Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.fw001

Organic Free Radicals

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Organic Free Radicals

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A symposium sponsored by
the Division of Organic
Chemistry at the 174th
Meeting of the American
Chemical Society, Chicago,
Illinois, August 29–
September 2, 1977.

ACS SYMPOSIUM SERIES **69**

AMERICAN CHEMICAL SOCIETY
WASHINGTON, D. C. 1978

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.fw001

Library of Congress CIP Data

Main entry under title:
Organic free radicals.
(ACS symposium series; 69 ISSN 0097-6156)

Includes bibliographies and index.

1. Radicals (Chemistry)—Congresses. 2. Chemistry, Physical organic—Congresses.
I. Pryor, William A. II. American Chemical Society. Division of Organic Chemistry. III. Series.

QD471.068 547'.1'224 78-1672
ISBN 0-8412-0421-7

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American Chemical
Society Library
1155 16th St. N. W.
Washington, D. C. 20036

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.fw001

ACS Symposium Series

Robert F. Gould, *Editor*

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.fw001

FOREWORD

The ACS SYMPOSIUM SERIES was founded in 1974 to provide a medium for publishing symposia quickly in book form. The format of the SERIES parallels that of the continuing ADVANCES IN CHEMISTRY SERIES except that in order to save time the papers are not typeset but are reproduced as they are submitted by the authors in camera-ready form. As a further means of saving time, the papers are not edited or reviewed except by the symposium chairman, who becomes editor of the book. Papers published in the ACS SYMPOSIUM SERIES are original contributions not published elsewhere in whole or major part and include reports of research as well as reviews since symposia may embrace both types of presentation.

PREFACE

The chapters in this volume are grouped into six sections. In the first, Walling provides a fascinating overview of the first forty years of free radical chemistry. His talk on this subject at the Chicago meeting ended with a heartfelt standing ovation.

The next nine chapters, grouped under the subheading of "Initiator Chemistry," are concerned with various aspects of research on topics of current interest dealing with the energetics and detailed mechanisms of radical production. The first chapter in this section summarizes Paul Bartlett's most recent results on photooxidation and the identity of the elusive epoxidation reagent. Other chapters treat MAH reactions, peroxide and perester reactions, cyclic endoperoxides, diazenes, cage effects, and radiation.

The third section deals with structures and rearrangement reactions of free radicals. This field has seen great advances in recent years, especially because of the use of electron spin resonance techniques.

In the section entitled, "Propagation Reactions of Free Radicals," topics ranging from molecular orbital calculations to detailed studies of electron transfer and radical displacement reactions are discussed. The reactions of sulfur, phosphorous, and nitrogen radicals are reviewed also.

Four presentations of the kinetics and mechanisms of radical ion reactions are presented in the section on radical ion chemistry. Again, electron spin resonance and other physical techniques play a large role.

The final three chapters cover termination reactions. The structural dependence of the rate of oxy-radical terminations, the technique of spin trapping, and pyridinyl radicals are discussed.

The chapters in this book present a review of contemporary research on radical reactions by U.S. and Canadian chemists. These chapters are meant to provide a broad-brush treatment of the research of these contributors, and an easily read introduction to their current interests. I and the other authors also hope that these chapters attest to the pleasure we have all had from our associations with Paul Bartlett and Cheves Walling.

Louisiana State University
Baton Rouge, Louisiana
January 17, 1978

WILLIAM A. PRYOR

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

INTRODUCTION

In late August, 1977, in connection with its 174th National Meeting in Chicago, the American Chemical Society sponsored a three-day symposium entitled, "Organic Free Radicals." At this symposium, 27 well-known radical chemists presented their current research in a program dedicated to the contributions that Paul D. Bartlett and Cheves Walling have made to free radical chemistry. Many more speakers could have participated, but the program was limited by the time made available by the ACS. Furthermore, some speakers were unable to attend because of conflicts with other international meetings held at about the same time.

The papers in this volume are based on talks given at the symposium —with one exception. Owing to an unfortunate accident, Paul Bartlett was laid up with a leg in a cast, and could not attend. However, he was present in spirit, and he agreed to include in this volume the talk that he would have given had Nature, on a dark night in Munich the month before, been slightly kinder.

The breadth and excitement of the current research in the free radical field is, I believe, represented excellently by these papers. And they all, both in explicit acknowledgments and in subtle and personal ways that are less obvious, demonstrate the enormous debt that today's radical chemists owe to these two pioneers.

Radical chemistry has had a tempestuous and interesting history. During the late 1800's, most chemists felt that free radicals could not exist. We were led from this wilderness by Moses—the remarkable Moses Gomberg, who demonstrated that the triphenylmethyl radical can be produced in rather concentrated solutions, and who, with clever and insightful intuition, worked out some of the chemistry of this still-interesting radical.

In subsequent years, a succession of brilliant physical chemists interested in the fundamental laws of chemical kinetics began to interpret their results in terms of radical reactions. In 1918, J. A. Christiansen, K. F. Herzfeld, and M. Polanyi independently suggested a radical chain process for the H_2–Br_2 reaction. In 1925, H. S. Taylor postulated the occurrence of the ethyl radical to rationalize a gas-phase photolysis. In 1931, Norrish suggested that radicals occur in the photolysis of carbonyl compounds. And then in 1939, in a very influential paper, F. Paneth showed that small alkyl radicals could be produced in a flowing gas stream and that their approximate lifetimes could be measured. In 1935, F. O. and K. K. Rice published their book, "The Aliphatic Free Radicals," and in 1946 E. W. R. Steacie published "Atoms and Free Radical Reactions."

Organic chemists apparently had little interest in radical chemistry in these early years. However, the enormous utility of the vinyl polymers and the critical need for synthetic rubber brought about by the second World War dramatically changed that.

The first suggestion that vinyl polymerization occurs by a radical chain mechanism was made by H. S. Taylor in 1927, and independently by H. Staudinger in 1932. In 1937, P. J. Flory developed the model further and introduced the concept of chain transfer. These developments may have appeared quite academic, but during the World War the Japanese first threatened, and then captured the areas in the Far East that supplied America's natural rubber. At first we began a stockpiling program, but our supply of natural rubber in 1941 was only two-thirds of one year's consumption. Germany already had developed a synthetic rubber based on the radical-initiated copolymerization of styrene and butadiene, and, because of a scientific exchange program between German and American industries, our government knew of this work. Thus, in the early 1940's, a huge and vitally important effort began to use and improve the process and product from a vinyl polymerization.

Paul Bartlett and Cheves Walling became involved in this effort to understand and use free radical chemistry in different ways. In 1941, Bartlett, then at Harvard as a young faculty member, began a long and fruitful program of research sponsored by the Pittsburgh Plate Glass Company. As Mike McBride relates in his dedication to Bartlett, even the earliest contributions from this program had the magic Bartlett touch—they were important, novel, and insightful. For example, I have used the Nozaki–Bartlett 1946 publications in my classes for years to illustrate the kinetics of initiator decompositions; these papers are as fresh and current today as they were the day they were published, and they form the cornerstone for all later studies of initiators. As is the Bartlett trademark, they are models of lucidity. The flow of fascinating research from the Bartlett group became a fixture and touchstone in the free radical field.

Cheves Walling, too, was in the forefront of the newly born study of vinyl polymerization process. As Earl Huyser relates in his dedication, Cheves obtained a PhD under Morris Kharash in 1939—a most propitious moment for a young man to arrive on the scene with a special talent for unraveling the mysteries of the kinetics and mechanisms of radical reactions. In his early years at the U. S. Rubber Company Laboratories, Cheves Walling contributed to the newly appreciated understanding of

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polymerization and copolymerization processes. Walling has become well known for his ability to see into the most complex and difficult system, and to reduce it to understandable equations. But it was Walling's book, "Free Radicals in Solution," published in 1957, that surely stands as his most remarkable contribution. Quite literally, this has served as the introduction to the field for a generation of radical chemists, and it remains a frequent source and cited reference in the field despite the fact that it is now over two decades old.

If I may be excused the pleasure of some personal remarks, both of these men played vital roles in my own entreé into the radical field. After receiving a PhD at Berkeley (and never having even heard the word radical during my university days), I started a happy and profitable period with the California Research Corporation. After a short induction period in an exploratory polymer group, I was fortunate to be chosen to direct the one-man basic research group and I began a study of sulfur as an oxidant and the mechanism of the oxidation of methylaromatics to benzoic acids by sulfur. That process proved to be a radical one—at least according to my evidence—and I purchased and studied Walling's newly published book. In addition, Cheves himself was an intermittent consultant to the company, and for the first time I observed his astounding ability to analyze tough kinetic problems in critical detail.

My relationship with Paul Bartlett began with my first visit to Harvard and the tour through his laboratories in about 1961, when I was a young faculty member. During that tour of Bartlett's labs years ago, and in subsequent years whenever any critical academic problem came up, like many other young men I sought to find the answer to the critical question, "How does PD handle that?". Paul Bartlett has stocked the universities and laboratories of America with persons that have looked to him as a teacher, a mentor, and a father figure for a period of nearly 40 years.

Both Paul Bartlett and Cheves Walling have many friends and admirers, and I feel privileged to be counted in that number. And with these many admirers, I dedicate this book to them both.

December 9, 1977 WILLIAM A. PRYOR

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

To Paul Bartlett

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DEDICATION TO PAUL BARTLETT

It is inadequate to characterize Paul Bartlett as a free radical chemist. His interests and contributions have ranged over the entire field of organic reaction mechanisms. Only about one-fourth of his 225 research publications deal directly with free radicals. Another fourth deal with the related topics of singlet oxygen and cycloadditions. Still, these contributions have assured his place as a founder of the modern school of organic free radical chemistry. Of 27 participants in this symposium, seven were his graduate students, two were his postdoctoral associates, and another four were students of his students or post-docs. Obviously his impact on the practitioners has been as strong as on the field itself.

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Bartlett did not begin his career with radical chemistry; he did not even participate directly in the emergence of the field during the 1930's. After graduating from Amherst in 1928 and earning his doctorate under Conant at Harvard in 1931 he rusticated in New York and Minnesota before returning to Cambridge as instructor in 1934. During the rest of the decade he became a leader in the study of ionic reactions and rearrangements. In 1938 this work brought him the first of many honors, the ACS Award in Pure Chemistry.

At the beginning of the war the Pittsburgh Plate Glass Company agreed to support Bartlett's laboratory in what became a long and fruitful program of research on vinyl polymerization. He entered the free radical field by proving with Saul Cohen that both phenyl and benzoyloxy radicals from halobenzoyl peroxide initiators were incorporated into polystyrene. Soon after this he and Nozaki began investigating the role of solvent in induced decomposition of dibenzoyl peroxide, but most of his dozen publications during the forties concerned the kinetics of polymerization itself and the role of inhibitors and retarders. Some of the most striking of these described his work with Swain, and later with Kwart and Broadbent, using light intermittency to measure absolute rate constants for steps in the polymerization of vinyl acetate. The rotating sector is a good example of Bartlett's ability and instinct to use a new, incisive approach that cuts to the heart of a problem. Another is his work with Tate using the kinetic isotope effect on the polymerization of dideuteroallyl acetate to establish the mode of chain transfer and termination.

Such clean experiments are Bartlett's hallmark, but with Hammond and Kwart he fearlessly entered the thicket of inhibitors and retarders and through the fifties followed its path to separate investigations of sulfur chemistry and the complex chemistry of iodine with styrene.

His work with Leffler on the decomposition of phenylacetyl peroxide appeared in 1950 and inaugurated new lines of investigation, focusing on the mechanism of initiator homolyses and on the properties of the free radicals they generate. The latter led to important stereochemical insights through studies of triptycyl, norbornyl, and decalyl radicals, but the former had still wider impact. He developed *tert*-butyl peresters which were a more reliable tool than diacyl peroxides and could be used to generate radicals over a broad temperature range. With Hiatt, Rüchardt, and their successors he demonstrated the place of simultaneous bond rupture and of substituent effects in radical formation. One of the most widely recognized contributions from this research was Bartlett's rationale for the correlation between the entropy and enthalpy of activation in terms of restricted rotation in the transition state for concerted perester homolysis.

Toward the end of the fifties Bartlett began a systematic study of the cage effect, popularizing galvinoxyl as an efficient scavenger, and naming it after Galvin Coppinger. In subsequent work with Nelson, McBride, Engel, and Porter he clarified the mechanism for photosensitized decomposition of azoalkanes and used these compounds to demonstrate the importance in radical-pair reactions of electron spin correlation and matrix rigidity.

The work with Porter on cyclic azo compounds coupled Bartlett's free radical studies into his ambitious effort to delineate the border between concerted and biradical cycloaddition mechanisms. Few demonstrations in chemistry have matched the clarity of his 1963 stereochemical proof with Montgomery that the 2 + 2 cycloaddition of dichlorodifluoroethylene to 2,4-hexadiene involves a biradical intermediate. Through the following decade Bartlett led the biradical parade. His long series of investigations on cycloaddition became particularly important in demonstrating nature's resourcefulness in coping with the supposedly inviolable constraints of orbital symmetry.

For the last ten years Bartlett has concentrated on the world's most important diradical, oxygen. This effort has its roots in his earlier studies of radical-chain autoxidation—Traylor's experiments with oxygen-36, Günther's with kinetics, and Guaraldi's with EPR—that together demonstrated the importance of tetroxide and trioxide in the chains involving cumyl- and *tert*-butyl peroxy radicals. Until recently it appeared that photosensitized oxidations could be explained efficiently by nonradical mechanisms involving singlet oxygen. But now Bartlett is uncovering

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important free radical pathways in ketone-sensitized photooxidation. As so often before, the definitive publications in a complex field will be his. The only perceptible change over a period of forty years is that the word that used to come from the Erving Professor at Harvard now comes from the Welch Professor at Texas Christian.

Bartlett's contributions have spanned free radical chemistry as they have spanned mechanistic chemistry as a whole. Perhaps the truest testimony to his importance in the field can be borne by those of us who missed him at this Chicago symposium. Of course we were sorry that a broken ankle had kept our friend from the occasion that was to honor him and Cheves Walling, and we felt cheated at not hearing the latest news on his photooxygenation studies. But most of all we missed seeing him in the front row, intently following all of our talks, and, through his questions, helping us see new possibilities in our own work.

Yale University
New Haven, Connecticut

J. MICHAEL MCBRIDE

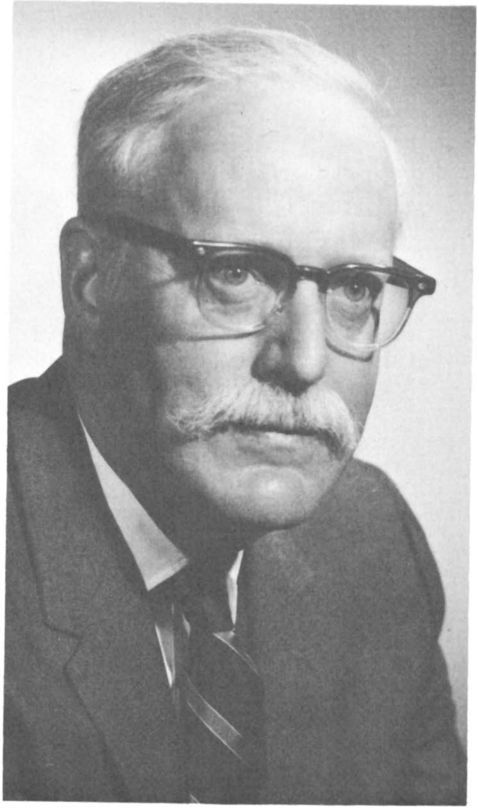
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

To Cheves Walling

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001



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DEDICATION TO CHEVES WALLING

For well over a quarter of a century, the name Cheves Walling has been synonymous with free radical chemistry. His contributions to this field of chemistry during its early years of development alone would have earned him this distinction. While it is an impressive experience to have a pioneer in any area of endeavor present at a symposium recognizing his contributions, it is even more impressive, as it is with Cheves Walling, when the recipient of such recognition is regarded as one of the more active and influential contributors to that field. Those of us who attend symposia and conferences in the general realm of mechanistic organic chemistry are accustomed to finding Cheves occupying a seat in the front row of the audience and to the fact that he can be counted on to contribute to (and often generate) the discussion that follows the presentation of a paper. This tradition was maintained in the best sense at this Chicago Free Radical Symposium.

From the beginning of his professional career, Cheves Walling has been involved intimately with free radical chemistry. After obtaining the AB degree from Harvard in 1937, he joined the research group of Professor M. S. Kharasch at the University of Chicago. Although his tenure as a graduate student was remarkably short (PhD in 1939), it provided the opportunity for him to participate in a significant period of the development of modern free radical chemistry. With Kharasch and Frank R. Mayo, he coauthored some of the early publications that demonstrated that the peroxide effect was a general phenomenon in the addition reactions of hydrogen bromide. In 1940, Walling and Mayo published a survey of free radical addition reactions in *Chemical Reviews*—that did much to establish the free radical chain mechanism of these additions as a general reaction of carbon–carbon unsaturated linkages.

Following his formal education, Cheves Walling spent over a decade as an industrial research chemist. Most notable were the years (1943–1949) when he was a research chemist at the General Research Laboratories of the U.S. Rubber Company. It was during this period that contributions were made by Walling and his co-workers (principal among them Frank Mayo, his colleague from his graduate school days in Chicago) that resulted in the elucidation of some of the fundamental kinetic principles of vinyl polymerization reactions. Among the important contributions made by the U.S. Rubber group was the research in the areas

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of chain transfer and the copolymerization reactions of vinyl monomers. The results of these investigations helped to unravel what appeared at the time to be a complex problem. The work by this group undoubtedly played a significant role in the fantastic growth of the polymer industry in succeeding years. A particularly exciting aspect of the copolymerization work by Walling and his collaborators during this period was the recognition of the resonance, steric, and polar factors that determine the reactivities of free radicals in chain propagating reactions thereby bringing free radical chemistry into the arena of mechanistic physical organic chemistry. The interpretive survey of copolymerization reactions by Walling and Mayo that appeared in *Chemical Reviews* in 1950 served as a basic reference manual for polymer scientists and free radical chemists for many years. The years he spent as an industrial research chemist had their influence on Cheves throughout his professional life in that not only has he been a successful industrial consultant but he always has been able to maintain a meaningful rapport with industrial chemists and their particular challenges.

In 1952, Cheves Walling joined the faculty of Columbia University as Professor of Chemistry, a position he held (serving as Department Chairman from 1963–1966) until 1970 when he became Distinguished Professor of Chemistry at the University of Utah. The research contributions to free radical chemistry by him and his students since the early fifties have been consistently innovative and incisive. An impressive aspect of his research is the breadth of areas in which publications by Walling and his co-workers have appeared. Basic and authoritative articles can be found concerning peroxide chemistry, free radical chemistry of organophosphorus compounds and sulfur compounds, the role of metal ions in free radical reactions, free radical cyclization reactions, halogenation reactions, and the use of high pressure techniques in investigating free radical reactions. His abiding interest in the chemistry of alkyl hypochlorites for over two decades has resulted not only in development of a useful synthetic reaction and information about alkoxyl radicals, but these studies also have provided insight into such subtle aspects of free radical chemistry as the nature of solvent and polar effects on radical reactions and the stereochemistry of allylic radicals. His book "Free Radicals in Solution," which appeared in 1957, must be regarded as one of the more influential publications in modern organic chemistry. In addition to being a comprehensive and interpretive survey of free radical chemistry up to the time of its publication, it both delineated the important areas of future investigations and established the criteria of meaningful research in this field. His scientific accomplishments have earned him membership in the National Academy of Sciences and the American Academy of Arts and Sciences. In 1971, he was the recipient of the James Flack Norris Award in Physical Organic Chemistry and was chosen Alumni Medalist of 1975 by the University of Chicago Alumni Association.

In addition to his scientific achievements, Cheves Walling has given generously of his time and talents in a variety of services to scientific professional organizations. The list of committees in which he has served or is serving presently is extensive and includes the Advisory Board of the Petroleum Research Fund, the Board of Directors of the Gordon Research Conferences, as well as various committee assignments in the American Chemical Society and the National Research Council. Noteworthy has been his work as Chairman of the Committee on Professional Training of the American Chemical Society during the period 1966–1973, a committee on which he serves presently as a consultant. Indicative of his continuing active concern and involvement with his profession is the fact that in 1975 he became editor of the *Journal of the American Chemical Society,* one of the world's most prestigious scientific periodicals. His high scientific and scholarly standards have been and are reflected in these efforts for his profession.

Before I became acquainted with him over two decades ago, Cheves Walling was described to me as a "chemist's chemist." During the time that I was privileged to work with him, it was quite apparent to me why he had earned this particular description. The many important contributions he has made to the chemical profession in succeeding years and the fact that his present activities indicate that there are many more to come give added significance to this unique title for a unique individual in the scientific community.

University of Kansas
Lawrence, Kansas
December 13, 1977

EARL S. HUYSER

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.pr001

1

Forty Years of Free Radicals

CHEVES WALLING

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch001

In a four-day symposium covering most of the developments of free radical chemistry, one retrospective paper seems appropriate to give some picture of the history of our field and how it got where it is. My title, "Forty Years of Free Radicals," was chosen for two reasons. First, although free radical chemistry really dates back to Moses Gomberg's discovery of triphenylmethyl, and the idea of small free radicals as intermediates in high temperature gas phase reactions had had considerable development in the early '30's, 1937 was a crucial year in the recognition that free radicals might be important in ordinary liquid-phase organic chemistry. It was in that year that Hey and Waters suggested that the arylation of aromatics by benzoyl peroxide was a radical process (1) and also that Kharasch proposed that the abnormal addition of hydrogen bromide, which he and Mayo had recognized in 1933 was a radical chain process and thus discovered that he was a free radical chemist (2).

Second, it was the year that I arrived at the University of Chicago, and, on the recommendation of Max Tishler, looked up Morris Kharasch as a possible research sponsor and was thus trapped by this new field. There I worked on some aspects of the abnormal addition problem, showing in part that it was not restricted to terminal olefins, and, with inate caution declined an invitation to investigate the chemistry of acetyl peroxide. Some idea of the rather rudimentary state of our concepts at the time is shown by the fact that at the Boston ACS meeting in September, 1939 I gave the first explanation, based on the energetics of chain propagation steps, why radical chain reactions had been observed with HBr, but not with other halogen acids. That ACS meeting is probably best remembered as the occasion when a large number of attendees came down with food poisoning from eating contaminated seafood at a now-defunct hotel in Swamscott. Fortunately I missed that celebration, but I spoke the next morning to a rather small audience. The interpretation was subsequently published in a review with Frank Mayo (3).

1937 was not long before World War II, and the war led to a

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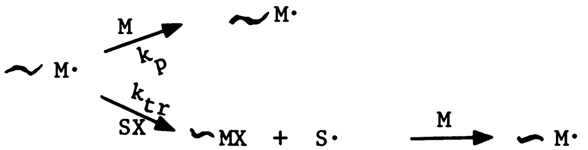
major turning-point in free radical chemistry. On the one hand, orthodox academic research was drastically curtailed; on the other, the Japanese occupation of S.E. Asia and the East Indies cut off our supply of natural rubber. The development of a synthetic rubber industry, almost from scratch, became a high-priority need, and polymer chemistry suddenly became a hot subject. A massive research program was launched in academic, industrial, and Government laboratories, all under the coordination of the Rubber Reserve Corp. In a way, the situation was a small scale preview of our present crisis over energy sources.

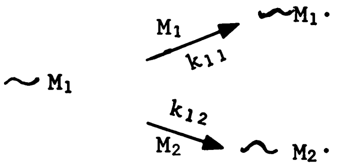
As it turned out, the short term solution, the immediate production of large quantities of synthetic rubber, depended primarily on engineering and modest improvements in German technology, knowledge of which was available large because of prior information exchange between the Standard Oil Co. of New Jersey (now Exxon) and the I.G. They got information about butyl rubber, while we learned about the manufacture of styrene-butadiene copolymer (GR-S), considerably the better part of the bargain. The research program, to be honest, contributed only modestly to war-time rubber production, but, as we shall see, had far-reaching later consequences.

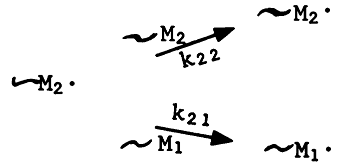
I got involved in this myself in early 1943 when I left Dupont and went to work for the U.S. Rubber Co. (now Uniroyal) on the top floor of an old silk mill in Passaic, New Jersey. U.S. Rubber had decided to launch a fundamental study of polymer chemistry to support their active applied work, and I joined the group headed by Frank Mayo, whom I'd known at Chicago. This was a marvellously exciting time. All sorts of new things were being learned and there were many groups in the field exchanging information quite freely. In particular Herman Mark was at Brooklyn Polytech where he was teaching Americans the extensive European lore on polymer chemistry and conducting regular Saturday morning seminars on the latest developments. Facilities at Brooklyn Poly were a bit primitive. I remember one investigation involving a high-pressure bomb which would hardly have met present standards of safety or equal opportunity. The bomb was in an alcove beween two buildings, hidden from the sidewalk by a thin piece of galvanized iron, and the controls could only be read from a toilet in the men's room. Nevertheless, the seminars were a great success, and attracted participants from all over the northeast.

At the point when I arrived, the Mayo group had already recognized and analyzed two fundamental problems, the kinetics of chain transfer and of copolymerization, and had obtained the first data showing their analysis worked. Unless polymer chemistry was to be a purely empirical art, understanding of both was critical. Chain transfer largely determines polymer molecular weight via the competition between chain growth and reaction of a growing chain with solvent or other transfer agent:



Similarly, copolymer compositions are determined by two competitions:





described by a copolymerization equation (4). In fairness, I should note that similar analyses were carried out by other workers - Alfrey, Goldfinger, and Tobolsky, among others. The success of the Mayo group lay in that we not only understood the theory, but provided the bulk of the experimental data. Frank set high experimental standards and one member of the group in particular, Fred Lewis, was a remarkably skillful devisor of new techniques. Equally important, we had the backup of a first class industrial analytical laboratory.

Beyond the practical import of these studies for polymer chemistry, the resulting data provided the first extensive body of information on the relation between structure and substrate reactivity in radical reactions and gave us the general picture we still use today: relative reactivities are determined by three factors - overall energetics (the usual picture in terms of resonance stabilization of reactants and products); steric hindrance (which for example explains the lowered reactivity of non-terminal olefins and much of the regioselectivity of radical additions); and the "polar effect" (increased reactivity between radicals with electron withdrawing groups and substrates with electron supplying groups, or vice versa). This last was quite unexpected and has proved to be quite general, although its detailed interpretation is still a subject of debate.

By about 1947 many of the major themes of free radical chemistry had emerged from this war-initiated polymer research: data on structure and reactivity and establishment of the utility of competitive kinetics for determining relative rates of chain propagation steps in chain reactions by product analyses as I've just described; the first good rate constants for elementary steps in chain processes - here the first really reliable results were on vinyl acetate polymerization from Paul Bartlett's laboratory (5); degradative chain transfer, first demonstrated by Bartlett and Altschul and showing how the length of kinetic

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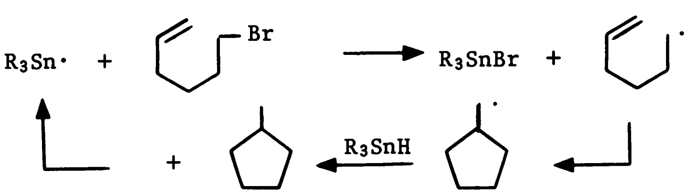
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch001

chains may be determined by the competition between radical addition to double bonds and attack on allylic hydrogen (6); the chemistry of inhibitors and of initiators - azo compounds and particularly peroxides with all their intricate chemistry; redox systems as radical sources. These are some of the examples I can mention, as is the recognition of the peculiar properties and advantages of emulsion polymerization. This last was the subject of intensive investigation by many distinguished scientists including Harkins and Debye, and the final picture was produced by Smith and Ewart (7). Ros Ewart worked in the lab next to mine and we shared a driving pool. I recall the day that he explained his solution to me on the way home from work; I was so fascinated that I drove through a red light and paid a $35 fine.

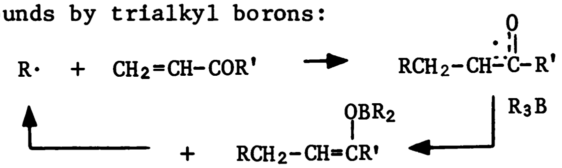
In the post-war period this new knowledge and enthusiasm for radical reactions shifted from polymer to small molecule chemistry. A logical bridge was the process of "telomerization," essentially polymerization carried out in the presence of such reactive chain transfer agents that the resulting product contained only a few monomer units per molecule. In retrospect, the idea was rather obvious, since the radical addition of mercaptans and HBr to olefins to give essentially monomeric products was already known, but its extension to reactions forming C-C bonds was stumbled on by several groups rather by chance. Workers at Dupont investigating the effect of solvents on the high pressure polymerization of ethylene discovered and named the process, but since they were working at high pressures produced relatively high molecular grease-like products which proved of limited interest.

At U.S. Rubber, we lacked the high pressure equipment, but Julian Little and his group quite independently undertook the study of ethylene polymerization in solvents at a pressure of a few atmospheres. To their considerable surprise, in CCl_4 ethylene was rapidly consumed, but no polymer precipitated. Rather, distillation yielded a series of low molecular weight products $Cl(C_2H_4)_nCCl_3$, (n=1-4). Again, apparently independently, Kharasch and his students, perhaps lacking any pressure equipment at all, tried the same reaction with 1-octene and CCl_4, obtaining similar products.

In the next few years the field saw intensive research, and it was shown that a large number of molecules with weak C-H or C-1 bonds could be added to olefins to give a remarkable variety of products. As a synthetic method the reaction has been a bit disappointing since only a few of the products proved to be of practical use, but it has had interesting ramifications, including radical cyclizations, which my students investigated at Columbia (8), e.g.



and which have been studied in detail by Julia (9). Another example is the interesting alkylation of α,β-unsaturated carbonyl compounds by trialkyl borons:



discovered by H. C. Brown, although I should note that the reaction was described some time before its radical chain nature was appreciated (10).

In 1947 I had the good fortune to attend the Faraday Society Discussion on "The Labile Molecule," which, despite its title, was largely concerned with free radical chemistry. This was an enormously exciting occasion, since, in those days chemists didn't make annual trips abroad, and, for the first time the American participants were exposed first hand to the British outlook and the considerable amount of research results which had accumulated during and right after the war. One of the most important ideas which I got from the meeting and visiting British laboratories was the potential significance of free radical autoxidation reactions, which had been brilliantly opened up by Farmer and his colleagues at the laboratories of the British Rubber Producers Association. Again, this was a subject originally investigated for practical reasons (BRPA was concerned with the rapid aging of natural rubber in air) but which had far-reaching results. When we got back to the U.S., we tried to interest our employer in the field with only modest success, but it certainly has had enormous ramifications since.

Since the intermediates in autoxidation are almost always peroxides, the growth of the field in turn focused attention on both their radical and polar reactions with some spectacular successes, as in the phenol synthesis from cumene via an intermediate peroxide rearrangement. As Dr. Porter's paper at this symposium on peroxides related to prostaglandins shows, Nature has known for a long time that the field was interesting, although it still receives neglible attention in organic textbooks.

Another area which received prominent attention at the 1947 Faraday Society Discussion was that of the role of free radicals in redox reactions. The unpredictable effects of trace metals on

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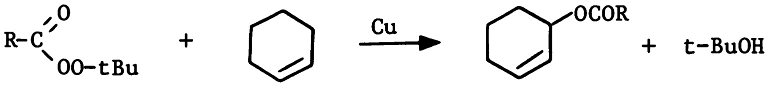
organic reactions had long been known, but for the first time the subject began to develop a rational interpretation. Again, the next few years were a period of rapid development, with Kharasch being an early leader in the U.S. Typical of his studies was the copper catalyzed reaction of perester with olefins (11).



At first there were conflicting ideas about mechanism, and I recall working out a scheme which I considered plausible in the middle '50's and describing it in a seminar at the Shell Development Co. This caused considerable confusion, since Jay Kochi and his colleagues there had worked out the same approach in considerable detail, but were restrained from publishing it because of industrial secrecy. Kochi of course has gone on to make fundamental contributions to the study of redox systems, identifying a variety of paths for transition metal-radical reactions (12).

Another area of radical chemistry which blossomed in the 50's with very practical results to synthetic chemists was free radical halogenation. In 1950 Mayo and I proposed that polar effects played an important role in halogen selectivity (13). A bit later Russell demonstrated remarkable solvent effects in chlorination which should still repay further study (14), and Poutsma showed that halogen-olefin systems initiate their own chains via molecule assisted homolysis (15). Most useful, I think, has been the work on what I call halogen carriers and intramolecular halogenation. The classic case of a potential halogen carrier is N-bromosuccinimide (NBS). By 1950 most chemists believed that the chain carrier in NBS bromination was the succinimide radical (the Bloomfield mechanism). In the late '60's the Goldfinger mechanism (bromine atom chains) took its place, chiefly on the basis of relative reactivity results with benzyl- and allylic substrates. More recently, the succinimide chain has resurfaced, and recent results are described at this symposium by Phil Skell. From my own point of view, this time sequence was fortunate. In 1952 the Bloomfield mechanism was in, and it seemed to me that chlorination via a t-butoxy radical chain using t-butyl hypochlorite might be a useful analog.
My expectations were realized: t-butyl hypochlorite proved to be a most useful allylic halogenating agent, and a convenient starting material for investigating alkoxy radical chemistry (16). With that done, a bit later I was able to participate in discrediting the Bloomfield mechanism for NBS (17), and Jim McGuiness in my group was able to show that chlorine atom chains could be observed with t-butyl hypochlorite as well (18).

We were led into intermolecular halogenation through Padwa's demonstration of very clean regiospecific intermolecular halogena-

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tion in long-chain hypochlorites to yield δ-chloroalcohol (19). Many other workers have taken independent advantage of this tendency of radicals to undergo intramolecular hydrogen transfer through 6-membered cyclic transition states to yield highly specific products as in the Barton reaction (20). Most recently, the concept has been extended by Breslow to highly specific substitutions at much more remote sites in the steroid series.(21)

Time doesn't permit my following all the other threads in the development of free radical chemistry, and I will just mention two. In the middle '50's photochemistry was pursued principally by two groups: a considerable number of physical chemists like W. A. Noyes, Jr, studying small molecules in the gas phase, and a few organic chemists living in hot countries with little equipment but a lot of sunshine (Schönberg and Mustapha in Egypt for example) who put things on the roof to see what would happen. About 1960 physical organic chemists discovered photochemistry, I think for two reasons. Gas chromatography had come in, so it was possible to analyze expeditiously complex mixtures of rather small molecules, and George Hammond and his students showed quite clearly that the photoreduction of benzophenone was a triplet process which could be studied conveniently by competitive kinetics (22). Triplet states are essentially biradicals and much of photochemistry turned out to be free radical chemistry. I've only had a mild hand in this area; Morton Gibian and I showed the close similarity in reactions of benzophenone triplets and t-butoxy radicals (23), but two of my former students, Al Padwa and Pete Wagner, have made substantial contributions to the field.

In the 1950's electron spin resonance (esr) equipment became available, and, for the first time, it became possible to see free radicals at very low concentrations. George Fraenkel at Columbia had built one of the first highly sensitive instruments, and in 1954 he and I were able to detect free radicals in polymerizing methyl methacrylate and show they had the expected structure (24). Unfortunately, for a long time, most of the people who knew how to operate esr spectrometers were interested primarily in interpreting esr fine-structure, and couldn't care less about reactions. Fortunately this is now changed, and starting with R. O. C. Norman's work on flow systems, many groups are applying the technique to the identification of radical intermediates and the measurement of elementary rate constants. Keith Ingold has told us about some recent examples here.

Where are we now? The years 1943-63 were probably the golden age of free radicals in terms of exponential growth of the field and introduction of new concepts. However, there is still activity. Aside from this symposium at this meeting, I count 15-20 papers in the organic section involving radical reactions, and a considerably larger number in the meeting as a whole. Free radicals permeate our world - they make smog in Los Angeles, and destroy ozone in the stratosphere. On a sunny day there are roughly 10^6 hydroxyl radicals/cc. in the air we breathe, and they've been detected in interstellar space (more encouraging to future space travellers, there is also lots of ethanol). If I try to look ahead, I'd say that some of our important unsolved problems lie, first, in the borderline between radical and polar reactions - when can the two have common rate determining transition states and when do reactions go via single electron transfer, rather than via two electron displacements? Ashby, for example, has shown that both paths occur in Grignard reactions.

Second, and closely related, there is much to be learned about the role of radicals in oxidation-reduction processes, and organometallic chemistry and in the chamistry of radical ions. Here, as an example, my colleagues and I have been able to greatly strengthen the concept that radical cations are intermediates in a variety of radical reaction with aromatic molecules.

Third, what is the role of radical reactions in biochemical processes? Do enzymes dare use them? Plainly they sometimes do, but how often?

Radical chemistry continues to be a rewarding area, and, if the past is any guide to the future, radical intermediates will continue to turn up in unexpected places. In the meantime I can only regret that textbooks are unwilling to give them equal time with carbonium ions and molecular orbitals.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch001

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch002

2

Free Radical Aspects of Photooxidation

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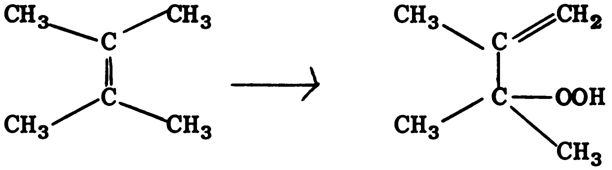
Photo-oxidation is defined, for our present purpose, as oxidation by molecular oxygen under the influence of light. The process may result in any product more oxidized than the starting material; and it may originate in the absorption of light by the oxygen, by the substrate, or by a third molecule (a "sensitizer") whose function may be to transfer excitation energy or to involve the reactants in short-lived reactive complexes or covalent intermediates. Many investigators of photo-oxidation may have entertained the hope of discovering a common mechanistic thread underlying all the kinds of photo-oxidation; but the current mood is more one of appreciation of the versatility of Nature, who does not reserve her subtleties only for complex biological systems, but lavishes them on even some of the smallest molecules that we have.

In principle, any compound that can be thermally oxidized can be oxidized by some application, direct or indirect, of light. But the things that are unique about photo-oxidation are seen mainly with unsaturated starting materials, and it is with them that the hope of sorting out mechanisms reaches a maximum. Included in such photo-oxidations are reactions leading to three general results:

1. The O-O bond remains intact in the product, which may be an allylic hydroperoxide (1) (1), a dioxetane (2) (2), or an "endoperoxide" (3) (3), depending on the nature of the starting material.



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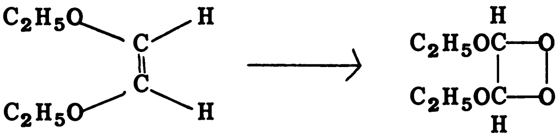

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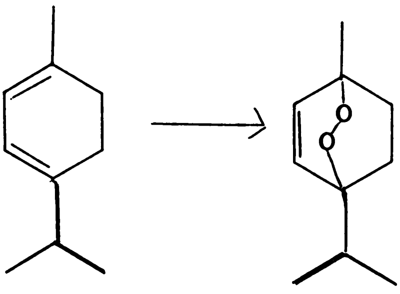

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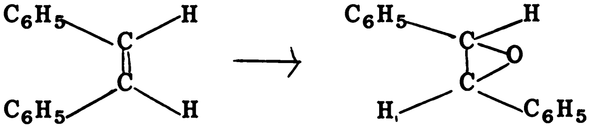
2. The product contains only one of the atoms of the oxygen molecule, as in the case of an epoxide (4) (4), or a sulfoxide (5) (5, 6)



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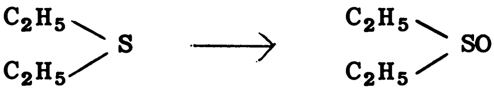

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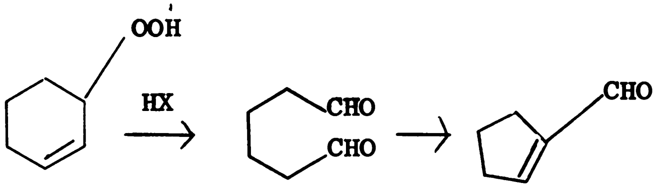
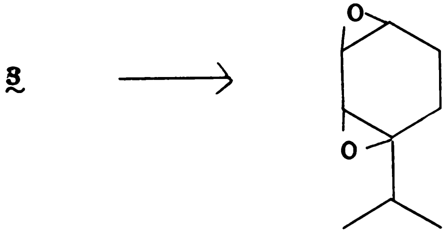
3. Cleavage products or rearrangement products are found, often attributable to an initial hydroperoxide (7) or peroxide (8) undergoing further reaction under the influence of light or thermally (9):





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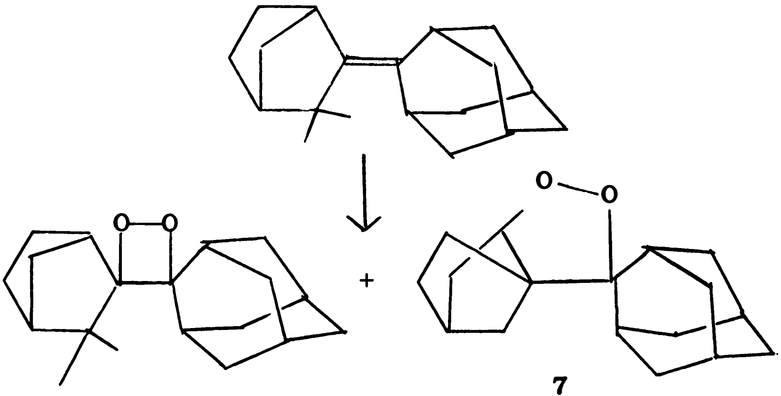

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The Development of Mechanistic Criteria

Not only is there a ramification of products from any particular photo-oxidation method, but there are some clear cases where one and the same product may be formed by two or more mechanisms. The study of this field has therefore demanded the development of some criteria for at least assigning observed oxidations to mechanistic categories.

General criteria for singlet oxygen:

1. The formation of singlet oxygen requires the input of energy, and a photo-system generating singlet oxygen ceases to operate when the light is turned off. It thus differs from a chain reaction operating under thermal initiation.

2. Quenchers, typified by β-carotene and by 1,4-diaza(2.2.2)bicyclooctane (DABCO), powerfully inhibit reactions in which singlet oxygen is the reactant, while normally leaving free-radical chain reactions and ground-state thermal processes unaffected.

3. On the other hand, reactions depending on singlet oxygen do not respond specifically to chain inhibitors, such as hydroquinones or stable free radicals which strongly interfere with thermal chain reactions.

4. Certain compounds, such as tetramethylethylene or diphenylisobenzofuran, which are very reactive to singlet oxygen, may serve as indicators of its presence when introduced into a photo-oxidation where the participation of singlet oxygen is suspected. The absence of the normal singlet oxygen reaction products of these agents is a generally reliable criterion of the absence of the excited species.

5. The ability of singlet oxygen to attack a double bond is a sensitive function of electron availability in the pi system being attacked. Some photo-oxidations actively involve electron-poor double bonds which are unreactive toward singlet oxygen; this can be a straightforward mechanistic criterion.

Special Criteria for Certain Kinds of Oxidations.

For a reaction leading to hydroperoxides, a useful criterion of mechanism is the product distribution when 1,2-dimethylcyclohexene is oxidized by that method. Autoxidation under initiation by free radicals leads to introduction of the hydroperoxy group at the 3-position to the extent of 54% (10), this mode of reaction being undetectably small when either thermally- or photo-generated singlet oxygen is the reactant.

Criteria that have been used in the case of dioxetane formation include stereospecificity of the reaction, comparison of reactivities with those toward known singlet oxygen sources, and the presence or absence of termination products from any possible chain-carrying species.

Application of such criteria as these has shown that among photo-oxidations retaining the O-O bond, hydroperoxides can be formed either from singlet oxygen or from radical chain reactions, while there is a growing number of cases of dioxetanes or endoperoxides being apparently formed in non-singlet oxygen reactions. The oxidation of 2-phenylnorbornene in the dark gave products which could have involved dioxetane formation, but could also be accounted for in part by a Mayo chain. (11)

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch002

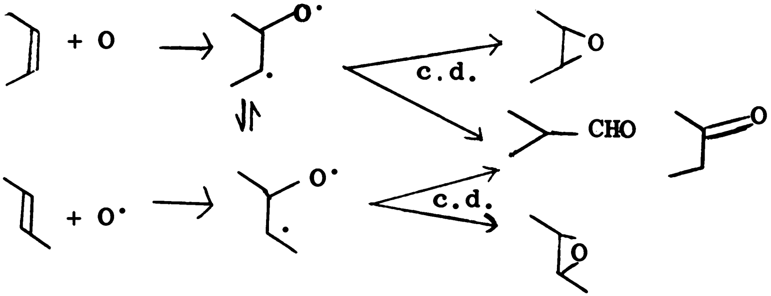
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch002

The Mechanistic Problem in Photo-epoxidation.

Epoxides can be produced stereospecifically from olefins by compounds so constituted that they can concertedly deliver an O atom and leave a stable molecule behind. Peroxyacids are prime examples of this capability. (12)

Substituent effects on this kind of concerted, stereospecific epoxidation indicate that the peroxyacid functions as an electrophile; electron-donating groups activate the olefin while electron-withdrawing groups strongly deactivate it. When the electron flow at the transition state is reversed by using electron-poor olefins and peroxy anions for epoxidation, the reaction is stepwise and stereo-equilibrating and both cis- and trans-olefins (e.g., benzalacetophenone) yield trans-epoxide. (13, 14)

What might appear the simplest model of a concerted epoxidation, the addition of a free gas-phase oxygen atom to an olefin, proves to be in fact a stepwise process as a result of the triplet character of ground-state oxygen atoms. (15)



Without the indicated "collisional deactivation" (c.d.), the epoxide and carbonyl isomers are largely replaced in the product by complex mixtures of cleavage products. The product figures of Cvetanovic extrapolated to infinite pressure, allow an estimate (16) that the energy-rich cis-biradical rotates to the trans-conformation 2.9 times as fast as it undergoes ring closure to the epoxide. Although this corresponds to a retention index of 2.1, which is quite normal for condensed-phase cycloadditions via biradicals, the gas phase systems cannot be perfect models of reactions in solution because of the high vibrational excitation which in this case leads to migration of hydrogen and methyl in amounts comparable to the amount of ring closure.

Thus the distinction between concerted and

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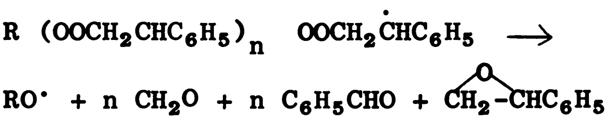
stepwise epoxidations is not a matter of neutral vs. ionic reactants, nor even of spin-paired vs. triplet systems, but rather has to do with the availability of a transition state allowing simultaneous bonding of the incoming oxygen atom to both carbon atoms of the double bond. The criteria for such a concerted mechanism are not understood on a level allowing prediction.

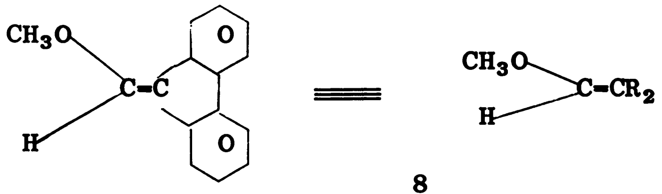
A clearly stepwise mechanism for epoxide formation was demonstrated in detail by Mayo and coworkers (18, 19). It was shown that in a chain copolymerization of styrene and molecular oxygen, any polymeric radical terminating in a styrene unit has the possibility of cleaving off an epoxide molecule from the end of the chain:



$$R\ (OOCH_2CHC_6H_5)_n\ \ OOCH_2\dot{C}HC_6H_5 \longrightarrow$$

$$RO^{\bullet} + n\ CH_2O + n\ C_6H_5CHO + \overset{O}{CH_2-CHC_6H_5}$$

In the case of styrene, because of rapid β-fission of the remaining chain, epoxide is a minor product, reaching its maximum yield in comparison to aldehydic fission products at a low oxygen pressure assuring a significant lifetime to the styrene-terminated radical. An example was recently found in the case of photo-oxidation of 9-methoxymethylenefluorene (8) where the cleavage of such a radical to epoxide is so favored over addition of oxygen that comparable amounts of epoxide and fluorenone are attained at and above room temperature (20) (Scheme 1):



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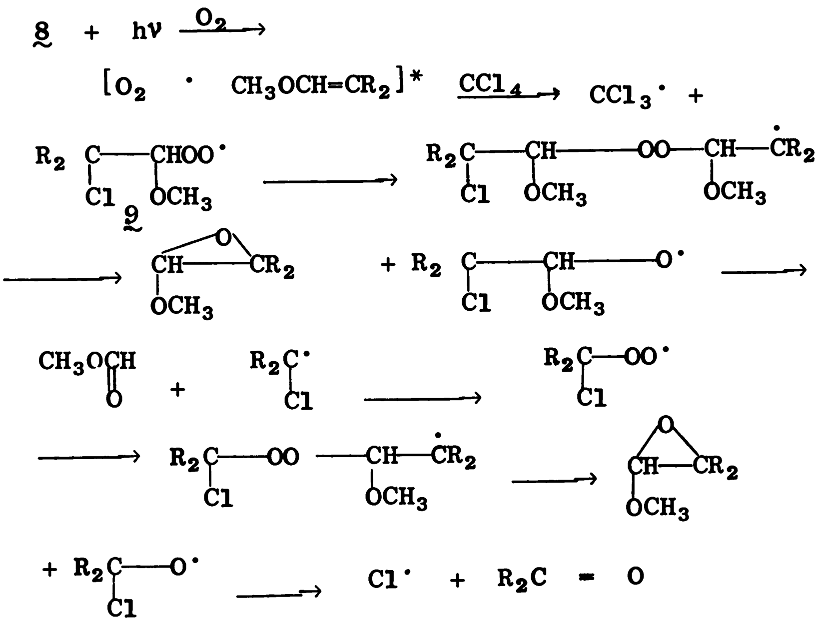
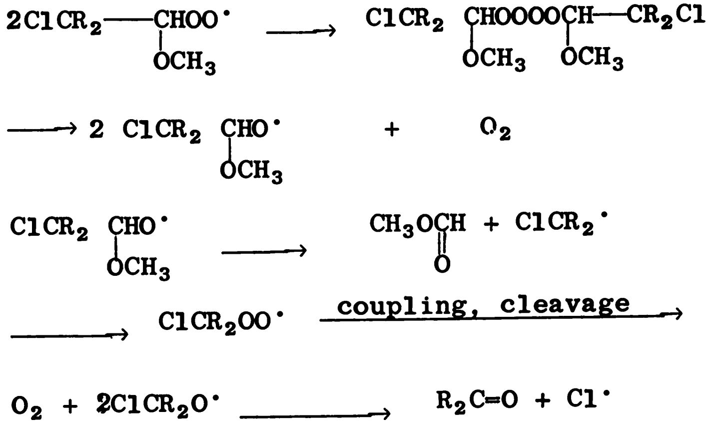
In a chain reaction involving peroxy radicals, coupling of these radicals is a very rapid process and can be the principal mechanism of chain termination. In the case of methoxymethylene fluorene, however, peroxy radical coupling in normal course does not lead to termination, but to fluorenone and a chlorine atom to continue the chain (Scheme 2).



Scheme 1.



Scheme 2.

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Coupling thus diverts intermediate radicals from forming epoxide to forming fluorenone. Since the activation energy for radical coupling is normally lower than for chain propagation, an explanation is at hand for the rather sharp reduction in the epoxide/fluorenone ratio as the temperature is lowered.

The compelling evidence in favor of a free radical mechanism for this reaction consisted in the fact that the results were identical when the reaction was initiated in the dark by generating the radical 9 from a hydroperoxide precursor with lead tetraacetate, and in the determination of a quantum yield of about 12 for the photo-initiated reaction.

Thus free radicals may readily be involved in a photo-epoxidation, and when they are they can be detected by establishing the chain character of the reaction and its response to initiators. If the example of 9-methoxymethylene-fluorene is of general significance, we may suspect that reactions leading cleanly to epoxides as single products will not be found to proceed through free radicals.

The Simultaneous Formation of Epoxides and Dioxetanes

The near-inseparability of conditions for the formation of dioxetanes and of epoxides was first observed when 7,7'-binorbornylidene was oxidized with photosensitizers in a series of solvents (21).

The ratio of epoxide to dioxetane increased 28-fold on going from methylene chloride to benzene with tetraphenylporphin as sensitizer, such solvents as pinacolone, dioxan, and acetone occupying intermediate positions. Systematic investigation showed that epoxide more often than not accompanies the dioxetane from sensitized oxygenation of norbornene (22) and of biadamantylidene (M. J. Shapiro, quoted in (23); (26)). For each solvent-sensitizer combination, the ratio of epoxide to dioxetane increased in the order: biadamantylidene < norbornene < binorbornylidene. This is also the decreasing order of reactivity of these olefins toward singlet oxygen. In the course of these and other investigations (24), much negative evidence has been accumulated concerning the mechanism. Since the hypothesis of an intermediate perepoxide was already an attractive one in offering a symmetry-allowed path for stereospecific dioxetane formation, it gained in attractiveness with

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the apparent possibility of explaining the accompanying formation of epoxides.

However, although we do not yet understand the full meaning of the observations, it is clear that the almost ubiquitous epoxide products in these experiments do not come from singlet oxygen. For example, in a series of controlled experiments by Dr. M. J. Shapiro, biadamantylidene is converted solely into dioxetane by the singlet oxygen generated from the decomposition of triphenylphosphite ozonide in methylene chloride at 0° in the dark, or in the photosensitized oxidation with visible light by crystal violet in the same solvent. On the other hand, three sensitizer systems in carbon tetrachloride -- rose bengal on polymer beads, iodine, and bromine -- have converted biadamantylidene entirely into its epoxide. In one photosensitizer system in benzene, the presence or absence of an ultraviolet cutoff filter has made a difference of a factor of 17 in the epoxide/dioxetane ratio.

Such observations eliminate suggested mechanisms of deoxygenation of the perepoxide, whether by solvent (27) or by singlet oxygen (23, 28, 29). The powerful effect of tetracyanoethylene as an additive (23) and of diphenyl sulfide as a solvent (30) in shifting the product over to epoxide would be compatible with deoxygenation of a perepoxide, but in the case of the diphenyl sulfide a different order of events seems more probable (5). Especially striking is the observation of Jefford and Boschung (26) that the amount of epoxide accompanying the dioxetane varies greatly with the concentration of the sensitizer: sometimes, as in the case of rose bengal, it increases with increasing sensitizer concentration, whereas with tetraphenylporphin it declines. These facts, plus the wavelength dependence of the epoxide/dioxetane ratio, require that the epoxide results from a photochemical sequence independent of that producing singlet oxygen. The conclusion is clear -- there is a photo-induced sequence, of which many sensitizers are capable, which leads to epoxide by a mechanism or mechanisms other than the direct transfer of energy to an oxygen molecule.

It should be mentioned parenthetically that the several roles which the perepoxide has been shown not to perform have not served to eliminate this intermediate from a possible central position on the reaction path from singlet oxygen to dioxetane. In deciding between the perepoxide as a way of removing the orbital symmetry barrier and the chief other possibility -- the 2s+2a cycloaddition -- McCapra's observation of polar-type rearrangements to dioxolanes instead of dioxetanes (9) can be interpreted as favoring the three-membered ring intermediate with its obvious polar capabilities. However, the rearrangement depends on the charge-bearing disposition of the camphenyl skeleton in the substrate, which might induce a polar rearrangement in any transition state en route to dioxetane.

Frimer, Bartlett, Boschung and Jewett (32) have recently observed by means of deuterium and tritium isotope effects that the transition states in the attack of singlet oxygen on 4-methyl-2,3 dihydro-4H-pyrans deviate from the "least motion" path for the direct formation of either dioxetane or allylic hydroperoxide, toward the type of transition state to be expected if perepoxide formation were the rate determining step. Any final judgment on the perepoxide as an intermediate in dioxetane formation must await evidence as specific as that which has eliminated it in the competitive photo-epoxidations.

The commonly used photosensitizers for generating singlet oxygen undergo π,π^* activation; this property is associated with their strong predisposition to transfer energy to other molecules rather than entering into some of the more specific chemistry associated with n,π^* excited states. Yet all these sensitizers have hetero-atoms with unshared electron pairs and hence, with light of the appropriate energy, they should be capable of n,π^* excitation.

Epoxidation with α-Diketones

We have observed that a change in sensitizer for olefin photo-oxidation from a π,π^* absorber to benzophenone, benzil, and finally biacetyl (4) shifts the reaction toward epoxidation at an accelerating rate, epoxidation with biacetyl being general, fast, and of high yield. The epoxidation does not respond to singlet oxygen quenchers, and is effective on many olefins which are quite inert to singlet oxygen. Although this reaction had little in common with the chain epoxidation of methoxymethylenefluorene, it was tempting at first to attribute the epoxidation to the more localized electron distribution in an n,π^* excited state and to postulate active intermediates having covalent interaction of

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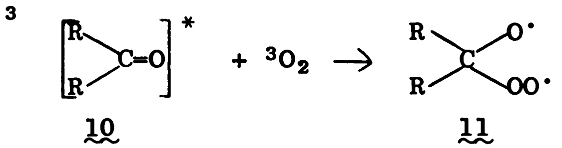
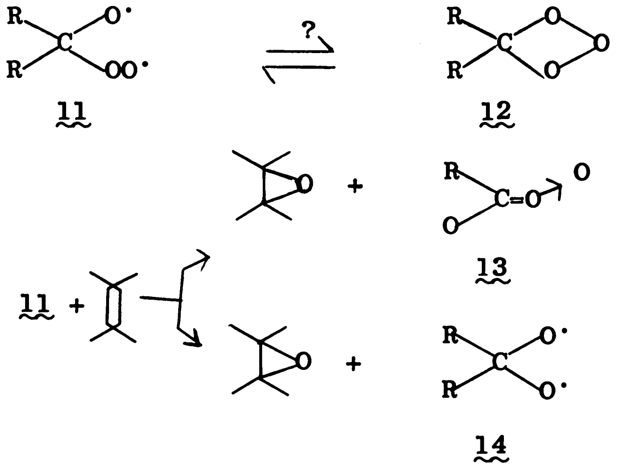
oxygen with the caronyl group.

An obvious possibility of the kind would be



11 formed from 10 by attack of triplet oxygen. Although 11, as a singlet species, might cyclize to 12 which could be the same kind of one-O-donor as a chelated peracid, yet 11 might also behave as a biradical in reacting with an olefin with the end result of donating a single oxygen atom to form the observed epoxide.



The remaining species, 13 and 14, are alternate forms of the caronyl oxide of the ketone. If the Criegee structure 13 were formed in the process, it would mean that the epoxide oxygen came not from the oxygen molecule but from the keto oxygen of the sensitizer. By either of these paths any sensitizer keto group which becomes regenerated must be either completely exchanged (in the case of 13) or half exchanged (in the case of 14) with the oxygen from O_2.

Dr. Johannes Becherer has tested this possibility of biradical involvement in the photo-epoxidation by carrying out the reaction with completely ^{18}O - labeled molecular oxygen, and unlabeled benzil and biacetyl. Small samples in benezene containing

0.33 millimoles of $^{36}O_2$ and 0.20 millimoles each of benzil or biacetyl and norbornene were irradiated through pyrex with a 450-W. Hanovia mercury vapor lamp. Under identical conditions, benzil on 15-minute irradiation underwent about 5% isotopic O-exchange in the absence of norbornene and 10% in its presence. In the same length of time the norbornene was converted 70% into norbornene oxide whose oxygen was 93% ^{18}O and 7% ^{16}O. A result like this could not have been produced by any obvious variant of the mechanism depicted above, but rather requires a reaction path by which the oxygen of O_2 is conveyed into the epoxide without ever having been covalently attached to the carbonyl group of the sensitizer.

The results with biacetyl are equally emphatic. In the absence of olefin biacetyl is rapidly destroyed by light and oxygen: on irradiation for 15 minutes the yellow color of the alpha-diketone had completely faded. The small amount of biacetyl remaining showed 42% incorporation of isotopic oxygen, still short of the calculated 62.5% for equilibration incidental to the photo-destruction. In the presence of equimolar norbornene after the same irradiation, the much larger amount of recovered diketone was only 8% exchanged, while there was a 90% conversion to norbornene oxide whose oxygen was 93% ^{18}O.

Ion Radicals in Photo-oxidation

These experiments having eliminated participation of both the biradical **11** and the hypothetical peracid analog **12**, there remains a large area where there are persistent indications of involvement of odd-electron species in oxidation processes. Single electron transfers occur in many of the same situations in which free radical initiation and photosensitization occur. There have been cases of this kind where superoxide radical ion, $O_2^{\cdot -}$, has been observed, and some of its interactions with singlet oxygen have been studied.

Jefford and Boschung (26) have interpreted their extensive experiments on the photooxidation of biadamantylidene in terms of an intervention of superoxide anion, generated in a secondary reaction between singlet oxygen and various ground-state sensitizers, especially rose bengal. In a series of steps, the resulting $RB^{+\cdot}$ takes an electron

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch002

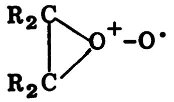
from $Ad{=}Ad$ and the resulting cation radical $Ad{=}Ad^{+\cdot}$ reacts with triplet ground state oxygen to give the cation radical of a perepoxide. This species in turn is converted by a second superoxide anion into the often-discussed pair, epoxide +ozone. The advantage of this sequence over the direct process via perepoxide and singlet oxygen is that it provides a picture of the special role played by each sensitizer in influencing the relative amounts of dioxetane (still formed via singlet oxygen and olefin) and epoxide. The authors show that DABCO, as a singlet oxygen quencher, stops both kinds of photo-oxidation, consistent with the view that singlet oxygen is a precursor of the epoxidizing reagent itself.

Specific tools used in these experiments included di-*t*-butyl-p-cresol as a radical inhibitor to interrupt selectively the radical chain, and the use of phenylglyoxylic acid to react specifically with superoxide anion (33).

Other probes that have been used for the occurrence of superoxide anion radical (36) in the presence of singlet oxygen include sulfite anion (34), selectively oxidized by superoxide, and superoxide dismutase (34, 35), which efficiently converts superoxide ion into oxygen and hydrogen peroxide.

In seeking a framework for the epoxidizing action of the alpha-diketones as photosensitizers, it is suggestive that these compounds are themselves very effective electron-acceptors, giving rise to the well characterized semidiones (37).

In terms of the Jefford-Boschung framework, we might then say that a sensitizer whose excited state is high enough in electron affinity (such as an α-diketone) can simplify the photo-oxidation sequence by taking an electron directly from the olefinic substrate rather than transferring any excitation energy to oxygen, and so can initiate an epoxidation sequence without intervention of singlet oxygen. Epoxidation could be completed in the absence of both superoxide ion and singlet oxygen if the perepoxide cation radical, **15**, could react with triplet oxygen to a species (**16**) which is converted by collision



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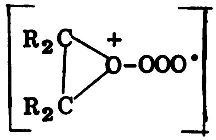

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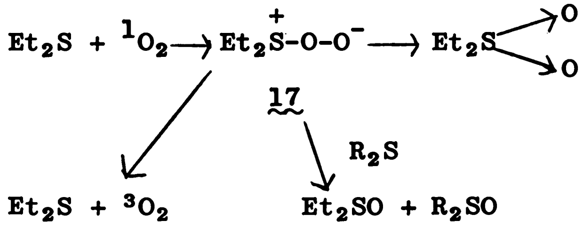
with the semidione into epoxide and ozone. Thus the inclusion of ion radicals among the reactive intermediates for photo-oxidation greatly widens the mechanistic possibilities among which a decision must be made.

Another sensitizer which might be expected to generate a radical anion on excitation in the presence of an electron donor is 9,10-dicyanoanthracene (31). Although Foote and co-workers found this to be a sensitizer for oxygenation without any evidence of singlet oxygen being involved, yet its action in producing benzophenone from tetraphenylethylene suggested that the oxidation product was a dioxetane; no epoxidation was observed.

Cation radicals are strongly implicated in the series of catalysts discovered by Barton and coworkers (38) which, some photochemically and some thermally, produce peroxides from ergosteryl acetate and other dienes in methylene chloride at -78°. These catalysts, including Lewis acids, carbonium ions, or aminium ion radicals, are in remarkable contrast to those just mentioned in that they have not been observed to produce any epoxides. Dr. M. J. Shapiro has also found that Barton's cation radical $(p\text{-}BrC_6H_4)_3N^{+\cdot}$ converts biadamantylidene into dioxetane and not into epoxide. It is striking in this connection that the cationoid radical complex $(CH_3)_2N{\cdot}ZnCl_2$ (39) reacts, also thermally, with oxygen and olefins to yield, not peroxides, but epoxides, as inferred from the structure and configuration of the aminoalcohols isolated.

Photo-oxidation of Sulfides

Dialkl sulfides, like olefins, can undergo one-O or two-O oxidation, with the obvious difference that in a sulfone the two oxygen atoms do not remain bonded to each other. Foote and Peters (5) developed convincing evidence that singlet oxygen reacts directly with diethyl sulfide to yield a reactive peroxysulfoxide (17) which is capable of converting



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another sulfide molecule into sulfoxide, or of rearranging more slowly into sulfone, in competition with quenching by dissociation into sulfide and triplet oxygen. Cleavages attending the photooxidation of benzyl alkyl sulfides (40) could also be formulated as involving peroxysulfoxides derived from singlet oxygen. However, the photo-oxidation of sulfides sensitized by 9,10-dicyanoanthracene (31) also produced sulfoxides and sulfones. This oxidation was not inhibited by β-carotene, and showed a strong reversal of the relative reactivities of diphenyl and diethyl sulfides compared to those in singlet oxygen oxidation.

Another kind of evidence for the involvement of ion radicals in photo-oxidation comes from the observation of cleavage of certain sulfides (41) with formation of *unoxidized disulfides*. Unlike the benzyl alkyl sulfides (40), di-*t*-butyl sulfide gives on oxidation with several photosensitizers, in addition to the sulfoxide and sulfone, amounts of di-*t*-butyl disulfide varying from traces with rose bengal or methylene blue in methanol to 97 and 100% in acetone with rose bengal free and bound on polymer beads, respectively. The yield of the disulfide may be a measure of the relative rate at which the cation radical **18** dissociated to the *t*-butyl cation and the *t*-butylthiyl radical in the various media:

$$\underset{\mathbf{18}}{(CH_3)_3C\overset{+\cdot}{S}C(CH_3)_3} \rightarrow (CH_3)_3C^+ + (CH_3)_3CS\cdot \rightarrow (CH_3)_3CSSC(CH_3)_3$$

The other products of the photo-oxidations are mixtures of di-*t*-butylsulfoxide and di-*t*-butylsufone, these mixtures becoming steadily richer in sulfone as the reaction progresses. Although singlet oxygen generated *thermally* was capable of producing the sulfoxide and sulfone, the disulfide was absent from such thermal product mixtures.

Neither was disulfide produced with sensitizer in the absence of oxygen. In parallel irradiations of di-*t*-butyl sulfide, one under oxygen and the other under argon, no cleavage or any other reaction is seen in the experiment without oxygen. These results show that oxygen plays an essential part in generating the cation radicals, even though direct attack of singlet oxygen on the sulfide (as shown in the experiments with chemical generation) is no part

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of the process. This is further evidence supporting some such multi-step electron transfer process as that proposed by Jefford and Boschung in some of the epoxidation reactions.

Not surprisingly, although superoxide anion is implicated in the genesis of the cation radicals, a solution of potassium superoxide-crown ether in methylene chloride was without effect on di-t-butyl sulfide alone.

Di-t-butyl sulfide could be converted to disulfide in two hours at room temperature by tris-(p-bromophenyl)-aminium fluoborate in a stream of oxygen, but neither tetrahydrothiophene nor diphenyl sulfide underwent cleavage under these conditions.

Conclusions

Photo-oxidation has been shown to proceed, not only by concerted reactions with singlet oxygen, but through stepwise mechanisms involving neutral free radicals and radical ions. In some of the latter cases singlet oxygen is implicated in the genesis of the radical ions and their precursors, and the resulting radical reactions compete with the direct reaction of the singlet oxygen. Radical and cation-radical processes appear to be especially important in photo-epoxidation.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch002

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

3

Radical Production from the Interaction of Closed-Shell Molecules

Part 7. Molecule-Assisted Homolysis, One-Electron Transfer, and Non-Concerted Cycloaddition Reactions

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For some time, my research group has been interested in the processes by which closed-shell, stable molecules interact to produce free radicals (1-6). We have divided these reactions into three mechanistic types: molecule-assisted homolyses (MAH), one-electron transfers, and non-concerted pericyclic reactions. These processes usually occur at surprisingly moderate temperatures and often have an intriguing and challenging kinetic and mechanistic complexity. A large number of reactions of all three mechanistic types are now known.

Many of these processes find practical use. For example, some processes that appear to involve MAH reactions are used in chemical industry: the commercial polymerization of styrene often is self-initiated (7); the autoxidation of acetaldehyde is initiated by ppm levels of ozone (8); and some halogenations are clearly MAH processes (1,9). Electron-transfer reactions find practical use as low-temperature initiation systems: for example, benzoyl peroxide and dimethylaniline produce radicals at temperatures as low as 10°, perhaps by an electron transfer process (3, 4). Radical production from [2+2] cycloaddition reactions also has been clearly demonstrated by a number of workers, using both experimental and theoretical techniques (9a). However, the interception of the intermediate 1,4-diradicals by added radical trapping reagents has been reported in only a few cases (5,10-16).

In the limited space available here, I will not attempt a complete summary or a detailed review of the three classes of reactions; rather, I will present an eclectic report of a few reactions on which my own group has done research in the past several years.

First, let me define the three classes of processes which we will consider. Molecule-assisted homolyses generally have a formulation like that given in eqs 1a or 1b, where the homolysis of the A-B bond is assisted by some type of bond-formation process

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with molecule(s) C.* Electron transfer reactions can be formulated as shown in eqs 2a or 2b; these reactions can be followed by

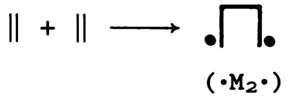
$$\text{A-B} + \text{C} \longrightarrow \text{A}\cdot + \text{BC}\cdot \qquad (1a)$$

$$\text{A-B} + 2\text{C} \longrightarrow \text{AC}\cdot + \text{BC}\cdot \qquad (1b)$$

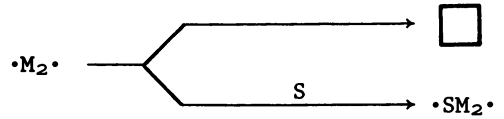
$$\text{A-B} + \text{C} \longrightarrow \text{A-B}\overset{+}{\cdot} + \text{C}\overset{-}{\cdot} \qquad (2a)$$

$$\text{AB} + \text{C:} \longrightarrow \text{AB}\overset{-}{\cdot} + \text{C}\overset{+}{\cdot} \qquad (2b)$$

the scission of the $\text{A-B}\overset{+}{\cdot}$ or $\text{A-B}\overset{-}{\cdot}$ bond. We shall limit our discussion of pericyclic reactions to [2+2] cycloadditions which lead to scavengable radicals; these processes can be described as in eqs 3 and 4, where S is a reactive molecule or radical that can trap the 1,4-diradical in competition with the ring closure reaction, eq 4a, leading to cyclobutanes.



(3)



(4a)

(4b)

Molecule-Assisted Homolyses

Introduction. The first systematic discussion of this field, to my knowledge, was by Semenov (17), in his book published in English translation in 1958. I discussed the principles of MAH reactions and reviewed a number of examples in my book in 1966 (1), and Benson (18) has considered the application of his thermochemical techniques to such processes. In 1974, Harmony presented a relatively complete survey of MAH reactions, including 150 references (9). Her review does not cover non-concerted cycloadditions, nor does she treat one-electron transfer reactions in depth. Her chapter also gives an unsatisfactory picture of

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*In the textbook "Free Radicals", ref. 1, I used the expression "molecule-induced homolysis" and the abbreviation MIH, a phraseology retained by Harmony (9). More recently, I have used "molecule-assisted homolysis" to avoid confusion of MAH processes with the induced decomposition of initiators caused by radicals, a propagation step, rather than an initiation process:

$$\text{AB} + \text{R}\cdot \longrightarrow \text{A}\cdot + \text{RB}$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

radical production from the self-initiated polymerization of various vinyl monomers ("thermal polymerizations"), but we have recently reviewed that area in detail (7). Nevertheless, her review does provide, for the first time, a compilation of most of the key references on MAH processes in non-polymer systems.

An accelerated homolysis is defined as one that proceeds at an accelerated rate over that expected for a simple unimolecular homolysis. If a compound A-B undergoes unimolecular homolysis, eq 5, the rate constant can be predicted from the Arrhenius equation, eq 6, where BDE(A-B) is the bond dissociation energy of the A-B bond (18). However, if AB undergoes an assisted homolysis

$$\text{A-B} \longrightarrow \text{A}\cdot + \text{B}\cdot \qquad (5)$$

$$k = A\exp(-E_a/RT) = 10^{16}\exp[-\text{BDE(A-B)}/RT]\ \text{sec}^{-1} \qquad (6)$$

with another molecule (or molecules) C, eq 7, then the heat of reaction for this process can only be calculated if the stoichiometry of the reaction is known. For example, if the process can be described by eq 1a, then the heat of reaction equals the BDE of the A-B bond minus that of the B-C bond; thus, the overall

$$\text{AB} + n\text{C} \longrightarrow \text{Radicals} \qquad (7)$$

endothermicity of the process is reduced. In general the activation energy also is reduced and an acceleration in the rate of the reaction is observed.

MAH Transfer of a Hydrogen Atom. The assisted transfer of a hydrogen atom, often from a C-H bond, is perhaps the most fascinating of these processes to an organic chemist. Assisted C-H bond homolyses were postulated very early to rationalize complex radical chain reactions. For example, in 1947 Hinshelwood (19) proposed that the primordial initiation process in hydrocarbon autoxidations is the spontaneous hydrogen abstraction reaction of oxygen, eq 8. This process remains controversial to this day (20, 21). Since oxygen is not a closed-shell molecule, but a ground

$$\text{RH} + \text{O}_2 \longrightarrow \text{R}\cdot + \text{HO}_2\cdot \qquad (8)$$

state triplet, eq 8 actually does not meet the formal definition of an MAH process. However, it is usually discussed with other examples, since it has a superficial similarity (and perhaps also because it has some of the same exasperatingly inaccessible experimental features).

A hydrogen atom transfer from carbon in an MAH process was proposed by Flory in 1937 to rationalize the spontaneous polymerization of styrene (7). He suggested that 1,4-diradicals are formed via eq 9 and are converted to monoradicals by the transfer reaction shown in eq 10. However, Hammond, Kopecky, and our group

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

have used kinetic isotope effects to rule out reaction 10 as the predominant process that converts diradicals to monoradicals in styrene (7).

$$2PhCH{=}CH_2 \longrightarrow Ph\dot{C}H{-}CH_2{-}CH_2{-}\dot{C}HPh \qquad (9)$$

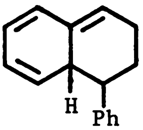
$$(\cdot M_2 \cdot)$$

$$\cdot M_2\cdot + M \longrightarrow PhCH{=}CH{-}CH_2{-}\dot{C}HPh + Ph\dot{C}H{-}CH_3 \qquad (10)$$

$$(HM_2\cdot) \qquad (HM\cdot)$$

Another mechanism for the spontaneous initiation reaction in styrene was proposed by Mayo in 1961 (7). It involves the reactions shown in eqs 11-12.

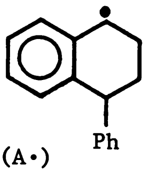
$$\underset{(M)}{2PhCH{=}CH_2} \xrightarrow[\text{dimerization}]{\text{Diels-Alder}}$$



(AH)

(11)

$$AH + M \xrightarrow{MAH}$$



$$+ HM\cdot \qquad (12)$$

(A·)

$$A\cdot\ (\text{or } HM\cdot) + M \longrightarrow M_n^{\cdot} \qquad (13)$$

(Growing polymeric chain radical)

Recently, the occurrence of the MAH process, eq 12, has been probed by two methods: (i) Buchholz and Kirchner (22) and Pryor and Patsiga (6a,20) used the uv absorption of AH to follow its rate of appearance and measure its steady state concentration. Buchholz and Kirchner obtain a steady state concentration for AH of about 0.6×10^{-4} M at 64°. (ii) We had previously published a computer simulation (23) of the thermal polymerization of styrene in which we assumed that eqs 11-12 were the only initiation mechanism; this simulation predicts the steady state concentration of AH to be 5×10^{-4} M at 60°. This certainly is in acceptable agreement with the later experimental measurement by Buchholz and Kirchner. In addition, our simulation gives the chain transfer constant for AH, i.e., k_{14}/k_{15}, to be about 1. Thus, AH is a remarkably reactive hydrocarbon toward radicals.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

(For example, the transfer constant of Ph_3CH is only 3×10^{-4} at 60^o (23a).)

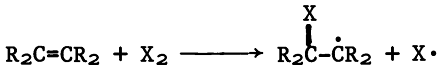
$$AH + M_n^\bullet \longrightarrow A^\bullet + M_n\text{-}H \tag{14}$$

$$M_n^\bullet + M \longrightarrow M_{n+1}^\bullet \tag{15}$$

A large number of MAH transfers of hydrogen atoms have been inferred, and in the space available here we can do no more than list a few to indicate the diversity and wide occurrence of the process. For example, reaction 16 was postulated by Semenov to rationalize gas phase cracking rates (17).

$$C_2H_5\text{-}H + CH_2{=}CH_2 \longrightarrow 2C_2H_5^\bullet \tag{16}$$

Many of the halogens give MAH reactions, but the mechanism usually involves attack on the halogen molecule by π-electrons from an unsaturated molecule as a halogen atom adds to the unsaturated linkage:



$$R_2C{=}CR_2 + X_2 \longrightarrow R_2\overset{X}{\overset{|}{C}}\text{-}\dot{C}R_2 + X^\bullet$$

However, some halogenations involve MAH H-atom transfers. The first example discovered, and perhaps the most clearly established occurs in the fluorination of organic materials (27). Here, the driving force is clearly the very large exothermicity of processes like eq 17; e.g., for propane, eq 17 would be 3 kcal/mole exothermic.

$$R\text{-}H + F_2 \longrightarrow R^\bullet + HF + F^\bullet \tag{17}$$

A variety of halogenation agents evidence MAH processes. Many of the reaction systems are quite complex, and it is not always clear whether C-H bond breaking is involved or not. For example, Walling and his coworkers have studied *tert*-butyl hypochlorite in detail. This reagent reacts with a variety of organic compounds, including ethers, aldehydes and alcohols in MAH processes (28).

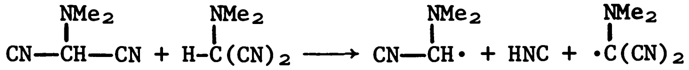
We have already mentioned the reaction of ozone with aldehydes, and the fact that an MAH process is used in commerce to initiate the autoxidation of acetaldehyde to produce peracetic acid. Ozone reacts with a wide variety of organic materials to produce radicals; these reactions are fascinating because they occur at very low temperatures and with almost every class of organic compound (29-33). Even alkanes react--in this case to give alcohols, eq 18.

$$RH + O_3 \longrightarrow [R^\bullet \; ^\bullet O_3H] \longrightarrow ROH + O_2 \tag{18}$$

Although the process is partially stereospecific, radicals are postulated to be involved (34,34a,35). We will return to this subject when we discuss reaction 19, in which the MAH of an O-H bond occurs.

$$\mathrm{ROOH + O_3 \longrightarrow ROO\cdot + HO\cdot + O_2} \qquad (19)$$

Radicals are produced in the low temperature reactions of dimethylaminomalononitrile, but the mechanism is unknown (36). An MAH scission of a C-H bond, eq 20, can be suggested (36), although this reaction would be strongly endothermic and probably too slow.



$$\mathrm{CN{-}\overset{NMe_2}{\overset{|}{C}}H{-}CN + H{-}\overset{NMe_2}{\overset{|}{C}}(CN)_2 \longrightarrow CN{-}\overset{NMe_2}{\overset{|}{C}}H\cdot + HNC + \cdot\overset{NMe_2}{\overset{|}{C}}(CN)_2} \qquad (20)$$

Assisted transfers of a hydrogen atom from two other atoms—sulfur and oxygen—might be mentioned to demonstrate the variety of MAH processes. Hiatt and Bartlett (24) have shown that ethyl thioglycolate and styrene react to produce radicals. At high thiol/styrene ratios, the rate of radical production is too fast to be accounted for by the thermal reaction of styrene with itself, and we (2,7) have suggested that the reaction is a direct MAH of an S-H bond, eq 21.

$$\mathrm{RSH + PhCH{=}CH_2 \longrightarrow RS\cdot + Ph\dot{C}H{-}CH_3} \qquad (21)$$

Styrene also reacts with hydroperoxides to produce radicals (25, 26). *A priori*, one might have thought that a hydrogen atom transfer would be involved, eq 22; however, isotope effect data of

$$\mathrm{ROOH + PhCH{=}CH_2 \longrightarrow ROO\cdot + Ph\dot{C}H{-}CH_3} \qquad (22)$$

Walling and Heaton do not support this formulation. This reaction system has some of the most complex and baffling kinetic and mechanistic difficulties of any MAH system yet studied.

Demonstration of MAH Hydrogen Atom Transfers from C-H Bonds.

The Self-Initiated Polymerization of Styrene and the Chemistry of Methylenecyclohexadiene (Isotoluene)

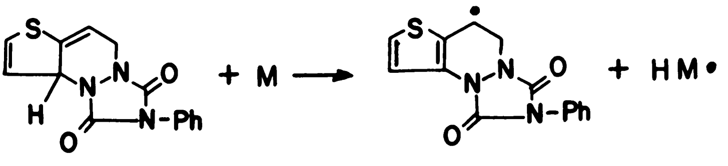
Introduction. The brief review given above indicates that MAH reactions in general, and assisted homolysis of C-H bonds in particular, can no longer be regarded *terra incognita*. Yet, few systems are well understood or have mechanisms that are known with certainty. Our love affair with this field began some twenty years ago with studies of the thermal polymerization of styrene.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

This is a particularly fascinating process. Styrene is an unusually stable molecule (it has only vinylic and aromatic hydrogens) and yet it initiates its own polymerization at a well-defined and reproducible rate. (The rate is about 1%/hr at 90°.) The initiation reaction has been convincingly shown to involve styrene itself, and not some adventitious impurity (7).

Currently the most popular mechanism to rationalize the self-initiated polymerization of styrene, eqs 11-13, involves the formation of the Diels-Alder adduct, AH, from two styrene molecules, and the MAH reaction of this dimer with a third styrene molecule. This novel and very elegant mechanism was originally suggested by Frank Mayo, and derived from his observation of phenyltetralin and phenylnaphthalene among the oligomers. It is clear that AH is the source of the phenyltetralin-type products. However, while a critical review (7) of the evidence establishes that AH is present during polymerization, there is no conclusive evidence that it is involved in eq 12, the MAH step.

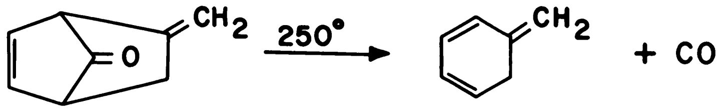
No synthesis or isolation of AH has been reported, although our recent work (6) suggests that AH could be prepared *in situ*, at least. However, we have reported the synthesis of an analogue of AH which was chosen so as to have a lower driving force for H-atom transfer (and consequently to be more easily isolable than AH) and still be sufficiently reactive so as to be able to initiate the polymerization of olefins by an MAH mechanism. The adduct, BH, formed from 2-vinylthiophene and 4-phenyl-1,2,4-triazoline-3,5-dione, appears to have this property. Solutions (0.01 to 0.1 M) of BH appear to initiate the polymerization of styrene and also of methyl acrylate, a monomer which does not initiate its own polymerization, eq 23.



(23)

(BH) (B•)

MAH Reactions of Methylenecyclohexadiene (Isotoluene). In a quest for a simpler and perhaps more reactive model for AH, my group (6,6a), and Kopecky and Lau (37) independently and simultaneously, have studied the reactions of methylenecyclohexadiene (MCH). Initially, both we and Kopecky utilized the synthesis invented by Bailey (38), but that method can provide only dilute solutions of MCH and requires repetitive and time-consuming preparative glpc separations. Therefore, both groups developed new syntheses. Ours utilizes the pyrolysis of compound I.



(24)

(I) (MCH)

Surprisingly, MCH is relatively stable in acid free, degassed heptane or benzene; however, MCH does rearrange to form toluene with a half life of about 50 hrs at 80^{o}.* However, MCH decomposes in styrene solution (ca. 10^{-3} M) with a first order rate constant of 4.3×10^{-4} sec^{-1} at 60^{o}, corresponding to a half life of 27 minutes. This accelerated disappearance of MCH in styrene could be due to several processes: (1) an MAH initiation reaction; (2) a Diels-Alder reaction of MCH with styrene or, less likely at the concentrations studied, with itself; (3) an ene reaction of MCH with styrene or itself; (4) chain transfer of MCH with the polystyryl radical produced from the self-initiated polymerization of styrene.

Fully expecting that MCH would initiate the polymerization of styrene, we investigated solutions from 0.001 to 0.01 M at 60^{o}. To our disappointment and considerable surprise, MCH does not cause an increase in the observed rate of thermal polymerization. Kopecky and Lau have reached the same conclusion.

As I have said, the half life of MCH is about 27 minutes in styrene at 60^{o}, and only a few percent of the styrene is converted to polymer in the first hour of reaction. Therefore, we were concerned that the transfer and ene reactions of MCH might be depleting its concentration so rapidly that there was none left to undergo the MAH reaction. That is, we were concerned that we had not used sufficiently high initial concentrations of MCH to observe initiation by it. However, as I will show below, this is not the case. Before we consider the possible reactions of MCH and the fraction of MCH undergoing each possible pathway, let's examine the possible reactions of AH itself.

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*The rate appears to be slower in the presence of hydroquinone, suggesting a radical chain mechanism for the rearrangement of MCH to toluene (6b). (In the presence of oxygen, the product of the reaction is benzyl hydroperoxide (6b).) However, it is difficult to find an inhibitor that produces a radical that does not abstract hydrogen from the super-reactive MCH. (For example, DPPH and galvinoxyl destroy MCH, and of course styrene cannot be used as an inhibitor.) Thus, it is difficult to prove that the rearrangement involves a radical chain.

Figure 1 shows the reactions of AH, and it can be seen that major processes using up AH are: the formation of trimer, the MAH process, and chain transfer. The rate constants for all three of these reactions can be estimated in the following way (6,6a). If it is assumed that all of the trimeric product A-Sty is produced by an ene reaction (eq f in Figure 1A) rather than by radical recombination, reaction h, then the rate constant for the ene reaction of AH can be calculated from the rate of appearance of the trimer A-Sty measured by Buchholz and Kirchner (22)* The rate constant for transfer of AH can be calculated from its transfer constant, obtained from our computer simulation (23), and the known value of k_p for styrene. And finally, the rate constant of the MAH reaction of AH can be calculated from the rate at which radicals are formed in styrene (calculated from the observed rate of thermal polymerization), assuming that all radicals come from this postulated MAH reaction. The steady state concentration of AH was measured by Kirchner, and is 6×10^{-5} M at about 60^{o}. Thus, knowing the rate constants for the ene, MAH, and transfer reactions of AH, and the steady-state concentration of AH, the fraction of AH that undergoes each of these three reactions can be calculated. Table I shows these rate constants and also shows the percent of AH that reacts by each of these paths. The data are quite surprising: 94% of AH undergoes an ene reaction, and only about 4% undergoes an MAH process. Transfer is even less important, despite the large transfer constant. Table I also gives the moles of AH that pass through each pathway in the first hour of reaction; as can be seen, 7×10^{-7} moles of free radicals are produced.

For MCH, a similar conclusion is reached (6,6a). Kopecky and Lau showed that almost all of the MCH is converted to the ene (or radical recombination) product. Thus, we can set the rate constant for the ene reaction as approximately equal to the total rate constant (measured by uv) for the disappearance of MCH. Again, the transfer constant is known (see below), from which the rate constant for transfer can be calculated. If we *assume* that the rate constants for the MAH reactions of MCH and AH are equal,

---

*It is not likely that all A-Sty trimer arises from an ene reaction. (I.e., from reaction f in Fig. 1A.) As I have pointed out (7), phenyltetralin probably arises from the disproportionation reaction of caged radicals, shown as eq i in Fig. 1A. (Any A· that diffuses into free solution would be expected to add to styrene and not to abstract hydrogen to give phenyltetralin.) If cage disproportionation occurs, then cage combination also must occur. (See eq h in Fig. 1A.) However, the conclusion reached here is not dependent on whether trimer arises from the combination of radicals within a cage or an ene process, since neither reaction produces free radicals that can initiate the polymerization of styrene.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

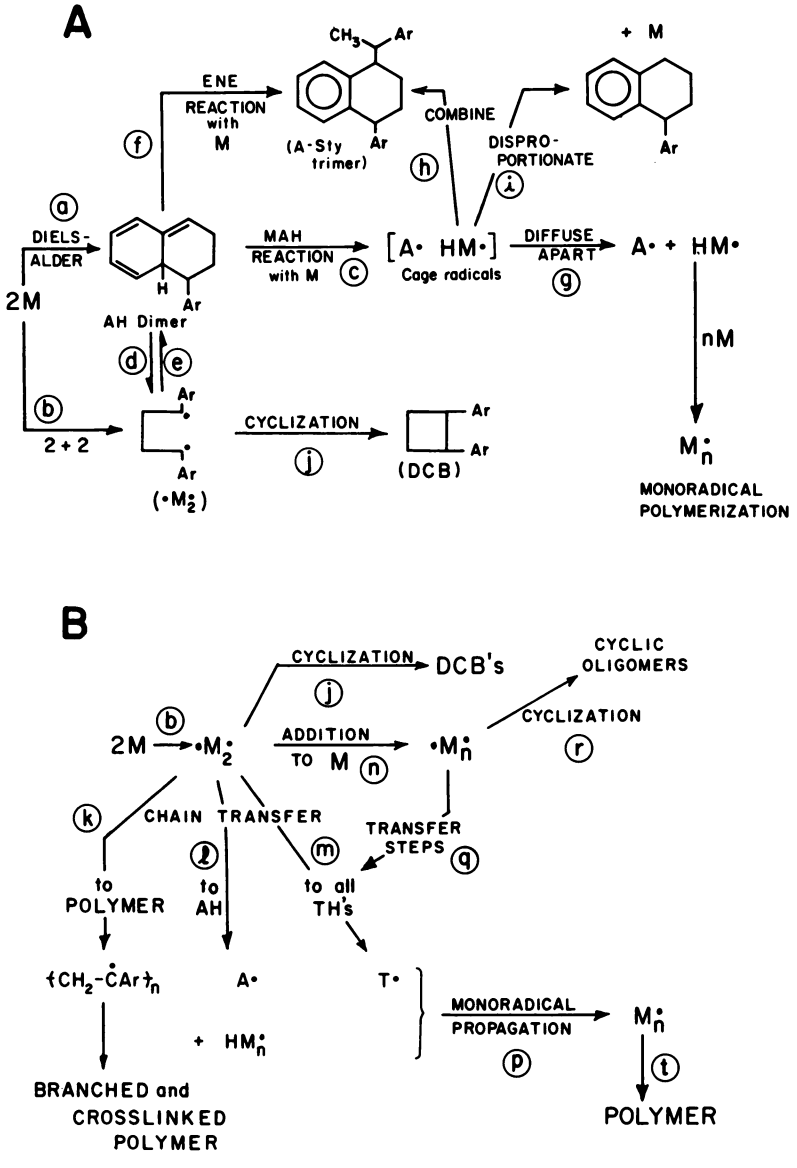

Figure 1. (A) This chart outlines the Diels–Alder dimerization of 2 styrene monomers (or similar vinyl aromatics) to form AH and the subsequent possible reactions of AH to give oligomers or to produce free radicals. The [2 + 2] cycloaddition of 2 monomer units to form the 1,4-diradical $\cdot M_2\cdot$ also is shown. (B) The reactions of 1,4-diradical that convert it to oligomers such as dicyclobutanes (DCB) or to monoradicals. (See Refs. 5, 6, and 7.*)*

then the data in Table I are obtained: virtually all of the MCH disappears by the ene reaction and less than 1% disappears by transfer or by an MAH process. However, by doing a point-by-point integration of the amount of MCH that goes through each reaction, the number of moles of MCH that would have undergone the MAH reaction in 1 hour is calculated to be 6 x 10^{-5}. Thus, if we assume that the rate constants for the MAH reactions of MCH and AH are identical, then 85-fold more moles of radicals would have been produced in 1 hour from a solution initially 0.01 M in MCH than are produced by the steady state (6 x 10^{-5} M) concentration of AH. If this were true, the rate of thermal polymerization (proportional to the square root of the rate of initiation) would be observed to increase by about 9-fold in the MCH solution. Since we could easily observe an increase in $R_{p,th}$ of 2-fold, the rate constant for the MAH reaction of MCH must be at least 21-times smaller than that for AH.

Thus, the calculations shown in Table I can be summarized as follows. If we assume that MCH and AH undergo an MAH reaction with the same rate constant, then an initially 0.01 M solution of MCH (the most concentrated we studied) would produce 85-times more radicals in 1 hour than does the steady state concentration of AH, despite the fact that only a very small fraction of MCH undergoes the MAH reaction. Since this would produce a rate of polymerization 9-times greater than the thermal rate, our initial assumption that MCH and AH undergo the MAH reaction with the same rate constant must be in error. In fact, since we could quite easily detect a 2-fold increase in the rate of polymerization, the rate of radical production from MCH must be at least 21-fold slower than for AH.

We also measured the transfer constant of MCH, and it is about 10 at 60°. Thus, MCH is extraordinarily reactive toward radicals; 10 is not only the world's record for a transfer constant for a hydrocarbon, but it is one of the largest transfer constants known. Only thiols and transition metal compounds have transfer constants this large or larger. For comparison, the transfer constant of triphenylmethane (in styrene at 60°) is about 10^5 smaller than that of MCH! Despite this strikingly large transfer constant, MCH undergoes the MAH reaction an order of magnitude (or more) more slowly than does AH. Surely this is extremely surprising and is hard to reconcile with the Diels-Alder mechanism for the initiation of styrene.

There are two possibilities at this point. The most conservative is that MCH is a poor model for AH; this allows the postulated MAH reaction of AH to be retained as the initiation process in styrene. The least conservative is that the entire Diels-Alder mechanism for styrene's initiation is wrong!

It certainly does seem possible that MCH is a poor model for AH, and that MCH might undergo a more nearly concerted ene reaction than does AH, thus giving a smaller yield of free radicals. Figure 2 outlines the reactions of an MCH-like molecule.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

Table I. A Comparison of the Rate Constants for Reaction and Moles Reacted in 1 Hour for AH and MAH in Styrene at 60° (6)

	$[AH]_{ss} = 6 \times 10^{-5}$[a]			$[MCH]_o = 0.01$[b]		
Process	k	Moles/hr[c]	%	k	Moles/hr[c]	%
Ene	8.5×10^{-6}[d]	1.6×10^{-5}	94.	--	--	80-100[h]
Transfer	145[e]	2×10^{-8}	0.1	10^3[i]	4×10^{-5}	0.5
MAH	3.7×10^{-7}[f]	7×10^{-7}	4.	$[3.7 \times 10^{-7}]$[j]	6×10^{-5}	0.7[k]
Total	9.0×10^{-6}[g]	1.7×10^{-5}	100.	5.3×10^{-5}[i]	8.2×10^{-5}	100.

(a) Steady state AH concentration (22). (b) The half life of MCH is 0.5 hr (6). (c) Moles reacted by this path in first hour by point-to-point integration. (d) from ref (22). (e) from ref (23). (f) Calculated from the rate of radical appearance indicated by the observed rate of thermal polymerization. (g) from the measured rate of AH appearance (22) and assuming that $-d[AH]/dt = +d[AH]/dt$ at the steady state. (h) Ref (37). (i) Ref (6). (j) Assumed as identical to the AH value. (k) Not in agreement with experiment. Clearly, the value of k_{MAH} must be smaller for MCH than for AH.

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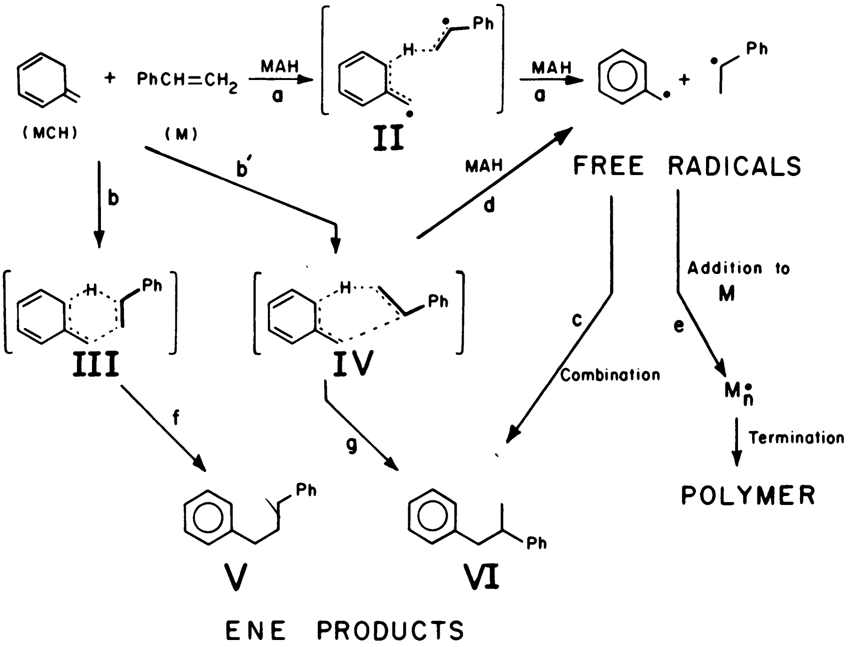


Figure 2. Possible reactions of methylenecyclohexadiene (MCH) and the formation of ene products. Compound VI can be produced either by a concerted ene reaction or by a process (Equations 2a and 2c) involving diradicals. The possible leakage of radicals from the ene reaction's extended transition state (II) to initiation polymerization is shown (6, 6a).

Ene products V and VI can be produced by reactions **b** and **b'**. In addition, one of the ene products, VI, can be formed by the recombination of free radicals, reactions **a**,**c**. (Kopecky and Lau have reported that V and VI are produced in approximately a 1:3 ratio from MCH.) For a more hindered molecule such as AH, models indicate that an extended transition state such as II may be relatively more preferable to III or IV, thus explaining the larger yield of radicals relative to ene products. Alternatively, it is possible that a transition state like IV may have a more distorted shape for AH, and that more radicals "leak out" of the ene reaction via eq **d**. In either case, the faster rate of radical production from AH relative to MCH is rationalized as due to the greater hindrance in the AH-styrene reaction relative to the MCH-styrene ene process.

Thus, the faster production of radicals from AH relative to MCH could be rationalized in terms of an ene reaction that involves a transition state with varying amounts of radical character and leading to varying yields of scavengable free radicals. As the argument has been presented above, this rationalization does not appear to be impossible. However, Figure 3 shows a tabulation of all of the model compounds synthesized to date in an attempt to model the behavior of AH. Although the second and third compounds in the list are reported to initiate polymerization, MCH does not. Furthermore, as shown in Figure 3, a compound that would appear to give an even more hindered ene reaction transition state than AH also does not initiate the polymerization of styrene (private communication from D. Aue). This is hard to reconcile with a rationalization of the lack of MAH reaction by methylenecyclohexadiene based on the hindrance of its ene reaction.

There are other problems with the Diels-Alder mechanism. For example, it appears from UV evidence that AH builds up to its steady-state concentration so slowly that an induction period should be observed in the rate of polymerization. However, none has been reported, although an induction period in chain transfer by AH is easily observed (6a).

Thus, I suggest that the Diels-Alder mechanism can continue to be accepted as the mechanism for initiation as long as it is clearly recognized that it is *not* conclusively established and that it may be incorrect. If the Diels-Alder mechanism *is* wrong, it is difficult to suggest a superior mechanism to take its place. The only mechanism that has been suggested and not yet disproven is one involving 1,4-diradicals (5,7), and it too has its difficulties (5). The only conclusive experiment appears to be the synthesis and testing of AH itself, and we are attempting to do that.

The Reaction of Ozone with *tert*-Butyl Hydroperoxide. An MAH Hydrogen Atom Transfer from Oxygen

Introduction. As we have remarked above, ozone reacts with

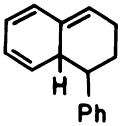
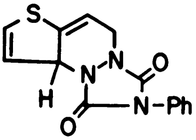
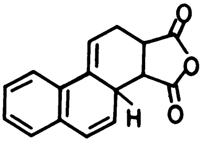
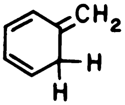
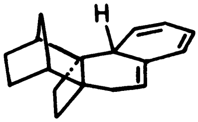
Compound	Initiation	Reference
	?	Pryor, Lasswell Adv. Free Radical Chem **5** (1975)
	Yes	Pryor, Coco, Houk, Daly JACS (1974)
	Yes	Sato, Abe, Otsu Makromol Chem 1977
	No	Pryor, Graham, Green 1977 Kopecky, Lau 1977
	No	D. Aue, A. Kos 1976 Unpublished

Figure 3. Compounds synthesized and tested as models for AH. The Diels–Alder adduct of styrene, AH itself, is shown at the top of the figure; it is postulated to initiate the polymerization of styrene. Of the models tested, two initiate and two do not.

virtually every type of organic molecule to form radicals (29,30, 31). Our interest in ozone was sparked by indications that the pathology caused by ozone in smog is partially due to the autoxidation of polyunsaturated fatty acids (PUFA) in lung lipids initiated by ozone (32,51). *A priori*, several mechanisms can be envisioned for radical production from O_3-substrate reactions.

(*i*) The simplest radical-producing reaction is the unimolecular homolysis of ozone, eq 25. The heat of this reaction is

$$O_3 \longrightarrow O_2 + O \qquad (25)$$

25 kcal/mole (assuming O_2 is formed in its ground state), predicting a half life for ozone of 10^4 hrs at -20°, 10^2 at 0°, and 10 min at $37^\circ C$ (18,39). Thus, eq 25 is too slow to be an important initiation process at the low temperatures at which ozonolyses are usually conducted, but it could play an important role at $37^\circ C$ in biological systems where ozone toxicity is observed.

(*ii*) Perhaps the next simplest radical-producing reaction would be an electron-transfer, eq 26. Bailey has suggested that

$$X + O_3 \longrightarrow X^{+}\cdot + O_3^{-}\cdot \qquad (26)$$

an initial electron transfer is responsible for the radical production observed at -78° in the reactions of ozone with trimesitylvinyl alcohol (40). If $O_3^{-}\cdot$ were produced, it might form reactive radicals. The rate constant for dissociation of $O_3^{-}\cdot$ in aqueous solution at 25°, eq 27, is 10^3 sec^{-1} (41). Thus, HO•

$$O_3^{-}\cdot + H_2O \longrightarrow O_2 + HO\cdot + HO^{-} \qquad (27)$$

could be the radical that initiates autoxidation (and pathology in bio-systems) in some of the reactions of ozone (42). This is reminiscent of the suggestion that the pathology caused by superoxide, $O_2^{-}\cdot$, is mediated by HO• radicals (43,43a,43b) generated by by the reaction of superoxide with H_2O_2, eq 28.*

$$O_2^{-}\cdot + H_2O_2 \longrightarrow O_2 + HO\cdot + HO^{-} \qquad (28)$$

---

*Reaction 28 is too slow to be important in biological systems (43b). However, we have recently shown that the reaction of the superoxide anion radical with organic hydroperoxides, eq *i*, is fast (45b). Since PUFA forms hydroperoxides *in vivo* both by an enzymatic path and by autoxidation, it appears that reaction *i* could be responsible for the HO• radicals observed in biological systems.

$$O_2^{-}\cdot + ROOH \longrightarrow O_2 + RO\cdot + HO^{-} \qquad (i)$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

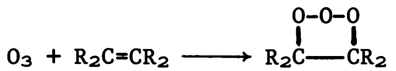
(*iii*) Ozone could undergo a concerted 1,3-dipolar insertion into a C-H bond or O-H bond, eq 29a (44,44a). When R-H is

$$R{-}H + \overset{\delta+}{O}{=}O{-}\overset{\delta-}{O} \longrightarrow RO_3H \longrightarrow ROO\bullet + HO\bullet \qquad (29a)$$

benzaldehyde, PhCO-OOOH is an intermediate and an insertion mechanism appears reasonable (35a). However, when R-H is an alkane, an MAH hydrogen abstraction mechanism is usually written, eq 29b, although the reaction is stereospecific (34,34a,35).

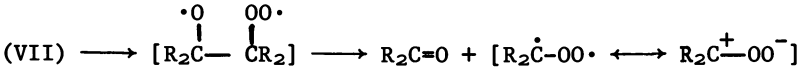
$$R{-}H + O_3 \longrightarrow [R\bullet \quad HO_3\bullet] \longrightarrow ROH + O_2 \qquad (29b)$$

(*iv*) Ozone reacts with olefins some 10^6 faster than with alkanes (44). Thus, in systems that contain olefinic unsaturation, the fastest reaction is addition of ozone to give the trioxide, eq 30. Even at 10^{-3} M olefin, this addition is so fast that ozone homolysis, eq 25, cannot compete at 37° C or below. The trioxide then undergoes rapid dissociation and recombination to form the Criegee ozonide, eqs 31-32.



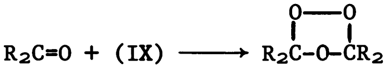
$$O_3 + R_2C{=}CR_2 \longrightarrow \begin{array}{c} O{-}O{-}O \\ |\qquad\quad | \\ R_2C{-}CR_2 \end{array} \qquad (30)$$

(VII)



$$\text{(VII)} \longrightarrow [R_2\overset{\bullet O}{\overset{|}{C}}{-}\overset{OO\bullet}{\overset{|}{C}}R_2] \longrightarrow R_2C{=}O + [R_2\dot{C}{-}OO\bullet \longleftrightarrow R_2\overset{+}{C}{-}OO^-] \qquad (31)$$

(VIII) (IX)



$$R_2C{=}O + \text{(IX)} \longrightarrow \begin{array}{c} O{-}O \\ |\qquad | \\ R_2C{-}O{-}CR_2 \end{array} \qquad (32)$$

Criegee ozonide

To the extent that the zwitterion-diradical, IX, has free radical character, it can be the source of initiating radicals:

$$\text{(IX)} + R'H \longrightarrow R_2\dot{C}OOH + R'\bullet$$

However, it appears doubtful that IX has sufficient lifetime and/or radical character to be the initiating species in PUFA autoxidations induced by ozone.

(*v*) We have shown that the Criegee ozonide does not homolyze to initiate autoxidation in PUFA-ozone-air systems (32,45). In contrast, the trioxide (VII) does dissociate at temperatures that are sufficiently low so as to rationalize radical production in olefins induced by ozone (46,47,48), but it is doubtful that the

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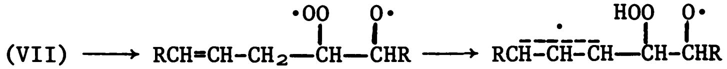
diradical produced in this dissociation, VIII, has sufficient lifetime to initiate PUFA autoxidation. In the gas phase, diradical VIII may undergo a "back-bite" reaction (51a):

$$\text{RHC}(\text{O}\cdot)\text{—CHR}(\text{OO}\cdot) \longrightarrow \text{RC}(=\text{O})\text{—CHR}(\text{OOH}) \tag{33a}$$

In analogy with this process, we have suggested (45a) that the trioxide formed from ozone addition to one of the double bonds in a polyunsaturated fatty acid can undergo the similar reaction, eq 33b, in which an allylic hydrogen atom is abstracted. Eq 33b



$$(\text{VII}) \longrightarrow \text{RCH=CH-CH}_2\text{—CH}(\text{OO}\cdot)\text{—CHR}(\text{O}\cdot) \longrightarrow \text{R}\overline{\text{CH-}\overset{\cdot}{\text{CH}}\text{-CH}}\text{—CH}(\text{HOO})\text{-CHR}(\text{O}\cdot) \tag{33b}$$

generates a diradical that may well have sufficient lifetime to initiate autoxidation.

(*vi*) Finally, radicals can be produced by MAH reactions of ozone with O-H bonds. In particular, the reaction of ozone with hydroperoxides might involve an MAH process, eq 34. We began

$$\text{ROOH} + \text{O}_3 \longrightarrow \text{ROO}\cdot + \text{HO}_3\cdot \tag{34}$$

investigating the reactions of ozone with hydroperoxides for several reasons. In the first place, radicals are produced at very low temperatures (47,48,49,50). Secondly, lipid hydroperoxides are produced during the autoxidation of PUFA by ozone-containing smog, and we wished to know if ozone reacts with these lipid hydroperoxides to produce radicals (32,51).

Analysis of the reaction of ozone with *tert*-butyl hydroperoxide in $CHCl_3$, CCl_4, or $CFCl_3$ as solvents at temperatures from 24 to -60° showed that the products are *tert*-butyl alcohol, acetone, water, and di-*tert*-butyl peroxide (44,44a). The reaction scheme, shown in eqs 35-43, rationalizes these products as resulting from free radical reactions of ozone and the hydroperoxide, where T = *tert*-C_4H_9.

$$\text{TOOH} + \text{O}_3 \xrightarrow{\text{i}} \text{TOO}\cdot + \text{HO}\cdot + \text{O}_2 \tag{35}$$

$$\text{HO}\cdot + \text{TOOH} \xrightarrow{\text{i}'} \text{H}_2\text{O} + \text{TOO}\cdot \tag{36}$$

$$2\text{TOO}\cdot \overset{K}{\rightleftharpoons} [\text{TO}_4\text{T}] \xrightarrow{a} [2\text{TO}\cdot + \text{O}_2] \xrightarrow{f} \text{TOOT} + \text{O}_2 \tag{37}$$

$$[2\text{TO}\cdot + \text{O}_2] \xrightarrow{(1-f)} 2\text{TO}\cdot + \text{O}_2 \tag{38}$$

$$\text{TO}\cdot + \text{TOOH} \xrightarrow{p} \text{TOH} + \text{TOO}\cdot \tag{39}$$

$$TO\cdot \xrightarrow{\beta} CH_3COCH_3 + CH_3\cdot \tag{40}$$

$$CH_3\cdot + O_2 \xrightarrow{o} CH_3OO\cdot \tag{41}$$

$$CH_3OO\cdot + TOO\cdot \xrightarrow{t'} \text{Non-radical products} \tag{42}$$

$$TOO\cdot + O_3 \xrightarrow{x} [TO_5\cdot] \longrightarrow TO\cdot + 2O_2 \tag{43}$$

Under conditions where the production of acetone is insignificant (e.g., in $CFCl_3$ at -4^o), kinetic analysis of eqs 35-43 gives the rate laws shown in eqs 44 and 45.

$$\text{Rate}(-O_3) = k_i(\text{TOOH})(O_3) + k_x\left(\frac{k_i}{k_t}\right)^{\frac{1}{2}} (\text{TOOH})^{\frac{1}{2}} (O_3)^{3/2} \tag{44}$$

$$\text{Rate}(-\text{TOOH}) = \frac{2k_i}{f}(\text{TOOH})(O_3) + k_x\left(\frac{k_i}{k_t}\right)^{\frac{1}{2}} (\text{TOOH})^{\frac{1}{2}}(O_3)^{3/2} \tag{45}$$

Eq 44 can be rearranged to give eq 46. Thus, a plot of the quantity of the left side of eq 46 versus $\{[\text{TOOH}]/[O_3]\}^{1/2}$ should give a straight line with slope equal to k_i and intercept $k_x(k_i/k_t)^{1/2}$. We have performed the analysis in $CFCl_3$ at -4^oC both for TOOH and for the deuterated hydroperoxide, TOOD.

$$\frac{\text{Initial rate}(-O_3)}{(O_3)^{3/2}\ (\text{TOOH})^{\frac{1}{2}}} = k_i\frac{(\text{TOOH})^{\frac{1}{2}}}{(O_3)^{\frac{1}{2}}} + k_x\left(\frac{k_i}{k_t}\right)^{\frac{1}{2}} \tag{46}$$

Our data give $k_i = 5.4\ M^{-1}\ sec^{-1}$ for *tert*-butyl hydroperoxide, and $k_H/k_D = 2.8$ for *tert*-BuOOD at -4^o. This primary isotope effect establishes the mechanism of eq 35 as an assisted scission of an O-H bond, rather than a rate limiting electron transfer followed by a rapid proton transfer, eqs 35a,b. In addition, the heat of

$$ROOH + O_3 \longrightarrow ROOH^{+}\!\cdot + O_3^{-}\!\cdot \tag{35a}$$

$$ROOH^{+}\!\cdot + O_3^{-}\!\cdot \longrightarrow ROO\cdot + HO_3\cdot \tag{35b}$$

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reaction of eq 35a can be shown to be too large for the electron transfer process to be facile (44).

