1983

Free-radical clocks in the aliphatic S[subscript RN]1 process and reactions of nucleophiles with 1,1-dinitro-2,2-diphenylethylene

Douglas Frederick Dedolph
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FREE-RADICAL CLOCKS IN THE ALIPHATIC S(RN)1 PROCESS AND REACTIONS OF NUCLEOPHILES WITH 1,1-DINITRO-2,2-DIPHENYLETHYLENE

Iowa State University PH.D. 1983

Free-radical clocks in the aliphatic $S_{RN}1$ process and reactions of nucleophiles with 1,1-dinitro-2,2-diphenylethylene

by

Douglas Frederick Dedolph

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PREFACE

As an organizational convenience, this thesis has been formated in two parts. The synthesis of and subsequent reaction of two free-radical clocks are described in Part I. Included in Part I are various other reactions which pertain to the investigation of the $S_{RN}1$ process. The reactions of various nucleophiles with 1,1-dinitro-2,2-diphenylethylene are presented in Part II.

Although a separate experimental section follows each section of results and discussion, descriptions of techniques and sources of starting materials are mentioned only once to avoid repetitions. Most items utilized in subsequent sections are to be located at the beginning of the experimental section under the heading of "General Considerations".

PART I. $S_{RN}1$ COUPLING REACTIONS

I. INTRODUCTION: A DISCUSSION OF THE $S_{RN}1$ PROCESS

In recent years, it has become evident that nucleophilic substitution at a saturated carbon atom (Eq. 1) may proceed by other possible mechanisms besides the

$$RX + A^- \longrightarrow RA + X^- \qquad (1)$$

limiting S_N1 and S_N2 cases. The only new and widely applicable substitution mechanism that has been added to the above limiting cases involving organic halides has been termed $S_{RN}1$ by Bunnett and Kim [1]. The $S_{RN}1$ process is distinctly different from the S_N2, S_N1, and S_NAr mechanisms, although the net reaction is similar. The new process is a multi-stage chain sequence involving free radicals and radical anion intermediates. A generalized description of the basic steps of the $S_{RN}1$ process is provided in Scheme 1.

Scheme 1

Step 1: Initiation

$$RX + A^- \xrightarrow{\text{E.T.}} RX^{\cdot -} + A\cdot$$

Step 2: Propagation

$$RX^{\cdot -} \longrightarrow R\cdot + X^-$$

Step 3: Propagation

$$R\cdot + A^- \longrightarrow RA^{\cdot -}$$

Step 4: Propagation

$$RA^{\cdot -} + RX \xrightarrow{\text{E.T.}} RA + RX^{\cdot -}$$

The chain initiation step of the $S_{RN}1$ process, presented in Step 1, is an electron transfer (E.T.) reduction of RX to form an unstable radical anion ($RX^{\cdot -}$). In propagation Step 2, the radical anion ($RX^{\cdot -}$) can fragment to form radical R· and anion X^-. This type of fragmentation is known in other contexts [2]. The radical R· can covalently combine with nucleophile A^- to form a new radical anion ($RA^{\cdot -}$) as shown in propagation Step 3. Propagation Step 3 would be identical with the reverse of propagation Step 2 if X^- was similar to A^-. Propagation Step 4 involves electron transfer from the powerful reducing agent ($RA^{\cdot -}$) to a neutral molecule of RX which regenerates the reactive intermediate ($RX^{\cdot -}$) as well as product (RA). The regeneration of $RX^{\cdot -}$ may continue the chain process by propagation Step 2. Step 1 only needs to occur at a rate that will offset chain terminating processes.

The $S_{RN}1$ mechanism involves three types of reactive intermediates, radical R·, and radical anions $RX^{\cdot -}$ and $RA^{\cdot -}$. Since generation of any one of the reactive intermediates will provide entry into the progagation cycle, there are various initiation processes which have been used to initiate the $S_{RN}1$ process. The most common initiation process in saturated systems involves the electron transfer reduction of the starting substrate by the nucleophile which also combines covalently with radical R·. In saturated systems, the substrate normally contains a nitro group which can readily accommodate an additional electron in its relatively low-lying antibonding pi-orbital. The case in which nitro compounds readily form radical anions by single electron transfer from anions is well-known [3,4]. The process where an electron is

transferred in the initiation step is believed to be some form of a charge transfer complex between A^- and RX [5]. The initiation step usually requires light to initiate the chain process, since Step 1 is often too endothermic to occur thermally at reaction temperatures.

Other initiation processes that have been utilized to initiate the $S_{RN}1$ process are reduction of substrate RX by solvated electrons [6] or electrochemical [7] methods, even though these methods have been used mainly on aromatic systems. Entrainment of $S_{RN}1$ reactions is also possible and may take one of several forms. One method possible utilizes a catalytic quantity of N^- which is a potent initiator to a solution that contains substrate RX and an inactive electron transfer anion A^- that is an adequate radical trap. This procedure has been reported in numerous aliphatic systems [8].

There are two major classes of substrates which are known to undergo $S_{RN}1$ reactions. The first class of substrates consists of molecules which contain a leaving group attached to a saturated carbon atom. Substitution in saturated systems by the $S_{RN}1$ process has been extensively reviewed by Kornblum [8]. The second major class of substrates which are known to be involved with the $S_{RN}1$ process are unsaturated or aromatic systems. Bunnett [9] has reviewed aromatic substitution by the $S_{RN}1$ mechanism. Recently, several excellent reviews, including both saturated and unsaturated systems, have been published [10,11,12]. The remainder of this introduction will focus on the aliphatic $S_{RN}1$ process since only saturated systems are involved in the free radical chain processes reported in this thesis.

During the past two decades, the majority of the investigations of the aliphatic $S_{RN}1$ process have centered around 2-chloro-2-nitropropane and p-nitrobenzylchloride [13,14,15]. The $S_{RN}1$ mechanism was originally proposed to explain the C-alkylation of anions of aliphatic nitro-compounds with the previously mentioned substrates. Subsequent anions commonly employed for the reduction of 2-chloro-2-nitropropane or p-nitrobenzylchloride were usually "soft nucleophiles" such as enolates of 1,3-dicarbonyl compounds [16]. In recent years, a wide variety of nucleophiles such as azide [17], sulfinates [18], thiolates [19], simple enolates [20], nitrite ion, and anions of dialkylphosphites [21] have been employed in the aliphatic $S_{RN}1$ process. As the list of nucleophiles that participate in the $S_{RN}1$ process increased, so did the list of nucleofuges.

In addition to the various halogens, an impressive array of nucleofuges, including nitrite, methylsulfide, trimethylamine, and phenylsulfinate to name a few, have been shown to be involved in the $S_{RN}1$ process. It is interesting to note that often poor nucleofuges in the S_N1 and S_N2 process can be involved in $S_{RN}1$ reactions.

A large number of substances have been frequently shown to inhibit radical chain processes and are often used as diagnostic tests for the $S_{RN}1$ process. A reaction involving radical anions may be inhibited by powerful one-electron acceptors such as m-dinitrobenzene. Inhibition by traces of radical scavengers such as di-t-butyl nitroxide or molecular oxygen is characteristic of radical chain reactions. The list of in-

hibitors of the $S_{RN}1$ process is long but di-t-butyl nitroxide and m-dinitrobenzene appear to be generally acceptable.

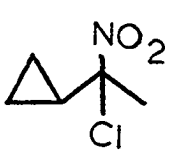
After two decades of investigation, it is now generally recognized that nucleophilic substitution at a carbon atom may proceed as an electron transfer chain reaction. It is noteworthy that in most aliphatic examples of the $S_{RN}1$ process, a nitro group is present either in the compound undergoing substitution or in the attacking nucleophile. When the substrate RX contains a nitro group, the radical anion $RX^{\cdot -}$ is made energetically accessible by the low-lying antibonding pi-orbital of the nitro moiety. Examples where the p-nitrophenyl substituent is not at the reaction center but is on the attacking nucleophile have been reported [22]. The presence of a nitro group is important for stabilization of the radical anion ($RA^{\cdot -}$) formed by propagation Step 3. On the basis of the available evidence, it appears that a nitro group is generally necessary for the $S_{RN}1$ process at a saturated carbon. Although, a few examples are known where neither $RX^{\cdot -}$ or $RA^{\cdot -}$ possess a nitro substituent [23].

II. SYNTHESIS OF 1-CHLORO-1-CYCLOPROPYL-1-NITROETHANE AND 2-CHLORO-2-NITRO-6-HEPTENE

A. Introduction

α-Chloro-α-nitroalkanes can be obtained by a variety of synthetic pathways. The prevalent method of forming α-chloro-α-nitroalkanes is by oxidation of the corresponding α-chloro-α-nitrosoalkanes with an assortment of very strong and nonselective oxidants. The intermediate nitrosoalkanes are in turn readily available from the parent ketones by chlorination of the oxime derivatives. Chlorination of oximes can be accomplished under a variety of conditions [24] usually involving a positively polarized chlorine. α-Chloro-α-nitroalkanes can also be synthesized from corresponding nitroalkanes which are available from a wide range of substrates.

In the preparation of 1-chloro-1-cyclopropyl-1-nitroethane 1 and 2-chloro-2-nitro-6-heptene 2, both of the possible synthetic pathways were employed in the synthesis of the appropriate free-radical clocks.



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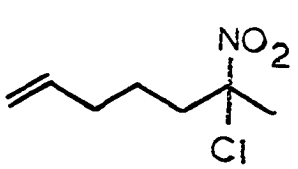


2

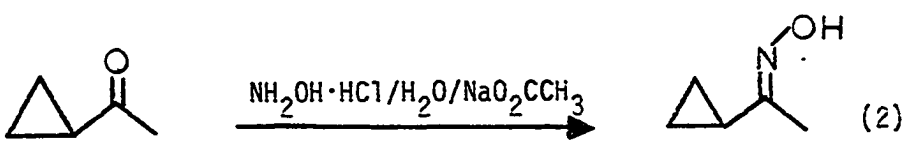
Chlorination and oxidation of the oxime formed from cyclopropyl methyl ketone was used in the synthesis of 1-chloro-1-cyclopropyl-1-nitroethane

1. While, chlorination of the anion of 2-nitro-6-heptene was employed in the synthesis of 2-chloro-2-nitro-6-heptene 2.

B. Results and Discussion

1. Preparation of 1-chloro-1-cyclopropyl-1-nitroethane

The decision to prepare 1-chloro-1-cyclopropyl-1-nitroethane from the oxime of cyclopropyl methyl ketone was influenced by expense, yield, and convenience. Although, numerous questions remained about the selectivity of the chlorination and oxidation reagents towards the highly reactive cyclopropyl ring. The oxime of cyclopropyl methyl ketone 3 was prepared by the method of Makosza [25] with a very reasonable yield (Eq. 2).



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Oximes are transformed into α-chloro-α-nitrosoalkanes using aqueous hypochlorous acid [26], nitrosyl chloride [27], chlorine [28], N-chlorosuccinimide [29], and alkyl hypoclorites [30]. Unfortunately, all of the previously mentioned chlorination reagents involves a positively polarized chlorine which could electrophilicly add to the oxime or the cyclopropyl ring. The oxidation of α-chloro-α-nitroso

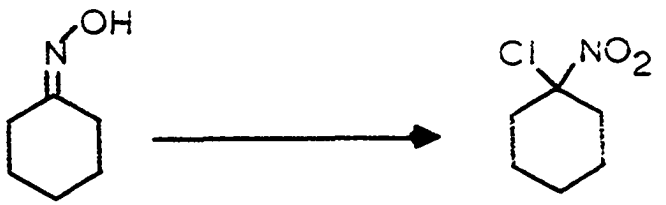
compounds are generally performed under extremely harsh reaction conditions, e.g., nitric acid [31], ozone [28], potassium permanganate, m-chloroperbenzoic acid at elevated temperatures, and tetra-n-butylammonium hypochlorite [26].

Although there are numerous chlorination and oxidation procedures, several combinations of reagents were used to optimize 1-chloro-1-nitrocyclohexane 4 with respect to purity and yield from the readily available cyclohexanone oxime. The results for the preparation of 1-chloro-1-nitrocyclohexane are listed in Table 1.

The yields using the various conditions vary widely and are explainable based on the difficulty of monitoring the completion of the reaction and isolation procedures. For instance, N-chlorosuccinimide (NCS) chlorination of the oxime of cyclohexanone generally gave lower yields due to the difficulty of decanting the product from large amounts of solid. While the nitric acid oxidations of α-chloro-α-nitrosocyclohexane were slow and often incomplete which resulted in low yields, the remaining two chlorination (Cl_2 and HOCl) and oxidation (O_3 and $n\text{-}Bu_4NOCl$) procedures appeared useful if competing electrophilic attack on the cyclopropyl ring could be eliminated. Unfortunately, the conditions of choice from Table 1 were not very encouraging because cyclopropyl rings are extremely susceptible to electrophilic attack.

Small scale reactions were performed with cyclopropyl methyl ketone oxime 3 using the four possible combination of reactants. Numerous unidentified reaction products were produced under the various reaction conditions. Some of the unidentified products contained three chlorine

Table 1. Preparation of 1-chloro-1-nitrocyclohexane using various reaction conditions



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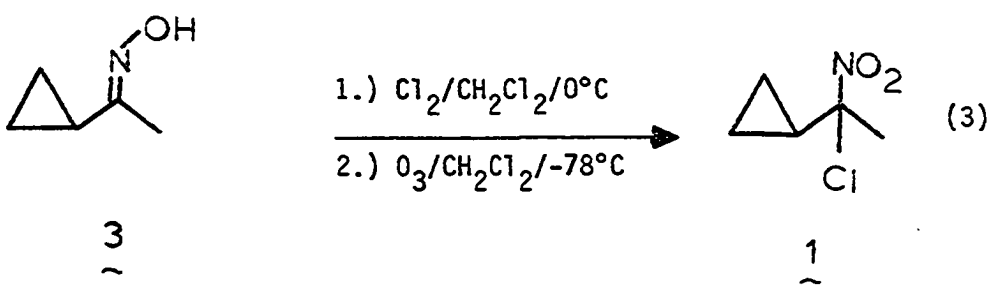
Reagents and Conditions	% Yield Isolated	Ref.
1. $Cl_2/CH_2Cl_2/0°C$ and $O_3/CH_2Cl_2/-78°C$	91	28
2. $Cl_2/CH_2Cl_2/0°C$ and cyclo-C_6H_{12}/HNO_3	64	28
3. $NCS/NaHCO_3/H_2O$ and $(n\text{-}Bu)_4N^+HSO_4^-/NaOCl/C_6H_6$	47	26,29
4. $NCS/NaHCO_3/H_2O$ and HNO_3/cyclo-C_6H_{12}	39	29
5. $HOCl$/pH 5.5/H_2O/C_6H_6 and $(n\text{-}Bu_4N^+HSO_4^-/NaOCl/C_6H_6$	87	26
6. $HOCl$/pH 5.5/H_2O/C_6H_6 and HNO_3/cyclo-C_6H_{12}	71	26
7. $NCS/NaHCO_3/H_2O$ and $O_3/CH_2Cl_2/-78°C$	55	28,29

atoms and no cyclopropyl rings as detected by G.C.M.S. and ^1H N.M.R. analyses. These presumably arise from electrophilic attack upon the cyclopropyl ring and the oxime functional group. Other products did not contain nitro groups as observed by G.C.I.R. Clearly, the optimal set of reaction conditions appeared to be chlorination using chlorine followed by ozonolysis.

After repeated attempts and slight modifications of the procedure described by Barnes and Patterson [28], a reasonable yield of 1 1-chloro-1-cyclopropyl-1-nitroethane (51%) was obtained. The alteration of conditions included titration of only one equivalent of chlorine slowly into the reaction mixture to minimize electrophilic attack of the cyclopropyl ring and ozonolysis at -78°C (Eq. 3). After the slight modifications of the reaction procedure, the preparation of 1-chloro-1-cyclopropyl-1-nitroethane 1 was consistently reproducible on a larger



3 1 (3)

scale. It appears chlorine preferentially attacks the oxime functionality over the cyclopropyl ring at low chlorine concentrations. The yields are low due to some competing electrophilic attack and

incomplete reaction evidence by the remaining unreacted oxime of cyclopropyl methyl ketone.

2. Preparation of 2-chloro-2-nitro-6-heptene

The synthesis of 2-chloro-2-nitro-6-heptene 2, to use as a free-radical clock for the investigation of the $S_{RN}1$ process, was significantly more complex than the preparation of 1-chloro-1-cyclopropyl-1-nitroethane 1. Although nitro compounds are accessible from a variety of substrates such as alkyl halides, oximes, amines, hydrocarbons, carboxylic acids, and alkenes [32], an appropriate seven carbon precursor for the synthesis of 2-chloro-2-nitro-6-heptene 2 was not readily available. Additional complications in the synthesis of 2-chloro-2-nitro-6-heptene were anticipated due to the experimental conditions usually employed for the conversion of the previously mentioned substrates to aliphatic nitro compounds. Many of the reagents that affect the conversion of suitable precursors to appropriate nitro compounds are known to react with carbon-carbon double bonds. An illustrative example is the conversion of oximes to α-chloro-α-nitroalkanes. All of the oxidizing agents (e.g., O_3, HOCl, and HNO_3) which are suitable for the oxidation of α-chloro-α-nitrosoalkanes readily react with carbon-carbon double bonds. Also, the conversion of secondary alkyl halides to secondary nitroalkanes by the Victor-Meyer reaction is complicated by the formation of alkyl nitrites.

In preparing a synthetic strategy for the synthesis of 2-chloro-2-nitro-6-heptene 2, it would be desirable to incorporate the double

bond and nitro groups into the molecule at the same time to avoid problems. Unfortunately, the apparent routes such as alkylation of nitronate anions or organometallic reagents with nitro compounds are unsatisfactory. Apart from the $S_{RN}1$ process forming highly substituted compounds, only a few examples of C-alkylation of simple nitronate anions have been reported [33,34]. These examples usually involve intramolecular cyclizations. The reaction of nitronate anions with alkyl halides normally results in O- and not C-alkylation.

Inherent problems exist with the reaction of organometallic compounds with nitroalkanes or nitroalkenes due to the plethoria of products which can be isolated at varying temperatures [35]. Michael addition to nitro-olefins is most successful with well-stabilized anions with yields often decreasing with increasing reactivity of the nucleophile. Although alkyl groups can be added as cadmium alkyls [36], this researcher could not reproduce reported results. Several elegant methods to incorporate both the nitro and carbon-carbon double bond functional groups at the same time all failed to give acceptable yields of products. These recently developed procedures included reactions of silyl nitronates with organolithium reagents [37] and α,α-doubly deprotonated nitroalkanes [38]. Reports in the literature suggest the α,α-doubly deprotonated nitroalkanes have dramatically improved the poor C-nucleophilicity of nitronate anions with alkyl bromides or iodides. Due to the limited experimental procedures reported, this researcher could not reproduce reported results.

After attempts to synthesize 2-nitro-6-heptene or 2-chloro-2-nitro-6-heptene 2 by a variety of routes failed, it became apparent that 2-nitro-6-heptene should be synthesized using improved variations of the Victor-Meyer reaction [39-41]. The reaction of silver nitrite with primary alkyl iodides or bromides

$$RX + AgNO_2 \longrightarrow AgX + RNO_2 + RONO$$

is an excellent method for the preparation of primary nitroalkanes [42]. Unfortunately, the conversion of secondary alkyl halides to secondary nitroalkanes by the Victor-Meyer reaction is complicated by the formation of alkyl nitrites or alkyl nitrates. Alkyl nitrates are formed if the silver nitrite is thermally allowed to decompose.

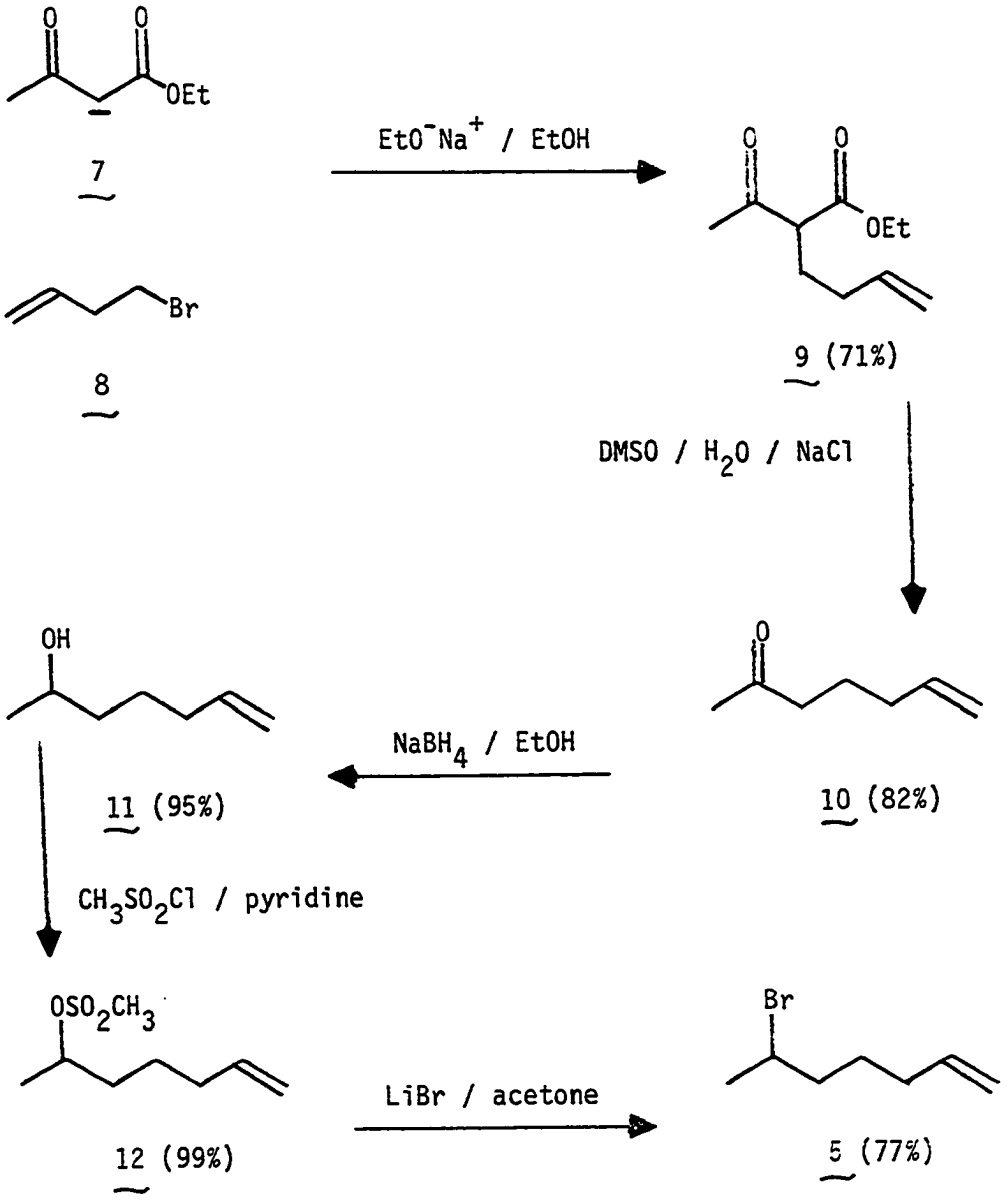
$$2AgNO_2 \longrightarrow AgNO_3 + Ag^0 + NO$$

$$AgNO_3 + RX \longrightarrow RNO_3 + AgX$$

Modifications using sodium nitrite with secondary alkyl bromides substantially increases the yields of secondary nitroalkanes over silver nitrite reactions [43]. With various modifications available, the preparation of 2-nitro-6-heptene was pursued, although questions concerning the formation of by-products and the selective chlorination of nitronate anions over a carbon-carbon double bond remained.

The preparation of 2-bromo-6-heptene 5 to use as a precursor for the synthesis of 2-nitro-6-heptene 6 involves several steps as shown in Scheme 2. The first step involves alkylation of ethyl acetoacetate 7 with 4-bromo-1-butene 8 in a S_N2 process. The yield was slightly

Scheme 2


OEt
7
EtO⁻Na⁺ / EtOH
OEt
9 (71%)
Br
8
DMSO / H2O / NaCl
OH
O
NaBH4 / EtOH
11 (95%)
10 (82%)
CH3SO2Cl / pyridine
OSO2CH3
Br
LiBr / acetone
12 (99%)
5 (77%)

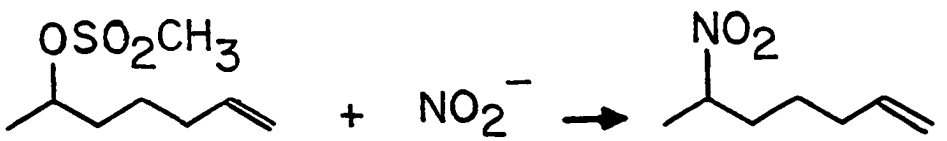
diminished (71.2%) due to dialkylation of starting ethyl acetoacetate. The decarbalkoxylations of a variety of geminal diesters, β-ketoesters, and α-cyanoesters by H_2O-DMSO with added salts is a convenient preparative route leading to esters, ketones, and nitriles, respectively [44]. This versatile reaction was used to prepare 6-heptene-2-one 10 from the previously prepared mono-alkylated ethyl acetoacetate 9 with a reasonable yield (82%). The majority of material isolated which was not 6-heptene-2-one 10 was unreacted β-ketoester [45].

2-Bromo-6-heptene 5 was prepared from 6-heptene-2-one 10 utilizing a well-known sequence of reactions. First, sodium borohydride reduction of 6-heptene-2-one afforded 6-hepten-2-ol 11 with an isolated yield of 95%. Second, the formation of 6-heptene-2-methanesulfonate 12 was prepared nearly quantitatively (99%) using established procedures. Third, 6-heptene-2-methanesulfonate 12 was treated with lithium bromide in refluxing dry acetone to yield (77%) 2-bromo-6-heptene 5 [46]. The synthetic sequence from 6-heptene-2-one to 2-bromo-6-heptene proceeded with an overall isolated yield of 72.4% utilizing known procedures.

Several reactions were performed, in an attempt to form 2-nitro-6-heptene 6 directly from 6-heptene-2-methanesulfonate 12, with silver nitrite or sodium nitrite. The results of these reactions are shown below in Table 2. The poor yields of 2-nitro-6-heptene 6 can easily be explained.

Two explanations suggest themselves for this progressive change in the character of the reaction. First, the formation of a silver-

Table 2. Reactions of 6-heptene-2-methanesulfonate with silver nitrite and sodium nitrite



12 → 6

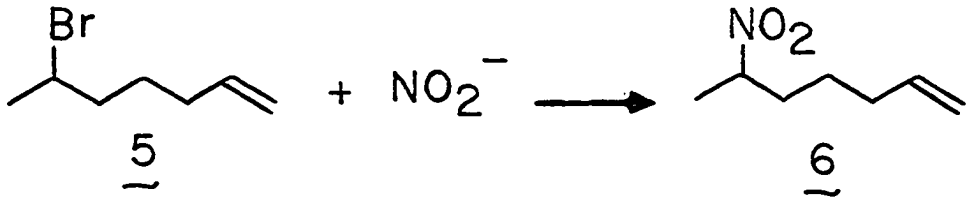
Counterion/Solvent	Time (hrs)	Yield	% Sulfonate Unreacted
Ag^+/Et_2O	72	no reaction	91
Na/DMSO	12	trace	0
Na/DMF	12	trace	0

halogen bond furnishes an important part of the driving force for the reaction of alkyl halides with silver nitrite; this is verified by the failure of 6-heptene-2-methanesulfonate to react with silver nitrite. Other sulfonate esters have been recovered unreacted using similar conditions in literature reactions, while the corresponding alkyl bromides and iodides react completely in a fraction of the time.

Second, the low yield of 2-nitro-6-heptene 6 using sodium nitrite can be rationalized by an increase in the carbonium character of the reaction due to the sulfonate ester. In a paper rationalizing the contrasting alkylation reactions of ambident anions, evidence was presented which supports the contention that preferential covalency formation at the atom having higher electron density is preferred when the transition state has a large carbonium component. This preference is taken to mean that in a reaction having a relatively large amount of S_N1 character, simple electrostatic forces govern the course of the reaction and, clearly with nitrite ion, the oxygens have a much higher electron density than nitrogen. The formation of nitrite esters over 2-nitro-6-heptene is verified by the major products of the reaction (6-hepten-2-ol 11 and 6-hepten-2-one 10) which are known products from the decomposition of nitrite esters.

Several reactions were performed in an attempt to maximize the yield of 2-nitro-6-heptene 6 from 2-bromo-6-heptene 5. These results are listed in Table 3. The lower yield of 2-nitro-6-heptene obtained when silver nitrite was reacted with 2-bromo-6-heptene can be explained by an increase in the carbonium character on the reaction when silver

Table 3. Reaction of 2-bromo-6-heptene with sodium and silver nitrite



5 6

Counterion/Solvent	Time (hrs)	% Yield Isolated
Ag/et_2O	24	7
Na/DMSO	48	39
Na/DMF	48	44

is used. This also was verified by the formation of appreciable amounts of 6-heptene-2-ol and 6-hepten-2-one.

The desired product, 2-nitro-6-heptene 6, was isolated from the reaction between 2-bromo-6-heptene and sodium nitrite with similar yields when DMF or DMSO were used as solvents. Pure 2-nitro-6-heptene was separated from the complex mixture of reaction products by flash chromatography [47]. Since the yields obtained were acceptable, no further attempts at maximizing the yield of 2-nitro-6-heptene using recently developed modifications were pursued. Some of the recent modifications include the use of tetra alkyl ammonium nitrites [39] or the use of crown ethers [41].

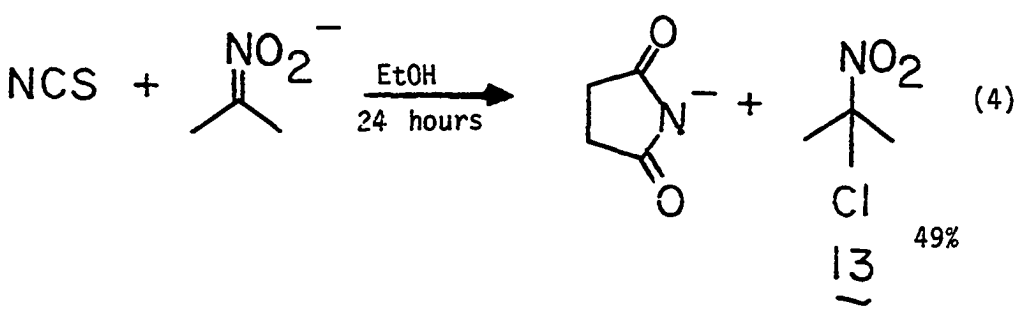
Although the synthesis of 2-nitro-6-heptene 6 was successful, several questions concerning the selective chlorination of the nitronate anion over a carbon-carbon double bond remained. In the synthesis of 1-chloro-1-cyclopropyl-1-nitroethane 1, one equivalent of chlorine (Cl_2) was titrated slowly into the reaction mixture to minimize the electrophilic attack on the cyclopropyl ring contained in the starting substrate. In order to prevent competing chlorination of the carbon-carbon double bond, other procedures were pursued.

The halogenation of ketones with N-bromosuccinimide have been reported to proceed by a free-radical mechanism and an ionic mechanism. Free-radical halogenation of ketones are frequently initiated by light, a peroxide, or some other free-radical initiator [48]. The ionic bromination mechanism of ketones using N-bromosuccinimide involves the electrophilic attack on the enol. Regiospecificity in the halogenation

of unsymmetrical ketones can be attained by treatment of appropriate enol borinate of the ketone with N-bromo- or N-chlorosuccinimide [49].

Although the use of N-chlorosuccinimide as an electrophile is well-documented and researched, examples of N-chlorosuccinimide quenching a nitronate anion were not found in the literature. In an attempt to minimize the chlorination of the carbon-carbon double bond during the chlorination of the nitronate of 2-nitro-6-heptene, the use of N-chlorosuccinimide as an electrophilic chlorination reagent was pursued.

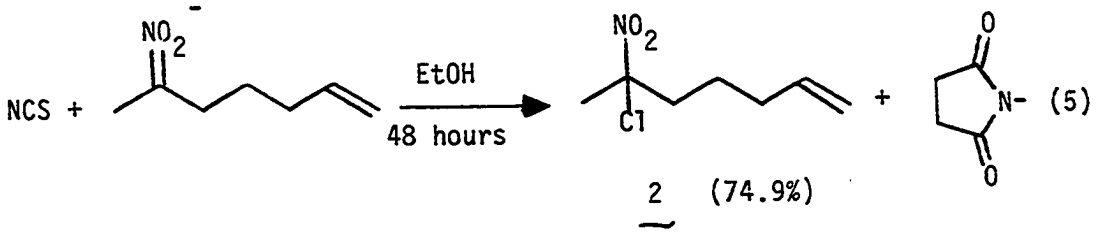
N-Chlorosuccinimide was reacted with the lithium salt of 2-nitropropane in absolute ethanol to yield 0.49 g (49%) of 2-chloro-2-nitropropane 13 (Eq. 4). The isolated 2-chloro-2-nitropropane



(4)

compared favorably to an authentic sample of 2-chloro-2-nitropropane by G.C., I.R., and ^{1}H N.M.R. Since the reaction of N-chlorosuccinimide appeared to give satisfactory results with the anion of 2-nitropropane, several precautions were taken to prevent allylic chlorination of 2-nitro-6-heptene.

The chlorination of the lithium salt of 2-nitro-6-heptene was performed under an oxygen atmosphere and in a flask wrapped with aluminum foil to exclude light. These precautions were taken in order to prevent allylic free-radical chlorination from occurring. N-Chlorosuccinimide was added to the lithium salt of 2-nitro-6-heptene to yield (74.9%) 2-chloro-2-nitro-6-heptene 2 after two days of stirring at room temperature (Eq. 5). G.C.M.S. analysis of the crude



2 (74.9%)

isolate indicated only a trace amount of allylic chlorination had occurred. It appears from the few experiments performed, chlorination of nitronate anions with N-chlorosuccinimide is a useful synthetic reaction.

C. Conclusion

The synthesis of 1-chloro-1-cyclopropyl-1-nitroethane 1 and 2-chloro-2-nitro-6-heptene 2, to use as appropriate free-radical clocks, have been described. These two previously unreported α-chloro-α-nitroalkanes were obtained by different synthetic pathways utilizing a variety of reactions and techniques. It is this author's opinion that

the synthesis of 1-chloro-1-cyclopropyl-1-nitroethane and 2-chloro-2-nitro-6-heptene are the first reported examples of α-chloro-α-nitroalkanes which contain reactive side chains. The presence of the carbon-carbon double bond and the reactive cyclopropyl ring made the synthesis of the two α-chloro-α-nitroalkanes challenging.

D. Experimental Section

1. General considerations

Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Preparative G.L.C. was performed on a Aerograph model A-90-P gas chromatograph. Analytical gas chromatography (G.L.C.) was performed on a Beckman G.C. 72-5 or a Varian 3700 gas chromatograph. High resolution mass spectra (M.S.) were recorded on an AEI MS 902 mass spectrometer. G.C. mass spectra (G.C.M.S.) were recorded on a Finnegan 4000 instrument. ^{1}H N.M.R. (60 MHz) were recorded on a Varian EM360, a Varian EM360A, a Varian EM360L, or a Hitachi-Perkin Elmer R-20B instrument. ^{1}H N.M.R. (300 MHz) were recorded on a Bruker WM-300. ^{13}C N.M.R. (22.6 MHz) were recorded on a Joel FX-90Q spectrometer. The Bruker WM-300 spectrometer was also used to record ^{13}P N.M.R. (36.4 MHz). Infrared spectra (I.R.) were recorded on a Beckman 4250 spectrophotometer or a Beckman Acculab 2 spectrophotometer. Ozonolysis was performed with a Welsbach T-23 using 90 volts, 0.04 C.F.M., and 7 lb/sq. in.

^1H N.M.R. yields were determined by integration comparison with a known amount of an appropriate reference (usually CH_2Cl_2, $CHCl_3$, C_6H_6, or DMSO).

All solvents were purchased from Fisher, Baker, or Mallinckrodt. Dimethyl sulfoxide (DMSO) was distilled from calcium hydride before use and stored over 4A molecular sieves under nitrogen. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride before use and stored over 4A molecular sieves under a nitrogen atmosphere. N,N-Dimethylformamide was distilled from calcium hydride before use and stored under nitrogen. Other solvents were purchased reagent grade, if available, and used without purification.

2-Nitropropane, cyclopropyl methyl ketone, 4-bromo-1-butene, and N-chlorosuccinimide were purchased from Aldrich. Cyclohexanone oxime and methanesulfonyl chloride were purchased from Eastman Organic. Ethyl acetoacetate, silver nitrite, and sodium borohydride were obtained from Fisher, while sodium nitrite was purchased from Mallinckrodt.

2-Chloro-2-nitropropane 13 was prepared by the addition of chlorine to an ice-cold aqueous solution of 2-nitropropane and sodium hydroxide. The resulting bottom layer was separated, washed with aqueous thiosulfate, dried, and distilled (b.p. 133-134°C/760 mm).

2. Preparation of the oxime of cyclopropyl methyl ketone

Hydroxylamine hydrochloride (53 g, 0.77 M) and sodium acetate (581 g, 0.71 M) were added to a suspended system of cyclopropyl methyl

ketone (50 g, 0.59 M) in 200 ml of water. The stirred mixture was heated for 18 hours at 90°C. After the solution cooled, it was extracted with three 100 ml portions of methylene chloride. The combined extracts were washed with 100 ml of 10% NaCl solution and dried ($MgSO_4$). The dried solution was distilled (58-62°C/1.8 mm) through a short distillation head to obtain 49.9 g (85.4%) of pure product which melted at 49.5°C.

^1H N.M.R. ($CDCl_3$) δ 9.9-9.3 (s, broad, 1H, -OH), 1.73 (s, 3H, $-CH_3$), 1.7-1.3 (m, 1H, $-CH-CH_2-$), 0.9-0.6 (m, 4H, $-CH_2-CH_2-$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 159.19, 15.19, 10.64, 4.42.

I.R. ($CDCl_3$, cm^{-1}) 3600 (s), 3300 (vs, broad), 1645 (m), 1370 (s), 1340 (m), 1310 (m), 1070 (m), 990 (m).

M.S. Calculated for C_5H_9NO: 99.06842. Measured: 99.06857. Error = +1.5 ppm.

3. Preparation of 1-chloro-1-cyclopropyl-1-nitroethane

The solid oxime of cyclopropyl methyl ketone (6.16 g, 62.2 mmol) was added to 100 ml of ice-cold methylene chloride. Chlorine gas (4.41 g, 62.2 mmol) dissolved in 100 ml of methylene chloride was slowly added over a period of one hour to the oxime solution with efficient stirring and constant cooling. The addition of chlorine turned the solution blue immediately. After the addition of all of the chlorine, the reaction mixture was stirred for an additional two hours. Excess chlorine was vented from the reaction flask under aspirator

vacuum at 0°C. After 2 hours, very little chlorine odor was evident in the reaction mixture. The remainder of the chlorine was purged by bubbling argon through the solution for 30 minutes. The solution was transferred to a 250 ml R.B. flask and ozonolysis performed at -78°C. The excess ozone was purged with argon. Methylene chloride was then removed under reduced pressure to give a slurry. Additional precipitate was formed upon the addition of ether. The resulting ether solution was filtered, dried (Na_2SO_4) and concentrated. The crude isolate was distilled (41-42°C/1.8 mm) to yield 4.7 g (51%) of 1-chloro-1-cyclopropyl-1-nitroethane 1.

