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Free radical chain reactions involving an electron transfer process

by

Woonphil Baik

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of the
Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Department: Chemistry
Major: Organic Chemistry

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Iowa State University
Ames, Iowa

1988

TABLE OF CONTENTS

I. INTRODUCTION

The $S_{RN}1$ terminology was proposed by Bunnett and Kim in 1970 [1]. The mechanistic description of a $S_{RN}1$ reaction is provided in Scheme 1.

Scheme 1

Step 1: Initiation

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

Step 2: Propagation

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

Step 3: Propagation

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

Step 4: Propagation

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

The $S_{RN}1$ reaction is distinctly different from the S_N2, S_N1 and S_NAr mechanisms, although the net reaction (Eq. 1) is similar. The $S_{RN}1$ reaction is a multi-step chain process

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

involving free radicals and radical anion intermediates. The chain initiating Step 1 may be an electron transfer (E.T.) reduction of RX to form an unstable radical intermediate ($RX^{-\bullet}$). In propagation Step 2, the radical anion ($RX^{-\bullet}$) fragments to form radical $R^{\bullet}$ and anion X^{-}. The radical $R^{\bullet}$ combines covalently with nucleophile A^{-} to form a new radical anion $RA^{-\bullet}$ in propagation Step 3. Propagation Step 4 involves an electron transfer from $RA^{-\bullet}$ to RX, regenerating the reactive intermediate $RX^{-\bullet}$ as well as the product RA. The regeneration of $RX^{-\bullet}$ continues the chain process. Step 1 needs to occur at a rate which will offset chain terminating processes.

There has been various methods of initiation used to start $S_{RN}1$ reactions. Among the initiation processes in $S_{RN}1$ reactions, the electron transfer reduction of the starting substrate (RX) by nucleophile (A^{-}) is often too endothermic to occur thermally at normal reaction temperatures but occurs readily under photostimulation. Such reactions are conducted in a simple commercial photochemical reactor or under a sunlamp. In saturated systems, the substrate generally contains an electron withdrawing group, such as nitro group which can easily accommodate an additional electron in its relatively low lying antibonding pi-orbital.

Examples in which nitro groups are readily reduced to form radical anions by photostimulation are well known [2,3,4]. The reduction of RX by solvated electrons supplied by alkali metal in ammonia is often used in the aromatic $S_{RN}1$ process [5]. Electrochemical methods which supply electrons at the cathode also initiate $S_{RN}1$ processes [6].

The mechanism of Scheme 1 has been proved in a number of ways. It was recognized early that molecular oxygen inhibits free radical chain reactions. This fact is easily understood on the basis of the proposed mechanism [7]. Di-*tert*-butyl nitroxide is also known to be a free radical scavenger [8]. In reactions proceeding by the $S_{RN}1$ mechanism, a small amount of di-*tert*-butyl nitroxide inhibits the reaction for a discrete period of time depending upon the rate of initiation. This is readily interpretable on the basis that $R^{\bullet}$ is an intermediate and that these are chain reactions (Scheme 1). A powerful one electron acceptor such as *p*-dinitrobenzene (p-DNB) or *m*-dinitrobenzene (m-DNB) can intercept the radical anions of the $S_{RN}1$ processes. Inhibition by these reagents is also diagnostic for $S_{RN}1$ processes [9]. Light often speeds up $S_{RN}1$ processes which sometimes do not occur in the dark. This observation is consistent with a photochemical process or with a photostimulated chain reaction with a high quantum yield. With quantum yields $\gg 1$ there can be no doubt that the process is a free radical chain reaction [9].

During the past two decades, two major classes of substrates have been recognized to undergo $S_{RN}1$ reactions. The first major class of substrates are unsaturated systems.

These systems have been extensively reviewed by Kornblum and Bunnett [9,10]. The second major class of substrates consists of aliphatic systems with good leaving groups. Russell has reviewed the $S_{RN}1$ reactions in aliphatic systems [11]. Most of the investigations of the aliphatic $S_{RN}1$ reactions have been focused on 2-chloro-nitropropane and p-nitrobenzyl chloride [2,3,10]. The mechanism of the aliphatic $S_{RN}1$ reactions was originally recognized by Russell and Kornblum to explain the carbon alkylation of the anions of secondary nitroalkanes with 2-substituted-2-nitropropanes. A wide variety of leaving groups such as halogens, nitrite, phenylsulfinate, dimethyl sulfide and trimethylamine have been employed in the aliphatic $S_{RN}1$ reactions. It is impressive that poor leaving groups in S_N1 and S_N2 process can be involved in the $S_{RN}1$ reactions.

Since 1970, numerous investigations of the aliphatic $S_{RN}1$ reactions have shown that a nitro group is usually required either in the substrate or in the attacking nucleophile. The importance of the nitro group must be connected with the low energy of its LUMO which leads to stability of $RA^{-\cdot}$ whenever R or A^- contains a nitro group.

II. PHOTOSTIMULATED REACTIONS OF 2-SUBSTITUTED-2-NITROPROPANES AND ALKOXIDE IONS IN ALIPHATIC $S_{RN}1$ PROCESS

A. Introduction

The radical chain substitution process, which has been labeled $S_{RN}1$, has been investigated for 2-substituted-2-nitropropanes and a wide variety of carbanions. The reaction proceeds via a free radical chain process as shown in Scheme 2. This process has been observed with tertiary carbanions

Scheme 2

$$R_2C(NO_2)X^{-\cdot} \longrightarrow R_2CNO_2^{\cdot} + X^-$$

$$R_2CNO_2^{\cdot} + N^- \longrightarrow R_2C(NO_2)N^{-\cdot}$$

$$R_2C(NO_2)N^{-\cdot} + R_2C(NO_2)X \rightarrow R_2C(NO_2)N + R_2C(NO_2)X^{-\cdot}$$

which are weak nucleophiles such as nitronate anions [2,3,8], enolates of β-dicarbonyl or β-cyano carbonyl compounds [12,13], malonitriles [12], aryl thiolates, aryl sulfinates [14,15] and dialkyl phophite or thiophosphite anions [16,17,18]. Evidence for the 2-nitro-2-propyl radical as an intermediate has been provided by the observation that competitive relative reactivities with two nucleophiles are independent of the nature of the leaving group X [19]. Enolate anions with 2-substituted-2-nitropropanes form both coupling and dimerization products by free radical chain processes as shown in Scheme 3 [20,21,22]. More easily oxidized carbanions

Scheme 3

$$\mathrm{Me_2C(NO_2)X^{-\cdot} + E^- \longrightarrow [\,X^- + Me_2C{=}NO_2^- + E^\cdot\,]} \longrightarrow$$

$$\left\{\begin{array}{l} \longrightarrow \mathrm{E{-}CMe_2NO_2^{-\cdot} + X^-} \\ \longrightarrow \mathrm{E^\cdot + Me_2C{=}NO_2^- + X^-} \end{array}\right.$$

$$\mathrm{E^\cdot + E^- \longrightarrow E{-}E^{-\cdot}}$$

$$\mathrm{E{-}CMe_2NO_2^{-\cdot} + Me_2C(NO_2)X \longrightarrow Me_2C(NO_2)X^{-\cdot} + ECMe_2NO_2}$$

$$\mathrm{E{-}E^{-\cdot} + Me_2C(NO_2)X \longrightarrow Me_2C(NO_2)X^{-\cdot} + E{-}E}$$

react with 2-substituted-2-nitropropanes to undergo dimerization with no evidence of formation of cross coupling products [23]. A modified non-chain pathway can lead to the dimerization of the carbanions (Scheme 4). When the carbanion contains a conjugated phenyl group which can lead to a substituted benzyl radical, Reaction 3 greatly predominates.

Other substitution which provide reasonance stabilization of $A^{\cdot}$ should also favor Reaction 3 over Reaction 2. The dimer

Scheme 4

$$\mathrm{Me_2C(NO_2)X^{-\cdot}} \longrightarrow \mathrm{Me_2CNO_2^{\cdot}} + \mathrm{X^-}$$

$$\mathrm{Me_2CNO_2^{\cdot}} + \mathrm{R_3C:^-} \longrightarrow \mathrm{Me_2C{=}NO_2^-} + \mathrm{R_3C^{\cdot}}$$

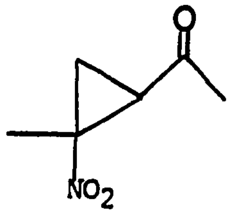
$$2\ \mathrm{R_3C^{\cdot}} \longrightarrow \mathrm{R_3C{-}CR_3}$$

A-A can be formed by coupling of two radicals in a non-chain reaction or possibly by a chain sequence in which the radical $A^{\cdot}$ is trapped by the anion A^-.

$$\mathrm{Me_2CNO_2^{\cdot}} + \mathrm{A:^-} \longrightarrow \mathrm{ACMe_2NO_2^{-\cdot}} \qquad (2)$$

$$\mathrm{Me_2CNO_2^{\cdot}} + \mathrm{A:^-} \longrightarrow \mathrm{Me_2C{=}NO_2^-} + \mathrm{A^{\cdot}} \qquad (3)$$

Another example of the $S_{RN}1$ process that has been investigated involves carbon-carbon bond scission in the nitrocyclopropane 1 upon reaction with the 2-nitro-2-propyl anion to form 2 [24]. The reaction apparently proceeds by the $S_{RN}1$ sequence as shown Scheme 5.



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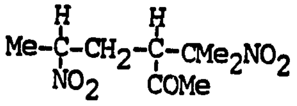
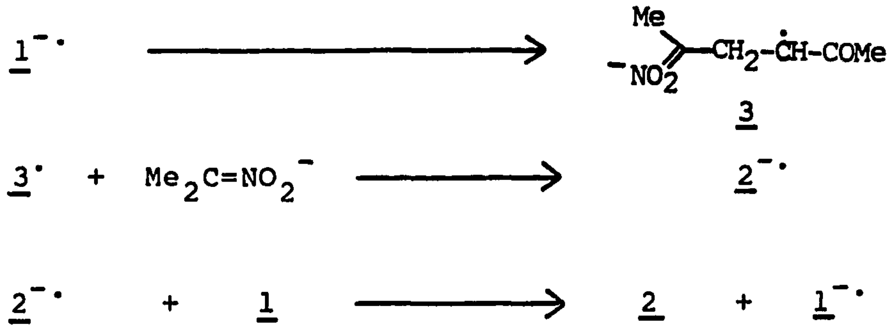


$\mathrm{Me{-}\overset{H}{\underset{NO_2}{C}}{-}CH_2{-}\overset{H}{\underset{COMe}{C}}{-}CMe_2NO_2}$

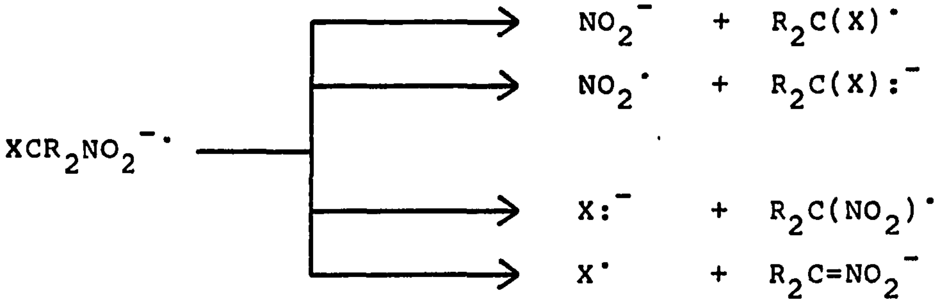
2

Scheme 5



In the propagation steps, the fragmentation of the generalized structure $XCMe_2NO_2^{-\cdot}$ is controlled by thermodynamic considerations and can lead to any of the four fragmentation routes in Scheme 6 [11].

Scheme 6



An alternative chain mechanism for nucleophilic aliphatic substitution has been suggested for certain systems (Scheme

3). The propagation steps of this $S_{RN}2$ mechanism are given in Scheme 7.

Scheme 7

$$RX^{-\bullet} + N^{-} \longrightarrow RN^{-\bullet} + X^{-}$$

$$RN^{-\bullet} + RX \longrightarrow RX^{-\bullet} + RN$$

Several experimental methods have been developed to distinguish between $S_{RN}1$ and the $S_{RN}2$ processes. The most common method has been the effect of the leaving group upon nucleophilic selectivity. When two anions are allowed to compete for a series of substrates containing a common R moiety, the relative reactivities of the anions should be independent of the leaving groups only if free $R^{\bullet}$ is an intermediate [25]. The stereochemical courses of the two processes are probably different also. Another possible distinction would be the intervention of a unimolecular rearrangement of $R^{\bullet}$ to $R'^{\bullet}$, which is possible only in the $S_{RN}1$ process [26].

In contrast to the reactions of 2-substituted-2-nitropropanes with a variety of nucleophiles which are recognized to participate in the $S_{RN}1$ processes, oxygen nucleophiles, such as alkoxide ions, have never been reported to be capable of participation in $S_{RN}1$ processes. A major goal of this investigation was to search for experimental evidence concerning the nature of the interaction of 2-nitro-2-propyl radicals with alkoxide ions with the hope of developing new $S_{RN}1$ processes.

B. Results and Discussion

1. Reaction of 2-bromo-2-nitropropane with methoxide ion

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 propagating step.

The sodium salt of methyl alcohol was found to react rapidly with 2-bromo-2-nitropropane 4 to produce 2,2-dimethoxypropane 5. A good yield of 2,2-dimethoxypropane 5 was obtained from the reaction of 2-bromo-2-nitropropane and 2 equivalents of methoxide ion after irradiation using a Rayonet photoreactor (350 nm) under a nitrogen atmosphere in methanol (Eq. 4). Examples and yields are listed in Table 1.

$$\underset{\underline{4}}{BrCMe_2NO_2} + 2\ CH_3O^- \xrightarrow[UV]{CH_3OH} \underset{\underline{5}}{Me_2C(OCH_3)_2} \qquad (4)$$

Light was absolutely necessary to carry out the reaction. Reactions run in aluminum foil-wrapped flasks to exclude light

Table 1. Characteristics of the reaction between 2-bromo-2-nitropropane with sodium methoxide in methanol

$$BrCMe_2NO_2 \quad + \quad NaOCH_3 \xrightarrow[N_2]{MeOH} Me_2C(OCH_3)_2$$

Amounts of $NaOCH_3$	Conditions[a]	% Yields[b]
2 eq.	5 h, 350 nm	96
1 eq.	5 h, 350 nm	45 (43)[c]
2 eq.	24 h, dark, 35 °C	0 (90)[c]
2 eq.	4 h, 350 nm, O_2	0
2 eq.	4 h, 350 nm, DTBN[d]	31
2 eq.	5 h, 350 nm, m-DNB[e]	51
2 eq.	5 h, room light	0 (88)[c]
0 eq.	5 h, 350 nm	2 (94)[c]
2 eq.	4 h, sunlamp[f]	93

[a] $[BrCMe_2NO_2]_o$= 0.10 M. Reactions were irradiated in the Rayonet photoreactor at 35 °C.

[b] GC yields measured by adding biphenyl as an internal standard.

[c] GC yields of 2-bromo-2-nitropropane.

[d] DTBN= 10 mol% of di-*tert*-butyl nitroxide.

[e] m-DNB= 10 mol% of *m*-dinitrobenzene.

[f] Irradition was carried out with a 275 W sunlamp positioned 15 cm from the Pyrex reaction tube.

and immersed in oil-bath (35 °C) to simulate the temperature inside a Rayonet photoreactor, showed no trace of 2,2-dimethoxypropane and 90% of the starting material, as determined by GC analysis, was recovered. Furthermore, no trace of product was observed when the reaction was run in the room light.

The 2,2-dimethoxypropanes were shown to arise from radical anion intermediates. The reactions did not occur in the presence of oxygen and were completely inhibited for a discrete period of time by 10% of di-*tert*-butyl nitroxide.

2. Reaction of 2-substituted-2-nitropropanes with methoxide ion

A variety of leaving groups in 2-substituted-2-nitropropanes 6 were examined in the reactions with methoxide ion in methanol solution with couterions such as Li^+, Na^+, K^+, K^+-18-crown-6, or $PhCH_2NMe_3^+$ (Eq. 5).

$$\underset{\underline{6}}{XCMe_2NO_2} + 2\ M^{+-}OCH_3 \xrightarrow[UV]{CH_3OH} \underset{\underline{5}}{Me_2C(OCH_3)_2} \qquad (5)$$

X= Cl, Br, NO_2, SO_2Ph, N_3

M^+= Li^+, Na^+, K^+, K^+-18-crown-6, $PhCH_2NMe_3^+$

The reactions were performed under standard conditions using a Rayonet photoreactor or a 275 W sunlamp, nitrogen

Table 2. Reactions of 2-substituted-2-nitropropanes with methoxide ions

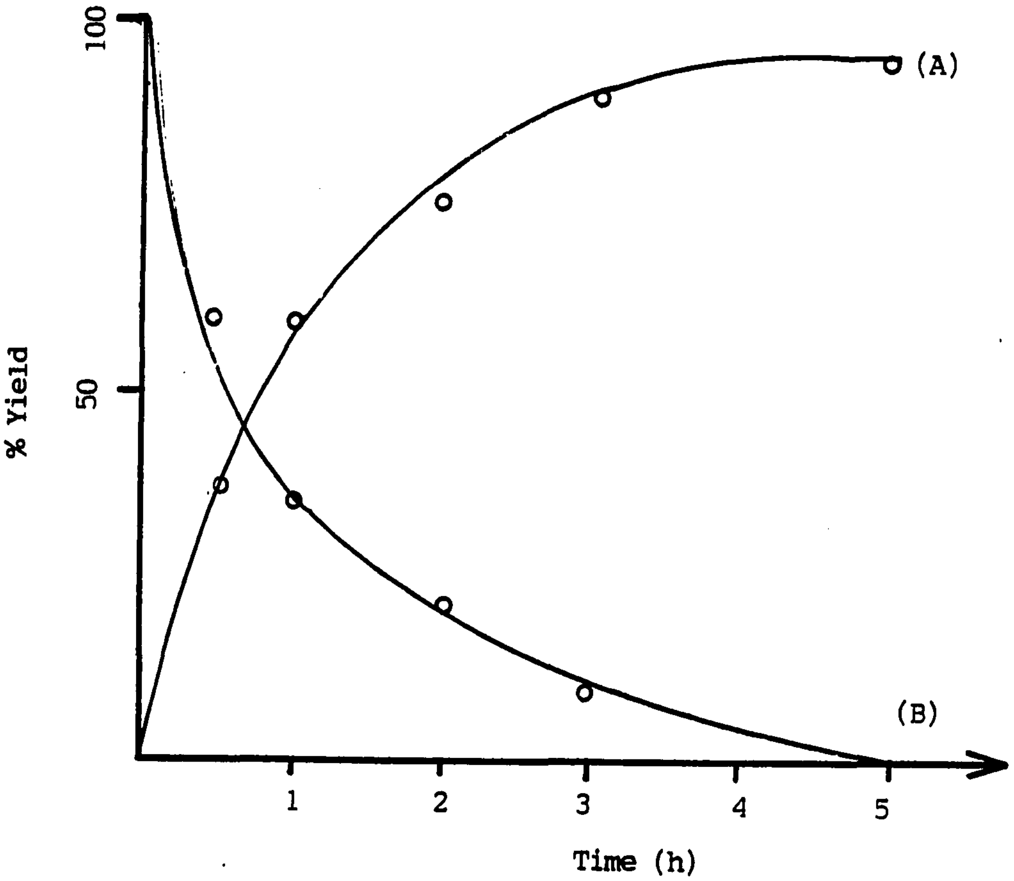
$$XCMe_2NO_2 \quad + \quad 2\ M^+\ {}^-OCH_3 \xrightarrow[N_2]{MeOH} Me_2C(OCH_3)_2$$

X	Counterions	Conditions[a]	% Yields[b]
Cl	Na^+	7 h	89
NO_2	Na^+	12 h	84
$PhSO_2$	Na^+	5 h	82
Br	K^+	6 h	81
Br	K^+-18-C-6	6 h	62
Br	Li^+	12 h	89
Br	$PhCH_2N(CH_3)_3^+$	12 h	84
Br	$PhCH_2N(CH_3)_3^+$	12 h, dark	0 (91)[c]
N_3	Na^+	2 h	74
p-ClC_6H_4S	Na^+	24 h	11
COOEt	Na^+	24 h	0 (89)[c]

[a] $[BrCMe_2NO_2]_o$= 0.10 M, $[ROM]_o$= 0.22 M. Reactions were irradiated for the time indicated in the Rayonet photoreactor at 35 °C.

[b] GC yields measured by adding internal standard.

[c] GC yields of unreacted starting material.



A. The formation of 2,2-dimethoxypropane

B. The disappearance of 2-bromo-2-nitropropane

Figure 1. Reaction of 0.10 M 2-bromo-2-nitropropane with 0.22 M sodium methoxide in methanol in a Rayonet photoreactor (350 nm) at 35 ^{o}C.

atmosphere, and an aqueous work-up. These results are listed in Table 2.

The formation of 2,2-dimethoxypropane by a S_N2 process can be excluded since the reaction did not occur in the dark. A free radical chain process in the reactions of 2-substituted-2-nitropropanes and methoxide ion was demonstrated by the effect of radical inhibitors. The formation of 2,2-dimethoxypropane were not only independent of the leaving group X but also independent of the counterions. However, the presence of the cyclic ether 18-crown-6 in the reaction with K^+ as the counterion resulted in a diminished yield of product.

The disappearance of 2-substituted-2-nitropropane was equal to the rate of formation of 2,2-dimethoxypropane and no intermediate, such as 2-methoxy-2-nitropropane, could be detected by ^1H NMR or GC analyses in methanol (Figure 1). Undoubtedly, these reactions occur via radical chain processes.

3. Reaction of 2-substituted-2-nitropropanes with ethoxide ion

Ethoxide ion was also allowed to react with a variety of 2-substituted-2-nitropropanes **6** under same conditions employed for methoxide ion (Eq. 6). The expected products were observed and are listed in Table 3. These reactions also

Table 3. Reactions of 2-substituted-2-nitropropanes with ethoxide ions

$$XCMe_2NO_2 \quad + \quad 2\ M^+\ {}^-OC_2H_5 \xrightarrow[N_2]{EtOH} Me_2C(OC_2H_5)_2$$

X	Counterions	Conditions[a]	% Yields[b]
Br	Na^+	4 h	51
Br	Na^+	5 h, dark	9 (81)[c]
Br	Na^+	5 h, DTBN[d]	21
Br	Na^{+e}	4 h	23 (41)[c]
NO_2	Na^+	12 h	45
NO_2	K^+	12 h	49
$PhSO_2$	Na^+	24 h	50

[a] $[XCMe_2NO_2]_o$= 0.10 M, [EtOM]= 0.22 M. Reactions were irradiated for the time indicated in the Rayonet photoreactor at 35 °C.

[b] GC yields were measured.

[c] GC yields of starting material.

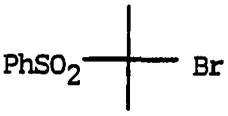
[d] DTBN= 10 mol% of di-*tert*-butyl nitroxide.

[e] 1 equivalent of sodium ethoxide was used.

smoothly under the influence of irradiation from a 275 W sunlamp placed 15 cm from the Pyrex reaction vessel. Like the reactions of methoxide ion in methanol, the reactions of ethoxide ions in ethanol were significantly retarded by the presence of radical inhibitors.

$$\underset{\underline{6}}{XCMe_2NO_2} \quad + \quad 2\ {}^{-}OC_2H_5 \xrightarrow[UV]{EtOH} \underset{\underline{7}}{Me_2C(OC_2H_5)_2} \quad (6)$$

It is worthwhile to note that the reaction of 2,2-dichloropropane with methoxide or ethoxide ions fails to form the 2,2-dimethoxypropane or 2,2-diethoxypropane, and the reaction of 2-methyl-2-nitropropane with methoxide ion also failed to form the 2-methoxy-2-methylpropane. α-Bromosulfones, such as 2-bromo-2-propyl phenyl sulfone 8 would be expected to be better substrates than 2,2-dichloropropane because the $PhSO_2$ group would increase the stability of $\underline{8}^{-\cdot}$ the same as the nitro group does. However, the reaction of



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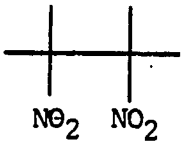

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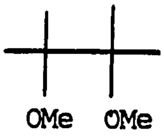

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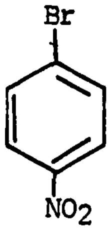

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8 with ethoxide ion in ethanol in the usual manner produced

none of the substitution product. The reaction of 2,3-dimethyl-2,3-dinitrobutane 9 , in which two nitro groups are separated by two carbons, with methoxide ion under the same conditions failed to form 2,3-dimethoxy-2,3-dimethylbutane 10. p-Bromonitrobenzene 11 also failed to react with methoxide ion in methanol under conditions which gave a high yield with the 2-substituted-2-nitropropanes. A simple S_N2 displacement of the leaving group by 1°-alkoxide ion would seem unlikely since these reactions of 2,2-dichloropropane, α-bromo-sulfones or p-bromonitrobenzene with 1°-alkoxide ions did not occur under the reaction conditions.

4. Reaction of 2-cyano-2-nitropropane with 1°-alkoxide ions

2-Cyano-2-nitropropane 12 failed to yield a substitution product with sodium methoxide. Instead, addition of methoxide ion yielded methyl 2-methyl-2-nitropropionimidate 13 (Eq. 7).

$$\underset{\underline{12}}{CNCMe_2NO_2} + NaOCH_3 \xrightarrow{MeOH} \underset{\underline{13}}{Me_2C(NO_2)C(OMe)=NH} \qquad (7)$$

The alkoxide catalyzed reaction of nitriles with alcohols has been previously studied [27,28,29]. The conversion of nitrile to imidate in methanol at 25 °C in the presence of a catalytic amount of sodium methoxide was observed by those workers for a wide variety of nitriles. Many electronegatively substituted

Table 4. The conversion of 2-cyano-2-nitropropane to imidate

$$Me_2C(CN)NO_2 \quad + \quad RO^- \xrightarrow[N_2]{ROH} Me_2C(NO_2)C(OR)=NH$$

R	Conditions[a]	% Yields[b]
Me	24 h, room light[c]	85 (71)[d]
Et	24 h, room light[c]	83 (72)[d]
Me	24 h, dark	85
Me	24 h, UV[e]	87
Me	24 h, dark, DTBN[f]	(70)[d]

[a] Equimolar amounts of substrates (1.00 mmol) were employed for the time indicated at room temperature in 10 mL of ROH.

[b] GC yields measured by adding naphthalene as an internal standard.

[c] Fluorecent light.

[d] Isolated yields.

[e] Irradiation was carried out in the Rayonet photoreactor at ambient temperature.

[f] DTBN= 10 mol% of di-*tert*-butyl nitroxide.

aliphatic and aromatic nitriles were converted to imidates extremely easily in useful yield by base-catalyzed reaction with alcohols (Eq. 8).

$$\text{R-CN} \quad + \quad \text{NaOR'} \quad \xrightarrow[\text{5-24 h}]{\text{R'OH, r.t.}} \quad \text{RC(OR')=NH} \qquad (8)$$

R = CH_3-, $PhCH_2$-, NC-CH_2-, Cl-CH_2-, $O_2NC_6H_4$-

The reactions of 2-cyano-2-nitropropane with sodium alkoxides were carried out under several conditions and the results are listed in Table 4. Table 4 shows that the reactions of 2-cyano-2-nitropropane with sodium alkoxides are independent of irradiation and are not affected by di-tert-butyl nitroxide. Undoubtedly, these reactions do not proceed via free radical chain processes.

5. Mechanistic considerations

The formation of 2,2-dimethoxypropane from the reaction between 2-substituted-2-nitropropane and methoxide ion can be rationalized by several possible pathways. One possible interpretation of these results is the free radical chain of Scheme 8. The α-nitro radical derived from the 2-substituted-2-nitropropane is trapped by the methoxide ion to form a radical anion which subsequently dissociates to form the 2-methoxy-2-propyl radical. It is known that the cyano and the

Scheme 8

$$XCMe_2NO_2^{-\cdot} \longrightarrow Me_2C(NO_2)^{\cdot} + X^-$$

$$Me_2C(NO_2)^{\cdot} + RO^- \longrightarrow Me_2C(OR)NO_2^{-\cdot}$$

$$Me_2C(OR)NO_2^{-\cdot} \longrightarrow ROCMe_2^{\cdot} + NO_2^-$$

$$ROCMe_2^{\cdot} + XCMe_2NO_2 \xrightarrow{E.T} ROCMe_2^+ + XCMe_2NO_2^{-\cdot}$$

$$X = Cl,\ Br,\ NO_2,\ N_3,\ SO_2Ph,\ \underline{p}\text{-}ClC_6H_4S$$

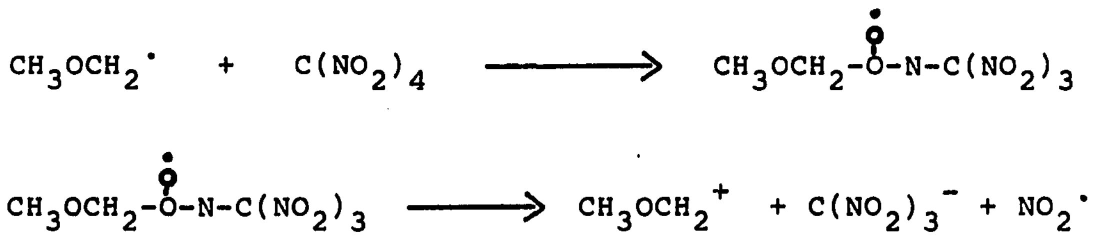
ester group in 2-substituted-2-nitropropane radical anions leads to fragmentation with loss of nitrite ion in $S_{RN}1$ process (Eqs. 9, 10). In a similar manner, the methoxy group can stabilize the radical formed by the fragmentation with loss of the nitrite anion.

$$NCCMe_2NO_2^{-\cdot} \longrightarrow NCCMe_2^{\cdot} + NO_2^- \quad (9)$$

$$EtO_2CCMe_2NO_2^{-\cdot} \longrightarrow EtO_2CCMe_2^{\cdot} + NO_2^- \quad (10)$$

The 2-methoxy-2-propyl radical should be easily oxidized by the 2-substituted-2-nitropropane to the cation. This unusual step for a chain reaction can be explained by the inner-sphere electron transfer process [30,31]. Steenken and co-workers reported that α-monoalkoxyalkyl radicals and α-hydroxyalkyl radicals can be oxidized by nitrobenzene or tetranitromethane (TNM) to carbocations. The reactions proceed via addition of the radicals to TNM ($k \sim 3 \times 10^{9}/M.S$) to form adducts which decompose in a first-order reaction to yield carbocations (Scheme 9).

Scheme 9



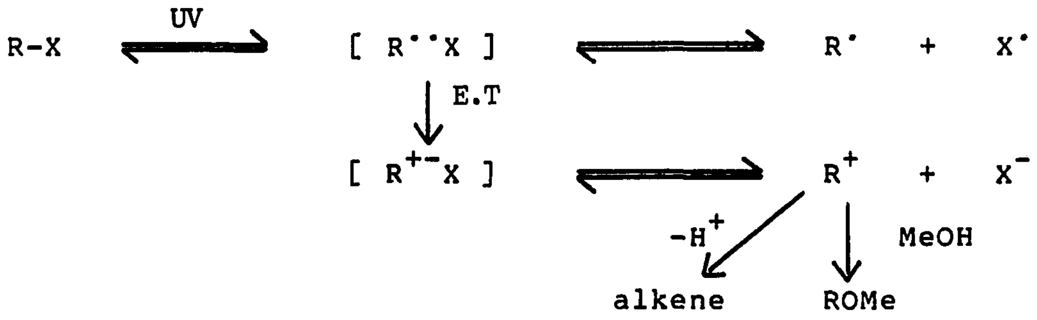
$$CH_3OCH_2^{\bullet} \quad + \quad C(NO_2)_4 \longrightarrow CH_3OCH_2{-}\overset{\overset{\bullet}{O}}{\overset{|}{O}}{-}N{-}C(NO_2)_3$$

$$CH_3OCH_2{-}\overset{\overset{\bullet}{O}}{\overset{|}{O}}{-}N{-}C(NO_2)_3 \longrightarrow CH_3OCH_2^{+} \; + \; C(NO_2)_3^{-} \; + \; NO_2^{\bullet}$$

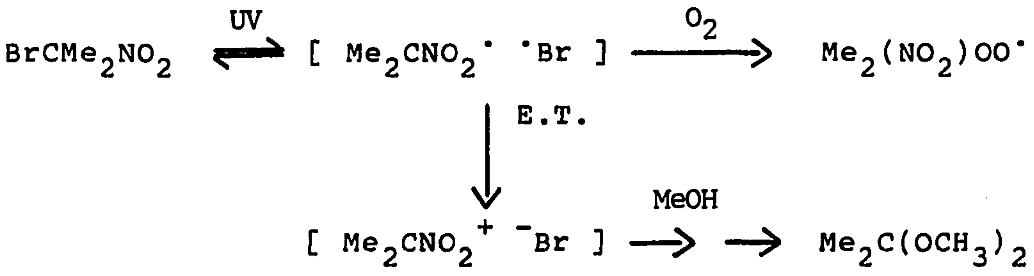
The presence of alkoxy substituent provides a driving force for the last two steps in Scheme 8 by stabilization of the 2-methoxy-2-propyl radical and carbocation. As mentioned previously, the effects of light and radical inhibitors strongly support the free radical chain mechanism. Furthermore, an initial kinetic chain length of 75 is calculated for the reaction of 2-bromo-2-nitropropane with potassium methoxide in methanol (the kinetic chain length will be discussed on next section). Thus, the reaction proceeds via a free radical chain mechanism as in Scheme 8.

Another possible interpretation for the formation of 2,2-dimethoxypropane is non-chain photochemical reaction. Kropp and co-workers have shown that irradiation of alkyl halides in methanol is a powerful method for the generation of carbocations via a process thought to be involve light-induced homolytic cleavage of the carbon-halogen bond followed by electron transfer within the initially formed caged radical pair [32-35](Scheme 10).

Scheme 10



Extension of the Kropp mechanism to 2-bromo-2-nitropropane is shown in Equation 11. Some of the experimental observation can be explained by this non-chain photochemical process.



(11)

Thus, the excited states in photochemical reactions can be deactivated by di-tert-butyl nitroxide or by oxygen, and the caged radicals which come from homolytic cleavage of carbon-halogen bond in photochemical reactions could perhaps also be trapped by these reagents. However, the photochemical process of Reaction 11 can be excluded by several observations. First, the reaction of 2-bromo-2-nitropropane with methanol in the absence of methoxide ion failed to give 2,2-dimethoxypropane. Furthermore, the reaction with 1.1 equiv. of methoxide ion resulted in the 45% yield which was half as much as the reaction with 2.2 equiv. of methoxide ion. Second, the failures of the reaction of 2,2-dichloropropane with methoxide ion in methanol and the reaction of 2-bromo-2-propyl phenyl sulfone 8 under the same conditions do not support the photochemical reaction. It is thus concluded that the experimental observations are consistent only with a chain mechanism with a considerable kinetic chain length and not with a photochemical reaction of the Kropp type.

6. Reaction of 2-bromo-2-nitropropane with 2^o- and 3^o-alkoxide ions

The 2^o- and 3^o-alkoxide ions generated from an excess of the alcohol, were allowed to react with 2-bromo-2-nitropropane under the same conditions employed for methoxide and other 1^o-alkoxide ions (Eq. 12). However, the expected products were not observed. These unexpected results are listed in Table 5 and summarized in Equation 12.

The 2°- and 3°-alkoxide ions are capable of causing 2-bromo-2-nitropropane to undergo an elimination reaction (Eq. 13). Subsequently, the addition of 2°-alkoxide ion to

$$BrCMe_2NO_2 \quad + \quad (CH_3)_2CHO^-Na^+ \quad \xrightarrow{ROH,\ UV}$$

$$\underset{\underline{9}}{O_2NCMe_2CMe_2NO_2} \quad + \quad \underset{\underline{14}\ (R=\underline{i}\text{-}Pr)}{ROCH_2CMe(NO_2)CMe_2NO_2} \qquad (12)$$

2-nitropropene generates a nitronate anion (Eq. 14). The reaction of this anion and 2-bromo-2-nitropropane can proceed via the $S_{RN}1$ process to give the coupled product (Eq. 15).

$$BrCMe_2NO_2 \quad + \quad 2^{\circ}\text{-}RO^- \quad \xrightarrow{E_2} \quad CH_2{=}C(Me)NO_2 \qquad (13)$$

$$CH_2{=}C(Me)NO_2 \quad + \quad 2^{\circ}\text{-}RO^- \quad \longrightarrow \quad 2^{\circ}\text{-}ROCH_2C(Me){=}NO_2^- \qquad (14)$$

$$2^{\circ}\text{-}ROCH_2C(Me){=}NO_2^- \quad + \quad BrCMe_2NO_2 \quad \xrightarrow{S_{RN}1}$$

$$2^{\circ}\text{-}ROCH_2CMe(NO_2)CMe_2NO_2 \qquad (15)$$

The formation of 2,3-dimethyl-2,3-dinitrobutane $\underline{9}$ can be explained by the generation of 2-nitro-2-propyl anion which reacts with 2-bromo-2-nitropropane via the $S_{RN}1$ process or by the coupling of 2-nitro-2-propyl radicals. The mechanism by

Table 5. Reactions of 2-bromo-2-nitropropane with 2°- and 3°-alkoxide ions[a]

$$BrCMe_2NO_2 \quad + \quad RO^- \ {}^+M \xrightarrow{ROH,\ N_2}$$

$$\underset{\underline{9}}{O_2NCMe_2CMe_2NO_2} + \underset{\underline{14}}{ROCH_2CMe(NO_2)CMe_2NO_2}$$

			% yields[c]	
R	M	Conditions[b]	9	14
Isopropyl	Na^+	24 h	(38)	(61)
Isopropyl	$Na^{+\ d}$	24 h	22	48
tert-Butyl	K^+	12 h	(43)	(25)
tert-Butyl	K^+-18-C-6	12 h	41	trace

[a] $[BrCMe_2NO_2]_o$= 0.10 M and $[ROM]_o$= 0.11 M were used in the corresponding alcohols.

[b] Reactions were irradiated for the time indicated in the Rayonet photoreactor at 35 °C.

[c] GC yields were measured by adding internal standard; and isolated yields are in parentheses.

[d] $[ROM]_o$= 0.22 M was used.

which the 2-nitro-2-propyl anion might be formed is unclear.

Consequently, 2°- and 3°-alkoxide ions do not participate in the $S_{RN}1$ process of Scheme 8 which occurs readily with 1°-alkoxide ions. It is unclear whether 2°- and 3°-alkoxide ions fail to react by Scheme 8 because the E_2 elimination occurs rapidly or because some step in Scheme 8 is does not occur with these anions. Attack of the 2-nitro-2-propyl radical upon 2°- and 3°-alkoxide ions may not lead to the formation of the adduct radical ion or the radical ion if formed may rapidly dissociate to the 2-nitro-2-propyl radical and the alkoxide ion. This could allow a slower E_2 reaction to dominate the reaction process. Furthermore, 2-nitro-2-propyl radicals when formed might be consumed by dimerization or electron transfer from the alkoxide ions to form the 2-nitro-2-propyl anion. With isopropoxide ion the possibility of α-hydrogen atom transfer to form 2-nitropropane is also a possibility.

7. Reaction of 2-bromo-2-nitropropane with a variety of 1 - alkoxide ions

A variety of the anions of alcohols were investigated and are listed in Table 6. The anions of allyl alcohol and *n*-butyl alcohol act as the nucleophiles in the $S_{RN}1$ process of Scheme 8, and also act as the bases which participate in the E_2 reaction follow by the $S_{RN}1$ process as observed for 2°- and

Table 6. Reactions of 2-bromo-2-nitropropane with the anions 1^{o}-alkoxide ions[a]

$$BrCMe_2NO_2 \quad + \quad 2\ RO^{-}\ {}^{+}M \xrightarrow{ROH,\ N_2}$$

$$\underset{\underline{15}}{Me_2C(OR)_2} \quad + \quad \underset{\underline{9}}{O_2NCMe_2CMe_2NO_2} \quad + \quad \underset{\underline{14}}{ROCH_2CMe(NO_2)CMe_2NO_2}$$

R	M	Conditions[b]	% Yields[c]		
			<u>15</u>	<u>9</u>	<u>14</u>
Allyl	Na^+	10 h, UV	35	13	10
n-Bu	Na^+	24 h, UV	21	20	36
2-Ethoxyethyl	Na^+	3 h, UV	46	0	0
2-Hydroxyethyl	Na^+	8 h, UV	0	0	0
Phenyl	K^+	10 h, UV	0	0	0
Acetyl	Na^+	12 h, UV, AcOH[d]	0	0	0
Benzyl	Na^+	24 h, UV	0	0	0

[a] $[BrCMe_2NO_2]_o$= 0.10 M, $[ROM]_o$= 0.22 M. Reactions were carried out in the corresponding alcohols.

[b] Reactions were irradiated for the time indicated in the Rayonet photoreactor.

[c] Isolated yields were measured.

[d] Acetic acid was used as a solvent.

3^{o}-alkoxide ions. However, the anion of 2-ethoxyethyl alcohol reacted to give exclusively the ketal product.

On the other hand, the anions derived from ethylene glycol, phenol, or acetic acid failed to react with 2-bromo-2-nitropropane under the standard conditions. The greatly diminished recovery of 2-bromo-2-nitropropane implies that the formation of 2-nitro-2-propyl anion was involved on the reaction, since the nitronate anion is removed on the aqueous work-up procedure employed. The peculiar result observed with ethylene glycol, a good solvating agent from the sodium cation, led to a consideration of solvent effect upon the ketal forming reaction.

