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VAPOR-PHASE ORGANIC POLLUTANTS

VOLATILE HYDROCARBONS AND OXIDATION PRODUCTS

Committee on
Medical and Biologic Effects of
Environmental Pollutants

DIVISION OF MEDICAL SCIENCES
ASSEMBLY OF LIFE SCIENCES
NATIONAL RESEARCH COUNCIL

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This document is a cooperative effort on the part of the members and consultants of the Panel on Vapor-Phase Organic Pollutants. Each chapter, and sometimes a separate section within a chapter, was the responsibility of an author who was expert in its subject matter. The chapters setting forth the general summary and conclusions and the recommendations for future research represent a consensus of the Panel membership.

Dr. Benjamin L. Van Duuren, initially Chairman of the Panel and later Co-chairman with Dr. John R. Goldsmith, was responsible for the introduction and wrote the section on carcinogenic effects for Chapter 6. Dr. Goldsmith was the author of Chapter 7, on the epidemiologic appraisal of human effects; he selected the excerpts on airborne contaminants that appear in Appendix C.

Dr. Julian B. Andelman was coordinator for Chapter 8, on interactions and effects on the total environment, and wrote the introduction for that chapter and the section on effects on natural waters. Dr. John C. Craig was coordinator for Chapter 5, on metabolism of vapor-phase organic pollutants in mammalian systems; wrote the sections on fatty acids and on lactones; and collaborated with Dr. Neal Castagnoli on the section on metabolism of alcohols and phenols.

Dr. Jerome Kleinerman was coordinator for Chapter 6, on biologic

effects of vapor-phase compounds on humans and other mammalian systems, and wrote the section on pathophysiology for that chapter. Dr. Hans L. Falk developed the section on synergism, antagonism, and tolerance, and Dr. Oscar J. Balchum participated in the discussion and review of that section.

Dr. Robert W. Murray and Dr. Daniel Swern were responsible for Chapter 3, on possible mechanisms of formation of oxygenated organic compounds in the atmosphere, with Dr. Swern contributing the section on formation from triplet oxygen (atmospheric oxygen) and Dr. Murray the sections on formation from singlet oxygen and formation from ozone.

Dr. Charles S. Tuesday was the author of all of Chapter 2, and Dr. Julian Heicklen was the author of all of Chapter 4. Those responsible for the various sections of Chapter 5 for which credit has not already been given were as follows: Dr. John W. Daly and Dr. Donald M. Jerina, the section on metabolism of hydrocarbons; Dr. Paul R. Ortiz de Montellano, the sections on epoxides and on ethers; Dr. Castagnoli, the sections on aldehydes and on ketones and, in collaboration with Dr. Craig, the section on metabolism of alcohols and phenols; Dr. Robert E. McMahon, the section on organic compounds containing nitrogen; and Dr. Paul Mazel, the section on organic compounds containing sulfur.

For Chapter 6, Dr. Hector Blejer wrote the section on absorption of vapor-phase organic pollutants, Dr. Frederick J. de Serres prepared the section on mutagenic effects, and Dr. Harold Kalter provided the section on teratogenic effects.

For Chapter 8, Dr. Jerome J. Perry wrote the section on effects on microorganisms. The section on effects on atmospheric properties was contributed by Dr. John Frohliger and that on effects on vegetation by Dr. Michael Treshow. Dr. Malcolm J. Campbell wrote the section on removal, fate, and persistence.

Dr. Reinhold A. Rasmussen developed Appendixes A and B, with the assistance of Dr. Campbell. Dr. E. Bingham Mattheis compiled her choices of excerpts to form Appendix D. The Panel is indebted to the anonymous reviewers whose services were elicited to review the work and to criticize it constructively.

The Panel is also indebted to Mr. Norman Grossblatt for his capable editing of the report and to Miss Barbara A. Murek and her successor, Miss Joan V. Stokes, for locating and verifying the many references. Miss Stokes was responsible for preparing the final reference list. In obtaining information and references for the use of the Panel in its deliberations and in the preparation of its report, much use was made of the National Research Council's Advisory Center on Toxicology, the National Academy of Sciences Library, the National Library of Medicine, the National Agricultural Library, the Library of Congress, and the Air Pollution Technical Information Center.

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Preface

In the spring of 1970, the Division of Medical Sciences, National Academy of Sciences–National Research Council, entered into a contract with what has since become the Environmental Protection Agency (EPA) to produce background documents for selected pollutants. When the panel to prepare a study on polycyclic organic matter was formed, it was immediately apparent to its members that the task was too broad for a single study; so they recommended to EPA that two studies be conducted. One was completed by the panel and published by the Academy in August 1972: *Particulate Polycyclic Organic Matter.* A second panel, formed to deal with other aspects of the subject, completed its task in the spring of 1975; the result of its work is the present document.

The purpose of this document is to prepare a balanced and comprehensive survey of selected organic pollutants in relation to health for the information of the scientific community and the general public and for the guidance of standard-setting and regulatory agencies. The report describes sources, physical and chemical properties, measurement, biologic effects, and interrelationships of a number of pollutants and offers recommendations for further research. Statements contained in the report are supported by references to the scientific literature whenever possible or are based on a consensus of members of the Panel on Vapor-Phase Organic Pollutants.

Contents

APPENDIXES

1

Introduction

This report, a companion to an earlier document, *Particulate Polycyclic Organic Matter*, concerns vapor-phase substances likely to be produced as community pollutants in sufficient amounts to affect health and well-being.

A number of compounds, some of which are less likely to have effects as community pollutants, have been included to illustrate reactions that occur in the atmosphere or to indicate the health and environmental effects of such materials and their metabolic transformations. The relationship between the concentrations likely to produce unfavorable reactions and those likely to be present in polluted atmospheres is considered in Chapter 6. Interpretations are related to several practical questions of policy and environmental protection.

In general, materials with low vapor pressure or high molecular weight have been treated only briefly, but are introduced to illustrate basic reaction pathways.

The Panel On Vapor-Phase Organic Pollutants did not consider the occupational health significance of vapor-phase pollutants, particularly those of industrial origin.

This document has four major parts. The first (Chapter 2) deals with the sources of vapor-phase organic pollutants. Natural sources of some of the lower-molecular-weight compounds and technologic sources (mostly from transportation) are considered. Chapter 2 is supported by Appendixes A and B, on collection and sampling techniques and analytic methods.

The second section (Chapters 3 and 4) is a thorough treatment of the possible mechanisms of formation of oxygenated organic hydrocarbon compounds in the atmosphere and of atmospheric reactions of organic molecules with oxides of nitrogen and sulfur, hydroxyl radicals, and oxygen atoms.

The third section (Chapters 5 through 8) deals with the toxicologic, pathophysiologic, and epidemiologic information on vapor-phase organic pollutants, their metabolism, and their effects on the total environment. Oxidized compounds are given special attention, because oxidation in the atmosphere is the principal process by which nature degrades vapor-phase hydrocarbons. Oxidation, often by photochemical mechanisms, produces materials that may be harmful and have variable half-lives in the atmosphere. Chapter 7 considers the importance of exposures to various classes of these materials. Special attention is given to the importance of formaldehyde, ozone, and other oxidants and to the significance of benzene, in view of the possibility of an increase in the aromatic content of motor fuel. Vapor-phase emission is not determined solely by fuel content, inasmuch as the processes of combustion cause important transformations of hydrocarbons. The interpretations concerning health effects depend largely on the evidence available from exposures in the Los Angeles area, because insufficient data are available for most other areas.

Little is known regarding the effects of short-lived (but potentially toxic) species (e.g., the toxic peroxyacetylnitrates). Although a balanced overview of the several possible mechanisms (involving singlet oxygen, hydroxyl radicals, and ozone) by which atmospheric—especially photochemical—oxidation occurs has been presented, present knowledge does not permit accurate assessment of the relative importance of the different pathways.

The report stresses the importance of oxidation reactions in the vapor phase and the human health hazards produced from the (more or less transient) products of oxidation. The review of metabolism indicates that, although vapor-phase hydrocarbon pollutants are modified usually by enzymatic oxidation within mammalian systems from nonpolar to polar compounds (which are then excreted by the kidney), this sometimes occurs with the production of toxic intermediates. These reactions occur mostly in the liver and to a lesser extent in the kidney, intestine, and lung.

A major gap in knowledge is represented by the uncertainties concerning atmospheric oxidation mechanisms. That is because the resources for studying vapor-phase reactions have been substantially less than those for studying liquid-phase reactions. A great deal more information is needed about human exposure to low dosages over long periods and their health implications. Most of our information is based on exposure of animals to high dosages of a small number of compounds; there is a lack of information about the carcinogenicity and mutagenicity of most of the compounds in question. Vapor-phase pollutants have not been studied in as great detail as the polycyclic aromatic compounds treated by the Panel on Particular Polycyclic Organic Matter. The most important practical problem lies in the possible health consequences if a greater fraction of the fuel stock is based on aromatic hydrocarbons. Benzene, the major representative of this class, is known under occupational circumstances to be capable of producing mutations and is considered by many as a carcinogen because of its likelihood of producing leukemia, as well as interfering with bone marrow function. The highest atmospheric concentration of benzene is one five-thousandth the concentration thought likely to damage health under occupational circumstances; for this reason, the present concentrations are not considered harmful. Increases in these concentrations, however, should not be permitted without careful evaluation of their possible health implications.

2

Sources of Atmospheric Hydrocarbon

Total hydrocarbon emission in the United States from mobile (transportation) and stationary man-made source and from natural sources is summarized in Table 2-1.[211,373,878,949,1186,1227] The differences between estimates are due primarily to differences in underlying assumptions and methods of calculation. Most investigators agree that emission estimates are improving as more is learned about pollution; as a result, the more recent estimates in Table 2-1 are probably the more reliable. In particular, the most recent estimate[878] of 25.4 million tons/year from stationary man-made sources is significantly higher than all previous estimates because of improved knowledge and the increased number of stationary sources.

One estimate of worldwide hydrocarbon emission is also given in Table 2-1. The U.S. emission is about 40% of the world total for both mobile and stationary man-made sources. Although natural hydrocarbon emission dwarfs man-made emission on a global basis, it generally occurs in relatively unpopulated areas. As a result, tonnage comparisons do not accurately reflect importance.

A detailed hydrocarbon emission inventory for the United States is presented in Table 2-2.[211] This is the latest authoritative inventory that includes both mobile and stationary man-made sources. In discussing the various source categories, the format of Table 2-2 will be followed.

TABLE 2-1 Estimates of Hydrocarbon Emission from Man-Made and Natural Sources

	Hydrocarbon Emission, million tons/year			
	Man-Made Sources			
Area	Mobile	Stationary	Natural Sources	Reference
United States	17.6	13.9	72	949
	12[a]	7	—	1186
	16.6	15.4	—	1227
	19.8	17.6	—	211
	13.8	—	—	373
	—	25.4	—	878
World	34	54	2,000	1026

[a] Automobiles only.

MOBILE MAN-MADE SOURCES OF HYDROCARBON EMISSION

Motor vehicles are by far the most important mobile man-made source of gaseous hydrocarbons. According to Table 2-2, they account for about 86%, whereas aircraft, railroads, marine vessels, and nonhighway use together account for only 14%. Nationwide total emission from motor vehicles has been decreasing since about 1966, because of the installation on new cars of crankcase control systems in 1963, exhaust control systems in 1968, and evaporative control systems in 1971.[128] Total hydrocarbon emission is expected to continue to decline into the 1980's,[128,373] even without additional controls. Some estimates of hydrocarbon emission from automobiles and other mobile sources for the years 1955–1985 are given in Table 2-3.[373] It should be pointed out that these National Petroleum Council estimates are somewhat lower than the Environmental Protection Agency (EPA) estimates in Table 2-2.

Gasoline-Powered Motor Vehicles

Gasoline-powered vehicles account for about 99% of all vehicular hydrocarbon emission; diesels account for the remainder. Of the emission from gasoline-powered vehicles (automobiles) in 1967, an estimated 55% came from exhaust, 25% from the crankcase (blowby),

TABLE 2-2 Hydrocarbon Emission by Source Category, United States, 1969[a]

Source	Hydrocarbon Emission, million tons/year	
Mobile (transportation)		
Motor vehicles, gasoline	16.9	
Motor vehicles, diesel	0.2	
Aircraft	0.4	
Railroads	0.1	
Vessels	0.3	
Nonhighway use	1.9	19.8
Fuel combustion—stationary		
Coal	0.1	
Fuel oil	0.1	
Natural gas	0.3	
Wood	0.4	0.9
Industrial processes		
Primary metals	0.3	
Petroleum refining	2.3	
Chemical processing	0.8	
Other	2.1	5.5
Solid-waste disposal		
On-site incineration	0.5	
Open dumps, burned	1.2	
Teepee burners	0.3	2.0
Miscellaneous		
Forest fires	2.9	
Structural fires	0.1	
Coal-refuse banks	0.1	
Agricultural burning	1.7	
Solvent evaporation	3.1	
Gasoline marketing	1.3	9.2
TOTAL POLLUTION		37.4
Natural		
Methane	50[b]	
Terpenes	22[c]	
Ethylene	0.04	72.0
TOTAL POLLUTION PLUS NATURAL		109.4

[a] Data from U.S. Environmental Protection Agency,[211] except as noted.

[b] Derived from Robinson and Robbins,[1026] assuming U.S. methane emission per square mile to be half world rate.

[c] Derived from Rasmussen and Went,[1008] assuming terpene emission to be uniformly distributed over forested lands of the world.

and 20% from carburetor and fuel tank evaporation.[1186] Presumably, this breakdown was for cars without any emission controls. Today, with emission controls on many cars, the proportions are different.

EXHAUST EMISSION

Several investigators have measured exhaust emission from car fleets. One of the earliest studies was a Coordinating Research Council (CRC) field survey in which the average exhaust hydrocarbon concentration (hexane equivalent) of 160 pre-1956 model cars from the Los Angeles area was reported to be 1,375 ppm.[1287] A California Motor Vehicle Pollution Control Board (MVPCB) survey of 200 pre-1966 cars showed an average concentration of 828 ppm.[183] A later survey of 583 1966 models with first-generation controls showed an average concentration of 290 ppm.[165] On the basis of its own two surveys and other data, the California MVPCB estimated the average hydrocarbon emission from automobiles to be 11.0 g/mile before controls and 3.4 g/mile for 1966 models with first-generation controls.[182] Differences in auto emission have been shown for different altitudes and for cars of different engine size.[730]

The development of gas-chromatographic procedures to measure individual hydrocarbons has greatly increased our understanding of the nature of exhaust gas.[317,541,598,624,825,955] We now know that exhaust gas contains low-molecular-weight hydrocarbons that are not present in the fuel, as well as fuel components. The low-molecular-weight hydrocarbons include methane, ethane, ethylene, acetylene, propylene, the four-carbon (C_4) olefins, and sometimes propadiene and

TABLE 2-3 Estimated Hydrocarbon Emission from Automobiles and Other Mobile Pollution Sources, United States, 1955–1985[a]

	Estimated Hydrocarbon Emission, million tons/year						
					Projected Estimates		
Source	1955	1960	1965	1970	1975	1980	1985
Automobiles	9.9	12.0	13.0	11.0	5.9	2.4	0.9
Trucks and buses	1.2	1.4	1.7	1.9	1.7	1.4	1.4
Aircraft	0.3	0.3	0.2	0.3	0.2	0.1	0.1
Off-highway	0.7	0.7	0.7	0.6	0.6	0.6	0.5
TOTAL	12.1	14.4	15.6	13.8	8.4	4.5	2.9

[a] Derived from *Environmental Conservation: The Oil and Gas Industries,* Vol. 1. National Petroleum Council, June 1971.[373]

methylacetylene. The fuel components include hydrocarbons heavier than butane and may number over 100. Typically, the low-molecular-weight hydrocarbons constitute 40–60% of the total (by volume), although the exact proportions depend on many engine-fuel variables.

The predominant hydrocarbons in gasoline exhaust have been reported in three studies, each of which covered a wide range of conditions and included many analyses.[622,874,955] The three agree remarkably well (Table 2-4), considering the diversity of the investigations. The low-molecular-weight hydrocarbons—methane, ethylene, acetylene, and propylene—are high on each list. Toluene and isopentane seem to be the major fuel components.

Fuel composition obviously will affect exhaust composition, but the fuel components in exhaust do not exactly match the original fuel. Some fuel hydrocarbons are preferentially burned, and some others are formed in the engine. To avoid undue complexity, some investigators have used simple hydrocarbon fuels to study the relations between fuel composition and exhaust composition. Fleming[412] used blends of isooctane, isooctene, and *m*-xylene and found that the exhaust may contain (aromatic) hydrocarbons heavier than those in the original fuel and that fuel paraffins produce more exhaust olefins than do fuel olefins. Ninomiya and Biggers[926] used blends of toluene, isooctane, and *n*-heptane and showed that the air:fuel ratio greatly affects the yields of aromatic products (ethylbenzene, styrene, benzene, benzaldehyde, and toluene) formed from these blends. The effects on other exhaust hydrocarbons (low-molecular-weight products and some heavier olefins) were reported in an earlier study.[927] Daniel[282] found methane, ethylene, ethane, acetylene, propylene, and propane in the exhaust from a single-cylinder engine burning pure propane. The concentrations depended greatly on the air:fuel ratio, spark timing, volumetric efficiency, and compression ratio.

The effect of gasoline composition on exhaust composition has been studied extensively by Dishart and his co-workers.[321,322,874] They concluded that ethylene is formed from saturates and olefins—propylene and butene primarily from saturates, and diolefins primarily from olefins—and that additional amounts of toluene, benzene, and xylenes are formed from higher aromatics and additional 2-methyl-2-butene from higher saturates. Doelling *et al.*[325] concluded that gasoline composition had no effect on the total hydrocarbon concentration in exhaust, but that the percentages of aromatics, olefins, and paraffins in exhaust were correlated with fuel composition. Wigg *et al.*[1312] concluded that aromatic exhaust emission is linearly related to the aromatic content of the fuel. Similarly, Neligan *et al.*[913] concluded that

TABLE 2-4 Predominant Hydrocarbons in Auto Exhaust

Hydrocarbon	Fraction of Total Exhaust Hydrocarbons, vol % 62-Car Survey[a]	 15-Fuel Study[b]	 Engine-Variable Study[c]
Methane[d]	16.7	18	13.8
Ethylene[d]	14.5	17	19.0
Acetylene[d]	14.1	12	7.8
Propylene[d]	6.3	7	9.1
n-Butane	5.3	4	2.3
Isopentane	3.7	4	2.4
Toluene	3.1	5	7.9
Benzene[d]	2.4	—	—
n-Pentane	2.5	—	—
m- and *p*-Xylene	1.9	—	2.5
1-Butene[d]	1.8	3[e]	6.0[e]
Ethane[d]	1.8	—	2.3
2-Methylpentane	1.5	—	—
n-Hexane	1.2	—	—
Isooctane	1.0	—	—
All others	22.2	30	26.9

[a] Data from Papa.[963]

[b] Data from Morris and Dishart.[874]

[c] Data from Jackson.[622]

[d] Combustion products.

[e] Includes isobutylene.

fuel olefinic exhaust emission is proportional to the olefin content of the fuel, but that the nature and concentration of the light, cracked products are independent of the olefin content of the fuel. Many others have investigated fuel composition effects, frequently expressing their results in terms of photochemical reactivity.[174,195,197,316,318,349,351,841,1084,1164,1165,1178]

Jackson[622] has reported the effects of the air:fuel ratio and spark timing on the concentrations of about 10 exhaust hydrocarbons. This is the only comprehensive engine-variable study using gasoline as fuel, although Ninomiya and co-workers[926,927] and Daniel[282] investigated engine variables with pure hydrocarbon fuels. In each of these three studies, the effect of engine variables was different for different hydrocarbons.

The use of tetraethyl lead (TEL) as a gasoline antiknock agent tends to increase exhaust hydrocarbon emission, both directly and indirectly, by promoting the buildup of engine deposits.[324,414,447,509,759,951] The direct lead effect increases hydrocarbon emission by about 5%; the indirect (deposit) effect, by an additional 7%, according to the summary study of Leikkanen and Beckman.[759] TEL does not affect the composition of exhaust hydrocarbons.[414]

Some emission controls, however, do affect exhaust hydrocarbon composition. Morris and Dishart[874] compared an uncontrolled car, a modified-combustion car, an air-injection car, and an advanced thermal-reactor car. The greatest differences they found were the high percentage (87%) of C_1 and C_2 hydrocarbons and the near absence of fuel components in the exhaust of the thermal-reactor car. Adams *et al.*[10] also found significantly higher percentages of methane and ethylene and lower percentages of aromatics in the exhaust of a lean-reactor car, compared with that of an unmodified car of the same model. Weaver[1293] reported that catalytic reactors selectively oxidize the olefins and aromatics in exhaust, but that the selectivity diminishes with catalyst age. Nebel and Bishop[907] also reported that catalytic reactors may be selective and that methane and ethylene are the most difficult hydrocarbons to oxidize. Jackson[622] found that an engine-modification emission[622] control system increased the photochemical reactivity of exhaust, but that an air-injection system had no effect.

Exhaust gases contain organic compounds besides hydrocarbons, such as aldehydes, ketones, alcohols, ethers, esters, acids, and phenols. These partial-oxidation products are called oxygenates. The total oxygenate concentration is about one-tenth the total hydrocarbon concentration. Aldehydes are generally believed to be the most important class of oxygenates.

Many investigators have measured formaldehyde[361,364,412] and total aldehyde[364,447,574,741,1164,1293] concentrations in auto exhaust with sensitive chemical tests.[233,685,954,1070] A few investigators have measured benzaldehyde[574,926,927] and phenol;[574] still others have qualitatively identified various aldehydes.[76,365] However, a reasonably complete quantitative analysis of exhaust aldehydes has not been possible until recently, when sophisticated gas-chromatographic techniques were developed.[92,432,934,1255,1342] The results of several of these detailed analyses are summarized in Table 2-5. They agree very well, considering that different engines, gasolines, and, to some extent, analytic techniques were used. Formaldehyde is by far the predominant aldehyde, constituting about 60–70% of the total (on a volume basis); acetaldehyde is next, at about 10%; and propionaldehyde, acrolein, benzaldehyde, and the tolualdehydes are all found in appreciable amounts. As might be expected, the nature of the gasoline burned influences the aldehydes formed.

There is almost no published information on noncarbonyl oxygenates, such as ethers, alcohols, epoxides, and peroxides. Seizinger and

TABLE 2-5 Exhaust Aldehyde Analyses

Aldehyde	Fraction of Total Exhaust Aldehydes, vol %					
	Wiggs *et al.*[1312a]		Oberdorfer[934]	Wodkowski and Weaver[1342a]		Fracchio *et al.*[432]
Formaldehyde	66.7	72.5	70.2	59.9	69.3	72.9
Acetaldehyde	9.3	8.7	7.2	14.3	7.5	8.5
Propionaldehyde[b]	15.7	—	0.4	7.0	0.7	6.4
Acrolein	3.2	—	9.8		2.6	
Butyraldehydes		4.3	0.4	3.0	1.0	1.7
Crotonaldehyde	—	—	0.4	1.4	0.4	0.4
Valeraldehydes	—	—	0.4	—	—	—
Benzaldehyde	3.2	7.0	8.5	3.3	5.4	4.3
Tolualdehydes	1.9	7.2	—	5.9	3.1	—
Other	—	0.3	2.7	5.2	10.0	5.8
TOTAL	100	100	100	100	100	100

[a] Exhausts from two different gasolines.

[b] Also includes acetone of unknown proportion.

Dimitriades measured 10 aldehydes, six ketones, and 16 noncarbonyl oxygenates in exhaust from 22 different simple fuels, each containing one, two, or three hydrocarbons.[1095,1096] They developed computational formulas from their data that can be used to estimate the oxygenate concentrations in gasoline exhaust.

The use of liquefied petroleum gas (LPG) or natural gas as a motor fuel does not in itself eliminate or even reduce exhaust hydrocarbon emission. These fuels, however, produce less complex exhaust than gasoline. Schwartz *et al.*[1090] reported finding mostly propane—plus small amounts of methane, ethane, ethylene, acetylene, and propylene and traces of C_4 hydrocarbons—in the exhaust from automobiles or lift trucks burning LPG. Fleming and Allsup[413] found mostly methane and smaller amounts of other (up to C_4) hydrocarbons in the exhaust from an automobile burning natural gas. They attributed the nonmethane hydrocarbons primarily to the ethane in natural gas. This was confirmed by Eccleston and Fleming's study in which natural gas and a synthetic pipeline gas derived from coal (Synthane) were compared as motor fuels.[352] The exhaust from Synthane—which was about 10% hydrogen, 88% methane, and less than 0.5% ethane—contained noticeably less C_2 and C_3 hydrocarbons than the exhaust from natural gas, whose composition was 89% methane, 9% ethane, and 2% propane and butane. The photochemical reactivity of the Synthane exhaust was also significantly lower. The exhausts from both the natural gas and Synthane contained small amounts of an unidentified aldehyde (or aldehydes).

EVAPORATION LOSSES

The evaporation of gasoline from carburetors and fuel tanks has been greatly reduced for 1971 and later automobiles, compared with older models, by 88% according to one estimate,[914] owing to the installation of evaporation control systems. Evaporative emission is still significant, however, because many older cars are in use.

Evaporative emission consists of the lighter components of gasoline, primarily C_4 and C_5 hydrocarbons. As many investigators have pointed out, the exact composition depends on the gasoline used, the temperature it attains, and the degree of "weathering" or prior evaporation.[299,348,351,597,623,826,887,1178,1262,1303] Some representative analyses of evaporative emission samples are summarized in Table 2-6. They are not complete analyses, covering only the C_4, C_5, and C_6 paraffins, the C_4 and C_5 olefins, and the C_6 and C_7 aromatics. The light paraffins and light olefins constituted about 70% of the carburetor emission and about 90% of the fuel-tank emission in these samples. Isopentane and *n*-

TABLE 2-6 Partial Analysis of Carburetor and Fuel-Tank Evaporation Losses

	Fraction of Total Evaporated Hydrocarbons, vol. %						
	Carburetor				Fuel Tank		
Hydrocarbon	Wade[1303a]		Caplan[197]	Muller *et al.*[887b]	Jackson and Everett[623]	McEwen[836c]	
Paraffins							
n-Butane	11.9	9.1	10.5	23.0	16.5	30.5	48.5
Isobutane	0.2	0.1	0.6	0.2	6.5	2.7	3.6
n-Pentane	2.0	2.0	9.9	1.5	7.2	8.6	6.9
Isopentane	45.3	40.9	17.8	36.0	23.2	26.4	20.3
n-Hexane	0.2	0.3		8.7	0.7	1.8	1.5
2,2-Dimethylbutane	0.1	0.0	15.5	3.7	0.1	—	—
2,3-Dimethylbutane	3.0	3.2			1.6	2.6	1.6
2-Methylpentane	2.3	2.4			1.9	3.4	2.4
3-Methylpentane	1.2	1.3			1.1		
Olefins							
1-Butene	0.3	0.2	0	0.9	4.6	—	—
trans-2-Butene	0.5	0.5	0.3		4.8	3.2	2.2
cis-2-Butene	0.3	0.2	0.2		4.2		
cis-, *trans*-2-Pentene	1.4	1.3	2.7	1.0	1.5	2.9	2.0
1-Pentene	0.3	0.3	0.7	0.8	5.6	4.5	2.8
2-Methyl-1-butene	0.7	0.6	1.7		4.3		
3-Methyl-1-butene	0.1	0.1	0.2		0.8		
2-Methyl-2-butene	1.6	1.6	3.9	1.2	7.3	3.4	2.7
Aromatics							
Benzene	0.5	0.5	1.8	0.1	0.4	0.4	0.3
Toluene	0.5	0.8	2.4	—	0.4	0.9	0.3
TOTAL	72.4	65.4	68.2	77.1	92.7	91.3	95.1

[a] Same gasoline at 163 and 177 F.

[b] Calculated values for 140 F.

[c] Different gasolines.

butane were by far the predominant hydrocarbons, together accounting for an average of about 50% of the total. It seems safe to generalize that isopentane and *n*-butane account for the major portion of all gasoline evaporation losses. The amounts of other paraffins and olefins varied from sample to sample, largely because of differences in gasoline composition.

The analyses in Table 2-6 confirm Jackson and Everett's[623] conclusion that fuel-tank emission is richer in the lighter components than carburetor emission. Presumably, this is because the gasoline in the carburetor is "distilled" at a higher temperature.

BLOWBY

Blowby or crankcase emission has been practically eliminated; all 1963 and later model cars have been equipped with positive crankcase ventilation (PCV). The PCV cure for this problem and the importance of blowby hydrocarbon emission were first recognized by Bennett and his co-workers.[97] They measured hydrocarbon concentrations of around 10,000 ppm and flow rates of a few cubic feet per minute for blowby and concluded that blowby accounted for about 40% of the total hydrocarbon emission from automobiles. They also found that blowby is predominantly carbureted mixture (85%) plus some combustion gases (15%) and that fuel composition determines which hydrocarbons are emitted from the crankcase. Later studies by other investigators essentially confirmed their findings on blowby composition.[961,1033,1114]

Possible contamination of blowby from lubricating oil was eliminated in a unique study by Domke, Lindley, and Sechrist.[326] Using an oilless engine with Teflon parts, they found that blowby hydrocarbon composition was roughly 50% aromatics, 35% saturates, and 15% olefins, regardless of the air:fuel ratio or the fuel used (gasoline or isooctane). They also found oxygenates at about 5 ppm in the blowby, of which only formaldehyde, acetaldehyde, methanol, and ethanol could be identified. Payne and Sigsworth[965] also detected oxygenates, as well as hydrocarbons, in blowby gases, although they did not recognize the importance of blowby as an emission source of their early (1952) study.

Hass and Scanlin[534] measured the blowby rates of 500 cars of various makes and ages and determined the flow-rate percentiles for various engine sizes. This basic information has been useful to designers of PCV systems. Voelz *et al.*[1254] tested over 75,000 vehicles in 15 metropolitan areas and found that 17% of the PCV systems needed maintenance and that 3.6% of the cars were discharging some crankcase fumes to the atmosphere. In a smaller survey of 483 cars in Cincinnati, Ohio, 29%

needed PCV maintenance and 5% were discharging some crankcase fumes.[251] The detailed data from these surveys suggest that the PCV systems in actual use are about 98% effective.

Diesel-Powered Motor Vehicles

As indicated in Table 2-2, diesel-powered motor vehicles account for about 1% of the hydrocarbon emission from all motor vehicles and about 1% from all mobile sources. Diesel emission originates exclusively from the exhaust; blowby and evaporative emission is practically nil.[770,830]

The gaseous hydrocarbon fraction of diesel exhaust is extremely complicated. Many investigators have shown that it consists of light, cracked hydrocarbons and heavy fuel-like components up to about C_{24}.[599,600,769,770,830,848,1009,1263] Except for methane, the light, cracked hydrocarbons are almost all olefins. Ethylene, acetylene, and propylene are the predominant light hydrocarbons, with smaller amounts of C_4 olefins and even smaller amounts of C_5 and C_6 olefins.[769,1009] Figure 2-1 shows the bimodal carbon-number distribution of diesel-exhaust hydrocarbons; interestingly, the proportions of light hydrocarbons are greater for the four-cycle engine than for the two-cycle engine.[599] Linnell and Scott[770] estimated that the light hydrocarbons constitute 10–25% of the total on a molar basis. Hurn and Seizinger[600] reported that the

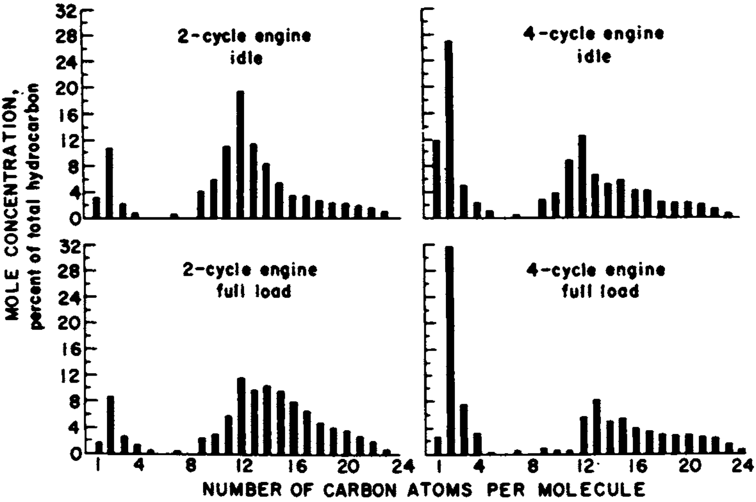

FIGURE 2-1 Distribution of hydrocarbons in diesel exhaust gas. (Reprinted with permission from Hurn and Marshall.[599])

proportions of light hydrocarbons are highest when the total hydrocarbon concentration is lowest.

Most of the analytic work on heavy hydrocarbons (C_{10-24}) has been directed toward identifying the odorous components.[334,763,1141] Caragay *et al.*[763] reported finding the following hydrocarbon classes in the "oily-kerosene" fraction of diesel-exhaust condensate: indans, tetralins, alkylbenzenes, naphthalenes, indenes, acenaphthenes, and benzothiophenes. Similar types of hydrocarbons were found by Dravnieks *et al.*[334] in a related odor study. Skala *et al.*[1120] identified several high-molecular-weight aromatic carbonyl compounds in diesel exhaust that they believe are important odorants. At present, we can say only that the fuel-like fraction of diesel exhaust consists of at least several hundred compounds; most of them are found in the fuel, but some—important to the odor problem—are formed during combustion.

Low-molecular-weight aldehydes have also been found in diesel exhaust. Formaldehyde and to a lesser extent acrolein have been reported most often.[64,360,600,769,770,865,1009,1038,1144] Vogh[1256] measured the following aldehydes in one diesel-exhaust sample: formaldehyde (18.3 ppm); acetaldehyde (3.2 ppm); acrolein, acetone, propionaldehyde, and isobutyraldehyde (2.9 ppm); *n*-butyraldehyde (0.3 ppm); crotonaldehyde and valeraldehyde (0.4 ppm); hexaldehyde (0.2 ppm); and benzaldehyde (0.2 ppm). The proportions were not greatly different from those shown in Table 2-5 for diesel auto exhaust.

Several investigators[360,848,1038] have attempted to correlate total aldehyde or formaldehyde concentration with diesel-exhaust odor, with limited success.

Other Mobile Sources

AIRCRAFT

Hydrocarbon emission from aircraft is estimated to be 400,000 tons/year, or about 2% of the emission from all mobile sources.[211] This estimate includes only gaseous hydrocarbons, not smoke or soot, although smoke is considered to be the major air pollution problem for aircraft.

Jet aircraft are by far the most important type from a fuel-consumption standpoint. In general, hydrocarbon emission from turbine engines is considerably lower than from comparable-sized reciprocating engines, and the concentrations are very much lower, owing to the large air consumption of turbine engines. Like those from reciprocating engines, the hydrocarbons in turbine-engine exhaust consist of light, cracked products plus fuel-like components. Figure 2-2 shows the carbon-number distribution of the hydrocarbons in the exhaust from an aircraft turbine and in the fuel (JP-4) burned to produce the exhaust.[215] The proportions of light hydrocarbons are much lower than for reciprocating engines powered by either gasoline or diesel fuel. Turbine-engine exhaust is unusual in another way, as shown in Figure 2-2: the

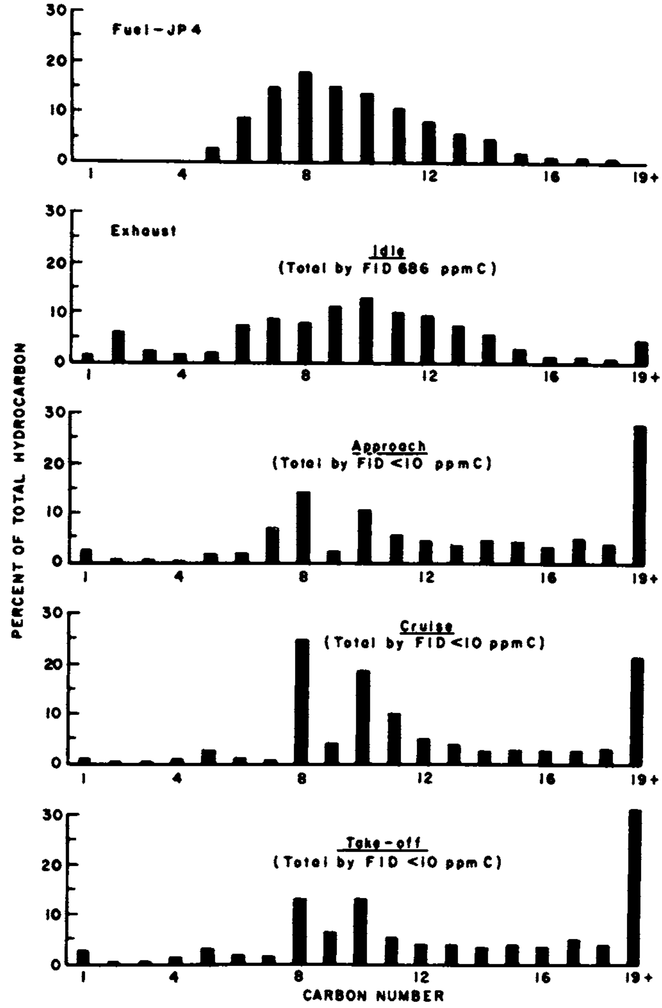

FIGURE 2-2 Distribution of hydrocarbons in jet-aircraft engine exhaust. (Reprinted with permission from Chase and Hurn.[215])

polymerization of the fuel components to form heavy hydrocarbons (C_{19} and heavier). Fuel polymerization does not occur in gasoline or diesel engines to nearly so great an extent, if it occurs at all. The C_{19} and heavier hydrocarbons in turbine exhaust are probably particulate, rather than gaseous.

Cornelius *et al.*[250] measured the concentrations of individual hydrocarbons in the exhaust from an automotive turbine engine, but reported only that their average photochemical reactivity "compared favorably" with that of gasoline-engine exhaust hydrocarbons. Korth and Rose[714] measured individual hydrocarbons in the exhaust from a turbine-powered automobile operated on unleaded gasoline. Compared with those from a conventional automobile (and adjusted for differences in air consumption), the turbine exhaust concentrations were very much lower for C_{1-5} olefins and C_{1-5} paraffins, slightly lower for C_{6-8} paraffins, and slightly higher for benzene. Moreover, the exhaust from the turbine car did not contain any aromatics above C_8, whereas the exhaust from the conventional car, operated on the same gasoline, did contain higher aromatics. The proportion of light olefins in the turbine exhaust was much less than that in the conventional exhaust. This agrees with Chase and Hurn's carbon-number distribution[215] (Figure 2-2).

Formaldehyde and total aldehyde concentrations in turbine exhaust have been measured,[215,250,714,785] but no detailed aldehyde analyses have been reported. What little information on aldehyde composition is available is conflicting. In one study involving aircraft turbines,[785] formaldehyde constituted about 70% of the total aldehyde, about the same proportion as in gasoline- or diesel-powered engine exhaust. However, in Korth and Rose's[714] study of the turbine-powered automobile, formaldehyde constituted only 10% of the total aldehyde.

RAILROADS

Hydrocarbon emission from railway locomotives is only about 100,000 tons/year.[211] Because locomotives are almost all diesel-powered, the character of their emission is essentially the same as that of diesel-powered vehicles, previously discussed.

MARINE VESSELS

Hydrocarbon emission from ships, barges, and other vessels is estimated at about 300,000 tons/year.[211] Larger vessels are powered by oil-fired and to a lesser extent coal-fired steam engines. Because no information is available about the gaseous emission from such vessels (although smoke is a problem on the Great Lakes), they cannot be discussed further here. Smaller vessels are usually diesel-powered. The character of their emission is essentially the same as that of diesel-powered vehicles. The special case of outboard motors is discussed in the following section, because they are similar in design to internal-combustion engines in some off-highway uses.

OFF-HIGHWAY USE

This category includes large construction equipment, farm tractors, snowmobiles, trail bikes, outboard motors, electric generators, garden tractors, power lawn mowers, and chain saws. Hydrocarbon emission from these sources is about 1.9 million tons/year, or about 10% of all mobile-source emission.[211] Off-highway emission appears to be increasing.

Many large off-highway vehicles and machines, such as heavy construction equipment and farm tractors, use gasoline or diesel engines that are very similar to those in motor vehicles. Their emission is probably also similar, so they will not be discussed further. However, many small off-highway vehicles and machines use small gasoline engines, which in general are less efficient and emit larger quantities of hydrocarbons than larger engines. Donohue *et al.*[327] estimated the hydrocarbon emission from these small engines at 169,000 tons/year for the United States. This is about 9% of the emission from all off-highway sources and less than 1% of the emission from all mobile sources. Eccleston and Hurn[350] tested 36 small utility engines and found the average hydrocarbon emission to be 8 g/hp-hr for four-cycle engines and 140 g/hp-hr for two-cycle engines. This large difference was attributed partly to the lower average size of the two-cycle engines, but mostly to the fact that two-cycle engines are scavenged by unburned fuel–air mixture. This scavenging action not only increases the total hydrocarbon concentration in the exhaust, but alters the composition. As shown in Figure 2-3, two-cycle engine exhaust contains a much higher proportion of fuel components.[350]

STATIONARY MAN-MADE SOURCES OF HYDROCARBON EMISSION

Many industrial, commercial, and domestic activities emit gaseous hydrocarbons and other organc compounds to the atmosphere. These

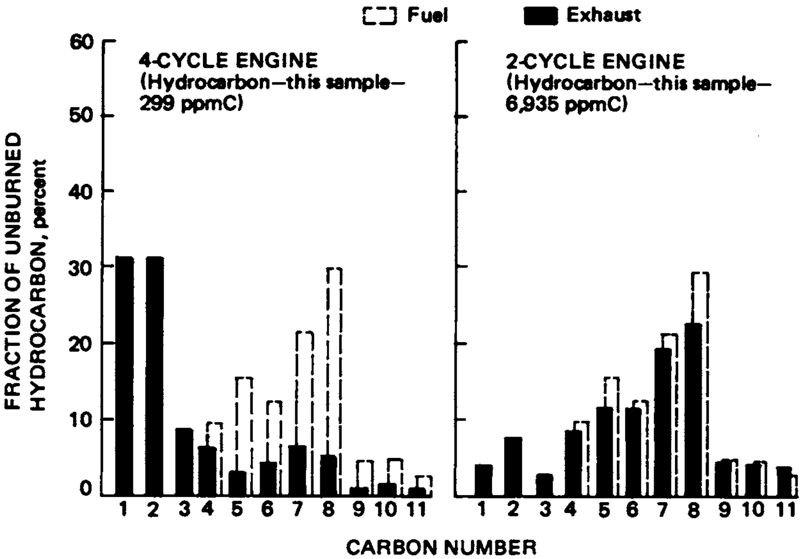

FIGURE 2-3 Distribution of hydrocarbons in exhaust from small utility engines. (Reprinted with permission from Eccleston and Hurn.[350])

sources, both numerous and widespread, include all kinds of fuel burning, solvent usage, and waste-disposal operations, as well as the more obvious chemical processing and petroleum refining and marketing. The total hydrocarbon emission from these sources is shown in Table 2-2. According to this 1969 estimate, stationary sources in the United States discharge 17.6 million tons of hydrocarbon per year, compared with 19.8 million tons from mobile sources. A more recent (1971) survey estimates stationary-source emission at slightly more than 25 million tons/year; it is summarized in Table 2-7 and is considerably different from the 1969 survey and presumably more accurate.

The composition of organic emission from various stationary sources is discussed in the following sections.

Fuel Combustion

The fuel burned by all stationary combustion sources in the United States during 1968 was the equivalent of 43.4 × 10^{15} Btu, of which 30% was provided by coal, 17% by distillate and residual fuel oil, 48% by natural gas, and 5% by miscellaneous fuels, such as coke, lignite,

TABLE 2-7 Most Recent (1971) Estimates of Organic Emission from Stationary Sources in the United States[a]

Stationary Source	Total Organic Emission, million tons/year
Solvent evaporation	7.1
Solid-waste combustion	4.5
Agricultural burning	4.2
Forest fires	2.4–3.0
Petroleum storage and marketing	2.2
Petroleum production and refining	2.0
Chemical processing	1.4
Other industrial processing	~1
Fuel combustion	0.4
Coal-refuse burning	0.2
TOTAL	25.4–26.0

[a] Data from MSA Research Corporation.[878]

wood, LPG, and waste gases.[1229] The major uses of fuel are in electric power plants, industrial processing, and space heating. In general, the gaseous hydrocarbon and other organic emission from specific stationary combustion sources is lower than and very different from those of specific automotive sources.

COAL

Electric power plants account for most of the coal burned in the United States. Cuffe, Gerstle, and their co-workers[267,268,458] reported hydrocarbon emission from several large coal-fired power plants to be between 0.1 and 0.2 lb/ton of fuel burned. Hangebrauck *et al.*[521] reported similar values for large power plants and considerably higher values (1–3 lb/ton) for coal-fired industrial boilers. Formaldehyde emission from the same units ranged from about 0.001 to 0.006 lb/ton of fuel, or about 1–2% of the hydrocarbon emission, and so appears to be unimportant. However, organic acids are important and actually exceed hydrocarbon emission in this type of equipment. Cuffe *et al.*[268] reported an average value of 12.4 lb of organic acid (as acetic) per ton of fuel burned for one large coal-fired plant. This was almost 70 times the hydrocarbon emission from the same plant. An EPA report[1229] stated that hydrocarbon emission from coal-fired equipment ranges from 0.3 lb/ton for large utility boilers to 3 lb/ton for commercial and domestic furnaces. Hovey *et al.*[584] reported that organic emission from the combustion of hard coal was only one-eighth that from soft coal.

No information is available on the composition of the hydrocarbons or organic acids that are discharged from coal-burning equipment.

FUEL OIL

Electric power plants, oil refineries, industrial plants, and space heating account for most of the fuel oil burned in the United States. Like that from coal-burning equipment, gaseous hydrocarbon and other organic emission from oil burners is very low. Chass *et al.*[217] reported hydrocarbon emission from oil-burning power plants, industrial boilers, and domestic and commercial furnaces to be about 0.2 lb/ton; aldehyde and ketone emission, about 0.15 lb/ton; and other organic emission (presumably organic acids), 0.4–0.8 lb/ton. The hydrocarbon and other organic emission from oil-fired equipment in petroleum refineries was about 1 and 3 lb/ton, considerably greater than from the other sources. Hangebrauck *et al.*[521] reported hydrocarbon emission of about 0.3 lb/ton and formaldehyde emission of about 0.006 lb/ton for large oil-fired equipment; emission from smaller equipment was somewhat higher—about 1.0 and 0.03 lb/ton, respectively. Chass and George[216] measured aldehyde emission from about 30 small industrial burners operated on oil, gas, or both. The oil-fired burners discharged 0.1–6.7 lb of aldehydes per ton of fuel burned and averaged 1.0 lb/ton. Wasser *et al.*[1277] studied the effect of excess air on the emission from a small domestic oil burner. The hydrocarbon emission was very low under optimal conditions—about 0.06 lb/ton—but increased to over 30 lb/ton when the air was reduced to stoichiometric proportions. An EPA literature survey[1229] estimated the hydrocarbon emission from oil-fired equipment to be about 0.5 lb/ton. Magill and Benoliel[800] reported somewhat higher emission for large oil-fired units than those quoted above in their early (1952) study.

NATURAL GAS

Space heating accounts for most of the natural gas consumed in the United States, although power plants and industrial processes are important users. Natural gas is considered to be clean-burning fuel, but it does produce some organic emission. Chass *et al.*[217] reported negligible hydrocarbon emission from gas-fired power plants, industrial boilers, and commercial and domestic heaters. Aldehyde emission from the same sources was less than 0.1 lb/ton, and other organic emission (presumably organic acids) was between 0.1 and 0.2 lb/ton. Chass *et al.*[217] reported appreciably higher emission for gas-fired units in petroleum refineries than for other gas-fired units, as they did for oil-fired equipment. Hydrocarbon emission reported by Hangebrauck *et al.*[521] for gas-fired equipment varied from 0.14 to 3.8 lb/ton; formaldehyde emission, from 0.005 to 0.12 lb/ton. Aldehyde emission from the small gas-fired burners tested by Chass and George[216] varied from near zero to about 3 lb/ton and averaged 0.5 lb/ton. The consensus values reported by the EPA[1229] were about 2.0 lb/ton for hydrocarbons, 0.15 lb/ton for aldehydes, and 0.2 lb/ton for other organics for gas-fired power plants and industrial boilers; emission was somewhat lower for domestic and commercial heating units. Magill and Benoliel[800] reported that the emission of all three organic classes was between 2 and 3 lb/ton for gas-fired equipment; no difference was noted between large and small units.

Methane is presumably the predominant hydrocarbon in the effluent from gas-fired equipment, but there are no published data to confirm this. Hall[510] reported that formaldehyde, acetaldehyde, and formic acid are produced when natural gas is burned in appliances with a deficiency of air.

WOOD

Wood is used as an industrial fuel only where it is a readily available by-product. Hydrocarbon emission from burning it depends on the proportions of wood and bark, the moisture content, and how well the furnace is designed and maintained. An EPA report[1229] gave typical emission from the combustion of wood in industrial boilers as 2 lb of hydrocarbon per ton and 0.5 lb of carbonyl per ton; these values are comparable with those reported for the combustion of other fuels.

Fritschen *et al.*[441] measured total hydrocarbon emission of 2–4 lb/ton from the burning of pine slash samples in laboratory apparatus. Methane was the predominant hydrocarbon, but smaller amounts of ethylene, ethane, acetylene, and propylene and traces of C_4 and C_5 olefins were also found. Several other investigators have reported a variety of oxygenated organics in wood smoke. Jahnsen[629] found 29 different organics in the effluent from hickory sawdust that was burned in Pyrex apparatus. Acetic acid was the principal organic acid; methyl alcohol, the principal alcohol; diacetyl, the principal carbonyl; and guaiacol and 2, 6-methoxypyrogallol, the principal phenols. Bellar and Sigsby[92] identified methyl alcohol, ethyl alcohol, acetone, acetaldehyde, acrolein, propyl alcohol, 2-methylpropyl alcohol, and butyl alcohol in the effluent from a trench incinerator burning wood. Hoff and Kapsalopoulou[578] reported finding 18 different alcohols, aldehydes, ketones, and ethers and benzene and toluene in the low-boiling fraction of smoke from a hickory fire used to smoke meats. Levaggi and Feldstein[760] measured amounts of formaldehyde, acetaldehyde, and acetone in parts per million and smaller amounts of propyl alcohol and methylethylketone in the effluent from a wood-burning fireplace.

SUMMARY

Some typical fuel combustion emission values are shown in Table 2-8. The purpose is to show the composition of the gaseous organic emission from different combustion sources, not to compare different fuels. Organic acids are the major constituent, followed by hydrocarbons and aldehydes. This is an entirely different order from auto exhaust, in which hydrocarbons are predominant, aldehydes secondary, and organic acids negligible.

It should be pointed out that the nationwide hydrocarbon emission summarized in Table 2-2 does not include organic acids, at least for the fuel combustion sources. On the basis of 1968 U.S. consumption of the three fuels and the emission values in Table 2-8, an additional 4.5 million tons of organic acids are emitted, of which 3.5 million tons are from coal, 0.5 million tons from oil, and 0.5 million tons from gas. These must be considered only rough estimates, but they do indicate that fuel combustion is a more important source of organic emission than implied in Table 2-2 or Table 2-7.

Industrial Processes

A wide variety of organic pollutants are emitted by industrial processes. Some of the more important are discussed below.

PRIMARY METALS

The production of coke is the main source of gaseous hydrocarbon emission associated with the primary metals industry. Coke-oven gases contain aromatic hydrocarbons and phenols, as well as inorganic pollutants. The emission occurs principally when coal is charged to the oven and when the coke is quenched and removed.[244] The recent development of a continuous coking process may greatly reduce coke-oven emission in the future.[74] The phasing-out of old beehive ovens, from which no attempt is even made to collect the coal tars, will also alleviate the problem.[135]

TABLE 2-8 Typical Emission of Several Classes of Compounds from Stationary Combustion Sources

Compounds	Emission, lb/ton of fuel		
	Coal	Oil	Gas
Hydrocarbons	0.3	1.0	1.0
Aldehydes	unknown	0.5	0.5
Formaldehyde	0.003	0.006	0.008
Organic acids	10	~5	2

PETROLEUM REFINING

Various refinery processing and storage operations discharge hydrocarbons to the atmosphere. Good design and housekeeping minimize this emission, however.[373] The more volatile C_4, C_5, and C_6 hydrocarbons probably account for most of the refinery emission. Petroleum refineries also discharge small amounts of organic sulfur compounds.

CHEMICAL PROCESSING

Many chemical processing plants discharge a variety of organic compounds to the atmosphere, depending on their operations. Fawcett[391] inventoried the emission from a phthalic anhydride plant and found that it included phthalic anhydride, maleic anhydride, naphthoquinone, benzoic acid, and various aldehydes. Lur'e[792] reported that butadiene, isobutylene, styrene, benzene, and ethyl alcohol vapors are discharged from a synthetic rubber plant. Walter and Amberg[1274] reported that α-pinene, methyl alcohol, and, to a lesser extent, acetone are the major organic compounds emitted from kraft paper mills (sulfur compounds excluded). No organic compound or group of compounds predominates in chemical plant emission.

OTHER INDUSTRIAL SOURCES

Levaggi and Feldstein[761] measured aldehyde emission from a variety of small industrial operations, such as coffee roasting, printing, paint spraying, and foundry-core preparation, many of which involved ovens and after burners. They found amounts of formaldehyde, acetaldehyde, and acetone in parts per million and smaller amounts of acrolein and other C_3 and C_4 aldehydes. The emission from many of these and from other small industrial operations arises from the use of chemical solvents. The EPA has compiled air pollutant emission rates for a variety of industrial processes.[1229]

Solid-Waste Disposal

The per capita solid-waste load in the United States is about 10 lb/day, about half of which is disposed of by incineration.[1229] This incineration produces a wide variety of organic air pollutants, whose amount and composition depend greatly on the nature of the wastes and how they are burned.

DOMESTIC, MUNICIPAL, AND INDUSTRIAL INCINERATORS

These incinerators vary widely in size, design, and effectiveness. In general, large, fully engineered units, many of which have stack controls, discharge smaller amounts of pollutants than small, domestic units. Tuttle and Feldstein[1216] reported much lower hydrocarbon emission from an adequately designed multichamber incinerator than from an inadequately designed incinerator; methane and ethylene were the predominant hydrocarbons from both units, but many other C_{2-6} hydrocarbons were found with the less efficient incinerator. Stenburg and co-workers[1150,1151] reported hydrocarbon emission of 1–2 lb/ton of refuse burned and formaldehyde emission of 0.01–0.02 lb/ton for a medium-sized multichamber incinerator. Carotti and Kaiser's data for a large municipal incinerator indicate hydrocarbon emission of about 0.2 lb/ton, aldehyde emission of about 0.1 lb/ton, and organic acid emission of about 3 lb/ton; most of the hydrocarbon was methane and ethylene.[199] Kaiser *et al.*[658] reported somewhat higher values for an apartment-house incinerator: organic acids, 18 lb/ton; esters, 10 lb/ton; aldehydes, 4 lb/ton; and benzene and phenol, about 0.1 lb/ton each. In addition, Kaiser *et al.* detected smaller amounts of methane, ethylene, propylene, acetaldehyde, methyl alcohol, ethyl alcohol, acetone, and unidentified higher-molecular-weight products totaling about 0.6 lb/ton. Still higher emission was reported by Yocum *et al.*[1352] for a backyard incinerator burning a high proportion of garden clippings: methyl alcohol, 9–23 lb/ton; ethylene, 8–61 lb/ton; acetone, > 8 lb/ton; methane, 23–150 lb/ton; acetylene, 4–73 lb/ton; olefins, > 6 lb/ton; carbon disulfide, > 3 lb/ton; benzene, > 3 lb/ton; organic acids, > 4 lb/ton; phenols, > 8 lb/ton; and aldehydes, 5–64 lb/ton. Magill and Benoliel[800] reported organic emission of several hundred pounds per ton for domestic incinerators burning paper or grass clippings, compared with only 1–2 lb/ton for municipal incinerators.

Bellar and Sigsby[92] measured individual oxygenates in the effluent from a trench incinerator burning wood. They found a much wider range of products when no forced air was added. With forced air, methyl and ethyl alcohol predominated. Bellar and Sigsby noted that the ratio of alcohols to aldehydes was considerably greater in the incinerator effluent than in auto exhaust.

OPEN BURNING

Gerstle and Kemnitz[459] reported the following emission values from the open burning of municipal refuse, landscape refuse, and automobile components: hydrocarbons, 30 lb/ton; organic acids, 15 lb/ton; and formaldehyde, 0.01–0.10 lb/ton. An EPA report[1229] showed that organic emission from open burning is generally higher than that from incineration.

TEEPEE BURNERS

Teepee (or wigwam) burners are large conical structures in which industrial and municipal wastes are burned. They are used only when more efficient (and costly) incinerators are not available. Kreichelt[725] reported that many teepee burners do not receive enough air for good combustion, because of poor maintenance or inadequate blowers. The organic emission from teepee burners depends on the waste material burned and is generally greater than that from incinerators, but less than that from open burning.

Miscellaneous Stationary Sources

The following sources account for over half the total gaseous organic emission from all stationary sources. Solvent evaporation is the largest single stationary source, 7.1 million tons/year according to the most recent EPA estimates (Table 2-7). Solid-waste combustion and agricultural burning are the next most important stationary sources.

FOREST FIRES

It is nearly impossible to measure emission from a forest fire, but at least one study has been made under field conditions closely simulating forest fires. Fritschen *et al.*[441] measured the gaseous organic emission from the burning of several acres of mature Douglas fir trees. They identified 25 different organics, ranging in molecular weight from that of ethylene to that of xylene; the most significant were ethylene, ethane, propylene, propane, methyl alcohol, and ethyl alcohol. Acetone, benzene, and toluene were also found in most of the samples. They estimated the total hydrocarbon emission from forest fires at 2–4 lb/ton burned, on the basis of these and other laboratory tests. This is considerably lower than the 166-lb/ton estimate of Feldstein *et al.*[392] for the open burning of land-clearing debris.

Stephens and Burleson[1155] reported an excess (compared with normal air) of olefins over paraffins in the air near a brush fire in Riverside, California; this finding is consistent with the results of laboratory studies on the combustion of agricultural wastes.

STRUCTURAL FIRES

The gaseous organic emission from structural fires, like that from forest fires, can be only roughly estimated. It is probably similar in composition to the emission from wood combustion and municipal-waste incineration and includes both hydrocarbons and oxygenated compounds.

COAL-REFUSE BANKS

Smoldering coal-refuse banks are a conspicuous source of air pollution in mining areas.[802] Carbon monoxide and sulfur dioxide are the major gases emitted,[177] but some organics are also produced. The composition of the gaseous organics is not known.

AGRICULTURAL BURNING

Agricultural wastes—such as cut grass and weeds, straw, felled trees, and other debris—are often disposed of by open burning. The relatively low temperatures associated with open burning tend to increase the emission of gaseous organics, compared with incineration.[392]

Darley *et al.*[284] measured the hydrocarbon produced by burning fruit prunings, barley straw, and native bush in a special tower that simulated field conditions. The average hydrocarbon emission from these agricultural wastes was about 13 lb/ton, of which 2 lb consisted of ethylene, 3 lb of other olefins below C_5, 1 lb of paraffins below C_6, and 7 lb of heavier hydrocarbons. Boubel *et al.*[126] reported similar values for the burning of grass and straw in the same apparatus. Gerstle and Kemnitz[459] reported a considerably higher hydrocarbon emission (30 lb/ton) for the open burning of landscape refuse. Feldstein *et al.*[392] reported still higher values for the open burning of land-clearing debris. They estimated (from other incinerator tests) total gaseous organic emission at 166 lb/ton, of which 30 lb would consist of ethylene, 30 lb of other olefins, 36 lb of saturated hydrocarbons, 11 lb of aromatic hydrocarbons, and 59 lb of oxygenated organics. Many of the low-molecular-weight alcohols and aldehydes in wood smoke are probably produced by the open burning of agricultural wastes.

SOLVENT EVAPORATION

Some of the more important uses of solvents include dry cleaning, surface coatings, metal degreasing, and chemical processing. Most solvents evaporate eventually, either inadvertently or by plan, and end up in the atmosphere. Therefore, the overall composition of solvent emission can be deduced accurately from usage data.

The usage or consumption of different solvents in the United States for 1968 is shown in Table 2-9. Petroleum naphtha, a generic name for hydrocarbon mixtures of varied composition and volatility, is by far the most important solvent from a tonnage standpoint, accounting for about 60% of the total usage. No other solvent accounts for more than 4%. In all, hydrocarbon-based solvents account for 70% of the total usage; ketones and other oxygenated hydrocarbons, 14%; and chlorinated hydrocarbons, 16%. It should be pointed out that the data in Table 2-9 indicate only the quantities of various chemicals consumed as solvents, rather than total amounts produced or consumed in all uses.

GASOLINE MARKETING

Vapor breathing losses from storage tanks at refineries and bulk plants and vapor displacement during filling of tank trucks, service station tanks, and automobile tanks account for almost all the emission associated with gasoline marketing. The vapor lost from breathing and filling consists primarily of the more volatile C_4, C_5, and C_6 hydrocarbons. The analyses of automobile evaporation losses shown in Table 2-6 are probably typical of gasoline marketing emission. Various control devices and practices minimize vapor losses at most storage facilities, but there are no vapor loss controls at retail service stations.

NATURAL SOURCES OF ATMOSPHERIC HYDROCARBONS

Many natural processes emit hydrocarbons to the atmosphere. The major natural sources that have been identified and for which quantita-

TABLE 2-9 Estimated Solvent Usage in the United States, 1968[a]

Solvent	Quantity Used As Solvent, tons/year
Petroleum naphtha	4,325,000
Perchloroethylene	285,000
Ethyl alcohol	265,000
Trichloroethylene	245,000
Toluene	240,000
Acetone	205,000
Xylenes	180,000
Fluorocarbons	175,000
Methylethylketone	160,000
1,1,1-Trichloroethane	140,000
Methylene chloride	140,000
Methyl alcohol	135,000
Ethylene dichloride	120,000
Ethylacetate	85,000
Cyclohexane	80,000
Methylisobutylketone	75,000
Hexanes	65,000
Benzene	50,000
n-Butyl alcohol	45,000
Nitrobenzene	25,000
Turpentine	20,000
Isopropylacetate	20,000
Ethyl ether	20,000
Monochlorobenzene	15,000
Isopropyl alcohol	10,000
Diethylene glycol	5,000
Methylacetate	5,000
Cresols	2,500
Phenol	[b]
Chloroethylene	[b]
Carbon tetrachloride	[b]
Pinene	[b]
Cyclohexyl alcohol	[b]
Cyclohexanone	[b]
Ethylbenzene	[b]
Isobutyl alcohol	[b]
Chloromethane	[b]
n-Butylacetate	[b]
TOTAL	7,137,500+

[a] Data from MSA Research Corporation.[878]

[b] Less than 2,500.

tive estimates are available are biologic decomposition of organic matter, seepage from natural gas and oil fields, and volatile emission from plants. However, information in the literature indicates that there are many other natural sources of hydrocarbons and oxygenates that have not been considered heretofore. Techniques sensitive enough to measure the minute concentrations of hydrocarbons and oxygenates present in remote areas have only recently become available. For example, methane, the predominant hydrocarbon in the atmosphere, was first identified as a trace constituent of the atmosphere as late as 1948.[858] As more-sensitive analytic techniques become available and more effort is channeled into attempts to understand the characteristics and role of natural emission, one would expect more and more minor sources (particularly in the biosphere) to be identified. This section discusses the major natural sources for which quantitative estimates are available and indicates some of the minor sources that have been identified.

Methane is produced in the anaerobic bacterial decomposition of organic matter in swamps, lakes, marshes, paddy fields, etc.[176,346] Koyama[722] has estimated the global production of methane as 2.7×10^{14} g/year (300 million tons/year), on the basis of his measurements of methane fermentation in various soils and lake sediments under controlled experimental conditions. Koyama estimated that paddy fields contribute two-thirds of the methane production and used Hutchinson's[602] estimate of enteric fermentation in animals to account for one-sixth. The other one-sixth of the methane in Koyama's estimate came from coalfields and soils in grassland and forest areas. Ehhalt[355] pointed out that Koyama did not include methane production from swamps, and Robinson and Robbins[1026] pointed out that methane production in humid, tropical areas should also be considered. Robinson and Robbins have estimated the production from swamps and humid tropical areas and added it to Koyama's figure to derive an estimate of methane production of 14.5×10^{14} g/year (1.6 billion tons/year).

Methane is the predominant hydrocarbon in natural gas; seepage from gas, oil, and coal fields constitutes another source.[18] However, Ehhalt[355] considered measurements of the carbon-14 content of atmospheric methane and concluded that up to 25% of the atmospheric methane is from "dead" carbon and could have come from oil-field seepage or the combustion of fossil fuels; 75% is of recent biogenic origin.

Our understanding of the natural sources of methane is still highly limited; as a result, current estimates of global production remain speculative.

Plants release a variety of volatile organic substances, including ethylene, isoprene, α-pinene, and a variety of other terpenes. Ethylene production by plants was noted as early as 1910[254] and rediscovered in 1932.[369] Burg[171] has compiled an extensive list of plants that have been shown to produce ethylene. Rates of production of ethylene in various fruits have been measured by Biale *et al.*[110] and in cotton plants by Hall *et al.*[512] Although some of the fruits were thought to produce no ethylene, later measurements by a more sensitive gas-chromatographic method have shown that very small amounts are produced.[171,172] Ethylene is a plant hormone that is continuously produced in plants and has been linked to fruit ripening.[1,170,265] The ripening of fruits,[110] the fading of flowers,[12] and injury from air pollutants[257] have all been shown to be associated with increased ethylene production. Abeles *et al.*[2] have estimated the natural production of ethylene from plants in the United States at 20,000 tons/year.

Other organic plant volatiles have not been studied as extensively. Ivanov and Yakobson[617] have reviewed the Russian literature and reported that a considerable number of plant species release low-molecular-weight hydrocarbons, aldehydes, and a wide variety of essential oil components.

Went[1301] hypothesized that the decomposition of carotenoids (lipochromes) and phytol results in emission of volatile organics to the atmosphere and that the fate of terpenes synthesized in plants is volatilization into the air. Went estimated that a total of 175 million tons of volatile organic material was emitted to the atmosphere of the whole world each year. Later, Rasmussen[999] and Rasmussen and Went[1008] reported ambient concentrations of plant volatiles (such as isoprene, α- and β-pinene, limonene, and myrcene) in air at remote sites. From the average concentration they measured (10 ppb), Rasmussen and Went estimated the global production of plant volatiles at 438 million tons/year. Although the estimates of worldwide terpene emission need considerable refinement,[1000] it is definite that there are large sources of natural, organic emission in the biosphere. Furthermore, Sanadze and Dolidze[1060] and Rasmussen[996] have identified isoprene as a natural volatile plant product and studied the physiology of isoprene emission.[1007,1059] Table 2-10 lists the various volatile plant products identified by Rasmussen.[999]

From the available estimates of methane and terpene emission, it is clear that worldwide natural hydrocarbon emission is about 2 billion tons/year. However, there is evidence that many other organic volatiles are naturally emitted to the atmosphere. These may be only trace amounts emitted on a local scale, but the total worldwide production can be very large.

TABLE 2-10 Volatile Plant Products[a]

α-Pinene	*n*-Heptane
β-Pinene	Isoprene
Myrcene	α-Ionone
D-Limonene	β-Ionone
Santene	α-Irone
Camphene	

[a] Identified by Rasmussen.[999]

Although natural gas consists predominantly of methane, it also contains varying amounts of ethane, propane, and butane and traces of heavier hydrocarbons.[18] It has been reported that trace quantities of ethane, acetylene, ethylene, propane, and propylene are present as products of methane fermentation.[175]

Studies of odorous compounds in natural waters[635] have shown that organic sulfur compounds—such as methylmercaptan, dimethylsulfide, isobutylmercaptan, and *n*-butylmercaptan—are produced. In addition, geosmin has been identified as a natural product.[843] Organic nitrogen compounds are also well-known odorous natural products.[173,1153,1176] Wilson *et al.*[1327] have found that ethylene and propylene are produced in illuminated cell-free distilled water or natural seawater systems to which dissolved organic matter produced by phytoplankton has been added. Furthermore, Cavanagh *et al.*[210] consider the small quantities of *n*-butyl alcohol, acetone, and ethyl alcohol in Point Barrow, Alaska, as products of a fermentation process in the tundra cover. Aldehydes have been identified as products of an illuminated mixture of plant extracts, oxygen, and water;[1314] and methane, ethane, ethylene, propane, propylene, and *n*-butane have been identified as products of the thermal treatment of marine mud slurries.[885]

Man is also a source of volatile organics. Body odors have been studied by the U.S. armed forces.[241,935,1202] Some atmospheric contaminants identified during a 30-day manned experiment are low-molecular-weight aliphatic acids and aldehydes, in addition to hydrocarbons and other compounds.

The annual hydrocarbon emission from natural sources in the United States can be estimated from the preceding information. If natural methane emission is uniform in all land areas, Robinson and Robbins's[1026] estimate of worldwide methane emission (1.6 billion tons/year) can be used to calculate a U.S. emission of 100 million tons/year. The assumption that natural methane is emitted uniformly from all land areas is probably in error, in that emission rates are higher in tropical than in nontropical areas. More realistically, assuming that the U.S. methane emission rate is half the world average, the U.S. natural methane emission would be 50 million tons/year. Similarly, if Rasmussen and Went's[1008] estimate of worldwide terpene emission (438 million tons/year) is based on uniform distribution over the forested areas of the world, the U.S. emission would be 22 million tons/year. Emission of ethylene from plants in the United States has been estimated at 20,000 tons/year.[2] Combining these estimates indicates a natural hydrocarbon emission in the United States of about 72 million tons/year.

ATMOSPHERIC CONCENTRATIONS OF GASEOUS HYDROCARBONS AND OXYGENATES

Many hydrocarbons are present in the atmosphere, and the exact composition varies enormously from place to place, but methane is the predominant hydrocarbon found in all locations. In remote areas, it is predominant by far. In populated areas, other hydrocarbons are present, but methane has the highest concentration.

Total Hydrocarbon Concentrations

The flame ionization detector, which measures total organically bound carbon, has been used to measure total hydrocarbon concentrations in various cities. It has been used in the Continuous Air Monitoring Program (CAMP) network since 1962.[1230] Yearly average carbon concentration ranges from 1.43 ppm in Washington, D.C., in 1962 to 3.3 ppm in Chicago in 1962, and yearly maximal 1-hr averages range from 8 to 17 ppm. Total hydrocarbons are also routinely measured at over 30 sites in the California air monitoring network.[184] Total hydrocarbon analyses have also been made for shorter periods in specific studies.[32,336,372,1092,1093]

Because the total hydrocarbon measurement does not discriminate between photochemically active hydrocarbons and methane, which is relatively inert, various techniques to separate the hydrocarbon mixture into classes have been developed.[698,948] One method,[948] which discriminates between methane and nonmethane hydrocarbons, has been used[1082,1227] to relate nonmethane hydrocarbons to oxidants formed in urban atmospheres. Diurnal patterns of nonmethane hydrocarbons at some CAMP and Los Angeles County sites are presented in *Air Quality Criteria for Hydrocarbons*.[1227] Ratios of nonmethane hydrocarbons to total hydrocarbons are reported to vary from 0.2:1 in Washington, D.C., to 0.5:1 in Los Angeles.[1082]

Methane

Methane was discovered in the telluric spectrum by Migeotte in 1948.[858] Later spectroscopic measurements established the average methane concentration of the atmosphere to be about 1.5 ppm.[398,475,476] From these spectroscopic measurements, which average over the entire air column, it was tentatively concluded that methane is uniformly distributed throughout the atmosphere, except for local variations near the surface. However, vertical profiles have shown that the methane concentration is somewhat variable in time and space.[69,355] Bainbridge and Heidt[69] measured a decrease in the methane concentration at the tropopause, indicating that the stratosphere is a sink for methane. Scholtz *et al.*[1077] have shown that the methane concentration near the stratopause is, indeed, less than 0.05 ppm (by volume).

A number of ground-level measurements of natural background methane concentrations in remote areas have been reported. Stephens and Burleson[1155] measured 1.39 ppm in southern California mountain areas during the time hot, dry Santa Ana winds were blowing. Cavanagh *et al.*[210] found an average methane concentration of 1.59 ppm at Point Barrow, Alaska. Swinnerton *et al.*[1180,1181] measured a mean concentration of 1.25 ppm during an oceanographic cruise between Washington, D.C., and Puerto Rico and concentrations between 1.25 and 1.50 ppm over the Pacific Ocean and on the island of Hawaii. All these measurements agree with Junge's estimate of the worldwide range (1.2–1.5 ppm).[656] However, Shearer[1107] has reported measurements at a rural site averaging 0.89 ppm. In inhabited areas, methane concentrations are higher.[32]

Other Individual Hydrocarbons

REMOTE LOCATIONS

There have been few measurements of individual hydrocarbons in remote locations. Cavanagh *et al.*[210] found fractional parts-per-billion concentrations of benzene, pentane, butane, ethane, ethylene, acetaldehyde, and acetone at Point Barrow, Alaska. They also found *n*-butyl alcohol at about 100 ppb, which they attributed to biologic sources. Turk and D'Angio[1215] showed that there is a complex mixture of organic vapors in remote locations. Rasmussen and Went[1008] have identified isoprene, α-pinene, β-pinene, limonene, and myrcene in the ambient air in remote locations in North Carolina, Virginia, Missouri, and Colorado. They measured terpene concentrations from 2 to 50 ppb and found that ambient concentrations increased with temperature and light intensity.

Particularly high concentrations were found when conditions associated with the death of cells were present, such as the dying of leaves in autumn and the mowing of meadows. Rasmussen[996] and Rasmussen and Hutton[1004] have also analyzed volatile organics in the ambient air in the humid tropics. Stephens and Burleson[1155] measured parts-per-billion concentrations of ethane, ethylene, and acetylene in the mountains of southern California during Santa Ana winds.

POPULATED LOCATIONS

Although the hydrocarbon composition of the ambient air in populated areas has been studied by a number of investigators, only the Los Angeles basin has been studied extensively. Neligan[911] analyzed 16 early-morning samples collected in central Los Angeles for C_{2-4} hydrocarbons. He compared his results with the composition of auto exhaust and showed that they were similar. However, he did find a relative excess of light paraffins in the atmosphere, compared with the composition of auto exhaust. He attributed these to natural gas leakage. Altshuller and Bellar[19] measured methane, C_{2-5} hydrocarbons, and C_{6-8} aromatics on separate days in downtown Los Angeles in the fall of 1961. They followed changes in concentrations during the day and showed that methane concentrations between 2 and 3 ppm were common, confirmed Neligan's finding that light paraffins are more abundant in the Los Angeles atmosphere than in auto exhaust, and showed that aromatic hydrocarbons contribute appreciably to the total hydrocarbon concentration.

Neligan and Leonard[912] reported the concentrations of a dozen C_{6-10} aromatics at five sites in Los Angeles and concluded that aromatics contribute significantly to the total hydrocarbon loading of urban atmospheres. The average results from over 200 early-morning analyses of C_{1-7} hydrocarbons in Los Angeles are summarized in *Air Quality Criteria for Hydrocarbons*.[1227] Stephens and Burleson[1154] analyzed the atmosphere in Riverside, California, for C_{1-6} hydrocarbons. Here, too, an abundance of light paraffins was found in the atmosphere, compared with auto exhaust. Because this phenomenon appeared to be more pronounced in the afternoon, Stephens and Burleson suggested that natural gas losses, gasoline evaporative losses, and possibly seepage from oil fields could contribute to the effect. In a later paper, Stephens *et al.*[1156] presented results of C_{1-7} analyses from various locations in Riverside, the San Francisco Bay area, and southern California oil fields. They concluded that gasoline evaporation alone could not account for the excess paraffins, but that natural gas leakage, seepage from oil fields, and gasoline evaporation all contribute.

Lonneman *et al.*[779] measured methane, total hydrocarbons, and individual C_{6-10} aromatics in 136 samples from Los Angeles during the fall of 1966. The average and maximal concentrations are shown in Table 2-11. Toluene was the most abundant aromatic, followed by *m*-xylene and benzene. Gordon *et al.*[483] followed the diurnal patterns of individual C_{2-5} hydrocarbons in downtown Los Angeles and Azusa in the fall of 1967. Altshuller *et al.*[31] measured the full range of individual C_{1-10} hydrocarbons in downtown Los Angeles and Azusa in the fall of 1967. The average concentrations of a number of individual hydrocarbons are shown in Table 2-12. Diurnal patterns for various individual hydrocarbons are shown in Figures 2-4 through 2-7. Although many hydrocarbons are present in urban atmospheres, Altshuller *et al.* found that methane and 10 other hydrocarbons (ethane, ethylene, acetylene, *n*-butane, isopentane, propane, toluene, *n*-pentane, *m*-xylene, and isobutane) account for about 90% of the total hydrocarbon loading.

The hydrocarbon composition of urban areas other than Los Angeles is not so well known. Williams[1316] has identified over 30 hydrocarbons on the University of British Columbia campus, and some measurements from Japan are available.[941] Grob and Grob[497] have qualitatively identified 108 C_{6-20} organics in the air of Zurich, Switzerland. Scott

TABLE 2-11 Average and Highest Concentrations of Various Aromatic Hydrocarbons in Los Angeles[a]

	Concentration, ppb (by volume)	
Aromatic Hydrocarbon	Average	Highest
Benzene	15	57
Toluene	37	129
Ethylbenzene	6	22
p-Xylene	6	25
m-Xylene	16	61
o-Xylene	8	33
Isopropylbenzene	3	12
n-Propylbenzene	2	6
3- and 4-Ethyltoluene	8	27
1,3,5-Trimethylbenzene	3	11
1,2,4-Trimethylbenzene, isobutylbenzene, and *sec*-butylbenzene	9	30
tert-Butylbenzene	2	6
TOTAL	106	330

[a] Data from Lonneman *et al.*[779]

TABLE 2-12 Aliphatic Hydrocarbon and Alkylbenzene Concentrations in Downtown Los Angeles (DLA) and Azusa[a]

	Concentration, ppb (by volume)					
	Concentration below Which 10% of Values Occur		Overall Average		Concentration Exceeded by 10% of Values	
Hydrocarbon	DLA	Azusa	DLA	Azusa	DLA	Azusa
Aliphatic hydrocarbons						
Methane	1,700	1,500	2,100	2,200	3,500	3,000
Ethane + ethylene	40	34	102	65	180	100
Acetylene + propane	30	18	76	43	120	65
Propylene	3	1	10.5	4	21	8
n-Butane	20	9	46	21	80	35
Isobutane	5	3	12	7	20	12
1-Butene + isobutene	2	1	5.5	3.5	10	5
2-Butene	1	1	2	1	5	2
1,3-Butadiene	1	1	2	1	5	2
n-Pentane	8	4	21	10	35	16
Isopentane	12	7	35	16	56	26
1-Pentane + 2-methyl-1-butene	—	—	3	—	—	—
Nonane + decane	2	1	5	3	8	6
Alkylbenzenes						
Toluene	10	6	30	14	50	23
Ethylbenzene	1	1	5	2.5	9	4
p-Xylene	2	1	5	2	10	4
o-Xylene	2	1	6.5	3	11	6
m-Xylene	4	2	12	5.5	21	10
Propylbenzenes	2	1	4.5	3	8	6
Ethyltoluenes	3	1	7.5	3	15	7
Other C_9 and C_{10} alkylbenzenes	3	1	12	6	23	13

[a] Data from Altshuller *et al.*[31]

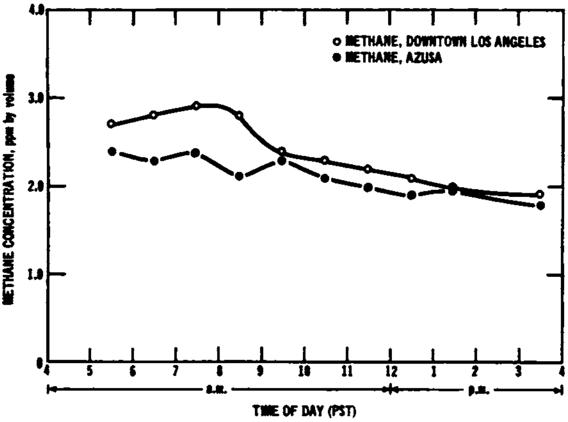

FIGURE 2-4 Diurnal variations in average hourly methane concentrations in downtown Los Angeles and Azusa. (Figures 2-4 through 2-7 reprinted with permission from Altshuller *et al.*[31])

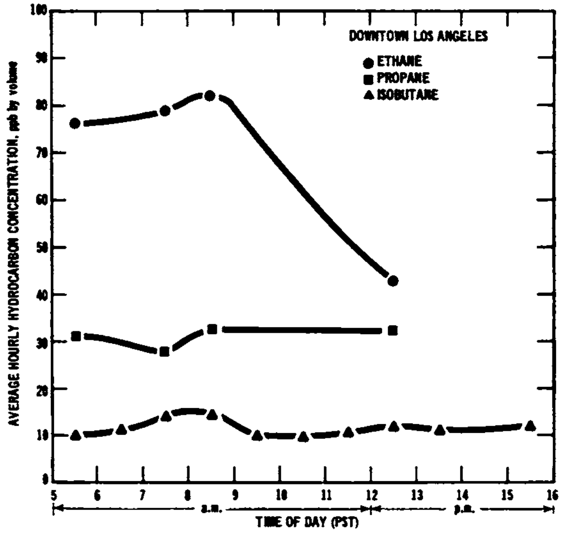

FIGURE 2-5 Diurnal variations in average hourly concentrations of ethane, propane, and isobutane in downtown Los Angeles.

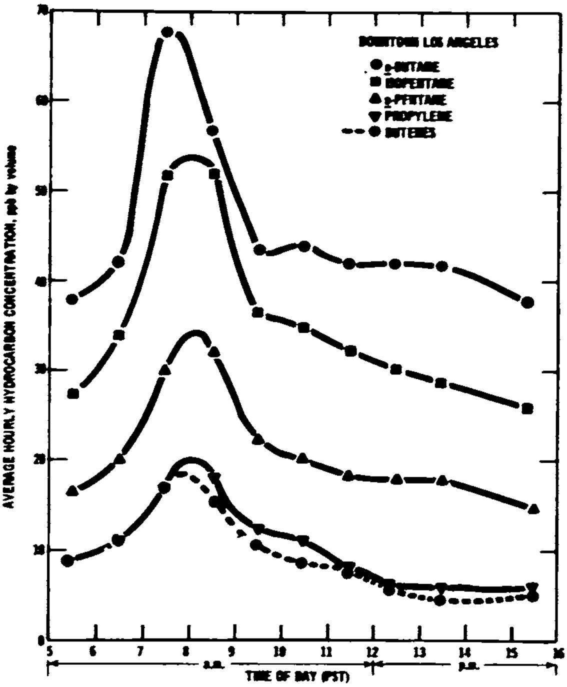

FIGURE 2-6 Diurnal variations in average hourly concentrations of *n*-butane, isopentane, *n*-pentane, propylene, and butane in downtown Los Angeles.

Research Laboratories[1092,1093] has measured individual C_{1-10} hydrocarbons at various sites in New York, as well as Los Angeles, but has not analyzed the results in detail. Lonneman and Kopczynski[780] have determined atmospheric hydrocarbon compositions in Los Angeles, Denver, and New York. Stephens and Burleson[1155] have measured the composition of light hydrocarbons in samples from Hawaii, Denver, New York, and Riverside and the Salinas Valley, California. They concluded that, as long as samples are not deliberately taken near sources of hydrocarbon pollution, the composition resembles that of auto exhaust, with the addition of natural gas and of C_{3-5} paraffins that resemble gasoline vapor. Samples taken in industrial areas and near a brush fire showed distinct differences in composition.

