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**THE IMPORTANCE OF CONFORMATION IN THE  
REACTIVITY OF RADICAL CATIONS**

by

**Allyson L. Perrott  
B.Sc. (Hons.) Dalhousie**

**Submitted in partial fulfillment of the requirements  
for the degree of Doctor of Philosophy**

at

**Dalhousie University  
Halifax, Nova Scotia  
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For my dad:  
the only thing he's ever asked of me.

For my mom:  
in lieu of the only thing she's ever asked of me.

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## ABSTRACT

The photosensitized (electron transfer) bond cleavage of radical cations has been investigated. In previous studies, the feasibility of the bond cleavage was thought to depend solely on the bond dissociation energy of the radical cation. However, this simple hypothesis led to several incorrect predictions. In this thesis, the hypothesis has been extended to include several conformational criteria. The most stable conformers of neutral molecules have been calculated with molecular mechanics; these calculations have been used to rationalize previous results and to predict the reactivity of new compounds.

In Chapter I, photosensitized (electron transfer) carbon-carbon bond cleavage of  $\beta$ -phenyl ethers is considered. The ethers studied are 2-methoxy-1-phenylpropane (11), 2-methoxy-1-phenylindane (13 cis and trans), 1-methoxy-2-phenylcyclopentane (15 cis and trans), 1-methoxy-2-phenylcyclohexane (18 cis and trans), 6-phenyl-1,4-dioxaspiro[4.5]decane (19), 2-methoxy-3-phenylbutane (27, both diastereomers) and 2-methyl-3-phenyltetrahydropyran (28 cis and trans).

In Chapter II, the feasibility of deprotonation (C-H bond cleavage) of the radical cations of 1-methyl-2-phenylcyclopentane (39 cis and trans) and 1-methyl-2-phenylcyclohexane (40 cis and trans) is investigated.

## LIST OF ABBREVIATIONS

A	electron acceptor
a	encounter distance
anal. calcd.	analysis calculated
D	electron donor
d	doublet
$e_0$	elementary charge, $1.602 \times 10^{-19}$ C
$\epsilon$	molar absorptivity
$\epsilon$	dielectric constant
$\epsilon_0$	permittivity of vacuum, $8.854 \times 10^{-12}$ C <sup>2</sup> N <sup>-1</sup> m <sup>-2</sup>
$E_{0,0}$	electronic excitation energy
$E_A$	reduction potential of the electron acceptor
$E_D$	oxidation potential of the electron donor
$E_{R\cdot}$	oxidation potential of radical
F	Faraday's constant, $9.6485 \times 10^4$ C mol <sup>-1</sup>
$\Delta G_{bdc}$	free energy for bond dissociation of neutral molecule
$\Delta G_{bet}$	free energy for back electron transfer
$\Delta G_c$	free energy for bond dissociation of radical cation
$\Delta G_{et}$	free energy for electron transfer
$\Delta G_f$	free energy for reduction of the radical fragment

gc/fid	gas chromatography/flame ionization detector
gc/ms	gas chromatography/mass selective detector
$\Delta H_{\text{nt}}$	bond dissociation enthalpy of neutral molecule
$\Delta H_{\text{c}}$	bond dissociation enthalpy of radical cation
HOMO	highest occupied molecular orbital
ir	infrared spectrum
J	coupling constant
LUMO	lowest unoccupied molecular orbital
m	multiplet
m	medium
ms	mass spectrum
m/z	mass-to-charge ratio
N	Avogadro's number, $6.022 \times 10^{23} \text{ mol}^{-1}$
nmr	nuclear magnetic resonance
Q	quencher
q	quartet
s	singlet
s	strong
$\Delta S_0$	entropy change for cleavage of neutral molecule
$\Delta S_{\text{c}}$	entropy change for cleavage of radical cation
SCE	saturated calomel electrode

SCF	self-consistent field
SE-30	100% methyl silicone gum
SOMO	singly occupied molecular orbital
t	triplet
w	weak

All other abbreviations are standard.

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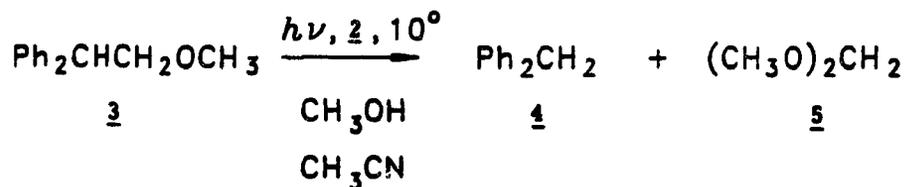
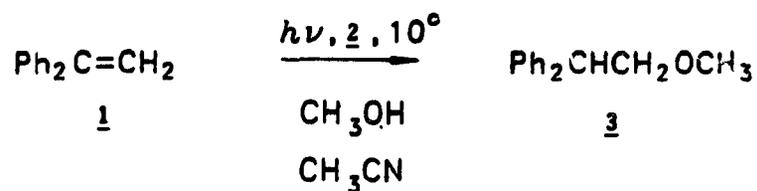
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# Chapter I: The Photosensitized (Electron Transfer) Carbon-Carbon Bond Cleavage of Radical Cations.

## 1. INTRODUCTION

In 1976, Arnold and Maroulis investigated the photochemical behavior of 1,1-diphenylethene (1) (1). The initial product upon irradiation of 1,1-diphenylethene at 10°C with 1,4-dicyanobenzene (DCB, 2) as a sensitizer was 2-methoxy-1,1-diphenylethane (3). However, upon prolonged irradiation, the primary photochemical product (3) underwent carbon-carbon bond cleavage to give diphenylmethane (4) and dimethoxymethane (5). The cleavage reaction proceeds via a radical cation intermediate, i.e. the neutral substrate is oxidized by the excited state of the sensitizer. This is the earliest known example of photosensitized (electron transfer) carbon-carbon bond cleavage, and it has led to further investigations of the bond cleavage reaction in order to clarify the mechanism and determine the scope (2-7).

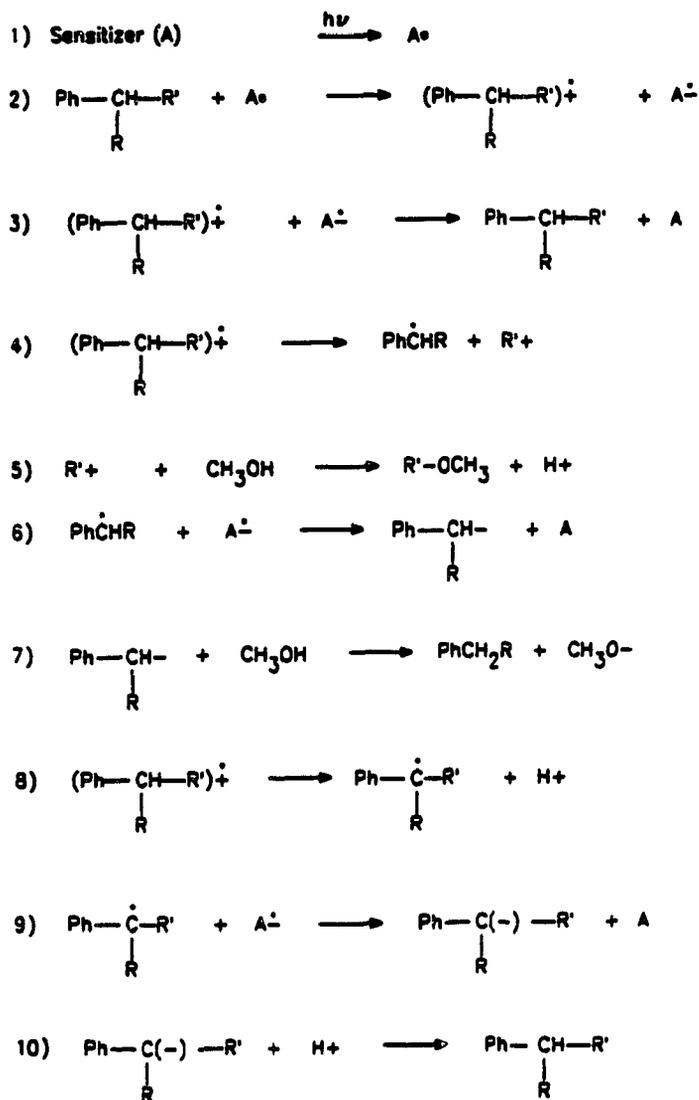
**Reaction 1:**

Initially, the feasibility of carbon-carbon bond cleavage in radical cations was thought to depend solely on the free energy of the process (4). However, this assumption led to several predictions which proved false experimentally (5,7). Accordingly, the hypothesis has been modified to include conformational criteria. The clarification and substantiation of this new hypothesis is the goal of this research.

## A. MECHANISM OF THE PHOTOSENSITIZED (ELECTRON TRANSFER) REACTION

The overall reaction mechanism for the photosensitized reaction is given in Scheme 1. Each step of the mechanism is important, and each will be considered separately below.

Scheme 1: The mechanism for the photosensitized (electron transfer) reaction.



### A.1 EXCITATION OF THE SENSITIZER

The ground state of the sensitizer, A, absorbs light to give one or more excited singlets. If the molecule is promoted to a singlet higher in energy than  $S_1$ , there is rapid internal conversion to  $S_1$ . It is possible for the sensitizer to undergo intersystem crossing to give the triplet  $T_1$  if the rate of intersystem crossing is greater than the rate of fluorescence from  $S_1$  to  $S_0$ .

Both the singlet and triplet excited states are capable of participating in the electron transfer (step 2). There are two important differences between these states, however. Because phosphorescence from  $T_1$  to  $S_0$  is a spin-forbidden process, the lifetime of the triplet is long (compared to the singlet). This means that the triplet has more time to react with the substrate molecule in the next step of the mechanism. However,  $E_{0,0}$  for the triplet is lower than for the singlet. The significance of this will become apparent in the next section.

Samples are commonly irradiated through Pyrex, which absorbs wavelengths less than 280 nm. 1,4-Dicyanobenzene (2), a common sensitizer, has an absorption maximum at 290 nm ( $\epsilon$  1600). However, this absorption extends out to 300 nm. If the donor molecule does not absorb at wavelengths greater than 280 nm, DCB can be irradiated directly while the Pyrex filter prevents excitation of the donor.

Fluorescence quenching of DCB (2) by several donors showed that the singlet excited state is involved (1). To confirm this conclusion, triplet sensitizers were added to acetonitrile-methanol solutions of DCB (2) and a  $\beta,\beta$ -diphenyl ether. A filter was used to prevent direct excitation of DCB (2) upon irradiation; energy transfer from the excited sensitizer gave the triplet excited state of 2. No cleavage of the ether was observed, indicating that electron transfer from the ether to the triplet of 2 does not occur.

#### A.2 ELECTRON TRANSFER

This step must be rapid in order to compete with deactivation of the sensitizer. If the electron transfer is exergonic by more than  $20 \text{ kJ mol}^{-1}$ , the reaction should occur at the diffusion-controlled rate (8). Direct evidence for diffusion-controlled electron transfer comes from observation of the fluorescence quenching of the sensitizer by the substrate. However, it is also possible to calculate the free-energy change for the process by using the Weller equation (8).

$$\Delta G_{et} = F (E_D - E_A - \frac{e}{4\pi\epsilon_0\epsilon a}) - E_{0,0} \quad (1)$$

where  $E_D$  is the oxidation potential of the electron donor,  $E_A$  is the reduction potential of the acceptor,  $\epsilon$  is the dielectric constant of the solvent and  $a$  is the encounter distance at which electron transfer takes place.

$(E_D - E_A)$  is the energy gap between the acceptor LUMO and the donor HOMO for the ground state molecules.  $E_{0,0}$  is the energy of the excited state of the sensitizer, as mentioned in section A.1. Effectively,  $E_{0,0}$  is the energy available for electron transfer. It can be seen that the greater the energy of the excited state, the more favourable the electron transfer will be. The remaining term in the equation is an electrostatic one, accounting for the energy released when the two oppositely charged ions are brought together from infinity. This term includes the dielectric constant of the solvent in the denominator: the magnitude of the electrostatic term is greater in nonpolar solvents. However, the polarity of the solvent also affects  $E_D$  and  $E_A$ . In addition, nonpolar solvents can not separate the ions formed before back electron transfer can occur (see section A.3), lowering the overall efficiency of the mechanism. In acetonitrile ( $\epsilon = 37$ ), the electrostatic term is very small ( $-5.4 \text{ kJ mol}^{-1}$  for  $a = 7 \text{ \AA}$  (8)).

The Weller equation applies for both excited-state electron donors and excited acceptors. Excitation of the



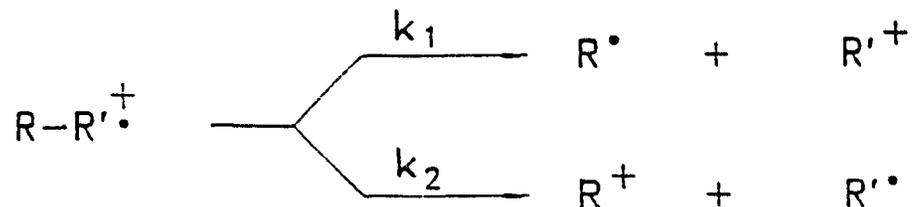
### A.3 BACK ELECTRON TRANSFER

The free-energy change associated with this step can be calculated by using equation 2. The process of back electron transfer is always distinctly exergonic, which usually makes this step rapid. However, when back electron transfer becomes greatly exergonic, it falls in the Marcus "inverted region" (9). That is, the more energetically favorable the back electron transfer is, the slower the reaction will be. This is a potentially useful complication, as slowing this step provides a greater opportunity for other reactions of the radical cation.

$$\Delta G_{\text{bet}} = F (E_A - E_D) \quad (2)$$

Back electron transfer effectively halts the mechanism by regenerating the starting materials. Any other reaction of the radical cation produced in step 2 must be very fast in order to compete.

## A.4 CARBON-CARBON BOND CLEAVAGE



The removal of an electron from the molecule weakens the bonding interactions, making the radical cation susceptible to carbon-carbon bond cleavage. The selectivity of the cleavage, i.e. which fragment will become the radical and which will be the cation, is known to depend on the oxidation potentials of the radicals  $R^{\cdot}$  and  $R'^{\cdot}$  (4,6,7): the radical with the lower oxidation potential becomes the cation. The cleavage is kinetically controlled (6): there is no equilibration of the solvent-separated radical-cation pairs.

The energetics of the cleavage process will be treated later, as will the importance of conformation.

#### A.5 NUCLEOPHILIC ATTACK ON THE CATIONIC FRAGMENT

When the irradiations are carried out in nucleophilic solvent systems (eg. containing methanol), the cation produced by the cleavage is rapidly trapped. The high concentration of the nucleophile minimizes the importance of side reactions. To avoid complication of the mechanism, the nucleophile should not compete for light absorption or interfere with the electron transfer.

#### A.6 REDUCTION OF THE RADICAL FRAGMENT BY THE RADICAL ANION OF THE SENSITIZER

Like back electron transfer, this process is very favorable energetically. However, the reaction is a bimolecular one. The concentration of the radicals is low, as is the concentration of the radical anion of the sensitizer. Therefore, the rate of this reaction can be slow enough to allow competition from various side reactions.

$$\Delta G_r = F (E_A - E_R) \quad (3)$$

where  $E_R$  is the reduction potential of the radical fragment.

### A.7 PROTONATION OF THE CARBANION

Because hydrocarbons have very low acidities, this reaction is essentially irreversible. When the irradiation is carried out in 3:1 acetonitrile-methanol, methanol serves as the proton donor. When  $\text{CH}_3\text{OD}$  is used in the solvent mixture, the anion will be deuterated.

### A.8 DEPROTONATION

Like the carbon-carbon bond cleavage, this is a fragmentation pathway for the radical cation. It is well established that kinetic and equilibrium acidities of a radical cation are greatly enhanced relative to the neutral molecule (10,11). For example, while the  $\text{p}K_a$  for toluene is only 41, the  $\text{p}K_a$  of its radical cation is -11.

The conformation of the radical cation is important in determining whether or not deprotonation will occur. The singly occupied orbital must overlap with the C-H bond in order for the radical cation to deprotonate (11).

As an alternative reaction pathway for the radical cation, this deprotonation is in competition with the carbon-carbon bond cleavage. Camaioni and Franz (12) have studied this competition for 1,2-diarylethanes. They have shown that 1,2-diarylethanes fragment primarily by loss of a benzylic proton, even in strongly acidic solution. However,

it is noted that the deprotonation of the radical cation of bibenzyl is slower than the carbon-carbon bond cleavage of the radical cation of bicumyl. Our investigations suggest that the dominant reaction pathway depends to a great extent on the conformation of the neutral molecule.

#### A.9 REDUCTION OF THE DEPROTONATED RADICAL

This step is essentially the same as reduction of the radical formed by the C-C cleavage.

#### A.10 REPROTONATION

The anion formed in step 9 is readily protonated by any acid. If the benzylic carbon is achiral in the neutral molecule, the product of reprotonation is the same as the starting material. Use of deuterated solvents can lead to incorporation of deuterium, allowing detection of the deprotonation-reprotonation sequence. If the benzylic carbon is chiral, the deprotonation and reprotonation can result in isomerization.

## B. ENERGETICS OF THE CARBON-CARBON BOND CLEAVAGE

As noted previously, back electron transfer from the radical cation of the substrate to the radical anion of the sensitizer is always exergonic and rapid. In order to be a competitive process, C-C bond cleavage must be rapid also. However, the bond cleavage is an endergonic process. According to the Hammond postulate, the transition state should be late, and the transition state will resemble the products (13). The activation barrier will be at least as large as the free-energy change for the process. In this consideration, the activation barrier is assumed to be approximately equal to the enthalpy change for the reaction (4). However, as will be seen later, this assumption is not always valid. Conformational requirements can have a significant effect on the activation barrier.

The free-energy change for the reaction is given by equation 4. Equation 5 applies to the enthalpy of the reaction. Fortunately, this equation can be simplified by assuming that the entropy change involved in the cleavage of the radical cation is roughly the same as that for the neutral molecule. That is, if  $\Delta S_0 \approx \Delta S_+$ , then equation 6 holds.

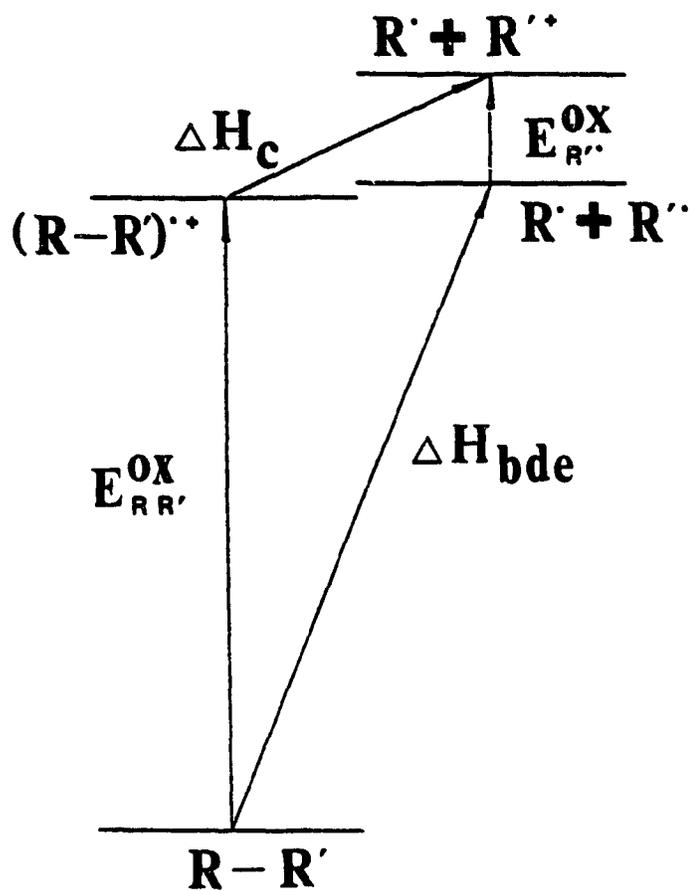
$$\Delta G_c = \Delta G_{bdc} + F (E_{R^{\cdot}}^{ox} - E_{RR^{\cdot}}^{ox}) \quad (4)$$

$$\Delta H_c = \Delta H_{bdc} + F (E_{R^{\cdot}}^{ox} - E_{RR^{\cdot}}^{ox}) - T (\Delta S_o - \Delta S_+) \quad (5)$$

$$\Delta H_c = \Delta H_{bdc} + F (E_{R^{\cdot}}^{ox} - E_{RR^{\cdot}}^{ox}) \quad (6)$$

The significance of equation 6 can be visualized easily by considering the thermochemical cycle in Figure 2.  $\Delta H_{bdc}$  is the bond dissociation energy for the neutral molecule; this energy can be calculated or determined from thermolytic measurements. The oxidation potential of the intact molecule can be obtained with a variety of electrochemical methods such as polarography or cyclic voltammetry. The oxidation potential of the radical which becomes the cation,  $E_{R^{\cdot}}^{ox}$ , is more difficult to obtain, because radicals are transient species. However, a newly developed photo-electrochemical technique (14) makes measurement of radical oxidation potentials possible. When all of these data are known, the bond dissociation energy of the radical cation,  $\Delta H_c$ , is easily obtained.

Figure 2: Thermochemical cycle for the determination of the bond dissociation energy of a radical cation.



From the thermochemical cycle, it can be seen that there are three different ways to lower the bond dissociation energy of the radical cation. First, the oxidation potential of the molecule could be increased. (However, this makes the original electron transfer reaction less favourable.) The bond dissociation energy of the intact molecule could be lowered. Finally, the oxidation potential of the radical could be lowered.

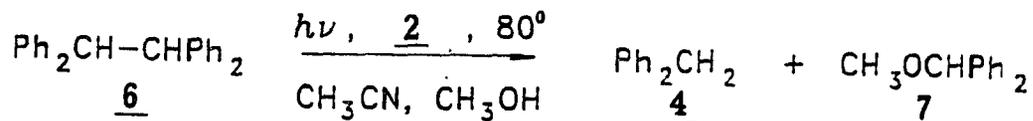
One question remains: what is the maximum value of  $\Delta H_c$  that will permit carbon-carbon bond cleavage to occur?

### C. EXAMPLES OF CARBON-CARBON BOND CLEAVAGE

The results of irradiations of some acyclic and cyclic compounds are summarized in Table 1.

1,1,2,2-tetraphenylethane (6) is unreactive at 10°C, but cleaves at 80°C to give diphenylmethane (4) and methoxydiphenylmethane (7) (4). These products result from the cleavage of the radical cation of 6 to give a diphenylmethyl radical and a diphenylmethyl cation. The radical is reduced by the radical anion of the sensitizer, and the resultant anion is protonated to give 4. The cation is attacked by a nucleophilic methanol molecule, followed by deprotonation to give 7.