8. Solvent considerations for the formation of 2,2-dialkoxypropane

The formation of the desired 2,2-dialkoxypropane 15 from the reaction between 2-bromo-2-nitropropane and alkoxide ion is solvent dependent. This is verified by the results presented in Table 7 which show that the yield of the product formed is sensitive to the nature of the solvent. A change in solvent from a protic solvent (alcohol) to aprotic solvent (DMSO, HMPA, DMF and THF) has a striking effect on the reaction to produce 2,2-dialkoxypropane 15.

The reaction to form 2,2-dialkoxypropane does not occur in polar aprotic solvents. The ketal forming reaction is not

Table 7. Solvent effects on the formation of 2,2-dialkoxypropane

$$BrCMe_2NO_2 \quad + \quad 2\ RO^{-}\ {}^{+}M \xrightarrow{ROH,\ N_2}$$

$$\underset{\underline{15}}{Me_2C(OR)_2} \quad + \quad \underset{\underline{9}}{O_2NCMe_2CMe_2NO_2} \quad + \quad \underset{\underline{14}}{ROCH_2CMe(NO_2)CMe_2NO_2}$$

			% Yields[a]		
R	M	Conitions[b]	<u>15</u>	<u>9</u>	<u>14</u>
Me	Na^+	5 h, MeOH + DMSO (1:1)	51	5	0
Me	Na^+	5 h, MeOH + DMSO (1:9)	0	19	0
Me	Na^+	5 h, DMSO	0	25	0
Me	Na^+	6 h, DMF	0	31	0
Me	Na^+	5 h, THF	0	29	0
Me	Na^+	12 h, MeOH + THF (1:4)	0	31	0
Me	Na^+	8 h, HMPA	0	18	0
tert-Bu	K^+	12 h, DMSO	0	27	2
tert-Bu	$K^{+\ c}$	12 h, DMSO	0	71	trace
tert-Bu	K^+-18-C-6	12 h, DMSO	0	29	0

[a] GC yields were measured by adding internal standard.

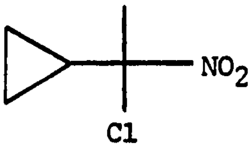
[b] $[BrCMe_2NO_2]_o$= 0.10 M, $[ROM]_o$= 0.22 M. Reactions were irradiated for the time indicated in the Rayonet photoreactor at 35 °C.

[c] $[ROM]_o$= 0.11 M.

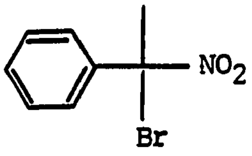
observed in DMSO or THF even in the presence of 10 and 25% of methanol, respectively. These peculiar observations will be discussed further in next section. The reaction to produce ketal obviously requires strong hydrogen bond formation and is restricted to reaction conditions employing the alcohol as solvent.

9. Reaction of methoxide ion with 1-chloro-1-cyclopropyl-1-nitroethane and 1-bromo-1-nitro-1-phenylethane

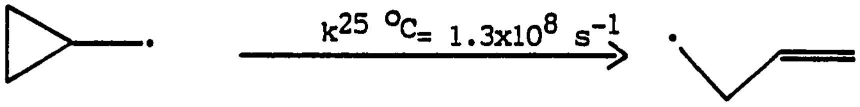
The reactions of 1-chloro-1-cyclopropyl-1-nitroethane 16 with various nucleophiles have been studied to determine the relative efficiency of various nucleophiles in trapping α-nitro radicals using free radical clocks [26]. However, it



16

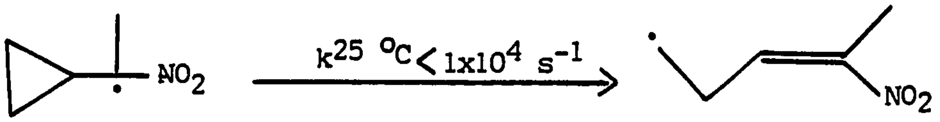


17



18 19

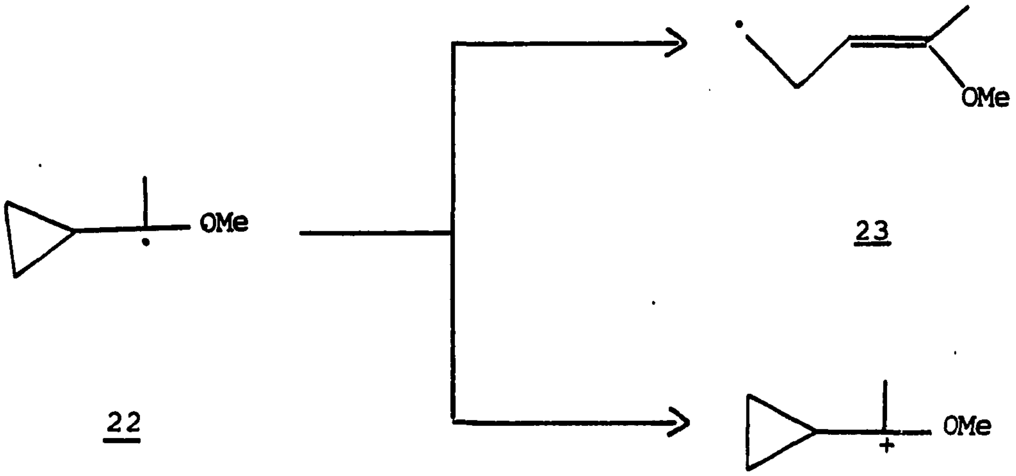
(16)



20 21

(17)

turns out that the α-nitro radical 20 derived from 1-chloro-1-cyclopropyl-1-nitroethane 16 does not readily undergo unimolecular rearrangement to the acyclic radical 21. The absence of the cyclopropylcarbinyl ring opening (Eq. 17) must be due to stabilization by a nitro group at the radical center. Russell and Dedolph [26] have indicated that the 20 → 21 interconversion has a rate constant less than 1×10^4 sec^{-1}. On the other hand, the kinetic rate constant for primary alkyl radical 18 at 25 °C is 1.3×10^8 sec^{-1} which is greater than that for 5-hexenyl radical.



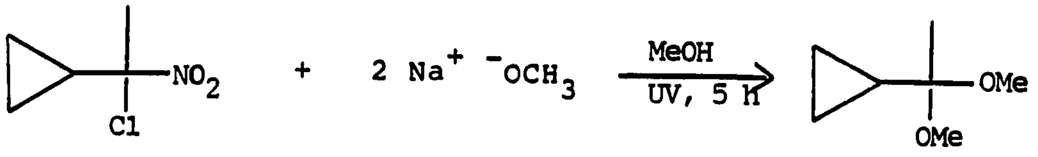
22

23

24

(18)

The reaction of 1-chloro-1-cyclopropyl-1-nitroethane <u>16</u> with methoxide ion under the same conditions in methanol was performed to study the unimolecular rearrangement of the α-methoxy radical <u>22</u> (Eq. 18). A satisfactory yield of 1-cyclopropyl-1,1-dimethoxyethane <u>25</u> was isolated after irradiation using a Rayonet photoreactor (350 nm) under a nitrogen atmosphere (Eq. 19). Analyses of the crude isolate by GC and ^{1}H NMR failed to indicate the presence of any ring-opened products.

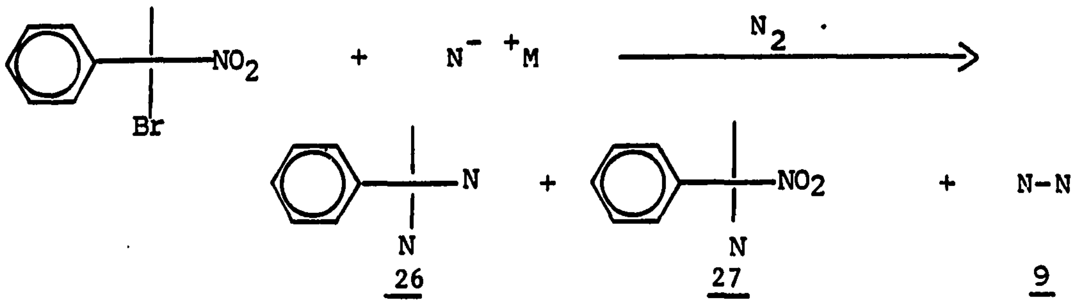


(19)

<u>16</u> <u>25</u> (68%)

This result indicates that the rate of the oxidation of α-methoxy radical <u>22</u> to the carbocation <u>24</u> must be greater than that of the ring opening of α-methoxy radical <u>22</u> to homoallylic radical <u>23</u>. The rate constant for the unimolecular decay of the α-ethoxyethyl radical-TNM adduct to the carbocation in Scheme 9 is about 10^6 sec^{-1} and is strongly enhanced by electron donating substituents at the alpha carbon. Furthermore, the rate constant for the formation of

Table 8. Reactions of 1-bromo-1-nitro-1-phenylethane with nucleophiles



			% Yields[a]		
N^-	M	Conditions[b]	26	27	9
MeO^{-c}	Na^+	7 h, MeOH	34	0	0
MeO^{-c}	Na^+	12 h, MeOH, dark	0 (89)[d]	0	0
$Me_2C{=}NO_2^-$	K^+	4 h, DMSO	0	0	20
$(EtO_2C)_2CEt^-$	K^+	5 h, DMSO	0	0	(82)[e]
$(EtO)_2PO^-$	K^+	5 h, DMSO	0	0	0

[a] GC yields were measured by adding internal standard.

[b] Equimolar amounts of substrates (1.0 mmol) were irradiated in the Rayonet photoreactor at 35 °C.

[c] 2.20 mmol of methoxide ion was used.

[d] GC yield of unreacted starting material.

[e] $(EtO_2C)_2CEtBr$ was formed.

the α-ethoxyethyl radical-TNM adduct is much greater than 10^9 M^{-1} sec^{-1}, so the decomposition of this adduct to the carbocation is usually the rate-determining step [31]. By analogy it seems reasonable that 22 is rapidly oxidized to 24 before the cyclopropylcarbinyl ring opening can occur. Another possible interpretation for the failure of ring opening process is the stability of the α-methoxy radical 22. It is well known that free radicals are stabilized by both electron acceptor groups and by electron donor groups [36,37,38].

1-Bromo-1-nitro-1-phenylethane 17 reacts smoothly with methoxide ion upon photolysis to produce 1,1-dimethoxy-1-phenylethane via the $S_{RN}1$ process. In DMSO, anions such as nitronate anion, dialkyl phosphite anion or malonate anion fail to form coupling products with this substrate (Table 8).

10. Reactions of α,α-disubstituted nitroalkanes with methoxide ion

α-Bromo-α-nitrobenzyl phenyl sulfone 28 and 1,1-dichloro-1-nitroethane 29 were employed in the reaction with methoxide ions. The results of these experiments are listed in Table 9. The formation of 1,1,1-trimethoxyethane 30 can be interpreted by $S_{RN}1$ process of Scheme 11.

Scheme 11

$$\mathrm{RC(X)(Y)NO_2^{-\bullet}} \longrightarrow \mathrm{RC(Y)NO_2^{\bullet}} + \mathrm{X^-}$$

$$\mathrm{RC(Y)NO_2^{\bullet}} + {}^{-}\mathrm{OCH_3} \longrightarrow \mathrm{RC(Y)(OCH_3)NO_2^{-\bullet}}$$

$$\mathrm{RC(Y)(OCH_3)NO_2^{-\bullet}} \longrightarrow \mathrm{RC(OCH_3)NO_2^{\bullet}} + \mathrm{Y^-}$$

$$\mathrm{RC(OCH_3)NO_2^{\bullet}} + {}^{-}\mathrm{OCH_3} \longrightarrow \mathrm{RC(OCH_3)_2NO_2^{-\bullet}}$$

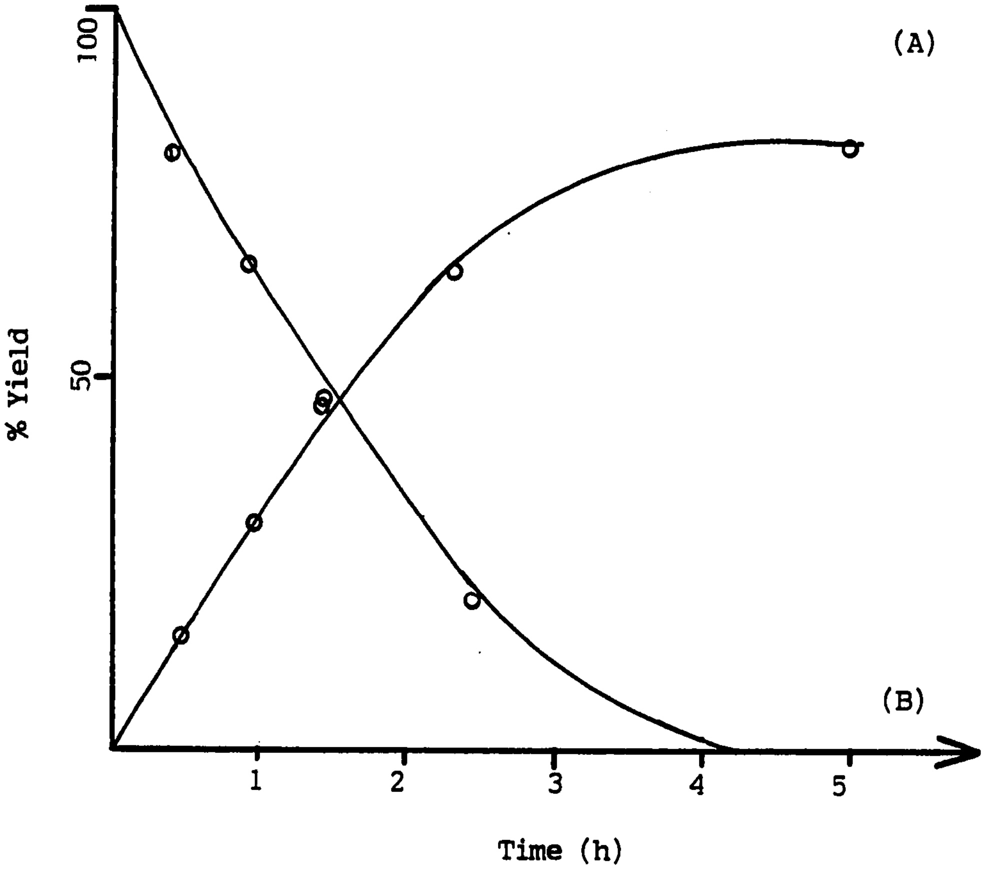
$$\mathrm{RC(OCH_3)_2NO_2^{-\bullet}} \longrightarrow \mathrm{RC(OCH_3)_2^{\bullet}} + \mathrm{NO_2^-}$$

$$\mathrm{RC(OCH_3)_2^{\bullet}} + \mathrm{RC(X)(Y)NO_2} \xrightarrow{\mathrm{E.T}} \mathrm{RC(OCH_3)_2^{+}} + \mathrm{RC(X)(Y)NO_2^{-\bullet}}$$

X,Y = Br, Cl, SO_2Ph

R = Me, Ph

Monitoring the reaction mixture of 1,1-dichloro-1-nitroethane <u>29</u> and methoxide ion in methanol-d_4 (deoxygenated with nitrogen) in the Rayonet photoreactor at 35 °C by ^1H NMR confirmed that 1,1-dichloro-1-nitroethane was consumed and only 1,1,1-trimethoxyethane <u>30</u> was formed as shown in Figure 2. Intermediates, such as 1-chloro-1-methoxy-1-nitroethane, cannot be detected ^1H NMR or GC analyses. The explanation of



A. The formation of 1,1,1-trimethoxyethane

B. The disappearance of 1,1-dichloro-1-nitroethane

Figure 2. Reaction of 0.10 M 1,1-dichloro-1-nitroethane and 0.33 M sodium methoxide in 0.5 mL of methanol-d_4 in a Rayonet photoreactor (350 nm) at 35 ^{o}C.

Table 9. Reactions of trisubstituted substrates with methoxide ions

$$RC(X)(Y)NO_2 \quad + \quad 3 \quad NaOMe \xrightarrow[N_2]{MeOH} RC(OMe)_3$$

R	X	Y	Conditions[a]	% Yields[b]
Me	Cl	Cl	5 h, UV	81
Me	Cl	Cl	5 h, UV	28[c]
Me	Cl	Cl	10 h, dark	0 (89)
Me	Cl	Cl	5 h, UV, DTBN[d]	32
Ph	$PhSO_2$	Br	12 h, UV	48[e]
Ph	$PhSO_2$	Br	24 h, dark	0 (91)

[a] Mixtures of $RC(X)(Y)NO_2$ (1.00 mmol) and sodium methoxide (3.30 mmol) in 10 mL of methanol in Pyrex reaction tube were irradiated in the Rayonet photoreactor.

[b] GC yields measured by adding internal standard; unchanged starting materials are in parentheses.

[c] 1.10 mmol of sodium methoxide was used.

[d] 10 mol% of di-tert-butyl nitroxide.

[e] Isolated yield.

these results is that the α-nitro radical derived from 1,1-dichloro-1-nitroethane 29 is trapped by the methoxide ion to form a radical anion which subsequently dissociates to form another α-nitro radical. The rate of the fragmentation of radical anion must be fast because of the failure to detect the formation of 1-chloro-1-methoxy-1-nitroethane. 1-Methoxy-1-nitroethyl radical is trapped again by the another methoxide ion to form a radical anion which dissociates to form 1,1-dimethoxyethyl radical. These results listed in Table 9 appear consistent with the $S_{RN}1$ process of Scheme 11.

11. Reaction of 2-bromo-2-nitropropane with thiolate ion in methanol

Thiolate ions derived from thiols and sodium methoxide react with 2-bromo-2-nitropropane in methanol to produce the disulfide 31 (Table 10). No evidence for the formation of 2,2-bis(alkylthio)propane was found in the reaction mixture. Bowman and Richardson have reported that thiolates undergo either a substitution reaction with 2-bromo-2-nitropropane in aprotic solvent, such as DMF, or are oxidized to disulfides by an ionic mechanism [39-41]. Russell et al. have also proposed a radical mechanism (Scheme 12) to account for the oxidative dimerization [23].

Table 10. Reactions of 2-bromo-2-nitropropane with thiolate ions in methanol

$$\mathrm{BrCMe_2NO_2} \quad + \quad 2\ \mathrm{RS^-\ {}^+Na} \xrightarrow[\mathrm{N_2}]{\mathrm{MeOH}} \underset{\underline{31}}{\mathrm{RS{-}SR}}$$

R	Conditions[a]	% yields[b]
Ph	3 h, UV	65
$PhCH_2$	5 h, UV	32
n-Bu	5 h, UV	71

[a] Mixtures of 2-bromo-2-nitropropane (1.0 mmol) and sodium thiolate (2.20 mmol) in 10 mL of methanol in Pyrex reaction tube were irradiated in the Rayonet photoreactor at 35 °C.

[b] GC yields were measured by adding internal standard.

Scheme 12

$$XCMe_2NO_2^{-\cdot} \longrightarrow Me_2CNO_2^{\cdot} + X^-$$

$$Me_2CNO_2^{\cdot} + RS^- \longrightarrow Me_2C{=}NO_2^- + RS^{\cdot}$$

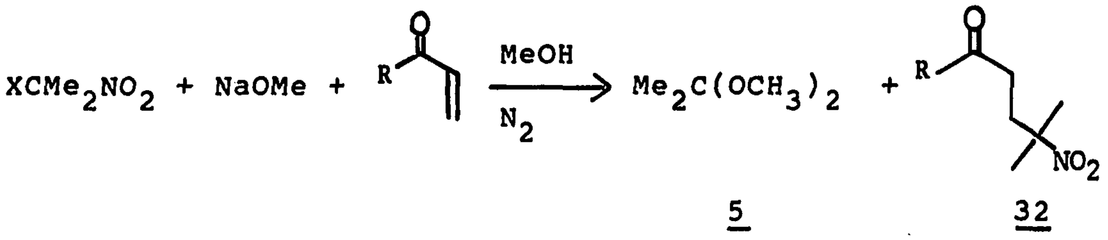
$$2\ RS^{\cdot} \longrightarrow \underset{\underline{31}}{RS{-}RS}$$

12. Reaction of 2-substituted-2-nitropropanes with methoxide ion in the presence of an α,β-unsaturated ketone

2-Bromo-2-nitropropane was allowed to react with methoxide ion in the presence of methyl vinyl ketone and methyl acrylate. The conjugate addition of nitronate anions to α,β-unsaturated carbonyl and nitrile compounds have been investigated in great detail [42,43,44]. The results as shown in Table 11 suggest that the conjugate addition products derived from the reaction mixtures in the presence of methyl vinyl ketone may be connected with the formation of the nitronate anion.

One interpretation of this result is that the nitronate anion is slowly formed by the reaction of methoxide ion with 2-bromo-2-nitropropane. The formation of the conjugate

Table 11. Reactions of 2-substituted-2-nitropropanes with methoxide ion in the presence of an α,β-unsaturated ketone or ester



X	R	Conditions[b]	% yields[a]	
			5	32
Br	Me	1:2:1, 24 h	15	31
Br	Me	1:1:1, 24 h	3	30
Br	Me	1:1:1, 24 h, dark	0	21 (13)[c]
Br	Me	1:1:2, 24 h	0	84
Br	Me	1:1:2, 24 h, dark	0	74
Br	Me	1:1:2, 24 h, DTBN	0	83
Br	MeO	1:1:2, 12 h	52	0
NO_2	Me	1:1:2, 12 h	36	0 (62)[c]
NO_2	MeO	1:1:2, 12 h	21	0 (68)[c]
$PhSO_2$	Me	1:1:2, 12 h	25	0 (71)[c]

[a] Irradiation was carried out in the Rayonet photoreactor for the time indicated.

[b] GC yields measured by adding internal standard.

[c] Recovered $XCMe_2NO_2$.

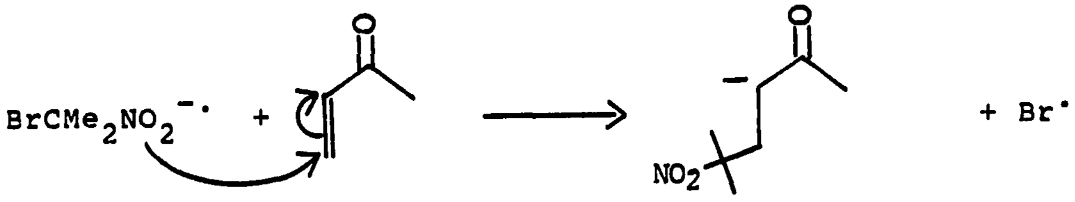
addition product derived from 2-bromo-2-nitropropane is independent of light and radical inhibitor. However, the reactions of 2,2-dinitropropane and 2-nitro-2-phenysulfonylpropane with methoxide ions in the presence of methyl vinyl ketone did not yield the conjugate addition product. Furthermore, with methyl acrylate the reaction mixtures did not yield the conjugate addition product; although reversibility of the Michael addition reaction cannot be ignored. Perhaps, the nitronate anion may be derived from

$$BrCMe_2NO_2^{-\cdot} \longrightarrow Me_2C{=}NO_2^{-} + Br^{\cdot} \qquad (20)$$

the fragmentation of the radical anion (Eq. 20). However, the fragmentation of the radical anion to the 2-nitro-2-propyl anion is very suspicious because of the absence of dimer **9** which is usually formed in the reaction of 2-bromo-2-nitropropane with the anion of 2-nitro-2-propane.

Another interpretation might be the occurrence of a process in which the radical anion of 2-bromo-2-nitropropane reacts directly with methyl vinyl ketone (Scheme 13). However, this interpretation cannot explain the lack of reaction with 1,1-dinitropropane and 1-nitro-1-phenylsulfonylpropane. Furthermore, the reaction occurs in the absence of light and in the presence of radical inhibitors; observation which do not support the interpretation of Scheme 13.

Scheme 13



$$\mathrm{Br}^{\bullet} + \mathrm{MeO}^{-} \longrightarrow \mathrm{HBr} + \mathrm{CH_2O}^{-\bullet}$$

$$\mathrm{HBr} + \mathrm{MeO}^{-} \longrightarrow \mathrm{MeOH} + \mathrm{Br}^{-}$$

$$\mathrm{CH_2O}^{-\bullet} + \mathrm{BrCMe_2NO_2} \longrightarrow \mathrm{CH_2O} + \mathrm{BrCMe_2NO_2}^{-\bullet}$$

The formation of the 2-nitro-2-propyl anion must compete with the formation of 2-nitro-2-propyl radical. However, the anion and the radical may well be derived from different pathways. The mechanism of the formation of the 2-nitro-2-propyl radical in the photostimulated reaction between 2-bromo-2-nitropropane and methoxide ion seems to be clear, but the mechanism of the formation of the 2-nitro-2-propyl anion in the reaction with methyl vinyl ketone is still ambiguous. The presence of methyl vinyl ketone or methyl acrylate seems to inhibit the photostimulated ketal forming reaction. Perhaps the α,β-unsaturated compounds trap the 2-nitropropyl radical and inhibit the chain process leading to ketal. This could allow a slow process forming the 2-nitro-2-propyl anion from 2-bromo-2-nitropropane to become the dominant reaction pathway.

13. Reaction of 2-bromo-2-nitropropane with methoxide ion in the presence of other anions and alkenes

A variety of anions and olefins were added to the photostimulated reaction of 2-bromo-2-nitropropane with methoxide ion. Anions, such as cyanide, azide, iodide and perchlorate did not affect the reactions of 2-bromo-2-nitropropane with methoxide ion which produced 2,2-dimethoxypropane in reasonable yields (Eq. 21). The olefins,

$$BrCMe_2NO_2 + 2\ {}^-OCH_3 + 5\ X^- \xrightarrow[UV]{MeOH} \underset{80-90\%}{Me_2C(OCH_3)_2} \qquad (21)$$

$X = CN^-, N_3^-, I^-, ClO_4^-$

such as 1,1-diphenylethylene, norbornylene and phenylacetylene also failed to trap the α-nitro radical derived from 2-bromo-2-nitropropane (Eq. 22).

$$BrCMe_2NO_2 + 2\ {}^-OCH_3 + 5\ X \xrightarrow[UV]{MeOH} \underset{80-90\%}{Me_2C(OCH_3)_2} \qquad (22)$$

$X = CH_2{=}C(Ph)_2,\ PhC{\equiv}CH$

The results from these experiments seem to indicate that either the α-nitro radical is not involved in the formation of

2,2-dimethoxypropane or that the 2-nitro-2-propyl radical is not trapped by the anions or alkenes employed. A more complete discussion concerning the reactivity of the α-nitro radical will be given later.

Electron-rich olefins, such as a vinyl ether, would be expected to intercept the α-nitro radical to produce a radical which could subsequently be oxidized by 2-bromo-2-nitropropane (Scheme 14).

Scheme 14

$$Me_2CNO_2^{\cdot} \quad + \quad CH_2{=}C(OMe)Ph \longrightarrow Me_2C(NO_2)CH_2\text{-}C(OMe)Ph^{\cdot}$$

$$Me_2C(NO_2)CH_2\text{-}C(OMe)Ph^{\cdot} \quad + \quad BrCMe_2NO_2 \longrightarrow$$
$$Me_2C(NO_2)CH_2\text{-}C(OMe)Ph^{+} \quad + \quad BrCMe_2NO_2^{-\cdot}$$

The reaction of 2-bromo-2-nitropropane(0.10 M) with ethoxide ion(0.22 M) in the presence of excess (1-methoxyethenyl)benzene(0.55 M) <u>33</u> in ethanol produced 35% of acetophenone, 50% of (2-ethoxy-1-methoxyethyl)benzene <u>34</u> and only 5% of 2,2-diethoxypropane. Although no radical addition

$$BrCMe_2NO_2 \quad + \quad 2\ NaOC_2H_5 \quad + \quad 5\ \underset{\underline{33}}{CH_2{=}C(OMe)Ph} \longrightarrow$$

$$\underset{5\%}{Me_2C(OC_2H_5)_2} \quad + \quad \underset{35\%}{PhCOMe} \quad + \quad \underset{\underline{34}\quad 50\%}{CH_2(OEt)CH(OMe)Ph} \qquad (16)$$

products were formed, the diminished yield of 2,2-diethoxypropane may be attributed to the interception of α-nitro radical by the vinyl ether. A diminished yield of 2,2-diethoxypropane was also observed in the reaction with excess 2-methoxypropene. In contrast to the simple olefins, such as 1,1-diphenylethylene, norbornylene and phenylacetylene, electron-rich olefins inhibit the reaction leading to the formation of the ketal. In an attempt to prove that an α-nitro radical would be readily trapped by an electron-rich olefin, the reaction of excess (1-methoxyethenyl)benzene(0.55 M) 34 and 2-bromo-2-nitropropane(0.10 M) with tributyltin hydride was studied. However, the reaction gave only 2-nitropropane in a 50% yield.

The α-nitro radical derived from the reaction of 2-bromo-2-nitropropane and 2-nitro-2-propyl anion upon photolysis is an accepted intermediate in the $S_{RN}1$ process. However, under the conditions where the $S_{RN}1$ coupling reaction to form 2,3-dimethyl-2,3-dinitrobutane occurs, the 2-nitro-2-propyl radical was not trapped by the electron-rich olefins to yield any isolable products.

14. Reaction of 1-methyl-1-nitroethyl p-chlorophenyl sulfide with methoxide ions

In an effort to determine whether the neutral and unknown 2-methoxy-2-nitropropane derived from the electron transfer from the radical anion of 2-methoxy-2-nitropropane to 2-bromo-2-nitropropane is rapidly converted to 2,2-dimethoxypropane by nucleophilic displacement of nitrite ion (Scheme 15), several attempts work made to synthesize 2-methoxy-2-nitropropane. Unfortunately, the synthesis of 2-methoxy-2-nitropropane

Scheme 15

$$BrCMe_2NO_2^{-\cdot} \longrightarrow Me_2CNO_2^{\cdot} + Br^-$$

$$Me_2CNO_2^{\cdot} + {}^-OCH_3 \longrightarrow Me_2C(OMe)NO_2^{-\cdot}$$

$$Me_2C(OMe)NO_2^{-\cdot} + BrCMe_2NO_2 \xrightarrow{E.T} Me_2C(OMe)NO_2 + BrCMe_2NO_2^{-\cdot}$$

$$Me_2C(OMe)NO_2 + {}^-OCH_3 \xrightarrow{fast} Me_2C(OCH_3)_2$$

turned out to be impossible. However, the known 1-methyl-1-nitroethyl *p*-chlorophenyl sulfide **35** was adapted to be a reasonable model for 2-methoxy-2-nitropropane.

1-Methyl-1-nitroethyl *p*-chlorophenyl sulfide **35** was reacted with methoxide ion in methanol under a nitrogen atmosphere in the Rayonet photoreactor to produce only 11% of 2,2-dimethoxypropane. 1-Methoxy-1-methylethyl *p*-chlorophenyl

$$\mathrm{Me_2C(\underline{p}\text{-}ClC_6H_4S)NO_2} + {}^{-}\mathrm{OCH_3} \xrightarrow{\mathrm{MeOH}} \mathrm{Me_2C(\underline{p}\text{-}ClC_6H_4S)OMe} \quad (23)$$

$\underline{35}$ $\underline{36}$

sulfide 36 was not produced (Eq. 23).

Like the previous ketal-favoring reactions, Reaction 23 required light to form 2,2-dimethoxypropane and was inhibited by di-*tert*-butyl nitroxide. For more detail observations, this reaction employing deuterated methanol in a ^{1}H NMR tube was performed in the dark. The anion of 2-nitropropane and the anion of *p*-chlorobenzenethiol were observed in the ^{1}H NMR spectrum. These results seem to be interpretable by the following mechanism shown in Scheme 16.

Scheme 16

$$\mathrm{Me_2C(\underline{p}\text{-}ClC_6H_4S)NO_2}^{-\cdot} \longrightarrow \mathrm{Me_2C{=}NO_2}^{-} + \underline{p}\text{-}\mathrm{ClC_6H_4S}^{\cdot}$$

$$\underline{p}\text{-}\mathrm{Cl\text{-}C_6H_4S}^{\cdot} + \mathrm{CH_3O}^{-} \longrightarrow \underline{p}\text{-}\mathrm{Cl\text{-}C_6H_4SH} + \mathrm{CH_2{=}O}^{-\cdot}$$

$$\mathrm{CH_2{=}O}^{-\cdot} + \mathrm{Me_2C(\underline{p}\text{-}ClC_6H_4S)NO_2} \longrightarrow \mathrm{Me_2C(\underline{p}\text{-}ClC_6H_4S)NO_2}^{-\cdot} + \mathrm{CH_2O}$$

$$\underline{p}\text{-}\mathrm{Cl\text{-}C_6H_4SH} + \mathrm{CH_3O}^{-} \longrightarrow \underline{p}\text{-}\mathrm{Cl\text{-}C_6H_4S}^{-} + \mathrm{CH_3OH}$$

It is now apparent from these results that the methanolysis of neutral 2-methoxy-2-nitropropane can be excluded in the ketal-favoring process.

15. Reaction of 2-bromo-2-nitropropane with 2-nitro-2-propyl anion in the presence of radicaphiles

2-Bromo-2-nitropropane reacts with the 2-nitro-2-propyl anion in the presence of excess cyanide ion upon photolysis in DMSO to give 2-cyano-2,3-dimethyl-3-nitrobutane 37 and 2,3-dimethyl-2,3-dinitrobutane. These results as shown in Table 12 seem to indicate that α-nitro radical derived from the radical anion of 2-bromo-2-nitropropane is trapped by an excess of cyanide ion (Scheme 17). The fragmentation of the resulting radical anion to 2-cyano-2-propyl radical has been previously documented [24]. The formation of 2-cyano-2,3-dimethyl-3-nitrobutane 37 occurs by the subsequent coupling of the 2-nitro-2-propyl anion with the 2-cyano-2-propyl radical.

Scheme 17

$$BrCMe_2NO_2^{-\cdot} \longrightarrow Me_2CNO_2^{\cdot} + Br^-$$

$$Me_2CNO_2^{\cdot} + CN^- \longrightarrow Me_2C(CN)NO_2^{-\cdot}$$

$$Me_2C(CN)NO_2^{-\cdot} \longrightarrow Me_2CCN^{\cdot} + NO_2^-$$

$$Me_2CCN^{\cdot} + Me_2C{=}NO_2^- \longrightarrow NCCMe_2CMe_2NO_2^{-\cdot}$$

Table 12. Reactions of 2-bromo-2-nitropropane with 2-nitro-2-propyl anions in the presence of radicaphiles

$$BrCMe_2NO_2 \quad + \quad Me_2C{=}NO_2^- \quad + \quad M^+ \ ^-X \quad \longrightarrow$$

$$\underset{\underline{A}}{NCCMe_2CMe_2NO_2} \quad + \quad \underset{\underline{B}}{O_2NCMe_2CMe_2NO_2}$$

MX	Conditions[b]	% Yields[a]	
		A	B
NaCN	1:1:8, 1 h	(75)	23
NaCN	1:1:20, 1 h	(87)	8
NaCN	1:1:2, 2 h	10	67
NaN_3	1:1:10, 5 h	0	81
$PhSO_2K$	1:1:10, 5 h	0	80
AcOK	1:1:5, 10 h	0	83
KSCN	1:1:5, 5 h	0	81
NaF	1:1:5, 10 h	0	85
NaI	1:1:5, 7 h	0	87
$(MeO)_3P$	1:1:5, 5 h	0	85

[a] GC yields measured by adding internal standard; isolated yields are in parentheses.

[b] Reaction mixture (1 mmol scale) in 10 mL of DMSO was irradiated in the Rayonet photoreactor.

$$\mathrm{NCCMe_2CMe_2NO_2}^{-\cdot} + \mathrm{BrCMe_2NO_2} \xrightarrow{\mathrm{E.T}}$$

$$\underset{\underline{37}}{\mathrm{NCCMe_2CMe_2NO_2}} + \mathrm{BrCMe_2NO_2}^{-\cdot}$$

However, a wide variety of other anions failed to trap the 2-nitro-2-propyl radical. Possibly, the fragmentation of the radical anion derived from the coupling of 2-nitro-2-propyl anion and other anions (Table 12) yields only the 2-nitro-2-propyl radical and not the 2-substituted-2-propyl radical.

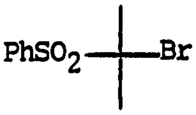
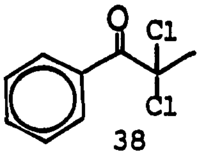
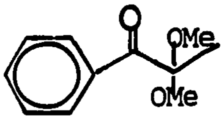
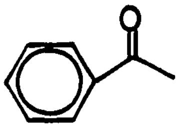
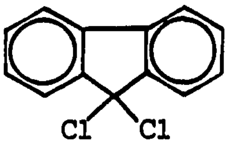
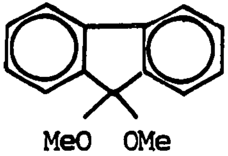
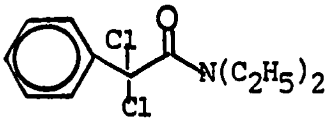
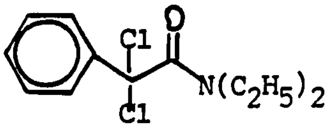
16. Reactions of various substrates not containing a nitro group with methoxide ion

In an attempt to discover reactions with other substrates not containing an α-nitro group which proceed via $S_{RN}1$ processes, reagents, such as 2-bromo-2-(phenylsulfonyl)propane 8, 9,9-dichlorofluorene 39, 2,2-dichloro-1-phenyl-1-propanone 38 and N,N-diethyl-α,α-dichlorophenylacetamide 40, were employed. The results are listed in Table 13.

The reactions of 2-bromo-2-(phenylsulfonyl)propane 8 and N,N-diethyl-α,α-dichlorophenylacetamide 40 with methoxide ions did not occur upon photolysis. The unchanged starting materials were recovered after work-up.

9,9-Dichlorofluorene 39 and 2,2-dichloro-1-phenyl-1-propanone 38 reacted with methoxide ions to give 9,9-

Table 13. Reactions of substrates with methoxide ions

Substrates	Conditions[a]	% Yields of products[b]
 8	24 h	8 (91)
 38	1 h	 41 63  5
38	dark, 1 h	41 69
38	dark, DTBN[c], 1 h	41 67
 39	2 h	 42 45
39	dark, 2 h	42 36
 40	2 h	 40 (92)

[a] $[\text{substrate}]_0$ = 0.10 M, [NaOMe]= 0.22 M. Reactions were irradiated for the time indicated in the Rayonet photoreactor at 35 °C.

[b] Isolated yields; GC yields of unreacted starting materials are in parentheses.

[c] DTBN= 5 mol% of di-*tert*-butyl nitroxide.

dimethoxyfluorene 42 and 2,2-methoxy-1-phenyl-1-propanone 41 respectively. But it seemed unlikely that the reactions of these two substrates proceed via the $S_{RN}1$ process, since the reactions occurred readily in the dark and the yields were not affected by the presence of di-*tert*-butyl nitroxide.

C. Conclusion

2-Substituted-2-nitropropanes (substituent= Cl, Br, N_3, $PhSO_2$, NO_2, *p*-Cl-C_6H_4S) reacted smoothly with 1°-alkoxide ions under the influence of ultraviolet light irradiation in the corresponding alcohol solutions to afford 2,2-dialkoxypropanes in good yields by reactions which proceed via a free radical chain mechanism. Among the evidence which supports a free radical chain mechanism are as following; (1) the reactions in the dark fail to give the product, (2) the rate of ketal formation is drastically retarded by the presence of 10 mol % of di-*tert*-butyl nitroxide (k.c.l. will be discussed in detail later), (3) the yields of product are significantly decreased by radical inhibitors, such as *p*-dinitrobenzene and *m*-dinitrobenzene, (4) the presence of oxygen also inhibits the reaction.

The intermediate 2-methoxy-2-nitropropane derived from electron transfer between the radical anion of 2-methoxy-2-

nitropropane and 2-bromo-2-nitropropane could not be detected by GC or ^{1}H NMR analyses after or before work-up. Evidence against a mechanism involving rapid solvolysis of the unknown 2-methoxy-2-nitropropane to give the ketal is based on the observation that 1-methyl-1-nitroethyl p-chlorophenyl sulfide 35 with methoxide ion in methanol fails to solvolyze to give 1-methoxy-1-methylethyl p-chlorophenyl sulfide.

It appears from the experiments reported that the α-nitro radicals derived from 2-bromo-2-nitropropane undergo coupling with methoxide ion before dimerization can occur. This step is followed by the fragmentation of nitrite ion from the radical anion of 2-methoxy-2-nitropropane to yield the 2-methoxy-2-propyl radical which can be oxidized by electron transfer to the 2-substituted-2-nitropropane. The free radical chain process leading to the ketal is inhibited by methyl vinyl ketone or (1-methoxyethenyl)benzene but not by 1,1-diphenylethylene or phenylacetylene.

2-Bromo-2-nitropropane also reacts with 2°- or 3°-alkoxy ions upon photolysis or in the dark to give two major products in reasonable yields. The reactions proceed in part by an E_2 elimination to form 2-nitropropene which reacts with the alkoxide ion to form $ROCH_2C(Me)=NO_2^-$ which subsequently undergoes coupling with the 2-bromo-2-nitropropane via the $S_{RN}1$ process. The other major product is the coupling product of $Me_2C=NO_2^-$ and $BrCMe_2NO_2$.

