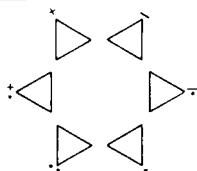# Cyclopropane derived
reactive intermediates

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Cyclopropane derived reactive intermediates

Cyclopropane derived reactive intermediates

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The Hebrew University of Jerusalem

Updates from the Chemistry of Functional Groups

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To Anne Marie and Paula

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Foreword

This is an additional volume in the new series entitled 'Updates from the Chemistry of Functional Groups'.

The volume presents the chapter on 'Cyclopropyl radicals, anion radicals and anions' from *The chemistry of the cyclopropyl group* (1987) volume in its original form, together with corrections and an appendix updating the material until about the end of 1989. In addition the authors, Professors G. Boche and H. M. Walborsky prepared three completely new chapters on reactive intermediates derived from cyclopropanes, namely on cations, carbenoids and cation radicals. The references in these chapters also include most of the year 1989.

We will appreciate any comment or suggestions regarding this volume as well as other volumes of the main series or their updates.

Jerusalem   SAUL PATAI
January 1990   ZVI RAPPOPORT

Preface

The present monograph constitutes an expanded and updated version of our earlier contribution 'Cyclopropyl radicals, anion radicals and anions' to the volume *The Chemistry of the Cyclopropyl Group*" edited by Z. Rappoport (John Wiley & Sons, 1987). The chapter on cyclopropyl cations is completely new as is the chapter on cyclopropyl carbenoids. In the latter emphasis is placed on the cationic nature of cyclopropyl carbenoids. As to cyclopropane cation radicals there exists no general review of the subject although the earlier volume contained a chapter on the chemistry of ionized cyclopropanes in the gas phase by H. Schwarz. Hence we discuss the most recent calculations and investigations of cyclopropane cation radicals in the gas phase and also summarize the situation in matrices and in solutions. Judging by the literature, there is increasing activity in the area of cyclopropane cation radicals. An appendix summarizes the most recent and exciting results dealing with cyclopropyl anions.

In conclusion we would like to stress that we have been selective in citing those articles which in our opinion demonstrate the singular importance of cyclopropane derived reactive intermediates as tools for understanding the general aspects of their chemistry and the mechanisms involved, especially if stereochemistry plays a significant role. We apologize if we have omitted any important references.

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Marburg, Germany
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January 1990

Contents

CHAPTER **1**

Cyclopropyl radicals, anion radicals and anions

I. GENERAL INTRODUCTION

This chapter deals with some of the reactive intermediates of cyclopropanes—radicals, anion radicals and anions. It is hoped that the reader will appreciate that the cyclopropane ring, because of its unique bonding, affords one with a tool to study the mechanism of a variety of reactions. The mechanism of many of these reactions will be discussed in some detail in this chapter. It should also be noted that whenever possible stereochemistry has been used as a mechanistic probe. Pertinent literature has been reviewed through most of 1985.

II. CYCLOPROPYL RADICAL[1]

A. Structure

The valence bond description, originating with Förster[2] and refined by Coulson and Moffitt[3], provides a useful model of the bonding in cyclopropane. In this approach two sets of hybridized orbitals are used, one set for the *endo* bonds and the other set for the *exo* bonds. The orbitals associated with the *endo* bonds are calculated to be $sp^{4.12}$ hybridized and those associated with the *exo* bonds $sp^{2.28}$ hybridized. This hybridization corresponds to a bond angle of 104° for the *endo* orbitals and 116° for the *exo* orbitals (Figure 1).
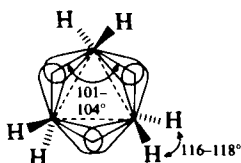
FIGURE 1.   *Exo* and *endo* bonds in cyclopropane

A refinement[3] of Coulson's and Moffitt's calculation suggests hybridization of the *endo* orbitals as sp^5 with a bond angle of 101° 32′ and the *exo* orbitals as sp$^{2.28}$ with a bond angle of 116°. The greater p character of the *endo* bonds and the greater s character associated with the *exo* bonds accounts for most of the physical and chemical properties of the cyclopropane[4, 5]. The molecule is highly strained with an estimated strain energy of 27.6 kcal mol^{-1} or 9.2 kcal mol^{-1} per CH$_2$ group. The strain is largely a result of bond angle distortion (Baeyer strain) and non-bonded repulsions (Pitzer strain)[6].

Converting cyclopropane to a planar cyclopropyl radical (Figure 2) would result in the relief of Pitzer strain (four H–H interactions), but would at the same time increase bond angle distortion (104°–120°), thereby causing greater internal (I)-strain[7].
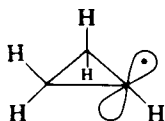
FIGURE 2.   Planar cyclopropyl radical

This latter effect may be one of the reasons for the observation that the cyclopropyl radical, in contrast to other cyclic and acyclic radicals, exists as a bent radical[8, *]. Delocalizing substituents (X = π-systems) attached to the radical site could convert the cyclopropyl σ radical to a π radical. On the other hand electronegative substituents (i.e. oxygen and fluorine) attached to a radical site have a tendency to convert what would ordinarily be a π radical to a σ radical[8]. Such substituents attached to the cyclopropyl radical site could reinforce the σ character of the radical and thereby decrease the rate of inversion. Unless constrained, for example at a bridgehead, a σ radical such as cyclopropyl would rapidly invert its configuration ($k_1 \simeq 10^{11}$ s^{-1} at 71 °C), with the inversion proceeding through a π radical transition state (Figure 3).
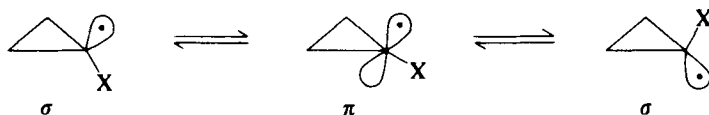
FIGURE 3.   Inversion via planar transition state

Hoffmann-type extended Hückel theory (EHT) calculations[9] have been carried out on the parent cyclopropyl radical[10]. The calculations were in reasonable agreement with the ESR spectral results obtained by Fessenden and Schuler[8]. However, the predicted α-

---

* The term σ radical is applied to those radicals in which the electron occupies an hybridized orbital and a π radical to those in which the electron occupies a p orbital.

proton coupling constant of 24.89 Gauss was in poor agreement with the observed value of 6.51 Gauss. The inversion barrier for flipping from one σ to another was calculated to be 0.5 kcal mol^{-1} and the out-of-plane angle for the α-CH bond was estimated to be 20°.

INDO calculations by Kochi and coworkers[11] gave an out-of-plane angle for the α-CH bond of 35° with an inversion barrier of 3.2 kcal mol^{-1}. The calculated coupling constants for the *syn* and *anti* β-protons are nearly equal to each other for all values of the bonding angle, which would indicate that this datum cannot necessarily be used as evidence for a rapidly inverting σ radical.

Ab initio Hartree–Fock (HF) calculations of the structure of the cyclopropyl radical by Dupuis and Pacansky[12] also showed that the α-CH bond is bent with an out-of-plane α-CH angle of 39.3° with an inversion barrier of 3.0 kcal mol^{-1}. Moreover, compared to cyclopropane itself, the α-CH bond is slightly shorter and the C–C bonds are no longer equivalent. The α-CC bond lengths are shorter (1.476 Å vs. 1.501 Å) and the β-CC bond length is longer (1.54 Å). This means that the σ radical causes the strengthening of the α-CC bonds and the weakening of the β-CC bond. This result is consistent with the observed mode of rearrangement of the cyclopropyl radical to the allyl radical (*vide infra*).

In addition the HF calculations show that no significant hyperconjugative interaction takes place between the σ radical center and the β-CH bonds. This view is contradicted by the ESR results of Kawamura and coworkers[39] who conclude from their data that the σ-cyclopropyl radical is hyperconjugatively coupled with the β-CH bonds and that the coupling is stronger with the *cis* bond than with the *trans* bond.

The heat of formation $(\Delta H^0_f)_{298}$ of the cyclopropyl radical has been determined[13] experimentally to be 66.9 ± 0.25 kcal mol^{-1}, and the C–H bond dissociation energy for the cyclopropyl carbon–hydrogen bond in cyclopropane was found to be 106.3 ± 0.25 kcal mol^{-1}. This bond dissociation energy is less than the C–H bond dissociation energy in ethylene (108 kcal mol^{-1}) and in benzene (110 kcal mol^{-1}) and is a reflection of hybridization (sp$^{2.28}$) of the exocyclic bonds in cyclopropane. The above data were obtained from the bimolecular rate constant for the reaction of chlorine atoms with cyclopropane to give hydrogen chloride and the cyclopropyl radical. Ion cyclotron double resonance spectroscopy[14] was in complete agreement giving $(\Delta H^0_f)_{298} = 66.6 \pm 0.1$ kcal mol^{-1} and a bond dissociation energy of 105.9 ± 2.2 kcal mol^{-1} for the cyclopropyl carbon–hydrogen bond, and a value of 111.1 ± 2.2 kcal mol^{-1} for the C–H bond in ethylene.
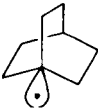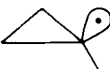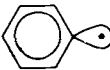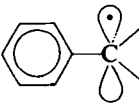
In general, σ radicals, such as cyclopropyl, are more electrophilic than π radicals[15]. The larger the s character of an orbital, the greater the electronegativity of that orbital and the greater is its electrophilic character (less nucleophilic).

B. Reactivity

Consistent with the σ nature of the cyclopropyl radical is its reactivity. In general, σ radicals are more reactive and less selective than π radicals. It has been found for example, that phenyl, vinyl and cyclopropyl σ radicals will abstract hydrogen atoms from saturated hydrocarbons at 77 K, conditions under which π radicals are unreactive[15]. From Rüchardt's[16] radical reactivity data (Table 1), one notes that the bridgehead 1-bicyclo[2.2.2]octyl radical, which should be a standard for σ radicals since it cannot invert its configuration, is the least selective. The benzyl radical, a delocalized radical, is the most selective. The cyclohexyl radical, a non-delocalized π radical, is intermediate in selectivity. The phenyl radical, a non-inverting σ radical in an sp^2 hybridized orbital shows greater selectivity than a non-inverting σ radical in an sp^3 hybridized orbital. The cyclopropyl radical, an inverting σ radical in an sp$^{2.28}$ hybridized orbital, most nearly resembles the non-inverting phenyl σ radical but is more selective and less reactive. The advantage of
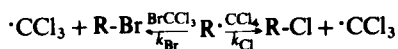
TABLE 1. Competition constant r for the reaction of R$^{\cdot}$ with BrCCl$_3$ and CCl$_4$[16]

R$^{\cdot}$	Type	T($^{\circ}$C)	r^a
	σ	80	59
	π	11	566
	σ	110	278
	σ	104	184
	π	80	1700
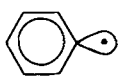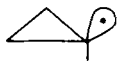
^{a} $r = k_{Br}/k_{Cl}$.

Rüchardt's experiments is that they minimize polar effects in the reaction of the radicals since the same leaving group, the $\cdot$CCl$_3$ radical, is involved in both radical abstraction reactions.

$$\cdot CCl_3 + R\text{-}Br \xrightarrow[k_{Br}]{BrCCl_3} R \xrightarrow[k_{Cl}]{CCl_4} R\text{-}Cl + \cdot CCl_3$$

From the relative reactivity data, shown in Table 2, which describes the thermal decomposition of biscyclopropanoyl peroxide in a series of substituted benzenes, Shono and Nishiguchi[17] have concluded that the cyclopropyl radical more closely resembles the

TABLE 2. Relative reactivity in homolytic aromatic substitution[17]

Aromatic			
PhCl	3.5	1.1	1.78
PhOMe	2.3	1.7	1.95
PhCN	2.7	3.7	3.59
PhMe	0.76	1.2	1.03
PhBu-t	0.28	0.64	0.59

phenyl[18] σ radical in its reactivity than it does the cyclohexyl[19] π radical. The 2-phenylcyclopropyl radical behaves similarly to the cyclopropyl radical[17].

In its relative reactivity toward toluene, ethylbenzene and cumene the more highly substituted 1-methyl-2,2-diphenylcyclopropyl radical[20], derived from the decomposition of the precursor diacyl peroxide, resembles the chlorine radical more than it does the phenyl radical (Table 3). Similarly, comparison of the relative reactivities of primary, secondary and tertiary aliphatic hydrogens toward chlorin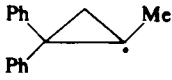e atoms (1.0:3.6:4.2)[21] and phenyl radicals (1.0:9.3:44)[21] with the relative reactivities of the C–H bond in the methanol/ethanol/2-propanol series toward the 1-methyl-2,2-diphenylcyclopropyl radical (1.0:2.4:3.5)[20] further confirms the low selectivity of the cyclopropyl radical. Again, this radical resembles the chlorine atom in its reactivity more than it does the phenyl radical.

TABLE 3. Relative reactivities (per hydrogen) of hydrogen donors toward a variety of radicals[20]

R–H/Radical	Br·	Me·	Ph·	Cl·	Ph—△—Me (Ph) ·
	40°	65°	60°	40°	65°
Toluene	1	1	1	1	1
Ethylbenzene	17.2	4.1	4.6	2.5	1.8
Cumene	37.0	12.9	9.7	5.5	2.5

In so far as the rate of formation of radicals reflects their stability or reactivity the findings of Hart and Wyman[22] are instructive. In carbon tetrachloride the rate of decomposition of benzoyl peroxide was twice as fast as that of biscyclopropanoyl peroxide. Ingold and coworkers[23] have found that in the photodecomposition of benzoyl and biscyclopropanoyl peroxides, in carbon tetrachloride at 298 K, the phenyl radicals produced reacted faster $(7.8 \times 10^6 \text{ M}^{-1} \text{ s}^{-1})$ than the cyclopropyl radicals $(1.5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1})$. These results are consistent with C–H bond dissociation energies for benzene (110 kcal mol) and cyclopropane (106 kcal mol^{-1}) which implies that the cyclopropyl radical should be less reactive than the phenyl radical. In subsequent work[23b] they also showed that at ambient temperatures radical reactivities decreased along the series: $k = $ Ph·> (Me)$_2$ C=CH· > cyclopropyl· > Me·. Table 4 records the absolute rate constants for the reaction of these radicals with tri-n-butylgermane.

Other findings which show the difficulty in forming the cyclopropyl radical by some radical molecule reactions are the failure of chlorine atoms to abstract the tertiary ring hydrogen from methylcyclopropane[24] and the failure of t-butoxy radicals[25] to abstract the tertiary hydrogen from a variety of alkylcyclopropanes. Hydrogen abstraction from the cyclopropylcarbinyl C atom is, as expected, preferred in these cases. The failure of

TABLE 4. Absolute rate constants for reactions of various radicals with tri-n-butylgermane[23]

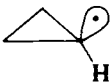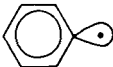| Radical	T(°C)	$10^{-6} k$, M^{-1} s^{-1}
Ph·	29	260 ± 28
(Me)$_2$ C=CH·	27	35 ± 5
△·	30	13 ± 2
Me·	27	0.5

cyclopropanecarboxaldehyde to undergo decarbonylation reaction with di-t-butyl peroxide[26] to yield the cyclopropyl radical is another good example of the difficulty in producing the cyclopropyl radical. The difficulty encountered in the decomposition of *trans*-azocyclopropane to cyclopropyl radicals has resulted in the appellation of 'reluctant azoalkane' for this molecule [P. S. Engel and G. A. Bodager, *J. Org. Chem.*, **53**, 4748 (1988)]. However, 1-methyl- and 1-phenylcyclopropanecarboxyaldehyde did decarbonylate to yield methyl- and phenylcyclopropane, respectively. Also, photochemical chlorination[27] and vapor phase nitration[28] of cyclopropane have been reported. The relative reactivity of cyclopropane vs. neopentane toward a variety of radicals is shown in Table 5.

TABLE 5. Relative reactivities of C–H bonds in cyclopropane (c) and neopentane (n) toward radicals

Radical	T(°C)	k_c/k_n
Cl⋅$_{(g)}$	250	0.03
Cl⋅$_{(l)}$	68	0.13
Me⋅	182	0.65
MeO⋅	250	0.4
t-BuO⋅	68	0.2

Of the cycloalkyl radicals, the cyclopropyl radical is the least nucleophilic. This is in keeping with the σ character of cyclopropyl radicals. Table 6 compares the *meta/para* ratios obtained from the reaction of phenyl σ radical, cyclopropyl σ radical and cyclohexyl π radical with substituted benzenes[17]. This demonstrates that cyclopropyl and phenyl σ radicals are less nucleophilic than the cyclohexyl π radical.

TABLE 6. The *meta/para* ratios in radical aromatic substitution of PhX[17]

X			
Cl	2.8	1.9	1.8
OMe	5.6	1.5	1.4
CN	0.09	0.43	0.33
t-Bu	2.5	1.9	1.8

It has also been shown in radical substitution at the 2-position of a series of 4-substituted (CN, MeO, Me) protonated pyridines, that the cyclopropyl radical is the least nucleophilic of the cycloalkyl radicals[29]. This low nucleophilicity is consistent with the observed difficulty[30] in oxidizing the cyclopropyl radical by Cu^{2+}. The lack of reactivity of the 2-phenylcyclopropyl radical, generated by the thermal decomposition of the 2-phenyl-cyclopropanepercarboxylic acid, towards the O–O peracid bond to yield 2-phenylcyclopropanol is also in line with the radical's weak nucleophilicity[31]. However from a study of relative rates of hydrogen abstraction to olefin addition of the cyclopropyl radical to a variety of olefins (Table 7) Stefani and coworkers[32] concluded that the cyclopropyl radical was decidedly nucleophilic.
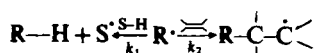
$$R—H + S\cdot \underset{k_1}{\overset{S-H}{\rightleftharpoons}} R\cdot \underset{k_2}{\overset{}{\rightleftharpoons}} R-\overset{|}{\underset{|}{C}}-\dot{C}\diagdown$$

TABLE 7. Relative rate constants for hydrogen abstraction from (k_1) and addition of cyclopropyl radicals (k_2) to olefins at 65°C[32]

Olefin	Mean k_2/k_1	Olefin	Mean k_2/k_1
$CH_2=CH_2$	23.4	$CH_2=CHCl$	40.6
E-MeCH=CHMe	5.7	E-EtO$_2$CCH=CHCO$_2$Et	630
$(Me)_2C=C(Me)_2$	1.7		

Moreover, cyclopropyl radicals, generated by the NaBH$_4$ reduction of cyclopropyl-mercuric bromide in the presence of excess olefins possessing one or two electron-withdrawing groups, yielded the addition product in good yields (60%)[33] (Table 8).

TABLE 8. Cyclopropyl radical addition to olefins XCH=CYZ[33]

X	Y	Z	Yield (%)
H	H	CO_2Me	53
H	H	CN	61
H	Cl	CN	61
CO_2Et	H	CO_2 Et	67

In summary, the cyclopropyl radical behaves as a highly reactive and poorly selective rapidly inverting σ radical with a degree of nucleophilicity that has not been firmly established.

C. Stereochemistry

If the cyclopropyl radical is a rapidly inverting σ radical $(k_1 = 10^8 \text{ s}^{-1}$ at $-175°C$ and 10^{11} s^{-1} at $71°C)$[8,23b] is there any possibility that such a radical, generated at a chiral center, could maintain its configuration? Obviously for this to happen the radical would have to react, i.e. abstract an hydrogen atom faster than it inverts. Since the inversion frequency $(\sim 10^{11} \text{s}^{-1})$ is close to that of the diffusion rate $(\sim 10^{11} \text{s}^{-1})$[34c] a reaction in which the configuration is maintained must occur at a rate faster than the diffusion of the radical through the solvent. The only hope of observing a chiral radical is either to slow down the inversion frequency (k_1) and/or increase the rate of reaction (k_R, k_S) with the solvent. The former might be accomplished by introducing a substituent X which is capable of decreasing the k_1 or by placing the radical on a solid surface with which it can somehow interact. A cage reaction, disproportionation or combination, would also lead to retention of configuration since k_R might be expected to be very close to or greater than k_1 (Scheme 1); see also Section II.C.3.

1. Effect of α-substituents

a. Theoretical considerations

In general, increasing the s character of the orbital containing the unpaired electron will stabilize the radical and decrease the rate of inversion[9]. Both cyclopropyl and vinyl radicals
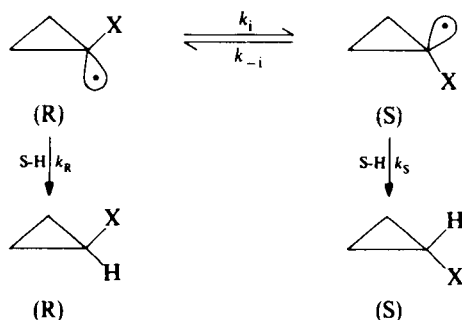
SCHEME 1

are bent σ radicals and their inversion barriers are larger than those of their acyclic and saturated counterparts[34a].

Two theories have been advanced to explain why electronegative substituents tend to cause the radical to be a σ radical. Walsh[35a] and Pauling[35b] propose that the effect is due to a difference in electronegativity which would cause the orbital occupied by the odd electron to have a greater amount of s character. Any highly electronegative substituent would therefore enhance the non-planarity of the radical and the substituent effect should parallel the electronegativities of the group. Wells[36] has published a critical review dealing with group electronegativities; a portion of this compilation of mutually consistent group electronegativities is presented in Table 9.
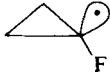
TABLE 9. Mutually consistent group electronegativities[36]

Group	Empirical values	Group	Empirical values
F	3.95	Cl	3.03
MeO	3.70	Br	2.80
H_2N	3.37	Me	2.30
CF_3	3.35	H	2.28

Dewar and Shanshal[34a] argue that the electronegativity of the substituent is not the factor which accounts for the increased configurational stability of the free radicals and that stabilization in the cyclopropyl radical is due to an antibonding interaction between the non-bonding electrons of the substituent and the MOs arising from the interactions between the singly occupied carbon AO and the MOs of the adjacent C bonds. As the result of MINDO/3 calculations it was predicted that the barrier to inversion, caused by a substituent at the radical site, should increase in the order $O < Cl < F$. This order is at variance with that predicted solely on the basis of group electronegativities which would be $Cl < OMe < F$. CNDO/2 calculations[37] of inversion barriers of a number of X-substituted cyclopropyl radicals are given in Table 10.

Electronegativity may be a necessary but not a sufficient property to cause a radical to maintain its configuration. As we can see from Table 9 the CF_3 group is highly electronegative yet the geometry of a carbon radical to which it is attached is not much affected by replacing the hydrogens with CF_3 groups[38]. Another important factor is whether or not there is a significant delocalization in the transition state for the inversion process when the σ radical becomes a π radical. When this type of delocalization becomes

TABLE 10. Calculated (CNDO/2) inversion barriers[37]

Radical	F	Cl	H
Inversion barrier (kcal mol^{-1})	10.5	4.0	0.8

significant then the energy barrier for inversion will be lowered. With second row elements such as N, O and F, contributions from this type of delocalization will be minimal. They will only become significant for higher row elements, i.e. X = S, Cl, Br and I or when X is part of a system such as a carbon in a vinyl, cyano, carbonyl, etc.
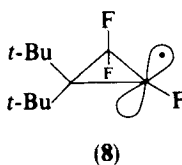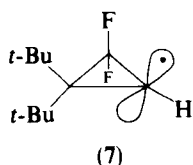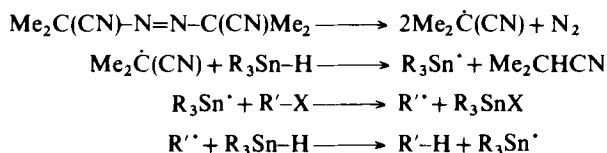
b. Fluorine

As the most electronegative element, fluorine would be expected to have the greatest effect on the stereochemical stability of the cyclopropyl radical and it does. When comparing ESR spectra of cyclopropyl radicals with 1-fluoro cyclopropyl radicals Kawamura and coworkers[39] found the inversion frequencies of **1, 2** and **3** at −99°C comparable to that found for the parent cyclopropyl radical, ∼ 10^8 s^{-1} at −175°C. In contrast, the inversion frequency of the α-fluorocyclopropyl radicals **4, 5** and **6** is estimated to be lowered to 10^6 s^{-1} at −108°C.
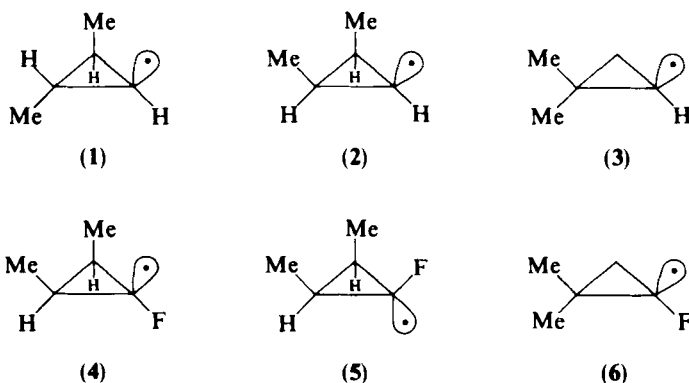
Steric effects also play a role in determining whether a cyclopropyl radical will be a rapidly inverting σ radical or a π radical. Ingold and coworkers[40] have concluded from an analysis of the ESR spectra of **7** and **8** that although the radical **3** is a σ radical having a pyramidal structure, **7** is a planar π radical. Moreover, **8** is also a planar or nearly planar π radical whereas **6** is an inverting bent σ radical. The unusual configuration of **7** and **8** is believed to be due to steric repulsion between the *t*-butyl groups and the α-hydrogen or α-fluorine which is minimized in the π radicals.

(7)   (8)

Can an α-fluorine substituent reduce the inversion frequency k_i of the cyclopropyl σ radical sufficiently so that it can maintain its stereochemistry in a chemical reaction? The answer is yes, when an efficient radical trap is available so that $k_R \gg k_i$ (Scheme 1). The tin hydrides provide such an efficient radical scavenger[41] as well as the means to generate radical intermediates by their reaction with alkyl halides[42]. The reaction usually involves the use of a radical initiator such as azobisisobutyronitrile (AIBN) or di-t-butyl peroxide (DTBP). The reaction mechanism is depicted in Scheme 2.

$$Me_2C(CN)\text{-}N=N\text{-}C(CN)Me_2 \longrightarrow 2Me_2\dot{C}(CN) + N_2$$

$$Me_2\dot{C}(CN) + R_3Sn\text{-}H \longrightarrow R_3Sn^{\cdot} + Me_2CHCN$$

$$R_3Sn^{\cdot} + R'\text{-}X \longrightarrow R''^{\cdot} + R_3SnX$$

$$R''^{\cdot} + R_3Sn\text{-}H \longrightarrow R'\text{-}H + R_3Sn^{\cdot}$$

SCHEME 2

Ando and coworkers[43] reduced a series of gem-halofluorocyclopropanes with tri-n-butyltin hydride to yield the corresponding monofluorocyclopropanes. Table 11 lists a number of representative gem-halofluorocyclopropanes that have been reduced. The results are striking in that the reactions are completely stereospecific under the conditions specified. The effect of the α-fluoro substituent in reducing the inversion frequency (k_i) of the radical combined with the propensity of the tin hydride to react rapidly with the radical[41] best accounts for these observations.

Kaplan[44] has compared the hydrogen-transfer ability of various Group IV hydrides toward radicals and found the order (k_R) $R_3Sn\text{-}H > R_3Ge\text{-}H > R_2Si\text{-}H > R_3Si\text{-}H$. Yamanaka[45] has shown that the same order is followed in the reduction of 1-bromo-1-fluoro-2-phenylcyclopropane. Whereas using tri-n-butyltin hydride gives stereospecific reduction, the use of di-n-butylsilicon dihydride gave slightly less retention (97%) and with tri-n-butylsilicon hydride the retention was reduced to 84%. Ando, Yamanaka and coworkers[46] have also demonstrated that the brominative decarboxylation (Hunsdiecker reaction) of the silver α-fluorocyclopropanecarboxylate derivatives 9 and 10 proceeds in a
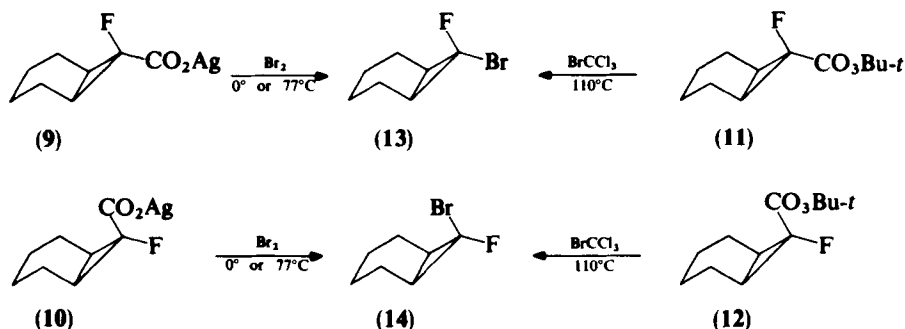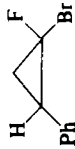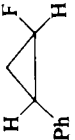

(9)   (13)   (11)

(10)   (14)   (12)
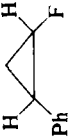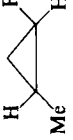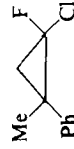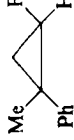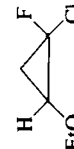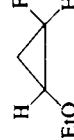
TABLE 11. Stereochemistry of reduction of gem-halofluorocyclopropane with tri-n-butyltin hydride[43]

Isomer(s) reduced	Isomer ratio	T(°C)	Product(s)	Isomer ratio
(H, Ph / F, Br cyclopropane)	100:0	135	(H, Ph / F, H cyclopropane)	100:0
(H, Ph / Br, F cyclopropane)	100:0	135	(H, Ph / H, F cyclopropane)	100:0
(H, Me, F : Cl, Me cyclopropane)	66:34	90	(H, Me : H, F, Me cyclopropane)	67:33
(Me, Ph, F : Cl, Ph cyclopropane)	52:48	135	(Me, Ph : H, F, Ph cyclopropane)	53:47
(H, EtO, F : Cl, EtO cyclopropane)	60:40	85	(H, EtO : H, F, EtO cyclopropane)	61:39
(F, Cl bicyclic)	58:42	90	(F, H bicyclic)	58:42[a]
(Cl, F, O bicyclic)	61:39	80	(F, H, O bicyclic)	65:35

[a] Na/NH$_3$ reduction was also stereospecific; see M. Schlosser, G. Heinz and L. Y. Chan, Chem. Ber., 104, 192 (1971).

stereospecific manner. This again reflects the ability of an α-fluorine substituent to stabilize the configuration of a cyclopropyl radical and suggests that the bromine radical is also an efficient radical trap. Moreover, they have shown that the thermal decomposition of *exo*- and *endo-t*-butyl 7-fluoronorcarane-7-peroxycarboxylates **11** and **12** in BrCCl₃ also produced the corresponding 7-bromo-7-fluoronorcaranes **13** and **14** with 100% retention of configurati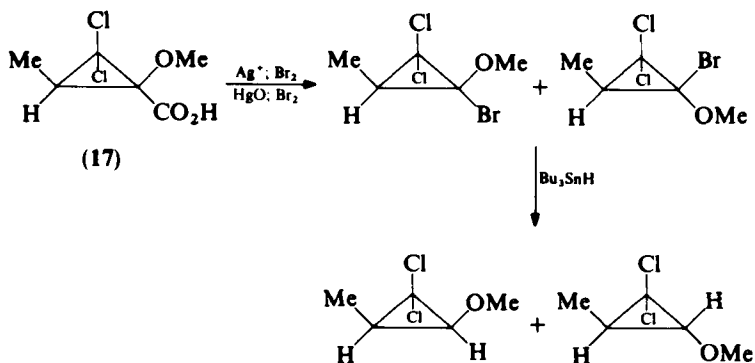on. Replacing BrCCl₃ as a solvent by a poorer radical trap solvent, such as toluene and cumene, reduced the stereospecificity by only 6–10%. Walborsky and Collins[47] found that the thermal decomposition of *t*-butyl (−)-(S)-1-fluoro-2,2-diphenylcyclopropanepercarboxylate (**15**) in tetrahydrofuran, a markedly inferior radical scavenger solvent, resulted in the formation of (−)-(S)-1-fluoro-2,2-diphenylcyclopropane (**16**) of overall retained configuration but only 47% optical purity, or 74% retention of configuration.

$$(-)\text{-}(S)\text{-}(\mathbf{15}) \qquad\qquad (-)\text{-}(S)\text{-}(\mathbf{16})$$
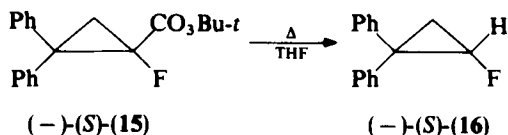
In summary, the α-fluoro substituent on a cyclopropyl radical has a marked effect on the ability of the radical to maintain its configuration. A strongly electronegative atom decreases the inversion frequency k_i of the cyclopropyl σ radical and in the presence of a good radical scavenger makes $k_R \gg k_i$ (Scheme 1) and results in a high retention of configuration.
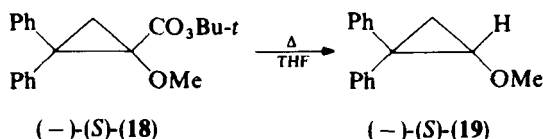
c. Methoxyl

An α-methoxyl group would also be expected to stabilize the configuration of the cyclopropyl radical since oxygen is an electronegative atom. There have been two investigations of the methoxyl group as a substituent. Ando and coworkers[48] reported on the Hunsdiecker reaction of *r*-1-methoxy-*c*-2-methyl-*c*-3,*t*-3-dichlorocyclopropane-carboxylic acid (**17**). At 0°C use of either the silver salt or the Cristol–Firth method (HgO) and bromine yielded a ~ 57:43 mixture of the bromo isomers with overall retention of configuration. However, at 77°C a ~ 39:61 ratio of isomers was produced indicating overall inversion of configuration. Unfortunately, decomposition of the *r*-1-methoxy-*t*-2-methyl-*c*-3,*t*-3-dichlorocyclopropanecarboxylic acid was not studied to ascertain whether the product ratios represented a thermodynamically or kinetically controlled reaction. That the reaction is probably thermodynamically controlled was indicated by tri-*n*-

butyltin hydride reduction of each of the isomers resulting from the Hunsdiecker reaction. Both isomers at 0°C gave approximately the same ratio (54:46) of products.

Walborsky and Collins[47] decomposed chiral t-butyl (−)-(S)-1-methoxy-2,2-diphenylcyclopropanepercarboxylate (18) in tetrahydrofuran and isolated, inter alia, (−)-(S)-1-methoxy-2,2-diphenylcyclopropane (19) with an optical purity of 8% or an overall retention of configuration of 54%.


$$(-)-(S)-(18) \qquad\qquad (-)-(S)-(19)$$

The results of these limited experiments suggest that an α-methoxyl group is not very effective in stabilizing the configuration of the cyclopropyl radical[49] and indicate that delocalization of the radical by the methoxyl group may be making a significant contribution to the stabilization of the π-radical intermediate or transition state. This is also reflected in the low reactivity of the α-methoxy cyclopropyl radical toward styrene and 1,4-cyclohexadiene as compared to the cyclopropyl and 1-methylcyclopropyl radical [L. J. Johnston and K. U. Ingold, J. Am. Chem. Soc., 108, 2343 (1986)].


$$\sigma \qquad\qquad\qquad \pi \qquad\qquad\qquad \sigma$$
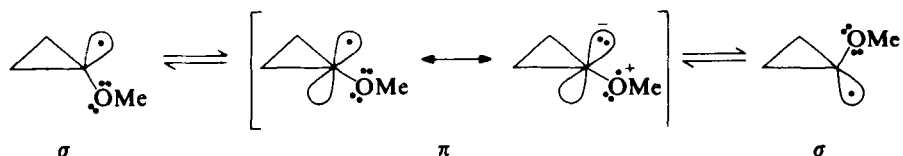
d. Chlorine, bromine and iodine

Singer and Chen[50] demonstrated the inability of an α-chlorine substituent to stabilize the configuration of a cyclopropyl radical. They showed that the photochemical decomposition of both exo- (20) and endo-t-butyl 6-chlorobicyclo[3.1.0]hexane-6-percarboxylate (21) in diisopropylbenzene resulted in an identical mixture of exo- (22) and endo-6-chlorobicyclo[3.1.0]hexane (23). A similar result[46] was obtained in the thermal decomposition of both exo- (24) and endo-t-butyl 7-chlorobicyclo[4.1.0]heptane-7-percarboxylate (25). In solvents such as toluene, cumene or bromotrichloromethane the same ratio (20:80) of exo-26 and endo-27 products was formed within experimental error.
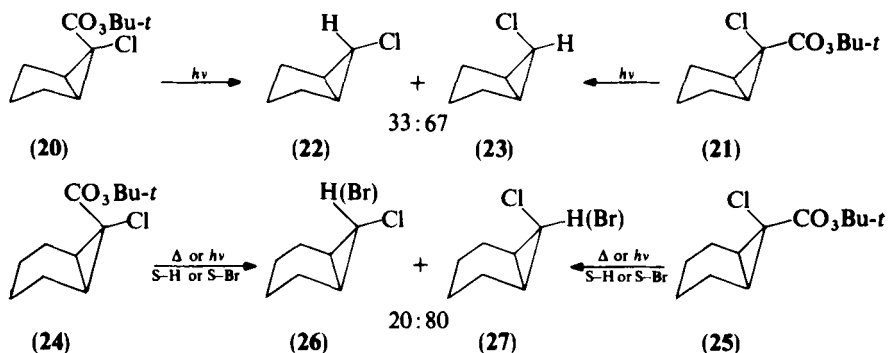
These observations are supported by the findings that the thermal decomposition of *t*-butyl (+)-(*S*)-1-chloro-2,2-diphenylcyclopropanepercarboxylate (**28**) in tetrahydrofuran resulted in completely racemic 1-chloro-2,2-diphenylcyclopropane (**29**)[47].

$$(+)\text{-}(S)\text{-}(\textbf{28}) \qquad\qquad (+)\text{-}(\textbf{29})$$
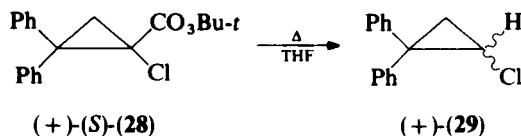
Surprisingly, the Hunsdiecker reaction using the silver salts of *exo*- and *endo*-7-chlorobicyclo[4.1.0]heptanecarboxylic acids and bromine at 0°C did not result in the same ratio of products but instead showed a high retention to inversion ratio of 88:12 for the *exo* acid and 88:12 for the *endo* acid[46]. This anomalous result may be a reflection of the bromine radical's ability to trap the cyclopropyl radical but this is unlikely. Altman and Baldwin[37] as well as Ando and coworkers[51] found that the reduction of each of the isomers of 7-bromo-7-chlorobicyclo[4.1.0]heptane, **30** and **31**, respectively, by the excellent radical scavenger triphenyltin hydride resulted in an identical mixture (21:79) of *exo*-(**32**) and *endo*-7-chlorobicyclo[4.1.0]heptane (**33**). This ratio of products is, within experimental error, identical with that found in the thermal decomposition of *exo*- and *endo*-*t*-butyl 7-chlorobicyclo[4.1.0]heptane-7-percarboxylate[46] in cumene.

| (**30**)	(**32**)	(**33**)	(**31**)

21:79
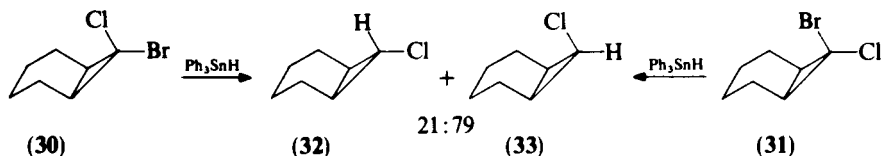
The reduction of 7,7-dibromobicyclo[4.1.0]heptane (**34**) by a variety of radical reactions leads to a similar product ratio of *exo*- (**36**) and *endo*-7-bromobicyclo[4.1.0]heptane (**35**) (Table 12). The product ratio is similar to that found for *exo*- and *endo*-7-chloro-7-bromobicyclo[4.1.0]heptane[37].