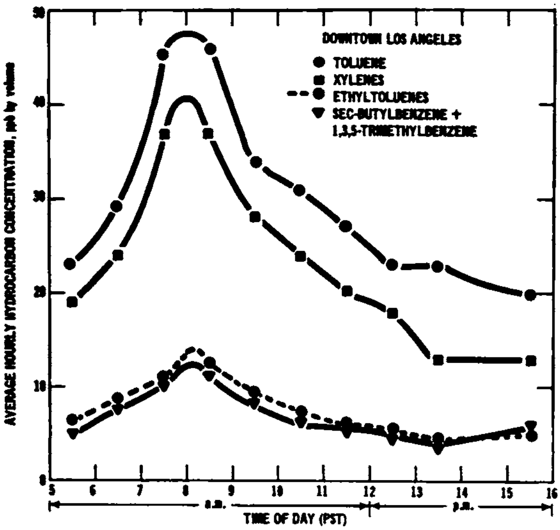

FIGURE 2-7 Diurnal variations in average hourly concentrations of toluene, xylene, ethyltoluene, *sec*-butylbenzene, and 1,3,5-trimethylbenzene in downtown Los Angeles.

Aldehydes and Other Oxygenates

A number of investigators have predicted that formaldehyde should be naturally present in the atmosphere as an intermediate in the oxidation of methane.[18,191,765,821,1299] Levy[765] calculated a steady-state daytime concentration of 2 ppb. These predictions are generally confirmed by the few aldehyde measurements that have been made in remote areas. Lodge and Pate[775] and Fischer *et al.*[402] measured aldehyde concentrations between 1 and 10 ppb in the jungles of Panama and in Antarctica. Although their method measured total aldehydes, it seems reasonable to assume that formaldehyde was the major, if not the only, aldehyde present. Thus, there is some evidence that formaldehyde is a natural constituent of the atmosphere at a few parts per billion.

The source of aldehyde data for populated areas is the U.S. National Air Surveillance Networks (NASN), which measured total aldehydes on an experimental basis in 1967. Insufficient data were obtained from this pilot study, however, to permit the computation of annual averages. The study was discontinued after 1967. The average estimated concentrations at 30 urban sites ranged from less than 0.01 to 0.06 ppm; the average daily maximal concentrations ranged from 0.01 to 0.13 ppm.[1224] Stahl[1143] has compiled atmospheric aldehyde data for the years before 1967. Some indication of the composition of atmospheric aldehydes can be obtained from total aldehyde, formaldehyde, and acrolein measurements made in the Los Angeles area.[1014,1092,1093] Formaldehyde was the predominant aldehyde, accounting for over 50% of the total, whereas acrolein accounted for only about 5%. Formaldehyde has also been measured in the air of Tokyo, Japan.[1349]

There are few atmospheric measurements of oxygenates other than aldehydes, primarily because suitable analytic methods are lacking. However, Bellar and Sigsby[92] have qualitatively identified methyl alcohol, acetaldehyde, and acetone in ambient air near motor-vehicle traffic.

3

Possible Mechanisms of Formation of Oxygenated Organic Compounds in the Atmosphere

Hydrocarbons are among the five most frequently encountered air pollutants in the United States. Although their concentration in the atmosphere is low (2–3 ppm), the total amount is large; data for 1965 are given in Table 3-1. The emission of hydrocarbons into the atmosphere of the United States has probably increased since 1965 as a consequence of the substantial increase in the number of automobiles and increased industrial and electric power production. As the table shows, approximately 63% of emitted hydrocarbon is from automobiles; industry accounts for approximately 21%.

FORMATION FROM TRIPLET OXYGEN (ATMOSPHERIC OXYGEN)

The first part of this chapter deals mainly with the reactions of hydrocarbons and atmospheric oxygen—molecular oxygen in its ordinary triplet ground state—and later sections with reactions of singlet oxygen and ozone. The emphasis is on the oxidation of hydrocarbons present in the atmosphere and the mechanisms by which selected oxidation products are produced, particularly those implicated in toxic or other physiologically undesirable manifestations. In addition, the discussion includes intermediate combustion–oxidation products of

TABLE 3-1 Hydrocarbon Emission into the Atmosphere, United States, 1965[a]

Source	Amount of Hydrocarbon Emitted, million tons	Fraction of Total Hydrocarbon Emitted, %
Automobiles	12	63
Industry	4	21
Electric power plants	1	5
Space heating	1	5
Refuse disposal	1	5
TOTAL	19	99

[a] Data from U.S. Department of Health, Education, and Welfare.[1226] More recent figures for mobile- and stationary-source emission will be found in Tables 2-1 and 2-2. The reader should also consult Table 2-3 for estimated and projected figures for mobile-source emission from 1955 to 1985. All cited figures must be considered as estimates only.

hydrocarbons derived from internal-combustion engines (excluding particulate and polycyclic aromatic hydrocarbons). Furthermore, because it is assumed that hydrocarbons are nontoxic at their atmospheric concentrations, the role of hydrocarbons as precursors of oxygenated compounds of relatively high reactivity—such as hydroperoxides, peroxides, epoxides, aldehydes, and ketones—is emphasized. The report is restricted to hydrocarbons emitted into the atmosphere because of technology; bacterial and other production of hydrocarbons is not considered.

The volatility of hydrocarbons varies with their carbon number, and the discussion in this chapter deals with hydrocarbons most likely to be encountered—those containing eight or fewer carbon atoms. Hydrocarbons containing more than eight carbon atoms are considered to be insufficiently volatile to contribute significantly to the air pollution problem. The emphasis here is on hydrocarbons in urban and heavily industrialized areas, because such areas contribute by far the largest fraction of volatile hydrocarbons. A major problem in discussing vapor-phase organic air pollutants is the difficulty in controlling and understanding all the variables involved in oxidative and other transformations that hydrocarbons can undergo in the presence of oxygen, sunlight, metals of variable valence, oxides of nitrogen and sulfur, ozone, and peroxides.

The reactions, kinetics, and mechanisms discussed here are based to a large extent on well-controlled laboratory experiments on the oxidation of hydrocarbons in the liquid phase, conducted usually at low temperatures (< 200 C) and often in the absence of photochemical energy and the wide variety of initiators likely to be encountered in the atmosphere. Higher-temperature vapor-phase oxidations are also discussed, inasmuch as they represent important reactions that occur in internal-combustion engines. (Reactions in internal-combustion engines occur at temperatures above 200 C.) Laboratory studies at either low or high temperatures have generally used one initiating system (at most, two), but such limitation is not feasible under atmospheric conditions, because components are present in uncontrolled and varying quantities. In the atmosphere and in internal-combustion engines, a wide variety of reactions are occurring simultaneously, proceeding from the original hydrocarbons through the intermediate products and ultimately to the final products, carbon dioxide and water. Unfortunately, environmental reactions do not always go to completion quantitatively, and small quantities of many oxidation products are present in the atmosphere in a more-or-less steady state.

Atmospheric hydrocarbons vary markedly in structure, from the relatively unreactive straight-chain saturated aliphatic hydrocarbons and benzene to branched-chain saturated aliphatic hydrocarbons, unsaturated hydrocarbons, alicyclic hydrocarbons, substituted aromatic hydrocarbons, diolefins, acetylenes, and many others. Table 3-2 is a partial list of hydrocarbons identified in urban environments.

Because rates of oxidation of hydrocarbons vary with structure, consumption is not uniform. The more reactive hydrocarbons are consumed considerably more rapidly than the least reactive ones; thus, relative concentrations are changing rapidly.[1155]

The rate of consumption of individual hydrocarbons is a summation of the rates of the various reactions by which they are consumed. Therefore, rates and mechanisms of oxidation of hydrocarbons are important to understand. Considerable data are now available on rates, kinetics, mechanisms, and activation dimensions of the oxidation of many hydrocarbons derived from model laboratory experiments. The data from these laboratory studies are used in discussions of oxidation of hydrocarbons under the complex sets of conditions that exist in the atmosphere and elsewhere. Such an extrapolation has some theoretical support; vapor-phase reaction rates have been predicted from liquid-phase data by Benson,[100] who used thermochemical information on various classes of peroxides to estimate rates for many hydrocarbon reactions. Benson's methods have been tested and found to be accurate in a substantial number of reactions for which experimental data are available, and it should be possible to extrapolate laboratory

TABLE 3-2 Partial List of Hydrocarbons Present in the Atmosphere[a]

Carbon Number	Saturated Aliphatic Hydrocarbons (Paraffins)	Unsaturated Aliphatic Hydrocarbons (Olefins)	Aromatic Hydrocarbons	Acetylenes	Diolefins	Alicyclic Hydrocarbons
1	Methane					
2	Ethane	Ethylene		Acetylene		
3	Propane	Propylene		Methylacetylene	Allene	
4	Butane Isobutane	1-Butene 2-Butenes, *cis*- and *trans*- Isobutylene			1,3-Butadiene	
5	Pentane Isopentane	1-Pentene 2-Pentenes, *cis*- and *trans*- 2-Methyl-1-butene 2-Methyl-2-butene 3-Methyl-1-butene			Isoprene	Cyclopentene Cyclopentane

6	Hexane	1-Hexene	Benzene	Methylcyclopentane
	2,2-Dimethylbutane	2-Hexenes, *cis*- and *trans*-		Cyclohexane
	2,3-Dimethylbutane	3-Hexenes, *cis*- and *trans*-		
	2-Methylpentane	4-Methyl-1-pentene		
	3-Methylpentane	2-Methyl-1-pentene		
		4-Methyl-2-pentene		
7	2,4-Dimethylpentane		Toluene	
	2,3-Dimethylpentane			
	2-Methylhexane			
8	2,2,4-Trimethylpentane		Xylenes	
9			Trimethylbenzenes	

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[a] Derived from *Air Quality Criteria for Hydrocarbons.*[1227]

results to account for the oxidative behavior of hydrocarbons in the vapor phase (particularly in urban environments), including the prediction of rates of development of secondary contaminants, as well as rates of consumption of various hydrocarbons in the atmosphere. A computerized simulation model for the kinetics of photooxidation of propylene has already been suggested.[1288]

Methods exist for measuring total hydrocarbons and classes of hydrocarbons, such as aldehydes, in the atmosphere, but there is no acceptable and universally used instrumental method for measuring all the oxidation products that are present simultaneously. It would be of considerable importance to be able to determine simultaneously some well-known components of the atmosphere that are irritants and derive from hydrocarbon oxidation—for example, formaldehyde, acrolein, and peroxyacylnitrates.

In addition to irritants, common alkylating agents present in the atmosphere include epoxides, peroxides, and lactones.[716,1065] Some expoxides and peroxy compounds have been shown to be carcinogenic[717,1234,1237,1239,1240,1242,1243,1296] and to have other physiologic effects.[716] Sources of these classes of compounds are liquid fuels, such as gasoline and diesel fuels, and partial combustion processes in internal-combustion engines and industry. In the unburned state, liquid fuels are reactive and readily undergo vapor-phase oxidation—especially in the presence of light, metals, and oxides of nitrogen—to produce a broad range of peroxides and epoxides. The unburned gasoline and other exhaust products emitted from automobiles contain ethylene, propylene, butenes, and other unsaturated hydrocarbons; under atmospheric oxidation conditions, these hydrocarbons can form many oxidation products.

Kinetics of Hydrocarbon Autoxidation

Kinetic studies of the liquid-phase, free-radical autoxidation of hydrocarbons by triplet molecular oxygen are numerous and well documented in the literature.[108,567,859,1268] Specific reaction rate constants and activation dimensions have been obtained with many systems. The basic equations of the free-radical chain reactions of oxygen with hydrocarbons in which kinetic chains are long and hydroperoxides are major primary products follow.

Initiation

$$X_2 \longrightarrow X\cdot \text{ (where } X\cdot \text{ is any radical)} \qquad (1)$$

$$RH + X\cdot \text{ (or } XO_2\cdot) \xrightarrow{R_i} R\cdot + XH \text{ (or } XO_2H) \qquad (2)$$

Propagation

$$R\cdot + O_2 \xrightarrow{k_a} RO_2\cdot \tag{3}$$

$$RO_2\cdot + RH \xrightarrow{k_p} RO_2H + R\cdot \tag{4}$$

Termination

$$2RO_2\cdot \xrightarrow{k_t} \text{ROOR (or alcohol or carbonyl)} + O_2 \tag{5}$$

In these equations, R_i is rate of initiation, and k_a, k_p, and k_t are specific reaction rate constants for addition, propagation, and termination, respectively. Because $k_a > > k_p$, termination at usual oxygen pressures is via bimolecular interaction of peroxy radicals (Reaction 5). Under these circumstances, the rate expression for hydroperoxide formation, and for oxygen consumption if its formation by Reaction 5 is neglected, is given in Eq. 6.

$$\frac{-d[O_2]}{dt} = \frac{-d[RH]}{dt} = \frac{d[RO_2H]}{dt} = k_p[RH](R_i/2k_t)^{1/2}, \tag{6}$$

where R_i combines Reactions 1 and 2. Reaction 3 is usually so fast and efficient that it can be neglected; it is reversible, however, at high temperatures. Using thermochemical data, Benson[99] has calculated ceiling temperatures at which the forward and reverse rates of Reaction 3 are equal. At 1 atm of oxygen pressure, they are above 500 C if R is alkyl, but only 300 or 160 C if R is allyl or benzyl, respectively.

The conditions under which the autoxidation of hydrocarbons occurs in the atmosphere are usually quite different from those under which the above rate expressions were obtained. For example, in laboratory studies at high temperatures or in the presence of metal catalysts, or both, negligible hydroperoxide accumulates, autoxidation rates are high, and a number of anomalies occur that are not immediately accommodated by the simple kinetic scheme given. Actual autoxidation rates may be considerably higher than would be predicted by the final rate equation and may be further increased by cooxidation of relatively small amounts of more easily oxidized substrates, typically aldehydes or ketones. Furthermore, some autoxidations take a much longer time to reach a maximal rate than that expected to build up a small steady-state concentration of hydroperoxide.

Many systems, however, obey Eq. 6 for consumption of oxygen and hydrocarbon (or formation of hydroperoxide) and k_p's and k_t's have been determined and correlated by using non-steady-state methods. The relatively low rate of Reaction 4 is particularly significant; the rate is somewhat dependent on $RO_2\cdot$, but is highly sensitive to R—H bond strengths and the presence of electron-donating or electron-withdrawing groups.

The overall rate of autoxidation depends on the ratio of k_p to $(2k_t)^{1/2}$, about which some qualitative generalizations can be made. Experiments show that the relative ease of autoxidation of RH roughly parallels the ease of breaking the C—H bond, and for hydrocarbons increases in the series *n*-alkanes < branched alkanes < aralkanes ≅ alkenes < alkynes. Both resonance and inductive effects on the stability of the resulting radical are important, especially the former.

More quantitative data are available for alkenes than for any other class of compounds. Bolland's rules[120] for substituted olefins of the type $^1CH_2 = {}^2CH—{}^3CH_3$ state that alkyl substitution on C-1 or C-3 increases the rate of autoxidation by 3.3^n at 45 C, where n is the number of substituents. Substitution of C-2 has little effect. These rules have been refined to include steric effects,[1247] with C-3 substitution by the *tert*-butyl group giving a rate only one-sixth as fast as substitution by methyl. The conclusion is that a fully formed carbon radical plus hydroperoxide is a poor model for the transition state of Reaction 4. Deuterium isotope effects support this conclusion. Measured values of the ratio $k_H:k_D$ (the ratio of the specific reaction rate constants for carbon–hydrogen bond cleavage and carbon–deuterium bond cleavage) for Reaction 4 vary from 1.05 to 5.8, depending on R.[1041,1042] For accurate predictions, it is best to consult tables of $k_p/(2k_t)^{1/2}$ measured experimentally, of which there are a large and growing number.[371,847,1247,1267]

Separate values for k_p and k_t have also been measured for many hydrocarbons, chiefly by Howard and Ingold,[585–589,591] by rotating-sector methods. A representative sample is presented in Table 3-3. In practical terms, however, conclusions from such data may be misleading. At 100–110 C without added initiators, ring-substituted cumenes autoxidize faster than cumene itself, although $k_p/(2k_t)^{1/2}$ values predict the reverse.[591] Under these conditions, the reaction is autocatalytic; the substituted α-cumylhydroperoxides decompose to radicals faster than do the unsubstituted hydroperoxides.

INITIATION BY THERMAL DECOMPOSITION OF HYDROPEROXIDES[1268]

First, we shall consider hydrocarbon systems that contain no added catalysts; the chief source of chain initiation, therefore, is thermal decomposition of hydroperoxides. If the initiation involves simple unimolecular homolysis (Reaction 7), initial scission of the

TABLE 3-3 Rate Constants[a] for the Autoxidation of Hydrocarbons

Hydrocarbon	$k_t(2k_t)^{1/2} \times 10^5$ At 70 C[b]	 At 30 C[b]	k_p/H at 30 C[b]	$k_t \times 10^{-6}$ at 30 C
Propylene	21.7	—	—	—
1-Butene	81	—	—	—
1-Hexene	38	—	—	—
1-Octene	—	6.2	50	130
Neopentylethylene	13	—	—	—
Isobutylene	20	—	—	—
Tetramethylethylene	1,120	—	0.14	0.32
Cyclopentene	220	—	1.7	3.1
Cyclohexene	175	—	1.5	2.8
Cyclooctene	10	—	—	—
Toluene	—	1.4	0.08	150
Ethylbenzene	—	21	0.65	20
Cumene	—	150	0.18	0.0075
1,1-Diphenylethane	—	110	0.34	0.047

[a] In liters per mole per second.
[b] For abstraction only.

hydroperoxide should be followed immediately by the steps shown in Reactions 8 and 9.

$$\text{ROOH} \xrightarrow{k_d} \text{RO}\cdot + \text{HO}\cdot \tag{7}$$

$$\text{RO}\cdot + \text{RH} \longrightarrow \text{ROH} + \text{R}\cdot \tag{8}$$

$$\text{HO}\cdot + \text{RH} \longrightarrow \text{H}_2\text{O} + \text{R}\cdot \tag{9}$$

Because the rate constants for the processes shown in Reactions 8 and 9 are large, probably around 10^4 and 10^8, respectively,[40,198,1269] termination steps involving these species are highly unlikely. Beyond this point, the autoxidation is assumed to continue by way of Reactions 3–5, leading to the usual steady-state expression for total radicals:

$$2k_d[\text{ROOH}] = 2k_t[\text{ROO}\cdot]^2 \tag{10}$$

When the reactions are conducted under conditions in which hydroperoxide does not accumulate—for example, at high temperatures—it also reaches a low steady state, as shown in Eq. 11:

$$\frac{d[\text{ROOH}]}{dt} = k_p[\text{ROO}\cdot][\text{RH}] - k_d[\text{ROOH}] = 0 \tag{11}$$

Equations 12 and 13 follow from Eqs. 10 and 11:

$$[\mathrm{ROO\cdot}] = k_p[\mathrm{RH}]/k_t \qquad (12)$$

$$[\mathrm{ROOH}] = k_p^2[\mathrm{RH}]^2/k_t k_d \qquad (13)$$

In these equations, k_d is the specific reaction rate constant for hydroperoxide decomposition. Hydrocarbon is consumed by two pathways, of which one is reaction with HO· and RO· (two molecules per molecule of hydroperoxide decomposed) and the other is reaction with ROO· (from Eq. 11, one molecule per molecule of hydroperoxide decomposed). Accordingly,

$$-d[\mathrm{RH}]/dt = 3k_d[\mathrm{ROOH}] = 3k_p^2[\mathrm{RH}]^2/k_t \qquad (14)$$

Because k_d and [ROOH] are inversely proportional (Eq. 14), both disappear from the rate expression. The actual rate constant for hydroperoxide decomposition is unimportant, provided it is large enough to ensure that hydroperoxide reaches a low steady-state concentration early in the reaction. Before this point, the autoxidation is autocatalytic; afterward, Eq. 14 is obeyed. If we assume E_p = 12–15 kcal/mol and E_t = 4 kcal, reasonable values for relatively unreactive hydrocarbons and secondary peroxy radicals, then E_{overall} = (24 to 30) − 4 = 20–26 kcal, about the same as predicted for a long-chain process with E_i = 30–40 kcal (E_p, E_t, E_{overall}, and E_i indicate the activation energy for propagation, termination, overall process, and initiation, respectively).

The above analysis, which is due to Walling,[1268] produces striking results when applied to cooxidation, the condition that exists under atmospheric oxidation and internal-combustion conditions. Such an analysis is too complex to be reproduced here; the original literature should be consulted. The most interesting cases arise when one of the substances is a very easily autoxidized material, such as an aldehyde, and the other compound is a hydrocarbon.

Equation 14 may be generalized to any initiation scheme, assuming Reactions 3–5 and a low steady-state concentration of ROOH; details are given in Walling's paper.[1268]

METAL-CATALYZED INITIATION AND OTHER REACTIONS

Metal-catalyzed initiation has been reviewed by Bawn[90] and, more recently, by Betts[108] and Walling.[1268] Compounds of some variable-valence (transition) metals are among the most important initiators for hydrocarbon autoxidation. At low concentrations, the chief effect of transition-metal salts is to initiate autoxidation by converting hydroperoxides to radicals, as shown in Reactions 15 and 16:[666–669,788]

$$M^{n+} + RO_2H \longrightarrow M^{(n+1)^+} + RO^{\cdot} + OH^-(k_m) \qquad (15)$$

$$M^{(n+1)^+} + RO_2H \longrightarrow M^{n+} + RO_2\cdot + H^+(k_n) \qquad (16)$$

In these equations, k_m and k_n are specific reaction rate constants for metal in valency states M^{n+} and $M^{(n+1)}$, respectively. Among the most important of these transition-metal compounds are salts of cobalt and manganese, which can alternate between adjacent valency states and undergo both reactions shown in Reactions 15 and 16, thereby decomposing hydroperoxides catalytically by a redox cycle when equilibrium has been established between the two valency states of the metal, $k_m[M^{n+}][RO_2H] = k_n[M^{(n+1)+}][RO_2H]$. The initiation rate is given by Eq. 17, where $[M] = [M^{n+}] + [M^{(n+1)+}]$:

$$R_i = [k_m(M^{n+}) + k_n(M^{(n+1)^+})][RO_2H] = 2k_mk_n[M][RO_2H]/(k_m + k_n) \qquad (17)$$

The autoxidation rate given by Reaction 16 depends on the square root of the total metal concentration. As hydroperoxide accumulates, the autoxidation accelerates, but the hydroperoxide concentration eventually attains a maximum, at which its decomposition by Reactions 15 and 16 exactly equals its formation by Reaction 4. On the assumption that the alkoxyl radicals produced in Reaction 15 react quantitatively with hydrocarbon according to Reaction 18, it may be shown that Eq. 19 applies:[666–669,1011]

$$RO\cdot(HO\cdot, RO_2\cdot) + RH \longrightarrow ROH(H_2O, RO_2H) + R\cdot \qquad (18)$$

$$-d[O_2]/dt = k_p{}^2[RH]^2/2k_t \qquad (19)$$

Thus, the limiting autoxidation rate is independent of the total metal concentration, a result that has been observed in various autoxidation systems. Equation 19 may not necessarily be a reliable source of $k_p/(2k_t)^{1/2}$ values, inasmuch as in its derivation no account is taken of alkoxyl radical attack on hydroperoxide. Moreover, the polarity of a medium rich in hydroperoxide and metal ions would probably affect the value of $k_p/(2k_t)^{1/2}$. Compounds of transition metals, particularly of cobalt and manganese, are reported to initiate autoxidation by oxidizing particularly reactive hydrocarbons,[163,164,1285] such as dienoic acids and alkyl aromatics, and it has been frequently suggested that such attack is important in producing initiating radicals in autoxidation, as shown in Reaction 20:

$$M^{(n+1)+} + RH \longrightarrow M^{n+} + R\cdot + H^+ \qquad (20)$$

Even in the absence of peroxidic species, cobaltous ion may react with molecular oxygen,[107,247,305] as formulated in Reactions 21 and 22:

$$Co^{2+} + O_2 \longrightarrow Co^{2+}\cdot O_2 \text{ (complex)} \qquad (21)$$

$$Co^{2+}\cdot O_2 + Co^{2+}(XH) \longrightarrow Co^{3+}\ X^- + HO_2\cdot + Co^{2+} \qquad (22)$$

Initiation is apparently effected by a reaction with oxygen to give a complex that oxidizes another cobaltous ion to cobaltic. The chain reaction continues through the activity of the hydroperoxy free radical.

Kinetic evidence has been reported[452] to show that similar reactions occur with ferrous ion in aqueous media, and other work[540] supports such reactions for three metallic salts—cobaltous, manganous, and cerous—in solvent media. Similar reactions have been observed with many cobalt compounds,[806] and manganese phthalocyanine[370] forms a reversible oxygen complex, which is an efficient autoxidation catalyst similar to ferrous and cobaltous phthalocyanines.

In the presence of hydroperoxides, the cobaltous ion is oxidized and free radicals are formed, as shown in Reaction 23:

$$Co^{2+} + ROOH \longrightarrow Co^{3+} + RO\cdot + OH^- \qquad (23)$$

With cobaltic ion in the presence of hydroperoxide, the accepted reaction in the presence of aldehydes and monounsaturated hydrocarbons is shown in Reaction 24:

$$Co^{3+} + ROOH \longrightarrow Co^{2+} + H^+ + RO_2\cdot \qquad (24)$$

Two recent studies of metal-catalyzed autoxidation involving either intermediates or added materials as cooxidants are worth noting. Brill has shown that the cobalt-catalyzed autoxidation of toluene or *p*-xylene in acetic acid at 90 C is markedly accelerated by 2-butanone. With 1 *M* *p*-xylene, a maximal rate of approximately 25%/hr is obtained, corresponding to $-d[RH]/(dt = 5.6 \times 10^{-5}$ mol/(liter-sec). At this temperature, $k_p^2/2k_t \cong 2.8 \times 10^{-7}$. Morimoto and Ogata[866,867] have reported a maximal rate of 5×10^{-5} mol/(liter-sec) for toluene autoxidation under the same conditions. The latter authors clearly implicate benzaldehyde as a critical cooxidant; they show that it is present at a constant concentration (4.5%, based on toluene) during most of the reactions and that the autoxidation does not reach its maximal rate until this concentration is reached. Addition of benzaldehyde greatly decreases the initial induction period.

In autoxidation reactions of hydrocarbons in the atmosphere, oxygen is present in great abundance. Thus, it may be that termination may occur with unsaturated, as well as with saturated, molecules, as illustrated in Reaction 5. In their lower valency states, transition metals can also terminate autoxidation chains by reducing alkylperoxy radicals to hydroperoxides and other products.[107,247,667,668,1106]

The behavior of transition-metal salts in the autoxidation of hydrocarbons depends heavily on the ligands attached to them. The recent book by Reich and Stivala[1011] should be consulted for a more detailed account of the chemical and kinetic behavior of transition metals in autoxidation systems.

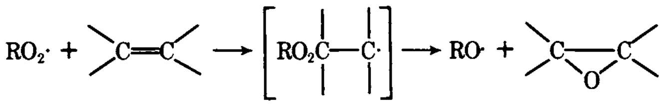
CONCLUSIONS

This brief analysis permits prediction of limiting rates of autoxidation that can be expected for "classic" hydroperoxide chain autoxidation of hydrocarbons under different conditions of chain initiation, using values of $k_p^2/2k_t$ obtained under conditions of slow reaction and long kinetic chains. At these limiting rates, substantial attack on hydrocarbon occurs via alkoxy or hydroxy radicals, and this may explain the large increases in rate that may arise in cooxidation involving intermediate oxygenated products or added easily autoxidized materials. Although some instances of metal-catalyzed autoxidation proceed near the predicted maximal rates, others are notably faster, but show kinetics inconsistent with this analysis. Under these conditions, it becomes likely that hydrogen abstraction by peroxy radicals from any substrate becomes unimportant, and either peroxy radicals participate in redox cycles with the metal or some entirely new chain carriers are involved. Although a number of such steps have been proposed, none has been conclusively identified, nor have their rates been established. The extensive data on the rates of individual steps in "classic" long-chain autoxidation may now make this possible and lead to understanding of a series of reactions of unusual scientific interest and technical importance, particularly in relation to the atmospheric oxidation of hydrocarbons.

Products of Hydrocarbon Autoxidation[404,859,1246]

Autoxidation either in the vapor phase or in nonpolar solvents involves free-radical chain processes. The kinetics and mechanisms of these reactions are indeed complex, because numerous free-radical intermediates are simultaneously involved and each has different lifetimes and numerous modes of further reaction. Recombination, disproportionation, decomposition, displacement, and addition are possible, and the natures and quantities of the products formed during autoxidation, gaseous oxidation, and pyrolytic decomposition depend on the relative rates of the competing processes.

The hydroperoxide theory of autoxidation has had considerable success in describing the mechanisms of low-temperature autoxidation of hydrocarbon, and it has long been recognized that the alkylperoxy radical $RO_2\cdot$ is a very important intermediate. Reactions 1–5 and Eq. 6 have been successful in describing many instances of autoxidation of hydrocarbons conducted on a well-controlled laboratory scale at low temperatures (<200 C). Although it is now generally accepted that termination in autoxidation (Reaction 5) involves interaction of two alkylperoxy radicals to form a dialkylperoxide (or other products) with liberation of oxygen, under appropriate conditions the dialkylperoxide formed may also decompose to form free radicals, thereby propagating chains; such a process must be considered important in both liquid-phase and vapor-phase oxidation (>200 C). Alkylperoxy radicals may add to unsaturated systems to form an alkoxy radical and epoxides, as shown in Reaction 25.



(25)

A wide variety of other oxidation products are also obtained, including saturated and unsaturated alcohols, aldehydes, and ketones, as illustrated by the recently published work on the autoxidation of 1-hexene[218] and cyclopentene.

Although most oxygenated intermediates—with the possible exceptions of ketones, lactones, and epoxides—would not be expected to build up appreciably, because they are more reactive than hydrocarbons, oxygenated intermediates are physiologically less desirable.

Recent work has established that a further important reaction of organic peroxy radicals is intramolecular rearrangement or isomerization, especially at higher temperatures (over about 200 C). These rearrangement reactions lead, by further reactions of the isomerized radical, to several interesting types of compounds, including carbonyl compounds and alcohols with carbon skeletons different from those of the original organic molecules, alkenes, *O*-heterocycles, and dihydroperoxides; under favorable conditions, as in oxygen-deficient systems, the yields of these can be quite high. Because several of these products are effective chain-branching agents, the occurrence of isomerization during oxidation is mechanistically important and in many cases may determine the overall rate, the course of reaction, and product distribution.

Competing Reactions of Organic Peroxy Radicals

Rearrangement reactions of peroxy radicals can be important chain-propagation steps in the oxidation of hydrocarbons only if they can compete successfully with intermolecular H abstraction. Radical rearrangements involve attack by the free electron of the radical on some other bond in the radical. These reactions occur by the intramolecular transfer of an atom or group, usually the hydrogen atom, and an active center migration. Free-radical isomerization is favored by high temperature and by low pressure. A typical example is the isomerization of the 1-pentylperoxy radical by 1:6 transfer of secondary H (Reaction 26) and the intermolecular abstraction of a secondary H atom from *n*-pentane by that radical (Reaction 27):

$$CH_3CH_2CH_2CH_2CH_2OO\cdot \xrightarrow[\text{transfer}]{\text{1:6 H}} CH_3\dot{C}HCH_2CH_2CH_2OOH \qquad (26)$$

$$CH_3(CH_2)_3CH_2OO\cdot + CH_3(CH_2)_3CH_3 \longrightarrow CH_3(CH_2)_3CH_2OOH + CH_3\dot{C}HCH_2CH_2CH_3 \qquad (27)$$

It has been estimated[951] that the activation energy for intermolecular displacement by $RO_2\cdot$ of secondary hydrogen is 10.5 kcal/mol. For 1:6 intramolecular transfer of secondary hydrogen,[403] $E \simeq 17$ kcal/mol.

Modes of Isomerization of Organic Peroxy Radicals

The simplest organic peroxy radical is $CH_3OO\cdot$, which is formed during the oxidation of methane (Reaction 28); it decomposes as illustrated by Reaction 29. It is evident that Reaction 29 must involve isomerization by 1:3 transfer of H from C to O (Reaction 30); this process has a high activation energy. The reaction sequence is therefore usually represented by a single step as shown in Reaction 31.

$$CH_3\cdot + O_2 \longrightarrow CH_3OO\cdot \qquad (28)$$

$$CH_3OO\cdot \longrightarrow CH_2O + \cdot OH \qquad (29)$$

$$CH_3OO\cdot \longrightarrow \cdot CH_2OOH \longrightarrow CH_2O + \cdot OH \qquad (30)$$

$$CH_3\cdot + O_2 \longrightarrow CH_2O + \cdot OH \qquad (31)$$

For higher alkylperoxy radicals, also, this well-established mode of decomposition to a carbonyl compound and a hydroperoxy radical must involve isomerization by hydrogen transfer in order that ·OH may be formed (Reaction 32):

$$\mathrm{RR'CHOO\cdot \longrightarrow RR'\dot{C}OOH \longrightarrow RR'C{=}O + \cdot OH} \qquad (32)$$

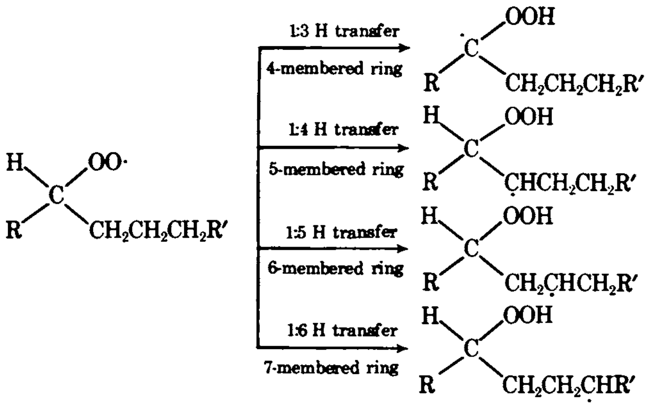
The products of photooxidation of methane, ethane, and propane illustrate the temperature dependence of such an isomerization reaction.[415,416] Below 100 C, peroxides are the only products of photooxidation; above 100 C, aldehydes are also produced, by the isomerization and decomposition sequence (Reaction 32). At higher temperatures, this mode of reaction of $RO_2\cdot$ occurs exclusively.

In more complex cases, several modes of isomerization are possible. Each of these may be followed by several decomposition reactions, leading to a variety of products, many of which are diagnostic of the occurrence of isomerization. These modes of isomerization can be grouped into three classes of reaction: H transfer, group transfer, and ring-opening reactions.

Isomerization by H transfer is by far the most frequent mode of isomerization of alkylperoxy radicals, forming hydroperoxyalkyl radicals (Reaction 33).

$$C_nH_{2n+1}OO\cdot \longrightarrow \cdot C_nH_{2n}OOH \qquad (33)$$

In complex radicals, transfer of H from several different carbon atoms can occur and can be classified as 1:3, 1:4, 1:5, or 1:6 H transfer (Reaction 34):



(34a)

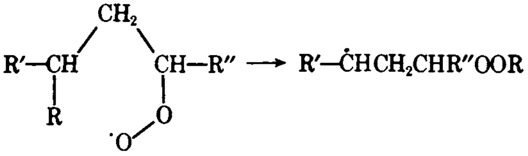
(34b)

(34c)

(34d)

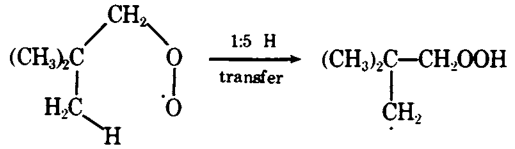
Thus, for example, in the 2,2,4-trimethyl-1-pentylperoxy radical, $(CH_3)_3CCH_2CH(CH_3)CH_2OO\cdot$, two H atoms can be transferred 1:3, one 1:4, five 1:5, none 1:6, and nine 1:7. The relative rates of these processes depend on the size of the ring in the necessarily cyclic transition states involved, because, although this does not affect the enthalpy change, account must be taken of the strain energy involved in calculating the probable activation energy.

Isomerization of an alkylperoxy radical by transfer of an alkyl group, producing an alkylperoxyalkyl radical (Reaction 35), is less favored energetically than isomerization by H transfer and has been postulated much less frequently in discussions of oxidation mechanisms.

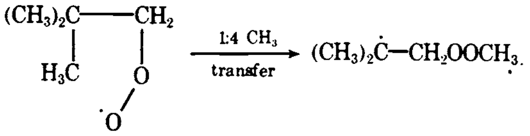


(35)

Group transfer can compete with H transfer, however, in the isomerization of alkylperoxy radicals for which only primary H is available. The best example of this is the neopentylperoxy radical in which H transfer (Reaction 36) and CH_3 transfer (Reaction 37) compete.[1359]



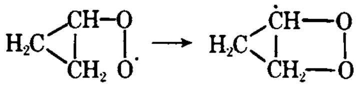
(36)



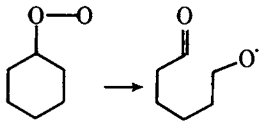
(37)

As would be expected, the products of oxidation reactions suggest that the larger an alkyl group is, the less likely it is to be transferred. Ethyl transfer in the 1-propylperoxy radical[1097] and in the 2-butylperoxy radical[929] has, however, been postulated.

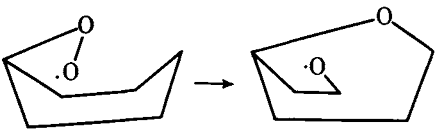
Isomerization by ring opening, a special case of group transfer, can occur in cycloalkylperoxy radicals. It can lead either to an increase in ring size (Reaction 38) or to scission of the O—O bond to give a carbonyl-substituted (Reaction 39) or epoxy-substituted (Reaction 40) alkoxy radical.



(38)



(39)



(40)

It has been suggested that increase in ring size is effected by Reaction 38 during the oxidation of cyclopropane,[823,824] cyclopentane,[827,828] methylclohexane,[861] and cyclohexane[550] and that Reactions 39 and 40 may play a minor part in the oxidation of cyclohexane.[1361]

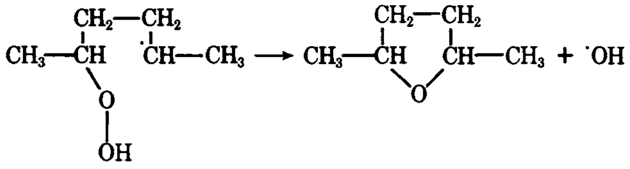
Isomerization by H transfer of cycloalkylperoxy radicals is more difficult than the corresponding reactions of peroxy radicals derived from acyclic alkanes because of restriction of rotation by the ring. In these circumstances, ring-opening isomerization reactions appear to compete with H transfer.

Decomposition Reactions of Hydroperoxyalkyl Radicals

Hydroperoxyalkyl radicals decompose by several routes to give a variety of stable or moderately stable products. In systems containing oxygen, oxidation of these radicals will compete with their decomposition, giving hydroperoxyalkylperoxy radicals. The nature of the stable products of these oxidation and decomposition reactions provides strong evidence of the participation of alkylperoxy radical isomerization as a chain-propagating step in vapor-phase oxidation reactions. The decomposition and oxidation reactions of alkylperoxyalkyl radicals are analogous to those of hydroperoxyalkyl radicals.

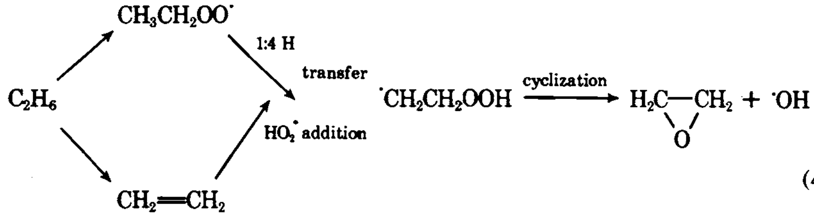
CYCLIZATION TO *O*-HETEROCYCLES

Homolysis of the O—O bond (the weakest bond) in a hydroperoxyalkyl radical is often accompanied by ring closure, to give an *O*-heterocycle and a hydroxyl radical. Thus, decomposition by this route of α-hydroperoxyalkyl radicals gives oxiranes, of β radicals gives oxetanes, of γ radicals gives tetrahydrofurans, and of δ radicals gives tetrahydropyrans. This important mode of decomposition is illustrated in Reaction 41, which shows the mechanism of formation of 2,5-dimethyltetrahydrofuran from the 5-hydroperoxy-2-hexyl radical:



(41)

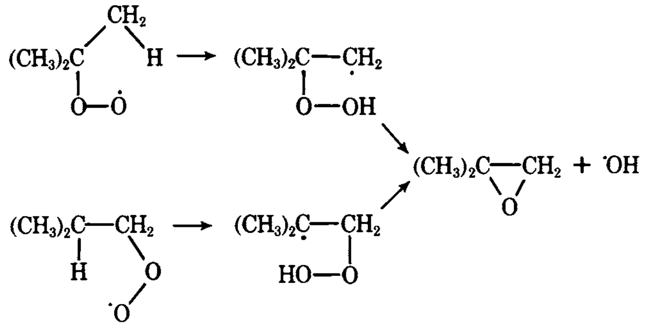
In the case of simple alkanes, such as ethane, the *O*-heterocycles formed are oxiranes. These are probably formed by cyclization of a hydroperoxyalkyl radical with elimination of ·OH or by cyclization of an alkylperoxyalkyl radical with elimination of ·OR. However, the 5-hydroperoxy-2-hexyl radical could have been formed either by alkylperoxy radical isomerization or by addition of a peroxy radical to an alkene[700] (Reaction 42), so that the formation of the *O*-heterocycle is not unequivocal evidence of the occurrence of isomerization.



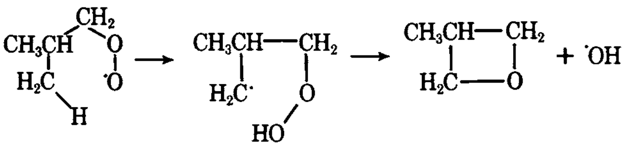
(42)

In the case of higher alkanes, however, the *O*-heterocyclic products include derivatives of oxetane, tetrahydrofuran, and tetrahydropyran, as well as oxiranes. These products do provide definite evidence of alkylperoxy radical isomerization; it is very difficult to write a mode of their formation that does not involve this reaction.

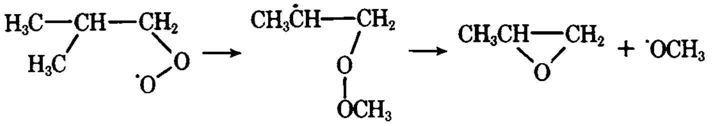
The slow oxidation of isobutane[1360] yields, in the second stage of the induction period, 2,3-dimethyloxirane (isobutene oxide) and methyloxirane (propylene oxide). In the third stage of the induction period, small amounts of 3-methyloxetane are formed. Rearrangement by 1:4 H transfer of the *tert*-butylperoxy radical or the isobutylperoxy radical followed by the elimination of ·OH gives 2,2-dimethyloxirane (Reaction 43). In the case of isobutylperoxy, two further possibilities occur: 1:6 H transfer and loss of ·OH, giving 3-methyloxetane (Reaction 44); and 1:4 CH_3 transfer and loss of $\cdot OCH_3$, giving methyloxirane (Reaction 45):



(43)



(44)



(45)

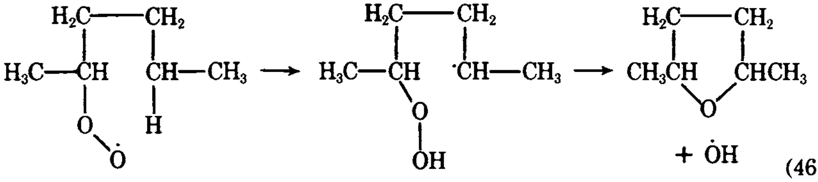
The oxidation of *n*-butane[106] produces 2-methyloxetane and 2-ethyloxirane by 1:5 and 1:4 H transfer, respectively, of butylperoxy radicals and cyclization of the hydroperoxybutyl radicals formed.

The alkylperoxy radical that should lead to a single conjugate *O*-heterocycle is the neopentylperoxy radical, in which 1:5 H transfer is the only possible mode of H transfer (Reaction 36). Cyclization of the resulting 3-hydroperoxy-2,2-dimethyl-1-propyl radical produces 3,3-dimethyloxetane, which has indeed been identified among the products of slow combustion of neopentane[1359] and is a major product of the *n*-pentane–oxygen cool flame.[408]

The occurrence in combustion condensates of saturated furans and pyrans was first reported from studies of the *n*-pentane–oxygen system.[1219,1220] More recently, it has been shown[222] that the *n*-pentane–

air reaction in an annular-flow reactor gives, by 1:6 H transfer and cyclization, 2-methyltetrahydrofuran over a wide variety of conditions of temperature and reactant ratio, the maximal yield being obtained at 450–500 C. In a static reactor, by contrast, the cool flames of the *n*-pentane–oxygen system at 278 C give 2-ethyl-3-methyloxirane and 2,4-dimethyloxetane as the predominant C_5 *O*-heterocycles.[272] It has been estimated that, in this system, 40% of the pentylperoxy radicals formed isomerize and decompose to C_5 *O*-heterocycles.[272]

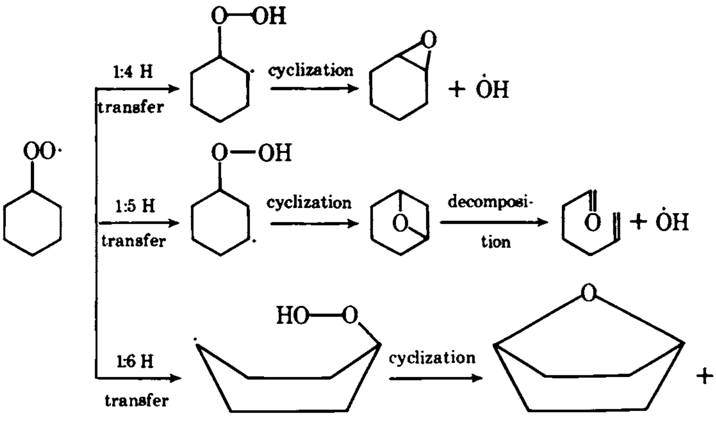
One of the earliest interpretations of *O*-heterocyclic products in terms of alkylperoxy radical isomerization followed by cyclization is that of Bailey and Norrish,[65] who found 2,5-dimethyltetrahydrofuran in the products of cool flames of *n*-hexane, thus providing unambiguous evidence of the participation and isomerization of the 2-hexylperoxy radical (Reaction 46):



(46)

The first discovery of oxetanes in gaseous oxidation of hydrocarbons resulted from studies of the oxidation of 2,2,4-trimethylpentane (isooctane) and 2,2-dimethylbutane.[1045] In addition to 2,2,4,4-tetramethyltetrahydrofuran, isooctane gave 2-*tert*-butyl-3-methyloxetane, whereas 2,3,3-trimethyloxetane was produced from 2,2-dimethylbutane.

Oxetanes and tetrahydrofurans are much less likely to be formed by cyclization of hydroperoxycycloalkyl radicals with elimination of ·OH than by the corresponding reaction of acyclic hydroperoxyalkyl radicals, because of the highly strained configurations of the bicyclo products that would result. In the oxidation of cyclohexane,[1361] however, 1,2-epoxycyclohexane is formed by 1:4 H transfer in the cyclohexylperoxy radical and cyclization of the resulting α-hydroperoxycyclohexyl radical, and 1,4-epoxycyclohexane (7-oxabicyclo [2·2·1] heptane) is formed from 1:6 H transfer in the boat configuration of the cyclohexylperoxy radical followed by cyclization. Also, the considerable yield of 5-hexenal probably arises by isomerization, cyclization, and (because of the strain in 1,3-epoxycyclohexane) decomposition (Reaction 47):

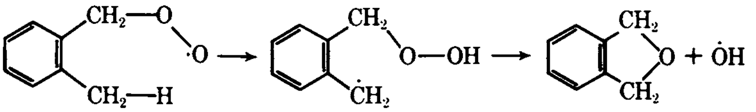


(47a)

(47b)

(47c)

The gaseous oxidation of aromatic hydrocarbons has been studied less intensively than that of alkanes. If, however, suitably positioned side chains are present, isomerization of arylperoxy radicals can occur. Thus, the oxidation of *o*-xylene[81,777,1067] yields a wide variety of oxygenated products, but phthalan (*o*-xylene oxide) predominates under a wide range of operating conditions. At low conversion, the yield of phthalan can exceed 50%.[777,1067] It is very probable that the mechanism of production of this compound involves isomerization by 1:6 H transfer of the *o*-xylylperoxy radical and cyclization (Reaction 48):



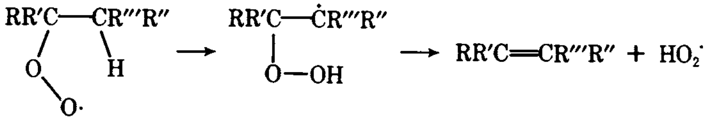
(48)

It is noteworthy that no *O*-heterocyclic products result from the oxidation under similar conditions of *m*- and *p*-xylenes, because the outer oxygen of the peroxy group and the hydrogen of the *m*- or *p*-methyl group cannot get close enough to each other. As a result, the kinetics of the oxidation of *o*-xylene differ markedly from those of the oxidations of *m*- and *p*-xylenes.

SCISSION OF C—O

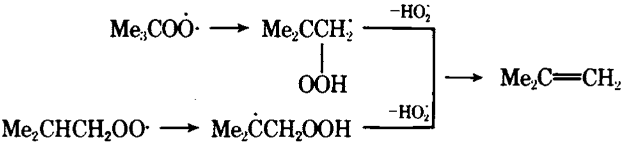
Scission of C—O (Reaction 49) is possible only when the original isomerization occurs by 1:4 H transfer, that is, only when the

O-heterocycle derived from the hydroperoxyalkyl radical by cyclization is an oxirane.



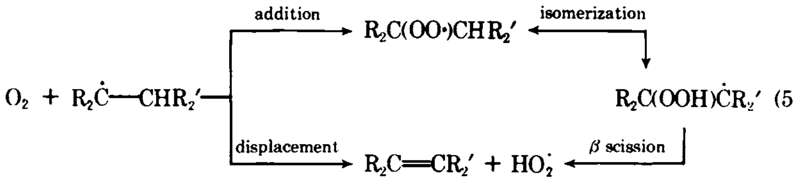
(49)

The proximity of the unpaired electron weakens the C—O bond in the β position. Alkenes result that are conjugate with the alkane from which the alkylperoxy radical was derived. Production of alkenes by this route is held responsible for the formation of isobutene as the major product during the induction period of the gaseous oxidation of isobutane[1360] (Reaction 50) and could account for the production of alkenes in high yield from a variety of hydrocarbons (e.g., 2-methyl-1-pentene and 2-methyl-2-pentene from 2-methylpentane,[403] styrene from ethylbenzene,[109] and cyclohexene from cyclohexane[1361]):



(50)

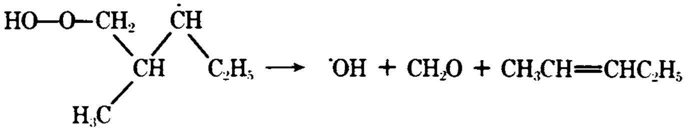
However, at temperatures over 400 C, alkenes are formed by direct abstraction of H by oxygen from alkyl radicals, and it has been suggested recently[700] that this reaction can occur at temperatures as low as 300 C, in which case it is in competition with addition of oxygen to alkyl radicals to form alkylperoxy radicals, followed by their rearrangement and decomposition (Reaction 51):



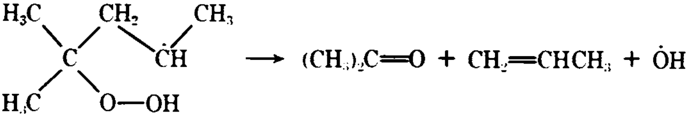
(51)

SCISSION OF C—C AND O—O

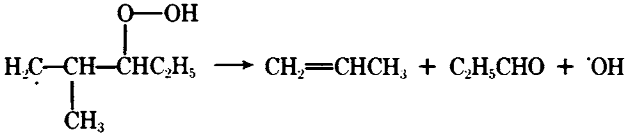
In many β-hydroperoxyalkyl radicals, β-scission reactions result in the formation of an oxygenate and an alkene (·OH being eliminated) without further H shift. The production in pairs of many of the alkenic and carbonyl scission products formed during the cool-flame oxidation of 2-methylpentane[406,407] can be accounted for qualitatively by this mode of decomposition (e.g., Reactions 52–57).



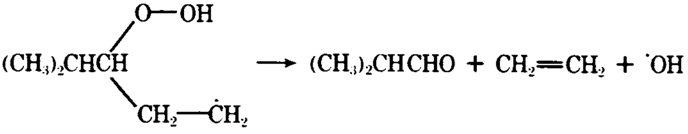
$$HO{-}O{-}CH_2CH(CH_3)\dot{C}HC_2H_5 \longrightarrow {}^{\cdot}OH + CH_2O + CH_3CH{=}CHC_2H_5 \qquad (52)$$



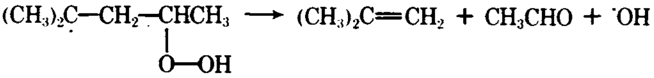
$$(CH_3)_2C(O{-}OH)CH_2\dot{C}HCH_3 \longrightarrow (CH_3)_2C{=}O + CH_2{=}CHCH_3 + \dot{O}H \qquad (53)$$



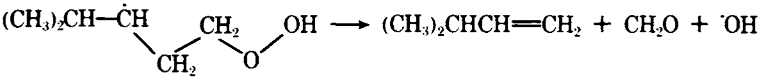
$$\dot{H_2C}{-}CH(CH_3){-}CH(O{-}OH)C_2H_5 \longrightarrow CH_2{=}CHCH_3 + C_2H_5CHO + {}^{\cdot}OH \qquad (54)$$



$$(CH_3)_2CHCH(O{-}OH)CH_2{-}\dot{C}H_2 \longrightarrow (CH_3)_2CHCHO + CH_2{=}CH_2 + {}^{\cdot}OH \qquad (55)$$

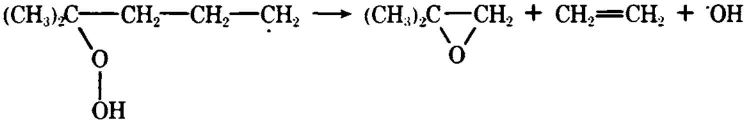


$$(CH_3)_2\dot{C}{-}CH_2{-}CH(O{-}OH)CH_3 \longrightarrow (CH_3)_2C{=}CH_2 + CH_3CHO + {}^{\cdot}OH \qquad (56)$$



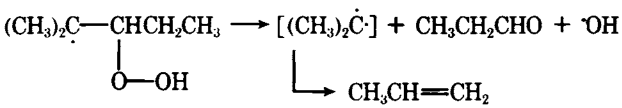
$$(CH_3)_2CH{-}\dot{C}H{-}CH_2{-}CH_2{-}O{-}OH \longrightarrow (CH_3)_2CHCH{=}CH_2 + CH_2O + {}^{\cdot}OH \qquad (57)$$

Similar *β*-scission reactions of *γ*- and *δ*-hydroperoxyalkyl radicals can occur, but lead to an alkene and an *O*-heterocycle as the scission products (Reaction 58):



$$(CH_3)_2C(O{-}OH){-}CH_2{-}CH_2{-}\dot{C}H_2 \longrightarrow (CH_3)_2\underset{O}{C{-}CH_2} + CH_2{=}CH_2 + {}^{\cdot}OH \qquad (58)$$

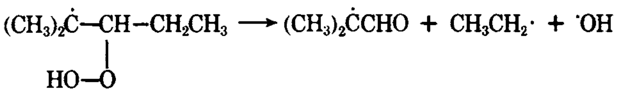
A second group of C—C and O—O scission reactions, *α* scission of *α*-hydroperoxyalkyl radicals, leads to oxygenated scission products in a similar way, but H shift in an alkylidene biradical is necessary to produce the alkene (Reaction 59):



$$(CH_3)_2\overset{\cdot}{\underset{\underset{\displaystyle O-OH}{|}}{C}}-CHCH_2CH_3 \longrightarrow [(CH_3)_2\dot{C}\cdot] + CH_3CH_2CHO + \cdot OH$$
$$[(CH_3)_2\dot{C}\cdot] \longrightarrow CH_3CH{=}CH_2$$

(59)

This isomerization is rapid,[1208] but the α-scission reaction involved is unlikely to compete effectively with β scission of C—O in α-hydroperoxyalkyl radicals. Again, scission may produce two radicals, instead of two molecules (Reaction 60). This group of reactions is energetically unfavorable and is not very important.

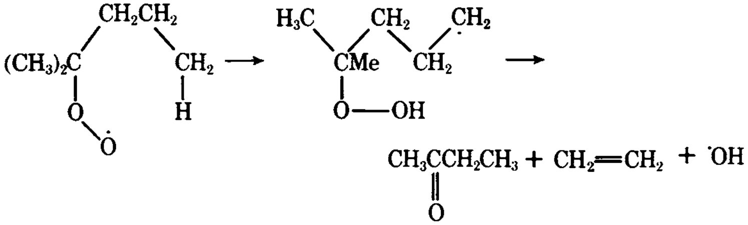


$$(CH_3)_2\dot{C}-\underset{\underset{\displaystyle HO-O}{|}}{CH}-CH_2CH_3 \longrightarrow (CH_3)_2\dot{C}CHO + CH_3CH_2\cdot + \cdot OH$$

(60)

It is unlikely that the total yields of carbonyl scission compounds formed in cool-flame combustion reactions can be explained by β scission of hydroperoxyalkyl radicals. At subatmospheric pressures, these carbonyl compounds are usually formed[222,406,407] in yields considerably greater than those of the alkenic scission products that are formed simultaneously by such β-scission reactions. Two possible alternative routes to carbonyl scission compounds are decomposition of alkoxy radicals[406,407] and decomposition of dihydroperoxy compounds. The discrepancies in yields of carbonyl and alkenic scission products may also result, in part, from attack of the π bonds of the alkenes formed by radicals (Reaction 25).

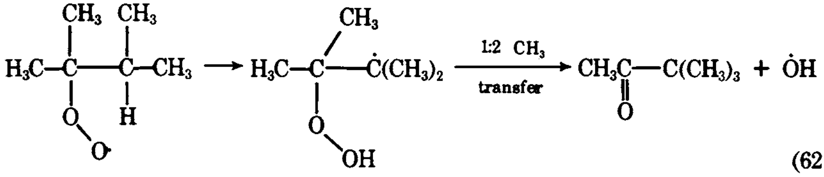
If intramolecular group transfer occurs during scission, scission products will result, one of which contains an arrangement of carbon atoms not present in the hydroperoxyalkyl radical decomposed and therefore not present in the original alkane. Group transfer accounts for the formation of butanone in the oxidation of 2-methylpentane (Reaction 61):



(61)

HOMOLYSIS OF O—O AND INTRAMOLECULAR TRANSFER OF AN ALKYL GROUP

This reaction has been postulated to account for the production, during gaseous oxidation, of carbonyl compounds with the same number of carbon atoms as the alkane molecule, but with different arrangements ofthem (e.g., pinacolone from 2,3-dimethylbutane,[1207] as in Reaction 62; 3-methyl-2-pentanone, 2-hexanone, and 3-hexanone from 2-methylpentane;[406,407] and butanone from isobutane[269]).



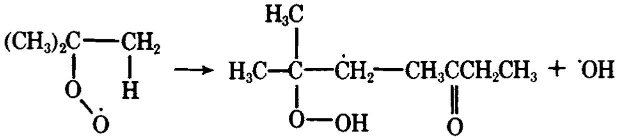
$$H_3C-\underset{\underset{O^{\cdot}}{O}}{\overset{CH_3}{C}}-\underset{H}{\overset{CH_3}{C}}-CH_3 \rightarrow H_3C-\underset{\underset{OH}{O}}{\overset{CH_3}{C}}-\dot{C}(CH_3)_2 \xrightarrow[\text{transfer}]{1{:}2\ CH_3} CH_3\underset{\underset{O}{\|}}{C}-C(CH_3)_3 + \dot{O}H$$

(62)

It has been suggested[124] that butanone arises from further reactions (Reaction 63) of acetone, which is a major product of the oxidation of isobutane.

$$CH_3COCH_3 \xrightarrow{-H\cdot} CH_3CO\dot{C}H_2 \xrightarrow{+\cdot CH_3} CH_3COCH_2CH_3 \qquad (63)$$

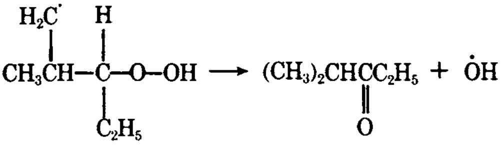
Alternatively, it can arise by 1:4 H transfer in the *tert*-butylperoxy radical followed by O—O homolysis and 1:2 methyl transfer (Reaction 64):



$$\underset{\underset{\dot{O}}{O}}{(CH_3)_2C}-\underset{H}{CH_2} \rightarrow H_3C-\underset{O-OH}{\overset{H_3C}{C}}-\dot{C}H_2-CH_3\underset{\underset{O}{\|}}{C}CH_2CH_3 + \cdot OH$$

(64)

Similar O—O homolysis reactions, accompanied by intramolecular transfer of an H atom (instead of an alkyl group), may compete with hydroperoxide decomposition in forming carbonyl compounds with the same carbon skeleton as the fuel (Reaction 65):

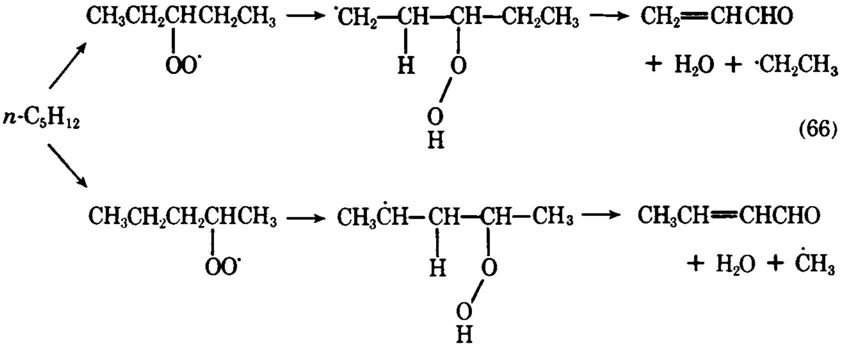


$$CH_3\overset{H_2C^{\cdot}}{CH}-\underset{C_2H_5}{\overset{H}{C}}-O-OH \rightarrow (CH_3)_2CH\underset{\underset{O}{\|}}{C}C_2H_5 + \dot{O}H$$

(65)

HOMOLYSIS OF O—O AND TWO OTHER BONDS

This mode of decomposition of hydroperoxyalkyl radicals is complex and may not occur as a single step. Nevertheless, substantial yields of unsaturated carbonyl compounds are formed in instances of combustion in which the formation of *O*-heterocycles and rearranged carbonyl compounds shows that rearrangement and decomposition of alkylperoxy radicals are important. Thus, the cool-flame oxidation of *n*-pentane yields acrolein[222,272] and crotonaldehyde,[801] with an ethyl and a methyl radical, respectively, being eliminated (Reaction 66):



(66)

Similarly, the cool-flame oxidation of 2-methylpentane[406,407] produces a variety of unsaturated carbonyl compounds, including acrolein, methacrolein, 1-buten-3-one, 2-pentenal, 1-penten-3-one, 1-penten-4-one, *trans*-2-penten-4-one, 2-methylbuten-3-one, 2-methyl-1-penten-3-one, 4-methyl-1-penten-3-one, 2-methyl-1-penten-4-one, 2-methyl-2-penten-4-one, 2-methyl-2-pentenal, and 4-methyl-2-pentenal. Again, acrolein, crotonaldehyde, and 1-buten-3-one are products of the slow low-temperature gaseous oxidation and cool flames of *n*-heptane.[1079]

It is likely, therefore, that these unsaturated carbonyl compounds arise from the hydroperoxyalkyl radicals known to be important in cool flames. Their formation from such radicals necessitates the scission of three bonds: the O—O bond, a C—H bond, and either a C—C bond or another C—H bond (Reaction 66). If we assume that the weak O—O bond breaks first, both of the other bonds broken are in position β to an atom bearing an unpaired electron; this complex reaction is another example of a β-scission process.

Oxidation of Hydroperoxyalkyl Radicals

Disubstituted products may be formed by further attack of oxygen at the free valency of a hydroperoxyalkyl radical, that is, at the position from which the H was transferred during the isomerization of the original alkylperoxy radical (Reaction 67).

$$\cdot C_nH_{2n}OOH + O_2 \longrightarrow \cdot OOC_nH_{2n}OOH \qquad (67)$$

The hydroperoxyalkylperoxy radical thus formed usually abstracts hydrogen intermolecularly (or, if a suitable hydrogen is available, intramolecularly) to form a dihydroperoxy compound (Reaction 68), whose decomposition leads to other dioxygenated products:

$$\cdot OOC_nH_{2n}OOH + RH \longrightarrow R\cdot + HOOC_nH_{2n}OOH \qquad (68)$$

One of the fullest studies of this reaction is the liquid-phase oxidation of 5-methylnonane.[46] At 90 C, attack on this hydrocarbon by oxygen and chain carriers removes tertiary hydrogen 19 times as frequently as secondary hydrogen, which, in turn, is removed 4 times as frequently as primary hydrogen. The predominant resulting alkyl radical is therefore $CH_3(CH_2)_3\dot{C}(Me)(CH_2)_3CH_3$, and the alkylperoxy radical formed by later addition of oxygen is $CH_3(CH_2)_3C(Me)(OO\cdot)(CH_2)_3CH_3$, in which there are three possible modes of transfer of secondary hydrogen (1:4, 1:5, and 1:6). Further oxidative attack at the carbon atoms from which H has been transferred will lead to three disubstituted 5-methylnonanes—4,5-, 3,5-, and 2,5-disubstituted products. The autoxidation products were reduced by lithium aluminum hydride, converting monosubstituted products into alcohols and disubstituted products (presumably dihydroperoxides) into the corresponding diols. The resulting hydroxy compounds were analyzed by gas–liquid chromatography, which showed that the ratios of diols produced were 2,5-diol:3,5-diol:4,5-diol = 8:4:1. Thus, 1:6 H transfer is the most frequent mode of rearrangement of the 5-methyl-5-nonylperoxy radical, whereas 1:5 H transfer is more frequent than 1:4 H transfer.

DIHYDROPEROXIDES

The formation of dihydroperoxides by Reactions 67 and 68 has been established both in solution and in the vapor phase.

Rust[1044] has studied the formation in solution of dihydroperoxides by autoxidation of dimethyl-substituted *n*-alkanes (2,3-dimethylpentane, 2,4-dimethylpentane, 2,5-dimethylhexane, and 2,6-dimethylheptane), and it is interesting to compare his findings with those of Arndt and his collaborators.[46] By comparing dihydroperoxide formation from these branched hydrocarbons, each of which has two tertiary hydrogen atoms, Rust showed that 1:5 H transfer was most frequent; considerable 1:6 H transfer also took place, but rearrangement by 1:4 or 1:7 H transfer was of little or no significance. The yields of 2,4-dihydroperoxy-2,4-dimethylpentane and of 2,5-dihydroperoxy-2,5-dimethylhexane from the corresponding alkanes were each about 90% of the total autoxidation product, illustrating the high efficiency of intramolecular H transfer when the hydrogen involved in the rearrangement reaction is tertiary and attached to a carbon atom that is separated by one or two atoms from the carbon atom bearing the peroxy group. The differences between the relative susceptibilities of 1:5 and 1:6 H transfer in monomethyl-substituted[46] and dimethyl-substituted[1044] hydrocarbons are believed to result from conformational differences introduced by the degree of chain branching. Dihydroperoxides (mainly formed by 1:6 H transfer) have also been produced during liquid-phase oxidation of *n*-alkanes (e.g., *n*-decane[1217]).

Paper-chromatographic techniques have been developed for the separation and identification of small amounts of organic peroxides[201] and applied to the products of the gaseous oxidation of *n*-heptane, 2,2,3-trimethylbutane, *n*-butane, propane, and cyclohexane.[202–205] The products from *n*-heptane, the fuel most extensively studied, included a dihydroperoxyheptane (in which the positions of the OOH groups were not determined) and the products of its addition and condensation reactions with aldehydes. It was also suggested that an unidentified peroxidic fraction of the products, completely nonvolatile *in vacuo* at room temperature, might contain trihydroperoxyheptane. If this is true, it is likely that its mode of formation involves two intramolecular rearrangements (Reaction 69):

$$C_7H_{17}OO\cdot \xrightarrow[\text{transfer}]{H} \cdot C_7H_{14}OOH \xrightarrow{O_2} \cdot OOC_7H_{14}OOH \xrightarrow[\text{transfer}]{H} \cdot C_7H_{13}(OOH)_2 \xrightarrow{O_2}$$

$$\cdot OOC_7H_{13}(OOH)_2 \xrightarrow{RH} C_7H_{13}(OOH)_3 \quad (69)$$

No dihydroperoxide could be detected in the products of slow combustion of propane or of 2,3,3-trimethylbutane. In the latter case, initial attack will remove the single tertiary hydrogen; rearrangement of the resulting $RO_2\cdot$ radical, $(CH_3)_3CC(OO\cdot)(CH_3)_2$, must involve primary hydrogen. Similarly, in the propane molecule, 1:5 H transfer is possible only if both initial attack and isomerization involve primary hydrogen and 1:4 H transfer only if one of these processes does. Butane yields dihydroperoxybutane only under very vigorous conditions (335–345 C; $C_4H_{10}:O_2 = 2:1$); 1:5 H transfer involves primary hydrogen once, but 1:4 H transfer involves only secondary hydrogen. The pattern of formation of dihydroperoxides from these fuels is thus consistent with the relative ease of rearrangements involving 1:3, 1:4, 1:5, and 1:6 intramolecular H transfer and with the strengths of primary, secondary, and tertiary C—H bonds.

Strong support for the formation of dihydroperoxides by a mechanism involving isomerization of alkylperoxy radicals followed by oxidation of the hydroperoxyalkyl radicals thus formed has resulted from studies of the effect of hydrogen bromide on the gaseous *n*-heptane–oxygen system.[527] In the absence of this additive, the peroxidic products are dihydroperoxides (Reaction 70); in its presence, monohydroperoxides are formed, owing to the successful competition of the reaction of alkylperoxy radicals with hydrogen bromide (which has a weak bond) with their isomerization (Reaction 71):

$$C_nH_{2n+1}OO\cdot \xrightarrow{\text{isomerization}} \cdot C_nH_{2n}OOH \xrightarrow[\text{RH}]{O_2,\ \text{then}} C_nH_{2n}(OOH)_2 \qquad (70)$$

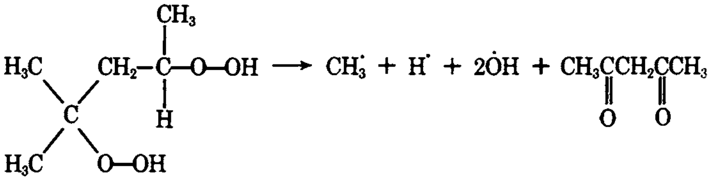
$$C_nH_{2n+1}OO\cdot + HBr \longrightarrow C_nH_{2n+1}OOH + Br\cdot \qquad (71)$$

DICARBONYL COMPOUNDS

The radical, $\cdot OOC_nH_{2n}OOH$, or the dihydroperoxide, $C_nH_{2n}(OOH)_2$, will decompose by homolytic O—O scission, producing carbonyl hydroperoxides and dicarbonyl compounds. Several early ultraviolet spectroscopic studies[353,354,1219,1220] of the preflame combustion of hydrocarbons detected a strong absorption at 2600 Å, and further work[84,85,1189] showed that this may be, in part, a result of the production of *β*-dicarbonyl compounds (e.g., CH_3COCH_2CHO from *n*-C_4H_{10} and $CH_3COCH_2COCH_3$ from *n*-C_5H_{12}), which are later consumed in the cool flame. More recent studies suggest, however, that unsaturated carbonyl compounds (e.g., 2-methyl-2-penten-4-one from 2-methylpentane) are more-important absorbing species. Nevertheless, *β*-dicarbonyl compounds are certainly formed, and yields as high as 10% (from the oxidation of *n*-pentane to pentane-2,4-dione below the cool-flame limit) have been reported. The involvement of isomerization in the mechanism of their formation is supported by the fact that none of the intermediate products of *n*-butane combustion (C_4 alkenes, butanone, crotonaldehyde, *n*-butyraldehyde, and 1-buten-3-one) yields 1-butanal-3-one on oxidation.

The tentative identification of $(CH_3)_2C(OH)CH_2COCH_2C(OOH)(CH_3)_2$ in the products of autoxidation of 2,6-dimethylheptane suggests that trihydroperoxides decompose similarly.[1044]

Dicarbonyl compounds and related species are not, however, the sole products of dihydroperoxide decomposition. Homolysis of both O—O bonds and β elimination of two hydrogen atoms or alkyl groups, leading to a dicarbonyl compound (Reaction 72), is the major fate of β- and γ-dihydroperoxides. The easiest mode of decomposition of α-dihydroperoxides, however, is homolysis to two hydroxyl radicals and two monocarbonyl scission products (Reaction 73):



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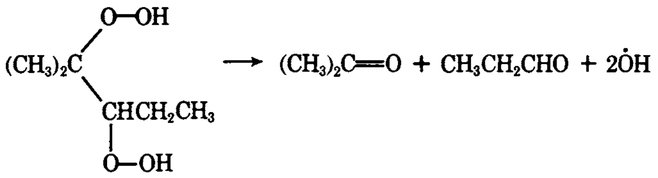


(73)

Chain Cycles

The formation, isomerization, and later decomposition or further oxidation of alkylperoxy radicals provide chain-propagation mechanisms that are important during the oxidation of hydrocarbons, particularly in the cool-flame and low-temperature two-stage ignition regions of gaseous systems. The basic chain cycle involved is shown in the sequence of Reactions 75–77.

$$C_nH\cdot_{2n+1} + O_2 \longrightarrow C_nH_{2n+1}OO\cdot \qquad (74)$$

$$C_nH_{2n+1}OO\cdot \xrightarrow{\text{isomerization}} \cdot C_nH_{2n}OOH \qquad (75)$$

$$\cdot C_nH_{2n}OOH \xrightarrow{\text{decomposition}} \text{products} + X\cdot \qquad (76)$$

$$X\cdot + C_nH_{2n+2} \longrightarrow XH + C_nH\cdot_{2n+1} \qquad (77)$$

X· is the radical produced by decomposition of hydroperoxyalkyl radicals. This radical X· can be ·OH (from cyclization and other modes of decomposition of $\cdot C_nH_{2n}OOH$ in which O—O is ruptured), $HO_2\cdot$ (from β scission of C—O in α-$\cdot C_nH_{2n}OOH$ radicals), or an alkyl radical or hydrogen atom (from complex decomposition reactions of $\cdot C_nH_{2n}OOH$, whose stable products are unsaturated carbonyl compounds). The relative yields of *O*-heterocycles and carbonyl scission products, alkenes, and unsaturated carbonyl compounds provide an approximate measure of the relative extents of formation of the radicals that accompany them: ·OH, $HO_2\cdot$, and R·, respectively. It has thus been shown [406,407] that ·OH is formed most frequently by far. In regimes in which isomerization and later decomposition is an important fate of alkylperoxy radicals, the hydroxyl radical is the predominant entity that attacks the alkane, to regenerate an alkyl radical (Reaction 78):

$$\cdot OH + C_nH_{2n+2} \longrightarrow H_2O + C_nH_{2n+1}^{\cdot} \qquad (78)$$

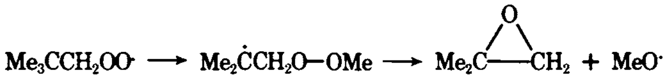
The activation energy for attack of an alkane by ·OH, although difficult to determine accurately,[491,575] is low [101] (1–2 kcal/mol). This has an important consequence. The reaction will be unselective, being almost insensitive to C—H bond strength (cf. the attack of alkanes by chlorine atoms[701,984]); every alkyl radical derived from the alkane skeleton will therefore be formed. To describe in detail the chain-propagation steps under conditions in which isomerization is a frequent fate of alkylperoxy radicals, it is necessary to consider every alkylperoxy radical derived from the alkane, not just the tertiary radicals.

If a substantial proportion of the hydroperoxyalkyl radicals formed by isomerization are oxidized, the position is more complicated. Hydroperoxyalkylperoxy radicals will also be potential abstracters of hydrogen from an alkane, giving dihydroperoxides (Reaction 79).

$$\cdot OOC_nH_{2n}OOH + C_nH_{2n+2} \longrightarrow HOOC_nH_{2n}OOH + C_nH_{2n+1}^{\cdot} \qquad (79)$$

Kinetically, Reaction 79 will resemble the abstraction of hydrogen from an alkane by an alkylperoxy radical (Reaction 2), the preexponential factor of Reaction 79 being somewhat lower because of the greater bulk of the radical reactant. This reaction is therefore much more selective than attack by ·OH, tertiary C—H bonds being attacked preferentially.

A further complication is involved if isomerization of alkylperoxy radicals by group transfer competes with that by H transfer, although this is rarely important. Decomposition reactions of alkylperoxyalkyl radicals, analogous to those of hydroperoxyalkyl radicals in which $\cdot OH$ is eliminated, will give $\cdot OR$ as the radical product (Reaction 80),[1359] whereas the analogue of β scission of C—O in hydroperoxyalkyl radicals will produce $RO_2\cdot$ (Reaction 81).[1360]



(80)

$$Me_2CHCH_2OO^\bullet \longrightarrow Me\dot{C}HCH_2{-}OOMe \longrightarrow MeCH_2{=}CH_2 + MeO_2^\bullet \qquad (81)$$

The attack of a hydrocarbon by an alkoxy radical has an activation energy of 3–11 kcal/mol, depending on the structure of the alkane.[102,104,1105] It is therefore more selective than that by a hydroxyl radical, but less selective than that by an alkylperoxy or hydroperoxyalkylperoxy radical.

The proportions of the various alkyl radicals that are formed during alkane oxidation are therefore sensitive to the nature of the attacking entity. The predominance of $\cdot OH$ (when alkylperoxy radical isomerization is important) ensures, however, that all these will participate. It is possible to write a qualitative chain-propagation scheme for the oxidation of a hydrocarbon by this mechanism. Because the products of oxidation are formed largely by propagation steps (branching being infrequent in degenerately branched reactions, such as the oxidation of alkanes), this scheme should account for the products found experimentally. For 2-methylpentane and *n*-pentane, it has been shown that the agreement between theory and experiment is good.[272,406,407]

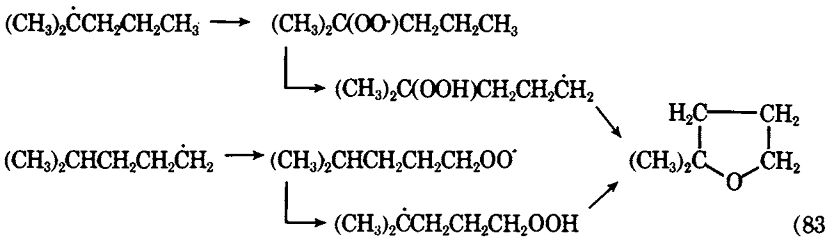
COMPETITION CYCLIZATION: THE RELATIVE YIELDS OF *O*-HETEROCYCLE

The estimated equilibrium constants of 1:4, 1:5, 1:6, and 1:7 H transfer in alkylperoxy radicals and the rates of cyclization of hydroperoxyalkyl radicals to give *O*-heterocycles enable the relative yields of the *O*-heterocycles derived from the carbon skeleton of the alkane to be calculated and compared with experimental results.

In the oxidation of 2-methylpentane, for example, the chain-propagation cycle that produces a C_6 *O*-heterocycle is Reaction 82.

$$C_6H_{14} + {}^\bullet OH \longrightarrow C_6H_{13}^\bullet \xrightleftharpoons{O_2} C_6H_{13}OO^\bullet \rightleftharpoons {}^\bullet C_6H_{12}OOH \longrightarrow C_6H_{12}O + {}^\bullet OH \qquad (82)$$

Five species of $C_6H_{13}\cdot$, five of $C_6H_{13}OO\cdot$, 21 of $\cdot C_6H_{12}OOH$, and 11 of $C_6H_{12}O$ *O*-heterocycles are involved. Each *O*-heterocycle (except 3-*n*-propyloxetane) is formed by two routes (Reaction 83):



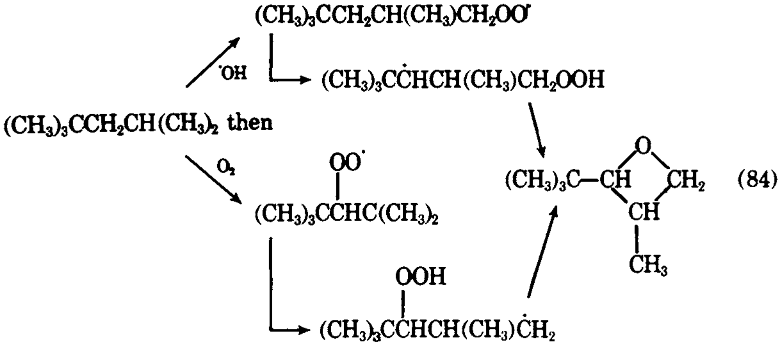
(83)

At high pressures in half-stoichiometric mixtures of 2-methylpentane with air, the presence of substantial amounts of 3-methyltetrahydropyran is also in agreement with the theory. At low pressures in RH:$2O_2$ mixtures, the absence of 3-methyltetrahydropyran is surprising, however; it appears that, under these conditions, δ-hydroperoxyalkyl radicals may decompose predominantly by homolysis of O—O and C—C, accompanied by methyl transfer to produce *n*-butyraldehyde and ethylene.[406,407] The amounts of 2,2,4-trimethyloxetane are also higher than those predicted theoretically.

The simple theory predicts that the concentration of C_6 oxiranes (notably 2,2-dimethyl-3-ethyloxirane, 2-methyl-2-*n*-propyloxirane, and 2-methyl-3-isopropyloxirane) will be lower than those found experimentally at both high and low pressures. This is readily explicable, however: Oxiranes may arise from the addition of $RO_2\cdot$ to alkenes followed by β scission of C—O and by the analogous addition of $HO_2\cdot$. But the latter reaction is not very important during the oxidation of large alkane molecules.[403,406,407]

In the oxidation of isooctane,[812,1045] the major *O*-heterocyclic products are 2,2,4,4-tetramethyltetrahydrofuran and 2-*tert*-butyl-3-methyloxetane; the absence of 2-isopropyl-3,3-dimethyloxetane suggests that the 2,2,4-trimethyl-5-pentylperoxy radical (not the 2,2,4-trimethyl-3-pentylperoxy radical) is the precursor of 2-*tert*-butyl-3-methyloxetane. This is in agreement with the theory; formation of the oxetane from the 5-alkylperoxy radical should theoretically be 25 times as fast as from the 3-alkylperoxy radical.

In general, it follows that, if the two routes to an *O*-heterocycle involve (1) abstraction by ·OH of a primary hydrogen followed by intramolecular transfer of a secondary or tertiary hydrogen and (2) abstraction by ·OH of a secondary or tertiary hydrogen followed by intramolecular transfer of a primary hydrogen (Reaction 84), then the former reaction is the faster:

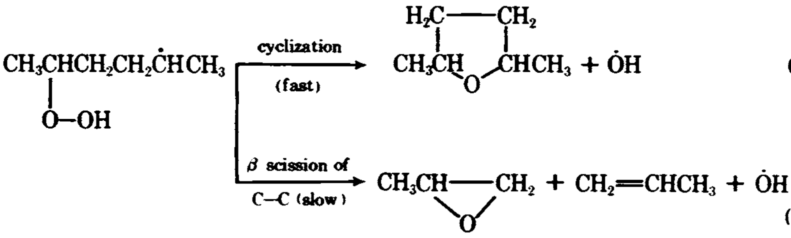


(84)

In other words, a high proportion of *O*-heterocycles results from primary alkylperoxy radicals; this is a reflection of the unselectivity of attack of a hydrocarbon by ·OH. This suggests that the formation of 2,2-dimethyltetrahydrofuran from 2-methylpentane occurs via the 2-methyl-5-pentylperoxy radical and that the formation of 2-methyloxetane from *n*-butane,[106] 2-methyltetrahydrofuran from *n*-pentane,[222,1219,1220] and 2-methyltetrahydropyran from *n*-hexane[65] results primarily from the isomerization of primary alkylperoxy radicals. The formation of oxetanes from *n*-pentane[408] and isobutane[1360] must, of course, involve primary radicals.