Although the kinetic law for the reaction of ozone with *tert*-butyl hydroperoxide is complex with a first order and a chain term, under conditions where the hydroperoxide is present in 10-30 mole excess, 50-80% of the reaction goes by the first order process. (That is, calculations show that most of the reaction is due to the first term in eqs 44 and 45.) Under these conditions, approximate values of k_1 can be obtained by simply measuring initial rates. Data obtained in this way give an apparent activation energy for the reaction of ozone and *tert*-butyl hydroperoxide of 7 kcal/mole and a log A value of 7. Reaction 35 can be calculated to be 14 kcal/mole endothermic (44,44a), and the heats of reaction and activation energies for eqs 36-43 have been measured or can be calculated using Benson's methods. Thus, the activation energies for the two terms in the kinetic law, eq 46, are calculated to be about 14 and (5 + 14/2 - 8/2) = 8 kcal/mole, respectively. Thus, depending on the kinetic chain lengths, the observed activation energy for this mechanism is predicted to be between 14 and 8 kcal/mole, in excellent agreement with the observed value of 7 kcal/mole.

The heat of reaction for a concerted 1,3-insertion by ozone into the O-H bond also can be calculated using Benson's estimate of the group term for an oxygen atom attached to two other oxygens (18). This calculation shows that the direct insertion to form *tert*-butyl hydropentoxide as an intermediate is far too endothermic to be allowed by our approximate activation energy of 7 kcal/mole (44,44a). The calculated heats of reaction for the insertion process are shown over the arrows in eq 35c.

$$\mathrm{TOOH} + \mathrm{O_3} \xrightarrow{\Delta H = +25} \mathrm{TO_5H} \xrightarrow{\Delta H = -11} \mathrm{TOO\cdot} + \mathrm{O_2} + \mathrm{HO\cdot} \qquad (35c)$$

By the same approximate technique that was used to obtain activation energies, the rates for reaction of ozone were determined for a variety of types of organic species. Table II gives data of this type. It can be seen that the relative rates of reaction of ozone with alkenes: ROOH: alkanes is approximately in the ratios of 10^6: 10^3: 10^1.

1,4-Diradicals from [2+2] Cycloaddition Reactions

1,4-Diradicals. Orbital symmetry arguments suggest the [2+2] cycloaddition should not be concerted, and experiments of various types suggest that these reactions do, indeed, involve diradicals (9a,53-55). The arguments are primarily based on the lack of stereospecificity in cycloaddition reactions. However, recently, several reports have been published in which 1,4-diradicals have been trapped by added reagents. Table III presents these data. Most of the diradicals are produced photochemically,

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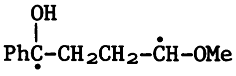
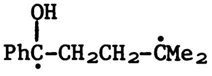
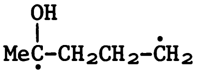
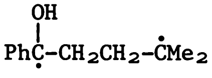
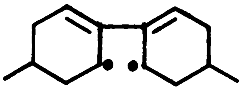
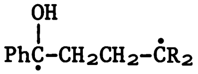
Table II. Approximate Second Order Rate Constants for the Reaction of Ozone with a Series of Organic Compounds in CCl_4 at 24° (44,57)

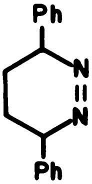
Substrate	$k(M^{-1}sec^{-1})$	k_{rel}
2,3-Dimethylbutane	0.2	(1)
Cyclohexane	0.02	0.1
tert-Butyl alcohol	0.02	0.1
Cyclopentanol	1.3	6.
Benzene	0.05	0.2
tert-Butyl hydroperoxide	37.	185.
1-Pentene	8×10^4	4×10^6

Table III. Trapping of 1,4-Diradicals by Scavengers

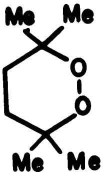
Diradical	Scavenger	Diradical half life (sec)	Ref
$C_6F_5\dot{C}H-CH_2CH_2-\dot{C}HC_6F_5$	$C_6F_5CH=CH_2$	-	(56)
 $\mathrm{Ph}\overset{\mathrm{OH}}{\underset{\bullet}{\mathrm{C}}}\mathrm{-CH_2CH_2-\dot{C}H-OMe}$	n-BUSH-d_1	10^{-6} - 10^{-7}	(10) (11)
 $\mathrm{Ph}\overset{\mathrm{OH}}{\underset{\bullet}{\mathrm{C}}}\mathrm{-CH_2CH_2-\dot{C}Me_2}$	O_2	-	(12)
 $\mathrm{Me}\overset{\mathrm{OH}}{\underset{\bullet}{\mathrm{C}}}\mathrm{-CH_2CH_2-\dot{C}H_2}$	HBr (gas)	$10^{-4.9}$	(14)
 $\mathrm{Ph}\overset{\mathrm{OH}}{\underset{\bullet}{\mathrm{C}}}\mathrm{-CH_2CH_2-\dot{C}Me_2}$	Methyl methacrylate	-	(13)
	$(t\text{-}Bu)_2NO\cdot$	-	(15)
 $\mathrm{Ph}\overset{\mathrm{OH}}{\underset{\bullet}{\mathrm{C}}}\mathrm{-CH_2CH_2-\dot{C}R_2}$	$(t\text{-}Bu)_2C=Se$	$10^{-6.4}$	(16)

and thus could be triplet series that must undergo intersystem crossing prior to ring closure to cyclobutanes. However, the recent report by Bottini in which a diradical produced by the thermal cycloaddition of 1-methyl-3,4-cyclohexadiene is trapped by a nitroxide suggests that sufficiently reactive trapping reagents can scavenge even singlet diradicals.

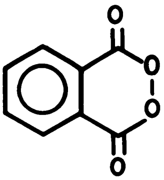
In addition to data of the type shown in Table III, a considerable literature exists for polymer systems; these latter data are much less well-known to chemists interested primarily in cycloaddition phenomena. The data are of two types. (*i*) Compounds that decompose to produce diradicals can, albeit somewhat inefficiently, initiate the polymerization of vinyl monomers. Compounds X-XIV are examples of diradical initiators that have



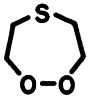
X



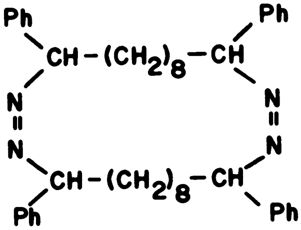
XI



XII



XIII



XIV

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been studied in this way (7). (*ii*) When olefins are heated in the presence of scavengers, the scavengers disappear. In the case of styrene, the scavengers often disappear faster than monoradicals are formed, and it has been suggested that the scavengers react with diradicals, with AH (Figure 1A), or with monomer directly. The field is complex, and we have reviewed all of the data in some detail (7).

Study of Pentafluorostyrene (PFS). A Particularly Likely Candidate for Initiation of Polymerization by 1,4-Diradicals? As was described above, my research group has been involved for some time with efforts to establish the Diels-Alder mechanism for initiation in the thermal polymerization of styrene suggested by Mayo. However, we also have argued that some of the initiation in styrene might be due to 1,4-diradicals. (See Figure 1B.)

It seems clear that all monomers do not undergo thermal polymerization by the same mechanism. For example, Table IV lists monomers that are susceptible to thermal spontaneous polymerization; at least some of those listed do not appear capable of forming a Diels-Alder adduct analogous to AH that could initiate by an MAH process. Furthermore, as is shown in Figure 1, the yields of dimers and trimers are indicative of the presence of oligomers that might be involved in initiation processes; and, as shown in Table V, the relative yields of dimers and trimers differ enormously when different monomers are compared.

In this regard, pentafluorostyrene (PFS) is particularly interesting. It undergoes a spontaneous polymerization at a rate that is slower than that of styrene, but still quite appreciable. There is some evidence that PFS might form diradicals (9a), but it does not appear to form a Diels-Alder adduct analogous to styrene's AH. Therefore, we have attempted to find evidence that the initiating species in the thermal polymerization of PFS is a 1,4-diradical (5). The stumbling block in any such diradical mechanism, and the factor that has mitigated against its general acceptance, is the mechanism by which the diradicals are converted to monoradicals (6,7). Since evidence of several sorts suggests that the polymer (at least in the styrene case) is formed via growth of monoradicals, and since it is clear that 1,4-diradicals would undergo rapid ring closure to form cyclobutanes (DCB's in Fig. 1B), a very rapid process must convert the diradicals to monoradicals if diradicals are to initiate polymerization.

We at first thought that this process for PFS might be that originally suggested for styrene by Flory, eq 10. Therefore, we investigated the polymerization of PFS-β,β-d_2. In this case, like that for styrene, no primary isotope effect is observed (5). Thus, if radicals are produced in PFS by eq 47, they are not converted to monoradicals by eq 48 to an appreciable extent.

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Table IV. Monomers that Undergo Thermal Polymerization (7)

Monomer	$R_{p,th}$ at 90° (%/hr)
Styrene	1
2-Bromostyrene	11
2-Fluorostyrene	2
PFS	0.03
3,4-Dichlorostyrene	7
2,4-Dichlorostyrene	20
2,5-Dichlorostyrene	15
2,6-Dichlorostyrene	0.01
Methyl methacrylate	0.01

Table V. Yields of Dimers and Trimers from Styrene and 2-Vinylthiophene (7)

	μ moles/100 g monomer			
		Dimers		
	Polymer	[4+2][a]	[2+2][b]	Trimers of A-Sty Type
Styrene, 85°	15	70	35	830
2-Vinylthiophene, 100°	20	900	--	0

(a) Derivatives of Diels-Alder dimers; e.g., phenyltetralin for styrene. (b) 1,2-Diarylcyclobutanes.

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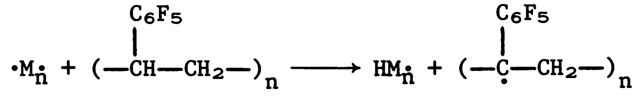
$$2\ \mathrm{PFS\text{-}d_2} \longrightarrow \mathrm{C_6F_5\text{-}\dot{C}H\text{-}CD_2\text{-}CD_2\text{-}\dot{C}H\text{-}C_6F_5} \qquad (47)$$

$$\mathrm{(XV)}$$

$$\mathrm{(XV)} + \mathrm{PFS\text{-}d_2} \longrightarrow \mathrm{C_6F_5\text{-}CH{=}CD\text{-}CD_2\text{-}\dot{C}H\text{-}C_6F_5} \qquad (48)$$

$$+ \mathrm{C_6F_5\text{-}\dot{C}H\text{-}CD_3}$$

In thinking about another mechanism by which diradicals might be converted to monoradicals in PFS, we became intrigued by the fact that very pure PFS precipitates at very low conversions and appears to be crosslinked. This suggests that the polymer is attacked by growing mono- or diradicals to cause branching and ultimately cross links, eq 49. Some of the oligomers that have

 (49)

$$\cdot\mathrm{M}_n^{\bullet} + (\text{—}\underset{}{\overset{\mathrm{C_6F_5}}{\mathrm{CH}}}\text{—}\mathrm{CH_2}\text{—})_n \longrightarrow \mathrm{HM}_n^{\bullet} + (\text{—}\underset{\bullet}{\overset{\mathrm{C_6F_5}}{\mathrm{C}}}\text{—}\mathrm{CH_2}\text{—})_n \qquad (49)$$

benzylic hydrogens could also undergo a transfer reaction of the same type; eq 50 shows this process for cyclobutanes.

 (50)

If chain transfer is the mechanism by which diradicals are converted to monoradicals, then the addition of transfer agents should cause an increase in the rate of polymerization. This experiment was tried very early in the study of styrene's thermal polymerization with negative results (7); in fact, it was one of the coffin nails in the diradical-initiation mechanism for styrene. However, for PFS, transfer agents such as toluene do increase the rate of polymerization (5). Table VI gives data on the effect of transfer agents on the rate of polymerization for both styrene and PFS (5). For styrene it can be seen that even very high concentrations of transfer agents do not affect the rate other than by diluting the concentration of monomer, and hence, reducing the rate of polymerization by a solvent effect. In contrast, for PFS, molecules with benzylic hydrogens such as toluene and diphenylmethane cause a dramatic increase in the rate of polymerization.

Figure 1B illustrates the possible fates of diradicals formed in styrene and PFS systems. They can cyclize to form cyclobutanes (eq j) or macrocyclic oligomers (eq x), they can react with polymer to yield polymer-radicals and HM• (eq k), or they can react with endogenous transfer agents that have benzylic hydrogens (TH's) to yield monoradicals (eq m). Possible TH molecules

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include the cyclobutanes and all other oligomers shown in Figure 1. Thus, our best suggestion at present for the mechanism of conversion of diradicals to monoradicals in PFS is that reaction m in Figure 1, the transfer process, is the critical monoradical-forming reaction (5). Although the arguments are not overwhelming, it does appear possible that the transfer reaction m could compete with the cyclization reaction j or r (5).

Table VI. Rates of Polymerization of PFS and Styrene in the Presence of Transfer Agents with Benzylic Hydrogens

Monomer	Transfer agent	Wht %	Rate %/hr	$R_{P,obs}/R_{P,calc}$ [c]
PFS[a]	None	--	0.17	(1)
	$PhCH_3$	8.3	0.24	1.5
	$PhCH_3$	8.4	0.28	1.8
	Ph_2CH_2	9.6	0.44	2.9
Styrene[b]	None	--	0.10	(1)
	PhH	43	0.05	0.9
	$PhCH_3$	47	0.05	0.9
	$PhCH_3$	43	0.05	0.9
	Ph_2CH_2	46	0.06	1.1

(a) 100°. (b) 60°. (c) The $R_{P,calc}$ values are obtained by assuming that the transfer agent acts only as an inert diluent, with no effect on the rate, and that polymerization is first order in monomer.

Abstract

A general review is presented of the mechanisms for reactions in which radicals are formed at accelerated rates by the interaction of closed-shell molecules. We have grouped these mechanisms into three classes: molecule-assisted homolysis, electron transfer, and non-concerted cycloaddition reactions.

The spontaneous thermal polymerization of styrene is postulated to involve an initiation step in which the reactive Diels-Alder dimer of styrene (AH in Figure 1A) undergoes a molecule-assisted homolysis reaction with another styrene molecule. The evidence for this process is reviewed, and it is concluded that it is not at all conclusive. Furthermore, methylenecyclohexadiene

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(MCH, eq 24) was synthesized, and, although it appears to be an excellent model for AH, it does not initiate the polymerization of styrene. The implications of this and similar experiments on the mechanism of the spontaneous initiation of styrene are discussed.

Reaction between *tert*-butyl hydroperoxide and ozone produces radicals at a rapid rate even at temperatures as low as -20°C. We have studied the kinetics of this reaction in $CFCl_3$ at -4°C and have obtained the kinetic isotope effect and an approximate activation energy. Using these data, both an electron-transfer reaction and a concerted 1,3-dipolar insertion reaction can be eliminated as mechanistic possibilities for the peroxide-ozone reaction. We conclude the mechanism involves a molecule-assisted homolysis:

$$TOOH + O_3 \longrightarrow TOO\cdot + O_2 + HO\cdot$$

The spontaneous polymerization of pentafluorostyrene (PFS) has been studied. It appears unlikely that this monomer undergoes an initiation by the Diels-Alder mechanism. Rather, we suggest it undergoes initiation by a mechanism involving 1,4-diradicals. Measurements of the kinetic isotope effects on the polymerization of PFS-β,β-d_2 prove that the 1,4-diradical is not converted to monoradicals by donating a hydrogen atom to another molecule of PFS. Instead, it appears that the 1,4-diradicals undergo chain transfer reactions with oligomers that possess benzylic hydrogens. (See Figure 1B.) If this is correct, then the capture of thermally produced 1,4-diradicals by transfer agents is sufficiently fast to compete with the closure of the diradicals to form cyclobutanes.

Acknowledgement

The work described in this report was done by a series of talented graduate students and post-doctoral fellows, and I want to acknowledge their considerable contributions. Without them, this chapter would not have been written. I particularly want to acknowledge the contributions of Professor Michael Kurz and Drs. W. David Graham, John G. Green, Masashi Iino, and Daniel Church.

This research was supported by grants from the National Science Foundation, the National Institutes of Health, and Dow Chemical Company. I express my sincere thanks to those agencies for their continuing support.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch003

4

Organic Peroxides as Free Radical Generators: Some Competitions

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch004

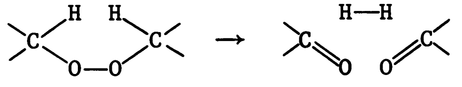
In the decomposition of peroxides many reactions compete with unimolecular homolysis and more than a few of these are thoroughly appreciated in a general, qualitative sense. Some quantitative information is available, but usually applies to conditions where the nonhomolysis reaction(s) predominate. Precise predictions for real-world situations fail through a superabundance of ignorance--a circumstance for which we offer no immediate remedy.

Three kinds of competing reactions are considered here: (1) electrocyclic decompositions; (2) free radical-induced decompositions; (3) decompositions by nucleophiles. Our results of the past few years, mainly for hydroperoxides and alkyl peroxides, are reviewed and some current specific problems are mentioned.

1. Electrocyclic Decompositions of Peroxides

A family of reactions involving concerted transfer of hydrogen from carbon to a hetero-atom may be discerned (1). Despite the dissimilarity of products, there are sufficient unifying

I. Peroxides



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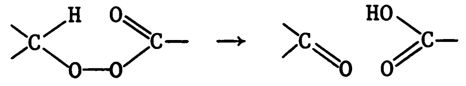
II. Peroxyesters



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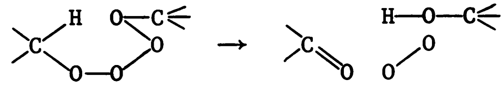
III. Tetroxides



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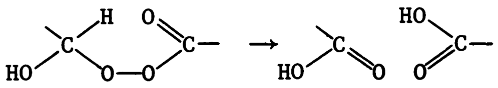
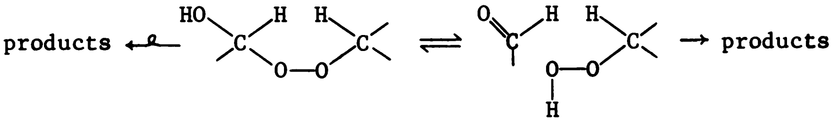
IV. Acylperoxy hemiacetals



(4)

features to justify the generic classification: all are thermally allowed and photolytically nonallowed by orbital symmetry rules. (Photolysis yields only alkoxy radicals in cases I and II. For III and IV the experiments would be much more difficult.) All proceed quite readily in nonpolar solvents but show a marked aversion to the vapor phase, in so far as known.[*] In some instances there are competing equilibria; e.g.,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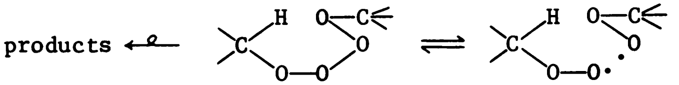
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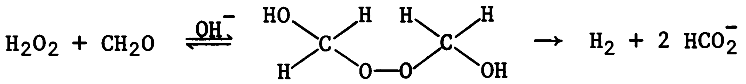
For all cases, the competing homolysis yields oxy radical pairs capable of self-disproportionation, a complicating feature for both product analyses and solvent-cage considerations.

Historically the reaction can be traced to Blank and Finkenbeiner (2) who found that dilute alkaline solutions of H_2O_2 and formaldehyde yielded H_2 quantitatively at room temperature.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The yield of H_2 obtained by heating hydroxymethylene peroxide in solution is also virtually quantitative, but very low upon vapor phase pyrolysis (3).

Yields of H_2 are only 40-75% in the thermal decomposition (80-110°C), of peroxyhemiacetals (4), but whether this reflects

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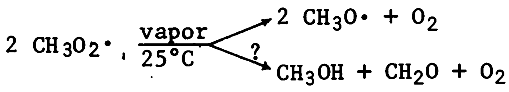
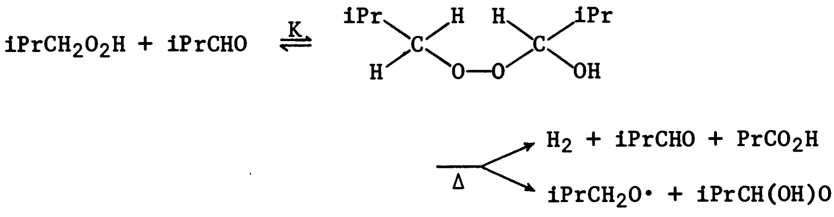
[*] For type III's the evidence is circumstantial. Gas phase kineticists evidently produce alkoxy radicals from peroxy radical species which in solution would yield only nonradical products. However for reactions such as



$$2\ CH_3O_2\cdot \xrightarrow[25°C]{vapor} \begin{cases} 2\ CH_3O\cdot + O_2 \\ ?\ CH_3OH + CH_2O + O_2 \end{cases} \quad (5)$$

the possibility of the competing electrocyclic route has not been considered and the efficiency of alkoxy radical production is unknown. For acylperoxyhemiacetals (type IV), there is as yet no reliable information.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch004



(9)

a more competitive homolysis or a partly dissociated peroxide is not clear.*

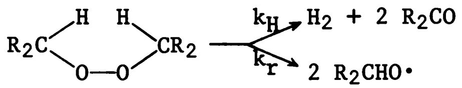
Table I reflects some of our own attempts to discover the

Table I. H_2 from Pyrolyses of Alkyl Peroxides (R_2O_2) in Solution

R	T°C	Solvent	% H_2^a	$10^5\ k_H^b$	E_{aH} kcal/mol
s-Bu	130.0	toluene	22	1.35	32.2
Ph_2CH	130.0	toluene	95	19.3	28.0
i-Pr	140.0	toluene	7.5	5.0	32.1
i-Pr	140.0	i-PrOH	8.4	28.5	
i-Pr	140.0	MeOH	30.5	67.2	17.2
i-Pr	140.0	H_2O	41.5	296	

[a] Based on total decomposition. [b] For H_2 formation, sec^{-1}.

factors governing the competition between homolysis and electro-



(10)

cyclic decomposition in sec-alkyl peroxides. Not unexpectedly a weaker C-H bond results in more rapid H_2 formation at the expense of O-O scission. (The α-hydroxyl groups, (vide supra), presumably exerts the same influence.)

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[*] Certainly some radicals are produced since induced decomposition is extensive in the absence of radical traps. However, measurements (5), (6) of the equilibrium constant at lower temperatures indicate that K can be no greater than 3-4 at 100°C. The variation in H_2 yields with initial concentration can be computer-modelled with fair success, assuming an induced term for free hydroperoxide decomposition.

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The phase effect has been more intriguing. Early attempts (7), (8) to demonstrate an effect of solvent polarity failed; neither k_H nor k_r is highly sensitive and the effects are qualitatively in the same direction. Recent work (9) using H_2O and alcohols as solvents (Table I) has shown a dependence. Log k_H correlates lineally with Kosower's Z-values (10). The acceleration in polar media may be due to the products being more polar than the starting peroxide or to dimunition of dipole-dipole interaction in the cisoid transition state--or both. In any case there is now an experimental basis for believing that the electrocyclic decomposition would proceed less rapidly in the vapor phase than in toluene or benzene.

The problem lies in the homolytic decomposition which also shows a real, if less pronounced, (and less readily explained) acceleration in more polar media. One correlation of log k_r with Z is not very good, but is excellent with the Hildebrand δ-values (11). Thus homolysis *should* be less rapid in the vapor phase than in toluene or benzene also, and should not completely overwhelm the electrocyclic decomposition--as it does. In fact, translation of alkyl peroxides from nonpolar solvents to the vapor phase has no measurable effect on their rates of homolysis, as the results of many workers attest (12), (13).

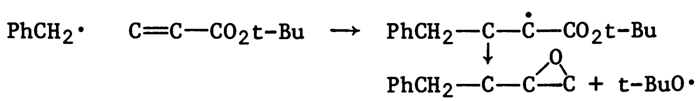
Of course, this new quandary is based on straight line mentality. Ideally a plot of log k_r vs. solvent "polarity" should curve upwards and have as slope assymptotically approaching zero at the low end of the scale. If we really understood the effect of medium on peroxide homolysis the correct solvent parameter probably would be obvious.

2. Free Radical-Induced Decomposition of Allylic Peroxides and Hydroperoxides

Alkyl peroxides may be attacked by free radicals at three sites: the O-O bond, a β C-H bond, or an α C-H bond, (if available). (The last mode has not been unambiguously demonstrated, except for Me_2O_2 in the vapor phase, where little else can happen.) Ordinarily it is not difficult to eliminate any induced component in a thermal decompositions; e.g., using toluene as solvent does the job for *sec*-alkyl peroxides.

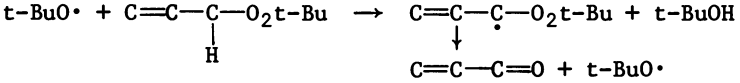
We have found allylic peroxides, i.e., allyl *tert*-butyl to be more susceptible (14). Heating 0.1-0.2 molar solutions in toluene at 130°C gives an estimated 14-15% induced decomposition, while DBPO-peroxide-toluene mixtures at 60°C yield similar results.

At the higher temperature at least half of the induced reaction results from benzyl radical addition followed by s_Hi.



(11)

At 60°C no epoxide was produced, although bibenzyl was, and the yield of t-BuOH was nearly quantitative. We conclude that the reaction here was

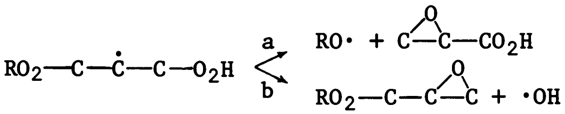


$$t\text{-}BuO\cdot + C{=}C{-}\underset{H}{C}{-}O_2t\text{-}Bu \rightarrow C{=}C{-}\dot{C}{-}O_2t\text{-}Bu + t\text{-}BuOH \downarrow C{=}C{-}C{=}O + t\text{-}BuO\cdot \quad (12)$$

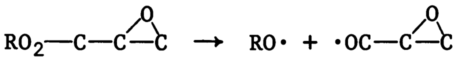
From the average peroxide concentration (0.14 M), the amount decomposed (0.0415 mmol), and the number of t-BuO•s involved (0.66 mmol), the rate constant for t-BuO• abstraction from $C{=}C{-}\overset{H}{C}{-}O{-}/H$ is calculated to be 5.5 times as great as for abstraction from $PhCH_3$. This seems about right,* and suggests that direct t-BuO• abstraction will also be a factor in the higher temperature self-induced decomposition.

Pyrolyses of allylic hydroperoxides have revealed a novel aspect of induced decomposition associated with addition to the double bond (16). Here there are peroxy radicals in the system as well, produced either from RO_2H by H-abstraction or from solvent radicals + O_2. Addition of peroxys leads to the sequence

$$RO_2\cdot + C{=}C{-}C{-}O_2H \rightarrow RO_2{-}C{-}\dot{C}{-}C{-}O_2H \quad (13)$$



(14)



(15)

Both branches are interesting: reaction 14a converts an inactive peroxy radical to alkoxy while converting the original hydroperoxide to a new one; reaction 14b + 15 converts a peroxy radical to three alkoxy's.

As yet we have not been able to isolate the presumed intermediates. Low temperature, extraneous radical-induced decompositions of 2,3 dimethyl-2-hydroperoxy-3-butene (TMEH) (16) gave some addition, and epoxide formation, when the radical was $CH_3\cdot$. With Ph_3C, however, the only induced product was Ph_3COH from S_H2 displacement. Clearly the propensities for alkyl radicals to attack at the several available sites require elaboration.

Thermal decompositions of allyl hydroperoxide have proved much more complicated than those of TMEH. For one thing, it is

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[*] Comparisons of t-BuO• and $t\text{-}BuO_2\cdot$ reactivity vs. $PhCH_3$ and Ph_3CH, and $t\text{-}BuO_2\cdot$ vs. $PhCH_3$ and $(PhCH_2)_2O$ (15) form the basis of this supposition.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch004

primary and subject to electrocyclic decomposition. H_2 is a major product and the kinetics are pseudo zero-order in RO_2H. Secondly, the allylperoxy radical loses O_2:

$$H_2C{=}CH{-}CH_2O_2\cdot \xrightleftharpoons{170°C} H_2C{=}CH{-}CH_2\cdot + O_2 \tag{16}$$

Products of allyl radical coupling are found, as well as solvent oxidation products, (PhCHO and $PhCH_2OH$).*

Thirdly, a problem with all allylic peroxides, but particularly severe here, the product α,β-unsaturated aldehyde (or ketone) polymerizes, incorporating other interesting products as well as some undecomposed hydroperoxide. The polymerization of acrolein by itself is gloriously complicated, and the nonvolatile residue from thermal decomposition of allyl hydroperoxide in toluene has so far defied analysis. Since the polymer constitutes the major, if not the only, chain termination product, some knowledge of its structure is necessary in order to obtain a free radical count and determine the efficacy of reaction 15.

3. Nucleophilic Reductions of Hydroperoxides

The extra oxygen of a hydroperoxide is readily removed by phosphines, arsenes and stibines (17). Other nucleophiles, e.g., sulfides and sulfoxides, amines, and olefines, accomplish this feat, though less rapidly (Table II).

Table II. $t\text{-}BuO_2H$ + Nucleophiles; Alone and with Vanadium Catalysis

N: (solvent)	$10^4\ k_2$[a]	(°C)	k_3, relative[b]	(°C)
Ph_3P (EtOH)	7200.	(35)	4×10^5	(25)
Ph_3Sb (EtOH)	5700.	(35)	1×10^6	(25)
Ph_3As (EtOH)	93.	(35)	2×10^5	(35)
Thioxane (H_2O)	1.35	(25)[c]	-	
Styrene (PhH)	0.0004	(70)[d]	6×10^3	(60)
Aniline (PhH)	-		1	(66)

[a] $M^{-1}sec^{-1}$. [b] Apparent third order rate constant with catalytic amounts of $VO(Acac)_2$ relative to aniline ($k_3 = 0.24\ M^{-2}sec^{-1}$). [c] Reference 18. [d] Reference 19.

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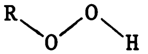
* The TMEH results are puzzling in contrast. Under identical conditions this hydroperoxide does not rearrange, as would be expected if eq. 16 were operative, nor are PhCHO and $PhCH_2OH$ among the products.



$$\mathrm{ROOH} + \mathrm{N\!:} \longrightarrow \mathrm{ROH} + \mathrm{N{\to}O} \qquad (17)$$

Competing with this reaction is the one-electron reduction giving MAH or MIRF (20). The 2-electron--but not 1-electron--reductions

$$\mathrm{RO_2H} + \mathrm{N\!:} \longrightarrow \text{Free Radicals} \qquad (18)$$

are enormously accelerated by certain metal ions or complexes; e.g., Mo^{VI}, V^{V}, some Fe porphyrins enzymes (Table II). Whether this says anything about MAH depends upon the mechanism of the metal catalyzed reaction.

The simplest view of the latter is that metal ion complexation reduces electron density on the peroxidic oxygen, facilitating nucleophilic displacement--just as H^+ catalyzes displacement by I^-. (If this is the case, MAH and 2-electron reduction can hardly share N^+—OH as a common intermediate.)

However there is some evidence for the involvement of metal ion-peroxo intermediates; $MoO(O_2)_2\cdot HMPA$ has been isolated from the reaction of MoO_3 with H_2O_2 and shown to epoxide olefins selectively (21), (22). Thus a more comprehensive sequence may be

$$\begin{tikzcd}
\mathrm{RO_2H + M} \arrow[r, shift left, "K"] & \mathrm{RO_2H\cdots M} \arrow[l, shift left] \arrow[r, "k_a", "\mathrm{N:}"'] \arrow[d, "k_b"] & \mathrm{[NOH^+\ ROM^-]} \arrow[r] & \mathrm{ROH + N{\to}O} \quad (19) \\
& \mathrm{M{-}O + ROH} & &
\end{tikzcd}$$

$$\mathrm{M{-}O + N\!:} \overset{K'}{\rightleftharpoons} \mathrm{M{-}O\cdots N} \xrightarrow{k_c} \mathrm{M + N{\to}O} \qquad (20)$$

The gross kinetics of the hydroperoxide-metal ion-nucleophile reaction can not distinguish between the two pathways. However, comparison of the apparent 3^d-order rate constants with the nucleophilicity of N--for a constant RO_2H—M system--might be useful. For very good and very poor nucleophiles, the rate will depend on nucleophilicity, with ka and $K'k_c$, respectively, rate controlling. Mediocre nucleophiles should not show this dependence since k_b will govern the rate.

Our own randomly collected data, Table II, show no evidence of this postulated triphasic curve. The leveling out in the P, As, Sb series might be the expected plateau, but could equally well indicate near diffusion control. More work is required. Additional work with $MoO(O_2)_2\cdot HMPA$ using a greater variety of nucleophiles, under conditions directly comparable to RO_2H—Mo date should also prove interesting.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch004

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

5

The Anchimeric Acceleration of *tert*-Butyl Perbenzoate Homolysis: Reactions on the Borderline between Radical and Ionic Chemistry

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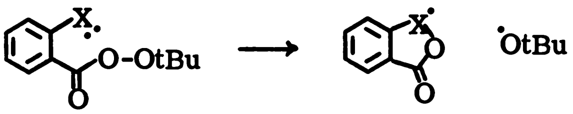
Substantial accelerations of radical formation by neighboring group participation in the homolysis of oxygen-oxygen bonds has been shown in several suitably substituted peresters and diacyl peroxides (1 - 8).



1 2

Ortho-substituted tert-butyl perbenzoates, 1, may show anchimerically accelerated bond homolyses leading to bridged radicals of type 2 plus tert-butoxy radicals.

Table I. Decomposition of 1 in Chlorobenzene

X	k_{rel} (60°)	ΔH*(kcal/mol)	ΔS*(eu)	Ref
SPh	2.78×10^4	23.0	-3.4	2
SCH_3	1.81×10^4	22.6	-5.5	2
SOPh	72.7	29.4	4.5	9
$CH{=}CPh_2$	67.0	26.3	-5.0	5
I	54.1	28.1	-0.7	2
$C(CH_3)_3$	3.8	34.2	12.5	2
SO_2CH_3	0.4^a	38.0	9.5	9
$C{\equiv}CPh$	1.8	35.4	15.0	10
H	1.0	34.1	10.0	4

[a] Relative to H at 120°C.

The formation of a stable bridged radical of type 2 requires the substituent to accommodate one additional electron beyond its ground state complement and one might expect the degree of

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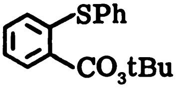
transition state stabilization from the formation of the X-O bond to reflect the ability of the substituent to provide a low energy orbital for this additional electron. We shall discuss reasons for expecting the parallel between the stability of 2 and transition state stabilization to be only approximate.

Mechanism of Reaction. The relative rates of Table I show that the largest accelerations so far observed result from participation of sulfide (sulfenyl) sulfur (2). The neighboring phenyl sulfinyl group shows a much smaller accelerating influence (9) while a sulfonyl substituent shows no acceleration (10). Neighboring iodine (2) and neighboring 2,2-diphenylvinyl (5) substituents provide substantial accelerations, while the very bulky *o-tert*-butyl (2) substituent shows no acceleration. This rules out explanations for the acceleration based on steric influences of the ortho substituent.



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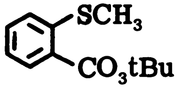
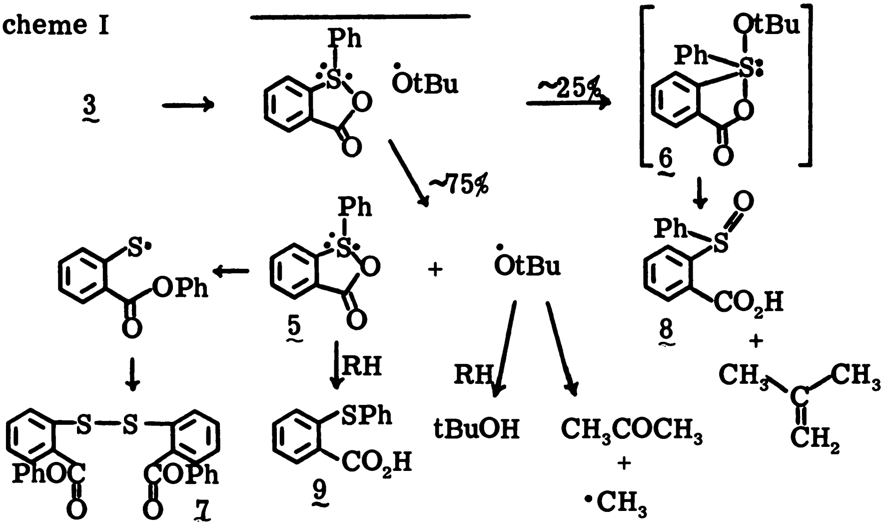


4

More work has been done (1-4, 6, 8) on systems with neighboring sulfenyl sulfur than on any of the other systems listed in Table I. The decompositions of 3 and 4 occur with very similar rates, both showing acceleration of more than 10^4 at 60° (2). We can therefore be reasonably sure that the sulfur of the phenylthio substituent, rather than the phenyl, is responsible for the observed acceleration. The products of decomposition of 3 observed in the original work of Bentrude (1, 2) are adequately explained by the mechanism originally proposed, that of Scheme I.

Scheme I

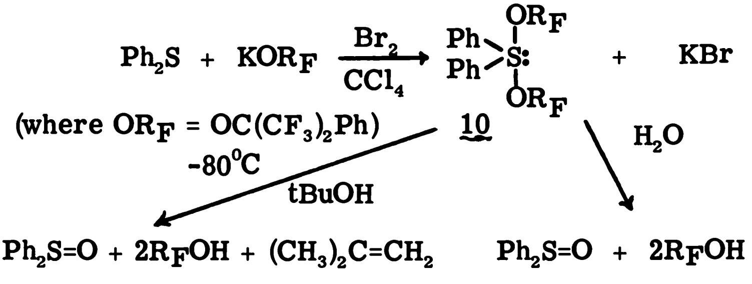


The initially formed cage radical pair was postulated to give free radicals to the extent of ca. 75% in chlorobenzene solution at 80°C, with free radical 5 giving 9 by hydrogen abstraction or 7 by S to O migration of the phenyl group. Under various conditions scavenging of reactive radicals produced in the reactions of Scheme I could be accomplished (using galvinoxyl as the scavenger) to the extent of 30-98% of the radicals expected.

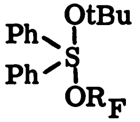
A minor pathway (ca. 25%) for the production of products from the radical pair was suggested to involve cage recombination to yield the tetracoordinate sulfur(IV) species 6. Although no precedents were at that time available for such species the postulate that 6 could serve as a reactive intermediate, precursor to 8 and isobutylene, provided an appealing economy of speculative mechanistic detail.

The suggested intermediacy of 6 led to the idea that a related species, lacking access to the pictured decomposition pathway in which a *tert*-butoxy ligand to sulfur loses a methyl proton to yield sulfoxide and isobutylene, might be stable enough to allow direct observation or isolation.

This idea was vindicated in the work of Arhart (11, 12) who succeeded in oxidative introduction of hexafluorocumyloxy ligands (OR_F) to the sulfur of diphenyl sulfide to give sulfurane 10, a crystalline material stable indefinitely at room temperature.



Sulfurane 10, a ketal analog of a sulfoxide, is very sensitive to moisture and reacts very rapidly at -80°C with *tert*-butyl alcohol to give isobutylene (13). Mechanisms studies (14) pointing to the intermediacy of a *tert*-butoxysulfurane 10a in the reaction of 10 with *tert*-butyl alcohol are consistent with the postulated intermediacy of 6 in Scheme I.

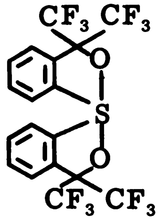


10a

The Five-membered Ring Effect. The remarkable stabilizing effect of a five-membered ring linking an apical with an equatorial position of a trigonal bipyramidal (TBP) molecule

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

has long been recognized in phosphorane chemistry (15) and has more recently been shown to be important in sulfuranes as well, since these sulfur(IV) species may be considered to have TBP geometry if the sulfur lone pair is considered to be one of the equatorial ligands. Sulfuranes stabilized by this five-membered ring effect (e.g., 11 and 12) are orders of magnitude less reactive than acyclic analogs 10 and 10a.



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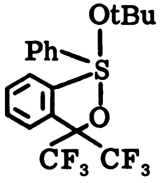
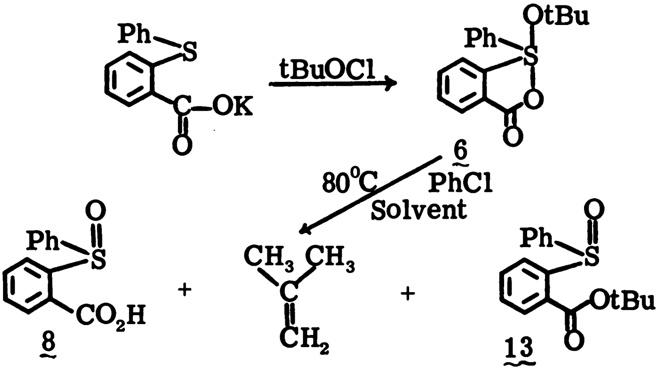


12

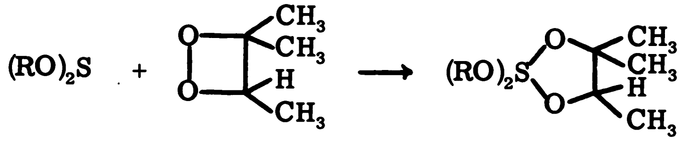
Characterization of the Sulfurane Intermediate. The great stability of these cyclic sulfuranes suggested the possibility that the postulated intermediate sulfurane (6) of Scheme I, a close analog of 12, might in fact have sufficient stability to allow its isolation and characterization. This was found by Livant (8) to be the case. The reaction of Scheme II produced 6 in high yield.

Scheme II



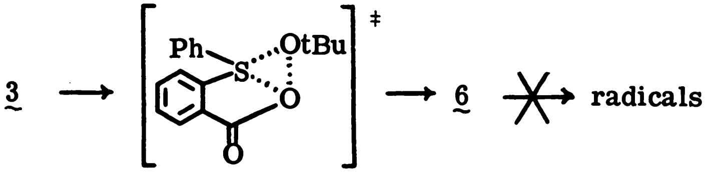
Sulfurane 6 was found to be a stable crystalline compound decomposing, by a reaction showing some autocatalysis by acid produced in the reaction, to give isobutylene and 8 in keeping with the postulate of Scheme I. An additional product, tert-butyl ester 13 was characterized in this reaction. It is sufficiently unstable that its conversion to 8 and isobutylene would probably have been complete after the long reaction times used in the earlier product studies of the decomposition of perester 3.

The failure to observe any radical products (9, 7 or acetone) in the decomposition of 6 allows us to rule out a mechanism for the anchimerically accelerated homolysis of 3 which begins with a biphilic insertion of sulfenyl sulfur into the O-O bond of 3 to yield 6 directly with 6 serving as the precursor to radical products. Analogous biphilic insertion reactions have been used to produce sulfuranes from the reaction between sulfoxylates and dioxetanes (18).



Since 6 does not produce free radicals we may rule out the mechanism of Scheme III for this anchimerically accelerated bond homolysis.

Scheme III



A reexamination of the thermolysis of perester 3 at 70°C in chlorobenzene, using ^{1}H NMR to monitor the reaction throughout its course, showed evidence for the intermediacy of 6. Indeed the finding that its stability is comparable to that of the perester requires an appreciable concentration of 6 to be built up at intermediate times if it is an intermediate in the reaction. Maximum concentrations of 6 approximately 19% of the original perester concentration were observed during the thermolysis of 3 after about 12 minutes at 70°C.

The Transition State. The polar nature of transition states for anchimerically accelerated bond homolyses of peresters of type 1 was established very early (2, 3, 4). For example, the dependence on substituent electronic effects of the rate of radical production from 3 was probed by kinetic studies of 14. The dependence on Hammett σ values for substituent X is described by a ρ value of -1.3.

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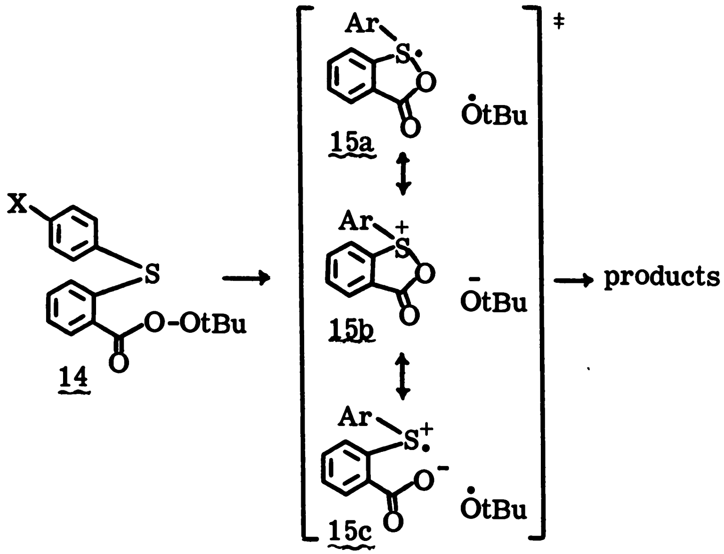

The polar character of the transition state for the decomposition of 3 is also manifested in a remarkably large dependence on solvent polarity. The fraction of radicals scavengeable varies with solvent in the range from 30 to 98% at 40°C, but not in a manner related to solvent polarity. The rate of decomposition of 3 in a variety of solvents is directly correlated with measures of solvent polarity such as the Kosower Z values (19) with a sensitivity to solvent polarity about 64% of that observed for the ionization of p-methoxyneophyl tosylate (20). It also shows a kinetic salt effect with a rate dependence of radical formation on the concentration of lithium perchlorate in tetrahydrofuran which provides strong evidence for appreciable transition state polarization.

The pronounced charge polarization in the transition state for bond homolysis is not limited to cases involving neighboring sulfenyl sulfur nor to peresters. One of the more thoroughly studied cases is that of a series of diaroyl peroxides showing accelerated bond homolysis from neighboring group participation of an olefinic double bond in the ortho position (5).

The rate of radical production from peroxides 16 in chlorobenzene solvent depends on substituents X and Y in a manner correlated with Hammett σ constants with $\rho_X = -1.2$ and $\rho_Y = +0.6$. The development of positive charge in the vinyl substituent and negative charge in the leaving carboxyl group is in keeping with the transition state charge distribution pictured for resonance structure 17b in the reactions examined in this study by Koenig (5).

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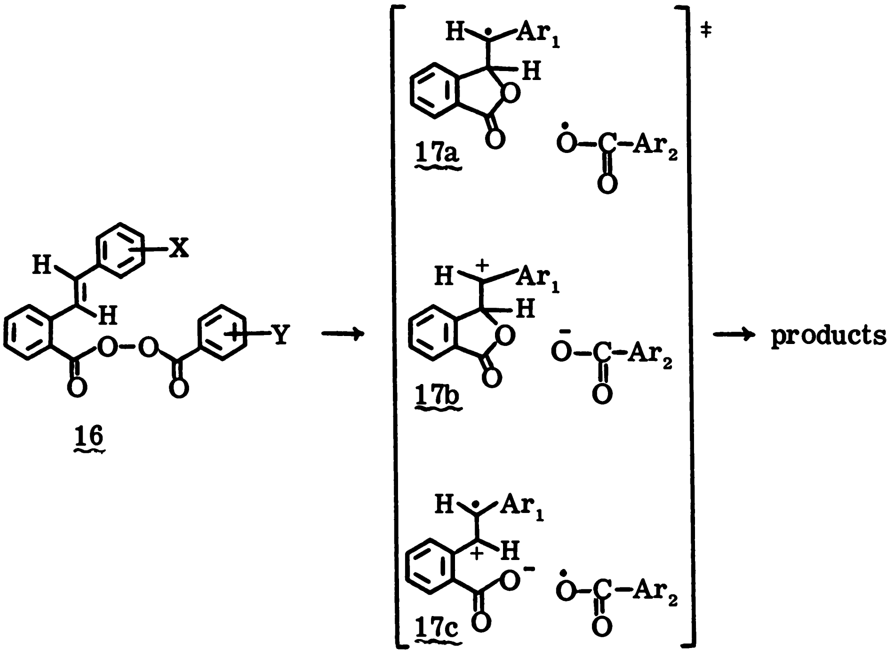
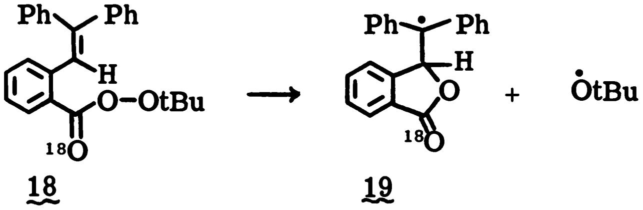
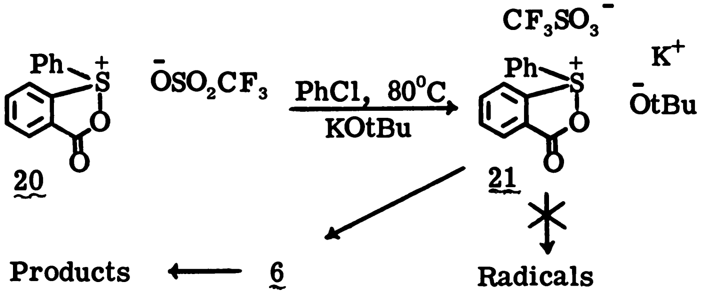


The closely related perester, 18, also shows a strongly accelerated rate of decomposition (Table I). It gives products from bridged radical 19 in which oxygen 18 tracer experiments indicate 88% retention of the label in the product carbonyl oxygen (21). This evidence for the maintenance of bond integrity in the intermediate radical 19 also points to bridging in the polar transition state leading to this radical.



The Nature of the First-formed Intermediate. Despite the very polar nature of the transition state, the products of the decomposition of 3 (or 14) are reliably free-radical. The high energy intermediate which is first encountered along the reaction pathway for decomposition of a radical initiation is a geminate radical pair, within the solvent cage. In the case of 3, the large degree of charge polarization in the transition state leading to this intermediate leads one to question whether the cage pair is better described as a radical pair, resembling transition state resonance structures 15a (or 15c), or an ion pair resembling 15b. If the latter were the case it should be possible to generate the same species by reaction of a sulfonium species with *tert*-butoxide anion. The ionic sulfonium triflate 20 was treated with potassium *tert*-butoxide in chlorobenzene at 80°C, the same conditions used for the product studies for the decomposition of 3. The products included isobutylene and sulfoxide acid 8, the products expected for the reaction via 6. None of the free radical products, specifically acetone, was observed. We may conclude that there is no crossover between the two sets of intermediates, the radical pair from the perester decomposition and the ion pair formed in the reaction of Scheme IV (8), either directly or by formation of perester by combination of the ion pair to form an O-O bond.

Scheme IV



The absence of radical products in the reaction of Scheme IV, and the formation of only a limited amount of product in the perester decomposition (Scheme III) which could have arrived by a non-radical path (via 6), could be explained in at least two ways. The two pair species, one from perester and the other from the pairing of ions, could differ in that the ion sources contribute potassium and triflate ions which could be included in an ion aggregate, 21, possibly more likely to give ionic products than is the unperturbed sulfonium--*tert*-butoxide pair. Further work will be required to confirm or deny this explanation. The associated uncertainty remains a defect in the experiment.

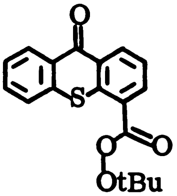
Another more interesting explanation of the failure to see extensive crossover of the two reaction paths is based on a possible difference in geometry between the sulfonium ion and the corresponding sulfuranyl radical derived from it by one-electron reduction. If this difference in geometry is sufficiently large a Franck-Condon factor could slow the electron transfer sufficiently to allow diffusion of radicals from the cage to compete with conversion to the ion pair.

While we can place considerable confidence in a prediction of strongly pyramidal geometry for the cyclic acyloxysulfonium

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

ion of 20, the preferred geometry of sulfuranyl radical, 5, is less obvious.

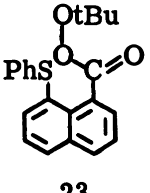
Geometry and Structure of the Sulfuranyl Radical. Evidence relating to the preferred geometry of the transition state leading to sulfuranyl radical from perester 3 has been sought in kinetic studies of model peresters of constrained geometry. For example, perester 22 differs from 3 in having the S-aryl substituent a part of a six-membered ring. The further perturbation of the system introduced upon going from 3 to 22 is the introduction of an electron-withdrawing acyl substituent on both aromatic rings in 22. After allowing for the rate retarding effect, which can be estimated from the known $\rho = -1.3$, the observed rate of decomposition of 22 is slower by a factor of ca. 10^3 (at 50°C) than the rate expected from the operation of this electronic effect alone (3). This factor was attributed to a steric effect in the study by Fisher (6).



22

Even if we concede that the transition state for the decomposition of 22 is constrained away from the geometry which is optimum for bridging to the neighboring sulfur it is clear that extrapolation from this to speculation on the geometry of the product radical is dangerous.

Evidence that these displacements by neighboring sulfur occur on the acyloxy oxygen, rather than the tert-butoxy oxygen, can be adduced from the observation of only slightly attenuated ($\Delta H^* = 23.7$ kcal/mole, $\Delta S^* = -5.5$ eu) anchimeric acceleration in perester 23. Participation at the tert-butoxy oxygen in this molecule would lead to a seven-membered ring in the transition state. Attack at the acyloxy oxygen as envisioned in the mechanism we have adopted leads to the six-membered ring in the transition state, more in keeping with the observed high level of anchimeric acceleration.



23

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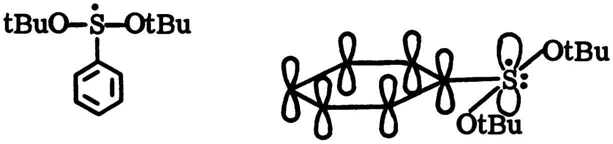
Literature models may be cited in support of three different bonding modes for bridged radical 5: (a) π-sulfuranyl radicals with a 3-center, 4-electron (3c-4e) bond and a π-delocalized unpaired electron, (b) σ-sulfuranyl radicals with a 3-center, 3-electron (3c-3e) bond, and (c) radicals containing a 2-center, 3-electron (2c-3e) bond.

(a) The direct observation of a number of sulfuranyl radicals, e.g., dialkoxyarylsulfuranyl radical 24 (22), by ESR provides evidence that π-sulfuranyl radicals may in some cases adopt a T-shaped geometry as shown for 24. The unpaired electron is delocalized over the aromatic π-system in this radical. The O-S-O bond linking the two apical alkoxy ligands to sulfur is therefore most likely a hypervalent (17) 3c-4e bond. On the basis of several analogies, this predicts a near colinearity of the two O-S axes. Radical 24 was formed by the reaction of *tert*-butoxy radicals with diphenyl disulfide.



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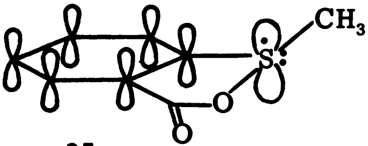
While sulfuranyl radicals derived from perester homolysis with neighboring sulfur participation have not been directly observed by ESR, results of CIDNP studies of the decomposition of 4 have been interpreted in terms of a π-sulfuranyl radical intermediate 25 (23).



25

The interpretation of observed (23) nuclear spin polarization of CH_3 protons in the earlier noted (2) products of decomposition of this perester was based on results of CNDO/2 SCF-MO calculations without minimizing energy with respect to geometry. Other bonding schemes must therefore still be considered possibilities.

(b) An alternative bonding scheme consistent with a geometry similar to that postulated in 25 would have the hypervalent colinear three-center bond occupied by three rather than four

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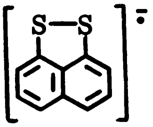
electrons. This scheme, which places two electron pairs on sulfur orthogonal to the apical three-center bond, has analogies in phosphoranyl radicals for which such a bonding scheme has been postulated from ESR studies (24, 25). In this bonding model the odd electron is in a 3c-3e bond along the O-S-C axis of 25, orthogonal to the π-system, hence we call such a radical a σ-sulfuranyl radical.

(c) The third model, which also has a three-electron bond orthogonal to the π-system, might be expected to differ in geometry from that with the O-S-CH_3 axis colinear. Analogies for a 2c-3e bonding scheme have been established from ESR studies of radical anion 26 (26). The one-electron reduction of the corresponding disulfide to give 26 introduces the electron into an orbital in the molecular plane which is approximately described as the antibonding combination of sulfur 3p atomic orbitals (26).

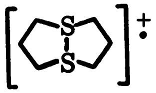


26

Similar bonding schemes may be invoked for the dialkylated analogs of 26, radical cations 27 (27), which shows equivalent hyperfine coupling to all twelve protons, and the more stable 28 (28), a possible beneficiary of a five-membered ring stabilizing effect similar to that noted earlier for closed shell sulfuranes.

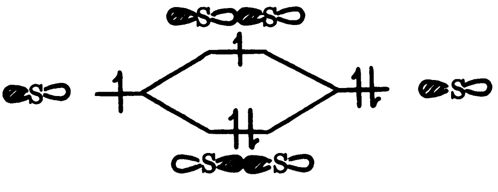
$$\left[Me_2S\text{-}SMe_2\right]^{+\bullet}$$

27

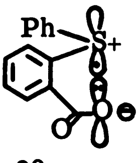


28

Species 27 and 28 are generated by one-electron oxidation of the dialkyl sulfide. The interaction between the resulting sulfide cation radical and another sulfide sulfur is overall a bonding interaction since the antibonding orbital is only singly occupied.



The interaction of a sulfide cation radical with any nucleophile might be expected to result in some net bonding by such an interaction. Radical 5 for example could be imagined to have an S-O bond formed by interaction of the doubly occupied oxygen 2p orbital of the carboxylate ion interacting intramolecularly with the singly occupied sulfur 3p orbital of the adjacent sulfide sulfur of 29.



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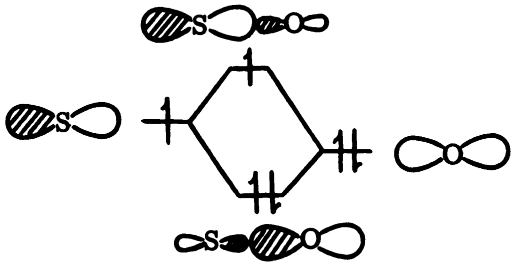
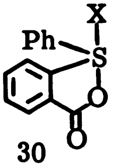


Polarity of the S-O Bond in 5. The MO scheme shown for the 2c-3e S-O bond in 29 (one representation of 5) shows the doubly occupied lower MO to have a heavier contribution from the lower energy oxygen 2p atomic orbital than from the higher energy sulfur 3p orbital. The S-O bond in such a species would therefore be polar with negative charge on oxygen and positive charge on sulfur.

An argument can be made for a similar charge polarization in the S-O bonds described by bonding schemes a (3c-4e) and b (3c-3e) as well. In both cases a three-center bond joins two apical ligands to sulfur. It has been shown that such bonds to sulfur, at least in the 3c-4e case, are highly polarizable (29, 30). Specifically to the point in the present case, it has been shown (29) that the carbonyl stretching frequency in sulfuranes of type 30 are very sensitive to the electron-withdrawing power of apical substituent X.



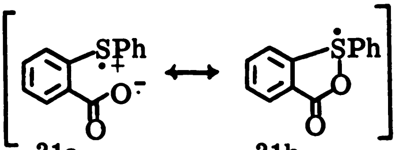
30

The change in $\nu_{C=O}$ as X is changed from OSO_2CF_3 (1832 cm^{-1}) to Cl (1740 cm^{-1}) to O-t-Bu (1640 cm^{-1}) suggests an appreciable increase in carboxylate anion character as the electron-withdrawing character of X decreases. One might expect a hypervalent radical of type 25 (or its 3c-3e analog) with a carbon-centered ligand at one apical position and a carboxylate oxygen at the other to be very dipolar.

One might therefore expect bridged radical 5 to be strongly dipolar no matter which bonding mode (a, b, or c) is properly involved to describe the S-O bond. It is possible that this dipolar character, reflecting a major contribution from 15c to the description of the transition state resonance hybrid, is largely responsible for the solvent dependence of rate of decompositions

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

observed for perester 3. The bridged radical product may be represented for any of the three structural hypotheses (a, b, or c) by the geometrically ambiguous resonance structures 31a and 31b.



31a 31b

Relationship to Electron Transfer Mechanisms. The intermolecular reactions of dialkyl or alkyl aryl sulfides with *tert*-butyl perbenzoates have been shown by Pryor and Hendrickson (31) to give only a small amount (0.7 - 3.5%) of scavengeable radical product. The rates of disappearance of the perbenzoates are strongly accelerated by addition of the sulfides. The mechanism which has been postulated involves an electron transfer from sulfur to the peroxide and kinetic isotope effect data have been presented in support of this mechanistic postulate (32). The interpretation of deuterium kinetic isotope effects, for substitution of D for H on a carbon bonded to the sulfur, invoked the change in C-H stretching force constants upon removing an electron from the delocalized HOMO of the sulfide, a molecular orbital with significant contributions from the hydrogen 1s orbitals.

It is clear from the arguments presented earlier in this paper that a continuum of transition state structures may obtain for such reactions with the free sulfide cation radical at one extreme and a variable amount of covalent bonding to a nucleophile, either intramolecularly or intermolecularly. For example, the relative contributions of the two resonance structures written for 31 can vary continuously with substitution or conditions.

The much larger fraction of radical products from the decomposition of 3, relative to the intermolecular analogs reported by Pryor (31, 32), can be explained as a manifestation of the five-membered ring effect discussed earlier. It is clear that a five-membered ring containing sulfonium sulfur is, because of angle strain and other factors, very much disfavored in comparison with such a ring containing sulfuranyl sulfur (16, 17, 33). The ionic pathway for decomposition of 3 leads to such a sulfonium species and is therefore disfavored, because of the five-membered ring effect, relative to the homolytic pathway leading to 5 which has a different, more favorable geometry about sulfur.

Simultaneous Participation of Multiple Neighboring Groups. The strength of a hypervalent 3c-4e bond increases with electronegativity of the apical ligands. In a sulfuranyl radical such as

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

25 (3c-4e, bonding mode a), or its σ-sulfuranyl radical analog (3c-3e, bonding mode b), one of the apical positions is occupied by an oxygen but the other is occupied by a more electropositive carbon. A stronger bond might be expected in the transition state if both apical ligands were oxygen-centered (17). A search for a radical initiator which might decompose through such a transition state led us to examine the possibility that three neighboring groups might, in a suitable molecule, be simultaneously involved in transition state bond-making. Perester 32, studied by Chau (7), provided the first example of such a radical initiator. It decomposes to give stable sulfurane 34 and tert-butoxy radicals.

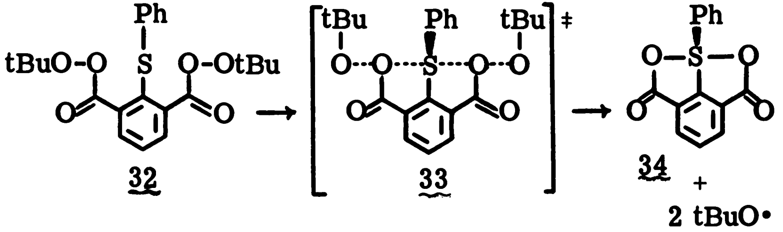


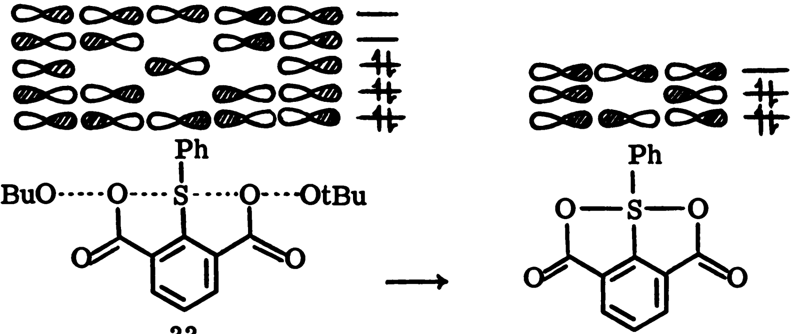
Table II. Perester Decomposition in Chlorobenzene

Compound	k_{rel}, 0°C	ΔH*(kcal/mol)	ΔS*(eu)	Ref
tert-butyl perbenzoate	1.	33.6	8.2	34
3	1.1×10^6	22.3	-5.7	2
32	8.9×10^7	17.6	-13.9	7
35	3.2×10^2	28.1	-0.66	2
36	3.9×10^4	22.4	-11.9	7
38	2.3×10^5	25.5	2.5	37

The data of Table II show that the decomposition of bis-perester 32 is anchimerically accelerated by a factor of 10^8 at 0°C, a temperature within the range at which rate measurements were made for 32. This is larger than the anchimeric acceleration noted for monoperester 3 by a factor of about 10^2. Evidence for the simultaneous breaking of two O-O bonds and formation of two S-O bonds, in the manner suggested in the drawing for transition state 33, is even more compellingly discernible in the activation parameters listed in Table II. The remarkable lowering of ΔH* for the decomposition of 32 (17.6 kcal/mol) compared to tert-butyl perbenzoate (33.6 kcal/mol) is accomplished only at the cost of achieving the very precisely ordered geometry of transition state 33. This lowers ΔS* from +8.2 eu (for the unsubstituted perbenzoate) to -13.9 eu (for 32). The monoperester, decomposing by a process forming one S-O bond simultaneously with cleavage of a single O-O bond via transition state 15, is intermediate in both ΔH^* and ΔS^*. The rate accelerations observed for 3 and 32 would be larger still were it not for these partially compensating entropy effects. The entropy effects are clearly consistent with the postulated transition state structures.

The bonds represented by dotted lines in transition state 33 could be described as a single extended five-center six-electron (5c-6e) bond. Molecular orbitals constructed from oxygen 2p and sulfur 3p orbitals are pictured below for both transition state and product.

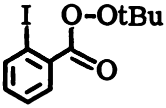
The description of 3c-4e bonds, the sort which Musher (35) has called hypervalent, in terms of linear combinations of p_z orbitals of the three colinear atomic centers is pictured for the product sulfurane (34) at the right below. The 5c-6e bond postulated for transition state 33 is illustrated in similar terms in the MO diagram to the left. Arduengo and Burgess (36) have discussed related multicenter bonds.



33

34

A very similar set of observations for 35 and 36, the iodo analogs of 3 and 32, provides further confirmation for this hypothesis. The simultaneous participation of three neighboring groups in the decomposition of 36, to give 37 and tert-butoxy radicals, is evidenced in a rate of decomposition 10^2 faster for 36 than for 35. This effect is amplified in ΔH^* values (Table II).



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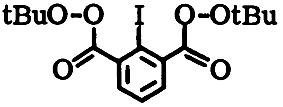

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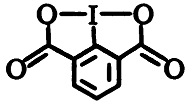
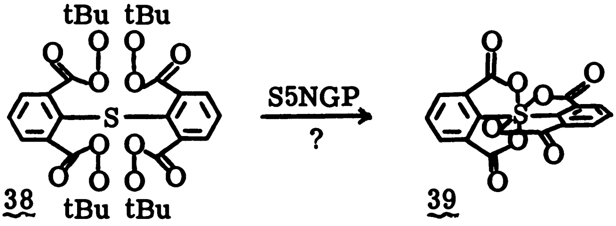


37

The simultaneous three-neighboring-group participation (S3NGP) mechanism favored for these molecules, via transition states such as 33, is in theory extendable to larger numbers of neighboring groups which might simultaneously engage in bond-making in a transition state. (Note that we have refrained from designating one group as a "reaction center" and another as a "neighboring group" but have simply counted all groups involved in bonding changes in a transition state.)

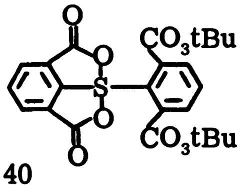
A search for an example of the S5NGP mechanism led Chau (37) to synthesize tetraperester 38. The pictured S5NGP process leading directly to persulfurane 39 appears not to be the major pathway for the decomposition of 38.

From a consideration of the kinetic data for 38 (Table II), and spectroscopic evidence for the intermediacy of 40 and 41 in the reaction, we suggest the major pathways for decomposition to be the two S3NGP processes possible for the tetraperester, leading first to 40 and 41 (37).



38

39



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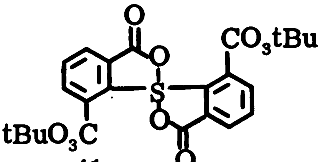
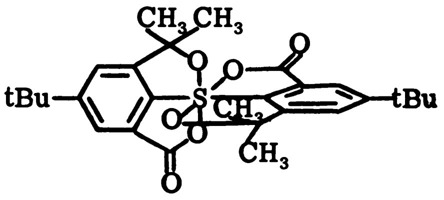


41

The conclusion that 39 was the eventual product of decomposition of 38 was clouded by our failure to find methods for purification which would allow us to obtain satisfactory elemental analyses for 39. The more recent complete characterization by Lam (38) of a related persulfurane (42) provides a model which makes our assignment of structure for 39 much firmer.



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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

Comparison of the product from thermolysis of **38**, which was assigned structure **39**, with the more rigorously characterized **42** makes it seem likely that **39** is indeed the proper structure of this product. The possibility of anchimeric acceleration by an S5NGP process remains open for this reaction, perhaps providing a minor pathway for decomposition. This prompts us to continue our search for a more favorable case for the observation of such a mechanism.

Acknowledgment. The research upon which this review is based was supported in part by grants from the National Cancer Institute (CA-13963) and the National Science Foundation (MPS75-17742).

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch005

6

The Chemistry of Cyclic Peroxides: The Formation and Decomposition of Prostaglandin Endoperoxide Analogs

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006

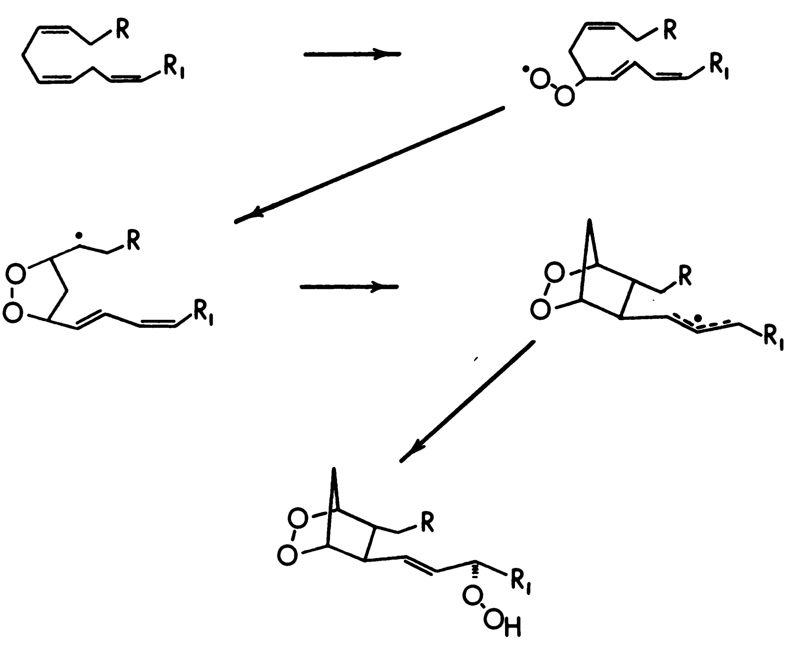
Interest in the chemistry and biochemistry of peroxides has been recently stimulated by the fact that the important class of natural products, the prostaglandins, has two members (PGG and PGH) that contain the peroxide linkage. Further, the proposed mechanism for the biosynthesis of these peroxides involves a novel peroxy radical bicyclization. Thus, one mechanism for biosynthesis of PGG, proposed in 1967 (1, 2), involves an autoxidative-type conversion of fatty acid to endoperoxide via a peroxy radical mechanism (Figure 1). For the past three years, our research has focused on aspects of peroxide and free radical chemistry related to the formation and decomposition of monocyclic and bicyclic peroxides analogous to these prostaglandin intermediates, and we present here our results concerning the formation and decomposition of these compounds.

Monocyclic Peroxides

Formation. Although a peroxy radical cyclization mechanism was proposed (1, 2) for prostaglandin biosynthesis, this mode of reaction had received little chemical attention. Early reports suggested that peroxy radical cyclization was an important variant in the autoxidation of polyunsaturated materials such as squalene (3) and cyclododecatriene (4). Products were not fully characterized in these studies, however, due to the difficulties of peroxide isolation and purification.

Perhaps the best documented case of peroxy radical cyclization was the report (5) that α-farnesene undergoes radical autoxidation to yield the completely characterized monocyclic peroxide, **1**. Autoxidative peroxy radical cyclization has precedent, then, but this autoxidation format is cumbersome for a systematic study.

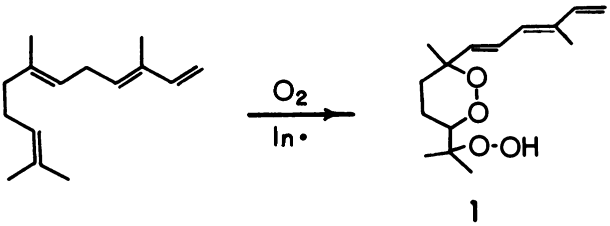
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006



PGG

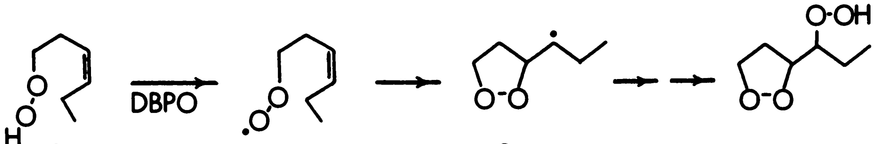
Figure 1. Proposed mechanism for prostaglandin biosynthesis (1, 2)

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006



1

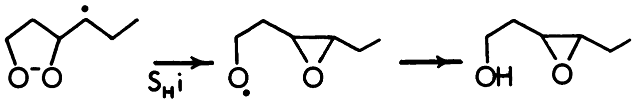
We developed a method for the study of peroxy radical cyclization based on the generation of peroxy radicals from unsaturated hydroperoxides (6, 7). Thus, treatment of the hydroperoxide 2, with free radical initiators such as DBPO (8) led to the formation of monocyclic peroxides that could be isolated by liquid chromatography and characterized by standard techniques.



2 3

Systematic investigation has shown that the ease of cyclization is [in the terminology proposed by Baldwin (9)] 5 or 6 exocyclic > 6 or 7 endocyclic cyclization.

The mechanism for cyclic peroxide formation presumably involves formation of β-peroxy alkyl radicals like 3 which can react with oxygen to yield ultimately cyclic peroxide products. An alternate pathway available to 3, however, is intramolecular radical attack on the peroxide linkage (10,11) yielding ultimately the epoxy-alcohol product. We wished to investigate this S_Hi pathway systematically and sought other, more controlled methods for the preparation of radicals like 3.



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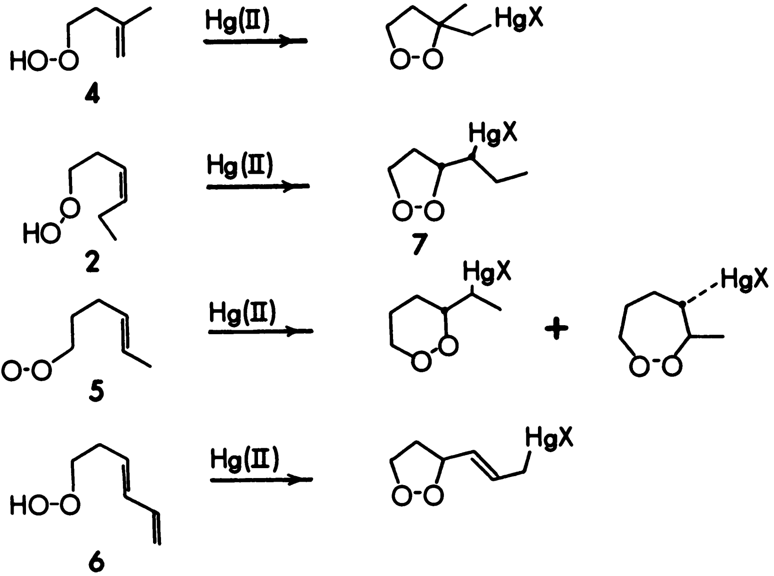
Potential methods for generation of radicals like **3** involve the use of β-mercurated cyclic peroxides. Alkyl-mercuric compounds react with borohydride to yield the corresponding alkyl radical (12, 13). The mechanism of radical production has been thoroughly investigated (14) and involves an intermediate alkylhydrido mercury compound, R-Hg-H. Chain propagation occurs as shown below by radical attack on R-Hg-H.

$$R\bullet + R\text{-}Hg\text{-}H \longrightarrow R\text{-}H + Hg + R\bullet$$

The crucial β-mercurated cyclic peroxide precursors of **3** can be prepared by mercuric nitrate initiated cyclization of unsaturated hydroperoxides (15). Yields are excellent and the compounds (as the bromide derivatives) can be purified by high pressure liquid chromatography (hplc). Exocyclic products are formed in cyclizations of **2**, **4**, and **6** with none of the 6-endo products being detected by nmr or hplc. **5** leads to a 3:1 ratio of 6-exo to 7-endo cyclization products. These isomers can be cleanly separated by hplc and quantities of all of the β-mercurated cyclic peroxides are thus readily available.

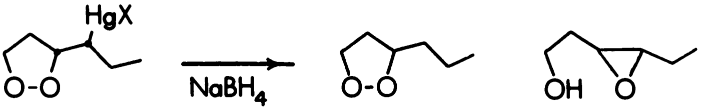


The predictions for cyclization developed by Baldwin (9) are rather vague when applied to these mercury initiated cyclizations. The rules, as stated for nucleophilic attack on 3-membered rings, "seem to lie between those for tetrahedral and trigonal systems, generally preferring exo modes." From our limited observation of peroxide attack on the three-membered ring mercurinium

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006

intermediate, we conclude that *exo* modes of cyclization are favored and that 6-*endo* cyclization is disfavored.

$S_{H}i$ Stereochemistry. Treatment of the β-mercurated cyclic peroxides with sodium borohydride leads to mixtures of demercurated cyclic peroxides and epoxy-alcohols. Thus, 7 reacts to give the cyclic peroxides and the epoxy-alcohol in a 3:1 ratio. As noted earlier, these are products expected from a β-peroxy radical; the cyclic peroxide resulting from H atom abstraction, the epoxy-alcohol from $S_{H}i$ radical attack on the peroxide linkage.

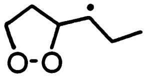
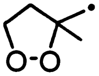
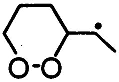
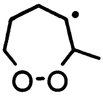


7

The relative amount of peroxide product and epoxy-alcohol is intimately dependent on the structure of the intermediate radical. In Table I is presented the product distribution of peroxide and $S_{H}i$ product (epoxy-alcohol) for a series of cyclic peroxide alkyl-radicals. Note that the exocyclic five-membered ring radicals 8 and 9 lead predominately to peroxide as does the endocyclic seven-membered ring radical 11. The exocyclic six-membered ring radical, on the other hand, gives primarily $S_{H}i$ products. The amount of peroxide and epoxy-alcohol produced does vary somewhat depending on how borohydride addition is carried out. The product compositions reported in Table I could be reproducibly obtained, however, by quickly syringing the borohydride reducing agent into a mixed phase CH_2Cl_2/H_2O solution of the β-mercurated cyclic peroxide at 0°. In addition, by reducing mixtures of the various β-mercurated peroxides, the product ratios presented could be confirmed.

We suggest that the $S_{H}i$ reaction reported here offers the possibility of studying the geometric requirements of $S_{H}2$ attack on the peroxide linkage. The data suggest that the critical geometric parameter for the $S_{H}i$ reaction is the dihedral angle, ϕ, about the OC bond between the attacking radical and the leaving oxygen. We assume that for maximum $S_{H}i$ reactivity, this dihedral angle must be 180°. A view down the O-C bond of a space-filling model of a six-membered ring peroxide with a $-CH_2\bullet$ center attached α to the peroxide linkage is presented in Figure 2. The critical dihedral angle about the O-C bond is 180°, or nearly so, for this six-membered ring radical. For the analogous radical derived from a five-membered ring, the O-C dihedral angle is substantially less than 180°, having a maximum of approximately 165° in the most favorable conformation for $S_{H}i$ attack. Thus, the

Table I. Product distribution from borohydride reduction of β mercurated cyclic peroxides.

	peroxide	S_Hi
 **8**	75	25
 **9**	90	10
 **10**	10	90
 **11**	100	–

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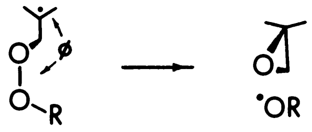


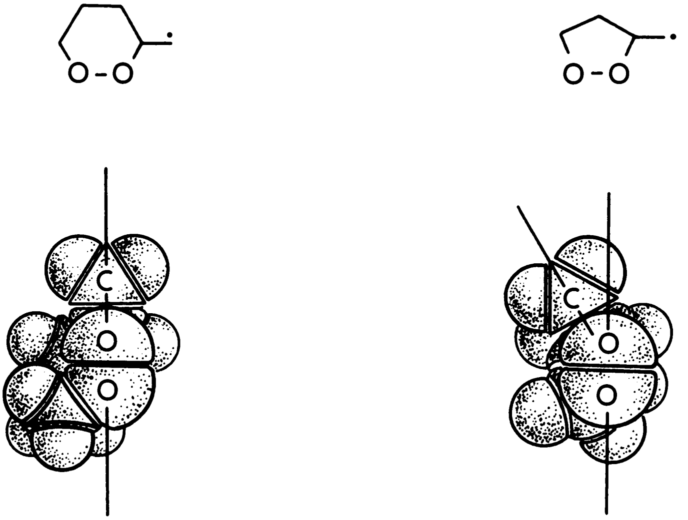


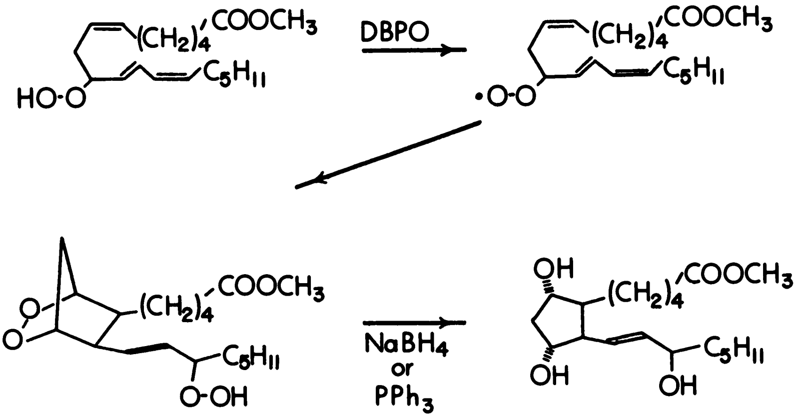
Figure 2. Geometric requirements of S_Hi radical attack on the cyclic peroxide bond

five-membered ring peroxides lead to less $S_{H}i$ product than the six-membered ring peroxides since the five-membered ring radical cannot attain the required transition state geometry without undue strain. It is impossible for radical **11** to assume the required conformation since the radical center is located within the ring (endocyclic) rather than on an exocyclic carbon chain. As a consequence, no $S_{H}i$ reaction from **11** is detected and only cyclic peroxide product is isolated.

Little is known about the stereochemical requirements of $S_{H}2$ radical attack on first row elements. An $S_{N}2$-type transition state has been proposed (16, 17) for radical attack on cyclopropane carbon and strong evidence has been presented that suggests that halogen atom attack on cyclopropane carbon occurs with stereochemical inversion. Our observation of alkyl radical attack on the peroxide linkage suggests that backside displacement is the rule here also, and it appears that this geometry may be generally required in $S_{H}2$ reactions (18, 19).

Bicyclic Peroxides

Formation. Although bicyclo[2.2.1]endoperoxides are important intermediates in prostaglandin chemistry, they have been synthetically elusive. Autoxidation of polyunsaturated fatty acids does lead to mixtures of compounds containing the endoperoxide structure (20, 21). We (22) were also able to isolate prostaglandin products from the sequence described below. The lipid hydroperoxide (prepared from soybean lipoxygenase and the fatty acid (23) was treated with a free radical initiator and the products, following borohydride reduction, were compared to authentic prostaglandins (24).



Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006

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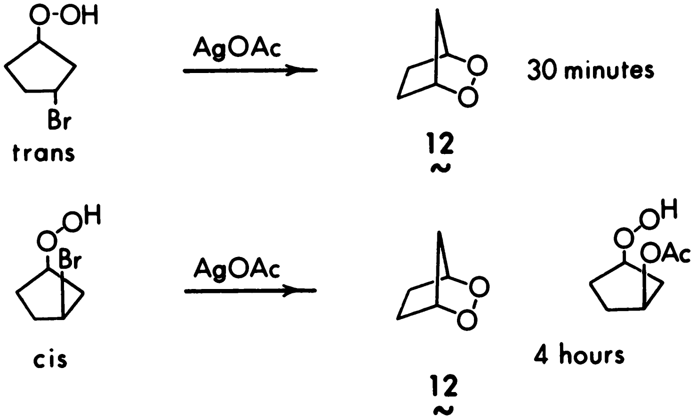
Any of these radical methods suffer from the fact that a serious mixture of diastereomers is formed and alternate routes to the bicyclo[2.2.1]endoperoxides have received considerable attention.

Recently, other methods of endoperoxide synthesis have been reported that make the parent 2,3-dioxabicyclo[2.2.1]heptane system, 12, readily available (25, 26, 27). For example, we have been able to prepare 12 from 3-bromocyclopentanehydroperoxide. The trans bromohydroperoxide is converted to 12 in 30 minutes by treatment with silver acetate. The cis bromohydroperoxide reacts much slower and leads to a mixture of products, including 12.



Decomposition of Endoperoxides. With 12 readily available, its chemistry relative to the prostaglandin endoperoxides can be explored. Salomon and collaborators (26) have reported on aspects of the thermal and base catalyzed decomposition of 12. We have chosen to initially concentrate on the reactions of the endoperoxide with Lewis acids such as Cu^{2+}.

Bartlett, Baumstark, and Landis (28) have shown that dioxetanes are subject to acid catalyzed decomposition (29) , and we reasoned that 12 would also be subject to catalytic Cu^{2+} decomposition. In fact, the interaction of endoperoxides and Cu^{2+} has been of interest in prostaglandin chemistry. For example, when enzymatic prostaglandin biosynthesis was allowed to occur with Cu^{2+} or Cu^{2+} and thiol present in the biosynthetic reaction mixture, significantly more PGF (diol) products were obtained than when no Cu^{2+} was added to the reaction mixture (30). Thus, the

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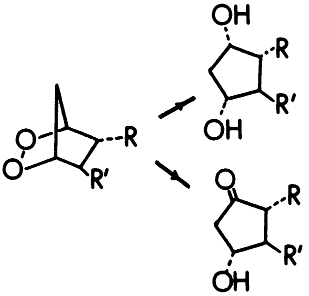
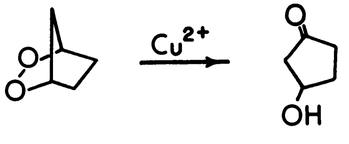
PGF (diol):PGE β-hydroxy cyclopentanone ratio obtained in prostaglandin biosynthesis increases from 2:3 with no added reagents to 1:1 with added Cu^{2+}. Addition of Cu^{2+} along with thiol increases the PGF:PGE ratio even more dramatically to 20:1.



	none	Cu^{2+}	Cu^{2+}/RSH
$\frac{F}{E}$	$\frac{2}{3}$	$\frac{1}{1}$	$\frac{20}{1}$

Treatment of 12 in EDTA distilled acetone with Cu^{2+} (7.1×10^{-4}M, 25°) leads to consumption of the endoperoxide at a rate of 8×10^{-4} min^{-1}. The only products detected are 3-hydroxycyclopentanone and 2-cyclopentenone. 2-Cyclopentenone has been shown to arise from the β-hydroxycyclopentanone under the conditions of the reaction and work-up. 3.5×10^{-3}M Cu^{2+} leads to consumption of 12 at a rate of 3.7×10^{-3} min^{-1} and this leads to a k_{cat} for Cu^{2+} catalysis of 1.1 min^{-1} M^{-1}. The endoperoxide decomposes very slowly at 25° in EDTA purified acetone with no added Cu^{2+}. If the acetone



is not prepurified by EDTA distillation, then decomposition of the endoperoxide in this solvent occurs at a significant rate, even without added Cu^{2+}. This emphasizes the sensitivity of endoperoxides to transition metal impurities and suggests that extreme care be exercised in pre-purification of solvents to be used in studies of endoperoxide chemical reactivity.

The finding that Cu^{2+} catalyzes conversion of 12 to β-hydroxy cyclopentanone presents an apparent anomoly. Addition of Cu^{2+} to the PG biosynthetic medium leads to more PGF (diol) products whereas PGE-type products result from reaction of the endoperoxide 12 with Cu^{2+}. This inconsistency is clarified by consideration of the fact that the enzymatic mixture contains endogenous thiol that can react with the added Cu^{2+}, thus modifying the Cu^{2+}

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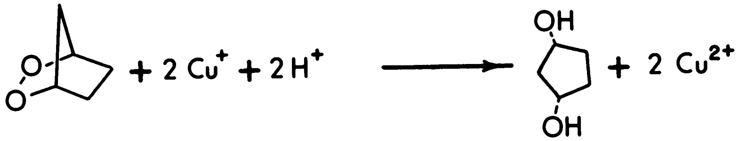
reactivity (31). To test this possibility, we reacted Cu^{2+} with various thiols and then determined by assay with 9,10-dimethyl phenanthroline (DMP) that copper was present as Cu^{1+} (32). Cu^{1+} (as the chloride in methanol) rapidly reduces the endoperoxide **12** to cis-1,3-cyclopentanediol (PGF-type product). In fact, even the Cu^{1+} bis-9,10-dimethylphenanthroline complex reduces **12** slowly to the diol; two Cu^{1+} equivalents being required for every diol equivalent formed.



It thus seems likely that in the biosynthetic studies, the true reactivity of the endoperoxide toward Cu^{2+} is masked by the presence of thiol in the biosynthetic medium. Cu^{2+} acts on the endoperoxide to give PGE products (β-hydroxy cyclopentanone) but this reactivity is never fully recognized since endogenous or exogenous thiol reduces Cu^{2+} to Cu^{1+}. Cu^{1+} then acts to reduce the endoperoxide to PGF-type products.

This study of endoperoxide-Cu^{2+} reactivity demonstrates how the examination of simple endoperoxide model systems can help to clarify the chemistry of the naturally-occurring PGH and PGG molecules and it seems likely that more model studies of this type will provide additional information about the reactivity of prostaglandins, thromboxanes, and prostacyclin.

Acknowledgement

This paper is dedicated to P.D. Bartlett on the occasion of his 70th birthday. The authors acknowledge the initial work in this area carried out by Drs. Max Funk and Ramdas Issac. N.A.P. acknowledges support from an NIH Career Development Award, J.R.N. from an NIH Pharmacology Training Grant, and D.W.G. from the C.R. Hauser Memorial Fellowship. N.A.P. acknowledges discussions with Dr. L.J. Marnett some six years ago that initially interested us in the area of lipid oxidation. Support of the research by NIH and ARO is gratefully acknowledged.

Abstract

Two aspects of the chemistry of cyclic peroxides have been investigated. Alkyl radicals β to the peroxide linkage in cyclic

peroxides attack the peroxide linkage in an S_Hi manner giving rise to epoxy-alcohols. The ease of this S_Hi reaction is dependent on the geometric arrangement of the attacking radical center and the peroxide bond. The preferred geometry appears to be an arrangement in which oxygen leaves by backside displacement from the attacking carbon radical. Bicyclic[2.2.1]endoperoxides have been shown to react with Cu^{2+} to yield β-hydroxy cyclopentanone by an acid catalyzed isomerization. Cu^{1+} reduces the endoperoxides to 1,3-cyclopentanediol, and it has been shown that thiol/Cu^{2+} mixtures act as does Cu^{1+} on the endoperoxide.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch006

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch007

7

Intramolecular Interactions of Acylperoxy Initiators and Free Radicals

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In a broad sense radical-induced decomposition may be considered as the reaction of any substrate promoted by a free radical, but the more common usage is to restrict consideration to those cases in which the molecule undergoing reaction is a free radical initiator (1,2). Thus radical-induced decomposition may be defined as reaction of a free radical with the primary source of the radical. This phenomenon is particularly noticeable when a free radical initiator does not react with first-order kinetics, but is consumed by the radicals it generates in chain processes. This case was originally elucidated for the kinetics of benzoyl peroxide decomposition in solvents such as ethyl ether (3-5), and was found to occur with radical displacement (the S_H2 reaction) (6) by solvent derived radicals on the peroxidic oxygen of benzoyl peroxide as shown in Fig. 1.

Another classic study of benzoyl peroxide involved the addition of solvent derived radicals to the *para* position of the initiator. For example, decomposition of benzoyl peroxide in cyclohexane led to the formation of *p*-cyclohexylbenzoic acid (7). The absence of *meta* product led to the suggestion (7,8) that *para* substitution was enhanced by *α*-lactone formation concerted with addition. An alternative route would involve addition followed by subsequent *α*-lactone formation (9) or transannular hydrogen transfer (Fig. 2) (10). In this case the absence of *meta* substitution product could be ascribed to reversibility of the addition, and this is known to occur (11). A preference for *para* substitution leading to formation of a radical intermediate stabilized by an adjacent carboxylate function would also be expected.

A related phenomenon is molecule induced homolysis.

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch007

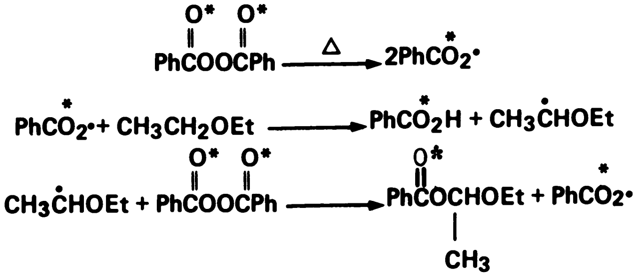

Figure 1. Radical-induced decomposition

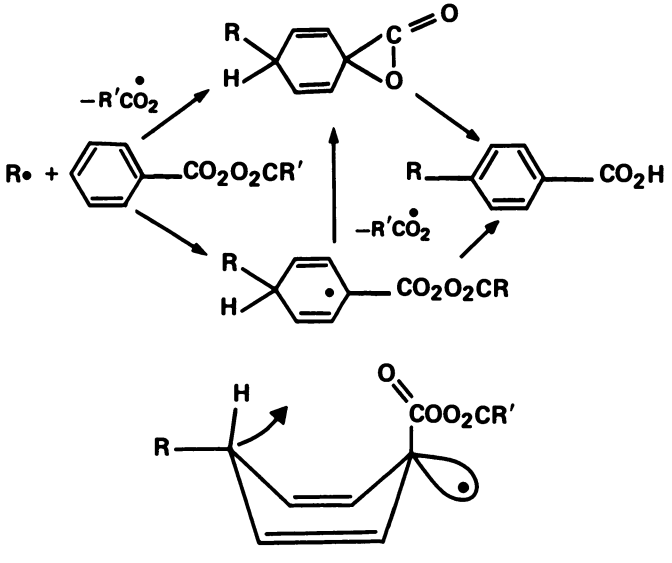

Figure 2. Transannular hydrogen transfer

This process, which has been recently reviewed (12), was defined as "an interaction of two or more non-radical species which results in the formation of free radicals", but is not the subject of primary concern here.

The present work deals with the intramolecular interaction of free radicals with peroxide initiators. Our original concept was to examine suitably constructed systems in which it was anticipated that the geometries of the interacting free radical and peroxidic sites could be accurately defined so that the factors which affect these interactions could be isolated. Intramolecular attack of a free-radical on an atomic center with displacement of a radical constitutes an SHi process, a subclass of the SH2 reaction, or homolytic substitution (6). The emphasis in our work is on such displacements on acylperoxy groups, but for a broader understanding of the phenomena ordinary ester groups are being examined as well.

The intramolecular reactivity of free radicals with acylperoxy groups as a function of distance between the two centers has been delineated by a number of investigations. These radicals were generated by homolysis, free radical addition, or atom abstraction to form the desired system. Radical sites α to acylperoxy groups lead to α-lactone formation as the characteristic reaction (eq. 1), whereas β-radicals lead to elimination (eq. 2-6).

An effort was made to examine the stereochemistry of β-elimination to give a stilbene system but this was thwarted since the first step in the reaction in eq. 7 did not occur to an appreciable extent (20). However the stereochemistry of formation of 2-butene from pyrolysis of the isomeric cyclic dl and meso -2,3-dimethylsuccinyl peroxides has been accomplished and found to be the same from either source (eq. 8) (21). The reaction in equation 2 was stereospecific as shown, and the resulting E-product is that expected from an anti-elimination from the preferred conformation of the starting material.

Radicals in γ or δ positions relative to acylperoxy groups also lead to lactone formation (eq. 9-12). In these lactone-forming reactions homolytic attack could occur either at carbonyl or peroxidic oxygen (eq. 13) but apparently this has yet to be determined for the examples noted in eq. 9-12.

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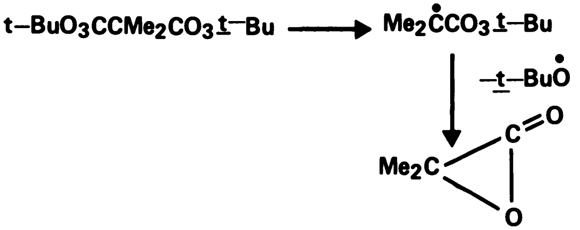

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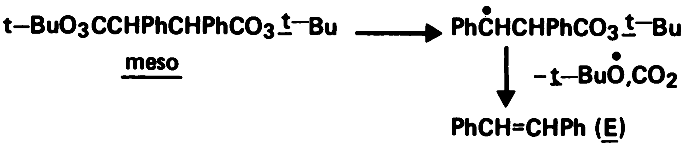

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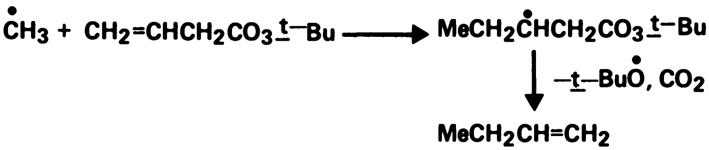

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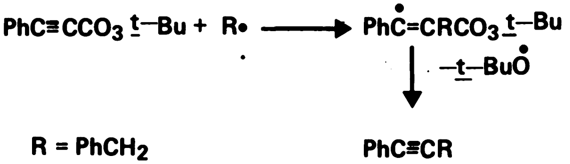
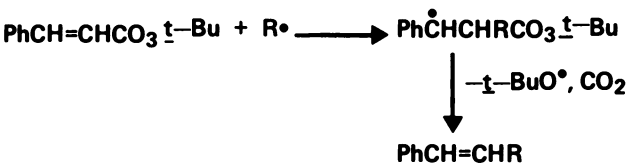
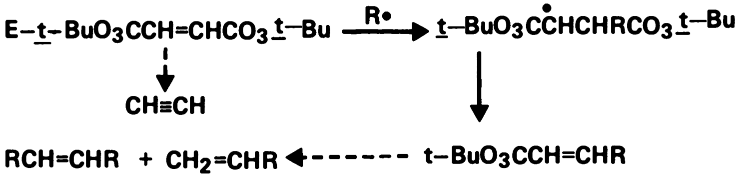


(4) 17



(5) 18



(6) 19

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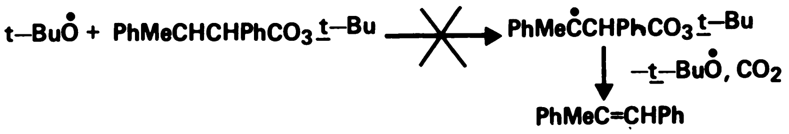

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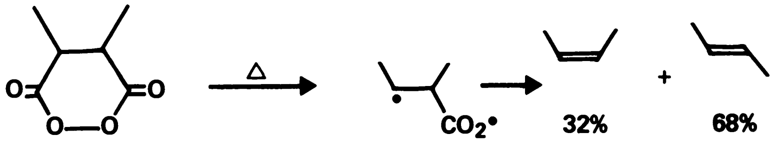
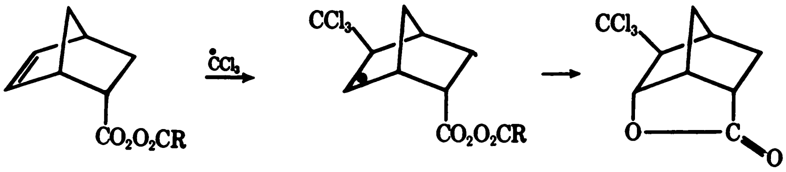


(8)[21]



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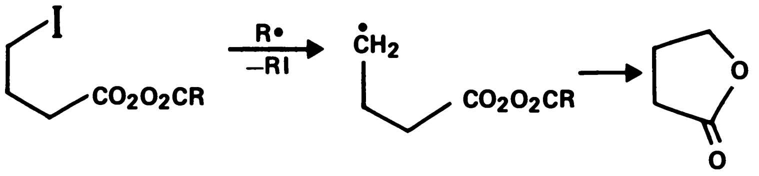

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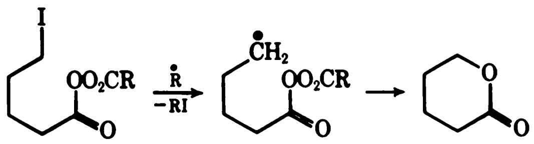

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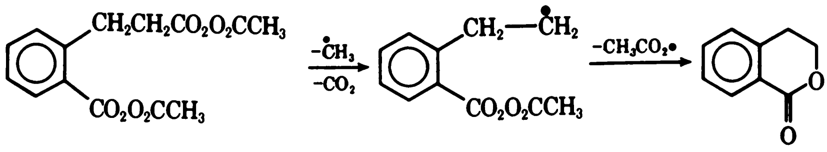
(12)[25]



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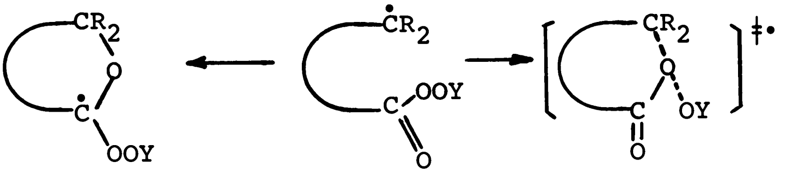
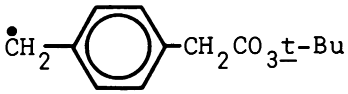


(13)

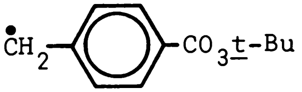
Some related lactone forming reactions have been observed in the reactions of acylperoxy alkenes in which the double bond participates in the homolysis (eq. 14,15). In the first case (eq. 14), the position of bond scission has been elucidated and found to occur at the peroxidic oxygen (27), in agreement with the results for benzoyl peroxide and *tert*-butyl perbenzoate which are attacked on peroxidic oxygen by a variety of radicals (5,30-32).

Some more compliated cases of reactions of bis-peroxides have also been reported (eq. 16,17). It was proposed (34) on the basis of a large negative $\Delta S^{\ddagger}$ that the reaction in eq. 17 proceeds by the 3-bond path indicated.

In our own work we were interested in the possibility that radicals delocalized in π-systems might interact with adjacent peroxy groups, for example in the systems **1** (35) and **2** (1). Induced decomposition paths can be visualized for both of these peresters; in the case of **1** the structure is a phenylene analog of a perester with a β-radical site (eq. 2,3,5) and decomposition to *p*-xylylene (**3**) could be contemplated. Similarly **2** is a phenylene analog of a perester with an α-radical site and decomposition to an *α*-lactone (**4**) could be contemplated. Radicals **1** and **2** were generated from the corresponding bisperesters **5** and **6**. The



1



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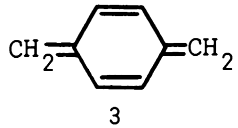

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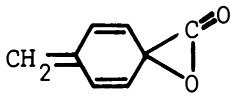

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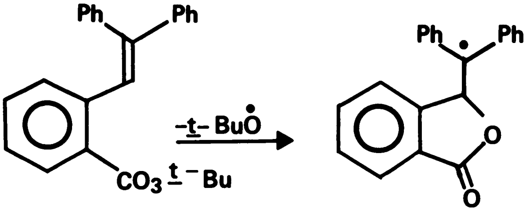
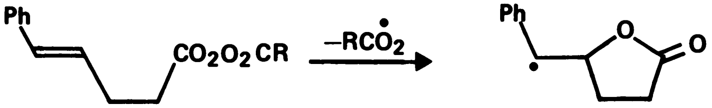
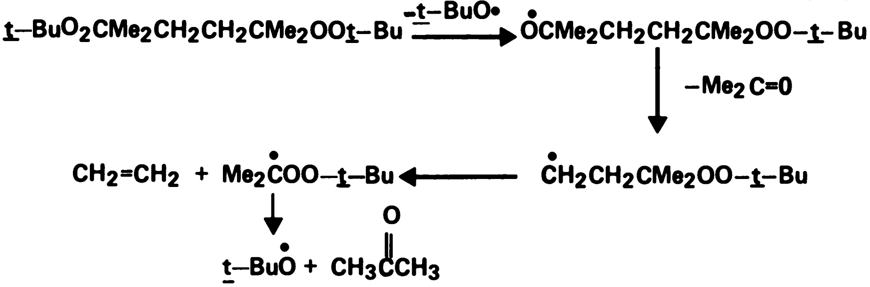


(14)[26]

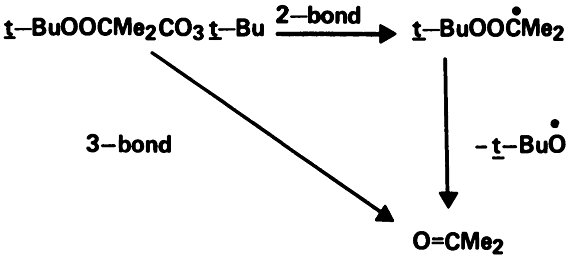
(15)[28,29]



(16)[33]

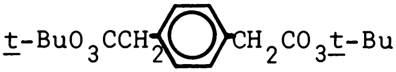
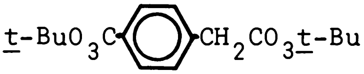
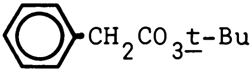
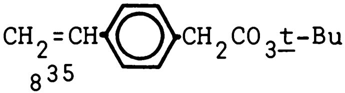


(17)[34]



kinetics of decomposition were normal for substituted phenylperacetates (Table 1). This result showed that the peresters underwent normal 2-bond cleavage in the rate determining step with formation of the radicals 1 and 2 as the initial intermediate and excluded the possibility of synchronous cleavage of more than two bonds giving the intermediates 3 and 4 directly. However the kinetic studies do not reveal the fate of the radicals 1 and 2 after they have been formed in the rate determining step.

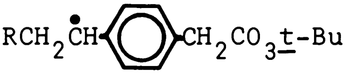
Table I. Kinetics of decomposition of substituted *tert*-butyl phenylperacetates at 80.0°C in cumene

Substrate	k(s^{-1} x10^5)	$\Delta H^\ddagger$ (kcal mol^{-1})	$\Delta S^\ddagger$ eu
 $t\text{-}BuO_3CCH_2\text{-}C_6H_4\text{-}CH_2CO_3t\text{-}Bu$ 5[35]	10.3	26.9	-1.0
 $t\text{-}BuO_3C\text{-}C_6H_4\text{-}CH_2CO_3t\text{-}Bu$ 6[1]	2.30[a]	29.2	3.1
 $C_6H_5CH_2CO_3t\text{-}Bu$ 7[35]	7.21	27.7	0.9
 $CH_2{=}CH\text{-}C_6H_4\text{-}CH_2CO_3t\text{-}Bu$ 8[35]	16.2	27.8	2.5
Copolymer of 8 and styrene[35]	23.4	27.2	1.7

[a] in toluene

Product studies were indicative as to the reaction pathways of 1 and 2. In the case of 2 the formation of 4 could be excluded as a significant reaction pathway, as the observed products were all derived from abstraction or radical coupling reactions of 2 (1). The perbenzoate group is thermally stable at the temperature at which 6 was decomposed and the products indicated that the peroxide group in 2 remained intact to form perbenzoate containing products. These were analyzed by hydrogenolysis of the peroxide group and separation of the derived products.

In the case of 1 products containing perester groups could not be isolated, and in any event any peresters derived from 1 by hydrogen abstraction or radical coupling would be expected to be at least as reactive as their precursor 5. However the product distribution was quantitatively what would be expected from reaction of 1 without formation of 3, and no products uniquely ascribable to 3 were observed. Perhaps more convincingly radical 9, analogous to 1, could be formed at 25°C and did not undergo decomposition in the time required for reaction with styrene. Thus an argument can be made that 1 is also stable at 70-100°C, although the evidence is indirect. Using the rate constants for benzyl radical combination and estimated diffusion constants for the radicals, average lifetimes could be estimated as $8x10^{-4}$s for 1 at 100°C and $6x10^{-3}$ s at 85°C for 2. This is the time which would be required before dimerization or coupling with solvent derived radicals occurred.



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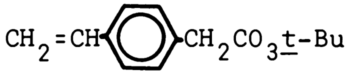
Once it had been established that 1 was probably stable in solution, and that 2 was definitely relatively stable it appeared that it would be possible to use the monomers 8 and 10 in free radical polymerizations to form polystyrenes with pendant phenylperacetate and perbenzoate groups. This indeed proved to be the case (36,37). Both 8 and 10 could be polymerized at 25°C with initiation by the low temperature initiator di-*tert*-butyl peroxyoxalate (DBPO) to give homopolymers with apparent quantitative retention of the peroxide functionality, or copolymerized with styrene by the same initiator. The resulting polymers were then heated to temperatures at which the pendant peroxide functions decomposed to give highly insoluble cross-



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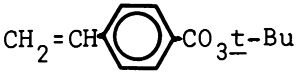
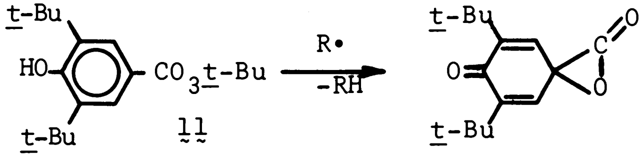


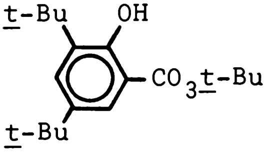
10

linked materials. If other monomers such as acrylonitrile were present graft-polymers were formed (Fig. 3).