TABLE 12. Stereochemistry of the reduction of 7,7-dibromo-bicyclo[4.1.0]heptane

(**34**)	(**35**)	(**36**)

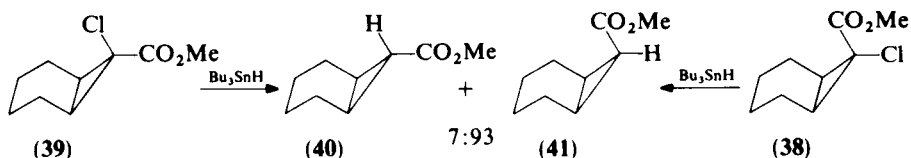| Reagent	*Endo*(%)	*Exo*(%)	Ref.
n-Bu$_3$SnH	72	28	52
LiAlH$_4$	75	25	53
NaBH$_4$	64	36	54
MeMgBr	72	28	55a
NaH/HMPT	67	33	55b

The only example of iodine as an α-substituent is that reported by Oliver and Rau[56]. The reduction of 1,1-diiodo-*cis*-2,3-dimethylcyclopropane (**37**) by tri-*n*-butyltin hydride yielded a 72:28 ratio of *cis* and *trans* products, a result comparable to that found for an α-chloro or an α-bromo substituent.
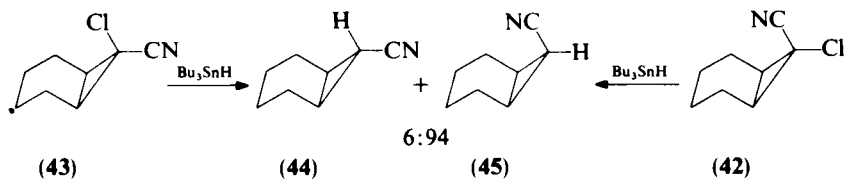
$$\text{Me} \quad \xrightarrow{n\text{-Bu}_3\text{SnH}} \quad \text{Me} \quad + \quad \text{Me}$$

(37)   28:72
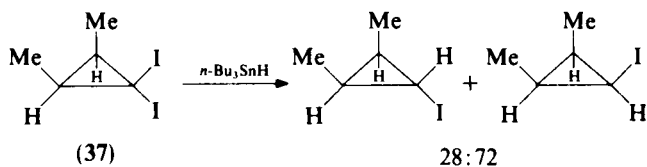
The available evidence points to the conclusion that α-chloro, α-bromo and α-iodo substituents on a cyclopropyl radical do not help to maintain its configuration. The radical is either a rapidly inverting σ-radical or a π-radical due to delocalization of the radical through the use of available d orbitals of the halogens (Cl, Br, I).

e. Carbomethoxyl and cyano

As expected, delocalizing substituents such as carbomethoxyl and cyano should decrease the barrier to inversion and perhaps may even convert the rapidly inverting σ radical to a linear π radical. The net result should be a loss of configuration. Ando and coworkers[51] have shown this to be the case in the tri-n-butyltin hydride reduction of the isomeric exo- (38) and endo-7-chloro-7-carbomethoxybicyclo[4.1.0]heptane (39). Both isomers gave the same (7:93) ratio of exo- (40) and endo-methyl bicyclo[4.1.0]heptane-7-carboxylate (41).

$$\text{(39)} \xrightarrow{\text{Bu}_3\text{SnH}} \text{(40)} \quad + \quad \text{(41)} \xleftarrow{\text{Bu}_3\text{SnH}} \text{(38)}$$

(39)   (40)   7:93   (41)   (38)

A similar result was obtained in the reduction of each of the isomeric exo- (42) and endo-7-chloro-7-cyanobicyclo [4.1.0] heptane (43). Both isomers gave the same (6:94) ratio of exo- (44) and endo-7-cyanobicyclo[4.1.0]heptane (45).

$$\text{(43)} \xrightarrow{\text{Bu}_3\text{SnH}} \text{(44)} \quad + \quad \text{(45)} \xleftarrow{\text{Bu}_3\text{SnH}} \text{(42)}$$

(43)   (44)   6:94   (45)   (42)

The triphenyltin hydride reduction of methyl (−)-(R)-1-bromo-2,2-diphenyl-cyclopropanecarboxylate (46) resulted in essentially racemic methyl 2,2-diphenylcyclopropanecarboxylate (47)[57].

$$\text{Ph} \quad \xrightarrow{\text{Ph}_3\text{SnH}} \quad \text{Ph}$$

(−)-(R)-(46)   (±)-(47)
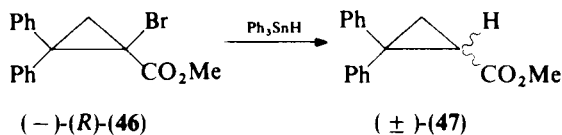
f. Methyl and trifluoromethyl

The accumulated evidence indicates that an α-methyl substituent attached to the cyclopropyl radical has very little, if any, effect in helping to maintain the configuration of

the radical. It has been shown[58,59] that thermal decomposition of the diacyl peroxide of (+)-(R)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid, (+)-(R)-(48) in THF yielded, *inter alia*, the hydrocarbon 1-methyl-2,2-diphenylcyclopropane (49) which was essentially racemic. Moreover, thermolysis in carbon tetrachloride produced racemic 1-chloro-1-methyl-2,2-diphenylcyclopropane (52) and even the addition of a good radical trap such as iodine produced only racemic 1-iodo-1-methyl-2,2-diphenylcyclopropane (50). The latter reaction presumably involves the formation of an intermediate hypoiodite which decomposes to the iodide by a radical pathway. Other reactions, which presumably involve similar intermediates, are the lead tetraacetate–iodine procedure for the decarboxylation of carboxylic acids[60] and the Cristol–Firth[61] reaction (HgO/Br$_2$ in CCl$_4$). Both reactions yield the corresponding racemic iodide (50) and bromide (51)[58,59] from (+)-(R)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid.
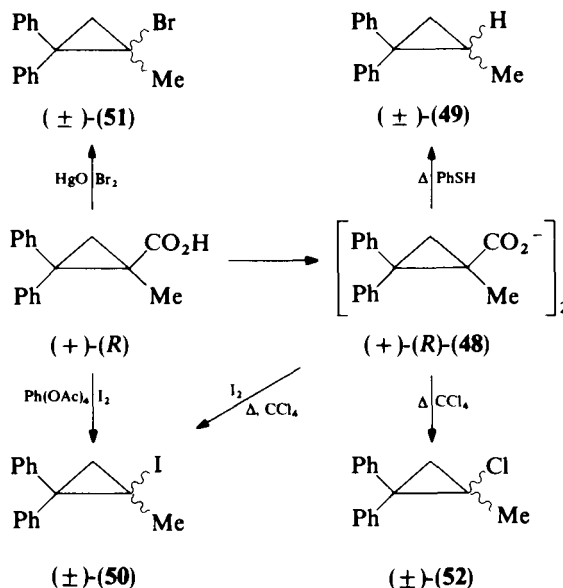
Further attempts to trap the chiral 1-methyl-2,2-diphenylcyclopropyl radical, before inversion, by using excellent radical scavengers as solvents were also abortive. Decomposition of the diacyl peroxide (48) in thiophenol and reduction of (−)-(R)-1-bromo-1-methyl-2,2-diphenylcyclopropane (51) with tri-*n*-butyltin hydride as solvent resulted in essentially racemic hydrocarbon (49)[58,59].
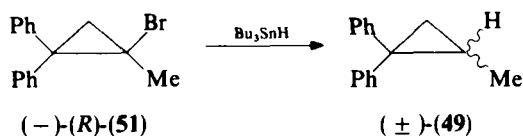

As was discussed earlier, although the CF$_3$ group is an electronegative substituent its influence on stabilizing the configuration of a cyclopropyl radical is similar to that of a methyl group rather than a fluorine atom[38]. Thus, Altman and Vederas[62] have shown that the reduction of *r*-1-bromo-1-trifluoromethyl-*c*-2-phenylcyclopropane (53) and of its

70:30

(53)   (55)   (54)
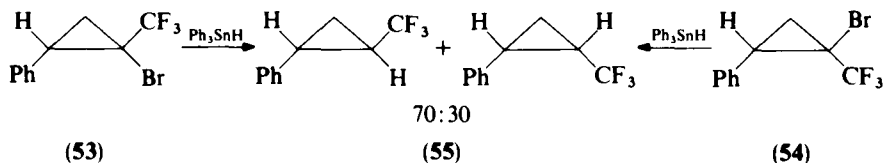
isomer **54** with a large excess of neat triphenyltin hydride gives rise to complete configurational equilibration of the radical: in both reactions the isomers of **55** have been found in a 70:30 *trans/cis* ratio.

g. Hydrogen and deuterium

Hunsdiecker reaction of the silver salts of both *cis*-(**56**) and *trans*-2-methylcyclopropanecarboxylic acid (**57**) yielded the same mixture of *cis*- (**58**) and *trans*-1-bromo-2-methylcyclopropane (**59**), thus demonstrating that the 2-methylcyclopropyl radical was incapable of maintaining its configuration[63a]. Brominative decarboxylation of the silver salts of *exo*- (**60**) and *endo*-norcarane-7-carboxylic acid (**61**) produced the same mixture (16:84) of *exo*- (**62**) and *endo*-7-bromonorcarane (**63**)[46]. Similarly, *cis*- and *trans*-silver 1,2-cyclopropanedicarboxylate gave rise to the same isomer ratio (24:76) of *cis*- and *trans*-1,2-dibromocyclopropane[64]. Consistent with these results is the report that the Hunsdiecker reaction with the silver salt of *trans*-2,2,3-d₃-cyclopropanecarboxylic acid (**64**) gives an equimolar mixture of *cis*- (**65**) and *trans*-2,2,3-d₃-cyclopropane (**66**)[63b].

35:65

(56)   (58)   (59)   (57)

16:84

(60)   (62)   (63)   (61)

1:1

(64)   (65)   (66)
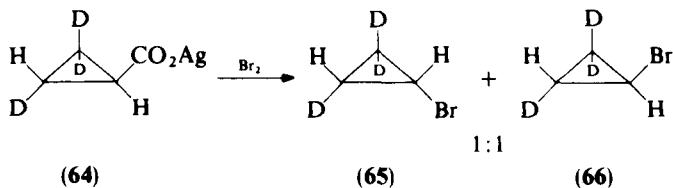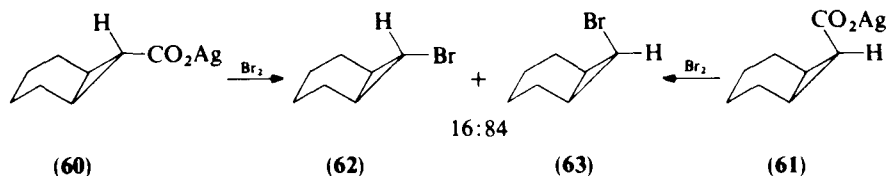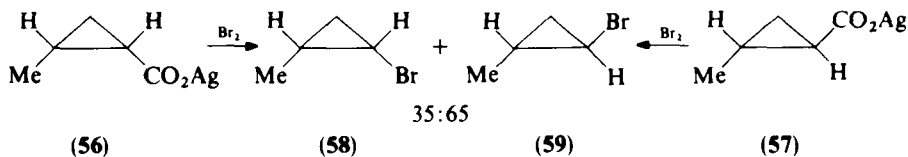
Moreover, an α-deutero substituent does not have any effect on the stereochemical outcome. Both mixtures (70:30 and 3:97) of *cis*- (**67**) and *trans*-1-bromo-1-deutero-2-phenylcyclopropane (**68**) gave, upon reduction with tri-*n*-butyltin hydride, the same mixture (95:5) of *cis*- (**69**) and *trans*-1-deutero-2-phenylcyclopropane (**70**)[65].

95:5

(68)   (69)   (70)   (67)
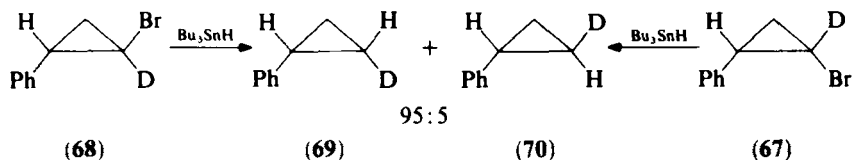
In summary, it can be stated that both secondary cyclopropyl radicals (α-H, α-D) and the tertiary radical (α-Me) are rapidly inverting radicals incapable of maintaining their configuration.

h. Trimethylsilyl

Recently, Paquette and coworkers[66a] reported on the stereochemical consequences of having a trimethylsilyl substituent at the radical site. The Hunsdiecker reaction, as well as the Cristol–Firth[56] modification thereof, on $(-)$-(R)-1-trimethylsilyl-2,2-diphenyl-cyclopropanecarboxylic acid (71) resulted in racemic $(\pm)$-1-bromo-1-trimethylsilyl-2,2-diphenylcyclopropane (72). The trimethylsilyl group, bulky as it is, could not slow down the inversion frequency of the cyclopropyl σ radical sufficiently to prevent complete racemization. More to the point, recent[66b] ESR studies have demonstrated that the radical intermediate is planar, or nearly so.


$(-)$-(R)-(71) $(\pm)$-(72)
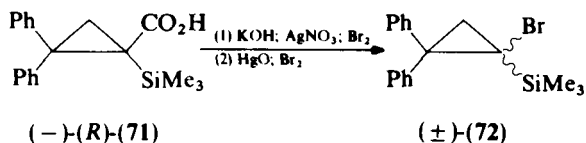
i. Phenyl and vinyl

Jensen and Patterson[67] have shown that a mixture of *exo-* (74) and *endo-*7-chloro-7-phenylbicyclo[4.1.0]heptane(73) was reduced with triphenyltin hydride to yield a mixture (99:1) of *endo-* (75) and *exo-*7-phenylbicyclo[4.1.0]heptane (76).


(73)   (74)   (75)   (76)

99:1
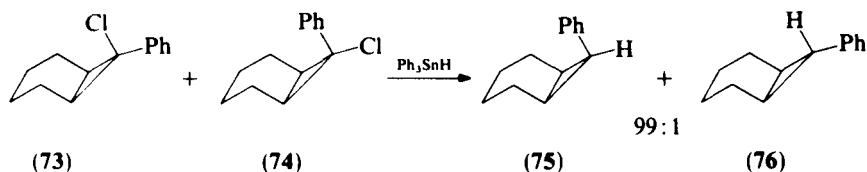
Pasto and Miles[68] have demonstrated that the regioselectivity of the radical addition of thiophenol to alkenylidenecyclopropane (77) is such that one generates a cyclopropyl radical having an α-vinyl substituent (78).

Whether these radicals are rapidly inverting σ radicals or π delocalized radicals cannot be ascertained but the almost exclusive product in both these cases is the thermodynamically less stable isomer 75 and 79. It is in the hydrogen abstraction step that the overall stereochemistry is controlled and not by the α-substituent (see below).

cis-(79), 98%
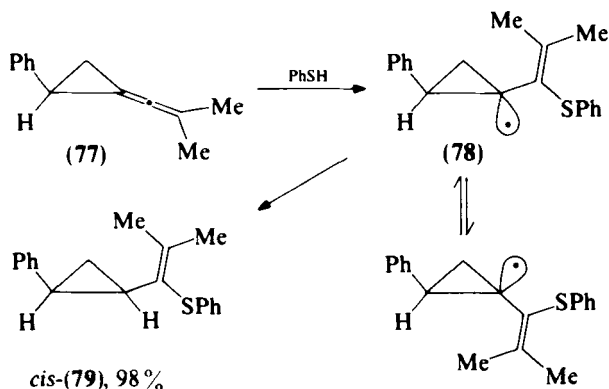
2. Effect of β-substituents

Do β-substituents effect the stereochemistry of the cyclopropyl radical? In order to evaluate the β-substituent effect let us examine a cyclopropyl radical that can maintain its configuration, such as one with an α-fluoro as a substituent, and determine whether a β-substituent will alter its configurational stability. Inspecting the data in Table 11 one would have to conclude that β-substituents such as methyl, phenyl and ether groups have no effect on the stereochemistry of the cyclopropyl radical[67]. Also, chlorine as a β-substituent does not have any effect on the stereochemistry. Jefford and coworkers[53] have shown that LiAlH₄ reduction of the tricyclic compound 80 (R=H, Cl) gave the same ratio (2:1) of anti-


(80), R = H, Cl   (81)   2:1   (82)
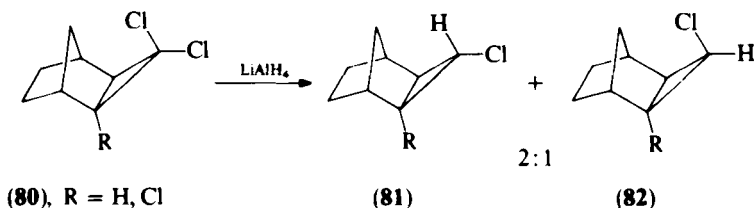
81 to syn-82 products. Schleyer and coworkers[69] have also concluded from their ab initio and MNDO calculations that β-chloro and fluoro substituents are only marginally more stable trans to the radical side than cis.

Of interest is the observation that the reduction of 1,1-dibromo-2,2-dimethyl-3-isopropylidenecyclopropane (83) by tri-n-butyltin hydride leads only to the formation of 1-bromo-2,2-dimethyl-3-isopropylidenecyclopropane (84) and no 1-bromo-2,2-dimethyl-3-isopropylcyclopropane (85)[70,71] is formed. Could it be that a π-system β to the radical site does not delocalize the π-radical intermediate of the rapidly inverting σ radical?

There are no examples of the effect of a β-vinyl group on the stereochemistry of a radical intermediate. However, a β-phenyl[65] group has been shown not to have an observable effect as far as stereochemistry or cyclization are concerned (see Table 11). An example of a β-allyl substituent is found in the tri-n-butyltin hydride reduction of 11,11-dibromotricyclo[4.4.1.0]undeca-3,7-diene (86) to a monobromo derivative (87). Again, there is no apparent interaction with the π-system as is evident by the lack of ring-closure product[72].

It is only when one gets to the β-homoallyl system (88) of Julia and coworkers[73] that one observes interaction of the cyclopropyl radical with the π-system resulting in a cyclization.

(83)

n-Bu₃SnH

(85)　　　　　　(84)

(86)　　　　　　(87)
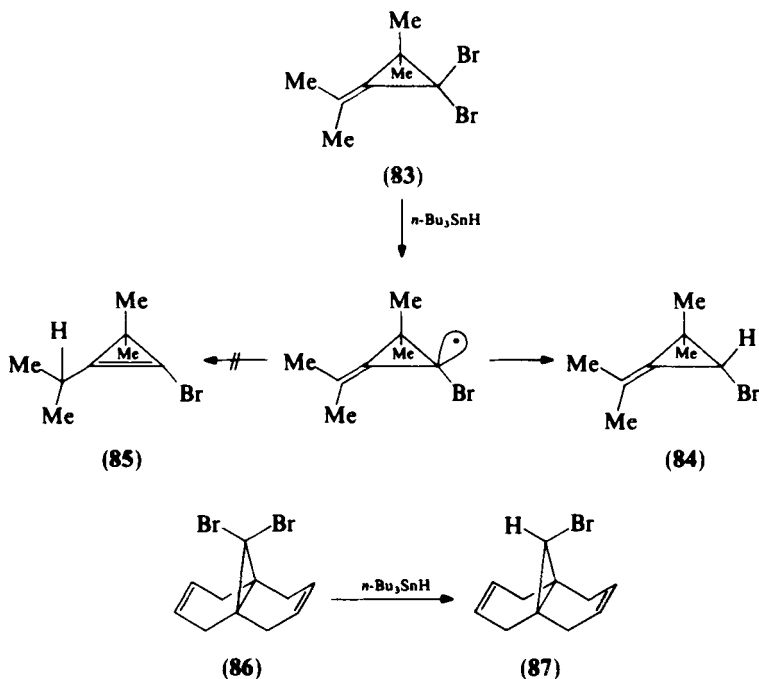
It should be noted that the radical cyclization proceeds to yield a five-membered ring and not a six-membered one. This is predicted by the 'Baldwin rules' for ring-closure and is classified as a 5-*exo*-trig closure[74]. LiAlH₄ has also been used to generate the cyclopropyl radical which also underwent a 5-*exo*-trig ring-closure[65].


(88)　　　　endo, 71%　　　　exo, 14%
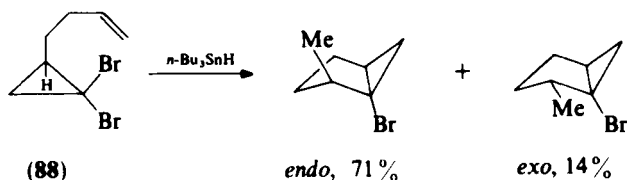
3. Regioselectivity of the rapidly inverting σ-radical

In those cases where the inversion rate (k_i) of the σ radical is faster than the trapping of the radical (k_{cis} or k_{trans}) the product(s) of the reaction will reflect the thermodynamic stability of the radical assuming that $k_{trans} = k_{cis}$ (Scheme 3).

This latter assumption is not necessary when the reaction is analyzed by ESR spectroscopy since one is observing the radical directly. Table 13 lists the structures of the thermodynamically (ESR) or chemically more favored cyclopropyl radicals. There are a number of factors which will influence the position of the equilibrium. Among them are steric effects and electronic effects. As can be seen in Table 13, entries 5, 6 and 13–21 are examples in which the position of the equilibrium is influenced by steric interactions. Entry 5 shows that the σ orbital containing the odd electron prefers to be *cis* to the phenyl group
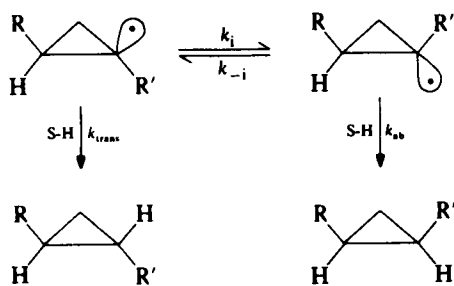
SCHEME 3

TABLE 13. Structure of favored σ radical

Entry	Structure	% Favored	Method[d]	Ref.
1		65	C(1)	63
2		92	C(3), C(4)	39, 75
3		80	C(2)	52
4		79	C(3)	75
5		70	C(2)	62
6[a]		mainly	C(4)	39
7		80	C(1)	46

TABLE 13. *Continued*.
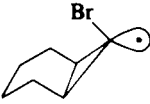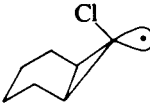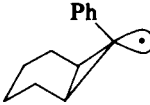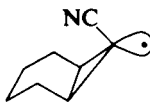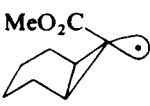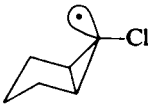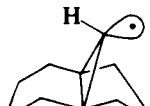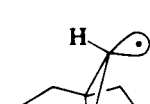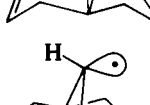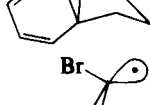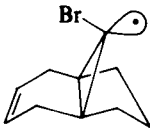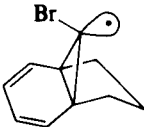
Entry	Structure	% Favored	Method[d]	Ref.
8[b]		75–80	C(1), C(5)	43
9[b]		80	C(2), C(5)	37, 46
10[b]		80	C(2)	67
11[b]		92	C(2)	51
12[b]		94	C(2)	51
13[b,c]		67	C(5)	50
14		94, 100	C(2)	76
15		94, 100	C(2)	76
16		95	C(2)	76
17		80	C(2)	76

TABLE 13. *Continued.*

Entry	Structure	% Favored	Method[d]	Ref.
18		77	C(2)	76
19		87	C(2)	76
20		70	C(3), C(4)	39, 77
21		100	C(2)	78

[a] Rapidly rearranges to the cyclobutenyl radical.
[b] This radical may well be a π radical.
[c] Result in toluene; opposite stereochemistry in diisopropylbenzene.
[d] C(1) (Hunsdiecker reaction); C(2) (tin hydride reduction); C(3) (dissolving metal reduction); C(4) (ESR); C(5) (acyl peroxide decomposition).

to avoid the more sterically hindered situation which would place the CF_3 and phenyl group *cis* to each other. A similar situation obtains in entries 20 and 21. Entry 13 illustrates the result of steric interaction between an *endo* substituent on C(6) and the *endo* hydrogens on C(2), C(3) and C(4). This *endo–endo* interaction is relieved when the C(6) σ-radical orbital occupies the *endo* position. This same type of interaction would account for the
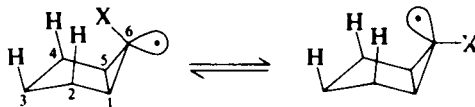
results observed with the radicals shown in entries 13–19. Steric interactions not only play an important role in determining the regioselectivity of the radical but, when severe, can even cause a σ radical to be converted to a π radical. This was demonstrated by Ingold and coworkers[40] in the case of the 1,2,2-trifluoro-3,3-di-*t*-butylcyclopropyl radical (**8**) as discussed above.

One could interpret the results of entries 1–4 and 7–12 as being due to electronic effects. Dewar and Bingham[34b] have suggested that there is a stabilizing interaction between the orbital containing the odd electron and *cis* hydrogen substituents on adjacent β-carbon
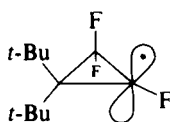
(8)

atoms. This suggestion has some support by ESR observations that there is a larger hyperfine splitting constant (hfsc) with the *cis* hydrogens than with the *trans* ones[39]. Such a stabilizing effect could account for the results observed.

The steric and electronic arguments are not all that clear cut. Without ESR evidence to the contrary one might interpret the results in entries 1–4 and 7–12 as being due to the radical being either a π radical (8–13) or rapidly inverting σ radical and that the regioselectivity observed is due to a difference in k_{cis} and k_{trans} caused by the approach of S–H from the least hindered side of the radical. At the current state of knowledge this interpretation is a possible one for these radicals but can certainly be excluded for entires 13, 20, 21 and possibly 15–19.

4. Rearrangements

The electrocyclic cyclopropyl radical–allyl radical rearrangement has been the subject of many theoretical investigations not all of which are in agreement.

Woodward and Hoffmann[79] on the basis of extended Hückel calculations suggested that the conrotatory mode is slightly preferred. At the same time Longuet-Higgins and Abrahamson[80] pointed out that both ring-opening modes were unfavorable because they are symmmetry forbidden. *Ab initio* calculations by Farnell and Richards[81] supported this latter view. Other calculations[82] led to energies of activation in the range of 30–40 kcal mol^{-1} for disrotatory opening and 40–50 kcal mol^{-1} for conrotatory opening of the cyclopropyl radical (Scheme 4).
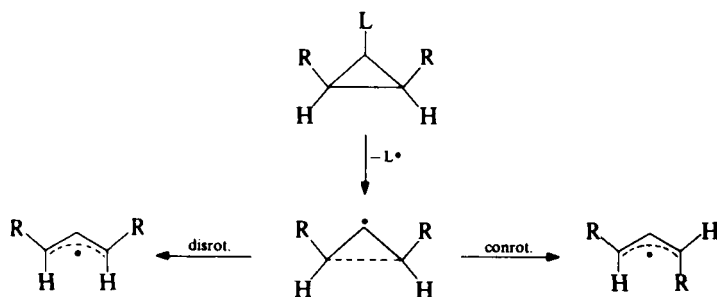
SCHEME 4

Haselbach's[83] analysis is of interest. His calculations indicated that the rupture of the ring precedes rotation of the resultant CH_2 groups. He is also in agreement with Longuet-Higgins and Abrahamson[80] that both electrocyclic modes of ring-opening are unfavorable. He favors a disrotatory opening if 'abstraction of the leaving group and ring opening occur in a concerted manner'. This qualification would exclude a concerted electrocyclic reaction since it is known from ESR observation and chemical evidence that the cyclopropyl radical exists in solution. To emphasize this point, it should be noted that in solution the unsubstituted cyclopropyl radical itself has never been observed to

rearrange to the more stable allyl radical in spite of the 30 kcal mol^{-1} stabilization predicted for this rearrangement. It is only with suitable substitution that the activation energy is lowered sufficiently to permit ring-opening.

As we have previously discussed the cyclopropyl radical is a very reactive radical. When in addition we consider the appreciable activation energy ($\sim$ 22 kcal mol^{-1})[82,84,85] necessary for the cyclopropyl radical to rearrange to the allyl radical we are not surprised that rearrangements are not always observed. The cyclopropyl radical prefers to react with solvent by abstracting hydrogen, the activation energy for which is reported[84] to be only $\sim$ 7 kcal mol^{-1}.
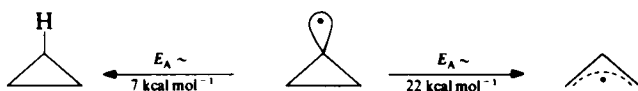

Only unrearranged cyclopropyl products were reported for photochemical chlorination[27,86] and vapor phase nitration[28] of cyclopropane. The Hunsdiecker reaction of silver cyclopropanecarboxylate[87] and the thermal decomposition of cyclopropanoyl peroxide[22] also gave exclusively unrearranged product as did the di-t-butyl peroxide initiated decarbonylation of 1-methyl and 1-phenylcyclopropanecarboxaldehyde[26]. In general one can predict that when a good radical scavenger, solvent or substrate, is present in the reaction, unrearranged product will result (i.e. see Tables 11 and 13).
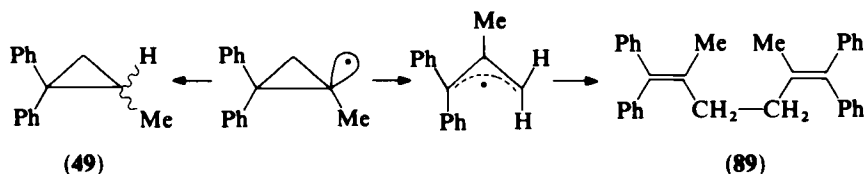
The first example of the rearrangement of a cyclopropyl radical to an allyl radical in solution was observed in the thermal decomposition of 1-methyl-2,2-diphenylcyclopropanecarbonyl peroxide[58,59]. The radical reacted by abstracting hydrogen from solvent or by rearranging to the 1,1-diphenyl-2-methylpropenyl radical which dimerized to yield 1,1,6,6-tetraphenyl-2,5-dimethyl-1,5-hexadiene (89). The proportion of dimeric product to that of cyclopropane is dependent on the solvent. If a good radical scavenger is used, such as chloroform, carbon tetrachloride or thiophenol, then only the unrearranged cyclopropane derivative is obtained. This is also the case when a radical trap such as iodine is added to a benzene solution.

The ratio of dimeric product to cyclopropane product is a measure of the reactivity of the solvent toward the cyclopropyl radical. Table 14 shows the results of such a study.

Similar rearrangements have been observed with 2,2-diphenylcyclopropyl radicals that have a variety of 1-substituents[47] (Scheme 5).


X = H, Me, F, Cl, Br, OMe   (89, X = Me)
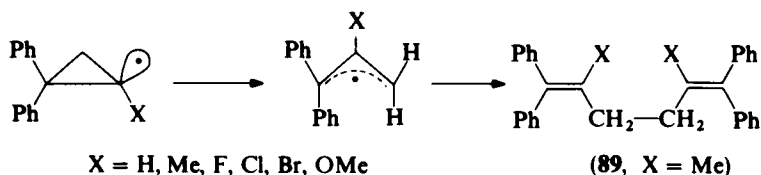
SCHEME 5

TABLE 14. Relative reactivity of various solvents toward the 1-methyl-2,2-diphenylcyclopropyl radical[59]

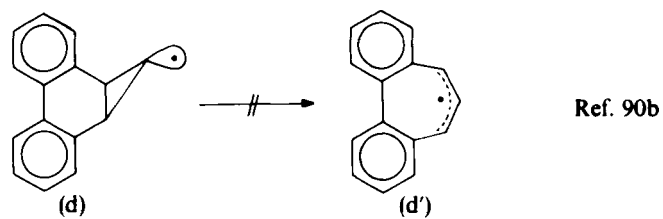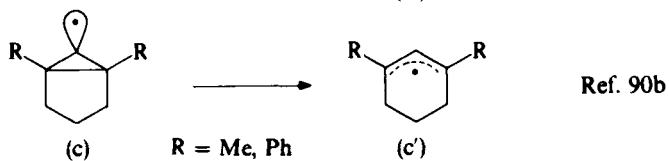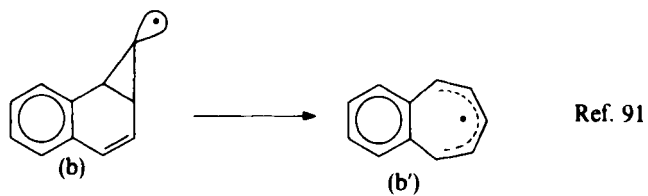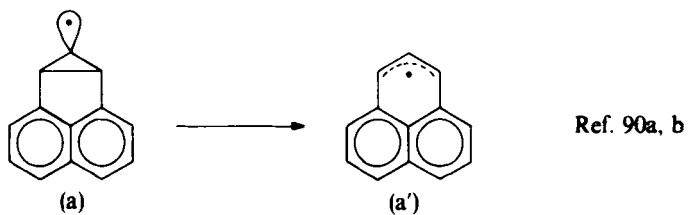| Solvent	Cyclopropane (%)	Dimer (%)	Relative reactivity[a] per active hydrogen
Benzene	5.85	11.95	0.23
Cyclohexane	3.98	7.14	0.30
t-Butanol	2.70	2.71	0.33
Acetone	6.77	6.77	0.51
Diethyl ether	7.37	9.61	0.57
Ethyl acetate	4.24	7.50	0.92
Toluene	7.41	8.34	1.00
Methanol	1.49	1.27	1.24
Tetrahydrofuran	6.98	6.45	1.44
Acetonitrile	8.35	4.62	1.76
Ethylbenzene	4.32	3.82	1.77
Cumene	1.45	1.77	2.50
Ethanol	3.00	1.53	3.05
2-Propanol	4.08	2.71	4.40

[a] Expressed in terms of reactivity of toluene as 1.

Chen[88] has demonstrated that one phenyl group in the 2-position of the cyclopropyl radical is insufficient to overcome the activation energy necessary to obtain the rearrangement. Thus thermal decomposition of trans-2-phenylcyclopropanecarbonyl peroxide in a poor hydrogen-donating solvent such as benzene yielded only 2-phenylcyclopropane. However, when two phenyl groups were located in the 2,3-position of the cyclopropane ring-rearranged products were obtained.

meso and d,l
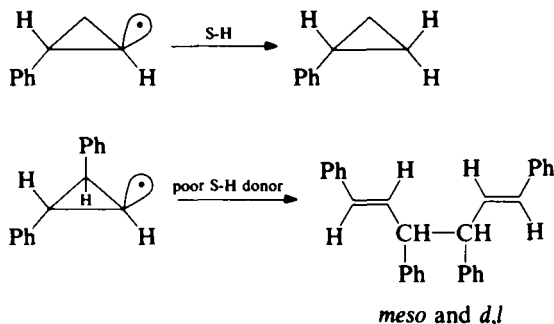
Thus, under the same conditions, thermolysis of cis,trans-2,3-diphenyl-cyclopropanecarbonyl peroxide gave a 30% yield of 1,3,4,6-tetraphenyl-1,5-hexadiene. Boche, Rüchardt and coworkers[89a] have confirmed this result. It was also shown that both cis,cis and trans,trans isomeric peroxides produced the same 1:1 mixture of d, l-and meso-rearranged products. An attempt to interpret these results on the basis of an electrocyclic ring-opening did not result in any definitive conclusion[89b]. The following cyclopropyl radicals have also been shown to undergo rearrangement. In each case the rearranged radical is a highly delocalized species thereby reducing the activation energy sufficiently for the rearrangement process to occur.

(a) → (a')   Ref. 90a, b

(b) → (b')   Ref. 91

(c)   R = Me, Ph   (c')   Ref. 90b

(d) → (d')   Ref. 90b

(e) → (e')   Ref. 92

(f) → (f')   Refs 93, 94

(g) → (g')   Refs 93, 94

(h) → (h')   Refs 39, 77
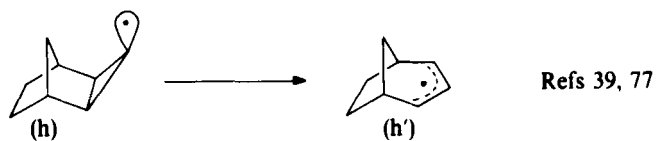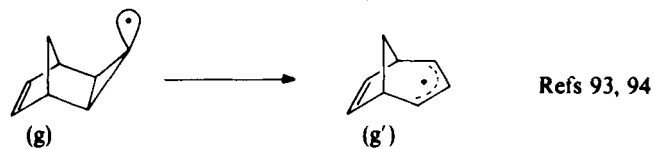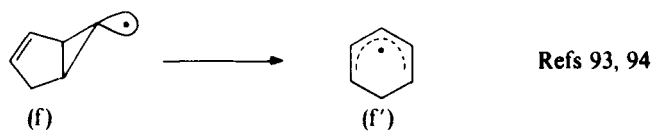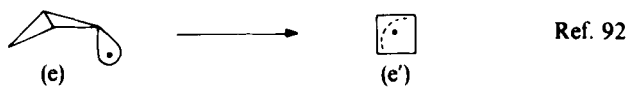
Surprisingly the dibenzonorcaradien-7-yl radical (d) is reported[90b] not to rearrange to the dibenzotropyl radical (d'), and whether the perinaphthenyl radical (a') is formed[90a,b] is also questionable[90b]. The ring-opening of 2-bicyclo[1.1.0]butyl radical (e) is not surprising[92], due to the strain and the cyclopropylcarbinyl nature of the radical. Although (f), (g) and (h) have been reported to give the rearrangement products (f'), (g') and (h')[93,94] alternative routes to the rearrangements for at least (f) and (g) have been presented[93]. Moreover, the rearranged radical (h')[39,77] could not be detected by ESR[39] nor when generated by other means[77].

Also noteworthy is that the following cyclopropyl radicals have been reported not to undergo rearrangement (see also Table 13).
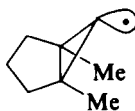

R = H, Me
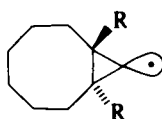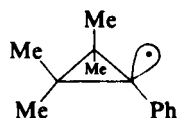
Refs: 54   95   95   95

5. Solvent cage reactions

With the possible exception of certain dissolving metal reactions (see Section III.B.2), the 1-methyl-2,2-diphenylcyclopropyl σ radical is incapable of maintaining its configuration in solution. In order to trap this cyclopropyl radical before complete racemization occurs, it must react at a rate equal to or greater than the inversion frequency determined to be $\sim 10^{11} s^{-1}$. Since the average time required for diffusion from a cage has been determined[96] to be 10^{-11} s, the most likely place to intercept a rapidly inverting σ radical would be within a solvent cage.

The thermal decomposition of $(-)-(R)$-methyl-2,2-diphenylcyclopropanoyl peroxide, $(+)-(R)$-48, in *pure* carbon tetrachloride yielded, besides the expected $(\pm)$-1-chloro-1-methyl-2,2-diphenylcyclopropane (52), a 2% yield of $(+)-(S)$-1-methyl-2,2-

$(+)-(R)-(48)$ $(\pm)-(52)$ $(+)-(S)-(49)$
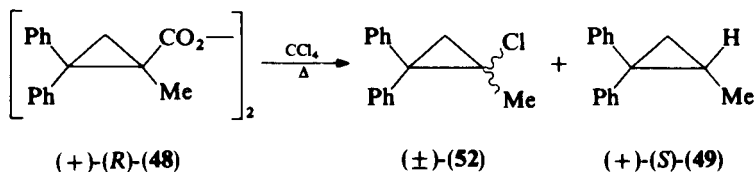
diphenylcyclopropane (49)[59]. Doubling the concentration of the peroxide had no effect on the yield of the hydrocarbon. Neither did addition of a good radical trap such as iodine. These observations are consistent with a solvent cage disproportionation reaction providing the hydrogen source for the formation of $(+)-(S)-(49)$.

Finally the most definitive evidence for a cage reaction was the observation that when an equimolar mixture of the peroxide (48) and the peroxide-d_{10} (48-D_{10}) were decomposed, no crossover products were obtained; only equal amounts of fully protonated hydrocarbon (49) and the hydrocarbon-d_6[59] (49-D_6) were formed. The optical purity of the isolated $(+)-(S)$-1-methyl-2,2-diphenylcyclopropane (49) was found to be 31–37% with a net retention of configuration. Thus, when the lifetime of the rapidly inverting σ radical is sufficiently great to permit diffusion out of the solvent cage the product formed by the

(48)   (48-D$_{10}$)

(49)   (49-D$_6$)
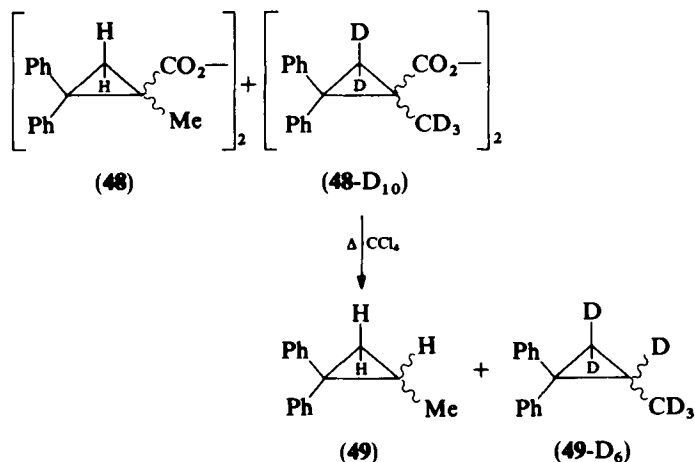
radical reacting with the substrate (CCl$_4$) will be essentially racemic. If the radical is constrained in a solvent cage and reacts within that cage, it will maintain its configuration to a large extent.


(+)-(S)-(49)   (90a)   (90b)
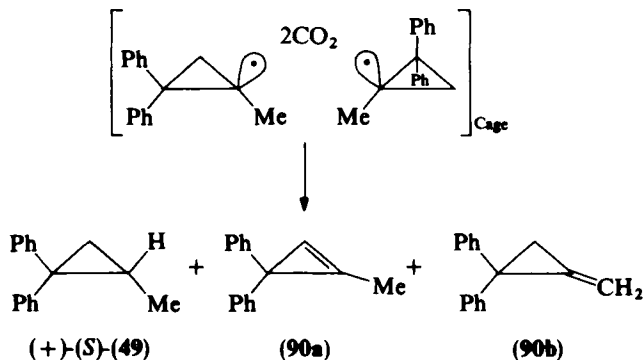
The disproportionation reaction is depicted above although other modes are possible[59]. β-Hydrogens are abstracted by the radical, either from the methyl group or the ring, to yield the hydrocarbon 49 with largely retained configuration and also the two olefins 90a, b. A cage disproportionation reaction has also been observed in the thermal decomposition of trans-2-phenylcyclopropanoyl peroxide in carbon tetrachloride.

(−)-(S)-(18)   (−)-(R)-(91)
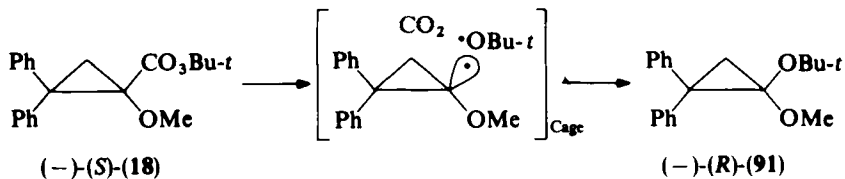
Similarly, a cage recombination reaction takes place in the thermal decomposition of t-butyl (−)-(S)-methoxy-2,2-diphenylcyclopropanepercarboxylate (18)[47]. A 0.8 % yield of 1-t-butoxy-1-methoxy-2,2-diphenylcyclopropane (91). $[\alpha]_{H_g}^{24} = 63°C$, was isolated from

the reaction mixture. Unfortunately, neither the absolute configuration nor the optical purity of the cage product was determined. The magnitude of the rotation would indicate that a high degree of retention of optical activity had occurred. In line with previous cage reactions the configuration is probably maintained as well.
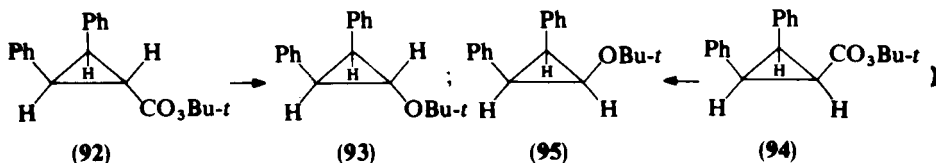
Thermal decomposition of *t*-butyl *trans,trans*-2,3-diphenylcyclopropanepercarboxylate (**92**) in ethylbenzene yielded (10%) exclusively *trans,trans*-2,3-diphenylcyclopropyl *t*-butyl ether (**93**) as a cage recombination product, wheras the *cis,cis* isomer (**94**) gave a low yield of recombination product consisting of 1% *trans,trans* 93 and 1.5% *cis,cis* 95. The low yield and the loss of stereoselectivity in the latter case are thought to be due to a steric effect[89].
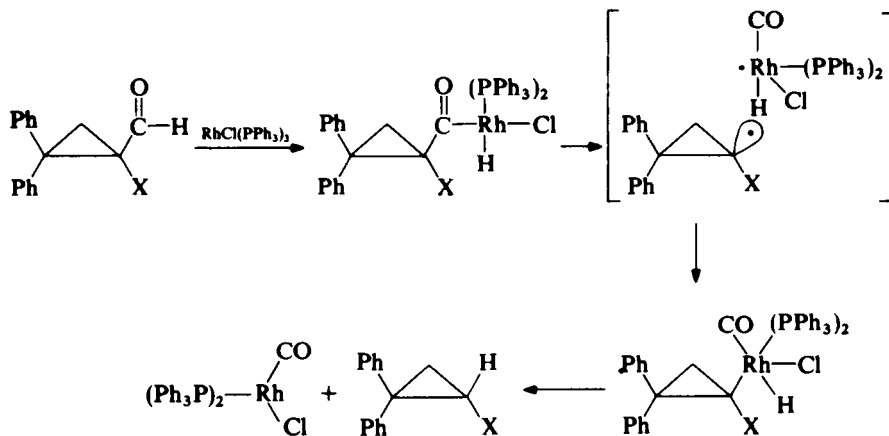
SCHEME 6

It has been proposed that the decarbonylation of aldehydes by the Wilkinson catalyst [RhCl(PPh₃)₃] involves a radical pair disproportionation or recombination reaction[97]. A radical pair intermediate in solution is equivalent to a cage reaction (Scheme 6). Table 15 shows the results obtained from the decarbonylation of a series of chiral cyclopropyl aldehydes[92, 98].