COMPETITION BETWEEN CYCLIZATION AND β SCISSION

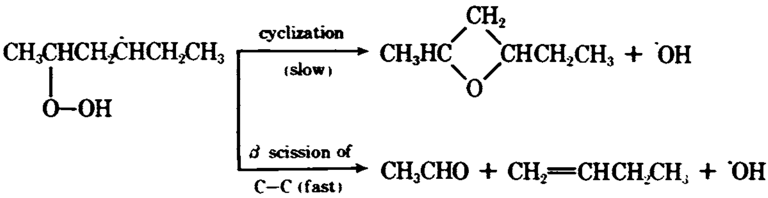
The competition between cyclization and scission reactions depends on the structure of the decomposing hydroperoxyalkyl radical. Both γ- and δ-hydroperoxyalkyl radicals cyclize rapidly, producing derivatives of tetrahydrofuran and tetrahydropyran. In the β scission of C—C in such radicals, small-ring *O*-heterocycles (oxiranes from γ radicals, oxetanes from δ radicals) are formed. In the β-scission reaction, the strain energy that must be overcome is greater than that in the cyclization reactions, with the result that cyclization is the faster reaction (85):



(85a)

(85b)

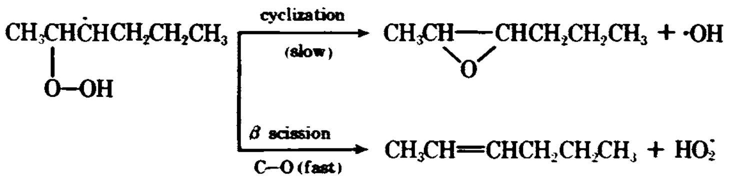
The cyclization of β-hydroperoxyalkyl radicals is slower than that of γ radicals, because oxetanes are forming. However, β scission of C—C gives carbonyl compounds (not *O*-heterocycles) plus alkenes; in this scission reaction, no strain energy is involved. In this case, the β scission is likely to be the faster reaction (86):



(86a)

(86b)

Similarly, the cyclization of α-hydroperoxyalkyl radicals, which produces oxiranes, is slow. In these radicals, β scission of C—O, not C—C, occurs, producing alkenes conjugate with the original alkane and $HO_2\cdot$ radicals. Again, because no strain energy is involved in β scission, this is the faster reaction (87):



(87a)

(87b)

COMPETITION BETWEEN DECOMPOSITION AND OXIDATION

Further oxidation of hydroperoxyalkyl radicals is analogous to the addition of oxygen to alkyl radicals. The activation energy of the reaction is zero.[96,220] Transition-state theory suggests that, at 550 K, the preexponential factor is about 10^{-13} cm^3/molecule-sec for large alkyl radicals; this result compares with the experimental value of $10^{-12.8}$ cm^3/molecule-sec for propyl and butyl radicals.[700] The constant for addition is therefore approximately 10^{-13} cm^3/molecule-sec. When the partial pressure of oxygen is 200 torr, then $k_{\mathrm{addition}}\,[O_2] = 10^{5.5}$/sec, which compares with the rough values for $k_{\mathrm{decomposition}}$ of $10^{5.5}$/sec, $10^{5.9}$/sec, 10^{11}/sec, $10^{3.5}$/sec, and $10^{7.8}$/sec for the formation of oxiranes, oxetanes, tetrahydrofurans, and tetrahydropyrans, conjugate alkenes, and carbonyl scission products, respectively.

Although these values are only very approximate, oxidation probably competes effectively with the formation of conjugate alkenes, oxiranes, and oxetanes, but not with that of tetrahydrofurans, tetrahydropyrans, and carbonyl scission products. It is, therefore, α-hydroperoxyalkyl radicals (and, to a small extent, β-hydroperoxyalkyl radicals) that will add to oxygen; γ- and δ-hydroperoxyalkyl radicals will decompose preferentially.

The addition of oxygen to α-hydroperoxyalkyl radicals gives α-hydroperoxyalkylperoxy radicals, which can abstract hydrogen intermolecularly or intramolecularly to produce α-dihydroperoxides or dihydroperoxyalkyl radicals. α-Dihydroperoxides will decompose by homolysis of both O—O bonds and β scission of the bond joining the two peroxidized carbon atoms (Reaction 73). This reaction may be capable of explaining the discrepancy in the yields of carbonyl scission products and alkenic scission products from oxidation reactions in regimes where alkylperoxy radical rearrangement is responsible for chain propagation. Decomposition of β-hydroxyalkyl radicals by scission of O—O and C—C bonds accounts qualitatively for the formation of these two types of scission product, but the two members of each alkene—carbonyl "pair" should be formed in equimolar yields if this is their sole mode of formation. In practice,[272,406,407] the yields of carbonyl scission products considerably exceed those of alkenic scission products. The decomposition of α-dihydroperoxides to give two carbonyl scission products and no alkenes affords a possible explanation for the relatively high yields of the former.[406,407] A further reaction contributing to the formation of carbonyl scission products is, however, decomposition of alkoxy radicals produced by O—O homolysis in monohydroperoxides.[272]

The addition of oxygen to β-hydroperoxyalkyl radicals will produce, eventually, β-dihydroperoxides. In these compounds, there is no C—C bond in the β position to both O—O bonds; their decomposition will probably lead, therefore, to dicarbonyl compounds (Reaction 72).

β-Dicarbonyl compounds are, indeed, formed in the low-temperature gaseous oxidations of *n*-butane and *n*-pentane.

IMPORTANCE OF OTHER REACTIONS

It is prohibitively difficult to estimate the rates of complex modes of reaction of hydroperoxyalkyl radicals, such as O—O scission with group transfer, C—C and O—O scission with group transfer, and scission to unsaturated carbonyl compounds. The formation, in considerable yields, of products diagnostic of these reactions during the gaseous oxidation of alkanes shows, however, that they compete well with the simpler modes of decomposition discussed above.

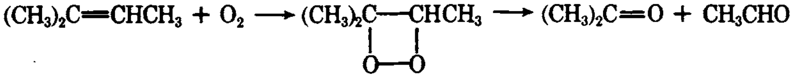
A further competitive reaction that must be considered is the "reverse isomerization" of a hydroperoxyalkyl radical to an alkylperoxy radical. The reverse isomerization of γ- and δ-hydroperoxyalkyl radicals is slow, compared with their decomposition to *O*-heterocycles, but reverse isomerization of α- and β-hydroperoxyalkyl radicals competes well with the fastest modes of their further reaction (decomposition or oxidation). Nevertheless, at the high temperatures characteristic of vapor-phase oxidation (internal combustion, for example), rearrangement of alkylperoxy radicals to give α- and β-hydroperoxyalkyl radicals is a viable mode of chain propagation, inasmuch as when such a hydroperoxyalkyl radical has isomerized back to an alkylperoxy radical, the likely fate of that radical is to isomerize again! Both γ- and δ-hydroperoxyalkyl radicals probably react directly to give stable or moderately stable products, and α- and β-hydroperoxyalkyl radicals eventually do so.

Related Reactions during Oxidation

Rearrangement reactions of alkylperoxy radicals containing a variety of substituent groups [e.g., HO—, R_2N—, O=C, and —O—C (=O)—] are important during the oxidation reactions of substituted alkanes.

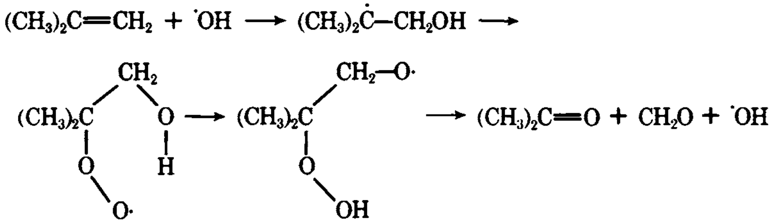
OXIDATION OF ALKENES

The low-temperature gaseous oxidation of alkenes is, in general, propagated by abstraction of hydrogen attached to an allylic carbon atom to give an allylic radical.[1121] A competing reaction, however, involves addition of oxygen or oxygenated radicals to the double bond to give, eventually, carbonyl scission products. This reaction is favored, and can predominate, in alkenes of which the hydrogen atoms on each allylic carbon are exclusively primary. During the early stages of the gaseous oxidation of 2-methyl-2-butene,[270,271] for example, large and equal yields of acetone and acetaldehyde are formed. Similarly, in the gaseous oxidation of isobutene,[1122] acetone and formaldehyde are formed in equimolar quantities. It has been proposed[270,271] that these scission products could arise from direct addition of oxygen to the double bond, cyclization, and breakdown of the moloxide formed (Reaction 88):



$$(CH_3)_2C{=}CHCH_3 + O_2 \longrightarrow (CH_3)_2C\!-\!CHCH_3 \longrightarrow (CH_3)_2C{=}O + CH_3CHO \quad (88)$$

This nonradical reaction seems rather unlikely, however. A more probable route[1122] is the addition of a hydroxyl radical to the double bond to form a hydroxyalkyl radical, followed by addition of oxygen to this. Isomerization by 1:5 H transfer of the hydroxyalkylperoxy radical thus formed will give a substituted alkoxy radical that can decompose by β scission, forming equimolar quantities of the two carbonyl scission products and regenerating a hydroxyl radical (Reaction 89):



$$(CH_3)_2C{=}CH_2 + {}^{\cdot}OH \longrightarrow (CH_3)_2\dot{C}{-}CH_2OH \longrightarrow$$

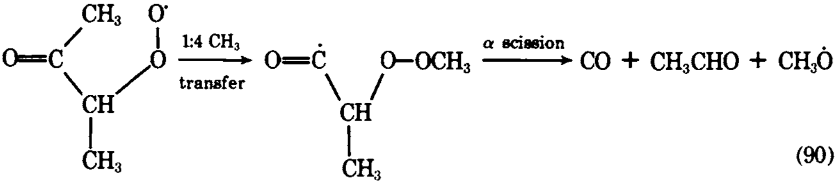
$$\longrightarrow (CH_3)_2C{=}O + CH_2O + {}^{\cdot}OH \quad (89)$$

The isomerization and decomposition of a hydroxyalkylperoxy radical therefore appear to be responsible for propagation of the primary chain during the gaseous oxidation of some alkenes, in a way analogous to that in which intramolecular reactions of unsubstituted alkylperoxy radicals propagate chains during the oxidation of alkanes.

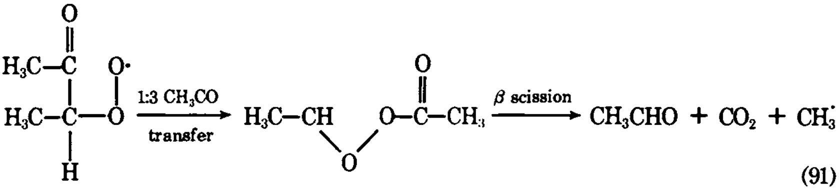
The formation of minor products (butanone, propionaldehyde, isopropyl alcohol, and *tert*-butyl alcohol) of the slow combustion of 2-methyl-2-butene, labeled in specific skeletal positions with carbon-14, has been described in terms of the isomerization reactions of peroxy biradicals formed by direct addition of oxygen to the double bond of the fuel.[270,271] The formation of the two alcohols can be explained on the basis of the mechanism involving addition of · OH followed by addition of oxygen, which accounts so well for the major carbonyl scission products.

OXIDATION OF KETONES

In the gaseous oxidation of ketones, scission reactions predominate, producing lower aldehydes and oxides of carbon.[77–80] From butanone, for example, acetaldehyde, carbon monoxide, and carbon dioxide are important products.[78] It is likely that these are formed from ketonylperoxy radicals by intramolecular group transfer and decomposition of the substituted alkylperoxyalkyl radical thus formed (Reactions 90 and 91):



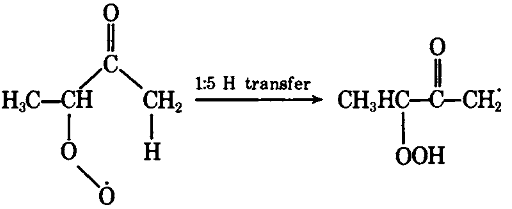
(90)



(91)

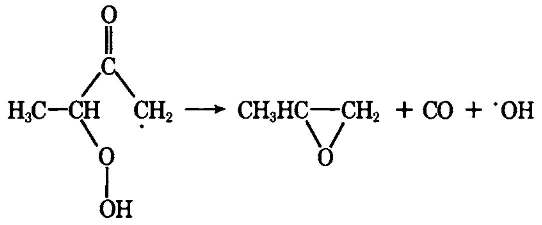
Similarly, acetone gives formaldehyde and oxides of carbon. The variation of the relative yields of carbon monoxide and carbon dioxide with temperature is interesting. Carbon dioxide decreases in importance as the temperature is raised;[79,80] comparison of the isomerization reactions involved suggests that the opposite should be true (1:3 CH_3CO transfer will have a higher activation energy than 1:4 CH_3 transfer), but comparison of the decomposition reaction leads to a result in agreement with experiment (β scission is easier than α scission). The results suggest that the mode of decomposition of the substituted alkylperoxyalkyl radical is the rate-controlling step.

If group transfer in ketonylperoxy radicals is important, the energetically favored H-transfer reaction should also occur (Reaction 92).



(92)

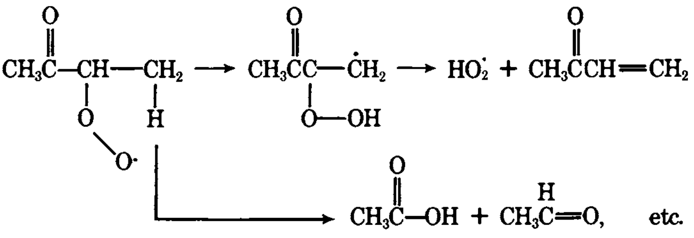
Cyclization of the radical thus formed, with elimination of OH, will be more difficult than that of the corresponding unsubstituted hydroperoxyalkyl radical, $CH_3CH(OOH)(CH_2CH_2\cdot)$, because the carbonyl oxygen and the three carbon atoms that are potential members of the ring are constrained in a planar configuration by the carbonyl π bond. It is perhaps not surprising that carbonyl-substituted *O*-heterocycles have not been formed in the products of the oxidation of ketones. If the carbonyl group can be "ejected" from the substituted hydroperoxyalkyl radical during ring closure, however, this constraint no longer applies, and substituted *O*-heterocycles should result (Reaction 93).



(93)

These *O*-heterocycles have, indeed, been formed among the products of ketone oxidation reactions (e.g., 2-ethyloxirane from 3-pentanone, methyloxirane from butanone, and oxirane from acetone), and their formation has been interpreted in this way.[78]

A further possible mode of isomerization of ketonylperoxy radicals is transfer of a hydrogen atom from a carbon atom on the same side of the carbonyl group as is the peroxy group. Decomposition by β scission of C—O of the resulting substituted hydroperoxyalkyl radical would result in a conjugated unsaturated ketone (Reaction 94a).



(94a)

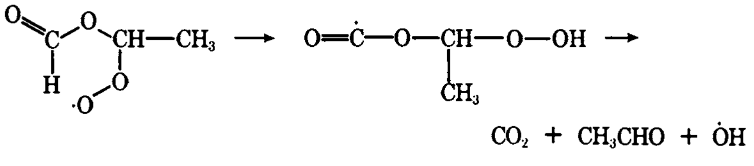
(94b)

1-Buten-3-one has, indeed, been found among the oxidation products of butanone.[78] Another mode of decomposition of α-ketohydroperoxides is cleavage to carbonyls and carboxylic acids (Reaction 94b).

The ease with which isomerization of ketonylperoxy radicals can occur is a function of the molecular structure of the ketone, just as that of alkylperoxy radicals is a function of alkane structure. The fact that 2,2-dimethylbutan-3-one gives no cool flame at subatmospheric pressures, suggests that the peroxy radicals derived from it cannot isomerize in the way characteristic of the radicals derived from acetone, butanone, 3-pentanone, and 3-methyl-2-butanone (each of which gives cool flames).[576] If, as discussed above, the two important modes of H transfer in ketonylperoxy radicals are 1:4 H transfer between atoms on the same side of the carbonyl group and 1:5 H transfer between atoms on opposite sides, then the absence of cool flames from the oxidation of 2,2-dimethylbutan-3-one is explicable, in that neither $\cdot OOCH_2C(CH_3)_2COCH_3$ nor $(CH_3)_3CCOCH_2OO\cdot$ can react in this way. It is difficult to see, however, why 1:6 H transfer in these radicals does not lead to cool flames, inasmuch as 1:5 transfer of primary hydrogen is capable of so doing during the oxidation of acetone. The probable explanation is that, because of the π bond, the C—C(=O)—C bond angle is 120°; that is, it is considerably higher than the $C—C(H_2)—C$ bond angle. In short, 1:6 H transfer is much more difficult in ketonylperoxy radicals than in alkylperoxy radicals.

OXIDATION OF ESTERS

During the oxidation of formates, 1:5 intramolecular H transfer in substituted alkylperoxy radicals is of major importance.[410] It is followed by β scission of a C—O bond (as well as the usual homolysis of the O—O bond) of the substituted hydroperoxyalkyl radical formed to give an aldehyde, carbon dioxide, and ·OH (Reaction 95).


(95)

In the oxidation of ethylformate, acetaldehyde is the sole nonperoxidic organic product at temperatures below 250 C. The oxidation reactions of esters of higher organic acids (acetates, propionates, etc.) do not exhibit an analogous temperature region, possibly because in these cases H transfer must involve a ring of at least seven members. The formation of cyclic transition states in these radicals is more difficult than that in the corresponding unsubstituted alkylperoxy radicals, given the constraint of planarity imposed on three ring members by the π bond.

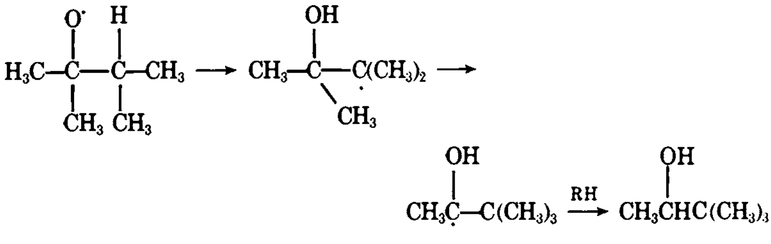
At somewhat higher temperatures (about 300 C), however, a wider variety of substituted alkylperoxy radicals derived from esters can isomerize. Again, the ability of esters to give cool flames has been explained in terms of this reaction.[576] At low pressures, ethylformate, ethylacetate, ethylpropionate, *n*-propylformate, *n*-propylacetate, isopropylacetate, and methyl-*n*-butyrate produce cool flames or associated phenomena, but methylformate, methylacetate, methylpropionate, and *tert*-butylacetate do not. It appears that 1:6 or 1:7 transfer of primary hydrogen occurs too slowly at these temperatures to lead to cool-flame reaction, but that 1:6 transfer of secondary hydrogen or 1:5 or 1:4 transfer of any hydrogen is sufficiently rapid to do so. The rates of these processes are, again, affected by steric constraints associated with the π bond.

These characteristics of the oxidation of ketones and esters show that two H-bearing centers are necessary for the formation of cool flames and therefore strongly support the argument that an isomerization reaction is an important chain-propagating step in this regime.

REARRANGEMENT OF ALKOXY RADICALS

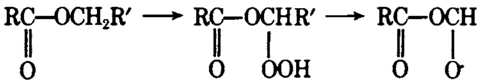
Direct decomposition to a carbonyl compound and an alkyl radical is generally the predominant mode of reaction of the alkoxy radicals formed during gaseous oxidation; intermolecular H abstraction (forming an alcohol) is also of considerable importance. Rearrangement reactions, by migration of an atom or group to oxygen, play only a minor role and have not been studied as fully as the corresponding reactions of alkylperoxy radicals.

In the vapor phase, RO· rearrangement involving 1:3 H transfer and 2:1 methyl transfer has been suggested to be responsible for the formation of pinacolyl alcohol during the slow combustion of 2,3-dimethylbutane (Reaction 96):



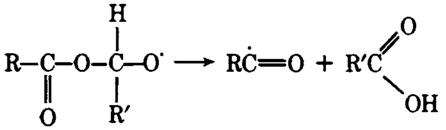
$$H_3C{-}C(O^{\cdot})(CH_3){-}CH(CH_3){-}CH_3 \longrightarrow CH_3{-}C(OH)(CH_3){-}\dot{C}(CH_3)_2 \longrightarrow CH_3\dot{C}(OH){-}C(CH_3)_3 \xrightarrow{RH} CH_3CH(OH)C(CH_3)_3 \quad (96)$$

Several modes of H transfer in and skeletal scission of alkoxy radicals play a major part in the oxidation of esters.[409,410] In the substituted alkoxy radical derived from an ester by the normal hydroperoxide chain mechanism and hydroperoxide decomposition (Reaction 97),

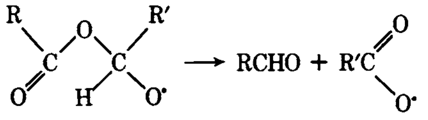


$$\underset{\underset{\displaystyle O}{\|}}{\mathrm{RC}}\mathrm{-OCH_2R'} \longrightarrow \underset{\underset{\displaystyle O}{\|}}{\mathrm{RC}}\mathrm{-}\underset{\underset{\displaystyle OOH}{|}}{\mathrm{OCH}}\mathrm{R'} \longrightarrow \underset{\underset{\displaystyle O}{\|}}{\mathrm{RC}}\mathrm{-}\underset{\underset{\displaystyle O^{\cdot}}{|}}{\mathrm{OCH}}\mathrm{R'} \qquad (97)$$

the presence of an ether linkage appears to affect the balance of competing decomposition and abstraction reactions, compared with those of unsubstituted alkoxy radicals derived from alkanes. Thus, although direct scission to a carbonyl compound, R'CHO, by detachment of the largest group, RC(=O)O—,[990] is still important, abstraction of hydrogen from a further substrate molecule to give RC(=O)OCH(OH)R' is negligible, and no alcohol is formed. Two modes of isomerization by H transfer and scission of an ether C—O bond also occur: 1:2 transfer of H from C to O (Reaction 98) gives an acid and an acyl radical; 1:3 transfer of H from C to C (Reaction 99) gives an aldehyde and an acyloxy radical.



(98)



(99)

These reactions explain qualitatively the pattern of product formation, its variation with temperature, and the effects of ester structure (i.e., the identities of R and R') on the course of oxidation.[410]

Alkoxy biradicals, formed by the addition of oxygen atoms to the π bonds of alkenes, are short-lived species that cyclize to give epoxides and isomerize by H transfer or group transfer to give carbonyl compounds.[122,273–275,634,650,1064,1065] The transfer of hydrogen atoms is entirely intramolecular; that of alkyl groups occurs by both intermolecular and intramolecular mechanisms. The epoxides and carbonyl compounds have excess vibrational energy on formation and decompose, unless deactivated by collision. From each nonaromatic alkene studied, all possible products are formed. A particularly striking example of biradical rearrangement is the production of carbonyl compounds from a cyclic alkene, which involves a reduction in ring size.

Variation of the Rate of Hydrocarbon Oxidation with Temperature

One of the most striking features of the gaseous oxidation of hydrocarbons and their derivatives is the complicated dependence of the rate on temperature. Rate–temperature curves for the slow combustion of a wide range of fuels show marked regions of "negative temperature coefficient," and this phenomenon of decrease in rate with increase in temperature is also reflected in the ignition limits of the fuels. Plots of ignition temperature against pressure for given mixtures of a hydrocarbon with air or oxygen show a low-temperature region, associated with the occurrence of "cool flames," and a high-temperature region. The former region shows "fine structure." Several maximal and minimal values of the pressure necessary for cool flames, or for ignition, occur as the temperature is raised; the number of these "lobes" is a sensitive function of the molecular structure of the fuel.[405,1272]

To explain these phenomena, it is necessary that repeated fluctuations of the net branching factor of the chain reaction occur as temperature increases. The most ready explanation is that the nature of the degenerate branching reaction (or of the reaction producing the branching agent) changes repeatedly with temperature.

At low temperatures, below those at which cool flames and spontaneous ignition occur (<250 C), it is commonly held that homolysis of alkyl hydroperoxides (Reaction 100) is responsible for degenerate branching, as in the liquid phase; at high temperatures, above those at which cool flames occur (>400 C), it is probable that homolysis of hydrogen peroxide fills a similar role (Reaction 101):

$$\mathrm{ROOH} \longrightarrow \mathrm{RO}\cdot + \cdot\mathrm{OH} \qquad (100)$$

$$\mathrm{HOOH} + \mathrm{M} \longrightarrow 2\cdot\mathrm{OH} + \mathrm{M} \qquad (101)$$

At the intermediate temperatures characteristic of cool flames, analysis of the products of the gaseous oxidation of many hydrocarbons has shown conclusively that alkylperoxy radical isomerization is the most important mode of chain propagation. Because this propagation process is unselective, these products include many species (e.g., aldehydes and *O*-heterocycles) with labile hydrogen atoms. Further reaction of these species with oxygen (Reaction 102) or with alkylperoxy radicals (Reaction 103) can lead to branching.

$$\mathrm{AH} + \mathrm{O_2} \longrightarrow \mathrm{A}\cdot + \mathrm{HO_2^{\cdot}} \qquad (102)$$

$$\mathrm{AH} + \mathrm{RO_2^{\cdot}} \longrightarrow \mathrm{A}\cdot + \mathrm{ROOH} \quad \mathrm{ROOH} \longrightarrow \mathrm{RO}\cdot + \cdot\mathrm{OH} \qquad (103)$$

Alkylperoxy radical isomerization therefore produces a variety of branching agents; it is very likely, indeed, that this process is responsible for the formation of cool flames and for the complex fine structure of the low-temperature ignition regime of hydrocarbon oxidation.

It has been proposed that a given mode of intramolecular H transfer in alkylperoxy radicals is responsible for a given lobe in the pressure–temperature locus of the ignition limit.[405,1272] These descriptions must be indirect, however, because it is the branching reaction, not the propagation reactions, that determines the "kinetic balance" of the reacting mixture and hence the limiting conditions for nonisothermal behavior. Moreover, there are no sharp changes in product distributions at the lobe boundaries, as there would be if a given mode of isomerization were exclusive to a given lobe.[406–408]

Aldehyde–Hydrocarbon Reactions

Photodecomposition of aldehydes can also result in free radicals (Reactions 104–106).

$$\mathrm{RCHO} + h\nu \longrightarrow \mathrm{RCHO}^* \qquad (104)$$

$$\mathrm{RCHO}^* \longrightarrow \mathrm{R}^\cdot + \cdot\mathrm{CHO} \qquad (105)$$

$$\mathrm{RCHO}^* \longrightarrow \mathrm{RH} + \mathrm{CO} \qquad (106)$$

This mechanism was explored by Altshuller and co-workers[26] in the photooxidation of propionaldehyde and by Johnston and Heicklen[648] with acetaldehyde. The alkyl and formyl radicals will either react with oxygen to produce peroxyalkyl and peroxyformyl radicals or, as is much less probable, react with olefins and aromatics directly. If the alkyl or formyl radicals react first with molecular oxygen, the resulting peroxyformyl and peroxyalkyl radicals can react with an olefin or aromatic hydrocarbon (Hc) (Reactions 107–109).

$$\mathrm{RO}_2^\cdot + \mathrm{Hc} \longrightarrow \mathrm{RO_2Hc}\cdot \qquad (107)$$

$$\mathrm{RO_2Hc} \longrightarrow \mathrm{HcO}\cdot + \mathrm{RO}\cdot \qquad (108)$$

$$\mathrm{RO_2Hc}\cdot \longrightarrow \mathrm{RO_2H} + \mathrm{R}\cdot \qquad (109)$$

In either case, a chain-propagating step(s) is occurring, and the photodecomposition of aldehydes should facilitate the reaction of hydrocarbons. Some of the reactions of methyl and methoxy, as well as ethoxy, radicals have been discussed.[307,524]

Altshuller and co-workers[25] showed that aliphatic aldehydes, when photooxidized in air with radiation of 3400 Å or lower, will produce intermediate species that react with olefinic and aromatic hydrocarbons. These reactions, even at low concentrations, proceed at significant rates in the absence of nitrogen oxides. These reactions were investigated with both sunlight fluorescent lamps (Σ_{max} = 3100 Å) and natural sunlight; data are shown in Tables 3-4 and 3-5. Although conversions of aldehyde and olefin mixtures in natural sunlight are low, the amounts consumed are significant. Comparisons of the rates of reaction of olefins under these conditions with those involving oxides of nitrogen are difficult. The rate of reaction of ethylene is approximately 10 times higher in the presence of nitrogen oxides than its rate of reaction with aldehydes. This comparison was made under the most favorable conditions of hydrocarbon:nitrogen dioxide ratio and with natural sunlight.

Ketone–Hydrocarbon Reactions

Another group of oxygenates, the aliphatic ketones, also contribute to the reaction of hydrocarbons. The primary quantum yield for the photodissociation of acetone at 3130 Å has been reported as 0.9. Acetone dissociates as shown in Reaction 110, where $\Phi_{II}/(\Phi_I + \Phi_{II}) = 0.07$ at 3130 Å and ambient temperature.

$$\begin{aligned} CH_3COCH_3 + h\nu &\longrightarrow CH_3\dot{C}O + \dot{C}H_3 \quad [I] \\ &\longrightarrow 2\dot{C}H_3 + CO \quad [II] \end{aligned} \tag{110}$$

Acetone and diethylketone have been irradiated in the presence of 2-methyl-1-butene and sunlight fluorescent lamps for periods ranging from 1 to 3 hr.[986] Table 3-6 shows the rates of reaction of the olefin and the products resulting from such an irradiation.

Synergistic Effects in the Photooxidation of Organic Substances

A synergistic effect is one in which the reactivity or the amount of product produced by a given compound is unpredictably affected by the presence of a second. Some indications of this effect were observed in 1964 with the photooxidation of ethylene.[923] When ethylene was irradiated in the presence of oxygenates and some aromatics, more formaldehyde was produced. This occurred not because more formalde-

TABLE 3-4 Photooxidation of Aldehyde–Hydrocarbon Mixtures in Air by Sunlight Fluorescent Lamps

Aldehyde and Hydrocarbon	Initial Concentration, ppm (vol)	Fraction Reacted with Irradiation, % in 1 hr	in 2 hr	in 3 hr	Other Products Identified
Formaldehyde	13	66	70	79	Methylethylketone
2-Methylbutene-1	10	11	23	33	
Formaldehyde	30	57	71	74	—
2,3-Dimethylbutene-2	10	29	54	74	
Formaldehyde	10	50	62	71	—
1,3,5-Trimethylbenzene	10	8	20	29	
Acetaldehyde	32	33	61	74	—
2-Methylbutene-1	10	5	20	38	
Propionaldehyde	22	53	79	—	Acetaldehyde, ethylhydroperoxide, hydrogen peroxide
Ethylene	10	2	6	—	
Propionaldehyde	22	53	—	—	Acetaldehyde, ethylhydroperoxide, hydrogen peroxide
trans-2-Butene	11	9	—	—	
Propionaldehyde	20	49	76	89	Acetaldehyde, methylethylketone, ethylhydroperoxide
2-Methylbutene-1	10	7	21	38	
Propionaldehyde	22	51	76	89	Acetone
2,3-Dimethylbutene-2	10	12	32	53	
Propionaldehyde	18	49	75	88	Acetone, methylethylketone, ethylhydroperoxide, hydrogen peroxide
2-Methylbutene-1	10	1	8	15	
2,3-Dimethylbutene-2	10	—	21	36	
Propionaldehyde	18	50	—	88	Formaldehyde
1,3,5-Trimethylbenzene	10	8	—	34	

TABLE 3-5 Photooxidation of Aldehyde–Hydrocarbon Mixtures by Natural Sunlight

Aldehyde and Hydrocarbon	Initial Concentration, ppm (vol)	Fraction Reacted with Irradiation, % in 5 hr	Fraction Reacted with Irradiation, % in 6 hr	Other Products Identified
Formaldehyde	15	61	—	Oxidant, hydrogen peroxide
2,3-Dimethylbutene-2	10	36	—	
Acetaldehyde	5	12	—	Oxidant
2-Methylbutene-1	10	4	—	
Propionaldehyde	19	—	25	Acetaldehyde, methylethylketone, oxidant, hydrogen peroxide
2-Methylbutene-1	10	—	10	

TABLE 3-6 Photooxidation of Ketone–Hydrocarbon Mixtures in Air by Sunlight Fluorescent Lamps

		Fraction Reacted with Irradiation, %					Other Products Identified		
Ketone or Mixture	Initial Concentration, ppm (vol)	in 38 min	in 60 min	in 120 min	in 150 min	in 180 min	in 60 min	in 120 min	in 180 min
Acetone	10	—	12.4	23.3	—	31.9	Total oxidant[a] (0.14)	Formaldehyde[b] (1.82) Hydrogen peroxide[c] (0.03) Methylhydroperoxide[d] ($T_{1/2}$ = 33 min) Total oxidant[a] (0.267)	Formaldehyde[b] (2.88) Total oxidant[a] (0.352)
Acetone	5	—	10.2	22.4	—	34.7			Formaldehyde[b] (0.93)
2-Methyl-1-butene	10	—	2.3	7.0	—	11.3			Total oxidant[a] (0.29)

Acetone	10	—	11.4	23.8	—	32.4		Formaldehyde[b] (1.8)
2-Methyl-1-butene	10	—	4.5	8.6	—	15.8		Total oxidant[a] (0.49) Slow oxidant ($T_{1/2}$ = 32 min)
Acetone	20	—	12.2	23.6	—	33.5		Formaldehyde[b] (3.84)
2-Methyl-1-butene	10	—	7.8	17.6	—	28.7		Total oxidant[a] (0.84)
Diethylketone	3	17.3	24.7	—	69.3	76.7	Ethylhydroperoxide ($T_{1/2}$ = 50 min)	

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[a] Ferrous thiocyanate method (absorbance per 1-liter sample).
[b] Chromotropic acid method (ppm).
[c] Titanium-8-quinolinol method.
[d] Kinetic colorimetry with molybdate-catalyzed potassium iodide.

hyde was produced per molecule of ethylene reacted, but because more ethylene reacted.

The importance of synergistic effects in actual atmospheric conditions has not been determined, given the lack of sufficiently good data from both atmospheric samples and laboratory measurements. Some data obtained from the irradiation of atmospheric samples are shown in Table 3-7. The data of Kopczynski and co-workers[712] and of Stephens and Burleson[1154] are the result of irradiating Los Angeles air samples, the data of Heuss and Glasson[566] and Schuck and Doyle[1083] are from the irradiation of pure components, and the data of Leach and co-workers[746] are from the irradiation of diluted auto exhaust. The data of Schuck and Doyle[1083] seem to disagree markedly with those of others. The single-component data are the only data in which synergistic effects are absent. If we ignore the data of Schuck and Doyle, the remaining values show that *n*-butane, *sec*-butylbenzene, and the olefins react more quickly when irradiated in multicomponent mixtures. Equally apparent is that the reactivities of toluene and the xylenes are essentially unchanged. It is not obvious why the data of Schuck and Doyle do not agree with any of the other data. More information is needed before definitive conclusions can be reached on synergistic effects in polluted atmospheres.

Oxidation of Aromatic Hydrocarbons[293,537]

Aromatic hydrocarbons, present in the atmosphere in minor amounts, are also subject to autoxidation by triplet oxygen in an environment containing metallic catalysts, ozone, oxides of nitrogen and sulfur, peroxides, and light to form species with reactive functional groups. The only hydrocarbons whose oxidation will be considered here are benzene, toluene, dimethylbenzene and trimethylbenzene, and isopropylbenzene (cumene); these are the major atmospheric hydrocarbons. Their reactions should be typical of those of other structurally similar aromatic hydrocarbons not specifically discussed.

In the liquid phase at ambient temperatures, benzene is relatively stable; it is not readily autoxidized by triplet oxygen in the absence of catalysts. In the atmosphere, however, the situation is very complex, and one can visualize the oxidative formation of arene epoxides and peroxides, phenol, polyhydric phenols, quinones, such ring-cleavage products as muconic acid, and low-molecular-weight oxidation products.

Toluene is more rapidly oxidized than benzene in the liquid phase and undergoes side-chain oxidation to benzylhydroperoxide as the

TABLE 3-7 Relative Reaction Rates of Selected Hydrocarbons (4-hr irradiation)[a]

	Kopczynski *et al.*[712]		Stephens and Burleson[1154] (4-hr irradiation)	Heuss and Glasson[566] (6-hr irradiation)	Leach *et al.*[746] (auto exhaust)	Schuck and Doyle[1083]
Hydrocarbon	Relative Rate	Standard Deviation				
Ethane	0.06	0.09	0	—	—	—
Propane	0.16	0.09	0.18	—	—	—
n-Butane	0.27	0.13	0.37	0.11	0.3	—
Isobutane	0.24	0.26	0.33	—	—	—
n-Pentane	0.37	0.07	—	—	—	0.037
Isopentane	0.43	0.13	0.58	—	—	0.037
2,4-Dimethylpentane	0.99	0.27	—	—	—	—
Acetylene	0.14	0.07	0.17	—	—	—
Ethylene	1.00	—	1.0	1.00	1.00	1.00
Propylene	2.33	0.42	2.5	1.6	1.95–2.50	12.6
1-Butene	1.62[b]	0.52	2.5	1.9	—	9.7
2-Methyl-2-butene	9.39[c]	1.99	—	2.1	—	60
Toluene	0.56	0.34	—	0.87	0.59	—
m-Xylene	1.14	0.45	—	1.2	1.13–1.59	—
o-Xylene	0.70	0.28	—	1.2	0.74–1.27	—
sec-Butylbenzene	1.25[d]	0.45	—	0.47	—	—

[a] Ethylene = 1.00.
[b] Contains isobutylene.
[c] Averaged over first hour of irradiation.
[d] Contains 1,2,4-trimethylbenzene.

initial product. This decomposes to benzaldehyde, which undergoes facile oxidation to benzoic acid, a stable end product in solution.

In the atmosphere, the initial hydroperoxidation and later decomposition would also be expected to occur, but it is not known whether benzoic acid would survive in the vapor phase with the variety of catalytic species present. In principle, a wide range of reaction products can be obtained from benzoic acid. In addition, toluene itself may undergo the same types of ring attack as benzene.

The alkylbenzenes (*o*-, *m*-, and *p*-xylene and trimethylbenzenes) are even more readily autoxidized in the liquid phase than benzene and toluene. Initial oxidation products are monohydroperoxide and polyhydroperoxide, which are converted to an exceedingly complex mixture containing acids, quinones, phenolic oxidation products, and products of ring attack. Atmospheric oxidation is also likely to be facile.

Isopropylbenzene (cumene) is rapidly oxidized by triplet oxygen in the liquid phase to the hydroperoxide in an efficient, high-yield process. The hydroperoxide undergoes ready cleavage to acetone and phenol in the presence of catalytic quantities of acids and to acetophenone in the presence of variable-valence metals. The products of hydroperoxide decomposition (acetone, phenol, and acetophenone) are also readily oxidized by triplet oxygen to form a broad spectrum of products. Atmospheric oxidation may follow similar pathways, but information on that point is not available.

Recent studies[566,712,746,1083,1154] on vapor-phase oxidation have shown that toluene, *o*- and *m*-xylene, and *sec*-butylbenzene are oxidized by triplet oxygen in the presence of light at rates comparable with that of ethylene. The reported results are somewhat confusing, with some authors reporting faster and some slower oxidation. All rate differences are minor, however, and lead to the tentative conclusion that aromatic hydrocarbons are oxidized at a reasonable rate by triplet oxygen in the presence of light. Oxidation products were not identified.

FORMATION FROM SINGLET OXYGEN

The possibility that singlet oxygen can be produced in the atmosphere and later react with selected hydrocarbons to yield oxygenated organic compounds has only recently received attention. Before considering this possibility in detail, it is perhaps worth while to review briefly what singlet oxygen is and the methods by which it is generated. This review is not meant to be comprehensive; several excellent reviews on the subject are already available.[420,421,479–481,671,678,679,976,1289,1335]

Nature of Singlet Oxygen

The highest occupied molecular orbitals in molecular oxygen are a pair of doubly degenerate antibonding orbitals containing two electrons. Application of Hund's rule leads to a triplet state for the ground state. Other possible electronic configurations lead to the formation of three excited singlet states. Two of these states are degenerate in energy, are 22 kcal above the ground state in energy, and are referred to as the $^1\Delta$ state. The third singlet state, the $^1\Sigma$ state, is 38 kcal above the ground state and is diamagnetic by virtue of a cancellation of orbital angular momentum in the two available π orbitals.

It is possible to predict the chemical behavior of these excited states of oxygen on the basis of orbital occupation. The first excited state is expected to be electrophilic in its chemical behavior—i.e., it is expected to undergo two-electron reactions. The second excited state has an orbital occupancy similar to that of the ground state and is expected to undergo the one-electron—i.e., free-radical—reactions usually associated with ground-state oxygen. Both these states have been amply identified spectroscopically.[678]

Because singlet molecular oxygen is an excited-state species, it is important to consider its lifetime. The radiative lifetime for the $^1\Delta$ state has been found to be 45 min.[63,920] The radiative lifetime for the $^1\Sigma$ state is 7–12 sec.[1265] These long radiative lifetimes reflect the spin-forbidden character of the transition to the ground state. Because of collisional deactivation, the expected lifetimes of the states in condensed phases are considerably shorter. They have been estimated to be 10^{-9} sec for $^1\Sigma$ and 10^{-3} sec for $^1\Delta$.[48] A more recent estimate of the $^1\Delta$ state, based on β-carotene quenching studies, predicts a solution lifetime of 200 μsec.[808] Merkel and Kearns have measured $O_2(^1\Delta g)$ lifetimes of 2–200 μsec, depending on the solvent.[847] Young *et al.*[1355] recently reported $O_2(^1\Delta)$ lifetimes in a variety of solvents that compare favorably with those of Merkel and Kearns. These reduced lifetimes, owing to the quenching of the excited states, suggest that it will be extremely difficult to observe any reactions of the $^1\Sigma$ state in solution.[48]

Photosensitized Oxidation and Singlet Oxygen

Most of the recent resurgence of interest in singlet oxygen stems from work indicating that singlet oxygen is the active oxidant in many photosensitized oxidations. The possibility that electronically excited singlet oxygen might be the actual oxidant in dye-sensitized photooxidation reactions was first suggested over 30 years ago by Kautsky.[675,676] The mechanism proposed by Kautsky is shown in Reactions 111–113.

$$S + h\nu \longrightarrow {}^1S \tag{111}$$

$${}^1S \longrightarrow {}^3S \tag{112}$$

$${}^3S + {}^3O_2 \longrightarrow S + {}^1O_2({}^1\Sigma \text{ or } {}^1\Delta) \tag{113}$$

According to this mechanism, the sensitizer molecule (S) absorbs the light and is excited to a singlet state (^1S). Intersystem crossing then occurs to give a sensitizer triplet (^3S). Finally, energy transfer occurs from the triplet excited sensitizer to ground-state oxygen. This energy transfer produces oxygen in an excited singlet state and returns the sensitizer to its ground state.

The Kautsky mechanism was ignored until recently, when additional evidence stirred renewed interest in his proposal, leading ultimately to its confirmation. In 1963, Khan and Kasha[687] investigated the red chemiluminescence that occurs in the reaction of hydrogen peroxide and sodium hypochlorite. They identified some of the emission bands as originating from electronically excited oxygen. It was later shown that one of the emissions occurs from a pair of excited oxygen molecules.[47]

Beginning in 1964,[425,426] Foote and co-workers have published a series of papers that demonstrate not only that the hydrogen peroxide–sodium hypochlorite system can effect chemical oxygenation reactions, but that the nature and selectivity of the products and the stereochemistry of these oxygenations are the same as those observed in photosensitized oxidations of the same substrates. Simultaneously with the 1964 Foote paper, Corey and Taylor[249] showed that the excited oxygen molecules produced in a radiofrequency discharge react with some substrates to give oxygenation products that are also identical with those obtained in photosensitized oxidations. Since these 1964 observations, singlet oxygen has received increasing attention from scientists in a wide range of disciplines. This increasing attention has led to the suspicion or confirmation that singlet oxygen is involved in a variety of reactions and phenomena. Of interest in this report is the possible involvement of singlet oxygen in photodynamic action, carcinogenicity, and mutagenicity.

Production of Singlet Oxygen

Largely as a result of the solution-phase work of Foote and co-workers, it is now clear that a major source of singlet oxygen is the transfer of energy from excited triplet states of sensitizer molecules to ground-state oxygen.[420,421,425,426] The photolysis of ozone serves as another photochemical method of producing singlet oxygen.[328,451,620,652,734,932,1354]

Oxygen in its triplet ground state absorbs very weakly in the red end of the visible spectrum. Because of this very low absorption probability, the direct excitation of ground-state oxygen to the singlet state has not been considered a likely source of singlet oxygen. Recently, however, it has been found that the emission at 6238 Å from a helium–neon laser almost exactly coincides with the transition required for the excitation of the ground state to the $^1\Delta$ state.[383] Using this method of excitation, Evans[383] has been able to produce enough singlet oxygen to oxygenate several organic substrates.

Radiofrequency discharge flow systems serve as a convenient source of singlet oxygen. This method was first shown to give singlet oxygen by Foner and Hudson in 1956.[417] The use of the singlet oxygen thus produced to oxygenate organic compounds was first shown by Corey and Taylor in 1964.[249] Since then, several groups have successfully used this method, as reviewed by Wayne[1289] and Furukawa *et al.*[445]

A growing number of chemical methods for generating singlet oxygen are available. One of the first of these is the hydrogen peroxide–sodium hypochlorite system described by Foote and Wexler.[425] Other methods available are the reaction of bromine with hydrogen peroxide,[833] the decomposition of alkaline solutions of peracids,[833] the decomposition of photoperoxides,[1279] the self-reaction of *sec*-butylperoxy radicals,[590] the base-induced decomposition of peroxyacteylnitrate,[1147] the decomposition of superoxide ion,[686] and the aqueous decomposition of potassium perchromate.[968] The decomposition of a number of oxygen-rich products formed from the reaction of ozone with a variety of organic compounds has also been shown to be a source of singlet oxygen.[896–898,900,901]

SINGLET OXYGEN IN THE UPPER ATMOSPHERE

This subject has been recently reviewed[1073] and will only be summarized here. The sky emits radiation known as the "airglow," which contains some emission from both $O_2(^1\Delta g)$ and $O_2(^1\Sigma)$. Indeed, the first evidence[649] of $^1O_2(\Delta)$ molecules in the upper atmosphere was obtained in 1958 and was based on the 1.58-μm (0,1 band) emission of this state observed from the ground. A separate emission from $^1O_2(\Delta)$ has also been observed from aircraft,[933] balloons,[385,501] and rockets.[384,533] This second emission, at 1.27 μm (0,0 band), is not readily visible from the ground, because it is reabsorbed by atmospheric oxygen molecules. These observations indicate that the $^1O_2(\Delta)$ concentration rises to a maximum of 4×10^{10} molecules/cm^3 at 50 km. It then decreases again to the limits of detection at about 100 km. There are large differences in the intensity of the emission bands between night and day. These differences suggest that the primary source of this singlet oxygen is photochemical. It is now believed that the source is the ultraviolet photolysis of ozone.

SINGLET OXYGEN IN THE LOWER ATMOSPHERE

Basic to any consideration of the role of singlet oxygen in the lower atmosphere is a consideration of the likelihood of producing singlet oxygen there. This subject has recently received considerable attention and has led to some differences of opinion regarding the role of singlet oxygen in polluted atmospheres. The polluted atmospheres referred to here are those to which photochemical smog is a major contributor, such as those in the Los Angeles basin. Leighton[757] was the first to consider the possible role of singlet oxygen in oxidation reactions in these atmospheres. The specific oxidation process of interest is the conversion of nitric oxide to nitrogen dioxide. It has been known for some time that the termolecular reaction between oxygen and nitric oxide cannot proceed rapidly enough to explain the buildup of nitrogen dioxide (Reaction 114).

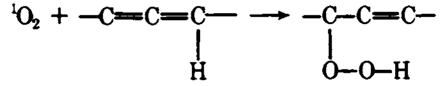
$$2NO + O_2 \longrightarrow 2NO_2 \qquad (114)$$

Once ozone is produced, it is consumed by reaction with nitric oxide (Reaction 115).

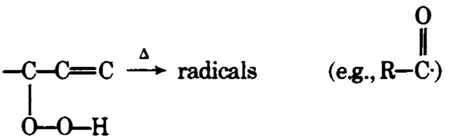
$$NO + O_3 \longrightarrow NO_2 + O_2 \qquad (115)$$

Nitrogen dioxide buildup generally precedes ozone buildup, however, so that the reaction of nitric oxide with ozone is not usually regarded as the important process for this oxidation. This situation has led to the speculation that singlet oxygen might be involved in the nitric oxide conversion process. Leighton first considered, then rejected, this possibility, on the grounds that the calculated rate of direct excitation from ground-state oxygen to singlet oxygen was too low. In 1964, Winer and Bayes[1339] recalculated this rate, taking into account the observation that $^1O_2(\Delta)$ is not efficiently quenched by O_2. On this basis, they concluded that singlet oxygen could be involved in smog formation. Furthermore, Winer and Bayes showed[1339] in 1966 that $^1O_2(\Delta)$, produced in a radiofrequency discharge, reacts with tetramethylethylene in the gas phase to give the same hydroperoxide product formed in solution.

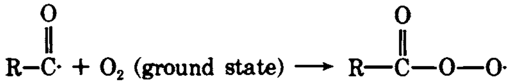
Beginning in 1967, Pitts and co-workers[688] have published a series of papers in which they revive the idea that singlet oxygen could be involved in the oxidation of nitric oxide to nitrogen dioxide in polluted atmospheres. Because the direct reaction of singlet oxygen (either Δ or Σ) with nitric oxide is endothermic and spin-forbidden (unless the products are produced in an excited state), Pitts *et al.* have proposed an indirect mechanism[975] for the involvement of ${}^1O_2$ in the nitric oxide oxidation. The essential steps of this proposed mechanism are presented in Reactions 116–122:



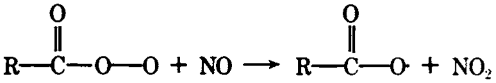
$${}^1O_2 + -C=C=\underset{\substack{|\\H}}{C}- \longrightarrow -\underset{\substack{|\\O-O-H}}{C}-C=C- \qquad (116)$$



$$-\underset{\substack{|\\O-O-H}}{C}-C=C \xrightarrow{\Delta} \text{radicals} \qquad (\text{e.g., } R-\overset{\substack{O\\\|}}{C}\cdot) \qquad (117)$$



$$R-\overset{\substack{O\\\|}}{C}\cdot + O_2\ (\text{ground state}) \longrightarrow R-\overset{\substack{O\\\|}}{C}-O-O\cdot \qquad (118)$$



$$R-\overset{\substack{O\\\|}}{C}-O-O + NO \longrightarrow R-\overset{\substack{O\\\|}}{C}-O\cdot + NO_2 \qquad (119)$$

$$NO_2 + h\nu \longrightarrow NO + O \qquad (120)$$

$$O + O_2 + M \longrightarrow O_3 + M \qquad \text{(where M is a third body)} \qquad (121)$$

$$O_3 + NO \longrightarrow NO_2 + O_2 \qquad (122)$$

Reaction 116 is simply an example of one of the known reactions of ${}^1O_2$ with olefins—namely, the "ene" reaction.[421] In Reaction 117, the allylic hydroperoxide produced in Reaction 116 is thermally decomposed to give radicals that include the acyl radical. The acyl radical then combines with ground-state oxygen (Reaction 118) to give a peroxy radical that then reacts with the nitric oxide (Reaction 119). Reactions 120 and 121 illustrate the usually accepted mechanism for the production of ozone in polluted atmospheres. Reactions 118 and 119 are identical with those involved in the mechanism generally accepted for the photooxidation of hydrocarbons in the presence of nitrogen oxides.[21,974]

If singlet oxygen is involved in this scheme, or in any other scheme permitting it to be involved in air pollution chemistry, then it seems likely that it must be the Δ state, and not the Σ state, that is involved. The several quenching studies that have been reported indicate that the Σ state is collisionally deactivated at a high rate, whereas the Δ state is inefficiently quenched.[48,397,808,847,903,1355] Kearns and Khan,[679] using correlation diagrams, have predicted that the Σ state will not react in a concerted reaction, such as that shown in Reaction 116. State correlation diagrams do indicate[679] that both Δ and Σ states could be involved in hydrogen abstraction reactions. Such a reaction is predicted to have an activation energy of 10 kcal for the Δ state and to proceed with little or no activation energy for the Σ state. Again, because of the rapid deactivation of the Σ state, such reactions are not expected to be observed. To date, there are no reports of vapor-phase reactions involving the Σ state. Later references to vapor-phase reactions of singlet oxygen in this report therefore pertain exclusively to the Δ state.

The proposals of Pitts and co-workers suggest that, in addition to the direct excitation process, several other possible ways for the generation of $O_2(^1\Delta)$ in the atmosphere need to be considered. It should be emphasized that, whereas there is still no direct evidence of the presence of singlet oxygen in the lower atmosphere, each of the methods to be considered has been verified as a source of singlet oxygen in laboratory experiments. In 1967, Pitts and co-workers suggested[688] that a high yield of singlet oxygen could be obtained in a system in which, first, the solar radiation is absorbed by a molecule capable of photosensitization and, second, there is a transfer to ground-state oxygen. One example of possible photosensitizing molecules is the group of polycyclic aromatic hydrocarbons produced in some combustion processes. It has now been demonstrated that such energy transfer processes do occur in the vapor phase.[246,680,732,1133,1148,1278]

The sensitizers used in these studies are among those one expects to find in fairly high concentrations in polluted atmospheres. Pitts *et al.* have also suggested[975] that excited nitrogen dioxide may act as a photosensitizer. This possibility has been realized experimentally (Reaction 123) by Frankiewicz, Berry, and Lehman.[105,433–435]

$$NO_2^* + O_2 \longrightarrow NO_2 + {}^1O_2 \qquad (123)$$

These workers have calculated that this mechanism alone could produce a steady-state $O_2(^1\Delta g)$ concentration in the atmosphere of

10^7–10^8 per cubic centimeter. They also point out that the concentration of oxygen atoms is seldom greater than 5×10^5 per cubic centimeter.[105] Thus, despite its lower reactivity relative to ozone and atomic oxygen, $O_2(^1\Delta g)$ could make a contribution to smog formation. Bufalini[166] points out that the oxygen atom reaction is most important in the initial stages of the smog-producing process, and its importance decreases with irradiation time. He concludes, on the basis of the expected concentrations and known reaction rates for oxygen atoms and $O_2(^1\Delta g)$, that the contribution of the $O_2(^1\Delta g)$ reaction is at best less than one-hundredth that of atomic oxygen. Frankiewicz and Berry argue that the contribution of $O_2(^1\Delta g)$ reactions could be 0.1–5%, depending on the class of compounds being considered.[434] Jones and Bayes have also demonstrated energy transfer from nitrogen dioxide to oxygen.[651] More recently, it has been shown that sulfur dioxide can also act as a photosensitizer to produce $O_2(^1\Sigma g+)$ from ground-state oxygen.[291]

Using computer simulation to study the changes that occur in smog chambers containing nitric oxide, nitrogen dioxide, *trans*-2-butene, and air, Calvert and co-workers[190,303] have concluded that $O_2(^1\Delta g)$ is an unimportant reactant in this system.

A second possibility for the production of singlet oxygen in the lower atmosphere referred to by Pitts is the ultraviolet photolysis of ozone. Wayne and Norrish had shown[930,1290] that the ultraviolet photolysis of ozone almost certainly leads to excited oxygen atoms in a singlet state. If this is the case, then the other product of this reaction ought to be singlet oxygen. In 1970, Gauthier and Snelling reported[451] that both $O_2(^1\Delta g)$ and $O_2(^1\Sigma)$ can be formed from the photolysis of ozone at 2537 Å (Reaction 124).

$$O_3(^1A) + h\nu \longrightarrow O_{25}(^1D) + O_2\ (\text{singlet}) \qquad (124)$$

In 1969, Kummler *et al.*[734] suggested that this ultraviolet photolysis of ozone could be a source of singlet oxygen in polluted atmospheres. Using the available data[1339] for the collisional quenching of $O_2(^1\Delta g)$ by ground-state oxygen, these authors compute the lifetime (τ) of $O_2(^1\Delta g)$ to be 0.57 sec at ground level. They then propose that a steady-state concentration of $O_2(^1\Delta g)$ will quickly be reached according to Eq. 125.

$$[O_2(^1\Delta g)] = ka[O_3]\tau \qquad (125)$$

Here, *ka* is the first-order rate constant for the formation of $O_2(^1\Delta g)$

from ozone photolysis. These authors contend that the concentrations of $O_2(^1\Delta g)$ thus calculated make singlet oxygen a more important oxidizing agent than atomic oxygen in these polluted atmospheres.

However, Hamming[519] has argued that singlet oxygen cannot be as important as oxygen atoms in the photochemical smog process during the early morning hours, when neither ozone nor, presumably, singlet oxygen would be present in measurable quantities. Additional data then became available, and Kummler *et al.*[733] made new calculations concerning the possible concentrations of singlet oxygen available from ozone photolysis. More accurate data[225] on the quenching of $O_2(^1\Delta g)$ by ground-state oxygen indicate that the effective lifetime of the singlet oxygen is 0.088 sec at ground level, a value lower than that used previously. Using this lifetime for $O_2(^1\Delta g)$, these authors calculate that the ratio of $O_2(^1\Delta g)$ to ozone will range from $8 \times 10^{-8}:1$ to $6 \times 10^{-7}:1$ at the early morning nitrogen dioxide peak. For any later time, these calculations indicate that the $O_2(^1\Delta g)$, produced by ozone photolysis, will exceed the oxygen atom concentration. However, it had been shown by Herron and Huie[563] in 1970 that $O_2(^1\Delta g)$ is less than one-thousandth as reactive as oxygen atoms with olefins. Thus, Kummler *et al.* conclude[733] that ultraviolet photolysis of ozone is not itself sufficient to generate enough singlet oxygen to make it an important reactant in polluted atmospheres. They point out, however, that other mechanisms for the production of singlet oxygen in the atmosphere could produce high enough concentrations to overweigh the reactivity disadvantage relative to oxygen atoms. One such mechanism could be the photosensitization process suggested by Pitts and co-workers; another could be the chemiexcitation process discussed next.

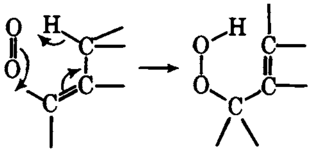
As described earlier, it has been shown that ozone can react with some organic substances to produce oxygen-rich intermediates that yield singlet oxygen on decomposition.[896–898,900,901] Most of this work has been done with solutions. In one case, however, Murray and Kaplan[896] have shown that the singlet oxygen so produced undergoes reactions in the vapor phase. These authors have suggested that such reactions may be important in polluted atmospheres. Murray *et al.* have also pointed out that these results indicate that ozone may have to be regarded as latent singlet oxygen.[899] The objection that singlet oxygen is expected to have a short lifetime in the atmosphere may not always be decisive, in that ozone could react with biologic substrates to produce singlet oxygen in proximity to those substrates.

Kummler and Bortner have identified[731] a number of inorganic atmospheric reactions of ozone, all of which could potentially produce singlet oxygen. To date, none of these inorganic reactions has been shown to give singlet oxygen. The same authors point out that, if an organic pollutant were present at 0.01 ppm and reacted with ozone at a rate comparable with that of nitric oxide, then such a reaction could produce singlet oxygen at the rate of 1.14 ppm/hr.

Finally, Pitts and co-workers have suggested that the alkaline hydrolysis of peroxyacylnitrate to give singlet oxygen[1147] could take place slowly in the lungs to produce singlet oxygen *in situ*.[4]

Vapor-Phase Reactions of Singlet Oxygen

Singlet oxygen undergoes various reactions with organic compounds in condensed phases. Because most work to date with singlet oxygen has been in condensed phases, a brief review might prove instructive regarding potential vapor-phase reactions. The reaction types that have been observed are the "ene" reaction[421] (126), the diene reaction[421] (127), the hydrogen-abstraction reaction[810] (128), reaction with enamines[423] (129), reaction to give dioxetanes[83,817] (130), reaction with amines[401] (131), and reaction with sulfides[4,422,424] and disulfides[4,6,895] (132 and 133). Most observed singlet oxygen reactions fall into these seven types.



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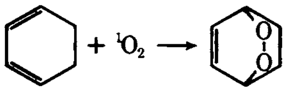

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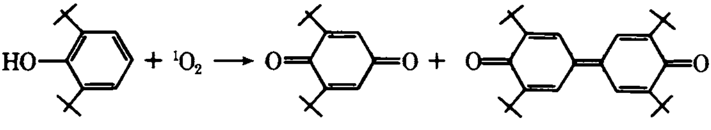

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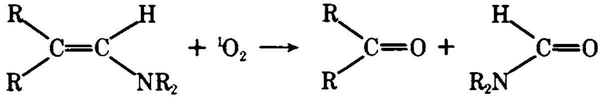

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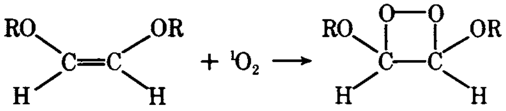

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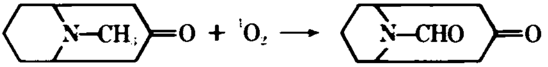

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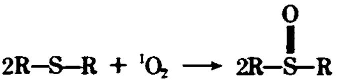
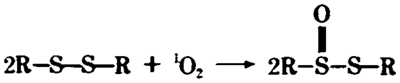


$$2R{-}S{-}R + {}^1O_2 \longrightarrow 2R{-}\overset{\overset{\displaystyle O}{\|}}{S}{-}R$$

(132)



$$2R{-}S{-}S{-}R + {}^1O_2 \longrightarrow 2R{-}\overset{\overset{\displaystyle O}{\|}}{S}{-}S{-}R$$

(133)

Of these general types, the reaction with amines (131) is still a subject of discussion, with some workers[82] arguing that singlet oxygen is not involved. The recent data of W. F. Smith, Jr.,[1130] however, seems to indicate clearly that singlet oxygen can oxidize some amines. In other cases, it seems clear that the oxidation does indeed involve singlet oxygen.

Singlet oxygen can be physically quenched in the vapor phase by a variety of substances, organic and inorganic. Although this subject has received much attention, it is distinct from reactions involving singlet oxygen and will not be discussed here. The reader is referred to a recent excellent review[678] for a comprehensive description of this subject.

The number of reactions of singlet oxygen in the vapor phase that have been reported is very small. It reacts with ozone to give atomic oxygen (Reaction 134).[228,229]

$$O_2({}^1\Delta g) + O_3 \longrightarrow 2O_2 + O({}^3P) \qquad (134)$$

Reported vapor-phase reactions of singlet oxygen with organic compounds are restricted to olefins, sulfides, disulfides, and one acetylene (3-hexyne). The one acetylene was used in a kinetic study in which products were not isolated.[560] Pitts and co-workers have reported that methylsulfide, ethylsulfide, and methyldisulfides are oxidized to the corresponding sulfoxides.

Many olefins have been oxidized in the vapor phase (Table 3-8). In most cases, products have not been isolated. In the cases of the less reactive olefins, the process measured is physical quenching, and no products have been formed from the olefin. Perhaps the first report of this type of reaction is that of Falick, Mahan, and Myers,[388] who showed in 1965 that introduction of ethylene reduces the paramagnetic resonance absorption signal due to $O_2({}^1\Delta g)$. Since then, additional reports have appeared. Singlet oxygen for use in vapor-phase reactions is usually produced by the discharge method. Photosensitized oxidation[246] and triphenylphosphite ozonide[424] have each been used in one such experiment. In most cases, the products of these vapor-phase reactions have not been isolated, as indicated in Table 3-8. Where they have been isolated, the products are the same as those produced in solution. Where more than one product can be produced, the vapor-phase reactions give small differences in product distributions with a variety of olefins.[470] Like the solution reactions, the vapor-phase reactions do not give the usual radical oxidation processes.

To date, there have been no reports of vapor-phase reactions of singlet oxygen with saturated hydrocarbons or terpenes.

The kinetics of the vapor-phase reactions of singlet oxygen with

TABLE 3-8 Vapor-Phase Reactions of Olefins with Singlet Oxygen

Olefin	Reference	Product
Ethylene	5,388,560,563	[a]
Propene	5,560,563	[a]
1-Butene	5,560,563	[a]
Isobutene	560,563	[a]
cis-2-Butene	4,445,560	[a]
	446	Allylic hydroperoxide
trans-2-Butene	4,445	[a]
2-Methyl-2-butene	4,445,559,560,563	[a]
	446,470	Allylic hydroperoxide
2-Hexene	445,560	[a]
2,3-Dimethyl-2-hexene	559	[a]
1-Nonene	560	[a]
Cyclopentene	560	[a]
1,2-Dimethylcyclopentene	559,560	[a]
Cyclopentadiene	445,560	[a]
Cyclohexene	560	[a]
	470	Allylic hydroperoxide
1,2-Dimethylcyclohexene	559,560,563	[a]
	470	Allylic hydroperoxide
1-Methylcyclohexene	445,560	[a]
1-Methylcyclopentene	445,560,563	[a]
4-Methylcyclohexene	560	[a]
1,3-Cyclohexadiene	445,560,563,896	[a]
1,4-Cyclohexadiene	560,563	[a]
2,5-Dimethylfuran	445,559-561,563,580	[a]
	155	Methoxyhydroperoxide
	469	Endoperoxide

[a] Product not isolated.

olefins have recently been examined by several groups. A summary of the available data on absolute rate constants is given in Table 3-9, and relative rate data are given in Table 3-10. Where more than one measurement on the same substrate is available, there is some variation in the reported values of absolute rate constants. This variation sometimes is an order of magnitude. It should be emphasized that some, perhaps even most, of the data were obtained under conditions in which physical and chemical quenching cannot be separated. There also appears to be some influence of pressure on the rate constant. It has been suggested[4] that this may be associated with the presence of a metastable intermediate. Both the absolute and the relative data support the conclusion that the reaction is electrophilic in the vapor phase, as well as in solution.

Herron and Huie[560,563] have compared the rate constants for the reactions of oxygen atoms and singlet oxygen with olefins and have concluded that singlet oxygen, which is approximately one-thousandth as reactive as oxygen atoms, will not play an important role in air pollution. This conclusion appears to be based on a consideration of ultraviolet photolysis as the only source of singlet oxygen. Kummler *et al.*[733] maintain that, when other possible atmospheric sources of singlet oxygen are considered, this conclusion may not be correct.

Because no products could be detected from the vapor-phase reactions of terminal olefins with singlet oxygen, Ackerman *et al.*[4] have concluded that the quenching in these cases is almost entirely physical. This means that the rate constants for chemical reactions of these olefins would be too low to allow singlet oxygen to compete with either oxygen atoms or ozone for removal of these olefins from the atmosphere. In the case of internally unsaturated olefins, products can be obtained; but the rate constants are low enough so that there is a question as to whether singlet oxygen could compete with oxygen atoms or ozone for reaction with these olefins in the atmosphere. What is still lacking is a good estimate or measure of the concentration of singlet oxygen in the atmosphere. Ackerman *et al.*[4] make the point, however, that, even if singlet oxygen did not compete favorably with ozone or oxygen atoms in the gross consumption of atmospheric olefins, the rates are such that quantities of products of singlet oxygen–olefin reactions of significance to air pollution could be produced. It seems unlikely, however, that atmospheric reactions of singlet oxygen are a major source of free radicals.

There are no reports of vapor-phase reactions of singlet oxygen with benzene derivatives. There are some reports of solution work with benzene derivatives, but none with pure hydrocarbons. Saito, Matsuura,

TABLE 3-9 Absolute Rate Constants for Vapor-Phase Reactions of Singlet Oxygen with Olefins

Olefin	k, liters/mol-sec	T, K[a]	Reference
Ethylene	1.1×10^{3}	RT	5
	$\leq 1 \times 10^{4}$	[b]	563
Propylene	1.3×10^{3}	RT	5
	$\leq 1 \times 10^{4}$	[b]	563
1-Butene	1.4×10^{3}	RT	5
	$\leq 1 \times 10^{4}$	[b]	563
2-Methyl-2-butene	1.0×10^{5}	298	445
	1.4×10^{4}	RT	4
	$\leq 1 \times 10^{4}$	[b]	563
2,3-Dimethyl-2-butene	9.5×10^{5}	298	445
	4.6×10^{5}[c]	RT	4
	1.2×10^{6}[d]	RT	4
	1.81×10^{6}	298	580
	8.6×10^{5}	300	559
	3.7×10^{5}	295	469
	1.0×10^{6}	300	561
	1.0×10^{6}	[b]	563
cis-2-Butene	2.5×10^{4}	298	445
	1.3×10^{4}	RT	4
trans-2-Butene	1.0×10^{4}	298	445
	3.0×10^{3}	RT	4
1,3-Butadiene	7.8×10^{3}	RT	4
2-Methyl-1,3-butadiene	9.5×10^{3}	298	445
1-Pentene	1.9×10^{3}	RT	5
cis-2-Pentene	2.0×10^{4}	298	445
2,3-Dimethyl-2-pentene	7.0×10^{5}	[b]	563
1,3-Pentadiene	6.3×10^{4}	RT	4
	$\leq 1 \times 10^{4}$	[b]	563
2-Hexene	6.7×10^{3}	298	445
Cyclopentadiene	8.8×10^{6}	298	445
1,2-Dimethylcyclopentene	4×10^{5}	[b]	563
1-Methylcyclopentene	1.5×10^{4}	[b]	563
	4.0×10^{5}	298	445
1-Methylcyclohexene	1×10^{4}	298	445
1,2-Dimethylcyclohexene	4×10^{5}	[b]	563
1,3-Cyclohexadiene	2.3×10^{5}	298	445
	$\leq 1 \times 10^{4}$	[b]	563
2,5-Dimethylfuran	2.8×10^{6}	298	445
	1.10×10^{7}	298	580
	1.5×10^{7}	300	559
	4.8×10^{5}	295	469
	1.46×10^{7}	300	560
	1.6×10^{7}	300	561

[a] RT = room temperature.

[b] Temperature not specified.

[c] 2–10 torr.

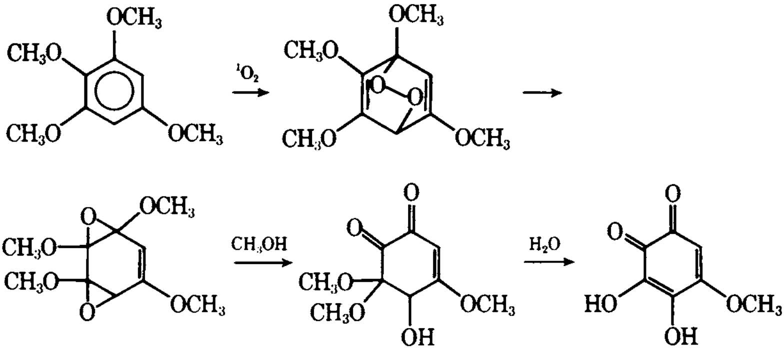
[d] 1 torr.

TABLE 3-10 Relative Rate Constants for Vapor-Phase Reactions of Singlet Oxygen with Olefins[a]

Olefin	Relative k[b]	Reference
Ethylene	<0.01	560
Propylene	<0.01	560
1-Butene	<0.01	560
cis-2-Butene	<0.01	560
2-Methyl-2-butene	<0.01	560
	0.044	559
2,3-Dimethyl-2-butene	1.00	559,560
trans-3-Methyl-2-pentene	<0.01	560
2,3-Dimethyl-2-pentene	0.69	559
	0.7	560
2,3-Dimethyl-2-hexene	0.66	559
1,3-Pentadiene	<0.01	560
1-Methylcyclopentene	0.015	560
2,2-Dimethylcyclopentene	0.4	560
1,2-Dimethylcyclopentene	0.4	560
	0.43	559
1,2-Dimethylcyclohexene	0.4	560
	0.38	559
1,3-Cyclohexadiene	0.09	560
1,4-Cyclohexadiene	<0.01	560
2,5-Dimethylfuran	17.0	559,560

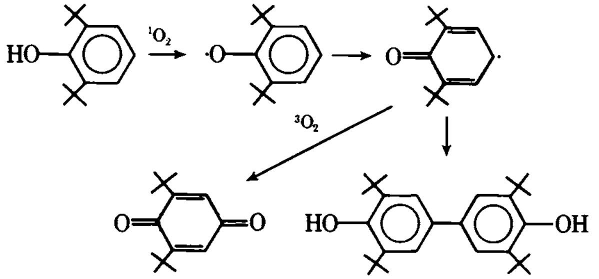
[a] All experiments at 300 K.
[b] Based on 1,2-dimethyl-2-butene = 1.0.

and co-workers[1049–1052] have reported the photosensitized oxidation of a number of methoxy derivatives of benzene. The reaction appears to be of the diene type, proceeding through an intermediate endoperoxide. Reaction 135 illustrates the case of 1,2,3,5-tetramethoxybenzene.



(135)

The same group has reported[809–811] that singlet oxygen produced via photosensitization or from a chemical source is able to accomplish a hydrogen abstraction reaction with some phenols. A similar reaction has been reported by Pfoertner and Böse[969] and is illustrated for 2,6-di-*tert*-butylphenol (Reaction 136):



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FORMATION FROM OZONE

Ozone in Polluted Atmospheres

Ozone in small quantities is a natural constituent of the atmosphere. It is produced in a photochemical reaction that occurs in the upper portions of the stratosphere.[181,494] Some of this ozone finds its way to the troposphere and contributes to the background ozone concentration in all atmospheres. A recent study by Ripperton *et al.* reported a background ozone concentration of 0.02–0.04 ppm.[1020] This background concentration generally ranges from 0 to 0.1 ppm.

When molecular oxygen absorbs radiation of approximately 2400 Å, it dissociates into atomic oxygen; the atomic oxygen then combines with molecular oxygen to produce ozone (Reactions 137 and 138).

$$O_2 + h\nu \longrightarrow O + O \qquad (137)$$

$$O_2 + O + M \longrightarrow O_3 + M \quad (M = \text{a third body}) \qquad (138)$$

This process leads to high stratospheric concentrations of ozone, reaching a maximum of approximately 2.0 ppm at an altitude between 12 and 22 miles. The ozone layer absorbs ultraviolet light, which would otherwise reach the earth's surface and present a hazard to life.

Ozone in the troposphere has four general sources: dissociation of oxygen as it occurs in the stratosphere, photochemical reactions involving nitrogen oxides and hydrocarbons in polluted atmospheres, lightning, and transfer from the stratosphere. Of these, only the second and fourth are significant. In atmospheres in which photochemical smog is prevalent, the second source is the major one and can lead to ozone concentrations as high as 1.0 ppm. The chemistry of photochemical smog that leads to ozone production has recently been reviewed[21,22,320,1152,1228] and will only be summarized here.

A major reaction leading to ozone formation in polluted atmospheres has its origin in the photolysis of nitrogen dioxide, which is produced in combustion processes as illustrated by Reaction 139–141:

$$2NO + O_2 \longrightarrow 2NO_2 \qquad (139)$$

$$NO_2 \xrightarrow{h\nu} NO + O \qquad (140)$$

$$O_3 + O_2 + M \longrightarrow O_3 + M \qquad (141)$$

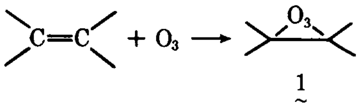
In the presence of hydrocarbons, there are clear indications of a separate path contributing to the conversion of nitric oxide to nitrogen dioxide. Several proposals have been offered for this alternative oxidation process (discussed earlier and in Chapter 4). The possibility that ozone–olefin reactions can contribute to this process is considered below.

Mechanism of Reaction of Ozone with Aliphatic Hydrocarbons

OLEFINS

Most of the work on the mechanism of the reaction of ozone with olefins has been carried out with solutions. The prevailing views on the mechanism are summarized here. Necessary modifications to the mechanism for vapor-phase reactions are considered below.

The most extensive proposal for the mechanism of ozonolysis of olefins was given by Criegee[262,263] on the basis of several years of work by him and his co-workers. According to this mechanism, ozone adds to the double bond to give an initial olefin–ozone adduct, 1, which is unstable and decomposes to give a zwitterion fragment, 2, and a carbonyl compound, 3 (Reactions 142 and 143). Recombination of 2 and 3 leads to the normal ozonide, 4 (Reaction 144). Depending on a number of factors—largely the reactivity of the carbonyl compound—the zwitterions may also react with themselves to give diperoxides, 5, and higher peroxides, 6 (Reaction 145). In reactive solvents, such as methyl alcohol, the zwitterion is diverted to other products, such as methoxyhydroperoxides, 7 (Reaction 146).



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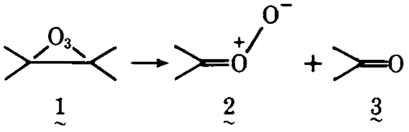

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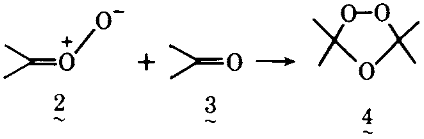

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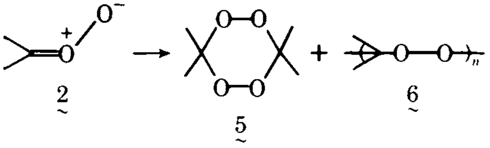

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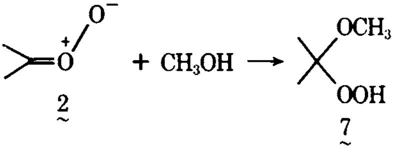

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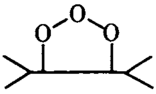
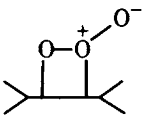
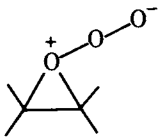
Depending on olefin structure, the initial adduct, 1, may have several possible structures (1a–1c).



1a



1b



1c

It now seems likely that 1a is the most common structure for the initial adduct,[68] whereas 1b is invoked when excess aldehyde is present[1166] and 1c is particularly likely for terminal olefins with bulky substituents.[67,902,1168] It is also possible that 1c is formed first and then proceeds to 1b or 1a, depending on olefin structure and specific reaction conditions.[1166] A number of experimental results have been obtained that are not fully explained by the Criegee mechanism. Perhaps the most significant is the failure of the Criegee mechanism to predict stereochemical consequences in the ozonide (or ozonides, where more than one is formed). These results have led to several additional proposals for the mechanism,[894] all of which retain the basic elements of the Criegee mechanism. One proposal[894,902,1168] suggests that the observed stereochemical results can be understood if the ozonolysis reaction is viewed as having several mechanistic paths available, of which that suggested by Criegee is one. Additional pathways include a direct conversion of the initial adduct, formulated as 1c, to ozonide, and the reaction of the initial adduct with aldehyde, to give ozonide in an aldehyde-exchange reaction. This proposal has been amplified[1166] to include suggestions that the initial adduct, formulated as 1b, can also undergo a Baeyer–Villiger[535] reaction to give ozonide or to oxidize aldehyde to acid. A second major alternative to the Criegee mechanism has been suggested by Bailey and co-workers.[88] The essence of this proposal is that olefin stereoisomers can give different distributions of *syn*- and *anti*-zwitterions and that these in turn will react with the carbonyl fragment, 2, to give different ozonide stereoisomer distributions. A further modification of this proposal has recently been given that is claimed to be more consistent with the experimental observations.[743]

SATURATED HYDROCARBONS

Reaction of ozone with saturated hydrocarbons has received far less attention than reaction with olefins. Saturated hydrocarbons are considerably less reactive than olefins. Two mechanisms have been considered for this reaction. One [1309] is a radical mechanism in which ozone abstracts a hydrogen atom from the hydrocarbon. Recombination of the fragments thus produced leads to a hydrotrioxide that decomposes further to give an alcohol and oxygen (Reactions 147–149):

$$\mathrm{R{-}H + O_3 \longrightarrow R. + .OOOH} \qquad (147)$$

$$\mathrm{R. + .OOOH \longrightarrow ROOOH} \qquad (148)$$

$$\mathrm{ROOOH \longrightarrow R{-}OH + O_2} \qquad (149)$$

A variation of this mechanism has been proposed and examined with the assistance of optically active tertiary hydrocarbons.[518] According to this view, the first step in the reaction is regarded as an insertion reaction of ozone into a carbon–hydrogen bond (Reaction 150). The transition state for the insertion is postulated as having considerable radical character. The mechanism suggests that the alcohol will be produced with retention of configuration or with racemization, depending on the relative importance of the two competing processes shown (Reaction 150a). Experimentally, it is found that alcohol is formed with 60–70% retention of configuration.

$$\text{R—H} + \text{O}_3 \longrightarrow [\text{R}\cdot\ .\text{OOOH}] \tag{150}$$

$$\begin{tikzcd}[][\text{R}\cdot\ .\text{OOOH}] \arrow[r] \arrow[dr] & \text{ROOOH} \arrow[r] & \text{ROH (retention)} + \text{O}_2 \\ & \text{R}^{\cdot} + \text{O}_2 + .\text{OH} \arrow[r, "\text{O}_2"] & \begin{array}{l}\text{ROH (racemized)} + \\ \text{O}_2 + \text{ketone} + \\ \text{peroxides and} \\ \text{fragmentation products}\end{array}\end{tikzcd} \tag{150a}$$

It seems likely that, if hydrotrioxides are produced in vapor-phase oxidation of saturated hydrocarbons with ozone, they would decompose, to give radicals.

Benson has suggested[98] that, in vapor-phase oxidation of hydrocarbons the reaction could involve an initiation step that gives atomic oxygen. The initiating atomic oxygen is postulated to abstract a hydrogen atom from the hydrocarbon. The reaction sequence then has propagating steps (Reactions 151–154), one of which involves ozone.

$$\text{M} + \text{O}_3 \rightleftarrows \text{O}_2 + \text{O} + \text{M} \tag{151}$$

$$\text{O} + \text{R—H} \longrightarrow \text{R}\cdot + \cdot\text{OH} \tag{152}$$

$$\text{R}\cdot + \text{O}_3 \longrightarrow \text{RO}\cdot + \text{O}_2 \tag{153}$$

$$\text{RO}^{\cdot} + \text{R—H} \longrightarrow \text{ROH} + \text{R}^{\cdot} \tag{154}$$

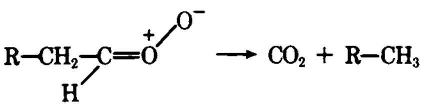
Because of the low temperatures used, it is not felt that this sequence is important in solution reactions. But Benson suggests that the radical abstraction process described above for solution reactions (150 and 150a) is also not very likely, given the endothermicity of the reaction and the temperatures used. He concludes that an intimate ion-pair mechanism cannot be ruled out.

$$O_3 + R{-}H \longrightarrow [R^+ + O_3H^-] \qquad (155)$$

Vapor-Phase Reactions of Ozone

Because ozone concentrations in polluted atmospheres are considerably higher than those found in the ambient tropospheric environment, studies of the vapor-phase reactions of olefins with ozone are essential to an understanding of the chemistry of photochemical smog. A summary of the reported reactions is given in Table 3-11. Leighton has given an excellent review of this subject through 1961.[757] The data in Table 3-11 include the earlier references, as well as reports up to the present.