D. Experimental Section

1. General Considerations

Analytical gas chromatography (GC) was performed on a varian 3700 gas chromatograph equipped with a Hewlett-Packard 3390A integrator. Melting points were determined on a Thomas-Hoover Capillary melting point apparatus and are uncorrected. GC mass spectra (GCMS) were recorded on a Finnegan 4000 spectrometer with Incos data system. High resolution mass spectra (MS) were recorded on a Kratos MS-50 spectrometer. Infrared spectra (IR) were recorded on a Beckman IR 4250 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Nicolet-300 spectrometer. Chemical shifts are reported in parts per million from tetramethylsilane(TMS). ^{1}H NMR yields were determined by integrated comparison with a known amount of an appropriate reference (benzene, dibromomethane).

Most products were isolated by either flash column chromatography on silica gel (Kiesel gel 60, 230-400 mesh ASTM, purchased from EM Regents Co.) with eluents of mixed solvents or by distillation. GC yields were determined by using an internal standard of biphenyl or naphthalene.

2. Solvents and reagents

Solvents were purchased from Fisher or Baker. Absolute methanol was dried by the reaction with magnesium methoxide prepared by placing 5 g of dry magnesium turnings and 0.5 g iodine in a flask, followed by 50 mL of methanol and warming the mixture until a vigorous reaction occurred. Up to 1 L of methanol was added, refluxed for one hour, and then distilled and stored over 4 A Molecular Sieves. Absolute ethanol was obtained by the same method. Allyl alcohol was dried with K_2CO_3 followed by distillation under nitrogen. Butanol was stirred over CaO, followed by refluxing, and distillation under nitrogen. Dimethyl sulfoxide (DMSO) was stirred with calcium hydride at 80 ^{o}C overnight, distilled and stored over 4 A Molecular Sieves. Tetrahydrofuran (THF) was refluxed with sodium metal by using benzophenone as an indicator to form sodium benzophenone ketyl (deep blue). After a few hours, the material was distilled and stored over 4 A Molecular Sieves.

Chemical reagents in high purity grades were purchased mostly from Aldrich. In most cases, the reagents were used without further purification. The ketals were synthesized by a known method [45]. The constitution of reagents which prepared by known methods was verified either by a comparison with the reported melting point or from the ^{1}H NMR spectrum.

3. Preparation of 2-substituted-2-nitropropanes

2-Halo-2-nitropropanes were prepared in the usual manner [46] by addition of halogen to an ice-cold aqueous solution of

2-nitropropane and sodium hydroxide. The oily product was collected from the bottom of the flask, washed with aqueous thiosulfate, dried and distilled.

2,2-Dinitropropane has been prepared by several methods [47-50]. The oxidative nitration of nitronate salts using ferricyanide as the oxidant was used. 2-Cyano-2-nitropropane was also prepared by the oxidative reaction of the nitronate salt with cyanide ion in the presence of ferricyanide.

2-Nitro-2-(phenylsulfonyl)propane was readily obtained in high yield by treating 2-bromo-2-nitropropane with sodium benzenesulfinate in DMSO solution in the light. The product was extracted with benzene, washed, dried and concentrated. The resulting white solid after one recrystallization from 95% ethanol gave 80% yield of the pure product (mp 106-100 °C, lit. [13] mp 104-110 °C).

^{1}H NMR (δ, $CDCl_3$) 1.95 (s, 6H), 7.71 (m, 5H).

2-Azide-2-nitropropane was prepared by either nucleophilic substitution or oxidative addition of azide ion [51,52]. 2-Bromo-2-nitropropane was added to a solution of sodium azide in HMPA at room temperature under nitrogen. After stirring 24 hours, the product was extracted from brine solution with methylene chloride. The extract was dried, concentrated and distilled with extreme caution.

1-Methyl-1-nitroethyl p-chlorophenyl sulfide 35 [8] was prepared by addition of 2-nitro-2-(phenylsulfonyl)propane to the solution of the sodium salt of p-chlorothiophenol in DMSO under the two 20 W fluorescent lights After stirring 3 hours, the reaction mixture was poured into ice-water and extracted with ethyl ether. The extracts were dried and the white solid left after evaporation of the ethyl ether was recrystallized from hexane (mp 111-113 ^{o}C, lit. [8] mp 109-110 ^{o}C).

^{1}H NMR (δ, $CDCl_3$) 1.83 (s, 6H), 7.37 (s, 4H). This compound has been prepared by another methods [14, 15, 40], but several of the methods reported by Bowman failed to yield any product.

Ethyl α-nitroisobutyrate [53] was prepared by the general procedure of Kornblum and co-workers from the sodium nitrite and ethyl α-bromopropinate in DMF.

4. Preparation of 1-bromo-1-nitro-1-phenylethane and 1-chloro-1-cyclopropyl-1-nitroethane

The phenylation of secondary nitro compounds with diphenyliodonium tosylates which has been developed by Kornblum and Taylor [54] was employed to prepare 1-nitro-1-phenylethane. Diphenyliodonium tosylate (9.04 g, 20 mmol) generated from potassium iodate, benzene and acetic anhydride in the solution of acetic anhydride and sulfuric acid was added to a magnetically stirred suspension of the sodium salt of 2-nitropropane (2.75 g, 25 mmol) in 25 mL of dry DMF. After 24 hours, the reaction mixture was poured into the brine solution and extracted with five 40 mL portions of petroleum ether (bp 35-37 °C). The combined petroleum ether extracts was washed, dried and removed under vacuum at room temperature. The residue was distilled (92-95 °C/1 torr) to obtain 2.20 g of pure 1-nitro-1-phenylethane.

^{1}H NMR (δ, $CDCl_3$) 1.89 (d, 3H, J=6.9 Hz), 5.62 (q, 1H, J=6.9 Hz), 7.51 (m, 5H).

1-Bromo-1-nitro-1-phenylethane <u>17</u> [46] was prepared by the bromination of the sodium salt of 1-nitro-1-phenylethane in methanol at 0 °C. The bromine (1.60 g, 10 mmol) was added over a period of 30 minutes to the stirred sodium salt of 1-nitro-1-phenylethane (1.70 g, 10 mmol) in 30 mL of dry methanol at 0 °C. The reaction was then warmed to room temperature and worked up as previously described to yield 1.84 g of product.

^{1}H NMR (δ, $CDCl_3$) 2.66 (s, 3H), 7.50 (m, 5H).

IR (neat, NaCl plates, cm^{-1}) 3200 (w), 2970 (m), 1610 (m), 1550 (m), 1430 (m), 1340 (m).

1-Chloro-1-cyclopropyl-1-nitroethane <u>16</u> was prepared by the addition of Cl_2 to the oxime of cyclopropyl methyl ketone in methylene chloride at 0 °C. This was followed by ozonolysis at -78 °C. Flash column chromatography gave the pure product. This method has been developed by Russell and Dedolph [26].

5. Preparation of α-bromo-α-nitrobenzyl phenyl sulfone

30% Hydrogen peroxide (44 g, 0.40 mol) was added over a period of 30 minutes to benzyl phenyl sulfide (20 g, 0.10 mol) in 100 mL of a 1:1 mixture of acetic anhydride and acetic acid at 0 °C. The mixture was stirred for 24 hours at room temperature to yield a white solid. The mixture was poured into ice-water, filtered and dried in the air. The crude product was recrystallized from ethanol to give an 82% yield of pure benzyl phenyl sulfone.

^{1}H NMR (δ, $CDCl_3$) 4.81 (s, 2H), 7.30 (m, 5H), 7.60 (m, 5H).

Benzyl phenyl sulfone (11.60 g, 0.05 mol) was added to a solution of potassium *tert*-butoxide (6.2 g, 0.055 mol) in 200 mL of dried THF under nitrogen at room temperature. The reaction mixture was stirred for 2 hours. After cooling to -35 °C, butyl nitrate (9.52 g, 0.08 mol) was added dropwise and stirring was continued for 4 hours. Glacial acetic acid (0.10 mol) was added dropwise and the reaction mixture was allowed to warm to room temperature. After the potassium acetate was removed by filtration, the solvent was removed in vacuo and the crude α-nitro sulfone was treated with 10% aqueous sodium hydroxide. The insoluble starting material was removed by filtration. The aqueous filtrate was cooled to 0 °C, carefully acidified with glacial acetic acid and the crude α-nitrosulfone removed by filtration. Recrystallization from ethanol gave 80% of the product (mp 135-137 °C, lit. [55] mp 137-139 °C).

^{1}H NMR (δ, $CDCl_3$) 6.51 (s, 1H), 7.1-7.8 (m, 10H).

Bromine (1.6 g, 0.01 mol) was added dropwise to the sodium salt of the α-nitro sulfone derived from sodium ethoxide and α-nitro sulfone in ethanol at room temperature. The mixture was stirred overnight. Removal of solvent, extraction with water and recrystallization from ethanol gave 88% of α-bromo-α-nitrobenzyl phenyl sulfone <u>29</u> (mp 91-92 °C, lit. [55] mp 90-91 °C).

6. Preparation of (1-methoxyethenyl)benzene

The (1-methoxyethenyl)benzene <u>33</u> was prepared by a method adapted from Loudon et al. [56]. A 500 mL flask, equipped with condenser and nitrogen inlet, was charged with methyl orthoformate (50 g, 0.48 mol), acetophenone (48 g, 0.40 mol), *p*-toluenesulfonic acid (0.25 g) and 200 mL of dry methanol. The mixture was refluxed for 16 hours and then cooled to room temperature. The condenser was replaced with a vigreux column and the methyl formate, methanol and excess methyl orthoformate was distilled. The reaction mixture was then heated to approximately 150 °C and allowed to remain there until no more methanol was produced. The reaction mixture was cooled and then distilled under vacuum to give 70% of (1-methoxyethenyl)benzene <u>33</u> as a colorless liquid.

^{1}H NMR (δ, $CDCl_3$) 3.73 (s, 3H), 4.21 (d, 1H, J=2.7 Hz), 4.65 (d, 1H, J=2.7 Hz), 7.6-7.3 (m, 5H).

GCMS m/e (relative intensity) 134 (87), 133 (100), 104 (68), 103 (62), 91 (52), 78 (48), 77 (48), 65 (20), 51 (46).

7. Preparation of 2.2-dichloro-1-phenyl-1-propanone

2.2-Dichloro-1-phenyl-1-propanone 38 was prepared as described by Kimpe et al. [57]. Thus, a solution of propiophenone (33.5 g, 0.25 mol) in 300 mL N,N-dimethylformamide was heated until a temperature of 80 °C inside the flask was reached. Chlorine gas was bubbled into the solution and the exothermic reaction raised the temperature to 100 °C. After 30 minutes the reaction was completed. The mixture was cooled, poured into 600 mL of 2 N hydrochloric acid and extracted with carbon tetrachloride. The solution was dried ($MgSO_4$), evaporated and distilled under vacuum to give 69% of 2,2-dichloro-1-phenyl-1-propanone 38.

^{1}H NMR (δ, $CDCl_3$) 2.25 (s, 3H), 7.5-8.2(m, 5H).

IR (neat, NaCl plates, cm^{-1}) 3100, 2950, 1690, 1360.

8. Preparation of N,N-diethyl-α,α-dichlorophenylacetamide

N,N-diethyl-α,α-dichlorophenylacetamide 40 was prepared by a method adapted from Smith and Speziale [58]. Thus, a mixture of phosphorus pentachloride (21.0 g, 0.1 mol) and phenylacetyl chloride (15.5 g, 0.05 mol) was refluxed at 140

^{o}C. After refluxing 24 hours, distillation gave phosphorous trichloride (bp 74-76 ^{o}C). The residue was again refluxed for 24 hours and phosphorus trichloride distilled. After an addition reflux period of 24 hours, distillation gave phosphorous trichloride and the acid chloride as a colorless liquid (bp 100 ^{o}C/6 torr) in 90% yield. Diethylamine (8.5 g, 0.12 mol) was added dropwise to the acid chloride (13.0 g, 0.058 mol) in 50 mL benzene. The benzene solution was dried over calcium chloride and evaporated. Distillation of the residue gave 65% of the product, N,N-diethyl-α,α-dichlorophenylacetamide 40.

^{1}H NMR (δ, $CDCl_3$) 0.75 (t, 3H), 1.10 (t, 3H), 3.02 (q, 2H), 7.5 (m, 5H).

9. Preparation of 9,9-dichlorofluorene

Several methods have been developed to prepare 9,9-dichlorofluorene 39 [59, 60]. Thus, fluorenone (18 g, 0.1 mol) and phosphorous pentachloride (22.8 g, 0.11 mol) were added to phosphorous oxychloride (3 g, 0.02 mol) in 60 mL of toluene. The mixture was heated for 3 hours and became dark brown in color. Vacuum distillation (25 torr) gave most of the phosphorous compounds. The residue was dissolved in benzene, washed with ice water and dried over calcium chloride. The benzene was removed under reduced pressure and the residue was recrystallized from glacial acetic acid. A

60% yield of colorless crystals was obtained (mp 104-105 °C, lit. [59] mp 102.9-103.1 °C).

10. Preparation of 2-bromo-2-(phenylsulfonyl)propane

Thiophenol (11.0 g, 0.10 mol) and potassium hydroxide (5.7 g, 0.10 mol) were dissolved in 50 mL of hot 95% ethanol. Isopropyl bromide (12.3 g, 0.10 mol) was added dropwise to this mixture kept at 70 °C. The reaction mixture was refluxed for 20 minutes, cooled and extracted from water with ethyl ether. After removal of solvent, the residue was distilled to give 61% of isopropyl phenyl sulfide. The oxidation of isopropyl phenyl sulfide with hydrogen peroxide was performed under the same procedure described previously. The bromination of isopropyl phenyl sulfone was carried out according to the procedure for the reaction of the sodium salt of 2-nitropropane with bromine. After distillation under vacuum, a 95% yield of pure 2-bromo-2-(phenylsulfonyl)propane 8 was obtained.

^{1}H NMR (δ, $CDCl_3$) 2.01 (s, 3H), 7.5-8.0 (m, 5H).

11. Photoreactions of 2-substituted-2-nitropropanes with methoxide ions

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL methanol in a Pyrex tube equipped with a rubber septum under nitrogen. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe through a septum to the solution of methoxide ion. The mixture was irradiated at 350 nm in the Rayonet photoreactor for a period of time (see Table 1). The reaction mixture was washed with brine solution. The mixture was dried over anhydrous magnesium sulfate and the solvent was removed very carefully by fractional distillation with a vigreux column. The crude isolate was purified for analysis by Kugelrohr distillation (83 °C/760 torr) to yield 83% of pure 2,2-dimethoxypropane as a colorless liquid.

^{1}H NMR (δ, $CDCl_3$) 1.31 (s, 6H), 3.19 (s, 6H).

IR (neat, NaCl plates, cm^{-1}) 2980 (s), 2880 (m), 1370 (s), 1210 (s), 1150 (s), 820 (s).

GCMS m/e (relative intensity) 89 (20), 73 (100), 43 (60).

Identification of the product was confirmed by comparison of their ^{1}H NMR and GCMS data with those of the authentic compound synthesized by known method [45].

A variety of 2-substituted-2-nitropropanes (1.0 mmol) were repeated with methoxide ion (2.2 mmol) under the same procedure. Yields of the products from the reaction of the 2-substituted-2-nitropropanes with methoxide ion were determined by GC by adding a known amount of biphenyl as an internal standard (see Table 2).

One equivalent of sodium metal (0.026 g, 1.1 mmol) was used in the reaction of 2-bromo-2-nitropropane (0.17 g, 1.0mmol) in 10 mL of methanol. The reaction mixture was worked up as previously described. GC analysis showed that the crude residue contained 45% of 2,2-dimethoxypropane and 43% of 2-bromo-2-nitropropane.

12. Effect of light on the reaction of 2-bromo-2-nitropropane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere 2-bromo-2-nitropropane (0.17 g, 1.0 mmol) was added to the solution. The Pyrex tube was wrapped tightly with several layers of aluminum foil to exclude light and placed in a Rayonet photoreactor at 40 °C. After 24 hours, the reaction mixture was worked up as previously described. GC analysis of the crude isolate revealed that the isolate contained 90% of starting 2-bromo-2-nitropropane. 2,2-Dimethoxypropane was not observed.

Another reaction mixture was prepared and was not wrapped with aluminum foil. The mixture was irradiated with a 275 W sunlamp approximately 15 cm from the Pyrex tube at ambient temperature for 4 hours. After completion, the usual work-up afforded 93% of 2,2-dimethoxypropane by GC analysis.

Another reaction mixture was also prepared and was not wrapped with aluminum foil. The reaction mixture was in room light for 4 hours. The reaction mixture was worked up as previously described. GC analysis showed that the crude isolate contained 88% of 2-bromo-2-nitropropane. None of 2,2-dimethoxypropane was observed.

13. Effect of di-tert-butyl nitroxide (DTBN) on the reaction of 2-bromo-2-nitropropane with methoxide ion

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added to a solution of methoxide ion (2.2 mmol) and di-*tert*-butyl nitroxide (0.014 g, 0.1 mmol) in 10mL of dry methanol under a nitrogen atmosphere. The reaction mixture was irradiated for 4 hours at 350 nm in the Rayonet photoreactor. The reaction mixture was worked up as previously described. GC analysis of the crude isolate showed that the residue contained 31% of 2,2-dimethoxypropanes. None of starting material was observed.

14. Effect of oxygen on the reaction of 2-bromo-2-nitropropane with methoxide ion

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added to a solution of methoxide ion (2.2 mmol) in 10 mL of dry methanol. As the mixture was being irradiated at 350 nm in the Rayonet photoreactor, oxygen gas was passed via a long needle through septum into the reaction mixture for 30 minutes. After 4 hours, the reaction mixture was worked up as previously described. GC analysis of the crude isolate showed that the residue did not contain 2,2-dimethoxypropane.

15. Effect of m-dinitrobenzene (m-DNB) on the reaction of 2-bromo-2-nitropropane with methoxide ion

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to a solution of methoxide ion (2.2 mmol) and *m*-dinitrobenzene (0.008 g, 0.05 mmol) in 10 mL of dry methanol solution under a nitrogen atmosphere. The reaction mixture was irradiated for 5 hours at 350 nm in the Rayonet photoreactor. The reaction mixture was worked up as previously described. GC analysis showed that the crude residue contained 51% of 2,2-dimethoxypropane.

16. Effect of counterions on the reaction of 2-bromo-2-nitropropane with methoxide ion

Sodium, potassium and lithium methoxides were prepared from the corresponding metals and methanol. Triton B ($PhCH_2N(CH_3)_3^{+-}OCH_3/MeOH$) was purchased from Aldrich. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added to a solution containing methoxide ion (2.2 mmol) with one of these counterions in methanol under a nitrogen atmosphere. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor. The reaction mixture was worked up as previously described. Yields are summarized in Table 2.

17. The consumption of 2-bromo-2-nitropropane and the formation of 2,2-dimethoxypropane in the reaction of 2-bromo-2-nitropropane with methoxide ion in deuterated methanol

Sodium metal (0.0025 g, 0.11 mmol) was dissolved in 0.5 mL of nitrogen-purged methanol-d_4 in a NMR tube equipped with a rubber septum and sealed with a parafilm. 2-Bromo-2-nitropropane (0.0085 g, 0.05 mmol) and benzene (0.01 mmol, internal standard) were added by syringe to the solution. After a ^1H NMR spectrum was obtained, the NMR tube was irradiated in the Rayonet photoreactor. The progress of the reaction was monitored by ^1H NMR and the consumption of 2-bromo-2-nitropropane was obtained by the integration of the signal for the six methyl protons compared with the internal standard. The consumption of 2-bromo-2-nitropropane and the formation of 2,2-dimethoxypropane are given in Figure 1 and Table 14.

18. Photoreactions of 2-substituted-2-nitropropanes with ethoxide ions

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL ethanol in a Pyrex tube under a nitrogen atmosphere. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe through a septum to the solution. The mixture was irradiated at 350 nm in the Rayonet photoreactor for a period of time (see Table 3). After completion of the reaction, ethyl ether

Table 14. Reaction of 2-bromo-2-nitropropane with methoxide ion in deuterated methanol

$$\underset{\text{A}}{BrCMe_2NO_2} \quad + \quad 2\ NaOCD_3 \xrightarrow{\text{UV, } N_2\ ^{a}} \underset{\text{B}}{Me_2C(OCD_3)_2}$$

Time (h)	% consumption of A[b]	% formation of B[b]
0	100	0
0.5	59.8	37.4
1	34.4	58.8
2	19.8	75.5
3	8.9	89.7
5	0	95.3
7	0	95.0

[a] Reaction of 2-bromo-2-nitropropane (0.10 M) and methoxide ion (0.22 M) was carried out in 0.5 mL of deuterated methanol in the Rayonet photoreactor at 35 °C.

[b] ^1H NMR yields measured by adding a known amount of benzene as an internal standard.

(10 mL) was added and washed with brine solution. The ethereal solution was dried over anhydrous magnesium sulfate and the solvent was removed carefully by fractional distillation. The crude isolate was further separated for analysis by distillation through a short distillation column to obtain 45% of pure 2,2-diethoxypropane.

^{1}H NMR (δ, $CDCl_3$) 1.32 (t, 2H), 1.38 (s, 3H), 3.50 (q, 3H).

IR (neat, NaCl plates, cm^{-1}) 2990 (s), 1420 (w), 1380 (m), 1190 (s), 1050 (s), 950 (s), 860 (m).

GCMS m/e (relative intensity) 117 (10), 87 (85), 59 (100), 43 (20).

Identification of the product was confirmed by comparison of the ^{1}H NMR and GCMS data with those of the authentic compound synthesized by known method [45].

19. Reaction of 2-cyano-2-nitropropane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL methanol in a Pyrex tube under a nitrogen atmosphere. 2-Cyano-2-nitropropane (0.26 g, 1.5 mmol) was added to the solution. The reaction mixture was stirred for 24 hours and poured into ice-water. The reaction mixture was extracted with methylene chloride, dried over anhydrous magnesium sulfate and the solvent evaporated under reduced pressure. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 7:3) to give 71% of methyl 2-methyl-2-nitropropionimidate 13.

^{1}H NMR (δ, $CDCl_3$) 1.796 (s, 6H), 3.764 (s, 3H), 7.780 (s, 1H).

^{13}C NMR (δ, $CDCl_3$) 23.89, 23.95, 53.85, 53.68, 167.37.

GCMS m/e (relative intensity) 15 (9), 100 (80), 73 (100), 68 (50), 58 (46), 41 (90).

High-resolution MS calculated for $C_5H_{11}N_2O_2$ (M+1) : 147.07698. Found : 147.07700. Error= + 0.1 pm.

20. Photoreaction of 2-bromo-2-nitropropane with isopropoxide ion

Sodium metal (0.026 g, 1.1 mmol) was dissolved in 10 mL 2-propanol in a Pyrex tube under a nitrogen atmosphere at 50 °C. The solution was allowed to cool to room temperature. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor for 24 hours. The reaction mixture was poured into 20 mL of brine and extracted with methylene chloride (3x10 mL). The combined methylene chloride extracts were washed, dried and concentrated. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1) to give 38% of 2,3-dimethyl-2,3-dinitrobutane 9 and 61% of 2,3-dimethyl-2,3-dinitrobutyl isopropyl ether 14, R=i-Pr (mp 99-102 °C).

14, R=i-Pr : ^{1}H NMR (δ, $CDCl_3$) 1.033 (d, 3H, J=6 Hz), 1.068 (d, 3H, J=6 Hz), 1.621 (s, 3H), 1.630 (s, 3H), 1.681 (s, 3H), 3.591 (m, 1H), 3.782 (d, 7H, J=9.9 Hz), 4.091 (d, 1H, J=10.0 Hz).

^{13}C NMR (δ, $CDCl_3$) 17.405, 21.706, 23.087, 23.447, 69.692, 73.153, 90.839, 94.115.

GCMS m/e (relative intensity) 219 (1), 175 (10), 141 (20), 116 (10), 99 (70), 85 (20), 43 (100).

IR (neat, NaCl plates, cm^{-1}) 2980 (w), 2800 (w), 1530 (s), 1375 (s), 1100 (s), 1040 (s).

High-resolution MS calculated for $C_8H_{15}N_2O_5$ (M^+ - CH_3) : 219.09810. Found : 219.09908. Error= +9.8 pm.

The ^{1}H NMR spectrum and GCMS of 2,3-dimethyl-2,3-dinitrobutane were identical to those of authentic compound.

21. Photoreaction of 2-bromo-2-nitropropane with tert-butoxide ion

Potassium metal (0.044 g, 1.10 mmol) was dissolved in 10 mL of dry tert-butyl alcohol in a Pyrex tube under a nitrogen atmosphere at 60 °C. The solution was allowed to cool to room temperature. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution of tert-butoxide ion. The reaction mixture was irradiated in the Rayonet photoreactor for 12 hours. The reaction mixture was worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2) to give 43% of 2,3-dimethyl-2,3-dinitrobutane 9 and 25% of 2,3-dimethyl-2,3-dinitrobutyl *tert*-butyl ether 14, R=*t*-Bu (mp 103-105 °C).

14, R=*t*-Bu : ^{1}H NMR (δ, $CDCl_3$) 1.157 (s, 9H), 1.671 (s, 3H), 1.702 (s, 3H), 1.757 (s, 3H), 3.748 (d, 2H, J=9.8 Hz), 4.137 (d, 2H, J=10.6 Hz).

^{13}C NMR (δ, $CDCl_3$) 17.405, 23.131, 23.489, 27.106, 63.854, 74.117, 90.958, 94.191.

GCMS m/e (relative intensity) 233 (1), 174 (8), 145 (5), 99 (70), 57 (100).

IR (neat, NaCl plates, cm^{-1}) 2995 (m), 2900 (m), 1540 (s), 1370 (s), 1130 (s), 1110 (s), 1030 (s).

High-resolution MS calculated for $C_9H_{17}N_2O_5$ ($M^+ - CH_3$) : 233.11372. Found : 233.11380. Error= + 0.8 pm.

22. Photoreaction of 2-bromo-2-nitropropane with sodium allyloxide

Fresh sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry allyl alcohol under a nitrogen atmosphere at 50 °C. The solution was allowed to cool to room temperature. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor for 10 hours. The reaction mixture was worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1) to give 35% of 2,2-diallyloxypropane 15, R=allyl, 13% of 2,3-dimethyl-2,3-dinitrobutane 9 and 10% of 2,3-dimethyl-2,3-dinitrobutyl allyl ether 14, R=allyl.

15, R=allyl : ^{1}H NMR (δ, $CDCl_3$) 1.397 (s, 6H), 3.971 (d, 4H, J=5.7 Hz), 5.131 (d,d, 2H, J=1.2, 10.2 Hz), 5.275 (d,d, 2H, J=1.5, 17 Hz), 5.901 (m, 2H).

^{13}C NMR (, $CDCl_3$) 24.660, 61.898, 63.002, 115.671, 135.096.

GCMS m/e (relative intensity) 141 (8), 99 (85), 41 (100).

Identification of the product was confirmed by comparison of the physical constants with those of the authentic compound synthesized by known method [45].

23. Photoreaction of 2-bromo-2-nitropropane with n-butoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry *n*-butanol under a nitrogen atmosphere at 60 °C. The solution was allowed to cool to room temperature. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor for 24 hours. The reaction mixture was worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane;ethyl acetate = 9:1) to give 21% of 2,2-dibutoxypropane 15, R=Bu, 20% of 2,3-dimethyl-2,3-dinitrobutane 9 and 36% of 2,3-dimethyl-2,3-dinitrobutyl *n*-butyl ether 14, R=Bu (mp 104-107 °C).

15, R=Bu : ^{1}H NMR (δ, $CDCl_3$) 0.922 (t, 6H) , 1.301 (m, 4H) , 1.343 (s, 6H), 1.411 (m, 4H).

GCMS m/e (relative intensity) 173 (5), 115 (53), 59 (100), 43 (20).

Identification of this product was confirmed by comparison of ^{1}H NMR and GCMS with those of the authentic compound synthesized by known method [45].

14, R=Bu : ^{1}H NMR (δ, $CDCl_3$) 0.833 (t, 3H), 1.267 (m, 2H), 1.450 (m, 2H), 1.683 (s, 6H), 1.695 (s, 3H), 3.392 (d, 1H, J=9.9 Hz), 4.105 (d, 1H, J=9.9 Hz).

^{13}C NMR (δ, $CDCl_3$) 14.254, 18.792, 23.961, 24.963, 25.008, 32.351, 69.235, 76.321, 91.001, 94.321.

GCMS m/e (relative intensity) 233 (5), 155 (40), 99 (100), 57 (80), 41 (75).

High-resolution MS calculated for $C_9H_{17}N_2O_5$ ($M^+ - CH_3$) : 233.11375. Found : 233.11323. Error= - 5.2 pm.

24. Photoreaction of 2-bromo-2-nitropropane with 2-ethoxyethoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry 2-ethoxyethanol under a nitrogen atmosphere at 40 °C.

The solution was allowed to cool to room temperature. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. After irradiation, the reaction mixture was worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 85:15) to give 45% of 2,2-di(2-ethoxyethoxy)propane <u>15</u>, R=2-ethoxyethyl.

<u>15</u>, R=2-ethoxyethyl : ^{1}H NMR (δ, $CDCl_3$) 1.13 (t, 6H), 1.311 (s, 6H), 3.3-3.6 (m, 12H).

^{13}C NMR (δ, $CDCl_3$) 15.31, 25.07, 60.21, 66.48, 70.01, 100.04.

GCMS m/e (relative intensity) 205 (10), 175 (5), 147 (25), 117 (5), 101 (5), 87 (10), 73 (81), 59 (15), 45 (100).

IR (neat, NaCl plates, cm^{-1}) 2990 (s), 2890 (m), 1450 (m), 1370 (s), 1350 (s), 1180 (s), 1100 (s), 1080 (s).

High-resolution MS calculated for $C_{10}H_{21}O_4$ ($M^+ - CH_3$) : 205.14399. Found : 205.14430. Error= + 2.1 pm.

25. Attempted photoreaction of 2-bromo-2-nitropropane with the sodium salt of ethylene glycol

A similar reaction employing 1.0 mmol of 2-bromo-2-nitropropane and 2.2 mmol of the sodium salt of ethylene glycol in 10 mL of dry ethylene glycol was performed under the same conditions. After work-up, GC and ^{1}H NMR analyses indicated that no product was formed.

26. Attempted photoreaction of 2-bromo-2-nitropropane with phenoxide ion in methanol

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe into a dry methanol solution containing potassium phenoxide (2.2 mmol) derived from the reaction of phenol and potassium methoxide under a nitrogen atmosphere. The reaction mixture was irradiated in the Rayonet photoreactor for 10 hours. After work up, GC and ^{1}H NMR analyses indicated that only 2,2-dimethoxypropane (25%) was formed. No phenoxide substituted product was formed.

27. Photoreaction of 1-chloro-1-cyclopropyl-1-nitroethane with methoxide ion

1-Chloro-1-cyclopropyl-1-nitroethane (0.15 g, 1.0 mmol) 17 was added by syringe to 10 mL of dry methanol containing sodium methoxide prepared from fresh sodium metal (0.051 g, 2.2 mmol) under a nitrogen atmosphere. The resulting solution was irradiated in the Rayonet photoreactor for 5 hours. After work up, the crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2) to give 68% of 1-cyclopropyl-1,1-dimethoxyethane <u>25</u>. GC and ^{1}H NMR analyses indicated that no ring-opened product was formed.

<u>25</u> : ^{1}H NMR (δ, $CDCl_3$) 0.4 (m, 2H), 0.5 (m, 2H), 1.0 (m, 1H), 1.253 (s, 3H), 3.211 (s, 6H).

GCMS m/e (relative intensity) 115 (26), 99 (100), 89 (60), 67 (40), 55 (5), 43 (60), 41 (55).

High-resolution MS calculated for $C_6H_{11}O_2$ ($M^+ - CH_3$) : 115.07591. Found : 115.057570. Error = - 2.1 pm.

28. Photoreaction of 1-bromo-1-nitro-1-phenylethane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere. 1-Bromo-1-nitro-1-phenylethane (0.23 g, 1.0 mmol) 17 was added to the solution. The resulting solution was irradiated in the Rayonet photoreactor for 7 hours and the reaction worked up as previously described. The crude isolate was purified by flash column chromatography on silica gel (hexane:ethyl acetate = 95:5) to give 1,1-dimethoxy-1-phenylethane 26. None of monomethoxy substituted product was formed.

26 : ^1H NMR (δ, $CDCl_3$) 1.540 (s, 3H), 3.192 (s, 6H), 7.4 (m, 5H).

GCMS m/e (relative intensity) 151 (20), 135 (100), 105 (19), 89 (12), 77 (19), 43 (68).

The ^1H NMR spectrum and GCMS of the product 26 were identical to those of the authentic compound [45].

29. Photoreaction of 1-bromo-1-nitro-1-phenylethane with 2-nitro-2-propyl anion

1-Bromo-1-nitro-1-phenylethane (0.23 g, 1.0 mmol) was added to a solution of the 2-nitro-2-propyl anion derived from 2-nitropropane and potassium tert-butoxide in DMSO. After irradiation for 4 hours in the Rayonet photoreactor under a nitrogen atmosphere, the reaction mixture was poured into brine and extracted with methylene chloride (3x10 mL). The combined methylene chloride extracts were washed, dried and concentrated under reduced pressure. GC and ^1H NMR analyses indicated that only the dimer of 2-nitropropane **9** was formed. No substituted product was formed.

30. Photoreaction of 1-bromo-1-nitro-1-phenylethane with the anion of diethyl ethylmalonate

1-Bromo-1-nitro-1-phenylethane (0.23 g, 1.0 mmol) was added to a solution containing potassium tert-butoxide and diethyl ethylmalonate (0.245 g, 1.0 mmol) in 10 mL of dry DMSO under a nitrogen atmosphere. The solution was irradiated (350 nm) for 5 hours. After irradiation was completed, the reaction mixture was poured into 20 mL of brine and extracted with methylene chloride (3x10 mL). The crude isolate was purified by flash column chromatography to give 82% of diethyl bromoethylmalonate. No cross coupled product was formed.

^1H NMR (δ, $CDCl_3$) 0.99 (t, 3H), 1.25 (t, 6H), 2.28 (q, 2H), 4.25 (q, 4H).

GCMS m/e (relative intensity) 269 (1, M^++2), 267 (1.1, M^+), 240 (4), 238 (4), 195 (19), 193 (21), 167 (40), 165 (42), 153 (38), 151 (40), 69 (45), 41 (100).

31. Attempted photoreaction of 1-bromo-1-nitro-1-phenylethane with the anion of diethyl phosphite

A similar reaction employing 1.0 mmol of 1-bromo-1-nitro-1-phenylethane and 1.0 mmol of the anion of diethyl phosphite in 10 mL of dry DMSO was performed. GC and ^{1}H NMR analyses indicated that no product was formed.

32. Photoreaction of α-bromo-α-nitrobenzyl phenyl sulfone with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of methanol under a nitrogen atmosphere. α-Bromo-α-nitrobenzyl phenyl sulfone (0.34 g, 1.0 mmol) **28** was added to a solution of methoxide ion. The resulting solution was irradiated in the Rayonet photoreactor for 12 hours and worked up as previously described. The crude isolate was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2) to give 48% of α,α,α-trimethoxytoluene.

^{1}H NMR (δ, $CDCl_3$) 3.11 (s, 9H), 7.5 (m, 5H).

GCMS m/e (relative intensity) 151 (100), 105 (55), 91 (15), 77 (35), 59 (15), 51 (14).

33. Photoreaction of 1,1-dichloro-1-nitroethane with methoxide ion in deuterated methanol

Sodium metal (0.0025 g, 0.11 mmol) was dissolved in 0.5 mL of nitrogen-purged methanol-d_4 in a NMR tube equipped with a rubber septum. 1,1-Dichloro-1-nitroethane (0.0072 g, 0.05 mmol) and benzene (0.01 mmol, internal standard) was added by microsyringe to a solution of methoxide ion. After a ^1H NMR spectrum was obtained, the NMR tube was irradiated in the Rayonet photoreactor. The progress of the reaction was monitored by the ^1H NMR. The consumption of starting material and the formation of product were obtained by the integration of the signal of three methyl protons ($CH_3C(OCD_3)_3$) comparing with an internal standard. The results are given in Figure 2 and Table 15.

^1H NMR (δ, $CDCl_3$) 1.376 (s, 3H), 3.213 (s, 9H).

GCMS m/e (relative intensity) 105 (10), 89 (50), 47 (15), 43 (100).

The ^1H NMR and GCMS of trimethyl orthoacetate were identical to those of the authentic compound.

34. Effect of light on the reaction of 1.1-dichloro-1-nitroethane with methoxide ion

Sodium metal (0.053 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere. 1,1-Dichloro-1-nitroethane (0.14 g, 1.0 mmol) <u>29</u> was added to a solution.

Table 15. Reaction of 1,1-dichloro-1-nitroethane with methoxide ion in deuterated methanol

$$\underset{\underline{A}}{MeC(Cl)_2NO_2} \quad + \quad 2 \quad NaOCD_3 \xrightarrow{UV,\ N_2\ ^a} \underset{\underline{B}}{MeC(OCD_3)_3}$$

Time (h)	% consumption of A	% formation of B	Total %[b]
0	100	0	100
0.5	81.0	17.8	98.8
1	65.5	30.2	95.7
1.5	48.0	47.3	95.3
2.5	20.0	68.0	88.0
5	0	81.1	81.1

[a] Reaction of 1,1-dichloro-1-nitroethane (0.10 M) and methoxide ion (0.22 M) was carried out in 0.5 mL of deuterated methanol in the Rayonet photoreactor.

[b] ^{1}H NMR yields measured by adding a known amount of benzene as an internal standard.

The tube was wrapped tightly with several layers of aluminum foil to exclude light and subsequently placed in the Rayonet photoreactor at 40 °C. The reaction mixture was worked up as previously described. GC and ^1H NMR analyses indicated that the isolate contained 89% of the starting material. None of trimethyl orthoacetate was observed.

35. Effect of di-tert-butyl nitroxide on the reaction of 1,1-dichloro-1-nitroethane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere. 1,1-Dichloro-1-nitroethane (0.14 g, 1.0 mmol) 29 and di-*tert*-butyl nitroxide (0.014 g, 0.1 mmol) were added to the solution. After irradiation for 5 hours, the reaction mixture was worked up as previously described. GC analysis of the crude isolate showed that the residue contained 32% of 1,1,1-trimethoxyethane 30.

36. Photoreaction of 2-bromo-2-nitropropane with thiolate anions in methanol

Several reactions of the anions of thiols (generated from the thiol and sodium methoxide) with 2-bromo-2-nitropropane failed to give substitution products in methanol after irradiation in the Rayonet photoreactor. The only observable product was the disulfide.

37. Reaction of 2-bromo-2-nitropropane with methoxide ion in the presence of methyl vinyl ketone

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) and methyl vinyl ketone (0.07 g, 1.0 mmol) were added to a solution of sodium methoxide (2.2 mmol) in 10 mL of dry methanol under a nitrogen atmosphere. After 24 hours of irradiation in the Rayonet photoreactor, the reaction mixture was worked up as previously described. GC analysis showed that the residue contained 15% of 2,2-dimethoxypropane and 31% of 3-methyl-3-nitrobutyl methyl ketone <u>32</u>. The products were purified by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2).

<u>32</u> : ^{1}H NMR (δ, $CDCl_3$) 1.599 (s, 6H), 2.167 (s, 3H), 2.468 (t, 2H), 3.201 (t, 2H).

GCMS m/e (relative intensity) 159 (1), 144 (2), 113 (15), 95 (10), 69 (20), 55 (10), 43 (100).

Identification of the product was confirmed by comparison of ^{1}H NMR and GCMS data with the authentic compound synthesized by known methods [42-44].

A similar reaction employing 1 equivalent of sodium methoxide was carried out under the same conditions. After a similar work-up procedure, the residue contained 3% of 2,2-dimethoxypropane and 30% of 3-methyl-3-nitrobutyl methyl ketone <u>32</u>.

Another similar reaction employing 2-bromo-2-nitropropane

(0.17 g, 1.0 mmol) methyl vinyl ketone (0.14 g, 2.0 mmol) and sodium methoxide (1.0 mmol) was irradiated using a Rayonet photoreactor for 24 hours. After work-up, the residue was determined to contain 84% of 3-methyl-3-nitrobutyl methyl ketone 32 by GC analysis. No 2,2-dimethoxypropane was observed.

38. Effect of light on the reaction of 2-bromo-2-nitropropane with methoxide ion in the presence of methyl vinyl ketone

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) and methyl vinyl ketone (0.14 g, 2.0 mmol) were added to a solution of sodium methoxide (1.1 mmol) in 10 mL of dry methanol under a nitrogen atmosphere. The tube was wrapped tightly with several layers of aluminum foil to exclude light and placed in the Rayonet photoreactor for 24 hours. After work-up, GC analysis showed that the residue contained 74% of 3-methyl-3-nitrobutyl methyl ketone.

39. Effect of di-tert-butyl nitroxide on the reaction of 2-bromo-2-nitropropane with methoxide ion in the presence of methyl vinyl ketone

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol), methyl vinyl ketone (0.14 g, 2.0 mmol) and di-*tert*-butyl nitroxide (0.014 g, 0.1 mmol) were added to a solution of sodium methoxide (1.1 mmol) in 10 mL of dry methanol under a nitrogen atmosphere.

After 24 hours of irradiation in the Rayonet photoreactor, the reaction mixture was worked up as previously described. GC analysis indicated that the residue contained 83% of 3-methyl-3-nitrobutyl methyl ketone 32.