TABLE 15. Decarbonylation of chiral 1-X-2,2-diphenylcyclopropanecarboxaldehyde[97]

X	Config.	Product. config.	% Optical purity
Me	(−)-(R)	(−)-(S)	94
Cl	(−)-(S)	(−)-(S)	83
F	(−)-(S)	(−)-(S)	73
OMe	(−)-(S)	(−)-(S)	6

$$\begin{bmatrix} Ph & & Me \\ & \triangle & \\ Ph & & Cu \end{bmatrix}_n \xrightarrow[(2)D_2O]{(1)\Delta}$$

(S)-(96)

(−)-(R)-(49)

28%

(90b)

1%

+ (+)-(R,R)-(97)

27%, and
4% (−)-(S,S)-(97)

+ (R, S)-(98)

19%

+ (89)

5%

SCHEME 7

R$^{(S)}$
|
R$^{(S)}$

(−)-(S,S)-(97)

+ 2Cu° + [(S)-(96)]$_{n-2}$

R$^{(S)}$
|
R$^{(R)}$ c

(R,S)-(98)

b

[R$^{(S)}$-Cu]$_n$
[(S)-(96)]$_n$

a

R$^{(R)}$
|
R$^{(R)}$ + 2Cu° + [(S)-(96)]$_{n-2}$

(+)-(R,R)-(97)

d

e

(−)-(R)-(49)

(90b)

f

(+)-(S)-(49)

h

i

(89)

g

S–H

(±)-(49)
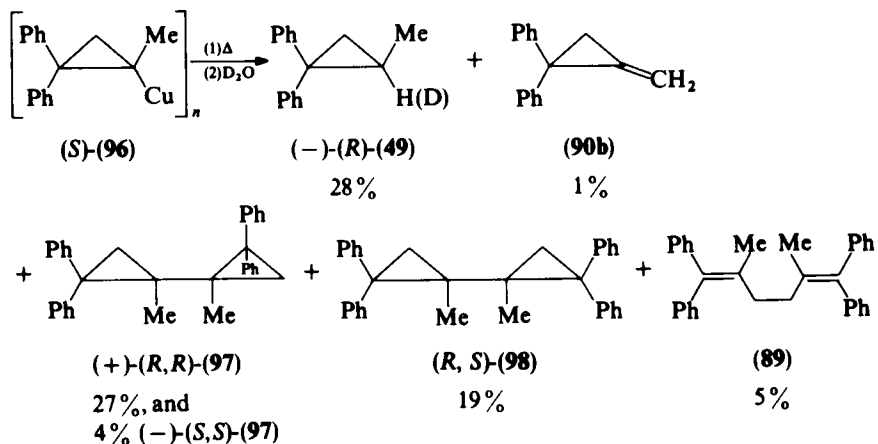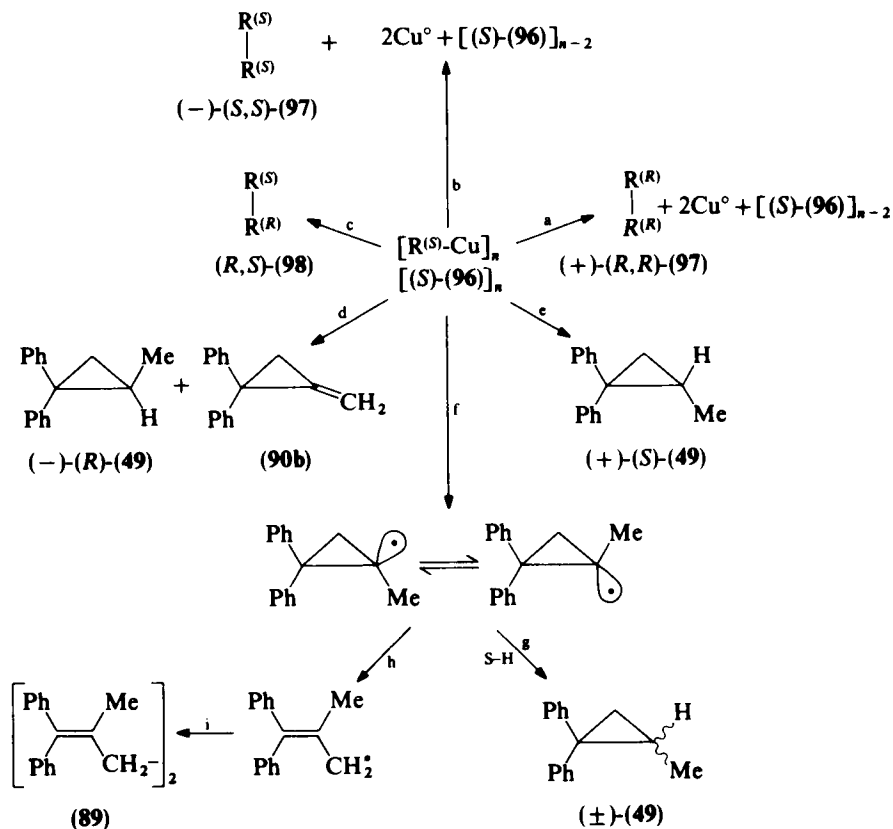
SCHEME 8.   Thermal decomposition of (S)-(1-methyl-2,2-diphenylcyclopropyl) copper
(96) (R = 1-methyl-2,2-diphenylcyclopropyl)

6. Aggregates (clusters)

The thermal reaction of chiral (S)-1-(methyl-2,2-diphenylcyclopropyl)copper (**96**) provides an interesting example of the effect of aggregates on the stereochemistry of the cyclopropyl radical[99]. The thermal decomposition of (S)-**96** led to the formation of a variety of products depicted in Scheme 7. Product analysis, including stereochemistry, led to the mechanism shown in Scheme 8. The aggregate mixture [(S)-**96**]$_n$ is assumed to exist in THF solution (colloidal?) where $n = 2$, 4, or 6.

The aggregates have been shown to be stable at 0°C for at least 1 h and are viewed as molecular species which exist in a solvent cage of THF. Upon thermolysis a homolytic cleavage of two R$^{(S)}$–Cu bonds occur (R = 1-methyl-2,2-diphenylcyclopropyl and superscript (S) or (R) relates to configuration) with the formation of Cu° and the concomitant coupling within the solvent cage (reaction a), of R$^{(S)}$ to yield (+)-(R$^{(R)}$, R$^{(R)}$)-**97** with retention of configuration. If within the cage one of the R$^{(S)}$ rotates 180°, this would lead to the formation of R$^{(R)}$, and coupling R$^{(S)}$ and R$^{(R)}$ would produce meso-(R, S)-**98** (reaction c). If two R$^{(S)}$ rotate 180° and then couple, this would lead to the formation of (−)-(S, S)-**97** (reaction b); combination with (+)-(R, R)-**97** results in the production of racemic compound (±)-(R, R/S, S)-**97**.

By itself, the formation of **97** takes on great significance. Its formation has never been observed in solution, only the products resulting from the reactions a, b and i, are observed[58, 59]. Also the 1-methyl-2,2-diphenylcyclopropyl radical does not dimerize to **97** even in a cage reaction[59] but instead it follows the usual course of a tertiary σ radical, it disproportionates. The only other time that dimerization of this radical has been observed was when the radical was formed on a magnesium metal surface[100]. *Thus, the reaction of the aggregates* [(S)-(**96**)]$_n$ *resembles a surface reaction* (see below).

III. ANION RADICALS

A. Introduction

In this section we are dealing predominantly with reactions of cyclopropyl halides with metal surfaces (heterogeneous) and with dissolving metals in solution (homogeneous). Although cyclopropyl metal bonds result from these reactions it is information regarding the *intermediates* leading to the formation of these metal bonds that we are seeking. Are radicals and/or radical anions formed as intermediates? What are the differences between heterogeneous and homogeneous reactions? To this end the cyclopropyl system provides a distinct advantage for this type of investigation since, in contrast to other saturated hydrocarbons, the lithium, magnesium, zinc and mercury compounds formed are configurationally stable. Another important feature is that the cyclopropyl radical is a σ radical which inverts its configuration at a rate of 10^{11} s^{-1}.

B. Electron Transfer to σ Bonds of Cyclopropyl Halides

1. Surface reactions

a. Lithium surface
The stereochemical results of radicals generated in solution and at metal surfaces can vary greatly. For example, genesis of the 1-methyl-2,2-diphenylcyclopropyl σ radical in solution, by decomposing its chiral diacyl peroxide precursor, leads to formation of completely racemic product. This is so even when good radical traps such as iodine or

thiophenol are present[58, 59] (*vide supra*). By contrast reaction of chiral (+)-(S)-1-bromo-1-methyl-2,2-diphenylcyclopropane (51) with lithium metal followed by carbonation leads to the formation of (−)-(S)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid (99) with 73 % retention of configuration[100] (45 % optical purity).

It was shown that the loss of configuration was not due to racemization of the lithium reagent, once formed in solution, since the preparation of the same lithium reagent by halogen–lithium exchange of the bromide 51 with butyllithium produced, after carbonation, the acid 99 with 100 % retention of configuration. Halogen–lithium exchange was shown to proceed with complete retention of configuration and the 1-methyl-2,2-diphenylcyclopropyllithium produced in this manner was shown to be configurationally stable at ambient temperatures and over extended periods of time[101].
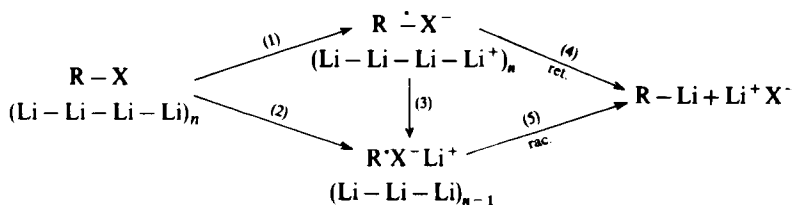

$$(−)-(S)-(99) \qquad\qquad (+)-(S)-(51) \qquad\qquad (−)-(S)-(99)$$
$$100\% \qquad\qquad\qquad\qquad\qquad\qquad\qquad 73\%$$
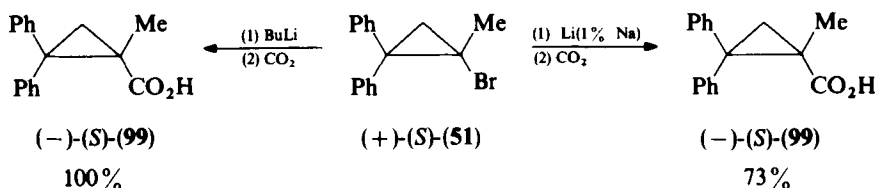
The nature of the lithium surface is important. Varying the particle size of the lithium dispersion from 25 μm with a surface area of 2782 cm^2 to 150 μm with a surface area of 464 cm^2 reduced the optical purity of the resulting acid by nearly 50 %. It was also demonstrated that the amount of sodium impurity in the lithium dispersion had a significant effect not only on the stereochemical results of the metallation reaction but also on the reactivity of the metal surface itself. For example, reaction of chiral 1-iodo-2,2-diphenylcyclopropane with 25 μm lithium dispersions containing 0.002 %, 0.02 % and 1 % sodium yielded after carbonation 1-methyl-2-cyclopropanecarboxylic acid (99) with optical purities of 13 %, 16 % and 36 %, respectively. The increase in optical purity with increase in sodium content may be a consequence of lowering the ionization potential of the metallic surface[102].

The stereochemistry of the reaction is also dependent on the halogen. The reaction of chiral 1-halo-2,2-diphenylcyclopropane with 25 μm lithium dispersions containing 1 % sodium produced the results shown in Table 16. It should be noted that the optical purity of the acid varies in the same order as the carbon–halogen bond strength Cl > Br > I.

TABLE 16. Lithiation of chiral 1-halo-1-methyl-2,2-diphenylcyclopropane followed by carbonation to give 99

Substrate	Halide	Temp. (°C)	Time (min)	Acid yield (%)	Optical purity
52	Cl	25	40	73	63
51	Br	26	42	70	45
50	I	25	41	60	36

The following mechanism[100] was proposed by Walborsky and Aronoff in 1965 for the lithiation reaction (Scheme 9). The stereochemistry of the reaction may be explained by a single electron transfer (SET) to the carbon–halogen bond which results in either the formation of an ion paired halide radical anion on the metal surface (pathway 1) or what is

$$
\begin{array}{c}
R \overset{\cdot}{-} X^- \\
(Li-Li-Li-Li^+)_n
\end{array}
$$

R — X
(Li — Li — Li — Li)$_n$

R$^{\cdot}$X$^-$Li$^+$
(Li — Li — Li)$_{n-1}$

(1) (2) (3) (4) rel. (5) rac.

R — Li + Li$^+$X$^-$

SCHEME 9. A mechanistic scheme for the formation of lithium reagent

in essence a Li$^+$X$^-$ complexed loose radical pair (pathway 2). The radical anion can collapse (pathway 4) to form lithium reagent with retention of configuration or dissociate (pathway 3) to the complexed loose radical pair. The radical (R $\cdot$) in the complexed loose radical pair can undergo rotation before the next SET occurs and this would yield the racemic lithium reagent. As the halogen (X) is changed from iodide to bromide to chloride reaction pathways 1 and 4 are favored and result in a decrease in the amount of complexed loose radical pair formation. Moreover, increasing the surface area and/or decreasing the ionization potential (increased sodium content) would also favor pathways 1 and 4 resulting in an increase of retention of configuration.

In solution the 1-methyl-2,2-diphenylcyclopropyl σ radical racemizes[58, 59] but when the radical is formed at the surface via intermediate ion radical precursors and/or complexes, the overall result is a retention of configuration. It may therefore be dangerous to draw conclusions about the stereochemical fate of σ radicals under these conditions[103]. For example, cis- and trans-1-bromo-2-methylcyclopropane when treated with metallic lithium yield products with 8–38 % retained configuration[104]. In one interpretation[104] it was claimed that the observed retention of configuration is due to the intrinsic stability of the intermediate σ cyclopropyl radical. More likely, the retention is due to a surface effect[102] as described above since it has previously been shown that the Hunsdiecker reaction with both cis- and trans-2-methylcyclopropanecarboxylic acids gave identical mixtures of products[63] thus demonstrating that the 2-methylcyclopropyl radical is incapable of maintaining its configuration in solution (at least under the Hunsdiecker conditions).

The effect of surface has also been demonstrated in the reduction[77] of anti-3-chloro-exo-tricyclo[3.2.1.0$^{2.4}$]octane (100). When the reduction is carried out by lithiation in ether followed by deuterolysis the ratio of syn product 102 to anti product 101 was about 2:1 whereas reduction under homogeneous conditions, lithium naphthalenide followed by deuterolysis, resulted in a 30:1 ratio. Again, there is greater retention on the metal surface. The syn σ radical was shown to be the thermodynamically more stable (Table 13).

anti-(100)   anti-(101)   +   syn-(102)
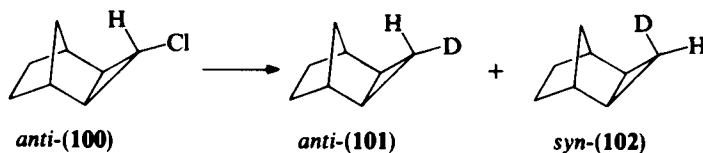
b. *Magnesium surface*
In 1961 it was reported that the reaction of chiral 1-bromo-1-methyl-2,2-diphenylcyclopropane (51) with magnesium metal produced a partially optically active Grignard reagent[105]. It was suggested that the racemization observed occurred in the Grignard formation step. In 1964 it was also established[106] that the racemization occurred

at some stage preceding Grignard formation by showing that once the Grignard reagent was formed it was optically stable. This was accomplished by preparing the Grignard reagent from the optically stable lithium reagent[101] by treatment with anhydrous magnesium bromide followed by carbonation. The acid produced in this manner was optically pure.

There is no doubt that the 1-methyl-2,2-diphenylcyclopropyl σ radical is incapable of maintaining its configuration when it is formed in solution[58, 59]. How then can one

$(+)\text{-}(S)\text{-}(51)$ $(-)\text{-}(S)\text{-}(99)$
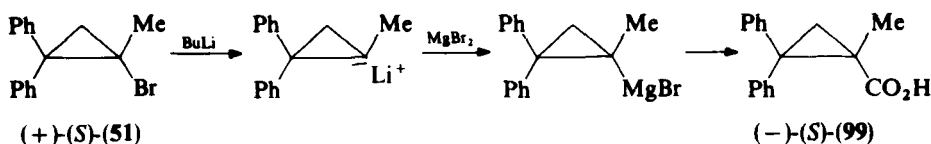
account for the retention of configuration and optical activity that is observed? In 1964 Walborsky and Young[106a] proposed the mechanism of Grignard formation (Scheme 10) which was elaborated upon in 1973[106b].

The processes pictured in Scheme 10 take place at the magnesium–metal solution interface. Interaction of the cyclopropyl halide and magnesium by pathway 1 involves electron transfer from the metal into the antibonding carbon–halogen bond to give a radical anion in close association with a univalent magnesium cation (ion paired radical anion). Collapse of this tight anion radical–cation radical pair, pathway 4, leads to Grignard reagent formation with complete rentention of configuration. Alternatively collapse may proceed by pathway 3 to a loose radical pair (M·MgX complexed loose radical pair) which may also be formed directly by pathway 2. Bodewitz and coworkers[107] have provided CIDNP evidence for pathway 2. It is in the complexed loose radical pair that racemization can take place. Combination of the cyclopropyl radical with the magnesious halide radical produces largely racemic Grignard reagent (pathway 5). The kinetic analysis of Grignard formation by Whitesides and coworkers[108] is also consistent with pathway 1 and/or 2 being involved in the rate-determining step.
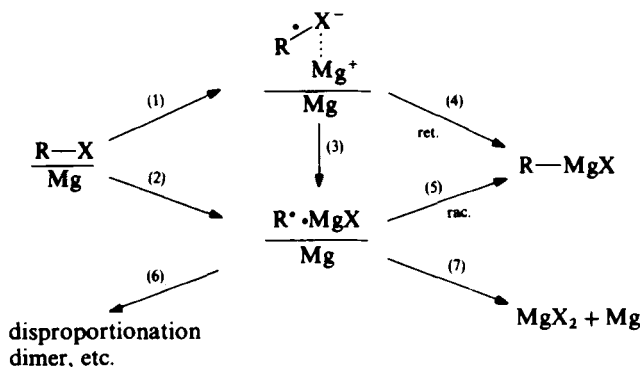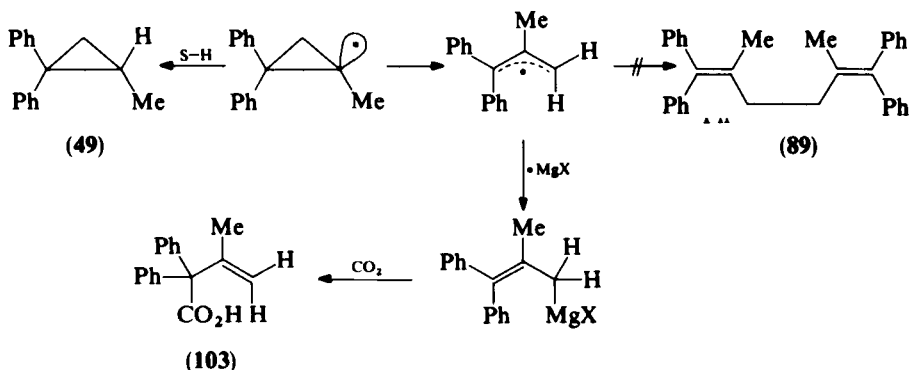

SCHEME 10.   A mechanistic scheme for Grignard reagent formation

The cyclopropyl radical may, however, escape capture by the magnesious halide and undergo typical radical reactions of disproportionation (90a, 90b) and dimerization (97, 98) (pathway 6), all at or very close to the surface. Or, some radical may leave the surface interface and abstract a hydrogen atom from the solvent. Consistent with the

Ph△D ←S-D Ph△(·) ⟶ Ph△=CH₂ + Ph△Me
Ph Me   Ph Me   Ph   Ph

(49-D)   **(90b)**   **(90a)**

Ph△—△Ph
Ph Me Me Ph

(97) + (98)
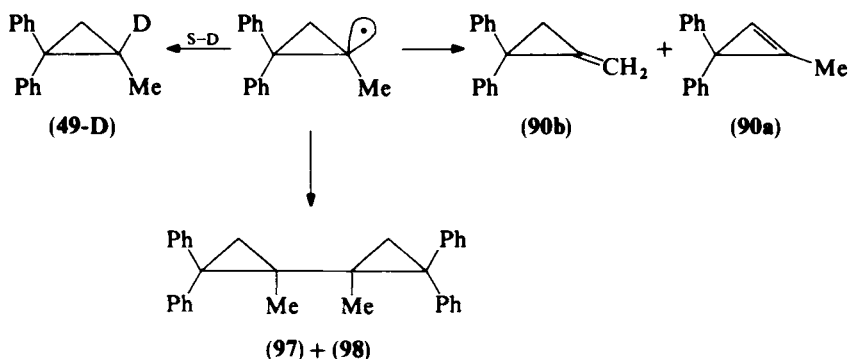
surface nature of the reaction is the observation that very little ring-opened product is observed. When the radical is generated in ether solution by thermal decomposition of the diacyl peroxide, the products consist of the cyclopropyl hydrocarbon and a dimeric product resulting from ring-opening[58, 59]. The only ring-opened product appears in the acid fraction, after carbonation of the Grignard solution. The allyl radical produced by the ring-opening does not dimerize as allyl radicals in solution normally do but rather is captured by the magnesious halide.

Ph△H ←S-H Ph△(·) ⟶ Ph—C(Me)···C—H ⟶∦→ Ph△Me Me△Ph
Ph Me   Ph Me   Ph   H   Ph   Ph

(49)   **(89)**

↓ ·MgX

Ph—C(Me)=C(H)—CO₂H ... H ←CO₂ Ph—C(Me)=C(H)—H ... H
Ph   Ph   MgX

(103)

Further confirmation of the surface nature of Grignard formation is the observation that when THF-d₈ and diethyl ether-d₁₀ were used as solvent only 28% and 6% deuterium, respectively, were found in the hydrocarbon fraction of the reaction[100]. The source of hydrogen atoms is the disproportionation of the surface radicals. Moreover, the yield of hydrocarbons from reaction in THF is only ~ 1.0–1.5% whereas in diethyl ether the yield is 20%. This is in accord with the greater solvating power of THF[109] which removes the metal organic species from the surface of the magnesium. Recent XPS analysis of the Grignard formation reaction is consistent with the surface nature of the reaction[110].

The effect of halogen X is evident in both the stereochemistry and the amount of Grignard reagent formed. The energy of the carbon–halogen bond increases in the order I < Br < Cl as do the optical purities (2%, 17% and 26% respectively) and yields of Grignard reagent (35%, 70% and 89% respectively). This is consistent with the amount of complexed loose radical pair formed at the surface, pathways 2 and 3 of Scheme 10, being determined by the strength of the carbon–halogen bond[100], i.e. the weaker the bond the greater the amount of loose radical pairs. As with lithiation the retention of configuration

and optical activity of the σ cyclopropyl radical is due to a surface interaction rather than to any intrinsic stability of the radical.

In our earlier discussion there did not seem to be any strong evidence for a stabilizing or unstabilizing effect of a β-substituent on the cyclopropyl radical. Recently Bickelhaupt and coworkers[111], in an extension of the early work of Wiberg and Bartley[112], have provided indirect evidence that a β-MgBr exerts a stabilizing interaction on the cyclopropyl radical. Both *trans*-104 and *cis*-1,2-dibromocyclopropane (105) when treated with magnesium in ether and then hydrolyzed with D_2O or carbonated with CO_2 formed *cis*-1,2-dideuterocyclopropane and *cis*-1,2-cyclopropanedicarboxylic acid, respectively. Based on this observation it was suggested that a *cis*-β-MgBr stabilized the σ-radical intermediate, which in turn would lead to the formation of a stabilized *cis*-α,β-dibromo-magnesium cyclopropane. The stabilized *cis*-β-MgBr σ radical has received support from *ab initio* calculations of Schleyer and coworkers[69] in which they determined that the *cis* isomer is 1.6 kcal mol^{-1} more stable than the *trans*. The reaction can be viewed as occurring on the surface[113] of the magnesium. After forming the first bond with the magnesium, the reagent is associated with the surface long enough to permit formation of the 1,2-dimagnesium bromide via radical pair pathway resulting in the formation of the thermodynamically more stable *cis* isomer (Scheme 11). As Bickelhaupt[111] has suggested because of the unique double bromine bridging[111, 112] and the entropic advantage of less ether fixation any *trans* isomer formed may be converted to *cis*.
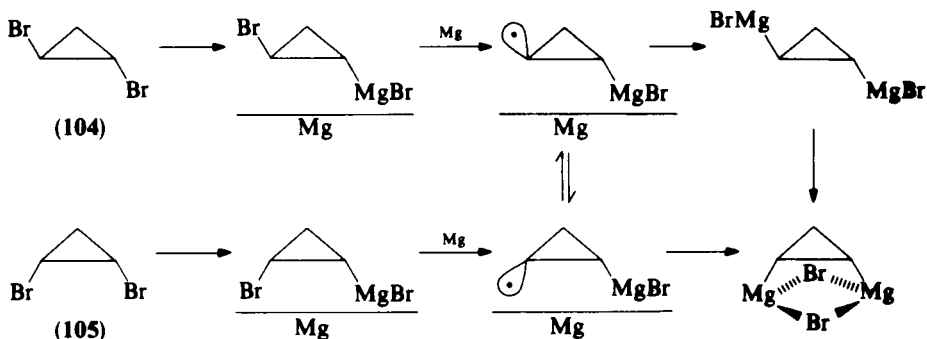
SCHEME 11.   Reaction of 1,2-dibromocyclopropane with magnesium

c. Zinc surface

Triphenyltin hydride reduction[37] of either isomer of *exo*-7-bromo-*endo*-7-chlorobicyclo[4.1.0]heptane (30) and *endo*-7-bromo-*exo*-7-chlorobicyclo[4.1.0]heptane (31) resulted in an identical 1:4 mixture of *exo*-32 and *endo*-7-chlorobicyclo[4.1.0]heptane (33). This same ratio was also obtained when *exo*-24 and *endo*-t-butyl 7-chlorobicyclo[4.1.0]heptane-7-percarboxylate (25) were thermally decomposed in cumene[46]. As previously discussed the α-chlorocyclopropyl σ radical, generated in solution, is incapable of maintaining its configuration and the 1:4 *exo*:*endo* product ratio represents the thermodynamically controlled reaction mixture (Table 13). By contrast, the reaction of *exo*-7-bromo-*endo*-7-chlorobicyclo[4.1.0]heptane (30) with zinc in an acetic acid–ethanol mixture yielded a mixture of *exo*-32 and *endo*-7-chlorobicyclo[4.1.0]heptane (33) with an *exo*:*endo* ratio of 1:19. This amounts to a heavily preferred retention of configuration for the reduction and a ratio of products far from that expected for a thermodynamically controlled reaction. Moreover, the *endo*-7-bromo isomer (31), under the same reaction conditions, gave an *exo*-32:*endo*-33 ratio of 5:1 for the product mixture

of *exo*-32 and *endo*-7-chlorobicyclo[4.1.0]heptanes. Again, a preferred retention of configuration is observed, with the thermodynamically less stable isomer predominating[114].
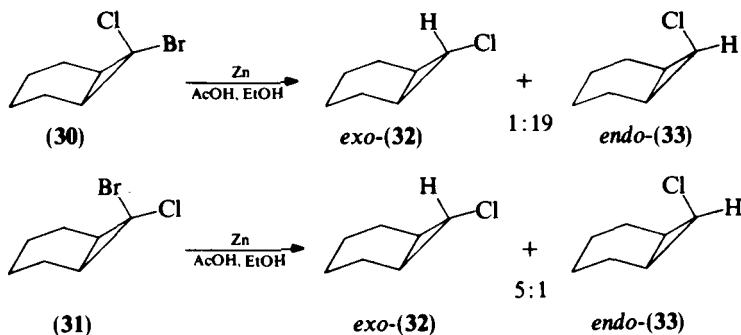

Annino and his coworkers[114] have postulated a mechanism for the reaction at the zinc surface patterned after the one proposed by Walborsky and coworkers for Grignard formation[100,106]. The organozinc intermediate formed is rapidly hydrolyzed by the protonic solvent. Note also that the reaction of zinc, in ethanol–10% KOH, with chiral 1-bromo-1-methyl-2,2-diphenylcyclopropane (51) yielded 1-methyl-2,2-diphenylcyclopropane (49) with 21% retention of configuration[115], a result comparable to the 15% retention that is found in Grignard formation.
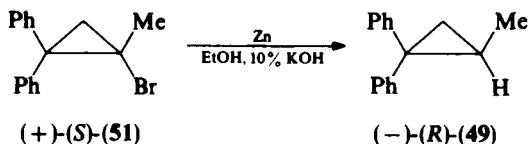
d. Mercury surface

As a first approximation one can view metallation and electrolytic reduction as a single class of reactions differing only in the ease with which electrons are transferred to the substrate. Ordinarily mercury metal does not react with alkyl halides because of its high ionization potential of 240 kcal mol^{-1} as compared with 124, 176 and 216 kcal mol^{-1} for lithium, magnesium and zinc, respectively. However, if one places a potential across mercury then it will readily react with alkyl halides in an electrolytic reaction.

Controlled potential electrolysis[116] of (+)-(S)-1-bromo-1-methyl-2,2-diphenyl-cyclopropane (51) in acetonitrile at −2.7 volts vs. SCE yielded the hydrocarbon
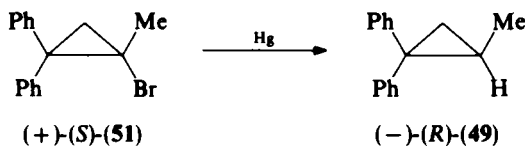
(−)-(R)-1-methyl-2,2-diphenylcyclopropane (49) with an optical purity of 25%. Current integration indicated that 1.98 electrons per molecule reacted. The reduction involves two single electron transfers (SET).

The reduction is viewed as occurring in the following manner[117].

(1) $RBr + e^- \rightarrow [R-Br]^{\dot{-}}$

(2) $[R-Br]^{\dot{-}} \rightarrow R^{\cdot} + Br^-$

(3) $R^{\cdot} + e^- \rightarrow R^-$

(4) $R^{\cdot} + Hg^{\circ} \rightarrow RHg_n^{\cdot}$

(5) $RHg_n^{\cdot} + e^- \rightarrow R^- + Hg^{\circ}$

(6) $RHg_n^{\cdot} + RHg_n^{\cdot} \rightarrow RHg_{2n}-R \rightarrow RHgR + Hg_{2n-1}^{\circ}$

(7) $RHgR + e^- \rightarrow R^- + RHg^{\cdot} \overset{Hg^{\circ}}{\rightarrow} RHg_n^{\cdot}$

(8) $R^- + CH_3CN \rightarrow R-H + {}^-CH_2CN$

(9) $R^- + Et_4N^+Br^- \rightarrow R-H + CH_2{=}CH_2 + Et_3N + Br^-$

As in direct metalation, the reaction occurs at the metal surface. An electron is transferred from the surface to the σ^* antibonding orbital of the carbon–bromine bond to produce the anion radical in the rate-determining step[114,116] (equation 1). The anion radical can then dissociate at the surface to the 1-methyl-2,2-diphenylcyclopropyl radical (equation 2). At this point some racemization may occur and the radical can undergo a number of indistinguishable reactions. The radical may pick up another electron to yield the anion (equation 3) or since mercury is such an efficient radical trap, the radical may become adsorbed on the mercury surface (equation 4) from which it can either take another electron to yield the anion (equation 5) or combine with another adsorbed radical to produce a dicyclopropylmercury (equation 6).

The formation of the dicyclopropylmercury alone or in combination with the adsorbed radical type intermediates accounts for the observation that the substrate disappears at a faster rate than the reduction product appears[116]. The dicyclopropylmercury can then accept an electron to produce the anion and a cyclopropylmercury radical which in combination with the mercury surface becomes an adsorbed radical (equation 7) which can be recycled through the pathway of equation 5 or equation 6. The anions formed in equation 3, equation 5, and equation 7 react at the surface with acetonitrile solvent (equation 8) to yield the hydrocarbon. When deuterated acetonitrile was used the hydrocarbon isolated contained 76 % deuterium[116]. The anion can also react with the electrolyte, tetraethylammonium bromide, in an elimination reaction (equation 9) to produce hydrocarbon, ethylene and triethylamine, all of which have been identified in the reaction mixture[116].

The surface reaction of lithium metal with the same chiral $(-)$-(S)-bromide (51) produces a product which has retained its optical activity to the extent of 46 %[100]. Reaction with magnesium results in 15–18 % retention of optical activity with overall retention of configuration[105]. The observation that the hydrocarbon produced in electrolytic reduction has retained 25 % of its optical activity (63 % retention of configuration) is consistent with the proposed surface nature of this reaction.

The controlled potential electrolysis of endo-7-bromo-exo-7-chlorobicyclo[4.1.0] heptane (31) and exo-7-bromo-endo-7-chlorobicyclo[4.1.0]heptane (30) resulted in a mixture of exo-32 and endo-7-chlorobicyclo[4.1.0]heptane (33) in which the retention–inversion ratio was 2.6:1 in each case. Overall retention of configuration is the usual observation[114]. However, this need not always be the case, since by changing the substituent at the reductive center from methyl in bromo-1-methyl-2,2-diphenyl-cyclopropane (51) to a carboxyl or carbomethoxyl group, the resulting product was still optically active (30–40 %) but the configuration was inverted[115].

2. Dissolving metal reductions (homogeneous)

The reduction of alkyl halides by solutions of dissolved metals like, e.g. sodium in ammonia or alkali metal naphthalenides in tetrahydrofuran, provides a convenient means of removing halogens to produce hydrocarbons or to prepare alkali metal organic compounds. It is generally accepted that these reductions involve free radical intermediates $R^{\cdot}$, (pathway A, Scheme 12)[118].
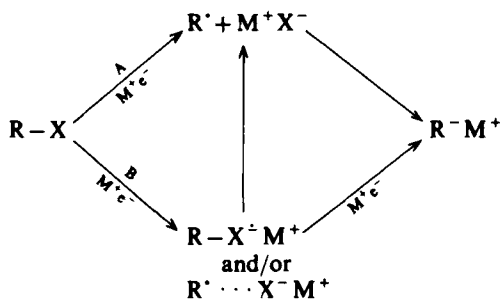
X = halide; M = alkali metal

SCHEME 12. Dissolving metal reductions

Are ion paired halide radical anions $R-X^{\div} M^{+}$ and/or weak radical $\cdots XM$ complexes $R\cdots X^{-}M^{+}$ also intermediates in such ET reactions (pathway B, Scheme 12)?

This timely question[119] is dealt with mainly in Section III.B.2.b.

a. Reductions in liquid ammonia

It is well established that lithium and sodium derivatives of 1-methyl-2,2-diphenylcyclopropane are capable of retaining their optical activity and configuration[100,101]. It has also been shown that when the corresponding radical is generated in solution the resulting product is racemic[58,59]. Only in a solvent cage[59] and on metal surfaces[100,102,105,106] can this rapidly inverting σ cyclopropyl radical be intercepted.

Because of these observations a study of optically active 1-halo-1-methyl-2,2-diphenylcyclopropanes with solutions of sodium in liquid ammonia was undertaken[120]. As will be seen, the stereochemical results observed were shown to be dependent on the concentration of sodium in ammonia, the nature of the halogen and a heterogeneity factor.

The chemical composition and physical properties of solutions of sodium in liquid ammonia have been known to depend upon the concentration. In particular, physical measurements have generally shown that such solutions pass from blue solutions where they contain essentially free solvated electrons at very high dilution (0.003 M), through dilute solutions having salt-like characteristics (0.003–1.0 M), to bronze solutions that behave as metals at very high concentrations[121]. The reduction of (+)-(S)-1-bromo-1-methyl-2,2-diphenylcyclopropane (51) using a highly diluted solution (0.026 M) of sodium in liquid ammonia yielded, *inter alia*, essentially racemic hydrocarbon (49). On the other hand, when a concentrated solution (6.5 M) was used the hydrocarbon produced was 46% optically pure with overall retention of configuration. These results are consistent with the interpretation that under highly diluted conditions the cyclopropyl radical is produced in solution and before the second SET occurs it racemizes. At high concentrations, ('metallic

bronze') the reaction is occurring at the metallic surface leading to a stereochemical result comparable to that observed with metallic sodium in ether[100,101].

The effect of halogen on the stereochemical course of the reduction is in the same order as that observed on metallic surfaces. The optical purity of the hydrocarbon **49** using a 4 M solution of sodium in liquid ammonia, decreases in going from chloride (58 %) to bromide (43 %) to iodide (17 %).

The above interpretation would seem adequate to account for the results. However, the reaction is of greater complexity and may involve the surface of the *crystalline halide* instead of the metal surface. If instead of adding crystalline chiral (+)-(S)-1-bromo-1-methyl-2,2-diphenylcyclopropane (**51**) to a 3–4 M solution of sodium in ammonia to obtain the hydrocarbon of 43 % optical purity, one adds an ammoniacal solution of the bromide **51** to the dissolving metal solution then the resultant hydrocarbon **49** is completely racemic. It is tempting to speculate that the observed optical activity in the product, when crystals are used, is due to the radical being formed and trapped at the surface of the crystal lattice. It is noteworthy that the crystals turn deep red as soon as they are added to the dissolving metal solution. Since most organic halides have limited solubility in liquid ammonia these results point to a danger in the interpretation of results obtained in such media. However, it is clear that when the 1-methyl-2,2-diphenylcyclopropyl σ radical is produced in solution under highly diluted dissolving metal conditions (Na/NH₃) it is incapable of maintaining its configuration and that its inversion frequency is greater than a second SET[75].

b. Reductions with alkali metal naphthalenides

Boche and coworkers[122] have reported that r-1-bromo-c-2,c-3-dimethyl- as well as r-1-bromo-t-2,t-3-dimethylcyclopropane (**106** and **107**), reacted with lithium naphthalenide (LiN) in THF and after carboxylation and methylation gave the identical 21:79 mixture of the corresponding carbomethoxy derivatives **108** and **109**. A completely analogous result was obtained with another secondary cyclopropyl bromide, *cis*- and *trans*-1-bromo-2-phenylcyclopropane[75].
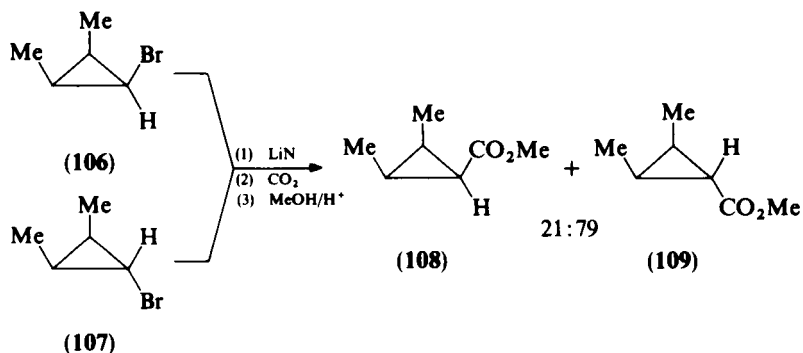
The reduction of tertiary cyclopropyl halides with alkali metal naphthalenides leads to a similar situation. After treatment of a 78:22 and a 25:75 mixture, respectively, of r-1-bromo-1-methyl-c-2-methyl-t-2-phenylcyclopropane (**110**) and its isomer (**111**) with LiN in THF at 20°C, protonation with methanol led to identical 45:55 mixtures of r-1-phenyl-1,c-2-dimethyl- and r-1-phenyl-1,t-2-dimethylcyclopropanes (**112** and **113**).

Reactions of r-1-chloro-1-methyl-t-2-phenylcyclopropane (**114–Cl**) and r-1-chloro-1-methyl-c-2-phenylcyclopropane (**115–Cl**) as well as of **114–Br** and **115–Br** with lithium, sodium and potassium naphthalenide (MN), respectively, demonstrate that neither the
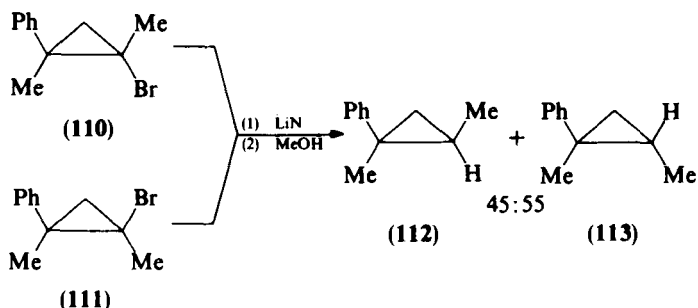
variation of the halide nor of the naphthalenide gegenion has any significant influence on the isomer ratio of the resultant cis- and trans-1-methyl-2-phenylcyclopropanes (116 and 117) (Table 17)[122]. Results of Freeman[77] and Ledlie and coworkers[123] fully confirm these findings.
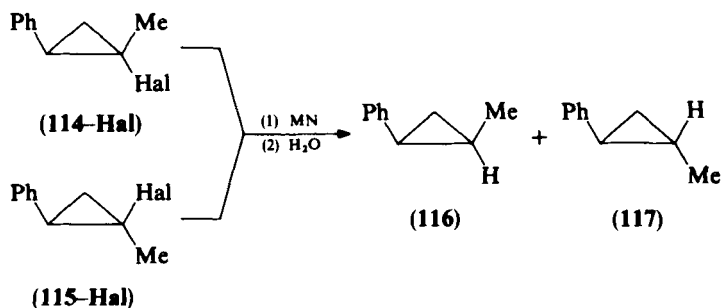
TABLE 17. Ratios 116/117 from the reactions of 114–Hal and 115–Hal with MN in THF at room temperature[122]

MN	114–Cl	40:60 114–Cl/115–Cl	114–Br	68:32 114–Br/115–Br
LiN	45:55	45:55	45:55	45:55
NaN	40:60	40:60	40:60	40:60
KN	39:61	39:61	39:61	39:61

The entirely different pathway of reduction in homogeneous solution and on a surface is nicely illustrated by a result of Dewar and Harris[104]. Reaction of 106 (107) with lithium metal leads to 54 (31)% of r-1-lithio-c-2,c-3-dimethylcyclopropane—the precursor of 108. As shown earlier, in the homogeneous LiN reductions, both bromides give 21% of 108.

Thus, the results in solution with the cyclopropyl halides mentioned lead to the following conclusions:

(1) Free secondary and tertiary cyclopropyl radicals reach their thermodynamic equilibrium before they are trapped by a *bimolecular* SET reaction from the alkali metal naphthalenides to give a configurationally stable alkali metal species. Net retention is not observed under such conditions (Scheme 13).
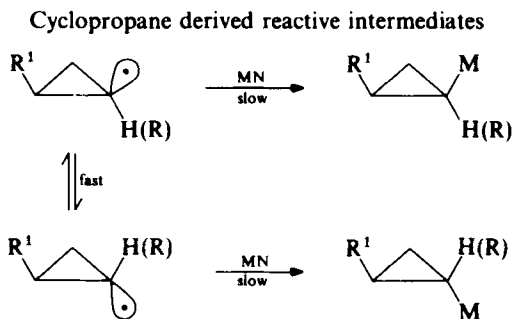
SCHEME 13.   Alkali metal naphthalenide reductions of cyclopropyl halides

This is in agreement with the general observation that the equilibration of isomeric cyclopropyl radicals is always faster than any of the known bimolecular trapping reactions of these radicals in solution.

(2) Assuming a similar rate constant for the reactions of cyclopropyl radicals with MN in THF as for the reaction of primary alkyl radicals with NaN in dimethoxyethane (DME) $(k = 1.6 \cdot 10^9 \, l \, mol^{-1})$[124a] the rate constant for the inversion of secondary and tertiary cyclopropyl radicals is $k \geqslant 5 \cdot 10^9 \, s^{-1}$ corresponding to $\Delta G^{\neq} \leqslant 3.7 \, kcal \, mol^{-1}$. This is in good agreement with the ESR results of Fessenden and Schuler[8] and Kawamura and coworkers[39].

(3) There is no experimental indication that either an ion paired cyclopropyl halide radical anion ($CprX^{-} \, M^{+}$) and/or cyclopropyl radical $\cdots$ XM complex ($Cpr \cdot \cdots \, XM$) participate in the product-determining step of these homogeneous bimolecular SET reactions. Kinetically all that would be required is that the reactivity of these species with one halide ion should differ from that with another[125a]. This is clearly not the case as shown in Table 17. Rather, the C–X bond is broken before the product partitioning step (Scheme 13). Either the halide containing species decompose very rapidly or dissociative SET takes place to give cyclopropyl radicals directly[119,124,125]. This is not unexpected since Garst came to the same conclusions for the reactions of 'normal' alkyl halides with sodium naphthalenide[124c].

An entirely different result has been reported by Jacobus and Pensak[126]. They found that the reduction of the optically active 1-bromo-1-methyl-2,2-diphenylcyclopropane (51) with sodium naphthalenide (NaN) in DME (0.5 M) yields the corresponding hydrocarbon 49 of 29% optical purity with net retention of configuration. This observation was interpreted to mean that the 1-methyl-2,2-diphenylcyclopropyl σ radical was being captured by a second SET from sodium naphthalenide to give the sodium derivative (which transforms in DME to 49) at a rate faster than its inversion frequency (Scheme 14).

In the light of the results discussed previously (*vide supra*) for the halides 106, 107, 110, 111, 114–Hal and 115–Hal, and many others, this interpretation seems unlikely. The following study of Boche and colleagues clearly demonstrates that the experimental results of Jacobus and Pensak are correct but that their interpretation is flawed[122].

Table 18 summarizes the net retentions of configuration of the cyclopropane 49 observed in the reactions of the optically active cyclopropyl halides 50–52 with alkali metal naphthalenides MN as the halide X, the gegenion M and the concentrations are varied. The effect of inverse versus normal addition is demonstrated in Table 19. The influence of the solvent is given in Table 20. Dicyclohexyl-18-crown-6 also affects the amount of retention of cyclopropane 49 (Table 21).