As indicated in Table 3-11, the products of the reaction of olefins with ozone in the vapor phase differ somewhat from those obtained in solution. It has generally been assumed that the first step in the mechanism is approximately the same as that observed in solution—i.e., an unstable olefin–ozone addition compound (1) is produced. After comparing calculated A factors for several possible transition states with the observed A factor, DeMore[304] concluded that the transition state in the cases of ethylene and propylene results from a concerted 1,3-dipolar addition of ozone to the double bond. This compound then presumably fragments to a carbonyl compound (3) and a zwitterion (2). In almost all cases, the expected aldehydes and ketones are found. In many cases, the acids corresponding to further oxidation of these materials are also found. Many of the reactions also gave carbon dioxide. This could arise from further decomposition of the zwitterion, as given by Reaction 156.



$$R{-}CH_2{-}CH{=}\overset{+}{O}{-}O^- \longrightarrow CO_2 + R{-}CH_3 \qquad (156)$$

In at least some cases, the hydrocarbon expected from this kind of decomposition has been found.[167] The variation in product composition from corresponding solution reactions could also indicate that the vapor-phase reactions are more likely to involve free-radical pathways. Two recent investigations bear directly on this question. Working at a total pressure of 3 torr, Finlayson, Pitts, and Akimoto[399] have obtained evidence of OH radical production in the ozonolysis of a number of

TABLE 3-11 Vapor-Phase Ozonolysis of Aliphatic Hydrocarbons

Hydrocarbon	Products	Reference
Ethylene	Formaldehyde, formic acid, unstable intermediate	151
	Water, formaldehyde, carbon monoxide, carbon dioxide, formic acid	1091
	Formaldehyde	51,167
	Acetaldehyde, formic acid	1259
	Formic acid, unstable intermediate	539
	[a]	180,304,526,1260
Propylene	Formaldehyde, acetaldehyde, formic acid, acetic acid	151,152
	Water, formaldehyde, acetaldehyde, carbon monoxide, carbon dioxide, ketene, an acid	1091
	Ketene, methyl alcohol, methane, carbon monoxide, carbon dioxide, formaldehyde, acetaldehyde	526
	Propylene ozonide	304
	Acetaldehyde, propionaldehyde, acetone, formic acid, methyl alcohol, carbon dioxide	1259
	Acetaldehyde[b]	1294
	[a]	180,1260
1-Butene	Ethane	167
	Propionaldehyde, propionic acid, unstable intermediate	150
	Acetaldehyde, propionaldehyde, *n*-butyraldehyde, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, propionaldehyde[b]	1294
	[a]	1260
2-Butene[c]	Acetaldehyde, acetic acid, unstable intermediate	150
Isobutene	Acetone	167
	Acetone, formaldehyde	51,526
	Acetone, formaldehyde, formic acid	150
	Isobutyraldehyde, acetone, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, acetone[b]	1294
	[a]	1260
trans-2-Butene	Acetaldehyde	167

TABLE 3-11 *Continued*

Hydrocarbon	Products	Reference
trans-2-Butene	Methyl alcohol, carbon monoxide, acetaldehyde	526
	Acetaldehyde, formic acid, carbon dioxide	1259
	Carbon dioxide, acetaldehyde[b]	1294
	[a]	1260
cis-2-Butene	Methyl alcohol, carbon monoxide, acetaldehyde	526
	Acetaldehyde, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde[b]	1294
	Formaldehyde, acetaldehyde, ketene, formic acid, methyl alcohol	51
	Acetaldehyde, 2-butanone, methylvinylketone	400
	[a]	167,180,1260
1-Pentene	Butyraldehyde, formaldehyde, ozonide	526
	Butyraldehyde, carbon dioxide, formic acid, unstable intermediate	525
	Water, formaldehyde, butyraldehyde, carbon monoxide, carbon dioxide, acid	1091
	Acetic acid, propionaldehyde, butyraldehyde, formic acid, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, propionaldehyde, butyraldehyde[b]	1294
	[a]	180,1260
2-Pentene[c]	[a]	1091
cis-2-Pentene	Acetaldehyde, propionaldehyde, butyraldehyde, methylethylketone, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, propionaldehyde[b]	1294
	[a]	1260
trans-2-Pentene	Acetaldehyde, propionaldehyde, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, propionaldehyde[b]	1294
	[a]	1260

TABLE 3-11 *Continued*

Hydrocarbon	Products	Reference
2-Methyl-1-butene	Acetaldehyde, methylethylketone, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, acetone, methylethylketone[b]	1294
	[a]	1260
3-Methyl-1-butene	Acetaldehyde, isobutyraldehyde, acetone, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, isobutyraldehyde, acetone[b]	1294
	[a]	1260
2-Methyl-2-butene	Acetaldehyde, acetone, formic acid, methyl alcohol, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, acetone[b]	1294
	[a]	1260
1,3-Butadiene	Acetaldehyde, acrolein, formic acid, carbon dioxide	1259
	[a]	1260
Tetramethylethylene	Acetone[b]	167,523,524,1294
	Formic acid, formaldehyde, acetone, methyl alcohol, carbon dioxide, acetic acid, esters	1127
	Acetaldehyde, acetone, formic acid, methyl alcohol, carbon dioxide	1259
	[a]	1260
1-Hexene	Pentyl alcohol, butane	167
	Ozonide, valeraldehyde, formaldehyde	526
	Formaldehyde, butyraldehyde, acetylene, carbon dioxide, water, hydroperoxides	1057
	Acetaldehyde, butyraldehyde, valeraldehyde, acetone, formic acid, carbon dioxide	1259
	Carbon dioxide, acetaldehyde, propionaldehyde, butyraldehyde, valeraldehyde[b]	1294
	[a]	180,1058,1260
1-Heptene	[a]	180

TABLE 3-11 *Continued*

Hydrocarbon	Products	Reference
3-Heptene[c]	[a]	1091
1-Octene	[a]	180
1-Decene	[a]	180
Cyclohexene	Formic acid, adipic acid, *trans*-1,2-cyclohexanediol	347
	Acetaldehyde, formic acid, carbon dioxide	1259
	[a]	180,1260
Styrene	[a]	167
Acetylene	[a]	179,304
3-Methyl-1-pentene	Carbon dioxide, acetaldehyde, propionaldehyde, isovaleraldehyde, acetone[b]	1294
4-Methyl-1-pentene	Carbon dioxide, acetaldehyde, isobutyraldehyde, isovaleraldehyde, acetone[b]	1294
2-Methyl-1-pentene	Carbon dioxide, acetaldehyde, propionaldehyde, acetone, methylpropylketone[b]	1294
2-Hexene[d]	Carbon dioxide, acetaldehyde, propionaldehyde, butyraldehyde[b]	1294
4-Methyl-2-pentene[c]	Carbon dioxide, acetaldehyde, propionaldehyde, isobutyraldehyde[b]	1294
2-Methyl-2-pentene[c]	Carbon dioxide, acetaldehyde, propionaldehyde, acetone[b]	1294
3-Methyl-2-pentene	Carbon dioxide, acetaldehyde, acetone, methylethylketone[b]	1294
Dipentene	Diozonide	1138
D-Limonene	Diozonide	1138
D-α-Pinene	Ozonide	1138

TABLE 3-11 *Continued*

Hydrocarbon	Products	Reference
α-Pinene	Aerosol	1019
Methane	Formic acid, carbon dioxide, carbon monoxide, methyl alcohol	1081
	Carbon monoxide, carbon dioxide, water, formic acid	313
	[a]	1080
Ethane	Carbon dioxide, water, formic acid, methyl alcohol	875
Propane	Formic acid, carbon dioxide, methyl alcohol, acetone	1081
	Carbon dioxide, water, acetone, formic acid, methyl alcohol	875
	[a]	1080
n-Butane	Formic acid, carbon dioxide, methyl alcohol	1081
	[a]	1080
Isobutane	Formic acid, carbon dioxide, acetone, *tert*-butyl alcohol	1081
	tert-Butyl alcohol, acetone, *tert*-butylhydroxymethylperoxide	1080
n-Pentane	[a]	1080

[a] Products not isolated.
[b] Yields of major products greater in the presence of molecular oxygen than in its absence.
[c] Stereochemistry not specified.
[d] *Cis–trans* mixture.

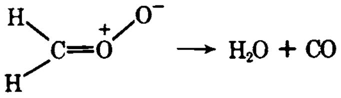
low-molecular-weight olefins. In a related study, Atkinson, Finlayson, and Pitts[51] have obtained evidence of a number of radical species, including HCO and HO_2, in the ozonolysis of low-molecular-weight olefins at a total pressure of 2 torr. A general treatment of vapor-phase ozonolysis making use of a radical mechanism has now been offered.

The usual recombination reaction between carbonyl compound and zwitterion to give normal ozonide (4) seems to be completely suppressed in the vapor phase. Although there are some reports that ozonides were isolated in vapor-phase reactions, the conclusion is based only on infrared spectra, and some reports have been found to be incorrect.

In a number of cases, aerosols were reported to form. It is possible that non-vapor-phase reactions could occur in these aerosols to produce ozonides and other peroxidic materials. As seen in Table 3-11, several groups of workers reported the formation of unstable materials. These are presumably peroxidic materials, including ozonides.

A more recent study indicates that the dark-phase reaction of ozone with open-chain monolefins in air produced no light-scattering aerosol. However, similar reactions with the cyclic olefins cyclohexene and α-pinene and the diolefin 1,5-hexadiene produced considerable quantities of light-scattering aerosol.[1019]

Decomposition of the zwitterion (2) has also been postulated to explain some of the other lower-molecular-weight products (Reactions 157 and 158):[1091]



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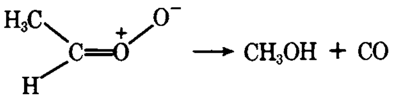

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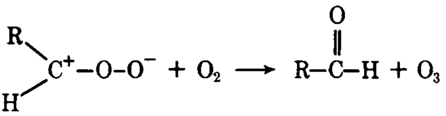
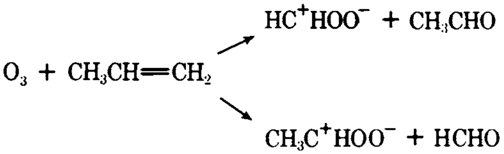
Yields of the carbonyl-containing products obtained are higher when ozone is used in oxygen than in nitrogen.[1259] Thus, some of the products probably result from further oxidation reactions after the initial attack of the ozone on the olefin. It should be pointed out, however, that these results are obtained when the reactants are used in the torr pressure range. Also, in the presence of oxygen about 1.4–2.0 mol of olefin are consumed per mole of ozone, whereas, when nitrogen is used as the diluent, a stoichiometric relation is observed.[1259] Apparently, some of the products produced are themselves capable of oxidizing olefins.

A possible explanation[167] for the higher aldehyde and ketone yields in the presence of oxygen is that the zwitterion reacts with oxygen, to give the carbonyl compound and ozone (Reaction 159):

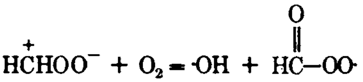


(159)

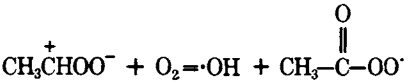
Niki has presented a comprehensive scheme for smog production in which he concludes that ozone–olefin reactions are important in all aspects of the total mechanism.[924] According to Niki, both the time of induction and the time of conversion of nitric oxide to nitrogen dioxide are lengthened if the ozone reactions are not considered. He proposes the following (Reaction 160 and Eqs. 161–166) as possibilities for the involvement of the ozone–olefin reaction, using propylene as the olefin.



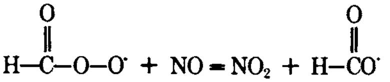
$$O_3 + CH_3CH{=}CH_2 \begin{array}{l} \nearrow\; HC^+HOO^- + CH_3CHO \\ \searrow\; CH_3C^+HOO^- + HCHO \end{array} \qquad (160)$$



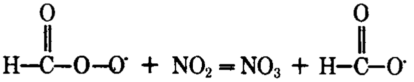
$$H\overset{+}{C}HOO^- + O_2 = \cdot OH + H\overset{O}{\overset{\|}{C}}{-}OO\cdot \qquad (161)$$



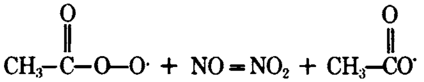
$$CH_3\overset{+}{C}HOO^- + O_2 = \cdot OH + CH_3{-}\overset{O}{\overset{\|}{C}}{-}OO\cdot \qquad (162)$$



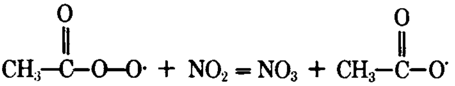
$$H{-}\overset{O}{\overset{\|}{C}}{-}O{-}O\cdot + NO = NO_2 + H{-}\overset{O}{\overset{\|}{C}}O\cdot \qquad (163)$$



$$H{-}\overset{O}{\overset{\|}{C}}{-}O{-}O\cdot + NO_2 = NO_3 + H{-}\overset{O}{\overset{\|}{C}}{-}O\cdot \qquad (164)$$



$$CH_3{-}\overset{O}{\overset{\|}{C}}{-}O{-}O\cdot + NO = NO_2 + CH_3{-}\overset{O}{\overset{\|}{C}}O\cdot \qquad (165)$$



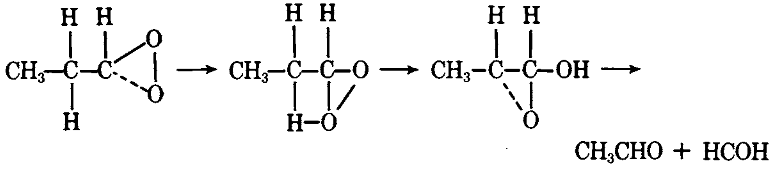
$$CH_3{-}\overset{O}{\overset{\|}{C}}{-}O{-}O\cdot + NO_2 = NO_3 + CH_3{-}\overset{O}{\overset{\|}{C}}{-}O\cdot \qquad (166)$$

Niki, Daby, and Weinstock conclude that the later stage of the process, which governs the terminal concentrations of ozone and nitrogen-containing smog products, is dominated by ozonolysis reactions.[925]

Jaffe and Loudon have also suggested[628] that the zwitterions produced on ozonolysis could react with oxygen, but they prefer the path giving ozone and a carbonyl compound (Reaction 159). They suggest further that such reactions could be responsible for the nonstoichiometric ratio of olefin to ozone in the presence of oxygen, which had been observed earlier by Vrbaski and Cvetanović.[1259]

It has been suggested[22] that the finding of a stoichiometric olefin–ozone relation in the presence of nitrogen could rule out the possibility that the zwitterion itself can attack hydrocarbons to initiate a chain oxidation reaction. This may be true only when there are limited quantities of olefins, such as were used in the kinetic studies in which the stoichiometric relation was found. In the gross reactions that take place in polluted atmospheres, the possibility of reaction between zwitterions and olefins, as well as other hydrocarbons, should probably not be ruled out. The zwitterion has been shown to epoxidize some olefins in solution.[264,736] A dipolar addition reaction between zwitterions and olefins has also been reported.[1167] Finally, it has been suggested[517] that the zwitterion can initiate the oxidation of saturated hydrocarbons.

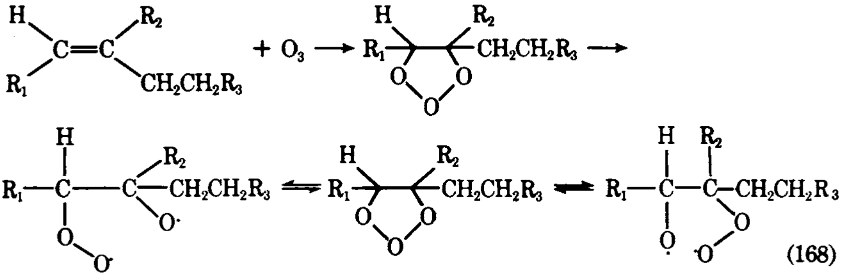
In some cases, aldehyde and ketone products are obtained that are not normal ozonolysis products, i.e., derived from direct cleavage of the double bond. It has been suggested[1294] that some of these products result from more complex rearrangements of zwitterions (Reaction 167).



(167)

Such possibilities must be regarded as highly speculative.

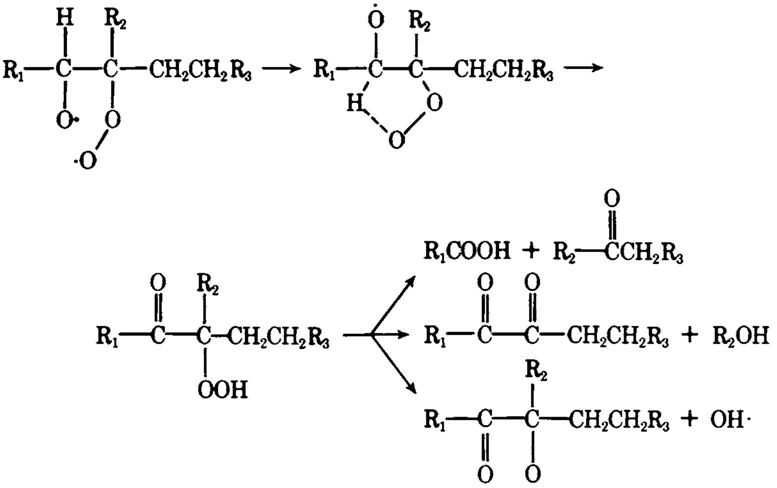
The observation that some of the products obtained from vapor-phase ozonolysis are different from those obtained in solution, and the general dissatisfaction with explanations for these products using the Criegee zwitterion mechanism has prompted one group to suggest[944] a mechanism for the vapor-phase reaction that is based on free-radical chemistry. According to this proposal, the Criegee zwitterion mechanism is seen as the least important of several reaction possibilities. The other possibilities proposed are based on a detailed kinetic and thermochemical analysis of the vapor-phase reaction. An outline of this new proposal is presented in Reaction 168.



(168)

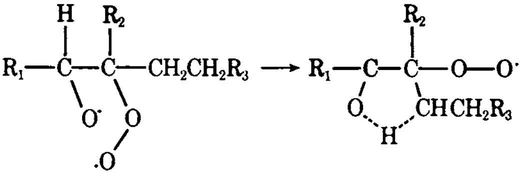
Ozone adds to the olefin to give the initial ozonide or trioxolane. This unstable intermediate is postulated as being in equilibrium with the two possible diradicals arising from homolysis of an oxygen–oxygen bond. The diradicals so formed have several possible fates. These are illustrated by Reactions 169–172 for one of the diradicals.

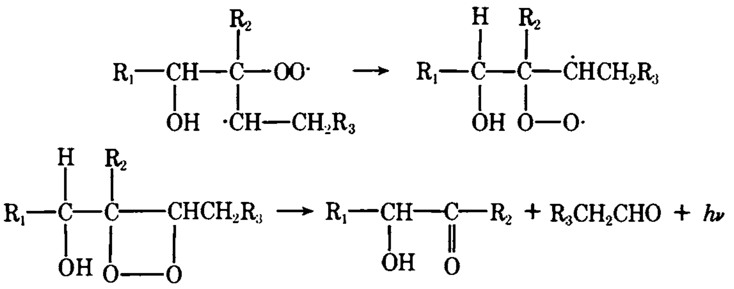
αH-abstraction path



(169)

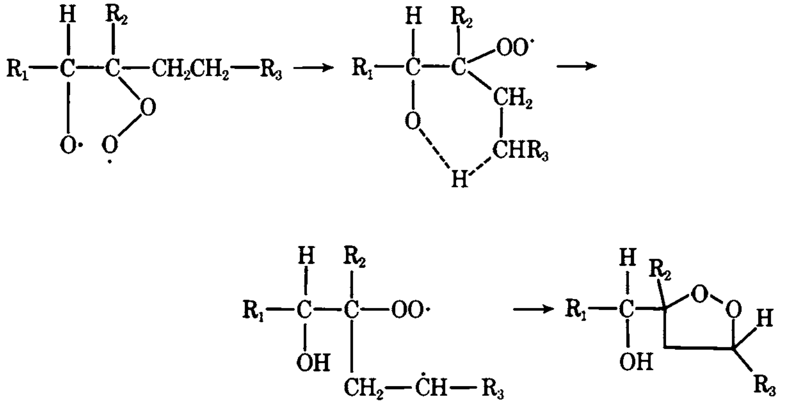
βH-abstraction path





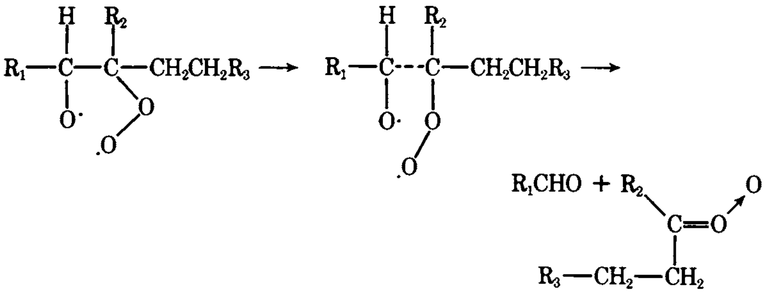
(170)

γH-abstraction path



(171)

Criegee split



(172)

This proposal retains the Criegee zwitterion formation as one of the fates of the diradical. It also postulates several new fates that do explain some of the products that are observed experimentally and that are not readily explained via the zwitterion route. In particular, this mechanism explains the formation of carbonyl compounds arising from cleavage of the carbon–carbon bond adjacent to the olefinic linkage. In a recent study of low-pressure vapor-phase ozone–olefin reactions, Finlayson *et al.*[400] have used this free-radical scheme of O'Neal and Blumstein[944] to explain most of their observed products.

In the case of saturated hydrocarbons, the vapor-phase products are again approximately the same as those obtained in solution.[1081] It has been suggested that these products are the results of free-radical reactions initiated by ozone.[1081]

A considerable number of vapor-phase ozone–olefin reactions have been subjected to kinetic analysis. Rate data for saturated aliphatic hydrocarbon reactions are more limited. The available data are summarized in Tables 3-12 (absolute rate constants) and 3-13 (relative rate constants). Cox and Penkett[256] have reported that they also have studied vapor-phase ozone-olefin reactions. They did not report their kinetic data, but state that second-order kinetics were observed and that their rate constants agreed well with those given by Leighton.[757]

On the basis of measured compositions of smoggy atmospheres[31] and the rate constants for the reaction of ozone with various species contained in such atmospheres, Stedman and Niki[1145] have concluded that, under typical atmospheric conditions, the carbon-containing species primarily removing ozone are olefins.

A major problem associated with most of the vapor-phase kinetic work is the nonstoichiometric relation between ozone and olefin. One assumes that the stoichiometry should be 1:1 and that second-order kinetics will be observed. As a result of the work of Wei and Cvetanović,[1294] it now seems clear that the failure to observe 1:1 stoichiometry is due to the use of oxygen as the carrier gas for ozone. When these workers used oxygen, they observed a stoichiometry that varied from 1.4:1 to 2.0:1 (olefin:ozone); in the presence of nitrogen, a clean 1:1 stoichiometry was achieved. In a more recent study of the vapor-phase ozonolysis of propylene and *trans*-2-butene, Stedman *et al.*[1146] have observed stoichiometry of unity with both air and nitrogen as diluents. In this work, the ozone and olefin concentrations were in the parts-per-million range, suggesting that the failure to observe unity stoichiometry in the presence of oxygen in the earlier study[1259] may be due to a concentration effect.

Because the vapor-phase ozonolysis probably proceeds through an initial olefin–ozone adduct, it seems prudent to determine the influence of different inert carrier gases on the rate constant, inasmuch as the observed rate constant may depend on the deactivation ability of the carrier gas.

TABLE 3-12 Absolute Rate Constants for Vapor-Phase Reactions of Ozone with Aliphatic Hydrocarbons

Hydrocarbon	*k*, liters/mol-sec	*T*, K[a]	Reference
Ethylene	1.6×10^3	303	167,180
	0.8×10^3	RT	236
	1.8×10^3	RT	1260
	1.0×10^3	RT	400
	0.93×10^3	299	1146
	[b]	Various	304
1-Propene	4.9×10^3	RT	526
	3.8×10^3	303	180
	5.1×10^3[c]	RT	1260
	7.5×10^3	299	1146
	[d]	Various	304
1-Butene	6.2×10^3	—	167
	3.9×10^3	RT	1260
trans-2-Butene	260×10^3	303	167
	17×10^3	RT	1260
	165×10^3	299	1146
cis-2-Butene	200×10^3	303	167
	2.9×10^3	RT	526
	13×10^3	RT	1260
	$60\text{–}92 \times 10^3$	RT	400
Isobutylene	1.4×10^3	303	167
	3.7×10^3	RT	526
	3.6×10^3	RT	1260
	$5\text{–}14 \times 10^3$	RT	400
3-Methyl-1-butene	3.0×10^3	RT	1260
2-Methyl-1-butene	4.0×10^3	RT	1260
2-Methyl-2-butene	450×10^3	303	167
	12×10^3	RT	1260
Tetramethylethylene	14×10^3	RT	1260
Butadiene	4.2×10^3	RT	1260
1-Pentene	4.5×10^3	RT	526
	3.2×10^3	303	180
	3.9×10^3	RT	1260
cis-2-Pentene	10×10^3	RT	1260
trans-2-Pentene	13×10^3	RT	1260
1-Hexene	6.8×10^3	303	167
	6.1×10^3	RT	526
	6.1×10^3	303	180
	5.5×10^3	RT	1058
	4.6×10^3	RT	1260
	6.6×10^3	299	1146
1-Heptene	4.9×10^3	303	180
1-Octene	4.9×10^3	303	180
1-Decene	6.5×10^3	303	180
Acetylene	4.7×10^1	303	179

TABLE 3-12 *Continued*

Hydrocarbon	k, liters/mol-sec	T, K[a]	Reference
	[e]	Various	304
	5.18×10^{1}	298	1145
Styrene	18×10^{3}	303	167
Cyclohexene	35×10^{3}	303	180
	14×10^{3}	RT	1260
Tetrafluoroethylene	81×10^{3}	RT	546
Perfluoropropene	13×10^{3}	RT	546
Perfluoro-2-butene[f]	1.1×10^{3}	RT	546
α-Pinene	99×10^{3}	RT	1019
Methane	0.85×10^{-3}	312.5	1081
	0.82×10^{-3}	298	313
Ethane	7.4×10^{-3g}	298	875
	5.79×10^{-3h}	298	875
Propane	4.1×10^{-3}	312.5	1081
	4.3×10^{-3g}	298	875
	3.75×10^{-3h}	298	875
n-Butane	5.9×10^{-3}	310.5	1081
Isobutane	12.2×10^{-3}	310.5	1081

[a] RT = room temperature.

[b] $\log k(M^{-1}\,\text{sec}^{-1}) = (6.3 \pm 0.2) - (4.7 \pm 0.2)/2.3\,RT$.

[c] This and other absolute rate constants taken from Vrbaski and Cvetanović[1260] were obtained from relative values by adopting a value of 1.8×10^{3} liters/mol-sec for ethylene.

[d] $\log k(M^{-1}\,\text{sec}^{-1}) = (6.0 \pm 0.4) - (3.2 \pm 0.6)/2.3\,RT$.

[e] $\log k(M^{-1}\,\text{sec}^{-1}) = (9.5 \pm 0.4) - (10.8 \pm 0.4)/2.3\,RT$.

[f] *Cis–trans* mixture.

[g] Oxygen added.

[h] No oxygen added.

As shown in Table 3-12, when more than one measurement is available for a given olefin, the results are in fairly good agreement. It should be kept in mind, however, that all these results were obtained in the presence of oxygen. In some cases, the differences reported are more than an order of magnitude. Examples include *cis*- and *trans*-2-butene. The higher values were obtained by Bufalini and Altshuller.[167] Such large discrepancies appear to be restricted to 2-olefins. More recently, Altshuller and Bufalini[22] have suggested that this difference may be due to the low olefin concentrations (about $10^{-8}\,M$) used in their work, compared with the values of about $10^{-3}\,M$ used by Wei and Cvetanović.[1294] Studies over a wide range of olefin concentrations are needed to understand this apparent discrepancy further.

These discrepancies are pointed out further in Table 3-13, where the relative reactivities of various olefins are summarized. When absolute rate constants are compared (Table 3-12), trimethylethylene (2-methyl-2-butene) is seen to be about 300 times as reactive as ethylene, but their

TABLE 3-13 Relative Rate Constants for Vapor-Phase Reactions of Ozone with Aliphatic Hydrocarbons[a]

Olefin	Relative k_{O_2}[b]	Relative k_{N_2}[c]	Reference
Ethylene	0.51	—	1260
	0.32	0.21	1294
Propylene	1.41	—	1260
	1.30	0.95	1294
1-Butene	1.08	—	1260
	1.10	0.85	1294
1-Pentene	1.07	—	1260
	1.10	0.85	1294
1-Hexene	1.28	—	1260
	1.25	1.05	1294
3-Methyl-1-butene	0.84	—	1260
	0.95	0.75	1294
3-Methyl-1-pentene	0.90	0.75	1294
4-Methyl-1-pentene	1.15	0.85	1294
2-Methylpropene	1.00	—	1260
	1.00	1.00	1294
2-Methyl-1-butene	1.11	—	1260
	1.30	1.25	1294
2-Methyl-1-pentene	1.30	1.25	1294
trans-2-Butene	4.56	—	1260
	4.30	2.20	1294
cis-2-Butene	3.69	—	1260
	3.40	2.00	1294
trans-2-Pentene	3.50	—	1260
	4.20	2.70	1294
cis-2-Pentene	2.84	—	1260
	3.50	2.60	1294
Cyclohexene	3.74	—	1260
2-Hexene[d]	3.60	2.70	1294
4-Methyl-2-pentene	3.50	2.30	1294
2-Methyl-2-butene	3.24	—	1260
	3.50	3.20	1294
3-Methyl-2-pentene	3.40	3.20	1294
2-Methyl-2-pentene	3.40	3.20	1294
Tetramethylethylene	3.80	—	1260
	4.80[e]	5.50[e]	1294
Butadiene	1.15	—	1260

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[a] All experiments at 298 K.

[b] Relative rate constant in the presence of oxygen.

[c] Relative rate constant in the presence of nitrogen.

[d] *Cis–trans* mixture.

[e] Mean value from several competition experiments.

relative reactivities (Table 3-13) indicate that trimethylethylene is only about 10 times as reactive as ethylene.

Table 3-13 also shows that the relative rates in the presence of nitrogen have the same electrophilic trend as found in solution studies (i.e., increasing the number of alkyl substituents at the double bond generally increases the rate). A major departure from this trend is found in the cases of 1,1-dialkyl olefins, whose rates are generally lower than those for the corresponding 1,2-dialkyl olefins. If ozone electrophilicity were the controlling factor, these rates should be approximately the same. Wei and Cvetanović have suggested[1294] that this apparent discrepancy may be due to a greater steric hindrance to approach of the ozone in the 1,1-dialkyl cases. At any rate, the data do not seem to be consistent with an initial radical attack. When ozonolysis is carried out in the presence of oxygen, the variation from an electrophilic trend is even greater (Table 3-13).

As shown in Table 3-12, olefins are considerably more reactive than saturated hydrocarbons with ozone. However, ozone is only 10^{-5}–10^{-4} as reactive with ozone as is atomic oxygen. Because ozone is present in much higher concentrations than atomic oxygen, the olefin–ozone reactions are still very important in polluted atmospheres. These reactions will lead to consumption of olefin, with the production of a variety of substances (Table 3-11). They may also serve as sources of radical reactions. The available rate data suggest that reaction of ozone with saturated hydrocarbons is not likely to be significant as an atmospheric reaction.

The reaction of ozone with benzene derivatives in the vapor phase has received very little attention. Bufalini and Altshuller have reported[167] that the rate constant for the reaction of ozone with 1,3,5-trimethylbenzene is less than 0.06×10^3 liter/mol-sec when measured in the vapor phase. The kinetics of ozonization of a number of polyalkylbenzenes have been studied in solution by Nakagawa, Andrews, and Keefer.[905]

A review of the reaction of ozone with hydrocarbon derivatives of benzene has been given by Bailey.[66] The reaction appears to involve both 1,3-dipolar cyclo addition at a carbon–carbon double bond and electrophilic ozone attack at individual carbon atoms. A study[1310] of the rate of ozone attack on methyl-substituted benzenes reveals the following trend: benzene < toluene < xylene < mesitylene < hexamethylbenzene. The reaction thus follows a trend consistent with an electrophilic attack. The peroxidic products of these reactions have not been characterized. The ultimate products are the expected ones—glyoxal, methylglyoxal, biacetyl, etc.

4

Atmospheric Reactions of Organic Molecules with Nitrogen and Sulfur Oxides, Hydroxyl Radicals, and Oxygen Atoms

The main feature of the chemistry of photochemical smog is the conversion of nitric oxide to nitrogen dioxide in the atmosphere. A number of possible mechanisms for the conversion have been proposed. The oxidants considered include O·, ·OH, ·OOH, and singlet oxygen.[190,303] Singlet oxygen is not expected to contribute significantly to the process (see Chapter 3). Of the remaining possibilities mentioned, the intervention of ·OH radicals is discussed in some detail below. The chemistry of this conversion is not yet fully understood.

OZONE PRODUCTION

When mixtures of hydrocarbons and nitrogen oxides are subjected to ultraviolet radiation in air, oxidant is produced.[105] The course of such an irradiation is shown in Figure 4-1 for a propylene mixture of nitric oxide and propylene. Initially, nitrogen dioxide and aldehydes are produced as the reactants are consumed. As the nitric oxide is exhausted, the nitrogen dioxide concentration passes through a maximum; and as the nitrogen dioxide is consumed, ozone and other oxidants, such as peroxyacetylnitrate (PAN), are produced. Such compounds as nitric acid and nitrates must also be present to account for the nitrogen

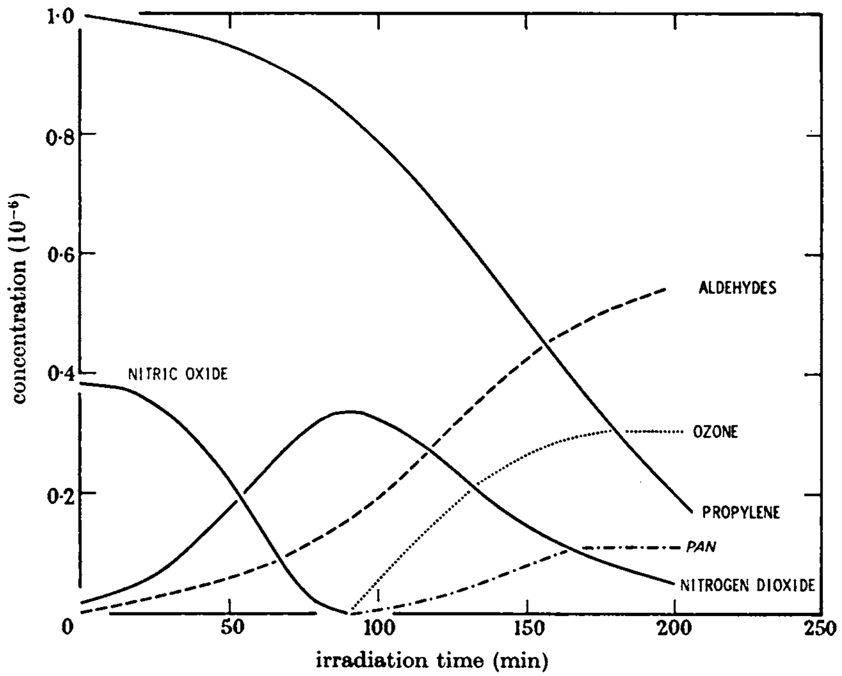

FIGURE 4-1 Typical concentration changes during ultraviolet irradiation of a propylene–nitric oxide mixture in air. PAN, peroxyacetylnitrate. (Reprinted with permission from Berry and Lehman.[105])

balance. It has been shown[711,738] that studies like that of Berry and Lehman[105] correlate with what happens in the atmosphere.

Most interestingly, although the reaction is imperceptibly slow in the dark, none of the initial gases (nitric oxide, propylene, oxygen, and nitrogen) absorbs the ultraviolet radiation (wavelength, >2900 Å). In fact, the absorbing species is nitrogen dioxide, and trace amounts of it must be present for the reaction to proceed. These are produced from a well-known, but slow, reaction (Reaction 1).[547]

$$2NO + O_2 \longrightarrow 2NO_2 \qquad (1)$$

The photochemical reaction is autocatalytic, and the nitrogen dioxide concentration rises at an increasing rate as long as sufficient nitric oxide is present.

The hydrocarbon–nitric oxide photooxidation has been studied in simulated atmospheres for several hydrocarbons and aldehydes.[24,319,465,466,689,709,1083] Measures of hydrocarbon reactivities have been based on the rates of hydrocarbon consumption and nitrogen dioxide production. Altshuller and Bufalini[22] have reviewed hydrocarbon reactivities. Hydrocarbons and aldehydes reported to be present in urban atmospheres (J. Garner, personal communication) are listed in Table 4-1, which includes for some the relative reactivity as calculated

TABLE 4-1 Reactivities of Some Hydrocarbons[a] Identified in Urban Air Sampling[b]

	Reactivity		Relative Rate Constant, per mol-sec	
Compound	Based on Hydrocarbons	Based on Nitric Oxide Oxidation	k_O	k_{OH}
Paraffins				
Methane	0.0[c]	—	6.2×10^{-7}[d]	0.00016[e]
Ethane	—	—	2.9×10^{-5}[d]	0.0047[f]
Propane	—	—	0.0072[g]	0.022[f]
Butane	—	—	0.0100[h]	0.049[e],0.063[i]
Isobutane	—	—	—	0.034[f]
n-Pentane	0.002[c]	—	—	—
Isopentane	0.002[c]	—	0.050[c]	—
2-Methylpentane	0.024[c]	<0.1[j]	—	—
3-Methylpentane	0.012[c]	<0.1[j]	—	—
Cyclohexane	0.004[c]	—	—	0.147[e]
2,3-Dimethylpentane	—	—	—	0.138[e]
Isooctane	0.30[c]	0.15[j]	0.44[h]	0.072[e]
Aromatics				
Benzene	—	0.15[j]	0.0016[k]	—
Toluene	0.30[l]	0.2[j]	0.0057[k]	—
o-Xylene	—	0.4[j],0.45[m]	—	—
m-Xylene	0.56[h]	1.0[j],0.90[m]	—	0.29[i]
p-Xylene	0.152[c],0.21[n]	0.4[j],0.45[m]	—	—
m-Ethyltoluene	—	0.90[m]	—	—
1,2,4-Trimethylbenzene	—	0.6[f],1.8[m]	—	—
1,3,5-Trimethylbenzene	—	1.2[j],2.4[m]	—	—
β-Methylstyrene	—	2.94[m]	—	—
Olefins				
Acetylene	—	0.1[j]	0.0095[q]	0.0029[s]
Ethylene	0.045[c],0.1[n]	0.4[k],0.49[p],0.54[m]	0.49[q],0.029[r]	0.079[s]
Propylene	0.57[c],0.73[n]	1[j],1.0[p]	0.19[q]	0.27[r]
1-Butene	0.44[c]	0.83[p]	0.25[q]	0.60[l]
cis-2-Butene	2.43[c],4.2[h]	2.0[f]	0.95[k]	0.94[i]
trans-2-Butene	4.05[c]	2[d],3.2[p]	1.13[k]	1.1[i]
Isobutene	1.0	1.0	1.0	1.0
1,3-Butadiene	0.80[c]	1.23[p]	0.97[k]	—

TABLE 4-1 *Continued*

Compound	Reactivity		Relative Rate Constant, per mol-sec	
	Based on Hydrocarbons	Based on Nitric Oxide Oxidation	k_O	k_{OH}
Olefins				
1-Pentene	0.50[f]	0.60[p]	—	—
cis-2-Pentene	—	1.54[p]	0.90[k]	} 1.4[i]
trans-2-Pentene	—	2.2[p]	—	
2-Methyl-1-butene	—	0.97[p]	—	—
2-Methyl-2-butene	2.70[f]	5.4[p]	3.17[k]	1.84[i]
3-Methyl-1-butene	—	0.77[p]	—	—
2-Methyl-1,3-butadiene	1.5[c]	1.05[p]	—	—
Cyclopentene	—	6.6[p]	1.19[k]	—
1-Hexene	—	0.49[p]	0.26[k]	—
trans-2-Hexene	—	1.71[p]	—	—
cis-3-Hexene	3.5[n]	—	—	—
trans-3-Hexene	—	1.68[p]	—	—
2-Methyl-1-pentene	—	0.66[p]	—	—
cis-4-Methyl-2-pentene	—	0.92[p]	—	—
trans-4-Methyl-2-pentene	—	1.28[p]	—	—
Aldehydes				
Formaldehyde	—	0.80[m]	0.023[t]	0.24[i]
Acetaldehyde	—	1.34[m]	0.025[k]	0.24[r]
Acrolein	—	0.86[m]	—	—
Propionaldehyde	—	2.26[m]	—	0.47[t]
Butyraldehyde	—	1.48[m]	—	—
Crotonaldehyde	—	1.20[m]	—	—
Benzaldehyde	—	0.15[m]	—	—
o-Tolualdehyde	—	6.06[m]	—	—
m-Tolualdehyde	—	0.23[m]	—	—
n-Tolualdehyde	—	0.18[m]	—	—

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[a] The compounds reported to be present in urban air (J. Garner, personal communication).
[b] Based on a relative reactivity of 1.0 for isobutene.
[c] Derived from Schuck and Doyle.[1063]
[d] Derived from Herron;[558] based on $k = 4.0 \times 10^9$ mol-sec for 1-C_4H_8.[596]
[e] Derived from Greiner,[492] assuming relative rate coefficient = 0.022 for C_3H_8.
[f] Derived from Greiner.[491]
[g] Derived from Saunders and Heicklen,[1068] assuming relative $k = 0.25$ for 1-C_4H_8.
[h] Derived from Herron and Huie;[562] based on $k = 4.0 \times 10^9$ mol-sec for 1-C_4H_8.[596]
[i] Derived from Morris and Niki.[871]
[j] Derived from Altshuller and Cohen.[24]
[k] Derived from Cvetanović.[273]
[l] Derived from Kopczynski,[709] assuming C_6H_6 reactivity = 0.15.
[m] Derived from Dimitriades and Wesson,[319] assuming C_3H_6 reactivity = 1.0.
[n] Derived from Stephens and Scott.[1159]
[o] Derived from Breen and Glass.[143]
[p] Derived from Glasson and Tuesday.[465]
[q] Derived from Atkinson and Cvetanović.[50]
[r] Derived from Morris *et al.*[872]
[s] Derived from Greiner.[493]
[t] Derived from Morris and Niki,[870] assuming relative $k = 0.025$ for CH_3CHO.

by one or both methods. Arbitrarily, isobutene is considered to have a relative reactivity of 1.0.

The two scales give similar results. Reactivity can be associated with structure. The paraffins are the least reactive. Except for isooctane, their relative reactivities are less than 0.1, and often much less. The aromatics have reactivities from 0.15 for benzene to more than 2 for some highly substituted benzenes. Most of the olefins have reactivities of about 0.5–2.2, although cyclopentene has a value of 6.6. The relatively high value of 2.94 for β-methylstyrene can be attributed to its being both aromatic and olefinic. The aldehyde reactivities cover the same range as those of the aromatics, except for the surprisingly high reactivity of *o*-tolualdehyde.

It seems reasonable to assume that the reactivity of a hydrocarbon is related to its rate coefficient for reaction with some active species in photochemical smog that reacts readily with hydrocarbons. Such species include $O(^3P)$ and HO radicals. Ozone is a product of the reaction and does not appear until the reaction is well advanced. Thus, it is probably not as important as oxygen or OH·, although it reacts readily with hydrocarbons. Other conceivable intermediates, such as peroxy and alkoxy radicals, are removed so much faster by other routes than by hydrocarbon attack that their role can be only minor. The same is true of photoexcited aldehydes and ketones. Nitric oxide and nitrogen dioxide react too slowly with hydrocarbons to be important. Photoexcited nitrogen dioxide may be quenched readily by hydrocarbons, but no report of chemical interaction has appeared.

The relative reactivities of the compounds with $O(^3P)$ and HO are also listed in Table 4-1. Not all the available data on any compound are included, but only the most likely value. For $O(^3P)$, the results from Cvetanović's[273] and Herron's[558,562,596] laboratories have been preferred. Both have made extensive studies and are therefore experienced; and any errors in values are likely to be internally consistent, so the relative values from a given laboratory may be correct, even if the absolute values are not. This is not to imply that other studies are less accurate. In fact, the differences in values among several laboratories are usually less than 50%. For HO radicals, the values of Greiner[491–493] are preferred, for the same reasons noted for $O(^3P)$ atoms.

For both $O(^3P)$ and HO, the reactivity of the hydrocarbon follows the same trends as the photochemical reactivity, although the detailed fit is not all that one might have expected. For methane and ethane, the reactivities are very small, but the other paraffin reactivities with $O(^3P)$ and HO, although still small, are larger than the photochemical reactivities. With the aromatics, the reverse seems to be the case, but the measurements are sparse. With the olefins, reasonably good matches are obtained in all cases except cyclopentene, which has an abnormally large photochemical reactivity. With the aldehydes, the data are again sparse, but the HO and O(^{3}P) reactivities are lower by factors of about 4 and 40, respectively, than the photochemical reactivities. Thus, it can be concluded that, in a general way, photochemical reactivity is associated with the reactivity toward O(^{3}P) or HO, but that the detailed correlation must be considerably more complex. Further evidence that some species in addition to O(^{3}P) and HO are attacking hydrocarbons comes from the work of Bufalini and Altshuller[168] and others,[27,923] who noticed synergistic effects when two hydrocarbons were photooxidized simultaneously.

OXIDATION OF NITRIC OXIDE

A mechanism for the photochemical conversion of nitric oxide to nitrogen dioxide in urban atmospheres has been proposed by Heicklen *et al.*[544,548] in which HO radical is the important chain carrier. With alkanes, the initiating reaction is HO radical attack to remove a hydrogen atom. For example, with butane, the sequence proposed was that presented in Reactions 2–6. Reaction 7 depicts the overall reaction. It should be noted that HO· is regenerated in Reaction 6 and can thus reinitiate the sequence.

$$C_4H_{10} + HO\cdot \longrightarrow C_4H_9\cdot + H_2O \tag{2}$$

$$C_4H_9\cdot + O_2 \longrightarrow C_4H_9O_2\cdot \tag{3}$$

$$C_4H_9O_2\cdot + NO \longrightarrow C_4H_9O\cdot + NO_2 \tag{4}$$

$$C_4H_9O\cdot + O_2 \longrightarrow C_3H_7CHO + HO_2\cdot \tag{5}$$

$$HO_2\cdot + NO \longrightarrow HO\cdot + NO_2 \tag{6}$$

$$C_4H_{10} + 2NO + 2O_2 \longrightarrow C_3H_7CHO + H_2O + 2NO_2 \tag{7}$$

With olefins, the scheme is slightly modified; HO· adds to the double bond, rather than abstracting hydrogen. Thus, for isobutene, the sequence might be as given in Reactions 8–14.

$$C_4H_8 + HO\cdot \longrightarrow HOC_4H_8\cdot \tag{8}$$

$$HOC_4H_8\cdot + O_2 \longrightarrow HOC_4H_8O_2\cdot \tag{9}$$

$$HOC_4H_8O_2\cdot + NO \longrightarrow HOC_4H_8O\cdot + NO_2 \tag{10}$$

$$HOC_4H_8O^{\cdot} \longrightarrow HOCH_2^{\cdot} + (CH_3)_2CO \quad (11)$$

$$HOCH_2^{\cdot} + O_2 \longrightarrow HOCH_2O_2^{\cdot} \quad (12)$$

$$HOCH_2O_2^{\cdot} + NO \longrightarrow HOCH_2O\cdot + NO_2 \quad (13)$$

$$HOCH_2O^{\cdot} \longrightarrow HO^{\cdot} + CH_2O \quad (14)$$

The overall reaction is shown as Reaction 15, which conforms to the findings of Schuck and Doyle,[1083] who observed that formaldehyde and dimethylketone were the major products of the photochemical oxidation of isobutene in the presence of nitric oxide.

$$C_4H_8 + 2NO + 2O_2 \longrightarrow (CH_3)_2CO + CH_2O + 2NO_2 \quad (15)$$

With aromatic compounds, the cycle is probably similar to that with olefins. The aldehydes should behave like the alkanes, but with a slight modification. For example, with acetaldehyde, the first few steps would proceed as Reactions 16 and 17.

$$CH_3CHO + HO^{\cdot} \longrightarrow CH_3\dot{C}O + H_2O \quad (16)$$

$$CH_3\dot{C}O + O_2 \longrightarrow CH_3O^{\cdot} + CO_2 \quad (17)$$

From Reaction 17, the sequence would proceed as in Reactions 5 and 6. Reaction 17 may not be a fundamental reaction, but may occur in several steps.

The implication of the above schemes is that carbon monoxide must also oxidize nitric oxide (Reactions 18, 19, and 6).

$$HO\cdot + CO \longrightarrow H\cdot + CO_2 \quad (18)$$

$$H\cdot + O_2 + M \longrightarrow HO_2^{\cdot} + M \quad (19)$$

$$HO_2^{\cdot} + NO \longrightarrow HO\cdot + NO_2 \quad (6)$$

Confirmation of the influence of carbon monoxide has been given several times in recent years. The first report was by Glasson,[464] who examined an atmosphere with 2-ppm ethene and 1-ppm nitric oxide. The addition of 400-ppm carbon monoxide doubled the rate of nitrogen dioxide production. Because the rate constant for HO· attack on ethylene[493,872] is 1–3 × 10^{10}/mol-sec and that for HO· attack on carbon monoxide[87] is 8.0 × 10^7/mol-sec, the relative reactivity between ethylene and carbon monoxide should be between 125 and 375. Because 200 times as much carbon monoxide as ethylene was used in Glasson's experiment, the expected rate of nitric oxide oxidation on the addition of carbon monoxide would be between 1.6 and 2.9 times that in its absence—in excellent agreement with the observed result. The effect of carbon monoxide with other hydrocarbons has been confirmed.[1307]

Simultaneously with the reports of Heicklen *et al.*,[544,548] Weinstock and his collaborators[1298] were using a very similar mechanism to do a complete computer study on propylene photooxidation. They estimated the chain length (number of nitric oxide molecules converted to nitrogen dioxide molecules per photochemical initiation step) to be about 280 and the lifetime of the HO radical to be 56 sec. Detailed computer studies have also been made by Westberg and Cohen[1305,1306] and Hecht and Seinfeld.[542]

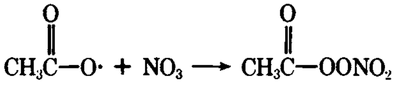
It is interesting to compare the estimated chain length of 280 with known rate coefficients for the reactions of HO· with propylene and nitric oxide. For the HO·–propylene reaction, the room-temperature rate coefficient[872,1118] is 10^{10}/mol-sec. Let us assume that three nitric oxide molecules are converted to nitrogen dioxide molecules during each chain cycle (one conversion per carbon atom in propylene). Then, to reach a chain length of 280, the rate coefficient for HO· removal by nitric oxide should be about 10^{8}/mol-sec. The estimated coefficient is at least 10 times this value.[868,1117,1172] Part of this discrepancy can be explained by the fact that the product of the HO·–nitric oxide interaction is nitrous acid, which photolyzes to reproduce HO· and nitric oxide; thus, the effective removal coefficient is lower. However, a chain length of 280 seems to be too large, given the known rate coefficient data.

The reaction steps outlined above were in some cases well established, but in other cases speculative. Reactions 2, 3, 16, 18, and 19 were certain. Some evidence existed for Reaction 5 with CH_3O and C_2H_5O radicals[545] and for Reaction 6 at high temperatures.[49,1218] Reactions 8–14 were all speculative and, except for Reaction 8, still are. The details and even the validity of Reaction 17 are still unknown.

Reaction 8 has now been verified for ethylene and propylene by Morris *et al.*[872] Studies have been undertaken by Heicklen and collaborators to verify Reactions 4–6. For CH_3O radicals, they have found[1311] that, at 25 C, the relative reactivities of CH_3O with oxygen, nitrogen dioxide, and nitric oxide are 4.7×10^{-5}, 0.83, and 1.0, respectively. Thus, under atmospheric conditions, the reaction with oxygen is at least 5 times as important as that with the oxides of nitrogen. Wiebe *et al.*[1311] also found that the principal fate of $HO_2\cdot$ was Reaction 6. The rate constant for this reaction has been reported[646] to be 1.2×10^{6}/mol-sec. This is not a large rate constant, but Reaction 6 still must be the dominant fate of $HO_2\cdot$ in the atmosphere. A more recent report[1117] indicates that this rate constant is greater than 10^{8}/mol-sec.

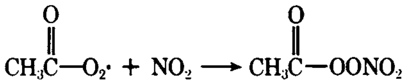
Spicer *et al.*[1140] examined the reaction of $CH_3O_2\cdot$ with nitric oxide and nitrogen dioxide in an attempt to verify Reaction 4. In neither case was CH_3O produced. The initial products were either the adduct peroxy compounds, peroxymethylnitrite and peroxymethylnitrate, or formaldehyde and nitric and nitrous acids. These reactions can thus explain the production of peroxy compounds and acids, but present a dilemma for the mechanism of the conversion of nitric oxide to nitrogen dioxide. It is not necessary that hydrocarbon peroxy radicals react with nitric oxide to produce nitrogen dioxide; that can be done by $HO_2\cdot$ via Reaction 6. However, it is essential that alkoxy radicals be formed. At the moment, this dilemma is unresolved, although Spicer *et al.* point out that the later photodecomposition of the peroxy nitrates and nitrites might produce alkoxy radicals. Thermal decomposition also would have the same effect.

In regard to peroxynitrate formation, particularly peroxyacetylnitrate (PAN), Hanst[522] has offered an interesting proposal. He suggests that PAN could be produced by Reaction 20,



$$CH_3\overset{\overset{O}{\|}}{C}-O\cdot + NO_3 \longrightarrow CH_3\overset{\overset{O}{\|}}{C}-OONO_2 \tag{20}$$

rather than (or in addition to) Reaction 21.



$$CH_3\overset{\overset{O}{\|}}{C}-O_2\cdot + NO_2 \longrightarrow CH_3\overset{\overset{O}{\|}}{C}-OONO_2 \tag{21}$$

His arguments reduce to three: (1) PAN formation is delayed past the onset of nitrogen dioxide formation and correlates with ozone production (see Figure 4-1); because nitrogen trioxide is produced from the ozone–nitrogen dioxide reaction, it is the precursor to PAN formation. (2) PAN is readily synthesized in the dark thermal reaction between acetaldehyde, oxygen, and nitrogen pentoxide, as shown by Tuesday.[1212] (3) PAN formation correlates with the nitrogen trioxide and not the nitrogen dioxide concentration.

Although Hanst's proposal is intriguing, it has weaknesses. The delay in PAN production can be attributed to the delay in acetaldehyde production, inasmuch as acetaldehyde is a necessary precursor to PAN. Also, although it is true that there is no explanation for PAN production in the dark thermal reaction between acetaldehyde, oxygen, and nitric oxide via Reaction 21, it is also true that there is no explanation of how the dark reaction leads to Reaction 20. Nevertheless, Hanst's proposal deserves attention, and further investigation is warranted.

The chain termination and initiation steps for the conversion of nitric oxide to nitrogen dioxide may be numerous. Principally, termination may involve reaction of HO, alkoxy, and alkylperoxy radicals. However, termination by these processes would be slower than the reaction rate constants indicate, because the products can be photolyzed to regenerate the radicals.

Initiation occurs as a result of the nitrogen dioxide photolysis to produce nitric oxide and $O(^3P)$. Most of the time, the oxygen atom reacts with oxygen to produce ozone. Occasionally, however, $O(^3P)$ reacts with a hydrocarbon. With alkanes and aldehydes, hydrogen atom abstraction results, and $HO\cdot$ is produced directly. With olefins, the initial product is an excited epoxide that can rearrange to an excited aldehyde or decompose to free radicals. If the excited aldehyde does not decompose to radicals, but is stabilized by collision, it can photodecompose to produce free radicals; these free radicals then enter the nitric oxide oxidation mechanism, and the chain is initiated.

Although an increase in hydrocarbon content increases oxidant production, an increase in the concentration of the oxides of nitrogen can either increase or decrease oxidant production. This effect was first reported by Haagen-Smit and Fox[505] and has since been substantiated with many hydrocarbons.[23,28–30,467,504,1031,1158,1211,1212] In one of the most recent studies, Glasson and Tuesday[467] reported this effect for several hydrocarbons. In particular, they found that for propylene and *m*-xylene the maximal rate of oxidation occurred for hydrocarbon:nitric oxide ratios of about 6:1 and about 1.5:1, respectively.

Perhaps the most dramatic demonstration of the nitric oxide inhibition was shown by Dimitriades.[314,315] He examined the reactivity of exhaust in an irradiated atmosphere. Because several hydrocarbons were present, the effective hydrocarbon concentration was computed on a per-carbon basis by summing over the products of the concentration and relative reactivity of each hydrocarbon. The measure of reactivity was the oxidant dosage, i.e., the product of the oxidant concentration and its time of existence. The results are shown in Figure 4-2. It can be seen that the oxidant dosage increases regularly with the hydrocarbon concentration at any concentration of the oxides of nitrogen; but for any hydrocarbon concentration, the oxidant dosage drops as the nitrogen oxide is increased. The effect for mixtures at a constant hydrocarbon:nitrogen oxide ratio is shown in Figure 4-3. For ratios below about 4:1, the oxidant dosage actually drops as the pollutants increase! The implication is that, if an automobile exhaust consists of hydrocarbons and oxides of nitrogen in an effective ratio of less than 4:1, reducing the exhaust pollutants will actually increase the oxidant dosage!

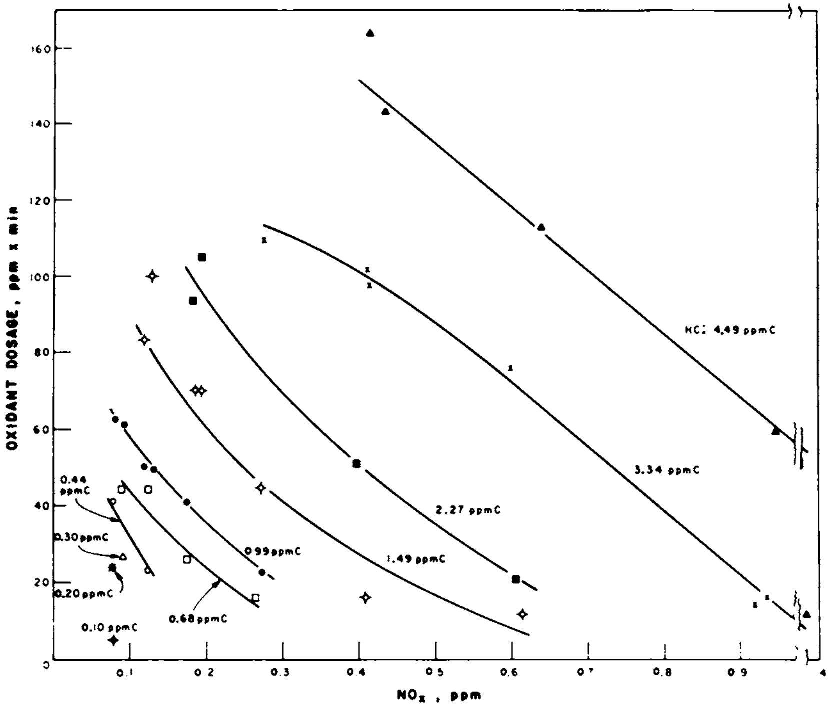


FIGURE 4-2 Oxidant-dosage reactivity of exhaust as a function of nitrogen oxide (NO_x) concentration at various hydrocarbon concentrations (HC). (Reprinted from Dimitriades.[315])

The effect of nitric oxide is easily explained. In the conversion of nitric oxide to nitrogen dioxide, nitric oxide is not involved in the chain-initiating step, but it is important in removing radicals in the termination steps. Its role in propagation is to react with $RO_2\cdot$ or $HO_2\cdot$. However, once enough nitric oxide is present to scavenge these radicals, further increases in its concentration lead to competition between nitric oxide and hydrocarbons for the HO radicals and between nitric oxide and oxygen for the alkoxy radicals. When either HO or alkoxy radicals react with nitric oxide, termination of the chain results.

An additional effect of excess oxides of nitrogen is to remove ozone by direct reaction. The ozonation of nitric oxide gives nitrogen dioxide, which when ozonized gives nitrogen pentoxide and ultimately nitric acid in the presence of water.

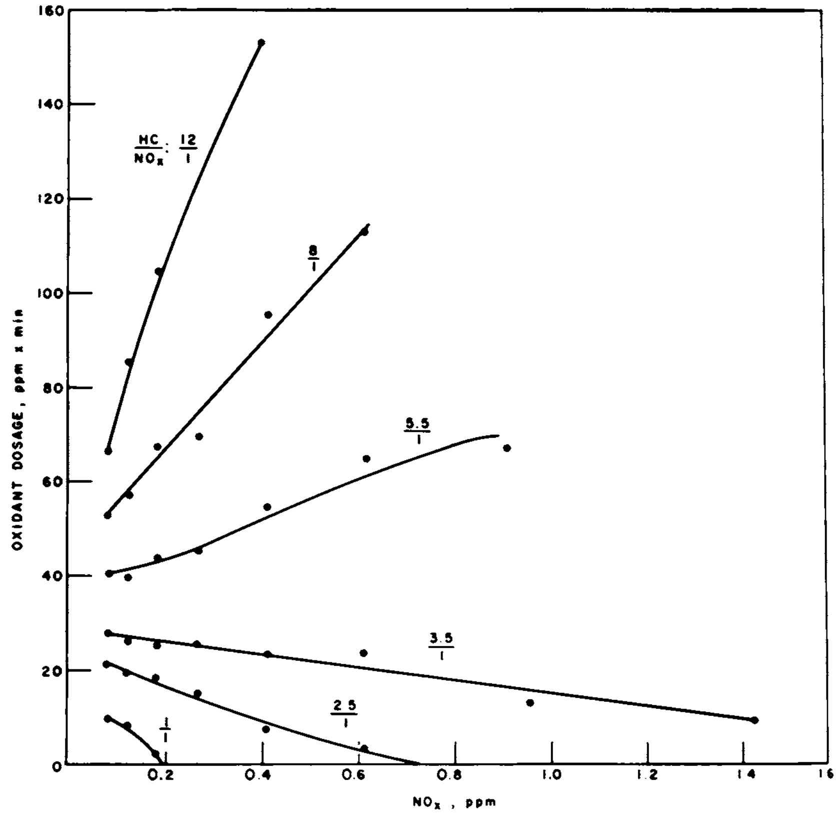


FIGURE 4-3 Oxidant-dosage reactivity of exhaust as a function of nitrogen oxide (NO_x) concentration at various hydrocarbon:nitrogen oxide concentration ratios. (Reprinted from Dimitriades.[315])

REACTION OF NITROGEN DIOXIDE WITH OLEFINS

Cottrell and Graham were first to report that nitrogen dioxide can react with olefins in the vapor phase.[252,253] At high temperatures, nitrogen dioxide reacted with ethylene[252] and propylene[253] by a rate law that was approximately second-order in nitrogen dioxide and first-order in hydrocarbon pressure. The Arrhenius parameters for the rate coefficient changed with temperature, but the activation energies were sufficiently large (greater than 12 kcal/mol) that the reaction is not of principal importance in urban atmospheres. They proposed the sequence of Reactions 22 and 23.

$$NO_2 + \text{olefin} \rightleftharpoons \text{adduct} \qquad (22)$$

$$NO_2 + \text{adduct} \longrightarrow \text{products} \qquad (23)$$

With ethylene, the products were almost entirely carbon dioxide, carbon monoxide, and nitric oxide. Also produced were an oil and a small amount of carbon-like material. The addition of nitric oxide or air had no effect, nor did changing the surface:volume ratio. With propylene, the results were similar, except that the reaction was 3–4 times faster.

Support for the above mechanism comes from the fact that free-radical products resulting from the addition have been observed by electron-spin resonance in condensed phases.[654,1182] It is also known that nitrogen dioxide can induce *cis–trans* isomerization of unsaturated compounds in the liquid phase. However, the first study of the vapor-phase isomerization appears to be very recent. Sprung *et al.* have measured the rate coefficient for the nitrogen dioxide-catalyzed isomerization of *cis*-butene-2,[1142] *trans*-butene-2 (J. L. Sprung, personal communication), and *cis*- and *trans*-pentene-2 (J. L. Sprung, personal communication). They found the rate law to be first-order in both nitrogen dioxide and olefin pressure, as expected from the above mechanism. Again, their rate constants are much too small for this reaction to be of principal importance in urban atmospheres.

The reaction of several olefins with nitrogen dioxide at 25–100 C was studied by Jaffe,[627] whose results were very different from those of the other investigators. He found the reaction to be first-order in both nitrogen dioxide and olefin pressure and the activation energies to be between 4 and 8 kcal/mol. He proposed that the initial step was the transfer of an oxygen atom to give excited aldehydes and epoxides, which reacted further to give the observed products—nitric oxide, carbon dioxide, nitrous oxide, water, methylnitrite, methylnitrate, dimethyl ester, and acetaldehyde.

The reaction of nitrogen dioxide with *trans*-butene-2 was studied in both the absence and presence of oxygen.[864] In both cases, a liquid product was found, but the kinetics of the reaction were different. In the absence of oxygen, the product is presumably the addition compound formed from the olefin with two molecules of nitrogen dioxide, i.e., the dinitro or nitro–nitrite compound. However, with excess oxygen, the initial adduct appears to add to oxygen before reacting with the second nitrogen dioxide molecule, suggesting a nitroperoxynitrate product.

Although there are discrepancies in the results from the various laboratories, it is clear that nitrogen dioxide does react with olefins, but not fast enough to be of major consequence in urban atmospheres. As far as we know, no one has reported chemical reaction between electronically excited nitrogen dioxide and hydrocarbons.

REACTIONS OF SULFUR DIOXIDE

Sulfur dioxide is an important air pollutant in some urban atmospheres, such as those of New York, Philadelphia, and Chicago. Not only is it harmful in itself, but it can undergo oxidation to produce the more toxic sulfur trioxide and sulfuric acid. It may react with zwitterions and oxygenated radicals, although almost nothing is known about such reactions. It is known that methyl radicals add to sulfur dioxide,[192] but this reaction is probably not important in the atmosphere, where alkyl radicals are readily scavenged by oxygen.

The possible reactions of sulfur dioxide and nitric oxide with zwitterions, R^+OO^-, are of considerable interest. These zwitterions are probably produced in the reaction of ozone with olefins, as discussed elsewhere. Presumably, the zwitterion rearranges most of the time, but other reactions are possible. Of pertinence here is the possibility of reaction with either nitric oxide (Reaction 24) or sulfur dioxide (Reaction 25), where RO is a stable aldehyde or ketone, and not a free radical. There is no evidence to support or refute Reaction 24; if it occurred, however, it could regenerate nitrogen dioxide. There is evidence of Reaction 25. Cox and Penkett[255] reacted ozone with *cis*-2-pentene in the presence of sulfur dioxide and moist air. In the dark, a rapid conversion of sulfur dioxide to sulfuric acid aerosol occurred, suggesting Reaction 25 followed by hydration of sulfur trioxide.

$$R^+OO^- + NO \longrightarrow RO + NO_2 \tag{24}$$

$$R^+OO^- + SO_2 \longrightarrow RO + SO_3 \tag{25}$$

The influence of sulfur dioxide on photochemical smog has been the subject of a recent extensive review.[169] Therefore, the work will not be discussed in detail here. In summary, the rate of disappearance of sulfur dioxide and the formation of aerosol increase when sulfur dioxide is photolyzed in the presence of olefinic hydrocarbons and the oxides of nitrogen.

Mixtures of sulfur dioxide, saturated and unsaturated hydrocarbons, nitrogen dioxide, and water do not react in the dark. However, if powdered oxides of aluminum, calcium, chromium, iron, lead, or vanadium are present, reaction occurs readily in the dark.[1231] In the same study,[1231] it was also noticed that, in the absence of the metal oxides, the photochemical oxidation of sulfur dioxide was noticeably faster in the presence of hydrocarbon and nitrogen dioxide than in their absence.

Wilson *et al.*[1337] reported an interesting study in which several hydrocarbons were photooxidized in the presence of sulfur dioxide and the oxides of nitrogen under atmospheric conditions. Although sulfur dioxide does not react with the hydrocarbon, ozone, nitric oxide, and nitrogen dioxide, its presence reduced the nitrogen dioxide concentration in the photolysis. Presumably, the reactions of sulfur dioxide with $O(^3P)$ and nitrogen trioxide are responsible for the inhibition. The oxidant production depended on the concentrations of water vapor, nitrogen dioxide, and sulfur dioxide. In the case of 1-butene, 1-heptene, and isooctane, oxidant was reduced by adding sulfur dioxide; in the case of toluene, the oxidant was enhanced.

Studies of the effect of sulfur dioxide in irradiated automobile exhausts were made by Wilson *et al.*[1336] They found that the addition of sulfur dioxide increased aerosol formation, but produced a decrease in eye irritation with many of the hydrocarbon–nitrogen oxide systems studied. These results are particularly intriguing, in that they showed that the photochemical aerosols generated from 1-heptene and nitrogen oxides in the absence of sulfur dioxide cause eye irritation, whereas the sulfuric acid aerosol produced in the photooxidations of sulfur dioxide in clean wet air did not cause eye irritation. It is clear that the role of sulfur dioxide in photochemical smog is complex and not well understood.

Sulfur dioxide absorbs radiation that enters the lower atmosphere. Weak absorption occurs below 3900 Å to a triplet state, whereas a much stronger absorption takes place below 3400 Å. The latter absorption band peaks at about 2900 Å, the cutoff for radiation entering the lower atmosphere.

The primary photophysical processes in sulfur dioxide when excited into the absorption band centered at about 3000 Å have been studied in detail for about a decade. These studies include the excellent work of Duncan and his co-workers,[208,490] Strickler and Howell,[1169] Mettee,[849,851] and Calvert and his co-workers.[236,942,993,994] The details of the primary process have been elucidated through lifetime measurements of emission, fluorescence, and phosphorescence yields during steady-state exposure and through biacetyl sensitization. The mechanism resulting from these studies is presented in Reactions 26–29.

$$^1SO_2 + SO_2 \longrightarrow 2SO_2 \qquad (26a)$$

$$^1SO_2 + SO_2 \longrightarrow {}^3SO_2 + SO_2 \qquad (26b)$$

$$^1SO_2 \longrightarrow SO_2 + h\nu_f \qquad (27a)$$

$$^1SO_2 \longrightarrow SO_2 \qquad (27b)$$

$$^1SO_2 \longrightarrow {}^3SO_2 \qquad (27c)$$

$$^3SO_2 \longrightarrow SO_2 + h\nu_p \qquad (28a)$$

$$^3SO_2 \longrightarrow SO_2 \qquad (28b)$$

$$^3SO_2 + SO_2 \longrightarrow 2SO_2 \qquad (29a)$$

$$^3SO_2 + SO_2 \longrightarrow SO_3 + SO \qquad (29b)$$

The superscripts 1 and 3 refer to excited singlet and triplet states, respectively. Rate constants have been determined for all the steps.

Furthermore, Thrush and his co-workers[513–516,832,1196] studied the emission of sulfur dioxide from the reactions of sulfur oxide with ozone or oxygen atoms. Their results are consistent with the above mechanism, except for minor discrepancies.[235]

Electronically excited sulfur dioxide is also known to react with oxygen to produce sulfur trioxide, although the quantum yield is small and the details of the process are not known.[758,1101] The quantum yield is too small to account entirely for the oxidation of sulfur dioxide to sulfur trioxide in urban atmospheres.[15] However, a more recent study suggests that sulfur trioxide does not form to any extent from reactions of excited sulfur dioxide with oxygen, water, or both.[440]

Dainton and Ivin[277,278] studied the photolysis of sulfur dioxide in the presence of several paraffins and olefins. The principal products were sulfinic acids. The quantum yields were independent of sulfur dioxide pressure, but increased with the hydrocarbon pressure to a maximum of about 0.35. A negative temperature coefficient was found between 15 and 100 C.

Aerosols have been seen when sulfur dioxide was irradiated in the presence of hydrocarbons,[647] and aerosol formation is enhanced in air[647,710] when sulfur dioxide is present.

More recently, Timmons[1199] has reexamined the photolysis of sulfur dioxide in the presence of alkanes. When isobutane was the added gas, he found that, for a sulfur dioxide pressure of 20 torr, the total quantum yield first increased with isobutane pressure and then became constant at approximately 0.090 for isobutane pressures above 200 torr. The addition of excess methane had almost no effect on the quantum yield. The negative temperature coefficient reported by Dainton and Ivin was confirmed.

Timmons[1199] also made a limited study of the photolysis of sulfur dioxide in the presence of carbon monoxide. For four runs at 25 C and

$[SO_2] = 20$ torr, he found that carbon dioxide was produced with a quantum yield increasing from 5.2×10^{-3} at 21 torr of carbon monoxide to 7.4×10^{-3} at 420 torr. A negative temperature coefficient was also found for this reaction.

Heicklen and co-workers[137,212] have studied the chemical reactions of electronically excited sulfur dioxide. In their first studies, done at 3130 Å, they examined the photolysis in the presence of carbon monoxide and in the presence of perfluoroethylene. With carbon monoxide, carbon dioxide was produced, although the quantum efficiency was small. However, the quantum yield of carbon dioxide, $\Phi\{CO_2\}$, increased proportionately with carbon monoxide pressure, but was independent of sulfur dioxide pressure at high sulfur dioxide pressures. Such a result is contrary to expectations based on the mechanism deduced from the light-emission studies, which require that $\Phi\{CO_2\}$ be a function of $[CO]/[SO_2]$. Furthermore, it was found that the addition of an atmosphere of nitrogen did not alter $\Phi\{CO_2\}$. Because the emitting sulfur dioxide states are readily quenched by nitrogen,[850] this observation also cannot be explained by the light-emission measurements.

With perfluoroethylene, the photoreaction proceeds readily to produce carbonylfluoride, cyclic perfluoropropylene, and polymer. At high C_2F_4 pressures, $\Phi\{CF_2O\}$ is approximately 0.05. Again, the addition of a large excess of nitrogen had no effect on the reaction.

At the pressures of sulfur dioxide used in these studies (i.e., at least 1 torr), Reactions 27 and 28 are unimportant,[849,993,1169] and the mechanism involving the emitting states reduces to the following sequence: Reactions 26a, 26b, 29a, and 29b.

$$^1SO_2 + SO_2 \longrightarrow 2SO_2 \tag{26a}$$

$$^1SO_2 + SO_2 \longrightarrow {}^3SO_2 + SO_2 \tag{26b}$$

$$^3SO_2 + SO_2 \longrightarrow 2SO_2 \tag{29a}$$

$$^3SO_2 + SO_2 \longrightarrow SO_3 + SO \tag{29b}$$

The steady-state concentrations of the excited states are inversely proportional to $[SO_2]$. If these states reacted with carbon monoxide or C_2F_4 to produce products, then the quantum yields of product formation should depend on the sulfur dioxide pressure. This expectation has been confirmed for $^3SO_2$ by the results of Jackson and Calvert[621] in the $^3SO_2$–carbon monoxide system.

The above results, as well as those of Dainton and Ivin,[277] show that the product quantum yields are independent of sulfur dioxide pressure at high sulfur dioxide pressures. The addition of nitrogen, a known quencher of both sulfur dioxide fluorescence and phosphorescence,[850] did not eliminate chemical reaction with either carbon monoxide, perfluoroethylene, or *n*-butane. The results of Timmons[1199] showed that excess methane, another known quencher of both sulfur dioxide fluorescence and phosphorescence,[850] did not eliminate chemical reaction. Finally, some recent experiments of McQuigg and Allen[840] have shown that sulfur dioxide is removed when irradiated at 3130 Å in the presence of oxygen. The quantum yield of sulfur dioxide disappearance was 7×10^{-3} and was independent of reactant pressures (oxygen, 20–400 torr; sulfur dioxide, 20–200 torr) or the addition of nitrogen or carbon dioxide.

It is clear that the electronic states predominantly involved in chemical reaction when sulfur dioxide is irradiated at 3130 Å must be different from the emitting states. Furthermore, results with the addition of small amounts of nitric oxide or biacetyl (two known triplet-quenchers) show that the reaction is inhibited, but not eliminated. Thus, two (or more) new states must be involved, one a singlet and one a triplet.

Cehelnik *et al.*[212] proposed a mechanism consistent with the known facts. For pure sulfur dioxide, the mechanism envisioned is depicted by Reactions 26b, 26c, 29a, 29b, and 30–32:

$$^1SO_2 + SO_2 \longrightarrow {}^3SO_2 + SO_2 \qquad (26b)$$

$$^1SO_2 + SO_2 \longrightarrow SO_2^* + SO_2 \qquad (26c)$$

$$^3SO_2 + SO_2 \longrightarrow 2SO_2 \qquad (29a)$$

$$^3SO_2 + SO_2 \longrightarrow SO_3 + SO \qquad (29b)$$

$$SO_2^* \longrightarrow SO_2^{**} \qquad (30)$$

$$SO_2^* + SO_2 \longrightarrow SO_2^{**} + SO_2 \qquad (31)$$

$$SO_2^{**} \longrightarrow SO_2 \qquad (32)$$

As noted above, $^1SO_2$ and $^3SO_2$ are, respectively, the singlet and triplet states that emit radiation; SO_2^* and SO_2^{**} are, respectively, the singlet and triplet states that do not emit radiation. In this mechanism, Reaction 26a of the previous mechanism has been replaced by Reaction 26c. Reactions 27 and 28 have been omitted, because they are unimportant at atmospheric pressure.

With carbon monoxide present, additional reactions are needed: Reactions 33–36.

$$^1SO_2 + CO \longrightarrow SO_2^* + CO \qquad (33a)$$

$$^1SO_2 + CO \longrightarrow SO + CO_2 \qquad (33b)$$

$$SO_2^* + CO \longrightarrow SO + CO_2 \quad (34)$$

$$SO_2^{**} + CO \longrightarrow SO + CO_2 \quad (35)$$

$$^3SO_2 + CO \longrightarrow SO_2 + CO \quad (36a)$$

$$^3SO_2 + CO \longrightarrow SO + CO_2 \quad (36b)$$

With hydrocarbons, the mechanism is not yet known. However, both nitrogen and oxygen are relatively insensitive quenchers of SO_2^* and SO_2^{**}. Thus, the reactions of these states with hydrocarbons and the oxides of nitrogen may be important in the atmosphere, especially if they are needed only as initiation reactions for aerosol formation.

It is now necessary to relate the four photochemical states of sulfur dioxide with the known spectroscopic states. The lowest excited state of sulfur dioxide is generally agreed to be $^3B_1$. This state is responsible for the weak absorption at 3900–3400 Å.[565] It is also the state that phosphoresces and is therefore the state designated $^3SO_2$. The phosphorescence is readily quenched by hydrocarbons.[62,1112] If the quenching is chemical, rather than physical, the quenching reactions may play a role in the atmosphere. The second absorption band at 3400–2600 Å is much stronger and is probably the corresponding singlet state, $^1B_1$.

One difficulty in the sulfur dioxide system is that the fluorescent lifetime of the excited singlet state is about 70 times greater than that computed from the integrated absorption coefficient.[490,1169] This anomaly has been discussed by Douglas,[331] who has ascribed the main effect to the mixing of the vibrational levels of the absorbing state with those of other electronic states. Walsh[1271] has suggested that an optically forbidden $^1A_2$ state should exist. Such a state has been observed in the electronically similar NO_2^- ion.[1170] Presumably, the $^1B_1$ and $^1A_2$ states are strongly coupled, and it may be that $^1B_1$ is the absorbing state, whereas $^1A_2$ is the emitting state.

The $^1A_2$ state should have a triplet state, $^3A_2$, that can be formed by intersystem crossing. Brand *et al.*[136] have suggested that this triplet state lies about 2.5–3 kcal/mol above $^3B_1$, and this would be SO_2^{**}.

5

Metabolism of Vapor-Phase Organic Pollutants in Mammalian Systems

The metabolic fates of many of the substances identified as vapor-phase organic pollutants have not been investigated, but their biologic transformation sequences should closely parallel the metabolism of the various functional groups to be discussed in this chapter, in which the emphasis is on biotransformation sequences in terms of chemical function.

Mammals convert nonpolar xenobiotic substances by enzymatic oxidation, reduction, hydrolysis, or hydration into more polar materials that are then easily excreted either by the kidney or by the intestine via the bile. These metabolic reactions occur principally in the liver and to a lesser extent in the kidney, intestine, and lung. The mode of metabolism and excretion differs widely among species. In general, however, such compounds as hydrocarbons, aldehydes, ketones, ethers, epoxides, esters, amides, tertiary amines, sulfides, and nitrogen compounds are enzymatically converted to more polar compounds—i.e., phenols, *vic*-glycols, acids, primary and secondary amines, sulfoxides, and sulfones. These polar metabolites are then excreted directly or after conjugation with glucuronic acid, sulfuric acid, glycine, or glutathione.

Epoxides, reactive alkyl and aryl halides, α,β-unsaturated carbonyl compounds, arylhydroxylamines, and some nitrated aromatics are metabolized by conjugation with the thiol group of glutathione. Before excretion, the peptide residue in the glutathione conjugate is converted to N-acetylcysteine. Compounds with a hydroxyl or amino function—such as phenols, alcohols, *vic*-glycols, amines, and hydroxylamines—are usually conjugated with the 4-hydroxy group of glucuronic acid to form glucuronides or with sulfuric acid to form sulfates or sulfamates. The aromatic dihydrodiols, a special class of *vic*-diols probably produced by enzymatic hydration of intermediate arene oxides, may be excreted directly or first conjugated with glucuronic or sulfuric acid before excretion. Esterases and amidases convert esters and amides to acids, which are then often conjugated with glycine to yield hippuric acids. Carbonyl and nitrogen compounds are often reduced to alcohols or amines. In the case of volatile organic compounds, a major portion is often exhaled unchanged. Reviews of the metabolism and toxicology of organic compounds, including many known vapor-phase organic pollutants, are available.[157,162,457]

Although little seems to be known about the metabolism of a number of highly reactive volatile air pollutants formed in the atmosphere—e.g., peroxides, peroxy acids, and ozonides (Chapter 3)—many of these compounds exhibit potent biologic effects (Chapter 6).

Initial oxidative metabolism of many foreign substances by mammals occurs primarily in the liver and is catalyzed by membrane-bound enzymes. The reaction incorporates one atom of the oxygen molecule into the organic substrate, whereas the other atom is concomitantly reduced to water. These monoxygenases thus require reducing equivalents in the form of reduced nicotinamide adenine dinucleotide phosphate. This metabolic system of oxidizing and reducing enzymes is frequently studied in hepatic membrane preparations referred to as microsomes. At least two general groups of monoxygenases have been identified in liver microsomes. The concentrations of the normal hepatic enzymes, referred to as cytochrome P-450, are greatly increased by pretreatment of animals with phenobarbital or related compounds.[157,457] Spectrally distinct enzymes, referred to as cytochrome P-448, appear in liver after pretreatment of animals with polycyclic hydrocarbons.[157,457] Both the extent of enzyme induction by such agents and basal concentrations of these enzymes vary greatly in different species and in individual humans.[242,762,1249] Cytochromes P-450 and P-448 catalyze such reactions as aliphatic hydroxylation, olefinic epoxidation, conversion of aromatic compounds to arene oxides and phenols, oxidation of sulfides to sulfoxides and sulfones, and oxidative dealkylation of amines and ethers. Because cytochrome P-450 and cytochrome P-448 have different substrate specificities,[786] exposure of animals or humans to drugs, polycyclic hydrocarbons, or other xenobiotic substances can markedly alter both the quantitative and the qualitative aspects of later organic substrate metabolism. Concomitant interaction of more than one xenobiotic substance with the hepatic enzyme system can result in altered metabolism of either substance. This chapter attempts to delineate representative metabolism of vapor-phase organic air pollutants. Many of the studies cited here have been performed with *in vitro* microsomal systems; thus, it should be stressed that *in vivo* metabolism can be very different, both quantitatively and qualitatively, from that observed *in vitro*. This difference often depends on the route, degree, and duration of administration of a substance.

The preceding discussion has stressed some of the complex factors pertinent to an evaluation of the pathway and extent of metabolism of vapor-phase organic air pollutants in man and lower animals. A recent comprehensive treatment of the metabolism of xenobiotic substances is available,[157] as is a monograph on drug metabolism in man.[1249]

HYDROCARBONS

Alkanes

Saturated hydrocarbons are metabolized both *in vitro* and *in vivo* to alcohols, which may be further metabolized to ketones, aldehydes, and acids. Vapor-phase air pollutants of this type include methane, ethane, propane, *n*-butane, isobutane, *n*-pentane, isopentane, cyclopentane, *n*-hexane, 2-methylpentane, 3-methylpentane, 2,2-dimethylbutane, cyclohexane, methylcyclopentane, 2-methylhexane, methylcyclohexane, 2,2,4-trimethylpentane, and *n*-octane.

The metabolism of *n*-butane, isobutane, *n*-pentane, isopentane, cyclohexane, and methylcyclohexane has been investrigated with hepatic microsomes from a variety of rodents.[443] The major metabolites from *n*-butane and *n*-pentane are 2-butanol and 2-pentanol, respectively. 3-Pentanol is also a significant metabolite from *n*-pentane. *n*-Butane, *n*-pentane, and isobutane form barely detectable amounts of the primary alcohol.[443] This is in contrast with the *in vitro* results obtained with hexane, octane, decane, and hexadecane,[290,603,735,820] for which oxidation of the terminal methyl groups is a significant pathway. Isopentane leads to all the possible alcohols, with the tertiary alcohol, 2-methyl-2-butanol, as the major metabolite.[603] It was concluded[443] that, in acyclic aliphatic hydrocarbons, the rate of hydroxylation at different positions was tertiary CH > secondary CH_2 > primary CH_3.