Other examples of polymers containing peroxidic groups are noted in ref. 36. A recent example containing 2 kinds of perester groups and a vinyl group in shown in figure 4 (38).

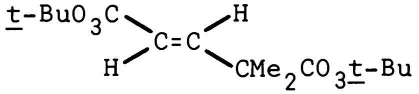
Radical 2 (39) and the analogous radical-diacyl peroxide (39) have also been prepared by abstraction of benzylic hydrogen and found to survive long enough to abstract halogen. However under these conditions the lifetimes of the radical species could not be estimated. The phenolic perester 11 underwent a radical-induced decomposition on abstraction of the phenolic hydroxyl, but interestingly the ortho isomer 12 was resistant to induced decomposition (40,41).





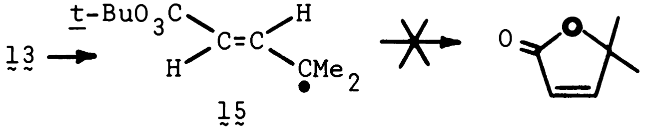
12

We have also studied the acylic bisperester 13 (42). Qualitative rate data indicate that 13 is about



13

10 times more reactive than trans-$MeCH{=}CHCH_2CO_3$t-Bu (14) (43). Inasmuch as 14 gives a primary allylic radical in the rate determining step whereas 13 could give a tertiary one the rate difference is not excessive and 13 may be presumed to have the same rate determining step as 14, namely two-bond scission to give an allylic radical (eq. 18). No lactone was formed from 13. This may seem surprising because other γ-percarboxy radicals formed lactones (eq. 9,10). Ring opening



(18)

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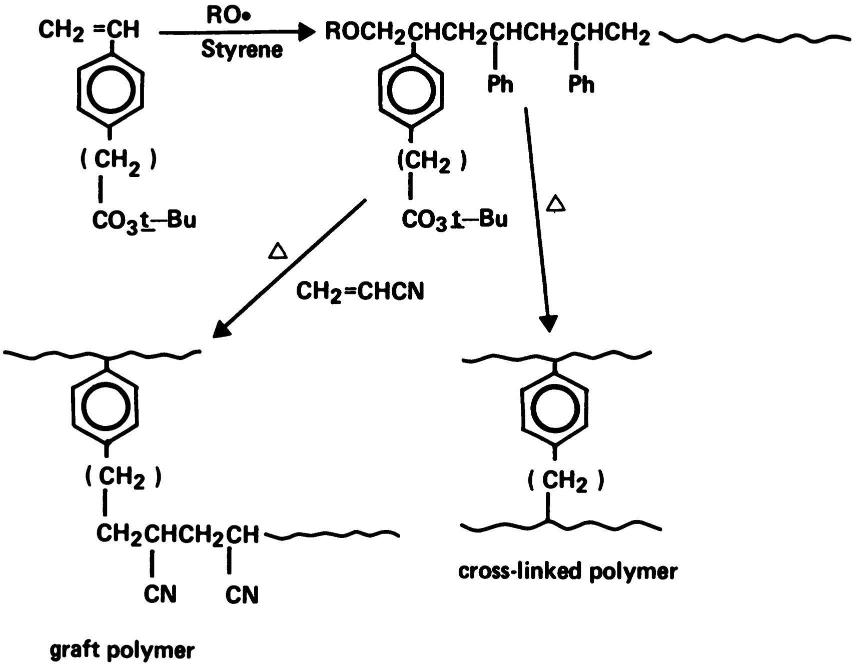


Figure 3. Graft-polymers

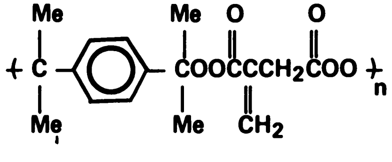
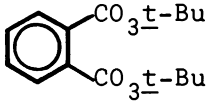


Figure 4. Polymer containing 2 types of perester groups

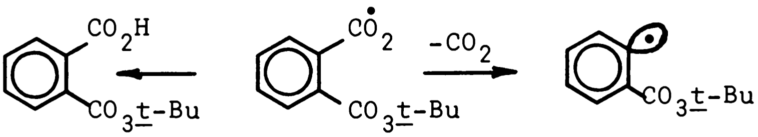
and lactone formation also occurred in the reaction of *trans*-di-*tert*-butylperoxy 3,3-diphenylcyclopropane-1,2-dicarboxylate (**16**) as shown in eq. 19 (44). The yield of **17** was 61% of the isolated material derived from the carbon skeleton of **16**; the remainder was 1,1-diphenylcyclopropane. Thus lactone formation was quite efficient in this case, in contrast to **15**. However it is to be expected that the cyclopropyl radical from **16** will be pyramidal (45), and will have a barrier to inversion (45), so that initially it will have the structure shown. In this geometry the preferred direction of ring opening would be to give the *cis*-allylic radical, as this gives maximum overlap during the ring opening (eq. 19). This geometry is favorable for lactone formation, whereas **15** would be formed in a *trans*-geometry unfavorable for lactone formation. A barrier of 21 kcal/mol for interconversion of allyl radicals has been reported (46). Lactone formation has also been observed in a related system (eq. 20) which does not suffer from geometrical restraints (47).

ortho-Substituted aryl peroxides should be a source of some interesting interactions between free radical centers and peroxides. Such substrates have fixed geometries with the radical site constrained to a relatively close proximity to the peroxide group. One example of such a system has already been cited (eq. 12). Another we have examined is *o*-di-*tert*-butyldiperphthalate (**18**) (48). This compound had a reactivity relative to *tert*-butyl perbenzoate of 0.9 and



18

similar activation parameters so with confidence may be assumed to undergo initial one-bond scission to radical **19**. The other observed products from **18** can be ascribed to arise from **20** and **21**, derived from **19** by hydrogen abstraction, and decarboxylation, respectively. Two possible induced decomposition pathways of **19** (eq. 21) are not required by the evidence. Phthalic anhydride is formed and there have been claims that this



20 **19** **21**

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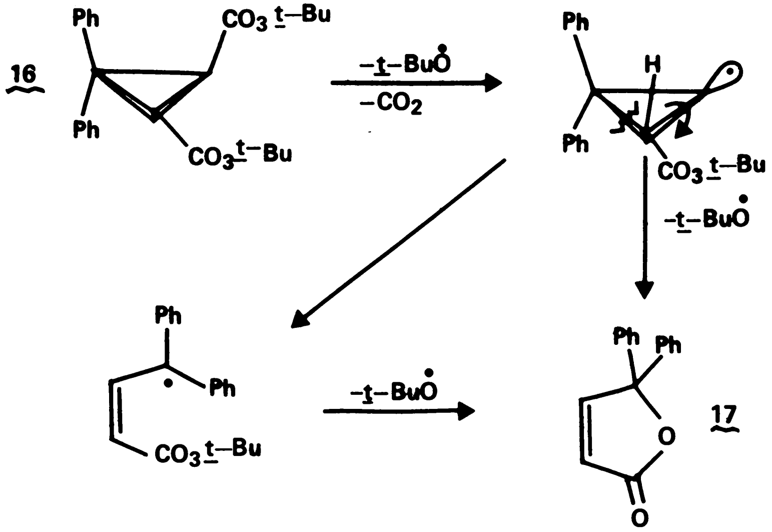
16
Ph
Ph
CO3 t-Bu
CO3 t-Bu
-t-BuO•
-CO2
Ph
Ph
H
CO3 t-Bu
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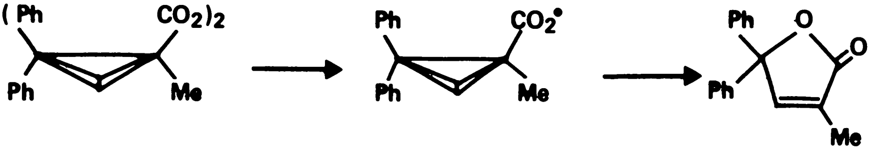
-t-BuO•
Ph
Ph
O
O
17

(19)

(20)


(Ph
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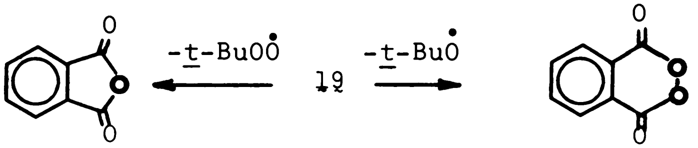
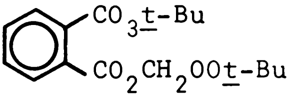


(21)

occurs by attack on carbon by a carboxylate radical to give anhydride with expulsion of a peroxy radical (25, 49). However, we found that phthalic anhydride was formed from 20 under the reaction conditions by a presumably non-radical pathway. Thus the unconventional SHi displacement of a peroxy radical is not required to explain the formation of anhydride. Another conceivable SHi reaction of 19 involves displacement of a tert-butyoxy radical and formation of phthalyl peroxide (eq. 21) but this product would also be reactive under the reaction conditions so its presence can neither be confirmed nor excluded.

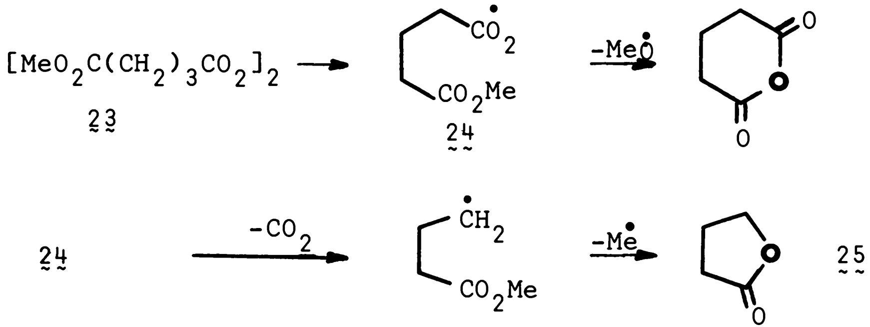
Compound 22, which is an interesting analog of 18, has recently been reported (50). However the rate of reaction of 22 in chlorobenzene is reported as 2.8



22

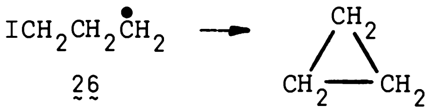
times that of 18 (in cumene) (48) at 115°, indicating that 22 reacts by the same rate-determining step as 18, namely initial 1-bond scission to give a carboxylate radical analogous to 19.

There has also been a recent report of radical displacement of an ordinary carboxylate ester (49). Numerous examples of such reactions involving percarboxylate functions have already been mentioned (cf. Fig. 1, eqs. 1, 9-12) but in the cases where the position of bond cleavage has been determined all have involved attack on peroxidic oxygen. The example reported for an ester would have to involve cleavage of the O-C bond (49).



23 24 25

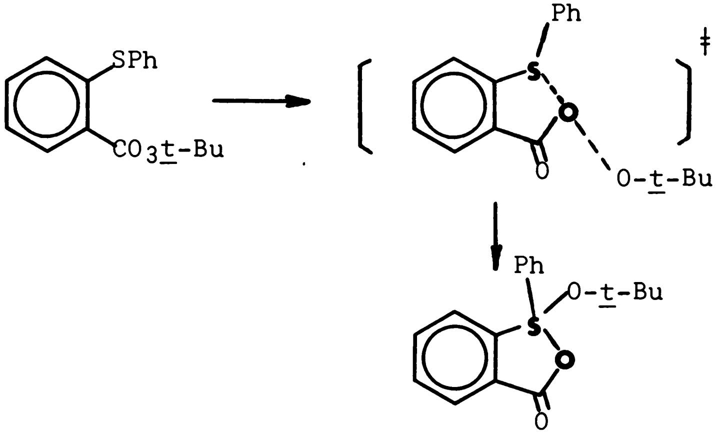
Radical displacement on carbon is extremely rare, excluding examples in which a strained ring is cleaved. One case that has been claimed involves the formation of cyclopropane from the 3-iodo-1-propyl radical (eq. 22). The mechanism in eq. 22 has been criticized (52) on the basis of the high strain generated in the



26

(22)[51]

reaction, and diradicals were proposed as a more likely source of the cyclopropane (52). The fact that radical 26 would combine would other radicals at near the diffusion controlled rate was felt to eliminate this possibility (51). Radical displacement on hetereo atoms are much more common. Some recent examples involving sulfur include spectroscopic observation of sulfurane 27, presumably formed by SHi attack of sulfur on the peroxidic oxygen (eq. 23) (53), and study of the electron transfer mechanism for some intermolecular

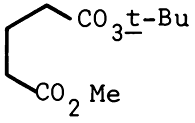


(23)

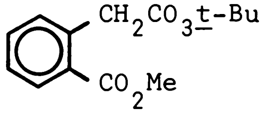
27

reactions of sulfides and peresters (54).

In the example mentioned above (49) butyrolactone (25) was claimed to be isolated to the extent of 35% (mol/mol) from 23 in HOAc. In order to further examine this phenomenon we have studied the decomposition of the peresters 28 and 29 (55). The kinetic parameters for 28 (Table II) show the decomposition rate of the perester is normal and not affected by the carbomethyoxy group beyond a possible slight inductive retardation. Similarly, the rate of 29 is half that of $PhCH_2CO_3$t-Bu (7), showing that 29 and 7 must react by the same rate-determining step with only a slight inductive role due to the carbomethoxy group.



28



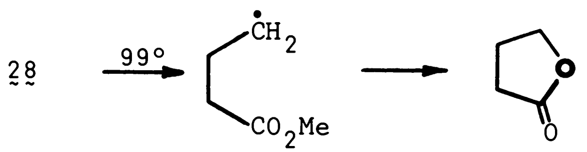
29

Table II. Rates of decomposition of peresters RCO_3t-Bu in cumene, extrapolated to 25°C

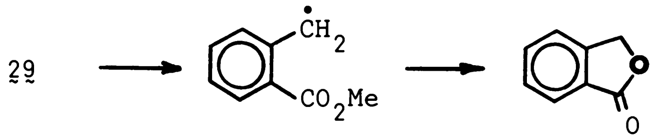
Perester	k_{rel}	$\Delta H^{\ddagger}$(kcal/mol)	$\Delta S^{\ddagger}$(eu)
$MeCO_3$t-Bu	0.5	36.9	17.2[a]
$EtCO_3$t-Bu	3.0	33.3	8.7[b]
28	1.0	36.1	16.1

[a] In ethylbenzene, ref. 56 [b] Ref. 57

The products from 28 and 29 both showed the formation of lactones (eq. 24,25). The yield of lactone from 28 decreased with the hydrogen atom donating abil-



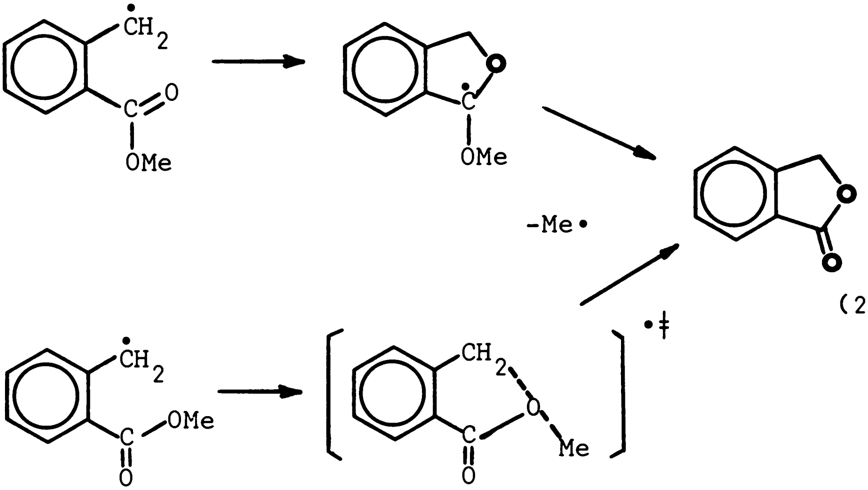
(24)



(25)

ity of the solvent, but in our hands was much less than that reported (49) for reaction in acetic acid solvent. The greater yield of lactone from 29 may be attributed to the fixed geometry of this intermediate which would encourage cyclization.

Thus SHi reaction is confirmed for 28 and 29. The question remains as to the mechanism of this process. Two possibilities to be considered are shown in eq. 26.



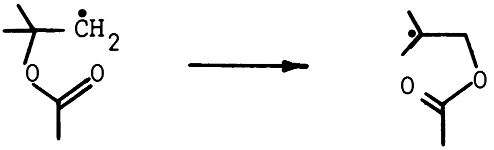
(26)

Formation of an intermediate by attack of carbonyl oxygen was favored by other authors (49). These routes should be distinguishable by O-18 labeling and such experiments are now underway.

Several analogies for this reaction are known. In an acylic case α-phenethyl benzoate reacts with tri-n-butyltin hydride by a free radical process (58), but it has not been demonstrated which oxygen is attacked by the radical (eq. 27). Radicals are known to attack intramolecularly on carbonyl oxygen in ketones (eq. 28) and esters (eq. 29), and attack on carbonyl carbon is even known (eq. 30).

$$n\text{-Bu}_3\dot{\text{S}}\text{n} + \text{PhCO}_2\text{CHMePh} \longrightarrow \text{PhCO}_2\text{Sn-}n\text{-Bu} + \text{Ph}\dot{\text{C}}\text{HMe} \quad (27)^{58}$$

(28)[59]



(29)[60]

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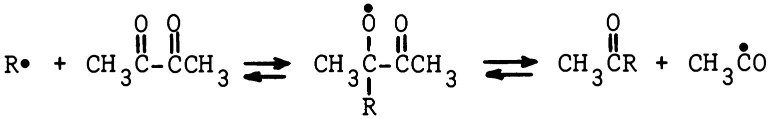

$$R\bullet + CH_3\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}CH_3 \rightleftharpoons CH_3\underset{R}{\overset{\overset{\bullet}{O}}{C}}-\overset{\overset{O}{\|}}{C}CH_3 \rightleftharpoons CH_3\overset{\overset{O}{\|}}{C}R + CH_3\overset{\bullet}{C}O \quad (30)^{61}$$

In summary the presence of an acylperoxy group and a free radical center in an intermediate may lead to intramolcular induced decomposition by one of several routes, or induced decomposition may not occur. Many interesting examples in which such processes may occur still await study.

Acknowledgements: Financial support by the U.S. Army Research Office-Durham, the Defence Research Board of Canada, and the National Research Council of Canada is gratefully acknowledged. Special thanks is due to my collaborators cited in the footnotes.

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RECEIVED December 23, 1977.

8

Decomposition of Diazenes and Diazene *N*-Oxides. Consideration of Three-Electron Stabilization.

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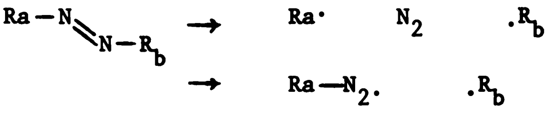
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch008

The carbon-nitrogen bond is a strong link of average bond energy 75 kcal/mole. There are, of course, many examples in which homolytic cleavage of this bond may be effected under relatively mild conditions. Diazenes (azo compounds) comprise a well-documented example (1). Decomposition of diazenes affords dinitrogen and radicals. The question of whether the rate-determining step involves synchronous two-bond cleavage (eq. 1) or one-bond cleavage (eq. 2) has received a great deal of study (1, 2). For alkyldiazenes (including aryl-substituted alkyl) the evidence strongly favors cleavage of both carbon-nitrogen bonds in the rate-determining step. A convincing line of evidence is the dependence of rate on substituent [e.g. Table 1 (3)].



(eq. 1)

(eq. 2)

Table 1
Rate of Decomposition of Diazenes, Ra—N=N—R_b

Ra	Rb	rel k, predicted, 200°C Synchron (eq. 1)	Stepwise (eq. 2)	rel k, Observed
1-Norbornyl	1-Norbornyl			1
1-Norbornyl	t-Butyl			$6.6\text{x}10^4$
t-Butyl	t-Butyl	$(6.6\text{x}10^4)^2$	$2(6.6\text{x}10^4)$	$7 \text{ x } 10^7$

Indeed, these findings might appear to be a logical consequence of a consideration of the energetics of the reaction. The enthalpy change, ΔH°, for eq. 1 is approximately +25 kcal/mole for R = alkyl, e.g. t-butyl (4); the enthalpy of activation is +42 kcal/mole (5). In comparison with the average bond energy of 75 kcal/mole for the carbon-nitrogen bond, the considerably lower activation energy (+42) can be achieved by some synchronous

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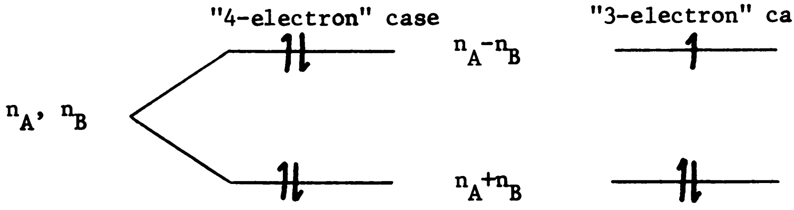
cleavage of both carbon-nitrogen bonds with the attendant recouping of the energy cost by partial formation of dinitrogen. Rate-determining cleavage of just one of the carbon-nitrogen bonds could be considered only if the resulting alkyl radical and diazenyl radical ($RN_2\bullet$) were stabilized to the extent of 30 kcal/mole (the average bond energy minus the observed enthalpy of activation). A tertiary alkyl radical is stabilized to the extent of only a few kcal/mole; a diazenyl radical usually has been considered to possess no stabilization (6).

With highly unsymmetrical diazenes, and particularly when Ra is phenyl, decomposition does appear to take place via diazenyl radicals (eq. 2). Several lines of evidence provide strong support for this view (7), including CIDNP observations of $PhN_2\bullet$, and studies of the dependence of rate on viscosity and on pressure. Consider the case of phenyltriphenylmethyldiazene (eq. 3). The activation enthalpy is +27 kcal/mole (1). There will be some

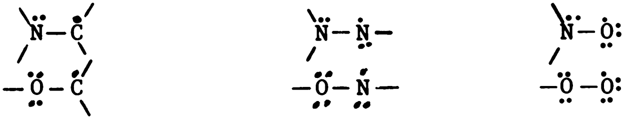
$$Ph{-}N{=}N{-}CPh_3 \rightarrow Ph{-}N{=}N\cdot + \cdot CPh_3 \quad \text{(eq. 3)}$$

destabilization of the ground state (steric) and considerable stabilization in the triphenylmethyl radical. Are these two sources sufficient to account for the observed 50 kcal/mole difference between the average carbon-nitrogen bond energy and the enthalpy of activation? Probably not; it appears reasonable to attribute part of this lowering to stabilization in the phenyldiazenyl radical, $PhN_2\cdot$. Although there have been numerous attempts to observe this species in the esr, they have not been successful, ascribable in part to the high exothermicity of the conversion of a diazenyl radical, $RN_2\cdot$, to $R\cdot$ and N_2. However, a diazenyl radical possesses an aspect that provides considerable stabilization in other systems, - an odd electron located on an atom adjacent to an atom containing a lone pair, $\dot{A}{-}\ddot{B}$. The stabilization provided by this "three-electron" bond is most easily seen in reference to the "four-electron" counterpart, $\ddot{A}{-}\ddot{B}$. Interaction between lone pairs results in formation of new energy levels, one bonding and one antibonding. In the



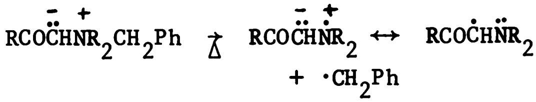
"four-electron" case, the net result is destabilizing (the antibonding combination is somewhat more destabilizing than the bonding combination is stabilizing). In the "3-electron" case, the net result is stabilizing. The magnitude of the stabilization obviously depends on the extent of the interaction of the odd electron with the adjacent lone pair, in turn dependent on the particular atoms involved, the geometry of the system, and the state of hybridization at each atom. Some examples are shown in Chart 1.

Chart 1



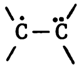
A qualitative resonance representation of the interaction is $\ddot{A}-\dot{B} \leftrightarrow {}^{+}\dot{A}-\ddot{B}^{-}$; i.e. one might expect the strength of the interaction to increase with increasing electronegativity of B and increasing shareability of the lone pair of A. Of those shown in Chart 1, the most stable "three-electron" species are the nitroxyls, R_2NO (8), in keeping with the simple generalization expressed above. Evidence is available on all of the systems shown in Chart 1 but will not be reviewed here. Suffice it to say that the adjacency of a lone pair may be a strongly stabilizing factor in radical stability. The question of stability is a complex one. In some instances the species in question may be subject to direct thermochemical measurement, e.g. some nitroxyls (9). In some instances, two species in question may be isomeric, and the question of relative stability may be answered unambiguously, e.g. R_2NO more stable than RNOR. In other cases, apparent stability may be related to drawbacks to dimerization. For example, dimerization of nitroxyls would entail the formation of the weak oxygen-oxygen bond, and the change from "three-electron" stabilization in nitroxyls to electron destabilization in the dimer from the four contiguous atoms each holding a lone pair. Other comparisons of stability in such cases might come from relative reactivity in atom transfer reactions. "Three-electron" bonding involving carbon radicals deserves further attention. Much evidence exists to show that hydrogen abstraction by alkoxyl radicals or halogen atoms is facilitated by the adjacency of nitrogen or oxygen (10). Much of this facilitation may be due to ionic contributions to the transition state of the abstraction process. Few experiments bear directly on the matter of how much ground state stabilization is present in radicals such as $R_2\ddot{N}\dot{C}R_2$ (11). Another index of "three-electron" stabilization is the relative ease of homolytic bond cleavages. In the Stevens rearrangement (12) a carbon nitrogen bond is broken homolytically at activation energies well below the carbon-nitrogen bond strength. The "three-electron" bond in the nitrogen-containing

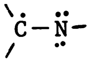
e.g.

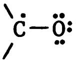


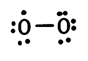
$$\text{RCO}\overset{-}{\ddot{\text{C}}}\text{H}\overset{+}{\text{N}}\text{R}_2\text{CH}_2\text{Ph} \xrightarrow[\Delta]{} \text{RCO}\overset{-}{\ddot{\text{C}}}\text{H}\overset{+}{\dot{\text{N}}}\text{R}_2 \leftrightarrow \text{RCO}\dot{\text{C}}\text{H}\ddot{\text{N}}\text{R}_2$$
$$+ \cdot\text{CH}_2\text{Ph}$$

moiety provides much stabilization thereby lowering the energy needed to effect cleavage. Many related rearrangements are also in this class (12), and provide information on the degree of stabilization in "three-electron" bonds. The scope of "three-electron" stabilization is far broader than the few cases shown in Chart 1. Some additional important charge types are shown below, and include radical anions of olefins and carbonyl compounds (ketyls), both substantially more stable than the corresponding carbon radical or alkoxyl radical.



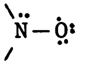




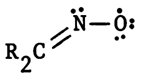


Mention should be made of "three-electron" bonding involving second row elements, e.g. the effect of adjacent atoms containing lone pairs on phosphorus or sulfur radicals ($\ddot{A}-\dot{B}$ in which B is P or S), and the effect of phosphorus or sulfur adjacent to a radical ($\dot{A}-\dot{B}$ in which A is R_2P or RS). The great increase in rate of decomposition of symmetrical diazenes containing α-RS substituents (13) is suggestive of stabilization in $RS-\dot{C}R_2$, a conclusion that is also supported by the ease of homolysis of sulfur-carbon bonds in sulfonium ylide rearrangements (12).

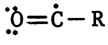
Extension to systems in different states of hybridization is also of interest. The odd electron in the iminoxyl radical is

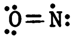


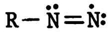
vs.



in an orbital interacting with the nitrogen lone pair and is distributed between the nitrogen and oxygen (14), not in a p orbital. Adjacent "three-electron" arrays are also found in systems containing a multiple bond between A and B. The reduced







strength of the aldehydic carbon-hydrogen bond compared to an alkyl carbon-hydrogen bond (80 vs. 100 kcal/mole) and the ease of abstraction of the aldehydic hydrogen by carbon radicals [e.g. in free radical chain decarbonylation reactions, (15)] are suggestive of greater stabilization in acyl radicals, RCO, than in vinyl or alkyl radicals. "Three-electron" stabilization may also be of consequence in diazenyl radicals, $RN_2\cdot$, the species under discussion at the beginning of this brief survey of "three-electron" stabilization. Some information on diazenyl radicals comes from consideration of the decomposition of diazene N-oxides.

On the Mechanism of Decomposition of Diazene N-Oxides

As indicated above, symmetrical diazenes decompose by a process involving synchronous cleavage of both carbon-nitrogen bonds (eq. 1). Some years ago we were interested in the question of

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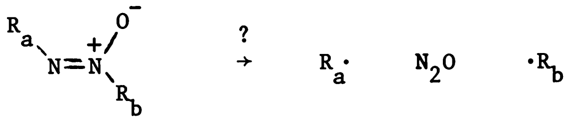
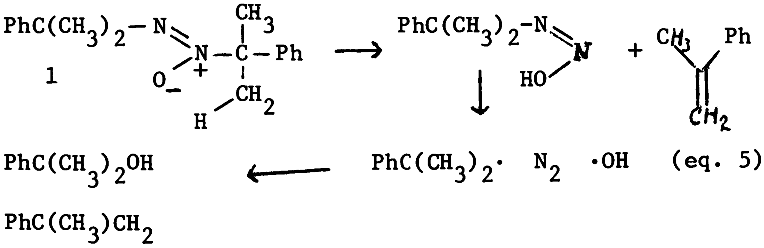
the possible use of diazene N-oxides as sources of free radicals (eq. 4). Examination of the literature revealed a compound re-



(eq. 4)

ported to be the N-oxide of azobisisobutyronitrile, AIBN-O (16). We repeated Aston and Parker's preparation. The compound does indeed have the structure claimed and is quite stable, requiring hours at 180° to effect decomposition. We have also prepared dicumyldiazene N-oxide, 1, and compared it with the corresponding diazene. Decomposition of 1, like AIBN-O, is very slow. The products of decomposition are α-methylstyrene, water, dinitrogen, and a small amount of cumyl alcohol. Nitrous oxide is not a product, and decomposition clearly is not proceeding by the process shown in eq. 4. The decomposition is most simply understood in terms of a cyclic decomposition, eq. 5, related to the Cope amine oxide decomposition (17).



(eq. 5)

The azo compound, dicumyldiazene (18), decomposes much faster than the corresponding N-oxide, kazo/kazozy = 10^5 (est. for 180°). In summary, diazenes that normally decompose by synchronous two-bond cleavage (eq. 1) decompose much more rapidly than the corresponding N-oxides. The failure of N-oxides to decompose synchronously to nitrous oxide is apparent from a consideration of the appropriate energy cycle (Fig. 1). A limiting factor is the paucity of thermochemical data for diazene N-oxides. The heat of oxidation of the diazene in Fig. 1 is from the heats of combustion of diphenyldiazene and the corresponding N-oxide (19). The energy cycle indicates that the decomposition of a diazene N-oxide into nitrous oxide and two radicals would be +65 kcal/mole, approximately 40 kcal/mole more endothermic than the decomposition of the related diazene into the same two radicals and dinitrogen. The major difference lies in the great stability of dinitrogen; oxidation of dinitrogen is endothermic whereas oxidation of the diazene is exothermic. Snyder has called attention to the great difference in stability of cyclic diazenes and diazene N-oxides in retrocycloaddition reactions (20). For example, 2,3-diazabicyclo [2.2.1]hepta-2,5-diene and the corresponding N-oxide are

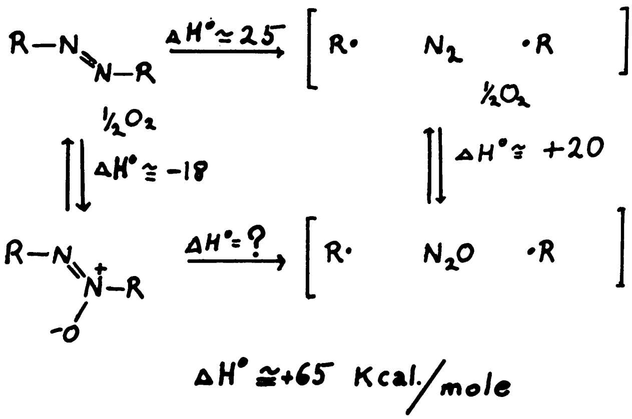


Figure 1. Estimated heat of reaction for conversion of a diazene N-*oxide into radicals and nitrous oxide*

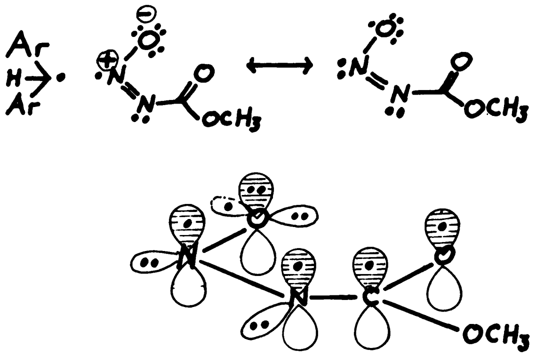


Figure 2. Representation of the transition state for decomposition of diazene N-*oxide 7*

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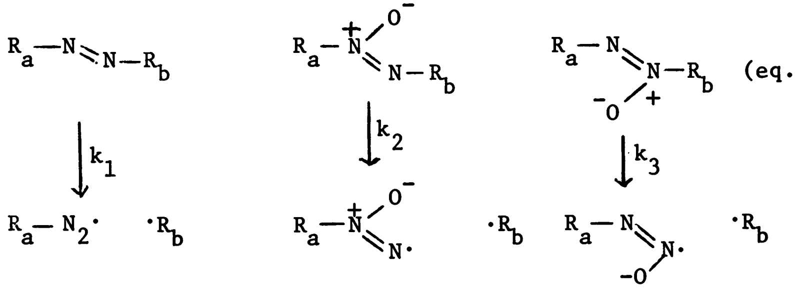
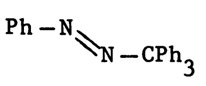
converted to cyclopentadiene and N_2 and N_2O, respectively; the diazene reacts seventeen powers of ten faster than the diazene N-oxide (20). Here, also, it seems likely that the types of differences noted in Fig. 1 are important. However, the synchronous nature of the decomposition of 2,3-diazabicyclo[2.2.1]hepta-2,5-diene and the corresponding N-oxide makes it more difficult to estimate differences in activation energies for these systems than for the endothermic, homolytic fragmentation reactions of diazenes and diazene N-oxides of Fig. 1.

We have indicated that diazenes with sufficiently different groups may undergo one-bond cleavage in the rate-determining step (eq. 2). How do these systems compare in rate with the corresponding N-oxides? The comparisons in eq. 6 are of interest.



(eq. 6)

An ideal system in which to make these comparisons would appear to be phenyltriphenylmethyldiazene, 2, and the corresponding N-oxides. Oxidation of the diazene with peroxytrifluoroacetic acid affords a diazene N-oxide, assigned structure 3 on the basis of spectroscopic data (principally, ultraviolet



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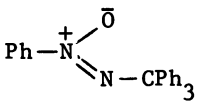
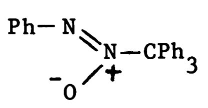


3



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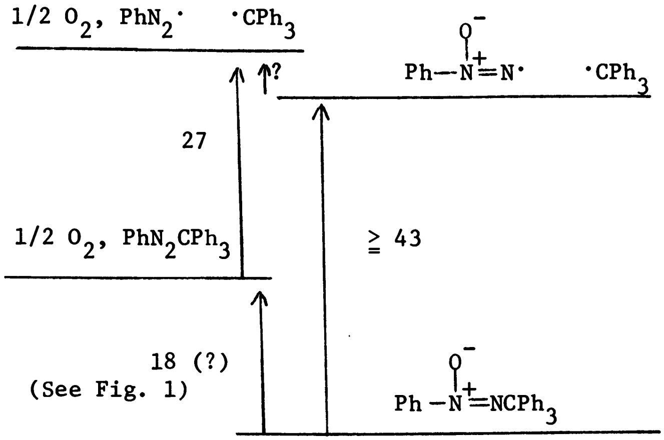
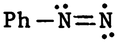
comparisons). Compound 3 is a very stable substance decomposing only slowly at 290°C (half-life ~ 50 min, a minimum value of 43 kcal/mole for $\Delta G^{\ddagger}$). Here, also, the diazene N-oxide is much more stable than the corresponding diazene, although the reason must be different from that operative with the symmetrical, two-bond-cleaving diazenes described above. The comparisons of interest are shown in Chart 2. There are many uncertainties, including a lack of knowledge of the mode of decomposition of diazene N-oxide, 3! One point is clear: for diazenes that decompose by one-bond cleavage in the rate-determining step, placement of an oxygen on the beta-nitrogen greatly decreases the rate of

Chart 2



decomposition, i.e., in eq. 6, $k_1 >> k_2$. Much of this difference may be attributable to the difference between 5 and 6. The



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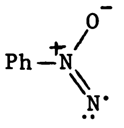

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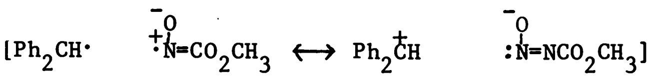
"three-electron" bonding possible in 5 is precluded in 6 by the presence of the oxygen. The uncertainties in Chart 2 are too great to allow placement of a number on the amount of "three-electron" stabilization in 5, but one should note in particular that a localized (non-stabilized) phenyldiazenyl radical would be expected to lie at a considerably higher level than that shown in Chart 2 (on the assumption that the heat of oxidation of localized $PhN_2\cdot$ to PhN(O)=N• would be comparable to the heat of oxidation of a diazene to a diazene N-oxide).

The third comparison of interest is that of a one-bond-cleaving diazene with the corresponding N-oxide in which the oxygen is on the alpha nitrogen (eq. 6, k_1 vs. k_3). A desirable point of comparison would be triphenylmethylphenyldiazene N-oxide, 4. Several approaches to prepare this compound have been unsuccessful. An alternative was the methyl triphenylmethyldiazenecarboxylate, $Ph_3CN_2CO_2CH_3$, a diazene that decomposes into radicals at a rate close to that of phenyltriphenylmethyldiazene (21). Efforts to obtain the N-oxide of the triphenylmethyldiazenecarboxylate were also unsuccessful. Consequently, we sought to answer the question by examination of a benzhydryl system. Efforts to prepare benzhydrylphenyldiazene N-oxide afforded only the unwanted isomer (oxygen on the nitrogen attached to phenyl). Success was achieved with methyl benzhydryldiazenecarboxylate. Oxidation of this diazene afforded the N-oxide in which the oxygen is on the benzhydryl nitrogen, 7a. Decomposition was carried out at 150° in o-dichlorobenzene, affording the products summarized in eq. 7 (the numbers are moles per mole of reactant). The products

$$7a,\ Ph_2CHN(O){=}NCO_2CH_3 \xrightarrow{150°}$$

$$\begin{array}{cccc} Ph_2CHOCO_2CH_3 & Ph_2CHOCH_3 & Ph_2CO & \\ 0.30 & 0.27 & 0.13 & \\ CH_3OH & Ph_2CHCHPh_2 & Ph_2C{=}CPh_2 & Ph_2CH_2 \\ 0.12 & 0.04 & 0.04 & \text{trace} \end{array} \qquad \text{(eq. 7)}$$

are strongly suggestive that decomposition involves radicals. The decomposition is first order in reactant, and the rate is not increased by the addition of bisbenzhydryldiazene or methyl triphenylmethyldiazenecarboxylate, sources of benzhydryl and carbomethoxy radicals, - two likely candidates for chain carriers in a possible free radical chain decomposition. Consequently, the decomposition of diazene N-oxide 7a appears to proceed by a unimolecular path. Is the rate-determining step simply a homolysis of the benzhydryl - N(O) bond, or are ionic contributions important in the transition state of this reaction? The electron-withdrawing nature of the carbomethoxy group might make this example susceptible to ionic contributions to the transition state of the carbon-nitrogen cleavage. Two related diazene N-oxides were



$$[Ph_2CH\cdot\quad \overset{^{-}O}{\overset{|}{{}^{+}\cdot N}}{=}CO_2CH_3 \longleftrightarrow Ph_2\overset{+}{C}H\quad :\overset{^{-}O}{\overset{|}{N}}{=}NCO_2CH_3]$$

prepared, the p, p′-dimethyl (7b) and the p, p′-dichloro (7c) derivatives. Decomposition of each afforded a product mixture similar to that from 7a (eq. 7). Rates of decomposition are summarized in Table 2. The effect of the para-methyl and the para-chloro substituents is small, both groups exerting a small rate acceleration. [For comparison, the corresponding rel k's for

Table 2

Decomposition of $(p\text{-}RC_6H_4)_2CHN(O){=}NCO_2CH_3$ in o-Dichlorobenzene at 150°

Cpd	R	rel k	σ
7a	H	1.0	0
7b	CH_3	5.0	-0.17
7c	Cl	1.2	+0.23

$(p\text{-}RC_6H_4)_2CHCl$ in ethanol, 25°C are H (1.00), CH_3(413), Cl (0.15)]

(22). Thus, in decomposition of diazene N-oxides, 7, there is little change in the degree of charge at the benzhydryl carbon in going from ground state to transition state. The small rate effects are in accord with simple homolysis of the benzhydryl carbon-nitrogen bond [eg. the rel k's for decomposition of p-RC$_6$H$_4$C(CH$_3$)$_2$N=NC(CH$_3$)$_2$C$_6$H$_4$-p-R at 43° in toluene are H (1.00), CH$_3$(1.46), Cl (2.67)] (23). A representation of the transition state for decomposition of diazene N-oxide 7 is shown in Fig. 2. Homolytic cleavage of the carbon-nitrogen bond at a cost of only 33 kcal/mole is possible in this case by the combined help of benzhydryl radical stabilization and "three-electron" stabilization in the diazenoxyl radical (Fig. 2).

How does the rate of decomposition of diazene N-oxide 7 compare with the corresponding diazene, 8? Direct measurement of the rate of decomposition of methyl benzhydryldiazenecarboxylate, 8, was complicated by tautomerization to the corresponding hydrazone, Ph$_2$C=NNHCO$_2$CH$_3$. The rate of decomposition of 8 was estimated from the measurement rate of decomposition of benzhydrylphenyldiazene (24) and the observation that the rates of decomposition of phenyltriphenylmethyldiazene and methyl triphenylmethyldiazenecarboxylate are the same (21). Relative rates of 7, 8, and a related nitrone, 9 (25) are summarized below.

		rel k, 150°	$\Delta G^{\ddagger}$, 150°
7	Ph$_2$CHN(O)=NCOOCH$_3$	1.0	33.3
8	Ph$_2$CHN=NCOOCH$_3$	(~10.)	(~31.5)
9	Ph$_2$CHN(O)=CPh$_2$	~1	33

Diazene 7, diazene N-oxide 8 and the nitrone 9 all decompose at a comparable rate. The diazene N-oxide and the nitrone should both be aided by "three-electron" stabilization in the diazenoxyl and the iminoxyl moieties, respectively (see Fig. 2). The implication (by reference to the type of diagram shown in Chart 2 but not repeated for the present case) is that considerable "three-electron" stabilization also may be present in the diazenyl radical. The comparison of 7 with 8 suffers from some uncertainty in the matter of one-bond vs. two-bond cleavage in the rate-determining step of the model system, benzhydrylphenyldiazene; there may be some weakening of the phenyl-nitrogen bond in the transition state. The greater rate for 8 (estimated) than for 7 may be more a consequence of some synchronous character to the decomposition of 8 than a consequence of comparable amounts of "three-electron" stabilization in the diazenyl radical, RN$_2$· and the diazenoxyl radical, RN$_2$O·. In either case, the conclusion from this example is that diazenes which decompose by one-bond cleavage in the rate-determining step (eq. 6) may decompose at a rate comparable to (or perhaps, less than) that of the corresponding N-oxide when the oxygen is on the nitrogen of the carbon-nitrogen bond undergoing homolysis (i.e. in eq. 6, $k_1 \lesssim k_3$).

In summary, the type of stabilization on which attention has been focussed here, "three-electron" bonding, appears to be an important factor in radical stabilization, applicable to many situations, and highly worthy of further investigation.

Acknowledgment. This work was supported, in part, by Public Health Service Research Grant CA-16592 and Training Grant 5T32 CA-09112 from the National Cancer Institute.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch008

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

9

Cage Effects in Peresters and Hyponitrites

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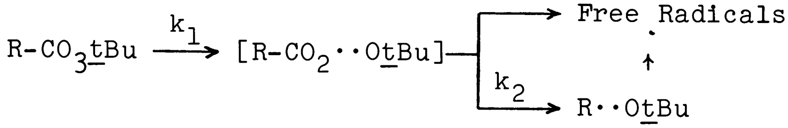
A. Introduction

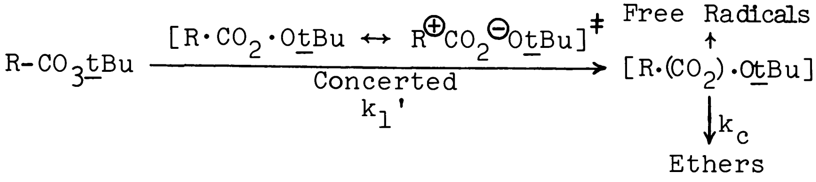
The studies of Bartlett and his coworkers (1) on decompositions of t-butyl peresters of a wide range of carboxylic acids clearly showed two mechanistic pathways for the production of free radicals. The first mechanism is the simple homolysis of the O-O bond to give an acyloxy t-butoxy (pair) intermediate which can decarboxylate in a subsequent step. This mechanism (A-1) pertains to the unimolecular free radical production for methyl, aryl, cyclopropyl and 1-norbornyl decarboxylation residues (R, equation A-1).

A-1



The second mechanism involves concerted cleavage of both the O-O and C-C bonds to give, through a single transition state, alkyl t-butoxy radical pairs. Activation parameters (2), isotope effects (3) and substituent effects (4) all indicate a change from stepwise (A-1) to concerted (A-2) mode of reaction when the decarboxylation residue has the stability of secondary alkyl or more. Hammet substituent constants

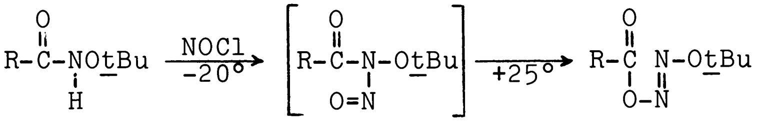
A-2



indicated a significant dipolar character (4) of the transition state for the concerted process (A-2) as shown.

The major factors determining the rates of free radical formation, as a function of the structure of the acyl group in peresters, are certainly well explained by these two mechanisms. Our investigation of the reactions of nitrosohydroxylamines (2), which rearrange to O-acyl-O'-*t*-butyl hyponitrites (3), were initiated with aim of providing a deaminative entry into the same formal intermediates as given by the corresponding peresters. The questions we hoped to answer were (i) to what extent would the deaminative process give rise to radicals which were atypical in reactions such as decarboxylation (k_2, A-1) and (ii) to what extent would the physical presence of the nitrogen molecule affect the observed yields of combination products (eg. k_c, A-2).

Our initial study (5) involved the low temperature nitrosation of the benzoyl hydroxyamate (1, R=Ø) to give the N-nitroso derivative (2, R=Ø) which, in turn, was expected to rearrange to the O-benzoyl-O'-*t*-butyl hyponitrite (3, R=Ø) by analogy with nitrosoamide rearrangements (6). Solutions of the nitroso hydroxamate were easily obtained and rearrangement to the hyponitrite was rapid at room temperature. It was somewhat surprising to find that the hyponitrite rearrangement product was relatively stabile at room temperature in view of the short lifetime of aryl diazoacylates towards dissociation to diazonium ions (7).



$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{N}O\underline{t}Bu} \xrightarrow[-20^\circ]{NOCl} \left[\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{O=N}{|}}{N}{-}O\underline{t}Bu}\right] \xrightarrow[+25^\circ]{} \mathrm{R{-}\overset{\overset{O}{\|}}{\underset{\underset{O-N}{|\quad\|}}{C\quad N}}{-}O\underline{t}Bu}$$

1 2 3

The decomposition of the benzoyl hyponitrite occurred at a slow rate at room temperature giving products typical of benzoyloxy and *t*-butoxy free radicals. A careful comparison (8) of the abstraction/β-scission competition showed that the radicals formed from the deamination give the same product ratios as the perbenzoate when extrapolated to a common temperature. Thus, the deaminative nature of this reaction does not give free radicals with any unusual tendency for decarboxylation or β-scission as might be expected if they were vibrationally excited above the barrier for the fragmentation.

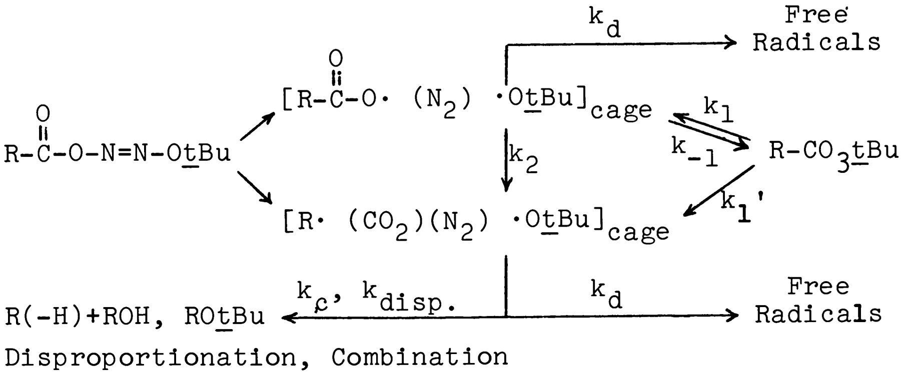
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

B. Acyloxy t-Butoxy Cage Reactions.

The most interesting product from the decomposition of this hyponitrite was t-butyl perbenzoate. The fact that free radicals accounted for the balance of the reaction products made it seem likely that the perester was formed by cage combination. This was supported by the observation that the yield of this product increased with increased solvent viscosity (5, 8). Furthermore, oxygen-18 labelling studies showed that the perester was formed with essentially complete randomization of the benzoyloxy oxygen atoms and that this randomization did not occur in any step preceding the decomposition of the hyponitrite (8). All of these observations are consistent with a cage combination process for the formation of the perester product.

One implication of cage combination of benzoyloxy t-butoxy pairs in the hyponitrite reaction was that the O-O bond homolysis of peresters, not proceeding by the concerted reaction (A-2), must be reversible. Conversely, hyponitrites corresponding to peresters which did undergo the concerted reaction should not give perester products. Finally, it was clear that comparison of ether yields, formed by cage combination of alkyl-t-butoxy pairs from peresters and hyponitrites, should shed light on the importance of the intervening small molecules (CO_2 or N_2 and CO_2) initially present. The phenomenological scheme which characterizes this kinetic situation is shown below (Scheme I).

Scheme I



This scheme shows the intervention of one class of cage radical pair which can decay exclusively by first order reactions (irreversible diffusive separation to

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

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free radicals (k_d), combination k_{-1} or k_c), disproportionation ($k_{disp.}$) or decarboxylation (k_2)). The observables from the two types of initiators may be related through the cage combination efficiency ratio F. These observables are the isolated yields of per-

$$F \equiv (1/(\text{Fraction cage efficiency})) - 1$$

ester (y_p) from the hyponitrite, the yield of ether (y_e) from the perester or the hyponitrite, the observed rate constant for decomposition of the perester (k_o) and the observed rate constant for scrambling of oxygen-18 from carbonyl labelled perester (k_s). The algebraic connection between these observables and Scheme I are as shown.

$$\text{B-1}\quad \frac{k_o}{k_1-k_o} = \frac{k_o}{k_s} = (\frac{1}{y_p}) - 1 = \frac{k_d}{k_{-1}} + \frac{k_2}{k_{-1}} = F_{perester}$$

$$\text{B-2}\quad k_1 = k_o + k_s$$

$$\text{B-3}\quad (\frac{1}{y_e}) - 1 = \frac{k_d}{k_c} + \frac{k_{disp.}}{k_c} = F_{ether}$$

If it is assumed that k_d (diffusive destruction of the cage pair) is the only solvent (viscosity) sensitive rate constant, then the qualitative implications of the scheme are obvious. The value of F should follow the fluidity (f = 1/viscosity). This means that the values of k_o for a perester undergoing simple O-O bond homolysis should increase with fluidity (viscosity decrease) while k_s should decrease with solvent fluidity. The yield of a perester product, from the corresponding hyponitrite, should increase with fluidity decrease (viscosity increase). The yields of ethers from either perester or hyponitrite should likewise increase with fluidity decrease. All of these qualitative expectation were in fact observed (Table I).

While these qualitative observations substantiate the gross features of the cage scheme, quantitative comparisons are necessary if one is interested in the effects such as those due to the (variable) intervening molecules on cage reactions. The value of k_1, the fundamental rate constant for O-O bond homolysis of a nonconcerted perester, is not directly available from any single experiment in condensed media. According to Scheme I and the assumption that k_d is the only viscos-

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

Table I

Cage Product Yields[a] from $R\text{-}CO_2\text{-}N_2\text{-}O\underline{t}Bu$, 32°C

R	% Perester (RCO_3tBu)	% O^{18} Scrambling[b]	% Ether (ROtBu)	Ref.
C_6H_5	9.0, 38.0	98.	<.1	5,8
Cyclopropyl[c]	21.0, 46.0	90.	-	9,21
CH_3	2.7, 10.2	93.	8.9, 41.7	10
i-Propyl	<.1	-	10.0, 25.0	11,21
2-Butyl	<.1	-	11.3, 27.8	12,13

a) Low viscosity (hexane, n ∿0.3cp) followed by high viscosity (Nujol, n ∿17.cp), percentages based on nitrogen evolved.

b) % oxygen-18 scrambling in the isolated and purified perester product from reaction of carbonyl-$\underline{O}^{18}$ labelled hyponitrite.

c) Denitrosation complicates the cyclopropyl products; T. Koenig, J. A. Hoobler and W. R. Mabey, J. Am. Chem. Soc., 94, 2514 (1972).

ity sensitive rate constant, k_1 should be obtained from extrapolation of values of k_o to infinite fluidity (zero viscosity) (14). Figure 1 shows such an extrapolation for *t*-butyl perbenzoate against the square root of solvent viscosity (8). The value of k_1, obtained from this extrapolation, can be used to obtain F_p values for (re)combination of benzoyloxy *t*-butoxy pairs with no intervening molecule using the values of k_o. Figure 2 shows a comparison of the combination efficiency ratios (F_p's) for the hyponitrite (squares) and perester (circles). Both plots appear to be linear with square root of fluidity and both pass through the origin. The zero intercept in such a plot implies that no other reaction (like decarboxylation, k_2, Scheme I) competes with combination except diffusive destruction of the cage pair and that the yield of cage product at infinite viscosity would be 100%. The difference in the two slopes in Figure 2 could be ascribed to the intervening nitrogen molecule (and temperature difference) in the hyponitrite reaction, amounting to a reduction in the k_c of the N_2 (hyponitrite) separated pair by a factor of one fourth.

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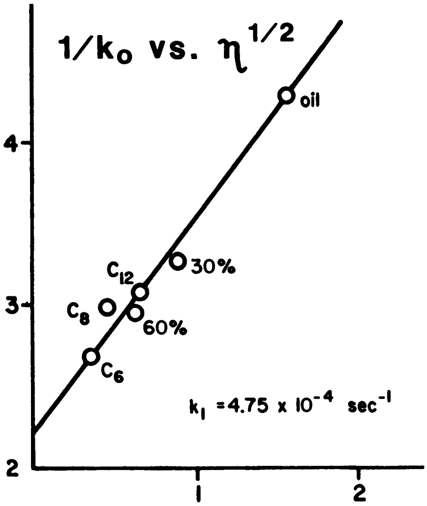

Figure 1. $1/k_o$ vs. square root viscosity. tert-*Butyl perbenzoate, 130°C (8).*

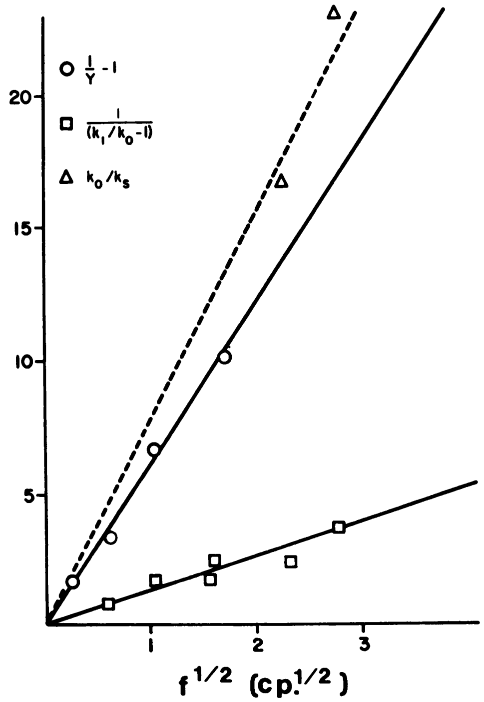

Figure 2. tert-*Butyl perbenzoate. F_p from 3 at 32°C (○), K_o (□), K_s (△) (8).*

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A second means of obtaining k_1 is from the sum of k_o and k_s. If k_d is really the only viscosity sensitive rate constant, then the k_o+k_s sum should be constant in all solvents and equal to the value obtained by extrapolation. This was not the case for either the perbenzoate (8) or the peracetate (3). Figure 2 also shows the F_p values from k_o/k_s which takes into account the variation of both k_o and k_s with solvent (triangles). The descrepancy the two means of estimating k_1 is very large and negates any conclusions concerning the N_2 effect.

During the course of this work, Neuman and his coworkers (15) measured activation volumes for a number of free radical initiators including t-butyl perbenzoate. It was clear that our hydrocarbon solvents of variable viscosity were also of variable internal pressure. The variations in k_o values for t-butyl perbenzoate were in accord with the +12cc/mole activation volume which Neuman found by external pressure variation. In order to remove objections concerning methods of estimating internal solvent pressure for our mixed solvent series, we used Neuman's +12cc/mole value for t-butyl perbenzoate to establish a set of differential solvent pressures for our mixed solvent system (using the experimental values of k_o) (16). The k_o+k_s sums for the perbenzoate and peracetate were then plotted (Fig. 3) versus the derived DSP solvent parameters to give activation volumes for the simple homolyses process (k_1). The activation volumes were within the range expected from external pressure studies. The variation in the k_o+k_s sums with varying solvent are entirely explainable in terms of the internal solvent pressure effect on k_1 which may be viscosity independent but is not solvent independent. The extrapolative method for estimating k_1 is therefore incorrect since there can be no constant value for this rate constant unless the corresponding activation volume is zero. Scheme I survives but the assumption that k_d is the only solvent sensitive rate constant in it, must be abandoned.

In order to avoid the large extrapolation to common temperature, required for comparison of the thermolysis of both t-butyl perbenzoate and the corresponding hyponitrite, we decided to study the photolysis of the perester under the same conditions of solvent and temperature as convenient for the thermal hyponitrite reaction (27°, hexane) (17). Product studies showed hexyl benzoate was formed from a chain induced reaction. The direct photolysis gave phenyl t-butyl ether and high relative yields of carbon dioxide. Both

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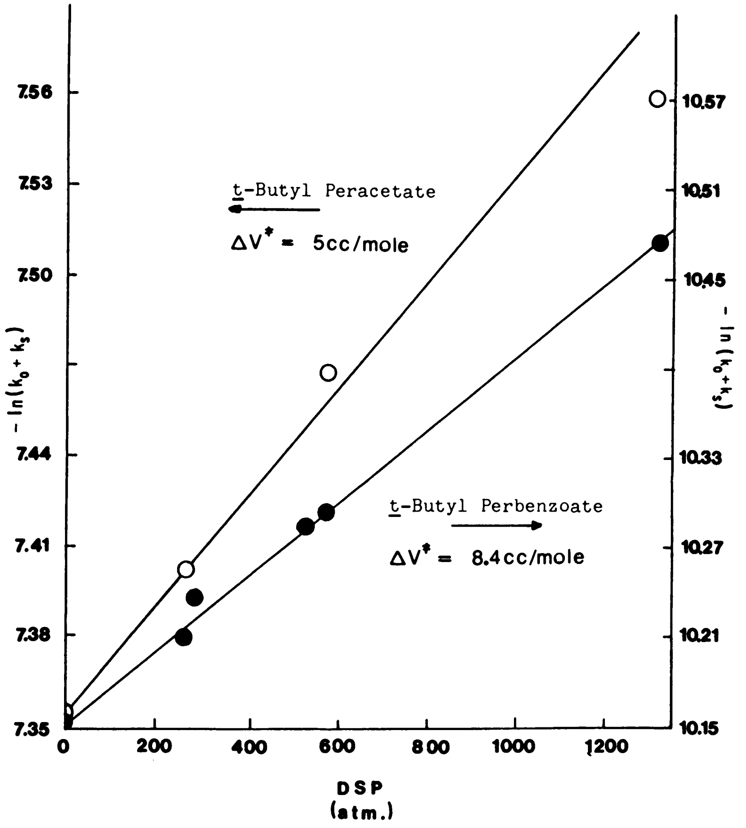

Figure 3. Activation volume from empirical differential solvent pressures (16)

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are indications that the reactive singlet excited state of the perester gives phenyl *t*-butoxy pairs, bypassing the benzoyloxy *t*-butoxy pair. Fortunately, the availability of the carbon dioxide yield data from the hyponitrite under nearly identical conditions allowed a correction for the fraction of the total photolysis which procedes in this manner. The fraction oxygen-18 scrambling of reisolated material after known fractions of overall perester disappearance and corrected for induced and concerted reactions, gave a minimum estimate of the fraction combination (0.18) which was twice the observed yield of perester from the hyponitrite (0.09) under nearly identical conditions. Acetophenone sensitized photolysis of the perester (presumably triplet) gave oxygen-18 scrambling corresponding to 8% cage reaction. The intervening nitrogen molecule and the spin barrier both appear to reduce the cage combination efficiency of benzoyloxy *t*-butoxy pair by a factor of one half.

A series of ring substituted benzoyl hyponitrites showed the rho value for combination of benzoyloxy *t*-butoxy pairs was +0.4 (18). The sign and magnitude of this reaction constant are both in accord with the O-O bond dipole repulsion (19) explanation of the rho value observed in perbenzoate homolysis ($\rho = -0.7$). The nonzero rho value observed for the benzoyloxy *t*-butoxy combination process implies a nonzero activation energy for combinations through the sign of the activation energy is left ambiguous.

C. Alkyl t-Butoxy Cage Reactions.

Isotope effects indicated that *t*-butyl isobutyrate underwent the concerted reaction (A-2) (20). Oxygen-18 scrambling of reisolated material, after partial decomposition showed the nonconcerted (A-1) process contributed only 2% to the overall reaction, exactly the amount estimated for the relative rate of *t*-butyl peracetate at the temperature used. The corresponding hyponitrite gave no detectable perester even at 0° in paraffin oil solvent (9). The isobutyryl system is thus one which gives i-propyl *t*-butoxy cage pairs with CO$_2$ or CO$_2$ and N$_2$ as intervening molecules. The cage efficiency ratio (F$_e$) for ether fromation gave a fairly linear correlation with square root fluidity ($1/\eta^{1/2}$) (21). According to Scheme I, the intercepts of such plot should give the ratio of k_{disp}/k_c. The observed intercepts ($\sim$2.3) was very close to the propylene-ether ratio found by Kochi and Sheldon in their studies of the photolysis of the perester in decalin solution. It

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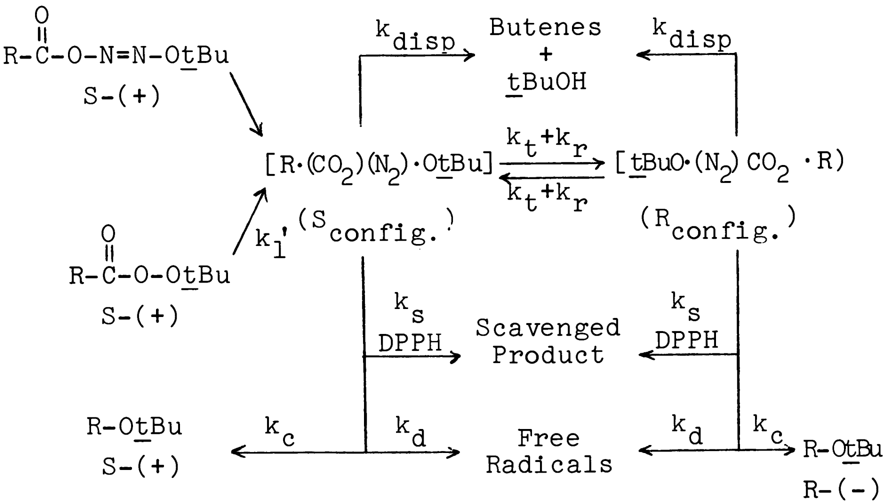
should be noted that intercepts of F_e correlations at zero fluidity give the ratio of k_{disp}/k_c through measurement of only the ether yield and the good numerical agreement of these intercepts with the value obtained from the measured ether olefin ratio lends strong support to the methodology associated with Scheme I.

These results on the isobutyryl system convinced us that both the perester and the hyponitrites with secondary alkyl side chains underwent concerted homolysis to give secondary alkyl-*t*-butoxy cage pairs in a single step. We decided to investigate the chiral 2-methylbutyrate systems which would allow an examination of the relative efficiency of the tumbling process of the 2-butyl radical compared with the combination and disproportionation. We also wanted to examine the effects of added scavengers on the ether yields and optical purities. These additional kinetic channels are added to the phenomenological cage model and shown as Scheme II.

Scheme II



Scheme II generates several new algebraic relationships between the observables of the system and the interpretative rate constants. The observables are the yields of 2-butyl *t*-butyl ether (y_e) and its optical urity (OP). The interpretative rate constants are that for combination to give the ether (k_c), that for disproportionation (k_{disp}), that for diffusive destruction of the cage pair (k_d), that for the tumbling of the 2-butyl radical with respect to the *t*-butoxy radical which racemizes the cage pair (k_s), that for internal rotation of the radical center about the ethyl group which racemizes the cage pair (k_r) and that for scavenging of the cage pair by DPPH. The algebraic relationships are shown below.

C-1 $$F_e = \frac{k_{disp.}}{k_c} + \frac{k_d}{k_c} + \frac{k_s[DPPH]}{k_c}$$

C-2 $$[F_e]_{[DPPH]} - [F_e]_o = \frac{k_s[DPPH]}{k_c}$$

C-3 $$\frac{1}{Y_e}\left(\frac{1-OP}{2(OP)}\right) = \frac{k_r}{k_c} + \frac{k_t}{k_c}$$

C-4 $$\left[\frac{2(OP)}{1-OP}\right]_{[DPPH]} - \left[\frac{2(OP)}{1-OP}\right]_o = \frac{k_s[DPPH]}{k_t+k_r}$$

Figure 4 shows the results of the combination efficiency ratio (F_e) for the perester at 102° (22) and the hyponitrite at 30° (12) against fluidity to the 0.75 power (eq. C-1, [DPPH]=0). The intercepts again measure the $k_{disp.}/k_c$ ratio. The difference in the intercepts can be explained by a 0.9 kcal/mole difference in the activation energies for disproportionation and combination. The slope of the perester line (1.49) is lower than that for the hyponitrite (1.96), suggesting the additional nitrogen molecule which intervenes between the two radicals of the cage pair reduces k_c to some extent. The higher temperature required for the perester tends to mask this effect.

The optical purity functions are again linear with $f^{0.75}$ (Figure 5, eqn. C-3) (12). The slopes are interpreted as measuring the ratio of 2-butyl radical tumbling to combination (k_t/k_c). The difference in the two provides an independent suggestion that k_c is reduced by the nitrogen molecule formed in the cage from the hyponitrite. The extent of reduction is the same as indicated by the relative slopes in Figure 4. The intercepts are interpreted as the ratio of the rate constants for internal rotation of the radical center to combination k_r/k_c and are again suggestive of a reduced k_c for the deaminative reaction.

Finally, the effect of DPPH on the yields of ether and its optical purity are shown in Figure 6 (12). The important result is that the cage scheme treats the scavenging reaction as a simple pseudo first order process and the linear plots are in good accord with these expectations. The observed ratio k_s/k_c is 3.66

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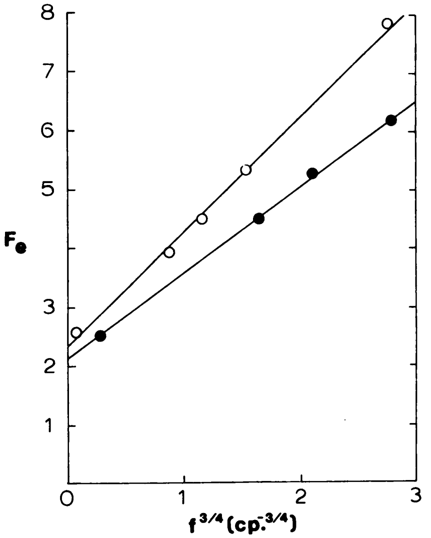

*Figure 4. (F_e) vs. $f^{3/4}$ for ether from 2-butyl-*tert*-butoxy radical pairs generated from perester (–●–) and hyponitrite (–○–) (13, 22)*

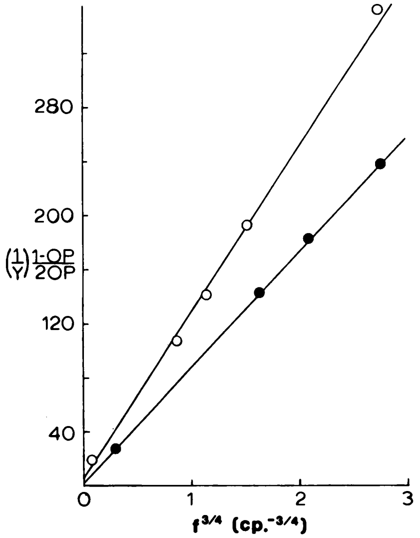

Figure 5. $(1/Y)[(1 - OP)/2OP]$ vs. $f^{3/4}$ for ether product produced from optically active hyponitrite (–○–) and perester (–●–) (22)

ℓ/mole in chloroform (η = 0.56 cp.). A stabile radical scavenger is capable of trapping about half the cage intermediate at concentrations around 1 M. The optical purity also responds in a systematic way to added DPPH. The ratio $k_s/(k_t+k_r)$ is 1.97×10^{-2} ℓ/mole in chloroform.

If the Debye-Stokes relationship and a tumbling radius for the 2-butyl radical of 2.0Å are assumed, the ratios of rate constants found here can be put in terms of absolute rate constants. These values are given in Table II (12) and we believe they correspond fairly well to the actual time scales of the reacting system. The nitrogen molecule effect is shown in the two values of k_c (1.0×10^9 for the hyponitrite at 32° vs. 1.8×10^9 for the perester at 102°). The temperature difference in the two sets of experiments makes this comparison less direct than one would like. The effective diffusion radius for destruction of the cage pair reflects the degree of internal consistency which these data possess.

Table II

Rate Constant Derived[a] from Scheme II

Reaction	Constant	Hyponitrite, 32°	Perester, 102°	E_a
Tumbling	k_t(1 cP)	(1.1×10^{11}sec^{-1})[a]	(1.5×10^{11}sec^{-1})[a]	0.0
Internal rotation	k_r	5.8×10^{10}sec^{-1}	6.7×10^{10}sec^{-1}	0.5 kcal/mole
Combination	k_c	1.0×10^{9}sec^{-1}	1.8×10^{9}sec^{-1}	0.0
Disproportionation	k_2	2.4×10^{9}sec^{-1}	3.8×10^{9}sec^{-1}	0.9
Scavenging	k_s(DPPH)	3.6×10^{9} l./(mol sec)		
Diffusion	k_d(1 cP)	2.0×10^{9}sec^{-1}	2.7×10^{9}sec^{-1}	0
$r_{diffusion}$[b]		3.3 Å	3.2 Å	
$\tau_{combination}$[c]		1.8×10^{-10}sec	1.2×10^{-10}sec	
$\tau_{retention}$[d]		6.0×10^{-12}sec	4.5×10^{-12}sec	

a) Assuming 2.0 Å as the effective tumbling radius of the 2-butyl radical and the Debye-Stokes relationship.

b) The effective radius for diffusion using the Stokes-Einstein relationship and the derived k_d.

c) The lifetime for all pairs giving combination.

d) The lifetime of the pairs giving retention.

D. A Suggested Model for the Cage Effect.

Our general conclusion from all of the above experiments was that a phenomenological scheme, which recognizes a single class of cage radicals undergoing cage (re)combination (k_c,k_{-1}) in competition with first order (irreversible) diffusive destruction to free radicals (k_d) and possibly other first order reactions

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(such as disproportionation ($k_{disp.}$), decarboxylation (k_2), molecular tumbling (k_t), internal rotation (k_r) and scavenging (k_s[Scavenger]), is the best way to view these reactions. The intercepts of F-fluidity correlations (at f=0) appear to give reasonable estimates of relative rates of competitive chemical reactions. Intervening molecules have a small but definite effect as evidenced by the slopes and intercepts of the F-fluidity correlations.

One additional observation from these experiments is that the common assumption that the rate constant for diffusive destruction of the cage pair (k_d) is the only one which responds to changes in solvent is untenable. A second is that the power of fluidity which is needed to give linear correlations with F ratios is highly variable. Our results at the low fluidity end gave correlations with powers less than 1 (0.5, Figure 2, 0.75, Figures 4, 5). Other cases (23,24) give powers equal to one out to fluidity of about 5 $cp.^{-1}$ with powers greater than unity applying to data obtained at fluidities greater than 5 $cp.^{-1}$ (more fluid, less viscous than hexane at 102°). First power fluidity correlations are expected on the basis of the model of Noyes (25) for geminate combination. However, a number of features make the Noyes model distinct from the cage idea of Frank and Rabinowitch (26) and it is difficult for it to accommodate the less than first power fluidity dependence which is sometimes observed. We therefore felt it worthwhile to attempt to develope a different mathmatical model for the cage effect which remained as close as possible to the phenomenological scheme discussed above.

The model begins with the postulate that a region of space in a solution may be defined as the cage. A pair of radicals inside this region are "caged" and those outside this region are "free". The radius of the cage is called ρ. For simplicity, we consider the cage to be spherical. We therefore begin with the equation (D-1) for a spherical source of particles diffusing into an infinite sink. This equation requires

D-1 $$P_{(r,t)} = \frac{A}{2}\left[\operatorname{erf}\left(\frac{r_N - r}{\sqrt{4Dt}}\right) + \operatorname{erf}\left(\frac{r_N + r}{\sqrt{4Dt}}\right) + \sqrt{\frac{4Dt}{\pi r^2}}\left\{\exp\left(\frac{-(r+r_N)^2}{4Dt}\right) - \exp\left(\frac{-(r_N - r)^2}{4Dt}\right)\right\}\right]$$

a second radius which contains all of the pair at t=0. This we call the normalization radius (r_N, $A=P_{(r_N, t=0)}$).

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The probability that a cage pair is destroyed by diffusive separation is the integral of the source equation (D-1) from the outside boundary of the cage (ρ) to infinity (equation D-2).

D-2 $$P_D(t) = \int_{\rho}^{\infty} 4\Pi r^2 P(r,t)dr$$

The probability the cage pair exists at time t ($\Theta(t)$, D-3) is taken as the product of the probability ($1-P_{D(t)}$) that it has not yet diffused times the probability that it has not yet reacted by any chemical reaction (k_i) ($e^{-\Sigma k_i t}$ were k_i pertains to any of the first order chemical reactions mentioned above; combination, disporportionation, scavenging, etc.)

D-3 $$\Theta(t) = e^{-\Sigma k_i t}(1-P_D(t))$$

The probability of forming combination product is simply obtained by integration as in any first order reaction. The final results of these integrations can

D-4 $$Y_c = \int_0^{\infty} k_c e^{-\Sigma k_i t}(1-P_D(t))dt$$

be written in fairly simple form using the parameters P (which is the ratio ρ/r_N) and B (which is $\sqrt{D/k_c r_N^2}$). Two solutions (D-5 and D-6) are required dependent on P(P>1 or P<1). The value of a cage product yield (Y_c)

$$P = \frac{\rho}{r_N} \qquad B = \sqrt{\frac{D}{\Sigma k_i r_N^2}}$$

D-5 $P > 1$

$$Y_c = \frac{k_c}{\Sigma k_i}\left\{1 - \frac{3B}{2}(P+B)\left[(1+B)\exp\left(-\frac{(P+1)}{B}\right) + (1-B)\exp\left(-\frac{(P-1)}{B}\right)\right]\right\},$$

D-6 $P < 1$

$$Y_c = \frac{k_c}{\Sigma k_i}\left\{P^3 - \frac{3B}{2}(1+B)\left[(P+B)\exp\left(-\frac{(P+1)}{B}\right) + (B-P)\exp\left(-\frac{(1-P)}{B}\right)\right]\right\}$$

depends on four variables, the effective diffusion coefficient for separation of the pair (D), the first order rate constants for chemical reactions ($k_i = k_c$, k_2, $k_{disp.}$, k_s[DPPH], etc.), the radius of the cage (ρ) and normalization radius require to enclose the pair as of t=0 when random motion begins (r_N). It is clear from D-5 that F ((1/Y)-1) values give $\Sigma k_i/k_c$ ($i \neq c$) when D=0 (fluidity of zero or infinite viscosity) so long as $\rho > r_N$ (P>1). This consideration applies to the (f=0) intercepts shown in Figure 4 where k_i is disproportionation ($k_{disp.}$). If all chemical reactions are negligibly slow compared to combination ($\Sigma k_i = k_c$ or k_i ($i \neq c$) = 0) and P>1, then the intercept of the F-fluidity correlation (f=0) should be zero as indicated for t-butyl perbenzoate (Figure 2).

On the other hand, with $\Sigma k_i (i \neq c) = 0$, a nonzero intercept (f=0, D=0) is predicted if $p<1$ in which case it should be interpreted as the ratio of the cage volume to the normalization volume at zero fluidity. This condition could apply to radicals studied by matrix isolation which experimentally require an intervening molecule in the generating reaction. In rigid media the effective radius of the cage could be smaller than the radius given by the generating reaction and a fraction of the pair could be infinitely stabile as predicted by D-6 (Figure 7). For a case with P<1 and $\Sigma k_i \neq k_c$, the value of F at D=0 would not be simple to interpret since it would be the product $P^3(\Sigma k_i)/k_c$.

It should be emphasized that D-5 and D-6 are general in effective diffusion coefficient (D), cage radius (ρ) and normalization radius (r_N). Analysis of the D=0 (f=0) limits was examined first since values for the yield, with no translational motion permitted, are independent of the connection one chooses between the effective diffusion coefficient of the pair and the macroscopic viscosity of the medium. We have used the Stokes-Einstein equation (D-7) for this purpose where f is fluidity ($1/\eta$, cp.) and b is the effective radius for diffusive separation of the pair.

D-7 $$D = \frac{kTf}{6\Pi b} = \frac{kT}{6\Pi\eta b}$$

This allows the basic parameters of the model to be expressed as three distinct radii, that for the cage (ρ), that for the normalization (r_N) and that for diffusive separation (b). One might hope that a single value of ρ and r_N would suffice for a given cage pair source in every solvent. However, consideration of the Noyes' model indicates this cannot be the case. The physical basis here is the distance which a pair separates during the short time while the relative velocity vectors of the cage partners are oriented towards separation. This relative velocity orientation is intrinsic to the initiation event. Variations in combination efficiency with solvent fluidity, in Noyes' model, are ascribed entirely to these small initial

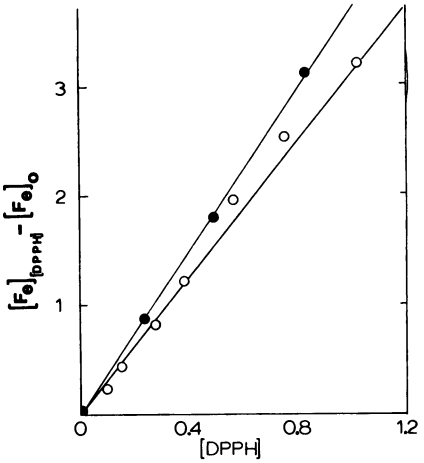

Figure 6. $[F_e]_{[DPPH]} - [F_e]_0$ vs. [DPPH] from decomposition of optically active hyponitrite (–●–) (22) and ketenimine (–○–) (30)

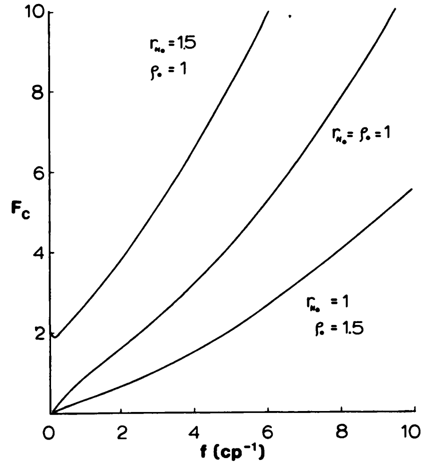

Figure 7. Calculated F_c vs. fluidity for a hypothetical initiator, $b = 1$Å, mass = 10, $k_b^\circ = 2 \times 10^{11}$ sec^{-1} various values of Δr_m and $\Delta \rho_m$

separations of the pair which vary with the frictional drag (viscosity) of the solvent. Translated into terms of the present model this means that the normalization radius will vary with solvent and we have taken this variation (Δr_N) to be that which Noyes derived (D-8).

D-8 $$\Delta r_N = \sqrt{\frac{3mD^2}{2kT}}$$

A second factor in the normalization radius is the effect of the intervening molecules which, when bonded to the radical partners in the starting material, will impart an initial separation (Δr_m). For the same cage pair partners, the normalization radius will thus vary with both the structure of the initiator and the solvent (D-9).

D-9 $$r_N = b + \Delta r_m + \sqrt{\frac{3mD^2}{2kT}}$$

The radius of the cage (ρ) should likewise be affected by solvent and intervening small molecules. We have approximated the small molecule(s) effect by an increment ($\Delta\rho_m$) equal to the radius of a sphere of the volume occupied by any small molecule eliminated by the initiation event. The solvent dependent factor ($\Delta\rho_\eta$, D-10) is taken from the mean increment in separation of Brownian particles during the time τ.

D-10 $$\Delta\rho_\eta = \sqrt{6D\tau}$$

The inclusion of the latter factor (D-10) is suggested by the studies of Walling and Lepley (27) on random jumps by a pair of particles in a cubic lattice. These workers showed that the pair has no chance of reencounter after 20 such jumps. During the timescale of the first 20 jumps, reencounters are possible. Alternatively, Noyes defined secondary recombination as those combination reactions involving a pair which had been separated and returned to collision. Either point of view leads to a sensitivity of the cage size (or radius of escape) to the effective diffusion coefficient like that expressed as D-10. The value of τ would roughly correspond to the time of 20 lattice jumps in the Walling-Lepley work and must be fixed empirically in the present model. The final equation for the cage radius (D-11) takes Noyes' secondary combination into account but, in the present model, it cannot be dis-

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

D-11 $$\rho = b + \Delta\rho_m + \sqrt{6D\tau}$$

tinguished from the "primary" events.

The other parameters of the model are the first order rate constants for chemical reaction of the cage pair. Each has an associated activation volume and is therefore subject to a small solvent effect over and above solvation energy considerations. We have ignored such effects except those for k_c, k_{-1} and $k_{disp.}$, all of which depend on collision between the cage partners. Analysis of the limiting behavior of equations D-5 and D-6 indicates that inclusion of the Noyes increment in normalization radius (D-8) demands that the rate constant for combination vary to an inverse power of fluidity greater than one. Equation D-12, which sets the variation in k_c in proportion to the normalization volume, satisfies this requirement. Here k_b^o

D-12 $$k_c = k_b^o (b/r_N)^3$$

refers to the combination rate constant for the pair in a sphere of radius b at zero fluidity.

While the parameterization of equation D-5 and D-6 is lengthy, it is also straightforward. The effective diffusion coefficient is approximated by the Stokes-Einstein relationship. This equation (D-7) requires the diffusion radius (b) of the pair which is simply estimated from Van der Walls radii. The normalization radius is simply the same value of b plus the increment of separation of the radical fragments given by the structure of the covalent initiator (Δr_m) and the viscosity term derived by Noyes (Δr_η). The latter term ultimately depends again of the radical size (b). The cage size is simply the same diffusion radius (b) plus an increment due to the excluded volume of any small molecules eliminated ($\Delta\rho_m$) plus a diffusion dependent term ($\Delta\rho_\eta$) requiring the time τ. Finally, the first order rate constants for chemical reaction of the pair in a sphere the size of the particle (b) are required. These rate constants also vary by the dilution volume of the intervening molecules and Δr_η.

Figure 7 demonstrates the sensitivity of the model to the increments in ρ and r_N for a hypothetical pair of mass 10 and diffusion radius 1 Å, reacting exclusively by combination and diffusive separation ($\Sigma k_i = k_c$ or $\sum_{i\neq c} k_i = 0$) with k_b^o equal to $1\times10^{12}\,\mathrm{sec}^{-1}$ at 25°C. These give a purely theoretical look at the possible effects of differing effective size of the cage and normalization volumes.

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To test the model against experimental data, only two parameters were varied: k_b^o (D-12) and τ (D-10). The values of b, Δr_m and $\Delta \rho_m$ were fixed from geometry considerations (Table III). We initially thought that τ could be obtained by a fit to one set of data and would be a constant for every pair. We chose the data of Szwarc and his coworkers (23) on perfluoroazomethane photolysis since these are the most extensive yield-fluidity results available for a single system. Figure 8 shows the fit of calculated (solid line) and experimental (eliptical points) values for F_c vs. fluidity at 65°C. The greater than first power fluidity dependence of the high fluidity region is easily reproduced. The upward curvature of the F_c correlation in the present model due to the downward curvature of P (ρ/r_N) and reduced values of k_c at high fluidity. The present model confirms the intuitive conclusion of Bartlett (27) and Szwarc (23) that highly fluid solvents act to separate the cage pair to a greater extent than simple viscosity considerations would suggest.

Figure 9 shows the fit of the data (28) for the same pair in a single solvent (2-methylbutane) from +90°C to -190°C. The values of all parameters were the same as those in Figure 8 except τ which varied inversely with the temperature (with the value at 65° being set by the fit of Figure 8). The very strong upward curvature (greater than first power fluidity dependence) in both Figure 8 and Figure 9 is directly attributable to the Noyes term in r_N (Δr_η) which causes decreasing values of P (ρ/r_N) and k_c at high fluidity.

Figure 10 shows the fit obtained to our data (22) on the ether formation from the 2-methylbutyryl perester. In this case, the calculated line shows downward curvature when plotted *vs*. fluidity to the first power. This downward curvature is related to the increase in the value of P at fluidities between 0 and 1 cp^{-1}. This feature, in the present model, is directly related to the inclusion of the fluidity dependent term in the cage radius ($\Delta\rho_\eta$) which is responsible for the initial rise in P (ρ/r_N) values. The physical interpretation is that, at low fluidities there is a relatively important increase in the chance for slight separation and return of the pair while at high fluidities the separation achieved while passing the transition state for homolysis (Δr_η) makes the start of random motion nearer the boundary of the cage limit.

Figure 11 shows the fit obtained for the hyponitrite source (12) of the 2-butyl-*t*-butoxy pair using the same value of k_b^o as obtained in Figure 10. That

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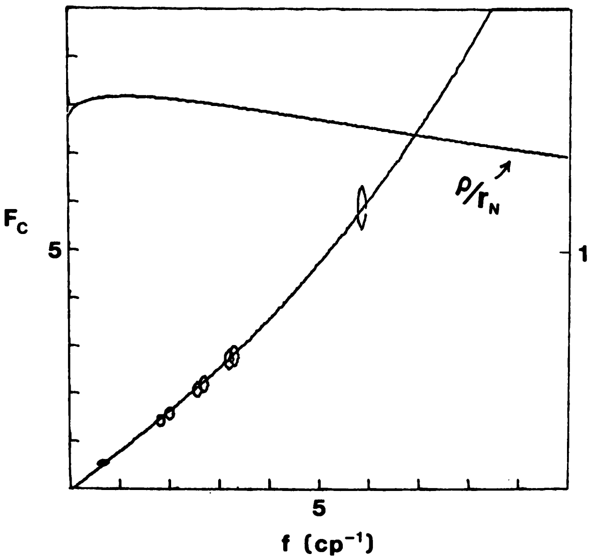

Figure 8. F_c vs. fluidity for $[CF_3 \cdot (N_2)CF_3 \cdot]$ (23)

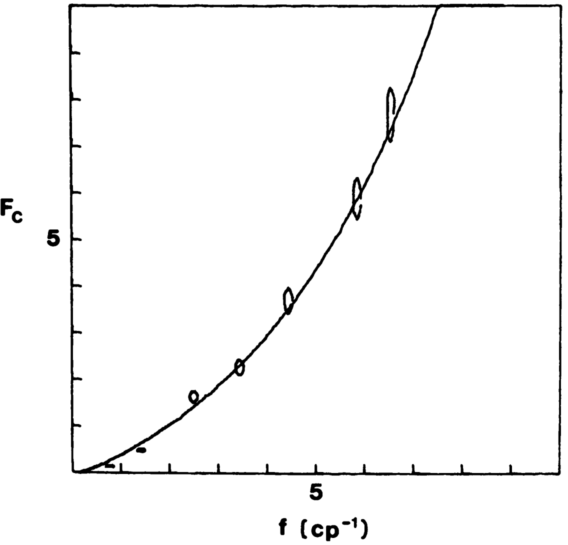

Figure 9. F_c vs. fluidity for $[CF_3 \cdot (N_2) \cdot CF_3]$ in 2-methylbutane (24)

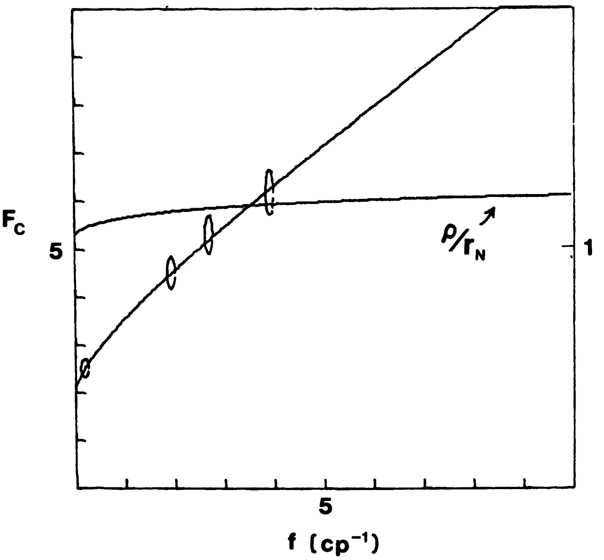

Figure 10. F_{ether} *vs. fluidity for* tert-*butyl 2-methylbutyl ether, perester 102°C (12).*

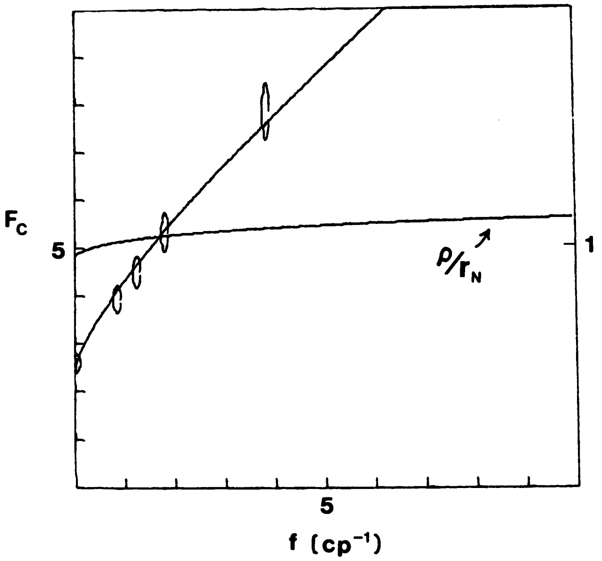

Figure 11. F_{ether} *vs. fluidity for* tert-*butyl 2-methylbutyl ether formation, hyponitrite (22) 32°C*

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is, the same value of k_c for a pair in a volume of radius b was used in both data sets (Figures 10 and 11). The actual k_c for the hyponitrite is lowered at all viscosities, due to the larger r_N resulting from the extra nitrogen molecule in the hyponitrite initiator. The intervening molecule effect deduced in the discussion of Figure 4 and Table II is thus reproduced here.

Figure 12 shows a fit to our data (5, 8) on the O-benzoyl-O-t-butyl hyponitrite. These data require an anomalously low value for $\Delta\rho_m$ (Table III) but, with that adjustment, a square root dependence of F_c on fluidity is observed in the theoretical curve over the viscosity range which was investigated.

Figure 13 shows a fit which was obtained for the data pertaining to di-tert-butyl peroxide formation from the corresponding hyponitrite (29). These data show the most variable apparent fluidity dependence of any available. The high viscosity (low fluidity) region is approximately linier with square root fluidity while the high fluidity (low viscosity) region varies with a power of fluidity greater than one. The fit of the calculated line, shown in Figure 15, required a fluidity sensitive factor in r_N (r_η, eqn. D-8) 10 times larger than the Noyes relationship. This relationship (D-8) gives a minimum value for the pair separation during the homolysis event since it assumes no excess translational energy (above kT) is available to the separating fragments. The deaminative nature of the hyponitrite reaction suggests that as much as 30 kcal/mole could be available for translational separation of the fragments (occurring in a time less than 10^{-13}sec). A magnification of the Noyes factor is not entirely unreasonable in such cases but additional experimental verification is needed before this factor can be considered a certainty.

Table III contains a summary of the parameters entering these calculations and shows the range of $k_c{}^o$ and τ values. The cage combination of benzoyloxy-t-butoxy and t-butoxy-t-butoxy pairs.have significantly lower rate constants for combination than that for perfluoromethyl pairs. An additional observation, which was interesting to us, is that the product of $k_c{}^o$ and τ is nearly constant. In other words, the τ required in D-10 is approximately a constant divided by $\Sigma k_i{}^o$ for the pair undergoing reaction. A pair undergoing a slow combination reaction should thus have a larger effective cage radius. There is an intuitive basis for this to be a real feature of cage reactions.

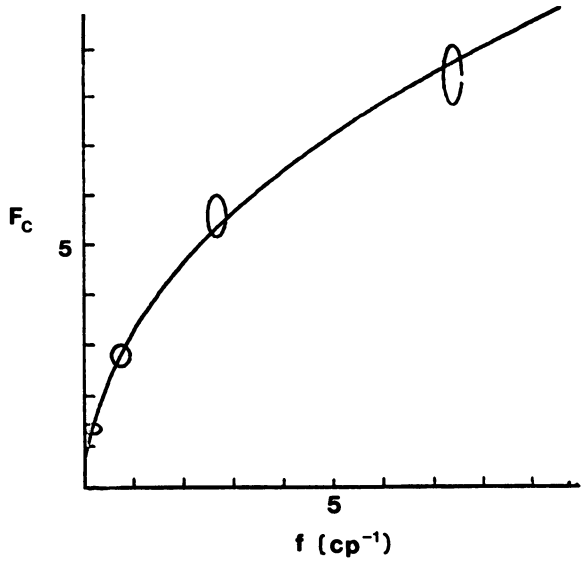

Figure 12. $F_{perester}$ vs. fluidity for tert-*butyl perbenzoate from the hyponitrite (8)*

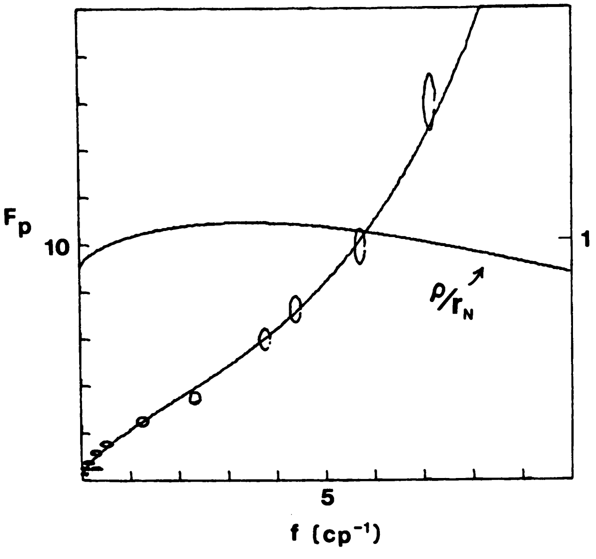

*Figure 13. F_c vs. fluidity for di-*tert-*butyl peroxide from the hyponitrite (9)*

Table III

Cage Model Summary

Fig.	Pair	T^oC	k_b^o x 10^{-11}sec.[f]	$k_c^{2cp^{-1}}$ 10^{-11}sec.[a]	τ psec.	b	Δr_m	$\Delta\rho_m$	$\Sigma k_i^o \cdot \tau^f$
8	$[CF_3\cdot\ N_2\ \cdot CF_3]$	65	2.70	0.59	0.14	1.35Å	0.67Å	1.74Å(N_2)	0.038[b]
9	$[CF_3\cdot\ N_2\ \cdot CF_3]$	Variable	2.70	0.59	48/T°K	1.35Å	0.67Å	1.74Å(N_2)	
10	$[2\text{-}Bu\cdot\ CO_2\ \cdot O\underline{t}Bu]$	102	0.39	0.11	0.39	3.20Å	1.60Å	1.84Å(CO_2)	0.040[c]
11	$[2\text{-}Bu\cdot\ CO_2\ N_2\ \cdot O\underline{t}Bu]$	32	0.39	0.06	0.48	3.20Å	2.26Å	2.26Å(CO_2,N_2)	0.057[d]
12	$[\underline{t}BuO\cdot\ N_2\ \cdot O\underline{t}Bu]$	45	0.20	0.03	1.5	2.70Å	1.60Å	1.74Å(N_2)	0.030[b,e]
13	$[ØCO_2^{\cdot}\cdot\ N_2\ \cdot O\underline{t}Bu]$	32	0.007	0.002	6.3	2.70Å	1.60Å	0.70Å(N_2)	0.043[b]

a) $k_o^{2cp.}$ is the rate constant for combination at a fluidity of 2 $cp.^{-1}$.
b) $\Sigma k_i^o = k_b^o$. c) $\Sigma k_i^o = k_b^o + k^o_{disp.} = 3.3\ k_b^o$. d) $\Sigma k_i^o = k_b^o + k^o_{disp.} = 3.1\ k_b^o$.
e) The value for Δr_η was x 10 that given by D-8. f) Super zero refers to f=0.

We believe the present model is distinct and superior to the version of Noyes. It uses structures and rate constants in familiar terms. It appears to deal with intervening molecule effects in a manner which is in keeping with experimental observations. It provides a rationalization for the variable power of fluidity which is needed to correlate F_c values. It supports the notion that the intercepts (at f=0) in F_c - fluidity correlation are generally due to chemical reaction competing with combination. Overall it provides a new framework for designing experimental tests of the effects of the several variables which may be controlled in chemical reactions.

On the negative side, it should be emphasized that the fits between experimental and calculated results shown in Figures 8-13 are not unique. A different criterion (within limits) for estimating b, Δr_m and/or $\Delta\rho_m$ would give equally acceptable fits using different values for k_b^o and τ. Application of picosecond laser methods or adaptation of the present model to CIDNP theory could remove some of this ambiguity and would serve as a more stringent test of the model than existing data allow.

Acknowledgement: Appreciation is due to Prof. R. M. Mazo for his assistance in the integrations involved in the development of the present model and to Drs. J. M. Owens, J. G. Huntington, W. R. Mabey, J. A. Hoobler and Max Deinzer whose doctoral theses contain much of the experimental work of this paper. Appreciation is also expressed to the National Science Foundation for financial support.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch009

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

10

Gamma Radiation-Induced Free Radical Chain Reactions

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The use of gamma radiation for the initiation of free radical chain reactions in liquids offers several advantages over the more conventional methods of initiation. With this technique radical reactions that are not readily accessible by other methods can be studied. Because of the wide temperature range within which radiolytic initiation can be applied this method allows an accurate determination of Arrhenius parameters and therefore can bring better understanding and deeper insight to the factors that control the rates and mechanism of free radical reactions.

At Soreq gamma radiolysis of liquid systems has been used in studies of various free radical chain reactions. The purpose of this work is to illustrate and demonstrate, through a survey of those studies, the advantages and limitations of the radiolytic method.

Radiolytic Initiation

General aspects. Most of the chain reactions that will be discussed in this work were initiated in alkane solutions by ^{60}Co gamma radiation. Therefore, the following rather brief and somewhat simplified discussion of the primary radiolytic processes will be limited mainly to alkanes and alkane solutions. An understanding of these processes is necessary in order to explain how radicals are generated by ionizing radiation and to understand the causes for the advantages and shortcomings of this technique. A detailed discussion of the primary steps that take place in a liquid exposed to ionizing radiation is beyond the scope of this work and can be found in several excellent texts (1-4).

In a pure alkane (RH) the radiolytic generation of radicals can be described by reaction 1. Surprisingly, this rather schematic formulation of the initiation

$$2RH \rightarrow 2R + H_2 + \text{products} \qquad (1)$$

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

process applies also to alkane solutions of various compounds *provided that a long chain reaction is initiated by the absorption of gamma radiation*.

How are those radicals formed? In a liquid that is exposed to ionizing radiation the formation of radicals is preceded by a number of rather complex steps. Basically, in the primary steps that follow the absorption of ionizing radiation the molecules of the absorbent become ionized or electronically excited. In nonpolar liquids such as alkanes, the charge neutralization processes are fast and therefore the lifetime of the charged species, molecular cations (RH^{+}) and electrons, is very short. The directly formed excited molecules (RH^{*}) or those that are created in the neutralization processes (RH^{**}) can lose their energy in processes such as radiative and nonradiative conversion to the ground state, collisional deactivation, etc. These processes do not result in a chemical change in the system. Alternatively, these excited molecules can dissociate into molecular products and free radicals. This latter chain of events, that leads to the formation of radicals, is summarized by reactions 2-11.

$$RH \rightarrow RH^{+} + e \qquad \text{(ionization)} \tag{2}$$

$$RH \rightarrow RH^{*} \qquad \text{(excitation)} \tag{3}$$

$$RH^{+} + e \rightarrow RH^{**} \qquad \text{(neutralization)} \tag{4}$$

$$RH^{*}, RH^{**} \rightarrow R + H \tag{5}$$

(radical formation)

$$RH^{*}, RH^{**} \rightarrow R' + R'' \tag{6}$$

$$RH^{*}, RH^{**} \rightarrow H_2 + \text{olefin} \tag{7}$$

(molecular products)

$$RH^{*}, RH^{**} \rightarrow P_1 + P_2 \tag{8}$$

$$H + RH \rightarrow H_2 + R \tag{9}$$

$$R' + RH \rightarrow R'H + R \qquad \text{(hydrogen transfer)} \tag{10}$$

$$R'' + RH \rightarrow R''H + R \tag{11}$$

It can be seen that the overall change caused by reactions 2-11 will be given by reaction 1, provided that the excited molecules RH^{*} and RH^{**} decompose primarily by the rupture of C-H bonds as in reaction 5. A priori, such selective bond cleavage seems to be rather unexpected since the gamma photons of ^{60}Co have a mean energy of 1.25 million electron volts (MeV), which by far exceeds the energy of any chemical bond. In fact, however, selective C-H bond rupture is indeed observed. For example, cyclohexene and bicyclohexyl comprise more than 95% of the carbon-containing products that are formed in the gamma

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

radiolysis of cyclohexane. A similar product distribution is observed in the radiolysis of other alkanes.

Chain reactions are usually studied in mixtures, where the situation is more complicated. In mixtures, processes such as electron capture (reaction 12), charge transfer (reaction 13) and energy transfer (reaction 14) might result in the preferential decomposition of the solute (SX) instead of the alkane solvent. However, even in that case, the transfer reactions 9-11 are replaced by reactions 19-21 so that the net effect is reduction in the yield of hydrogen and the regeneration of alkyl radicals. If reactions 19 and 20 are faster

$$e + SX \rightarrow S + X^- \text{ or } SX^- \qquad \text{(electron capture)} \qquad (12)$$

$$RH^+ + SX \rightarrow RH + SX^- \qquad \text{(charge transfer)} \qquad (13)$$

$$RH^*,\ RH^{**} + SX \rightarrow RH + SX^* \qquad \text{(energy transfer)} \qquad (14)$$

$$X^- + RH^+ \rightarrow RH + X \qquad (15)$$

$$SX^- + RH^+ \rightarrow RH + SX^* \qquad (16)$$

$$SX^+ + e \rightarrow SX^* \qquad (17)$$

$$SX^* \rightarrow S + X \qquad (18)$$

$$S + RH \rightarrow HS + R \qquad (19)$$

$$X + RH \rightarrow HX + R \qquad (20)$$

$$X^- + RH^+ \rightarrow HX + R \qquad (21)$$

than the termination reactions of S and X radicals and if R radicals participate in a long chain reaction, then the schematic description of the initiation step by reaction 1 can still be used.

Let us now consider some quantitative aspects of radiolytic initiation. The radiolytic yield, G value, is defined as the number of molecules that 'react' per 100 eV of absorbed energy. In alkanes and alkane solutions, G(radicals) does not exceed 10. This value is practically independent of temperature (5). Therefore, product formation with a G value that exceeds 10 indicates that this product is formed, at least in part, in a chain reaction.

The amount of γ radiation energy absorbed per unit volume of an absorbent is determined by the number of electrons in that volume. This number is known as electron density (E_d) and is given by expression I, where Z is the apparent atomic number of a molecule,

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(I) $$E_d = dZN/M$$

i.e. the sum of the atomic numbers of the elements in the molecule [$Z(CCl_4) = 6 + 4x17 = 74$], N is Avogadro's number and d is the density of the absorbent. Since many of the organic compounds have nearly the same electron density, the energy absorbed per unit volume of pure solvent and the energy absorbed by the same volume of a concentrated solution are almost equal. In other words, the rate of radiolytic initiation is practically independent of the composition of the irradiated solution.

The advantages and limitations of radiolytic initiation. Radiolytic initiation is particularly useful in kinetic studies of liquids phase free radical chain reactions. The advantages of this technique can best be seen by comparing it with other commonly used methods of initiation, photolysis and thermal decomposition of initiators.

The determination of the time dependence of the rate of a chain reaction and the study of the effects of reactants concentrations and of incident light intensity are the most commonly used techniques for the elucidation of the kinetics and mechanism of chain reactions. The best way to establish the effect of these three parameters is to change them separately. However, only radiolytic initiation allows such 'one at a time' variation of parameters. In this case the rate of initiation is independent of the composition of the solution and it is constant in time and in space (neglecting 'spur reactions'). In comparison, photochemical initiation is possible only when one of the components of the solution absorbs ultra violet or visible light. The concentration of this absorbent is constantly depleted. In solutions with low absorbance this change in concentration is accompanied by a decrease in the rate of initiation. This is a particularly serious problem when the light absorbent is also one of the reactants in the chain reaction. While it is true that the concentration change in solutions that absorb a large fraction of the incident light has a small effect on the overall rate of initiation, the rate of initiation in regions that are removed from the light source is considerably lower than in regions that are close to it. In other words, the rate of initiation is not uniform in space. Thermal initiation is uniform in space but not in time. As in the case of photochemical initiation, thermal decomposition of the initiator and its consumption in a subsequent chain reaction present the most complicated situation.

Because of its high penetrating power, gamma radiation induced reactions can be carried out in opaque vessels and metal autoclaves. Consequently, the temperature range within which a chain reaction can be studied in a given solution, extends from its freezing point to its critical temperature. Thermally induced reactions can also be studied in autoclaves. However, the tempe-

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rature range in which thermal initiation can be employed is usually quite narrow as it is determined by the thermal stability of the initiator. Furthermore, even within this narrow region, the rate of initiation is temperature dependent. In contrast, the rate of radiolytic initiation is independent of temperature. Photochemical initiation on certain cases is also independent of temperature. However, the need for transparent cells limits the pressure and therefore the temperature at which photochemical studies can be carried out.

Finally, side reactions of the absorbent or the initiator may compete with and inhibit the chain reaction under investigation. The products of these side reactions interfere with the determination of the main reaction products. When radiolytic initiation is used the solvent is the main source of radicals and consequently these complications are minimized.

Radiolytic initiation is not free from limitations and shortcomings. We have previously seen that ions are formed in the initial steps that follow the absorption of gamma radiation. While in pure alkanes the lifetime of the ions is very short, this is not necessarily the situation in the presence of solutes. In some cases, solute anions and cations formed by electron capture and charge transfer, respectively, may have considerably long lifetimes. If this occurs, it is possible that ionic reactions take place and therefore the free radical mechanism of the chain reaction has to be established. This can be done by various methods such as the addition of electron, charge and radical scavengers, and the determination of the effect of these additives on the chain reaction. Another method is to show that the same reaction can also be initiated thermally or photochemically.

The second complication encountered in radiolytic studies in which a radical derived from the solvent participates in the reactions, arises from the fact that the termination reaction of this radical and the initiation can result in the formation of the same product. Further clarification of this problem seems to be in order and it brings us back to the details of the initiation step. It has been found that formation of some of the radiolytic products cannot be suppressed by the addition of radical scavengers. These products are known as 'molecular products', which is misleading since not all these products are formed by a true molecular mechanism. There are various reasons for the inability of radical scavengers to suppress their formation, but they will not be discussed here. For the purpose of this work, the important consequence of the formation of 'molecular products' lies in the fact that if a certain product is formed both by a molecular mechanism and in a radical termination reaction, then the yield of this product cannot, as such, be used for the estimation of the steady state concentration of radicals. For example, in cyclohexane a significant portion of the radiolytic yield of cyclohexene and bycyclohexyl is 'molecular'. These 'molecular yields have to be subtracted from the total yields of those products and only the corrected values represent the amounts of cyclohexene and bicyclohexyl that are formed in the termination reactions of the cyclohexyl radicals. It should be noted that the complications arising from the formation of 'molecular products' are similar to those encountered in photochemically and thermally induced reactions in which the 'cage' effect is important.

Experimental

Thoroughly degassed solutions in glass ampules were irradiated in a ^{60}Co gamma source. Irradiation at elevated temperatures was made possible by the use of metal autoclaves in which the ampules were immersed in solution of the same composition as the sample. This procedure ensures that an increase in the irradiation temperature brings about an equal change in pressure on both sides of the ampule. This irradiation apparatus was devised by Katz (6) and is shown in Figure 1. Gas chromatography was the main method used for product analysis.