Ph ⋀ Br / Ph ⋀ Me (57–Br) → NaN → Ph ⋀ (•) / Ph ⋀ Me → NaN fast → Ph ⋀ Na⁺ / Ph ⋀ Me → DME

(slow) ↕ → Ph ⋀ Me / Ph ⋀ (•)

Ph ⋀ H / Ph ⋀ Me

(49)
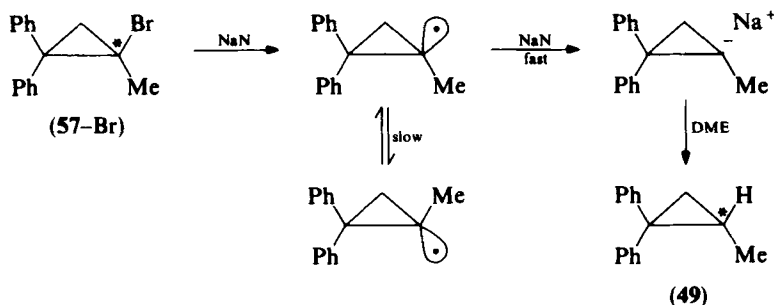
SCHEME 14. Proposed mechanism for the sodium naphthalenide reduction with retention of configuration[126]

TABLE 18. Percent net retention of configuration of cyclopropane 49 formed in the reactions of the halides 50–52 (0.9 M) with MN (0.9 M) in THF at 20 °C, followed by hydrolysis after 1 min

Halide	LiN[a]		NaN[c]		KN[c]	
	normal[b]	diluted[a]	normal[a]	diluted[a]	normal[a]	diluted[a]
52–Cl	0.2	< 0.1[100]	0.8	0.1[100]	3	1.2[100]
51–Br	32	15 [25]	49	42 [100]	53	56 [25]
50–I	57	43 [100]	48	42 [100]	41	47 [100]

[a] Normal addition (MN in THF is added dropwise to the halides in THF). Diluted solutions, e.g. [25] fold dilution: MN (0.36 M), halide (0.1 M), [ ] = dilution factor.
[b] ≤ 1 equivalent.
[c] ≥ 2.5 equivalents.
[d] Yields of 49: 73 ± 16%.

TABLE 19. Percent net retention of configuration of cyclopropane 49 formed in the reactions of the halides 50–52 (0.9 M) with KN (0.9 M) in THF at 20°C, followed by hydrolysis after 1 min

	52–Cl	51–Br	50–I
Inverse[a] addition	3	53	41
Normal addition	3	53	41

[a] Inverse addition (the halide in THF is added dropwise to KN in THF).

TABLE 20. Percent net retention of configuration of cyclopropane 49 formed in the reactions of 51–Br (0.9 M) with MN (0.9 M) in THF, DME and hexamethylphosphoric acid triamide (HMPT) (normal addition)

MN	THF	DME	HMPT
LiN	32	17	3
NaN	49	31	3
KN	53	43	2

TABLE 21. Percent net retention of configuration of cyclo-
propane **49** from the reactions of **51–Hal** (0.9 M) in THF with
KN (0.9 M), without and in the presence of dicyclohexyl-18-
crown-6 ('crown ether') (normal addition)

	Without crown ether	With crown ether
52–Cl	3	0
51–Br	53	7
50–I	41	18

The following points emerge from Tables 18–21.

(1) The amount of net retention of configuration of **49** is strongly *halogen* dependent (Table 18). In contrast to the surface reductions with, e.g. Li and Mg in which the chloride gave the highest net retention, under homogeneous conditions it is just the other way around: the chloride **52–Cl** shows almost no retention!

(2) With LiN, the iodide **50–I** gives the highest net retention but with KN it is the bromide **51–Br** that gives the highest net retention (Table 18). Thus the amount of net retention of configuration of **49** is also dependent on *the gegenion* M^+.

(3) The strong influence of *solvent* (Table 20) and *crown ether* (Table 21) on the net retention is in agreement with the dissociation of X^- *and the solvated* M^+ in the product-determining step. One would not expect such an influence with a free cyclopropyl radical in the product-determining step, as can be seen from Table 17.

(4) Normal, inverse addition (Table 18) and the dilution experiments (Tables 18 and 19) lead to almost the same amounts of net retention for **49**. This essentially excludes an involvement of a *bimolecular* SET in the product-determining step. In the case of a bimolecular reaction increasing concentrations of MN should lead to an increase of net retention in **49**.

(5) The almost negligible net retention observed in the reactions of the *chloride* **52–Cl** with LiN, NaN and KN excludes even the involvement of a cyclopropyl *radical* trapping reaction as being responsible for the distinct net retentions observed in the reductions of the bromide and the iodide **51–Br** and **50–I**, respectively.

Reactions of 1-bromo- and 1-chloro-1-methyl-2,2-biphenylenecyclopropane **118–Br** and **118–Cl** with KN in THF support the findings with **50–52**: the resultant 1,1-biphenylene-2-methylcyclopropane (**119**) shows net retention of configuration, and the amount of retention is dependent on the nature of the halogen (Table 22)[122].

What is the reason for the alternative pathways in the reactions of the cyclopropyl halides **106, 107, 110, 111, 114–Hal, 115–Hal** and **50–I, 51–Br, 52–Cl, 118–Hal** with alkali metal naphthalenides?

Undoubtedly, in the case of the cyclopropyl halides **106, 107, 110, 111, 114–Hal** and **115–Hal** the normal mechanism with the cyclopropyl radical participating in the product-determining step is observed. The cyclopropyl halides **50–52** and **118–Hal**, however, seem to react in such a way that cyclopropyl halide radical anions $CprX^{\overline{\cdot}}\, M^+$ and/or cyclopropyl radical complexes $Cpr^{\cdot} \cdots X^- M^+$ are kinetically significant. The question whether species of this type indeed exist 'is an important issue'[125b].

The first experimental hint for a 'finite lifetime' of an 'alkyl halide anion radical' in homogeneous etheral solution was provided by Garst and coworkers in 1977[124b]. From the reduction of 5-hexenyl chloride, bromide and iodide with disodium tetraphenylethylene in 2-methyltetrahydrofuran (MTHF) at 20°C they concluded that radical anions $R–X^{\overline{\cdot}}\, Na^+$ were involved and that the order of their stability was $R–I^{\overline{\cdot}} Na^+ > R–Br^{\overline{\cdot}} Na^+ > R–Cl^{\overline{\cdot}} Na^+$.

TABLE 22. Percent net retention of configuration of cyclopropane **119** formed in the reactions of **118** (0.1 M) with KN (0.4 M) in THF at 20°C (normal addition)

(118–Hal)		**(119)**

Hal	% Net retention
Br	75
Cl	11

Symons[125b] critically discussed the results of Garst and coworkers. He points out that although it is very unlikely that an ion paired halide radical anion $R-X^{\cdot-} M^+$ exists in the case of R = 5–hexenyl, $R^{\cdot} \cdots X^- M^+$ complexes possessing weak residual charge-transfer interactions would also be expected to differ kinetically from each other as the halide is varied. Of special significance for the interpretation of the results obtained with the *cyclopropyl* halides **50–52** and **118–Hal** are the following conclusions of Symons[125]:

(1) Genuine σ^* radical anions exist only if the corresponding radical is naturally bent or pyramidal—as this is the case with the cyclopropyl radical but not with normal aliphatic π radicals.

(2) Since iodide I^- is the best electron donor of the halide ions, it can be expected that $R^{\cdot} \cdots I^- M^+$ will be the most thermodynamically stable of the $R^{\cdot} \cdots X^- M^+$ complexes towards dissociation[127], and the least reactive as a donor of $R^{\cdot}$. This is precisely what is observed in the homogeneous reductions that we have been discussing.

Recent model *ab initio* calculations by Clark and Illing[128a] on $MeCl^{\cdot-} M^+$ ion pairs (M = Li, Na, K) suggest a modest barrier to dissociation and not a dissociative SET. Furthermore, they clearly show the influence of different gegenions Li^+, Na^+ and K^+: the leaving group is $X^- M^+$ rather than X^- which is in accord with the results given in Table 18.

In agreement with the first-order kinetics in the product-determining step in the reactions of **50–52** and **118–Hal** with MN, and with all other experimental facts outlined in detail above, the following *intra*molecular SET reactions are proposed to account for the net retention observed with these cyclopropyl halides (Scheme 15).

Because of the good electron accepting qualities of the two aromatic substituents in **50–52** and **118–Hal** (which are not present in the 'normal' cyclopropyl halides **106, 107, 110, 111, 114–Hal** and **115–Hal**) the first SET leads to A with the extra electron predominantly in the aromatic part of the molecule (see Section III.C), and not in the σ^* orbital of the C–X bond. The second SET may lead directly to the final product B (route 1), or to C as an intermediate (route 2). *Formation of B from C via route 3 corresponds to the intramolecular SET trapping with retention of configuration of a $CprX^{\cdot-} M^+$ and/or $Cpr^{\cdot} \cdots X^- M^+$ species and thus to a kinetic proof of their existence.* At the moment it is not clear whether a σ^* radical anion $CprX^{\cdot-} M^+$ or a cyclopropyl radical complex $Cpr^{\cdot} \cdots X^- M^+$ is trapped although a σ^* radical anion is much more likely with
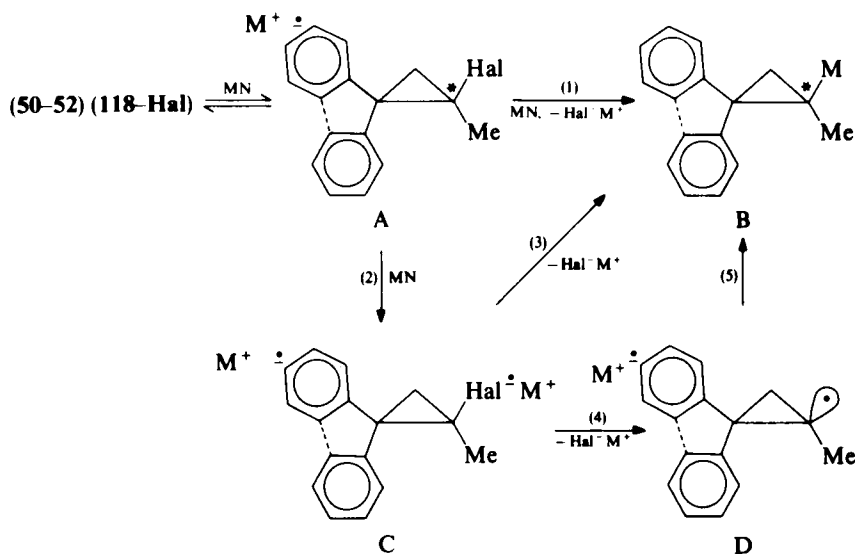
SCHEME 15.   Alternative pathway for the alkali metal naphthalenide reduction of the cyclopropyl halides **50–52** and **118–Hal**[122]

cyclopropyl than with 'normal' aliphatic halides[125b]. Dissociation to give D (route 4) followed by *intra*molecular trapping of the rapidly inverting cyclopropyl radical (route 5) should lead mostly to *racemic* B as indicated by the very low retentions observed with the *chlorides* **52–Cl** and **118–Cl**.

The formation of cyclopropyl halide radical anion pairs as intermediates is also invoked in $S_{RN}1$ type substitution reactions by Rossi[135] and Meijs[136]. It seems that the photostimulated reaction of cyclopropyl bromides like 7-bromonorcarane (**120**) with $Ph_2P^-M^+$ to give **121** involves a radical chain, and halogen-containing radical anions as chain carrier.
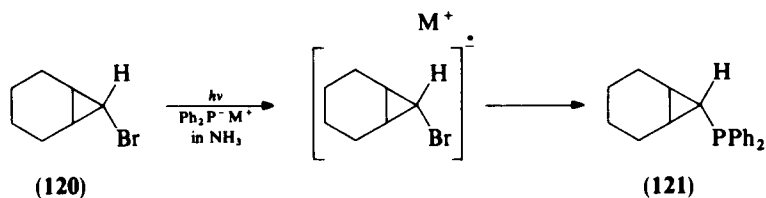
In view of the results with the halides **50–52** and **118–Hal** it is not surprising that in the reaction of optically active 1-isocyano-1-methyl-2,2-diphenylcyclopropane with sodium naphthalenide in DME a similar result was observed. The cyclopropane **49** showed 13 % net retention of configuration as observed by Niznik and Walborsky[137].

Walborsky and Powers also reported on the reduction of optically active 1-fluoro-1-methyl-2,2-diphenylcyclopropane (**122**) under homogeneous (sodium naphthalenide and Na/NH_3) as well as heterogeneous (lithium metal) conditions[138]. The most important outcome of this work is to show the facile acceptance of electrons by the electrophoric[139] phenyl groups causing, in this case, a substantial fragmentation of cyclopropyl C–C bonds because of the low reactivity of the C–F bond[140]. Relevant products and their distribution in the reaction with Li in THF followed by workup with CO_2 are given on the next page.

(122)

(1) Li/THF
(2) CO₂

(49), 21%

2.5% o.p.

(99), 22%

2.6% o.p.

(123), 2%

(124), 0.5%

(125), 26%

(126), 7%
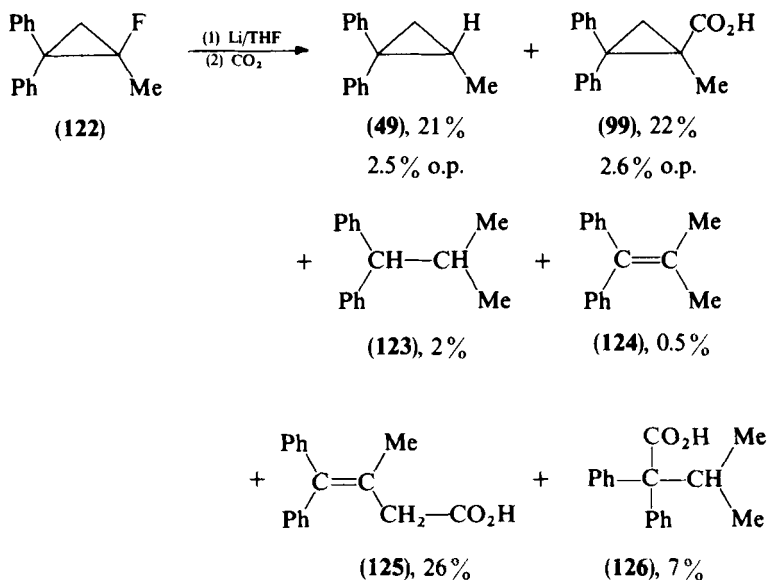
In the Na/NH_3 reduction only the ring-opened **123** was observed, while in the rather slow NaN reduction besides little cyclopropane **49** (6%) mostly the ring-opened **124** (58%) and **123** (17%) were formed. It has been pointed out before that the NaN reduction of **50–52** results only in the cyclopropane **49**. As far as the formation of the cyclopropane **49** and the acid **99** in the Li reduction of **122** is concerned, a similar mechanism has been discussed as outlined in Scheme 15 for the reduction of **50–52** and **118–Hal** in homogeneous solution. The marginal retentions of **49** (2.5% o.p.) and **99** (2.6% o.p.) are in line with the expected instability of the corresponding fluoride containing radical anion.

In summary, SET reactions under homogeneous conditions on the cyclopropyl halides **50–I, 51–Br, 52–Cl, 122–F**, the corresponding isonitrile and **118–Cl, Br** which are strongly halide, gegenion and solvent dependent clearly reveal a pathway with halide- and gegenion-containing intermediates (pathway B in Scheme 12). Normally—with one exception[124b]—SET reactions of this type occur exclusively via radical intermediates (pathway A, Scheme 12), as, for example, clearly demonstrated by the reactions of the cyclopropyl halides **106, 107, 110, 111, 114–Hal** and **115–Hal**.

C. Electron Transfer to π-bonded Substituents of Cyclopropanes

1. Introduction

Electron transfer to cyclopropane should lead to the cyclopropane radical anion which, in principle, can isomerize to the ring-opened trimethylene radical anion. Further reduction of the trimethylene radical anion should give a 1,3-dianion. A less likely two-electron transfer to cyclopropane could conceivably give the ring-opened 1,3-dianion via the corresponding cyclopropane dianion.

The preparation of the cyclopropane radical anion was published in 1963[141]. However, in 1966 it was reported that upon failing to repeat the earlier results there is no 'adequate basis for further discussion of the species previously observed'[142,143]. Cyclopropanes with
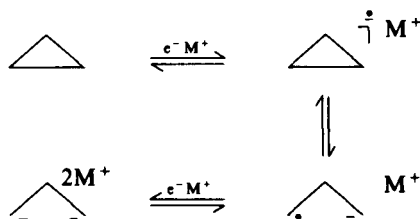
electrophoric[139] substituents (e.g. π-electron systems like carbonyl or aromatic groups) on the other hand, easily accept electrons.

Stable substituted 'cyclopropyl radical anions' have been prepared by Bauld and coworkers[144] and Russell and coworkers[145].

$$(127^{\cdot-}) \qquad\qquad (128^{\cdot-}) \qquad\qquad (129^{\cdot-})$$
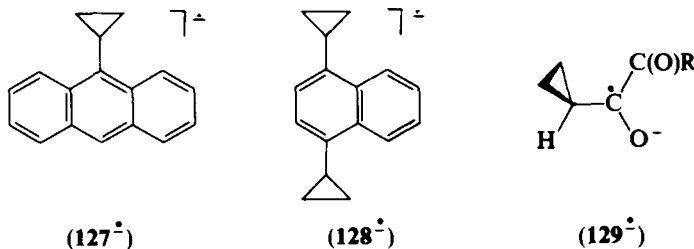
Most interestingly, reduction of 9-cyclopropylanthracene and 1,4-dicyclopropyl-naphthalene led to the planar cyclopropyl conformations in $127^{\cdot-}$ and $128^{\cdot-}$ as opposed to the normally observed bisected[155] cyclopropyl conformations as, for example, in ·the cyclopropylsemidione $129^{\cdot-}$. In all other cyclopropane derivatives previously studied except $127^{\cdot-}$ and $128^{\cdot-}$, q_1, the excess charge density present in the relevant p orbital of the electrophore, is zero or positive. Even in semidione radical anion systems q_1 is calculated (HMO) to be positive ($\sim +0.10$). Thus it is reasonable to assume that the change in the conformational preference of cyclopropyl may be related to the change in sign of q_1.

The underlying reason could be that the Walsh model of cyclopropane has a quasi-cyclopropenyl ring system which could be more effective at accepting an electron pair than the external p system, which is so adept at electron pair donation. Delocalization into the former one would require the planar conformation observed for the radical anions 127^- and 128^-.

Another stable cyclopropane radical anion was possibly observed by Papa[146] when he reacted the cyclopropane 130 with nucleophiles such as potassium iodide, potassium cyanide and triethylamine.

$$(130) \qquad\qquad\qquad (130^{\cdot-})$$
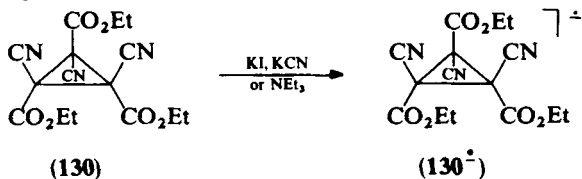
An ESR spectrum 'consistent with the cyclopropane structure $130^{\cdot-}$' was obtained on electrolytic reduction of 130. Undoubtedly $130^{\cdot-}$, if it has the proposed structure, will owe its stability to the many and excellent electrophoric substituents as this is the case with $127^{\cdot-}$, $128^{\cdot-}$ and $129^{\cdot-}$. The facile ET to 130 from the nucleophiles mentioned is remarkable.

2. *Reductive cleavage of cyclopropanes*

a. Regioselectivity

The first report on the reduction of a *carbonyl* substituted cyclopropane was published in 1949[147]. Reactions of methyl cyclopropyl ketone (131) with sodium in liquid ammonia in the presence of ammonium sulfate yielded instead of the expected methyl cyclopropyl-carbinol (132) only a mixture of 2-pentanone (133) and 2-pentanol (134).
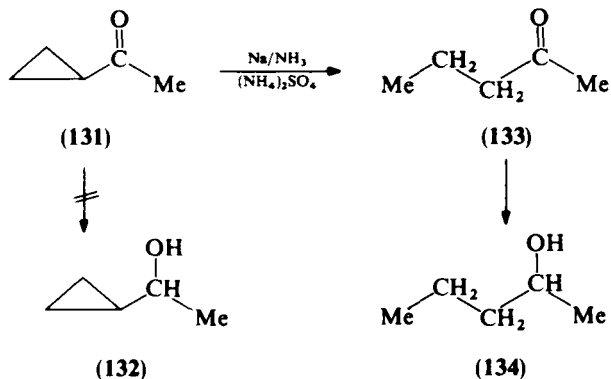
Norin[148b] showed in 1965 that the reduction of conjugated cyclopropyl ketones with lithium in liquid ammonia proceeds via a highly stereospecific opening of the three-membered ring. The steric course of the reductions appears to be determined by the configuration of the starting material. The cyclopropane bond which is cleaved is the one possessing maximum overlap of the Walsh orbitals with the π orbital of the carbonyl group, as exemplified by the following transformations.
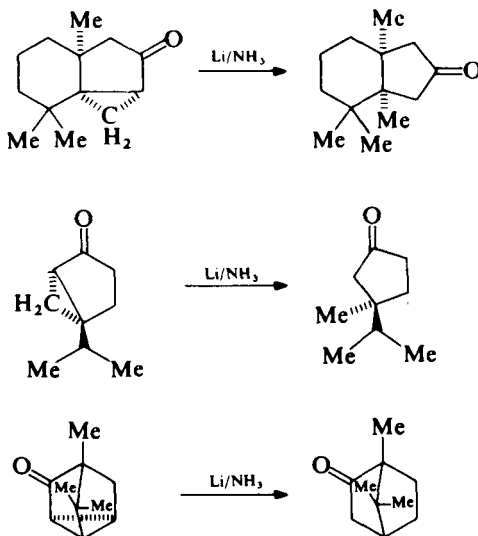
The importance of the geometrical factor in rigid systems was confirmed by Dauben and coworkers[149] who also pointed out that in such systems the process is not controlled by thermodynamic considerations. It is not necessarily the most stable (= least substituted) carbanion which is formed ('electronic factor').

In a further study using the cyclopropyl ketones 135, cis-136 and trans-136, in which two bonds of the cyclopropane ring, C(1)–C(2) and C(1)–C(3), are free to overlap with the carbonyl π-system, the importance of electronic versus steric factors was evaluated[149b].

(135)   (cis-136)   (trans-136)
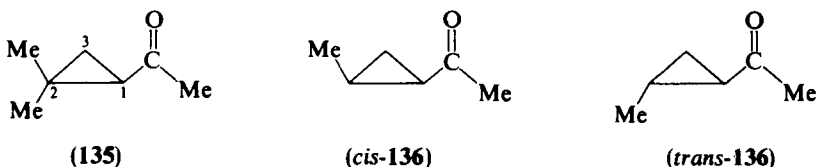
The reduction products that predominate in the reaction mixture from the cleavage of the 2,2-dimethyl-135 and the cis-2-methyl cyclopropyl ketone (cis-136) arise from C(1)–C(2) bond breaking. In contrast, the trans-2-methyl cyclopropyl ketone (trans-136) fragments at the C(1)–C(3) bond. The observed ring-opening pattern suggests that steric factors can control the direction of cleavage 'presumably through unsymmetrical overlap of the carbonyl π system with one of the cyclopropane bonds'. In the absence of these steric elements as in the case of the trans-substituted trans-136 the bond that cleaves is the one
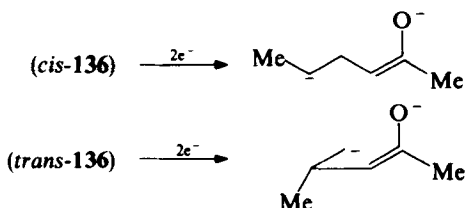
that gives the more thermodynamically stable carbanion intermediate Fraisse-Jullien and Frejaville[150] and House and Blankley[151] arrived at similar conclusions.

Overlap control by steric factors of phenyl substituents in cyclopropanes additionally containing a carbonyl group have been described by Zimmerman and coworkers[152] in the liquid ammonia reduction of the isomeric diphenyl cyclopropyl ketones cis- and trans-137.
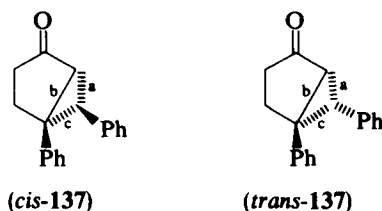
(cis-137)   (trans-137)

In cis-137, bond a is more easily broken than bond b; the reverse is true in the case of trans-137. Interestingly, the reductive degradation of cis- and trans-137, respectively, with Li/NH₃, is related to stereoelectronic control in the photochemical transformations of these compounds.

The reduction of 1-methyl-2,2-diphenylcyclopropane 49 and of one of its enantiomers, (+)-(R)-49, with Na/NH₃ to give 1,1-diphenylbutane (138) and 1,1-diphenyl-2-

methylpropane (123) in a ~ 5.5:1 ratio over a wide concentration range has been studied by Walborsky and Pierce[153a].
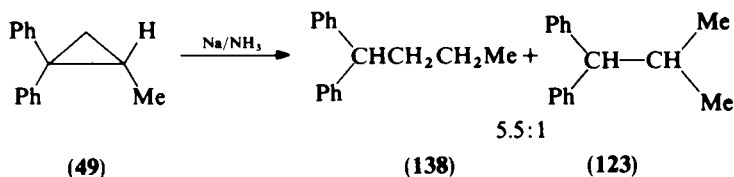
From the well known ability of phenyl groups to accept electrons from sodium in NH_3[154] the mechanism outlined in Scheme 16 was proposed for the opening of the cyclopropane ring in 49 and other phenyl-substituted cyclopropanes.
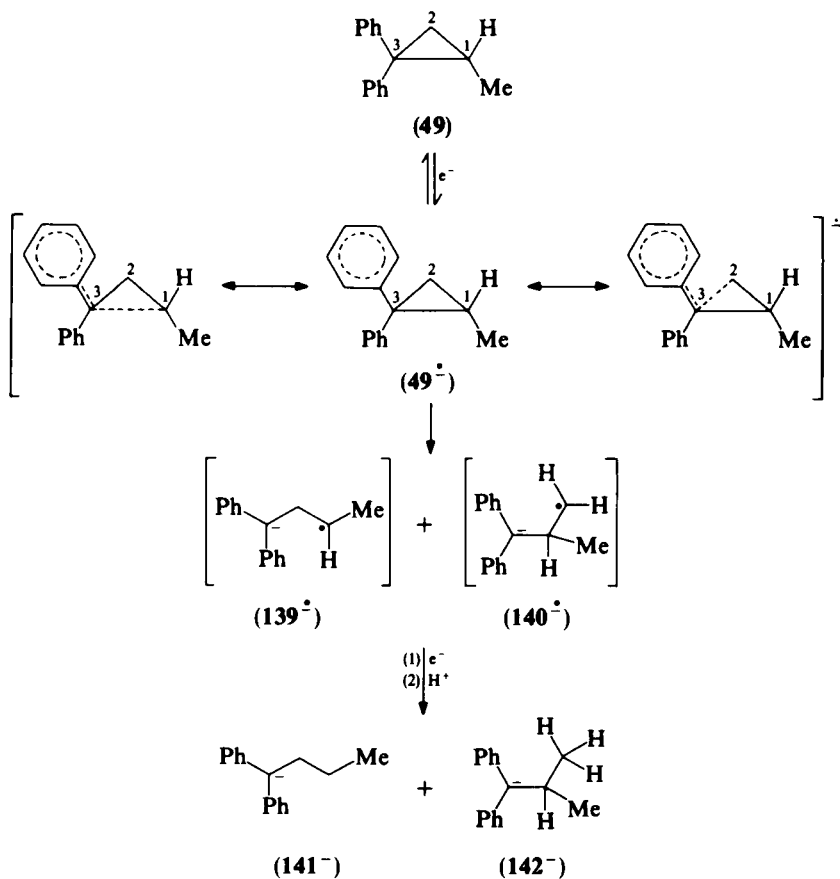
SCHEME 16. Proposal for the reduction of 1-methyl-2,2-diphenylcyclopropane 49 and other phenyl-substituted cyclopropanes with sodium in NH_3[153a].

It has been found that at least one phenyl group attached to the cyclopropane ring is a necessary condition for the ring-opening: 2,2-diphenyl- and *trans*-2-phenyl-cyclopropanecarboxylic acid are opened by Na/NH_3 while 2,2-dimethyl- and cyclopropanecarboxylic acid are not opened[153a].

From these results it is quite understandable that the parent cyclopropyl radical anion is not observable by ESR (*vide supra*), and that ring-opening to give the parent trimethylene radical anion, the parent 1,3-dianion or any follow-up products also does not occur[141-143].

The role of the phenyl group is to accept an initial electron to form the short-lived radical anion **49**$^{\dot{-}}$. ESR experiments, however, failed to demonstrate the existence of species such as **49**$^{\dot{-}}$, or the trimethylene radical anions **139**$^{\dot{-}}$ and **140**$^{\dot{-}}$. This means that if **49**$^{\dot{-}}$ is formed it must readily open to **139**$^{\dot{-}}$ and **140**$^{\dot{-}}$ which themselves must quickly add another electron to form a dianion which is protonated by the solvent to give the anions **141**$^-$ and **142**$^-$, respectively.

Moreover, the ring-opening of **49**$^{\dot{-}}$ to **139**$^{\dot{-}}$ and **140**$^{\dot{-}}$ is *irreversible* in the presence of sodium in ammonia since optically active (+)-(R)-**49** is recovered without loss of optical activity[153b].

That intermediates such as **139**$^{\dot{-}}$, not unexpectedly, would cause loss of optical activity was shown by using (−)-(R)-1-*n*-pentyl-1-methyl-2,2-diphenylcyclopropane (**143**) as the starting material. The resulting **144** was completely racemic[153a].

$$Ph \underset{Ph}{\overset{n\text{-}C_5H_{11}}{\bigwedge}} Me \xrightarrow{\text{Na/NH}_3} \underset{Ph}{\overset{Ph}{\underset{}{}}}CHCH_2\overset{Me}{\underset{}{C}}H\text{-}C_5H_{11}\text{-}n$$

(143)   (144)
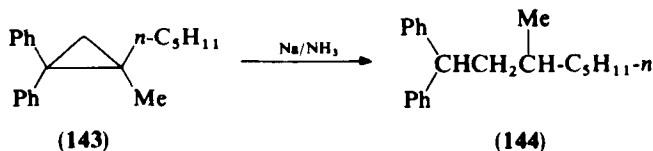
The predominant formation of **138** from **49** via 1,2-bond cleavage of **49**$^{\dot{-}}$ to give **139**$^{\dot{-}}$ is expected on the basis that the radical anion **139**$^{\dot{-}}$ would be predicted to be more stable than the isomeric radical anion **140**$^{\dot{-}}$. This argument presumes that there is almost no negative charge on the carbon atom bearing the methyl substituent; otherwise **140**$^{\dot{-}}$ should be more stable. This assumption seems reasonable because the negative charge is very well stabilized by two phenyl substituents. Furthermore it seems unlikely that instead of **139**$^{\dot{-}}$ and **140**$^{\dot{-}}$ the corresponding 1,3-dianions have been formed *directly* from their common cyclopropane dianion precursor. This, however, has not been excluded rigorously by means of these experiments.

Reductions of 1,1-biphenylene-2-methylcyclopropane **119** with Na/NH_3, $Na/NH_3/t$-BuOH, Li/NH_3, electrolysis, Na/glyme and sodium naphthalenide/glyme/25°(−78°C) essentially confirm the results with **49**, although under any conditions a higher ratio of C(1)–C(2) bond cleavage is observed in the case of **119**[153b].

What is the underlying reason? In **119**, the phenyl groups are frozen in the preferred bisected[155] conformation for interaction with the Walsh orbitals of both the C(1)–C(2)

(119)   81–96% : 19–4%
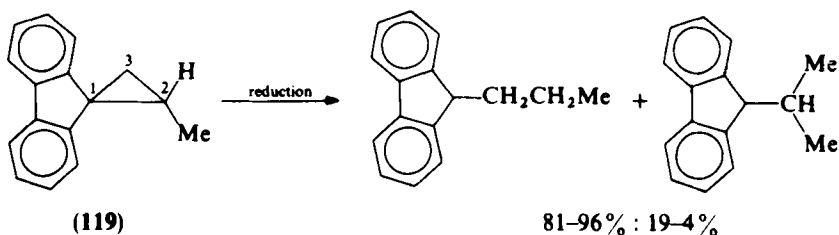
and the C(1)–C(3) bond. Thus electronic considerations are more important than steric ones. Therefore, the direction of the cleavage should even more be determined by the stability of the ring-opened radical anions corresponding to **139**$^{\div}$ and **140**$^{\div}$ which again are believed to be intermediates. This makes sense since a negative charge is more stabilized in a fluorenyl than in a diphenyl methyl anion thus making the fluorenyl trimethylene radical anion, which corresponds to **139**$^{\div}$, even more stable.

Steric and electronic factors in the reductive cleavage of methyl-substituted phenyl cyclopropanes (**145**) and in spiro[2.4]hepta-4,6-dienes like **146** have been investigated by Staley and Rocchio[156].

| (*trans*-**145**) | (*cis*-**145**) | (**146**) |
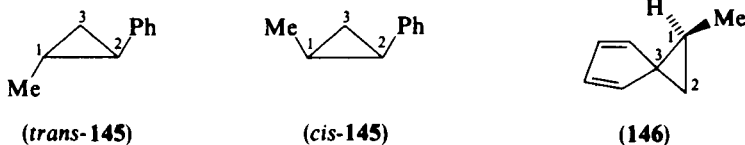
In *trans*-**145** Li/NH$_3$ reduction cleaved primarily the C(2)–C(3) bond (k(2)–(3)/k(2)–(1) = 360 ± 20) whereas the *cis*-**145** is cleaved in the opposite direction (k(2)–(1)/k(2)–(3) = ~ 70).

The high regioselectivity in the cleavage of *trans*-**145** (in which there is no steric bias for either pathway) shows that a methyl group exerts a destabilizing effect relative to hydrogen for the cleavage. This is consistent with a description of the activated complex in the case of *trans*-**145** with a substantial negative charge also on the cyclopropyl β-carbon of the bond undergoing cleavage.

In the case of *cis*-**145** the conformation of maximum overlap for cleavage of bond C(2)–C(3) possesses a substantial steric interaction between the methyl group and the *ortho* hydrogen atom of the phenyl ring. Therefore, the cleavage of C(2)–C(1) is favored.

From the very different reduction products from *cis*- and *trans*-**145**, respectively, with sodium in NH$_3$ one can conclude that a possible trimethylene radical anion intermediate is not *reversibly* formed. Otherwise, both stereoisomers *cis*- and *trans*-**145** should lead to the same reduction products. An irreversible ring-opening has similarly been observed in the Na/NH$_3$ reduction of (+)-(*R*)-**49**[153b], as shown earlier. Comparable results to those of *cis*- and *trans*-**145** have been observed with the corresponding cyclopropyl ketones *cis*- and *trans*-**136**[149b] (see above).

The destabilizing effect of a methyl group relative to hydrogen is also observed in the cleavage of the spiro[2.4]hepta-4,6-diene **146**. Na/NH$_3$ reduction leads to 1- and 2-*n*-propyl-, and 1- and 2-isopropylcyclopentadienes in a 1 : 4.8 ± 0.3 ratio. Since the rigid **146** does not provide conformational advantage to the breaking of either bond C(3)–C(2) or C(3)–C(1) the moderate preference for the cleavage of C(3)–C(2) indicates a small amount of excess negative charge on the methyl-substituted carbon atom C(1) in the activated complex, in agreement with the negative charge being largely delocalized in the incipient cyclopentadienyl ring. Although the results of **146** are strongly suggestive of radical anion in favor of dianion intermediates it has been pointed out by Staley and Rocchio that one cannot distinguish between these two mechanisms (or a combination thereof) on the basis of the present data[156].

SET reduction of dibenzonorcaradiene (**147**) with lithium, sodium or potassium naphthalenide followed by quenching with water led to 9-methylphenanthrene (**148**) (16–24%), 9-methyl-9,10-dihydrophenanthrene (**149**) (33–43%) and 6,7-dihydro-5-*H*-dibenzo[a,c]cycloheptane (**150**) (23–34%)[139].

The intermediate formation of the radical anion **147**$^{\div}$ is assumed because of the green colour of the solution due to an electrophore which encompasses at least the biphenyl

(147)   **(147$\dot{}^-$)**

(148)   **(149)**   **(150)**
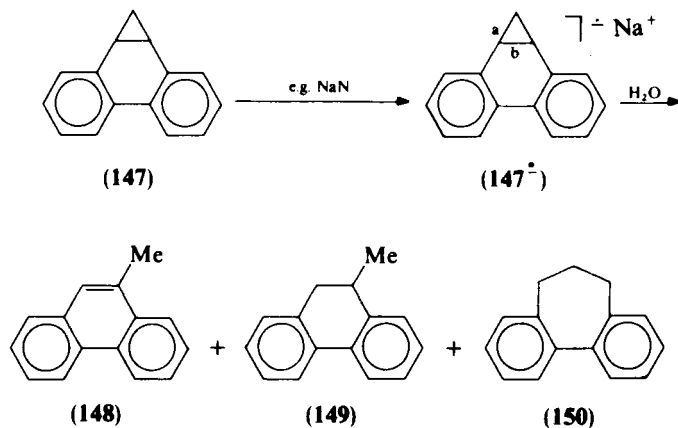
electrophore. Preferential cleavage of bond a is caused by a stereoelectronic effect: the external cyclopropane bonds are well oriented for overlap with the biphenylene π-system; the internal bond is nearly perpendicular to that system. Why still 23–24 % **150** is formed although the cleavage of bond b is 'an apparent violation of the orbital symmetry prediction' is not quite clear.

Ring-opening, again presumably of the radical anion, is observed in the reduction of **151** to give the radical anion **152$\dot{}^-$**. Reduction of **153**, in contrast, gives the 'closed' radical anion **153$\dot{}^-$** [145a].

(151)   **(152$\dot{}^-$)**

(153)   **(153$\dot{}^-$)**
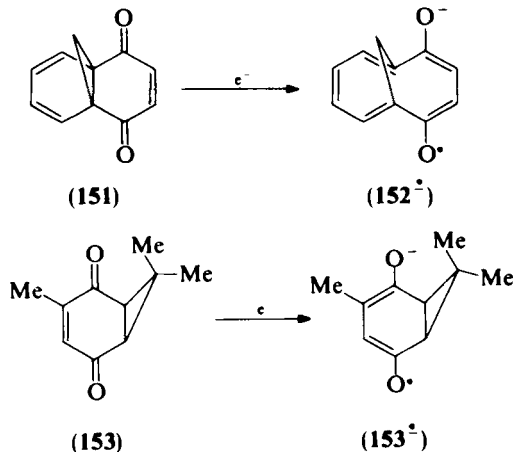
The reduction of *cis*- and *trans*-bicyclo[6.1.0]nona-2,4,6-triene (*cis*- and *trans*-**154**, respectively) under various conditions has been studied by several groups[157,158].

Reduction of *cis*-**154** proceeds through the nine-electron homoaromatic radical anion **155$\dot{}^-$** to give the delocalized monohomocyclooctatetraene dianion **155$^=$** [157].

In contrast, the bicyclic radical anion *trans*-**154$\dot{}^-$** is produced exclusively upon reduction of *trans*-**154** with a potassium mirror in THF or DME solution at $-90°C$ [158]. These observations agree fully with orbital symmetry considerations if the highest occupied MOs of *cis*- and *trans*-**154** are the levels which control reactivity, thus requiring disrotatory bond

(cis-154)   (155$\overline{\cdot}$)   (155$^=$)
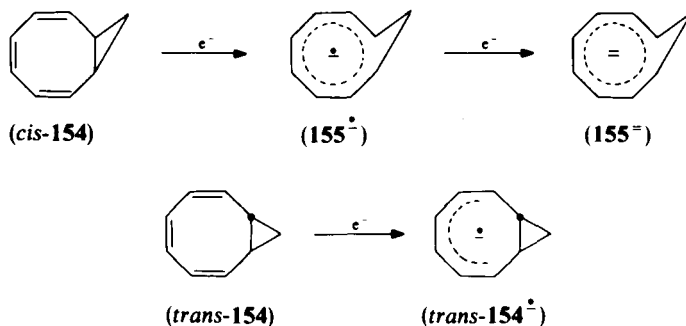
(trans-154)   (trans-154$\overline{\cdot}$)

cleavage of the central cyclopropane bond[157d]. Disrotatory ring-opening of cis-154 to give cis,cis,cis,cis-cyclononatetraene radical anion (155$\overline{\cdot}$) is accordingly favorable while the analogous reaction channel starting from trans-154 is prohibited by the high-strain energy and poor p-π overlap in the trans,cis,cis,cis-cyclononatetraene radical anion. However, the ring-opening process is not as clear if the symmetries of all occupied orbitals in starting material and product(s) are considered. The orbital correlation diagram for disrotatory and conrotatory modes of cyclopropyl ring-opening in cis-154$\overline{\cdot}$ show that both processes are formally disallowed as the symmetries of starting material and product are different. However, if one assumes $\beta_{1,8} = 1.0\beta_0$ for the ring-opened product 155$^=$, a disrotatory mode is allowed for the dianion. Thus it is possible that the dianion undergoes ring-opening. Again, we are confronted with the unsolved question which species opens the ring.

Reaction of bullvalene (156)[159a] with Na/K alloy in THF or DME at room temperature led to the bicyclo[3.3.2]decatrienyl dianion 157$^=$ 2K$^+$.

(156)   (157$^=$ 2K$^+$)

(158)   (159$^=$)
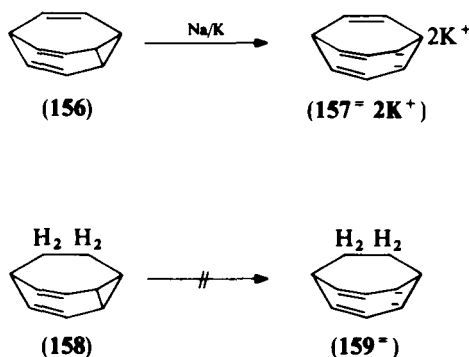
The lithium salt was accessible by LiBr metathesis. The facile formation of 157$^=$ 2K$^+$ in contrast to the unsuccessful reduction of dihydrobullvalene (158) which does not give the corresponding dianion 159$^=$, has been discussed along the lines of longicyclic stabilization of 157$^=$ as opposed to the bishomoantiaromatic nature of the bicyclo[3.3.2]decadienyl dianion 159$^=$. The value of such qualitative theoretical argument has increasingly been questioned in recent years, and particularly as it applies to anions. A literature survey of such criticism is given in Ref. 159b.

Reduction of semibullvalene (160) should lead to the destabilized [3.3.0]dianion 161$^=$. A symmetry-allowed and thermodynamically attractive isomerization to the cyclooctatet-

raenyl dianion $162^=$ would be difficult to resist. Treatment of **160** with lithium in THF or dimethyl ether even at $-78°C$ leads to 'dilithium semibullvalenid' which actually exists as the C_{2h} and D_2 diastereoisomers of bis(bicyclo[3.3.0]octa-3,7-diene-2,6-dyil)tetralithium (**163**), the first structurally characterized pair of diastereoisomeric organolithium

(160)   (161⁻)

(163)   (162⁻)
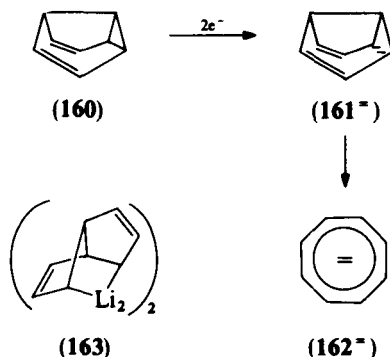
compounds[159b–d, 160]. 'Dilithium semibullvalenid' (**163**), as expected, isomerizes at 0°C with an apparent first-order rate constant $k = 9.0(1) \cdot 10^{-5}\,s^{-1}$ to **162** $2Li^+$.

The potassium species $161^= 2K^+$ could not be prepared by deprotonation of a mixture of tetrahydropentalenes (e.g. **164**) with a 1:1 n-butyllithium/potassium t-pentoxide mixture[161].
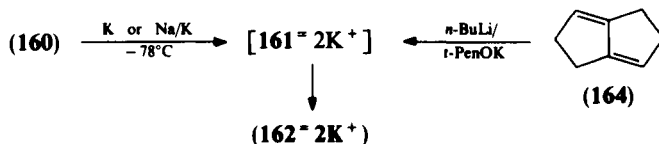
Instead, the dipotassium salt of the cyclooctatetraenyl dianion $162^= 2K^+$ was detected exclusively. This result was confirmed by Goldstein and Wenzel[159c]: reduction of semibullvalene (**160**) with potassium or sodium/potassium alloy even at $-78°C$ resulted only in $162^= 2K^+$.

