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FREE RADICAL CHEMISTRY OF α-HYDROPEROXYDIAZENES: SYNTHETIC APPLICATIONS AND MECHANISTIC STUDIES

by

Emmanuel Yaw Osei-Twum, B.Sc., M.Sc.

A Thesis
Submitted to the School of Graduate Studies in
Partial Fulfillment of the Requirement for the
Degree
Doctor of Philosophy

McMaster University

FREE RADICAL CHEMISTRY
OF α-HYDROPEROXYDIAZENES

To the Memory of my Parents

and

to Adwoa Asantewaa.

DOCTOR OF PHILOSOPHY (1984)

McMASTER UNIVERSITY
Hamilton, Ontario

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ABSTRACT

The structures of the products of autoxidation of hydrazones were first established in the early 1950's. Although those compounds have been known for many years, relatively little is known about their chemistry. Recent reports indicate that they can be used as oxidizing agents for a number of organic substrates and as sources of hydroxyl and carbon-centered radicals. The free radical chemistry of the title compounds is the main subject of this thesis.

Alkyl(1-hydroperoxy-1-methylethyl)diazenes (28) [$(CH_3)_2C(OOH)N{=}NR$: a, R = CH_2CF_3; b, R = $CH_2CH_2OCH_3$; c, R = $CH_2CH_2OC_6H_5$; e, R = $CH(CH_3)_2$; f, R = $C(CH_3)_3$; g, R = $CH_2C_6H_5$] and phenyl(1-hydroperoxy-1-methylethyl)-diazene, 28d, were prepared in solution by autoxidation of the corresponding hydrazones of acetone. These compounds show broad bands between 3600 and 3200 cm^{-1} in their infrared spectra. The intensities of the bands decrease at different rates with decreasing hydroperoxydiazene concentration indicating the presence of hydrogen-bonded species.

Thermolysis of 28 in enol ethers produces carbonyl compounds; thus 28b decomposed in 1-ethoxyethylene (ethyl vinyl ether) and in 2-methoxypropene to give 4-methoxybutanal and 5-methoxy-2-pentanone, respectively. Yields ranged between 50% and 70%. In some alkenes the compounds decompose to give alcohols. For example, 28a decompose in 1,1-diphenylethylene to give 45% of 1,1-diphenyl-4,4,4-trifluorobutanol.

Other alkenes, particularly those that are highly hindered, give hydroalkylation products and epoxides. For example, decomposition of 28a in bicyclo[2.2.1]hept-2-ene (norbornene) leads primarily to formation of 2-(2,2,2-trifluoroethyl)norbornane and exo-2,3-epoxynorbornane.

The reactions of 28 in olefinic substrates involve free radical intermediates. Products formation takes place via radical chain hydroxyalkylation and radical chain hydroalkylation. The chain-initiation step involves the unimolecular decomposition of the hydroperoxydiazene to give alkyl and hydroxyl radicals with concomittant formation of nitrogen and acetone.

In the case of hydroxyalkylation, the first chain-propagating step involves addition of the alkyl radical to the double bond. The adduct radical so formed chain-transfers by inducing the decomposition of 28 at the hydroperoxyl oxygen. According to this mechanism, the first-formed products from enol ethers are hemiacetals and hemiketals which do not survive the reaction conditions but decompose to the corresponding carbonyl compounds.

In hydroalkylation reactions, the sterically crowded alkyl radical, formed by addition of R· to the hindered alkene, propagates by abstracting the hydroperoxyl hydrogen to generate α-azoperoxyl radical and alkane. The peroxyl radical, in the next step, adds to the alkene and the adduct β-peroxyalkyl radical undergoes intramolecular induced decomposition by γ-scission to give the epoxide. In less reactive, and in hindered alkenes, additions seem to be slow and that leads to very poor yields of epoxide.

Evidence for the mechanisms is presented and discussed.

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TABLE OF CONTENTS

Page

ABSTRACT iii

ACKNOWLEDGEMENTS iv

CONTENTS viii

LIST OF TABLES xi

LIST OF FIGURES xiii

INTRODUCTION 1

I1. GENERATION OF FREE RADICALS 3

I1.1. Thermolysis 4

I1.2. Radiation-Induced Bond Homolysis 6

I1.3. Electron Transfer Reactions 8

I2. DETECTION OF FREE RADICALS 9

I2.1. Electron-Spin Resonance Spectroscopy 9

I2.2. Spin Trapping 13

I3. FREE RADICAL REACTIONS 19

I3.1. Radical Addition Reactions 20

I3.2. Radical Substitution at Hydrogen and Oxygen 32

I3.3. Autoxidation 35

I3.4. Free Radical Rearrangements 38

I4. ORGANIC HYDROPEROXIDES 42

I5. AZO COMPOUNDS 47

Page

I5.1. Acyclic Azoalkanes 47
I5.2. α-Hydroxydiazenes 54
I5.3. α-Hydroperoxydiazenes 57

RESULTS AND DISCUSSION 61
RD1. SYNTHESIS AND PROPERTIES OF α-HYDROPEROXYDIAZENES 61
RD1.1. Synthesis 61
RD1.2 Physical Properties 67
RD2. CHEMISTRY OF α-HYDROPEROXYDIAZENES 74
RD2.1. Synthetic Applications 74
RD2.2. Mechanistic Studies 92

EXPERIMENTAL 139
E1. GENERAL 139
E2. SYNTHESIS 141
E3. THERMOLYSIS 145
E3.1. Thermolysis of Hydroperoxydiazenes in Unsaturated Substrates 145
E3.2. Kinetics 146
E3.3. Spin Trapping 149
E4. INFRARED STUDIES 149

APPENDIX I. SPECTRA OF MINOR PRODUCTS 150
APPENDIX II. KINETIC METHODS 160
AII.1. Treatment of First-Order Reactions 160

Page

AII.2. Treatment of Half-Order Reactions 162

REFERENCES 172

LIST OF TABLES

Page

1. Arrhenius Parameters for H-Abstraction from Alkanes by Methyl Radicals at 164°C 26
2. Arrhenius Parameters for H-Abstraction from Substituted Methanes by Methyl Radicals at 164°C 27
3. Bond-Dissociation Energies 34
4. Energies of Activation for Decomposition of 15 49
5. Data on the Decomposition of 18 50
6. Secondary Deuterium Isotope Effects in 18a and 18b 51
7. Kinetic Effects for Pyrolysis of Compound 19 52
8. Differences in Free Energy of Activation Between Symmetrical and Unsymmetrical Diazenes 53
9. ^{1}H NMR Spectra of Hydrazines (H_2NNHR) 62
10. Spectra of Acetone Hydrazones ($(CH_3)_2C=N-NHR$) 63
11. Spectral Data of α-Hydroperoxydiazenes ($(CH_3)_2C(OOH)N=NR$) 68
12. Hydroxytrifluoroethylation of Unsaturated Compounds 76
13. Hydroxy-2-methoxyethylation of Unsaturated Compounds 78
14. Hydroxy-2-phenoxyethylation of Unsaturated Compounds 80
15. ESR Parameters for Spin Adducts 38 101
16. Rate Constants for the Unimolecular Decomposition of $(CH_3)_2C(OOH)N=NR$, 28, at 50°C in Benzene 117

Page

17. Calculated Lifetimes, τ, of Diazenyl Radicals (R-N=N·) at 298°C 120

18. Products and Yields from Reactions of 28 and of ^{2}H-Labelled 28 with Norbornene 134

19. Products and Yields from Reactions of 28 and of ^{2}H-Labelled 28 with 3,3-Dimethyl-1-butene 138

A1. Raw Kinetic Data for Unimolecular Decomposition of 28 in Benzene at 50°C 165

A2. Raw Kinetic Data for Unimolecular Decomposition of 28 in Benzene at 50°C 166

A3. Raw Kinetic Data for Unimolecular Decomposition of $(CH_3)_2C(OOH)N{=}NCH_2CH_2OCH_3$ in Benzene in Presence of Norbornene at 50°C 167

A4. Raw Kinetic Data for the Half-Order Reactions of 28b,c in Ethyl vinyl Ether at 50°C 171

LIST OF FIGURES

Page

1. Electron Spin Energy Levels as a Function of External Magnetic Field Strength 11
2. Energy Level Diagram for $S = \frac{1}{2}$, $I = \frac{1}{2}$ 12
3. IR Spectra of 28c in CCl_4 Showing the O-H Band ($3400\ cm^{-1}$) with Decreasing Concentration 71
4. Mass Spectrum of Product Identified as 4-Hydroxy-2-(2-phenoxyethyl)butanal 85
5. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazyl-2,2,2-trifluoroethylnitroxyl Radical 95
6. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazyl-2-methoxyethylnitroxyl Radical 96
7. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazylphenylnitroxyl Radical 97
8. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazylisopropylnitroxyl Radical 98
9. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazyl-t-butylnitroxyl Radical 99
10. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazylbenzylnitroxyl Radical 100
11. Kinetics of Decomposition of $(CH_3)_2C(OOH)N{=}NCH_2CH_2OCH_3$ in Presence of TMPO 103

Page

12. Kinetics of Decomposition of $(CH_3)_2C(OOH)N=NR$ in Absence of TMPO 104

13. ESR Spectrum of (2,4-Diphenyl-1-methyl)pyrazyl-(1-ethoxy-4-phenoxy)butylnitroxyl Radical 106

14. Kinetics of Unimolecular Decomposition of $(CH_3)_2C(OOH)N=NR$ 115

15. Kinetics of Unimolecular Decomposition of $(CH_3)_2C(OOH)N=NR$ 116

16. Kinetics of Unimolecular Decomposition of $(CH_3)_2C(OOH)N=NCH_2CH_2OCH_3$ in Presence of Norbornene at 50°C 130

A1. Mass Spectrum of 5-Phenoxypentanal 151

A2. Mass Spectrum of 3-Ethoxy-6-phenoxyhexanal 151

A3. Mass Spectrum of 3-(2-phenoxyethyl)tetrahydrofuran 152

A4. Mass Spectrum of 3-(2-Phenoxyethyl)-2,3-dihydrofuran 152

A5. Mass Spectrum of Bis-2,3-dihydrofuran 153

A6. Mass Spectrum of 2-Hydroxy-3-(2,2,2-trifluoroethyl)-norbornane 154

A7. Mass Spectrum of 2-Hydroxy-3-(2-methoxyethyl)norbornane 154

A8. Mass Spectrum of 2-Hydroxy-3-(2-phenoxyethyl)norbornane 155

A9. Mass Spectrum of 2-Hydroxy-3-(2-norbornyl)norbornane 155

A10. Mass Spectrum of 2-(2,2,2-Trifluoroethyl)-3-(2-norbornyl)norbornane 156

A11. Mass Spectrum of 2-(2-Methoxyethyl)-3-(2-norbornyl) norbornane 156

A12. Mass Spectrum of t-Butylethylene oxide 157

Page

A13: Mass Spectrum of 2,3-Dihydro-4,5-benzofuran 157
A14. Mass Spectrum of 2,2-Dimethyl-5-phenoxypentane 158
A15. Mass Spectrum of Phenoxyacetaldehyde 158
A16. Mass Spectrum of 2,2-Dimethyl-3-hydroxy-6-phenoxyhexane 159
A17. Mass Spectrum of 2,2-Dimethyl-6-phenoxyhexan-3-one 159
A18. Mass Spectrum of 1,3-Diphenoxypropane 160
A19. Mass Spectrum of 1,4-Diphenoxybutane 160

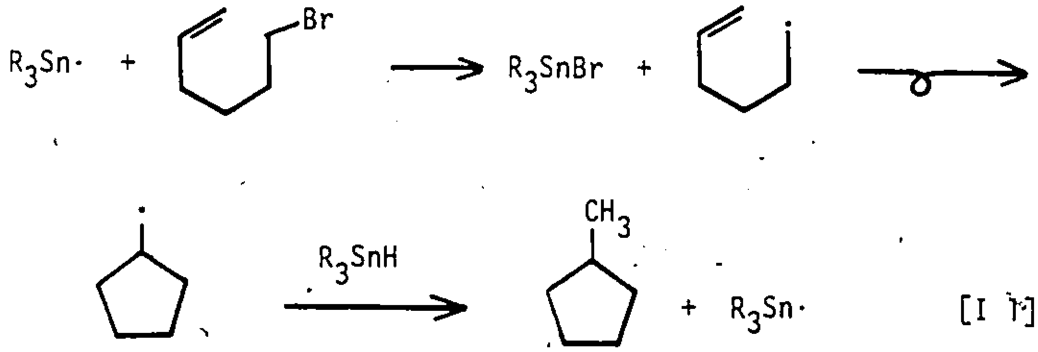
INTRODUCTION

The chemistry of free radicals dates back to 1900 when Gomberg[1] discovered the first free radical, triphenylmethyl radical. This discovery by Gomberg was followed by physical chemists' reinterpretation of their fundamental laws of chemical kinetics in terms of radical reactions; in 1918 Christiansen[2], Hertzfeld[3], and Polanyi[4] independently suggested a radical chain process for the H_2-Br_2 reaction.

The importance of organic free radicals as reaction intermediates was first recognised in 1937 by Hey and Waters[5] in England who suggested that arylation of aromatic compounds by benzoyl peroxide was a radical process, and by Karasch[6] in the United States who proposed that the abnormal (anti-Markownikoff) addition of HBr to double bonds, which he and Mayo had recognized in 1933, was a radical chain process.

The early 1940's ushered in a need for synthetic rubber. The two fundamental problems, the kinetics of radical chain transfer and of copolymerization, that were associated with free radical polymerization were recognized and analysed. Vigorous research activities were also centered on such subjects as structure and reactivity relationships, degradative chain transfer reactions, the chemistry of inhibitors and initiators, and redox systems as sources of free radicals.

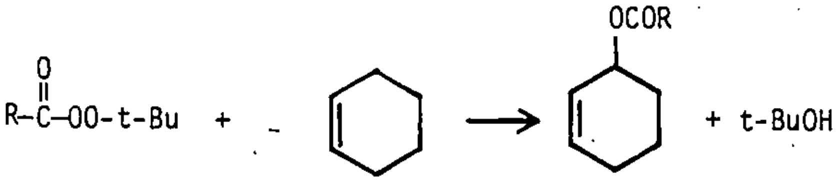
The knowledge and enthusiasm that were generated in free radical chemistry in the early 1940's were shifted from polymers to small molecules in the late 1940's. The field saw intensive research in the addition of molecules containing weak C-H or C-X(X=Cl, Br, I) bonds to olefins to give a remarkable variety of products, eq. I1. These reactions led to the discovery, by Walling and students[7], of radical cyclizations which were later studied in detail by Julia[8]. Another important discovery was the potential significance of autoxidation reactions[9] which led to such



[I 1]

interesting industrial processes as phenol synthesis from cumene. The mechanisms of biosynthesis of prostaglandins[10,11] have been shown to involve autoxidation of unsaturated fatty acids.

Free radicals in redox reactions have received much attention. Karasch in the early 1950's demonstrated the copper-catalysed reaction of peresters with olefins[12], eq. I2. Another area of free radical



[I 2]

chemistry which received much attention in the 50's and which had practical results for synthetic organic chemists was free radical halogenation. Halogenating agents which Walling called halogen carriers were discovered and their mechanisms of halogenation were worked out. N-Bromosuccinimide (NBS) was first reported to be a convenient brominating agent by Ziegler in 1942[13]. Although the reaction was quickly recognized as a free radical chain process, the actual mechanism involved has been the subject of recurrent controversy[14]. Another class of halogenating agents that has been used quite extensively is the hypochlorites; an example is found in the Barton reaction[15].

In the 1950's electron spin resonance (ESR) spectroscopy became available to the chemist and for the first time it was possible to detect free radicals at very low concentrations. Such techniques as spin-trapping which followed afterwards have been extensively studied. Phenomena such as chemically induced dynamic nuclear polarization (CIDNP) and chemically induced dynamic electron polarization (CIDEP) were discovered in the late 1960's and early 1970's and they have been applied in the studies of free radicals and their reactions. For example, Howard and Ingold[16] used ESR and other techniques to measure absolute rate constants for hydrocarbon autoxidation.

The foregoing section is an overview of historical developments in free radical chemistry. Many of the areas mentioned above will be discussed in more detail in the following sections.

I 1. GENERATION OF FREE RADICALS

There are generally three different ways in which free radicals can be generated: (a) thermal scission of a bond; (b) irradiation of molecules leading to homolysis of a bond; and (c) one-electron oxidation-reduction processes.

I 1.1 Thermolysis

When molecules are heated to sufficiently high temperature, bond homolysis takes place producing radicals. The normal C-C bond energy is about 90 kcal mol^{-1} and thermal excitation of molecules becomes sufficient to break these bonds at temperatures in the range of 450°-650°C. There are, however, some compounds that have exceptionally weak bonds and which can therefore decompose to form radicals at lower temperatures. Many of these compounds contain either peroxy(O-O), or azo(-N=N-) bonds, or both, and can be used to initiate radical reactions at temperatures between 10° and 150°C. These compounds undergo decomposition by one or more of three mechanisms: (a) unimolecular decomposition; (b) bimolecular decomposition induced by some free radical; (c) bimolecular decomposition induced by closed-shell molecules (molecule-assisted homolysis, MAH). For example, t-butylhydroperoxide is known to decompose in solution at 150°-180°C by mechanisms (a) and (b), eq. I 3 and I 4, respectively. The decomposition is found to proceed thermally by a

$$(CH_3)_3COOH \longrightarrow (CH_3)_3CO\cdot + \cdot OH \qquad [I\ 3]$$

$$\left.\begin{matrix}(CH_3)_3CO\cdot \\ \text{or} \\ \cdot OH\end{matrix}\right\} + (CH_3)_3COOH \longrightarrow (CH_3)_3COO\cdot + \left\{\begin{matrix}(CH_3)_3COH \\ \text{or} \\ H_2O\end{matrix}\right. \qquad [I\ 4]$$

$$2(CH_3)_3COO\cdot \longrightarrow 2(CH_3)_3CO\cdot + O_2 \qquad [I\ 5]$$

mechanism with 1.5-order kinetics[17,18]. Thus it is a chain reaction initiated by a unimolecular decomposition of the peroxide (eq. I 3) followed by attack on the unreacted hydroperoxide by the radicals, eq. I 4. An example of radical production from the interaction of closed-shell molecules involving t-butylhydroperoxide and ozone was given by Pryor.[19] Ozone was shown to react rapidly at -60° to 24°C with t-butylhydroperoxide in various halogenated solvents to produce t-butyl alcohol, acetone and di-t-butyl peroxide. A reaction scheme involving both peroxy and alkoxy radicals in radical chain reactions was proposed to account for the products. Equation I 6 shows the steps involved in the production of the peroxy radicals. The overall Arrhenius parameters for this reaction were found to be $E_a \simeq 7$ kcal mol^{-1} and

$$(CH_3)_3COOH \quad + \quad O_3 \quad \xrightarrow[-60°C]{} \quad (CH_3)_3COO\cdot \quad + \quad \cdot OH \quad + \quad O_2 \qquad [I\ 6]$$

log $A \simeq 7$. Another example of a MAH reaction is found in the fluorination of hydrocarbons. Molecular beam study[20] of the reaction between fluorine and methane at 300-400°K indicates that the dominant initiation reaction is the interaction of closed-shell molecules (eq. I 7) with log A = 9.3 ± 0.3 and $E_a = 11.2 \pm 2$ kcal mol^{-1}.

$$CH_4 \quad + \quad F_2 \quad \longrightarrow \quad CH_3\cdot \quad + \quad H\text{-}F \quad + \quad F\cdot \qquad [I\ 7]$$

The formation of free radicals by a 'spontaneous' reaction between nitroso compounds and other organic compounds such as alcohols or ethers has often been ascribed to MAH. However, Ingold and Chatgilialoglu[21] have shown that in several such reactions, the radicals are formed by simple photolysis of the nitroso compound by laboratory light.

The C-N and N=N bonds in azo compounds have bond energies of about 70 and 100 kcal mol^{-1}, respectively. These values may suggest that azo compounds would be poor initiators. However, the formation of molecular nitrogen in the dissociation of these compounds provides a driving force for the process. Compounds such as azobisisobutyronitrile are known to be good radical initiators at temperatures around 80°C

I 1.2. Radiation-Induced Bond Homolysis

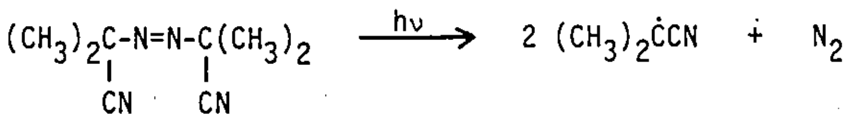
The energy necessary to cause bond scission can be supplied by any form of electromagnetic radiation (for example visible or ultraviolet light, or X- or γ-rays) or by corpuscular radiation (for example high energy electrons, α- or β-particles, neutrons, or protons). Many compounds will undergo photodecomposition on absorbing visible or ultraviolet light. The most familiar examples are the photodissociation of molecular chlorine and bromine in the halogenation of hydrocarbons, eq. I 8. Both peroxides and azo compounds undergo temperature-independent photodecompositions, eq. I 11 and I 12.

$$X_2 \xrightarrow{h\nu} X_2^* \longrightarrow 2X. \qquad [I\cdot 8]$$

$$X\cdot + RH \longrightarrow R\cdot + HX \qquad [I\ 9]$$

$$R\cdot + X_2 \longrightarrow RX + X\cdot \qquad [I\ 10]$$

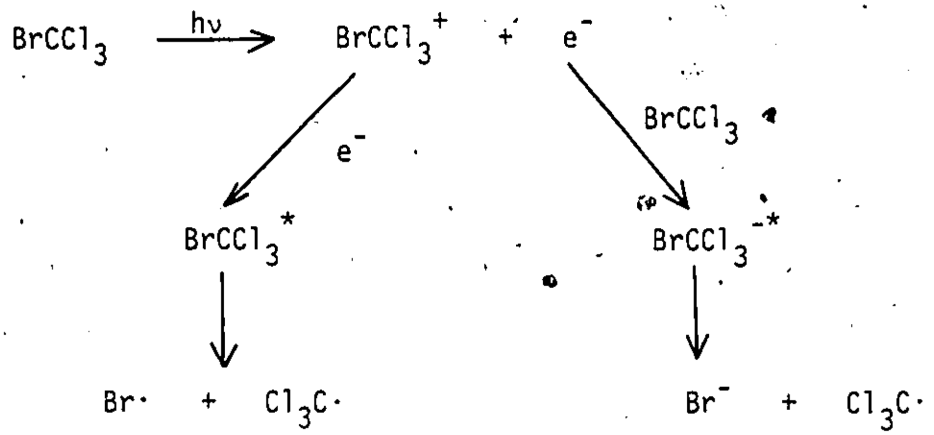
$$(CH_3)_3COOC(CH_3)_3 \xrightarrow{h\nu} 2\ (CH_3)_3CO\cdot \qquad [I\ 11]$$



$$(CH_3)_2C(CN)\text{-}N{=}N\text{-}C(CN)(CH_3)_2 \xrightarrow{h\nu} 2\ (CH_3)_2\dot{C}CN + N_2 \qquad [I\ 12]$$

Much attention has been given to the formation of free radicals by the action of γ-rays (from a ^{60}Co Source), X-rays, or high-energy electrons (from a van de Graaf generator). These techniques produce radical ions. Radical-cations can combine with low-energy electrons to yield excited molecules which decompose into free radicals. A molecule can capture an electron to produce a radical-anion which fragments into an anion and a free radical. An example of these processes is found in the radiolysis of bromotrichloromethane (Scheme 1).

SCHEME 1

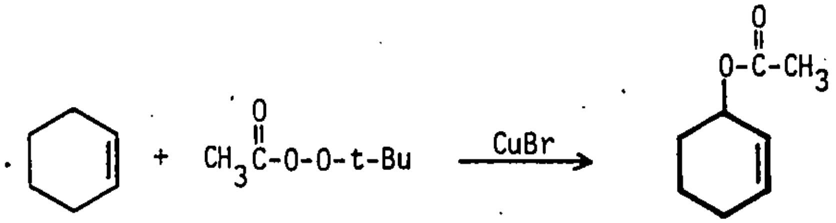


I 1.3. Electron Transfer Reactions

Some redox reactions produce, among other species, free radicals. The most important of these are those which involve a metal ion that can undergo one-electron transfer. Of these, the Fenton reaction is one of the oldest and best known. Haber and Weiss, in 1932, proposed the presently accepted mechanism,[22] eq. I 13 and I 14. Analogous reactions occur with ions of other metals and with hydroperoxides, peroxides, and peresters. Such reactions have been used successfully in the manufacture of styrene butadiene copolymer initiated with cumene hydroperoxide and ferrous ion, and in copper-catalysed reactions; the reaction of t-butylperacetate with cyclohexene catalysed by cuprous bromide (eq. I 15) is an example of the latter.

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + HO\cdot \qquad [I\ 13]$$

$$Fe^{3+} + H_2O_2 \longrightarrow Fe^{2+} + HO_2\cdot + H^+ \qquad [I\ 14]$$



[I 15]

I 2. DETECTION OF FREE RADICALS

Most organic radicals are very reactive and because of that they exist in solution at concentrations of 10^{-6}M or lower. The earliest methods of detecting free radicals included magnetic susceptibility measurements using the Gouy balance, IR spectroscopy, and UV spectrophotometry. These methods are quite insensitive since they can detect radical species only at concentrations far higher than 10^{-6}M.

Newer methods such as electron spin resonance (ESR) spectroscopy, chemically induced dynamic nuclear polarization (CIDNP), chemically induced dynamic electron polarization (CIDEP), and muon-spin rotation (μSR) spectroscopy have been developed for detection of free radicals. ESR, CIDEP, and μSR techniques are direct methods for the detection of radicals while the CIDNP technique is an indirect method for radical detection. The technique of ESR spectroscopy and its applications in spin trapping are discussed.

I 2.1. Electron-Spin Resonance Spectroscopy

Electron-spin resonance spectroscopy is a technique for the study of species containing one or more unpaired electrons. The scope of the method includes the detection and characterization of some transition metal ions, simple molecules and ions (eg. O_2, NO, NO_2, and CO_2^-), and organic radicals including biradicals and triplet states.

Basic Principles. As a charged particle creates a magnetic field, an unpaired electron or paramagnetic species will possess a magnetic moment. There are two possible contributions to the total moment; (a) one derived from the motion of the electron about the nucleus of an atom (the orbital magnetic moment), and (b) the spinning of the electron about an axis through its center (the spin magnetic moment). In the majority of cases the total electric dipole is essentially determined by the spin magnetic moment with only a small orbital contribution.

In a magnetic field of strength H, the magnetic moment of the electron interacts with the field to give rise to two energy states ($m_s = \pm \frac{1}{2}$). Those electrons whose spin magnetic moments are aligned parallel to the direction of the field have lower energy than those with their magnetic moments antiparallel to the field (Fig. 1). The difference in energy of these spin states is given by eq. I 16.

$$\Delta E = h\nu = g\beta H \qquad [\text{I } 16]$$

where g is the spectroscopic splitting factor, β is the Bohr Magneton = $e\hbar/(2mc) = 0.927 \times 10^{-20}$ erg Gauss^{-1}, e is the charge on the electron, ħ is Planck's constant divided by 2π, m is the electronic mass, and c is the speed of light. Irradiation of the system with a frequency ν, induces a transition between the two states.

There are three important characteristics of ESR spectra.

(i) <u>The g-Factor</u>. The electron free-spin g-factor has a value of 2.00232. However, in a radical the electron has a slightly different effective magnetic moment due to spin-orbit coupling. Consequently the condition for resonance is altered so that for a given

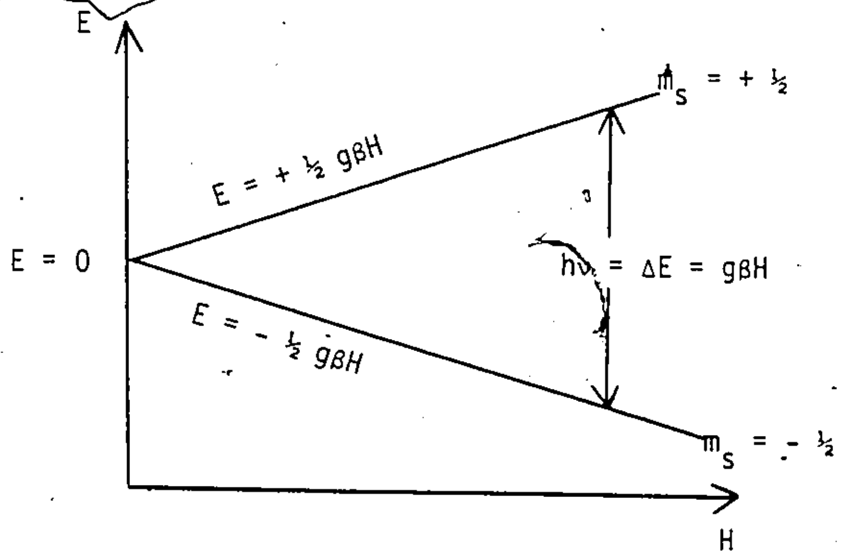


Fig. 1 Electron Spin Energy Levels as a Function of External Magnetic Field Strength.

frequency, radicals with different g-values resonate at different field strengths.

(ii) Hyperfine Splitting Constants. Most radicals contain one or more atoms with magnetic nuclei, so that the unpaired electron interacts not only with the applied field but also with internal fields. This is referred to as "hyperfine interactions" and results in the splitting of the resonance lines into two or more components. There are two types of hyperfine interactions. The first is the classical interaction between two dipoles, $\vec{\mu}_S$ (for the electron) and $\vec{\mu}_I$ (for the nucleus) separated by a distance $\vec{\gamma}$. This interaction depends on the angle between the vector that joins the two dipoles and the magnetic field vector, and it is called the anisotropic (or dipolar) hyperfine interaction. The second type of interaction is non-classical and arises from the finite probability of finding the electron at the nucleus; that is, it is proportional to the square of the electronic wavefunction at the nucleus. This is called the isotropic (or Fermi Contact) interaction. Interaction of the electron with a nucleus of spin I splits the resonance line into (2I + 1) components. For example, for a system with $s=\frac{1}{2}$ and $I=\frac{1}{2}$, the energy diagram appears as shown in Fig. 2.

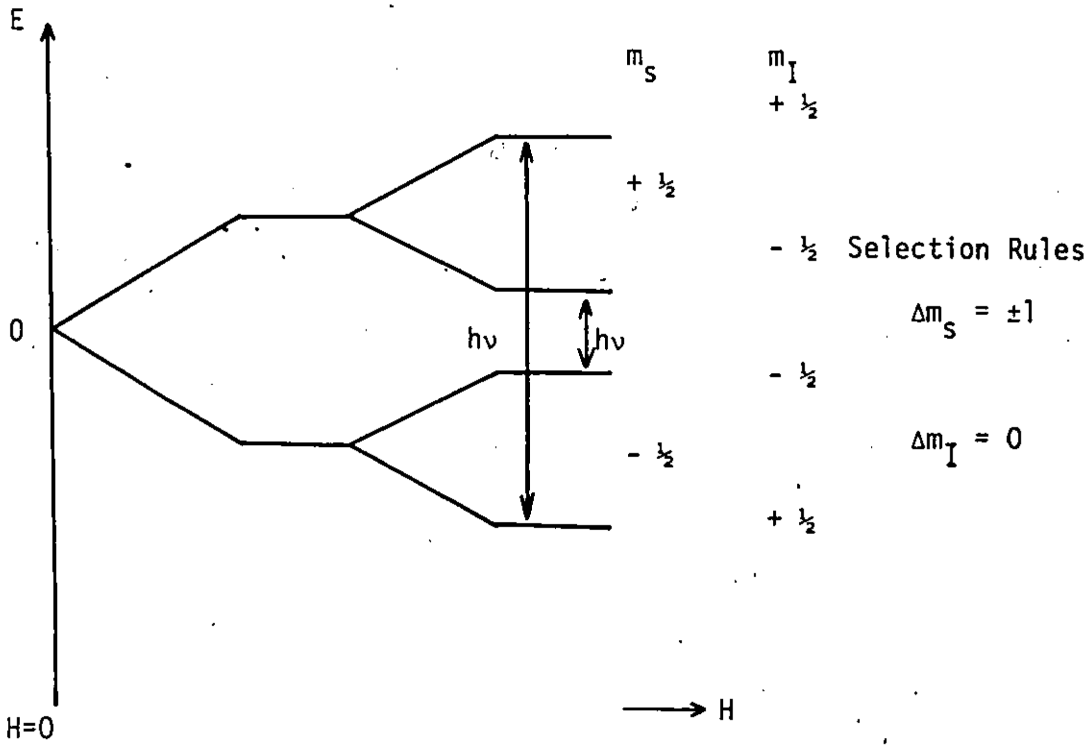


Figure 2. Energy Level Diagram for $S = \frac{1}{2}$, $I = \frac{1}{2}$.

(iii) Line-Widths. The line-widths of ESR absorptions in solution may be as narrow as a few milligauss. Some factors affecting line-shape and line-width in solution have been discussed by Carrington[23].

The width of the lines in solution spectra is increased if the life-time of an excited spin-state is reduced. The relaxation time of an excited spin-state can be reduced by spin-lattice, spin-orbit, and spin-spin interactions. Uncertainty in the lifetime of a spin-state, and the consequent line-broadening, also arises in two other general circumstances. First, it results when the radical takes part in a rapid chemical reaction, such as the electron exchange which occurs between the naphthalene radical-anion and naphthalene.[24] Secondly, it arises when there is uncertainty in the position of an interacting nucleus.

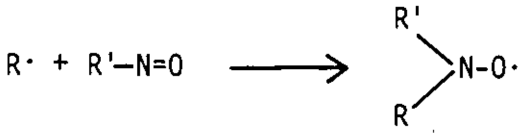
A combination of g-factor, hyperfine splitting constants, and line-widths has been used to establish the structures of a number of free radicals in solution.[25]

I 2.2. Spin Trapping[26]

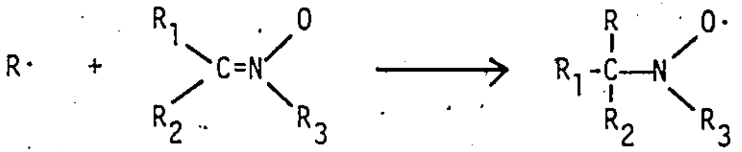
Electron spin resonance spectroscopy is among the most sensitive spectroscopic techniques. However, in liquid solutions many organic free radicals undergo bimolecular self-reaction at rates close to the diffussion-controlled limit. Thus their detection and characterization by ESR spectroscopy is limited to experimental conditions under which radicals are being created at correspondingly high rates. It is only with such techniques that the concentrations of such reactive radicals can be raised to levels (above steady state concentrations) adequate for detection. Examples of these techniques include the use of continuous flow cells[27]; the use of high intensity UV light and ionizing radiation at low temperatures[28], or of the more recently developed flash photolysis.[29] An alternative to these techniques is the use of diamagnetic radical scavengers which lead to relatively longer-lived paramagnetic products. This technique, referred to as "spin-trapping", was developed in the late 1960's.[30-32] The principle is based on the addition to the reaction system of a small quantity of a diamagnetic substance, the "spin-trap", that has a high affinity for reactive radicals. The product of the resulting reaction, the "spin-adduct", must be persistent in which case its concentration will build up to readily detectable levels ($> ca\ 10^{-7} - 10^{-6}M$). The general reaction is represented by eq. I 17.

$$\underset{\text{spin trap}}{R\cdot + ST} \longrightarrow \underset{\text{spin adduct}}{[R\text{-}ST]\cdot} \qquad [I\ 17]$$

Various spin traps have been investigated. The reactions of C-nitroso compounds and nitrones with radicals were studied by Lagercrantz and Forshult,[30] by Perkins,[31] and by Janzen and Blackburn,[32] eq. I 18 and I 19. Lagercrantz and Forshult used 2-methyl-2-nitrosopropane to spin-



[I 18]



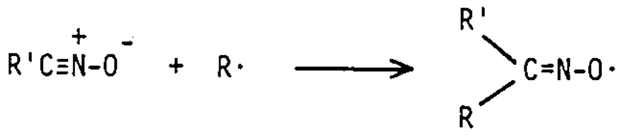
[I 19]

trap a series of radicals generated by γ-irradiation of a number of organic compounds including sodium acetate, glycine, DL-α-alanine, succinic acid, and L-glutamic acid hydrochloride. The nitrogen hyperfine splitting constants (a_N) were in the range of 15.5-16.2 Gauss and the α-hydrogen splitting constants (a_H^α) ranged between 4.1 Gauss and 8.4 Gauss.

Janzen and Blackburn were the first to investigate the feasibility of using phenyl t-butyl nitrone as a radical trap for the identification of reactive short-lived free radicals. They argued that the information necessary to define the structure of the radical trapped must lie in the magnitude of the β-hydrogen hyperfine splitting constant (a_H^β) and a_N. The a_H^β depends on the dihedral angle which in turn depends on the bulk of R; the magnitude of a_H^β decreases with increasing bulk of R. The a_N, on the other hand, is sensitive to the electronegativity of R, inductive electron withdrawal producing a smaller a_N. Free radicals such as methyl, trifluoromethyl, phenyl, ethyl, benzyl, n-butyl, benzoyloxyl, and acetoxyl radicals were trapped.[32]

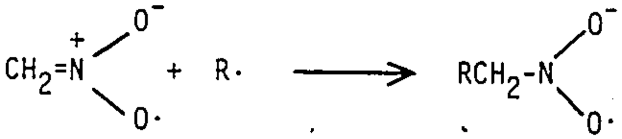
Perkins was first to point out the potential value of spin-trapping with C-nitroso compounds as a probe for exploring the mechanisms of free-radical reactions in solution. Using 2-methyl-2-nitroso propane he studied the polymerization of styrene initiated by t-butyl peroxyoxalate. By varying the concentration of the spin-trap he was able to trap either the initiating butoxyl radicals or the first-formed carbon radical from the addition of the butoxyl radicals to styrene molecules.[31]

These two classes of compounds (C-nitroso and nitrones) have become the most widely-used spin-traps. However, various alternatives to these have been used. Addition of radicals to nitrile oxides to form persistent imino-oxyl radicals has been described[33] (eq. I 20) and so has the use of the conjugate base of nitromethane, $CH_2NO_2^-$, to trap various radicals to give the corresponding nitroalkane radical anions,[34,35] eq. I 21. Thioketones have also been used as spin-traps. For example,



$$R'C\equiv\overset{+}{N}-O^- + R\cdot \longrightarrow (R')(R)C=N-O\cdot$$

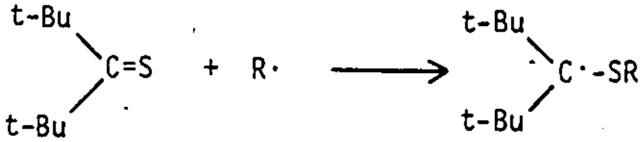
[I 20]



$$CH_2=\overset{+}{N}(O^-)(O\cdot) + R\cdot \longrightarrow RCH_2-N(O^-)(O\cdot)$$

[I 21]

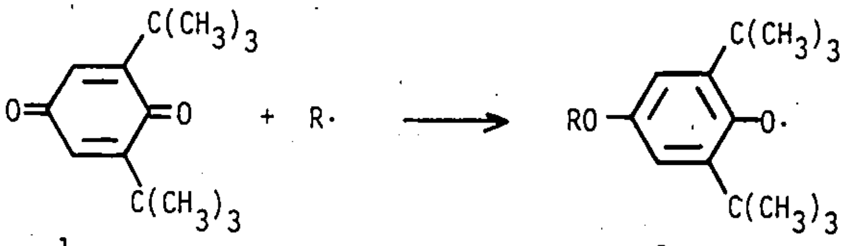
persistent thioalkyl radicals are formed by radical addition to di-t-butylthioketone.[36] Roginskii and Belyakov[37] have also described the



$$(t\text{-}Bu)_2C=S + R\cdot \longrightarrow (t\text{-}Bu)_2C\cdot-SR$$

[I 22]

use of 2,6-di-t-butyl-p-benzoquinone as a spin trap, eq. I 23.



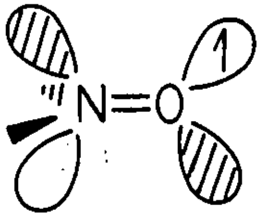
1

2

[I 23]

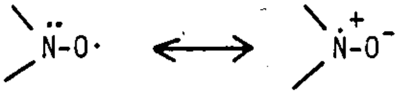
The rest of this section deals with the structure and stability of the nitroxide radicals, the chemistry of which has been extensively reviewed.[38-43]

Nitroxide radicals are π-radicals with the unpaired electron occupying a π^* orbital between the oxygen and nitrogen atoms. Also present is an N-O σ-bond and a π-bond. Thus the effective N-O bond order is 1.5. The nitroxide function can be represented in valence bond terms



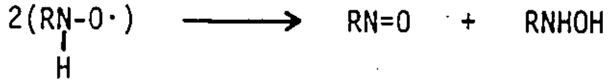
3

as a hybrid of two structures, 4a and 4b. The result of this electron



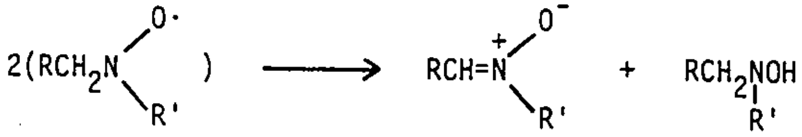
4a 4b

delocalization is a relatively stable structure. Di-t-alkyl, diaryl and many aryl t-alkyl nitroxides are particularly "stable". They are sufficiently persistent to be isolated. Perkins and Ward[44] and Alewood[45] have shown that several aryl t-alkyl nitroxides can also be obtained pure. There are other nitroxides that are less persistent. Monosubstituted nitroxides, RN(H)O·, rapidly disproportionate to nitroso-compound and hydroxylamine (eq. I 24), and nitroxides with a β-hydrogen also disproportionate to give nitrones and hydroxylamine, eq. I 25.



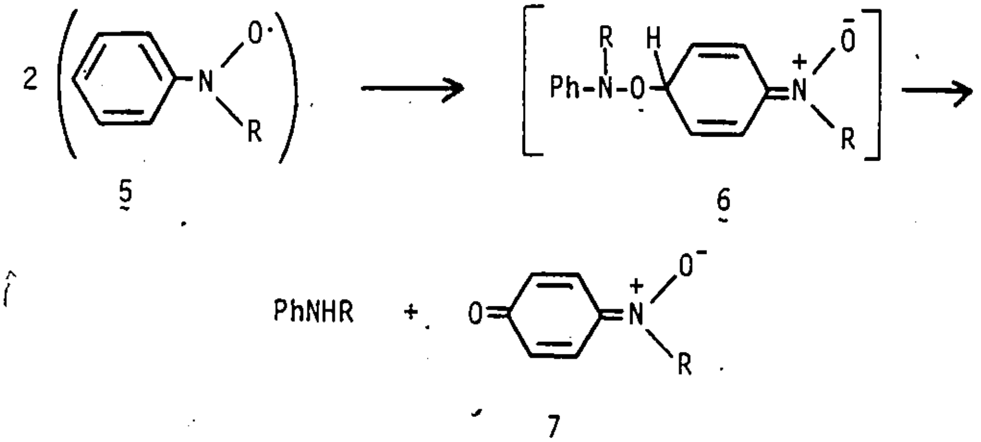
$$2(\underset{\mathrm{H}}{\underset{|}{\mathrm{RN}}}\text{-O}\cdot) \longrightarrow \mathrm{RN{=}O} + \mathrm{RNHOH}$$

[I 24]



[I 25]

In spin trapping the more stable nitroxides may decay slowly by a bimolecular process when the concentrations are very high, eq. I 26. This process does not occur if steric constraints twist the aryl group out of conjugation with the nitroxide function. The disappearance of nitroxides may also occur by unimolecular reactions. For example t-butoxy-t-butyl nitroxide is known to be a relatively short-lived species



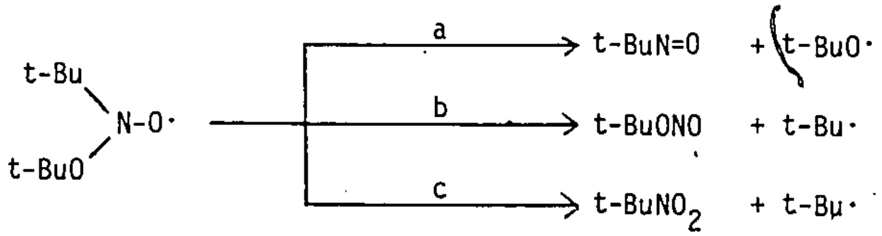
5

6

7

[I 26]

for which three fragmentation pathways are possible, eq. I 27.



[I 27]

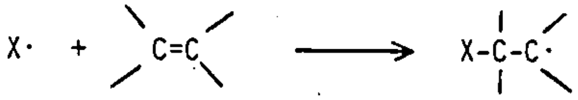
The spin-trapping technique provides a convenient route to many nitroxides that contain structural features of the scavenged radical. The spin-adduct spectra reveal hyperfine splittings due to the nitrogen and to hydrogen when it is directly attached to the nitrogen or is in the β-position. The β-hydrogen splittings arise predominantly by a hyperconjugative mechanism so that they have a pronounced angular dependency. The spectra also often reveal hyperfine splittings due to substituent atoms other than hydrogen. Fluorine, chlorine, and bromine splittings have been encountered, and many nitroxide spectra have been reported in which there were splittings by a second nitrogen, by phosphorus, or even by a metal atom.

I 3. FREE RADICAL REACTIONS

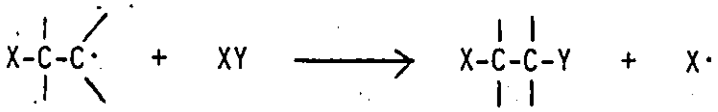
Three classes of free-radical reactions will be discussed in this section. These are (a) Radical Addition Reactions, (b) Radical Substitution Reactions, and (c) Radical Rearrangements. These are by no means the only and most important classes of free radical reactions; they have been chosen to reflect on the work reported and discussed in the next chapter.

I 3.1. Radical Addition Reactions

A number of free-radical reactions are known to proceed by a radical chain mechanism. The addition of a substrate, XY, to a multiple bond can be accomplished by a free-radical chain sequence which consists of two principal steps: the chain propagating step in which the free radical X· adds to the double (or multiple) bond to form adduct free radical, and the chain-transfer step in which the adduct radical abstracts group Y from the substrate XY to give the addition product and to regenerate the radical X·. The second step can, in fact, be described as radical substitution at Y.

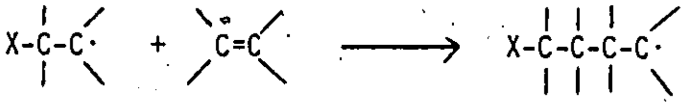


[I 28]



[I 29]

Competing with the chain-transfer step (eq. I 29) is addition of the adduct radical to a second molecule of olefin, eq. I 30. The addition reaction, eq. I 30, is likely to occur if D(X-Y), the X-Y bond dissociation energy, is high, or if X-Y is in very low concentration, or if X-C-C· is particularly reactive and the ΔE for chain transfer with



[I 30]

another olefin molecule is low. This will result in the formation of telomer or polymer.

In a chain addition mechanism, a number of points have to be considered. These include (a) the initiation step, (b) the orientation of addition to the double bond, (c) the energetics of the propagation steps, (d) the stereochemistry of the process, (e) the activation energies and rates of reaction for the various steps, (f) the structure of the olefin, including polar and steric factors, and (g) the mode of termination of the chain reaction. Many of these points are discussed below.

Kinetic Aspects of Radical Chain Additions. In any chain reaction, the initation and termination steps have to be considered as part of the overall reaction even though termination reactions are relatively unimportant as product-forming reactions if the chain-sequence is long. In kinetics, initation and termination are found to play very significant roles.

The basic mechanism for the formation of a 1:1 addition product by a radical chain reaction (eq. I 31) is shown in Scheme 2. Let us

$$XY + CH_2{=}CHZ \longrightarrow XCH_2CHYZ \qquad [I\ 31]$$

assume that $XCH_2\dot{C}HZ$ is very unstable kinetically. Its concentration will be very low and termination by step 6 will therefore not take place. If step 4 is chosen as the termination step, then the kinetic chain length, which is defined as the rate of one of the propagating reactions (R_p) divided by the rate of termination reaction (R_t), is given

SCHEME 2

INITIATION

$$\mathrm{In} \longrightarrow \mathrm{In.}$$

$$\mathrm{In.} + \mathrm{XY} \xrightarrow{k_1} \mathrm{InY} + \mathrm{X\cdot}$$

PROPAGATION

$$\mathrm{X\cdot} + \mathrm{CH_2{=}CHZ} \xrightarrow{k_2} \mathrm{XCH_2CHZ\cdot}$$

$$\mathrm{XCH_2CHZ\cdot} + \mathrm{XY} \xrightarrow{k_3} \mathrm{XCH_2CHYZ} + \mathrm{X\cdot}$$

TERMINATION

$$2\mathrm{X\cdot} \xrightarrow{k_4} \mathrm{X_2}$$

$$\mathrm{X\cdot} + \mathrm{XCH_2CHZ\cdot} \xrightarrow{k_5} \mathrm{CH_2CHZX}$$

$$2\mathrm{XCH_2CHZ\cdot} \xrightarrow{k_6} \mathrm{XCH_2CHZCHZCH_2X}$$

by equation I 32. It is evident from eq. I 32 that the kinetic chain

$$\text{Kinetic Chain Length} = \frac{R_p}{R_t} = \frac{k_2[\mathrm{X\cdot}][\mathrm{CH_2{=}CHZ}]}{k_4[\mathrm{X\cdot}]^2} = \frac{k_2[\mathrm{CH_2{=}CHZ}]}{k_4[\mathrm{X\cdot}]}. \qquad [\text{I } 32]$$

length is inversely proportional to the concentration of the chain-carrying radical and directly proportional to the concentration of the substrate.