Chlorovinylation of Alkanes

Gamma radiolysis of alkane (RH) solutions of chloroethylenes (ECl_2) i.e., C_2Cl_4(7-10), C_2Cl_3H (9-11), cis- and trans- $C_2Cl_2H_2$ (9,10,12) and C_2Cl_3F (13), results in the formation of hydrogen chloride and chlorovinyl substituted alkanes. These products are formed in almost equal yields with G values that exceed 1000 at 200°C (9,13), clearly indicating that a chain mechanism is operative. The free radical character of this mechanism was established in experiments with added inhibitors (7) in which it was shown that the radical scavengers, iodine and pentene, strongly inhibit the chain reaction, while SF_6 and N_2O, known to be efficient electron scavengers, do not. The propagation step of the radical chain mechanism that is consistent with these findings is given by reactions 22 through 25 and the termination step by reactions 26 through 31. This reaction sequence is identical to the one suggested for peroxide (14, 15) and photo (16) initiated chlorovinylation.

$$R + ECl_2 \rightarrow RECl_2 \tag{22}$$

$$RECl_2 \rightarrow RECl + Cl \tag{23}$$

$$RECl_2 + RH \rightarrow RECl_2H + R \tag{24}$$

$$Cl + RH \rightarrow HCl + R \tag{25}$$

$$2R \rightarrow R_2 \tag{26}$$

$$2R \rightarrow \text{cyclohexene} + RH \tag{27}$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

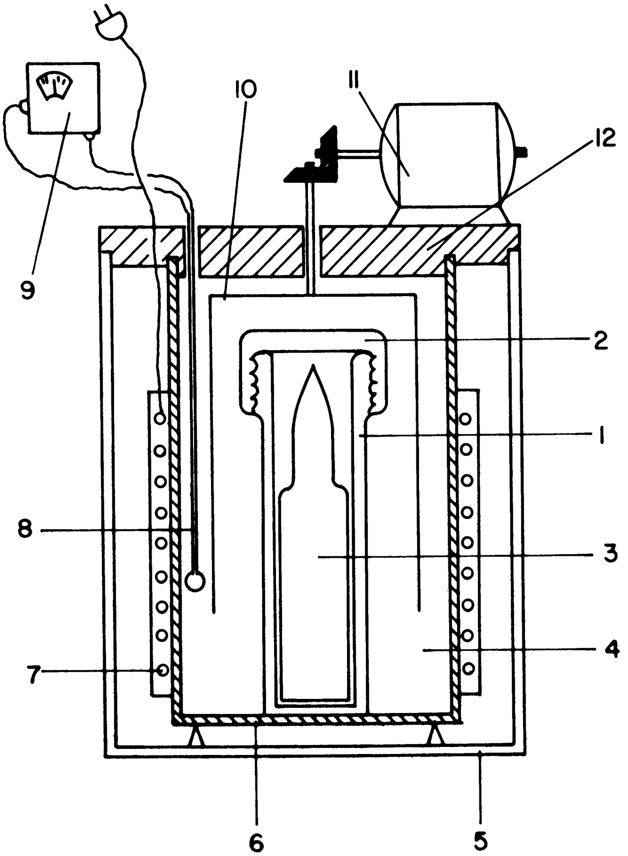

Figure 1. Controlled temperature apparatus for gamma irradiation. 1. autoclave, 2. cover, 3. ampule, 4. silicon–oil bath, 5. glass beaker, 6. aluminum beaker, 7. heater, 8. thermocouple, 9. potentiometer, 10. stirrer, 11. motor, 12. cover.

$$R + RECl_2 \rightarrow RCl + RECl \qquad (28)$$

$$R + RECl_2 \rightarrow \text{cyclohexene} + RE \qquad (29)$$

$$2RECl \rightarrow (RECl)_2 \qquad (30)$$

$$2RECl \rightarrow RE + RECl_2 \qquad (31)$$

It should be noticed that all possible reactions do not always take place. Thus chlorine elimination (reaction 23) from c-$C_6H_{11}CCl_2CClF$ and c-$C_6H_{11}C_2Cl_3$ radicals is so fast that reaction 24 cannot compete with it. Also, cyclohexyl radicals add only to the less substituted end in trichloroethylene. When reaction 24 does occur, it is of minor importance, as is indicated by the fact that G(RECl)>>G($RECl_2H$).

We will now demonstrate how the radiolytic method can be used for the determination of the rate constants for the addition of cyclohexyl radicals to chloroethylenes in terms of the above outlined reaction scheme. Using the steady state assumption under conditions of a long chain reaction it can be shown that the rate of formation of $RECl_2$ is given by expression II. According to this expression k_{22} can be determined

$$\text{(II)} \qquad [R_{RECl}] = k_{22}[R][ECl_2] = k_{23}\ RECl_2$$

provided that the steady state of the cyclohexyl radicals can be estimated from the rates of formation of the termination products cyclohexene and bicyclohexyl. Unfortunately, both products are also formed by 'molecular processes' and, therefore, only the corrected values, obtained by the subtraction of the molecular yields from the experimental values, can be used for the estimation of the steady state concentration of cyclohexyl radicals. This is a rather inaccurate method, particularly when the difference between the experimental and the molecular yields is small, and should therefore be used only when there is no other alternative.

The alternative method for the derivation of the steady state concentration of cyclohexyl radicals utilizes the fact that the rate of radiolytic generation of cyclohexyl radicals is not affected by the presence of chloroethylenes. Assuming that the sum of the steady state concentrations of the R and $RECl_2$ radicals is constant and that it is equal to the steady state concentration of R radicals in pure alkane, it can be shown that G($RECl_2$) should be given by the following expression:

$$\text{(III)} \qquad \frac{1}{G(RECl_2)} = \left[\frac{2\alpha(k_{26}+k_{27})}{G(R_o)}\right]^{\frac{1}{2}} \left[\frac{1}{k_{23}} + \frac{1}{k_{22}[ECl_2]}\right]$$

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where $G(R_o)$ is the yield of cyclohexyl radicals in pure cyclohexane, which is equal to 5.7 (17) and α is a constant that converts G values into rates of formation in units of mole ℓ^{-1} sec^{-1}. The applicability of this relation was verified for $ECl_2 = C_2Cl_4$, C_2Cl_3H and C_2Cl_3F.

Since $G(R_o)$ is known, the ratio $k_{22}/(k_{26}+k_{27})^{\frac{1}{2}}$ can be determined from the slope of the plot of $1/G(RECl_2)$ versus the reciprocal of the concentration of chloroethylene. The advantage of this method is that it does not require the determination of the termination products, which can be difficult for a long chain reaction. When such a reaction occurs the chloroethylene may be consumed long before a detectable amount of termination products is formed. Furthermore, at sufficiently low ECl_2 concentrations, when $k_{23} >> k_{22}[ECl_2]$, expression III reduces to the linear form given in expression IV. Reversing this argument, it can be seen that if $G(RECl_2)$

$$\text{(IV)} \qquad G(RECl_2) = k_{22}\left[\frac{G(R_o)}{2\alpha(k_{26}+k_{27})}\right]^{\frac{1}{2}}[ECl_2]$$

is proportional to $[ECl_2]$, then $k_{23} >> k_{22}[ECl_2]$ and therefore $[R] >> [RECl_2]$. In other words, when expression IV is obeyed the steady state concentration of R radicals is constant. This approach was used in the derivation of the rate constants and Arrhenius parameters for the addition of cyclohexyl radicals to C_2Cl_4. The Arrhenius expression for the rate constants for the addition of cyclohexyl radicals to the other chloroethylenes were obtained from competitive studies. These results are summarized in Table I.

Inspection of the results given in Table I reveals that the reactivity trends in the addition reaction are determined by steric and inductive effects. Thus, trichloroethylene is more reactive than the dichloroethylenes because of the electron withdrawing effect of the additional chlorine atom. However, in tetrachloroethylene this effect is offset by the steric effect and therefore this compound is less reactive than trichloroethylene. Particularly interesting is the comparison between C_2Cl_4 and C_2Cl_3F. Fluorine has a strong inductive effect. Unlike chlorine it does not sterically hinder the reaction and therefore the addition of c-C_6H_{11} radicals to C_2Cl_3F requires an activation energy that is lower by 1.2 kcal/mole than the activation energy needed for the addition of those radicals to C_2Cl_4. On the other hand, the same inductive effect lowers the reactivity of the CCl_2 site in C_2Cl_3F to the extent that it requires an energy of activation that is higher by 1.2 kcal/mole than the activation energy for the addition to C_2Cl_4.

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Table I. Arrhenius Parameters and Relative Rate Constants for the Addition of c-C_6H_{11} Radicals to Chloroethylenes (ECl_2)

ECl_2 (a)	$\log k_{22}/k_{22}(C_2Cl_4)$ at 150°	$\log A_{22}$ (b) $M^{-1}sec^{-1}$	E_{22} (b) kcal/mole	Ref.
cis-$C_2Cl_2H_2$	4.92	8.72	7.30	10
trans-$C_2Cl_2H_2$	5.35	9.13	7.25	10
$\underline{HCC}l{=}CCl_2$	5.58	9.10	6.75	10
C_2Cl_4	4.88	8.68	7.30	10
$\underline{HCF}{=}CCl_2$	5.32	8.64	6.38	13
$HCF{=}\underline{CCl}_2$	4.30	8.72	8.49	13

(a) the site of addition is underlined.
(b) derived by taking $2(k_{26}+k_{27}) = 2x10^9\ M^{-1}sec^{-1}$ (16) and $E_{dif} = 4.56$ kcal (19)

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

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Chain Reactions of Halomethanes and Haloethanes

General. The free radical chain decomposition of halogen (mainly chlorine) substituted methanes (XM) and haloethanes (XEtY), was studied in cyclohexane. The propagation step of the chain reaction of halomethanes is given by reactions 32 and 33 while reactions 34 through 37 describe the chain decomposition of haloethanes. These reactions can be

$$R + XM \rightarrow RX + M \qquad (32)$$

$$M + RH \rightarrow MH + R \qquad (33)$$

$$R + XEtY \rightarrow RX + EtY \qquad (34)$$

$$EtY \rightarrow Et + Y \qquad (35)$$

$$EtY + RH \rightarrow EtYH + R \qquad (36)$$

$$Y + RH \rightarrow HY + R \qquad (37)$$

divided into three groups: halogen transfer, hydrogen transfer and halogen elimination. In addition, in some cases, hydrogen transfer from XM and XEtY to the R radical also becomes important.

Chlorine transfer reactions. The rate constants and Arrhenius parameters of chlorine transfer reactions, given in Table II, were determined by competition studies in solutions that contained another compound, SX, in addition to the chloromethane (ClM) or chloroethane ($EtCl_2$) under investigation. The reaction of SX with cyclohexyl radicals (reaction 38) served as a reference.

$$R + SX \rightarrow P \qquad (38)$$

In these systems, the rate constant for chlorine transfer, K_{Cl}, is given by expression V. At low conversions, expression V reduces to expression VI. The indices i,f and av indicate initial, final and average concentrations, respectively. The same equations

$$(V) \qquad \frac{k_{Cl}}{k_{38}} = \frac{\log[ClM]_i/[ClM]_f}{\log[SX]_i/[SX]_f}$$

$$(VI) \qquad \frac{k_{Cl}}{k_{38}} = \frac{G(RCl)[SX]_{av}}{G(P)[ClM]_{av}} = \frac{G(MH)[SX]_{av}}{G(P)[ClM]_{av}}$$

are used for solutions containing chloroethane, by substituting [$EtCl_2$] for [ClM].

The chlorine transfer data given in Table II can be treated in various ways and grouped accordingly. Thus the compounds $ClCCl_3$, $HCCl_3$, CF_3CCl_3, CH_3CCl_3, CCl_3CCl_3, CH_2ClCCl_3 and CCl_3CN are included in a series having the general form $XCCl_3$, while $ClCCl_2H$, $HCCl_2H$, $HCCl_2CH_2Cl$, CH_3CHCl_2 and $CHCl_2CN$ are in the $XCHCl_2$ series. As can be seen from Figure 2, within each series, the chlorine transfer rate constants correlate well with the Taft polar substituent constants σ_x^* .

Another way to treat the results of Table II is to compare reactivity trends in pairs such as CCl_4- CCl_3CN, $CHCl_3$ - $CHCl_3CN$ and CH_2Cl_2 - CH_2ClCN. This approach shows that substitution of a chlorine atom by the cyano group lowers the activation energy E_{Cl} by 3.6 kcal/mole. This effect reflects the lower C–Cl bond strength in chloroacetonitriles, and the stabilization of the radicals formed by chlorine transfer reactions of those compounds.

Hydrogen transfer reactions. Hydrogen transfer reactions of CCl_3 (25,26), CCl_2CN (24) and CH_2CN (27) radicals, generated by chlorine and bromine atom transfer from CCl_4, CCl_3CN and $BrCH_2CN$, respectively, were studied in alkanes. In these systems combination is the only termination reaction. Therefore, G(MH) and G(RX) are given by expression VII, where k_t

$$M + M \rightarrow M_2 \qquad (39)$$

$$\text{(VII)} \qquad G(RX) = G(MH) = \frac{k_H}{k_t^{1/2}}\,\alpha^{1/2} G(M_2)^{1/2}[RH]$$

= k_{39} and k_H = k_{33} and α is a known coefficient that converts G values into rates of formation.

It should be noticed that the products M_2 are derived from the solute and therefore are not formed by 'molecular processes'. Consequently the experimentally determined values of G(M_2) can be substituted directly into expression VII. Since [RH] and α are known, this expression can then be used to obtain the rate constant ratio $k_H/k_t^{1/2}$ and the respective relative Arrhenius parameters E_H–$0.5E_t$ and $A_H/A_t^{1/2}$. This method was used in the derivation of rate constants and Arrhenius parameters of the H transfer reactions of trichloromethyl radicals in cyclohexane and n-hexane.

Another situation exists in $BrCH_2CN$ and CCl_3CN solutions, where at very low solute concentrations, G(CH_3CN) and G($CHCl_2CN$) reach constant values. Since the alkane concentration is constant this can happen only if [M]>>[R]. Under these conditions expression VIII can be used for the derivation of $k_H/k_t^{1/2}$. The relative Arrhenius parameters of the H transfer reactions of

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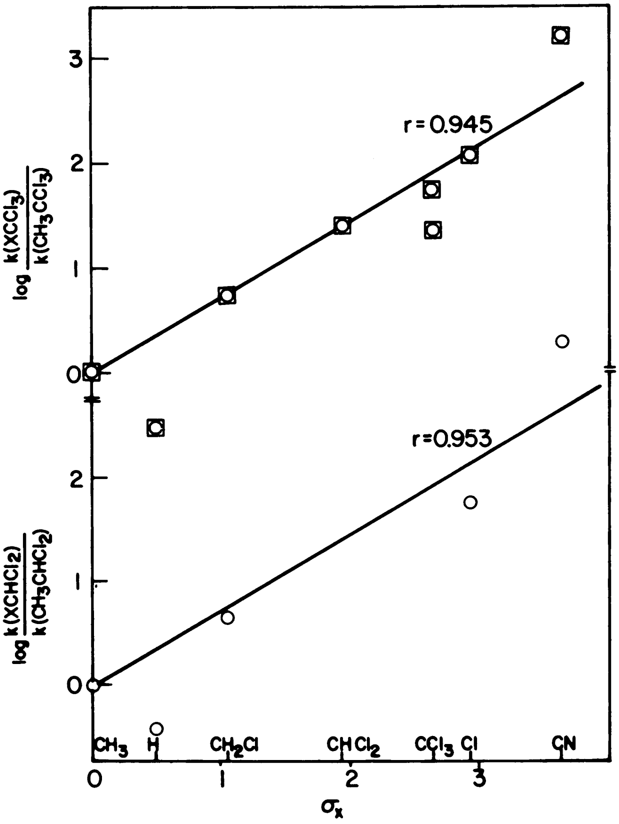

Figure 2. Plot of relative values of log k_{Cl} at 80° vs. Taft σ^* parameters, r = linear correlation coefficient.

Table II. Rate Constants and Arrhenius Parameters of Cl Atom Transfer Reactions of Cyclohexyl Radicals(a)

Compound	log A_{Cl} $M^{-1}sec^{-1}$	E_{Cl} kcal/mole	Temp. ^{o}K	log k_{Cl} (c) $M^{-1}sec^{-1}$	Ref.
CCl_4	9.40	5.88	333–453	5.76	20
CCl_3H	9.45	10.16	392–492	3.16	20
CCl_2H_2	9.24	13.67	463–523	0.98	20
CF_3CCl_3	8.97	6.33	333–473	5.05	21
CCl_3CCl_3	9.56	6.17	295–463	5.74	21
$CHCl_2\underline{CCl}_3$	8.69	5.80	333–473	5.10	21
$CH_2Cl\underline{CCl}_3$	9.46	8.18	373–493	4.40	21
CH_3CCl_3	9.46	9.32	373–498	3.69	21
$CH\underline{Cl}_2CH_2Cl$	8.98	11.17	423–523	2.01	22
$CH\underline{Cl}_2CH_3$	8.81	11.93	403–523	1.42	22
CH_2ClCH_2Cl	9.18	14.87	423–523	−0.62	22
CH_2ClCN	8.58	9.99	413–483	2.40	23
$CHCl_2CN$	8.80	6.55	423–513	4.75	23
CCl_3CN	8.20	2.09	373–523	6.91	24

(a) The absolute values are based on log $k_{22}(M^{-1}sec^{-1})$ = 8.68–7300/2.303RT.

(b) The site of attack by the cyclohexyl radical is underlined.

(c) at 353°K.

CCl_2CN radicals in cyclohexane, given in Table III, were

$$\text{(VIII)} \qquad G(RX) = G(MH) = \frac{k_H}{(2k_t)^{\frac{1}{2}}} \alpha^{\frac{1}{2}} G(R_o)^{\frac{1}{2}} [RH]$$

determined using both expressions VII and VIII. The good agreement between the two results supports the validity of the assumptions that were made in the derivation of the two expressions.

Table III. Relative Arrhenius Parameters of H Atom Transfer Reactions

Radical	Alkane	$\log A_H - \frac{1}{2}\log A_t$ $M^{-\frac{1}{2}}$ $sec^{-\frac{1}{2}}$	$E_H - \frac{1}{2}E_t$ kcal/mole	Ref.
CCl_3	cyclohexane	3.28	8.81	25
CCl_3	n-hexane	3.69	9.62	26
$CCl_2CN^{(a)}$	cyclohexane	3.68	13.24	24
$CCl_2CN^{(b)}$	cyclohexane	3.95	13.70	24
CH_2CN	cyclohexane	4.22	11.96	27

(a) Determined using expression VII.
(b) Determined using expression VIII.

Now, in order to obtain E_H and A_H from the relative values of Table III, the absolute values of E_t and A_t have to be known. Unfortunately, in liquids, rate constants of radical termination reactions have, at best, been determined at only one temperature. If k_t is known, as it is for CCl_3 radicals (28), then it is possible to calculate A_t, provided that E_t can be estimated. According to Patrick (29), radical metathesis reactions should have the same activation energies in the gas and liquid phase. This theoretical prediction is satisfied when the self-reaction of trichloromethyl radicals is assumed to be diffusion controlled, that is, when E_t is equated to the activation energy of diffusion in cyclohexane of 4.54 kcal. The Arrhenius expression for k_H obtained from the results of Table III, assuming that E_t = 4.54 kcal/mole is:

$$\log k_H(CCl_3) = 8.8 - 11,100/2.303RT \ (M^{-1}sec^{-1})$$

The assumption that $E_t = E_{diff}$ is further supported by the fact that the difference between E_H−0.5E_t values in cyclohexane and n-hexane is 0.8kcal/mole. This is very close to half the difference between the diffusion energies in these two alkanes.

The termination rate constants for the reactions of CCl_2CN and CH_2CN radicals are not known. However, for $(CH_3)_2CCN$ radicals $k_t = 4x10^9M^{-1}sec^{-1}$ at 25° (30). Therefore, it is safe to assume that the termination reactions of CH_2CN and CCl_2CN radicals are diffusion controlled. In these cases the results of Table III give E_H values of 14.23 and 15.97 kcal/mole, respectively. Comparison of these values with the E_H value for CCl_3 shows that the cyano substituted radicals require a considerably higher activation energy for hydrogen abstraction. This effect can be ascribed to the stabilization of the abstraxting radical by the cyano group. The stability of cyano-substituted radicals thus manifests itself in two ways - they react slowly but can be generated easily in reactions such as halogen transfer.

Chlorine elimination reactions. Chloroethyl radicals (ClEt) formed by Cl or Br transfer reactions in cyclohexane can subsequently eliminate a Cl atom by reaction 34 or abstract a H atom from the solvent by reaction 35. The rate constant ratio $k_{34}/k_{35} = k_{el}/k_H$ and the related Arrhenius parameters can be obtained with the use of expression IX. These data

$$\text{(IX)} \qquad \frac{k_{el}}{k_H} = \frac{G(ClEH)}{G(Et)[RH]}$$

are summarized in Table IV. The absolute Arrhenius parameters of Cl elimination, given in the table, were derived by assuming that the Arrhenius parameters of H atom transfer are the same for all the chloroethyl radicals and equal to the gas phase Arrhenius parameters of H atom transfer from cyclohexane to the CCl_3 radical. Small differences between the reactivity of various chloroethyl radicals are expected. However, gas phase data shows that these differences in E_H are small when compared to the differences in E_{el}.

In the gas phase addition of Cl atoms to chloroethylenes, reaction-35, requires

$$Cl + Et \rightarrow ClET \qquad (-35)$$

activation energies that are very close to zero and therefore $E_{el} \sim D(Et\text{-}Cl)$. In cyclohexane one would expect E_{-35} to be slightly higher than in the gas phase. Hence, the cyclohexane

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

Table IV. Arrhenius Parameters for Cl Atom Elimination Reactions of Chloroethy Radicals

Radical	$\log A_{el}/A_H$ (a) M	$E_{el}-E_H$ (a) kcal/mole	$\log A_{el}$ sec^{-1}	E_{el} kcal/mole	Ref.	D(C–Cl) (b) kcal/mole
CCl_3CCl_2	5.52	6.45	14.3	17.17	31	17.77
$CHCl_2CCl_2$	5.28	7.60	14.1	18.27	32	21.38
$CHCl_2CHCl$	5.53	6.26	14.3	16.98	32	19.66
CH_2ClCCl_2	5.00	8.69	13.8	19.37	33	21.85
$CH_2ClCHCl$	5.74	8.43	14.5	19.10	34	22.57

(a) Data from references (31)-(33) corrected for the change in the density of cyclohexane.

(b) Gas phase data.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

E_{el} values are the upper limit of the C-Cl bond dissociation energies in chloroalkyl radicals. Inspection of the results of Table IV shows that E_{el} in cyclohexane is consistently lower than D(C-Cl). Solvation of the Cl atoms in cyclohexane can be envisaged as the possible cause of the lower D(C-Cl) bond dissociation energies in cyclohexane.

Radiolytic Decomposition of Alkanesulfonyl Chlorides

The free radical mechanism of the gamma radiation induced decomposition of alkanesulfonyl chlorides (RSO_2Cl) in cyclohexane was studied (35-37) to obtain kinetic and thermochemical information on the reactions of alkylsulfonyl radicals (RSO_2). Previously discussed systems are relatively simple and their kinetic analysis is almost straightforward. The radiolysis of alkanesulfonyl chlorides presents a more complex situation. The problems encountered in the radiolysis of alkanesulfonyl chlorides will be illustrated in the $c\text{-}C_6H_{12}$ - $MeSO_2Cl$ system (36,37).

The main products of the radiolysis of methanesulfonyl chloride solutions in cyclohexane are methane, SO_2 and chlorocyclohexane. In addition, small amounts of methylchloride are also formed. The yields of these products satisfy the material balance relations XI and XII.

$$\text{(XI)} \qquad G(MeCl) + G(RCl) = G(SO_2) = G(-MeSO_2Cl)$$

$$\text{(XII)} \qquad G(RCl) = G(MeH)$$

Two mechanims are consistent with these findings. The first mechanism is given by reactions 40-47 while the second mechanism includes, in addition to these reactions, reactions 48 through 51, as well. However, since the formation of MeCl by a chain

$$Me + MeSO_2Cl \rightarrow MeCl + MeSO_2 \qquad (40)$$

$$R + MeSO_2Cl \rightarrow RCl + MeSO_2 \qquad (41)$$

$$MeSO_2 \rightarrow Me + SO_2 \qquad (42)$$

$$Me + RH \rightarrow MeH + R \qquad (43)$$

$$R + SO_2 \rightarrow RSO_2 \qquad (44)$$

$$2MeSO_2 \rightarrow \text{products} \qquad (45)$$

$$2RSO_2 \rightarrow \text{products} \qquad (46)$$

$$MeSO_2 + RSO_2 \rightarrow \text{products} \qquad (47)$$

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$$MeSO_2 + RH \rightarrow [MeSO_2H] + R \qquad (48)$$

$$[MeSO_2H] \xrightarrow{fast} MeH + SO_2 \qquad (49)$$

$$RSO_2 + RH \rightarrow RSO_2H + R \qquad (50)$$

$$[RSO_2H] \xrightarrow{fast} RH + SO_2 \qquad (51)$$

reaction was observed, reactions 48 and 49 cannot completely replace reactions 42 and 43 as a source of methane. Furthermore, the ratio [MeCl]/[MeH] is independent of $MeSO_2Cl$ and SO_2 concentrations. Kinetic analysis shows that this can occur only if methane formation through the intermediacy of methanesulfinic acid is negligible. Incidentally, the [MeCl]/[MeH] ratios observed in the thermal decomposition of $MeSO_2Cl$ in cyclohexane at 150° are the same as in the radiolytic experiments at this temperature (36), although the rate of the thermal reaction is markedly lower than the rate of the gamma radiation induced reaction. This observation further supports the radical mechanism of the radiolytic reaction.

In the RH-$MeSO_2Cl$ system the rates of MeH, RCl and SO_2 formation sharply decrease with irradiation time, even at very low conversions of $MeSO_2Cl$. This effect can be explained with the help of expression XIII that applies when MeH>>MeCl, as observed. According to

$$\text{(XIII)} \quad -R_{MeSO_2Cl} = R_{MeH} = \frac{k_{-42}\, k_{43}[RH][MeSO_2]}{k_{42}[SO_2] + k_{43}[RH] + k_{41}[MeSO_2Cl]}$$

this expression R_{MeH} decreases because $k_{42}[SO_2] \gg k_{43}[RH] + k_{41}[MeSO_2Cl]$. In other words, even when very small amounts of SO_2 are formed R_{MeH} is given by expression XIV. At these

$$\text{(XIV)} \quad R_{MeH} = \frac{k_{-42}k_{43}[RH]}{k_{41}\, SO_2}[MeSO_2]$$

SO_2 concentrations the equilibrium of reaction 42 is far to the left, i.e. $[MeSO_2] \gg [Me]$ and therefore R_{MeH} should be proportional to the reciprocal of SO_2 concentration. This behavior was verified in experiments in which small amounts of SO_2 were added to the RH-$MeSO_2Cl$ system. With sufficiently large amounts of added SO_2, $MeSO_2Cl$ decomposes at a constant rate. Expression XIV shows, that under those conditions, the ratio $k_{-42}k_{43}/k_{42}$ can be determined provided that $MeSO_2$ is known.

Obviously, $MeSO_2$ concentration can be estimated from the rate of formation of its termination products. Unfortunately, these products are known to be unstable and therefore their determination is difficult. The advantage of radiolytic systems of a constant and known rate of initiation can again be utilized to derive the concentration of $MeSO_2$ radicals. This estimation is based on the assumption that $[MeSO_2] \gg [Me]$ and $[RSO_2] \gg [R]$ so that

$$[R]_o = [RSO_2] + [MeSO_2]$$

where $[R]_o$ is the steady state concentration of cyclohexyl radicals in cyclohexane.

When the necessary kinetic analysis, based on this assumption and expression XIV is carried out (37), the temperature dependence of $K_{-42} = k_{-42}/k_{42}$ is found to be given by the following expression:

$$\log K_{-40}(M^{-1}) = 4.99 \pm 0.52 - (14.94 \pm 0.92)/2.303RT$$

Accordingly, the bond dissociation energy $D(Me{-}SO_2)$ in cyclohexane is 14.94 kcal/mole. This value is lower by 6 kcal/mole than the average of the gas phase estimations (38-40). It is worth noting that the difference of 6 kcal/mole between the gas and liquid phase bond dissociation energies is almost equal to the heat of vaporization of SO_2.

Radiolytic Studies of the Reactions of Cl_3Si and Et_3Si Radicals

The use of gamma radiation for the initiation of free radical chain reactions is not limited to alkane solutions. Reactions of other radicals can be studied by this method. For example, silyl radicals are generated in silane solutions and their subsequent reactions with added solutes can be investigated.

In trichlorosilane the chain decomposition of chloromethanes, ClM, proceeds by reactions 52 and 53. In the Cl_3SiH–ClM systems the relative Arrhenius parameters of the Cl atom transfer, reaction 52, were determined in competitive studies (41). The same method was

$$Cl_3Si + ClM \rightarrow Cl_4Si + M \tag{52}$$

$$M + Cl_4Si \rightarrow MH + Cl_3Si \tag{53}$$

used for the determination of relative Arrhenius parameters of the analogous Cl transfer reactions of Et_3Si radicals with chloromethanes and chloroethanes (42).

In general, chlorine transfer reactions of silyl radicals were found to be much faster and less selective than the analogous

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch010

reactions of cyclohexyl radicals. The higher reactivity of silyl radicals can be ascribed to the fact that Si-Cl bond is stronger than the C-Cl bond while the Si-H bond is considerably weaker than the C-H bond. Consequently, the Cl atom transfer reactions of silyl radicals are more exothermic than the reactions of alkyl radicals and have lower activation energies. However, the trends in reactivity cannot be explained entirely by changes in activation energies since in both the Cl_3SiH-ClM and Et_3SiH-ClM systems large differences between the preexponential Arrhenius coefficients were observed.

Particularly interesting is the chain mechanism of the decomposition of chloroethylenes in triethylsilane (43). For C_2Cl_3H solutions in Et_3SiH the propagation step of the decomposition reaction is given by reactions 54 through 58.

$$Et_3Si + HCCl{=}CCl_2 \rightarrow Et_3SiCl + HCCl{=}CCl \tag{54a}$$

$$Et_3Si + HCCl{=}CCl_2 \rightarrow Et_3SiCl + HC{=}CCl_2 \tag{54b}$$

$$Et_3Si + HCCl{=}CCl_2 \rightarrow Et_3SiCHClCCl_2 \tag{55}$$

$$Et_3SiCHClCCl_2 \rightarrow Et_3SiCH{=}CCl_2 + Cl \tag{56}$$

$$HCCl{=}CCl + Et_3SiH \rightarrow (cis,\ trans)\text{-}C_2Cl_2H_2 + Et_3Si \tag{57a}$$

$$HC{=}CCl_2 + Et_3SiH \rightarrow CH_2{=}CCl_2 + Et_3Si \tag{57b}$$

$$Cl + Et_3Si \rightarrow HCl + Et_3Si \tag{58}$$

At 80° $k_{55}/k_{54a} = 1.09\pm0.11$ and $k_{54a}/k_{54b} = 37\pm14$.

The ability of triethyl silyl radicals to remove the strongly bound vinylic chlorine from trichloroethylene (reaction 54) is a characteristic feature of the reactions of triethylsilyl radicals with other chloroethylenes. Radical addition to acetylenes is the method used most frequently to generate vinyl radicals. The formation of vinyl radicals by Cl atom transfer from chloroethylenes to silyl radicals thus offers an interesting alternative to this method.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

11

Some Applications of Free Radical Rearrangements

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I have chosen to discuss some applications of free-radical rearrangements in solution for a number of reasons. In the first place, this Symposium is intended to honour Paul Bartlett and Cheves Walling for their many contributions to free-radical chemistry. Early work on free-radical rearrangements by both Bartlett (1) and Walling (2) played vital roles in the subsequent development of the subject (3-5). Secondly, this Symposium is being held in the city in which the first free-radical rearrangement, the neophyl rearrangement, was discovered by Urry and Kharasch in 1944 (6). Third and finally, our own wish to put free-radical chemistry on a quantitative footing has led us to measure the rate constants and Arrhenius parameters for a number of well-known rearrangements using the technique of kinetic electron spin resonance spectroscopy (7-11).

Rate constants for radical rearrangements (9) [and for radical scission reactions (12)] can be measured directly by E.S.R. However, it is usually simpler to obtain such rate constants in two separate experiments (7, 8, 10-16). It is first necessary to measure the concentrations of the unrearranged radical, $\mathbf{U}$, and the rearranged radical, $\mathbf{R}$, formed from some source of $\mathbf{U}$ under steady-state conditions. Provided the radicals react according to the following scheme,

$$\mathbf{U} \xrightarrow{k_i} \mathbf{R}$$

$$\left.\begin{array}{l} \mathbf{U} + \mathbf{U} \xrightarrow{k_t^{\mathbf{U}}} \\ \mathbf{U} + \mathbf{R} \xrightarrow{k_t^{\mathbf{UR}}} \\ \mathbf{R} + \mathbf{R} \xrightarrow{k_t^{\mathbf{R}}} \end{array}\right\} \text{nonradical products}$$

the usual steady-state treatment (12-14) yields equation I.

© 0-8412-0421-7/78/47-069-187$05.00/0

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

$$\frac{1}{[\mathbf{R}]} = \frac{2k_t^{\mathbf{R}}[\mathbf{R}]}{k_i[\mathbf{U}]} + \frac{2k_t^{\mathbf{UR}}}{k_i} \qquad \text{(I)}$$

The relative and absolute concentrations of $\mathbf{U}$ and $\mathbf{R}$ can be varied by changing the rate of radical production. A plot of $1/[\mathbf{R}]$ against $[\mathbf{R}]/[\mathbf{U}]$ will yield a straight line of slope $2k_t^{\mathbf{R}}/k_i$. The rearrangement rate constant is then obtained following direct measurement of $2k_t^{\mathbf{R}}$ by the usual kinetic E.S.R. method (17, 18) under similar experimental conditions [solvent, temperature, etc.]. In certain cases, it can be safely assumed that $k_t^{\mathbf{UR}} = k_t^{\mathbf{R}}$, in which case equation I can be simplified to

$$k_i/2k_t^{\mathbf{R}} = ([\mathbf{R}]^2/[\mathbf{U}]) + [\mathbf{R}] \qquad \text{(II)}$$

and only one measurement of the $\mathbf{U}$ and $\mathbf{R}$ concentrations is necessary (7).

The Neophyl Rearrangement

Urry and Kharasch's pioneering discovery of the neophyl rearrangement arose from an investigation into the factors influencing the course and mechanism of Grignard reactions (6). It was found that although neophyl chloride did not react with pure phenyl magnesium bromide, it reacted vigorously in the presence of cobaltous chloride to give *tert*-butylbenzene (27%), isobutylbenzene (15%), 2-methyl-3-phenyl-propene (9%), β,β-dimethylstyrene (4%), and a mixture of dimers and biphenyls - all of these products having to be identified by boiling point, refractive index, etc. It was concluded that the neophyl free radical, $\mathbf{1U}$, had rearranged to the β,β-dimethylphenethyl radical, $\mathbf{1R}$.

$$\underset{\mathbf{1U}}{C_6H_5C(CH_3)_2\dot{C}H_2} \xrightarrow{o} \underset{\mathbf{1R}}{C_6H_5CH_2\dot{C}(CH_3)_2}$$

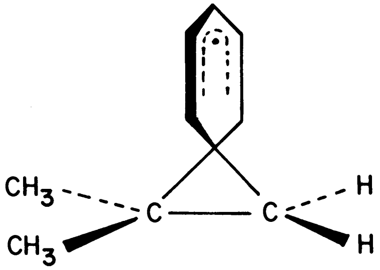
The occurrence of this rearrangement can, nowadays, be very simply verified by uv photolysis of a di-*tert*-butyl peroxide solution of *tert*-butylbenzene in the cavity of an E.S.R. spectrometer. At room temperature and below the spectrum due to $\mathbf{1U}$ is observed (8, 19).

$$(CH_3)_3COOC(CH_3)_3 \xrightarrow{h\nu} 2(CH_3)_3CO^{\bullet}$$

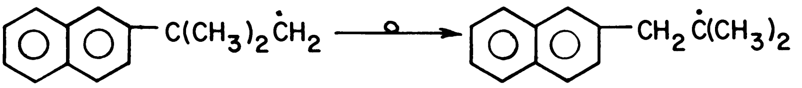
$$(CH_3)_3CO^{\bullet} + C_6H_5C(CH_3)_3 \longrightarrow (CH_3)_3COH + \mathbf{1U}$$

At higher temperatures the spectrum due to $\mathbf{1R}$ is also present and so the rate constant for the rearrangement can be measured by the method described above. Although this was the first free-radical rearrangement to be discovered it requires quite a large activation energy (see Table I) and so it is relatively slow $[k_i^{\underset{\sim}{1}} = 59\ \text{sec}^{-1}$ at 25°C ($\underline{8}$)].

The neophyl rearrangement must proceed through a spiro [2.5] octadienyl type of intermediate or transition state, viz.,



It is clear that the rearrangement will be accelerated if this structure is stabilized by better delocalization of the unpaired electron into the aromatic ring. For this reason, the analogous rearrangements involving the β-naphthyl system,

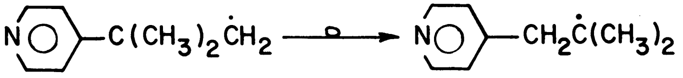


(2)

$\underset{\sim}{2U}$

$k_i^{\underset{\sim}{2}} = 2.9 \times 10^3\ \text{sec}^{-1}$ at 25°C (8)

and 4-pyridyl ring,



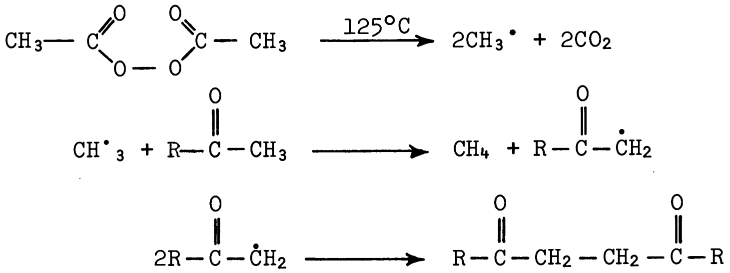
(3)

$\underset{\sim}{3U}$

$k_i^{\underset{\sim}{3}} = 1.4 \times 10^3\ \text{sec}^{-1}$ at 25°C (8) are appreciably faster than the neophyl rearrangement (see also Table I). It is, I think, worth noting that the first report of a substituent effect on the migratory abilities of aromatic rings in free-radical rearrangements is due to Bartlett and Cotman (1).

The Benzoylmethyl Rearrangement

In 1948 Kharasch, McBay, and Urry (20) found that the reaction of aliphatic ketones with acetyl peroxide, at temperatures where the latter undergoes thermal decomposition, provided a convenient synthetic route to 1,4-diketones.

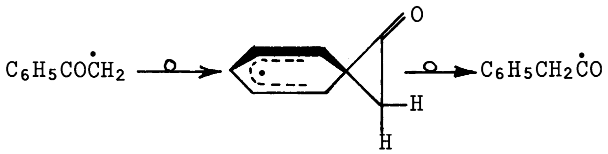


$$CH_3-\overset{O}{\overset{\|}{C}}-O-O-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{125^\circ C} 2CH_3^{\bullet} + 2CO_2$$

$$CH^{\bullet}_3 + R-\overset{O}{\overset{\|}{C}}-CH_3 \longrightarrow CH_4 + R-\overset{O}{\overset{\|}{C}}-\dot{C}H_2$$

$$2R-\overset{O}{\overset{\|}{C}}-\dot{C}H_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-R$$

However, all attempts to synthesize 1,2-dibenzoylethane and related diketones by dehydrodimerization of the appropriate alkyl phenyl ketones using the same procedure were unsuccessful, only resinous polymeric material being obtained. This was subsequently attributed (21) to a "neophyl-like" rearrangement of the benzoylmethyl radical, 4U, via an intermediate 1-keto spiro [2.5] octadienyl radical, 4I, to form the phenylacetyl radical, 4R.



(4)

4U 4I 4R

The phenylacetyl radical then undergoes an α-scission to yield the benzyl radical, 5, and carbon monoxide.

$$C_6H_5CH_2\dot{C}O \xrightarrow{k_5} C_6H_5\dot{C}H_2 + CO \qquad (5)$$

4R 5

We have recently reinvestigated this sequence of reactions by E.S.R. spectroscopy (11). Our kinetic data show that the forma-

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

tion of resinous products rather than dimers in the reaction of alkyl phenyl ketones with acetyl peroxide is unrelated to the rearrangement that benzoylalkyl radicals can undergo.

The benzoylmethyl radical was generated in the E.S.R. spectrometer by two different photolytic methods.

$$\text{(a)}\quad (\underline{n}\text{-}Bu_3Sn)_2 \xrightarrow{h\nu} 2\ \underline{n}\text{-}Bu_3Sn^{\bullet}$$

$$\underline{n}\text{-}Bu_3Sn^{\bullet} + C_6H_5COCH_2Br \longrightarrow \underline{n}\text{-}Bu_3SnBr + C_6H_5CO\dot{C}H_2$$

$$\text{(b)}\quad (\underline{t}\text{-}BuO)_2 \xrightarrow{h\nu} 2\ \underline{t}\text{-}BuO^{\bullet}$$

$$\underline{t}\text{-}BuO^{\bullet} + C_6H_5COCH_3 \longrightarrow \underline{t}\text{-}BuOH + C_6H_5CO\dot{C}H_2$$

At temperatures of -50°C and lower the benzoylmethyl radicals decayed with second order kinetics at a rate that was close to the diffusion-controlled limit ($2k_t^{4U} = 5 \times 10^8\ \underline{M}^{-1}\ sec^{-1}$ at -70°C). The product was 1,2-dibenzoylethane.

$$2C_6H_5CO\dot{C}H_2 \xrightarrow{2k_t^{4U}} C_6H_5COCH_2CH_2COC_6H_5$$

At temperatures above about 80°C, 4U decayed with first order kinetics ($k = 1.7 \times 10^3\ sec^{-1}$ at 100°C). At 120°C the spectrum due to 4U was replaced by that of the benzyl radical, 5. At no temperature between 100 and 200°C was it possible to detect the spiro-octadienyl radical, 4I, (which may be only a transition state in the rearrangement rather than a discrete intermediate) or the phenylacetyl radical, 4R. However, 4R can be detected when it is generated at low temperatures (22). Photolysis of a cyclopropane solution of di-tert-butyl peroxide and phenylacetaldehyde at -116°C gave the E.S.R. spectra of 4R and 5 simultaneously (11). At this temperature $k_5 \approx 9 \times 10^2\ sec^{-1}$, while at 125°C, the temperature at which the original attempt was made to prepare 1,2-dibenzoylethane from acetophenone (20), we can estimate that k_5 would be ca. $10^9\ sec^{-1}$ (11). It is clear that at 125°C, no bimolecular reaction of 4R could be fast enough to compete with its decarbonylation. Hence, radical 4R cannot itself be directly involved in any of the reactions that lead to resinous materials in the acetophenone-acetyl peroxide reaction.

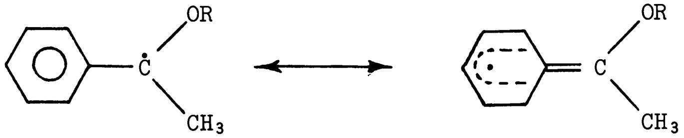
The rearrangement of the 2-benzoyl-2-propyl radical, 6, is very much slower than the rearrangement of the benzoylmethyl radical. In fact, 6 decays with second order kinetics even at temperatures as high as 130°C.

$$\underset{6}{2C_6H_5CO\dot{C}(CH_3)_2} \xrightarrow{2k_t^{6}} \text{Products} \qquad (6)$$

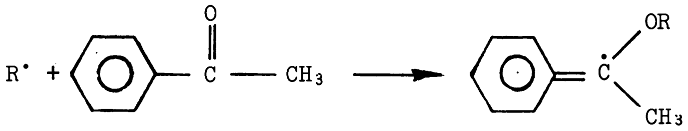
$$2k_t^{6} = 2.4 \times 10^9\ \underline{M}^{-1}\ sec^{-1} \text{ at } 130°C(\underline{11}).$$

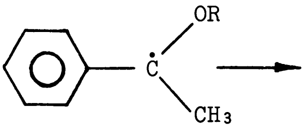
Since the reaction of acetyl peroxide with phenyl isopropyl ketone at 115°C did give resinous material (20) we must conclude that isomerization products of 6 could not have been involved in the formation of this material.

Since the rearrangement of benzoylalkyl radicals is unrelated to the production of resinous materials (instead of the anticipated dimers) in the acetyl peroxide - alkyl phenyl ketone reactions, we must look elsewhere for an explanation. Once we come to this conclusion the fact that acetophenone is isoelectronic with α-methylstyrene immediately becomes significant. That is, radical additions to the carbonyl oxygen of phenyl ketones will be facilitated by resonance stabilization of the adduct, just as is the case with α-methylstyrene or styrene, i.e.

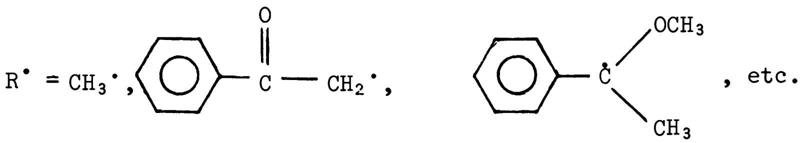


The overall route to the formation of resinous materials can, we believe, therefore be represented as:





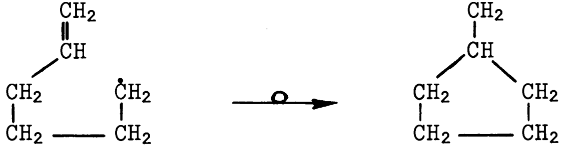
A mixture of dimers and of disproportionation products.



The formation of resinous material at the temperatures employed by Kharasch, McBay, and Urry (20) in their attempted dehydrodimerizations of alkyl phenyl ketones is, after the event, perhaps not too surprising.

The 5-Hexenyl Cyclization.[23]

In the foregoing we have seen how kinetic E.S.R. spectroscopy has been used to solve a long-standing problem in reaction mechanism. I now want to turn to a different radical rearrangement reaction, the cyclization of the 5-hexenyl radical, **7U**, to the cyclopentylmethyl radical, **7R**.

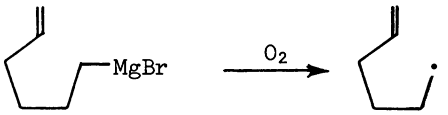


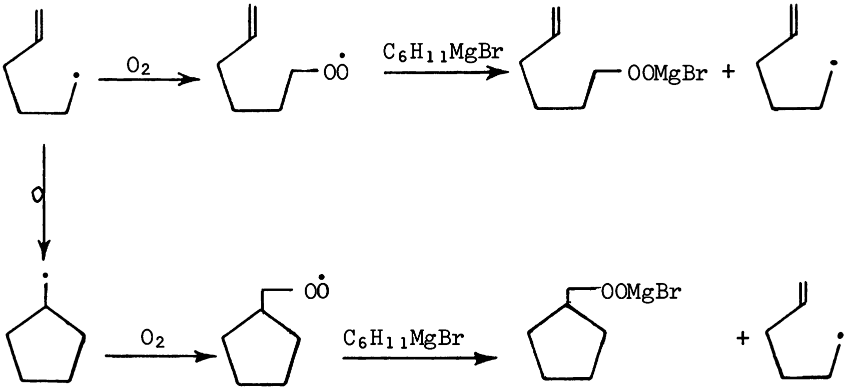
7U **7R** (7)

Our initial kinetic E.S.R. study of this reaction (7) has now led us into a quantitative investigation of the "spin-trapping" (24) of **7U** and other primary alkyl radicals.

Free-radical cyclizations have a long history (2) but of all known cyclizations that of the 5-hexenyl radical has proved most useful as a mechanistic probe. This is because the anion corresponding to **7U** does not cyclize (25) while, as Bartlett has shown (26), the corresponding cation cyclizes to yield products having a *six*-membered ring. Therefore, in reactions that involve the 5-hexene moiety, the formation of products containing the *five*-membered ring is diagnostic of a homolytic process and any potential heterolytic mechanism can be ruled out. This criterion has been used extensively by Walling (27-29) and by Lamb and Garst (25,30,31) and their coworkers to investigate reactions which might, in principle, proceed by homolytic or by heterolytic or concerted pathways. A case in point, is the autoxidation of Grignard reagents (29,30). Attempts to inhibit such autoxidations by conventional free-radical inhibitors have not been successful, probably because the inhibitors that have been tried are rapidly removed by reaction with the Grignard reagents. However, the autoxidation of 5-hexenylmagnesium bromide with an excess of oxygen at low temperatures yields 5-hexenylperoxymagnesium bromide whereas, if the oxygen supply is restricted, or if the temperature is raised, a substantial amount of cyclopentylmethylperoxymagnesium bromide is formed. The overall reaction can therefore be represented as:

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011





The 5-hexenyl cyclization is clearly under kinetic rather than under thermodynamic control since the thermodynamically favoured product would be the cyclohexyl radical. It has been suggested that the 5- rather than the 6-membered ring is produced because bond formation requires the approach of the radical within the plane of the π-orbital and along an axis extending above one of the terminal atoms of the double bond either approximately vertically (32, 33), or at an angle of about 109° to the double bond (34). In the latter case, the angle subtended between the three interacting atoms is maintained during the reaction pathway and becomes the angle between these atoms in the product. On the basis of a series of elegant experiments on the cyclization of related radicals, Beckwith and Gara (35) have, however, concluded that intramolecular radical cyclizations are kinetically favoured if the newly formed bond and the semi-occupied orbital at the new radical center can become completely coplanar. The 5-hexenyl radical and analogous species yield the five-membered ring because coplanarity is readily achieved by the free rotation of the exocyclic C–C bond. Complete coplanarity cannot be achieved in

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forming the six-membered ring and so cyclization to the six-membered ring is kinetically disfavoured (35).

Our own interest in reaction 7 began when we were able to estimate its rate constant at ambient temperatures (36). This first estimate of k_i^{7} was obtained by combining some product studies of Walling (28) with a rotating-sector kinetic study of our own on the trialkyltin hydride - alkyl halide reaction. We have subsequently investigated reaction 7 by kinetic E.S.R. spectroscopy (7) and have confirmed our earlier rate constant (see also, Table I):

$$k_i^{7} = 1 \times 10^5 \text{ sec}^{-1} \text{ at } 25°\text{C} \quad (7).$$

Since the rate constants for this, and for related (36), cyclizations are known these reactions can be used to determine the rates of reaction of primary alkyls with such diverse species as cupric ion (32, 37) and tert-butyl hypochlorite (38). However, there can be no doubt that some of the most interesting radical-molecule reactions are those involved in "spin-trapping". This is a technique which has been used qualitatively for several years to detect and identify transient free-radicals (24). Its quantitative use in mechanistic studies has been hampered by the paucity of data available for the rate constants, k_a, for the addition of radicals to the spin traps, T.

$$R^\bullet + T \xrightarrow{k_a} R\,T^\bullet \qquad (a)$$

What little rate data is available rests on competitive experiments with reactions having "known" rate-constants but, unfortunately, even these "known" rate constants are somewhat uncertain. In view of the great potential of spin-trapping we have begun a program to determine accurate rate constants for the trapping of some commonly encountered radicals, starting with primary alkyls (39).

Since the 5-hexenyl and cyclopentylmethyl radicals are both primary alkyls the spin adducts that they form with a trap will have similar kinetic and thermodynamic stabilities, which is an advantage, and similar E.S.R. spectra, which is a handicap. However, a nice distinction between the spectra of the two spin adducts, 7UT• and 7RT•, can be obtained by labelling the 5-hexenyl radical with carbon-13 (I = ½) in the 1-position. In most cases, hyperfine splitting by this C-13 should be detectable in the E.S.R. spectrum of 7UT• because of the proximity of the C-13 to the orbital containing the unpaired electron in this adduct. However, in 7RT• the C-13 will be too remote from the unpaired electron to produce any appreciable hyperfine splitting. The rate constant for the addition of 7U to the trap can be calculated from the trap concentration and the measured ratio of the concentrations of the two spin-adducts in the early stages of the reaction, i.e.

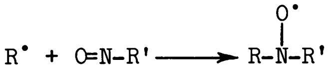
$$k_a^{7} = k_i^{7}\,[T]\,\frac{[7\,UT\cdot]}{[7\,RT\cdot]}$$

The spin-adduct ratio must be extrapolated to zero time if it shows any variation and the total concentration of adducts must not be allowed to approach its steady-state level (see below).

Our source of C-13 labelled 7U is di(2-^{13}C-6-heptenoyl) peroxide (90 atom % ^{13}C) which can be decomposed thermally or photochemically in an inert solvent, such as benzene, containing a known concentration of a spin trap (39).

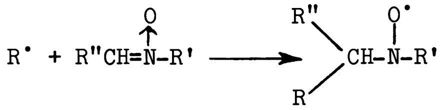
$$[CH_2{=}CH(CH_2)_3{}^{13}CH_2C(O)O]_2 \xrightarrow[h\nu]{\Delta} 2CH_2{=}CH(CH_2)_3{}^{13}CH_2^{\cdot} + 2CO_2$$

We have investigated a number of the usual nitroso traps,



$$R^{\cdot} + O{=}N{-}R' \longrightarrow R{-}\overset{O^{\cdot}}{N}{-}R'$$

and nitrone traps,



as well as a few less commonly employed spin traps such as di-tert-butyl thioketone,

$$R^{\cdot} + S{=}C[C(CH_3)_3]_2 \longrightarrow R{-}S{-}\dot{C}[C(CH_3)_3]_2$$

Values of k_a^7 at 40°C for some of the spin-traps studied are listed in Table II. Some of the data in this Table has been obtained with the n-hexyl radical, 8, (from n-heptanoyl peroxide) by competitive experiments in the presence of two spin traps that give readily distinguishable E.S.R. spectra.

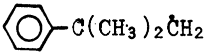
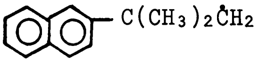
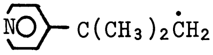
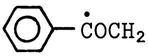
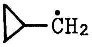
$$\underset{8}{CH_3(CH_2)_5^{\cdot}} + T_1 \longrightarrow CH_3(CH_2)_5T_1^{\cdot} \qquad (8)$$

$$CH_3(CH_2)_5^{\cdot} + T_2 \longrightarrow CH_3(CH_2)_5T_2^{\cdot}$$

In all cases where confirmation has been sought, it has been found that the rate constant ratios $(k_a^7)_{T_1}/(k_a^7)_{T_2}$ and $(k_a^8)_{T_1}/(k_a^8)_{T_2}$ are equal, as we would expect since 7U and 8 are both primary alkyls.

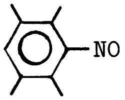
By monitoring the initial rate of formation of the spin-adduct it is possible to measure the rate, V_i, at which the

Table I. Rate Constants and Arrhenius Parameters for the Rearrangement of Some Primary Alkyl Radicals.

Reaction	Radical U	k_i, sec^{-1} at 25°C	log A_i, sec^{-1}	E_i, kcal/mol	Ref.
1		59	11.7_5	13.6	8
2		2.9×10^3	11.7_5	11.3	8
3		1.4×10^3	11.8	11.8	8
4		10^a	11.8^b	14.7^a	11
7	$CH_2{=}CH(CH_2)_4^{\bullet}$	1.0×10^5	10.7	7.8	7
9		1.3×10^8	12.5	5.9	10

[a]Calculated from the measured rate constant of 1.7×10^3 sec^{-1} at 102°C and the assumed pre-exponential factor. [b]Assumed.

Table II. Some Rate Constants for the Spin-Trapping of Primary Alkyl Radicals in Benzene at 40°C

Spin-Trap	$k_a\times10^{-5}$, M^{-1} sec^{-1}
$(CH_3)_3CNO$	90
	394
$CH_2{=}N(O)C(CH_3)_3$	31
$C_6H_5CH{=}N(O)C(CH_3)_3$	1.3
$[(CH_3)_3C]_2CS$	0.45

peroxide is decomposing to form free-radicals (40). We have found (39) that if the reaction is allowed to continue until the spin-adduct concentration reaches a steady-state then, by measuring this concentration, it is possible to obtain the rate constants for the two processes that normally will lead to its consumption, viz.,

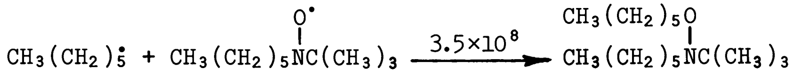
$$R^\bullet + R\mathbf{T}^\bullet \xrightarrow{k_b} \text{Products} \qquad (b)$$

$$R\mathbf{T}^\bullet + R\mathbf{T}^\bullet \xrightarrow{2k_c} \text{Products} \qquad (c)$$

Radical formation at a rate V_i, followed by reactions a, b, and c yields the relation (32):

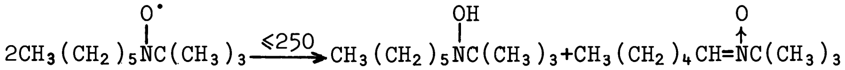
$$\left\{\frac{k_a[\mathbf{T}]}{[R\mathbf{T}^\bullet]_{ss}} - k_b\right\} \bigg/ \left\{\frac{k_a[\mathbf{T}]}{[R\mathbf{T}^\bullet]_{ss}} + k_b\right\} = \frac{2k_c}{V_i}[R\mathbf{T}^\bullet]_{ss}^2 \qquad (III)$$

This application of the kinetic E.S.R. technique can be illustrated for $R^\bullet$ = *n*-hexyl and $\mathbf{T}$ = 2-methyl-2-nitrosopropane in benzene at 40°C. Measurement of the initial rate of $R\mathbf{T}^\bullet$ formation gave $V_i = 2 \times 10^{-8}$ M sec^{-1}. Taking $k_a = 9.0 \times 10^6$ M^{-1} sec^{-1} (see Table II), the steady-state concentrations of $R\mathbf{T}^\bullet$ at various trap concentrations could best be correlated by taking $k_b = 3.5 \times 10^8$ M^{-1} sec^{-1} and $2k_c \approx 125$ M^{-1} sec^{-1}. The value found for k_b is in range generally observed for the addition of other alkyl radicals to sterically hindered, persistent, nitroxides such as di-*tert*-butyl nitroxide (41, 42).



$$CH_3(CH_2)_5^\bullet + CH_3(CH_2)_5\overset{\overset{\displaystyle O^\bullet}{|}}{N}C(CH_3)_3 \xrightarrow{3.5\times10^8} CH_3(CH_2)_5\overset{\overset{\displaystyle CH_3(CH_2)_5O}{|}}{N}C(CH_3)_3$$

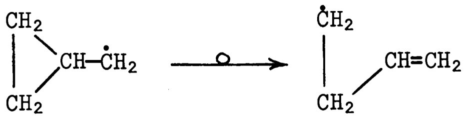
This technique would, therefore, appear to provide a simple method for studying reactions between alkyl radicals and transient nitroxides and also, possibly, for studying other "cross" radical-radical reactions. The value obtained for $2k_c$ was found to be in reasonable agreement with that obtained by a direct measurement of the bimolecular decay of *n*-hexyl-*tert*-butyl nitroxide, viz., $\leqslant 250$ M^{-1} sec^{-1} (39):



$$2CH_3(CH_2)_5\overset{\overset{\displaystyle O^\bullet}{|}}{N}C(CH_3)_3 \xrightarrow{\leqslant 250} CH_3(CH_2)_5\overset{\overset{\displaystyle OH}{|}}{N}C(CH_3)_3 + CH_3(CH_2)_4CH{=}\overset{\overset{\displaystyle O}{\uparrow}}{N}C(CH_3)_3$$

The Cyclopropylmethyl Ring-Opening Reaction

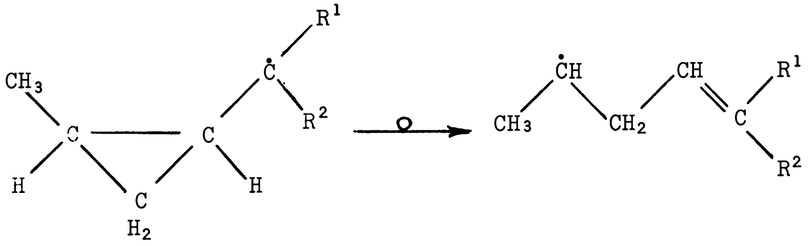
Another example of a mechanistically useful rearrangement of a primary alkyl radical is provided by the extremely facile ring-opening of cyclopropylmethyl, **9U**, to yield the 3-butenyl radical, **9R**.



(9)

9U 9R

The effect that ring substituents have on the direction of ring opening, which has been unravelled by Davies and Pereyre and their co-workers (43-49), provides a fascintaing picture of the subtle stereoelectronic factors that control such processes. At low temperatures, cis-2-methylcyclopropylalkyl radicals, 10U, undergo ring opening to give the thermodynamically preferred secondary alkyl radical, 10R.

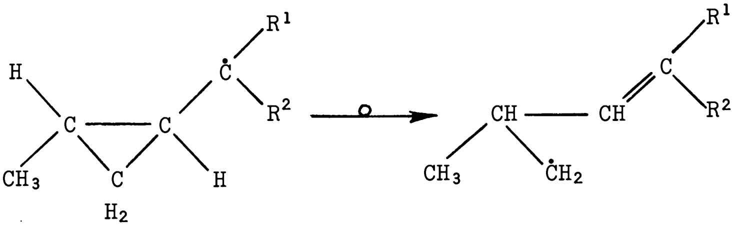


(10)

10U 10R

R^1=H; R^2=H, OH, $OSn[(CH_2)_3CH_3]_3$, $OSi(CH_3)_3$, etc.

However, trans-2-methylcyclopropylalkyl radicals, 11U, undergo ring opening at low temperatures to give the thermodynamically disfavoured primary alkyl, 11R. [At high temperatures and low concentrations of radical trapping agents, 11U, gives an increasing proportion of the thermodynamically preferred products from 10R because the ring opening is reversible (48)].

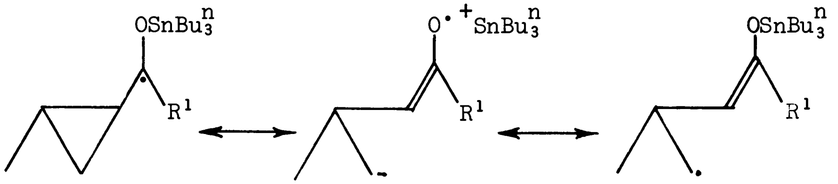


(11)

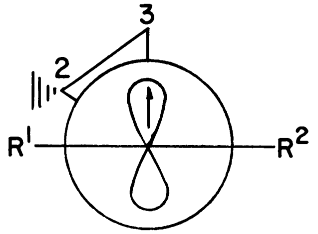
11U 11R

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

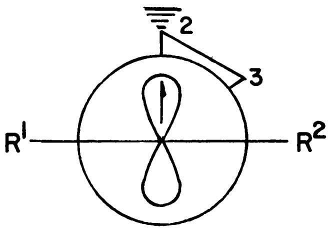
The remarkably selective formation of the primary alkyl **radical** from 11U was initially thought to be due to polar contributions to the transition state which conferred some carbanionic character on the incipient alkyl (43, 44), e.g.,



However, further work (49) showed that the regioselectivity of the ring openings did not depend on the presence of a polar OSnBu$_3^n$ or OH substituent at the initial radical center. It was therefore suggested that the methyl substituent interacts with the polarizable electrons of the cyclopropyl ring to render the C^1-C^3 bond electronically non-equivalent with the C^1-C^2 (and C^2-C^3) bond. Interaction between the semi-occupied orbital and the C^1-C^3 bonding orbital could cause conformer 11Ua to be more highly populated than 11Ub, which would lead to preferential cleavage of the C^1-C^3 bond, and hence to the production of 11R.



11Ua



11Ub

However, in the case of the cis radical, 10U, electronic factors could be overwhelmed by steric effects so that conformer 10Ub (or b')- which is the precursor of the secondary alkyl radical, 10R - would be preferred to conform 10Ua (or a').

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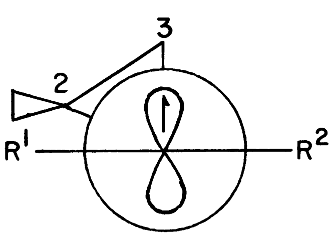
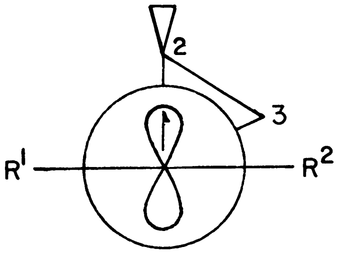


10Ua



10Ub

R^1 and R^2 reversed for conformers **10Ua'** and **10Ub'**.

Our own work on the ring opening of cyclopropylalkyl radicals has been confined to measuring the rate for the cyclopropylmethyl radical, i.e. reaction 9, by kinetic E.S.R. spectroscopy at low temperatures. Radical **9U** was generated by photolysis of *tert*-butyl cyclopropylperacetate in methylcyclopropane as solvent.

$$\overline{\mathrm{CH_2CH_2C}}\mathrm{HCH_2CO_2C(CH_3)_3} \xrightarrow{h\nu} \overline{\mathrm{CH_2CH_2C}}\mathrm{H\dot{C}H_2 + CO_2 + (CH_3)_3CO^{\bullet}}$$

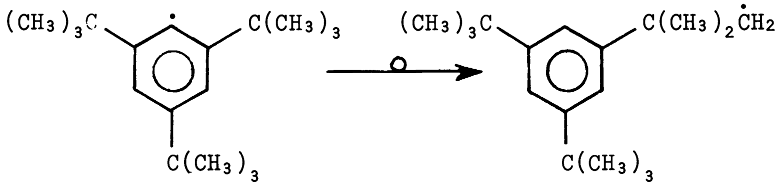
$$\mathrm{(CH_3)_3CO^{\bullet} + \overline{CH_2CH_2C}HCH_3} \longrightarrow \mathrm{(CH_3)_3COH + \overline{CH_2CH_2C}H\dot{C}H_2}$$

Both **9U** and **9R** could be detected at temperatures in the range -120 to -145°C. Extrapolation of the measured rate constants for the isomerization to room temperature (see Table I) yielded,

$$k_i^{9} = 1.3 \times 10^{8}\ \mathrm{sec}^{-1} \text{ at } 25^{\circ}\mathrm{C} \qquad (\underline{10})$$

The Tri-tert-butylphenyl Isomerization

The majority of intramolecular hydrogen atom transfers proceed *via* 6-center cyclic transition states and so involve a 1,5 migration of hydrogen. The 2,4,6-tri-*tert*-butylphenyl radical, **12U**, however, undergoes an intramolecular H-transfer *via* a 5-center cyclic transition state (i.e., a 1,4 H-migration) to produce the 3,5-di-*tert*-butylneophyl radical, **12R**, (9).



(12)

12U **12R**

The unusual feature about this reaction is that it provides the first authentic example of quantum-mechanical tunneling in an intramolecular H-transfer, that is, the H atom is transferred through a potential barrier, rather than over the top of the barrier as would be required by classical mechanics. Both **12U** and **12R** can be observed by ESR spectroscopy and k_i^{12} has been measured by both the direct and indirect methods for hydrogen and for deuterium atom transfer (9). The occurrence of tunneling is indicated four kinetic phenomena. Firstly, the kinetic deuterium isotope effect, $\left(k_i^{12}\right)_H / \left(k_i^{12}\right)_D$, is much greater at all temperatures than the classically calculated "maximum" value, which is based on the assumption that the maximum isotope effect arises when all zero-point energy is lost in the transition state. Thus, the "maximum" isotope effects at -30 and -150°C are calculated to be 17 and 260, respectively, while the measured values are 80 and 13,000. Secondly, the Arrhenius plots are strongly curved, the temperature dependence of the reaction becoming less as the temperature is lowered. In fact, the hydrogen transfer occurs at an appreciable rate at temperatures not far above absolute zero (38). The third and fourth pieces of evidence for tunneling are the values of the Arrhenius pre-exponential factors and the activation energies. That is, although the usual Arrhenius equation cannot realistically be applied to reaction (12), over any limited range of temperature it is possible to draw straight lines through the data in the normal manner. The A-factors and activation energies derived in this way are enormously different from those which would be expected if the reaction obeyed classical mechanics. They can only be explained satisfactorily by invoking the wave nature of hydrogen and deuterium atoms.

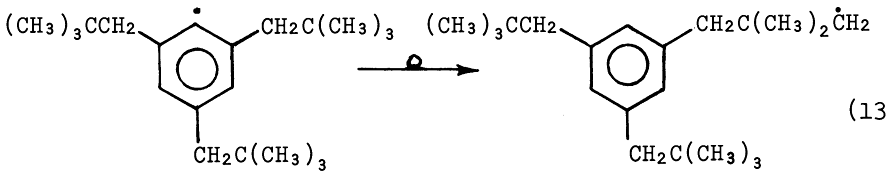
The curved Arrhenius plot for H-transfer can be described by the modified Arrhenius equation:

$$k_i^{12}(T) = A\Gamma(T)\ e^{-V_o/RT}$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

in which V_0 is the height of the potential barrier through which tunneling takes place (i.e., V_0 = the classical activation energy), A has essentially the same significance as in the usual equation, and $\Gamma(T)$ is a temperature dependent function which gives the ratio of quantum-mechanical to classical transmission rates from one side of the barrier to the other. The data for H-transfer can be fitted extremely well by a barrier having the shape proposed by Eckart (50) with a height of 14.5 kcal/mol and with an A factor of 10^{11}sec^{-1}, while for the D-transfer zero-point energy effects cause V_0 to increase to 14.9 kcal/mol (9).

The analogous isomerizations of several other aryl radicals that are structurally related to 12U also occur slowly and by quantum-mechanical tunneling (9,38). In contrast, the 2,4,6-tri-neopentylphenyl radical, 13U, isomerizes by a 1,5 hydrogen transfer which is so fast that only the rearranged radical, 13R, could be detected by ESR spectroscopy even at -160°C (9).



13U 13R

(13)

Conclusion.

A glance at the k_i values found for the radicals listed in Table I will show that we now have available an extremely versatile STABLE (51, 52) of primary alkyl radical rearrangements. Within this stable we can find radicals whose rearrangement rates will enable them to compete in a wide variety of radical-molecule races. That is, amongst these radicals we can find entrants suitable for competition against reactions whose speed varies from the gallop of,

$$R^{\bullet} + O_2 \longrightarrow ROO^{\bullet}$$

to the walk of,

$$R^{\bullet} + RH \longrightarrow RH + R^{\bullet}$$

We would very much like to expand this stable and obtain accurate rates for the rearrangement of additional primary alkyl

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch011

radicals. This would enable us both to "plug the gaps" in the range of k_i values that is available and to provide a wider choice of radicals which could be used in any particular competition. A few possible new candidates for this stable are listed below

$$C_6H_5CH_2{}^*CH_2^{\bullet} \xrightarrow{\circ} C_6H_5{}^*CH_2CH_2^{\bullet}$$

$$H_2C{=}CHC(CH_3)_2CH_2^{\bullet} \xrightarrow{\circ} H_2C{=}CHCH_2\dot{C}(CH_3)_2$$

$$(C_6H_5)_3CCH_2^{\bullet} \xrightarrow{\circ} C_6H_5CH_2\dot{C}(C_6H_5)_2$$

$$CCl_3CH_2^{\bullet} \xrightarrow{\circ} ClCH_2\dot{C}Cl_2$$

Rate constants for one or two of these rearrangements have been estimated (5, 36) but for none of these reactions are reliable Arrhenius parameters available.

The ordered growth and future development of homolytic chemistry will, to quite a large extent, be dependent on the building of additional free-radical stables, set up to cater to the rearrangement or fragmentation of other breeds of free radicals. Limited data is already available on the α-scission of certain acyl radicals (11,13,15,53), on the β-scissions of some tetra-alkoxyphosphoranyl radicals (12,14), some alkoxyalkyls (54), and some dialkoxyalkyls (16, 54), and on the rearrangement of some β-acyloxyalkyl radicals (55,56). An extension of such data to cover a wider variety of reactive free radicals is an important task for the future.

Abstract.

Measurement of the rate constants and Arrhenius parameters for the rearrangement of a variety of primary alkyl radicals by E.S.R. spectroscopy is briefly described. At 25°C these rate constants vary from a low of 10 sec^{-1} for the reaction: $C_6H_5COCH_2^{\bullet} \xrightarrow{\circ} [C_6H_5CH_2\dot{C}O] \longrightarrow C_6H_5CH_2^{\bullet} + CO$; to a high of 1.3×10^8 sec^{-1} for the reaction $\overline{CH_2CH_2\dot{C}}HCH_2 \xrightarrow{\circ} \dot{C}H_2CH_2CH{=}CH_2$. These isomerizations provide useful probes in mechanistic studies and can be used to determine the rates with which primary alkyls react with a variety of molecules. The latter use is illustrated by the measurement of the rates of spin trapping of the 5-hexenyl radical by some common traps. Aryl radical isomerizations that proceed by quantum-mechanical tunneling are reviewed briefly.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

12

EPR Studies of Radical Pairs. The Benzoyloxy Dilemma.

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For the past ten years we have been using free-radical systems to study the chemistry of organic solids. This work originated with studies of the photolysis of solid azoalkanes in P. D. Bartlett's laboratory at Harvard. (1,2) Much of our effort has been devoted to epr spectroscopy of radical pairs generated in low concentration by photolyzing single crystals of such standard radical initiators as azoalkanes and diacyl peroxides. In several cases this tool has allowed us to determine where molecules in a solid move during chemical reaction and how easily they move. (3,4)

Since single-crystal epr spectra contain information about electron spin distribution, it is necessary to know how the electron spin is distributed about the nuclear framework of a radical in order to infer how the radical is oriented. When the spin distributions of isolated radicals are known from independent sources, epr gives detailed information about the arrangement of the radicals in pairs. Naturally knowing this arrangement can be uniquely helpful in determining the factors which influence reactions of organic solids.

Sometimes radical structure and spin distribution are not known reliably. Epr results can then be useful in determining radical structure as well as in studying the arrangement of pairs. This paper focuses on what solid systems can tell about radical structure rather than on what radical systems can tell about the chemistry of solids. Its first purpose is to show what information about radical structure and pair arrangement is contained in single crystal EPR spectra. Its second is to show, using pairs including benzoyloxy radicals as an example, how the spectra sometimes confuse us by providing more information than appears to be consistent with simple explanations.

EPR of Radical Pairs

The radicals we study are immobilized in pairs separated by 3.5 to 8 Å. At these distances the bonding between them is weak enough that for temperatures above about 10 K (20 cal/mole) the

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

triplet state predominates over the singlet, which is presumably the ground state, by the statistical factor of three. The residual bonding remains strong enough, however, that for most magnetic purposes (perhaps 0.01 to 0.001 cal/mole) the pair must be considered as a triplet state with electron spins exchanging rapidly between the radicals, rather than as a pair of independent doublet states each with its own spin. (3) In addition to the normal electron Zeeman splitting there are three types of magnetic interactions which have a strong influence on the epr spectra of triplet radical pairs. These are:

1) interaction between electron spins and nuclear spins, which gives rise to hyperfine splitting (hfs) and is described by an A tensor for each magnetic nucleus;

2) indirect interaction between the electron spins and the applied field mediated by orbital angular momentum, which determines how much the field at the center of the pattern differs from that for a free electron, and is described through the g tensor; and

3) interaction between the two electron spins, which gives rise to spectral fine structure (fs) and is described by the D tensor.

What information do the A, g, and D tensors contain? The six independent elements of each tensor (D, being traceless, has only five) may be transformed to yield three sets of values consisting of one, two, and three members. These sets contain different types of information and may be determined under different conditions. The set of one member (which D lacks) is the isotropic or average value of the interaction and may be determined from samples in any phase. The set with two members describes the magnitude of the interaction's anisotropy and contains symmetry information. Its determination usually requires a rigid sample. The set of three members describes the orientation of the anisotropy, giving for example the spherical polar coordinates of a molecular symmetry axis and the phase of rotation about it. The orientation can only be determined with an oriented sample, usually a single crystal.

Hyperfine Splitting. The isotropic value of the hfs depends on electron spin density at the nucleus in question. Since p orbitals have a node at the nucleus, it shows how much spin density resides in the atom's s orbitals. For the 2s orbital of carbon the proportionality constant is 1110 gauss/electron; for the 1s orbital of hydrogen, 507. (5) The magnitude of the hfs anisotropy depends on how much the spin density in the neighborhood of the nucleus departs from spherical, and how much from axial symmetry. Since the through-space interaction is attenuated by the cube of the electron-nuclear distance, it samples primarily the immediate vicinity of the nucleus. For C-13 the anisotropic hfs commonly has an axis of symmetry and may be interpreted in terms of spin density in the 2p orbitals of the atom. The splitting by a C-13 nucleus of an electron localized in its p orbital would vary over a range of 97 gauss.(5) For hydrogen the interpretation is in terms of spin density on its neighbor. The orientational information can then tell which 2p orbital of carbon bears the electron spin.

For radicals in a triplet pair the observed hfs is the average of what it would be for the individual radicals. Since the spin of a nucleus on one radical has negligible direct interaction with the electron spin on the other, the hfs is half of the value for the isolated radical. The C-13 hfs of pairs of bridgehead triptycyl radicals provides an example. Pairs which persist at -100°C in a photolyzed single crystal of the related diacyl peroxide show signals with satellite doublets from splitting by bridgehead C-13 in natural abundance.(6) The isotropic value of this splitting is 49.9 G and the anisotropy shows approximate axial symmetry with a range of about 38 G. The isolated radical thus has (2 x 49.9 / 1110) = 9% spin density in the 2s orbital of the bridgehead carbon and (2 x 38 / 97) = 77% density in its 2p orbital. Thus some 86% of the spin density is localized on the bridgehead carbon in an sp^9 hybrid. The direction of the symmetry axis shows how the orbital is oriented in the solid, and the existence of a single pair of satellites shows that the two radicals in a pair are close enough to antiparallel that their bridgehead carbons give equivalent splitting.

Spin-Orbit-Field Coupling. Even a nondegenerate radical can acquire orbital angular momentum when an applied magnetic field mixes electronically excited states with the ground state by the $\underline{H}\cdot\underline{L}$ interaction.(7) In an LCAO-MO picture this mixing is the resultant of contributions from each atomic p orbital in the singly occupied MO, which after rotation by 90° about the applied field direction would overlap a p orbital in another MO of similar energy. For example, if the singly occupied MO had a large coefficient from p_x of a particular atom, and a vacant MO had a large coefficient for p_y of the same atom, a field in the z direction would tend to mix them through the L_z operator, which "rotates" p_x into $i\hbar$ p_y (at the same time rotating p_y into $-i\hbar$ p_x, and destroying p_z). The magnitude of the mixing depends directly on the extent of rotation and the amount of overlap it generates (that is on the field strength and the product of the coefficients of coupled AOs in the two MOs) and inversely on the energy gap between the MOs. The sign of the mixing and the sense of the orbital angular momentum depend on the sign of the energy gap (that is on whether mixing is with a lower-energy doubly occupied orbital or with a higher vacant one). The influence of the resulting orbital angular momentum on the electron spin through $\underline{L}\cdot\underline{S}$ depends on the strength of the spin-orbit coupling constant of those atoms whose p orbitals make a significant contribution to the mixing. The following expression for the effective g-value summarizes these effects:

$$g = 2.0023 - 2 \sum_n \sum_k \langle \psi_o \mid \zeta_k L_k \mid C_n \psi_n \rangle$$

where 2.0023 is the g value for the free electron; ψ_o is the singly occupied MO; ψ_n is another MO; ζ_k is the spin-orbit coupling constant of atom k; L_k is the orbital angular momentum operator which rotates the p orbitals of atom k about the applied field direction; and C_n is the amount of ψ_n mixed into ψ_o.

$$C_n = \langle \psi_n | L_k | \psi_o \rangle / (E_n - E_o).$$

The isotropic value of the shift in g from the free electron value shows the magnitude of spin-orbit-field coupling averaged over all field directions. It gives qualitative information about whether there is significant spin density on atoms of high spin-orbit coupling and whether there exist low-energy vacant or high-energy doubly occupied orbitals. The anisotropy of g shows what the extremes in spin-orbit-field coupling are and gives information about molecular symmetry. The orientation of the g tensor is especially valuable, since by showing the field directions which give strong and weak coupling it helps assign the ground state and low-lying excited states of the radical. Such an application is exemplified by benzoyloxy radical below.

For radicals in a triplet pair the observed g tensor is the average of the appropriately oriented tensors of the consitituent free radicals. Thus if the g tensor of one member of the pair is known, that of the other may be found by subtracting the known tensor from twice the observed tensor.

Electron-Electron Splitting. The fine structure splitting in a radical pair, unlike hfs and g, is not an average of values for the separate radicals. Since it arises from interaction of the radicals, it depends more on their separation than on their individual orientations. To first order the fs line separation is 3D:

$$3D = \langle (1-3\cos^2\theta)/r^3 \rangle \cdot 27{,}853 \text{ gauss } Å^3,$$

where r is the distance between electron spins and θ is the angle between the spin-spin vector and the applied field. (8) The average is taken over all pairs of sites between the two radicals and weighted according to the product of the spin densities of the sites. If only one site is important in each radical the "point dipole" approximation holds, and the largest splitting is observed when the field lies along the radical-radical vector so that the average in the 3D expression is $-2/r^3$. Spin delocalization in the radicals will affect 3D in obvious ways, and contributions from pairs of sites with opposite spin density may partially cancel contributions from pairs with the same sign. The

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

point-dipole approximation overestimates the "average" spin-spin distance when the spins are delocalized in directions perpendicular to their average separation. If the spin distribution and orientation of the radicals is known, 3D is readily calculable for any field direction and interradical vector.

Since $(1-3\cos^2\theta)$ averages to zero over a spherically symmetric set of spin-spin vectors within a species, D has no isotropic value and is unobservable by epr for a rapidly tumbling sample. The anisotropy of D tells by how much the relative spin distribution departs from spherical symmetry. If a spherical distribution is distorted by stretching along one direction and compressing along the others to preserve the average spin-spin separation, the splitting measured with the field in the stretching direction becomes negative (the average $\cos^2\theta$ increases). Splittings measured with fields in the plane perpendicular to the stretching become positive but, of course, remain equal to one another. If the cylindrical symmetry is broken by additional stretching along some direction in the plane, 3D in that direction becomes less positive. The magnitude of the anisotropy of D (the familiar "D" and "E" values) depends on the symmetry and interradical distance of the pair, while the orientation of the tensor assigns directions to the distortions.

The fs of radicals separated by 6 to 10 Å is less sensitive than hfs to details of their individual internal spin distributions and, unlike g, is insensitive to the energy gaps between ground states and various excited states. Given a reasonably accurate model for the spin distributions and orientations of two radicals, the fs gives precise information about the interradical vector. For example the pair of triptycyl radicals mentioned above has an axially symmetric fs with a maximum (negative) splitting of 319 G. For point dipoles this would correspond to a separation of 5.58 Å. The splittings measured with an accuracy of 2.5 G fix the length of this vector within 0.02 Å and its direction within 1°. The direction of maximum splitting lies within 5° of the symmetry axis of the C-13 hfs, so the interaction should be calculated for electrons in antiparallel sp^9 hybrid orbitals rather than for point dipoles centered on the nuclei. Using Slater orbitals we calculate a larger separation of 6.22 Å between the bridgehead nuclei. So the fs provides highly precise geometrical information, but to interpret it properly we must know the spin distribution within the radicals.

Σ or Π ? The Benzoyloxy Dilemma

Benzoyloxy is one radical for which the spin distribution is questionable. Despite its chemical importance neither the electronic ground state nor the equilibrium geometry is certain. Various semi-empirical and *ab initio* SCF-MO methods, with and

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

without spin and spacial restrictions, have been used to study acyloxy radicals. (9,10) They agree that most of the spin density (in all cases greater than 75%) resides on oxygen, but how is it distributed between the oxygens? If the radical is symmetrical (C_{2v}), the oxygens should of course share the spin density equally. If, however, the radical possesses only a plane of symmetry (C_s), as would a carboxylic acid with the hydroxyl hydrogen removed, the spin would be unevenly distributed. Figure 1 illustrates the question by showing the form of the molecular orbitals which are singly occupied in various states of the formyloxy radical. (3) For the C_{2v} geometry the candidates are a π orbital (a_2, the out-of-phase combination of the oxygen p π orbitals), and two σ orbitals (a_1, the in-phase, and b_2, the out-of-phase combinations of in-plane oxygen p orbitals). For the C_s geometry the π possibility is a", a distorted version of a_2, and the σ possibility is a', a distorted sum of a_1 and b_2. In either geometry the orbitals which are not singly occupied are filled.

Since distortion from C_{2v} to C_s mixes a_1 with b_2, it is not surprising that all molecular orbital calculations have predicted that the lowest-energy Σ radical is the $^2A'$ state. (9,10) The energy of the Π radical is less sensitive to distortion, and SCF-MO methods differ in assigning its equilibrium geometry. Newton has found that even with an STO 4-31G basis set, the C_{2v} formyloxy radical shows doublet instability, meaning that the calculated energy is minimized by an unsymmetrical electron distribution. (10) This is physically unreasonable and is but one of many symptoms of the inadequacy of single-determinant methods as applied to this system. The 5-15 kcal/mole differences they predict among the lowest states and geometries vary in sign as well as magnitude and are certainly untrustworthy. At least until CI calculations become available, (10) we can depend on theory only to give us the form of the orbitals in the various states. Only experimental data would allow a confident choice between a Σ state with most of the spin on one oxygen and a Π state with equal spin on both.

To understand such chemical properties of the benzoyloxy radical as the rates of decarboxylation and of oxygen scrambling one should know its electronic structure. We had hoped by studying the epr spectra of pairs including this radical to determine its ground state experimentally.

Acetyl Benzoyl Peroxide

Methyl Motion and the D Tensor. Photolysis of crystalline acetyl benzoyl peroxide with O-18 in the peroxy positions gives methyl benzoate with most of the O-18 bound to methyl rather than scrambled between the carbonyl and ether positions. (11) In attempting to understand this discrimination we studied the epr spectrum of the methyl-benzoyloxy radical pair (M-B) trapped in a photolyzed crystal of the peroxide at low temperature. (3)

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

The first row of Table I expresses in several ways the two items of non-orientational information from the electron-electron fs of M-B. The first two entries, Z and X, are the extreme values of splitting (in gauss) and correspond to the maximum and minimum components, respectively, of the average spin-spin distance. The third entry, Y, is the splitting in the third orthogonal direction, and its difference from X shows by how much the distribution departs from axial symmetry. The next two entries express this same information in wave numbers as the D and E parameters. The last entry is the separation (in Å) between point dipoles which would give the same Z. As discussed above this provides an upper limit to the distance between delocalized spins.

Table I. Electron-Electron Splittings of Radical Pairs.

Pair	Z	X	Y	D	E	Dist.
M-B	-375	199	176	0.0175	0.0003	5.30
M-P	-259	135	125	0.0121	0.0001	5.99
P-B	-329	173	156	0.0154	0.0003	5.53
P-P	-197	98	92	0.0092	0.0001	6.56
B-B	-1256	943	313	0.0587	0.0098	3.54
B-B'	-1320	1024	296	0.0617	0.0113	3.48

More of the fs information is presented in Figure 2D, where a heavy arrow indicating the direction of maximum spin separation (Z) is shown relative to the framework of the peroxide precursor in two orthogonal projections. The length of this arrow is 5.30 Å, corresponding to the point dipole limit for the observed splitting. The forked line indicates the direction of minimum spin-spin separation (X). Since the site of spin in methyl is obvious, we could use the arrow to locate the radical relative to benzoyloxy, if we knew the spin distribution and orientation of the latter.

On the assumption that benzoyloxy is C_{2v} and that it is immobile in the crystal, we suggested earlier that the methyl radical moves from its position in starting peroxide by 2.4 Å. The motion can be visualized approximately in Figure 2 by translating the heavy arrow so that its origin is centered between the oxygens of benzoyloxy. Benzoyloxy delocalization would shorten the point dipole arrow by about 0.1 Å.

While this motion seems to explain the preference for methyl attack at the original peroxidic oxygen, it is surprising in light of the fs of the methyl-phenyl radical pair (M-P), which can be generated from M-B by photolysis at 800 nm. This fs is summarized in the second entry of Table I, and the point dipole vector it predicts is illustrated by the light arrow in Figure 2D. The origin of this arrow is more certain than that of M-B, since the

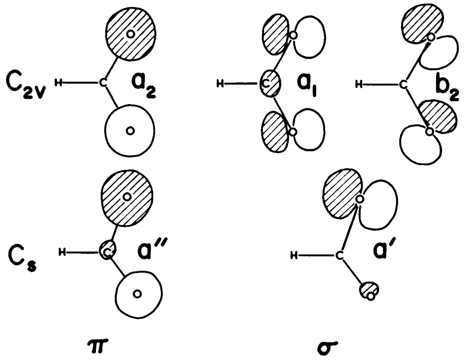

Figure 1. Orbitals that might be singly occupied, low energy states of an acyloxy radical in the C_{2v} and C_s geometries. The plane of the drawing is the nodal plane of the π orbitals. The most likely candidates for single occupancy in the ground state are a_2 (π) and a′ (σ).

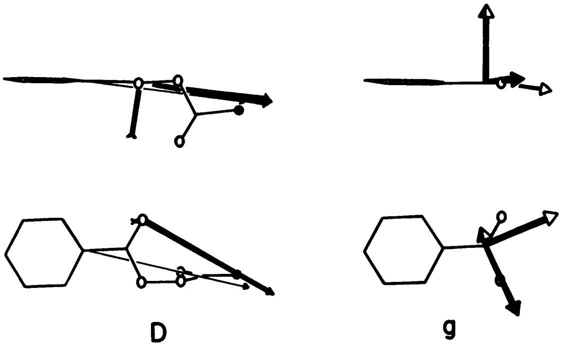

Figure 2. M–B and M–P tensors relative to acetyl benzoyl peroxide.

*The two orthogonal projections (above and below) show the orientation of the D tensors of M–B and M–P (left) and of the g tensor of benzoyloxy (right). D. Open circles denote oxygen atoms; a filled circle, the methyl group. The heavy line with a forked tail shows the direction of minimum spin–spin separation of M–B. The heavy arrow represents the point dipole approximation to the spin–spin vector of M–B in length and direction. The light arrow presents the same information for M–P. g. The principal directions for the g shift of benzoyloxy are denoted by heavy vectors 2-Å long. The filled and open triangles denote the most and least positive g shifts, respectively (*see *Table II).*

phenyl radical is mostly localized. (13) The arrow's head falls very near the original methyl position. If methyl moves by 2.4 Å in forming M-B, it must move back again when benzoyloxy decarboxylates. This coincidence is conceivable, but suspicious.

The geometry of M-P would have been less surprising if we had assigned benzoyloxy a C_s Σ electronic state with most of its spin density on the oxygen which was originally carbonyl. The origin of the heavy arrow would then have been as shown in Figure 2D, and methyl would undergo only modest displacements from peroxide to M-B to M-P. If the C_s Σ benzoyloxy radical had its spin on the oxygen which was originally peroxy, the arrow would originate on that oxygen, and the excursion of the methyl radical would be even lengthier than for the Π. If benzoyloxy radical had a Σ ground state, one might expect the two geometries to coexist and give a doubling of the peaks in the epr spectrum, which we have not observed. But the lattice forces which impose a 5-6 kcal/mole barrier on radical recombination could easily bias an equilibrium toward one of the Σ geometries.

If we wished to be parsimonious about the amount of methyl motion in the crystal, we would choose the Σ benzoyloxy radical with spin on the original carbonyl oxygen, although the direction of minimum spin-spin distance is more consistent with the Π than with this Σ radical.

The g Tensor of Benzoyloxy. By subtracting the isotropic g value of methyl radical from twice the g tensor of M-B, we determined an approximate g tensor for benzoyloxy. Shifts of its principal values from 2.0023 are presented in the first row of Table II. Since the shifts are positive, filled orbitals must predominate over vacant ones in mixing with the singly occupied orbital.

Table II. Benzoyloxy g Shifts.[a]

Partner	iso	X	Y	Z
$CH_3\cdot$	94	205	59	18
Ph•	99	221	61	15
$PhCO_2\cdot$	86 (89)	207 (239)	113 (83)	-64 (-58)
		212 (209)	37 (36)	9 (20)

a) g shift = (g - 2.0023) x 10^4, where g is calculated from twice the g tensor observed for the radical pair of benzoyloxy with a partner minus the g tensor of the partner. The parenthetical values in the $PhCO_2\cdot$ entries are for B-B', the others for B-B. The last two rows correspond to different tensor assignments, one of which is incorrect, as explained under The B-B Pairs in the text.

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How the g shifts help choose the ground state can be seen by examining Figure 1. The C_{2v} Π state ($^2A_2$) would be strongly mixed with $^2B_2$ by a field in the oxygen-oxygen direction, since the oxygen orbitals of a_2 rotated about that axis give high overlap with those of b_2 (they have the wrong phase to overlap with a_1). A field along the molecular symmetry axis would in principle mix a_1 with a_2, but in fact the shape of the a_1 orbital is such that very little overlap would result, and only a small g shift would be expected. A field perpendicular to the molecular plane would not mix the Π state with any other state, and would give no g shift. Thus a Π radical should display a large g shift along the O-O direction, a small g shift along the symmetry axis, and no g shift perpendicular to the nuclear plane.

The C_s Σ state ($^2A'$) would be strongly mixed with $^2A''$ by a field along the bond connecting the radical oxygen to the carboxyl carbon. A field perpendicular to the bond and in the nuclear plane would not mix the $^2A'$ state, since it would lie along the axis of the spin-bearing p orbital of oxygen. A field perpendicular to the plane would mix $^2A'$ with higher-energy Σ states. Thus the Σ radical would show a strong g shift along the C-O single bond, a weak shift perpendicular to the plane, and no shift in the third orthogonal direction.

The orientation of the g tensor shown in Figure 2g is just what would be expected for the $^2A'$ benzoyloxy radical with spin on the original peroxy oxygen. Kim, Kikuchi, and Wood have used this agreement to argue for a Σ benzoyloxy radical with spin on this oxygen. (14) Their interpretation may well be correct, but it is disturbing that this assignment is the one for which the D tensor requires maximum motion of the methyl radical. As we suggested earlier, the Σ radical with spin on the original carbonyl oxygen, which gives the least-motion interpretation of the D tensor, gives the worst agreement with the g tensor. (3)

Thus the D and g tensors give conflicting indications of the geometry of M-B and of the ground state for benzoyloxy. To decide on a radical pair geometry which will help us understand the solid state reaction we must resolve this conflict. Unfortunately the additional data we have been able to collect have served more to sharpen the conflict than to resolve it.

Dibenzoyl Peroxide.

The P-B Pair. Partly to assess the reliability of the experimental tensors for M-B, we determined D and g tensors for the analogous phenyl-benzoyloxy pair (P-B) in photolyzed dibenzoyl peroxide. This species, like M-P, was first reported by Lebedev. (15) We used perdeuterated crystals to remove phenyl hfs from the highly overlapped spectra of four symmetry-related versions of each radical pair (there would have been eight, each corresponding to loss of one of the CO_2 groups in the $P2_12_12_1$ unit cell, if it were not for an approximate, non-crystallographic two-fold symmetry axis, which almost converts a screw axis to a translation). Box has determined the D tensor for the phenyl-phenyl pair (P-P) in dibenzoyl peroxide. (16) Figure 3 presents our D and g tensors for P-B, and Box's D tensor for P-P in the same format as Figure 2. Comparison of Figures 2 and 3 and of the corresponding data in Tables I and II shows that the tensors of the pairs with methyl and phenyl as partner have almost the same magnitude and the same orientation in the molecular frame, although the crystalline environments are completely different. This increases our confidence in the experimental tensors. More importantly it requires that whatever motion methyl undergoes in acetyl benzoyl peroxide, phenyl must undergo in dibenzoyl peroxide.

Far from resolving our dilemma about the ground state of benzoyloxy radical, this additional information has made it more acute. If we favor the Σ radical with spin on the original peroxy oxygen, which in its initial orientation is consistent with the g tensor, the D tensor forces us to accept that in their different crystals M-B and P-B pairs undergo identical large (about 3 Å) displacements relative to the peroxide geometry, although the M-P and P-P pairs have geometries very similar to those in the peroxide. If we favor the Π radical, the g tensor is anomalous and no longer attributable to experimental error, and the methyl or phenyl excursion is still substantial. Again the Σ radical with spin on the original carbonyl carbon allows minimal radical motion but seems unlikely to have the observed g tensor.

The B-B Pairs. While measuring the spectra of P-B we noticed weak doublets with greater electron-electron splitting than P-B and no hfs, even in undeuterated samples. Their strong g anisotropy, resistance to saturation at low temperature, and rapid decay at 35 K (P-B can be observed at 63 K) confirmed our inference that they were due to benzoyloxy-benzoyloxy pairs (B-B). Box has mentioned observing B-B after subjecting a solid solution of dibenzoyl peroxide in dibenzoyl disulfide to ionizing radiation. His B-B recombined at "a few degrees above 4.2 K."(16) After brief photolysis at 20 K and cooling to 6 K we observed eight doublets rather that the four required by symmetry for a single species. Thus there are two different metastable arrangements of the B-B pair. One pair, which we denote B-B', converts rapidly to the other on warming to 25 K. We determined D and g tensors for both B-B' and B-B in hopes of answering two questions. What can these pairs tell us about the ground state of benzoyloxy? How can radical pairs be stable when they are not separated by an intervening molecule, such as CO_2 or N_2?

Since the crystalline unit cell contains four symmetry-related molecules, spectra of four B-B orientations are measured simultaneously in one crystal mounting. However this experimental efficiency comes at a high price, because there is no direct method for determining which of four symmetry-related tensors goes

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with a particular molecular orientation. The previous radical pairs were sufficiently separated that the point dipole approximation permitted a unique choice of the correct tensor. For B-B (and B-B') two of the four choices may be excluded as giving spin-spin extension in directions nearly orthogonal to reasonable ones. The remaining two possibilities are plotted in Figures 4 and 5 for B-B. Plots for B-B' analogous to Figures 4 and 5 would be practically indistinguishable from 4 and 5, except in the end-on view of 5, where the B-B' vectors are included and indicated by squares. In both figures we have started the spin-spin arrow from the carbonyl oxygen, which seemed to be the best origin for the M-B and the P-B pairs in terms of predicting minimal motion. As before the arrow should terminate near the center of spin density of the other radical in the pair, which in this case is also benzoyloxy. The g tensors of the second benzoyloxy in B-B and B-B' were calculated as before by subtracting the g tensor of the first (assumed equivalent to that found from the P-B pair) from twice the observed tensor. The next to last row of Table II corresponds to the tensor assignment of Figure 4, and the last row to that of Figure 5.

The arrow of Figure 4D suggests that the spin density in the second benzoyloxy radical, as in the first, resides mostly near the original carbonyl oxygen. It does require some motion of this atom, which could be achieved by twisting the carboxy group about the C-phenyl bond. The same sense of rotation is suggested by the orientation of the g tensor for this radical. The magnitudes of the principal g shifts (Table II) are similar to those of the previous benzoyloxy radicals, but differ from them by much more than they differ from one another. If this is the correct tensor assignment, the stability of the B-B pair could perhaps be attributed to the twist, which separates the peroxy oxygens enough that their bonded attraction cannot overcome a lattice barrier to the twist back. The attraction may be particularly weak if most of the spin resides on the original carbonyl oxygens. B-B and B-B' are remarkably similar, differing by less than 0.4 Å in point dipole vectors and 6° in g orientation. The source of a barrier between two such similar geometries is not obvious. As for the M-B and P-B pairs, the D and g tensors suggest spin localization on different oxygens.

The tensor assignment of Figure 5 suggests that the average spin position of the second benzoyloxy radical is very near the carbonyl carbon, as would be expected for a C_{2v} radical. Furthermore the g shifts for this radical in B-B are precisely those that would be predicted for an almost unmoved Π state, both in magnitude and in orientation. The g orientation of the corresponding radical in B-B' differs from this by rotation of 11° about the C-phenyl bond, as shown in the end-on view of Figure 5. It is remarkable that the principal values of these g tensors are so similar to those of the other radical, if that radical is in a Σ state. If this assignment is correct, the barrier to recombi-

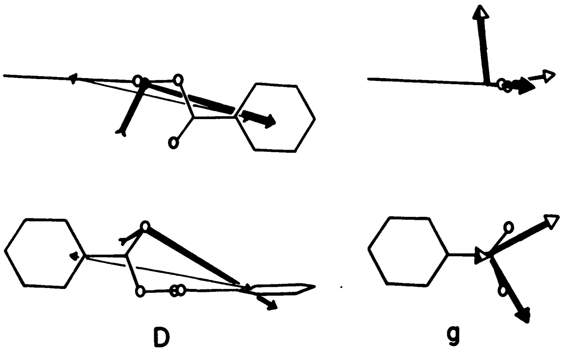

Figure 3. P–B and P–P tensors relative to dibenzoyl peroxide. Presentation analogous to that of Figure 2, except that the double-headed arrow representing the spin–spin vector of P–P is centered between the substituted ring carbons of the peroxide.

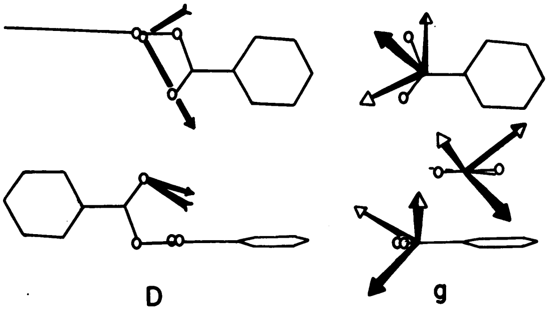

Figure 4. B–B tensors relative to dibenzoyl peroxide. Tensor assignment of the next-to-last row in Table II. Presentation analogous to Figure 2, except that the middle diagram in the g column is an end-on view obtained by rotating the lower diagram by 90° to the right about a vertical axis in the page.

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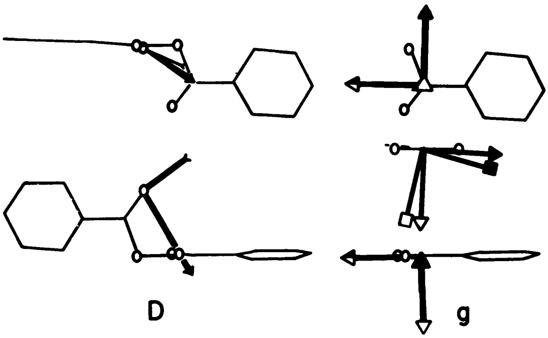

Figure 5. B–B tensors relative to dibenzoyl peroxide. Tensor assignment of the last row in Table II. Presentation analogous to Figure 4, except that the end-on view includes the g tensor of B–B′ denoted by squares instead of triangles.

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nation of the radicals may be due to a failure of a Σ-Π radical pair state to correlate with the ground state of peroxide.

Summary and Conclusions

Although we have now measured D and g tensors for four different radical pairs containing the benzoyloxy radical, we cannot yet be certain of the radical's electronic state. If we consider only the g tensors, we would feel confident that the radical in the M-B and P-B pairs is in a Σ state with its spin on the oxygen which was originally peroxidic. However, the D tensors would then indicate that the other radical, methyl or phenyl, must undergo surprisingly large (and similar) motion after the first decarboxylation but return to its initial location after the second.

If we considered only the D tensors of these pairs, we would conclude that the benzoyloxy is in a Σ state with spin on the original carbonyl oxygen, and that very little radical motion occurs during the decarboxylations. The g tensors do not seem consistent with this interpretation.

An unmoved Π benzoyloxy radical would not give such flagrant disagreement with one of the tensors as one or the other of the Σ radicals does. Neither would it give such good agreement with the other tensor.

We could cease trying to understand the nature of the benzoyloxy radical in M-B and P-B and assume only that its spin is near the original site of the carbonyl oxygen and that it has the observed g tensor. This might result from some unanticipated motion or distortion of the radical. If we then risk supposing that one of the benzoyloxy radicals of B-B has these same properties, we may determine the g tensor and spin location of the other. The same is true of B-B'. In either instance one of two plausible interpretations is incorrect. Either 1) the second radical has the same anomalous properties as the first and has its carboxyl group twisted about the C-phenyl bond, or 2) the second radical is in a Π electronic state and is essentially unmoved in B-B but twisted by 11° about the C-phenyl bond in B-B'.

Obviously we must do much more work before claiming that we understand acyloxy radicals and their behavior in solids. Still the work described above shows that single-crystal epr spectroscopy of radical pairs can provide unique, if not always unambiguous, information about the structure and chemistry of free radicals.

Acknowledgments

This work has been supported by the National Science Foundation (DMR 76-01996) and by a Camille and Henry Dreyfus Teacher-Scholar Grant. We thank Dr. Marshall D. Newton and Professor D. E. Wood for helpful discussions of their unpublished work.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch012

Abstract

Low-temperature epr spectra yield A, g, and D tensors for radical pairs generated by uv photolysis of single crystals of diacyl peroxides. The precise, but sometimes ambiguous, information these tensors contain about the structure of the radicals and about their arrangement in pairs is discussed with examples. Pairs including a benzoyloxy radical together with methyl, phenyl, or another benzoyloxy radical are perplexing in that D tensors seem to indicate that electron spin resides mostly on the original carbonyl oxygen, while g tensors seem to indicate that most of the spin resides on the original peroxy oxygen. The radicals in the benzoyloxy-benzoyloxy pair may be in different electronic states.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch013

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Molecular Orbital Correlations of Some Simple Radical Reactions

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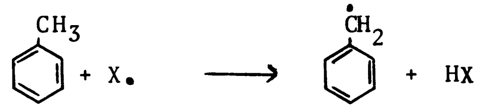
The application of relatively simple molecular orbital theory to problems involving the formation and reactivity of organic radicals has lagged behind related studies on charged trigonal species. This is somewhat surprising for although radical forming reactions are often judged by the uninitiated to be much less sensitive to structural changes, post hoc evidence indicates that a judicious choice of system can obviate such problems. There also exists a compensating factor in that the uncharged radical system may be simpler to treat theoretically than its charged counterparts due to the absence of a pronounced electric field (1). A too sanguine overview, however, can be adopted. Through the early sixties surprisingly few investigations were planned to make use of potential molecular orbital calculations. Even more disturbing was the observation that in certain studies where such correlations were attempted, overall agreement was unsatisfactory.

The best of the early experimental work is a series of investigations involving radical aromatic substitution by alkyl radicals studied by Szwarc and co-workers (2-6). This and still earlier work by Kooyman and Farenhorst with the trichloromethyl radical (7) have allowed for systematic variation in the steric and electronic properties of the attacking species. Experiments indicate that there is rather little variation in relative rate trends as a function of attacking radical. Theoretically, it can also be pointed out that there is little difference among correlations utilizing parameters determined from ground state calculations and those utilizing calculated energy differences (see below).

A second type of investigation can be typified by the work of Kooyman in the generation of arylmethyl and similarly delocalized radicals and the attempted correlation with calculated molecular orbital parameters (8). Studies of this type represent but part of the overall subject of arylmethyl reactivity which includes not only radical generating hydrogen abstraction processes, Equation 1, but also the corresponding carbonium ion and

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch013

carbanion reactions, Equations 2 and 3.



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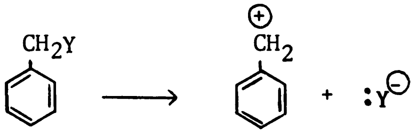

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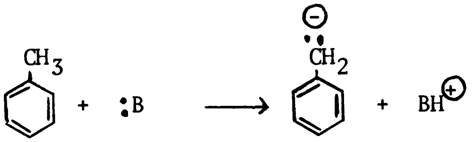

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Kooyman's investigation utilized the relative rates of hydrogen abstraction from a series of aralkyl compounds (and one olefin) by the trichloromethyl radical (8). The experimental results are shown in Table I.

Table I. Relative rates of Hydrogen Abstraction from Selected Hydrocarbons by the Trichloromethyl Radical.

Hydrocarbon	Relative Rate
Toluene	1.0
Diphenylmethane	7.98
2-Octene	11.67
Triphenylmethane	17.90
3-Phenylpropene	28.57
Indene	111.9

A linear correlation between logs of the relative rate constants and calculated HMO pi energy differences between the delocalized product radical (assumed equivalent to the transition state) and the initial unsaturated compound was attempted. The results were quite poor. A correlation coefficient of only 0.47 was obtained. (A formalism strongly analogous to the Hammett equation will be employed throughout the discussion. The slopes of the correlations, unlike rho values, have little recognized physical meaning and are not even comparable if energy differences are calculated by different methods. The numerical values of these slopes well therefore be ignored. However, correlation coefficients shall be given and considered as a measure of the reliability of the calculation employed. All such coefficients are obtained from linear least squares analyses of the correlations.)

Although this poor correlation may be attributable in part to utilization of the overly simple HMO approach and to experimental problems in evaluation of rate constants, there also exist underlying difficulties concerning the choice of systems. Benzylic radicals derived from diphenylmethane, triphenylmethane and 3-phenylpropene cannot achieve complete planarity and arguments based on delocalization in planar systems cannot be safely applied. As shall be seen most subsequent workers in the field of benzylic reactivity have opted to study series of compounds of overall greater similarity than those utilized by Kooyman.

Benzylic Reactivity and Molecular Orbital Correlations.

The formation of unsubstituted polycyclic benzylic carbonium ions has been studied for over twenty years (9, 10). While much of the earlier work was apparently planned with application of Hückel molecular orbital theory in mind, the problem continues to attract workers and more recent publications have combined experimentally more precise results with advanced theoretical techniques (11).

The corresponding carbanions have also been generated utilizing the reaction of polycyclic arylmethanes with strong bases (12, 13). Initial theoretical calculations were again with HMO theory.

Irrespective of the complexity of the molecular orbital approach employed, it is possible to attempt correlations using some calculated energy difference, e.g. Kooyman's results (8), or some parameter derived from the isolated aromatic starting material. While the latter approach has worked well in correlating the results of electrophilic and radical aromatic substitution (14), it has been less frequently applied to the generation of charged benzylic species. Mechanistically this neglect is reasonable. The transition states for generation of the benzylic ions must show a strong resemblance to the charged intermediate. Any approach which ignores this will probably be incorrect. The utilization of energy differences should also be applicable to relatively endergonic radical forming reactions as well (15).

The HMO correlations of relative rates of formation of the polycyclic benzylic ions lead to some interesting conclusions. Compounds of an α-naphthyl type (i.e. those having the exo-cyclic methylene unit attached to a carbon adjacent to a point of annelation) always show a reactivity less than that expected based on compounds of the β-naphthyl type. A tendency to treat data in terms of dual correlations has been thus developed. The infrequent inclusion of nonalternant (i.e. non-benzenoid) systems would usually generate data which could not be accommodated by either the α-naphthyl or β-naphthyl correlations. These findings for the generation of arylmethyl anions (12, 13) are illustrated in Figure 1. A single HMO correlation including data from both α-naphthyl and β-naphthyl type systems yields a correlation

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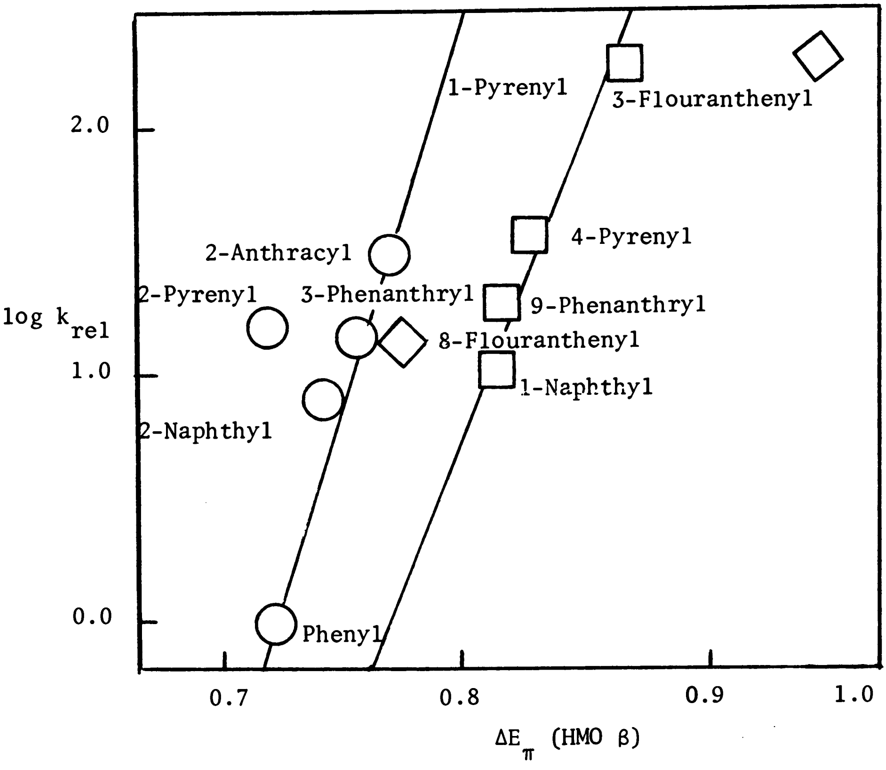

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Figure 1. Correlation of the relative rates of formation of arylmethyl anions with calculated HMO energy differences: (○), β-naphthyl compounds; (□), α-napthyl compounds; (◇), non-alternant compounds.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch013

coefficient of only 0.82. If a dual correlation is employed correlation coefficients of 0.97 (α-naphthyl) and 0.99 (β-naphthyl, excluding one point) are found. Inclusion of the data from non-alternant systems, as pointed out, decreases the reliability.