Müllen and coworkers[160b] were able to transform barbaralane (**165**) with lithium into the dianion $166^=$. In the presence of potassium, 3,4-homotropilidene (**167**), in contrast, first isomerizes to **168** which then deprotonates to give the monoanion 169^-. Interestingly, the three-membered ring is not cleaved in that case. In all these cases it is not clear which species opens the ring.

(165)   (166⁼)

(167)   (168)   (169⁻)
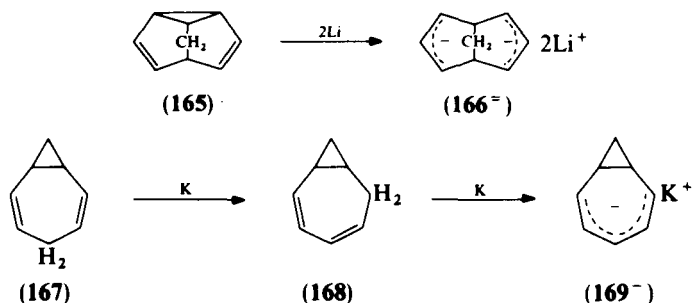
In the following examples ET reactions to cyclopropanes have been presumed to account for the observed cyclopropane → propene isomerizations.

2,3,4-Triphenyl-*endo*-tricyclo[3.2.1.0^{2,4}]octane (**170a**) isomerizes in the presence of base, e.g. *t*-BuOK in DMSO (70°C, 20 h), to 2,3,4-triphenylbicyclo[3.2.1]oct-2-ene (**173a**) (Scheme 17). Originally this was proposed by Mulvaney and coworkers[162] to occur via forbidden disrotatory ring-opening of the cyclopropyl anion **171a**$^-$ to give the allyl anion **172a**$^-$ which is then protonated to give **173a** (pathway A).

	R^1	R^2
a:	H	Ph
b:	H	CN
c:	Me	CN
d:	H	Me
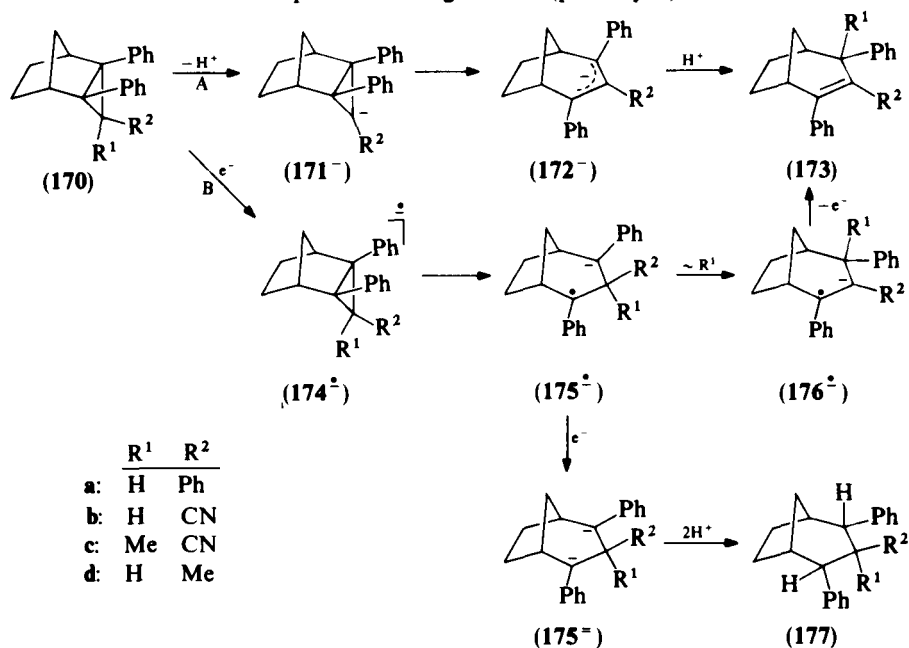
SCHEME 17. Reactions of *endo*-tricyclo[3.2.1.0^{2,4}] octanes with base and ET reagents (gegenions omitted)

It was concluded later[163] that 'the reaction of **170a** with *t*-BuOK in DMSO or HMPA (25°C, 24 h), or with dimsyl potassium in DMSO (70°C, 24 h) appears to proceed by a radical pathway'. The authors proposed that an initial SET from base to **170a** affords radical anion **174a**$^{\pm}$ which opens to **175a**$^{\pm}$. The latter was envisaged to rearrange to **176a**$^{\pm}$ which loses an electron 'possibly to **170a**', to give **173a** (pathway B).

In order to shed some more light on the mechanism of this isomerization reaction Boche and Marsch[164] investigated the reactions of the *endo*-bicyclo[3.2.1.0^{2,4}]octanes **170a–d** with different bases and ET reagents, respectively. It was shown that the cyclopropyl anion **171b**$^-$, transforms completely and in a disrotatory manner into the allyl anion **172b**$^-$, even at −75°C within 1 h, which strongly suggests a similar pathway in the case of **170a** with base. Further support is provided by the reaction of **170a** with the 'superbase' potassium 3-aminopropylamide (KAPA) in 1,3-diaminopropane[165]: **170a** is completely transformed into **173a** after 1 h at 0°C. In the reaction of 2,3,4-triphenyl-*endo*-tricyclo[3.2.1.0^{2,4}]octene with lithium 2-aminoethylamide in ethylenediamine at 100°C a similar cyclopropyl/allyl anion pathway has been formulated by Martin[166].

A totally different picture emerges if **170c** and **170d** are used (Scheme 17). Treatment of the methylcyanocyclopropane **170c** with base (LDA, THF, −75°C, 1 h; *t*-BuOK, DMSO,

25°C, 24 h; *t*-BuOK, DMSO, 70°C, 5 h) leads to complete recovery of starting material. **170d** is also unreactive towards base (*t*-BuOK, DMSO, 70°C, 6 h; KAPA, 1,3-diaminopropane, 25°C, 24 h). Thus replacing the acidic H-3 in **170b** by a methyl group as in **170c** or making it comparatively non-acidic as in **170d**, prevents deprotonation and therefore does not lead to a reaction with base although the proposed[163] SET reaction still could occur. With a real SET reagent (Na/K alloy, THF) **170d** is transformed into **177d** in a manner analogous to the transformation of **170a** to **177a** by sodium naphthalenide, followed by protonation[163].

The behavior of **170c** and **170d** therefore supported the cyclopropyl anion pathway A in favor of the ET mechanism B. Furthermore, as far as the proposed rearrangement of the proposed radical anions **175**$^{\overline{\cdot}}$ → **176**$^{\overline{\cdot}}$ is concerned, it is shown later in this section that in similar trimethylene radical anions such rearrangements do not take place.

One can therefore conclude that the base-catalyzed cyclopropane → propene isomerization **170a** → **173a** is induced by an acid–base and not by an ET reaction.

It is also rather doubtful whether the reaction of a 72:28 mixture of *cis*- and *trans*-1,2-diphenylcyclopropane (**178a**) with *t*-BuOK in DMSO or in HMPA at 25°C for 70 days leading, i.e., to 23% 1,3-diphenylpropene (**179a**) is caused by electron transfer[163].
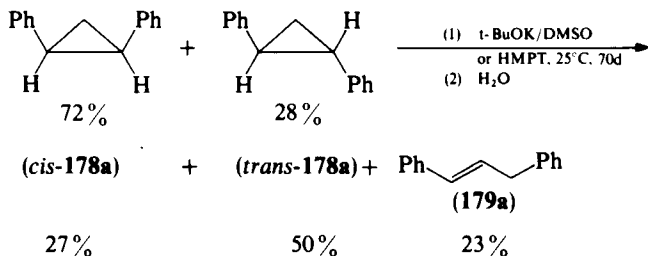
The authors of this work[167] at least suggested that 'further investigation is required to determine the mechanism of the described reaction'.

b. Electron transfer catalyzed stereoisomerization

Electron transfer reactions to various cyclopropanes with special concern for the question of the formation of radical anion intermediates and their chemistry have been studied by Boche and coworkers[168]. A typical example is given by the reaction of *cis*-1,2-diphenylcyclopropane (*cis*-**178a**) with Na/K alloy at 0°C to yield on protonation *trans*-1,2-diphenylcyclopropane (*trans*-**178a**), *trans*-1,3-diphenylpropene (*trans*-**179a**, together with some *cis*-**179a**), and 1,3-diphenylpropane (**181a**). The time-dependent amounts of *cis*-**178a**, *trans*-**178a**, *trans*(+ *cis*)-**179a** and **181a** are shown in Table 23. Table 23 can be summarized as follows:

(1) The cyclopropane *cis*-**178a** disappears steadily; after 40 min nothing is left.

(2) The concentrations of the stereoisomeric cyclopropane *trans*-**178a** and of the propane **181a** pass through a maximum. This demonstrates the intermediacy of *trans*-**178a** and of the 1,3-dianion **180a**$^{=}$; **180a**$^{=}$ gives the propane **181a** on protonation, as confirmed by deuteration (Scheme 18).

(3) The concentration of the propene **179a** resulting from protonation of the allyl anion **182a**$^{-}$ increases steadily.

Similar results have been observed when the reaction was started with the thermodynamically more stable *trans*-cyclopropane *trans*-**178a**, and at different temperatures. Obviously, two different reactions take place:

(1) the *stereoisomerization* of the cyclopropanes *cis*-178 and *trans*-178, and

(2) the transformation of the cyclopropanes *cis*- and *trans*-178 into the *ring-opened products* 179 and 181.

TABLE 23. Time-dependent yields of *cis*-178a, *trans*-187a, *trans*(+*cis*)-179a and 181a in the reaction of *cis*-178a with Na/K alloy in THF at 0°C, followed by protonation with water

	(*cis*-178a)	(*trans*-178a)	(*trans*(+*cis*)-179a)	(181a)
Time (min)		Yield %		
0	95	5	—	—
10	83	5	—	12
45	8	57	5	30
120	1	28	30	41
240	—	9	53	38

	R
a:	H
b:	D
c:	Me
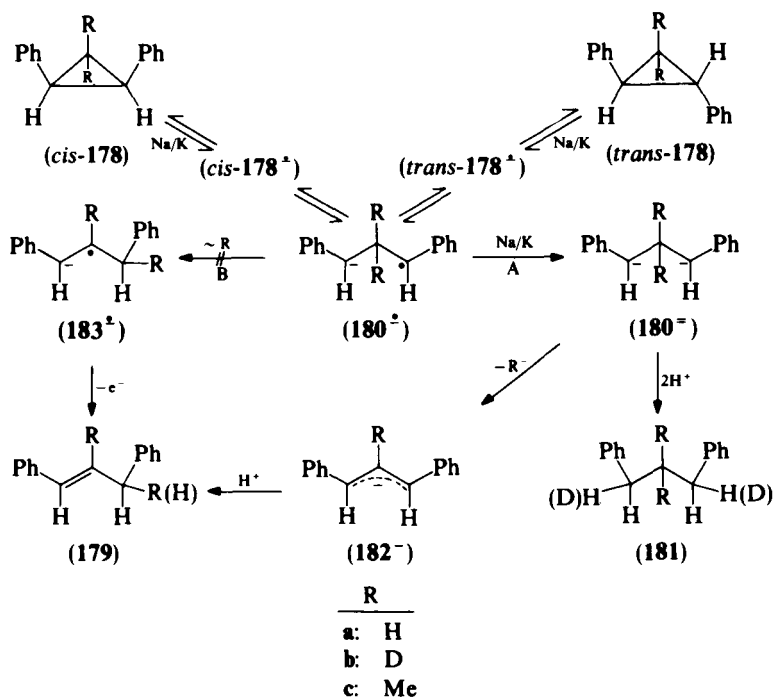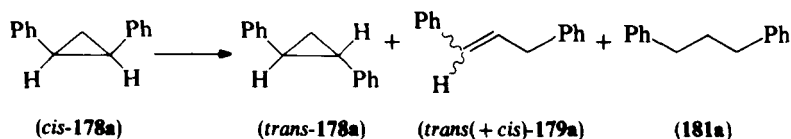
SCHEME 18. *Cis/trans* isomerization of the *cis*- and *trans*-1,2-diphenylcyclopropanes (*cis*- and *trans*-178a–c) and formation of the 1,3-diphenylpropanes (181a–c) and 1,3-diphenylpropenes (179a,b) with Na/K in THF (gegenions omitted).

The suggestion that the *stereoisomerization* is an *ET-catalyzed* reaction occurring via the stereoisomeric trimethylene radical anions **180**$^{\doteq}$ (Scheme 18) is confirmed by the following three results:

(1) The *thermal* isomerization *cis*-**178a** → *trans*-**178a**, having a rate constant $k = \sim 10^{-4}$ s^{-1} at 200°C, as measured by Rodewald and DePuy[169], extrapolates to a half-life at 0°C of $\sim 10^9$ years. Clearly, the observed reaction in the presence of Na/K is not a thermal one: *cis*-**178a** has disappeared completely after 40 min.

(2) The *cis–trans* isomerization in the case of the 1,2-diphenylcyclopropanes **178a** in the presence of Na/K is not a *base-catalyzed* reaction with the cyclopropyl anions **183**$^-$ as

$$(cis\text{-}\textbf{178a}) \;\overset{-H^+}{\underset{H^+}{\rightleftharpoons}}\; \text{Ph}\!\!\diagup\!\!\diagdown\!\!\text{Ph} \;\rightleftharpoons\; \text{Ph}\!\!\diagup\!\!\diagdown\!\!K^+ \;\overset{H^+}{\underset{-H^+}{\rightleftharpoons}}\; (trans\text{-}\textbf{178a})$$

$$(\textbf{183}^-)$$
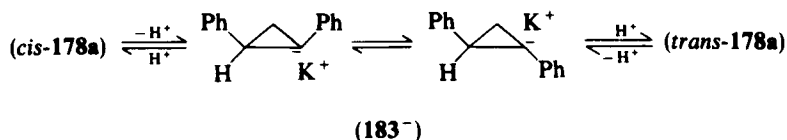
intermediates. This is nicely shown by the work mentioned in the previous section: *cis*-**178a**, in the presence of *t*-BuOK in DMSO or HMPA, isomerizes to *trans*-**178a** even within 70 days at 25°C only slightly[167].

(3) The stereoisomerization of the cyclopropanes **178** via 'dianions' **180**$^=$ (Scheme 18) is also rigorously excluded. *A priori*, this is not a totally unlikely pathway since Lagendijk and Szwarc[170] have deduced from kinetics that it is the dianion that breaks the C–C bond in the reaction of electron sources with 1,2-di-α-naphthylethane to give α-naphthylmethyl anions. Similarly, Grovenstein and coworkers[171] have recently found that bond cleavage in the reaction of 1,2-di-*p*-tolylethane with Cs/K/Na alloy occurs at the dianion stage.
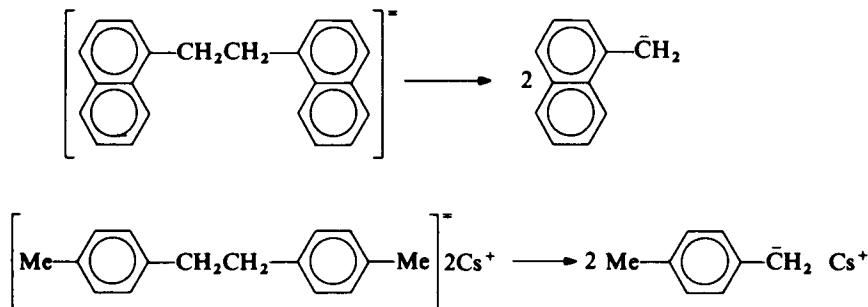
The formation of the 1,3-dianions **180**$^=$ from the corresponding cyclopropane dianions would correspond exactly to these reactions. If the dianions **180**$^=$ were intermediates in the ET-catalyzed stereoisomerization of the cyclopropanes the *reverse reaction*—formation of the cyclopropanes **178** from the dianions **180**$^=$—should also take place. Preparation of the 1,3-dianion **180a**$^=$ 2K$^+$(Li$^+$) from the cyclopropane *cis*-**178a** with Na/K alloy or with lithium at -78°C shows clearly that **180a**$^=$ 2K$^+$ (Li$^+$) is stable at -78°C (Scheme 19).

Whether this is also the case at 0°C cannot be decided with **180a**$^=$[172] because it loses hydride between $-78°$ and 0°C to give the allyl anion **182a**$^-$. If the methylene hydrogens in **180a**$^=$ are replaced by two methyl groups as in **180c**$^=$ then elimination does not take place. **180c**$^=$ is stable up to 0°C; importantly, ring-closure to give *cis*- or *trans*-**178c** is not observed! The corresponding cyclopropanes *cis*- and *trans*-**178c**, however, isomerize in the presence of Na/K alloy.

$(cis\text{-}178a) \xrightleftharpoons[\text{THF, }-78°\text{C}]{\text{Na/K or Li}} (trans\text{-}178a) \xrightleftharpoons[\text{THF, }-78°\text{C}]{\text{Na/K or Li}}$

Ph H $2K^+(Li^+)$ Ph $\xrightarrow[-78° \text{ to } 0°\text{C}]{-\text{MH}}$ Ph H $K^+(Li^+)$ Ph

H H H

(180a$^=$)

H H

(182a$^-$)

Me $2K^+(Li^+)$

Ph Ph $\xrightarrow{\quad\not\!\!\longrightarrow\quad}$ no ring-closure

H Me H

(180c$^=$)
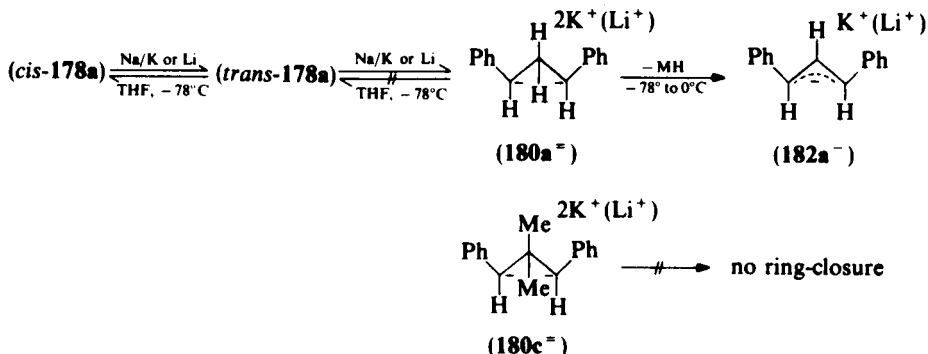
SCHEME 19. 1,3-Dianions are not intermediates in the ET-catalyzed isomerization of cyclopropanes

The difference between a *base-catalyzed* and an *ET-catalyzed cis/trans*-isomerization of cyclopropanes is also nicely demonstrated by the following example.

The *base-catalyzed* t-BuOK, DMSO, 100°C, 17 h isomerization of r-1-phenyl-c-2, c-3-dimethyl- and r-1-phenyl-t-2-, t-3-dimethylcyclopropane (*cis,cis-*184 and *trans,trans-*184), as studied by Closs and Moss[173], and the ET-catalyzed (Na/K, THF, 20°C, 16 min) reaction of these cyclopropanes are shown below.

Ph Me Me H Me Me
H $\xrightleftharpoons[100°\text{C, }17\text{ h}]{t\text{-BuOK, DMSO}}$ Ph

H H H H

(*cis, cis-*184) (*trans, trans-*184)

1 99

(*cis, cis-*184) $\xrightleftharpoons[20°\text{C, }16\text{ min}]{\text{Na/K, THF}}$

Ph Me H
H

H Me

(*cis, trans-*184)

$\xrightleftharpoons[20°\text{C, }16\text{ min}]{\text{Na/K, THF}}$ (*trans, trans-*184)

1 : 44 : 55
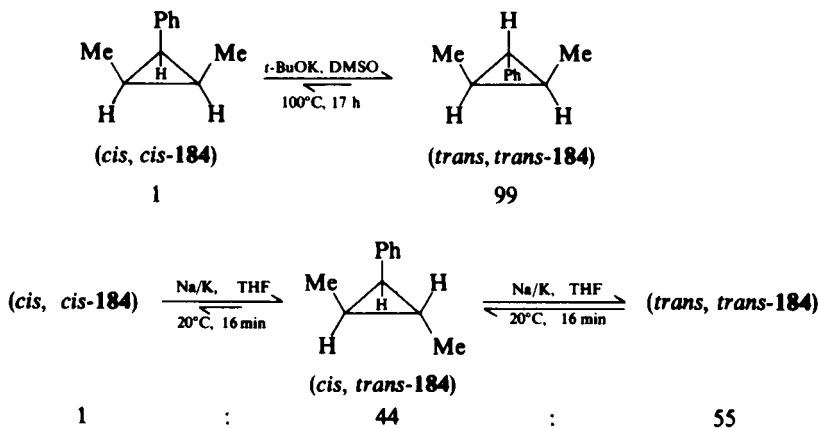
It is not only the conditions of temperature and time which are totally different in these two reactions. In the *base-catalyzed* reaction only *cis,cis-* and *trans,trans-*184 are formed as expected if the cyclopropyl anion 185$^-$ is the intermediate.

In the much faster ET-catalyzed reaction a new stereoisomer, r-phenyl-c-2,t-3-dimethylcyclopropane (*cis,trans-*184) shows up in equilibrium with the isomers *cis,cis-* and *trans, trans-*184. This excludes the possibility that the cyclopropyl anion pathway occurs exclusively. It also excludes the belief that under base-catalyzed conditions ET-catalyzed isomerizations must play a significant role. This result also supports the conclusion[164] that in the base-catalyzed reaction of 170a the proposed ET mechanism[163] is not valid (see

Ph K⁺
Me—⟨—Me
   H   H
(185⁻)

Ph
Me—⟨—H·Me
   H   H
(186·̄)
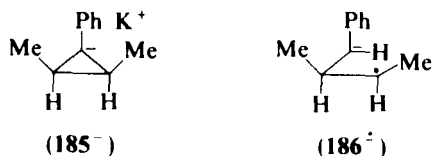
previous section). The formation of *cis,trans*-184 requires that in the course of the equilibration a cyclopropane bond is broken. As in the case of stereoisomerization of the 1,3-diphenylcyclopropanes 178 with Na/K alloy a trimethylene radical anion, here 186·̄, should be an intermediate.

That 186·̄ indeed is an intermediate is shown by a prolonged reaction of the equilibrium mixture of the cyclopropanes 184 with Na/K. After 60 h at 20°C the following reactions have been observed (Scheme 20).

182

          Me K⁺   Me 2K⁺   K⁺   Me
Ph—C̄—C—C·—H   →(Na/K, A)→   Ph—C̄—C—C̄—H   →(THF)→   Ph—C̄—C—CH₂
     │ │ │   │ │ │   │ │ │
     H H Me   H H Me   H H Me

      (186·̄)   (186⁼)   (187⁻)

  Dimer │ B   CH₂=CH₂ │

                                                                 Me
                      2K⁺   K⁺   Ph │
     Me   Me   C̄H₂—CH₂—C—C—CH₂
Ph—C̄—C—C—C—C̄—Ph   │ │ │
    │ H H │ H H │ │   H H Me
    H   Me Me   H
                                                        (188⁻)
     (189⁼)

                                                          THF │

                                                              Ph   Me
                                                                │   │
                                                    Me—CH₂—C—C—CH₂
                                                              │ │ │
                                                              H H Me

                                                              (188)
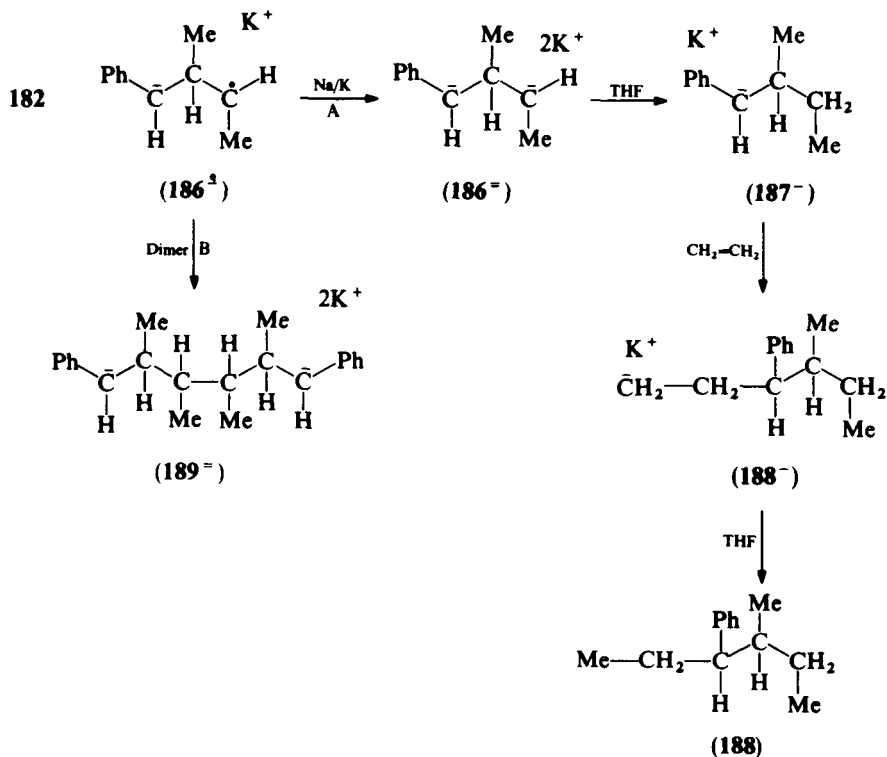
SCHEME 20. Reactions of the trimethylene radical anion 186·̄ after 60 h at 20°C, followed by workup with water

Pathway A: 186·̄ is further reduced to the dianion 186⁼ which is immediately protonated by THF to give the benzylic anion 187⁻. The ethylene formed on decomposition of THF reacts with some 187⁻ to give 188⁻ which is also protonated by

THF to give **188** in 47% yield. On workup with water protonated **187**⁻ is formed and isolated in 16% yield.

Pathway B: more importantly, the dimer **189**⁼ of the radical anion **186**˙⁻ is also formed. Protonation with water leads to the corresponding hydrocarbon **189** in 37% yield.

In summary, the results shown leave no doubt that the reversible stereoisomerizations of the cyclopropanes **178a**, **178c** and **184** in the presence of alkali metals in THF occur via trimethylene radical anions like **180**˙⁻ and **186**˙⁻. These ET-catalyzed reactions do not occur in a thermal or base-catalyzed process or via 1,3-dianion intermediates and they differ greatly from the *irreversible* electron transfer reactions with sodium in NH₃, as observed with (+)-(R)-**49**[153b] and with the *cis,trans*-isomeric cyclopropanes **145**[156] because of the very fast protonation steps in NH₃. Undoubtedly, however, in the later cases, as strongly suggested by the regioselectivity of the bond cleavages (*vide supra*) trimethylene radical anions are also intermediates. Spectroscopic evidence for a trimethylene radical anion is not available to date.

Other reversible ET-catalyzed stereoisomerizations of cyclopropanes have been observed with *cis*-1-methyl-2-phenyl-, *r*-1-phenyl-1-methyl-*c*-2-methyl- and optically active 1-methyl-2,2-diphenylcyclopropane (**190**, **191** and (+)-(R)-**49**, respectively)[168a]. Experimental evidence for the existence of intermediate cyclopropane radical anions like *cis*- or *trans*-**178**˙⁻ (Scheme 18) has not been found in the course of these investigations.

Ph ∧ Me	Ph ∧ Me	Ph ∧ Me
H H	Me H	Ph H
(190)	**(191)**	**((+)-(R)-49)**
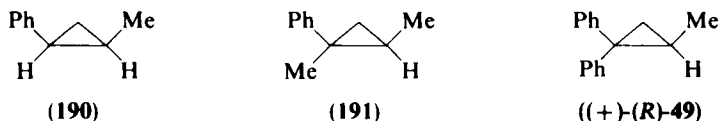
A simple MNDO calculation of the phenyltrimethylene radical anion **192**˙⁻[174] is in good agreement with experimental results reported by Staley and Rocchio[156]: not only C(1) which bears the phenyl group, but also C(3) has an appreciable amount of

(192˙⁻)   **(trans-145)**
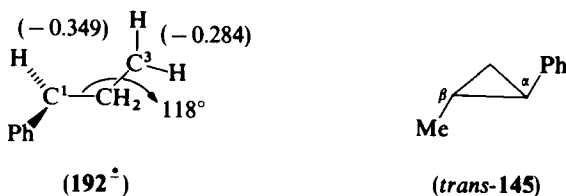
undergoing cleavage. MNDO and AM1 calculations on the ET-catalyzed stereoisomerization of *cis*-**178a** and *trans*-**178a** are consistent with the experimental findings, as well as with the mechanistic discussion given above for this system (E. Hänsele, T. Clark and P. v. R. Schleyer, private communication, 1988).

c. Mechanism of formation of isomeric acyclic olefins

In Section III.C.2.b. above clear evidence has been presented that the trimethylene radical anions **180**˙⁻ are intermediates in the stereoisomerization of the cyclopropanes **178** under ET catalysis (see also Scheme 18). This is also true for other cyclopropanes.

The formation of the *ring-opened* propene (**179**) and propane (**181**) also seems straightforward from Scheme 18, pathway A: the trimethylene radical anion **180**˙⁻ is further reduced to the dianion **180**⁼ which, as a function of time (Table 23), loses β-hydride H⁻ (if the β-carbon atom bears hydrogen atoms); protonation of the reaction mixture gives propene (**179**) and propane (**181**). Thus, the structural isomer propene (**179**) *does not result from an ET-catalyzed rearrangement reaction* (pathway B in Scheme 18)!

The literature offers an alternative pathway for the formation of propenes from cyclopropanes in the presence of electron sources as mentioned earlier: rearrangement of the trimethylene radical anion **175a⁻** to give **176a⁻** is the important step, see also pathway B, Scheme 17[163].

A similar rearrangement has been proposed to occur in the trimethylene radical anion **193⁻** to give **194⁻**[175].

(175a⁻·)   (176a⁻·)

(193⁻·)   (194⁻·)
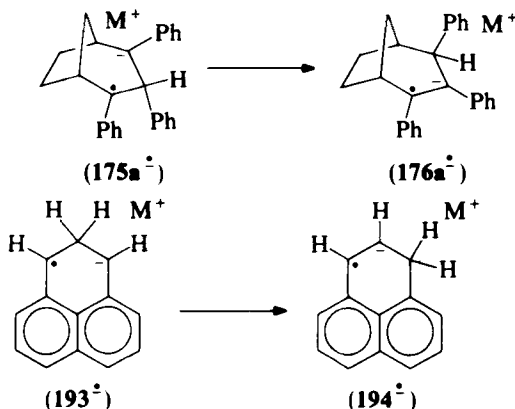
Although the radical anion pathway requiring the rearrangement of **175a⁻** to give **176a⁻** is rather unlikely on the basis of the experimental results presented earlier in Section III.C.2.a, this alternative ET-catalyzed route to yield propenes from cyclopropanes via *migration of an atom or a group* has been checked with the cyclopropanes **178**[168b].

When the bis-deuterated cyclopropane *trans*-**178b**-d₂ was reacted with Na/K in THF at 0°C one observed on protonation after 1 h besides 16% *trans*-**178b**-d₂, 6% propene **179**-d₁ and 78% propane **181b**-d₂.

(*trans*-**178b**-d₂)   (**179**-d₁)   (**181b**-d₂)

(**179b**-d₂)   (**182**-d₁⁻)   (**180b**-d₂⁻)
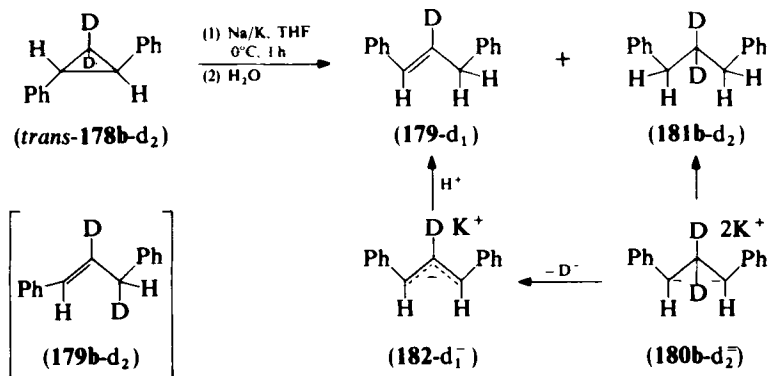
It is thus unambiguously clear that the propene **179**-d₁ is formed exclusively from the dianion **180b**-d₂⁻ by loss of D⁻ to give the allyl anion **182**-d₁⁻, followed by protonation. This route corresponds to pathway A in Scheme 18. Pathway B in Scheme 18, the proposed alternative[163, 175], which in the case of *trans*-**178b**-d₂ should lead to the bis-deuterated propene **179b**-d₂, is not a viable process. This is in agreement with the general observation that the *intra*molecular 1,2-migration of hydrogen (deuterium) is not a facile reaction in either radicals[176] or carbanions[177].

Finally, it should be noted that geometrical and structural isomerizations of substituted cyclopropanes by means of ET-catalyzed reactions, via intermediate trimethylene radical anions, is only one pathway to perform these reactions. Other possibilites are the thermal reaction via trimethylenes[178], the light induced reaction [179], the photosensitized reaction via trimethylene radical cations[180], the Pd/C-catalyzed reaction[181], and the base-catalyzed reaction[167, 173].

IV. ANIONS

A. Introduction

Cyclopropyl anions have a high synthetic potential, see Section IV.D. Their direct preparation from cyclopropyl halides with metals, by halogen–metal exchange as well as by alkali metal naphthalenide has been discussed in Section III.

In the following sections we concentrate on structural aspects of the cyclopropyl anion and of substituted cyclopropyl anions. Since the structure of these anions and the acidity of the corresponding cyclopropanes correlate intimately with each other, it is inevitable to combine these two subjects in a discussion of cyclopropyl anions and their structure.

B. Formation from Cyclopropane and its Stereochemistry

Theoretical calculations[3, 183, 185a, c] and a variety of experimental results indicate rather early that the hybridization of the C–H bonds in cyclopropane is not sp^3 but rather $sp^{2.28}$ which due to the greater s character, should increase their acidity[182]. However, it wasn't until 1969[184] that the (kinetic) acidity of cyclopropane was finally measured by using cesium cyclohexylamide in N-tritiated cyclohexylamine and it was shown that the exchange rate of cyclopropane is $7.0 \pm 0.9 \times 10^4$ faster than that of cyclohexane (Table 24).

TABLE 24. Kinetic acidities of cyclopropane and cyclo-hexane toward cesium cyclohexylamide at $50°C$[184]

	Rel. rate	$J(^{13}C–H)$
Cyclopropane	$7.0 \pm 0.9 \times 10^4$	161
Cyclohexane	1.00	123

The linear correlation[184] between the log of the relative rates and the coupling constants $J(^{13}C–H)$, which is 161 Hz in the case of cyclopropane and 123 Hz in the case of cyclohexane, supports the thesis that the dominant factor in cyclopropane acidity is the amount of s character in the exocyclic C–H bonds.

Accurate anion proton affinities are now available from theoretical calculations[185a] and this enables one to estimate the proton affinity as well as the relative energy of hypothetical carbanion configurations, as, for example, the cyclopropyl anion in the pyramidal C_s and the planar C_{2v} configuration.

	MP2/4-31 + G//4-31 + G (Hartrees)	Rel. energy (kcal mol^{-1})
Cyclopropyl anion, C_s	− 116.48368	0.0
Cyclopropyl anion, C_{2v}	− 116.45966	15.1

The 15.1 kcal mol^{-1} higher stability of the pyramidal C_s configuration is in agreement with the experimental results given in detail in Sections III.B.1 and III.B.2. on the

configuration and the configurational stability of various cyclopropyl metal compounds.

An X-ray crystal structure determination of di-μ_3-bromo-di-μ_3-cyclopropyl-tetralithio-tetrabis (diethyl ether) $[2LiBr \cdot 2c\text{-}C_3H_5Li \cdot 4(C_2H_5)_2O]$ published by Schmidbaur and coworkers[185b] shows nicely the pyramidal configuration of the anionic carbon atom, in agreement with the calculations. The cyclopropyl anion in the gas phase has been studied by Sguires and coworkers[185c].
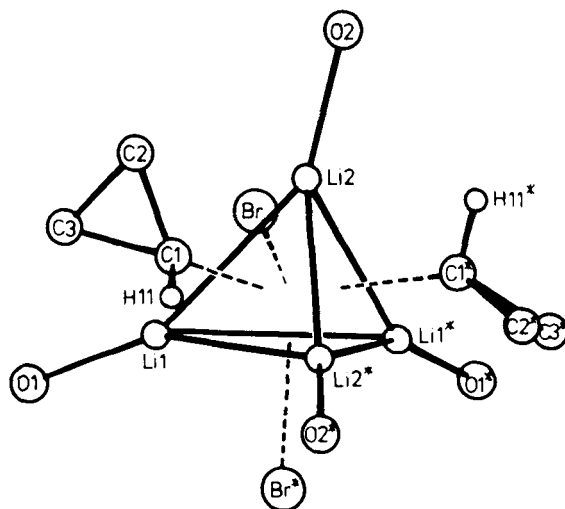
FIGURE 4.   Solid state structure of $[2LiBr \cdot 2c\text{-}C_3H_5Li \cdot 4(C_2H_5)_2O]$[185b].

Reproduced with permission from Schmidbaur et al., Chem. Ber., 116, 1938 (1983).

1. Effect of substituent

a. α-Carbonyl and α-carboalkoxyl
   The chemistry of cyclopropanes substituted with C(O)R groups goes back to the turn of the century. Kohler and his group studied the reaction of the cyclopropane 195 with sodium methoxide which eventually leads[186a] to the formation of 197.

(195)   (196)   (197)
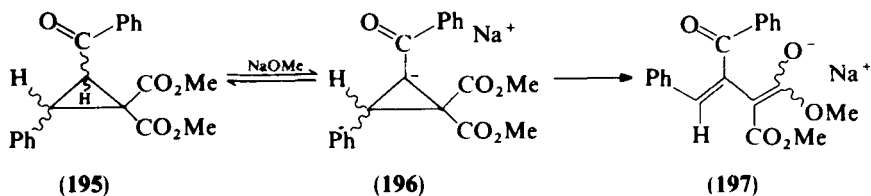
It was Smith and Showell[187] who inferred that 195 is deprotonated to give the cyclopropyl anion 196 which isomerizes to the allyl anion 197 (the cyclopropyl ⇌ allyl anion rearrangement is treated in detail in Section IV.C.).

(198)
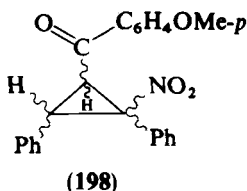
Similar behaviour has been observed by Kohler and Allen[186b] and by Smith and Showell[187] on treating the tertiary nitrocyclopropyl ketone **198** with a base. Base catalyzed stereoisomerizations of ketones like **198** had also been observed by Kohler and Smith[186c] and by Smith and Showell[187] and were in agreement with the deprotonation of such cyclopropanes to the corresponding cyclopropyl anions. It thus did not seem as if the deprotonation of C(O)R-substituted cyclopropanes would cause any problems.

This conclusion had to be revised when Piehl and Brown[188] showed that although they were able to repeat Haller's work on the alkylation of phenylcyclopropyl ketone (**199**) by means of sodium amide and methyl iodide to give **200**[189] (a reaction which they thought was wrong), unexpected reactions occurred in the case of ethyl cyclopropanecarboxylate (**201**). With sodium amide the amide (**202**), and with triphenylmethyl sodium the ketone (**203**) is formed. The latter reaction is normally typical of esters having no α-hydrogen atom!

Piehl and Brown[188] concluded 'that α-hydrogens in *monofunctional* derivatives of cyclopropane are relatively unreactive in accordance with I-strain theory[7] because deprotonation of α to an electron-accepting group should lead to additional strain in exocyclic double-bonded forms', as in the case of the ester enolate of **201**.

The comparatively low acidity of monofunctional C(O)R-substituted cyclopropanes has been repeatedly confirmed in the literature as shown by the following examples.
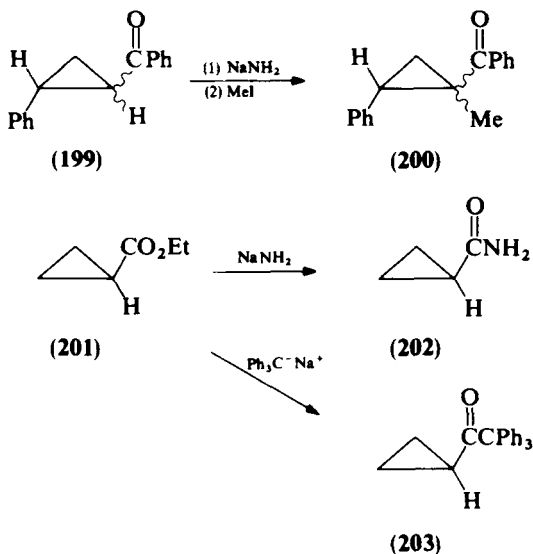
For *cyclopropanecarboxaldehydes* de Boer and coworkers[190, 191] have investigated the base-catalyzed reaction of the parent compound **204** and compared its acidity with that of the cyclobutanecarboxaldehyde **207**.

(204)   (205)   (206)

(207)   (208)
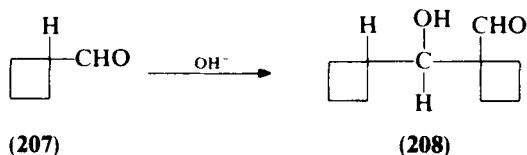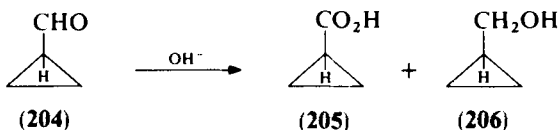
In the case of the cyclopropanecarboxaldehyde (204) only the Cannizzaro products 205 and 206 were formed. Thus, 204 behaves as if it had no α-hydrogen atom—like the ester 201. In contrast, in the case of the cyclobutanecarboxaldehyde (207), as expected, the normal aldol condensation is much faster, leading to 208 (under the reaction conditions 208 was not actually isolated; instead the Cannizzaro products of this tertiary aldehyde were obtained in 90% yield).

More investigations have been performed with *cyclopropyl ketones*. The isomerization of the *cis*-cyclopropyl ketone 209 to its *trans* isomer 210 was only achieved by means of the rather basic dimsyl sodium in dimethyl sulfoxide at 60°C[192a]. Similarly, esters of cyclopropane carboxylic acids have been isomerized[192b].

(209)   (210)
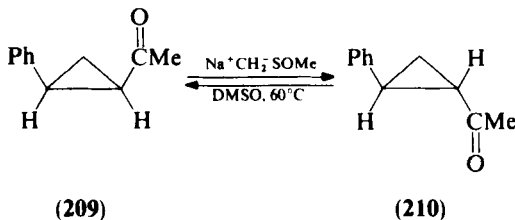
The relative acidities of the α-hydrogens in 209 and 210 have been determined by Itoh and coworkers[193]. In the *cis* compound 209 the hydrogen is exchanged faster than in the *trans* species 210 by a factor of 100. From these and other results it is concluded that the cyclopropyl anion derived from 209 is more stable than that which results on deprotonation of 210. This has been confirmed by CNDO/2 calculations, however, there is no obvious explanation available. It is also noteworthy that the H/D-exchange in 209 is faster than the base-catalyzed isomerization to give 210.

Another successful alkylation of a cyclopropyl ketone was reported by Handel and coworkers[194a] when they reacted cyclopropyl phenyl ketone (211) with excess potassium hydride (5 M equivalents) in the presence of [2.2.2]cryptand: methylation with methyl iodide gave 212 in 90% yield. The conditions are crucial: without the cryptand, 211 is reduced to the corresponding secondary alcohol in 82% yield.