The kinetic situation presented here (that is, a slow initiation step followed by rapid chain-propagating reactions and a very fast termination step) dictates that the concentrations of all free radicals be very small and that these concentrations remain effectively unchanged. At the start of the reaction, the concentrations of the free radicals in solution are very low and destruction of the radicals by termination reactions is insignificant. With time these concentrations build up to levels at which they are removed rapidly and the rate of termination becomes equal to the rate of initiation. The concentration at which this occurs is termed the steady-state concentration. At this concentration the rates of the propagation reactions in the chain sequence must be the same.

When the addition step is the slow, rate-controlling reaction in the chain sequence, the rate of formation of the product is given by eq. I 33,

$$\frac{d[P]}{dt} = k_2[X\cdot][CH_2{=}CHZ] \qquad [I\ 33]$$

where [P] is the concentration of product. If step 4 is the chain termination reaction, the rate of termination will be

$$\frac{-d[X\cdot]}{dt} = 2k_4[X\cdot]^2 = R_i \qquad [I\ 34]$$

where R_i is the rate of initiation. Thus

$$[X\cdot] = (\tfrac{1}{2}\frac{R_i}{k_4})^{\frac{1}{2}}.$$

substituting for the radical concentration in eq. I 33 gives eq. I 35.

$$\frac{d[P]}{dt} = k_2[CH_2{=}CHZ](R_i/2k_4)^{1/2} \qquad [I\ 35]$$

To obtain a good yield of the product of 1:1 addition, k_2 must be large and the chains must be as long as possible to minimize the loss of reactant in termination reactions and to increase the efficiency of conversion.

When the chain-carrying radical, $X_h\cdot$, has the radical center on a hetero-atom, the addition step is frequently reversible, eq. I 36.

$$X_h\cdot + CH_2{=}CHZ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} X_hCH_2\dot{C}HZ \qquad [I\ 36]$$

$$X_hCH_2\dot{C}HZ + X_hY \xrightarrow{k_3} X_hCH_2CHYZ + X_h\cdot \qquad [I\ 37]$$

The carbon-heteroatom bond formed in the propagating step is generally weak and there may therefore be appreciable decomposition of the adduct radical even at room temperature. Reversible additions have been established for such atoms and groups as iodine,[46] organotin,[47] and thiyl[48] radicals.

Application of the steady-state approximation to the kinetics of addition reactions, including the reverse decomposition, leads to the following expression for the rate of product formation. In this

$$\frac{d[P]}{dt} = k_2[CH_2{=}CHZ](R_i/k_4)^{\frac{1}{2}}\{1/(1 + k_{-2}/k_3[X_hY])\} \qquad [I\ 38]$$

case the rate of product formation depends not only on the rate constant of addition (k_2), but also on the concentration of the radical source, $[X_hY]$, and on the ratio of the rate constant of decomposition to rate constant for transfer (k_{-2}/k_3) of the adduct radicals.

Factors Influencing Chain Transfer.[49] The various factors which influence the chain-transfer step include bond strengths, steric effects, resonance stabilization, and polar effects. The strength of the bond being broken has been shown to be very important. In the H-abstraction from alkanes by methyl radicals at 164°C, the changes in the rate constant were found to be entirely due to differences in the activation energy term with very little variation in log A[49a] (see Table 1).

There are three type of steric effects which are important in radical transfer reactions: steric hindrance, which inhibits approach of the initial radical to a particular reaction site; steric inhibition of resonance, which prevents the incipient radical from being stabilized by electron delocalization; and steric compression, which is partly released in forming the new radical. The familiar decrease in C-H bond strengths from primary to secondary to tertiary, can be attributed partly to steric compression which is released when the new radical forms.

If the adduct radical formed is stable, it will exhibit reluctance to continue on into chain transfer. This reluctance to react is the results of two factors: (a) a high energy of activation for chain transfer

Table 1

Arrhenius Parameters for H-Abstraction from Alkanes by Methyl Radicals at 164°C.[49]

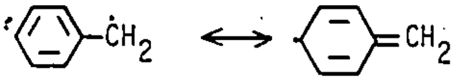
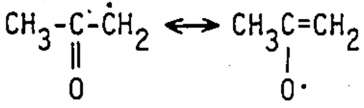
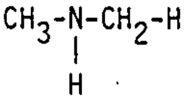
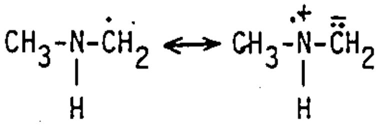
Alkane	log A/(L $mol^{-1}s^{-1}$)	Ea/(kcal mol^{-1})	log k/(L $mol^{-1}s^{-1}$)
CH_4	8.76	14.23	1.65
CH_3CH_3	8.83	11.83	2.96
$(CH_3)_2CH_2$	8.82	10.13	3.75
$(CH_3)_3CH$	8.38	8.03	4.36

because of high radical stability; and/or (b) a high energy of activation because of a high X-Y bond strength. Radical stability arises as a result of resonance. With considerable resonance stabilization, the concentration of the radical will build up and may lead to chain termination and, therefore, shorter chain lengths. However, if the adduct radical is very reactive, and therefore short-lived, the reaction may have long chain lengths and the termination step will be different (for example dimerization of X·) and the kinetics of the process will change.

"Resonance stabilization" has been shown to be small. A comparison of data from Tables 1 and 2 indicates that the variation of reactivity in H-abstraction from the alkanes, CH_3-H to $(CH_3)_3$C-H, which do not have any resonance stabilization is greater than for those compounds that provide some form of resonance stabilization to the radical.

Table 2

Arrhenius Parameters for H-Abstraction from Substituted Methanes by Methyl Radicals at 164°C.[49]

RCH_2-H	Resonance	Log A[a]	E_a[b]	k[a]
CH_3CH_2-H	$H\text{-}CH_2\dot{C}H_2 \leftrightarrow H\cdot CH_2{=}CH_2$	8.1	10.4	8.0×10^2
FCH_2-H	$F\text{-}\dot{C}H_2 \leftrightarrow \overset{+\cdot}{F}\text{-}\overset{-}{\ddot{C}}H_2$	8.2	11.8	2.0×10^2
$CH_3CH{=}CHCH_2$-H	$CH_3CH{=}CHCH_2 \leftrightarrow CH_3\dot{C}HCH{=}CH_2$	8.1	7.6	2.0×10^4
$C_6H_5CH_2$-H		8.6	9.5	7.1×10^3
CH_3COCH_2-H	 $CH_3\text{-}\underset{\underset{O}{\Vert}}{C}\text{-}\dot{C}H_2 \leftrightarrow CH_3\underset{\underset{O\cdot}{\vert}}{C}{=}CH_2$	8.5	9.7	4.5×10^3
CH_3OCH_2-H	$CH_3\text{-}O\text{-}\dot{C}H_2 \leftrightarrow CH_3\text{-}\overset{\cdot+}{O}\text{-}\overset{-}{\ddot{C}}H_2$	8.6	10.0	4.0×10^3
 $CH_3\text{-}\underset{\underset{H}{\vert}}{N}\text{-}CH_2\text{-}H$	 $CH_3\text{-}\underset{\underset{H}{\vert}}{\dot{N}}\text{-}\dot{C}H_2 \leftrightarrow CH_3\text{-}\underset{\underset{H}{\vert}}{\overset{\cdot+}{N}}\text{-}\overset{-}{\ddot{C}}H_2$	8.4	8.9	8.9×10^3

[a] Units in L $mol^{-1}s^{-1}$. [b] Units in kcal mol^{-1}.

Polar forces in the transition state are known to play a significant role in certain free radical reactions. It is very significant that while the activation energy for H-abstraction from methane by trifluoromethyl radicals (E_a = 11.2 kcal mol^{-1}) is lower than that for abstraction by methyl radicals (E_a = 14.0 kcal mol^{-1}), the order is reversed in the H-abstraction from hydrogen chloride (5.0 kcal mol^{-1} for $\cdot CF_3$ and 2.5 kcal mol^{-1} for $\cdot CH_3$). Tedder[49] has explained this to be because in the latter reactions $\cdot CF_3$ radicals, being more electronegative, resist formation of a polar transition state, while the $\cdot CH_3$ radicals, being more electron-donating, facilitate the formation of a polar transition state. Evidence for the importance of polar forces in determining the course of radical transfer reactions is well documented. Relationships of the Hammett $\sigma\rho$-type have been investigated for H-transfer reactions.[50]

Orientation and Stereochemistry of Addition. One aspect of interest in radical addition reactions is the orientation of addition, that is, which carbon of the double bond of an unsymmetric alkene is attacked. Two isomeric products are formed when the adduct radicals abstract Y from

$$X\cdot \;+\; CH_2{=}CHZ \begin{array}{l} \overset{k_\alpha}{\nearrow}\; XCH_2\dot{C}HZ \\ \underset{k_\beta}{\searrow}\; XCHZ\dot{C}H_2 \end{array} \qquad [I\ 39]$$

$$XCH_2\dot{C}HZ \;+\; XY \longrightarrow XCH_2CHYZ \qquad [I\ 40]$$

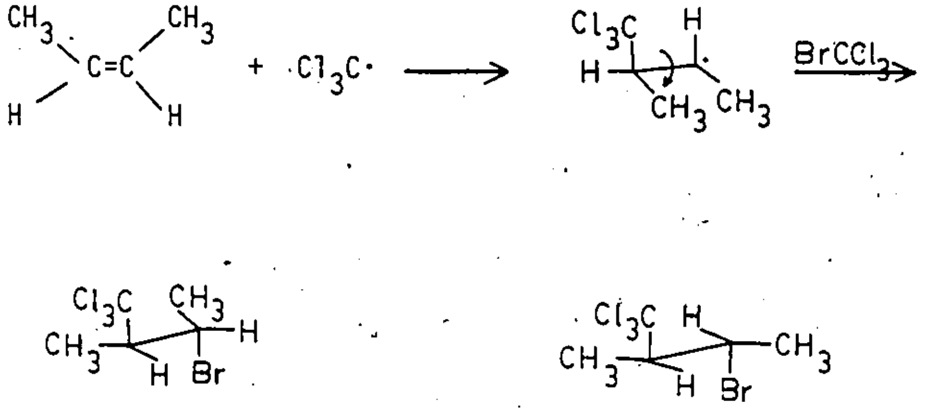
$$XCHZ\dot{C}H_2 \;+\; XY \longrightarrow XCHZCH_2Y \qquad [I\ 41]$$

the chain-transfer agent XY. Mono-substituted alkenes and 1,1-disubstituted alkenes always give predominantly the product from initial addition to the unsubstituted end, irrespective of the nature of the radical, or the substituents on the alkene. This is associated with steric compression in the adduct radical. For 1,2-disubstituted, and trisubstituted alkenes, the major product usually comes from addition to the least substituted end. The orientation ratio (OR) is defined as the ratio of the rate constant for addition to the most substituted end (β) to the rate constant for addition to the least substituted end (α), eq. I 42. Studies of orientation ratios for various haloalkenes and various radicals suggest that both polar (or electronic) and steric

$$OR = k_\beta/k_\alpha \qquad [I\ 42]$$

factors are important in the orientation of addition to the double bond.

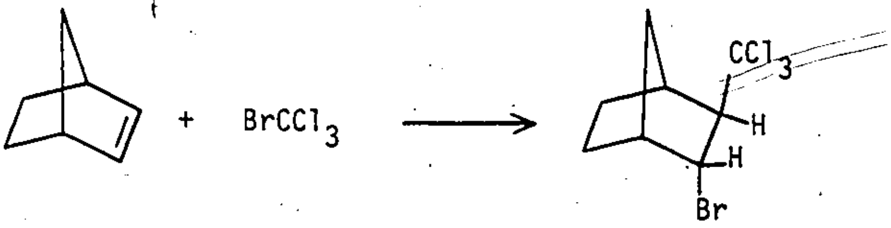
Radical addition to 1,2-disubstituted alkenes is generally found to be non-stereospecific. For example, the light-induced additions of bromotrichloromethane to cis-2-butene and tran-2-butene yield the same



[I 43]

mixture of the threo and erythro addition products.[51] The lack of stereospecificity in this addition reaction (and many others) can be attributed to reaction of the same adduct radical, in the transfer step, with bromotrichloromethane. The adduct radicals resulting from addition of the trichloromethyl radical to the 2-butenes apparently undergo conformational equilibration faster than they react in the chain transfer step with the bromotrichloromethane.

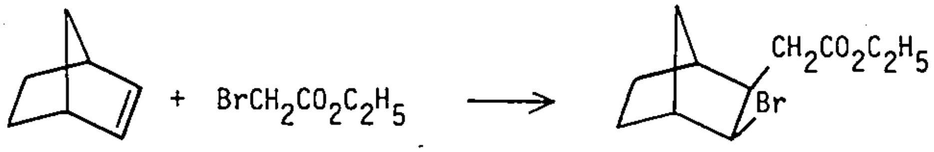
In contrast to the reaction with the 2-butenes, the free-radical addition of bromotrichloromethane to norbornene appears to be highly stereoselective in that elements of the polyhalomethane add trans to the unsaturated bond of this alkene.[52] A plausible explanation for the



[I 44]

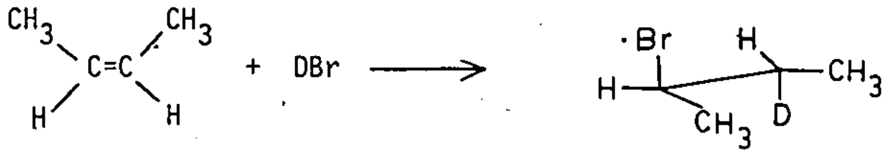
stereoselective trans additions of the bromotrichloromethane to such bicyclic systems stem from a combination of two factors: the steric effect rendered by the trichloromethyl group and the methylene bridge, and the fact that rotation about the carbon-carbon σ bond is prohibited. Trans addition occurs because the adduct radical formed from the exo-addition of trichloromethyl radicals to norbornene is sterically hindered on the exo side by both the methylene bridge and the trichloromethyl group. The results from the reactions of the 2-butenes indicate that reactions of the norbornene show a high degree of stereoselectivity due to steric effects rather than to an inherently stereospecific addition.

Interestingly, free-radical addition reactions of other reagents to norbornene and its derivatives appear to be cis. Ethyl bromoacetate reacts with norbornene to yield exo-cis-2-carboethoxymethyl-3-bromonorbornane,[53] eq. I 45. In this case the steric effect of the ethylene bridge in the adduct radical likely outweighs the combined steric effects of the methylene bridge and the carboethoxymethylene group.



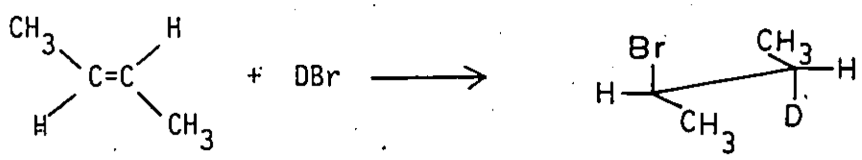
[I 45]

In contrast to the reaction discussed above, free-radical additions of hydrogen bromide to unsaturated bonds appear to be truly stereospecific. Reactions of cis- and trans-2-butenes with deuterium bromide yield exclusively the threo- and erythro-products, respectively, the products of a stereospecific trans-addition of the elements of the adding reagent to the alkenes.[54] The stereospecificity observed in these addition



[I 46]

Threo



[I 47]

Erythro

reactions is attributed to a combination of two factors. The first of these is the very high reactivity of the hydrogen halide in displacement reactions with free radicals. The second and probably the most important factor is the preference shown by intermediate β-bromoalkyl radicals for the staggered conformation in which the radical center is non-planar.[55] This staggered, non-planar radical is known[56] to have a relatively high barrier to rotation which is similar to the activation energy of racemization reported for the so-called "bridged" β-bromoalkyl radicals.[57]

A large number of reagents are known to add across unsaturated bonds. These include hydrogen halides, halogens, thiols and hydrogen sulfide, alkylpolyhalides, nitrogen and phosphorus compounds, group IV organometallic hydrides, aldehydes, alcohols, esters and acids, and ethers and acetals.[58]

I 3.2 Radical Substitution at Hydrogen and Oxygen

Free radical substitution (S_H2) reactions are defined operationally as homolytic processes in which one atom or group of atoms in a molecule is replaced with another without regard to details of mechanism.

Radical substitution reactions take place at hydrogen in halogenation (eq. I 48) and in autoxidation (eq. I 49) and oxidation, at halogen in halogenation (eq. I 50) and dehalogenation (eq. I 51), and at oxygen in induced decomposition of peroxides, eq. I 52. Substitution

$$X\cdot + RH \longrightarrow XH + R\cdot \qquad [I\ 48]$$

$$ROO\cdot + RH \longrightarrow ROOH + R\cdot \qquad [I\ 49]$$

also takes place at such atoms as boron, phosphorus, sulfur, silicon,

$$R\cdot + X_2 \longrightarrow RX + X\cdot \qquad [I\ 50]$$

$$R_3Sn\cdot + RX \longrightarrow R_3SnX + R\cdot \qquad [I\ 51]$$

$$R\cdot + R'OOR \longrightarrow ROR' + RO\cdot \qquad [I\ 52]$$

tin, magnesium and mecury.[59] However, substitutions at these atoms are believed to be two-step involving an addition-elimination mechanism. Substitutions at hydrogen and oxygen, which are of relevance to this thesis, are discussed here.

Substitution at Hydrogen. Substitution at hydrogen is one of the widely studied subjects in free radical chemistry.[60] Activation energies for H-abstraction by various atoms vary quite substantially. Hydrogen-abstraction by fluorine atom is found to have a very low (or zero) activation energy while that by iodine is high, ca. 12-35 kcal mol^{-1}. The reactivities of the halogen atoms are in the order F > Cl > Br > I. Also the activation energies for H-abstraction by t-butylperoxyl radical from various compounds is very low (ca. 0-6 kcal mol^{-1}).[58e]

Hydrogen abstraction studies using electronegative radicals indicate that the activation energies for such radicals as chlorine, t-butoxy, and trifluoromethyl are lower than the activation energies for H-abstraction by methyl radicals because of polar contributions to the transition state.

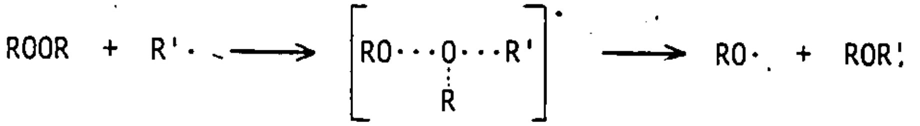
The facility of S_H2 attack at various kinds of X-H bonds can be crudely predicted from their bond dissociation energies (see Table 3). For any given column of the periodic table, attack will be faster at the molecule with the weaker X-H bond.

Table 3

Bond-Dissociation Energies, D (kcal mol^{-1})

Bond	D	Bond	D	Bond	D
F-H	136	CH_3O-H	102	$(CH_3)_2N$-H	86
Cl-H	103	CH_3S-H	88	ØNH-H	80
Br-H	87	ØS-H	75	CH_3-H	104
I-H	71			ØCH_2-H	85

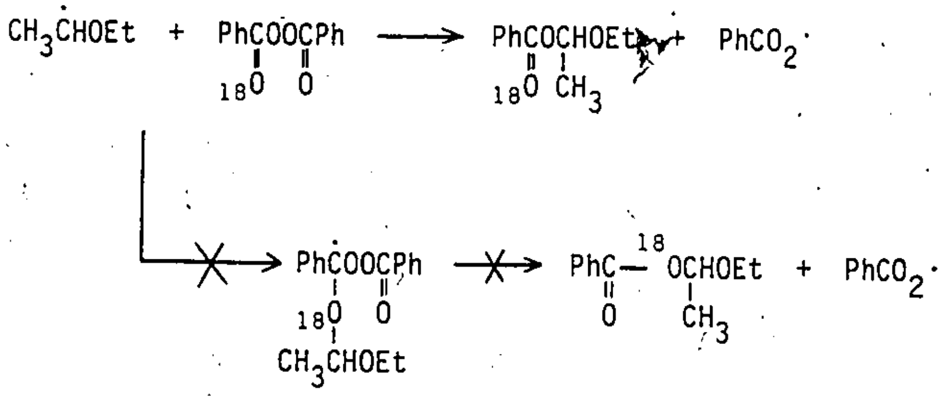
<u>Substitution at Oxygen</u>. Evidence for S_H2 reactions at oxygen comes from studies of induced decomposition of peroxides. One of several modes of radical attack on peroxides has been identified as the S_H2 process, eq. I 53. This step is usually thermochemically favorable, the replacement



$$\mathrm{ROOR} + \mathrm{R'}\cdot \longrightarrow \left[\begin{array}{c}\mathrm{RO\cdots O\cdots R'}\\ \vdots\\ \mathrm{R}\end{array}\right]^{\cdot} \longrightarrow \mathrm{RO}\cdot + \mathrm{ROR'} \qquad [I\ 53]$$

of an 0-0 bond by, for example, a C-0 bond being about 45 kcal mol^{-1} exothermic. In the case of diacyl peroxides in ether, labelling studies[61,62] showed that attack was largely, if not totally, at the peroxidic oxygen (eq. I 55a) and did not occur by the two-step addition-elimination sequences, eq. I 55b. In trialkyltin hydrides, the diacyl peroxides

$$R\cdot + CH_3CH_2OEt \longrightarrow RH + CH_3\dot{C}HOEt \qquad [I\ 54]$$



$$CH_3\dot{C}HOEt + Ph\underset{{}^{18}O}{\underset{\|}{C}}OO\underset{O}{\underset{\|}{C}}Ph \longrightarrow Ph\underset{{}^{18}O}{\underset{\|}{C}}O\underset{CH_3}{\underset{|}{C}}HOEt + PhCO_2\cdot \qquad [I\ 55a]$$

$$\not\longrightarrow Ph\dot{C}\underset{\underset{CH_3CHOEt}{|}}{\underset{{}^{18}O}{|}}OO\underset{O}{\underset{\|}{C}}Ph \not\longrightarrow Ph\underset{O}{\underset{\|}{C}}-{}^{18}O\underset{CH_3}{\underset{|}{C}}HOEt + PhCO_2\cdot \qquad [I\ 55b]$$

decompose even faster than in alcohols and ethers. This is attributed to the very facile attack of stannyl radicals at the 0-0 bond.[63]

I 3.3 Autoxidation

Autoxidation is a subject that has attracted the attention of a large number of organic chemists, and which is still being studied.[64]

A wide variety of organic compounds react with atmospheric oxygen to yield hydroperoxides and other oxygenated compounds such as peroxides, alcohols, ketones, aldehydes, epoxides and acids. The complex series of elementary processes leading to these products is collectively referred to as autoxidation. This can be described by the following free-radical chain sequence:

Initiation:

production of free radicals [I 56]

Propagation:

$$R\cdot + O_2 \longrightarrow ROO\cdot \qquad [I\ 57]$$

$$ROO\cdot + RH \xrightarrow{k_p} ROOH + R\cdot \qquad [I\ 58]$$

Termination:

$$2\ ROO\cdot \xrightarrow{2k_t} \text{non-radical products} \qquad [I\ 59]$$

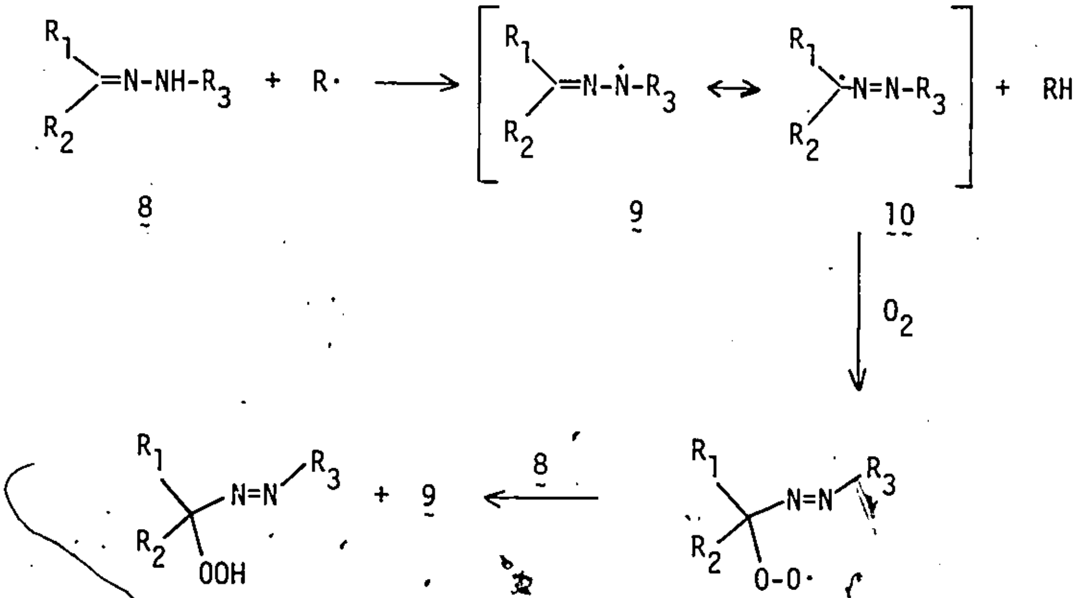
Using the usual steady-state assumptions, the overall rate of oxidation is given by:

$$-\frac{d[O_2]}{dt} = -\frac{d[RH]}{dt} = \frac{d[ROOH]}{dt} = \frac{k_p[RH]R_i^{\frac{1}{2}}}{2(k_t)^{\frac{1}{2}}} \qquad [I\ 60]$$

where k_p and k_t are the rate-controlling propagation and termination rate constants, and R_i is the rate of chain initiation.

Autoxidation of hydrazones has been studied extensively.[65] Pausacker[65a] and Criegee and Lohaus[65b] were the first to suggest a radical mechanism for the autoxidation process. The chain process (Scheme 3) involves the abstraction of hydrogen to give a hydrazyl radical. This radical can be represented by two cannonical forms with one being a carbon-centered species. The carbon-centered form (10) reacts with

SCHEME 3



oxygen to give an α-azoperoxyl radical which reacts with a hydrazone molecule to regenerate the hydrazyl radical intermediate and give an α-azohydroperoxide. The initiation and termination reactions would conceivably be similar to those in autoxidation of other organic compounds.

Autoxidation usually has a detrimental effect on organic compounds because it leads to loss of the desirable properties of the original material. Thus prevention of the oxidative degradation of organic materials has attracted the attention of research scientists for many years. This has resulted in a wide variety of antioxidants that are commercially available and widely used in industry. The most important and probably the most thoroughly investigated class of antioxidants is the chain-breaking class of antioxidants. These include hindered phenols and aromatic amines. They reduce the rate of autoxidation by reacting with chain propagating alkylperoxyl radicals, eq. I 61 and I 62. A second class of antioxidants is the preventive antioxidants. These include metal ion deactivators, UV light deactivators, and peroxide decomposers. They prevent chain initiation or reduce the rate of initiation. An example of a UV light deactivator is o-methylbenzophenone. Organic sulfur compounds are found to be very good peroxide decomposers.

$$RO_2\cdot + AH \longrightarrow ROOH + A\cdot \qquad [I\ 61]$$

$$RO_2\cdot + A\cdot \longrightarrow ROOA \qquad [I\ 62]$$

I 3.4 Free Radical Rearrangements

De Mayo[66] defined rearrangement as the occurrence of any "change in atomic disposition in the molecule (with concomitant bond cleavage, σ or π, and reformation)". Thus radical rearrangement is looked at as unimolecular reactions of organic radicals to form isomeric radicals. The subject of free radical rearrangement has been studied extensively.[67] The area of radical rearrangements, namely group migration, which has some relevance to this work is discussed here.

Group transfers can be represented by the generalized one-step, or concerted, reaction shown in eq. I 63. The most common of the group transfer reactions involve 1,2-shifts (n=0) of unsaturated groups such

$$A\text{-}B\text{-}C_n\text{-}\dot{D} \longrightarrow \dot{B}\text{-}C_n\text{-}D\text{-}A \qquad [\text{I } 63]$$

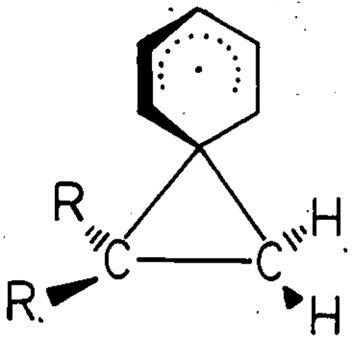
as phenyl. More remote group transfers are also known, including 1,4-shifts (n=2) and 1,5-shifts (n=3).

For radical rearrangement in solution to be fast enough to compete with the other processes by which the radical can be destroyed, its activation energy must be less than 15 kcal mol^{-1}. The favorable direction for the rearrangement is determined by the thermodynamic stabilities of the unrearranged and rearranged species. Intramolecular group transfer will occur readily at carbon, provided that there is a low-lying unfilled orbital available to accept the unpaired electron in the transition state and/or intermediate. The process is similar to bimolecular homolytic substitution (S_H2)[59] (vide supra). Homolytic substitution at sp^2 carbon is generally a facile process,[68] and so aryl, vinyl and similar unsaturated groups migrate readily; but substitution at sp^3 carbon occurs only under special circumstances.[59,69] The lowest energy pathway by which a simple alkyl group such as methyl or t-butyl can migrate in a radical involves group elimination and readdition. Group transfers by 1,2-shifts (involving three-membered cyclic transition states) are much more common than 1,3-shifts and somewhat more than 1,4- and 1,5-shifts. This is so because, although the stability of a ring system depends on its internal strain, its ease of formation depends on how much time the two reactive centers spend in close proximity. This decreases with increasing separation of the two centers since the number of possible conformations that an acyclic system can assume increases with the length of the system.

Migration of Unsaturated Groups. Urry and Karasch[67] identified the first radical rearrangement, the neophyl rearrangement, eq. I 64.

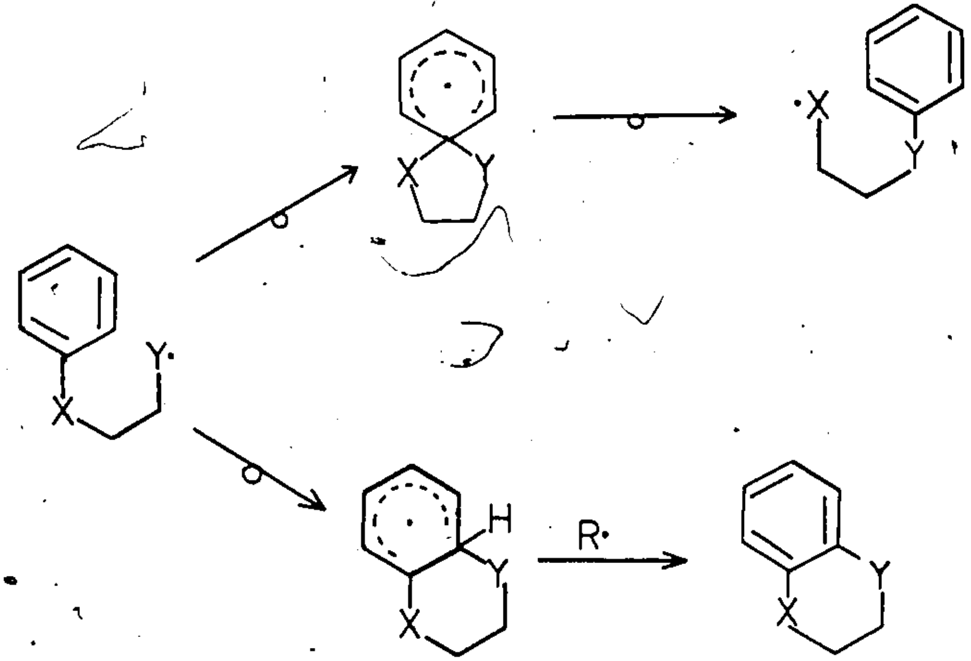
$$C_6H_5C(CH_3)_2\dot{C}H_2 \longrightarrow C_6H_5CH_2\dot{C}(CH_3)_2 \qquad [I\ 64]$$

This rearrangement has been investigated extensively and the reaction is known to be intramolecular in nature.[65c] It must therefore proceed through a spiro[2.5]octadienyl radical, 11, as an intermediate or transition state. However, this "intermediate" is so short-lived that it is not observed.



11

1,2-Aryl shifts are known to occur between carbon and heteroatoms where the migration origin is the carbon atom; migrations from heteroatoms to carbon are not known. No authentic 1,3-aryl shifts are known. On the other hand, 1,4- and 1,5-aryl shifts are known. In these two rearrangements, the aryl group may migrate between two carbon atoms, between a carbon atom and a heteroatom, or between two heteroatoms. 1,4-Aryl shifts are often accompanied by an Ar_2-6 reaction which usually leads to products of the tetralin type, eq. I 65.



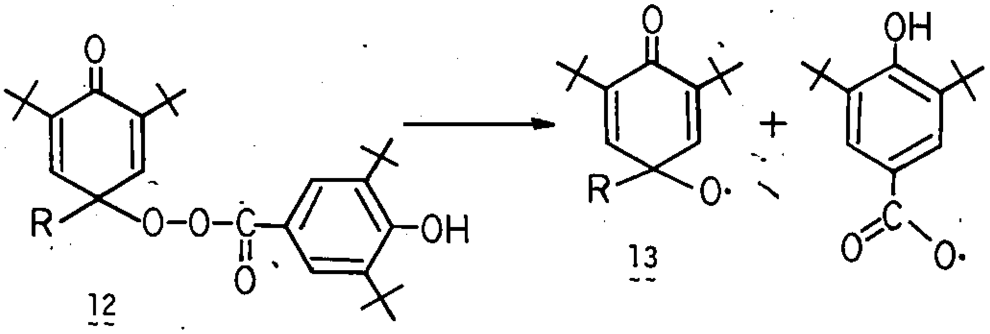
[I 65a]

[I 65b]

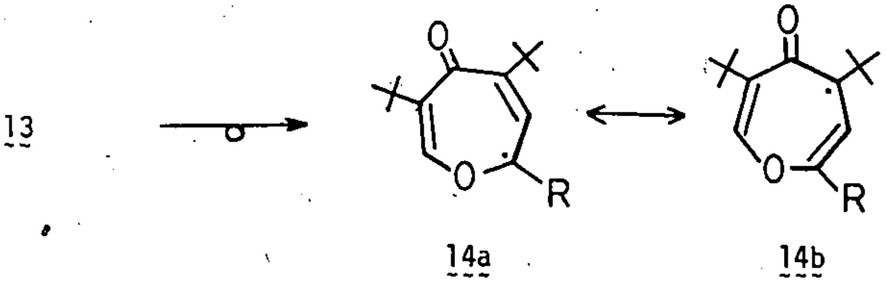
Vinyl groups are known to undergo a 1,2-shift via cyclopropylcarbinyl radicals as discrete intermediates.[70-72] This type of radical rearrangement is the fastest known to date.[73] Warkentin and Ingold recently reported the rate constant for the overall rearrangement of the 2,2-dimethyl-3-buten-1-yl radical to 1,1-dimethyl-3-buten-1-yl radical to be 4.3×10^{7} sec^{-1} at 25°C (see eq. I 66). Of particular interest to the work reported in this thesis is 1,2-vinyl migration from carbon

$$H_2C{=}CHC(CH_3)_2\dot{C}H_2 \longrightarrow H_2C{=}CHCH_2\dot{C}(CH_3)_2 \qquad [I\ 66]$$

to oxygen. Nishinaga[74] recently studied the intramolecular rearrangement of the quinoxyl radicals, **13**, which are formed by the peroxy bond homolysis in compound **12**. 1,2-Vinyl migrations in simple alkyl oxyl radicals are not known. This is rationalised on the basis of the known stabilities of oxygen and carbon radicals. Thus, even ~~if~~ addition to the double bond



[I 67]



[I 68]

took place the reverse β-scission pathway towards the alkyl oxyl radicals is very easy and very fast.[75-79] In oxiranyl alkyl radicals the C-C bond cleavage is known to take place only when the resulting carbon radical is stabilized.[77,80]

I 4. ORGANIC HYDROPEROXIDES

Synthesis of organic hydroperoxides is well documented.[64,81] These compounds are synthesized from (a) hydrogen peroxide, (b) molecular oxygen, (c) ozone, and (d) by hydrolysis of organic peroxides.

Physical Properties of Hydroperoxides. Most alkyl hydroperoxides are liquids at room temperature and the lower members are soluble in water and are explosive.

Hydroperoxides have characteristic infrared absorption bands in the 880-820 cm^{-1} (due to C-O-O-H deformation and stretching vibrations) and 3600-3400 cm^{-1} (due to -O-H stretch) regions. Like alcohols, hydroperoxides in solution exhibit two absorption maxima in the 3600-3400 cm^{-1} region of their ir spectra. The sharper band is attributed to the monomeric species and the broader band, which appears at lower wavenumbers, is attributed to the hydrogen-bonded species.[82-84] A number of reports on infrared and nmr studies of hydrogen bonding[85,86] and the effect of the H-bonding on stabilities of the hydroperoxides[87,88] are found in the literature.

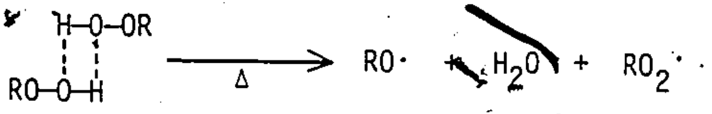
Nuclear magnetic resonance spectroscopic studies showed the hydroperoxyl proton resonance at approximately $\delta = 9.0$ ppm. This signal is close to that of the carboxylic proton in aliphatic acids. In fact organic hydroperoxides are known to be more acidic than the corresponding alcohols,[89-91] with their pK_a values lying between 11 and 13.

Radical Reactions of Hydroperoxides. Hydroperoxides undergo five general types of homolytic reactions:

1) Unimolecular homolysis:

$$RO\text{-}OH \xrightarrow[\text{or } h\nu]{\Delta} RO\cdot + \cdot OH \qquad [I\ 69]$$

2) Bimolecular homolysis (A special case of MAH):



$$\begin{matrix} H\text{—}O\text{—}OR \\ \vdots \quad \vdots \\ RO\text{—}O\text{—}H \end{matrix} \xrightarrow{\Delta} RO\cdot + H_2O + RO_2\cdot \qquad [I\ 70]$$

3) Molecule assisted homolysis:

$$RO\text{-}OH + A \longrightarrow RO\cdot + AOH \qquad [I\ 71]$$

4) Hydrogen abstraction:

$$RO\text{-}O\text{-}H + R'\cdot \longrightarrow RO_2\cdot + R'H \qquad [I\ 72]$$

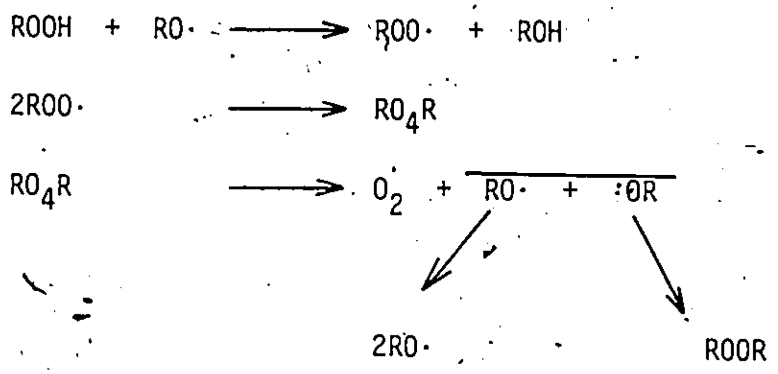
5) Radical substitution at oxygen:

$$RO\text{-}OH + R'\cdot \begin{array}{l} \nearrow ROR' + \cdot OH \\ \searrow R'OH + RO\cdot \end{array} \qquad [I\ 73]$$

The unimolecular decompositions of hydroperoxides are usually complicated by higher-order reactions. Using low initial concentrations (0.01-0.001M in toluene) to minimize these complications, Hiatt and Irwin[92] determined the rate constant for the unimolecular decomposition of t-BuOOH to be 2.6×10^{-5} sec^{-1} at 182°C. They also determined that the rate constant for homolytic cleavage of O-O bond at 170-215°C is about $10^{15.8} e^{-43,000/RT}$. Their results led Hiatt to conclude that any hydroperoxide decomposition that is significantly more rapid than the above must in large part be due to other reactions.[93] Several observations[64k,87,88] support a bimolecular homolysis of hydroperoxides (eq. I 70) and this process has been explained in terms of hydrogen bonding between the molecules to give dimers.

By far the major process involved in the thermal decomposition of hydroperoxides is the attack by free radicals at either the oxygen or hydrogen of the hydroperoxy group. The rates of decomposition of tertiary alkyl hydroperoxides initiated by a more thermally labile peroxyester,[94] peroxide,[95] or azo compound[96] are found to be independent of hydroperoxide concentration and first-order in initiator concentration. The mechanism for the decomposition of the tertiary alkylhydroperoxides is illustrated by the sequence of reactions in Scheme 4. The rate of

SCHEME 4



H-abstraction from the hydroperoxide is often surprisingly fast. For example, the thermoneutral reaction between tetralin hydroperoxide and cumylperoxyl radicals (or vice versa), (eq. I 74), has a rate constant of about 10^3L mol^{-1}sec^{-1} at 30°C.[60e,97] Similarly, the reaction between phenoxyl radicals and tetralin hydroperoxide, (eq. I 75) has a rate constant $\geq 2\text{x}10^5$L mol^{-1}sec^{-1}.[98] The reverse has a rate constant of $5\text{x}10^3$L mol^{-1}

$$R'OOH + ROO\cdot \rightleftharpoons ROOH + R'OO\cdot \qquad [I\ 74]$$

sec^{-1}.[99-101]

$$C_6H_5O\cdot + ROOH \rightleftharpoons C_6H_5OH + ROO\cdot \qquad [I\ 75]$$

At hydroperoxide concentrations of 0.01M and above in toluene, Hiatt and Irwin[92] found that the peroxy-type of induced decomposition (see Scheme 4) was effectively suppressed. The hydroperoxide underwent bimolecular decomposition induced by radical attack at oxygen. For 0.01M t-BuOOH in toluene the rate constant for hydroxyl-abstraction was found to be 1×10^4 L mol^{-1} sec^{-1} at 182°C.

Non-Radical Reactions. Two of the non-radical reactions which hydroperoxides undergo are discussed here.

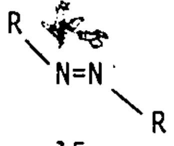
Hydroperoxides react with alkyl and acyl halides to give organic peroxides, eq. I 76. This is one of the methods for the synthesis of dialkyl and diacyl peroxides.

$$\mathrm{ROOH} + \mathrm{R'X} \longrightarrow \mathrm{ROOR'} + \mathrm{HX} \qquad [\mathrm{I}\ 76]$$

Hydroperoxides have also been used as oxidizing agents for many organic compounds; olefins are oxidized to epoxides,[102] phosphines and phosphites to their corresponding oxides,[103-105] sulfides to sulfoxides[106-108] which are further oxidized to sulfones, and amines to N-oxides.[107d] Various mechanisms have been proposed for the uncatalysed epoxidation of olefins; these are discussed in Section RD2.2, page 127.

I 5. AZO COMPOUNDS

Compounds containing the -N=N- bond are referred to as azo compounds. They may be acyclic or cyclic, symmetric or asymmetric, and may contain other functional groups. Examples of this group of compounds are:

(a) 

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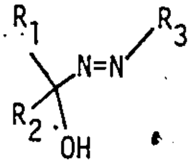
acyclic azoalkanes (R = alkyl or aralkyl);

(b) 

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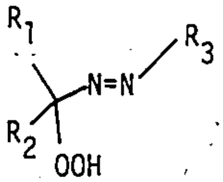
α-hydroxydiazenes (or α-azocarbinols);

(c) 

17

α-hydroperoxydiazenes (or α-azohydroperoxides)

These three classes of azo compounds are discussed in this section.

Azo compounds have been known since 1909[109]. They undergo such reactions as isomerization, cyclization, Diels-Alder reactions, and free radical reactions. A number of reviews on azo compounds are available.[110-116]

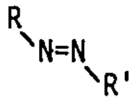
I 5.1 Acyclic Azoalkanes

Azo compounds may decompose in a one-step or two-step process to give three fragments, eq. I 77 and I 78. The question of whether azo

$$R\text{-}N{=}N\text{-}R' \longrightarrow R\cdot + N_2 + \cdot R' \qquad [I\ 77]$$

$$\begin{tikzcd}
R\text{-}N{=}N\text{-}R' \arrow[r] & R\cdot + \cdot N{=}N\text{-}R \arrow[d] & \\
 & N_2 + \cdot R' & [I\ 78]
\end{tikzcd}$$

compounds decompose by the one-step or by the two-step mechanism was addressed first by Ramsperger.[117] In his study of the azoalkanes 15, he assumed that if the decomposition of the compounds occurred by a single bond scission followed by elimination of nitrogen from the diazenyl radical (eq. I 78), then the energy of activation of 15c



15a, R = R' = CH_3; 15b, R = R' = i-Pr; 15c, R = CH_3; R = i-Pr

would be very nearly that of 15b, for the first bond to break would be the weaker isopropyl bond; if, however, the reaction occurred by simultaneous rupture of both bonds, the energy of activation would be intermediate between those of 15a and 15b. His results, Table 4, pointed to a one-step (that is the two-bond concerted cleavage) mechanism eq. I 78. The activation energy for 15b used by Ramsperger was incorrect; the best current value is 47.9 kcal mol^{-1}.[118] If the value for 15c is reliable, these results would point in the direction of a one-bond scission; the opposite of what Ramsperger found.

Table 4

Energies of Activation for Decomposition of 15

R	R'	E_a/kcal mol^{-1}	Recent Value
CH_3	CH_3	51.2	
i-Pr	i-Pr	40.9	47.9
CH_3	i-Pr	47.5	

Crawford studied the gas-phase pyrolysis of simple azoalkanes, 18, which provided resonance stabilization to the radicals formed.[119-121] It should be expected that if the two-step mechanism (eq. I 78) were

$CH_2=CHCH_2-N=N-R$

18a, R = $CH_2=CHCH_2$; 18b, R = CH_3

18c, R = n-Pr; 18d, R = t-Bu

operative then all the energies of activation would be nearly that of 18a. Comparison of observed and calculated rate constants, Table 5, shows that these compounds decomposed by the two-step mechanism.

If the generalized Polanyi equation (I 79), applicable to unsymmetrical diazenes, were applied to compounds 18, assuming that $\alpha + \alpha' = 1.0$ and c = 48.4, then the compounds fit only when $\alpha = 0.9$ to

$$E_a = \alpha\ D(R-H) + \alpha'\ D(R'-H) - C \qquad [I\ 79]$$

Table 5

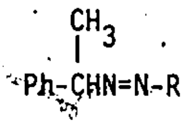
Data on the Decomposition of 18

Compound	E_a/kcal mol^{-1}	Log A	$\Delta S^{\neq}$	Rate Constants (s^{-1})			
				Rel.	Obs.x10^6	Calc'd x 10^6	
						1-step	2-step
18a	36.1	15.54	9.8	1.00	-		
18b	35.5	14.36	4.6	0.13	4.90	0.0001∿0.069	1.8∿180
18c	35.6	14.80	6.6	0.339	12.0	0.0021∿0.29	1.8∿180
18d	29.8	12.72	-2.8	4.92	174	0.14 ∿14	1.8∿180

1.0 and α' = 0.1 to 0.0. These results implied that there was an insignificant stretching of the alkyl-N bond associated with a fully stretched allyl-N bond in the transition state.

Further evidence in support of the two-step mechanism is obtained by examination of the secondary deuterium isotope effects, Table 6. The $\Delta\Delta G^{\neq}$ values obtained by assuming a two-step mechanism are found to be more consistent within themselves and with those generally found ($\Delta\Delta G^{\neq}$ 80-120 cal mol^{-1}).[122]

In a series of papers[123] Seltzer provided clues on the mechanism of decomposition of α-phenethylazo compounds, 19. Alpha-deuterium



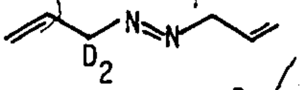
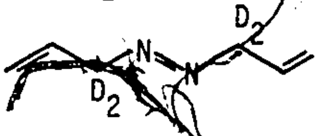
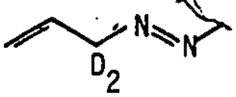
$\mathrm{Ph\text{-}\overset{\overset{\large CH_3}{|}}{C}HN{=}N\text{-}R}$

19

19a, R = $CH(CH_3)Ph$; 19b, R = $CH(CH_3)_2$; 19c, R = CH_3

Table 6

Secondary Deuterium Isotope Effects in 18a and 18b

		k_H/k_D	$\Delta\Delta G^{\neq}/D$ (cal mol^{-1})	
			Two-step	One-step
	18a-d_2	1.14	121	56
	18a-d_4	1.26	99	50
	18b-d_2	1.28	98	98

isotope effects on the thermal decomposition of 19 revealed changes in the mechanism in going from 19a to 19c, Table 7. He observed[121a] that a large body of data on secondary α-deuterium isotope effects indicate that an average value of 1.12, at 105°C, corresponds to a system where only one bond is being broken in the slow step. From this observation he concluded that since the measured effect for 19a (k_H/k_D = 1.27) was about twice as large, it appeared that both C-N bonds were being broken simultaneously. Observed effects in the decomposition of 19c indicated that the CH_3-N bond is not stretched in the transition state; in fact, Seltzer[123c] proposed a small tightening of the CH_3-N bond possibly because of three-electron resonance in the resulting diazenyl radical. For 19b a transition state wherein the two [illegible] bonds are stretched simultaneously but not to the same degree was [illegible]ed.