40. Photoreaction of 2-substituted-2-nitropropanes with methoxide ion in the presence of methyl vinyl ketone

2,2-Dinitropropane (0.134 g, 1.0 mmol) and methyl vinyl ketone (0.14 g, 2.0 mmol) were added to a solution of sodium methoxide (1.1 mmol) in 10 mL of dry methanol under a nitrogen atmosphere. After 24 hours of irradiation, the reaction mixture was worked up as previously described. GC analysis showed that the residue contained 36% of 2,2-dimethoxypropane. No Michael addition product was observed.

A similar reaction employing 2-bromo-2-(phenylsulfonyl)propane (0.23 g, 1.0 mmol) instead of 2,2-dinitropropane was carried out under the same conditions. GC analysis showed that the residue contained 25% of 2,2-dimethoxypropane. No michael addition product was observed.

41. Photoreaction of 2-bromo-2-nitropropane with methoxide ion in the presence of methyl acrylate

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) and methyl acrylate (0.16 g, 2.0 mmol) were added to a solution of sodium methoxide (1.1 mmol) in 10 mL of dry methanol under a nitrogen atmosphere. After 24 hours of irradiation in the Rayonet photoreactor, the reaction mixture was worked up as previously described. GC analysis showed that the residue contained 52% of 2,2-dimethoxypropane. No michael addition product was observed.

42. Effects of added nucleophiles on the photoreaction of 2-bromo-2-nitropropane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) and an excess of nucleophile, such as NaCN, NaN_3, NaI or $KClO_4$, were dissolved in 10 mL of dry methanol. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor for 5 hours. After work-up, GC analysis showed that the formation of 80-90% of 2,2-dimethoxypropane.

43. Effects of added olefins on the photoreaction of 2-bromo-2-nitropropane with methoxide ion

Sodium metal (0.051 g, 2.2 mmol) and the excess of 1,1-diphenylethylene, norbornylene or phenylacetylene were dissolved in 10 mL of dry methanol. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added by syringe to the solution. The reaction mixture was irradiated for 5 hours and worked up as previously described. GC analysis indicated the formation of 80-90% of 2,2-dimethoxypropane.

44. Effect of an added methyl vinyl ether on the photoreaction of 2-bromo-2-nitropropane with ethoxide ion

2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) and (1-methoxyethenyl)benzene (0.67 g, 5.0 mmol) were added by syringe to a solution of sodium ethoxide (2.0 mmol) in 10 mL of dry ethanol under a nitrogen atmosphere. The reaction mixture was placed in the Rayonet photoreactor for 7 hours and worked up as previously described. GCMS analysis indicated the formation of 35% of acetophenone, 50% of (2-ethoxy-1-methoxyethyl)benzene **34**, 5% of 2,2-diethoxypropane and the presence of a large amount of unreacted (1-methoxyethenyl)benzene.

34 : GCMS m/e (relative intensity) 180 (1), 165 (9), 149 (32), 135 (72), 121 (15), 105 (25), 91 (7), 77 (30), 43 (100).

45. Reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane in the presence of excess cyanide ion

Sodium cyanide (1.0 g, 20 mmol) was dissolved in a solution of the anion of 2-nitropropane derived from the reaction of potassium *tert*-butoxide and 2-nitropropane (0.09 g, 1.0 mmol) in 10 mL of dry DMSO. 2-Bromo-2-nitropropane (0.17 g, 1.0 mmol) was added to the solution. The reaction mixture was irradiated in the Rayonet photoreactor for an hour and worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 3:7) to give 87% of 2-cyano-2,3-dimethyl-3-nitrobutane <u>37</u> and 8% of 2,3-dimethyl-2,3-dinitrobutane.

<u>37</u> : ^{1}H NMR (δ, $CDCl_3$) 1.391 (s, 6H), 1.687 (s, 6H).

^{13}C NMR (δ, $CDCl_3$) 22.740, 22.939, 23.289, 90.594, 121.748.

GCMS m/e (relative intensity) 156 (1), 110 (35), 94 (10), 68 (100), 55 (40), 41 (95).

A similar reaction employing methanol (instead of DMSO) was carried out under the same conditions. GC analysis indicated that the residue contained no product.

46. <u>Effect of added nucleophiles on the reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane</u>

Using the same technique employed for sodium cyanide in the previous section, 5.0 mmol of the nucleophiles listed in Table 10 were dissolved in a solution of the anion of 2-nitropropane (1.0 mmol) in DMSO. 2-Bromo-2-nitropropane (1.0 mmol) was added and the solution irradiated. After work-up, GC analysis showed that the residue contained only 2,3-dimethyl-2,3-dinitrobutane.

47. Attempted photoreaction of 2-bromo-2-(phenylsulfonyl)propane with methoxide ion

Sodium metal (0.053 g, 2.2 mmol) was dissolved in 10 mL of methanol under a nitrogen atmosphere. 2-Bromo-2-(phenylsulfonyl)propane (0.26 g, 1.0 mmol) was added to the solution. The reaction mixture was irradiated in the Rayonet photoreactor for 24 hours and worked up as previously described. The crude isolate appeared to be only starting material as revealed by ^{1}H NMR and GC analyses.

48. Reaction of 2,2-dichloro-1-phenyl-1-propanone with methoxide ion

Sodium metal (0.053 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere. 2,2-Dichloro-1-phenyl-1-propanone (0.20 g, 1.0 mmol) **38** was added to a solution. The reaction mixture was irradiated at 350 nm in the Rayonet photoreactor for 1 hours, then worked up as previously described. The crude isolate was separated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1) to give 63% of 2,2-dimethoxy-1-phenyl-1-propanone **41** and 5% of methyl benzoate.

41: ^{1}H NMR (δ, $CDCl_3$) 1.512 (s, 3H), 3.28 (s, 6H), 7.5 (m, 5H)

GCMS m/e (relative intensity) 163 (9), 135 (5), 105 (11), 89 (100), 77 (17)

49. Effect of light on the reaction of 2,2-dichloro-1-phenyl-1-propanone with methoxide ion

2,2-Dichloro-1-phenyl-1-propanone (0.20 g, 1.0 mmol) 38 was added to a solution of sodium methoxide (2.2 mmol) in 10 mL of dry methanol. The flask was wrapped tightly with several layers of aluminum foil to exclude light. The reaction mixture was worked up as previously described. GC analysis showed that the crude isolate contained 69% of 2,2-dimethoxy-1-phenyl-1-propanone 41.

A similar reaction employing di-*tert*-butyl nitroxide (0.014 g, 0.1 mmol) was carried out in dark under a nitrogen atmosphere. The reaction mixture was worked up as previously described. GC analysis showed that the crude isolate contained 67% of 2.2-dimethoxy-1-phenyl-1-propanone 41.

50. Attempted photoreaction of N,N-diethyl-α,α-dichlorophenylacetamide with methoxide ion

Sodium metal (0.053 g, 2.2 mmol) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere. N,N-diethyl-α,α-dichlorophenylacetamide (0.26 g, 1.0 mmol) 40 was added to a solution. The reaction mixture was irradiated in the Rayonet photoreactor for 2 hours and worked up. The crude isolate appeared to be only starting material as revealed by GC analysis.

III. KINETIC CHAIN LENGTHS AND REACTION KINETICS IN THE REACTION OF 2-BROMO-2-NITROPROPANE WITH ALKOXIDE ION AND THE ANION OF 2-NITROPROPANE

A. Introduction

Chemical kinetics is closely related to the development of reaction mechanism. The proposed reaction mechanism may account for the results, but these postulates are not always proved. Often a large body of experimental results supports only one credible mechanism. On the other hand, sometimes the experimental results are consistent with several mechanistic possibilities. To narrow the range of possibilities, reaction kinetics are a valuable tool.

A chain reaction is one whose mechanism involves low concentrations of reactive intermediates, such as radical anions (chain carriers), that participate in a cycle of reaction steps such that the radical anions are regenerated after each cycle. The radical anions (chain carriers) are formed in a chain initiation step which is one of three main reaction steps, termed initiation, propagation and termination. Chain propagating steps are often bimolecular reactions of one intermediate and one substrate. Free radical chain reactions can be interrupted by a termination step which converts the active chain-carrying intermediates to stable molecules, such as products, reactants or inert by-products.

The concept of kinetic chain length is of great importance and may be defined as the average number of reactant molecules consumed for every radical which initiates a chain reaction [61]. It may also be considered the number of successful chain propagation steps resulting from a single original chain carrier [62]. To calculate the kinetic chain length, the rate of chain initiation must be known. This rate is conveniently measured from the inhibition period observed with known amounts of free radical chain inhibitors. Free radical chain reactions are commonly susceptible to inhibition in which a mere trace of inhibitor can cause a marked decrease in the rate. The reactions of 2-substituted-2-nitropropanes with 1^{o}-alkoxide ions have been shown to be a free radical chain process since the reactions fail to occur in the absence of light, the reactions are inhibited by addition of small amounts of radical inhibitors and the reactions are retarded by molecular oxygen.

The following sections will present the results of the determination of kinetic chain lengths and relative reactivities in the reactions of 2-substituted-2-nitropropanes with 1^{o}-alkoxide ions and the anion of 2-nitropropane.

B. Results and Discussion

1. Determination of kinetic chain length of the reaction between 2-bromo-2-nitropropane and methoxide ion

The kinetic chain length of a reaction can be formulated as shown in Equation 24. Experimentally, the initial kinetic

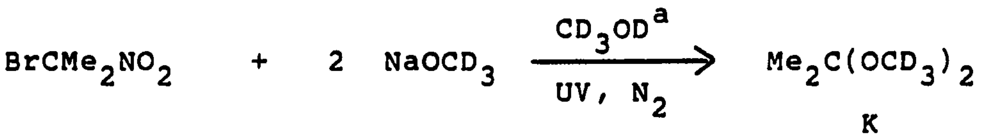
$$\text{Kinetic Chain Length} = \frac{\text{Initial Reaction Rate}}{\text{Rate of Initiation}} \qquad (24)$$

chain length can be measured from the initial reaction rate and the rate of initiation. The initial reaction rate can be calculated by following either the rate of consumption of the substrate or the rate of formation of product. The rate of initiation also can be calculated in the presence of small amounts of a radical inhibitor by measurement of the inhibition period. Kinetic chain length varies over the course of a reaction and depends upon the concentrations of reagents. As the reactant is consumed and the rate of the reaction approaches zero, the kinetic chain length will also approach zero. The kinetic chain lengths measured by Equation 24 thus apply only under the initial reaction concentrations.

Sodium metal was dissolved in nitrogen-purged deuterated methanol (0.5 mL) in a 5 mm NMR tube to give a 0.22 M solution of sodium methoxide. 2-Bromo-2-nitropropane was added by microsyringe through a rubber septum to give a 0.10 M solution. The reaction mixture was checked by ^{1}H NMR and then irradiated in a Rayonet photoreactor at 35 °C at 350 nm. The progress of the reaction was monitored at different periods of time by ^{1}H NMR. The formation of the product was determined by the integration of the signal for the six methyl protons of $Me_2C(OCD_3)_2$ by comparison with a known amount of internal standard (benzene). The reaction in the presence of 10 mol % of di-*tert*-butyl nitroxide (DTBN) was carried out under the same conditions to calculate the rate of inhibition. Yields of ketal resulting from both reactions are presented in Table 16 and the plots of the yield of product vs. time are shown in Figure 3.

The initial rate of the reaction is obtained from the slope of the curve at the beginning of the reaction by using a tangent meter as shown in Figure 3. The rate of inhibition with DTBN is obtained from the concentration of DTBN divided by the time needed to consume all of the DTBN which can be calculated from the Figure 3. The calculation, of course, assumes that each molecule of DTBN captures one radical which would otherwise lead to chain initiation.

Table 16. Reaction of 2-bromo-2-nitropropane with sodium methoxide in deuterated methanol



$$BrCMe_2NO_2 + 2\ NaOCD_3 \xrightarrow[UV,\ N_2]{CD_3OD^a} Me_2C(OCD_3)_2$$

K

Time (minutes)	% formation of K[b]	
	without DTBN	with DTBN[c]
0	0	0
10	3.7	0
20	22.9	0
40	42.1	0
60	58.0	3.7
80	68.4	13.0
120	83.7	23.1
240	94.8	41.0

[a] $[BrCMe_2NO_2]_o$ = 0.10 M, $[NaOCD_3]_o$ = 0.22 M and $[benzene]_o$ =0.01 M (internal standard). The reaction mixture in a 5 mm NMR tube was irradiated for the time indicated in a Rayonet photoreactor (350 nm) at 35 °C.

[b] Yields were determined by ^1H NMR.

[c] DTBN = 10 mol % of di-*tert*-butyl nitroxide (0.01 M).

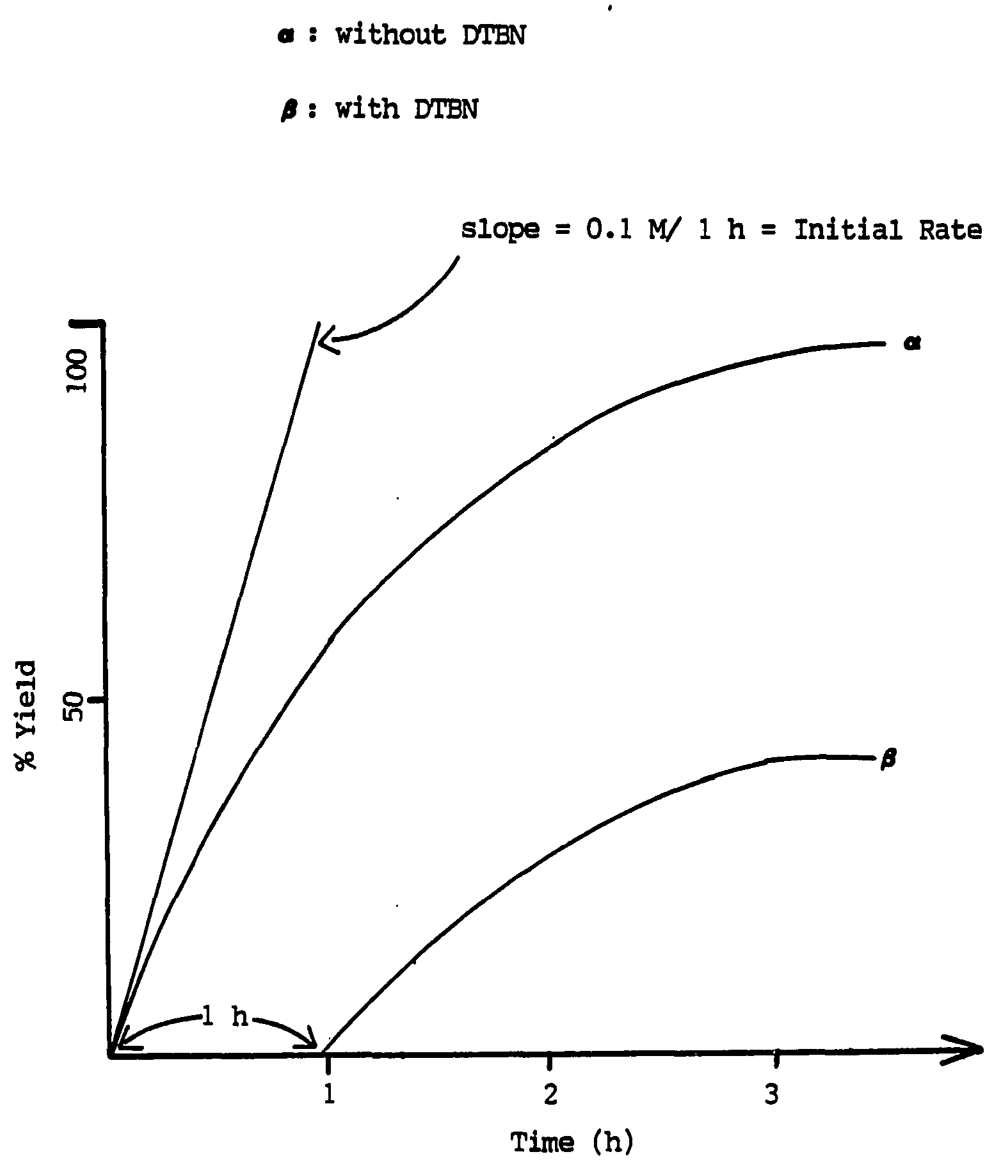


Figure 3. Formation of $Me_2C(OCD_3)_2$ vs. time for the reaction of $BrCMe_2NO_2$ and $NaOCD_3$ in deuterated methanol in the absence and presence of DTBN

From Figure 3,

Initial Rate = 0.10 M / 1 h

Rate of Initiation = 0.01 M / 1 h

Initial Kinetic Chain Length = 10

A similar reaction employing potassium metal to prepare the methoxide ion was also performed under the same conditions. The initial kinetic chain length of this reaction in deuterated methanol was measured (Table 17 and Figure 4).

From Figure 4,

Initial Rate = 0.10 M / 2 h

Rate of Initiation = 0.01 M / 7.5 h

Initial Kinetic Chain Length = 38

The rate of initiation was much greater with sodium methoxide than for potassium methoxide. Usually, free radical chain reaction occur at a rate proportional to the square root of rate initiation ($Ri^{1/2}$). Thus, the kinetic chain length should be proportional to $Ri^{1/2}$. The observed kinetic chain lengths (10 and 38) are roughly proportional to the values of $Ri^{1/2}$.

Table 17. Reaction of 2-bromo-2-nitropropane with potassium methoxide in deuterated methanol

$$\mathrm{BrCMe_2NO_2} \quad + \quad 2\ \mathrm{KOCD_3} \xrightarrow[\mathrm{UV,\ N_2}]{\mathrm{CD_3OD^a}} \underset{\underline{K}}{\mathrm{Me_2C(OCD_3)_2}}$$

Time (h)	% formation of $\underline{K}^b$	
	without DTBN	with DTBN[c]
0.3	21.8	0
0.6	35.4	0
1.0	46.3	0
2.0	68.6	0
3.0	81.0	0
7.0	90.0	0
8.0	90.0	10.0
9.0	-	29.2
12.0	-	55.4
13.0	-	55.2

[a] $[\mathrm{BrCMe_2NO_2}]_o$ = 0.10 M, $[\mathrm{KOCD_3}]_o$ = 0.22 M and $[\mathrm{benzene}]_o$=0.01 M. The reaction mixture was irradiated for time indicated in a Rayonet photoreactor at 35 °C.

[b] Yields were determined by ^{1}H NMR.

[c] DTBN = 10 mol % of di-*tert*-butyl nitroxide (0.01 M).

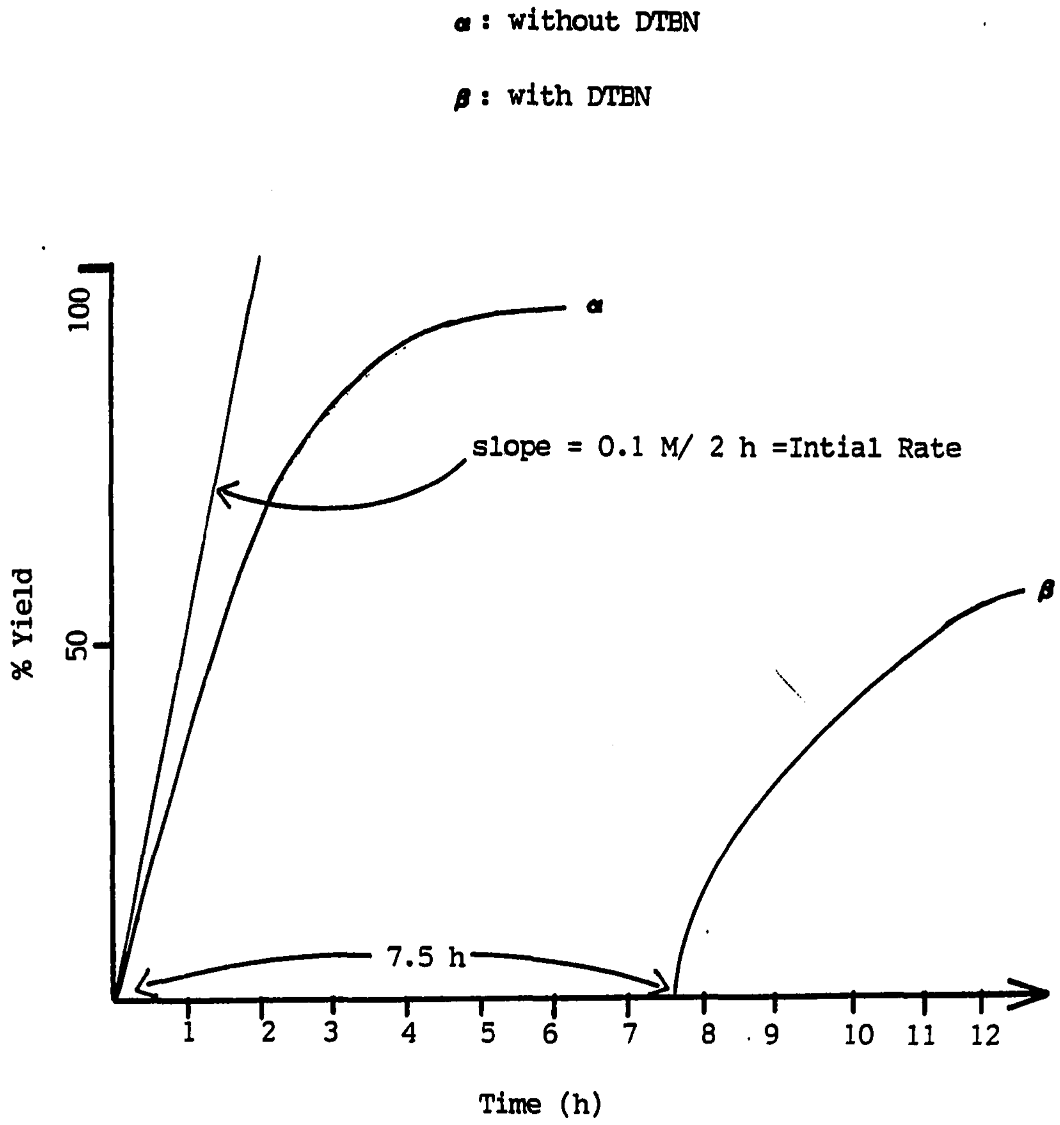


Figure 4. Formation of $Me_2C(OCD_3)_2$ vs. time for the reaction of $BrCMe_2NO_2$ and $KOCD_3$ in deuterated methanol in the absence and presence of DTBN

2. Determination of kinetic chain length of the reaction between 2-bromo-2-nitropropane and sodium ethoxide

Sodium metal was dissolved in ethanol under a nitrogen atmosphere to give a 0.22 M solution of sodium ethoxide. 2-Bromo-2-nitropropane was added by syringe through a rubber septum to give a 0.10 M solution. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm. The progress of the reaction was monitored periodically by quenching a known amount of the reaction mixture and measuring the yield of product by GC. A similar reaction in the presence of 3 mol % of di-*tert*-butyl nitroxide was carried out under the same conditions. These results are given in Table 18. Figure 5 shows the plots of the yield of 2,2-diethoxypropane vs. time. The initial kinetic chain length is obtained by the same method as previously described.

From Figure 5,

Initial Rate = 0.038 M / 1 h

Rate of Initiation = 0.003 M / 3 h

Initial Kinetic Chain Length = 38

A similar reaction employing potassium metal in ethanol was also performed under the same conditions, The progress of the reaction was monitored by GC. The product yields with and without 3 mol % of di-*tert*-butyl nitroxide are given in Table

Table 18. Reaction of 2-bromo-2-nitropropane with sodium ethoxide in ethanol

$$\mathrm{BrCMe_2NO_2} \quad + \quad 2\ \mathrm{NaOC_2H_5} \xrightarrow[\mathrm{UV,\ N_2}]{\mathrm{EtOH}^{a}} \underset{\underline{\mathrm{K}}}{\mathrm{Me_2C(OC_2H_5)_2}}$$

Time (h)	% formation of $\underline{K}$[b]	
	without DTBN	with DTBN[c]
0	0	0
0.3	9.9	0
0.6	17.1	0
1.0	21.0	0
2.0	31.1	0
3.0	39.5	1.8
4.0	43.1	4.5
7.0	43.0	10.1
10.0	-	10.4

[a] $[\mathrm{BrCMe_2NO_2}]_o$ = 0.10 M and $[\mathrm{NaOC_2H_5}]_o$ =0.22 M. The reaction was irradiated for the time indicated in a Rayonet photoreactor (350 nm) at 35 °C.

[b] Yields were measured by adding a known amount of biphenyl by GC analysis.

[c] DTBN = 3 mol % of di-tert-butyl nitroxide (0.003 M).

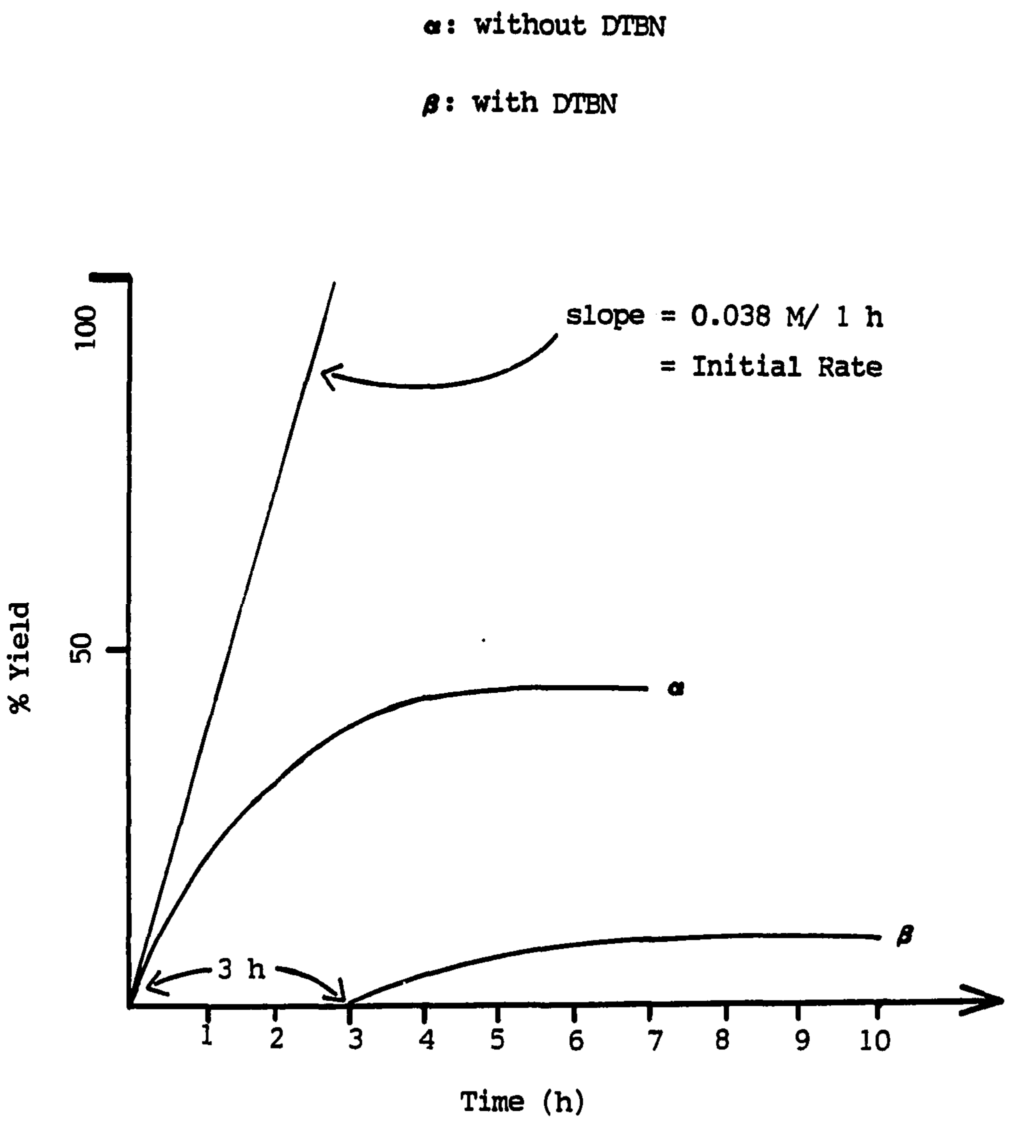


Figure 5. Formation of $Me_2C(OC_2H_5)_2$ vs. time for the reaction of $BrCMe_2NO_2$ and $NaOC_2H_5$ in ethanol in the absence and presence of DTBN

Table 19. Reaction of 2-bromo-2-nitropropane with potassium ethoxide in ethanol

$$\mathrm{BrCMe_2NO_2} \quad + \quad 2\ \mathrm{KOC_2H_5} \xrightarrow[\mathrm{UV,\ N_2}]{\mathrm{EtOH}^{a}} \underset{\underline{K}}{\mathrm{Me_2C(OC_2H_5)_2}}$$

Time (h)	% formation of <u>K</u>[b]	
	without DTBN	with DTBN[c]
0.3	24.1	0
0.6	41.2	0
1.0	44.9	0
2.5	57.2	0
4.0	63.5	0
5.0	65.1	0
6.0	-	4.2
8.0	-	16.3
12.0	-	19.0

[a] $[\mathrm{BrCMe_2NO_2}]_o$ = 0.10 M and $[\mathrm{KOC_2H_5}]$ = 0.22 M. The reaction mixture was irradiated for the time indicated in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding a known amount of biphenyl as an internal standard.

[c] DTBN= 3 mol % of di-*tert*-butyl nitroxide (0.003 M).

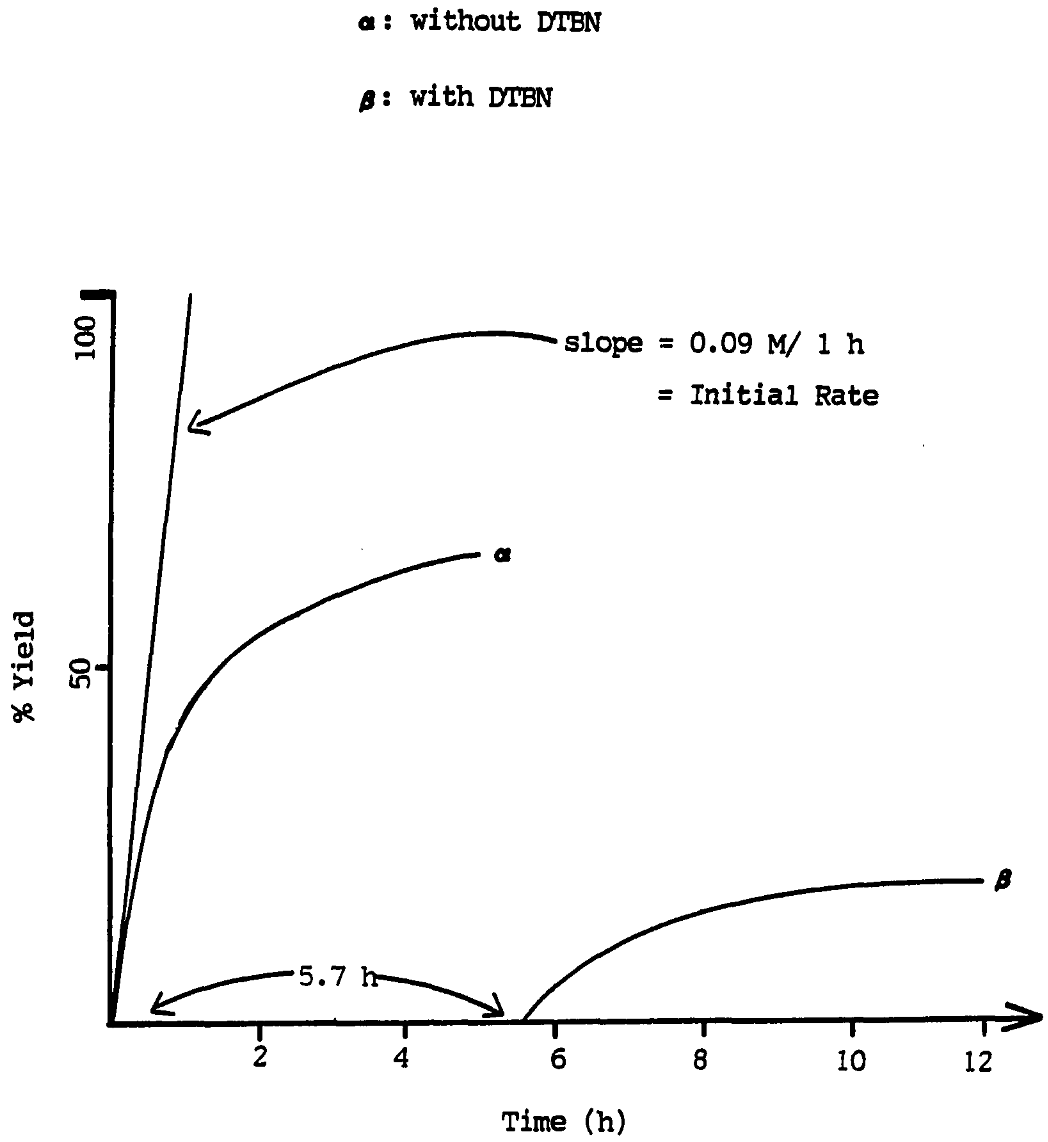


Figure 6. Formation of $Me_2C(OC_2H_5)_2$ vs. time for the reaction of $BrCMe_2NO_2$ and KOC_2H_5 in ethanol in the absence and presence of DTBN

19. Figure 6 shows the plots of the yield of 2,2-diethoxypropane vs. time.

From Figure 6,

Initial Rate = 0.09 M / 1 h

Rate of Initiation = 0.03 M / 5.7 h

Initial Kinetic Chain Length = 171

The reactions of 2-bromo-2-nitropropanes with ethoxide ion with initial kinetic chain lengths of 38 and 171 are free chain processes. Although the rate of initiation was somewhat slower for potassium ethoxide than for sodium ethoxide, the initial reaction rate and initial kinetic chain length were much greater for the potassium alkoxide. In general, the relative rates of propagation and termination reactions depend upon reaction conditions as well as kinetic chain length [62]. Apparently, the propagation reaction involving the potassium alkoxide occurs more readily than the propagation reaction with sodium as the conterion. Alternately,the termination reaction with the sodium cation may be slower than with potassium cation.

3. Determination of kinetic chain length of the reaction between 2-bromo-2-nitropropane with the anion of 2-nitropropane

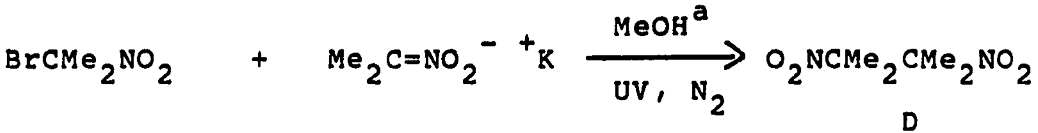
The kinetic chain lengths of the reaction of 2-bromo-2-nitropropane with the potassium salt of 2-nitropropane in both methanol and ethanol have also been determined. Thus, potassium metal (0.12 M) was dissolved in methanol under a nitrogen atmosphere. 2-Nitropropane was added to give a 0.10 M solution and the reaction mixture was stirred for 30 minutes. A slight excess of potassium methoxide must ionize all of 2-nitropropane to the anion of 2-nitropropane, because the pKa of methanol (16-18) is greater than that of 2-nitropropane (10) [63]. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm. The progress of reaction was monitored at different periods of time by GC. Yields of product were determined by adding a known amount of biphenyl as an internal standard. A similar reaction in the presence of 5 mol % of di-*tert*-butyl nitroxide was also carried out under the same conditions. Yields of the product (2,3-dimethyl-2,3-dinitrobutane) from both reactions are listed in Table 20 and the plots of the yield of product vs. time are shown in Figure 7.

From Figure 7,

Initial Rate = 0.075 M/ 1 h

Rate of Initiation = 0.005 M/ 3 h

Table 20. Reaction of 2-bromo-2-nitropropane with potassium salt of 2-nitropropane in methanol



$$BrCMe_2NO_2 \quad + \quad Me_2C{=}NO_2^{-}\ {}^{+}K \xrightarrow[UV,\ N_2]{MeOH^{a}} \underset{\underline{D}}{O_2NCMe_2CMe_2NO_2}$$

Time (h)	% formation of $\underline{D}$[b]	
	without DTBN	with DTBN[c]
0	0	0
0.3	16.7	0
0.6	26.1	0
1.0	40.1	0
1.5	51.1	0
3.5	74.5	16.2
5.0	82.0	44.2
7.0	82.1	43.1

[a] $[BrCMe_2NO_2]_o = 0.10$ M and $[Me_2C{=}NO_2^{-}{}^{+}K]_o = 0.10$ M. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm.

[b] GC yields were determined by adding a known amount of bihpeyl as an internal standard.

[c] DTBN= 5 mol % of di-*tert*-butyl nitroxide (0.005 M).

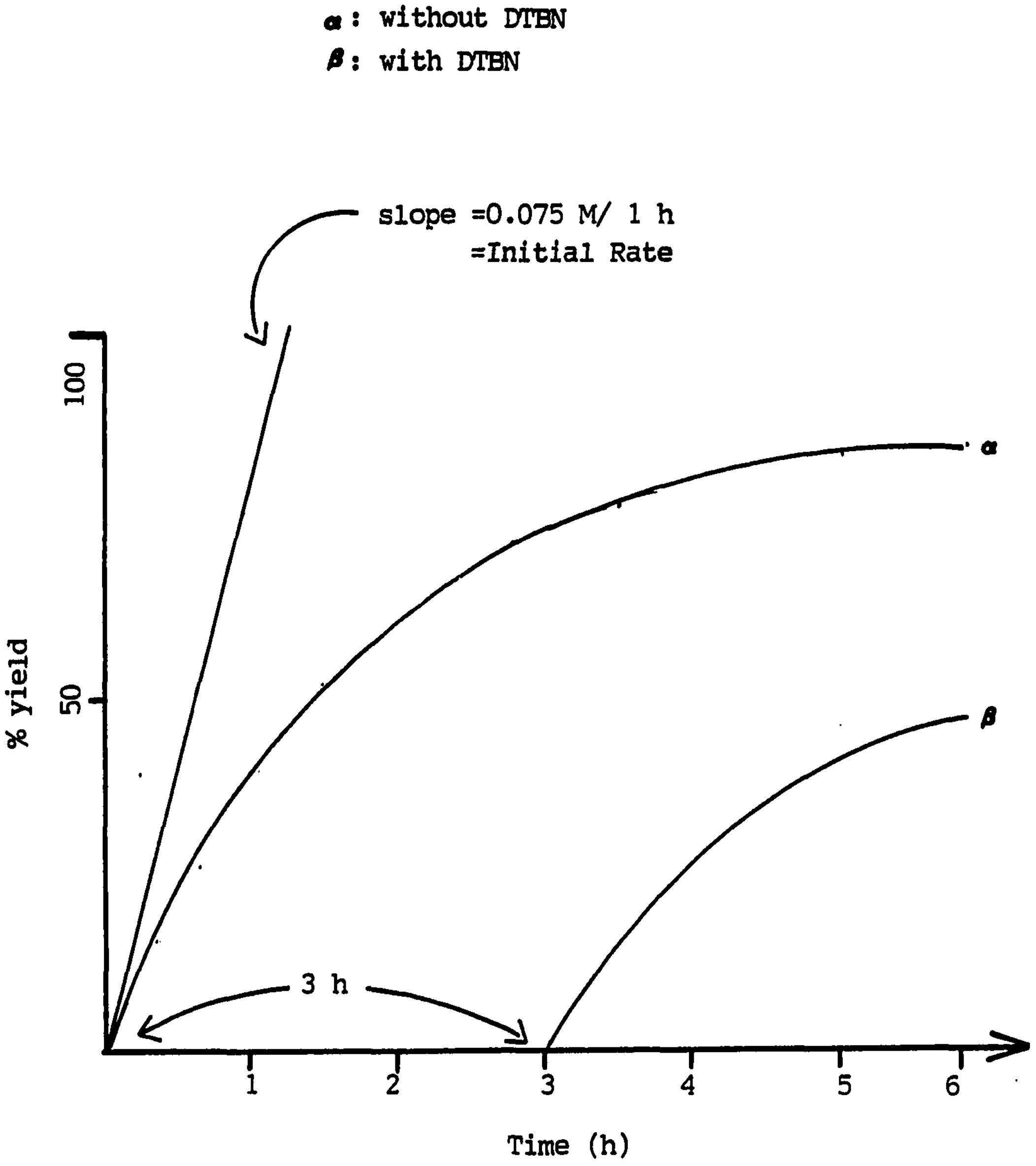


Figure 7. Formation of $O_2NCMe_2CMe_2NO_2$ vs. time for the reaction of $BrCMe_2NO_2$ and the potassium salt of 2-nitropropane in methanol in the absence and presence of DTBN

Table 21. reaction of 2-bromo-2-nitropropane with potassium salt of 2-nitropropane in ethanol

$$BrCMe_2NO_2 \quad + \quad Me_2C{=}NO_2^{-}\ {}^{+}K \xrightarrow[UV,\ N_2]{EtOH^{a}} \underset{\underline{D}}{O_2NCMe_2CMe_2NO_2}$$

Time (h)	% formation of D[b]	
	without DTBN	with DTBN[c]
0	0	0
0.2	54.5	0
0.4	71.0	0
1.0	82.0	0
2.0	91.0	0
3.5	91.0	2.1
5.0	-	36.3
7.0	-	58.5
12.0	-	58.1

[a] $[BrCMe_2NO_2]_o$= 0.10 M and $[Me_2C{=}NO_2^{-+}K]_o$= 0.10 M. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding an internal standard.