Reaction 2:



The thermochemical cycle for 6 is shown in Figure 3. The bond dissociation energy of the radical cation has been calculated to be 47 kJ mol<sup>-1</sup>. Since 6 cleaves at 80°C but not at 10°C, this bond dissociation energy can be regarded as a threshold value. What happens in systems with a higher bond dissociation energy than this?

Table 1: Summary of results of irradiations.

Starting material	Condition	Products
1,1,2,2-tetraphenyl-ethane (6) <sup>c</sup>	a	diphenylmethane (4) methoxydiphenylmethane (7)
1,1,2-triphenyl-ethane (8) <sup>d</sup>	b	no reaction
1-methoxy-2-phenyl-ethane (10) <sup>d</sup>	b	no reaction
2-methoxy-1-phenyl-propene (11) <sup>d</sup>	a	toluene (25%) 1,2-diphenylethane (15%) (4-cyanophenyl)phenylmethane (25%) 1,1-dimethoxyethane
5-methyl-3-phenyl-2,3-dihydro-benzofuran (12) <sup>e</sup>	a	<u>cis</u> - and <u>trans</u> -2-methoxy-5-methyl-3-phenyl-2,3-dihydrobenzofuran
<u>cis</u> -2-methoxy-1-phenylindane (13) <sup>e</sup>	a	<u>trans</u> -2-methoxy-1-phenylindane (13)
2-methoxy-1,1-diphenyl-cyclopentane (14) <sup>e</sup>	a	5,5-diphenylpentanal dimethyl acetal
<u>cis</u> -1-methoxy-2-phenyl-cyclopentane (15) <sup>f</sup>	a	<u>trans</u> -1-methoxy-2-phenyl-cyclopentane (15)
<u>trans</u> -1-methoxy-2-phenyl-cyclopentane (15) <sup>f</sup>	a	5-phenylpentanal dimethyl acetal 5-(4-cyanophenyl)-5-phenyl-pentanal dimethyl acetal
2-methoxy-1,1-diphenyl-cyclohexane (16) <sup>f</sup>	a	6,6-diphenylhexanal dimethyl acetal (95%)
6,6-diphenyl-1,4-dioxaspiro[4.5]decane (17) <sup>f</sup>	a	2-methoxy-2-(5,5-diphenyl-pentyl)-1,3-dioxolane (50%)
<u>cis</u> - or <u>trans</u> -1-methoxy-2-phenyl-cyclohexane (18) <sup>f</sup>	b	no reaction

6-phenyl-1,4-dioxaspiro[4.5]decane      a      no reaction  
(19)<sup>f</sup>

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<sup>a</sup>Irradiation at 10°C, DCB as sensitizer, 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OH solvent.

<sup>b</sup>Irradiation at 80°C, DCB, 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OH.

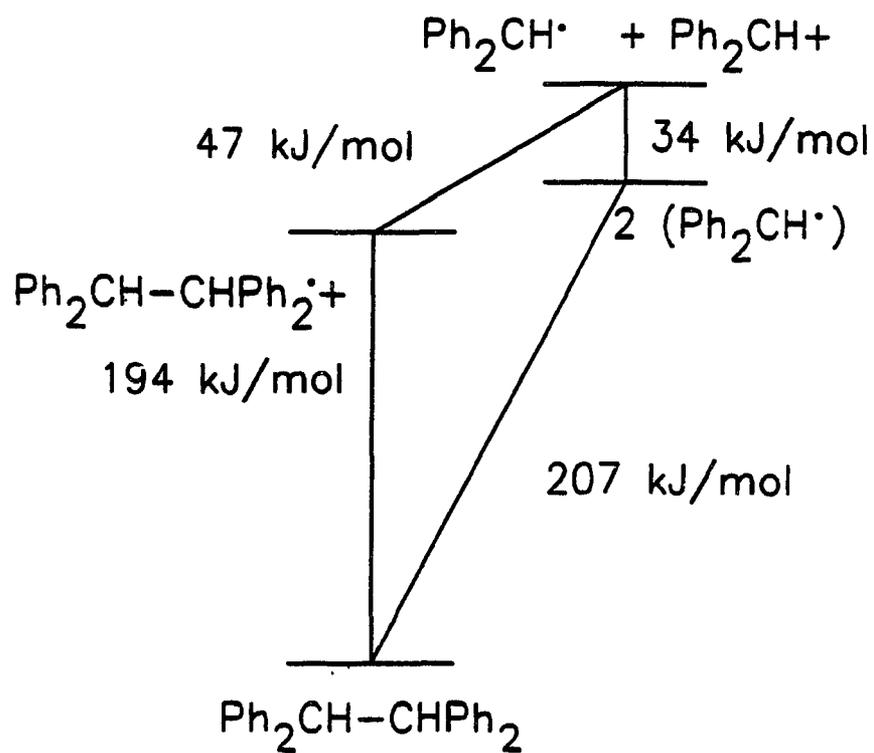
<sup>c</sup>Reference 4.

<sup>d</sup>Reference 7.

<sup>e</sup>Reference 5.

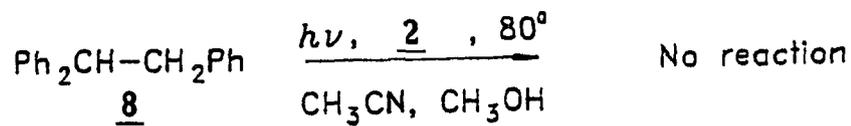
<sup>f</sup>Reference 15.

Figure 3: Thermochemical cycle for the bond dissociation energy of the radical cation of 1,1,2,2-tetraphenylethane (6).



One could predict that cleavage of 1,1,2-triphenylethane (8) in the presence of methanol would give toluene and methoxydiphenylmethane (7) (via a benzyl radical and a 2° diphenylmethyl cation). These products are preferred over diphenylmethane (4) and methoxyphenylmethane (9) (formed from a 1° cation), since stabilization of the cation is more important than stabilization of the radical. That is, the oxidation potential of the diphenylmethyl radical is lower than that of the benzyl radical.

Reaction 3:



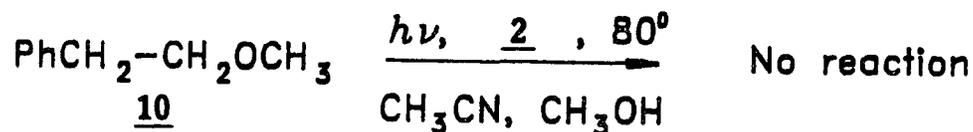
Experimentally, however, no reaction is observed (7). Making the radical 1° instead of 2° raises the bond dissociation energy of the neutral molecule. This causes the bond dissociation energy of the radical cation to be increased to the point where cleavage will not occur. This energy has been calculated to be 70 kJ mol<sup>-1</sup> (6).

It is known that an  $\alpha$ -oxy group can stabilize a cationic center (16). Substitution of a methoxy group on the carbon atom which becomes the cationic center should lower the oxidation potential of the corresponding radical significantly (relative to an alkyl substituent). This

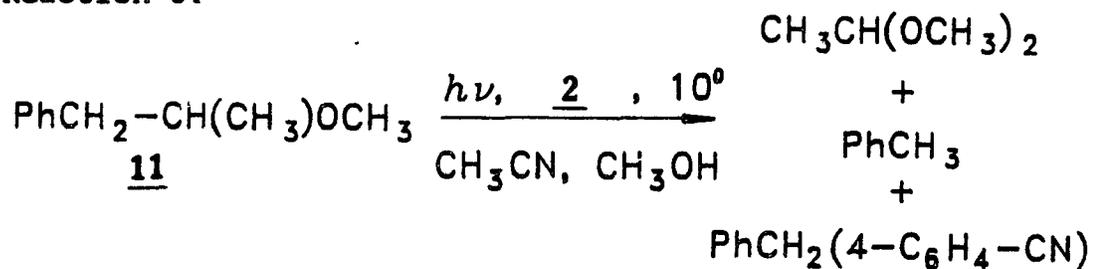
would lower the bond dissociation energy of the radical cation, making cleavage more favourable.

This has been verified experimentally. While 1,1,2-triphenylethane (8) did not cleave, 2-methoxy-1,1-diphenylethane (3) did (reaction 1). However, the stabilizing effect of the oxygen is insufficient to allow reaction of 1-methoxy-2-phenylethane (10), which would involve a 1° radical as well as a 1° cation (7). In the case of 2-methoxy-1-phenylpropane (11), the cation formed is 2°, and the cleavage can occur (7).

Reaction 4:

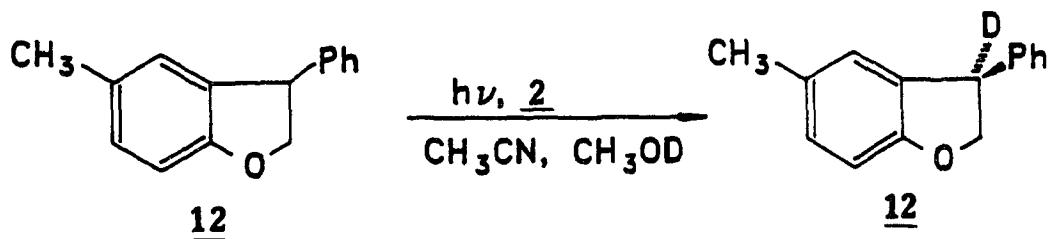


Reaction 5:

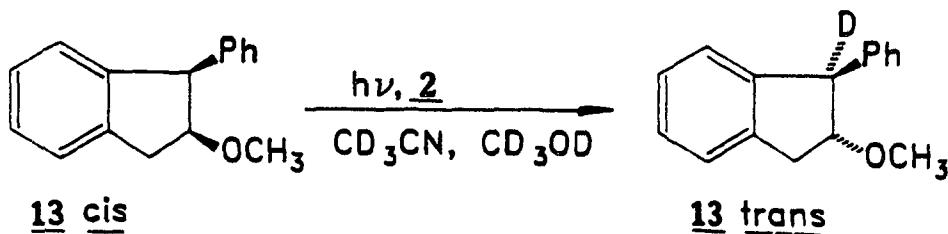


Some unexpected results were obtained when cyclic systems were investigated (5). Under the same reaction conditions as before, 5-methyl-3-phenyl-2,3-dihydrobenzofuran (12) did not cleave. The cis isomer of 2-methoxy-1-phenylindane (13) isomerized to the trans, but neither isomer could be induced to cleave. This may seem strange, as the behavior of these compounds is predicted to be about the same as that of 2-methoxy-1,1-diphenylethane (3) on energetic grounds.

Reaction 6:

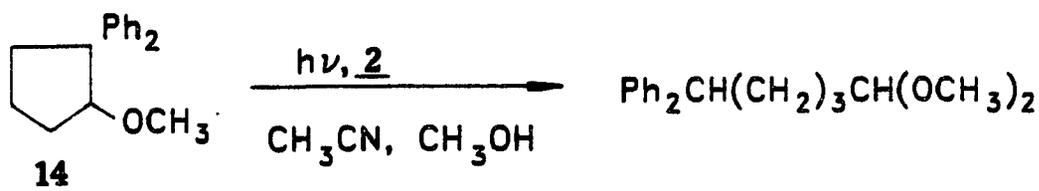


Reaction 7:



1,5-Radical cations have been generated as intermediates in the photosensitized carbon-carbon bond cleavage of five-membered cyclic compounds (3,5,7)<sup>a</sup>. An example of such a reaction is the cleavage of 2-methoxy-1,1-diphenylcyclopentane (14) when irradiated with DCB in 3:1 acetonitrile-methanol (5).

Reaction 8:

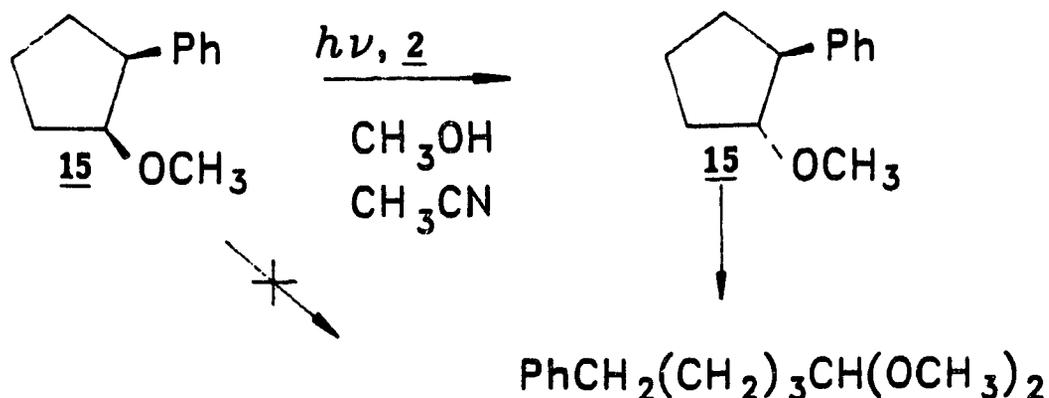


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<sup>a</sup>Griffin and coworkers have generated a 1,5- and a 1,6-radical cation (3). For example, the photosensitized (electron transfer) irradiation of meso-1,2-dimethoxy-1,2-dimethylacenaphthene (20) or rac-9,10-dimethoxy-9,10-dimethyl-9,10-dihydrophenanthrene (21) in acetonitrile with 1,4-dicyanonaphthalene resulted in the formation of the diastereomers. In these cases, carbon-carbon cleavage is considerably different from that in reactions 8 and 9, since both the radical and cationic centers are conjugatively coupled through the  $\pi$ -system. Hence, orbital symmetry rules may be involved here.

It has been reported that the monophenyl analogue 15 also undergoes carbon-carbon cleavage under identical reaction conditions (7). Deprotonation of the radical cation of 15 at the benzylic position and subsequent cis-trans isomerization were also indicated. However, investigation of the isolated cis and trans forms of 15 showed that the isomers have differing reactivities (15). Although the trans isomer undergoes carbon-carbon bond cleavage, the cis isomer does not. Instead, the radical cation of the cis isomer deprotonates at the benzylic position, resulting in isomerization to the trans.

Reaction 9:



The possibility of generating a 1,6-radical cation has also been investigated by extending photoinduced carbon-carbon bond cleavage to six-membered cyclic analogues (15). These include 2-methoxy-1,1-diphenylcyclohexane (16), 6,6-diphenyl-1,4-dioxaspiro[4.5]decane (17), the cis and trans

isomers of 1-methoxy-2-phenylcyclohexane (18), and 6-phenyl-1,4-dioxaspiro[4.5]decane (19). The diphenyl compounds both underwent C-C bond cleavage when irradiated in the presence of an electron-accepting photosensitizer, as predicted on energetic grounds. However, the monophenyl compounds were inert under the irradiation conditions.

The carbon-carbon bond strengths in the radical cations of the diphenyl compounds are well below the threshold for cleavage. Although the carbon-carbon bond strengths in the monophenyl compounds are closer to the threshold (at least 17 kJ mol<sup>-1</sup> higher than for the diphenyl compounds), these monophenyl compounds were predicted to cleave a priori. It was therefore surprising that all but one of these compounds, 15 trans, failed to cleave under the irradiation conditions.

Obviously, consideration of the bond dissociation energy of the radical cation alone is insufficient to give useful predictions. This simple approach has led to several predictions which have proven false experimentally. In order to rationalize these results and permit accurate predictions for other compounds with bond strengths near the cleavage threshold, conformational criteria are now suggested.

#### D. THE IMPORTANCE OF CONFORMATION IN CARBON-CARBON BOND CLEAVAGE

As mentioned previously, the SOMO of the radical cation must overlap with the C-H bond in question in order for deprotonation to occur. It seems rational to suggest, therefore, that the SOMO must overlap with the C-C bond before cleavage will take place (6).

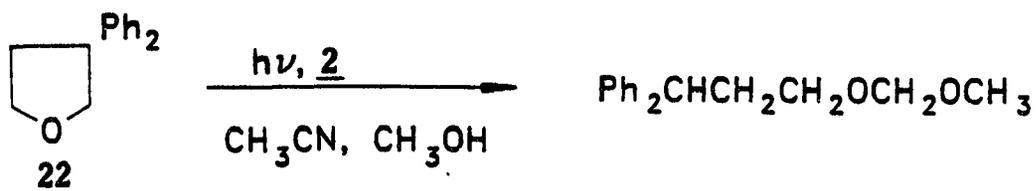
Consider 5-methyl-3-phenyl-2,3-dihydrobenzofuran (12). The oxidation potential of 12 is significantly lower than that of the diphenylmethyl derivatives. This indicates that the SOMO of the radical cation is largely associated with the fused phenyl ring, which bears electron-donating substituents. The fused phenyl ring is held in roughly the same plane as the benzylic C-C bond that is expected to cleave. There can be no overlap between the SOMO (perpendicular to the phenyl ring) and this bond, and no cleavage is observed.

This explanation is still insufficient to explain the lack of reactivity for the isomers of 1-methoxy-2-phenylcyclohexane (18) and the cis isomer of 1-methoxy-2-phenylcyclopentane (15). These phenyl rings are not fused, and yet no cleavage is observed. It is not enough for the phenyl ring to be able to orient perpendicular to the C-C bond. The lifetime of the radical cation is insufficient to permit this conformational reorientation before back

electron transfer occurs. The conformation of the phenyl group must be correct in the neutral molecule if the radical cation is to cleave.

There is some experimental evidence for a proper alignment of phenyl groups in compounds which cleave. 3,3-Diphenyltetrahydrofuran (22) was found to cleave when irradiated (7). X-ray crystallography has shown that there is an angle of 62° between the bis-benzylic carbon-carbon bond and the plane of one of the phenyl rings (17). Therefore, overlap between the SOMO of the radical cation and the carbon-carbon bond is possible.

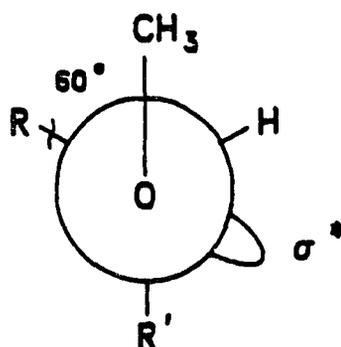
Reaction 10:



Another conformational requirement is now suggested for ethers. It is known that the  $\alpha$ -oxy group must stabilize the cationic fragment formed by the cleavage if this process is to be competitive with back electron transfer. It now seems that one of the lone pairs on the oxygen atom must feed into the C-C antibonding orbital to stabilize the transition state. Figure 4 shows the proper orientation of the alkoxy group as a Newman projection along the O-C bond.

Figure 4: Preferred conformation for carbon-carbon bond cleavage of the radical cation.

a) Illustrated with a Newman projection along the O-C bond.



b) Illustrated with dashed-wedged line notation.



This is another illustration of the kinetic anomeric effect (18-22). This effect is an example of a more general phenomenon: the stereoelectronic control of reactivity (23). Originally, the anomeric effect was defined (18) as the tendency for an electronegative substituent on C1 of a pyranoid ring to be in the axial position, despite the fact that steric considerations would favour the conformation with the equatorial substituent. When the electronegative substituent is in the axial position, the axial lone pair on the oxygen is antiperiplanar to the polar bond, allowing good  $n-\sigma^*$  overlap (Figure 5). The stabilizing effect of this delocalization, sometimes referred to as back-bonding (22), is sufficient to override the effect of the repulsive 1,3-diaxial interactions.

This type of  $n-\sigma^*$  interaction is also responsible for the gauche effect, first discussed by Wolfe (24). This is the tendency for molecules to adopt a conformation with the maximum number of gauche interactions between vicinal lone pairs and/or polar bonds. For example, the dihedral angle between the fluorine atoms in FOOF is  $87.5^\circ$ , allowing the maximum number of gauche interactions between lone pairs (Figure 6). More significantly, it guarantees that there is a lone pair antiperiplanar to both O-F bonds. The delocalization of the electrons is reflected in a short O-O bond (1.22 Å) and a long O-F bond (1.58 Å) (25).

Figure 5: Preferred conformation of a pyranoid ring with an electronegative substituent at C1.

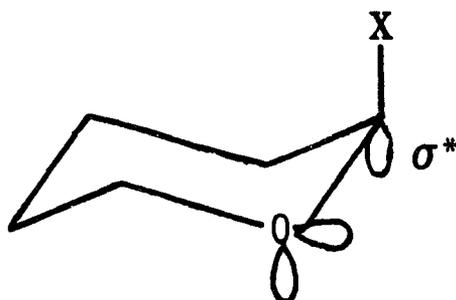
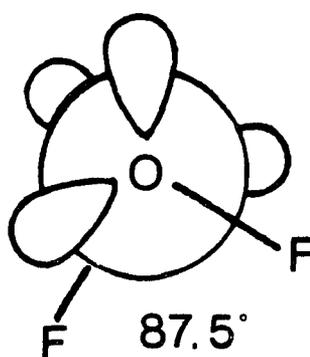


Figure 6: Preferred conformation of FOOF.