In order to explain this duality, recourse was made to special steric factors operative in the α-naphthyl series which could increase the energy difference between ground and transition states. This peri effect is a specific result of non-bonded interaction between the methylene unit and the atom or group on the "other side" of the point of annelation as is shown for the α-naphthylmethyl carbanion in Figure 2A. A rotation of ninety degrees around the exocyclic carbon-carbon bond shown in Figure 2B can remove this unfavorable interaction but only with complete loss of conjugation between the exocyclic carbon and the remainder of the system. A semi-quantitative estimate of these interactions may be gleaned if recourse is made to models of the systems and standard values for hydrogen-hydrogen and carbon-hydrogen repulsion terms (16). Initially models were constructed using an average aromatic carbon-carbon bond length of 1.40 Å and a carbon-hydrogen bond length of 1.085 Å. The pertinent internuclear distances and repulsive interactions giving rise to the peri effect are shown in Figure 2. It is assumed that some practical compromise is reached with the resulting lessened delocalization causing a decreased reactivity. In the above carbanion case, for example, a rotation of seventeen degrees from planarity is estimated (13).

It is possible, however, that intuitively attractive as the peri effect is, there is no need to invoke it for simple, unsubstituted, polycyclic arylmethyl intermediates. The complete neglect of electron repulsion which underlies HMO calculations cannot be justified. While this approach can yield reasonable results for alternant hydrocarbons because of the uniform electron distribution, there is less reason to believe that it will be satisfactory for odd-alternant ions (17) as, in fact, is observed above. Dewar and Thompson (18) have applied the results of SCF calculations to the problem of carbanion formation. These workers were able to incorporate α-naphthyl, β-naphthyl and non-alternant derivatives into a single relationship with a correlation coefficient of 0.97. This is shown in Figure 3. The SCF approach can also make use of a bond order-bond length relationship to determine two center resonance and repulsions integrals (19). It is thus possible to arrive at consistent molecular structures as well as energies. Such structures for α-naphthyl species also tend to predict a slightly decreased importance for the peri interaction, relative to that obtained from the usual HMO approximation. This is due to greater calculated internuclear separations being obtained for those atoms causing the repulsive peri effect.

Although it is clear that some of the discrepancy between

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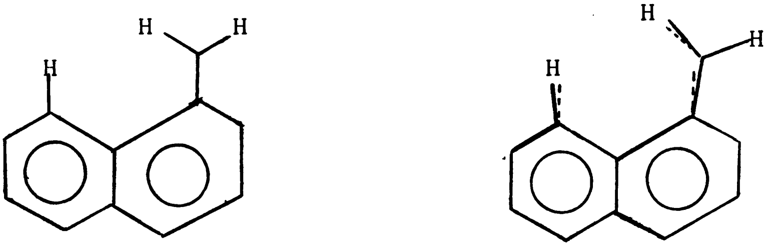
A) Planar, standard bond lengths

C---H	2.44 Å
H---H	1.71 Å
E_{C--H}	0.725 kcal/mole
E_{H--H}	4.175 kcal/mole
strain	4.900 kcal/mole

B) As A, CH_2 rotated 90°

C---H	2.44 Å
H---H	2.74 Å (2)
E_{C--H}	0.725 kcal/mole
E_{H--H}	0.050 kcal/mole
strain	0.725 kcal/mole



C) Planar, SCF bond lengths

C---H	2.49 Å
H---H	1.76 Å
E_{C--H}	0.529 kcal/mole
E_{H--H}	3.520 kcal/mole
strain	4.049 kcal/mole

D) As C, 3° in-plane bends

C---H	2.62 Å
H---H	1.97 Å
E_{C--H}	0.261 kcal/mole
E_{H--H}	1.484 kcal/mole
strain	1.745 kcal/mole
angle strain	0.544 kcal/mole
total strain	2.289 kcal/mole

Figure 2. Various geometries of the α-naphthylmethyl system with accompanying peri interactions and calculated strains

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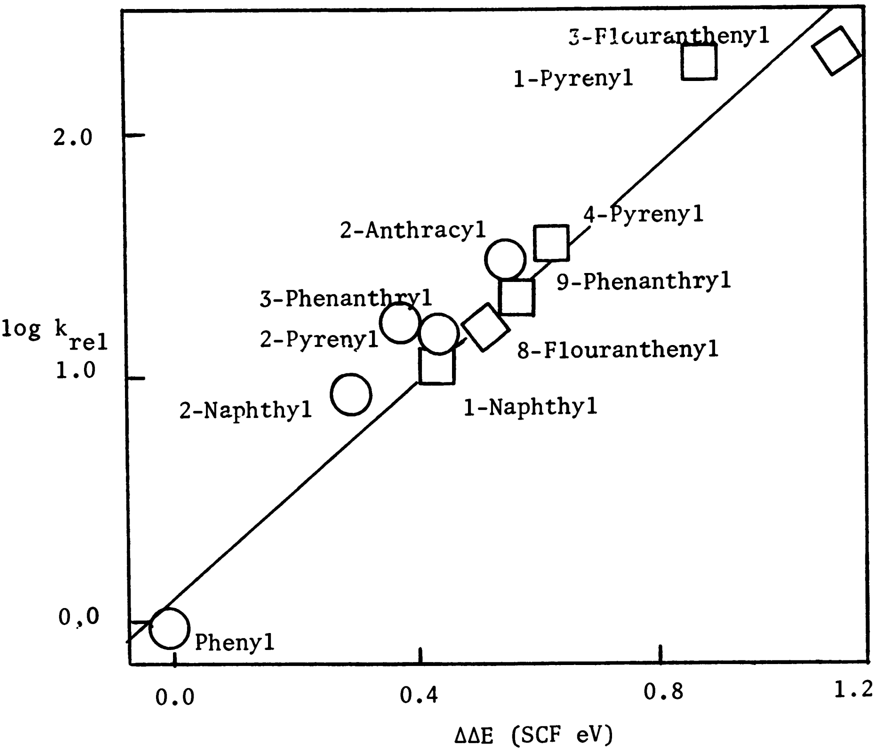

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Figure 3. Correlation of the relative rates of formation of arylmethyl anions with calculated SCF energy differences

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α-naphthyl and β-naphthyl type systems hitherto assigned to peri effects is not steric but rather electronic in origin, such an effect might still be important in arylmethyl reactivity. A quantitative evaluation of the peri effect has been undertaken (20). Based upon bond lengths determined from SCF calculations, it is shown in Figure 2C that the non-bonded interactions involving the exo-cyclic atoms were smaller than thought. These interactions could be further diminished by slight (three degree) in-plane deformations without any loss of delocalization. This is shown in Figure 2D. Out of plane bending of hydrogen atoms may further reduce peri interactions. Inclusion of atoms or groups larger than hydrogen within the potential peri interaction tions, however, may well necessitate a rotation from co-planarity of the exo-cyclic group.

Formation of Arylmethyl Radicals by Hydrogen Abstraction.

Unlike the corresponding ions, benzylic radicals are true alternant hydrocarbon species. It was deemed of interest to see whether rates of formation of such species could be related to changes in delocalization and also whether a similar dichotomy of results between HMO and SCF correlations would be observed. To examine these questions a series of arylmethanes was reacted with bromotrichloromethane at 70° (21, 22). The reactions were initiated with trace amounts of benzoyl peroxide, Equation 4.

$$ArCH_3 + BrCCl_3 \xrightarrow{\text{peroxide}} ArCH_2Br + HCCl_3 \qquad 4$$

Although subsequent research in other laboratories have led to claims that bromine atom is the chain carrying species in hydrogen abstractions utilizing bromotrichloromethane (28), our original presentation of results was based on the rate determining step shown in Equation 5.

$$ArCH_3 + {}^{\bullet}CCl_3 \longrightarrow ArCH_2^{\bullet} + HCCl_3 \qquad 5$$

The relatively endothermic nature of this process should allow for utilization of of a calculated energy difference as a structural parameter with which to correlate reaction rates.

This particular reaction is not free from complications. The trichloromethyl radical is known to attack the rings of polycyclic aromatics (7). In order to correct for this, it was assumed that any enhanced reactivity of the methylarene relative to the parent arene reflected only hydrogen abstractions. A competition between these two species can thus be used to determine (allowing for statistical correction) the amounts of hydrogen abstraction and ring substitution for each arylmethane. Such an approach presumes that the methyl substituent does not electronically influence attack in the aromatic unit. At the time, however, both experimental (24) and theoretical (25) results seemed to justify this view for the trichloromethyl radical.

Table II presents the originally obtained percent of reaction at the methyl group and corrected relative rates of hydrogen abstraction. Also shown are the calculated relative energy differences between the arylmethyl radical and the initial arene. It can be seen that a large range of experimental reactivities, nearly three powers of ten, is encountered.

Table II. Relative Rates of Hydrogen Abstraction from a Series of Unsubstituted Arylmethanes by Trichloromethyl Radical at 70°.

Arylmethane	% methyl Hydrogen abstraction	(k_X/k_0) H abstr	ΔΔE (SCF)
Toluene	100	0.172 ± 0.008	(0.000)
1-Methyltriphenylene	84.6	0.362 ± 0.027	0.076
2-Methyltriphenylene	69.1	0.395 ± 0.014	0.068
3-Methylphenanthrene	86.9	0.547 ± 0.027	0.060
1-Methylphenanthrene	69.5	0.569 ± 0.035	0.139
2-Methylnaphthalene	68.4	0.682 ± 0.057	0.076
9-Methylphenanthrene	91.0	0.845 ± 0.056	0.178
1-Methylnaphthalene	94.3	(1.00)	0.175
6-Methylchrysene	77.0	2.19 ± 0.04	0.214
2-Methylanthracene	74.5	5.89 ± 0.47	0.215
1-Methylanthracene	54.3	13.1 ± 1.4	0.340
1-Methylpyrene	76.5	18.7 ± 1.0	0.352
9-Methylanthracene	86.4	112.0 ± 5.0	0.519

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Although the arylmethyl radicals are alternant hydrocarbons, the Hückel method again proved inadequate in correlating the data. The compounds fell into the usual two sets. While the separate correlation coefficients of 0.948 for the α-naphthyl points and 0.904 for the β-naphthyl points were good and fair, the overall correlation coefficient of 0.86 was unacceptable. The single SCF correlation is shown in Figure 4. The overall correlation coefficient is now 0.977. Some slight improvement can still be made if a dual correlation is utilized with the two new correlation coefficients now being greater than 0.99. Perhaps this does reflect a small peri effect.

Why does the Hückel method still fail in treating arylmethyl reactivity even in neutral systems? This must be attributable to the neglect of electronic interaction terms in general and specifically neglect of spin polarization. The latter is particularly important in odd electron systems and is due to differential interactions between electron pairs of the same and opposite spin. Hückel calculations cannot account for fine

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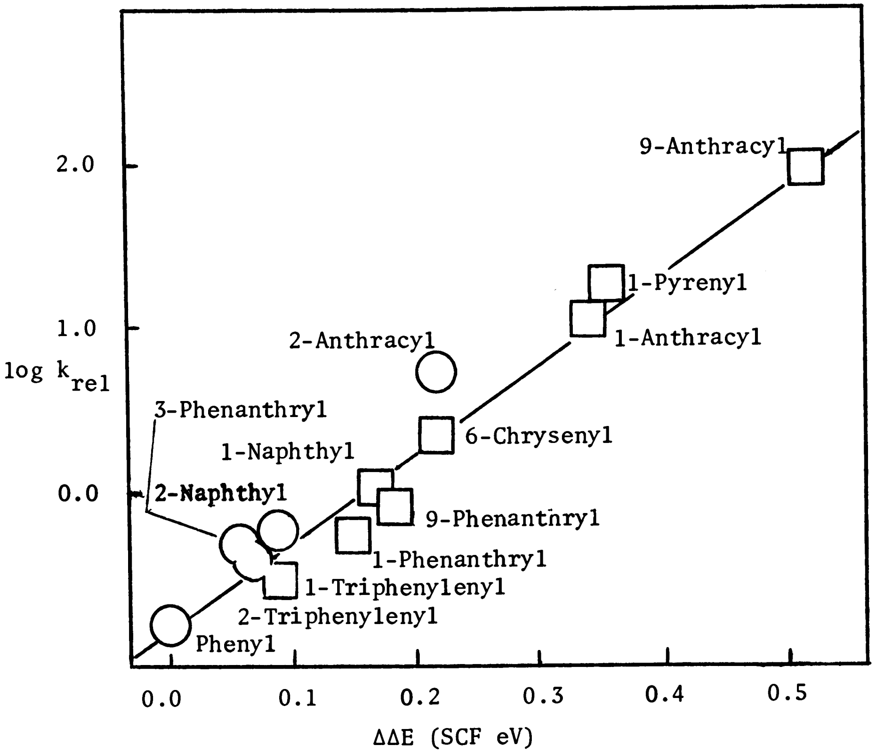

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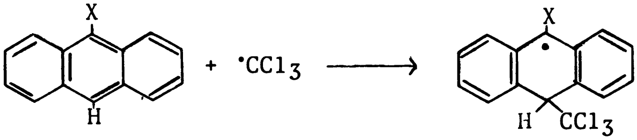
Figure 4. Correlation of the relative rates of hydrogen abstraction from polycyclic arylmethanes by the trichloromethyl radical with calculated SCF energy differences

structure in the esr spectra of allyl and benzyl radicals caused by spin polarization while SCF calculations can (26).

Although it was felt that a correlation with a calculated energy difference was in keeping with the view that a large degree of carbon-hydrogen bond breaking occurs in hydrogen abstraction by trichloromethyl radical, correlation with several ground state parameters (14) was also undertaken. In all cases the resulting correlations were much poorer than that discussed above. The use of negative evidence is suspect of course. However, it is felt that these results give some support to the view that a late transition state is encountered in this process. (22)

It was at this point that concern over one of the initial assumptions developed. The problem that a methylarene might undergo ring substitution at a significantly different rate than the parent system, could not be ignored. This question seemed to be particularly important for 9-methylanthracene. This compound should not only be most susceptible to ring substitution, but, because of its high reactivity in the hydrogen abstraction reaction, can disproportionately influence that overall correlation. In order to evaluate the importance of this possible effect the trichloromethylation of a series of 9-substituted anthracenes was studied in accord with Equation 6.



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The meso position(s) of anthracenes is known to be most prone to reaction and has been shown to account for about ninety percent of radical substitution (27).

The results are given in Table III. As can be seen there is a substituent effect with electron donating groups favoring, as might be expected, the trichloromethylation of the ring (28). This data may be treated within a standard Hammett type correlation to produce a rho value of -0.83 (correlation coefficient of 0.970) when plotted against σ_ρ^+. The data for 9-methylanthracene, however, shows a significant upwards deviation from the correlation. This is indicative of an additional mode of disappearance for this compound which must be hydrogen abstraction from the methyl group. The total reactivity of 9-methylanthracene is due mostly (65%) to this latter process. The original amount of reaction at this site was believed to be 86% of the total reactivity of this compound. Most serendipitously, however, the original correlation for hydrogen abstraction from arylmethanes is only slightly changed. There is only a two percent decrease in the slope of the correlation and a change in the correlation coefficient from 0.977 to 0.973.

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Table III. Relative Reactivities of 9-Substituted Anthracenes toward Trichloromethyl Radical Addition at 70.0°.

Substituent	k_X/k_H
NO_2	0.71 ± 0.10
CN	0.34 ± 0.04
CO_2CH_3	0.74 ± 0.07
Br	1.00 ± 0.04
Cl	1.02 ± 0.04
H	1.00
C_6H_5	2.28 ± 0.43
$i\text{-}C_3H_7$	2.38 ± 0.30
C_2H_5	3.39 ± 0.44
CH_3	6.85 ± 0.89
OCH_3	5.52 ± 0.60

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It is of interest that 9-ethyl and 9-isopropylanthracene do not show the same large deviation from the correlation for ring substitution. The simplest conclusion is that exocyclic hydrogen abstraction is less likely here because of peri effects caused by replacing one or both of the methylene hydrogens by methyl groups.

Two other studies involving hydrogen abstraction from polycyclic arylmethanes have also been reported in the literature. Gilliom and coworkers have studied many of the same compounds discussed above in reaction with bromine atom (29). It was observed that methylanthracenes and methylpyrenes underwent exclusive ring reactions. The other compounds employed showed reactivities in this reaction which paralleled those observed in the trichloromethyl radical reaction. One must again conclude that appreciable radical character is again developed in the trasition state based upon the good correlation with SCF calculated energy differences. The reaction of the arylmethanes with t-butyl hypochlorite was also undertaken (22). It was hoped that the less selective t-butoxy radical might cause a reactivity trend which could be correlated with ground state properties. Although chlorine atom traps were employed, exclusive ring chlorination was observed for several of these molecules. The remaining systems showed marginal selectivity. All attempt at correlation with either calculated energy differences or ground state parameters were unsuccessful.

Formation of Arylmethyl Radicals by Addition.

In an attempt to determine whether ground state molecular orbital parameters could correlate a relatively exothermic radical reaction, attention was directed away from atom abstraction and toward an addition process. The addition of a thiyl radical to vinylarenes is shown in Equation 7 (30). No measurable attack by the thiyl radical in the polycyclic portion

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of the olefin takes place; thus making the reaction in theory a simple one to study. The results are presented in Table IV. The overall range of reactivities is much smaller than that

Table IV. Relative Reactivities of Vinylarenes toward Thiophenol at 70°.

Compound	k_X/K_{std}	ΔΔE (SCF)
Styrene	1	0
2-Vinylnaphthalene	2.8 ± 0.3	0.061
9-Vinylphenanthrene	2.0 ± 0.2	0.125
1-Vinylnaphthalene	4.0 ± 0.5	0.140
6-Vinylchrysene	3.8 ± 0.2	0.142
2-Vinylanthracene	5.9 ± 1.2	0.167
1-Vinylanthracene	6.5 ± 1.5	0.209
1-Vinylpyrene	11.5 ± 3.0	0.234
9-Vinylanthracene	1.8 ± 1.2	0.424

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found in the corresponding hydrogen abstraction study and is indicative of the expected more exothermic process. Failure was again encountered, however, in the attempted utilization of ground state properties to correlate the experimental data. The two most likely of such parameters, free valence on the terminal carbon and bond order of the exocyclic double bond, both yielded correlation coefficients of less than 0.5. A much better correlation could again be obtained with a calculated SCF energy difference. This is shown in Figure 5. The correlation coefficient, while only 0.932,is still fair. Improvement is noted if the data are separated into the traditional two sets. Correlation coefficients of 0.95 (α-naphthyl) and 0.97 (β-naphthyl) are now found. Peri interactions must be very real in these systems as the exocyclic portion of the supposed transition state is no longer a simple methylene group. Indeed, as can be seen, it is impossible to incorporate the results for 9-vinylanthracene within any of the above correlations as no planar conformation is possible for the intermediate radical without a particularly severe peri interaction. The remaining

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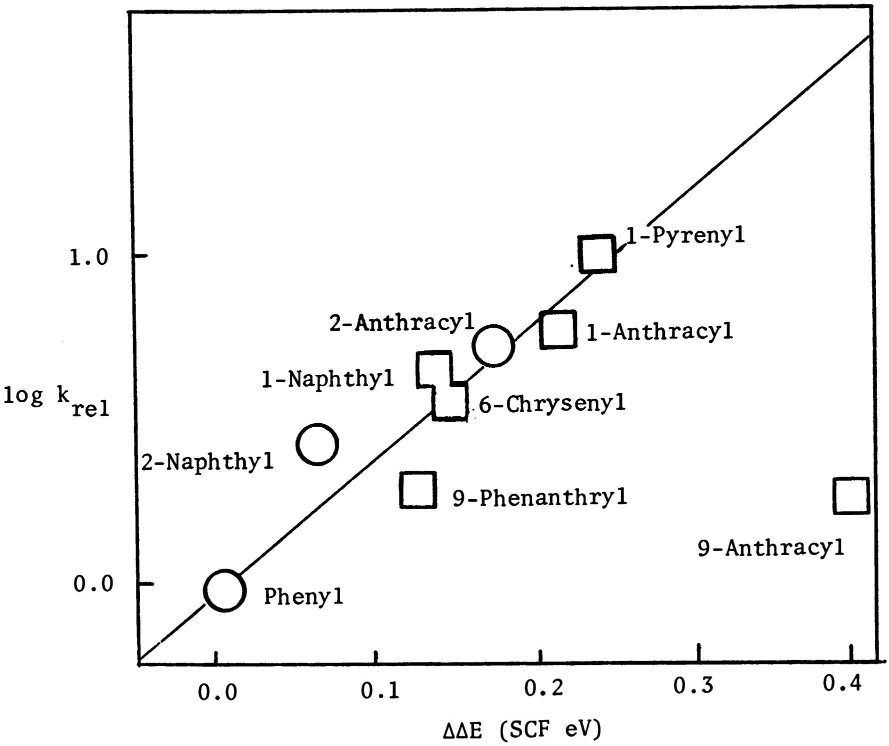

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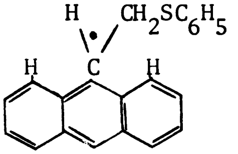
Figure 5. Correlation of the relative rates of thiyl radical addition to polycyclic vinylarenes with calculated SCF energy differences



α-naphthyl compounds may adopt a conformation with the bulky exocyclic group directed away from the peri hydrogen. Support for this view is obtained from a consideration of similar thiyl radical addition to a homologous series of isopropenylarenes as shown in Equation 8. (30). The data in Table V show all

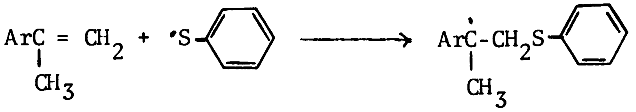


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Table V. Relative Reactivities of Isopropenyl Arenes toward Thiophenol at 70.0°.

Compound	k_X/k_{std}
α-Methylstyrene	1.0
2-Isopropenylnaphthalene	1.55 ± 0.12
1-Isopropenylnaphthalene	0.14 ± 0.01
9-Isopropenylphenanthrene	0.05 ± 0.002
9-Isopropenylanthracene	0.02 ± 0.005

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members of the α-naphthyl series to now possess greatly reduced reactivity attributable to steric effects as it is now impossible for all large groups on the exocyclic carbon to "point away from" the peri hydrogen.

Conclusions.

Certain distinct conclusions may be drawn from these studies. Firstly, as might have been expected, is the obvious fact that delocalization can have a tremendous effect on the ease of benzylic radical formation. The peri effects, invoked by earlier mechanicians, seem to be less important than claimed for non-substituted systems, but, may exert a large effect if substituents are attached to either the exocyclic atom or the peri site. (Although only rate retarding peri effects have been treated above, accelerative counterparts can be easily imagined.) Finally, from the theoretical point of view, all of the work on formation of benzylic like radicals cited enforce the view that calculations which do not include interelectron terms are inadequate and that ground state parameters cannot successfully

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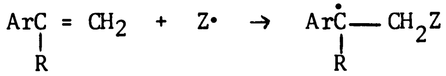
correlate the data.

Abstract

The correlation of the rates of formation of arylmethyl free-radicals by molecular orbital theory will be discussed. Different levels of sophistication among pi-electron methods lead to conflicting conclusions concerning the degree of possible electron localization and the importance of non-bonded interactions with the principal radical site. The arylmethyl radical systems have been generated both by hydrogen abstraction (1) and addition (2) reactions.

$$ArCH_3 + X\cdot \rightarrow ArCH_2\cdot + HX \qquad (1)$$



$$\underset{R}{ArC} = CH_2 + Z\cdot \rightarrow \underset{R}{Ar\dot{C}}-CH_2Z \qquad (2)$$

The sensitivity toward steric factors varies and is much more pronounced in the latter process.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch013

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Nucleophilic Reactions of Superoxide Anion Radical

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

Superoxide ion, $O_2^{\cdot -}$, is the anion radical derived by addition of an electron to molecular oxygen. It is one of the simplest anion radicals and, undoubtedly, the most important. This species is capable of reacting with a variety of substrates owing to its anionic, radical, and redox nature although the nuceophilic and reducing electron transfer processes appear to be the predominate reaction pathways. This report will attempt to review the important features of the nucleophilic behavior of $O_2^{\cdot -}$ with well-defined chemical reactants. No attempt will be made to cover the vast biochemical literature involving or implicating $O_2^{\cdot -}$.

Although $O_2^{\cdot -}$ is a stable anion radical, easily generated or even available commercially as the potassium salt, its chemical behavior has received significant attention only within the last several years. Chemical interest was spawned by the discovery of Fridovich and coworkers (1) that *superoxide dismutase*, an enzyme present in all aerobic organisms studied, has as its function the dismutation of $O_2^{\cdot -}$ into H_2O_2 and O_2 (equation 1). Since

$$2\ O_2^{\cdot -} + 2\ H^+ \longrightarrow H_2O_2 + O_2 \qquad (1)$$

superoxide dimutase is so common among respiring organisms, $O_2^{\cdot -}$ is thought to be a deleterious species whose cytotoxicity has promoted the evolution of such defenses. In fact, superoxide has been suggested to be involved in various biological disorders such as radiation damage to tissue, cancer, aging processes and oxygen toxicity; it may have beneficial effects in biological defense mechanisms.

Chemical studies have employed either electrogenerated $O_2^{\cdot -}$ or solutions or suspensions of KO_2. Dipolar aprotic solvents are usually used in either case as $O_2^{\cdot -}$ is quite sensitive to proton sources. The electrogenerated tetraalkylammonium superoxides are both soluble and stable in a variety of dipolar aprotic solvents (DMSO, DMF, CH_3CN, pyridine, acetone) (2). The

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

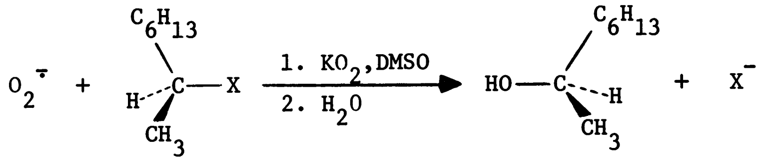
solubility of KO_2 in such solvents is not particularly high, e.g., the estimated concentration of saturated KO_2 in DMSO is only about 0.02 M (3). However, the use of crown ethers such as 18-crown-6 greatly enhances the solubility of KO_2 (4) and the commercial availability of both KO_2 and crown ethers has resulted in their rather common usage for chemical studies of $O_2^{\cdot-}$.

Superoxide ion exhibits spectral properties in the ultraviolet region. The λ_{max} for $O_2^{\cdot-}$ is 250 nm in acetonitrile with a reported extinction coefficient of 2580±300 $M^{-1}cm^{-1}$ (5). The reduction potential for oxygen in DMSO is −0.77 V versus SCE (2) and the pK_a for HOO·, the conjugate acid of $O_2^{\cdot-}$, has been determined to be 4.8 (6).

I. Reactions with Alkyl Halides and Sulfonate Esters

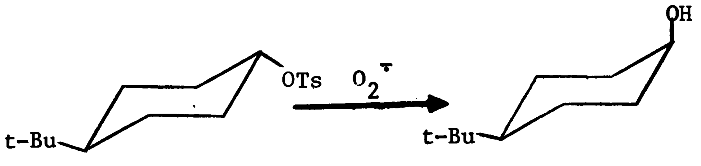
A. Mechanism. Alkyl halides undoubtedly represent the most well-tested functional group for nucleophilic reactivity. That superoxide ion reacts with alkyl haldies by an S_N2 mechanism has been demonstrated. Dietz, *et al.*, (7), observed a relative reactivity which fell in the series *n*-BuBr > *sec*-BuBr > *i*-BuBr > *t*-BuBr for variation of alkyl group structure and in the series *n*-BuBr > *n*-BuOTs > *n*-BuCl for variation of leaving group. The former order is consistent with a S_N2 reaction mechanism and the latter order suggests that superoxide anion radical is a strong nucleophile.

Results obtained by San Filippo and co-workers (8) paralleled those of Dietz concerning substrate reactivity but indicated further that substitution was predominant with primary halides, whereas substantial elimination occurred with secondary and tertiary systems. These workers, as well as Johnson and Nidy (9) reported the essentially complete inversion of configuration at the chiral center in the carbon-oxygen bond formation which is typical of a S_N2 Walden inversion mechanism (eq. 2).



(2)

In a similar manner, Corey, *et al.*, (10) have reported that the p-toluenesulfonate of *trans*-4-*t*-butylcyclohexanol was converted into pure *cis*-4-*t*-butylcyclohexanol in 95% yield (eq. 3) in DMSO-DME. Likewise, the *cis*-methanesulfonate was transformed into pure *trans*-4-*t*-butylcyclohexanol in 96% yield.



(3)

These workers (10,11) have also utilized $O_2^{\cdot-}$ to achieve an important synthetic objective in the prostaglandin field, namely the efficient conversion of 15-*R* (unnatural) prostaglandins into the 15-*S* (natural) isomers by nucleophilic displacement. These data all demonstrate the S_N2 inversion character of $O_2^{\cdot-}$ reacting with alkyl halides and sulfonate esters.

As noted by equation 2, the alcohol is the ultimate reaction product in DMSO solvent. However, there are several reactions that take place when $O_2^{\cdot-}$ is mixed with an alkyl halide. Equations 4-10 list the overall mechanism originally proposed by

$$RX + O_2^{\cdot-} \longrightarrow RO_2\cdot + X^- \quad (4)$$

$$RX + O_2^{\cdot-} \longrightarrow R(-H) + HO_2\cdot + X^- \quad (5)$$

$$HO_2\cdot \rightleftharpoons H^+ + O_2^{\cdot-} \quad (6)$$

$$HO_2\cdot + O_2^{\cdot-} \longrightarrow HO_2^- + O_2 \quad (7)$$

$$RO_2\cdot + O_2^{\cdot-} \longrightarrow RO_2^- + O_2 \quad (8)$$

$$RO_2^- + RX \longrightarrow RO_2R + X^- \quad (9)$$

$$RO_2^- + Me_2SO \longrightarrow RO^- + Me_2SO_2 \quad (10)$$

Dietz, et al., (7) which was subsequently expanded by Gibian and Ungermann (12). The course of the reaction is dependent upon both the alkyl halide structure and the reaction solvent. For a primary alkyl halide, the displacement of halide ion (eq. 4) is dominant over the elimination reaction (eq. 5) as determined by product analysis; e.g., for the reaction of KO_2 with 1-bromooctane and 2-bromooctane in DMSO, olefins were isolated in yields of 1% and 34%, respectively (8). It is apparent that secondary halides give significant olefin yields under these experimental conditions. The $HO_2\cdot$ formed in equation 5 may ionize to superoxide (eq. 6) or be reduced (eq. 7). The bulk reaction of the alkyl peroxy radical with $O_2^{\cdot-}$ (eq. 8) is the analogue to equation

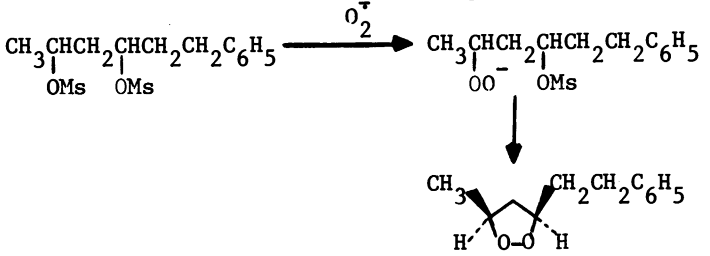
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

7 and is equally exothermic. Finally, the peroxy anion can undergo either reaction 9 or 10 to form products. The displacement reaction of RO_2^- with an alkyl halide is quite facile but equation 10 is favored by at least a factor of four when DMSO is the solvent (12).

Equation 9 can be made the principal reaction pathway and Johnson and Nidy (9) have reported a convenient and synthetically useful preparation of dialkyl peroxides using benzene as solvent and solubilizing the KO_2 with crown ethers. Alcohols were frequently formed as by-products, probably resulting from reduction of the dialkyl peroxides with $O_2^{\cdot-}$ (13).

Interestingly, Corey, et al., (10) produced a cyclic peroxide in DMSO. The peroxide shown in equation 11 was formed



(11)

in 35% yield in DMSO. Apparently, the close proximity of the second mesylate group in the proposed peroxy mesylate allowed the intramolecular cyclization process to compete favorably with reaction with DMSO. Such a process may be of value in the synthesis of biologically important prostaglandin endoperoxides.

B. Kinetics of Reaction with Alkyl Halides (14). Prior to the work of Danen and Warner, (14,15) few rate constants for the reaction of $O_2^{\cdot-}$ with alkyl halides had been reported. In an electrochemical study, Merritt and Sawyer (16) had determined the pseudo-first-order rate constants at 28°C for three butyl chlorides in DMSO solvent. In a similar manner, Dietz, et al., (7) had reported a pseudo-first-order rate constant for 1-bromobutane reacting with electrogenerated $O_2^{\cdot-}$ in DMF containing tetra-n-butylammonium perchlorate. San Filippo and coworkers (8) had determined the relative reactivity of several alkyl halides but had not reported any absolute rate constants.

Danen and Warner (15) have reported the rate constants in Table I for reaction of KO_2 in DMSO with a series of alkyl bromides. The rates were determined by stopped-flow spectrophotometry under pseudo-first-order conditions. The usual reactivity order characteristic of a S_N2 process was evident in the series MeBr > EtBr > n-BuBr > i-PrBr >> 1-bromoadamantane, which reflects the increasing inaccessibility of the reaction center. However, the 10-fold difference in reactivity between CH_3Br and i-PrBr is smaller than frequently observed; Streitwieser (17) noted a 1000-fold difference in average relative reactivity

Table I. Rate Constants for the Reaction of KO_2 with Alkyl Bromides in DMSO at 25.0°

Alkyl Bromide	k_2 ($M^{-1}s^{-1}$)
CH_3Br	$(6.7 \pm 0.2) \times 10^2$
CH_3CH_2Br	$(3.5 \pm 0.2) \times 10^2$
$CH_3(CH_2)_3Br$	$(1.5 \pm 0.1) \times 10^2$
$(CH_3)_2CHBr$	$(6.5 \pm 0.1) \times 10^1$
1-bromoadamantane	$<<1.0$[a]

[a] Too slow to measure by stopped-flow spectrophotometry.

towards nucleophiles for these two alkyl groups.

The unreactivity of 1-bromoadamantane with $O_2^{\cdot-}$ demonstrated a lack of any appreciable electron transfer type substitution process (eq. 12). Although an electron transfer type mechanism has been demonstrated for nitroaromatic halides (see Section II. C), the difference in reduction potentials between $O_2^{\cdot-}$ and aliphatic bromides is apparently too great to allow such a transfer to occur.

$$RBr \xrightarrow[-O_2]{O_2^{\cdot-}} [RBr]^{\cdot-} \xrightarrow[-Br^-]{} R\cdot \xrightarrow{O_2} RO_2\cdot \longrightarrow \text{Products} \qquad (12)$$

The rate constants reported in Table I are very large for a nucleophilic reaction at 25°. Danen and Warner (15) compared $O_2^{\cdot-}$ with other nucleophiles under comparable conditions and noted that $O_2^{\cdot-}$ reacts several orders of magnitude faster than many nucleophiles indicating that $O_2^{\cdot-}$ is a very potent nucleophile. Although there are numberous factors which determine the nucleophilicity of various anions toward organic substrates, it was suggested that a possible important factor in determining $O_2^{\cdot-}$ nucleophilicity is a significant electron-transfer contribution in the transition state (eq. 13). Since similar

$$O_2^{\cdot-} + RBr \longrightarrow \left[O_2^{\cdot-}\text{---}R\text{---}Br \leftrightarrow \dot{O}_2\text{---}R\text{---}Br^-\right]^{\ddagger} \longrightarrow RO_2\cdot + Br^- \qquad (13)$$

contributions can be drawn for all nucleophiles, the key factor for $O_2^{\cdot-}$ is the inherent stability of molecular oxygen.

The Arrhenius parameters, E_a and $\Delta S^{\ddagger}$, have been determined to be 11.0 kcal/mole and -15.6 e.u., respectively, for the reaction of $O_2^{\cdot-}$ with 1-bromobutane (18). For comparison purposes, the activation parameters for various nucleophiles reacting with

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

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alkyl bromides in dipolar aprotic solvents are presented in Table II along with the values for superoxide. The low E_a for $O_2^{\cdot-}$ is reflected in its nucleophilic reactivity. The entropy of activation for $O_2^{\cdot-}$ is indicative of a bimolecular displacement reaction. Since entropy is measure of randomness or disorder, a negative $\Delta S^{\ddagger}$ implies that the transition state is more ordered than the reactants. This is the normal trend observed in most bimolecular reactions, since for reaction to take place two molecules in random motion must come together. For S_N2 Walden inversion reactions, where specific backside attack is required, a significantly negative $\Delta S^{\ddagger}$ value is usually observed as evident from the data in Table II.

Table II. Energies and Entropies of Activation of Some Displacement Reactions (14)

Nucleophile	Substrate	Solvent	E_a	$\Delta S^{\ddagger}$
$O_2^{\cdot-}$	n-BuBr	DMSO	11.0	-15.6
I^-	n-BuBr	acetone	20.5	-13.9
Cl^-	n-BuBr	acetone	17.5	-21.1
N_3^-	n-BuBr	DMSO	16.91	+ 1.62
$C_6H_5S^-$	n-BuBr	DMF	13.3	- 9.4
N_3^-	MeBr	DMF	16.7	-12.9
SCN^-	MeBr	DMF	16.0	-17.5

The effects of halogen atom substituents on the reactivity of alkyl bromides toward $O_2^{\cdot-}$ have been determined for a series of α-, β-, and γ-halogen substituted alkyl bromides. Rate constants were determined by stopped-flow techniques and are listed in Table III. Since displacement of chloride by $O_2^{\cdot-}$ is much slower

Table III. Rate Constants for the Reaction of KO_2 with Halogen Substituted Alkyl Bromides in DMSO at 25.0° (14)

Dihalide	$k_2 (M^{-1}s^{-1})$	Relative Rate[b]
$BrCH_2Br$[a]	$(1.28 \pm 0.02) \times 10^1$	0.037
$ClCH_2Br$	$(4.0 \pm 0.2) \times 10^1$	0.11
$BrCH_2CH_2Br$[a]	$(2.42 \pm 0.02) \times 10^2$	0.69
$ClCH_2CH_2Br$	$(2.67 \pm 0.02) \times 10^2$	0.76
$ClCH_2CH_2CH_2Br$	$(4.71 \pm 0.04) \times 10^2$	1.35

---

[a] Corrected for statistical factor of two.

[b] Relative to ethyl bromide ($350\ M^{-1}s^{-1}$).

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than that of bromide, the rate constants given are assumed to be for bromide displacement only.

The largest effect on reactivity was caused by α-halogen substitution as indicated by the relative rates shown in Table III. The relative rates for the first two entries are characteristic of an S_N2 process. For example, the nucleophilic displacement reaction of KI in acetone with the same alkyl bromide series (Et-, $ClCH_2$-, $BrCH_2$-) gave the relative rates 1.0:0.13:0.041 (19).

The decrease in reactivity upon halogen substitution in the α-position can be accounted for as follows. Halogen atoms, which are more electronegative than carbon, tend to destabilize the developing positive charge on carbon and, in turn, increase the energy of the transition state. Since reactivity is decreased by introduction of either an α-methyl (electron donating) or an α-halogen (electron withdrawing), it is likely that the decrease is at least partially due to steric hindrance. Finally, and closely related to steric hindrance, is the effect called neighboring orbital overlap, which is due to electron repulsion between the incoming nucleophile and the α-position halogen.

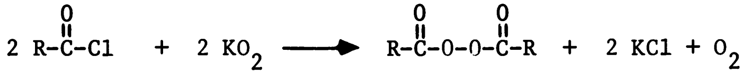
The effect of β-halogen substituents on the reactivity was in the anticipated direction as a result of the electronegativity effect but of less magnitude than usually observed, i.e., the rates of reaction of β-haloethyl bromides with thiophenoxide ion in methanol are a factor of about seven less than that of ethyl bromide (20).

In contrast to the decrease in reactivity exhibited by the other entries in Table III. the γ-halogen substituted example showed increased reactivity. This was a trend that had been previously observed (21) for S_N2 reactions with γ-oxygen substituents but a satisfactory explanation for this behavior has not been advanced.

In summary of this section, it has been conclusively demonstrated that the reaction of $O_2^{\overline{\cdot}}$ with primary alkyl halides and tosylates occurs by an initial S_N2 displacement process. Secondary and tertiary substrates give significant amounts of elimination products. In DMSO solvent, alcohols are the ultimate reaction product while dialkyl peroxides are formed in synthetically useful yields in benzene using crown ethers to solubize the KO_2. The available rate data indicate that $O_2^{\overline{\cdot}}$ is a very potent nucleophile.

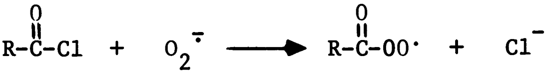
II. Other Nucleophilic Reactions of Superoxide.

A. Reaction with Acyl Chlorides and Esters. In view of the facile reaction of $O_2^{\overline{\cdot}}$ with alkyl halides, it is not unexpected that acyl halides should react rapidly with $O_2^{\overline{\cdot}}$. Johnson (22) has reported that diacyl peroxides are conveniently produced in the reaction of KO_2 with acyl chlorides according to equation 14. The reaction proceeds readily in benzene even

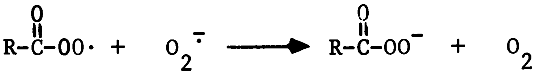


$$2\ \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}Cl} + 2\ \mathrm{KO_2} \longrightarrow \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}O{-}O{-}\overset{O}{\overset{\|}{C}}{-}R} + 2\ \mathrm{KCl} + \mathrm{O_2} \qquad (14)$$

without crown ether. In fact, the present authors (3) have demonstrated that diacyl peroxides are rapidly consumed by KO_2 solubilized in benzene with 18-crown-6 generating the anion of the corresponding acid. Even without crown ether, Johnson has noted that it is advantageous to work-up the acyl chloride-KO_2 reactions as soon as the acyl chloride has been consumed to avoid production of the acid. The mechanism of formation of diacyl peroxides almost certainly involves steps 15-17 analogous to the



$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}Cl} + \mathrm{O_2^{\cdot -}} \longrightarrow \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OO^{\cdot}} + \mathrm{Cl^-} \qquad (15)$$

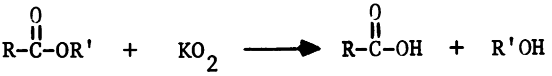


$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OO^{\cdot}} + \mathrm{O_2^{\cdot -}} \longrightarrow \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OO^-} + \mathrm{O_2} \qquad (16)$$

$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OO^-} + \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}Cl} \longrightarrow \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OO{-}\overset{O}{\overset{\|}{C}}{-}R} + \mathrm{Cl^-} \qquad (17)$$

production of dialkyl peroxides as discussed above.

San Filippo and coworkers (23) have shown that a variety of carboxylic esters are cleaved by KO_2 in benzene with crown ether to produce after acidic work-up the corresponding carboxylic acid and alcohol in good to excellent yields (eq. 18). A mechanism involving alkyl-oxygen cleavage was ruled out by stereochemical studies involving esters derived from chiral alcohols. A



$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OR'} + \mathrm{KO_2} \longrightarrow \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OH} + \mathrm{R'OH} \qquad (18)$$

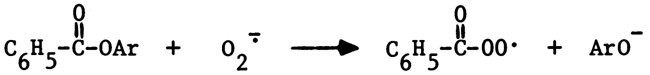
mechanism involving initial additon of $O_2^{\cdot -}$ to the carbonyl carbon was favored although the subsequent steps were only speculated; peroxy intermediates were implicated. An initial addition-elimination mechanism is consistent with the influence the departing alkoxide ion exerts on the rate of reaction; i.e., R^1 = phenyl > primary > secondary > tertiary.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

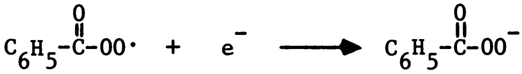
Triphenyl phosphate was readily cleaved by $O_2^{\cdot -}$ but tri-n-octyl phosphate showed no appreciable reactivity. Simple amides and nitriles were also largely unaffected by $O_2^{\cdot -}$ under conditions equivalent to those employed for ester cleavage.

Magno and Bontempelli (24) have reported on the reaction kinetics of electrogenerated $O_2^{\cdot -}$ in DMF with phenyl benzoate and p-chlorophenyl benzoate; second-order rate constants of 3.0±0.3 and 25±5 $M^{-1}sec^{-1}$, respectively, were determined by electrochemical techniques. An e.c.e. (electron transfer-chemical reaction-electron transfer) mechanism was shown to be operative and the following mechanism was suggested (equations 19-23). The

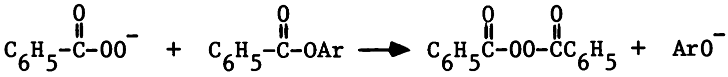
$$O_2 + e^- \longrightarrow O_2^{\cdot -} \qquad (19)$$



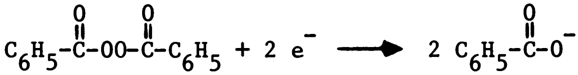
$$C_6H_5-\overset{O}{\overset{\|}{C}}-OAr + O_2^{\cdot -} \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-OO\cdot + ArO^- \qquad (20)$$



$$C_6H_5-\overset{O}{\overset{\|}{C}}-OO\cdot + e^- \longrightarrow C_6H_5-\overset{O}{\overset{\|}{C}}-OO^- \qquad (21)$$



$$C_6H_5-\overset{O}{\overset{\|}{C}}-OO^- + C_6H_5-\overset{O}{\overset{\|}{C}}-OAr \longrightarrow C_6H_5\overset{O}{\overset{\|}{C}}-OO-\overset{O}{\overset{\|}{C}}C_6H_5 + ArO^- \qquad (22)$$

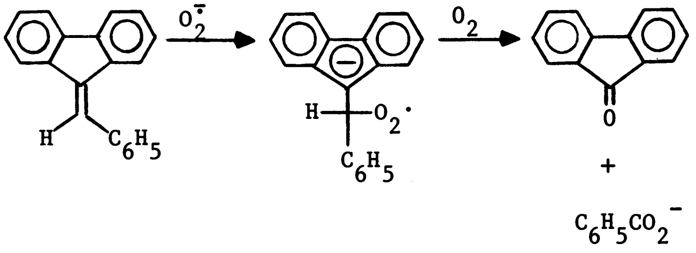


$$C_6H_5-\overset{O}{\overset{\|}{C}}-OO-\overset{O}{\overset{\|}{C}}-C_6H_5 + 2\ e^- \longrightarrow 2\ C_6H_5-\overset{O}{\overset{\|}{C}}-O^- \qquad (23)$$

greater reactivity of the p-chlorophenyl ester is consistent with reaction 20 being the rate-limiting step.

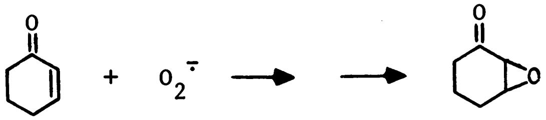
B. Nucleophilic Addition to Double Bonds. There are at least two reports of $O_2^{\cdot -}$ adding in nucleophilic fashion to a carbon-carbon double bond. Although the reaction mechanisms were not elucidated in detail, in both reports the double bond was activated for nucleophilic addition.

Benzylidenefluorene, a hydrocarbon susceptible to nucleophilic attack, was shown by Dietz, *et al*. (7) to react with electrogenerated $O_2^{\cdot -}$ in the presence of O_2 to produce fluorenone and benzoate. It was proposed that $O_2^{\cdot -}$ initiated an autoxidation reaction (equation 24); one equivalent of $O_2^{\cdot -}$ was necessary to remove the hydrocarbon completely.



(24)

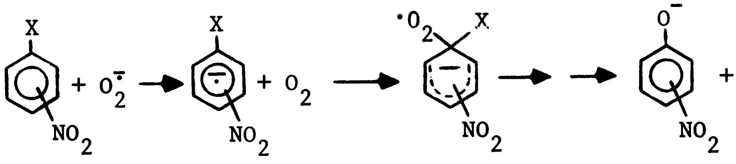
These authors also showed that electrogenerated $O_2^{\cdot-}$ reacted with cyclohexen-3-one to give the corresponding epoxide in 30% yield (equation 25). Cyclohexene, in contrast, gave no epoxide implying that a double bond activated towards a Michael-type of addition is required.



(25)

C. Electron Transfer Reactions Mimicking Nucleophilic Attack. There are several reports in which $O_2^{\cdot-}$ nominally appears to react as a nucleophile but, in fact, involve an initial electron-transfer from $O_2^{\cdot-}$ followed by reaction of O_2 with the radical anion generated from the organic substrate. These results appear appropriate for this review. There are certainly other reactions which occur by such a process instead of a simple nucleophilic displacement but isotopic labeling studies or chiral reactants must be utilized to distinguish between the two mechanisms. Because of the relatively low reduction potential for O_2, -0.77 V versus SCE (2), any substrate with a more negative reduction potential will likely be reduced by $O_2^{\cdot-}$ via an electron transfer process. Depending upon the substrate, the ultimate product(s) of such a reaction may or may not resemble those expected from a simple nucleophilic reaction.

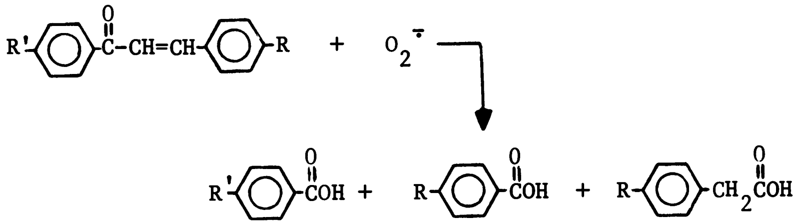
Frimer and Rosenthal (25) have demonstrated that the reaction of $O_2^{\cdot-}$ with nitro substituted aromatic halides occurs via an electron transfer from $O_2^{\cdot-}$ to the substituted benzene to yield the anion radical which is subsequently scavenged by molecular oxygen (equation 26). They were able to distinguish this reaction pathway from direct addition of $O_2^{\cdot-}$ to the aromatic ring as in normal nucleophilic aromatic substitution by utilizing


(26)

^{18}O-enriched KO_2. By conducting the reaction with enriched KO_2 in benzene saturated with unlabeled O_2, mass spectroscopic analysis of the resulting phenol revealed the presence of an ^{18}O tag of less than 10%. This result implied that the phenolic oxygen was incorporated in large part after the equilibration with molecular oxygen dissolved in solution.

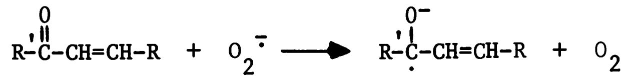
Dougherty, et al., (26) have observed a similar reaction in the gas phase. The negative chemical ionization spectra of 4-bromobenzophenone, 4-nitrochlorobenzene, and 2,4-dinitrochlorobenzene were all replaced by spectra of the corresponding phenolate anions when $O_2^{\cdot -}$ was generated in the system.

Another nominally nucleophilic reaction of $O_2^{\cdot -}$ is the efficient production of carboxylic acids from chalcones (equation 27). Rosenthal and Frimer (27) have also studied this reaction


(27)

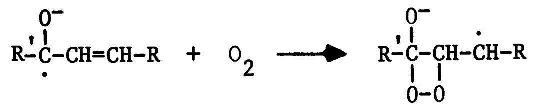
utilizing ^{18}O-enriched KO_2 and determined that oxygen is not incorporated into the product carboxylic acids by direct nucleophilic attack of $O_2^{\cdot -}$. Instead, the reaction proceeds by a preliminary electron transfer from $O_2^{\cdot -}$ to the enone system and the resulting anion radical then reacts with the surrounding molecular oxygen as depicted in equations 28-32. A similar mechanism enabled the understanding of the surprising formation of 2-hydroxy-2,4,5-triphenylfuranone-3 in the reaction of KO_2 with tetracyclone (28)(equation 33).

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014



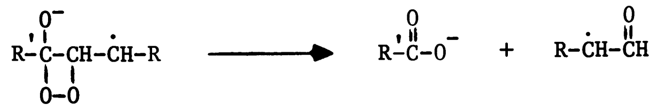
$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH{=}CH\text{-}R + O_2^{\overline{\cdot}} \longrightarrow R\text{-}\underset{\cdot}{\overset{\overset{O^-}{|}}{C}}\text{-}CH{=}CH\text{-}R + O_2$$

(28)



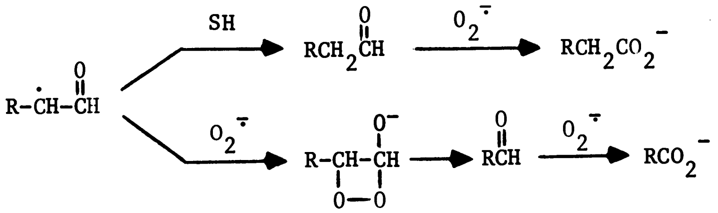
$$R\text{-}\underset{\cdot}{\overset{\overset{O^-}{|}}{C}}\text{-}CH{=}CH\text{-}R + O_2 \longrightarrow R\text{-}\underset{\underset{O-}{|}}{\overset{\overset{O^-}{|}}{C}}\text{-}\underset{\underset{O}{|}}{\dot{C}H}\text{-}CH\text{-}R$$

(29)



$$R\text{-}\underset{\underset{O-}{|}}{\overset{\overset{O^-}{|}}{C}}\text{-}\underset{\underset{O}{|}}{CH}\text{-}\dot{C}H\text{-}R \longrightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O^- + R\text{-}\dot{C}H\text{-}\overset{\overset{O}{\|}}{C}H$$

(30)

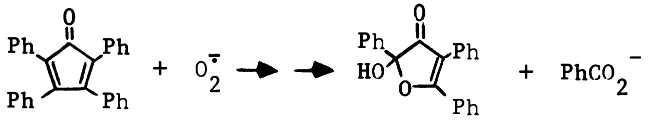


$$R\text{-}\dot{C}H\text{-}\overset{\overset{O}{\|}}{C}H \xrightarrow{SH} RCH_2\overset{\overset{O}{\|}}{C}H \xrightarrow{O_2^{\overline{\cdot}}} RCH_2CO_2^-$$

(31)

$$R\text{-}\dot{C}H\text{-}\overset{\overset{O}{\|}}{C}H \xrightarrow{O_2^{\overline{\cdot}}} R\text{-}\underset{\underset{O-}{|}}{CH}\text{-}\underset{\underset{O}{|}}{\overset{\overset{O^-}{|}}{C}H} \longrightarrow R\overset{\overset{O}{\|}}{C}H \xrightarrow{O_2^{\overline{\cdot}}} RCO_2^-$$

(32)



(33)

In conclusion of this review of the nucleophilic properties of $O_2^{\overline{\cdot}}$, the versatile nature of this unique anion radical should be emphasized. This chapter attempted to cover only the main features of the nucleophilic reactions of $O_2^{\overline{\cdot}}$ with well-defined chemical substrates; no attempt was made to treat any of the biochemical reactions. Moreover, in addition to nucleophilic properties, $O_2^{\overline{\cdot}}$ is capable of reacting as a free radical as well as an electron transfer agent or electron acceptor. Thus, the understanding of this ubiquitous anion radical is probably only in its late infancy even though a computer search of the 1972-mid 1977 Chemical Abstracts revealed 850 references to "superoxide".

III. Acknowledgement

This work was written while W. C. Danen was on sabbatical leave at the Los Alamos Scientific Laboratory, Los Alamos, New Mexico. This author would like to express his appreciation to the personnel of AP Division, in particular John H. Birely and Samuel M. Freund, for their hospitality during that time.

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch014

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Kinetic Analysis of the Methylene Blue Oxidations of Thiols

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch015

Kinetics traditionally have been among the more powerful tools available for the study of organic reation mechanisms. Much of our present understanding of the behavior of free radicals as reaction intermediates can be attributed to data accumulated by various competitive kinetic investigations (e.g. the determination of transfer and copolymerization constants in vinyl polymerization reactions). Somewhat less exploited as a means of gaining insight into the mechanistic details of free radical chain reactions has been the examination of the rate laws of such reactions. Neglect of this area of investigation is surprising because those reactions that have been subjected to such studies (e.g., vinyl polymerizations, brominations, autoxidations) have yielded valuable information concerning the overall mechanisms of free radical chain reactions. The lack of extensive effort in this area may be due, at least in part, to the fact that the experimentally determined rate constants are combinations of the rate constants of the several individual steps in the overall reaction. Generally, these observed rate constants are not readily resolvable into the rate constants of the individual steps of the reaction and thereby available for the classical examination the activation parameters of these reactions. Furthermore, the observed rate laws often involve fractional kinetic orders of the reactants (and sometimes the products). Further, these kinetic orders often depend on experimental conditions, in particular the relative concentrations of the reactants (and sometimes the products). While such factors as inconsistent kinetic orders may appear at the outset to be detrimental to the study of a reaction mechanism by kinetic analysis, these same factors may, in some instances, prove to be valuable probes for investigation of the mechanisms of free radical chain reactions. The work presented here describes such an investigation.

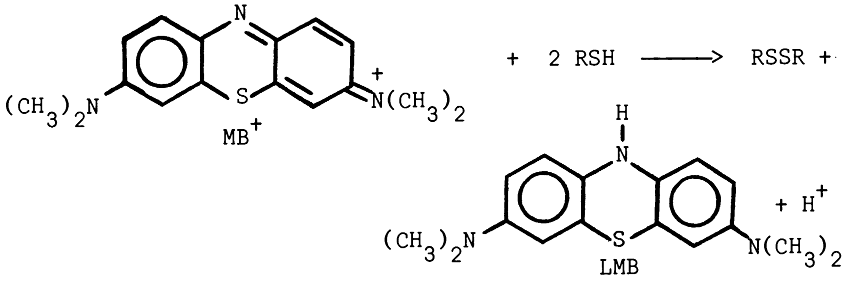
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch015

Methylene Blue Oxidations of Thiols

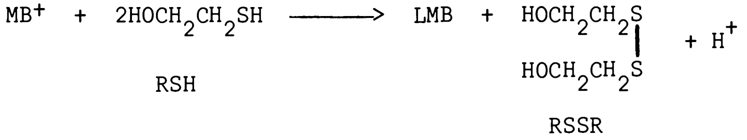
The oxidations of thiols to disulfides, reactions encountered in a variety of biological processes, have been accomplished in the laboratory by a variety of oxidizing agents

$$2\ RSH + Ox \longrightarrow RSSR + OxH_2$$

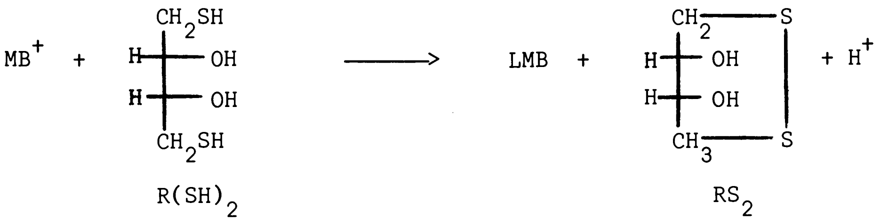
(e.g. molecular oxygen, ferricyanide, quinones, flavins, and azocompounds) (1). In this study, methylene blue (MB^+) was used as the oxidizing agent (2). The thiols subjected to oxidation by



MB^+ were mercaptoethanol (RSH) and dithioerythritol ($R(SH)_2$) which were oxidized to the corresponding disulfides (RSSR and RS_2, respectively) with concurrent reduction of MB^+ to leucomethylene blue (LMB).



$$\underset{}{MB^+} + \underset{RSH}{2HOCH_2CH_2SH} \longrightarrow LMB + \underset{RSSR}{\begin{array}{l} HOCH_2CH_2S \\ \quad\quad\quad\;\;\, | \\ HOCH_2CH_2S \end{array}} + H^+$$



The reaction rates of the oxidations of mercaptoethanol and dithioerythritol were determined at various concentration ratios of the thiols with respect to MB^+ over a range of pH's and ionic strengths in both water and D_2O by following the decrease in the absorption maximum of MB^+ at 650 nm. The high molar extinction coefficient of MB^+ (ε = 51,200) allows for rate determinations at very low concentrations of this reagent. That the reactions investigated actually do occur was established by isolation of both leucomethylene blue and the corresponding disulfides as reaction products.

MB^+ Oxidations of Mercaptoethanol. A mechanism for the oxidation of mercaptoethanol with MB^+ that is consistent with our data for the reaction is shown in the sequence 1-10. This mechanism evolved for the most part from our kinetic studies of the reaction. Steps 2-4 of the reaction scheme comprise a free

$$RS^- + MB^+ \xrightarrow{k_1} RS\cdot + MB\cdot \qquad (1)$$

$$RS\cdot + RS^- \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} RS\dot{\bar{S}}R \qquad (2)$$

$$RS\dot{\bar{S}}R + MB^+ \xrightarrow{k_3} MB\cdot + RSSR \qquad (3)$$

$$MB\cdot + RSH \xrightarrow{k_4} LMB + RS\cdot \qquad (4)$$

$$2\ RS\cdot \xrightarrow{k_5} RSSR \qquad (5)$$

$$RS\cdot + MB\cdot \xrightarrow{k_6} RS^- + MB^+ \qquad (6)$$

$$RS\cdot + RS\dot{\bar{S}}R \xrightarrow{k_7} RS^- + RSSR \qquad (7)$$

$$MB\cdot + RS\dot{\bar{S}}R \xrightarrow{k_8} MB^+ + 2\ RS^- \qquad (8)$$

$$2\ MB\cdot + H^+ \xrightarrow{k_9} MB^+ + LMB \qquad (9)$$

$$2\ RS\dot{\bar{S}}R \xrightarrow{k_{10}} 2\ RS^- + RSSR \qquad (10)$$

radical chain sequence that accounts of the stoichiometry of the oxidation of mercaptoethanol by MB^+. The sulfur-sulfur linkage of the disulfide is effected in the formation of the radical anion $RS\dot{\bar{S}}R$, a radical which is partitioned between fragmenting to the species from which it was formed and transfering of an electron to MB^+ to yield the disulfide as a reaction product and the methylene blue derived radical $MB\cdot$. The latter propagates the chain by abstracting the sulfur-bonded hydrogen from the thiol yielding leucomethylene blue (LMB) and a chain-carrying thiyl radical ($RS\cdot$). The overall reaction, which occurs at room temperature, is initiated (step 1) by an interaction (possibly an electron transfer) between a sulfide ion and MB^+. There are six termination reactions possible (steps 5-10) for a chain sequence involving three different chain-carrying radicals. Our rate data indicate that only those shown in 5-8 are likely termination processes for the reaction.

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Examination of this mechanism reveals that both the thiol and the sulfide ion are required as reactants. The pH of the medium, which determines the relative amounts of these components, therefore, has a significant influence on the rate of the oxidation reaction. Table I shows the oxidation rates of mercaptoethanol by MB^+ are pH dependent in that the reaction rate is greatest at a pH roughly one pH unit greater than that required for about equal distribution of the thiol and sulfide ion as dictated by the ionization constant of mercaptoethanol (pK_A = 9.34) (3). The lower oxidation rates above pH 10.3 indicate involvement of the thiol in a rate-limiting step when the thiol concentration is low.

Table I

Effect of pH on MB^+-Oxidation

Rates of Mercaptoethanol

pH[a]	Rate x 10^6 M sec^{-1}
8.20	1.01 (0.05)
8.60	2.14 (0.08)
9.00	4.89 (0.08)
9.30	6.51 (0.26)
9.60	7.40 (0.08)
9.90	7.66 (0.13)
10.30	8.36 (0.09)
10.70	7.66 (0.32)

a. Buffered with borate. All solution adjusted to ionic strength = 0.4 with KCl.

The observed rate laws for the oxidation of mercaptoethanol by methylene blue under different reaction conditions are consistent with the steady-state rate laws derived from the proposed mechanism. If step 2 of the reaction sequence, namely formation of the disulfide radical anion from a thiyl radical and a sulfide ion, is the rate limiting step of the chain sequence, and therefore only termination by 6 (coupling of thiyl radicals) occurs, the derived rate law for the reaction is Eq. 11. This rate law, which takes into account the distribution of the thiol and sulfide as determined by the K_A of the thiol and the acidity of the medium, predicts that the observed rate law would be half order in MB^+ and three halves order in mercaptoethanol. This is the rate law expected, however, only if the concentration of MB^+ is sufficiently high so that the second term in the denominator is neglible. At pH's below the pH maximum, and at a sufficiently

$$\text{Rate} = \frac{(k_1/2k_5)^{1/2}k_2[MB^+]^{1/2}(K_A[RSH]/[H^+])^{3/2}}{1 + k_{-2}/k_3[MB^+]} \qquad (11)$$

high concentration of MB+, the formation of the disulfide radical anion may well be expected to be the only limiting reaction in the chain sequence since the reactants for the other two steps (MB+ and RSH) are present in sufficient concentrations to obviate their participation in rate limiting steps. Table II shows the kinetic orders of MB+ and RSH for the oxidation reaction at pH 9.9.* The rate law for the reaction at pH 9.9 very closely follows the derived rate law shown in Eq. 11 in that at the higher concentrations of MB+, the reaction is three-halves order in RSH and half order in MB+. However, the derived rate law indicates that at lower concentrations of MB+ the second term in the denominator could be significant and the observed kinetic order of MB+ would be greater than one half. The increase in kinetic order of MB+ observed at lower concentrations of MB+ is therefore likely a reflection of the less effective partioning of the $RS\hat{S}R$ to the MB+.

At pH > 10.3, the concentration of RSH relative to RS^- is small and reaction 4, the hydrogen atom abstraction from RSH by the methylene blue derived radical MB·, is a rate limiting factor. If reaction 4, along with the disulfide radical anion formation in reaction 2, are the rate limiting steps in the chain sequence, the reaction would follow the derived rate law shown in Eq. 12. Note that, in terms of the measurable kinetic

$$\text{Rate} = \left(\frac{k_1k_2k_4[MB^+]([RSH]-K_A[RSH]/[H^+])}{k_6(1 + k_{-2}/k_3[MB^+])}\right)^{1/2} K_A[RSH]/[H^+] \qquad (12)$$

orders of MB+ and RSH, the expected observed rate law at pH 10.7 is not distinguishable from the observed rate law for the reaction at pH 9.9, namely that the reaction is half order in MB+ and three-halves order in mercaptoethanol. Table III shows that at the higher concentrations of MB+, the reaction at pH 10.7

*A word concerning these kinetic orders and those in subsequent Tables is warranted. All kinetic orders were determined by the method of initial rates. The kinetic order listed at each concentration of MB+ is the average calculated from at least three (generally four or five) determinations of the reaction rate at that concentration of MB+. The value in parenthesis following the kinetic order indicates the outside limits of certainty based on the calculation of the kinetic order from the fastest and slowest rates at that particular concentration.

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Table II

Kinetic Data for MB^+ Oxidations

of Mercaptoethanol at pH 9.9[a]

$$\text{Rate} = k_{obs}[MB^+]^{\alpha}[RSH]^{\beta}$$

Kinetic Orders

$[MB^+] \times 10^6$	α	β[b]
		1.48 (.11)[c]
7.84	.47 (.12)[c]	
		1.49 (.13)
5.92	.50 (.12)	
		1.48 (.11)
4.36	.48 (.10)	
		1.50 (.12)
3.05	.50 (.10)	
		1.48 (.13)
1.66	.74 (.05)	
		1.50 (.16)
.78	.89 (.18)	
		1.52 (.10)
.59	1.07 (.18)	
		1.49 (.11)

a. Borate buffered, $\mu = 0.40$.
b. $[RSH] = 8.15 \times 10^{-3}$ and 5.78×10^{-3}.
c. Extreme limits of reliability.

is indeed three halves order in RSH and half order in MB^+.

At lower concentrations of MB^+, the increase in kinetic order of this reagent reflects less favorable partitioning the disulfide radical anion $RS\dot{S}R$ to MB^+ as noted at pH 9.9. The decrease in the kinetic order of RSH at lower MB^+ concentrations indicates that $RS\dot{S}R$ is possibly involved in a termination reaction.

The derived rate law for the reaction if steps 3 and 4 are rate limiting is shown in Eq. 13 and indicates that if reaction

$$\text{Rate} = \left(\frac{k_1k_3k_4(K_A[RSH]/[H^+])}{k_8(1 + k_{-2}/k_3[MB^+])}\right)^{1/2}[MB^+][RSH]^{1/2} \qquad (13)$$

3 is a rate limiting step, the kinetic order of RSH is unity.

<u>MB^+ Oxidations of Dithioerythritol</u>. Although the kinetic rate laws observed for the mercaptoethanol oxidations are

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Table III

Rate Data for Mercaptoethanol Oxidations at pH 10.7[a]

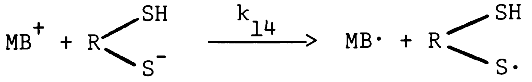
$$\text{Rate} = k_{obs}[MB^+]^{\alpha}[RSH]^{\beta}$$

$[MB^+] \times 10^6$	α	β[b]
		1.50 (.10)
7.84	0.50 (.16)	
		1.49 (.09)
5.92	0.48 (.13)	
		1.50 (.08)
4.36	0.55 (.11)	
		1.47 (.08)
3.05	0.51 (.09)	
		1.45 (.08)
1.66	0.72 (.05)	
		1.38 (.10)
.78	0.81 (.16)	
		1.35 (.06)
.59	0.93 (.04)	
		1.28 (.04)
.44	1.02 (.12)	
		1.25 (.13)
.30	1.17 (.16)	
		1.18 (.13)

a. Borate buffered, $\mu = 0.40$.
b. $[RSH] = 6.38 \times 10^{-3}$ and 3.89×10^{-3}.

consistent with those expected for the proposed mechanism, these studies were somewhat less than satisfying because the derived rate laws predict the same observed rate laws at pH's above and below the pH of the rate maximum. The oxidations of dithioerythritol are more informative because, owing to the unimolecularity of the disulfide radical anion formation (in contrast to the bimolecularity of the disulfide radical anion formation in the case of mercaptoethanol), the observed and derived rate laws are pH-dependent. The mechanism proposed for the dithioerythritol oxidations by MB^+ is shown in the sequence 14-23.

As in the case of the mercaptoethanol oxidations, the oxidation rates of dithioerythritol are pH-dependent showing a maximum at pH ∿ 9.6 (see Table IV). The lower pH observed for the maximum rate relative to that observed for mercaptoethanol (see Table I) parallels the lower pK_A for the first ionization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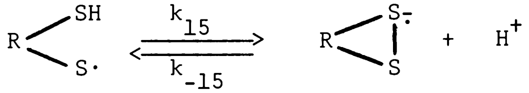
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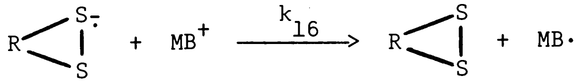
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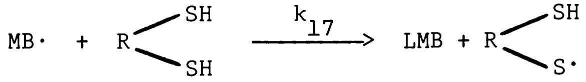
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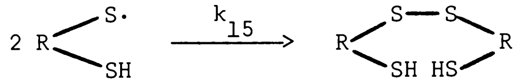
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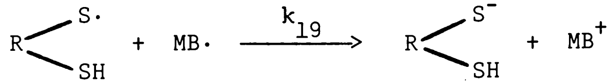
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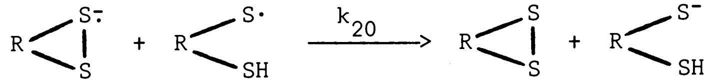
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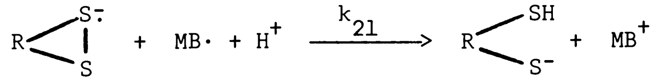
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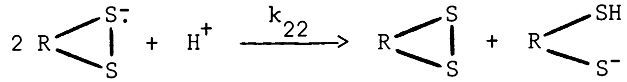
(22)

$$2\ MB\cdot + H^+ \xrightarrow{k_{23}} LMB + MB^+ \qquad (23)$$

constant of dithioerythritol (9.0) (4) relative to that of mercaptoethanol. Not shown is a second rate maximum observed at pH ∿ 11 reflecting the dibasic character of dithioerythritol (second pK_A = 9.9) (4). For the present study, only the rate maximum associated with the first ionization is pertinent.

If the dithioerythritol oxidations do indeed follow the same mechanistic path as the mercaptoethanol oxidations with respect to relative reagent concentrations, at pH's below that observed for the maximum rate and at the high concentrations of MB^+, only the unimolecular disulfide radical anion formation (reaction 15) would be rate limiting. The derived rate law based on only

Table IV

Effect of pH on MB^+-Oxidation Rates of Dithioerythritol[a]

pH	Rate x 10^6 M sec^{-1}
8.21	0.11 (0.01)
8.44	0.28 (0.03)
8.86	0.62 (0.02)
9.28	1.08 (0.09)
9.58	1.37 (0.13)
9.88	1.12 (0.09)
10.24	1.03 (0.02)
10.56	0.80 (0.02)

a. Ionic strength = 0.40.

termination by reaction 18, the chain-carrying radical in the rate limiting step, is Eq. 24. This derived rate law predicts that at a pH below 9.6 and relatively high concentrations MB^+ the

$$\text{Rate} = \frac{(k_{14}/2k_{18})^{1/2}k_{15}([MB^+]K_A[R(SH)_2]/[H^+])^{1/2}}{1 + k_{-15}/k_{16}[MB^+]} \qquad (24)$$

observed rate law would be half order in both MB^+ and dithioerythritol, a prediction that is consistent with rate law obtained at pH 9.0 (Table V) when the MB^+ is sufficiently high.

However, the derived rate law indicates that the kinetic order of MB^+ should increase with decreasing concentration of MB^+. The latter effect, as in the mercaptoethanol reactions, reflects the less effective partitioning of the disulfide radical anion toward the MB^+ at the lower concentrations of MB^+.

In the pH range above that observed for the rate maximum, hydrogen atom abstraction by MB· from the thiol (reaction 17) is a rate limiting step in the chain sequence. If termination occurs by reaction 19 and the derived rate law for the reaction (Eq. 25) predicts that the reaction would be half order in MB^+

$$\text{Rate} = \left(\frac{k_{14}k_{15}k_{17}[MB^+]([RSH]-K_A[R(SH)_2]/[H^+])(K_A[R(SH)_2]/[H^+])}{k_{19}(1 + k_{-15}/k_{16}[MB^+])}\right)^{1/2} \qquad (25)$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch015

Table V

Kinetic Data for MB^+ Oxidations

of Dithioerythritol at pH 9.0[a]

$$\text{Rate} = k_{obs}[MB^+]^{\alpha}[R(SH)_2]^{\beta}$$

Kinetic Orders

$[MB^+] \times 10^6$	α	β[b]
		.52 (.04)
7.84	.52 (.14)	
		.51 (.03)
5.92	.74 (.13)	
		.52 (.04)
4.36	.86 (.12)	
		.51 (.04)
3.05	1.08 (.10)	
		.51 (.05)
1.66	1.25 (.07)	
		.49 (.05)
1.13	1.38 (.08)	
		.45 (.12)

a. Borate buffer, $\mu = 0.40$.
b. $[RSH] = 2.59 \times 10^{-3}$ and 1.01×10^{-3}.

and first order in dithioerythritol. The kinetic orders observed for the dithioerythritol oxidation by MB^+ at pH 10.3 (Table VI) show the reaction is indeed first order in dithioerythritol and half order in MB^+ at the higher concentrations of the latter reagent. The kinetic order of MB^+ at lower concentrations of MB^+ is greater than half order and indicates the involvement of the fractional term in the denominator of derived rate law resulting from less effective partitioning of the disulfide radical anion toward the MB^+ at low concentrations of this reagent.

The observed rate laws for the methylene blue oxidations of both mercaptoethanol and dithioerythritol at the different pH's are consistent with the mechanisms proposed for these oxidations. The most significant effect of the pH on the reaction is that of establishing the relative amounts of thiol and sulfide ion. Initiation of the chain sequence by the reaction of a sulfide ion with MB^+ would be expected to be more rapid, and therefore the overall oxidation faster, if the pH of the medium is increased. However, at the higher pH's where the relative amount of undissociated thiol is small, the reaction rate diminishes indicating not only that the thiol is likely a reactant in the overall reaction but that it is involved in a rate limiting step of the reaction at higher pH's. While not as supportive as the

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Table VI

Kinetic Data for MB^+ Oxidations

of Dithioerythritol at pH 10.3[a]

$$\text{Rate} = k_{obs}[MB^+]^{\alpha}[R(SH)_2]^{\beta}$$

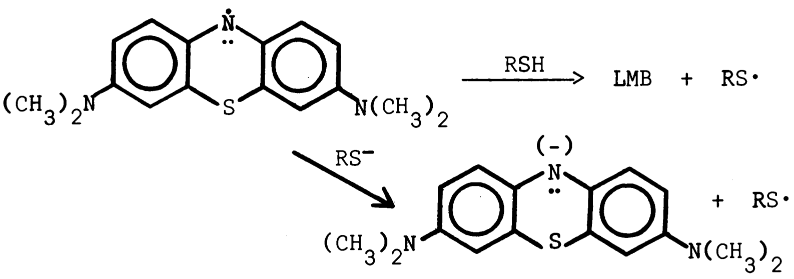
Kinetic Orders

$[MB^+] \times 10^6$	α	β[b]
		.99 (.04)
7.84	.49 (.12)	
		.98 (.03)
5.92	.50 (.14)	
		.98 (.04)
4.36	.53 (.14)	
		.99 (.05)
3.05	.67 (.13)	
		1.01 (.06)
1.66	.79 (.09)	
		.98 (.03)
1.13	.89 (.13)	
		.99 (.07)

a. Borate buffer, $\mu = 0.40$.
b. $[RSH] = 1.56 \times 10^{-3}$ and 5.58×10^{-4}.

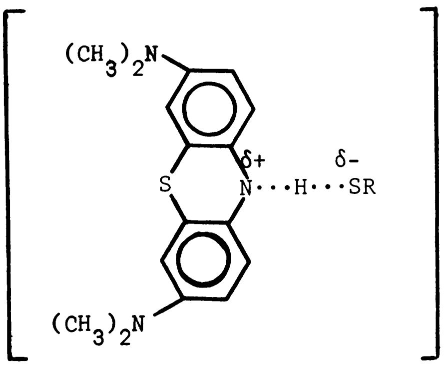
rate laws for the dithioerythritol oxidations, the observed rate laws for the mercaptoethanol oxidation are consistent with the hypothesis that hydrogen atom abstraction from the thiol is a rate limiting step at higher pH's where the concentration of thiol is small.

Finding hydrogen atom abstraction from the thiol is the chain propagating step that produces the chain-carrying thiyl radical rather than electron transfer from a sulfide ion is not unexpected in terms of the expected chemical behavior of the methylene blue derived radical MB·. The most probable structure



MB^-

of MB· is the hybrid radical having as a major contributor to the hybrid the structure with the unpaired electron localized on heterocyclic nitrogen. If electron transfer from RS^- to this species did occur, it would yield MB^-, the conjugate base of the weakly acidic leucomethylene blue. On the other hand, hydrogen atom abstraction from the thiol not only yields a more stable MB· derived reaction product, namely LMB, than electron transfer but the reaction itself involves a favorable polar effect in that the thiol is a good electron acceptor substrate and the MB· a good electron donor radical.



Solvent Isotope Effects. The involvement of the abstraction of the hydrogen atom from the thiol by MB· as a rate limiting factor at the higher pH's is supported by comparison of the oxidation reaction rates in H_2O and D_2O at different pH's. Table VII lists the observed rate constants for the oxidations of both mercaptoethanol and dithioerythritol at different acidities.

Examination of the solvent isotope effects as measured by k'_H/k'_D (where, in the case of mercaptoethanol at each pH, k' is the observed reaction rate constant calculated from the rate law $v = k_{obs}[RSH]^{3/2}[MB^+]^{1/2}$ and in the case of dithioerythritol, k' is calculated from the rate law $v = k_{obs}[R(SH)_2]^{1/2}[MB^+]^{1/2}$ at the lower pH's and from $v = k_{obs}[R(SH)_2][MB^+]^{1/2}$ at the highest pH) shows that an isotope effect is observed only under those conditions where breaking and S-H bond is a rate limiting factor, namely at the higher pH's where the free thiol concentrations are low. The inverse isotope effects at the lower pH's in both cases can be ascribed to the difficulties encountered in comparing the sulfide to thiol ratios in H_2O and D_2O at a designated pH (5). It is possible that at the lower pH's the higher observed rate constant in D_2O reflects an increased rate of initiation owing to a higher concentration of sulfide ion in D_2O relative to that in the H_2O solution with which it is compared. At the higher pH, this factor is outweighed by the positive isotope effect resulting from the involvement of the

Table VII

Solvent Isotope Effects

pH	k'_H	"pD"	k'_D	k'_H/k'_D
		Mercaptoethanol		
9.90	1.69	10.6	1.88	0.92
10.30*	2.08	11.0*	2.44	0.85
10.80	2.05	11.2	1.83	1.12
		Dithioerythritol		
9.30	1.06	9.90	1.17	0.91
9.60*	1.32	10.20*	1.43	0.92
9.90	1.20	10.60	0.91	1.31

* pH or "pD" at which maximum rate is observed.

breaking of the S-H bond in a rate limiting step. Thus, the observed isotope effect at the higher pH's as measured by the k_H/k_D values in Table VII likely are considerably smaller than the actual isotope effect operative in the hydrogen atom abstraction from the thiols by the methylene blue derived radical.

Ionic Strength Considerations. Reactions involving charged reactants may be expected to be influenced by the ionic strength of the medium in which the reaction occurs. The most profound effects are observed in reactions between two charged species, either both with the same charge or each oppositely charged. The effect of a change in the ionic strength of the medium on the rate constant of a reaction between ionic species can be expressed in the Eq. 26 which is a combination of Brønsted equation and the Debye-Hückel rate limiting law (6). This equation, where k_o and k are the rate constants at infinite

$$\ln k = \ln k_o + 2\, Z_A Z_B\, \alpha \sqrt{\mu} \qquad (26)$$

dilution of any charged species in solution and at ionic strength μ, respectively, α is a constant related to the solvent and temperature (α = 0.509 in water at 25°) and Z_A and Z_B are the charges of the ionic species A and B, respectively, predicts that the rate constant for a reaction between species of like charges will increase with increasing ionic strength of the medium. Conversely, the rate constant of a reaction between species of opposite charge should be expected to decrease with increasing

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch015

ionic strength. Examination of the proposed mechanisms for the methylene blue oxidations of mercaptoethanol and dithioerythritol shows that in each case there are two steps in the reaction sequence that involve interactions between species that are oppositely charged. These are the initiation reactions (the reaction between MB^+ and the sulfide ion, reactions 1 and 14) and the chain propagating electron transfer reactions between the disulfide radical anions and MB^+ (reactions 3 and 16).

That interactions between charge species are rate limiting factors in these oxidations was evident in the early stages of our work in that reliable rate data could not be obtained for these oxidations unless precautions were taken to maintain a constant ionic strength by addition of a strong electrolyte (KCl was used in this work). All of the data presented in the work covered up to this point was obtained at an ionic strength of 0.4. It should be noted that at ionic strengths greater than about 0.01, the Debye-Hückel limiting law is no longer strictly valid and corrections must be made to account for the changes in the activities of the charged species in media of high ionic strength. The inclusion of the correction factor "b" is necessary to accommodate these changes in the activities of the charged species at high ionic strengths as shown in Eq. 27.

$$\ln k = \ln k_o + 2 Z_A Z_B \alpha \sqrt{\mu} - b\mu \qquad (27)$$

Not having quantitative values for "b" for the reactions of MB^+ with either the sulfide ions or the disulfide radical anions, we can evaluate the effects of ionic strength in these reactions at high ionic strength only in a semi-quantitative manner.

Table VIII lists the rates of oxidation of mercaptoethanol by methylene blue at various ionic strengths. Note that at any given concentration of MB^+ the rate of the reaction decreases with increasing ionic strength. At the higher concentrations of MB^+, only the initiation reaction rate constant would be influenced by the change in the ionic strength of the solution. The observed decrease in the reaction rate at the higher ionic strengths is consistent with a decrease in the value of the rate constant of the initiation reaction.

As pointed out earlier, the electron transfer reaction of the disulfide radical anion with MB^+ is a rate limiting factor at low concentrations of MB^+. The extent to which this reaction is a rate limiting factor, as evidenced by the change in the kinetic order of MB^+, depends not only on the concentration of MB^+ but also on the reaction rate constant for this chain propagating reaction. Equation 28, which relates the expected change in the kinetic order of MB^+ ($\Delta\alpha$) and the change in ionic strength of two solutions in which the rate law is determined for a given concentration of MB^+, can be derived from the Eq. 26 and the assumption that the rate law changes can be ascribed only to a change of the value of the reaction rate constant for the reaction

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Table VIII

Effect on Ionic Strength on

Mercaptoethanol[a] Oxidation Rates[b]

	Rate x 10^8 M sec^{-1}			
	$[MB^+] \times 10^6$			
μ	5.88	4.33	3.02	1.89
0.1	7.88	6.78	5.64	4.46
0.4	5.41	4.63	3.83	2.91
1.0	5.14	4.40	3.61	2.68
2.0	3.00	2.57	2.07	1.47

a. $[RSH] = 1.57 \times 10^{-2}$.
b. pH 10.3.

of the disulfide radical anion with MB^+. The equation predicts that the magnitude of the change in the kinetic order of MB^+ is

$$\Delta\alpha = -1.08 \left| \mu_{(1)}^{1/2} - \mu_{(2)}^{1/2} \right| / \log [MB^+] \qquad (28)$$

inversely related to the concentration of MB^+ and that changes in the kinetic order of MB^+ may be observable experimentally only if the rate laws are measured in solutions with markedly different ionic strengths.

Table IX shows the rate laws for the oxidation of mercaptoethanol by MB^+ at pH 10.3 at different ionic strengths. At the highest concentration of MB^+, the rate law, as expected, is not influenced by the ionic strength of the medium because the reaction of the disulfide radical anion is not a rate limiting factor. At the lower concentrations of MB^+, however, there is evidence that the rate law for the oxidation is dependent on the ionic strength of the medium. The rate law changes at the high ionic strength and low MB^+ concentrations are consistent with the changes that would be predicted if the rate constant for the electron transfer reaction from the disulfide radical anion to MB^+ were decreased in value, namely an increase in the kinetic order of MB^+ and a decrease in the kinetic order of the thiol. These are the same rate law changes observed at constant ionic strength when the concentration of MB^+ is very low (see Table III).

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Table IX

Effect on Ionic Strength on Kinetic Orders of Reactants

$$\text{Rate} = k_{obs}[MB^+]^{\alpha}[RSH]^{\beta}$$

μ	α	β
	$[MB^+] = 5.11 \times 10^{-6}$	
.1	.49 (.13)	1.51 (.13)
.4	.51 (.09)	1.51 (.17)
1.0	.51 (.09)	1.50 (.07)
2.0	.51 (.10)	1.42 (.08)
	$[MB^+] = 3.67 \times 10^{-6}$	
.1	.51 (.05)	1.52 (.10)
.4	.55 (.06)	1.51 (.09)
1.0	.55 (.05)	1.45 (.11)
2.0	.60 (.12)	1.35 (.10)
	$[MB^+] = 2.46 \times 10^{-6}$	
.1	.50 (.11)	1.48 (.04)
.4	.59 (.11)	1.42 (.18)
1.0	.64 (.11)	1.40 (.15)
2.0	.73 (.17)	1.27 (.10)

Summary

The agreement between the changes in the observed rate laws of the MB^+ oxidations of thiols with changes in the reactant concentrations, pH and ionic strength and the changes predicted from the steady-state derived rate laws based on the proposed mechanism for disulfide formation support this mechanism. Of particular interest to us is that it is possible to extract information concerning the behavior of a free radical chain reaction by kinetic analysis of the reaction. Such kinetic analysis of other redox reactions may be expected to be of value in not only establishing the possible intermediacy of free radicals but also the details of steps in the chain sequence in which free radicals are reaction intermediates.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch015

Abstract

The effects of pH, ionic strength, reagent concentration ratios and deuterium substitution of the sulfur-bonded hydrogens on both the rates and rate laws for the methylene blue oxidations of mercaptoethanol and dithioerythritol have been determined. A free radical chain mechanism consistent with the observed kinetic behavior of the oxidation reactions is proposed. A key feature of the proposed mechanism is the formation of the sulfur-sulfur linkage of the disulfide in the reversible formation of a disulfide radical anion ($\mathrm{RS\overset{\dot{-}}{S}R}$) as a chain propagating step in the chain sequence.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch016

16

The Geometry of Free Radical Displacements at Di- and Trivalent Sulfur

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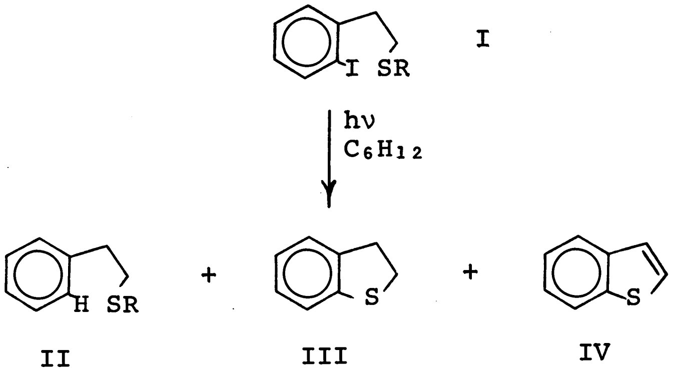
The displacement reaction (eq. 1) is one of the fundamental unit processes in free radical chemistry.

$$X\cdot + Y - Z \rightarrow X - Y + Z\cdot \qquad (1)$$

This process, with suitable variation in X, Y, and Z, serves to organize a very large number of free radical reactions.(1,2) The determination of rate constants (or relative rate constants) for these reactions has been a major preoccupation of free radical chemists. (1,2) It is striking, however, that we have very little understanding of the geometrical characteristics of these reactions. The historical reason for this is easy to see; free radical displacements at potentially chiral reaction centers are not common, thereby prohibiting the classical experimental approaches to stereochemical questions. For example, free radical displacements at carbon are rare and seem, in general, to be confined to the reactions of strained ring systems.(3-5) A few reaction centers (e.g., P, Si, some metals) can be prepared in chiral form and do invite the use of standard techniques.(6) However, many important displacement reactions take place at mono- or divalent reaction centers, where there is no possibility of using a chiral probe of mechanism. In this paper, we report the results of experiments designed to probe the preferred geometry and mechanism of radical displacements at divalent sulfur, a reaction center characterized by a plane of symmetry. Further, the technique is general and can presumably be used to study the geometries of other displacement reactions at centers which are inherently achiral or cannot be easily prepared in chiral form.(7)

Photolysis of methyl 2-(o-iodophenyl)ethyl sulfide (I, R=CH_3) in a cyclohexane solution gives a reduction product, methyl 2-phenylethyl sulfide (II, R=CH_3) and two displacement products, dihydrobenzothiophene (III) and benzothiophene (IV) (eq. 2). A control experiment involving the photolysis of



(2)

iodobenzene in cyclohexane containing dihydrobenzothiophene shows smooth conversion of dihydrobenzothiophene to benzothiophene. Benzothiophene is a secondary product and the yield of displacement product from the photolysis of the iodosulfide (I) is, therefore, taken as the sum of the yields of III and IV. Typical results for the photolysis of the methyl sulfide (I) are shown in Table I. Mass balances are good, showing that the important reaction products are identified; conversions are relatively low to minimize secondary reactions.

Table I.
Products of Photolysis of Methyl 2-(o-Iodophenyl)ethyl Sulfide[a] (I)

Solvent	$\frac{10^2\ \text{Red'n}^b}{\text{Red'n + Disp'}}$	% Conversion	Mass Balance
CH_3CN	10	23	96
Cyclohexane	17	20	94
Cyclohexane/0.5M BuSH	75	-	-
Cyclohexane/3M BuSH	87	11	100
BuSH (NEAT)	97	12	101

a. [I]~0.1M; 254 nm b. 10^2 [II]/([II]+[III]+[IV])

The key point to be derived from the data in Table I is that the displacement reaction is progressively interrupted by the reduction reaction as the hydrogen donor ability of the medium increases. This

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch016

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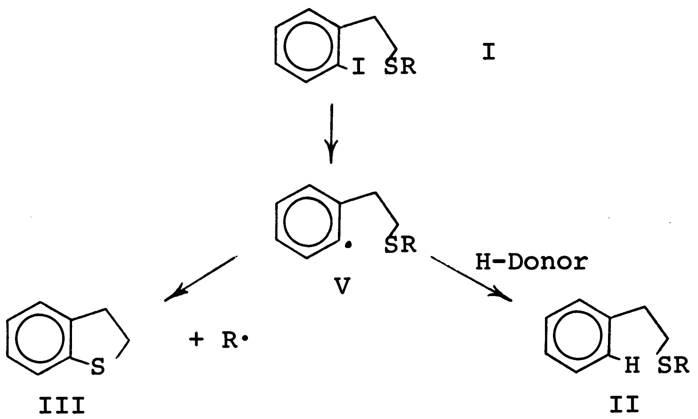
is clear evidence that displacement and reduction are competitive fates of a common precursor. Since the reduction reaction involves capture of the aryl radical (V) from the photolysis of the iodo sulfide precursor, (8,9) radical V is implicated as the source of the displacement product (eq. 3). Table II reports data showing that this displacement reaction proceeds with a number of leaving groups covering a wide range of "stability" as free radicals. We have investigated the fate of the leaving group (R·) in some of these displacement reactions and find typical free radical products (e.g., I, R=C_6H_5 gives C_6H_6 and C_6H_5I).



(3)

Table II

Products of Photolysis of Various 2-(o-Iodophenyl)ethyl Sulfides (I) in Media of Different H-Donor Ability[a]

R	10² Red'n/(Red'n + Disp')[b]		
	C_6H_{12}[c]	C_6H_{12}/BuSH[d]	BuSH[e]
C_6H_5[f]	28-40	-	97
CF_3	35	63	96
CH_3	17	75	97
C_2H_5	12	62	96
t-C_4H_9	9	71	95
$CH_2C_6H_5$[f].	9	52	92

a. [I]~0.1 M; 254 nm b. 10^2 [II]/[II]+[III]+[IV])
c. cyclohexane solvent d. 0.5 M n-BuSH
e. n-BuSH solvent
f. Mass balances are poor for these two cases due to competitive photochemical homolysis of $ArCH_2CH_2$--SC_6H_5 and $ArCH_2CH_2S$--$CH_2C_6H_5$. Mass balances are >95% in the other cases.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch016

Any concern that the displacement product originates in an excited state reaction or in competitive photolysis of the S-R bond is mitigated by the observation that reaction of iodosulfides (I) with tri-n-butyltin radicals, via the $Bu_3SnH/Bu_3Sn\cdot$ chain, also gives the reduction and displacement products (II and III); the distribution of products is a function of the concentration of the hydrogen donor, tri-n-butyltin hydride (Table III).

Table III

Distribution of Products in the Reaction of 2-(o-Iodophenyl)ethyl Sulfides (I) with Tri-n-Butyltin Hydride

	10^2 Red'n/(Red'n + Disp')[a]	
R	0.1 M Bu_3SnH[b]	~2.2 M Bu_3SnH[c]
C_6H_5	57	86
CH_3	49	-
$CH_2C_6H_5$	16	44

a. 10^2 [II]/([II]+[III]) b. In cyclohexane at 105°-110°, AIBN as initiator c. No solvent; 105°-110°

We conclude that we are dealing with a free radical displacement at divalent sulfur (eq. 3). We arrived at a similar conclusion in a study of the prototype of the system described in this paper.(10) Other free radical displacements at the divalent sulfur of sulfides are known.(11-17)

The salient point in this study is that radical V has, in principle, two displacement opportunities. One gives dihydrobenzothiophene, as described; the alternative would give radical VI, which should be reduced to an o-ethylphenyl sulfide (VII)(eq. 4). We have searched carefully for the product (VII) of this alternative displacement in every reaction described in this paper; VII is stable to the reaction conditions and is never observed.(18) Authentic radical VI($R=C_6H_5$, CH_3, $CH_2C_6H_5$) is available in cyclohexane from the thermal or photochemical decomposition of the corresponding peresters (VIII)and gives rise, *inter alia*, to dihydrobenzothiophene and the expected reduction product VII; the product of the alternative displacement, II, is not formed. Since it is experimentally established that the radicals V and VI are captured by cyclohexane to

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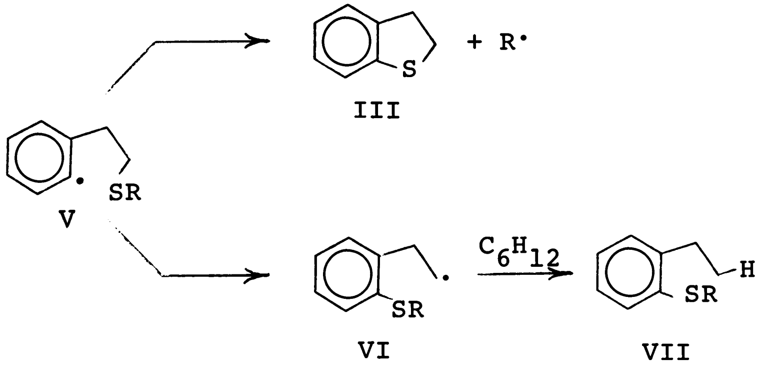

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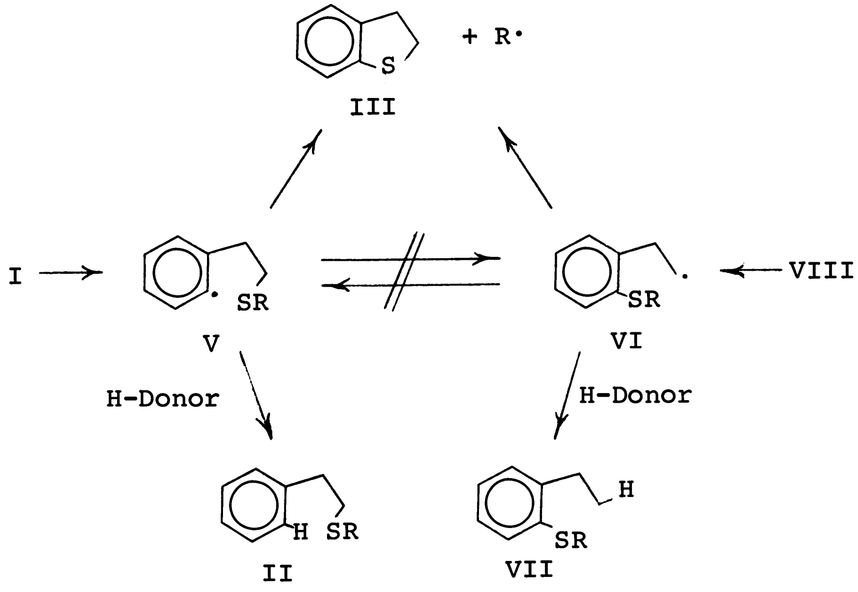
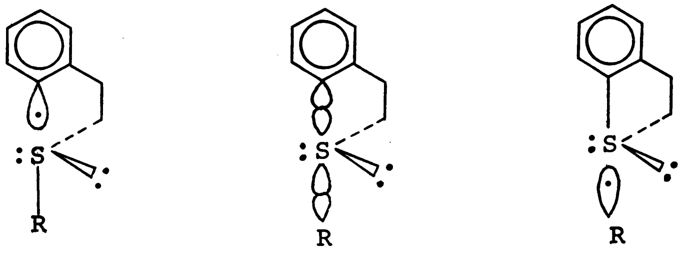
give stable products II and VII, respectively, it is certain that alternative displacement paths are less favorable than those giving dihydrobenzothiophene. These observations are summarized in Scheme I.

Scheme I



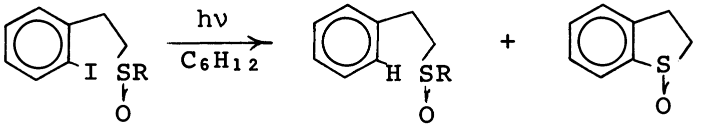
The displacement reactions which give dihydrobenzothiophene are exocyclic pathways; the alternative displacements are forced, and refuse, to follow an endocyclic pathway. The clear preference for the exocyclic pathway cannot, in the case of radical V, be assigned to differences in leaving group ability. For radical V, R=C_2H_5, the leaving groups in the two competing displacements are both $\cdot CH_2\sim$; for R=C_6H_5, CF_3 and CH_3, an argument based on the relative stability of the leaving group favors the endocyclic path, contrary to observation. In fact, the distinction between the two displacement reactions resides in the different geometries available to the competing displacement paths. In particular, the endocyclic path is constrained to a non-linear geometry by the cyclic nature of the reaction, whereas the exocyclic path can attain a linear arrangement of the three centers involved in the reaction. We conclude, therefore, that these free radical displacements at divalent sulfur involve a linear, back-side, "inversion" path; the alternative non-linear path has the character of a front-side, "retention" reaction. A three-center, three-electron description (IX) of the reaction path (Scheme II) is consistent with the observed geometrical preference. (19)

Scheme II



V IX II

An analogous free radical displacement reaction is observed at sulfoxide centers, but fails for the corresponding sulfone. Thus, photolysis of methyl 2-(*o*-iodophenyl)ethyl sulfoxide (X, R=CH_3) in cyclohexane gives methyl 2-phenylethyl sulfoxide (XI, R=CH_3) and dihydrobenzothiophene oxide (XII) (eq. 5). Photolysis of ethyl(2-*o*-iodophenyl)ethyl sulfone in cyclohexane gives only the reduction product, ethyl-



X XI XII (5)

2-phenylethyl sulfone. The results of the photolysis of the sulfoxides are given in Table IV.

Table IV

PRODUCTS OF PHOTOLYSIS OF ALKYL 2-(o-IODOPHENYL) ETHYL SULFOXIDES[a] (X) IN CYCLOHEXANE

R	$\frac{10^2\ \text{Red'n}}{\text{Red'n + Disp'}}$
CH_3[c]	47
CH_3[d]	54
$C(CH_3)_3$[c]	16

a. 254 nm in cyclohexane
b. $10^2[XI]/([XI]+[XII])$.
c. $[X] \sim 10^{-4}$ M.
d. $[X] \sim 10^{-2}$ M.

The course of these radical displacements at the trivalent sulfur center of the sulfoxides is analogous to that observed for the sulfides; the exocyclic displacement path obtains. Methyl (or t-butyl) o-ethylphenyl sulfoxide, the ultimate product of the alternative, endocyclic, displacement path is not observed. Our conclusion is also analogous; the free radical displacements at the sulfoxide sulfur involve a linear, back-side, "inversion" path. A three-center, three-electron description (analogous to IX) of the reaction path is consistent with these observations. It is useful to note that sulfoxide centers can be prepared in chiral form. These conclusions are, therefore, subject to test by classical techniques. Other free radical displacements at sulfoxide centers are known. (20,21)

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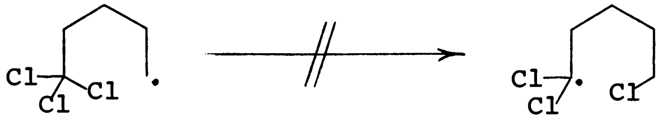
In summary, we note that the preference for the linear displacement geometry observed in this work probably obtains to free radical displacement at many other centers such as hydrogen, oxygen, halogen, and phosphorous. In other cases, suggestive results are already available.(22,23) For example, the failure (24) of the displacement at chlorine in eq. 6 is reasonably attributed to the non-linear, endocyclic geometry of the reaction path. In any case, the approach we have used to define the preferred geometry of the displacement at divalent and trivalent sulfur is, in principle, applicable to a variety of other systems where classical chiral techniques are not readily accessible.



(6)

It is important to consider the detailed nature of these displacement reactions at di- and trivalent sulfur centers; i.e., is the three-center, three-electron species (IX) a transition state or an intermediate on the displacement path? In fact, the present system was specifically designed to provide information on this question. As we have previously described, radical V partitions competitively between reduction and displacement paths. In Scheme III, mechanisms A and B involve the three-center, three-electron species as transition state and intermediate, respectively. If the concentration and the nature of the reducing agent (H-donor) are held constant, then the rate of formation of reduction product should be a constant, independent of the nature of substituent on sulfur, since the S-R bond is not involved in the rate-determining step of the reduction reaction. This reaction, therefore, can serve as a kinetic reference point. If the displacement reaction involves a simple one-step reaction (path A), the rate of formation of

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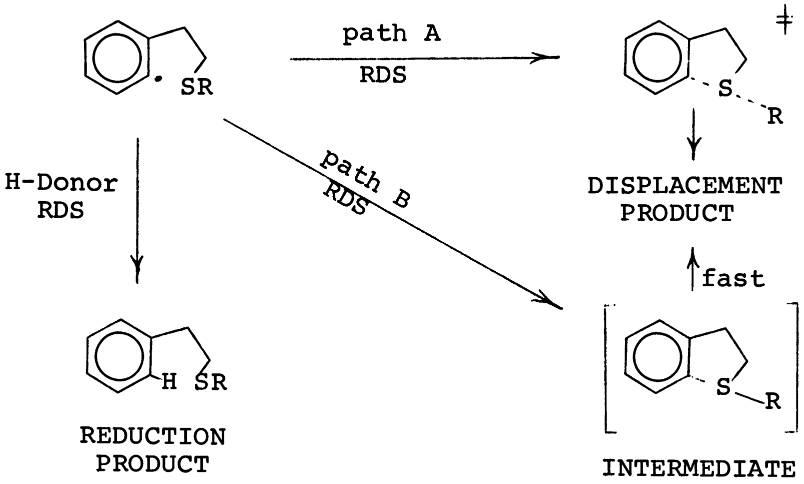
Scheme III



displacement product will vary with the nature of the leaving group (R). In the alternative mechanism involving rate-determining formation of an intermediate followed by fast product formation (path B), the rate of the displacement will, to a first approximation, not depend on substituent R, since the S-R bond is broken in a subsequent, fast step. Thus, the influence of the substituent R on the ratio of the yields of reduction to displacement product in a given solvent provides a potential distinction between mechanisms A and B.

In actual fact, a control experiment shows that this simple analysis cannot be strictly correct. Thus, the photolysis of 0.1*M* ethyl 2-(*o*-iodophenyl)ethyl sulfide in cyclohexane-d_{12} (I, R=C_2H_5) gives ethyl 2-(*o*-deuteriophenyl)ethyl sulfide (~16%) and ethyl 2-phenylethyl sulfide (~84%). Thus, there are sources of hydrogen, other than solvent, participating in the reduction reaction. In fact, the formation of benzothiophene as a side product in these reactions implicates dihydrobenzothiophene as a reductant. In addition, the starting material (I) has a variety of reactive C-H bonds α to sulfur and to the aromatic ring. As the nature of the substituent (R) is varied, the reducing ability of the starting material will vary and, therefore, the assumption that the rate of

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reduction is independent of $\dot{R}$ cannot be strictly true. On the other hand the 16/84 competition observed between reaction with C_6D_{12} and other H-donors clearly demonstrates that these different reductions have comparable rates. This is confirmed, in a related case, by the observation that the experimental reduction/displacement ratio is independent of the absolute concentration of the starting material and reaction products. Thus, photolysis of I (R=Me) at 0.1 M concentration gives reduction/displacement = 17/83, while photolysis at 10^{-4} M concentration of I gives a product ratio of 19/81. Thus, although the precise details of the reduction reaction may vary with the specific system, the total rate of reduction is approximately constant.

Tables II and III present the results of the determination of the distribution of products between reduction and displacement paths in cyclohexane solution as the nature of the substituent (R) is varied through a series of sulfides. The striking result is that big changes in the nature of the leaving group have little effect on the distribution of products. The relative rates of displacement by phenyl radical on the hydrogens of various alkanes is a model for the leaving group effect in a direct, one-step, displacement reaction. As shown in Table V, these displacements are very sensitive to the nature of the leaving group.

Table V

$$\phi\cdot + H\text{-}R \rightarrow \phi H + R\cdot$$

R	Rel. Rate(25)
CH_3	1
C_2H_5	40
$CH(CH_3)_2$	300
$C(CH_3)_3$	1600

The relative rates of displacement by phenyl at sulfur can be obtained from the data in Table II by assuming that the rate of reduction is independent of substituent (R). These relative rates are 1.0 ($R=CH_3$), ~1.5 ($R=C_2H_5$), ~2 ($R=t\text{-}C_4H_9$). The contrast is striking and clearly indicates that the S-R bond is not significantly involved in the rate-determining step for the formation of displacement product. A similar lack of sensitivity to leaving group is seen for the displacements at sulfoxide centers (Table IV). The displacement at hydrogen and sulfur are comparably exothermic and so it does not seem reasonable to dismiss the absence of a leaving group effect by an "early transition state" argument. Rather, these results would seem to argue clearly for the rate-determining formation of an intermediate, followed by a fast cleavage of the S-R bond (mechanism B).

However, the results of the competition between reduction and displacement at a sulfoxide center contradict this simple interpretation. Thus, radical V ($R{=}CH_3$) in the sulfide series gives a reduction/displacement ratio of 17/83 in cyclohexane. The corresponding radical derived from the methyl sulfoxide (X, $R{=}CH_3$) distributes approximately 50/50 between reduction and displacement paths in cyclohexane. This change in product distribution reflects a trivial change in the rate of displacement as the reaction center is changed from divalent sulfide to trivalent sulfoxide. Unfortunately, we do not have suitable models for the expected variations in rate with variations in the reaction center in the addition-fragmentation mechanism (mechanism B). The rates of addition of phenyl radical to sulfide and sulfoxide centers might just be coincidentally identical, although this seems very unlikely. Rather, the comparison of sulfide and sulfoxide reactions centers indicates that the formation of the new aryl-sulfur bond is also not involved in the rate determining step of the displacement reaction.

We are confronted, therefore, with a displacement reaction in which a new bond is formed to sulfur and an old bond to sulfur is broken and, yet, neither of these processes seems to be involved in the rate determining step. A clue to dissecting this dilemma is found in a comparison of the behavior of the prototype radical (XIII) with the radical involved in the present studies

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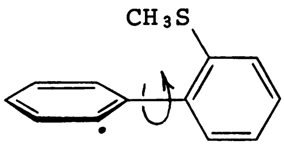
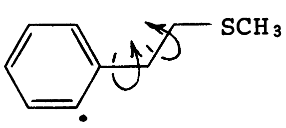


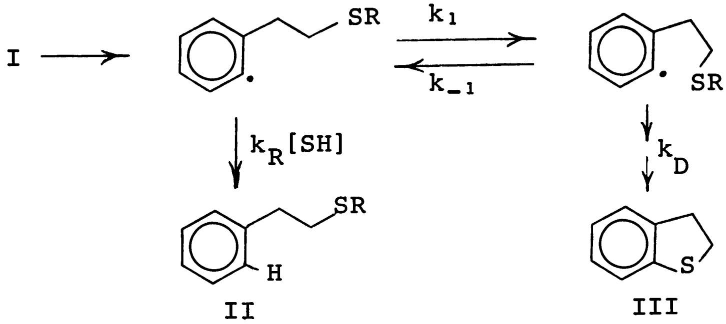
XIII



XIV

(XIV). In the presence of a very good reducing agent (*n*-butanethiol) as solvent, radical XIII still gives >95% displacement to give dibenzothiophene. In contrast, radical XIV is trapped under comparable conditions to give >95% reduction product. This structural change from XIII to XIV is, in fact, the only way in which we have been able to vary the rate of the displacement reaction. The significant difference between the two radicals is a conformational difference. Radical XIII needs only to "rock" about the central bond to bring the radical and the sulfur centers into juxtaposition; in XIV, significant rotation around the central "ethane" bond is required. As argued earlier, the distribution of the radicals between reduction and displacement products does not seem to be determined by the relative rates of radical attack on H-donor and the sulfur centers. Rather, the distribution of products is consistent with a competition between the rate of reduction and the rate of rotation around C-C bonds required to convert radicals XIII and XIV into conformations suitable for the displacement reactions at sulfur. This competition between reduction and conformational change has nothing to do with the sulfur and, therefore, changes in the ease of bond formation and/or bond breaking are irrelevant. This analysis is summarized in Scheme IV. When k_D is large, the product composition is determined by the ratio, $k_R[SH]/k_1$.