[c] DTBN= 10 mol % of di-tert-butyl nitroxide (0.01 M).

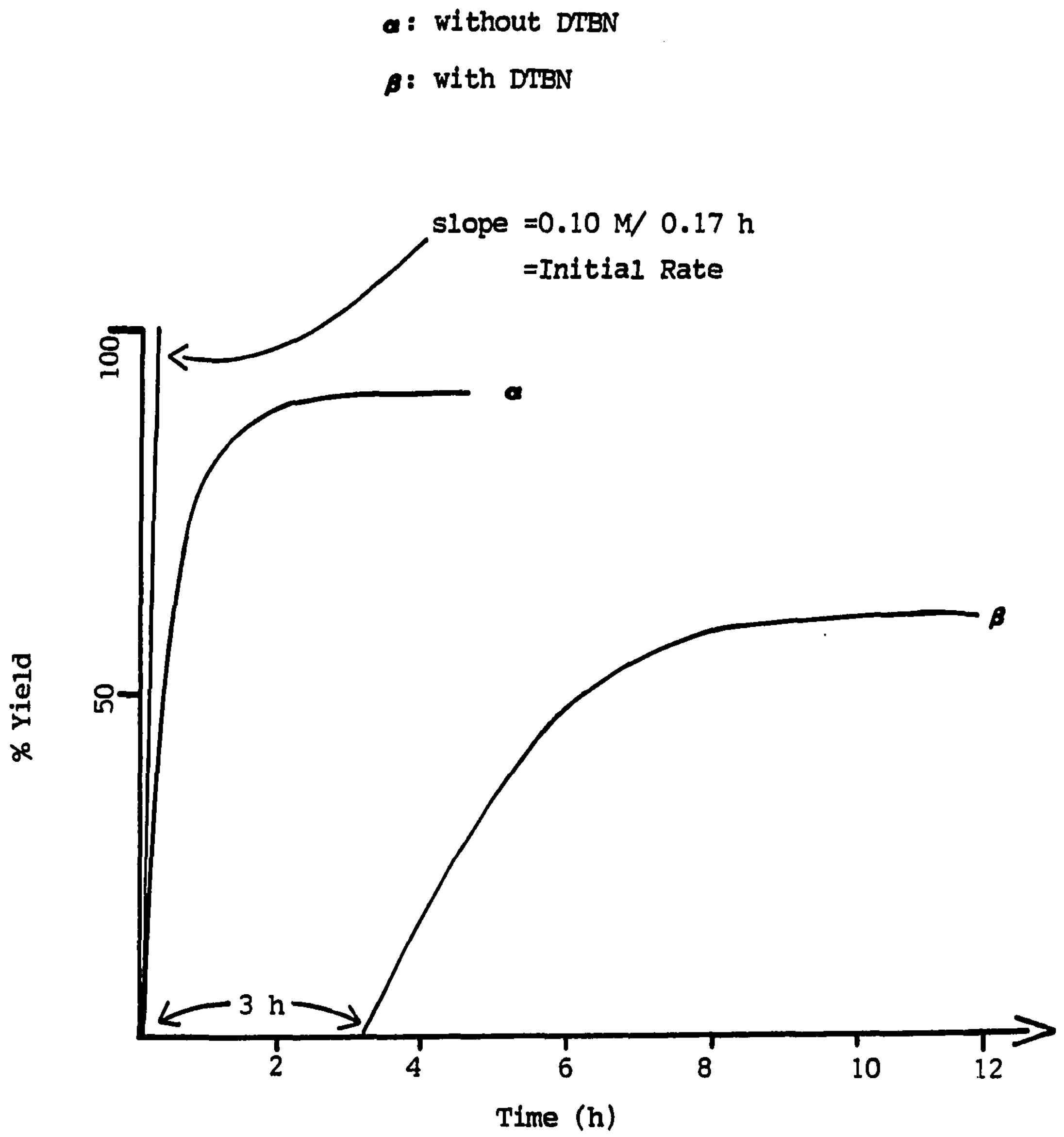


Figure 8. Formation of $O_2NCMe_2CMe_2NO_2$ vs. time for the reaction of $BrCMe_2NO_2$ and the potassium salt of 2-nitropropane in ethanol in the absence and presence of DTBN

Initial kinetic Chain Length = 45

A similar reaction employing potassium metal in ethanol was performed under the same conditions with 2-nitropropane and 2-bromo-2-nitropropane. The progress of the reaction was monitored by GC. The product yields with and without 10 mol % of di-tert-butyl nitroxide are given in Table 21. Figure 8 shows the plots of the yield of product vs. time.

From Figure 8,

Initial Rate = 0.10 M / 0.17 h

Rate of Initiation = 0.01 M / 3.0 h

Initial Kinetic Chain Length = 179

The potassium ethoxide in ethanol gave both a more rapid rate of initiation and a longer initial kinetic chain length than potassium methoxide in methanol. Apparently, there is a significant solvent effect in the reaction of 2-nitro-2-propyl radical with the anion of 2-nitropropane.

4. Kinetic study of the competitive reaction of the anion of 2-nitropropane and 1 -alkoxide ions with 2-bromo-2-nitropropane

The photostimulated reaction of 2-bromo-2-nitropropane with 1°-alkoxide ions was influenced by the presence of the anion of 2-nitropropane. The formation of 2,2-dialkoxypropane (K) and 2,3-dimethyl-2,3-dinitrobutane (D) in the reaction of

2-bromo-2-nitropropane with a mixture of a 1°-alkoxide ion and the nitronate anion appears to proceed via competitive $S_{RN}1$ processes in which 2-nitro-2-propyl radical is trapped by either 1°-alkoxide ion or nitronate anion.

The photostimulated reaction of 2-bromo-2-nitropropane (0.107 M) with the potassium salt of 2-nitropropane (0.111 M) and potassium methoxide (0.125 M) in the Rayonet photoreactor under a nitrogen atmosphere gave 49.2% of 2,2-dimethoxypropane and 41.6% of 2,3-dimethyl-2,3-dinitrobutane by GC analysis. A series of metal ions, such as Na^+, K^+ and Li^+, with different solvents have been employed and these results are listed in Table 22. It turned out that the photostimulated reaction of 2-bromo-2-nitropropane with 1°-alkoxide ion and nitronate anion is sensitive to both the nature of the solvent and the counterion.

The formation of 2,2-dialkoxypropane in the photostimulated reaction of 2-bromo-2-nitropropane with 1°-alkoxide ion in the absence of the nitronate anion was observed in the presence of Na^+, K^+, K^+-18-C-6, Li^+ or $PhCH_2N(CH_3)_3^+$, but the rates of the formation of 2,2-dialkoxypropane were different. The counterion, Na^+, gave more 2,2-dialkoxypropane than K^+ or Li^+, and the solvent methanol favored the formation of 2,2-dimethoxypropane more than ethanol (Tables 1, 2 and 3).

The formation of 2,3-dimethyl-2,3-dinitrobutane in the

Table 22. Photostimulated reaction of 2-bromo-2-nitropropane with primary alkoxide ion and nitronate anion

$$BrCMe_2NO_2 + RO^{-+}M + Me_2C{=}NO_2{}^{-+}M \xrightarrow{ROH,\ UV^{a}} \underset{\underline{K}}{Me_2C(OR)_2} + \underset{\underline{D}}{O_2NCMe_2CMe_2NO_2}$$

R	M	$[BrCMe_2NO_2]_o{}^b$	$[ROM]_o{}^b$	$[Me_2C{=}NO_2{}^-]_o{}^b$	% yields[c]	
					<u>K</u>	<u>D</u>
Me	K	0.107	0.111	0.125	49.2	41.6
Me	Na	0.106	0.110	0.123	83.2	5.2
Me[d]	Li	0.114	0.153	0.153	51.6	23.5
Et	K	0.083	0.082	0.090	38.8	59.1
Et[d]	Na	0.083	0.083	0.087	21.7	4.5
Et[d]	Li	0.114	0.153	0.153	29.8	15.4

[a] Reagents in 10 mL of nitrogen-purged solvent were irradiated in a Rayonet photoreactor for 5 hours at ambident temperature.

[b] Initial concentration, M.

[c] GC yields were measured by adding internal standard.

[d] Irradiation period was 24 hours.

reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane in the absence of 1°-alkoxide ion was also studied in the presence of Na^+, K^+ and Li^+ (Table 23). With Na^+ as the counterion in methanol, the competitive reaction of 2-bromo-2-nitropropane with methoxide ion and the anion derived from 2-nitropropane, greatly favored the formation of ketal. This preference decreased upon going to ethanol or upon using lithium or potassium as the counterions. Undoubtedly, ion-pairing effects [64] are important in the competitive reactions of the anions with different counterions and in different solvents toward 2-bromo-2-nitropropane.

The rate of formation of 2,2-dimethoxypropane was measured in the photostimulated reaction of 2-bromo-2-nitropropane with potassium methoxide in the presence of the potassium salt of 2-nitropropane. The rate of formation of 2,2-dimethoxypropane was decreased by the addition of nitronate anion. Figure 9 shows that the rate of formation of 2,2-dimethoxypropane in the reaction of 2-bromo-2-nitropropane with potassium methoxide is faster than that in the reaction of 2-bromo-2-nitropropane with potassium methoxide in the presence of nitronate anion. This result confirms the supposition that 1°-alkoxide ion competes with nitronate anion towards the 2-nitro-2-propyl radical as shown in Scheme 18.

Table 23. Reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane

$$\mathrm{BrCMe_2NO_2} \quad + \quad \mathrm{Me_2C{=}NO_2{}^{-+}M} \quad \xrightarrow[\mathrm{UV}]{\mathrm{ROH}^{a}} \quad \mathrm{O_2NCMe_2CMe_2NO_2}$$

M	R	Time	% yield[b]
K	Me	2	82
Na	Me	5	42
Li	Me	3	75
K	Et	1	91
Na	Et	5	43
Li	Et	3	85
K	Et	3[c]	79
Na	Et	10[c]	8
Li	Et	5[c]	32

[a] Equimolar amounts of substrates (1.0 mmol) in 10 mL of solvent were irradiated for the time indicated in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding a known amount of naphthalene as an internal standard.

[c] Reactions were carried out in the room light.

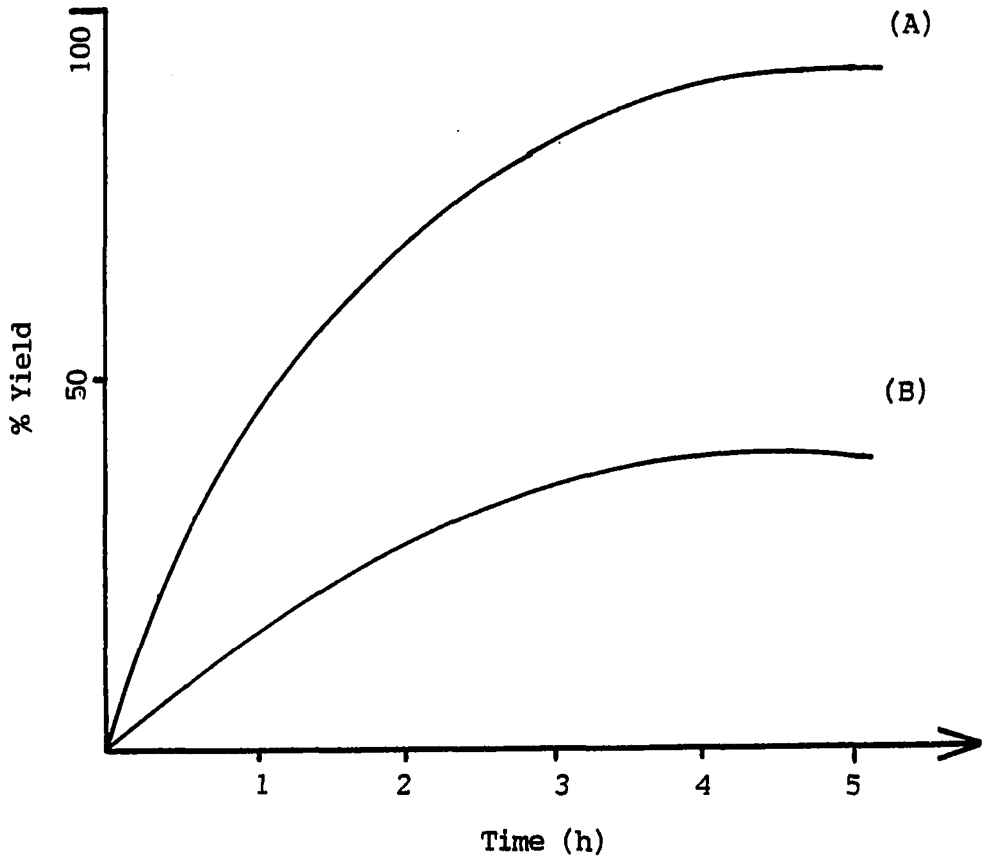


Figure 9. Plot of formation of K vs.time; (A) $[BrCMe_2NO_2]$= 0.101 M, $[KOCH_3]$= 0.220 M in 10 mL of methanol, (B) $[BrCMe_2NO_2]$= 0.100 M, $[KOCH_3]$= 0.210 M, $[Me_2C{=}NO_2{}^{-+}K]$= 0.111 M in 10 mL of methanol. Reactions were irradiated in a Rayonet photoreactor at 350 nm

Scheme 18

$$BrCMe_2NO_2^{-\cdot} \longrightarrow Me_2CNO_2^{\cdot} + Br^{-}$$

$$Me_2CNO_2^{\cdot} + Me_2C{=}NO_2^{-} \xrightarrow{k_N} \underline{D}^{-\cdot} \longrightarrow \underline{D} \qquad (25)$$

$$Me_2CNO_2^{\cdot} + 1^{\circ}\text{-}RO^{-} \xrightarrow{k_O} Me_2C(OR)NO_2^{-\cdot} \longrightarrow \longrightarrow \underline{K} \qquad (26)$$

The photostimulated reaction of 2-substituted-2-nitropropanes with the potassium salt of 2-nitropropane and potassium methoxide was performed to determine the ratio of *K*/*D* during the reaction period. To minimize the experimental error, two reactions were performed. The average of the two experiments are given in Tables 24 and 25. Figure 10 shows the plots of yield ratio of *K*/*D* vs. time. The product ratio of *K*/*D* with 2,2-dinitropropane was observed to be the same as that observed with 2-bromo-2-nitropropane and with both substrates the product ratio of *K*/*D* did not change during the reaction period. This means that the competitive reaction of the anion of 2-nitropropane and 1°-alkoxide ion is independent of the nature of leaving group (X = Br, NO_2) and the extent of the reaction. The observed constant values of *K*/*D* (0.86 ± 0.03) support the simple radical competition reaction between nitronate anion and 1°-alkoxide ion towards the intermediate 2-nitro-2-propyl radical. In general, distinction between the

Table 24. Photostimulated reaction of 2-bromo-2-nitropropane with the potassium salt of 2-nitropropane and potassium methoxide

$$\underset{\underline{4}}{\mathrm{BrCMe_2NO_2}} + \mathrm{KOMe} + \mathrm{Me_2C{=}NO_2^{-+}M} \xrightarrow{\mathrm{MeOH,\ UV^a}} \underset{\underline{K}}{\mathrm{Me_2C(OCH_3)_2}} + \underset{\underline{D}}{\mathrm{O_2NCMe_2CMe_2NO_2}}$$

Time (h)	% yields[b]			K/D[c]
	4	K	D	
0.5	74.20 (± 2.50)	7.86 (± 3.54)	11.78 (± 4.42)	0.67
1	57.31 (± 2.87)	18.17 (± 1.34)	20.82 (± 0.71)	0.87
2	18.97 (± 2.91)	33.79 (± 2.79)	39.34 (± 1.94)	0.86
3	10.53 (± 2.13)	38,85 (± 3.08)	46.38 (± 2.39)	0.84
4	7.21 (± 0.53)	39.60 (± 2.91)	48.20 (± 2.73)	0.86
8	0	42.00 (± 2.98)	50.10 (± 1.69)	0.88

[a] $[\mathrm{BrCMe_2NO_2}]_o$= 0.10 M, $[\mathrm{KOMe}]_o$= 0.090 M and $[\mathrm{Me_2C{=}NO_2^{-+}K}]_o$= 0.128 M. Reactions were irradiated for the time indicated in a Rayonet Photoreactor at 350 nm.

[b] GC yields were measured by adding a known amount of naphthalene as an internal standard; the deviations from the average value were given in parentheses.

[c] Product ratios.

Table 25. Photostimulated reaction of 2,2-dinitropropane with potassium salt of 2-nitropropane and potassium methoxide

$$\underset{\underline{6}}{Me_2C(NO_2)_2} + KOMe + Me_2C{=}NO_2^{-+}K \xrightarrow{MeOH,\ UV^{a}} \underset{\underline{K}}{Me_2C(OCH_3)_2} + \underset{\underline{D}}{O_2NCMe_2CMe_2NO_2}$$

Time (h)	% yields[b]			K/D[c]
	6	K	D	
1	75.28 (± 2.54)	10.21 (± 1.65)	12.69 (± 0.91)	0.80
2	54.31 (± 1.42)	19.98 (± 0.97)	22.97 (± 1.12)	0.87
4	20.12 (± 3.21)	34.01 (± 2.13)	38.21 (± 1.99)	0.89
6	10.41 (± 2.99)	37.29 (± 3.19)	43.87 (± 2.15)	0.85
8	3.29 (± 0.34)	39.11 (± 2.98)	45.48 (± 1.55)	0.86
12	0	40.19 (± 2.22)	46.19 (± 1.99)	0.87

[a] $[Me_2C(NO_2)_2]_o$ = 0.10 M, $[KOMe]_o$ = 0.091 M and $[Me_2C{=}NO_2^{-+}K]_o$ = 0.134 M. Reactions were irradiated in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding a known amount of naphthalene as an internal standard; the deviations from the average value were given in parentheses.

[c] Product ratios.

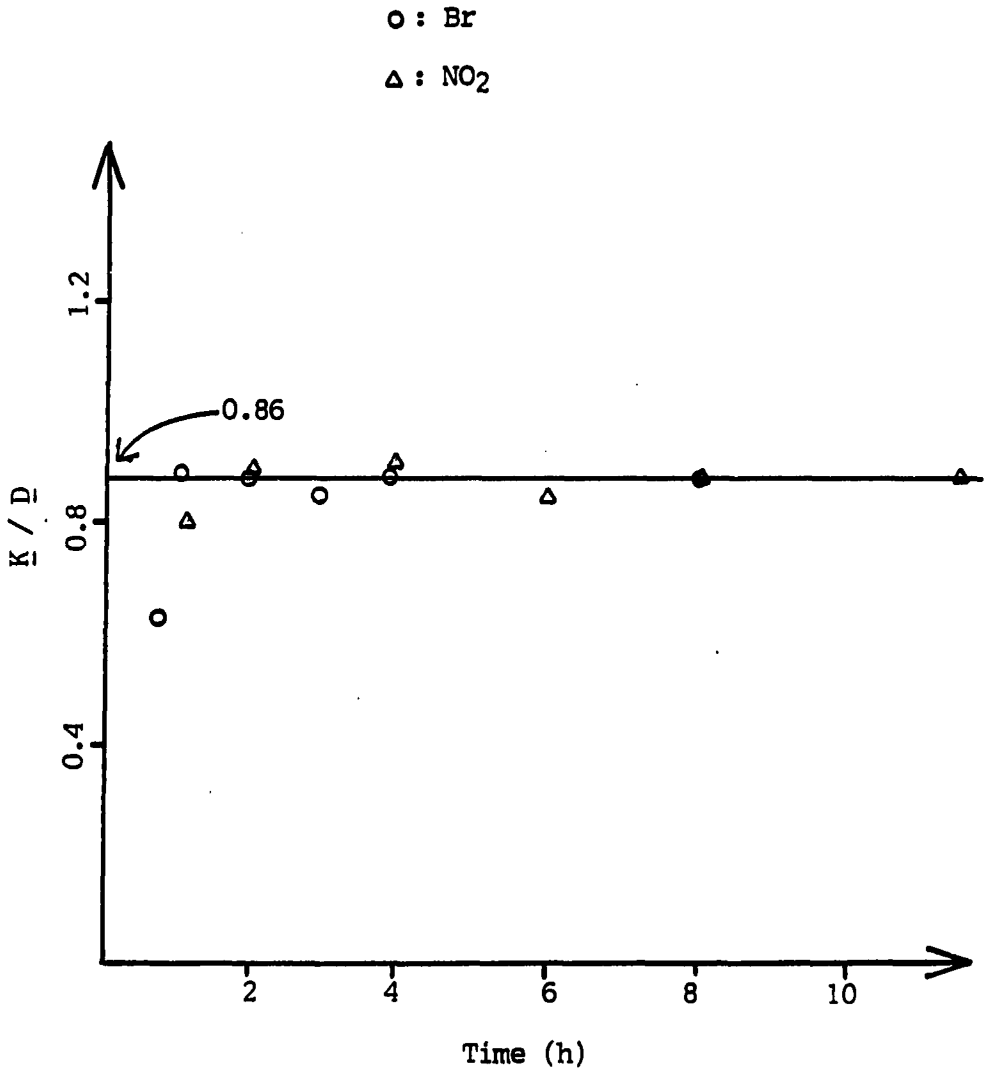


Figure 10. Products ratio (K/D) vs. time for the reaction of $XCMe_2NO_2$ (X = Br, NO_2) with the potassium salt of 2-nitropropane and potassium methoxide in methanol in a Rayonet photoreactor at 35 °C

$S_{RN}1$ process of Scheme 18 and the $S_{RN}2$ process of Scheme 7 can be made on the basis of evidence for the 2-nitro-2-propyl radical as an intermediate. The fact that the ratio of K/D is independent of the leaving group in the 2-substituted-2-nitropropanes is taken as evidence for the formation of the free 2-nitro-2-propyl radical as an intermediate and excludes an $S_{RN}2$ process in the photostimulated reaction of 2-substituted-2-nitropropanes with 1^{o}-alkoxide ion.

In the reactions described in Table 24 and 25, the concentrations of the 2-substituted-2-nitropropanes varied widely during the course of the reactions. However, the relative yields of K and D were nearly constant. If the 2-nitro-2-propyl radical reacts reversible with the methoxide and nitronate anion to yield radical anions which then undergo electron transfer with the 2-substituted-2-nitropropane, one would expect the ratio of K/D to vary with the concentration of the electron acceptor. Either the radical trapping is not reversible or the product determining steps do not depend upon the concentration of the electron acceptor. It is generally assumed that the trapping of 2-nitro-2-propyl radical by nitronate anion is irreversible. However, the reaction with 1^{o}-alkoxide ion might be reversible. This reversibility might not show up in the competitive reactions if the radical anion of 2-methoxy-2-nitropropane is converted to a ketal precursor in an irreversible reaction not involving the 2-

substituted-2-nitropropane as shown in Scheme 19.

Scheme 19

$$XCMe_2NO_2 + N^- \longrightarrow XCMe_2NO_2^{-\cdot} + N^\cdot \qquad (27)$$

$$XCMe_2NO_2^{-\cdot} \longrightarrow Me_2CNO_2^\cdot + X^- \qquad (28)$$

$$Me_2CNO_2^\cdot + 1^\circ\text{-}RO^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Me_2C(OR)NO_2^{-\cdot} \xrightarrow{k_2}$$

$$Me_2COR^\cdot + NO_2^- \qquad (29)$$

$$Me_2COR^\cdot + XCMe_2NO_2 \longrightarrow Me_2COR^+ + XCMe_2NO_2-. \qquad (30)$$

$$Me_2COR^+ + 1^\circ\text{-}RO^- \longrightarrow \underline{K} \qquad (31)$$

$$Me_2CNO_2^\cdot + Me_2C{=}NO_2^- \xrightarrow{k_N} \underline{D}^{-\cdot} \longrightarrow \underline{D} \qquad (32)$$

If Scheme 19 is followed, the differential rate equation 33 can be written

$$\frac{-d[1^\circ\text{-}RO^-] / dt}{-d[M_2C{=}NO_2^-] / dt} = \frac{2\ k_o\ [1^\circ\text{-}RO^-]\ [Me_2CNO_2^\cdot]}{k_N\ [Me_2C{=}NO_2^-]\ [Me_2CNO_2^\cdot]} \qquad (33)$$

where $k_o = k_1k_2 / (k_{-1}+k_2)$.

When the ratio of $[1^\circ\text{-RO}^-]/[Me_2C{=}NO_2^-]$ remains constant, Equation 34 results

$$\frac{\underline{K}}{\underline{D}} = \frac{k_O \; [1^\circ\text{-RO}^-]}{k_N \; [Me_2C{=}NO_2^-]} \qquad (34)$$

The integration of Equation 33 yields,

$$\frac{\int_o^t d[1^\circ\text{-RO}^-] \;/\; [1^\circ\text{-RO}^-]}{\int_o^t d[Me_2C{=}NO_2^-] \;/\; [Me_2C{=}NO_2^-]} = \frac{\int_o^t 2\; k_O \; dt}{\int_o^t k_N \; dt} \qquad (35)$$

$$\frac{\log\, [1^\circ\text{-RO}^-]_t \; - \; \log\, [1^\circ\text{-RO}^-]_o}{\log\, [Me_2C{=}NO_2^-]_t \; - \; \log\, [Me_2C{=}NO_2^-]_o} = \frac{2\; k_O}{k_N} \qquad (36)$$

where $[1^\circ\text{-RO}^-]_t = [1^\circ\text{-RO}^-]_o - 2\,[\underline{K}]$

$[Me_2C{=}NO_2^-]_t = [Me_2C{=}NO_2^-]_o - [\underline{D}]$

The value of k_O/k_N can be expressed by the rate constants k_1, k_{-1} and k_2 in Reaction 29 as shown in Equation 37.

$$\frac{k_O}{k_N} = \frac{k_1 \; k_2}{(k_{-1} + k_2)\; k_N} \qquad (37)$$

In an attempt to prove the rate expression of Equation

33, several different initial concentrations of $[MeO^-]_o$ and $[Me_2C{=}NO_2^-]_o$ were employed in the reaction of 2-bromo-2-nitropropane. The photostimulated reactions of 2-bromo-2-nitropropane (0.082 M) with the potassium salt of 2-nitropropane (0.111 M) in the presence of different concentrations of potassium methoxide gave the expected variation in the product ratio K/D. As the concentration of potassium methoxide was increased, the yield of K increased as did the ratio of K/D (Table 26). The plot of the product ratio of K/D vs. the ratio of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ in Figure 11 gave a straight line. The slope of this plot permits the evaluation of the desired reactivity ratio k_O/k_N, provided the ratio $[MeO^-]/[Me_2C{=}NO_2^-]$ remains constant (Eq. 34).

Values of k_O/k_N corrected for the variation in the $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ ratio can be calculated from the data of Table 26 by use of the integrated form of the competitive rate expression (Eq.35, 36). A series of experiment here performed where the ratio of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ was held constant and $[K^+]$ was varied by using different initial concentrations of the both anions. Values k_O/k_N obtained in this manner are given in Table 27. One possible reason for the variation in k_O/k_N as calculated in Table 27 is the variation in $[K^+]$ as the initial concentrations of the two anions was changed. Figure 12 gives a plot of k_O/k_N as a function of $[M^+]$. The value of k_O/k_N at $[K^+]_{total} < 0.3$ M (1.6-1.9) for the reaction

Table 26. Photostimulated reaction of 2-bromo-2-nitropropane with the potassium anion of 2-nitropropane and potassium methoxide

$$\mathrm{BrCMe_2NO_2} \;+\; \mathrm{KOMe} \;+\; \mathrm{Me_2C{=}NO_2^{-+}K} \xrightarrow{\text{MeOH, UV}^{a}} \underline{\mathrm{K}} + \underline{\mathrm{D}}$$

$[MeO^-]_o$ (M)	$[MeO^-]_o/[Me_2C{=}NO_2^-]_o$	% yields[b]		$\underline{K}/\underline{D}$
		$\underline{K}$	$\underline{D}$	
0.037	0.33	23.11	57.74	0.40
0.056	0.50	34.96	59.09	0.59
0.059	0.53	29.34	64.41	0.46
0.111	1.00	47.82	36.78	1.30
0.132	1.19	60.48	36.60	1.74
0.136	1.23	62.45	32.30	1.93
0.214	1.93	62.50	22.80	2.75

[a] $[BrCMe_2NO_2]_o$= 0.082 M, $[Me_2C{=}NO_2^-]_o$=0.111 M. Reactions were irradiated for 5 hours in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding internal standard.

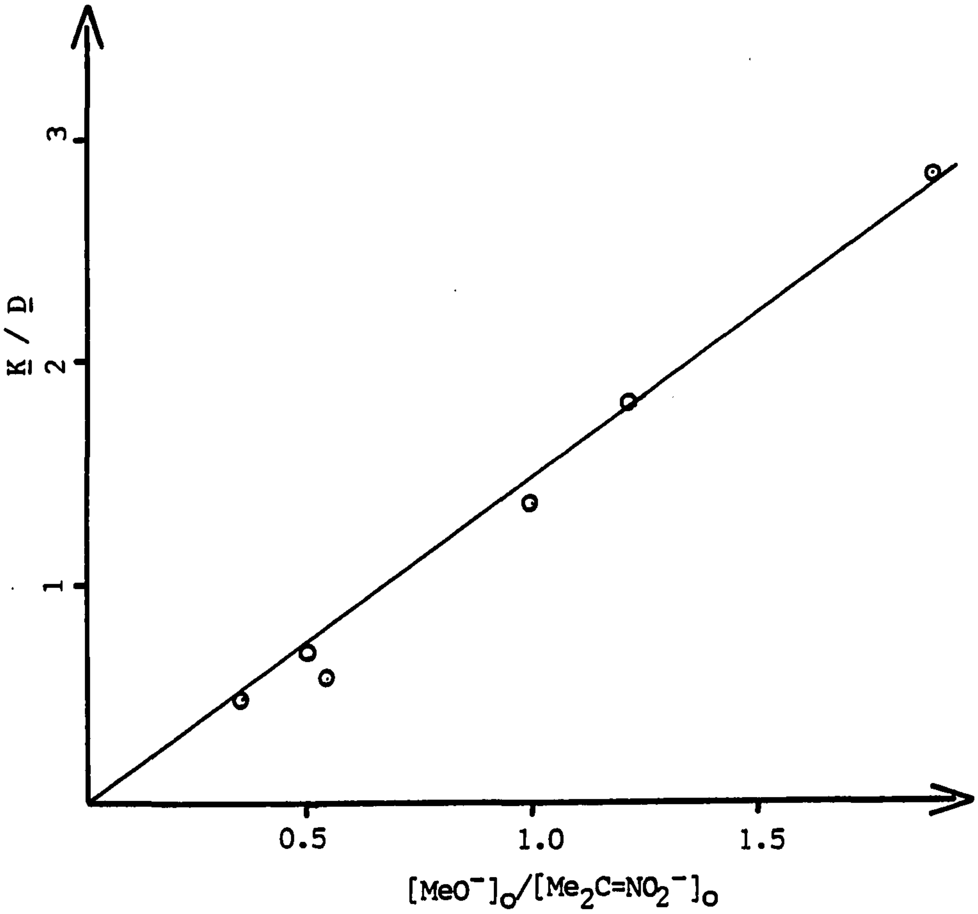


Figure 11. Plot of the products ratio (K/D) vs. $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$. Reactions employing K^+ as counterion and $BrCMe_2NO_2$ (0.082 M) were irradiated for 5 hours in a Rayonet photoreactor at 350 nm

Table 27. Photostimulated reaction of 2-bromo-2-nitropropane with the potassium salt of 2-nitropropane and potassium methoxide with different concentrations of $[K^+]$

$$BrCMe_2NO_2 + MeOK + Me_2C{=}NO_2{}^{-+}K \xrightarrow{MeOH,\ UV^a} \underline{K} + \underline{D}$$

$[K^+]_{total}$ (M)	$Me_2C{=}NO_2{}^{-b}$ (mmol)	% yield[c] $\underline{K}$	% yield[c] $\underline{D}$	$k_O/k_N{}^d$
0.063	0.623	51.0	48.0	1.75
0.100	0.795	53.6	42.8	1.84
0.161	0.784	52.1	44.0	1.66
0.220	0.792	54.3	41.0	1.85
0.291[e]	0.767	55.2	40.8	1.90
0.312	0.790	58.3	38.0	2.33
0.420	1.323	76.2	19.9	3.10

[a] $BrCMe_2NO_2$ = 0.500 mmol. Reactions were irradiated in a Rayonet photoreactor at 350 nm.

[b] $[Me^2C{=}NO_2{}^-]_o = [MeO^-]_o = 1/2\ [K^+]_{total}$. Units are mmol.

[c] GC yields were measured by adding internal standard.

[d] $k_O/k_N = k_1k_2/(k_{-1}+k_2)k_N$.

[e] 0.291 M of 18-crown-6 was added in the solution of potasssium methoxide.

with different concentrations of [K^+] at a constant ratio of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ is similar to that for the reaction with different ratios of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ (Figure 11 gives $k_O/k_N = 1.5 \pm 0.2$). It is now apparent that the proposed mechanism in Scheme 19 is well fitted by the observed kinetics. Similar kinetics studies of the photostimulated reactions with the counterions Li^+ and $PhCH_2N(CH_3)_3^+$ under the same conditions were performed to calculate the value of k_O/k_N ($= k_1k_2/(k_{-1}+k_2)k_N$). The results are listed in Table 28 and Figure 12. The values of k_O/k_N at low concentrations of the counterions Li^+ and $PhCH_2N(CH_3)_3^+$ are about 1.50 ± 0.40 and 1.00 ± 0.40, respectively. Within the experimental errors, these values are very similar to that for K^+.

When the counterion Na^+ was employed in the photostimulated reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane and sodium methoxide in methanol where the ratio of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o$ was held constant and [Na^+] was varied, the value of k_O/k_N was much different from that observed for K^+, Li^+ or $PhCH_2N(CH_3)_3^+$. Table 29 and Figure 12 show that the value of $k_O/k_N > 50$ is observed with $[Na^+]_{total}$ <0.23 M. Small amounts of D were observed, only when both the anion of 2-nitropropane and 2-bromo-2-nitropropane were present at relative high concentrations. At low concentrations of 2-bromo-2-nitropropane, no D was observed at the highest concentration of $Me_2C{=}NO_2^-$ employed. At low

Table 28. Photostimulated reaction of 2-bromo-2-nitropropane with the anion of 2-nitropropane and methoxide ion with different concentration of [M^+]

$$BrCMe_2NO_2 + MeO^{-+}M + Me_2C{=}NO_2^{-+}M \xrightarrow{MeOH,\ UV^a} \underline{K} + \underline{D}$$

M	[M^+]$_{total}$ (M)	% yields[b]		k_O/k_N[c]
		$\underline{K}$	$\underline{D}$	
Li[d]	0.072	47.0	39.3	1.65
Li	0.179	53.2	41.7	1.27
Li	0.238	48.2	44.6	1.51
Li	0.358	45.5	47.2	1.28
Li	0.715	49.2	38.4	1.87
$PhCH_2N(CH_3)_3$[e]	0.045	45.3	44.8	1.33
$PhCH_2N(CH_3)_3$	0.084	46.2	44.8	1.40
$PhCH_2N(CH_3)_3$	0.191	37.3	60.3	0.68
$PhCH_2N(CH_3)_3$	0.445	32.8	56.8	0.63

[a] Reactions with 0.500 mmol of 2-bromo-2-nitropropane were irradiated in a Rayonet photoreactor at 350 nm.

[b] GC yields were measured by adding internal standard.

[c] $k_O/k_N=k_1k_2/(k_{-1}+k_2)k_N$.

[d] 0.715 mmols of $Me_2C{=}NO_2^-$ and MeO^- were used.

[e] 0.67 mmols of $Me_2C{=}NO_2^-$ and MeO^- were used.

Table 29. Photostimulated reaction of 2-bromo-2-nitropropane with the sodium salt of 2-nitropropane and sodium methoxide with different concentrations of $[Na^+]$

$$\mathrm{BrCMe_2NO_2} + \mathrm{MeO^{-+}Na} + \mathrm{Me_2C{=}NO_2{}^{-+}Na} \xrightarrow{\mathrm{MeOH,\ UV^a}} \underline{K} + \underline{D}$$

$[Na^+]_{total}$ (M)	$Me^2C=NO_2^-$ (mmol)	$BrCMe_2NO_2$ (mmol)	% yields[b]		k_O/k_N[c]
			K	**D**	
0.076	0.59	0.50	56.1	0	-
0.108	0.59	0.50	57.0	0	-
0.168	0.63	0.50	66.1	0	-
0.235	0.65	0.50	41.7	1.5	53.5
0.417	0.65	0.50	35.5	6.0	6.3
0.433	0.65	0.50	36.7	7.2	7.3
0.441	0.66	0.25	57.9	0	-
0.570[d]	0.75	0.50	57.1	0	-

[a] Reactions were irradiated for 5 hours in a Rayonet photoreactor a 350 nm.

[b] GC yields were measured by adding internal standard.

[c] $k_O/k_N=k_1k_2/(k_{-1}+k_2)k_N$.

[d] 4.20 mmol of $NaClO_4$ was added to a solution of sodium methoxide.

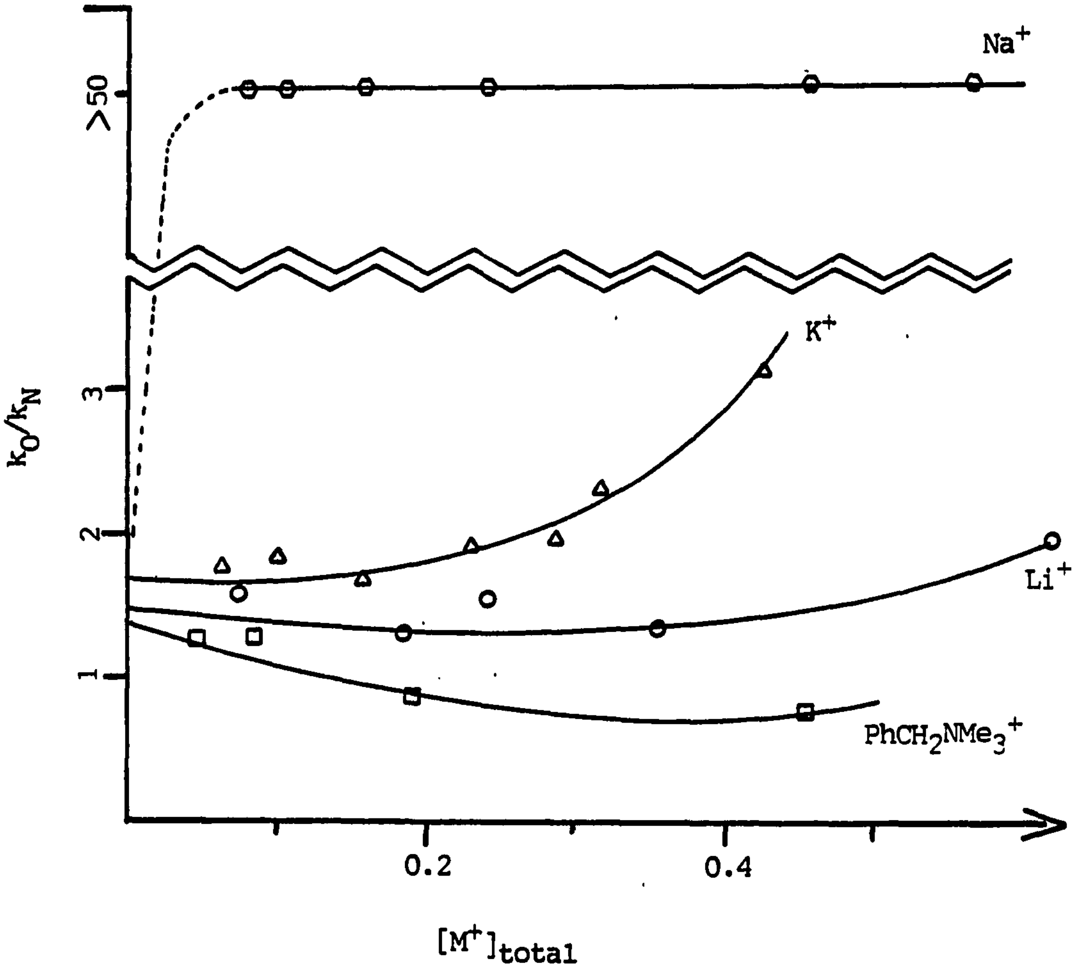


Figure 12. Plot of the ratio of k_O/k_N vs. $[M^+]_{total}$ at constant initial ratio of $[MeO^-]_o/[Me_2C{=}NO_2^-]_o = 1$ where $k_O/k_N = k_1k_2/(k_{-1}+k_2)k_N$

concentration of $Me_2C{=}NO_2^-$ and high concentration of $BrCMe_2NO_2$, $\underline{D}$ was not observed even when excess sodium perchlorate was added to give a relatively high concentration of $[Na^+]_{total}$. The formation of $\underline{D}$ at high concentration of both $Me_2C{=}NO_2^-$ and $BrCMe_2NO_2$ may reflect a reaction not involving free 2-nitro-2-propyl radical, but involving Reaction 38 or 39. In Reaction 38,

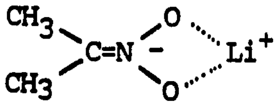
$$Me_2C{=}NO_2{}^{-+}Na \ + \ BrCMe_2NO_2 \xrightarrow{UV} [Me_2CNO_2{}^{\cdot} \ \ Na^{+-}Br \ \ Me_2CNO_2{}^{\cdot}]_{cage} \longrightarrow \underline{D} \tag{38}$$

$$2\ Me_2C{=}NO_2{}^{-+}Na \rightleftharpoons O_2NCMe_2CMe_2NO_2{}^{-2} \xrightarrow{UV,\ BrCMe_2NO_2} \underline{D} \tag{39}$$

the formation of $\underline{D}$ occurs directly from the dimerization of 2-nitro-2-propyl radicals in the cage. Alternately, two anions of 2-nitropropane might be coupled by photolysis and subsequently oxidized by 2-bromo-2-nitropropane to give the dimer as shown in Equation 39.