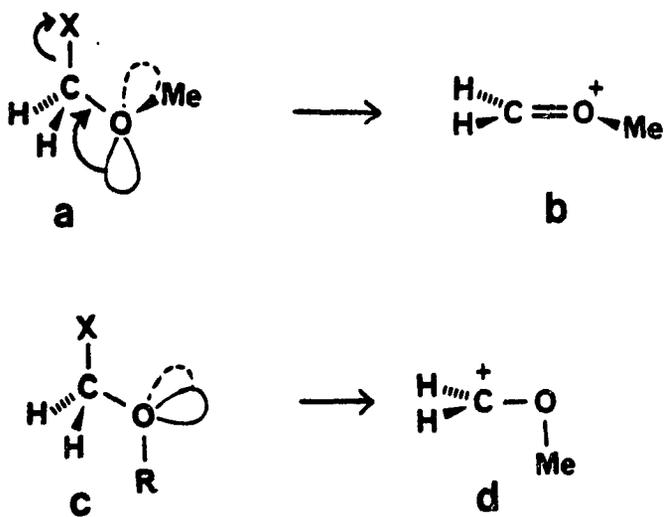
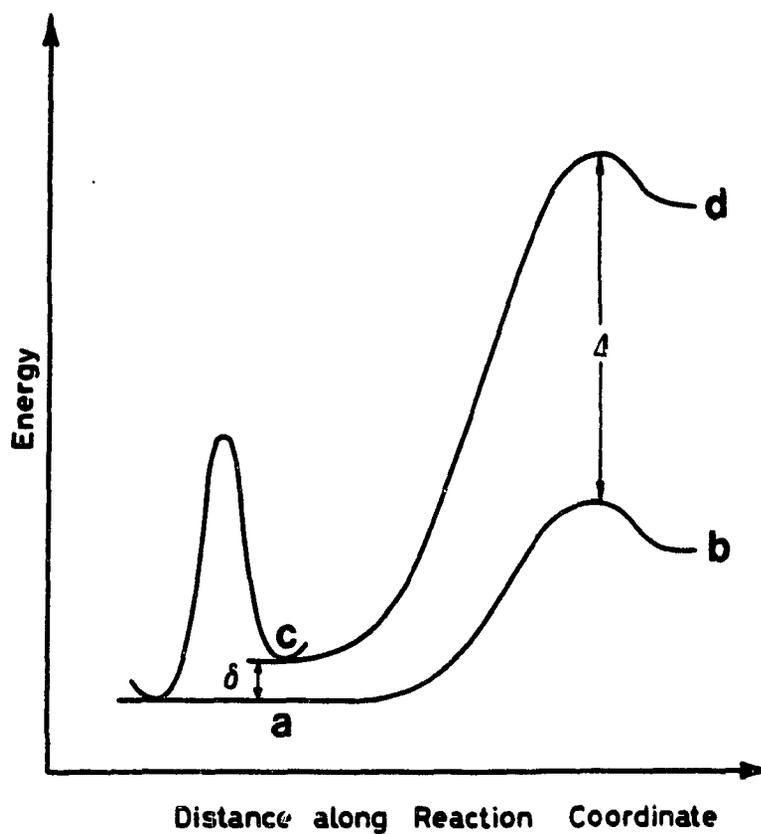


The nature of the orbitals containing the oxygen lone pairs is important to this thesis. The simple picture most commonly used in organic chemistry involves a pair of equivalent  $sp^3$ -hybridized orbitals. In terms of molecular orbitals, it is more correct to use nondegenerate orbitals: one with  $\sigma$  symmetry, and one with  $\pi$  symmetry (19). The  $\pi$ -type orbital is higher in energy, and therefore, this is the orbital which makes the major contribution to electron donation. However, the  $\sigma$ -type orbital also contributes to the back-bonding. After considering the two lone-pair models, Kirby has concluded that the use of the more common  $sp^3$  orbitals is justified (19).

As originally defined, the anomeric effect applies to ground-state conformations of molecules. It is a thermodynamic effect, influencing the equilibrium populations of various possible conformers. The kinetic anomeric effect is based on the same principles, but applies instead to the stabilities of transition states.

Consider the energy profile diagram for the elimination of X from  $CH_3OCH_2X$  (Figure 7). This is an endothermic process, and therefore the transition state should resemble the intermediate carbocation. When X is eliminated from the more stable gauche conformer, the resultant carbocation is in the appropriate conformation for good overlap between the empty orbital on the carbon atom and a lone pair on oxygen. Elimination from the slightly less stable

Figure 7: Energy profile diagram for the elimination of X<sup>-</sup> from CH<sub>3</sub>OCH<sub>2</sub>X.



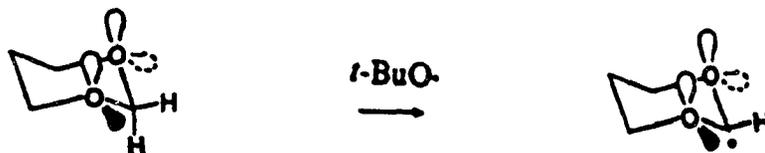
antiperiplanar conformation produces a cation with the vacant p-orbital perpendicular to the lone pairs. The difference in energies between the transition states is much larger than the difference between the starting conformations: the reaction from the gauche conformer is much faster than from the antiperiplanar rotamer. The energy difference between the transition states is approximately the same as the barrier to rotation about the double bond in  $\text{CH}_2=\text{O}^+-\text{Me}$ , which has been calculated to be about  $85 \text{ kJ mol}^{-1}$  (26).

According to the Curtin-Hammett principle, this rate enhancement will be observed only when the barrier to interconversion of the ground-state conformers is greater than the barrier to the bond cleavage (27). This can be achieved when the vulnerable bond is a very weak one, or when the ground-state molecule is rigid.

There are many examples of the kinetic anomeric effect in the literature (20,21). Beckwith and Easton have carried out a kinetic investigation of hydrogen abstraction from some 1,3-dioxanes (20a). The rate of H abstraction is 11 times greater when a lone pair on an oxygen included in the ring is antiperiplanar to the H abstracted (reaction 11). (Interestingly, an exocyclic methoxy group geminal to the hydrogen does not accelerate the reaction. This appears to be due to the orientation of the methoxy group. If the methyl group is antiperiplanar to the hydrogen, there can be

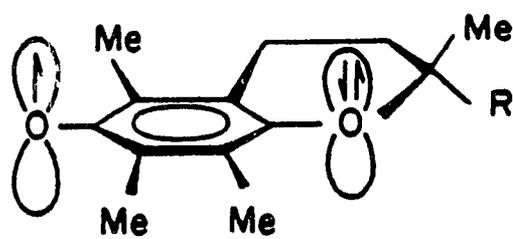
no interaction between the C-H bond and one of the oxygen lone pairs.) A similar effect was observed in other studies of hydrogen abstraction from ethers (20b,c).

Reaction 11:



The kinetic anomeric effect has also been used to explain the high efficiency of  $\alpha$ -tocopherol (23) as an antioxidant (21). Phenols inhibit the free-radical peroxidation of organic materials by donating the phenolic hydrogen to the intermediate peroxy radicals, thereby terminating the chain reaction. A 4-methoxy substituent can increase the efficiency of the phenol as a hydrogen atom donor if the SOMO can interact with a lone pair on the methoxyl oxygen. In  $\alpha$ -tocopherol, a fairly rigid six-membered ring holds the alkoxy oxygen in the proper conformation for good interaction (Figure 8). In contrast, 4-methoxy-2,3,5,6-tetramethylphenol (24) is much less reactive. The steric interactions between the methoxy group and the two adjacent methyl groups force the methoxy group into a conformation unsuitable for such a delocalizing interaction.

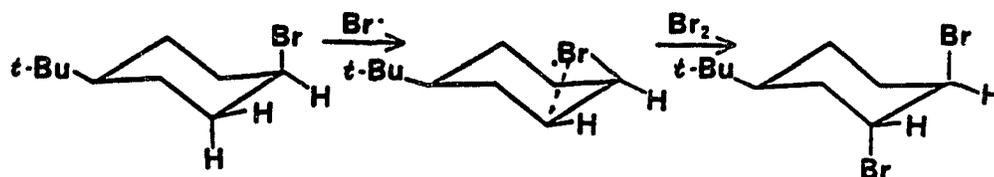
Figure 8: Preferred conformation of the radical derived from  $\alpha$ -tocopherol.



The anomeric effect involves the stabilization that results from interactions with n-orbitals on oxygen; interactions with  $\sigma$ -bonds are referred to as hyperconjugation (28,29). The phenomenon of hyperconjugation is responsible for the enhanced stability of the ethyl cation relative to the methyl cation (30): in the ethyl cation, the C-H  $\sigma$  bonds can interact with the vacant p orbital on the adjacent carbon. Hyperconjugation can also involve C-C bonds.

The kinetic anomeric effect involves the donation of a lone pair from an  $\alpha$  substituent. The free-radical bromination of 1-bromo-4-tert-butylcyclohexane (25) (31) illustrates a more general stereoelectronic phenomenon. While the trans isomer is substituted randomly, the cis isomer gives only trans-dibromide. This is because the bromine atom in the cis isomer is antiperiplanar to the hydrogen which is abstracted in the course of the reaction. The electrons on the bromine can feed into the C-H antibonding orbital. This electron donation makes abstraction of this hydrogen much more favorable than the abstraction of any other. In this case, the stabilizing lone pair is on a  $\beta$ -Br. The bridging in the intermediate is an example of neighbouring group participation (32); the resulting acceleration of the reaction is referred to as anchimeric assistance.

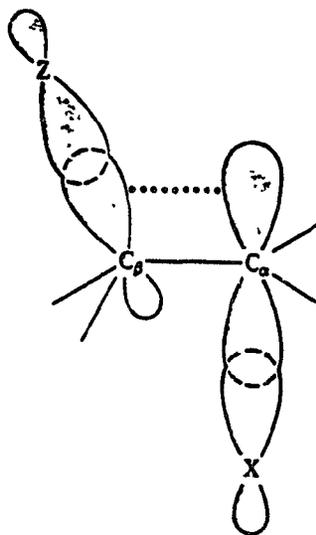
## Reaction 12:



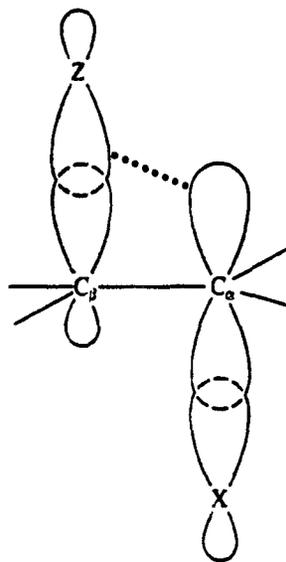
Hyperconjugation and neighbouring group participation are closely related but distinct topics. The formal distinction is illustrated in Figure 9. Neighbouring group participation requires motion of nuclei toward the reaction center, while the concept of hyperconjugation merely recognizes that the organic chemist's persistent use of valence-bond theory is sometimes a misleading simplification of more precise molecular-orbital theory. However, both ideas fall under the larger heading of stereoelectronic effects, and both may operate simultaneously. Many researchers have worked to distinguish between these effects (33), but such distinctions can be difficult and perhaps pointless. The important conclusion is that the conformations of molecules can influence reactivity; the nature of the stereoelectronic interaction is of secondary importance.

Figure 9:

a) Orbital interactions involved in hyperconjugation.



b) Orbital interactions involved in neighbouring group participation.



In many photochemical investigations, the conformations of ground-state molecules have been shown to influence the reactivity of short-lived intermediates. In organic crystals, rotations are hindered: the constraining influence of the crystalline structure has been shown to affect the nature of the products in a wide range of photoreactions (34). The inclusion of organic substrates in cyclodextrin complexes has also been shown to affect their photochemical properties (35). Even in solution, the reactivity can be affected: photoinduced cyclization of the ethylene glycol ketal of 1-methylindol-2-yl 1-chloroacetyl-3-piperidylmethyl ketone (26) produces the less stable conformer because this product corresponds to the more stable ground-state conformer of the starting material (36).

Our working hypothesis is as follows. In order for the radical cation of a 2-phenylalkyl ether to undergo carbon-carbon bond cleavage:

- 1) the C-C bond dissociation energy in the radical cation must be less than about  $50 \text{ kJ mol}^{-1}$ ;
- 2) in the neutral molecule, the phenyl group must be roughly perpendicular to the C-C bond;
- 3) the conformation of the neutral molecule must be such that an oxygen lone pair can feed into the C-C antibonding orbital.

MMP2 and MM3 calculations have been used to determine the lowest energy conformers of the ethers. From these, the reactivities can be rationalized.

## E. MOLECULAR MECHANICS CALCULATIONS

Since the ethers under investigation are liquids, the conformations can not be obtained from x-ray crystallography. It was therefore decided that the optimized structures would be calculated. If the molecules under consideration contained fewer atoms, ab initio calculations could be used to obtain optimized geometries. However, with structures of this size, the use of ab initio optimization becomes exceedingly time consuming. In order to reduce the computer time required, molecular mechanics calculations were chosen.

It was hoped that the results of the calculations could be used to assess orbital overlap; similar approaches have been utilized in the past (37). Ingold was able to rationalize the relative rates of hydrogen atom abstraction from ethers by estimating orbital overlap with Dreiding models (20c): use of molecular mechanics calculations should provide a much clearer picture of conformations and permit far more accurate predictions of reactivity.

Molecular mechanics calculations employ a set of empirical, classically derived equations to compute the energy of a given structure as a function of nuclear positions (38). This set of potential functions is known as the force field. The force field makes use of many different kinds of potential functions, including terms for

bond stretching, bending and torsion; a stretch-bend term; electrostatic terms; and van der Waals functions to account for steric interactions.

The force field contains many adjustable parameters. The values of these parameters have been determined by fitting the properties of a set of archetypal compounds. As more compounds are studied and more experimental data have become available, the force field has been improved and the parameters have been updated. MM2 is an order of magnitude more accurate than STO-3G calculations, provided that the parameterization is valid for the compounds studied (39). However, since the development of the MM2 program, much more experimental data has become available. Also, users of the program have discovered some systematic errors in the results of the calculations (40). One of the failings of MM2 is an inability to reproduce correct bond lengths for eclipsed single bonds. This error is especially notable in the case of five-membered rings.

In order to alleviate some of the deficiencies inherent in the MM2 program, MM3 has been developed. Although the force field is similar to MM2, a new torsion-stretch interaction has been included. In addition, cyclopentane rings have been given new parameters, distinct from those used for straight-chain alkanes. The MM3 results for five-membered rings should therefore be more reliable.

Molecular modelling programs can provide several

different pieces of information. They are perhaps most useful as a means of optimizing a structure from a set of rough coordinates. In addition, molecular modelling can provide the heat of formation and the strain energy for a given structure. Recently, molecular modelling programs such as PCMODEL (41) have been developed, allowing the starting structures to be sketched on the computer screen with a mouse and eliminating the need to calculate initial coordinates by hand.

The dihedral driver option of the MM2 and MM3 programs can be very useful. A specified dihedral angle is fixed at a given value, and the rest of the structure is optimized. The value of the dihedral angle is then incremented, and the calculation is repeated. The variation in the steric energy with dihedral angle can be informative.

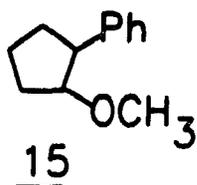
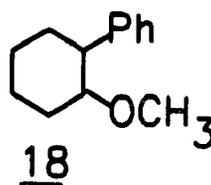
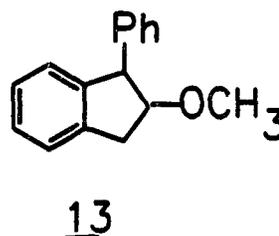
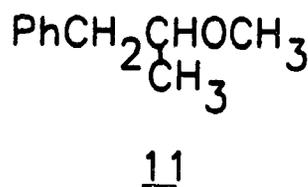
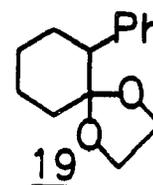
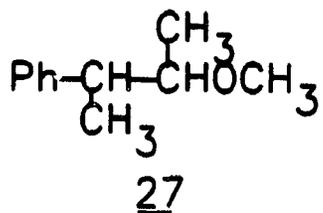
The original MM2 program worked especially well for unconjugated hydrocarbon systems. However, it was unable to accurately predict the properties of conjugated  $\pi$  systems. The effect of bond order variation must be considered. This problem was corrected by the introduction of the MMP2 program. MMP2 makes use of the self-consistent field (SCF) method to determine the bond orders for the conjugated  $\pi$  system. There is a good correlation between bond order and bond length. Therefore, the results of the SCF calculation can be used in the ordinary MM2 calculation to optimize the structure. If the optimized structure is significantly

different from the original geometry, the SCF calculation is repeated and the structure is reoptimized. The procedure is repeated until an internally consistent solution is achieved. When MMP2 is used, the Dewar resonance energy can be obtained as part of the output. This SCF calculation is also part of the more recently developed MM3 program.

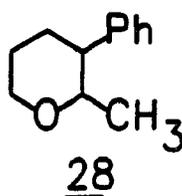
## 2. RESULTS

The compounds of interest are shown in Chart 1; all of these were investigated with molecular mechanics. The diastereomers of 2-methoxy-3-phenylbutane (27) and the cis isomer of 2-methyl-3-phenyltetrahydropyran (28) were prepared and used in the photochemical investigation.

Chart 1: Compounds of interest.

cis and transcis and transcis and trans

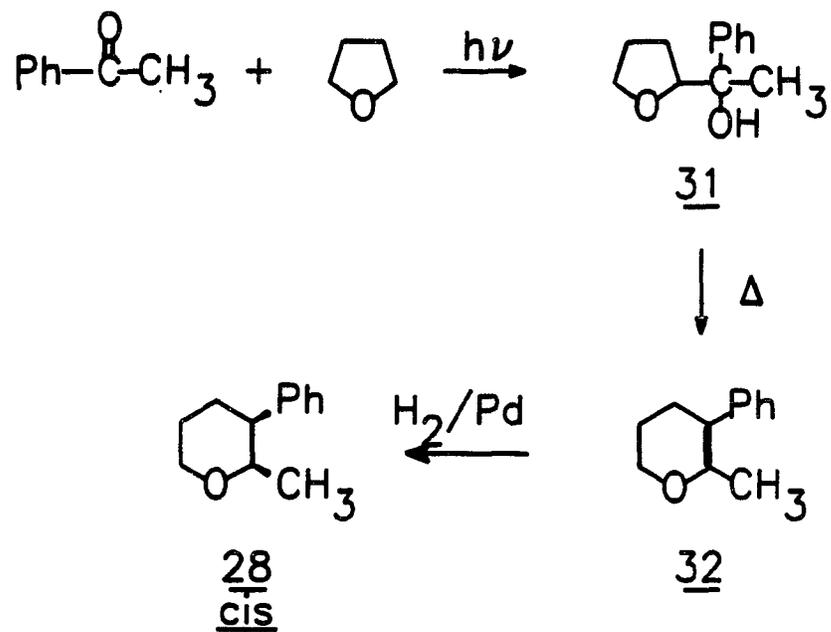
(2R,3R)/(2S,3S) and  
(2R,3S)/(2S,3R)

cis and trans

2-Methoxy-3-phenylbutane (27) is a known compound. 3-Phenyl-2-butanol (29) was prepared by the addition of a methyl Grignard reagent to DL-2-phenylpropionaldehyde (30). The resultant diastereomeric alcohols were separated by ester derivatization followed by fractional crystallization (42). The separated diastereomers were converted back to alcohols by base-catalyzed hydrolysis, and the alcohols were then methylated with sodium hydride and dimethyl sulfate. Both diastereomers of 2-methoxy-3-phenylbutane (27) were characterized by  $^1\text{H}$  nmr spectroscopy.

Cis-2-methyl-3-phenyltetrahydropyran (28) is a new compound, and was prepared by a three-step synthesis (Scheme 2). Acetophenone was irradiated in the presence of tetrahydrofuran, producing  $\alpha$ -methylphenyltetrahydrofuryl carbinol (31). 2-Methyl-3-phenyl-5,6-dihydropyran (32) was prepared from this carbinol by pyrolysis on neutral alumina (43). Hydrogenation over 10% Pd on activated carbon yielded the desired isomer of 2-methyl-3-phenyltetrahydropyran (28). It was fully characterized by  $^1\text{H}$  nmr,  $^{13}\text{C}$  nmr, ir spectroscopy, mass spectroscopy, and elemental analysis.

Scheme 2: Synthesis of cis-2-methyl-3-phenyltetrahydropyran (28).



Solutions of the ether and 1,4-dicyanobenzene (2), the electron-accepting photosensitizer, in 3:1 acetonitrile-methanol were degassed by nitrogen ebullition and irradiated through Pyrex in a constant temperature bath held at 10°C. Reaction progress was followed by gas chromatography with flame ionization detection (gc/fid) and by gas chromatography with mass selective detection (gc/ms). The results of the irradiations are summarized in Table 2.

All three of the ethers cleaved, albeit inefficiently. The identification of the products was by comparison of gc/ms retention times and mass spectra with those of authentic samples, or from analysis of the  $^1\text{H}$  and  $^{13}\text{C}$  nmr spectra. Identification of trace amounts of the diastereomers of 2,3-diphenylbutane (33) rests tentatively on the observed mass spectra. Acetaldehyde methyl 4-phenylbutyl acetal (34) was identified after acid hydrolysis of the reaction mixture to yield 4-phenyl-1-butanol (35). The retention time and mass spectrum of this alcohol were compatible with an authentic sample.

Table 2: Results of irradiations.

Starting material	Products (yield <sup>a</sup> , %)
(2R,3S)- and (2S,3R)- 2-methoxy-3-phenyl- butane ( <u>27</u> )	ethylbenzene (8%) 1-(4-cyanophenyl)- 1-phenylethane ( <u>36</u> ) (20%) 2,3-diphenylbutane ( <u>33</u> ) (trace)
(2R,3R)- and (2S,3S)- 2-methoxy-3-phenyl- butane ( <u>27</u> )	ethylbenzene (6%) 1-(4-cyanophenyl)- 1-phenylethane ( <u>36</u> ) (24%) 2,3-diphenylbutane ( <u>33</u> ) (trace)
<u>cis</u> -2-methyl-3-phenyl- tetrahydropyran ( <u>28</u> )	acetaldehyde methyl 4-phenylbutyl acetal ( <u>34</u> ) (21%)

-----  
<sup>a</sup>All yields are based on consumption of ether.

The percent conversion of the starting materials was determined by using gc/fid, with cyclododecane as an internal standard. Cyclododecane was also used as an internal standard in the determination of the yield of ethylbenzene by gc/ms. The detector was calibrated with solutions containing known ratios of ethylbenzene to cyclododecane. The yield of 4-phenyl-1-butanol (35) was determined similarly. The crude photolysates from the irradiations of the diastereomers of 27 were chromatographed on silica gel: the yield of 1-(4-cyanophenyl)-1-phenylethane (36) was determined by analysis of <sup>1</sup>H nmr spectra of fractions containing a mixture of 36 and recovered ether 27.

Deuterium-incorporation studies were carried out as described above, using CH<sub>3</sub>OD in the solvent mixture. The reactions were followed with gc/ms, using selected ion monitoring. There was no evidence of deuterium incorporation in either diastereomer of 27, or in 28 cis.

Oxidation potentials were determined by cyclic voltammetry. The voltammograms were typical of irreversible oxidation; the oxidation potentials were determined by correcting the anodic peak potentials (44,45). The free energies of the electron-transfer reactions were calculated by using the measured oxidation potentials (equation 1). The values are summarized in Table 3.

Table 3: Oxidation potentials and calculated free energies for electron transfer from ethers.

	$E_D$ (V) <sup>a</sup>	$\Delta G_e$ (kJ mol <sup>-1</sup> ) <sup>b</sup>
<u>cis</u> -1-methoxy-2-phenyl-cyclopentane (15)	2.02 <sup>c</sup>	-59
<u>trans</u> -1-methoxy-2-phenyl-cyclopentane (15)	2.02 <sup>c</sup>	-59
<u>trans</u> -1-methoxy-2-phenyl-cyclohexane (18)	2.22 <sup>c</sup>	-39
6-phenyl-1,4-dioxaspiro-[4.5]decane (19)	2.08 <sup>c</sup>	-53
2-methoxy-1-phenylpropane (11)	2.18 <sup>d</sup>	-43
<u>trans</u> -2-methoxy-1-phenylindane (13)	2.01 <sup>c</sup>	-60
(2R,3S)- and (2S,3R)-2-methoxy-3-phenylbutane (27)	2.36	-26
(2R,3R)- and (2S,3S)-2-methoxy-3-phenylbutane (27)	2.27	-35
<u>cis</u> -2-methyl-3-phenyl-tetrahydropyran (28)	2.38	-24

-----  
<sup>a</sup>Reported vs saturated calomel electrode.