(211)   (212)
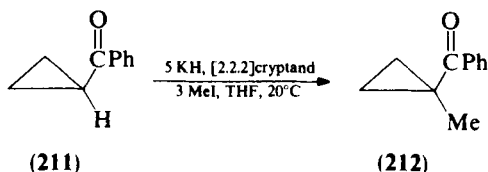
As far as *salts of cyclopropanecarboxylic acids* are concerned 'exceedingly low rates' for the deuterium oxide catalyzed H/D exchange have been observed by Bottini and Davidson[195] in the case of the sodium salts **213, 214** and **215**.
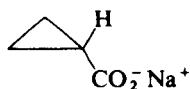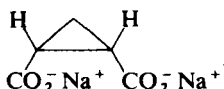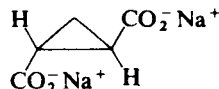
(213)   (214)   (215)

After 100 h at $152 \pm 2°C$ (> 0.2 N NaOD), exchange of the α-hydrogens was to the extent of $0 \pm 16\%$ (**213**), $3 \pm 4\%$ (**214**) and $4 \pm 4\%$ (**215**).

In agreement with these results Krapcho and Jahngen's[196] attempts to utilize cyclopropanecarboxylic acid (**216**) in the reactions of α-anions of cycloalkanecarboxylic acid salts with cycloalkanones have been unsuccessful.
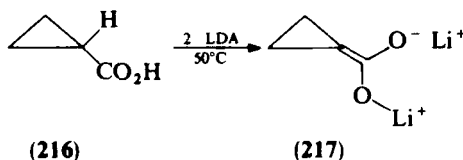
(216)   (217)

No condensation products have been isolated and upon quenching with D_2O the starting material **216** was recovered in 25 % yield showing no incorporation of deuterium. The remainder of the isolated product 'appears to be dimeric'. Pinnick and coworkers[197] confirmed these results.

A different result was obtained later by Warner and Le[198] who showed that when the reactions were performed at room temperature it was possible to alkylate and to silylate **217**. It was also found that **217** remained unchanged after 22 h at 80°C. Thus only the reversible aldol formation appeared to be unfavorable in this instance. Jahngen[199]— coauthor with Krapcho[196]—recently confirmed the results of Warner and Le. In addition he found that the earlier formulated 'dimeric' product[196] was the condensation product 1-(cyclopropylcarbonyl)cyclopropanecarboxylic acid.

The problems with α-deprotonations of salts of carboxylic acids are also nicely exemplified by a study of Ford and Newcomb[200] with the isomeric acids **218** and **222**. Reaction of the *cis, trans* acid **218** with LDA in THF at 0°C for 30 min resulted in the desired allyl anion **220** which was protonated to give the two isomeric α-benzylcinnamates (**221**).

In contrast the *trans, trans* acid (**222**) was deprotonated at the *benzylic* position to give the allyl anion (**224**), which upon protonation gave as expected, **225**. It has not been possible to prove the existence of the cyclopropyl anions **219** and **223** (only in the case of the methyl ester enolates the cyclopropyl anion corresponding to **219** has been shown by deuteration to exist at $-78°C$). Thus, deprotonation of cyclopropyl carbonyl compounds may be strongly dependent on the structural details of the cyclopropane, as previously demonstrated by the relative acidities of **209** and **210**.

Of interest, with regard to synthetic applications are *cyclopropane ester enolates* and their reactions.

Unsuccessful attempts to α-methylate the carboethoxy cyclopropane **226** have been reported by Fitzsimmons and Fraser-Reid[201].

(218)

LDA, THF
0°C, 30 min

(219)

(220)

H⁺

(221)

(222)

LDA, THF
25°C, 30 min

(223)

(224)

H⁺

(225)

(226)
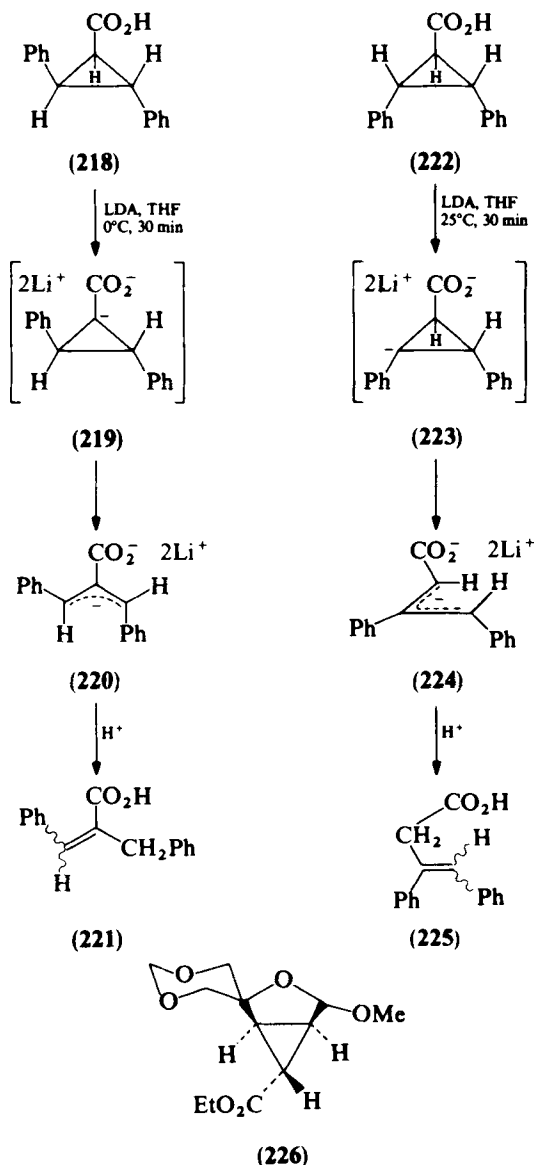
The low tendency of cyclopropyl esters to form the ester enolate is also documented by the following examples: Boche and Martens[202] have reported that methyl cis-bicyclo[6.1.0]nona-2,4,6-triene-anti-9-carboxylate (227) loses a proton at C(1) when treated with LDA to give, probably via the cyclopropyl anion 228⁻, the allyl anion 229⁻. Russell and coworkers[203] have shown that ethyl 2-methyl-2-nitrocyclopropanecarboxylate (230) gives the 2-methylenecyclopropanecarboxylate (231) when treated with sodium hydride. However, 231 may also be the result of isomerization of 2-methylcyclopropenecarboxylate, which was formed by elimination of nitrite ion from the α-anion of 230.

(227)   (228⁻)   (229⁻)

(230)   (231)
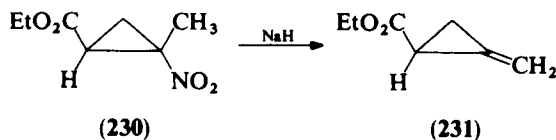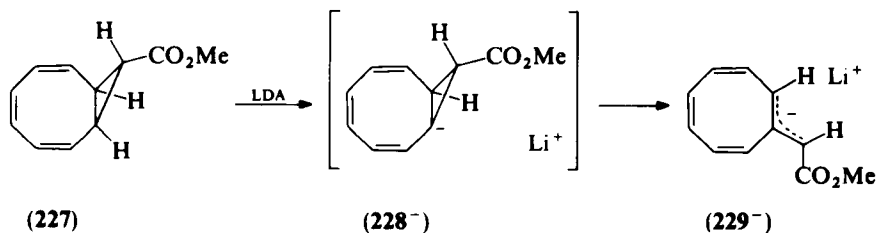
A successful trapping reaction of a cyclopropyl ester enolate with trimethylsilyl chloride (TMSC) was first performed by Ainsworth and coworkers[204]. In the reaction of **232** with lithium diisopropyl amide at − 78°C, followed by addition of TMSC, the ketene acetal **233** was formed in 10% yield as well as the silylated cyclopropane **234** (40%). Ketene acetals other than **233** are formed in yields > 90%.

(232)   (233)   (234)
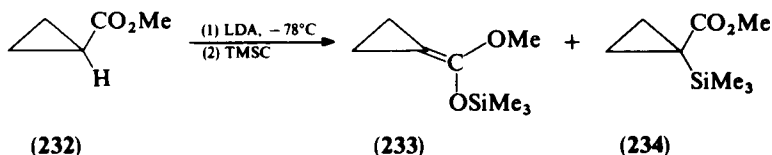
Pinnick and coworkers[197] reported similar attempts to α-functionalize ethyl cyclopropanecarboxylate (**235**) by treatment with base. Depending on the reaction conditions they were able to isolate the ketene acetal (**236**) and the α-silylated ester (**237**) as analogously reported by Ainsworth and coworkers[204].

(235)   (236)

(237)   (238)
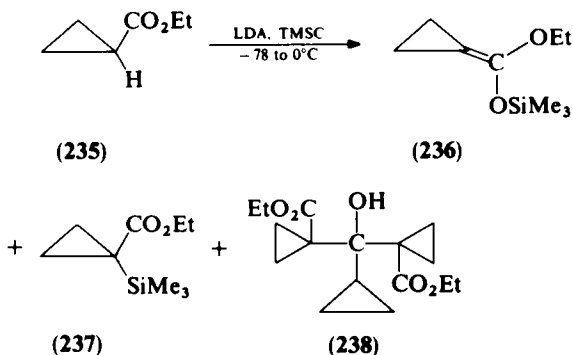
In addition, **238** was found which is undoubtedly the result of a two-step Claisen-aldol sequence. The formation of **238** has been confirmed by Seebach and coworkers[205a]. This clearly indicates that the anion of ethyl cyclopropanecarboxylate is formed by the action of LDA on **235**, but that the anion is very reactive in agreement with the low acidity of **235**. When trityllithium reacted with **235** only **238** was obtained after quenching with AcOD. Potassium hydride together with several trapping reagents gave neither **238** nor the expected trapping products.

Because of the difficulties encountered in the case of the esters **232** and **235** Wemple[206] investigated similar reactions with *thiol esters* of cyclopropanecarboxylic acids. As shown, deprotonation of **239** with LDA followed by treatment with benzaldehyde leads to **240** in 76% yield.
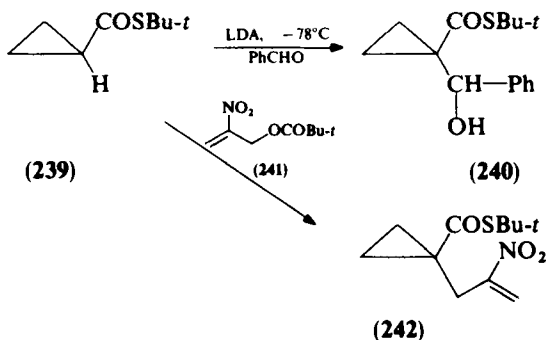
Knochel and Seebach[207] similarly converted **239** to **242** by condensation with **241**. The successful reaction of the thiol ester enolate anion of **239** with electrophiles seems to result from the higher kinetic acidity of the thiol ester as compared to the acidity of the normal ester[208].

Thorough investigations on the deprotonation and diastereoselective alkylation of 2-siloxy[209a] and other substituted methyl cyclopropanecarboxylates, **243** and **244**, respectively, have recently been published by Reissig[209b].
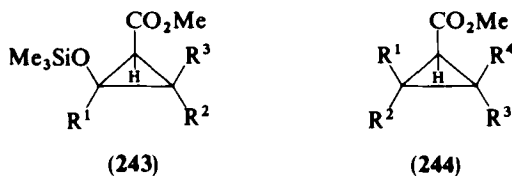
Most importantly with regard to the topic of this chapter, all cyclopropanecarboxylates may be deprotonated with LDA at $-78°C$ (normally after 2 h). The question is whether it is possible to trap these energy-rich enolates with, for example, alkylating reagents, before self-condensation occurs with not yet deprotonated ester. Whether one is successful or not is a function of the substituents R^1–R^3 in **243** and R^1–R^4 in **244** as indicated early by the results of Kohler[186] and Smith and their coworkers[187] with, for example, **195** and **198**, and by the following data published by Koyanagi and coworkers[210]. Although additional substituents may increase the acidity of the hydrogen atom α to the carboxylate group, at the same time steric hindrance by these substituents can cause self-condensation to be unfavorable. Steric hindrance of self-condensation should also be responsible for the high-yield transformations of the esters **244a** and **b** with LDA or *t*-butyllithium followed by reaction with electrophiles E like alkyl halides, aldehydes or acid chlorides into **244-E'a** and **b**[205b–d]
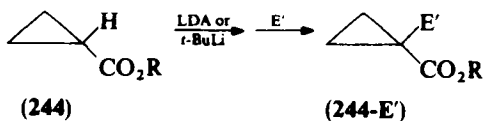
a: R = *t*-butyl
b: R = 2,6-di-*t*-butyl-4-methylphenyl
For further synthetic preparations see Section IV.D.

Koyanag and coworkers[210] have determined the relative acidities of the *cis/trans* isomeric phenylthiocyclopropanecarboxylates **245** and **246**, respectively, as compared to phenylcyclopropane carboxylate (**247**). H/D exchange experiments have shown that the ester **245** is 18.4 and **246** is 8.0 times more acidic than **247**. Thus, a *cis*-phenylthio group stabilizes a negative charge much better than, for example, a phenyl group.

(**245**)   (**246**)   (**247**)
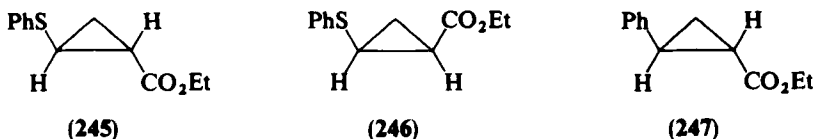
One could envision a stabilization of the gegenion by the sulfur atom as the underlying reason. Again, no *cis* ⇌ *trans* isomerization takes place during the H/D exchange reaction (ethanol, pyridine, 70° C). Unfortunately, no quantitative data are available as to the acidity of cyclopropanes like **195** and **198** which are 'heavily loaded' with acceptor substituents.

Base-catalyzed stereoisomerization of the cyclopropyl carboxylate **248** to give **249** has been observed by Martin and coworkers[211].

(**248**)   (**249**)
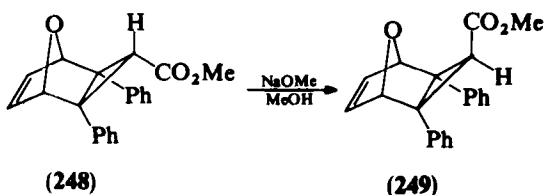
De Boer[190, 191] and Rappe[212] and their coworkers were the first to report on quantitative measurements of the kinetic acidity of cyclopropyl C(O)R-substituted compounds in comparison to their open ring analogs, the corresponding isopropyl species. Bordwell and

TABLE 25. Relative rate constants for the exchange reaction of RD in MeONa/MeOH at 53.2°C[190, 191]

Isopropyl	$k_{D,rel}$	Cyclopropyl	$k_{D,rel}$	$\dfrac{k_{iso}}{k_{cyclo}}$
	1330 ± 100		1	1330 ± 100
	1550 ± 100		1.8 ± 0.2	850 ± 100
	4000 ± 400		24 ± 2	170 ± 20
	4.4 ± 0.3		0.42 ± 0.65	10 ± 2
	24.7		28.2	

* Equilibrium acidities (pK_a) in DMSO.

coworkers have measured equilibrium acidities in dimethyl sulfoxide[213]. Their data are presented in Table 25.

The data from Table 25 clearly emphasize the lower acidity of *cyclopropyl ketones* as compared to *isopropyl ketones*, the factor ranging from 1330 to 10 in the case of the *t*-butyl species. These data are in contrast to earlier findings of Shechter and coworkers who reported that an α-hydrogen atom in benzoylcyclopropane exchanges 14 times faster than in isobutyrophenone, but they agree with later work of this group[214]. Breslow[215] compared the relative rates of cyclopropyl and cyclopropenyl ketones with regard to antiaromaticity of the cyclopropenyl anion. This is expected for a largely *mesomeric* substituent leading to a planar enolate anion which adds additional strain, as pointed out in earlier publications[188,214c,216a].

The instability and high reactivity of cyclopropyl enolates encountered throughout in this chapter are also nicely documented by electrochemical reductions of bis(α-bromocyclopropyl)ketones[217]. Reduction of cyclopropane **250** requires a much more negative potential than, for example, reduction of the ring-opened reference substance **251**.

(250)   (251)

$E_{1/2}$ V(vs. S(E)) -0.85 -0.23
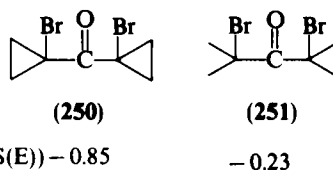
That it is indeed the planarity of cyclopropyl (ester) enolates that causes extra strain and thus instability and high reactivity of such anions, as well as low acidity of the corresponding C(O)-substituted cyclopropanes, has been firmly established[191c,216a]. It was shown that treatment of $(-)$-(R)-1-benzoyl-2,2-diphenylcyclopropane $((-)$-(R)-**252**) with 0.1 M sodium methoxide in methanol-O-D gave $k_{rac}/k_{ex} = 1$; this means that the anion is planar.

$((-)$-(R)-**252**)
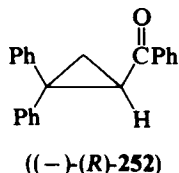
b. α-Cyano

Pioneering work with cyclopropyl nitriles, their acidities, stereochemistry and the reactions of the corresponding carbanions has been published by Walborsky and coworkers[216b-f].

Optically active $(-)$-(R)-**253** is deprotonated by LDA in ether at $-65°$C completely in less than 10 min, as shown by methylation, to give the racemic product **254**.

$((-)$-(R)-**253**)   racemic (**254**)
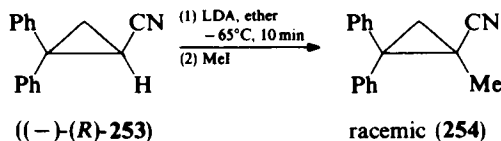
When H/D exchange was performed with 1.0 M sodium methoxide in methanol-O-D the ratio of racemization (k_{rac}) to exchange (k_{ex}) was 1.2×10^{-4} corresponding to 99.9 % retention of configuration. This is evidence for a *pyramidal* anion which has a considerable barrier to inversion.

Comparison of cyclopropyl nitriles with isopropyl nitriles, and of the nitriles with the corresponding ketones is accessible from work of Walborsky[216], and de Boer[190,191] and their coworkers (Table 26).

TABLE 26. Relative rate constants k_D for H/D exchange reactions

Isopropyl	$k_{D, rel}$	Cyclopropyl	$k_{D, rel}$	$\dfrac{k_{iso}}{k_{cyclo}}$
(255)	1330 ± 100^a	(256)	1^a	1330 ± 100
(257)	0.81 ± 0.06^a	(258)	11.8 ± 0.7^a	0.067 ± 0.006
(259)	$1^{b,c}$	$((-)-(R)-253)$	$31^{b,c}$	0.033

^a MeONa/MeOH at 53.2°C[191].
^b MeONa/MeOD at 50.0°C[216].
^c The relative rates of (−)-(R)-253 and 259 are not related to the data of 255–258.

A comparison of compounds (−)-(R)-253 and 255–259 clearly demonstrates that the cyclopropyl nitriles (−)-(R)-253 and 258 are more acidic than their open-ring analogs 259 and 257, respectively. This situation is reversed to what is observed in the ketone series 255 and 256. Thus, deprotonation α to a cyano group does not lead to a compound which is similarly strained as cyclopropyl enolates, or (in agreement with the ratio $k_{rac}/k_{ex} = 1.2 \times 10^{-4}$ observed with (−)-(R)-253), a cyano group stabilizes a negative charge at a *pyramidal* C-atom much better than a C(O)R-group. Thus, in the case of the C(O)R group mesomeric stabilization is more important than in the case of the cyano group which stabilizes largely via its dipole (field) effect as well. A recent X-ray structure determination of α-cyano-benzyllithium is in agreement with this conclusion[218b].

The literature offers more examples of facile deprotonations of cyclopropyl nitriles. Boche and coworkers[202,218a,219] and Ford and Newcomb[200b,c] observed the deprotonation of the nitriles 260 and 261 as well as their alkylation; 262 has been deprotonated by Wittig and coworkers[90a]. Similarly, 263 is easily deprotonated to give the α-cyano anion— in contrast to the corresponding ester 227 which is deprotonated exclusively at C(1) instead[202]! Compound 264 also gives the corresponding α-cyano cyclopropyl anion[164].

(260)   (261)   (262)   (263)   (264)
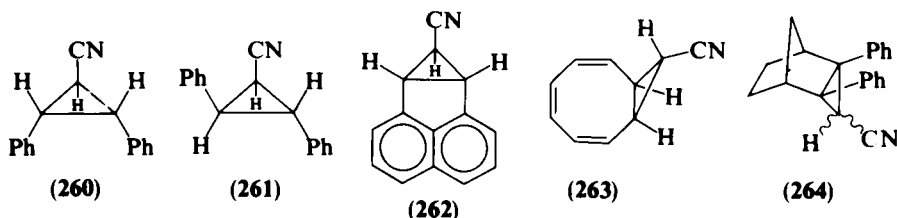
Pinnick and coworkers[197] reported that addition of cyclopropanecarbonitrile to LDA in THF at −78°C (LDA and similar bases have also been used in the reactions of 260–264)

followed by allyl bromide gave after warming to room temperature the expected allyl nitrile. Deprotonation with potassium hydride and reaction with allyl bromide, benzaldehyde and methyl benzoate, respectively, failed however to give any of the expected trapping products. This, of course, may be due to the potassium hydride reacting with the nitrile group itself.

c. α-Isocyano

It has been demonstrated by Walborsky and Periasamy[220,221] that, in contrast to the 1-cyano-2,2-diphenylcyclopropyl anion (see above), the 1-isocyano-2,2-diphenylcyclopropyl anion in ether solvents is configurationally stable at − 72 °C: deprotonation of (+)-(S)-265

((+)-(S)-265)   ((+)-(S)-266)
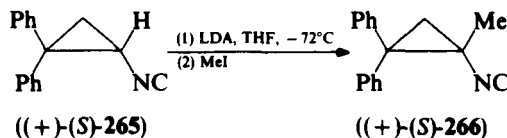
with LDA in THF at − 72 °C, followed by reaction with methyl iodide led to (+)-(S)-266 with almost complete retention of configuration (99 % o.p.).

The barrier to the inversion imposed by the isocyano group permitted the evaluation of the effect of gegenion, solvent and temperature on this cyclopropyl anion. As is evident from Table 27 only at − 5 °C is the loss of configuration very rapid. This would be consistent with the view that there is a great deal of ionic character associated with the lithium–carbon bond[221].

TABLE 27. Effect of temperature on configurational stability

Temp. (°C)	((+)-(S)-265) Yield (%)	((+)-(S)-266) Optical purity (%)
− 72 ± 2	96	98
− 52 ± 1	75	93
− 25 ± 1	92	58
− 5 ± 1	80	0.3

Moreover, using the cation exchange technique[222] the lithium cation was exchanged for sodium and potassium cations and the stereochemical results were the same as for lithium: essentially complete retention of configuration at − 72 °C. Finally, at − 72 °C changing the solvent to a mixture of THF and dimethoxyethane or adding cation complexing reagents such as TMEDA, triglyme or HMPA also resulted in complete retention of configuration. Even the addition of crown ethers such as 12-crown-4, 15-crown-5, 18-crown-6 or dicyclohexyl-18-crown-6, did not affect the configurational stability of the 1-lithio-1-isocyano-2,2-diphenylcyclopropane.

Hence, in the case of the electronegative isocyano group which possesses a π-system for delocalization (as the carbonyl and the nitrile group) but additionally a non-bonding pair of electrons on nitrogen, even a 'free' or 'naked'[223] anion is capable of maintaining its configuration.

d. α-Nitro.

Nitrocyclopropane is about 10 orders of magnitude less acidic than its open chain analog 2-nitropropane[191c, 213, 214c] as determined in DMSO (equilibrium acidities)[213].

	Me
	$\searrow$
	CH—NO$_2$
	$\nearrow$
	Me

pk(DMSO)   16.89 ±0.02   ~ 27
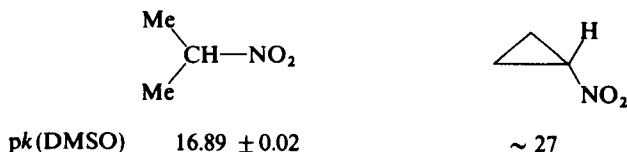
Bordwell and coworkers[213] note that nitrocyclopropane under the conditions of exchange rapidly decomposes. Thus, the nitrocyclopropyl anion is not easily formed and is therefore very reactive, similar, for example, to cyclopropyl ethyl ester enolates (Section IV.B.1.a).

The pK measurements are nicely supported by efforts of Seebach and coworkers to get hold of the 'elusive' nitrocyclopropyl anion[205a]. When nitrocyclopropane was treated at temperatures between − 80 and − 110° C with bases such as butyllithium, LDA or potassium hexamethyldisilylamide in THF, yellow to red solutions have been obtained which were thought to contain the lithium salt of acinitrocyclopropane (267a). Workup after any amount of time, raising the temperature, or addition of any electrophile with or without oxidizing properties, always led to the isolation of mixtures of the colorless dinitro-compound 268, and of the deep-blue nitro-nitroso compound 269.

(267a)   (267b)   (268)   (269)
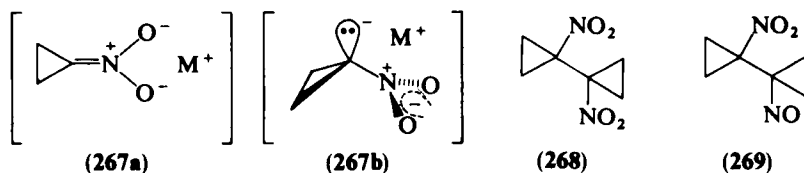
The nitronate 267 'might be expected not to have a planar structure 267a but to be the bent species 267b, stabilized more by polar than conjugative effects'[205a].

The formation of 268 and 269 is believed to occur by two possible pathways[205a]:

(1) reaction of the probably very reactive nitronate 267 with the probably very reactive products 270 resulting from 267 by addition of an electrophile E$^+$ to an oxygen atom (route A). This is followed by loss of MOE to give 269. This route is similar to the one leading to the self-condensation product 238 formed from the cyclopropane carboxylate 235 with LDA.

A   (267) +   OE $\xrightarrow{-\text{MOE}}$ (269)

(270)

B   (267) $\xrightarrow{\text{internal} \atop \text{ET}}$ (271) $\longrightarrow$ (272) $\xrightarrow{-\text{M}_2\text{O}}$ (269)

oxidation

(268)   (269)
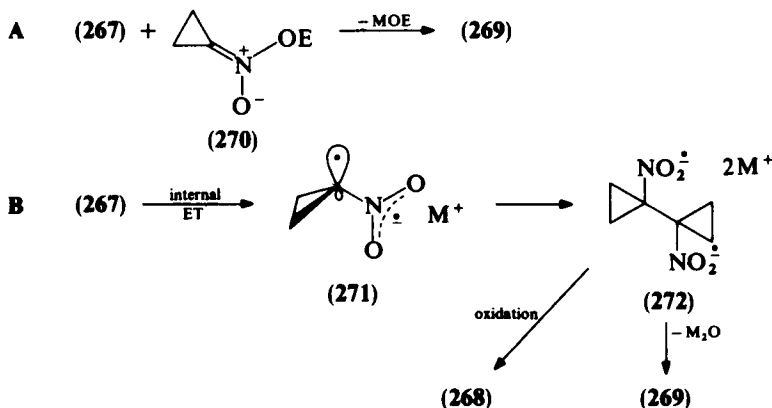
(2) An ET-mechanism would be also in accord with the results (route **B**). Internal ET within **267** should give the cyclopropyl radical–nitro radical anion species **271** which might easily dimerize to give **272**. On addition of electrophiles/oxidants the observed products **268** and **269** would be formed.

The question whether the nitrocyclopropyl anion might have a triplet structure (possibly similar to **271**) is discussed in Section IV.B.1.l.

The solid state structure of [α-nitrobenzyllithium ethanol]$_n$ has recently been determined[242b].

e. α-Sulfonyl and derivatives

As far as the situation of the sulfonyl group and derivatives of the sulfonyl group is concerned, there are conflicting results in the literature—at least at first sight. Zimmerman and Thyagarajan[224] (measurements in ether and hydrocarbon solvents) and Cram and coworkers[225] (measurements in DMSO) reported that the equilibrium acidities of isopropyl- and cyclopropyl phenyl sulfone, **273** and **274**, respectively, are roughly equal.
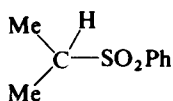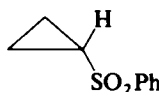
(273)   (274)

De Boer and coworkers' H/D exchange measurements[190,191] ($k_{H,rel}$ for the exchange of 30% of RH in MeOD/MeONa (0.22 M) at 53.2°C) indicate a lower acidity of the open-chain **273** than of the cyclopropane derivative **274** ($k_{273}/k_{274} = 0.029 \pm 0.001$).

Bordwell and coworkers[213], on the other hand, report the following equilibrium acidities in DMSO (Table 28).

TABLE 28. Cyclopropyl effects on equilibrium acidities in DMSO[213]

X	pK_a(MeX)	p$K_a \left(\triangle^H_X \right)$	ΔpK
S(O)(N̄Me$_2$)Ph	14.4	20.9 ± 0.3	6.5 + 0.3
SO$_2$CF$_3$	18.8	26.6	7.8
S(O)(NSO$_2$Ph)Ph	24.5	28.8 ± 0.2	4.3 ± 0.2
SO$_2$Ph	29.0	> 32	> 3.0

According to these results the sulfone and the related sulfoximine and oxosulfonium cation groups lead to higher acidities of the methyl derivatives. The corresponding cyclopropanes are less acidic. Isopropyl phenyl sulfone (**273**) has a pK value > 32 (the pK_a limit in DMSO), as does cyclopropyl phenyl sulfone (**274**)[213] (which, of course, does not exclude equal acidities). From his results, Bordwell[213] reaches the conclusion that the similarity of cyclopropyl effects on acidities in substituted cyclopropanes when the substituent is NO$_2$, C(O)R, SO$_2$CF$_3$, S(O)(N$^+$Me$_2$)Ph or S(O)(NSO$_2$Ph)Ph can be interpreted in terms of a demand for p character from cyclopropyl anions, which suggests that α-sulfonyl carbanions, as well as nitronate and enolate anions, have planar structures. The α-C atom in [α-(phenylsulfonyl)-benzyllithium-tetramethylethylenediamine]$_2$ has recently been shown by Boche and coworkers to be planar in the solid state[226a]. This result was confirmed by a study of Gais and coworkers[226b] on the structure of [CH$_2$(SO$_2$Ph)Li(TMEDA)]$_2$. As far as the structure of a cyclopropyl α-sulfonyl anion is concerned, Zimmerman and Thyagarajan[224] conclude from their data that only some of the stabilization derives from electron delocalization and that there is only an approach to

the planar geometry associated with such stabilization. Cram and coworkers[225] similarly favor a pyramidal structure in the cyclopropyl case.

It is not easy to establish the question—planar or pyramidal cyclopropyl α-sulfonyl anion—from solution studies. There seem to be, however, more arguments in favor of a pyramidal structure. Cram[225] performed NMR measurement with the lithium species **275** in DMSO/THF between 30 and 80°C which indicates definitively that this anion is very 'stable'. The NMR measurements do not, however, allow one to distinguish between an inversion of the pyramidal species **275** and a hindered rotation around the C–S bond of a planar anion.

(275)   (276)
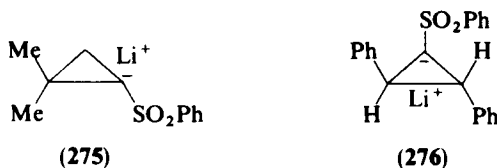
The lithium salt **276** has been prepared by Boche and coworkers[219] with MeLi in ether, n-BuLi in THF and LDA in THF; it reacts with D_2O to give the corresponding 1-D-compound. Thus, **276** is also comparatively 'stable'. The cis,cis-sulfone **277** reacts with n-BuLi in THF, followed by protonation after 5 min, to give the trans,trans-sulfone **278** (undoubtedly via the corresponding Li compounds at which stage the isomerization takes place although stereoselective protonation of a pyramidal or planar carbanion is not excluded)[215a, 219].

(277)   (278)
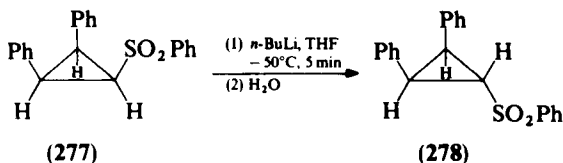
It thus seems that there is no problem to prepare cyclopropyl α-sulfonyl carbanions—like the α-cyano species which have been shown experimentally to be pyramidal[216]. This is in striking contrast to the situation of the α-NO_2 and α-C(O)R-cyclopropyl anions which are difficult to prepare, extremely reactive and, at least in the case of the enolates, planar.

As far as the previously mentioned 'conflicting' pK results are concerned it is important to note that Zimmerman's and Cram's *equilibrium* acidities have been determined in ether, hydrocarbon solvents and in DMSO, respectively. This excludes a solvent effect at least in these solvents, as being responsible for the almost equal acidities of **273** and **274**. The situation, however, may be different in the case of de Boer's *kinetic* acidity measurements in methanol resulting in a higher acidity of the cyclopropyl sulfone **274**. Bordwell's higher acidity of the *methyl* sulfone also does not exclude **274** have the same acidities: one should use the less acidic isopropyl and not the methyl sulfones in a comparison with the cyclopropyl sulfones. Very recent H/D exchange measurements (0.5 NaOD/D_2O) by Kirmse[279] support the suggestion that the pyramidal configuration of the anionic C atom of an α-sulfonyl carbanion is not necessarily unfavorable. Thus, the cyclopropyl α-hydrogen in **278a** is kinetically more acidic ($k[s^{-1}]$, 75°C) than the isopropyl hydrogen. This is also the case in the tricyclic sulfone **278b** ($k[s^{-1}]$, 35°C) in which planar configurations of the anionic C atoms are hard to imagine. The comparatively high acidity of **278b** is also remarkable.

Interesting results as far as a possible pyramidal configuration of an α-sulfonyl cyclopropyl anion is concerned are furthermore supplied by the results in the following section and in Section I.

(278a)   **(278b)**

75°C $1.2\cdot10^{-6}$ $2.6\cdot10^{-4}$ $1.1\cdot10^{-6}$ $1.5\cdot10^{-3}$
35°C $4.3\cdot10^{-6}$
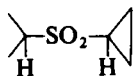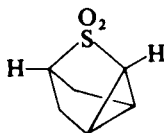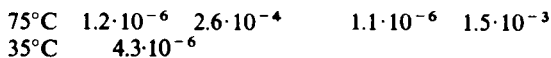
f. α-Triphenylphosphonium and α-phosphonyl

Triphenylphosphonium cyclopropylide (**279**), although not a 'carbanion', is of interest because its structure has been determined by X-ray crystallography by Schmidbaur and coworkers[227]. The most important feature is the pyramidal configuration of the ylidic C-atom: the P-atom is bent out of the plane of the cyclopropyl carbon atoms by 58°! There is no analogy to planar methylenecyclopropanes like **280** nor to other ylids all of which are planar[227a]. As Schmidbaur points out[227a] the description of the ylid 'double bond' is becoming a problem.
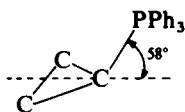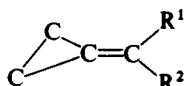
(279)   **(280)**

This is even more so if one compares the relative acidities of the hydrogen atoms in the isopropyl and cyclopropyl substituents of the phosphonium salts **281** and **282**.

(283)

(281)   **(284)**

(282)   **(285)**

(286)
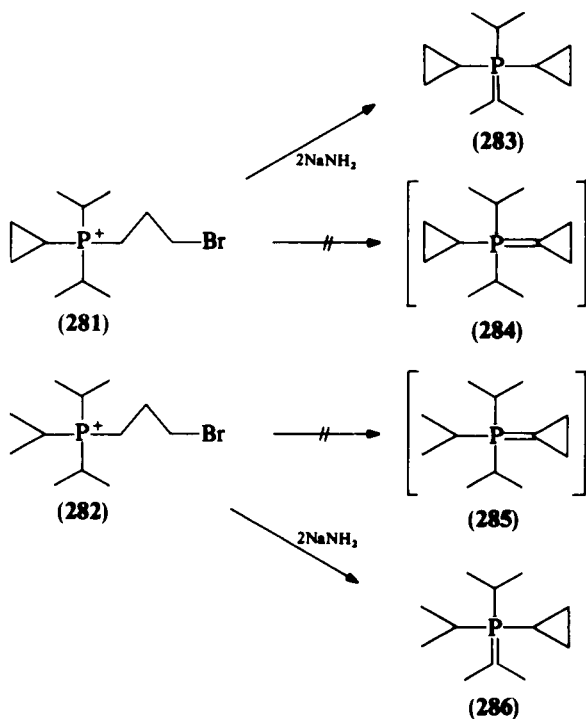
Deprotonation of **281** (**282**) does not give the cyclopropylid **284** (**285**); rather the isopropyl group is deprotonated to give **283** (**286**)[227b]. It is concluded from the low acidity of the cyclopropyl hydrogens in **281** and **282** that the carbanion-stabilizing properties of the phosphonium substituent are not only inductive in nature but that delocalization of the negative charge should also be important[227b].

The X-ray structure of the pyramidal and thermally very stable ylid **279**, however, rigorously excludes that the cyclopropyl hydrogens of the phosphonium salts **281** and **282** might be less acidic than the isopropyl hydrogens because in the latter the ylid is planar, as is the case with cyclopropyl enolates! Does R_4P^+ really lead to a 'violation of the acidity rule'[227b]?

It may rather be that in the case of third row substituents like R_4P^+ the relative acidity of cyclopropyl and isopropyl hydrogens is not as indicative of the carbanion configuration as in the case with the second row substituents C(O)R, CN and possibly NO_2. As far as cyclopropyl sulfones are concerned one would therefore predict that the corresponding α-sulfonyl cyclopropyl anions may have a pyramidal configuration. The deprotonation of cyclopropyl phosphonates, followed by reaction with aldehydes, was recently published by Hirao and coworkers[227d, e].

g. α-Sulfide, α-sulfoxide and α-diphenylsulfonium

The facile preparation of cyclopropane sulfides, e.g. **287**, by means of a phase transfer catalyzed reaction has been described by Boche and Schneider[228].
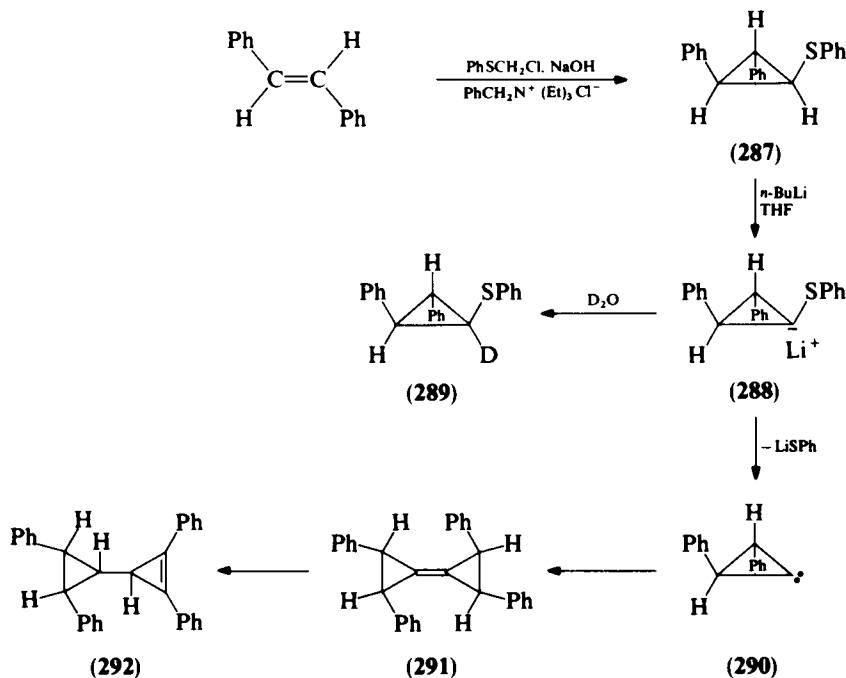
The lithium species (**288**) is easily accessible by deprotonation with *n*-butyllithium in THF, as shown by deuteration to give **289**[219]. The concomitant formation of **292** is probably due to the carbenoid nature of **288**. Dimerization of the cyclopropylidene **290** should give **291** which under basic conditions isomerizes to give **292**[219].

The configurational stability of such anions has been demonstrated by Trost and coworkers[229].

(293)   **(294)**   **(295)**
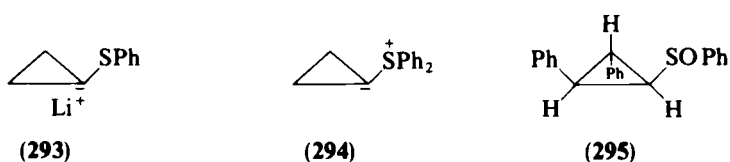
It has been found that the AA'BB' type NMR spectrum of **293** shows no temperature dependence between $-78°C$ and ambient temperature. The higher barrier to inversion compared to the α-sulfonyl anion **275** may be attributed to lone pair–lone pair repulsions that destabilize the flattening of the carbon atom, an effect similar to that found for the anion of the isocyanide **265**[221] (see above).

The inversion in the case of the diphenylsulfonium ylide **294** is also slow on the NMR time scale[229].

The anion of the cyclopropyl sulfoxide **295** has been prepared with n-butyllithium in THF at $-20°C$[219] as shown by deuteration. The stereochemistry of the anion has not been investigated so far.

h. α-Phenyl, α-vinyl and α-acetylene

1-Lithio-1-phenylcyclopropane **296** has first been prepared by Schlosser[230]; the pyramidal structure and dynamic behaviour of **297** have been investigated by Müllen and coworkers[231] who showed that it isomerizes at 4°C with a free energy of activation $\Delta G^{\ddagger}_{(4°C)} = 13.4 \pm 0.5 \text{ kcal mol}^{-1}$.

(296)   **(297)**   **(298)**
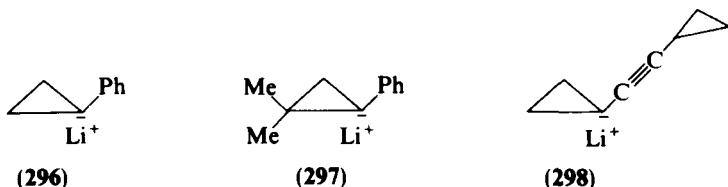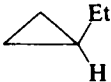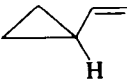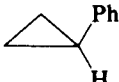
A similar situation is observed in cyclopropyl(1-lithiocyclopropyl)acetylene (**298**). The compound has a pyramidal configuration at the anionic carbon atom but isomerization occurs easily at a rate which is dependent on the composition of the benzene/THF mixture[232]. In the case of **297** the phenyl substituent should stabilize the negative charge mostly by delocalization while the acetylenic group in **298** should operate more inductively.

The reaction of vinylcyclopropanes[233] with n-butyllithium/TMEDA leads to several lithium species: **299**, for example, gives mainly **300**, but also **301**.

(299)   **(300)**   **(301)**

                  50%   20%
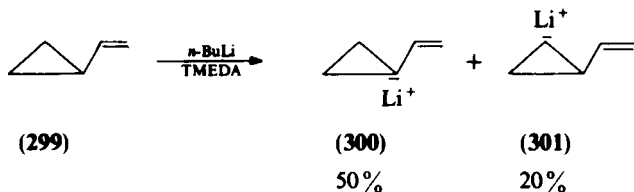
Thus, there is not much preference for the formation even of the 'allyl' species **300**, possibly because it has a pyramidal configuration at the carbanionic C-atom.

Shatenstein and coworkers performed kinetic acidity measurements[234] with **302, 299** and **303** by exchange with KND_2/ND_3 and obtained the following rate constants.

	Temp. ($^{\circ}$C)	k (s^{-1})
(302)	120	$\sim 10^{-7}$
(299)	25	$\sim 10^{-4}$
(303)	25	$\sim 10^{-4}$

The ethyl-substituted **302** does not exchange at 25°C; only at 120°C is exchange observable; however, at much slower rate than with **299** and **303** whose acidities are comparable.

i. α-Trifluoromethyl

The kinetic acidity of trifluoromethyl cyclopropane (**304**) and of the corresponding isopropyl compound **305** have been determined by de Boer and coworkers[190,191]. As expected for the inductively operating CF_3 group the cyclopropyl compound **304** exchanges with deuterium $5 \times 10^3 - 5 \times 10^4$ times faster than **305**.