Engel and Bishop[124] have recently compared the free energies of activation for the thermolysis of symmetrical and unsymmetrical alkyl

Table 7

Kinetic Effects for Pyrolysis of Compound 19

Compound[a]	k_H/k_D	Temp (°C)
19a-d_2	1.27	105
19b-α-d	1.14	143
19b-α'-d	1.03	143
19c-α-d	1.13	161
19c-α'-d	0.97	161

[a] α Refers to the phenethyl group and α' refers to the other.

diazenes (Table 8). Mechanism (I 78) suggests that the nature of the less stable free-radical $\cdot R_1$ should have no effect on $\Delta G^{\neq}$ for the thermolysis of $R_1N{=}NR_2$ so that $\Delta\Delta G^{\neq}{}_2$ should be zero. If this was in fact true, then $\Delta G^{\neq}$ values for $R_1N{=}NR_2$ and $R_2N{=}NR_2$ should be equal. In general, $\Delta\Delta G^{\neq}{}_2$ is less than $\Delta\Delta G^{\neq}{}_1$ but it is equal to zero only in a few cases.[121,125] The fact that $\Delta G^{\neq}$ for thermolysis of $R_1N{=}NR_2$ lies closer to that for $R_2N{=}NR_2$ than to that for $R_1N{=}NR_1$ suggests that the R_2-N bond is more broken than the R_1-N bond in the transition state. The evidence so far seems to support the hypothesis that symmetrical azoalkanes decompose by the concerted two-bond cleavage (eq. I 77) whereas greatly different R groups lead to unequal stretching of the two C-N bonds. In the extreme case of arylazoalkanes, the evidence is in favour of one-bond cleavage.[126,127]

Table 8

Differences in Free Energy of Activation Between Symmetrical and Unsymmetrical Diazenes

R_1	R_2	$\Delta\Delta G_1^{\neq}$ (kcal mol^{-1})[a]	$\Delta\Delta G^{\neq}_2$ (kcal mol^{-1})[b]
Me	i-Pr	3.5	0.7
Me	α-Phenethyl	13.7	3.8
i-Pr	α-Phenethyl	10.2	3.1
i-Pr	Cumyl	11.4	6.0
t-Bu	Cumyl	8.4	3.3
Me	Allyl	14.0	1.0
n-Pr	Allyl	10.3	0.5
t-Bu	Allyl	7.5	-2.5

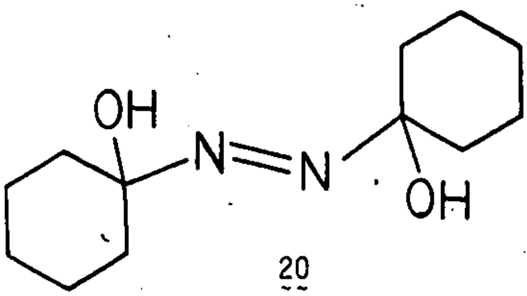
[a] Free-energy difference between azoalkane listed and its more stable symmetrical counterpart ($R_1N{=}NR_1$).

[b] Free-energy difference between azoalkane listed and its less stable symmetrical counterpart ($R_2N{=}NR_2$).

A recent MNDO calculation on azoethane,[128] and a solution-phase pressure study of azo-1-adamantane[129] have led to the conclusion that even symmetrical azoalkanes may decompose by a stepwise homolysis. Engel and Gerth[130] also recently carried out further studies into the thermal decomposition of cis and trans azoalkanes. The results of these recent studies are presented and discussed, together with those from this work, in section RD2.2 (page 92).

I 5.2 α-Hydroxydiazenes

α-Hydroxydiazenes (or α-azocarbinols) have received some attention since 1,1'-dihydroxyazocyclohexane, 20, was first synthesized.[131] Until recently,[132] α-monohydroxydiazenes of type 16 were rare and little was known about their chemistry.



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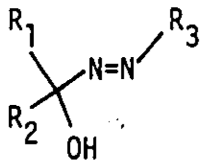
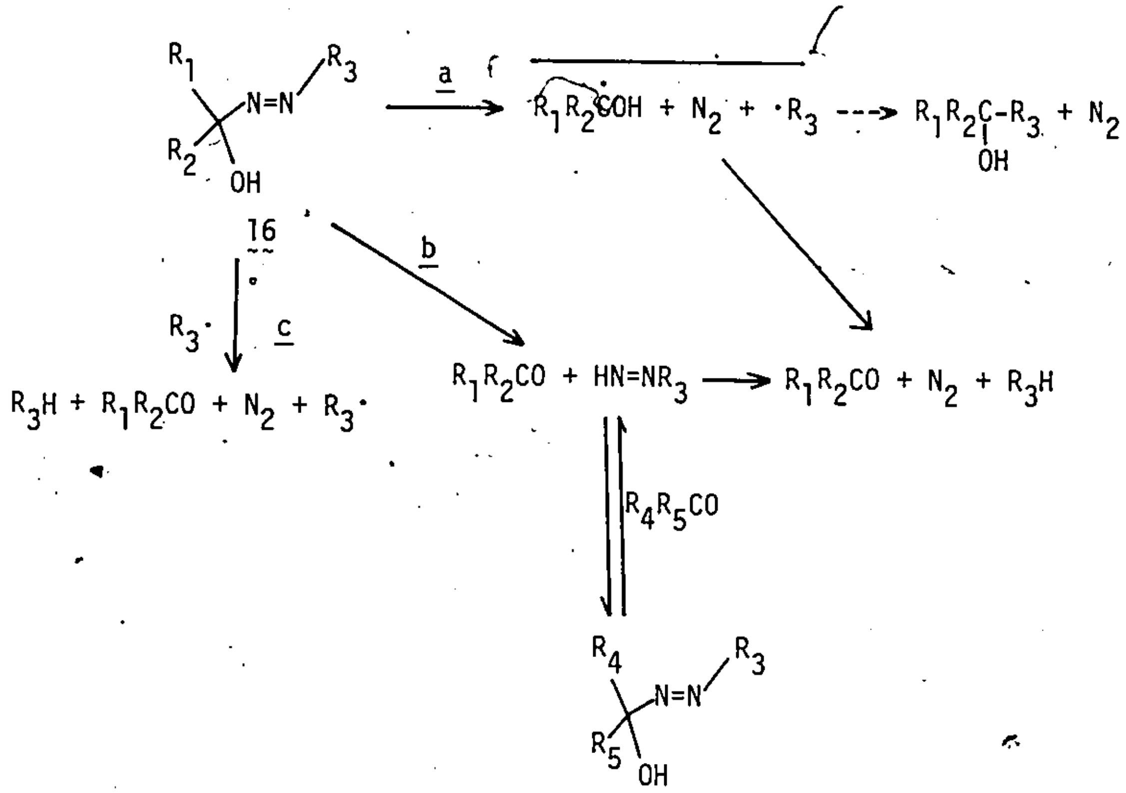
These compounds have been shown to display three main types of chemistry (see Scheme 5): (a) normal unimolecular decomposition to



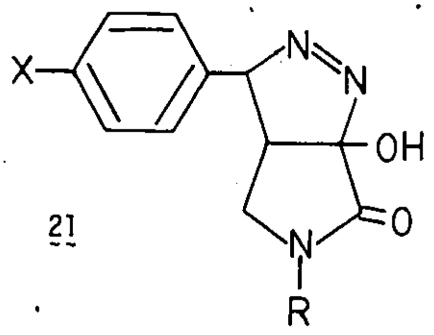
16

produce ketyl radicals, $R_1R_2\dot{C}OH$, and alkyl (or aryl) radicals which disproportionate in the cage; (b) reversible dissociation to carbonyl compound and diazene; and (c) bimolecular decomposition induced by radical attack at the hydroxyl hydrogen.

SCHEME 5

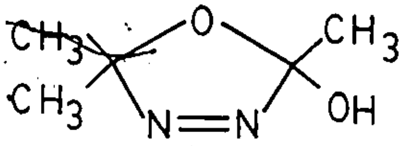


Southwick and coworkers[133] suggested that, in their fragmentations to cyclopropanes, 5-substituted-6a-hydroxy-6-oxo-3-phenyl-3,3a,4,5,6,6a-hexahydropyrrolo[3,4-c]pyrazoles, 21, did so by mechanism a (Scheme 5). Hünig[132] demonstrated that under strongly alkaline condi-



21

tions mechanism b operated where the intermediate diazene (R-N=NH) can lose the proton to become nucleophilic and thereby exchange carbonyl groups. Mechanism c was proposed and proven by Warkentin and Knittel.[134-136] They observed quite an interesting chemistry of 2-hydroxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline, 22. It decomposed readily in solution

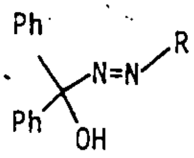


22

at moderate temperatures to isopropyl acetate. Evidence for a radical chain induced-decomposition by attack at hydroxyl hydrogen included (a) reaction of 22 with alkenes to give hydroalkylation compounds as the major products; (b) spin trapping of 2-acetoxy-2-propyl radical by nitrosobenzene with esr detection, and (c) inhibition by Ph_3SnH. "Stable" free radicals were found to initiate decomposition.

Recent work in this laboratory by Warkentin and Nazran[137], however, indicates that at low concentrations, diphenylpicrylhydrazyl (DPPH) free radical inhibited the rapid decomposition of 2-[(1-hydroxy-1-methylethyl)azo]ethanenitrile (16, $R_1=R_2=CH_3$, $R_3=CH_2CH_2CN$). However, at higher DPPH concentrations rapid decomposition was observed indicating that the DPPH initiated the decompositon of the azocarbinol. Ordinarily abstractions of hydroxyl hydrogen in solution are unfavorable so that the chain decomposition of 16 ($R_1=R_2=CH_3$, $R_3=CH_2CH_2CN$) can be attributed to a concerted mechanism which tends to lower the activation energy for decomposition considerably.

The radical chain additions to olefins by the azocarbinols were exploited for their synthetic values by Warkentin and Knittel[136] and by Warkentin and Yeung.[138,139] The latter pair employed an acylic system, 23, to generate a variety of radicals R· (eq. I 80) which added RH across double bonds by the radical chain mechanism.



23

$$\xrightarrow{\text{In.}} \text{InH} + \text{Ph}_2\text{CO} + \text{N}_2 + \text{R}\cdot \qquad [\text{I } 80]$$

$R = CH_3, C_2H_5, CH(CH_3)_2, C(CH_3)_3, C_6H_5, C_6H_5CH_2$

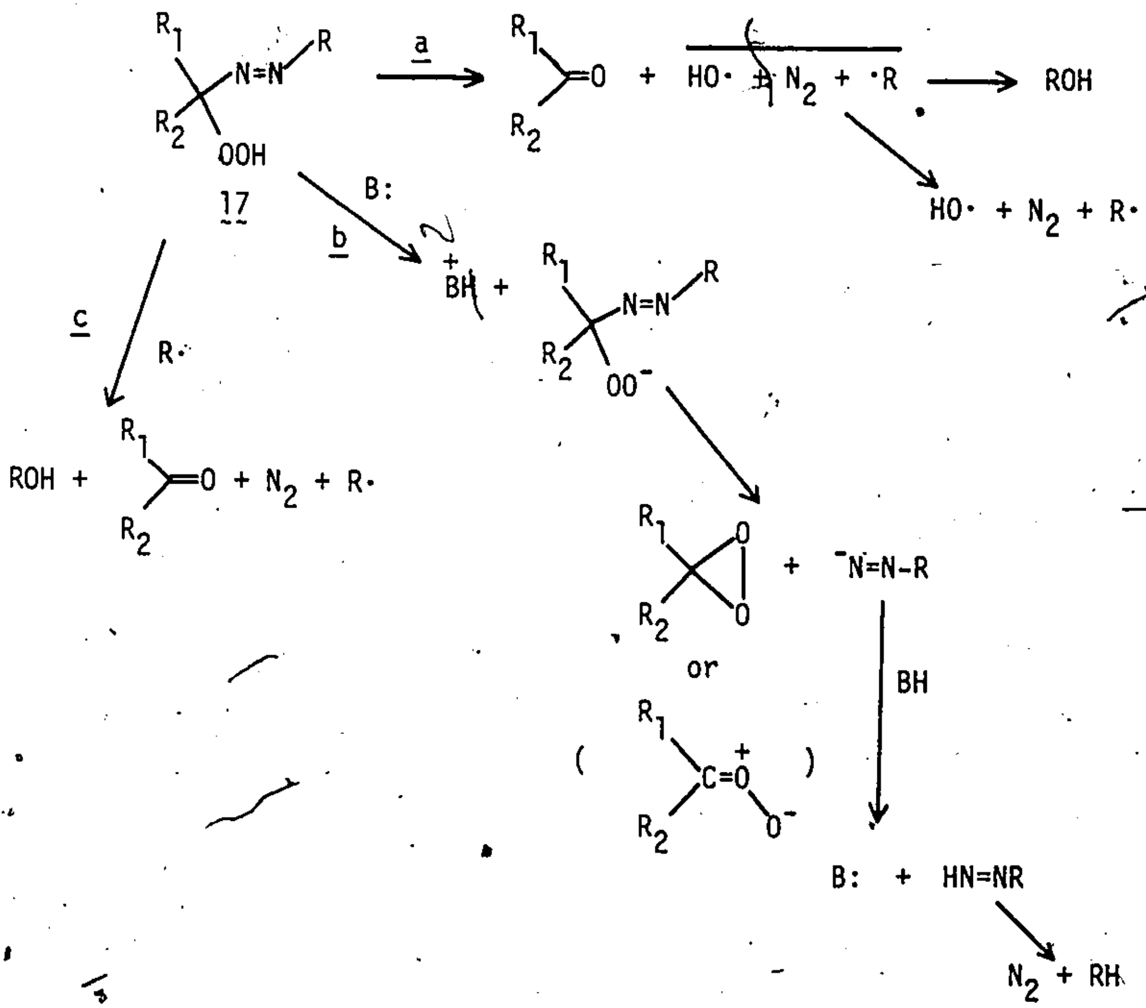
$CH_2CH_2OH, CH_2CH{=}CH_2,$

I 5.3 α-Hydroperoxydiazenes

Although the structure of α-hydroperoxydiazenes (or α-azohydroperoxides) was established as far back as 1951,[64] it was only recently that organic chemists began to investigate their chemistry. They were first used as polymerization initiators by MacLeay[140] who later synthesized a series of these compounds and their corresponding alkaline and alkaline earth metal salts[141] and azocarbinols.[142] Tezuka and coworkers have used p-bromo-[(1-hydroperoxybenzyl)azo]benzene, 24, as a source of hydroxyl radicals in aromatic hydroxylation reactions,[143] and as oxidizing agent for epoxidation of olefins[144] and sulfoxidation of sulfides to sulfoxides.[145] The compounds are readily reduced to the corresponding azocarbinols by reducing agents such as Ph_3P[146], lithium aluminium hydride,[144] and the iodide ion.[137]

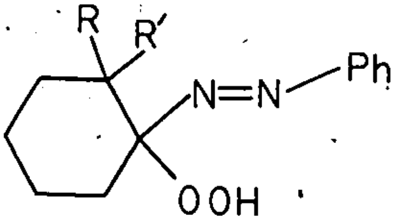
Both free radical and ionic mechanisms have been proposed for the decomposition of α-hydroperoxydiazene (see Scheme 6).

SCHEME 6



Tezuka[143] proposed a unimolecular decomposition of compound 24 to give hydroxyl and aryl radicals, and a carbonyl compound and nitrogen (mechanism a, Scheme 6). He also proposed a base-catalysed conversion of 24 to a dioxirane (or a carbonyl oxide) intermediate which was said to be the oxidizing agent in the epoxidation of olefins and in sulphoxidation reactions. However, he has not positively proved the intermediacy of the dioxirane (or carbonyl oxide).

Takeda[147] recently showed that α-hydroperoxydiazenes underwent C-C bond cleavage when treated with acids,bases,-or reducing agents. The presence of a 2-hydroxyl group in the cyclohexane rings of the compounds (25) seemed to play an important role for the cleavage. Baumstark and Landis[148], in their study of compound 26, observed that



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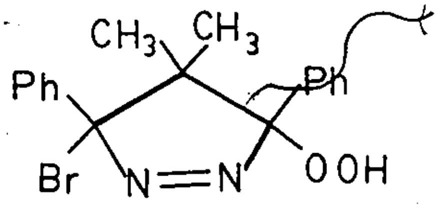
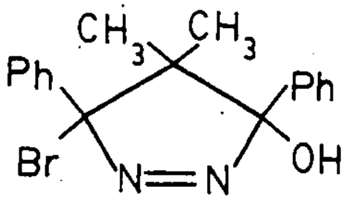
it reacted with 2,3-dimethyl-2-butene to give 3-bromo-4,5-dihydro-



26

4,4-dimethyl-3,5-diphenyl-3H-pyrazole (27) and tetramethylethylene oxide. In more recent studies Baumstark[148a] showed that α-hydroperoxydiazenes reacted with olefins and with organic sulfides via a bimolecular mechanism; the reactions were found to be first order with respect to α-hydroperoxydiazene and to alkene or sulfide.



27

We have independently proposed[149] the unimolecular decomposition mechanism (mechanism a in Scheme 6) and have also proposed and proved a radical-chain abstraction of the hydroxyl group of the hydroperoxyl function (mechanism c, Scheme 6). A fourth mechanism proposed in this laboratory involves a radical-chain abstraction of the hydroperoxyl hydrogen.

All the mechanisms proposed above are discussed in detail in the next chapter.

RESULTS AND DISCUSSION

RD 1. SYNTHESIS AND PROPERTIES OF α-HYDROPEROXYDIAZENES

RD 1.1. Synthesis.

α-Hydroperoxydiazenes, 28, were synthesized according to Scheme 7. The first step involved the preparation of the alkyl hydrazine by reacting hydrazine hydrate with the alkyl bromide or the alkyl tosylate. The alkyl tosylate was prepared from the alcohol and p-toluenesulphonyl chloride.[150] The results and the spectroscopic data are given in Table 9. Yields ranged between 71% and 95%. In many cases the hydrazine was used in the next step without purification.

In the second step the hydrazines were condensed with acetone to give the acetone hydrazones. Table 10 lists the hydrazones and their spectroscopic data. Yields of the distilled hydrazones were in the range of 46-90%. The distillation ensured purer hydrazones for autoxidation; long induction periods were sometimes encountered in autoxidation of undistilled hydrazones.

The hydrazones were converted to the α-hydroperoxydiazenes via oxidation with oxygen at about 5°C in petroleum ether (bp 30-60°C) or in benzene. Oxygen uptake was monitored by a gas burette. The reaction was judged complete when the gas volume remained constant for 4h or more. Completion of the reaction was also checked for by ^{1}H NMR spectroscopy to ensure that the separate methyl singlets of the hydrazone had given

Table 9: ^{1}H NMR Spectra of Hydrazines (H_2NNHR)

R	Yield (%)	^{1}H NMR[a]
CH_2CF_3	-	3.30 (s, br, 3H); 3.41 (q, 2H, J=9.0 Hz).[b]
$CH_2CH_2OCH_3$	85	2.90 (t, 2H, J=6.3 Hz); 3.35 (s, 3H); 3.50 (m, 5H).
$CH_2CH_2OC_6H_5$	95	3.02 (t, 2H, J=5.9 Hz); 3.37 (s, br, 3H); 4.01 (t, 2H, J=5.9 Hz); 7.05 (m, 5H).
C_6H_5	-	3.82 (s, br, 3H); 6.70 (m, 5H).
$CH(CH_3)_2$	71	1.05 (d, 6H, J=6.0 Hz); 2.81 (sept., 1H, J=6.0 Hz); 3.50 (s, br, 3H).
$C(CH_3)_3$	92	1.18 (s, 9H); 3.30 (s, br, 3H).
$CH_2C_6H_5$	97	3.25 (s, br, 3H); 3.80 (s, 2H); 7.30 (s, 5H).

[a] In $CDCl_3$ with internal Me_4Si. The numbers are δ values followed, in parenthesis, by the multiplicity, the relative signal intensity, and, where appropriate, by the coupling constant in Hertz. [b] ^{19}F chemical shift, relative to external $CFCl_3$, $\delta = -66.3$ (t, J_{FH}=9.0 Hz).

Table 10: Spectra of Acetone Hydrazones ($(CH_3)_2C{=}N{-}NHR$)

R	Yield (%)	^1H NMR[a]	^{13}C NMR[b]	M.S. (m/z)[c]
CH_2CF_3	78	1.70 (s, 3H);	14.91 ($\underline{Z}$ Me);	154, $M^{+\cdot}$
		1.89 (s, 3H);	24.36 ($\underline{E}$ Me);	139, $[M-CH_3]^+$
		3.60 (m, 2H, J=9.0 Hz, J=4.0 Hz);	51.79 (q, $-\underline{\underline{C}}H_2-$, ($J_{CF}$=31.0 Hz);	85, $[M-CF_3]^+$
		4.77 (s, br, 1H)	125.09 (q, $\underline{\underline{C}}F_3$, J_{CF}=279.6 Hz)	56, $[(CH_3)_2C{=}N)]^+$
			147.17 ($(CH_3)_2\underline{\underline{C}}{=}N$)	
$CH_2CH_2OCH_3$	46	1.73 (s, 3H);	14.56 ($\underline{Z}$ Me);	130, $M^{+\cdot}$
		1.90 (s, 3H);	24.16 ($\underline{\underline{E}}$ Me);	85, $[C_4H_9N_2]^+$
		3.27 (t, 2H, J=5.1 Hz);	49.66 ($N-\underline{\underline{C}}H_2-$);	72, $[C_3H_8N_2]^+$
		3.34 (s, 3H)	57.75 ($-\underline{\underline{C}}H_2-O$);	56, $[(CH_3)_2C{=}N]^+$
		3.50 (t, 2H, J=5.1 Hz);	70.32 ($-O-\underline{\underline{C}}H_3$);	45, $[C_2H_5O]^+$
		4.75 (s, br, 1H)	144.80 ($(CH_3)_2\underline{\underline{C}}{=}N$)	

..... continued

Table 10: Spectra of Acetone Hydrazones ($(CH_3)_2C{=}N\text{-}NHR$) (continued)

R	Yield (%)	^1H NMR[a]	^{13}C NMR[b]	M.S. (m/z)[c]
$CH_2CH_2OC_6H_5$	86	1.73 (s, 3H); 1.90 (s, 3H); 3.50 (t, 2H, J=5.0 Hz); 4.05 (t, 2H, J=5.0 Hz); 4.88 (s, br, 1H); 7.05 (m, 5H).	14.75 (Z Me); 24.41 (E Me); 49.51 ($N\text{-}\underline{\underline{C}}H_2\text{-}$); 65.86 ($\text{-}\underline{\underline{C}}H_2\text{-}O$); 114.03 (meta); 120.19 (para); 128.88 (ortho); 145.40 ($(CH_3)_2\underline{\underline{C}}{=}N$) 158.43 (ipso).	192, $M^{+\cdot}$ 107, $[C_7H_7O]^+$ 99, $[M-C_6H_5O]^+$ 94, $[C_6H_6O]^{+\cdot}$ 56, $[(CH_3)_2C{=}N]^+$
C_6H_5	93	1.66 (s, 3H); 1.93 (s, 3H); 6.96 (m, 6H, $C_6\underline{\underline{H}}_5+N\underline{\underline{H}}$).	14.99 ($\underline{\underline{Z}}$ Me); 24.78 ($\underline{\underline{E}}$ Me); 112.75 (meta); 119.19 (para); 128.87 (ortho); 143.75 (ipso) 145.86 ($(CH_3)_2\underline{\underline{C}}{=}N$).	148, $M^{+\cdot}$ 133, $[M-CH_3]^+$ 92, $[C_6H_6N]^+$ 77, $[C_6H_5]^+$ 65, $[C_5H_5]^+$ 56, $[(CH_3)_2C{=}N]^+$

...continued

Table 10: Spectra of Acetone Hydrazones ($(CH_3)_2C{=}N{-}NHR$) (continued)

R	Yield (%)	^1H NMR^a	^{13}C NMR^b	M.S. (m/z)^c
$CH(CH_3)_2$	69	1.12 (d, 6H, J=6.0 Hz);	14.84 ($\underline{\underline{Z}}$ Me)	114, $M^{\dot{+}}$
		1.71 (s, 3H)	21.64 ($CH(\underline{\underline{C}}H_3)_2$)	99, $[M-CH_3]^+$
		1.90 (s, 3H);	24.51 ($\underline{\underline{E}}$ Me)	71, $[C_3H_7N_2]^+$
		3.40 (sept., 1H, J=6.0 Hz);	49.98 ($N-\underline{\underline{C}}H(CH_3)_2$)	56, $[(CH_3)_2C{=}N]^+$
		4.10 (s, br, 1H).	144.39 ($(CH_3)_2\underline{\underline{C}}{=}N$)	56, $[(CH_3)_2C{=}N]^+$
$C(CH_3)_3$	87	1.21 (s, 9H);	14.51 ($\underline{\underline{Z}}$ Me)	128, $M^{\dot{+}}$
		1.73 (s, 3H);	24.79 ($\underline{\underline{E}}$ Me)	113, $[M-CH_3]^+$
		1.91 (s, 3H);	28.14 ($C(\underline{\underline{C}}H_3)_3$)	85, $[M-C_3H_7]^+$
		4.30 (s, br, 1H)	52.43 ($N\underline{\underline{C}}(CH_3)_3$)	72, $[C_4H_{10}N]^+$
			142.67 ($(CH_3)_2\underline{\underline{C}}{=}N$)	56, $[(CH_3)_2C{=}N^+]$

..... continued

Table 10: Spectra of Acetone Hydrazones ($(CH_3)_2C=N-NHR$) (continued)

-R	Yield (%)	^1H NMR[a]	^{13}C NMR[b]	M.S. (m/z)[c]
$CH_2C_6H_5$	83[e]	1.63 (s, 3H);	14.45 (Z Me)	162, $M^{\ddagger}$
		1.85 (s, 3H);	23.95 (E Me)	147, $[M-CH_3]^+$
		4.18 (s, 3H);	54.16 ($N-\underline{C}H_2C_6H_5$)	91, $[C_7H_7]^+$
		7.25 (s, 5H).[f]	125.97 (meta)	71 $[(CH_3)_2C=NNH]^+$
			127.27 (ortho,para)	
			139.15 (ipso)	
			144.06 ($(CH_3)_2\underline{C}=N$)	

[a] In $CDCl_3$, unless otherwise noted, with internal Me_4Si. The numbers are δ values followed, in parenthesis, by the multiplicity, the relative signal intensity, and, where appropriate, by the coupling constant in Hertz.

[b] In $CDCl_3$ with the solvent signal as internal reference.

[c] Probable ion assignments in parenthesis.

[d] ^{19}F chemical shift, relative to external $CFCl_3$, $\delta = -65.9$ (t, J=9.0 Hz).

[e] Yield based on starting benzyl chloride.

[f] In carbon tetrachloride.

SCHEME 7

$$H_2NNH_2 + RX \xrightarrow{EtOH} H_2NNHR \qquad (X = \text{hal., OTs})$$

$$(CH_3)_2CO + H_2NNHR \xrightarrow[\text{catalytic } CH_3CO_2H]{Et_2O} (CH_3)_2C{=}NNHR$$

$$(CH_3)_2C{=}NNHR \xrightarrow[\text{Pet. Ether (or benzene)}]{O_2} \underset{28}{(CH_3)_2C(OOH)N{=}NR}$$

way to the single gem dimethyl signal of the product. Spectroscopic data for compounds 28 are given in Table 11.

RD 1.2 Physical Properties.

Pausacker[65a] and Criegee and Lohaus[65b] were the first to propose the correct structure of the products of autoxidation of phenylhydrazones. Busch and Dietz[151] had earlier assigned a wrong structure to the autoxidation products. The structure of α-hydroperoxydiazenes is now well established and the spectroscopic information on the compounds (28) in this work substantiates the structure proposed by Pausacker[65a] and by Criegee and Lohaus.[65b]

Compounds 28 show infrared bands at 3400 cm^{-1} and 845 cm^{-1}. These bands are indicative of the hydroperoxyl group; the 3400 cm^{-1} band is due to O-H stretching and 845 cm^{-1} is due to O-O stretching.

Table 11: Spectral Data of α-Hydroperoxydiazenes $((CH_3)_2C(OOH)N{=}NR$

R	^{1}H-NMR^a	^{13}C NMR^b	IR (cm^{-1})^c	UV (λ_{max}, nm)
CH_2CF_3	1.40 (s, 6H);	21.30 $((\underline{C}H_3)_2C)$;	3520 (br, str)	372
	4.27 (q, 2H, J_{HF}=9.0 Hz);	68.58 (q, $-\underline{C}H_2CF_3$,	3450 (br, str)	
		J_{CF}=29.1 Hz);	850	
	8.80 (s, br, 1H).	104.22 $((CH_3)_2\underline{C})$		
		123.69 (q, $CH_2\underline{C}F_3$,		
		J_{CF}=251.0 Hz).		
$CH_2CH_2OCH_3$	1.32 (s, 6H);	21.43 $((\underline{C}H_3)_2C)$;		365
	3.30 (s, 3H);	58.64 $(-\underline{C}H_2O)$;		
	3.91 (m, 4H);	68.09 $(N-\underline{C}H_2-)$;		
	8.92 (s, br, 1H).	69.40 $(O\underline{C}H_3)$;		
		104.76 $((CH_3)_2\underline{C})$.		
$CH_2CH_2OC_6H_5$	1.32 (s, 6H);	21.71 $((\underline{C}H_3)_2C)$	3520 (br, med.)	280, 365
	4.19 (t, 2H, J=6.0 Hz);	64.91 (NCH_2-)	3430 (br, str)	
	4.48 (t, 2H, J=6.0 Hz);	67.70 $(-CH_2O-)$	3300 (br, str)	
	6.94 (m, 3H)	103.32 $((CH_3)_2\underline{C})$	1600 (s, str)	
	7.28 (m, 2H)	114.91 (meta)	850 (s, med)	
	9.30 (s, br, 1H)	121.32 (para)	685 (s, str)	
		129.63 (ortho)		
		158.66 (ipso)		

..... continued

Table 11: Spectral Data of α-Hydroperoxydiazenes ($(CH_3)_2C(OOH)N{=}NR$) (continued)

R	^{1}H-NMR^a	^{13}C NMR^b	IR (cm^{-1})^c	UV (λ_{max}, nm)
C_6H_5	1.50 (s, 6H);	21.98 ($(\underline{\underline{C}}H_3)_2C$)	3640 (s, str)	260, 372
	7.55 (m, 5H);	103.99 ($(CH_3)_2\underline{\underline{C}}$)	3450 (br, str)	
	9.10 (s, br, 1H).	122.68 (meta)	850 (s, str)	
		127.25 (para)		
		131.45 (ortho)		
		151.21 (ipso)		
$CH(CH_3)_2$	1.27 (d, 6H, J=6.0 Hz)	20.27 ($CH(\underline{\underline{C}}H_3)_2$)	3520 (br, m)	362
	1.42 (s, 6H);	21.62 ($(\underline{\underline{C}}H_3)_2C$)	3350 (br, str)	
	3.70 (sept., 1H,	67.92 ($N\underline{\underline{C}}H(CH_3)_2$)	850 (s, str)	
	J=6.0 Hz);	102.45 ($(CH_3)_2\underline{\underline{C}}$)	835 (s, str)	
	9.50 (s, br, 1H)			
$C(CH_3)_3$	1.20 (s, 9H);	21.58 ($(\underline{\underline{C}}H_3)_2C$)	3630 (s, m)	363
	1.33 (s, 6H);	26.68 ($(\underline{\underline{C}}H_3)_3C$)	3538 (s, str)	
	9.21 (s, br, 1H).	67.97 ($(CH_3)_3\underline{\underline{C}}$)	3380 (br, str)	
		102.75 ($(CH_3)_2\underline{\underline{C}}$)	852 (s, m)	

..... continued

Table 11: Spectral Data of α-Hydroperoxydiazenes ($(CH_3)_2C(OOH)N{=}NR$) (continued)

R	^1H NMR[a]	^{13}C NMR[b]	IR (cm^{-1})[c]	UV (λ_{max}, nm)
$CH(CH_3)_2$	1.27 (d, 6H, J=6.0 Hz);	20.27 ($CH(\underline{\underline{C}}H_3)_2$)	3520 (br, m)	362
	1.42 (s, 6H);	21.62 ($(\underline{\underline{C}}H_3)_2C\cdot$)	3350 (br, str)	
	3.70 (sept., 1H, J=6.0 Hz);	67.92 ($N\underline{\underline{C}}H(CH_3)_2$)	850 (s, str)	
			835 (s, str)	
	9.50 (s, br, 1H)	102.45 ($(CH_3)_2\underline{\underline{C}}$)	835 (s, str)	
$C(CH_3)_3$	1.20 (s, 9H);	21.58 ($(\underline{\underline{C}}H_3)_2C$)	3630 (s, m)	363
	1.33 (s, 6H);	26.68 ($(\underline{\underline{C}}H_3)_3C$)	3538 (s, str)	
	9.21 (s, br, 1H).	67.97 ($(CH_3)_3\underline{\underline{C}}$)	3380 (br, str)	
		102.75 ($(CH_3)_2\underline{\underline{C}}$)	852 (s, m)	
$CH_2C_6H_5$	1.35 (s, 6H);	21.52 ($(\underline{\underline{C}}H_3)_2C$)		
	4.88 (s, 2H);	73.24 ($N\text{-}\underline{\underline{C}}H_2C_6H_5$)		
	7.27 (s, 5H);	103.03 ($(CH_3)_2\underline{\underline{C}}$)		
	9.11 (s, br, 1H)[d]	127.73 (meta)		
		128.70 (para)		
		128.83 (ortho)		
		134.76 (ipso)		

---

[a] In $CDCl_3$, unless otherwise indicated, with internal Me_4Si. [b] In $CDCl_3$ with the solvent as internal reference. [c] In CCl_4 with signal shape and intensity in parenthesis; br=broad, s=sharp, m=medium, str=strong. [d] In CCl_4.

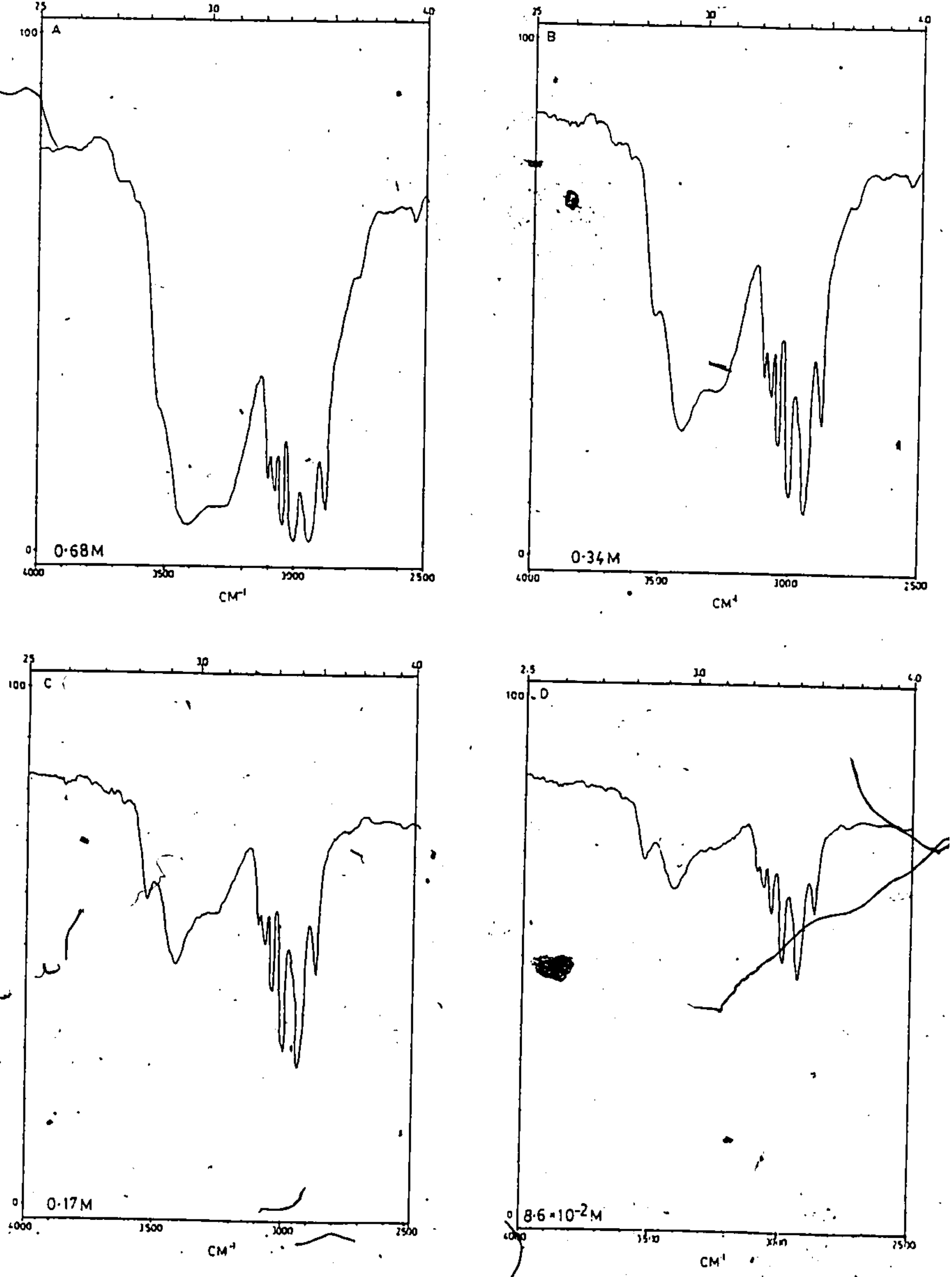
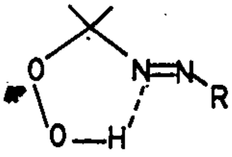
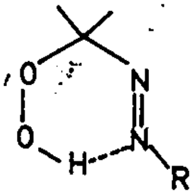


Fig. 3: IR Spectra of 28c in CCl$_4$ Showing the O-H Bands (3400 cm^{-1}) with Decreasing Concentration

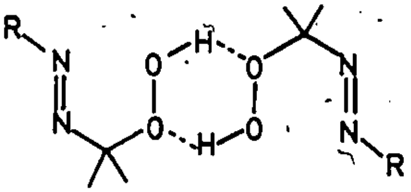
The 3400 cm^{-1} band is very broad and strong and is shown to consist of three bands (Fig. 3). Figure 3 shows changes in the 3400 cm^{-1} bands as a function of concentration of the hydroperoxydiazene in CCl_4. The three bands appear at about 3530 cm^{-1} (2.83 μm), 3420 cm^{-1} (2.92 μm), and 3290 cm^{-1} (3.05 μm). The intensity of the band at 3290 cm^{-1} is observed to decrease much faster than those of the other two bands with decreasing hydroperoxydiazene concentration. This fast-disappearing band is assigned to intermolecularly hydrogen-bonded species while the other two bands are assigned to intramolecularly hydrogen-bonded species and possibly non-hydrogen bonded species. There are a number of these possible secondary structures that the compounds can have; some of these structures are shown below (29-33).



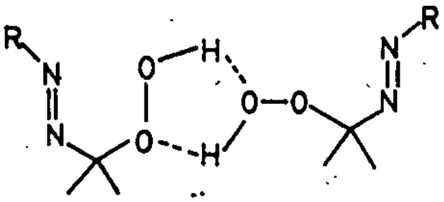
29



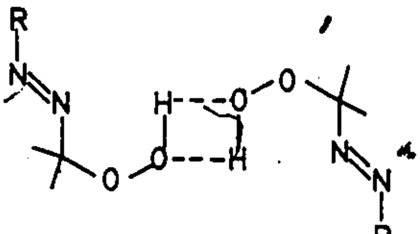
30



31



32



33

The information from the infrared studies is not enough for unambiguous assignment of the structures in solution.

Table 11 lists the ultraviolet spectra of compounds 28. The absorption maxima are typical of diazenes. Those compounds that contain only alkyl substituents (R) show one band at approximately 365 nm which is assigned to an n→π* transition due to the azo function. Compounds 28 (R = $CH_2CH_2OC_6H_5$ and R = C_6H_5) which contain the aromatic group show a second band at 280 nm and 260 nm, respectively. This band is assigned to a π→π* transition due to the aromatic ring. There is a red shift for the n→π* band in compounds 28 (R = C_6H_5 and R = CH_2CF_3). In the case where R = C_6H_5 this shift can be attributed to conjugation of the -N=N- bond with the aromatic system. No simple explanation can be offered for the shift in the case where R = CH_2CF_3.

^1H NMR spectra also show the characteristic features of the α-hydroperoxydiazenes. The separate methyl signals of the hydrazones, at δ 1.7 ppm and 1.9 ppm, collapse into one singlet at δ 1.4 ppm when the hydrazones are oxidized. A new signal appears in the low field region of the spectra. This signal is assigned to the hydroperoxy hydrogen. The chemical shift of δ 9 ppm is an indication that the hydroperoxyl group is fairly acidic. It was mentioned in the Introduction (see page 43) that the pK_a values of hydroperoxides lie between 11 and 13. Acidity of the hydroperoxydiazenes is also indicated by the ease with which the alkaline and alkaline earth metal salts are prepared; MacLeay and Sheppard[141] have synthesized these salts from the metal hydroxides.

^{13}C NMR spectra show that the signals of the Z and E methyls in the hydrazone, at approximately 15 ppm and 25 ppm, respectively, became a single signal at about 21.5 ppm for the gem dimethyls in the hydroperoxydiazene (see Tables 10 and 11) once the oxidation was complete. Also the signal of the ethylidene carbon at approximately 145 ppm is shifted to about 103 ppm in the α-hydroperoxydiazene.

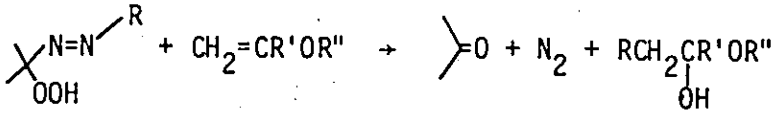
Compounds **28** show different solubilities in petroleum ether (bp 30°-60°C). All the compounds, except **28c** (R = $CH_2CH_2OC_6H_5$) are soluble in the solvent at room temperature. Compound **28c** is insoluble in petroleum ether and precipitates out of solution when the corresponding hydrazone ~~is~~ autoxidized in that solvent. The other compounds are partially soluble in petroleum ether at -15°C; they fall out of solution as liquids.

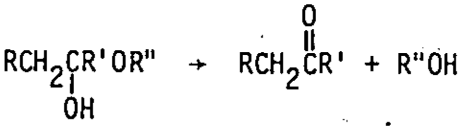
At room temperature compound **28c** is a colorless crystalline solid. The melting point was not determined because analogous hydroperoxydiazenes are reported[140] to be very sensitive to shock in their pure form. Caution: Although hydroperoxydiazene samples as large as 0.5 g did not give any problems using the procedures outlined in the Experimental, they should be handled with care and with adequate shielding because of their explosive nature.

RD 2. CHEMISTRY OF α-HYDROPEROXYDIAZENES

RD 2.1. Synthetic Applications

Decomposition in Enol Ethers. Thermal decomposition of the hydroperoxydiazenes, **28**, in ethyl vinyl ether and in 2-methoxy propene afforded carbonyl compounds as the major products. The carbonyl compounds are postulated to arise from an intermediate hemiacetal or hemiketal (eq. Rl and R2) which arises via a radical chain mechanism. The mechanism of the reaction is discussed in the next section.


[R1]



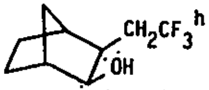
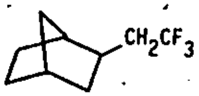
$$RCH_2C(OH)R'OR'' \rightarrow RCH_2C(=O)R' + R''OH$$

[R2]

R = CH_2CF_3, $CH_2CH_2OCH_3$, $CH_2CH_2OC_6H_5$; R' = H, CH_3.

Careful analysis of the product mixtures from reactions of compounds **28a-c** with ethyl vinyl ether and with 2-methoxy propene provided the identity and yields of the major products as well as those of many of the minor products. In all cases acetone is formed as a major co-product as a result of decomposition of **28**. Ethyl vinyl ether and 2-methoxypropene, respectively, gave ethanol and methanol. Most of the minor products were identified from their mass spectra, obtained from GC/MS analyses, and from their GC retention times. Equation R3 gives the products and their approximate yields from the reaction of **28c** (R = $CH_2CH_2OC_6H_5$) with ethyl vinyl ether. Particularly significant among the minor products are 5-phenoxypentanal, 2,3-dihydro-5,6-benzopyran, and phenyl propyl ether. These compounds probably arise from the major product, 4-phenoxybutanal, via free radical processes. Full discussion on how they arise is presented in the next section. The results from the reaction of **28a-c** with different olefinic substrates are reported in Table 12, 13, and 14. Mass spectra of the minor products are provided in Appendix I.

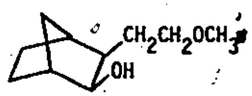
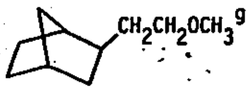
Table 12: Hydroxytrifluoroethylation of Unsaturated Compounds

	Products						
Reagent	Structure	Yield (%)[a]	^{1}H NMR[b]	^{13}C NMR[c]	IR(cm^{-1})[d]	MS(m/z)[e]	Derivative
$CH_2=C(C_6H_5)_2$	$CF_3CH_2CH_2C(OH)(C_6H_5)_2$	45	2.15(m,4H); 4.30(s,1H); 7.21(s,br,10H)		3540(ν_{OH})	263[M-OH]$^+$ 262[M-H_2O]$^+$ 183[Ø$_2$COH]$^+$ 105[C_7H_5O]$^+$	
$CH_2=CHOC_2H_5$	$CF_3CH_2CH_2CHO$[f]	70	2.50(m,4H); 9.87(s,1H);		2740(ald.C-H) 1730(ν_{CO})	126 M$^{+\cdot}$ 98[M-CO]$^+$ 77[M-CH_2FO]$^+$	2,4-DNP[g] (mp 179-181°C)
	 [h]	14	1.04-2.53(m,12H); 3.80(d,1H,J=6.3Hz)			194, M$^{+\cdot}$ 176[M-H_2O]$^+$ 67[C_5H_7]$^+$	
		62	1.07-2.07(m,11H); 2.11(s,br,1H); 2.26 (s,br,1H)	28.45; 29.77; 35.32; 35.76 36.64; 38.25 39.49; 39.71 41.02; 41.32 42.34		178 M$^{+\cdot}$ 163[M-15]$^+$ 95[M-$C_2H_2F_3$]$^+$ 67[C_5H_7]$^+$	
	 [i]	60	0.63(d,1H,J=9.5Hz); 1.18-1.47(m,5H); 2.39 (s,2H); 2.88(s,2H)	25.01; 26.11 36.57; 51.26		110, M$^{+\cdot}$ 67[C H_7]$^+$ 66[C_6H_6]	

Footnotes to Table 12

[a] Yields are based on the amount of 28a determined by iodometric titration. [b] $CDCl_3$ solvent, unless otherwise indicated, with Me_4Si as internal reference. [c] $CDCl_3$ solvent and as internal reference. [d] $CDCl_3$ solvent, unless otherwise indicated. [e] Probable ion assignments in parethesis; only major ions shown. [f] High-resolution m.s., m/z 126.02, calc'd for $C_4H_5F_3O$ m/z 126.03. [g] Low-resolution m.s., m/z 306($M^{\ddagger}$); high-resolution m.s., found 306.06, calc'd for $C_{10}H_9F_3N_4O_4$ m/z 306.06. [h] High-resolution m.s., found m/z 176.08 calc'd for $C_9H_{11}F_3([M-H_2O]^+)$ m/z 176.08. [i] The ^1H NMR spectrum matched the reported spectrum[152]

Table 13: Hydroxy-2-methoxyethylation of Unsaturated Compounds

	Products					
Reagent	Structure	yield (%)[a]	^1H NMR[b]	^{13}C NMR[c]	IR(cm^{-1})[d]	MS(m/z)[e]
$CH_2{=}C(C_6H_5)_2$	$CH_3OCH_2CH_2CH_2C(C_6H_5)_2$ OH	40	2.07(m,2H); 2.39(t, 2H,J=6.3Hz); 3.29(s, 3H); 3.38(t,2H,J=6.1Hz); 7.24(s,br,10H)			239[(M-OH)$^+$ 238[(M-H_2O)$^+$]
$CH_2{=}CHOC_2H_5$	$CH_3OCH_2CH_2CH_2CHO$	52	1.99(m,2H); 2.59(t, 2H,J=6.9Hz); 3.38(s,3H); 3.47(t,2H,J=6.0Hz); 9.85(s,1H)		1735(CO)	74[(M-CO)$^+$] 58[(M-C_2H_4O)$^+$] 45[(C_2H_5O)$^+$]
$CH_2{=}C(CH_3)OCH_3$	$CH_3OCH_2CH_2CH_2COCH_3$[f]	67	1.91(m,2H); 2.59(t,2H, J=6.9Hz); 2.21(s,3H); 3.24(t,2H,J=6.1Hz); 3.38(s,3H)		1720(CO)	104[M$^+$] 89[(M-CH_3)$^+$]
		7				152[(M-H_2O)$^+$] 95[(M-C_3H_7O)$^+$] 67[(C_5H_7)$^+$] 45[(C_2H_5O)$^+$]
		64	1.0-1.6(m,11H); 1.97(s,br, 1H); 2.19(s,br,1H); 3.23 (S,3H); 3.25(t,2H,J=6.2Hz)	28.68; 29.98; 35.18; 36.50; 36.64; 38.09; 38.68; 41.10; 58.43; 71.52	122[(M-CH_4O)] 67[(C_5H_7)$^+$] 66[(C_5H_6)$^+$] 45[(C_2H_5O)$^+$]	
		33				

Footnotes to Table 13

[a] Yields are based on the amount of 28b determined by iodometric titration. [b] $CDCl_3$ solvent with Me_4Si as internal reference. [c] $CDCl_3$ solvent and as internal reference. [d] $CDCl_3$ solvent, unless otherwise indicated; only diagnostic bands given. [e] Probable ion assignments in parenthesis; major ions given. [f] ^1H NMR matched the reported spectrum;[153] lit. IR 1720 cm^{-1}.[153] [g] High-resolution m.s., found m/z 164.08, calc'd for $C_{10}H_{12}O_2$ m/z 164.08. [h] see Table 12 for spectra.