<sup>b</sup>Calculated by using the Weller equation:

$E_{0,0} = 408.4 \text{ kJ mol}^{-1}$ ,  $E_A = -1.66 \text{ V (vs SCE)}$ , and the electrostatic term was taken to be  $5.40 \text{ kJ mol}^{-1}$ .

<sup>c</sup>Reference 15.

<sup>d</sup>Reference 7.

<sup>e</sup>Reference 5.

The structures of 1-methoxy-2-phenylcyclopentane (cis and trans) (15), 1-methoxy-2-phenylcyclohexane (cis and trans) (18), and 6-phenyl-1,4-dioxaspiro[4.5]decane (19) were optimized (steric energies were minimized) with the 1987 force field of the MMP2 program. The acyclic ethers 2-methoxy-1-phenylpropane (11) and 2-methoxy-3-phenylbutane (27) (both diastereomers) were optimized with the 1988 force field of the MM3 program, as were the cis and trans isomers of both 2-methyl-3-phenyltetrahydropyran (28) and 2-methoxy-1-phenylindane (13).

The dihedral driver option of the molecular mechanics program was used to investigate the effect of rotation about bonds. For the 1-methoxy-2-phenylcyclopentane (15) and 1-methoxy-2-phenylcyclohexane isomers (18), the OCH<sub>3</sub> group was rotated first. Initial calculations used angle increments of 30°. Large step sizes can give inaccurate results, but the minima were always reinvestigated with smaller increments. Once the minima were located, the dihedral driver option was used again to rotate the phenyl group, giving fully optimized structures. In the acyclic systems, the first rotation was about the central C-C bond, followed by rotation of the methoxy group.

Although it is the radical cation which deprotonates, molecular mechanics calculations were carried out on the neutral molecules. The lifetime of the radical cation is short, and little reorientation will take place in the

period between electron transfer and disappearance of the radical cation.

For each molecule, a number of starting conformations was considered. Not all initial conformations led to distinct conformers. The results of the optimizations are tabulated in Tables 4-15: magnitudes of selected dihedral angles are reported. The structures of the global minima are shown in Figures 10-19, 21, and 22.

### 3. DISCUSSION

The first three steps of the proposed mechanism for the cleavage reaction (Scheme 1) should occur readily.

Calculated values of the free energy for electron transfer between excited 1,4-dicyanobenzene and the ethers are all more negative than  $-20 \text{ kJ mol}^{-1}$  (Table 3): electron transfer should take place at the diffusion-controlled rate. Back electron transfer is extremely exergonic, and although it should be in the Marcus inverted region, it will still be sufficiently rapid to make this pathway the most likely for the radical cation (i.e. the quantum yield for the cleavage should be low).

Step 4 is the actual carbon-carbon bond cleavage of the radical cation. When the bond strength is well below the threshold value, cleavage will occur readily. If the bond energy is markedly above the threshold, no cleavage will be observed. However, when the carbon-carbon bond energy in the radical cation is near the threshold value ( $50 \text{ kJ mol}^{-1}$ ), other factors become important. In earlier considerations, it was assumed that the activation barrier to the cleavage step was approximately the same as the enthalpy change for the process. This assumption is not always valid.

In previous cases (7), lack of reactivity has been attributed to insufficient overlap of the singly occupied molecular orbital (SOMO) with the carbon-carbon bond

expected to cleave. In the radical cations of all of the compounds under investigation, the SOMO is largely associated with the phenyl group. Therefore, in order for cleavage to occur, the plane of the phenyl ring must be roughly perpendicular to the benzylic C-C bond. Also, the O-R moiety of the ether should be gauche to the vulnerable C-C bond. It is not sufficient for the molecule to be able to attain this conformation. The lifetime of the radical cation is too short for rotation to occur before back electron transfer takes place. The conformation must be correct in the neutral molecule if the radical cation is to cleave.

It has been found that the cis and trans isomers of 1-methoxy-2-phenylcyclohexane (18) and 6-phenyl-1,4-dioxaspiro[4.5]decane (19) are inert when irradiated in 3:1 acetonitrile-methanol in the presence of DCB (2) (15). This lack of reactivity can be rationalized with the results of the molecular mechanics optimizations.

The lowest energy conformer of cis-1-methoxy-2-phenylcyclohexane (18) (as determined with MMP2) is shown in Figure 10. The absolute value of the dihedral angle between the methyl group bonded to the oxygen and the C-C bond to be cleaved was calculated to be 170°: in the most stable conformer, this methyl group is nearly antiperiplanar to the C-C bond. The dihedral angle of the phenyl group with respect to the geminal hydrogen was calculated to be 26°;

the angle with respect to the C-C bond was  $94^\circ$ .

A Karplus-type relationship can be used to evaluate the degree of overlap between orbitals (46). In order for deprotonation to occur, the SOMO and the benzylic C-H bond must overlap. For maximum overlap, the angle between the SOMO and the C-H bond should be  $0^\circ$ . Since the molecular mechanics program calculates the positions of atoms, not orbitals, it is more convenient to consider the angle between the plane of the phenyl ring and the C-H bond. The orbital overlap is maximum when this angle is  $90^\circ$ . The fraction of maximum overlap is  $(1 - \cos^2\phi_{\text{Ph-CH}})$ , where  $\phi_{\text{Ph-CH}}$  is the dihedral angle between the C-H bond and the plane of the phenyl ring. Similarly, in order for carbon-carbon bond cleavage to take place, the dihedral angle between the plane of the phenyl group and the C-C bond should approach  $90^\circ$ : the degree of overlap is  $(1 - \cos^2\phi_{\text{Ph-CC}})$ . If  $\phi_{\text{OCH}_3}$  is the dihedral angle between the C-C bond and the O-CH<sub>3</sub> bond, then the degree of overlap between an  $sp^3$ -type lone pair and the C-C antibonding orbital is  $\cos^2(\phi_{\text{OCH}_3} - 60^\circ)$ , since  $60^\circ$  is the angle at which this overlap will be maximum.

Table 4: Conformers of cis-1-methoxy-2-phenylcyclohexane (18).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{Ph-CH} $ , (overlap)	$ \phi_{Ph-CC} $ , (overlap)	$ \phi_{OCMe} $ , (overlap)
28.1 (Ph ax)	16°, (8%)	79°, (96%)	95°, (67%)
24.8 (Ph eq)	32°, (28%)	83°, (99%)	86°, (81%)
20.9 (Ph ax)	59°, (74%)	61°, (76%)	72°, (96%)
15.8 (Ph ax)	47°, (54%)	13°, (5%)	167°
14.2 (Ph ax)	45°, (50%)	13°, (5%)	57°, (100%)
14.0 (Ph ax)	44°, (48%)	14°, (6%)	67°, (98%)
7.15 (Ph eq)	56°, (69%)	1°, (0%)	170°
0.0 (Ph eq)	26°, (19%)	94°, (100%)	170°

Table 5: Conformers of trans-1-methoxy-2-phenylcyclohexane (18).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{Ph-CH} $ , (overlap)	$ \phi_{Ph-CC} $ , (overlap)	$ \phi_{OCMe} $ , (overlap)
39.6 (Ph ax)	24°, (16%)	42°, (45%)	73°, (99%)
20.0 (Ph ax)	61°, (76%)	6°, (1%)	80°, (88%)
18.9 (Ph ax)	62°, (78%)	7°, (1%)	168°
18.7 (Ph ax)	60°, (75%)	56°, (69%)	82°, (86%)
18.0 (Ph ax)	58°, (72%)	58°, (72%)	170°
8.08 (Ph eq)	1°, (0%)	61°, (76%)	70°, (97%)
0.0 (Ph eq)	2°, (0%)	63°, (79%)	160°

Table 6: Conformers of 6-phenyl-1,4-dioxaspiro[4.5]decane (19).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{Ph-CH} $ , (overlap)	$ \phi_{Ph-CC} $ , (overlap)	$ \phi_{OR} $
0.79	19°, (11%)	80°, (97%)	155°, 155°
0.50	24°, (17%)	85°, (99%)	115°, 141°
0.0	20°, (12%)	81°, (98%)	137°, 112°

Figure 10: Global-minimum conformer of cis-1-methoxy-2-phenylcyclohexane (18), viewed along the plane of the phenyl ring.

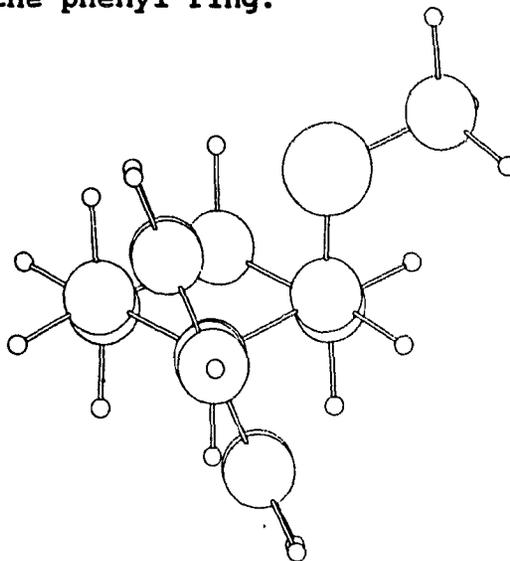
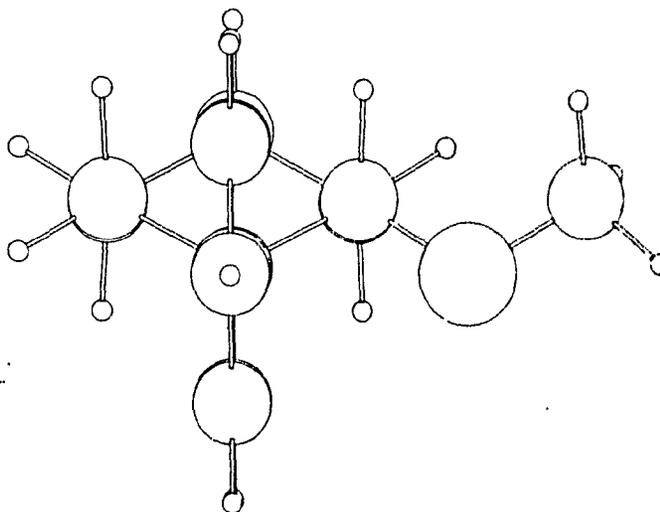


Figure 11: Global-minimum conformer of trans-1-methoxy-2-phenylcyclohexane (18), viewed along the plane of the phenyl ring.



Although the phenyl group is well aligned for cleavage in the global-minimum conformer of the cis isomer of 18, the orientation of the methyl group prevents interaction of the nonbonding electrons on oxygen with the C-C antibonding orbital. The lowest energy conformer suitably aligned for cleavage was calculated to have a heat of formation 20.9 kJ mol<sup>-1</sup> above that of the global minimum.

In order to incorporate deuterium or isomerize, the substrate molecule must deprotonate from the benzylic position. In the global-minimum conformer of 18 cis, the dihedral angle of the phenyl group with respect to the benzylic C-H bond is small, preventing good overlap of the SOMO with the benzylic C-H bond (26° = 19% overlap). The conformer closest in energy to the global minimum was calculated to have a Ph-CH angle of 56°. Deprotonation of this conformer may be feasible. However, this conformer was calculated to have a heat of formation 7.15 kJ mol<sup>-1</sup> above that of the most stable conformer. The population of this conformer is evidently too small to contribute to the reactivity of this isomer.

Similarly, the global-minimum conformer of trans-1-methoxy-2-phenylcyclohexane (18) is expected to be unreactive (Figure 11). The nearest conformer suitably aligned for cleavage was calculated to be 8.08 kJ mol<sup>-1</sup> above this, and the lowest energy conformer which could deprotonate was calculated to be 18.0 kJ mol<sup>-1</sup> above the

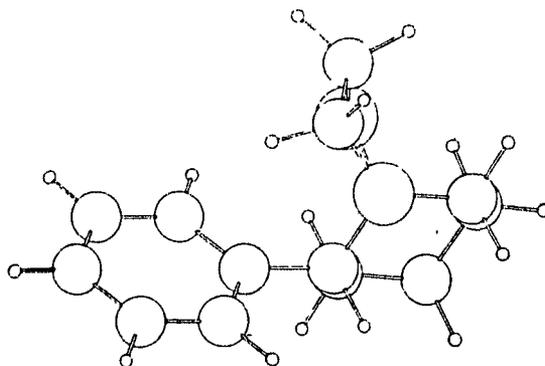
global minimum. (The most stable conformer of this isomer was 4.52 kJ mol<sup>-1</sup> lower in energy than that of the cis isomer.) As for the cis isomer, the MMP2 results rationalize the lack of reactivity.

Optimization of 6-phenyl-1,4-dioxaspiro[4.5]decane (19) resulted in the identification of three conformers (Table 6, Figure 12). In all three, the phenyl group is suitably oriented for C-C bond cleavage but not for deprotonation at the benzylic position. However, in all cases, the orientation of the dioxolane ring makes cleavage unfeasible. The calculations are in agreement with the observed lack of reactivity.

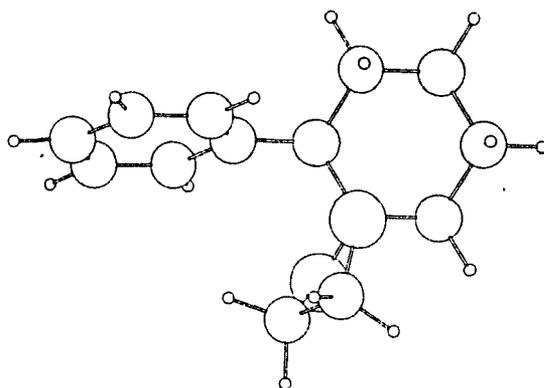
The structure of the lowest energy conformer of cis-1-methoxy-2-phenylcyclopentane (15) is shown in Figure 13. The orientation of the methoxy group prevents interaction of the nonbonding electrons with the C-C antibonding orbital, preventing cleavage of the radical cation. However, the orientation of the phenyl group should allow sufficient overlap of the SOMO and the benzylic C-H bond ( $64^\circ \approx 81\%$  overlap), making deprotonation and isomerization feasible. This is in accord with the experimental results. (The lowest energy conformer which could cleave was calculated to be 5.82 kJ mol<sup>-1</sup> above the global minimum.)

Figure 12: Global-minimum conformer of 6-phenyl-  
1,4-dioxaspiro[4.5]decane (19).

a) Looking down the oxygen (equatorial)-carbon bond.



b) Looking down the oxygen (axial)-carbon bond.



c) Viewed along the plane of the phenyl ring.

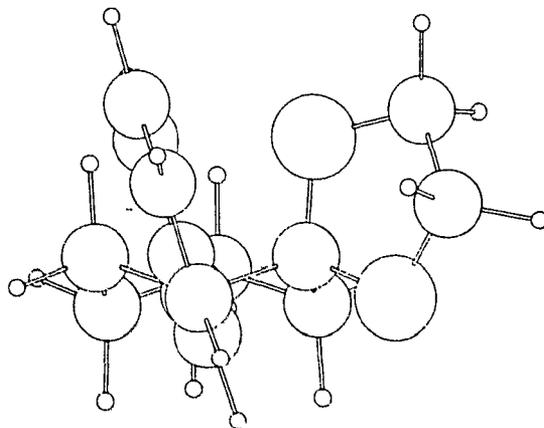


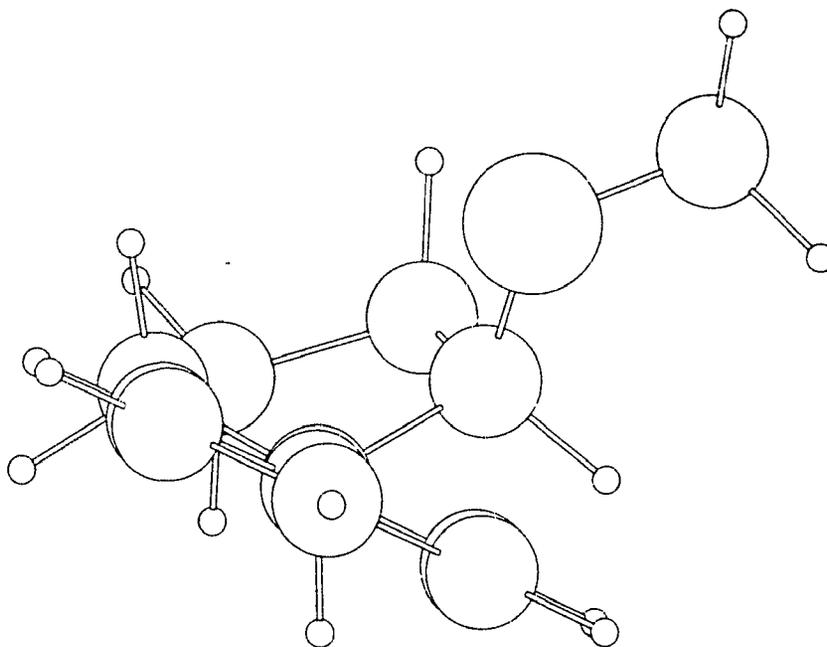
Table 7: Conformers of cis-1-methoxy-2-phenylcyclopentane (15).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $ , (overlap)	$ \phi_{\text{Ph-CC}} $ , (overlap)	$ \phi_{\text{OCH}_3} $ , (overlap)
15.2	70°, (88%)	48°, (55%)	56°, (100%)
8.49	15°, (7%)	76°, (94%)	73°, (95%)
7.62	29°, (24%)	31°, (26%)	168°
7.15	24°, (16%)	34°, (31%)	68°, (98%)
5.82	51°, (60%)	68°, (86%)	100°, (59%)
4.94	33°, (30%)	89°, (100%)	170°
0.0	64°, (81%)	55°, (67%)	165°

Table 8: Conformers of trans-1-methoxy-2-phenylcyclopentane (15).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $ , (overlap)	$ \phi_{\text{Ph-CC}} $ , (overlap)	$ \phi_{\text{OCH}_3} $ , (overlap)
15.0	53°, (64%)	1°, (0%)	46°, (94%)
14.5	5°, (1%)	61°, (76%)	48°, (96%)
10.3	40°, (41%)	81°, (98%)	163°
9.83	34°, (31%)	25°, (18%)	162°
1.8	4°, (0%)	59°, (74%)	82°, (86%)
0.2	5°, (1%)	54°, (66%)	71°, (96%)
0.2	56°, (69%)	0°, (0%)	174°
0.0	0°, (0%)	59°, (74%)	173°

Figure 13: Global-minimum conformer of cis-1-methoxy-2-phenylcyclopentane (15), viewed along the plane of the phenyl ring.



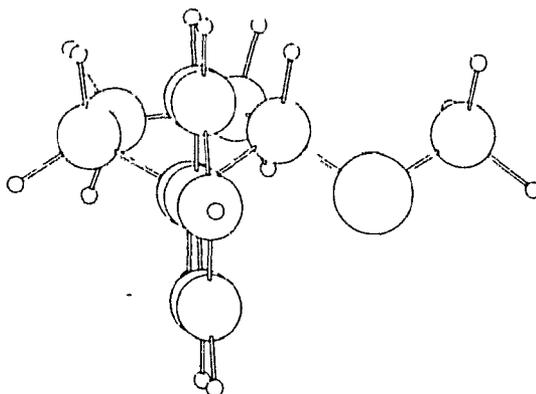
Analysis of the trans isomer of 1-methoxy-2-phenylcyclopentane (15) was more complicated. Instead of one easily recognizable global minimum, optimization resulted in three local minima of comparable energy (Table 8, Figure 14).

The global minimum is predicted to be inert. However, there are two conformers calculated to be only 0.2 kJ mol<sup>-1</sup> above this. Cleavage does not appear to be feasible for the first of these, although deprotonation may be possible. However, the methyl group in the other conformer is gauche to the C-C bond to be cleaved: the nonbonding electrons should be able to stabilize the transition state for the cleavage. Experimentally, this isomer does undergo carbon-carbon bond cleavage.

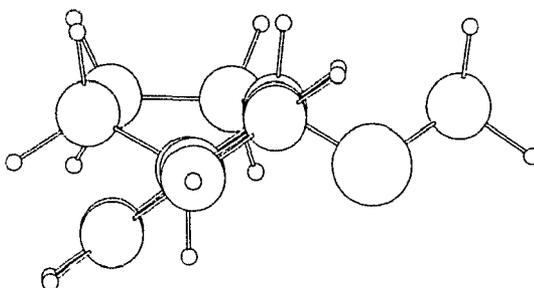
It could be argued that relief of strain plays a part in the cleavage of these cyclic systems: the cleavage of the more strained isomer would be expected to have a greater driving force. This effect does not seem to play an important role in this case. The calculated difference in steric energies for the cis and trans isomers of 15 is only 2.8 kJ mol<sup>-1</sup>. The trans isomer is more stable, and yet this is the isomer that undergoes C-C bond cleavage.

Figure 14: Low-energy conformers of trans-1-methoxy-2-phenylcyclopentane (15), viewed along the plane of the phenyl ring.

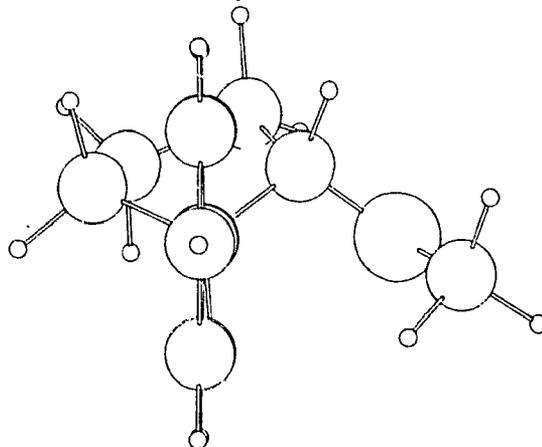
a) The global-minimum conformer.



b) An unreactive conformer (0.2 kJ mol<sup>-1</sup> above the global minimum).



c) The reactive conformer (0.2 kJ mol<sup>-1</sup> above the global minimum).



In addition to these cyclic systems, Arnold and Lamont have studied the behavior of the radical cation of 2-methoxy-1-phenylpropane (11) (7). The bond dissociation energy of this radical cation is greater than that of the cyclic radical cations considered above: cleavage would give a 1°, not 2°, benzylic radical. Based on energetic criteria alone, it is surprising that this ether cleaves readily (reaction 5) while many of the analogous cyclic ethers are inert.