The ions and ion pairs derived from MeO^- and $Me_2C{=}NO_2^-$ with Li^+, K^+ or $PhCH_2NMe_3^+$ as the counterion have a similar reactivity towards 2-nitro-2-propyl radical. However, with Na^+ as the counterion, MeO^- is much more reactive than

$Me_2C{=}NO_2^-$. This probably reflects selective ion pairing with $Me_2C{=}NO_2^-$ because the $S_{RN}1$ coupling reaction between $BrCMe_2NO_2$ and $Me_2C{=}NO_2^{-+}M$ in ethanol also occurs readily with $M^+ = K^+$, Li^+ or $PhCH_2N(CH_3)_3^+$ but not with Na^+. It is surprising that ion pairing of $Me_2C{=}NO_2^-$ with Na^+ decreases the reactivity of $Me_2C{=}NO_2^{-+}Na$ towards 2-nitro-2-propyl radical, whereas ion pairing with Li^+ increases the reactivity of $Me_2C{=}NO_2^{-+}Li$. Perhaps the structure of the ion pairs is important. With Li^+ perhaps a tight ion pair,



exists which has a reactivity towards radical attack similar to the essentially free $Me_2C{=}NO_2^-$ observed with K^+ and $PhCH_2N(CH_3)_3^+$. With Na^+ the structure of the ion pair may be different and a low reactivity is observed towards 2-nitro-2-propyl radical.

Solvent effects may play an important role on the reactivity of the anions in $S_{RN}1$ process [65]. The competition reactions between 1°-alkoxide ion and nitronate anion towards 2-nitro-2-propyl radical generated from the radical anion of 2-bromo-2-nitropropane, produced only 2,3-dimethyl-2,3-dinitrobutane <u>D</u> in aprotic solvents, such as DMSO, DMF and HMPA. It seemed likely that the 1°-alkoxide ion would still react with the 2-nitro-2-propyl radical to form the radical anion of 2-alkoxy-2-nitropropane in these solvents. However, in aprotic solvents perhaps this radical anion fails to dissociate to form 2-alkoxy-2-propyl radical (k_2 in Scheme 19) because the rate of the reverse process (k_{-1}) is much faster than the rate of dissociation (k_2). This result is perhaps formulated as shown in Equation 40.

$$k_2 \mathbin{/} k_2 + k_{-1} = 0$$

$$\text{in aprotic solvents, } (k_{-1} \gg k_2) \qquad (40)$$

C. Conclusion

The initial kinetic chain lengths in the reactions of 2-bromo-2-nitropropane (0.10 M) with 1°-alkoxide ion (0.22 M) in a solution of the alcohol and with the anion of 2-nitropropane (0.10 M) in methanol and ethanol were determined. The measured initial kinetic chain lengths for sodium methoxide and potassium methoxide in methanol were 10 and 38, respectively. The initial kinetic chain lengths of 38 and 171 were measured from the reaction with sodium ethoxide and potassium ethoxide in ethanol, respectively. Initial kinetic chain lengths of 45 and 179 were measured from the reaction with the potassium salt of 2-nitropropane in methanol and ethanol, respectively. These results indicate that these reactions proceed via free radical chain processes. Possibly, the rates of the propagating steps of the reactions with potassium counterion are faster than those of the reactions with sodium as the cation. Longer initial kinetic chain length for the reactions of sodium or potassium ethoxide in ethanol than for the alkali methoxides in methanol were always observed.

Relative reactivities of 1°-alkoxide ions and the anion of 2-nitropropane (k_O/k_N) towards the 2-nitro-2-propyl radical have been determined from the product analysis. In the reaction with 2-substituted-2-nitropropanes (X= Br, NO_2), 1°-alkoxide ions competes with the nitronate anion to form the ketal (K) and the dimer (D). The constant values of K/D and the independence of this ratio upon the leaving group observed during a reaction period in which the concentration of the 2-substituted-2-nitropropane changes are good evidences supporting the simple competitive reaction of the 2-nitro-2-propyl radical with the two anions. It is now apparent that the photostimulated reaction of 2-substituted-2-nitropropanes with 1°-alkoxide ions cannot proceed via an $S_{RN}2$ process.

Constant values of k_O/k_N were observed with the counterions K^+, Li^+ and $PhCH_2N(CH_3)_3^+$ in methanol for the reactions of the 2-nitro-2-propyl radical with different initial concentrations and ratios of $[MeO^-]_o$ and $[Me_2C{=}NO_2^-]_o$. Furthermore, there was no appreciable change in the values of k_O/k_N when the potassium counterion was complexed with 18-crown-6 ether. Ion pairing effect for these counterions are not significant. In contrast to the constant values of k_O/k_N for these counterions, the value of k_O/k_N for the counterion Na^+ dramatically increased to >50 with low concentration of $[Na^+]_{total}$. This large change of k_O/k_N values appears to be associated with an increase in ion pairing. Specific ion pairing effects with sodium may lower the reactivity of the nitronate anion relative to methoxide ion towards 2-nitro-2-propyl radical.

By changing to an aprotic solvent, such as DMSO, DMF and HMPA, the relative reactivities of 1^o-alkoxide ion and nitronate anion can be dramatically changed and little or no ketal is formed. Possibly, the dissociation rate (k_2) of the intermediate radical anion of 2-alkoxy-2-nitropropane to yield the 2-alkoxy-2-propyl radical is significantly smaller than the dissociation to form the 2-nitro-2-propyl radical (k_{-1}) in aprotic solvents.

The relative reactivities of the 1^o-alkoxide ions and the anion of 2-nitropropane in the photostimulated reaction with 2-bromo-2-nitropropane are depend upon the counterions and the nature of solvents and are independent of the concentration of

2-bromo-2-nitropropane, the extent of reaction, or of the initial ratio of $[MeO^-]/[Me_2C{=}NO_2^-]$. The initial kinetic chain length measurements and the reactivity studies of the photostimulated reactions of 2-substituted-2-nitropropanes with 1°-alkoxide ions strongly support a free radical chain processes in the formation of the ketal.

D. Experimental Section

1. General considerations

^1H NMR spectra were recorded on a Nicolet Magnetic Corp. NMC-1280 spectrometer (300 MHz) in methanol-d_4. Product yields were determined by ^1H NMR integration with a known amount of benzene or Gas Chromatographic analysis was performed on a 3700 Varian Gas Chromatograph with a packed Chromosorb W (80-100 mesh) column coated with 7% ov-3 and a thermal conductivity detector. Product yields were determined by addition of a known amount of biphenyl or naphthalene as an internal standard.

2. Determination of kinetic chain length in the reaction of 2-bromo-2-nitropropane and methoxide ion

Sodium metal (0.0025 g, 0.110 mmol) was dissolved in 0.5 mL of nitrogen-purged deuterated methanol in a NMR tube equipped with a rubber septum and sealed with a piece of parafilm. 2-Bromo-2-nitropropane (0.0085 g, 0.050 mmol) was added by microsyringe to a 0.22 M solution of methoxide ion. Internal standard (benzene, 0.01 mmol) was also added to the solution. After a ^1H NMR spectrum was obtained, the NMR tube was irradiated in a Rayonet photoreactor at 35 °C at 350 nm. The progress of the reaction was monitored by the ^1H NMR spectrum and the formation of ketal was obtained by the integration of the increased signal of six methyl protons of $Me_2C(OCD_3)_2$ comparing with the internal standard. The formations of ketal at different periods of time are given in Table 16 for methanol-d_4. The reaction of 2-bromo-2-nitropropane and sodium methoxide in the presence of 10 mol % of di-*tert*-butyl nitroxide (DTBN) was carried out under the same conditions. The progress of the reaction was also followed by ^1H NMR and the yields of ketal obtained at different periods of time are given in Table 16.

A similar reaction with potassium metal instead of sodium metal was carried out under same conditions. Thus, potassium metal (0.0037 g, 0.110 mmol), 2-bromo-2-nitropropane (0.0850 g, 0.050 mmol) and were dissolved in 0.5 mL of nitrogen-purged methanol-d_4. After a ^1H NMR spectrum was obtained, the mixture was irradiated in the Rayonet photoreactor. The progress of the reaction was followed by ^1H NMR under the same conditions described above. The yields of ketal obtained at different periods of time are given in Table 17. The reaction of 2-bromo-2-nitropropane and potassium methoxide in the presence of 10 mol % of DTBN were carried out under the same conditions. The yields of ketal are given in Table 17.

3. Determination of kinetic chain length in the reaction of 2-bromo-2-nitropropane and ethoxide ion

Sodium metal (0.051 g, 2.20 mmol) was dissolved in 10 mL of dry ethanol in a Pyrex tube equipped with a rubber septum and sealed with a piece of parafilm. 2-Bromo-2-nitropropane (0.168 g, 1.00 mmol) was added to a solution of ethoxide ion. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. The progress of the reaction was monitored by quenching a known amount of reaction mixture and measuring the yield of product by GC. The yields of ketal obtained at different periods of time are given in Table 18. The reaction of 2-bromo-2-nitropropane and sodium ethoxide in the presence of 3 mol % of DTBN was carried out under same conditions. The reaction was followed by GC analysis and the formations of ketal obtained at different periods of time are given in Table 18.

A similar reaction with potassium metal was carried out under the same conditions. Potassium metal and 2-bromo-2-nitropropane were dissolved in 10 mL of dry ethanol to give a solution 0.10 M in $BrCMe_2NO_2$ and 0.22 M in $K^{+-}OEt$. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. The progress of the reaction was followed by GC analysis as described above. The yields of ketal are given in Table 19. The reaction of 2-bromo-2-nitropropane and potassium ethoxide in the presence of 3 mol % of DTBN was carried out under the same conditions. The yields of ketal obtained by GC analysis are given in Table 19.

4. Determination of kinetic chain length in the reaction of 2-bromo-2-nitropropane and the anion of 2-nitropropane

Potassium metal (0.047 g, 1.20 mmol) was dissolved in 10 mL of dry methanol to give a 0.12 M solution of potassium methoxide. 2-Nitropropane (0.089 g, 1.00 mmol)was added and stirred for 20 minutes. Then, 2-bromo-2-nitropropane (0.168 g, 1.00 mmol) was added via syringe to a solution under a nitrogen atmosphere. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C at 350 nm. The progress of the reaction was monitored by quenching a known amount of reaction mixture and measuring the yield of product by GC. The yields of dimer obtained at different periods of time are given in Table 20. The reaction of 2-bromo-2-nitropropane and potassium methoxide in the presence of 5 mol % of DTBN was carried out under the same conditions. The yield of dimer obtained by GC are given in Table 20.

A similar reaction with ethanol was carried out under the same conditions. Thus, a solution of 2-bromo-2-nitropropane (0.10 M) and the potassium salt of 2-nitropropane (0.10 M) were dissolved in 10 mL of dry ethanol. The yields of dimer are given in Table 21. The reaction of 2-bromo-2-nitropropane and the potassium salt of 2-nitropropane in the presence of 10 mol % of DTBN was carried out under the same conditions. The yields of dimer obtained by GC are given in Table 21.

5. <u>Determination of product ratio in the reaction of 2-substituted-2-nitropropanes with potassium methoxide and the potassium salt of 2-nitropropane</u>

Potassium metal (0.1022 g) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere to give a 0.262 M solution of potassium methoxide. 2-Nitropropane (0.1139 g, 1.280 mmol) was added via syringe to the solution and the mixture was stirred for 20 minutes. 2-Bromo-2-nitropropane (0.168 g, 1.00 mmol) was added to the reaction mixture. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. The progress of the reaction was monitored by quenching an aliquot of the reaction mixture and measuring the yields of ketal and dimer by GC. The yields of ketal and dimer are given in Table 24.

A similar reaction with 2,2-dinitropropane was carried out under the same conditions. The yields of ketal and dimer are given in Table 25.

6. Determination of relative reactivities in the reaction of 2-bromo-2-nitropropane with different ratios of anions

Potassium metal (0.0577 g) was dissolved in 10 mL of dry methanol under a nitrogen atmosphere to give a 0.148 M solution of potassium methoxide. 2-Nitropropane (0.0988 g, 1.110 mmol) was added and the mixture was stirred for 20 minutes. Then, 2-bromo-2-nitropropane (0.1386 g, 0.820 mmol) was added to the solution. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. After 5 hours, the reaction mixture was poured into a brine solution and extracted with methylene chloride (3 x 10 mL). The combined methylene chloride extracts were washed and dried over anhydrous magnesium sulfate. The product ratio was measured by GC. Several similar reactions with different amounts of potassium metal were carried out under the same conditions. The product ratio are given in Table 26.

7. Determination of relative reactivities in the reaction of 2-bromo-2-nitropropane and anions with different concentrations of potassium salts

Potassium metal (0.0486 g, 1.246 mmol) was dissolved in 20 mL of dry methanol under a nitrogen atmosphere to give a 0.623 M solution of potassium methoxide. 2-Nitropropane (0.0554 g, 0.623 mmol) was added and stirred for 20 minutes. Then, 2-bromo-2-nitropropane (0.0840 g, 0.50 mmol) was added by syringe to the solution. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. After 5 hours, the reaction mixture was worked up as previously described. The product ratio was determined by GC analysis with an internal standard.

Several similar reactions with different amounts of potassium metal and solvent were carried out under the same conditions. The yields of ketal and dimer are listed in Table 27.

8. **Determination of relative reactivities in the reaction of 2-bromo-2-nitropropane and anions with different concentrations of lithium salts**

Several similar reactions with different amounts of lithium metal were carried out under the same conditions. Thus, lithium metal (0.0099 g, 1.430 mmol) and 2-nitropropane (0.0636 g, 0.715 mmol) were dissolved in dry 20 mL of methanol. 2-Bromo-2-nitropropane (0.0840 g, 0.50 mmol) was added to the solution. The reaction mixture was irradiated under a nitrogen atmosphere. After work-up, the yields of products were determined by GC analysis and are listed in Table 28.

9. Determination of relative reactivities in the reaction of 2-bromo-2-nitropropane and anions with different concentrations of benzyltrimethlyammonium salts

Benzyltrimethylammonium methoxide (1.340 mmol) and 2-nitropropane (0.670 mmol) were dissolved in 30 mL of dry methanol under a nitrogen atmosphere. 2-Bromo-2-nitropropane (0.50 mmol) was added to the solution. The reaction mixture was irradiated in the Rayonet photoreactor for 5 hours. After work-up as previously described, the yields of products were determined by GC analysis.

Several similar reactions with different concentrations of benzyltrimethylammonium salts were carried out under the same conditions. The yields of ketal and dimer are listed in Table 28.

10. Determination of relative reactivities in the reaction of 2-bromo-2-nitropropane and anions with different concentrations of sodium salts

Sodium metal (0.0271 g, 1.180 mol) was dissolved in 15 mL of methanol under a nitrogen atmosphere. 2-Nitropropane (0.0525 g, 0.590 mmol) was added and the mixture was stirred for 20 minutes. 2-Bromo-2-nitropropane (0.50 mmol)was added by syringe to the solution. The reaction mixture was irradiated in the Rayonet photoreactor for 5 hours. After work-up as previously described, the yields of products were determined by GC analysis. A similar reaction with sodium perchlorate was carried out under the same conditions. Thus, sodium metal (1.496 mmol) and sodium perchlorate (4.201 mmol) are dissolved in 10 mL of dry methanol. 2-Nitropropane (0.750 mmol) was added to give a 0.569 M solution of sodium salts and the mixture stirred for 20 minutes. 2-Bromo-2-nitropropane (0.50 mmol) was then added to the solution. After irradiation of the reaction mixture for 5 hours, the reaction mixture was worked up. The yields of products are listed in Table 29.

IV. ADDITION OF tert-BUTYL RADICALS TO α,β-UNSATURATED KETONES

A. Introduction

Organomercury halides were known to participate in free radical chain reactions with a variety of substrates. The reduction of alkylmercury halides by metal hydrides has been proved to be a radical reaction [66-68]. The mechanism of this reaction is outlined in Scheme 20. Giese and co-workers

Scheme 20

Initiation:

$$\mathrm{RHgX} + \mathrm{NaBH_4} \longrightarrow \mathrm{RHgH} + \mathrm{NaBH_3X}$$

$$\mathrm{RHgH} \longrightarrow \mathrm{R^{\bullet}} + \mathrm{Hg^{o}} + \mathrm{H^{\bullet}}$$

Propagation:

$$\mathrm{R^{\bullet}} + \mathrm{RHgH} \longrightarrow \mathrm{RH} + \mathrm{RHg^{\bullet}}$$

$$\mathrm{RHg^{\bullet}} \longrightarrow \mathrm{R^{\bullet}} + \mathrm{Hg^{o}}$$

have studied the addition of alkyl radicals, generated from an alkylmercury halide with sodium borohydride, to electron deficient olefins [69-73]. The reaction has been shown to proceed via a free radical chain mechanism as shown in Scheme 21. The alkylmercury halide is reduced by sodium borohydride

Scheme 21

Initiation:

$$RHgX \quad + \quad NaBH_4 \longrightarrow RHgH \quad + \quad NaBH_3X$$

$$RHgH \longrightarrow R^{\bullet} \quad + \quad Hg^{0} \quad + \quad H^{\bullet}$$

Propagation:

$$R^{\bullet} \quad + \quad CH_2{=}CR^1R^2 \longrightarrow RCH_2\dot{C}R^1R^2$$

$$RCH_2\dot{C}R^1R^2 \quad + \quad RHgH \longrightarrow RCH_2CHR^1R^2 \quad + \quad RHg^{\bullet}$$

$$RHg^{\bullet} \longrightarrow R^{\bullet} \quad + \quad Hg^{0}$$

to produce the alkylmercury halide which spontaneously initiates the reaction since alkylmercury hydrides are not stable and decompose to generate the alkyl radical ($R^{\bullet}$). In the propagating step, the alkyl radical adds to the alkene to form an adduct radical, which reacts with alkylmercury hydride to form the product and alkylmercury radical ($RHg^{\bullet}$). The alkylmercury radical decomposes readily to form another alkyl radical which continues the chain reaction.

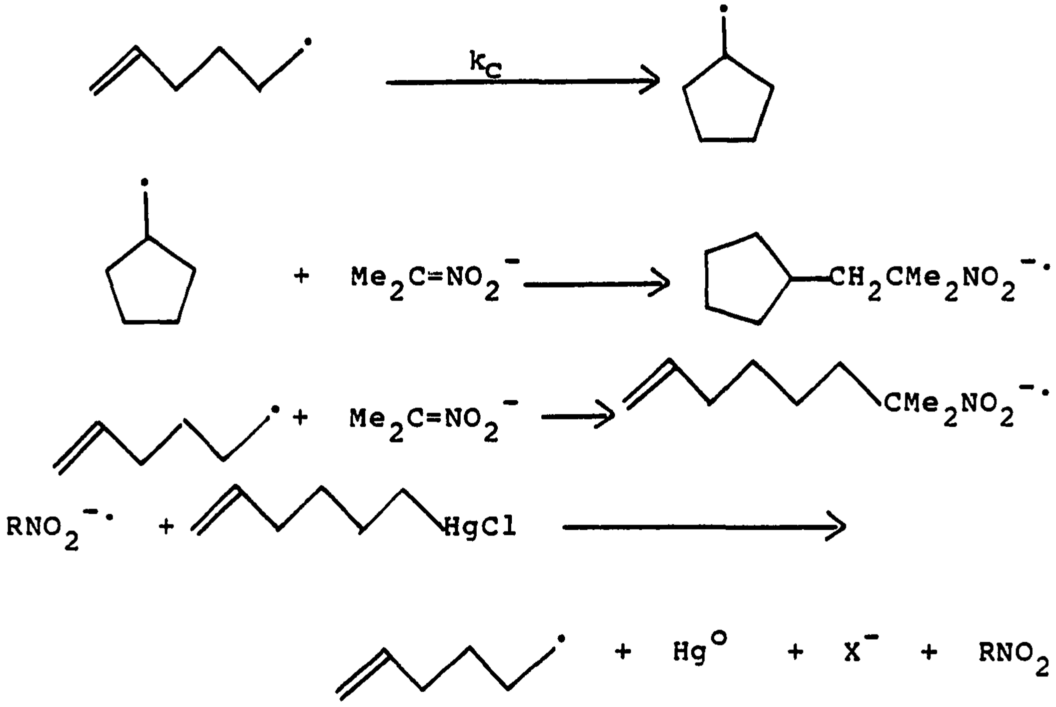
Alkylmercury halides have been found to participate in a photostimulated free radical chain reaction with a wide variety of carbanions as shown in Scheme 22 [74-76]. Strong support for the $S_{RN}1$ process involving radical anions and free radicals is provided by the fact that the cyclization of the 5-hexenyl radical, generated by electron transfer to 5-

Scheme 22

$$R^{\bullet} + N^{-} \longrightarrow RN^{-\bullet}$$
$$RN^{-\bullet} + RHgX \longrightarrow RN + RHgX^{-\bullet}$$
$$RHgX^{-\bullet} \longrightarrow R^{\bullet} + Hg^{o} + X^{-}$$

hexenylmercury chloride, to the cyclopentylcarbinyl radical occurred in the presence of the anion of 2-nitropropane to form the radical anion of adduct as shown in Scheme 23 [77]. The reduction of alkylmercury halides by $LiAlH_4$ has also been suggested to proceed by the $S_{RN}1$ process [78].

Scheme 23



The photostimulated reactions of alkylmercury halides with phenyl disulfide, phenyl diselenide, arylsulfonyl phenyl selenides and benzenesulfonyl chloride also occur by a free radical chain mechanism involving the alkyl free radical as an intermediate [79]. Alkenylmercury halides readily undergo photostimulated free radical chain substitution reactions with sulfinate anions, disulfides and benzenesulfonyl chloride as shown in Equation 41-43 [80, 81].

$$\mathrm{RCH{=}CHHgX} \quad + \quad \mathrm{R^{\circ}Y{-}YR^{\circ}} \xrightarrow{\mathrm{UV}} \mathrm{RCH{=}CHYR^{\circ}} \quad + \quad \mathrm{XHgYR^{\circ}} \tag{41}$$

$Y = S, Se, Te$

$R^{\circ} =$ alkyl, aryl

$$\mathrm{RCH{=}CHHgX} \quad + \quad \mathrm{Z{-}Q} \xrightarrow{\mathrm{UV}} \mathrm{RCH{=}CHZ} \quad + \quad \mathrm{XHgQ} \tag{42}$$

$Z = PhSO_2, \quad Q = Cl$

$$\mathrm{RCH{=}CHHgX} \quad + \quad \mathrm{A^-} \xrightarrow{\mathrm{UV}} \mathrm{RCH{=}CHA} \quad + \quad \mathrm{XHgQ} \tag{43}$$

$A^- = RS^-, RSO_2^-, (RO)_2PO^-$

Recently, several free radical reactions of organomercury halides with alkenes and alkynes have been shown to proceed via a free radical addition-elimination sequence [82-84]. The reaction involves regioselective addition of $R^{\bullet}$ to substrate followed by the β-elimination of $Q^{\bullet}$ as shown in Scheme 24. The chain reaction continues by virture of the attack of $Q^{\bullet}$

upon RHgX to regenerate the $R^\bullet$ by either S_H2 attack upon Hg by $Q^\bullet$ or electron transfer from $Q^\bullet$ to RHgX. The addition and elimination reactions in the chain sequence can lead to the substitution with the retention of configuration of alkenes.

Scheme 24

$$R^\bullet \quad + \quad R^1R^2C{=}CHQ \xrightarrow{\text{add.}} R^1R^2C{-}CHQR$$

$$R^1R^2C{-}CHQR \xrightarrow{\text{elim.}} R^1R^2C{=}CHR \quad + \quad Q^\bullet$$

$$RHgX \quad + \quad Q^\bullet \xrightarrow{S_H2} R^\bullet \quad + \quad QHgX$$

or

$$RHgX \quad + \quad Q^\bullet \xrightarrow{\text{E.T.}} R^\bullet + Hg^0 + Q^+ \quad + X^-$$

R = t-Bu, i-Pr, cyclohexyl, PhS

Q = I, HgCl, $PhSO_2$, n-Bu_3Sn, PhS

The photostimulated addition of alkylmercury chlorides to substituted acetylenes or electronegatively monosubstituted ethylenes has been studied by Russell et al. [85]. Alkylmercury halides react with alkenes followed by sodium borohydride reduction to afford the addition adducts as shown in Equation 44. The intermediate $RCH_2CH(HgCl)E$ involved in free radical chain sequence has been trapped by formation of the corresponding iodide $RCH_2CH(I)Q$ from work-up of the product with iodine.

$$\mathrm{RHgCl} \quad + \quad \mathrm{CH_2{=}CHE} \xrightarrow{\mathrm{NaBH_4}} \mathrm{RCH_2CH_2E} \quad + \quad \mathrm{Hg^{o}} \qquad (44)$$

$E = \mathrm{P(O)(OEt)_2},\ \mathrm{PhSO_2}$

$R = \underline{t}\text{-Bu},\ \underline{i}\text{-Pr},\ \underline{n}\text{-Bu},\ \text{cyclo-}C_6H_{11}$

Alkylmercury halides have been found to react with alkynes to form the (E) and (Z) adduct olefins as shown in Scheme 25. The adduct radical 43 is stabilized by electron delocalization by the phenyl ring.

Scheme 25

Initiation:

$$\underline{t}\text{-BuHgCl} \xrightarrow{\mathrm{UV}} \underline{t}\text{-Bu}^{\bullet} \quad + \quad {}^{\bullet}\mathrm{HgCl}$$

Chain Propagation:

$$\underline{t}\text{-Bu}^{\bullet} + \mathrm{Q{-}C{\equiv}C{-}Y} \longrightarrow \underset{\underline{43}}{\mathrm{Q{-}\dot{C}{=}C(\underline{t}\text{-Bu})Y}}$$

$$43 \quad + \quad \underline{t}\text{-BuHgCl} \longrightarrow \underset{\underline{44}}{\mathrm{Q(HgCl)C{=}C(\underline{t}\text{-Bu})Y}} \quad + \quad \underline{t}\text{-Bu}^{\bullet}$$

$$\begin{tikzcd} & \mathrm{QCH{=}C(\underline{t}Bu)Y} \\ \underline{44} \arrow[ur, "\mathrm{NaBH_4}"] \arrow[dr, "\mathrm{I_2}"'] & \\ & \mathrm{Q(I)C{=}C(\underline{t}\text{-Bu})Y} \end{tikzcd}$$

$Q = \mathrm{Ph},\ \mathrm{COOEt},\ \mathrm{COMe}$

$Y = \mathrm{H},\ \mathrm{COOEt}$

The photostimulated conjugate addition of the alkyl radicals derived from alkylmercury halides to 2-cycloalkenone systems has never been reported. On the other hand, the conjugate 1,4-additions of organocopper reagents to α,β-unsaturated ketones have been investigated in great detail by House and co-workers [86-90]. The mechanisms of organocopper conjugate addition are currently a matter of speculation, but the accepted mechanistic hypothesis involves partial or complete electron transfer from organocuprate to unsaturated substrate forming either a charge-transfer complex or an ion radical. The mechanistic study performed with methylcuprate or _n_-butylcuprate shows that this reaction does not involve organic free radicals [91, 92].

The following sections will present the photostimulated reaction of alkylmercury halides with 2-cycloalkenones in the presence of iodide ion. A discussion concerning the possibility of the _tert_-butyl radical being involved in the reaction of di-_tert_-butylcuprate with 2-cycloalkenones will be presented. Some other possible sources of _tert_-butyl radicals will also be considered.

B. Results and Discussion

1. Photostimulated reactions of alkylmercury halides with 2-cycloalkenones in the presence of iodide ion

2-Cyclohexenone was allowed to react with tert-butylmercury chloride in dimethyl sulfoxide (DMSO) under UV irradiation. A gray precipitate appeared after irradiation for 30 minutes. After work-up, this reaction gave the "1,4-addition" product, 3-tert-butylcyclohexanone in low yield. However, the photostimulated reaction of 2-cyclohexenone and tert-butylmercury chloride in the presence of iodide ion or a surprisingly high yield of the 1,4-addition product as shown in Table 30. DMSO was used as the solvent because the reaction seemed to proceed well in this solvent and all the starting materials and product were readily dissolved. After the reaction was completed, DMSO and the mercury salt were easily removed by washing the reaction mixture with aqueous sodium thiosulfate solution while the organic product was extracted into methylene chloride. The mixture was then analyzed by GC, GCMS and ^{1}H NMR. Recently, the role of added iodide ion in the photostimulated reaction of alkylmercury halide with bromotrichloromethane has been investigated by Herron [93]. They have made the observation that the addition of iodide ion to the reaction mixture of alkylmercury halide and bromotrichloromethane significantly increased the efficiency of photostimulated free radical reaction. The isopropylmercury halide produces the isopropylmercurate in the presence of halide ions. In the free radical chain reaction with bromotrichloromethane, the ate complex is consumed at a rate faster than it can be regenerated by the equilibrium between isopropylmercury halide and halide ion (Eq. 45).

$$(CH_3)_2HCHgX \quad + \quad Y^- \rightleftharpoons [(CH_3)_2HCHgXY]^- \qquad (45)$$

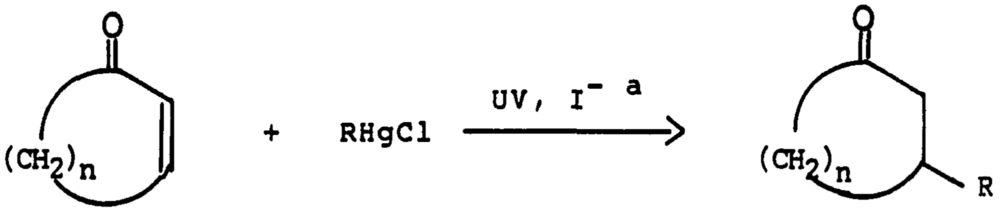
Futhermore, as the concentration of the halide ion is increased, the initial reaction rate is also increased. Initial kinetic chain lengths have been calculated to be at least 38000. The isopropylmercurate solutions react with bromotrichloromethane to produce excellent yields of isopropyl halide and small amounts of chloroform. The trichloromethyl radical is reduced by the isopropylmercurate to produce the trichloromethyl anion and the tricovalent mercury species, $(CH_3)_2HCHgXY^\cdot$, which readily decomposes to give the isopropyl radical and mercuric halide as shown in Eqs. 46 and 47.

$$Cl_3C^\cdot + [(CH_3)_2HCHgXY]^- \longrightarrow Cl_3C^- + [(CH_3)_2HCHgXY]^\cdot \qquad (46)$$

$$[(CH_3)_2HCHgXY]^\cdot \longrightarrow (CH_3)_2HC^\cdot \quad + \quad HgXY \qquad (47)$$

Like the photostimulated reaction of alkylmercury halide and bromotrichloromethane with halide ion, the "1,4-addition "

Table 30. Photostimulated reaction of 2-cycloalkenone with alkylmercury chloride in the presence of iodide ion



n	R	Conditions[b]	% Yields[c]
2	t-Bu	2, 4 h	89 (72)
2	n-Bu	2, 12 h	(45)
3	t-Bu	0, 12 h	37
3	t-Bu	2, 4 h	85 (73)
3	t-Bu	1, 10 h	65
3	t-Bu	0, 12 h, Dark	3
3	t-Bu	3, 4 h	89
3	n-Bu	2, 12 h	36 (25)
3	i-Pr	2, 5 h	75
4	t-Bu	2, 5 h	(69)

[a] [2-cycloalkenone]$_0$=0.10 M and [RHgCl]$_0$=0.22 M. Reaction mixure in 10 mL of dry DMSO was irradiated with a 275 W sunlamp placed 15 cm from the Pyrex tube.

[b] Number of equivalent of sodium iodide based upon the concentration of RHgCl and reaction period.

[c] Yields in parenthesis were determined by isolation.

of alkylmercury halide to 2-cycloalkenones in the presence of iodide ion seems to proceed by a radical chain process in which the alkylmercurate, $[RHgClI]^-$ or $[RHgI_2]^-$ is involved. The photostimulated reaction of 2-cyclohexenone with tert-butylmercury chloride in the absence of iodide ion gave only 37% of the addition product as measured by GC analysis. This result can be interpreted to mean that the tert-butyl radical generated by the photolysis of tert-butylmercury halide adds to the β-position of 2-cyclohexenone to form an adduct radical similar to the addition of alkyl radicals to the β-position of substituted vinyl compounds as shown in Eq. 44. However, the resulting radical generated by the addition of an alkyl radical to 2-cyclohexenone, does not react readily with RHgX.

The 2-alkylcyclohexanones were not observed in the GC analysis of the reaction product from 2-cyclohexenone and alkylmercury chlorides in the presence of excess iodide ion. Attack of the alkyl radical occurred at the 3-position to form the enolyl radical. This result can be interpreted as an electronic or steric effect. Giese and co-workers have proposed that steric effects have a considerable influence on the reactivity of selectivity of addition of alkyl radicals to alkenes [94]. The nucleophilic alkyl radical does not attack the alkene at the center of the double bond, but approachs the π-system from the side. An approach of the alkyl radical from the side is hampered by substituents which are located at the vinylic carbon atom being attacked. The steric α-effect of 2-cycloalkenone may hinder the formation of the radical leading to the 2-alkylcyclohexanone. The 1,2-addition product of alkyl radicals to 2-cycloalkenones, that is addition at the carbonyl carbon, was not observed. In general, radicals do not added to carbonyl groups and addition would not form a resonance stabilized enolyl radical.

The low yield of 1,4-addition product of 2-cycloalkenone with n-butyl radical may be due to the low nucleophilicity of n-butyl radical. n-Butyl radical is less nucleophilic than tert-butyl radical. In general, 1^{o}-RHgX give lower yields than 3^{o}-RHgX in many radical reactions, since the chain propagation step with 1^{o}-RHgX is not as good as with 3^{o}-RHgX.

2. Photostimulated reaction of alkylmercury halides with 5-methyl-2-cyclohexenone

tert-Butylmercury chloride and sodium iodide were dissolved in DMSO followed by the addition of 5-methyl-2-cyclohexenone. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm. After work-up, GC analysis indicated that the crude isolate consisted of cis and trans 3-tert-butyl-5-methylcyclohexanone.

Isopropylmercury chloride and n-butylmercury chloride were also employed and found to give the cis and trans 1,4-

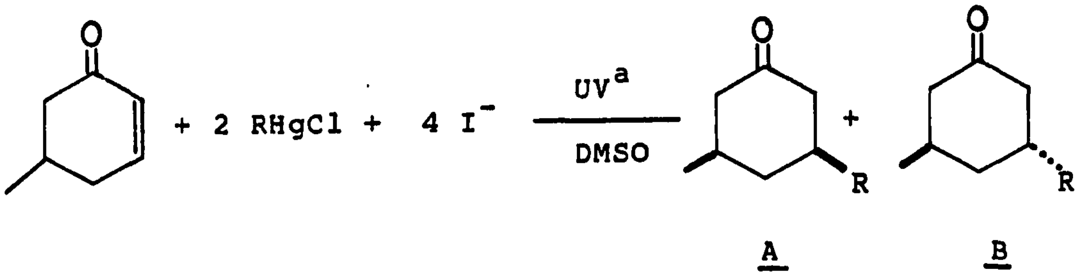
addition products. The results are listed in Table 31.

Although the stereochemical course of the photostimulated reaction of alkylmercury halides with a variety of substituted alkenes and alkynes have been studied in detail, no sterochemical study dealing with 5-methyl-2-cyclohexenone and alkyl radicals has been reported. Fortunately, important trends were observed. 5-Methyl-2-cyclohexenone exhibits trans selectivity with alkylmercury halide, ranging from 81:19 in the addition of *n*-butyl radical to 55:45 in the addition of *tert*-butyl radical. This high trans selectivity of *n*-butyl radical is analogous to the trans selectivity which is observed in the addition of curprates to 5-alkyl-2-cyclohexenones [95]. The observed results of stereochemistry suggest that the conformation of 5-methyl-2-cyclohexenone and the size of incoming radicals are of importance.

3. Photostimulated reaction of tert-butylmercury chloride with 5,6-dihydro-2H-pyran-2-one

tert-Butylmercury chloride and sodium iodide were dissolved in DMSO followed by the addition of then 5,6-dihydro-2H-pyran-2-one. The reaction mixture was irradiated in a Rayonet photoreactor at 350 nm. After work-up, the conjugate addition product, 4-*tert*-butyl-3,4,5,6-tetrahydro-2H-pyran-2-one, was formed in 81% yield as shown in Reaction 48.

Table 31. Photostimulated reaction of 5-methyl-2-cyclohexenone with alkylmercury halides in the presence of iodide ion.

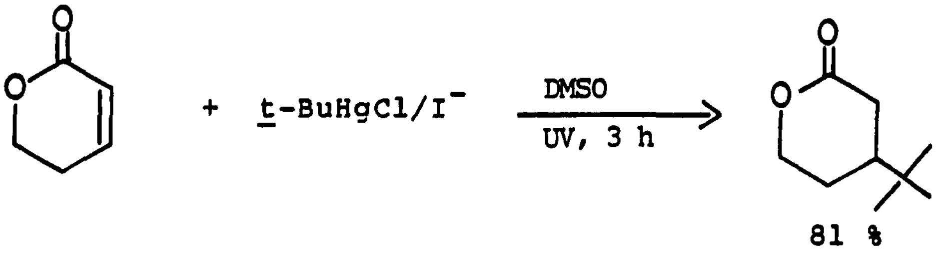


R	Conditions	Product Ratio[b] =A : B	Overall yields[c]
t-Bu	5 h	45 : 55	91 (76)
i-Pr	12 h	26 : 74	85 (71)
n-Bu	12 h	19 : 81	(31)

[a] [5-methyl-2-cyclohexenone]$_o$=0.1 M and [RHgCl]$_o$=0.22 M and [NaI]$_o$=0.44 M. Reaction mixture in 10 mL of dry DMSO was irradiated in a Rayonet photoreactor at 35 °C.

[b] Product ratio was determined by ^{1}H NMR and GC analysis.

[c] Overall yields were measured by GC with internal standard. Yield in parenthesis was determined by isolation.



(48)

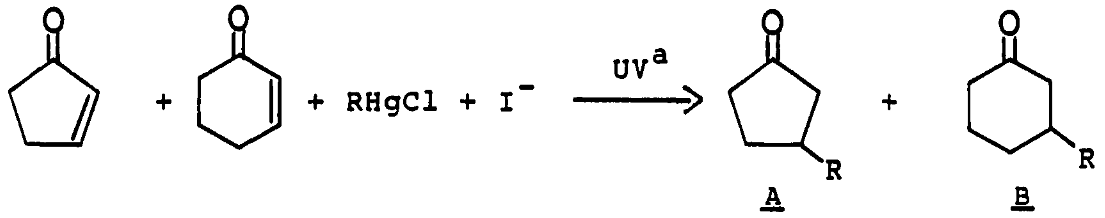
4. The relative reactivity of 2-cyclohexenone and 2-cyclopentenone towards alkylmercury halides

The relative reactivities of 2-cyclopentenone and 2-cyclohexenone towards alkyl radical was measured as shown in Table 32. A five-fold or two-fold excess of each cycloalkenone was employed. The observed product ratios indicate that alkyl radicals preferentially add to 2-cyclopentenone. The slightly increased product ratio from *n*-butylmercury halide to *tert*-butylmercury halide can be attributed to the fact that reactivity decreases and selectivity increases from 1°— to 2°— to 3°— alkyl radicals.

5. The relative reactivity of 2-cyclohexenone and 2-cycloheptenone towards alkylmercury halides

Five-fold or two-fold excesses of equal amounts of 2-cyclohexenone and 2-cycloheptenone were added to the DMSO solution of the alkylmercury chloride and sodium iodide. After irradiation in the Rayonet photoreactor, the reaction mixture was worked up. The product ratios were measured by GC

Table 32. Relative reactivities of 2-cyclohexenone and 2-cyclopentenone with alkylmercury halides.



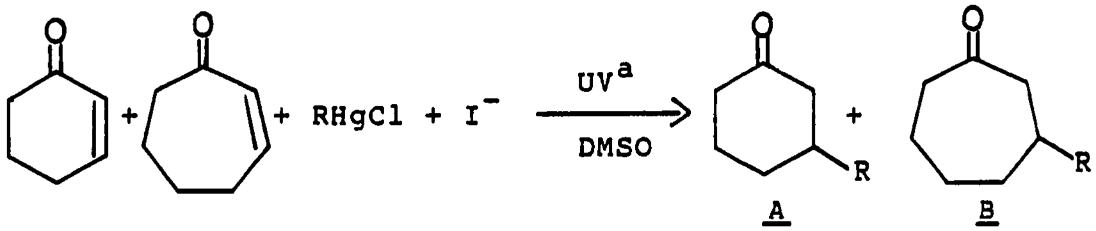
R	Conditions[b]	Products ratio (= A/B)	Overall yields[c]
t-Bu	1:1:0.2:0.4, 4 h	3.30	79
t-Bu	1:1:0.5:1.0, 5 h	3.32	81
i-Pr	1:1:0.2:0.4, 10 h	2.90	72
i-Pr	1:1:0.5:1.0, 10 h	2.90	75
n-Bu	1:1:0.5:1.0, 12 h	2.30	34

[a] [2-cyclohexenone]=[2-cyclopentenone]=0.10 M. Reaction mixture in 10 mL of dry DMSO was irradiated in a Rayonet photoreactor at 35 °C.