Table 14: Hydroxy-2-phenoxyethylation of Unsaturated Compounds

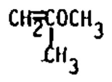
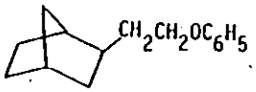
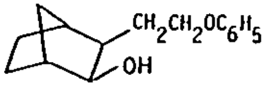
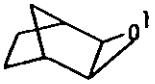
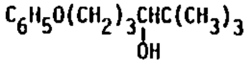
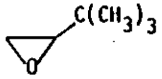
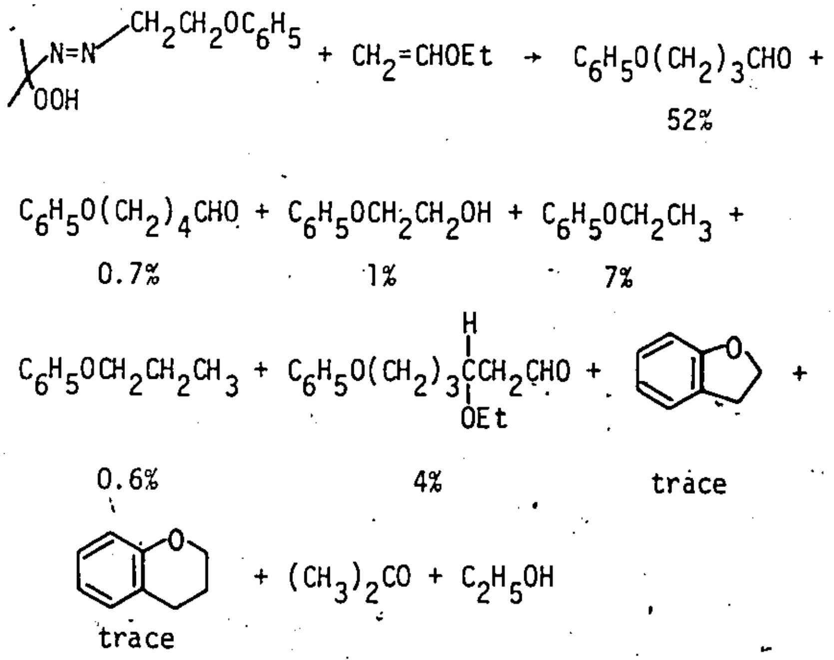
Reagent	Products						
	Structure	Yield (%)[a]	^1H NMR[b]	^{13}C NMR[c]	IR(cm^{-1})[e]	MS(m/z)[e]	Derivative
$CH_2=CHOC_2H_5$	$C_6H_5O(CH_2)_3CHO$[f]	65	2.12(m,2H); 2.67(t, 2H, J=7.1Hz); 4.01(t, 2H,J=6.1Hz); 6.94(m,3H); 7.28 (m,2H); 9.84(t,1H, J=1.4Hz)	22.65(-$\underline{\underline{C}}H_2$-) 40.77(-$\underline{\underline{C}}H_2CHO$) 67.47(-O-$\underline{\underline{C}}H_2$-) 115.22(meta) 121.20(para) 129.98(ortho) 159.82(ipso) 205.78(-$\underline{\underline{C}}HO$)	2735(ald. C-H) 1728(C=O)	164,$M^{\dot{+}}$ 94$[C_6H_6O]^+$ 71$[M-C_6H_5O]^+$ 43$[C_2H_3O]^+$	2,4-DNP (mp 102-103°C)[g]
$CH_2=\underset{CH_3}{\underset{\vert}{C}}OCH_3$	$C_6H_5O(CH_2)_3COCH_3$[h]	76	2.10(m,2H); 2.15(s,3H); 2.65(t,2H,J=7.5Hz); 3.96(t,2H,J=6.0Hz); 6.93(m,3H); 7.27(m,2H)	24.12(-$\underline{\underline{C}}H_2$-) 29.59(CO $\underline{\underline{C}}H_3$) 39.95(-$\underline{\underline{C}}H_2CO$-) 67.56(-O-$\underline{\underline{C}}H_2$-) 115.21(meta) 121.15(para) 130.04(ortho) 160.02(ipso) 204.56(-$\underline{\underline{C}}O$-)	1718(CO)	174, $M^{\dot{+}}$ 94$[C_6H_6O]^+$ 85$[M-C_6H_5O]^+$ 43$[C_2H_3O]^+$	2,4-DNP (mp 103-105°C)[i]
		70	1.09-1.60(m,9H); 1.61-1.78(m,2H); 2.04(s,br,1H); 2.22(s,br,1H); 3.87(t,2H, J=6.4Hz); 6.73-6.82 (m,3H); 7.15(m,2H)	28.78; 30.04; 35.31; 36.34; 36.64; 38.17; 38.76; 41.17; 66.68; 114.64; 120.51; 129.45		216; $M^{\dot{+}}$ 123$[M-C_6H_5O]^+$ 94$[C_6H_6O]^+$ 81$[C_6H_9]^+$ 67$[C_5H_7]^+$	

Table 14 (continued) Hydroxy-2-phenoxyethylation of Unsaturated Compounds

Reagent	Products, Structure	Yield (%)[a]	^1H NMR[b]	^{13}C NMR[c]	IR(cm^{-1})[d]	MS(m/z)[e]	Derivative
		2				232, $M^{+\cdot}$[k] 95$[M-C_8H_9O]^+$ 94$[C_6H_6O]^+$	
	 [l]	20					
$CH_2=CHC(CH_3)_3$	 $C_6H_5O(CH_2)_3\underset{OH}{CH}C(CH_3)_3$					222, $M^{+\cdot}$ 165[M-t-Bu]$^+$ 129$[M-C_6H_5O]^+$ 94$[C_6H_6O]^+$ 71$[C_5H_{11}]^+$	
	$C_6H_5O(CH_2)_4C(CH_3)_3$	35	0.88(s,9H); 1.19-1.89(m,6H); 3.39 (t,2H,J=6.0Hz); 6.93(m,3H); 7.28 (m,2H)			206, $M^{+\cdot}$ 191$[M-CH_3]^+$ 150$[M-C_4H_8]^+$ 112$[M-C_6H_6O]^+$ 94$[C_6H_6O]^+$ 57$[C_4H_9]^+$	
		1.5	m			100, M^+ 85$[M-CH_3]^+$ 57[t-Bu]$^+$ 41$[C_3H_5]^+$	

Footnotes to Table 14

[a] Yields are based on the amount of 28c determined by iodometric titration. [b] $CDCl_3$ solvent with Me_4Si as internal reference. [c] $CDCl_3$ solvent and as internal reference. [d] $CDCl_3$ solvent, unless otherwise indicated; only diagnostic bands are given. [e] Probable ion assignments in parenthesis; major ions are given. [f] High-resolution ms, found m/z 164.08, calc'd for $C_{10}H_{12}O_2$ m/z 164.08. [g] 2,4-DNP m.p. 95-95.5[154]; high resolution ms, found m/z 344.11, calc'd for $C_{16}H_{16}N_4O_5$ m/z 344.11. [h] High-resolution ms, found 178.10, calc'd for $C_{11}H_{14}O_2$ m/z 178.10; mp 51-53°C. [i] High-resolution ms, found 358.12, calc'd for $C_{17}H_{18}N_4O_5$ m/z 358.13. [j] High-resolution ms, found m/z 216.15, calc'd for $C_{15}H_{20}O$ m/z 216.15. [k] See Figure A8 for mass spectrum. [l] See Table 12 for spectral data. [m] This compound was not collected. Its identity was inferred from the mass spectrum and from GC analysis by co-injection with authentic t-butylethylene oxide.

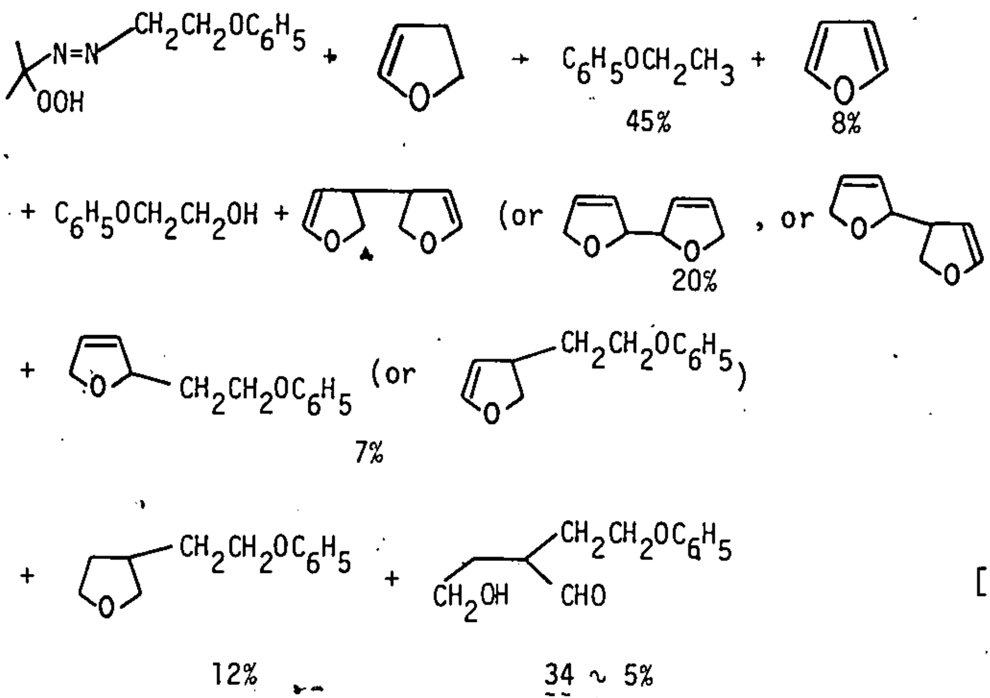


[R3]

The results demonstrate the synthetic utility of α-hydroperoxydiazenes in hydroxyalkylations of olefinic substrates. Those carbonyl compounds formed in the reaction of the hydroperoxydiazenes with enol ethers were in high yields (see Tables 12 to 14). Thus it is possible to incorporate into small molecules a number of substituents that may provide handles for the synthesis of many important compounds. The synthetic applications of these α-hydroperoxydiazenes were recently reported by Warkentin and co-workers.[149]

Unfortunately, enol ethers with abstractable allylic hydrogens give analogous products in very low yields. For example compound 28c decomposed in 2,3-dihydrofuran to give only about 5% of the expected hydroxyalkylation product, 4-hydroxy-2-(2-phenoxyethyl)butanal, 34. The presence of this compound, 34, was inferred from the chemical shift (δ 9.9) of the aldehydic proton in the ^1H NMR spectrum of the product mixture and from the mass spectrum obtained from GC/MS analysis of the product mixture. Figure 4 shows the mass spectrum of compound 34. The major product from the reaction is phenyl ethyl ether. Other products, identified from their mass spectra, include 2,3-dihydro-4,5-benzofuran; furan; 2-phenoxyethanol; bis-2,3-dihydrofuran; 3-(2-phenoxyethyl)tetrahydrofuran; and 2,3-dihydro-3-(2-phenoxyethyl)furan (or an isomer of it; see Fig. A in Appendix I); see eq. R4. Bis-2,3-dihydrofuran probably arises from coupling of two 2,3-dihydrofuranyl radicals(), and 2,3-dihydro-3-(2-phenoxyethyl)furan (or its isomer) probably arises from a similar reaction between 2-phenoxyethyl and 2,3-dihydrofuranyl radicals.

The results indicate that there are some limitations, imposed by



[R4]

the reactivity of the olefinic substrate, to hydroxyalkylation reactions of α-hydroperoxydiazenes. Other limitations, such as steric factors, are discussed below.

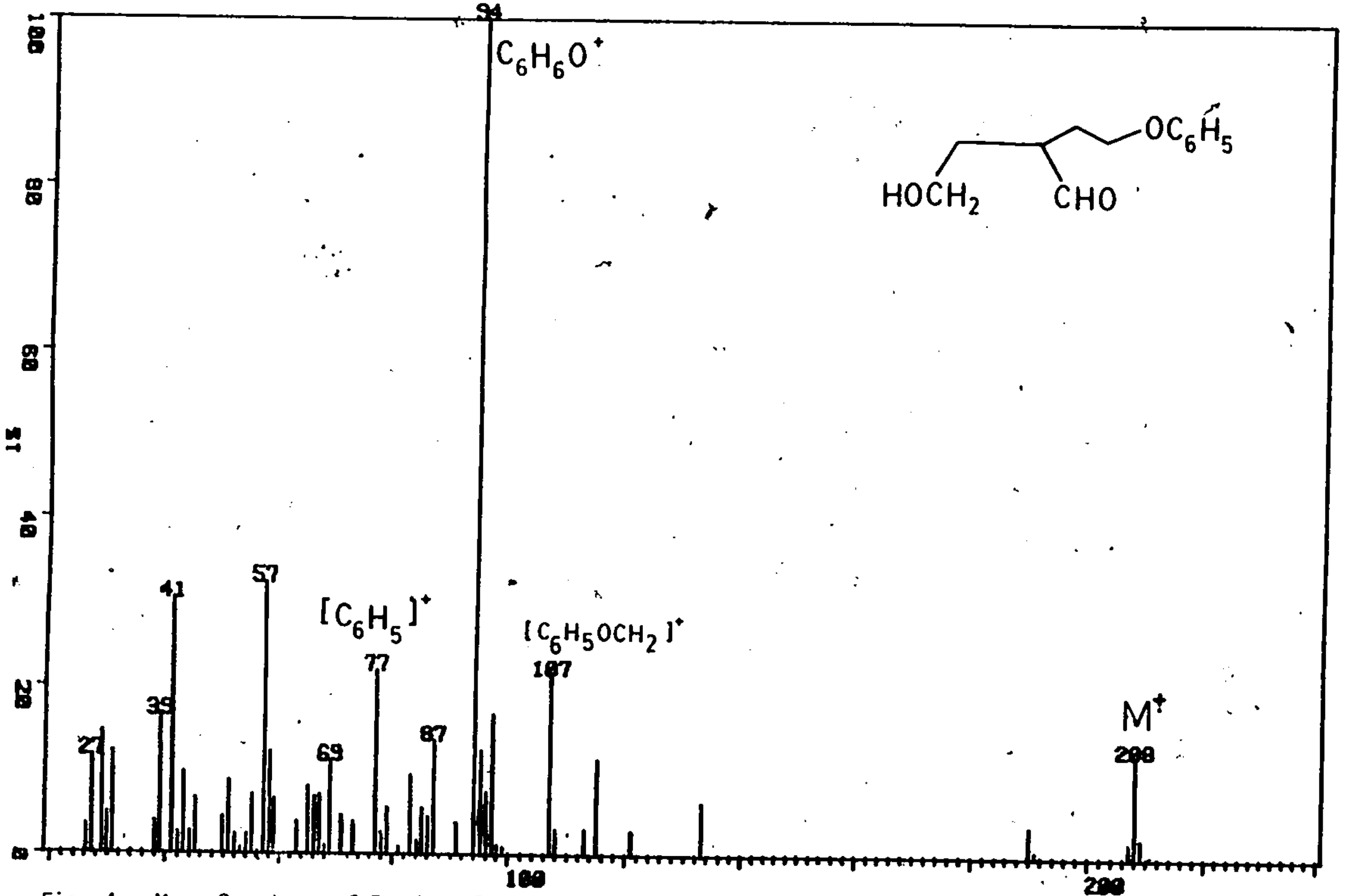
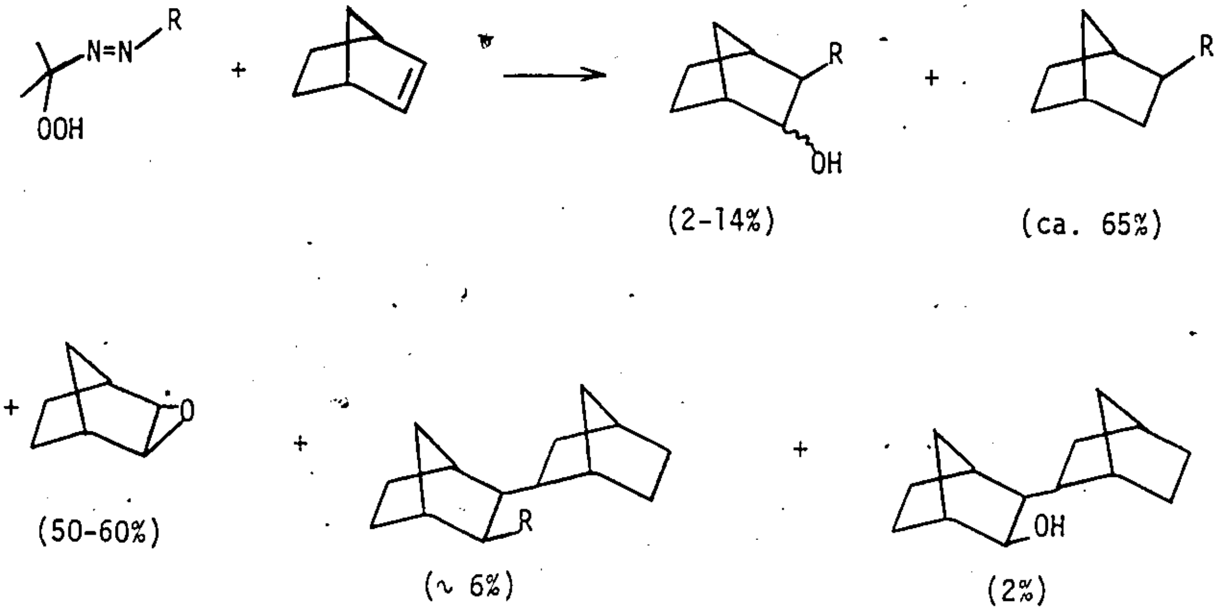


Fig. 4: Mass Spectrum of Product Identified as 4-Hydroxy-2-[2-phenoxy]ethyl butanal (compound 34).

Decomposition in Alkenes. Thermal decomposition of 28a,b in an alkene such as 1,1-diphenylethylene gave the hydroxyalkylation products in 40 to 45% yield. 1,1-Diphenylethylene oxide was found in only about 5% yield. Epoxide formation is discussed below in this section and in the next section. The thermolysis chemistry of the hydroperoxydiazenes in bicyclo[2.2.1]heptene (norbornene) and in 3,3-dimethyl-1-butene (t-butyl ethylene) was found to be strikingly different from that of other alkenes. In the case of norbornene, although the expected products of hydroxyalkylation with 28a-c were found, the major products were those of hydroalkylation and the epoxide of norbornene, eq. R5. The major products were identified from their mass spectra and from their ^{1}H NMR and ^{13}C NMR spectra. the results are reported in Tables 12, 13, and 14. The minor products were

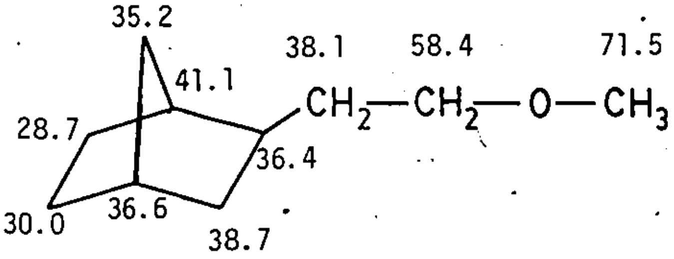


+ Other products [R 5]

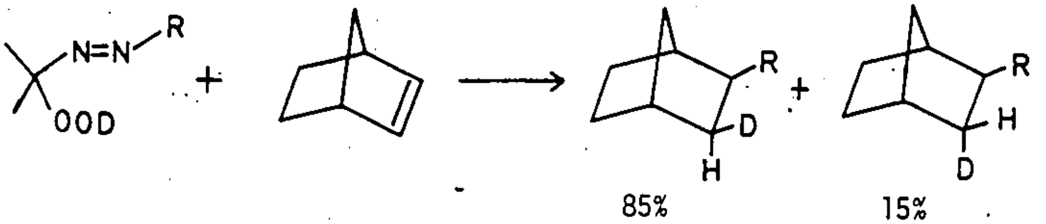
identified from their mass spectra obtained from GC/MS analyses of the product mixtures, see Appendix I. Reaction of deuterio analogues (28-OOD) of compounds 28 gave the hydroxyalkylation products in higher yields and the hydroalkylation and the epoxide in lower yields. The hydroalkylation products were found to incorporate about 50% deuterium.

The products from the reactions of 28 with norbornene were not known until recently[149] and it was therefore necessary to establish their stereochemistries and of the addition reactions.

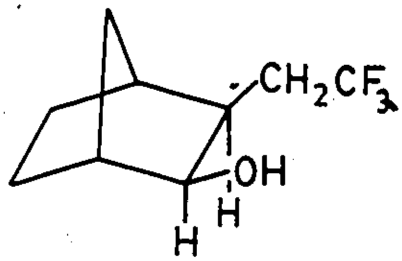
In their studies of free radical addition of bromotrichloromethane to norbornene, Karasch and Friedlander[52] observed that the elements of the polyhalomethane added trans to the double bond with the trichloromethyl group going to the exo position. Weinstock[53] showed that radical addition reactions of other reagents to norbornene and its derivatives are cis in nature with both substituents in the exo position. Thus in a typical example, ethyl bromoacetate reacts with norbornene to yield exo-cis-2-carboethoxymethyl-3-bromonorbornane.[53] From these analogies and from a comparison of the ^{13}C NMR spectra of the 2-alkylnorbornanes to that of exo-2-methylnorbornane[155] it is concluded that the alkyl groups in the 2-alkylnorbornanes are in the exo position. The ^{13}C NMR assignments are shown below for 2-[2-methoxyethyl]norbornane.



There are two signals, separated by 0.42 ppm, in the ^2H NMR spectrum of the deuterioalkylation products obtained from reaction of 28-OOD with norbornane, eq. R6. These signals at δ 1.14 and δ 1.56 are in a ratio of 6:1. The exo-exo assignment to the major product (eq. R6) is based on the analogy for the exo-cis addition of ethyl bromoacetate to norbornene[53] (see page 31), and on the results obtained from ^1H NMR decoupling experiments with 2-hydroxy-3-(2,2,2-trifluoroethyl)norbornane, 36. The ^1H NMR spectrum of compound 36 showed the resonance of the proton bonded to the hydroxyl-bearing carbon at δ 3.82 as a doublet. Proton decoupling studies showed that this proton is coupled to another proton which resonates at δ 1.85 which is also a doublet. The coupling constant is J = 6.3 Hz. Exchange of the hydroxyl hydrogen of 36 by shaking the solution with a drop of D_2O removed a signal at approximately δ 1.10 while those at δ 1.85 and δ 3.82 remained unchanged. That result indicates that the 6.3 Hz coupling is not to OH but to an adjacent CH. The dihedral angle must be almost zero for them to have the normal coupling constant. The results point to these two protons as being endo-cis at C-2 and C-3. This puts the hydroxyl group in the exo position at C-2.



[R6]



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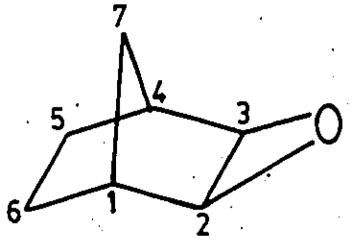
The ^1H NMR spectrum of the 2,3-epoxynorbornane matched the reported spectrum of exo-2,3-epoxynorbornane.[152] ^{13}C NMR assignments for the compound are given below



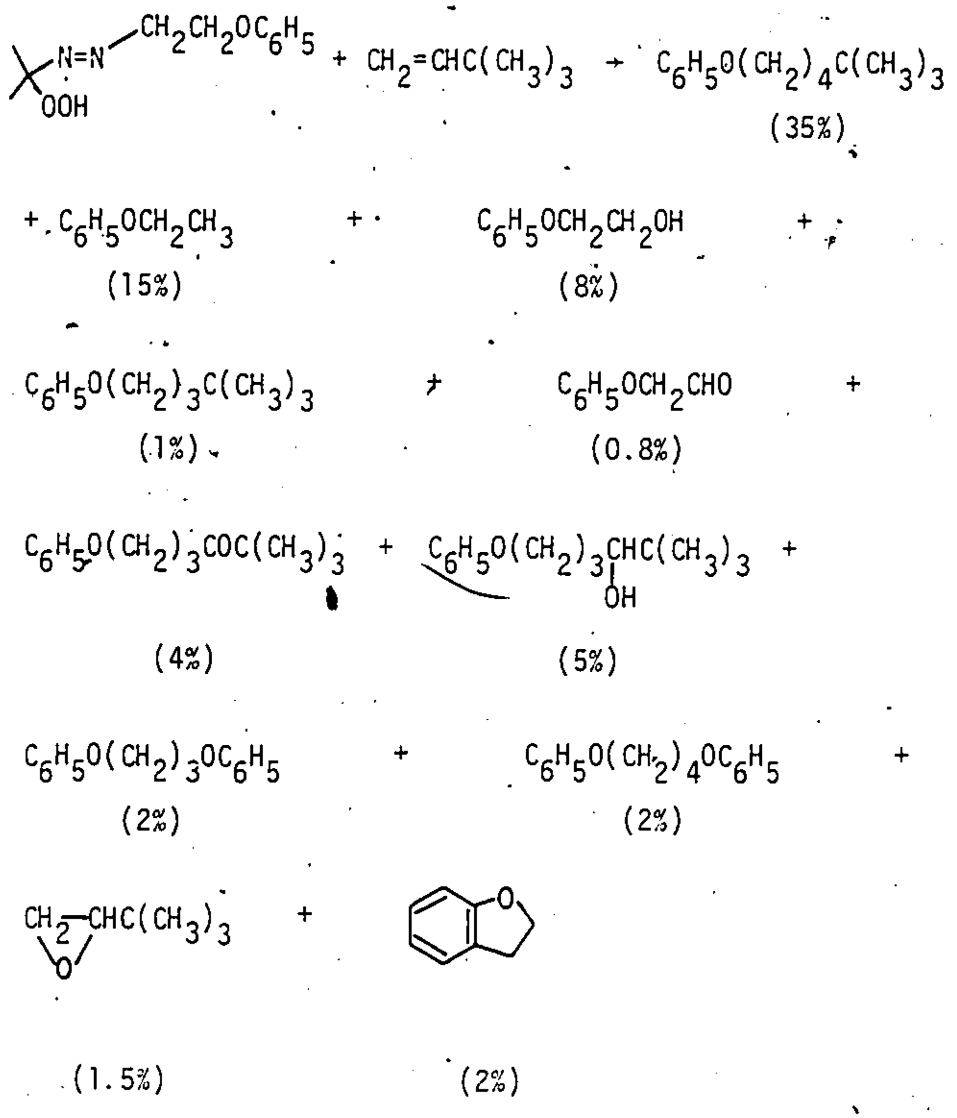
C_1,C_4	C_2,C_3	C_5,C_6	C_7
26.1	51.3	25.0	36.6

The results from the studies of the chemistry of the α-hydroperoxydiazenes in norbornene indicate that these azo compounds are poor in hydroxyalkylating norbornene and probably other hindered alkenes. They can be used for monodeuteriation of norbornenes; however, they do not compare favorably with the α-hydroxydiazenes which are known to give 87% deuterium incorporation.[138]

Thermolysis of 28c in t-butylethylene gave 2,2-dimethyl-6-phenoxyhexane as the major product. Other products include phenyl ethyl ether, 2-phenoxyacetaldehyde, 2,2-dimethyl-5-phenoxypentane, 2,2-

dimethyl-6-phenoxyhexan-3-one, 1,3-diphenoxypropane, and 1,4-diphenoxybutane. Only about 5% of the hydroxyalkylation product, $C_6H_5O(CH_2)_3$-$CH(OH)C(CH_3)_3$, is formed and, although the major product comes from hydroalkylation as in the case of norbornene, only about 1.5% of t-butylethylene oxide is formed. Equation R7 gives the products and their approximate yields from the reaction of 28c with t-butylethylene.

Particularly interesting is the fact that the epoxide is formed in very low yield and also interesting is the presence of such compounds



[R7]

as 2,3-dihydro-4,5-benzofuran, 1,3-diphenoxypropane and 1,4-diphenoxybutane in appreciable yields. These observations point to a low reactivity of the alkene towards addition of free radicals. This allows build-up in the concentrations of the radicals and leads to couplings and cyclizations to give those products.

Details of the reaction mechanisms in norbornene and in t-butylethylene are discussed in the next section.

Summary of "Synthetic Applications". Hydroxyalkylations of unsaturated substrates with α-hydroperoxydiazenes, reactions discussed in the preceeding section, are the first known reactions of their kind. Studies of the synthetic applications of the α-hydroperoxydiazenes suggest that formation of the hydroxyalkylation products depends on the reactivity of the olefin towards radical additions as well as on the structure of the olefin. When the olefin is reactive and the intermediate adduct radical is sterically unhindered, as in the case of ethyl vinyl ether, the yield of hydroxyalkylation product is high. However, when the olefin is reactive but the intermediate adduct radical is sterically crowded, as in the case of norbornene, the reaction pathway is altered and the major products result from hydroalkylation and epoxidation. For unreactive olefins which give sterically crowded intermediate adduct radical, hydroalkylation is the major route and epoxidation is drastically reduced.

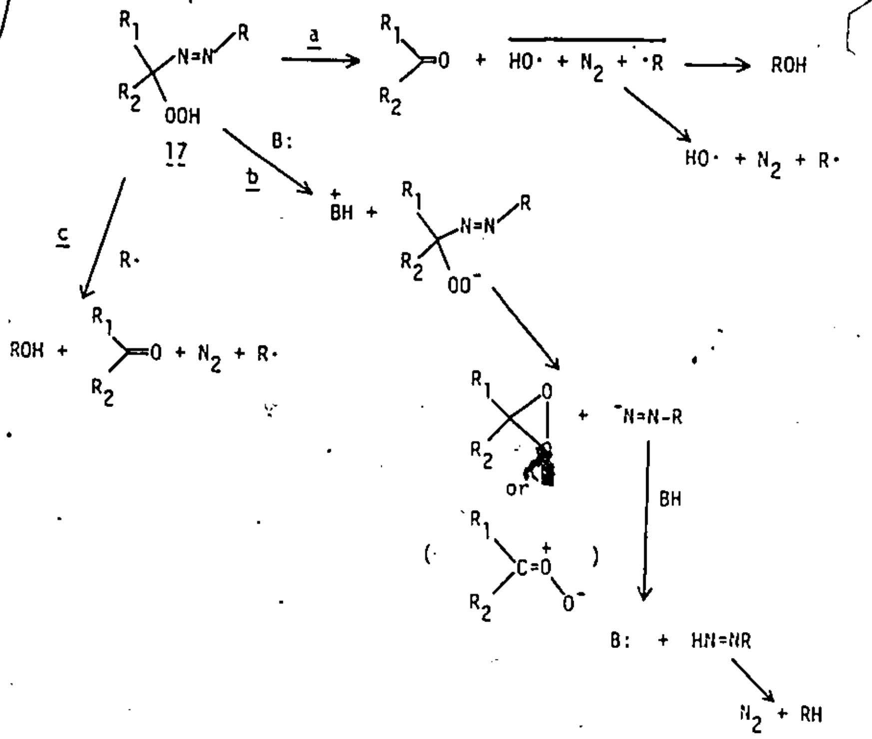
Deuteriation of the azo compounds in the hydroperoxy group increases the yields of the hydroxyalkylation products from 2-14% to between 12 and 29% and at the same time decreases the yields of the alkylnorbornanes and epoxynorbornane from about 65% to about 30%.

Deuterium is incorporated into the alkylnorbornanes at C-2 in the exo and endo positions in a ratio of 6:1.

RD 2.2. Mechanistic Studies

As pointed out in the Introduction (Section I 5.3, p 57) a number of mechanisms have been put forward for the decomposition of α-hydroperoxydiazenes. Scheme 6, repeated below, shows three of the mechanisms: (a) unimolecular fragmentation of the compounds to give a carbonyl compound, hydroxyl radical and an alkyl (or aryl) diazenyl radical (R-N=N·) which dissociates rapidly to nitrogen and alkyl (or aryl) radical; (b) base-catalysed fragmentation to give a dioxirane (or carbonyl oxide); and (c) radical chain abstraction of the hydroxyl group to give a hydroxy compound, a carbonyl compound and an alkyl radical.

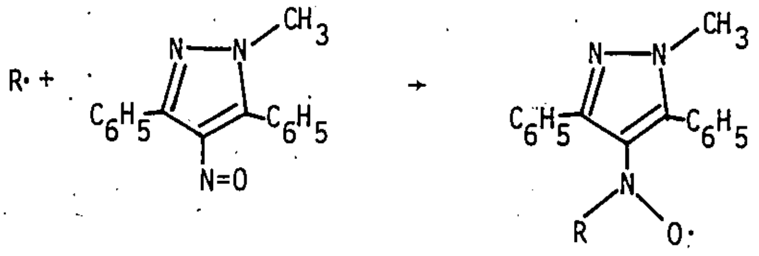
SCHEME 6



It should be pointed out that in his proposed mechanism, Tezuka[144,145] failed to indicate the fate of the aryldiazenyl group in compound 24. Formation and decomposition of the alkyl (or aryl) diazene in mechanism b (Scheme 6) is postulated by this author.

Evidence in support of the unimolecular mechanism (a) and the bimolecular decomposition induced by free radicals (mechanism c) which are proposed in this laboratory, is given and discussed, together with mechanism b, in this section.

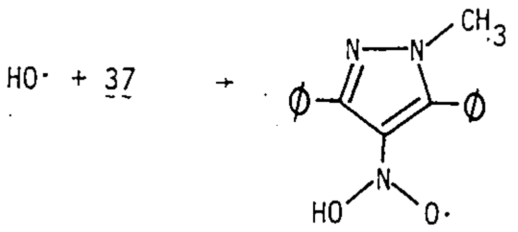
Spin Trapping. Approximately 0.15 mmole of compounds 28 were decomposed in benzene containing approximately 0.1 mmole of 3,5-diphenyl-1-methyl-4-nitrosopyrazole (DMNP, 37) as the spin trap. The radicals formed by the decomposition of 28 were captured by 37 to give the nitroxide radical, 38, eq. R8.



[R8]

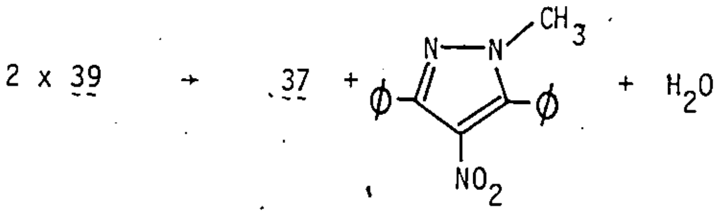
37 38

The nitroxide radicals (spin adducts) were detected by ESR spectroscopy, Fig. 5-11. A second set of resonances which were observed in the ESR spectra and which disappeared rather rapidly with time was assigned to the spin adduct 39 resulting from reaction of hydroxyl radicals with DMNP, eq. R9. The spin adduct 39 must be very unstable. This can possibly be accounted for in terms of self-reactions (eq. R10) to give the original nitroso compound (in this case DMNP), a nitro compound, 40



[R9]

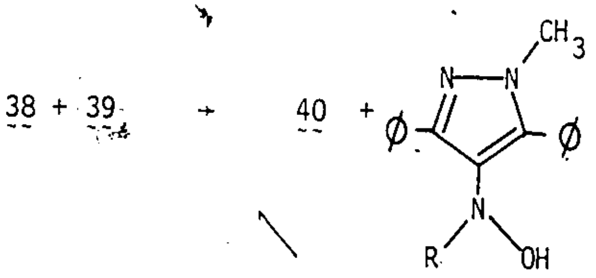
39; $a^N = 7.83G$, $a^H = 5.00G$



40

[R10]

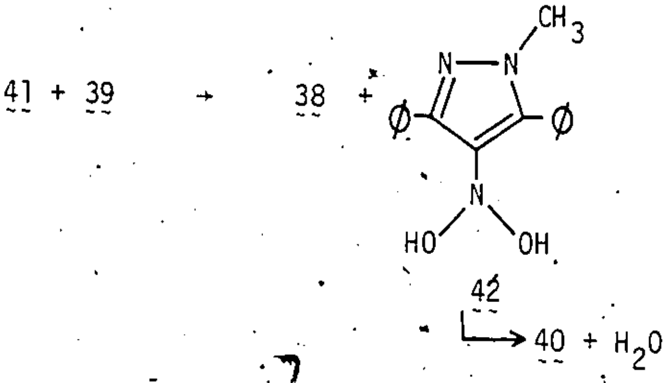
and H_2O, or in terms of disproportionation with the spin adduct 38 to give the nitro compound, 40, and a hydroxylamine derivative, 41, eq. R11.



41

[R11]

The spin adduct 38 can be regenerated by a reaction between the hydroxylamine, 41, and spin adduct 39, eq. R12.



42

[R12a]

[R12b]

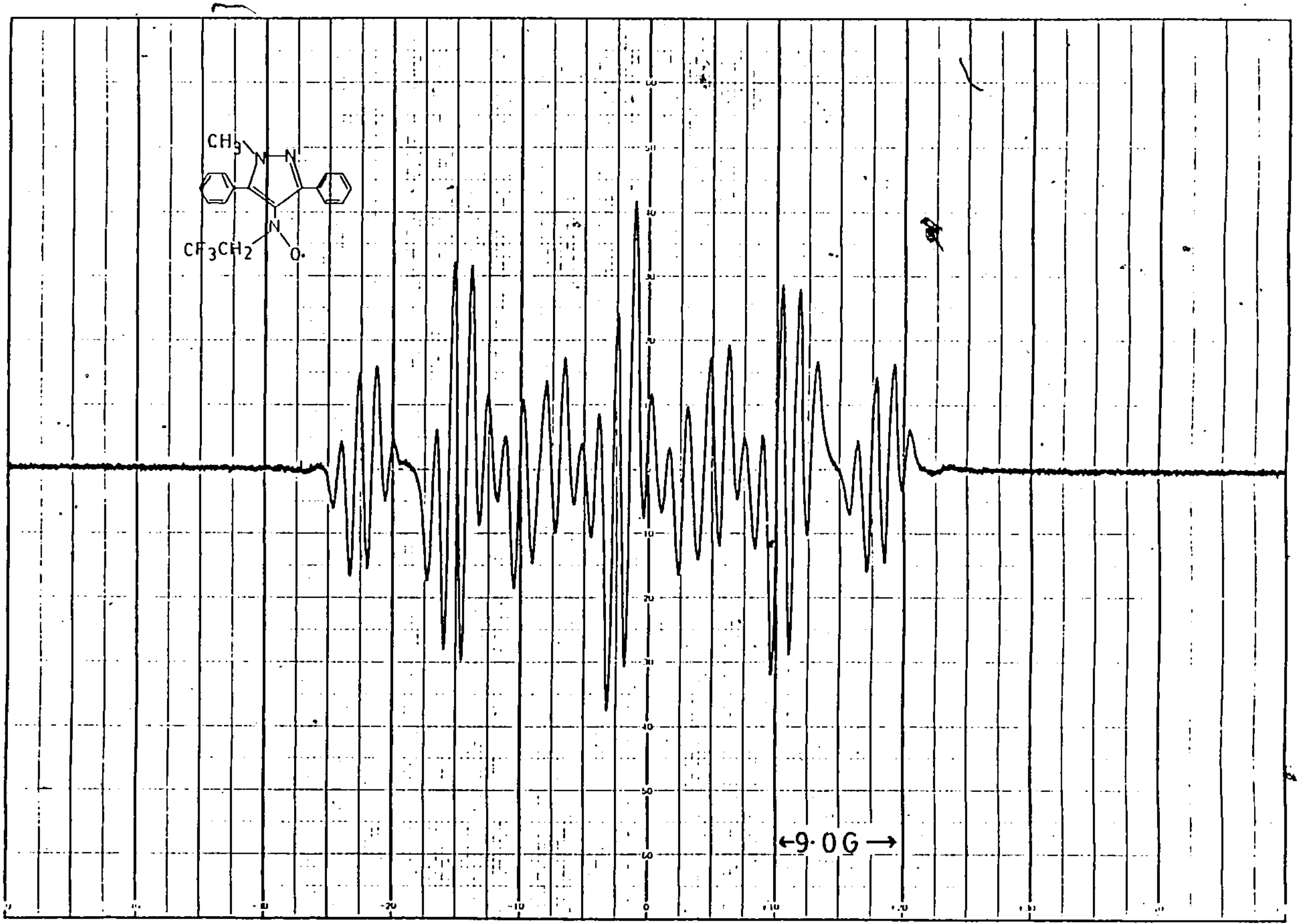


Fig. 5: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl-2,2,2-trifluoromethyl nitroxyl Radical.

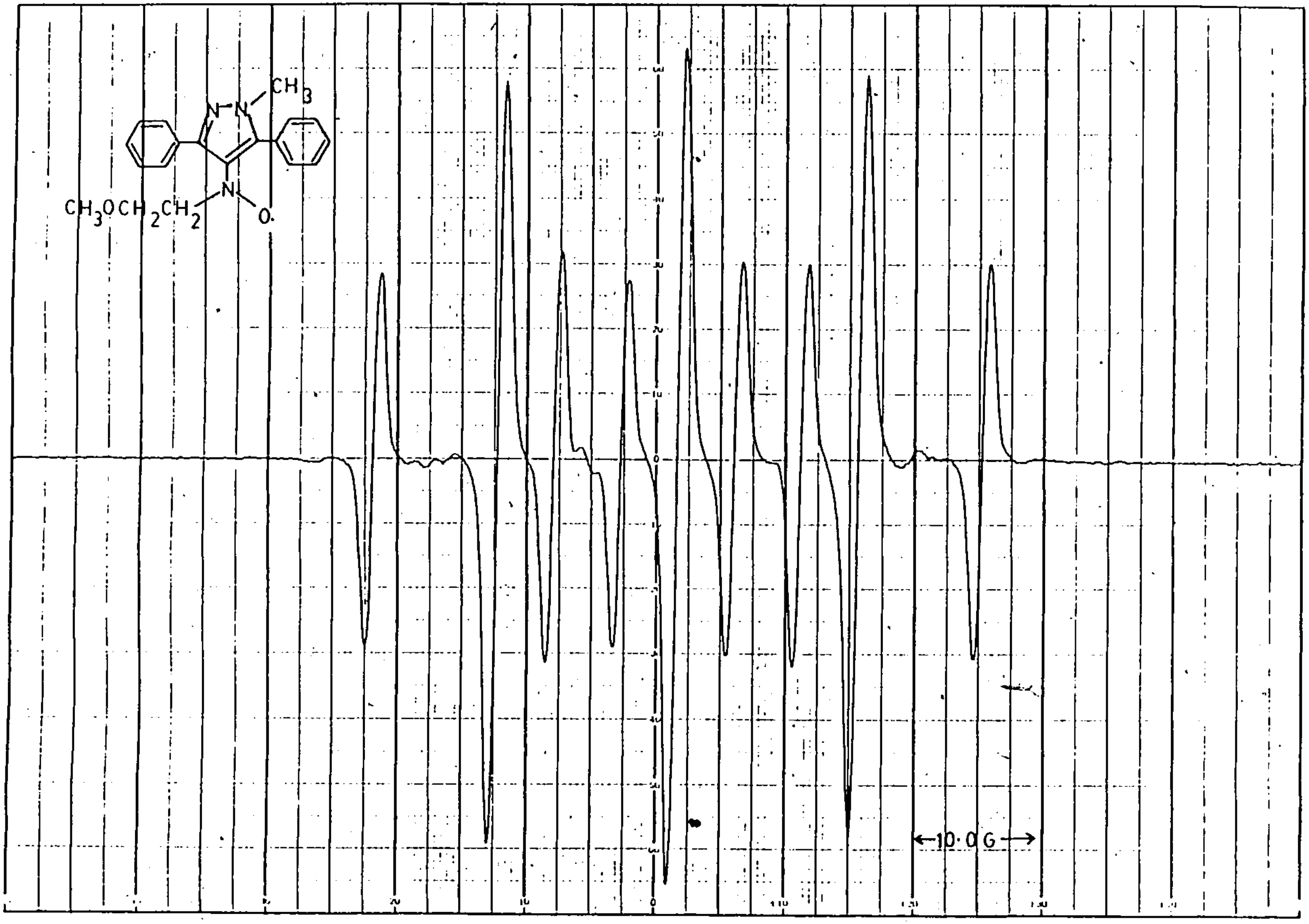


Fig. 6: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl-2-methoxyethyl nitroxyl Radical.

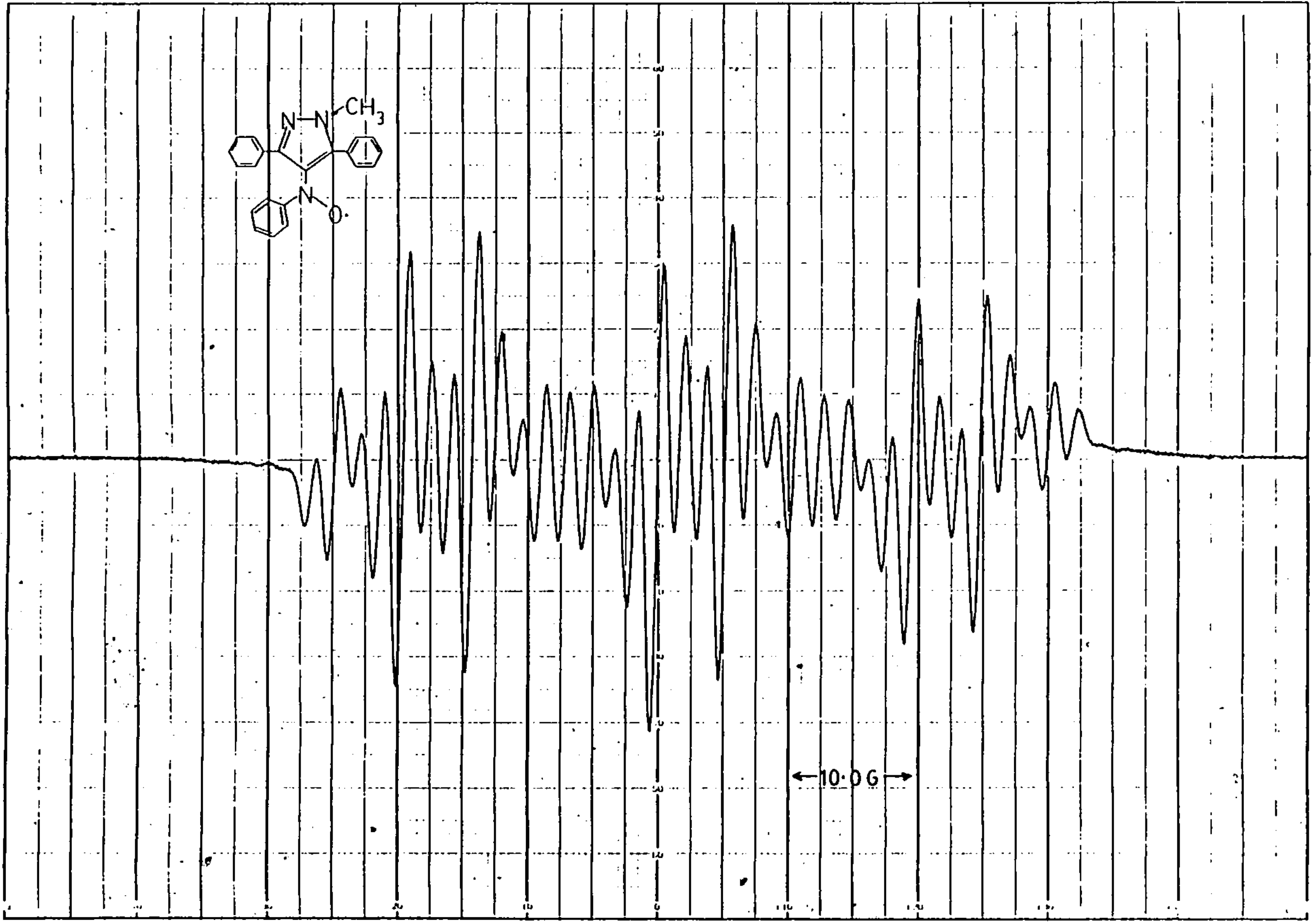


Fig. 7: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl phenyl nitroxyl Radical.