Calculations with MM3 suggest that the global-minimum conformer of 2-methoxy-1-phenylpropane (11) should be inert (Table 9). Although the phenyl group is well oriented for cleavage, the methoxy group is antiperiplanar to the susceptible C-C bond. However, potentially reactive conformers were identified 0.59 kJ mol<sup>-1</sup> and 4.23 kJ mol<sup>-1</sup> higher in energy than this. The populations of these conformations must be sufficient for this ether to react.

The reactivities of the cis and trans isomers of 2-methoxy-1-phenylindane (13) have also been investigated (5). It was initially predicted that the bis-benzylic C-C bond would cleave, since the bond dissociation energy in the radical cation is below the threshold. However, neither isomer cleaved: instead, they interconverted via the deprotonation-reprotonation mechanism.

Table 9: Conformers of 2-methoxy-1-phenylpropane (11).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $ ; (overlap)	$ \phi_{\text{Ph-CC}} $ ; (overlap)	$ \phi_{\text{OCH}_3} $ ; (overlap)
17.9 (Ph anti H)	36°, 27°; (35%, 21%)	87°, (100%)	92°, (72%)
12.4 (Ph anti Me)	27°, 37°; (21%, 36%)	84°, (99%)	72°, (96%)
9.46 (Ph anti OMe)	42°, 22°; (45%, 14%)	79°, (96%)	67°, (99%)
4.23 (Ph anti H)	25°, 40°; (18%, 41%)	84°, (99%)	83°, (85%)
3.3 (Ph anti H)	25°, 39°; (18%, 40%)	84°, (99%)	165°
1.1 (Ph anti Me)	33°, 30°; (30%, 25%)	90°, (100%)	159°
0.59 (Ph anti OMe)	45°, 19°; (50%, 11%)	78°, (96%)	82°, (86%)
0.0 (Ph anti OMe)	44°, 20°; (48%, 12%)	78°, (96%)	161°

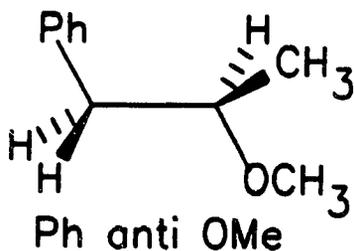
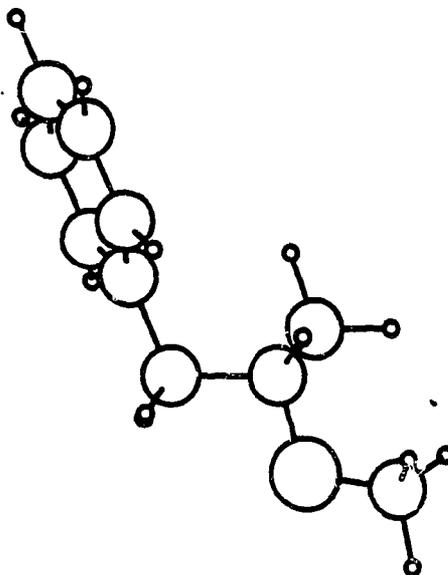
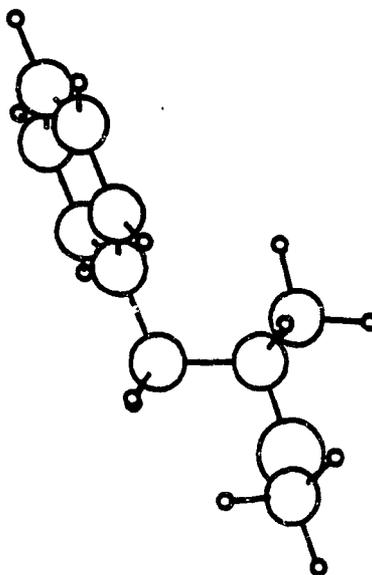


Figure 15: Low-energy conformers of 2-methoxy-1-phenylpropane (11).

a) The global-minimum conformer.



b) A reactive conformer (0.59 kJ mol<sup>-1</sup> above the global minimum).



The lack of cleavage was easily explained. An electron can be more easily removed from the more highly substituted fused ring than from the unfused phenyl group. Therefore, the SOMO of the radical cation will be largely associated with the fused ring. The bis-benzylic C-C bond is held in roughly the same plane as the fused ring, preventing overlap with the SOMO and making C-C cleavage unfeasible. The bis-benzylic C-H bond is much more suitably aligned for cleavage.

The orientation of the unfused ring becomes important when substitution on the rings alters the site of the SOMO. Arnold, Du, and Henseleit studied the effect of a methoxy group on the unfused ring (47). This lowered the oxidation potential to the point where the SOMO was localized on the unfused ring: it was hoped that this would allow overlap between the SOMO and the bis-benzylic C-C bond. No C-C cleavage was observed for either trans-2-methoxy-1-(3-methoxyphenyl)indane (37) or trans-2-methoxy-1-(4-methoxyphenyl)indane (38). However, this was explained in terms of energetics, not conformation. The substitution of the methoxy group on the phenyl ring lowers the oxidation potential of the indane to the point where the C-C bond energy in the radical cation is above the cleavage threshold.

Currently, other members of the Arnold group are working to substitute a cyano group on the fused ring. This

electron-withdrawing group would make it more difficult to remove an electron from the fused ring, and so the SOMO would be localized on the unfused ring. The oxidation potential of this molecule should be high enough to allow the cleavage to occur.

Molecular mechanics calculations were carried out to add support to these arguments. Only the parent compound, 2-methoxy-1-phenylindane (13), was considered, since the substitutions on the benzene rings should have little effect on the conformation. The orientations of both benzene rings were examined (Table 10,11).

If the SOMO is considered to be localized on the fused ring, cleavage is indeed unlikely: the overlap between the SOMO and the bis-benzylic C-C bond was calculated to be less than 13% in all conformers of both the cis and trans isomers. Deprotonation of both isomers is feasible, however. The geometry of the global-minimum conformer of the trans isomer is almost perfect for deprotonation (99% overlap). The lowest energy conformer of the cis isomer deviates considerably from the ideal, but the overlap between the SOMO and the C-H bond is still almost 50% of the the maximum possible. Even if this were insufficient to permit deprotonation, there is a conformer only 2.9 kJ mol<sup>-1</sup> above the global minimum which is almost perfectly aligned. In any case, it is not surprising that the parent compound reacted as it did.

Table 10: Conformers of cis-2-methoxy-1-phenylindane (13).

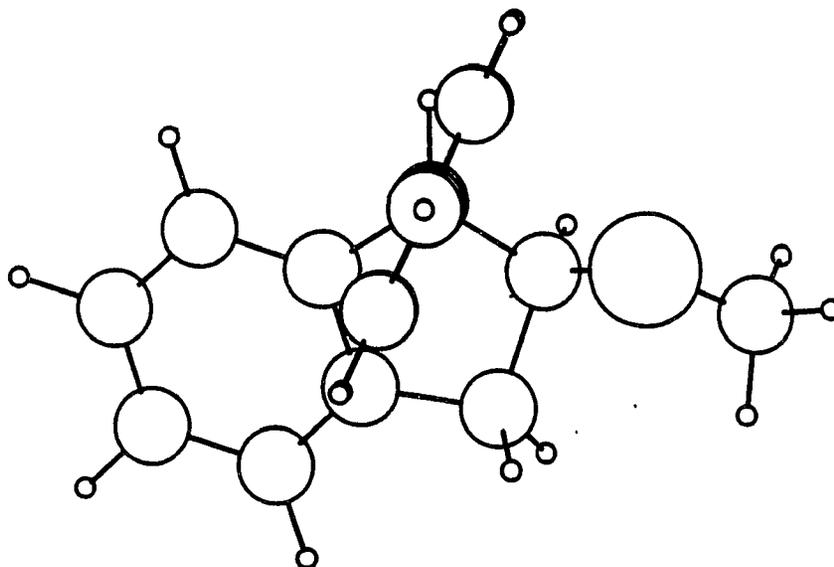
Energy above global minimum (kJ mol <sup>-1</sup> )	fused ring		unfused ring		
	$ \phi_{\text{Pb-CH}} $	$ \phi_{\text{Pb-CC}} $	$ \phi_{\text{Pb-CH}} $	$ \phi_{\text{Pb-CC}} $	$ \phi_{\text{OCH}_3} $
20.0	82°	17°	40°	78°	72°
17.9	43°	21°	34°	89°	92°
4.1	84°	18°	20°	80°	103°
2.9	85°	19°	19°	80°	160°
0.59	46°	19°	6°	64°	79°
0.0	44°	21°	26°	83°	171°

Table 11: Conformers of trans-2-methoxy-1-phenylindane (13).

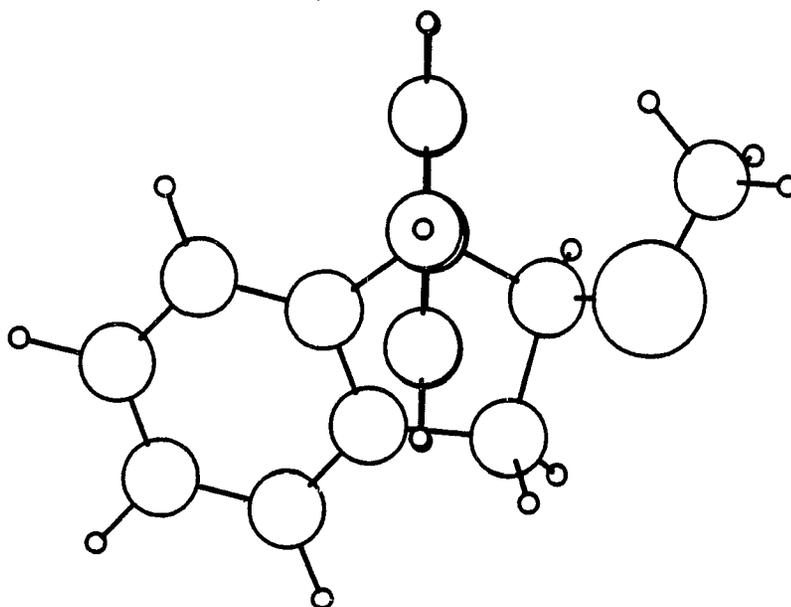
Energy above global minimum (kJ mol <sup>-1</sup> )	fused ring		unfused ring		
	$ \phi_{\text{Pb-CH}} $	$ \phi_{\text{Pb-CC}} $	$ \phi_{\text{Pb-CH}} $	$ \phi_{\text{Pb-CC}} $	$ \phi_{\text{OCH}_3} $
17.3	84°	20°	12°	69°	50°
13.9	45°	17°	24°	81°	61°
4.44	45°	19°	27°	85°	162°
4.1	45°	18°	26°	83°	85°
0.67	85°	19°	2°	61°	80°
0.0	85°	20°	12°	70°	170°

**Figure 16: Low-energy conformers of cis-2-methoxy-1-phenylindane (13), viewed along the plane of the unfused phenyl ring.**

**a) The global-minimum conformer.**

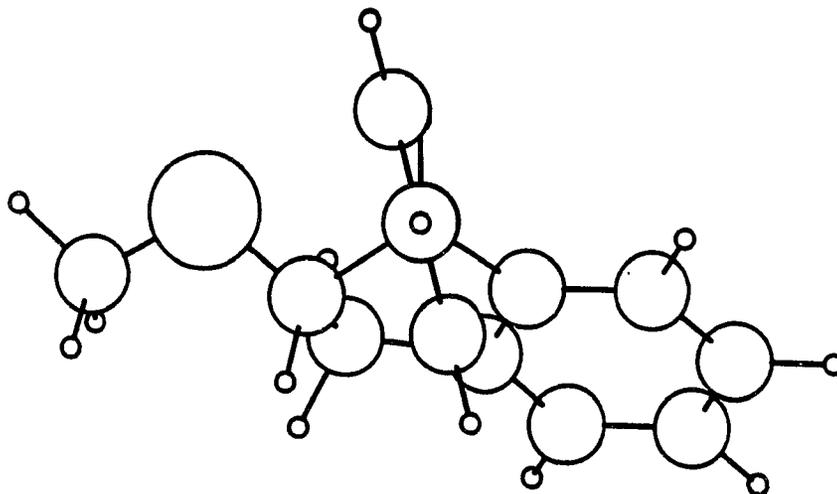


**b) A reactive conformer (0.59 kJ mol<sup>-1</sup> above the global minimum).**

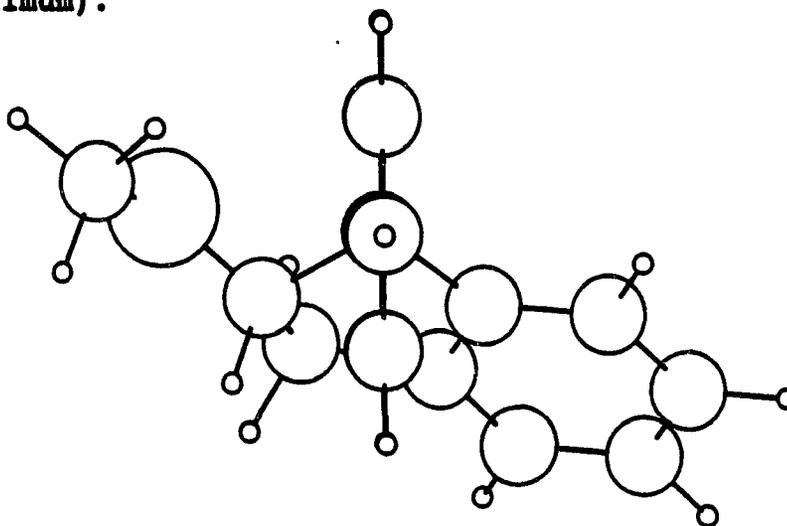


**Figure 17:** Low-energy conformers of trans-2-methoxy-1-phenylindane (**13**), viewed along the plane of the unfused phenyl ring.

**a) The global-minimum conformer.**



**b) A reactive conformer (0.67 kJ mol<sup>-1</sup> above the global minimum).**



If the SOMO is considered to be localized on the unfused ring, the expected reactivities are different. The cis isomer is predicted to undergo C-C bond cleavage, since there is a conformer only 0.59 kJ mol<sup>-1</sup> above the global minimum which is properly aligned. (The global minimum may deprotonate inefficiently, since the overlap of the SOMO with the benzylic C-H bond is 19% of the maximum possible.) The results for the trans isomer are similar: in this case, the conformer that could potentially cleave is 0.67 kJ mol<sup>-1</sup> above the global minimum. (The trans isomer was calculated to be 6.57 kJ mol<sup>-1</sup> more stable than the cis isomer.)

The molecular mechanics investigation of these ethers seemed to lend support to the conformational hypotheses. The ultimate goal was to use the calculations to predict the reactivity in systems which had not yet been studied experimentally. The two diastereomers of 2-methoxy-3-phenylbutane (27) were chosen as acyclic analogues of the 1-methoxy-2-phenylcycloalkanes: as before, cleavage of the radical cations of these molecules would produce a 2°  $\alpha$ -oxy carbocation and a 2° benzylic radical. Therefore, the energetics of the cleavage are about the same as in the cyclic systems, and any differences in reactivity should be attributable to differences in conformation.

The results of the calculations on the (2R,3R) isomer of 2-methoxy-3-phenylbutane (27) are tabulated in Table 12. The global-minimum conformer is not predicted to cleave, due

to an unfavourable orientation of the OCH<sub>3</sub> group. Because the phenyl group is parallel to the geminal hydrogen, deprotonation is also unlikely. However, two potentially reactive conformers were found 9.83 kJ mol<sup>-1</sup> and 10.8 kJ mol<sup>-1</sup> above the global minimum. Both of these conformers could undergo carbon-carbon bond cleavage; the (2R,3R) isomer will cleave if the populations of these conformers is sufficient. No conformers that might undergo deprotonation and isomerization were found.

Similarly, the global-minimum conformer of the (2S,3R) isomer was predicted to be inert under the irradiation conditions (Table 13). The orientation of the methoxy group would prevent the cleavage of the three most stable conformers. However, a conformer was found 4.77 kJ mol<sup>-1</sup> above the global minimum in which the methoxy group is more favourably aligned. Therefore, cleavage of the (2S,3R) isomer seemed feasible.

Although there was no evidence for deprotonation of either diastereomer, it was found that both diastereomers of 27 cleaved inefficiently when subjected to the standard irradiation conditions. Cleavage of this molecule produces a 2° 1-phenylethyl radical and a 2° α-oxy cation. Reduction of the radical by the radical anion of the sensitizer and subsequent protonation gives ethylbenzene, which was observed in roughly 7% yield (gc/ms). Coupling of the radical fragments gives two diastereomers of 2,3-

diphenylbutane (33), which were detected in trace amounts. Coupling of the radical fragment at the ipso position of the radical anion of DCB (2) followed by loss of cyanide ion yields 1-(4-cyanophenyl)-1-phenylethane (36), which was the major product for both diastereomers.

All of the observed products involve the radical fragment. The relative amounts of these products is related to the reduction potential of the radical. The reduction potential of 2 is -1.66 V, while the reduction potential of the 1-phenylethyl radical is -1.60 V (48). Therefore, the reduction of the radical by the radical anion of 2 should be exergonic. However, the difference between these reduction potentials is not great, and it is not surprising that some products result from reactions of the unreduced radical.

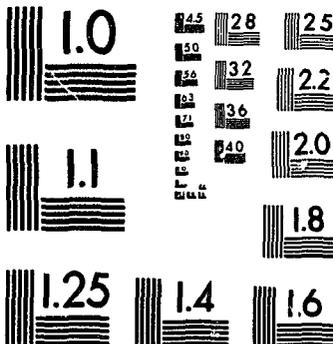
2-Methyl-3-phenyltetrahydropyran (28) was of special interest. The barriers to rotation in the acyclic systems are very low, and it is difficult to predict a priori which orientation will be most favourable. However, since tetrahydropyrans can be expected to adopt chair conformations, the equatorial lone pair on the oxygen atom can be predicted to be antiperiplanar to the C-C bond to be cleaved.

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PRECISION<sup>SM</sup> RESOLUTION TARGETS

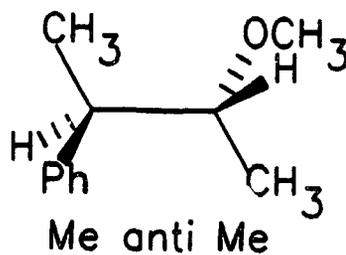
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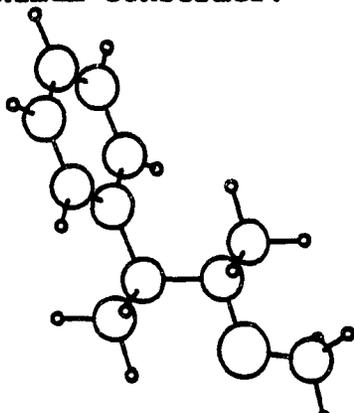
Table 12: Conformers of (2R,3R)-2-methoxy-3-phenylbutane (27).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $ , (overlap)	$ \phi_{\text{Ph-CC}} $ , (overlap)	$ \phi_{\text{OCH}_3} $ , (overlap)
27.5 (Me anti H)	6°, (1%)	71°, (89%)	97°, (64%)
22.7 (Me anti OMe)	14°, (6%)	79°, (96%)	90°, (75%)
10.8 (Me anti OMe)	24°, (17%)	89°, (100%)	84°, (83%)
9.83 (Me anti Me)	2°, (0%)	63°, (79%)	69°, (98%)
9.54 (Me anti OMe)	23°, (15%)	89°, (100%)	164°
6.53 (Me anti H)	8°, (2%)	72°, (90%)	160°
0.0 (Me anti Me)	1°, (0%)	62°, (78%)	160°

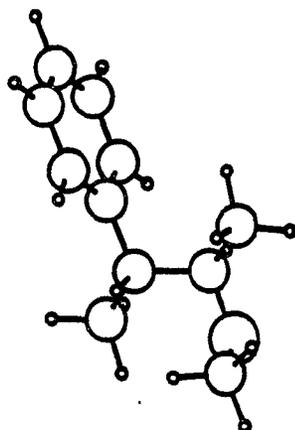


**Figure 18: Low-energy conformers of (2R,3R)-2-methoxy-3-phenylbutane (27).**

a) The global-minimum conformer.



b) A reactive conformer (9.83 kJ mol<sup>-1</sup> above the global minimum).



c) A reactive conformer (10.8 kJ mol<sup>-1</sup> above the global minimum).