[b] Ratio of 2-cyclopentenone:2-cyclohexenone:RHgCl:I$^-$ and reaction period.

[c] GC yields were measured by adding internal standard and were based upon the concentration of alkylmercury chloride.

Table 33. Relative reactivities of 2-cyclohexenone and 2-cycloheptenone with alkylmercury halides.



R	Conditions[b]	Product Ratio =A/B	Overall yields[c]
t-Bu	1:1:0.2:0.4, 4 h	2.50	92
t-Bu	1:1:0.5:1.0, 4 h	2.47	91
n-Bu	1:1:0.2:0.4 12 h	1.05	36
n-Bu	1:1:0.5:1.0 12 h	1.12	34

[a] [2-cyclohexenone]=[2-cycloheptenone]=0.10 M. Reaction mixture in 10 mL of dry DMSO was irradiated in Rayonet photoreactor at 35 °C.

[b] Ratio of 2-cyclohexenone:2-cycloheptenone:RHgCl:I⁻, reaction period.

[c] GC yields were measured by adding internal standard and were based upon the concentration of alkylmercury chloride.

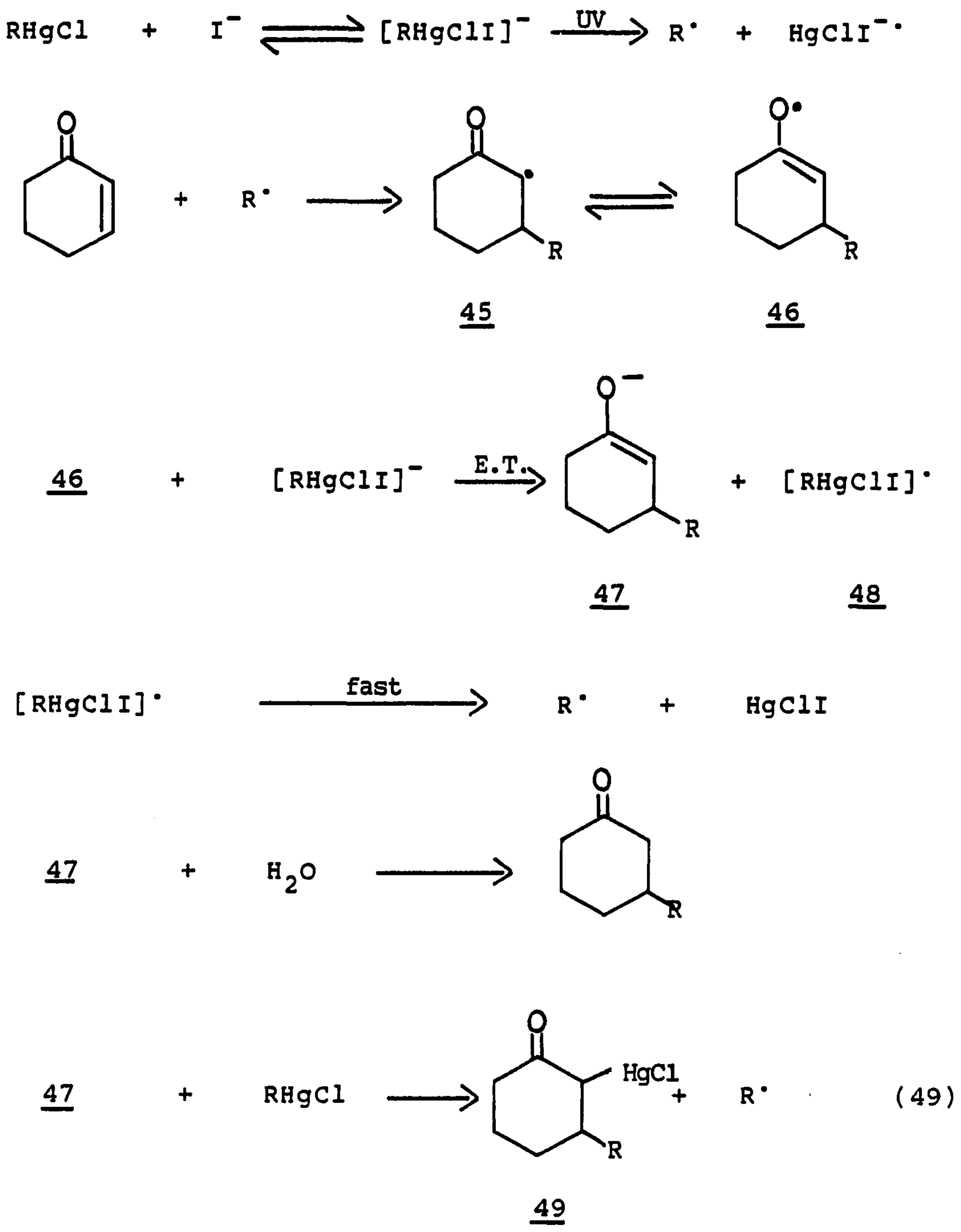
analysis and listed in Table 33. tert-Butyl radical preferentially add to 2-cyclohexenone. However, n-butyl radical has almost same relative reactivity towards 2-cyclohexenone and 2-cycloheptenone. These results indicate that the relative reactivities towards tert-butyl radicals follow the sequence 2-cyclopentenone > 2-cyclohexenone > 2-cycloheptenone. While the relative reactivities toward n-butyl radical have the order of 2-cyclopentenone > 2-cyclohexenone $\cong$ 2-cycloheptenone

6. Mechanistic considerations

Like the photostimulated reaction of alkylmercury chloride with alkenes and alkynes, the 1,4-addition of alkylmercury chloride to 2-cycloalkenone in the presence of excess iodide ion proceeds via a free radical chain process as shown in Scheme 26.

The radical intermediate 46 is an electron-acceptor radical which easily undergoes the electron-transfer process with the organomercurate to give the enolate anion 47 and the unstable radical 48. The unstable radical 48 can readily decompose to generate the alkyl radical (R$^\bullet$) and mercuric salt. An alternative mechanism of the step as shown in Equation 49 can be excluded because no intermediate 49 was detected.

Scheme 26


RHgCl + I⁻ ⇌ [RHgClI]⁻ —UV→ R· + HgClI⁻·
+ R·
R
45
46
46 + [RHgClI]⁻ —E.T.→
+ [RHgClI]·
47
48
[RHgClI]· —fast→ R· + HgClI
47 + H₂O
47 + RHgCl
HgCl
+ R·
(49)
49

Unlike the enolate anion generated from 2-cyclohexenone with organocuprates in THF, the enolate anion **47** generated from 2-cyclohexenone with alkylmercury halide in the presence of excess iodide ion could not be trapped by electrophiles. The choice of solvents and counterions of enolates used in the conjugated addition reaction are known to influence the outcome of alkylation reaction [96]. Possibly the reaction conditions involving DMSO solvent and mercuric salts are not suitable for the trapping of enolate anions by alkyl halides.

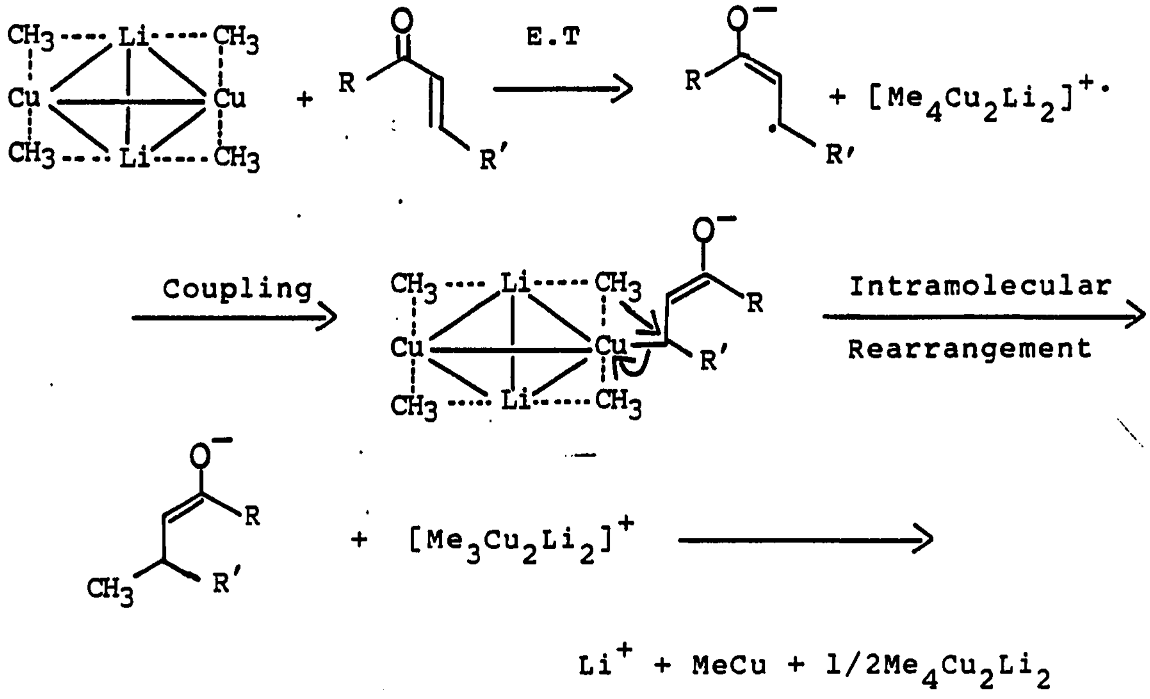
7. The relative reactivity of 2-cyclohexenone and 2-cyclopentenone towards dialkylcuprates

Evidence concerning the possibility of a mechanism involving *tert*-butyl radicals in di-*tert*-butylcuprate reaction has been found in the substitution and addition reactions of alkynes and alkenes with di-*tert*-butylcuprate in our research group. The substitution and addition product ratio in the reaction of 1-alkenyl phenyl sulfones with di-*tert*-butylcuprate has the same value as with the *tert*-butyl radical generated from *tert*-butylmercury chloride. The relative reactivities of $PhCH{\equiv}CHSO_2Ph$, $PhCH{\equiv}CHSPh$, $PhC{=}CSO_2Ph$ and $PhC{=}CSPh$ in *tert*-butylation reaction are similar for *tert*-butylmercury chloride upon photolysis and di-*tert*-butylcuprate without photolysis.

In an attempt to prove the existence of *tert*-butyl radical in di-tert-butylcuprate reaction, the relative reactivities of 2-cyclopentenone of 2-cyclohexenone towards dialkylcuprates and trialkylzincates were studied. An excess of equal amounts of 2-cyclohexenone and 2-cyclopentenone were added to a solution of di-tert-butylcuprate generated from tert-butyllithium and copper(I) iodide at 78 °C in ether. The product ratio was measured by GC analysis after work-up. Di-sec-butylcuprate and di-n-butylcuprate were also employed. Table 34 gives the relative reactivities of a series of dialkylcuprate in ether.

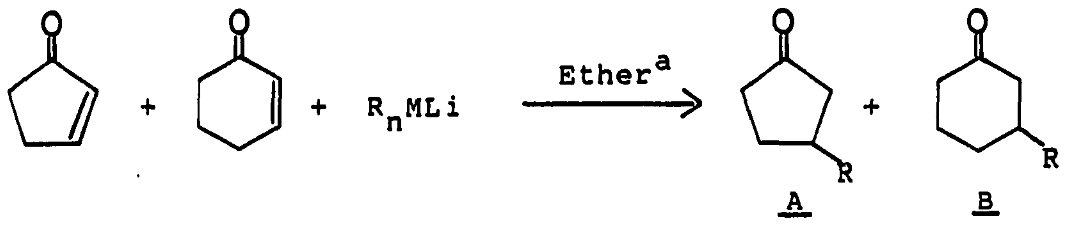
The relative reactivities of 2-cyclohexenone and 2-cyclopentenone were reversed from di-tert-butylcuprate to di-n-butylcuprate. The value of 3.60 with di-tert-butylcuprate at -78 °C is very similar to the value of 3.30 with tert-butylmercury chloride at 35 °C in DMSO. However, the values of 0.18 and 0.33 with di-n-butylcuprate and di-sec-butylcuprate, respectively, are reversed from the values of 2.30 and 2.90 with n-butylmercury chloride and isopropylmercury chloride. Like the tert-butyl radical generated from tert-butylmercury chloride, di-tert-butylcuprate favors 2-cyclopentenone in a competitive reaction. However, di-n-butylcuprate and di-sec-butylcuprate prefer 2-cyclohexenone to 2-cyclopentenone. House and Wilkins have suggested that the 1,4-addition of dimethylcuprate to 2-cyclohexenone involves an electron transfer and subsequent coupling as shown in Scheme 27 [97, 98]. Free alkyl radicals are excluded as intermediates by the observation that isoprene

Scheme 27



does not interfere with the 1,4-addition of dimethylcuprate and diethylcuprate [91]. The stereochemistry of 1,4-addition of divinylcuprates to 2-cyclohexenone has been studied by Casey and Boggs [92]. The cis-and trans-1-propenyl groups are transferred with retention of configuration. This stereospecifity provides further evidence against the intermediacy of free radicals in the conjugate additions. The conjugate addition of dialkylcuprates derived from endo-2-

Table 34. Relative reactivities of 2-cyclohexenone and 2-cyclopentenone with ate complex



R$_n$MLi	Conditions^b	Products ratio =A/B	Overall yields^c
(*n*-Bu)$_2$CuLi	1:1:0.2, 2 h, -78	0.18	78
(*n*-Bu)$_2$CuLi	1:1:0.5, 2 h, -78	0.19	73
(*n*-Bu)$_2$CuLi	1:1:0.5, 2 h, 0	0.20	62
(*s*-Bu)$_2$CuLi	1:1:0.2, 2 h, -78	0.33	51
(*t*-Bu)$_2$CuLi	1:1:0.2, 2 h, -78	3.60	91
(*t*-Bu)$_2$CuLi	1:1:0.2, 2 h, -30	4.20	79
(*t*-Bu)$_2$CuLi	1:1:0.1, 2 h, -78	4.30	58
(*n*-Bu)$_3$ZnLi	1:1:0.5, 3 h, -78	0.45	88
(*t*-Bu)$_3$ZnLi	1:1:0.5, 2 h, -78	3.50	62

[a] [2-cyclohexenone]$_0$=0.1 M, [2-cyclopentenone]$_0$=0.10 M. Reaction was carried out in 10 mL of ether at the temperature indicated.

[b] Ratio of 2-cyclopentenone:2-cyclohexenone:ate complex, reaction period and reaction temperature.

[c] GC yields based upon the concentration of ate complex.

norbornylcopper(I) occurred with complete retention at carbon-2 position of the norbornyl moiety, an observation which excludes a mechanism involving the free 2-norbornyl radical [99].

The reversed relative reactivities of dialkylcuprate with primary and secondary alkyl groups compared with the alkyl radicals generated from alkylmercury halides indicates that free alkyl radicals were not involved in these conjugate additions.

However, Table 34 presents strong evidence for the existence of *tert*-butyl radicals in the conjugate addition of di-*tert*-butylcuprate and 2-cycloalkenones. The lack of a constant trend between *n*-butyl, *sec*-butyl and *tert*-butylcuprates suggest a change in mechanism for the *tert*-butylation process.

8. The relative reactivity of 2-cyclohexenone and 2-cyclopentenone towards triorganozincates

Lithium triorganozincates (R_3ZnLi) are known to participate in the 1,4-addition of alkyl groups to the unsaturated carbonyl compounds [100-102]. The reagent can readily be prepared in THF by mixing a saturated THF solution of zinc chloride (or zinc chloride-TMEDA complex) and alkyllithium in a 1:3 ratio.

The relative reactivities of 2-cyclohexenone and 2-

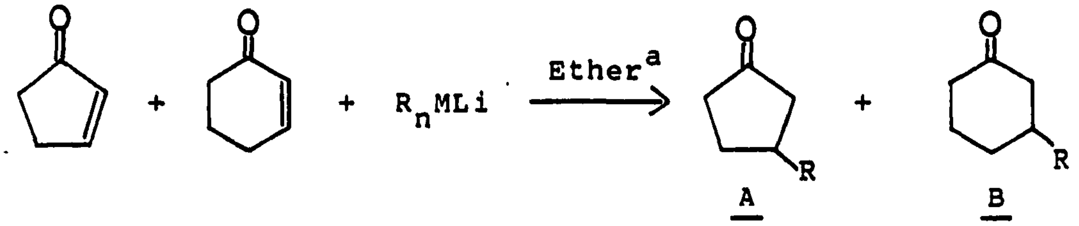
cyclopentenone towards triorganozincates were measured in a manner similar to that employed with the cuprates. The results in Table 34 demonstrate that tri-*tert*-butylzincate and tri-*n*-butylzincate shows different relative reactivities. The lower relative reactivity of tri-*n*-butylzincate as compared with *n*-butylmercury chloride seems to indicate that the free alkyl radical is not involved in the case of the zincate. However, the values of 3.5 for tri-*tert*-butylzincate and 3.6 for di-*tert*-butylcuprate at -78 °C appear consistent with those obtained from *tert*-butyl radical formed from *tert*-butylmercury chloride at 35 °C.

9. The relative reactivity of 2-cyclohexenone and 2-cyclopentenone towards higher order organocuprate and organocopper phosphine complex

The higher order organocuprates $R_2CuCNLi_2$ are known to be highly reactive towards conjugated ketones transferring the R group very efficiently in a Michael type process [103]. The conjugate addition of (t-Bu)$_2$CuCNLi$_2$ to 2-cycloalkenones gave 3-*tert*-butyl-2-cycloalkanones in higher yield than (t-Bu)$_2$CuLi [103]. Furthermore, (t-Bu)$_2$CuCNLi$_2$ is relatively stable at 0 °C and stable more than 2 hours at -78 °C.

Table 35 lists the examples studied which suggest that the organocuprates, $R_2CuCNLi_2$, give higher yields of 1,4-addition products than simple organocuprates, R_2CuLi. No 1,2-

Table 35. Relative reactivities of 2-cyclohexenone and 2-cyclopentenone with organocopper reagents



R_nMLi	Conditions	Products ratio =A/B	Overall yields[b]
$(n\text{-Bu})_2CuCNLi_2$	2 h, -78	0.25	85
$(n\text{-Bu})_2CuCNLi_2$	2 h, -30	0.27	83
$(t\text{-Bu})_2CuCNLi_2$	1 h, -78	0.30	96
$(t\text{-Bu})_2CuCNLi_2$	1 h, -30	0.14	79
$(n\text{-Bu})_2CuLi\cdot PBu_3$	2 h, -78	0.25	85
$(t\text{-Bu})_2CuLi\cdot PBu_3$	1 h, -78	0.27	85
$(t\text{-Bu})_2CuLi\cdot PBu_3$	1 h, -30	0.18	92

[a] $[\text{2-cyclohexenone}]_o=[\text{2-cyclopentenone}]_o=0.10$ M, $[R_nMLi]_o=0.05$ M. Reaction was carried out in 10 mL of ether at the temperature indicated.

[b] GC yields based upon the concentration of organocuprate.

addition product was observed by GC analysis. The primary butyl group of $R_2CuCNLi_2$ was delivered to 2-cyclohexenone with a 4:1 preference over 2-cyclopentenone at -30 or -78 °C. Interestingly, $R_2CuCNLi_2$ transferred the tert-butyl and n-butyl groups to 2-cycloalkenones with a similar selectivity. This unexpected finding concerning about the reversal in relative reactivities of $(t\text{-Bu})_2CuCNLi_2$ and $(t\text{-Bu})_2CuLi$ is consistent with the possibility that only $(t\text{-Bu})_2CuLi$ reacts by a mechanism involving the tert-butyl radical.

The organocopper phosphine complex, $R_2CuLi \cdot PBu_3$, as been prepared and its reactivity studied with organic halides [88]. This complex is also known to participate in 1,4-addition to conjugated carbonyl compounds. This organocopper phosphine complex prepared by adding 2 equivalents of alkyllithium to 1 equivalent of tetrakisiodo(tri-n-butylphosphine)copper(I) at -78 °C is stable indefinitely at -78 °C.

The data of Table 35 summarize observations concerning the relative reactivities of 2-cycloalkenones towards the organocopper phosphine complexes. The value of relative reactivities obtained using $(n\text{-Bu})_2CuLi \cdot PBu_3$ and $(t\text{-Bu})_2CuLi \cdot PBu_3$ were similar and not significantly different from the relative reactivities observed with the cyano cuprates.

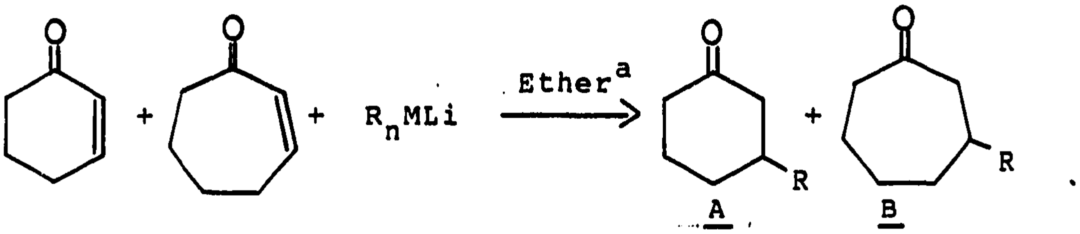
Comparison of entries 1, 2 and 5 of Table 35 and 1-4 and 8 of Table 34 establishes that the reaction of 2-

cycloalkenones and ate complex with primary and secondary alkyl groups appear to proceed by House s mechanism in which no free alkyl radical is involved. The 1,4-addition of ($\underline{t}$-Bu)$_2$CuCNLi$_2$ and ($\underline{t}$-Bu)$_2$CuLi•PBu$_3$ to 2-cyclopentenone and 2-cyclohexenone gives roughly the same relative reactivity as the ate complexes with primary and secondary R groups with 2-cyclopentenone being 0.18-0.30 as reactive as 2-cyclohexenone at -78 °C. However, with ($\underline{t}$-Bu)$_2$CuLi or ($\underline{t}$-Bu)$_3$ZnLi 2-cyclopentenone was 3.3 times as reactive as 2-cyclohexenone, which is a characteristic ratio of tert-butyl radical attack.

10. The relative reactivity of 2-cyclohexenone and 2-cycloheptenone towards organocuprates

A slight preference for attack on 2-cyclohexenone was observed in the competitive reaction of 2-cyclohexenone and 2-cycloheptenone with tert-butylmercury chloride (Table 33). With $\underline{n}$-butylmercury chloride 2-cyclohexenone and 2-cycloheptenone had approximately the same reactivity in conjugate radical addition. Table 36 lists the relative reactivities of 2-cyclohexenone and 2-cycloheptenone observed with organocuprates. The product ratios with ($\underline{n}$-Bu)$_2$CuLi and ($\underline{n}$-Bu)$_2$CuCNLi$_2$ were very similar to that observed with $\underline{n}$-butylmercury chloride. The product ratios of about 2.50 with ($\underline{t}$-Bu)$_2$CuLi and ($\underline{t}$-Bu)$_2$CuCNLi$_2$ in the competitive reactions of 2-cyclohexenone and 2-cycloheptenone were also very similar

Table 36. Relative reactivities of 2-cyclohexenone and 2-cycloheptenone with organocuprates



R_nMLi	Conditions	Product ratio A/B	Overall yields[b]
($\underline{t}$-Bu)$_2$CuLi	1 h, -78	2.45	69
($\underline{t}$-Bu)$_2$CuCNLi$_2$	2 h, -78	2.60	72
($\underline{t}$-Bu)$_2$CuCNLi$_2$	2 h, -30	2.58	83
($\underline{n}$-Bu)$_2$CuLi	2 h, -78	1.20	85
($\underline{n}$-Bu)$_2$CuLi	3 h, -30	1.16	91
($\underline{n}$-Bu)$_2$CuCNLi$_2$	3 h, -30	1.21	91

[a] $[2\text{-cycloalkenone}]_o$=0.10 M, $[R_nMLi]_o$=0.05 M, Reactions were carried out in 10 mL of ether solution at the temperature indicated.

[b] GC yields were measured and based upon the concentration of ate complex.

to these observed with tert-butylmercury chloride. This observation seems to be inconsistent with the relative reactivities of previous section. However, possibly the relative reactivities of 2-cyclohexenone and 2-cycloheptenone are not sensitive to the mechanism of the alkylation process.

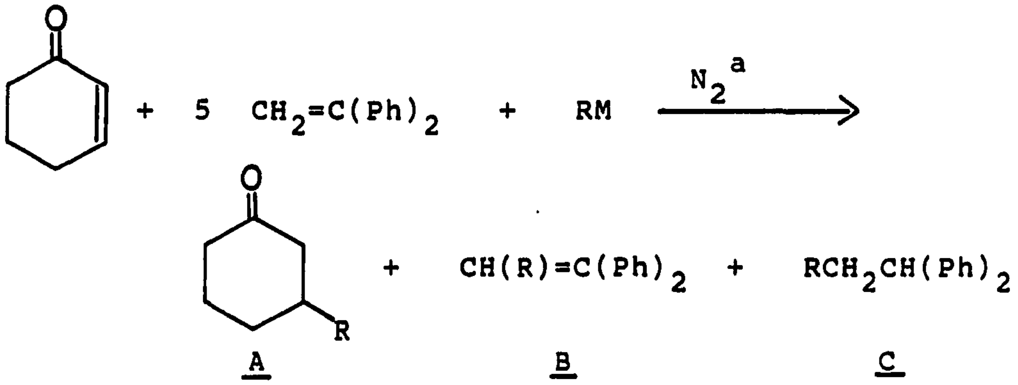
11. The trapping of alkyl radicals with 1,1-diphenylethylene

The work presented in this section was designed to detect free alkyl radicals that might be present as intermediates in 1,4-addition reactions. Alkyl radicals are known to be very reactive toward 1,1-diarylethylene [104].

In an effort to trap free alkyl radicals in organocuprate reactions, an excess of 1,1-diphenylethylene was employed in the 1,4-addition of 2-cyclohexenone. The photostimulated reaction of 2-cyclohexenone with tert-butylmercury chloride and sodium iodide in the presence of 5 equivalents of 1,1-diphenyethylene leads to trapping of the tert-butyl radical as expected. In contrast to the failure to trap a free radical in dimethylcuprate reaction with excess isoprene, the free tert-butyl radical derived from the reaction of 2-cyclohexenone and di-tert-butylcuprate was trapped by 1,1-diphenylethylene and the yield of 1,4-addition product was significantly decreased. And the products, $\underline{t}$-BuCH=C(Ph)$_2$ and $\underline{t}$-BuCH$_2$-CH(Ph)$_2$, were formed in a 1.3:1 ratio from the disproportionation of $\underline{t}$-BuCH$_2$-$\overset{\bullet}{C}$(Ph)$_2$ (Table 37). The reaction of 2-cyclohexenone with di-n-butylcuprate was not affected by the presence of 5 equivalents of 1,1-diphenyethylene, and the yield of 1,4 addition product was not reduced even with 10 equivalents of 1,1-diphenylethylene. This confirms the prediction that the 1,4 addition of organocuprate with primary and secondary alkyl groups does not take place through a free radical process.

The failure of trapping of free radicals and the high yields of 1,4 addition product with $(\underline{t}\text{-Bu})_2CuCNLi_2$ and $(\underline{t}\text{-Bu})_2CuLi{\cdot}PBu_3$ indicate that the conjugate addition with these ate complexes does not involve free alkyl radicals as intermediates. The different characteristic of $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_2CuCNLi_2$ or $(\underline{t}\text{-Bu})_2CuLi{\cdot}PBu_3$ suggests that the same mechanistic conclusions can not be applied to these reactions. No mechanistically significant interpretation concerning the 1,4-addition of $(\underline{t}\text{-Bu})_2CuCNLi_2$ and $(\underline{t}\text{-Bu})_2CuLi{\cdot}PBu_3$ to 2-cycloalkenone can be drawn at present. However, the 1,4-addition of $(\underline{t}\text{-Bu})_2CuLi$ to 2-cycloalkenone may proceed via a free radical process as shown in Scheme 28. As shown in Scheme 28, the tert-butyl radical derived from the unstable $(\underline{t}\text{-Bu})_2CuLi$ attacks the β-carbon of the unsaturated carbonyl compounds to generate the radical intermediates 45 which can readily be reduced by $(\underline{t}\text{-Bu})_2CuLi$. The difference between $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_2CuCNLi_2$ or $(\underline{t}\text{-Bu})_2CuLi{\cdot}PBu_3$ could be due to a different rate of the initiation process or

Table 37. Reaction of 2-cyclohexenone with alkylmercury chloride and ate complexes in the presence of excess of 1,1-diphenylethylene



RM	Condition[b]	% Yields[c]	
		A	B+C
t-BuHgCl/I$^-$	3 h, UV, DMSO	21	38 (1.2:1)
(t-Bu)$_2$CuLi	2 h, -78	42	36 (1.3:1)
(n-Bu)$_2$CuLi	2 h, -78	95	0
(n-Bu)$_2$CuLi[d]	2 h, -30	95	0
(t-Bu)$_2$CuCNLi$_2$,	2 h, -78	83	trace
(t-Bu)$_2$CuLi·PBu$_3$	1 h, -30	85	0

[a] 5 Equivalents of 1,1-diphenylethylene were employed.

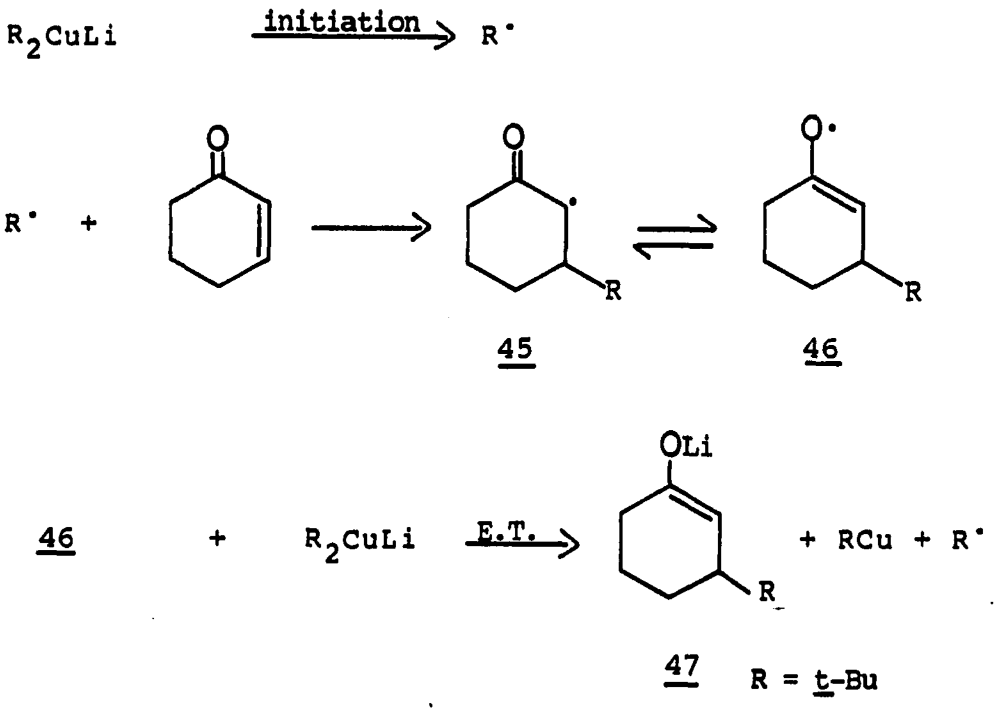
[b] Reactions were carried out in ether solution unless otherwise indicated.

[c] GC yields were measured. The ratios in parenthesis were % yield ratio of product B and C.

[d] 10 Equvialents of 1,1-diphenylethylene were employed.

to a different rate in the electron transfer step.

Sheme 28

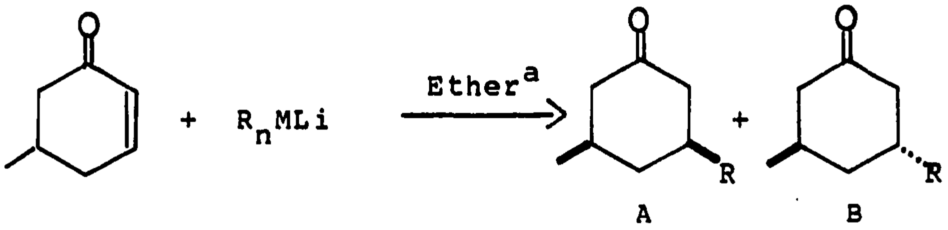


12. Reaction of 5-methyl-2-cyclohexenone with organocuprates

The stereochemical aspects of addition reactions with *tert*-butyl ate complexes was investigated with the 5-methyl-2-cyclohexenone. As expected from the earlier work with Me_2CuLi, the trans isomer is the predominant product with $BuCu \cdot BF_3$ [105]. The increase in the cis/trans ratio observed with *n*-butylmercury chloride (Table 31) indicates that *n*-butyl radical addition is somewhat less stereoselective than *n*-butyl group transfer from *n*-butyl or *sec*-butylcuprates.

The stereochemistry of 1,4-addition with $(\underline{s}\text{-}Bu)_2CuLi$ or $(\underline{n}\text{-}Bu)_2CuLi$ to 5-methyl-2-cyclohexenone is listed in Table 38.

Table 38. Reaction of 5-methyl-2-cyclohexenone with organocuprates



R_nMLi	Conditions	Product ratio A:B	Overall yields[b]
$(\underline{t}\text{-Bu})_2\text{CuLi}$	1 h, -78	41:59	65
$(\underline{t}\text{-Bu})_3\text{ZnLi}$	1 h, -78	46:54	61
$(\underline{t}\text{-Bu})_2\text{CuCNLi}_2$	1 h, -78	9:91	71
$(\underline{s}\text{-Bu})_2\text{CuLi}$	2 h, -78	9:91	62
$(\underline{n}\text{-Bu})_2\text{CuLi}$	3 h, -30	9:91	81
$(\underline{n}\text{-Bu})_2\text{Cu}\cdot\text{BF}_3$[c]	1 h, -78	9:91	72[d]

[a] All reactions were carried out on a 1 mmol scale.

[b] Isolated yields.

[c] The result is cited from reference [105].

[d] GC yield.

The cis/trans product ratios were 9/91. Comparison of entries 2 and 3 of Table 31 establishes that the stereoselectivity of free alkyl radical addition depends upon the size of alkyl radical. On the contrary, the stereoselectivity of organocuprates with primary and secondary alkyl group is independent of the size of alkyl group.

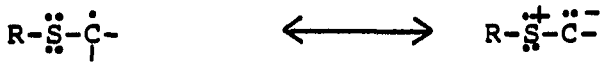
It was observed that the amount of cis-product is significantly increased with ($\underline{t}$-Bu)$_2$CuLi and ($\underline{t}$-Bu)$_3$ZnLi. The observed cis/trans product ratios are very similar to these observed with tert-butylmercury chloride. This is consistent with a mechanism involving tert-butyl radical addition in the reaction of ($\underline{t}$-Bu)$_2$CuLi and ($\underline{t}$-Bu)$_3$ZnLi with 2-cycloalkenone. On the other hand, ($\underline{t}$-Bu)$_2$CuCNLi$_2$ gave a vastly different cis/trans product ratio.

13. The relative reactivity of 2-cyclohexenone and 2-cyclopentenone with organocuprates generated from methylthiomethyllithium

In an attempt to find another example of a free alkyl radical process in the conjugate addition of an organocuprate to a 2-cycloalkenone, a new organocuprate generated from methylthiomethyllithium and copper(I) iodide was studied. The reaction involving free alkyl radical addition may be facilitated by the presence of sulfide group due to the conjugation of the unshared electron pairs as shown in

Eq. 50. Russell and co-workers found that the hydrogen atom abstraction from a methyl group by the phenyl radical is facilitated by the presence of α-sulfur atom and explained this result in terms of the stabilization of the incipient radical by electron-releasing conjugative effect of α-sulfur atom as shown in Equation 51 [106].

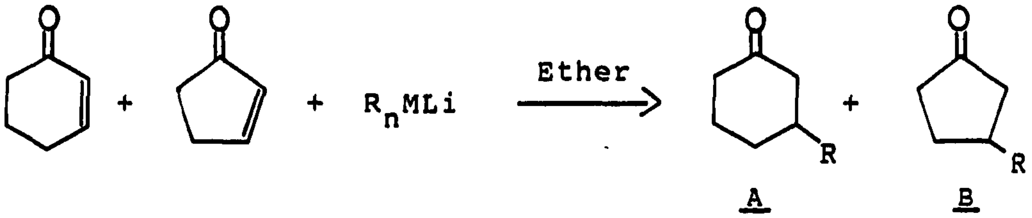
$$CH_3-\overset{\cdot\cdot}{\underset{\cdot\cdot}{S}}-\dot{C}H_2 \longleftrightarrow CH_3-\overset{\cdot}{\underset{\cdot\cdot}{S}}=CH_2 \qquad (50)$$



$$R-\overset{\cdot\cdot}{\underset{\cdot\cdot}{S}}-\overset{\cdot}{\underset{|}{C}}- \longleftrightarrow R-\overset{\cdot+}{\underset{\cdot\cdot}{S}}-\overset{\cdot\cdot\,-}{C}- \qquad (51)$$

The unknown ate complex was prepared from methylthiomethyllithium and copper(I) iodide in ether at 0 °C. 2-Cycloalkenone was added to a solution at the same temperature. After one hour, the reaction mixture was worked up to give the results listed in Table 39. The conjugate addition products with 2-cycloalkenones were obtained in high yields. However, the relative reactivity of 2-cyclohexenone and 2-cyclopentenone towards $(CH_3SCH_2)_2CuLi$ of 2.3:1 indicates that this ate complex has a similar reactivity to $(\underline{n}\text{-Bu})_2CuLi$. Furthermore, the organolithium reagent CH_3SCH_2Li also gives a similar relative reactivity of 3.1:1. It is apparent from these results that the carbanions are involved in the conjugate addition of 2-cycloalkenones with $(CH_3SCH_2)_2CuLi$.

Table 39. Reactions of 2-cycloalkenone with oragonocuprate generated from methylthiomethyllthium



R_nMLi	Conditions[a]	Product ratio A/B	Overall yields[b]
$(CH_3SCH_2)_2CuLi$	1:0:1, 2 h	-	(91)
$(CH_3SCH_2)_2CuLi$	1:0:1 2 h, -20	-	61
$(CH_3SCH_2)_2CuLi$	0:1:1 1 h	-	85
$(CH_3SCH_2)_2CuLi$	1:1:0.5 1 h	2.3:1	65
CH_3SCH_2Li	1:1:0.5 1 h	3.1:1	51
$(CH_3SCH_2)_2CuLi$[c]	1:1:0.5 1 h	-	trace

[a] All reactions were carried out on a 1 mmol scale at 0 °C, except where otherwise indicated. Entry 1, 2 and 3 were carried out with either 2-cyclohexenone or 2-cyclopentenone.

[b] GC yields (isolated yield given in parentheses).

[c] 1 Equivalent of *p*-dinitrobenzene was added.

C. Conclusion

The photostimulated reaction of 2-cycloalkenones with alkylmercury halides and iodide ion produced the conjugate addition products in yields comparable to those of the organocuprates. This reaction was significantly facilitated by the presence of excess iodide ion. Possibly, the alkylmercurate ($RHgI_2^-$) promotes the formation of alkyl radicals and reduces the adduct radical to the enolate anion by electron transfer. The mechanism involved in the conjugate addition observed in these reactions is presumably a free radical chain process as shown in Scheme 26. The cis preference of alkyl radical attack in the conjugate addition to 5-methyl-2-cyclohexenone with alkylmercury halide increased with the size of incoming alkyl radical as expected. The alkyl radicals generated from alkylmercury halide always react preferentially with 2-cyclopentenone rather than with 2-cyclohexenone, ratios for the relative reactivities ranged from 2.3-3.3 : 1. This reactivity sequence appears to be unique for radical attack and is possibly diagnostic for a mechanism involving free radical addition.

Although several pieces of evidence have established that the 1,4-addition reaction of 2-cycloalkenones with organocuprates containing primary and secondary alkyl groups does not involve a free radical as an intermediate, the ate complex with tert-butyl groups appears to proceed via a free radical chain process. The preference for reaction with 2-cyclopentenone over 2-cyclohexenone for the conjugate addition with $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_3ZnLi$ is characteristic of a free radical process. In contrast to $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_3ZnLi$, cuprate or zincate complexes with primary and secondary alkyl groups react preferentially with 2-cyclohexenone rather than 2-cyclopentenone. The more stable ate complexes with the tert-butyl group, such as $(\underline{t}\text{-Bu})_2CuCNLi_2$ and $(\underline{t}\text{-Bu})_2CuLi \cdot PBu_3$ also undergo preferential reaction with 2-cyclohexenone.

The significantly reduced yield of the conjugate addition product in the reaction of 2-cyclohexenone with $(\underline{t}\text{-Bu})_2CuLi$ in the presence of an excess of 1,1-diphenylethylene suggests that the tert-butyl radical is trapped and produces the adduct radical of 1,1-diphenylethylene. This observation is consistent with the trapping of free alkyl radicals in the photostimulated conjugate addition reaction of 2-cyclohexenone with alkylmercury halide in the presence of an excess of 1,1-diphenylethylene. The conjugate addition with organocuprates with primary and secondary alkyl groups, $(\underline{t}\text{-Bu})_2CuCNLi_2$ or $(\underline{t}\text{-Bu})_2CuLi \cdot PBu_3$ are not affected by an excess of 1,1-diphenylethylene. Apparently, no free alkyl radical is involved in these reactions.