Cyclohexane is metabolized by hepatic microsomes *in vitro* to cyclohexanol,[1223] whereas cyclohexanol and *trans*-1,2-dihydroxycyclohexane are the major urinary metabolites *in vivo* in ratios from 3:1 to 8:1 at different dosages.[362] Pretreatment of rats with phenobarbital enhances microsomal metabolism of cyclohexane, and pretreatment with a polycyclic hydrocarbon retards metabolism.[1223]

Metabolism of methylcyclohexane *in vitro* by rodent microsomes yields the following products: 3-hydroxy-1-methylcyclohexane > 4-hydroxy-1-methylcyclohexane ≅ 1-hydroxy-1-methylcyclohexane > 2-hydroxy-1-methylcyclohexane >> 1-hydroxymethylcyclohexane.[443] The *in vivo* metabolism of methylcyclohexane in rats is similar, except that the 1-hydroxy-1-methyl and 1-hydroxymethyl metabolites have not been reported.[363]

Alkenes

Olefinic compounds may be oxidized at saturated positions to yield alkenols. However, the major metabolism of such compounds *in vitro* is conversion to *vic*-glycols via intermediate epoxides. The epoxidation is catalyzed by the hepatic monoxygenase system; the resulting epoxide is converted to a *vic*-glycol by a *trans* addition of the elements of water catalyzed by microsomal epoxide hydrase. A variety of olefins have been reported as air pollutants, including ethylene, propylene, 1-butene, *cis*- and *trans*-2-butene, isobutene, 1,3-butadiene, 1-pentene, *cis*- and *trans*-2-pentene, 2-methyl-1-butene, 2-methyl-2-butene, 3-methyl-1-butene, 2-methyl-1,3-butadiene, cyclopentene, 1-hexene, *cis*- and *trans*-2-hexene, *cis*- and *trans*-3-hexene, 2-methyl-1-pentene, 4-methyl-1-pentene, and 4-methyl-2-pentene. The aromatic olefin, styrene, has also been detected as a pollutant.

1,3-Butadiene has been reported to be metabolized to 3-butene-1,2-diol and erythritol with rat liver microsomes, presumably via intermediate epoxides.[564] The same products are formed from 1,2-epoxy-3-butene. 1-Octene and *trans*-4-octene are converted to the corresponding epoxides with liver microsomes.[813] The intermediate epoxides are further metabolized by the microsomal epoxide hydrase(s) to the corresponding *vic*-glycols. 3-Ethyl-2-pentene is also converted to the *vic*-glycol.[813] Styrene is converted with microsomal preparations to styrene glycol[755] via intermediate formation of styrene oxide.[756] Volatile cycloalkenes—such as cyclopentene, cyclohexene, and cycloheptene—are converted to the corresponding *trans*-diols with microsomal preparations.[753]

Epoxides have proved difficult to isolate as microsomal metabolites, unless further metabolism to glycols by epoxide hydrase is prevented by the addition of an inhibitor of the latter enzyme. Structure–activity correlations of epoxides as substrates or inhibitors of hepatic epoxide hydrase have been extensively studied.[938] Monosubstituted, 1,1-disubstituted, and *cis*-1,2-disubstituted oxiranes are much better substrates than *trans*-1,2-disubstituted oxiranes, and trisubstituted and tetrasubstituted oxiranes are nearly inactive as substrates. An alternate metabolism of intermediate epoxides is conjugation with glutathione.

Little is known of the relative rates of conversion of various substituted olefins to epoxides with the microsomal system. The rates of conversion of three olefins to *vic*-glycols are 1-octene > *trans*-4-octene > 3-ethyl-2-pentene.[813] However, the oxides corresponding to the latter two olefins are increasingly less active as substrates for epoxide hydrase.[813,938]

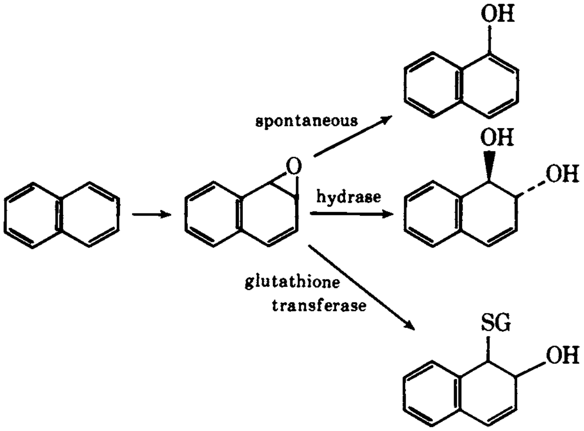
In vivo metabolism of simple alkenes does not appear to have been investigated. *In vivo*, styrene is converted to benzoic and mandelic acids, in addition to styrene glycol.[367] A trace amount of 4-vinylphenol has been detected as a metabolite in rats.[73]

Acetylenic and allenic compounds—such as acetylene, methylacetylene, and propadiene—have been reported as organic air pollutants. Little is known of the metabolism of such compounds. Phenylacetylene is metabolized *in vivo* to phenylacetic acid.[756]

Arenes

Aromatic hydrocarbons are metabolized both *in vitro* and *in vivo* to arene oxides, which isomerize to phenols, are enzymatically hydrated to the so-called dihydrodiols, and are conjugated with glutathione. The dihydrodiols are further metabolized to catechols by dehydrogenation. A major route of metabolism of alkyl-substituted arenes consists of aliphatic hydroxylation of a substituent, usually at the benzylic position.

The route of metabolism of an aromatic hydrocarbon has been firmly established in the case of naphthalene, where it has been shown that naphthalene-1,2-oxide is the obligatory intermediate leading from naphthalene to 1-naphthol, *trans*-1,2-dihydroxy-1,2-dihydro-naphthalene, and a glutathione conjugate[640] (Reaction 1).



(1)

Many such arene oxides are extremely unstable, thus rendering their direct demonstration difficult in biologic systems.[639,642,674] Evidence of their formation is usually indirect. Thus, dihydrodiols, catechols, and mercapturic acids formed during metabolism of aromatic substrates are certainly derived from intermediate arene oxides. Phenolic metabolites may, however, be formed directly from the arene by an oxygen-insertion reaction similar to that involved in the formation of alcohols from aliphatic hydrocarbons or may result from formation and later isomerization of an intermediate arene oxide. Isomerization of such oxides to phenols occurs with a concomitant migration and retention of isotopic hydrogen[130,639] similar in magnitude to that observed during enzymatic phenol formation from the appropriate parent arene. Thus, the occurrence of the NIH shift,* an almost ubiquitous phenomenon associated with monoxygenase-catalyzed formation of phenols,[638] provides strong evidence that formation of a phenolic metabolite involves the intermediacy of the corresponding arene oxide. Arene oxides, such as bromobenzene oxide, may react nonenzymatically with macromolecular tissue constitutents and thus cause tissue necrosis.[158]

Benzene is a vapor-phase organic pollutant. Metabolism *in vivo* in rabbits leads primarily to phenol.[956] Minor *in vivo* metabolites include *trans*-1,2-dihydro-1,2-dihydroxybenzene,[1066] catechol, hydroquinone, phenylmercapturic acid, and *trans-trans*-muconic acid.[956] As indicated earlier, the hydroxylated products may be further converted into, and

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* The NIH shift is the phenomenon by which the substituent (^{2}H, ^{3}H, Cl, or Br) displaced by the entering hydroxy group during enzymatic hydroxylation of aromatic substrates migrates to an adjacent position in the aromatic ring.[638]

excreted as, a variety of conjugates (e.g., glucuronides and sulfates). *In vitro,* benzene is converted to phenol, but neither *trans*-1,2-dihydro-1,2-dihydroxybenzene nor benzene oxide has been detected as a product.[641]

As variety of alkylbenzenes have been identified as organic air pollutants, including toluene, ethylbenzene, isopropylbenzene, *n*-propylbenzene, *sec*- and *tert*-butylbenzene, *o*-, *m*-, and *p*-xylene, 1,2,4-trimethylbenzene, and mesitylene.

Such alkylbenzenes are metabolized *in vivo* both to phenols and to products resulting from side-chain oxidation. Thus, toluene is metabolized *in vivo* primarily to benzoic acid[142,1322] via intermediate formation of first benzyl alcohol and then benzaldehyde. Both *o*-cresol and *p*-cresol are also detected as minor *in vivo* metabolites of toluene.[73] *In vivo*, ethylbenzene, *n*-propylbenzene, and *n*-butylbenzene afford side-chain oxidation products.[368] Initial oxidation appears to occur primarily at the benzylic position. Ethylbenzene is converted in rats to small amounts of 4-ethylphenol,[73] but the major metabolite is methylphenylcarbinol.[73,1128] Isopropylbenzene apparently is not converted *in vivo* to phenolic metabolites,[638] nor is benzylic hydroxylation to 2-phenyl-2-propanol the major pathway for side-chain oxidation.[73,130] Instead, 2-phenyl-1-propanol is the major alcoholic metabolite.[73,1021] Xylenes are metabolized *in vivo* primarily by oxidation of a methyl group to yield toluic acids.[140] Phenols are also detected as minor metabolites.[73] The trimethylbenzenes are metabolized to acids and to trace amounts of phenols.[73,1322]

The *in vitro* metabolism of alkylbenzenes has not been studied extensively. Ethylbenzene yields mainly methylphenylcarbinol[837] and small amounts of 2- and 4-ethylphenol.[674] The phenolic metabolites obtained from toluene, xylenes, and mesitylene with rat microsomal preparations have been compared with the phenols obtained on isomerization of the analogous arene oxides.[639,674] It has been concluded that phenol formation from alkylbenzenes is in all instances compatible with the intermediacy of one or more arene oxides. The proposed intermediate arene oxides are all remarkably unstable and rearrange rapidly to phenols. Because of their instability, it is likely that such alkylarene oxides do not survive long enough to be enzymatically converted to *trans*-dihydrodiols or to premercapturic acids. Such metabolites apparently have not been detected from alkylbenzenes.

Oxidative metabolism at the aromatic carbon atoms of three additional volatile arenes—aniline, nitrobenzene, and chlorobenzene—should be mentioned briefly. Aniline is metabolized *in vivo* to a mixture of *o*- and *p*-aminophenol.[956] The proportions of these phenols differ markedly in different species. Nitrobenzene in rabbits gives rise to *m*- and *p*-nitrophenol and lesser amounts of *o*-nitrophenol.[956] Other metabolites include aniline and the three aminophenols. The presence of 4-nitrocatechol and 4-nitrophenylmercapturic acid indicates the intermediacy of 4-nitrobenzene oxide. Chlorobenzene is metabolized in rabbits to 3-chlorophenol, 4-chlorophenol, and a minor amount of 2-chlorophenol.[637] Apparently, 4-chlorobenzene oxide is formed as an intermediate, inasmuch as 4-chlorocatechol and its two mono-O-methyl ethers, the corresponding dihydrodiol, and 4-chlorophenylmercapturic acid are detected as metabolites. 3-Chlorobenzene oxide must also be formed, as evidenced by the isolation of its hydration product, the corresponding dihydrodiol (D. M. Jerina and J. W. Daly, unpublished data).

EPOXIDES

In general, our knowledge of the metabolic fate of epoxides is derived from a correlation of *in vitro* studies with the epoxides themselves and *in vivo* studies with the precursor olefins. This is due to the chemical instability of epoxides, particularly in acid conditions like those in the stomach, and to the relatively recent interest in their biologic role. The few metabolic studies in which the epoxides themselves have been administered by injection confirm the conclusions drawn from the correlated evidence. Owing to the paucity of data on the metabolism of volatile epoxides, nonvolatile substances are also discussed here.

Two general pathways have been found for the metabolism and excretion of epoxides. In one, the epoxide is hydrolyzed to a vicinal *trans*-diol by the action of an epoxide hydrase enzyme. The diol is then excreted directly or as a glucuronic acid conjugate, or it may undergo further oxidative metabolism. Phenyl-1,2-ethanediol obtained by the metabolism of styrene, for example, is not only excreted as such, but is further oxidized to mandelic and benzoic acids.[367] The hydrolysis of epoxides invariably yields the *trans*-diol and has been found to be stereospecific.[643] The hydrolysis of *cis*-stilbene oxide by rabbit liver microsomes, for example, gives only D-*threo*-1,2-diphenylethanediol, whereas only the *meso*-diol is obtained from *trans*-stilbene oxide.[1280] The rate of epoxide hydrolysis depends heavily on the degree of substitution and the stereochemistry about the epoxide ring. In general, the rate of hydrolysis decreases in traversing the series monosubstituted, disubstituted, trisubstituted, and tetrasubstituted, whereas *cis*-disubstituted epoxides are more readily hydrolyzed than the *trans*-

isomers.[938,1280] These effects of substitution on the rate of hydrolysis are most probably due to steric, rather than electronic, factors.

The second major pathway for the metabolism of epoxides involves enzyme-catalyzed conjugation with glutathione. The sulfhydryl group of the cysteine residue in glutathione adds to the epoxide, yielding an α-hydroxythioether. The resulting conjugate then either is excreted or undergoes hydrolysis of the glutathione moiety. This cleavage of the glutathione group, which probably occurs in the kidney,[123] leads to eventual excretion of the cysteine or N-acetylcysteine conjugate. Little is known about the structure–activity relations of this sequence.

In addition to the two major metabolic pathways summarized above, a number of alternative biologic fates have been identified for some epoxides. Of these, the most important is the nonenzymatic intramolecular rearrangement of epoxides to give the corresponding carbonyl compounds. This transformation is observed with epoxides that are particularly unstable. Two examples are the rearrangement of 1,2-oxido-1,2-dihydronaphthalene to give 1-naphthol[640] and the probable conversion of trichloroethylene via its epoxide to trichloroacetaldehyde.[281]

The enzyme fumarase from swine heart, which normally catalyzes the addition of water to the double bond of fumarate, also catalyzes the hydrolysis of *trans*-2,3-epoxysuccinate to give *meso*-tartrate.[13] Because similar reactions have been observed with enzymes from nonmammalian sources, it is possible that biosynthetic enzymes that catalyze the hydration of double bonds will also catalyze the hydrolysis of the corresponding epoxides.

The enzyme 2,3-oxidosqualene lanosterol cyclase from liver has been found to cyclize 2,3-oxidosqualene analogues, in some cases competing with the hydrolysis of the epoxides to the diols.[248]

Epoxides are sufficiently reactive to undergo purely chemical alkylation reactions with proteins and nucleic acids under physiologic conditions. Propylene oxide, for example, alkylates the guanine and adenine residues of DNA on incubation at a pH of 7.[745] Although the significance of these alkylation reactions in live animals is not clear, they must be kept in mind in any discussion of the biologic fate of epoxides.

Epoxides of Four or Fewer Carbons

The metabolic fate of the simplest epoxide, ethylene oxide, is unknown. It is not eliminated in expired air, however, and its hydrolysis to ethylene glycol is considered likely.[507,1325] Only preliminary data are available on ethylene, the precursor olefin, but its conversion to carbon dioxide and urinary metabolites has been reported.[1245] Trichloroacetic acid and the glucuronide of trichloroethanol have been isolated from rat urine after ingestion of trichloroethylene.[281] It was shown that the chlorine rearranges intramolecularly, suggesting that the corresponding trichloroethylene oxide was an intermediate. This unstable species would rearrange spontaneously to trichloroacetaldehyde, which then undergoes oxidation or reduction to the observed products.

1,2-Oxidobutane administered to rabbits and rats is excreted at least in part as N-acetyl-S-(2-hydroxybutyl)-L-cysteine.[632] This is probably derived from initial conjugation with glutathione. Butadiene and 1,2-oxido-3-butene are converted *in vitro* to the diol (3-butene-1,2-diol) and tetraol (erythritol).[564] In both cases, the concentration of the diol rises and then falls as the erythritol concentration increases, indicating that the hydrolysis is faster than the oxidation reaction. An early *in vivo* study of the metabolism of inhaled butadiene failed to find urinary metabolites, but it cannot be relied on, because it preceded the use of radioactive labels.[200] The diepoxide from butadiene is conjugated to glutathione by rat liver preparations.[134] Although no comprehensive study has been carried out with the various butane epoxides, and no *in vivo* data are available, the data suggest that these compounds are readily metabolized by the two major pathways.

2,3-Oxidopropanol (glycidol) is conjugated with glutathione by rat liver preparations,[134] and trichloromethylethylene oxide undergoes both *in vitro* conjugation to glutathione[937] and slow hydrolysis to the diol.[938]

Epoxides of Five to Eight Carbons

N-Acetyl-S-(2-hydroxycyclopentyl)-L-cysteine can be isolated from rabbit urine after injection of either cyclopentene or 1,2-oxidocyclopentane.[633] The conversion of cyclopentene to 1,2-cyclopentanediol by rat liver microsomes has also been noted.[753]

The *in vitro* oxidation of cyclohexene to 1,2-oxidocyclohexane and its later hydrolysis to 1,2-cyclohexanediol has been reported.[752] The isolation of the epoxide in this case is probably due to the relatively slow hydrolysis to the diol.[938] 1,2-Oxidocyclohexane injected into rabbits is excreted in the urine as N-acetyl-S-(2-hydroxycyclohexyl)-L-cysteine.[633] The probable origin of this product from an initial glutathione conjugate is supported by the *in vitro* conjugation of 1,2-3,4-dioxidocyclohexane with glutathione.[134]

Cycloheptene and its epoxide injected into rabbits are excreted in the urine as N-acetyl-S-(2-hydroxycycloheptyl)-L-cysteine.[633]

Liver preparations convert 1-octene, 4-octene, and 3-acetyl-2-

pentene, as well as the corresponding epoxides, to diols.[813] The isolation of only 4,5-oxidooctane instead of the diol when 4-octene was incubated in the presence of 1,2-oxidooctane as a hydrase inhibitor indicated that the epoxide was an obligatory intermediate between olefin and diol.

The metabolism of styrene and styrene epoxide has been extensively studied. Both styrene and styrene epoxide are converted to phenyl-1,2-ethanediol by liver microsomes.[755] The epoxide is also conjugated with glutathione *in vitro*.[134] The *in vivo* metabolism of styrene in rabbits resulted in the formation of phenyl-1,2-ethanediol (as its glucuronide), mandelic acid, and hippuric acid.[367] The same authors found mandelic and hippuric acids in rabbit urine after administration of styrene epoxide, but no diol. Because the epoxide was given orally, however, this result is ambiguous. The formation of mandelic and hippuric acids from styrene diol was verified by the isolation of these products as metabolites of the diol itself. The other products that have been isolated from styrene metabolism are benzoic acid in rabbits,[1139] carbon dioxide arising from the methylene group in rats,[283] and traces of *p*-hydroxyphenylethylene in rats.[73] All these are consistent with metabolism via the epoxide and the diol.

Epoxides of More Than Eight Carbons

Indene *in vitro* gives indan-1,2-epoxide[756] and the corresponding diol.[754] Indan-1,2-epoxide is hydrolyzed to the diol by rabbit or rat liver preparations,[754,938] but it does not give a glutathione conjugate.[134] Not surprisingly, indene is excreted in the urine of rabbits and rats as the free glucuronide conjugate indan-1,2-diol.[159]

1,2-Dihydronaphthalene is one of the most extensively studied compounds. Both the parent olefin and its epoxide have been found to give *trans*-diols on incubation with rat liver slices.[123] The glutathione conjugate is also formed from these two compounds in the same enzyme system. When the glutathione conjugate is incubated with rat kidney homogenate, the glutathione group is hydrolyzed, leaving only the cysteine residue attached at C-1 of 1,2,3,4-tetrahydro-2-hydroxynaphthalene. This is one of the strongest pieces of evidence that the cysteine or N-acetylcysteine conjugates are derived from initial glutathione conjugates. Both 1,2-dihydronaphthalene and 1,2,3,4-tetrahydro-1,2-oxidonaphthalene are excreted in the urine of rabbits in part as the free glucuronide conjugate diol.[133]

The free diol, its glucuronide conjugate, and the glutathione addition product are all found in the bile of rats that have received either 1,2-dihydronaphthalene or the epoxide derived from it.[132] The two general metabolic pathways for epoxides have therefore been demonstrated *in vitro* and *in vivo* with these substrates.

The formation of epoxides from chlorinated insecticides, such as Aldrin, and the later metabolism to diols have long been known. An extensive review of the data on these compounds is available.[160]

The presence of uroterpenol glucuronide in human urine as a metabolite of ingested or inhaled limonene has been established.[1261]

The *in vitro* hydrolysis of epoxides to diols has been demonstrated for a number of steroids and their precursors. These include squalene analogues, such as 1,1-desmethyl-2,3-oxidosqualene,[248] 2,3-oxidocholestanes,[1281] and $16\alpha,17\alpha$-epoxyestratriene-3-ol.[147] The excretion of this last compound as the glucuronide conjugated diol by humans has been reported.[146] Oleic acid and its epoxide are converted to *threo*-dihydroxystearic acid by rat liver microsomes.[1282]

ETHERS

Ethers are oxidatively metabolized, with the exception of epoxides, whose reactivity is dominated by the inherent ring strain. Aliphatic ethers are cleaved to an alcohol and an aldehyde, probably via initial hydroxylation at the α carbon to give an unstable hemiacetal that undergoes nonenzymatic cleavage.[157] The initially formed alcohol and aldehyde are directly excreted or, more commonly, undergo further oxidative, reductive, and conjugative transformations before elimination. *p*-Nitroanisole, for example, is cleaved to *p*-nitrophenol and formaldehyde,[59] but the products primarily excreted in the urine are the corresponding glucuronide and sulfate.[139]

The rate of demethylation for a series of ring-substituted anisoles is greater for *para* than for *meta* substitution, although a simple correlation between the rate and the electronic properties of the substituent cannot be made.[59] However, it has been clearly shown that the rate of dealkylation decreases as the size of the alkyl group increases through the series ethyl > *n*-propyl > isopropyl > *n*-butyl > *n*-hexyl.[835,836] Compounds with chains larger than propyl are often metabolized by side-chain oxidation, rather than dealkylation.[863,1353]

The cleavage of alkylarylethers has been shown to occur by oxidative rupture of the alkyl–oxygen, rather than the aryl–oxygen, linkage.[1013] No label appeared in the *p*-hydroxyacetanilide formed by enzymatic demethylation of the corresponding ether in the presence of ^{18}O-enriched oxygen or water.

The enzyme system(s) mediating these dealkylations is primarily in the liver microsomes and requires oxygen and reduced pyridine nucleotide as cofactors.[59] The differential inhibition of codeine and *p*-ethoxyacetanilide dealkylation by such inhibitors as SKF 525-A* suggests the presence of more than one enzyme.

A microsomal enzyme in the liver and intestine has been found to catalyze the cleavage of fatty acid glycerylethers.[1134,1197] This enzyme system requires not only oxygen and reduced pyridine nucleotides, but also tetrahydropteridine. Unlike the first enzyme system discussed, it is capable of efficiently cleaving ethers with long alkyl chains.

Most of the evidence on ether metabolism is based on studies of alkylarylethers. Little is actually known about the specific metabolism of volatile dialkylethers. There is indirect evidence that these compounds are metabolized by the pathways discussed above. Diethylether and related halogenated ethers, for example, appear to be metabolized to ethanol and acetaldehyde, which enter the acetate pool of normal body metabolism.[487,1245] Thus, administration of labeled diethylether results in labeling of steroids and fatty acids.[487]

Cyclic saturated ethers, such as tetrahydrofuran, may be formed from the interaction of ground-state oxygen and hydrocarbons (see Chapter 3). The evidence available, although meager, indicates that tetrahydrofurans are metabolized in the same manner as acyclic ethers. The substituted tetrahydrofuran obtained from thiamine tetrahydrofurfuryldisulfide, for example, is oxidized to the corresponding lactone, presumably via a hemiacetal intermediate.[693]

ALCOHOLS AND PHENOLS

The general pathway for the types of compounds under consideration is primarily oxidative, in many instances ultimately leading to the formation of carboxylic acids. The conversion of primary alcohols to aldehydes and thence to carboxylic acids is a common metabolic sequence in mammals. In the case of secondary alcohols, oxidative metabolism generates ketones, which in special cases can be further metabolized oxidatively. However, such reactions involve carbon–carbon cleavage and are less common. An alternative pathway is reduction to the original secondary alcohol, which itself can be conjugated with glucuronic acid. Conjugation of primary alcohols is less common (presumably because of greater susceptibility to the available

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* Diethylaminoethyl-2,2-diphenylvalerate.[803]

oxidative pathway), whereas tertiary alcohols, not susceptible to oxidative enzymes, are excreted primarily either unchanged or as glucuronide conjugates. Because of the predominance of oxidative reactions involved in the metabolism of these types of compounds, this review will start with a consideration of the molecular species at the lower oxidative state, namely, the alcohol. Consideration of aldehydes and ketones will follow. We are concerned only with vapor-phase organic air pollutants, so our attention will focus on small molecules (C_{1-5}), which are the more likely species to be found in the atmosphere we breathe.

Ethanol

The metabolism of primary alcohols ($R—CH_2OH$) has been investigated more extensively than that of any other class of molecules to be considered in this report, because of man's consumption of ethanol. The literature dealing with the metabolism of ethanol is far too extensive to be reviewed here; key review articles and books may be consulted.[538,789,1062] As is the case with primary alcohols, in general, the metabolism of ethanol is dominated by the pathway involving oxidation, in this case to acetaldehyde. This conversion can be effected by three independent enzyme systems. Catalase mixed-function oxidase and alcohol dehydrogenase in the presence of hydrogen peroxide converts ethanol to acetaldehyde and water.[681] However, convincing evidence has been presented[789] that, although the catalase pathway may function *in vitro*, its role in the net metabolism of ethanol *in vivo* is only minor. A second source of enzymatic oxidation of ethanol to acetaldehyde that has been described is the mixed-function oxidase system of the liver endoplasmic reticulum.[947] However, there is some controversy over whether contamination of the microsomal preparation, which was used to demonstrate this conversion with catalase, was responsible for the observed oxidation. By far the most important enzyme system responsible for the oxidation of ethanol is the NAD^+-dependent oxidoreductase, alcohol dehydrogenase.[1188] This enzyme is probably a collection of enzymes found in many tissues, as well as in the liver.[1266] In addition to ethanol, many primary and secondary alcohols are oxidized by this system;[834] therefore, it is probably of considerable importance in the metabolism of vapor-phase organic air pollutants. In addition to the acetaldehyde pathway, several minor routes for the metabolism of ethanol have been described. Sulfate and glucuronide conjugates have been found in the urine,[125,664] and there is some evidence of formation of fatty acid esters.[482] However, these pathways are quantitatively insignificant.

Methanol

After ethanol, the metabolism of methanol has been examined more extensively than that of any other aliphatic alcohol, in part to understand better its toxic effects on mammals. The metabolism of methanol has been reviewed.[705] Its primary metabolic pathway, too, is oxidative, presumably to formaldehyde, which is then further metabolized to formic acid and then to carbon dioxide. The role of the oxidoreductase, aldehyde dehydrogenase, in the oxidation of methanol is not so obvious as with ethanol. Several workers (for example, Theorell[1187]) have been unable to demonstrate activity with purified enzyme preparations from horse liver, although human liver is reported to catalyze the oxidation of methanol at about one-tenth the rate at which it catalyzes the corresponding oxidation of ethanol.[113] In contrast with the metabolism of ethanol, catalase apparently can participate in the oxidation of methanol in animal tissues.[706] The possibility that species variations are important has been stressed.[804] Because methanol is a C-1 unit, it is not surprising that it can contribute to the C-1 "active methyl" pool, although the incorporation of methanol into the choline methyl group is not a simple transmethylation process.[345]

Higher Alcohols

It is of interest that such alcohols as isoamyl and *n*-butyl alcohol disappear much more rapidly than ethanol or methanol from rat blood.[449] Although this phenomenon may be a consequence of partition coefficients, the relative initial rates of oxidation of these and several other alcohols *in vitro* through the action of horse liver alcohol dehydrogenase are considerably higher than for ethanol.[1338] In addition to alcohol dehydrogenase, catalase has been demonstrated to be an effective catalyst for the oxidation of the propyl alcohols.[448] Presumably, conjugations of higher alcohols, particularly secondary and tertiary alcohols, can play an important role in the metabolism of these substances.[665] In a recent report,[485] the metabolism of the α,β-unsaturated compound crotyl alcohol has been examined. As is the case in the metabolism of allyl alcohol,[677] crotyl alcohol is excreted in rats as a glutathione derivative, 3-hydroxy-1-methylpropylmercapturic acid. The evidence suggests that formation of the mercapturic acid proceeds via the corresponding crotonaldehyde.

Phenols

Phenols present in the atmosphere[138] can arise from combustion processes, including those leading to automobile exhaust[239] and tobacco smoke.[579] Phenolic substances present in the vapor phase will be principally lower-molecular-weight materials, such as phenol or the isomeric cresols, which have boiling points between 180 and 200 C at atmospheric pressure.

Another major source of phenols in the atmosphere is the photochemical oxidation of the parent hydrocarbons (see Chapter 3), and a third mechanism by which man is exposed to phenols is the metabolism of aromatic hydrocarbons found in the atmosphere (see Chapter 2). The mixed-function oxidase system found in both liver and lung tissues has been demonstrated[280] to convert these aromatic hydrocarbons, both *in vivo* and *in vitro,* into arene oxides, which isomerize to phenols.

Another relatively little information is available on the metabolic fate of the various lower-molecular-weight phenols, it appears from animal studies[300] that they exhibit toxicity of about equal magnitude. Phenol itself is rapidly absorbed from the stomach (40% in 1 hr) at both acid and alkaline pH.[1071] However, phenol gains access to the body from all sites of administration and can reach the circulation even if applied to the intact skin.[377]

In a recent paper,[196] the metabolic fate of ^{14}C-labeled phenol was studied in man and in 18 animal species. The conjugation and oxidation of phenol *in vivo* were first described by Baumann and Preusse.[89] The conjugation products of phenol and cresol are now known to be their sulfuric and glucuronic acid esters.[957(p.146),958,1320(p.278)] Detailed discussions of the sulfate and glucuronide conjugation mechanisms are given by Williams [1320(p.278)] and Roy.[1039] Phenol and the cresols are further susceptible to oxidative metabolism, leading to *ortho-* and *para-*hydroxylated products.[141,1320(p.297)] These oxidative metabolites are then also transformed into their conjugates.[1320(p.278)] Another enzymatic pathway for phenol and cresols appears to be O-methylation mediated by catechol-O-methyltransferase.[60,72] Although earlier reports indicated that substantial amounts of phenol and cresols appeared in the urine in their free state,[1320(p.294)] more recent data using ^{14}C-labeled material suggest that the conjugated metabolites predominate.[196,958] Sulfate and glucuronide conjugation appear to occur with about equal facility, although significant species variation has been reported.[196]

In a 24-hr urine collection from a 25-mg/kg dose of [^{14}C]phenol, total excreted radioactivity accounted for 31–95% in the species studied. In man, with a dose of 0.01 mg/kg, 90% of the excreted radioactivity appeared in the first 24 hr, 70% as the sulfate and 16% as the glucuronide conjugate, with only trace amounts of the conjugated quinols.

ALDEHYDES

The oxidative metabolism of aldehydes to the corresponding carboxylic acids can be catalyzed by three groups of enzymes—aldehyde dehydrogenase,[987] aldehyde oxidase,[988] and xanthine oxidase.[989] In the case of acetaldehyde, the aldehyde dehydrogenase appears to be the main biologic catalyst.[790,1043]

Chemically, aldehydes are reactive species that are readily oxidized to the corresponding carboxylic acids and may also undergo condensation reactions with a variety of nucleophiles. Acetaldehyde and formaldehyde, in addition to being susceptible to oxidative enzymes, may participate in biologic condensation reactions. For example, there is good evidence that acetaldehyde will combine with pyruvic acid *in vivo* to form acetoin.[221,690] Recent studies[295,1273] have indicated that acetaldehyde may also form tetrahydroisoquinolines through their interaction with catecholamines. A similar report on the *in vitro* and *in vivo* condensation of acetaldehyde with 5-methoxytryptamine to form a β-carboline has also been noted.[829] It is likely that these condensation pathways are quantitatively minor. However, it is not at all clear whether they may play an important role in the overall pharmacology and toxicology of the parent alcohol ingested.

In the case of the volatile α,β-unsaturated aldehyde crotonaldehyde, there is good evidence of the formation of a glutathione adduct involving a Michael addition across the activated double bond.[131] Oxidation and reduction of the aldehyde moiety may also occur.[485] Presumably, these metabolic reactions are characteristic of α,β-unsaturated aldehydes.

Unlike acetaldehyde and higher aldehydes, formaldehyde may be regarded as a normal metabolite in mammals.[11,706] Thus, it is not surprising that it may undergo a number of potentially important metabolic conversions, including condensations with pyruvic acid[568] and the amino group of α-amino acids.[1323] In general, formaldehyde enters into the metabolic pool of "one-carbon compounds" and via an intermediate adduct with tetrahydrofolic acid may be utilized in many physiologic metabolic processes.[104,114,344] However, these "synthetic" reactions are presumably minor, compared with oxidation to formic acid, the principal metabolic pathway of formaldehyde.[1308] In addition to liver involvement, monkey and human retinal extracts will form formic acid from formaldehyde in the presence of glutathione.[694]

KETONES

In general, the metabolism of ketones does not involve oxidative pathways, because the cleavage of carbon–carbon bonds requires that fairly high-energy processes be involved.[162(pp.412–462)] An alternate pathway often followed involves reduction of the keto group to a secondary alcohol, which may then be excreted unchanged or undergo conjugation and be excreted as its glucuronide conjugate.

An important exception to this generalization is the metabolic fate of acetone. It has been well established by use of ^{14}C-labeled acetone[982,1053] that, at least in small doses, a large percentage of the label appears as carbon dioxide, which implies the involvement of oxidative pathways. With larger doses, excretion of unchanged compound via kidneys, lungs, and even skin predominates.[960] For a summary of metabolic and toxicologic data on low-molecular-weight ketones, see Browning.[162(pp.412–462)]

FATTY ACIDS

The volatile acids considered are the saturated and unsaturated aliphatic fatty acids containing up to five carbon atoms and having boiling points ranging from 100 to 200 C.[1320]

The major metabolic pathway of organic acids is an oxidative degradation, leading ultimately to carbon dioxide and water. Fatty acid (FA) metabolism occurs in muscle, adipose tissue, mammary gland, brain, and liver. In man, FA is converted to carbon dioxide in liver and in extrahepatic tissues at about the same rate (0.10 and 0.12 mmol/min) and requires oxygen consumption of 52–62 ml/min. The enzymatic capacity available for oxidation of short-chain FA is always in excess of the measured amount of oxidation of long-chain FA by intact mammalian cells,[442] and the oxidation of short-chain FA occurs much more rapidly *in vivo* and *in vitro* than does the oxidation of long-chain substrates.[782] Whereas long-chain fatty acids are partially incorporated into triglycerides, oral administration of short-chain fatty acids has shown them to unergo rapid oxidation without direct incorporation into triglycerides to any significant extent.[782] Short-chain fatty acids enter the capillaries and are carried in the portal vein to the liver, which is the major site of transformation of FA in higher animals.[118,438]

Short-chain fatty acids occur in plasma, and formate and acetate have been found in human blood.[44,418]

Formic acid is a special case, owing to its greater acidity (pK_a, 3.7, compared with 4.7 for other saturated aliphatic acids) and its greater ease of oxidation. The principal hazard appears to be that of direct irritant effect of the acid on skin, eye, and mucous membranes. No evidence of cumulative toxicity exists, presumably because of the rapid metabolism of the acid.

Fatty acids are metabolized by oxidative processes that can be summarized as α, β, and ω oxidation. The enzyme sequence catalyzing the oxidation of FA has been extensively reviewed.[213,444,695,1173]

The process of α oxidation has been observed in mammalian tissues and occurs by α hydroxylation, a stereospecific replacement of an α H by a hydroxyl function with an overall retention of configuration, as shown by the preservation or loss of a tritium label in the D or L position at C-2.[873] In brain tissue and in liver preparations, an enzyme system (requiring Fe^{2+} and ascorbic acid and inactivated by ethylenediaminetetraacetate, EDTA) catalyzes the oxidative decarboxylation of the α-OH acid to the acid with one less carbon atom.[772,795] Detection of the 2-keto acid suggests that this is an intermediate and that the process occurs by Reaction 2.

$$RCH_2COOH \longrightarrow RCHOHCOOH \longrightarrow RCOCOOH \longrightarrow RCOOH + CO_2 \quad (2)$$

The process of ω oxidation is represented in Reaction 3 and occurs in liver microsomes, requiring reduced triphosphopyridine nucleotide (TPNH) and oxygen.[768]

$$RCH_3 \longrightarrow RCH_2OH + H_2O \quad (3)$$

However, the major degradative route for FA metabolism in all forms of life is the so-called β-oxidation pathway, originally proposed by Knoop[699] to involve oxidation to the β-keto derivative, followed by removal of the carboxy-terminal two-carbon fragment as acetate and repetition of the reaction sequence.

The active form of the substrate for oxidation is the acyl coenzyme A (acyl-CoA) derivative of the FA, with the intermediates in the oxidation similarly bound to coenzyme A (CoA).[794]

The acyl-CoA synthetase activates the FA to its CoA ester by catalyzing the reversible Reaction 4.

$$\mathrm{RCOOH + CoASH \rightleftharpoons RCOSCoA + H_2O} \qquad (4)$$

Acyl-CoA synthetase activity dependent on adenosine triphosphate (ATP) was found in all tissues, with the highest concentrations in liver, heart, and kidney.[1063]

The acyl-CoA derivative then undergoes the sequence of reactions referred to as the "FA oxidase spiral,"[793] involving successive α,β dehydrogenation, hydration, oxidation, and thiolytic cleavage by CoA to yield the acyl-CoA derivative containing two carbon atoms fewer than the original compound. The four steps are shown in Reactions 5–8.

$$\mathrm{RCH_2CH_2COSCoA \longrightarrow RCH{=}CHCOSCoA} \qquad (5)$$

$$\mathrm{RCH{=}CHCOSCoA \longrightarrow RCHOHCH_2COSCoA} \qquad (6)$$

$$\mathrm{RCHOHCH_2COSCoA \longrightarrow RCOCH_2COSCoA} \qquad (7)$$

$$\mathrm{RCOCH_2COSCoA + CoASH \longrightarrow RCOSCoA + CH_3COSCoA} \qquad (8)$$

A general review of the enzymes catalyzing these reactions has been given by Green and Wakil.[486] Acyl dehydrogenases (Reaction 5) specific for a narrow range of chain length have been isolated; in each case, the unsaturated product has the *trans* configuration. The enoyl hydratase enzyme (Reaction 6) appears to be independent of chain length[1161] and proceeds with stereospecificity, giving the L-β-hydroxyacyl-CoA derivative. The β-hydroxyacyl dehydrogenase catalyzing Reaction 7 is independent of chain length, but specific for the L configuration of the substrate.

Thiolytic cleavage of the β-ketoacyl-CoA occurs by β-ketothiolase catalysis (Reaction 8), producing acetyl-CoA, as well as the new acyl-CoA derivative. When this acyl-CoA product is acetoacetate, β-ketothiolase cleavage will lead to the formation of two molecules of acetyl-CoA (Reaction 9).

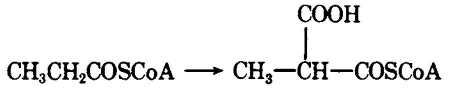
$$\mathrm{CH_3COCH_2COSCoA + CoASH \rightleftharpoons 2CH_3COSCoA} \qquad (9)$$

Acetyl-CoA is the form in which fragments then enter the citric acid (or tricarboxylic acid) cycle, where they undergo complete oxidation to carbon dioxide and water.[724]

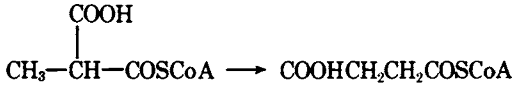
Other pathways for acetoacetate comprise reduction to β-hydroxybutyrate or cleavage to acetone and carbon dioxide; the acetone is then further cleaved (e.g., in muscle and other extrahepatic tissues) to acetyl fragments, which enter the acetyl pool.[982] When plasma FA concentrations are increased, there is evidence of increased oxidation to carbon dioxide, as well as increased formation of ketones.[1149]

The original β-oxidation theory has been extended into the "β-oxidation–condensation" theory, in which it is generally agreed that, in higher animals, cleavage of FA into two-carbon units is followed by condensation of these units into four-carbon (acetoacetate) units. Recent experimental data using ^{13}C-labeled acids have entirely supported this hypothesis.[797,798,1297]

An odd-numbered FA will ultimately leave a three-carbon chain, yielding one molecule of propionyl-CoA and one of acetyl-CoA as the final products. The propionyl-CoA is known to undergo metabolic carboxylation to methylmalonyl-CoA (Reaction 10), which rearranges to succinyl-CoA (Reaction 11) and enters the citric acid cycle and is oxidized further.[673]



$$CH_3CH_2COSCoA \longrightarrow CH_3-\overset{\displaystyle COOH}{\overset{|}{C}}H-COSCoA \qquad (10)$$

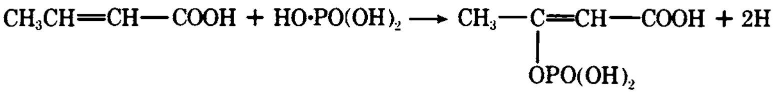


$$CH_3-\overset{\displaystyle COOH}{\overset{|}{C}}H-COSCoA \longrightarrow COOHCH_2CH_2COSCoA \qquad (11)$$

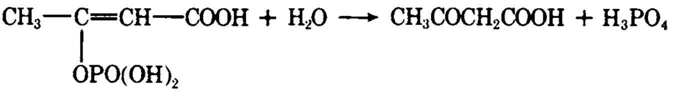
Propionic acid therefore does not accumulate under normal conditions.

An alternative route for propionate metabolism is the dehydrogenation of propionyl-CoA to acrylyl-CoA, followed by hydration to L-lactoyl-CoA. This undergoes dehydrogenation to pyruvate.[329] Under aerobic conditions, pyruvate is oxidized in animal cells to acetyl-CoA and carbon dioxide by the pyruvate dehydrogenase system; under anaerobic conditions—e.g., in vertebrate muscle—pyruvate is reduced to lactate in a reversible reaction.[329]

Little is known about the mode of oxidation of unsaturated fatty acids.[842] Acrylic acid is oxidized by kidney and liver enzymes. Sodium acrylate fed to dogs in doses up to 1.5 g underwent complete oxidation *in vivo,* no acrylate being excreted in the urine.[1320] Crotonic acid is also reported to undergo oxidation in rat kidney preparations[697] and with rat liver slices,[771] giving β-hydroxybutyrate and acetoacetate. Under the same conditions, acetoacetate was also formed from butyrate. It was postulated[771] that oxidation of crotonic acid may proceed by a dehydrogenation accompanied by addition of, for example, phosphate, to form an enol phosphate intermediate (Reaction 12) that would hydrolyze to the keto compound (Reaction 13).



$$CH_3CH{=}CH{-}COOH + HO{\cdot}PO(OH)_2 \longrightarrow CH_3{-}\underset{\displaystyle OPO(OH)_2}{\underset{|}{C}}{=}CH{-}COOH + 2H \qquad (12)$$



$$CH_3{-}\underset{\displaystyle OPO(OH)_2}{\underset{|}{C}}{=}CH{-}COOH + H_2O \longrightarrow CH_3COCH_2COOH + H_3PO_4 \qquad (13)$$

LACTONES

Some photochemical transformations (see Chapter 3) have indicated the possible atmospheric formation of lactones. These very reactive substances may be regarded as internal esters that are readily transformed into the corresponding hydroxy acids by lactone-hydrolyzing enzymes found in mammalian liver and kidney tissue.[156,693,1340] For most lactones (except the β-lactones containing a strained four-membered ring), this hydrolysis is reversible.[693] The hydroxy acids will then be further metabolized by the routes indicated above for alcohols and carboxylic acids. However, a second metabolic pathway may involve the interaction of lactones with biologic amines, leading either to an amino acid or to the amide of a hydroxy acid, and this ability to combine with cellular constituents could cause toxic effects if the compounds were ingested.[619]

ORGANIC COMPOUNDS CONTAINING NITROGEN

The principal nitrogen-containing compounds to be covered in this section arise from the photochemical interaction of airborne hydrocarbons and nitrogen oxides (Chapter 4). They include peroxyacylnitrates like peroxyacetylnitrate and may include alkyl and acyl nitrites and nitrates. The literature contains little information on the mammalian absorption, fate, and excretion of the specific compounds present in air as pollutants. However, some studies concerning the metabolic disposition and fate of compounds closely related to those present as air pollutants are discussed below.

Peroxyacylnitrates

From the toxicologic standpoint, the most important of the nitrogen-containing pollutants are the peroxyacylnitrates, of which peroxyacetylnitrate (PAN) is the most widely studied.[340,1184] The fate of PAN and its relatives has not yet been studied in intact mammals. Because PAN is an important phytotoxic air pollutant,[1184] some studies of its biochemical properties have been reported. Most importantly, PAN is known to react readily with sulfhydryl groups.[880,882,883] For example, the reaction of PAN with reduced glutathione produces a mixture of oxidized glutathione and S-acetylglutathione.[880,883] The fate of PAN during sulfhydryl oxidation has not been reported. During the oxidation of olefins, however, PAN is converted to a mixture of methylnitrate and nitromethane.[289] In contrast, the base-catalyzed decomposition of PAN yields acetate ion, nitrate ion, and molecular oxygen.[1147] Further studies will be required to assess the role of these reactions in the *in vivo* metabolism of PAN and related compounds in mammals. Such studies are urgently needed.

Alkylnitrite Esters

Like amylnitrite (a coronary vasodilator), alkylnitrite esters present as air pollutants could enter the body by inhalation and be rapidly absorbed from the lungs. Amylnitrite is destroyed by gastric juice, so unchanged compound does not enter the body orally.

The fate of amylnitrite, once absorbed, appears to be a straightforward hydrolysis to amyl alcohol and nitrite ion.[1324] It is currently generally thought that amylnitrite exerts its pharmacologic effect through the intact molecule, rather than by virtue of its hydrolysis to nitrite. Nickerson[921] has recently discussed this point and other aspects of the pharmacology of amylnitrite.

The nature of the *in vivo* hydrolysis of alkylnitrite esters is unknown. For example, it is apparently not known whether the reaction is catalyzed by an enzyme or is a nonenzymatic process. *In vitro* studies with tissue homogenates are needed to clarify this point.

Finally, there is the question of the fate of the nitrite ion formed by hydrolysis. Studies as early as 1893 indicated that nitrite is largely oxidized to nitrate in the intact animal.[751] Heppel and Porterfield[556] have studied this reaction in some detail and found that hydrogen peroxide serves as the oxidant and that the reaction depends on catalase. Thus, nitrite was readily oxidized to nitrate in the presence of hydrogen peroxide-producing enzymes, such as D-aminooxidase, when catalase was added. Nitrite ion is also known to react with hemoglobin to produce methemoglobin.

Alkylnitrate Esters

No studies have been reported on the fate of nitrate esters of monohydric alcohols, i.e., nitrate esters of the type that would occur as air pollutants. However, nitrate esters of polyhydric alcohols (used as coronary vasodilators) have been extensively studied. Their pharmacology has been reviewed by Nickerson[921] and Angelakos,[43] and Litchfield[773] has recently summarized the various aspects of the metabolism of nitrate esters of polyhydric alcohols.

Glycerol trinitrate, "nitroglycerin," is reasonably volatile at room temperature. It is customarily administered sublingually and is efficiently absorbed from the mucous membranes of the mouth. When given orally to man, it is rather ineffective, either because of poor absorption from the gut or because of destruction in the gut.[1016] In the rat, however, [^{14}C]nitroglycerin given orally was found to be well absorbed.[309] Nitroglycerin is also readily absorbed through unbroken skin and from the lung. This point is of considerable toxicologic importance in the case of workers in explosive plants. These data suggest strongly that any volatile nitrate esters present as atmospheric pollutants would readily enter the body via skin, lungs, and oral mucosa.

No thorough study of the distribution of intact alkylnitrate esters into body tissues has yet been reported. Some data from radiocarbon labeling studies are available. However, because only radiocarbon concentrations were measured, it is not clear whether intact nitrate ester was being measured or whether only metabolites were present.

Once absorbed, nitroglycerin is rapidly metabolized by loss of the nitrate ester groups.[309,910] The initial metabolite is a mixture of glycerol-1,2-dinitrate and glycerol-1,3-dinitrate. There is no apparent initial preference for the primary or secondary ester. The ultimate metabolites are glycerol-1-nitrate and glycerol and its degradation products. The partially cleared esters, as well as glycerol itself, are excreted in urine. Recently, Crew and co-workers[261] have shown that the mononitrate, dinitrate, and trinitrate esters of pentaerythritol are excreted as glucuronides in the rat. Furthermore, Sisenwine and Ruelius[1119] found that 5-isosorbide mononitrate glucuronide undergoes *in vivo* denitration to isosorbide glucuronide. Reed and co-workers[1010] have also discussed the glucuronides of isosorbide mononitrate.

The formation of glucuronides of partially nitrated polyols is of some interest, because it has been speculated that β-hydroxyalkylnitrates may be present as air pollutants (see Chapter 4). The metabolism of two such compounds, ethyleneglycol mononitrate and propyleneglycol mononitrate, has been investigated.[223,224] Both disappear rapidly from the body, but no attempt has been made to identify glucuronides as possible metabolites.

The metabolic reaction involved in the denitration of alkylnitrates is not a simple ester hydrolysis, in that the product is nitrite ion, rather than the expected nitrate (Reaction 14).[43,260,1324]

$$RONO_2 \longrightarrow ROH + NO_2^- \qquad (14)$$

The nature of the reductive cleavage of alkylnitrate esters has been the subject of a relatively large number of investigations. In 1940, Krantz and co-workers[723] proposed that nitrate esters are reduced to nitrite esters, which in turn undergo facile hydrolysis to carbinol and nitrite ion (Reaction 15).

$$RONO_2 \xrightarrow{+2H} RONO \xrightarrow{H_2O} ROH + NO_2^- \qquad (15)$$

Oberst and Snyder[936] later demonstrated that incubation of nitroglycerin with rabbit liver homogenates at 37 C and a pH of 8.4 resulted in a rapid release of nitrite ion. Heppel and Hilmoe[555] observed that nitrate esters reacted with reduced glutathione to produce oxidized glutathione and nitrite ion. The reaction was catalyzed by liver homogenate. The enzymatic activity responsible for the reaction is localized in the soluble fraction of liver[909,910] and has been referred to as glutathione–organic nitrate reductase.[909] Reduced nicotinamide adenine dinucleotide phosphate (NADPH) is required, to maintain a pool of reduced glutathione, a step mediated by glutathione reductase. The rate of disappearance of NADPH can be used as a measure of glutathione–organic nitrate reductase.[909] The overall reactions are Reactions 16–19.

$$2NADPH + GSSG \longrightarrow 2NADP^+ + 2GSH \qquad (16)$$

$$2GSH + RONO_2 \longrightarrow GSSG + H_2O + RONO \qquad (17)$$

$$\underline{RONO + H_2O \longrightarrow ROH + HNO_2} \qquad (18)$$

$$2NADPH + RONO_2 \longrightarrow 2NADP^+ + ROH + HNO_2 \qquad (19)$$

Pretreatment of rats with phenobarbital stimulated the metabolism of nitrate esters in the *in vitro* system.[910] The effect may be a consequence of an increase in glutathione reductase. In any event, later studies[740,908] indicate that tolerance to nitroglycerin is not due to increased *in vivo* metabolism. Considerably more work will be required before the nature of the enzyme glutathione–organic nitrate reductase (enzyme classification 1.8.6.1—glutathione:polyolnitrate oxidoreductase) is completely understood. In particular, it has not been demonstrated that the organic nitrites are indeed true reaction intermediates. This may be revealed as part of a substrate structure–activity study, which should be pursued and should involve nitrate esters of simple aliphatic monohydric carbinols.

Alkylnitrate esters are also known to be readily degraded to nitrate ion by blood serum. The reaction in rat serum was investigated[310] in some detail recently and found to require neither NADPH nor glutathione. The reaction is nevertheless considered to be enzymatic. It is possible that, in the intact animal, degradation in the serum is of greater importance than in the liver.

Acylnitrates

Another class of compounds found are the anhydrides of carboxylic acids and nitric acid. Acetylnitrate is a well-known example of this class. Acetylnitrate is a colorless hydroscopic liquid that readily hydrolyzes to acetic and nitric acids.[972] Nothing is known concerning its fate in mammals. It is reasonable to suppose, however, that it would be readily absorbed by humans and would undergo *in vivo* breakdown. Whether it would be directly hydrolyzed to acetate and nitrate or would undergo reductase cleavage to acetate and nitrite is open to conjecture.

Other Compounds Containing Nitrogen

In addition to the classes of compounds discussed above, other nitrogen compounds occur in the atmosphere, particularly in some industrial locations. These include such classes of organic solvents as aliphatic and aromatic nitro compounds and aliphatic and aromatic amines. Compounds of these classes are also thought to be formed photochemically in the atmosphere in minimal concentrations. Aromatic nitro compounds are characteristically metabolized in mammals by reductive mechanisms.[462,862] Among the products formed are arylhydroxylamines and aromatic nitroso compounds. These metabolites are thought to cause the methemoglobinemia seen after ingestion of some nitroaromatics. The metabolism of the nitroparaffins has not been fully studied. The major route of metabolism, however, appears to be oxidative cleavage to aldehyde and nitrite.[594,1320]

The reactions by which amines are metabolized depend on the chemical nature of the amine, i.e., whether the amines are primary, secondary, or tertiary and whether they are aromatic or aliphatic. Low-molecular-weight aliphatic primary amines, as well as benzylamines and β-phenethylamines, are metabolized to aldehydes and ammonia by the soluble enzyme, monoamine oxidase.[1364] More lipid-soluble amines and those which are α branched appear to be oxidatively deaminated by the hepatic microsomal system.[959] An interesting recent observation has been that ketoximes are formed in the course of microsomal deamination of α-branched primary amines.[594]

The oxidative dealkylation of tertiary and secondary amines to aldehydes and dealkylated amines has been extensively reviewed.[484,835] This reaction, which appears to be catalyzed by hepatic cytochrome P-450, is a key reaction in the inactivation of ingested amines. In contrast with aliphatic amines, aromatic amines, such as aniline, undergo N-hydroxylation in the body.[1221] This route of metabolism is very important, because the N-hydroxy derivatives of aromatic amines have been implicated not only in methemoglobin formation, but in carcinogenesis and mutagenesis.[860,1222]

There is no convincing evidence of the occurrence of N-nitrosamines in the atmosphere. However, because they are considered to be potential carcinogens, a systematic search for them will be necessary. Nitrosamines are thought to be metabolized *in vivo* to diazo compounds, which in turn form covalently bonded structures with macromolecules. The carcinogenic process could then be initiated by these altered cell constituents.[860]

ORGANIC COMPOUNDS CONTAINING SULFUR

Pollution of the atmosphere by various sulfur compounds has received a great deal of attention in recent years.[8,682,1025] A reading of recent reviews and a close search of the literature indicate that information concerning volatile organic sulfur compounds in the atmosphere is very limited. Thus, although a recent review by Kellogg *et al.*[682] states that about 95% of the sulfur emitted to the atmosphere is in the form of "sulfur dioxide," other evidence suggests the ubiquitous occurrence of dimethylsulfide in the atmosphere.[783]

Many organic sulfur compounds affect mammalian systems and have been discussed from the toxicologic viewpoint.[963] Although these compounds are not expected to be formed by any of the mechanisms discussed in Chapter 4, a knowledge of their metabolic transformations should be helpful in predicting the various ways in which other vapor-phase organic sulfur compounds may be handled by the mammalian detoxifying system.

The metabolic pathways by which organic sulfur compounds are handled by mammalian systems are basically similar to the limited number of pathways for the metabolism of other foreign compounds, i.e., by enzymatic detoxifying systems localized in the liver. These include, in part, reduction, oxidation, conjugation, S-methylation, and formation of thiosulfate esters.

Reduction

Disulfides have been shown to be reduced to the corresponding mercaptans. The general reaction is Reaction 20.

$$\mathrm{RSSR'} \rightleftharpoons \mathrm{RSH} + \mathrm{R'SH} \qquad (20)$$

Thus, diethyldisulfide is reduced to ethylmercaptan,[957,1320] tetraethylthiuram disulfide (Antabuse) is reduced to diethyldithiocarbamic acid,[957,1321] and dibenzyldisulfide is reduced to the corresponding benzylmercaptan.[1320] A nonspecific nucleotide-dependent disulfide reductase is present in rat liver and catalyzes the overall reaction (Reaction 21).[1198]

$$\mathrm{NADPH^+} + \mathrm{RSSR} \longrightarrow 2\mathrm{RSH} + \mathrm{NADP} + \mathrm{H^+} \qquad (21)$$

This nonspecific disulfide reductase may be responsible for the metabolism of dimethyldisulfide that is emitted into the atmosphere.[8] Reduction of dimethyldisulfide would yield methylmercaptan, which would then be oxidized to carbon dioxide and inorganic sulfate.

The sulfur compounds generally undergo more than one type of biotransformation. Thus, after the reduction of the diethyldisulfide to yield the mercaptan, the mercaptan may undergo methylation to form the methylalkyl sulfide, which may then be oxidized to the sulfoxide and finally to the sulfone. Furthermore, a substantial portion of the sulfur may be excreted as inorganic sulfate.[957,1320]

Dimethylsulfoxide has been reported to be metabolically reduced to dimethylsulfide,[323,957] and diaminodiphenylsulfoxide is reduced to diaminodiphenylsulfide.[816]

Oxidation

Lower mercaptans have been reported to be metabolized eventually to inorganic sulfate and carbon dioxide.[194,1320]

Dimethylsulfide has been shown to be oxidized to dimethylsulfoxide,[1317] which is further oxidized to dimethylsulfone.[593,957] There are a number of cases in which sulfide compounds are initially oxidized to sulfoxides and then to sulfones. Thus, the propylmercaptan moiety of thiamine propyldisulfide is oxidized partly to the sulfone and excreted in part as inorganic sulfate.[928] S-Methylthiophenol is oxidized to the sulfoxide and then to the sulfone.[818] Mustard gas (*bis-b*-chloroethylsulfide) is in part oxidized to the sulfone,[297] diaminodiphenylsulfide is oxidized to the sulfoxide,[463] and the thio analogue of phenylbutazone is oxidized to the sulfoxide.[298]

A number of thioethers, including 6-methylmercaptopurine and S-methylbenzothiazole, have been shown to be oxidatively cleaved by mammalian liver enzymes.[815] The formaldehyde formed in the process probably enters the one-carbon metabolic pool. The other products include mercaptans and mercaptan derivatives. Oxidative dealkylation is a pathway to be considered in the metabolism of organic sulfur compounds; Reaction 22 illustrates this.

$$\mathrm{RSCH_3} \xrightarrow[\mathrm{O_2}]{\mathrm{NADPH}} \mathrm{HCHO} + \mathrm{RSH} \qquad (22)$$

It is possible for some mercaptans to be oxidized to disulfides. However, it is more likely that the disulfides would be reduced to the corresponding mercaptan.

Conjugation

Conjugation with glucuronic acid is one of the main *in vivo* routes by which both exogenous and endogenous substances are detoxified and inactivated. In a manner similar to that of hydroxy compounds, thiols form S-glucuronides. Thus, thiophenol and 2-mercaptobenzothiazole have been shown[237,460,672,818,1171,1320] to be metabolized to the S-glucuronides.

Methylation

Sulfhydryl groups are methylated *in vivo*. Thus, thiophenols, ethylmercaptan, and thiouracil are converted to their S-methyl analogues by S-methyltransferases, using the donor S-adenosylmethionine.[818,1061,1321]

Formation of Thiosulfate Esters

In a manner similar to that of an alcohol or phenol, thiols might be expected to form thiosulfate esters. Phenylthiosulfate has been reported to be a possible metabolite of thiophenol, because an increase in sulfate ester was found after the administration of thiophenol.[1320]

It is possible for a sulfite to react with any suitable disulfide according to the general Reaction 23.[1039]

$$SO_3^- + RSSR \rightleftharpoons RSH + RSSO_3^- \qquad (23)$$

Thus, sulfate ester formation after ingestion of a disulfide must be entertained as a distinct possibility in the metabolism of vapor-phase volatile organic sulfur compounds. It has recently been suggested[169] that both sulfinic and sulfonic acids may be among the products obtained from the reaction of sulfur dioxide and hydrocarbons.

6

Biologic Effects of Vapor-Phase Organic Pollutants in Man and Other Mammals

ABSORPTION

Vapor-phase organic pollutants (VPOP) are absorbed through four routes: the respiratory and gastrointestinal tracts, the eye, and the skin.[61] Discussion of routes and mechanisms of absorption of a pollutant requires reference to its physicochemical properties, such as vapor pressure, stability, reactivity, and solubility. The metabolism, excretion, and toxicology—including ability to produce acute and chronic inflammatory reactions, allergenicity, and carcinogenicity—are discussed elsewhere and are mentioned only briefly here.

Respiratory Tract

The volume of air normally breathed by a normal human adult at rest approximates 8 liters/min, or about 11,500 liters/day. Moreover, during vigorous exercise, the volume, and accordingly the amount of pollutants in the breathed air, can increase by a factor of 10 or more—to 80–100 liters/min—for relatively short periods. It can be assumed that the respiratory tract tissues are exposed to more air contaminants than the tissues of any other route of absorption, and more so during vigorous effort.[34]

Generally, pollutants cross mucosal membranes—such as those of the alveoli, conjunctivae, etc.—via three mechanisms. Through the first, pollutants are actively absorbed, with energy derived from the cells themselves. The second mechanism is vesicular transport, or cellular ingestion of the pollutant substance. It has also been called pinocytosis, or "drinking" by the cell. Although it is certainly the main mechanism for the systemic absorption of large particles and colloids via the gastrointestinal tract, it is of little importance with regard to the absorption of VPOP via the respiratory tract, the eye, and the skin. An exception would be VPOP absorbed onto such particles or colloids and absorbed through pinocytosis in the gastrointestinal tract. The third and main mechanism is diffusion. For inhaled soluble pollutants in the vapor phase, this is the main mode of absorption.[61]

In the respiratory tract, where a pollutant is absorbed and how much is absorbed depend mainly on the pollutant's solubility in water. Highly water-soluble VPOP, such as formaldehyde, are absorbed mainly in the upper respiratory tract, where they first come into contact with the moist surfaces of the respiratory passages. Thus, the proximal upper respiratory tract's nasal, buccal, nasopharyngeal, and laryngotracheal areas are the sites of absorption of highly water-soluble compounds. However, poorly water-soluble VPOP can reach the distal lower respiratory tract and can affect the alveolar and bronchiolar epithelium and the interstitial tissue, permitting entrance into the bloodstream. The chlorinated camphene pesticide toxaphene and the products of incomplete combustion in smoke from fires and tobacco are examples of compounds absorbed mainly in the distal respiratory tract.[116]

Once VPOP reach the alveoli, the rate of alveolocapillary transfer and of systemic absorption is high. Anesthetic gases and vapors can be measured in distant tissues, such as the brain, within seconds after inhalation. In a limited sense, the bronchial tree functions as a system of elastic pipes conducting air in and out of the alveoli. Thus, although the bronchial mucosal and other luminar cells are exposed to most air pollutants, these tissues absorb only the VPOP that are highly to moderately water-soluble, with this absorption being local and nonsystemic. VPOP that are only poorly water-soluble can also interact with the bronchial mucus to some degree, but may not be directly absorbed systemically. Acute and chronic inflammatory reactions, as well as hyperreactivity, affect the mucosal and other cells and tissues of the nose, nasopharynx, and bronchial tree, which are the first tissues to contact VPOP. This is especially so for water-soluble materials, but such reactions depend on the specific toxicologic properties of the pollutant.[116] These types of reactions may also affect the absorption of VPOP positively or negatively.

Deichmann *et al.*[301] noted rapid absorption of nitroolefins at various concentrations from the respiratory tract of exposed rats, chicks, and rabbits, as evidenced by peripheral vasodilatation and marked irritation of the respiratory mucous membrane. At high relative humidity, there was greater pulmonary damage than in animals exposed to the same compounds at low humidity.

Agricultural workers and pest-control operators are often adversely affected by simultaneous respiratory, conjunctival, and dermal exposures to aerosolized pesticides during spraying of crops, fumigation, and similar operations. Pesticides are commonly dispersed with the aid of hydrocarbon dilutants or propellants, such as kerosene for agricultural application and halogenated hydrocarbons (Freons) for household and other applications. This gives particular importance to experimental and field experience with pesticides, inasmuch as pesticide uptake could act as a tracer for the mechanism of human uptake of vapor-phase hydrocarbons. Too few quantitative data are available from uncontrolled occupational exposures to indicate the degree to which different exposure routes contributed to the systemic absorption and resulting toxic effects. On the basis of clinical toxicologic evidence, dermal exposure is thought to play an important role in the uptake of organophosphorous pesticides. This type of exposure is of special importance, because of the extensive household use of these compounds.

VPOP may be adsorbed onto or absorbed by finely divided atmospheric particles, whether these belong to the natural background or man-produced aerosols—such as asbestos, road dust, soot, fly ash, and metal fume—or arise from biologic sources—such as animal decidua, pollens and other vegetable particles, spores, and fungi. In urban areas, many of these particles, notably the first five, normally enter the respiratory tract and reach the alveoli when the particle size is 0.5–5 μm. Only a small fraction of particles of this size are absorbed through the alveoli and retained in the body.[906]

Gastrointestinal Tract

Most inhaled VPOP will generally reach the gastrointestinal tract, where they will not be readily absorbed, except for highly water-soluble compounds absorbed in the buccal and pharyngoesophageal areas. As noted, gastrointestinal exposure to and absorption of VPOP through pinocytosis can occur from the ingestion of air-suspended particles onto which VPOP have been adsorbed and from the swallowing of bronchial phlegm containing similar particles with adsorbed VPOP. Moreover, some gastrointestinal exposure to and absorption of such pollutants can conceivably occur from ingestion of VPOP adsorbed onto edible materials, like produce. No quantitative data are available regarding any of these.

There are data on experimentally induced gastrointestinal absorption of liquid organic air pollutants—such as aldehydes, benzene, kerosene, toluene, and xylene—and on the effects of accidental ingestion of liquid pesticides. But quantitative data pertaining to absorption and oral toxicity of organic pollutants in liquid form cannot be applied directly to the study of gastrointestinal absorption of vapor-phase organic air pollutants.

Eye

Except during sleep, the conjunctival membranes and corneas are almost continuously exposed to VPOP, much as the respiratory tract and skin. However, although very small amounts of air pollutants, such as acrolein and formaldehyde, contact these eye tissues, it is usually there that the first uncomfortable reactions are felt. Such reactions can range from mild irritation to acute inflammation, depending on concentration of the VPOP, their irritant properties, etc. Highly water-soluble pollutants are most likely to be absorbed by the conjunctiva locally and systemically.[116,301]

Skin

Scant information is available regarding the amount of percutaneous absorption of VPOP. In general, skin absorption is a function of the solubility of a substance in a water–lipid system. Thus, because most VPOP are very soluble in lipids and few are highly water-soluble, percutaneous absorption of VPOP at large is likely to be greater via the skin lipids, hair follicles, and sebaceous glands for lipid-soluble VPOP, and less through sweat glands for water-soluble compounds (Scheuplein and Blank[1072] and R. J. Feldmann, personal communication).

Although the low permeability of the keratinized intact stratum corneum has been considered one of the skin's major protections, newer data reveal that this thin, uppermost epidermal layer permits some percutaneous absorption of vapors. In the absence of pores or air-filled interstices in the stratum corneum, molecules able to dissolve in that intact tissue can exhibit appreciable permeability through it. For example, the transport of alkane vapors does indeed increase with their solubility in the epidermal tissues. The more water-soluble VPOP, such as acrolein and formaldehyde, are thus more likely to penetrate. In general, the trend is as follows: (1) The diffusion (as measured by sorption) of alcohols and alkanes decreases with increase in molecular weight; (2) the presence of hydroxyl groups promotes the solubility of alcohol vapors, but decreases their diffusion markedly; and (3) the diffusion of vapors like alcohols and the higher alkanes is considerably lower than for nonreactive permanent gases, such as nitrogen, carbon dioxide, and oxygen.[1072]

It has been shown that nitroolefins can produce damage to the lung by percutaneous absorption.[301] Although nitroolefins have not been shown to be important pollutants, cutaneous absorption may be an overlooked route for systemic toxicity.

Occupational health studies involving aerosols of the organophosphorous pesticide parathion indicated that spraymen absorb much more parathion through the skin than through the respiratory tract. However, these studies also indicated that the body absorbed only a small fraction of the total dermal exposure, whereas the absorption through the respiratory tract exposure appeared to be total.[343] Other occupational experience has shown that dermal absorption related to exposure to pesticides is highly influenced by the type of pesticide, the diluent or solvent used, the physical state of the material, the size and hydration (sweatiness) of the exposed area of skin, the part of the body exposed, and the condition (intactness) of the exposed skin's stratum corneum.[187,188] Dermal absorption of VPOP is most likely influenced by the same factors.

Comparison of Various Routes of Absorption

Evaluation of common routes of human exposure to pesticides leads to the general conclusion that toxic chemicals at equivalent dosages are absorbed more rapidly and completely from the respiratory tract than from the skin.[382] Although not stated specifically about VPOP, it has been demonstrated that the hazard—and, by inference, the degree of absorption—from respiratory exposures with the same "dose" may be 3 times as great as that from dermal exposure and 10 times as great as that from oral exposure.[45] Oral exposures, as discussed elsewhere, usually involve detoxification or modification in the liver.

PATHOPHYSIOLOGIC EFFECTS

The consequences of inhalational exposure of hydrocarbons in mammalian organisms are complex, because the inhaled substances are always mixtures. This intermingling of compounds makes it virtually impossible to incriminate any single material as the villainous agent in the causation of pathologic changes. In addition, the chemical events that occur spontaneously in the atmosphere as a result of photooxidation cause the formation of additional compounds, which are derived from hydrocarbon material. These materials, which include aldehydes and such complex oxidants as peroxyacetylnitrate, are among the most important irritants of the atmospheric contaminants to which man and other mammals are exposed.

These two factors, the complex mixtures of hydrocarbons and other chemicals in the atmosphere and the spontaneous production of additional oxidizing agents involving hydrocarbon substrates, preclude the identification of any agent as the causative factor in any pathologic change in urban exposures. An additional factor causing confusion in the interpretation of the effects of these agents in human exposures is the background of disease and hyperreactivity to additional insults that may exist in the populations under study. These responses may be the result of genetic deficiency states, such as deficiencies of serum α_1-antitrypsins; prolonged and heavy inhalation of cigarette smoke, which may aggravate and amplify disease states; intercurrent infection or allergic hypersensitivity; and underlying "sensitivity" to atmospheric materials.

These difficulties have made it necessary to resort to controlled human exposure studies or animal exposures in order to evaluate the responses to single agents of the hydrocarbon groups known to exist in the polluted urban atmosphere. Even with artificial exposures, minimal changes in the tissues are difficult to detect. This may be due to the insensitivity of the methods used in reported studies and to the very limited anatomic changes produced by many of the atmospheric hydrocarbons.

Methods for Detecting Effects on the Respiratory System

The effects of many common pollutants on the airways are best assessed by measurement of specific airway conductance and resistance at a known lung volume, usually the functional residual capacity (FRC) or the lung volume at the end of an ordinary breath. For total pulmonary resistance (TRP) measurements (of lungs and chest) in such animals as the guinea pig, a pulsating pressure is applied to the whole-body plethysmograph containing the animal, and rate of airflow is measured by a screen pneumotachygraph applied by means of a mask over the nose and head. TPR is the ratio of the pressure difference to the rate of airflow.

Transfer factor (diffusion capacity), related to the rate of transfer of tracer carbon monoxide from lung spaces into the blood, can be measured and is useful when pollutants cause pulmonary edema, in both man and animals. Arterial blood can be sampled, and pO_2, pCO_2, pH, and bicarbonate can be measured.

All the foregoing are reasonably objective measurements. Spirometry in humans, which involves recording the deepest breath that can be inhaled and then exhaled by a maximal rapid (forced) exhalation, measures vital capacity (FVC or FEV) or the amount exhaled rapidly. Indexes related to rate of exhalation are the FEV_1 (the volume exhaled during the first second) and the rate (liters/min) during the middle 50% of the vital capacity (MMEF, or maximal midexpiratory flow rate) and during the range 200–1,200 cm^3 of exhalation (MEFR, or maximal expiratory flow rate). Measurements after the inhalation of nebulized bronchodilator are useful in assessing the degree of reversible bronchoconstriction. The first part (40–50%) of maximal expiratory flow is subjective, in that several recordings are necessary to assume that maximal forced exhalation has been achieved.

Neither spirometry nor body plethysmography assesses small-airway (bronchioles 2 mm or less in diameter) resistance in humans. Critical closing capacity, or the volume at which small airways close during exhalation, is being assessed for implications in inhalation effects.

Effects of Specific Classes of VPOP

ALIPHATIC HYDROCARBONS.

Straight-chain hydrocarbons are virtually inert, and no demonstrable pathologic changes have been reported. Methane and ethane cause death only by asphyxiation or anoxia. The higher saturated aliphatic compounds, as well as the unsaturated or olefinic hydrocarbons, produce anesthesia in higher concentration. Heptane and octane are reported to cause incoordination and vertigo after 4 min of inhalation at 5,000 ppm, and inhalation of octane at 10,000 ppm or heptane at 15,000 ppm produces narcosis within 30–60 min. Ethylene produces little or no effect in concentrations of 5,500 ppm for periods of several hours. Inhalation of acetylene at 350,000 ppm for 5 min will produce unconsciousness. This applies to hydrocarbons in the CH_4–C_8H_{18} series.[1227]

ALICYCLIC HYDROCARBONS.

Alicyclic hydrocarbons have effects similar to those of the straight-chain compounds. In general, higher concentrations act as depressants or anesthetics. They are retained but sparingly in tissue and blood, and their toxicity is low. Cumulative toxicity due to continued or repeated exposures to low concentrations is considered to be unlikely. Single exposures to cyclohexane vapor at 18,000 ppm in air for 5 min produce slight muscle tremors in mice and rabbits; 25–30 min of such exposure produces muscular incoordination and paralysis. This dose does not produce effects in guinea pigs. Chronic exposures to cyclohexane vapor at up to 3,330 ppm in air for 6 hr/day for 60 days in rabbits and 1,240 ppm for similar periods in monkeys produce no noticeable effects. Chronic exposures to methylcyclohexane vapor (2,800 ppm for 24 hr/day for 70 continuous days) also produce no noticeable effects.[1227]

AROMATIC HYDROCARBONS

Aromatic hydrocarbons are biochemically active and more irritating to mucous membranes than are aliphatic and alicyclic hydrocarbons in equivalent concentrations. Some, particularly benzene, produce leukopenia and anemia with chronic exposure. In general, benzene, toluene, or xylene in acute and chronic exposures at concentrations above 100 ppm may result in fatigue, weakness, confusion, skin paresthesias, and mucous membrane irritation (eye and nose), and at concentrations above 2,000 ppm, in prostration and unconsciousness. Styrene in concentrations above 1,000 ppm produces mucous membrane irritation in some animals, but unconsciousness and death in others. Styrene concentrations of 200 ppm produce mucous irritation in man.

Apparently, no human health effects have been reported for benzene below 25 ppm or for the other unsubstituted aromatic hydrocarbons at this concentration. Of 102 men studied in the rotogravure printing industry, 74 had evidence of chronic benzene poisoning of various degrees of severity.[489] Savilahti[1069] found blood abnormalities in 107 of 147 workers in a shoe factory. The source of benzene was cement, and the concentrations were reported to have ranged from 318 to 470 ppm. One death occurred. Winslow[1341] reported blood changes in workers where concentrations of benzene vapor below 100 ppm were found. Heimann and Ford [549] found one death from benzene poisoning and three other cases of blood changes where air analysis for benzene showed a concentration of 105 ppm. Wilson [1333] reported three fatal cases in a plant where the average concentration of benzene vapor was 100 ppm. Hardy and Elkins[528] reported one death from benzene poisoning and several other cases of blood changes in a plant where repeated air analyses indicated benzene vapor concentrations of about 60 ppm.

Hematologic changes may occur without general symptoms, such as headache, fatigue, dizziness, anorexia, nervousness, and irritability. The opposite was also observed—that is, general symptoms of toxicity without hematologic change.

Acute exposures in man to toluene at 50–100 ppm produce no apparent effects, but paresthesia, fatigue, and confusion have been reported after exposure to 220 ppm for 8 hr.[456,966] After exposure to 600 ppm for 8 hr, confusion, dyscoordination, staggering gait, nausea, headache, dizziness, and dilated pupils have been observed. In acute exposures, 6,700 ppm is the LC_{50} in mice. Hematologic effects are not observed with toluene toxicity.

ALDEHYDES

Aldehydes are formed from hydrocarbons in the atmosphere. Formaldehyde and other mucous-membrane irritants—such as ketones, PAN, and other oxidants—are formed in and may be consumed in the atmosphere through photochemical actions. Their toxicity is predominantly related to their irritant properties.[1227] The principal effect of low concentrations of aldehydes is irritation of the skin and the mucous membranes of the eyes, nose, and throat. The aldehydes of lower molecular weight are more soluble and act chiefly on the eyes and upper respiratory tract. The higher-molecular-weight and less soluble aldehydes reach more deeply and may affect the lungs.

Aldehydes are frequent contaminants in the urban atmosphere, as well as in industrial situations, but detailed information concerning the effects of this family of compounds in human experience and chronic animal studies is limited. No evidence of disease or injury due to cumulative exposures has been described.

Although nearly all aldehydes produce irritation of the mucosal surfaces on exposure, the unsaturated olefinic aldehydes and the halogenated aldehydes generally cause greater irritative effects than do saturated ones. Aromatic and heterocyclic aldehydes cause less severe irritation.[238] Within a given aldehyde series, the irritant effect decreases with increasing length of the carbon chains.[1116] Low-molecular-weight aldehydes act primarily on the eyes and upper respiratory tract, and longer-chain aldehydes, which are less soluble, tend to affect the lower respiratory tract and pulmonary parenchyma. Many aldehydes have anesthetic properties, which appear to vary inversely with increasing molecular weight of the aldehyde group.[1122] In general, because they are rapidly metabolized, aldehydes are not good anesthetic agents. Acute exposure to high concentrations of aldehyde vapors may produce injury to the alveolar capillary membranes, pulmonary edema, focal hemorrhage, and exudation. A variety of sequelae after acute high-dose exposures have been reported. These effects—which include pneumonic consolidation, alveolar wall thickening, and parenchymal destruction—are unusual and may be the result of complicating infection. Low concentrations of aldehyde cause a decrease in mucociliary activity of the respiratory epithelium after acute exposures. Little is known of the responses of the respiratory ciliary apparatus after chronic, intermittent, or continuous exposures to aldehydes.

Of the specific aldehydes present in the general urban atmosphere, two are relatively important. Formaldehyde and acrolein are present in greater concentrations than other aldehyde forms. Formaldehyde may be perceived by its odor at concentrations between 0.060 and 0.5 ppm.[844,845,1160] Irritant effects on the eyes (producing lacrimation) and on the nasal and pharyngeal mucosa (causing sneezing, rhinorrhea, cough, sore throat, a sense of substernal oppression, or a combination of these) are reported at concentrations below 1 ppm, varying from 0.1 to 1.0 ppm.[127,845,869,1085] Other studies[390] have incriminated concentrations of about 2–3 ppm as necessary to produce these symptoms. Some tolerance or adaptation to formaldehyde exposure can occur, and concentrations of 2–3 ppm may be tolerated by some subjects for periods of 8 hr. Above 5 ppm, discomfort becomes very pronounced after 10–30 min in many subjects. These symptoms persist for an hour or more after removal from the irritant atmosphere. Serious chemical bronchitis, laryngitis, and even bronchopneumonia are reported at concentrations above 5 ppm.[805,1264]

Formaldehyde exposures also occur in industrial settings. Dermatitis was observed in 25 men engaged in the manufacture of phenol–formaldehyde and urea–formaldehyde resins.[530] Eczematoid reactions of an acute and chronic type and a combination of the two were observed. These work exposures usually involved direct contact with liquid, solid, or resinous formaldehyde materials and differ in this respect from the usual vapor exposures in air pollution episodes. Skin eruptions due to formaldehyde vapors are rare, but exacerbations of skin lesions from this material after reexposure have been noted. Fatal formaldehyde poisonings that have been reported are uniformly the result of ingestion of this agent[427] Sensitization of the skin or respiratory tract in man is uncommon, and asthma-like symptoms are seldom noted.

Animal studies have demonstrated the similar effects of irritation of mucous membranes and skin, but with some study and confirmation at the cellular or tissue level. Ciliary activity ceased in the anesthetized tracheotomized rat on exposure to 0.5 ppm for 150 sec or to 3 ppm for 50 sec.[258,279,684]

Inhalation of formaldehyde by the intact animal produces an increase in residual volume and a decrease in tidal volume. That these effects involve apparent airway receptors and scrubbing of the upper airway due to this soluble gas is shown by the fact that increases in pulmonary resistance and tidal volume occur in tracheotomized animals along with a decrease in respiratory rate.

Inhalation of formaldehyde vapors as an aerosol with sodium chloride or other materials increases the work of respiration when the formaldehyde concentration exceeds 0.3 ppm, and the aerosol increases the time necessary for recovery after discontinuation of the exposure. Increases in aerosol concentration incrase the resistance to air flow and potentiate and prolong the effects.[35,737]Inhalation of formaldehyde vapors also can produce effects in organs other than the lung. Alkaline phosphatase activity in the liver increased after exposure to vapors of 3.5 ppm for 18 hr.[891] Higher concentrations (19 ppm for up to 10 hr) produce edema and hemorrhage in the lungs and hyperemia of the liver.[1054] Exposure to higher concentrations produces pleural and peritoneal fluid and pneumonitis.[1124]

Acrolein, an unsaturated aldehyde, is generally much more toxic and irritant than the saturated aldehydes.[207] Acute exposures produce irritations to mucous membranes and skin, similar to those produced by formaldehyde. Chronic toxicity studies have not been reported. Human subjects experience a sense of irritation of the eyes and nose within 5 min of exposure to acrolein at 0.25 ppm.[572,1126] Lacrimation occurs at 0.67 ppm after 20 sec and at 1.04 ppm within 5 sec.[245,552] The eye irritation becomes almost intolerable at the latter concentration after 5 min of exposure, and higher concentrations are tolerable for even shorter periods.[1126] At 21 ppm, pulmonary edema has been observed, and inhalation of 150 ppm for 10 min is lethal in man. The American Conference of Governmental Industrial Hygienists suggests that workplace concentrations of acrolein vapor should not exceed 0.01 ppm, to prevent mucosal sensory irritation.

In animal studies, exposure to acrolein vapor at 6 ppm for 87 min produces a 50% survival time of 87 min. This is half the survival time related to similar formaldehyde concentrations. The LC_{50} for rats in 0.5 hr is 0.05 ppm, only one-sixth the concentration of formaldehyde vapor needed for similar lethality. Chronic exposures of rats to acrolein vapors at 0.57 ppm over several weeks caused loss of weight, decreases in whole-blood cholinesterase activity, a decrease in urinary coproporphyrin excretion, and a change in conditioned-reflex activity.[500] Rabbits exposed to 0.57 ppm for 30 days showed no apparent ill effects; at 1.9–2.6 ppm for 4 hr, enzyme alterations in eye tissues were observed[571,852] and hepatic alkaline phosphatase was increased.[891]

Animals exposed to higher concentrations develop pulmonary edema and desquamation and degeneration of the bronchial epithelium.[1054,1124] A concentration of 10.5 ppm for 6 hr is fatal to 50% of mice and guinea pigs;[962] but cats—although they develop lacrimation, evidence of respiratory tract irritation, and narcosis—return to apparent normal function within 2–3 hr after exposure. Residual lung damage has been reported in rats 6 months after exposure to 200 ppm for 10 min once a week for 10 weeks.[207]

Murphy studied the physiologic effects in guinea pigs at concentrations closely approximating those present in some industrial exposures. At 0.06 ppm, total pulmonary resistance and tidal volume increased, and respiratory rate decreased. These changes were accentuated with increasing concentration and were reversed when the animals were removed to clean air. The increased resistance was believed to be due to a reflex bronchospasm mediated through the autonomic nervous system.[892] Mineral oil, sodium chloride, and silica gel aerosols potentiate the damaging effects of acrolein. Exposure to acrolein by aerosol potentiated the effects seen at comparable vapor concentrations, as was the case with formaldehyde exposures.[737]

Acetaldehyde is almost nonirritating in man at 50 ppm, although it may be perceived at 25 ppm by some. Human volunteers exposed to 50 ppm for 15 min show some evidence of eye irritation;[962,1115,1116] this is pronounced, and nose and throat irritation is observed, at 200 ppm.