^{1}N.M.R. ($CDCl_3$) δ 2.07 (s,3H, $-(NO_2)C(CL)\underline{CH_3}$), 2.0-1.5 (m, 1H, $-(NO_2)C(CL)-\underline{CH}-$), 0.83 (s, broad, 2H, $-\underline{CH_2}-$) 0.70 (s, broad, 2H, $-\underline{CH_2}-$).

^{13}N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 105.93, 27.98, 21.53, 4.36, 3.49.

I.R. (neat, NaCl plates, cm^{-1}) 3020 (w), 2900 (w), 1565 (vs), 1450 (m), 1390 (s), 1370 (m), 1340 (s), 1230 (m), 1190 (m), 1115 (m), 1035 (m), 850 (s).

In the M.S. of α-chloronitroalkanes, the parent ion was never observed. This is typical of aliphatic nitro compounds. The P-46 ion (loss of NO_2) was measured. Calculated for C_5H_8Cl: 103.03146. Measured: 103.03185. Error = +3.8 ppm.

Elemental analysis. Calculated for $C_5H_8NO_2Cl$: C, 40.15; H, 5.39; N, 9.36; O, 21.39; Cl, 23.70. Found: C, 40.39; H, 5.42; N, 9.33; Cl, 23.97.

4. Alkylation of the anion of ethylacetoacetate with 4-bromo-1-butene

Metallic sodium (3.1 g, 138 mmol) was gradually added to 70 ml of absolute ethanol. After all of the sodium dissolved, ethylacetoacetate (18 g, 0.138 mmol) was added to the ethanol solution. The resulting solution was heated to gentle boiling with constant stirring. 4-Bromo-1-butene (25 g, 151 mmol) was added to the refluxing solution over a period of two hours. The refluxing and stirring were continued until a sample of the solution was neutral to litmus paper.

The cooled solution was decanted and the remaining NaBr was washed with 20 cc of absolute ethanol. The combined ethanol solution was distilled through a short distillation head to remove the solvent. Distillation of the resulting crude mixture (85-90°C/2mm) afforded 18.1 g (71.2%) of product 9.

^{1}H N.M.R. ($CDCl_3$) δ 6.2-5.4 (m, 1H, CH_2=C<u>H</u>-), 5.3-4.8 (m, 2H, <u>CH_2</u>=CH-), 4.2 (q, 2H, -O<u>CH_2</u>CH_3, J_H=7H_2), 3.15 (t, 1H, -COC<u>H</u>CO), 2.18 (s, 3H, <u>CH_3</u>CO, J_H = 7 Hz).

I.R. (neat, NaCl plates, cm^{-1}) 3095 (m), 2995 (s), 2945 (m), 1730 (vs), 1645 (s), 1450 (m), 1365 (m), 1250 (m), 1030 (m), 920 (m).

5. Preparation of 6-hepten-2-one by decarbalkoxylation of alkylated ethyl acetoacetate

In a 100 ml rb flask equipped with a magnetic stirrer and a reflux condenser was placed previously prepared β-ketoester 9 (5.0 g, 27 mmol), dimethylsulfoxide (30 ml, as received), water (0.5 ml) and NaCl (3.17 g, 54 mmol). The mixture was heated overnight at 170°C. The cooled solution was poured into 30 ml of brine and 30 ml of water. The

resulting aqueous solution was then extracted three times with 30 ml of ether. After combining the ether extracts, they were washed with three 30 ml portions of H_2O and 30 ml of brine. The resulting ether solution was dried (Na_2SO_4) and evaporated. Distillation (82-84°C/98 mm) of the residue afforded 2.5 g (82%) of the desired 6-hepten-2-one 10. This compound has been prepared by another method [45,50].

^1H N.M.R. ($CDCl_3$) δ 6.15-5.5 (m, 1H, $CH_2=C\underline{H}-$), 5.4-4.8 (m, 2H, $\underline{CH_2}=CH-$), 2.13 (s, 3H, $\underline{CH_3}CO-$), 2.16-1.0 (m, 6H, $CH_2=CH-(\underline{CH_2})_3-$).

I.R. (neat, NaCl plates, cm^{-1}) 3080 (w), 2990 (m), 2940 (s), 1710 (vs), 1640 (m), 1415 (m), 1370 (s), 1165 (m), 1090 (m), 910 (s), 730 (m).

6. Preparation of 6-hepten-2-ol by sodium borohydride reduction of 6-hepten-2-one

A slurry of sodium borohydride (0.3 g, 8 mmol) in 15 ml of absolute ethanol was added to 6-hepten-2-one (1.68 g, 15 mmol). The resulting solution was refluxed for one hour. The cooled solution was treated with 15 ml of 10% NaOH until the precipitate dissolved. The alkaline solution was transferred to a separatory funnel and extracted with three 25 ml portions of methylene chloride. The combined methylene chloride extracts were washed with brine, dried (Na_2SO_4), and evaporated. The 6-hepten-2-one was completely consumed as shown by I.R. and N.M.R. The crude alcohol was purified by Kugelrohr distillation (70°C/13 mm) to yield 1.66 g (97%) of pure 6-hepten-2-ol 11.

In a scaled-up reaction using the same procedure, the crude product was distilled through a 5 inch vacuum jacketed Viqreaux column (64-65°C/ 13 mm) to obtain 95% pure product.

^{1}H N.M.R. ($CDCl_3$) δ 6.2-5.5 (m, 1H), 5.2-4.7 (m, 2H), 3.95 (m, 1H), 3.1 (s, 1H, broad), 1.15 (d, 3H, J_H = 6 Hz).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 138.66, 114.45, 67.69, 38.65, 33.61, 24.99, 23.22.

I.R. (neat, NaCl plates, cm^{-1}) 3360 (vs, broad), 3100 (m), 2990 (s), 2940 (s), 1645 (m), 1380 (m), 1130 (m), 995 (m), 905 (m), 810 (s), 755 (m).

7. Preparation of the 6-heptene-2-methanesulfonate

Methanesulfonyl chloride (20.1 g, 175 mmol) was added to a cooled solution (0°C) of 6-hepten-2-ol (10 g, 88 mmol) and 75 ml of pyridine. The flask was refrigerated for 12 hours. The reaction mixture was poured into 300 ml of ice water. The resulting aqueous solution was extracted with ether washed with an equal volume of cold HCl, washed with water, and dried ($MgSO_4$). The ether was concentrated to yield 15.44 g of organic residue. ^{1}H N.M.R. and I.R. analyses of the isolate revealed that no 6-hepten-2-ol was present and 6-heptene-2-methanesulfonate 12 was isolated with a 99% yield.

^{1}H N.M.R. ($CDCl_3$) δ 6.1-5.3 (m, 1H, $H_2C=C\underline{H}-CH_2-$), 5.2-4.5 (m, 2H, $\underline{H_2}C=CH-$), 2.96 (s, 3H, $-OSO_2-\underline{CH_3}$), 1.37 (d, 3H, $-(OSO_2CH_3)CH(\underline{CH_3})$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.99, 114.82, 79.71, 38.38, 35.78, 32.96, 24.08, 20.83.

I.R. (neat, NaCl plates, cm^{-1}) 2995 (m), 2975 (m), 1645 (m), 1350 (vs, broad), 1175 (vs), 970 (s), 905 (vs, broad), 795 (m).

8. Preparation of 2-bromo-6-heptene

Reagent grade acetone, protected from moisture, was refluxed with the mesylate of 6-hepten-2-ol (13.46 g, 76.4 mmol) and lithium bromide (19.0 g, 212 mmol). Magnetic stirring prevented serious bumping. The acetone was removed on a rotary evaporator and the residual oil was taken up in ether. The ether solution was washed well with water, brine, and dried ($MgSO_4$). Distillation (60-62°C/23 mm) afforded 10.4 g (77%) of 2-bromo-6-heptene 5.

^1H N.M.R. ($CDCl_3$) δ 6.2-5.4 (m, 1H, $H_2C=\underline{CH}-CH_2$), 5.2-4.6 (m, 2H, $\underline{H_2C}=CH-$), 4.4-3.7 (m, 1H, $-\underline{HC}(Br)CH_3$), 2.4-1.1 (m, 6H, $CH_2=CH-\underline{(CH_2)_3}-$), 1.7 (d, 3H, $-HC(Br)-\underline{CH_3}$, J_H = 6 Hz).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 138.01, 114.82, 51.11 40.44, 32.96, 26.89, 26.41.

I.R. (neat, NaCl plates, cm^{-1}) 3060 (m), 2965 (s), 2920 (s), 1630 (m), 1430 (m, broad), 1370 (m), 1210 (m), 980 (m), 900 (s).

M.S. Calculated for $C_7H_{13}Br$: 176.02006. Measured: 176.02025. Error = +1.1 ppm.

9. Attempted reaction of 6-heptene-2-methanesulfonate with silver nitrite

6-Heptene-2-methanesulfonate (1.0 g, 5.68 mmol) was added slowly to an ice-cold solution of silver nitrite (1.31 g, 8.52 mmol) in 30 ml of ether. The reaction flask was wrapped tightly with several layers

of aluminum foil to exclude light. The reaction mixture was allowed to stir 12 hours at 0° and then 72 hours at room temperature. The silver salts were filtered, washed with more ether, and the washings added to the filtrate. The ether solution was concentrated to yield 0.74 g of organic residue. ^{1}H N.M.R. analysis of the crude isolate revealed that 91% of 6-heptene-2-methanesulfonate was recovered unreacted.

10. Reaction of 6-heptene-2-methanesulfonate with sodium nitrite

6-Heptene-2-methanesulfonate (1.0 g, 5.68 mmol) was syringed into a stirred solution of sodium nitrite (0.68 g, 9.85 mmol) and 5 ml of dry DMF. The reaction flask was immersed in a water bath held at room temperature. After stirring for 12 hours, the reaction mixture was poured into 15 ml of water and extracted (3 x 15 ml) with ether. The combined ether extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated to yield 0.62 of organic residue. G.C.M.S., ^{1}H N.M.R., and I.R. analyses of the crude isolate revealed that all of 6-heptene-2-methanesulfonate was reacted. The major products identified were 6-hepten-2-ol and 6-hepten-2-one. Only a trace amount of the desired 2-nitro-6-heptene was observed.

An identical experiment using dried DMSO and sodium nitrite gave similar results.

11. Preparation of 2-nitro-6-heptene

2-Bromo-6-heptene (1.38 g, 7.8 mmol) was added to an ice-cooled solution of sodium nitrite (0.91 g, 13.3 mmol) in 5 ml of

N,N-dimethylformamide. The reaction mixture was allowed to warm up to room temperature and stir for 48 hours. The resulting solution was poured into 10 ml of water and extracted three times with 20 ml of ether. The resulting ether solution was washed with water and brine. The organic layer was then dried over sodium sulfate and concentrated to give 980 mg of a yellow oil. Purification by flash chromatography using hexanes:ethyl acetate (6:1) as eluent afforded 0.491 g (44%) of 2-nitro-6-heptene 6 (Rf = 0.61).

^{1}H N.M.R. ($CDCl_3$) δ 6.2-5.4 (m, 1H, CH_2=C<u>H</u>-), 5.2-4.8 (m, 2H, <u>CH_2</u>=CH-), 4.5 (m, 1H, -<u>H</u>C(NO_2)CH_3), 1.52 (d, 3H, -HC(NO_2)<u>CH_3</u>, J_H = 6 Hz).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.41, 115.19, 83.26, 34.32, 32.80, 24.73, 18.98.

I.R. (neat, NaCl plates, cm^{-1}) 3080 (m), 2980 (m), 2940 (m), 2860 (m), 1680 (m), 1550 (vs), 1450 (m, broad), 1385 (s), 1350 (s), 980 (m), 900 (m).

M.S. (P-46 peak measured). Calculated for C_7H_{13}: 97.10173. Measured: 97.10202. Error = +3.0 ppm.

12. Reaction of 2-bromo-6-heptene with silver nitrite

2-Bromo-6-heptene (1.23 g, 6.95 mmol) was added slowly via syringe to an ice-cold solution of silver nitrite (1.61 g, 10.4 mmol) in 20 ml of ether. The reaction flask was wrapped tightly with several layers of aluminum foil to exclude light. The reaction mixture was allowed to stir for 4 hours at 0°C and then 24 hours at room temperature. The

resulting reaction mixture was filtered from silver salts. The salts were washed with more ether. The combined ether solution was concentrated to yield 0.66 g of crude product. Purification by flash chromatography using hexanes:ethyl acetate (6:1) as eluent afforded 69 mg (7%) of 2-nitro-6-heptene (Rf = 0.61). The major products were 6-hepten-2-ol and 6-hepten-2-one which probably result from the decomposition of the form nitrite ester.

13. Preparation of 2-chloro-2-nitropropane by the reaction of N-chlorosuccinimide with the anion of 2-nitropropane

N-Chlorosuccinimide (1.08 g, 8.11 mmol) was added to an ice-cold solution of the lithium salt of 2-nitropropane (0.769 g, 8.09 mol) in 10 ml of absolute ethanol. The reaction was saturated with oxygen and foil-covered before and after the addition of N-chlorosuccinimide. The reaction mixture was allowed to warm-up to room temperature and stirred for 24 hours. The resulting solution was poured into brine and extracted three times with 25 ml of ether. The combined ether extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated to give 0.52 g of organic residue. The isolate was compared favorably to an authentic sample of 2-chloro-2-nitropropane by G.C., I.R., and N.M.R. The crude residue was purified by bulb to bulb distillation (140°/760 mm) to give 0.49 g (49%) of pure 2-chloro-2-nitropropane 13.

14. Preparation of 2-chloro-2-nitro-6-heptene by the reaction of N-chlorosuccinimide with the anion of 2-nitro-6-heptene

Lithium metal (0.0469 g, 6.75 mmol) was dissolved in 15 ml of absolute ethanol. After all of the lithium dissolved, 2-nitro-6-heptene (0.95 g, 6.64 mmol) was added to the foil wrapped flask containing lithium ethoxide. After 30 minutes, the resulting solution was cooled to 0°C with an ice-bath and throughly saturated with oxygen for 15 minutes. N-Chlorosuccinimide (0.9043 g, 6.75 mmol) was added to the reaction mixture and cooling was continued for 2 hours. The reaction mixture was then allowed to stir at room temperature for 2 days. The resulting solution was poured into brine and extracted with three 25 ml portions of ether. The combined ether extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated to give 0.97 g or organic residue. The crude isolate was purified by flash chromatography using hexane:ethyl acetate (6:1) as eluent which afforded 2-chloro-2-nitro-6-heptene 2 (0.885 g/74.9%/ Rf = 0.69).

^{1}H N.M.R. ($CDCl_3$) δ 6.2-5.4 (m, 1H, CH_2=C<u>H</u>-), 5.3-4.7 (m, 2H, <u>CH_2</u>=CH-), 2.7-1.0 (m, 6H, CH_2=CH-<u>$(CH_2)_3$</u>-), 2.13 (s, 3H, -(NO_2)C(CL)<u>CH_3</u>).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.03, 115.74, 104.69, 42.33, 32.69, 29.28, 23.64.

I.R. (neat, NaCl plates, cm^{-1}) 3095 (w), 2995 (2), 2950 (m), 1645 (m), 1560 (vs), 1450 (m), 1390 (s), 1345 (s), 1095 (m), 995 (m), 920 (s, broad), 850 (m).

M.S. (P-35 peak measured). Calculated for $C_7H_{12}NO_2$: 142.08681. Measured: 142.08712. Error = +2.2 ppm.

Elemental analysis. Calculated for $C_7H_{12}NO_2Cl$: C, 47.33; H, 6.81; N, 7.89; O, 18.01; Cl, 19.96. Found C, 46.45; H, 6.82; N, 8.26; O, 18.12; Cl, 20.63.

III. FREE-RADICAL CLOCKS AND THE ALIPHATIC $S_{RN}1$ PROCESS

A. Introduction

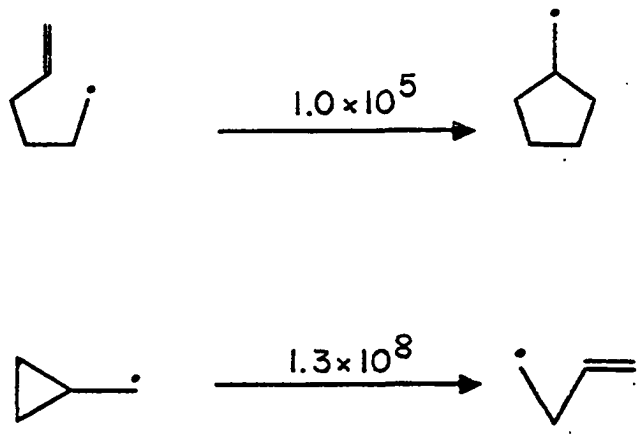
Electron-transfer substitution at a saturated carbon atom is now well-established. Although the $S_{RN}1$ process is well-documented, little if anything is known about the rate of the various propagation steps. There is no completely general method for measuring the absolute rate constants of radical-molecule reactions. Various techniques have been developed to study radical-molecule reactions such as flash photolysis, pulse radiolysis, and the well-known "rotating sector" method [51]. Due to various limitations of the previously mentioned special techniques, these methods are unattractive to an organic chemist. Qualitative timing devices (free-radical clocks) have been used for many years to investigate the rates of radical-molecule reactions.

Free-radical clocks use competing unimolecular radical reactions as a qualitative method for determining the rates of radical-molecule reactions. The relevant information is usually obtained by careful product analysis. Recently, about a dozen alkyl radicals have been studied by EPR spectroscopy and their room-temperature-rearrangement rate constants cover more than seven order of magnitude. Consequently, there is a suitable free-radical clock for almost any reaction involving a molecule and a primary alkyl radical [52].

A major goal of this investigation is to determine the relative efficiency of various nucleophiles at trapping α-nitro radicals using appropriate free-radical clocks. Surprisingly, very few results appear in the literature concerning the relative efficiency with which anions

trap radicals. Saveant [7] reports the softness of the attacking atom in the nucleophile is important since sulphur and phosphorous nucleophiles are very efficient radical traps. Tolbert has indicated that the basicity of the nucleophile may influence the radical-anion formation to a greater extent than the stability of the resulting radical ion [53]. The majority of information on trapping of radicals by anions has been obtained by using competitive reactions in studies involving the $S_{RN}1$ process. Results obtained from competitive reactions are reliable even when the rate of initiation is nucleophile dependent. By using appropriate free-radical clocks (competing unimolecular radical reactions), substantial information should be provided concerning the lifetimes of α-nitro radicals and the trapping efficiency of various nucleophiles. The relevant information is ascertained from the products formed and their distribution ratios.

Since radical intermediates are usually short-lived, it was desirable to select free-radical clocks which are not too many orders of magnitude different from the calculated diffusion-controlled limit. Diffusion controlled rate constants at ambient temperatures in a variety of low viscosity solvents are generally 8×10^9 M^{-1} sec^{-1} [54]. 1-Chloro-1-cyclopropyl-1-nitroethane 1 and 2-chloro-2-nitro-6-heptene 2 were selected as suitable free-radical clocks for investigating the aliphatic $S_{RN}1$ process, due to the difference in room-temperature-rearrangement rate constants of the 5-hexenyl and cyclopropyl carbinyl radical unimolecular reactions [55,56]. With the difference in rate constants of the two selected free-radical probes and their general

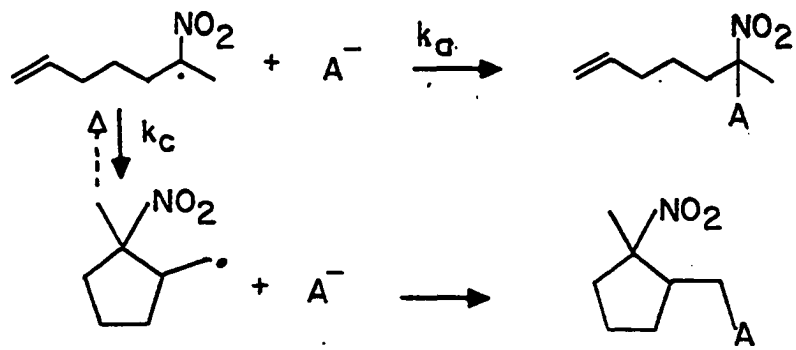


proximity to the diffusion-controlled limit, a good approximation of the lifetime of an α-nitro radical should be obtainable.

Some generalizations and assumptions regarding the treatment and analysis of the data obtained from the free-radical probes should be discussed. First, the cyclization and ring-opening unimolecular radical reactions of the free-radical clocks have to be assumed irreversible (Scheme 3). Second, the trapping of intermediate α-nitro radicals by various nucleophiles has to be assumed irreversible. Third, cyclized product formed by the 5-hexenyl rearrangement includes both five and six-membered rings. Fourth, the value of the rearrangement rate constant of the free-radical clock is assumed to be within close proximity of the model unsubstituted primary alkyl radical. With these four assumptions, an approximate lifetime of the intermediate α-nitro radical and the relative efficiency with which various nucleophiles can trap radicals can be determined. The validity of these

assumptions will be treated in the following results and discussion section.

Scheme 3



$$\frac{[A^-]\,k_a}{k_c} = \frac{[open]}{[closed]}$$

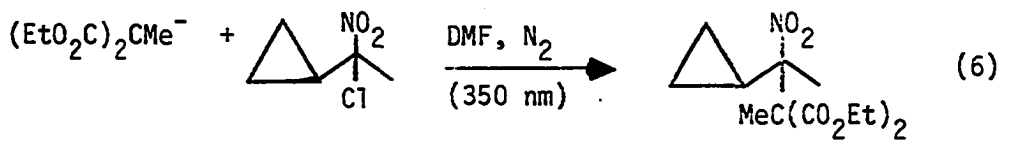
B. Results and Discussion

1. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the anion of diethyl methylmalonate

A nucleophile must perform two functions to enable it to participate in the $S_{RN}1$ process. First, the nucleophile must act as a single electron donor in the initiation step of the $S_{RN}1$ process. Secondly, the nucleophile must be an efficient radical trap in the key propagating step. The enolate derived from diethyl methylmalonate 14 has been shown previously to participate in the $S_{RN}1$ process.

The enolate derived from diethyl methylmalonate (generated with sodium hydride in DMF) reacts with 1-chloro-1-cyclopropyl-1-nitroethane 1

to produce 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15 (Eq. 6). A satisfactory yield of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15 was isolated after irradiation using a Rayonet photoreactor (350 nm) under a nitrogen atmosphere. Analyses



14 1 15 (77%) (6)

of the crude isolate by G.C., I.R., and ^{1}H N.M.R. failed to indicate the presence of any ring-opened products.

Light is necessary for the efficient formation of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15 from the anion of diethyl methylmalonate and 1-chloro-1-cyclopropyl-1-nitroethane. Reactions run in aluminum foil-wrapped flasks to exclude light and immersed in an oil-bath (35°C) to simulate the temperature inside the Rayonet photoreactor, formed 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane with only a 7% yield as determined by G.C. analysis. The greatly diminished yield of cross-coupling product implies that a slow thermal initiation or a S_N2 process are competing alternatives to a photostimulated reaction.

The formation of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15 by a S_N2 process is unlikely since the anion of diethyl

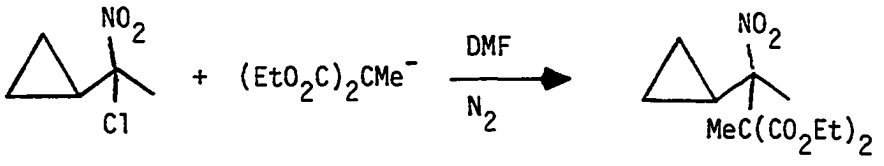
methylmalonate 14 is a very weak nucleophile. This alternative can be excluded since a similar reaction wrapped with aluminum foil, the presence of 10% di-t-butyl nitroxide completely inhibited the formation of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane. Chain character for the reaction between the anion of diethyl methylmalonate and 1-chloro-1-cyclopropyl-1-nitroethane was further demonstrated when an irradiated (350 nm) sample containing 10% di-t-butyl nitroxide yielded 60% of the cross-coupled product. The slightly diminished yield can be attributed to the long reaction time involved after the nitroxide was consumed.

2. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the anion of 2-methyl-1,3-cyclopentanedione

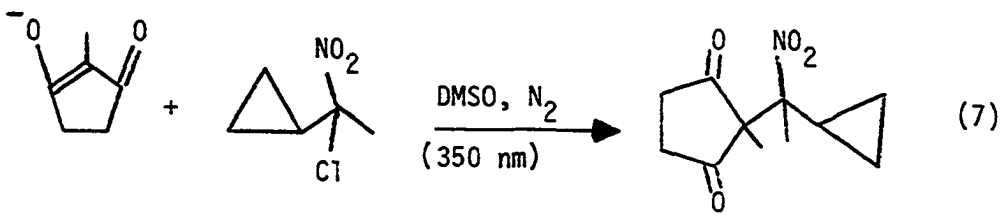
In an attempt to determine if the failure of the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane to undergo unimolecular rearrangement was nucleophile dependent, another stabilized enolate was used. 1-Chloro-1-cyclopropyl-1-nitroethane 1 reacts with the anion of 2-methyl-1,3-cyclopentanedione 16 in DMSO to produce exclusively 2-(1-cyclopropyl-1-nitroethane)-2-methyl-1,3-cyclopentanedione 17 (Eq. 7).

The reaction was performed under standard conditions using a Rayonet photoreactor (350 nm), nitrogen atmosphere, and an aqueous work-up. It is worthwhile to note that careful analyses of the crude isolate failed to reveal the presence of any ring-opened cross-coupled products or dimers. These results appear consistent with those obtained from reactions with the anion of diethyl methylmalonate.

Table 4. Characteristics of the reaction between 1-chloro-1-cyclopropyl-1-nitroethane with the anion of diethyl methylmalonate



Time (hrs)	Conditions	% Yield
30	(350 nm), N_2	77 (isolated)
30	(350 nm), N_2, 10% di-t-butyl nitroxide	60 (G.C.)
30	dark, N_2, 35°C	7 (G.C.)
30	dark, N_2, 10% di-t-butyl nitroxide	0 (G.C.)



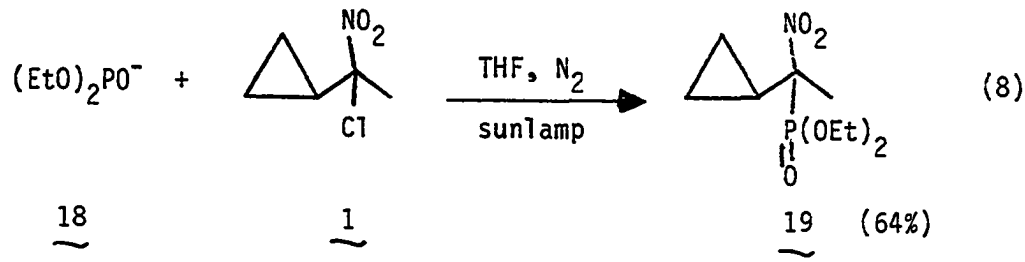
(7)

16 1 17 (53%)

3. The reaction of diethyl phosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

After observing the lack of ring-opened cross-coupled products from the reaction between the anion of diethyl methylmalonate and 1-chloro-1-cyclopropyl-1-nitroethane, it seemed imperative to try other nucleophiles such as dialkyl phosphites. Dialkyl phosphites are known to participate as nucleophiles in the aliphatic $S_{RN}1$ process. Hopefully, the anion of diethyl phosphite would be less efficient at trapping α-nitro radicals so a series of relative reactivities of various nucleophiles could be established. In order to determine any type of scale of relative reactivities of nucleophiles, the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane would have to rearrange to some extent.

The anion 18 generated from diethyl phosphite and potassium t-butoxide reacts with 1-chloro-1-cyclopropyl-1-nitroethane to produce exclusively 1-cyclopropyl-1-nitro-1-(diethoxy phosphinyl)ethane 19 in THF (Eq. 8). Although the formation of α-nitroalkyl phosphonates has been reportedly initiated by an extremely facile thermal initiation



(8)

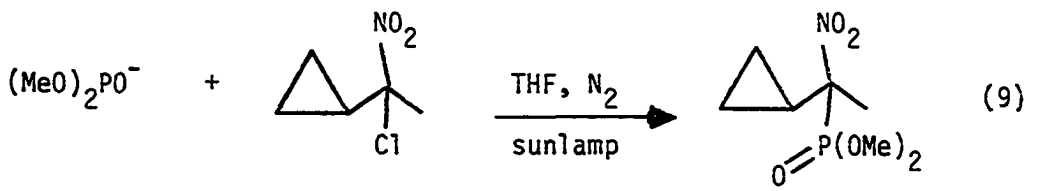
18 1 19 (64%)

process, sunlamp irradiation was included to ensure formation of cross-coupled products. 1-Cyclopropyl-1-nitro-1-(diethoxy phosphinyl)ethane 19 was isolated with a reasonable yield of 64% since the product is somewhat water soluble and an aqueous isolation procedure was performed on the reaction mixture. It is worthwhile to note that careful analyses of the crude isolate after aqueous work-up failed to reveal the presence of any ring-opened cross-coupled products of dimers as determined by ^{1}H N.M.R. and G.C. analyses. Consequently, it appears the α-nitro radical is more stable or rearranges slower than anticipated. Discussion of rates and stability of α-nitro radicals will be addressed later in this section.

4. The reaction of dimethyl phosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

The potassium salt of dimethyl phosphite 20 (generated by the action of potassium t-butoxide on dimethyl phosphite) was found to react with 1-chloro-1-cyclopropyl-1-nitroethane in THF (Eq. 9). After sunlamp irradiation of the reaction mixture (23 hours) and an aqueous work-up, the crude isolate was analyzed. The only cross-coupled product to form

was 1-cyclopropyl-1-nitro-1-(dimethoxy phosphinyl)ethane 21 (42% isolated). ^{1}H N.M.R. and G.C. analyses failed to reveal the presence of any dimers in the crude isolate.

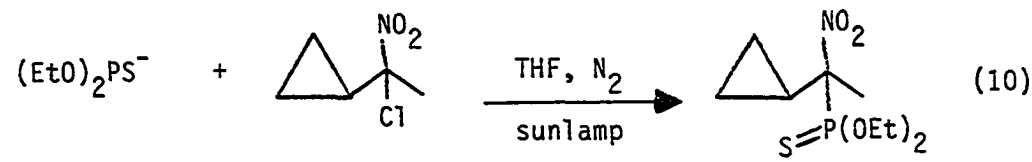


20 1 21 (42%) (9)

5. The reaction of diethyl thiophosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

The anion of diethyl thiophosphite 22 (generated from diethyl thiophosphite and potassium t-butoxide in THF) reacts with 1-chloro-1-nitroethane to produce exclusively 1-cyclopropyl-1-nitro-1-(diethoxy thiophosphinyl)ethane 23 (Eq. 10). A reasonable yield (54%) was obtained, although the product is somewhat water soluble and some thermal decomposition accompanied the bulb to bulb distillation of 1-cyclopropyl-1-(diethoxy thiophosphinyl)ethane 21. Careful analyses of the crude isolate failed to indicate the formation of any ring-open cross-coupled products as determined by G.C. and ^{1}H N.M.R.

All of the reactions of the various dialkyl phosphite anions with 1-chloro-1-cyclopropyl-1-nitroethane yielded similar results. Products containing the rearranged α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane were never observed.



(10)

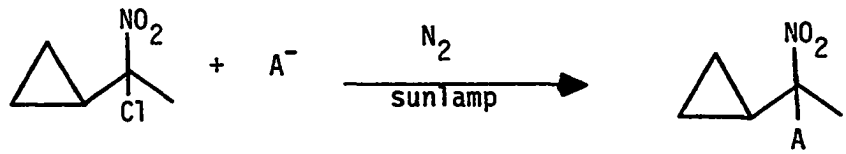
22 1 23 (54%)

6. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane

It has been previously established by competitive reactions that the anion of 2-nitropropane is relatively more reactive toward α-nitro radicals than diethyl phosphite anion in DMSO with K^+ or Li^+ as the counterion. The difference in reactivities of the nucleophiles has been shown to be solvent and counterion dependent [57]. Consequently, the anion of 2-nitropropane should trap the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane before intramolecular rearrangement of the free-radical clock since diethyl phosphite anion exclusively formed the cross-coupled product with the cyclopropyl group still remaining intact.

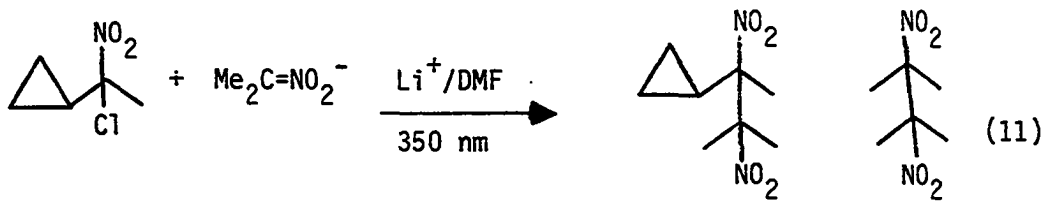
A DMF solution containing the lithium salt of 2-nitropropane 24 and 1-chloro-1-cyclopropyl-1-nitroethane 1 was irradiated (350 nm) for 24 hours under a nitrogen atmosphere (Eq. 11). After an aqueous work-up, the crude isolate was analyzed by G.C. and several products had formed as determined by a change of retention times. It was determined that the crude isolate contained 2,3-dimethyl-2,3-dinitrobutane 25

Table 5. Reaction of dialkylphosphites and thiophosphites anions with 1-chloro-1-cyclopropyl-1-nitroethane



A^-	Counterion/Solvent	Time	% Yield N.M.R.	% Isolated
$(EtO)_2PO^-$	K^+/THF	48	72	64
$(MeO)_2PO^-$	K^+/THF	23	54	42
$(EtO)_2PS^-$	K^+/THF	33	86	54

(0.05 g, 21%) and 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.24 g, 45%) when compared to authentic samples.



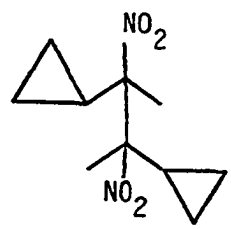
1 24 26 (45%) 25 (21%)

An authentic sample of 2-cyclopropyl-3 methyl-2,3-dinitrobutane 26 was purified for characterization using preparative G.L.C. ^{1}H N.M.R. also revealed that no vinyl protons were observable in the crude isolate. This confirms the prediction that the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane would not undergo intramolecular rearrangement before being trapped by the anion of 2-nitropropane.

7. Preparation of 2,3-dicyclopropyl-2,3-dinitrobutane from the reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 1-cyclopropyl-1-nitroethane

Before determining the distribution of products from the reaction between 1-chloro-1-cyclopropyl-1-nitroethane and the anion of 2-nitropropane using various counterions and solvents, it seemed imperative to obtain a pure sample of 2,3-dicyclopropyl-2,3-dinitrobutane 27. 1-Cyclopropyl-1-nitroethane was prepared by reductive dechlorination of 1-chloro-1-cyclopropyl-1-nitroethane according to a literature procedure of Corey and Estreicher (see experimental section) [26].

A dry DMSO solution containing lithium t-butoxide, 1-chloro-1-cyclopropyl-1-nitroethane, and 1-cyclopropyl-1-nitroethane was irradiated (350 nm) for 48 hours under a nitrogen atmosphere. After an aqueous isolation procedure, the crude isolate contained 2,3-dicyclopropyl-2,3-dinitrobutane 27 (89%) existing as an approximate equal amount of two diastereomers. Recrystallization of the crude isolate from hexane yielded 0.42 g (54%) of white crystals of 2,3-dicyclopropyl-2,3-dinitrobutane which contained the two diastereomers as observed by ^{1}H N.M.R. in a ratio of 5.2:1.0. Identification of the two diastereomers was not pursued further.

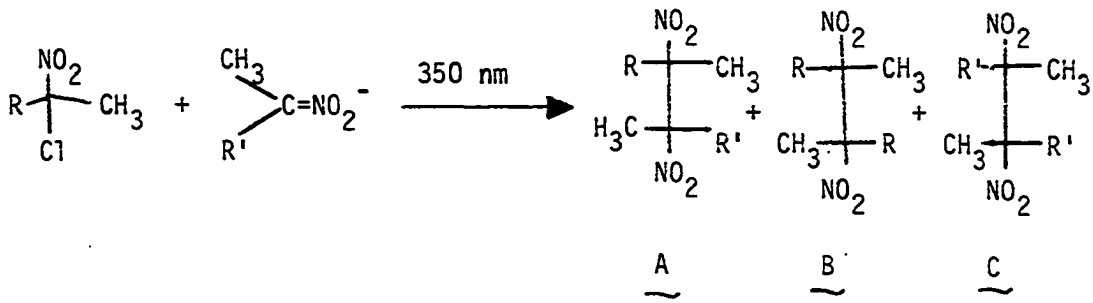


27

8. Reactions of 1-chloro-1-cyclopropyl-1-nitroethane with the anion of 2-nitropropane employing various counterions and solvents

In an attempt to maximize the yield of 2-cyclopropyl-3-methyl-2,3-dinitrobutane and minimize the yield of oxidative dimers, several reactions were performed using various solvents and counterions. The results of these experiments are listed in Table 6. The experimental procedures employed are described in the experimental section.