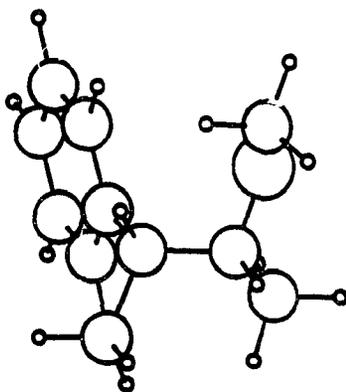
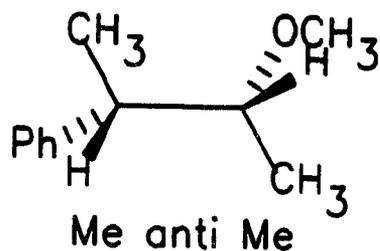


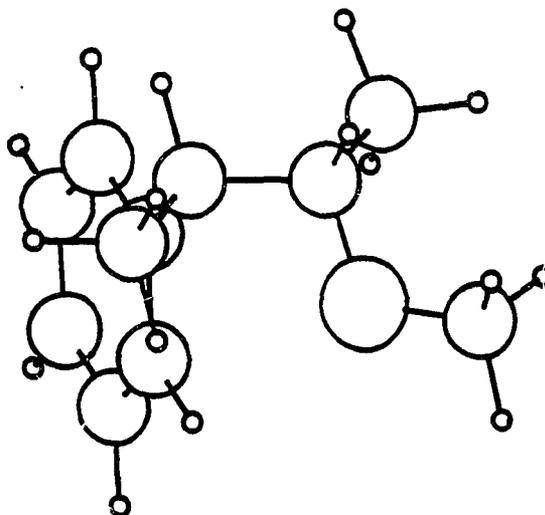
Table 13: Conformers of (2S,3R)-2-methoxy-3-phenylbutane (27).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $ , (overlap)	$ \phi_{\text{Ph-CC}} $ , (overlap)	$ \phi_{\text{OCH}_3} $ , (overlap)
23.6 (Me anti OMe)	24°, (17%)	90°, (100%)	100°, (59%)
19.0 (Me anti Me)	23°, (15%)	88°, (100%)	98°, (62%)
10.6 (Me anti OMe)	1°, (0%)	59°, (73%)	67°, (99%)
4.77 (Ph anti OMe)	27°, (21%)	89°, (100%)	80°, (88%)
4.48 (Ph anti OMe)	27°, (21%)	89°, (100%)	160°
1.4 (Me anti OMe)	5°, (1%)	67°, (85%)	153°
0.0 (Me anti Me)	9°, (2%)	72°, (90%)	164°

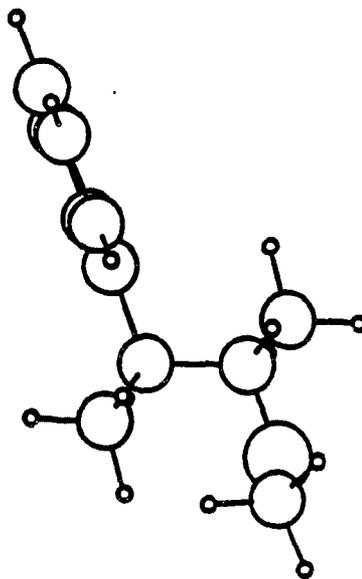


**Figure 19: Low-energy conformers of (2S,3R)-2-methoxy-3-phenylbutane (27).**

**a) The global-minimum conformer.**



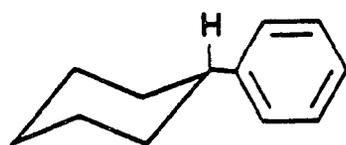
**b) A reactive conformer (4.77 kJ mol<sup>-1</sup> above the global minimum).**



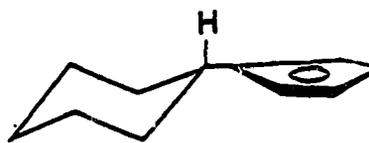
An MM1 study by Allinger and Tribble (49) has shown that the most stable conformer of phenylcyclohexane has the phenyl group in the equatorial position, with the ring parallel to the geminal C-H bond (Figure 20a). This orientation of the phenyl group minimizes interactions between the ortho hydrogens and the equatorial hydrogens on C2 and C6. However, if additional substituents on the cyclohexane ring force the phenyl group to be in the axial position, the most favorable conformer will have the phenyl ring perpendicular to the geminal C-H bond (Figure 20d). In this way, interactions between the ortho hydrogens and the axial hydrogens on the cyclohexane ring are minimized. The conformational free energy difference between the axial and equatorial conformations of phenylcyclohexane (i.e. the A value) is reported to be 8.4 - 13 kJ mol<sup>-1</sup> in favour of the equatorial (50). Allinger has calculated the free-energy difference to be 15.3 kJ mol<sup>-1</sup>. Since there is no substituent geminal to the phenyl group in 2-methyl-3-phenyltetrahydropyran (28), it was expected that the phenyl group would be in the equatorial position, oriented parallel to the geminal C-H bond. Although this would make deprotonation of the radical cation unlikely, this would give reasonably good overlap between the SOMO and the C-C bond. As mentioned above, the orientation of the lone pairs also seemed suitable. Before the structures were optimized with MM3, it was believed that both the cis and trans

isomers of this compound would undergo photosensitized carbon-carbon bond cleavage.

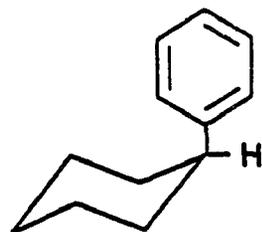
Figure 20: Possible conformations of phenylcyclohexane.



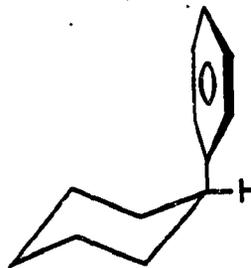
(a)



(b)



(c)



(d)

Two of the starting conformations used in the optimization of cis-2-methyl-3-phenyltetrahydropyran (28) were based on a chair structure: one with the phenyl group in the axial position; the other, equatorial. Despite the initial assumption that the most stable conformers of 28 would be based on a chair-like conformation, the PCMODEL program was used to generate starting conformations with the six-membered ring in a boat conformation. However, when these structures were input into the MM3 program, the resulting conformers were all at least 21.4 kJ mol<sup>-1</sup> higher in energy than the chair-based global minimum.

The global minimum structure of the cis isomer is shown in Figure 21. The phenyl group is not in the equatorial position: the conformer with the axial phenyl group is 4.35 kJ mol<sup>-1</sup> more stable than the equatorial conformer. This calculated result is supported by the <sup>1</sup>H nmr spectrum of the compound. The proton geminal to the phenyl group has no coupling constant larger than 4 Hz, indicating that the hydrogen must be in the equatorial position. In retrospect, this result is not surprising. In this conformation of the tetrahydropyran ring, the axial Ph group has a 1,3-diaxial interaction with only one hydrogen. Although the conformation of the ring does indeed guarantee that one of the lone pairs can assist the C-C bond cleavage, the axial phenyl group is twisted so that the overlap of the C-C bond and the SOMO is only 41% of the maximum possible. At best,

the cleavage of this conformer would be inefficient. The deprotonation of this conformer also seems unlikely.

The conformation with the phenyl group in the equatorial position is perfectly aligned for cleavage. However, the energy gap between this conformer and the global minimum is moderately large. It was uncertain whether the population of this conformer would be sufficient to allow this isomer to react.

There was no evidence of deprotonation of the cis isomer of 28. However, this isomer cleaved inefficiently when irradiated in the presence of DCB (2), giving acetaldehyde methyl 4-phenylbutyl acetal (34). Either the population of the more favourably aligned conformer is large enough to allow the reaction to occur, or the 41% overlap in the global minimum is sufficient to account for the inefficient cleavage.

Table 14: Conformers of cis-2-methyl-3-phenyltetrahydropyran (2E).

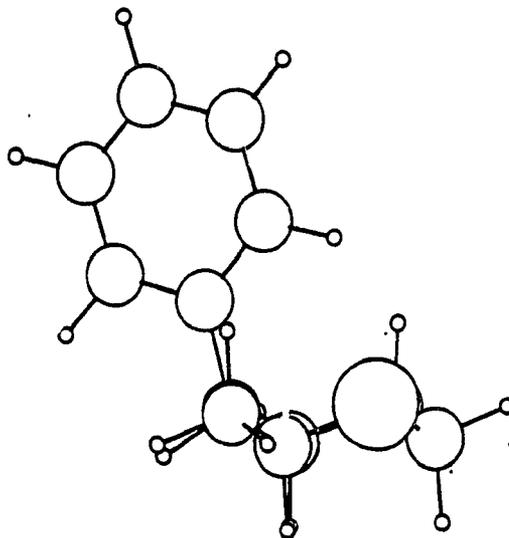
Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{m-CH}} $ , (overlap)	$ \phi_{\text{m-CC}} $ , (overlap)	$ \phi_{\text{OR}} $ , (overlap)
4.35 (Ph eq)	23°, (15%)	89°, (100%)	59°, (100%)
0.0 (Ph ax)	19°, (11%)	40°, (41%)	64°, (100%)

Table 15: Conformers of trans-2-methyl-3-phenyltetrahydropyran (2E).

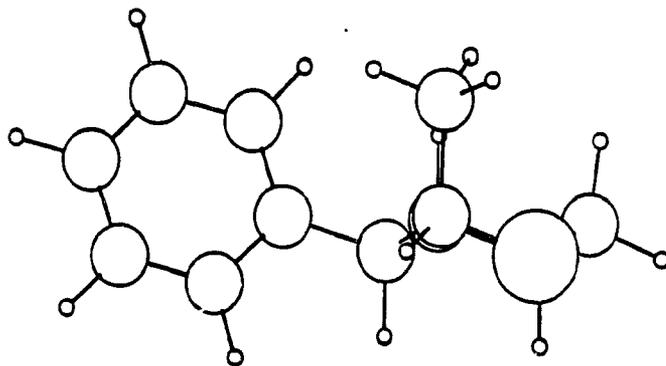
Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{m-CH}} $ , (overlap)	$ \phi_{\text{m-CC}} $ , (overlap)	$ \phi_{\text{OR}} $ , (overlap)
21.3 (Ph ax)	28°, (22%)	31°, (26%)	56°, (100%)
0.0 (Ph eq)	2°, (0%)	59°, (74%)	65°, (99%)

Figure 21: Low-energy conformers of cis-2-methyl-3-phenyltetrahydropyran (**28**).

a) The global-minimum conformer.

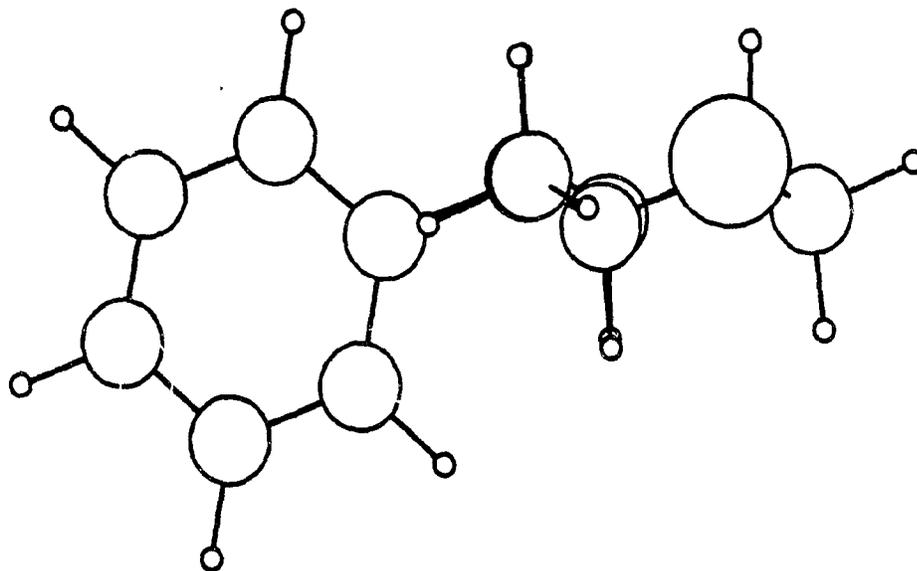


b) A reactive conformer (4.35 kJ mol<sup>-1</sup> above the global minimum).



Only chair conformations of trans-2-methoxy-3-phenyltetrahydropyran (28) were considered. In this isomer, the structure with the equatorial phenyl group was indeed found to be lower in energy than the conformer with the phenyl group in the axial position. In agreement with the original expectations, the most stable conformer had the equatorial phenyl group aligned parallel to the geminal hydrogen. This orientation would prevent deprotonation and isomerization to the cis isomer. However, this conformer is well aligned for cleavage. The trans isomer is therefore predicted to be reactive. (The trans isomer was calculated to be 12.0 kJ mol<sup>-1</sup> more stable than the cis isomer.)

Figure 22: Global-minimum conformer of trans-2-methyl-3-phenyltetrahydropyran (28).



#### 4. CONCLUSIONS

When the activation barrier is lower than about 50 kJ mol<sup>-1</sup>, a radical cation can undergo C-C bond cleavage before back electron transfer occurs. The C-C bond dissociation energies of the radical cations considered in this investigation are all below this threshold value. When the conformation is suitable, the bond dissociation energy is a good estimate of the activation barrier for cleavage. However, when the plane of the phenyl group is parallel to the vulnerable benzylic bond or the alkyl portion of the alkoxy group is antiperiplanar to the C-C bond, the barrier is substantially higher than the bond dissociation energy, and cleavage becomes much more unlikely.

Deprotonation of the radical cation is in competition with C-C bond cleavage. Conformation is important in this reaction, too. Deprotonation will not occur if the plane of the phenyl group is parallel to the benzylic C-H bond.

Molecular mechanics calculations have been used to identify which of the ethers studied are suitably aligned for cleavage. These calculations have shown that C-C bond cleavage is unfeasible for the radical cations of cis- and trans-1-methoxy-2-phenylcyclohexane (18), 6-phenyl-1,4-dioxaspiro[4.5]decane (19), cis-1-methoxy-2-phenylcyclopentane (15), and cis- and trans-2-methoxy-1-phenylindane (13). However, the radical cations of low-

energy conformers trans-1-methoxy-2-phenylcyclopentane (15) and 2-methoxy-1-phenylpropane (11) are suitably aligned for C-C cleavage. In all cases, the molecular mechanics calculations are in agreement with the experimental results.

For a few of the ethers studied, the results of the calculations were not conclusive. The global-minimum conformers of (2R,3R)- and (2S,3R)-2-methoxy-3-phenylbutane (27) and cis-2-methyl-3-phenyltetrahydropyran (28) were predicted to be inert. However, for all three of these ethers, other conformers that might undergo C-C bond cleavage were identified. For the (2R,3R) isomer of 27, the potentially reactive conformer was 9.83 kJ mol<sup>-1</sup> above the global minimum; for the (2S,3R) isomer, the reactive conformer was 4.77 kJ mol<sup>-1</sup> above the global-minimum conformer; and for the cis isomer of 28, the suitably oriented conformer was 4.35 kJ mol<sup>-1</sup> above the most stable conformer. All three of these ethers were found to cleave inefficiently.

There is experimental evidence for the deprotonation of the radical cations of cis-1-methoxy-2-phenylcyclopentane (15) and the cis and trans isomers of 2-methoxy-1-phenylindane (13). Although C-C cleavage of these radical cations is unfeasible, the conformations of the global-minimum structures are suitable for deprotonation. The calculated values of  $\phi_{\text{Ph-CH}}$  were 64° (15 cis), 44° (13 cis), and 85° (13 trans). In each of the ethers found to be

inert, the value of  $\phi_{\text{Pb-CH}}$  was calculated to be less than  $26^\circ$ .

Although the radical cation of trans-2-methyl-3-phenyltetrahydropyran (28) has not been studied experimentally, the results of the calculations permit the prediction that C-C cleavage will occur readily. The global-minimum conformer is almost perfectly aligned for cleavage; this is the only such global-minimum structure that was identified.

## 5. EXPERIMENTAL

### GENERAL INFORMATION

The  $^1\text{H}$  nmr spectra were recorded on a Nicolet Instruments Corp. narrow bore 360-MHz spectrometer or on a Bruker AC250 spectrometer, as noted. Chemical shifts are reported in parts per million relative to tetramethylsilane. Infrared spectra were recorded on a Perkin Elmer 283B IR spectrometer and frequencies are reported in wavenumbers, relative to the  $1602\text{ cm}^{-1}$  stretch for polystyrene. Gas chromatography with mass selective detection (gc/ms) was carried out on a Hewlett Packard 5890 gc/5970 mass selective detector interfaced with a Hewlett Packard 9816 microcomputer. The column used was 25 m x 0.2 mm 5% phenyl methyl silicone on fused silica with a film thickness of  $0.25\ \mu\text{m}$ . Gas chromatography with flame ionization detection (gc/fid) was carried out on a Hewlett Packard 5890. The column used was 25 m x 0.25 mm OV-1701 fused silica. Preparative gas chromatography was carried out on an Aerograph A-700 gc fitted with a thermal conductivity detector. Combustion analyses were done by Canadian Microanalytical Service Limited, Delta, B.C..

## ELECTROCHEMICAL MEASUREMENTS

Oxidation potentials were obtained by cyclic voltammetry using a three-electrode cell, which has been described previously (44). The working electrode was a platinum sphere (1 mm diameter) and the counter electrode was a platinum wire. The reference electrode was saturated calomel (SCE). The electrolyte was 0.1 M tetraethylammonium perchlorate (TEAP) in acetonitrile. Substrate concentrations were approximately 1 mM.

The peak potentials were measured with a 100 mV/s sweep rate. No cathodic wave was detected following the anodic sweep. The reported oxidation potentials correspond to corrected anodic peak potentials (45).

## MATERIALS

Solvents were distilled prior to use. Acetonitrile and 1,4-dicyanobenzene (2) (Aldrich) were purified as reported previously (4b). Tetrahydrofuran (BDH) was distilled over sodium before use. DL-2-Phenylpropionaldehyde (30), phthalic anhydride, 3-nitrophthalic anhydride, dimethyl sulfate, and 4-phenyl-1-butanol (35) were obtained from the Aldrich Chemical Company. Iodomethane was obtained from BDH, acetophenone was obtained from Fisher, and cyclododecane was obtained from K & K Laboratories.

## CALCULATIONS

Molecular mechanics calculations were carried out on a VAX 8800 mainframe computer. The 1988 force field of MM3 and the 1987 force field of MMP2 were used. In some cases, PCMODEL (41) was used for preliminary molecular mechanics calculations.

## PREPARATIONS

### Preparation of 3-phenyl-2-butanol (29)

3-Phenyl-2-butanol (29) was prepared from DL-2-phenylpropionaldehyde (30) via a Grignard reaction. Iodomethane (100. mL, 228 g, 1.61 mol) was added dropwise with stirring to magnesium (50. g, 2.1 mol) in anhydrous diethyl ether. The flask was chilled in an ice bath throughout the addition. After the addition was complete, DL-2-phenylpropionaldehyde (106 mL, 107 g, 0.799 mol) was added dropwise. The resulting mixture was stirred for 16 h and then poured into a slurry of saturated  $\text{NH}_4\text{Cl}$  and ice. Concentrated HCL was added until the aqueous layer was acidic. The aqueous layer was extracted several times with ether; the combined organic extracts were washed with 5%  $\text{NaHCO}_3$ , dilute  $\text{NaHSO}_4$ , and distilled water. The solution was dried over  $\text{MgSO}_4$ , and the ether was evaporated. A mixture of

the diastereomers of 3-phenyl-2-butanol (29) was obtained by vacuum distillation (107.8 g, 29.8% yield).

#### Separation of the diastereomers of 3-phenyl-2-butanol (29)

The diastereomers were separated with a few slight modifications of Cram's procedure (42). A mixture of the isomers of 3-phenyl-2-butanol (29) (80.5 g, 0.536 mol) was refluxed with phthalic anhydride (60.0 g, 0.405 mol) and pyridine (100 mL) for 2 h. The mixture was cooled and diluted with an equal volume of benzene. The solution was washed with excess 1 M H<sub>2</sub>SO<sub>4</sub> and with water, and then dried over MgSO<sub>4</sub>. The solvents were evaporated, and the residue was diluted with two volumes of ethyl acetate. Low-boiling petroleum ether was added until the solution became slightly turbid. The crystals that formed upon standing were recrystallized from ethyl acetate and petroleum ether to yield 21.4 g of the acid phthalates of the (2R,3S) and (2S,3R) enantiomers of the alcohol. Some of these crystals (10.0 g) were hydrolyzed back to the alcohol by refluxing for 16 h with a solution of NaOH (8.0 g) in water (40 mL). The crude hydrolysis mixture was extracted with diethyl ether, and the organic layer was washed with water. The solution was dried over MgSO<sub>4</sub> and the ether was evaporated. The conversion from the acid phthalate to the alcohol was quantitative.

The (2R,3R)/(2S,3S) pair of isomers was obtained by refluxing a mixture of the alcohol diastereomers (24.3 g, 0.162 mol) with 3-nitrophthalic anhydride (23.4 g, 0.121 mol) in pyridine (35 mL) for 1 h. The solution was diluted with an equal volume of benzene, washed with excess 1 M H<sub>2</sub>SO<sub>4</sub> and distilled water, and dried over MgSO<sub>4</sub>. The solvent was evaporated, and the resulting viscous oil was dissolved with two volumes of ethyl acetate. Low-boiling petroleum ether was added until the solution became slightly turbid, but crystallization could not be induced. Therefore, the crude reaction mixture was chromatographed on silica gel, using ethyl acetate as the eluent. Some of the fractions were induced to crystallize by adding two volumes of ethyl acetate, followed by sufficient petroleum ether to produce turbidity. The resulting solid product was recrystallized from ethyl acetate and petroleum ether to yield 1.2 g of acid 3-nitrophthalate. This was converted back to the alcohol by refluxing for 14 h with a solution of NaOH (2.0 g) in water (20 mL); work-up of the reaction mixture as before yielded the desired alcohol diastereomer (77% yield from the acid 3-nitrophthalate).

#### Preparation of 2-methoxy-3-phenylbutane (27)

The separated diastereomers of 3-phenyl-2-butanol (29) were methylated with dimethyl sulfate. The (2R,3S)/(3R,2S)

alcohol (5.20 g, 0.0346 mol) was dissolved in anhydrous diethyl ether (150 mL). NaH (6.0 g of 60% suspension in mineral oil, 0.15 mol) was added, followed by dropwise addition of dimethyl sulfate (14 mL, 19 g, 0.15 mol). After the suspension was refluxed for 29 h, gc/ms showed that the reaction was not complete. More dimethyl sulfate (10 mL, 13 g, 0.11 mol) was added and the mixture was refluxed for an additional 23 h. The reaction was quenched by the addition of distilled water. The aqueous layer was extracted with diethyl ether; the combined organic extracts were washed with concentrated  $\text{NH}_4\text{OH}$  and saturated NaCl. The solution was dried over  $\text{MgSO}_4$  and the solvent was removed from the potentially volatile ether by distillation with a fractionating column. Chromatography on silica gel with 1:4  $\text{CH}_2\text{Cl}_2$ -hexanes yielded 2-methoxy-3-phenylbutane (27) in quantitative yield; integration of the gc/ms spectrum gave the ratio of isomers as 95:5;  $^1\text{H}$  nmr (250 MHz) in  $\text{CDCl}_3$  (lit. (51)): 7.23(m, 5H), 3.43(dq, 1H,  $J = 6.3$  Hz,  $J = 5.8$  Hz), 3.27(s, 3H), 2.93(dq, 1H,  $J = 7.2$  Hz,  $J = 5.8$  Hz), 1.25(d, 3H,  $J = 7.2$  Hz), 1.05(d, 3H,  $J = 6.3$  Hz).

The same procedure was used to methylate the (2R,3R)/(2S,3S) isomers of 3-phenyl-2-butanol (29) (78% yield, 96:4 ratio of isomers);  $^1\text{H}$  nmr (250 MHz) in  $\text{CDCl}_3$  (lit. (51)): 7.16 - 7.31(m, 5H), 3.35(s, 3H), 3.34(dq, 1H,  $J = 6.1$  Hz,  $J = 6.6$  Hz), 2.73(dq, 1H,  $J = 7.2$  Hz,  $J = 6.6$  Hz), 1.25(d, 3H,  $J = 7.2$  Hz), 0.96(d, 3H,  $J = 6.1$  Hz).

Preparation of cis-2-methyl-3-phenyltetrahydropyran (28)

2-Methyl-3-phenyl-5,6-dihydropyran (32) was prepared via a two step synthesis, following the method of Descotes (43). The first step involved the synthesis of  $\alpha$ -methylphenyltetrahydrofuryl carbinol (31). A stirred solution of acetophenone (12 mL, 12 g, 0.10 mol) in tetrahydrofuran (200 mL, 177 g, 2.46 mol) was irradiated through Pyrex with a 400-W mercury lamp. Nitrogen was bubbled through the solution during the irradiation; the total irradiation time was 24 h. Evaporation of unreacted THF left 28 g of a mixture containing the carbinol. This crude carbinol was used in the next step of the synthesis without further purification.