(304)   **(305)**
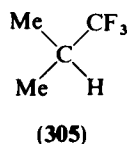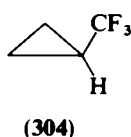
j. α-Trimethylsilyl, methyl, chloro, fluoro and methoxyl

It has been shown recently by Paquette and coworkers[235] based on the earlier work of Walborsky and coworkers[236] that under the conditions of a Haller–Bauer cleavage the optically active ketone **306** is transformed into the optically active trimethylsilyl species **307** with complete retention of configuration.

$$\xrightarrow[\text{C}_6\text{H}_6]{\text{NaNH}_2}$$

$((+)-(R)$-**306**) $((-)-(R)$-**307**)
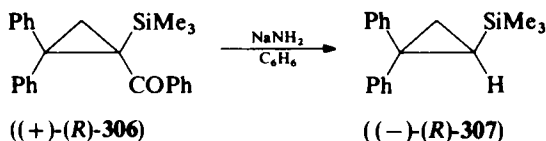
Thus, under the reaction conditions the intermediate α-trimethylsilyl anion is configurationally stable. One should also mention that the Haller–Bauer cleavage proceeds with complete retention of configuration when Me^{236}, H^{237} and possibly Cl^{236}, F^{236} and OMe^{236} replace the $SiMe_3$ of **306**.

k. β-Alkoxyl

Ortho-lithiation of aromatic compounds has become a useful synthetic reaction[238]. It is interesting that similar methodology also provides selectivity in the lithiation of cyclopropanes. Klumpp and coworkers reported[239] on the directed lithiation of cyclopropylcarbinyl ethers, as shown by the arrow in the following examples.

BuLi, hexane
64 h, 56 %

BuLi, hexane
20 h, 80 %

i-prop. Li, ether/pentane
48 h, 76 %
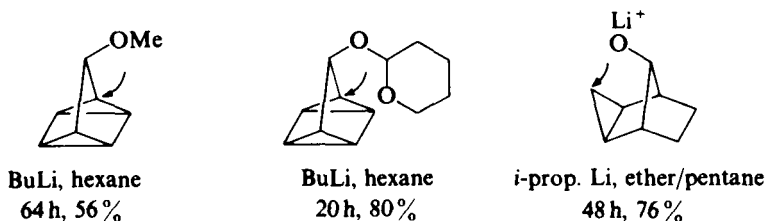
Padwa and Wannamaker[239c] have also demonstrated the remarkable effect of a β-methoxy groups. The carbanion obtained by deprotonation of either *cis*- or *trans*-2,2-dimethyl-3-methoxycyclopropyl phenyl sulfone with LDA at $-78°C$ reacted smoothly with a variety of electrophiles $EX(D_2O, MeI, CH_2CHCH_2Br, ClCO_2Me)$ to give exclusively a single stereoisomer in which the electrophile was *cis* to the methoxy group.
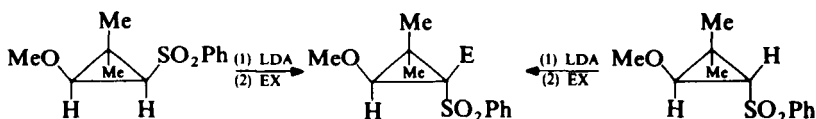
l. α-Substituent effects: theoretical studies

In order to examine whether the acidities observed in α-C(O)R, α-NO$_2$, α-CN and α-CF$_3$ substituted cyclopropanes are correctly explained by a predominating mesomeric effect in the case of the α-C(O)R and α-NO$_2$ substituents, and a stronger dipole (field) effect with α-CN and α-CF$_3$ substituents Wagner and Boche[240] investigated this subject by means of STO-3G calculations. It was of interest to determine whether the calculations are able to reproduce the relative acidities of cyclopropyl and isopropyl compounds, as well as the configuration of the corresponding cyclopropyl anions.

Table 29, column 1 reveals the influence of a substituent X in comparison to H at a methyl group. Columns 2 and 3 give the relative acidities of X-substituted 2-propanes and cyclopropanes. As one can see, the mostly mesomerically stabilizing substituents CHO,

TABLE 29. Calculated proton affinities (kcal mol^{-1}) related to the calculated proton affinity of CH$_3^-$ $(= 559.7$ kcal mol$^{-1})$[240]

X	$\underset{H}{\overset{H}{\diagdown}}C^-\diagup X$	$\underset{Me}{\overset{Me}{\diagdown}}C^-\diagup X$	$\triangle^- X$
H	0	−15.8	−32.0
CF$_3$	−44.9	−45.1	−61.6
CN	−63.0	−69.0	−75.4
CHO	−56.8	−66.3	−60.6
COOH	−62.8	−69.7	−64.7
NO$_2$	−84.5	−93.1	−88.2

COOH and NO_2 acidify the 2-propanes more than the cyclopropanes, thus confirming that they create I-strain to delocalize the negative charge of the cyclopropyl anion in those cases. The opposite applies for CN and CF_3. Both results are in excellent agreement with the experimental results discussed in earlier sections.

Next, the energy difference between the planar and the pyramidal configuration has been calculated (Table 30).

TABLE 30. Energy difference (kcal mol^{-1}) between planar and pyramidal carbon configuration[a]

X	H $\overset{H}{\underset{X}{\diagdown}}C^-$	Me $\overset{Me}{\underset{X}{\diagdown}}C^-$	$\triangle\!\!\!-X$
H	23.9	18.4	32.5
CF_3	10.5	2.1	22.4
CN	0.5	0	9.3
CHO	0	0	0.7
COOH	0	0	1.9
NO_2	0	0	11.9

[a] Zero means that the planar structure is an energy minimum[240].

In agreement with Walborsky's results[216] and a recent X-ray structure determination of α-cyano-benzyllithium[218b] the calculations nicely show that $H_2\bar{C}$–CN (0.5 kcal mol^{-1})[241] and $Me_2\bar{C}CN$ (0 kcal mol^{-1}) have almost no inversion barrier while the α-cyano cyclopropyl anion has a sizeable one (9.3 kcal mol^{-1}). Whether in the case of the CHO and COOH substituted cyclopropyl anions a pyramidal configuration with a very small barrier (0.7 and 1.9 kcal mol^{-1}, respectively) exists, is not clear. The barrier may be an artifact of the small basis set, and the enolates may well be planar. In any case, the calculations are again in agreement with the experimental result according to which k_{ex}/k_{rac} in the case of the optically active cyclopropyl phenyl ketone $(-)$-(R)-252 is unity[216f] (see Section IV.B.1.a).

The NO_2 result is interesting: the anion is pyramidal according to the calculations and has a rather high barrier to inversion (11.9 kcal mol^{-1}). This indicates that the NO_2 group exerts not only a strong mesomeric effect (compare the acidities of the isopropyl and cyclopropyl NO_2 compounds in Table 29) but also a strong dipole (field) effect, which is supported by experimental facts[205a]. Other calculations of Wagner and Boche[242a] revealed a triplet ground state for the nitrocyclopropyl anion. This result would nicely explain the experimental findings with regard to the 'elusive' α-nitrocyclopropyl anion[205a] because it would quickly dimerize.

As far as the phenylsulfonyl substituent is concerned it has been demonstrated by means of recent 3-21G* calculations by Bors and Streitwieser[243] that in the methylsulfonyl-methyl anion 308 the dominating mechanism of carbanion stabilization can be described as a classical polarization involving the SO_2 group and n–σ* orbital interactions. The carbanionic center is planar although d–p–π conjugation is not an important factor in stabilizing the anion.
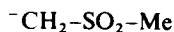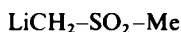
$$^-CH_2\text{–}SO_2\text{–}Me \qquad LiCH_2\text{–}SO_2\text{–}Me$$
$$(308) \qquad\qquad\qquad (309)$$

In the more realistic lithiomethyl methyl sulfone (309) the lack of importance of conjugative bonding is nicely demonstrated by the pyramidal carbanion center. This result

is important with respect to the relative acidities of 2-propyl and cyclopropyl sulfonyl compounds (Table 28, Section IV.B.1.e) and the structure of α-sulfonyl anions. It questions whether the 'low' acidities of the cyclopropyl compounds really mean that they are *planar*[213]. The formation of a pyramidal C-atom even in the case of **309** rather suggests a pyramidal structure of an α-sulfonyl cyclopropyl anion (see also the discussion in Section IV.B.1.f. in connection with the pyramidal structure of the cyclopropyl phosphonium ylid **279**).

C. Cyclopropyl–Allyl Anion Transformations

Although reactions of cyclopropanes as **195** or **198** with base to give ring-opened products have been investigated broadly by the groups of Kohler and coworkers[186] at the turn of the century and later by Smith and coworkers it has not been clearly established whether a cyclopropyl anion like **196** is formed as a discrete intermediate[187], or whether deprotonation and ring-opening to give the allyl anion **197** occur synchronously[188] (see page 768).

It was only after Woodward and Hoffmann in 1965 had predicted a conrotatory mode for the thermal cyclopropyl–allyl anion transformation[79] that a new interest developed in this reaction. By means of the iso-π-electronic aziridine **310** Huisgen and coworkers[244] succeeded in demonstrating that the thermal reaction gave a conrotatory formation of azomethine ylid (**311**) and that the light-induced reaction resulted in a disrotation to give **312**.

                (312)   (310)   (311)
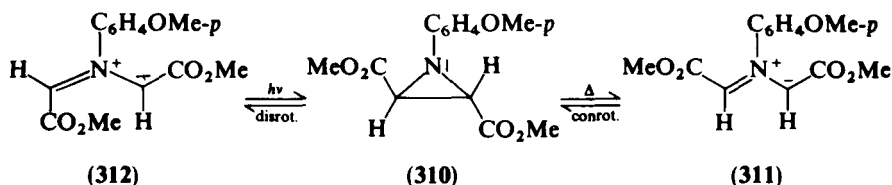
The same stereochemical modes have been observed by the same group in the oxirane ⇌ carbonyl oxide transformations[245, 246].

Kauffmann and coworkers[247] prepared N-lithio-cis-2,3-diphenylaziridine (**313**) which transforms into endo,exo-1,3-diphenyl-2-azallyllithium (**314**) at 40–60°C, this establishing the thermal conrotation in this system.

                (313)   (314)   (315)
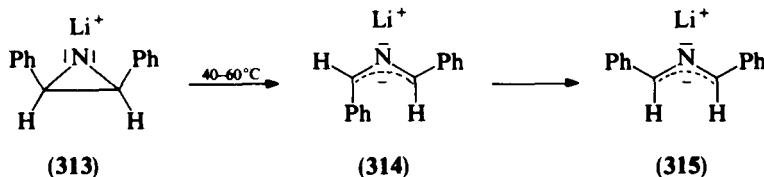
The isomerization of **314** to give **315** competes successfully with the trapping reaction of **314** with trans-stilbene which established the stereochemistry of **314**.

The cyclopropyl–allyl anion case itself turned out to be more of a problem. Mulvaney and Savage[248] reacted the trans,trans-1,2,3-triphenylcyclopropane (**316**) with n-butyllithium/TMEDA which led to one (or more) of the isomeric 1,2,3-triphenylallyl anions (**317**).

Since the corresponding cis,cis-isomer **318** with potassium t-butoxide in DMSO-d_6 led to the tris-deuterated trans,trans-cyclopropane **316-D_3** Mulvaney and Savage concluded that the 1,2,3-triphenylcyclopropyl anion is capable of existing for a finite period of time as an intermediate without undergoing ring-opening. Therefore this cyclopropyl anion

(316)

(317)

(318)   (316-D$_3$)
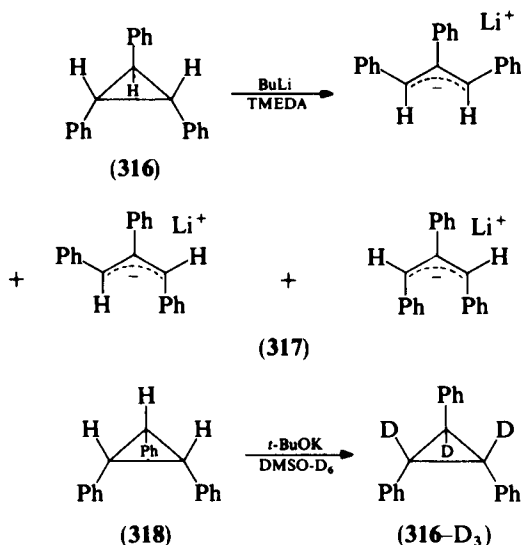
should also be an intermediate in the reaction of **316** with *n*-butyllithium/TMEDA to give the allyl anion(s) **317**. Huisgen and Eberhard[249] arrived at similar conclusions with the cyclopropane **319**.

(319)   (320$^-$)

(322)   (321$^-$)
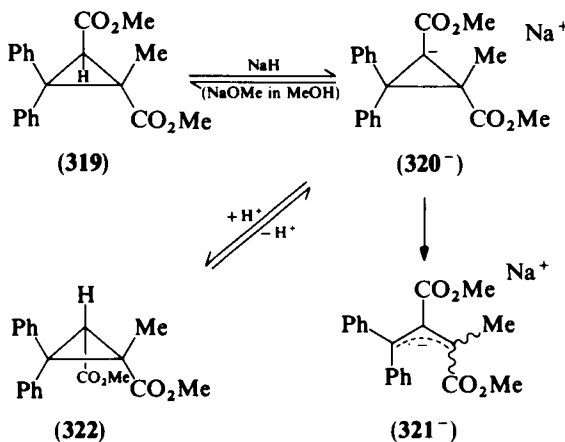
The cyclopropyl anion **320**$^-$ should be the intermediate both in the *cis–trans* isomerization to give **322** (NaOMe in MeOH) and in the ring-opening reaction (NaH in DMF) to give **321**$^-$ whose stereochemistry is unknown. From these studies it seemed reasonable that cyclopropyl anions did indeed thermally isomerize to give allyl anions.

If one compares the 1,2,3-triphenylcyclopropyl anion as well as the cyclopropyl anion **320**$^-$ with the many more cyclopropyl anions not showing the ring-opening reaction such as all cyclopropyl 'anions' with H or alkyl groups at C(1) like the parent **323**[250] or Walborsky's **324**$^-$ [216] it is immediately clear that substituents which stabilize a negative charge at *both* carbon atoms which become terminal centers of the allyl anion facilitate the ring scission. If the cyclopropyl anion is prepared by deprotonation of a cyclopropane it is

additionally necessary to put the appropriate substituent at the forthcoming carbanionic carbon atom in order to provide regioselective deprotonation.

(323)　　　　　　　　　**(324)**
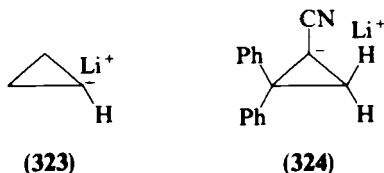
The necessity of both prerequisites is illustrated by the following examples which, for different reasons have not been useful in determining the stereochemistry of the cyclopropyl–allyl anion transformation.

(218)　　　　　　**(219$^=$)**　　　　　**(220$^=$)**

(Ref. 200)

(222)　　　　　　**(223$^=$)**　　　　　**(224$^-$)**

(Ref. 200)

(227)　　　　　　**(228$^-$)**　　　　　**(229$^-$)**

(Ref. 202)

(325$^-$)　　　　　　**(326$^-$)**　　　　(Ref. 251)
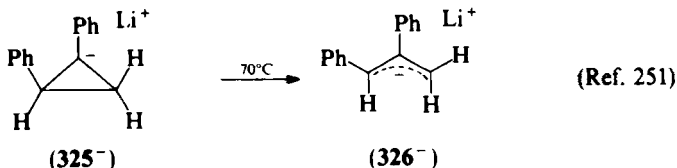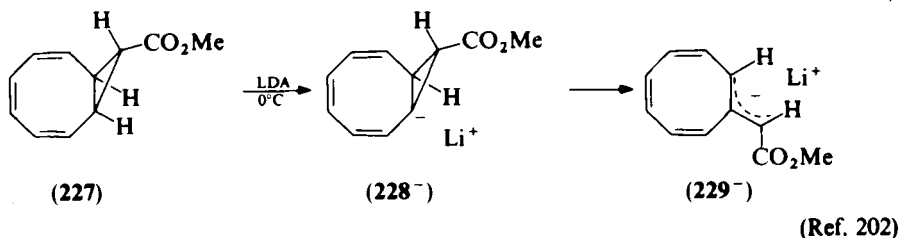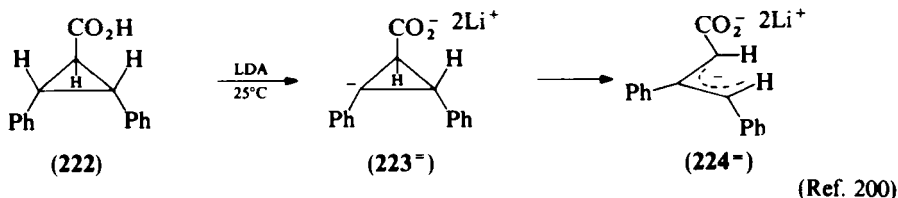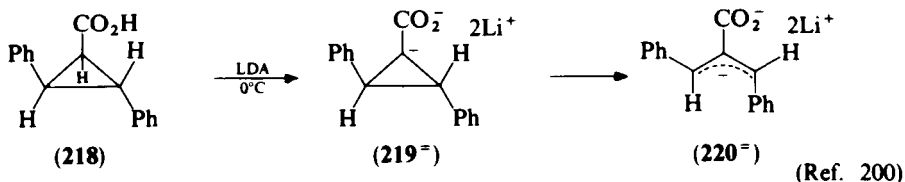
Ring-opening reactions in tricyclic systems (e.g. **171$^-$** → **172$^-$**) which are likely to occur via a cyclopropyl–allyl anion rearrangement have been discussed in more detail in Section III.C.2.a.

In these systems as well as in the case of the cyclopropyl anions **327$^-$** which gives **328$^-$** slowly at 100°C and **329$^-$** which gives **330$^-$** slowly at 0°C, which were studied by Wittig and coworkers[90a], the ring-opening reactions can not occur in a conrotatory fashion. The slow disrotatory opening of **329$^-$** (R = CN), however, was useful in elaborating a kinetic criterion for the cyclopropyl–allyl anion transformation by the groups of Boche[218a,219]

Ph
-Ph
R²

(171⁻)

Ph
R²
Ph

(172⁻)

R Li⁺
H   H

R Li⁺
H   H

(327⁻; R = H)
(329⁻; R = CN)

(328⁻; R = H)
(330⁻; R = CN)

CN
Ph   H
H   Ph

(261)

$\xrightarrow{\text{2 LDA} \atop \text{THF}}$

CN Li⁺
Ph   H
H   Ph

(331⁻)

conrot.

disrot.

conrot.

Li⁺ CN
H   H
Ph   Ph

(332⁻)

CN Li⁺
H   Ph
Ph   H

(333⁻)

CN Li⁺
Ph   Ph
H   H

(334⁻)

disrot.

conrot.

disrot.

CN
H   H
Ph   Ph

(260)

$\xrightarrow{\text{2LDA} \atop \text{THF}}$

CN Li⁺
H   H
Ph   Ph

(335⁻)
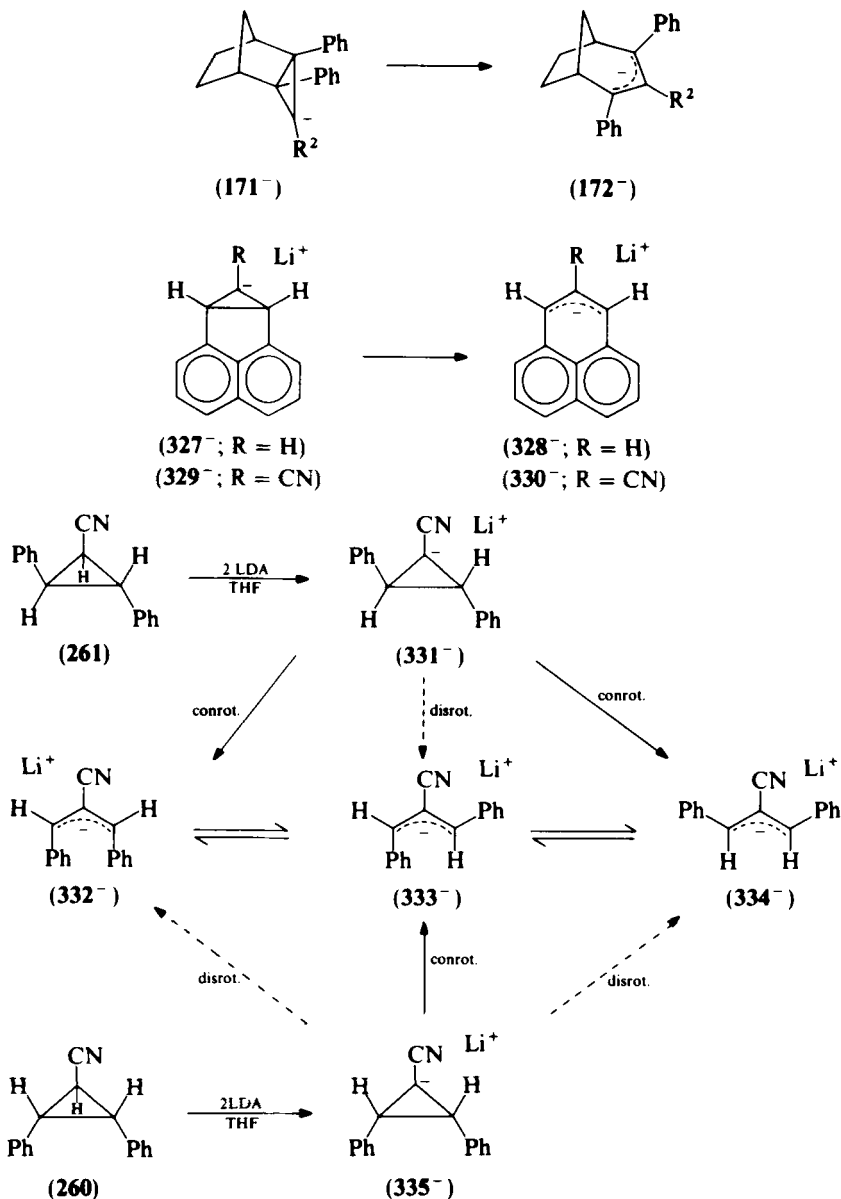
and Ford[200b,c] using in addition the isomeric 2,3-diphenylcyclopropyl nitriles 260 and 261. Deprotonation of 261 with 2 molar equivalents of lithium diisopropylamide in THF at − 30°C led to the *trans*-cyclopropyl anion 331⁻ which on warming to 20°C gave mainly the *endo, exo*-ally anion 333⁻ besides 4.5% of the *exo, exo*-isomer 334⁻ (and less likely *endo, endo*-isomer 332⁻) as shown by ¹H-NMR spectroscopy and protonation.

The similarly formed *cis*-cyclopropyl anion 335⁻ (from 260) led exactly to the same

result as in the case of **331**$^-$, with **333**$^-$ being formed predominantly. It thus seems that the fast isomerization of the allyl anions **332**$^-$, **333**$^-$ and **334**$^-$ accumulates quickly the thermodynamically most stable isomer **333**$^-$, which prevents the experimental verification of the thermal conrotation by determining the structure of the allyl anions formed in the two ring-opening reactions. That this was indeed the case was confirmed by kinetic studies of the ring-opening and isomerization reactions (Scheme 21).
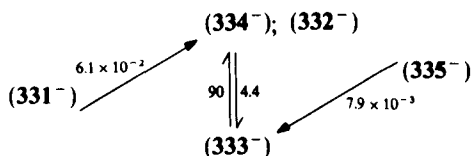
SCHEME 21. Rate constants for ring-opening reactions of the cyclopropyl anions **331**$^-$ and **335**$^-$ (s^{-1} at 20°C), and of isomerization reactions of the allyl anions **333**$^-$ and **334**$^-$ (**332**$^-$) (s^{-1} at 24.5°C)

The ring-opening reaction, e.g. of **331**$^-$ to give **334**$^-$ (and/or **332**$^-$ which is not clear from the available data), is about 1500 times slower than the isomerization of the allyl anion **334**$^-$ (and/or **332**$^-$) to give the more stable **333**[252]. A similar situation obtains for **335**$^-$.

A comparison of the rate constants given in Scheme 21 with the rate constant of the disrotatory ('forbidden') ring-opening reaction in the related Wittig system[90a] **329**$^-$ → **330**$^-$, however, allows the evaluation of a kinetic criterion for the thermal conrotation in the cases of **331**$^-$ and **335**$^-$. At 20°C the following ratios of rate constants are calculated:

$$\frac{k_{331^-}}{k_{329^-}} = 5500; \qquad \frac{k_{335^-}}{k_{329^-}} = 740$$

The 'forbidden' disrotation of **329**$^-$ thus is much slower than the ring-opening reactions of **331**$^-$ and **335**$^-$ which are not hindered to occur in the 'allowed' conrotatory fashion.

The generally slow conrotatory ring-opening reaction of cyclopropyl anions as compared to the fast isomerization of the corresponding allyl anions has been supported by means of MO calculations with the parent anions (Table 31)[219]

TABLE 31. Relative energies (kcal mol^{-1}) of the cyclopropyl–allyl anion transformation and the allyl anion isomerization[219]

STO-3G	66.7	25.3
4-31G	38.0	27.6

The experimental data obtained with the cyclopropyl anions **331**$^-$ and **335**$^-$, and the allyl anions **332**$^-$, **333**$^-$ and **334**$^-$, are therefore symptomatic of the cyclopropyl–allyl *anion* system.

It is interesting to mention the entirely different situation in the cyclopropyl–allyl *cation* system: the ring-opening reaction is very fast as compared to the isomerization of the allyl cation. In agreement with this situation the disrotatory mode of the cyclopropyl–allyl cation transformation has been 'much easier' to verify[253].

The electrocyclic transformation of the β-lithiocyclopropyloxirane **336**$^-$ also occurs in a conrotatory fashion as suggested by the formation of **338** (after protonation) from the

intermediate **337** which has been trapped in a Diels–Alder reaction to give the *trans*-fused adduct **339**[254].

(336⁻)   (337)   (338)

(339)
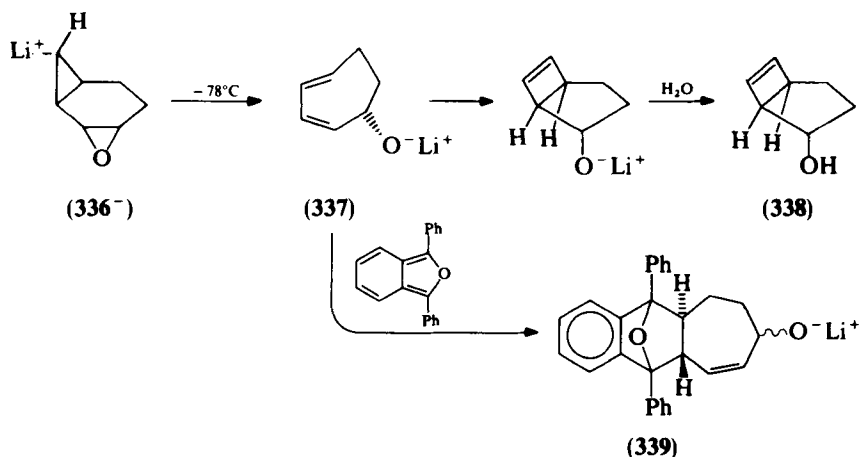
This ring-opening contrasts sharply with the normally observed stability of cyclopropyllithium compounds with hydrogen at C(1) and alkyl substituents at C(2) snd C(3) as mentioned above. In this electrocyclic transformation combined with a Grob-type heterocyclic fragmentation the ring-opening reactions of both three-membered rings must therefore be concerted[255a]. A special case of a cyclopropyl anion rearrangement has been observed by Ogle and coworkers[255b]. When phenylcyclopropane is treated with n-BuLi/t-BuOK, it seems that only the phenyl cyclopropyl potassium which is also metallated at the phenyl ring undergoes ring opening and not the monometallated potassium 1-phenyl cyclopropane.
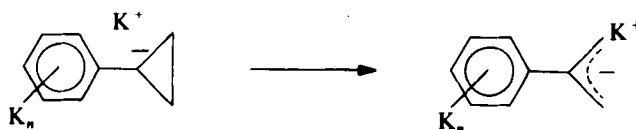
Photochemical cyclopropyl–allyl anion transformations with some of the cyclopropyl anions described above have been observed by Newcomb and Ford[200c] and by Fox[256].

(331⁻; X = CN)   (333⁻; X = CN)
(340⁻; X = CO₂Me)   (341⁻; X = CO₂Me)
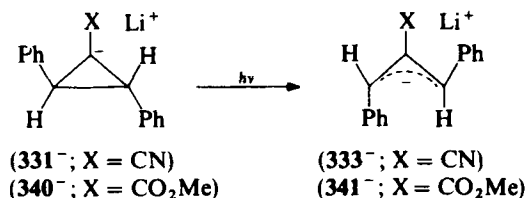
Thus with the cyclopropyl anions **331**⁻ and **340**⁻ it has been established that the disrotatory mode, as predicted by Woodward and Hoffmann[79], is the preferred one. It is however not clear whether a photochemical cyclopropyl–allyl anion or a thermal

cyclopropyl radical ring-opening (the latter caused by photochemical electron ejection) takes place. It has also been realized that systems with X = vinyl or Br (**342⁻** and **343⁻**, respectively) do not open photochemically[256c].

(**342⁻**; X = vinyl)
(**343⁻**; X = Br)
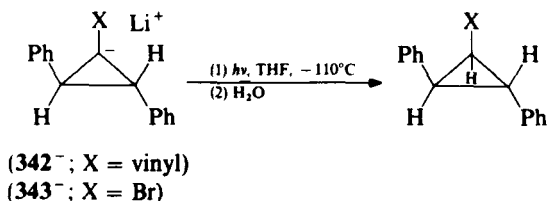
These results have been attributed[256c] to an 'increased ionicity' of the carbon–lithium bond in the case of **331⁻** and **340⁻** as compared to **342⁻** and **343⁻**. This conclusion is supported by electrochemical measurements and MNDO calculations[257]. A similar conclusion had been reached earlier by Boche and Martens[219] for thermal cyclopropyl–allyl anion transformations.

D. Synthetic Applications

The generation and alkylation of electronegatively substituted cyclopropyl anions, under preparatively useful conditions is not a straightforward procedure. For example, attempts to deprotonate ethyl cyclopropanecarboxylate have led to formation of a Claisen aldol condensation product[197,205a] (**238**; Section IV.B). Although the dianion of cyclopropanecarboxylic acid is capable of reacting with some electrophiles at 20°C[198], it dimerizes rapidly at 50°C to yield **344**[196,197]. Nitrocyclopropane[205a,242a] also undergoes a self-condensation under the influence of strong base to produce **268** and **269**.

(**238**)   (**344**)   (**268**)   (**269**)
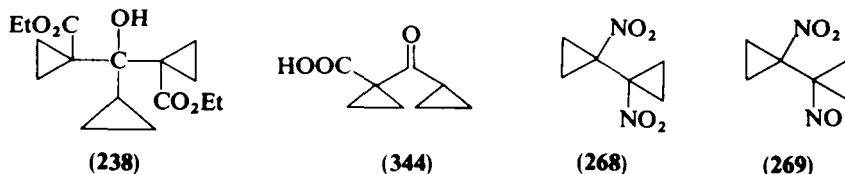
The propensity for self-condensation may sometimes be reduced or eliminated by placing bulky substituents beta to the electron-withdrawing group[216] or even attached to the electron-withdrawing group[206]. The latter methodology has been elaborated very recently by Seebach and coworkers[205b] (see also Section IV.B.1.a). Cation chelating substituents in the beta positions are also effective in reducing self-condensation[209]. A

(**345**)   (**346**)   (**347**)
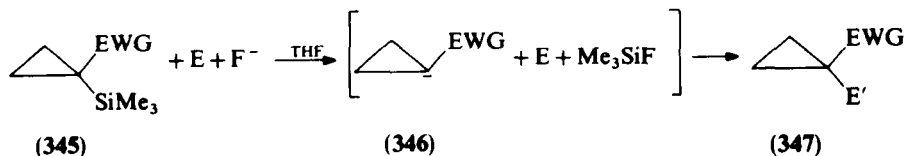
method, developed by Paquette and coworkers[258], provides a means for avoiding the problem of self-condensation. It takes advantage of the fluoride ion desilylation of α-trimethylsilylcyclopropanes containing an electron-withdrawing group (EWG) in the α-

TABLE 32. Desilylation and condensation reactions

EWG in 345	Fluoride source	E	Product	Yield (%)
COOMe	TBAF[a]	MeCHO (acetaldehyde)	cyclopropyl-C(COOMe)-CHMe-OH	90
	TBAF	Me-CO-Me (acetone)	cyclopropyl-C(COOMe)-C(Me)(Me)-OH	68
	TBAF	cyclohexanone	cyclopropane-spiro cyclohexane COOMe, OH	45
CN	BTAF[b]	Ph-CHO	cyclopropyl-C(CN)-CHPh-OH	83
	BTAF	Me-CO-Me (acetone)	cyclopropyl-C(CN)-C(Me)(Me)-OH	55
CH₃-C(=O)- (acetyl)	BTAF	PhCHO	cyclopropyl-C(=O)Me-CHPh-OH	63
3-methylcyclohex-2-enone	BTAF	PhCHO	product, cyclohexenone with cyclopropyl and CHPh-OH	73
2-ethylidenecyclohexanone	BTAF	PhCHO	product with cyclohexanone, cyclopropyl, CHPh-OH	45

[a] Tetrabutylammonium fluoride.
[b] Benzyltrimethylammonium fluoride.

position (345). The desilylation produces, *in situ*, an α-anion **346** which can condense with an electrophile E that is already present in solution to yield **347**. The overall reaction is depicted above and Table 32 records some results.

If the electron-withdrawing group is such that self-condensation does not occur then the anion can be generated in the normal manner. Thus, the anion **349** of cyclopropyl phenyl sulfone (**348**) can be readily prepared by treatment of the parent compound with *n*-butyllithium at 0°C in THF. The anion has been shown to condense in excellent yield with aldehydes, ketones, methyl iodide and allyl and benzyl bromides[259] to yield **350**. The phenyl sulfone group can be readily removed by reduction with sodium amalgam[259] to produce desulfurized **351**.

If the electron
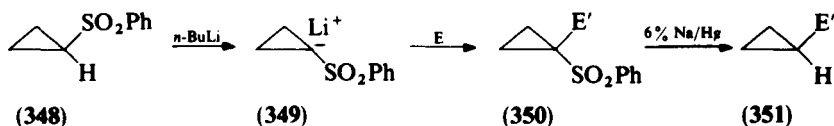
1-(Lithio)cyclopropylsilanes are useful intermediates since they can readily be transformed to synthetically useful alkylidene and allylidene derivatives when used in the Peterson olefination[260]. Treatment of 1-phenylthio-1-trimethylsilylcyclopropanes (**352**) with lithium 1-(dimethyl-amino)-naphthalenide (LDMAN) produces 1-lithio-1-(trimethylsilyl)-cyclopropanes (**353**) which can be condensed with a variety of carbonyls[260,261]. The products are converted by elimination to the exocyclic olefin (**354**).
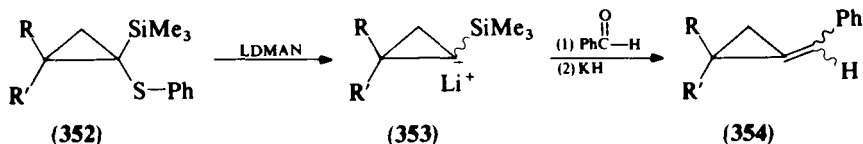
The formation of carbon–carbon bonds by means of three carbon homologating agents (d³ synthons)[262] can provide a useful and desirable methodology for the preparation of *inter alia*, α,β- and β,γ-unsaturated aldehydes.

The d³-synthons that lead to the formation of β,γ-unsaturated aldehydes (**358**) are E- and Z-2-methoxycyclopropyllithium[263] (**356**) which can be readily prepared, at −78°C, by treatment of E- and Z-2-methoxycyclopropyl bromide (**355**) with *t*-butyllithium. The lithium reagent is condensed with a carbonyl compound to yield the corresponding cyclopropylcarbinol which is converted to its mesylate derivative **357**. The mesylates,
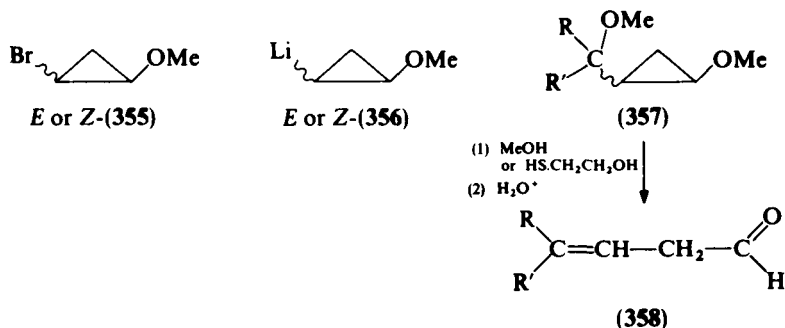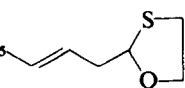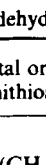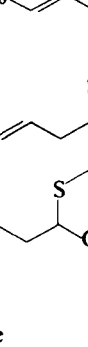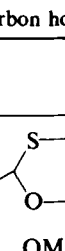
TABLE 33. β,γ-Unsaturated aldehydes by three carbon homologation

R	R'	Acetal or hemithioacetal	(% Yield)	β,γ-Unsaturated aldehyde (% Yield)
Me(CH$_2$)$_5$	H	Me(CH$_2$)$_5$ ~~~ (1,3-oxathiolane)	77	93
Me(CH$_2$)$_5$	H	Me(CH$_2$)$_5$ ~~~ CH(OMe)$_2$	97	96
NC(CH$_2$)$_6$	H	NC(CH$_2$)$_6$ ~~~ (1,3-oxathiolane)	82	93
cyclohexyl	H	cyclohexyl–CH=CH–CH$_2$–(1,3-oxathiolane)	72	91
(CH$_2$)$_5$		cyclohexylidene–CH$_2$–CH$_2$–(1,3-oxathiolane)	81	95
(Me)(H)C=C(Me)	H	Me$_2$C=C(Me)–CH=CH–CH$_2$–(1,3-oxathiolane)	61	67

which are not isolated, are solvolysed in methanol or 2-mercaptoethanol to yield the corresponding acetals or hemithioacetals. The latter can be especially useful because, although relatively acid resistant, they are readily hydrolyzed under neutral conditions with mercuric ion assistance or via the S-methyl sulfonium derivative. Examples for the process are given in Table 33.

The anion of 2-(methoxyethoxymethoxy)cyclopropyl phenyl sulfone (methoxyethoxymethoxy = MEM) is a d^3-synthon for α,β-unsaturated aldehydes[264]. The anion is readily formed by treating 2-(MEM)cyclopropyl phenyl sulfone (359) with n-butyllithium in THF at $-78°$C. Treatment of the anion 360 with aliphatic primary bromides or allyl bromide produces the alkylated sulfone 361 in very good yields. Hydrolysis of the MEM-protecting group was readily performed by treatment with aqueous tetrafluoroboric acid to furnish the cyclopropanol sulfone (362). Treatment with aqueous sodium bicarbonate produced the corresponding aldehydes 363 in 70–90% yields.

Although the anion is used as a means of derivatizing the sulfone the key step to this method is the generation of a homoenolate anion and its subsequent rearrangement. The subject of homoenolate anions and their synthetic applications has been extensively reviewed elsewhere[265].
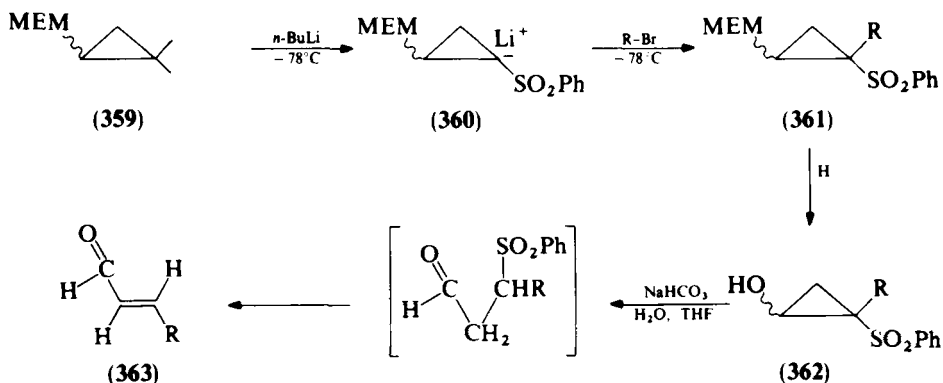
Cyclobutanones have become very useful intermediates for synthesis since their introduction by Trost as a means of secoalkylation[266]. The key element in the synthesis was diphenylsulfonium cyclopropylide (365) which is generated from its precursor diphenylcyclopropylsulfonium fluoroborate (364) by treatment with potassium hydroxide.
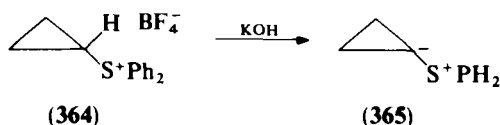
The use of the ylide in secoalkylation and secoalkylative annelation is shown in Scheme 22[266a,b]. Cyclobutanones can also serve as precursors to five-[267], six-[268] and eight-membered[269] rings as well as a variety of highly functionalized acyclic[266b,270] molecules.
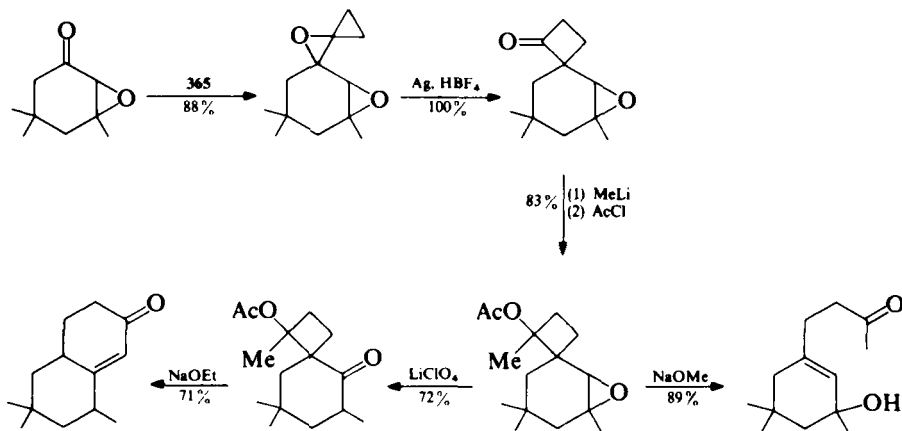
SCHEME 22. Secoannelation and secoalkylation

Besides ylids, carbenoids (366) can also be used since they too can condense with ketones to yield oxaspiropentanes (367) or heteroatom-substituted cyclopropylcarbinols (368), both of which rearrange to cyclobutanone derivatives (369) under acid catalysis. The 1-ethoxycyclopropyllithium is the carbenoid reagent of choice because of its ease of

preparation and condensation with carbonyls. Also the rearrangement to the cyclobutanone derivatives is greatly accelerated and cleaner[274,275].