Other higher-molecular-weight aldehydes have received little study. In man, exposure to crotonaldehyde at 4 ppm for 10 min produces lacrimation and respiratory mucosal irritation.[962] Propionaldehyde at 134 ppm for 30 min is mildly irritating to the exposed mucosal surfaces, whereas butyraldehyde and isobutyraldehyde at approximately 200 ppm for 30 min are almost nonirritating.[1116]

The results of animal studies involving exposures to isolated hydrocarbons are difficult to relate to human and animal studies of true atmospheric exposures, because many of the naturally occurring hydrocarbons are degraded and altered by reactions encouraged by photochemical energy and naturally occurring oxidants in the atmosphere. As a result, additional groups of pollutant substances are generated, including oxidants and complex reaction products, such as PAN.

HYDROCARBON MIXTURES

The hydrocarbons in the atmosphere are altered to other compounds during ultraviolet irradiation by sunlight. Hydrocarbon–oxidant relationships in experimental exposures are often ill-defined; therefore, difficulty is encountered in determining the cause of the effects noted.

Murphy *et al.*[893] exposed guinea pigs to irradiated and nonirradiated automobile exhaust for 4 hr. The response to nonirradiated exhaust was relatively small, whereas flow resistance and tidal volume increased and respiratory rate decreased during exposure to irradiated exhaust. The latter showed photochemical formation of aldehydes, nitrogen dioxide, and total oxidant at the expense of nitric oxide and olefins. The greatest response was to an atmosphere of 2.4-ppm formaldehyde, 0.2-ppm acrolein, 0.8-ppm ozone, and 2.7-ppm nitrogen dioxide. The effects produced could be simulated nearly quantitatively by exposing animals to 0.6-ppm acrolein, whereas 0.7-ppm ozone produced negligible effect on flow resistance; even at an exhaust dilution of 1,000 : 1 with hydrocarbon concentrations well within the range of community air pollution, the same effects were detected. In this exposure, total oxidant concentration was 0.4 ppm; that of formaldehyde was 0.5 ppm.

That oxidants were not responsible for these effects was shown by study of a 150 : 1 dilution of nonirradiated exhaust. Although no oxidant was present, the respiratory effects were identical with those of irradiated exhaust in a 1,140 : 1 dilution. The effective agents are therefore present in raw exhaust gases and are multiplied by irradiation. Because quantitatively identical pulmonary effects are produced by acrolein and similar effects by formaldehyde, it is a good hypothesis that these effects are caused by aldehydes.

Eye irritation in man is similarly related to total aldehyde concentration. Renzetti and Bryan[1014] found a good direct relationship with aldehyde concentrations ranging from 0.035 to 0.35 ppm. This direct relationship held for formaldehyde (0.01–0.1 ppm), but was nonlinear for acrolein, of which concentrations of 0.003–0.015 ppm resulted in more eye irritation than concentrations greater than 0.015 ppm. Tuesday *et al.*[1213] also noted a high correlation of eye irritation with formaldehyde and a linear relationship between formaldehyde accumulation and initial hydrocarbon concentration, although only light eye irritation was noted. Initial hydrocarbon concentrations ranged from 0.3 to 2.6 ppm (as hexane), and those of oxides of nitrogen, from 0.1 to 1.1 ppm. Formaldehyde concentrations were up to 0.3 ppm; eye irritation occurred with formaldehyde as low as 0.15 ppm.

Romanovsky *et al.*[1031] irradiated synthetic atmospheres in a series of tests using ethylene, propylene, isobutane and gasoline mixture, and auto exhaust. They noted a high correlation of eye irritation with formaldehyde content, which ranged from 0.1 to 4 ppm.

A series of 29 hydrocarbons, which included 12 aromatic hydrocarbons, was studied in irradiation of synthetic atmospheres by Heuss and Glasson.[566] The aromatic hydrocarbons, particularly styrene and β-methylstyrene, were more potent than nonaromatic hydrocarbons in producing eye irritation. Some systems produced peroxybenzoylnitrate, 200 times more potent as a lachrymator than formaldehyde. In the photooxidation of styrene, formaldehyde accumulated to a concentration of 0.4 ppm. It is thus likely that formaldehyde was responsible for most of the eye irritation in this experimental photochemical pollution system.

Altshuller *et al.*[28] studied irradiated synthetic atmospheres containing alkylbenzenes. Eye irritation was of the same magnitude as that with propylene photooxidation. Toluene, *m*-xylene, and 1,3,5-trimethylbenzene produced eye irritation greater than ethylene, and *o*-xylene resulted in less. They concluded that paraffinic hydrocarbons, acetylene, and benzene in photochemical air pollution do not contribute appreciably to eye irritation.

Altshuller *et al.*[30] showed that the addition of propylene or toluene to *n*-butane or *n*-butane–ethane mixtures with nitrogen oxides produced large increases in oxidant dosages, in formaldehyde and PAN yields, and in eye irritation. Next to ethylene, propylene is the most abundant olefin in the urban atmosphere. Toluene is the most abundant alkylbenzene and, with xylene, constitutes about half the total amount of alkylbenzenes present. The results clearly show that oxidant dosage and PAN yields decrease by 35–95% when propylene or toluene is removed or reduced, depending somewhat on the nitrogen oxide concentration. When hydrocarbon concentration is 4 ppm and nitrogen oxide concentration is 1.5 ppm, the relative eye irritation responses are as follows: to toluene, 2.3 units; to *m*-xylene, 1.9; to *o*-xylene, 0.9; to 1,3,5-trimethylbenzene, 2.2; to ethylene, 1.1; and to 2-methyl-2-butene, 1.6.

Effects of Photochemical Reaction Products

Bils[111] studied the ultrastructural alterations in lung tissue of mice after exposure for 2–3 hr to natural urban atmospheres whose total oxidant concentration was 0.4 ppm. The older mice showed the most severe changes. Bils and Romanovsky[112] studied the ultrastructural effects on mice of a 3-hr exposure to synthetic photochemical smog containing oxidant material at 0.50–0.75 ppm. The results were similar to those observed in mice exposed to natural smog. The pattern of observations indicated irreversibility of lesions after 15 months of exposure, with marked sensitivity of the endothelium and edema after 21 months of exposure.

Because nitric oxide was one of the constituents of the synthetic smog used in the study, it is necessary to evaluate its own effects on lung tissue. Rounds and Bils[1037] studied the effects of sodium nitrite on organ cultures of alveolar wall cells of rabbits and rats *in vitro*. Ultrastructural study of the exposed cells *in vitro* showed alterations in the shape, size, and structure of the nuclei and mitochondria resulting from a single exposure to the equivalent of nitrogen dioxide at 20 ppm for 1 hr and chronic exposures equivalent to nitrogen dioxide at 15 ppm for 4 hr/day for 10 days.

Bils[111] and Bils and Romanovsky[112] have reported apparent ultrastructural changes in the lungs of mice exposed to synthetic photochemical smog. It is not possible to interpret these data in relation to any specific vapor-phase organic air pollutant.

Coffin and Blommer[230] exposed mice to automobile exhaust containing carbon monoxide at 12–100 ppm and oxidant materials at 0.08–0.67 ppm for 4 hr. Control animals were exposed to clean air. After exposure, the animals of both control and oxidant groups were treated with a streptococcal aerosol (group C) of 100,000 bacteria/animal. Animals exposed to carbon monoxide at 100 ppm and oxidants at 0.35–0.67 ppm had an increased mortality rate from streptococcal pneumonia, compared with controls. Exposures to carbon monoxide at 25 ppm and oxidants at 0.12 ppm apparently did not compromise resistance to the streptococcal aerosol.

Ozone at 0.08 ppm has also been reported to affect susceptibility to respiratory infection and augment mortality.

If mice were pretreated with α-naphthylthiourea (15 mg/kg) 30 min before exposure to irradiated and nonirradiated automobile exhaust, there was a small but consistently greater mortality in the mice exposed to the irradiated exhaust.[893] This change, although statistically significant at the 2% level, was not interpreted by the authors as an effect of the oxidant materials produced in the irradiated exhaust. Because ozone and nitrogen dioxide increase susceptibility to respiratory infection, it is not necessary to attribute the effect observed by Coffin and Blommer[230] to photooxidized hydrocarbons alone.

PAN is one of the better defined and studied products of the photochemical oxidation of naturally occurring atmospheric hydrocarbons. It is recognized to be exceedingly irritant, especially to the eye. The effects of short-term exposures to PAN in healthy young male volunteers have been studied; PAN at 0.3 ppm was administered for 5 min, and the oxygen uptake was measured during a 5-min bicycle ergometer exercise period and during a 5-min recovery period. A 2.3% increase in oxygen uptake was observed during exercise; this is claimed to be statistically significant. No difference in oxygen uptake between exposed and control groups was observed in recovery. Expiratory flow velocity was reduced after exercise. Both these changes—the increase in oxygen uptake and the increased flow resistance—could be due to an increase in airway resistance, which is reflected in an increase in the work of breathing and in the oxygen cost of breathing.[1129]

Studies of the toxicity of PAN in mice have shown that mice exposed to PAN at 110 ppm or more for 2 hr or more die within a month of exposure; the higher the concentration, the earlier the death. Most deaths occur in the second and third weeks after exposure. Increased age and chamber temperature tended to increase mortality, but variation in relative humidity did not. No mortality was observed with exposure to 97 ppm during the 4-week period of observation, and death immediately after exposure was not observed.[193] Spontaneous activity of C57 black male mice was considerably reduced (50%) by exposure to PAN at 4 ppm for 6 hr. Dungworth and associates[340] studied the chronic effects of PAN on strain A mice. Exposure to 15 ppm for 130 daily 6-hr periods over 6 months produced an 18% mortality, primarily due to bronchopneumonia of bacterial origin. Weight loss occurred consistently in the exposed group. The major features of the reaction to injury by PAN occurred in the epithelial structures of the airways. A papillary proliferation of epithelium was observed, with foci of squamous metaplasia in some 50% of the animals. Mucous cells were usually reduced in number in the bronchial epithelium, and cilia were often absent. Unique to this lesion is the formation of acinar structures lined by ciliated and mucous cells. In some cases, the bronchial walls were ulcerated and scarred; in other cases, the epithelial structures extended into the bronchial wall. Bronchiolectasis was common, and epithelial hyperplasia was often present; bronchiolitis fibrosa obliterans was infrequent. Hypertrophy of peribronchiolar and adjacent alveolar epithelium was common. Centriacinar emphysema was mild. Some focal pneumonitis was present. Atypical squamous metaplasia was not seen, and no neoplasia or adenomata were observed.

SYNERGISM, ANTAGONISM, AND TOLERANCE

The study of biologic effects of air pollution has been complicated by evidence of synergism and antagonism among physical, chemical, and biologic components of pollution that have adverse effects on susceptible organisms. This discussion will focus on biologic interactions of reaction products from engine exhaust, excluding particles and polycyclic aromatic hydrocarbons, irritants like ozone, and oxides of nitrogen and sulfur.

Evaluations of interactions that result in either unexpected severity or unexpected mildness of toxicity suffer greatly from a lack of information on human experience after exposure to specific air pollutants. Epidemiologic studies of proper design, of which there are few, could confirm results of laboratory experiments in which some of the typical components of pollution seem to exert synergistic or antagonistic effects.

Synergism that has been observed in experimental animals has usually been studied only with regard to specific physiologic mechanisms leading to an exaggerated response or death. The underlying mechanism of the interaction, nonetheless, is often not understood, even in studies based on clear physiologic responses.

The interaction of inert particles and vapor-phase pollutants can alter the physiologic response to the pollutants. This could be considered a synergistic effect, even though it is based only on physical factors that cause adsorption of a gaseous irritant on a particle, which leads to a different degree of penetration and a greater concentration of the chemical at the site of its deposition. The irritant effect, rather than being increased by the very presence of particulate matter, may depend on particle size and chemical properties, which would be responsible for the capacity of the particle to adsorb first and allow desorption later. Thus, chemical and physical properties of adsorbate and adsorbent are important.

Amdur[35,36] noted a synergistic effect on respiratory flow resistance and decreased compliance in guinea pigs after inhalation of formaldehyde with a sodium chloride aerosol. The sodium chloride aerosol was of very small particle size (average diameter, 0.04 μm) at a concentration of 10 mg/m^3. The aerosol alone had no effect on flow resistance. The synergistic effect was observed with formaldehyde at 0.3–47 ppm. It was not present at the lowest concentration of formaldehyde, 0.07 ppm; but the higher the concentration of formaldehyde, the greater the resistance. After the hour-long exposure, the resistance remained high for another hour.

In comparable experiments with formic acid, the sodium chloride aerosol did not increase respiratory flow resistance, but it prolonged the period of high resistance after exposure. The increase in toxicity of aldehydes in the presence of inert aerosols or particulate materials has also been explored by La Belle and co-workers,[737] who investigated formaldehyde and acrolein for their toxicity when administered in the presence and absence of specific aerosols. The greatest degree of synergism was observed for aerosols of triethylene glycol, mineral oil, celite, glycerin, and sodium chloride in studies with formaldehyde. In studies with acrolein, significant synergism was seen only with mineral oil, sodium chloride, and Santocel CF.* It was concluded that, when aerosol penetration exceeds vapor penetration, toxicity is increased. It is apparent that aerosols are readily at hand in community air pollution, so aldehyde toxicity may be increased.

An example of antagonism is given by the studies of Salem and Cullumbine,[1055] who studied acute aldehyde inhalation toxicity in guinea pigs, mice, and rabbits with high doses of acetaldehyde or acrolein alone or in combination with kerosene smoke produced by incomplete combustion in a kerosene lamp. Black smoke was introduced into the inhalation chamber via a baffle that limited the size of the smoke particles. The mean fatal dose was calculated from the concentration of aldehydes found in the chamber and the interval until death. The concentrations of aldehydes were many times those encountered in the atmosphere, and extrapolation of these data to realistic concentrations of soot and aldehyde is not possible.

The observation of reduced toxicity of air pollutants was originally described for ozone, which is not a vapor-phase comound itself, but rather a product of atmospheric chemical reactions. A lethal exposure to ozone could be tolerated by mice and rats if they were exposed earlier for a short period to a nontoxic concentration of ozone.[846] Tolerance starts 1 day after the nonlethal exposure and lasts for at least 100 days. A variety of oxidants or other chemicals can substitute for ozone for either tolerance induction or later challenge.[1163] Such protective action could be found in several species. It is not known whether it appears in man.

Extending these studies to ketene, considered a likely air pollutant, showed the existence of a similar but short-lived tolerance to lethal doses of ketene after pretreatment with ketene. Pretreatment with ozone also protected against a lethal dose of ketene, and ketene pretreatment produced tolerance to ozone. The effective dose of ketene for mice was a 10-min exposure at 6–7 ppm, which produced tolerance to a lethal dose if exposure came at least 2 days after treatment. Ketene-induced tolerance lasted for at least 2 weeks. Pretreatment with ketene produced tolerance to ozone the very next day, but it lasted for less than a week. Pretreatment with ozone at 1 ppm for 4 hr produced tolerance to ketene after 48 hr, which lasted for 2 weeks without decline.

Later studies on other air pollutants and unrelated chemicals showed that cross-tolerance may or may not be developed (e.g., cumene hydroperoxide provided tolerance against hydrogen peroxide, but not

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*Amorphous silica preparation, Monsanto Co.

against ozone, nitrogen dioxide, or even cumene hydroperoxide itself). Attempts have been made to illuminate the mechanism of tolerance; for details, the reader is referred to a paper by Fairchild.[386]

Synergism between air pollution and microbial infections in humans has been postulated on the basis of animal experimentation.[488,791,985] Diluted automobile exhaust was irradiated by Coffin *et al.*[230–232] to produce smog atmospheres comparable with that encountered in areas of human habitation. Mice were exposed for 4 hr to such atmospheres containing carbon monoxide at 100 ppm, oxidant at 0.35–0.67 ppm, nitrogen dioxide at 0.5–1 ppm, and nitric oxide at 0.03–1.96 ppm. After this exposure, immediate inhalation of an aerosol of streptococci, calculated to give 100,000 organisms/mouse, led to a fivefold increase in mortality, compared with the results of streptococcal aerosol exposure after filtered-air inhalation. When the exhaust was further diluted, the synergistic effect disappeared, with a threshold at 0.15-ppm oxidant, 0.3-ppm nitrogen dioxide, and 25-ppm carbon monoxide. It was concluded that the critical component must be the oxidant, inasmuch as the nitrogen dioxide concentrations were below the toxicity threshold by a factor of 10. The oxidant concentration, however, was similar to the threshold for synergism due to ozone, previously determined by Coffin *et al.*, i.e., 0.08 ppm.

In similar experiments, the enhancing effect of cold was studied with ozone and streptococcal infection in combination with exposure for 2 hr at 6–9 C. A 30% increase in mortality after exposure by aerosol to 30,000 organisms/mouse was attributed to this additional factor.[791]

A suggestion regarding the mechanism was proposed by Coffin and Blommer[231] in the depression of pulmonary bactericidal activity, which was attributed to a decrease in the number of pulmonary macrophages and in their activity after exposure to ozone at 0.3 ppm for 3 hr. The synergism between artificial smog (ozonized gasoline) and influenza viral infections was studied in C57 black mice. The artificial smog was maintained continuously at 1–2 ppm throughout the experiment. A few pulmonary adenomas were observed in each group of C57 black mice; but squamous cell carcinomas of the lung were seen only in the group that was subjected to a combination of continuous exposure to smog and the three influenza virus intubations—33 of 328 survivors had squamous cell cancers in their lungs.[715]

A modification of these experiments was undertaken, with exposure to only one virus (PR-8). Mice of the C57 black strain were exposed to the same "artificial smog" as in the earlier experiments. Lung tumors were observed, but they were all of the adenomatous type.[917] Introduction of the influenza viral infection reduced lung-tumor growth. The results differed from those of the earlier studies in the lack of squamous lung cancer.

Synergism between formaldehyde and hydrogen peroxide with respect to their mutagenic action has been reported for Neurospora.[311,637] Similar synergistic effects on neurospora have been reported for formaldehyde and ultraviolet radiation.[311] X radiation also increased the mutagenic action of formaldehyde in drosophila spermatids.[1135] However, synergism in drosophila was not reported for treatment with a combination of formaldehyde and hydrogen peroxide, and the explanation offered was that catalase in the flies destroyed hydrogen peroxide. Synergism could, however, be observed if catalase was inactivated by treatment of the flies with hydrogen cyanide or other catalase poisons.[1136] In this connection, it can be postulated that mutagenesis will be increased not only in species deficient in catalase or peroxidase, but also in mammalian species if enzymatic decomposition is blocked or, more important from the point of view of air pollution, if the hydroperoxide is more complex and cannot be attacked by the enzymes.[717] Thus, synergism in mutagenesis was observed between *tert*-butylhydroperoxide and ultraviolet radiation in drosophila eggs.[16]

Synergism between simple alkanes and alkenes in mice and rats has been described by Shugaev.[1111] Butane and isobutylene were inhaled for 2 or 4 hr, and the LD_{50} was reached for both species at much lower brain concentrations of the hydrocarbons when combinations of the two were inhaled.[1111]

Ethylene oxide has been found to be antagonistic to ethylene. It acts as a reversible antiripening agent for fruit and prevents aging of flowers. This effect may turn out to be useful in allowing longer life for flowers, but it may cause damage to fruit by preventing normal ripening.[767]

The situation is complicated further by the antagonistic interaction between ethylene and carbon dioxide in cut flowers.[1131] Ethylene at very low concentration in the air (0.05 ppm) causes a reduction in the vase life of cut flowers, such as carnations or narcissi, which can be countered by addition of 5% carbon dioxide to the air. Lower concentrations of carbon dioxide also protect flowers from rapid wilting due to ethylene.

Synergistic or antagonistic interactions of air pollutants in biologic systems have generally been considered rare. Gusev[499] stressed that toxicologists generally were concerned only with the evaluation of toxicity of single chemicals and did not pay enough attention to combinations of toxic substances. The conclusions he reached on the basis of available data, however, were that only an additive effect would be expected and that toxicity could be calculated in a simple fashion for any number of combinations of air pollutants.

In a study[1132] in which a large number of solvents in a 1:1 ratio were tested regarding their combined LD_{50} in rats that received them orally, the authors concluded that most toxicologic results could be interpreted as additive, but that 5% of all the combinations produced either higher or lower toxicity than expected from straight additive action. The solvents involved in the synergistic effects were limited to three of a total of 27—formaldehyde, tetrachloroethylene, and acetonitrile. These chemicals and the ones with which the synergistic effect was observed deserve more study and attention. The pairs that produced less than the expected toxicity appear to be less important, because rapid chemical reaction between them could alter the expected toxicity, as in the case of combinations of epoxides and alcohols or of amines and aldehydes.

MUTAGENIC EFFECTS

Air pollutants have many adverse effects; among them is their potential for eliciting genetic changes. This review deals with published information pertinent to the mutagenic potential of selected air pollutants. The compilation is neither fully comprehensive nor exhaustive, but rather is an attempt to focus attention on one aspect of the potential hazards that such pollutants may pose to man.

Literature from the Environmental Mutagen Information Center on selected chemicals was used in preparing this section. Detailed information has been published on the mutagenic effects of air pollutants in general;[375,886,1103] of specific compounds and groups of compounds, including benzene,[428,429,474,531,970,977,1204] diepoxybutane,[55–57,375,707,726,807,916,1036] diepoxycyclohexane,[1036] epoxides and other derivatives of cyclic hydrocarbons,[592] epoxy compounds,[573] formaldehyde,[14,53,54,670] nitric oxide,[692] oxygen,[103,153,240,393,461,691,692,729,877] ozone,[153,154,219,394,395,979,1362,1364] phenol compounds,[37,728] and toluene;[429] and of ultraviolet radiation[153,219] and X radiation.[394,395,692,1363]

Methods for testing mutagenicity of atmospheric pollutants are presented in detail in the National Research Council report *Particulate Polycyclic Organic Matter*.

Fractions of particulate atmospheric pollutants collected on filters in New York City during 1967 were tested for the induction of dominant lethal mutations in mice.[374,375] Although most of the samples tested were found to be nonmutagenic, one oxyneutral pentane 28% ether fraction was found to be significantly mutagenic, and another aliphatic air pollutant fraction was slightly mutagenic. Organic extracts of atmospheric particulate pollutants collected during 1966 by continuous air monitoring over Birmingham, Boston, and Wheeling did not significantly increase the frequency of dominant lethal mutations.[375]

Benzene

Several studies have been reported on the effects of occupational chronic exposure (1–26 years) to benzene or chromosome abnormalities in peripheral blood lymphocytes or bone marrow.[428,429,531,977,1204] The concentration of benzene in vapors to which the subjects were exposed varied from 12 to 532 ppm. Exposure to very low concentrations, 12 ppm, for up to 26 years did not result in significant change in frequencies of chromosome or chromatid abnormalities.[1204] Much higher concentrations of benzene, however, resulted in various chromosome abnormalities, such as simple chromosome or chromatid breaks, deletions,[428,531,977] trisomy, chromosome loss,[428] and other unstable chromosome changes.[429,977] Similar chromosome damage was detected in workers exposed to mixtures of benzene and toluene in high concentrations.[429]

Inhaled benzene induced biochemical changes and inhibited nucleic acid synthesis in pregnant albino rats.[474] Furthermore, subcutaneous injection of benzene into rats evoked an immediate effect—chromatid breaks in bone marrow cells—with full recovery 36 hr after treatment.[970] Whether such chromosome damage represents a true index of mutagenicity or lethal cellular effects cannot be determined; nonetheless, exposure of man, particularly chronic, to benzene should not exceed the maximal allowable limits.

Diepoxybutane

Diepoxybutane (DEB) is an active radiomimetic substance capable of inducing various biologic changes, such as cancer, depression of the hemopoietic system, and mutations. It has been tested for mutagenic potential in bacteria (*Escherichia coli,* salmonella), fungi (neurospora, penicillium, saccharomyces), insects (drosophila, housefly), higher plants (vicia, allium, barley, maize, tomato, arabidopsis), and mammals (rats, mice).[411]

Subcutaneous injection of DEB at 1–3 mg/kg into rats resulted in chromosome abnormalities, such as stickiness, clumping, breaks, and a decrease in mitotic index of cultured blood lymphocytes.[916] No significant increase in dominant lethal mutation frequency was detected, however, in mice given DEB at 17 mg/kg.[916] Chromosome abnormalities were also observed in vicia root tip cells[807] and in maize pollen.[726] Treatment of neurospora with DEB resulted in marked increase in adenine and inositol revertants.[57] Furthermore, DEB interacted synergistically with ultraviolet radiation, resulting in a twofold increase in the frequency of adenine revertants.[55,56]

Formaldehyde

Formaldehyde has been tested for mutagenic potential in drosophila, bacteria, neurospora, and mammals. Exposure of young male drosophila to formaldehyde vapors for 30–60 mn did not increase the frequency of recessive sex-linked lethal mutation.[54] Inclusion of formaldehyde in the foods of drosophila larvae, however, resulted in a moderate to high increase in recessive sex-linked lethal mutation frequency, but adenylates were necessary for expression of the formaldehyde effect.[14,53,670] No significant increase in frequency of dominant lethal mutations was observed when mice received intraperitoneal injections of formaldehyde.[374,375] As with benzene, exposure of pregnant rats to formaldehyde during the entire gestation period raised the requirement for ascorbic acid and inhibited nucleic acid biosynthesis.[474]

Formaldehyde is highly reactive with a wide range of chemicals. Several of the reaction products may be mutagenic; for example, caseine treated with formaldehyde was mutagenic to drosophila. This is especially significant, because skim milk fed to animals is stabilized with formaldehyde.[411]

Ozone

The mutagenic potential of ozone has been tested on nucleic acids *in vitro*,[219,979] higher plants,[394] human cells in culture,[395] rabbits,[154] mice,[154] and Chinese hamsters.[1362,1363]

A 30-min exposure of vicia roots to ozone resulted in chromosome damage equivalent to that induced by 100-r x rays; most aberrations were dicentric bridges and double deletions.[394] Chinese hamsters inhaling 0.2-ppm ozone for 5 hr showed a marked increase in chromosome aberrations in their circulating lymphocytes.[1363] Chromatid breaks were detected after exposure of human tissue in culture to 8-ppm ozone for 5–10 min.[395] Mice or rabbits inhaling 0.2-ppm ozone 5–7 hr/day for 3 weeks showed a marked increase in neonatal mortality and slight rupture in the nuclear envelope of myocardial fibers; these animals recovered fully 4 weeks after cessation of ozone exposure.[154] Treatment of nucleic acids with ozone *in vitro* resulted in base changes.[979] In view of the biologic damage induced by very low ozone concentrations in other forms of life, the limits of ozone to which man is currently exposed may be too high.

Oxygen under High Pressure

The effects of oxygen under pressure may resemble the toxic effects of ozone. Therefore, studies of oxygen under pressure are included. Exposure of higher plants to oxygen under high pressure (500–2,000 lb/in.^{2}, or 30–60 atm) increased the frequencies of chromosome aberrations and chlorophyll mutations.[103,240,691,729,877] Prolonged exposure of bacteria to oxygen under high pressure markedly increased the mutation frequency.[393,461]

Phenol Compounds

Several phenol compounds have been tested for their potential to induce biologic changes in vicia root tip cells.[37] Many of these substances—such as *o*-nitrophenol, *p*-nitrophenol, *p*-chlorophenol, 2,4-dichlorophenol, pentachlorophenol, α-naphthol, β-naphthol, and 2,4-dichloronaphthol—induced a host of cytologic and genetic changes, such as C-mitosis, chromosome stickiness, dicentric bridges, fragments, binucleate cells, and micronuclei. Furthermore, a marked reduction in mitotic index was observed.

Quinones

Several quinones were tested for mutagenic potential in the Allium test for mitotic chromosome aberrations.[728] Hydroquinone and pyrocatechol were not very effective in inducing genetic damage. However, other quinones, such as *p*-benzoquinone and *o*-benzoquinone, significantly increased the frequencies of chromosome aberrations, observed as dicentric bridges and fragments. Chromosome stickiness and C-metaphase were also detected.

Miscellaneous

Several other chemicals that may become air pollutants were tested for mutagenic potential. Several epoxides and derivatives of cyclic hydrocarbons increased the forward-mutation frequency (8-azaguanine resistance) in Chinese hamster cells; however, polycyclic hydrocarbons needed metabolic reactivation to become mutagenically active.[592] Four diepoxides were also tested in mice and found to increase the frequency of dominant lethal mutations and to induce chromosome changes.[573]

TERATOGENIC EFFECTS

There are two ways of being alerted to the teratogenic potential of environmental agents for human beings: environmentally induced congenital malformations may be detected by surveillance[582] of human births and abortions and reporting all agreed-on abnormalities to a recording and analyzing headquarters;[749] and the toxicity of chemicals may be tested prenatally in animals. The methods for such tests have been extensively described and discussed in the last 10 years.[71,145,436,437,439,952,983,1028,1209,1210,1329,1331]

The type and frequency of embryotoxic effects of chemicals administered to experimental animals during pregnancy have been found to depend on numerous conditions or combinations of conditions, including the type and dosage of chemical, the stage of pregnancy, and the genetic sensitivity of the stock or species.[436,663,1329]

In general, the types of embryotoxic effects, as seen at or near the end of gestation, are in three broad categories: intrauterine growth retardation, physical maldevelopment (i.e., teratogenicity), and death.[1328] Malformation ultimately can result only from interference with events that occur in the embryo and early fetus; and in general, the type of malformation produced is related to when the chemical acts.[1276,1330,1331]

All other things being equal, the factor determining the relative frequency of the three general categories of embryotoxic effect is dosage.[889,890] Below some dosage, these phenomena are rare in experimental animals; this dosage, which by convention is termed the "no-effect" dosage, must be determined empirically for each chemical and each set of experimental circumstances. At the other end of the scale are dosages large enough to kill all or most offspring. Between these extremes, typically, is a range of dosages that permits a significant fraction of the offspring to survive to term, but may cause some to be stunted, malformed, or both. This "in-between" range may be so narrow for some chemicals or in some experimental situations—the balance between normality and lethality may be so delicate—that it is difficult to demonstrate a teratogenic effect at all. Commonly, however, the in-between range is broad enough to permit detection of teratogenicity and growth retardation readily and to allow analysis of the dose–response relations for all three types of embryotoxicity.

The species most often used (mice, rats, hamsters, and rabbits) are chosen usually for convenience: They cost little, they are small, they breed rapidly, and much knowledge of their biology is already at hand. The present system of using several rodent or other small species or some primates to evaluate teratogenicity is the only experimental method available.

Few vapor-phase organic air pollutants have been tested for possible effect on mammalian reproduction and prenatal development or for postnatal consequences of administration during pregnancy. Many studies done with this handful of agents were not directed specifically to teratogenesis, and most of the substances were not administered by inhalation.

In a study using benzene,[42] female mice received injections of benzene at 4 ml/kg on day 6, 9, or 12 of gestation. Litter size and postnatal viability were not affected. Watanabe and Yoshida[1283] gave CF1 female mice benzene subcutaneously at 3 mg/kg on one of days 11–15 of gestation and examined the offspring just before term for external and skeletal defects. The only gross defects found were cleft palate and jaw abnormalities, and the highest total frequency (7.9%) was produced by treatment on day 13. Fetal mortality was unaffected. No difference was found between females with and without malformed offspring in increase of body weight or decrease in white-cell count after treatment.

Wilson[1330] gave pregnant rats carbon tetrachloride in corn oil daily, 0.3 ml orally or 0.8 ml subcutaneously for 2–3 successive days, beginning on gestation days 8–12; 21% of pregnant females died; 38% of females resorbed their entire litters; 41% carried young to term with 9.1% of young resorbed. Malformations were not found, and only one litter contained growth-retarded young. Adams *et al.*[7] fed pregnant rabbits carbon tetrachloride in arachis oil, 0.6 ml/kg on gestation day 5 or 1 ml/kg on days 4–5—i.e., before uterine implantation. Blastocysts were removed and examined at day 6.5 and were found to be normal after the smaller dose, but to have some cellular degeneration and (in some cases) to contain very large nuclei with prominent nucleoli after the larger dose. Their later embryologic fate, however, was not determined.

Ranström[992] gave pregnant "white" rats 6% formalin subcutaneously, 0.25 ml twice a day throughout gestation. Young were examined just before term; none was growth-retarded, but the fetal adrenal weight was reduced. Prenatal mortality and developmental abnormalities were not mentioned. Schnürer[1075] gave pregnant Wistar rats 2% formalin subcutaneously, 0.25 ml twice a day throughout gestation. This dose was not toxic to the females and produced no increased fetal death and no malformation or growth retardation; twice this dosage produced some maternal death.

Gofmekler and Bonashevskaya[473] continually exposed pregnant albino rats to formaldehyde by inhalation (1 or 0.012 mg/m^3, time of exposure during pregnancy unstated) and examined the offspring (age of examination unstated) for external and internal developmental abnormalities. No gross abnormalities were found, but histologic deviations were noted in only some tissues (liver, kidney, etc.) of offspring of females exposed to the higher concentration.

Piekacz[973] administered two phthalate esters to pregnant rats (stock unstated) by stomach tube daily in amounts corresponding to 1 and 5% of the LD_{50} for 3 months before conception and for almost the entire gestation period. The mean litter size and fetal weight were reduced in some cases, but malformations were apparently not found, nor were there any differences between the control and test groups with respect to minor skeletal variations. Peters and Cook[967] gave pregnant rats (stock unstated) intraperitoneal injections of three phthalate esters at 0.5, 1, 2, and 4 mg/kg on gestation days 3, 6, and 9. One of the chemicals apparently prevented implantation, and the others greatly reduced the mean litter size and number of offspring weaned. Two anophthalmic offspring were noted.

Kotin and Thomas[720] exposed young C57 black male and female mice in an inhalation chamber to smog formed by reacting gasoline with ozone or urban atmosphere. Results indicated that low concentrations of atmospheric pollutants impaired the conception rate, marginally reduced the litter size, and were severely harmful to preweaning offspring. Congenital malformations were not mentioned. Heuter *et al.*[595] exposed LAFI mice to irradiated and nonirradiated automobile exhaust and also noted marked decreases in fertility and postnatal survival of neonates; again, no malformations were mentioned. Lewis *et al.*,[766] in an elaborate extension of the studies noted above with irradiated and nonirradiated automobile exhausts, essentially confirmed these results. In addition, some exposed females were killed near term, but no increase in fetal resorption was found. In the above mentioned three studies, lack of effects should not be referred to vapor-phase organics, in that ozone and other photochemical products were probably also present. Decreased fertility and poorer survival of the litter have been noted in mice exposed to irradiated exhaust.[595] The materials in this exposure included ozone at 0.6–1.0 ppm, carbon monoxide at 60–100 ppm, hydrocarbons at 20–36 ppm, and nitrogen dioxide at 2.9–3.9 ppm. When males were preconditioned by exposure to artificially produced oxidant smog, the nonpregnancy incidence doubled beyond the increase produced by exposing virgin females to the exhaust. Additional experiments indicated that the preconditioning of the males produced an increased number of neonatal deaths in the mice.[532]

Younoszai *et al.*[1358] placed pregnant Holtzman rats in chambers where they were forced to inhale smoke from various types of cigarettes for 4 min five times a day on gestation days 3–22. Fetuses from all experimental groups were growth-retarded, but those from females exposed to tobacco cigarette smoke were most severely affected. Reduction in maternal food consumption may have accounted for some, but probably not all, of the retardation. Litter size was not reduced. Congenital malformations were not mentioned.

CARCINOGENIC EFFECTS

In studies of air pollution, much emphasis has been placed on carcinogenic aromatic hydrocarbons, aromatic heterocycles, and their chemical transformation products. This is the main subject of an earlier document.[906]

Two major efforts at reviewing carcinogenic exposures are under way. The first is by the National Cancer Institute, which publishes and periodically updates a survey of materials evaluated for carcinogenic risk.[1192–1194] This survey can be consulted for any particular compound to see who has tested it, what animals were used, the duration of exposure, and the results. Such a survey is not intended to interpret the carcinogenicity. The second type of review, through the International Agency for Research on Cancer (IARC), is a comprehensive and interpretative review of both experimental and human population experience and consists of a series of monographs entitled *Evaluation of Carcinogenic Risk of Chemicals to Man.* Seven such volumes have been published so far.[607–613] Few of the compounds of interest to this panel have been the subject of IARC monographs.

There is increasing evidence from chemical[1040] and biologic[1234] studies that vapor-phase nonaromatic compounds in polluted air contribute to the total carcinogens present. It is known that aliphatic and olefinic hydrocarbons are major vapor-phase organic air pollutants from a variety of sources. These compounds themselves have not been shown to be active carcinogens. However, some of their chemically reactive transformation products obtained by interaction with singlet oxygen, molecular oxygen, ozone, sulfur oxides, and nitrogen oxides might be expected to be carcinogenic. In addition to or rather than being carcinogenic, vapor-phase organic pollutants might be tumor-promoting or cocarcinogenic agents.[1048]

A number of basic considerations related to carcinogenesis are route of exposure, test methods and group sizes, dose–response relations, tolerance limits, effects of chronic irritation on carcinogenesis, and aging versus carcinogenesis. These are discussed elsewhere,[906] and many authoritative reviews on these subjects have appeared in recent years.[226,302] They will therefore be elaborated on in this section only if directly relevant to vapor-phase organic pollutants.

Of the many known or suspected vapor-phase organic pollutants, only a few have been tested for carcinogenicity. Moreover, the route of exposure most relevant to human lung cancer induction due to air pollutants—i.e., inhalation exposure—has not been commonly used for known vapor-phase components. It has been used, however, in the exposure of mice to ozonized gasoline.[718,719] A few compounds have also been tested by intragastric instillation in rats.[1239] Most of the compounds tested were examined by skin application, subcutaneous injection, or intraperitoneal injection in mice or rats.[396,717,1179,1234,1237,1238,1240,1241,1270,1296]

A built-in difficulty in the carcinogenicity assay of the compounds of interest is the fact that many are highly reactive chemically. The chemical reactivity of these agents is discussed elsewhere in this volume. The compounds undergo a wide variety of reactions, *in vivo,* most of which probably bear no relation to the process of cancer induction. The bioassay of these compounds has usually resulted in the induction of tumors only at the site of administration and only with high dosages.

An examination of the chemistry of VPOP presented in earlier sections of this document reveals that only a few compounds of interest have actually been detected in polluted air. Many have been produced in the laboratory in solutions, and a few have been detected in vapor-phase experiments. These are described in other sections of this report. In evaluating the known carcinogenicity data on VPOP, it is therefore wise to consider structurally related chemicals, also.

On the basis of limited bioassays, the following compound types have generally been classed as noncarcinogenic: aliphatic and olefinic hydrocarbons, aldehydes, ketones, fatty acids and esters, and simple ethers. However, some of these compounds, notably long-chain aliphatic hydrocarbons and some fatty acids, have been implicated as cocarcinogens or tumor-promoters, on the basis of mouse skin experiments.[1048] These will be discussed later. Some of the known compounds in these classes have not been adequately tested for carcinogenic activity.

Some of the oxidized products of VPOP have been shown in experimental animals to have carcinogenic properties. These include epoxides, β-lactones, hydroperoxides, peroxides, and the peroxy acids and esters. Van Duuren[1234] has reviewed these experimental findings.

Very few, if any, of these oxidized hydrocarbons have been determined to be present in air; the compounds that have been tested have been tested by skin applications or subcutaneous injection in mice or rats, and they were determined to be carcinogenic when used at relatively high dosages—for example, 0.1–10 mg/application once or twice a week for 1–2 years. Because these materials are highly reactive chemically, with reactions occurring at these dosages, the data indicate that in this system they are weak carcinogens. Community exposures to these substances would occur, if at all, at very low dosages. Such exposures might indeed be a matter of concern, but cannot be evaluated without further data.

It is reasonable to question whether the induction of subcutaneous sarcomas by such compounds at the site of injection, particularly in the rat, implies carcinogenicity for humans. But the results of experiments in which several routes of administration were used, including subcutaneous injection in rats, indicates good agreement among the various test systems.[1240]

The most extensively studied group of compounds in this series are the epoxides. On the basis of these bioassays and studies on chemical reactivity—e.g., rate of hydrolysis and reactions with a variety of nucleophiles[1237]—it has become possible to draw some conclusions about chemical structure and reactivity, on the one hand, and carcinogenicity, on the other.[1234] Thus, bifunctional epoxides are more likely to be carcinogenic than monoepoxides. This may be due, in part, to their cross-linking ability. Carcinogenicity is more often observed in bifunctional epoxides whose structures are flexible than in those whose structures are rigid. An excellent example of this is diepoxybutane, an open-chain flexible structure, which is carcinogenic. Its rigid cyclic analogue, 1,2,3,4-diepoxycyclohexane, is noncarcinogenic.

No carcinogenicity data are available on ozonides; and, even for the other compound types listed, except epoxides, the data are extremely sparse.

A series of aliphatic nitro compounds have been tested for carcinogenic activity by a variety of routes. These experiments are summarized by Weatherby[1292] and Treon and Dutra.[1205]

A number of VPOP components may not be carcinogenic, but may exhibit cocarcinogenic or tumor-promoting activity. When used in animal studies, these two types of agents usually result in little, if any, tumorigenic activity. However, when they are applied at various intervals before, with, or after another agent (usually a moderate exposure to a carcinogen), they result, in positive tests, in a high incidence of tumors. The best-known laboratory model is the mouse skin system.[1235] In tumor-promotion tests, a single application of 7,12-dimethylbenz[*a*]-anthracene is followed by repeated application of the material being tested as a tumor-promoter. In cocarcinogenesis experiments, the two agents are applied simultaneously and repeatedly. In these tests, the compound being tested as a cocarcinogen is applied with a low dose of carcinogen, such as benzo[*a*]pyrene. In both tests, the combination of agents results in a much higher yield of tumors than either agent alone, and tumors appear much more rapidly. Not all cocarcinogens have tumor-promoting activity, and vice versa.

Most of the components expected in vapor-phase organic pollution have not been tested for tumor-promoting or cocarcinogenic activity. An exception is phenol.[1236] Additional studies are needed to determine whether this kind of biologic activity is to be expected from vapor-phase pollutants. The long-chain hydrocarbon dodecane has both tumor-promoting[1048] and cocarcinogenic[583] activity. Several long-chain alcohols, particularly the C_{12} and C_{14} compounds, have shown accelerating activity when applied with benzo[*a*]pyrene.[583]

It is probably well to point to the experience with another well-known environmental carcinogen—cigarette smoke. It is generally agreed that the carcinogenic aromatic hydrocarbons of cigarette smoke do not account satisfactorily for its carcinogenicity on mouse skin.[1244] Two-stage carcinogenesis tests with 7,12-dimethylbenz[*a*]anthracene as initiating agent followed by repeated application of cigarette tar have resulted in marked tumor-promoting effect.[1244] Some of the components of cigarette smoke are known to have such promoting activity—e.g., phenol.[1236] Long-chain aliphatic hydrocarbons, alcohols, and carboxylic acids are expected to be biologically active cofactors (cocarcinogens or promoters) in cigarette-smoke condensates.

7

Epidemiologic Appraisal of Human Effects

ANALYTIC STRATEGY

Vapor-phase organic air pollutants constitute a large class of substances, and community exposures are usually to mixtures of several of them. Although mechanisms of action and sometimes of uptake and metabolism of individual pollutants are often known, these facts are not necessarily adequate to evaluate the likely effects on a given population of a given exposure. For such an evaluation, epidemiologic studies are needed. However, few such studies are known; and when effects are studied, it may be difficult to separate those of a specific substance from those of other substances present.

Despite these difficulties and because it is believed that the usefulness of available knowledge is related to what is done about exposures, a strategy is proposed here to make the best possible use of all the information we have and to focus attention on the types of information still needed.

The strategy consists of classifying the vapor-phase organic pollutants according to major chemical class; estimating the average and maximal population exposures in terms of concentration and duration for exposed groups that vary in susceptibility; identifying available data on human population effects; classifying estimated maximal exposures into regions of indifference, incremental effect, imperative action, and ignorance; stipulating, on the basis of experimental studies, which substances might be important if suitable population studies were done; and interpreting the findings with respect to policies that affect control and research. This strategy can be applied to three types of exposure situation: community-wide atmospheric pollution, occupational exposure, and household or other localized exposure. Among community-wide exposures, motor-vehicle exhaust hydrocarbons in photochemical smog are of greatest concern. Occupational exposures, although not the primary focus of this Panel's work, account for a substantial portion of our knowledge of the effects of specific substances on human populations. Localized exposures are the hardest to recognize and hence to study. Uses of vapor-phase organic pesticides in the home provide the paradigm for these exposures.

The proposed classification consists of five major classes: aliphatic substances (A), aliphatic oxygenated substances (O), aromatic substances (R), transient products of vapor-phase hydrocarbon pollutant reactions (T), and relatively stable products of such reactions (S). Each class has subclasses. It is suggested that the subclasses of chief interest be the following:

A_1, saturated aliphatic hydrocarbons
A_2, monounsaturated aliphatic hydrocarbons
A_3, unsaturated aliphatic hydrocarbons of higher order
A_4, sulfur- and nitrogen-containing aliphatic hydrocarbons
O_1, saturated aldehydes
O_2, unsaturated aldehydes
O_3, ketones
O_4, organic acids
R_1, benzene
R_2, toluene and xylene
R_3, other substituted benzene compounds
T_1, active states of oxygen produced in hydrocarbon reactions
T_2, free radicals produced in hydrocarbon reactions
T_3, other high-energy compounds produced in hydrocarbon reactions
S_1, ozone, which may be produced in hydrocarbon reactions
S_2, PAN, nitroolefins, and homologues produced in hydrocarbon reactions
S_3, nitrogen dioxide, which may be produced in hydrocarbon reactions
S_4, other products of hydrocarbon reactions

Table 7-1 presents the data available[31,1227] for the average and maximal community exposure to air pollutants of the A, O, and R classes in the form of atmospheric concentrations. The data are from Los Angeles. Table 7-2 gives some similar data[185,1228] for T and S classes. Statements from the American Conference of Governmental Industrial Hygienists (ACGIH),[38,39] on the effects of specific substances, particularly on workmen, are given in Appendixes C and D. Exposures of workmen are often more intense, more sharply restricted in time, and better defined in composition and involve less-sensitive populations than community exposures. Hatch[536] has analyzed the role of permissible limits for hazardous airborne substances in the working environment. This classification procedure is based partly on his analysis.

EXPERIENCE WITH CLASSIFYING POLLUTANT EFFECTS

The next step in the strategy deals with the fundamental relationship of the epidemiologic evidence on health effects to the policy implications of this evidence.

When the relationships of health to environmental exposures were first subjected to systematic study, the dramatic illness was the phenomenon that attracted attention—for example, typhoid fever, cholera, lead poisoning, radiation-induced skin cancer, and deaths or illness during air pollution disasters. Qualitative associations were the first objects for study; later, epidemiologic and toxicologic studies of quantitative dose–response relationships were made, to determine how much reduction in exposure was needed to avoid these devastating effects.

In the 1950's, nondisease effects of pollutant exposures[478] began to be noted, and qualitative and then quantitative effects of exposures of populations were reported. In 1959, when California first established air quality standards on a scientific basis, three categories were proposed—"adverse," "serious," and "emergency," reflecting different degrees of apparent health risk.[189] This policy was reflected in the following statements:

> The effects of air pollutants vary both in kind and in severity. The seriousness of the effect determines the urgency of control. A graded set of standards was established which recognized this relationship. Three levels of air pollutants were defined as follows:
>
> I. "Adverse" Level. The first effects of air pollutants are those likely to lead to untoward symptoms or discomfort. Though not known to be associated with the development of disease, even in sensitive groups, such effects are capable of disturbing the population stability of residential or work communities. The "adverse" level is one at

TABLE 7-1 Community Air Concentrations of Aliphatics, Aliphatic Oxygenates, and Aromatics, Los Angeles, 1965–1967

Class and Subclass	Substance	Average Concentration, ppm 1965 (218 samples)[a]	Sept.–Nov. 1966 (26 days)[a]	Autumn 1967[b]	Maximal Concentration, ppm[c]
A_1	Methane	3.22	—	3.0	
	Ethane	0.098	—	0.08	
	Propane	0.049	—	0.03	
	n-Butane	0.064	—	0.07	
	Isopentane	0.043	—	0.05	
	n-Pentane	0.035	—	0.03	
A_2	Ethylene	0.06	—	0.08	
	Propene	0.018	—	—	
	1-Butene + isobutylene	0.007	—	—	
A_3	Acetylene	0.039	—	0.08	
O_1	Formaldehyde	—	0.05–0.12[d]	—	
O_2	Acrolein	—	0.004–0.009[e]	—	0.011
R_1	Benzene	0.032	0.015	—	0.057
R_2	Toluene	0.053	0.037	0.048	0.129
	Xylene	—	0.03	0.038	0.12

[a] Data from *Air Quality Criteria for Hydrocarbons.*[1227]

[b] Data from Altshuller *et al.*[31]

[c] Three to four times average unless indicated otherwise.

[d] 1951 data; total aldehydes, 0.20–1.30 ppm.

[e] For Sept. 25–Nov. 15, 1961.

TABLE 7-2 Threshold Limit Values for Chemical Substances in the Workroom Environment, 1972[a]

Class and Subclass	Substance	TLV ppm	TLV mg/m^3
A_1	Methane	None cited; these are simple asphyxiants	
	Ethane		
	Propane		
	n-Butane		
	Isopentane	None cited	
	n-Pentane	500	1,500
A_2	Ethylene	Simple asphyxiant	
	Propene	None cited	
A_3	Acetylene	Simple asphyxiant	
O_1	Formaldehyde	2[b]	3[b]
O_2	Acrolein	0.1	0.25
R_1	Benzene	25[b]	80[b]
R_2	Toluene	100	375
	Xylene	100	435
S_1	Ozone	0.1	0.2
S_2	Nitrogen dioxide	5[b]	9[b]

[a] Derived from American Conference of Governmental Industrial Hygienists.[39]

[b] Not to be exceeded.

which eye irritation occurs. Also in this category are levels of pollutants that lead to costly and undesirable effects other than those on humans. These include damage to vegetation, reduction in visibility, or property damage of sufficient magnitude to constitute a significant economic or social burden.

II. "Serious" Level. Levels of pollutants, or possible combination of pollutants, likely to lead to insidious or chronic disease or to significant alteration of important physiological function in a sensitive group, define the "serious" level. Such an impairment of function implies a health risk for persons constituting such a sensitive group, but not necessarily for persons in good health.

III. "Emergency" Level. Levels of pollutants, or combination of pollutants, and meteorological factors likely to lead to acute sickness or death for a sensitive group of people, define the "emergency" level.

In 1963, at a World Health Organization Symposium on Air Quality Criteria and Methods of Measurement, following Ryazanov's suggestion, the three-category system was modified by adding a "no-effect" category. The system defined boundaries for pollution exposures that produce specified effects, expressed as follows:[1348]

1. Criteria for guides to air quality are the tests which permit the determination of the nature and magnitude of the effects of air pollution on man and his environment.
2. Guides to air quality are sets of concentrations and exposure times that are associated

> with specific effects of varying degrees of air pollution on man, animals, vegetation and on the environment in general.
>
> 3. In the light of present knowledge, guides to air quality may be presented as four categories of concentrations, exposure times and corresponding effects. These four categories are defined by limiting values which may vary for a given pollutant according to the anticipated effect or the criteria used and in relation to other co-existing pollutants and the relevant physical factors, and which take into account the varying responses of different groups of human beings. The Symposium agreed to define the four categories in terms of the following levels:
>
> Level I. Concentration and exposure time at or below which, according to present knowledge, neither direct nor indirect effects (including alterations of reflexes or of adaptive or protective reactions) have been observed.
>
> Level II. Concentrations and exposure times at and above which there is likely to be irritation of the sensory organs, harmful effects on vegetation, visibility reduction, or other adverse effects on the environment.
>
> Level III. Concentrations and exposure times at and above which there is likely to be impairment of vital physiological functions or changes that may lead to chronic diseases or shortening of life.
>
> Level IV. Concentrations and exposure times at and above which there is likely to be acute illness or death in susceptible groups of the population.
>
> For some known pollutants, it may not be possible to state concentrations and exposure times corresponding to all four of these levels because (*a*) the effects corresponding to one or more of these levels are not known to occur with the substance in question, or (*b*) exposures producing effects corresponding to certain levels also produce more severe effects, or (*c*) the present state of knowledge does not permit any valid quantitative assessment (e.g., of threshold levels for carcinogenic substances).
>
> The possibility that some pollutants may have mutagenic effects must be borne in mind; however, at the present time, too little is known about this subject to permit classification of such pollutants in the above categories.

In the meantime, "criteria" and "standards" were being distinguished. "Criteria" referred to exposures that, on the basis of cited evidence, could produce specified effects on a defined population—for example, sufficient exposure to photochemical oxidant to increase the likelihood of an attack of asthma in a population of adult asthmatics.[1076] "Standards" were numerical objectives of an air pollution control program, formulated by a politically authorized agency of government and presumably related in some systematic way to criteria.[186]

DIFFICULTIES IN INTERPRETATION OF POLLUTANT-EFFECT CLASSIFICATION

Standards, whether supposedly differing in the gravity of their health effects, as in California, or based on different criteria, as with those set by the EPA, all tended to be perceived as though their violation implied a risk of widespread disease or of increased mortality. Disease and nondisease effects tended to be considered without distinction, and some types of nondisease effects—for example, annoyance or other responses to odorous pollution[683]—were largely ignored, in part because of this lack of discrimination. At present, if a standard has been set, it is inferred that it must be met, regardless of cost or secondary effects. In the view of some, this is an extreme interpretation of the available data and should be reconsidered.

Because the present report may become input to such a process, this portion properly considers the classification of effects of community exposures. It is proposed that the ideal output from studies of the biologic effects of pollutants on human populations consist of two sets of boundary conditions and the dose–response function(s) connecting these boundaries. Figure 7-1 shows diagrammatically what these boundary conditions imply. For most pollutants, a dose can be denoted that is not known on the basis of generally accepted data to have any effect (called by Hatch[536] the upper limit of normal psychophysiologic function). With sufficient research, the several concentration–duration dosages that are without effect on even sensitive population groups can be cited, along with the slightly higher exposures tolerated without known effect by the more robust sectors of the population. Such data define the lower boundary conditions shown. The boundary conditions may not be very precisely defined, but the variations in population sensitivity tend to make the boundary curved. Above this boundary there is a zone of nondisease effects within which decreased pollution is associated with decreased health risks for the population, and increased pollution with increased health risk. The second set of boundary conditions is that above which, for at least some sector of the population, there is likely to be production or aggravation of illness or fatality.

Note that such boundary conditions require four statements for a full description of what is known or believed to be true: concentration of a pollutant (or index of pollution), duration of exposure, target population, and probability of a defined effect.

The usual dose–response relationships of interest are those which define nondisease effects for various groups, for these also define the magnitude of health impairment that control of pollution, under some conditions, can prevent or avoid.

Associated with the three regions defined by the two boundary conditions for a pollutant or combination of pollutants are appropriate regions whose names imply corresponding community responses. Below the boundary of no health effect, there is a region of "indifference." Although other effects of pollution may be occurring, such as on materials or on visibility, any change in pollution within the region is a matter of indifference from the point of view of health. Above the upper set of boundary conditions is a region of "imperative action" to protect health. Action is needed, regardless of cost or disruption of other activities, for health is threatened and the damage may be irreversible. The intermediate region is one of "incremental health benefit." The lower the pollution, the better health is protected. But in this region, cost of reducing pollution is relevant and is appropriately compared with health benefits and other possible applications of the available resources to other problems.

The public health objective with respect to pollution is ultimately to maintain conditions in the region of indifference for all people at all times. However, such an objective cannot be achieved at once, ignoring all other social goals. Furthermore, research tends to move the left-hand (lower) boundary to the left as new nondisease effects of low concentration are found. The objective must be modified when this occurs.

For many pollutants we do not know enough about the two boundaries, much less about the dose–response relationships. Nevertheless, we can often rank pollutant exposures according to those probably in the region of indifference and those probably in the region of incremental health benefit, using as a basis for reference what is known about the upper boundary and its "distance" from the given exposure conditions. For some pollutants, we know so little that we can say only that we are in a "region of ignorance."

The foregoing proposal is based on exposures of human populations. Data on animals are, as it were, on another plane; although such data influence the nature of studies undertaken and their interpretations, the quantitative exposure conditions for animals define only a projection or shadow area on the plane of dose–probability–population relationships for man.

Concerning the vapor-phase organic pollutants, we may now apply

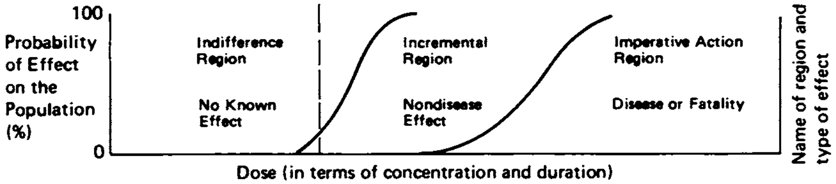

FIGURE 7-1 Diagram showing a proposed classification of pollutant effects in terms of probability, dose, and "regions" associated with different classes of effects. Broken line represents possible "no-appreciable-effect" dose.

this scheme to the available epidemiologic data on population exposure, using occupational exposure data where no other data are available. In carrying out such a classification, it is important to recognize some limitations. Short-term effects, such as irritation, are more likely to be recognized than are long-term effects, symptomatic effects more likely than asymptomatic ones, and specific more likely than nonspecific ones. Furthermore, the importance of identifying sensitive groups and studying their responses must be stressed. These problems can be illustrated by the discussion of specific pollutant exposures. However, there is a further set of problems derived from the nonspecific nature of the effects of pollutants on human populations.

Although photochemical oxidant is largely ozone, ozone does not account for the eye and respiratory irritation. Ozone experimentally[1085] causes alterations in pulmonary function that persist after exposures are terminated, but this is not usually detected epidemiologically (with sufficient effort, it probably could be). Association of oxidant with asthma cannot be attributed to any single agent. Cigarette-smoking exposures and air pollutant exposures often coexist, and exposures to nitrogen oxides, particles, polycyclic aromatic hydrocarbons, and carbon monoxide occur in both smoke and pollution exposures, although in different time–concentration relationships. Although there is an urban excess of lung cancer that appears to be independent of the effect of cigarette-smoking, the roles of specific pollutants and even the contribution of urban air pollution cannot be isolated for purposes of estimating dose–response relationships. Yet, by weighing the available evidence and looking at it carefully from many points of view, we may make some reasonable statements, as the work of groups like the American Conference of Governmental Industrial Hygienists (ACGIH) and some of the work on water and air quality and radiation protection criteria and standards illustrate.

INTERPRETATION OF AVAILABLE DATA

The numbers that are available are shown in Table 7-1. The first class of paraffins is headed by methane, which in Los Angeles from September to November 1966 averaged 3.22 ppm. The maxima in 1965 were 3–4 times these concentrations. We might say that the maximal concentration of exposure to methane that could occur in Los Angeles is 10–12 ppm, with concentrations of other members of the class being proportionately lower, according to the approximate ratios derived from Table 7-1. Similar statements could be made from Table 7-1 about ethylene, benzene, toluene, total aldehydes (or formaldehyde), and acrolein. It is likely that these are the highest community-wide values for human population exposures from motor-vehicle exhaust. Locally higher concentrations could occur because of solvent usage and petroleum refining, distributing, and marketing.

Using the data on threshold limit values (TLV's) of the ACGIH in Table 7-2, we see that the primary pollutants in subclass A_1 are considered "simple asphyxiants" and that, except for *n*-pentane, no TLV's are given. Thus, in subclasses A_1, A_2, and A_3, none of the exposures is outside the region of indifference.

For benzene, the TLV is 25 ppm; for toluene, 100 ppm. Thus, the exposure to benzene is within two orders of magnitude of the TLV, and the effect is a long-range one. Exposures to benzene may be in the region of indifference, but they deserve further discussion because of the possibility of long-term effects.

Epidemiologic Evidence on Benzene

Benzene, a widely used solvent, has had to be used with restrictions because of its tendency to produce changes in red-cell formation, apparently through toxic effects on bone marrow (see Chapter 6).

The results of excessive occupational exposures are aplastic anemia and other serious hematologic problems. The latent period for low exposure is very long. In some respects, the effects resemble those of exposures to radiation. The lowest persistent exposures that had effects were to about 100 ppm. Exposures to 5–25 ppm have no known effects. These findings are related to disease effects and do not necessarily reflect the application of such methods for detecting nondisease effects, for which an example might be mean red-cell turnover rates. Another example of a possible nondisease effect has recently been reported by Forni *et al.*,[430] who examined lymphocytes from 25 people who had recovered from occupational benzene poisoning. A high frequency of stable and unstable chromosome abnormalities was found in the exposed populations, compared with control groups. For example, the cells from control subjects showed 0.5% abnormal metaphase patterns, whereas the cells from the subjects with past benzene hemopathy showed 1.9% abnormal patterns.

We may assume that the affected people were regularly exposed to more than 100 ppm 8 hr/day. Therefore, both the concentrations of the material and the durations were much greater than those likely in community exposures.

The data in Table 7-1 for Los Angeles mean that the average concentration was 0.032 ppm for 1965 and 0.015 ppm for autumn 1966 and the highest measured was 0.057 ppm in terms that are equivalent to the data for occupational health exposure. Thus, the TLV is about 450 times the highest atmospheric concentration. The average in 1966 was 0.015 ppm, about half that in 1965, 0.032 ppm.[1227] It is important in citing such numbers to know the concentrations in areas remote from the influence of motor-vehicle emission and to know more about the minimal detectable concentration and differences in concentrations.

In view of the widely discussed possibility that, in response to the need for unleaded gasoline, a higher proportion of aromatic fuel stocks may be used to sustain octane ratings, we may need to assess the health importance of increasing use of motor fuel containing benzene and related compounds. This assessment should be based on several considerations that go beyond the available data. Evaluation of past occupational exposures would be of critical importance for this assessment. First, monitoring of benzene should be systematically undertaken at highly polluted and remote sites; second, exposures of and possible effects in persons who fill gasoline tanks should be assessed; and third, estimates of benzene in exhausts from the various types of vehicles and control systems in use should be made. From the available evidence, we conclude that community exposure to benzene is in the region of indifference as far as health is concerned; but, if any substantial increase in aromatic motor-vehicle fuel is contemplated, these three steps will need to be undertaken to ensure that no avoidable health hazard occurs.

Evaluation of Other Hydrocarbons

For toluene, the TLV is 200 ppm, and maximal exposure is so much lower that this also is in the region of indifference.

For formaldehyde, the TLV is 2 ppm; the maximal value for total aldehydes is 1.3 ppm. The effect of formaldehyde at low concentrations is that of an irritant. Much of the effect of photochemical oxidant on the eyes and respiratory tract is attributed to the irritating effects of formaldehyde.[1085] Thus, exposures to formaldehyde may very well be in the region of incremental effects. However, these circumstances need to be defined further; to the best of our knowledge, the effects would be transient. The matter is discussed below.

Although the more complex compounds (subclasses O_2, O_3, and O_4) may very well be much more toxic or irritating, their concentrations are almost certainly less than those shown in Table 7-1. Chlorinated or other substituted homologues may have greater toxicity, but are unlikely to be atmospheric pollutants in the usual community-wide sense. They may be occupationally important, and they may contribute to localized pollution. Therefore, from the point of view of community exposure, we should concentrate attention on formaldehyde.

Epidemiologic Evidence on Formaldehyde

Of necessity, this section deals with total aldehydes expressed as formaldehyde, as well as with what is known of the individual agents. Two recent reviews are available and are appropriately summarized and compared: *Air Quality Criteria for Hydrocarbons*[1227] and *Community Air Quality Guides*.[238]

To summarize from the former:

> The most characteristic and important effect of aldehydes, particularly of low-molecular-weight aldehydes in both humans and animals is the primary irritation of the eyes, upper respiratory tract, and skin. Aldehyde concentrations have been shown to correlate with the intensity of odor of diesel exhaust and to some extent with the intensity of eye irritation during natural and chemically produced smogs. . . . Aldehyde levels referred to as "low" in toxicological reports are usually much greater than concentrations routinely found in ambient air. . . . In most cases, the general and parenteral toxicities of these aldehydes appear to be related mainly to these irritant effects. The unsaturated aldehydes are several times more toxic than the corresponding aliphatic aldehydes, and toxicity generally decreases with increasing molecular weight within the unsaturated and aliphatic aldehyde series. . . . Sensitization of the respiratory tract is produced rarely, if at all, by inhalation of aldehydes.

Renzetti and Bryan[1014] have shown an association between eye irritation in a panel and aldehyde concentrations in Los Angeles. Regression curves of the effect of atmospheric concentrations of total aldehydes and formaldehyde on panel eye irritation are given in Figures 7-2 and 7-3, respectively.

From Figure 7-2 we may infer that, with total aldehyde above 0.05 ppm, there is likely to be a progressive increase in eye irritation with exposure. Of course, this association does not prove that aldehyde is the cause; other photochemical products are also likely to be present.

However, Schuck *et al.*[1085] have demonstrated (Figure 7-4) that substantial eye irritation from irradiated synthetic atmospheres containing nitrogen dioxide and various hydrocarbons can be explained by concentrations of formaldehyde. They suggest that formaldehyde concentrations as low as 12 $\mu g/m^3$ (0.01 ppm) could cause eye irritation.

Other substances probably contribute to the eye irritation of photochemical pollution, but most scientists accept a significant contribution of aldehydes.

Community Air Quality Guides[238] states that, "as constitutents of photochemical smog, acrolein and formaldehyde are highly suspected

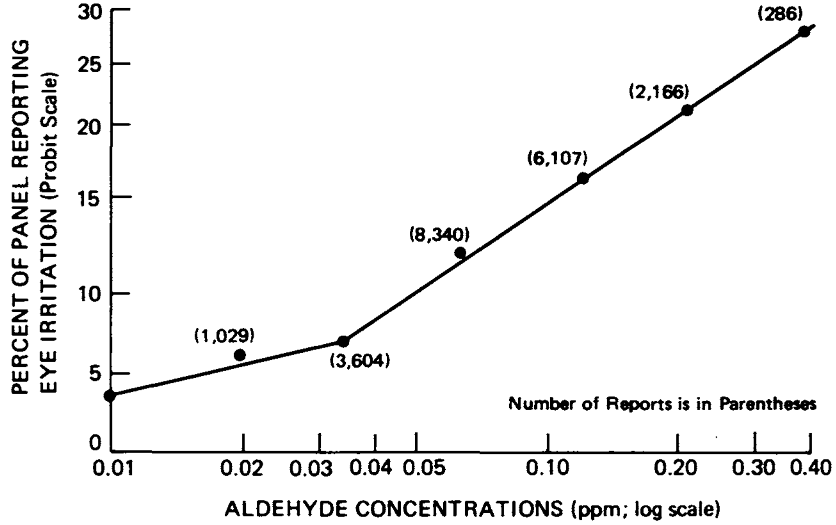

FIGURE 7-2 Regression curve of effect of aldehyde concentrations on eye irritation in panel studies. (Reprinted with permission from Renzetti and Bryan.[1014])

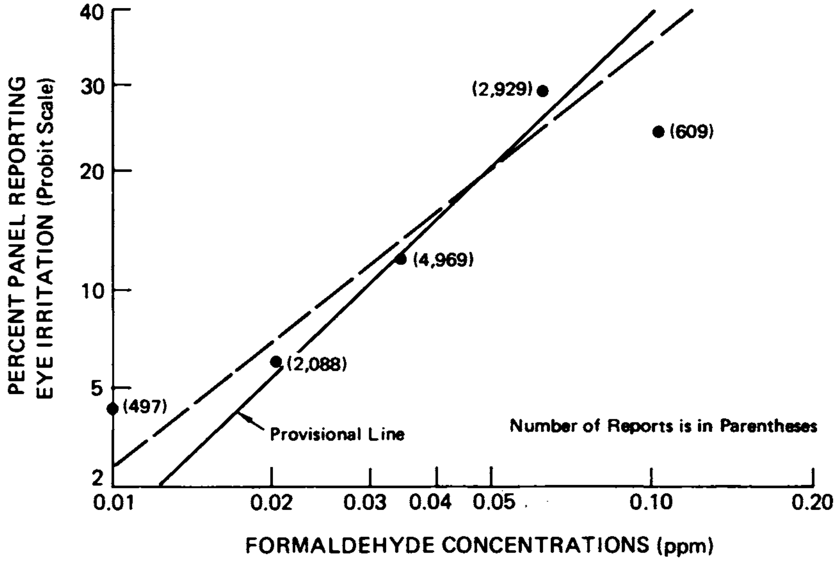

FIGURE 7-3 Regression curve of effect of formaldehyde concentrations on eye irritation in panel studies. (Reprinted with permission from Renzetti and Bryan.[1014])

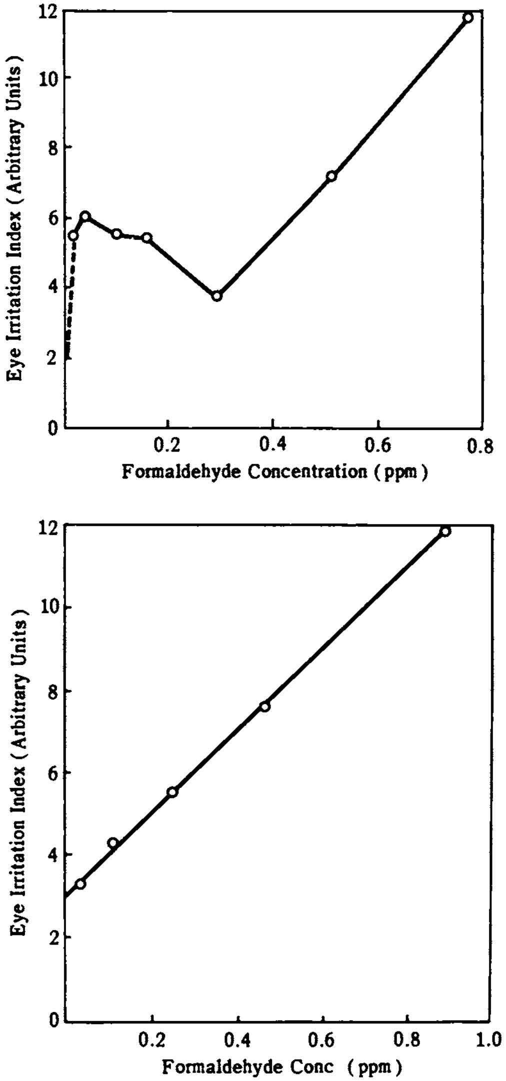

FIGURE 7-4 Average reported eye irritation intensities of 12 subjects during photooxidation with ethylene (top) and propylene (bottom), related to observed formaldehyde concentrations. (Reprinted with permission from Schuck *et al.*[1085])

eye irritants." Although noting that 35% of the panelists[1014] experienced eye irritation at 0.10-ppm formaldehyde, it nevertheless concludes that "there is no evidence to suggest that sensory irritation of any form will be present if the atmospheric aldehyde concentrations are held under:

0.1 ppm	formaldehyde
0.01 ppm	acrolein
0.2 ppm	total aldehyde as formaldehyde.

The evidence of Renzetti and Bryan[1014] and Schuck *et al.*[1085] refutes this conclusion. Admittedly, the work leaves many questions, concerning unusually sensitive groups, other substances, and the consistency between experimental and epidemiologic data.

The TLV's for formaldehyde and acrolein are within about an order of magnitude of the maximal observed values in Los Angeles. We conclude that in Los Angeles, but possibly not elsewhere, aldehyde exposures have been in the incremental region, on the basis of their probable role in producing eye and respiratory tract irritation. These effects are due largely to photochemical reaction products, and not solely to aldehydes emitted as such to the atmosphere.

TABLE 7-3 Eye Irritation Potency of Various Hydrocarbons in Irradiated Synthetic Atmospheres[a]

Hydrocarbon	Potency[b]	Hydrocarbon	Potency[b]
n-Butane	0	*m*-Xylene	2.9
n-Hexane	0	1,3,5-Trimethylbenzene	3.1
Isooctane	0.9	1-Hexene	3.5
tert-Butylbenzene	0.9	Propylene	3.9
Benzene	1.0	Ethylbenzene	4.3
Ethylene	1.0	Toluene	5.3
1-Butene	1.3	*n*-Propylbenzene	5.4
Tetramethylethylene	1.4	Isobutylbenzene	5.7
cis-2-Butene	1.6	*n*-Butylbenzene	6.4
Isopropylbenzene	1.6	1,3-Butadiene	6.9
sec-Butylbenzene	1.8	α-Methylstyrene[c]	7.4
2-Methyl-2-butene	1.9	Allylbenzene[c]	8.4
trans-2-Butene	2.3	β-Methylstyrene[c]	8.9
o-Xylene	2.3	Styrene[c]	8.9
p-Xylene	2.5		

[a] Derived from Heuss and Glasson.[566]
[b] Conditions: hydrocarbon at 2 ppm and nitric oxide at 1 ppm, except where noted.
[c] Conditions: hydrocarbon at 1 ppm and nitric oxide at 0.5 ppm.

Appraisal of Transient Reaction Products

The transient reaction products of concern are peroxyacetylnitrate (PAN), peroxybenzoylnitrate and its homologues, and singlet oxygen. In the first case, the maximal concentration is 0.1 ppm and the minimal concentration that under experimental conditions produces health effects is about 0.3 ppm. Thus, this substance may be relevant to community exposures. However, few systematic measurements have been made, and no epidemiologic data are available. We are therefore in the region of ignorance for PAN and homologous substances.

Concerning singlet oxygen, we need to know the maximal concentration and the minimal concentration that produces health effects. We will therefore have to carry out further research to evaluate this problem. We are in the region of ignorance for singlet oxygen.

Concerning ozone, the maximal concentration is 0.90 ppm, and the minimal concentration that produces health effects (based on the TLV for 8 hr) is 0.1 ppm. From epidemiologic data, for ozone, at least in Los Angeles, we are well into the region of incremental effects. This is discussed more fully below.

Epidemiologic Evidence on Ozone and Oxidants

There are at least two separate problems to be considered here: the contributions of specific hydrocarbons to the noxiousness of photochemical pollution and the epidemiologic data on the effects of oxidant pollution. With respect to the latter, data from Los Angeles, scant as they are, constitute the major source of useful information. With respect to the former, there is always a risk that the use of yields of ozone, aldehydes, or phytotoxins will not adequately reflect the short- or long-term health effects. For the present, we must assume that potency with respect to eye irritation or alterations of pulmonary function in animals is equivalent to health impact of hydrocarbon ingredients in photochemically reacted atmospheres.

A representative result for eye irritation is shown in Table 7-3.[566] Table 7-4 is similar, but uses a different criterion for potency: the reactivity for photooxidation of nitric oxide to nitrogen dioxide.

Heuss and Glasson[566] sought relationships between eye irritation and hydrocarbon reactivity. Yeung and Phillips[1351] have identified the structures of hydrocarbon molecules that relate photochemical reaction to eye irritation potency. The most potent is that which yields benzaldehyde, a precursor of the highly potent, but transient, peroxybenzoylnitrate. Next in importance is the structure that yields

TABLE 7-4 Reactivities of Hydrocarbons Based on Ability To Participate in Photooxidation of Nitric Oxide to Nitrogen Dioxide

	Relative Reactivities		
Hydrocarbon	Altshuller and Cohen (1963)[24a]	Glasson and Tuesday (1970)[465]	Levy *et al.* (1970)[764a]
2,3-Dimethylbutene-2	—	5.3	—
2-Methyl-2-butene	—	1.7	—
trans-2-Butene	2	2	2
Isobutene	1	0.6	—
Propylene	1	0.6	—
Ethylene	0.4	0.3	0.3
1,3,5-Trimethylbenzene	1.2	0.9	0.5
m-Xylene	1	0.7	0.3
1,2,3,5-Tetramethylbenzene	0.9	0.6	—
1,2,4-Trimethylbenzene	0.6	0.6	—
o- and *p*-Xylenes	0.4	0.4	—
o- and *p*-Diethylbenzenes	0.4	0.3	—
Propylbenzenes	0.3	0.2	—
Toluene	0.2	0.2	0.1
Benzene	0.15	0.05	0.02
n-Nonane	0.15	0.2	—
3-Methylheptane	0.15	0.2	—
n-Heptane	—	0.1	—
Methylpentanes	<0.1	0.2	—
Pentanes	—	0.1	—
2,2,4-Trimethylpentane	0.15	0.1	—
Butanes	—	0.1	—
Ethane	—	0.03	—
Methane	—	<0.01	—
Acetylene	0.1	—	—

[a] Arbitrarily adjusted to the Glasson and Tuesday value for *trans*-2-butene to permit comparison.

formaldehyde, and then that which forms aliphatic aldehydes or lower yields of formaldehyde. Fully substituted olefins, for example, the class that yields ketones, produce weak or minor eye irritants with photochemical irradiation. Some compounds—for example, 1,3-butadiene—form two eye irritants (in this case, formaldehyde and acrolein) per reactive molecule, and special categories of reactivity need to be set up for them.

It appears that the basis for eye irritation is more complex than a single substance (see Figure 7-4, for example; the methods and scales differ from those of Figures 7-3 and 7-5).

Data on ozone and oxidant effects have been reviewed.[185,186,189,1076,1228,1348] The results are summarized in Tables 7-5 and 7-6.

We may summarize these findings as showing evidence of disease aggravation (asthma) at oxidant concentrations of 0.25 ppm (peak) or 0.20 ppm (hourly average) and impairment of lung function in persons with chronic respiratory disease, eye irritation, and impairment of athletic performance at about 0.10 ppm (hourly average). There is evidence of an increased likelihood of motor-vehicle accidents in Los Angeles during periods with increased oxidant.[1233] The quantitative relationships of the exposures that produce such an effect have not been established.

The disease aggravation data can be interpreted as putting a peak dose of 0.25 ppm briefly or 0.20 ppm for an hour in the imperative-action

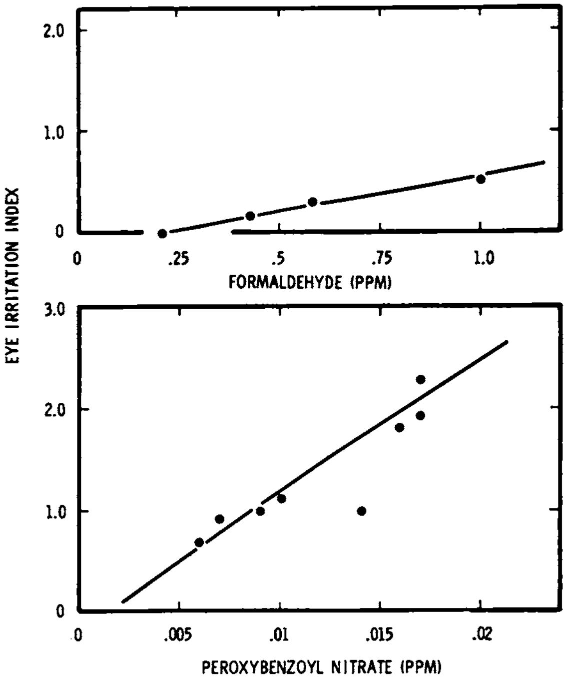

FIGURE 7-5 Eye irritation of peroxybenzoylnitrate and formaldehyde. (Reprinted with permission from Heuss and Glasson.[566])

TABLE 7-5 Health Effects of Experimental and Occupational Exposures to Ozone as an Air Pollutant[a]

Effect	Exposure, ppm	Duration	Comment	Reference
Odor detection	0.02	5 min	Odor detected in 9 of 10 subjects within 5 min	553
Respiratory irritation (nose and throat), chest constriction	0.3	Continuous during working hours (8 hr)	Occupational exposure of welders (other pollutants probably also present)	696
Changes in pulmonary functions:				
Diminished FEV8$_{1.0}$ after 8 weeks	0.5	3 hr/day 6 days/week for 12 weeks	Experimental exposure; change returns to normal 6 weeks after exposure; no changes observed at 0.2 ppm	95
Small decrements in VC, FRC, and DL_{CO} in 3, 2, and 1, respectively, of 7 subjects	0.2–0.3	Continuous during working hours	Occupational exposure; all 7 subjects smoked; normal values for VC, FRC, and DL_{CO} based on predicted values	1357

Impaired diffusion capacity (DL_{CO})	0.6–0.8	2 hr	Experimental exposure of 11 subjects	1356
Increased airway resistance	0.1–1.0	1 hr	Increase in 1 of 4 at 0.1 ppm and 4 of 4 at 1.0 ppm	J. R. Goldsmith and J. A. Nadel, unpublished data
Reduced VC, severe cough, inability to concentrate	2.0	2 hr	High temperatures; one subject	496
Acute pulmonary edema	9.0	Unknown	Refers to peak concentration of occupational exposure; most of exposure was to lower concentration	696

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[a] Derived from California Air Resources Board.[185]

TABLE 7-6 Epidemiologic Effects of Oxidant Pollution in Los Angeles[a]

Effect	Exposure, ppm	Duration	Comment	Reference
Eye irritation	0.1	5 min	Result of panel response	1015
Impairment of pulmonary function (airway resistance)	Regression about 0.1	1 week in room containing ambient air	Subjects were smokers and nonsmokers; most subjects had emphysema	1012, 1232
Aggravation of respiratory disease—asthma	0.25[b]	Peak value	Patients exposed to ambient air; value refers to oxidant content at which number of attacks increased	1076
Impaired performance of student athletes	Regression about 0.1	1 hr or more	Exposure for 1 hr immediately before race	1291

[a] Derived from California Air Resources Board.[185]

[b] Equivalent to 0.20 ppm as an hourly average.

region involving sensitive groups. However, this is based on a single study, and equivalent concentrations of oxidant at other times and places may well differ from those in Pasadena in 1956. An hourly average of 0.1 ppm is near the lower boundary of the region of incremental effects. The experimental and occupational exposure data in Table 7-5 are consistent with the community exposure data on respiratory system effects due to ozone. The effects on eye irritation and on track performance are not likely to be due to ozone alone.

Recent studies with hamster lymphocytes[1362,1363] indicate that respiratory exposures to ozone at 0.2 ppm for 5 hr produce stable chromosome breaks, which are interpreted as evidence of a mutagenic effect of the agent. The authors suggest that the margin of safety for permitted community exposures to ozone based on mutagenic effect is less than one-hundredth the margin of safety permitted for radiation exposures. These findings and interpretations are of serious import and deserve prompt and thorough evaluation. Because a similar question arises for exposure to benzene, ozone effects should be added to the evaluation previously proposed for benzene as a mutagen. The authors[1362,1363] do evaluate the interaction of ozone and irradiation for 5 hr to 230 rad and find that ozone and radiation effects are approximately additive.

A recent evaluation of the effects of oxidant pollution was that of the World Health Organization's Expert Committee on Air Quality Criteria and Guides for Urban Air Pollutants.[1347] The foregoing analysis is entirely consistent with the WHO report.[1348]

Epidemiologic Evidence on Oxides of Nitrogen

Nitrogen dioxide is produced by photochemical reactions of vapor-phase hydrocarbons and nitric oxide. Nitrogen dioxide on a molar basis is several times more toxic than nitric oxide. The epidemiologic and toxicologic bases for air quality criteria were reviewed at an Air Pollution Control Association symposium in 1969.[884] The contributors to the symposium and the WHO expert committee[1348] agreed that the data do not permit quantitative statements about epidemiologic aspects of nitrogen dioxide. The WHO expert committee said:

> A study of second-grade (6–8 years of age) schoolchildren in Chattanooga, Tenn., USA, comparing two low control areas and two "high" pollution areas (one for NO_2 and one for suspended particulates) showed that the reported $FEV_{0.75}$ values were significantly higher in the control areas than in the "high" NO_2 area. The levels of suspended particulates and SO_2 did not seem to account for the health effects. Another finding was that the incidence of acute respiratory illness in the schoolchildren, their siblings, and their parents was significantly greater in the "high" NO_2 area. . . .

> The average NO_2 level of 190 $\mu g/m^3$ (0.10 ppm) in the "high" area was exceeded on 40%, 18%, and 9% of the days respectively at the three monitoring stations; in the control areas this level was exceeded on 17% of the days at only one station.

Thus, differences in exposure to nitrogen dioxide were not shown, even though differences in respiratory disease were demonstrated. The WHO committee concluded that "the Committee believes that there is insufficient information upon which to base specific air quality guides at this time."

It is concluded that the epidemiologic data on health effects of nitrogen dioxide exposure are in the region of ignorance.