Scheme IV



$$\frac{[II]}{[III]} = \frac{k_R[SH]k_{-1}}{k_D k_1} + \frac{k_R[SH]}{k_1}$$

$$k_D > k_1,\ k_{-1} \sim k_R[SH]$$

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch016

Trotman-Dickenson reported an activation energy of 6.7 kcal/mol for the reaction of phenyl radicals with isobutane in the gas phase.(26) On the basis of this, we were confident that conformational interconversion (k_1, k_{-1}) would be rapid with respect to other reactions and that the product composition would be determined by the ratio $k_R[SH]k_{-1}/k_D k_1$. Recent experimental work by J. P. Lorand,(24) however, shows that the rate of reaction of phenyl radicals with the tertiary hydrogens of alkanes is about 10^2 times faster than that reported by Trotman-Dickenson. A competition between $k_R[SH]$ and k_1 is, therefore, plausible.

In summary, these experiments give a clear insight into the geometric course of the displacement reaction at sulfide and sulfoxide centers. The kinetic analyses do not permit a distinction between concerted one-step displacements and two-step mechanisms involving an intermediate because the processes in competition are probably reduction and conformational change. By implication, the rates of reaction at sulfur must be very rapid; they must be faster than either reduction or conformational change. The rate of reaction of hydroxyl radical with dimethylsulfoxide is reported to be diffusion controlled.(28) B. P. Roberts and coworkers have estimated the rate constant for displacement by t-butoxy radical at the sulfur of thietan at be 6×10^6 ℓ/m/sec at 243°K.(17) The addition of alkoxy radicals to dialkylsulfoxylates is competitive with the addition of these alkoxy radicals to phosphites, a reaction that proceeds at close to the diffusion controlled rate at room temperature.(29)

Finally, if the three-center, three-electron species is an intermediate, the observed geometric selectivity of the displacement requires that formation of products must be faster than equilibration of various isomeric three-center, three-electron species. Trialkoxy sulfuranyl radicals have been observed by e.s.r. These species are assigned a T-shape (like IX); equilibration of apical and equatorial substituents is slow on the e.s.r. time scale.(30,31)

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RECEIVED December 23, 1977.

17

Succinimidyl and Related Radicals

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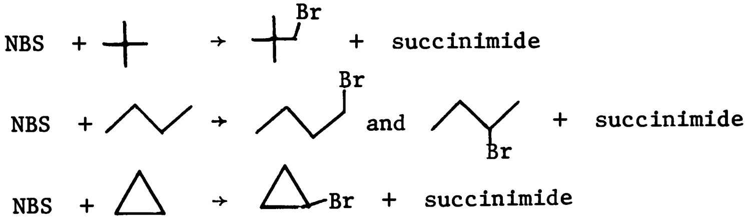
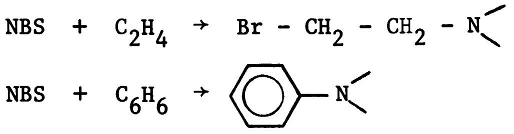
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch017

The chemical properties of succinimidyl radicals remained a mystery until the simultaneous recognition in the laboratories of Professor J. G. Traynham (1) and ours (2) that the radical could be a chain carrier in the sense first suggested by Bloomfield (3), albeit incorrectly (4), for the allylic bromination reaction.

For substrates which react readily with bromine atoms, succinimidyl mediated brominations are carried out in the presence of bromine scavengers (ethylene or t-butylethylene), employing a good solvent for NBS such as methylene chloride. In these circumstances bromination occurs with a selectivity which closely resembles Cl• mediated chlorinations.



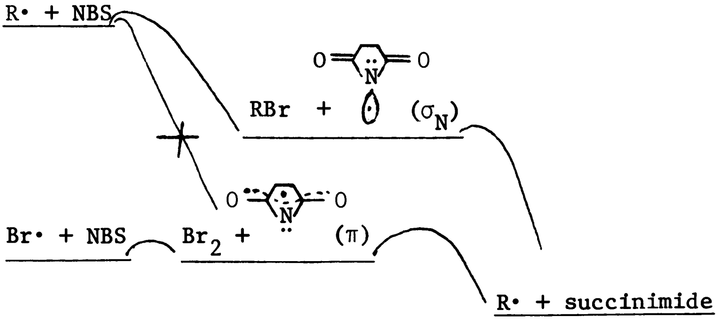
Additions to alkenes and arenes also occur readily.



In all of these reactions the selectivities are remarkable for radical reactions, being characteristic of no-stabilization of transition states by contributions from product structures. Each of these reactions appears to be an encounter-controlled reaction. As an illustration, succinimidyl radical adds to styrene as follows: to the double bond twice as rapidly as to the phenyl nucleus.

With substrates which do not react with bromine atoms, a mixture of Br_2 and NBS is effective in bromination, succinimidyl abstracting the H-atom, the product radical reacting with Br_2, and the Br• reacting with NBS to regenerate the succinimidyl radical.

These two methods for generating succinimidyl radicals (in the presence of olefins or bomrine) produce different succinimidyl radicals, ground state (π) in the presence of Br_2 and excited state (σ_N) in the presence of olefins (the evidence is described elsewhere).



The ring opening reaction, NBS → β-bromopropionyl isocyanate, is a reaction of σ, but not π.

Financial support came from the Air Force Office of Scientific Research (2748C).

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18

The Chemistry of Some Nitrogen-Centered Radicals

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch018

The chemistry of nitrogen-centered radicals has been reviewed comprehensively by Nelsen (1), and, more recently, by Forrester (2). The present paper deals largely with the chemistry of a more restricted group of these radicals, the dialkylamino radicals.

These radicals are an intriguing class because of their seemingly dichotomous behavior. Besides being normal, electron deficient, and therefore, electrophilic species, they are also basic and hence could exhibit nucleophilic properties. The pK_A of Me_2NH+ has been estimated to be 6.5-7.3 (3). Profound changes in amino radical reactivity are produced by protonation, complexation by metals, and by substitution with electron attracting groups. These effects can be seen as a result of changes in electron density around the central atom, i.e. these changes which reduce non-bonding electron density at nitrogen tend to make the radical more electrophilic, and, therefore, more reactive in typical radical reactions. It is convenient to discuss the reactivity of amino radicals in terms of the aforementioned types--protonated radicals, metal complexed radicals, those substituted by electron attracting substituents and, finally, the unadulterated, neutral amino radicals.

Protonated Amino Radicals. The reaction of hydroxylamine with $TiCl_3$ in aqueous, acidic methanol results in the formation of the simplest protonated amino radical, $NH_3^{+}\cdot$. This radical added readily to butadiene and to simple olefins to form products which were the result of coupling of the intermediate β-aminoalkyl radicals (4). The addition reactions of protonated dialkylamino radicals were described in a series of elegant papers by Neale and his co-workers (5-10). The radicals were generated from the appropriate N-chloroamines in presence of the unsaturated system. The most effective acid solvent combination was found to be 4M sulfuric acid in glacial acetic acid, but other acid/solvent combinations were also used. The reactions proceeded by chain mechanisms, which were initiated by light or by

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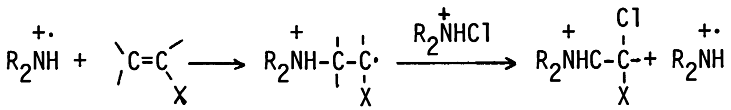
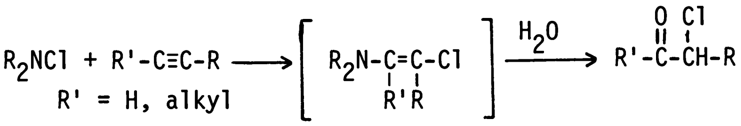
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch018

Fe(II) salts, although spontaneous initiation was also observed.



$$\overset{+\cdot}{R_2NH} + \;\rangle C=C\langle_{X} \longrightarrow R_2\overset{+}{N}H-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{X}{C}}\cdot \xrightarrow{R_2\overset{+}{N}HCl} R_2\overset{+}{N}HC-\overset{Cl}{\underset{X}{C}}- + \overset{+\cdot}{R_2NH}$$

The reaction was most effective when X was an electron withdrawing substituent, but only because this suppressed the competing ionic chlorination of the double bond. In some cases, the ionic chlorination was the predominant reaction. Protonated amino radical addition to unsubstituted olefins, acetylenes and allenes, however, gave acceptable yields of products, particularily in the case of the sterically unhindered substrates. The products obtained from the acetylenes were the α-chloroketones or aldehydes.

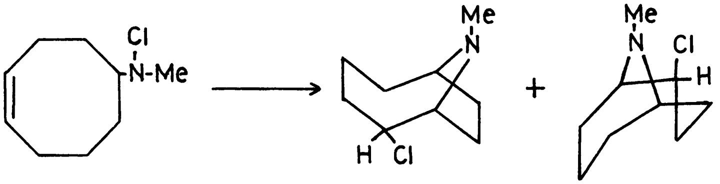


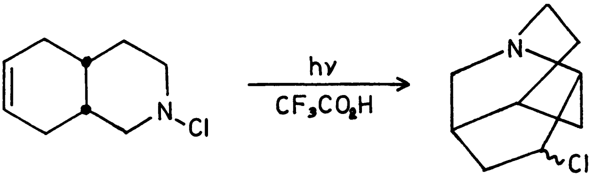
$$R_2NCl + R'-C\equiv C-R \longrightarrow \left[R_2N-\underset{R'}{C}=\underset{R}{C}-Cl \right] \xrightarrow{H_2O} R'-\overset{O}{\overset{\|}{C}}-\overset{Cl}{CH}-R$$

$R' = H$, alkyl

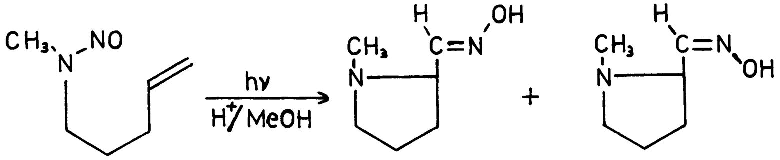
One interesting aspect of the reactivity of protonated amino radicals is that the reactivity toward unsaturation is much higher than toward allylic abstraction. There is essentially no competing allylic abstraction even in very favorable cases (7).

Intramolecular addition of protonated amino radicals has been examined by several groups. The following reaction has been carried out using silver perchlorate in acetone, ferrous sulfate or acidic (4M H_2SO_4) conditions (11). The yields varied, depending on conditions, but the authors concluded that either a metal-coordinated or a protonated amino radical was the reactive species. The elegant synthesis of the azatwistane also probably involved the protonated amino radical (12). Chow (13) has



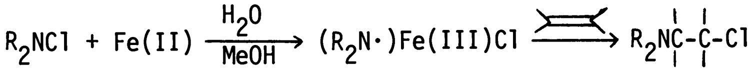


studied acid catalyzed photolysis of N-nitrosamines. The photolysis leads to protonated amino radicals, which add to alkenes to produce, generally, amino oximes. In the intramolecular case, efficient ring closure to the five membered ring occurs, as in the following example (14,15).



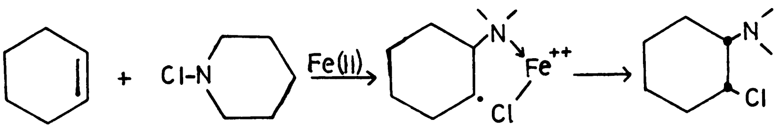
The question of amination of aromatics by protonated amino radicals has been examined extensively by Minisci and co-workers (16). Benzene is aminated in good yields by a variety of N-chloroamines in acidic solutions, catalyzed by iron(II) sulfates. With activated aromatics competing chlorination and sulfonation complicates the reactions, but in many cases good yields of the substituted anilines are obtained. In the case of alkylbenzenes, benzylic chlorination competes with nuclear amination. The latter is favored by high acid concentrations. Thus, the reaction of toluene with N-chlorodimethylamine (17) gives 95 percent amination and 6 percent benzylic chlorination in neat H_2SO_4, but 100 percent benzylic chlorination in neat acetic acid. The amount of nuclear amination increases with the concentration of H_2SO_4 in acetic acid.

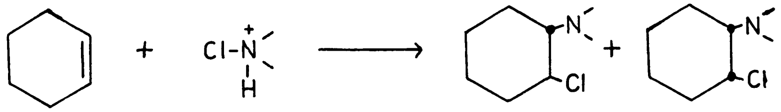
Complexed Amino Radicals. Since protonated amino radicals perform so well in addition reactions it is not altogether surprising that metal complexed amino radicals also add well to unsaturated substrates. This area of amino radical chemistry has been studied by Minisci and his co-workers (18-21).



$$R_2NCl + Fe(II) \xrightarrow[MeOH]{H_2O} (R_2N\cdot)Fe(III)Cl \xrightarrow{>C=C<} R_2N\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-Cl$$

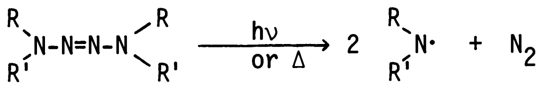
For example, the addition of N-chloropiperidine to cyclohexene, catalyzed by iron(II) sulfate, gives predominately the cis product in good yield (21),



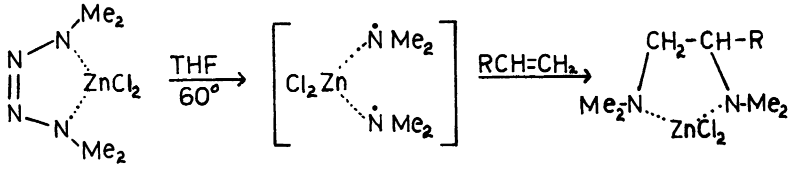


The protonated amino radicals give a mixture of cis and trans products. The stereoselectivity of the complexed radical is presumably due to the intramolecular transfer of the chlorine atom. A decided advantage of the addition of N-chloramines catalyzed by a redox process in neutral media as opposed to the acid catalyzed reaction, is that the reaction conditions are much milder and ionic chlorination is not a competing process.

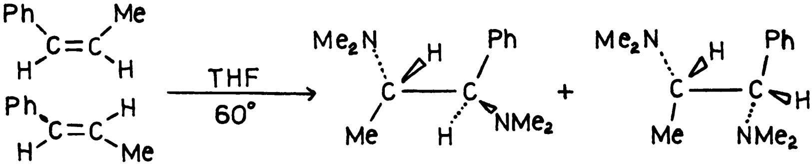
Tetralkyl-2-tetrazenes are excellent, general sources of dialkylamino radicals because they are prepared readily from the corresponding unsym-dialkylhydrazines by oxidation, and can be decomposed to the radicals either by thermal or photochemical methods (see below).



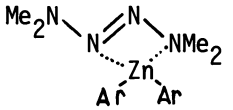
In keeping with their amine origins, tetrazenes are basic and can act as ligands in coordination complexes. Noltes and van den Hurk (22) reported that tetrazenes formed isolatable 1:1 complexes with zinc halides, zinc alkyls and aryls. They found that the zinc chloride complex was particularly unstable and lost nitrogen on heating between 40° and 60°. The structure which these workers proposed for the complex and its ready loss of nitrogen suggested to us (23) that the following reaction was occurring with tetramethyl-2-tetrazene (TMT).



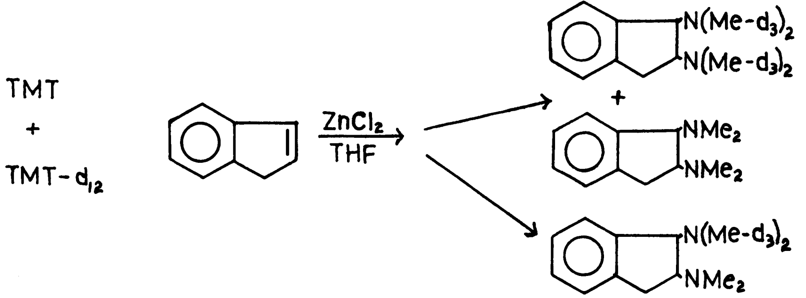
The putative biradical intermediate was trapped by styrene and α-methylstyrene in 30-40 percent yields. That the reaction was not concerted was shown by the fact that cis and trans-β-methyl styrenes gave an identical mixture of threo and erythro diamine adducts (24).



Doubts about the validity of the biradical intermediate arose when the single crystal x-ray structure of the bis(perfluorophenyl)tetramethyl-2-tetrazenezinc(II) was shown to be the following (25).



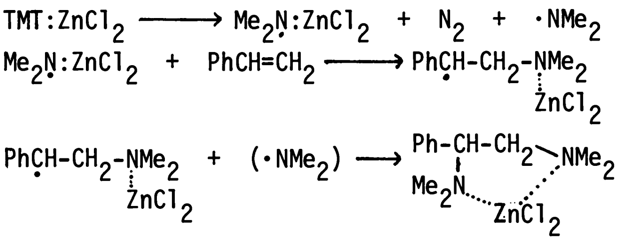
The transoid stereochemistry of the tetrazenes seems to be more stable than the cisoid, as suggested by other x-ray structures of tetrazenes, carried out in our laboratories (26). It thus became difficult to rationalize the biradical on the basis of the structure of the final complex. The crucial evidence, which destroyed the biradical hypothesis, was the result of the following isotope scrambling experiment. A mixture of TMT and TMT-d_{12} was treated with zinc chloride in refluxing THF in the presence of excess indene. If the reaction to form the diamine adduct proceeded via the biradical, the resulting diaminoindane would have been either fully labelled in methyl groups or not at all. If, on the other hand, the dimethylamino groups came from different tetrazenes, the product would have contained approximately half-labelled and half-unlabelled methyl groups. The experiment showed that the latter case obtained and, therefore, the biradical could not be an intermediate.



Indene was used instead of styrene in this experiment because the diamine adduct of styrene failed to give a molecular ion in the mass spectrum.

The addition of the amino radicals from TMT to styrene catalyzed by zinc chloride is now seen to be a stepwise process.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch018



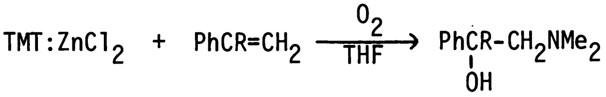
$$TMT{:}ZnCl_2 \longrightarrow Me_2\underset{\bullet}{N}{:}ZnCl_2 + N_2 + {\cdot}NMe_2$$

$$Me_2\underset{\bullet}{N}{:}ZnCl_2 + PhCH{=}CH_2 \longrightarrow Ph\underset{\bullet}{C}H\text{-}CH_2\text{-}\underset{\underset{ZnCl_2}{\vdots}}{N}Me_2$$

$$Ph\underset{\bullet}{C}H\text{-}CH_2\text{-}\underset{\underset{ZnCl_2}{\vdots}}{N}Me_2 + ({\cdot}NMe_2) \longrightarrow Ph\text{-}\underset{|}{C}H\text{-}CH_2\text{-}NMe_2 \quad Me_2N\cdots ZnCl_2$$

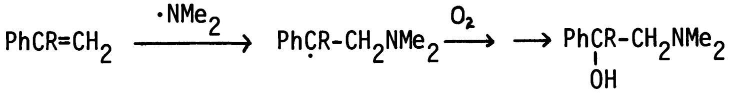
The product crystallized out of the reaction mixture as the zinc chloride complex. The state of the dimethylamino radical shown in brackets in the last equation is uncertain. It may or may not be coordinated with zinc chloride or it may originate from an S_H2 displacement by styryl radical on the TMT:ZnCl$_2$ complex. Curiously no dimerization or disproportionation of the β-aminostyryl radical was observed. Perhaps the coordination by zinc chloride prevents other reactions from occurring, allowing the combination with the second amino radical to occur reasonably efficiently. The reaction works well only with conjugated alkenes. Only slight reactions were observed with olefins such as 1-octene.

The addition reactions of the zinc chloride-complexed amino radicals, described above were carried out in the absence of oxygen. When oxygen was bubbled through the reaction mixture, the products were not the corresponding diamines but rather amino alcohols were isolated (27). Thus with styrene and α-methylstyrene, the reaction proceeded in the following fashion.



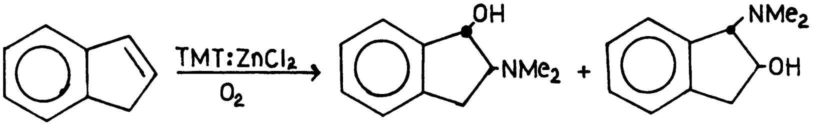
$$TMT{:}ZnCl_2 + PhCR{=}CH_2 \xrightarrow[THF]{O_2} Ph\underset{\underset{OH}{|}}{C}R\text{-}CH_2NMe_2$$

These products could be accounted for by assuming the addition of an amino radical to the styrene, followed by capture of the intermediate radical by oxygen and the reductive breakdown of the resulting hydroperoxide to the alcohol. A reaction of that type has been discussed by Minisci and Galli (28).



$$PhCR{=}CH_2 \xrightarrow{{\cdot}NMe_2} Ph\underset{\bullet}{C}R\text{-}CH_2NMe_2 \xrightarrow{O_2} \longrightarrow Ph\underset{\underset{OH}{|}}{C}R\text{-}CH_2NMe_2$$

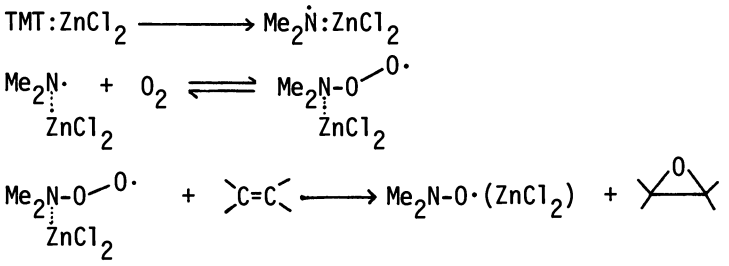
This mechanism, however, does not explain the behavior of the other alkenes studied. Thus indene gave two amino alcohols. Only one of them, trans-2-(dimethylamino)-1-indanol, could



have been formed by the radical addition mechanism above. Likewise, the reaction of cis and trans-β-methylstyrenes gave products which were difficult to rationalize by that mechanism. Thus, the cis isomer gave exclusively the threo-products, 1-(dimethylamino)-1-phenyl-2-propanol and 2-(dimethylamino)-1-phenyl-1-propanol, while the trans isomer gave exclusively erythro-1-(dimethylamino)-1-phenyl-2-propanol. The stereospecificity of this reaction, as well as the wrong regiospecificity, are sufficient grounds to reject the radical addition mechanism.

All of these products can be accounted for by the assumption that the initial products of the reaction are the alkene epoxides, which then react with either dimethylamine or TMT to form the amino alcohols. Thus, when authentic cis and trans-β-methylstyrene epoxides were treated with dimethylamine or the TMT:ZnCl$_2$ complex in THF solution precisely the same amino alcohols were formed as in the TMT:ZnCl$_2$:O$_2$ reaction. The same was true for the other alkenes studied. The incursion of the radical reaction, however, can be detected with indene because the only product formed from indene epoxide and dimethylamine was trans-1-(dimethylamino)-2-indanol and, hence, the other regioisomer must have been formed by the radical reaction. The epoxidation hypothesis was strengthened considerably by the observation that cyclooctene reacted with the TMT:ZnCl$_2$:O$_2$ mixture to give cyclooctene oxide in 12 percent isolated yield. This epoxide resists nucleophilic ring opening because the backside approach to the epoxide function is sterically hindered. In accord with this, no amino alcohol was formed when cyclooctene oxide was treated with dimethylamine or with the TMT:ZnCl$_2$ mixture.

The epoxidation reaction proceeds in the following fashion.



$$\mathrm{TMT{:}ZnCl_2} \longrightarrow \mathrm{Me_2\dot{N}{:}ZnCl_2}$$

$$\underset{\vdots\;\mathrm{ZnCl_2}}{\mathrm{Me_2N\cdot}} + \mathrm{O_2} \rightleftharpoons \underset{\vdots\;\mathrm{ZnCl_2}}{\mathrm{Me_2N{-}O{-}O\cdot}}$$

$$\underset{\vdots\;\mathrm{ZnCl_2}}{\mathrm{Me_2N{-}O{-}O\cdot}} + \mathrm{{>}C{=}C{<}} \longrightarrow \mathrm{Me_2N{-}O\cdot(ZnCl_2)} + \text{epoxide}$$

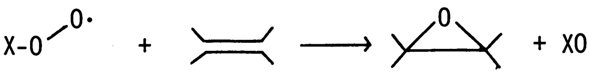
When the reaction was carried out in the cavity of an esr spectrometer a transient spectrum of a radical was observed, which

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch018

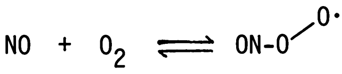
could be simulated adequately by using the literature values for the hyperfine coupling constants for dimethylnitroxyl (a_N = 15.2G, a_H = 12.3G). The line-width (3.9G) was broadened, probably by the presence of oxygen. Nitroxyl radicals which have α-hydrogens decay relatively rapidly by disproportionation to the corresponding hydroxylamine and nitrone (29). Our reaction mixtures always contained considerable quantities of dimethylhydroxylamine. The reaction of the dimethylamino radical with oxygen is reversible because no epoxidation was observed when the temperature of the reaction mixture was increased to 100° or when the oxygen supply was restricted. Under these conditions the diaminated products were formed.

The formation of the simplest amino peroxyl radical, NH_2O_2, has been observed in the reaction of potassium ozonide with ammonia under photolytic conditions (30) if Raman spectrum has been determined. This radical has also been postulated as an intermediate in the reaction of NH_2 with oxygen (31).

The concept of a direct oxygen atom transfer from a radical precursor to an alkene to give an epoxide and another radical ought to be a general reaction. Its energetics, however, require that the final product radical be a stable one, at least substantially more stable than the precursor peroxy radical.

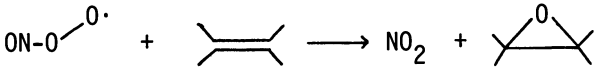


The above conditions are met by the radical formed from nitric oxide and oxygen, the nitrosoperoxyl radical (32). This radical,



$$NO + O_2 \rightleftharpoons ON\text{-}O\text{-}O\cdot$$

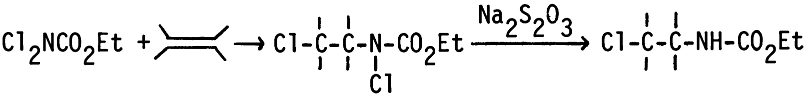
if left alone presumably reacts with another nitric oxide molecule to form two molecules of nitrogen dioxide. In the presence of an alkene however, the ONOO· radical can transfer an oxygen atom to give the epoxide and nitrogen dioxide.



The reaction is remarkably clean for some alkenes, notably cyclooctene, which is transformed to the epoxide with no side products. Other alkenes, however, give a plethora of products, many containing nitrogen, together with some epoxide. Reactive olefins sometimes undergo rapid reactions but no epoxides are isolated. For example α-methylstyrene is cleaved quantitatively to acetophenone. This is also the fate of α-methylstyrene oxide when that substance is exposed to the NO/O_2 mixture. The cleavage of the styrene epoxide does not make the substance an obligatory intermediate in the reaction of α-methylstyrene with NO/O_2, but the general instability of unprotected epoxides in reaction mixtures containing NO, NO_2 and O_2 makes such a hypothesis reasonable.

An interesting reaction of the NO/O_2 system is with a mixture of α- and β-cedrene. The β-isomer is left intact.

Amino Radicals Substituted by Electron Attracting Substitutents. The reactivity of these radicals, particularly toward addition reactions, in greatly enhanced, relative to dialkylamino radicals. The photochemically initiated reaction between N-bromo-*bis*-trifluoromethylamine and ethylene gave a 95% yield of the addition product (33). The *bis*-trifluoromethylamino radical was the chain carrying species. Although the authors also reported efficient addition to several polyfluoroolefins, no attempt was made to add this interesting radical to olefins containing allylic hydrogens. Neale and Marcus have reported good to excellent yields of addition of N-halocyanamides and N-halosulfonamides to conjugated and non-conjugated olefins (34). The amidyl radicals generated from N-chlorourethanes add to unsaturated systems efficiently (35-37). Both N-monochloro and N,N-dichlorourethanes can be used, although the latter have been studied more frequently. Some competition from allylic abstraction has been observed with the radicals derived from the N-halourethanes. The additions of dichlorourethanes are spontaneous but are accelerated by light, exhibit an induction period, and are retarded by oxygen.



$$\mathrm{Cl_2NCO_2Et} + \mathrm{C{=}C} \longrightarrow \mathrm{Cl{-}C{-}C{-}}\underset{\mathrm{Cl}}{\mathrm{N}}\mathrm{{-}CO_2Et} \xrightarrow{\mathrm{Na_2S_2O_3}} \mathrm{Cl{-}C{-}C{-}NH{-}CO_2Et}$$

In spite of earlier reports to the contrary, the addition of amidyls derived from N-halocarboxamides has been shown to be an efficient reaction (38) as long as the temperature of the reaction mixture was kept low. Thus high yields of addition of N-chloro or N-bromoacetamide to cyclohexene were observed at -70°. At higher temperatures allylic abstraction predominated. The addition was also quenched by N-methylation of the amidyl radical.

Neutral Amino Radicals. It is generally accepted that dialkylamino radicals add to olefins very reluctantly. This is a little surprising because thermodynamic calculations, based on the best thermochemical values (39), indicate that the addition of NH_2 to ethylene ought to be exothermic by about 17 kcal/mole. The apparent lack of reactivity suggests therefore that there is a relatively high activation barrier to this reaction. Indeed, this was found to be the case in the *ab initio* SCF-MO-CI calculation of the potential surface of the NH_2 plus ethylene reaction (40, 41). The best activation energy for that reaction appears to be in the range of 16-20 kcal/mole (41). However, Lesclaux and Khe (42) reported that NH_2 radicals in the gas phase generated from the flash photolysis of ammonia, reacted with ethylene, propene and 1-butene with an energy of activation of $\sim$4 kcal/mole, in all three cases. Bamford (43) found, on the other hand, that dimethylamino radicals gave exclusively allylic hydrogen abstraction from propene, in the gas phase. No product studies were carried out by Lesclaux and Khe, and it is possible that their kinetics might be complicated by allylic abstraction in the propene and butene case. Addition of dimethylamino radicals to ethylene was reported in the gas phase, but no yields were given (44). Whatever the true value of the activation energy might be, there is no doubt that amino radicals do not add to alkenes rapidly.

Dialkylamino radicals are likewise sluggish in H-abstraction reactions. Nelsen and Heath (45) found that arylmethylamino radicals, generated from the corresponding diaryldimethyl-2-tetrazenes, are difficult to scavenge with H-atom donors. These workers found, however, that the radicals induced the decomposition of the parent tetrazenes, presumably by H-atom abstraction. We (46) also found that induced decomposition was an important reaction in the thermal decomposition of tetramethyl-2-tetrazene when the concentration of the tetrazene was greater than 0.2M. The relative rates of benzylic hydrogen abstraction from substituted toluenes by the dimethylamino radicals were correlated by the Hammett equation, using σ^+ values; the ρ-value of -1.1 indicated that the radical is moderately electrophilic in abstraction reactions (46). The deuterium isotope effect for that reaction was found to be 4.0. Interestingly, the ρ-value for H-atom abstraction from toluenes by a protonated amino radical, the piperidinium radical, was found to be -1.34 (47). Thus it appears that protonation does little to change the electrophilicity of the radical in abstraction reactions.

Although neutral dialkylamino radicals generally do not add to simple alkenes it was possible to observe some addition of dimethylamino radicals to styrene and α-methylstyrene (48). Photolysis of tetramethyl-2-tetrazene (TMT) in cyclohexane, at room temperature, in the presence of α-methylstyrene resulted in the formation of small but reproducible yields of addition products. The bulk of the amino radicals were consumed in the formation of tetramethylhydrazine and dimethylamine. The relative rate of formation of the adducts from substituted α-methylstyrenes were correlated by the Hammett equation yielding a $\rho = +0.69 \pm 0.03$ (corr. coeff. .99). This result indicates that the dimethylamino radical behaves like a nucleophile in addition reactions i.e. the styrenes substituted by electron attracting substituents reacted more rapidly than the electron rich styrenes. This result is in marked contrast to that obtained for dimethylamino radicals coordinated by zinc chloride (48). These

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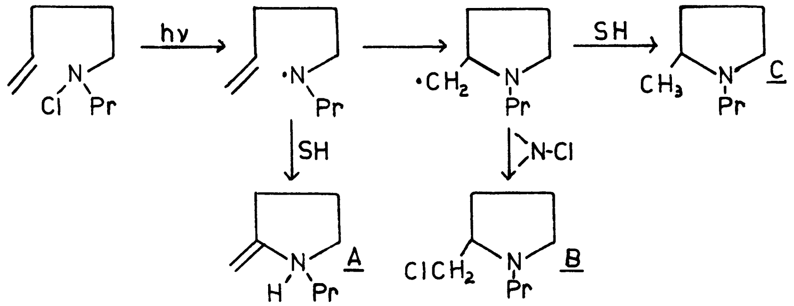
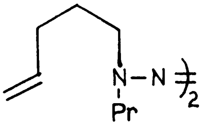
radicals generated from the TMT:$ZnCl_2$ complex (see above) added reasonably efficiently to α-methylstyrenes. The Hammett correlation yielded a ρ value of -0.98 ± .04 (corr. coeff. .99). This cross-over from nucleophilicity to electrophilicity illustrates very graphically how the lone pair on nitrogen influences amino radical reactivity.

The intramolecular cyclization of amino radicals, where the nitrogen is not coordinated by a metal or the proton, has not been studied extensively. Surzur, Stella and Tordo (49) reported the photolysis of N-chloro-N-(4-pentenyl)-N-propylamine in various neutral solvents. The data were accounted for by the following scheme.

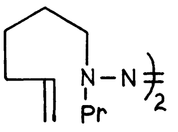


The photolysis was carried out in acetic acid/water, in methanol and in isopropyl alcohol. In the first solvent B was formed exclusively, but in the alcohols, mixtures of A, B, and C were obtained. While some of the details of this reaction are not clear, the evidence for the intramolecular addition of the neutral amino radical seems to be strong.

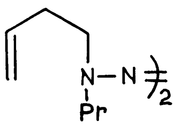
We (50) prepared the following tetrazenes in an effort to provide unequivocal sources of the alkenyl-substituted amino radicals.



D



E



F

The pentenyl tetrazene D gave on photolysis or thermolysis the same radical as that reported by Surzur and co-workers. The tetrazene E led to a radical which could cyclize to a 6 or a 7-membered ring, while the radical from F had only the possibility of cyclization to a 5-membered ring (a 4-membered ring being unlikely).

Photolysis of the tetrazene D through Pyrex in cyclohexane

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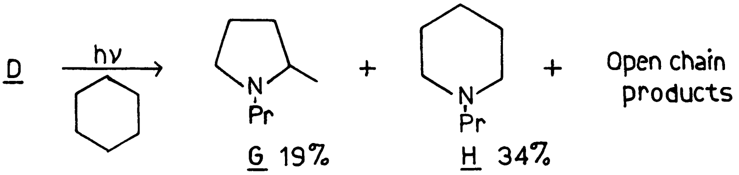
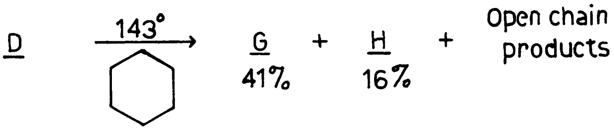
gave a large number of products. However, the cyclization products were formed in reasonable yields. It is interesting to

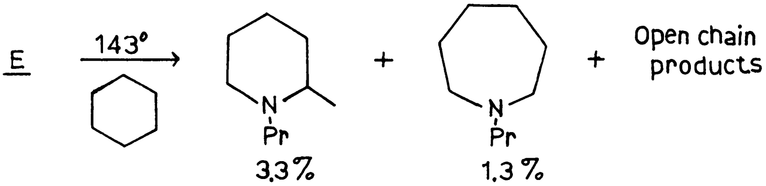


note that photolysis of D at room temperature leads to almost twice as much of the N-propylpiperidine H as the pyrrolidine G. Surzur et al (49) did not observe any H in their system. Interestingly, however, the thermolysis of D at 143° in cyclohexane (reaction carried out in sealed tubes) led to only 16% of H but 41% of G.



Thus the ratio of the cyclic products was inverted at the two temperatures. The reason for this inversion is not at all clear. One possible explanation, however, might be that at higher temperatures the reaction is less selective, i.e. the transition state is less bound, and hence the kinetically favored product G is formed predominatly. At the lower temperature of the photochemically generated radical, the reaction is more selective, the transition state is more product-like and hence the 6-membered ring product H is formed. This argument is really a loose interpretation of the observations in terms of the reactivity-selectivity principle (51).

Thermolysis of the hexenyl tetrazene E in cyclohexane gave the following cyclic products.



The photolysis gave no detectable cyclized materials. The open chain products were either monomers or dimers of the intermediate N-propyl-N-(5-hexenyl)amino radical, presumably by the Hofmann-Loeffler type of rearrangement.

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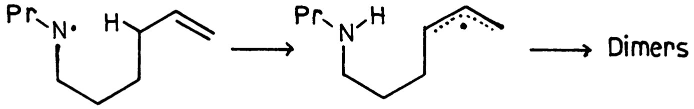
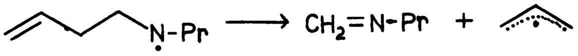


These various rearranged dimers corresponded to approximately 65 percent of the product. The hydrazine, the product of the N-N-coupling of the first formed radical, was isolated in less than one percent yields. Thus, in the hexenyl radical case the cyclization does not compete well with rearrangement.

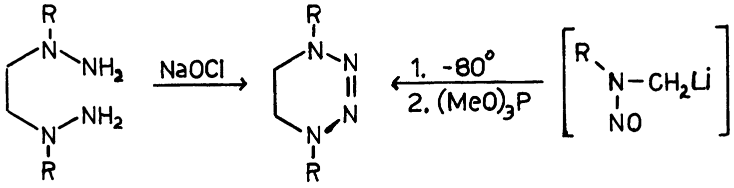
No cyclic products were obtained from either the photolysis or the thermolysis of the butenyl tetrazene, F. The principal isolated product in the photochemical reaction was the parent amine, N-propyl-N-(3-butenyl)amine, formed in about 50 percent yield. In the thermolysis reaction the principal reaction was the β-scission.



The allyl radical then entered into a variety of cross-combination reactions. The β-scission of amino radicals had been observed previously in the case of the methyl-(2-phenylethyl)-aminium radical (52).

The preferred transoid geometry of tetraalkyl-2-tetrazenes is in common with other azo compounds. In this case, however, the cisoid form of the acylic tetrazenes has never been isolated. In fact Roberts and Ingold (53) suggested that the photochemical decomposition of tetrazenes involved the photochemical *trans* to *cis* isomerization followed by the thermal loss of nitrogen from the *cis*-isomer. Some acylated *cis*-tetrazenes have been reported (54,55), but the chemical behavior of these substances differs substantially from the tetraalkyl analogs.

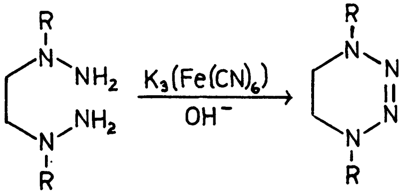
Nelsen and Fibiger (56) prepared the first authentic *cis*-tetrazene, 1,4-dimethyl-1,4,5,6-hexahydro-1,2,3,4-tetrazine.



The *cis*-cyclic tetrazene was formed in 5 percent yield by basic oxidation of the precursor dihydrazine (R=Me) with sodium hypochlorite. A general synthesis of tetrazenes of this type was worked out by Seebach and co-workers (57,58,59). The method involves the low temperature self-condensation of the lithium derivatives of nitrosamines to give the corresponding tetrazene N-oxides. The oxygen is then readily removed by treatment with trimethylphosphite.

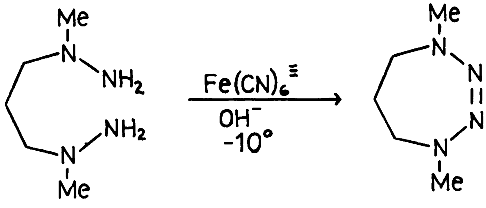
Nelsen and Fibiger studied the thermal decomposition of the *cis*-tetrazene in tetralin over the temperature range of 130 to 144°. The activation parameters, $\Delta H^{\ddagger} = 38$ kcal/mole and $\Delta S^{\ddagger} = 17$ eu, obtained from the kinetic data, were surprisingly high. The activation parameters for tetramethyl-2-tetrazene, for comparison, are $\Delta H^{\ddagger} = 36.1$ kcal/mole and $\Delta S^{\ddagger} + 4.7$ eu. These were obtained from a gas phase study (60), but indications are that they do not change significantly in solution (56). This unexpected result was explained by Nelsen on the basis of a conformational effect, i.e. that restricted movement of the *cis*-cyclic structure prevents the attainment of the most favorable conformation which leads to reaction. Thus, the six-membered ring *cis*-tetrazene is to be considered as a special case, its stability being the product of the conformationally restricted structure.

It was of interest to prepare and study the next higher homolog. Kreher and Wissman (61) reported the preparation of several 1,4-diaryl- and 1,4-dialkyl-1,4,5,6-tetrahydro-D-tetrazines by oxidation of the corresponding hydrazines.



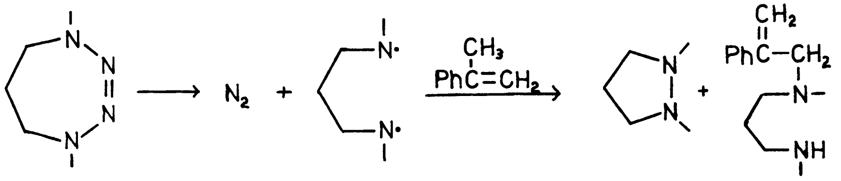
$R = C_6H_5$, p-MeC_6H_4, C_6H_{11}

They also reported unsuccessful attempts to prepare the higher homologs. We repeated this procedure using N,N'-dimethyl-N,N'-diaminopropylenediamine as the starting hydrazine. Careful, low temperature isolation of the product yielded the corresponding seven membered ring *cis*-tetrazene in up to 50 percent yield.



The thermolysis of this tetrazene (1,4-dimethyl-1,2,3,4-tetraaza-2-cycloheptene) indicated that the material behaved as expected for the *cis*-structure. The rates were measured at five degree intervals over the temperature range of 65-90°. The Arhennius parameters calculated from the kinetic data were, $\Delta H^{\ddagger} = 19 \pm 1$ kcal/mole, $\Delta S^{\ddagger} = -10.5 \pm 1$ eu. Based on differences in the activation enthalpies between *trans* and *cis* azoalkanes, Nelsen (56) predicted that the difference between the *cis* and *trans* tetrazene activation energies ought to be on the order of 6-8 kcal/mole. It is apparent now that the difference is approximately double of that seen in azoalkanes. The primary reason that our tetrazene could be isolated at all is that the entropy of activation is quite negative, suggesting that the rather loose seven-membered ring must become more rigid in the transition state. It is therefore entirely possible that Ingold and Roberts may have been correct in their assumption that the photochemical decomposition of acyclic tetrazenes proceeds by photoisomerization to the *cis* form and the thermal decomposition of that isomer to the amino radicals.

The products of the decomposition the tetraazacycloheptene are the five-membered ring hydrazine plus other, as yet unidentified, materials. When the decomposition was carried out in a large excess of α-methylstyrene some of the initial biradical was trapped as a radical addition product.



Acknowledgement: We are grateful to NSF for support through grants MPS 7411792 and CHE 76-24095 and to Dr. H. E. Baumgarten for his help.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch018

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch019

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Early Intermediates in Hydrazine Oxidations: Hydrazine Cation Radicals, Hydrazyls, and Diazenium Cations

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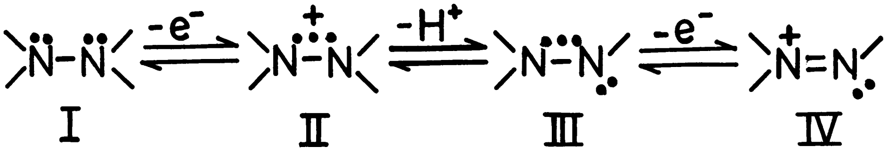
We have put considerable effort over the past several years into study of the early intermediates expected in hydrazine (I) oxidation. As indicated in Scheme 1, electron and proton loss should alternate in the presence of a one electron oxidant, giving hydrazine radical cations (II), hydrazyl radicals (III), and trisubstituted diazenium cations (IV). Other types of oxidants would bypass some of these intermediates; a hydride abstraction would convert I directly to IV, and hydrogen atom abstraction would give III. Under most oxidation conditions, II-IV do not build up to observable concentrations. IV deprotonates easily if one of the substituents is hydrogen, giving either azo compounds (often isolable), or 1,1-disubstituted diazeniums (N-aminonitrenes) which have a complex chemistry of their own (1). Our interest in the intermediates of Scheme 1 was sparked by the great conformational charge which must occur between the four unshared electron, two center hydrazine I, well known to be approximately tetrahedral at nitrogen and prefer a gauche orientation of the lone pairs (2), and the diazenium cation IV, which should have sp^2 hybridized, pi bonded nitrogens. We thought the great conformational charge which must occur would make the electron transfer steps unusual, and wished to probe the geometric consequences of the three electron, two center bonding shown for II and III.

Scheme 1



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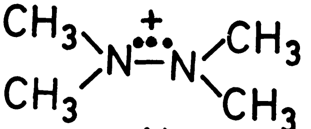
Analogous bonding occurs in several important classes of free radicals, including nitroxides, peroxy radicals, ketone radical anions, and superoxide, all of which also have a spin-bearing center adjacent to an atom bearing an unshared pair of electrons.

There had been considerable study of variously substituted examples of II-IV before our work began. The most studied example of II was tetraphenylhydrazine cation radical, whose purple color led Hünig to coin the term "violenes" (3a) for the series of vinologous species his group has studied extensively (3). The solution ESR spectrum of hydrazine radical cation had been recorded in a flow system (4). Aromatic examples of III had received extensive study (5), and diphenylpicrylhydrazyl was the first example of a neutral radical stable both to dimerization and reaction with oxygen. The chemistry of 1,1-dimethyldiazenium cation had been studied (6), and interesting electrochemical work on arylhydrazine oxidations had been carried out by Cauquis and Genies (7).

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch019

The Hydrazyine,Hydrazine Radical Cation Redox Equilibrium

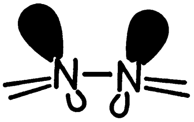
Our work on the first electron transfer, I $\rightleftharpoons$ II, became possible when it was realized that tetraalkylhydrazine radical cations have a reasonably long lifetime in solution, even at room temperature. This discovery was made completely by accident, when tetramethylhydrazine radical cation, $1^{\dot{+}}$ was observed by ESR



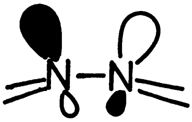
$1^{\dot{+}}$

during attempted study of tetramethyl-2-tetrazine maleic anhydride charge-transfer complexes (8a), and nearly simultaneously by Michejda and coworkers (8b), who had methylated the tetrazene, and observed $1^{\dot{+}}$ as a decomposition product. The long lifetime of tetraalkyl-II cation radicals made possible measurements of the relative free energy differences between I and II by electrochemical determination of E^{o}, the standard potential for the redox equilibrium (9), and also allowed convenient ESR study of II with a variety of structural constraints (10).

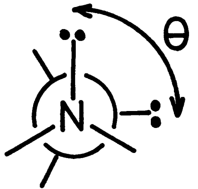
The four point substitution of hydrazines provides a unique opportunity to control the geometry at the N-N bond of I, and thus allows placing structural constraints upon II which are not possible with other three electron, two center species. The highest occupied molecular orbitals of a hydrazine are expected to be the symmetric and antisymmetric lone pair combination orbitals, n_+ and n_-. Since the energy separa-



n_+



n_-



V

tion between n_+ and n_- should be sensitive to the lone pair,lone pair dihedral angle θ (see V), one would predict that the energy of the highest occupied molecular orbital (homo) for a hydrazine would be sensitive to θ. It was well established that solution redox potentials correlate linearly with the energy of the homo for several aromatic cases (11), and a surprisingly good linear correlation of solution oxidation potential with vapor phase ionization potential was found by Miller and coworkers (12) for a very wide range of structural types of compounds. Photoelectron spectroscopy studies by our group (13) and that of Rademacher (14) have verified the expectation of a great sensitivity of ΔE^o to θ; $\Delta E = 2.3$ eV (53 kcal/mole) for hydrazines with θ near 0° and 180° (13), and the minimum ΔE is near 0.5 eV (11.5 kcal/mole) for gauche, acyclic hydrazines (9b). The photoelectron spectrum for hydrazines provides a convenient method for determining the approximate θ for a hydrazine in the vapor phase, and the short pe timescale allows observation of conformational mixtures in compounds which interconvert too rapidly for investigation by NMR techniques (13e). Nevertheless, E^o is not very sensitive to θ, partially because of compensating energy changes in lower-lying orbitals. An excellent example is provided by the ee and ae conformations of dimethyl hexahydropyridazine 2. Although ΔE differs by a substantial amount, 1.3 eV (30 kcal/mole) because of the large difference in θ, 2ee and 2ae only differ in free energy by about 0.2 kcal/mole (15), requiring that their E^o values are virtually identical, since both give the same cation, $2^{+\cdot}$. Their first ionization potentials are also

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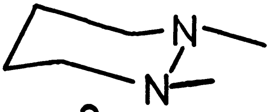
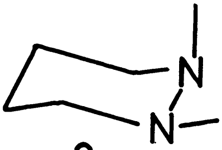


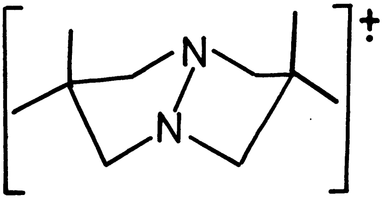
2ee



2ae

virtually the same (13,14), showing that the average of the n_+ and n_- energies is not constant as θ is changed.

Comparison of E^{o} values for various tetraalkylhydrazines shows that there is a great increase in RN,NR steric interaction in the cation relative to the neutral species and that six-ring hydrazines have substantially higher E^{o} values than five- and seven-ring compounds, both of which indicate considerable flattening at the nitrogens of the cation radical (9b). ESR studies of the nitrogen splitting constant have demonstrated that although the nitrogens of hydrazine radical cations are considerably flattened compared to those of the neutral compounds, the equilibrium geometry is not planar for some cases in which planarity would destabilize cyclic substituents. The double



3^{+}

nitrogen inversion barrier of 3^{+} is only about 3.4 kcal/mole (10c), considerably less than the 12 kcal/mole of the neutral hydrazine. If relatively unstrained tetraalkylhydrazine cation radicals are not planar at nitrogen in their equilibrium geometry, the barrier to double nitrogen inversion is quite low. Tetraalkylhydrazine cation radicals clearly are more easily bent than hydrazine radical cation (10c); even the lower nitrogen splitting constant examples such as 1^{+} (a(N) = 13.4 gauss) have larger nitrogen splittings than does hydrazine radical cation (a(N) = 11.5 gauss (4)) despite the fact that hyperconjugation to the alkyl groups must decrease the total spin density at nitrogen.

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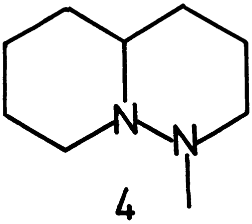
The ease of twist at the three electron pi bond of II is being studied by comparing E° values for **4**-**6** (16). Although E° was found to be the same for **4** and **5**, it is 0.38 V (9 kcal/mole) higher for **6** than for **4**. We attribute the lack of detected strain in $\mathbf{5}^{+\cdot}$ to the ease of bend at the nitrogens, which decreases the amount of torsional strain applied by the bicyclic system, and a



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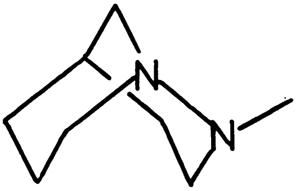

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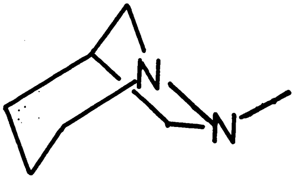
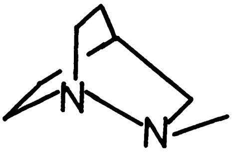


6



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smaller barrier to twisting in a three electron than a two electron pi system. The corresponding olefin has been found to have about 12 kcal/mole of strain relative to 3-ethyl-3-hexene by Turner and coworkers (17). The strain apparent in $\mathbf{6}^{+\cdot}$ demonstrates that substantial torsional twist of the three electron pi bond is difficult. For **7**, where even greater twist is required, the cation is so destabilized that it is short-lived, and a thermodynamic E° value is not currently available.

In contrast to the small effect of θ on E°, the rate of electron transfer is very sensitive to θ, as has been demonstrated by low temperature cyclic voltammetry experiments. Electron transfer from axial, equatorial ($\theta \sim 60^{\circ}$) conformations of six ring hydrazines is far slower than from diequatorial ($\theta \sim 180^{\circ}$) conformations, resulting in a kinetic resolution of the oxidation peaks for these two types of conformations (18). This phenomenon allows the use of low temperature cyclic voltammetry to determine both equilibrium and rate constants for conformational change in these

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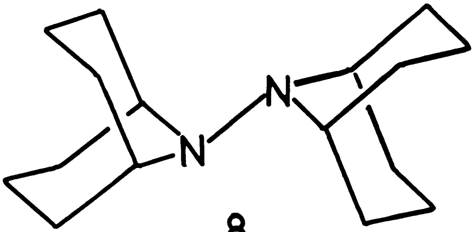
compounds (19).

Many tetraalkylhydrazine radical cations last for hours to days in solution, but attempts to isolate them only led to their rapid decomposition. Since the hydrazine dications were known to be very short-lived from cyclic voltammetry experiments (only an irreversible second oxidation wave was observed) we thought the problem in isolation was caused by electron transfer disproportionation, followed by very rapid proton transfer. We found that **8**, which has Bredt's rule destabilization of the transition state for α-deprotonation,



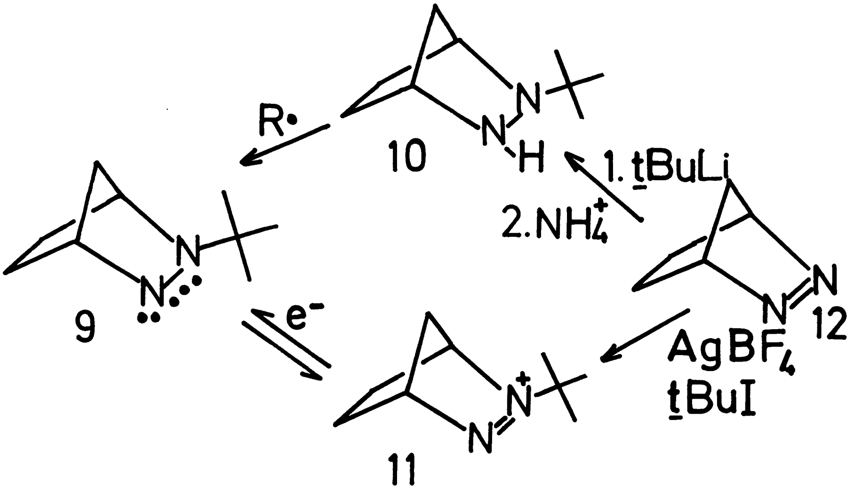
8

gives a dication which is long-lived on the cyclic voltammetry timescale, and shows E^{o} values for mono- and dication formation of -0.01 and +1.18 V vs. sce (20). These E^{o} values require a minute value for the electron transfer disproportion constant $K_d = [\mathbf{8}^{+2}][\mathbf{8}]/[\mathbf{8}^{+\cdot}]^2$ of 1×10^{-20}. It is not surprising that $\mathbf{8}^{+\cdot}$ has the smallest K_d value yet observed for cation radical, because the small, two atom pi system involved will maximize electrostatic effects. We find that $\mathbf{8}^{+\cdot}$ $\mathbf{PF_6}^{\ominus}$ is indefinitely storable, both in solution and as the solid (20). Preliminary X-ray diffraction data for $\mathbf{8}^{+\cdot}$ $\mathbf{PF_6}^{\ominus}$ (21) indicate that the nitrogens are coplanar with their four α-carbons (for neutral **8**, the N-N bond forms an angle of 58^{o} with the CNC plane), and the N-N distance is surprisingly short 1.28 A^{o} (neutral **8** has a 1.51 A^{o} N-N distance, unusually long for a hydrazine (22)).

The Hydrazyl, Diazenium Salt Redox Equilibrium

Several groups reported esr studies on non-aromatic hydrazyl radicals during the period 1972-1974 (23), the most detailed work being that of Ingold's group. Our approach to the problem of studying these compounds was to devise trialkylhydrazyls which would have conveniently long lifetimes. Since extensive work on the isoelectronic nitroxides had shown that α-hydrogen atom transfer disproportionation is the irreversible decomposition pathway, and that Bredt's rule effects were sufficient to make norpseudopelletierine-N-oxyl (24) long-lived, we selected the tert-butyl-bicyclo[2.2.1]heptyl system 9 as the most easily available long-lived hydrazyl. Two routes were developed to generate 9 from a bicyclic azo compound 12, as shown in Scheme 2. Although 9 is easily formed by

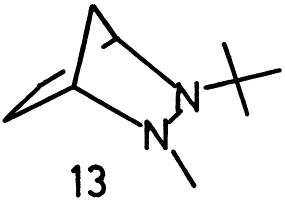
Scheme 2.



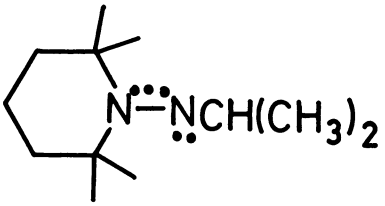
hydrogen abstraction from the trialkylhydrazine 10, the great sensitivity of 10 to air makes it an inconvenient precursor. In contrast, the diazenium salt 11 is an air stable solid which is easy to handle, and 9 is conveniently prepared by electrochemical reduction of 11. There is no problem with over-reduction of 9 to the hydrazine anion; indeed, E^0 for this process is more than 1.8 V negative of the 9,11 E^0 in acetonitrile (25), and 1.5 V more negative in dimethylformamide (26) facts which require that the hydrazine anion is remarkably basic, presumably because of lone pair-lone pair interactions. The electron transfer disproportionation constant is even lower for 9 than for 8^{+}. Preparation

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch019

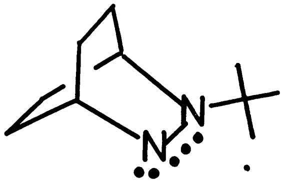
of the 2-methyl and 2-ethyl analogues of 11 was carried out, and these compounds give only irreversible reduction waves (26), demonstrating that α-hydrogen transfer is in fact rapid when abstractable α-hydrogens are present in trialkylhydrazyl radicals. The E^{o} for the 9,11 couple is -0.72 V vs. SCE in acetonitrile, 0.89 V (20 kcal/mole) negative of the 13,$13^{\dot{+}}$ couple E^{o}. Removal


13

of the third pi electron from 9 is thus considerably more fascile than generation of a three pi electron system by electron removal from 13. The ESR spectrum of 9 has nitrogen splittings of 11.03 and 10.25 gauss (26a), indicating nearly equal spin densities at the nitrogens. No evidence for dimerization was observed, even at low temperature, but admission of air to solutions of hydrazyl 9 results in immediate destruction of its ESR signal, and appearance of the hydrazyloxy radical 14. Several other hydrazyl radicals also have been shown to give hydrazyloxy radicals in the presence of air (27). In the absence of oxygen, however, 9 decomposes in several hours to give 10 and a ca. 10:1 mixture of 15 and 16. This process seems best described as "homodisproportionation", since a β-hydrogen is removed to give 15 and 16. The β-scission process, which is rather rapid for 16 (23h), does not occur at all rapidly for N-*tert*-butyl bicyclic systems, presumably because the bicyclic system enforces poor

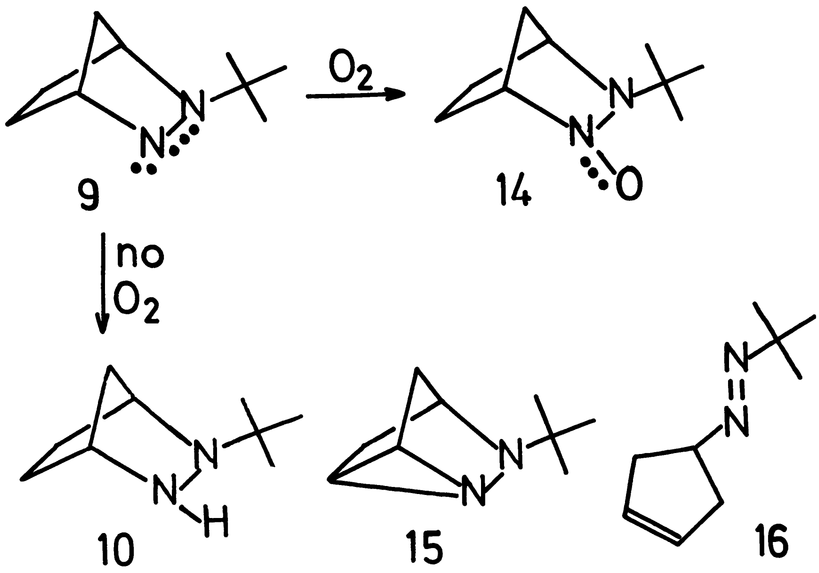


17



18

Scheme 3.



orbital allignment for loss of a tertiary radical. Surprisingly, 18, the bicyclo[2.2.2]octyl analogue of 9, is far longer lived, having a lifetime in solution of months instead of hours (26).

Air oxidation of 10 in cyclohexene gives remarkably high yields (>95% (28)) of a ca. 10:1 mixture of 15 and 16 (29). Obtaining the same oxidation products in similar ratio in the autoxidation reaction as in the self-decomposition of 9 suggests that 9 is the precursor of 15 and 16, although it is not clear why 9 is not intercepted by oxygen under these conditions. In acetonitrile, although 15 and 16 are still found in low yield, the principal product is the diazenium salt 11, with unknown counterion. Much remains to be learned about this unusual autoxidation reaction (30).

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch019

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30. It is a pleasure to thank my coworkers who have worked on the aspects of hydrazine oxidation discussed here, P. J. Hintz, R. T. Landis ,II, J. M. Buschek, Dr. L. Echegoyan, G. R. Weisman, V. E. Peacock, W. C. Hollinsed, C. R. Kessel, and W. P. Parmelle. Prof. D.H. Evans has given us invaluable assistance in the electrochemical aspects of this work.

RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch019

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Aspects of Phosphoranyl Radical Chemistry

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch020

Phosphoranyl radicals (1) are tetracovalent species most typically formed by the oxidative addition reaction shown in

$$Z\cdot + \ddot{P}Z_3 \rightarrow Z\dot{P}Z_3 \qquad 1 \qquad (1)$$

equation 1 (1). ESR evidence concerning the structure of such radicals is abundant and a very recent review is available (2). The majority are near-trigonal-bipyramidal (TBP) in structure

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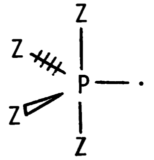

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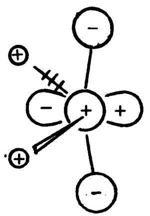

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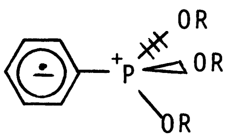

with the vacant position or phantom ligand equatorial, and often are represented by structure 2. A number of theoretical calculations (3-7) are consistent with a somewhat distorted TBP structure and also with the results of anisotropic ESR investigations (8-12) which show a high degree of spin density residing on the apical ligands. Structure 3 represents the HOMO calculated (3) for $\dot{P}H_4$. Certain but not all phosphoranyl radicals phosphorus-substituted by aryl groups appear to be tetrahedral (13-17) with the odd electron in the π-system, 4. A C_{3v} geometry is proposed for $Ph\dot{P}Cl_3$ (18,19).

The superficial similarity of 1 to pentacovalent phosphorus systems is apparent in their common TBP geometries and is emphasized by structure 2. Structure 2 is useful for stereochemical representations and also because it is easily written, though we acknowledge its inability to represent accurately electronic structure.

Phosphoranyl radicals (5) are postulated as probable intermediates in several types of radical processes involving trivalent phosphorus compounds (1) as demonstrated in the scheme below.

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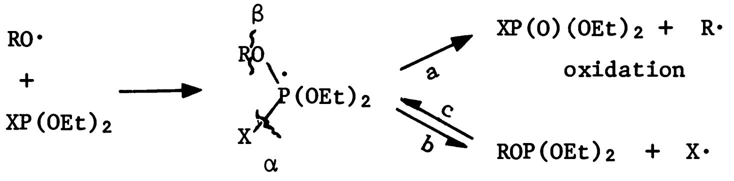
(α and β scission processes were first proposed by Walling (1).)



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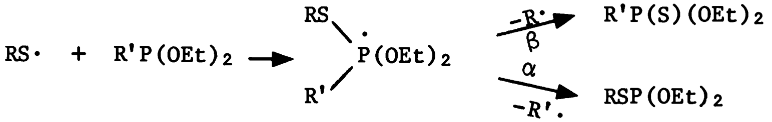
Alkoxy radical addition followed by rapid β-scission (process a) leads to overall oxidation. Alternatively, a rapid β scission reaction (path b) of 5 yields the product of substitution. Addition of X· (path c) followed by β scission is a third overall reaction, a free radical Arbuzov (reaction 2) (20).

$$X\cdot + ROP(OEt)_2 \rightarrow 5 \rightarrow XP(O)(OEt)_2 + R\cdot \qquad (2)$$

Both product and ESR studies show the ratio of β/α scission (oxidation/substitution) to be dependent on changes in the stabilities of radicals R· and X·. Effects of structure changes on the competition depicted by equation 3 are recorded in Table I (21).



(3)

TABLE I. E_a and A-Factor Effects on the Competition between Oxidation and Substitution in the Reaction RS· + R'P(OEt)2

RS·	R'	$E_\alpha - E_\beta$[a]	A_α/A_β	k_β/k_α (60°C)
i-PrS[b]	$PhCH_2$	0.36 ± 0.01	0.81	2.12
t-BuS[c]	$PhCH_2$	0.48 ± 0.06	0.44	4.74
p-$MeC_6H_4CH_2S$[c]	$PhCH_2$	9.9 ± 0.1	1.3	13.2
i-PrS	t-Bu	3.2 ± 0.2	5.4	22.9

[a] 95% confidence limit [b] Based on GLC measurements of i-PrSP(S)(OEt)2 and $PhCH_2P(S)(OEt)_2$ [c] Based on toluene and $PhCH_2P(S)(OEt)_2$ [d] Based on i-PrSP(S)(OEt)2 and t-BuP(S)(OEt)2

The increase in β/α ratio in the series i-PrS·, t-BuS·, p-$MeC_6H_4CH_2S$· and corresponding increase in E_α-E_β are consistent with the above idea. So is the effect of change of R' from $PhCH_2$ to t-Bu. It is notable that these parameters vary with both RS·

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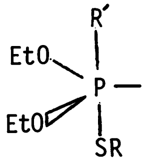
and R'· change. This rules out possible exclusive control of β/α scission by configurational effects. E.g. 6 might undergo only α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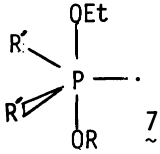
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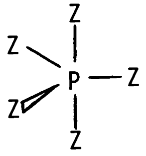
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scission making the proportion of α scission dependent solely on the statistics of 6 formation, which are likely to be unrelated to R'· stability. The importance of configurational effects in addition to radical stability factors is emphasized by the interpretation (22) given the decrease in overall rate of decomposition of 7 observed with bulky but relatively stable R' such as t-butyl. A reversible permutational isomerization which puts bulky substituents where they interact sterically with each other prior to α scission was postulated. The kinetics of phosphoranyl radical decay via C-O β scission (reaction 4) also has been investigated by ESR. E_a values which reflect changes in R· stability are found (23).

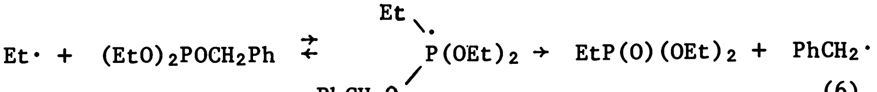
The rate of α or β scission of a phosphoranyl radical intermediate also can greatly effect the overall reactivity of a given radical towards a particular trivalent phosphorus derivative (26). Alkoxy radicals react with trialkyl phosphites with k_1 (reaction 4) about 10^8 sec^{-1} mol^{-1} and E_a~2 kcal/mol (24). For R equal t-

$$RO\cdot \;+\; P(OEt)_3 \xrightarrow{k_1} RO\dot{P}(OEt)_3 \xrightarrow[-R\cdot]{k_2} OP(OEt)_3 \qquad (4)$$

butyl, subsequent β-scission has E_a=8-10 kcal/mol. (24,25). Phenyl radical similarly adds very rapidly to phosphites (27). In these reactions, the first step is rate-determining. With Et· by contrast a free radical Arbuzov process, reaction 5, does not occur (28) although ΔH for the reaction is favorable by

$$Et\cdot \;+ (EtO)_3P \rightleftarrows Et\dot{P}(OEt)_3 \xrightarrow{-Et\cdot} EtP(O)(OEt)_2 \qquad (5)$$

>40 kcal/mol. ESR work shows (23) that Me· adds reversibly to trialkyl phosphites. However, if a very rapid β scission can follow Me· or Et· addition, then an overall reaction ensues (23, 28), reaction 6. Rapid α scission also can trap the initial



$$Et\cdot + (EtO)_2POCH_2Ph \rightleftarrows (Et)(PhCH_2O)\dot{P}(OEt)_2 \rightarrow EtP(O)(OEt)_2 + PhCH_2\cdot \qquad (6)$$

adduct (29), as in process 7 with R· various alkyls. The same sorts of reactions occur with dialkylamino radicals (28). Over-

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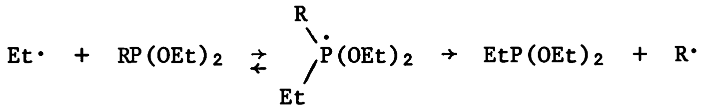


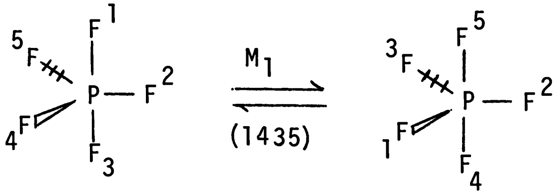
$$Et\cdot + RP(OEt)_2 \rightleftarrows \overset{R}{\underset{Et}{\dot{P}}}(OEt)_2 \rightarrow EtP(OEt)_2 + R\cdot \quad (7)$$

all reactivity in these systems requires a rapid second step.

A third class of radicals are simply too stable and don't add to phosphorus at all. The $PhCH_2\cdot$ of reaction 6 does not give $PhCH_2P(O)(OEt)_2$. Isopropyl radical also is unreactive in processes 6 and 7 (29).

These three reactivity cases are illustrated in Figure 1. The isoenergetic representation of the phosphoranyl radicals, $R'O\dot{P}(OR)XY$, is a minor oversimplification as they likely will have stabilities which depend somewhat on substituent. RO· adds irreversibly, but radical X· forms a relatively weak X-P bond in a reversible addition which gives substitution or Arbuzov product only if subsequent α or β scission is rapid (low $\Delta G^{\ddagger}$). The species Y· falls in the third reactivity class, because the P-Y bond is too weak to form at all.

The superficial structural similarity of phosphoranyl radicals, 2, and truly pentacovalent phosphorus derivatives, 8, is quite striking as noted earlier. Similar trends in substituent apicophilicities are noted also (30,31). It is therefore of interest to ascertain whether or not the analogous sort of Mode



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(8)

one (M_1 - see Musher (32)) permutational process which is known to be rapid for various PX_5 (where Z may be all the same or different) is also operative with $\cdot PZ_4$. E.g., the process illustrated above for PF_5, has a rate too fast to allow kinetic study by NMR. Calculations (33) place limits of 5 kcal/mol on its activation energy.

Two methods for gaining information on the types of permutations available for $\cdot PZ_4$ are ESR studies and stereochemical investigations. In the former, effects of temperature on hyperfine splittings, line shapes and patterns are observed. In the stereochemical approach, the overall stereochemistry of a free-radical oxidation, substitution, or Arbuzov reaction is determined. One then asks whether the operation of a given permutational mode on the presumed phosphoranyl radical intermediate is allowed by the stereochemical outcome. For example, if 9 were to undergo the

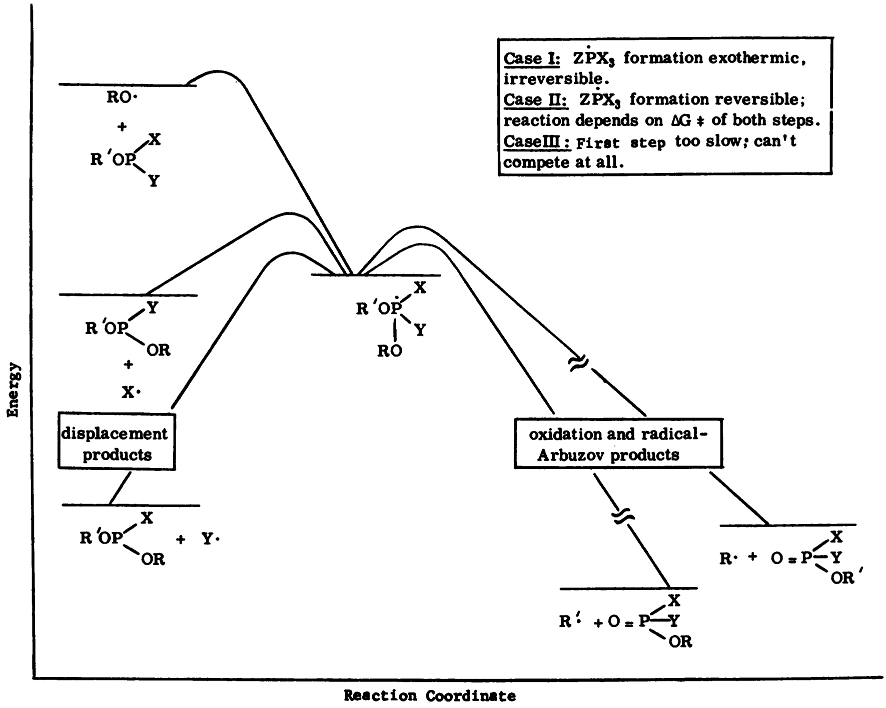

Figure 1. *Reactivities of radicals toward trivalent phosphorus derivatives*

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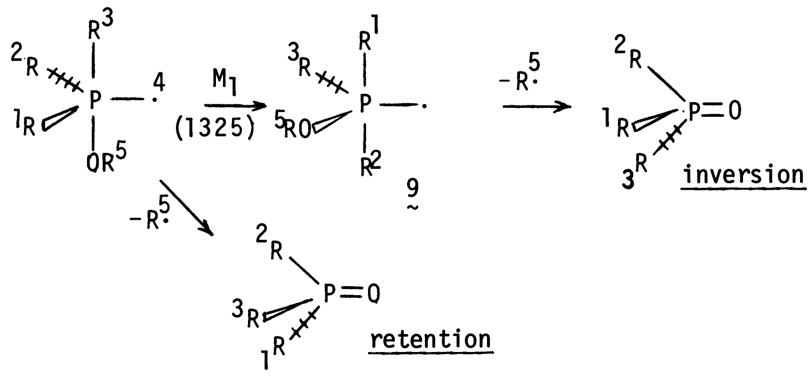
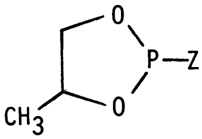
sort of M_1 permutation of substituents shown below prior to β scission, phosphine oxide of configuration opposite to that



formed on direct β scission of **9** would result.

Our stereochemical studies have involved the use of five- and six-membered ring derivatives of trivalent phosphorus, **10**



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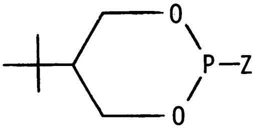

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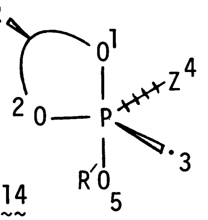
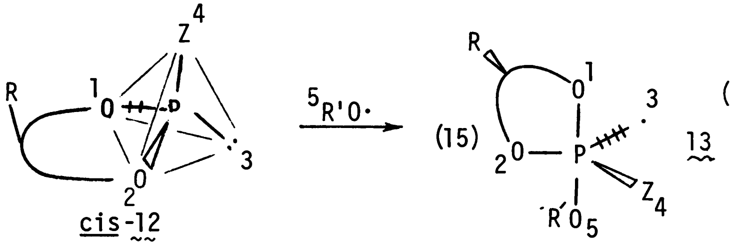


14 (15)

and **11**, whose cis or trans geometries and conformations we have characterized thoroughly (34,35). t-Butoxy radicals, generated thermally or photochemically, were found to transfer oxygen to both five- and six-membered ring phosphites (**10** and **11** with Z = CH_3O) nearly stereospecifically with retention of configuration about phosphorus. Since these results are already in the literature (36), the data will not be reproduced here.

In discussing the implications of these results, it is helpful to be able to refer to the various permutational isomers by the sorts of designations now commonly applied to pentacovalent phosphorus species (37,38). In equation 9 we show reaction of a cis isomer, **12**, (generalized to represent a ring of any size) to give the permutamer, **13**. This isomer, in the formalism employed in discussion of pentacovalent phosphorus intermediates, results



cis-12 13 (9)

from facial attack opposite the ring oxygen numbered one. The designation (15) shows which ligands are apical and indicates that the groups 2, 3, and 4 are arrayed in clockwise order. Isomer ($\overline{15}$) from the same reaction of trans-12 is shown above (structure 14) for comparison.

Figure 2 is a topological representation (37,38) which shows the M_1 interconversions of all 18 permutamers (the vertices of the hexasterane diagram) which can be formed from reactions of R'O· with *cis*- and *trans*-12. The edges of the diagram connect permutamers which can be interconverted by M_1 isomerizations. The C-T plane (perpendicular to the page) separates initial adducts which could be formed from attack of R'O· on either cis (left side) or trans phosphite. The P-O plane separates permutamers whose β scission gives trans product from the cis phosphate generating ones. The position of R'O in each permutamer is shown by eq or ap. The retentive nature of the observed oxidations excludes 14, $\overline{24}$, and $\overline{35}$ as initially formed phosphoranyls from *cis*-12 or $\overline{14}$, 24, 35 from *trans*-12. *Clearly, no extensive amount of M_1 isomerization of any of the remaining potential initial adducts occurs*, *e.g*. $\overline{25}$ → 14 or 13 → $\overline{24}$ → 15, as loss of retentive oxidation stereospecificity would result. Since $\Delta G^{\ddagger}$ for β-scission of these intermediates with R' equal *t*-Bu is at least 11 kcal/mol (24,25), the M_1 permutations have overall barrier greater than this.

Further simplification of this scheme is possible. Consider reaction of *cis*-12. From ESR evidences it is clear that only odd electron equatorial phosphoranyls have enough stability to be observed (2). Initial adducts with odd electron apical (13, 23, 34), therefore, should be rapidly converted to more stable ones: 24, $\overline{14}$, $\overline{45}$, $\overline{25}$, or 15. Moreover, preferential initial introduction of R'O apical is also likely ($\overline{45}$, $\overline{25}$, 15 formation) since apical bonds are expected to be longer and presumably weaker (3,4). *Ab initio* calculations (3) for the reaction H· + PH_3 → ·PH_4 favor apical attack as well. (Such an assumption is generally made in pentacovalent phosphorus chemistry. (37)) We can thus center our attention on $\overline{45}$, $\overline{25}$, and 15.

That intermediate $\overline{45}$ (14) should give *cis*-phosphate (retention) is not surprising since inversion would require isomerization *via* ($\overline{13}$) or (23) prior to β-scission. Such odd-electron-

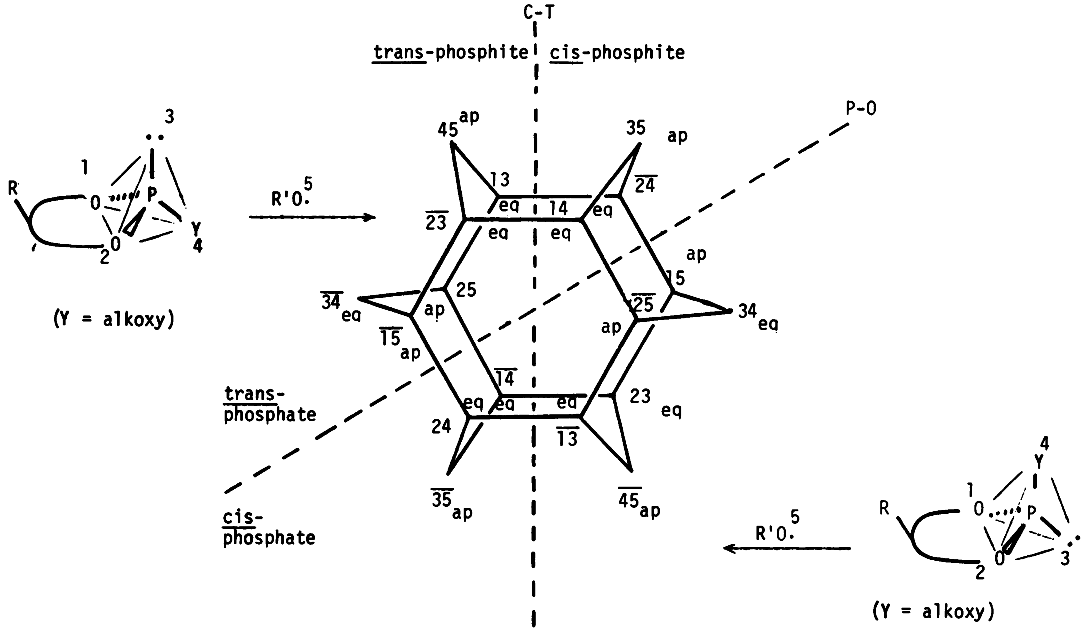
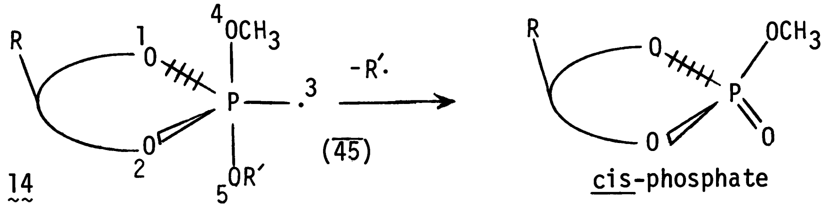
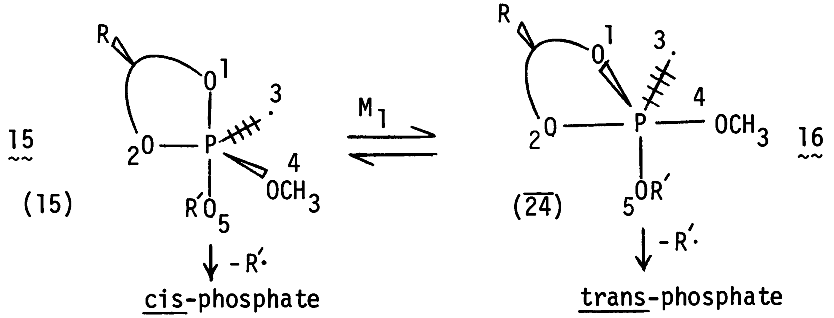


Figure 2. Formation and permutational isomerization of cyclic tetraalkoxy phosphoranyl radicals



apical intermediates may well be relatively high energy species.



However, the evidence is very strong (30) that in such reaction systems those phosphoranyl radicals observed by ESR have five-membered dioxa ring systems attached to phosphorus apical-equatorial as in 15 (15) and its mirror form 25[‡]. This applies to six-membered ring 1,3-diaza species too (39). The apparent failure of the isomerization of radical 15 to 16 (24) (a thermoneutral process which keeps the odd electron equatorial) to compete with loss of R′· (R′ = *t*-Bu), indicates that *the cyclic phosphoranyl radicals are not simple analogs of pentacovalent phosphorus intermediates, at least where permutational properties are concerned*. Thus by contrast to the apparent high $\Delta G^{\ddagger}$ of >11 kcal/mol assigned to process M_1 of 15 (15 → 24), that for the isomerization of the corresponding pentaalkoxy compound, 17, must be fewer than 10 kcal/mol. This follows since the equilibra-

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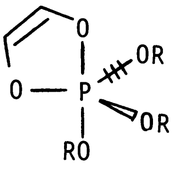

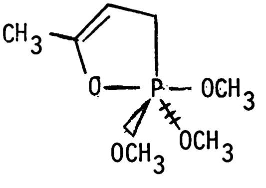

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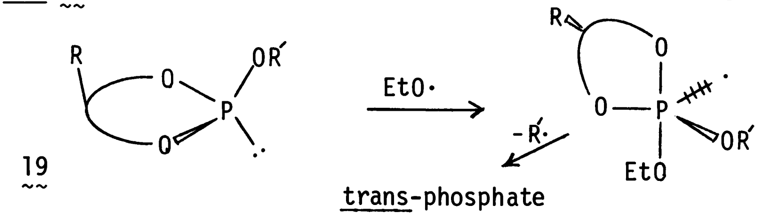
[‡] The arguments which follow also apply to permutamers 24 and 14 which have ap-eq ring attachment and differ from 25 and 15 only in that the R′O and CH_3O groups are interchanged. ESR work also suggests that the rapid interconversions 25 $\rightleftarrows$ 24 and 15 $\rightleftarrows$ 14 occur. (See later discussion.)

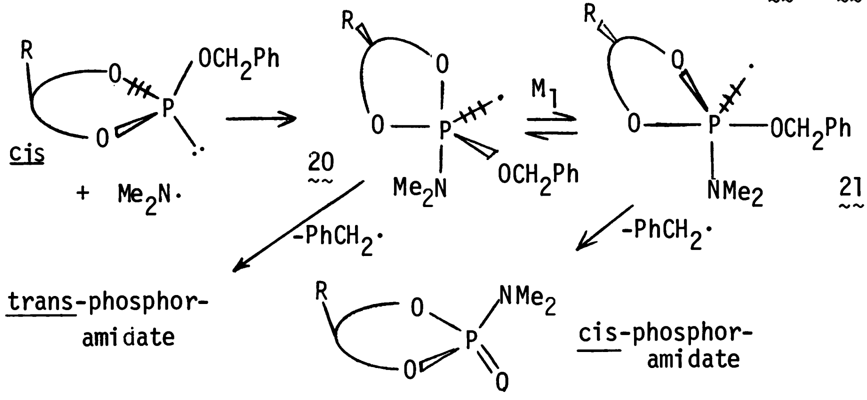
tion of CH_3O groups in 18, which requires the CH_2 to become apical (energetically unfavorable), has a $\Delta G^{\ddagger}$ value of only 10 kcal/mol (40). (See earlier comments on PF_5 barriers.)

An objection to the above is the possibility that 16 (24) cannot undergo β scission since R'O has become equatorial. However cis/trans mixtures of 19 (36) gave the outcome expected from direct β-scission of R'O equatorial as illustrated below for the cis-19. Mode 1 isomerization of the intermediate to place R'O



apical as in 15 would have inverted product stereochemistry.

Likewise, the stereochemistry of free-radical Arbuzov reaction of $Me_2N\cdot$ with cis/trans 5- and 6-membered benzyl phosphites failed to reveal any evidence of such an M_1 permutation (20 → 21).



Product phosphoramidate trans/cis ratios corresponded closely to cis/trans ratios of the starting phosphites (20). Some driving force for the permutation 20 → 21 could come from the slightly greater apicophilicity of Me_2N over $PhCH_2O$ (39). This is compensated for, however, by the greater rate of β-scission giving $PhCH_2\cdot$ than that for the t-butoxy radical.

Free-radical substitution processes occur only rarely at carbon but more often at heteroatoms. The stereochemistry of such a process cannot normally be ascertained, however. Trivalent phosphorus derivatives are perhaps uniquely suitable for such studies since phosphorus is sufficiently stable configurationally, and free radical substitution at phosphorus occurs with ease.

For reaction 10, we find (28,29) that the series of substituents shown constitute a kind of substitution order in which

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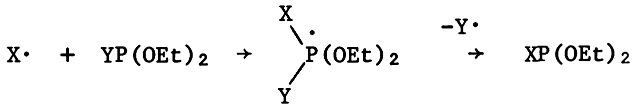


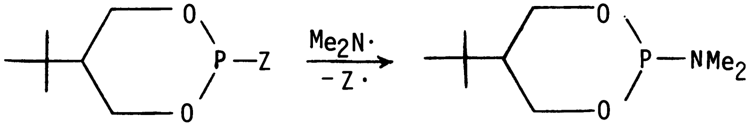
$$X\cdot + YP(OEt)_2 \rightarrow \overset{X}{\underset{Y}{\dot{P}(OEt)_2}} \xrightarrow{-Y\cdot} XP(OEt)_2 \qquad (10)$$

$RO\cdot > \phi O\cdot > R_2N\cdot > R\cdot$ (X and Y)

any one may serve as X· to replace any of those (Y) to the right of it.

In Figure 3 is pictured the formation of intermediate **22** in a manner analogous to that proposed for the oxidation and Arbuzov reactions. Subsequent M_1 permutation places the leaving group in the apical position. Departure of Y· then is predicted to yield product with retention of configuration at phosphorus.

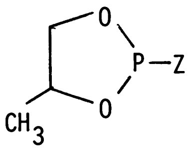
We previously published (41) the results of study of the stereochemistry of reaction 11 which occurs with inversion of



(11)

11 Z = t-Bu, $PhCH_2$

phosphorus configuration. We have since also looked at the five-membered ring system, **10**, (Z equal t-Bu, $PhCH_2$) and again observed (42) inversion of configuration about phosphorus in the



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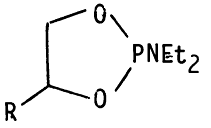

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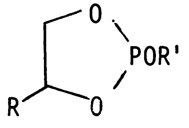

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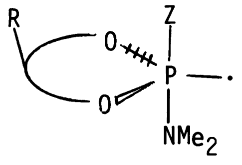
product phosphoramidite (**10**, Z = Me_2N). With the 5-membered ring, structure **22** should be especially favored.

Most recently we have examined (43) the reaction of **23** (R = t-Bu or Me) with R'O· to give phosphite **24**. Our earlier substitution stereochemical studies are open to some ambiguity of interpretation in that the intermediate phosphoranyl radical is too unstable to be detected by ESR, so no circumstantial evidence is available supporting its presence or suggesting its geometry. Inversion is most easily explained then by intermediate **25** or its corresponding transition state. In fact, since $Me_2N\cdot$ additions are reversible, initial intermediate **22** could conceivably not lead to product at all but break down instead to reform $Me_2N\cdot$ and reactant which then give product via 25. By contrast, RO• additions to trivalent phosphorus are irreversible (44,45).



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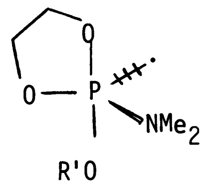

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Furthermore, ESR results (39) show clearly the formation of radicals of structure 26 from R'O• and an unsubstituted phosphoramidite analog of 23 (R equals H, Et_2N equals Me_2N).

In Table II are found results of some of our studies of reactions of EtO• and sec-BuO• with 23 (R equal Me and t-Bu). The product ratios are not the thermodynamic equilibrium ones. The conclusion is that here again substitution is with inversion about phosphorus. As before, the stereochemical outcome is inconsistent with an M_1 permutation of 22.

TABLE II. Substitution Stereochemistry

R	R'O•	cis/trans 23	cis/trans 23 consumed[a]	trans/cis 24[b] formed
CH_3	EtO•	37/63	40/60	39/61
CH_3	sec-BuO•	36/64	39/61	39/61
t-Bu	EtO•	19/81	25/75	24/76

[a] At 14-37% consumption of 23 [b] Yields 64-85%

A further question remains. What other permutational modes of the five (plus the identity) categorized by Musher (32) are consistent with the observed stereochemistries? In a series of definitive ESR investigations, B. P. Roberts and coworkers have shown (30,39) that very rapid M_4 permutational isomerizations are undergone by certain cyclic phosphoranyl radicals, 27. The so-called M_4 (exocyclic) process is more rapid and operative at lower temperatures than is the M_4 (ring) permutation. M_4 (exocyclic) for 26 occurs (39) with rate constant about 10^7 sec^{-1} at -120°. Although the exchange rates for M_4 (exocyclic) are dependent on the relative apicophilicities (30), such processes are surely rapid at room temperatures where our stereochemical work was done. Shown in Figure 4 is the predicted effect of an

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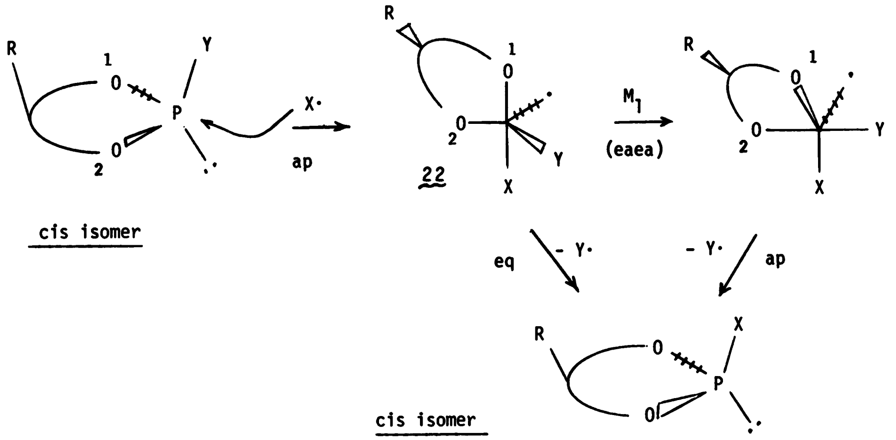


Figure 3. Potential effect of M_1 permutation on substitution stereochemistry

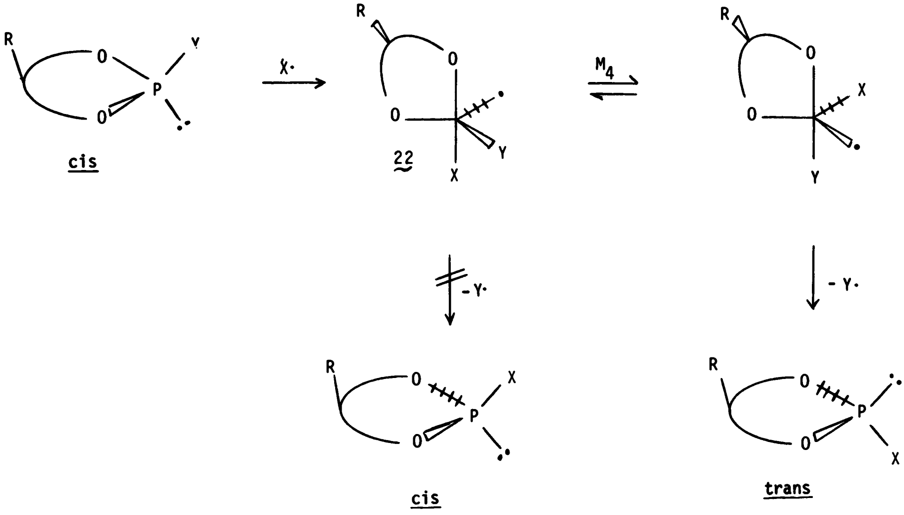
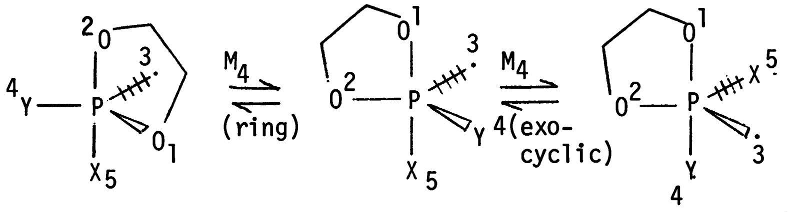


Figure 4. Potential effect of M_4 permutation on substitution stereochemistry



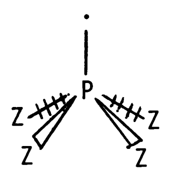
28 **27** **29**

M_4 (exocyclic) isomerization on substitution stereochemistry. This process moves the departing Y (Me_2N) into an apical position where its leaving (presumably favored by microscopic reversibility) gives product of inverted phosphorus configuration as is observed experimentally. An M_4 (ring) permutation of the type **27** → **28** would not alter substitution stereochemistry, but neither would it place the Me_2N apical.

In Figure 5 are shown the effects of M_4 (exocyclic) isomerizations on the stereochemistries of oxidation and free-radical Arbuzov as well as the substitution process discussed above. All three are stereochemically consistent with rapid M_4 (exocyclic) permutations although the results do not require that such processes be rapid, especially in the oxidation and Arbuzov reactions. Mode 5 processes (socalled disrotatory Berry) also fit the stereochemistry but not the ESR results. Modes 2 and 3 are ruled out by our stereochemical work. It is to be emphasized that the statements as to allowed permutation modes are made under the assumption that odd electron apical and ring diequatorial structures are excluded energetically.

Theoretical calculations (3,5) predict that a square pyramidal, odd-electron-apical geometry (**30**) is much higher in energy

30



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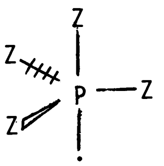

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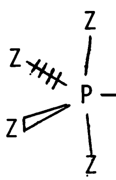
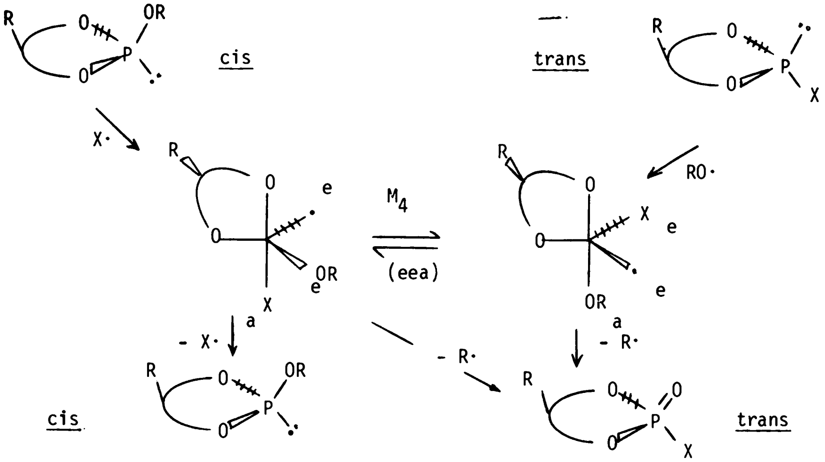


than the optimized distorted trigonal bipyramidal one (**32**). Values for the energy increase include: 35 kcal/mol, ab initio, Z = H (3); 39 kcal/mol, ab initio, Z = F (3); 25 kcal/mol, CNDO/2, Z = F (5). If the physical mechanism for an M_1 process with odd electron as equatorial pivot involves **30** as the barrier geometry (a true Berry pseudorotation process), then the reluctance of phosphoranyl radicals to undergo such M_1 isomerizations (equation 12) is reasonable. By comparison, this energy dif-



Free-Radical Arbuzov: cis → trans

Oxidation: trans → trans

Substitution: trans → cis

Figure 5. Stereochemical effects of M_4 isomerizations on stereochemistries of free radical oxidation, Arbuzov, and substitution reactions

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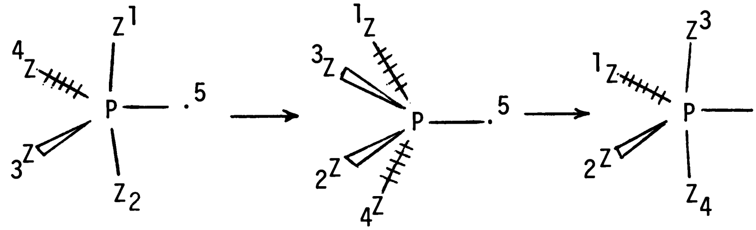
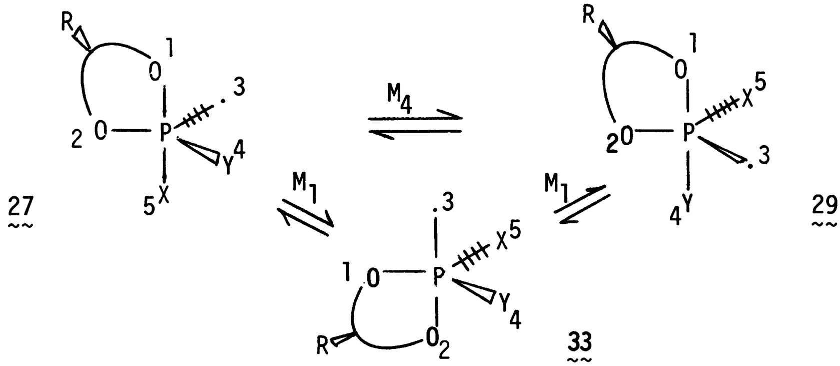


(12)

ference for PZ_5 compounds is calculated to be <5 kcal/mol (3,33). Clearly, theory predicts a Berry mechanism M_1 exchange of this type to be much more rapid with PZ_5 than with $\cdot PZ_4$. This is consistent with both the stereochemical and ESR findings.

Moreover, it is notable that the calculations predict $\cdot PZ_4$ structures with odd electron apical, **31**, to be of lower energy than those with geometry **30**, being 20 kcal/mol (3) above that of the optimized geometry for $\cdot PH_4$ (ab initio) and 3.4 kcal/mol (5) for $\cdot PH_3OH$ (CNDO/2). Again it is apparent that a phosphoranyl radical is not simply a pentacovalent phosphorus species with the odd electron as electropositive phantom ligand. A further significance of this is that M_1 processes via intermediates or barrier geometries with the odd electron apical may be more rapid than those with odd electron as equatorial pivot. Such a structure (**33**) could then represent an intermediate in a two-step $M_1 \times M_1$ process which is permutationally equivalent to the M_4. A sequential $M_2 \times M_2$ process exchanging substituents 3 and 5, then 4 and 5 of **27** will accomplish the same thing. As has been



noted (32), once restraints as to permutamers which are energetically accessible are removed, it is not possible, except for M_1, to separate individual permutation modes (M_2 through M_5) from combinations of other modes which are permutationally equivalent.

Fluxional behavior has been noted as well by ESR for acyclic phosphoranyls: $RO\dot{P}F_3$ (46); $(EtO)_2\dot{P}(NMe_2)_2$ (39); *t*-$BuO\dot{P}H_3$ (47); and $RO\dot{P}(CH_3)_3$ (22). The mode of exchange has not been assigned experimentally.

In a paper delivered at this symposium J. A. Kampmier of the University of Rochester presented data on radical substitutions at sulfide sulfur. The effects of stereochemical constraints on the products formed led to the conclusion that a linear array of attacking radical, sulfur, and leaving radical ($X^{\delta\cdot}$ - - - S - - - - - $Y^{\delta\cdot}$) is required. If a sulfuranyl radical ($R_3S\cdot$) is present in such reactions, permutational isomerizations should allow other groups to assume apical positions where they then could depart. A high barrier to permutation may be operative in such systems, as is found (48) by ESR for $(RO)_3S\cdot$. Evidence that $(RO)_3S\cdot$ results from apical introduction of $RO\cdot$ was also reported (48).

Acknowledgement. The author thanks the National Science Foundation, the National Cancer Institute of the Public Health Service, and the Petroleum Research Fund for grants supporting work described here.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch020

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Radical, Anion, Anion-Radical Reactions with Organic Halides

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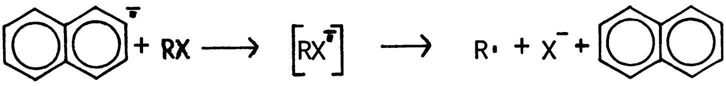
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch021

Interesting similarities in the behavior of the three reactive species, having one or two electrons, led us to study their reactions with organic halides from the point of view that comparisons of product and kinetic data could lead to correlations, and of equal importance the lack thereof, of the various mechanisms.

Aromatic radical anions have been studied in depth beginning in 1867 with Bertholet's discovery (1), and continuing with Schlenk and Bergmann's pioneering work (2) around the turn of the century. Although radical anions exhibit complex chemical behavior, their ability to function as reducing agents by electron transfer processes is reasonably well understood. In this regard, reduction of organic halides was selected as a model for election transfer reactions of radical anions.

The products of the reaction of radical anions, for example sodium naphthalene, with bromides and chlorides are the hydrocarbon, the olefin and alkylated dihydronaphthalene. Reaction with iodides gives hydrocarbon dimer in addition. The mechanism as shown is a result of numerous product and kinetic studies (3, 4, 5). Two steps that merit further investigation are the



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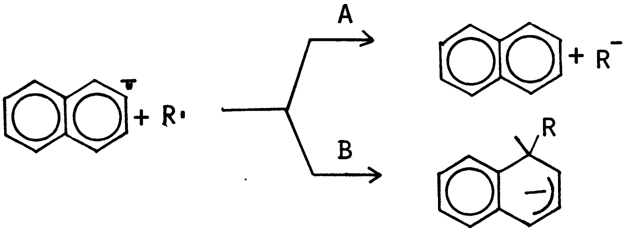

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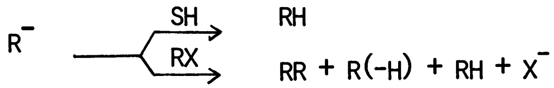

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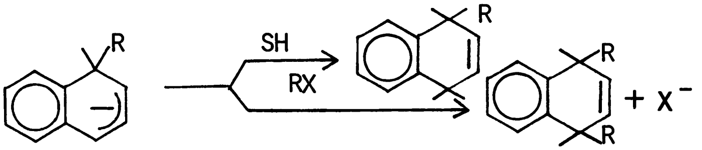

(4)

initial electron transfer (eq. 1) and the coupling reaction (eq.2).

Two possibilities for the first step are that the species, RX$^{\bar{\cdot}}$, is a transition state for a single-step bond dissociation, and that the species is an intermediate organic halide radical anion. The first possibility is generally accepted, however, extensive kinetic data (4C) for a series of organic radical anions and halides indicate a change in the nature of the transition state in going from a highly exothermic to a less exothermic reaction. These changes could result from differences in timing along the reaction path in a one-step bond cleavage, or from a superposition of the two proposed mechanisms.

In an attempt to resolve this dilemma, the reaction rates were measured for a series of organic bromides with sodium anthracene (Table I) and correlated with two model systems. The model for the first possibility, a one-step process with bond dissociation, is the tri-n-butyltin hydride reaction with these same halides (6). Correlation of the reaction rates would indicate that the transition state for anthracene radical anion reduction is similar to the transition state for radical formation by tri-n-butyltin radical. On the other hand, the model for the second possibility, the organic halide reduction potential, is a measure of organic halide radical anion formation (7).

Table I. Second-Order Rate Constants for Reaction of Sodium Anthracene with Alkyl Bromides in THF at 0°C.^{a}

Alkyl Bromide	k, $M^{-1}sec^{-1}$	k(rel.)	Logk(rel.)
n-Butyl	242^b	1.0	0.0
sec-Butyl	938^c	3.9	0.59
tert-Butyl	2402^c	9.9	1.0
Phenyl		0.0015^d	-2.82
Benzyl		25.0^e	1.40

(a) Measured with stopped-flow apparatus at 775 nm (b) The rate was unaffected by the addition of tert -butanol in excess. (c) tert- Butanol was added to prevent build-up of strongly absorbing anion. (d) From ref 4c at 20°C. (e) Estimated from competition experiments (8, 9).

The relationship in Figure 1 between the known radical reaction and the radical anion reaction is monotonic and there-

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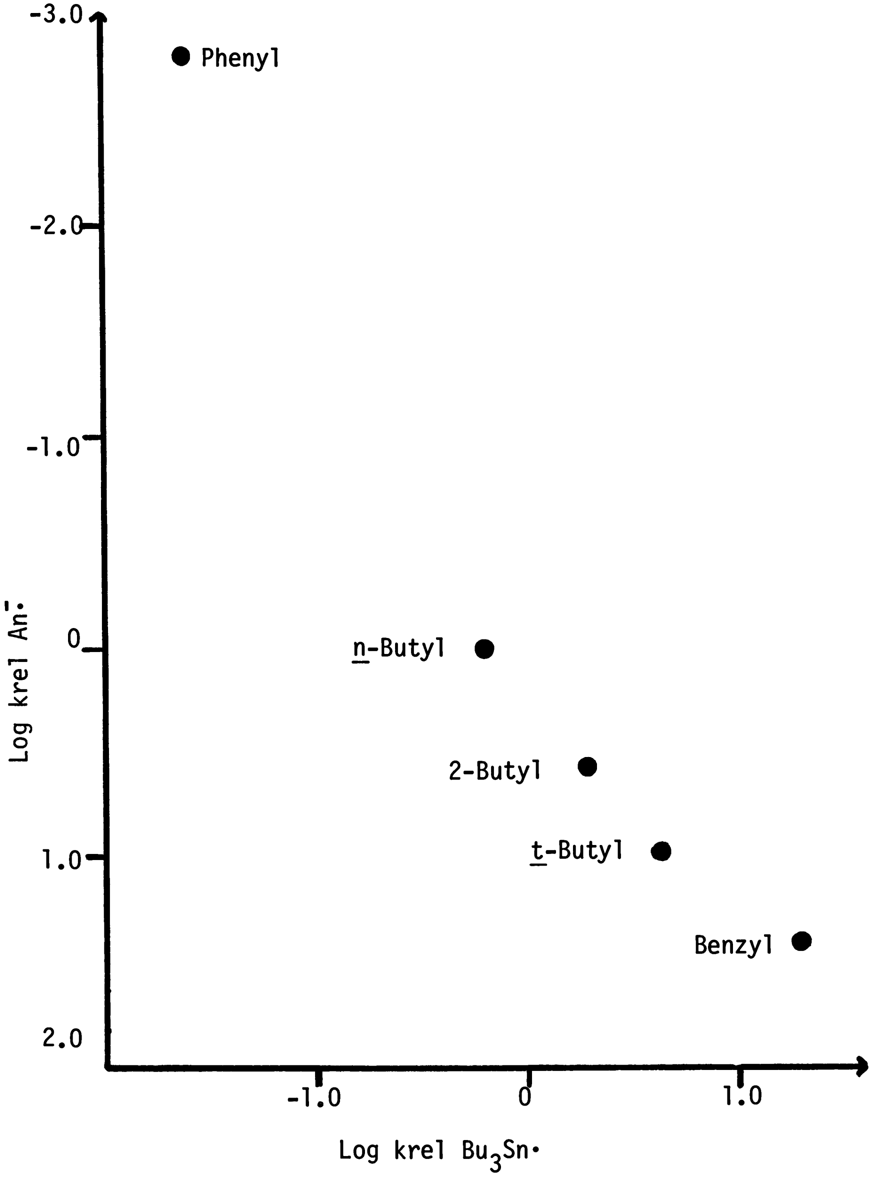

*Figure 1. The relationship between the logs of the relative rates of reaction of sodium anthracene and tri-*n*-butyltin hydride with select bromides*

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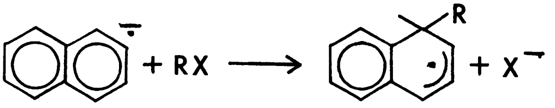
fore similar reaction factors are likely to be involved. This definitive correlation compared to the decided lack of correlation in Figure 2 indicates that for sodium anthracene the formation of $RX^{\cdot}$ is not involved to any great extent, but rather the transition state resembles that for a radical reaction.