$\alpha$ -Methylphenyltetrahydrofuryl carbinol (31) was converted to 2-methyl-3-phenyl-5,6-dihydrofuran (32) by pyrolysis on neutral alumina (activity 1). The pyrolysis was carried out in a cylindrical Electric Multiple Unit Furnace (Cenco) at 320°C. The alumina (14 g) was packed into a Pyrex tube (2 cm diameter), which was clamped vertically in the furnace. It was found that the pyrolysis was most successful if 7 g of alumina recovered from previous pyrolyses was mixed with 7 g of unused alumina. The crude carbinol mixture was pyrolyzed in batches of roughly 5 g each. With the entire apparatus under vacuum (0.25 mmHg), the carbinol was allowed to drop slowly onto

the alumina, and the product was collected in a flask immersed in liquid nitrogen. On average, about 40% of the mass of the carbinol mixture was recovered. The pyrolyzed mixtures were chromatographed on silica gel, using a 1:1 mixture of  $\text{CH}_2\text{Cl}_2$  and hexanes. The fractions containing 2-methyl-3-phenyl-5,6-dihydropyran (32) were combined.

These combined fractions were hydrogenated over 10% Pd on activated carbon. Filtration of the suspension and careful distillation of the solvent from the volatile product gave 1.0 g of cis-2-methyl-3-phenyltetrahydropyran (28), a new compound (6% yield);  $^1\text{H}$  nmr (360 MHz) in  $\text{CDCl}_3$ : 7.14-7.42(m, 5H), 4.03(m, 1H), 3.92(dq, 1H,  $J = 3.26$  Hz,  $J = 6.7$  Hz), 3.61(m, 1H), 2.83(m, 1H), 1.91(m, 4H), 1.04(d, 3H,  $J = 6.7$  Hz);  $^{13}\text{C}$  nmr (90 MHz) in  $\text{CDCl}_3$ : 142.6, 129.3, 128.0, 125.9, 75.4(d), 66.5(t), 44.7(d), 28.8(t), 22.1(t), 17.6(q); ir neat: 3080(w), 3050(w), 3020(w), 2940(s), 2840(s), 1600(m), 1495(s), 1450(s), 1380(s), 1340(m), 1270(s), 1225(s), 1190(s), 1140(m), 1110(s), 1090(s), 1075(s), 1040(s), 1030(m), 960(w), 930(w), 880(w), 850(s), 835(w), 810(w), 745(s), 730(m), 690(s), 655(w); MS m/z (rel. intensity): 176(12.0), 132(9.9), 117(14.0), 115(10.4), 104(100), 91(19.7); Anal. Calcd. for  $\text{C}_{12}\text{H}_{16}\text{O}$ : C 81.77, H 9.15; found: C 81.42, H 9.08.

## IRRADIATIONS

All irradiations were carried out in Pyrex tubes, using either a General Electric 1-kW or Ace Glass 450-W medium-pressure mercury vapour lamp, as noted. Both lamps were surrounded by a Pyrex cooling jacket; all irradiations were carried out in a constant temperature bath held at 10°C. Samples were degassed by nitrogen ebullition for five minutes prior to irradiation.

Irradiations of 2-methoxy-3-phenylbutane (27)

(2R,3S)/(2S,3R):

A solution of 2-methoxy-3-phenylbutane (27) (0.2085 g,  $1.269 \times 10^{-3}$  mol), 1,4-dicyanobenzene (2) (0.1147 g,  $8.952 \times 10^{-4}$  mol), and cyclododecane (38.0 mg,  $2.26 \times 10^{-4}$  mol) in 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OH (30 mL) was irradiated with the 1-kW lamp. After 7 d, there was still no evidence of reaction. The solution was irradiated with stirring for an additional week (450-W lamp). Finally, the mixture was transferred to nmr tubes and irradiated for a third week with the 1-kW lamp (22% conversion). The yield of ethylbenzene was 8% (calibrated gc/ms). The photolyzed solution was evaporated and chromatographed on silica gel with hexanes and CH<sub>2</sub>Cl<sub>2</sub>. The attempt at chromatographic separation was only partially successful: the yield of 1-(4-cyanophenyl)-1-phenylethane

(36) was determined by analysis of fractions containing only 36 and recovered starting material 27 (20% yield);  $^1\text{H}$  nmr (250 MHz) in  $\text{CDCl}_3$ : 7.56(d, 2H,  $J = 6.6$  Hz), 7.16 - 7.32(m, 7H), 4.19(q, 1H,  $J = 7.1$  Hz), 1.64 (d, 3H,  $J = 7.1$  Hz);  $^{13}\text{C}$  nmr (63 MHz) in  $\text{CDCl}_3$ : 151.9, 144.7, 132.3, 129.1, 128.7, 128.4, 127.5, 119.0, 110, 44.9, 21.4; MS m/z (rel. intensity): 207 (37.7), 192 (100), 165 (35.4), 105 (5.4), 77 (17.7).

A solution of 2-methoxy-3-phenylbutane (27) (ratio of isomers 93:7, 43.9 mg,  $2.67 \times 10^{-4}$  mol), 2 (23.2 mg,  $1.81 \times 10^{-4}$  mol), and cyclododecane (6.4 mg,  $3.8 \times 10^{-5}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OH}$  (2 mL) was irradiated for 7 d (21% conversion). The ratio of isomers remained constant. Small amounts of ethylbenzene and 1-(4-cyanophenyl)-1-phenylethane (36) were identified by gc/ms. Trace amounts of the diastereomers of 2,3-diphenylbutane (33) were also detected (gc/ms). The identification of these diastereomers is tentatively based on the observed mass spectra; MS m/z (rel. intensity): 210 (1.2), 105 (100), 77 (14.4).

A solution of 2-methoxy-3-phenylbutane (27) (45.4 mg,  $2.76 \times 10^{-4}$  mol) and 2 (27.0 mg,  $2.11 \times 10^{-4}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OD}$  (2 mL) was irradiated for 7 d. There was no evidence of deuterium incorporation in the starting material (gc/ms with selected ion monitoring).

(2R,3R)/(2S,3S):

A solution of 2-methoxy-3-phenylbutane (27) (0.1491 g,  $9.078 \times 10^{-4}$  mol), 2 (0.0791 g,  $6.17 \times 10^{-4}$  mol), and cyclododecane (35.1 mg,  $2.09 \times 10^{-4}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OH}$  (20 mL) was placed in nmr tubes and irradiated with the 1-kW lamp for 7 d (22% conversion). The yield of ethylbenzene was 6% (calibrated gc/ms). Trace amounts of the diastereomers of 2,3-diphenylbutane (33) were also detected. The photolyzed solution was evaporated and chromatographed on silica gel with hexanes and  $\text{CH}_2\text{Cl}_2$ : the yield of 1-(4-cyanophenyl)-1-phenylethane (36) was determined as before (24% yield).

A solution of 2-methoxy-3-phenylbutane (27) (21.3 mg,  $1.42 \times 10^{-4}$  mol) and 2 (16.3 mg,  $1.27 \times 10^{-4}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OD}$  (1 mL) was irradiated for 7 d with the 1-kW lamp. There was no evidence of isomerization or incorporation of deuterium in the starting material (gc/ms with selected ion monitoring).

Irradiations of cis-2-methyl-3-phenyltetrahydropyran (28)

A solution of cis-2-methyl-3-phenyltetrahydropyran (28) (0.2174 g,  $1.233 \times 10^{-3}$  mol), 2 (0.1235 g,  $9.639 \times 10^{-4}$  mol), and cyclododecane (46.0 mg,  $2.7 \times 10^{-4}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OH}$  (30 mL) was irradiated for 7 d with the 1-kW lamp. Gc/ms

indicated small amounts of products at 22% conversion. The solution was then irradiated with stirring for an additional week (450-W lamp). The yield of products still appeared very low: the solution was transferred to nmr tubes, and these were irradiated for a third week with the 1-kW lamp (47% conversion in total). The photolyzed solution was yellow. In order to identify the proposed cleavage product, acetaldehyde methyl 4-phenylbutyl acetal (34), most of the solvent was removed by distillation with a fractionating column, and the residue was subjected to acid hydrolysis as follows.

5% HCl (75 mL) was added to the crude photolysis mixture. Dioxane (about 5 mL) was added to improve the solubility. The mixture was refluxed for 2 h and extracted with diethyl ether. The organic layer was washed with saturated NaHCO<sub>3</sub> and with water before drying with MgSO<sub>4</sub>. Use of the gc/ms showed the disappearance of the suspected acetal peak and the appearance of a new peak. This peak was attributed to 4-phenyl-1-butanol (35) after comparison of the retention time and mass spectrum with an authentic sample. The yield of 4-phenyl-1-butanol (35) was determined after calibrating the gc/ms with solutions containing a known alcohol/cyclododecane ratio (21% yield at 47% conversion).

A solution of cis-2-methyl-3-phenyltetrahydropyran (28) (32.6 mg,  $1.85 \times 10^{-4}$  mol), 2 (20.8 mg,  $1.62 \times 10^{-4}$  mol), and

cyclododecane (3.1 mg,  $1.8 \times 10^{-5}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OH}$  (2 mL) was irradiated for 7 d with the 1-kW lamp. The irradiation resulted in a 40% conversion of the starting material.

A solution of cis-2-methyl-3-phenyltetrahydropyran (28) (37.5 mg,  $2.13 \times 10^{-4}$  mol) and 2 (19.5 mg,  $1.52 \times 10^{-4}$  mol) in 3:1  $\text{CH}_3\text{CN}-\text{CH}_3\text{OD}$  (2 mL) was irradiated with the 1-kW lamp for 7 d. Selected ion monitoring with the gc/ms showed no incorporation of deuterium in the ether.

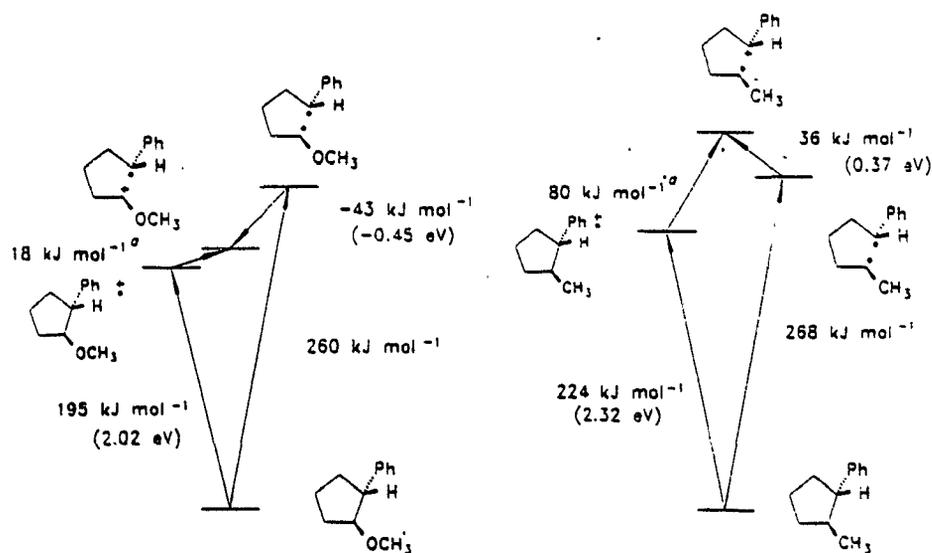
## Chapter II: Photosensitized (Electron Transfer) Carbon-Hydrogen Bond Cleavage: Changing Configuration at a Saturated Carbon Center.

### 1. INTRODUCTION

Molecular mechanics calculations have proven valuable in explaining the reactivity of the ether systems. Carbon-carbon bond cleavage can be predicted, as can deprotonation and isomerization. In the cyclic ether systems, the bond dissociation energies of the radical cations are low enough so that the C-C cleavage reaction competes with deprotonation. However, if the alkoxy group were replaced with an alkyl group, the bond dissociation energy would be increased to the point where C-C cleavage need not be considered.

The thermochemical cycle for the estimation of the C-C bond dissociation energy of 1-methyl-2-phenylcyclopentane (39) is shown in Figure 23. For 1-methyl-2-phenylcycloalkanes, deprotonation is the only probable reaction.

Figure 23: Thermochemical cycles used for the estimation of the bond dissociation energies of the vulnerable benzylic carbon-carbon bonds of the radical cations of trans-1-methoxy-2-phenylcyclopentane (15) and trans-1-methyl-2-phenylcyclopentane (39) (15).



\*Value calculated by completing the cycle

It is well established that the thermodynamic acidity of a radical cation is greatly enhanced relative to the neutral molecule (10,11). Despite this, it has been found that the kinetic acidity of a radical cation can be extremely low if the singly occupied molecular orbital does not overlap with the C-H bond. The radical cation will not deprotonate if the conformation is unsuitable.

In Chapter 1, molecular mechanics calculations were used to rationalize and predict the reactivity of some  $\beta$ -phenyl ethers. Here, MMP2 and MM3 are used to predict the feasibility of the deprotonation-isomerization of the cis and trans isomers of both 1-methyl-2-phenylcyclopentane (39) and 1-methyl-2-phenylcyclohexane (40).

The main goal of this study was to provide an example in which configuration at a saturated carbon center could be changed. The interconversion of diastereomers could prove to be a reaction of considerable synthetic utility. This reaction could be used to convert a mixture to a single diastereomer, with no waste. Also, if one diastereomer were more difficult to synthesize than the other, photosensitized isomerization could be used to produce the more difficult one.

## 2. RESULTS

Molecular mechanics programs were used to find the conformers of the cis and trans isomers of both 1-methyl-2-phenylcyclopentane (39) and 1-methyl-2-phenylcyclohexane (40). The isomers of 39 were synthesized for use in a photochemical investigation.

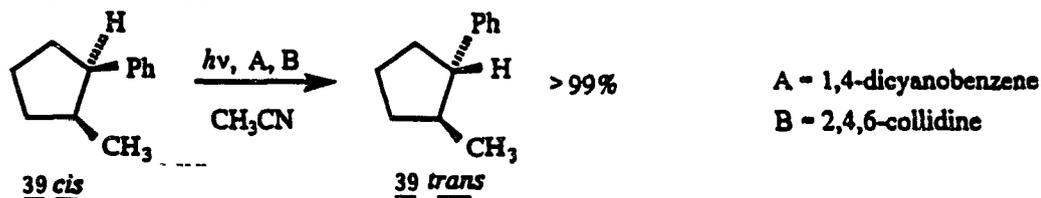
Both cis and trans 1-methyl-2-phenylcyclopentane (39) are known compounds. In order to synthesize the cis isomer, phenylmagnesium bromide was added to 2-methylcyclopentanone (41), the alcohol was dehydrated with p-toluenesulfonic acid, and the resultant alkene was hydrogenated at atmospheric pressure over 10% Pd on carbon. Chromatography on silica gel with hexanes as eluent was used to obtain the cis isomer in 95% purity. Purer (99%) samples could be obtained by using preparative gas chromatography.

The trans isomer was synthesized via a two-step procedure (52). First, 6-phenyl-1-hexene (42) was synthesized from 3-phenylpropylmagnesium bromide and allyl bromide. 6-Phenyl-1-hexene (42) was cyclized to the trans isomer of 39 with potassium. Pure trans isomer was isolated by using preparative gas chromatography.

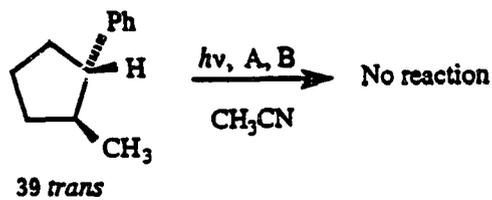
The irradiation procedure was similar to that used in earlier studies. Solutions of the cycloalkane, 1,4-dicyanobenzene (2), cyclododecane, and 2,4,6-collidine (a nonnucleophilic base) in acetonitrile or in a 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OD

mixture were degassed by nitrogen ebullition and then irradiated through a Pyrex filter using a medium-pressure mercury vapour lamp. The irradiation vessel was kept at 10°C by a circulating water bath. The reaction was followed by capillary column gas chromatography with a flame ionization detector (gc/fid). The cyclododecane served as an inert internal standard for determination of percent conversion and yield. The results of the irradiations are illustrated in reactions 13-16.

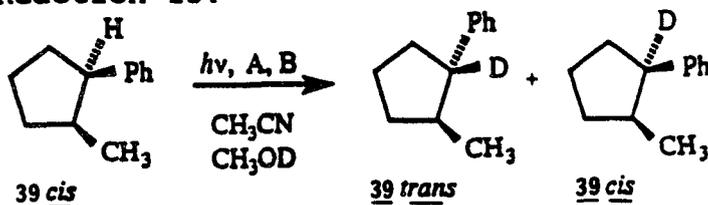
Reaction 13:



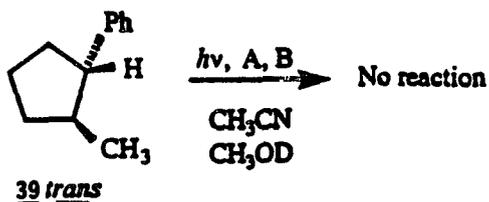
Reaction 14:



Reaction 15:



Reaction 16:



Irradiation of the pure cis isomer of 39 resulted in isomerization to its diastereomer. After four days, 50% conversion was achieved. However, the yield of trans isomer was only 24%. In addition to the isomerization, irradiation resulted in the formation of a 1:1 cycloalkane-dicyanobenzene adduct, 1-(4-cyanophenyl)-2-methyl-1-phenylcyclopentane (43). The stereochemical assignment (4-cyanophenyl- and methyl- trans) is based on the <sup>1</sup>H nmr evidence. The yield of this product is insufficient to account for the loss of starting material. No other volatile products were detected by gc/fid or gc/ms. When the irradiation of the cis isomer was carried out in 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OD, capillary column gas chromatography with a mass selective detector (gc/ms) showed that all of the trans isomer produced in the reaction contained deuterium. Also, some of the cis isomer incorporated deuterium at the benzylic position.

Irradiations that did not include added base did not result in the desired isomerization. Most of the starting material disappeared rapidly, resulting in only 7% yield and 74% conversion after only one day. No volatile products, not even the 1:1 adduct, were observed by gc/fid.

Prolonged irradiation of the trans isomer of 1-methyl-2-phenylcyclopentane (39) did not result in the formation of any cis isomer. Some of the starting material was consumed (15% conversion after six days), but no volatile products

were observed by gc/fid. Gc/ms showed that irradiation in the presence of  $\text{CH}_3\text{OD}$  did not lead to the incorporation of deuterium.

The oxidation potentials of both isomers were measured by cyclic voltammetry. The values are recorded in Table 16.

Stern-Volmer analysis showed that both cis and trans-1-methyl-2-phenylcyclopentane (39) quenched the fluorescence of 1,4-dicyanobenzene (2) with a rate constant of  $2.8 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$ , confirming that in both cases, the electron transfer takes place at the diffusion-controlled rate (Figure 24).

**Table 16: Oxidation potentials and calculated free energies for electron transfer.**

	$E_D$ (V) <sup>a</sup>	$\Delta G_a$ (kJ mol <sup>-1</sup> ) <sup>b</sup>
<u>cis</u> -1-methyl-2-phenyl-cyclopentane ( <u>39</u> )	2.27	-35
<u>trans</u> -1-methyl-2-phenyl-cyclopentane ( <u>39</u> )	2.32	-30.

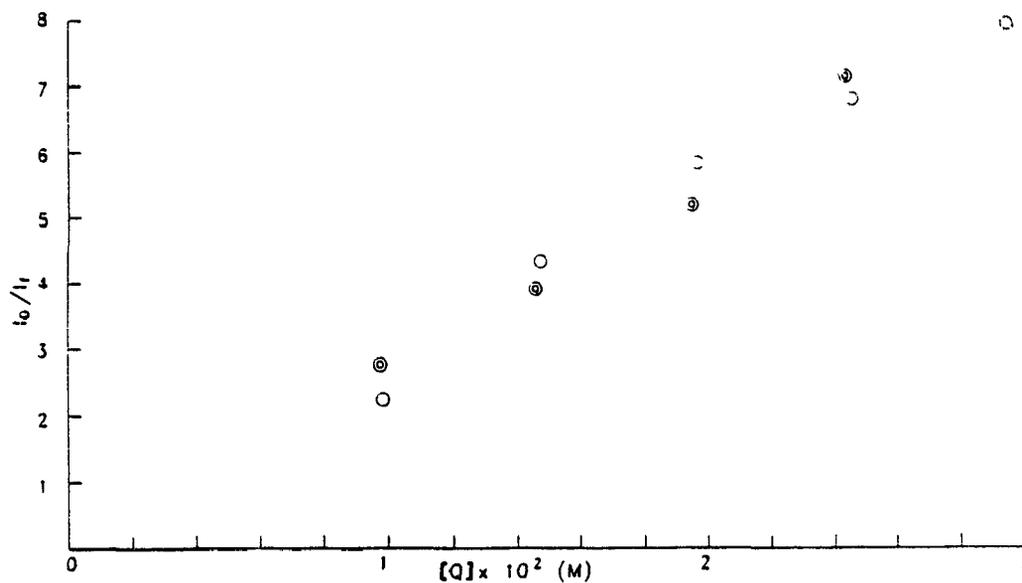
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<sup>a</sup>Reported vs saturated calomel electrode.

<sup>b</sup>Calculated by using the Weller equation:

$E_{0,0} = 408.4$  kJ mol<sup>-1</sup>,  $E_A = -1.66$  V (vs SCE), and the electrostatic term was taken to be 5.40 kJ mol<sup>-1</sup>.

Figure 24: Stern-Volmer plots of the fluorescence intensity from 1,4-dicyanobenzene (2) as a function of the concentration of cis- and trans-1-methyl-2-phenylcyclopentane (39).



⊙ 39 trans

$$k_{qT} = 249.9$$

$$r^2 = 0.974$$

○ 39 cis

$$k_{qT} = 245.4$$

$$r^2 = 0.971$$

Since MM3 is considered more reliable for five-membered rings, this was the program used to calculate the most stable conformers of the two isomers of 1-methyl-2-phenylcyclopentane (39) (Table 17,18). The starting conformations were based on the envelope structure and included all possible permutations with the phenyl or methyl group on either side of the "flap". The global-minimum conformers are shown in Figures 25 and 26.

MMP2 was used to identify the conformers of both isomers of 1-methyl-2-phenylcyclohexane (40). Only chair conformations were used as starting conformations. The results of the calculations are tabulated in Tables 19 and 20. The global minima are illustrated in Figures 27 and 28.