Table 6. Counterion and solvent effects on the formation of 2-cyclopropyl-3-methyl-2,3-dinitrobutane

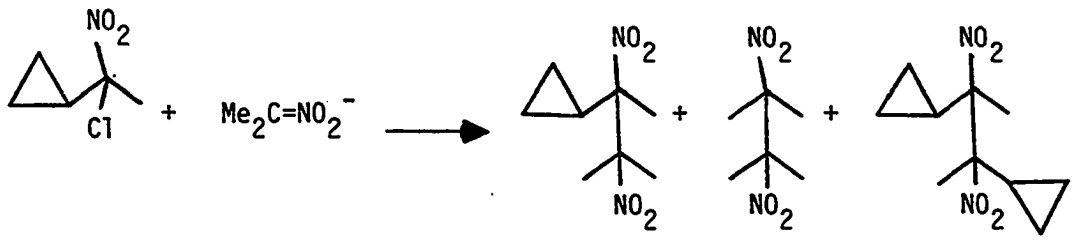


A B C

R	R'	Counterion/Solvent	Time	% Yield (G.C.) A	B	C
cyclo-C_3H_5	CH_3	Li^+/THF	24	1.2	0	7.8
cyclo-C_3H_5	CH_3	Li^+/ETOH	24	21.2	trace	36.2
cyclo-C_3H_5	CH_3	Li^+/DMF	48	57.7	8.7	22.8
cyclo-C_3H_5	CH_3	Li^+/DMSO	48	64.1	10.3	12.4
cyclo-C_3H_5	CH_3	Na^+/DMSO	48	69.9	3.6	17.1
cyclo-C_3H_5	CH_3	K^+/DMSO	48	68.1	4.7	14.7
cyclo-C_3H_5	CH_3	$N(\underline{n}\text{-Bu})_4^+$/DMSO	48	74.0	trace	4.9
cyclo-C_3H_5	CH_3	$N(CH_3)_4^+$/DMSO	48	62.8	2.1	14.3
cyclo-C_3H_5	CH_3	$N(CH_3)_3(CH_2C_6H_5)^+$/DMSO	48	71.4	trace	23.9
cyclo-C_3H_5	cyclo-C_3H_5	Li^+/DMSO	48	89	0	0
CH_3	cyclo-C_3H_5	Li^+/DMF	48	37.9	6.6	48.7
CH_3	cyclo-C_3H_5	Li^+/DMSO	48	42.0	12.9	43.8
cyclo-C_3H_5	CH_3	$N(\underline{n}\text{-Bu})_4^+$/DMF	48	78.1	trace	13.5

9. Solvent and counterion considerations for the formation of 2-cyclopropyl-3-methyl-2,3-dinitrobutane

The formation of the desired cross-coupled product (2-cyclopropyl-3-methyl-2,3-dinitrobutane 26) from the reaction between 1-chloro-1-cyclopropyl-1-nitroethane and the anion of 2-nitropropane appears to be solvent and counterion dependent. This is verified by the results presented in Table 6 which indicates the yield of the three products formed is sensitive to the nature of the solvent and the counterion.



1 24 26 27 25

Previously, Russell, Ros and Mudryk have shown that the $S_{RN}1$ reaction between 2-chloro-2-nitropropane and enolate anions is very sensitive to a change in counterion or solvent [57]. By changing the counterion, Russell et al. have demonstrated the relative reactivities of malonate and nitronate anions can be dramatically reversed.

The variations observed in Table 6 probably result from changes in the overall reactivities of the nitronate anion due to varying degrees of ionic association. Tight ion-pairing apparently decreases the reactivity of the nitronate anion towards α-nitro radicals, thus lowering the yield of the desired cross-coupled product. In THF, the yield of 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 is low presumably due to the presence of tight ion-paired species, while a loose ion-pairs,

such as the ammonium salts of 2-nitropropane in DMSO, show a dramatic increase in the amount of cross-coupled product formed.

A change in solvent from DMSO or DMF to the less polar THF has a striking effect on the reactivity of the lithium salt of 2-nitropropane with 1-chloro-1-cyclopropyl-1-nitroethane. This change can be attributed to an increase in ion-pairing and a decrease in reactivity of the nitronate anion as the polarity of the solvent decreases. It seems apparent from the results listed in Table 6 that an increase in solvent polarity and a decrease in ion-pairing will minimize the competing dimerization processes and increase the overall efficiency of forming the desired cross-coupled product.

10. Mechanistic considerations for the formation of dimers from the reaction of 1-chloro-1-cyclopropyl-1-nitroethane and the anion of 2-nitropropane

The formation of dimers (2,3-dimethyl-2,3-dinitrobutane 25 and 2,3-dicyclopropyl-2,3-dinitrobutane 27) from the reaction between 1-chloro-1-cyclopropyl-1-nitroethane and the anion of 2-nitropropane can be rationalized as occurring by several possible pathways. One interpretation of these results is that the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane is trapped by the anion of 2-nitropropane (Eq. 12) to form a radical anion which subsequently dissociates to form the anion of 1-cyclopropyl-1-nitroethane and the resonance stabilized free radical of 2-nitropropane (Eq. 13). The

$$(\text{cyclo-}C_3H_5)(Me)\dot{C}NO_2 + Me_2C{=}NO_2^- \longrightarrow (\text{cyclo-}C_3H_5)(Me)C(NO_2)C(NO_2)(Me)_2^{\cdot-} \quad (12)$$

$$(\text{cyclo-}C_3H_5)(Me)C(NO_2)C(NO_2)(Me)^{\cdot-}_2 \longrightarrow$$

$$(\text{cyclo-}C_3H_5)(Me)C{=}NO_2^- + Me_2\dot{C}NO_2 \qquad (13)$$

formation of 2,3-dimethyl-2,3-dinitrobutane could subsequently result in the coupling of the anion of 2-nitropropane with the α-nitro radical of 2-nitropropane (Eq. 14). While the major source of 2,3-dicylcopropyl-

$$Me_2C{=}NO_2^- + Me_2\dot{C}NO_2 \longrightarrow Me_2C(NO_2)C(NO_2)(Me)^{\cdot-}_2 \qquad (14)$$

2,3-dinitrobutane is presumably the known $S_{RN}1$ process of Eq. 15, an

$$(\text{cyclo-}C_3H_5)(Me)C{=}NO_2^- + (\text{cyclo-}C_3H_5)(Me)C(NO_2)(Cl) \longrightarrow$$

$$(\text{cyclo-}C_3H_5)(Me)C(NO_2) - C(NO_2)(Me)(\text{cyclo-}C_3H_5) \qquad (15)$$

intermolecular electron transfer between the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane and the anion of 2-nitropropane could result with similar intermediates as shown in the combined form of Eqs. 12 and 13 (Eq. 16). The two products formed in Eq. 16 can

$$(\text{cyclo-}C_3H_5)(Me)\dot{C}NO_2 + Me_2C{=}NO_2^- \xrightarrow{\text{E.T.}} (\text{cyclo-}C_3H_5)(Me)C{=}NO_2^- + Me_2\dot{C}NO_2 \qquad (16)$$

undergo reactions similar to Eqs. 14 and 15 to yield the dimers.

The dimer of 1-chloro-1-cyclopropyl-1-nitroethane can also be formed by coupling of two radicals in a nonchain reaction (Eq. 17).

$$2(\text{cyclo-}C_3H_5)(Me)\dot{C}NO_2 \longrightarrow$$

$$(\text{cyclo-}C_3H_5)(Me)C(NO_2)C(NO_2)(Me)(\text{cyclo-}C_3H_5) \qquad (17)$$

Another possible interpretation for the formation of dimers is chlorine atom transfer which could result from nucleophilic attack on chlorine (Eq. 18). Several papers in the literature support this

$$(\text{cyclo-}C_3H_5)(Me)C(NO_2)(Cl) + (Me)_2C{=}NO_2^- \longrightarrow$$
$$(\text{cyclo-}C_3H_5)(Me)C{=}NO_2^- + Me_2C(NO_2)(Cl) \qquad (18)$$

contention since chloroketones have been isolated and identified from reactions involving various enolate anions with 2-chloro-2-nitropropane [58]. Support for an ionic mechanism comes from experiments where chloroketones are formed in the presence or absence of radical chain inhibitors [59].

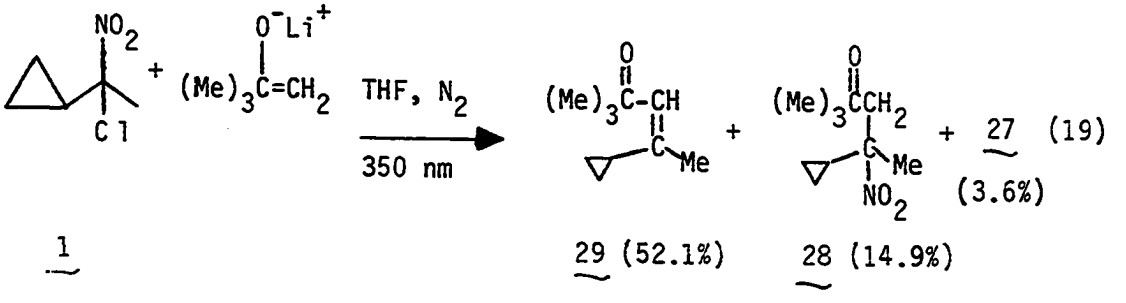
Although it is difficult to ascertain which of the possible competing dimerization reactions are important, it is possible to maximize the yield of cross-coupled product (2-cyclopropyl-3-methyl-2,3-dinitrobutane 26) by selecting a loose ion-pair and a polar solvent. In fact, all of the possible reactions yielding dimers may be operative to some extent, depending on the steric considerations.

11. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the enolate of pinacolone

A variety of mono-enolate anions have been condensed with 2-chloro-2-nitropropane by the $S_{RN}1$ process to yield products of a controlled crossed aldol condensation. The conversion of a primary or secondary enolate anion into the α-alkylidene ketone, the β-nitroketone, and enolate dimer by the $S_{RN}1$ process appears to be a good synthetic transformation. However, the ratio of cross-coupled products to oxidative dimers

appears to depend upon a number of variables including the counterion, the solvent, the leaving group, and the structure of the enolate anion [20]. Since a variety of products are formed when primary or secondary enolates are allowed to react with 2-chloro-2-nitroethane, it seemed worthwhile to investigate 1-chloro-1-cyclopropyl-1-nitroethane further.

Treatment of pinacolone with lithium diisopropylamide in THF, followed by addition of 1-chloro-1-cyclopropyl-1-nitroethane, yielded several products after subsequent irradiation using a Rayonet photoreactor (350 nm). After an aqueous work-up, the crude isolate was shown to contain 5-cyclopropyl-2,2-dimethyl-5-nitro-3-hexenone 28 (14.9%) and a mixture of E,Z-5-cyclopropyl-2,2-dimethyl-4-hexen-3-one 29 (52.1%) and unreacted 1-chloro-1-cyclopropyl-1-nitroethane (26.7%). Also present in the isolate was a small amount of 2,3-dicyclopropyl-2,3-dinitrobutane 27.



1 29 (52.1%) 28 (14.9%)

The two isomers of 5-cyclopropyl-2,2-dimethyl-4-hexen-3-one are probably formed by E2 elination of 5-cyclopropyl-2,2-dimethyl-5-nitro-3-hexanone. The ratio of β-nitroketone to α-alkylidene ketone depends upon the reaction and isolation conditions. In a scaled-up reaction employing

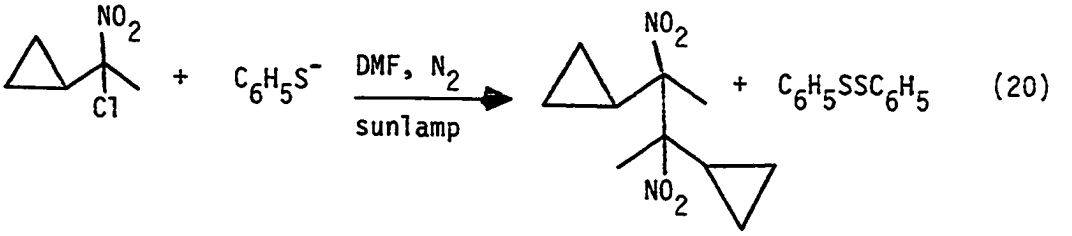
equivalents of pinacolone enolate with one equivalent of 1-chloro-1-cyclopropyl-1-nitroethane, a reasonable yield of 5-cyclopropyl-2,2-dimethyl-4-hexen-3-one (55.7%) was obtained. Analyses of both reaction mixtures failed to indicate the presence of any products not containing a cyclopropyl ring. This result agrees with previous experiments which seem to indicate the 1-chloro-1-cyclopropyl-1-nitroethane does not undergo any appreciable rearrangement or the rearrangement is reversible and the α-nitro radical stability is a controlling feature.

It has been reported previously that secondary and tertiary enolates give rise to appreciable amounts of enolate dimers when reacted with 2-chloro-2-nitropropane [60]. The literature suggests that the formation of oxidative dimers with secondary enolates reflects the increased ease of one-electron oxidation of the secondary enolate anions. When the enolate of propiophenone was treated with 1-chloro-1-cyclopropyl-1-nitroethane under similar reaction conditions, as previously described for pinacolone enolate, the oxidative dimer of propiophenone (2,3-dimethyl-1,4-diphenyl-1,4-butanedione) was formed along with other predicted cross-coupled products. G.C.M.S. and ^{1}H N.M.R. analyses of the crude isolate verified the formation of 2,3-dimethyl-1,4-diphenyl-1,4-butanedione existing as a mixture of diastereomers. Although no products were isolated, the formation of oxidative dimers from a secondary enolate anion with 1-chloro-1-cyclopropyl-1-nitroethane appears consistent with literature reports. ^{1}H N.M.R. failed to reveal the presence of any vinyl protons in the crude isolate which corresponds favorably with previous results. The lack of vinyl protons indicates

the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane did not rearrange to an appreciable extent.

12. Reaction of benzenethiolate with 1-chloro-1-cyclopropyl-1-nitroethane

Benzenethiolate (generated from benzenethiol and potassium t-butoxide) reacts with 1-chloro-1-cyclopropyl-1-nitroethane in DMF to produce phenyl disulfide 30 and 2,3-dicyclopropyl-2,3-dinitrobutane 27 with similar yields (Eq. 20). No evidence for the formation of α-nitrosuliphide was found in the reaction mixture. There is evidence that thiolates undergo substitution reactions with 2-substituted-2-nitropropane by the $S_{RN}1$ process [19,61] or are oxidized to disulphides by an ionic mechanism [62]. Recent reports suggest that there are several possible pathways leading to α-nitrosuliphides or disulphides, depending upon the nature of the α-substituted nitro compounds and the thiolate.



1 27 (11%) 30 (10.4%)

Russell, Jawdosiuk and Makosza have proposed a radical mechanism (Scheme 4) to account for the oxidative dimerization of benzenethiolate anion [63].

Scheme 4

$$Me_2C(X)NO_2 + RS^- \longrightarrow [Me_2C(X)NO_2]^{\cdot -} + RS\cdot$$

$$[Me_2C(X)NO_2]^{\cdot -} \longrightarrow Me_2\dot{C}NO_2 + X^-$$

$$Me_2\dot{C}NO_2 + RS^- \longrightarrow Me_2C{=}NO_2^- + RS\cdot$$

$$2RS\cdot \longrightarrow RSSR$$

13. Reactions of tri-n-butyltin hydride with 1-chloro-cyclopropyl-1-nitroethane

It is generally accepted that reduction of simple halides with organotin hydrides proceeds by a free-radical chain mechanism [64], shown below in Scheme 5. Evidence that the intermediate is a free-

Scheme 5

$$SnH + Q\cdot \longrightarrow Sn\cdot + QH$$

$$Sn\cdot + RX \longrightarrow R\cdot + SnX$$

$$R\cdot + SnH \longrightarrow RH + Sn\cdot$$

radical follows from catalysis (azobisisobutyronitrile and light) and retardation (hydroquinone) studies.

Since various nucleophiles react with 1-chloro-1-cyclopropyl-1-nitroethane without intramolecular rearrangement taking place, several possibilities exist which could explain the previous reported results. First, the substitutions are proceeding by a S_N2 mechanism instead of the $S_{RN}1$ process. Second, the presence of a nitro group on the intermediate α-nitro radical stabilizes the aliphatic radical sufficiently to prevent the competing unimolecular rearrangement from occurring.

Third, the unimolecular rearrangement is reversible and product stability is a controlling factor. The generation of the α-nitro radical from 1-chloro-1-cyclopropyl-1-nitroethane by an alternative method with tri-n-butyltin hydride should elucidate the stability of the intermediate α-nitro radical or verify the interpretation that substitutions occur through a S_N2 process. The desired information can be obtained provided the chloro substituent is reduced preferentially over the nitro substituent when reducing α-chloro-α-nitroalkanes.

A competitive reduction pathway is a definite problem due to recent reports concerning the reduction of tertiary nitro groups with trialkyltin hydride. Tanner, Blackburn, and Diaz [65] have reported the reduction (trialkyltin hydride) of tertiary nitro groups involves an electron transfer chain mechanism as shown below (Scheme 6). The reduction of a tertiary nitro group by the anion of methanethiol has been proposed to proceed via a similar mechanism as described above [66].

Scheme 6

$$R_3CNO_2 + R'_3Sn\cdot \longrightarrow R_3CNO_2^{\cdot-} + R'_3Sn^{+}$$

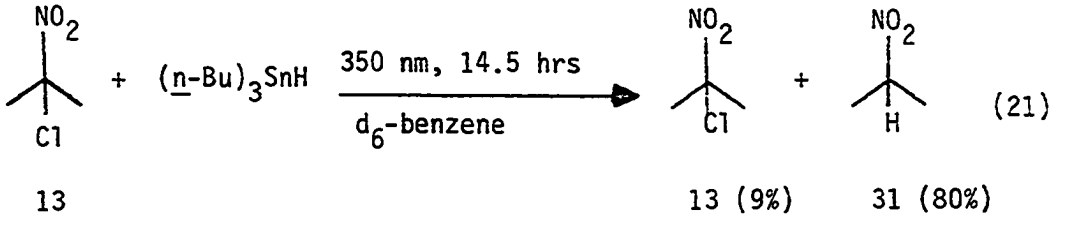
$$R_3CNO_2^{\cdot-} \longrightarrow R_3C\cdot + NO_2^{-}$$

$$R_3C\cdot + R'_3SnH \longrightarrow R_3CH + R'_3Sn\cdot$$

Which of the two mechanisms (Scheme 5 or 6) will prevail in a competitive sense depends upon the ability of the stannyl radical to act as an electron transfer agent and the capability of the electrophilic groups to participate in one-electron transfers [67]. Although the two

mechanisms are quite different, the end result should show reduction of the halide preferentially over the nitro substituent since the radical anion formed in Scheme 6 should dissociate to an intermediate α-nitro radical which is similar to the intermediate radical in Scheme 5. The loss of halide over nitrite is well-documented by the work of Russell and Kornblum involving radical anions.

A benzene-d_6 solution (degassed with nitrogen) containing 2-chloro-2-nitropropane and tri-n-butyltin hydride was irradiated (350 nm) for 14.5 hours. G.C. and ^{1}H N.M.R. analyses of the reaction mixture revealed the solution contained 2-nitropropane 31 and 2-nitro-2-chloropropane 13 as the only volatile products (Eq. 21). No tri-n-butyltin hydride remained as indicated by the absence of a signal from the proton attached to the tin atom in the region around 4-5 ppm. Periodic observation of

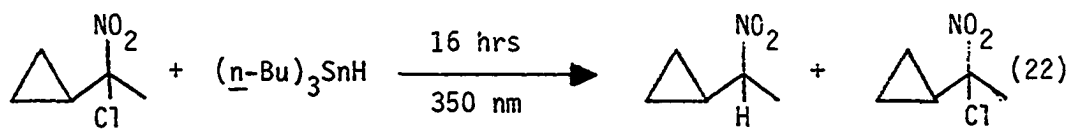


13 13 (9%) 31 (80%)

similar experiments also failed to reveal the presence of 2-chloropropane. The discrepancy between reactants consumed and products formed can be explained by chain terminating reactions or the subsequent reduction of secondary 2-nitropropane. The formation of tri-n-butyltin chloride was verified by the precipitation of fluoride salts [68]

which were removed by filtration. A similar experiment using 1-chloro-1-nitrocyclohexane also showed preferential reduction of the chloro substituent since ^1H N.M.R. analysis failed to reveal the presence of 1-chlorocyclohexane in the reaction mixture.

Since the reduction of α-chloro-α-nitroalkanes with tri-n-butyltin hydride appears to preferentially form intermediate α-nitro radicals over α-chloro radicals, the reaction of 1-chloro-1-cyclopropyl-1-nitroethane with tri-n-butyltin hydride should elucidate the stability of intermediate α-nitro radicals. Tri-n-butyltin hydride reacts with 1-chloro-1-cyclopropyl-1-nitroethane 1 to form 1-cyclopropyl-1-nitroethane 32 as the only observable product when light (350 nm) is used to initiate the homolytic cleavage of the organotin-hydride bond (Eq. 22). Authentic samples of 1-cyclopropyl-1-nitroethane prepared by reductive chlorination [26] of 1-chloro-1-cyclopropyl-1-nitroethane verified the presence of the product. Analysis of the reaction mixture failed to indicate the formation of any products containing vinyl protons.



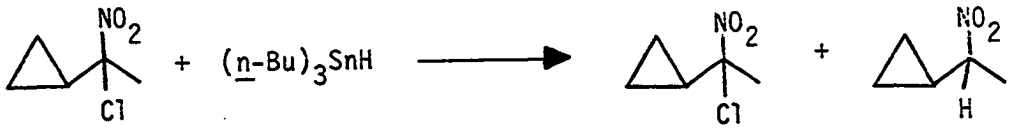
1 32 (46%) 1 (23%)

In an attempt to determine if the subsequent reduction of 1-cyclopropyl-1-nitroethane is a viable alternative for the poor observed mass balance, a similar experiment was performed with five equivalents of tri-n-butyltin hydride. Monitoring the reaction mixture confirmed that 1-cyclopropyl-1-nitroethane was formed and subsequently consumed under the reaction conditions as shown in Table 7. The reduction of 1-cyclopropyl-1-nitroethane would form an unstabilized alkyl radical which could undergo intramolecular rearrangement to form 2-pentene. Unfortunately, ethylcyclopropane or 2-pentene were not identified by G.C. or ^{1}H N.M.R. analyses. The formation of the carbon-carbon double bond of 2-pentene may have been overlooked since hydrostannation also proceeds by a free-radical mechanism [69]. The resulting tetraalkyltin compound would not be distinquishable by either G.C. or ^{1}H N.M.R. analyses if formed. Reactions employing five equivalents of tri-n-butyltin hydride with 1-chloro-1-cyclopropyl-1-nitroethane and using 10% azobisisobutyronitrile or 10% phenylazotriphenylmethane as initiators yielded similar results (see Table 7).

Assuming that the mechanism shown in Scheme 5 is correct, the relative ease with which an organotin radical abstracts a halogen atom can be determined. This can be done by placing a halide in competition with another halide for an insufficient quantity of hydride. Several competition reactions were performed involving 1-chloro-1-cyclopropyl-1-nitroethane.

A benzene-d_6 solution (deoxygenated with nitrogen) containing 2-chloro-2-nitropropane and 1-chloro-1-cyclopropyl-1-nitroethane and

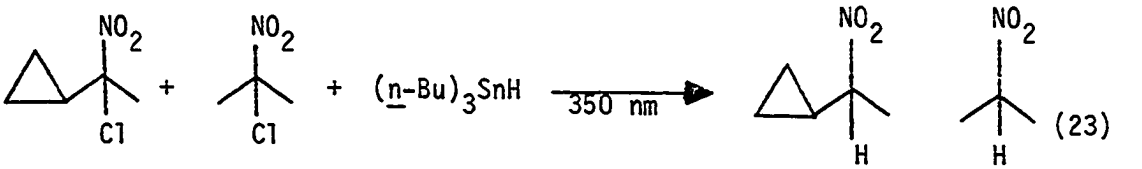
Table 7. Reactions of 1-chloro-1-cyclopropyl-1-nitroethane with five equivalents of tri-n-butyltin hydride



A B

Initiator	Time (hrs)	% A (G.C.)	% B (G.C.)
hv (350 nm)	16	21.4	43.1
hv (350 nm)	18	14.0	51.1
hv (350 nm)	20	9.3	53.7
hv (350 nm)	22	7.4	46.0
hv (350 nm)	24	7.0	41.0
AIBN (60°C)	24	34.8	38.3
PAT (60°C)	24	37.2	19.6

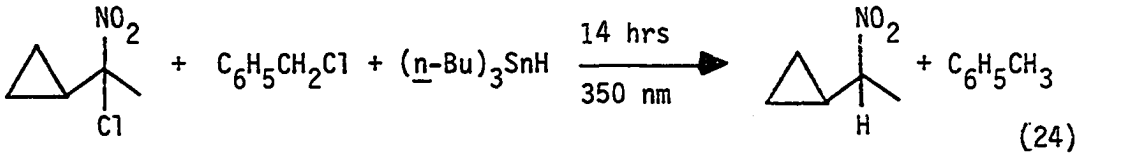
tri-n-butyltin hydride was irradiated (350 nm) for 15 hours. G.C. and ^{1}H N.M.R. analyses of the reaction mixture revealed the solution contained 2-nitropropane 31 (41.8%), 1-cyclopropyl-1-nitroethane 32 (17.4%), and unreacted tri-n-butyltin hydride (22.5%) (Eq. 23). Due to



1 13 32 (17.4%) 31 (41.8%)

the inability to effectively account for all of the starting materials, the possibility of the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane participating in an unimolecular rearrangement cannot be excluded. Assuming that the two α-nitro radicals formed from the α-chloro-α-nitroalkanes undergo further reduction with a similar rate, it appears 2-chloro-2-nitropropane is reduced faster than 1-chloro-1-cyclopropyl-1-nitroethane with tri-n-butyltin hydride.

In a similar reaction, equal molar quantities of 1-chloro-1-cyclopropyl-1-nitroethane 1 and benzyl chloride 33 were irradiated in the presence of tri-n-butyltin hydride for 14 hours. Careful analysis of the reaction mixture revealed it contained toluene 34 (34.8%) and 1-cyclopropyl-1-nitroethane 32 (15.3%) (Eq. 24). Approximately equal amounts of 1 and 33 were consumed in the reaction. The result seems to indicate that the halogen abstraction by tri-alkyltin radicals proceeds

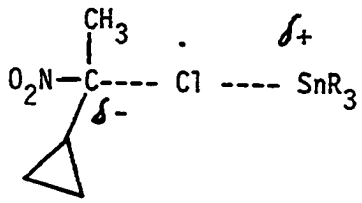


(24)

1 33 32 (15.3%) 34 (34.8%)

with approximately equal rates for the two starting substrates. This is a somewhat surprising result since benzyl halides have been reported to be considerably more reactive than alkyl halides towards halogen abstraction reactions in numerous reports in the literature.

Perhaps, these results can be rationalized if one considers the organotin radical to be an electron donor and that the polar factor plays a role in stabilizing the transition state as shown in the following diagram. The reduction of alkyl and aryl halides by trialkyltin hydrides

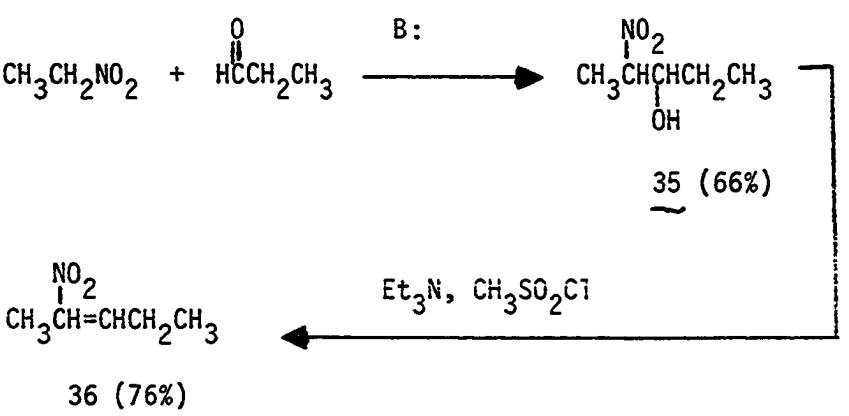


has been more thoroughly studied than any other halogen abstraction reaction [70]. The results obtained follow a trend expected if one assumes that the strength of the carbon-halogen bond being broken and the

stability of the resulting carbon radical are important factors for the reaction in question. The results obtained by the competition studies between benzyl chloride and 1-chloro-1-cyclopropyl-1-nitroethane can be rationalized as showing the α-nitro radical having unpredicted stability since a carbon-chlorine bond was broken from each substrate. Perhaps, the unpredicted stability of the α-nitro radical can best be explained by the concept of radical stabilization by capto-dative substituent effects. This concept will be further discussed later in this section.

In an attempt to clarify how fast 2-nitro-2-pentene would be consumed by a competing hydrostannation reaction, several experiments were performed. 2-Nitro-2-pentene was synthesized according to the following route (Scheme 7). The first step involves the addition of the nitronate of nitroethane to propionaldehyde, called the Henry of nitro-aldol reaction [71]. This is a classical method for carbon-carbon bond

Scheme 7



formation and the procedure is normally carried out in the presence of only catalytic quantities of base due to the ease of its reversibility. The product (2-nitro-3-pentanol 35) was dehydrated to 2-nitro-2-pentene 36 according to a mild method previously reported in the literature [72] with a suitable yield (76%).

A solution containing 2-nitro-2-pentene and tri-n-butyltin hydride was irradiated in a Rayonet photoreactor (350 nm) for 6 hours. After irradiation was completed, ^{1}H N.M.R. analysis failed to reveal the presence of any remaining tri-n-butyltin hydride or 2-nitro-2-pentene (absence of vinyl protons). Although no products were isolated or characterized, the hydrostannation of 2-nitro-2-pentene was perceived as occurring as shown in the following Eq. 25 due to the lack of characteristic protons alpha to the nitro group.

$$CH_3CH_2CH{=}C(NO_2)CH_3 + (n\text{-}Bu)_3SnH \longrightarrow CH_3CH_2CH_2\text{-}\underset{\displaystyle Sn(n\text{-}Bu)_3}{\overset{\displaystyle NO_2}{\overset{|}{\underset{|}{C}}}}\text{-}CH_3 \quad (25)$$

In an effort to determine the approximate rate of hydrostannation compared to the reduction of α-chloro-α-nitroalkanes, a reaction mixture containing 1-chloro-1-cyclopropyl-1-nitroethane 1, 2-nitro-2-pentene 36, and tri-n-butyltin hydride was irradiated (350 nm) for 6 hours. After irradiation was completed, ^{1}H N.M.R. revealed that all of the tri-n-butyltin hydride had been consumed. Careful G.C. and ^{1}H N.M.R. analyses of the reaction mixture indicated the solution contained unreacted

1-chloro-1-cyclopropyl-1-nitroethane 1 (88%), unreacted 2-nitro-2-pentene 36 (7%), and 1-cyclopropyl-1-nitroethane 32 (6.1%).

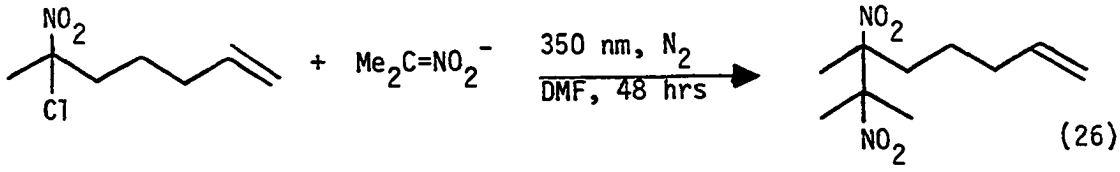
Although the 2-nitro-2-pentene may undergo polymerization once addition occurs to the carbon-carbon bond, it seems reasonable to assume that the tri-aklyltin radical is more reactive towards the double bond of 2-nitro-2-pentene than towards halogen abstraction from 1-chloro-1-cyclopropyl-1-nitroethane. With these results, it is difficult to exclude the possibility that the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane undergoes intramolecular rearrangement because of the poor observed mass balance. Although the generation of α-nitro radicals by the $S_{RN}1$ process with various nucleophiles failed to indicate the formation of any ring-opened products, it seems unlikely to this author that the α-nitro radical intermediate formed by halogen abstraction would participate in the unimolecular rearrangement. The poor mass balance can best be explained by reduction of 1-cyclopropyl-1-nitroethane and subsequent rearrangement of the unstabilized alkyl radical followed by rapid hydrostannation of 2-pentene.

14. Reaction of 2-chloro-2-nitro-6-heptene with the lithium salt of 2-nitropropane

The results from the previous experiments with 1-chloro-1-cyclopropyl-1-nitroethane and various nucleophiles seem to indicate that the α-nitro radical does not undergo any appreciable rearrangement or the rearrangement is reversible and the α-nitro radical stability is a controlling feature. A more complete discussion concerning the stability of α-nitro radicals will be addressed later in this section.

Since the cyclopropyl carbinyl radical unimolecular rearrangement is significantly faster than the 5-hexenyl rearrangement and the factors controlling the α-nitro radical's stability are similar, one could rationalize that the α-nitro radical derived from 2-chloro-2-nitro-6-heptene will not undergo any appreciable cyclization before being trapped by various nucleophiles.

The lithium salt of 2-nitropropane 24 reacts with 2-chloro-2-nitro-6-heptene 2 to produce only one cross-coupled product (2,3-dimethyl-2,3-dinitro-7-octene 37 (Eq. 26). G.C.M.S. and ^{1}H N.M.R. failed to



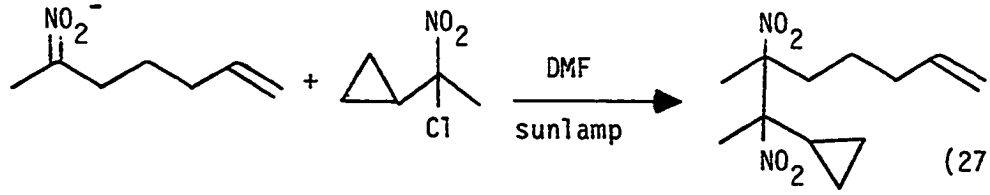
(26)

2 24 37 (63%)

indicate the formation of cross-coupled products containing 5- or 6-membered rings. The crude isolate was purified by flash chromatography to yield 2,3-dimethyl-2,3-dinitro-7-octene 37 (63.1%). The formation of 2,3-dimethyl-2,3-dinitro-7-octene was accompanied with a slight amount of 2,3-dimethyl-2,3-dinitrobutane which is consistent with previous reported experiments.

15. Preparation of 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene

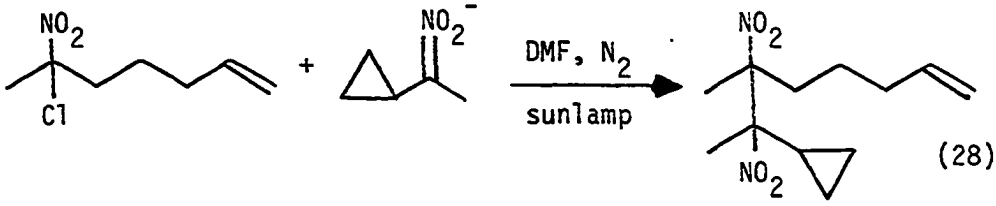
The potassium salt of 2-nitro-6-heptene reacts with 1-chloro-1-cyclopropyl-1-nitroethane to yield 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene 38 (56.4%) as the only cross-coupled product formed in the reaction. Although only one cross-coupled product was formed, several dimers resulting from a variety of possible pathways were also formed. The formation of 6,7-dimethyl-6,7-dinitrododeca-1,11-diene 39 agrees with previous results. The isolated 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene consisted of a mixture of the two diastereomers (52:48).



(27)

1 38 (56.4%)

The potassium salt of 1-cyclopropyl-1-nitroethane (generated by the action of potassium-t-butoxide on 1-cyclopropyl-1-nitroethane) reacts with 2-chloro-2-nitro-6-heptene to yield 60.8% of 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene 38 (Eq. 28) existing as the two diastereomers (51:49). Quantitative G.C. analysis of the crude isolate revealed it contained 2-chloro-2-nitro-6-heptene (10.9%), 2,3-dicyclopropyl-2,3-dinitrobutane (28%), 6,7-dimethyl-6,7-dinitrododeca-1,11-diene (2%), and desired 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene (61%). The

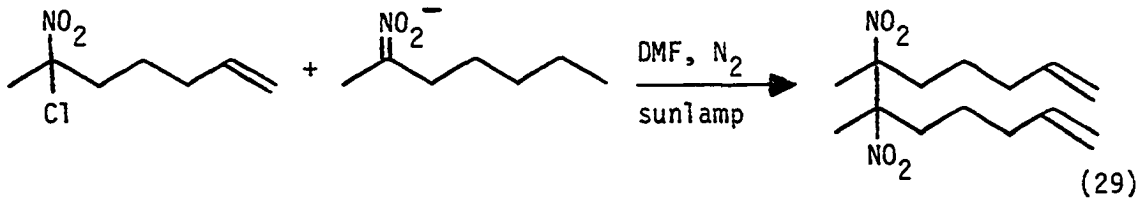


2 38 (60.8%)

formation of dimers and the lack of a noticeable amount of rearranged products is consistent with expected results based upon previously discussed experiments. It is interesting to note that the two experiments employed for the preparation of 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene gave approximately the same ratio of diastereomers.

16. Reaction of 2-chloro-2-nitro-6-heptene with the potassium salt of 2-nitro-6-heptene

The anion of 2-nitro-6-heptene (generated from potassium-t-butoxide and 2-nitro-6-heptene in DMF) reacts with 2-chloro-2-nitro-6-heptene to produce exclusively 6,7-dimethyl-6,7-dinitrododeca-1,11-diene 39 after sunlamp irradiation. After an aqueous workup, G.C.M.S. and ^{1}H N.M.R. analyses of the crude isolate verified that no detectable amount of cyclization of the α-nitro radical had occurred. If cyclization had occurred, several novel compounds containing an open alkyl chain and a cyclized alkyl chain would have resulted. After purification of the crude isolate, the 6,7-dimethyl-6,7-dinitrododeca-1,11-diene (72.1%) existed as a mixture of two diastereomers (72:28).



(29)

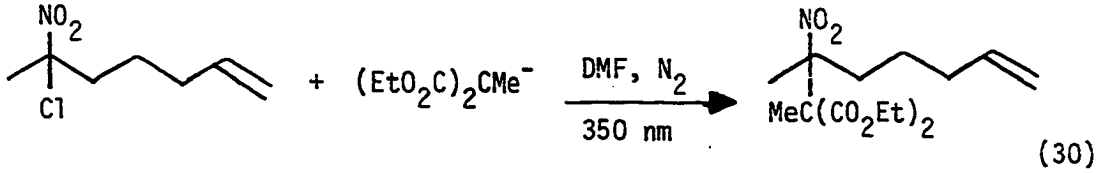
2 39 (72.1%)

The formation of two diastereomers and the noticeable absence of ring products is completely consistent with expected results. All of the reactions of various nitronate anions with 2-chloro-2-nitro-6-heptene failed to indicate the formation of cyclized products. This supports the contention that the α-nitro radical derived from 2-chloro-2-nitro-6-heptene does not undergo intramolecular cyclization due to the stability of the intermediate α-nitro radical.

17. Reaction of 2-chloro-2-nitro-6-heptene with the anion of diethyl methylmalonate

The enolate derived from diethyl methylmalonate 14 (generated with sodium hydride in DMF) reacts with 2-chloro-2-nitro-6-heptene to produce exclusively 2-(diethyl methylmalonate)-2-nitro-6-heptene 40 (Eq. 30). A satisfactory yield of 2-(diethyl methylmalonate)-2-nitro-6-heptene was isolated after irradation for 48 hours using a Rayonet photoreactor (350 nm) under a nitrogen atmosphere. G.C. and G.C.M.S. analyses of the crude isolate verified the presence of only one cross-coupled product. The formation of a substituted open alkyl chain product is consistent

with the known relative reactivity of the anion of diethyl methylmalonate and the apparent stability of the derived α-nitro radical.