In contrast, for reaction of organic halides with metallic magnesium, Whitesides (7) found a poor correlation with the rates of tri-*n*-butyltin hydride, and a reasonable correlation, especially with primary bromides, with reduction potentials, suggesting the formation of $RX^{\overline{\cdot}}$. Sodium naphthalene reductions also correlate with reduction potentials for primary halides (4b). Moreover, reaction rates are faster in solvents favoring loose ion pairs over tight, further evidence for an early transition state involving election transfer and little bond dissociation. (4c)

Therefore, one can conclude that for the less exothermic reduction by sodium anthracene,eq. 1 is a one-step radical formation. For radical anions of higher reduction potential, the possibility for the species, $RX^{\overline{\cdot}}$, must still be considered.

Turning now to equation 2 in the mechanism, the genesis of the alkylated aromatic raises the question of possible contributions from displacement reactions, and more generally the question of possible stereochemical integrity. Steps 5 and 6 were considered



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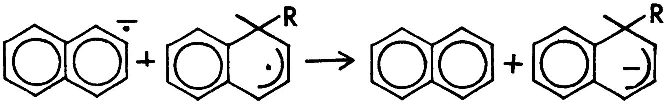

(6)

to contribute foremost to the mechanism (10) before experiments by Sargent (5b) and Garst (3c) showed little dependence either on the structure or on the halogen of the alkyl halide in the ratio of alkylated to reduced products. Data from experiments with chiral substrates (11) however, suggests that an S_N2 process might contribute to some extent. An important prediction of such a path is of course inversion of configuration at the reaction site. This is moreover a stringent test for the timing of steps 1 and 2A, for if there is a stereochemical preference for step 2A and if reaction is faster than racemization of the radical, then stereochemical integrity can be preserved.

Bridgehead tertiary halides were chosen as the experimental model because rear-side attack is not possible, and therefore, if displacement is involved, there would be a decrease in the amount of alkylated products. The results in Table II are consistent

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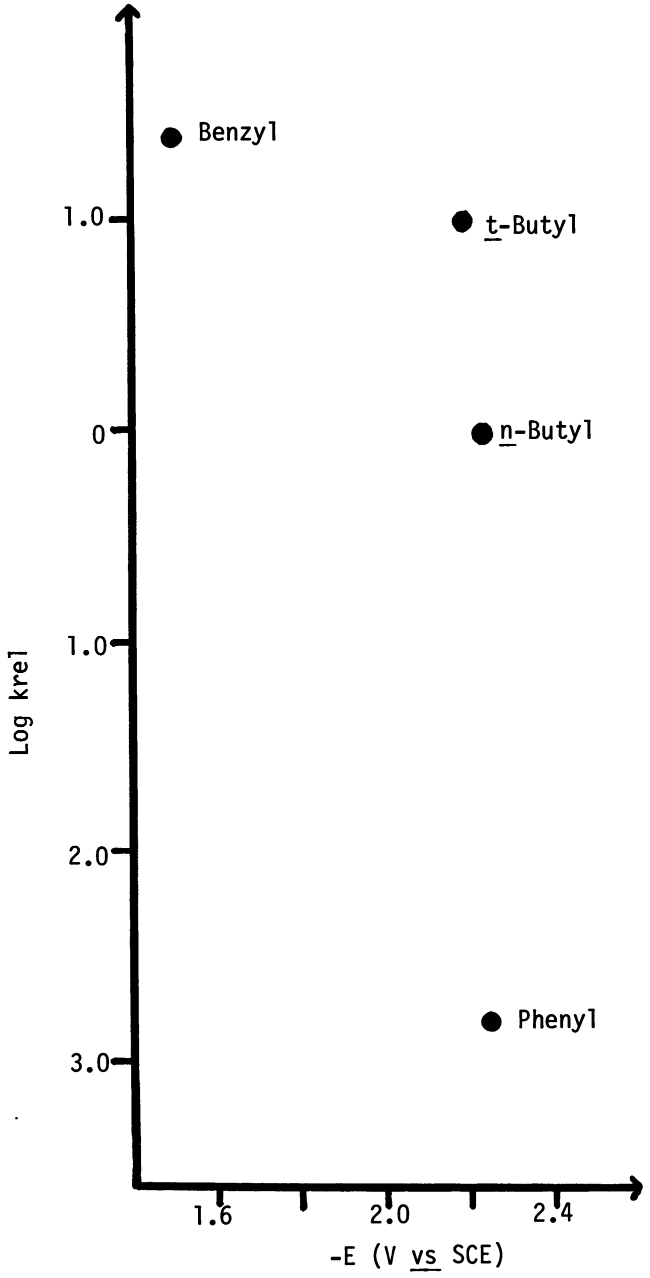


Figure 2. The relationship between the log of the relative rates of reaction of sodium anthracene with select bromides and their reduction potentials

Table II. Reaction of Bridgehead Bromides with Sodium Naphthalene

Bromide	R-H%	R-Naph-H%·[c]
1-Adamantyl	41[b]	59[d]
1-Bicyclo[2.2.2.]octyl	42[b]	(58)
4-Bicyclo[2.2.2.]-1-azooctyl	50[b]	(50)

(a) In THF at 20°C.

(b) Analyses were by vpc on a U.C. W 98 column.

(c) Determined by difference from the yields of aliphatic products.

(d) Isolated by liquid chromatography and characterized by mass spectroscopy and proton n.m.r.

with yields from primary halides. (4b) They agree as well with experiments by Sargent (5b) who found 61% alkylation from reaction with tert-pentyl iodide. In all cases it appears that the alkylation reaction is insensitive to stereochemistry which in turn is inconsistent with an S_N2 mechanism. The insensitivity further indicates that the radical, which is clearly implicated, has sufficient time to equilibrate before reaction. These results additionally provide estimated rate limits for reactions bearing on stereochemical integrity. From competition experiments, the rate constant for the coupling step was determined to be $\sim 1\times10^{9}\ M^{-1}\ sec^{-1}$ (12). Accordingly, loss of stereochemical integrity must be faster to account for the commonality of results with the acyclic and bridgehead bromides. A parallel scheme for electron transfer processes with anions (eq. 8 and 9) is suggested and this precludes any stereochemical integrity unless there is some special feature about the coupling step.

The tenfold increase in rate (Table I) in going from a primary to a tertiary bromide is in direct contrast to the expected structural effect for a displacement reaction. This supports further the conclusion that alkylation products arise neither by an S_N2-like process, nor by any process with strong stereochemical requirements.

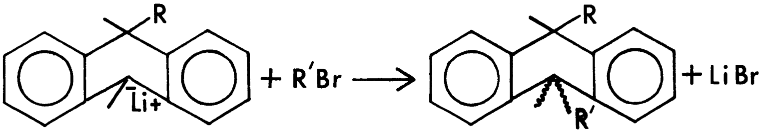
A potential, common surface for the chemistry of anions and radicals involves organometallic compounds and organic halides. In addition to the usual two-election displacement (eq. 7), a stepwise scheme (eq. 8 and 9) can explain the products of reaction. The electron transfer step (eq.8) has been implicated by

$$An^{-} + RX \longrightarrow An\text{-}R + X^{-} \qquad (7)$$
$$An^{-} + RX \longrightarrow An^{\bullet} + R^{\bullet} + X^{-} \qquad (8)$$
$$An^{\bullet} + R^{\bullet} \longrightarrow An\text{-}R \qquad (9)$$

the observation of radicals using ESR (13) and CIDNP (14) techniques. These observations prompted a search for the quantitative contributions of radicals and their role in the transition state for anion reactions.

To provide the quantitative data we have focused attention on the kinetics of the reaction of select anions with halides. This approach concentrates on the rate determining step and the factors that affect it. Two kinds of anionic species have been investigated, 9-alkyl-10-lithio-9,10-dihydroanthracenyl anions and lithio di-and tri-pehnylmethyl anions.

The stereochemistry of the alkylanthracenyl anion reactions with halides has in fact fascinating results. In the main, reaction with primary halides leads to a predominance of the cis product, while reaction of the secondary halides leads to the trans (15). We have used kinetic measurements to sort out the factors influencing the transition states for cis and trans products.



(10)

Table III. Second-Order Rate Constants for Reaction of 9-Alkyl-10-Lithio-9,10-Dihydroanthracene with Alkyl Bromides[a]

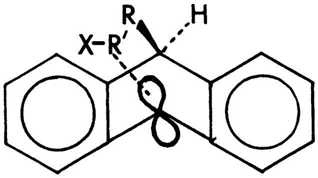
Bromide	9-Alkyl	k(corr.)[b]	cis/trans	k(cis)	k(trans)
n-Hexyl	H	2673			
	Et	1473	76/24	1124	346
	iPr	574	59/41	337	237
	tBu	312	10/90	31	280
i-Propyl	H	62			
	Et	40	25/75	10	30
	iPr	37	13/87	5	32
	tBu	36	2/98	0.7	35

(a) Measured with stopped-flow apparatus described previously, in THF at 20° at 400 nm. (b) Absolute rate constants were corrected for the elimination reaction (<15%).

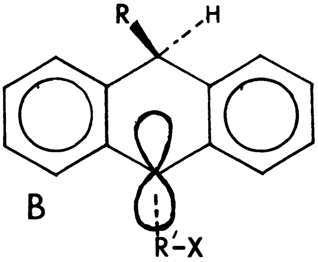
The rate and product date in Table III indicate that, for both primary and secondary halides, the transition state leading to cis product is a marked function of the size of the substituent in the 9-position. In direct contrast, the transition state leading to the trans product is insensitive to the substituent.

The geometry of the anion is not known with certainty and in fact might be a mixture of conformers (16), nevertheless, the geometry of the transition state leading to the cis product is most likely an axial-axial orientation shown as A. This orientation

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch021



A



B

accommodates the steric effects and the stereochemical preferences and allows anion stabilization by π orbital overlap. In the case of trans, whereas there are several possible conformers leading to the product, it is clear that the 9-substituent has little affect on the reaction rate. A reasonable model for the transition state is depicted in B. This absence of a steric effect suggests alternative mechanisms, perhaps involving electron transfer. We delay consideration of this point until a later section.

We consider now the relationships between anions and radical anions by comparing the corresponding reaction rates with organic halides reported in Table IV.

Table IV. Absolute and Relative Rate Constants for Anion and Radical Anion Reactions with Primary and Secondary Halides[a]

Halide/ Anion	n-$C_6H_{13}Cl$	n-$C_6H_{13}Br$	n-$C_6H_{13}I$	sec-C_3H_7Br	sec-C_3H_7I
Anth$^{\overline{\cdot}}$	1.3×10^{-1}	6.6×10^{2}	4.4×10^{4}	2.6×10^{3}	
AnthH^{-}	10	2.7×10^{3}	2.2×10^{4}	6.2×10	3.4×10^{3}
Napth$^{\overline{\cdot}}$	4.0×10^{2}	1.5×10^{5}	4.4×10^{7}		
NaphH^{-}	8.4				
Φ_2CH^-	10	2.7×10^{3}	5.0×10^{4}	1.9×10^{2}	5.0×10^{3}
Φ_3C^-		3.1×10	2.0×10^{3}	1.9	(5.0×10^{2}) [b]
Anth$^{\overline{\cdot}}$/AnthH$^-$	0.021	0.24	2.0	41.5	
Φ_2CH^-/Φ_3C^-		86.0	25	103	(10)

(a) In lit/mole/sec. Measured with stopped-flow apparatus.
(b) Uncorrected for elimination reaction.

Of initial interest is the comparative reactivity of the anthracenyl radical anion and the anion with a primary bromide. The anion is four times more reactive than the radical anion. This reactivity order means, therefore, that dialkylation is faster than initial alkylation of anthracene radical anion by

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primary bromide (k4b>kl).

The opposite is true for naphthalene where the radical anion is faster than the anion in reaction with primary chloride. The difference arises from disparate reactivity of the respective radical anions and shows the danger in extrapolating from one radical anion-anion pair to another. Another point of interest is the much greater reactivity of naphthalene radical anion *vs.* anthracene, which suggests alternate mechanisms for the electron transfer step, again raising the possibility for the existence of $RX^{\overline{\cdot}}$ for the naphthalene system.

The comparative reactivity order for $Anth^{\overline{\cdot}}$ *vs.* $Anth^{-}$ with chlorides and bromides is contrary to what is expected on the basis of their respective reduction potentials (17). This rate ratio changes by an order of magnitude in going from chlorides to bromides to iodides. For the iodides the rates of the two reactions are comparable but this surprising similarity may be fortuitous and may not in fact mean a similarity in mechanisms. Further discussion of this point appears in a subsequent section.

Focusing last on the rate ratios of di- and triphenylmethyl anions, we note that in contrast to the reduction potential order ($E_{\frac{1}{2}}\,\Phi_3C^- = 1.3v$ (18) $> E_{\frac{1}{2}}\,\Phi_2CH^- = 1.1v$ (19)) but in concert with the basicity order ($pka\ \Phi_2CH^- = 33.1 > pka\ \Phi_3C^- = 31.5$) (20), the diphenylmethyl anion is more reactive. This rate difference of about two powers of ten is ~3kcal/mole in ΔG† for primary and secondary bromides and decreases to 1.7 kcal/mole in ΔG† for primary and secondary iodides. It appears as if factors affecting basicity contribute more than factors affecting reduction potential for both primary and secondary systems.

The proposed comparisons of radical, radical anion and anion reactions are now described by two reactivity grids for organic halide reductions. Table V records patterns for a wide variety of reagents. There are definite trends, however for the chlorides, Figure 3 shows significant overlapping of reactivities of the three species. In particular, at log reactivity ratio of -2.7, there is an overlapping of all three reagents. The kinetic data as such is not likely to provide clear distinctions of mechanistic paths.

On the other hand reactivity ratios for the iodides offer a useful diagnostic for mechanistic distinctions. This is based on two considerations. First, there is no overlap of the three species. The full spread of S_N2 values for both dipolar aprotic solvents as well as protic solvents is quite distinct from the radical values, which in turn are distinct from radical anion valves. Second, the differences are sufficiently large to be useful. At the midpoints of the radical anion, radical and S_N2 ranges, the iodides would be 282, 68 and 6 times more reactive than the corresponding bromides. These values should lend confidence to predictions.

The second reactivity grid describes the structural effects

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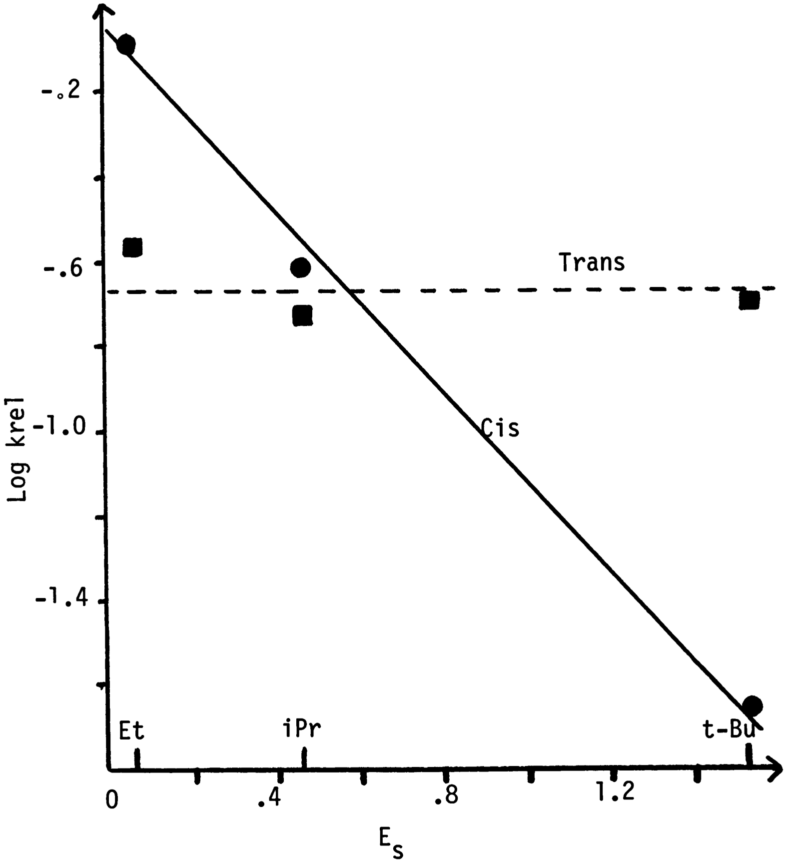

Figure 3. The relationship between the log of relative rates of reaction of 9-alkyl-10-lithio-9,10-dihydroanthracenyl anions with hexyl bromide, and the Taft steric constants for the alkyl groups

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of the halide. The rate ratio of primary to secondary halides in Table VI fall into a pattern such that radical and radical anion reactivities are similar and at midpoint the secondary halide is three times more reactive than the primary. Displacement reactivity ratios are distinct and the primary is 10-15 times more reactive than the secondary.

Table VI. The Ratios of Reaction Rates for Primary *vs.* Secondary Halides with Various Reducing Reagents

Reagent	Rate 1°/2°	Ref.
$Bu_3Sn^{\bullet}H$ + RBr	0.33	(6)
$Cr(en)_2II$ + RBr	0.11	(21)
$Phenyl^{\bullet}$ + RI	0.57	(27)
$An^{\bar{\cdot}}$ + RBr	0.26	(4e)
S_N2 average	15.5	(24, 25)
Φ_2CH^- + RBR	14.2	(26)
Φ_2CH^- + RI	10.1	(26)
$9\text{-}RAnH^-$ + RBr	9.0 (trans)	(26)

We now attempt to utilize these diagnostics for our study of organometallic reagents and the reaction scheme in equations 7, 8 and 9. In table V, the reactivity ratios for chlorides is, as expected in the overlapping region of radical, radical anion and S_N2 mechanisms. The iodide ratio is distinct, however, and although the reactivities are high and near those for radicals, the patterns for structural changes correspond to displacement reactions. In this regard, for reaction of alkyl dihydroanthracenyl anions to give trans product, the similarities of the rate ratios with those of other anions mitigates against the mechanistic change.

The predominate mechanistic pathway for the reaction of these anions and halides is consistent with a two-electron process (eq. 7), however this kind of kinetic evidence cannot exclude contributions of ~10% from an alternative scheme and clearly any contributions below 1% are undetectable. To assess small contributions to any certainty will probably require structural changes that augment those contributions.

In conclusion, do the similarities and differences in the reactivity patterns for these reactive species with organic halides indicate a basic relationship or are these similarities fortuitous and does nature provide distinct pathways of comparable energy. Of the three mechanistic possibilities considered for radical anions, electron transfer, radical-like and nucleophic substitution, electron transfer is indicated for highly exothermic reactions, and a radical-like process is likely for the less

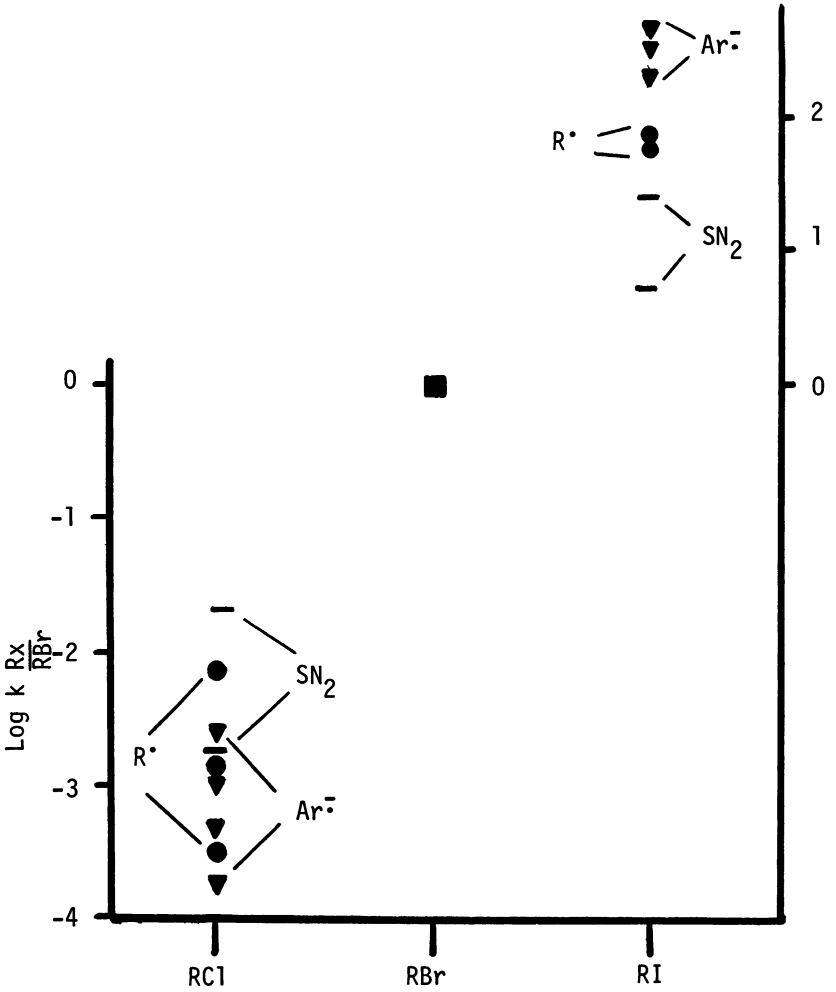

Figure 4. Correlations of anion, radical, and radical anion reactions with organic halides and the halide effect

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Table V. The Log of the Ratio of Second-Order Rate Constants for Chlorides and Iodides vs. Bromides with Various Reducing Reagents.

Reagent	RCl	RI	Reference
Bu_3SnH	-2.82	1.80	(6)
$Cr(en)_2$ (II)	-2.15	1.85	(21)
$Py^{\cdot}$ + Benzyl	-3.47		(22)
$Naph^{\overline{\cdot}}$	-2.58	2.50	(4d)
$Pyrene^{\overline{\cdot}}$	-2.96	2.27	(4d)
$Anth^{\overline{\cdot}}$	-3.71	2.57	(4d)
$Py^{\cdot}$ + NO_2-Benzyl	-3.36		(23)
S_N2 Typical	-1.7	0.7	(24)
ΦS^- in EtOH	-2.1	0.54	(25)
EtO^- in EtOH	-2.62	0.28	(25)
N_3^- in DMF	-2.66	0.83	(25)
N_3^- in MeOH	-2.13	1.05	(25)
SCN^- in DMF	-2.67	0.84	(25)
SCN^- in MeOH	-2.31	0.48	(25)
Φ_2CH^- in THF	-2.44	1.35	(26)
$HAnH^-$ in THF	-2.43	0.91	(26)

exothermic. Except for the fact that energetics of reaction sometimes are comparable for radical anion and displacement reactions (9), there is no compelling evidence that mechanistic similarities apply. In this regard a better concept of radical anions is as radicals with high reduction potentials rather than as anions. Moreover, the relatively weak basicity and reactivity towards proton donors does not fit well with connotations of anions (28).

For the case of anions, radical-like or pathways involving single electron transfer are not in evidence from the work described here. The products and reactivity patterns are expressed adequately by two-electron processes. A critical difference between the one and two-electron process is the contribution of bond making to the latter. Apparently this provides a substantial energy lowering that makes this path dominate in the systems studied in spite of the fact that electron transfer is possible. Conceivably this situation will be reversed for these kinds of anions when bond making is rendered less important, or when bond breaking more important, as for example *via* steric effects.

Acknowledgments. We are appreciative of the assistance of coworkers and collaborators whose names appear in the references. The financial assistance of NATO Grant No. RG 1069 is gratefully acknowledged.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch022

22

Electrophilic Reactions of Aromatic Cation Radicals

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A list of reactive intermediates in organic reactions would include the following: carbonium ions, carbanions, free radicals, carbenes (and nitrenes, etc.), arynes, anion radicals, and cation radicals. Among these the chemistry of all but the ion radicals has been well established and documented. Involvement of carbonium ions and free radicals in organic reactions was deduced long before these intermediates were detected directly (i.e., spectroscopically). In contrast, with the advent of esr spectroscopy a large number of ion radicals became identified and characterized before much interest was shown in their chemistry (1). This situation has changed during the last several years, particularly with respect to cation radicals. A number of reactions of cation radicals have been discovered and explored by both chemical and electrochemical techniques.

A cation radical is formed by the removal of an electron from a neutral molecule (eq. 1). The species so formed is at the same

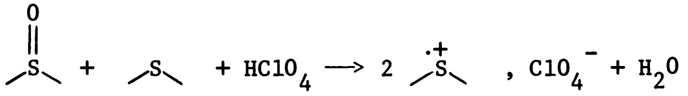
$$M - e^{-} \longrightarrow M^{\cdot +} \qquad (1)$$

time a cation and a radical (the remaining unpaired electron). Its chemistry therefore is of two kinds - both cationic and radical in nature.

The one-electron oxidation of eq. 1 may be achieved with chemical oxidants (e.g., sulfuric and perchloric acids, polyvalent metal ions) and anodic oxidation. The former methods are very useful for preparative-scale chemistry, while the latter is more versatile for exploring the mechanisms of cation-radical reactions (2, 3). Physical methods for gas-phase (pulse-radiolysis, electron-impact) and solution or glass-phase work (photoionization) can also be used.

It is understandable that electron-rich molecules, i.e., aromatics, heteroaromatics and alkenes, are among the most well explored in present cation radical chemistry, since such molecules are relatively easily oxidized. Some aromatics and heteroaromatics, furthermore, give cation radicals which are so stabilized by electron delocalization that they can be isolated as crystalline salts. It is, for the most part, cation radicals of this sort (from compounds 1-11) with which we have been working and whose chemistry will be described.

All of the cation radicals of 1-11 have been isolated as solid perchlorate salts. Compounds 1 (4) and 2 (5) are best oxidized by perchloric acid in anhydrous solvents. The cation radicals of 3 (6), 5 (7), 7, 8 (8), 10 (9), and 11 (10) can be made by oxidation with iodine-silver perchlorate. The crystalline cation radical perchlorates can be separated out or used in mixture with the solid silver iodide. The cation radical of 4 (7), as well as that of 3(6) is obtained by an interesting disproportionation reaction of the parent compound and its 5-oxide in perchloric acid (eq. 2). The reaction probably involves the dication and the parent (eqs. 3,4), but this has never been established. Although we have prepared the perchlorate of 6 chemically [using potassium dichromate in perchloric acid (11)], the more reliable method has been anodic oxidation in ethyl acetate solution (12). The cation radical of 10 is also obtainable anodically (13), but the method we prefer is electron exchange with $6^{\cdot+}$ (eq. 5) (14). We ran into so many problems with the dimerization of $7^{\cdot+}$ that we abandoned its preparation in favor of $8^{\cdot+}$ (8). In contrast, the preparation of $9^{\cdot+}$ is so easy that oxidation by iodine alone gives $9^{\cdot+}I^-$ (15). We have also prepared a number of crystalline cation radical tetrafluoroborates by reaction of the parent substance with $NOBF_4$ (16), but are not satisfied yet that they can entirely replace isolated perchlorates for chemical studies.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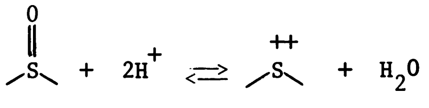
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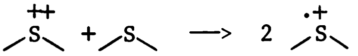
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$$10 + 6^{\cdot+}ClO_4^- \longrightarrow 10^{\cdot+}ClO_4^- + 6 \qquad (5)$$

Chemical studies amount mostly to reactions with nucleophiles; that is, the known chemistry is mostly of the cationic nature of cation radicals. Most of the reactions, furthermore, have the stoichiometry of eq. 6, where ArH and Nu^- are used in

$$2ArH^{\cdot+} + Nu^- \longrightarrow ArNu + ArH + H^+ \qquad (6)$$

general terms. The stoichiometry shows that a molecule of parent compound is obtained for each molecule of substitution product, and it is in this way, of course, that unpaired electrons eventually become paired.

A number of cases are now known in which the details of the reaction shown in eq. 6 have been worked out, principally by Blount (17, 18) and Parker (19, 20). The particular reactions will be described, but, in general terms, most of the reactions now documented occur by what Blount (17) and others term the half-regeneration mechanism (eq. 7-9). The rate-determining

$$\mathrm{ArH}^{\cdot+} + \mathrm{Nu}^{-} \rightleftharpoons (\mathrm{ArH\text{-}Nu})^{\cdot} \qquad (7)$$

$$(\mathrm{ArH\text{-}Nu})^{\cdot} + \mathrm{ArH}^{\cdot+} \rightleftharpoons (\mathrm{ArH\text{-}Nu})^{+} + \mathrm{ArH} \qquad (8)$$

$$(\mathrm{ArH\text{-}Nu})^{+} + \mathrm{B}^{-} \longrightarrow \mathrm{ArNu} + \mathrm{HB} \qquad (9)$$

step in this sequence may be either in eq. 8 or eq. 7, depending on the cation radical, nucleophile, and medium.

Reactions With Water

Polynuclear aromatics, e.g., perylene (9), and dibenzodioxin (12, 21) cation radicals are converted into quinones. The reaction must involve quite a number of steps since the stoichiometry is complex, eq. 10. Organosulfur cation radicals (except $3^{\cdot+}$) are

$$6\mathrm{ArH}^{\cdot+} + 2\mathrm{H_2O} \longrightarrow 5\mathrm{ArH} + \mathrm{O{=}Ar{=}O} + 6\mathrm{H}^{+} \qquad (10)$$

converted into sulfoxides, with the stoichiometry of eq. 11, where $R_2S^{\cdot+}$ represents the cation radicals of, for example, 1 and 2. Reaction of $1^{\cdot+}$ with water has been studied in detail and has been

$$2\mathrm{R_2S}^{\cdot+} + \mathrm{H_2O} \longrightarrow \mathrm{R_2S{=}O} + \mathrm{R_2S} + 2\mathrm{H}^{+} \qquad (11)$$

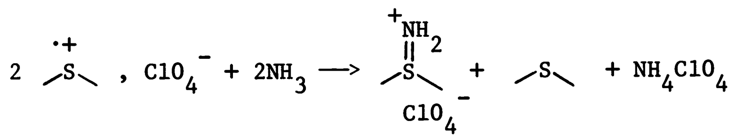
shown by Blount to be a half-regeneration reaction, which is in fact third order in water (eq. 12) (17). This is in contrast to

$$-d(1^{\cdot+})/dt = k_{\mathrm{total}}[1^{\cdot+}]^2[\mathrm{H_2O}]^3/[\mathrm{H_3O^+}] \qquad (12)$$

the proposal for a disproportionation mechanism, made when this reaction was first discovered (4).

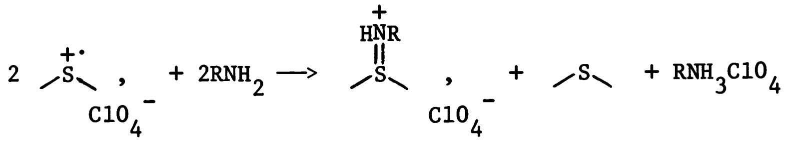
Reactions With Ammonia and Amines

The organosulfur cation radicals $1^{\cdot+}$, $2^{\cdot+}$, $4^{\cdot+}$, and $5^{\cdot+}$ react with ammonia and alkyl- and dialkylamines at their sulfur atoms. In principle, reaction with ammonia should give the sulfilimine salt, as in eq. 13. In practice, we have achieved this only with


(13)

$2^{\cdot+}$, the phenoxathiin sulfilimine being obtained if a rapid stream of ammonia is bubbled into a solution of $2^{\cdot+}$ (5). If the flow of ammonia is slow another product is obtained (12b). It is this type of product (12a, c, d) which is obtained from reaction of ammonia with $1^{\cdot+}$, $4^{\cdot+}$, and $5^{\cdot+}$, (7, 22). The products 12 arise apparently from formation and continued reaction of the sulfilimine.

Reaction of primary and secondary alkylamines with cation radicals has received limited attention. Sioda (23) reported that when DPA$^{\cdot+}$ reacted with ammonia and some primary alkylamines DPA was formed in half the amount of the DPA$^{\cdot+}$ used; that is, as if reaction had occurred according to eq. 6. However, the substitution product, if formed, was not sought. The only complete reactions we are aware of are our own with organosulfur cation radicals (7, 24–26). These react with primary amines to give *N*-alkylsulfilimine salts (eq. 14). Reaction with dialkylamines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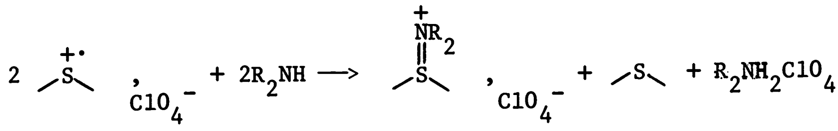
gives *N*,*N*-dialkylaminosulfonium salts (eq. 15). Over 60 examples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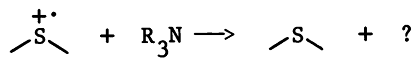
these two reactions have been carried out. Tertiary alkylamines do not react in this way. Among the few reactions we have carried out we observed only electron transfer (eq. 16) (7). We do not yet know what has happened to the amine; that is, if $R_3N^{\cdot+}$ was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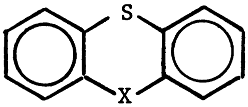
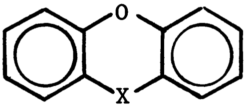
R = Me, Et

formed and underwent other reactions, such as dealkylation. The failure of trimethyl- and triethylamine to react is somewhat surprising in view of the reactivity of pyridine (see below) and the reaction of triethylamine with DPA$^{\cdot+}$ to give 13 (27). On the other hand the oxidation potentials of trialkylamines are in the

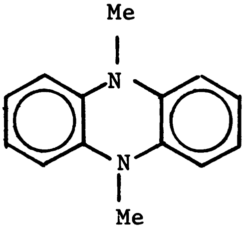
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch022



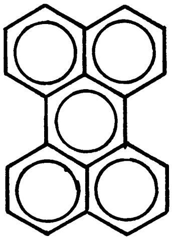
1, X = S (Thianthrene)
2, X = O (Phenoxathiin)
3, X = NH (Phenothiazine)
4, X = NMe
5, X = NPh



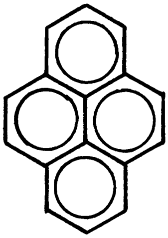
6, X = O (Dibenzodioxin)
7, X = NH (Phenoxazine)
8, X = NPh



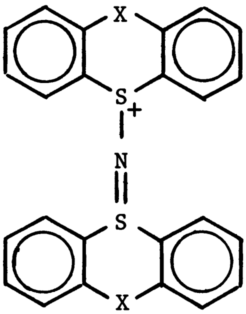
9
(5,10-Dimethyl-5,10-dihydrophenazine)



10
(Perylene)

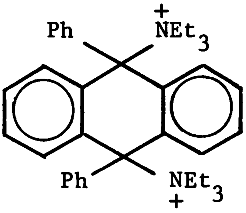


11
(Pyrene)



12

12a, X = S; 12c, X = NMe
12b, X = O; 12d, X = NPh



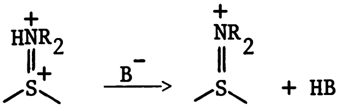
13

range 0.8-1.0 V (vs. SCE) as compared with 2.1 V for pyridine, so electron transfer from the tertiary amines is a lot easier than from pyridine.

A side reaction that occurs between primary alkylamines and the organosulfur cation radicals is the formation of 12 (particularly 12a, c, d). We do not yet know how this occurs.

The reaction of pyridine (and picolines and lutidines) with cation radicals is one of the earliest to be established and documented. In fact, it is referred to as the pyridination reaction. Reaction occurs at the pyridine's nitrogen atom. That is, electrophilic aromatic substitution (see below) does not occur, the pyridine ring being too unreactive for this. The pyridine behaves as a nucleophile and leads, for example, with $DPA^{\cdot +}$ to 14, and with $10^{\cdot +}$ to 15. The reaction with $DPA^{\cdot +}$ has been particularly well studied, and has been shown to be a half-regeneration reaction (28).

Reaction of the organosulfur cation radicals gives ring-pyridinated products, not S-pyridinated (e.g., 16 not 17). We supplied an explanation for this and its difference from the ammonia and alkylamine reactions [and the water reaction (6)]. It is that at some stage of product formation a dication intermediate is required (18). In order for the intermediate to lead to a



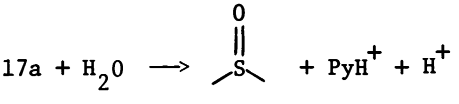
18

(17)

stable product proton loss must be possible, and this cannot occur from the dication 17. This idea has been validated by Blount, who has shown, kinetically, however, that 17d ($X = NC_6H_5$) is formed but is not stable to reaction with pyridine (eq. 18) (18). That

$$17d + Py \longrightarrow 16d + PyH^{+} \qquad (18)$$

is, the pyridination reaction in that case is second order in pyridine. Blount has also shown kinetically that 17a (X = S) is formed and is unstable to reaction with water (17). But in this case reaction occurs again at sulfur (eq. 19), the sulfoxide being formed.



(19)

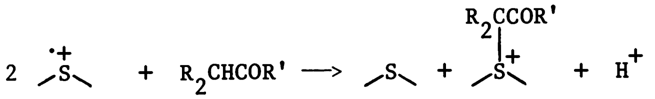
Reaction of arylamines with cation radicals usually leads to electron transfer (eq. 20). The coupling of arylamines leading,

$$ArH^{\cdot +} + ArNH_2 \longrightarrow ArH + ArNH_2^{\cdot +} \qquad (20$$

for example, to benzidines, is a cation radical reaction explored a great deal electrochemically, but is outside the scope of our discussion.

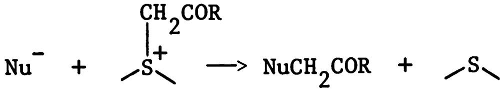
Reaction With Ketones

One would not ordinarily regard ketones as nucleophiles. An interesting reaction occurs, though, between dialkyl- and alkyl aryl ketones and organosulfur cation radicals. The products are β-ketoalkylsulfonium salts, the stoichiometry of whose formation follows the usual pattern (eq. 21). A variety of ketones has been used (29-31), such as acetone, butanone, methyl isopropyl



$$2\ {\diagup}\overset{\cdot+}{S}{\diagdown} + R_2CHCOR' \longrightarrow {\diagup}S{\diagdown} + {\diagup}\overset{\overset{R_2CCOR'}{|}}{S^+}{\diagdown} + H^+ \qquad (21)$$

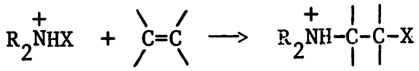
ketone, indanone-1, tetralone-1, and some cycloalkanones. The mechanism of reaction has not been investigated, but it has been suggested that reaction occurs between the cation radical and the enolic form of the ketone (31). Those β-ketosulfonium salts with an α-H are readily converted into sulfur ylides by treatment with base. In some cases the ylide is so readily formed that it is obtained directly from the cation radical reaction. The β-ketosulfonium salts have also been found very useful for preparing α-substituted ketones by nucleophilic displacement (e.g., eq. 22).



$$Nu^- + {\diagup}\overset{\overset{CH_2COR}{|}}{S^+}{\diagdown} \longrightarrow NuCH_2COR + {\diagup}S{\diagdown} \qquad (22)$$

Reactions With Alkenes and Alkynes

In contrast with the great wealth of information on both cationic and free-radical additions to alkenes and alkynes, not too much is known about analogous cation radical reactions. The most commonly known among these are additions of aminium radicals. The overall reaction is that of, say, an N-chloramine or N-nitrosamine in acid solution, brought about photochemically or by reaction with ferrous ion (eq. 23) (2). A chain reaction occurs in which $R_2NH^{\cdot+}$ is a participant.



$$\overset{+}{R_2NHX} + {>}C{=}C{<} \longrightarrow \overset{+}{R_2NH}-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-X \qquad (23)$$

We have discovered an entirely different addition of organosulfur cation radicals, resulting in the formation of alkane disulfonium salts (eq. 24) and vinyl disulfonium salts (eq. 25) (32).

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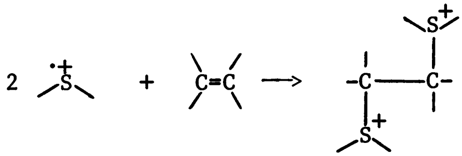

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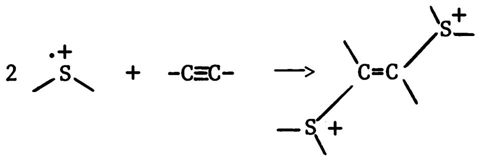
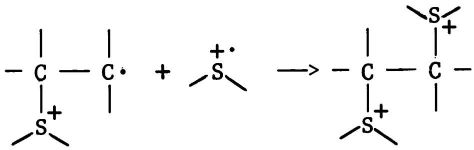


(25)

Here, again, we have used only the cation radicals 1 and 2. The phenothiazine cation radicals 4 and 5 react only very slowly. Among alkenes and alkynes reacting successfully are ethene, propene, 2-butene, cycloalkenes, acetylene, propyne, diphenylacetylene. The products are written in eq. 24 and 25 as trans adducts but we have not yet studied the stereochemistry of addition. Whether or not thiiranium and thiirenium ion radical intermediates are involved is an interesting conjecture yet to be explored.

These additions must be radical in nature in that an adduct is presumably formed first and then pairs with another cation radical (e.g., eq. 26). At the same time, however, the unsaturated compound is inactivated by electron withdrawing groups (e.g., as in propargyl chloride), so that the transition state to addition must also have much cationic character.

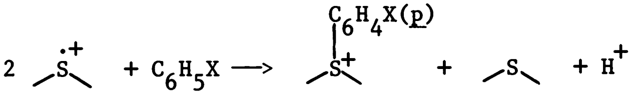


(26)

The adducts themselves are interesting classes of compounds in which the potential for competition between elimination and substitution reactions is being studied.

Reactions With Aromatics

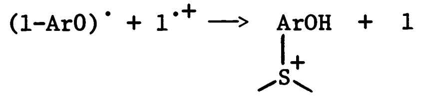
Cation radicals react as electrophiles with aromatics. The scope of this type of substitution is not too well explored, though. Amination of aromatics with dialkylaminium radicals has been known for some time (2). In recent years the arylation of organosulfur cation radicals was discovered in our own laboratories (eq. 27) (33, 34). The reaction is limited in that the



(27)

substituent X must be a good electron donor (OMe, OH, Me, NHAc), and that reaction occurs, apparently, only at the *para*-position. It was thought initially that the reaction was preceded by disproportionation of the cation radical, the electrophile then being the dication (33), but this was shown by Parker to be incorrect (19, 20). In the case of anisole and $1^{\cdot+}$ the reaction follows the half-regeneration steps (eqs. 7-9) (19). In the case of phenol, though, reaction follows these steps in acidic but not neutral solutions. In the latter, the reaction is first-order in $1^{\cdot+}$, the initial complex undergoing rate-determining deprotonation followed by faster oxidation by the second molecule of cation radical (eq. 28, 29) (20). Not many other examples of this type arylation are known. Anthracene and 9-phenylanthracene

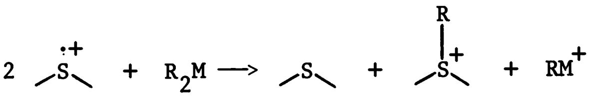
$$(1\text{-ArOH})^{\cdot+} \longrightarrow (1\text{-ArO})^{\cdot} + H^{+} \tag{28}$$



$$(1\text{-ArO})^{\cdot} + 1^{\cdot+} \longrightarrow \underset{\overset{|+}{\diagup S \diagdown}}{\text{ArOH}} + 1 \tag{29}$$

cation radicals are arylated at the 9,10- and 10-positions respectively (35). Even benzene and chlorobenzene can be used, whereas their reactions with $1^{\cdot+}$ are too slow to be useful.

We have more recently discovered a more versatile method of arylating heterocyclic organosulfur cation radicals, using organometallics R_2Hg and R_2Zn (eq. 30) (14). The reaction is even wider in scope in that dialkylmetals can be used too, which,



$$2 \; \diagup\overset{\cdot+}{S}\diagdown + R_2M \longrightarrow \diagup S \diagdown + \diagup\overset{\overset{R}{|}+}{S}\diagdown + RM^{+} \tag{30}$$

of course, is not possible as an analogue of direct arylation (eq. 27). The advantage of the newer method is that substitution at any position (o-, m-, p-) in the aryl ring can be achieved exclusively provided the right Ar_2M is used (e.g., di-o-tolylmercury, di-m-chlorophenylmercury). Furthermore, moderately deactivated aryl rings can be introduced (phenyl and chlorophenyl) which was not possible in the older method. Apparently, the polarization of the aryl-metal bond is sufficient to make reaction with the organosulfur cation radical feasible. Strongly deactivated rings, as in di-m-nitrophenyl- and di-perfluorophenylmercury cannot be used, though.

Although the cation radicals $1^{\cdot+}$ and $2^{\cdot+}$ react with R_2Hg and R_2Zn, $4^{\cdot+}$ and $5^{\cdot+}$ react only with the more active R_2Zn (R = Et, C_6H_5). Limited experiments, also, with $1^{\cdot+}$ and BuLi and Grignard reagents resulted in electron transfer.

These organometallic reactions are of further interest in that they may proceed with retention of configuration, as in other reactions of organomercurials (36). That is, optically

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active groups from $R_2{}^*Hg$ would then be introduced on sulfur. Furthermore, groups such as neopentyl and camphenyl may be attachable to sulfur with the use of the appropriate R_2Hg (37), and this may turn out to be the only way of making such attachments.

But, we do not know yet how these organomercury reactions do occur. The good yields and the absence of by-products in most of the reactions suggest that the alkyl and aryl groups are not free of the organometal before attachment to sulfur occurs. Electron transfer from R_2Hg to the cation radical prior to alkyl- or aryl group transfer may occur in analogy with other reactions of R_2Hg (38), although the high oxidation potential (1.8 V vs. Ag/Ag^+) of diphenylmercury (39) is not too persuasive of this possibility. The fact that we carry out the reactions in air without apparent interference by oxygen (cf. 38) suggests that free alkyl radicals are not involved. These reactions and their stereochemistry are under study.

Reactions With Inorganic Anions

The reactions we refer to here are with halide (F^-, Cl^-, Br^-, and I^-), cyanide, nitrite and nitrate ions. We have carried out a number of reactions with some of the cation radicals among $1^{\cdot+}$ - $10^{\cdot+}$. The mechanisms of the reaction in some cases need to be re-examined.

The simplest reaction to be expected with halide ions is nucleophilic halogenation (eq. 31). This seemingly simple

$$2\ ArH^{\cdot+} + X^- \longrightarrow ArX + ArH + H^+ \tag{31}$$

reaction has complexities, however, that need untangling. One of these complexities is electron exchange (eq. 32). This reaction

$$ArH^{\cdot+} + X^- \rightleftharpoons ArH + 1/2\ X_2 \tag{32}$$

occurs in all cases of our experience (except that of $9^{\cdot+}$) with iodide ion, and is used, in fact, in the iodometric assay of our cation-radical salts. The electron exchange is reversible, and in the case of iodine the reverse reaction is often used to prepare cation radicals. In that case a silver salt ($AgClO_4$, $AgBF_4$) is a co-reactant used to carry the equilibrium to the left. We do not, ourselves, know of cases in which iodide ion reacts as in eq. 31. The cation radical $9^{\cdot+}$ is stable toward iodide ion.

The possibility of electron exchange with chloride and bromide ion is a problem. In several cases exchange is thought to occur and to be followed by electrophilic halogenation (eq. 33). The final result is no different from that of eq. 31 and

$$ArH + X_2 \longrightarrow ArX + HX \tag{33}$$

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in most cases a proper distinction has not been made between the two processes.

Reaction of chloride ion with $1^{\cdot+}$ resulted in part in electron exchange since some chlorine was removed by nitrogen flow and was assayed (9%). Thianthrene (47%), thianthrene 5-oxide (18, 33%) and a very small amount (0.3%) of 2-chlorothianthrene (19) were also obtained (4). Since molecular chlorine slowly chlorinates thianthrene and since thianthrene 5-oxide can be prepared by oxidation of thianthrene with chlorine in wet solvents, the cation radical results are thought to "fit together" (eqs. 34-37). Nevertheless a proper kinetic and mechanistic study needs to be made.

$$1^{\cdot+} + Cl^- \longrightarrow 1 + 1/2\ Cl_2 \qquad (34)$$

$$1 + Cl_2 \longrightarrow 1(Cl_2) \qquad (35)$$

$$1(Cl_2) \longrightarrow 19 + HCl \qquad (36)$$

$$1(Cl_2) + H_2O \longrightarrow 18 + 2HCl \qquad (37)$$

Reaction of $1^{\cdot+}$ with bromide ion has not been studied. Reaction of $3^{\cdot+}$ with chloride and bromide ion gave 3 (about 45%), the 3-halogenophenothiazine (20, about 35%) and some 3,7-dihalogenophenothiazine (21, about 5%) (6). The formation of 21 was particularly perplexing, and led to the feeling that electron exchange (eq. 32) had occurred and electrophilic halogenation was responsible for the formation of 20 and 21. We do not know though that we can rule out successive half-regeneration reactions (eq. 38-42) since it is probable that the relative oxidation potentials of 3 and its halogenoderivatives would not entirely inhibit the successive steps.

$$3^{\cdot+} + X^- \longrightarrow (3\text{-}X)^{\cdot} \qquad (38)$$

$$(3\text{-}X)^{\cdot} + 3^{\cdot+} \longrightarrow 3 + 20 + H^+ \qquad (39)$$

$$20 + 3^{\cdot+} \longrightarrow 20^{\cdot+} + 3 \qquad (40)$$

$$20^{\cdot+} + X^- \longrightarrow (20\text{-}X)^{\cdot} \qquad (41)$$

$$(20\text{-}X)^{\cdot} + 3^{\cdot+} \longrightarrow 21 + 3 + H^+ \qquad (42)$$

In some of our earlier work it was reported that electron exchange also occurred between $10^{\cdot+}$ and chloride and bromide ion, leading only to the formation of 10 (9). We now think that this is not entirely correct. We now know that the chloride ion reaction leads to 3-chloro- (22) and a dichloroperylene (23), presumed to be the 3,9-isomer (40). Whether or not their formation

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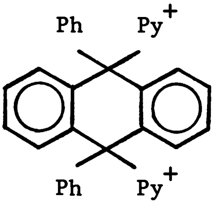

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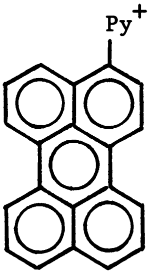

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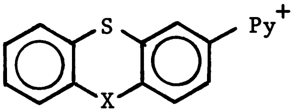

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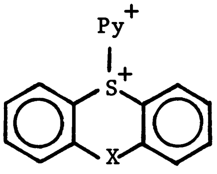

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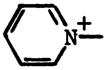
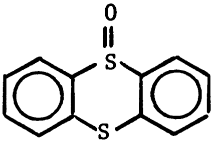
16a, 17a: X = S; 16c, 17c: X = NMe
16b, 17b: X = O; 16d, 17d: X = NPh

Py$^+$ = 



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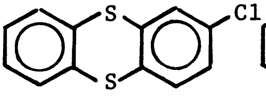

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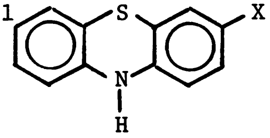

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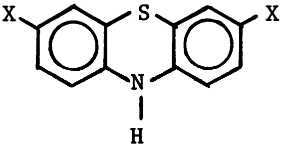

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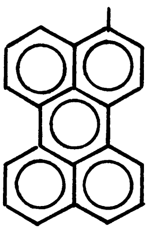

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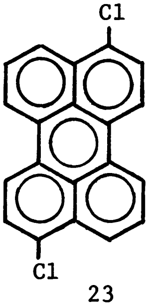

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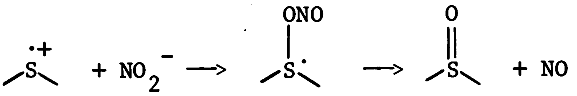
is preceded by electron exchange is still not settled but we feel that it probably is not. The bromide ion reaction also leads to the halogenoperylenes, but here preliminary electron exchange still appears to be likely. Reaction of chlorine with perylene also rapidly gives 22 and 23 (40). In fact the preparation of 22 appears, from the literature, never to have been achieved earlier. The great difficulty with the perylene work is in separating perylene from the monohalogeno and, to a lesser extent, the dihalogenoperylenes. Separation of the chloro compounds has now been achieved by multiple-plate TLC and column chromatography, and the products have been identified by mass spectrometry.

Fluoride-ion reactions are the most perplexing of all. A fairly large number of anodic fluorinations have been reported in the literature (41). These are anodic oxidations of aromatics and alkenes at potentials well below that of fluoride ion. Yet, examples of fluorination of isolated cation radicals are, so far, very rare. Reaction of fluoride ion with $3^{\cdot+}$ gave 3 (38%), its 3,10'-dimer (18%) and the well-known green dimer cation (6). In leading to the dimer, fluoride ion has behaved as a base. For some years it appeared that fluoride ion was too poor a nucleophile to react as in eq. 31, but we believe now that this is not correct. Mass spectrometry has shown that a monofluoro-N-phenylphenoxazine dimer is obtained from $8^{\cdot+}$ (8). Most recently mass spectrometry has also shown that a small amount of fluoroperylene is formed from $10^{\cdot+}$, in contrast with our earlier report (9). The major problem encountered here is in separating fluoroperylene and perylene. This has not been possible at all by TLC (40). It is evident now, therefore, that fluoride ion is indeed a poor nucleophile but reaction does occur to a small extent. Some cation radicals are inert even in anodic fluorination reactions, e.g., that of tetraphenylethylene (42). However, why many other anodic fluorinations are successful and "chemical" reactions are not is yet to be answered. Possibly, the answer lies in the second oxidation step (eq. 43) which may be easy at an anode but difficult by, say, $ArH^{\cdot+}$ in "chemical" reactions.

$$(ArHF)^{\cdot} -e^{-} \longrightarrow (ArHF)^{+} \longrightarrow ArF + H^{+} \qquad (43)$$

The summation appears to be that halide ion reactions need much further study. The only reaction which has been studied kinetically is that of $DPA^{\cdot+}$ with chloride ion, a reaction which follows the half-regeneration pathway, leading eventually to dichloro-DPA (43). In contrast, incidentally, $DPA^{\cdot+}$ and bromide ion undergo exclusive electron exchange (23).

Our experiences with nitrite-ion reactions show that both nitration and oxygen-atom transfer can occur. Thus, $6^{\cdot+}$ and $10^{\cdot+}$ give 2-nitrodibenzodioxin (12) and 3-nitroperylene (10) respectively according to eq. 6. The cation radical of zinc tetraphenylporphyrin is similarly nitrated at one of the pyrrolic carbon atoms (44). The perylene reaction is so facile that it can be carried out *in situ*, that is by shaking a solution of perylene with silver nitrite and iodine, but the perylene must be in large excess, say five-fold, over the iodine, to avoid polynitration, suggesting that in this case nitrogen dioxide may be the nitrating agent (10, 14). Pyrene can be nitrated similarly (10). The cation radical $9^{\cdot+}$ is converted *entirely* into mononitro-10 in what appears to be a two-stage reaction. We think that the first stage follows eq. 6, and then the 9 formed in that stage is slowly nitrated by nitrous acid (15). Reaction of $3^{\cdot+}$ gives 3-nitrophenothiazine also according to eq. 6 (6), and this is in accord with nitration of 6 with ferric chloride-nitrite ion (45). In contrast, $1^{\cdot+}$ and $2^{\cdot+}$ are converted entirely into the corresponding 5-oxides (6, 46). The last reactions have been interpreted (6) as in eq. 44, but we do not really know if,



(44)

perhaps, electron exchange does not occur first, that is, that if reaction is not between, say, 1 and NO_2. The oxidation potential of nitrite ion in acetonitrile is 0.96 V (vs. SCE), so that electron exchange with nitrite in cation radical reactions is a distinct possibility, as has been noted by Dolphin (47). This applies not only to reactions of $1^{\cdot+}$ and $2^{\cdot+}$ but to the other cation radical reactions too. In that they are all "clean" reactions it would appear that if electron exchange does occur in these reactions the NO_2 must react immediately and completely with the redox partner. A more complicated reaction has been noted with $5^{\cdot+}$ and nitrite ion, the products being not only 10-phenylphenothiazine 5-oxide but nitro- and dinitro-10-phenylphenothiazine 5-oxides, too (48).

Reactions with nitrate ion are similar to those of nitrite ion. That is, $6^{\cdot+}$ gave 2-nitrodibenzodioxin (12) and $1^{\cdot+}$ gave thianthrene 5-oxide (6). The last reaction was interpreted analogously to eq. 44, but the mechanism of the ring nitration is entirely unknown. Anodic nitrations which appear to be cation radical-nitrate ion reactions can be found in the literature, and their mechanisms are also unsolved.

Not much is known about the last of our inorganic ion reactions, that of cyanide ion. A number of anodic "cyanations" and cyanation-methoxylation reactions are in the literature. These, anodic oxidations in solutions (methanol usually) of cyanide ion, are reactions of cyanide with cation radicals. Yet, the only successful "chemical" reactions, we are aware of are with $10^{\cdot+}$ which gave small yields of 1- and 3-perylene nitrile (13), and with zinc octaethylporphyrin cation radical, which gives 68% of meso-cyanooctaethylporphyrin (49).

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch022

Acknowledgements

Support for research in cation-radical chemistry was received from the Robert A. Welch Foundation (Grant D-028), the National Science Foundation (Grant CHE 75-02794), and Texas Tech University Institute for Research.

Abstract

Aromatic and heteroaromatic cation radicals are readily prepared by one-electron oxidation of the parent compound. A number of these cation radicals are sufficiently stable to be isolated as solid salts, usually the perchlorates. These cation radicals react with a variety of nucleophiles, such as water, halide ions, nitrite, and cyanide ions. Reactions with purely aromatic cation radicals lead to ring-substituted aromatics. Reactions of aromatic organosulfur cation radicals occur more often at the sulfur atom, and lead to sulfonium salts of various kinds. Examples of the last type are reactions with aromatics (e.g., anisole), dialkyl- and diarylmercurials, primary and secondary alkylamines, and dialkyl and alkylaryl ketones. Addition of organosulfur cation radicals to alkenes and alkynes is also described. It is also possible that a cation radical and nucleophile undergo electron exchange instead of or prior to the substitution reaction. This possibility is particularly strong in reactions with halide ions and nitrite ion, and in these cases subsequent product-forming reactions may, in fact, be those of electrophilic substitution. Discussion of reactions of this kind is given.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch022

23

Use of the Semidione Spin Probe to Study Molecular Rearrangements *(1)*

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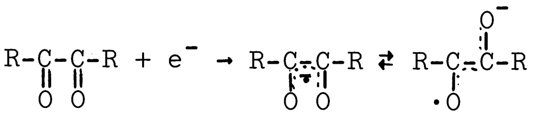
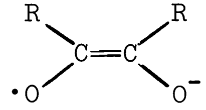
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch023

Radical ions derived formally by the one electron reduction of α-diones are termed 1,2-semidiones.



$$\mathrm{R{-}\underset{O}{\overset{}{\underset{\|}{C}}}{-}\underset{O}{\underset{\|}{C}}{-}R + e^- \rightarrow R{-}\underset{O}{\underset{\vdots}{C}}\cdots\underset{O}{\underset{\vdots}{C}}{-}R \rightleftarrows R{-}\underset{\cdot O}{\underset{\vdots}{C}}\cdots\overset{O^-}{\overset{\vdots}{C}}{-}R} \qquad (1)$$

Spin density is about equally distributed over the four atoms in the π-system, an estimate of the carbonyl carbon spin density being 0.35 for *cis*-dimethylsemidione and 0.28 for cyclohexane-1,2-semidione (2). This leads to considerable double bond character between the carbonyl carbon atoms of a *cis*-semidione in the range of 30%. Use of the valence bond structure 1 emphasizes



1

this double bond character and classifies the 1,2-semidione as an olefin derivative. This paramagnetic olefin derivative can be observed by esr spectroscopy during molecular reorganizations which may intimately involve the carbonyl carbon atoms. Since the paramagnetic center may be involved directly in the reaction the semidione group is not really a spin label for a double bond, when the carbonyl carbon atoms are directly involved in the rearrangement reaction.

Semidiones exist in equilibrium with the α-dione and the enediol dianion, equation 2. Low temperatures and ion-pairing favor the diamagnetic components of

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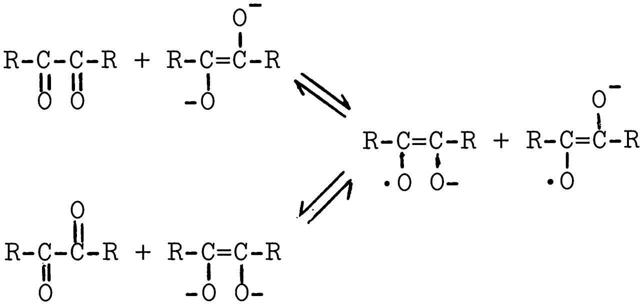
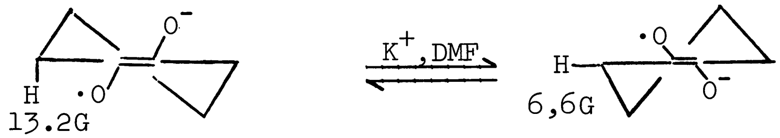
$$2\ RC(O\cdot)=C(O^-)R \rightleftarrows RCOCOR + RC(O^-)=C(O^-)R \qquad (2)$$

equation 2. Acyclic semidiones exist as a thermodynamic mixture of the *cis* and *trans*-isomers shown in equation 1, at least *in* a *static* system of DMSO plus alkali metal cation. The equilibrium is dramatically affected by ionic association; for example with lithium as the gegenion only the *cis*(lithium chelated)-ion pair can be observed in DMSO *whereas* with cesium as the gegenion only the *trans*(free ion)-semidione is observed (3). With *sodium or* potassium mixtures of the *cis and trans*-species are observed. Perturbation *of equilibrium* (2), for example by UV irradiation does not affect the observed *cis/trans*-ratio. This is not because the *cis* and *trans-semidione* are readily interconverted *by rotation about* the partial double bond. Instead the further equilibrium of Scheme 1 can serve to establish a thermodynamic ratio of the two isomers.

Scheme 1



The semidione group more nearly fulfills the definition of a spin label when the conformational equilibria of the cycloalkane-1,2-semidiones are considered. Thus, by esr spectroscopy the $\Delta H^{\ddagger}$ for ring flip of this cyclohexene derivative has been measured as 4 kcal/mole which corresponds to a magnetic coalescence temperature of -85° (4). This value can be compared with a $\Delta F^{\ddagger}$ of 5.3 *kcal*/mole observed for



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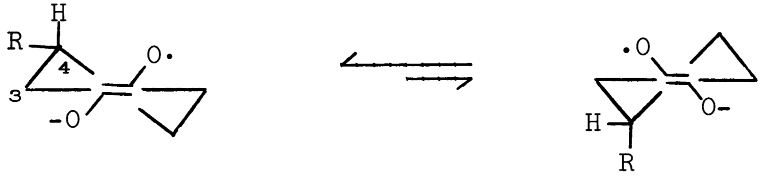
ring inversion of cis-3,3,4,5,6,6-d_6-cyclohexene in bromotrifluoromethane by p.m.r. (coalesence temperature = -165°) (5). It appears that in this case the semidione is a reasonable spin label for the olefin.

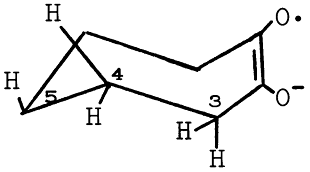
At 4-t-butyl group freezes the cyclohexane semidione into conformation 2 up to at least 90°. On the other hand for a 4-methyl substituent both 2 and 3 are



2 3

populated with 2 being preferred by an enthalapy difference of 1.4 kcal/mole ([3]/(2] = 0.13 at 40°) (4).

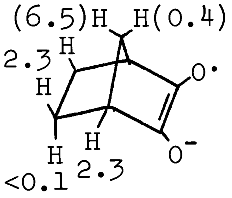
Cycloheptane-1,2-semidione is a rigid species ($\tau > 10^{-7}$ sec.) up to at least 90°. From an analysis of the esr hyperfine interactions it can be concluded that the single populated conformation is the staggered conformation 4 (6).



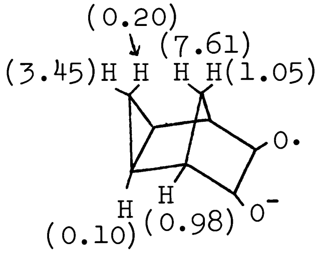
4

a^H(G)	C_3	C_4	C_5
equatorial	0.28	2.05	0.54
axial	6.60	0.28	<0.05

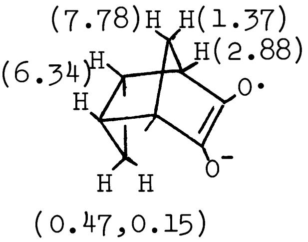
Cycloheptane semidione illustrates a rich long range hyperfine splitting due to π-σ delocalization. This interaction is maximized when the carbon-hydrogen bond involved forms one leg of a coplanar zigzag arrangement of bonds and the carbonyl carbon p_z-orbital. Two further examples of this long range interaction are given in structures 5 and 6.



5, a^H in G (ref. 7)



6a, a^H in G (ref. 6)

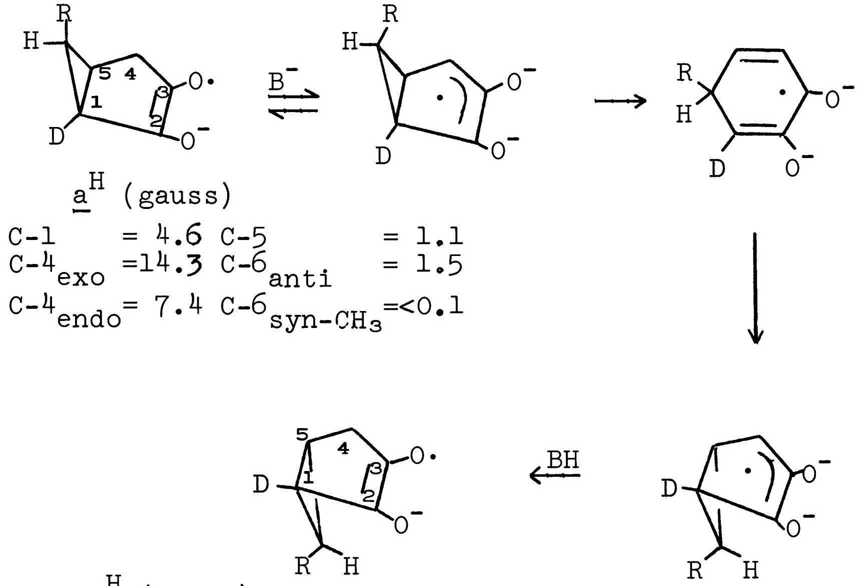


6b, a^H in G (ref. 6)

Valence Isomerization of Semidiones

The first case of molecular rearrangement in an aliphatic semidione was discovered by chance in an investigation of the long-range splitting in bicyclo-[3.1.0]hexan-2,3-semidion, Scheme 2 (8).

Scheme 2



a^H (gauss)

$C\text{-}1 = 4.6$ $C\text{-}5 = 1.1$

$C\text{-}4_{exo} = 14.3$ $C\text{-}6_{anti} = 1.5$

$C\text{-}4_{endo} = 7.4$ $C\text{-}6_{syn\text{-}CH_3} = <0.1$

a^H (gauss)

$C\text{-}1 = 4.3$ $C\text{-}5 = 0.40$

$C\text{-}4_{exo} = 14.6$ $C\text{-}6_{syn} = 0.90$

$C\text{-}4_{endo} = 7.6$ $C\text{-}6_{anti\text{-}CH_3} = 0.40$

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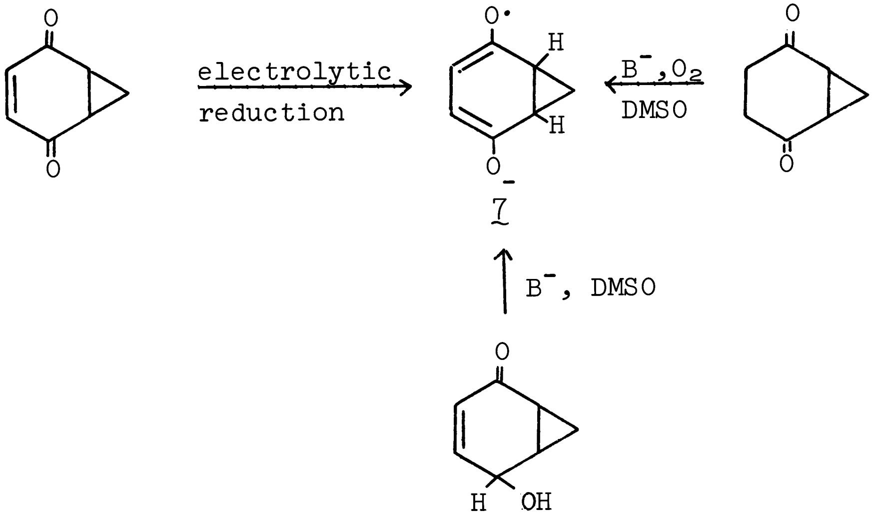
The isomerization of Scheme 2 occurs more rapidly the higher the concentration and the stronger the base. This, as well as hydrogen-deuterium exchange at the C-4_{exo} position implicate the radical dianion. The reaction also requires a steric driving force at 25°. The isomerization is not observed when R=D and is faster when R=C_2H_5 or CH_2OCH_3 than when R=CH_3. With R=CH_3 the reaction goes to completion, presumably because the isomer with the C-6_{anti} methyl group is thermodynamically more stable because of non-bonded interactions. These observations have led us to search for analogous bicyclic-monocyclic equilibria in systems analogous to the classical cycloheptatriene-norcaradiene and cyclooctatetraene-bicyclo[4.2.0]octatriene systems.

Paramagentic Analogues to the Cycloheptatriene-Norcaradiene Equilibrium. The 1,4-semidione (7) prepared as shown in Scheme 3 unquestionably exists in the bicyclic structure (9). This is easily ascertained

Scheme 3



by an examination of 7 and its analogue with methyl groups at the bridgehead positions. For the monocyclic valence isomer, equation 3 , one would expect $a^H_{1,5}$ to be approximately equal in magnitude to

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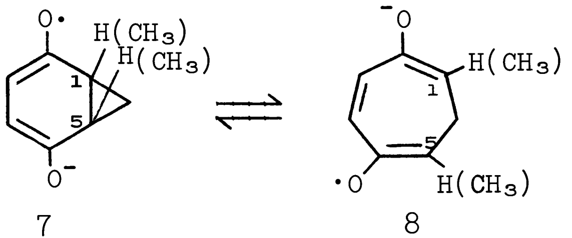
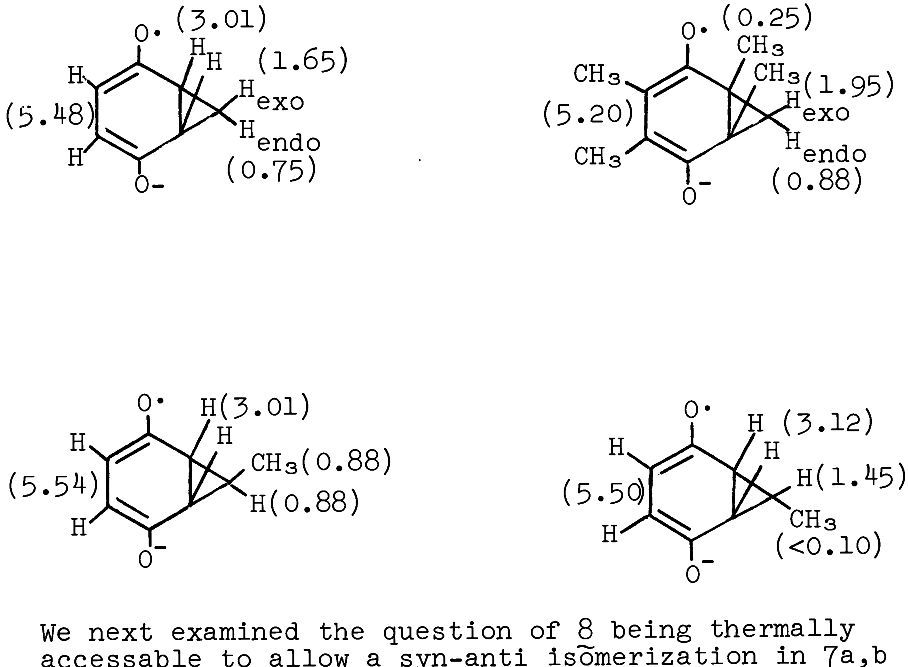


7 8 (3)

$a^{H}_{CH_3}(1,5)$ since as is well known, (e.g., ethyl radical) that $|Q^{H}_{\dot{C}H}| \cong |Q^{H}_{\dot{C}CH_3}|$. Instead the following values of the hsc are observed, as ecpected for the bicyclic structure.

Chart 1. Hyperfine Splitting Constants (gauss) for Bicyclo[4.1.0]hept-3-ene-2,5-semidiones(10).



We next examined the question of 8 being thermally accessable to allow a syn-anti isomerization in 7a,b as observed in the bicyclo[3.1.0]hexane system. It was expected that 7b would be more stable than 7a

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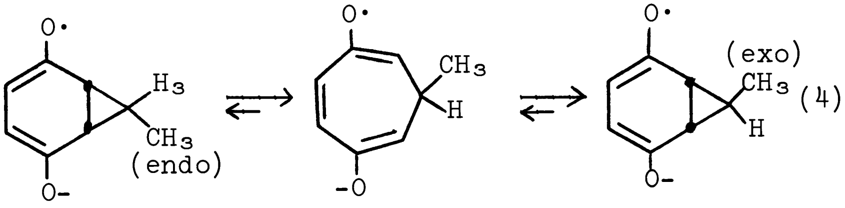
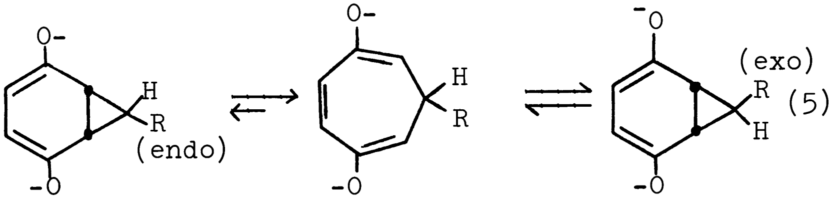


7a 8 7b

because of non-bonded interactions. The isomeric enedione precursors to 7a and 7b were synthesized and did not isomerize. Upon electrolytic reduction each dione initially formed its own 1,4-semidione which could be observed in the absence of the isomeric semidione. The equilibrium of equation 4 is either excluded or else must occur very slowly. However, upon extensive reduction either of the 1,4-enediones gave the same ratio of 7a/7b = 4 parts/96 parts. The simpliest explanation is that upon extensive reduction the dianions have an appreciable concentration. Although equilibrium (4) must occur slowly, the analogous equilibrium (5) apparently occurs quite readily at 25°. The observed 96/4 ratio of 7b/7a



probably reflects not only the thermodynamic stability of these isomers but may also reflect the various disproportion equilibrium constants similar to those of equations 2 and Scheme 1. The latter do not seem to be too important because the 96/4 ratio of semidiones did not vary significantly with the extent of reduction once an appreciable fraction of the starting dione had been reduced.

The formation of the 2,5-semidiones in the bicyclo[4.2.0]octane system has also been investigated. The two isomeric saturated diones shown in Scheme 4 both gave the same semidione upon base-catalyzed oxidation. Perhaps again valence isomerization at the dianion stage has occurred although in this case a base-catalyzed stepwise epimerization of the bridgehead hydrogen atoms in the semidione may be responsible for the isomerization assumed to occur for the

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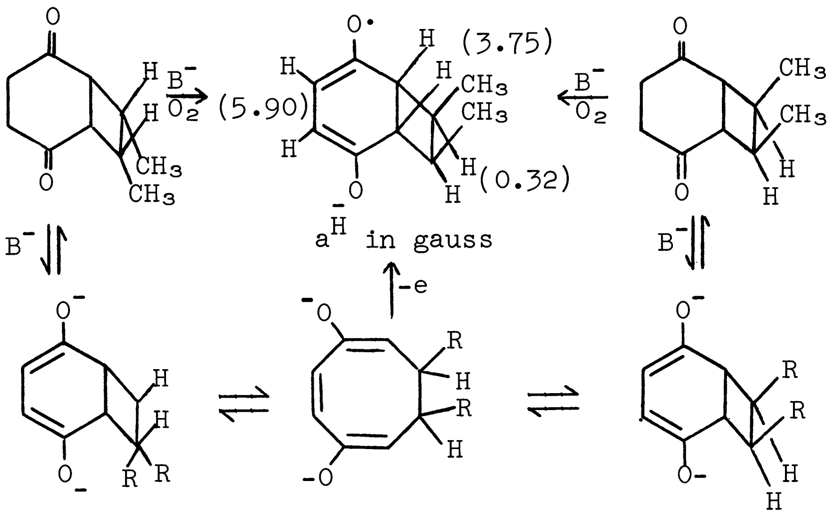
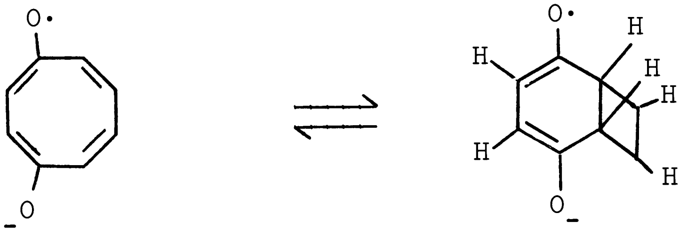
syn,syn-7,8-dimethyl isomer. Hydrogen-deuterium exchange at the bridgehead position occurs readily under the reaction conditions.

Scheme 4



1,4-Semidiones Derived from $(CH)_8$ Hydrocarbons. We have examined the possible valence isomerization shown in equation 6. Semidione 9 is stable and easily



(6)

8 9

prepared as shown in Scheme 5.

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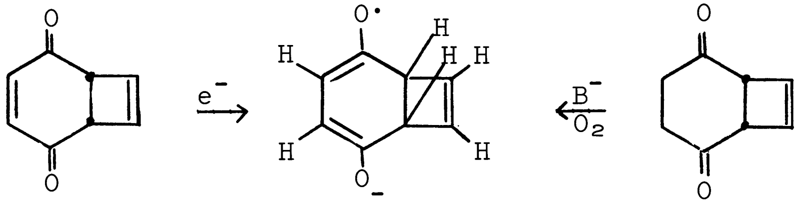
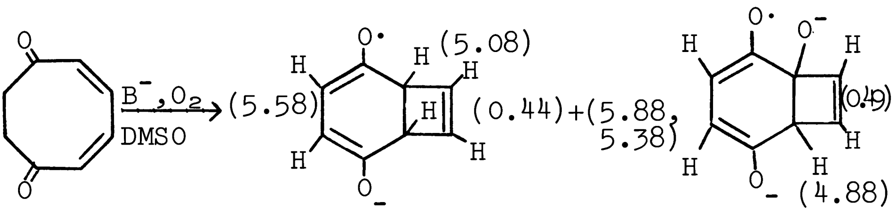
Scheme 5



Attempts to reduce the known cycloocta-1,3,6-triene-5,8-dione (11) electrochemically failed to produce any interpretable esr signals. The reduction polarographically involved a clean 2-electron wave (-1.0 v. relative to s.c.e.) apparently the result of 8 being more easily reduced than the parent dione. Base catalyzed oxidation of octa-1,3-diene-5,8-dione produced semidione 9 and a new species assigned structure 10 (equation 7).

(7)



9
a^H in gauss

10
a^H in gauss

The source of 9 is not certain because the monocyclic diene-dione was prepared by thermolysis of the bicyclic precursor and traces of this precursor could be responsible for the observation of 9. The formation of 10 requires valence isomerization between the monocyclic and bicyclic structure since semidione 10 is not formed from oxidation of 9 or its bicyclic precursor. Scheme 6 presents a possible rationalization for the formation of 10.

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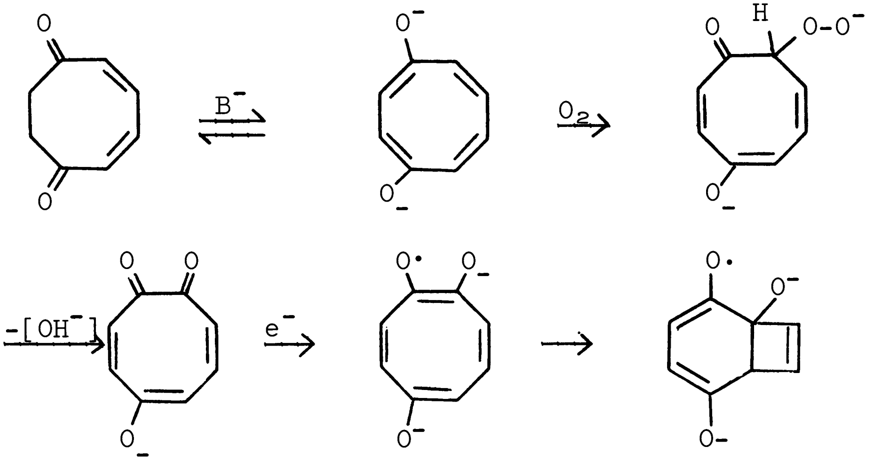
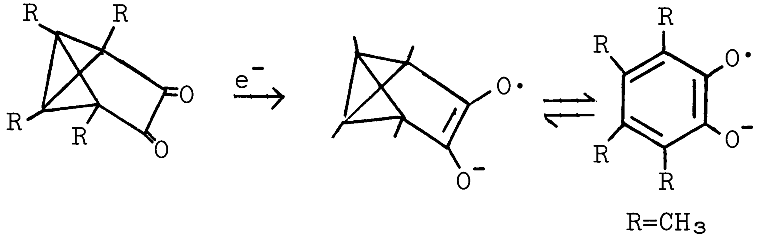
Scheme 6



10

1,2-Semidiones Derived from $(CH)_6$ Hydrocarbons. The possibility of reaction 8 was investigated by the electrolytic reduction of the stable dione 11 (12).

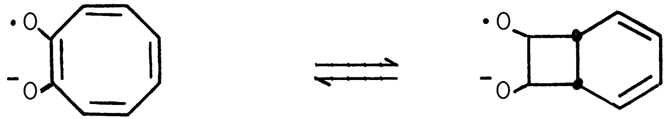


(8)

11 12 13

Dione 11 when reduced at -40° gave a broad singlet absorption which might be 12. The paramagnetic species was not stable and could be observed only when electrolysis was occurring. At 25° electrolytic reduction of 11 produced only 13. Apparently the expected valence isomerization of this system occurs readily at 25° but it is impossible to state whether rearrangement involves 12 or the analogous dianion.

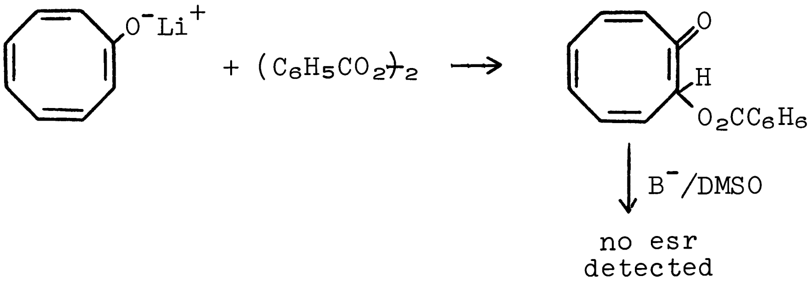
1,2-Semidiones Derived from $(CH)_8$ Hydrocarbons. A number of attempts have failed to produce the 1,2-semidione derived from cyclooctetraene (14), equation 9. Treatment of the appropriate α-benzoyloxy



14 ⇌ 15 (9)

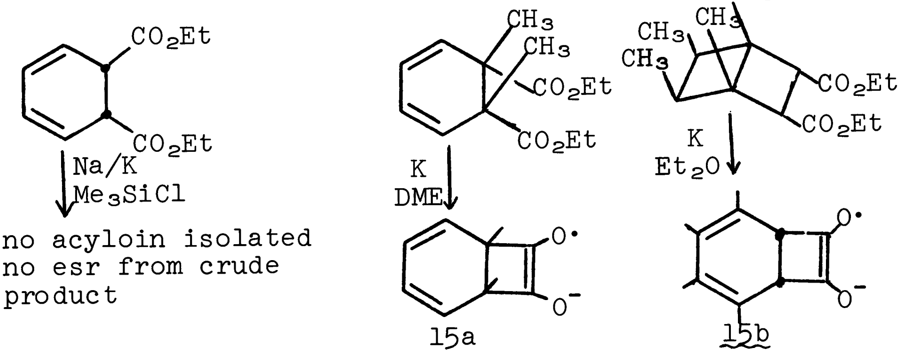
ketone with base/DMSO in a flow system has up to now failed to produce the semidione 14, Scheme 7.

Scheme 7



Two derivatives of 15 have been produced via the acyloin condensation of diesters. Unfortunately the acyloin condensation works very poorly for the diesters in Chart 2 and even in the presence of trimethylsilyl chloride pure acyloin condensation products could not be isolated. The spectra of semidiones 15a and 15b

Chart 2. Acyloin Dondensations of cis-5,6-carboethoxy-cyclohexa-1,3-dienes.



15a

a^H=0.08(2CH₃),
0.91(2),
0.44(2)

15b

a^H=7.2(2),
0.48(2CH₃),
0.24(2CH₃)

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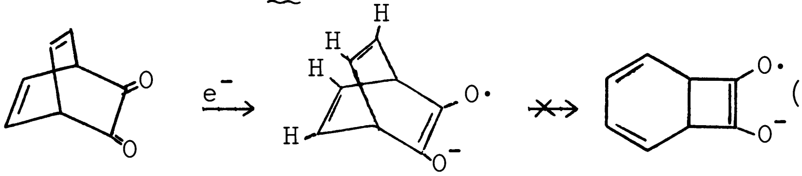
are shown in Figure 1. The large difference in hfsc for α-H and α-methyl require that these groups occupy bridgehead positions which is possible only in the bicyclic structure. The bicyclo[2.2.2]octadienesemidione (16) is perfectly stable and shows no rearrangement to structure 15 (equation 10).



(10)

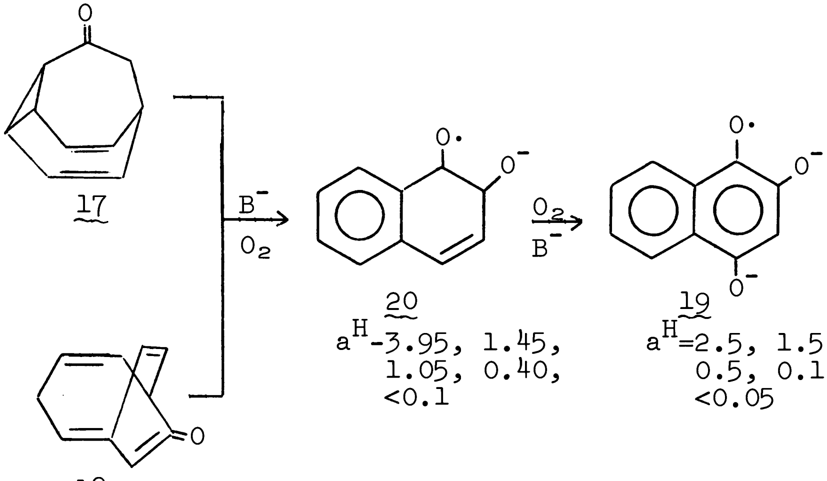
a^H=0.61G(4)

16

The hfsc for hydrogen atoms in a large number of cyclobutane semidiones are in the range 10-14 gauss (11,13). The value of 7.2 gauss assigned to structure 15b is definitely too low. This suggests that perhaps for 15b (but presumably not for 15a) a rapid equilibrium may exist between the bicyclic and monocyclic structures (i.e., equation 9).

1,2-Semidiones Derived from $(CH)_{10}$ Hydrocarbons. Treatment of 17 or 18 with oxygen in basic DMSO produce the extremely stable semiquinone 19 (12-14). With more limited amounts of oxygen 20 can be detected as the precursor to 19 (Scheme 8). It seems quite

Scheme 8



17

20

a^H-3.95, 1.45, 1.05, 0.40, <0.1

19

a^H=2.5, 1.5 0.5, 0.1 <0.05

18

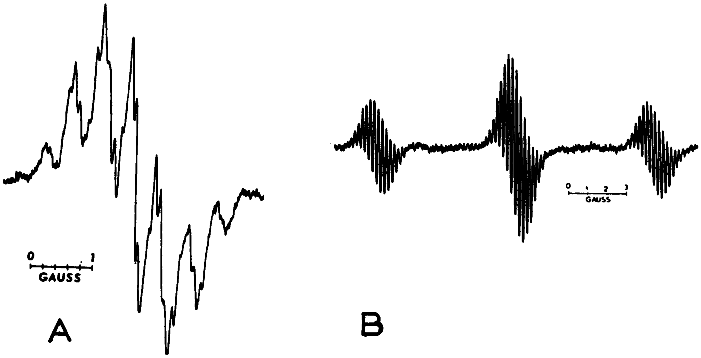


Figure 1. ESR spectra of bicyclo[4.2.0]octa-2,4-diene-7,8-semidiones in dimethyl sulfoxide solution at 25°C: (A) spectrum assigned to 15(a) (1,6-dimethyl); (B) spectrum assigned to 15(b) (2,3,4,5-tetramethyl).

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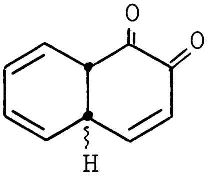
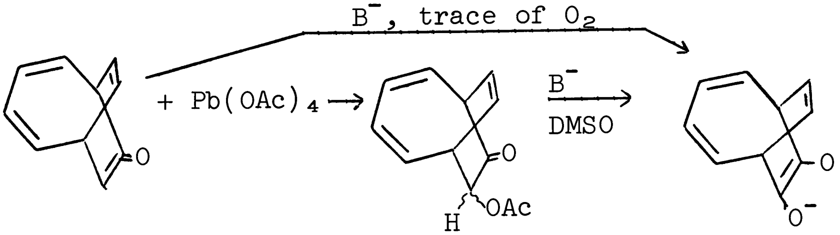
reasonable that the observed rearrangement-oxidation occurs via some oxidation state of the 9,10-dihydronaphthalene derivative 21.



21

Working with more limited amounts of oxygen it becomes apparent that there are additional stable paramagnetic intermediates preceeding the formation of 20. The semidione of 18 can be detected but it is very sensitive to traces of oxygen. When prepared from the acetoxy ketone (Scheme 9), 22 is the only paramagnetic

Scheme 9

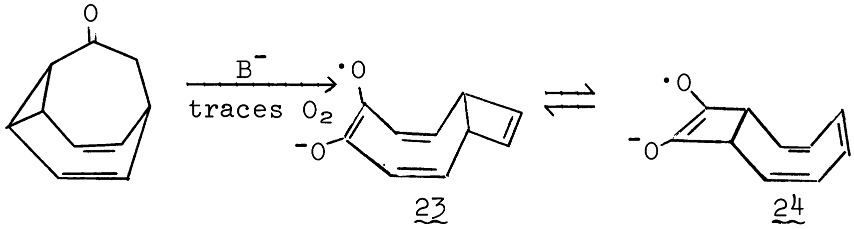


a^H=2.95(2),
1.30(2),
0.33(2)

22

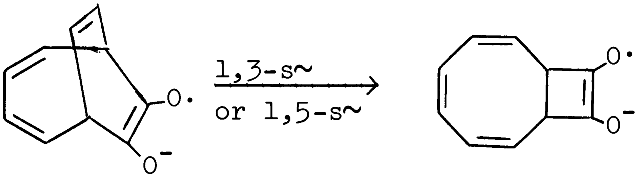
species detected. Furthermore 22 is quite stable in DMSO in the absence of oxygen for extended periods of time. Treatment of 17 with traces of oxygen at 0° in DMSO form an isomeric semidione which is also quite stable but is converted by additional oxygen into 19. The hfsc for this species suggest structures 23 or possibly a rapidly equilibration mixture of 23 and 24. There is no evidence for any equilibration between this species and 22 although such an interconversion

Scheme 10



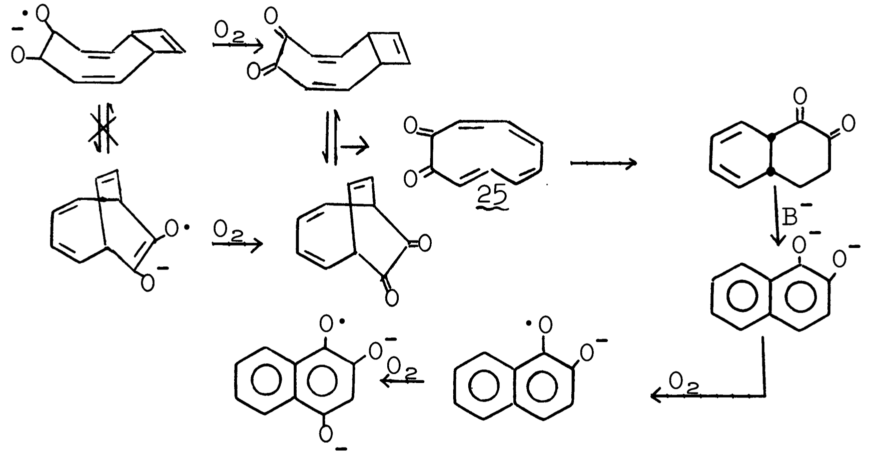
a^H=5.46(2),0.86(2),0.27(2),0.13(2)

could be readily achieved by a sigmatropic shift (equation 10). Both 22 and 23 are destroyed when treated with oxygen to yield cleanly 19; intermediate degrees of oxidation give mixtures of 19 and 22 or 23. Molecular oxygen will remove the electron from a semidione to yield the free dione. Can we in this instance be observing the molecular rearrangement of the diones? Scheme 11 presents a working hypothesis which seems to fit all of the observed facts.



(10)

Scheme 11



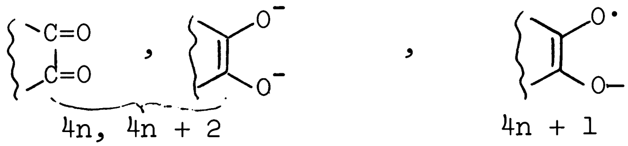
UV-Photolysis of semidione 23-24 forms still another apparently isomeric radical anion which also is destroyed by oxygen with the formation of 19. The photochemically formed radical anion possesses a low symmetry, perhaps 8 chemically different hydrogen atoms (equation 11). One reasonable suggestion for

$$23 \xrightarrow{h\nu} [\text{semidione}] \xrightarrow{O_2} 19 \qquad (11)$$

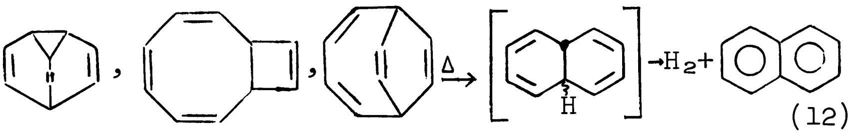
$$a^{H}=1.52, 0.76, 0.43$$
$$0.34, 0.17(4)$$

the structure of this semidione is the monocyclic cyclodecatetraenesemidione, $25^{\bullet -}$.

Perhaps the most important conclusion to be reached from this study of the isomeric semidione derived from $(CH)_{10}$ hydrocarbons, is that in this case the radical anions are themselves thermally stable at 25° in respect to valence isomerization. On the other hand apparently the diones rapidly equilibrate. It begins to appear that when the following three oxidation states are considered, that one or the other of



dione or dianion will possess the proper number of π or σ electrons for a low energy transition state of the Hückel-type (4n + 2) or of the Möbius-type (4n). The radical anion, on the other hand, never possesses the proper number of electrons to completely stabilize either a Hückel or Möbius-transition state. Finally, the overal course of the oxidation of ketones 17 and 18 at 25° appears to resemble the high temperature pyrolysis or the photolysis of the corresponding olefins which proceeds to naphthalene via the 9,10-dihydronaphthalenes (equation 12) (15).



(12)

1,3-Sigmatropic Rearrangements of Semidiones

A number of pairs of semidiones radical anions, which could be interconverted by a 1,3-sigmatropic

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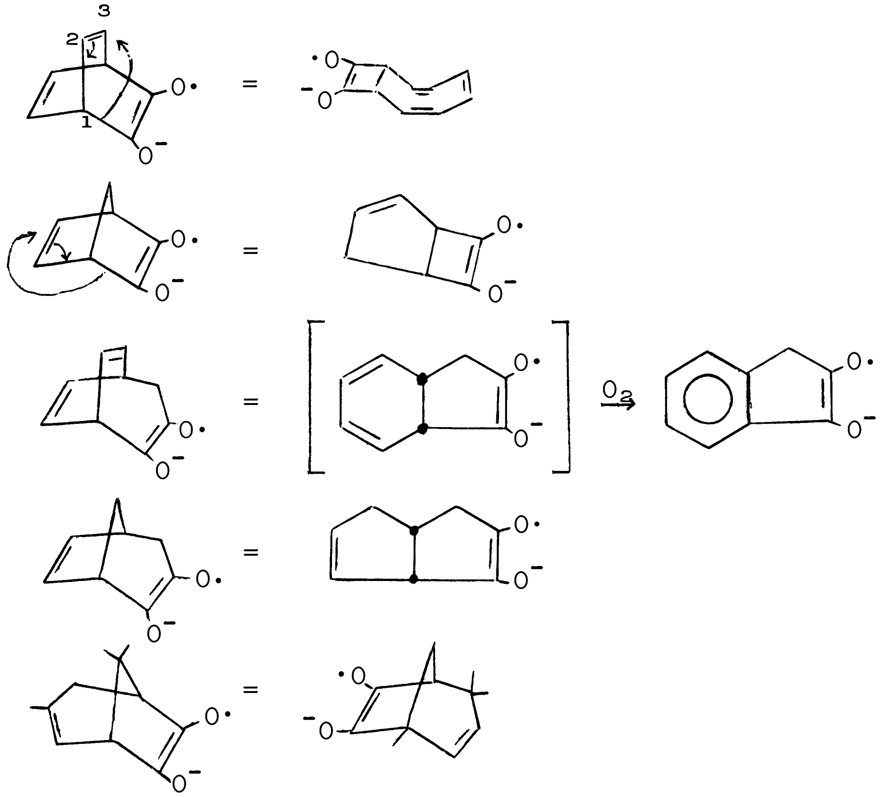
rearrangement, are recognized to not undergo thermal isomerization at 25°. Some of the pairs of semidiones are listed in Chart 3. Nevertheless, the formation of semidiones from α-acetoxy ketones plus base or from a methylene ketone plus base and oxygen has in two different cases led to the products of a 1,3-rearrangement.

Chart 3. Non-equilibrating Pairs of Semidiones



When exo- or endo-hydroxynorbornene-2-one is treated with base in DMSO the first esr signal that can be detected (~0.1sec. after mixing) is that of the rearranged semidione, bicyclo[3.2.0]hept-2-ene-6,7-semidione (16). On the other hand when norbornene-2,3-dione is reduced electrolytically, or 3-alkoxynorbornene-2-ones are oxidized in basic solution the unrearranged semidione is observed, Scheme 12. In both

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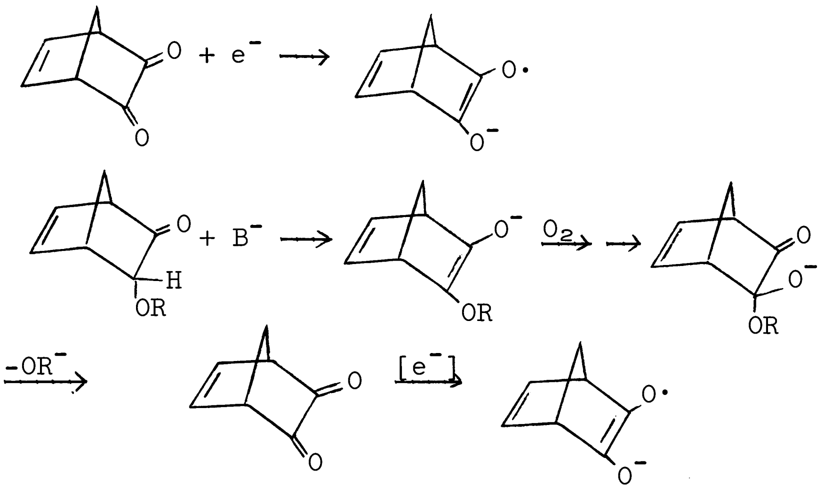
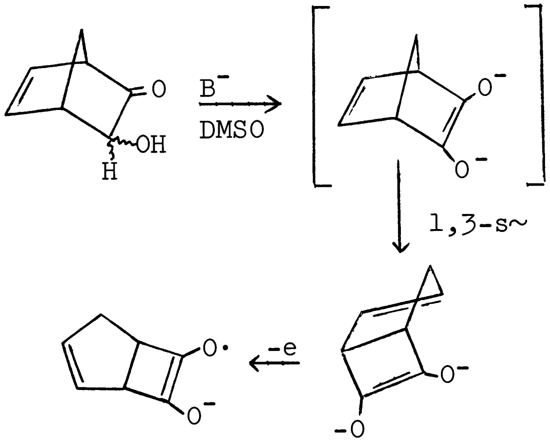
Scheme 12



of these cases the unrearranged semidione can be formed without going through the enediol dianion. On the other hand, starting from the α-hydroxy ketone the enediol dianion is first formed and it is apparently the dianion which undergoes molecular rearrangement, Scheme 13.

Scheme 13



The rearrangement of the dianion is apparently reversible. Thus, the three monomethyl derivatives shown in Scheme 14 all produce roughly the same ratio of the isomeric semidiones **26** and **27**. A second case where

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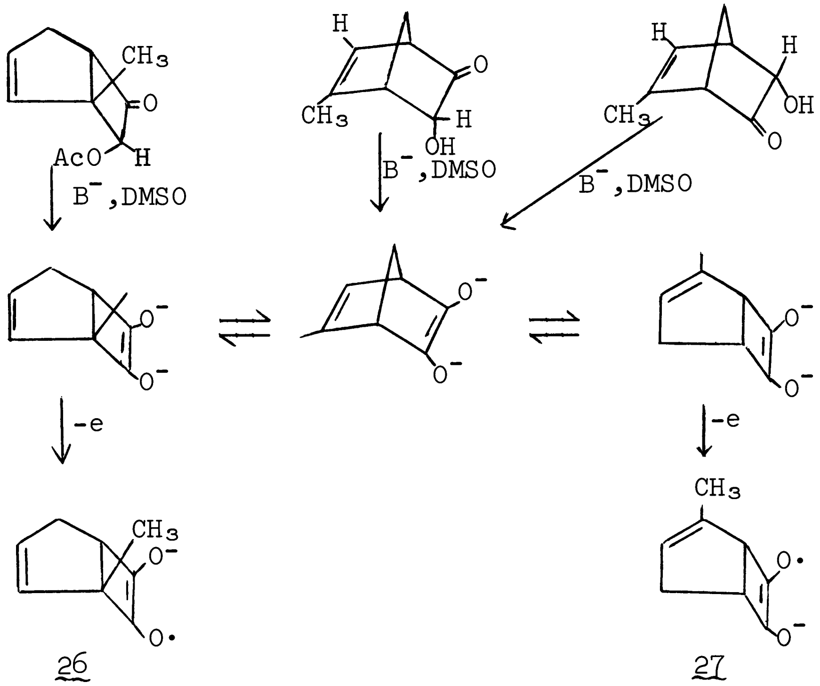
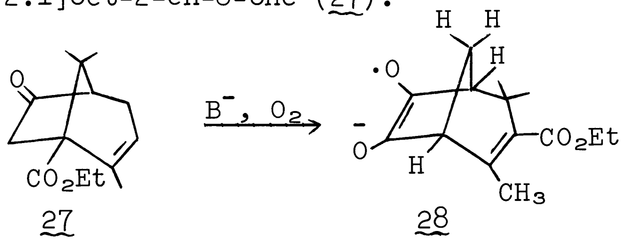
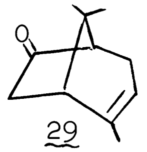
Scheme 14



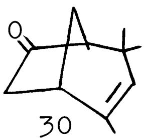
this type of rearrangement has been noted is in the oxidation of 1-carboethoxy-2,8,8-trimethylbicyclo-[3.2.1]oct-2-en-6-one (27).



The structure of the semidione 28 is assigned as the basis of the hfsc which cannot be rationalized with an unrearranged structure. On the other hand, 29 and 30 yield the unrearranged semidiones. The assignment of



29



30

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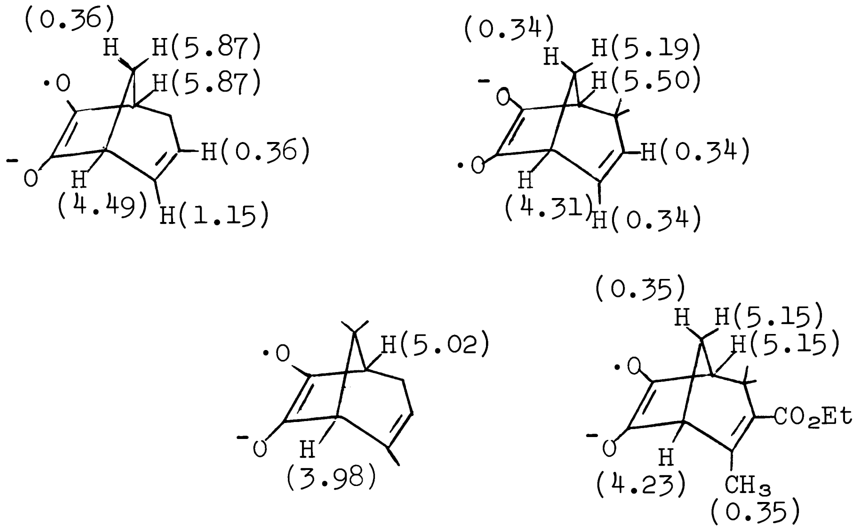
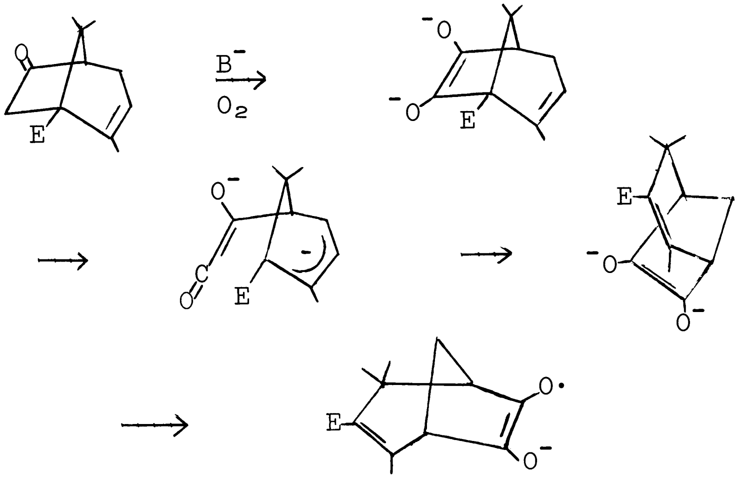
hfsc in the [3.2.1]-system are shown in Chart 4.

Chart 4. Bicyclo[3.2.1]hept-2-ene-6,7-semidiones, a^H in gauss



The presence of the carboethoxy group in 27 facilitates the rearrangement. This is quite reasonable if the rearrangement proceeds via the enediol dianion. Scheme 15 illustrates how this could occur in a stepwise manner. A stepwise rearrangement may also be

Scheme 15 E=EtO$_2$C-



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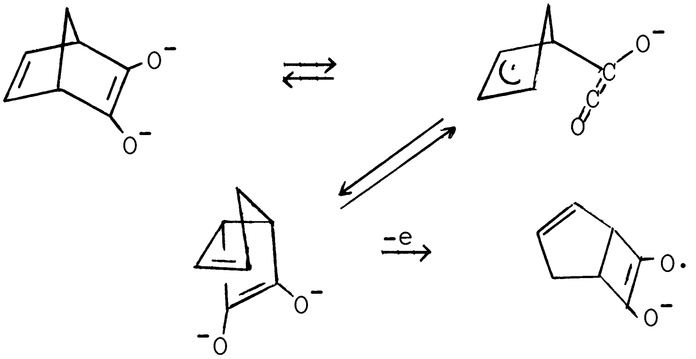
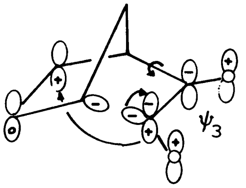
involved in the rearrangement of the dianion of the enediol in the bicyclo[2.2.1]heptene system. Scheme 16 illustrates how this process may occur.

Scheme 16



Another possible rationalization involves the formation of a transition state for a concerted rearrangement having a sextet of electrons. The concerted 1,3-migration would involve transition state 31. The argument can be advanced that a pair of electrons



31

in the carbonyl p_z-orbital will be more nearly available in the dianion than in the semidione since ρ_C in the dianion will be approximately twice ρ_C in the radical anion (approximately 0.38 and 0.76, respectively).

Photochemical 1,3-sigmatropic rearrangements occur readily for many of the ketones related to the semidiones shown in Chart 3. Observation of thermal rearrangements for the radical anions would in a way be an example of photochemistry without light. However it appears that these reactions require more than just having a single electron in the π^*-orbital of the carbonyl group as in the semidione. Photochemical rearrangements of the thermally stable semidiones are, of course, also possible. Thus the facile transformation of 32⇌33 has been observed.

32

a^H=0.91,0.40(3),
0.14(2) gauss

33

a^H=8.20,0.40(3),0.21,
0.14 gauss

Conclusions

Open shell species, such as the semidiones, are not more prone to undergo pericyclic reactions than their closed shell analogs. Indeed, it appears as if one or the other of the diamagnetic analogues (dione or dianion) undergo rearrangement more readily than the radical anion. In general this seems to be connected with the diamagnetic molecules possessing either the 4n or 4n+2 π plus σ electrons required for a low energy Möbius or Hückel transition state. On the other hand the dianion or diketone may simply posess higher energy contents (because of electrostatic considerations), thus leading to a lower energy barrier for a thermodynamically favorable rearrangement of the bicyclic skeleton.

Abstract

Bicyclic—monocyclic valence isomerization of a radical dianion in the bicyclo[3.1.0]hexanesemidione system has been demonstrated. Symmetrical 1,4-semidiones formally derived from cycloheptatriene and cycloöctatetraene perfer to exist in the bicyclic (4.1.0 and 4.2.0) structures. Bicyclic—monocyclic valence isomerization in the bicyclo[4.1.0]hept-3-ene-2,5-dione system occurs more readily for the dianion than for the radical anion. Several radical anions derived from the (CH)$_{6-10}$ annulenes are reported. In the case of the 1,2-oxygenated derivatives of (CH)$_{10}$ the dianions or radical anions are stable, but the diones undergo valence isomerization and under oxidatime conditions are converted to 4-hydroxynaphthalene-1,2-semiquinone. Enediol dianions in the bicyclo [2.2.1]hepta-2,5-dione and 1-carboalkoxybicyclo[3.2.1] octa-2,6-diene systems have been observed to undergo

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch023

thermal 1,3-signatropic rearrangements under conditions where the semidiones are stable. Photochemical 1,3-sigmatropic rearrangement has been observed for bicyclo [3.2.0]hept-7-ene-2,3-semidiones.