SUMMARY AND DISCUSSION

There appear to be three substantive questions to which this epidemiologic appraisal of vapor-phase organic air pollutants is relevant: (1) What is the demonstrated or reasonably inferred effect on health of likely exposures to these pollutants in the general community? (2) What health consequences are likely to follow a modification of the concentration or type of such pollutants, and in particular the increase in aromatic content of gasoline stocks? (3) What are the crucial gaps in our knowledge of health effects and with what priority should we try to fill them? In particular, are significant health threats implied by toxicologic or experimental data that do not match with epidemiologic data?

This task has been approached by a strategy consisting of classifying the major pollutants; estimating the average and maximal population exposure; relating these estimates to likely effects on human health, based mostly on occupational health considerations; classifying the maximal estimated exposures into regions with respect to expected effects on human health, implying differing attitudes or action (indifference, incremental effect, imperative action, or ignorance); and discussing likely or possible effects of classes not in the region of indifference.

Judgments concerning community exposures that are classed in the region of indifference are based largely on occupational exposure information and must therefore be qualified.

Direct human health effects of the following classes of pollutants under conditions of likely exposure were believed to be in the region of indifference:

A_1, saturated aliphatic hydrocarbons
A_2, monounsaturated aliphatic hydrocarbons
A_3, unsaturated hydrocarbons of higher order

R_1, benzene (but with qualifications—see discussion above)
R_2, toluene and xylene

In the region of incremental effects are

O_1, saturated aldehydes
S_1, ozone (possibly in the region of imperative action with respect to sensitive groups)

In the region of ignorance are possible effects of

T_1, T_2, T_3, transient products
S_2, PAN, nitroolefins, and homologous compounds
S_3, nitrogen dioxide produced in hydrocarbon reactions

8

Interactions and Effects on Total Environment

The basic orientation of most of this report is the assessment of the mechanism and extent of formation of vapor-phase organic pollutants (VPOP) in the atmosphere and their effects on humans, but it is also appropriate to consider their possible effects on atmospheric properties, on materials with which the air comes into contact, on natural waters, including aquatic life, on microorganisms, and on vegetation.

Hardly any information is available on the effects of VPOP at their typical ambient concentrations on building materials, clothing, paint, etc. This chapter therefore does not attempt to consider such effects. The available information on the incidence and effects of organic compounds in general in natural or treated waters is also sparse. Thus, there is no attempt here to assess the possible effects on aquatic life of VPOP that may find their way into such waters. Consideration of the effects on natural waters is limited for the most part to the relatively limited information on the interaction between organic compounds in air and natural waters and their possible effects on the latter. The contributions of VPOP to such effects and their significance is necessarily largely speculative.

Consideration is given to the possible role of VPOP on atmospheric properties, and their known effects on microorganisms and vegetation are treated in some detail.

EFFECTS ON ATMOSPHERIC PROPERTIES

The reported concentrations of vapor-phase organic materials in the atmosphere[31,210,1155] indicate that these materials are probably not prevalent enough to affect the physical properties of the atmosphere significantly. Robinson[1022] attributed the major effects on visibility, fog formation, precipitation, and solar radiation to the presence of particulate matter in the atmosphere.

Altshuller *et al.*[31] studied the hydrocarbon concentrations in the Los Angeles basin in 1967 and found that, excluding methane, over 80% of the remaining hydrocarbon concentration can be accounted for by 10 hydrocarbons: ethane, ethylene, acetylene, *n*-butane, isopentane, propane, toluene, *n*-pentane, *m*-xylene, and isobutane. Stephens and Burleson[1155] also examined the distribution of hydrocarbons in the atmosphere and reported that the composition of air samples resembled that of auto exhaust with an addition of natural gas and of C_{3-5} paraffins that resemble gasoline vapor. They determined that the background concentration of methane is 1.39 ppm. This concentration agrees with the results reported by Fink *et al.*[398] Cavanagh *et al.*[210] reported the methane concentration at Point Barrow, Alaska, to be 1.59 ppm. Stephens and Burleson[1155] concluded that the use of natural gas increases the methane concentration significantly in urban areas.

Visibility

The direct effect of vapor-phase organic pollutants in decreasing visibility has not been demonstrated. Loss of visibility has been attributed only to the effects of absorption and scattering of light by the particulate matter in the air. Charlson[214] and Ettinger and Royer[380] have both demonstrated a correlation between the aerosol mass concentration and visibility.

Solar Radiation

Many measurements have indicated that solar radiation is considerably less intense in polluted atmospheres than in clean air. Randerson[991] compared the spectral distribution of solar radiation in the 450- to 700-nm band near Houston, Texas, in a clean air mass and a heavily polluted air mass. He observed a 23% loss in solar radiation, which he attributed to attenuation by pollution in the atmosphere. The loss of solar radiation depends on wavelength, with the shorter wavelengths showing the greater loss. Randerson attributed this to the greater scattering of the shorter-wavelength radiation by the particulate matter in the atmosphere. Nader and White[904] investigated the ultraviolet radiation in urban atmospheres in the 300- to 380-nm region and observed a loss in energy in polluted atmospheres. They also attributed the loss to particulate matter in the atmosphere.

Atmospheric Color

Robinson[1022] discussed the effect of nitrogen dioxide, which imparts a brown color to the sky. The change in color is due to the absorption in particular regions of the spectrum. The vapor-phase constituent of the atmosphere must absorb radiation in the visible region of the spectrum (400–800 nm) if the compound is to impart a color to the sky. Most VPOP do not absorb radiation in this region of the spectrum and therefore will not impart a color to the sky.

Cloud Formation and Precipitation

Urban areas have been shown to have a more complex climate than nonurban ones. Landsberg[739] has pointed out that the climate of an urban area when compared with the climate of a nonurban area in the same region can be characterized by 5–10% more cloudiness, 100% more winter fog, 30% more summer fog, and 5–10% more precipitation. Robinson[1022] stated that fog persistence is related to the number of nuclei that produce fogs with smaller drops. Little is known of droplet chemistry and the role that VPOP can play in fog formation and persistence.

There are no data that would link VPOP to changes in precipitation patterns. The major effect of air pollution on such patterns is thought to be the addition of condensation nuclei to the system.[1022]

REMOVAL, FATE, AND PERSISTENCE

Over a decade ago, Junge[656] remarked about atmospheric cleansing mechanisms that "our knowledge of these processes is rather vague." In the intervening years, progress has been made in understanding the detailed life cycles of a small number of atmospheric contaminants; and for the remaining multitude of pollutants, agreement has been reached on the general processes by which they disappear from the atmosphere. However, quantitative data, as are available on the sources of organic pollutants, are largely unavailable for the removal mechanisms, and Junge's remark remains a fair summary of the situation.

The subject has more recently been reviewed by Haagen-Smit and Wayne,[506] by Robinson and Robbins,[1023] and in *Inadvertent Climate Modification.*[604] A major aspect of the problem, precipitation scavenging, was the subject of a U.S. Atomic Energy Commission conference report.[980]

The gas-phase reactions that transform pollutants after they enter the atmosphere and are mixed by diffusion and turbulence are discussed elsewhere. It is assumed here that any of these gas-phase reactions that proceed faster than the atmospheric cleansing processes have occurred. In other words, we will concern ourselves with the ultimate mechanisms that remove the products of organic pollutants, including unchanged compounds, from the atmosphere. It is worth noting that only a very few compounds, such as the Freons,[784] appear to be without a removal mechanism of the type that provides for almost all the other recognized VPOP a residence time in the atmosphere of less than a few years. Even such stable compounds as the Freons are not immune to reactions promoted by ambient ionization from cosmic rays, airborne radioactivity, and lightning discharges, although their residence time against these processes may be exceedingly long.

The low concentration of VPOP products in the atmosphere, except close to their sources, makes it safe to assume that removal processes will be first-order. If c is the ambient concentration at time t, we may write, for the removal of a VPOP,

$$-\frac{dc}{dt}=\frac{c}{T} \qquad (1)$$

where T is the residence time of the VPOP before removal under the prevailing conditions. If the VPOP is entering the well-mixed volume V under consideration at a rate dm/dt, then, when a steady state has been reached,

dt

$$\frac{1}{V}\frac{dm}{dt}=\frac{c}{T} \qquad (2)$$

or

$$c=\frac{T}{V}\frac{dm}{dt} \qquad (3)$$

with c in this case being the steady-state concentration.

The assumption that VPOP are widely dispersed in a time that is short, compared with T, will often not be true, especially when the steady state being considered is a global one; a more detailed examination of this case has been made by Schutz and co-workers.[1089] Nevertheless, the above result holds approximately for VPOP with residence times of weeks or longer and can be used to derive the residence time in cases where the ambient concentration can be measured and the production rate estimated.

For only a handful of low-concentration atmospheric components have residence times been estimated, and these are mostly the simpler compounds, such as methane, carbon monoxide, and nitrous oxide. Table 8-1 shows the current best estimates of the concentrations, production rates, and residence times of compounds for which reasonably reliable data are available.

What mechanisms are available for removal of VPOP from the atmosphere? It will be useful to classify these mechanisms according to the form of the VPOP when undergoing removal. A trivial case is the degradation of a VPOP to yield water, carbon dioxide, or other major constituents of the atmosphere; such a pathway will be followed by a large fraction of the total VPOP load (the oxidation processes in the atmosphere will bear analogy to slow combustion), but are of no interest here. This case apart, the products of the VPOP will ultimately be removed as either gases or solids/liquids. Although the mechanisms are not necessarily different, we will consider them separately.

Removal as a Gas

The principles of gaseous removal were set forth by Junge.[656] References to more recent work may be found in *Precipitation Scavenging (1970)*.[980] The following ultimate fates will be discussed briefly:

Diffusion to the upper atmosphere

Diffusion to the ground, including ultimate utilization by plants, animals, and microorganisms

Dissolution in cloud or rainwater, including reaction with the water or its solutes

DIFFUSION TO THE UPPER ATMOSPHERE

The definition of "upper atmosphere" in this case depends somewhat on the VPOP being considered. For most purposes, a VPOP penetrating the tropopause may be considered as lost to the lower atmosphere and lost to the biosphere. However, some compounds, such as methane, are resistant to dissociation by the ultraviolet of the lower stratosphere and

TABLE 8-1 Estimated Global Concentrations, Production Rates, and Residence Times of Some Trace Gases in the Atmosphere

Compound	Ambient Concentration, ppm (vol)	Production Rate, 10^{12} g/yr	Residence Time, yr	Reference
Methane	1.4	500–1,000	4–7	356
Carbon monoxide	0.2–0.05	700	0.7–1.5	657,919,1094
Nitrous oxide	0.26	—	12–13	822
Freon	50×10^{-6}	0.44	16	784
Methyliodide	10^{-6}	40	0.003	784
Carbon tetrachloride	7×10^{-5}	1.7	1	784

to oxidation by ozone; hence, the methane pool should be considered as encompassing both the troposphere and the lower stratosphere. As an extreme example, penetration of a gas into the stratosphere may lead to its incorporation into the stratospheric aerosol, with later return to the troposphere; however, it is unlikely that the product of this slow process (taking years) will chemically resemble the original gas.

Crossing of the tropopause is more often the result of large-scale turbulence, as in storms, than of diffusion on a molecular scale.

DIFFUSION TO THE GROUND

This process, too, is dominated by turbulent diffusion, with eddy diffusion coefficients of about 3×10^4 cm^2/sec being typical. Much research on the converse question, diffusion away from the ground, has been performed in connection with radon emission from the soil[234] and the evaporation of ground moisture. The concept of a deposition velocity, discussed later for aerosols, has been applied also to the case of gases[656] that diffuse to some sink at the ground surface; in this case, the deposition velocity may be best regarded as the ratio of the eddy diffusion coefficient to an appropriate scale length. Values of about 1 cm/sec have been found for deposition velocities of iodine vapor[234] and sulfur dioxide;[644] these values are about 10 times higher than the deposition velocities of aerosols.

A closer examination of diffusion to the ground raises the question of what establishes the concentration gradient above the soil. Clearly, there must be an efficient sink for the diffusing gas in the soil surface or in the biota resident within and on the surface of the soil. There is strong evidence[2,606,1005] that biologic scavenging by soil ecosystems is, at normal ambient concentrations, an efficient sink for a wide variety of atmospheric trace gases, including light hydrocarbons, carbon monoxide, and sulfur dioxide.

DISSOLUTION IN CLOUD OR RAINWATER

This is an inefficient process for atmospheric cleansing in the case where the gas merely dissolves in the water droplet, without undergoing hydration or reacting with other solutes. Junge[656] has pointed out that typically only 10^{-7} of the gas in a given volume of cloud will reside in the water, inasmuch as clouds contain only about 1 g of water per cubic meter.

The efficiency is greater, but still low, for gases that undergo hydration and dissociation in solution—for example, ammonia and sulfur dioxide. Only in the case where two solutes can participate in a reaction that either is irreversible or has a very large equilibrium constant is the rate of removal appreciable. The best known example of this process is the joint removal of ammonia and carbon dioxide, but obviously many such reactions are potentially able to occur.

Recent experimental work[1177] supports the theory of removal of gases, such as sulfur dioxide, that react with water; the case of "insoluble" gases is less clear.

Despite the low efficiency of removal of many of the trace gases, rainout and washout will be important, because of the repeated exposure to precipitating mechanisms, for the highly oxygenated and polar end products of VPOP degradation and will produce small but possibly important concentrations of some compounds in ground water.

Removal by Aerosol Formation

A major part of atmospheric organic pollutants is olefins and other reactive hydrocarbons. VPOP reaction products of these reactive species are believed to be removed by free-radical polymerization processes that result in macromolecular particles that grow in size to become the visible haze of, for example, photochemical automobile smog. The process producing natural haze from the olefins and terpenic emission of vegetation is probably similar. Light, during at least some phases of the reaction, seems essential for aerosol production.

The formation of aerosol from man-made pollutants has been reviewed by Altshuller and Bufalini[22] and Haagen-Smit and Wayne,[506] and many other reaction schemes involving free-radical intermediates capable of initiating radical polymerization have been suggested. Studies on the reactions involved in the formation of aerosols are intrinsically more difficult than those on vapor-phase reactions, and few have been attempted under conditions resembling those in the real atmosphere; much of the available information is gained indirectly by studying reaction rates (as measured by the disappearance of the reactant, and perhaps the total mass of particulate matter accumulated) as functions of reactant pressures, light intensities, and temperatures.

The systems used to model aerosol production from automobile exhaust have generally shown low yields of aerosol, as measured by the ratio of carbon in the aerosol to the total carbon of the original reactants. Much higher yields have been obtained by Rasmussen and coworkers[1001] in experiments with cyclic olefins, such as α-pinene. It is not clear that any of these experiments adequately model the processes in the real atmosphere, where, for example, small (less than 0.01 μm) particles are always present to act as nuclei for the growth of the polymeric particles produced by the reactions under study. Such nucleation may greatly facilitate aerosol production because of the energy barrier caused by surface effects when particle production *de novo* is attempted; the existence of nucleating particles will certainly alter the size distribution of the synthetic aerosol.

The experiments of Goetz and Klejnot[472] deserve attention. They demonstrated that even large aerosol particles are often only metastable and are prone to disappear, especially in the presence of ultraviolet light. Altshuller and Bufalini[22] point out that this metastability may have compromised the accuracy of some measurements of the yield of aerosols in photochemical chambers from synthetic gas reactions.

Aerosol formation from VPOP in chamber experiments is promoted by sulfur dioxide, but the resulting aerosol often contains little organic material. Nitrogen dioxide promotes aerosol formation, especially by the higher olefins, but nitric oxide is a powerful inhibitor. The most plausible explanation of this inhibitory effect of nitric oxide is that nitric oxide competes for atomic oxygen produced in the photodissociation of nitrogen dioxide more effectively than molecular oxygen, thus limiting the later formation of ozone. Ozone efficiently converts cyclic olefins to aerosol, even in the absence of light.[1001] Other experiments[148] indicate that aerosol formation can occur in the absence of any of these adjuvants, provided only that ionization produced by airborne radioactivity and cosmic rays is present.

The newly formed aerosol in the real atmosphere is certainly not a simple polymer; at the very least, it will be a copolymer formed from the diverse monomers present in the atmosphere, and it may incorporate compounds that, when used as the sole monomer species in chamber experiments, are insufficiently reactive to form aerosol.

Removal by Preexisting Aerosols

There is general agreement that the principal path for removal of the products of organic pollutants is aerosol formation from the products themselves. However, not all such products can be conceived as undergoing polymerization, or even copolymerization, to yield macromolecules for aerosol particle formation. We consider here a number of ways in which these products may be removed by a preexisting aerosol. Very little experimental evidence is available to judge the importance of these processes, and the following list is not intended to be exhaustive: reaction with aerosols; dissolution in aerosols; adsorption on the surface of aerosols; liquefaction in the interstices of aerosols; and reaction with a compound already dissolved in or attached to an aerosol. Some of these processes are well understood in contexts other than those involving aerosols, and it is worth considering them briefly before leaving the question of aerosol removal processes.

REACTION WITH AEROSOLS

This mechanism has been suggested[656] for the removal of ammonia, by reaction with acidic aerosols, particularly sulfuric acid droplets. In general, young aerosols formed from VPOP will be highly reactive, containing organic peroxides and hydroperoxides,[799] as well as low concentrations of radicals. The natural aerosol from vegetation-produced terpenes,[1008] when newly formed, may play a major role in removing VPOP; the efficiency of this process deserves investigation.

DISSOLUTION IN AEROSOLS

This process and the following one may provide paths for the removal of unreactive products present in very low concentrations. They are of no significance for the removal of most compounds, because of their relative inefficiency, but they are effective in changing the composition of aerosols in ways that may be biologically important. The removal by aerosols will be competing (except for very hydrophobic gases) with removal by rain and cloud droplets, which will typically be 10^4 times as abundant by mass over each unit area of the earth's surface. Nevertheless, clouds tend to be remote from sources of VPOP; thus, even with hydrophilic gases, solution in the ubiquitous aerosol may be significant. As with dissolution in cloud droplets, the most favorable case arises when the gas–aerosol partition coefficient is unusually large (for example, in the case of a polymeric aerosol particle that dissolves its own monomer). In less favorable situations, the fraction of VPOP in the aerosol particles will be too small (approximately 10^{-14}) to be of practical significance.

ADSORPTION ON THE SURFACE OF AEROSOLS

If one treats aerosol particles as spheres and calculates the surface area per unit volume of air, one finds areas of around 0.1 cm^2/m^3. In fact, as Cartwright and colleagues[206] and later workers have shown by electron micrography, many particles in common aerosols are composite structures apparently formed by coagulation of sizable numbers of much smaller particles. The total area may be 10 times larger than the simplistic calculation would suggest, although it could hardly be 100 times larger. In terms of surface area per unit *mass*, such an aerosol material is comparable with active carbon. There is no information on the adsorption properties of common aerosols, but no reason to believe them to be poor adsorbers. Sorption by aerosols may be a significant removal process for some VPOP. Under conditions of unusually high aerosol density, it may be an important process.

LIQUEFACTION IN THE INTERSTICES OF AEROSOLS

This represents an obvious extension of the proceding discussion, relevant to VPOP with low saturation vapor pressures at normal temperature. The most likely material to condense in the interstices of a complex particle—where surface forces encourage condensation that would not occur on a simple, spherical particle—is water.

REACTION WITH A COMPOUND ALREADY DISSOLVED IN OR ATTACHED TO AN AEROSOL

Just as these mechanisms are important in promoting the removal of gases by rain and cloud droplets, and indeed are essential in causing such removal at a significant rate in many cases, so we may speculate that they play a comparable part in aiding removal by aerosol particles.

Removal of Aerosol Particles from the Atmosphere

In the preceding sections, we have discussed aerosol formation from the products of organic pollutants and raised some questions about the removal of VPOP by preexisting aerosols. In this section, we mention briefly the final process, the removal of the aerosol itself from the atmosphere. This subject has been studied in considerable depth, largely because of the concern in the 1950's over the radioactive aerosol resulting from tests of nuclear weapons. This radioactive aerosol behaves, as far as has been observed, very similarly to the ambient, nonradioactive aerosol, presumably because of coagulation between the two. The decay of the radioisotopes in this aerosol permits a quantification of aerosol density and an identification of a particular aerosol as it ages and mixes with foreign aerosols, which are otherwise difficult to attain.

The mechanism of aerosol removal has been reviewed recently by Robinson and Robbins.[1024] Removal by hydrometeors was the subject of a 1970 U.S. Atomic Energy Commission conference.[980]

Approximately 10% of aerosol radioactivity is deposited in dry form on the ground and its covering; this is called "fallout." The remainder of the radioactivity appears in precipitation and is known as "washout" if the aerosol is captured below the clouds and "rainout" if the capture occurs inside the clouds. Three main physical mechanisms seem responsible for these phenomena: impaction, the result of the aerosol particle's possessing greater inertia than the air molecules around it; diffusion, the Brownian movement of the smaller particles in particular; and condensation nucleation, in which the particle acts as a nucleus for the formation of a droplet out of supersaturated water vapor. In addition, gravitational sedimentation will be important for very large particles (larger than a few micrometers), and other processes, such as diffusiophoresis and electric effects, may be found to be important.

Dry fallout is due to diffusion to the ground; to impaction on leaves, grass, structures, etc., of the windborne aerosol; and to gravitational sedimentation. The varied nature of the ground cover and the varying wind patterns make distinction between the component mechanisms academic. It is usual to characterize the rate of fallout by a deposition velocity that is the ratio of the (ideally, mass) deposition rate per unit area to the (mass) density per unit volume of the aerosol; deposition velocities for typical aerosols tend to cluster around and below 0.1 cm/sec.

The details of wet removal, rainout, and to a lesser extent washout are gradually becoming clear. Washout is well understood for large particles (above 1 μm), but these particles are mostly from ground-level sources (stack emission, duststorms) and only rarely represent the organic gases in their final guise. For smaller particles, impaction is less effective, and the collection process is best visualized as diffusion of the particle across the boundary layer around the falling raindrop. Aspects of this problem have been discussed by Davies.[294] Experimental measurements have been made of the efficiency of washout—the ratio of the mass of aerosol collected to the mass present in the volume swept out by the scavenging drops—and lead to values much less than unity when the aerosol particle size is 0.1–1.0 μm.[520]

Rainout is generally more significant in particle removal than washout, but is less well understood. Additional processes, such as condensation on the particle as a nucleus and possibly electric effects, become important, and the relatively long lifetimes of cloud droplets more than compensate for their low velocities, compared with those of raindrops. Cycles of coagulation of cloud droplets and reevaporation of the resulting raindrop have the effect of increasing the size of aerosol particles by aggregating them.

The overall lifetimes of aerosol particles with respect to wet removal are well determined from studies on aerosols from low-altitude nuclear weapons; they range from 40 days in the upper troposphere to about 10 in the lowest kilometer.[727] Weather variability and local peculiarities of climate will permit much longer or shorter lifetimes at particular times or places and perhaps more significantly will affect the size to which the aerosol particles have grown by the time they are removed. However, coagulation and growth of particles are universal processes from which no newly formed aerosol is exempt; we do not expect unusual aerosols to have a lifetime with respect to removal significantly longer than those of other aerosols formed in the same location at the same time.

EFFECTS ON NATURAL WATERS

Interactions between Air and Water

In assessing the quantities of VPOP from hydrocarbons that may be contributed by the air to terrestrial waters, one should consider the various mechanisms for their removal from air: precipitation (rainfall, snow, and washout); diffusion across the interface of surface water and air; and fallout. It should also be noted that movement takes place in the reverse direction and can be a major source of organics in air, by such mechanisms as evaporation and aerosol formation from sea spray. These are in addition to more direct emission from man-made pollutants, as well as materials transported to the air indirectly from soil particles. These mechanisms must be considered in relation to the specific chemical and physical forms of the organics in air. Thus, one must distinguish among mechanisms involving organics in the vapor form; those absorbed onto the surface of airborne biota, such as spores, as well as minerals and other particulate matter; and those dissolved or suspended in rainwater.

In general, information as to the possible contributions of VPOP from hydrocarbons by air to surface waters is not available. Indeed, aside from such types of organics as polynuclear aromatic hydrocarbons and pesticides, knowledge about the incidence of organics in precipitation is scanty. Although some specific organics have been measured in precipitation, the data available are often simply the total organic concentration measured as chemical oxygen demand (COD) or weight of organic residue per volume of precipitation.

However, many of these data are, nevertheless, useful in assessing possible contributions by air to surface waters and will be considered here. Thus, for example, Weibel and colleagues[1295] compared organics in rainfall and surface runoff with those contributed by sanitary sewage in an urban and a rural area in the United States. As noted in Table 8-2, the concentrations of both COD and organic chloride are smaller in rainfall than in urban or rural runoff; however, it was concluded that, in comparison with domestic sewage, these contribute much greater quantities of organics to terrestrial waters. Although terrestrial sources of organics, both man-made and natural, are large, one cannot dismiss precipitation as a contributor.

A useful comparison in this regard is the transport of DDT in the biosphere, which was reviewed and analyzed as a case study by Woodwell *et al.*[1346] They concluded that the movement of DDT in the atmosphere is the most important route, that the dominant mechanism for its removal from the atmosphere is probably rainfall, and that most of

TABLE 8-2 Comparison of Average Concentrations of Organic Materials in Rainfall and Runoff in Urban and Rural Areas of the United States[a]

	Average Concentrations			
	Urban Area		Rural Area	
	Rainfall	Runoff	Rainfall	Runoff
Chemical oxygen demand, mg/liter	16	111	9.0	79
Organic chloride, μg/liter	0.28	1.70	0.22	0.43

[a]Derived from Weibel *et al.*[1295]

it so removed goes into the ocean. An input–output analysis for a steady-state distribution of dissolved organic matter in the ocean indicates that rain (using a value of 0.1 mg of carbon per liter) contributes about 1% of the organic carbon to the oceans, the rivers about 0.1%, and primary productivity the balance.[1319] Thus, although the most important source of organics in seawater is primary productivity, one must consider rainfall as a source, particularly when such man-made organics as DDT are of concern.

Junge[656] is a useful source of data on the incidence of organic compounds in precipitation. Data cited by him (Table 8-3) indicate some concentrations and ranges of organic materials measured in rain and snow. The values for albuminoid (proteinaceous) nitrogen reported in Table 8-3 were obtained at specific locations in the countries named. It was indicated that these nitrogenous compounds were insoluble materials, either from windborne soil or from unidentified sources. The organic nitrogen and carbon reported for rain and snow were fairly uniform in concentration throughout Sweden. It was speculated that about 70% of the organic nitrogen was protein and that a sea-spray mechanism may have been the source of the organic material. Amino acids have also been reported in rainwater.[419]

Vapor-phase pollutants can be adsorbed directly by water by diffusion across the water–air interface. A large number of alkanes, alkenes, acetylenes, and aromatic hydrocarbons have been identified and quantified in ambient air.[31,1227] Although their solubilities in pure water are variable and often low, accumulations of lipids at a water surface would be likely to increase the rate of absorption from air;[1346] in general, organic contaminants in water are capable of increasing the "solubility" of other organic species through such mechanisms as solubilization and hydrotrophy.[41]

Methane is an example of a hydrocarbon that has been measured in air and whose interactions with surface water have been studied. Most of the concentrations measured in one study of urban atmospheres were between 1.5 and 2.5 ppm, and it was concluded that the normal geophysical concentration is 1.0–1.2 ppm.[20] To determine the extent of equilibration between air and water, samples were taken from a boat in both phases near the air–water interface at several sample points along the Potomac River, in the Chesapeake Bay, and 250 miles out into the Atlantic Ocean.[1181] The concentration of methane in water decreased from a high of 500 ml/liter at Washington, D.C., and leveled off at 250 ml/liter downstream in the Potomac and out into the Atlantic. The high concentration of methane in air was approximately 4 ppm at Washington, and the concentration generally decreased out into the

TABLE 8-3 Typical Concentrations of Organic Material in Rain and Snow[a]

Species	Location	Nature of Precipitation	Concentration, mg/liter
Formaldehyde[308]	India	Rain	0.5
Albuminoid nitrogen[376]	United States	—	0.4
	Canada	—	1.1
	India	—	2.6
	England	—	2.0
Organic carbon[918]	Sweden	Rain	1.7–3.4
		Snow	0.8–1.9
Organic nitrogen[918]	Sweden	Snow	up to 0.35
Organic material[557]	Nova Scotia	Rain	13
		Snow	2.7

[a] Data cited by Junge.[656]

Atlantic, the lowest being 0.075 ppm. On the basis of solubility calculations, it was found in all cases that the concentrations in water were higher than would be predicted from those in air, but the difference decreased markedly from the Potomac River out into the Atlantic. The higher water values were attributed to pollution in the river and bay, and it was concluded that methane in these regions was probably transported from the water to the atmosphere. However, it is not clear whether the ocean is acting as a source of or a sink for methane. It may be concluded that vapor-phase hydrocarbons and their reaction products are transferred directly across the water–air interface. However, estimates of the magnitude of such transfer are not available.

Finally, particulate matter in air is of interest as a source of organics in water through the mechanisms of settling and washout. Both natural and synthetic organics are likely to be found in such particles. It has been noted that most of the water-insoluble materials in these particles in polluted areas are organic substances and ashes, whereas in unpolluted areas the ashes are replaced by mineral dust.[656] However, a significant amount of the particulate matter is composed of fungal spores that can carry organic matter by absorption onto their surfaces.[742] Uredospores of stem and leaf rust fungi constitute an example of such a material that is present in the summer and was found to contain alkanes with chain lengths of C_{18-35} (average, 150), free fatty acids with chain lengths of

C_{14-24}, a C_{18} epoxy acid, and other organics, including several carotenoid pigments, high-molecular-weight ketones, and a variety of aromatic compounds.[742]

The organic material in airborne particles is often more highly concentrated in urban areas than in nonurban, as noted in Table 8-4, and it has been estimated that there is a natural background concentration of about 3-6 $\mu g/m^3$.[656] The total insoluble material is about 70–80%; it contains both minerals and combustible organic compounds, and the concentration of organic material seems to decrease with the size of the urban community, as noted in Table 8-4. Some data available from Los Angeles indicate some of the percentages of types of organic compounds that have been found in airborne particles, and these are also shown in Table 8-4. The relatively high percentage of water-soluble species, which include organic acids and alcohols, indicates that these are likely to be readily leached when the particles are deposited into surface waters or washed out from the air by precipitation. Thus, one can conclude that aerosol particles are a source of organics that can add to the load of terrestrial waters. However, as is the case for the other sources in air, an estimate as to the magnitude of their contribution is problematic.

Incidence of Organic Substances in Surface and Ground Water

Much less is known about the nature and amount of organic matter in saline and fresh water than about the inorganic constituents, although there is a reasonable amount of information available concerning nonspecific organic content, such as that shown in Table 8-5. These results were obtained from analyses that involved either adsorption by and later extraction from activated carbon or oxidation of organic constituents and later measurement of the carbon dioxide produced. In surface regions of the oceans (0–300 m), the dissolved organic content is typically about 0.5–1.2 mg of carbon per liter, with an average of about 1.0 mg/liter, whereas, in deeper waters, the average is about 0.5 mg/liter. The particulate organics represent about another 10% in the surface regions, and 2–10% in the deeper ones.[1275,1319] In many fresh waters, approximately 10 times these dissolved organic concentrations are found,[750] and the particulate concentrations, including colloidal organic matter, are similarly small, perhaps around 10%. However, there is considerable variability in the organic carbon content of both surface and ground fresh waters, as shown in Table 8-5. In some cases, this variability can be associated with sources of pollution. Thus, waters known to be unusually clean often contain carbon–chloroform extract at

TABLE 8-4 Typical Concentrations of Organic Matter in Aerosol Particles of the United States[a]

Location	Material	Amount
		Concentration, $\mu g/m^3$
Seven cities	Acetone-soluble	16–32
Five nonurban areas	Acetone-soluble	6–13
Los Angeles basin	Organic material	60
New York and Chicago	Organic material	40
Cities under 2 million	Organic material	25
		Approximate Fraction, %
Los Angeles	Organic acids and other water-soluble	40
	Saturated hydrocarbons	20
	Two- to five-ring aromatics	5
	Polynuclear aromatics	5

[a] Derived from Junge.[656]

less than 0.025 mg/liter, whereas waters known to be polluted with industrial wastes have been found to contain 10 or 100 times as much.[853] Nevertheless, much of the organic matter in surface waters is due to the excretory and degradative products of aquatic biota.[750]

Polynuclear aromatic hydrocarbons and pesticides have been found in marine and fresh waters.[41,774] In a survey[774] of the scientific literature for the period 1960–1970, aside from these two groups of compounds, perhaps 20 different organic compounds were reported in fresh waters; most of these are shown in Table 8-6. Several of them were associated with specific known sources of pollution. Specific amino acids have also been found in lake water, with concentrations of 2–23 μg/liter,[601] and polychlorinated biphenyls at concentrations of 0.02–2 μg/liter in the Milwaukee River.[1248]

A relatively large number of organic compounds of biologic interest have been determined in seawater,[1018] including specific sugars, carboxylic acids, amino acids, fatty acids, and urea, usually at concentrations of less than 0.1 mg/liter. Nevertheless, it has been estimated that only about 10% of the total dissolved organic carbon in surface and subsurface marine waters has been identified, using the northeast Pacific Ocean as an example; furthermore, it was concluded that little is known about the molecular nature of such materials in the sea and that "such identification may be as intractable as the identity of 'humus' in soils."[1319]

In trying to assess the possible effects of VPOP from hydrocarbons in air on marine and fresh waters, we are, therefore, confronted with the fact that there is a dearth of information about the nature and amounts of the organic compounds therein. In turn, the problem is compounded by a similar lack of knowledge of the specific organic contributions that air makes to these waters. Thus, any judgment as to their possible effects will be at best speculative and will have to rely on analogy with the limited number of laboratory or field investigations that have attempted to define or study the effects of model organic compounds or "organic matter" on the behavior of natural water systems.

Effects of Organic Compounds in Water

A variety of effects of organics on water are important, either because they influence the general quality and character of the water, sediments, and biota or because they degrade or have an economic impact on a particular water use. In general, it is most difficult to evaluate such possible effects and attribute them to the contributions of VPOP from hydrocarbons in air. This section therefore focuses on the known and hypothesized effects of a variety of organic compounds that may influence water quality.

Several water quality criteria and standards are concerned with organic compounds and related to both municipal and industrial use. These involve health considerations, as well as aesthetics and the

TABLE 8-5 Typical Gross Organic Content of Surface and Ground Waters

Constituent	Water Type	Concentration, mg/liter
Carbon chloroform extract[853]	Typical large U.S. rivers	0.02–0.4
Total organic carbon[1102]	Ohio River system at Pittsburgh	2–22
Total organics by carbon adsorption[495]	Missouri springs	0.2–0.3
	Missouri deep wells	0.01–0.06
Organics by carbon adsorption[1027]	Illinois well waters	1.5–7.3
Dissolved organic carbon[1318]	Amazon River	1.6–6.3
Dissolved organic carbon[1319]	Northeast Pacific Ocean	
	0–300 m	1.0
	300–3,000 m	0.5

TABLE 8-6 Some Specific Organic Compounds (Other Than Pesticides and Polynuclear Aromatics) Found in Fresh Waters and Reported in the Period 1960–1970[a]

Compound	Location	Concentration
Methane	Well water, Illinois	0.8–87 ml/liter
Aniline	River, U.S.S.R.	0–trace
Benzidine and naphthylamine	River, Japan	0.29–0.39 mg/liter
C_{2-6} carboxylic acids	Ohio River	0.2–25 μg/liter
Terephthalic acid	Industrial reservoir	0.1 mg/liter
Alkylbenzene sulfonate	Various surface and well waters	up to 100 mg/liter
Phenol	Various surface waters	up to 0.4 mg/liter
Nitrochlorobenzene	Mississippi River	1–37 μg/liter
Methylmercuric chloride	Agano River, Japan	14.4 mg/liter

[a] Derived from Arthur D. Little, Inc.[774]

quality and economics of industrial processes. Thus, U.S. Public Health Service Drinking Water Standards[1225] recommend that drinking water contain no more than 0.2 mg of carbon–chloroform extract per liter. It states that, although a higher concentration does not necessarily indicate the presence of toxic organic compounds, it does represent an exceptional and unwarranted dose of ill-defined chemicals to the consumer. A recent survey of finished waters in community water supply systems serving about 10% of the U.S. population indicated that about 1% of the people in this group were exposed to water exceeding this standard; the highest concentration found was 0.56 mg/liter.[819]

Similarly, a variety of water quality criteria for surface waters used for public water supplies—as well as waters used for food processing, agriculture, and industrial use—specify limits for pesticides, herbicides, and unspecified organic compounds.[1284] These indicate, for example, that waters at the point of use should not exceed carbon tetrachloride extract at 0.2 mg/liter for industries involving canning food, drying and freezing fruits and vegetables, bottling soft drinks, and finishing leather, whereas the criterion is 1 mg/liter for the hydraulic cement industry. These criteria indicate a need to limit the concentrations of unspecified organic compounds in raw waters, inasmuch as high concentrations will have economic consequences as a result of requiring a higher degree of treatment or as a result of a decrease in the quality of products.

There are also specific effects on the taste and odor of water related to drinking water quality. The Public Health Service Drinking Water Standard of 1 μg/liter for phenol is set "because of the undesirable taste often resulting from chlorination of waters containing extremely low concentrations of phenol."[1225] However, a large number of other organic compounds are known to impart taste and odor to drinking water. Several of these, isolated from a river polluted with industrial wastes, are listed in Table 8-7 with their mean threshold odor concentrations.[1035] The threshold odor concentrations vary widely. It has been noted that chemical and refinery wastes have the greatest potential for odor, but such organisms as actinomycetes and algae are also a common cause of taste and odor, and there is a direct relationship between the amounts of organic material present in water and the odor intensity.[1034] Although conventional water treatment practices have some utility in the removal of taste- and odor-causing organic compounds, the application of powdered activated carbon is often required as well. Nevertheless, for highly polluted waters, even this may not be effective. For such a water heavily polluted with various organic industrial wastes, it was found that "in spite of double aeration and relatively high powdered-carbon and chlorine doses at the water plant, the odor and carbon chloroform extract . . . values frequently exceed recommended levels."[330] As shown in Table 8-8, conventional water treatment is not always effective, whereas the addition of filtration with granular activated carbon after conventional treatment reduced the specific organic chemicals to concentrations below the detection limit. However, it should be noted that such a treatment technique is rarely used, and one cannot rely on more conventional municipal treatment methods to remove organic compounds from a raw water supply.

TABLE 8-7 Mean Threshold Odor Concentrations of Some Organic Compounds Isolated from a Polluted River[a]

Compound	Mean Odor Threshold Concentration, μg/liter
Naphthalene	6.8
Tetralin	18
2-Methyl-5-ethylpyridine	19
Styrene	37
Acetophenone	65
Ethylbenzene	140
bis-(2-Chloroisopropyl)ether	200
2-Ethylhexanol	270
bis-(2-Chloroethyl)ether	360
Diisobutylcarbinol	1,300
Phenylmethylcarbinol	1,450

[a] Derived from Rosen *et al.*[1035]

There is also the possibility of contamination by organic compounds in the distribution system after the water leaves the treatment plant. This can result from runoff or contributions from the air to a holding reservoir. In one instance, it was shown that in an impoundment the chemical oxygen demand, a measure of organic load, was typically 10 mg/liter in the cooler months and rose to as high as 18 mg/liter in the warmer ones.[243] It was concluded that in some reservoirs the organic load is established by the character of the runoff.

The persistence of organic compounds in natural waters is highly variable and is determined by such mechanisms as biologic, chemical, and photochemical degradation, evaporation, and removal by interaction with biota and suspended and bottom sediments. The rate of biologic oxidation in river waters is affected by several factors, including temperature, the nature of the biologic population, metabolic lag, concentration and nature of the organic compound, and the presence of nutrients, such as nitrogen and phosphorus.[381] As an indication of this variability, it was estimated that the persistence of phenol at 4 C is about 5 days in a river with a recent history of phenolic pollution, compared with approximately 20 days in a relatively pure river. Some variations in the rate of biochemical oxidation of synthetic organic chemicals are shown in Table 8-9, which lists the percentages of the theoretical

TABLE 8-8 Effect of Conventional Municipal Water Treatment Alone and in Conjunction with Activated-Carbon Filtration on the Removal of Organic Contaminants from Polluted River Water[a]

	Concentration, μg/liter			
	Conventional Treatment		Conventional Plus Carbon Filtration	
Compound	Raw	Treated[b]	Raw	Treated[b]
Ethylbenzene	11	11	—	—
Styrene	18	nd	—	—
bis-(2-Chloroethyl)ether	55	10	154	nd
2-Ethylhexanol	110	8	—	—
bis-(2-Chloroisopropyl)ether	24	nd	48	nd
α-Methylbenzyl alcohol	—	—	26	nd
Acetophenone	19	nd	29	nd
Isophorone	90	nd	25	nd
Tetralin	—	—	57	nd

[a] Derived from Dostal *et al.*[330]

[b] nd = not detected.

TABLE 8-9 Biochemical Oxygen Demand of Several Organic Chemicals Initially at Concentrations of 2.5 mg/liter in Mineralized Dilution Water with Settle Sewage Seed at 20 C for 10 days[a]

Chemical	Biochemical Oxygen Demand, % of theoretical
Monoethanolamine	58.4
Triethanolamine	0.8
Monoisopropanolamine	34.0
Butylamine	48.8
Methanol	62.7
Methylisobutylketone	49.3
Diethylketone	12.3
Acetone	71.8
Pentanedione-2,4	40.0

[a] Derived from Ettinger.[381]

maximal biochemical oxygen demand exerted in 10 days in a 20 C incubation with nutrients and settled sewage.[381]

Although the readily biodegradable compounds affect the health of a stream principally by reducing its dissolved oxygen content, the more resistant ones may cause damage owing to undesirable color, toxicity to aquatic life, tainting of fish, and impairment of aesthetic or recreational value.[381] In addition to the previously noted taste and odor relationships and the possible effect on the quality of water for industrial use, the presence of organic compounds in water can also result in coagulation difficulties and a higher chlorine demand in municipal water plants.

Organic compounds in both fresh water and seawater are known to interact with trace elements, especially through the mechanisms of complex and chelate formation.[750,1113] A large percentage of the copper in seawater has been shown to be associated with organic compounds in nonlabile combinations, as has up to 99% of the copper present in soil solutions. Other trace elements, such as cobalt and boron, have been similarly associated with organic materials, and it has been concluded that the control and initiation of phytoplankton productivity in seawater may be the most vital effect of metal–organic interactions in the environment.[1113]

Through complexing mechanisms and their control on the solubility, the sorption of trace elements on suspended and bottom sediments, and their uptake by biota, organic compounds are likely to have a major influence on the transport of trace elements in natural waters. Certainly, naturally occurring organic species like fulvic acid, which can complex these metals and sorb onto such clay minerals as montmorillonite, are important in this regard,[1074] but organic pollutants may also play a role. They can also concentrate at the air–water interface, where they have been shown to enrich the concentrations of such trace elements as lead, iron, copper, and nickel.[337] Once concentrated in the surface layer, these organics and their associated trace metals can enter the food chain and be concentrated in higher trophic members.

Organic compounds in water and soil–water systems can affect the oxidation state of trace elements; this has a strong influence on their behavior, such as their solubility and ability to absorb and to exchange ions.[750] Thus, for example, the reducing environment created by organic pollution may cause the reduction of Cr^{6+} to Cr^{3+}, thereby affecting its transport in water, in that sediments and the biomass have different capacities for sorbing these two species.[471] Complexing of trace elements by organics can also influence both the rate and the equilibria of their redox reactions.[750]

The sorption of organics onto minerals has implications for and possible effects on both water and soil–water systems. The capacity of soil for fixing organic substances depends on its physicochemical properties, with clays in particular promoting their sorption.[708] There are indications that such organic materials as humic substances, proteins, organophosphorus compounds, nucleic substances, and carbohydrates sorb by clay minerals, and this favors their preservation and gradual incorporation into the biologic cycle.

It has also been noted that the phytotoxicity of herbicides is reduced by as much as 99% by the presence of organics in soil, and it was suggested that this reduction is due to the sorption of herbicides by the soil organics, thereby making them unavailable to plants.[1304] Another important sorption effect is the ability of organics in water to coat such minerals as calcite, thereby inhibiting their equilibration with natural waters.[1174] Experiments in this regard have indicated that the dissolved organic carbon in seawater samples from different sources is reduced by 10–14% after exposure to calcite particles.[1174] This can also be a mechanism for the concentration and transport of organic compounds of limited solubility in water.[41]

Finally, the solubility of other organic compounds in water can be increased by the presence of natural organic compounds or pollutants. Thus, sodium humate solutions have been shown to increase greatly the solubility of DDT in water,[1304] and polynuclear aromatic hydrocarbons are known to be similarly affected by the presence of other, more soluble organic compounds.[41]

In conclusion, there are a large variety of important effects of organic compounds, both natural and synthetic, on natural water and soil–water relationships that can influence both aqueous systems and their use by man. The specific effects of VPOP from hydrocarbons are not readily assessable in this regard. However, to the extent that they add to the organic load and composition of the soil and water systems, they are of potential concern.

EFFECTS ON MICROORGANISMS

The biosphere contains three major living systems—plant, animal, and microbial. About 50% of the living biomass on earth is microbial, with plants representing 30–35% and animals the remainder of the cellular protoplasm. The microbe and its functions are necessary for the continuation of plant and animal life on earth. That microbial activities are indispensable is well illustrated by considering that there is a 30-year supply of carbon dioxide in the air and that microbial degradation of organic matter produces over 80% of the carbon dioxide released into the atmosphere. When one considers the effects of pollution on man's well-being, it is essential to consider the effect of pollutants on the total biosphere. The introduction of low concentrations of toxic nonbiodegradable pollutants into the biosphere over an extended period can bring about dramatic changes in the ecology.[1098] This section is concerned with the effects of vapor-phase hydrocarbon pollutants on the microbial populations of the earth.

Many studies have been conducted on the effect of air pollutants on microbial metabolism and growth. Estes and co-workers found that exposure of *Escherichia coli* to an oxidant air pollutant mixture inhibited its growth.[378,953] The amount of inhibition was a function of the initial concentration of reactants. The active component in the pollution mixture was isolated and identified as peroxyacetylnitrate (PAN). Glutamic dehydrogenase was isolated from *E. coli*, and exposure of the enzyme to the photochemical reaction products resulted in inactivation of the enzyme. Another study[379] suggested that photochemical reaction products of aldehydes would also yield products that inhibited the activity of glutamic dehydrogenase from *E. coli*. Mudd[881] found that both PAN and ozone oxidized the reduced form of nicotinamide adenine dinucleotide. The reaction product of PAN treatment was biologically active; that from ozone treatment was not. The author suggests that inactivation of enzymes by PAN is probably due to the oxidation of the sulfhydryl groups in the enzymes.

The effect of vapor-phase hydrocarbons on the germination of bacterial spores was ascertained by Rode and Foster.[1029] Spore-forming bacilli are abundant in all fertile soils. Many of the vapor-phase hydrocarbons tested were effective inhibitors of spore germination. Among the inhibitors were propane, *n*-butane, propylene, 1-butene, *trans*-2-butene, 1,3-butene, 3-methyl-1-butene, isobutane, and chloropropanes. Ethylene was slightly effective in inhibiting spore germination, but methane and ethane were not. Spore suspensions of *Bacillus megaterium*, *B. subtilis*, *B. cereus*, and *B. licheniformis* remained dormant under a partial atmosphere of *n*-butane, but germinated when the gas was removed. When pasteurized soil was exposed to vapor-phase hydrocarbons, the spore-formers present in the soil did not germinate until the gas was removed. Studies with *Rhizobium meliloti*[1344] demonstrated that the viability of this symbiotic nitrogen-fixing organism was affected by exposure to nitrogen dioxide, sulfur dioxide, and aldehydes. The lethal effect of aldehydes was enhanced by high humidity. Jacumin *et al.*,[625] using *Serratia marcescens* as a test organism, measured the effect of low concentrations of various pollutants on survival. He found that the photochemical product of 1-hexene and nitrogen dioxide, at concentrations found in polluted air, gave significant killing of bacterial cells. The toxicity of the products of the photochemical reaction in the 1-hexene–nitrogen dioxide system was greater than the simple additive effect of the individual components.

Luminescence in bacteria can be adversely affected by exposure to air pollutants. Serat *et al.*[1099,1100] developed an assay for air pollutants based on the fact that *Photobacterium phosphoreum*, a luminescent bacterium, was sensitive to photochemical oxidation products. Cells of *P. phosphoreum* treated with a gas stream containing products formed by the photochemical oxidation of *cis*-2-butene and nitric oxide lost both luminescence and viability. The rate of luminescence decrease depended on the initial concentration ratio of the reactants. Ozone, nitrogen dioxide, formaldehyde, acetaldehyde, and PAN were also examined in this system. PAN and ozone were effective in decreasing luminescence of *P. phosphoreum*. This organism might be useful in rapidly determining the extent of air pollution.

Several studies have been conducted on the effect of hydrocarbon pollutants on soil fertility. Harper[529] found that natural-gas seepage killed the plant cover over the area of leakage. This was shown by Hoeks[577] and Garner[450] to be due to the utilization of all available oxygen from the area during aerobic hydrocarbon degradation, resulting in a high degree of anaerobiosis. There was an increase in anaerobic organisms in the soil and in total nitrogen, probably owing to nitrogen fixation by various *Clostridia* species. Similar results were obtained by other workers.[78,366] The effect of halogenated hydrocarbons on soil microflora has been examined. Koike[704] found that 1,3-dichloropropene, 1,2-dichloropropane, and ethylene dibromide all retard nitrification in soil for an extended period. Wensley[1300] found that methylbromide suppressed the growth of bacteria and had less effect on fungi. Members of the Penicillia and Aspergilli species are more abundant in fumigated soil. Nitrifiers and cellulose-decomposers were most adversely affected by methylbromide treatment.

All vapor-phase organic air pollutants eventually are carried onto the surface of the earth by various forms of precipitation. They dissolve in water or attach to plant or soil particles. Abeles *et al.*[2] studied the fate of air pollutants using ethylene as a model. They estimated that 15×10^6 tons of ethylene were released as pollutants in 1966 and examined soil for the ability to remove ethylene from the atmosphere. No ethylene uptake occurred in sterilized soil or in the absence of oxygen. There was a 24-hr lag after exposure to ethylene before uptake of the gas by soil occurred. This suggests that microorganisms are responsible for the ethylene assimilation. Abeles *et al.* made a conservative estimate that 7×10^6 tons of ethylene can be removed from the atmosphere each year by microbial degradation.

Some consideration has been given by Lubowe[787] to the effect of air pollution on the normal microbial flora of human skin. Deposition of soot, dust, and air pollutants on skin could affect bacterial growth and later physiologic activities of the normal skin microflora.

Microbes utilize and produce a number of vapor-phase air pollutants. Anaerobic microorganisms in the intestine of ruminants and in swamps produce great quantities of methane (marsh gas). A single cow produces 60–70 liters of methane daily. Methane accumulation from microbial metabolism can, in rare instances, be hazardous, but in general the methane concentration (1.5–2.5 ppm) in polluted urban air is not toxic, nor does it react photochemically.[20] These methanogenic organisms do create one environmental pollution problem.[1345] When elemental mercury is present in anaerobic areas of ponds, rivers, estuaries, or oceans, the methyl group attached to Co^{3+} of the vitamin B_{12} in methanogenic microbes, which normally is evolved as methane, is passed to the Hg^{2+} molecule. Thus, mercury is transformed to methylmercury and dimethylmercury, its most toxic forms.

Microbes present in cow dung have been shown to produce ethane, ethylene, propane, and propylene.[296] *Penicillicum digitatum* produces acetylene, ethylene, propylene, ethane, and propane in small quantities.[296] Nickerson[922] found that *Blastomyces dermatiditis* can produce ethylene at 140 mg/liter during growth in liquid culture.

Microorganisms present in soil and water and on skin and plants throughout the surface of the earth play a very important role in prevention of any significant buildup of vapor-phase organic hydrocarbons. These scavengers utilize a great number of these compounds as a source of carbon and energy.[1005] In many cases, they convert potentially hazardous compounds to less toxic products by cooxidation.[747]

The ability of microorganisms to utilize hydrocarbon substrates has long been known.[431] Hydrocarbon-utilizing microbes are present in all surface soil and water, suggesting that hydrocarbons are constantly introduced into the environment. Studies on the oxidation of gaseous hydrocarbons are abundant in the literature[117,645,747,748,831,1250,1251] and will not be detailed here. These hydrocarbon-utilizing organisms act to keep the amount of saturated and unsaturated vapor-phase hydrocarbons in the environment at a low concentration. Jones[653] has developed a respirometric technique for demonstrating hydrocarbon utilization in the natural environment.

One of the dangers associated with increased concentrations of vapor-phase hydrocarbons in the environment is the introduction of these pollutants into the food chain through microorganisms. The lipids in microorganisms can be changed drastically[341,342,1251] by growth on hydrocarbon substrates, and these might also find their way into the food chains and into the bodies of higher animals.

EFFECTS ON VEGETATION

Vapor-phase organic pollutants are universal; many are natural components of plants and are normally vaporized into the atmosphere or released in combustion. The organics include a variety of partially oxidized products of combustion, particularly C_{1-10} compounds of carbon and hydrogen, plus the nitrogenated peroxyacetylnitrates.

Of these chemicals, only PAN and ethylene are known to be injurious to vegetation, and then only when their local concentrations exceed background concentrations by many times. Methane, benzene, acetylene, etc., are almost unreactive.

However, Adams and Ellis[9] report that chemical and physical changes may occur in soils saturated with natural gas. Plant growth may be retarded or completely inhibited in gas-saturated soils. The instances are so infrequent that studies have been limited. Mass-spectrometric analysis of affected soils showed the presence of 80–90% methane, with the remainder of the gas mostly ethane. It was suggested that the disturbance in iron–manganese relationship caused by the gases may have been one of the major factors in the detrimental influence of gas-saturated soils on vegetative growth.

Aldehydes have occasionally been blamed for plant injury, but their impact is more likely indirect, involving only their contribution to photochemical reactions yielding phytotoxic oxidants.[144,569] Hydrocarbons are included among the varied components of "photochemical" smog, and herein lies their significance. Briefly, some hydrocarbons react with nitrogen oxides in the atmosphere to produce the varied chemicals discussed earlier, of which the most important phytotoxicant is PAN.[288]

PAN was not defined as a specific pollutant until after "smog" injury was first described in the 1940's.[857] Evidence that injury was associated with automobile exhaust emission was slow to accumulate, and it was 1950 before Middleton *et al.*[857] demonstrated this relation. Haagen-Smit *et al.*[503] discovered in 1952 that hydrocarbon and nitrogen oxides emitted in exhausts react in the presence of sunlight to yield toxic gases that cause plant damage, eye irritation, and reduced visibility. Darley *et al.*[288] later reported the presence of an ozone–olefin complex. Stephens *et al.* began in 1956 to isolate the toxic component that later turned out to be PAN.[1157]

Few measurements have been made of ambient PAN concentrations or their correlations with symptoms, but controlled fumigations indicate the concentrations at which visible symptoms might be expected. Chemical analyses for PAN in California and Utah show concentrations of 0.01–0.02 ppm on average days and up to 0.05 ppm on "smoggy" days.[286,1200] Stephens and Scott[1159] reported that lesions developed on sensitive petunia and tobacco varieties after 5 hr of fumigation with 0.1 ppm. Observations in Salt Lake City after "natural" fumigations indicated that injury could be produced by as little as 0.02 ppm for 2–4 hr. Sensitive plants were injured when PAN concentrations averaged 0.025–0.03 ppm for a few hours. Taylor *et al.*[1185] and Jaffe[626] found that sublethal effects included a reduction in dry fresh weight at concentrations of 0.005–0.015 ppm for 8 hr and reduced flowering and stem elongation at 0.1–0.2 ppm.

Symptoms attributed to "smog" now seem to be caused primarily by PAN and its homologues—that is, the reaction products of photolyzed nitrogen oxides with unsaturated hydrocarbons. The symptoms produced include most of those once designated to be caused by "smog" or photochemical oxidants[1184] and are worldwide.[854,1302]

The precise nature of the symptoms depends as much on environmental factors, tissue, maturity, concentrations, and duration of fumigation as on the toxicant. Many symptoms may arise. Consequently, it is desirable to designate one general category as "PAN injury."[626]

Darley *et al.*[285] distinguished the PAN symptoms from those caused by products of ozone–olefin reactions. The symptoms were essentially similar, but the ozone–olefin reaction products were most toxic to young, fully expanded leaves, causing uniform or indiscriminately distributed glazing over the lower leaf surface. The banding that appears on plants in the field or when PAN is present was not observed.

Symptoms of PAN injury cover a considerable range of expression, depending on the concentration, duration of exposure, and nature and maturity of the leaf tissue exposed.[1184,1206] High concentrations, 0.5–1.0 ppm for 30 min, may cause complete collapse of the expanding leaves, but such concentrations have not been found to occur naturally. Lower concentrations, 0.3–0.5 ppm for 30 min, may cause the complete collapse of the tissue in a diffuse band across the leaf. Still lower concentrations, 0.1–0.3 ppm for 4–8 hr, higher than found in the field, may cause bronzing or glazing with little or no collapse visible on the upper leaf surface. Below 0.1 ppm, visible symptoms consist mostly of chlorosis.

Fumigations of sensitive species at the University of Utah (F. K. Anderson, unpublished data) with PAN at concentrations of 0.02–0.1 ppm for 2–6 hr provided a clear picture of symptomatology in a concentration range characterizing urban environments. Symptoms in Ranger alfalfa, one of the most sensitive species, first consisted of a very light yellow to white stippling, appearing mainly on the upper surface, but evident also on the lower. Stippling characteristically developed between secondary veins, but distribution along the leaf varied with maturity. Bleaching was most prominent at the tip of terminal leaves and base of older leaves. When concentrations approached 0.1 ppm, local areas of tissue collapsed completely, producing bleached, white necrotic lesions.

Lima bean plants fumigated with PAN occasionally developed a chlorotic green to white stipple scattered over the entire upper leaf surface. More typically, a silvery to lead-colored glaze developed in bands over the lower surface. Bronzing was often accompanied by a tan stippling.

Symptoms in corn consisted of chlorotic or necrotic streaks principally on the upper leaf surface. These streaks were largely interveinal, 0.5–2 in. long, and extended across the leaf at various distances from the tip. Light gray to chlorotic stipple symptoms, developing in similar bands, appeared on other leaves.

Endive developed a light green, overall chlorosis with slight marginal necrosis; lower surface, interveinal, silvery to bronzed glazing was most frequent and prominent.

The symptoms of smog injury in herbaceous plants in the field, as described in the Los Angeles area, generally consist of some type of glazing or bronzing distributed irregularly over the underside of the leaf.[287,855,856] In 1952, it became apparent that the area of the leaf damaged was related to its maturity.[119,468] When plants were exposed to a single fumigation, only a few leaves at a particular stage of maturity were marked. The youngest leaf would be injured at the tip, the next youngest about one-third of the way down from the tip, and the oldest near the base. This banding was especially prominent on leaves of petunia, rye grass, and annual blue grass. Sensitive broad-leaved plants, such as spinach, were most often marked about one-third of the way down from the leaf tip. Banding was also observed in the field on beets, chard, mimulus, chickweed, pigweed, dock, and others.

Banding is extremely helpful in identifying PAN injury. However, if exposure occurs on successive days, the newly differentiating cells may be injured each day, so a general glazing appears over the entire leaf. This has been the more characteristic expression in the polluted areas of California, where toxic PAN concentrations occur daily.

Photochemical pollutants, including PAN, enter the leaf through the mature, functional stomata. Once within the substomatal chambers, the pollutant attacks the mesophyll cells bordering the intercellular spaces. The morphologic and histologic effects of ozonated olefins, and later PAN, were studied on representative sensitive species.[119,468] The earliest visible indication of injury was the oily, shiny, water-soaked appearance of sensitive tissues on the lower leaf surface. By the time this appeared, tissue alterations were already apparent. Tiny, raised blisters appeared; they were formed by the swelling of guard cells and other epidermal cells nearest the stomata. These became swollen with water and increased in width, causing the stomata to enlarge further. By the time the epidermal cells collapsed, the entire leaf became turgid. Permeability may be damaged, so that excessive water enters the affected cells, which stretch as they absorb water, giving the underside of the leaf its shiny, water-soaked appearance. If the fumigation does not persist, or is not too severe, the turgid cells may recover after a few hours, leaving no trace of visible injury.

Cells of the spongy mesophyll nearest the intercellular spaces are affected after the epidermis. Thomson *et al.*,[1195] using electron microscopy, found that small, electron-dense granules appeared in the chloroplast stroma soon after fumigation. "Crystalline" arrays of granules appeared later, and the shape of the chloroplast was altered. The granules seemed to fuse into rods and then into an organized system of plates that persisted and even seemed to continue to develop. Finally, the integrity of the chloroplast was lost, and the membranes disrupted. As the chloroplasts broke down and became dispersed into the cytoplasm, the entire protoplast aggregated into a large mass, which condensed in the interior of the cell, causing the cell to collapse. The plasmodesmatal connections with neighboring cells appeared to persist. Although the lower surface was usually injured first, owing to the greater amount of intercellular space, the reverse may also be true.

Internal, as well as external, symptoms vary with the structure of the plant. Broad-leaved herbaceous plants—such as table beet, sugar beet, lettuce, and spinach—are most sensitive and characterized by a "silvering," and sometimes bronzing, of the lower leaf surface. Monocotyledonous plants—including oats, corn, barley, and grasses—appear dark green, as though water were trapped beneath the epidermis. As cell damage progresses, the dark-green, water-soaked areas develop into yellow streaks, which follow the zones where stomates are densest. The yellow soon turns to brown, and longitudinal necrotic streaks appear between the larger veins.[1056,1206]

The histologic changes and visible symptoms caused by air pollutants are basically caused by impaired metabolic processes. Enzyme activity, respiration, photosynthesis, ion absorption, and carbohydrate and protein synthesis all may be impaired by PAN concentrations far lower than necessary to produce any leaf chlorosis or necrosis.[1184]

To understand how PAN might affect metabolism, it is desirable first to know how the chemical is incorporated into the plant constituents. Stephens *et al.*[1157] synthesized PAN labeled with carbon-14, so that its pathway in the plant might be followed. When the cells were fractionated, much of the carbon-14 treated plants appeared in the chloroplasts, and it is in these organelles that one might first look for deleterious effects.[339] Early damage to the chloroplasts was shown first by histologic, microscopic studies, but later physiologic studies confirmed the damaging effect of PAN on the chloroplasts.[721] The mechanism of action is not clearly defined; it may be caused partly by injury to the enzymes necessary for photophosphorylation. Dugger *et al.*[339] showed that PAN inhibited photosynthetic carbon dioxide fixation in pinto bean plants.

PAN may also be harmful in oxidizing critical sulfhydryl groups of some enzymes. Mudd[879] showed that enzymes that contained free sulfhydryl groups for catalytic action were especially sensitive to PAN. Dugger *et al.*[338] have shown that a correlation exists between the sulfhydryl content of bean plants and their susceptibility to PAN.

Damage may be prevented by spraying sulfhydryl reagents that protect the sulfhydryl groups on intact plants or, in *in vitro* studies, adding the reagents to enzyme reaction mixtures, chloroplasts, or mitochondrial suspensions.

Oxidation of the sulfhydryl group would impair the activity of many enzymes. Inhibition of an enzyme, such as phosphoglucomutase, that is vital to the synthesis of glucose may be directly responsible not only for inhibition of glucose synthesis, but also for inhibition of the synthesis of closely related carbohydrates—including galactose, xylose, arabinose, and polymers that constitute such wall fractions as cellulose.[945] The cell wall expansion phase of plant cell growth depends on growth hormone-induced changes in cell wall plasticity. PAN also has been found to inhibit one of the enzymes, glucan hydrolase, that is necessary for the metabolic breakdown of the cell wall.

PAN inhibition of enzymes essential to both cell wall synthesis and degradation may well account for reduced cell enlargement and growth associated with PAN damage.[946]

A knowledge of the mechanism by which an air pollutant acts on specific metabolic processes provides the background for understanding the effects of air pollutants on growth and reproduction in the field. This threat is the ultimate concern of anyone attempting to grow plants and may be a critical factor in the well-being of natural plant populations. The multitude of variables affecting growth and production make it extremely difficult to measure losses that might be attributed solely to air pollutants, and relatively few studies provide much of a clue as to the extent of such losses.

Studies of growth suppression have consisted largely of exposing plants to ambient, polluted atmospheres and filtering air in which comparable control plants were grown.[1191] Total oxidant concentrations in the field were known, but the specific composition of the polluted air was not.

Ambient-atmosphere studies fail to delimit the effects of PAN alone on growth and production, but they do provide an excellent picture of the actual impact of ambient polluted atmosphere. The limited studies of the effects of Los Angeles "smog" on plant growth were summarized by Todd *et al.*[1201] Kentia palms were especially sensitive. When grown in ambient air, plants were small, and leaves were stunted and chlorotic. Palms in carbon-filtered atmospheres were noticeably larger, averaged one leaf more than on plants in ambient air, and had longer leaves, which were dark green. Avocado trees grown in ambient and filtered atmospheres responded similarly, with stem diameter significantly greater in the filtered air after 6 months.

Comprehensive studies of the effect of ambient atmospheres on citrus production in the Los Angeles area were undertaken by Thompson and Taylor.[1190,1191] Trees exposed to the naturally polluted air had up to 30% more leaf drop, and the average yield was often only half what it would have been in clean air. But much of this effect may have been caused by ozone.[1184]

Of the numerous hydrocarbons in urban atmospheres, only ethylene is recognized to affect plants significantly. Ethylene is produced naturally by plants and regulates various growth and maturation processes, including abscission and senescence.[511,512,543] Because of its low concentrations in the atmosphere, measurements of ethylene concentrations are infrequent. Data provided by Altshuller and Bellar[19] and the California State Department of Public Health suggest that background concentrations are in the parts-per-billion range. Concentrations in the few urban atmospheres monitored for ethylene are 0.004–0.3 ppm. Higher concentrations have been recorded around industries producing ethylene products.[543]

Ethylene has been recognized as an air pollutant since at least 1871 (Kny, cited in Sorauer[1137]), when it was found to escape from underground utility lines carrying illuminating gas. This gas was produced by the combustion of coal in retorts and used in early street lighting. The wooden or cast-iron pipes often leaked, releasing the gas, which contained about 3% ethylene, into the surrounding soil, where it damaged roots of nearby trees. Because coal gas is no longer used, this source does not provide a threat to the surrounding environment; however, ethylene as a more general air pollutant has been recognized since 1943, when it was discovered in automobile exhausts.[1030] The internal-combustion engine is the major source of ethylene in metropolitan atmospheres, but additional ethylene is contributed by combustion of natural gas, coal, or wood or as a blowoff gas from the cracking of natural gas in petrochemical plants. These and other hydrocarbon sources have been discussed earlier.

Ethylene is sufficiently toxic to plants to be responsible for crop losses near metropolitan areas.[631,855] The ambient concentrations may be 100 times greater than the threshold for injury to the more sensitive species. Ethylene content of samples collected in Los Angeles over a 10-month period averaged 0.07 ppm. Over a 4-month period, ethylene averaged 0.2 ppm, with peaks of 1.42 ppm.[93,312]

The deleterious effects of prolonged exposures to low ethylene concentrations, well under 1 ppm, were recognized after tremendous economic losses to the commercial orchid growers of Los Angeles.[285,292] The first indication of the disease was that the showy, petaloid sepals of the flower became chlorotic and dried from the tips down just as they were emerging from the bud; the earliest expression was the slight yellowing of the bud. Often, the bud dropped before opening; but, if it remained, the sepal tips were typically translucent to necrotic. Even when necrosis was not perceptible, the flower remained fresh for only a few days, rather than the 10–14 days required in the orchid trade. Davidson[292] found that the dry sepal disease, as it became known, could be produced by as little as a 24-hr exposure to ethylene at 0.002 ppm or a 6-hr exposure at 0.05 ppm. Even 0.002 ppm affected the commercial value of the bloom, decreasing the price by 25%.

The costly loss of orchids caused many growers to relocate beyond the urban limits of Los Angeles and San Francisco, but those who remained suffered losses estimated to exceed $100,000 a year in the San Francisco area alone.[631] Additional greenhouse crops and many field-grown floricultural species sustained equal or even greater losses. The demise of the cut-flower industry in Los Angeles and San Francisco was due at least in part to ethylene. Carnations, snapdragons, roses, camellias, and chrysanthemums were among the most critically damaged.

The "sleepiness" disease of carnation caused an estimated $700,000 loss to growers in 1963 (H. Jones, personal communication). This ethylene-caused disease has been known since 1908,[266] but has been more destructive since the intensification of automobile pollution. Petals turn yellow and wither, buds remain partly or wholly closed, and flowers open slowly, if at all.

Studies concerning the air pollution potential of ethylene received a substantial stimulus after severe losses in cotton and other economic crops near a Texas Gulf Coast polyethylene manufacturing plant.[543] Ethylene concentrations in the field ranged from 0.04 to 3 ppm, depending on distance and direction from the source. The cotton crop within a mile of the facility was completely destroyed. Less severe field symptoms included leaf abscission, scattered seedling death, vinelike growth habit, and fruit abscission. Vegetative and reproductive organs were malformed, with symptoms much like those produced by 2,4-D.[512] Young cotton plants were severely defoliated in fields close to the ethylene source. More distant plants exhibited "leaf puckering," reddening, and chlorosis; apical dominance was lost, and axillary buds were forced. Flowering was stimulated, but most fruits abscised.

Heck and Pires[543] fumigated 93 different species with ethylene at concentrations of 2.5–10 ppm. Symptoms on sensitive species consisted of yellowing and occasionally necrosis of the lower leaves, chlorosis of the flower buds, and inhibition of terminal growth, with an increase in the number of nodes and young leaves. These plants recovered rapidly when fumigation was stopped, but leaves formed during treatment never expanded normally. A still milder type of expression was characteristic of grasses and other more tolerant species. Plants developed no apparent injury, but leaf elongation was permanently and measurably inhibited. Abscission in the absence of chlorosis occurred on some plants. The oldest small branchlets of juniper and arborvitae dropped readily, and light shaking after fumigation caused more than 50% of the older branchlets to fall. More than half the arborvitae cones dropped on touch. Floral injury appeared on all 22 species that were in bloom during fumigation. Death or abscission was noted in eight species. Such an effect could result in the complete loss of economically valuable crops.

The profound effects of ethylene on the normal development of plants are due to its hormonal nature in being absorbed, transported, and assimilated readily by the vegetative organs. Abscission, for instance, is normally caused by the balance between auxin and ethylene in the petiole.[511] An artificial increase in ethylene through pollution would upset this balance and cause early defoliation.

Various mineral oils and hydrocarbons have been used to kill insect pests, and their phytotoxic properties have been applied in their use as herbicides.[618] Comparisons of the toxicity of hydrocarbons applied as sprays show the more volatile aromatic series to be most toxic, the olefins and cycloparaffins intermediate, and the paraffins least toxic. These hydrocarbons were toxic only at concentrations of over 2%; most were toxic only at concentrations of over 30%. Despite the significance of the herbicidal properties of these chemicals when applied to the soil, toxic concentrations are unlikely to be present in even the most polluted atmospheres.

9

General Summary and Conclusions

SOURCES OF HYDROCARBON EMISSION

Estimates of total hydrocarbon emission in the United States are 12–20 million tons/year from mobile sources, 7–25 × 10^6 tons/year from stationary sources, and 72 × 10^6 tons/year from natural sources. The U.S. emission is about 40% of the world total for both mobile and stationary sources. Most natural emission of hydrocarbons consists of methane and terpenes. Only a minor fraction of man-made pollutants are in this category.

Motor vehicles are by far the most important mobile source of gaseous emission, accounting for about 86%, whereas aircraft, railroads, marine vessels, and nonvehicular combined account for the rest.

Gasoline-powered vehicles account for about 99% of all vehicular emission, and diesel-powered vehicles account for the rest. The hydrocarbons in exhaust gases are chiefly low-molecular-weight compounds. The total oxygenate concentration is about one-tenth of the total hydrocarbon concentration. Aldehydes are generally believed to be the most important class of oxygenates.

Diesel-powered motor vehicles account for about 1½% of the emission from all motor vehicles and about 1% of that from all mobile sources. The gaseous hydrocarbon fraction of diesel exhaust is extremely complicated; it consists of light, cracked hydrocarbons and heavy fuel-like components up to about C_{24}. Low-molecular-weight aldehydes have also been found in diesel exhaust.

Hydrocarbon emission from aircraft is estimated at 0.4×10^6 tons/year, or about 2% of the emission from all mobile sources. Formaldehyde and total aldehyde concentrations in turbine exhaust have been measured, but no detailed aldehyde analyses have been reported.

Emission from railway locomotives is only about 0.1×10^6 tons/year; that from ships, barges, and other marine vessels is estimated at about 0.3×10^6 tons/year. Such emission from off-highway mobile sources is about 1.9×10^6 tons/year, or about 10% of all mobile-source emission, and appears to be increasing.

Total organic emission from stationary sources has been estimated (1971) at slightly over 25×10^6 tons/year. Organic acids are the major constituents, followed by hydrocarbons and aldehydes. This is an entirely different order from that in auto exhaust, where hydrocarbons predominate, aldehydes are second, and organic acids are negligible.

Solvent evaporation is the largest single stationary source of VPOP, 7.1×10^6 tons/year. Products from solid-waste combustion and agricultural burning are the next most important stationary sources.

Vapor breathing losses from storage tanks at refineries and bulk plants and vapor displacement in the filling of tank trucks, service-station tanks, and automobiles account for almost all the emission associated with gasoline marketing. Various control devices and practices minimize vapor losses at most storage facilities. There are few vapor-loss controls, however, at retail service stations.

Of the many hydrocarbons present in the atmosphere, methane is predominant in all locations, 1.2–1.5 ppm worldwide, and higher in inhabited areas. Yearly averages of total hydrocarbons in urban areas of the United States range from 1.43 to 3.3 ppm (measured as carbon) and yearly maximal 1-hr averages range from 8 to 17 ppm. In Los Angeles, methane and 10 other hydrocarbons (ethane, ethylene, acetylene, *n*-butane, isopentane, propane, toluene, *n*-pentane, *m*-xylene, and isobutane) account for about 90% of the total hydrocarbon load.

Formaldehyde appears to be a natural constituent of the atmosphere, at a concentration of a few parts per billion. However, there are few atmospheric measurements of oxygenates other than aldehydes.

MECHANISMS OF FORMATION OF OXYGENATED ORGANIC COMPOUNDS IN THE ATMOSPHERE

The atmosphere is a fertile medium for a wide variety of oxidation processes and products, because it contains a virtually unlimited quantity of oxidizing agents, oxidizable organic substances, and oxidation initiators and catalysts. Aromatic hydrocarbons, present in the atmosphere in minor amounts, are subject to autoxidation by triplet oxygen in an environment containing metallic catalysts, ozone, oxides of nitrogen and sulfur, peroxides, and light to form species with reactive functional groups.

Singlet oxygen has been suggested as a possible contributor to the chemistry of photochemical smog formation. Processes other than direct excitation of ground-state oxygen are possible important contributors to the production of singlet oxygen in the atmosphere. Available rate data indicate that both ozone and atomic oxygen are more reactive toward olefins than is singlet oxygen. It is difficult to assess the importance of any contributions from singlet oxygen without more information on its concentration in the atmosphere. On the basis of the available data, it does not seem likely that $O_2(^1\Delta g)$ is contributing more than 5% to the basic reactions that convert nitric oxide to nitrogen dioxide in polluted atmospheres. Whatever reactions occur would be expected to produce peroxides, hydroperoxides, and the carbonyl compounds derived from them.

Atmospheres affected by photochemical smog contain relatively high concentrations of ozone. Ozone reacts with olefins and saturated aliphatic hydrocarbons in the vapor phase. In the case of saturated hydrocarbons, the products are similar to those obtained in solution. A free-radical mechanism has been offered to explain these products.

With olefins, the vapor-phase products are similar to those obtained in solution, except that there is no good evidence of the formation of ozonides in the vapor phase. The products observed are aldehydes, ketones, alcohols, and acids derived from the olefins, along with carbon monoxide, carbon dioxide, water, methane, and small amounts of other saturated hydrocarbons in some cases. The reactions also produce peroxidic materials that have not been further identified.

Olefins are considerably more reactive than saturated hydrocarbons. Rate data for olefins obtained in the presence of oxygen show a nonstoichiometric olefin : ozone ratio. When nitrogen is used as carrier gas, the expected 1 : 1 stoichiometry is observed. There is some variation in the absolute rate data, which is probably related to the widely different concentrations used or the presence of oxygen. The relative rates of olefin reaction generally follow a trend that is consistent with initial electrophilic attack of ozone and inconsistent with initial radical attack.

REACTIONS OF OXIDES OF NITROGEN AND SULFUR, HYDROXYL RADICALS, AND OXYGEN ATOMS WITH ORGANIC MOLECULES IN THE ATMOSPHERE

When mixtures of hydrocarbons and nitrogen oxides are subjected to ultraviolet radiation, nitric oxide is transformed to nitrogen dioxide, the nitrogen dioxide photodissociates, and oxidant (primarily ozone) is produced. The exact mechanism for this process is uncertain, but it may involve a chain process in which the hydroxyl radical is the chain carrier. Contrary to earlier beliefs, carbon monoxide can enter the cycle and promote the conversion of nitric oxide to nitrogen dioxide. Nitric oxide is involved in both chain propagation and termination. Increasing the nitric oxide concentration at first enhances the production of nitrogen dioxide, but then retards the production, as the terminating reactions become more important than the propagating reactions. Increasing the hydrocarbon content enhances the conversion, because hydrocarbons are important primarily in the propagation steps.

If sulfur dioxide is also present, oxidant production may be either enhanced or retarded, sulfuric acid is produced, and organic aerosol formation is increased. The detailed reactions of sulfur dioxide are not understood, but it can react with alkyl radicals and perhaps with alkoxy and alkylperoxy radicals and with zwitterions. Furthermore, sulfur dioxide absorbs radiation above 2900 Å to produce at least four excited electronic states, each of which can interact with both inorganic and organic molecules.

METABOLISM OF VPOP IN MAMMALIAN SYSTEMS

The mammalian metabolism of hydrocarbons and their oxygenated derivatives (epoxides, ethers, alcohols, phenols, aldehydes, and ketones) generally results in their conversion into more polar compounds, which are excreted either as such or as their conjugates with glucuronic or sulfuric acid. In the case of sulfur compounds, conjugation occurs with glutathione.

Little seems to be known about the metabolism of a number of highly reactive substances that may be formed in the atmosphere, such as peroxides, hydroperoxides, peroxy acids, volatile nitrates and nitrites, lactones, and ozonides, many of which exhibit potent biologic effects.

BIOLOGIC EFFECTS OF VPOP IN HUMAN AND OTHER MAMMALIAN SYSTEMS

Absorption of VPOP

Vapor-phase organic air pollutants from hydrocarbons are absorbed through four routes: the respiratory and gastrointestinal tracts, the eye, and the skin. Owing to the comparatively enormous volume of VPOP-containing air exchanged in human lungs at rest and during exercise, the respiratory tract is directly and indirectly the most important route of exposure and absorption. Almost all available data on this subject are occupational and reveal that the respiratory tract generally absorbs toxic chemicals at equivalent doses more rapidly and completely than the skin and that the toxic hazard at equivalent doses from respiratory exposure is about 3 times greater than that from oral exposure and 10 times as great as that from dermal exposure.

Pathophysiologic Effects

Short-term exposure to irradiated auto exhaust results in increased flow resistance, minute volume, and tidal volume, all of which return to normal immediately after exposure. Agents that can cause pathophysiologic effects are also present in raw auto exhaust gases and are multiplied by the photochemical effects of irradiation. Similar effects are produced by acrolein and formaldehyde; the effects of auto exhaust on respiratory function are possibly caused by aldehydes.

Alkylbenzenes and olefins are more effective precursors of biologically active photochemical agents than paraffins, benzene, and acetylenes. Effective eye irritants that are products of photochemical reactions are formaldehyde, acrolein, peroxyacetylnitrate, and peroxybenzoylnitrate. Eye irritation can be appreciable when oxidants are negligible.

The effects of the many hydrocarbons present in the urban polluted atmosphere on the human and animal respiratory tract have not been studied sufficiently at low concentrations or over long periods, although there are data on the effects of concentrations much higher than are likely in community air pollution. Studies of these effects in man are complicated by the inability to separate the changes due to pollutant materials alone from those due to other factors, such as tobacco-smoke inhalation, spontaneous infection, genetic factors, industrial vapor exposures, and aging. Pathologic study of domestic or laboratory animals exposed to urban atmospheres has yielded relatively little information. This may be due in part to the relative insensitivity of the methods used. Limited and incomplete studies of the effects of real urban atmospheres on laboratory animals have been performed with ultrastructural techniques.

Synergism, Antagonism, and Tolerance

Synergistic and antagonistic action has been demonstrated in a few situations involving hydrocarbons and oxidizing pollutants.

Mutagenic Effects

Some vapor-phase organic air pollutants have been shown to have mutagenic effects on various laboratory test organisms and may therefore pose a potential hazard to man.

Teratogenic Effects

The prenatal safety of exposure to vapor-phase organic air pollutants has not been adequately assessed.

Carcinogenic Effects

Most of the vapor-phase organic compounds expected to be present in polluted atmospheres have not been tested for carcinogenic or cocarcinogenic activity. Several classes of compounds are known to have carcinogenic activity on injection and dermal application at relatively high dosages. These classes of compounds are all oxygenated hydrocarbons.

EPIDEMIOLOGIC APPRAISAL OF HUMAN EFFECTS

Compounds with established unfavorable effects are formaldehyde, ozone (and other oxidants), and a group of lachrymators that is not very well defined, but probably includes PAN and peroxybenzoylnitrate.

INTERACTIONS AND EFFECTS OF VPOP ON THE TOTAL ENVIRONMENT

Effects on Atmospheric Properties

There are no known effects of VPOP on the physical properties of the atmosphere. They might influence nucleation and the formation of droplets in the atmosphere, thereby affecting fog and cloud formation. However, the significance of such an effect is largely speculative. There is virtually no information on their effects at their typical ambient concentrations on building materials, clothing, and paint, although such effects may be considerable.

VPOP from hydrocarbons in air may be transported to terrestrial waters by precipitation, fallout, and diffusion across the surface water–air interface. Information on the extent of these contributions to the amounts and distributions of these compounds in such waters is not available. There are some data on the gross organic-compound content of precipitation, air, and air particles, as well as some additional characterization by types and some specific organic compounds.

Removal, Fate, and Persistence

Two contrasting situations present themselves for vapor-phase and aerosol removal.

Although the residence times of a few compounds that are removed as gases have been measured, experimental confirmation of the adequacy of the theories of removal is still sparse. As a result, we remain unsure of the generality of the proposed removal mechanisms, and our ability to predict the removal rates of gases for which no data are available is very limited.

For aerosol removal, we have no similar problem. Although here, too, experimental confirmation of mechanisms is sparse, there is a large body of empirical evidence, arising mostly from studies on radioactively labeled particles, that permits us to estimate with some confidence the lifetime of any aerosol before removal from the atmosphere. A weakness in this empirical approach is that we know little about the influence of particle size on the rate of removal and little about the rate at which particles grow to the sizes most subject to removal.

But the most urgent problem in aerosol removal of VPOP products is the conversion of the gas into particles. Only the sketchiest of estimates are available of the proportion of VPOP products that ultimately appear in aerosol form, and no information is available on the question of whether unreactive compounds that release energy on oxidation (for example, paraffins) can be ultimately incorporated into particles.

There is a pressing need for at least preliminary answers to these questions.

Effects on Natural Waters

A variety of effects of organic compounds on terrestrial waters are of possible concern because of their influence on the general quality of the water, sediments, and biota or because they may degrade or have an impact on a particular water use. There are quality criteria for the organic content of water for several industrial and agricultural uses. Taste and odor effects in drinking water have been associated with specific organic compounds, and one cannot rely on conventional municipal water treatment to remove all organic compounds from a raw water supply.

In general, terrestrial waters themselves are not well characterized as to their organic-compound composition, although some specific types of compounds, such as pesticides and polynuclear aromatic hydrocarbons, have been reasonably well studied. Because of this dearth of information, conclusions as to the possible effects of VPOP from hydrocarbons on the receiving waters will at best have to be speculative or extrapolated from studies of model organic compounds or "organic matter" in simulated natural water systems.

Through complexation processes, organic compounds are likely to have a profound effect on the transport of trace elements in natural waters. They can have similar effects on other organic compounds through their ability to associate with or solubilize them. The sorption of organic compounds onto minerals can affect their stability and gradual incorporation into the biologic cycle. This can also be a mechanism for their concentration and transport in water, even when they have limited solubility.