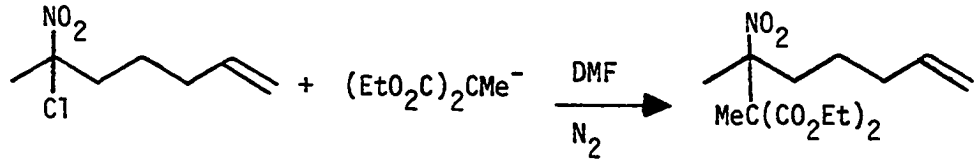
(30)

2 14 40 (62%)

Light is necessary for the efficient formation of 2-(diethyl methylmalonate)-2-nitro-6-heptene 40 from the anion of diethyl methylmalonate and 2-chloro-2-nitro-6-heptene. Reactions run in aluminum foil-wrapped flasks to exclude light and immersed in an oil-bath (35°C) to simulate the temperature inside the Rayonet photoreactor formed 2-(diethyl methylmalonate)-2-nitro-6-heptene in only a 4% yield as determined by G.C. analysis.

In a reaction employing 10% di-t-butyl nitroxide with 2-chloro-2-nitro-6-heptene and the anion of diethyl methylmalonate, a reduced yield of 2-(diethyl methylmalonate)-2-nitro-6-heptene was observed (see Table 8). The slightly diminished yield can be attributed to the long reaction time involved after the nitroxide was consumed. The formation of 2-(diethyl methylmalonate)-2-nitro-6-heptene appears to involve the photostimulated $S_{RN}1$ process due to the effect of light and 10% di-t-butyl nitroxide.

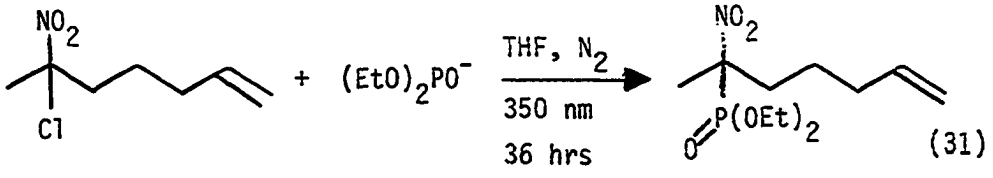
Table 8. Characteristics of the reaction between 2-chloro-2-nitro-6-heptene with the anion of diethyl methylmalonate



Time (hrs)	Conditions	% Yield
48	N_2, 350 nm	62 (isolated)
48	N_2, dark, 35°C	4 (G.C.)
48	N_2, 350 nm, 10% di-t-butyl nitroxide	56 (G.C.)

18. The reaction of diethyl phosphite anion with 2-chloro-2-nitro-6-heptene

Since diethyl phosphite anion reacts with 1-chloro-1-cyclopropyl-1-nitroethane without intramolecular rearrangement and the rearrangement of α-nitro radical derived from 2-chloro-2-nitro-6-heptene is perhaps even slower, it is apparent that the diethyl phosphite anion will react with 2-chloro-2-nitro-6-heptene without an appreciable amount of cyclization occurring. Indeed, the anion generated from diethyl phosphite and potassium t-butoxide reacts with 2-chloro-2-nitro-6-heptene to produce exclusively 2-nitro-2-(diethoxy phosphinyl)-6-heptene 41 (Eq. 31). The cross-coupled product was isolated with a reasonable yield of 49% since 2-nitro-2-(diethoxy phosphinyl)-6-heptene is somewhat water soluble and unreacted 2-chloro-2-nitro-6-heptene (35%) was isolated.



(31)

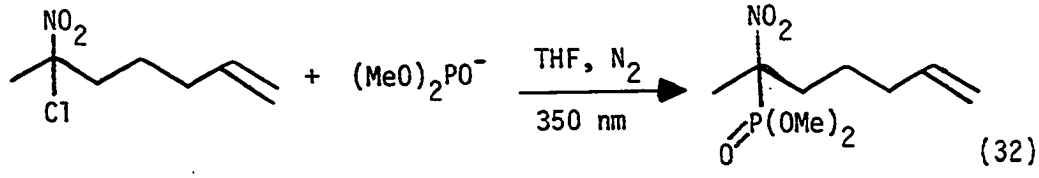
2 18 41 (49%)

Although the formation of α-nitroalkyl phosphonates has been reportedly initiated by an extremely facile thermal initiation process, a similar reaction was performed without irradiation. A reaction mixture wrapped in aluminum foil and containing 2-chloro-2-nitro-6-heptene with the anion of diethyl phosphite in THF was heated (36°C) for 36 hours.

After an aqueous work-up, only 13.5% of 2-nitro-2-(diethyl phosphinyl)-6-heptene was formed. Discounting the loss of product due to the solubility of 2-nitro-2-(diethyl phosphinyl)-6-heptene, it appears not all α-nitroalkyl phosphonates have an efficient thermal initiation process.

19. The reaction of dimethyl phosphite anion with 2-chloro-2-nitro-6-heptene

The potassium salt of dimethyl phosphite was found to react with 2-chloro-2-nitro-6-heptene in THF to yield 2-nitro-2(dimethoxy phosphinyl)-6-heptene 42 (Eq. 32). G.C. analysis of the crude isolate failed to reveal the presence of any dimers and only one crossed-coupled product was formed.



(32)

2 20 42 (63%)

The formation 2-nitro-2-(dimethoxy phosphinyl)-6-heptene as the only observable reaction product is consistent with the formation of only one crossed-coupled product arising from the reaction of various dialkyl phosphite anions with 1-chloro-1-cyclopropyl-1-nitroethane. The formation of a straight chain α-nitroalkyl phosphonate is also consistent with the prediction that the anions of dialkyl phosphites would react with

2-chloro-2-nitro-6-heptene without a detectable amount of cyclization occurring.

20. Reaction of tri-n-butyltin hydride with 2-chloro-2-nitro-6-heptene

Although hydrostannation of 2-chloro-2-nitro-6-heptene may effectively prohibit the formation of 2-nitro-6-heptene with tri-n-butyltin hydride, a reaction involving the previously named substrates was performed. A solution of tri-n-butyltin hydride and 2-chloro-2-nitro-6-heptene in benzene-d_6 was irradiated for 12 hours in a Rayonet photoreactor (350 nm). G.C. and ^{1}H N.M.R. analyses of the reaction mixture revealed all of tri-n-butyltin hydride was completely consumed. The only observable reaction products detected by G.C. were 2-nitro-6-heptene (16.9%) and some unreacted 2-chloro-2-nitro-6-heptene. The identity of 2-nitro-6-heptene was verified by G.C. retention times and G.C.M.S. fragmentation when compared to an authentic sample of 2-nitro-6-heptene.

The low yield of product can be attributed to a competing hydrostannation of the carbon-carbon double bonds of 2-chloro-2-nitro-6-heptene and 2-nitro-6-heptene. The addition of tri-alkyltin hydride to the double bonds makes G.C. analysis of tetra-alkyltin compound impossible due to decomposition and long retention times. The lack of cyclized products appears to favorably agree with previous experiments using 1-chloro-1-cyclopropyl-1-nitroethane and 2-chloro-2-nitro-6-heptene.

The lack of evidence for the rearrangement of the two free-radical probes seems to indicate several flaws in the initial assumptions made concerning the feasibility of determining the rate of propagation Step 3 (Scheme 1) and the assumptions made in an attempt to determine the efficiency of various nucleophiles at trapping α-nitro radicals. A complete discussion of the stability of α-nitro radicals is addressed in the next section.

21. Considerations for the apparent stability of α-nitro radicals

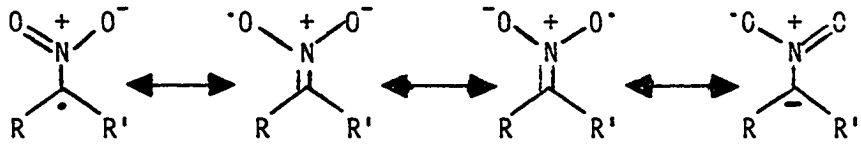
It is apparent from previous experiments that the α-nitro radicals derived from 1-chloro-1-cyclopropyl-1-nitroethane 1 and 2-chloro-2-nitro-6-heptene 2 did not undergo unimolecular rearrangements to any appreciable extent. The failure of the two free-radical clocks to participate in the competing unimolecular rearrangements severely limited the amount of relevant information obtained. Due to the absence of rearranged products, the approximate rate of propagation Step 3 (Scheme 1) and the relative efficiency of various nucleophiles at trapping radicals were not determined. Using hindsight, a more thorough discussion of the original assumptions and generalizations pertaining to the treatment of data should be addressed.

An original assumption pertaining to the irreversibility of cyclizations appears questionable because of several literature reports. The original assumption of irreversibility was based upon the results of studies concerning the cyclization of 5-hexenyl radicals. All previous studies support the contention that cyclization of the 5-hexenyl radical is irreversible [73].

However, when the 5-hexenyl acyclic radical is stabilized by electron accepting groups such as cyano and carboethoxy, irreversibility has been demonstrated [74]. Under such conditions, product stability then becomes a controlling feature. Because in cases where closure to five- and six-membered ring radicals can occur, the kinetic preference is for the former, while the thermodynamic preference is for the latter. As the cyclizations change from irreversible (unstabilized acyclic radical) to reversible (stabilized acyclic radical), the control passes from kinetic to thermodynamic as the proportion of the stabler six-membered ring product increases. It appears that substitution of an electron accepting nitro group on the acyclic radical may also effect the irreversibility of the cyclization.

Several resonance stabilized structures of α-nitro radicals can be drawn to help rationalize the apparent stability, as shown in Scheme 8.

Scheme 8



A B C D

Resonance structure D does little to help stabilize the α-nitro radical since the negative charge is located on the more electropositive atom (carbon). Thus, apparently, structures A, B, and C are important for

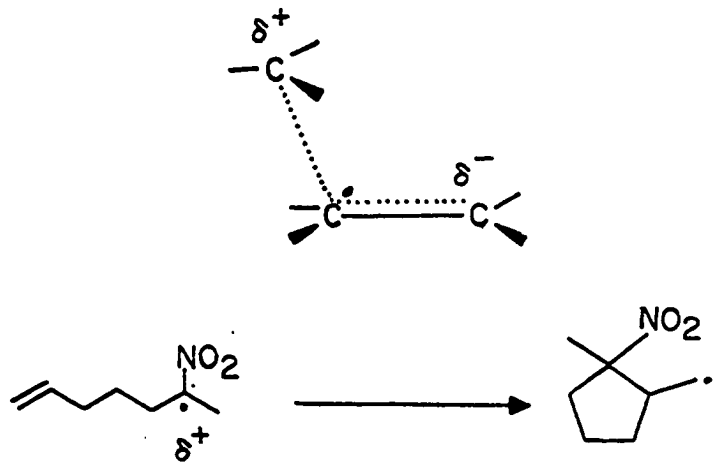
the resonance stabilization of α-nitro radicals. However, ESR studies indicate the nitro group has relatively little effect on stabilizing radicals because the spin density remains predominately on carbon [75].

Another concept capable of explaining the stability of α-nitro radicals derived from 1-chloro-1-cyclopropyl-1-nitroethane and 2-chloro-2-nitro-6-heptene is the concept of radical stabilization by capto-dative substitution. Recently, several aspects of capto-dative substitution have been discussed [76,77]. It has been reported that the stabilization of a radical substituted with an electron donating and an electron withdrawing group has a greater stabilization than the sum of the substituent effects [78]. The α-nitro radicals investigated in this thesis have electron withdrawing and donating groups associated with the intermediate radicals. The extent of orbital interactions involved in the stabilization of α-nitro radicals will depend upon the relative magnitude of the interactions with the two substituents. Although the concept of radical stabilization by capto-dative substitution is still in its infancy, this concept may have influenced the inability of the α-nitro radicals derived from the two free-radical clocks to undergo rearrangement.

Another original assumption concerning the irreversible trapping of α-nitro radicals by various nucleophiles also appears questionable. First, the trapping of α-nitro radicals by various nucleophiles is essentially the reverse of propagation Step 2 (Scheme 1). Second, the reversibility of trapping α-nitro radicals with nitronate anions has

been suggested earlier as a possible explanation for the formation of dimers.

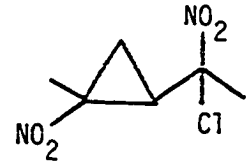
Initially, the cyclopropyl carbinyl radical derived from 1-chloro-1-cyclopropyl-1-nitroethane was predicted to undergo unimolecular rearrangement at a faster rate than the α-nitro radical formed from 2-chloro-2-nitro-6-heptene. This prediction was based upon the difference in room temperature-rearrangement rate constants of the unstabilized radicals. A number of theoretical treatments now support structure 43 as the transition state for homolytic addition to a carbon-carbon double bond [79,80]. The recent reports indicate that the dominant interaction for attack of an alkyl radical on a olefinic bond involves orthogonal overlap of the semioccupied 2p orbital with one lobe of the vacant pi-antibonding orbital. Consequently, the transition complex is dipolar: the incoming radical behaves as a nucleophile and assumes a fractional positive charge whereas the olefinic moiety becomes fractionally negative [81]. With a positive charge developing on the α-nitro radical derived from 2-chloro-2-nitro-6-heptene, it can be rationalized that cyclization is not favorable due to electronic influence of the nitro group at destablizing the transition state. A similar treatment would predict that the α-nitro radical derived from 1-chloro-1-cyclopropyl-1-nitroethane would undergo rapid ring opening due to the electronic influence of the transition state.



C. Conclusion

In this work, several interesting results were obtained. First, the free-radical clocks did not perform as was originally envisioned. The failure of the free-radical clocks to participate in the competing unimolecular rearrangements can be attributed to the stability of the α-nitro radicals. Second, the formation of dimers from competing side reactions can be minimized by the use of polar solvents and lose ion pairs.

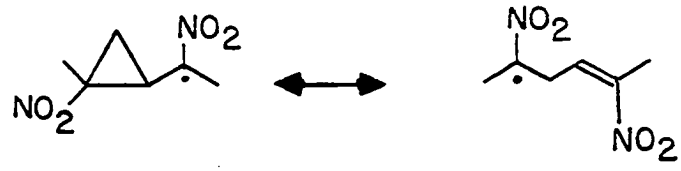
Several attempts at synthesizing 1-chloro-1-(2-methyl-2-nitrocyclopropyl)-1-nitroethane 44 were performed. The various routes had complications which prevented the total syntheses of compound 44.



44

1-Chloro-1-(2-methyl-2-nitrocyclopropyl)-1-nitroethane was a desirable compound to investigate, since the α-nitro radical derived from 44 could potentially open the cyclopropyl ring to yield an intermediate with similar stability (Scheme 9).

Scheme 9



If 1-chloro-1-(2-methyl-2-nitrocyclopropyl)-1-nitroethane could participate in the unimolecular rearrangement while 1-chloro-1-cyclopropyl-1-nitroethane did not undergo rearrangement, this would further support the contention that stabilization of the α-nitro radical is influenced by capto-dative effects.

Lastly, several attempts at synthesizing 5-chloro-2-nitro-2-pentene were also pursued without success. Reactions of 5-chloro-2-nitro-2-pentene with tri-n-butyltin hydride would have further supported the contention of stabilization of α-nitro radicals if cyclization had occurred, since the rate of cyclization is slower than the ring-opening reaction for unstabilized alkyl radicals.

D. Experimental Section

1. General considerations

Nitroethane, diethyl phosphite, dimethyl phosphite, tri-n-butyltin chloride, pinacolone, 2-methyl-1,3-cyclopentanedione, 2,3-dimethyl-2,3-dinitrobutane, propronaldehyde, tetrabutylammonium hydroxide,

N-benzyltrimethylammonium hydroxide, diethyl methylmalonate, and potassium t-butoxide were purchased from Aldrich. Benzenethiol, triethyl amine, and tetramethylammonium hydroxide were purchased from Eastman Organic. Sodium hydride, lithium t-butoxide, and n-butyllithium were purchased from Alfa Products.

Di-t-butyl nitroxide [82], diethyl thiophosphite [83], and the lithium salt of 2-nitropropane [84] were prepared by literature procedures.

Tri-n-butyltin hydride [85] was prepared by the addition of tri-n-butyltin chloride to a solution of lithium aluminum hydride in ice-cold ether. After 3 hours, the reaction mixture was hydrolyzed. The resulting organic layer was washed with water, dried ($MgSO_4$), and distilled (bp 68-74°C/0.3 mm).

2. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the anion of diethyl methylmalonate

1-Chloro-1-cyclopropyl-1-nitroethane (0.8618 g, 5.77 mmol) was syringed into an ice-cold solution of sodium hydride (0.1385 g, 5.77 mmol) and diethyl methylmalonate (1.005 g, 5.77 mmol) in 15 ml of dry DMF under a nitrogen atmosphere. The solution was allowed to warm to room temperature and then irradiated at 350 nm in a Rayonet photoreactor for 30 hours. After irradiation, the reaction mixture was poured into 30 ml of water and extracted (3 x 25 ml) with ether. The combined ether extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated to yield 1.43 g of organic residue. G.C.M.S. and ^1H N.M.R. analyses of the

crude isolate revealed that only one product was formed by the cross-coupling reaction and it did not contain any vinyl protons. The crude isolate was purified for analyses by Kugelrohr distillation (137°C/ 2.0 torr) to yield 1.27 g (77%) of pure 1-(cyclopropyl)-1-(diethyl methylmalonate)-1-nitroethane 15 as a colorless liquid.

^{1}H N.M.R. ($CDCl_3$) δ 4.38-4.10 (m, 4H, $-OCH_2CH_3$), 1.71 (s, 3H, $-C(NO_2)CH_3$), 1.31 (s, 3H, $COC(CH_3)CO$), 1.29 (t, 3H, $-OCH_2CH_3$, J = 7.08 Hz), 1.26 (t, 3H, $-OCH_2CH_3$, J = 7.08 Hz), 0.77-0.50 (m, 4H, $-CH_2CH_2-$).

I.R. (neat, NaCl plates, cm^{-1}) 2995 (m), 2950 (w), 1730 (vs), 1555 (vs), 1470 (m), 1455 (m), 1400 (m), 1370 (m), 1350 (m), 1270 (vs), 1230 (s), 1100 (s), 1020 (m), 915 (m), 860 (m), 840 (m), 730 (m).

M.S. (P-46 peak measured). Calculated for $C_{13}H_{21}O_4$: 241.14399. Measured: 241.14338. Error = -2.5 ppm.

Elemental Analysis: Calculated for $C_{13}H_{21}NO_6$: C, 54.37; H, 7.37; N, 4.88; O, 33.41. Found: C, 54.65; H, 7.54; N, 4.73.

3. Effect of light on the reaction of the anion of diethyl methylmalonate with 1-chloro-1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.2370 g, 1.58 mmol) was added by syringe to an ice-cold solution of sodium hydride (0.0381 g, 1.58 mmol) and diethyl methylmalonate (0.2765 g, 1.59 mmol) in 10 ml of dry DMF under nitrogen. The solution flask was wrapped tightly with several layers of aluminum foil to exclude light. After stirring for 30 hours (immersed in an oil bath 35°C), the reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate

showed that the isolate contained 0.032 g, (7%) of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15.

4. Effect of di-t-butyl nitroxide on the reaction of 1-chloro-cyclopropyl-1-nitroethane with the anion of diethyl methlymalonate

1-Chloro-1-cyclopropyl-1-nitroethane (0.3652 g, 2.44 mmol) was added to a solution of sodium hydride (0.0587 g, 2.44 mmol) and diethyl methylmalonate (0.4260 g, 2.44 mmol) and di-t-butyl nitroxide (0.035 g, 0.25 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated for 30 hours at 350 nm in a Rayonet photoreactor. The reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate showed that the residue contained 0.42 g (60%) of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane 15 and 0.106 g of unreacted 1-chloro-1-cyclopropyl-1-nitroethane 1.

5. Effect of light and di-t-butyl nitroxide on the formation of 1-cyclopropyl-1-(diethyl methylmalonate)-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.3130 g, 2.09 mmol) was syringed into an aluminum foil-wrapped flask that contained diethyl methylmalonate (0.3652 g, 2.09 mmol), sodium hydride (0.0503 g, 2.09 mmol), and di-t-butyl nitroxide (0.03 g, 0.21 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. After 30 hours of stirring at ambient temperature, the reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate showed that the residue contained no 1-cyclopropyl-1-(diethyl methylmalonate) 15 and only unreacted starting materials.

6. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the anion of 2-methyl-1,3-cyclopentanedione

1-Chloro-1-cyclopropyl-1-nitroethane (1.52 g, 10.4 mmol) was added by syringe into a dry DMSO solution (25 ml) containing potassium hydride (0.4178 g, 10.4 mmol) and 2-methyl-1,3-cyclopentanedione (1.1662 g, 10.4 mmol) under a nitrogen atmosphere. After 40 hours of irradiation (350 nm), the reaction mixture was poured into 35 ml of brine and extracted with ether (3 x 50 ml). The combined ether extract was washed (water and brine), dried ($MgSO_4$) and concentrated. ^1H N.M.R. and G.C. analyses of the crude isolate failed to indicate the presence of any cross-coupled product which contained vinyl hydrogens. The crude isolate was purified by flash chromatography using hexane:ethyl acetate (4:1) as eluent which afforded 1.4 g of crude product. Recrystallization of the crude product yielded 2-(1-cyclopropyl-1-nitroethane)-2-methyl-1,3-cyclopentanedione 17 (1.24 g, 52.8%, m.p. 79°C).

^1H N.M.R. ($CDCl_3$) δ 2.83 (s, 3H, -C(O)C($\underline{CH_3}$)C(O)), 1.36-1.2 (m, 1H), 1.18 (s, 3H, -C(NO_2)$\underline{CH_3}$), 0.78-0.3 (m, 4H, -$\underline{CH_2}$-$\underline{CH_2}$-). For a more complete description, see the appendix.

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 214.99, 213.04, 88.70, 54.82, 36.35, 34.66, 34.27, 23.08, 14.50, 4.88, 4.62.

I.R. (KBr pellet, cm^{-1}) 3000 (w), 2985 (w), 2965 (w), 2935 (w), 1740 (vs), 1545 (vs), 1450 (w), 1420 (2), 1390 (m), 1370 (w), 1290 (m), 1085 (m), 1060 (s), 1020 (m), 990 (m), 910 (w), 840 (w).

M.S. Calculated for $C_{11}H_{15}NO_4$: 225.10011. Measured: 225.09906. Error = -4.7 ppm.

7. Preparation of 1-cyclopropyl-1-nitro-1-(diethoxy phosphinyl) ethane by the reaction of diethyl phosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.55 g, 3.68 mmol) was added to an ice-cold solution of potassium t-butoxide (0.417 g, 3.71 mmol) and diethyl phosphite (0.513 g, 3.71 mmol) in 10 ml of dry THF under nitrogen. The solution was irradiated with a 275 Watt sunlamp for 48 hours after the ice-cold reaction mixture was allowed to warm to room temperature. The THF was vacuum evaporated and the residue was extracted from brine with ether. The combined ether solution was dried ($MgSO_4$) and evaporated. The resulting residue was shown to contain 1-cyclopropyl-1-nitro-1-(diethoxy phosphinyl) ethane 19 (72%) by ^1H N.M.R. The crude isolate was purified by Kugelrohr distillation (122°C/0.4 mm) to yield 0.59 g (64%) of pure colorless product 19.

^1H N.M.R. ($CDCl_3$) 4.33-4.1 (m, 4H, $-OCH_2-CH_3$), 1.8 (d, 3H, $-C(NO_2)(CH_3)$, J_{PH} = 14.5 Hz), 1.37 (t, 6H, $-OCH_2CH_3$, J_H = 7 Hz), 1.0-0.2 (m, 4H, $-CH_2-CH_2-$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 90.22 (d, $-C(NO_2)CH_3$, J_{PC} = 153.8 Hz), 64.22 (d, $-P(OCH_2CH_3)$, J_{PC} = 6.1 Hz), 63.9 (d, $-P(OCH_2CH_3)$, J_{PC} = 7.3 Hz), 16.44 (s, $-OCH_2CH_3$), 16.17 (s, $-OCH_2CH_3$), 14.95 (d, $-C(NO_2)CH_3$, J_{PC} = 10.37 Hz), 4.09 (s), 1.49 (s), 1.06 (s).

^{31}P N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from H_3PO_4) 17.46 (singlet).

I.R. (neat, NaCl plates, cm^{-1}) 2950 (m), 1545 (vs), 1460 (w), 1390 (m), 1370 (m), 1330 (m), 1260 (vs), 1160 (m), 1090 (m), 1030 (vs, broad), 970 (s, broad), 855 (m), 835 (m), 780 (m).

M.S. (P-46 peak measured). Calculated for $C_9H_{18}PO_3$: 205.09937. Measured: 205.09868. Error = -3.4 ppm.

Elemental Analysis. Calculated for $C_9H_{18}NO_5P$: C, 43.03; H, 7.22; N, 5.58; O, 31.84; P, 12.33. Found: C, 42.86; H, 7.31; N, 5.38; P, 12.50.

8. Preparation of 1-cyclopropyl-1-nitro-1-(dimethoxy phosphinyl) ethane by the reaction of dimethyl phosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

Reaction of 1-chloro-1-cyclopropyl-1-nitroethane (0.77 g, 5.1 mmol) with dimethyl phosphite (0.63 g, 5.7 mmol) and potassium t-butoxide (0.64 g, 5.7 mmol) yielded 1-cyclopropyl-1-nitro-1-(dimethoxy phosphinyl) ethane 21 (54%) as shown by ^1H N.M.R. of the crude isolate. The previously described procedure was performed in a similar manner except the reaction mixture was irradiated for 23 hours. The 1-cyclopropyl-1-nitro-1-(dimethoxy phosphinyl) ethane 21 was isolated by Kugelrohr distillation (115°C, 0.4 mm) to give (0.49 g, 42%) of pure product.

^1H N.M.R. ($CDCl_3$) δ 3.91 (d, 3H, $-OCH_3$, J_{PH} = 10.9 Hz), 3.88 (d, 3H, $-OCH_3$, J_{PH} = 10.8 Hz), 1.47 (d, 3H, $-C(NO_2)CH_3$, J_{PH} = 14.6 Hz), 1.0-0.2 (m, 4H, $-CH_2-CH_2-$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 90.06 (d, J_{PC} = 153.8 Hz, $-C(NO_2)CH_3$), 54.44 (d, J_{PC} = 6.12 Hz, $-P(OCH_3)$),

54.14 (d, J_{PC} = 7.32 Hz, -P(O$\underline{C}H_3$)), 14.84 (d, J_{PC} = 10.37, -C(NO_2)$\underline{C}H_3$) 3.87 (s), 1.44 (s), 1.00 (s).

I.R. (neat, NaCl plates, cm^{-1}) 1545 (vs), 1460 (w), 1390 (m), 1335 (m), 1260 (vs), 1180 (m), 1030 (vs, broad), 860 (m), 830 (m), 790 (m), 770 (m).

M.S. (P-46 peak measured). Calculated for $C_7H_{14}O_3P$: 177.06806. Measured: 177.06779. Error = -1.5 ppm.

Elemental Analysis. Calculated for $C_7H_{14}NO_5P$: C, 37.67; H, 6.32; N, 6.28; O, 35.84; P, 13.88. Found: C, 37.06; H, 6.68.

9. Preparation of 1-cyclopropyl-1-nitro-1-(diethoxy thiophosphinyl) ethane by the reaction of diethyl thiophosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.62 g, 4.2 mmol) was reacted with diethyl thiophosphite (0.72 g, 4.67 mmol) and potassium t-butoxide (0.5243 g, 4.67 mmol) according to the procedure given for the reaction of diethyl phosphite anion with 1-chloro-1-cyclopropyl-1-nitroethane with one exception. The reaction mixture was irradiated for 33 hours instead of the 44 hours in the standard procedure. After an aqueous isolation procedure, the crude isolate (1.01 g, 86% N.M.R. yield) was purified for analyses by Kugelrohr distillation (130°C/0.9 torr) to yield 1-cyclopropyl-1-nitro-1-(diethoxy thiophosphinyl) ethane 23 (0.63 g, 54%).

^{1}H N.M.R. ($CDCl_3$) δ 4.55-3.8 (m, 4H, -)$\underline{C}H_2CH_3$), 1.81 (d, 3H, -C(NO_2)$\underline{C}H_3$, J_{PH} = 16.5 Hz), 1.32 (t, 6H, -O$CH_2\underline{C}H_3$, J_{PH} = 6 Hz), 1.0-0.3 (m, 4H, -$\underline{C}H_2$-$\underline{C}H_2$-).

I.R. (neat, NaCl plates, cm^{-1}) 2950 (m), 1545 (vs), 1460 (w), 1390 (m), 1335 (m), 1160 (m), 1095 (m), 1030 (vs, broad), 960 (vs, broad), 860 (m), 835 (m), 790 (m, broad), 675 (m).

M.S. (P-46 peak measured). Calculated for $C_9H_{18}O_2PS$: 221.07652. Measured: 221.07635. Error = <1.0 ppm.

10. Preparation of 2-cyclopropyl-3-methyl-2,3-dinitrobutane by reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane

1-Chloro-1-cyclopropyl-1-nitroethane (0.4034 g, 2.7 mmol) was added by syringe to a solution of the lithium salt of 2-nitropropane (0.2570 g, 2.7 mmol) in 15 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated for 24 hours using a Rayonet photoreactor (350 nm). The resulting reaction mixture was poured into 15 ml of brine and extracted three times with 20 ml of ether. The combined ether extract was washed with water and brine. The resulting organic solution was dried ($MgSO_4$) and concentrated to yield 0.43 g of residue. G.C. analysis revealed that the crude residue contained 0.05 g of 2,3-dimethyl-2,3-dinitrobutane, 0.24 g (45%) of 2-cyclopropyl-3-methyl-2,3-dinitrobutane, and recovered 1-chloro-1-cyclopropyl-1-nitroethane. 2-Cyclopropyl-3-methyl-2,3-dinitrobutane 26 was purified for analysis using preparative G.L.C.

^1H N.M.R. ($CDCl_3$) δ 2.04 (s, 3H, $-CH_3$), 1.96 (s, 3H, $-CH_3$), 1.54 (s, 3H, $-CH_3$), 1.09-0.18 (m, 4H, $-CH_2CH_2-$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 95.37, 92.71, 23.64, 23.48, 15.25, 14.28, 6.04, 2.19.

I.R. (neat, NaCl plates, cm^{-1}) 1550 (vs), 1470 (m), 1415 (m), 1400 (m), 1385 (m), 1350 (s), 1120 (m), 1035 (w), 920 (m), 735 (m).

M.S. (P-46 peak measured). Calculated for $C_8H_{14}NO_2$: 156.10246. Measured: 156.10304. Error = +3.7 ppm.

11. Preparation of 1-cyclopropyl-1-nitroethane by reductive dechlorination of 1-chloro-1-cyclopropyl-1-nitroethane

To a suspension of active magnesium turnings (77.8 mg, 3.2 mmol) in dry THF (16 ml) was added 1-chloro-1-cyclopropyl-1-nitroethane (0.3 g, 2.0 mmol). The magnesium turnings (0.102 g, 4.2 mmol) were activated by treatment with dibromoethane (0.19 g, 1.0 mmol). The suspension was stirred at 26°C under an argon atmosphere for 2 hours. The resulting solution was then decanted from the residual magnesium with additional THF. Glacial acetic acid (4.0 equiv.) was added to the decanted solution and stirring was continued for 15 minutes. The acidic solution was extracted with ether (3 x 15 ml) and the combined ether solution was washed with bicarbonate and water. After drying ($MgSO_4$) the ether solution, bulb to bulb distillation (80°C/166 torr) yielded 1-cyclopropyl-1-nitroethane (0.21 g, 92%).

^1H N.M.R. ($CDCl_3$) δ 4.06-3.96 (dxq, 1H, J_H = 6.83 Hz, -$\underline{H}C(NO_2)(CH_3)$, 1.82 (d, 3H, $-HC(NO_2)\underline{CH_3}$, J_H = 6.35 Hz), 1.75-1.34 (m, 1H), 1.04-0.51 (m, 4H, $-\underline{CH_2}-\underline{CH_2}-$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 88.22, 18.66, 15.95, 4.09.

I.R. (neat, NaCl plates, cm^{-1}) 3000 (w), 1550 (vs), 1450 (m), 1400 (s), 1390 (m), 1360 (s), 1300 (m), 1115 (m), 1050 (m), 1030 (m), 920 (m), 865 (m), 830 (m).

M.S. (P-46 peak measured). Calculated for C_5H_9: 69.07043. Measured: 69.07047. Error = +0.6 ppm.

12. Preparation of 2,3-dicyclopropyl-2,3-dinitrobutane by the reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.51 g, 3.4 mmol) was syringed into a solution of lithium t-butoxide (0.2798 g, 3.5 mmol) and 1-cyclopropyl-1-nitroethane (0.40 g, 3.45 mmol) in 15 ml of dry DMSO under a nitrogen atmosphere. The resulting solution was then irradiated for 48 hours in a Rayonet photoreactor (350 mn). After irradiation, the reaction mixture was poured into 20 ml of brine and extracted three times with 25 ml of ether. The combined ether extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated to yield 0.72 g of crude isolate. The crude isolate contained 0.69 g (89%) of 2,3-dicyclopropyl-2,3-dinitrobutane 27 and 0.02 g of 1-chloro-1-cyclopropyl-1-nitroethane as observed by G.C. analysis. G.C. analysis also revealed that 2,3-dicyclopropyl-2,3-dinitrobutane exists as an approximate equal amount of two diastereomers. Recrystallization from hexane yielded 0.42 g (54%) of white crystals of 2,3-dicyclopropyl-2,3-dinitrobutane 27 which contained the two diastereomers as observed by ^1H N.M.R. in a ratio of 5.2:1.0.

^{1}H N.M.R. ($CDCl_3$) δ major isomer 1.80 (m, 1H, -C(H)CH_2-), 1.44 (s, 3H, -C(CH_3), 0.92-0.43 (m, 4H, -CH_2CH_2-). Minor isomer 2.04 (m, 1H, -C(H)CH_2-)), 1.36 (s, 3H, -C(CH_3)).

I.R. (KBR pellet, cm^{-1}) 1550 (vs), 1465 (m), 1415 (m), 1400 (m), 1385 (m), 1350 (s), 1120 (m), 1040 (m), 920 (m), 850 (m), 735 (m).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS). Major isomer: 96.67, 15.14, 14.87, 6.31, 2.63. Minor isomer: 15.52, 14.65, 2.03.

In the M.S. of 2,3-dinitro alkanes, the parent ion was not observed. The P-93 ion (loss of HN_2O_4) was measured. The loss of P-93 appears in general to all 2,3-dinitroalkanes compared. Calculated for $C_{10}H_{15}$: 136.12520. Measured: 136.12527. Error = +0.5 ppm.

Elemental Analysis. Calculated for $C_{10}H_{16}N_2O_4$: C, 52.62; H, 7.07; N, 12.27; O, 28.04. Found: C, 52.80, H, 7.35; N, 12.25.

13. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane in THF

1-Chloro-1-cyclopropyl-1-nitroethane (0.2734 g, 1.83 mmol) was added to a solution containing the lithium salt of 2-nitropropane (0.1727, 1.82 mmol) in 9 ml of dry THF under a nitrogen atmosphere. The reaction mixture was irradiated (350 nm) for 24 hours. After irradiation was complete, the THF was vacuum evaporated and the residue was extracted from brine with ether (3 x 15 ml). The combined ether extract was dried ($MgSO_4$) and concentrated to yield 0.2714 g of crude isolate. G.C. analysis indicated little or no 2,3-dicyclopropyl-2,3-dinitrobutane 27. The yields of 2-cyclopropyl-3-methyl-2,3-

dinitrobutane 26 (4.5 mg, 1.2%) and 2,3-dimethyl-2,3-dinitrobutane 25 (12.5 mg, 7.8%) were analytically determined using G.C. analyses techniques. The yield of 2,3-dimethy,-2,3-dinitrobutane was calculated from the amount of lithium salt originally present, while the yield of 2-cyclopropyl-3-methyl was based upon 1-chloro-1-cyclopropyl-1-nitroethane.

14. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane in ethanol

1-Chloro-1-cyclopropyl-1-nitroethane (0.2381 g, 1.59 mmol) was syringed into a solution of the lithium salt of 2-nitropropane (0.1524 g, 1.6 mmol) in 5 ml of EtOH under a nitrogen atmosphere. The resulting solution was irradiated for 24 hours in a Rayonet photoreactor (350 nm). After irradiation, the EtOH was removed under reduced pressure. The remaining residue was extracted from brine with ether (3 x 15 ml) and the combined ether extract was dried ($MgSO_4$) and concentrated. The crude isolate (0.2001 g) was analyzed by G.C. which reveal the presence of 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (68.3 mg, 21.2 %), 2,3-dimethyl-2,3-dinitrobutane 25 (50.8 mg, 36.2%), and only a trace of 2,3-dicyclopropyl-2,3-dinitrobutane 27 along with some unreacted 1-chloro-1-cyclopropyl-1-nitroethane.

15. Effect of light on the reaction of 2-nitropropane anion with 1-chloro-1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.2821 g, 1.89 mmol) was added via a syringe through a foil-covered septum to a solution containing the lithium salt of 2-nitropropane (0.180 g, 1.9 mmol) in 5 ml

of absolute EtOH under nitrogen. The flask was wrapped tightly under several layers of aluminum foil to exclude light. After stirring for 24 hours, the reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.9 mg, 0.23%) and 2,3-dimethyl-2,3-dinitrobutane 25 (1.1 mg, 0.33%).

16. Effect of di-t-butyl nitroxide on the reaction of 2-nitropropane anion with 1-chloro-1-cyclopropyl-1-nitroethane

1-Chloro-1-cyclopropyl-1-nitroethane (0.2491 g, 1.67 mmol) was added to a solution of the lithium salt of 2-nitropropane (0.1597 g, 1.68 mmol) and di-t-butyl nitroxide (24 mg, 0.16 mmol) in 5 ml of absolute EtOH under a nitrogen atmosphere. The solution was irradiated for 24 hours using a Rayonet photoreactor (350 nm). The reaction was worked-up as previously described to yield 0.2026 g of crude product. The crude product was analyzed by G.C. to contain 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (44.7 mg, 13.2%) and 2,3-dimethyl-2,3-dinitrobutane 25 (38.7 mg, 13.2%).

17. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane in DMF

1-Chloro-1-cyclopropyl-1-nitroethane (0.2892 g, 1.94 mmol) was added by syringe to a solution of the lithium salt of 2-nitropropane (0.1842 g, 1.94 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. The reaction mixture was worked-up as previously described after 48 hours of irradiation in a Rayonet photoreactor (350 nm). G.C. analysis of the 0.3109 g of the crude residue revealed it contained

2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (226.3 mg, 57.7%), 2,3-dimethyl-2,3-dinitrobutane 25 (38.9 mg, 22.8%), and 2,3-dicyclopropyl-2,3-dinitrobutane 27 (19.2 mg, 8.7%).

18. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the tetrabutylammonium salt of 2-nitropropane in DMSO

1-Chloro-1-cyclopropyl-1-nitroethane (0.2734 g, 1.83 mmol) was syringed into a solution of 2-nitropropane (0.163 g, 1.83 mmol) and tetrabutylammonium hydroxide (0.4774 g, 1.84 mmol) in 10 ml of dry DMSO under nitrogen. The resulting solution was irradiated for 48 hours in a Rayonet photoreactor (350 nm). The resulting reaction mixture was poured into 15 ml of brine and extracted three times with 25 ml of ether. The combined ether extract was washed with water and brine. The resulting ether solution was dried ($MgSO_4$) and concentrated to yield 0.381 g of crude isolate. G.C. analysis of the crude isolate revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.3091 g, 74%), 2,3-dimethyl-2,3-dinitrobutane 25 (16.1 mg, 4.9%), and only a trace amount of 2,3-dicyclopropyl-2,3-dinitrobutane 27.

19. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the lithium salt of 2-nitropropane in DMSO

1-Chloro-1-cyclopropyl-1-nitroethane (0.185 g, 1.23 mmol) was added to a solution of the lithium salt of 2-nitropropane (0.117 g, 1.23 mmol) in 10 ml of dry DMSO under nitrogen. After 48 hours of irradiation at 350 nm using a Rayonet photoreactor, the reaction mixture was worked-up as previously described to yield 0.218 g of crude product. The crude product was analyzed by G.C., and the crude

isolate contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (159.8 mg, 64.1%), 2,3-dimethyl-2,3-dinitrobutane 25 (17.4 mg, 12.4%), and 2,3-dicyclopropyl-2,3-dinitrobutane 27 (14.5 mg, 10.3%). G.C. yields of 2-cyclopropyl-3-methyl-2,3-dinitrobutane and 2,3-dicyclopropyl-2,3-dinitrobutane are based on the amount of starting 1-chloro-1-cyclopropyl-1-nitroethane, whereas the yield of 2,3-dimethyl-2,3-dinitrobutane was equated from the amount of lithium salt initially used.

20. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the sodium salt of 2-nitropropane in DMSO

1-Chloro-1-cyclopropyl-1-nitroethane (0.2106 g, 1.41 mmol) was added by syringe to a stirred solution of 2-nitropropane (0.1263 g, 1.42 mmol) and sodium t-butoxide (0.1355 g, 1.41 mmol) in 10 ml of dry DMSO under a nitrogen atmosphere. The resulting reaction mixture was irradiated for 48 hours in a Rayonet photoreactor (350 nm). A similar aqueous isolation procedure as described earlier was performed on the reaction mixture to yield 0.23 g of crude isolate. ^{1}H N.M.R. analysis of the crude isolate failed to reveal the presence of any ring-opened products. The crude residue contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.1993 g, 69.9%), 2,3-dicyclopropyl-2,3-dinitrobutane 27 (9.0 mg, 5.6%), and 2,3-dimethyl-2,3-dinitrobutane 25 (21.2 mg, 17.1%) as determined by G.C. analysis.

21. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the potassium salt of 2-nitropropane in DMSO

1-Chloro-1-cyclopropyl-1-nitroethane (0.1538 g, 1.03 mmol) was added by syringe to 10 ml of dry DMSO solution containing 2-nitropropane

(0.0919 g, 1.03 mmol) and potassium t-butoxide (0.1162 g, 1.035 mmol) under a nitrogen atmosphere. The reaction mixture was worked-up as previously described after 48 hours of irradiation in a Rayonet photoreactor (350 nm). Quantitative G.C. analysis of the 0.181 g of crude residue revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.1418 g, 68.1%), 2,3-dicyclopropyl-2,3-dinitrobutane 27 (5.5 mg, 4.7%), and 2,3-dimethyl-2,3-dinitrobutane 25 (13.3 mg, 14.7%).

22. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the tetramethylammonium salt of 2-nitropropane in DMSO

A solution of 10% tetramethylammonium hydroxide in water (2.01 g, 2.21 mmol) was added dropwise with cooling to 2-nitropropane (0.196 g, 2.2 mmol) in 5 ml of dry DMSO. The mixture was allowed to warm to room temperature and stirred for one hour. After degassing with nitrogen, 1-chloro-1-cyclopropyl-1-nitroethane (0.3286 g, 2.3 mmol) was syringed into the DMSO solution. The resulting solution was irradiated for 48 hours in a Rayonet photoreactor (350 nm). The reaction was worked-up as previously described to yield 0.3104 g of crude isolate. G.C. analysis of the crude isolate revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.2565 g, 62.8%), 2,3-dicyclopropyl-2,3-dinitrobutane 27 (4.8 mg, 2.1%), and 2,3-dimethyl-2,3-dinitrobutane 25 (25.4 mg, 14.3%).

23. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the N-benzyltrimethyl ammonium salt of 2-nitropropane in DMSO

A solution of 40% N-benzyltrimethyl ammonium hydroxide in methanol (0.63 g, 1.5 mmol) was added dropwise with cooling to 2-nitropropane

(0.1292 g, 1.45 mmol) in 10 ml of dry DMSO. The mixture was allowed to stir at room temperature for 1 hour. After degassing with nitrogen, 1-chloro-1-cyclopropyl-1-nitroethane (0.2165 g, 1.45 mmol) was syringed into the DMSO solution. After the addition of 1-chloro-1-cyclopropyl-1-nitroethane, the resulting solution was irradiated (350 nm) for 48 hours. A similar aqueous work-up as described earlier was performed on the reaction mixture to yield 0.245 g of crude isolate. Quantitative G.C. analysis of the crude residue revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.2093 g, 71.4%), 2,3-dimethyl-2,3-dinitrobutane 25 (30.5 mg, 23.9%), and only a trace of 2,3-dicyclopropyl-2,3-dinitrobutane 27 was observed. No evidence for the formation of any ring-opened products was detected by ^{1}H N.M.R.

24. Reaction 2-chloro-2-nitropropane with the lithium salt of 1-cyclopropyl-1-nitroethane in DMSO

2-Chloro-2-nitropropane (0.1831 g, 1.48 mmol) was added to a solution of lithium t-butoxide (0.1224 g, 1.53 mmol) and 1-cyclopropyl-1-nitroethane (0.1709 g, 1.48 mmol) in 10 ml of freshly distilled DMSO under a nitrogen atmosphere. The reaction mixture was worked-up as previously described after 48 hours in a Rayonet photoreactor (350 nm). G.C. analysis of the 0.30 g of crude residue revealed it contained 2,3-dicyclopropyl-2,3-dinitrobutane 27 (74.1 mg, 43.8%), 2,3-dimethyl-2,3-dinitrobutane 25 (16.9 mg, 12.9%), and 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (126.2 mg, 42.0%). Yields are calculated as previously described.

25. Reaction of 2-chloro-2-nitropropane with the lithium salt of 1-cyclopropyl-1-nitroethane in DMF

2-Chloro-2-nitropropane (0.2042 g, 1.65 mmol) was added by syringe to a solution of lithium t-butoxide (0.1333 g, 1.66 mmol) and 1-cyclopropyl-1-nitroethane (0.1904 g, 1.65 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated for 48 hours using a Rayonet photoreactor (350 nm). The resulting reaction mixture was poured into 10 ml of brine and extracted three times with 30 ml of ether. The combined ether extract was washed with water and brine. The resulting ether solution was dried ($MgSO_4$) and concentrated to yield 0.3614 g of a mixture of products. G.C. analysis revealed the crude isolate contained 2,3-dicyclopropyl-2,3-dinitrobutane 27 (92.5 mg, 48.7%), 2,3-dimethyl-2,3-dinitrobutane 25 (24.1 mg, 16.6%), and 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.1269 g, 37.9%). G.C. yields of 2-cyclopropyl-3-methyl-2,3-dinitrobutane and 2,3-dicyclopropyl-2,3-dinitrobutane are based upon the initial amount of 1-cyclopropyl-1-nitroethane. Yields of 2,3-dimethyl-2,3-dinitrobutane were calculated from 2-chloro-2-nitropropane.

26. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the tetrabutylammonium salt of 2-nitropropane in DMF

A solution of 40% tetrabutylammonium hydroxide in water (1.34 g, 2.07 mmol) was added dropwise with cooling to 2-nitropropane (0.184 g, 2.065 mmol) in 10 ml of dry DMF. The resulting mixture was allowed to stir at room temperature for 1 hour to ensure deprotonation of 2-nitropropane. After degassing with nitrogen, 1-chloro-1-cyclopropyl-

1-nitroethane (0.3091 g, 2.07 mmol) was added by syringe to the DMF solution. The resulting solution was irradiated for 48 hours in a Rayonet photoreactor (350 nm). The resulting reaction mixture was poured into 15 ml of brine and extracted three times with 25 ml of ether. The combined ether extract was washed with water and brine. The resulting ether solution was dried ($MgSO_4$) and concentrated to yield 0.353 g of crude isolate. G.C. analysis of the crude isolate revealed it contained 2-cyclopropyl-3-methyl-2,3-dinitrobutane 26 (0.3268 g, 78.1%), 2,3-dimethyl-2,3-dinitrobutane 25 (24.5 mg, 13.5%), and only a trace amount of 2,3-dicyclopropyl-2,3-dinitrobutane 27. The work-up procedure described above is representative of similar reactions involving salts of 2-nitropropane with 1-chloro-1-cyclopropyl-1-nitroethane.

27. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the enolate of pinacolone

n-Butyllithium in hexane (2.4 ml, 3.75 mmol) was added to a dry THF solution containing diisopropyl amine (0.38 g, 3.75 mmol) at -78°C under nitrogen. The solution was warmed to 10°C and subsequently cooled to -30°C where pinacolone (0.377 g, 3.77 mmol) was added dropwise over a period of 15 minutes to give a reaction mixture approximately 0.4 M in pinacolone enolate. 1-Chloro-1-cyclopropyl-1-nitroethane (0.553 g, 3.71 mmol) was added to the enolate solution at 0°C. The resulting solution was irradiated for 48 hours using a Rayonet photoreactor (350 nm). After the irradiation period was completed, the THF was removed under reduced pressure. The material remaining was dissolved in

ether and then washed with water and brine. After drying ($MgSO_4$), the ether solution was condensed to yield 0.85 g of crude isolate. ^{1}H N.M.R. and G.C.M.S. analyses of the crude isolate revealed it contained unreacted 1-chloro-1-cyclopropyl-1-nitroethane 1 (0.148 g, 26.7%), E,Z-5-cyclopropyl-2,2-dimethyl-4-hexen-3-one 29 (0.321 g, 52.1%), 5-cyclopropyl-2,2-dimethyl-5-nitro-3-hexanone 28 (0.118 g, 14.9%), and 2,3-dicyclopropyl-2,3-dinitrobutane 27 (1.7 mg, 36%). All yields are based upon 1-chloro-1-cyclopropyl-1-nitroethane.

In a scaled-up reaction (5.3 mmol of 1-chloro-1-cyclopropyl-1-nitroethane) using the same procedure with two equivalents of pinacolone enolate, the crude product was distilled by Kugelrohr distillation (50°C, 10 torr) to yield 0.49 g (55.7%) of two isomers of 5-cyclopropyl-2,2-dimethyl-4-hexen-3-one 29 (63:38).

^{1}H N.M.R. ($CDCl_3$) δ 6.28 (s, broad, 1H, -C<u>H</u>=C(CH_3)(R')), 1.9 (d, 3H, J_H = 1 Hz), 1.53 (d, 3H, J = 1 Hz), 1.16 (s, 9H, -C(<u>CH_3</u>)$_3$), 0.95-0.60 (m, 4H, -<u>CH_2-CH_2</u>-).

I.R. (neat, NaCl plates, cm^{-1}) 2960 (s), 1665 (vs), 1470 (m), 1385 (m), 1090 (m), 1055 (m), 1000 (w), 910 (s), 870 (m), 800 (m).

M.S. (M^+ peak measured). Calculated for $C_{11}H_{18}O$: 166.13577. Measured: 166.13584. Error = <1.0 ppm.

Elemental Analysis. Calculated for $C_{11}H_{18}O$: C, 79.46; H, 10.91; O, 9.62. Found: C, 79.09; H, 10.68.

28. Reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the potassium salt of benzenethiol

1-Chloro-1-cyclopropyl-1-nitroethane (0.2067 g, 1.38 mmol) was added via a syringe to a solution of potassium t-butoxide (0.1554 g, 1.38 mmol) and benzenethiol (0.1524 g, 1.38 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated for 22 hours with a 275 Watt sunlamp placed 15 cm from the Pyrex flask. Biphenyl (0.0476 g, 0.3 mmol) was added as an internal standard after irradiation was complete. G.C. analysis of the reaction mixture revealed it contained phenyl disulfide 36 (31.4 mg, 10.4%) and 2,3-dicyclopropyl-2,3-dinitrobutane 27 (34.6 mg, 11%) as the only formed volatile products. Similar reactions employing the Rayonet photoreactor and/or DMSO gave results consistent with the formation of the two dimers in approximately equal yields.

29. Reduction of 2-chloro-2-nitropropane with tri-n-butyltin hydride

Tri-n-butyltin hdride (0.5009 g, 1.72 mmol) was added by syringe through a septum to a solution of 2-chloro-2-nitropropane (0.2177 g, 1.76 mmol) in benzene-d_6 (0.158 g, 1.87 mmol) in a 5 mm N.M.R. tube. The solution was briefly degassed with nitrogen and irradiated in a Rayonet photoreactor (350 nm) for 14.5 hours. After irradiation, methylene chloride (26.7 mg) was added as an internal standard to determine the yield of 2-nitropropane by ^{1}H N.M.R. Integration of the resulting solution revealed it contained 2-nitropropane (0.121 g, 80%) and no 2-chloropropane or unreacted tri-n-butyltin hydride was detected. Periodic observation of similar experiments also failed to reveal the presence of 2-chloropropane.

30. Reduction of 1-chloro-1-cyclopropyl-1-nitroethane with tri-n-butyltin hydride

Tri-n-butyltin hydride (0.4388 g, 1.51 mmol) was added via a syringe to a solution of 1-chloro-1-cyclopropyl-1-nitroethane (0.2255 g, 1.51 mmol) in benzene-d_6 (0.127 g, 1.51 mmol) under a nitrogen atmosphere. The resulting solution in a N.M.R. tube was irradiated (350 nm) for 16 hours. Methylene chloride was added as an internal standard after irradiation was complete. ^{1}H N.M.R. analysis revealed the solution contained 1-cyclopropyl-1-nitroethane (0.0805 g, 46.5%) and no 1-cyclopropyl-1-chloroethane. Analysis also failed to indicate any products containing vinyl protons as determined by ^{1}H N.M.R.

31. Competitive reaction between 1-chloro-1-cyclopropyl-1-nitroethane and 2-chloro-2-nitropropane for tri-n-butyltin hydride

Tri-n-butyltin hydride (0.1471 g, 0.505 mmol) was added via a syringe to a solution of 1-chloro-1-cyclopropyl-1-nitroethane (87.5 mg, 0.586 mmol) and 2-chloro-2-nitropropane (79.2 mg, 0.643 mmol) in benzene-d_6 (0.145 g, 1.72 mmol). The resulting 5 mm N.M.R. tube solution was briefly flush with nitrogen and subsequently irradiated (350 nm) for 15 hours. ^{1}H N.M.R. and G.C. analyses (after the addition of appropriate internal standards) revealed the solution contained 1-chloro-1-cyclopropyl-1-nitroethane (64.5 mg, 73.8%), 1-cyclopropyl-1-nitroethane (11.7 mg, 17.4%), 2-chloro-2-nitropropane (38.9 mg, 48.1%), and 2-nitropropane (23.9 mg, 41.8%). ^{1}H N.M.R. also revealed 33.2 mg of tri-n-butyltin hydride remained unreacted.

32. A competitive reaction between 1-chloro-1-cyclopropyl-1-nitroethane and benzyl chloride for tri-n-butyltin hydride

Tri-n-butyltin hydride (0.3260 g, 1.12 mmol) was added by syringe to a benzene-d_6 solution containing 1-chloro-1-cyclopropyl-1-nitroethane (0.1623 g, 1.08 mmol) and benzyl chloride (0.1472 g, 1.16 mmol). The resulting solution in a N.M.R. tube was briefly degassed with nitrogen. After 14 hours of irradiation (350 nm), ^{1}H N.M.R. and G.C. analyses revealed the solution contained 1-cyclopropyl-1-nitroethane (19.1 mg, 15.3%) and toluene (37.3 mg, 34.8%). Analysis also showed that unreacted 1-chloro-1-cyclopropyl-1-nitroethane (0.1184 g, 73%), benzyl chloride (91.8 mg, 62.4%), and tri-n-butyltin hydride (0.1245 g, 38.2%) remained in the solution.

33. Preparation of 2-nitro-3-pentanol from nitroethane and propionaldehyde

Freshly distilled propionaldehyde (60.63 g, 1.04 M) was added slowly to a well stirred solution consisting of nitroethane (78.37 g, 1.04 M) and 2 ml of 10 N NaOH in 50 ml absolute ethanol. The temperature of the reaction mixture was maintained below 35°C by external cooling. When approximately 60% of the propionaldehyde was added, an additional 2 ml of 10 N NaOH was added. After addition of the aldehyde was complete, the solution was allowed to stand at ambient temperatures for 4 days. The alkali was neutralized with an equivalent amount of HCl and the ethanol was distilled from the reaction mixture. Distillation (99°C/ 10 torr) afforded 91.5 g (66%) of 2-nitro-3-pentanol 35.

^{1}H N.M.R. ($CDCl_3$) δ 4.57 (m, 1H, -$\underline{H}$C(CH_3)NO_2), 3.95 (m, 1H, -($\underline{H}$)C(OH)-), 3.13 (s, 1H, -O$\underline{H}$), 1.55 (d, 3H, J = 7 Hz, -CH(NO_2($\underline{CH_3}$).

I.R. (neat, NaCl plates, cm^{-1}) 3420 (s, broad), 2980 (m), 2960 (m), 2935 (m), 1540 (vs), 1450 (s), 1380 (s), 1350 (m), 970 (m), 860 (m).

M.S. (P-29 peak measured). Calculated for $C_3H_6NO_3$: 104.03477. Measured: 104.03507. Error = +2.9 ppm.

34. Preparation of 2-nitro-2-pentene by dehydration of 2-nitro-3-pentanol

2-Nitro-3-pentanol (5.32 g, 0.40 mmol) was dissolved in 40 ml of CH_2Cl_2 at 0°C under a nitrogen atmosphere, and methanesulfonyl chloride (4.6 g, 40 mmol) was added in one portion. Triethyl amine (16.0 g, 160 mmol) was then added dropwise and the reaction mixture was stirred for 15 minutes at 0°C. The reaction mixture was then transferred to a separatory funnel with the aid of 40 ml of CH_2Cl_2 and then washed with water, 5% aqueous HCl, and brine. The dried solution (Na_2SO_4) was concentrated and purified by distillation (85°C/20 torr) to yield 2-nitro-2-pentene 36 (3.5 g, 76%).

^{1}H N.M.R. ($CDCl_3$) δ 2.13 (s, 3H, -(=C($\underline{CH_3}$)NO_2), 1.13 (t, 3H, J = 7 Hz, -$CH_2\underline{CH_3}$), 7.17 (t, 1H, -(=C($\underline{H}$)CH_2CH_3).

I.R. (neat, NaCl plates, cm^{-1}) 2990 (w), 2970 (w), 2940 (w), 1670 (w), 1520 (vs), 1390 (m), 1335 (m).

35. A competitive reaction between 1-chloro-1-cyclopropyl-1-nitroethane and 2-nitro-2-pentene for tri-n-butyltin hydride

Tri-n-butyltin hydride (0.3085 g, 1.06 mmol) was added by syringe into a degassed (nitrogen) 5 mm N.M.R. tube containing 1-chloro-1-

cyclopropyl-1-nitroethane (0.1553 g, 1.04 mmol) and 2-nitro-2-pentene (0.1161 g, 1.01 mmol) in benzene-d_6. After 6 hours of irradiation (350 nm) with periodic observation, all of the tri-n-butyltin hydride was comsumed as indicated by the absence of a signal from the proton attached to the tin atom in the region around 4-5 ppm. G.C. and ^1H N.M.R. analyses of the reaction mixture revealed the solution contained 1-chloro-1-cyclopropyl-1-nitroethane (0.1366 g, 88%), 1-cyclopropyl-1-nitroethane (7.3 mg, 6:1%), and 2-nitro-2-pentene (8.1 mg, 7%).

36. Preparation of 2,3-dimethyl-2,3-dinitro-7-octene by the reaction of 2-chloro-2-nitro-6-heptene with the lithium salt of 2-nitropropane

2-Chloro-2-nitro-6-heptene (0.2272 g, 1.28 mmol) was added by syringe to a solution of the lithium salt of 2-nitropropane (0.139 g, 1.46 mmol) in 7 ml of DMF under a nitrogen atmosphere. The solution was irradiated with a 275 Watt sunlamp placed 16 cm from the Pyrex flask for 48 hours. The resulting reaction mixture was poured into brine and extracted three times with 30 ml of ether. The combined ether extract was washed with water and brine. The resulting organic solution was dried ($MgSO_4$) and concentrated to yield 0.26 g of crude isolate which was shown to contain 2-chloro-2-nitro-6-heptene (27 mg, 12%) and 2,3-dimethyl-2,3-dinitrobutane (40 mg, 0.23 mmol) by G.C. analysis. G.C.M.S. and ^1H N.M.R. analyses of the crude residue revealed that one cross-coupled product was formed. The crude isolate was purified by flash chromatography using hexane:ethyl acetate (6:1) as eluent which afforded 2,3-dimethyl-2,3-dinitro-7-octene 37 (0.186 g, 63.1%, Rf = 0.37).

^{1}H N.M.R. ($CDCl_3$) δ 5.81-5.67 (m, 1H, -C<u>H</u>=CH_2), 5.06-4.97 (m, 2H, -CH=C<u>H_2</u>), 1.75 (s, 3H, -C(NO_2)C<u>H_3</u>), 1.69 (s, 3H, -C(NO_2)C<u>H_3</u>), 1.59 (s, 3H, -C(NO_2)C<u>H_3</u>).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.14, 115.63, 94.72, 92.28, 33.99, 33.23, 23.32, 23.05, 18.33.

I.R. (neat, NaCl plates, cm^{-1}) 3070 (w), 2995 (w), 2970 (w), 2940 (m), 2860 (m), 1635 (m), 1540 (vs), 1450 (m), 1400 (m), 1380 (s), 1370 (m), 1335 (s), 905 (s), 840 (m), 750 (s).

M.S. (P-93 peak measured). Calculated for $C_{10}H_{17}$: 137.13303. Measured: 137.13334. Error = +2.3 ppm.

Elemental Analysis. Calculated for $C_{10}H_{18}N_2O_4$: C, 52.16; H, 7.88; N, 12.27; O, 27.79. Found: C, 51.98; H, 7.79; N, 12.03; O, 27.86.

37. <u>Preparation of 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene by the reaction of 1-chloro-1-cyclopropyl-1-nitroethane with the potassium salt of 2-nitro-6-heptene</u>

1-Chloro-1-cyclopropyl-1-nitroethane (0.2803 g, 1.87 mmol) was added by syringe to a solution of potassium <u>t</u>-butoxide (0.2287 g, 1.87 mmol) and 2-nitro-6-heptene (0.2683 g, 1.87 mmol) in 5 ml of dry DMF under a nitrogen atmosphere. The reaction mixture was irradiated with a 275 Watt sunlamp located 16 cm from the Pyrex flask for 72 hours. After irradiation, the reaction was extracted from brine with ether (3 x 15 ml). The combined ether extract was washed with water and brine. The resulting ether solution was dried ($MgSO_4$) and concentrated to yield 0.3489 g of crude isolate. The crude isolate was purified by flash chromatography using hexanes:ethyl acetate (10:1) as eluent which

afforded 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene (0.27 g, 56.4%, Rf = 0.34). G.C. analysis of the crude isolate before chromatography revealed the presence of recovered 1-chloro-1-cyclopropyl-1-nitroethane (28.7 mg, 10.2%) and 6,7-dimethyl-6,7-dinitrododeca-1,11-diene (15.9 mg, 5.9%). Analysis of the isolated 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene 38 revealed it was a mixture of two diastereomers (52:48).

^{1}H N.M.R. ($CDCl_3$) δ 5.85-5.67 (m, 1H, -C<u>H</u>=CH_2), 5.1-4.93 (m, 2H, -CH=C<u>H_2</u>), 1.70 and 1.65 (s, 3H, -C(NO_2)C<u>H_3</u>), 1.32 and 1.34 (s, 3H, -C(NO_2)C<u>H_3</u>), 0.95-0.42 (m, 4H).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS, mixture of two diastereomers) 137.25, 115.58, 96.29, 96.07, 95.96, 34.26, 33.34, 23.32, 18.88, 15.09, 14.98, 14.76, 14.60, 14.00, 6.26, 6.09, 2.36, 2.14.

I.R. (neat, NaCl plates, cm^{-1}) 3015 (w), 2970 (w), 2940 (w), 1643 (w), 1545 (vs), 1455 (w), 1390 (m), 1340 (m), 1100 (w), 1030 (m), 910 (m), 840 (m).

M.S. (P-93 peak measured). Calculated for $C_{12}H_{19}$: 163.14868. Measured: 163.14906. Error = +2.3 ppm.

38. <u>Preparation of 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene by the reaction of 2-chloro-2-nitro-6-heptene with the potassium salt of 1-cyclopropyl-1-nitroethane</u>

2-Chloro-2-nitro-6-heptene (0.2413 g, 1.36 mmol) was added to a solution of potassium <u>t</u>-butoxide (0.1526 g, 1.36 mmol) and 1-cyclopropyl-1-nitroethane (0.1564 g, 1.36 mmol) in 5 ml of dry DMF under nitrogen. The solution was irradiated for 72 hours using a 275 Watt sunlamp. The resulting reaction mixture was poured into 5 ml of brine and extracted

three times with 15 ml of ether. The combined ether extract was washed (water and brine), dried ($MgSO_4$), and concentrated to yield 0.316 g of crude isolate. G.C. analysis of the crude isolate revealed it contained recovered 2-chloro-2-nitro-6-heptene 2 (26.5 mg, 10.9%), 2,3-dicyclopropyl-2,3-dinitrobutane (44.3 mg, 28%), 6,7-dimethyl-6,7-dinitrododeca-1,11-diene (4 mg, 2%), and 2-cyclopropyl-3-methyl-2,3-dinitro-7-octene 38 (0.212 g, 60.8%) existing as two diastereomers (51:49).

39. Preparation of 6,7-dimethyl-6,7-dinitrododeca-1,11-diene by the reaction of 2-chloro-2-nitro-6-heptene with the potassium salt of 2-nitro-6-heptene

2-Chloro-2-nitro-6-heptene (0.2722 g, 1.53 mmol) was added by syringe to 5 ml of dry DMF containing potassium t-butoxide (0.1715 g, 1.53 mmol) and 2-nitro-6-heptene (0.2197 g, 1.53 mmol) under a nitrogen atmosphere. The reaction mixture was irradiated for 136 hours with a 275 Watt sunlamp placed 25 cm from the Pyrex flask. The resulting mixture was poured into 10 ml of brine and extracted with ether (3 x 25 ml). The combined ether extract was washed (water and brine), dried ($MgSO_4$), and concentrated to yield 0.3703 g of crude residue. G.C. and ^1H N.M.R. analyses of the crude residue verified that no detectable amount of cyclization had occurred. The residue was purified by flash chromatography using hexane:ethyl acetate (6:1) as eluent which afforded 6,7-dimethyl-6,7-dinitrododeca-1,11-diene 39 (0.314 g, 72.1%, Rf = 0.53) and recovered 2-chloro-2-nitro-6-heptene (46.9 mg, 17.2%) The isolated 6,7-dimethyl-6,7-dinitrododeca-1,11-diene 39 existed as a mixture of two diastereomers (72:28).

^{1}H N.M.R. ($CDCl_3$) δ 5.85-5.63 (m, 1H, -C<u>H</u>=CH_2), 5.1-4.9 (m, 2H, -CH=C<u>H_2</u>), 1.62 (major isomer, s, 3H, -C(NO_2)C<u>H_3</u>), 1.55 (minor isomer, s, 3H, -C(NO_2)C<u>H_3</u>).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) major isomer: 137.19, 115.74, 95.80, 34.15, 33.34, 23.48, 18.82.

I.R. (neat, NaCl plates, cm^{-1}) 3090 (w), 3010 (w), 2975 (w), 2885 (w), 1645 (w), 1558 (vs), 1460 (m), 1395 (m), 1342 (m), 990 (m), 920 (m), 845 (w), 800 (w).

M.S. (P-93 peak measured). Calculated for $C_{14}H_{23}$: 191.17998. Measured: 191.17955. Error = -2.3 ppm.

40. Preparation of 2-(diethyl methylmalonate)-2-nitro-6-heptene from the reaction of 2-chloro-2-nitro-6-heptene with the anion of diethyl methylmalonate

2-Chloro-2-nitro-6-heptene (0.3417 g, 1.93 mmol) was added by syringe into an ice-cold solution containing sodium hydride (0.051 g, 2.16 mmol) and diethyl methylmalonate (0.3856 g, 2.21 mmol) in 10 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated (350 nm) for 48 hours. After irradiation was complete, the reaction mixture was poured into 20 ml of water and extracted with ether (3 x 25 ml). The combined ether extract was washed (water and brine), dried ($MgSO_4$), and concentrated to yield 0.62 g of crude organic residue. G.C. and G.C.M.S. analyses of the crude isolate revealed that only one product resulting from a cross-coupling reaction was present. The residue was purified by flash chromatography using hexane: ethyl acetate (6:1) as eluent which afforded 2-(diethyl methylmalonate)-2-nitro-6-heptene 40 (0.38 g, 62%, Rf = 0.39).

^{1}H N.M.R. ($CDCl_3$) δ 6.45-5.7 (m, 1H, -C<u>H</u>=CH_2), 5.5-5.0 (m, 2H, -CH=C<u>H_2</u>), 4.4 (q, 4H, J = 7 Hz, -O<u>CH_2</u>CH_3), 1.79 (s, 3H), 1.74 (s, 3H), 1.35 (t, 6H, J = 7 Hz, -OCH_2<u>CH_3</u>).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 169.40, 169.01, 137.34, 115.10, 94.09, 61.77, 60.80, 34.98, 33.10, 22.89, 18.98, 13.78, 13.52.

I.R. (neat, NaCl plates, cm^{-1}) 2980 (m), 2930 (m), 1730 (vs), 1640 (w), 1545 (vs), 1450 (m), 1255 (s), 1090 (m), 910 (m), 850 (m).

M.S. (P-46 peak measured). Calculated for $C_{15}H_{25}O_4$: 269.17529. Measured: 269.17467. Error = -2.3 ppm.

41. Effect of light on the reaction of 2-chloro-2-nitro-6-heptene with the anion of diethyl methylmalonate

2-Chloro-2-nitro-6-heptene (0.1723 g, 0.97 mmol) was added by syringe into an ice-cold solution (0°C) containing sodium hydride (0.0233 g, 0.97 mmol) and diethyl methylmalonate (0.1694 g, 0.97 mmol) in 5 ml of dry DMF under a nitrogen atmosphere. The solution flask was wrapped tightly with several layers of aluminum foil to exclude light, and subsequently immersed in an oil bath (35°C) to simulate the temperature inside the Rayonet photoreactor. After stirring for 48 hours, the reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate revealed that 0.0122 g (4%) of 2-(diethyl methylmalonate)-2-nitro-6-heptene 40 was formed.

42. Effect of di-t-butyl nitroxide on the reaction of 2-chloro-2-nitro-6-heptene with the anion of diethyl methylmalonate

2-Chloro-2-nitro-6-heptene (0.2419 g, 1.36 mmol) was added to a dry DMF solution (6 ml) containing sodium hydride (0.0327 g, 1.36 mmol), diethyl methylmalonate (0.2402 g, 1.38 mmol), and di-t-butyl nitroxide (0.0216 g, 0.15 mmol) under a nitrogen atmosphere. The solution was irradiated for 48 hours in a Rayonet photoreactor (350 nm). The reaction mixture was worked-up as previously described. G.C. analysis of the crude isolate revealed the presence of 2-(diethyl methylmalonate)-2-nitro-6-heptene 40 (0.24 g, 56%) and recovered 2-chloro-2-nitro-6-heptene 2 (0.0748 g, 31%).

43. Preparation of 2-nitro-2-(diethoxy phosphinyl)-6-heptene from the reaction of diethyl phosphite anion with 2-chloro-2-nitro-6-heptene

2-Chloro-2-nitro-6-heptene (0.645 g, 3.63 mmol) was added to an ice-cold solution of potassium t-butoxide (0.41 g, 3.62 mmol) and diethyl phosphite (0.53 g, 3.84 mmol) in 10 ml of dry THF under nitrogen. The solution was irradiated for 36 hours in a Rayonet photoreactor (350 nm) after the ice-cold reaction mixture was allowed to equilibrate at room temperature. After irradiation, the THF was vacuum evaporated and the residue was extracted from brine with ether. The resulting ether solution was dried ($MgSO_4$) and condensed. G.C. and ^1H N.M.R. analyses of the crude residue verified that only one cross-coupled product was formed in the reaction mixture, and no detectable amount of cyclization had occurred before coupling of diethyl phosphite anion with the intermediate α-nitro radical formed from 2-chloro-2-

nitro-6-heptene. The resulting residue was purified by flash chromatography using hexane:ethyl acetate (1:1) as eluent which afforded 0.497 g (49%) of 2-nitro-2-(diethoxy phosphinyl)-6-heptene 41 (Rf = 0.39). Unreacted 2-chloro-2-nitro-6-heptene 2 (0.226 g, 35%) was also isolated by flash chromatography. Considering the amount of 2-chloro-2-nitro-6-heptene consumed in the reaction, a yield of 2-nitro-2-(diethoxy phosphinyl)-6-heptene 41 (75%) can be envisioned.

^{1}H N.M.R. ($CDCl_3$) δ 5.82-5.68 (m, 1H, -C<u>H</u>=CH_2), 5.06-4.97 (m, 2H, -CH=C<u>H$_2$</u>), 4.28-4.07 (m, 4H, -O<u>CH_2</u>CH_3), 1.78 (d, 3H, J_{PH} = 14.6 Hz, -C(NO_2)<u>CH_3</u>), 1.36 (t, 6H, J_H = 7.1 Hz, -OCH_2<u>CH_3</u>).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.14 (s, -<u>C</u>H=CH_2), 115.36 (s, -CH=<u>C</u>H_2), 89.84 (d, J_{PC} = 149 Hz, -<u>C</u>(NO_2)CH_3), 64.11 (d, J_{PC} = 7.3 Hz, -P(O)(O<u>C</u>$H_2$$CH_3$)), 63.95 (d, J_{PC} = 7.3 Hz, -P(O)(O<u>C</u>$H_2$$CH_3$)), 34.97 (s), 33.07 (s), 22.34 (d, J_{PC} = 9.8 Hz, -C(NO_2)<u>C</u>H_3), 18.93 (s), 16.33 (s, 3H, -OCH_2<u>C</u>H_3), 16.06 (s, 3H, -OCH_2<u>C</u>H_3).

^{31}P N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from H_3PO_4) one singlet 17.89.

I.R. (neat, NaCl plates, cm^{-1}) 3075 (w), 2980 (s), 2930 (m), 2860 (m), 1640 (m), 1540 (vs), 1440 (m), 1380 (m), 1365 (w), 1335 (m), 1255 (vs), 1160 (m), 1090 (m), 1040 (vs, broad), 1015 (vs, broad), 965 (s), 905 (m), 855 (m), 785 (m), 745 (m).

M.S. (P-46 peak measured). Calculated for $C_{11}H_{22}O_3P$: 233.13067. Measured: 233.13089. Error = -3.4 ppm.

Elemental Analysis. Calculated for $C_{11}H_{22}NO_5P$: C, 47.31; H, 7.94; N, 5.01; O, 28.64; P, 11.09. Found: C, 46.95; H, 8.06; N, 4.92; P, 11.26.

44. Effect of light on the reaction of diethyl phosphite anion with 2-chloro-2-nitro-6-heptene

2-Chloro-2-nitro-6-heptene (0.3547 g, 1.99 mmol) was added by syringe to a cold solution (0°C) of potassium t-butoxide (0.2260 g, 1.99 mmol) and diethyl phosphite (0.2910 g, 2.1 mmol) in 5 ml of dry THF under a nitrogen atmosphere. The reaction flask was wrapped tightly with several layers of aluminum foil to exclude light. The reaction mixture was slowly allowed to warm to room temperature, and subsequently immersed in an oil bath (36°C) to simulate the temperature inside a Rayonet photoreactor. After 36 hours of heating, an aqueous work-up similar to the previously described procedure was performed on the reaction mixture. Careful G.C. and ^1H N.M.R. analyses of the crude isolate revealed it contained 2-nitro-2-(diethyl phosphinyl)-6-heptene 41 (0.0778 g, 13.5%) and unreacted 2-chloro-2-nitro-6-heptene.

45. Preparation of 2-nitro-2-(dimethoxy phosphinyl)-6-heptene from the reaction of dimethyl phosphite anion with 2-chloro-2-nitro-6-heptene

2-Chloro-2-nitro-6-heptene (0.31 g, 1.75 mmol) was added to an ice-cold solution of potassium t-butoxide (0.233 g, 2.07 mmol) and dimethyl phosphite (0.228 g, 2.07 mmol) in 5 ml of dry THF under a nitrogen atmosphere. After 36 hours of irradiation (350 nm), the reaction mixture was worked-up as previously described for the diethyl phosphite reaction with 2-chloro-2-nitro-6-heptene. G.C. analysis of the crude

isolate showed 28% of 2-chloro-2-nitro-6-heptene remained unreacted. The crude isolate was purified by flash chromatography using hexane: ethyl acetate (1:1) as eluent which afforded 2-nitro-2-(dimethoxy phosphinyl)-6-heptene 42 (0.276 g, 63%, Rf = 0.24) as the only cross-coupled product formed.

^{1}H N.M.R. ($CDCl_3$) δ 5.74-5.61 (m, 1H, -C<u>H</u>=CH_2), 4.99-4.90 (m, 2H, -CH=C<u>H$_2$</u>), 3.81 (d, 3H, J_{PH} = 11.0 Hz, -O<u>C</u>H$_3$), 3.79 (d, 3H, J_{PH} = 11.0 Hz, -O<u>C</u>H$_3$), 1.72 (d, 3H, J_{PH} = 14.6 Hz, -C(NO_2)<u>C</u>H$_3$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 137.19 (s, -<u>C</u>H=CH_2), 115.58 (s, -CH=<u>C</u>H$_2$), 89.98 (d, J_{PC} = 150.1 Hz, -<u>C</u>(NO_2)CH_3), 54.66 (d, J_{PC} = 6.1 Hz, -P(O)(O<u>C</u>H$_3$)), 54.39 (d, J_{PC} = 6.1 Hz, -P(O)(O<u>C</u>H$_3$)), 35.24 (s), 33.13 (s), 22.45 (d, J_{PC} = 9.8 Hz, -C(NO_2)<u>C</u>H$_3$), 19.20 (s).