Acknowledgement

We gratefully thank Dr. E. Weissberger for a gift of ketones **29** and **30** and Dr. W. Erman for ketone **27**.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch023

24

Aromatic Anion Radicals as Bronsted Bases

Correlation of Protonation Rates with Singlet Energies of the Precursor Aromatic Hydrocarbon*

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Notre Dame, IN 46556

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

One of the aims of physical organic chemistry is to derive generalizations regarding structure-reactivity relationships which can be related to the fundamental electronic properties of a molecule. In this paper are described experiments and interpretations of these experiments which seem to indicate that there is a fundamental correlation between the singlet energy of an aromatic hydrocarbon and the rate of protonation of its anion radical.

Anion radicals of aromatic hydrocarbons are known to undergo protonation in protic media (1-5). The spectrophotometric pulse radiolysis technique has been used to demonstrate this process in alcoholic solutions of several aromatic compounds (2). In such experiments, the anion radicals are produced by the reaction of the hydrocarbon with the solvated electron

$$\mathrm{Ar} + e^-_{\mathrm{solv}} \xrightarrow{k_1} \mathrm{Ar}^{\bullet -} \qquad (1)$$

Protonation can take place by reaction of the anion radical with the solvent molecule

$$\dot{\mathrm{A}}\mathrm{r}^- + \mathrm{ROH} \xrightarrow{k_2} \dot{\mathrm{A}}\mathrm{rH} + \mathrm{RO}^- \qquad (2)$$

The additional protonation process is the reaction of $\dot{\mathrm{A}}\mathrm{r}^-$ with ROH_2^+ produced in the pulse

$$\dot{\mathrm{A}}\mathrm{r}^- + \mathrm{ROH}_2^+ \rightarrow \dot{\mathrm{A}}\mathrm{rH} + \mathrm{ROH} \qquad (3)$$

which is negligible at low dose rates. Dorfman and coworkers (2) found that the rates of reaction 2 were strongly dependent on the acidity of the solvent, e.g., i-PrOH<EtOH<MeOH. In a particular solvent, k_2

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

varied over several orders of magnitude for the various compounds. Even the rate constants for protonation of two isomeric forms of the same compound, i.e., cis- and trans-stilbene, were found to be different (3).

In a previous study, the rates of reaction of sodium naphthalenide and anthracenide with water in THF as solvent were determined by a stopped-flow technique (4) and found to be faster for the former anion radical. The authors indicated, however, that this behavior seemed to be in disagreement with predictions of reactivities from molecular orbital calculations.

Rates of protonation of aromatic anion radicals also have been estimated from polarographic measurements by observation of changes in the curve shape upon protonation (5). These experiments were carried out in DMSO as solvent with various phenols as proton donors. This method, however, is applicable only within a limited range of protonation rates and is less reliable than the direct observation of the kinetic process. Furthermore, correlation of the protonation rates (5) with calculated electron densities does not appear to be satisfactory.

In an attempt to determine the factors which control the rate of protonation, we examined the correlation of these rates with some basic properties of the molecules, such as electron affinity, ionization potential, and singlet energy, which are known to be interrelated for alternant aromatic hydrocarbons.

Experimental Results

Protonation rate constants of various aromatic anion radicals in 2-propanol were measured by the pulse radiolysis technique as described previously for stilbene (3). The aromatic compound was dissolved in the alcohol, usually in the range of 10^{-5} to 10^{-3} M. Certain compounds, such as tetracene and the dibenzanthracenes, which were difficult to dissolve directly in the 2-propanol, were first dissolved in a small amount of dry THF and then diluted by the alcohol. The amount of THF in the irradiated solution was always less than 5%. The solutions were deoxygenated by prolonged bubbling with ultrapure nitrogen or argon and were kept in the dark. Irradiation was carried out at room temperature using 9 MeV electrons from an ARCO LP-7 linear accelerator. The pulse duration was usually 5 ns, although longer duration pulses were sometimes used to achieve higher doses.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

Table I

Kinetics of Formation and Protonation of Aromatic Anion Radicals

No.	Aromatic Hydrocarbon	λ(nm)[a]	$k_5(M^{-1}s^{-1})$[b]	$k_2(s^{-1})$[b]	$\Delta E_{S_1 \leftarrow S_0}$ (cm^{-1})[c]	I(ev)[d]
	Alternant					
1	cis-Stilbene[e]	496	$<10^7$	$6.4x10^5$	31500	
2	Naphthalene[f]	810		$5.7x10^5$	32200	8.15
3	Phenanthrene[f]	1000		$3.4x10^5$	28900	7.86
4	Triphenylene[g]	410	$<10^8$	$3.0x10^5$	29900	7.89
5	trans-Stilbene[e]	486	$<10^7$	$7.3x10^4$	30400	7.60
6	Anthracene[f]	720		$4.7x10^4$	26700	7.47
7	Chrysene[h]	460-500	$<10^8$	$2.0x10^4$	27700	7.60
8	Pyrene[i]	492	$1.1x10^8$	$1.0x10^4$	26900	7.41
9	1,2,3,4-Dibenzanthracene[i]	790	$4.0x10^8$	$3.2x10^3$	26700	7.44
10	Benzo(a)pyrene[i]	583	$7.0x10^8$	$2.5x10^3$	24700	7.12
11	Tetracene[j]	810	$1.2x10^9$	$4x10^2$	21200	7.04
12	1,2,5,6-Dibenzanthracene[i]	790	$1.5x10^8$	$2x10^2$	25300	7.38
13	Perylene[i]	576	$1.4x10^9$	20	23000	7.06
	Non-Alternant					
14	Acenaphthylene[k]	387	$1.4x10^9$	$4x10^2$	21500	8.22
15	Fluoranthene[j]	445	$7.2x10^8$	~ 7	25300	7.95
16	Azulene[i]	425	$1.5x10^9$	1.5	14200	7.43

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Footnotes to Table I

a. wavelenths at which most of the kinetic measurements were done, usually it is one of the main peaks of the anion radical absorption.
b. The rate constants are accurate to ±15% except for the very low values which may have a larger experimental error.
c. taken from "Photophysics of Aromatic Molecules" by Birks, J.B., Wiley-Interscience, London (1970) p. 70, except for the values of acenaphthylene from Heilbronner, E., Weber, J.P., Michl, J. and Zahradnik, R., Theoret. Chim. Acta (Berl.), (1966) 6, 141.
d. Ionization potentials taken mostly from Boschi, R, Clar, E. and Schmidt, W., J. Chem. Phys. (1974) 60, 4406, and from Birk's book (footnote b, p. 457).
e. from ref. 3.
f. from Arai, S., Tremba, E.L., Brandon, J.R. and Dorfman, L.M., Can. J. Chem. (1967) 45, 1119, see also ref. 2.
g. obtained from K&K Laboratories.
h. purified by zone refining.
i. obtained from Aldrich Chemical Co., highest purity available.
j. obtained from Eastman Organic Chemicals
k. purified by sublimation.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

The experiments consisted of observation of the time profile of the formation and decay of the optical absorption of the various anion radicals. For all cases the transient spectrum was examined to verify the position of the maxima. These peaks were found to be in agreement with the literature values for the corresponding anion radicals in MTHF glasses (6). The wavelengths in which the kinetic measurements were performed with each compound are given in Table I. In some cases, such as chrysene and triphenylene, the transient absorption did not decay down to zero at all wavelengths. The spectra were then recorded before and after decay in order to verify that the observed decay is due to the dissappearance of the anion radical. The remaining absorption was sometimes assignable to the solvent radical (7). In most cases, however, the kinetic measurements were carried out at wavelengths above 450 nm where neither the solvent radical nor the product of protonation show any considerable absorption.

The irradiation of dilute alcoholic solutions produces mainly solvated electrons and solvent radicals with no direct action on the solute. The solvent radicals may be initially positive ions $\dot{R}OH^+$ which will convert very rapidly into carbon centered radicals. For example, in 2-propanol the main radicals will be $(CH_3)_2\dot{C}OH$. A small amount of acid, ROH_2^+, is also produced.

The reaction of all polynuclear aromatic compounds with the solvated electron (reaction 1) is very rapid (2,3), $>10^9 M^{-1}s^{-1}$, and in most cases it is diffusion controlled. Under the experimental conditions used, this process was complete long before the protonation took place.

The anion radicals can protonate by reaction with the solvent molecule (reaction 2) and by the small amount of acid produced by the radiation pulse (reaction 3). The latter reaction was minimized by use of very low doses, producing only $1\text{-}2\times10^{-6}$ M of ROH_2^+. However, when the rate of reaction 2 becomes lower than $\sim10^4 s^{-1}$ the contribution of reaction 3 cannot be neglected. It was, therefore, necessary to overcome this complication by adding a small amount of base. For this purpose, sodium metal was dissolved in 2-propanol prior to the experiment to produce a solution of $(CH_3)_2CHO^-Na^+$ in the required concentration. Since the concentration of this base was only in the mM range it was not expected to affect the rate of reaction 2. Experiments have shown that the addition of base has no effect on the rates of protonation when they are higher than $10^4 s^{-1}$. A small decrease in rate was noticed upon addition of base when k_2 was in the range of 10^4-$10^3 s^{-1}$, as expected.

The use of base has another effect on this system. The radical from 2-propanol, $(CH_3)_2\dot{C}OH$, dissociates into $(CH_3)_2\dot{C}O^-$ with a mid-point at $7x10^{-4}M$ of $(CH_3)_2CHO^-Na^+$ (8).

$$(CH_3)_2\dot{C}OH + (CH_3)_2CHO^- \rightleftarrows (CH_3)_2\dot{C}O^- + (CH_3)_2CHOH \qquad (4)$$

The basic form of this radical is known to be a stronger reducing agent than the neutral form (9). Thus, it was found to reduce the better electron acceptors among the compounds used in the present study. In such cases, the initial rapid formation of $\dot{A}r^-$ by reaction 1 is followed by a slower increase in absorption due to reaction 5

$$Ar + (CH_3)_2\dot{C}O^- \rightarrow \dot{A}r^- + (CH_3)_2CO \qquad (5)$$

Rate constants for this electron transfer process were determined from measurements of the rate of formation at various concentrations of Ar and the results are given in Table I along with the rates of protonation.

Discussion

The reactivities of aromatic compounds have been correlated with various physical parameters, such as ionization potentials, triplet energies, free valence, and energy levels of lowest unoccupied orbitals (10,11). It was noted that simplified HMO calculations were sufficient to account for many experimental observations. However, the reactivities of aromatic anion radicals toward proton donors have not been successfully correlated with any physical parameter. Such a correlation may shed light on the mechanism and allow prediction of unknown rates.

In the early work on aromatic anion radicals, Paul, Lipkin, and Weissman (1) correlated the reactivities of these radicals with electron affinities derived from their spectra. Bank and Bockrath (4) compared the rates of protonation of naphthalene and anthracene anion radicals and concluded that the higher rate for naphthalene was in contradiction to their prediction from molecular orbital localization energy calculations. Fry and Schuettenberg (5) correlated the rates of protonation of various aromatic

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anion radicals with the calculated electron densities at the position of highest electron density in each of these radicals. This correlation also appears unsatisfactory. It seems that parameters derived from simple MO calculations are not adequate to explain the reactivity of anion radicals.

In even alternant aromatic hydrocarbons, the difference in energy between the lowest unoccupied molecular orbital (LUMO) and the highest occupied one (HOMO) is essentially equal to the singlet energy difference $\Delta E_{S_1 \leftarrow S_0}$. The unpaired electron in the anion radical occupies the LUMO. Upon protonation of this radical an odd alternant structure is formed in which the unpaired electron occupies the non-bonding orbital. The exothermicity upon protonation is, therefore, $\sim\frac{1}{2}\Delta E_{S_1 \leftarrow S_0}$. If this energy change affects the rate of protonation one would expect a correlation between these rates and $\Delta E_{S_1 \leftarrow S_0}$. Fig. 1 shows that a plot of log k_2 vs $\Delta E_{S_1 \leftarrow S_0}$ gives a reasonable linear dependence. Deviations from linearity appear to be relatively larger when the rates of protonation are low, probably because the lower rates are more susceptible to experimental complications, particularly impurity effects. It should be noted that the protonation rates determined by Fry and Schuettenberg (5) also give a reasonable straight line when we plot them against $\Delta E_{S_1 \leftarrow S_0}$. As expected for alternant hydrocarbons, linearity is also obtained when log k_2 is plotted versus the ionization potential I (plot not shown, see values in Table I). In principle, k_2 can be correlated also with electron affinity (12) or with the polarographic reduction half-wave potential, but the literature values for these parameters are widely scattered. The molecular dimensions seem to have little effect on k_2.

Non-alternant hydrocarbons do not appear to fit easily into the linear relation with the singlet separation (Fig. 1). Also, they do not fit on the line of log k_2 versus ionization potential. For example, the ionization potential of azulene is similar to that of anthracene but the rate of protonation of the former is four orders of magnitude slower (see Table I), which is in line with the large difference between their respective $\Delta E_{S_1 \leftarrow S_0}$ values. The same considerations hold also for fluoranthene and acenaphthylene. Because of sparse experimental data the apparent fit of these latter compounds with the line in Fig. 1 should be treated cautiously. These findings indicate

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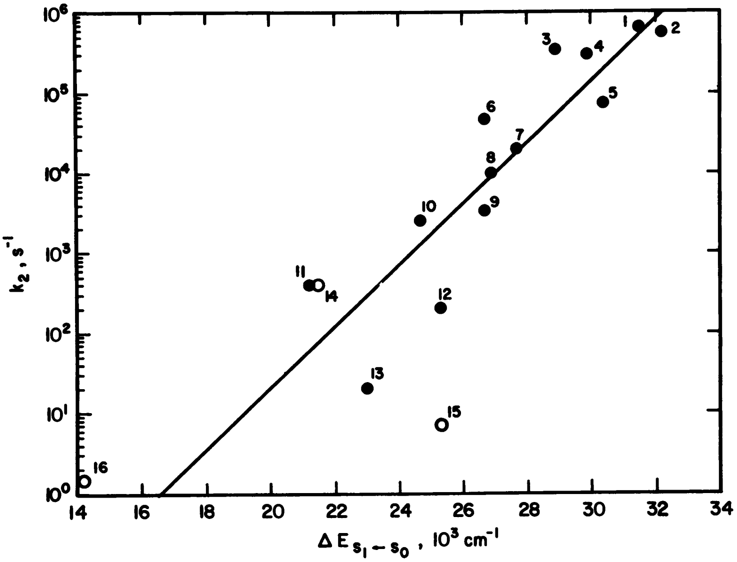

Figure 1. Correlation of protonation rate constants (k_2) with singlet–singlet separation ($\Delta E_{s_1 \leftarrow s_0}$). The compounds are identified by the numbers as given in Table I.

the relation between ionization potential and singlet-singlet separation does not hold for non-alternant hydrocarbons as discussed in detail by Michl and Thulstrup (13) for the case of azulene.

The present study shows that the rate of protonation of an aromatic anion radical can be correlated with the energy level (LUMO) of the unpaired electron. This finding suggests, on the basis of Hammond's postulate (14), that the transition state in the protonation process resembles the anion radical more than it resembles the product (neutral radical).

The correlation described by Fig. 1 does not hold for biphenyl and the three terphenyls whose rates of protonation (2) deviate from the line, most probably because of non-planarity.

The rates of reduction of the aromatic compounds (Table I), appear to increase as $\Delta E_{S_1 \leftarrow S_0}$ and I decrease, in contrast with the behavior of k_2. This trend is to be expected since k_5 reflects the electron affinity which decreases when I and $\Delta E_{S_1 \leftarrow S_0}$ increase. The values of k_5 also can be related to the polarographic half-wave potentials, $E_{1/2}$, of the aromatic hydrocarbons and the general trend is, of course, a decrease in k_5 when $E_{1/2}$ is more negative.

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*The research described herein was supported by the Division of Basic Energy Sciences of the Department of Energy. This is Document No. NDRL-1839 from the Notre Dame Radiation Laboratory.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch024

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

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Self-Reactions of Alkylperoxy Radicals in Solution (1)

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In 1967 Benson (2) noted that the most important area of disagreement, or perhaps uncertainty, which had been raised at the International Oxidation Symposium in San Francisco (3-5) was the nature of the termination reaction of alkylperoxy radicals. In the ten years that have elapsed since that meeting numerous papers have appeared on the kinetics and mechanisms of the self-reactions of these radicals and it is true to say that we are no closer to a complete understanding of the mechanisms of these reactions than we were in 1967.

Prior to 1957 the termination reaction for liquid-phase hydrocarbon autoxidation at oxygen pressures above *ca.* 100 torr was generally written as

(1) $RO_2^{\bullet} + RO_2^{\bullet} \longrightarrow$ non-radical products.

Kinetic results were consistent with a bimolecular termination reaction whereas reaction products and mechanisms were something of a mystery. At that time it was known that the termination rate constant for autoxidation of cumene (6) is about three orders of magnitude smaller than the termination rate constant for autoxidation of tetralin (7). It was, however, generally accepted that the termination rate constants for tertiary (8) and secondary (9) alkylperoxy radicals are insensitive to the structure of the hydrocarbon residue in the radical.

Russell (10) was the first to propose an acceptable mechanism for the termination of primary and secondary alkylperoxy radicals while Blanchard (11) made the important discovery that cumylperoxy radicals are capable of undergoing non-terminating as well as terminating interactions during autoxidation of cumene. These two pieces of work stimulated a great deal of further research on the self-reaction of alkylperoxy radicals. The results of this work, which are reviewed here, have provided compelling evidence that tertiary and secondary (and primary) alkylperoxy radicals can terminate by different mechanisms in the liquid-phase. For this reason these two types of radicals will be discussed separately.

© 0-8412-0421-7/78/47-069-413$05.00/0

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

Tertiary alkylperoxy radicals will be discussed first because the mechanism for these radicals is reasonably well understood. On the other hand the mechanism for self-reaction of secondary and primary alkylperoxy radicals is still in doubt and these radicals are considered in the second part of this review.

Tertiary Alkylperoxy Radicals

t-Butylperoxy. The simplest tertiary alkylperoxy radical is *t*-butylperoxy and there is considerable experimental evidence in support of the mechanism given in Scheme I for self-reaction of this radical.

Scheme I

$$(2)\quad 2t\text{-BuO}_2{}^{\bullet} \rightleftharpoons t\text{-BuO}_4\text{Bu-}t$$

$$(3)\quad t\text{-BuO}_4\text{Bu-}t \xrightarrow{k_3} [t\text{-BuO}^{\bullet}\,\text{O}_2{}^{\bullet}\text{OBu-}t]_{\text{cage}}$$

$$(4)\quad [t\text{-BuO}^{\bullet}\,\text{O}_2{}^{\bullet}\text{OBu-}t]_{\text{cage}} \xrightarrow{k_4} t\text{-BuOOBu-}t + \text{O}_2$$

$$(5)\quad [t\text{-BuO}^{\bullet}\,\text{O}_2{}^{\bullet}\text{OBu-}t]_{\text{cage}} \xrightarrow{k_5} 2t\text{-BuO}^{\bullet} + \text{O}_2$$

The alkoxy radicals formed in (5) may react with the solvent SH to give, in the presence of oxygen, solvent derived peroxy radicals or scavenge a $t\text{-BuO}_2{}^{\bullet}$,

$$(6)\quad t\text{-BuO}^{\bullet} + \text{SH} \xrightarrow{\text{O}_2} t\text{-BuOH} + \text{SO}_2{}^{\bullet}$$

$$(7)\quad t\text{-BuO}^{\bullet} + t\text{-BuO}_2{}^{\bullet} \longrightarrow t\text{-BuO}_3\text{Bu-}t$$

The initial reaction between $t\text{-BuO}_2{}^{\bullet}$ (2) must involve a head-to-head interaction because if peroxy radicals labelled with oxygen-18 ($t\text{-Bu}^{18}\text{O}^{18}\text{O}^{\bullet}$) are allowed to react with normal peroxy radicals ($t\text{-Bu}^{16}\text{O}^{16}\text{O}^{\bullet}$) the oxygen evolved has a total mass of 34 (12).

The existence of di-*t*-butyl tetroxide was deduced from studies of the influence of temperature on the concentration of *t*-butylperoxy radicals by electron spin resonance spectroscopy (13, 14). Thus it was shown that at temperatures below 193K the radical concentration can be increased by raising the temperature and decreased by lowering the temperature with no apparent loss in radical concentration. The influence of temperature on the concentration of $t\text{-BuO}_2^{\bullet}$ is shown in Figure 1. If the tetroxide is completely dissociated at the highest temperature equilibrium constants for reaction (2), K_2, can be calculated from

$$K_2 = \frac{[t\text{-BuO}_4\text{Bu-}t]}{[t\text{-BuO}_2^{\bullet}]^2}$$

because

$$[t\text{-BuO}_4\text{Bu-}t] = \tfrac{1}{2}\,\{[t\text{-BuO}_2^\bullet]_{max} - [t\text{-BuO}_2^\bullet]\}$$

where $[t\text{-BuO}_2^\bullet]$ is the measured radical concentration and $[t\text{-BuO}_2^\bullet]_{max}$ is the maximum radical concentration.

Equilibrium constants obtained at different temperatures are given in Table I. Plots of $\ln K_2$ against the reciprocal of the absolute temperature yielded values of ΔH_2° and ΔS_2° between -8.0 and -8.8 kcal mol^{-1} and -27 and -34 cal deg^{-1} mol^{-1}, respectively, depending on the method of radical preparation (14, 15). It would, therefore, appear that although ΔH_2° is known with a fair degree of accuracy there is some uncertainty about the magnitude of ΔS_2°, probably because of errors involved in measuring $[t\text{-BuO}_4\text{Bu-}t]$.

Table I Equilibrium constants for $t\text{-BuO}_2^\bullet$ - $t\text{-BuO}_4\text{Bu-}t$ equilibrium

Temperature/K	183	173	163	153
$10^{-4}(K_2/M^{-1})$	0.1	0.4	1.8	10

Heats of formation of $t\text{-BuO}_4\text{Bu-}t$ and $t\text{-BuO}_2^\bullet$ have been estimated (16) to be -47 ± 8 and -21.5 ± 2.5 kcal mol^{-1}, respectively, which give a calculated ΔH_2° ~-5 kcal mol^{-1} which is ~3 kcal mol^{-1} smaller than the measured value. This difference is probably because the tetroxide is more stable than was predicted (16).

Above 193K $t\text{-BuO}_2^\bullet$ decay irreversibly with second-order kinetics, i.e.,

$$(8) \quad \frac{-d[t\text{-BuO}_2^\bullet]}{dt} = 2k_a[t\text{-BuO}_2^\bullet]^2$$

The maximum value of $2k_a$ is $4k_3K_2k_5/(k_4 + k_5)$ and is obtained if all $t\text{-BuO}^\bullet$ are removed by (7). Values of this rate constant have been obtained for radicals prepared by photolysis of 2,2'-azoisobutane in oxygenated CF_2Cl_2 and by complete oxidation of t-BuOOH with a large excess of Ce(IV) in CH_3OH using kinetic e.s.r. spectroscopy (17). Values of $2k_a$ at 303K from 2.5×10^2 to 2.5×10^4 M^{-1} s^{-1} have been reported with a "best" value of $\sim 10^4$ M^{-1} s^{-1}. The most reliable Arrhenius equation for this rate constant (14) appears to be

$$\log(2k_a/M^{-1}s^{-1}) = 9.7 - 8.7/\theta$$

where $\theta = 2.303\ RT$ kcal mol^{-1}.

In the presence of large concentrations of t-butyl hydroperoxide the t-butoxy radicals formed in (5) abstract the hydroperoxidic hydrogen to regenerate $t\text{-BuO}_2^\bullet$.

$$(9) \quad t\text{-BuO}^\bullet + t\text{-BuOOH} \longrightarrow t\text{-BuOH} + t\text{-BuO}_2^\bullet$$

Consequently irreversible radical decay is slower than it is in the absence of *t*-BuOOH with a second-order rate constant $k_b = 2k_3K_2k_4/(k_4 + k_5)$.

There have been many determinations of this composite rate constant by KESR and the hydroperoxide method (17). Absolute values at 303K vary from 7×10^1 to 3×10^5 M^{-1} s^{-1}, values of $\log(A_b/M^{-1}\ s^{-1})$ from 5.5 to 12, and activation energies from 4.5 to 10 kcal mol^{-1} (17). It has, however, been concluded that the "best" Arrhenius equation is (18).

$$\log(2k_b/M^{-1}\ s^{-1}) = 9.2 - 8.5/\theta$$

Product and kinetic studies of the initiated decomposition of *t*-BuOOH (19,20) have been particularly useful in elucidating the relative importance of (4) and (5). Induced hydroperoxide decomposition can be described by reactions (2) to (6) plus an initiation reaction such as the decomposition of di-*t*-butylperoxyoxalate (10).

(10) $t\text{-BuOOC(O)C(O)OOBu-}t \longrightarrow 2t\text{-BuO}^\bullet + 2CO_2$

A kinetic analysis of this reaction gives

$$\frac{k_5}{k_4} = \frac{-d[t\text{-BuOOH}]/dt}{R_i} - 1 = \frac{2d[O_2]/dt}{R_i} - 1$$

where R_i is the rate of chain initiation. These equations have been verified experimentally and Hiatt, Clipsham, and Visser (19) obtained values of $(-d[t\text{-BuOOH}]/dt)/R_i$ in the range 6-10 at 45°, implying $k_5/k_4 \sim 7$. The ratio of *t*-BuOH to *t*-BuOOBu-*t* (corrected for alcohol produced from the initiator) was consistent with this ratio. Factor, Russell and Traylor (20) confirmed these results and found that $d[O_2]/dt/R_i$ is ~10 in chlorobenzene.

The ratio k_5/k_4 increases with an increase in temperature (18,21) with $E_5 - E_4 = 5.3$ to 6.6 kcal mol^{-1} and $\log(A_5/A_4) = 4.6$ to 5.2. If it is assumed that the reaction of *t*-BuO$^\bullet$ in the cage requires no activation energy, E_5, the energy required to diffuse out of the cage, must be about 6 kcal mol^{-1}. The difference in A-factors for (5) and (4) of about 5 orders of magnitude is consistent with a bimolecular cage reaction and first-order diffusion out of the cage. These differences in activation parameters are, however, not consistent with the "best" values for k_a and k_b given above. Thus $2k_a/2k_b = 2k_5/k_4$ and $\log(k_a/k_b) = 0.5$ and $E_5 - E_4 = 0.2$ kcal mol^{-1}. Clearly, there are discrepancies in the kinetic data for self-reaction of *t*-BuO$_2^\bullet$ which will require further investigation before they are resolved.

Adamic, Howard and Ingold (14) have used the thermodynamic parameters for the *t*-BuO$_2^\bullet$ -*t*-BuO$_4$Bu-*t* equilibrium and activation parameters for irreversible radical decay to calculate activation parameters for irreversible tetroxide decomposition. Decay

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

constants for *t*-$BuO_2^{\bullet}$ prepared by photolysis of 2,2'-azoisobutane in CF_2Cl_2 were used and it was assumed that $k_5/(k_4+k_5)$ is equal to 1 at the temperature of the experiments. The rate constant $2k_a$ is, therefore, equal to $4K_2k_3$ and

$$\ln A_a - \frac{E_a}{RT} = \ln 4 + \frac{\Delta S_2^o}{R} - \frac{\Delta H_2^o}{RT} + \ln A_3 - \frac{E_3}{RT}$$

Using $A_a = 10^{9.7}\ M^{-1}\ s^{-1}$, $E_a = 8.7$ kcal mol^{-1}, $\Delta H_2^o = -8.8$ kcal mol^{-1}, and $\Delta S_2^o = -34$ cal deg^{-1} mol^{-1} values of $A_3 = 10^{16.6}\ s^{-1}$ and $E_3 = 17.5$ kcal mol^{-1} were calculated. It was concluded (14) from the magnitude of the A-factor that only one bond in the tetroxide is cleaved in the rate determining step.

(11) $t\text{-}BuO_4Bu\text{-}t \longrightarrow t\text{-}BuO_3^{\bullet} + {}^{\bullet}OBu\text{-}t \longrightarrow t\text{-}BuO^{\bullet} + O_2 + {}^{\bullet}OBu\text{-}t$

In support of the intermediacy of *t*-$BuO_3^{\bullet}$ there is some evidence that it can be prepared from *t*-butoxy and oxygen (22,23) while $CF_3O_3^{\bullet}$ has been unambiguously identified (24).

It should, however, be noted that Barlett and Guaraldi (13) and Mill and Stringham (25) obtained low A-factors ($10^{9.3}$ and $10^{12}\ s^{-1}$, respectively) for irreversible decomposition of *t*-BuO_4 Bu-*t* and concluded that decomposition must be concerted.

There have been several reports of *t*-butylperoxy radicals undergoing self-reaction with first-order kinetics (21,26). Now it is well known that decay of certain radicals can be first-order if the radical is in equilibrium with a diamagnetic dimer and substantial concentrations of dimer are present at the decay temperature (27-28). *t*-Butylperoxy radicals do not fall into this category because the tetroxide is completely dissociated before irreversible radical decay occurs. Other less persistent *t*-$RO_2^{\bullet}$ do, however, decay irreversibly in the presence of tetroxide and in these cases first-order decay kinetics are observed (29) because radical decay monitors tetroxide decomposition.

Cumylperoxy. The initial reaction between cumylperoxy radicals ($RO_2^{\bullet}$) involves a head-to-head interaction to give dicumyl tetroxide (30)

(12) $RO_2^{\bullet} \rightleftharpoons RO_4R$

The equilibrium constants for this process, K_{12}, (17) fit the relation

$$\log(K_{12}/M^{-1}) = (-7 \text{ to } -10.5) + (9.2 \text{ to } 11.2)/\theta$$

Product analyses (11, 31, 32) have shown that the cumylperoxy radical undergoes non-terminating and terminating reactions during autoxidation of cumene.

(13) $\mathrm{RO_4R \longrightarrow [RO^\bullet\ O_2\ {}^\bullet OR]_{cage}}$

(14) $\mathrm{[RO^\bullet\ O_2\ {}^\bullet OR]_{cage} \longrightarrow ROOR + O_2}$

(15) $\mathrm{[RO^\bullet\ O_2\ {}^\bullet OR]_{cage} \longrightarrow 2RO^\bullet + O_2}$

The cumyloxy radicals produced by non-terminating interactions either abstract a H-atom from cumene or undergo β-scission at ambient temperatures to give acetophenone and methyl radicals, the latter being converted to methylperoxy by reaction with oxygen.

(16) $\mathrm{RO^\bullet + RH \longrightarrow ROH + R^\bullet}$

(17) $\mathrm{RO^\bullet \xrightarrow{O_2} CH_3O_2^\bullet + C_6H_5C(O)CH_3}$

Methylperoxy radicals either propagate autoxidation by reacting with cumene or terminate the reaction by reacting with cumylperoxy radicals.

(18) $\mathrm{CH_3O_2^\bullet + RH \longrightarrow CH_3OOH + R^\bullet}$

(19) $\mathrm{CH_3O_2^\bullet + RO_2^\bullet \longrightarrow ROH + CH_2O + O_2}$

The absolute termination rate constant, $2k_t$, obtained from rotating sector studies of autoxidation of neat cumene is, therefore, an *overall* rate constant and is given by

(20) $$2k_t = 2fk_{13}K_{12} + 2(1-f)k_{13}K_{12}\left[\frac{k_{17}}{k_{17}+k_{16}[RH]}\cdot\frac{4k_{19}[RO_2^\bullet]}{4k_{19}[RO_2^\bullet]+k_{18}[RH]}\right]$$

where $f = k_{14}/(k_{14} + k_{15})$.

The magnitude of this rate constant depends on k_{13}, K_{12}, f, the fraction of cumyloxy radicals which undergo β-scission, and the fraction of methylperoxy radicals which are consumed in the termination reaction (19).

The absolute value of $2k_t$ at 30° = 1.5×10^4 M^{-1} s^{-1} with $\log(2k_t/M^{-1}\ s^{-1}) = 10.1 - 9.2/\theta$ (17). The value of E_t is much larger than the value of ~0 kcal mol^{-1} found by Melville and Richards (6) and Thomas (21). This high activation energy has, however, been confirmed by KESR (14).

Traylor and Russell (32) made the important discovery in 1965 that the rate of oxidation of cumene is increased by the addition of cumene hydroperoxide. Thus the rate depends on the hydroperoxide concentration until a limiting rate is reached whereupon addition of more hydroperoxide has no effect on the rate

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

(Figure 2). This increase in rate was attributed (31) to reaction of cumyloxy and methylperoxy radicals with the hydroperoxide thus preventing $CH_3O_2^\bullet$ from undergoing chain termination reactions.

$$(21)\qquad \left.\begin{matrix} RO^\bullet \\ \\ CH_3O_2^\bullet \end{matrix}\right\} + ROOH \longrightarrow \left\{\begin{matrix} ROH \\ \\ CH_3OOH \end{matrix}\right. \quad + \quad RO_2^\bullet$$

Measurement of the termination rate constant $2k_b$ under these conditions gave a value of $6 \times 10^3\ M^{-1}\ s^{-1}$ with $\log(2k_b/M^{-1}\ s^{-1}) = 10.7 - 9.5/\theta$ (17).

Values of A_b and E_b in conjunction with ΔS°_{12} and ΔH°_{12} have been used to calculate the activation parameters $\log(A_{13}/s^{-1}) = 17.1$ and $E_{13} = 16.5$ kcal mol^{-1} for irreversible decomposition of dicumyl tetroxide (14). Although there is little difference between the activation parameters for di-cumyl- and di-*t*-butyl-tetroxides it would appear that the former is somewhat less stable towards irreversible decomposition.

Fukuzumi and Ono have very recently concluded that the termination reaction for oxidation of cumene with manganese dioxide or cobalt oxide supported on silica (33) and during autoxidation of cumene initiated by reaction of cumene hydroperoxide with lead oxide (34) is strictly first-order with respect to the concentration of cumylperoxy radicals. These workers proposed an unprecedented 1,3-methyl shift followed by O-O bond cleavage to account for these unusual kinetics,

$$RO_2^\bullet \longrightarrow C_6H_5(CH_3)\dot{C}OOCH_3 \longrightarrow C_6H_5C(O)CH_3 + CH_3O^\bullet$$

whereas a pseudo-first order reaction is more plausible.

Other *t*-alkylperoxys. The self-reactions of a wide variety of other *t*-alkylperoxy radicals have been examined by hydrocarbon autoxidation and KESR (14, 17, 35, 36) and they all exist in equilibrium with *t*-RO_4R-*t*. Unfortunately, most of these radicals are less persistent than *t*-$BuO_2^\bullet$ and values of ΔS° could not be determined with any degree of accuracy because [*t*-RO_4R-*t*] could not be measured. Estimates of ΔS° and ΔH° have, however, been made (17, 36) and it has been concluded that the nature of R has very little influence on the magnitude of these parameters. In addition, the nature of R appears to have little or no influence on the ratio of rate constants for non-terminating and terminating interactions (37).

Absolute values of overall termination rate constants ($2k_t$) and rate constants for self-termination ($2k_b$) have been measured and typical values are presented in Table II.

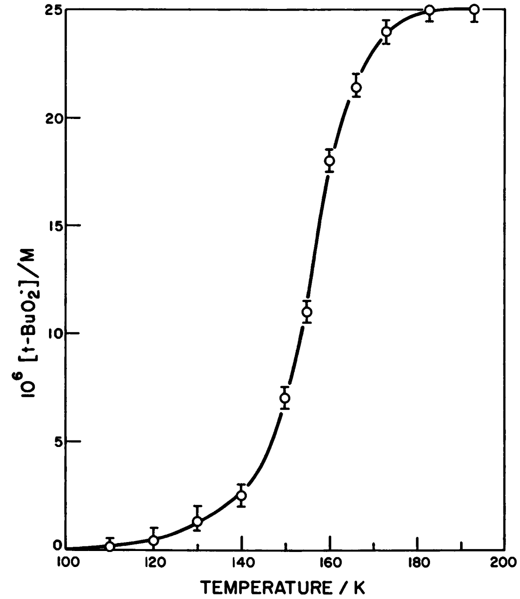

Figure 1. Variation of the concentration of $(CH_3)_3$-$CO_2\cdot$ with temperature in the range where irreversible decay does not occur

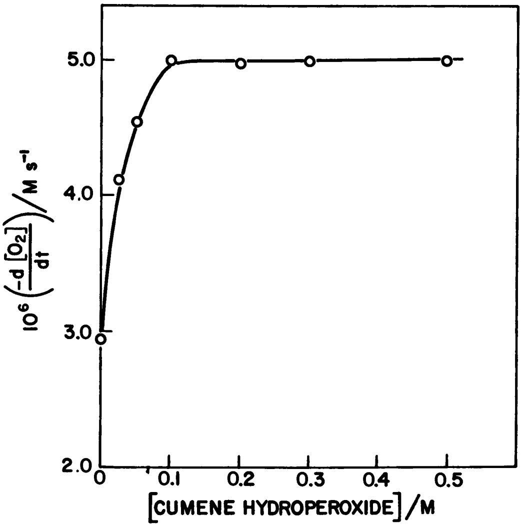

Figure 2. Rate of oxidation of cumene (3.6M) in chlorobenzene as a function of cumene hydroperoxide concentration at 330.2 K (31)

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Table II Overall and self-termination rate constants for some tertiary alkylperoxy radicals (17).

Peroxy radical	$10^{-4}(2k_t)^a$ $(M^{-1}\ s^{-1})$	$10^{-4}(2k_b)^b$ $(M^{-1}\ s^{-1})$
Cumylperoxy	1.5	0.6 - 0.8
2-Phenyl-2-butylperoxy	18	3.2
1,1-Diphenylethylperoxy	13	6.4
1-Methylcyclopentylperoxy	-	0.6 - 23
2-Cyano-2-propylperoxy	-	100

[a] From rotating sector studies of hydrocarbon autoxidation.

[b] From rotating sector studies of hydrocarbon autoxidation in the presence of hydroperoxide or by KESR in the presence of hydroperoxide.

Values of $2k_t$ for these radicals will be given by an equation similar to (20) and as might be expected $2k_t$ depends on the nature of R because the *t*-RO$^\bullet$ produced by non-terminating interactions exhibit different susceptibilities to β-scission. Somewhat more surprisingly values of $2k_b$ also depend on the nature of R. For instance the self-termination rate constant for 1,1-diphenylethylperoxy is over an order of magnitude larger than $2k_b$ for *t*-$BuO_2^\bullet$. Since K and f do not depend on R it has been concluded that differences in k_b are due to differences in the rate constants for unimolecular decomposition of *t*-RO_4R-*t*.

Acylperoxy radicals

Traylor and co-workers have recently provided evidence from autoxidation of acetaldehyde (38-40) and induced decomposition of peracetic acid (41) for a mechanism for the self-reaction of the acetylperoxy radical which involves a non-terminating interaction via a tetroxide.

$$(22)\quad 2CH_3C(O)O_2^\bullet \longrightarrow CH_3C(O)O_4C(O)CH_3 \longrightarrow 2CH_3^\bullet + 2CO_2 + O_2$$

Acetyl peroxide, methyl acetate, dimethyl peroxide and ethane are not produced in these reactions indicating that there is no cage collapse of the radicals. Instead the methyl radicals diffuse out of the cage and react with oxygen to give methylperoxy. This means that autoxidation of acetaldehyde is terminated either by reaction of methylperoxy with acetylperoxy or by self-reaction of methylperoxy (23) and (24).

(23) $CH_3O_2^{\bullet} + CH_3C(O)O_2^{\bullet} \longrightarrow CH_3C(O)OH + CH_2O + O_2$

(24) $2CH_3O_2^{\bullet} \longrightarrow CH_2O + CH_3OH + O_2$

Termination rate constants for autoxidation of some aldehydes (42) are given in Table III. The value for acetaldehyde must be a composite one containing contributions from $2k_{23}$ and $2k_{24}$. If reactions (22), (23), and (24) apply to the other aldehydes all the rate constants in this table will be composite ones.

Benzoyloxy radicals do not undergo decarboxylation as readily as other acylperoxy radicals. The termination rate constant is, however, close to the diffusion controlled limit. This apparent anomaly has been attributed (42) to irreversible formation of the tetroxide followed by complete dimerization of benzoyloxy radicals in the cage.

(25) $2C_6H_5C(O)O_2^{\bullet} \longrightarrow C_6H_5C(O)O_4C(O)C_6H_5 \longrightarrow$

$C_6H_5C(O)O^{\bullet}\ O_2\ {}^{\bullet}OC(O)C_6H_5 \longrightarrow C_6H_5C(O)O_2C(O)C_6H_5$

Table III. Termination rate constants for aldehyde autoxidation[a]

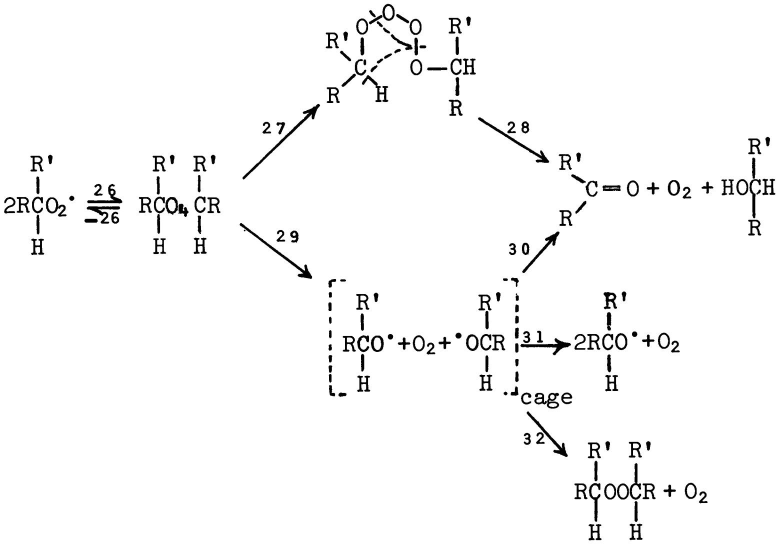
Aldehyde	$10^{-7}(2k_t)$ $/M^{-1}\ s^{-1}$
Acetaldehyde	10.4
Heptaldehyde	5.4
Octaldehyde	7.0
Cyclohexanecarboxaldehyde	0.7
Pivaldehyde	0.7
Benzaldehyde	176

[a] At 273°K.

Primary and secondary alkylperoxy radicals.

Two mechanisms have been considered for the self-reaction of primary and secondary alkylperoxy radicals, the Russell mechanism (10) reactions (26), (27), and (28) and a mechanism involving the intermediacy of alkoxy radicals (43, 44) reactions (29), (30), (31), and (32). The reactions involved in these two mechanisms are presented in Scheme II.

Scheme II



Russell (10) suggested that the bimolecular self-reaction of *s*-RO$_2^\bullet$ involves the concerted decomposition of a cyclic tetroxide formed by combination of the radicals. This mechanism was deduced from a consideration of the results of a kinetic and product study of the autoxidation of ethylbenzene. Thus Russell found that almost one molecule of acetophenone is produced per two kinetic chains and that $C_6H_5CH(CH_3)O_2^\bullet$ interact to form non-radical products nearly twice as fast as $C_6H_5CD(CH_3)O_2^\bullet$. The former result is only compatible with (29) if all the alkoxy radicals disproportionate in the solvent cage (30) while the deuterium isotope effect requires a H-atom transfer reaction to be rate controlling, which is unlikely for the radical pathway.

Support for the Russell mechanism came from Howard and Ingold (45) who found that some of the oxygen evolved from self-reaction of *s*-butylperoxy radicals is in the electronically excited singlet delta state ($^1\Delta g$) as required by the Wigner spin conservation rule for concerted decomposition to give singlet ketone and singlet alcohol. Kellogg (46) has, however, suggested that tetroxide decomposition gives triplet ketone and triplet oxygen and that singlet oxygen is formed by cage encounters of these two species. On the other hand Beutel (47) has argued that ketone can be produced either in a vibrationally excited singlet state from which it may undergo an inefficient adiabatic transition to the triplet manifold or in an electronically excited singlet state followed either by fluorescence or intersystem crossing. Although

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the exact mechanism for the production of chemiluminescence during autoxidation is debatable there is no doubt that emission spectra from triplet ketones have been observed and the intensity of chemiluminescence during non-stationary state autoxidation has been used to provide kinetic data for termination reactions (17).

Production of singlet oxygen (both $^1\Sigma g^+$ and $^1\Delta g$) by self-reaction of *s*-butylperoxy radicals and the peroxy radicals derived from linoleic acid has very recently been confirmed by analysis of the emission spectra observed during ceric ammonium nitrate oxidation of the appropriate hydroperoxide (48).

Howard and Ingold (49) confirmed Russell's conclusion that the rate constant for termination of *s*-alkylperoxy radicals depends on the strength of the α-C-H bond. Thus the average isotope effect for this reaction at 303K, $(2k_t)_H/(2k_t)_D$, is 1.37 ± 0.14 which provides compelling evidence for abstraction of this hydrogen in the rate controlling step (Table IV). Furthermore $2k_t$ for cyclohexenylperoxy is 2.8 times larger than $2k_t$ for cyclohexylperoxy which is consistent with the former radical having the weaker α-C-H bond.

Table IV. Deuterium isotope effects on rate constants for self-reaction of *s*-$RO_2^\bullet$

Peroxy radical	Temperature/K	$(2k_t)_H/(2k_t)_D$
$(C_6H_5)_2CH(D)O_2^\bullet$	303	1.36
$C_2H_5(CH_3)CH(D)O_2^\bullet$	303	1.37
cyclo-$C_5H_9(D_9)O_2^\bullet$	180	4.0

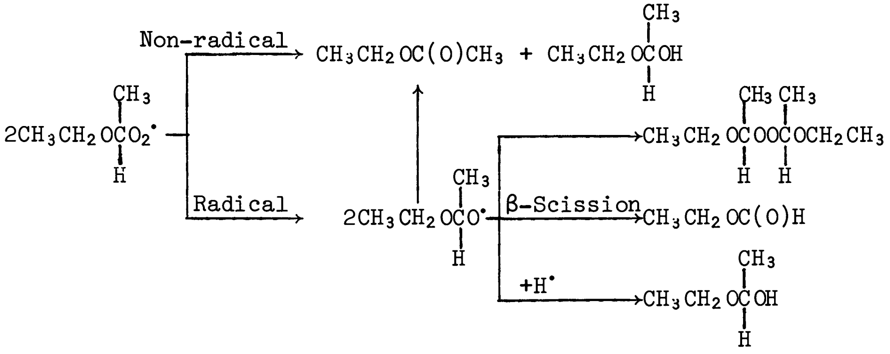
Hiatt and Zigmund (50) provided further evidence for the Russell mechanism when they discovered that the interaction of two *s*-butylperoxy radicals does not give di-*s*-butyl peroxide at 318K, a product that might be expected if the reaction involves the intermediacy of *s*-butoxy radicals. Diaper (51), however, reported that 1-methoxy- and 1-*t*-butoxy-nonane-1-hydroperoxides are oxidized to di-(1-alkoxyalkyl) peroxides by 1 equiv of Ce (IV) in methanol at 273K. Since Ce(IV) oxidizes alkyl hydroperoxides to the corresponding alkylperoxy radical in high yield these results are not compatible with Hiatt and Zigmund's findings or the Russell mechanism.

Other product studies (25, 52-54), mainly at ambient temperatures, have shown that almost equal yields of alcohol and ketone are formed from the self-reaction of *s*-$RO_2^\bullet$ as predicted by (27) and (28) or by (29) and (30).

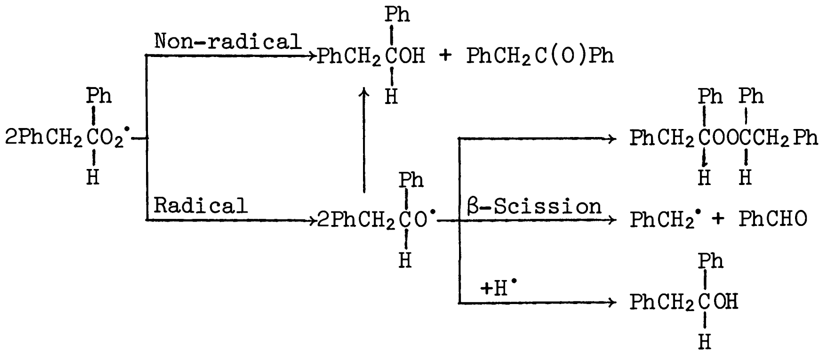
In addition Hiatt and co-workers (55) found chain lengths of 0.7 to 1.0 for di-*t*-butyl peroxyoxalate induced decomposition of n-butyl-, *s*-butyl-, and α-tetralyl-hydroperoxides at 318K indicating that interactions of the *s*-$RO_2^\bullet$ from these hydroperoxides are almost always terminating at this temperature.

Lindsay *et al* (56) made a thorough study of the products of the self-reaction of 1-ethoxyethylperoxy and 1,2-diphenylethylperoxy radicals at ambient temperatures, radicals which would be expected to give the products outlined in Schemes III and IV.

Scheme III



Scheme IV



1-Ethoxyethylperoxyls were prepared by a variety of methods and react to give ethyl acetate, ethanol, acetaldehyde and ethyl formate. (Table V). There was no evidence for the formation of di-(1-ethoxyethyl) peroxide, a result that is not entirely incompatible with Diaper's work in view of the large difference in the size the peroxy radicals studied by the two groups of workers. The absolute yields of the products were difficult to ascertain with any degree of certainty because of secondary reactions. The high yield of ethyl formate is, however, diagnostic for the intermediacy of alkoxy radicals and indicates that at least 20% of the self-reactions of 1-ethoxyethylperoxyls occur via the radical mechanism.

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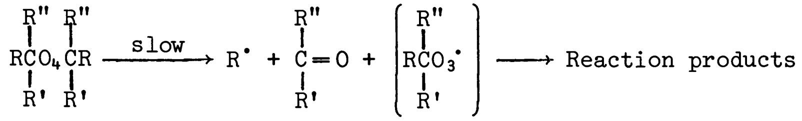
Table V. Products[a] from oxidation of 1-ethoxyethyl hydroperoxide

Oxidant	Solvent	Ethyl formate	Ethyl acetate	Ethyl alcohol	Acetaldehyde	O_2
Ce(IV)	CH_3OH	0.20	0.3	0.46	0.23[b]	0.4
t-BuO$^{\bullet c}$	CCl_4-C_6H_6	0.04-0.32	0.43	0.18	0.2	-
Ag_2O	C_6H_6	0.12	0.12	0.52	0.36	-

[a] mol per mol of hydroperoxide, [b] as 1,1-dimethoxyethane, [c] from di-*t*-butyl hyponitrite.

1,2-Diphenylethylperoxy radicals undergo self-reaction to give almost equal yields of benzaldehyde, benzyl alcohol, 1,2-diphenylethanol, and benzoin. Benzaldehyde is produced by β-scission of 1,2-diphenylethoxyls while 1,2-diphenylethanol and benzoin are formed by a non-radical process.

The work of Lindsay *et al* provides good evidence that not all *s*-$RO_2^\bullet$ undergo bimolecular self-reaction at ambient temperatures entirely by the Russell mechanism. It would, however, appear from their work that the yield of alkoxy radicals is very dependent on the structure of the peroxy radical. This lead these workers (56) to propose that the tetroxide may decompose by multiple bond scission by a concerted but non-cyclic mechanism.



$$\underset{R'}{\overset{R''}{RC}}O_4\underset{R'}{\overset{R''}{C}}R \xrightarrow{\text{slow}} R^\bullet + \underset{R'}{\overset{R''}{C}}{=}O + \left[\underset{R'}{\overset{R''}{RC}}O_3^\bullet\right] \longrightarrow \text{Reaction products}$$

Structural factors may, therefore, have a profound influence not only on the rate constants for termination of *s*-$RO_2^\bullet$ but also on the reaction mechanism.

Product studies have indicated (57) that the fraction of *s*-$RO_2^\bullet$ interactions that terminate during autoxidation of neat n-butane is 0.3-0.6 at 373K and 0.18-0.35 at 398K. Furthermore, the non-radical concerted reaction provides most of the termination for *s*-$BuO_2^\bullet$ at 373K whereas at the higher temperature a major fraction of the interactions give free *s*-$BuO^\bullet$. These results are quite compatible with all *s*-$BuO_2^\bullet$ self-reactions being terminated via a concerted non-radical process at 303K.

Very recently Bennett and Summers (58) reported a product study of the low temperature self-reaction of *s*-butylperoxy, *s*-hexylperoxy cycloheptylperoxy, and cyclopentylperoxy radicals. Although alcohol to ketone ratios close to 1.0 are produced at ambient temperatures this ratio *decreases* as the temperature is reduced. For instance the ratio of cyclopentanol to cyclopentanone is 0.06 at 173K. Furthermore significant yields of hydrogen

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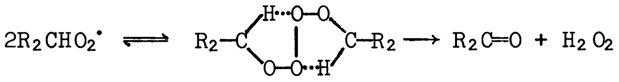
peroxide are obtained. These results prompted Bennett and Summers to propose an alternative transition state to the Russell mechanism which increases in importance as the temperature is lowered.



Kinetic data for self-reaction of *p*-$RO_2^\bullet$ and *s*-$RO_2^\bullet$ have been obtained by EPR spectroscopy and rotation sector studies on hydrocarbon autoxidation (17). These reactions usually obey the kinetic expression

$$\frac{-d[RO_2^\bullet]}{dt} = 2k_t[RO_2^\bullet]^2$$

where $2k_t$ is the bimolecular termination rate constant.

It has generally been found that *p*-$RO_2^\bullet$ have termination rate constants in excess of 10^8 $M^{-1}s^{-1}$ while *s*-$RO_2^\bullet$ exhibit a wide variation in $2k_t$ which, with a few exceptions, can be classified according to whether the radical is derived from a benzylic, allylic, cyclic, or alkyl system. In the benzylic group are compounds such as ethylbenzene, n-butylbenzene, and styrene, with $2k_t$'s of $2\text{-}6 \times 10^7$ $M^{-1}s^{-1}$. Secondary alkylperoxy radicals from alkenes undergo termination more slowly than benzylic peroxy radicals. This is partly due to steric effects associated with the alkyl moiety of the peroxy radical since $2k_t$'s increase as the size of the olefin is decreased and partly due to an increase in the strength of the α-C-H bond. Cyclic hydrocarbons such as tetralin and cyclohexene have termination rate constants in the range $2\text{-}8 \times 10^6$ $M^{-1}s^{-1}$. Addition of secondary alkyl hydroperoxides, e.g., α-tetralin hydroperoxide to the parent hydrocarbon has no effect on the magnitude of $2k_t$ indicating that in these cases non-terminating self-reactions are not significant. Values of $2k_t$ for some *p*-$RO_2^\bullet$ and *s*-$RO_2^\bullet$ are given in Table VI.

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Table VI. Termination rate constants at 303K for some typical primary and secondary alkylperoxy radicals.

Alkylperoxy radical.	$10^{-6}(2k_t)/M^{-1}s^{-1}$	Reference
Methylperoxy	500^a	59
Ethylperoxy	80^a	59
n-Butylperoxy	40^c, 300^b	17,59
2-Propylperoxy	3^b	59
2-Butylperoxy	1.5^c, 9^b	17,59
Cyclohexylperoxy	2.0^c, 10^b	17,59
Cyclohexenylperoxy	5.6^c	17
α-Tetralylperoxy	7.6, 7.2^d	17
Benzylperoxy	300^c	17
1-Phenylethylperoxy	40^c	17
Poly(peroxystyrylperoxy)	42^c	17
Tetrahydrofuranylperoxy	31^c	17

[a] Determined in the gas phase using molecular modulation spectroscopy (59). [b] Determined in the liquid-phase by KESR (59). [c] Rotating sector study of autoxidation (17). [d] In the presence of 0.2 M α-tetralin hydroperoxide (17).

Rate constants for methylperoxy and ethylperoxy were obtained in the gas-phase by molecular modulation spectroscopy (59) and it was concluded in this work that changing from the liquid to the gas phase has only a minor influence on the magnitude of $2k_t$. The order of reactivity, $CH_3O_2^{\bullet} > C_2H_5O_2^{\bullet} > (CH_3)_2CHO_2^{\bullet}$ is contrary to the previous conclusion that $2k_t$ increases as the α-hydrogen becomes weaker. It would, therefore, appear for these radicals that the relative stability of the incipient carbonyl compound overshadows a bond strength effect.

It should be noted that there is a significant discrepancy between the values of $2k_t$ determined by the rotating sector method and KESR for some of the radicals in Table VI. At the present time we are inclined to favour the values obtained from hydrocarbon autoxidation because values of the propagation rate constant are also obtained by this method, the magnitude of which gives an internal check on the value of $2k_t$.

Accurate Arrhenius parameters have been determined for a few primary and secondary $RO_2^{\bullet}$'s and examples are given in Table VII.

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Table VII. Arrhenius parameters for self-reaction of some primary and secondary alkylperoxy radicals.

Alkylperoxy	$\log(A_t/M^{-1}s^{-1})$	E_t/kcal mol^{-1}	Reference
Methylperoxy	8.7	0	59
Ethylperoxy	7.9	~0.5	59
s-Butylperoxy	9.0	2.7	60
Cyclopentylperoxy	10.0	3.1	60

The pre-exponential factors for these radicals are close to the normal values for liquid-phase bimolecular reactions while the activation energies are small and *positive*.

There is evidence from e.p.r. studies (29,36) that *s*-$RO_2^{\bullet}$ exist in equilibrium with a tetroxide below 173K and in this respect behave analogously to *t*-$RO_2^{\bullet}$. Unfortunately *s*-$RO_2^{\bullet}$ decay irreversibly before the tetroxide is completely dissociated and values of the equilibrium constant cannot be estimated. It would, however, appear that the thermodynamic parameters for *s*-$RO_2^{\bullet}$ are similar to those for *t*-$RO_2^{\bullet}$, e.g., $\Delta H^{\circ} \sim -7$ kcal mol^{-1} and $\Delta S^{\circ} < -25$ cal deg^{-1} mol^{-1} for isopropylperoxy.

The difference in termination rate constants between secondary (and primary) alkylperoxys and tertiary alkylperoxys is, therefore, almost entirely due to differences in the rate constants for irreversible tetroxide decay. Thus at 303K $2k_b$ for *t*-$BuO_2^{\bullet} = 1.2 \times 10^3$ $M^{-1}s^{-1}$ and $2k_t$ for *s*-$BuO_2^{\bullet} = 10^7$ $M^{-1}s^{-1}$. That is $k_t/k_b = 8.3 \times 10^3$. Now Ingold (61) has suggested that ΔS° for (27) ≈ -14.4 cal $deg^{-1}mol^{-1}$ because of the entropy loss from four hindered internal rotors (4×3.6 cal $deg^{-1}mol^{-1}$). Thus A_t/A_b and $E_b - E_t$ should be 10^{-3} and 9.6 kcal mol^{-1}, respectively, for *t*-$BuO_2^{\bullet}$ and *s*-$BuO_2^{\bullet}$, i.e., E_t should be *ca* 1 kcal mol^{-1} *negative*. Neither of these predictions are observed experimentally and we are forced to conclude that kinetic data for self-reaction of *s*-$RO_2^{\bullet}$ provides further evidence against the complete acceptance of the Russell mechanism.

Conclusions

There is no doubt that all alkylperoxy radicals interact to give a tetroxide which decomposes to give either radical or non-radical products. Furthermore, it would appear that the structure of the tetroxide determines the overall rate and mechanism of the reaction. Di-*t*-alkyl tetroxides decompose either by a concerted or two step process to give *t*-alkoxy radicals, a fraction of which combine in the cage. This reaction pathway is also available to primary and secondary alkylperoxy radicals but seems to be preferred at higher temperatures. At temperatures below 373K these radicals appear to react principally by a non-radical concerted process (Russell mechanism) although reaction products and kinetics are not entirely consistent with this mechanism.

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RECEIVED December 23, 1977.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch025

26

The Spin Trapping Reaction

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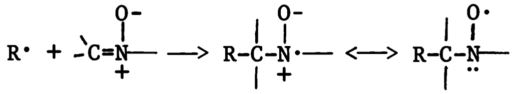
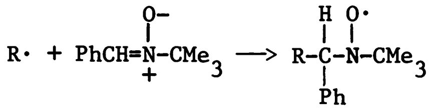
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

A number of different kinds of radicals add to the nitrone function to produce esr detectable (2) and sometimes isolable nitroxides (3):



$$R\cdot + {>}C{=}\overset{O^-}{\underset{+}{N}}{-} \longrightarrow R{-}\overset{|}{\underset{|}{C}}{-}\overset{O^-}{\underset{+}{N}}\cdot{-} \longleftrightarrow R{-}\overset{|}{\underset{|}{C}}{-}\overset{O\cdot}{\underset{\cdot\cdot}{N}}{-}$$

The α-phenyl N-t-butyl nitrones (PBN's) have been studied in greatest detail (4):

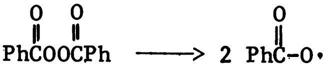


$$R\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3 \longrightarrow R{-}\overset{H}{\underset{Ph}{C}}{-}\overset{O\cdot}{N}{-}CMe_3$$

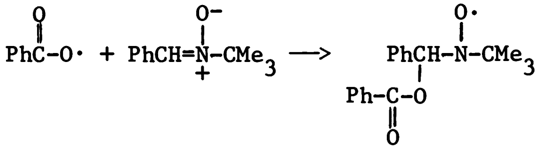
The magnitude of the β-hydrogen hyperfine splitting depends mainly on the bulk of R and indirectly on the group electronegativity of R. Since the spin density on the nitrogen atom and thus the g-value of the nitroxide is sensitive to the polar character of R the β-hydrogen splitting will vary depending on the group electronegativity of R. If R contains atoms with nuclear spin additional hyperfine splitting can be expected. Thus in principal each trapped radical should produce a unique spin adduct spectrum. This technique has been named spin trapping.

Quantitative Studies

It is of some interest to know what fraction of radicals can be trapped by nitrones at suitable concentrations. The first quantitative measurements were made with benzoyl peroxide in benzene at room temperature (5).



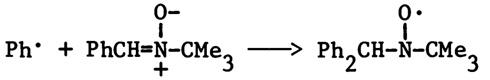
$$Ph\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}Ph \longrightarrow 2\,Ph\overset{O}{\overset{\|}{C}}{-}O\cdot$$



$$PhC(=O)-O\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}-CMe_3 \longrightarrow PhCH(O\text{-}C(=O)\text{-}Ph)-\overset{O\cdot}{N}-CMe_3$$

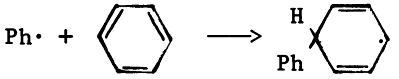
Initial slopes of the build-up of the benzoyloxy adduct of PBN are linear as a function of time for 5-15 minutes at 32-48° when PBN=0.001-1M for 0.1M benzoyl peroxide or when PBN=0.1M and benzoyl peroxide is varied between 0.05-0.5M. Rates obtained from these initial slopes show that adduct formation is 1st order in benzoyl peroxide and almost zeroth order in PBN as long as PBN > 0.075M. At lower concentrations of PBN decarboxylation of benzoyloxy radicals competes with trapping and phenyl radicals are detected:

$$PhCO_2\cdot \longrightarrow Ph\cdot + CO_2$$



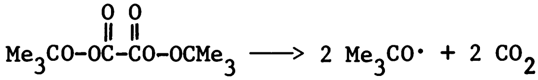
$$Ph\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}-CMe_3 \longrightarrow Ph_2CH-\overset{O\cdot}{N}-CMe_3$$

Benzene as solvent also competes for phenyl radicals at low concentrations of PBN to produce non-detected phenylcyclohexadienyl radicals:

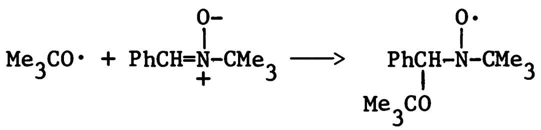


It was also shown that the rate constants for thermal decomposition of benzoyl peroxide as a function of temperature obtained by esr are in good agreement with those previously reported in the literature. Thus we conclude that benzoyloxy radicals are trapped quantitatively by PBN at suitable concentrations in benzene at room temperature and that induced decomposition of benzoyl peroxide by PBN or the spin adducts of PBN is not an important part of the spin trapping process.

Similar results were obtained with di-t-butyl peroxalate (DBPO) (6):



$$Me_3CO-O\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}O-OCMe_3 \longrightarrow 2\ Me_3CO\cdot + 2\ CO_2$$



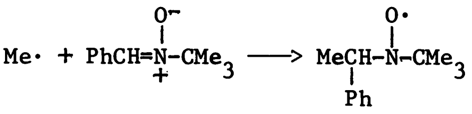
$$Me_3CO\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}-CMe_3 \longrightarrow PhCH(OCMe_3)-\overset{O\cdot}{N}-CMe_3$$

The reaction is 1st order in DBPO and zeroth order in PBN over the range of concentration studied: DBPO=0.001-0.1M and PBN=0.02-0.2M.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

Initial slopes of the build-up of the t-butoxy spin adduct were used for this study. The rate constants for thermal decomposition of the peroxalate obtained by esr as a function of temperature are in good agreement with those reported previously. At low concentrations of PBN some cleavage of t-butoxy radicals takes place and methyl radicals are detected:

$$\mathrm{Me_3CO\cdot \longrightarrow Me\cdot + MeCOMe}$$



$$\mathrm{Me\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3 \longrightarrow Me\underset{Ph}{C}H{-}\overset{O\cdot}{N}{-}CMe_3}$$

Thus in the thermal decomposition of DBPO all t-butoxy radicals are trapped at appropriate concentrations of PBN and induced decomposition of the peroxalate by PBN or the spin adducts can not be detected.

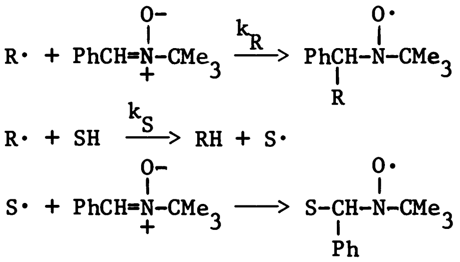
The thermal decomposition of phenylazotriphenylmethane (7) (PAT) in benzene containing PBN produces the phenyl spin adduct and triphenylmethyl radicals (detectable after longer periods of time).

$$\mathrm{Ph{-}N{=}N{-}CPh_3 \longrightarrow Ph\cdot + N_2 + Ph_3C\cdot}$$

The kinetics are complicated by the competition of benzene for phenyl radicals. An analysis of the data as a function of [PBN] in benzene gives a rate constant for the thermal decomposition of PAT which is in good agreement with literature values. Thus it appears that in an inert solvent phenyl radicals would be trapped quantitatively by PBN.

Spin Trapping Rate Constants of PBN

If at appropriate concentrations PBN can trap radicals quantitatively the rate constant of trapping must be quite large. By means of competitive kinetics estimates of the spin trapping rate constants have been obtained:



$$\mathrm{R\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3 \xrightarrow{k_R} Ph\underset{R}{C}H{-}\overset{O\cdot}{N}{-}CMe_3}$$

$$\mathrm{R\cdot + SH \xrightarrow{k_S} RH + S\cdot}$$

$$\mathrm{S\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3 \longrightarrow S{-}\underset{Ph}{C}H{-}\overset{O\cdot}{N}{-}CMe_3}$$

Thus when R· is t-butoxy radical and SH is cyclohexane the ratio

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

of the initial slopes of the build-up of the two signals due to the spin adducts is equal to the ratio of the appropriate rate constants times the ratio of the concentrations of PBN and cyclohexane:

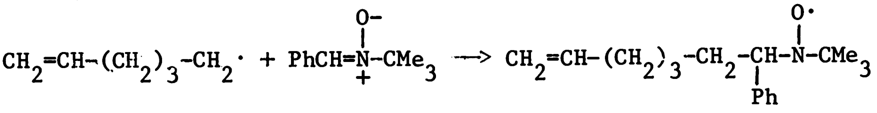
$$\left[\frac{\dfrac{d(\mathrm{SA\text{-}PBN})_R}{dt}}{\dfrac{d(\mathrm{SA\text{-}PBN})_S}{dt}}\right]_{t=o} = \frac{k_R[\mathrm{PBN}]_o}{k_S[\mathrm{SH}]_o}$$

Since the rate constant for hydrogen atom abstraction from cyclohexane by t-butoxy radicals has been estimated (8) (namely $1\mathrm{x}10^5$ M^{-1} sec^{-1} at ambient temperatures) a rate constant of $5.5\mathrm{x}10^6$ M^{-1} sec^{-1} for the trapping of t-butoxy radicals can be determined. (Actually a cyclic nitrone trap, 5,5-dimethylpyrroline-1-oxide (DMPO) was used for this study since a serious peak overlap problem was encountered with the two spin adducts of PBN (6). The rate constant for PBN was related to that of DMPO by further competitive experiments).

A similar approach was used to obtain the rate constant of trapping phenyl radicals (7). In this case the reported rate constant of hydrogen atom abstraction from methanol by p-methylphenyl radicals was used to obtain the rate constant of trapping phenyl radicals by PBN. A value of $1.2\mathrm{x}10^7$ M^{-1} sec^{-1} was obtained.

By combining some decarboxylation rate data of benzoyloxy radicals with those of phenylation of benzene an estimate of $4\mathrm{x}10^7$ M^{-1} sec^{-1} for the rate constant of trapping benzoyloxy radicals by PBN is obtained (7).

Ingold and Schmid (9) have obtained a rate constant for spin trapping 5-hexenyl radical by PBN equal to $1.7\mathrm{x}10^5$ M^{-1} sec^{-1} at 40^o in benzene.



$$CH_2{=}CH{-}(CH_2)_3{-}CH_2\cdot + PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3 \longrightarrow CH_2{=}CH{-}(CH_2)_3{-}CH_2{-}\underset{Ph}{CH}{-}\overset{O\cdot}{N}{-}CMe_3$$

We thus have the following summary of PBN spin trapping rate constants in benzene at room temperature.

$CH_2{=}CH{-}(CH_2)_3{-}CH_2\cdot$	$1.8\mathrm{x}10^5$ M^{-1} sec^{-1}
$Me_3CO\cdot$	$5.5\mathrm{x}10^6$
$Ph\cdot$	$1.2\mathrm{x}10^7$
$PhCO_2\cdot$	$4\mathrm{x}10^7$

It should be pointed out that the latter three values are based on estimates with large possible errors. The numbers may be correct only within an order of magnitude.

Spin Trapping Rate Constants of Other Nitrones

By competitive experiments spin trapping rate constants of other nitrones were obtained for t-butoxy and benzoyloxy radicals (5, 6). The values found are given in Table 1. Two features of the rate data are noteworthy: (1) Phenyl or methyl substitution on the carbon atom of the nitronyl function slows the reaction; (2) For benzoyloxy radical electron-withdrawing substituents on the phenyl group decrease the trapping rate constant whereas electron-donating substituents increase the rate constant although the effect is small. For t-butoxy radical the substituent effect is not clear.

The slowing effect of the phenyl group in the α-position when methyl radical adds to substituted ethylenes is well known from work of Szwarc (10):

Me· addition to	abstraction/addition	
$CH_2=CH_2$	34	(1)
$CH_2=CH-Ph$	796	(23)
$CH_2=CPh_2$	1590	(47)
PhCH=CHPh (trans)	104	(3)
(cis)	29	(0.9)
$PhCH=CPh_2$	48	(1.4)
$Ph_2C=CPh_2$	8	(0.2)

The rate enhancement in styrene or 1,1-diphenylethylene as compared to ethylene is easily accounted for by increased resonance stabilization of the radical in the addition products. However in <u>trans</u> stilbene the second phenyl group goes to stabilize the ground state and doesn't help to declocalize the unpaired electron in the addition product. Simple HMO calculations provide the following picture:

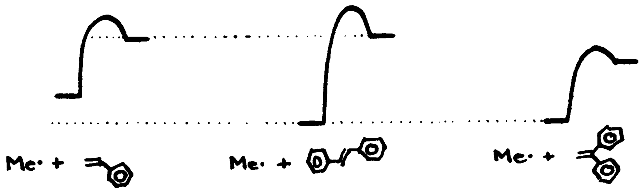
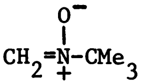
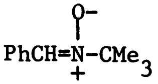
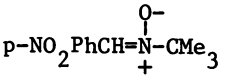
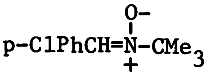
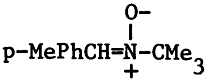
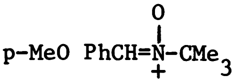
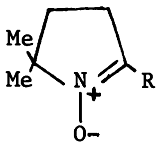


Table I

	with $Me_3CO\cdot$ (M^{-1} sec^{-1})		with $PhCO_2\cdot$ (M^{-1} sec^{-1})	
 $CH_2{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3$	$3\text{-}5\times10^8$	(100)		
 $PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3$	5.5×10^6	(1)	4×10^7	(7.3)
 $p\text{-}NO_2PhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3$	9×10^6	(1.6)	1.8×10^7	(3.3)
 $p\text{-}ClPhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3$	6.5×10^6	(1.2)	3×10^7	(5.5)
 $p\text{-}MePhCH{=}\overset{O^-}{\underset{+}{N}}{-}CMe_3$	3.4×10^6	(1.6)	6.3×10^7	(11)
 $p\text{-}MeO\ PhCH{=}\overset{O}{\underset{+}{N}}{-}CMe_3$	5.5×10^6	(1.0)	9.3×10^7	(17)



DMPO

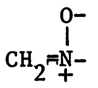
R=H	5×10^8	(100)
R=Ph	1.3×10^7	(2.4)
R=Me	9×10^6	(1.6)

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

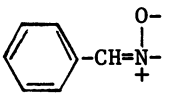
Thus resonance of the phenyl group can slow down the radical addition reaction in certain cases.

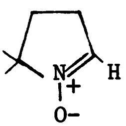
However if this were the only effect one would expect the cis isomer to give about the same rate of addition as the trans isomer. There must also be a steric effect to the addition of the radical. It is generally accepted that the transition state for radical addition is rather loose and resembles a σ-complex more than it does a π-complex (11, 12). The phenyl rings in cis-stilbene will have an ortho hydrogen blocking easy approach to the appropriate p-orbital of the ethylenic function. Perhaps some steric hindrance to approach also exists in the addition to trans-stilbene because the phenyl rings may not be entirely planar in this isomer.

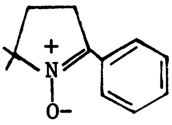
In applying the above conclusions to nitrone spin trapping we have the same α-phenyl substitution pattern when the unsubstituted nitrone is compared with PBN and DMPO with 2-phenyl-DMPO:



$CH_2{=}\overset{O^-}{\underset{+}{N}}-$

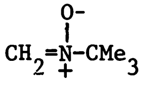




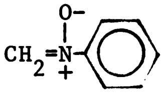


relative scale 1 0.01 1 0.03

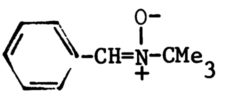
Probably a major factor is resonance although some steric hindrance to approach may also exist depending on the strucutre of these nitrones. X-ray diffraction studies of PBN crystals are planned. It would of course be of interest to compare the spin trapping rate constant of N-t-butyl nitrone with N-phenyl nitrone but this compound has never been synthesized:

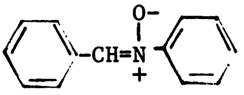


$CH_2{=}\overset{O^-}{\underset{+}{N}}-CMe_3$



We may have to be satisfied with comparing PBN with α-phenyl N-phenyl nitrone.





There may be a third effect influencing the rate of radical addition, namely steric hindrance to product formation associated with resistance of groups to move into the direction of the initial conformation of the addition product. Examples of this effect appear in the addition of methyl radical to methyl substituted ethylenes as seen in Table II (13). The relative rates are ethylene (1.0), propylene (0.7), cis- and trans- 2-butene (0.23 and 0.33), 1,1-dimethylethylene (1.1), trimethylethylene

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

Table II

Relative Rate Constants for Reaction of Radicals With Olefins(13)

OLEFIN	$CH_3\cdot$	$H\cdot$	$CF_3\cdot$	$\cdot NF_2$	$\cdot OH^{14}$	$\cdot OH^{15}$
	(453°K)	(298°K)	(338°K)	(373°K)	(298°K)	(305°K)
$F_2C=CF_2$	9.51		0.12			
$Cl_2C=CCl_2$						0.3
$Cl_2C=CHCl$						0.6
$H_2C=CH_2$	1	1	1	1	1	1
$CH_3CH=CH_2$	0.7	1.8	1.2	4.4	10	3.3
$CH_3CH=CHCH_3$ (CIS)	0.23	0.8	0.9	10.3	36	7.5
$CH_3CH=CHCH_3$ (TRANS)	0.33	1.1	1.0	10.4	42	
$(CH_3)_2C=CH_2$	1.1	4.4	3.7	20	38	
$(CH_3)_2C=CH(CH_3)$	0.32	-	-	34	70	
$(CH_3)_2C=C(CH_3)_2$	0.20	1.5	1.3	99	90	
$CH_2=CH-CH=CH_2$	12.0	8.7	8.7	-	-	9

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(0.32) and tetramethylethylene (0.20). Consider the reaction course from the first formed σ-complex through the initial conformation to the final conformation for the various ethylenes. The relative rate for addition to 1,1-dimethylethylene is the same as for ethylene probably because no serious new steric hindrance to the approach of the radical exists and the initial conformation is also the most stable final conformation for the $CH_3CH_2\dot{C}(CH_3)_2$ radical. The gain in producing a more stable tertiary radical as a product must be approximately offset by the fact that alkyl-substituted ethylenes are more nucleophilic olefins than ethylene. The addition to propylene is slower than to ethylene or 1,1-dimethylethylene probably because the initial conformation is not a particularly stable one - the barrier between the σ-complex and the final conformation of the addition product is greater in this case and the reaction is slower. The addition rate to trans-2-butene is much slower than the rate of addition to propylene although the initial conformation produced in trans-2-butene suffers from methyl interaction essentially in the same way as does the initial conformation produced from propylene. The slower rate in this case can be attributed to steric hindrance of approach to the appropriate p-orbital for σ-complex formation. The rates of addition in the case of cis-2-butene, trimethylethylene and tetramethylethylene are all slow probably because of a combination of the above effects.

In the case of nitrones when t-butoxy radicals adds the initial conformation is the most stable one for N-t-butyl nitrone (or very close to the most stable) but not for PBN. The same problem exists in the addition of t-butoxy to DMPO and 2-phenyl DMPO. In the latter case the steric resistance of the 5,5-dimethyl group contributes to the slower rate of addition.

Polar effects also appear to exist in the addition reactions of certain radicals to substituted ethylenes. It is clear from Table II that for electronegative radicals like difluoroamino or hydroxy and to a lesser extent trifluoromethyl radical and hydrogen atom, substitution with donor groups like methyl increases the rate of addition. Substitution with electronegative atoms like fluorine or chlorine has the effect of slowing the rate of addition by hydroxy or trifluoromethyl radicals but the rate of addition of methyl radicals is increased.

Similar rate constants for trifluoromethyl radical are obtained in solution phase as in the gas phase when the solvent is a hydrocarbon (16). However in water the addition seems to be faster:

$$CF_3\cdot + CH_2 = CH_2 \rightarrow CF_3CH_2CH_2\cdot$$

$k=3.5\times10^6$ (gas phase) (17), 3×10^6 (cyclohexane or heptane) (18), 4.0×10^7 (water) (19). The substituted effect and the solvent effect both point to a transition state where some charge transfer is occurring: e.g.

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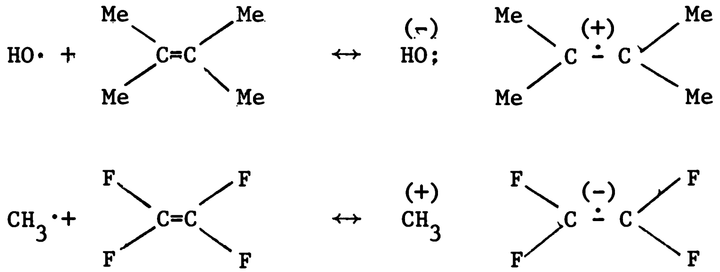
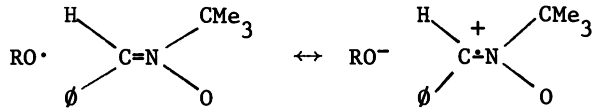


Unfortunately the same radicals have not as yet been studied quantitatively by spin trapping. However if one assumes that t-butoxy, benzoyloxy and phenyl radicals are similar to hydroxy and trifluoromethyl radicals comparisons can be made. In PBN the Hammett slope is slightly positive with benzoyloxy radical, i.e. some charge transfer is indicated in the transition state:



Although the effect is relatively small it is in the same direction as found for electronegative radicals adding to substituted ethylene.

t-Butoxy radical seems to behave both as an electronegative and as a nucleophilic radical with p-substituted PBN's. However the effect is very small. Examples of similar behaviour are available among certain haloalkyl radical additions to fluoroethylenes (12): e.g.

$\cdot CHF_2 + CH_2 = CH_2$	1.0 (relative rate constant)
$\cdot CHF_2 + CH_2 = CHF$	0.38
$\cdot CHF_2 + CH_2 = CF_2$	0.12
$\cdot CHF_2 + FCH = CF_2$	0.29
$\cdot CHF_2 + F_2C = CF_2$	1.10

Similar trends but with less marked changes in direction are found in the addition of $\cdot CH_2Cl$, $\cdot CFBr_2$ and $\cdot CF_3$ to these fluoroethylenes (12).

Thus in the addition to PBN of benzoyloxy or t-butoxy radicals, both electronegative radicals, one gets the picture that the nitronyl function is rather electrophilic itself or the site of radical attack is quite elctrophilic, for if it were otherwise

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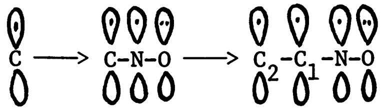
one might expect to see a larger polar effect. It would be interesting to investigate the same substitutent effect using an alkyl radical. Perhaps the Hammett slope would be positive in this case indicating charge acceptance by the nitronyl function. If charge transfer in the transition state is important the rates could be faster in aqueous media.

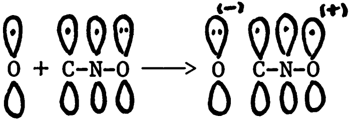
We explored the question of charge transfer in the transition state by a simple HMO approach. If one imagines tearing away carbon-2 from vinyl nitroxide the reverse process would resemble at the initial stages the addition of a kind of methyl radical (i.e. a radical with an unpaired electron in a p-orbital centered on carbon) to the nitrone function:



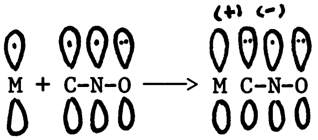
Nitrone Vinyl Nitroxide

The spin and π-electron densities were calculated for vinyl nitroxide using simple HMO theory and coulomb integral values for nitrogen and oxygen (α_N and α_O) which provided best fits for nitroxides in previous studies (20). To simulate the approach of the methyl radical β for C_1-C_2 was increased from 0.0 to 1.0.

Of interest are the simulations of the addition of an oxy radical to the nitronyl function. Here instead of using the parameters for a carbon atom for C_2 an atom with $\alpha_O=\alpha_C + 1.0\beta$ was used. At $\beta_{1-2}=0.0$ the approaching radical has no spin but instead a full negative charge. Thus HMO predicts charge transfer when an oxy radical approaches a nitrone function:



Similarly if a donor radical with the unpaired electron centered on M is used where $\alpha_M=\alpha_C - 1.2\beta$ again electron transfer is indicated but now to the nitronyl function (accidental degeneracy exists at $\alpha_M=\alpha_C - 1.0\beta$ and at $\alpha_M=\alpha_C - 0.8\beta$ no charge transfer occurrs):



A comparison of the magnitudes of the absolute rate constants of addition is also of interest. It would seem at first sight that the rapid rate of radical addition to the nitronyl function is unusual since unsaturated functions containing heteroatoms are not known to accept radicals readily. Radicals preferentially

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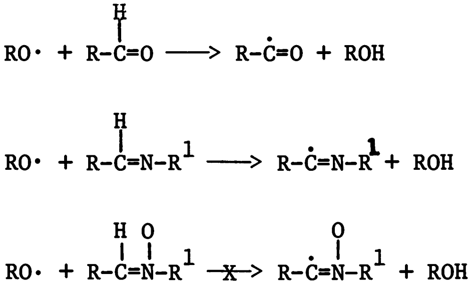
abstract the "vinyl" hydrogen in aldehydes and imines (21) but no evidence for vinyl hydrogen abstraction could be found in nitrones (22):

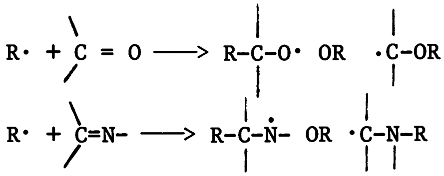


$$RO\cdot + R{-}\overset{H}{\overset{|}{C}}{=}O \longrightarrow R{-}\dot{C}{=}O + ROH$$

$$RO\cdot + R{-}\overset{H}{\overset{|}{C}}{=}N{-}R^1 \longrightarrow R{-}\dot{C}{=}N{-}R^1 + ROH$$

$$RO\cdot + R{-}\overset{H}{\overset{|}{C}}{=}\overset{O}{\overset{|}{N}}{-}R^1 \not\longrightarrow R{-}\dot{C}{=}\overset{O}{\overset{|}{N}}{-}R^1 + ROH$$

Although a few examples of radical additions to carbonyl compounds are known (23, 24), none are known to the authors for imines (25):

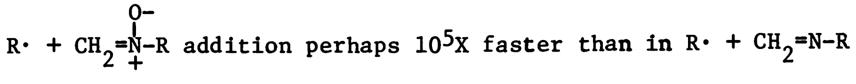


$$R\cdot + \rangle C = O \longrightarrow R{-}\underset{|}{\overset{|}{C}}{-}O\cdot \text{ OR } \cdot\underset{|}{\overset{|}{C}}{-}OR$$

$$R\cdot + \rangle C{=}N{-} \longrightarrow R{-}\underset{|}{\overset{|}{C}}{-}\dot{N}{-} \text{ OR } \cdot\underset{|}{\overset{|}{C}}{-}\underset{|}{N}{-}R$$

The radical addition to a nitrone is actually more analogous to the addition of a radical to butadiene because in both cases the unpaired electron in the addition product is stabilized by delocalization in a π-orbital over two or three atoms. The 9-12 fold increase in rate constant of addition produced by attaching the vinyl substituent to ethylene (butadiene) is much greater when an oxygen atom is attached to the nitrogen of an imine to make a nitrone:

$R\cdot + CH_2{=}CH{-}CH{=}CH_2$ addition 9-12X faster than in $R\cdot + CH_2{=}CH_2$



$R\cdot + CH_2{=}\underset{+}{\overset{O^-}{\overset{|}{N}}}{-}R$ addition perhaps 10^5X faster than in $R\cdot + CH_2{=}N{-}R$

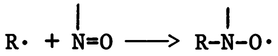
(when R· is t-butoxy radical in benzene at room temperature (22). The stabilization of the unpaired electron by delocalization over the two heteroatoms of the nitroxyl function in the addition product produces a rapid rate of addition which otherwise is very slow.

The absolute rate constants of radical addition to butadiene are $1.25\text{x}10^6\ M^{-1}\ sec^{-1}$ for methyl (26) and $4.0\text{x}10^7\ M^{-1}\ sec^{-1}$ for trifluoromethyl (19) both in aqueous solution. These values are of the same order of magnitude as estimated for additions to nitrones in benzene.

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch026

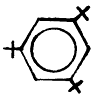
Spin Trapping Rate Constants with Nitroso Compounds

Carbon, oxygen and nitrogen centered radicals are known to add to the nitroso function to produce nitroxides:



$$R\cdot + \overset{|}{N}{=}O \longrightarrow R\text{-}\overset{|}{N}\text{-}O\cdot$$

Alkoxy nitroxides are not particularly stable but can be detected by ESR. The rate constants of addition for certain nitroso compounds are given here for completeness.

			Reference
$(Me)_3CN{=}O$	$MeO\cdot$	$1.3\times10^8\ M^{-1}\ sec^{-1}$	27
$(Me)_3CN{=}O$	$Me_3CO\cdot$	$1.5\times10^6\ M^{-1}\ sec^{-1}$	6
$(Me)_3CN{=}O$	$CH_2{=}CHCH_2CH_2CH_2\cdot$	$8.8\times10^6\ M^{-1}\ sec^{-1}$	9
 —N=O	$CH_2{=}CHCH_2CH_2CH_2\cdot$	$5.9\times10^5\ M^{-1}\ sec^{-1}$	9

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RECEIVED December 23, 1977.

27

Pyridinyl Paradigm Proves Powerful

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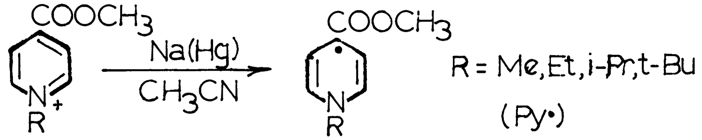
Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch027

Radicals stable enough to be transferred from one environment to another have been useful for (a) analyzing the effect of the molecular milieu on the reactions of radicals and (b) probing the viscosity and polarity of the domain in which the radical is located. The simplicity and chemical reactivity of pyridinyl radicals, generated through chemical reduction of pyridinium halides (Eq.1), has provided the opportunity for studies on the mechanisms of radical reactions and on the properties of π-complexes of radicals.

(1)



Halocarbon Reactions

Pyridinyl radicals (in most cases, this term will refer to a 4-carbomethoxy-1-alkylpyridinyl radical as shown in Eq.1) react with halocarbons in revealing ways. The kinetic constants shown in Table 1 for the reactions with dichloromethane, bromochloromethane and iodochloromethane illustrate (a) discrimination between C-Cl, C-Br and C-I bonds (b) rates which are convenient to measure by conventional techniques. The overall reaction is given in Eq. 2.

(2) $$2Py^{\bullet} + RX \longrightarrow Py^{+}X^{-} + PyR$$

In order to establish the mechanism of the reaction, the solvent effect on the reaction of pyridinyl radical with dibromomethane was investigated. As the results listed in Table 1 show, there is no solvent effect on the rate of the reaction. How could one reconcile the formation of a salt with the lack of solvent polarity effect on the rate? Since the initial state ($Py^{\bullet}$ + RX) is not very polar (pyridinyl radical with a 1-ethyl group is soluble in n-hexane, $BrCH_2Br$ has a dipole moment of ca. 1 Debye), the lack of

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch027

solvent effect requires that the transition state for the rate limiting step be also weakly polar. The only possible reaction which could account for this result is that of atom-transfer, in which a bromodihydropyridine is formed as a first intermediate. (Eq. 3).

To explore the mechanism of the reaction further, the rates of reaction of pyridinyl radical with a series of substituted benzyl chlorides were measured. The idea was that the Hammett ρ-value would help us to understand the possible charge separation in the transition state. The rate constants (Table 1) indicated that the effect of substituent was very small except in the case of the 4-nitrobenzyl chloride-pyridinyl radical reaction. The rate constant for the latter reaction was so high and so different from those for the other benzyl chlorides that a change in mechanism was likely, with an electron-transfer reaction being a reasonable possibility in view of the electron-withdrawing character of the nitro-group. This could be confirmed by a study of the effect of solvent polarity on the rate constants for the reaction of pyridinyl radical with 4-nitrobenzyl chloride, for which a very large effect was found. (Table 1).The criterion of solvent polarity used was the Z-value, an empirical solvent polarity parameter which I introduced in 1958, and which is based on the charge-transfer light absorption of 1-ethyl-4-carbomethoxy-pyridinium iodide. (Eq.4). The theoretical model for the solvent effect underlying the Z-values suggests that a reasonable estimate for the transfer of ion-pairs from one solvent to another may be made by dividing the difference in Z-values by two. We could then compare the $\frac{1}{2}\,\Delta Z$ thus obtained with the $\Delta\Delta G$ values derived from the transition state energies for the rate constants for the 4-nitrobenzyl chloride-pyridinyl radical reaction. The similarity of the two numbers for the solvents, 2-methyltetrahydrofuran and acetonitrile, shows that the interpretation of the reaction as an electron-transfer reaction is not only qualitatively valid but is quantitatively consistent with such a formulation. (Eq. 5).

Further details on the halocarbon reaction with pyridinyl radicals may be found in a review (1) and in the original papers with Schwager (2) and Mohammad (3).

Bimolecular Reactions of Pyridinyl Radicals in Water

1-Alkyl-3-carbamidopyridinyl radicals (e.g. $3^{\cdot}$) are of considerable significance biologically, since such radicals represent potential intermediates in biochemical reactions involving the coenzyme, NAD^{+}(NADH). The $3^{\cdot}$ radicals are, in general, not sufficiently stable to be isolated and transferred from one medium to another, but can readily be produced by pulse radiolysis (4) of 1-alkyl-3-carbamidopyridinium ions in water. The $3^{\cdot}$ radicals disappear in bimolecular reactions at rates which are close to diffusion-controlled and independent of pH. (5,6). The product of $3^{\cdot}$ reaction with $3^{\cdot}$ is the dimer. (Eq. 6).

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch027

TABLE I. Rate Constants for the Reaction of 1-Ethyl-4-carbomethoxypyridinyl Radical with Halides and Polyhalides at 25°C

Halide	Solvent	Rate constant ($M^{-1}sec^{-1}$)	Ref.
Group a: Element effect—atom-transfer reactions			
$ClCH_2Cl$	CH_3CN	2.6×10^{-8}[a]	2
$BrCH_2Cl$	CH_3CN	5.0×10^{-5}	2
ICH_2Cl	CH_3CN	1.3×10^{-1}	2
ICH_3	CH_3CN	5.0×10^{-6}	2
Group b: Substituent effect—aromatic ring			
$ClCH_2C_6H_4OCH_3$	CH_3CN	11.3×10^{-4}	17
$ClCH_2C_6H_4CH_3$	CH_3CN	3.68×10^{-4}	17
$ClCH_2C_6H_5$	CH_3CN	3.31×10^{-4}	17
$ClCH_2C_6H_4Cl$	CH_3CN	6.5×10^{-4}	17
$ClCH_2C_6H_4NO_2$	CH_3CN	$240{,}000{,}000 \times 10^{-4}$	17
Group c-1: Solvent effect—atom transfer			
$BrCH_2Br$	CH_3CN	1×10^{-4}	2
	CH_2Cl_2	0.48×10^{-4}	2
	i-PrOH	0.94×10^{-4}	2
	EtOH	1.7×10^{-4}	2
Group c-2: Solvent effect—electron transfer			
$ClCH_2C_6H_4NO_2$	MTHF[b]	1.62	3
	DME[c]	8.3	3
	CH_2Cl_2	75	3
	CH_3COCH_3	450	3
	DMF[d]	1.2×10^{4}	3
	CH_3CN	2.4×10^{4}	3

[a] Estimated from data at higher temperatures.

[b] 2-Methyltetrahydrofuran.

[c] 1,2-Dimethoxyethane.

[d] N,N-Dimethylformamide.

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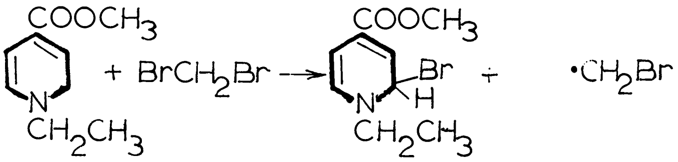

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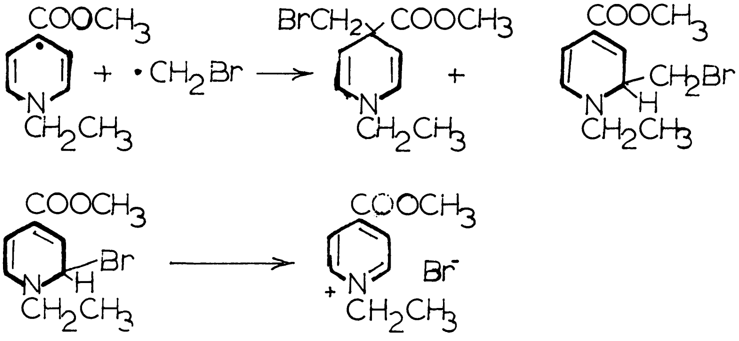
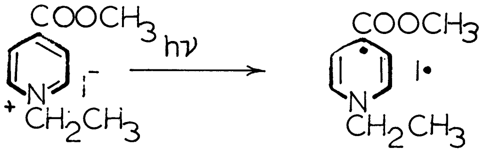
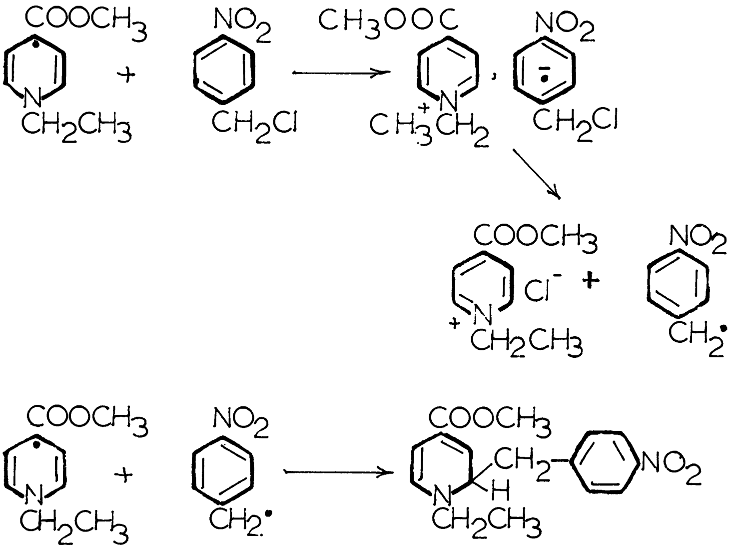


(4)



(5)



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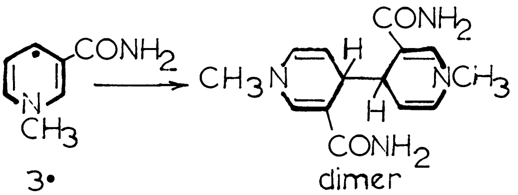
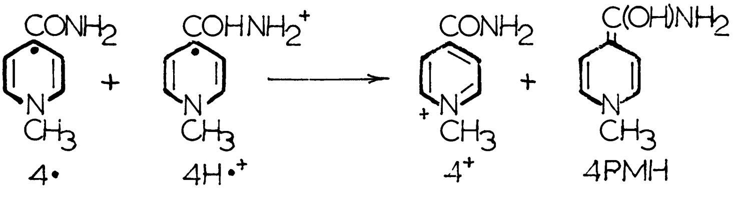
(6)



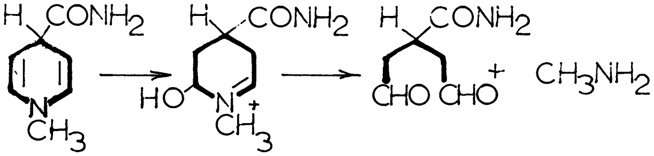
1-Alkyl-4-carbamidopyridinyl radicals (4•) react with one another in a pH-dependent reaction (7). A protonated radical can be demonstrated at low pH and its pK_a has been estimated as 2.3 for the 1-hexyl derivative (8). The disappearance of 4• can be described as a reaction between an electron-transfer reaction between 4• and 4H•+. (Eq. 7).

(7)



The 4PMH is not stable in aqueous solution. After hydration, another proton is consumed, yielding a product which slowly hydrolyzes to an alkylamine. Methylamine has been detected after radiolysis of 1-alkyl-4-carbamidopyridinium ions. (Eq. 8).

(8)



We have demonstrated a particularly clear and simple technique for evaluating the reactions of pyridinyl radicals in water through measurement of the pH changes resulting from radiolysis of pyridinium ions in unbuffered aqueous solutions containing isopropyl alcohol (6). Radiolysis generates one proton for each pyridinyl radical, as set forth in Eq. 9. (4).

$$\begin{array}{ll} & 3\,H_2O \xrightarrow{\gamma\text{-radiation}} 3\,{\cdot}OH + 3H^+ + 3e^- \\ (9) & 3e^- + 3Py^+ \longrightarrow 3Py{\cdot} \\ & 3\,{\cdot}OH + 3\text{ i-PrOH} \longrightarrow 3\,H_2O + 3\,(CH_3)_2C(OH){\cdot} \\ & 3\,(CH_3)_2C(OH){\cdot} + 3Py^+ \longrightarrow 3Py{\cdot} + 3H^+ + 3\,(CH_3)_2CO \\ \hline & 3\,H_2O + 6\,Py^+ + 3\text{ i-PrOH} \longrightarrow 6Py{\cdot} + 6H^+ + 3\,(CH_3)_2CO \end{array}$$

Each 1-methyl-x-carbamidopyridinium ion behaves differently upon radiolysis, with the results being summarized in Eq. 10-12.

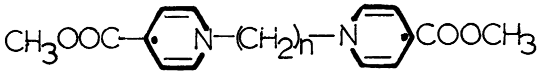
(10) $3{\cdot} + 3{\cdot} \longrightarrow$ 3-3 dimer (No H^+ consumption)

(11) $2{\cdot} + 2{\cdot}\ H^+ \longrightarrow 2^+ + 2H$ (1 H^+ consumed per2Py•formed)

(12) $4{\cdot} + 4{\cdot}+ 2H^+ \longrightarrow 4^+ + 4HH^+$ (1 H^+ consumed per Py• formed)

Pyridinyl Diradicals and Their Magnesium Complexes

The stability evident for 1-alkyl-4-carbomethoxypyridinyl radicals stimulated the preparation of a series of pyridinyl diradicals, with the general formula shown below (9,10). In many cases, as for the case of magnesium, calcium or other strongly reducing metals, a diradical-metal ion complex is produced, from which the metal ion is removed with great difficulty.



n = 3-10

The most striking property of the diradicals, most evident in their magnesium complexes, is that of π-merization. π-mers are defined as charge-transfer complexes between two identical or similar π-systems. The effect of π-merization upon the spectrum of a pyridinyl radical is illustrated with the cases of three pyridinyl diradicals (n = 3,4,5) in Fig. 1. The spectrum of the diradical with n = 5 is very similar to that of pyridinyl monoradical. The dramatic effect of magnesium complex formation is shown for the case of the diradical 3 in Fig. 2. (11). Magnesium complexation does not alter the epr properties of the diradicals, in so far as the spin concentrations are concerned. The diradical 3 is almost entirely spin-paired (spin/radical = 2%), the diradical 4 exhibits 20% spin and the diradical 5, 100% spin. A most interesting case is that of the 1,8-biphenylenyl-bis methyl 4-carbomethoxypyridinyl diradical (formula shown). The uv-visible spectrum of the diradical implies little interaction between the two pyridinyl radical moieties, whereas the epr spectrum shows

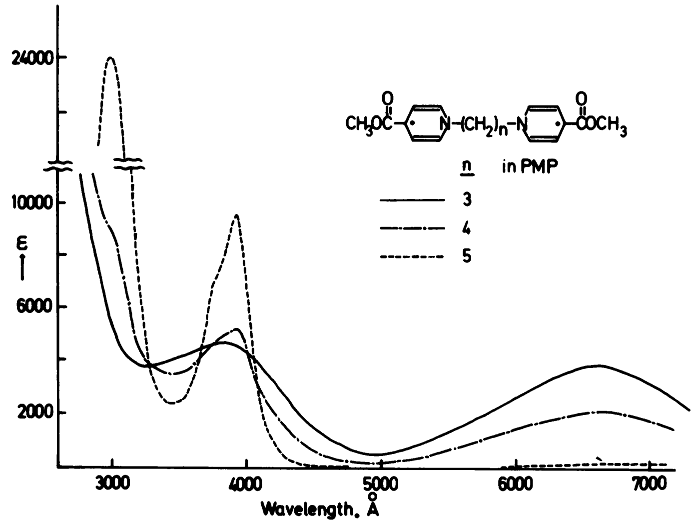


Figure 1. The effect of π-merization on the spectrum of a pyrinyl radical

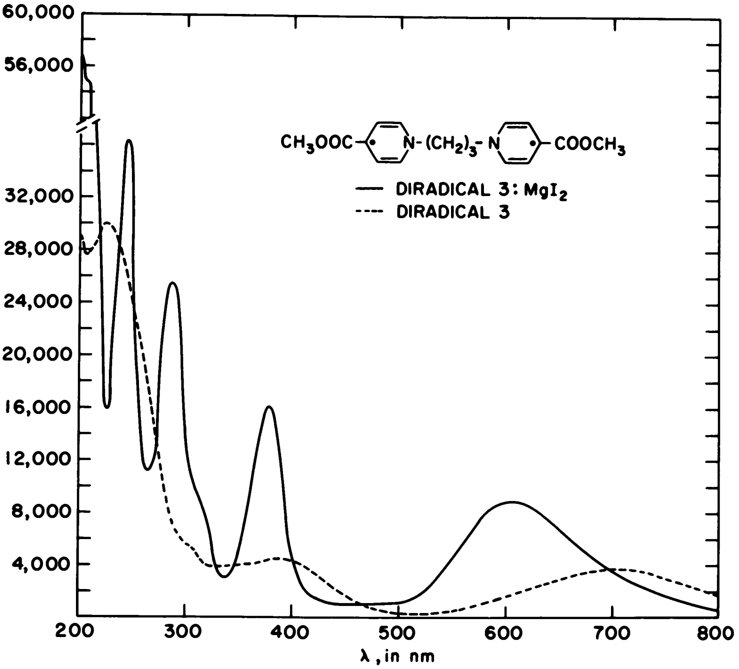
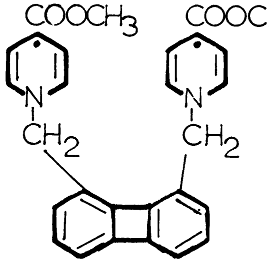
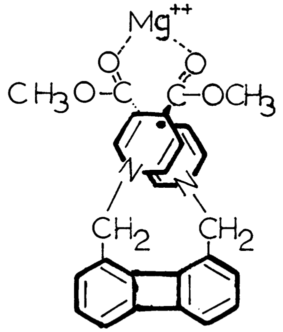


Figure 2. The effect of magnesium complex formation for the diradical 3

Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch027

exchange narrowing. The magnesium complex has a uv-visible spectrum which shows substantial interaction between the radicals, but the epr spectrum is very similar to that of the diradical in shape and width. Since the distance between the 1 and 8-positions in biphenylene is ca. 3.8A, the pyridinyls must bend towards one another for effective interaction. Apparently, magnesium ion can promote an interaction which does not occur easily in the diradical (12).

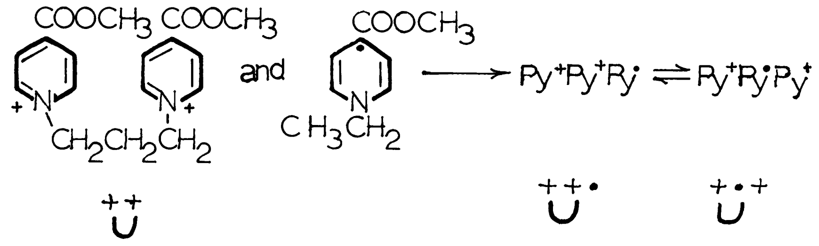




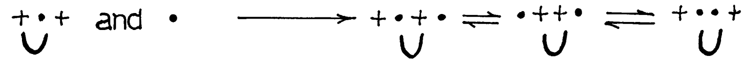
Pyridinyl Radical-Bis-Pyridinium Ion Complexes

In the course of an attempted titration of 1,1'-trimethylene-bis-(4-carbomethoxypyridinium) ion (++) with 1-ethyl-4-carbomethoxypyridinyl radical (•), we discovered that these species formed a strong complex, quite stable in acetonitrile at room temperature. (Eq. 13). Epr spectra exhibited exchange narrowing and possibly two overlapping spectra, but the most significant property of the complex was a near infrared band (λ_{max} 1360 nm (ε_{max} 1500)) which was assigned to an intervalence transition. (13). Addition of another equivalent of pyridinyl radical to the complex results in the formation of a second complex, accompanied by a shift of the near infrared band to λ_{max} 3200 nm. (Eq. 14).

(13)



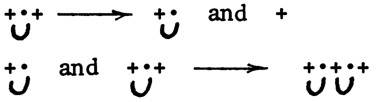
(14)



Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ch027

The +•+ complex stability is dependent upon the nature of the anion and on temperature, with the activation energy for the disappearance of the complex (followed with the near infrared absorption) varying from 45 kcal/mole for the iodide to 26 kcal/mole for the tetraphenylborate. The epr signal disappears in parallel with the loss of the near infrared band. The mechanism for the loss fo the complex is explained as due to the dissociation of the initial complex to a cation radical (+•) which combines with another molecule of the initial complex to yield a diradical complex. (Eq. 15). Further changes in the spectrum ensue, which are presumed to result in the formation of higher complexes, with continued heating.

(15)



Analogous complexes can be found for tetracyanoquinodimethane (TCNQ or T) including T, T^-, T_2^-, T_2^{--}, T_3^{--}, T_4^{--}. Indicating the pyridinium ring or pyridinyl radical by P, the following complexes have been detected: $P, P^+, P_2, P_2^+, P_3^{++}, P_4^{++}, P_5^{+++}$ and P_6^{++++}. If we bear in mind that considerable variation in the structure of P is possible, the variety of possible complexes is staggering.

Additional Information

We have discussed primarily our own work, especially that which is still in progress. No discussion of pyridinyl radical π-mers would be complete without citing the discovery of the dimerization of pyridinyl radicals by Itoh and Nagakura (14) and the work of Ikegami (15) on different π-mer triplets. The original impetus for the study of pyridinyl radical reaction with halocarbons was given by the discovery by Westheimer, Kurz and Hutton (16) that dihydropyridines were converted into pyridinium compounds via free radical reactions in the presence of tetrachloromethane. An extensive review of pyridinyl radicals has been published elsewhere (1). New ways of measuring the low temperature spectra of pyridinyl radicals are under development (18).

Acknowledgements

No report of our research would be complete without mention of those who have actively contributed to the progress of the work, including William Schwarz, jr., Edward J. Poziomek, Irving Schwager, John Cotter, Leroy Butler, Harold P. Waits, Yusaku Ikegami, Michiya Itoh, Mahboob Mohammad, Joseph Hajdu, J.B. Nagy, A. Lewis, N.F. McFarlane, Avraham Teuerstein and Joshua Hermolin. Senior colleagues from other institutions included A. John Swallow (Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester, England) and Hugh D. Burrows (now at the University of Ife, Ile-Ife, Nigeria).

Support for the research was provided over many years by the National Institutes of Health, supplemented by grants from Edgewood Arsenal and the Israel Academy of Sciences.

Abstract

Simple pyridinyl radicals, Py·, like those derived from 1-ethyl-4-carbomethoxy-pyridinium ion through 1e reduction, have proven useful for the investigation of properties of radicals, including complexes, and the study of the mechanisms of their reactions. Discoveries include: (a) distinction between atom-transfer and electron-transfer reactions by means of solvent effect on rate constants. (b) intramolecular radical complexes (π-mers) within pyridinyl diradicals and pyridinyl diradical:metal halide complexes, (c) occurrence of either electron-transfer or dimerization between pyridinyl radicals in water according to structure and (d) complexation between pyridinium ions and pyridinyl radicals. Consideration of actual and potential biological roles for pyridinyl radicals is aided by these discoveries.

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RECEIVED December 23, 1977

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Publication Date: June 1, 1978 | doi: 10.1021/bk-1978-0069.ix001

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