VPOP from hydrocarbons are only one source of the rather complex and often undefined collection of organic compounds in terrestrial waters that may contribute to some of these effects. It is likely that their contributions are not decisive. However, there is not sufficient information to make a judgment.

Effects on Microorganisms

Microorganisms are sensitive to ozone, peroxyacetylnitrate, unsaturated hydrocarbons, and many pollutants that are constantly introduced into the environment. Gaseous hydrocarbon seepage into soil results in an anaerobic condition that destroys the normal microbial flora and causes infertility of the soil. The activities of nitrifying bacteria in soil are disrupted by gaseous halogenated hydrocarbons. The microbes in soil and on plant surfaces are responsible for mineralization of vast amounts of terpenes, carbon monoxide, ethylene, and other naturally occurring compounds. Interfering with the mineralization of these naturally occurring compounds by introducing an overburden of organic pollutant into the environment can be dangerous.

Effects on Vegetation

The effects of most VPOP on vegetation are due largely to their participation in atmospheric photochemical reactions with the production of ozone and PAN. Concentrations of PAN in urban atmospheres are high enough to reduce growth and production of sensitive crop and ornamental plant species. Enzyme activity, respiration, photosynthesis, ion absorption, and carbohydrate and protein synthesis all may be impaired. Even for brief periods, concentrations of 0.05–0.1 ppm cause general chlorosis and the characteristic bronzing or glazing of the affected leaves. Broad-leaved herbaceous plants—including chard, lettuce, table beets, and spinach—are among the most sensitive.

Ethylene is probably the only hydrocarbon that has a directly adverse effect on higher plants at ambient concentrations. Orchids are most sensitive, but damage has also been reported to carnations, roses, camellias, and chrysanthemums. It is probable that other species have also sustained significant damage from this growth-regulating chemical, but the phytotoxic nature of ethylene has not been studied thoroughly.

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Recommendations for Future Research

MECHANISMS OF FORMATION OF OXYGENATED ORGANIC COMPOUNDS IN THE ATMOSPHERE

Triplet Oxygen

To reduce the quantity of organic pollutants from the oxidation of hydrocarbons in the atmosphere, research should be undertaken to determine practical means of eliminating or markedly reducing the quantity of hydrocarbons available for atmospheric oxidation or of oxidizing the hydrocarbons completely to carbon dioxide and water before emission from combustion processes.

There has been a plethora of research studies on the liquid-phase oxidation of hydrocarbons, but studies of oxidation in the vapor phase in the presence of metallic catalysts, ozone, oxides of nitrogen and sulfur, and light are sparse. Extensive research on the vapor-phase oxidation of hydrocarbons, including kinetics and mechanisms of oxidation and quantitative product identification and analysis, is highly desirable, with emphasis on more efficient processes for conversion to carbon dioxide and water.

Singlet Oxygen

More basic work should be conducted to determine the concentration of singlet oxygen in the atmosphere. More work is also needed on vapor-phase reactions of singlet oxygen and the rates of these reactions with hydrocarbons and their oxidation products. Polluted atmospheres are known to contain olefinic hydrocarbons. Because some reactions of singlet oxygen with olefins are expected to occur, the toxicity of the products of these reactions—such as hydroperoxides, methoxyhydroperoxides, endoperoxides, and perhaps some of the decomposition products of these peroxidic materials—needs to be determined.

Ozone

Polluted atmospheres contain a variety of hydrocarbons with which ozone would be expected to react. Many of the products of these reactions are known to be toxic. More work must be done on olefin–ozone reactions in the vapor phase with respect to both product analysis and kinetic studies, to assess the importance of such reactions in the atmosphere. The question of whether ozonides are formed needs a more decisive answer. Rate studies are needed over wide concentrations of olefin to attempt to determine the reason for the present discrepancies in the reaction rate data. Additional inert carrier gases need to be tried to determine the effect on the observed rate constant. More work is needed on the reaction of ozone with oxygenated products of the reaction of ozone and olefins. The role of radical reactions in the kinetics and production of products should be clarified. Information obtained from research should be useful in controlling the number and quantity of ozone–hydrocarbon reaction products.

REACTIONS OF OXIDES OF NITROGEN AND SULFUR, HYDROXYL RADICALS, AND OXYGEN ATOMS WITH ORGANIC MOLECULES IN THE ATMOSPHERE

The details of all the reactions involved in the production of oxidant in photochemical smog are still not known. Further work should be done to elucidate all reactions, and additives that reduce the conversion rate should be sought.

No mechanism can yet fully explain the oxidation of sulfur dioxide, the formation of organic aerosols, or the influence of sulfur dioxide on oxidant production. Aspects of the atmospheric chemistry of sulfur dioxide require further study, including the possible reactions of photoexcited sulfur dioxide with hydrocarbons and the reactions of oxides of sulfur with hydrocarbons catalyzed by trace-metal contaminants.

METABOLISM OF VPOP IN MAMMALIAN SYSTEMS

Further work is needed for an evaluation of the pathway and extent of metabolism of peroxides, hydroperoxides, peroxy acids, volatile nitrates and nitrites, lactones, and ozonides in man and lower animals.

BIOLOGIC EFFECTS OF VPOP IN HUMAN AND OTHER MAMMALIAN SYSTEMS

Absorption of VPOP

Any discussion of routes and mechanisms of absorption of vapor-phase organic air pollutants uncovers a paucity of understanding of these mechanisms, as well as many unanswered questions, owing especially to the lack of studies of long-term subacute and chronic human exposures and related adverse health effects. So far, these exposures and the resulting absorption effects have been difficult to study and identify properly, and they constitute a subject requiring additional study.

Pathophysiologic Effects

Inadequate attention has been paid to the monitoring of aldehydes (especially formaldehyde and acrolein) in photochemically polluted atmospheres. More extensive monitoring is recommended and more careful evaluations of the health effects of these agents, experimentally and epidemiologically, are recommended.

Photochemical reactions of VPOP produce irritating effects, but indexes of such effects have received little attention. Experimental tests in animals and systematic studies of human reactions in normal and occupationally polluted atmospheres should be carried out.

More information must be obtained on the physiologic effects of hydrocarbon oxidation products, such as hydroperoxides, peroxides, epoxides, ethers, lactones, aldehydes, ketones, and other species with reactive functional groups. Studies should be conducted not only on individual products, but also on mixtures of oxidation products to assess potentiating or other unexpected biologic effects.

Ultrastructural studies should be done with sophisticated techniques—e.g., scanning electron microscopy; autoradiographic study of cell turnover in the lung and bronchial tree; biochemical studies of the effects of mucin production, surfactant production, histamine and serotonin metabolism, and the effects on collagen and elastin; and studies of capillaries using electron-dense intravascular markers to study altered permeability.

The effects of acute and chronic exposures to single or multiple pollutants on pulmonary resistance to infection and invasion by bacteria and viruses must be evaluated more completely. This will require the use of several animal species of different ages, as well as a variety of microorganisms. These studies should include evaluation of the effects of pollutants on the activity and synthesis of immunoglobulins.

It is important that animals used in these studies have appropriate anatomic characteristics. For example, in studying the effects of chronic exposures to air pollutants on mucin secretion, the animals used should have adequate glandular structures in the tracheobronchial tree. The effects of alterations in collagen and elastin after experimental hydrocarbon exposures should be thoroughly studied by a multidisciplinary approach. Ultrastructural alterations in these fibers and chemical changes involving cross-linking and amino acid composition of the substances in question should be evaluated in conjunction with physiologic studies of compliance of whole lungs or similar studies involving lung strips or isolated lung fibers. All these studies should be performed with appropriate consideration and control of the effects of aging in these proteins.

Synergism, Antagonism, and Tolerance

Extensive experimental efforts should be made to understand the underlying mechanisms of synergism, antagonism, and tolerance in humans, rather than test all the possible combinations in all possible ways for all possible effects in different species. The human health implications of experimental data should also be evaluated further.

Mutagenic Effects

Industrial workers exposed to relatively high concentrations of benzene have shown persistent chromosome changes. Workmen exposed to air pollutants suspected of mutagenicity should be periodically subjected to chromosome analysis of blood samples or biochemical tests.

Any chemical substance released into the atmosphere should be evaluated for its mutagenic potential, and combinations of two or more pollutants should be included to detect possible interactions.

Teratogenic Effects

Numerous pharmacologic, toxicologic, biochemical, and embryologic aspects need study:

The nature and causes of differences in drug response between individuals and species must be intensively investigated.

It is necessary to discover, for many chemicals and in many species, which indexes (e.g., plasma content, tissue content, surface area) are most closely correlated with intensity of response to chemicals and to document the comparability of species for these relations.

There should be large-scale studies comparing the relation, or ratio, between maternal and fetal toxic dosages, in various species, stocks, and strains of animals, and for many classes of chemicals.

The pharmacologic effects on fetuses and, especially, embryos should be studied.

Because of its potential importance in terms of infant mortality and childhood morbidity, a nationwide system or rapid reporting of all malformations and collateral information should be set up.

Experimental animal studies should be carried out that are adjuncts to and relevant to epidemiologic probes of the possible harmful effects of vapor-phase organic pollutants in human embryos.

Carcinogenic Effects

There is no extensive background of *in vitro* studies of carcinogenic VPOP. *In vitro* methods should be expanded as a means to identify the class of carcinogenicity into which environmental pollutants fall. Human tissues should be used for *in vitro* studies whenever possible.

EPIDEMIOLOGIC APPRAISAL OF HUMAN EFFECTS

If the aromatic content of gasoline is increased, three steps should be undertaken: more careful monitoring of hydrocarbons and reaction products; the use of physiologic and metabolic indexes in studies of persons occupationally exposed in filling gasoline tanks and otherwise handling or refining aromatic fuels; and estimation of alterations in aromatic content of emission of vehicles with various types of control systems.

Epidemiologic and experimental studies of concentrations of nitrogen dioxide to which humans are exposed should be carried out.

The measurement of PAN, peroxybenzoylnitrate, and transient reaction products and the detection of human reactions deserve priority, along with defining and detecting reactions associated with exposures to mutagens, carcinogens, and teratogens.

INTERACTIONS AND EFFECTS OF VPOP ON THE TOTAL ENVIRONMENT

Research is required to determine the influence of VPOP on the formation of atmospheric droplets and, hence, fog and cloud formation and precipitation patterns.

Research is required to determine the extent of the contributions of VPOP from air to natural waters and their concentrations and stabilities therein.

More information is required on the effects of microbial cometabolism on VPOP (and other organic pollutants), which can result in a reduction of toxicity, such as for DDT, or an increase, such as for mercury.

Research is required on the possible use of microbial systems as monitors for VPOP.

Additional research is required on microbial and plant metabolism of VPOP, the ability of VPOP to affect such metabolism, and the movement of VPOP in aquatic and terrestrial food chains.

Additional research is required to clarify and quantify the mechanisms of removal of VPOP and organic aerosols from the atmosphere.

Appendix A

Collection and Sampling Techniques for Vapor-Phase Organic Air Pollutants

Vapor-phase organic air pollutants are generally present at very low concentrations in large volumes of air. The proper evaluation of these organic pollutants by instrumental analysis depends directly on their collection and transport to the laboratory with a minimum of chemical reactions. Because vapors mix freely with the ambient atmosphere, they are easier to sample than dusts or fumes. But, because of their reactive nature and susceptibility to adsorption, they present many difficult problems. This review will outline methods of direct collection by plastic bags, glass bottles, valved gas syringes, and stainless-steel cans; indirect enrichment methods of condensation and sorption with and without chemical reaction; and the more specialized and complex techniques of whole-air liquefaction and reversion gas chromatography.

DIRECT METHODS

Plastic Bags

A popular method of sampling and storing atmospheric gases for analysis at a central home laboratory uses flexible plastic bags. The advantages of plastic over rigid containers include the following: the bags are light and inexpensive, no dilution corrections are necessary when material is removed from the containers, and reasonably large volumes of air (~150–200 liters) can be collected. However, caution must be used against their indiscriminate use, because some substances in some kinds of plastic bags—i.e., styrene—will be rapidly lost. Consequently, the specific conditions of each type of chemical compounds in a variety of gas mixtures in a specific plastic bag must be reported.

It should be remembered that no container can prevent vapor-phase reactions, which result in decreased concentrations of starting materials; that, if the sample is initially saturated with water vapor, condensation of the water will readily remove soluble chemical species, such as formaldehyde, organic acids, and alcohols; and that no collection system obviates precautions against leaks.

The most studied vapor-phase organic air pollutants include numerous low-molecular-weight paraffins and olefins, formaldehyde, and acrolein. Semiquantitative data on stability are available for many other substances, including aromatic hydrocarbons, phenols, crotonaldehyde, and alcohols. Data have been reported on the stability of olefins, formaldehyde, and acrolein in samples of automobile exhaust effluents and diluted irradiated automobile exhaust stored in plastic bags.

The stability of various organic substances at atmospheric and source concentrations in plastic containers over storage periods as long as several days has been investigated by Wilson and Buchberg,[1332] Baker and Doerr,[70] Altshuller *et al.*,[33] and Clemons and Altshuller.[227] Baker and Doerr studied the storage of ethylene, 1-pentene, 2-methylpentane, benzene, acetone, and butyraldehyde at 30–130 ppm for periods of 16–67 hr in Mylar, aluminized Mylar, Saran, Scotchpak, and aluminized Scotchpak bags. They concluded that these organic gases could be stored satisfactorily in the plastic bags as single components and as complex mixtures if the film were impermeable to the studied gases, because diffusion characteristics alone controlled possible hydrocarbon loss. They recommended that double film bags be used. The inner film should be impermeable to the gases of interest, and the outer film to moisture. Aluminized Mylar and aluminized Scotchpak were shown to be the least permeable to moisture.

Altshuller *et al.*[33] also have reported that Scotchpak bags were satisfactory over 24-hr periods for storing synthetic and atmospheric samples of aliphatic hydrocarbons and acrolein, but not formaldehyde.

Mylar bags were satisfactory for synthetic mixtures of formaldehyde; a 5% loss occurred over a 24-hr period. However, formaldehyde in atmospheric gases sustained a 5–10% loss in only 2 hr.

Clemons and Altshuller[227] further studied systematic changes in aliphatic C_{2-5} hydrocarbons during a 10-day period. Paraffinic hydrocarbons showed no changes in concentrations in the containers during the storage time; but slow losses of ethylene and acetylene apparently occurred. A loss of the major portion of the aromatic hydrocarbons occurred even after only a few days of storage. Some of the aromatic hydrocarbons later reappeared in the container. These studies indicated that several precautions are necessary. First, long-term storage of aromatic hydrocarbons in these containers should be avoided. Second, new bags should be conditioned for several hours with the specific gases of interest in at least the concentrations of the samples. The greater the losses experienced with new bags, the more essential is repetitive conditioning before actual use. With increasing time, the rates of adsorption and desorption become equal, as the surface-active sites are saturated and equilibrium for the chemicals being studied is reached.

Clemons and Altshuller[227] also reported that a substance with the same retention time as *o*-xylene was very slowly desorbed from the walls in Mylar bags. This material was interpreted to be an oxygenated component or decomposition product of the plasticizer in the Mylar film.

Altshuller *et al.*[33] found that the stability of aliphatic and aromatic hydrocarbons stored in plastic bags made of Tedlar over 6-hr periods was very good. The concentrations varied by no more than 5%, with no significant trends. Most of the variability could be attributed to limitations in analytic precision in the sub-parts-per-million range. H. Mayrsohn (personal communication), W. A. Lonneman (personal communication), and P. Groblicki (personal communication) have found that Tedlar bags are superior to bags of other plastics. Within a 24-hr period, negligible hydrocarbon–Tedlar interaction occurs (Mayrsohn, personal communication). However, in a 5-day study, a 15% decrease in the hydrocarbon content of the bags was measured after several days. Both wall adsorption of the heavier hydrocarbons (such as the aromatics) and diffusion losses of the lighter hydrocarbons (like ethylene and acetylene) through the Tedlar are implicated.

Currently, fluorinated plastic film, such as Teflon and Tedlar, for constructing plastic bags is gradually replacing all the previously decribed types. Unfortunately, although it is generally recognized that

Teflon and Tedlar are superior materials for fabricating sampling bags, because of their very low surface–wall adsorption characteristics, no systematic studies that define these superior qualities are yet available.

Glass Bottles

Stainless-steel and glass containers are commonly used for storage of gases, because of their convenience and ready availability. Specifically, stainless-steel containers are usually used for sampling high-pressure sources, whereas glass containers are used at atmospheric pressure. Baker and Doerr[70] have reported that the storage of a mixture of sulfur dioxide, nitrogen dioxide, and 2-pentene in stainless-steel cylinders at atmospheric pressure showed no significant loss at 40 hr. Comparable storage in glass flasks showed a high loss of sulfur and nitrogen dioxide, but no significant loss of 2-pentene. These vacuum glass sample containers are unsuitable for storing other reactive gases, such as hydrogen sulfide, at trace concentrations. Altshuller *et al.*,[31] studying raw automobile exhaust, reported that no formaldehyde could be detected, even when collection was made into dry glass flasks. These severe losses of formaldehyde from the raw exhaust were probably due to the transport of formaldehyde to the container walls with the water-vapor condensate.

However, glass flasks have been successfully used for sampling atmospheres for the analyses of such gases as carbon dioxide, carbon monoxide, hydrogen, nitrogen, oxygen, methane, and a variety of light hydrocarbons. Stephens and Burleson[1154,1155] have collected air samples both in 20-liter glass carboys and in 300-ml glass sample tubes. Their system for extensive field collection of ambient air samples in urban locales involved 12 glass vacuum tubes with stopcocks at each end packaged in a padded wooden box; the workability of this system was demonstrated by the analysis of light hydrocarbons in their laboratory in California, after collection and shipment of air samples from Denver, New York, and Honolulu. Unfortunately, these rigid containers hold only small samples, thereby restricting the analytic measurements to gas-chromatographic (GC) analysis for hydrocarbons. Nevertheless, Stephens and Burleson[1155] could obtain three 100-ml syringe samples from the original 300-ml glass collection tubes with a positive-pressure diluent technique, although a twofold loss in sensitivity occurred with each successive withdrawal.

Hydrocarbons are collected for analysis in many laboratories in gastight syringes, enabling the sample to be injected directly into a gas chromatograph. Because of the limitations on the volume that may be injected into a GC column, this method is satisfactory only when the concentrations of the components being analyzed provide an adequate response to the detector. However, the great sensitivity of the flame-ionization detector has enabled many investigators to obtain almost routine sensitivities to a few parts per billion with air samples of 1–10 ml. The syringes used are normally constructed of stainless steel, glass, and Teflon.

A recent development in gas syringes promises to establish the syringe even more firmly as the preferred gas-sampling device. The innovation consists of a miniature gastight valve integral to a syringe that incorporates a resilient O-ring in the Teflon plunger seal. The O-ring ensures a leaktight seal against high backpressures and the cold-flow property of Teflon. This leaktight, valved syringe is commercially available (Precision Sampling Corporation, Baton Rouge, La.). It allows the gas sample not only to be sealed in the syringe from the point of sampling to the point of analysis, but also to be pressurized. Pressurization is achieved by pressing the plunger in the syringe barrel before injection, with the barrel sealed by closing the built-in valve. Rasmussen[998] has reported that pressurizing a gas sample before injection greatly improves the performance of the syringe in injecting the sample into a gas chromatograph. M. D. LaHue (personal communication) has used this new type of syringe to send air samples collected in Brazil and Panama by airmail to his home laboratory in Colorado for analysis of trace atmospheric hydrocarbons.

Although glass vessels have been found very satisfactory for storing trace concentrations of hydrocarbon gases with slight vessel-well effects, a surface–wall reactivity of glass for trace concentrations of the oxygenated products exists. A comparative study of the adsorptive properties of glass in altering the true proportions of trace concentrations of such gases as aldehydes, ketones, alcohols, lactones, epoxides, peroxides, hydroperoxides, peroxyacids, and ozonides should be investigated, if the chemistry of air pollutants stored or held static in glass vessels is to be regarded as representative of the real atmosphere.

Stainless-Steel Canisters

As previously mentioned, stainless-steel containers were found satisfactory for the storage of the oxides of sulfur and nitrogen at normal atmospheric pressures. In addition, Baker and Doerr[70] made some interesting tests on compressing prepared gas mixtures into stainless-steel tanks to 150 psig. This compression sampling allowed the transfer of large volumes of gas from the field to the laboratory in containers of reasonable size. Ketones, aldehydes, aromatics, and saturated and unsaturated hydrocarbons were tested, as well as nitrogen oxides and sulfur dioxide. Analyses before and after compression (150 psig) and with various storage periods were obtained. Acetone and butyraldehyde were slightly affected; 2-methylpentane, benzene, and 2-pentene showed no significant change; and nitrogen oxides and sulfur dioxide showed appreciable losses. Therefore, Baker and Doerr concluded that compression sampling was apparently satisfactory for hydrocarbons, but not for oxides of nitrogen and sulfur. The stainless-steel containers used by Baker and Doerr had only the normal manufactured surface without any modification.

Major technologic steps occurred in regard to the practical utility of reduced metal–surface reactivity with the advent of the Apollo program and its stringent requirements for extreme surface cleanliness and passivity. The steps were the development and perfection of the methods and the necessary solvent chemicals for electropolishing stainless-steel surfaces (U.S. patent 764462). It is now possible to use a nontoxic, nonfuming electrolytic solution, such as developed in Molectric's Summa process, that enables oxygen to combine with the chrome nickel of the stainless-steel alloy to create a pure chrome nickel oxide skin on the basic crystalline structure of the metal. The formation of this oxide not only gives a tremendous passive "wetting cushion" to the surface of the metal, which aids in retarding trace gases from reacting with the metal, but also results in a superpolish with a microinch finish as fine as 1½ Å. Ordinarily, a drawn metal surface has a microinch RMS (root mean square) finish of No. 32. With the appropriate mechanical polish, this surface can be improved to a No. 10 RMS. The Summa process will lower an already high polish (No. 10 RMS) finish to a No. 4 or less RMS, which has a very-high-luster polished surface.

Besides the advantages of better corrosion resistance, a surface free of imbedded residues from a mechanical polish, and a chemically pure and surgically clean surface, the chemical purity of the exposed metal surface is completely compatible with such fuels as hydrogen peroxide, liquid oxygen, fuming nitric acid, and fluorine. This latter point was not appreciated until a few serious accidents in the Apollo program showed that impurities imbedded in mechanically polished and deburred surfaces were excellent catalytic agents able to trigger explosions in missile and space systems. Interestingly, these same catalysts can react with trace oxides of sulfur, nitrogen, and other reactive air pollutants.

With these considerations in mind and with the ready availability of techniques and solvents for passivating stainless steel, the almost negligible absorptivity of electropolished stainless-steel surfaces should be investigated for special cases that require an extremely rugged and functional collection–storage system.

INDIRECT METHODS

This section reviews methods of collection of complex mixtures of vapor-phase organic air pollutants by sorption techniques with and without chemical reaction. These substances can be studied best after their isolation or partial concentration from the air. Prefiltering to remove particulate matter and adequate metering of the total volume of sampled air are necessary steps in the analyses. Metering of the air is necessary to obtain a true value of the total air volume sampled as the filter for removing the particles gradually becomes clogged, which results in a continuously changing resistance to flow.

Adsorption

At ambient or subambient temperatures, gases adhere variably to solid surfaces; this phenomenon is called adsorption. In porous solids, both external and internal surfaces (some possessing a vast network of intensely minute channels and submicroscopic pores) are exposed. The degree of adsorption depends on the relationship between pore structure and the size and shape of the contaminant molecules, as well as on the strengths of molecular attractive forces. Some of these solids—activated carbon, silica gel, activated alumina, and the porous organic polymer sorbents (Chromosorb and Porapaks) used in gas chromatography—are practical adsorbents.

Recently, Kaiser[659] reported a new type of porous carbon black (Carbosieve) produced by thermal degradation of polymeric polyvinylidene chloride. This carbon black has both adsorbent and molecular sieve properties and an extremely nonpolar surface; on this adsorbent, water is eluted before methane. Graphitized thermal carbon black has also been reported by Kalaschinikova *et al.*[662] to have excellent adsorption properties for C_{1-6} alkanes, alkenes, alkadienes, alkynes, cyclanes, cyclenes, and benzene and by Eisen *et al.*[357] for C_{6-10} *n*-alkenes.

Polar substances have a strong mutual attraction; water is highly polar, and polar adsorbents retain water from a humid atmosphere in preference to electrically nonpolar organic gases. In the sampling of vapor-phase organic pollutants from ambient air, nonpolar activated carbon preferentially adsorbs organic material. In fact, previously adsorbed moisture is displaced from the carbon surface as other organic gases are adsorbed, making it unnecessary to dehumidify the air before its passage through the carbon bed. Any prior dehumidification is also undesirable, inasmuch as alteration or loss of organics may occur in the dehumidification process.

Chemisorption of low-boiling-point organics like ethylene has been accomplished by impregnating the activated carbon with bromine, and stabilized sodium sulfite on activated carbon has been used for formaldehyde.[1214]

In extensive identification studies of the trace contaminants in enclosed atmospheres—such as submarines, space simulators, and manned and unmanned space cabins—activated charcoal has been found to afford one of the most practical sampling techniques available.[1047] However, correct interpretation of the data from charcoal sampling depends on a knowledge of the adsorption and desorption efficiency of each individual component on charcoal. Hence, although inferences can be drawn, no general quantitative values can be assigned.

Saalfeld *et al.*[1047] reported several shortcomings of the charcoal sampling method: Many contaminants in an enclosed atmosphere either cannot be recovered from charcoal or may be chemically altered by the adsorption–desorption process. The charcoal itself may pick up or acquire a background of contaminants during its handling and storage. The contaminants collected on the charcoal filter usually represent a long exposure. Thus, contaminants with short retention times are eluted from the charcoal bed. With increasing exposure time, the filter is depleted of these contaminants and enriched with contaminants having a long retention time. The three methods of recovering the adsorbed contaminants—vacuum–thermal desorption, solvent extraction, and steam desorption—are strenuous desorption techniques.

Another interesting charcoal-filter collection–enrichment technique has been reported by Grob and Grob;[497] it uses a very-small-capacity filter. The trap contains 25 mg of wood charcoal with an average particle size of 0.08 mm; the air flow is set at 2.5 ml/min, so that 25 m^3 of air are filtered within 8 days. To determine the adsorption of the substances of interest, a second filter was inserted behind the first. Carbon disulfide was used to extract the materials from the filters. Both qualitative and quantitative investigations were made on C_{6-20} volatile organics in city air with this system.[497] Unfortunately, like the saturation method of frontal analysis,[931] this technique gives excellent results for only a single major substance, but is inadequate for studying long-term loading of complex mixtures with a wide range in volatility, because several phenomena occur. First, the firm bonding to the active sites by initially well-adsorbed components prevents more volatile and less well-adsorbed substances from reaching their saturation equilibrium. Second, some substances, even if present in relatively high concentrations, may be greatly reduced on the charcoal bed in the course of prolonged loading. It is interesting to note the similarities (including fundamental difficulties) between Grob and Grob's more refined carbon disulfide solvent extraction scheme using 25-mg charcoal filters[497] and Turk and d'Angio's carbon tetrachloride solvent extraction scheme using 325-g charcoal filters.[1215]

In general, siliceous and metallic oxides like silica gel and activated alumina are polar adsorbents that retain atmospheric moisture. However, as long as the adsorbent does not become saturated with moisture before sampling is complete, both silica gel and activated alumina can be used for short-duration sampling from relatively dry atmospheres. Although silica gel has a lower retentivity for organic gases than does activated carbon, it possesses the advantages of greater selectivity and easier desorption.

Absorption

Equipment for absorption has usually consisted of simple bubblers, bubblers with diffusers, spiral absorbers, and packed towers. Absorption equipment of this type, with gas–liquid contact efficiencies of over 90%, usually has the disadvantage of relatively low flow capacities. Owing to the sampling time essential to collect measurable quantities of organic gases, repeated replacement of evaporated solvent may be necessary. Also, when trace organic gases have been collected in the form of a very dilute solution in an organic solvent, the problem of their recovery is formidable. In general, the problem of sampling trace gases (such as aliphatic aldehydes, hydrogen sulfide, and mineral oxides) in the atmosphere requires that the gases be extracted from the atmosphere by washing the air sample with aqueous reagents. For example, formaldehyde is the only organic vapor-phase contaminant currently measured in the atmosphere that relies on the principle of absorption for later colorimetric analyses.[1108]

Condensation

The collection of vapor-phase organic air pollutants by condensation at low temperatures has at least two distinct advantages over the other collection methods: the collected organics are immediately available for analysis, without requiring either removal of solvents or desorption from an adsorbent; and condensation is the most reliable method for preserving the organics without the further occurrence of chemical reactions. The main disadvantage of collection by condensation is that large quantities of water condense simultaneously with the collected organic gases.

SIMPLE COLD-SURFACE TRAPS

A special problem of condensation of organic gases in open-bore cold traps is the formation of condensation mists. Such mists are composed of solid or liquid particles of a few micrometers or less that often pass through the cold traps in sufficient proportions to reduce significantly the collection efficiency of the equipment. Shepherd *et al.*[1109] have described a simple glass-wool filter (additional to the prefilter used to remove ambient atmospheric particles) seated between the liner walls of a cold trap to minimize such losses.

For condensing some gases, the refrigerant used must be cold enough for a sufficient decrease in the vapor pressure of the trapped material to occur to prevent significant evaporation during the sampling. The choice of coolant is dictated by the requirement of keeping the vapor pressure of the condensed gases at less than 1 mm Hg in the cold trap. Normally, a cryogen colder than − 160 C is needed to condense C_{2-4} compounds efficiently, whereas a dry ice–acetone bath (–78 C) is usually appropriate for compounds of C_5 and above. However, the convenient availability of liquid nitrogen and dry ice has resulted in their preferred usage. Generally, liquid oxygen is a better cryogen than liquid nitrogen or liquid air, because at low sampling rates there is no condensation of atmospheric oxygen in the trap. However, there are some safety precautions necessary in handling liquid oxygen that have generally placed it in disfavor. Liquid argon has restricted usage, largely because it is difficult to obtain.

One feature of liquid nitrogen and dry ice that has not been very widely taken advantage of is the spongelike nature of dry ice for holding liquid nitrogen. Apportioning the appropriate amounts of liquid nitrogen with powdered or finely crushed dry ice enables a wide range of cryogenic temperatures to be obtained—between –193 and –80 C. This containment of the liquid nitrogen within the granular structure of the dry ice is especially useful under field conditions, inasmuch as there is no sloshing of liquid in the Dewar flasks.

The method most commonly used to deploy open-bore glass freeze-out traps involves using them as a series of traps held at progressively lower temperatures. The stepwise cooling action results in some degree of fractionation and water condensation before the last trap, which is the most efficient stage of condensation.

During the early investigatory period in the Los Angeles air pollution episodes, Cadle *et al.*,[178] Haagen-Smit,[502] Shepherd and colleagues,[1108,1109] and others reported that many volatile contaminants could be efficiently collected from the atmosphere with simple cold condensation surfaces. Shepherd *et al.*[1109] were the first to concentrate air pollutants in a cold trap and analyze the concentrates by mass spectrometry. The isolated, frozen concentrate was separated by isothermal distillation or sublimation at low temperature and high vacuum in the mass spectrometer. About 60 compounds were identified from the isolation of the vapor-phase pollutants on a filter at liquid oxygen temperatures.

Simple open-bore, cold-surface traps are now seldom used in air pollution studies, unless there is a need to freeze out the water from the air to examine the organic materials dissolved in the water.[1004,1006]

PACKED COLD-SURFACE TRAPS

Vapor-phase organic air pollutants from hydrocarbons are usually identified and quantified by gas chromatography. An enrichment step before analysis and measurement is required to detect concentrations of the different types of hydrocarbons at less than 0.01 ppm (i.e., 0.01 μl/liter), even with the different types of highly sensitive ionization detectors available. Various organic gases have been concentrated in traps containing small volumes of purified charcoal, silica gel, glass beads, stainless-steel washers, porous polymers, and gas–liquid chromatography partition substrates coated or bonded on refined diatomaceous earths. The lower limit of measurements of the C_{3-5} hydrocarbons can be extended to 0.1 ppb by concentrating 100 ml of the air sample in a freezeout trap packed with the appropriate adsorbent or gas–liquid partition substrate. Liquid oxygen is used in the freeze trap, rather than liquid nitrogen, to avoid condensation of oxygen in freezing the air sample. Dry ice–acetone is commonly used to collect aliphatic hydrocarbons on silica gel; however, ethylene is not retained. At reduced temperatures, neither silica gel nor charcoal offers any readily apparent advantage over gas–liquid partition substrates for concentrating compounds of C_3 and above. Consequently, most current investigations on the collection of atmospheric hydrocarbons have used short, packed columns similar to those used for the separation of hydrocarbons.

If the concentrations are high enough, the air sample is analyzed directly by pulling the atmospheric gases containuously through the gas-sampling valve connected to the inlet system of the chromatograph. If an intermediate step, such as freezeout trapping or collection in a container, is involved, the stability of the substances retained must be determined. Losses not only of reactive substances, such as peroxyacylnitrates, but also of oxygenated hydrocarbons occur in the containers and in the inlet and column system of the gas chromatograph.

The trapping procedures for concentrating aliphatic, aromatic, and terpenic hydrocarbons for transfer for analysis on packed, SCOT (support-coated open tubular), and capillary columns generally use one or a combination of the following: an external freezeout loop, on-column freezeout, a precolumn inlet freezeout system, and specially designed low-volume injector-needle freezeout assemblies. The essential details of these trapping techniques have been reported elsewhere.[91,94,259,483,779,1002,1154,1155]

Equilibration with Partitioning Substrates

Mackay *et al.*[796] were among the first to compare the results of a direct sampling technique for analyzing trace amounts of organics with the results of using a gas-chromatographic column itself as a concentration or enrichment device. The most valuable feature of the direct sampling technique is that all the artifact-introducing processes that may grossly alter the balance of constituents are bypassed by sampling the volatiles in their natural representative proportions and subjecting them to stresses no more severe than the forces encountered in the gas-chromatographic column. Mackay *et al.* concluded that an enrichment column held at 75–100 C cooler than the separation column did not indicate changes in the apparent composition of the organic volatiles being analyzed, but afforded increased sensitivity. The low-temperature bath used for cooling the enrichment column was not used intentionally as a cold trap, but rather as a means of slowing the passage of the volatiles through the precolumn so that a longer time for equilibration was available for absorption of the volatile organics by the partitioning substrate.

Recently, Dravnieks and Krotoszynski[332] advanced this type of enrichment when they reported a high-speed collection system for organic vapors from the atmosphere. The essential feature of their sampler was a fluidized bed of Teflon powder coated with Apiezon L, which collected atmospheric organics through equilibration with the partitioning phase. The fluidized bed was used to produce the best possible contact with air. Only Apiezon L, of the many conventional gas-chromatographic phases tried, permitted recovery of the dissolved organics without artifacts from the decomposition of the trapping phase itself. The bed temperature was limited to 80 C by incipient thermal decomposition of the Apiezon L phase. During collection, the bed was kept at ambient temperatures; the rate-limiting factor for equilibration was the diffusion of the organic material into the Apiezon L partition phase on the Teflon. Air flow rates of 0.5–0.75 liter/sec kept the powder constantly floating, providing uniform contact with the air. Normally, at such flow rates, the bed reached equilibrium within 45 min. Organic components dissolved in the partition phase were recovered by displacement with helium at 80 C and transferred to a thin-wall injector needle held at –196 C. Each collection yields only one sample for analysis. Quantitation depends on knowledge of the partition coefficient for each component trapped. Unfortunately, this technique, in its present developmental state,[333] has had a very limited evaluation for use in air pollution studies.

The primary problem involved in the condensation of air samples of 1–100 liters of greater is the large amount of water vapor relative to the organic fraction present in the air. For example, 1 liter of air at 25 C and 70% relative humidity contains 16.1 mg of water, whereas the organic burden in the same volume of air varies between 2 and 200 ng. Because the overloading of open tubular columns occurs with more than 50 mg of material, the introduction of a few milligrams of water or more is a very serious problem. In addition, the pumping units on the ionization sources of most conventional mass spectrometers are unable to maintain a vacuum of 10^{-5}–10^{-4} torr if milligram quantities of water are introduced into the mass spectrometer. Conventional small-bore cold traps that have become almost standard analytic instruments in trace analysis are also affected by milligram quantities of water. Even the performance of the most commonly used column type, a 1/8-in.-O.D. packed column 6 or 12 ft long and using a water-insoluble silicone phase, is affected by more than 50 mg of water.

These difficulties presented by the large amount of water present in ambient air relative to the organic species have led to various attempts to separate trace organics from water vapor. The most common method is the use of precolumns packed with desiccants that, interestingly, have given different investigators varied success and reliability. Unfortunately, the possibility always exists that the desiccant can irreversibly adsorb and absorb some of the organics from the air under study, especially inasmuch as the sorption properties fluctuate as more water is taken up by the desiccant.

In attempts to circumvent the problems associated with desiccants, several investigators[333,781,876,1087] have used polymeric adsorbents of the styrene–divinylbenzene type for separating and concentrating organic components from water vapor. The technique involves the trapping of the organic volatiles in a short precolumn at ambient temperature while the water vapor is discarded with a sweep gas. The adsorbed sample constituents are eluted from the precolumn at high temperature (150–180 C) with or without reversed flow. There are several advantages of the technique: The amounts of collected components are proportional to their concentrations in the atmosphere; sample storage is convenient and safe; most of the water vapor is rejected; and the organic constituents adsorbed are readily released on heating. The major disadvantages are interferences from the bleeding of extraneous compounds from the packing, the chemical instability of the packing, possible chemical alteration of the sample constituents during the heat-release treatment, and the limited retention volume before equilibration is reached and the collected materials begin to pass through the collector.

In an earlier report on the concentration of the trace contaminants in air on porous polymer beads, Williams and Umstead[1315] concentrated chlorinated and brominated hydrocarbons at ambient temperature on the same column that was later used for the gas-chromatographic analysis. They reported that the interference from water was minimized, because it was eluted as an early peak, thus eliminating the need to dry the air samples before injection onto the column. The original report on the feasibility of concentrating the organics in air samples on porous polymer beads was probably that of Hollis,[581] who stated that porous polymer beads gave low-molecular-weight hydrocarbons retention times that were very long, compared with those obtained on conventional gas–liquid chromatographic substrates, but allowed the rapid passage of water through the column.

Recently, Aue and Teli[52] reported the sampling of air pollutants with support-bonded chromatographic phases at ambient temperatures. The use of very high loading (26%) of the liquid silicone, $(C_{18}H_{37}SiO_{3/2})_n$, phase support-bonded to a coarse Chromosorb support permitted maximal retention and rapid gas flow of air pollutants. The trapped compounds were solvent-extracted, and the concentrated extracts analyzed by gas chromatography. Unfortunately, the extraction of minor trace compounds from the chromatographic phases and the restriction to the collection of organics above C_7 limited the amount of information obtained on the ambient air samples reported. Also, no quantitative investigation of the collection efficiencies or recovery efficiencies with extraction was reported. Identification of the collected compounds from atmospheric sampling was beyond the defined scope of the study.

Obviously, the copious water present in air samples must be circumvented if accurate, routine collections and analysis of atmospheric vapor-phase organic pollutants are ever to become a reality. The problem of interferences from large amounts of water is even more acute in the analysis of source emission, such as stack gases and auto exhaust. In an attempt to solve this problem, C. W. Skarstrom and J. Kertzman (personal communication) developed a new, self-regenerative air drier that selectively removes water vapor from saturated air or automobile exhaust without affecting the hydrocarbon concentration. The drier has demonstrated efficiencies of removing water in a saturated ambient air stream to less than 10 ppm by volume. The basic element is a special hygroscopic permeable membrane that removes water from the feed gas. The membrane does not have any of the aging or attrition characteristics of conventional solid desiccants. The efficiency of water removal depends on the length of the tube bundle, normally 40–72 in. The present available rates of 0.5–3.0 liters/min depend on the diameters (0.5–0.75 in.) of the tube bundle used. The drier consists of a single unit that samples continuously; the unit is self-regenerative.

The very newness of this selective water removal device limits the quantity of performance data available. However, by providing water reductions of better than 500:1, this concentration process promises to provide air pollution investigators with a means of obtaining better accuracy, higher precision, and greater repeatability of pollution measurements.

MISCELLANEOUS METHODS

In the category of miscellaneous collection methods are several hybrid enrichment–analysis systems that deserve to be included here, although some of their essential points belong in Appendix B.

Reversion Gas Chromatography

Kaiser[661] recently reported automated continuous trace organic analysis in concentrations of parts per billion to parts per million with a reversion gas chromatograph. The novel feature of the technique is that the air sample under investigation is continuously frozen out on the head of the column. Removable Peltier cooled copper blocks provide a chilled enrichment zone. Separation occurs discontinuously by means of an oven that moves along the length of the column. The oven provides the necessary temperature field within which the appropriate temperature gradient can be adjusted to the needs of the analysis. Both the upper limit of the temperature field and the column material determine the substances that can be eluted per analysis cycle, their rate of elution, and the coherence of the concentration of the separated compounds.

The procedure can be programed to permit an automatic analysis in intervals of 10, 15, or 30 min. If the flow rate, freezeout time, number of temperature fields, and other operational characteristics are changed, versatile continuous analyses on trace concentrations of light hydrocarbons are possible. Kaiser believes that, because the entire sample volume passes through the detector in a continuous flow, there are no problems of sampling, storage, transportation, aging, contamination, quantitative calibration, etc. However, the reversion procedure is limited by the following factors: Separation efficiency is low; at present, only homologues of light hydrocarbons can be separated; and direct calibration is difficult and a known detector constant is necessary for each unknown substance. The main advantage of the system is that practical ultratrace analyses with restricted resolution are possible through continuous sample on-column enrichment, because both nonsystematic and systematic analytic error is minimized in the sampling procedure.

Automated Airborne Collections

Cavanagh[209] reported on the development of instrumentation for automated airborne collections of atmospheric organic chemicals. The basic design feature of the sampling system was a concentration procedure that used gas-chromatographic column packing material to retain organics selectively while permitting the permanent gases of the atmosphere to pass through the trap. The broad range—methane to C_{10} terpenes—of organics for which the system was developed required that the collection system be divided into two channels to provide efficient enough collection of the C_{1-4} organics on one channel and the C_{5-10} organics on the second channel for quantitative analysis.

Two successive stages, each with a thousandfold concentration step, were used to achieve a 10^6-fold total concentration. Liquid argon (−186 C) was used as the cryogen. Trap design evaluations included selection and evaluation of packing material for compatibility of the organics of interest with the packing substrate and the efficiency of collection. Water removal from the atmospheric samples was necessary before concentration of the C_{5-10} organics. Desiccants were thoroughly evaluated on the basis of transmission of terpenes without loss or decomposition. In addition, methods were developed and tested to remove particulate material from the incoming air sample before the cryogenic traps.

Field tests with the prototype sample collector made by Cavanagh indicated that the principles of the cryogenic technique were valid and that good collection and measurement of trace C_{5-10} organics could be achieved. Unfortunately, in the automatic system later built from Cavanagh's prototype, the engineering of the automatic cryotrap sequence in the integrated system has not performed satisfactorily, owing to cold spots in the transfer lines between the first- and second-stage traps (B. Tyson, personal communication). The system has also been found to be too elaborate for routine field use, in that it is very sensitive to flow fluctuations and requires an intricate array of seven mass flowmeters with solenoids, two vacuum pumps, and several prefilter water sorption and desorption traps.

Cryocondenser—Whole-Air Liquefaction

The development of a portable air sampling instrument that can collect and enrich large representative samples of both urban and nonurban atmospheres has been reported by Rasmussen.[995] The principle of operation is the cryogenic technique of liquefying air. This simple and straightforward approach results in several benefits to air pollution scientists: It allows economical and practical transportation of a large volume of the atmosphere from the field sampling site to the laboratory, where careful, repetitive analysis can be made on the composition of its trace contaminants; it permits preservation of the whole composition until the appropriate analyses can be performed; it offers a simple means of collecting usable samples in remote areas or under difficult circumstances (industrial, urban, rural, etc.), in that the necessary equipment includes simply a Dewar flask with liquid nitrogen and an appropriately calibrated cryocondenser; external electric lines to service pumps or mass flowmeters with recorders are obviated; the entire system, including the Dewar flask, is constructed of electropolished stainless steel, has no moving parts, and is extremely rugged; and, at the temperature of the present refrigerant, liquid nitrogen (–196 C), nearly all the air pollution constituents (except carbon monoxide) have negligible vapor pressures.

The cryogenic sampler developed, a cryocondenser, consists of a multiple-column heat exchanger fitted to a reservoir for receiving liquefied air. The unit requires no external power to operate. Air is taken in by creating a vacuum in the trap through the condensation of the incoming air on the walls of the heat exchanger and collection reservoir. All the air that enters the cryocondenser is condensed; therefore, the unit can be considered to be 100% efficient. As the air condenses on the large cryogenic surface provided by the heat exchanger, the condensed (liquid) air flows to the reservoir can. In this way, an active cryogenic surface is maintained in the heat exchanger.

The intake rate is controlled with a critical orifice to give a uniform sampling rate over a sampling period of 10–60 min.[776] The repeatability of the volume of air collected has been measured under laboratory conditions at ± 1.2–2.3%, depending on the pumping capacity of the unit and the orifice size. Under field conditions, it is more convenient and accurate to use a battery-operated mass flowmeter with a ratemeter and a digital totalizing counter. This measuring device eliminates the tedious calculations necessary for standardizing the volume of air collected under field conditions at the different and changing altitudes experienced during samplings from an aircraft.

At the end of the sampling period, the inlet valve is closed and the cryocondenser is left in the Dewar flask with liquid nitrogen for transport to the laboratory, where the liquid air can be distilled precisely with maximal retention of the collected organics. Samples for gas-chromatographic analysis of the organic gases, carbon dioxide, water vapor, and other gases in the cryocondenser can be taken either directly with a valved syringe (Pressure-lok) or indirectly under conditions of isothermal and isobaric distillation or helium displacement, so that specific fractions can be trapped for specialized analysis. Syringe samples enable repetitive and range-finding analyses to be made on the contents of the cryocondenser, whereas fractionation and secondary enrichment of the entire contents of the cryocondenser can provide several hundred nanograms of material, to permit combined gas-chromatographic and mass-spectrometric analyses.

The major disadvantages of the system are that generally 24 hr are required between collection and analysis and that water-soluble organics dissolve in the water condensed in the unit when it is brought to room temperature. However, because everything that went into the cryocondenser can be recovered at cryogenic temperatures either by helium displacement or under vacuum, the types of analysis are limited only by the perseverance of the investigator and the amount of material available for analysis.

Appendix B

Analytic Techniques for Vapor-Phase Organic Air Pollutants

Understanding and effective regulation of the potential long-term biologic effects of vapor-phase organic pollutants at trace concentrations in the atmosphere will be possible only if appropriate analytic methods are developed. The chemical and physical instrumental methods for measuring this very broad range of organic chemical species have generally been restricted to colorimetry for the more reactive aldehydes and peroxidic species, gas chromatography (GC) with a flame ionization detector for hydrocarbons, flame photometry for organic sulfur compounds, electron capture for halogenated and nitrated species, and limited approaches for measuring the volatile ketones, alcohols, and acids.

The analysis of VPOP in ambient air with such sophisticated instrumentation techniques as high-resolution GC, mass spectrometry (MS), and combined GC and MS has been successful only for hydrocarbons and halogenated hydrocarbons. There has not been much success in the analysis of the oxygenated and nitrated chemical species. This results partly from the lack of adequate concentration procedures for these more reactive trace VPOP.

The essential first step in an accurate analysis is to obtain a sample that is representative and adequate (both in volume and in concentration). Inasmuch as both GC and MS require discrete samples for analysis, various preparation steps are necessary to concentrate the atmospheric contaminants into sample volumes compatible with the particular system's sample inlet requirements. It is important, when assessing the validity of reported data on the concentrations of atmospheric contaminants measured in ambient air, that the adequacy of sampling and preparation be considered, as well as the combined errors of the measurement technique and the calibration procedure. The purpose of this appendix is to describe the best approach to the analysis of atmospheric vapor-phase organic pollutants in trace amounts. A comprehensive review of all current analytic methods will not be undertaken here.

GAS CHROMATOGRAPHY

In measuring the trace contaminants that constitute the complex mixture of organic components in polluted air masses, air pollution scientists need methods that offer high specificity, high accuracy, and speed.

Since the original work of James and Martin,[630] the application of gas–liquid chromatography to the separation and identification of complex mixtures of organic materials has increased enormously. A wide variety of column types and packings are now used, extending from conventional packed columns to open tubular capillary columns, support-coated capillary columns, and, more recently, packed capillary columns. However, gas-chromatographic analyses of the hydrocarbon contaminants in polluted atmospheres have remained almost the exclusive realm of packed columns. This is unfortunate, because the classical packed columns (1/8–1/4 in. O.D.) do not provide sufficient resolution to separate adequately the broad range of components detected in urban atmospheres or to make the highly accurate retention-time measurements needed for identification purposes. Furthermore, the identification of the numerous compounds measured in the urban atmosphere by retention time is especially limited in the analyses of the higher-molecular-weight VPOP. A comparison of column characteristics relevant to VPOP analyses is given in Table B-1.

It is significant that, after more than 10 years of GC investigation of the VPOP measured in the urban atmosphere, there are no accepted standard referee methods for the analysis of the primary emission, including light hydrocarbons and the intermediate-weight hydrocarbons (C_{5-10} aliphatics, aromatics, oxygenated and halogenated hydrocarbons, etc.), and the many intermediate and terminal reaction products from the primary VPOP have not been accurately measured, primarily because of

TABLE B-1 Comparison of Column Characteristics for VPOP Analyses

Characteristic	Packed (1/8–1/4 in.)	Capillary (0.01 in.)	SCOT (0.02 in.)	Packed Capillary (0.02–0.03 in.)
Resolution	Low	Very high	High	Moderate
Number of separating phase/supports available	High	Low	Low	Moderate
Ease of fabrication	Good	Poor	Poor	Good
Prior use in VPOP studies	Large	Small	Small	Small
Durability	Very good	Poor	Very good	Good
Sample capacity	Large	Very small	Small	Moderate
Cost	Low	High	High	Moderate

insufficient sensitivity and the problem of surface adsorption of trace contaminants currently inherent in the techniques of GC, MS, and GC and MS combined that are available for the needed sophisticated analyses.

Low-Molecular-Weight Hydrocarbons

A standard referee method for light-hydrocarbon analyses is one of the important analytic tools lacking in air pollution study. At present, none of the many "operational" GC-column systems have demonstrated sufficient superiority to be accepted for preferred use by the many investigators performing daily GC analyses of light hydrocarbons in urban atmospheres. It would be especially desirable to use a method with the advantages of high-resolution GC. Up to now, the analysis of light hydrocarbons in the atmosphere has been mostly by packed columns of 1/8 in. O.D. with a wide variety of support materials and stationary phases. Most of these column-packing material combinations are tailored by the individual to be so specialized that duplication by other investigators of the GC-column system is very difficult, if not impossible. Therefore, there has arisen a multitude of individual procedures for the analysis of light hydrocarbons. Of course, the individuality of these measurements has been necessitated by the specific needs and the equipment available to the analysts.

There are too many published papers in this field to report them individually. However, several of the more popular columns in use are Porapak N for C_1 and C_2 hydrocarbons, dimethylsulfolane for C_{3-6} materials, and the Durapaks *n*-octane and β,β'-oxydipropionitrile (OPN) on Porasil C for C_{2-6} compounds. W. A. Lonneman (personal communication) has been successful in routinely analyzing ethylene, acetylene, and the C_{2-5} paraffins with a silica-gel column, although the breakthrough of water onto the column from the preparative sample freezeout loop has to be carefully guarded against.

Optimal GC separation and measurement of the VPOP in the atmosphere has been hindered not only by the low resolution inherent in packed columns but also by the use of isothermal analyses that do not fully utilize all the available column efficiency for maximal separation. The introduction by most GC instrument manufacturers of temperature programing capability, especially subambient oven control, offers a means of significantly increasing the resolution in packed columns. However, packed-column isothermal analyses of C_{1-5} hydrocarbons have been successfully applied to routine air pollution studies. These studies have focused their efforts on optimal resolution of compounds over a narrow range, such as ethylene from ethane and acetylene, allene from methylacetylene, and butenes from butanes. Unfortunately, complicated mixtures of liquid phases, the use of multiple columns, critical optimal temperature, precise flow characteristics, and, in many cases, the operation of two or more gas chromatographs are necessary to obtain these separations. The elaborateness of many of these GC-column systems precludes their use in mobile field laboratories.

The present Intersociety Committee method[614] for determining light hydrocarbons in the atmosphere uses β,β'-oxydipropionitrile on activated alumina packed in 10-ft, 1/8-in.-O.D. stainless-steel tubing. Unfortunately, the necessary resolution of ethane and ethylene is reduced with the use of concentrated ambient air samples of 100–300 ml, so that these two compounds are not separated sufficiently for accurate measurement. The resulting poor separation of ethylene from ethane in large air samples is responsible for the sparse use of this column.

An evaluation of the methods using low-resolution packed columns indicates that it would be desirable to incorporate the advantages of high-resolution GC in the analyses of light hydrocarbons. The major advantage to be gained would be rapid, high-resolution trace analysis of the C_{2-5} light-hydrocarbon air pollutant burden under conditions of one analysis. Specifically, a GC-column method is needed that would resolve, on one column in one analysis, the following light hydrocarbons: ethane, ethylene, acetylene, propane, propene, isobutane, *n*-butane, 1-butene, isopentane, *n*-pentane, and 1-pentene.

The recent development of organic stationary liquid phases bonded to porous silica beads reported by Halász and Sebastian,[508] commercially available as Durapak and Spherosils, promises to provide thermally stable column materials with reduced column bleed for lower detection limits. These materials also offer a way to construct more reproducible columns. This is especially important, in that the fabrication of column packing is a highly individualistic art and therefore difficult to duplicate from one laboratory to another. Present results indicate that, using subambient temperatures, 1/8-in. packed columns and 1/16-in. packed capillaries with OPN and *n*-octane on Porasil C have sufficient selectivity to separate all the C_{2-5} saturated and unsaturated chemical species relevant to air pollution measurements. Certainly, the need for a standard referee method of analysis of light hydrocarbons is great enough to warrant further development, with the objective of selecting an optimal column type.[997]

Intermediate-Molecular-Weight Hydrocarbons

The aromatic and aliphatic (C_6 and higher) VPOP compounds have been resolved by a more diverse selection of column types for their routine analysis, although generally open tubular columns have tended to dominate the analysis. Lonneman *et al.*[713] have reported separating aromatic hydrocarbons on a 300-ft, 0.06-in.-I.D. copper wall-coated open tubular (WCOT) column with *m-bis-*(*m*-phenoxyphenoxy) benzene and Apiezon-L at 70 C. This large-bore column is tolerant of larger sample loads than the more commonly used 0.01- and 0.02-in.-I.D. capillary WCOT columns. Adequate resolution and sensitivity for the alkylbenzenes associated with air pollution were obtained with this column on a routine analysis time schedule.

P. Groblicki (personal communication), Mayrsohn *et al.*,[814] Z. Tomaras (personal communication), and Belsky and Kaplan[94] have used temperature programing in conjunction with small-diameter (0.01-in.-I.D.) WCOT to achieve higher resolution of the atmospheric burden of C_{6-12} organics, also on a routine basis. However, the restrictive sample capacity of the 0.01-in.-I.D. capillary columns limits the air sample volume for analysis to 50 ml, which greatly curtails the lower sensitivity limits obtainable for trace analysis. Rasmussen and Holdren[1003] reported using a 200-ft, 0.02-in.-I.D. support-coated open tubular (SCOT) column with an OV-101 substrate operated in a subambient temperature program mode for routine analysis of C_{6-12} aliphatic and aromatic organics at trace (0.1-ppb) background concentrations. The SCOT column was chosen because of its inherent larger sample capacity than

0.01-in.-I.D. capillary columns, its proven durability, and its high resolution. This column has the advantages characteristic of open tubular and packed columns, without the great pressure drop of packed columns or the low sample capacity of capillary WCOT columns.[58]

One of the remarkable features of the analyses[1003] was the maintenance of the high resolution inherent in SCOT columns during the analysis of large (1–10 liters) air sample volumes. This was accomplished by transferring a "slug" sample from an external freezeout loop onto the head of the column and then zone-freezing it there, before initiating the subambient temperature program to obtain the increased column efficiency and therefore the higher resolution inherent in this low-temperature mode of operation. The use of the external freezeout loop apparently accommodates the excessive amounts of water in the large volume of air necessary for detection of the trace constituents. Also, the SCOT columns are more durable than standard capillary columns in the routine usage necessary for hourly air pollution analyses.

The use of packed columns for analysis of C_{6-9} aromatics and a variety of other atmospheric components has been optimized by E. R. Stephens and F. R. Burleson (personal communication), who reported good resolution of benzene and toluene from the xylenes, as well as acetone, using three 1/8-in.-O.D. columns in series: 10-ft, 5% 1,2,3-*tris*-(2-cyanoethoxy)propane; 5-ft, 5% Bentone 34 with 5% dinonylphthalate; and 8-ft, 10% Carbowax E-600 at 65 C. However, packed columns do not give the analyst the same important advantage that high-resolution columns provide for routine analysis, namely, an interim solution to the problem of better identification of the 50–100 (or more) readily measured hydrocarbons in urban atmospheres.

High-Molecular-Weight Hydrocarbons

In view of the many studies of the hydrocarbons in urban atmospheres, it is surprising how little has been published regarding the broad spectrum of organic substances expected in these atmospheres. Kaiser[660] has postulated that, at the parts-per-billion concentration, the number of potential organic chemicals that may be present in urban air is greater than 10^5. Although higher-molecular-weight organic compounds in particles have been studied extensively, the wide range of C_{10-20} volatile substances present in polluted atmospheres has been practically disregarded. This is especially true for the ambient air analyses of the tricyclic (C_{14}) and tetracyclic (C_{18}) polynuclear aromatics that are not collected in the standard methods used for measurement of particulate organic material. Also, very few analyses of naphthalenes and substituted naphthalenes in polluted atmospheres have been reported.

Stevens and O'Keeffe,[1162] in their report on the modern aspects of air pollution monitoring, mentioned methane as the only organic compound being studied *per se*. Is it to be inferred that routine analyses monitoring VPOP are not warranted, not possible, or not yet possible? Recently, instrumental field systems for automated GC analyses of methane, ethylene, ethane, and acetylene have become commercially available.

Altshuller's review[17] of the use of GC in air pollution studies reported that the majority of papers dealt with low-molecular-weight hydrocarbons, while recognizing that the higher-molecular-weight organic compounds represented very complex mixtures, possibly involving hundreds of compounds. Altshuller observed that most investigators reported on improvements and modifications of existing techniques, rather than devoting their studies to in-depth, long-term analyses of the components in the atmosphere.

Obviously, the trace character of the materials available for study in the atmosphere has intensified the difficulties of conducting routine studies. Nevertheless, there are now appropriate sampling techniques for VPOP for qualitative and quantitative analyses, commercially available high-resolution columns, and GC–MS systems with the necessary data-reduction equipment and interfacing technology to realize the full potential of the separation power of high-resolution columns working in the nanogram range.

MASS SPECTROMETRY

Mass spectrometry, coupled with appropriate auxiliary techniques (such as GC, computer-assisted data processing, and specific-ion detection), has the potential to be used to advantage to determine the various relevant organic air pollutants present in the nanogram to picogram range. MS is advantageous for use in gaseous air pollutant analyses for the following reasons: It has relatively uniform high sensitivity for all chemical species that can be volatilized (in contrast with the electron-capture GC technique, in which differences in sensitivity of 10^5 or greater are observed); it has excellent selectivity from interfering materials by use of specific-ion detection or high resolution (as opposed to the nonpositive identification of chemical species based on relative retention times associated with GC); and it can identify unexpected compounds easily.

The application of MS to model problems of environmental contamination has been described by Abramson.[3] However, the actual use of the technique in authentic air pollution problems is very limited. This limitation is directly related to the high cost of the mass spectrometer and the dedicated-computer system. An additional factor has been the difficulty of adequate sample preparation of discrete trace gases in the presence of an excessive overburden of water and the hitherto adequate information content available in other, less sophisticated and less expensive methods. However, present concern for more specific information on the types of products formed from the hydrocarbons reacting in the atmosphere and a need to know more about the persistence or chemical degradation—in air, water, soil, and biologic systems—of primary emission and its products require the use of the highly sophisticated analytic capabilities that MS affords.

Of particular importance in the use of MS is the flexibility in the type of data that can be obtained from analyses that incorporate the high sensitivity and selectivity of the mass spectrometer. In addition, many extra capabilities are afforded by the data acquisition and processing systems now available. For example, computer-reconstructed mass chromatograms are possible when the total number of ions in each scan is plotted against the scan number. The major peaks resolved at particular scan numbers can be entered into a library search routine for scanning with the appropriate search algorithm for identification. In addition, the data processor can construct a significant peak table, which is an ordered listing of various masses with respect to their relative abundance in each spectrum, for aiding in the identification process. Other important aspects of the computer-based data acquisition and processing system are the high volume of data that can be recorded continuously, the construction of library search algorithms, and the background subtraction that is available for analyses of complex systems with small trace vapor-phase samples.

Much lower detection limits are made possible by using single-ion monitoring, rather than scanning. Focusing the mass spectrometer on a strong mass signal in the mass spectrum has permitted detection limits of as little as 10 picograms of organic lead compounds in the atmosphere.[744] To obtain maximal sensitivity, the appropriate molecular ion selected as the diagnostic species may be enhanced by operating the mass spectrometer at lower ionizing voltages, to suppress the formation of fragment ions formed from background molecules, which often interfere with mass-number characterization.

An alternative approach to elegant chromatographic separation of many components in a mixture is the use of the superior resolving power of the high-resolution mass spectrometer to determine the constituents without separation of the mixture by GC. An advantage of high-resolution MS is its potential for determining, from an exact mass, the chemical formula for the ion.

Very little has been done with high-resolution MS in determining the constituents of VPOP. However, an interesting application of high-resolution MS to VPOP analyses has been accomplished by Schuetzle *et al.*[1086] A high-resolution MS was interfaced with a digital computer and adapted for multicomponent analyses of air pollutants. The major effort of the research was the development of a sophisticated computer program for identifying the inorganic and organic constituents in airborne particles. However, Schuetzle *et al.* were also able to introduce directly into the mass spectrometer the gaseous pollutants collected on Chromosorb 102 and desorbed by a thermal–vacuum technique.

One of the problems of using a high-resolution instrument is that data acquisition is complicated by the volume and rate of the incoming data. Also, data reduction is a difficult mathematical problem on a small computer, because of the computational precision required. Nevertheless, this new method for characterizing atmospheric VPOP certainly warrants further investigation.

A traditional method of performing high-resolution experiments is peak-matching by use of an oscilloscope to monitor the output from the mass spectrometer, which is being slowly alternated (approximately once every second) between two masses—one a reference mass (typically a perfluorokerosene) and one the unknown mass. Exact mass is determined by superimposing the position of the unknown peak on the position of the reference mass on the oscilloscope and reading the difference in mass from a calibrated dial. Another traditional method for gathering high-resolution ion data is scanning at 10–100 sec/decade. The latter method is too insensitive for satisfactory detection of GC effluents containing trace constituents.

High-resolution single-peak monitoring of GC effluents provides much of the definitive characteristics of a high-resolution analysis, with sensitivity limits even better than those of low-resolution scanning. The method is to alternate the two channels of the peak-matching unit between a reference mass and the unknown molecular ion with correct centering. Detection limits below 0.5 ng have been reported with this technique.[3]

The power inherent in MS as a tool for sophisticated analyses of environmental contaminants has recently been further increased by the development of a mass spectral search system that can be used by anyone with a teletype and an acoustic coupler. The program search is available from the National Institutes of Health at no cost to the user.[971] This interactive conversational system runs on a DEC PDP-10 time-sharing computer. Use of the programs and system is simple, and no knowledge of how the programs work or of program languages is required. About 9,000 spectra are in the data base, and there are plans to add about 5,000 more from the Aldermaston (England) collection. Experience with the system has shown that much information can be learned, even if the spectra sought are not on file. A manual gives directions on the use of the system, and a simple phone call brings the system into play. Programs now available performe the following: search for peaks, search for molecular weight, search for peaks with molecular formula, search for peaks with molecular weight, search for complete or partial molecular formula, search for molecular weight with molecular formula, print out peaks and intensities, comment and complain, and enter new spectra.

GAS CHROMATOGRAPHY–MASS SPECTROMETRY

The dominant instrument, both in total use and in projected growth, for measuring VPOP is the gas chromatograph. This is no surprise; since its inception in 1953, chemists all over the world have been quick to grasp the potential of GC. The intense activity continues today, with application to pollution analysis and control. The simplicity of the technique and its almost unlimited capacity to solve seemingly insoluble problems have contributed much to its predominant position.

Nevertheless, GC as an analytic technique is severely limited by the scarcity of standard reference methods to ensure proper standardization. This is especially critical when identification must rely solely on retention time and detector response for compound identification. The basic nature of MS removes many of these ambiguities of identification when used as the GC detector, by providing identification of the components resolved by GC in terms of their mass spectra.

Interfacing gas chromatographs to other instruments, especially computers and mass spectrometers, has particularly enhanced the gas chromatograph's present importance and potential for trace atmospheric analyses. The GC–MS system has found such wide acceptance in trace analyses that the major interest now in mass spectrometers is for this combined system. Gas chromatographers experienced in the technique quickly conclude that a dedicated computer is almost a necessity, so much so that an integrated GC–MS–computer system is the preferred analytic instrument.

The successful applications of the GC–MS system have essentially been in the biomedical and space sciences, in the food-flavor industry, in pollutant analyses with respect to pesticides, and in connection with the high-molecular-weight polycyclic organic materials recoverable from high-volume glass-fiber (Hi-Vol) filters. Unfortunately, pollution analyses of VPOP with GC–MS systems have been very few.

The most noteworthy contribution to VPOP analyses with GC–MS systems is that of Grob and Grob,[497] who reported using capillary columns in a GC–MS investigation of C_{6-20} organic compounds present in the urban atmosphere of Zurich, Switzerland. Most of the 108 substances identified were aliphatic and aromatic hydrocarbons. Benzaldehyde and several of its alkyl derivatives, which may be oxidation products of aromatic hydrocarbons, were also found.

To identify the trace components eluted from their high-resolution capillary columns, Grob and Grob reported that GC–MS was indispensable. The two most important considerations in their analyses were the availability of only a limited quantity of material for analysis and the necessity of preventing the separated substances from mixing again before reaching the ion source in the mass spectrometer; the higher the GC resolution of the complete mixture, the more important the latter is.

The means of interfacing GC to MS is one of the most difficult technical problems encountered. Essentially, the column effluent at atmospheric pressure must be delivered to the MS source, which is at high vacuum. The interfacing device must ensure transfer of the column eluates quantitatively and without degradation of the GC resolution. Therefore, the purpose of the interface is to conserve the sample—minimal loss of sample with maximal removal of the carrier gas and no significant loss of sample components because of interaction of the sample and the interfacing separator. Specifically, the interface must enrich the sample: carrier gas ratio while reducing the gas flow to the ion source. The pressure at the ionization source must be maintained at 10^{-5} torr or lower to ensure optimal operation and to prevent burnout of the filaments in electron impact sources. Chemical ionization of high-pressure MS is not limited by this high-vacuum-source problem; however, it also is influenced by inherent interface-related losses of substances or reduced GC resolution.

To overcome these limitations, the column flow rates used by Grob and Grob[497] were optimized so that the total column effluent was delivered to the ion source of the mass spectrometer for improved resolution and sensitivity. The technical details are described by Schulze and Kaiser.[1088] From the standpoint of conservation and precise quantitative control of the sample, the best interface is the avoidance of any interface separators or splitting devices. Direct coupling ensures that the GC resolution is fully retained; all the effluent is available to the MS, enabling it to be a more sensitive detector than the flame ionization detector.

Henderson and Steel[551] also reported recently that GC–MS instruments have been used predominantly with packed columns and that, with few exceptions, the advantages of coupling high-resolution columns to a mass spectrometer have not been realized. They concluded that the drawback to using high-resolution columns in GC–MS systems involves the limitations of the interface, which result in loss of resolution and sensitivity. Ryhage and Wikström[1046] recently reviewed the problems of interfacing GC with MS for a wide variety of separators.

To overcome the limitation of the separator, Henderson and Steel[551] developed a system that allows the introduction of the total GC effluent, up to 20 ml/min, directly into the ion source of the mass spectrometer. The system has been used effectively with high-resolution columns on a wide range of sample types, including fixed gases and C_{10-40} hydrocarbons. The direct coupling of the GC column effluent to the ion source of the mass spectrometer is made possible by high-speed differential pumping of the source and analyzer with all-stainless-steel diffusion pumps.

The effects of flow rate on ion source and analyzer pressures, overall sensitivity, and resolving power of the system were evaluated and reported. The sensitivity of the GC–MS varied by only a factor of 2 over a helium flow range of 1.1–7.2 ml/min, measured with cholesterol trimethylsilylether at a sample flow rate of 10^{-11} g/sec. The resolution was not significantly changed when the separation of a doublet at nominal mass 156 (separation, 136.38 millimass units) was monitored as a static system, and then a dynamic system with helium flows of 2.5 and 7.2 ml/min.

The concept of a differentially pumped mass spectrometer removes the need to maintain the ion source at an extremely low pressure to preserve resolution. Grob and Grob,[497] Schulze and Kaiser,[1088] and Henderson and Steel[551] have provided the logical extension of this concept by using diffusion pumps of much larger capacity to handle the GC effluent while maintaining low source pressures. This application should significantly advance the use of GC–MS instruments for pollution analysis, especially the hitherto forgotten sector of C_{10-22} VPOP.

The preceding discussions have dealt almost exclusively with the universally used electron-impact (EI) MS ionization source. The exciting new technique in MS is the development[888] of the chemical ionization (CI) source. Bonelli and Story[121] reviewed the features of the EI with the CI source and concluded that CI offers the advantages of simpler cracking patterns, intense quasimolecular ions, and easy-to-interpret spectra. Fales[387] recently reviewed the newer ionization techniques available to MS and concluded that CI is possibly the most significant new source for general MS work.

The CI principle of operation is a form of high-pressure MS (0.5–1.5 torr) in which the sample components react with reactant ions. Methane is the most common source of the reactant ions, which are formed by a combination of electron impact and ion–molecule reactions. The reaction of these reactant ions with the material to be chemically ionized occurs by ion–molecule reaction. However, it is possible to use many different gases as reactants and thus produce spectra from reactant ions of different energies.

In interfacing GC to MS with a CI source, the same two problems that confront the use of EI–MS systems must be overcome: high gas flow rates and low sample:carrier gas ratio. However, in the CI–MS, the low sample:carrier (reactant) gas ratio is an asset, because, with a CI source, the reactant gas:sample gas ratio must be at least 100:1. It is therefore advantageous to consider not using a separator or splitter to interface the GC effluent to the MS. The reality of directly introducing the total GC effluent to the CI source promises to extend the operational sensitivity of this system to the subnanogram range for VPOP analyses.

Appendix C

Airborne Contaminants*

Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit, a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.

. . .

Threshold limit values refer to time-weighted concentrations for a 7 or 8-hour workday and 40-hour workweek. They should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous concentrations. . . .

Threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance;

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* Excerpted from American Conference of Governmental Industrial Hygienists.[39(pp.1–3)]

protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may form the basis for others.

The amount and nature of the information available for establishing a TLV varies from substance to substance; consequently, the precision of the estimated TLV is also subject to variation and the latest *Documentation* should be consulted in order to assess the extent of the data available for a given substance.

. . .

In spite of the fact that serious injury is not believed likely as a result of exposure to the threshold limit concentrations, the best practice is to maintain concentrations of all atmospheric contaminants as low as is practical.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, (2) in the evaluation or air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures, (4) as proof or disproof of an existing disease or physical condition, or (5) for adoption by countries whose working conditions differ from those in the United States of America and where substances and processes differ.

Appendix D

Toxicity Data on Occupational Exposure to Selected Substances*

ACETALDEHYDE

Most of the subjects of Silverman, Schulte, and First[1115] experienced some eye irritation at 50 ppm, but were willing to work an 8-hr day in the presence of 200 ppm.

ACETIC ACID

Vigliani and Zurlo[1252,1253] reported that workers exposed for 7–12 years to 60 ppm and for 1 hr to 100–260 ppm had no injury except slight irritation of the respiratory tract, stomach, and skin. Parmeggiani and Sassi (cited in Fassett[389]) found conjunctivitis, bronchitis, pharyngitis, and erosion of exposed teeth, apparently in the same workers.

ACETONE

Vigliani and Zurlo[1252] found chronic respiratory tract irritation and dizziness in workers inhaling 1,000 ppm 3 hr/day. F. L. Oglesby *et al.*

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* Adapted from American Conference of Governmental Industrial Hygienists.[38]

(unpublished data) concluded, as a result of extensive studies on thousands of workers exposed to acetone in the manufacture of cellulose acetate yarn, that 200–400 ppm was detectable only on immediate contact, that 700 ppm cannot be detected after a brief period, and that 2,500–3,000 ppm caused, at most, only minor irritation of the eyes and nose.

ACETYLENE

The inhalation of 100,000 ppm has a slight intoxicating effect on man; marked intoxication occurs at 200,000 ppm, incoordination at 300,000 ppm, and unconsciousness within 5 min of exposure to 350,000 ppm.[454]

ACROLEIN

Prentiss[981] reported that concentrations as low as 0.25 ppm may cause some irritation, and 1 ppm is almost intolerable and can cause lacrimation and marked eye, nose, and throat irritation within 5 min.

BENZENE

Bowditch and Elkins[129] concluded that, of 11 deaths caused by exposure to benzene, three resulted from concentrations of 200 ppm or more, four from concentrations of more than 100 but less than 200 ppm, and three from concentrations estimated to be below 100 ppm (the concentration in one case varied). Greenburg *et al.*[489] described nine cases of benzene poisoning, with one death, in the rotogravure printing industry; of 48 air analyses, 20 showed less than 100 ppm. Savilahti[1069] found that 107 of 147 workers in a shoe factory had blood abnormalities; the source of benzene was cement, and the concentrations were reported as 318–470 ppm; one death occurred. Winslow[1341] reported blood changes in workers where concentrations of benzene vapor below 100 ppm were found. Heimann and Ford[549] found one death and three cases of blood changes where air analysis for benzene showed a concentration of 105 ppm. Wilson[1333] reported three fatal cases in a plant where the average concentration of benzene vapor was 100 ppm. Hardy and Elkins[528] reported one death and several cases of blood changes in a plant where repeated air analyses indicated benzene vapor concentrations of about 60 ppm. Blaney[115] found little evidence of benzene intoxication in a group of 90 workers regularly exposed to 25 ppm for about 13 years. Pagnotto *et al.*[950] found that rubber-spreaders were exposed to benzene vapor at 6–25 ppm; some blood studies showed abnormalities, but no apparent correlation with exposure; none of this group developed serious blood dyscrasias.

1,3-BUTADIENE

Two human volunteers breathed 8,000 ppm for 8 hr with no effects other than slight irritation of the eyes and upper respiratory tract.[454]

n-BUTANOL

Tabershaw *et al.*[1183] reported eye irritation in workmen exposed to concentrations above 50 ppm, but no systemic effects below 100 ppm. Nelson *et al.*[915] reported mild irritation at 25 ppm, which became objectionable and was followed by headaches at 50 ppm.

BUTANONE (METHYLETHYLKETONE)

Elkins,[359] reporting on industrial exposures, noted that human exposures to 700 ppm in the air were without evidence of permanent ill effects. Smith and Mayers[1125] reported that dermatoses were common among workers handling butanone; some workers exposed to 300–600 ppm complained of numbness of the fingers and arms.

tert-BUTYL ALCOHOL

Contact with human skin produced only slight erythema and hyperemia.[939]

CROTONALDEHYDE

Skog[1124] reported that crotonaldehyde produced symptoms similar to those of acrolein. L. D. Pagnotto (personal communication) reported a case of sensitization in a laboratory worker who handled small amounts of crotonaldehyde. Rhinehart[1017] found that exposure to 45 ppm was very disagreeable, and conjunctival irritation was observed; at 15 ppm, the odor was strong, but not intolerable, and no eye irritation was observed after brief exposures.

CYCLOHEXANE

Gerarde[455] reported that 300 ppm was detectable by odor and somewhat irritating to the eyes and mucous membranes.

CYCLOHEXANOL

Browning[161] reported one case of suspected intoxication—characterized by vomiting, coated tongue, and slight tremors—in a worker engaged in spraying leather with a preparation that contained butylacetate and cyclohexanol.

1,2-DICHLOROPROPANE (PROPYLENE DICHLORIDE)

1,2-Dichloropropane causes mild irritation on the open skin and some eye irritation.[615]

ETHYLBENZENE

Experimental exposure of six men showed that a concentration of 1,000 ppm was very irritating to the eyes, but that the irritation decreased on continued exposure, until, after a minute or two, it was scarcely noticeable; at 2,000 ppm, one observer stayed in the atmosphere 5 min and found that irritation to the eyes and throat gradually disappeared, but that vertigo developed.[456(p.1232)]

ETHYLENE DIBROMIDE (1,2-DIBROMOETHANE)

Kochmann[703] reported a case of subacute poisoning due to the accidental breathing of vapors in a plant; he said that a concentration of 50 ppm could be dangerous to man. Olmstead[943] described a fatality caused by the ingestion of several capsules containing a total of 4.5 ml of ethylene dibromide; autopsy findings were hepatic necrosis and renal damage.

ETHYLENE OXIDE

Joyner,[655] in a study of 37 chemical operators who worked in ethylene oxide production for over 10 years, failed to detect any evidence of ill effects due to exposure to this gas; in general, long-term exposure appeared to be to 5–10 ppm, with very few tests indicating concentrations above 50 ppm.

FORMALDEHYDE

Henderson and Haggard[552(p.128)] and Elkins[358(pp.116,231)] reported that formaldehyde irritates the eyes, respiratory tract, and skin. Henderson and Haggard noted that persons may become more susceptible on repeated exposure. Elkins also reported complaints from persons exposed to a maximal concentration of 5–6 ppm; eye irritation was noted in "unacclimated" persons exposed to much lower concentrations. Morrill[869] and Bourne and Seferian[127] reported irritation in the form of itching eyes, dry and sore throats, disturbed sleep, and unusual thirst on awakening in a few workers exposed to 1–2 ppm. Shipkowitz,[1110] in an environmental study of formaldehyde vapor emission in the permanent-press fabrics industry (eight plants), based on workers' complaints, revealed formaldehyde concentrations ranging generally from 0.3 to 2.7 ppm (sewing area), with an average of 0.68 ppm; complaints consisted of annoying odor, constant prickling irritation of the mucous membranes, and disturbed sleep. Harris[530] reported that the only positive finding among 25 men engaged in the manufacture of urea–formaldehyde and phenol–formaldehyde resins, in concentrations well below 10 ppm, was dermatitis in four of the men.

FORMIC ACID

J. P. Fahy and H. B. Elkins (unpublished data) reported that workers exposed to formic acid and acetic acid, averaging 15 ppm, in a textile plant complained of nausea; such concentrations were judged to be very irritating.

HEPTANE

Patty and Yant[964] reported that 1,000 ppm caused slight dizziness in man after exposure of 6 min; higher concentrations for shorter periods resulted in marked vertigo, incoordination, and hilarity; brief exposures (4 min) to 5,000 ppm produced complaints of nausea, loss of appetite, and a gasoline taste that persisted for several hours after exposure.

HEXANE

Patty and Yant[964] reported that 10 min of exposure to 5,000 ppm resulted in dizziness and a sensation of giddiness. Drinker *et al.*[335] found slight nausea, headache, and eye and throat irritation after exposure to 1,400–1,500 ppm. Nelson *et al.*[915] found no irritation at 500 ppm in unacclimated subjects.

2-HEXANONE (METHYL-2-BUTYLKETONE)

Schrenk *et al.*[1078] exposed human volunteers for several minutes to 1,000 ppm, which produced moderate eye and nasal irritation.

ISOVALERALDEHYDE (2-METHYLBUTYRALDEHYDE)

Wilkinson[1313] reported that exposure of chemists to high concentrations resulted in nausea, vomiting, headache, and weakness.

METHANOL

McNally[839] stated that occupational methanol poisoning has often caused death or blindness; several cases resulted from work in confined spaces, e.g., varnishing beer vats where the concentration was 500–6,000 ppm. Browning[162(pp.311–323)] stated that cases of chronic poisoning from repeated exposure to methanol vapor were manifested by conjunctivitis, headache, giddiness, insomnia, gastric disturbances, and failure of vision. Henson[554] reported that workers exposed to 300 ppm during the operation of duplicating machines complained of headaches.

METHYLBROMIDE

Von Oettingen[1257] recorded 47 fatal and 174 nonfatal cases of methylbromide intoxication. Hine[570] reviewed 10 cases (two fatal) where the concentration was 100 ppm. Ingram[605] reported that tests made in date-processing and -packing houses, where a number of employees had been stricken, showed concentrations ranging from 100 to over 1,000 ppm. Watrous[1286] described nausea, vomiting, headache, and other symptoms of mild systemic poisoning in workers exposed for 2 weeks to concentrations below 35 ppm.

2-METHYL-1-BUTENE-3-ONE (METHYLISOPROPENYLKETONE)

Human experience has shown this ketone to be a definite skin irritant; several minutes may elapse before blistering and pain develop (Biochemical Research Laboratory, Dow Chemical Co., unpublished data).

PENTANE

Human exposures for 10 min to 5,000 ppm did not cause mucous membrane irritation or other symptoms.[964]

2-PENTANONE (METHYL-*n*-PROPYLKETONE)

Yant, Patty, and Schrenk[1350] reported that 1,500 ppm had a strong odor and was markedly irritating to the eyes and nasal passages of humans.

PHENOL

Intermittent industrial exposure (5–10 min/hr) inside a conditioning room for phenol-impregnated asbestos resulted in marked irritation of the nose, throat, and eyes; the average phenol concentration in the room was 48 ppm, although formaldehyde (8 ppm) was also found; workers at the same plant, continuously exposed during winding operations (average concentration, 4 ppm), experienced no respiratory irritation (Connecticut Bureau of Industrial Hygiene, unpublished data).

PROPANE

Wolf and Menne[1344] reported the case of a man who was exposed to propane (concentration unknown) from a leaking tank in an automobile;

he exhibited colicky pains, stupefaction, disorientation and excitement, narrowing of the pupils, and marked salivation; he recovered, but suffered from retrograde amnesia. Gueffroy[498] reported a study of five women workers who were exposed to propane that escaped through improper pipe fittings; headache, numbness, a "chilly feeling," and vomiting were reported.

TOLUENE

Longley and co-workers[778] reported that 26 men were overcome by toluene vapor aboard ship; there were no deaths or serious aftereffects. Wilson[1334] found that, among workers exposed to toluene at less than 200 ppm, there were some complaints of headache, lassitude, and nausea, but that physical findings were essentially negative. Knox and Nelson[702] described an instance of permanent encephalopathy involving a man who inhaled toluene regularly for over 14 years. Powars[978] reported six cases of aplastic anemia, one of them fatal, among glue-sniffers. Von Oettingen and co-workers[1258] found that human subjects exposed to 200 ppm suffered slight but definite changes in muscular coordination. Ogata *et al.*[940] found that experimental human subjects exposed to 200 ppm for 7 hr showed prolongation of reaction time, decreased pulse rate, and decreased systolic blood pressure.

TRIMETHYLBENZENE

Bättig *et al.*[86] described human exposure to two isomers of trimethylbenzene—mesitylene and pseudocumene. Workers exposed for a number of years to vapor concentrations of 10–60 ppm had symptoms of nervousness, tension, and anxiety and asthmatic bronchitis; in addition, the peripheral blood showed a tendency to hypochromic anemia and a deviation from normal in coagulability.

m-XYLENE

Gerarde[453] listed headache, fatigue, lassitude, irritability, and gastrointestinal disturbances—such as nausea, anorexia, and flatulence—as the most common symptoms among workers exposed to xylene. Browning[162(pp.77–89)] recorded reports of gastrointestinal and neurologic disturbances and injury to heart, liver, kidneys, and nervous system among workers exposed to xylene; in addition, she noted a number of reports of blood dyscrasias, some of them fatal, associated with xylene exposures. De Oliveria[306] described the death from aplastic anemia of a lithographer who used xylene for several years. Goldie[477] reported a patient who had an apparent epileptiform seizure after relatively brief exposure to xylene vapor.

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