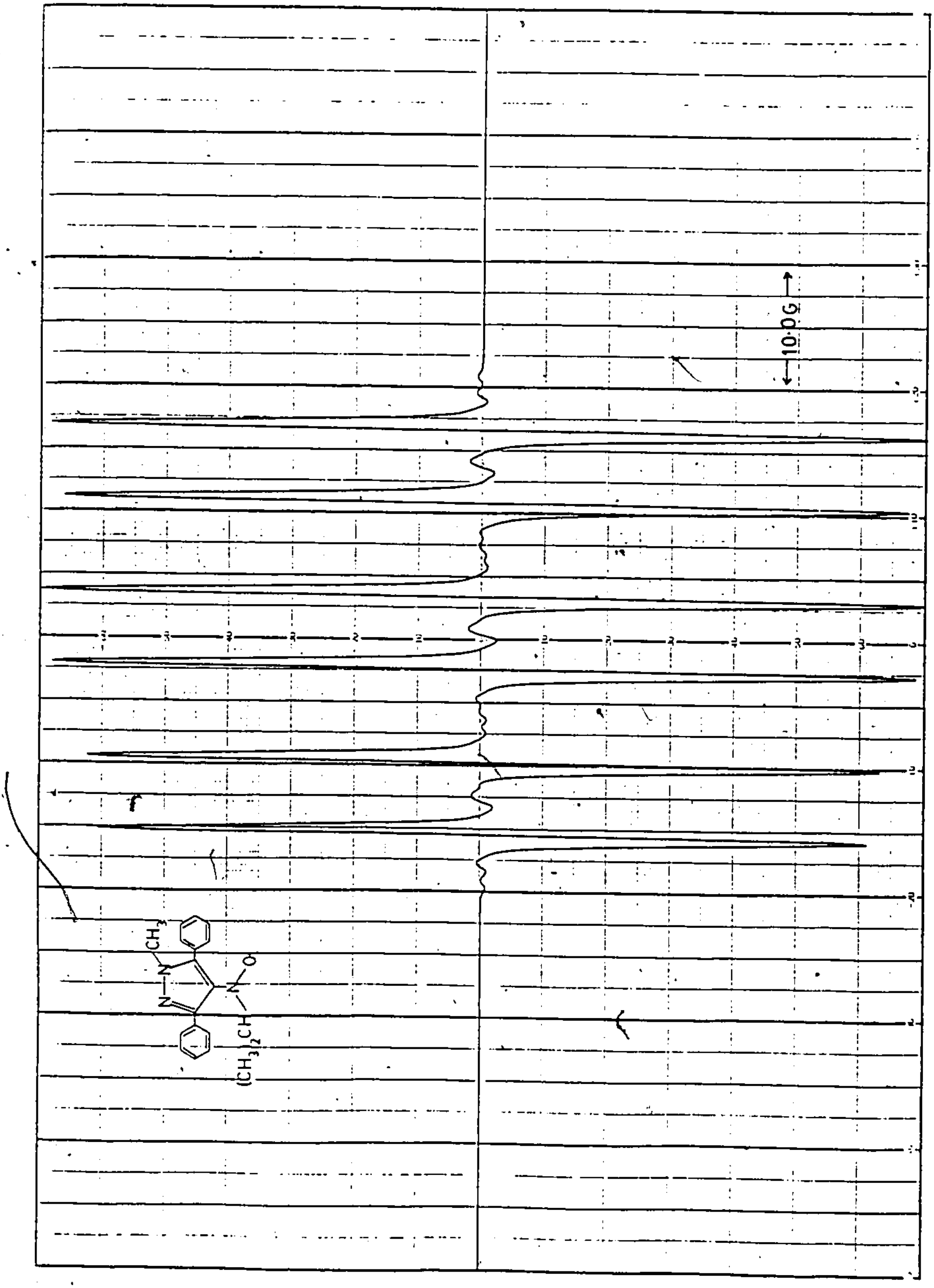


Fig. 8: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazylisopropyl nitroxyl Radical.

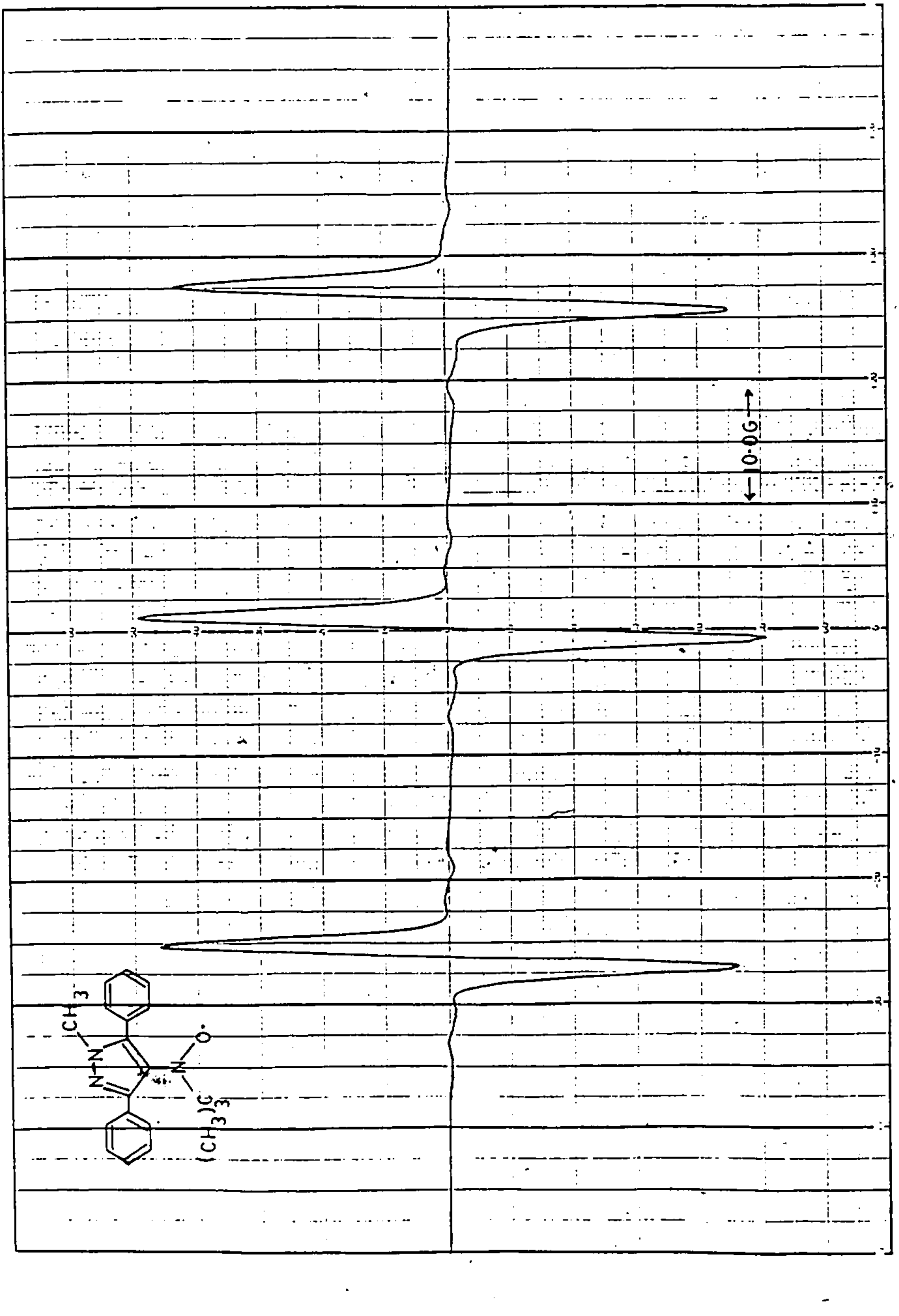


Fig. 9: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl-t-butyl nitroxyl Radical.

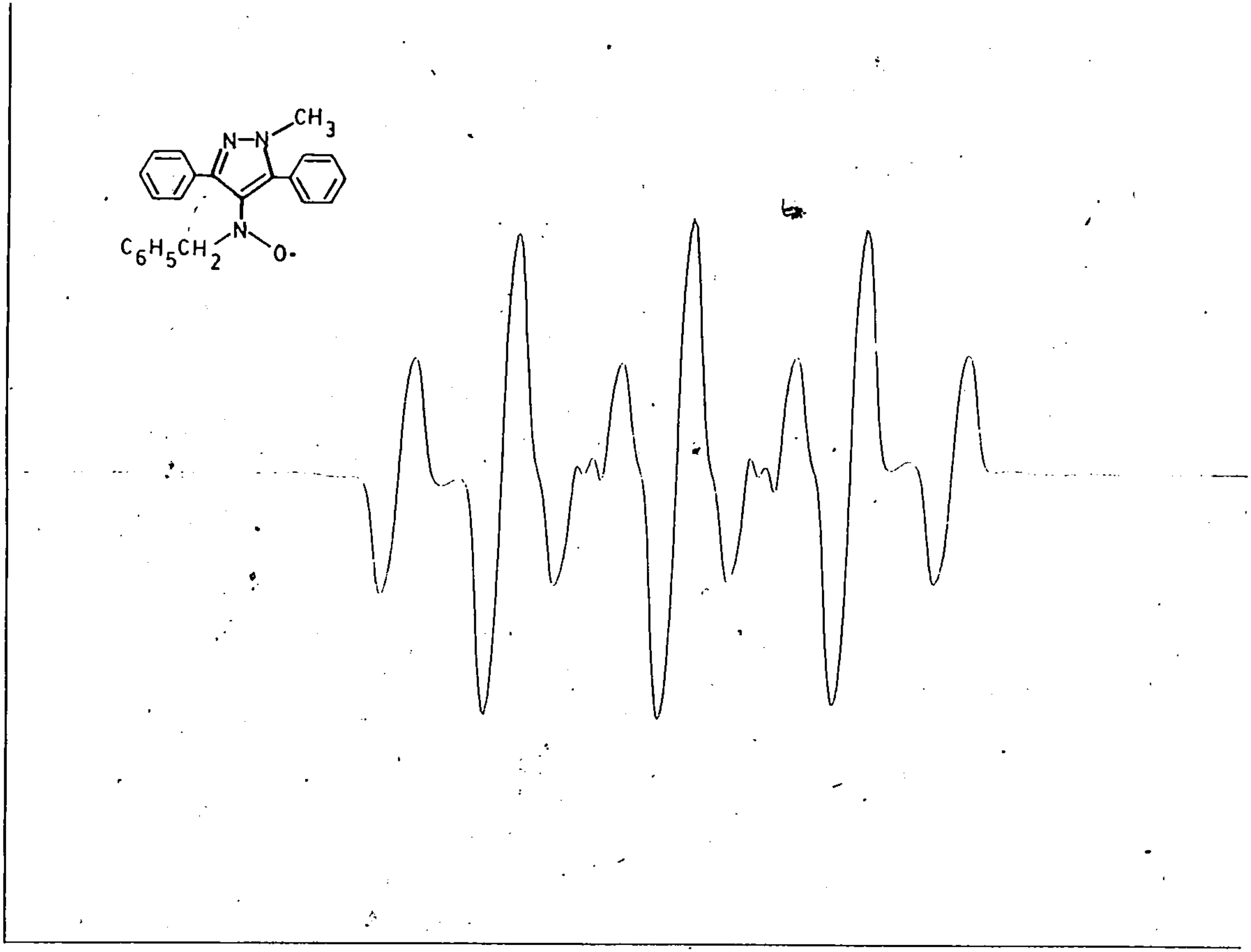


Fig. 10: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl benzyl nitroxyl Radical.

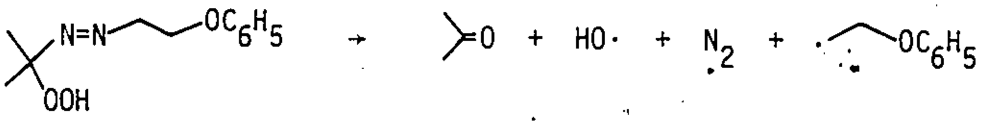
Spin trapping of the hydroxyl radical with nitrones is well known;[156-158] however, there is only one reported case[159] of spin-trapping with a nitroso compound. Konaka and Sakata[159] were unable to determine the half-life of the spin adduct from the reaction between hydroxyl radicals and 2,4-dimethyl-3-nitrosobenzenesulfonate (sodium salt), presumably because the adduct radical is very short-lived. The ESR parameters for the spin adduct 38 (see Table 15) are in good agreement with literature values.[160]

Table 15: ESR Parameters for Spin Adducts 38.

R in 38	g-value[a]	h.f.s. (Gauss)		
		a_N	a_H^{α}[b]	a_{other}
CH_2CF_3		11.48	6.30	a_F^{β} = 1.13
$CH_2CH_2OCH_3$		12.61	8.78	
C_6H_5	2.0056	9.75	-	$a_H^{o,p}$ = 2.63; a_H^{m} = 0.85
$CH(CH_3)_2$	2.0061	13.10	5.75	
$C(CH_3)_3$		14.35	-	
$CH_2C_6H_5$	2.0068	13.0	7.53	

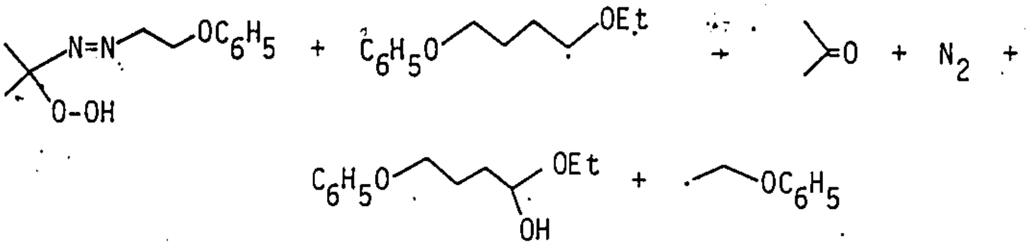
[a] Absolute. [b] α refers to the proton position in the first-formed radical.

Thermolysis Chemistry in Olefins. Compounds 28 decompose rapidly in olefins at 50°C. This rapid decomposition, the poorer fit of the kinetic data to the first-order rate equation (vide infra), and the spin trapping of the radicals in benzene were the initial indicators of a free radical chain mechanism. The rapid decompositions of **28** are strongly inhibited by 2,2,6,6-tetramethylpiperidine-N-oxyl (TMPO, **43**) radical, and return to the fast rate is observed only after all the TMPO is consumed, see Fig. 11. This observation provides a confirmation of the chain hypothesis. Samples of **28b** (R = $CH_2CH_2OCH_3$) and **28c** (R = $CH_2CH_2OC_6H_5$) in ethyl vinyl ether, but without added TMPO, decompose without induction periods, Fig. 12. Inhibition of the rapid decompositions of **28** exposes a slower rate of decomposition. This slower rate is attributed to the unimolecular decomposition of α-hydroperoxydiazenes. Results from the inhibition studies and from spin trapping suggest that the chain initiation involves the unimolecular decomposition of **28** (eq. R13), see mechanism a of Scheme 6. The above observations and the nature of products suggest

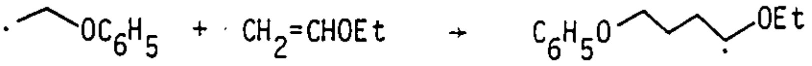


[R13]

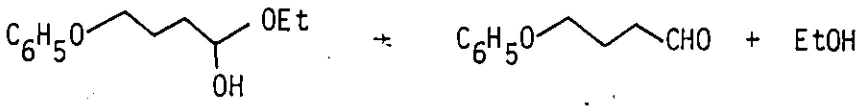
the chain-carrying steps of eq. R14 and R15 and hemiacetal (or hemiketal) decomposition step, eq. R16.



[R14]



[R15]



[R16]

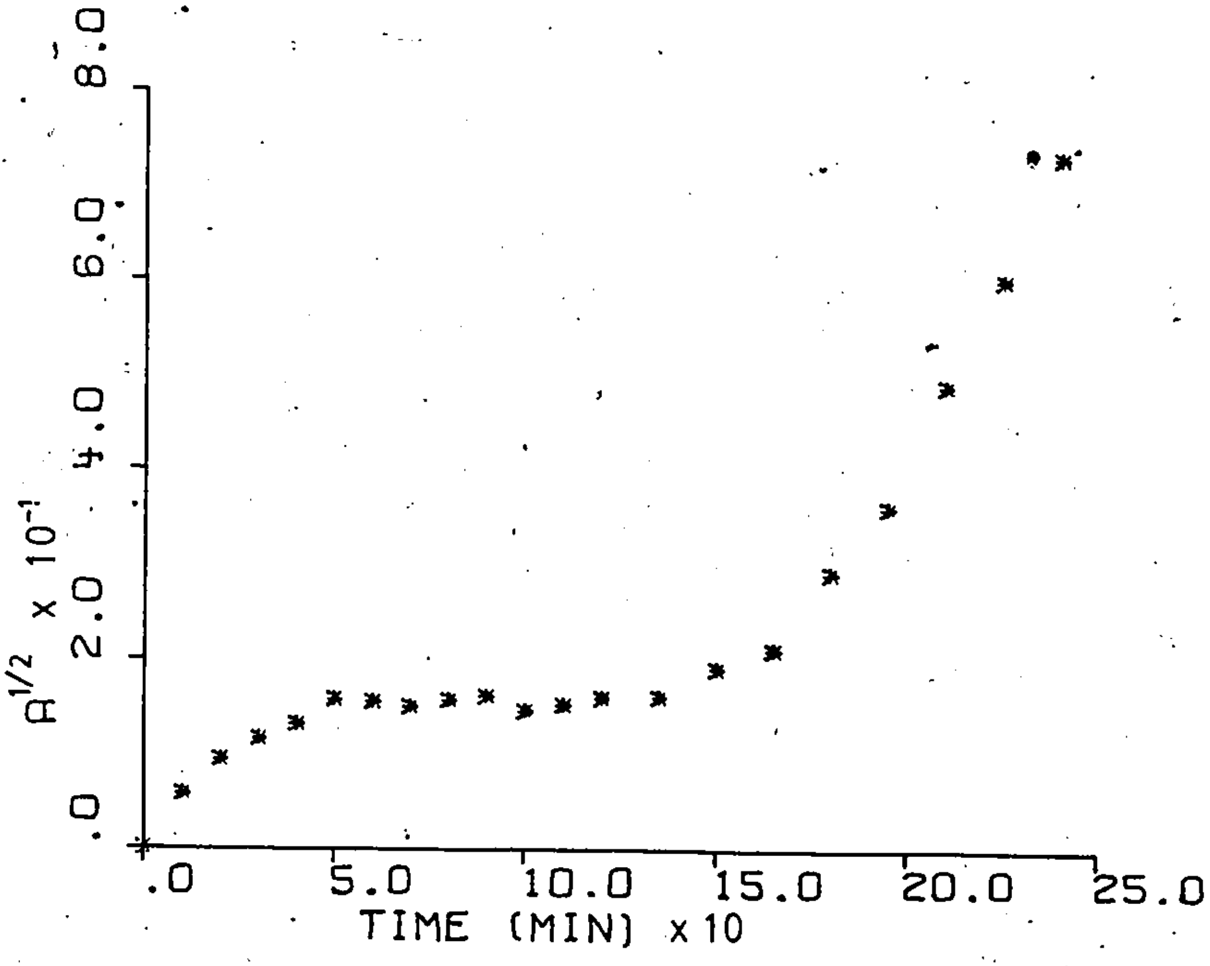


Fig. 11: Kinetics of Decomposition of 0.060M $(CH_3)_2C(OOH)-N{=}N-CH_2CH_2OCH_3$ in Ethyl Vinyl Ether in the Presence of TMPO at 50°C.

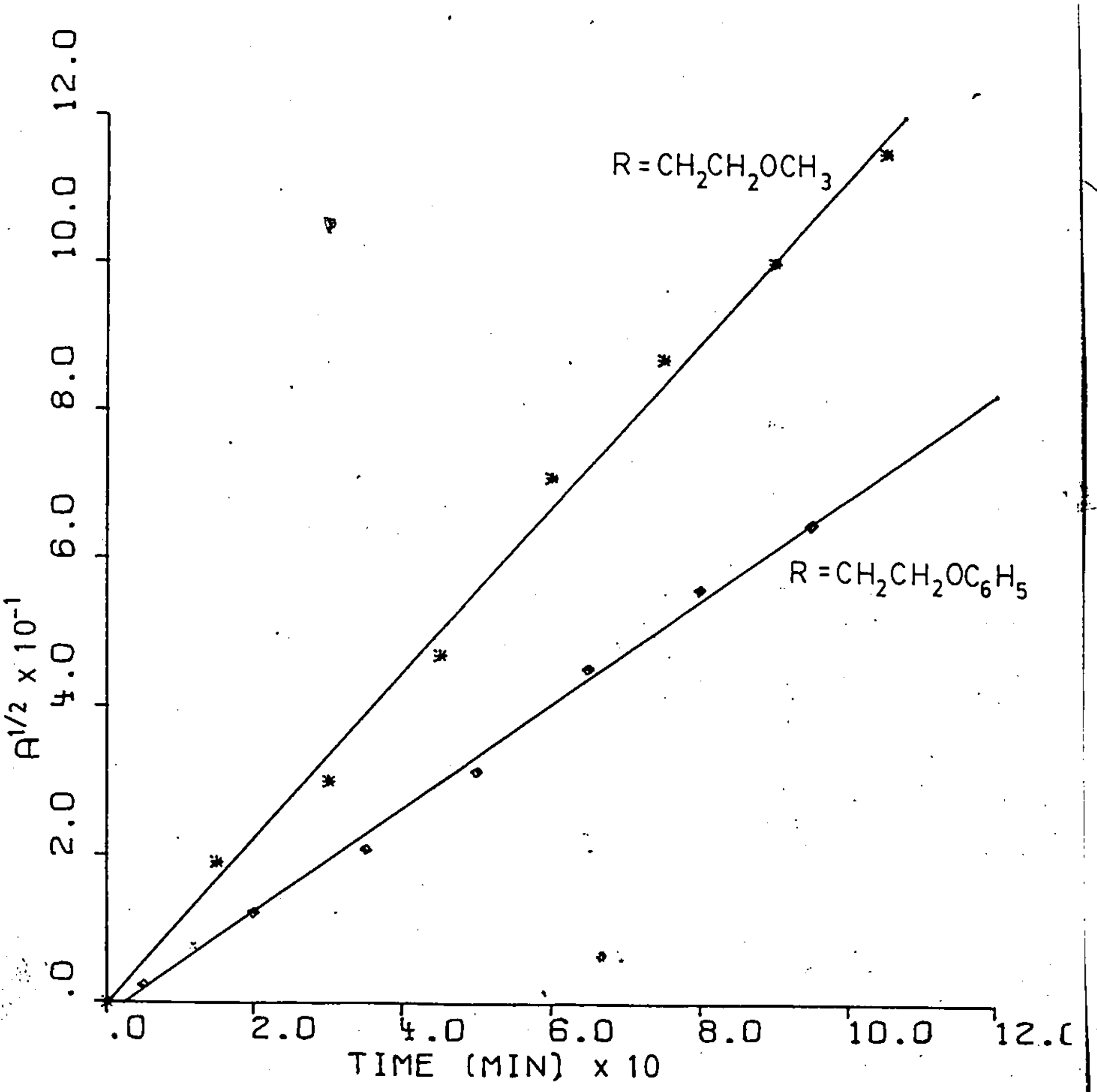
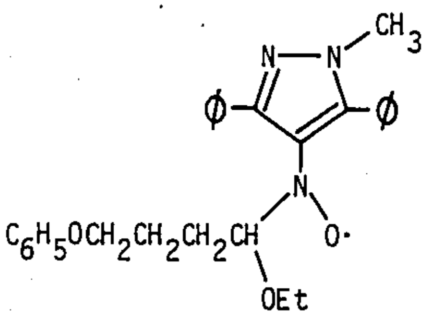


Fig. 12: Kinetics of Decomposition of 0.08M $(CH_3)_2C(OOH)N{=}NR$ in Ethyl Vinyl in the Absence of TMPO at 50°C.

The secondary α-ethoxyalkyl radical in eq. R15 was successfully spin-trapped when 28c was decomposed in a 1×10^{-3} M solution of DMNP, 37, in ethyl vinyl ether. The major signals in the ESR spectrum (Fig. 13) were assigned to the spin adduct 44 from 1-ethoxy-4-phenoxybutyl radical. The measured g-value for 44 compares very well with the values obtained by Merritt and Johnson[161] for spin adducts 45 from reaction of secondary alkoxy radicals ($R_2CHO\cdot$) with N-tert-butyl—α-phenylnitrone. The nitrogen and α-proton hyperfine splitting constants differ by only 1.7G and 2.3G, respectively, although the two spin adducts are not exactly the same. Also present in the ESR spectrum are some minor signals which are assigned to the spin adduct from the first-formed primary radicals ($C_6H_5OCH_2CH_2\cdot$) and DMNP, see eq. R8. The ESR parameters of this second adduct are a_N = 12.56G and a_H^α = 8.65G. The above results lend support to the hypothesis for the propagation steps.



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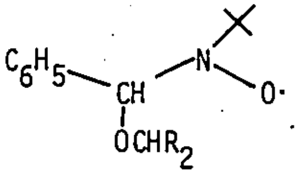


45

g-value	a_N	a_H^α
2.0063	12.0G	4.25G
2.0063	13.7G	1.77G

Since the products isolated from reactions of 28 with enol ethers

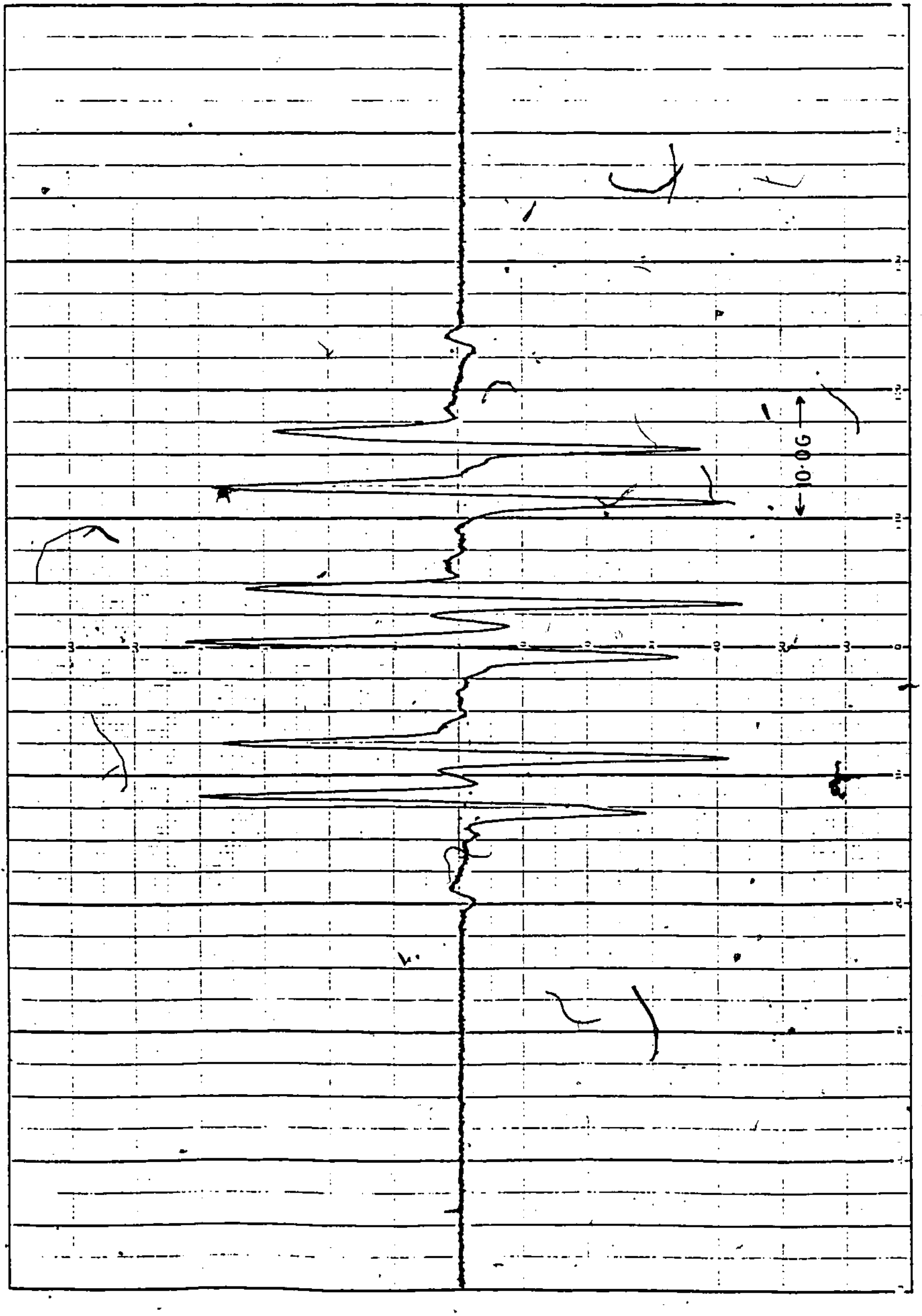
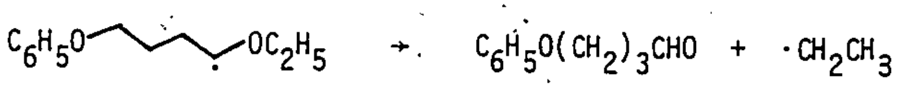


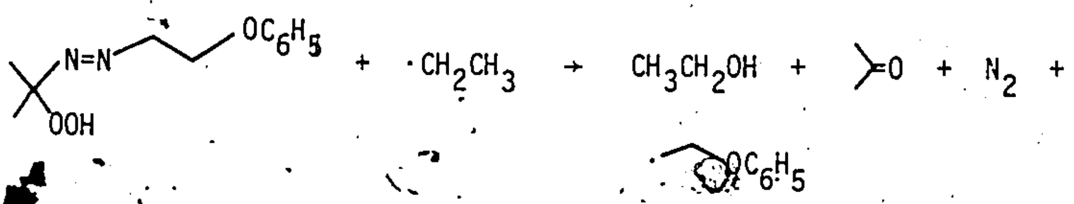
Fig. 13: ESR Spectrum of [2,4-Diphenyl-1-methyl]pyrazyl-[1-ethoxyl-4-phenoxy]butyl nitroxyl Radical.

were aldehydes and ketones, an alternative mechanism for the production of these compounds has to be considered. The carbonyl compounds could possibly arise by β-scission of the α-alkoxyalkyl radical (eq. R17) to generate an alkyl radical. The alcohol, which is a major co-product, would then be attributed to induced decomposition of 28 by the alkyl



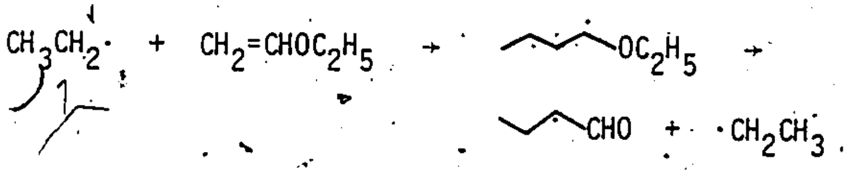
[R17]

radicals (eq. R18) instead of to decomposition of a first-formed hemiacetal (or hemiketal) (eq. R16). If the processes of eq. R17 and R18 were



[R18]

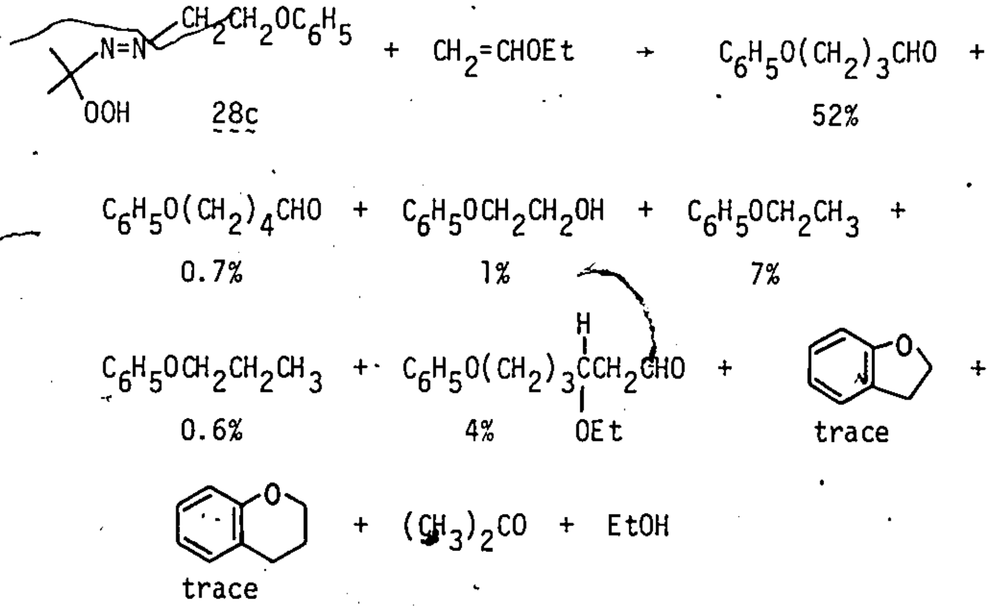
important during the thermolysis of compound 28 in ethyl vinyl ether, then butyraldehyde should be a major co-product since ethyl radicals too would add to ethyl vinyl ether (eq. R19).



[R19]

Butyraldehyde was not detected as a by-product of any reaction with ethyl vinyl ether. These results indicate that the β-scission process is at most a minor competing step in the cases that were studied.

A careful search for minor products in the case of the reaction of 28c with ethyl vinyl ether provided some interesting results which indicated that the major product was reacting further to give other products, see eq. R3. Particularly significant among the products were



[R3]

5-phenoxypentanal, 2,3-dihydro-5,6-benzopyran, and phenyl propyl ether which probably arose from the major product by a sequence of reactions in Scheme 8. Formation of 5-phenoxypentanal and phenyl propyl ether as minor by-products provides further support for the radical mechanism. Abstraction of aldehyde hydrogen and subsequent decarbonylation (first two steps of Scheme 8) are well known in free radical chemistry.[162,163] The resulting 3-phenoxy-1-propyl radical should then participate in the available abstraction and addition processes, leading to phenyl propyl ether, 5-phenoxypentanal, and 2,3-dihydro-5,6-benzopyran, the observed minor by-products with one more carbon atom than would be expected from consideration of the structures of the reactants. Another minor, but interesting, by-product was identified tentatively as 3-ethoxy-6-phenoxyhexanal. This compound probably arises via addition to a second molecule of ethyl vinyl ether by the first formed intermediate α-ethoxy-

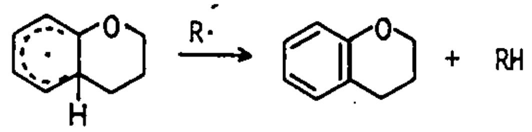
SCHEME 8

$$C_6H_5O(CH_2)_3CHO + R\cdot \rightarrow RH + C_6H_5O(CH_2)_3\dot{C}O$$

$$C_6H_5O(CH_2)_3\dot{C}O \rightarrow CO + C_6H_5O(CH_2)_2\dot{C}H_2$$

$$C_6H_5O(CH_2)_2\dot{C}H_2 + H\text{ donor} \rightarrow C_6H_5O(CH_2)_2CH_3$$

$C_6H_5O(CH_2)_2\dot{C}H_2 \rightarrow$



$$C_6H_5O(CH_2)_2\dot{C}H_2 + CH_2{=}CHOEt \rightarrow C_6H_5O(CH_2)_4\dot{C}HOEt$$

$$C_6H_5O(CH_2)_4\dot{C}HOEt + \mathbf{28c} \rightarrow C_6H_5O(CH_2)_4\underset{\displaystyle OH}{\underset{|}{C}}HOEt + \text{other products}$$

$$C_6H_5O(CH_2)_4\underset{\displaystyle OH}{\underset{|}{C}}HOEt \rightarrow C_6H_5O(CH_2)_4CHO + EtOH$$

alkyl radical. The radical then participates in hydroxyl abstraction followed by decomposition of the hemiacetal to give the compound, see Scheme 9.

SCHEME 9

$$C_6H_5OCH_2CH_2\cdot + CH_2{=}CHOEt \rightarrow C_6H_5O(CH_2)_3\dot{C}HOEt$$

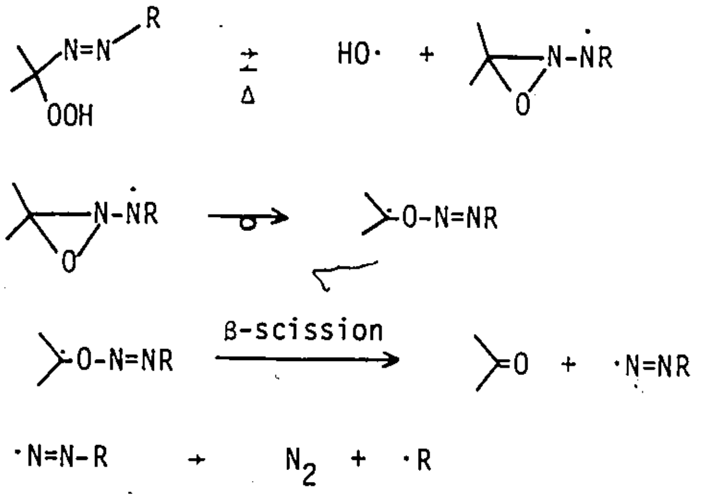
$$C_6H_5O(CH_2)_3\dot{C}HOEt + CH_2{=}CHOEt \rightarrow C_6H_5O(CH_2)_3\underset{\displaystyle OEt}{\underset{|}{C}}HCH_2\dot{C}HOEt$$

$$C_6H_5O(CH_2)_3\underset{\displaystyle OEt}{\underset{|}{C}}HCH_2\dot{C}HOEt + \mathbf{28c} \rightarrow C_6H_5O(CH_2)_3\underset{\displaystyle OEt}{\underset{|}{C}}HCH_2\underset{\displaystyle OH}{\underset{|}{C}}HOEt + \text{other products}$$

$$C_6H_5O(CH_2)_3\underset{\displaystyle OEt}{\underset{|}{C}}HCH_2\underset{\displaystyle OH}{\underset{|}{C}}HOEt \rightarrow C_6H_5O(CH_2)_3\underset{\displaystyle OEt}{\underset{|}{C}}HCH_2CHO + EtOH$$

Mechanism of Decomposition of Hydroperoxydiazenes. As mentioned in the Introduction (section I 3.4, page 41), 1,2-vinyl migration is not known for simple allyloxyl radicals. Nevertheless, an analogous pathway, 1,2-azo migration, must be considered in the thermal decomposition of α-hydroperoxydiazenes, see Scheme 10. Unfortunately there are no

SCHEME 10

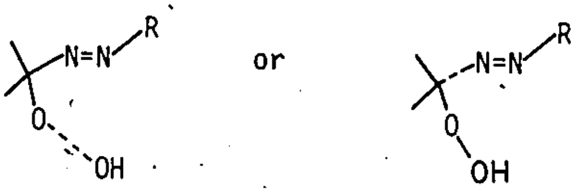


precedents for such a mechanism. In spite of the lack of examples, it can be predicted that if the O-O bond scission in concert with addition to form a hydrazyl radical is the rate-determining step, then substituents, R, capable of stabilizing the nitrogen-centred radical by resonance should increase the rate of decomposition of the hydroperoxydiazenes. This would mean that the decomposition of 28d (R = C_6H_5) must be faster than the decomposition of 28f (R = $C(CH_3)_3$). The products fit for this mechanism, because cyclization is only a little more than the first step of the rearrangement of a radical of the homoallyl type,[164] and would be followed by ring opening and by β-scission (Scheme 10). Results from this work (vide infra) indicate that compound 28f decomposes much faster than compound 28d. Thus decompositions of 28 probably do not proceed by the mechanism proposed in Scheme 10.

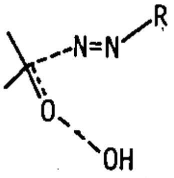
Other mechanisms for which the products fit include (a) one-bond cleavage involving the O-O bond or a C-N bond; (b) concerted two-bond cleavage involving the O-O bond and its nearest C-N bond; or (c) concerted three-bond cleavage involving the O-O bond and the two C-N bonds, see Scheme 11.

SCHEME 11

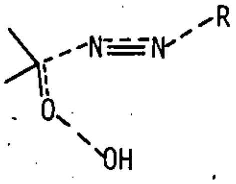
A. One-Bond Cleavage



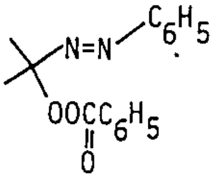
B. Two-Bond Cleavage



C. Three-Bond Cleavage



In a recent paper, Warkentin and Nazran[165] reported their studies of the thermal decomposition of azoperester 46. They chose tert-butyl perbenzoate, 47, as a model for the stepwise thermolysis of the azoperester 46.



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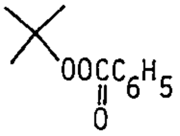
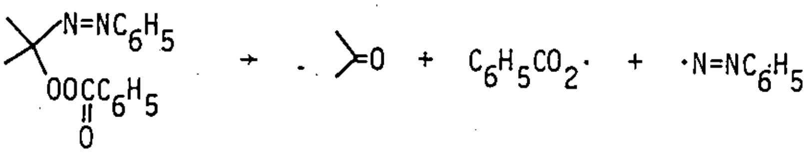


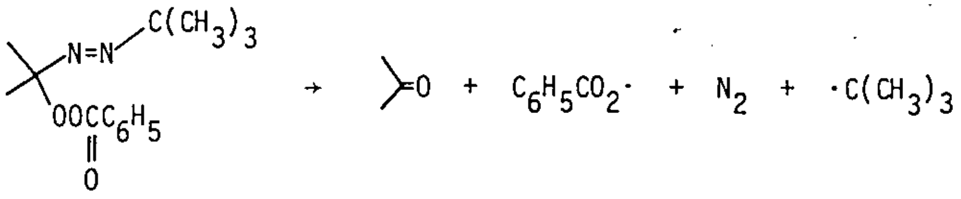
47

Perester 47 is well known to decompose by peroxy O-O bond cleavage in the rate-determining step[166] and if 46 were using that mechanism also, there ought to be only a small effect of substituting the $N{=}NC_6H_5$ for CH_3. The first-order rate constant for homolytic decomposition of 46 is 4.5×10^{-4} s^{-1}[165] at 10°C and that for 47 is 3.38×10^{-5} s^{-1} at 110°C.[167] Warkentin and Nazran[165] estimated that at 10°C 46 decomposes with a rate constant about 10^8 times larger than that for 47. Compound 46 was postulated to decompose by a concerted two bond cleavage, eq. R20. Attempts to isolate perester 48 failed and this was interpreted



[R20]

to indicate a faster rate of decomposition of 48. Warkentin[165] proposed that compound 48 decomposes by a concerted three-bond cleavage (mechanism C in Scheme 11), eq. R21. Further evidence in support of these mechanisms for the azoperesters is provided by the rate constants for decomposition



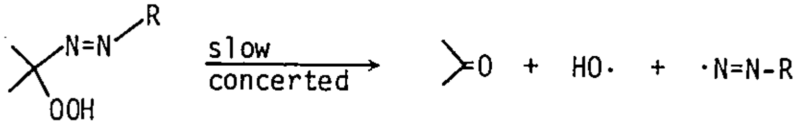
48

[R21]

of analogous azoalkanes[116] and tert-butylhydroperoxide.[93] The rate constant for decomposition of phenyl tert-butyl diazene is 1.06×10^{-3} s^{-1} at 300°C.[116] The rate constant at 10°C would thus be much smaller than the value obtained from compound 46. From the generalized rate equation, $\log k = 15.8 - (4.3\times10^{4})/(2.303RT)$, for unimolecular decomposition of tert-butylhydroperoxide,[93] the rate constant is 3.14×10^{-18} s^{-1} at 10°C and 4.17×10^{-14} s^{-1} at 50°C. The rate constant for decomposition of 46 at 10°C is about 10^{13} times larger than that for decomposition of tert-butylhydroperoxide. Phenyl tert-butyl diazene and tert-butylhydroperoxide are known to decompose by one-bond cleavage. Thus the azoperesters must decompose by the proposed mechanisms B and/or C in Scheme 11.

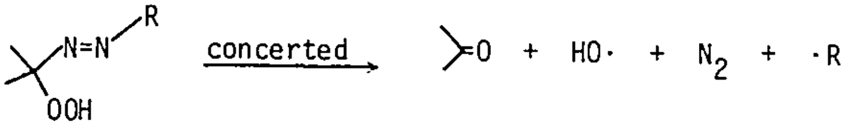
Based on these analogies it is proposed that the α-hydroperoxydiazenes undergo unimolecular decomposition by either the concerted two-bond cleavage to form diazenyl radical intermediates (eq. R22) which rapidly fragment to N_2 and ~~alkyl~~ (or aryl) radicals (eq. R23) or by the concerted three-bond cleavage, eq. R24. Induced decomposition of the hydroperoxydiazene can also be imagined to go by either concerted two-bond or concerted three-bond cleavage.

Evidence in support of either or both mechanism was provided by kinetic studies of the unimolecular decomposition of compounds 28. The radical chain decomposition of the compounds was inhibited by addition



[R22]

$$\cdot N{=}N{-}R \xrightarrow{\text{fast}} N_2 + \cdot R$$ [R23]



[R24]

of TMPO to the reaction mixtures. The first-order plots are shown in Fig. 14 and 15. Each plot is an average of three runs. Decomposition of 28 was followed by monitoring the disappearance of the gem dimethyl signal at δ 1.6 in the ^{1}H NMR spectrum using as internal standard for integration the sum of the gem dimethyl signal of 28 and the acetone signal at δ 1.9. The rate constants together with the correlation coefficients are given in Table 16.

Very recently Solomon and co-workers[168] have reported the rate constants and activation parameters for the unimolecular decomposition of 28f ($R = C(CH_3)_3$) in cyclohexane. From the generalized rate constant, $k = 9.58x10^{14}exp(-1.47x10^4/T)s^{-1}$, the value at 50°C in the cyclohexane is estimated to be $1.68x10^{-5}$ s^{-1}. This is 11.5 times smaller than the value obtained in this laboratory. As would be noted, the kinetic measurements in this laboratory were done in benzene. According to literature data[65e,85,86,169] and to the earlier discussion in this thesis (see Section RD 1.2) several types of associations are possible for organic hydroperoxides. It has been established that the structure and heat of formation of these hydrogen-bonded species affect considerably the Arrhenius parameters of decomposition of hydroperoxides.[85,169] For

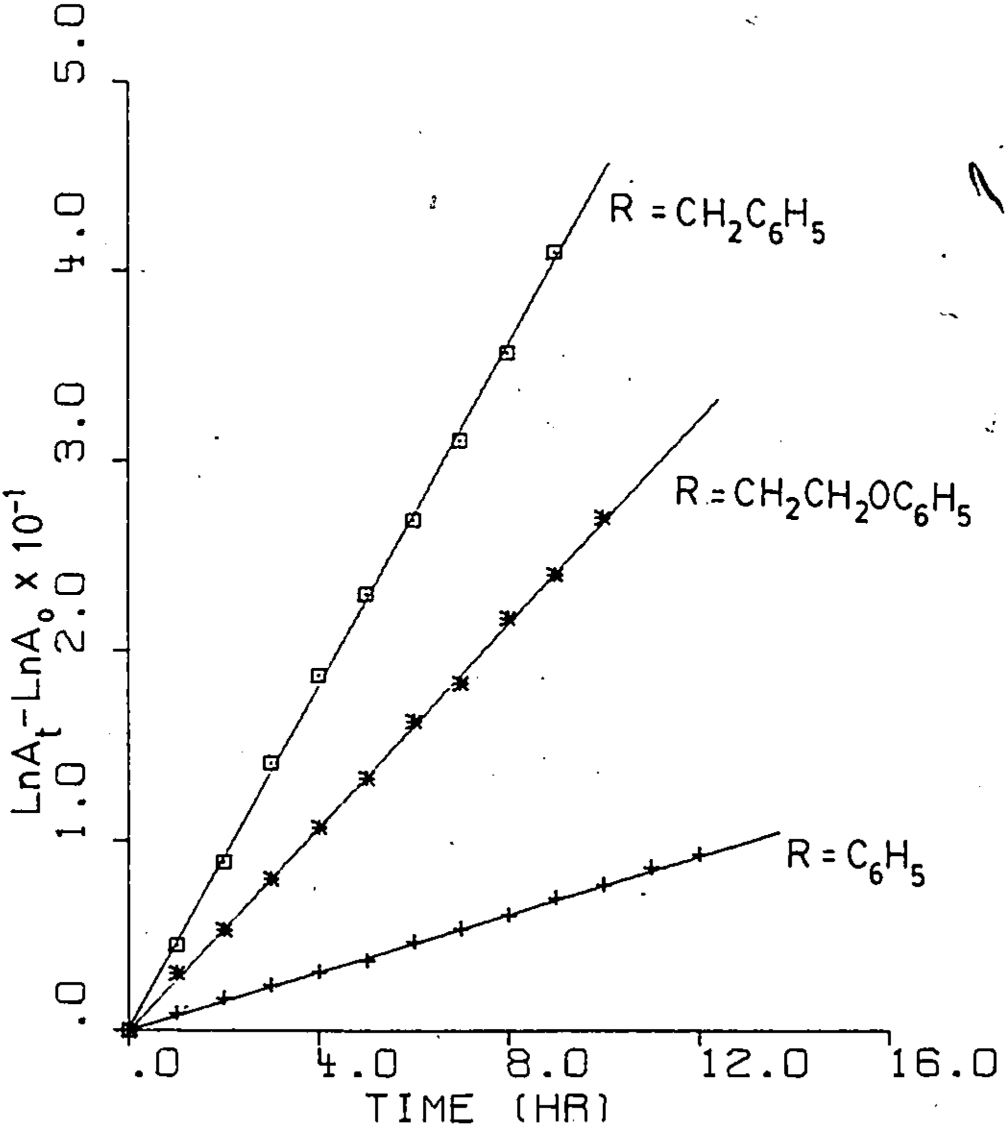


Fig. 14: Kinetics of Unimolecular Decomposition of (0.08M-0.09M) $(CH_3)_2C(OOH)N{=}NR$ in Benzene at 50°C.