It is apparent that the conjugate addition of 2-cycloalkenone with $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_3ZnLi$ involves the free *tert*-butyl radical as an intermediate and proceeds via a free radical chain process in which the propagating step is very similar to that for the conjugate reaction with alkylmercury halide in the presence of excess iodide.

D. Experimental Section

1. General consideration

The alkylmercury halides were prepare by the literature procedure [107]. Usually, they were prepared by the reaction of the corresponding Grignard reagents with mercury salts in 1:1 ratio in THF or ether. Thus, a solution containing mercuric chloride (0.2 mol, dried at 80 °C) in dry THF was stirred in an ice bath under nitrogen while a solution of 0.2 mol of *tert*-butylmagnesium chloride prepared from *tert*-butylchloride and magnesium in THF was added dropwise. After addition, the mixture was stirred overnight at room temperature. Ether (75 mL) and water (75 mL) were then slowly added to the mixture at 0 °C. The mixture was separated and aqueous layer was extracted by ether (2x50 mL). The combined ether was dried and the solvent was removed under reduced pressure. The white precipitate was recrystallized from hexane-ethanol (90:10). *tert*-Butylmercury chloride slowly decomposes to give mercury metal under room light at room temperature. Therefore, it was kept in a closed container wrapped with aluminum foil in a refrigerator. The melting points of alkylmercury chlorides are as follows; *n*-butylmercury chloride (Lit. [108] mp 127 °C), isopropylmercury chloride (Lit. [109] mp 94.5-95.5 °C), and *tert*-butylmercury chloride (Lit. [110], 110-113 °C). All the mercurials employed had melting points in agreement with the literature values.

All solvents were purified according to the procedure previously described. All solvents and solutions of organometallic reagents were transferred by using hypodermic syringes or stainless steel cannula under an atmosphere of nitrogen. Solutions of *n*-butyllithium in hexane (2.1 *M*) was obtained from Alfa Inorganics. Solutions of *sec*-butyllithium in cyclohexane (1.3 *M*) and *tert*-butyllithium in pentane (1.7 *M*) were purchased from Aldrich Chemical Co. Solutions of methylthiomethyllithium was prepared by the literature procedure [112]. Thus, to the *n*-butyllithium-TMEDA complex (0.05 mol) prepared by the dropwise addition of TMEDA (5.8 g, 0.05 mol) to *n*-butyllithium in hexane (0.05 mol, 2.1 *M*), was added dimethyl sulfide (3.0 g, 0.05 mol). Subsequent to 0.5 hour of stirring, a white precipitate was observed. The reaction mixture was stirred for ten hours before utilization of the metylthiomethyllithium. Copper(I) iodide was purified according to a previously described procedure [87]; the precipitated salt was washed successively with water, ethanol and pentane and then dried under reduced pressure. The $ZnCl_2$ TMEDA complex [101] was prepared by mixing 19 mL of a saturated $ZnCl_2$-THF solution and 5 mL of TMEDA and allowing the mixture to stand for several hours at room temperature. The crystals which separated were collected and recrystallized from THF.

2. General procedure for the reactions of alkylmercury chloride with 2-cycloalkenones in the presence of iodide ion

Sodium iodide (0.66 g, 4.44 mmol) was placed in a flame-dried Pyrex tube equipped with a rubber septum. The tube was flamed dry under a stream of nitrogen. DMSO (10 mL) was added using a hypodermic syringe. The resulting solution was stirred until the sodium iodide was completely dissolved. Alkylmercury chloride (2.2 mmol) was added to the solution, and immediately the 2-cycloalkenone (1.0 mmol) was added via syringe. The reaction mixture was irradiated with a 275 W sunlamp placed 15 cm from the Pyrex reaction tube. Normally a dark brown solution resulted after one hour of irradiation. For work-up, aqueous sodium thiosulfate solution (20 mL) was added and the mixture stirred for 10 minutes. The aqueous mixture was then extracted by methylene chloride (2x10 mL). The combined methylene chloride extracts were dried over anhydrous magnesium sulfate and concentrated to afford a liquid which was analyzed by GC and GCMS. The pure products were isolated by flash column chromatography and characterized by ^{1}H NMR.

3. **Photostimulated reaction of tert-butylmercury chloride with 2-cycloalkenone in the presence of iodide ion**

The reaction mixture containing *t*-BuHgCl (0.65 g, 2.2 mmol), 2-cyclopentenone (0.082 g, 1.0 mmol) and sodium iodide (0.66 g, 4.4 mmol) was irradiated for 4 hours. After irradiation, the mixture was worked up according to the general procedure. 3-*tert*-Butylcyclopentanone was obtained. And pale-yellow liquid isolated by flash column chromatography with hexane and ethyl acetate as the eluent (9:1).

^{1}H NMR (δ, $CDCl_3$) 0.888 (s, 9H), 1.85-2.05 (m, 3H), 2.07-2.25 (m, 4H).

IR (neat, NaCl plates, cm^{-1}) 1755 (s), 1345 (s).

GCMS m/e (relative intensity) 140 (M^+, 20), 125 (9), 97 (3), 84 (46), 83 (40), 69 (15), 57 (100), 41 (30).

High-resolution MS calculated for $C_9H_{16}O$ (M^+): 140.24965. Found: 140.24699. Error= + 0.4 ppm.

A similar reaction employed 2-cyclohexenone (0.196 g, 1.0 mmol) was carried out under the same procedure. 3-*tert*-Butylcyclohexanone was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1).

^{1}H NMR (δ, $CDCl_3$) 0.853 (s, 9H), 1.31-1.82 (m, 5H), 2.10-2.40 (m, 4H).

IR (neat, NaCl plates, cm^{-1}) 1715 (s), 1350 (s).

GCMS m/e (relative intensity) 154 (M^+, 32), 139 (8), 121 (6), 98 (85), 97 (30), 83 (30), 57 (100), 41 (61).

High-resolution MS calculated for $C_{10}H_{18}O$ (M^+):154.13577. Found: 154.13575. Error= - 0.1 ppm.

A similar reaction employed 2-cycloheptenone (0.11 g, 1.0 mmol) was carried out under the same procedure. 3-*tert*-Butylcycloheptanone was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2).

^{1}H NMR (δ, $CDCl_3$) 0.882 (s, 9H), 1.80-2.51 (m, 11H).

IR (neat, NaCl plates, cm^{-1}) 1702 (s), 1365 (s).

GCMS m/e (relative intensity) 156 (M^+, 7), 141 (1), 127 (7), 113 (15), 99 (100), 86 (10), 55 (21).

High-resolution MS calculated for $C_{11}H_{20}O$ (M^+):168.15142. Found: 168.15157. Error= + 1.5 ppm.

4. Photostimulated reaction of isopropylmercury chloride with 2-cyclohexenone in the presence of iodide ion

The reaction mixture containing *i*-PrHgCl (0.62 g, 2.2 mmol), 2-cyclohexenone (0.096 g, 1.0 mmol) and sodium iodide (0.66 g, 4.4 mmol) was irradiated for 5 hours. After work-up as previously described, the solvent was concentrated. 3-Isopropylcyclohexanone was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1)

^{1}H NMR (δ, $CDCl_3$) 0.843 (d, 6H, J=6.6 Hz), 1.38-2.40 (m, 10H).

IR (neat, NaCl plates, cm^{-1}) 1710 (s), 1355 (s).

GCMS m/e (relative intensity) 140 (M^+, 21), 125 (11), 110 (9), 98 (79), 83 (21), 69 (10), 42 (100).

High-resolution MS calculated for $C_9H_{16}O$ (M^+): 140.12012. Found: 140.12001. Error= -1.1 ppm.

5. Photostimulated reaction of n-BuHgCl with 2-cycloalkenones in the presence of iodide ion

A Pyrex tube containing n-BuHgCl (0.65 g, 2.2 mmol), 2-cyclopentenone (0.082 g, 1.0 mmol) and sodium iodide (0.66 g, 4.4 mmol)was irradiated for 12 hours. After irradiation, the mixture was worked up as previously described. 3-n-Butylcyclopentanone was isolated by flash column chromatography (hexane:ethyl acetate = 8:2)

^{1}H NMR (δ, $CDCl_3$) 0.931 (br t, 3 H), 1.10-1.70 (m, 6H), 1.90-2.40 (m, 7H).

IR (neat, NaCl plates, cm^{-1}) 1742 (s), 1465 (m), 1455 (m), 1405 (m), 1155 (s).

GCMS m/e (relative intensity) 140 (M^+, 9), 125 (2), 111 (5), 97 (25), 83 (100), 69 (12), 55 (70), 41 (4).

Identification of the product was confirmed by comparison of the ^{1}H NMR, IR and GCMS data with those of an authentic sample [113].

A similar reaction employing 2-cyclohexenone (0.096 g, 1.0 mmol) was carried out with the same procedure. 3-*n*-Butylcyclohexanone was isolated by flash column Chromatography on silica gel (hexane:ethyl acetate = 8:2).

^{1}H NMR (δ, $CDCl_3$) 0.938 (br t, 3 H), 1.11-1.60 (m, 6H), 1.72-2.41 (m, 9H).

GCMS m/e (relative intensity) 154 (M^+, 21), 139 (3), 125 (7), 97 (100), 83 (12).

The identity of the product was established by coinjection with authentic sample.

6. Effect of iodide ion in the reaction of t-BuHgCl and 2-cyclohexenone

A Pyrex tube containing *t*-BuHgCl (0.65 g, 2.2 mmol) and 2-cyclohexenone (0.096 g, 1.0 mmol) was irradiated for 12 hours. After irradiation, $NaBH_4$ (3 mmol) was added to the reaction mixture. After stirring for 10 minutes, the reaction mixture was poured into brine solution (20 mL) and extracted with methylene chloride (2x10mL). The combined methylene chloride extracts dried over $MgSO_4$ and concentrated to afford a liquid. GC analysis revealed that the isolate contained 37% of 3-*tert*-butylcyclohexanone.

Another reaction mixture employed 1 equivalent of sodium iodide was irradiated for 10 hours. After work-up as described in section 2, GC analysis of the crude isolate showed that the isolate contained 65% of 3-tert-butylcyclohexanone.

7. Photostimulated reaction of alkylmercury halides with 5-methyl-2-cyclohexenone in the presence of iodide ion

A Pyrex tube containing t-BuHgCl (0.65 g, 2.2 mmol), 5-methyl-2-cyclohexenone (0.11 g, 1.0 mmol) and sodium iodide (0.66 g., 4.4 mmol) was irradiated for 5 hours. After irradiation, the reaction mixture was worked up as previously described. The product, 3-tert-butyl-5-methylcyclohexanone was isolated by flash column chromatography (hexane:ethyl acetate = 95:5). The capillary GC and ^{1}H NMR of this material indicated that two stereoisomers were present, in a cis/trans ratio of 45:55. The cis and trans stereoisomers were determined by the comparison of the ^{1}H NMR chemical shifts of the methyl groups in the two stereoisomers and by the retention time of capillary GC analysis.

^{1}H NMR of cis product (δ, $CDCl_3$) 0.899 (s, 9H), 1.058 (d, 3H, J=6.3 Hz), 1.40-2.60 (m, 8H).

^{1}H NMR of trans product (δ, $CDCl_3$) 0.888 (s, 9H), 0.964 (d, 3H, J=7.5 Hz), 1.40-2.60 (m, 8H).

GCMS m/e (relative intensity) 168 (M^+, 20), 153 (3), 135 (1), 112 (75), 69 (41), 57 (100), 55 (60).

IR (neat, NaCl plates, cm^{-1}) 2965 (m), 2880 (s), 1715 (s), 1365 (s).

High-resolution MS calculated for $C_{11}H_{20}O$ (M^+): 168.15142. Found: 168.15203. Error= + 6.1 ppm.

A similar reaction employed i-PrHgCl was carried out under the same procedure. The product 3-isopropyl-5-methylcyclohexanone was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 9:1) The ^1H NMR spectrum of this material indicated that stereoisomers were present, in a cis/trans ratio of 26:74.

^1H NMR of cis product (δ, $CDCl_3$) 0.859 (d, 6H, J=6.9 Hz), 0.997 (d, 3 H, J=6.3 Hz), 1.40-2.40 (m, 9H).

^1H NMR of trans product (δ, $CDCl_3$) 0.859 (d, 6H, J=6.9 Hz), 0.926 (d, 3H, J=7.0 Hz), 1.40-2.40 (m, 9H).

IR (neat, NaCl plates, cm^{-1}) 2960 (m), 2875 (m), 1715 (s), 1385 (s), 1365 (s).

GCMS m/e (relative intensity) 154 (M^+, 20), 139 (9), 121 (3), 111 (50), 96 (39), 83 (18), 69 (50), 55 (100).

High-resolution MS calculated for $C_{10}H_{18}O$ (M^+): 154.13577. Found: 154.13597. Error = + 2.0 ppm.

A similar reaction employed n-BuHgCl was carried out under the same procedure. The product 3-n-butyl-5-methylcyclohexanone was isolated by flash column chromatography on silica gel (hexane:ethyl acetate = 8:2). The ^1H NMR spectrum of the this material indicated that stereoisomers were present in a cis/trans ratio of 19:81.

^1H NMR of cis product (δ, $CDCl_3$) 0.851 (br t, 3H), 1.004

(d, 3H, J=4.8 Hz), 1.15-1.40 (m, 6H), 1.70-2.39 (m, 8H).

^{1}H NMR of trans product (δ, $CDCl_3$) 0.851 (br t, 3H), 0.959 (d, 3H, J=6.9 Hz), 1.15-1.40 (m, 6H), 1.70-2.39 (m, 8H).

GCMS m/e (relative intensity) 168 (15), 111 (100), 69 (15), 55 (21), 43 (9), 41 (21).

Identification of the product was confirmed by comparison of the ^{1}H NMR, and GCMS data with those of an authentic sample [105].

8. Photostimulated reaction of tert-butylmercury chloride with 5,6-dihydro-2H-pyran-2-one in the presence of iodide ion

A Pyrex tube containing t-BuHgCl (0.65 g, 2.2 mmol), 5,6-dihydro-2H-pyran-2-one (0.098 g, 1.0 mmol) and sodium iodide (0.66 g, 4.4 mmol) was irradiated for 3 hours in the Rayonet photoreactor at 350 nm. After irradiation, the reaction mixture was worked up as previously described. The product, 5-tert-butyl-trihydro-2H-pyran-2-one, was isolated by flash column chromatography (hexane:ethyl acetate =8:2).

^{1}H NMR (δ, $CDCl_3$) 0.801 (s, 9H), 1.42-1.85 (m, 3H), 2.10-2.25 (m, 1H), 2.45-2.55 (m, 1H), 4.08-4.18 (m, 1H), 4.25-4.34 (m, 1H).

GCMS m/e (relative intensity) 157 (M^++1, 9), 141 (8), 100 (100), 85 (4), 69 (21), 57 (76), 41 (56).

IR (neat, NaCl plates, cm^{-1}) 1745 (s), 1600 (m), 1530 (m), 1350 (s), 1200 (s).

High-resolution MS calculated for $C_8H_{13}O_2$ (M^+-CH_3) : 141.09156. Found: 141.09121. Error= - 3.5 ppm.

9. General procedure for the competition reaction of 2-cyclohexenone and 2-cyclopentenone with alkylmercury halides in the presence of iodide ion

A Pyrex tube containing sodium iodide (1.0 mmol) was flamed dry under a stream of nitrogen. DMSO (10 mL) was added by a hypodermic syringe. The resulting solution was stirred until the sodium iodide was completely dissolved. Then, alkylmercury chloride (0.5 mmol) was added to the solution and immediately the mixture of 2-cyclohexenone (1.0 mmol) and 2-cyclopentenone (1.0 mmol) was added via syringe. The reaction mixture was irradiated in the Rayonet photoreactor at 35 °C. An aqueous sodium thiosulfate solution (20 mL) was added and stirred for 10 minutes. The aqueous mixture was extracted by methylene chloride (2x10 mL). The combined methylene chloride extracts were dried over $MgSO_4$ and concentrated. The ratio of the products was obtained from the GC analysis and corrected by the independently determined GC response factors. All the products were confirmed by the comparison of their GC retention times with those of the authentic compounds. The results are presented in Table 32.

10. General procedure for the competition reaction of 2-cyclohexenone and 2-cycloheptenone with alkylmercury halides in the presence of iodide ion

A similar reaction employed 2-cyclohexenone (1 mmol) and 2-cycloheptenone (1 mmol) was carried out under the same procedure as described in section 8. After work-up, the ratio of products was determined by GC analysis. The results are presented in Table 33.

11. General procedure for the competition reaction of 2-cyclohexenone and 2-cyclopentenone with lithium dialkylcuprates

Lithium di-*n*-butylcuprate was prepared by the reaction of *n*-butyllithium with copper(I) iodide using the following procedure. Copper(I) iodide (0.2-0.5 mmol) was placed in a Pyrex tube. The tube was capped with a rubber septum, and flamed dry under a stream of nitrogen. Ether (10 mL) was added to the tube, and the resulting suspension was cooled to -30 °C. At this temperature, *n*-butyllithium (0.5-1.2 mmol) was added. The tube was shaken vigorously for 10 minutes while holding the temperature between -40 and -20 °C.

Lithium di-*tert*-butylcuprate and lithium di-*sec*-butylcuprate were prepared by the reactions of the lithium reagent with copper(I) iodide. The temperature must be kept at -78 °C while adding *tert*-butyllithium (or *sec*-butyllithium) to the suspension of copper(I) iodide.

The typical competition reaction employing dialkylcuprate is as follows. 2-Cyclohexenone (1 mmol) and 2-cyclopentenone (1 mmol) were placed in a Pyrex tube capped with a rubber septum. The tube was flushed with nitrogen and its contents diluted with ether (0.5 mL), then transferred by cannula to a Pyrex tube containing the dialkylcuprate solution at -78 °C. Under the above conditions, a rapid reaction occurred, yielding a pale brown to dark solution. The resulting mixture was stirred for several hours at -78 °C and then allowed to warm to room temperature. The resulting mixture was poured into aqueous NH_4Cl adjusted to pH 8-9 (by the addition of aqueous NH_3), extracted with ether (3x10 mL) and washed with brine. The combined ethereal extracts were dried, concentrated and analyzed by GC. The product ratios presented in Table 34 were determined by adding biphenyl as an internal standard.

12. General procedure for the competition reaction of 2-cyclohexenone and 2-cyclopentenone with lithium trialkylzincate

The 1:1 complex of $ZnCl_2$ and TMEDA was used as the source of $ZnCl_2$·TMEDA (0.5 mmol) was dissolved in 10 mL of ether which was stirred in a Pyrex tube filled on nitrogen. This solution was cooled to 0 °C and *n*-butyllithium (1.6 mmol) was added. The white suspension was stirred for 10 minutes at 0 ^{o}C. To the suspension of tri-n-butylzincate at -78 ^{o}C, a mixture of 2-cyclohexenone (1.0 mmol) and 2-cyclopentenone (1.0 mmol) in 0.5 mL of ether was added by cannula under a nitrogen atmosphere. The reaction mixture was stirred for 3 hours at -78 ^{o}C and then allowed to warm to room temperature before work-up as described in section 11.

Lithium tri-tert-butylzincate was prepared by the reaction of tert-butyllithium (1.6 mmol) and $ZnCl_2$ TMEDA (0.5 mmol) in ether at -40 ^{o}C. The procedure of competition reaction employing tri-tert-butylzincate was the same as above. These results are presented in Table 34.

13. General procedure for the competition reaction of 2-cyclohexenone and 2-cyclopentenone with high-order organocuprate

The typical competition reaction employing $R_2CuCNLi_2$ was performed as follows. CuCN (0.5 mmol) was placed in a Pyrex tube capped with a rubber septum. The CuCN was flushed with nitrogen. Ether (10 mL) was introduced and the slurry was cooled to -30 ^{o}C, to which was then added the alkyllithium (1.1 mmol) via syringe. The resulting mixture was allowed to stir until complete dissolution of the CuCN. The solution was then cooled to -78 ^{o}C, and the mixture of 2-cyclohexenone (1.0 mmol) and 2-cyclopentenone (1.0 mmol) in 0.5 mL of ether was added. The solution was permitted to stir at -78 °C for the time needed to consume the ate complex. The solution was allowed to warm to room temperature and poured into aqueous NH_4Cl solution adjusted to pH 8-9 by addition of aqueous NH_3. The reaction mixture was extracted, dried and concentrated. The product ratios presented in Table 35 were determined by GC analysis with biphenyl as an internal standard.

14. General procedure for the competition reaction of 2-cyclohexenone and 2-cyclopentenone with lithium dialkyl(tri-n-butylphosphine)cuprate

The solution of lithium dialkylcuprate containing tri-*n*-butylphosphine was prepared by the reaction of 2 equivalents of alkyllithium and 1 equivalent of tetrakisiodo(tri-*n*-butylphosphine)copper(I). The copper(I) complex (0.5 mmol) was placed in a Pyrex tube capped with a rubber septum, and flushed with nitrogen. Ether (10 mL) was added to dissolve the complex and the clear solution was cooled to -78 °C. Alkyllithium (1.1 mmol) was added via cannula to a solution at -78 °C. The resulting solution was clear upon stirring for 20 minutes at this temperature. The mixture of 2-cyclohexenone (1.0 mmol) and 2-cyclopentenone (1.0 mmol) was added to the solution and the resulting mixture was stirred for the time needed to consume the ate complex at -78 °C. The work-up procedure employed was the same method used in the previous section. The product ratio was obtained by GC analysis and are presented in Table 35.

15. General procedure for the competition reaction of 2-cyclohexenone and 2-cycloheptenone with the ate complex

To an ethereal solution of ate complex (0.5 mmol) prepared by the same method as previously described, a mixture of 2-cyclohexenone (1.0 mmol) and 2-cycloheptenone (1.0 mmol) in 0.5 mL of ether was added at -78 °C. The reaction mixture was allowed to stir at -78 °C (or -30 °C) and for the time indicated in Table 36. The reaction mixture was warmed to room temperature and worked up as previously described. The product ratios were determined by GC analysis.

16. Photostimulated reaction of 2-cyclohexenone and tert-butylmercury chloride in the presence of 1,1-diphenylethylene

Sodium iodide (0.66 g, 4.4 mmol) was placed in a Pyrex tube and flamed dry under a stream of nitrogen. DMSO (10 mL) was added using a syringe and the solution was stirred until sodium iodide was completely dissolved. *tert*-Butylmercury chloride was added followed by a mixture of 1,1-diphenylethylene (5.0 mmol) and 2-cyclohexenone (1.0 mmol). The reaction mixture was irradiated with a 275 W sunlamp placed 15 cm from the Pyrex tube. After 3 hours of irradiation, the reaction mixture was worked up as described in section 2. The products were confirmed by coinjection with authentic samples and GCMS analysis.

17. General procedure for the reaction of 2-cyclohexenone and ate complexes in the presence of 1,1-diphenylethylene

To an ethereal solution of ate complex (0.5 mmol) prepared by the same method as previously described, the mixture of 2-cyclohexenone (1.0 mmol) and 1,1-diphenylethylene (5.0 mmol) was added at -78 °C. The reaction mixture was allowed to stir for the time indicated in Table 37 at -78 °C and warmed to room temperature. After work-up as previously described in section 11, the product ratios were determined by GC analysis.

18. General procedure for the reaction of 5-methyl-2-cyclohexenone with ate complexes

5-Methyl-2-cyclohexenone (1.0 mmol) was added to an ethereal solution of ate complex (1.2 mmol) at -78 °C. The reaction mixture was allowed to stir for the time indicated in Table 38 at -78 °C, and then warmed to room temperature. After work-up, the reaction mixture was extracted by ether (2x10 mL). The combined ether extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The product was isolated by flash column chromatography on silica gel. The cis/trans ratio was determined by the comparison of the ^1H

NMR integrals of the methyl groups in the two stereoisomers.

19. General procedure for the reaction of 2-cycloalkenones with lithium di(methylthiomethyl)cuprate

To an ethereal solution of ate complex (1.2 mmol) prepared by the reaction of Cu(I) iodide (1.2 mmol) and methylthiomethyllithium (2.4 mmol) at 0 °C, the 2-cycloalkenone (1.0 mmol) was added at 0 °C. The reaction mixture was allowed to stir for the time indicated in Table 39. The reaction mixture was warmed to room temperature and worked up as previously described. The product generated from the reaction of 2-cyclohexenone with ate complex (3-[(methylthio)methyl]cyclohexanone) was isolated by flash chromatography on silica gel (hexane:ethyl acetate = 7:3).

^1H NMR (δ, $CDCl_3$) 1.60-2.15 (m, 9H), 2.202 (s, 3H), 2.372 (dd, 2H, J=13.5 Hz).

GCMS m/e (relative intensity) 158 (M^+, 49), 143 (8), 97 (100), 85 (27), 69 (39), 55 (71), 41 (98).

IR (neat, NaCl plates, cm^{-1}) 2980, 2860, 1715, 1430, 1375.

High-resolution MS calculated for $C_8H_{14}OS$ (M^+):158.07654. Found: 158.07694. Error= + 4.0 ppm.

The product generated from the reaction of 2-cyclopentenone with ate complex (3-[(methylthio)methyl]cyclopentanone) was isolated by flash chromatography on silica gel (hexane:ethyl acetate = 8:2).

^{1}H NMR (δ, $CDCl_3$) 1.85-2.20 (m, 7H), 2.208 (s, 3H), 2.415 (dd, 2H, J=14.1 Hz).

GCMS m/e (relative intensity) 144 (M^+, 9), 126 (9), 83 (100), 62 (71), 55 (35).

High-resolution MS calculated for $C_7H_{12}OS$ (M^+):144.06089. Found:144.06043. Error= -4.6 ppm.

V. SUMMARY

The photostimulated reactions of 2-substituted-2-nitropropanes with a variety of alkoxide ions have been studied. The reactions with 1°-alkoxide ions in alcohol solution occurred by a free radical chain process involving an electron transfer and which forms the ketal. The reaction is not observed in aprotic solvents such as DMSO, HMPA, DMF or THF. Evidence for this mechanism includes photostimulation, the failure of the reaction to proceed in the dark, the retardation by radical inhibitors and the inhibition of the formation of ketal by vinyl methyl ketone or (1-methoxyethenyl)benzene. The reactions with 2°- or 3°-alkoxide ions proceed by an E_2 elimination to form 2-nitropropene which react with the alkoxide ion and subsequently undergo coupling with 2-bromo-2-nitropropane.

Initial kinetic chain lengths have been measured for the photostimulated reactions of 2-bromo-2-nitropropane with 1°-alkoxide ions and with the anion of 2-nitropropane in alcohol solution. The measured kinetic chain lengths (10 for $NaOCH_3$, 75 for $KOCH_3$, 38 for NaOEt, 171 for KOEt) indicate that these reactions are definitely free radical chain processes. The relative values of the rate constant for the trapping of 2-nitro-2-propyl radical by methoxide ion (k_O) and by nitronate anion (k_N) were measured from the yields of $Me_2C(OCH_3)_2$ and

$O_2NCMe_2CMe_2NO_2$. The values of k_O/k_N are independent of $[BrCMe_2NO_2]_o$, the extent of reaction, the nature of the irradiation employed or of the initial ratio of $[MeO^-]/[Me_2C{=}NO_2^-]$ but depend upon the nature of counterions and solvent. The values of $k_O/k_N = 1.5 \pm 0.2$ are observed at low concentrations of Li^+, K^+ or $PhCH_2N(CH_3)_3^+$ in MeOH. The value of k_O/k_N is > 50 with Na^+ in MeOH.

The photostimulated reactions of 2-cycloalkenone with alkylmercury chlorides in the presence of excess iodide ion are presented in Part IV of this dissertation. The conjugate addition reaction yielding the 3-alkylcycloalkenone is believed to be a radical chain process possibly involving the organomercurate complex, $RHgClI^-$ or $RHgI_2^-$, generated from the reaction of the alkylmercury chloride and iodide ion. The relative reactivities of alkyl radicals toward 2-cyclohexenone and 2-cyclopentenone indicate that the alkyl radicals preferentially react with 2-cyclopentenone. A similar chemoselectivity was observed in the reactions with $(\underline{t}\text{-Bu})_2CuLi$ and $(\underline{t}\text{-Bu})_3ZnLi$ in ether at -78 °C. However, 1°- and 2°-alkyl cuprates or zincates, $(\underline{t}\text{-Bu})_2CuCNLi_2$ or $(\underline{t}\text{-Bu})_2CuLi\cdot PBu_3$ preferentially alkylated 2-cyclohexenone. The supposition that $(\underline{t}\text{-Bu})_2CuLi$ or $(\underline{t}\text{-Bu})_3ZnLi$ react by a radical chain involving the <u>tert</u>-butyl radical ion was confirmed by the trapping of the <u>tert</u>-butyl radical by added 1,1-diphenylethylene.

VI. BIBLIOGRAPHY

1. Bunnett, J. F.; Kim, J. K. J. Am. Chem. Soc. 1970, 92, 7463.

2. Russell, G. A.; Danen, W. C. J. Am. Chem. Soc. 1966, 88, 5663

3. Russell, G. A.; Danen, W. C. J. Am. Chem. Soc. 1968, 90, 347.

4. Bunnett, J. F.; Rossi, R. A. J. Org. Chem. 1973, 38, 1407.

5. Bunnett, J. F.; Rossi, R. A. J. Org. Chem. 1972, 37, 3570.

6. Saveant, J. M. Acc. Chem. Res. 1980, 13, 323.

7. Russell, G. A. J. Am. Chem. Soc. 1953, 75, 5100.

8. Kornblum, N.; Boyd, S.D.; Ono, N. J. Am. Chem. Soc. 1974, 96, 2580.

9. Kornblum, N. Angew. Chem. Int. Ed. Engl. 1975, 14, 734.

10. Bunnett, J. F. Acc. Chem. Res. 1978, 11, 413.

11. Russell, G. A. Adv. Phys. Org. Chem. 1987, 23, 271.

12. Russell, G. A.; Norris, R. K.; Panek, E. J. J. Am. Chem. Soc. 1971, 93, 5939.

13. Russell, G. A.; Mudryk, B.; Jawdosiuk, M. Synthesis 1981, 62.

14. Bowman, R. W.; Richardson, G. D. Tetrahedron Lett. 1981, 22, 1551.

15. Bowman, R. W.; Richardson, G. D. J. Chem. Soc. Perkin Trans. I, 1980, 1407.

16. Russell, G. A.; Hershberger, J. J. Chem. Soc. Chem. Commun. 1980, 216.

17. Russell, G. A.; Ros, F.; Mudryk, B. J. Am. Chem. Soc. 1980, 102, 7691.

18. Russell, G. A.; Hershberger, J.; Tashtoush, H. J. Org. Chem. 1982, 47, 1480.

19. Russell, G. A.; Ros, F.; Mudryk, B. J. Am. Chem. Soc. 1980, 102, 7601.

20. Russell, G. A.; Mudryk, B. J. Org. Chem. 1982, 47, 1879.

21. Russell, G. A.; Mudryk, B.; Jawdosiuk, M. J. Am. Chem. Soc. 1981, 103, 4610.

22. Russell, G. A.; Jawdosiuk, M.; Ros, F. J. Am. Chem. Soc. 1979, 101, 3378.

23. Russell, G. A.; Jawdosiuk, M.; Makosza, M. J. Am. Chem. Soc. 1979, 101, 2355.

24. Russell, G. A.; Dedolph, D. F. J. Org. Chem. 1985, 50, 2378.

25. Galli, C.; Bunnett, J. F. J. Am. Chem. Soc. 1979, 102, 6137.

26. Russell, G. A.; Dedolph, D. F. J. Org. Chem. 1985, 50, 2498.

27. Schaefer, F. C.; Peters, G. A. J. Org. Chem. 1961, 26, 412.

28. Williams, V. A.; Miller, J. J. Am. Chem. Soc. 1956, 78, 1975.

29. Miller, J. J. Am. Chem. Soc. 1954, 76, 448.

30. Jagannadhan, V.; Steenken, S. J. Am. Chem. Soc. 1984, 106, 6542.

31. Eibenberger, J.; Schulte-Frohlinde, D.; Steenken, S. J. Phys. Chem. 1980, 84, 704.

32. Kropp, P. J.; Sawyer, J. A.; Snyder, J. J. J. Org. Chem. 1984, 49, 1583.

33. Kropp, P. J. Acc. Chem. Res. 1984, 17, 131.

34. Kropp, P. J.; McNeely, S. A.; Davis, R. D. J. Am. Chem. Soc. 1983, 105, 6907.

35. Kropp, P. J.; Gibson, J. R.; Snyder, J. J. Tetrahedron Lett. 1978, 207.

36. Klessinger, M. *Angew. Chem. Int. Ed. Engl.* 1980, *19*, 908.

37. Viehe, H. G.; Stella, L.; Janousek, Z.; Merenyi, R. *Angew. Chem. Int. Ed. Engl.* 1978, *17*, 691.

38. Viehe, H. G.; Merenyi, R.; Stella, L.; Janousek, Z. *Angew. Chem. Int. Ed. Engl.* 1979, *18*, 917.

39. Bowman, R. W.; Richardson, G. D. *Tetrahedron Lett.* 1981, *22*, 1551.

40. Bowman, R. W.; Richardson, G. D. *Tetrahedron Lett.* 1977, 4519.

41. Bowman, R. W.; Richardson, G. D. *J. Chem. Soc. Perkin Trans. I,* 1980. 1407.

42. Jones, J. B.; Young, J. M. *J. Med. Chem.* 1968, *11*, 1176.

43. Zoretic, P. A.; Chiang, J. *J. Org. Chem.* 1977, *42*, 2103.

44. McMurry, J. E.; Melton, J. *J. Org. Chem.* 1973, *38*, 4367.

45. Lorette, N. B.; Howard, W. L. *J. Org. Chem.* 1960, *25*, 521.

46. Hass, H. B.; Seigle, L. W. *J. Am. Chem. Soc.* 1940, *62*, 100.

47. Kaplan, R. B.; Shechter, H. *J. Am. Chem. Soc.* 1961, *83*, 3535.

48. Grakauskas, V.; Baum, K.; Garver, L. C. *J. Org. Chem.* 1985, *50*, 1699.

49. Kornblum, N.; Singh, H. K.; Kelly, W. J. *J. Org. Chem.* 1983, *48*, 332.

50. Kornblum, N.; Delly, W. J.; Destner, M. M. *J. Org. Chem.* 1985, *50*, 4720.

51. Bowman, W. R.; Al-Khalil, S. *Tetrahedron Lett.* 1982, *23*, 4513.

52. Bowman, W. R.; Al-Khalil, S. *J. Chem. Soc. Perkin Trans. I,* 1986, 555.

53. Kornblum, N.; Blachwood, R.; Powers, J. *J. Am. Chem. Soc.* 1957, *79*, 2507.

54. Kornblum, N.; Taylor, H. J. *J. Org. Chem.* 1963, *28*, 1424.

55. Truce, W. E.; Klingler, J. E.; Poar, J. E.; Wu, D. K. *J. Org. Chem.* 1969, *34*, 3104.

56. Loudon, G. M.; Smith, C. K.; Zimmerman, S. E. *J. Am. Chem. Soc.* 1974, *96*, 465.

57. Kimpe, N. D.; Buyck, L. D.; Verhe, R.; Schamp, N. *Synthetic Commun.* 1979, *9*, 575.

58. Smith, L. R.; Speziale, A. J. *J. Am. Chem. Soc.* 1962, *84*, 1868.

59. Albertson, C. E.; Ray, F. E. *J. Am. Chem. Soc.* 1948, *70*, 1954.

60. Jayaraman, B.; Singh, P. R. *Chem. Lett.* 1976, 1333.

61. Walling, C. " Free Radical in Solution", John Wiley & Son, Inc., New York, 1957, p. 80.

62. Espenson, J. H. " Chemical Kinetics and Reaction Mechanism", McGraw-Hill Book Co., New York, 1981, Charpter 7.

63. House, H. O. " Modern Synthetic Reactions", Benjamin Publishing Co., Menlo Park, 1972, p. 494.

64. Bunnett, J. F. " Investigations of Rates and Mechanisms of Reactions: General considerations and Reactions at Conventional Rates", Wiley-Interscience, New York, 1974, p. 161-165.

65. Moon, M. P.; Wolfe, J. F. *J. Org. Chem.* 1979, *55*, 4081.

66. Pasto, D. J.; Gontarz, J. A. *J. Am. Chem. Soc.* 1969, *91*, 719.

67. Whitesides, G. M.; Filippo, J. S., Jr. *J. Am. Chem. Soc.* 1970, *92*, 6611.

68. Hill, C. L.; Whitesides, G. M. *J. Am. Chem. Soc.* 1974, *96*, 870.

69. Giese, B. *Angew. Chem. Int. Ed. Engl.* 1983, *22*, 753.

70. Giese, B. *Angew. Chem. Int. Ed. Engl.* 1985, *24*, 553.

71. Giese, B.; Horler, H.; Zwick, W. Tetrahedron Lett. 1982, 23, 931.

72. Giese, B.; Kretzschmar, G. Angew. Chem. Int. Ed. Engl. 1981, 20, 965.

73. Giese, B.; Meister, J. Angew. Chem. Int. Ed. Engl. 1977, 16, 178.

74. Russell, G. A.; Khanna, R. K. Tetrahedron, 1985, 41, 4133.

75. Russell, G. A.; Hershberger, J.; Owens, K. J. Am. Chem. Soc. 1979, 101, 1312.

76. Russell, G. A.; Khanna, R. K. J. Am. Chem. Soc. 1985, 107, 1450.

77. Russell, G. A.; Guo, D. Tetrahedron Lett. 1984, 25, 5239.

78. Singh, P. R.; Khanna, R. K. Tetrahedron Lett. 1983, 24, 1411.

79. Russell, G. A.; Tashtoush, H. J. Am. Chem. Soc. 1983, 105, 1398.

80. Russell, G. A.; Hershberger, J. J. Am. Chem. Soc. 1980, 102, 7603.

81. Russell, G. A.; Hershberger, J. J. Chem. Soc. Chem. Comm. 1980, 476.

82. Russell, G. A.; Tashtoush, H.; Ngoviwatchai, P. J. Am. Chem. Soc. 1984, 106, 4622.

83. Russell, G. A.; Ngoviwatchai, P. Tetrahedron Lett. 1985, 26, 4975.

84. Russell, G. A.; Ngoviwatchai, P. Tetrahedron Lett. 1986, 27, 3479.

85. Russell, G. A.; Jiang, W.; Hu, S. S.; Khanna, R. K. J. Org. Chem. 1986, 51, 5499.

86. House, H. O.; Respess, W. L.; Whitesides, G. M. J. Org. Chem. 1966, 31, 3128.

87. House, H. O.; Fischer, W. F. J. Org. Chem. 1968, 33, 949.

88. House, H. O.; Whitesides, G. M.; Fischer, W. F.; Filippo, I. S. *J. Am. Chem. Soc.* 1969, *91*, 4871.

89. House, H. O.; Fischer, W. F. *J. Org. Chem.* 1969, *34*, 3615.

90. House, H. O.; Wilkins, J. M. *J. Org. Chem.* 1976, *41*, 4031.

91. House, H. O.; Traficante, K. K.; Evans, R. A. *J. Org. Chem.* 1963, *28*, 348.

92. Casey, C. P.; Boggs, R. A. *Tetrahedron Lett.* 1971, *27*, 2455.

93. Herron, S. Ph. D. Dissertation, Iowa State University, Ames, IA., 1988.

94. Giese, B.; Lachhein, S. *Angew. Chem. Int. Ed. Engl.* 1981, *20*, 967.

95. Heathcock, C. H.; Germroth, T. C.; Graham, S. L. *J. Org. Chem.* 1979, *44*, 4481.

96. Taylor, R. J. K. *Synthesis* 1985, 364.

97. House, H. O.; Wilkins, J. M. *J. Org. Chem.* 1978, *43*, 2443.

98. House, H. O.; Wilkins, J. M. *Acc. Chem. Res.* 1976, *9*, 59.

99. Kendall, P. E.; Whitesides, G. M. *J. Org. Chem.* 1972, *37*, 3718.

100. Kjonaas, R. A.; watson, R. A. *Tetrahedron Lett.* 1986, *27*, 1437.

101. Oshima, K.; Nozaki, H.; Tuchmantel, W. *Chem. Ber.* 1986, *119*, 1581.

102. Isobe, M.; Kondo, S.; Nagasawa, N. *Chem. Lett.* 1977, 679.

103. Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *J. Org. Chem.* 1984, *49*, 3938.

104. Russell, G. A.; Khanna, R. K.; Guo, D. *J. Chem. Soc. Chem. Comm.* 1986, 633.

105. Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* 1982, *47*, 123.

106. Russell, G. A.; Bridger, R. F. *J. Am. Chem. Soc.* 1965, *85*, 3754.

107. Makarova, L. G.; Nesmeyanov, A. N. " The Organic Compounds of Mercury", Vol. 4, North-Holland Publishing Co., Amsterdam, 1967.

108. Marvel, C. S.; Gauerke, C. G.; Hill, E. L. *J. Am. Chem. Soc.* 1925, *47*, 3009.

109. Robinson, J. H.; Wright, G. F. *Can. J. Chem.* 1960, *38*, 21.

110. Kharash, M. S.; Swartz, S. *J. Org. Chem.* 1938, *3*, 405.

111. Kaufman, G. B.; Teter, L. A. *Inorg. Syn.* 1963, *7*, 9.

112. Peterson, D. J. *J. Org. Chem.* 1967, *32*, 1717.

113. Langer, W.; Seebach, D. *Helv. Chim. Acta* 1979, *62*, 1710.

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