I.R. (neat, NaCl plates, cm^{-1}) 3090 (w), 2975 (m), 2870 (w), 1645 (m), 1550 (vs), 1465 (m, broad), 1390 (m), 1345 (m), 1270 (vs), 1190 (m), 1055 (vs, broad), 1030 (vs, broad), 920 (m), 840 (m).

M.S. (P-46 peak measured). Calculated for $C_9H_{18}O_3P$: 205.09936. Measured: 205.09984. Error = +2.4 ppm.

Elemental Analysis. Calculated for $C_9H_{18}NO_5P$: C, 43.03; H, 7.22; N, 5.58; O, 31.84; P, 12.33. Found: C, 43.35; H, 7.25; N, 5.36; P, 12.05.

46. Reduction of 2-chloro-2-nitro-6-heptene with tri-n-butlytin hydride

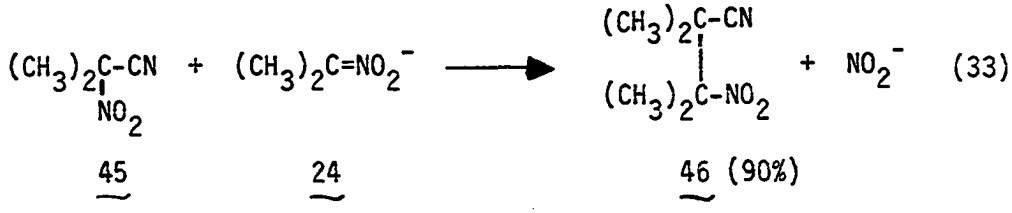
Tri-n-butyltin hydride (0.3167 g, 1.09 mmol) was added to a 5 mm N.M.R. tube containing 2-chloro-2-nitro-6-heptene (0.1934 g, 1.09 mmol)

in benzene-d_6 (0.08 g, 0.95 mmol). After degassing with nitrogen for 10 minutes, the resulting solution was irradiated for 12 hours in a Rayonet photoreactor (350 nm). G.C. and ^{1}H N.M.R. analyses of the reaction mixture revealed the 2-nitro-6-heptene (0.026 g, 16.9%) was the only observable reduction product formed. ^{1}H N.M.R. analysis showed the tri-n-butyltin hydride was completely consumed. G.C. and G.C.M.S. indicated no cyclization products were formed and some 2-chloro-2-nitro-6-heptene remained unreacted.

IV. A RADICAL CHAIN REACTION INVOLVING 2-METHYL-2-NITROCYCLOPROPYL METHYL KETONE

A. Introduction

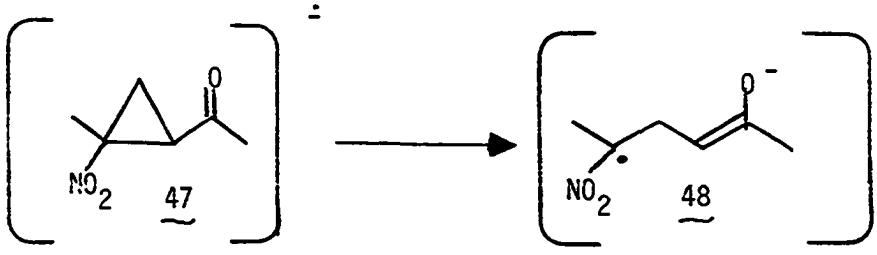
A growing list of α-substituted nitroalkanes have been shown to undergo nucleophilic substitution by the $S_{RN}1$ process. Consequently, an impressive array of leaving groups have been reported in the literature, including a variety of nucleofuges which do not participate in S_N1 or S_N2 processes. As the list of leaving groups increased, the conspicuous absence of carbon bonded nucleofuges was magnified. Several substrates which possess suitable leaving groups, potentially involving the reductive cleavage of a carbon-carbon bond, have lost nitrite ion instead. 2-Nitroisobutyronitrile 45 was a potentially good choice of substrate since it could lose relatively stable cyanide ion. Kornblum and Boyd [86] have shown that 2-nitroisobutyronitrile reacts with the anion of 2-nitropropane by the $S_{RN}1$ process with a loss of nitrite ion instead of cyanide ion (Eq. 33). Other nitro substrates that contain carbon bonded functional groups (e.g., α-nitro esters and α-nitro



45 24 46 (90%) (33)

ketones) undergo nucleophilic substitution by the $S_{RN}1$ process with the loss of nitrite ion instead of reductive cleavage of a carbon-carbon bond [87].

In an attempt to observe an example of a carbon centered leaving group in the aliphatic $S_{RN}1$ process, a substrate was selected that would hopefully incorporate an enolate as the nucleofuge. It was reasoned that the formation of a resonance stabilized enolate hopefully would prevent the loss of nitrite ion. 2-Methyl-2-nitrocyclopropyl methyl ketone 47 was selected as a suitable substrate to observe the reductive cleavage of a carbon-carbon bond in the aliphatic $S_{RN}1$ process. The radical anion of 2-methyl-2-nitrocyclopropyl methyl ketone 47 was envisioned to form a resonance stabilized enolate 48 as shown in Eq. 34. An additional



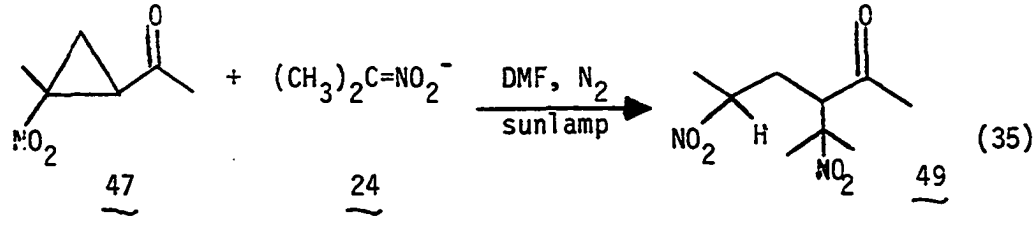
(34)

influence on the course of the reaction involves the relief of ring strain due to the opening of the highly strained cyclopropyl ring. It is the opinion of this author that the relief of ring strain and formation of a relatively stable enolate anion should circumvent the loss of nitrite ion from the radical anion of 2-methyl-2-nitrocyclopropyl methyl ketone.

B. Results and Discussion

1. Reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane

The lithium salt of 2 nitropropane reacts with 2-methyl-2-nitrocyclopropyl methyl ketone to produce 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 (Eq. 35). A reasonable yield could be achieved when the reaction was irradiated with a sunlamp while using dry N,N-dimethylformamide (DMF) as the solvent under a nitrogen atmosphere.



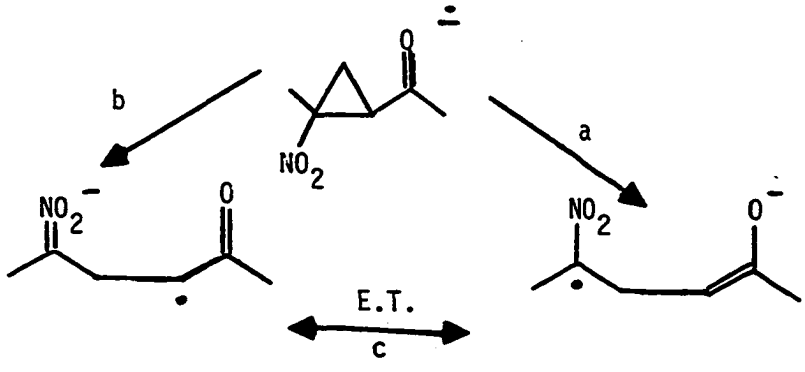
47 24 49 (35)

Like many aliphatic $S_{RN}1$ reactions, light was required for the formation of 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49. Reactions run in aluminum foil-wrapped flasks to exclude light revealed only 2-methyl-2-nitrocyclopropyl methyl ketone was present in the isolate after work-up. Careful product analyses by G.C. and ^1H N.M.R. failed to reveal the presence of any ring-opened products. Complete inhibition of the reaction between the lithium salt of 2-nitropropane and 2-methyl-2-nitrocyclopropyl methyl ketone by saturating the DMF solution with oxygen demonstrated that radical intermediates were involved in the formation of 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49. Strong support for a chain reaction involving radical anions is provided by the fact

that 10% of di-t-butyl nitroxide and 10% p-dinitrobenzene (p-DNB) completely inhibits the reaction of 2-methyl-2 nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane (see Table 9).

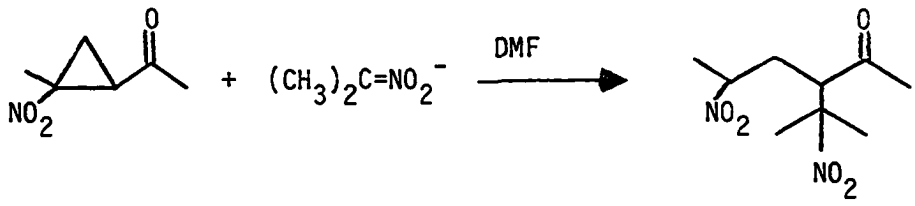
The unexpected formation of 3(2-nitro-2-propyl)-5-nitro-2-hexanone from the reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane can be rationalized as originating from an alternative pathway (b) rather than the anticipated reductive cleavage (a) as shown in Scheme 10.

Scheme 10



The predicted reductive cleavage (a) of 2-methyl-2-nitrocyclopropyl methyl ketone according to pathway (a) was based upon the desired observation of an enolate anion as a nucleofuge in the aliphatic $S_{RN}1$ process and the resultant stabilities of the enolate anion and the resonance stabilized α-nitro radical. The stabilization of the formed α-nitro radical (pathway a) is a logical extension of the capto-dative substituent effect as discussed in the previous section.

Table 9. Characteristics of the reaction between 2-methyl-2-nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane



47 49

Time (hrs)	Conditions	% Yield (N.M.R.)	% Unreacted Ketone (N.M.R.)
14.5	sunlamp, N_2	58.2	27.3
14.5	dark, N_2	0	91.5
14.5	sunlamp, O_2	0	91.2
14.5	sunlamp, N_2, 10% di-t-butyl nitroxide	0	92.5
14.5	sunlamp, N_2, 10% p-DNB	0	89.6

Using hindsight, it appears the combined stabilities of the α-nitro radical and enolate anion (a) are significantly less than the totaled stabilities resulting from the radical adjacent to the carbonyl group and nitronate anion. The stability of the formed carbanions or conjugate bases are proportional to the acidity of the carbon acids. The pK_a values of secondary nitro compounds and ketones are well-documented relative to water (approximately 10 and 21, respectively). Based upon the reported pK_a values, it appears the weaker conjugate base (nitronate anion) by pathway b should thermodynamically be preferred over pathway a. Due to the limited reported results on the magnitude of stabilization of capto-dative substituted radicals, it would be pure speculation to surmise which of the radicals formed from pathway a or b would be more stable. At this point in time, it is reasonable to assume the difference in acidities of the conjugate bases have a greater effect on the reaction pathway than the stabilization of capto-dative substituted radicals.

A third reaction pathway (c) also can be imagined involving intramolecular electron transfer between enolate anion and α-nitro radical that arose from pathway a to form nitronate anion and a radical alpha to the carbonyl group, which is identical to the ring opened intermediate formed from pathway b. If reaction pathway c is a viable alternative, then other nucleophiles should compete for the α-nitro radical, since it is generally recognized that nucleophiles not containing a nitro moiety are generally ineffective at trapping aliphatic radicals. It should be possible to differentiate between pathway b or c, since

the formation of a radical anion is made energetically accessible by the low-lying antibonding pi-orbital of the nitro moiety, thus only α-nitro radicals would be trapped by various nucleophiles not containing a nitro moiety.

2. Attempt to react 2-methyl-2-nitrocyclopropyl methyl ketone with sodium benzenesulfinate

Considering the unexpected formation of 3(2-nitro-2-propyl)-5-nitro-2-hexanone from the reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the anion of 2-nitropropane, it seemed likely that by changing the nucleophile the expected α-nitro radical may be trapped instead of the α-keto radical. Consequently, reactions of 2-methyl-2-nitrocyclopropyl methyl ketone with the sodium salt of benzenesulfinate were attempted in dimethyl sulfoxide and N,N-dimethylformamide. Even with extensive sunlamp irradiation in both cases, the only identifiable isolate was the starting 2-methyl-2-nitrocyclopropyl methyl ketone.

3. Attempts to react 2-methyl-2-nitrocyclopropyl methyl ketone with potassium benzenethiolate

Potassium benzenethiolate (generated by the action of potassium t-butoxide on thiophenol) was irradiated with 2-methyl-2-nitrocyclopropyl methyl ketone in dry dimethyl sulfoxide under nitrogen for 18 hours. After an aqueous work-up, ^{1}H N.M.R. analysis of the crude isolate revealed that only 2-methyl-2-nitrocyclopropyl methyl ketone was present. The absence of aromatic hydrogens by ^{1}H N.M.R. reveal that no cross-coupling had occurred.

In an additional attempt to trap the possible intermediate α-nitro radical, a five-fold excess of potassium benzenethiolate was employed under similar reaction conditions as mentioned above. Unfortunately, similar results were obtained when only 2-methyl-2-nitrocyclopropyl methyl ketone was identified from the crude isolate.

4. Attempts to react 2-methyl-2-nitrocyclopropyl methyl ketone with the anion of diethyl methylmalonate

Considering the number of enolates derived from mono- and di-carbonyl compounds that are capable of participating in the $S_{RN}1$ process with α-halonitroalkanes, it seems likely that the anion of diethyl methylmalonate might react with 2-methyl-2-nitrocyclopropyl methyl ketone. The enolate of diethyl methylmalonate (generated with sodium hydride) was allowed to react with 2-methyl-2-nitrocyclopropyl methyl ketone in N,N-dimethylformamide under a nitrogen atmosphere. Several attempts with extensive sunlamp irradiation failed to yield any cross-coupled products as revealed by careful G.C. and ^1H N.M.R. analyses. In a similar reaction employing a Rayonet photoreactor (350 nm) for irradiation, the crude isolate after an aqueous work-up was determined to contain only recovered diethyl methylmalonate (67.5%) and recovered 2-methyl-2-nitrocyclopropyl methyl ketone (76%).

5. Mechanistic considerations

Although 3(2-nitro-2-propyl)-5-nitro-2-hexanone was unexpectedly isolated from the reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the anion of 2-nitropropane, the formation of product can clearly

be explained by the $S_{RN}1$ process. With the radical chain character of the reaction well-established by inhibition studies, only two possible chain processes remained as alternatives. Since various nucleophiles which are capable of initiating the $S_{RN}1$ process and trapping α-nitro radicals failed to demonstrate the intermediacy of an α-nitro radical, the alternative mechanism containing an intramolecular electron transfer (Scheme 10, pathway c) appears unjustifiable.

It seems that pathway b of Scheme 10 is operative to a large extent. A description of the basic steps for the formation of 3(2-nitro-2-propyl propyl)-5-nitro-2-hexanone is provided in Scheme 11.

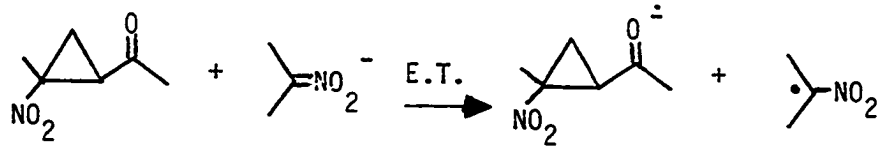
Scheme 11 describes the reaction of the anion generated from 2-nitropropane with 2-methyl-2-nitrocyclopropyl methyl ketone occurring via reductive cleavage of the cyclopropyl ring to form an α-keto radical (pathway b). Although the best explanation of the observed results coincide with pathway b, a very rapid intramolecular electron transfer (Scheme 10, pathway c) from enolate ion to α-nitro radical cannot be totally excluded.

6. Sodium dithionite reduction of 2-methyl-2-nitrocyclopropyl methyl ketone

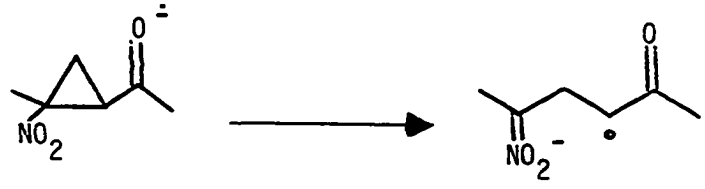
Recently, Krapcho and Seidman have studied the stereochemistry of the sodium dithionite ($Na_2S_2O_4$) reduction of cyclic ketones and found that cyclohexanones yielded mainly equatorial alcohols while bicyclic ketones gave primarily endo alcohols. On the basis of this stereochemical result, they suggested that reduction of the carbonyl group

Scheme 11

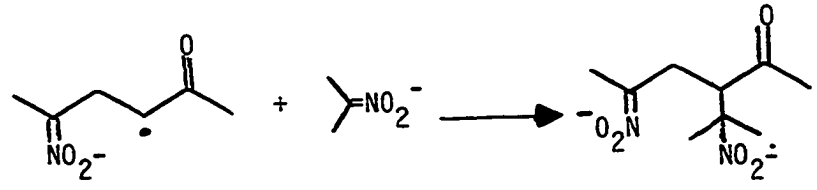
Step 1: Initiation



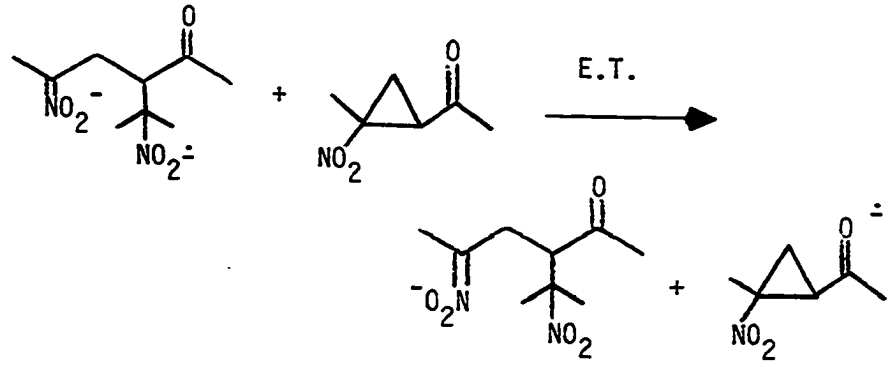
Step 2: Propagation



Step 3: Propagation



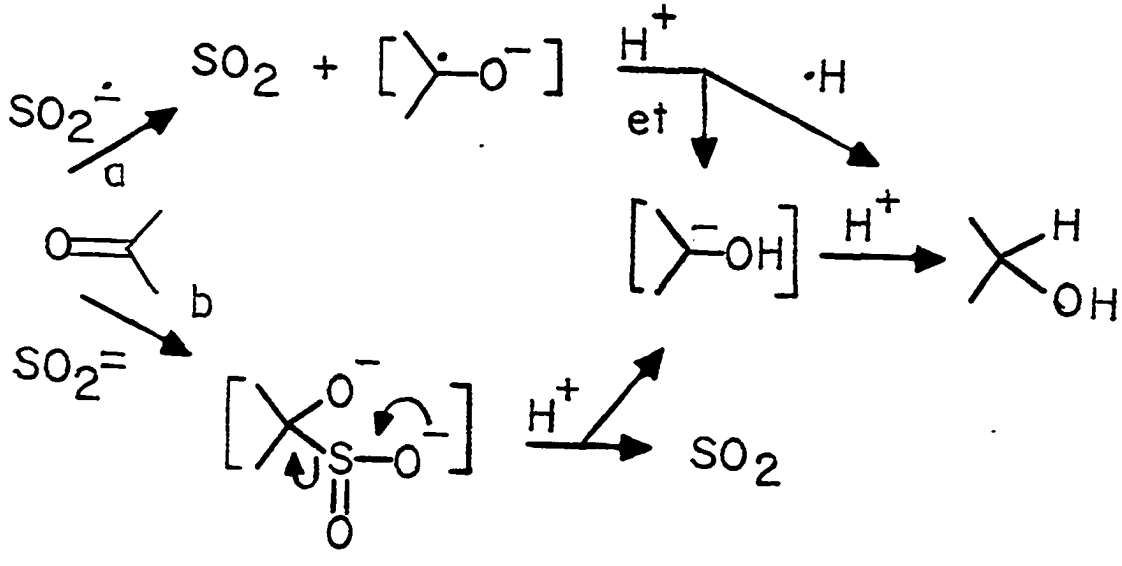
Step 4: Propagation



by $Na_2S_2O_4$ proceeded by an electron transfer mechanism in a manner similar to that of dissolving metal reductions of ketones [88].

There are basically two distinct mechanisms that are possibilities for the $Na_2S_2O_4$ reduction of carbonyl compounds as shown in Scheme 12, since the identity of the immediate reducing species is not yet clear. Although dithionite ions are known to dissociate reversibly to $SO_2^{\cdot-}$ radical anions in aqueous solution [89], electron exchange may be possible between the radical anions to form SO_2 and $SO_2^{=}$ dianion as reducing species.

Scheme 12

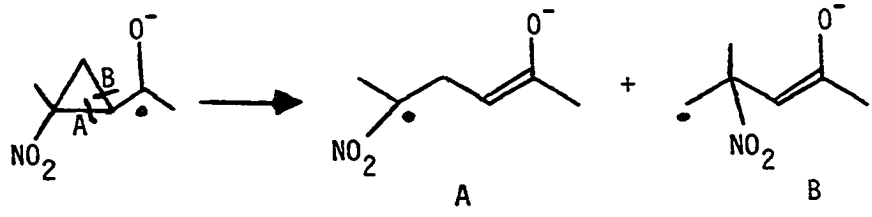


The first mechanism (pathway a) involves stepwise electron transfer from the reducing agent ($Na_2S_2O_4$) to the carbonyl group to form a ketyl radical intermediate. The ketyl radical intermediate can undergo a variety of reactions, such as abstraction of a hydrogen atom from the medium, dimerization, further reduction, or intramolecular rearrangement.

It is interesting to note that dissolving metal reductions of cyclopropyl ketones invariably gives the ring-opened products despite the well-documented efficiency of the second electron reduction of the conditions [90].

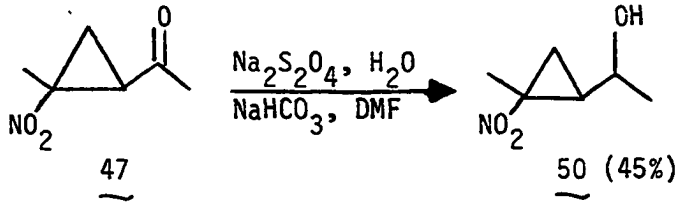
The second pathway (b) involves a nucleophilic addition of the $SO_2^=$ dianion or its equivalent to the carbonyl group to form an intermediate α-hydroxy sulfinate which then loses SO_2 to give a carbanionic species. If reduction occurs by a stepwise electron transfer mechanism, the $Na_2S_2O_4$ reduction of 2-methyl-2-nitrocyclopropyl methyl ketone should yield a ring-opened product from the intermediates shown below in Scheme 13.

Scheme 13



It should seem apparent based upon the previous section that should the ketyl radical undergo a ring-opening reaction, intermediate A should be formed preferentially over intermediate B. The prediction that the cleavage of the carbon-carbon bond would occur along pathway A is based upon the expected stabilization of the α-nitro radical compared to the unstabilized primary alkyl radical.

The reduction of 2-methyl-2-nitrocyclopropyl methyl ketone was carried out with $Na_2S_2O_4$ and $NaHCO_3$ in an aqueous DMF at 110°C under a nitrogen atmosphere. Only one reduction product was isolated from the reaction mixture. The reduction of 2-methyl-2-nitrocyclopropyl methyl ketone 47 with $Na_2S_2O_4$ yielded (0.39 g, 45%) of 2-methyl-2-nitrocyclopropyl methyl carbinol 50 (Eq. 36). 2-Methyl-2-nitrocyclopropyl methyl



47 50 (45%) (36)

carbinol 50 obtained by sodium dithionite reduction of 2-methyl-2-nitrocyclopropyl methyl ketone 47 compared favorably with an authentic sample of 50 obtained by sodium borohydride reduction. Careful G.C. and ^1H N.M.R. analyses of the crude isolate failed to reveal the presence of any ring-opened compounds. The yield of 2-methyl-2-nitrocyclopropyl methyl carbinol was low due to the incomplete reaction as verified by unreacted (29%) 2-methyl-2-nitrocyclopropyl methyl ketone.

7. Sodium dithionite reduction of cyclopropyl methyl ketone

Recently, Chung has reported the reduction of phenyl cyclopropyl ketone with sodium dithionite to yield phenyl cyclopropyl carbinol without any evidence for ring-opened products [91]. On the basis of

Chung's results, he suggests that reduction of the carbonyl group proceeds with the formation of a α-hydroxy sulfinate intermediate (pathway b, Scheme 12). His choice of substrates to use as a free-radical clock to determine the mechanisms of sodium dithionite reduction seems questionable, since the formation of a relatively stable intermediate benzyl ketyl radical could significantly affect the ring opening of the cyclopropyl free-radical probe. This argument can be justified as a logical extension of the effects observed in the previous section.

A more prudent choice of substrate to determine the mechanistic pathway of sodium dithionite reduction would be cyclopropyl methyl ketone. The reduction of cyclopropyl methyl ketone was carried out with $Na_2S_2O_4$ and $NaHCO_3$ in an aqueous DMF solution at 110°C under nitrogen. The reduction product was found to be cyclopropyl methyl carbinol (88.1%) as compared with an authentic cyclopropyl methyl carbinol obtained by sodium borohydride reduction of cyclopropyl methyl ketone. Careful product analyses by G.C., G.C.M.S., and ^1H N.M.R. failed to reveal the presence of any ring-opened products.

8. Sodium dithionite reduction of 6-hepten-2-one

Considering the results of the sodium dithionite reduction of 2-methyl-2-nitrocyclopropyl methyl ketone and cyclopropyl methyl ketone, it seemed worthwhile if not likely that the reduction of 6-hepten-2-one should be attempted. Consequently, the sodium dithionite reduction of 6-hepten-2-one yielded 6-hepten-2-ol (83%) and unreacted 6-hepten-2-one (8.7%) under similar reaction conditions as previously discussed. G.C.

and ^1H N.M.R. analyses of the crude isolate failed to reveal the presence of ring-cyclized products as would be predicted if the sodium dithionite reduction occurred by a stepwise electron transfer mechanism.

In summary, it appears the reduction of carbonyl compounds occurs with the nucleophilic addition of the SO_2 dianion to form an intermediate α-hydroxy sulfinate based upon the previously reported results, although the electron transfer pathway may become available if the adduct formation becomes difficult due to steric reasons.

C. Conclusion

A novel reaction involving 2-methyl-2-nitrocyclopropyl methyl ketone was investigated. Strong support for a chain reaction involving radical anions was provided by the fact that 10% di-t-butyl nitroxide and 10% p-dinitrobenzene completely inhibits the reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane. The cleavage of a carbon-carbon bond represents the first example of a carbon bonded leaving group in the aliphatic $S_{RN}1$ process. The unexpected mode of ring-opening undoubtedly occurs due to the thermodynamical preference of forming a weaker conjugate base. Several attempts to observe an alternate pathway of ring cleavage with various nucleophiles failed.

Also, results of reducing several ketones with sodium dithionite appear to indicate reduction of carbonyls occurs with the nucleophilic addition of SO_2^{-2} to form an intermediate α-hydroxy sulfinate instead of an electron transfer process.

D. Experimental Section

1. General considerations

2-Methyl-2-nitrocyclopropyl methyl ketone was prepared by the general intramolecular cyclization procedure of Russell, Makosza, and Hershberger [92] for the synthesis of nitrocyclopropanes. Sodium hydride was slowly added to a solution of 5-chloro-5-nitrohexan-2-one in DMF. After the evolution of hydrogen stop and an aqueous work-up, the vacuum distillation (103°C/25 torr) of the crude isolate afforded 2-methyl-2-nitrocyclopropyl methyl ketone 47 (71%).

5-Chloro-5-nitrohexan-2-one was prepared by the Michael addition of the anion of 1-chloro-1-nitroethane generated with Triton B (40% methanol) to methyl vinyl ketone in acetonitrile. After acidification (dilute hydrochloric acid), the product was extracted with methylene chloride and vacuum distilled (84°C/0.8 torr) to yield 72% of 5-chloro-5-nitrohexan-2-one. This compound has been previously prepared and characterized.

1-Chloro-1-nitroethane was prepared by the addition of chlorine to an ice-cold aqueous solution of nitroethane and sodium hydroxide. The resulting bottom layer was separated, washed with aqueous thiosulfate, dried ($MgSO_4$), and distilled to yield 83% of 1-chloro-1-nitroethane.

An authentic sample of cyclopropyl methyl carbinol was prepared by sodium borohydride reduction of cyclopropyl methyl ketone.

Methyl vinyl ketone, nitroethane, and p-dinitrobenzene were purchased from Aldrich. Sodium dithionite was purchased from Matheson.

2. Preparation of 3(2-nitro-2-propyl)-5-nitro-2-hexanone by the reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the lithium salt of 2-nitropropane

2-Methyl-2-nitrocyclopropyl methyl ketone (0.66 g, 4.6 mmol) was added to a solution of the lithium salt of 2-nitropropane (0.44 g, 4.6 mmol) in 10 ml of dry DMF under nitrogen. The solution was irradiated with a 275 Watt sunlamp placed 16 cm from the Pyrex flask. After 22 hours of irradiation, the reaction mixture was poured into 20 ml of water and extracted three times with 15 ml of ether. The combined extract was washed with water and brine. After drying with magnesium sulfate, the ether solution was concentrated. The crude isolate was purified for analysis by Kugelrohr distillation (85°C/2.9 mm) to yield 0.54 g (50.4%) of pure colorless product 49.

^{1}H N.M.R. ($CDCl_3$) δ 4.55 (m, 1H, $-(CH_3)C(\underline{H})NO_2$), 2.82 (m, 2H, $-\underline{CH_2}-$), 2.32 (s, 3H, $-C(O)\underline{CH_3}$, 1.9 (s, 3H, $-C(\underline{CH_3})(NO_2)$), 1.83 (s, 3H, $-C(\underline{CH_3})(NO_2)$), 1.5 (d, 3H, J_H = 6 Hz, $-\underline{CH_3}CH(NO_2)$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 204.59, 141.44, 132.27, 82.07, 35.26, 30.95, 22.89, 21.59, 18.59.

I.R. (neat, NaCl plates, cm^{-1}) 3000 (m), 2980 (m), 1690 (s), 1550 (vs), 1460 (m), 1400 (m), 1360 (m), 1300 (m), 1195 (m), 1145 (m), 1105 (m), 860 (m).

M.S. (P-93 peak measured). Calculated for $C_9H_{15}O$: 139.11229. Measured: 139.11235. Error = +0.4 ppm. M.S. (P-62 peak measured). Calculated for $C_8H_{12}NO_3$: 170.08172. Measured: 170.08228. Error = +3.3 ppm.

3. Effect of light on the reaction of 2-nitropropane anion with 2-methyl-2-nitrocyclopropyl methyl ketone

2-Methyl-2-nitrocyclopropyl methyl ketone (0.366 g, 2.56 mmol) was added *via* a syringe through a foil-covered septum to a solution containing the lithium salt of 2-nitropropane (0.247 g, 2.6 mmol) in 5 ml of dry DMF under nitrogen. The flask was wrapped tightly with several layers of aluminum foil to exclude light. After stirring for 14.5 hours, the reaction mixture was worked-up as previously described. ^{1}H N.M.R. analysis of the crude isolate showed that no 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 had been formed and (0.335 g, 91.5%) of 2-methyl-2-nitrocyclopropyl methyl ketone 47 remained.

4. Effect of oxygen on the reaction of 2-nitropropane anion with 2-methyl-2-nitrocyclopropyl methyl ketone

2-Methyl-2-nitrocyclopropyl methyl ketone (0.251 g, 1.75 mmol) was added *via* a syringe through a septum to a solution containing the lithium salt of 2-nitropropane (0.179 g, 1.88 mmol) in 5 ml of dry DMF saturated with oxygen. The solution was irradiated with a 275 Watt sunlamp located 17 cm from the Pyrex flask. After 14.5 hours, the reaction was worked-up as previously described. ^{1}H N.M.R. analysis showed that no 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 had been formed and 2-methyl-2-nitrocyclopropyl methyl ketone 47 (0.229 g, 91.2%) remained.

5. Effect of di-t-butyl nitroxide on the reaction of 2-nitropropane anion with 2-methyl-2-nitrocyclopropyl methyl ketone

2-Methyl-2-nitrocyclopropyl methyl ketone (0.307 g, 2.14 mmol) was added *via* a syringe through a septum to a solution containing the

lithium salt of 2-nitropropane (0.205 g, 2.16 mmol) and di-t-butyl nitroxide (0.031 g, 0.2 mmol) in 5 ml of dry DMF under nitrogen. The solution was irradiated with a 275 Watt sunlamp located 16 ml from the Pyrex flask. After 14.5 hours, the reaction mixture was treated as previously described. ^{1}H N.M.R. indicated little or no 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 was formed and only starting material 47 (92.2%) remained.

6. Effect of p-dinitrobenzene on the reaction of 2-nitropropane anion with 2-methyl-2-nitrocyclopropyl methyl ketone

2-Methyl-2-nitrocyclopropyl methyl ketone (0.286 g, 2.0 mmol) was added via a syringe through a septum to a solution containing the lithium salt of 2-nitropropane (0.195 g, 2.05 mmol) and p-dinitrobenzene (0.034 g, 0.2 mmol) in 5 ml of dry DMF under a nitrogen atmosphere. The solution was irradiated with a 275 Watt sunlamp located 16 cm from the Pyrex flask. After 14.5 hours, the reaction mixture was worked-up as previously described. ^{1}H N.M.R. analysis showed that no 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 had been formed and 2-methyl-2-nitrocyclopropyl methyl ketone 47 (0.256 g, 89.6%) remained.

7. Reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with anion of 2-nitropropane

2-Methyl-2-nitrocyclopropyl methyl ketone (0.250 g, 1.74 mmol) was added via a syringe to a solution containing the lithium salt of 2-nitropropane (0.166 g, 1.75 mmol) in 5 ml of dry DMF saturated with nitrogen. The solution was irradiated with a 275 Watt sunlamp located 16 cm from the Pyrex flask for 14.5 hours. The reaction mixture was

worked-up as previously described. ^{1}H N.M.R. analysis showed that (0.235 g, 58.2%) of 3(2-nitro-2-propyl)-5-nitro-2-hexanone 49 was formed and 2-methyl-2-nitrocyclopropyl methyl ketone 47 (0.068 g, 27.3%) remained.

8. Attempted reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with sodium benzenesulfinate

2-Methyl-2-nitrocyclopropyl methyl ketone (0.49 g, 3.43 mmol) was added to an ice-cold DMSO solution containing sodium benzenesulfinate (0.59 g, 3.6 mmol). The nitrogen flushed reaction mixture was irradiated with a 275 Watt sunlamp for 24 hours. The reaction mixture was extracted from brine with ether. The extract was washed with water, dried (Na_2SO_4), and concentrated to yield 0.397 g of liquid. ^{1}H N.M.R. revealed the isolate to contain only 2-methyl-2-nitrocyclopropyl methyl ketone (81%).

9. Attempted reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with potassium benzenethiolate

2-Methyl-2-nitrocyclopropyl methyl ketone (0.4433 g, 3.1 mol) was syringed into a solution of potassium t-butoxide (0.3725 g, 3.32 mmol) and thiophenol (9.365 g, 3.31 mol) in 10 ml of dry DMSO under a nitrogen atmosphere. The Pyrex reaction flask was irradiated for 18 hours at ambient temperatures with a 275 Watt sunlamp placed 17 cm away. The reaction mixture was extracted from brine with ether. The extract was washed with water and brine. The resulting organic solution was dried ($MgSO_4$) and concentrated to yield 0.29 g of crude isolate. ^{1}H N.M.R. analysis of the crude isolate revealed 66% of the starting ketone 47

had been recovered. There was no evidence of $CH_3(NO_2)C(SC_6H_5)CH_2CH_2C(O)$-$CH_3$ or $CH_3(NO_2)CHCH_2CH(SC_6H_5)C(O)CH_3$ being present.

10. Attempted reaction of 2-methyl-2-nitrocyclopropyl methyl ketone with the anion of diethyl methylmalonate

2-Methyl-2-nitrocyclopropyl methyl ketone (0.78 g, 5.45 mmol) was added to a solution of sodium hydride (0.1268 g, 5.28 mmol) and diethyl methylmalonate (0.932 g, 5.35 mmol) in 15 ml of dry DMF under a nitrogen atmosphere. After 19 hours of irradiation with a 275 Watt sunlamp, the solution was extracted from brine with ether. The ether solution was consecutively washed with water and brine, dried ($MgSO_4$), and concentrated. The crude isolate appeared to be only starting material as revealed by ^1H N.M.R. and G.C. analyses.

A similar reaction employing 2-methyl-2-nitrocyclopropyl methyl ketone (0.8847 g, 6.19 mmol), diethyl methylmalonate (1.09 g, 6.25 mmol), and sodium hydride (0.1485 g, 6.19 mmol) was irradiated using a Rayonet photoreactor (350 nm) for 53 hours. After a similar work-up procedure, the crude isolate (1.4 g) was determined to contain diethyl methylmalonate (0.73 g, 67.5%) and 2-methyl-2-nitrocyclopropyl methyl ketone (0.69 g, 76%) by ^1H N.M.R. and G.C. analyses.

11. Sodium borohydride reduction of 2-methyl-2-nitrocyclopropyl methyl ketone

A slurry of sodium borohydride (72.7 mg, 1.9 mmol) in 10 ml of isopropanol was added to a cooled (0°C) flask containing 2-methyl-2-nitrocyclopropyl methyl ketone (0.55 g, 3.8 mmol). The resulting solution was refluxed for one hour. The cooled solution was treated with

10 ml of 10% NaOH until all of the precipitate dissolved. The alkaline solution was transferred to a separatory funnel and extracted with three 15 ml portions of methylene chloride. The combined methylene chloride extract was washed with brine, dried (Na_2SO_4), and evaporated.

2-Methyl-2-nitrocyclopropyl methyl ketone was completely reduced as shown by I.R. and ^1H N.M.R. analyses. The resulting crude alcohol (0.495 g) was recrystallized from hexane to yield 0.447 g of a white solid which has a sharp melting point (89-90°C). 2-Methyl-2-nitrocyclopropyl methyl carbinol 50 was isolated with a 80% yield.

^1H N.M.R. ($CDCl_3$) δ 3.4 (m, 1H, -$\underline{H}$C(OH)CH_3), 1.83 (s, 3H, $\underline{CH_3}C(NO_2)$-), 1.35 (d, 3H, -HC(OH)$\underline{CH_3}$).

^{13}C N.M.R. (proton decoupled, $CDCl_3$, reported in ppm from TMS) 68.28, 64.38, 37.14, 23.10, 22.39, 14.87.

I.R. (KBr pellet, cm^{-1}) 3250 (vs, broad), 2990 (m), 1570 (vs), 1450 (m), 1390 (m), 1370 (m), 1350 (vs), 1170 (m), 1110 (s), 1080 (s), 1060 (m), 965 (m), 880 (s), 860 (m), 720 (m).