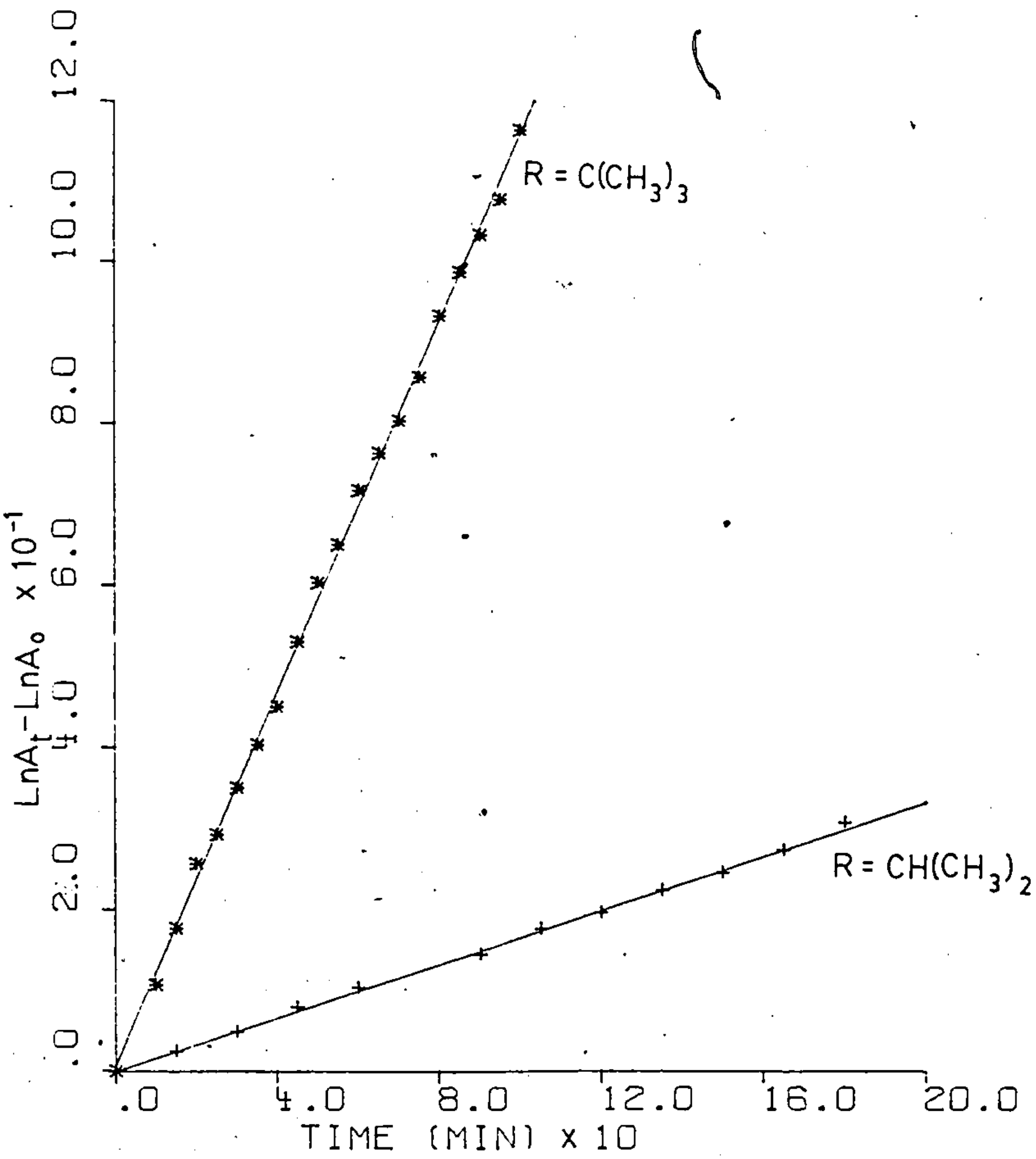


Fig. 15: Kinetics of Unimolecular Decomposition of (0.75M-0.80M) $(CH_3)_2C(OOH)N{=}NR$ in Benzene at 50°C.

Table 16: Rate Constants for the Unimolecular Decomposition of $(CH_3)_2C(OOH)N{=}NR$ at 50°C in Benzene

R	$k^{50°C} \times 10^6\ s^{-1}$	Corr. Coeff.
C_6H_5	2.1 ± 0.3^a	0.9996
$CH_2CH_2OCH_3$	9.6 ± 0.7	0.999
$CH_2CH_2OC_6H_5$	7.4 ± 0.4	0.9997
$CH_2C_6H_5$	12.3 ± 0.5	0.9996
$CH(CH_3)_2$	28 ± 2	0.9994
$C(CH_3)_3$	190 ± 5	0.9949

[a] Errors are standard deviations from the mean.

example, Kucher et al[169] found that the activation energy of the decomposition of cumene hydroperoxide is much lower in nitrosobenzene (50 kJ mol^{-1}) than in cumene (108 kJ mol^{-1}). The larger value for the rate constant of unimolecular decomposition of 28f in benzene, obtained in this work, can be explained in terms of the lowering of the Arrhenius parameters and of higher concentrations of the hydroperoxydiazene in benzene. Assuming that the rate constant for the disappearance of 28f in benzene is given by $k = 9.5 \times 10^{10} \exp(-1.103 \times 10^4/T) s^{-1}$ (the value reported by Solomon et al. is $k = 9.58 \times 10^{14} \exp(-1.47 \times 10^4/T) s^{-1}$)[168], the rate constant at 50°C is $1.46 \times 10^{-4}\ s^{-1}$. This value compared favorably with the experimental value in Table 16, and the difference between these values can be accounted for by differences in concentrations of the hydroperoxydiazene in the laboratories of Solomon's (∼ 0.035M) and of Warkentin's (0.06-0.10M).

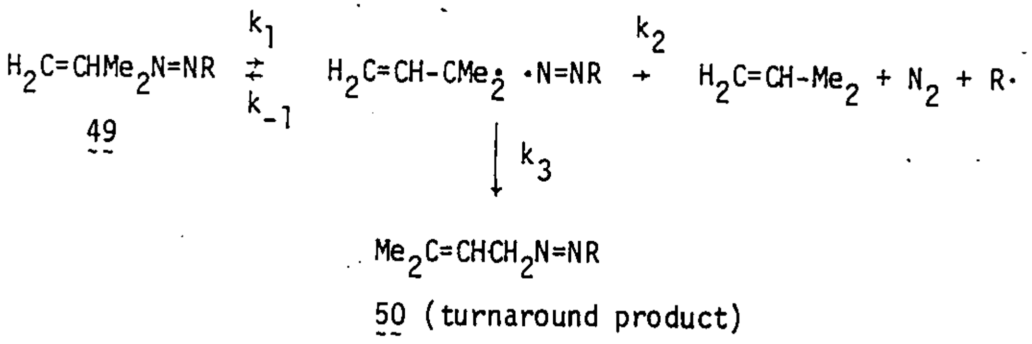
As pointed out in the Introduction (Section I 5.1, page 47), the mechanism by which azo compounds lose nitrogen has been debated since Ramsperger[117] first posed the question in 1929. The question, the status of which has oscillated between "essentially settled" and "still unanswered", is whether homolytic decomposition is concerted (eq. R25) or stepwise, eq. R26. The major criteria of mechanism (discussed in the

$$R^1N{=}NR^2 \rightarrow R\cdot^1 + N{\equiv}N + R\cdot^2 \qquad [R25]$$

$$R^1N{=}NR^2 \rightarrow R\cdot^1 + \cdot N{=}NR^2 \rightarrow R\cdot^1 + N_2 + R\cdot^2 \qquad [R26]$$

Introduction) that have been applied include the effect of substituents (R^1 and R^2, including isotope labelling) on the observed rate constant,[113,116] the results from theoretical calculations,[128] and the effects of pressure on the rate constant for solution-phase decomposition.[129] Engel[116,130] summarized the earlier results as follows. "Azoalkane thermolysis seems to proceed by a continuum of mechanisms between concerted (eq. R25) and stepwise (eq. R26) and the more unsymmetrical the azo compound, the more unsymmetrically it cleaves." Recent results[128,129] showed that even symmetrical dialkyl diazenes can decompose by the stepwise mechanism making the above generalization inadequate. Conclusive evidence for stepwise homolysis of a number of unsymmetric dialkyl diazenes (49) was provided recently when "turnaround products" (50), which could only arise from recombination of an alkyl-diazenyl radical pair (Scheme 12), were isolated.[130] Although Engel and Gerth's paper[130] contributed substantially to the clarification of diazene decomposition mechanism, one ambiguity remained. They observed that, for example, 49 (R = t-butyl) does not lead to a

SCHEME 12



$$\begin{tikzcd} H_2C{=}CHMe_2N{=}NR \arrow[r, shift left, "k_1"] & H_2C{=}CH{-}CMe_2^{\bullet}\ {\cdot}N{=}NR \arrow[l, shift left, "k_{-1}"] \arrow[r, "k_2"] \arrow[d, "k_3"] & H_2C{=}CH{-}Me_2 + N_2 + R\cdot \\ & Me_2C{=}CHCH_2N{=}NR & \end{tikzcd}$$

49

50 (turnaround product)

detectable amount of turnaround product and yet is much more labile than 49 (R = methyl) which forms turnaround product. The substituent effect can be accounted for in two ways. First, Scheme 12 could describe the mechanism for both compounds. For Scheme 12, $k_{obsd} = k_1[1 - \frac{k_{-1}}{(k_{-1}+k_2+k_3)}]$, and k_{obsd} would be essentially k_1 for the t-butyl system if k_2 were large relative to both k_{-1} and k_3 and turnaround product would not be detectable. For the methyl system k_{obsd} would be smaller if it had k_2 small relative to k_{-1} and k_3 and turnaround product would be formed. Engel calculated that the rate of N_2 loss from R-N=N· at 298°C exceeds the rate of rotation of dimethylallyl radical ($k_{rot} = 3.4\text{x}10^{10}\ s^{-1}$ at 298°C) within the cage when R is t-butyl but not when it is, say, isopropyl (see Table 17). Second, eq. R26 could describe the mechanism for the methyl system only; the t-butyl system adopting the concerted mechanism, eq. R25. The latter mechanism accomodates the enhanced lability of the t-butyl system easily and, of course, there is no possibility of turnaround products from an alkyldiazenyl radical pair because such a pair is never formed.

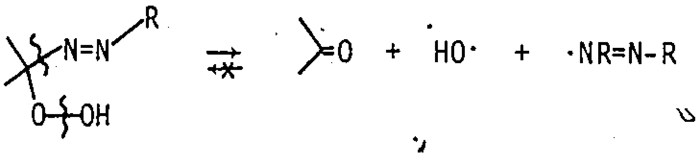
Substituent effects on the rate constants for unimolecular

Table 17: Calculated Lifetimes, τ, of Diazenyl Radicals (R-N=N·) at 298°C.[a]

R	k_D^b, s^{-1}	τ, s
C_6H_5	1.1×10^6	6.3×10^{-7}
Cyclopropyl	3.7×10^7	1.9×10^{-8}
CH_3	9.0×10^7	7.7×10^{-9}
$CH(CH_3)_2$	1.9×10^9	3.7×10^{-10}
$C(CH_3)_3$	1.5×10^{11}	4.6×10^{-12}
$CH_2{=}CHC(CH_3)_2$	6.2×10^{12}	1.6×10^{-13}

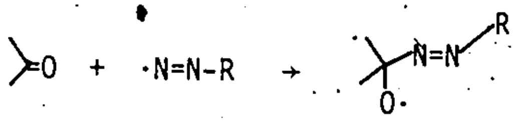
[a] Ref. 130. [b] Rate constant for dissociation of R-N=N· at 298°C.

decomposition of hydroperoxydiazenes 28 (b R = $CH_2CH_2OCH_3$, c R = $CH_2CH_2OC_6H_5$, d R = C_6H_5, e R = $CH(CH_3)_2$, f R = $C(CH_3)_3$, g R = $CH_2C_6H_5$) point to a fully-concerted mechanism for 28f and by extrapolation, to a concerted mechanism for the Engel systems which are left mechanistically ambiguous by failure of the "turnaround" criterion. It appears very unlikely that there will be internal returns in the thermolysis of hydroperoxydiazenes, eq. R27. Two-bond concerted homolysis, as implied by the azoperester model would require that internal return by the concerted process be termolecular; an unlikely event. If, however, return

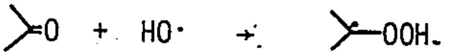


[R27]

were non-concerted, then the first step for the formation of the starting compound must involve addition of diazenyl or hydroxyl radicals to the carbonyl compound, eq. R28 and R29, respectively. There is no precedent



[R28]

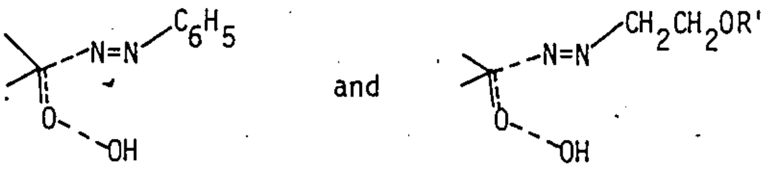


[R29]

for either of these processes and it is quite unlikely, in any case, that the necessary radical addition steps could compete with loss of N_2 from RN=N·. The rate constant for the latter process at 20°C has been estimated at $1.1\text{x}10^{6}\ \text{s}^{-1}$[130,170] for the case $R = C_6H_5$, which must be one of the slowest (Table 7). Thus the only likely reaction the diazenyl radicals can undergo is dissociation to N_2 and alkyl (or aryl) radicals or coupling with hydroxyl radicals. If all hydroperoxydiazenes decompose irreversibly by the concerted two-bond cleavage to give diazenyl radical intermediates, then the observed rate constant should show only small substituent effects.

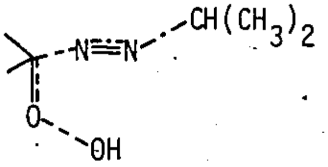
The phenyl diazenyl radical is a well-known radical intermediate[170] and it is therefore proposed to be formed in the thermolysis of 28d. Thus compound 28d probably decomposes by mechanism B, Scheme 11. If the other hydroperoxydiazenes decompose by the same mechanism, then their rate constants ought to be close to that for compound 28d. If, on the other hand, the compounds decompose by different mechanisms, then there ought to be large differences in their rate constants. Results in Table 16 show that compound 28f decomposes with a rate constant which is about

90 times larger than that of 28d while 28b and 28c have rate constants which are only 4 times larger than that of 28d. Compound 28e has a rate constant which is 13 times larger than that of 28d. The results point to the concerted two-bond cleavage for compounds 28b and 28c, and a concerted three-bond cleavage for compound 28f. Compound 28e probably

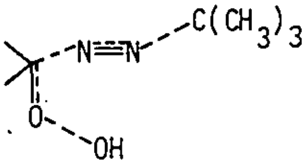


B. Concerted Two-Bond Cleavage

decomposes by a concerted, but less synchronous, three-bond cleavage.

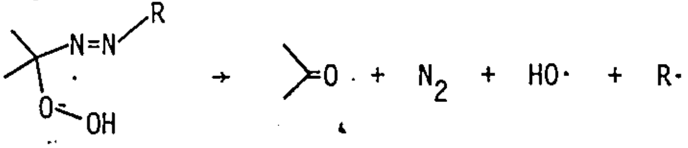


C1. Concerted, Less Synchronous



C2. Fully Concerted

Surprisingly, the benzyl system (28g) has a rate constant which is only 6 times larger than that for the phenyl system and 15 times less than that for the t-butyl system (28f). If resonance stabilization of the benzyl radical were an important factor during the decomposition of 28, then the rate constant for its decomposition ought to be much larger. In fact, the benzyl resonance is known to be very important. For example, bromination of alkylbenzenes which has a late transition state is enormously selective for benzyl sites while chlorination which has an early transition state is relatively unselective. The energetics of the decomposition of the hydroperoxydiazenes point to an exothermic process, eq. R30 and R31. According to Hammond's Postulate the decomposition of


[R30]

$$\Delta H_{rxn} = (2x69) + 100 + 45 + 83 - 226 - 172 = -42\ \text{kcal mol}^{-1}$$ [171] [R31]

the hydroperoxydiazenes has early transition states. Thus in the benzyl system the small energy gained at the transition state in terms of benzyl resonance could be offset by entropy cost of stopping rotation about the Ph-C bond. This early transition state should therefore make the rate constant smaller than one would expect.

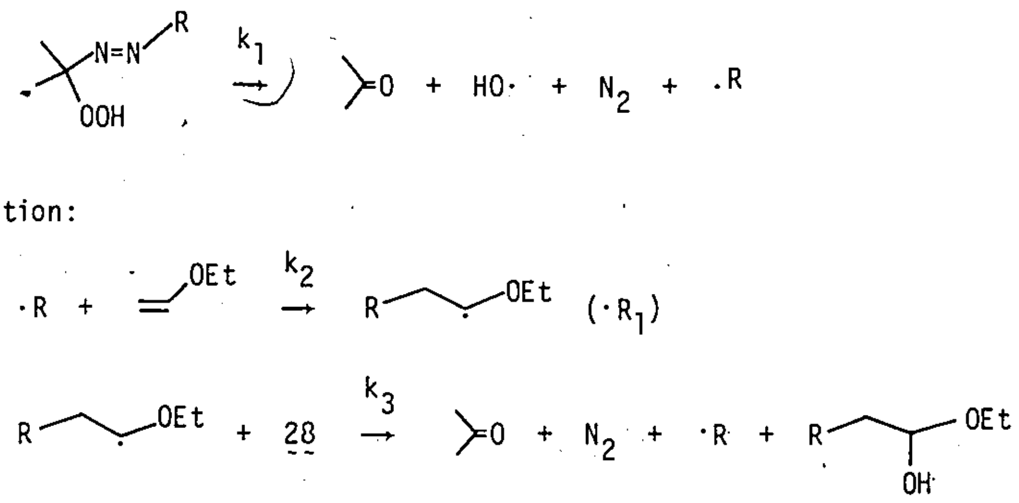
The results suggest that steric factors are also very important in the decomposition of the hydroperoxydiazenes. Overberger and coworkers[172] have earlier recognized the importance of steric factors in the decomposition of dialkyl diazenes. These factors were later examined by others.[173-175] The results from the studies by Timberlake and Engel[174] and by Timberlake[175] were shown to be most consistent with a concerted mechanism for the decomposition of sterically crowded dialkyl diazenes.

The large increase in the rate constant for the decomposition of the tert-butyl system can be explained in terms of changes in the geometry of the tert-butyl group. In going from the starting diazene to the free radical, the geometry of the tert-butyl group changes from tetrahedral to trigonal planar (or near-planar), thus changing the internal angles from approximately 109° to 120° and placing the methyl groups further away from each other.

The Reaction Kinetics. The overall reaction mechanism for compounds 28 in the olefins is given in Scheme 13.

SCHEME 13

Initiation:



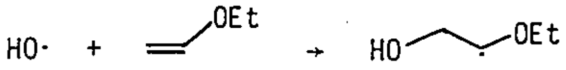
Termination:

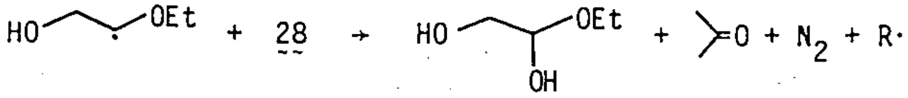
$$2R\cdot \xrightarrow{k_4} R\text{-}R$$

$$R_1\cdot + R\cdot \xrightarrow{k_5} R_1\text{-}R$$

$$2R_1\cdot \xrightarrow{k_6} R_1\text{-}R_1$$

A second set of propagation sequences involves the addition of hydroxyl radicals to the double bond followed by chain transfer on the hydroperoxydiazene, eq. R32 and R33.


[R32]


[R33]

This set of sequences is unimportant when the kinetic chain is long. Also if the chain is long the concentration of the secondary adduct radical will be very low and thus it will be prevented from being involved in chain termination processes; that is, steps 5 and 6 in Scheme 13 would be unimportant. Product analysis of the reactions of compounds **28** with the olefins showed none of the products that might have arisen from the second propagation sequence. Since the involvement of the hydroxyl radicals in the propagation sequence is not important, their self-dimerizations do not constitute chain termination. Thus only step 4 constitutes the chain termination process.

The rate of decomposition of the hydroperoxydiazenes is given by eq. R34, where [A] is the concentration of hydroperoxydiazene. At a

$$-\frac{d[A]}{dt} = k_1[A] + k_3[A][R_1\cdot] \qquad [R34]$$

steady-state radical concentration the rate of decomposition of compounds **28** is given as

$$-\frac{d[A]}{dt} = k_1[A] + k[A]^{\frac{1}{2}} \qquad [R35]$$

where $k = (k_1/k_4)^{\frac{1}{2}}(k_2/k_3)[S]$ and [S] is the constant concentration of the olefin (substrate), present in large excess. See Appendix II for a complete deduction of the above rate equation.

If it is assumed that $k[A]^{\frac{1}{2}} >> k_1[A]$, then eq. R35 becomes

$$-\frac{d[A]}{dt} \simeq k[A]^{\frac{1}{2}} \qquad [R36]$$

which leads to the integral rate equation R37.

$$[A]_t^{\frac{1}{2}} - [A]_0^{\frac{1}{2}} = -kt \qquad [R37]$$

where $[A]_0$ and $[A]_t$ are the hydroperoxydiazene concentrations at time zero and time t, respectively. The data that were plotted are given in Appendix II, Section AII.2 (see Fig. 12 for representative plots). The plots gave good straight lines with correlation coefficients of 0.9975 and 0.9982 for 28b and 28c, respectively, for at least 90% of the decomposition.

Chain Length. The chain length was defined in the Introduction (Section I 3.1, page 21) as the rate of one of the propagating reactions divided by the rate of the termination reaction. An operational estimate of the chain length for the case where chains are long, may be given as

$$\text{chain length} \simeq \frac{k_{obs}[A]^{\frac{1}{2}}}{2k_1[A]} \qquad [R38]$$

where k_{obs} is the observed rate constant and k_1 is the rate constant for the unimolecular decomposition of the hydroperoxydiazene. For compound 28b ($R = CH_2CH_2OCH_3$) in 2-methoxyethylene, $k_1 = 9.6 \times 10^{-6}\ s^{-1}$ and $k_{obs} = 1.7 \times 10^{-4}\ M^{\frac{1}{2}}\ s^{-1}$. At an initial concentration of 0.04M hydroperoxydiazene, the chain length is calculated to be approximately 45.

Concluding Remarks. Evidence has been given in the foregoing section to show that products from the reaction of hydroperoxydiazenes with olefinic substrates are formed via a free radical chain mechanism.

The evidence came from product analysis which showed incorporation of parts of the hydroperoxydiazenes in the products, from spin trapping of the alkyl radicals which were found as parts of the products that came from the starting diazene, and from kinetic studies.

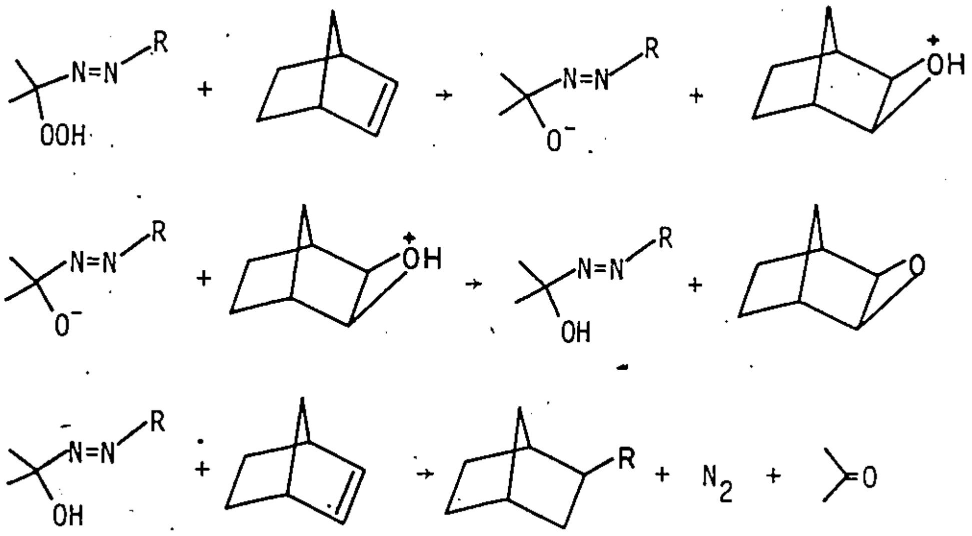
Evidence is also given to show that the chains are initiated by the unimolecular decomposition of the hydroperoxydiazenes and that those compounds containing primary alkyl groups decompose by a concerted two-bond cleavage while those compounds containing tertiary alkyl groups decompose by fully concerted three-bond cleavage. Hydroperoxydiazenes containing secondary alkyl groups probably decompose by a concerted but less-synchronous three-bond cleavage. The high likelihood that hydroperoxydiazenes decompose irreversibly means that substituent effects on thermolysis rate constants can be interpreted unambiguously, in favourable cases, in terms of mechanism. Extrapolation of the present results to alkyl-allyl diazene homolysis suggests that those with tertiary alkyl groups decompose by a concerted mechanism.

Thermolysis Chemistry in Presence of Hindered Alkenes. As was recently reported,[149] the thermolysis of 28a-c in norbornene took a course different from that in enol ethers and in other alkenes, yielding mainly the products of hydroalkylation and epoxidation with very little of the product of hydroxyalkylation. The results of tests for three mechanisms of epoxidation by hydroperoxides that are most likely are discussed below.

Scheme 14 depicts a bimolecular reaction between 28 and norbornene, leading directly to the conjugate acid of norbornene epoxide, ion-paired with the conjugate base of α-hydroxydiazene.

Proton transfer between the ions leads to the α-hydroxydiazene and epoxynorbornane. A mechanism of this type was first proposed by Farmer and co-workers[9,176] who, however, did not present evidence in favour of such a mechanism. A variation of this mechanism was later proposed by Brill[177] who showed that in the uncatalysed epoxidation of olefins with t-butylhydroperoxide, the epoxide forming reaction is a polar process which proceeds through an intermediate complex, Scheme 15. The complex led to the epoxide and 2-methyl-2-propanol or it led to oxygen and 2-methyl-2-propanol, regenerating the olefin. Expoxidation of olefins with an α-hydroperoxyketone, ester, amide, or nitrole,[178] or with an α-hydroperoxypyrazole (26)[148] has been shown to be first order in both hydroperoxide and olefin, suggesting a mechanism with a first step like that of Scheme 14, or the concerted modification of Scheme 15. There is precedent also for the last line of Scheme 14. Hydroalkylation of alkenes with α-hydroxydiazenes is a radical chain process,[134-136] the chain carrying steps of which add up

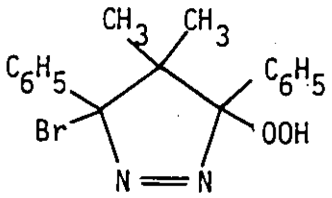
SCHEME 14



SCHEME 15

t-BuOOH + olefin → Complex
Complex → epoxide + t-BuOH
Complex → Olefin + t-BuOH + $\frac{1}{2}O_2$

to the overall reaction shown in that line.



26

It is clear that if mechanism 14 or mechanism 15 were applicable then the rate of decomposition of 28 should increase with norbornene concentration. Figure 16 shows pseudo first order plots of the rates of disappearance of 28b at 50°C in benzene containing norbornene in excess. A tenfold increase in the concentration of norbornene, from 0.3 M to 3.0 M lead to a small decrease in k_{obsd}, from 1.5 ± 0.5x10^{-5} s^{-1} to 1.2 ± 0.3x10^{-5} s^{-1}. In an attempt to suppress any free radical reaction that might overshadow the polar mechanisms, the above studies were carried out in the presence of TMPO as radical scavenger. Analysis of the products showed only trace amounts of the epoxynorbornane and the hydroalkylation product; no hydroxyalkylation product was found. The major product, 51, probably arose from radical pair reaction between 2-methoxyethyl radical and TMPO, eq. R39. The ^{1}H NMR spectrum of 51 had signals at δ 1.17 (s, 12H); δ 1.49 (s, 6H); δ 3.42 (s, 3H); δ 3.55 (t, 2H, J=5.0Hz); δ 3.95 (t, 2H, J=5.0Hz). The kinetic results cannot

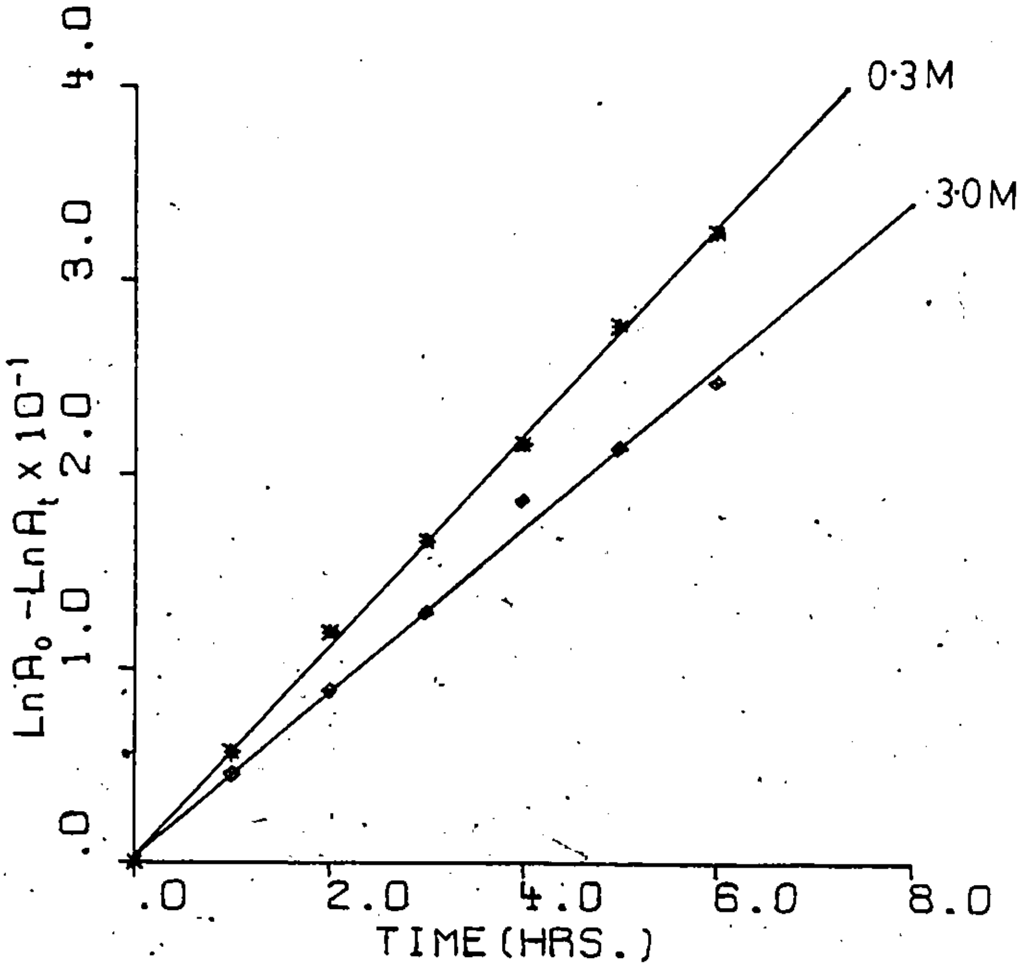
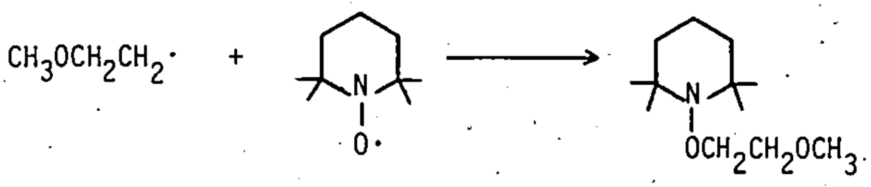


Fig. 16: Kinetics of Unimolecular Decomposition of $(CH_3)_2C(OOH)N{=}N{-}CH_2CH_2OCH_3$ in Presence of Norbornene.



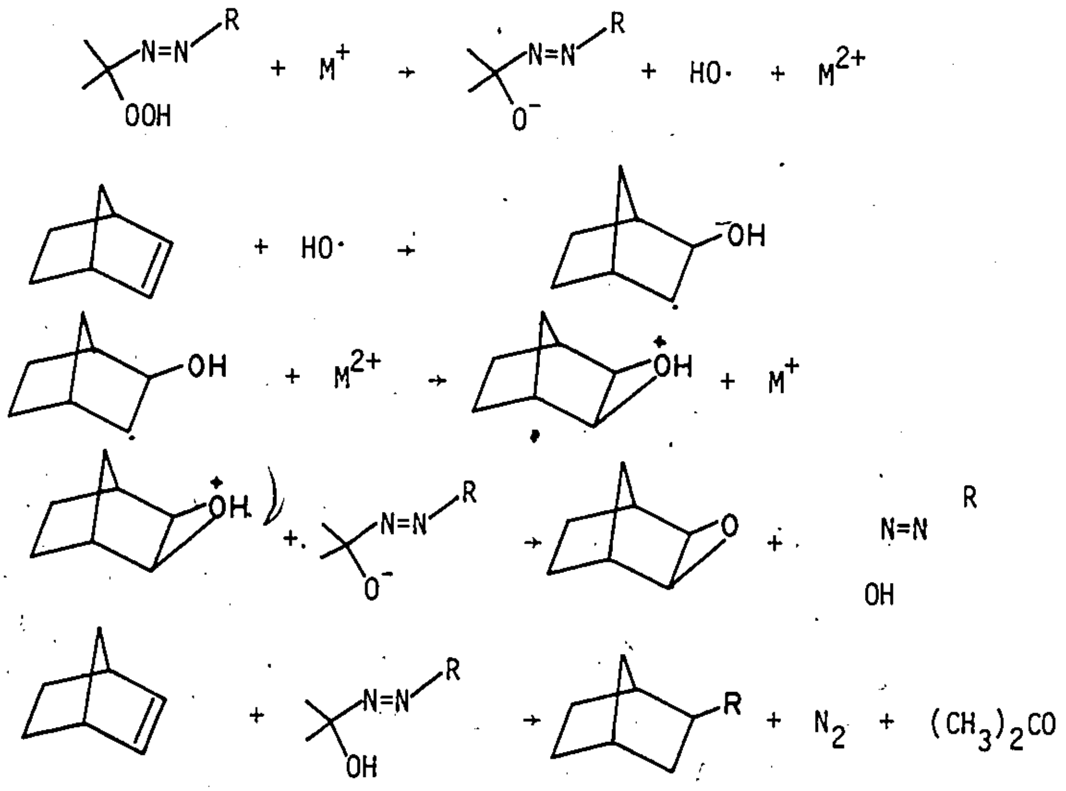
51

[R 39]

be accommodated within the framework of Scheme 14 or Scheme 15 so that the polar or ionic mechanism is ruled out. The reaction must therefore proceed by a mechanism which involves only the hydroperoxydiazene in the rate-determining step or by a mechanism which involves the diazene and a trace amount of some catalyst. Tezuka[144] postulated, very recently, that the reactions of α-hydroperoxydiazenes take place via oxenoid intermediates (see Section I 5.3, page 58 and Section RD 2.2, page 92). The formation of these oxenoid intermediates requires a base as catalyst. Norbornene should therefore not be epoxidized in the absence of base. When pyridine was added to the reaction of 28b with norbornene, neither the products nor their yields changed. The above results suggest that expoxidation with hydroperoxydiazenes does not need base as a catalyst.

Scheme 16 shows a mechanism involving catalysis by a redox couple (M^+/M^{2+}) such as Cu^+/Cu^{2+}. One electron transfer from cations such as cuprous copper or ferrous iron to α-hydroperoxydiazenes is known,[179] and the complementary reaction of Scheme 16, namely oxidation of carbon-centered radicals to cations, is also well documented.[180] Redox chemistry of the sort shown in Scheme 16 ought to be prevented by a reagent that would render any metal ion impurities inactive. In the present case, addition of EDTA did not affect either the rate of decomposition of 28b or the distribution of products from its reaction with norbornene. Thus the redox mechanism of Scheme 16 is unlikely to be the operating mechanism.

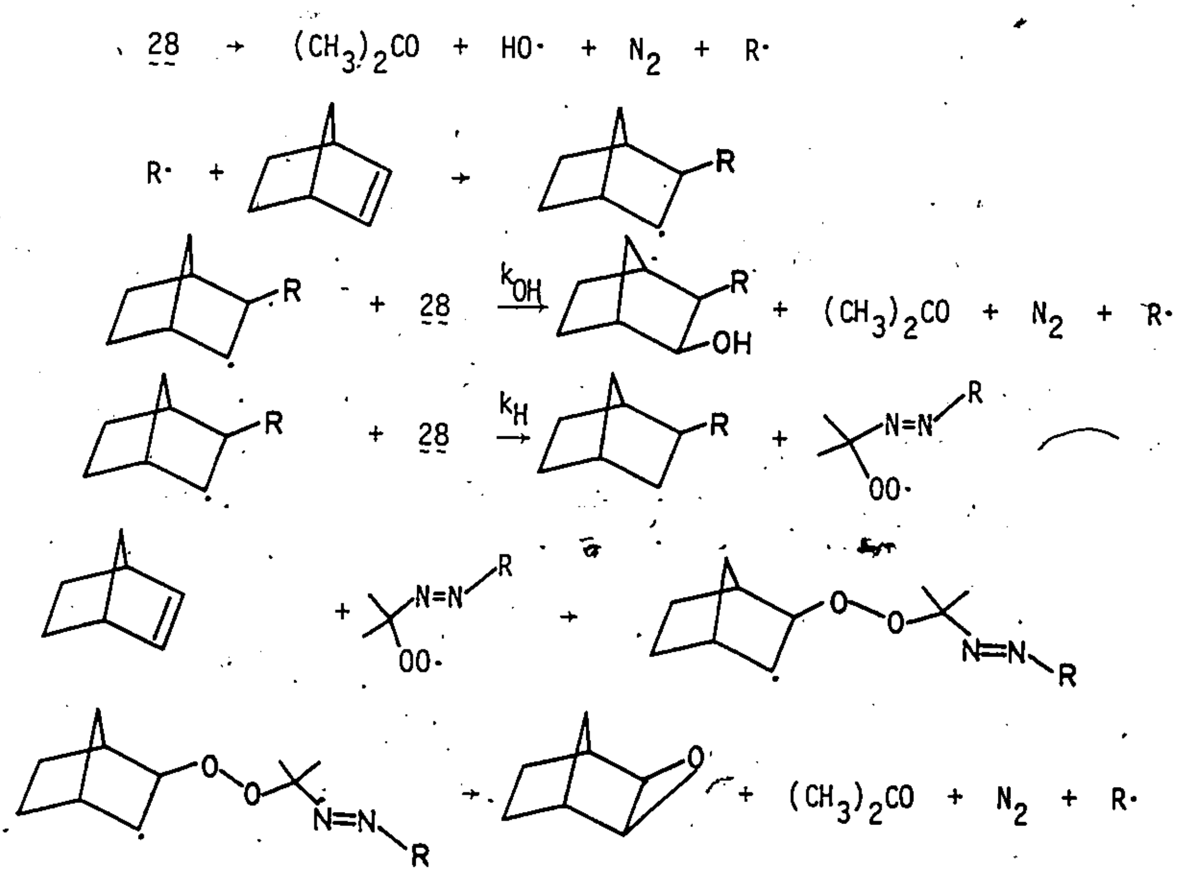
SCHEME 16



All principal products according to Scheme 17 arise from two radical chain processes that have the initiation and the first chain propagating step in common. The chain transfer steps involve abstraction of either OH or H from 28 by the adduct radical formed from R· and norbornene. Abstraction of H leads to a peroxy radical which adds to norbornene to from β-peroxyalkyl radical. Intramolecular induced decomposition of the peroxy function (γ-scission) leads to epoxynorbornane and to the regeneration of R·.

There is ample precedent for the chemistry of Scheme 17. Abstraction of hydroperoxyl hydrogen by radicals is well known,[60e,97-101] as is the addition of peroxy radicals to alkenes.[181] Radicals similar to the β-peroxyalkyl radical in Scheme 17 have been prepared from β-

SCHEME 17

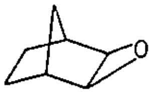
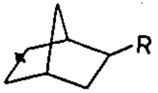
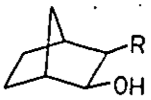


peroxyalkyl bromides and silyl or stannyl radicals. They undergo γ-scission with rate constants near 7×10^5 s^{-1} at 25°C to form oxiranes.[182]

A test for the mechanism in Scheme 17 involved the use of 28 labelled with ^{2}H in the hydroperoxyl (OOH) group. Hydrogen abstraction should be subject to a substantial primary H/D isotope effect while OH abstraction should be insensitive to isotope substitution because the O-H bond is not broken in that process. Labelling of 28 with ^{2}H should therefore alter the product distribution; yields of hydroxyalkylation product should be increased and yields of hydroalkylation product and of epoxide should be reduced. Moreover, the hydroalkylation product (exo-2-alkylnorbornane) should contain deuterium. The results in

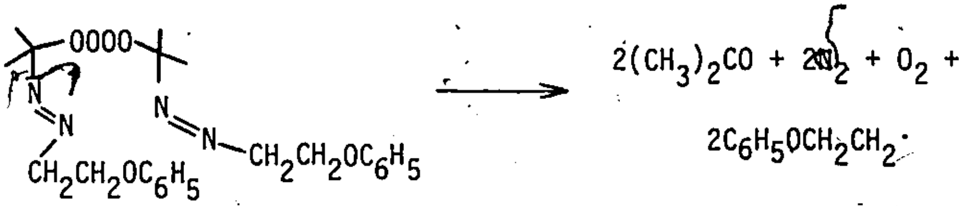
Table 18 are in accord with those expectations. There is a large increase in the yields of the hydroxyalkylation products as a result of using ^{2}H-labelled 28. A substantial reduction in yields of the 2-alkylnorbornanes and of the epoxynorbornane is observed. Mass spectrometric analysis of the 2-alkylnorbornanes showed that only about 50% deuterium incorporation is achieved, suggesting that H-abstraction is not exclusively from the OOH group. A careful search for other products from reaction of 28a-c with norbornene indicated the presence of compounds that could have come from 5-norbornenyl radical or the rearranged radical therefrom, suggesting some abstraction from norbornene. Unfortunately, these by-products were present in quantities too small to allow for their isolation and characterization by NMR.

Table 18: Products and Yields from Reactions of 28 and of ^{2}H-Labelled 28 with Norbornene

R	Peroxy Group			
CH_2CF_3	OOH	60	62	14
	OOD	48	24	29
$CH_2CH_2OCH_3$	OOH	31	64	7
	OOD	22	26	18
$CH_2CH_2OC_6H_5$	OOH	54	70	2
	OOD	36	30	12

A control experiment, in which 28a-c were treated with H_2O instead of D_2O, did not change the product distribution from that obtained with dry 28a-c and norbornene. The effects of deuteriation on the product distribution are therefore not a result of effects of hydration of 28a-c on the various reaction rates. Thus Scheme 17 appears to be the operating mechanism.

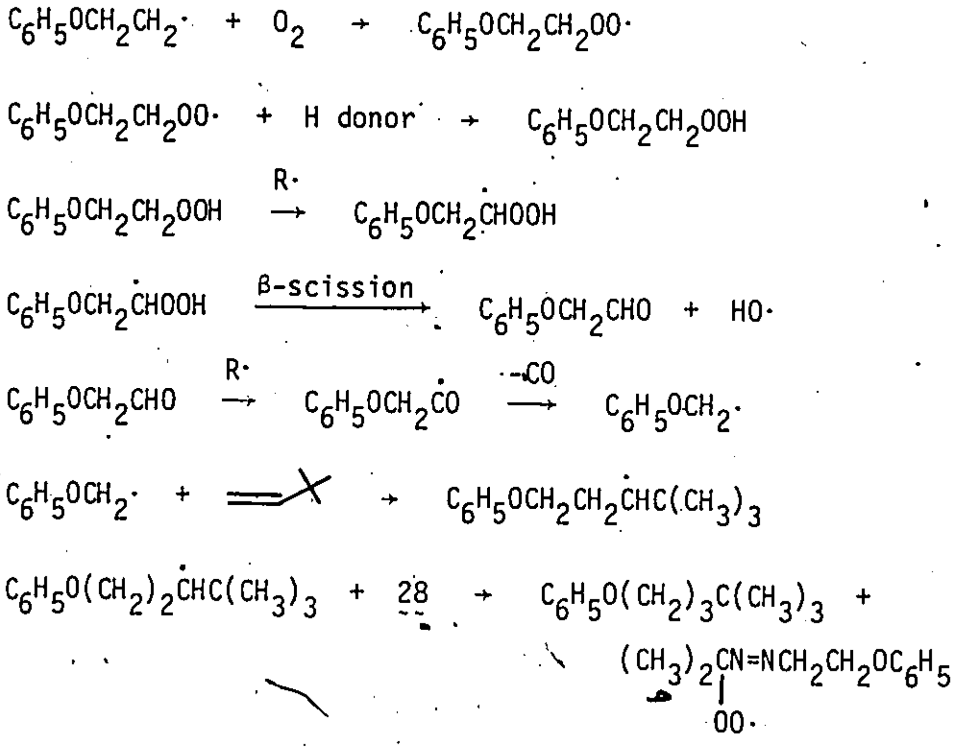
From the foregoing results it appears that steric hindrance at the transition state for reactions of the exo-2-alkyl-1-norbornyl radical determines whether OH or H is abstracted. For a hindered radical the free energy for substitution at oxygen in 28 could be raised, because of non-bonded interactions, to the point where reaction at the more accessible H-atom becomes favoured, in spite of the higher OH bond strength. This means that other hindered alkenes should also give products similar to those from the reactions in norbornene. Thermolysis of 28c in neat 3,3-dimethyl-1-butene afforded hydroalkylation product (2,2-dimethyl-6-phenoxyhexane) in 35% yield but very little of either the epoxide (1.5%) or the hydroxyalkylation product (3-hydroxy-2,2-dimethyl-6-phenoxyhexane, 5% . The very high ratio of hydroalkylation to epoxidation is not expected on the basis of the mechanism in Scheme 17. A tentative explanation is that the peroxy radicals (and β-phenoxyethyl radicals) from 28c add more slowly to 3,3-dimethyl-1-butene than to norbornene and, as a consequence, there is a build-up in concentration of the radicals. Many of them undergo coupling to tetroxide which then decomposes according to eq. R40. In keeping with this post-



[R 40]

ulate was the finding of 2,3-dihydrobenzofuran (2%); phenyl ethyl ether (15%); 2-phenoxyethanol (8%); 2-phenoxyacetaldehyde (0.8%); 2,2-dimethyl-5-phenoxypentane (1%); 2,2-dimethyl-6-phenoxyhexan-3-one (4%); 1,3-diphenoxypropane (2%); and 1,4-diphenoxybutane (3%). 1,3-Diphenoxypropane and 1,4-diphenoxybutane probably arise from termination steps involving radical pair reactions. The presence of carbonyl compounds is supported by absorption bands at 1735 cm^{-1} and 1715 cm^{-1} in the ir spectrum of the reaction mixture. 2,2-Dimethyl-6-phenoxyhexan-3-one, isolated by semi-preparative GC, was identified from the carbonyl band at 1712 cm^{-1} in its ir spectrum. It was also identified from its mass spectrum (m/z 220). Mass spectra of the minor products are provided in Appendix I. A rationale for the carbonyl compounds and 2,2-dimethyl-5-phenoxypentane is given in Scheme 18 and Scheme 19.

SCHEME 18



$C_6H_5OCH_2CH_2\cdot + O_2 \rightarrow C_6H_5OCH_2CH_2OO\cdot$

$C_6H_5OCH_2CH_2OO\cdot + \text{H donor} \rightarrow C_6H_5OCH_2CH_2OOH$

$C_6H_5OCH_2CH_2OOH \xrightarrow{R\cdot} C_6H_5OCH_2\dot{C}HOOH$

$C_6H_5OCH_2\dot{C}HOOH \xrightarrow{\beta\text{-scission}} C_6H_5OCH_2CHO + HO\cdot$

$C_6H_5OCH_2CHO \xrightarrow{R\cdot} C_6H_5OCH_2\dot{C}O \xrightarrow{-CO} C_6H_5OCH_2\cdot$

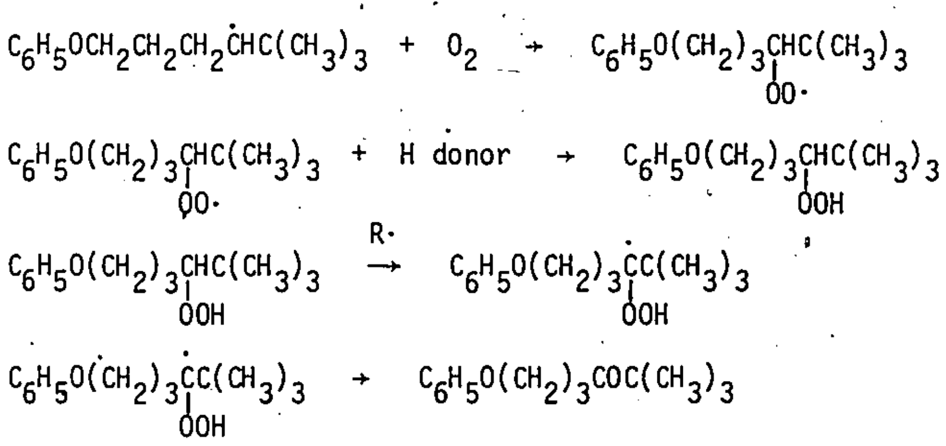
$C_6H_5OCH_2\cdot +$ ═╱ $\rightarrow C_6H_5OCH_2CH_2\dot{C}HC(CH_3)_3$

$C_6H_5O(CH_2)_2\dot{C}HC(CH_3)_3 + \underset{\sim}{28} \rightarrow C_6H_5O(CH_2)_3C(CH_3)_3 + \underset{\displaystyle OO\cdot}{(CH_3)_2\overset{}{C}}N{=}NCH_2CH_2OC_6H_5$

Oxygen from the tetroxide is captured by radicals in solution leading to alkylhydroperoxides. The alkylhydroperoxides are postulated to undergo H abstraction to give α-hydroperoxyalkyl radicals. β-Scission of the α-hydroperoxyalkyl radicals results in carbonyl compounds and hydroxyl radicals. 2-Phenoxyacetaldehyde undergoes further radical reactions similar to those depicted in Scheme 8.