### 3. DISCUSSION

The mechanism elucidated in Chapter 1 (Scheme 1) is also applicable to the deprotonation. The only distinction is that the C-C bond cleavage (step 4) is no longer energetically feasible.

The first step in the proposed mechanism involves excitation of the photosensitizer, 1,4-dicyanobenzene (2). The absorption of 2 extends out to 300 nm, beyond the cutoff of the Pyrex filter. All of the other components of the irradiation mixtures were transparent in this region.

The excited photosensitizer can accept an electron from the neutral substrate molecule. The free-energy change associated with this electron transfer can be calculated from the oxidation potential of the substrate by using the Weller equation (equation 1). For both the cis and trans isomers of 1-methyl-2-phenylcyclopentane (39), the electron transfer was calculated to be exergonic by at least 30 kJ mol<sup>-1</sup>. The electron transfer was therefore expected to occur at the diffusion-controlled rate. This expectation was confirmed by the fluorescence quenching study.

Any reaction of the radical cation produced in step 2 must be very fast in order to compete with back electron transfer. The deprotonation will be sufficiently rapid only if the SOMO is correctly oriented with respect to the C-H bond. That is, the plane of the phenyl group should be

perpendicular to the benzylic C-H bond.

As discussed in Chapter 1, the magnitude of the overlap should follow a Karplus-type relationship, varying with  $\cos^2\phi_{\text{Ph-CH}}$ . The maximum overlap occurs when the angle between the plane of the phenyl group and the C-H bond is  $90^\circ$  and the minimum is at  $0^\circ$ .

This angle was calculated to be only  $1^\circ$  in the minimum energy conformer of the trans isomer of 1-methyl-2-phenylcyclopentane (39) (Figure 25). Therefore, it is not surprising that this isomer is unreactive. However, the plane of the phenyl group was found to be twisted away from the benzylic C-H bond in the cis global-minimum conformer (Figure 26). The angle was calculated to be  $34^\circ$  (31% overlap). Although this is not ideal, this isomer can deprotonate when irradiated in the presence of 1,4-dicyanobenzene (2).

Table 17: Conformers of cis-1-methyl-2-phenyl-cyclopentane (39).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $	overlap
0.5	25°	18%
0.0	34°	31%

Table 18: Conformers of trans-1-methyl-2-phenyl-cyclopentane (39).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $	overlap
21.1	4°	1%
14.9	32°	28%
0.0	1°	0%

Figure 25: Global-minimum conformer of cis-1-methyl-2-phenylcyclopentane (39), viewed along the plane of the phenyl ring.

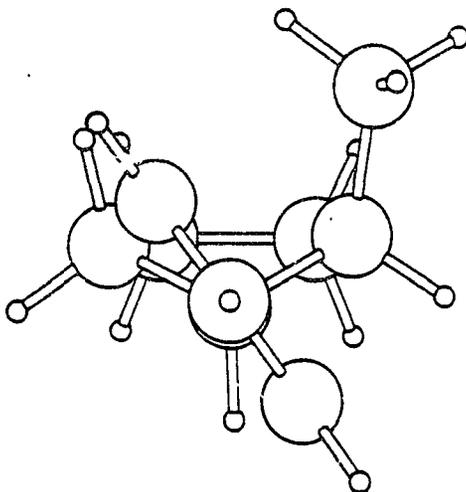
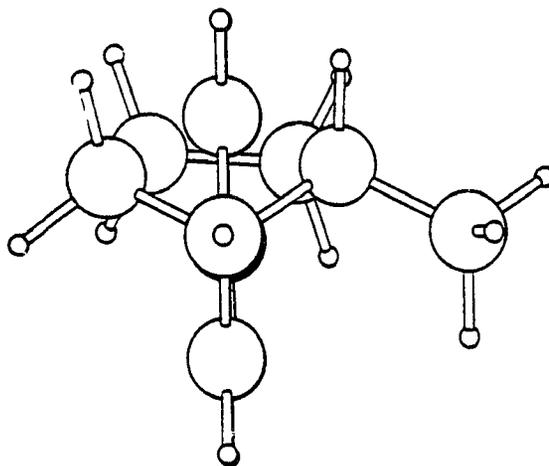


Figure 26: Global-minimum conformer of trans-1-methyl-2-phenylcyclopentane (39), viewed along the plane of the phenyl ring.



The radical cation of 1-methyl-2-phenylcyclohexane (40) has not been investigated experimentally. However, MMP2 results suggest that the trans isomer will be inert, and that the cis isomer may isomerize inefficiently. The phenyl group is parallel to the benzylic C-H bond in the global-minimum conformer of the trans isomer; the conformers with more favourable alignment are 22.3 kJ mol<sup>-1</sup> higher in energy, and they are therefore unlikely to influence the reactivity of this isomer. In the most stable conformer of the cis isomer,  $\phi_{\text{Ph-CH}}$  is 39°; 34° was sufficient to allow the isomerization of the cyclopentyl analog.

The radical cations have great thermodynamic acidity. The solvent, acetonitrile, should be sufficiently basic to remove the benzylic proton from the radical cation of the cis isomer of 1-methyl-2-phenylcyclopentane (39). It seems somewhat peculiar that the addition of 2,4,6-collidine was necessary before isomerization would take place. However, this is not unprecedented. Arnold and Mines (53) found that the addition of base was required to affect the deconjugative tautomerization of phenyl alkenes. The role of the added base remains unclear.

Table 19: Conformers of cis-1-methyl-2-phenylcyclohexane (40).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $	overlap
9.43 (Ph ax)	5°	1%
0.0 (Ph eq)	39°	40%

Table 20: Conformers of trans-1-methyl-2-phenylcyclohexane (40).

Energy above global minimum (kJ mol <sup>-1</sup> )	$ \phi_{\text{Ph-CH}} $	overlap
22.3 (Ph ax)	59°	73%
22.3 (Ph ax)	56°	69%
0.0 (Ph eq)	2°	0%

Figure 27: Global-minimum conformer of cis-1-methyl-2-phenylcyclohexane (40), viewed along the plane of the phenyl ring.

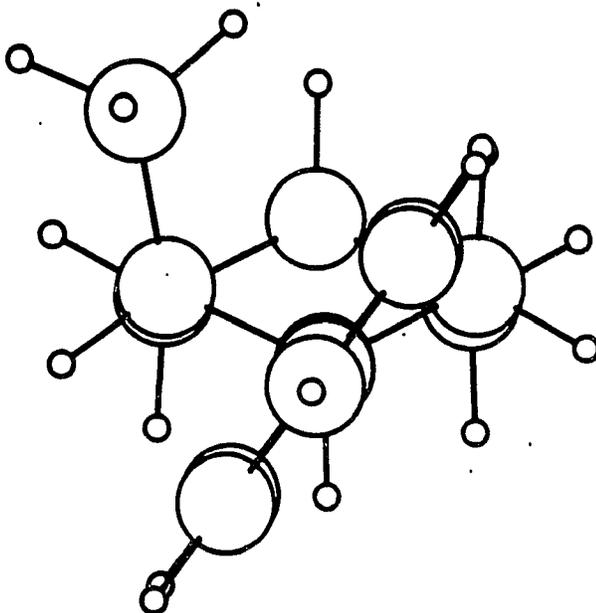
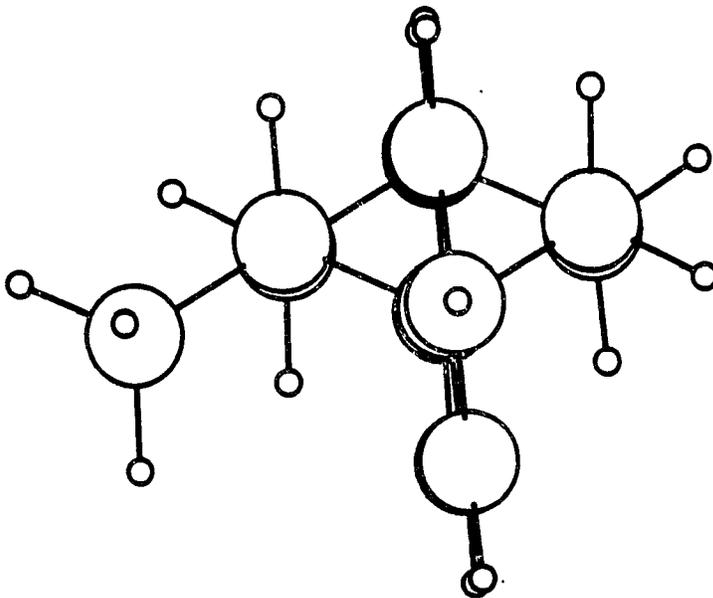


Figure 28: Global-minimum conformer of trans-1-methyl-2-phenylcyclohexane (40), viewed along the plane of the phenyl ring.



Step 9 in the proposed mechanism is reduction of the benzylic radical by the radical anion of 1,4-dicyanobenzene (2). In addition, the benzylic radical could couple with the radical anion at the ipso position. Loss of cyanide ion from this coupling product would produce 1-(4-cyanophenyl)-2-methyl-1-phenylcyclopentane (43), a product which was observed when the cis isomer of 1-methyl-2-phenylcyclopentane (39) was irradiated. The coupling product provides further evidence that the benzylic radical is produced from the cis radical cation; the absence of this 1:1 adduct in the trans irradiation mixture supports the conclusion that this radical cation does not deprotonate.

The final step in the mechanism is reprotonation of the benzylic anion (step 10). Since the benzylic carbon is chiral in the neutral molecule, reprotonation can give either diastereomer. However, formation of the cis isomer simply regenerates reactive starting material, while the trans isomer is inert.

In order to confirm that reprotonation gave both isomers, CH<sub>3</sub>OD was included in the solvent mixture. When the cis isomer of 39 was irradiated in 3:1 CH<sub>3</sub>CN-CH<sub>3</sub>OD, all of the trans isomer produced had incorporated a deuterium atom in the benzylic position. Incorporation of deuterium was also detected in the cis isomer. Irradiation of the trans isomer in the deuterated solvent did not result in any deuterium incorporation, adding to the evidence that the

radical cation of this isomer does not deprotonate.

We have been unable to convert a sample of pure 39 cis to pure 39 trans. The solutions turn bright yellow upon prolonged irradiation, indicating the production of side products that will absorb most of the light. However, prolonged irradiation of a mixture which was initially 86% trans and 14% cis showed that the photostationary state is more than 97% trans. Irradiations of 99% trans indicate that the photostationary state is virtually 100% trans.

Attempts to thermally equilibrate the diastereomers of 39 have proven unsuccessful. The alkali metal catalyzed cyclization of 6-phenyl-1-hexene (42) in refluxing n-butylcyclohexane reported by Pines (52b,c) gave a trans/cis ratio of 5.1. This was assumed to be an equilibrium mixture, corresponding to a free-energy difference of 6.1 kJ mol<sup>-1</sup> at 180°C. We repeated this synthesis in decalin, obtaining a ratio of 8.6 in favour of the trans ( $\Delta G = 8.3$  kJ mol<sup>-1</sup> at 190°C). The difference in the heats of formation calculated with MM3 was 11 kJ mol<sup>-1</sup>. Despite the lack of quantitative agreement among these results, it is evident that the photostationary state lies further in favour of the trans than the thermodynamic equilibrium does.

#### 4. CONCLUSIONS

Deprotonation of a radical cation will take place if the overlap between the SOMO and the C-H bond is sufficient. Deprotonation will occur even if the calculated value of  $\phi_{\text{R-CH}}$  deviates considerably from the ideal ( $90^\circ$ ): the cis isomer of 1-methyl-2-phenylcyclopentane (39) was found to isomerize to the trans, even though the calculated angle is only  $34^\circ$ . The radical cation of the cis isomer of 1-methyl-2-phenylcyclohexane (40) is predicted to deprotonate, since the calculated value of  $\phi_{\text{R-CH}}$  is  $39^\circ$ .

For 1-methyl-2-phenylcyclopentane (39), both the photostationary state and the thermodynamic equilibrium favour the trans isomer. The conformational criterion for reactivity in no way demands that this be true. It may be possible to use this photosensitized (electron transfer) isomerization reaction to synthesize the less thermodynamically favoured isomer. The ability to change the configuration at a saturated carbon should prove to have great synthetic utility if the efficiency can be improved.

## 5. EXPERIMENTAL

### MATERIALS

Bromobenzene, 2-methylcyclopentanone (41), and 1-bromo-3-phenylpropane (44) were obtained from the Aldrich Chemical Company. Decalin and 2,4,6-collidine were obtained from BDH, o-chlorotoluene was obtained from Matheson Coleman and Bell, and allyl bromide was obtained from Fisher.

### FLUORESCENCE QUENCHING MEASUREMENTS

Fluorescence quenching experiments were performed by using a Perkin-Elmer MPF-66 fluorescence spectrophotometer with a Perkin-Elmer MPF-66 xenon lamp power supply interfaced to a Perkin-Elmer 7500 computer. Solutions were 0.01015 M in 1,4-dicyanobenzene (2). The quencher concentrations ranged from 0.01 M to 0.03 M. All solutions were degassed on a vacuum line by using three freeze-pump-thaw cycles. The excitation wavelength was 293 nm; the emission was monitored at 309.4 nm. From the previously measured singlet lifetime of 2 (54),  $8.8 \times 10^{-9}$  s, both isomers were calculated to quench the fluorescence with a rate constant of  $2.8 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$ .

## PREPARATION OF COMPOUNDS

Preparation of cis-1-methyl-2-phenylcyclopentane (39)

2-Methyl-1-phenylcyclopentanol (45) was prepared by a Grignard reaction (52a). Bromobenzene (43 mL, 64 g, 0.41 mol) was added to magnesium turnings (10 g, 0.41 mol) in anhydrous diethyl ether. When reaction was complete, the flask was cooled in ice, and 2-methylcyclopentanone (41) (15 mL, 14 g, 0.14 mol) was added dropwise. The reaction mixture was poured into a mixture of concentrated HCl and ice, and then extracted with ether. The combined organic layer was washed with 5% NaHCO<sub>3</sub> and with distilled water. Finally, the organic layer was dried over MgSO<sub>4</sub> and the solvent was evaporated.

The alcohol was refluxed with p-toluenesulfonic acid in benzene. Water was removed by using a Dean-Stark trap. The crude 1-methyl-2-phenylcyclopentene (46) was chromatographed with hexanes on silica gel.

The cyclopentene 46 was hydrogenated over 10% Pd on carbon in ethanol. Chromatography of the crude product on silica gel with hexanes gave cis-1-methyl-2-phenylcyclopentane (39) in 88% purity, 30% yield. Preparative gas chromatography (6 ft x  $\frac{1}{8}$  in. 20% SE-30 on Chromosorb 60/80 W column) was used to prepare samples of 98% purity; <sup>1</sup>H nmr (360 MHz) in CDCl<sub>3</sub>: 7.1-7.3(m, 5H), 3.1(m,

1H), 2.3(m, 1H), 1.8-2.0(m, 4H), 1.7(m, 1H), 1.4(m, 1H), 0.6(d, 3H, J = 7.1 Hz).

#### Preparation of trans-1-methyl-2-phenylcyclopentane (39)

The synthesis of the trans isomer followed the procedure of Pines (52b,c). The first step involved the synthesis of 6-phenyl-1-hexene (42). 1-Bromo-3-phenylpropane (44) (24 mL, 31 g, 0.16 mol) was added to magnesium turnings (3.8 g, 0.16 mol) in anhydrous diethyl ether. When reaction was complete, allyl bromide (14 mL, 20 g, 0.16 mol) was added dropwise. After the addition was complete, the reaction mixture was refluxed for 16 h. The mixture was cooled and poured into a slurry of concentrated HCl and ice. The aqueous layer was extracted with ether, and the combined organic extracts were washed with 5% NaHCO<sub>3</sub> and then with distilled water. The organic extract was dried over MgSO<sub>4</sub> and the solvent was evaporated. The crude product was chromatographed on silica gel with hexanes. 6-Phenyl-1-hexene (42) was obtained in 68% yield.

Potassium (0.94 g, 0.024 mol) and o-chlorotoluene (0.40 mL, 0.43 g, 0.0034 mol) were refluxed in decalin (25 mL) for 15 min. 6-Phenyl-1-hexene (42) (7.43 g, 0.046 mol) was added dropwise, and the mixture was refluxed for 25.5 h. The black, sludgy reaction mixture was chilled in ice, and isopropanol was added to decompose any remaining potassium.

The mixture was diluted with hexanes (100 mL), and the mixture was filtered to remove the sediment. The filtrate was washed with distilled water until neutral. The organic layer was dried over  $\text{CaCl}_2$ , and the hexanes were evaporated. The remaining solution was distilled under reduced pressure to remove most of the decalin. The residue was chromatographed on silica gel with hexanes as the eluent to give 85% pure trans in 34% yield from 6-phenyl-1-hexene (42). Small amounts of pure 39 trans were obtained by preparative gas chromatography (6 ft x  $\frac{1}{4}$  in. 20% SE-30 on Chromosorb 60/80 W column);  $^1\text{H}$  nmr (360 MHz) in  $\text{CDCl}_3$ : 7.1-7.3(m, 5H), 2.4(m, 1H), 1.9-2.1(m, 3H), 1.7-1.8(m, 3H), 1.3(m, 1H), 0.9(d, 3H,  $J = 6.4$  Hz).

## IRRADIATIONS

Irradiations of cis-1-methyl-2-phenylcyclopentane (39)

A solution of 99% pure cis isomer (14 mg,  $8.7 \times 10^{-5}$  mol), 1,4-dicyanobenzene (2) (7.2 mg,  $5.6 \times 10^{-5}$  mol), 2,4,6-collidine (17 mg,  $1.4 \times 10^{-4}$  mol), and cyclododecane (5.2 mg,  $3.1 \times 10^{-5}$  mol) in acetonitrile (3 mL) was irradiated for 4 d. The progress of the reaction was followed by gc/fid, using cyclododecane as an internal standard. The yield of trans isomer was 24% at 50% conversion (gc/fid). Small amounts of 1-(4-cyanophenyl)-2-methyl-1-phenylcyclopentane (43) were detected.

A solution of 99% pure cis (15 mg,  $9.5 \times 10^{-5}$  mol), 2 (8.8 mg,  $6.9 \times 10^{-5}$  mol), 2,4,6-collidine (20 mg,  $1.6 \times 10^{-4}$  mol), and cyclododecane (6.3 mg,  $3.7 \times 10^{-5}$  mol) was irradiated in  $\text{CH}_3\text{CN}-\text{CH}_3\text{OD}$  (3 mL, 3:1) for 4 d. The trans isomer was formed in 17% yield at 46% conversion (gc/fid). Small amounts of 1-(4-cyanophenyl)-2-methyl-1-phenylcyclopentane (43) were detected. Some of the cis isomer and all of the trans incorporated deuterium (gc/ms). Analysis of the  $^1\text{H}$  and  $^2\text{H}$  nmr spectra indicated that the exchange took place at the benzylic position.

A solution of 95% pure cis (9.2 mg,  $5.7 \times 10^{-5}$  mol), 2 (6.4 mg,  $5.0 \times 10^{-5}$  mol), and cyclododecane (4.4 mg,  $2.6 \times 10^{-5}$  mol) in acetonitrile (2 mL) was irradiated for 1 d. At

74% conversion, the yield of the trans isomer was 7% (gc/fid). There was no evidence of the 1:1 adduct, 1-(4-cyanophenyl)-2-methyl-1-phenylcyclopentane (43).

A stirred solution of 99% pure cis isomer (0.18 g,  $1.1 \times 10^{-3}$  mol), 2 (0.56 g,  $4.4 \times 10^{-3}$  mol), and 2,4,6-collidine (0.28 g,  $2.3 \times 10^{-3}$  mol) in acetonitrile (60 mL) was irradiated for 1 d. The photolysate was chromatographed on silica gel using 1:1 hexanes- $\text{CH}_2\text{Cl}_2$  as the eluent. 1-(4-Cyanophenyl)-2-methyl-1-phenylcyclopentane (43) was isolated in 36% yield (72% conversion);  $^1\text{H}$  nmr (360 MHz) in  $\text{CDCl}_3$ : 7.0 - 7.5(m, 9H), 2.8(m, 1H), 2.6(m, 1H), 1.8 - 2.1(m, 3H), 1.6(m, 1H), 1.4(m, 1H), 0.8(d, 3H);  $^{13}\text{C}$  nmr (90 MHz) in  $\text{CDCl}_3$ : 155.4(s), 145.0(s), 131.8(d), 128.8(d), 128.0(d), 127.8 (d), 126.0(d), 119.1(s), 109(s), 58.8(s), 39.3(d), 38.8(t), 32.1(t), 21.4(t), 17.6(q); ir neat: 3065(w), 3040(w), 3010(w), 2940(s), 2860(s), 2215(s), 1730(w), 1600(s), 1500(m), 1490(s), 1455(m), 1445(m), 1400(w), 1375(w), 1015(w), 885(w), 815(s), 740(m), 715(m), 685(s); MS m/z (rel. intensity): 261(41.2), 218(51.1), 205(100), 190(43.9), 177(7.3), 165(10.3), 140(16.5), 128(7.2), 115(17.7), 91(16.6), 77(10.6). Exact mass calcd. for  $\text{C}_{19}\text{H}_{19}\text{N}$ : 261.1517; found: 261.1517.

Irradiations of trans-1-methyl-2-phenylcyclopentane (39)

A solution of 86% trans (14% cis) (12 mg,  $7.8 \times 10^{-3}$

mol), 1,4-dicyanobenzene (2) (11 mg,  $8.7 \times 10^{-5}$  mol), and 2,4,6-collidine (15 mg,  $1.2 \times 10^{-4}$  mol) in acetonitrile (3 mL) was irradiated for 7 d. The ratio of isomers in the irradiated mixture was 97:3 trans/cis.

A solution of 99% pure trans (10 mg,  $6.2 \times 10^{-5}$  mol), 2 (6.1 mg,  $4.8 \times 10^{-5}$  mol), 2,4,6-collidine (14 mg,  $1.2 \times 10^{-4}$  mol), and cyclododecane (4.3 mg,  $2.6 \times 10^{-5}$  mol) in acetonitrile (3 mL) was irradiated for 6 d. No volatile products were detected by gc/fid.

A solution of 99% pure trans (10 mg,  $6.5 \times 10^{-5}$  mol), 2 (5.4 mg,  $4.2 \times 10^{-5}$  mol), 2,4,6-collidine (14 mg,  $1.2 \times 10^{-4}$  mol), and cyclododecane (4.2 mg,  $2.5 \times 10^{-5}$  mol) in  $\text{CH}_3\text{CN}-\text{CH}_3\text{OD}$  (3 mL, 3:1) was irradiated for 6 d. No volatile products were detected by gc/fid. No deuterium incorporation was detected by gc/ms.

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