M.S. (P-15 peak measured). Calculated for $C_5H_8NO_3$: 130.05042. Measured: 130.05018. Error = -1.9 ppm.

12. Sodium dithionite reduction of 2-methyl-2-nitrocyclopropyl methyl ketone

Sodium dithionite (2.09 g, 12 mmol) was added slowly to a solution at 100°C containing sodium bicarbonate (2.01 g, 24 mmol) and 2-methyl-2-nitrocyclopropyl methyl ketone (0.87 g, 6.08 mmol) in 14 ml of DMF under a nitrogen atmosphere. Water (6 ml) was added to the reaction mixture immediately after the addition of sodium dithionite. After the

reaction mixture was heated (110°C) for 2 hours, the solution was cooled and 30 ml of cold water was added. The resulting solution was extracted with 3 x 25 ml of methylene chloride. The methylene chloride solution was washed with water (2 x 25 ml) and dried (Na_2SO_4). The solvent was removed under reduced pressure to yield 0.64 g of crude isolate.

G.C. analysis of the volatile compounds revealed that only two major compounds existed in the crude isolate. ^1H N.M.R. revealed that the crude isolate contained 2-methyl-2-nitrocyclopropyl methyl ketone (0.25 g, 28.7%) and 2-methyl-2-nitrocyclopropyl methyl carbinol 50 (0.39 g, 45%) which compares favorably to the alcohol 50 previously isolated from the sodium borohydride reduction of 2-methyl-2-nitrocyclopropyl methyl ketone.

13. Sodium dithionite reduction of cyclopropyl methyl ketone

Sodium dithionite (8.25 g, 47.4 mmol) was added slowly to a warm solution (100°C) of cyclopropyl methyl ketone (2.0 g, 23.7 mmol) and sodium bicarbonate (8.0 g, 95.2 mmol) in 45 ml of DMF under a nitrogen atmosphere. After the addition of sodium dithionite, 15 ml of water was immediately added to the reaction mixture. The mixture of reactants was heated (110°C) for 2 hours and then allowed to cool to room temperature. G.C. and G.C.M.S. analyses of the DMF solution reveal the presence of only two volatile compounds. Comparison of the G.C. retention time and G.C.M.S. fragmentation pattern of the reaction mixture with authentic samples of cyclopropyl methyl carbinol and cyclopropyl

methyl ketone verified that no ring-opened reduction products were formed. G.C. analysis of the reaction mixture showed that 88.1% of the cyclopropyl methyl ketone was reduced.

14. Sodium dithionite reduction of 6-hepten-2-one

Sodium dithionite (5.2 g, 30 mmol) was added to a solution of 6-hepten-2-one (1.6 g, 14.3 mmol) and sodium bicarbonate (5.04 g, 60 mmol) in 35 ml of DMF under a nitrogen atmosphere. After the addition of sodium dithionite, 15 ml of water was immediately added to the reaction mixture. The mixture of reactants was heated (110°C) for 2 hours and then allowed to cool to room temperature. The resulting solution was poured into 50 ml of water and extracted with 4 x 30 ml of methylene chloride. The combined methylene chloride solution was washed (water and brine) and dried (Na_2SO_4). The resulting solution was concentrated to yield 1.5 g of crude isolate. G.C. and ^1H N.M.R. analyses revealed that the crude isolate contained 1.35 g of 6-hepten-2-ol (83%) and 0.14 g of unreacted 6-hepten-2-one (8.7%). There was no evidence of any other compounds in the crude isolate.

PART II. REACTIONS OF NUCLEOPHILES WITH 1,1-DINITRO-2,2-DIPHENYLETHYLENE

I. REACTIONS OF NUCLEOPHILES WITH 1,1-DINITRO-2,2-DIPHENYLETHYLENE

A. Introduction

It is interesting to note that many nucleophiles which engage in aliphatic substitution reactions by the $S_{RN}1$ process are usually quite unreactive towards aromatic substrates. For example, the anions formed from β-carbonyl compounds, such as malonic esters, acetoacetic esters, and 2,4-pentanedione, are unreactive towards both halobenzenes [93] and 2-haloquinolines [94], although β-carbonyl compounds readily react with 2-chloro-2-nitropropane by the $S_{RN}1$ process. It appears the range of nucleophiles which are known to participate in $S_{RN}1$ reactions are dependent on the class of substrates (aliphatic or aromatic).

One possible explanation for the difference in reactivities of the various nucleophiles can be rationalized as arising from the concept of π- and σ-electronic structures of free radicals. A π-radical is a radical in which the unpaired electron is delocalized over a set of p-orbitals, whereas a σ-radical is a radical in which the unpaired electron is in an orbital with s-character. The difference in electronic structures of σ- and π-radicals may explain the difference in reactivities of various nucleophiles with the substrates that participate in the $S_{RN}1$ process. A considerable amount of research continues to address the controversy of reactivities of π- and σ-radicals at this time.

In Part II of this dissertation, reactions of various nucleophiles with 1,1-dinitro-2,2-diphenylethylene 51 will be discussed. It was

$Ph_2C{=}C(NO_2)_2$

51

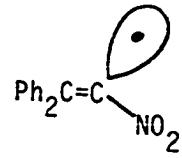
originally envisioned that 1,1-dinitro-2,2-diphenylethylene might undergo substitution (Eq. 37) by an electron transfer process similar to

$$Ph_2C{=}C(NO_2)_2 + N^- \longrightarrow Ph_2C{=}C(N)NO_2 + NO_2^- \qquad (37)$$

51 52

the $S_{RN}1$ reaction which occurs readily for 2,2-dinitropropane and other 2-substituted-2-nitro alkanes. If 1,1-dinitro-2,2-diphenylethylene undergoes substitution by an electron transfer process which involves an intermediate σ-radical (Scheme 14), then it could be rationalized that 1,1-dinitro-2,2-diphenylethylene should have a similar reactivity as halobenzenes since both would involve the intermediacy of σ-radicals.

Scheme 14



σ- radical

Evidence for the difference of reactivities of π- and σ-radicals could be demonstrated if 1,1-dinitro-2,2-diphenylethylene reacts with nucleophiles that only participate in the aromatic $S_{RN}1$ process. It is interesting to note that a $S_{RN}1$ process with 1,1-dinitro-2,2-diphenylethylene would represent the first example of a vinyl analog in the $S_{RN}1$ process.

B. Results and Discussion

1. Reactions of 1,1-dinitro-2,2-diphenylethylene with various enolates

There are numerous examples of enolates adding to sterically unhindered activated nitro olefins in the literature. We originally throught that 1,1-dinitro-2,2-diphenylethylene might undergo substitution (Eq. 37) by an electron transfer process due to the steric hindrance of the two phenyl groups. However, a competing conjugate addition process with various nucleophiles may predominate with small nucleophiles since the olefin is strongly activated by two nitro groups. It was previously mentioned that the Michael addition reaction is most successful with well-stabilized anions with yields often decreasing with increasing reactivity of the nucleophiles.

Several attempts at reacting the anion of dimethyl malonate (stabilized enolate) with 1,1-dinitro-2,2-diphenylethylene failed to yield substitution products after irradiation with a sunlamp in THF. The only observable compounds after irradiation and subsequent isolation procedures were identified as starting materials. In a similar experiment, acidification of the reaction mixture failed to yield a Michael-type adduct. Reactions employing the anion of diethyl methylmalonate with 1,1-dinitro-2,2-diphenylethylene yielded results similar to those obtained with the anion of dimethyl malonate. However, primary enolates, such as those derived from acetone and pinacolone, readily add to 1,1-dinitro-2,2-diphenylethylene (Eq. 38). The Michael adducts of the primary enolates have been protonated, isolated, and

$$Ph_2C{=}C(NO_2)_2 + N^- \longrightarrow Ph_2\overset{N}{\overset{|}{C}}\text{-}\bar{C}(NO_2)_2 \xrightarrow{H^+} Ph_2\overset{N}{\overset{|}{C}}\text{-}CH(NO_2)_2 \quad (38)$$

characterized completely (Table 10). Reactions employing primary enolates with 1,1-dinitro-2,2-diphenylethylene and sunlamp irradiation, followed by an aqueous isolation procedure without acidification, failed to yield substitution-type products. These results compare favorably to those obtained with secondary and tertiary enolates.

Presumably, steric hindrance is the reason for the failure of secondary and tertiary enolates to add to 1,1-dinitro-2,2-diphenylethylene. However, the possibility exists that for these enolates, the Michael adducts were unstable and underwent reversion during the isolation procedure.

2. Reactions of 1,1-dinitro-2,2-diphenylethylene with the anion of 2-nitropropane

The possibility that Michael adducts are unstable and may undergo reversion during the isolation procedure has been supported by several experiments with the anion of 2-nitropropane and 1,1-dinitro-2,2-diphenylethylene. Recently, Bernasconi, Carré, and Kanavarioti have reported the complete kinetic analysis of hydrolytic cleavage of the carbon-carbon double bond of 1,1-dinitro-2,2-diphenylethylene to form benzophenone and dinitromethane anion [95]. However, under the isolation procedure employed in this work, hydrolysis was negligible and recovered yields of 1,1-dinitro-2,2-diphenylethylene of 97-98% could be isolated from reactions with nucleophiles such as azide (N_3^-) or thiocyanate (SCN^-).

Table 10. Reaction of 1,1-dinitro-2,2-diphenylethylene with various enolates in THF

$$Ph_2C{=}C(NO_2)_2 + N^- \xrightarrow{H^+,THF} Ph_2C(N)CH(NO_2)_2$$

N^-	Yield %[a]	
	$Ph_2C(N)CH(NO_2)_2$	$Ph_2C{=}C(NO_2)_2$
$(EtO_2C)_2CMe^-$	0	94 (G.C.)
$(MeO_2C)_2CH^-$	0	97 (G.C.)
$MeCOCH_2^-$	51 (I), 63 (N.M.R.)	28 (G.C.)
$Me_3CCOCH_2^-$	42 (I), 57 (N.M.R.)	33 (G.C.)
$PhCOCH_2^-$	64 (N.M.R.)	++ (G.C.)

[a](I), isolated yield; (N.M.R.), ^1H N.M.R. yield with internal standard; (G.C.), G.C. yield with internal standard.

Evidence for a possible unstable Michael adduct with 1,1-dinitro-2,2-diphenylethylene and the anion of 2-nitropropane follows from the observation that treatment of the reaction mixture with brine led to a high yield of recovered 1,1-dinitro-2,2-diphenylethylene, whereas treatment of the reaction mixture with mineral acids led to a high yield of benzophenone ($Ph_2C{=}O$). In this example, the adduct apparently reverted to 1,1-dinitro-2,2-diphenylethylene during an aqueous work-up, but in an acidic solution, the adduct was hydrolyzed via $Ph_2C(OH)CH(NO_2)_2$ to benzophenone (see Table 13). The reaction products discussed so far in this section can all be explained by the initial Michael addition of the various nucleophiles to 1,1-dinitro-2,2-diphenylethylene instead of the envisioned electron transfer process.

3. Reaction of 1,1-dinitro-2,2-diphenylethylene with the sodium salt of phenylsulfinic acid

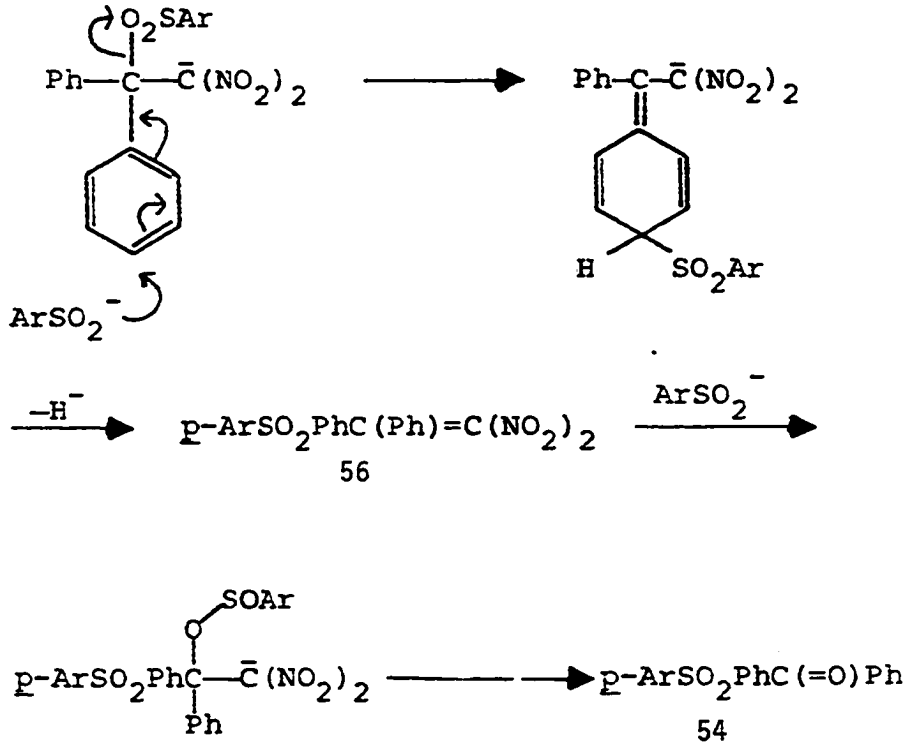
The sodium salt of phenylsulfinic acid ($PhSO_2^-$) reacts with 1,1-dinitro-2,2-diphenylethylene to produce p-phenylsulfonyl-benzophenone 54 and benzophenone 55 (Eq. 39). These products are assumed to be

$$\underset{\sim\sim}{53}\ PhSO_2^- + \underset{\sim\sim}{51}\ Ph_2C{=}C(NO_2)_2 \longrightarrow \underset{\sim\sim}{54}\ (21\%)\ p\text{-}ArSO_2PhC(=O)Ph + \underset{\sim\sim}{55}\ (74\%)\ Ph_2{=}O \qquad (39)$$

formed from initial conjugate addition of the nucleophile to 1,1-dinitro-2,2-diphenylethylene to form an intermediate Michael adduct. Evidence for the intermediary of a Michael adduct stems from the observation that with $PhSO_2^-$ in DMSO, a mixture of benzophenone and p-$ArSO_2PhCOPh$ were produced. Since benzophenone does not yield the

keto sulfone under similar reaction conditions, it appears that the intermediate Michael adduct of 1,1-dinitro-2,2-diphenylethylene may have reacted with a second equivalent of $PhSO_2^-$ to yield the substituted 1,1-dinitro-2,2-diphenylethylene 56 according to Scheme 15.

Scheme 15



The formation of p-phenylsulfonyl-benzophenone 54 can be rationalized by the mechanism in Scheme 15 which is similar to the nucleophilic aromatic substitution mechanisms (S_NAr). The loss of $PhSO_2^-$ in aromatic substitution processes is well-documented. The reaction of 1,1-dinitro-2,2-diphenylethylene with the sodium salt of p-toluene sulfinic acid

yielded the same type of reaction products as previously described with a comparable yield (see Table 13).

Several reactions were performed with one-half of an equivalent of sulfinic acid, sodium salt, and one-half of an equivalent of diethyl phosphite anion or methoxide with 1,1-dinitro-2,2-diphenylethylene to see if other substituted benzophenones could be synthesized. Unfortunately, these attempts were unsuccessful.

4. Reactions of 1,1-dinitro-2,2-diphenylethylene with anions of dialkyl phosphites and dialkyl thiophosphites

Several attempts at reacting the anion of diethyl phosphite (generated from diethyl phosphite and potassium t-butoxide) with 1,1-dinitro-2,2-diphenylethylene failed to yield substitution products in DMSO after irradiation with a sunlamp or Rayonet photoreactor (350 nm) for extended periods of time. The only observable product identified after an aqueous isolation procedure was unreacted 1,1-dinitro-2,2-diphenylethylene.

In a similar experiment, acidification of the reaction mixture yielded a stable Michael adduct for 1,1-dinitro-2,2-diphenylethylene with the anion of diethyl phosphite. Also, Michael adducts of a series of dialkyl phosphites and dialkyl thiophosphites have been protonated, isolated, and characterized completely (Table 11). It appears the anions of a variety of dialkyl phosphites undergo Michael addition to 1,1-dinitro-2,2-diphenylethylene instead of the envisioned electron transfer process.

Table 11. Reactions of 1,1-dinitro-2,2-diphenylethylene with dialkyl phosphite anions in DMSO

$$Ph_2C{=}C(NO_2)_2 + N^- \xrightarrow[DMSO]{H^+} Ph_2C(N)CH(NO_2)_2$$

N^-	Time (h); Temp. (0°C)	Yield %[a]	
		$Ph_2C(N)CH(NO_2)_2$	$Ph_2C{=}C(NO_2)_2$
$(MeO)_2P(=O)^-$	0.5; 25°	75 (I)	14 (G.C.)
$(EtO)_2P(=O)^-$	0.5; 25°	69 (I)	22 (G.C.)
$(MeO)_2P(=S)^-$	0.5; 25°	65 (I), 87 (N.M.R)	17 (G.C.)
$(EtO)_2P(=S)^-$	0.5; 25°	74 (N.M.R.)	++ (G.C.)

[a](I), isolated yield; (N.M.R.), ^1H N.M.R. yield with internal standard; (G.C.), G.C. yield with internal standard.

Michael adducts were also observed for $MeSO_2CH_2^-$ and $MeSOCH_2^-$ in DMSO with 1,1-dinitro-2-2-diphenylethylene. In methanol or ethanol, Michael adducts were also observed for methoxide (CH_3O^-) and cyanide (CN^-) anions, while no evidence was observed for the Michael addition of SCN^- in ethanol or Me_2SO nor in DMSO for nitrate (NO_3^-), azide (N_3^-), or diisoproylamide ($\underline{i}$-Pr)$_2N^-$. Steric hindrance may have prohibited the Michael adduct from forming with diisoproylamide, while it is this author's opinion that the Michael adducts of nitrate and azide probably underwent reversion.

5. Reaction of 1,1-dinitro-2,2-diphenylethylene with the anion of benzenethiol

The potassium salt of benzenethiol reacts with 1,1-dinitro-2,2-diphenylethylene to produce 1-nitro-1-phenylsulfide-2,2-diphenylethylene 56a (Eq. 40) in DMSO. The reaction was very fast at room temperature as

$$\underset{\sim\sim}{Ph_2C{=}C(NO_2)_2} + C_6H_5S^-K^+ \longrightarrow \underset{\sim\sim\sim}{Ph_2C{=}C(NO_2)SC_6H_5} + K^+NO_2^- \qquad (40)$$

51 56a (85%)

verified by the complete absence of 1,1-dinitro-2,2-diphenylethylene after less than 1 hour. We have found no evidence for a free radical chain reaction as judged by the lack of photostimulation and the absence of retardation by di-$\underline{t}$-butyl nitroxide.

Various other sulfur or selenium nucleophiles react with 1,1-dinitro-2,2-diphenylethylene to give similar substitution products 56a as shown in Table 12. We believe the substitutions are formed by the initial Michael attack of the nucleophiles followed by an internal

Table 12. Reaction of 1,1-dinitro-2,2-diphenylethylene with various nucleophiles to form 1-nitro-1-substituted-2,2-diphenylethylene

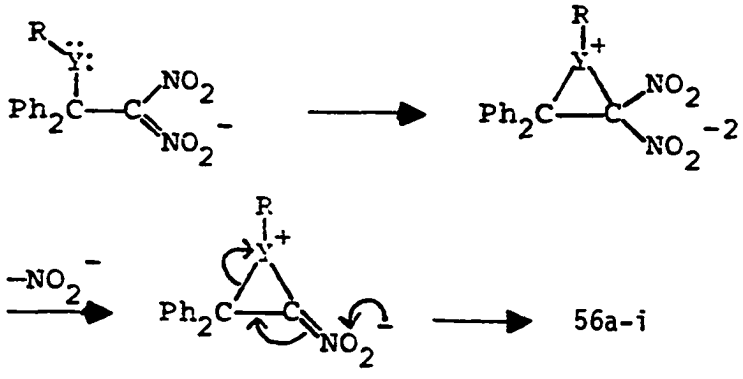
$$Ph_2C{=}C(NO_2)_2 + N^-K^+ \longrightarrow Ph_2C{=}C(N)NO_2 + K^+NO_2^-$$

56a-i

56	N^-	Time (h); Temp. (0°C)	% Yield Isolated
a	PhS^-	1; 25°	85
b	Me_3CS^-	1; 25°	32
c	p-$ClPhS^-$	1; 25°	68
d	p-$MePhS^-$	1; 25°	87
e	p-O_2NPhS^-	1; 25°	47
f	$PhSe^-$	1; 25°	48
g	PhO^-	36; 25°	49
h	p-$MeOPhO^-$	48; 25°	0
i	p-O_2NPhO^-	48; 25°	0

nucleophilic attack by an unbonded lone-pair of electrons on the original nucleophile and subsequent elimination of nitrite. Scheme 16 presents a possible rationale for this process.

Scheme 16



Y = O, S, Se; R = alkyl or aryl

The requirement for the formation of substitution products (Eq. 40) appears to be that a fairly nucleophilic O, S, or Se atom is attached to the diphenylmethyl carbon atom in the intermediate Michael adduct. The lack of reactivity of $\underline{p}$-O_2NPhO^- and low reactivity of $\underline{p}$-O_2NPhS^- is consistent with the formation of an oxiranyl or episulfonium zwitterion. The reactivity of $\underline{p}$-O_2NPhS^- appears to be lower than other substituted thiophenoxide nucleophiles because unreacted 1,1-dinitro-2,2-diphenylethylene was observed.

The yields of substituted products from the thiophenoxide nucleophiles appear to be significantly higher than the anions of phenoxide nucleophiles. The greater distribution of charge on the intermediate episulfonium zwitterion due to the larger sulfur atom may explain the

increased yields when thiophenoxide nucleophiles were used. Also, with sulfur atoms, the proximity of the unbonded pair of electrons is closer due to the larger orbitals, thus benefiting neighborhood participation.

The low yield of substituted product corresponding to $(CH_3)_3CS^-$ may be due to the incomplete ionization of the thiol. It is interesting to note that tert-butyl thiolate undergoes internal nucleophilic attack instead of β-elimination to form thiobenzophenone (see the following discussion). Analyses of the reaction mixture of 1,1-dinitro-2,2-diphenylethylene with tert-butyl thiolate by G.C. and G.C.M.S. failed to reveal the presence of any appreciable amount of thiobenzophenone.

6. Mechanistic considerations for the formation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene

Our investigations of the reactions of 1,1-dinitro-2,2-diphenylethylene support the hypothesis that a multi-step mechanism (Scheme 16) is occurring which involves initial Michael addition of the nucleophile (attack at C_β) to form an intermediate dinitromethide ion followed by an internal nucleophilic attack by an unbonded lone pair of electrons on the original nucleophile and subsequent elimination of nitrite. Evidence for the existence of an initial Michael adduct is supported by the observation of the dinitromethide ion intermedate (λ_{max} = 380 nm) with various sulfur and oxygen nucleophiles. However, the observation of the dinitromethide ion intermediate does not ensure the intermediacy when a leaving group is present.

Further support for a multi-step process leading to the formation of 1-substituted-1-nitro-2,2-diphenylethylene comes from the isolation

of a Michael adduct of 1,1-dinitro-2,2-diphenylethylene with methoxide at -78°C. Presumably, other Michael adducts were not isolated due to a competing β-elimination process or the increased ability of the nucleophiles to undergo internal nucleophilic attack due to the larger orbitals of sulfur or selenium atoms.

The lack of reactivity of $\underline{p}$-O_2NPhO^- and low reactivity of $\underline{p}$-O_2NPhS^- is consistent with the formation of an oxiranyl or episulfonium ion intermediate. However, the decrease in nucleophicity of the nucleophiles may also explain these results.

Although the formation of 1-substituted-1-nitro-2,2-diphenylethylene has been proposed to proceed by a multi-step process with initial Michael addition, there are other processes which should be discussed briefly which may be involved to some extent. The terms "addition-elimination", "synchronous addition-elimination", and "direct substitution" have been used to describe nucleophilic attack on C_α in a single or multi-step process. It has been previously mentioned that the transition state in nucleophilic vinylic substitution is variable [96]. The various possible intermediates depend on the nucleophile, on the solvent, and on the structural features of the substrate. Most of the possible routes available for vinylic substitution have been previously reviewed [97].

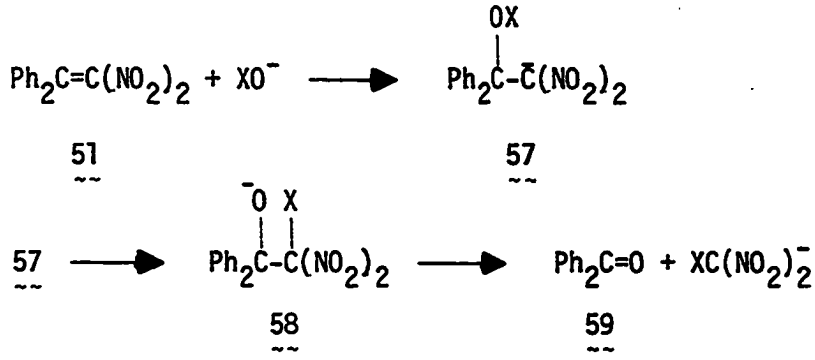
It seems unlikely to this author that sulfur nucleophiles will attack the alpha carbon, while all other nucleophiles appear to add to the beta carbon to form a Michael adduct. The above mentioned fact, along with the observation of the dinitromethide ion (380 nm) with the

anion of benzenethiol, also supports the multi-step process. Presumably, the substitution products are formed with sulfur, selenium, and oxygen nucleophiles because they contain an unbonded pair of electrons which are required for the neighborhood participation process shown in Scheme 16.

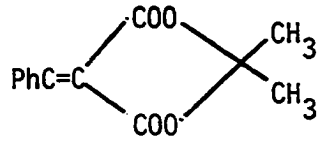
7. Reactions of 1,1-dinitro-2,2-diphenylethylene which yield predominately benzophenone

Reactions employing various oxyanions with 1,1-dinitro-2,2-diphenylethylene 51 yielded predominately benzophenone as the major reaction product. However, Michael adducts and substitution products were isolated for several oxyanions. Benzophenone was produced with nucleophiles such as NO_2^-, $ArSO_2^-$, $CH_3CO_2^-$, CH_3COS^-, EtO^-, and Me_3CO^-. It seems apparent to this author that the above mentioned nucleophiles initially add to 1,1-dinitro-2,2-diphenylethylene to yield a dinitromethide ion intermediate which presumably rearranged to a substituted benzhydrol intermediate 57 and then this benhydrol intermediate rapidly hydrolyzes to benzophenone 59 (Scheme 17).

Scheme 17



Bernasconi et al. have performed complete kinetic analyses of the hydrolytic cleavage of 1,1-dinitro-2,2-diphenylethylene 51 in acidic and basic solutions. Their results suggest that when X = H, the formation of intermediate 58 is very fast and the breakdown into benzophenone and dinitromethane anion is also very rapid. The departure of a carbanionic leaving group is remarkably rapid, but was accounted for by the low basicity of the carbanion (pK_a = 3.57) [98]. Jencks has mentioned that the expulsion of weakly carbanionic leaving groups for similar intermediates is very fast [99]. Bernasconi and Leonarduzzi have also studied the hydrolysis of benzylidene Meldrum's acid 60 which leads to



60

Meldrum's acid (pK_a = 4.83) and benzaldehyde [100]. They proposed a similar process for the hydrolysis of 60 as was suggested for the hydrolysis of 1,1-dinitro-2,2-diphenylethylene.

Support for the formation of benzophenone from 1,1-dinitro-2,2-diphenylethylene by a similar benzhydrol intermediate as the one proposed by Bernasconi comes from several sources, First, hydrolysis was negligible and recovered yields of 1,1-dinitro-2,2-diphenylethylene (97-98%) could be isolated from reactions with azide or thiocyanate. Second, attempts at trapping the initially formed dinitromethide ion intermediate formed with ethoxide, tert-butoxide, and phenoxide failed. However, the reaction of methoxide with 1,1-dinitro-2,2-diphenylethylene

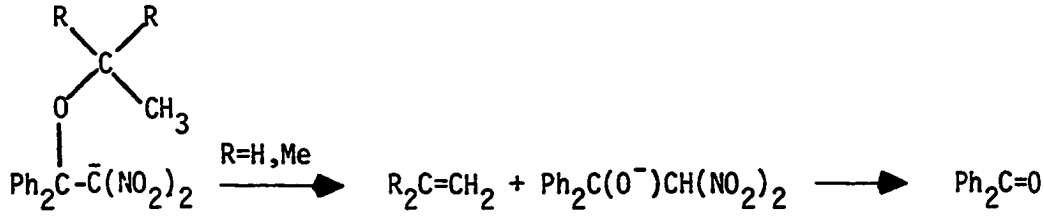
yields the Michael adduct (1,1-dinitro-2-methoxy-2,2-diphenylethane 61) upon acidification at -78°C. It is interesting to note that 1,1-dinitro-2-methoxy-2,2-diphenylethane could not be isolated under standard room temperature hydrolysis. The isolation at -78°C of 61 agrees with a

$Ph_2C(OMe)CH(NO_2)_2$

61

previous report by Rappoport, Albeck, and Hoz [101].

With nucleophiles such as ethoxide or tert-butoxide β-elimination of the initially formed Michael adduct is now a possibility (Eq. 41) which may explain why isolation of the Michael adducts were unsuccessful.



(41)

However, with N^- = alkoxide, it is difficult to exclude the formation of $Ph_2C=O$ from the hydrolysis of substitution products (see the following discussion).

The substitution product 62 derived from 1,1-dinitro-2,2-diphenylethylene and methoxide was identified but not isolated. There was ^1H N.M.R., G.C.M.S., and G.C.I.R. evidence for the existence of methyl vinyl ether 62, which formed benzophenone during attempts at isolation

$Ph_2C=C(OMe)NO_2$

62

of pure 1-nitro-1-methoxy-2,2-diphenylethylene 62. The formation of 1-nitro-1-methoxy-2,2-diphenylethylene is assumed to proceed by the same pathway that was previously presented for the formation of a series of vinyl nitro sulfides.

It appears the formation of benzophenone is more pronounced for the oxyanions than for the corresponding sulfur nucleophiles (Table 13). Benzophenone may have arisen from a competing reaction involving β-elimination of tert-butoxide, since potassium tert-butoxide was used in a slight stoichiometric excess to generate the anions employed. Alternately, the 1-nitrovinyl ethers and thioethers may have been hydrolyzed during isolation procedures. If this is the case, it suggests that thioethers are less readily hydrolyzed than their oxygen analogs.

Several attempts at monitoring the hydrolysis of 1-nitrovinyl ethers and thioethers in H_2O-p-dioxane at 25°C using the extinction coefficient of $Ph_2C{=}O$ at 256 nm apparently indicates that 1-nitrovinyl ethers are hydrolyzed faster than 1-nitrovinyl thioethers. Apparently, these qualitative rates reflect the basicities of the nitromethanes formed by acid catalyzed hydrolysis.

8. Oxidation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene

1-Nitro-1-phenylsulfide-2,2-diphenylethylene reacts with 30% hydrogen peroxide in glacial acetic acid to produce 1-nitro-1-phenylsulfoxide-2,2-diphenylethylene 63 with a satisfactory yield of 94%. However, a slight excess of two equivalents of 30% hydrogen peroxide

Table 13. Reactions of 1,1-dinitro-2,2-diphenylethylene with various nucleophiles in DMSO[a]

N^-	Yield %[b]			
	Recovered 51	$Ph_2C(N)CH(NO_2)_2$	$Ph_2C{=}C(N)NO_2$	$Ph_2C{=}O$
HO^-	0	0	0	96 (I)
MeO^-	4 (G.C.)	0	7 (N.M.R.)	73
$MeO^-(MeOH)$[c]	0	0[d], 42 (I)[e]	0	14 (G.C.)[d], 26 (G.C.)[e]
EtO^-	4 (I)	0	0	83 (I)
Me_3CO^-	1 (G.C.)	0	0	91 (I)
$ArSO_2^-$	5 (I)	0	0	74 (I)[f]
p-$MeArSO_2^-$	2 (I)	0	0	68 (I)[g]
NO_2^-	0	0	0	94 (I)
NO_3^-	95 (I)	0	0	2 (G.C.)
PhO^-	0	0	49 (I), 67 (G.C.)	31 (G.C.)
p-$MeOPhO^-$	4 (G.C.)	0	0 (G.C.)	86 (G.C.)
p-O_2NPhO^-	90 (I)	0	0 (G.C.)	3 (G.C.)
$MeCO_2^-$	74 (I)	0	0	19 (G.C.)
$MeC(=S)O^-$	67 (I)	0	0	21 (G.C.)

$Me_2C{=}NO_2^-$	92 (I)	0	0	0[h]

[a]Typical reactions on a 2 mmol scale involved a 1:1 ratio of 51 and K^+N^- (~0.05 M) under N_2 which was poured into brine from which reaction products were extracted.

[b](I), isolated yield; (G.C.), G.C. yield with internal standard.

[c]Ratio of N^-:51 = 13:1.

[d]Upon treatment of reaction product with mineral acid at 25°C, a 61% yield of the methyl ketal of $Ph_2C{=}O$ was also isolated.

[e]Acidification at dry ice-acetone temperature.

[f]A 21% yield of p-$PhSO_2PhCOPh$ was isolated.

[g]A 22% yield of p-(p-$MePhSO_2$)$^-$PhCOPh was isolated.

[h]Acidification by mineral acid gave an 88% yield of $Ph_2C{=}O$.

failed to form any observable amount of 1-nitro-1-phenylsulfonyl-2,2-diphenylethylene 64 as determined by I.R. analysis.

1-Nitro-1-phenylsulfonyl-2,2-diphenylethylene was prepared from 1-nitro-1-phenylsulfoxide-2,2-diphenylethylene and m-chloroperbenzoic acid in chloroform. Pure 1-nitro-1-phenylsulfonyl-2,2-diphenylethylene was obtained by recrystallization from ethyl acetate to afford 64 (65%). Epoxidation of the carbon-carbon double bond did not appear to interfere with the oxidation of the sulfoxide. This can be rationalized by the presence of electron withdrawing groups which are known to decrease the rate of epoxidation.

$Ph_2C{=}C(NO_2)S(O)Ph$ (63)

$Ph_2C{=}C(NO_2)SO_2Ph$ (64)

C. Conclusion

1,1-Dinitro-2,2-diphenylethylene reacts with a variety of nucleophiles to form several types of products. With nucleophiles (N^-), such as RS^- (R = tert-butyl, Ph, p-ClPh, p-O_2NPh, p-MePh), $PhSe^-$, or PhO^-, the intermediate dinitromethide ion undergoes rearrangement via an oxiranyl or episulfonium zwitterion to form $Ph_2C{=}C(NO_2)N$. Also, Michael adducts were formed with enolates, dialkyl phosphites, cyanide, and methoxide anions. With nucleophiles such as hydroxide, tert-butoxide, and ethoxide, the intermediate dinitromethide ion undergoes rearrangement to form benzophenone, presumably through an α-substituted benzhydrol intermediate.

Although no evidence was observed for an electron transfer process with 1,1-dinitro-2,2-diphenylethylene, several novel compounds were prepared. Perhaps, additional work with substituted phenyl groups may restrict nucleophilic addition to the dinitro olefin, thus allowing an electron transfer substitution process to occur.

D. Experimental Section

1. General considerations

1,1-Dinitro-2,2-diphenylethylene [102] and dimethoxy thiophosphite [103] were prepared by literature procedures.

Dimethyl malonate, methyl sulfide, 1,1-diphenylethylene, m-chloroperoxybenzoic acid, p-thiocresol, p-chlorothiophenol, 2-methyl-2-propanethiol, p-nitrothiophenol, phenol, 4-nitrophenol, and p-methoxyphenol were purchased from Aldrich. Acetophenone, potassium thiocyanate, and potassium nitrate were purchased from Baker. Reagent grade acetone, 30% hydrogen peroxide, and sodium methylate were purchased from Fisher, while sodium azide and sodium cyanide were purchased from Mallinckrodt.

2. General procedure for the reaction of enolates with 1,1-dinitro-2,2-diphenylethylene

The procedure for the reaction of 1,1-dinitro-2,2-diphenylethylene with the enolate of pinacolone is representative. n-Butyllithium (1.19 ml, 1.55 M in hexane) was added to a stirred solution of diisopropylamine (0.26 ml, 1.85 mmol) in dry THF (30 ml) under a nitrogen atmosphere at 0°C. After 30 minutes, the solution was cooled to -78°C

and pinacolone (0.232 ml, 1.85 mmol) was added slowly with a syringe. After 40 minutes, 1,1-dinitro-2,2-diphenylethylene (0.50 g, 1.85 mmol) in 10 ml of THF was added to the enolate solution.

After the solution was allowed to warm to room temperature, the THF was removed under reduced pressure. Ether was added to the resulting solid to form a suspension which was acidified with dilute hydrochloric acid. The ether layer was extracted, washed (brine), and dried (Na_2SO_4). A solid resulted after the removal of solvent under reduced pressure, which was subsequently recrystallized from methanol to afford 2,2-dimethyl-6,6-dinitro-5,5-diphenyl-3-hexanone (0.287 g, 42%, mp 146-147°C).

^1H N.M.R. ($CDCl_3$) δ 8.52 (s, 1H, $-\underline{CH}(NO_2)_2$), 7.17 (s, 10H), 3.63 (s, 2H, $-\underline{CH_2}-C(O)$), 0.76 (s, 9H, $C(\underline{CH_3})_3$).

I.R. (KBr pellet, cm^{-1}) 3030 (m), 2995 (m), 1695 (s), 1580 (vs), 1450 (m), 1370 (m), 1340 (m), 1080 (m), 750 (m), 700 (s).

M.S. Calculated for $C_{20}H_{22}N_2O_5$: 370.15288. Measured: 370.15268. Error = -0.5 ppm.

Elemental Analysis. Calculated for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.98; N, 7.56; O, 21.59. Found: C, 65.05; H, 5.98; N, 7.54.

3. Preparation of 5,5-dinitro-4,4-diphenyl-2-pentanone

Preparation of 5,5-dinitro-4,4-diphenyl-2-pentanone was carried out by the same procedure as described for 2,2-dimethyl-6,6-dinitro-5,5-diphenyl-3-hexanone. Recrystallization of the crude isolate from methanol yielded 5,5-dinitro-4,4-diphenyl-2-pentanone (51%, mp 137°C).

^{1}H N.M.R. ($CDCl_3$) δ 8.18 (s, 1H, -C<u>H</u>$(NO_2)_2$), 3.52 (s, 2H, -C(O)<u>CH_2</u>-), 1.69 (s, 3H, <u>CH_3</u>C(O)-).

I.R. (KBr pellet, cm^{-1}) 3010 (m), 1700 (s), 1580 (s), 1560 (s), 1350 (m), 1320 (m), 760 (m), 730 (m), 690 (m).

M.S. Calculated for $C_{17}H_{16}N_2O_5$: 328.10593. Measured: 328.10540. Error = -1.6 ppm.