A test for the reaction mechanism for thermolysis of 28 in 3,3-dimethyl-1-butene involved the use of ^{2}H-labelled 28c. Thermolysis of 28c, labelled in the OOH group, in 3,3-dimethyl-1-butene should show a reduction

SCHEME 19



$$C_6H_5OCH_2CH_2CH_2\dot{C}HC(CH_3)_3 + O_2 \rightarrow C_6H_5O(CH_2)_3\underset{OO\cdot}{C}HC(CH_3)_3$$

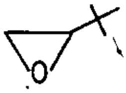
$$C_6H_5O(CH_2)_3\underset{OO\cdot}{C}HC(CH_3)_3 + \text{H donor} \rightarrow C_6H_5O(CH_2)_3\underset{OOH}{C}HC(CH_3)_3$$

$$C_6H_5O(CH_2)_3\underset{OOH}{C}HC(CH_3)_3 \xrightarrow{R\cdot} C_6H_5O(CH_2)_3\underset{OOH}{\dot{C}}C(CH_3)_3$$

$$C_6H_5O(CH_2)_3\underset{OOH}{\dot{C}}C(CH_3)_3 \rightarrow C_6H_5O(CH_2)_3COC(CH_3)_3$$

in the yields of epoxide and of hydroalkylation product and an increase in the yield of the hydroxyalkylation product. Results in Table 19 are in accord with those expectations.

Table 19: Products and Yields from Reactions of **28c** and ^{2}H-Labelled **28c** with 3,3-Dimethyl-1-butene.

Peroxy Group		$C_6H_5O(CH_2)_4C(CH_3)_3$	$C_6H_5O(CH_2)_3\underset{OH}{CH}C(CH_3)_3$
OOH	1.5	35	5
OOD	0.5	20	22

Concluding Remarks. The above results show that the more reactive alkenes which give sterically hindered intermediate radicals react with hydroperoxydiazenes to give hydroalkylation products and epoxides in high yields and hydroxyalkylation products in poor yields. Less reactive and sterically crowded alkenes give high yields of hydroalkylation products but poor yields of epoxide and hydroxyalkylation products.

All the products are shown to arise via free radical mechanisms with H abstraction being a major pathway which leads to formation of α-azoperoxy radicals. In the alkenes that have higher rates for radical additions, the peroxy radicals react to give epoxides whereas in less reactive alkenes the peroxyl radicals form tetroxides that decompose to oxygen and other products. Radicals in solution react with oxygen to give alkyl hydroperoxides. The presence of the alkylhydroperoxides is inferred from products of their decomposition, namely carbonyl compounds and possibly some alcohols.

EXPERIMENTAL

E 1. GENERAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Infrared (ir) spectra ($CDCl_3$ solutions unless otherwise indicated) were obtained on a Perkin-Elmer model 283 spectrophotometer using 0.5 mm KBr cells. Only major and diagnostic bands (transmittance) are reported.

Proton magnetic resonance (pmr) spectra were recorded on either a Varian EM-390, a Bruker WP-80, or a Bruker WM-250 spectrometer. Tetramethylsilane was used as the internal reference unless otherwise specified. Carbon-13 spectra were recorded on the Bruker WP-80 instrument and the internal reference is specified in each case. Fluorine-19 spectra were recorded on a Bruker WH-90 instrument with $CFCl_3$ as the external reference.

Electron spin resonance (esr) spectra were obtained on a Bruker ER100D spectrometer equipped with a TE_{102} rectangular cavity and operating at a normal frequency of 9.6 GHz.

Electron impact mass spectra were recorded on a VG7070 mass spectrometer (VG Micromass, Altricham, U.K.). Samples were introduced via a direct insertion probe system or through a gas chromatographic column via a jet separator. The ion source temperature was 200°C. The spectra were obtained at an accelerating voltage of 4KV and electron energy of 70eV with emission of 100 μA. The spectra were acquired and processed with a VG 2035 data system.

Gas chromatography was performed on a Varian VISTA 6000 gas chromatograph equipped with an off-column flash injector at 220°C and a flame ionization detector (FID) at 300°C. The column (glass, 2.5 m x 2 mm I.D.) was packed with 3% OV-17 (phenyl silicone) on 80/100 mesh Chromosorb W. The column oven temperature was programmed from 40°C to 280°C at 5°/min. The carrier gas was nitrogen at a flow rate of 25 ml/min. The data were acquired and processed with the Varian VISTA 402 chromatographic data system. Semi-preparative GC was performed on a Varian Aerograph A90-P3 instrument equipped with a thermal conductivity detector (TCD) at 300°C and an off-column flash injector at 250°C. The column (1.8 m x 4 mm I.D., steel) was packed with 10% OV-17 on 80/100 mesh Chromosorb W. The carrier gas was helium at a flow rate of 20 ml/min. The chromatograph was operated at column oven temperatures between 40° and 300°C.

Chemicals were purchased from Aldrich Chemical Co. (Milwaukee, Wisconsin), J.T. Baker (Phillipsburg, New Jersey), British Drug House (Poole, England), Matheson (Whitby, Ontario), and Fisher Chemical Co. (Toronto, Ontario). Chromatographic materials were obtained from Chromatographic Specialities (Brockville, Ontario). Solvents were supplied by Caledon (Georgetown, Ontario). The reagents were used without purification unless otherwise noted. Solvents were purified by distillation and stored over molecular sieves.

3,5-Diphenyl-1-methyl-4-nitrosopyrazole (DMNP) was provided by Dr. P.A. Risbood.

<u>p-Toluenesulphonyl Chloride</u>. p-Toluenesulphonyl Chloride was purified using the Pelletier[183] method. Impure (10.0 g, 0.053 mole) p-toluensulphonyl chloride was dissolved in a minimum amount of chloroform (25 ml) and the solution was diluted with 5 volumes of petroleum ether

(bp 30-60°C) to precipitate the impurities. Activated charcoal was added to the solution and the resulting mixture was filtered through a bed of Celite. The solution was concentrated to give pure p-toluenesulphonyl chloride.

E 2. SYNTHESIS

1,1,1-Trifluoro-2-hydrazinoethane. This compound, supplied as a solution in water (70% hydrazine by weight) by Aldrich Chemical Co., was used directly in the next step.

1,1,1-Trifluoro-2-[(1-methylethylidene)hydrazino]ethane. A solution of aqueous 1,1,1-trifluoro-2-hydrazinoethane containing 7.0 g (0.062 mole) of the reagent and 50 mL of ether was added slowly to a solution of acetone (6.0 g, 0.10 mole) in ether (20 ml) with stirring and cooling (10°C). The reactants were kept under nitrogen during the mixing and during a 1-h period of stirring after the addition. The solution was washed three times with 30 mL of water, and the ether layer was dried over $mgSO_4$. Evaporation of the ether and vacuum distillation of the residue gave 7.45 g (78%) of the title hydrazone (bp 28°C, 10 torr) with spectral data listed in Table 10.

2-Methoxyethyl-p-toluenesulphonate.[150] Dry pyridine (48.0 g, 0.6 mole) was added dropwise to a mixture of 2-methoxyethanol (23.0 g, 0.3 mole) and p-toluenesulphonyl chloride (63.0 g, 0.33 mole) at 0-5°C during 2h. Cooling and stirring were continued for another 2h. After acidification with 10% hydrochloric acid solution, the mixture was extracted with 3 x 50 mL of ether. The ether solution was washed with 50 mL of brine and dried with Na_2SO_4. The ether was taken off to give 2-methoxy-p-toluenesulphonate (60.1 g, 87%) as an oil. This was used in the next step without purification.

1-Methoxy-2-hydrazinoethane. 2-Methoxyethyl tosylate (29.5g, 0.13 mole) was added, dropwise, to a vigorously stirred solution of hydrazine hydrate (128.6 g, 2.57 mole) in absolute ethanol (50 ml) at 0-5°C. Addition was complete in 20 min. and stirring was continued thereafter for 2h. After removal of the ethanol with a rotary evaporator, the residue was extracted with 250 mL of ether (continuous extractor) for two days. The ether layer was dried with Na_2SO_4, the ether was evaporated and the residue was distilled under N_2 to give the pure 1-methoxy-2-hydrazinoethane[184] (10.7 g, 91%; bp 146-147.5°C, 760 torr). See Table 9 for spectral data.

1-Methoxy-2-[(1-methylethylidene)hydrazino]ethane. Acetone (10 ml) was added slowly and with stirring to 1-methoxy-2-hydrazinoethane (9.0 g, 0.10 mole) in 20 ml of dry benzene. The resulting solution was refluxed for 20 min, cooled, and washed with 30 mL of water and with 30 mL of brine before it was dried over Na_2SO_4. The benzene was evaporated and the residue was distilled to give the title hydrazone: 6.0 g (46%); bp 31°C, 6 torr; ^1H NMR data in Table 10.

1-Phenoxy-2-hydrazinoethane. 1-Bromo-2-phenoxyethane (40 g, 0.20 mole) in ethanol was dropped, during 20 min., into a solution of hydrazine hydrate (150 g, 3.0 mole) in ethanol (50 ml) at 20°C. The resulting solution was stirred for 1h at 20°C and for 1.5h at 40°C before the ethanol was removed on a rotary evaporator. The residue was extracted continuously with 250 mL of ether for 48h. The ether solution was dried and the ether was evaporated to give 28.9 g (95%) of the desired hydrazine which was used without purification in the next step. ^{1}H NMR data are given in Table 9.

<u>1-Phenoxy-2-[(1-methylethylidene)hydrazino]ethane</u>. Condensation of 1-phenoxy-2-hydrazinoethane (28.9 g, 0.19 mole) with acetone (50 mL) by following procedures analogous to that described for 1-methoxy-2-[(1-methylethylidene)hydrazino]ethane (page 142) gave 34.6 g (90%) of the title compound (Table 10) by 124-126°C (2.5 torr).

<u>2-Methyl-2-hydrazinopropane</u>. Tert-butylhydrazine hydrochloride (12.5 g, 0.1 mole) was added in small batches to aqueous potassium hydroxide (16.9, 0.30 mole) solution (60 mL H_2O) at 0°C. The resulting solution was extractd continuously for 36h with 250 mL of ether. The ether solution was dried with $MgSO_4$ and the ether was removed to give the title compound (8.2 g, 92%) as a light green liquid. The compound was used in the next step without purification.

<u>2-Methyl-2-[(1-methylethylidene)hydrazino]propane</u>. 2-Methyl-2-hydrazinopropane (8.2 g, 0.09 mole) was condensed with acetone (50 mL, 0.8 mole) by following procedures analogous to those described above for 1-methoxy-2-[1-methylethylidene)hydrazino]ethane (page 142) to give 10.3 g (87%) of the title compound (bp 87-90°C, 50 torr).

<u>[1-Methylethylidene]hydrazinobenzene</u>. Phenylhydrazine (10.8 g, 0.1 mole) was condensed with acetone (50 mL, 0.8 mole) to give 14.0 g (93%) of the pure title hydrazone (bp 101°C, 2 torr).

<u>2-Hydrazinopropane</u>. 2-Bromopropane (25 g, 0.20 mole) in 25 mL ethanol was added dropwise to hydrazine hydrate (50 g, 1 mole) in 50 mL ethanol. The solution was stirred at 15° during addition. The homogeneous solution was kept in the refrigerator at 0°C for 5 days after which it was heated at 40°C for 1h. The ethanal was removed and the residue

was extracted continuously for 2 days with 300 mL of ether. The ether solution was dried with $MgSO_4$ and the ether was taken off to give the title hydrazine (10.5 g, 71%). ^{1}H NMR data are given in Table 9. The compound was used in the next step without purification.

2-[(1-Methylethylidene)hydrazino]propane. 2-Hydrazinopropane (10.5 g, 0.14 mole) was condensed with acetone (50 mL) to give 11.2 g (60%) of the required hydrazone (bp 67°C, 63 torr).

Benzylhydrazine. Benzylchloride (21.9 g, 0.17 mole) in 25 mL ethanol was dropped, during 20 min, into a solution of hydrazine hydrate (89.27 g, 1.7 moles) in 50 mL of ethanol at 20°C. The resulting solution was stirred for 1 h at 20°C and for 1 h at 40°C. The ethanol was removed on a rotary evaporator and the residue was extracted continuously with 300 mL of ether for 3 days. The ether solution was dried and the ether was evaporated to give 20.45 g (97%) of the benzylhydrazine which was used in the next step without purification. ^{1}H NMR data are given in Table 9.

Phenyl-[(1-methylethylidene)hydrazino]methane. Benzylhydrazine (20.45 g, 0.17 mole) in ether (25 mL) was added slowly to a solution of acetone (20 mL, 0.32 mole) in 50 mL of ether with stirring and cooling (15°C). Acetic acid (3 drops) was added at the start of the reaction. The solution was stirred for 1 h before the ether layer was washed two times with 50 mL of water and once with brine (60 mL). It was then dried over $MgSO_4$. Evaporation of the ether and distillation of the residue gave 23.1 g (85%) of the title hydrazone (bp 109°C, 6 torr).

Autoxidation of Hydrazones to α-Hydroperoxydiazenes. The hydrazones described above autoxidized spontaneously as solutions in petroleum ether (bp 30-60°C) or in benzene. Undistilled hydrazones did not autoxidize reliably, in some cases absorbing O_2 only after induction period of several hours. Samples autoxidized at one time ranged from about 5 to 30 mmol. The following procedure for 1,1,1-trifluoro-2-[(1-methylethylidene)hydrazino]ethane is typical.

1,1,1-Trifluoro-2-[(1-methylethylidene)hydrazino]ethane (1.0 g, 6.4 mmol) in 50 mL petroleum ether (bp 30-60°C) was exposed to oxygen from a gas burette. Uptake of O_2 was spontaneous. When the gas volume remained constant for 4 h or more, indicating completion of the oxidation, an aliquot containing about 15 mg of product was removed and the petroleum ether was taken off either with a rotary evaporator, with rotating bulb in cold water, or with a stream of N_2 directed onto the surface of the solution in a flask cooled in a cold water bath. The ^{1}H NMR spectrum of the product (Table 11) had no signals of the E- and Z-methyl groups of the starting hydrazone indicating that autoxidation was complete.

The yields of the resulting hydroperoxydiazenes, determined by iodometric titration (vide infra), ranged from 76% to 95%. These yields are probably due to slow decomposition of the products during autoxidation.

E 3. THERMOLYSIS

E 3.1 <u>Thermolysis of Hydroperoxydiazenes in Unsaturated Substrates</u>. In a typical procedure, a hydroperoxydiazene sample ranging from about 15 mg to 0.7 g in weight was obtained by one of the solvent removal procedures described above. The desired olefin or enol ether (neat, about 0.5 mL/25 mg of hydroperoxydiazene) was then added and the resulting solution was transferred to a glass tube for degassing and sealing. Norbornene

In the case of norbornene, thermolysis was carried out in 3M solution of alkene in benzene since it is a solid at room temperature. Thermolysis in the presence of EDTA was carried out in a glass tube pretreated with 0.3M EDTA in water and by adding 15 mg EDTA to the reaction mixture. Similarly thermolysis of the α-hydroperoxydiazenes in norbornene solution in the presence of pyridine was carried out by adding 2-3 drops of pyridine to the reaction mixture.

For the larger scale runs, several samples of hydroperoxydiazene in alkene were combined before the degassing step. Sealed tubes were heated at 50°C in an oil bath for 10-24 h before they were opened for analysis. Products were analysed by GC/FID, GC/MS, and NMR. The products were quantitated by the internal standard method using GC/FID. Exo-isoborneol was used as the internal standard for products from norbornene reactions and p-methylacetophenone and 2-hexanol were used in reactions that produced carbonyl compounds and alcohols, respectively. NMR analysis involved isolation of products by semipreparative GC followed by NMR spectra acquisition. For spectral data of products see Tables 12, 13 and 14 (pages 76-82).

E 3.2 Kinetics

Rate constants for the unimolecular decomposition of the hydroperoxydiazenes were determined by following the disappearance of the gem dimethyl signal or the appearance of the acetone signal in the ^1H NMR spectra, or by iodometric titration of the remaining hydroperoxydiazene. The overall (observed) rate constant for the reaction of the hydroperoxydiazenes with enol ethers was determined by following the appearance of the acetone signal in the ^1H NMR spectra. Details of the data treatment are given in Appendix II.

NMR Method. The rate constants for unimolecular decomposition of the hydroperoxydiazenes were determined in benzene and, for a limited number, in ethyl (or methyl) vinyl ether. A sample of hydroperoxydiazene was freed from its solvent using one of the methods described above. This was then dissolved in benzene or enol ether containing 2,2,6,6-tetramethylpiperidine-N-oxyl (TMPO, 0.015-0.025M) to make a solution of 0.06-0.08M in hydroperoxydiazene. The enol ether solutions contained CH_2Cl_2 as internal standard. The solution was transferred to an NMR tube joined to a glass adaptor and it was degassed three times, using the freeze-pump-thaw cycles at a pressure of about 5 millitorr, and sealed. The tubes were heated at 50°C in an oil bath, and they were removed at time intervals and chilled immediately for analysis by ^1H NMR spectroscopy. ^1H NMR spectra were acquired with the Varian EM 390 spectrometer operating at a probe temperature of 35°C. The decompositions were followed for 10-13 h. These translate into half of one half-life. In benzene the decrease in intensity of the gem dimethyl signal of the starting hydroperoxydiazene was monitored and the sum of the heights of the acetone and gem dimethyl signals was used as the internal standard. This method involves the assumption that the sum of these two signals remained constant. In the enol ethers, the increase in the intensity of the acetone signal was monitored and the height of the dichloromethane signal was used as the internal standard. The rate constants for unimolecular decomposition were obtained by plotting $\ln A_t - \ln A_o$ vs time, where $A = \frac{H_{acetone} + H_{hydroper}}{H_{hydroper}}$, $H_{acetone}$ and $H_{hydroper}$ are the peak heights of acetone and of hydroperoxydiazene gem dimethyl signals respectively. Appendix II contains the raw data that were plotted and

Figures 14 and 15 (See pages 115 and 116) have the representative plots. The plots have correlation coefficients of between 0.9994 and 0.9997.

The observed rate constant for the decomposition of the compounds in the enol ethers was determined by ^1H NMR spectroscopy with no added TMPO. The increase in the intensity of the acetone signal was monitored and the height of the CH_2Cl_2 signal was used as the internal standard. The rate constants were obtained from the slope of the plot of $[(H_{acetone})/(H_{CH_2Cl_2})]^{\frac{1}{2}}$. Representative plots are given in Figure 11 (page 103). In this method as in that for the unimolecular decomposition, it is assumed that the ratios of the signal heights are proportional to the fraction of hydroperoxydiazene that has decomposed at the time of analysis.

Iodometric Titrimetry. The iodometric method[157] was used to determine the rate constant for unimolecular decomposition of hydroperoxydiazene in the presence of norbornene.

A stock solution of the hydroperoxydiazene in benzene (0.05M) containing norbornene (0.3M or 3.0M) and TMPO (0.03M) was prepared using the method described above. Aliquots (1.0 mL) of the solution were transferred into glass tubes which were degassed and sealed, vide supra. The tubes were heated at 50°C in an oil bath and they were removed one at a time at 1 h intervals. They were quenched in liquid nitrogen and opened. The sample was transferred into a cold, glass-stoppered Erlenmeyer flask (12 [illegible] Cold methanol (4 mL) and Dry Ice (ca. 0.1 g) were added and the [illegible] swirled to displace O_2 with CO_2. Freshly-prepared aqueous KI solution (saturated, 1 mL) and glacial acetic acid (15 mL) containing $FeCl_3$ (ca. 0.002%) were added. The flask was stoppered after making sure that no Dry Ice remained and it was placed in the dark for 10 minutes. Water (50 mL) was added and the resulting solution was titrated with 0.01N (5×10^{-3}M) sodium thiosulfate to the starch end point. A blank titration was performed on a sample that was allowed to go to complete thermolysis. The volume of titrant from this was subtracted from all the other volumes.

E 3.3 Spin Trapping

About 0.5 mL of between 0.1M and 0.2M solution of hydroperoxydiazene in benzene containing 3,5-diphenyl-1-methyl-4-nitroso pyrazole (DMNP, 0.1M) was placed in an NMR tube joined to a glass adaptor. The sample was degassed, using the freeze-pump-thaw cycles, and sealed, vide supra. ESR signals of the spin adducts from reaction between free radicals produced by unimolecular decomposition of the hydroperoxydiazene and the nitroso pyrazole were recorded at ambient temperature on the Bruker ER100D spectrometer.

Spin trapping in ethyl vinyl ether using 1×10^{-3}M DMNP was achieved in the same manner as described above.

E 3.4 Infrared Studies

Infrared spectra of 1-phenoxy-2-[(hydroperoxy-1-methylethyl)azo]-ethane in CCl_4, using a cell of 0.5 mm path length, were obtained at concentrations ranging between 0.086M and 0.68M. The spectra (see Fig. 3, page 71) showed a broad band between 3600 cm^{-1} and 3200 cm^{-1}. The band is observed to contain other bands which decrease in intensity at different rates with decreasing concentration of the hydroperoxydiazene.

APPENDIX I. SPECTRA OF MINOR PRODUCTS

Many of the compounds produced in the small-scale reactions of α-hydroperoxydiazenes with olefinic substrates, although mechanistically important, were present in quantities too small for their isolation and characterization by NMR spectroscopy. Analyses of the reaction mixtures containing these compounds, by GC/MS, afforded their mass spectra from which structure assignments, in some cases tentative, were made. Presented in this Appendix are the mass spectra of these minor but important by-products.

Bis-2,3-dihydrofuran (or two possible isomers) (Fig. A5) which does not give a molecular ion but the M/2 ion and ions therefrom at electron energy of 70eV was identified from its GC retention time.

The compound in Fig. A4 was assigned as 2-(2-phenoxyethyl)-2,3-dihydrofuran or its 3-isomer from the fragmentation pattern. The ion appearing at m/z 69 is assigned to the 2,3-dihydrofuranyl cation which can arise from elimination of the 2-phenoxyethyl group from the molecular ion.

The probable assignments for major peaks are shown in the mass spectra of all the compounds.

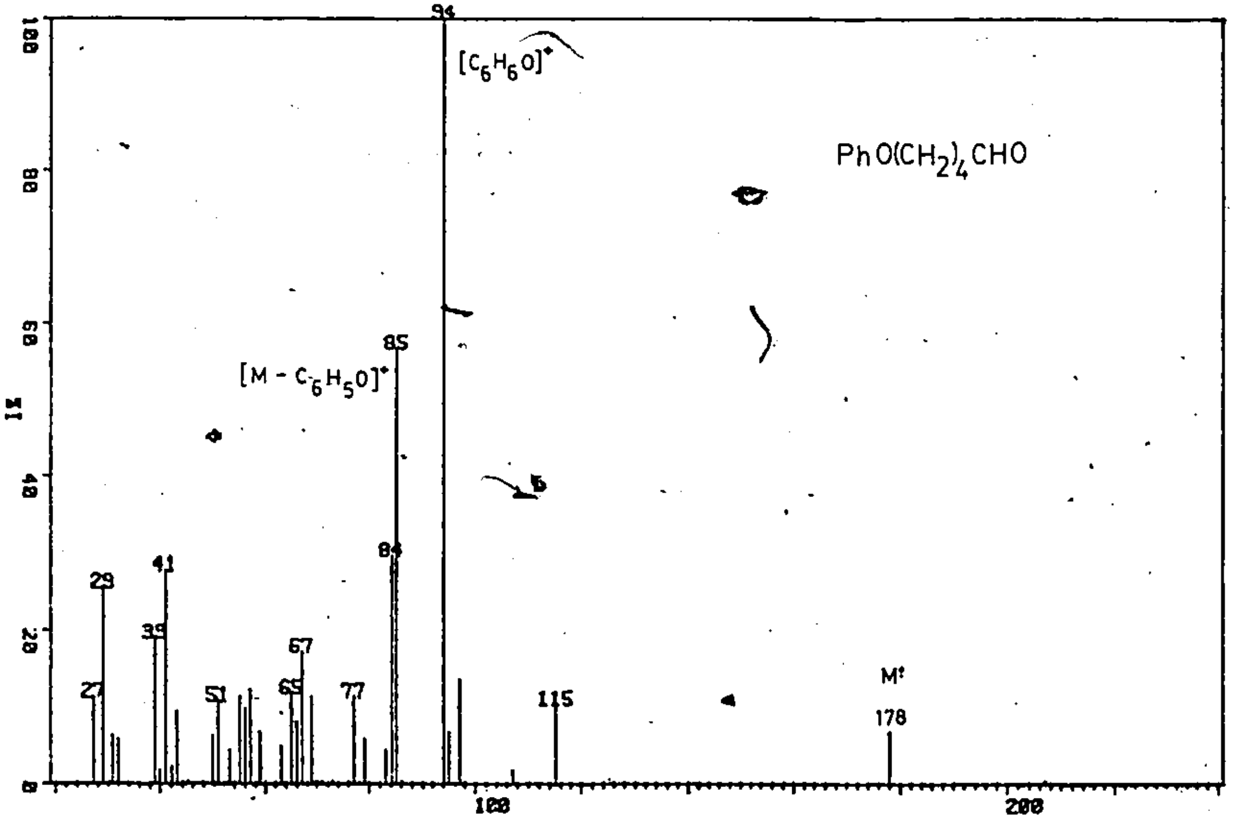


Fig. A1: Mass Spectrum of 3-Ethoxy-6-phenoxyhexanal

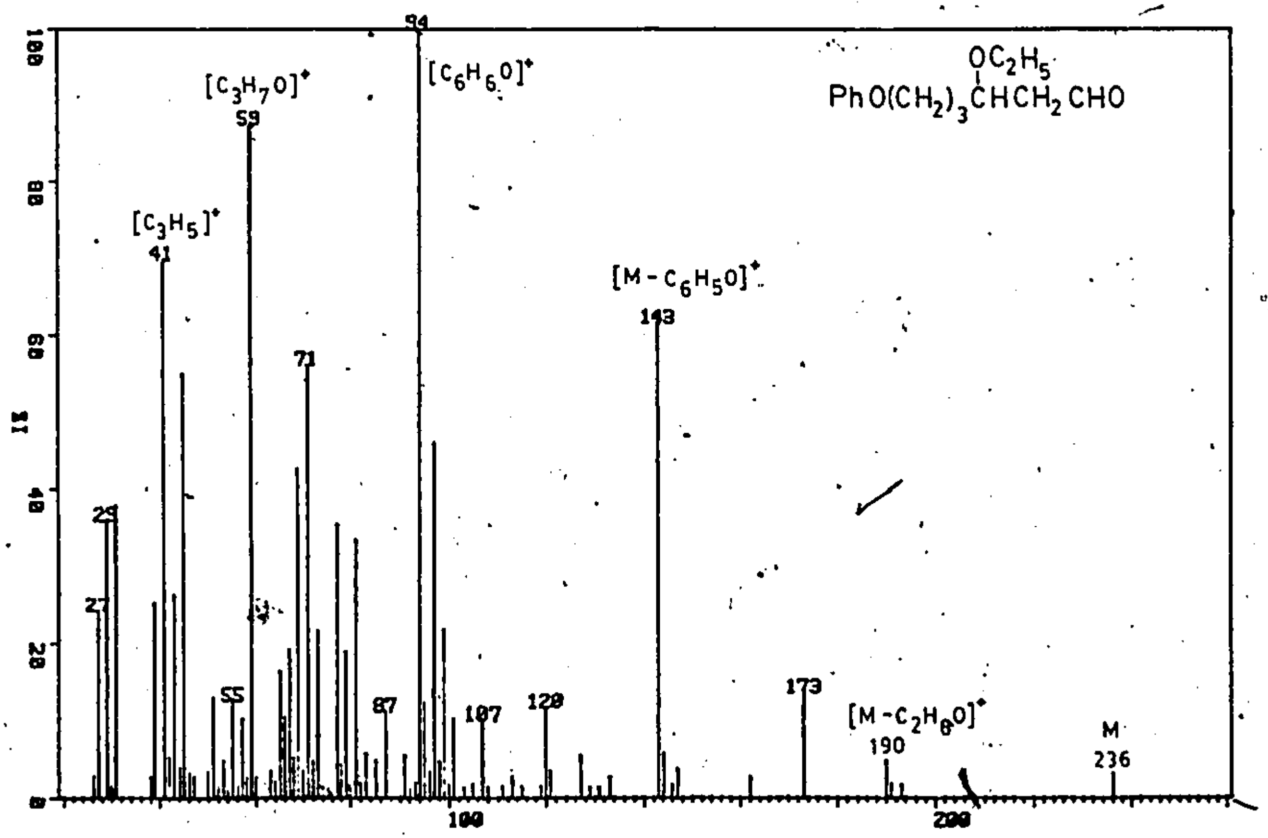


Fig. A2: Mass Spectrum of 3-Ethoxy-6-phenoxyhexanal

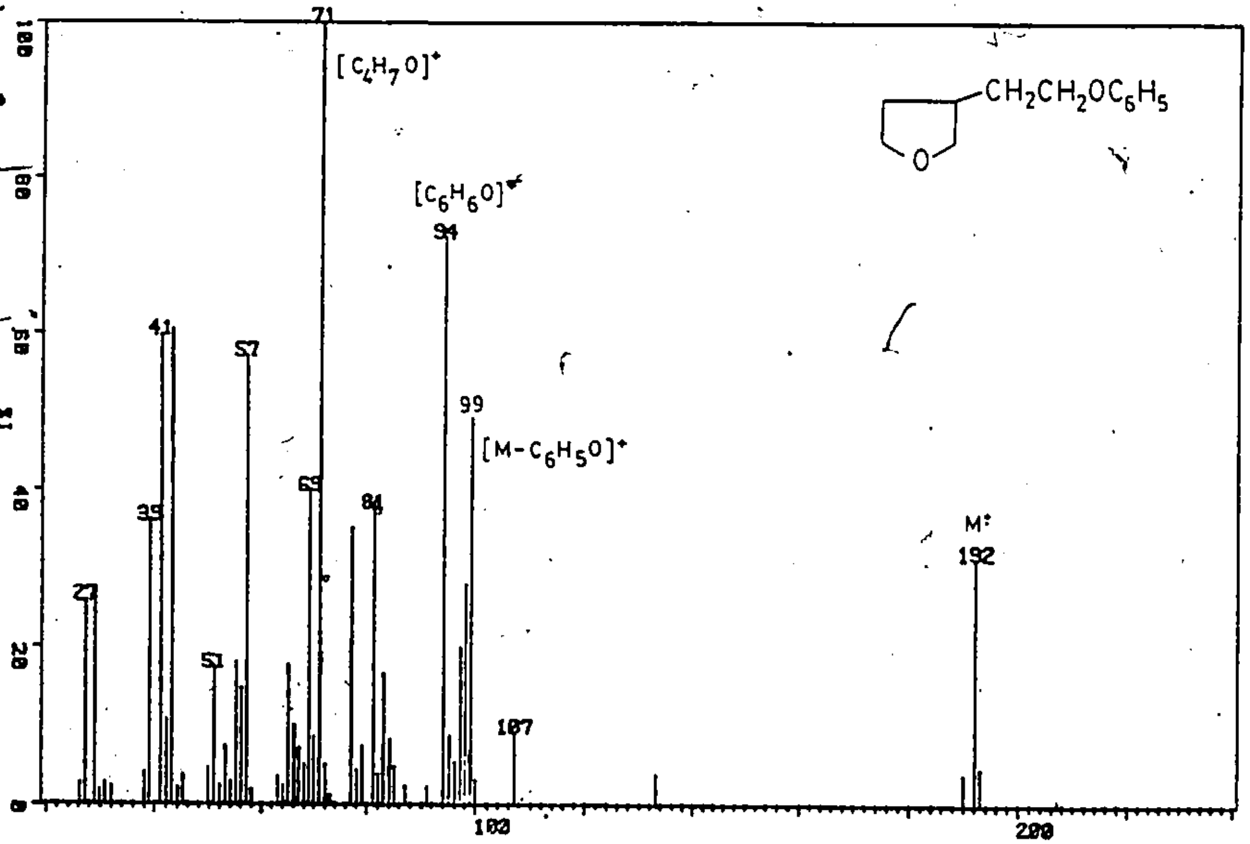


Fig. A3: Mass Spectrum of 3-(2-Phenoxyethyl)tetrahydrofuran

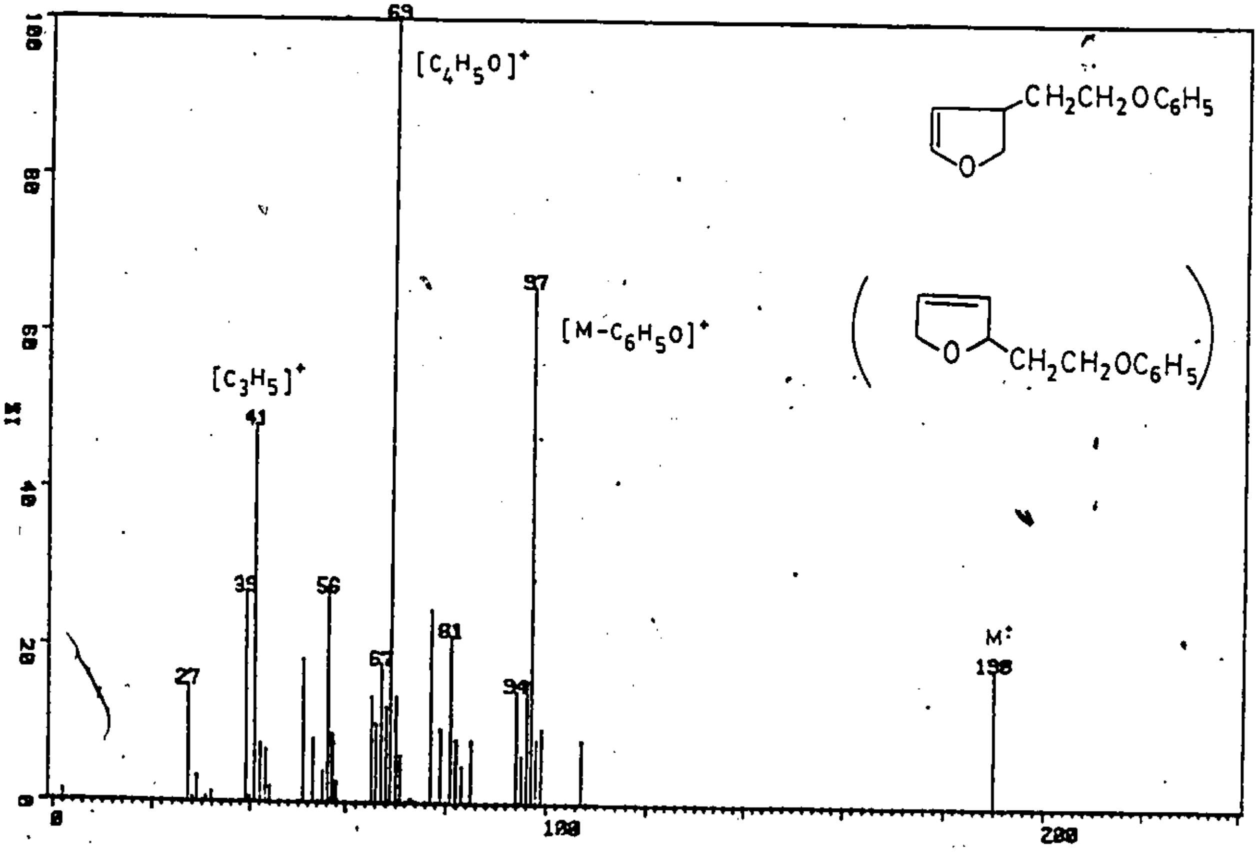


Fig. A4: Mass Spectrum of 2-(2-Phenoxyethyl)-2,3-dihydrofuran or its 3-isomer.

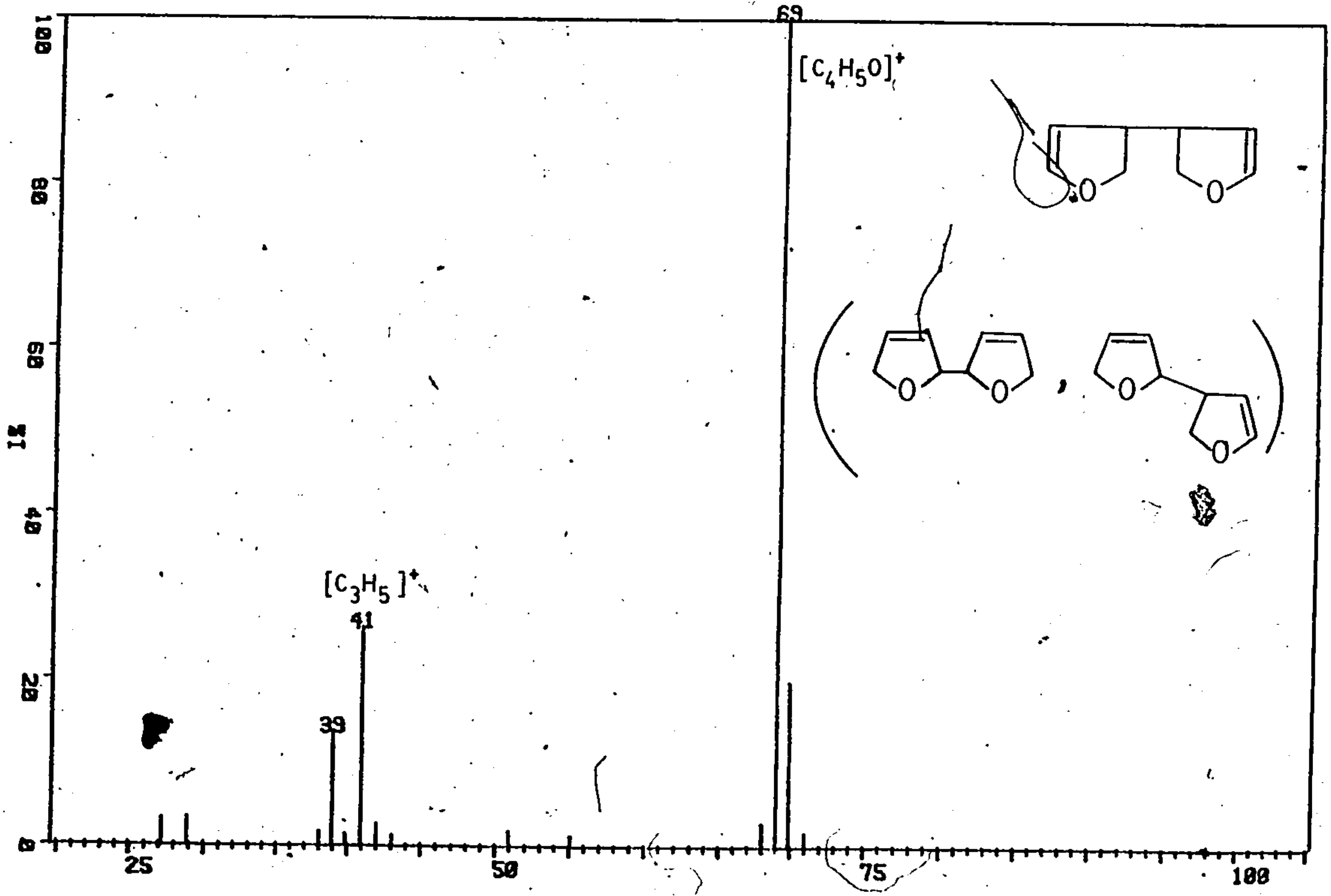


Fig. A5: Mass Spectrum of 3-Bis-2,3-dihydrofuran or isomers.