Elemental Analysis. Calculated for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91, N, 8.53; O, 24.36. Found: C, 61.99; H, 5.11; N, 8.40.

4. Preparation of p-methyl-p-phenylsulfonyl-benzophenone

A solution of 1,1-dinitro-2,2-diphenylethylene (0.693 g, 2.56 mmol) in 10 ml of N,N-dimethylformamide was transferred under nitrogen to a stirred solution of p-toluene sulfinic acid sodium salt dihydrate (0.55 g, 2.56 mmol) in 20 ml of DMF at 25°C. The reaction mixture was allowed to stir overnight. The resulting black solution was poured into 75 ml of brine and extracted with ether (3 x 50 ml). The combined ether extracts were washed with water (3 x 50 ml) and then washed with 50 ml of brine. The resulting ether solution was dried ($MgSO_4$) and evaporated. The remaining residue was recrystallized from methanol to yield p-methyl-p-phenylsulfonyl-benzophenone (0.15 g, 22%, mp 199-200°C).

I.R. (KBr pellet, cm^{-1}) 1650 (s), 1595 (m), 1395 (m), 1320 (s), 1290 (s), 1160 (vs), 1100 (m), 750 (m), 690 (m), 670 (m).

M.S. Calculated for $C_{20}H_{16}O_3S$: 336.08202. Measured: 336.08180. Error = -0.6 ppm.

^{1}H N.M.R. ($CDCl_3$) δ 8.06-7.27 (m, 13H), 2.42 (s, 3H, $-\underline{CH_3}$).

Elemental Analysis. Calculated for $C_{20}H_{16}O_3S$: C, 71.41; H, 4.79; O, 14.27; S, 9.53. Found: C, 71.33; H, 4.88; S, 9.69.

5. Preparation of p-phenylsulfonyl-benzophenone

Preparation of p-phenylsulfonyl-benzophenone 54 was carried out by the same procedure as described for p-methyl-p-phenylsulfonyl-benzophenone. Recrystallization of the crude isolate from methanol yielded p-phenylsulfonyl-benzophenone 54 (21%, mp 142.5-143.5°C).

I.R. (KBr pellet, cm^{-1}) 1645 (s), 1445 (m), 1390 (m), 1315 (s), 1290 (s), 1155 (vs), 1100 (m), 745 (m), 705 (m), 685 (m).

M.S. Calculated for $C_{19}H_{14}O_3S$: 322.06637. Measured: 322.06493. Error = -4.47 ppm.

6. General procedure for the reaction of dialkyl phosphite anions with 1,1-dinitro-2,2-diphenylethylene

The reaction procedure is representative of reactions of diaklyl phosphite anions with 1,1-dinitro-2,2-diphenylethylene. A solution of dimethyl phosphite (0.209 g, 1.9 mmol) and potassium t-butoxide (0.2132 g, 1.9 mmol) in 25 ml of dimethyl sulfoxide was allowed to stir for thirty minutes at ambient temperature. 1,1-Dinitro-2,2-diphenyl-ethylene (0.5047 g, 1.87 mmol) in 10 ml of DMSO was added to the solution containing the anion of dimethyl phosphite. The resulting solution was allowed to stir for 30 minutes and then the solution was poured into 50 ml of brine. The resulting brine solution was acidified with 5% hydrochloric acid and subsequently extracted with ether (3 x 30

ml). The combined ether extract was washed with H_2O (3 x 50 ml), washed with brine (50 ml), and dried (Na_2SO_4). Removal of the solvent gave a solid which was recrystallized from methanol to afford 2-(dimethoxy phosphinyl)-1,1-dinitro-2,2-diphenylethane (0.5306 g, 74.7%, mp 133°C (d)).

^1H N.M.R. ($CDCl_3$) δ 7.73 (d, 1H, -C<u>H</u>$(NO_2)_2$, J_{PH} = 11 Hz), 7.44-7.05 (m, 10H), 3.46 (d, 6H, -P(O)(O<u>CH$_3$</u>)$_2$, J_{PH} = 11.5 Hz).

I.R. (KBr pellet, cm^{-1}) 3050 (m), 2990 (m), 1595 (vs), 1580 (vs), 1510 (m), 1450 (m), 1375 (m), 1330 (m), 1255 (s), 1060 (vs), 1040 (vs), 700 (m).

M.S. Calculated for $C_{16}H_{17}N_2O_7P$: 380.07735. Measured: 380.07706. Error = -0.8 ppm.

7. <u>Reaction of the anion of diethyl phosphite with 1,1-dinitro-2,2-diphenylethylene</u>

The reaction of 1,1-dinitro-2,2-diphenylethylene with the anion of diethyl phosphite was performed with a similar procedure as described previously for the preparation of 2-(dimethoxy phosphinyl)-1,1-dinitro-2,2-diphenylethane. Recrystallization of the crude isolate from methanol yielded 2-(diethoxy phosphinyl)-1,1-dinitro-2,2-diphenylethane (68.9%, mp 128-129°C (d)).

^1H N.M.R. ($CDCl_3$) δ 7.72 (d, 1H, -C<u>H</u>$(NO_2)_2$, J_{PH} = 11.5 Hz), 7.65-7.15 (m, 10H), 4.2-3.7 (m, 4H, -P(O)(O<u>CH$_2$</u>CH$_3$)$_2$), 1.15 (t, 6H, -P(O)(OCH$_2$<u>CH$_3$</u>)$_2$, J_H = 7 Hz).

I.R. (KBr pellet, cm^{-1}) 3010 (m), 3000 (m), 1590 (vs), 1570 (vs), 1405 (m), 1370 (m), 1330 (m), 1250 (s), 1040 (s), 1005 (s), 740 (m), 695 (m).

M.S. Calculated for $C_{18}H_{21}N_2O_7P$: 408.10865. Measured: 408.10817. Error = -1.2 ppm.

Elemental Analysis. Calculated for $C_{18}H_{21}N_2O_7P$: C, 52.94; H, 5.18, N, 6.86; O, 27.42; P, 7.58. Found: C, 53.17; H, 5.46; N, 6.88; P, 7.57.

8. Reaction of the anion of dimethyl thiophosphite with 1,1-dinitro-2,2-diphenylethylene

The reaction of 1,1-dinitro-2,2-diphenylethylene with the anion of dimethyl thiophosphite was performed using a similar procedure as described previously for the preparation of 2-(dimethoxy phosphinyl)-1,1-dinitro-2,2-diphenylethane. Recrystallization of the crude isolate from methanol yielded pure 2-(dimethoxy thiophosphinyl)-1,1-dinitro-2,2-diphenylethane (65%, mp 137°C (d)).

^1H N.M.R. ($CDCl_3$) δ 8.01 (d, 1H, $-C\underline{H}(NO_2)_2$, J_{PH} = 12 Hz), 7.72-7.22 (m, 10H), 3.5 (d, 6H, $-P(S)(O\underline{CH_3})_2$, J_{PH} = 12 Hz).

I.R. (KBr pellet, cm^{-1}) 2950 (m), 2920 (m), 1560 (vs), 1540 (vs), 1470 (m), 1330 (m), 1050 (s), 1025 (vs), 810 (m), 790 (s), 690 (s).

M.S. Calculated for $C_{16}H_{17}N_2O_6PS$: 396.05450. Measured: 396.05548. Error = +2.5 ppm.

9. Preparation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene by the reaction of 1,1-dinitro-2,2-diphenylethylene with the anion of benzenethiol

The procedure for the preparation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene is representative. A solution of 1,1-dinitro-2,2-diphenylethylene (0.50 g, 1.85 mmol) in 20 ml of dimethyl sulfoxide was added under nitrogen to a solution of potassium t-butoxide (0.208 g, 1.85 mmol) and benzenethiol (0.19 ml, 1.85 mmol) in 25 ml of DMSO. The reaction mixture was allowed to stir at room temperature for one hour and then poured into a brine solution. The resulting brine solution was extracted repeatedly with ether. The combined ether extract was washed with water (3 x 25 ml) and brine (25 ml) and subsequently dried ($MgSO_4$). Removal of the ether yielded a solid which was recrystallized from methanol to afford 1-nitro-1-phenylsulfide-2,2-diphenylethylene 56a (0.523 g, 85%, mp 152-153°C).

I.R. (KBr pellet, cm^{-1}) 1520 (s), 1440 (m), 1330 (m), 770 (m), 740 (m), 680 (m).

M.S. Calculated for $C_{20}H_{15}NO_2S$: 333.08236. Measured: 333.08180. Error = -1.7 ppm.

Elemental Analysis. Calculated for $C_{20}H_{15}NO_2S$: C, 72.05; H, 4.54; N, 4.20; O, 9.60; S, 9.61. Found: C, 71.81; H, 4.63; N, 4.27; S, 9.45.

10. Synthesis of 1-nitro-1-t-butylsulfide-2,2-diphenylethylene

Preparation of 1-nitro-1-t-butylsulfide-2,2-diphenylethylene 56b was carried out by the same procedure as described for 1-nitro-1-phenylsulfide-2,2-diphenylethylene. Recrystallization of the crude

isolate from methanol yielded a yellow solid of 1-nitro-1-t-butylsulfide-2,2-diphenylethylene 56b (32%, mp 118-119°C).

^{1}H N.M.R. ($CDCl_3$) δ 7.5-6.9 (m, 10H), 1.27 (s, 9H, $-SC(CH_3)_3$).

I.R. (KBr pellet, cm^{-1}) 1520 (vs), 1450 (m), 1370 (m), 1340 (m), 1170 (m), 775 (m), 700 (s).

M.S. Calculated for $C_{18}H_{19}NO_2S$: 313.11366. Measured: 313.11313. Error = -1.7 ppm.

Elemental Analysis. Calculated for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; S, 10.22; N, 4.46; O, 10.20. Found: C, 68.83; H, 5.99; S, 10.05; N, 4.70.

11. Synthesis of 1-nitro-1-p-chlorophenylsulfide-2,2-diphenylethylene

1-Nitro-1-p-chlorophenylsulfide-2,2-diphenylethylene 56c was recrystallized from methanol to afford pure 56c (68.4%, mp 151-152°C).

I.R. (KBr pellet, cm^{-1}) 1520 (vs), 1475 (m), 1440 (m), 1390 (m), 1330 (s), 1090 (m), 1000 (m), 815 (vs), 770 (m), 760 (m), 745 (m), 710 (m), 690 (s).

M.S. Calculated for $C_{20}H_{14}NO_2SCL$: 367.04338. Measured: 367.04396. Error = +1.6 ppm.

12. Synthesis of 1-nitro-1-p-methylphenylsulfide-2,2-diphenylethylene

1-Nitro-1-p-methylphenylsulfide-2,2-diphenylethylene 56d was recrystallized from methanol to yield 56d (87%, mp 162-163°C).

I.R. (KBr pellet, cm^{-1}) 1520 (vs), 1490 (m), 1440 (m), 1340 (s), 800 (s), 765 (m), 745 (m), 690 (s).

^{1}H N.M.R. ($CDCl_3$) δ 2.32 (s, 3H, $-\underline{CH_3}$), 7.7-7.0 (m, 14H).

M.S. Calculated for $C_{21}H_{17}NO_2S$: 347.09801. Measured: 347.09939. Error = +4.0 ppm.

13. Synthesis of 1-nitro-1-p-nitrophenylsulfide-2,2-diphenylethylene

Preparation of 1-nitro-1-p-nitrophenylsulfide-2,2-diphenylethylene 56e was carried out by the same procedure as described for the preparation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene. Recrystallization of the crude isolate from methanol yielded a yellow solid which was identified as 1-nitro-1-p-nitrophenylsulfide-2,2-diphenylethylene 56e (46.8%, mp 137-138°C).

I.R. (KBr pellet, cm^{-1}) 1575 (m), 1515 (vs), 1475 (m), 1445 (m), 1340 (vs), 1110 (m), 1080 (m), 1005 (m), 850 (s), 840 (s), 740 (m), 700 (m).

M.S. Calculated for $C_{20}H_{14}N_2O_4S$: 378.06743. Measured: 378.06875. Error = +3.5 ppm.

14. Synthesis of 1-nitro-1-phenylseleno-2,2-diphenylethylene

The preparation of 1-nitro-1-phenylseleno-2,2-diphenylethylene 56f was carried out by the same procedure as described for 1-nitro-1-phenylsulfide-2,2-diphenylethylene. The crude isolate was recrystallized from methanol to yield 1-nitro-1-phenylseleno-2,2-diphenylethylene 56f (48%, mp 138-139.5°C).

I.R. (KBr pellet, cm^{-1}) 1515 (vs), 1490 (m), 1470 (m), 1440 (m), 1335 (s), 990 (m), 770 (m), 740 (m), 690 (s).

M.S. Calculated for $C_{20}H_{15}NO_2Se$: 381.02680. Measured: 381.02643. Error = -1.0 ppm.

Elemental Analysis. Calculated for $C_{20}H_{15}NO_2Se$: C, 63.16; H, 3.97; N, 3.68; O, 8.41; Se, 20.76. Found: C, 62.98; H, 3.92; N, 3.55; Se, 20.56.

15. Synthesis of 1-nitro-1-phenoxy-2,2-diphenylethylene

1-Nitro-1-phenoxy-2,2-diphenylethylene 56g was prepared by the same procedure as previously described for the preparation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene. Recrystallization of the crude isolate from methanol yielded pure 1-nitro-1-phenoxy-2,2-diphenylethylene 56g (49.3%, mp 136.5-137.5°C).

I.R. (KBr pellet, cm^{-1}) 1525 (vs), 1490 (s), 1440 (m), 1335 (s), 1230 (vs), 1180 (m), 1160 (m), 1130 (m), 750 (s), 690 (s).

M.S. Calculated for $C_{20}H_{15}NO_3$: 317.10520. Measured: 317.10497. Error = -0.7 ppm.

Elemental Analysis. Calculated for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41; O, 15.13. Found: C, 75.92; H, 4.77; N. 4.36.

16. Oxidation of 1-nitro-1-phenylsulfide-2,2-diphenylethylene with hydrogen peroxide

To a solution of 1-nitro-1-phenylsulfide-2,2-diphenylethylene (0.55 g, 1.65 mmol) in 10 ml of glacial acetic acid, was added a slight excess of two equivalents of 30% hydrogen peroxide. The reaction mixture was then allowed to stir overnight at room temperature. The reaction mixture was poured onto cracked ice and subsequently filtered

and washed with water. The resulting solid was recrystallized from ethyl acetate to afford 1-nitro-1-phenylsulfoxide-2,2-diphenylethylene 63 (0.575 g, 94%, mp 187.5-189°C).

I.R. (KBr pellet, cm^{-1}) 3030 (m), 1520 (vs), 1440 (m), 1340 (s), 1080 (s), 1040 (m), 770 (m), 730 (m).

M.S. Calculated for $C_{20}H_{15}NO_3S$: 349.07728. Measured 349.07712. Error = -0.4 ppm.

Elemental Analysis. Calculated for $C_{20}H_{15}NO_3S$: C, 68.75; H, 4.33; N, 4.01; O, 13.74; S, 9.18. Found: C, 68.86; H, 4.33; N, 4.02; S, 9.39.

17. Oxidation of 1-nitro-1-phenylsulfoxide-2,2-diphenylethylene with m-chloroperbenzoic acid

To a stirred solution of 1-nitro-1-phenylsulfoxide-2,2-diphenylethylene (0.31 g, 0.88 mmol) in 10 ml of chloroform cooled to 5°C, was added (0.155 g, 0.90 mmol) of m-chloroperoxybenzoic acid in portions at such a rate that the temperature did not exceed 30°C. The reaction mixture was stirred overnight at room temperature. The precipitated m-chlorobenzoic acid was removed by filtration and washed with a small amount of chloroform. The combined filtrate and washings were shaken and washed with sodium bicarbonate, dried ($MgSO_4$), and evaporated to yield crude product. The resulting solid was recrystallized from ethyl acetate to afford 1-nitro-1-phenylsulfonyl-2,2-diphenylethylene 64 (0.21 g, 65%, mp 200.5-202°C).

I.R. (KBr pellet, cm^{-1} 1540 (s), 1440 (m), 1350 (vs), 1160 (s), 1080 (m), 560 (m).

M.S. Calculated for $C_{20}H_{15}NO_4S$: 365.07219. Measured: 365.07228. Error = +0.3 ppm.

Elemental Analysis. Calculated for $C_{20}H_{15}NO_4S$: C, 65.74; H, 4.14; N, 3.83; O, 17.51; S, 8.77. Found: C, 65.75; H, 4.14; N, 3.82; S, 8.82.

AN OVERALL SUMMARY

Although Parts I and II initially appeared unrelated, they both increased the overall understanding of the scope and limitations of the aliphatic $S_{RN}1$ process. Unfortunately, all of the desired objectives and aspirations were not met with success during the course of this work. Nevertheless, a substantial amount of relevant information was obtained pertaining to the aliphatic $S_{RN}1$ process.

APPENDIX

This appendix contains ^1H N.M.R. spectra of 2-(1-cyclopropyl-1-nitroethane)-2-methyl-1,3-cyclopentanedione (Figure 1) at selected temperatures (293°K-383°K) in $CDCl_3$ or o-dichlorobenzene. The interest in this molecule developed from this author's inability to completely explain the observed ^1H N.M.R. spectrum using a Varion 360L (60 MHz) spectrometer 1. Of particular interest were the four protons located on the cyclopentanedione ring. The remaining hydrogens were easily assigned because of the presence of characteristic high field protons due to the cyclopropyl ring and the presence of two singlet methyls.

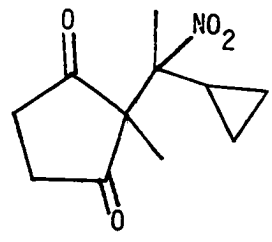


Figure 1

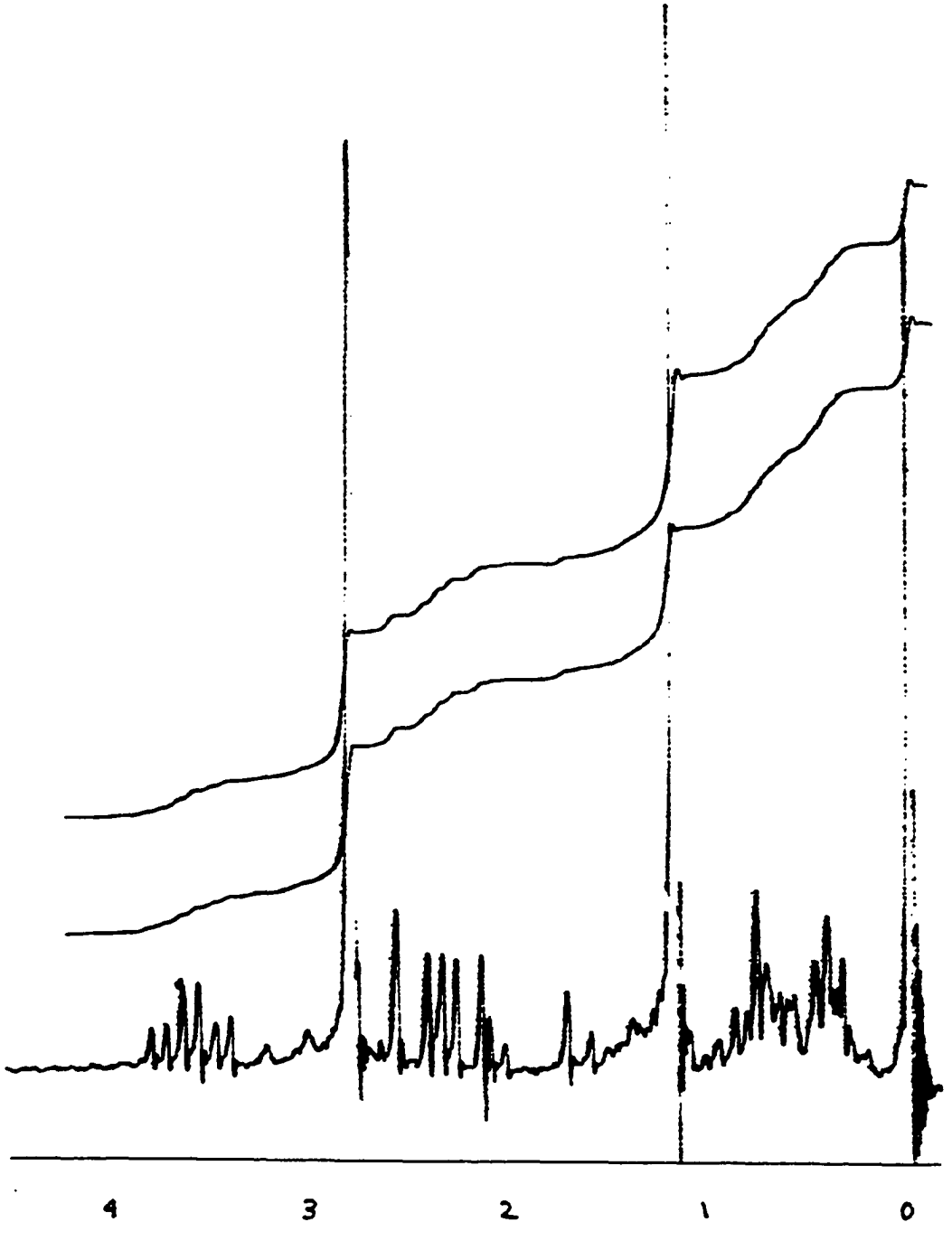
In an effort to ascertain the observed splitting pattern of the protons on cyclopentanedione ring, spectra were recorded on the Bruker WM-300 (300 MHz) and Joel FX-90Q (90 MHz) spectrometers in $CDCl_3$. However, these only confused the issue, since one of the assigned methyl singlets became a complex multiplet when observed on the Bruker WM-300 spectrometer (Spectra 2). Spectra 3 recorded on the Joel FX-90Q (90 MHz) afforded a splitting pattern which was intermediate in complexity between those obtained with the 60 MHz or 300 MHz spectrometers. The singlet

(60 MHz) that formed a multiplet (300 MHz) was now a broad singlet (90 MHz).

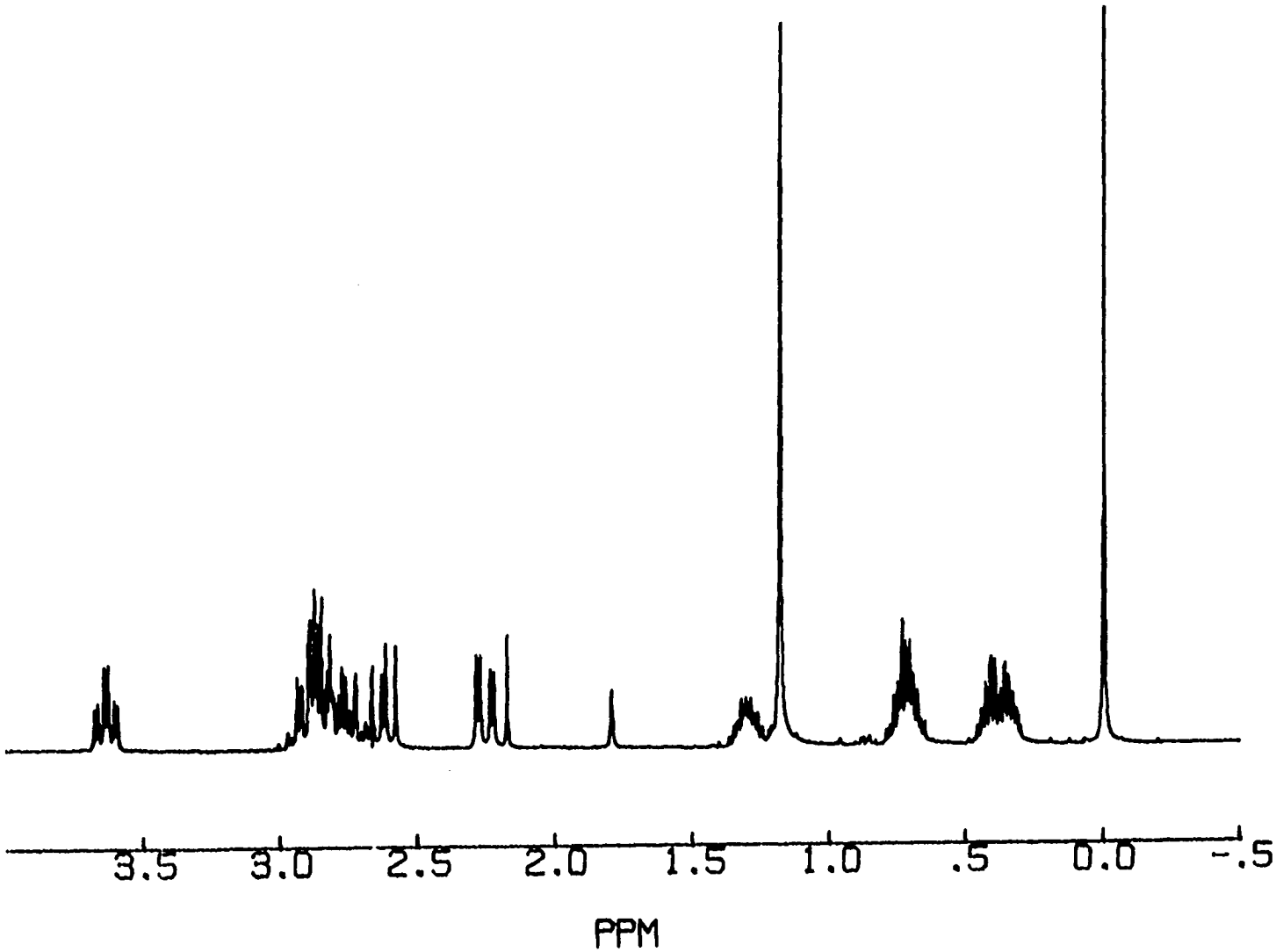
A reasonable explanation for these observations is that restricted rotation around a carbon-carbon bond gives rise to three different protons on the faster time scale (300 MHz). The three protons collapsed to a singlet on the slower time scale (60 MHz) while a broad singlet is observed for the 90 MHz spectrum. The broad singlet and sharp singlet are essentially a result of time averaging. If this assumption is correct, then the multiplet in the region of 2.5-3.0 ppm (300 MHz) should collapse at higher temperatures.

The following spectra were recorded on the Bruker WM-300 at temperatures ranging from 293°K to 343°K. The highest temperature was determined by the volatility of $CDCl_3$. It seems apparent that the multiplet in question is collapsing at higher temperatures as evidence in the following three spectra (4-6).

In an effort to observe the further collapse of the multiplet between 2.5-3.0 ppm, o-dichlorobenzene was used because of its higher boiling point. The following spectra (7-10) were obtained on the Bruker WM-300 using o-dichlorobenzene at temperatures ranging from 296°K to 383°K. Although it appears the observed multiplet (2.5-3.0 ppm) is different in o-dichlorobenzene, the multiplet has collapsed further at 383°K than 343°K in $CDCl_3$. This was the maximum temperature allowed on the Bruker WM-300 spectrometer.

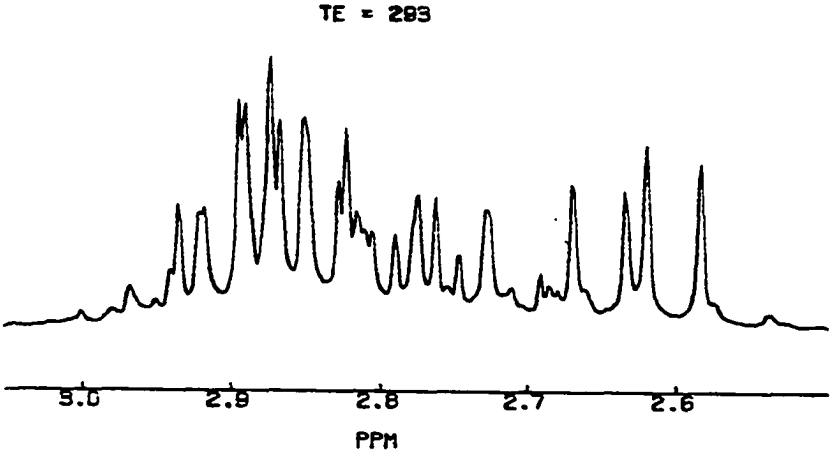


Spectra 1. 60 MHz

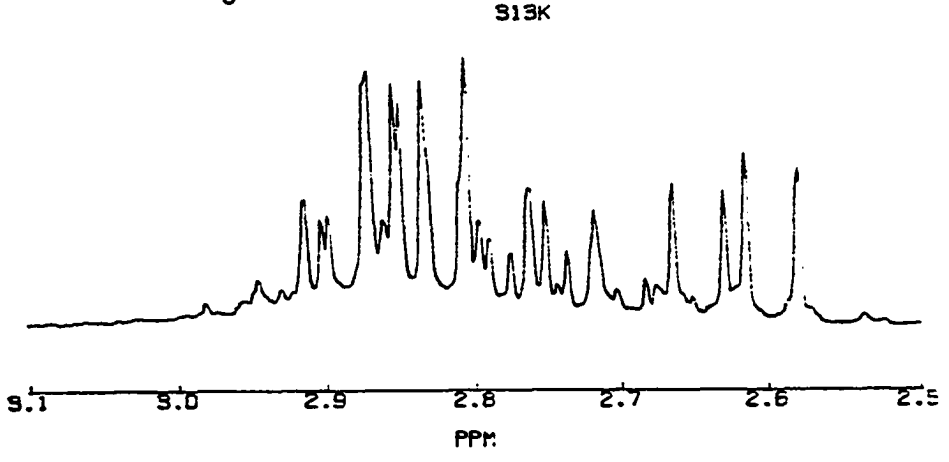


Spectra 2. 300 MHz, 293°K

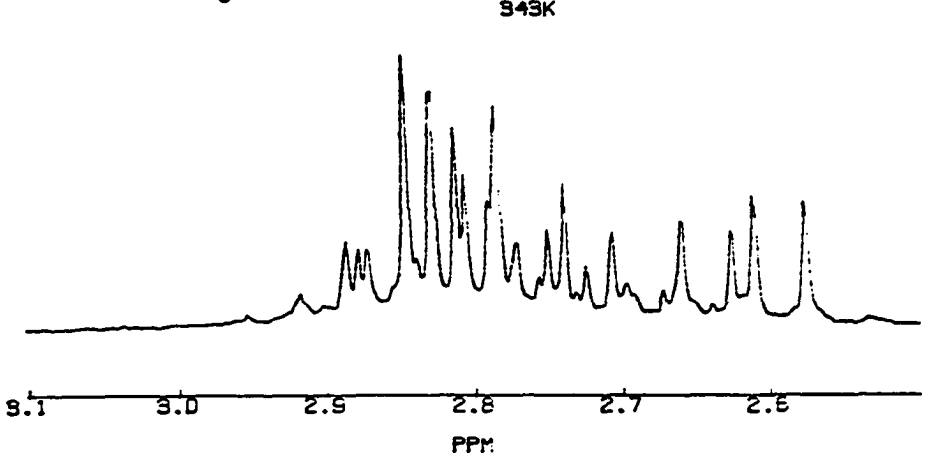
Spectra 3. 90 MHz



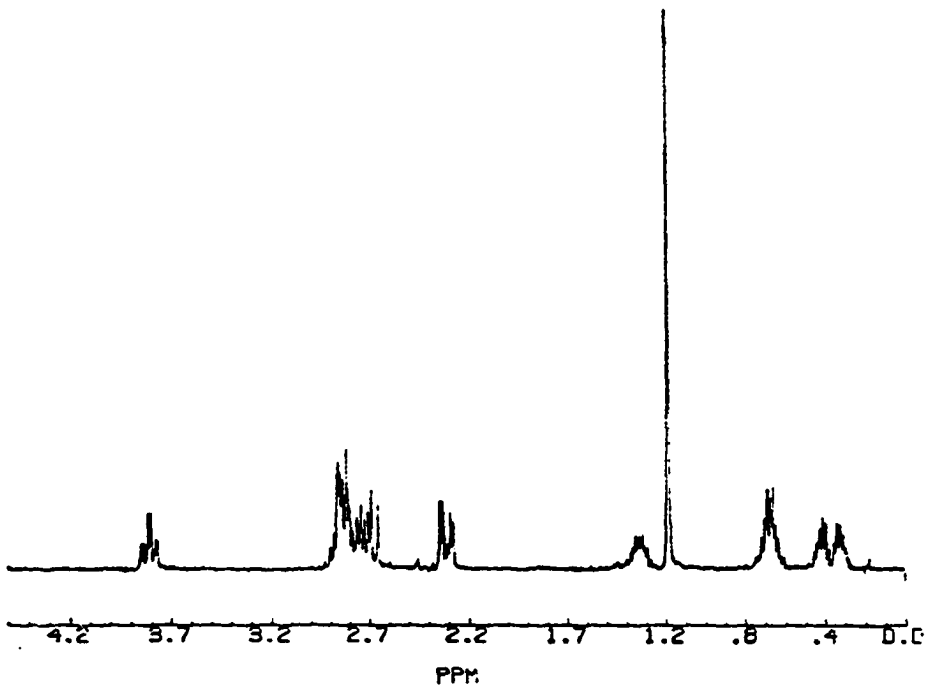
Spectra 4. $CDCl_3$



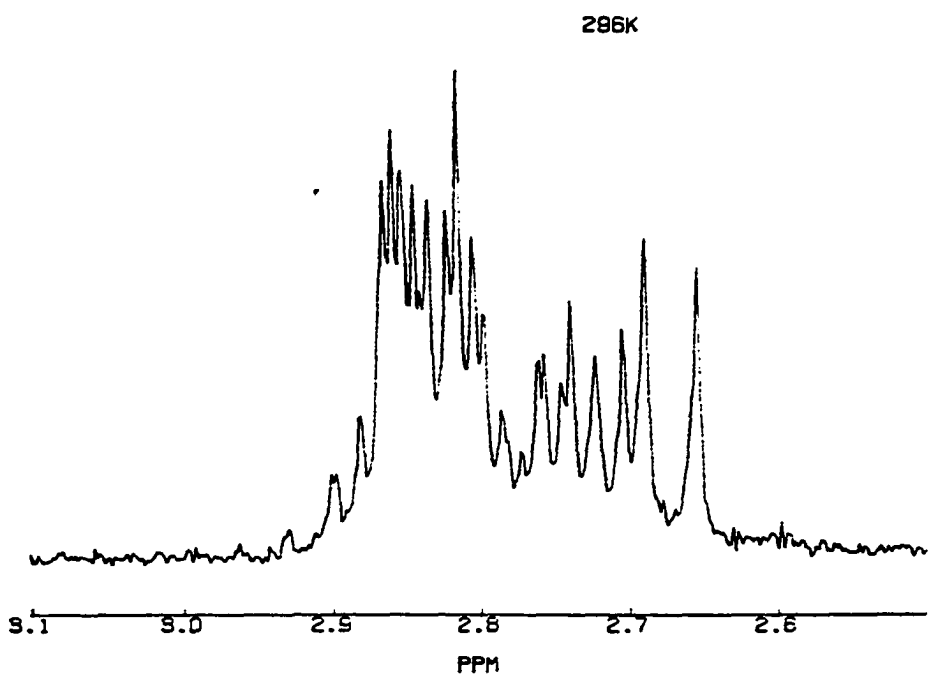
Spectra 5. $CDCl_3$



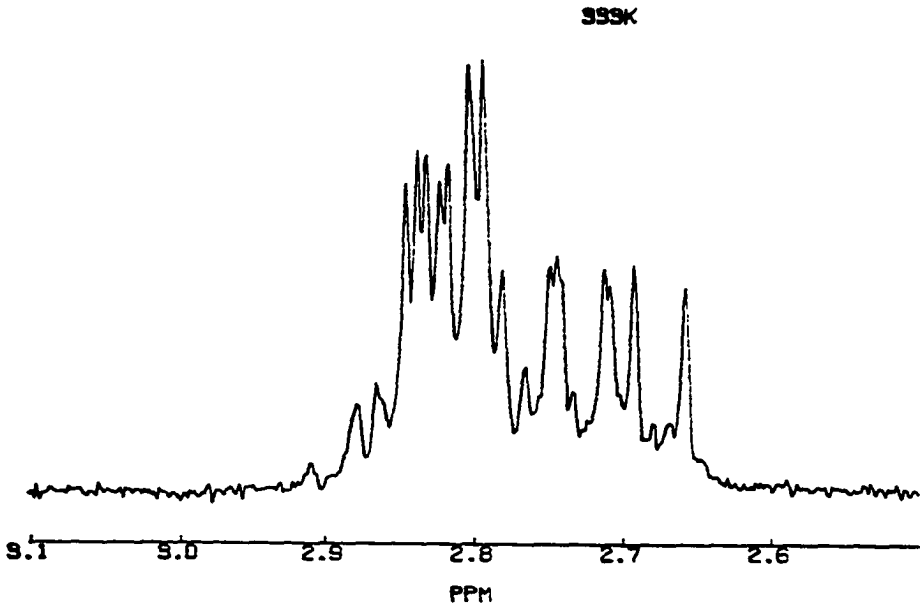
Spectra 6. $CDCl_3$



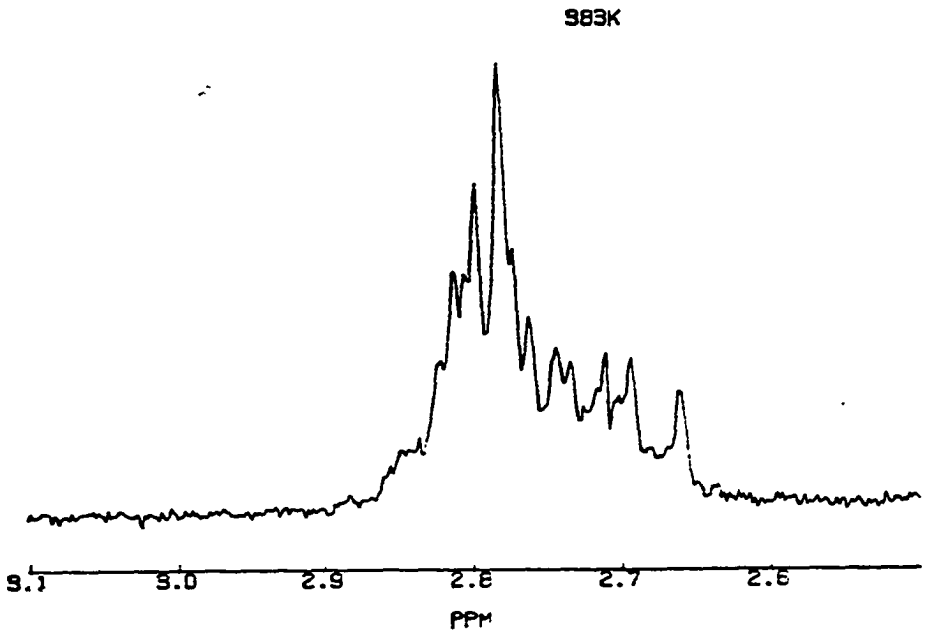
Spectra 7. 296K



Spectra 8. 296K



Spectra 9. 333K



Spectra 10. 383K

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