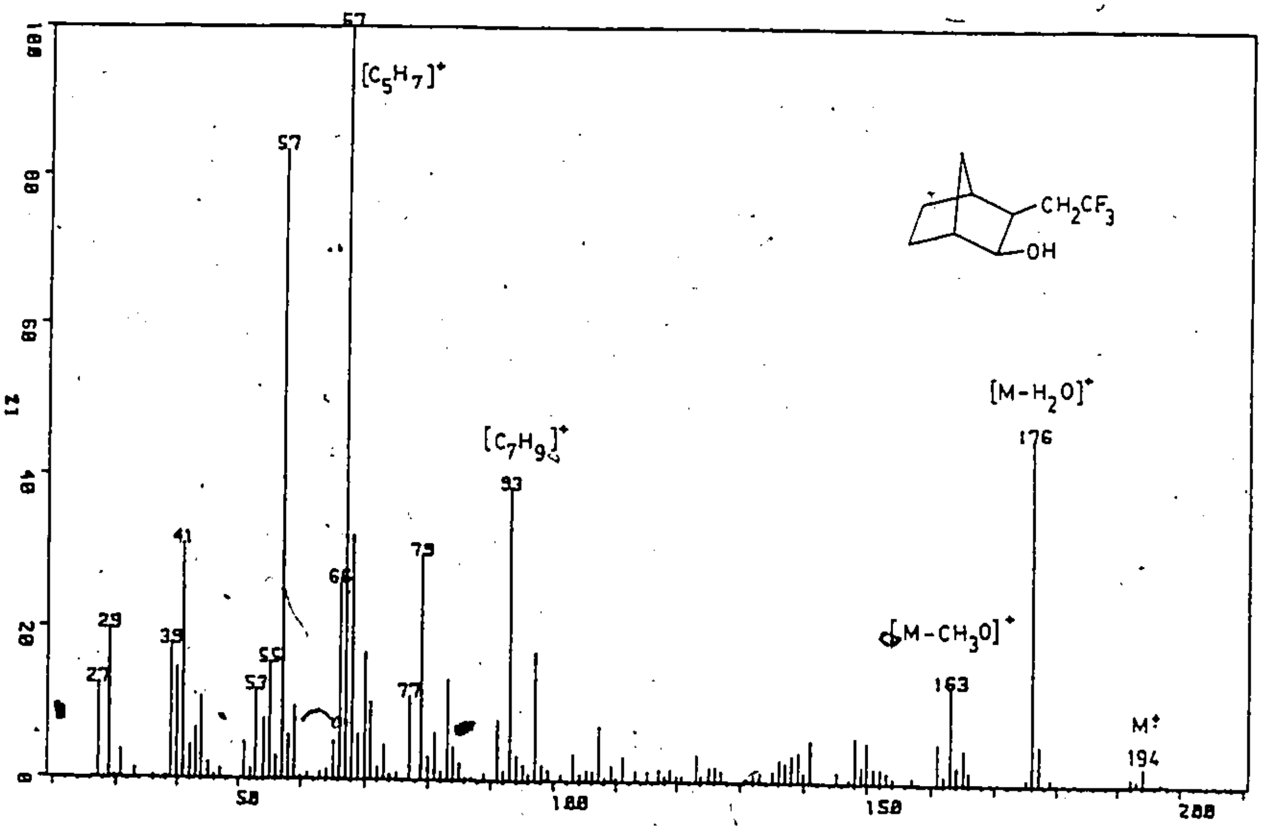


Fig. A6: Mass Spectrum of 2-Hydroxy-3-(2,2,2-trifluoroethyl)norbornane

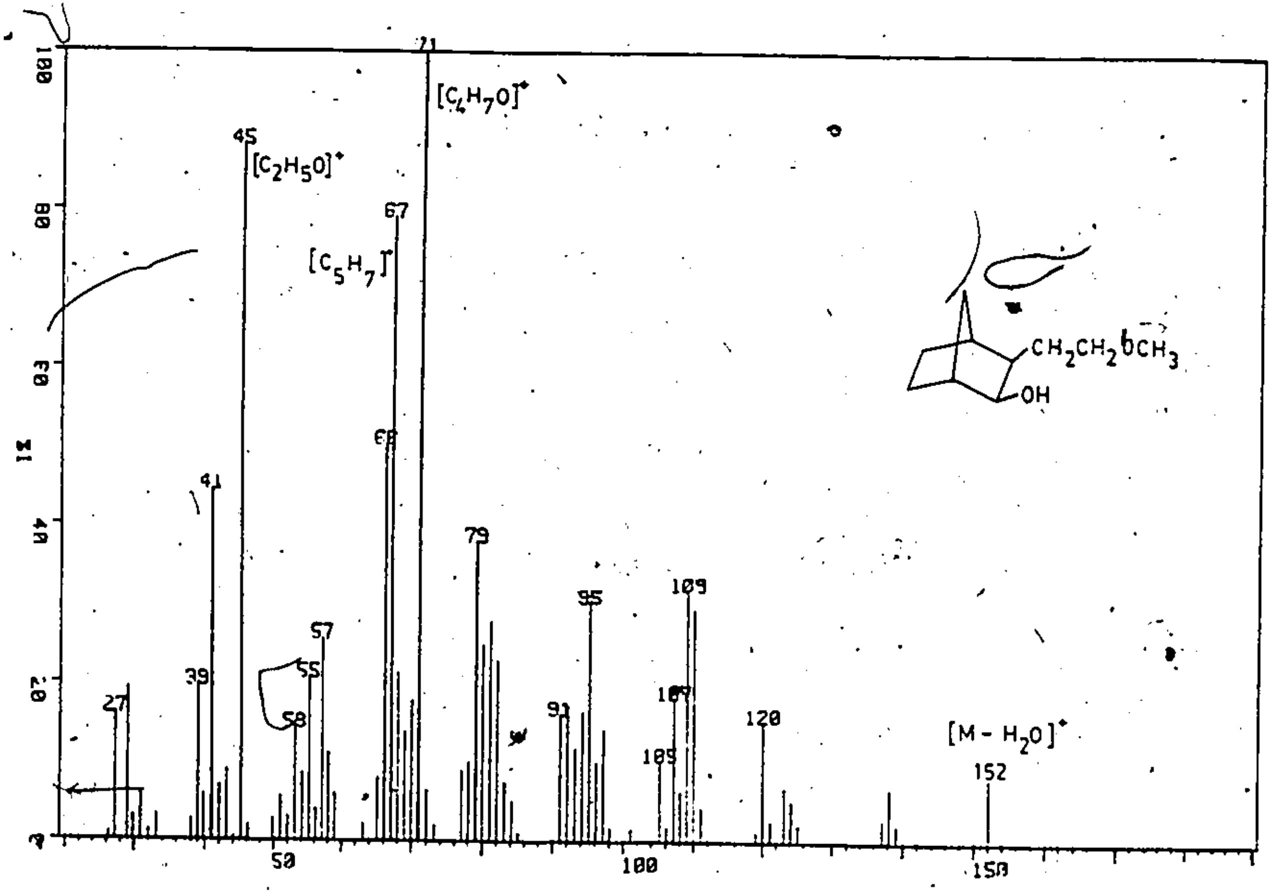


Fig. A7: Mass Spectrum of 2-Hydroxy-3-(2-methoxyethyl)-norbornane

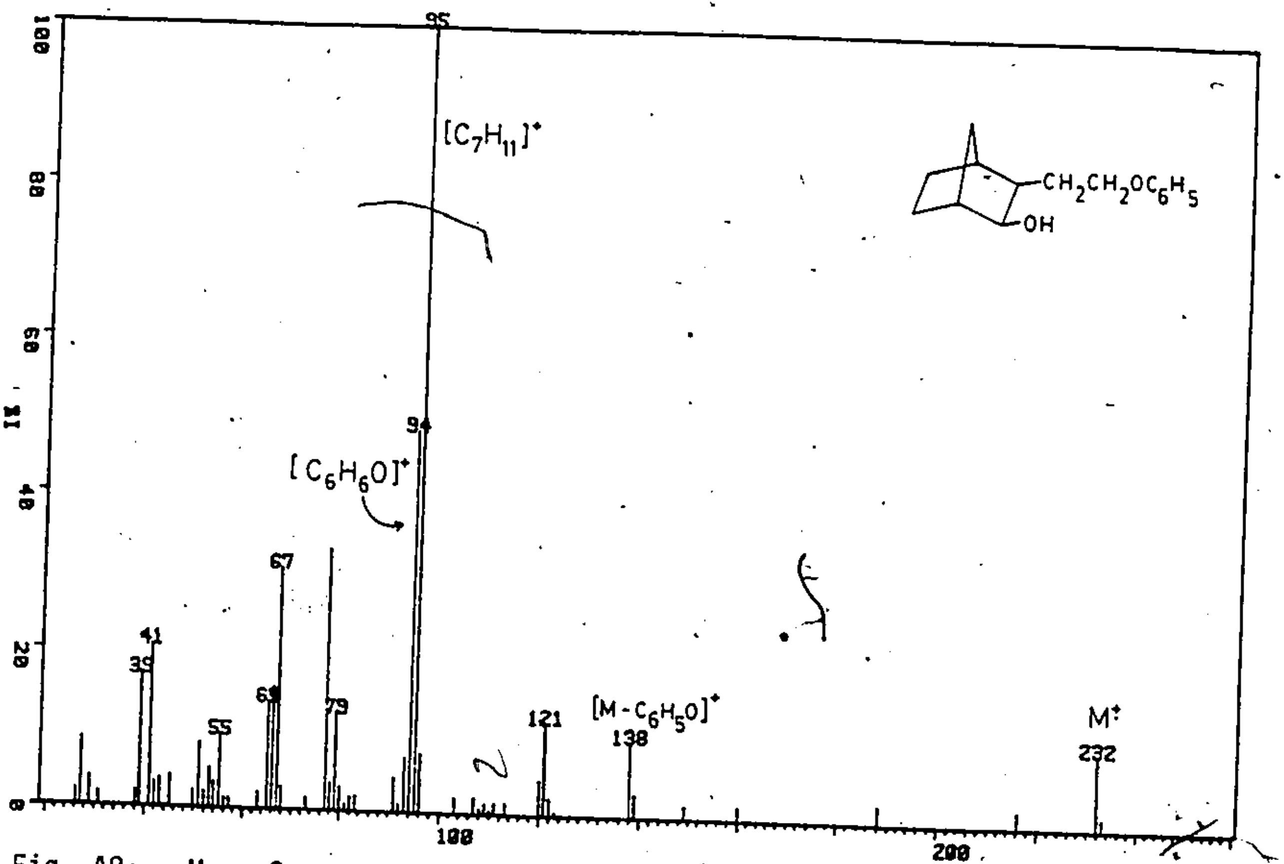


Fig. A8: Mass Spectrum of 2-Hydroxy-3-(2-phenoxyethyl)norbornane

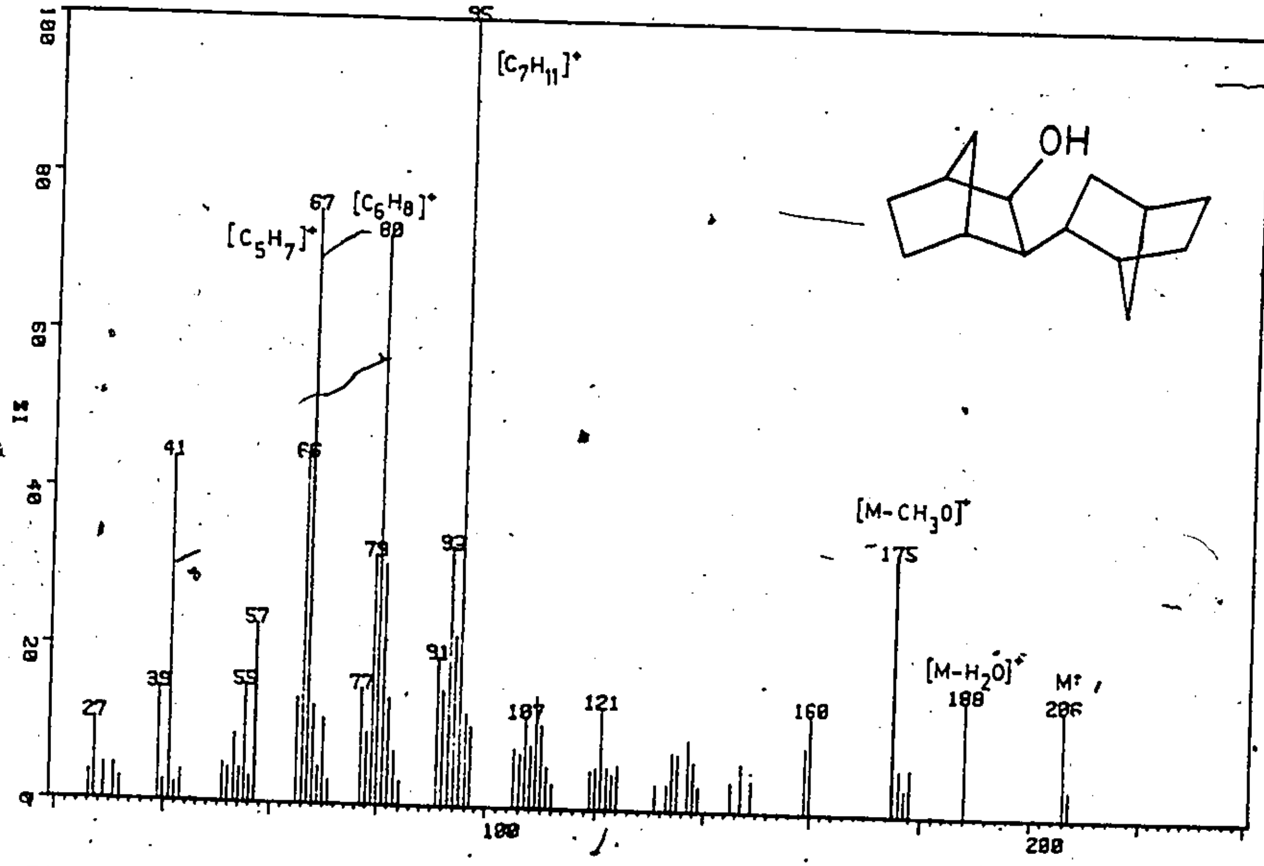


Fig. A9: Mass Spectrum of 2-Hydroxy-3-(2-norbonyl)norbornane

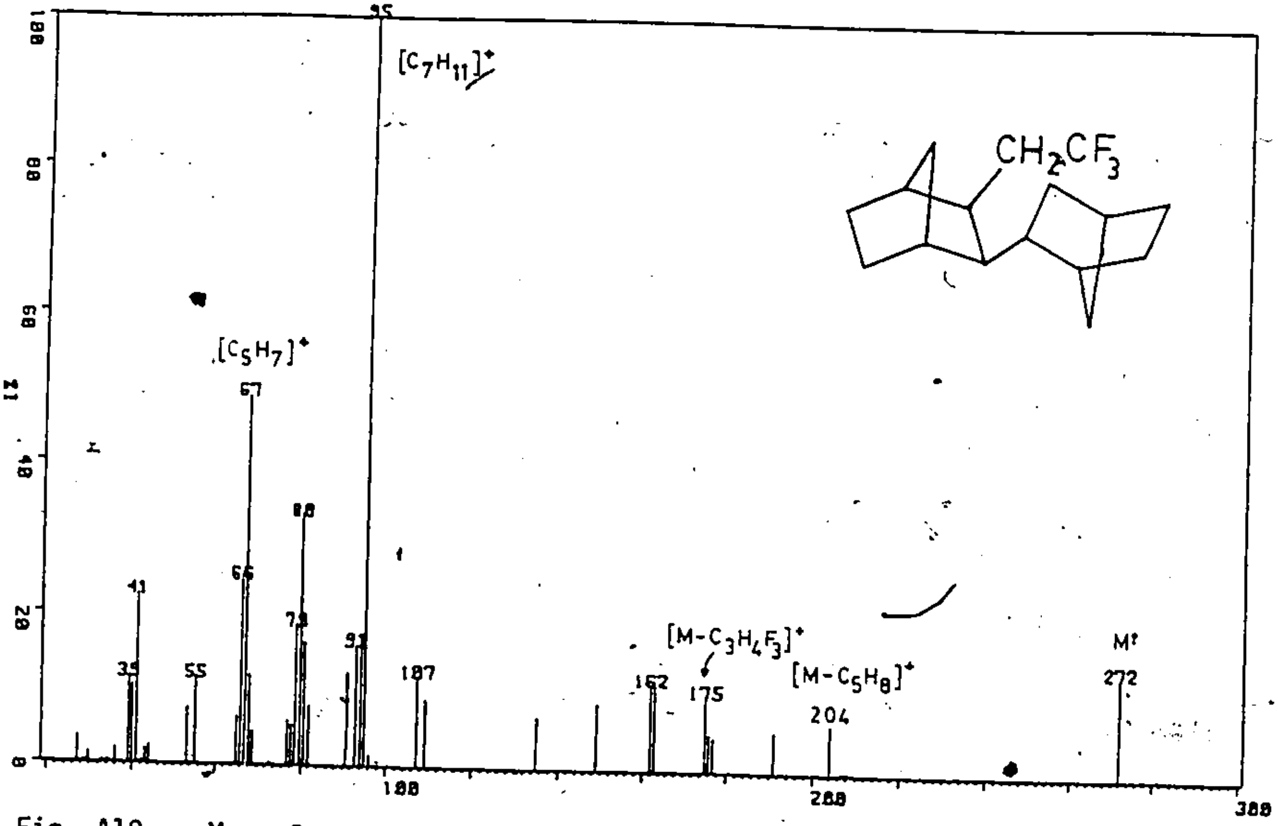


Fig. A10: Mass Spectrum of 2-(2,2,2-Trifluoroethyl)-3-(2-norbornyl)norbornane

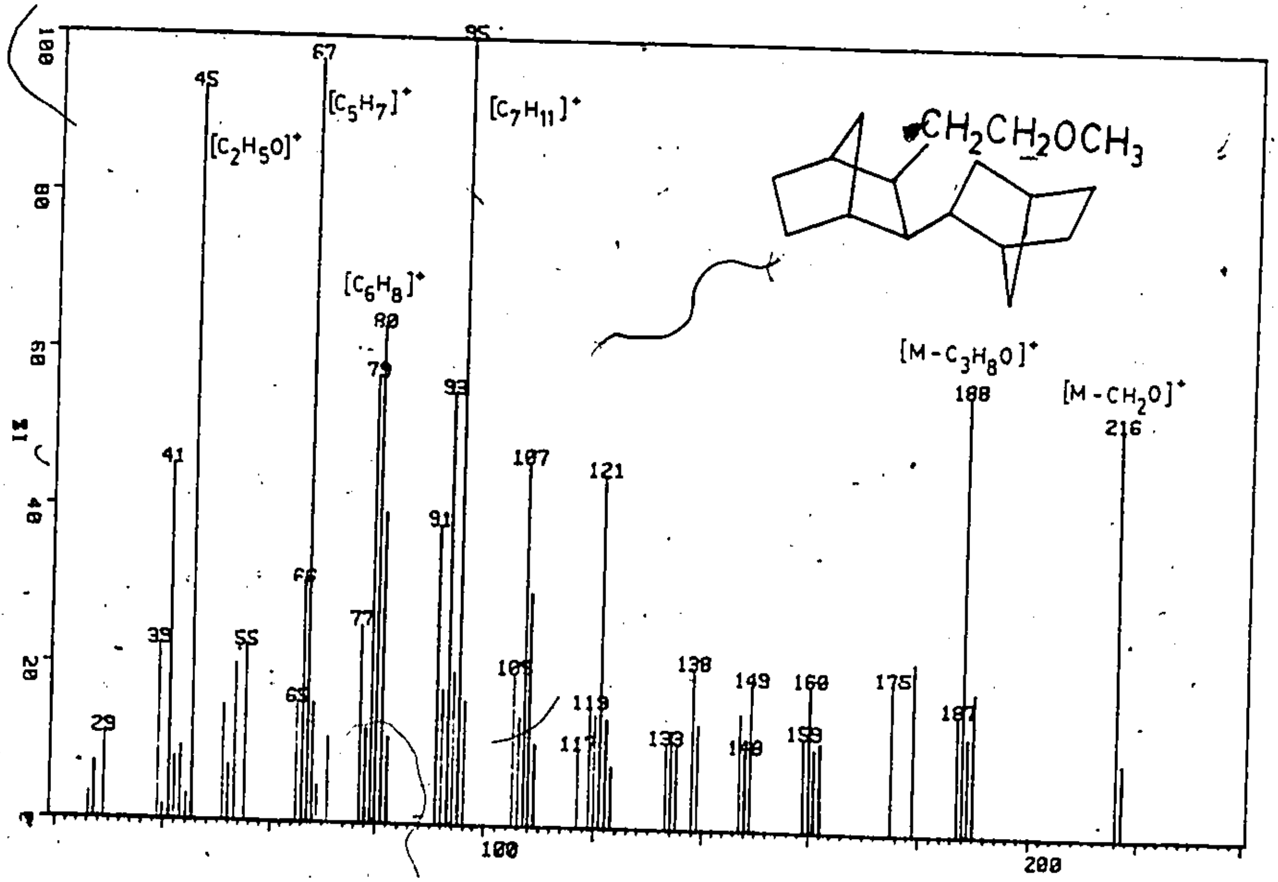


Fig. A11: Mass Spectrum of 2-(2-Methoxyethyl)-3-(2-norbornyl)norbornane

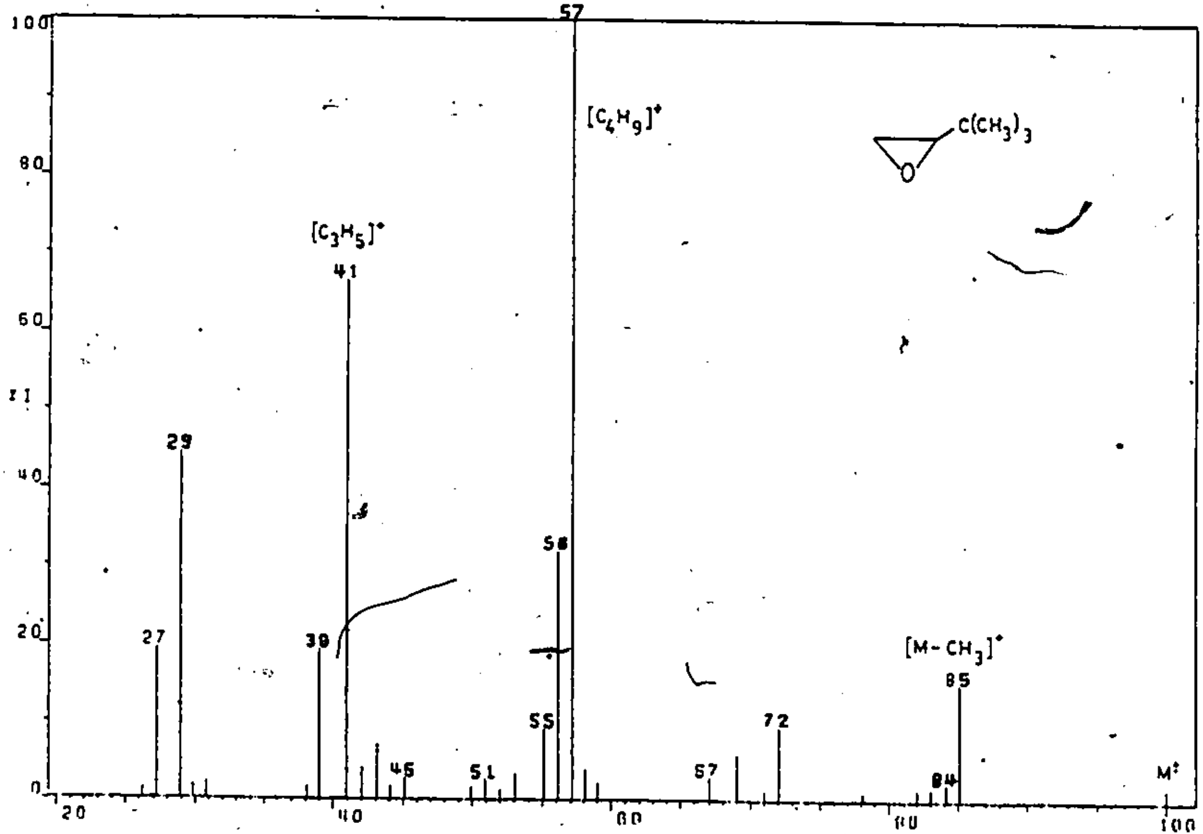


Fig. A12: Mass Spectrum of t-Butylethylene Oxide

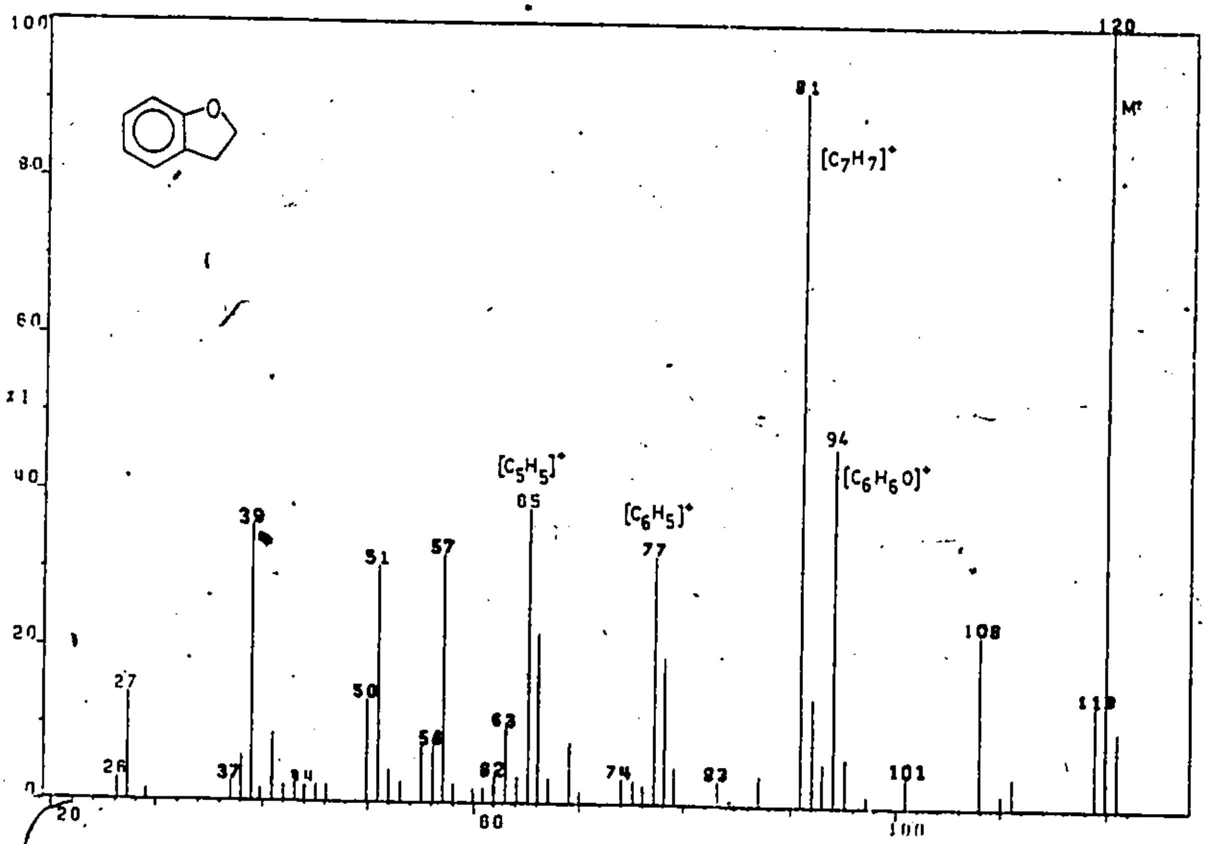


Fig. A13: Mass Spectrum of 2,3-Dihydro-4,5-benzofuran

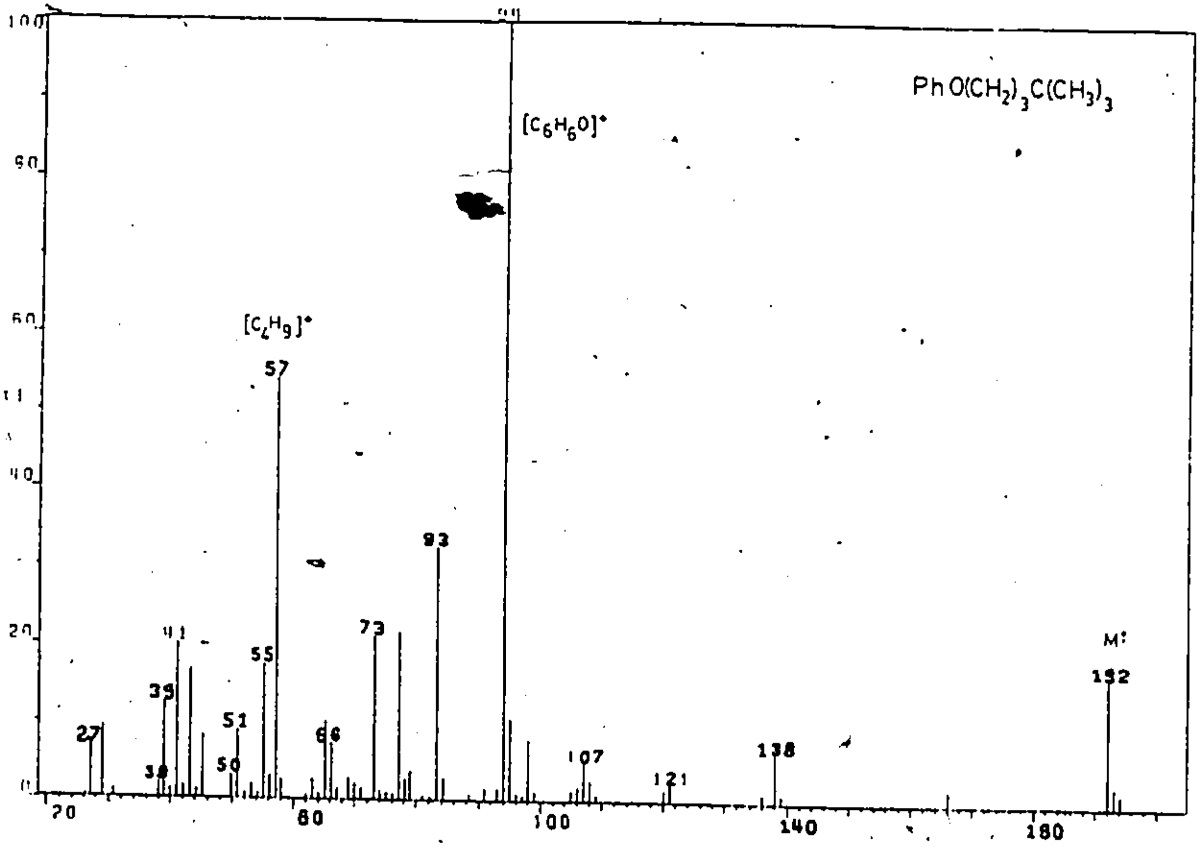


Fig. A14: Mass Spectrum of 2,2-Dimethyl-5-phenoxypentane

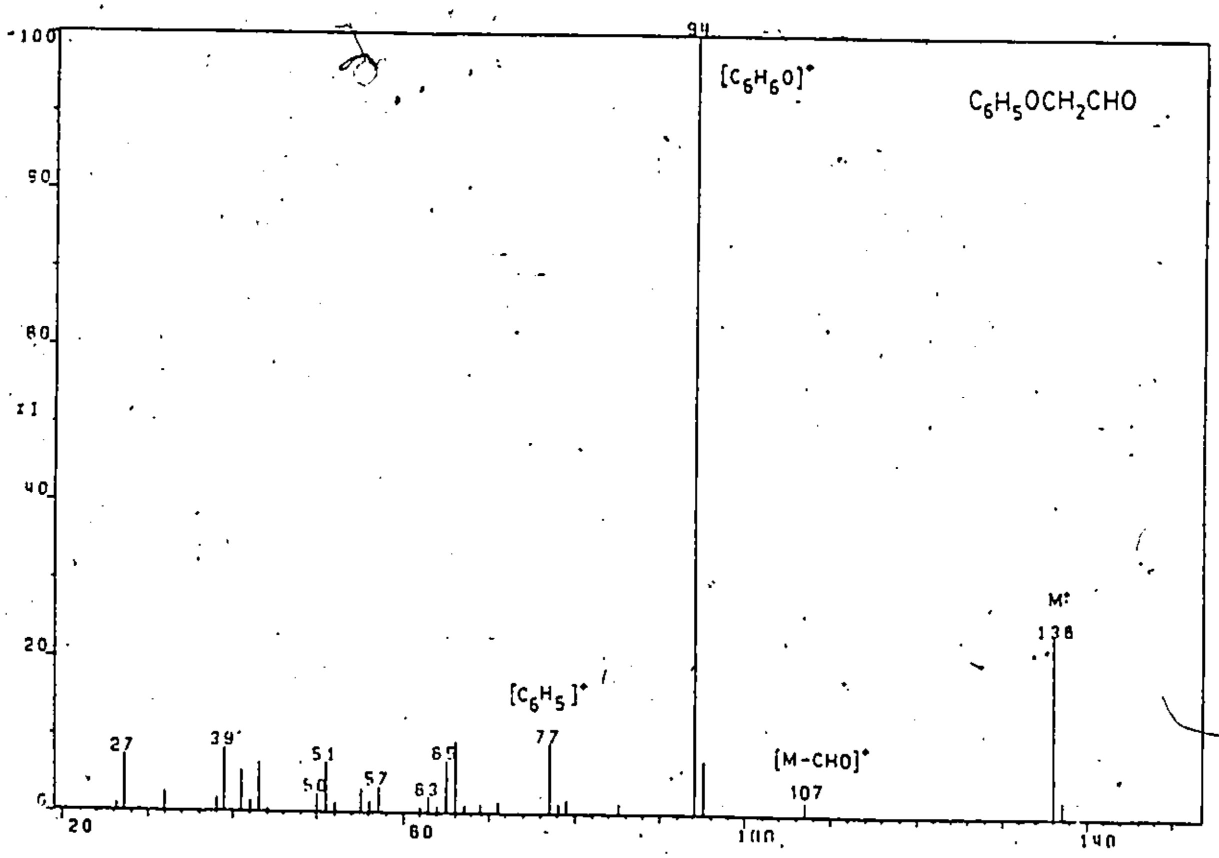


Fig. A15: Mass Spectrum of Phenoxyacetaldehyde

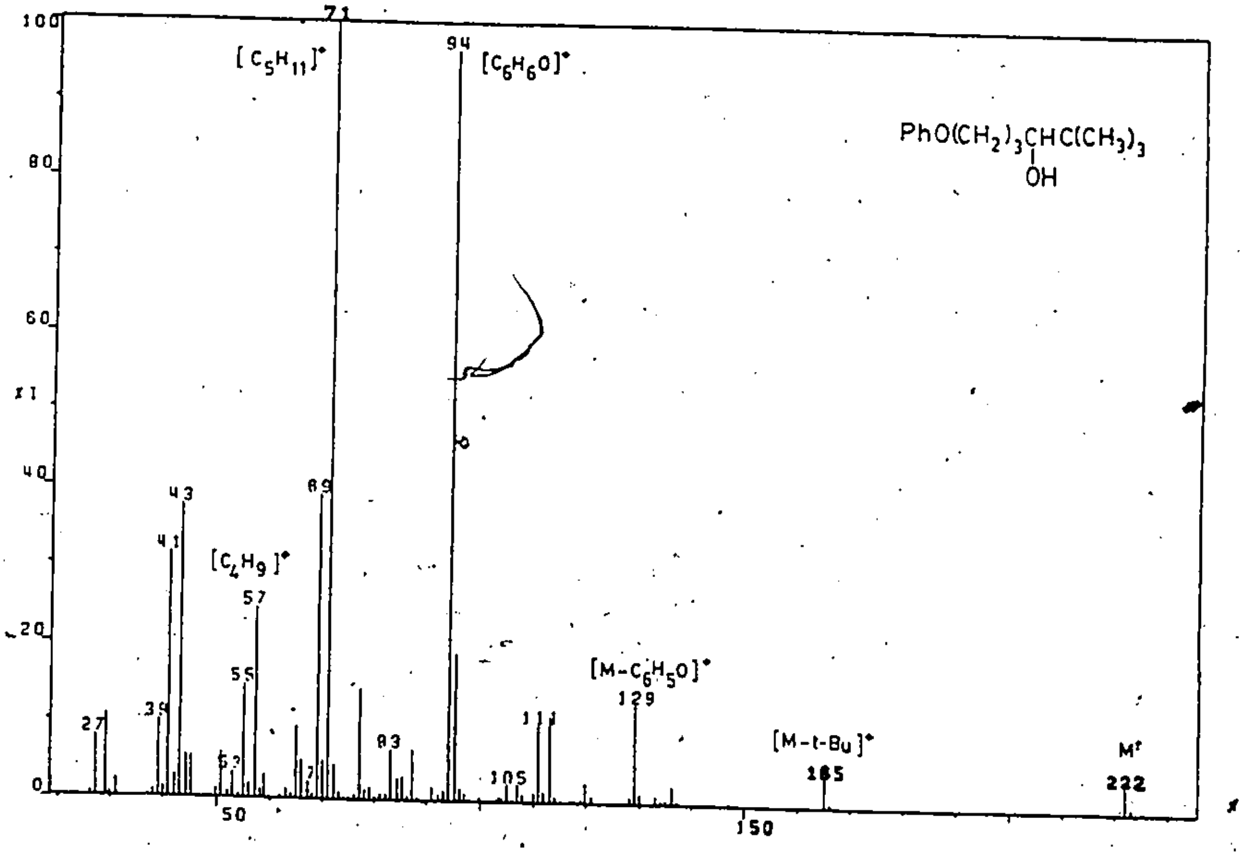


Fig. A16: Mass Spectrum of 2,2-Dimethyl-6-phenoxyhexan-3-ol

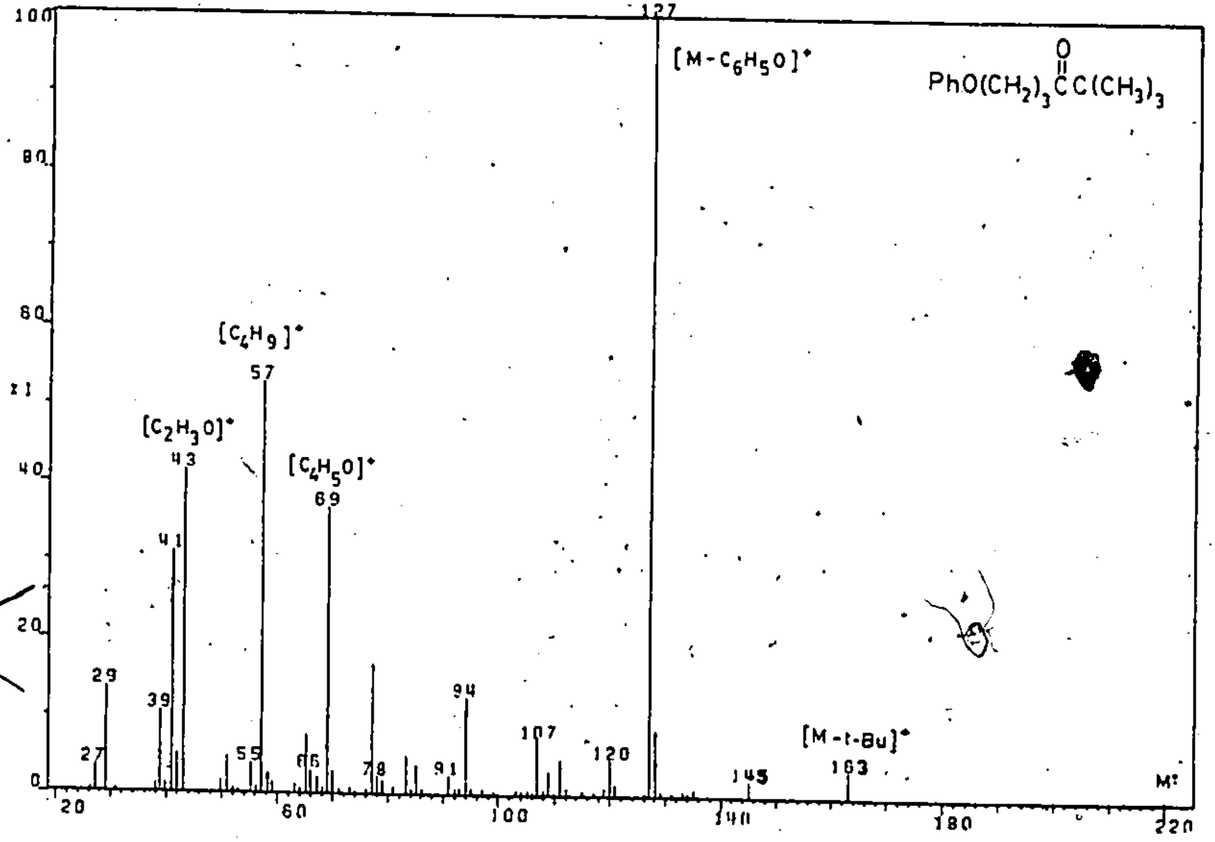


Fig. A17: Mass Spectrum of 2,2-Dimethyl-6-phenoxyhexan-3-one

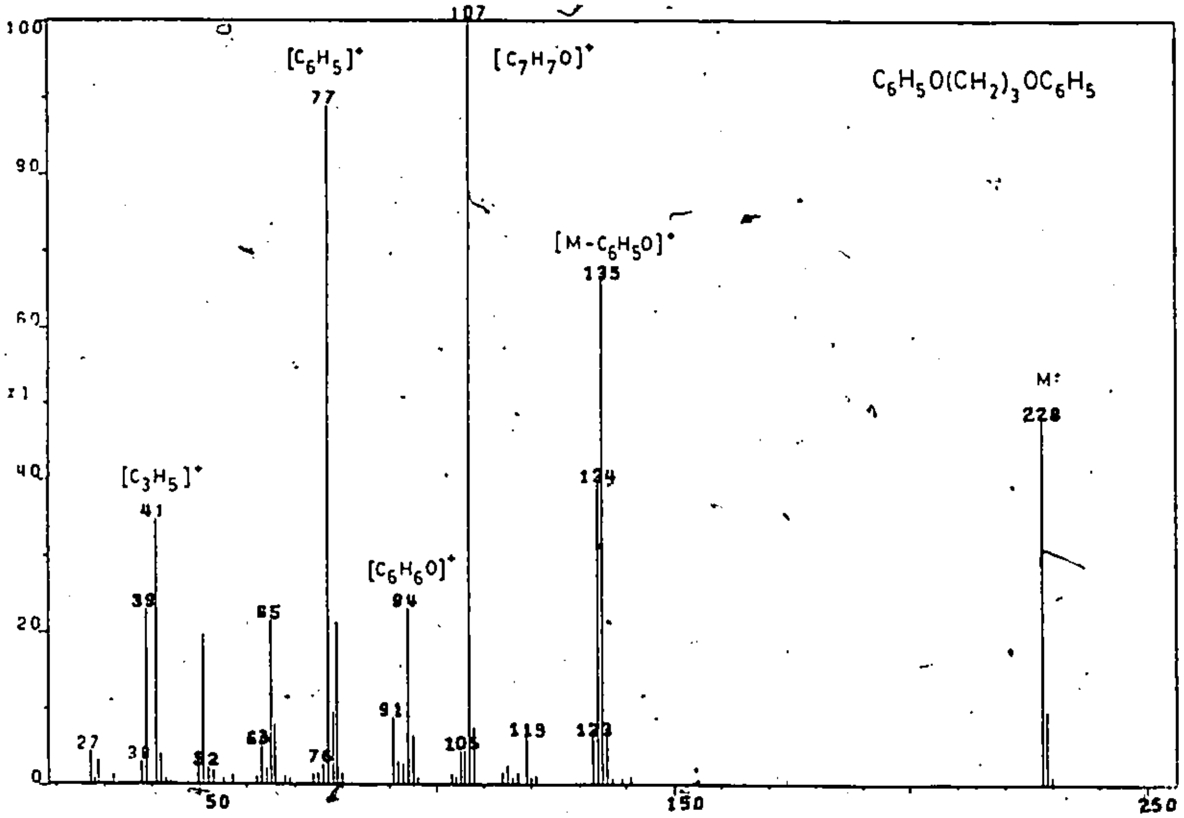


Fig. A18: Mass Spectrum of 1,3-Diphenoxypropane

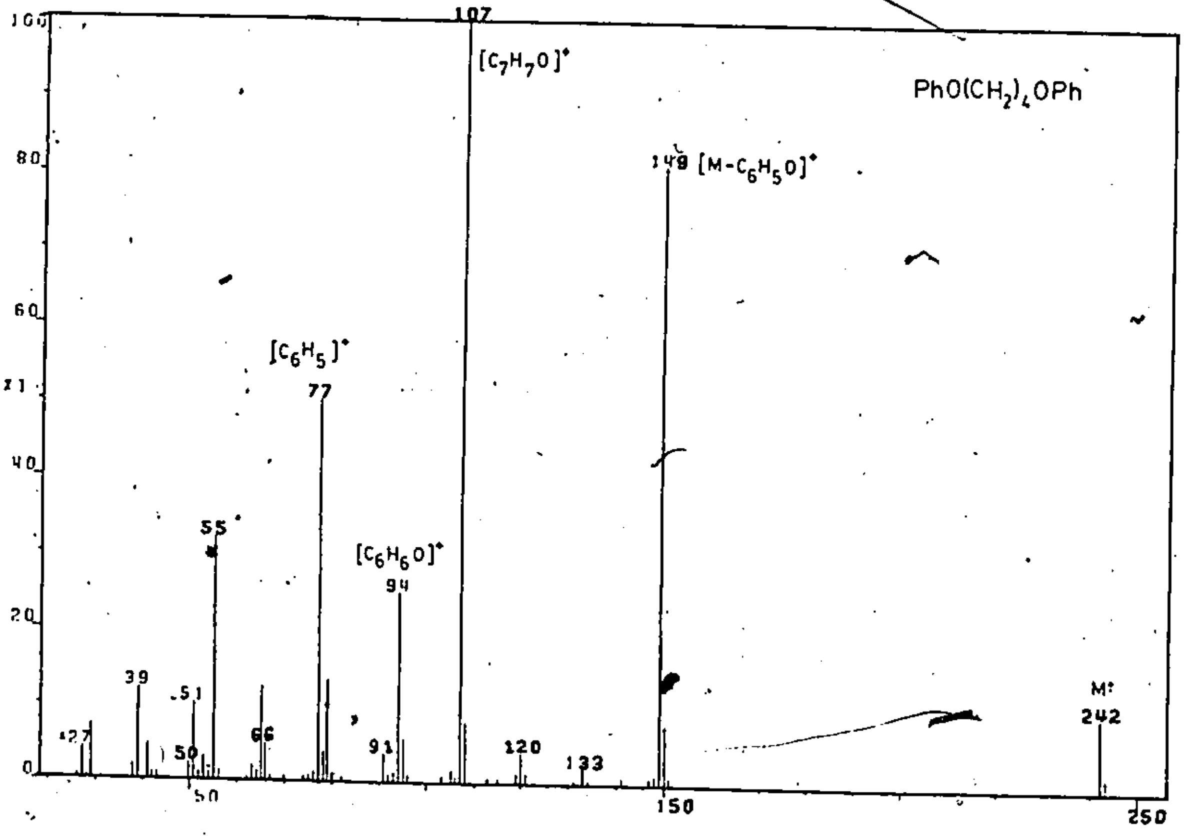


Fig. A19: Mass Spectrum of 1,4-Diphenoxybutane

APPENDIX II. KINETIC METHODS

AII. 1. TREATMENT OF FIRST ORDER REACTIONS

All the thermal decompositions of α-hydroperoxydiazenes investigated during this research were of first order with respect to hydroperoxydiazene concentration when a radical scavenger such as 2,2,6,6-tetramethylpiperidine-N-oxyl radical was present. For a simple, irreversible first-order process (eg. eq. A 1), the rate constant, k, is given by integration of the differential rate equation (eq. A 2 and A 3)

$$\text{Azo} \xrightarrow{k} \text{P} \qquad [\text{A } 1]$$

$$\frac{d[\text{Azo}]}{dt} = -k[\text{Azo}] \qquad [\text{A } 2]$$

$$\ln[\text{Azo}]_t = \ln[\text{Azo}]_o - kt; \; [\text{Azo}]_t = [\text{Azo}]_o e^{-kt} \qquad [\text{A } 3]$$

where Azo is the hydroperoxydiazene (azohydroperoxide). The rate constant, k, may be estimated by fitting measured concentration vs time data to the linear form of the integrated rate equation (eq. A 3). An important feature of first order rate equations is that the validity of the equation is independent of the arbitrary assignment of time zero. A general feature of these equations is that absolute concentrations of the compound may be replaced by any variable which is proportional to the concentration (for example absorption intensities in ir, uv-vis, or NMR spectrum). Suppose the measured quantity, A', is related to [Azo] by

$$A' = a[\text{Azo}] \qquad [\text{A } 4]$$

then the linear form of eq. A 3 becomes

$$\ln A'_t = \ln A'_o - kt \qquad [A\ 5]$$

In the NMR kinetics the rate of disappearance of the gem dimethyl signal of the hydroperoxydiazene in the ^{1}H NMR was followed. The sum of the absorption intensities of the acetone signal and of the gem dimethyl signal was used as the internal standard.

A' is defined as

$$A' = \frac{Hg}{Ha + Hg} \qquad [A\ 6]$$

where Hg and Ha are the absorption intensities of the gem dimethyl signal and of the acetone signal, respectively. Equation A 5 becomes

$$\ln\left(\frac{Hg}{Ha + Hg}\right)_t = \ln\left(\frac{Hg}{Ha + Hg}\right)_o - kt \qquad [A\ 7]$$

This equation may be written as

$$\ln\left(\frac{Ha + Hg}{Hg}\right)_t - \ln\left(\frac{Ha + Hg}{Hg}\right)_o = kt \qquad [A\ 8]$$

If $A' = \frac{1}{A}$, then equation A 8 becomes

$$\ln A_t - \ln A_o = kt \qquad [A\ 9]$$

The rate constant, k, can thus be estimated by plotting ($\ln A_t - \ln A_o$) vs t. The rate constants for the unimolecular decompositions of the hydroperoxydiazenes reported in this thesis are the averages of three runs, the value for each run being an average of three intensity measurements. The errors, reported as standard deviations, ranged from ±0.3 to ±5, see Table 16.

In the iodometric kinetics the rate of disappearance of the hydroperoxydiazene was followed (see Experimental) and the data was plotted as ln C vs t, where C is the hydroperoxydiazene concentration.

The data used in Figures 14 and 15 and in Figure 16 are given in Tables A1, A2, and A3, respectively.

AII. 2. TREATMENT OF HALF-ORDER REACTIONS

Virtually all the thermolysis reactions of the α-hydroperoxydiazenes in the alkenes were of the half-order with respect to hydroperoxydiazene concentration. The proposed reaction mechanism which fits this half-order kinetics, using ethyl vinyl ether (S) as the substrate, is given below.

INITIATION:

$$\underset{\textbf{28 (trans)}}{(CH_3)_2C(OOH)N{=}NR_1} \xrightarrow{k_1} (CH_3)_2CO + N_2 + HO\cdot + R_1\cdot \qquad [A\ 10]$$

PROPAGATION:

$$R_1\cdot + \underset{\textbf{S}}{CH_2{=}CHOEt} \xrightarrow{k_2} \underset{\textbf{R}_2\cdot}{R_1CH_2\dot{C}HOEt} \qquad [A\ 11]$$

$$R_2\cdot + \underline{\underline{28}} \xrightarrow{k_3} R_1CH_2CH(OH)OEt + N_2$$

$$+ (CH_3)_2CO + R_1\cdot \qquad [A\ 12]$$

TERMINATION:

$$2R_1\cdot \xrightarrow{k_4} R_1\text{-}R_1 \qquad [A\ 13]$$

The rate of decomposition of the hydroperoxydiazene in this solvent, in the absence of a radical scavenger such as TMPO, is given by eq. A 14. At a steady state concentration of $R_2\cdot$ the rate of its

$$-\frac{d[Azo]}{dt} = k_1[Azo] + k_3[Azo][R_2\cdot] \qquad [A\ 14]$$

formation must be equal to the rate of its destruction. Thus

$$k_2[S][R_1\cdot] = k_3[Azo][R_2\cdot] \qquad [A\ 15]$$

and

$$[R_2\cdot] = \frac{k_2}{k_3}\,\frac{[S][R_1\cdot]}{[Azo]} \qquad [A\ 16]$$

Also, at the steady state concentration of $R_1\cdot$,

$$k_1[Azo] = k_4[R_1\cdot]^2 \qquad [A\ 17]$$

Table A1: Kinetic Data for Unimolecular Decomposition of $(CH_3)_2C(OOH)N{=}NR$ in Benzene at 50°C

t(hr)	$(\ln A_t - \ln A_o)$		
	$R=C_6H_5$ (0.090M)	$R=CH_2CH_2OC_6H_5$ (0.080M)	$R=CH_2C_6H_5$ (0.085M)
0.0	0.00	0.00	0.00
1.0	0.009	0.030	0.045
2.0	0.017	0.053	0.089
3.0	0.024	0.080	0.141
4.0	0.031	0.107	0.187
5.0	0.037	0.133	0.230
6.0	0.047	0.163	0.269
7.0	0.054	0.183	0.311
8.0	0.061	0.217	0.357
9.0	0.070	0.240	0.410
10.0	0.077	0.270	
11.0	0.086		
12.0	0.093		

Table A2: Kinetic Data for Unimolecular Decomposition of $(CH_3)_2C(OOH)N{=}NR$ in Benzene at 50°C

t(min.)	$(\ln A_t - \ln A_o)$	
	$R{=}CH(CH_3)_2$ (0.080M)	$R{=}C(CH_3)_3$ (0.075M)
0.0	0.00	0.00
10.0		0.107
15.0	0.025	0.177
20.0		0.257
25.0		0.293
30.0	0.049	0.350
35.0		0.403
40.0		0.450
45.0	0.080	0.530
50.0		0.603
55.0		0.650
60.0	0.104	0.717
65.0		0.763
70.0		0.803
75.0		0.857
80.0		0.933
85.0		0.987
90.0	0.146	1.033
95.0		1.077
100.0		1.163
105.0	0.177	
120.0	0.197	
135.0	0.225	
150.0	0.247	
165.0	0.275	
180.0	0.309	

Table A3: Kinetic Data[a] for Unimolecular Decomposition of 0.10M $(CH_3)_2C(OOH)N{=}NCH_2CH_2OCH_3$ in Benzene in the Presence of Norbornene at 50°C.

	$(\ln C_o - \ln C_t)^b$	
t(hr.)	0.3M Norbornene	3.0M Norbornene
0.0	0.00	0.00
1.0	0.057	0.046
2.0	0.119	0.089
3.0	0.116	0.129
4.0	0.216	0.189
5.0	0.277	0.214
6.0	0.325	0.248

[a] Kinetic data obtained by iodometric titration (see Experimental section).

[b] The rate constants are 1.55 x $10^{-5}s^{-1}$ for the 0.3M norbornene and 1.19 x $10^{-5}s^{-1}$ for the 3.0M norbornene; they have correlation coefficients of 0.9867 and 0.9963, respectively.

and

$$[R_1\cdot] = \left(\frac{k_1}{k_4}\right)^{\frac{1}{2}} [\mathrm{Azo}]^{\frac{1}{2}} \qquad [\mathrm{A}\ 18]$$

Substituting for $[R_1\cdot]$ in eq. A 16, $[R_2\cdot]$ becomes

$$[R_2\cdot] = \left(\frac{k_1}{k_4}\right)^{\frac{1}{2}} \left(\frac{k_2}{k_3}\right) \frac{[S]}{[\mathrm{Azo}]^{\frac{1}{2}}} \qquad [\mathrm{A}\ 19]$$

The rate equation (eq. A 14) becomes

$$-\frac{d[\mathrm{Azo}]}{dt} = k_1[\mathrm{Azo}] + \left(\frac{k_1}{k_4}\right)^{\frac{1}{2}} \left(\frac{k_2}{k_3}\right)[S][\mathrm{Azo}]^{\frac{1}{2}} \qquad [\mathrm{A}\ 20]$$

In the presence of excess substrate, [S] is a constant and the rate equation may be expressed as

$$-\frac{d[\mathrm{Azo}]}{dt} = k_1[\mathrm{Azo}] + k_{obsd}[\mathrm{Azo}]^{\frac{1}{2}} \qquad [\mathrm{A}\ 21]$$

where $k_{obsd} = \left(\frac{k_1}{k_4}\right)^{\frac{1}{2}} \left(\frac{k_2}{k_3}\right)$ [S]. Assuming that $k_1[\mathrm{Azo}] << k_{obsd}[\mathrm{Azo}]^{\frac{1}{2}}$ for the chain reaction, equation A 21 becomes

$$-\frac{d[\mathrm{Azo}]}{dt} \simeq k_{obsd}[\mathrm{Azo}]^{\frac{1}{2}} \qquad [\mathrm{A}\ 22]$$

and

$$\int_0^t \frac{d[\mathrm{Azo}]}{[\mathrm{Azo}]^{\frac{1}{2}}} = k_{obsd}t \qquad [\mathrm{A}\ 23]$$

Equation A 23 leads to the integral rate equation, A 24.

$$[\text{Azo}]_t^{\frac{1}{2}} - [\text{Azo}]_o^{\frac{1}{2}} = k_{obsd}t \qquad [\text{A } 24]$$

In these reactions the rate of disappearance of the hydroperoxydiazene is assumed to be directly proportional to the rate of appearance of acetone. Thus, in terms of appearance of acetone, equation A 24 can be represented as

$$[\text{Acet}]_t^{\frac{1}{2}} - [\text{Acet}]_o^{\frac{1}{2}} = kt \qquad [\text{A } 25]$$

The appearance of acetone was followed in the ^{1}H NMR of the reaction mixture. Suppose the normalized absorption intensity, A, is related to [Acet] by

$$A = a[\text{Acet}] \qquad [\text{A } 26]$$

equation A 25 becomes

$$A_t^{\frac{1}{2}} - A_o^{\frac{1}{2}} = kt \qquad [\text{A } 27]$$

The normalized absorption intensity is given by

$$A = \left(\frac{H_{acet}}{H_{CH_2Cl_2}}\right) \qquad [\text{A } 28]$$

The rate constant, k_{obsd}, was obtained by plotting $A_t^{\frac{1}{2}}-A_o^{\frac{1}{2}}$ vs t. The plots for compounds 28b and 28c are shown in Figure 12 (page 104) and the raw data are given in Table A4.

Table A4: Kinetic Data for the Half-Order reactions of 0.08M trans$(CH_3)_2C(OOH)N{=}NR$ in Ethyl vinyl ether at 50°C.

	$(A_t^{\frac{1}{2}} - A_o^{\frac{1}{2}})$	
t(min.)	$R{=}CH_2CH_2OCH_3$	$R{=}CH_2CH_2OC_6H_5$
0.00	0.00	0.00
5.0		0.023
15.0	0.19	
20.0		0.122
30.0	0.30	
35.0		0.208
45.0	0.47	
50.0		0.314
60.0	0.71	
65.0		0.452
75.0	0.87	
80.0		0.559
90.0	1.00	
95.0		0.647
105.0	1.15	

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