(366)   **(367)**   **(368)**   **(369)**

$$X = Br^{271}, \quad SPh^{272}, \quad SePh^{273}, \quad OMe^{274}, \quad OEt^{275}$$
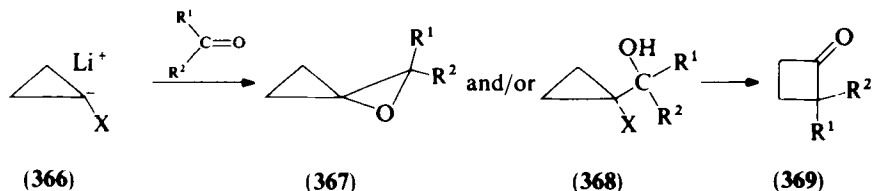
The ylid **371** prepared by treating cyclopropyltriphenylphosphonium bromide (with lithium diisopropylamide (LDA) produces a useful synthon on reaction with ethyl chloroformate[276]. The fluoroborate salt (**372**) was shown to be an excellent reagent for cycloalkenylation of carbonyl compounds. The ylid was used successfully in the total synthesis of Spirovetivanes[277].
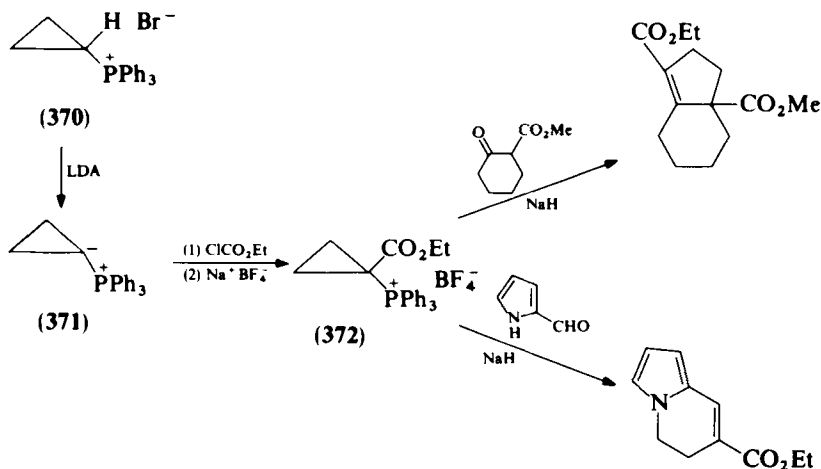
The reaction involves nucleophilic attack at the beta cyclopropyl carbon and cleavage of the cyclopropyl ring which produces an ylid that condenses intramolecularly with the carbonyl moiety.
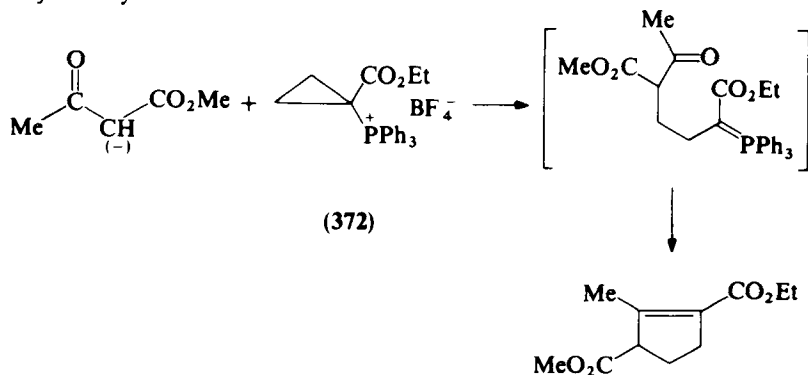
Replacing the carboethoxy group by a thiophenyl group in the cyclopropyltriphenyl-phosphonium salt generates a new synthon **373** which is useful in cyclopentanone synthesis[278].
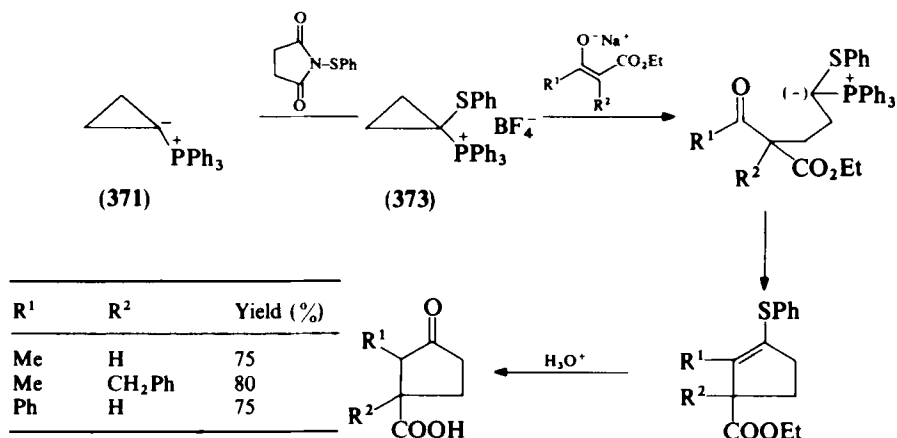
R¹	R²	Yield (%)
Me	H	75
Me	CH₂Ph	80
Ph	H	75

V. ACKNOWLEDGEMENT

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CHAPTER **2**

Appendix to 'Cyclopropyl radicals, anion radicals and anions'[†]

   b. α-Cyano.
(i) The solid state structure of [1-cyano-2,2-dimethylcyclopropyllithium · tetra-hydrofuran]$_\infty$. From the solution studies especially of Walborsky[216], and de Boer[190, 191] (see Table 26) it is apparent that α-cyano cyclopropyl 'anions' should not be planar but rather have a pyramidalized or even tetrahedral configuration at the anionic carbon atom. This has been nicely confirmed by a recent solid state X-ray structure determination of 1-cyano-2,2-dimethylcyclopropyllithium (**374**) which crystallizes from a THF solution in the form of the polymer (**374** · THF)$_\infty$ (Figure 5)[280]. Most importantly, the axis C1–Li2' is 51.8(3)° bent out of the plane of the cyclopropane ring [Li2' lies 1.685(8) Å below this plane]. Similarly, C6 of the cyano group is 57.4° bent out of the plane of the cyclopropane ring. The tetrahedral configuration of C1 in (**374** · THF)$_\infty$ together with the higher acidity of cyclopropyl nitrile as compared to isopropyl nitrile thus clearly demonstrate that the (inductive) field effect plays a major role in the stabilization of a

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[†] The material in this Appendix is divided in the same manner as in the original chapter (Chapter 1). The section numbers in the Appendix are preceded by an asterisk; only those sections are updated (and section numbers given) to which a coherent contribution has been made since 1987. The numbers of structures, equations, tables and references run continuously in Chapter 1 and this Appendix.

$$(374) \qquad\qquad (374\cdot THF)_\infty$$
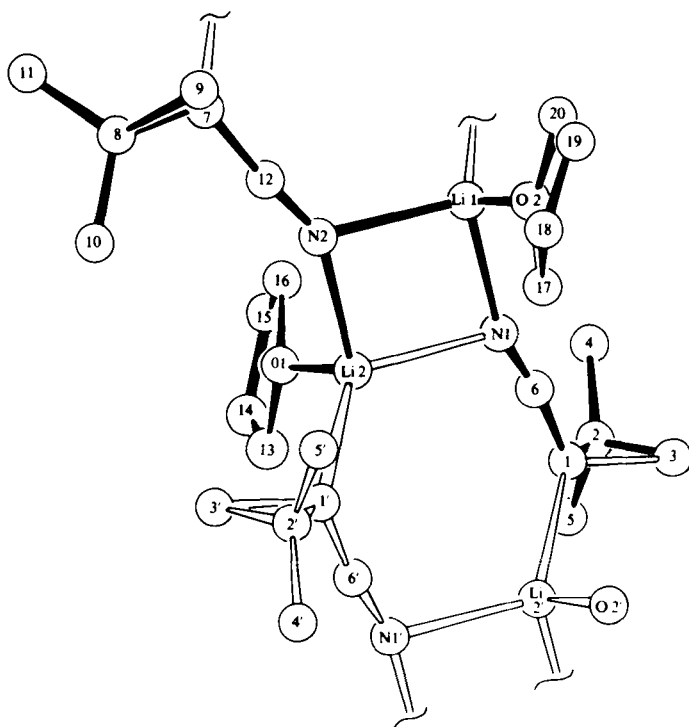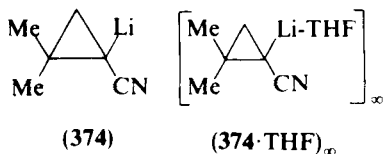
FIGURE 5. Solid state structure of $(374\cdot THF)_\infty$. Reproduced with permission from Boche and coworkers, *J. Am. Chem. Soc.*, **110**, 6925 (1988)

negative charge by a cyano group. In agreement the bond lengths C1–C6 [1.400(0.7) Å] and C6–N1 [1.178(0.7) Å] are not very different from those in cyclopropyl nitriles (e.g. in 1,1,2,2-tetracyanocyclopropane C–C: 1.442 Å; C≡N: 1.150 Å)[281].

The bond lengths within the three-membered ring are also of interest: the distal C2–C3 bond [1.473(0.7) Å] is shorter than the two vicinal bonds [C1–C2 1.500(0.7) Å; C1–C3 1.522(0.7) Å]. Such a pattern of bond length asymmetry has been predicted for acceptor-substituted cyclopropanes if there is an interaction between the occupied cyclopropane 3e' and an unoccupied acceptor π orbital[282, 283]. It is generally observed in cyano-substituted cyclopropanes[281]. Since it is also observed in the cyanocyclopropyl anion $(374\cdot THF)_\infty$, the cyano group not only interacts with the 'anionic' but also with the 3e' orbital. There are indications that this might be a general phenomenon: in the rearrangement of the 9-cyano-*cis*-bicyclo[6.1.0]nona-2,4,6-trien-9-yl 'anion' (375) a vicinal bond is broken to give 376 rather than the distal C–C bond which will give 377[202].
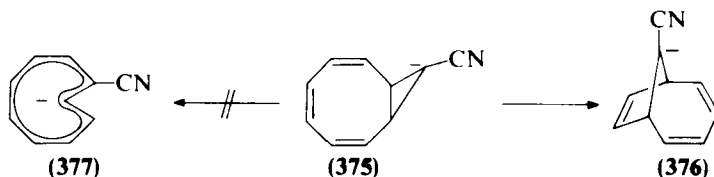
There is another feature of interest disclosed by the structural investigations: of all the lithiated cyano compounds studied so far by X-rays[280b], it is only in the case of the lithiated cyanocyclopropane $(374 \cdot \text{THF})_\infty$ that a carbon–lithium bond [C1–Li2′ 2.143(0.9) Å] is observed. This coordination, which leads to a genuine α-lithionitrile, is probably due to the high electron density in the exocyclic, 'anionic' three-membered ring orbital. This explanation is corroborated by a similar situation in the cyclopropylsulfonyl 'anion' $386 \cdot \text{DME}(2/3)$. The consequence in the case of $(374 \cdot \text{THF})_\infty$ is that, in addition to the generally observed (Li–N–Li–N) four-membered ring[280b], a (C–C–N–Li–C–C–N·Li) eight-membered ring aggregation pattern is observed. It is interesting to mention that both the four- and eight-membered ring have been predicted by means of calculations[241b]: in the case of a solvated Li$^+$ the four-membered ring should be preferred, as, e.g., 'in the solid state'; if, however, Li$^+$ is unsolvated, the eight-membered ring coordination should be the favored one. This last situation, of course, is equal to one in which Li$^+$ is solvated but the anionic carbon has a higher charge density than normal, and that is exactly the case with $(374 \cdot \text{THF})_\infty$. What a perfect agreement between theoretical prediction and experimental observation!

*d. α-Nitro

Compared with acyclic aliphatic nitro compounds, α-nitrocyclopropane is little acidic[191c, 213, 214c], and the α-nitrocyclopropyl anion is rather unstable: Bordwell and coworkers[213] noted the instability under the conditions of H/D exchange in DMSO, and Seebach and coworkers[205a] were unable to get hold of the 'elusive' nitrocyclopropyl anion (prepared by deprotonation with different bases) using all sorts of electrophiles.

In a recent publication, however, O'Bannon and Dailey report on the intermediate formation and trapping of the α-nitrocyclopropyl anion[284]. When they heated either 378 or 379 in anhydrous 1:1 (v:v) DMSO/benzaldehyde solution at temperatures between 40 and 80°C, they isolated the isomeric nitroaldol adducts 381 and 382 in yields of 50 to 80% (e.g. at 80°C, 381:382 = 1:2 in 70% combined yield).
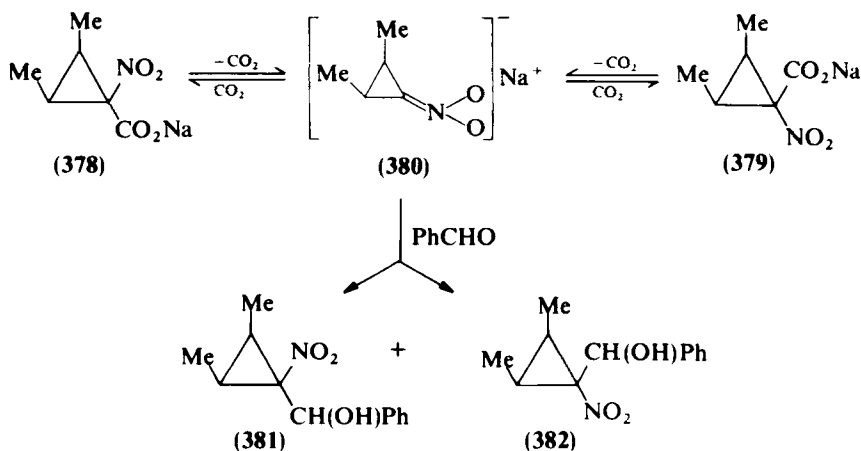
Remarkably, no carbon dioxide formation is observed in the absence of a suitable electrophile. It is assumed that the nitrocyclopropyl anion **380** is still formed under such conditions, but it recombines with the liberated carbon dioxide. The reversible formation of the 1-nitrocyclopropyl anion was demonstrated by warming an unhydrous DMSO-D$_6$ solution of pure **378** or **379** to 80 °C for one hour and examining the ^{1}H and ^{13}C NMR spectrum of the mixture. Regardless of which isomer is the precursor, a 3:1 mixture of **378:379** results. In contrast to Seebach's observations[205a], no dimer is formed, presumably because of the low concentration of the nitrocyclopropyl anion **380**.

When the nitrocyclopropyl anion is substituted by geminal groups on another carbon of the ring, it undergoes reactions with electrophiles without difficulties even when it is prepared under deprotonation conditions. For example, when 2,2-dimethyl-1-nitrocyclopropane **383** was added to a solution of LDA and benzaldehyde at −78 °C, the nitroaldol adduct **384** was formed in 51% yield as a 10:1 mixture of diastereomers.

(385)   (383)   (384)
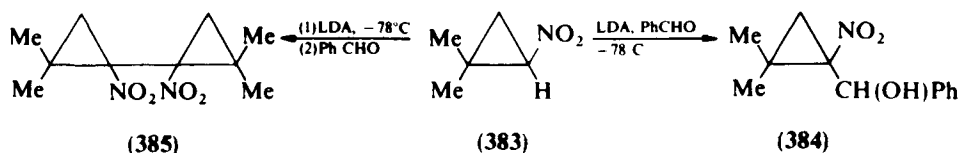
However, when the anion is generated first at −78 °C and then quenched by benzaldehyde, only dimer **385** is obtained.

The authors also performed *ab initio* calculations on the parent nitrocyclopropyl anion. At the HF/6−31+G*//6−31G*+ZPE level the anion prefers a nonplanar C$_s$ geometry by 2.1 kcal mol^{-1} over the planar C$_{2v}$ structure. A nonplanar structure was also found by Wagner and Boche[240]. Calculations at the ROHF/6-31+G*//6-31G* level indicate that the triplet state of the nitrocyclopropyl anion lies 29 kcal mol^{-1} higher in energy than the singlet ground state. The ease of dimerization of the nitrocyclopropyl anion was earlier ascribed (among other explanations) to a triplet ground state[205a], which was supported by a nonoptimized STO-3G calculation[242a].

e. α-Sulfonyl and derivatives, and α-selenonyl.
(i) The solid state structure of 2,2-diphenyl-1-(phenylsulfonyl)cyclopropyllithium·dimethoxyethane(2/3). The question of whether the anionic carbon atom in α-sulfonyl 'carbanions' has to display a planar, pyramidal or tetrahedral configuration is intimately related to the question of how a sulfonyl group stabilizes a negative charge. Theoretical investigations by Bors and Streitwieser[285] on the energy of different configurations and conformations of such an anion indicated that there is no reason to assume p$_\pi$–d$_\pi$ conjugation between the lone pair of electrons on C$_\alpha$ and the sulfonyl group. Calculations of bond lengths, proton affinities and electron densities gave the same result, which can only mean that the n$_C$–σ*$_{S-R}$ interaction is crucial for stabilization of the negative charge[285]. Thus, the anion of a cyclopropyl sulfone need not be planar. Hydrogen/deuterium exchange reactions by Kirmse and Mrotzek[279] supported the theoretical findings nicely. Unambiguous structural evidence was provided by an X-ray structure investigation of 2,2-diphenyl-1-(phenylsulfonyl)cyclopropyllithium **386** which crystallized from dimethoxyethane (DME) to give **386·DME(2/3)** (Figure 6)[280b, 286].

386·DME(2/3) forms a dimer, the lithium atoms being bonded to the O atoms of the sulfonyl groups and to two of the three dimethoxyethane molecules. This leads to an (S–O–Li–O–S–O–Li–O) eight-membered ring characteristic of lithiosulfones[280b]. The third molecule of dimethoxyethane cocrystallizes. Relevant to the introductory remarks is

$$Ph \triangle Li \atop Ph \qquad SO_2Ph$$

(386)

$$\left[Ph \triangle Li \atop Ph \qquad SO_2Ph \right]_2 \cdot 3DME$$
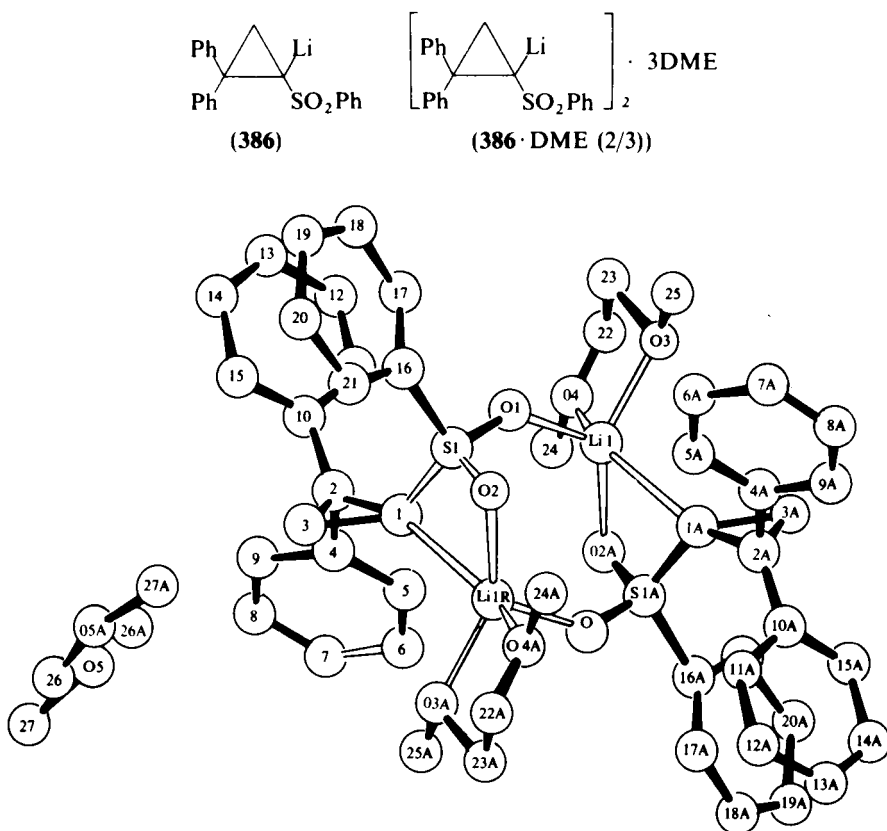
(386·DME (2/3))

FIGURE 6. Solid state structure of **386**·DME(2/3). Reproduced with permission from Boche and coworkers *Angew. Chem.*, **100**, 868 (1988); *Angew. Chem., Int. Ed. Engl.*, **27**, 846 (1988)

the finding that the $PhSO_2$ group is bent out of the plane of the cyclopropyl ring by 61.7(5)° [S1 lies 1.315(3) Å above this plane], leading to a tetrahedral configuration at the α-C atom. A salient feature of lithiosulfones is the additional coordination of the Li atom to the α-C atom [C1–Li1A 2.440(14) Å]. Although this is not a short C–Li bond it is formed in **386**·DME(2/3) presumably because of the comparatively high charge density in the exocyclic orbital containing the negative charge. The bond axis C1–Li1A is bent by 24.9(6)° out of the plane of the three-membered ring [Li1A lies 1.03(1) Å below this plane]. A comparable situation—only the corresponding cyclopropyl lithium compound shows a C–Li contact—was observed in the case of α-cyano 'anions' as described in a foregoing section on the structure of $(374 \cdot THF)_\infty$. This supports a special cyclopropyl effect with regard to the C–Li bond.

(ii) The solid state structure of $[c-C_3H_4-SO_2Ph]_2Ti[OCH(CH_3)_2]_2$. Considering the unusual C–Li bond in the solid state structure of the lithiated cyclopropyl sulfone **386**·DME(2/3), it is not surprising that a titanium–carbon bond is found in the solid state structure of the titanated cyclopropyl sulfone **387**[287].

387 is a diorganotitanium compound with two (phenylsulfonyl)cyclopropyl groups of opposite configuration. The Ti–C distance is normal (2.177 Å) and the average Ti–O

(387)
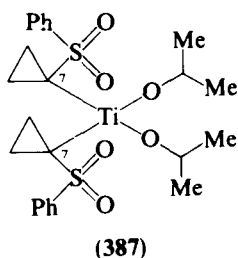
distance (1.763 Å) is short. Each titanium atom is coordinated to one O atom of each sulfonyl group, thus leading to hexacoordinated Ti. The existence of (O–S–C–Ti) four-membered rings is demonstrated by the Ti–O distance (2.229 Å), the torsion angle C–Ti–O–S (3.5 °) and the bond angle Ti–C–S (average 95.4 °). It is not surprising that C7 has a pyramidal configuration.

(iii) α-Selenonyl. Selenones have been shown to be useful synthetic intermediates, since they not only act to stabilize an α-carbanionic center but the $RSeO_2$-anion was also proven to be an excellent leaving group[288a–c]. Krief and coworkers have demonstrated that treating cyclopropyl phenyl selenone (388) with potassium t-butoxide in THF and in the presence of a ketone results in the formation of an oxaspirane (389) in excellent yield.
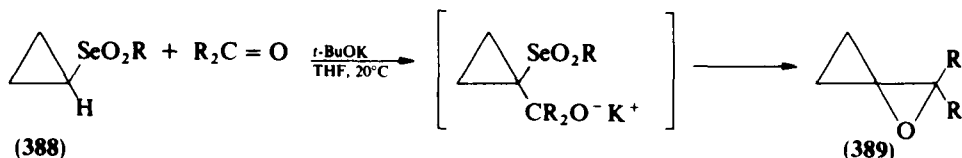
This reaction does not take place with the phenyl sulfone analogue but does occur when the phenyl selenone moiety is replaced by bromine[288d, e].
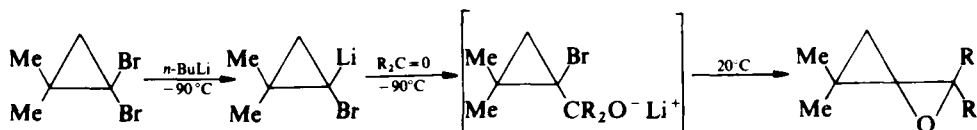
At first sight it is tempting to believe that the oxaspirane is produced by an intramolecular S_N2 displacement of the $RSeO_2^-$ or Br^- by the nucleophilic alkoxide. However, S_N2-type displacements on a cyclopropane are rare and usually very difficult, and we would therefore like to suggest the following alternative mechanism for the epoxide formation: the intermediate proposed in both examples undergoes cleavage to

(392)   (389)
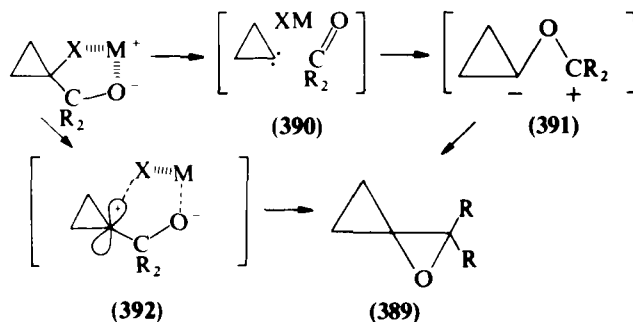
yield a carbene and carbonyl in a solvent cage (**390**). The electrophilic carbene can then recombine within the cage at the oxygen of the carbonyl to give the zwitterion **391**, which yields product **389**. Another possibility is that metal-assisted ionization (see Chapter 4 on carbenoids) helps to develop positive charge on the cyclopropyl carbon and the zwitterionic intermediate (**392**) collapses to product **389**. Experiments are required in order to decide between the possible alternatives.

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Note Added in Proof

a. α-Carbonyl and α-carboalkoxyl
Cyclopropylcarbonyl compounds **393** are much less acidic than the corresponding isopropyl compounds. On the other hand their enolates **394** are more difficult to handle because of their high reactivity.

(393)   (394)
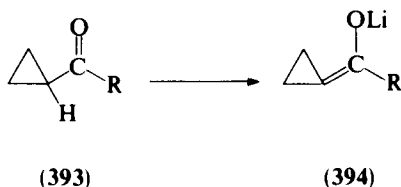
R = H, alkyl, aryl, OR, SR

This is due to the stabilization of a negative charge by a carbonyl group which, in contrast to nitrile or sulfonyl substituents (see Chapter 1, IV.B.1b, e and 2, *IV.*B.*1*b, *e), delocalizes the charge and forms enolates. In cyclopropyl enolates (**394**) this leads to an additional strain of *ca.* 13 kcal mol^{-1} [289]. The solid state structures of the lithiated cyclopropyl nitrile (374·THF)$_\infty$ and cyclopropyl sulfone **386**·DME (2/3) (see below), support the different modes of negative charge stabilization. In both cases the anionic carbon is tetrahedral and a lithium contact to this carbon atom is observed.

Thiol esters of cyclopropanecarboxylic acids are more amenable to α-lithiation[206-208] followed by reactions with electrophiles than other cyclopropylcarbonyl compounds. The

lithium enolate of the thiolester **395** has now been characterized by X-ray diffraction as the TMEDA and hexane complex [**395** · TMEDA · hexane]$_2$[290].

(**395**)
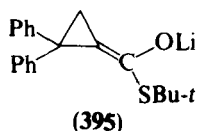
As with other TMEDA coordinated enolates, a Li–O–Li–O four-membered ring is formed[291] and each lithium is in contact with one TMEDA molecule. No Li/C interaction is observed in contrast to (**374** · THF)$_\infty$ and **386** · DME (2/3). The 'anionic' carbon Cl is very weakly ($\Delta = 0.07$ Å) pyramidalized. The C=C and C–O bond lengths are identical to those in other ester enolates[291] (Figure 7).
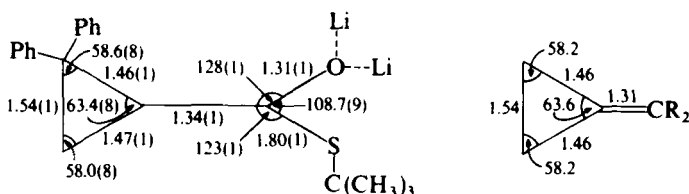
FIGURE 7. Some bond lengths (Å) and bond angles (degrees) in (**395**·TMEDA · hexane)$_2$ (left) and in other methylene cyclopropanes[292] (right).

The shortening of the vicinal bonds Cl–C2 and Cl–C3 and the lengthening of the distal bond C2–C3 (compared with cyclopropane (C–C: 1.509 Å[281])) agrees well with the bond lengths found in other methylene cyclopropanes[292]. In contrast, in [**374** · THF]$_\infty$ and in **387** the distal bonds are shorter than the vicinal bonds. It has been suggested that this is due to the acceptor substituents[280] and to the metals[290] attached to the carbon.

Enolate **395** forms clathrates with n-hexane to give [**395** · TMEDA · hexane]$_2$ with completely disordered hexane molecules. Interestingly in **386** · DME (2/3) one DME molecule similarly cocrystallizes[293].

m. α-Nitramine

The first nitramine anion known is one formed at a three-membered ring. In a recent work. Lillya and Sassi[294] reacted N-methyl N-nitro-1-(trimethylsilyl)cyclopropyl amine with Et$_4$NF in the presence of electrophiles such as water or MeCHO. From the products in which H or CH(Me)OH, respectively, replaced the SiMe$_3$ group, the intermediate formation of the α-anion of N-methyl-N-nitrocyclopropylamine is inferred.

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CHAPTER **3**

Cyclopropyl cations

I. INTRODUCTION

The topic of cyclopropyl cations has been extensively reviewed[1], the most recent review being that of Friedrich in 1987. This chapter will include a discussion of the structure of the cyclopropyl cation and how substituents in the α and β positions of the cyclopropane ring affect the structure and reactivity of the cation. Some applications to syntheses will be covered where deemed appropriate.

II. STRUCTURE

A. Open Structure

In our discussions of the cyclopropyl radical and the cyclopropyl anion we noted that the electron or the electron pair of these reactive intermediates occupied a σ orbital. However, the empty orbital of the cyclopropyl cation would be expected to be a p orbital which would result in a planar cationic center. Although the presence of a planar center would reduce Pitzer strain[2], it would severely increase the angle strain (Baeyer or I strain)[3]. This would account, in part, for the low relative rate of solvolysis of 1 ($\simeq 10^{-5}$) as compared with 3, since going to the cationic intermediate would be expected to have a very high activation energy. Under these constraints the cyclopropyl cation, if formed, would be expected to quickly convert, by ring opening, to the strain-free and more stable allyl cation (equation 1).

$$ (1) $$
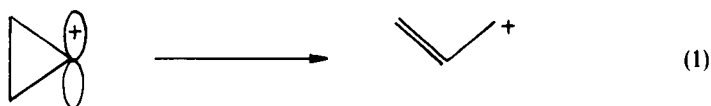
Indeed, *ab initio* molecular orbital calculations by Radom, Hariharan, Pople and Schleyer[4a] have shown that the allyl cation is 39 kcal mol^{-1} more stable than the cyclopropyl cation. Moreover, as will be shown, the cyclopropyl cation need not exist at all since it would be expected to be converted to the allyl cation with little or no activation energy[4a]. Relative solvolysis rates have been used to support this thesis. Kinetic analysis of the rates of solvolysis of cyclopropyl tosylate (1), 7-norbornyl tosylate (2) and cyclohexyl tosylate (3) showed the relative rates to be 10^{-5}, 10^{-7} and 1, respectively. Thus, the rate of cyclopropyl tosylate was enhanced in spite of the fact that the bond angle at the reaction site was smaller (60°) than that of 7-norbornyl tosylate (94°). The opposite would have been expected, since going to a planar cyclopropyl cation (120°) would increase the I strain[3]. Foote[4b] and Schleyer[4b] both concluded that the enhanced solvolysis rate of cyclopropyl tosylate was due to concerted ionization and ring opening. Although arriving at the correct conclusion, the argument presented may well be flawed since the bonds in cyclopropane are not true σ bonds, making bond angles of 60°, but are 'bent bonds'[5] whose orbitals overlap at angles of 101–104°.

     (1)   **(2)**   **(3)**
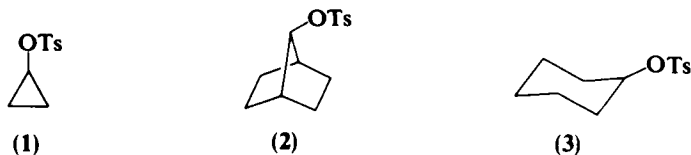
DePuy and coworkers[6] also concluded that the solvolysis of cyclopropyl tosylates involved a concerted ionization and ring opening. This conclusion was also based on a kinetic argument. Both *cis*- and *trans*-2-phenylcyclopropyl tosylate solvolyze faster than cyclopropyl tosylate, even though the inductive effect of the phenyl group would have been expected to decrease the rate. Moreover, the product of the solvolysis was solely the

ring-opened product cinnamyl acetate and no 2-phenylcyclopropyl acetate could be found.

Earlier, Woodward and Hoffmann[7, 8] as well as Longuet-Higgins and Abrahamson[9] and also Fukui[10] had proposed that the cyclopropyl–allyl rearrangement was an example of a 2π concerted electrocyclic ring opening and predicted that the reaction should be stereospecific and should occur, according to the rules governing conservation of orbital symmetry, in a disrotatory manner (the conrotatory is disallowed).

In principle, of course, there exist two disrotatory modes. DePuy and coworkers[6], based on their observation that cis-2-phenylcyclopropyl tosylate solvolyzed at one-fifteenth the rate of trans-2-phenylcyclopropyl tosylate, concluded that 'the direction of rotation is dependent upon the stereochemistry of the leaving group': cis substituents move inwards leading to the less stable endo-substituted allyl cation, while trans substituents move outwards giving the thermodynamically more stable exo-substituted allyl cation (equation 2).

$$(2)$$
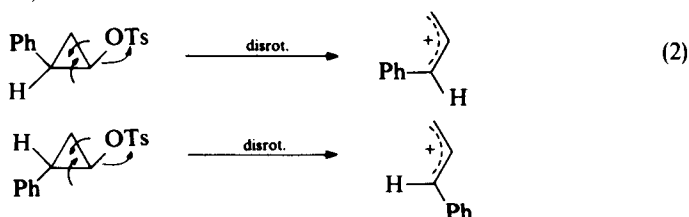
The suggestion of DePuy was reinforced by further molecular orbital calculations[8, 10, 11]. The 'Principle of Least Motion'[12] was also applied to the cyclo-propyl–allyl rearrangement and similarly predicted that the above-mentioned mode would be, by far, the most favorable reaction path[13]. Direct experimental verification was provided by Schleyer, Saunders and coworkers[14a] who demonstrated, by ^{1}H-NMR spectrometry at $-100\,°C$ in strong acid medium, that the isomeric 2,3-dimethyl-cyclopropyl chlorides 4, 6 and 8 yielded the stereoisomeric allyl cations 5, 7 and 9, respectively (equation 3).

$$(3)$$
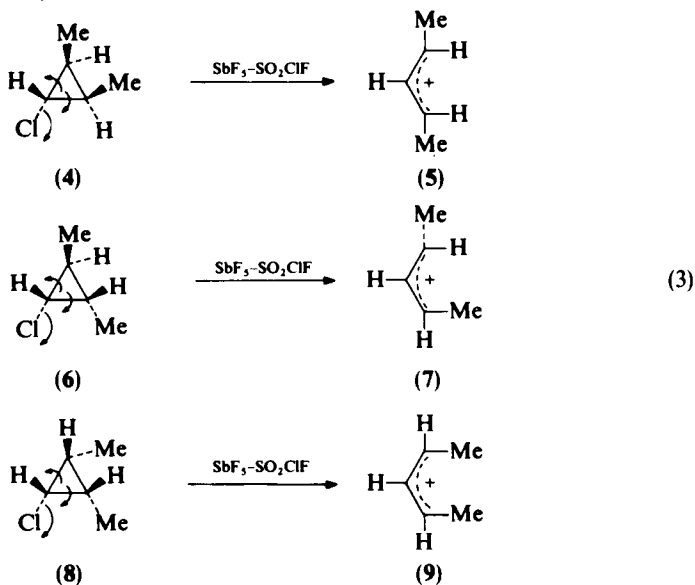
Also consistent with this interpretation are the observed rates of acetolysis of the isomeric chlorides[15a] **4, 6** and **8** relative to cyclopropyl chloride at 100 °C; $k_4 = 1.3 \times 10^6$, $k_6 = 2.0 \times 10^4$ and $k_8 = 1.7 \times 10^2$. The corresponding tosylates were [15b] in the same relative order 3.8×10^4, 4.6×10^2 and 2.2. Ledlie and MacLean[16] took advantage of the Woodward–Hoffmann–DePuy rules to separate r-1-chloro-1-phenyl-cis-2,3-dimethyl-cyclopropane (**10**) from a mixture with its isomer r-1-chloro-1-phenyl-trans-2,3-dimethylcyclopropane (**11**) by treating the mixture with methanolic $AgNO_3$ at room temperature for 10 hours. Pure **10** was readily isolated from the product mixture since **11** had rearranged and solvolyzed to the allyl ether **12** (equation 4).
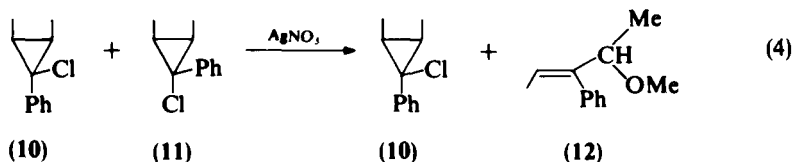
In summary, both the kinetics and stereochemistry of the cyclopropyl(halide or tosylate)–allyl cation ring-opening reactions are best described as concerted processes in which carbons C-2 and C-3 of the ring rotate in a disrotatory manner. The disrotation occurs in such a way that the C-2–C-3 bonding electrons are rotated into a position enabling them to behave as a neighboring group and do a backside displacement of the leaving group. Hence, the cyclopropyl cation is best viewed as an open allyl structure.

B. Half-opened Structure

The products obtained from the acetolysis of endo- and exo-bicyclo[n.1.0]alkyl tosylates (Table 1) are of special significance [17, 18]. In the endo isomer (**13**$_n$) where $n = 3-6$, the solvolysis yields the product expected for a disrotatory ring opening: the cis,cis-allyl cation (**14**$_{3-6}$) which is converted to the cis-eneacetate (**15**$_{3-6}$) (equation 5).
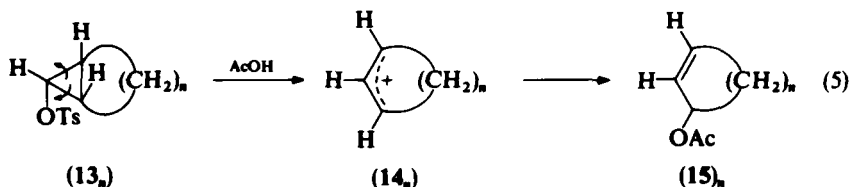
TABLE 1. Relative acetolysis rates of endo- and exo-bicyclo[n.1.0]alkyl tosylates **13**$_n$ and **16**$_n$ at 100 °C[17, 18]

(**13**$_n$), $n =$	Relative rate[a]	(**16**$_n$), $n =$	Relative rate[a]
3	2.5×10^4	3	10^{-4}
4	62	4	1.7
5	3.1	5	2.5×10^3
6	3.5	6	1.0×10^4

[a] Relative to cyclopropyl tosylate[19]; $k = 3.89 \times 10^{-8} s^{-1}$.

However, the disrotation should be strongly disfavored for the *exo* tosylates (16_n) because of strain factors, since ionization would lead to a *trans,trans*-allyl cation 17_n which gives the eneacetate 18_n (equation 6).

$$(16_n) \qquad\qquad (17_n) \qquad\qquad (18)_n \qquad (6)$$
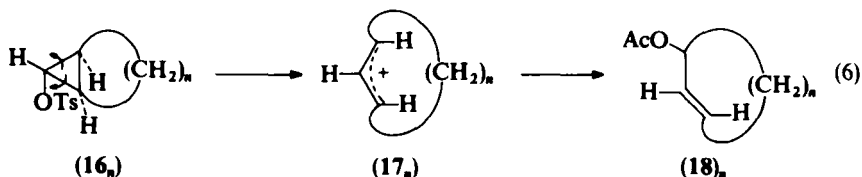
As a matter of fact 90% of 16_3 is recovered after being heated for three months in acetic acid at 150 °C[17]. This is a remarkable affirmation of the validity of the Woodward–Hoffmann–DePuy rule.

As *n* increases in 16_n, and assuming that the Woodward–Hoffmann–DePuy rule operates, one might expect an increase in rate since the (*trans, trans*) intermediates 17_n are becoming less strained (more stable). However, models indicate that the 17_n can only be completely strain-free when $n = 9$ or 10. Schöllkopf[17] and Schleyer and Bremer[18] suggested that the *exo* derivatives give only a 'half-open' cation 19_n, which is somewhere

$$(19_n)$$
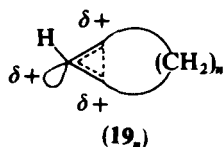
between a cyclopropyl and an allyl cation, a compromise between strain energy and delocalization energy. Note that the hydrogen attached to the cationic center is out of the plane and that the empty orbital is pyramidal[18]. This would account for the relative rates observed for the *exo*-tosylates 16_n (Table 1), $n = 6 > 5 > 4 \gg 3$. Moreover, the 'half-open' cation 19_4 accounts nicely for the formation of *exo*-acetate 20_4 and *cis*-cycloheptyl-1,3-diacetate (22)[20] (equation 7). The latter is formed by the expected addition of acetic acid to the initially formed, strained *trans*-3-cycloheptenyl acetate (21). The retention of configuration observed for the *exo*-acetate 20_4 is the expected consequence of a nonplanar carbocation such as 19_4.

$$(16_4) \qquad\qquad (19_4) \qquad\qquad (21) \qquad\qquad (22) \qquad (7)$$

$$(20_4)$$
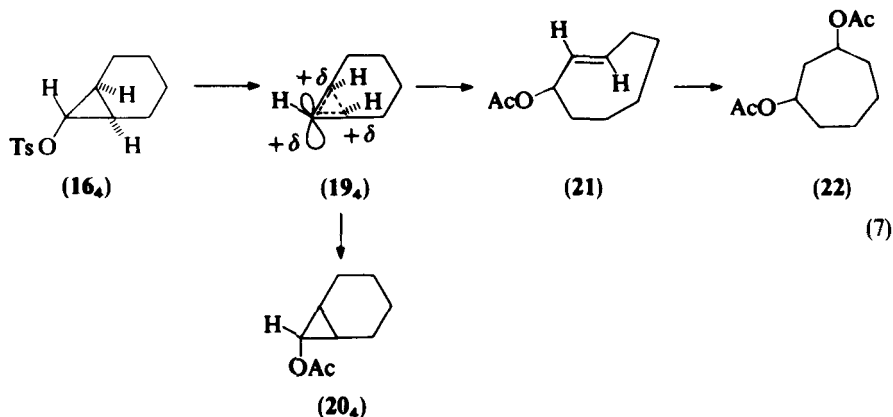
Theoretical confirmation by *ab initio* molecular orbital theory of the 'half-opened' structure for 19_{3-6} has recently been provided[18]. These calculations also show that 13_2 would not yield a 'half-opened' cation on solvolysis but would instead go directly to the essentially planar cyclopentenyl cation due to the relief of *ca* 54 kcal mol^{-1} of strain energy, a conclusion reached earlier by Jorgensen[21] and observed experimentally by Schöllkopf[22a] and Tufariello[22b] and their coworkers. Direct observation of the postulated 'half-opened' cyclopropyl cation has been made by Olah, Ledlie and coworkers[23] in their ^{1}H- and ^{13}C-NMR analyses of the species **24** obtained by dissolving 11-methyl-11-bromotricyclo[4.4.1]undecane (**23**) in sulfuryl chloride fluoride and slowly adding it to a solution of antimony pentafluoride in sulfuryl chloride fluoride at $-120°$ C (equation 8). Analysis of the spectra was consistant with a 'bent, distinct cyclopropyl cation stabilized by homoconjugation'. This description is equivalent to, but not necessarily identical with, the postulated 'half-opened' cyclopropyl cation. These authors view **24** as a bent cyclopropyl cation.

$$\text{Br, Me (23)} \xrightarrow[-120°C]{SbF_5-SO_2ClF} \text{Me (24)} \qquad (8)$$
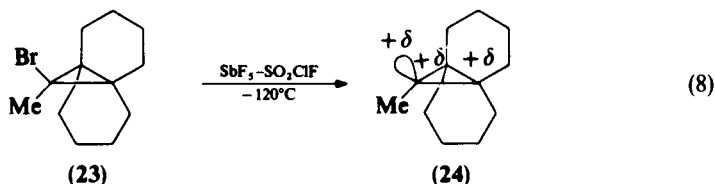
In keeping with the proposed 'half-opened' structure **24** is the observation of Ledlie and coworkers[24] that in the silver-ion-assisted methanolysis of the isomers **25** and **26**, the reactions proceeded with 87% and 97% retention of configuration, respectively (equation 9).

$$\text{Br, Me (25)} \xrightarrow[MeOH]{Ag^+} \text{MeO, Me} \qquad (9)$$

$$\text{Me, Br (26)} \xrightarrow[MeOH]{Ag^+} \text{Me, OMe}$$
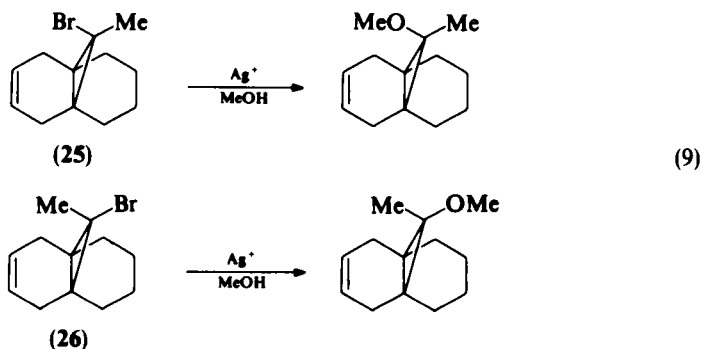
Further stereochemical evidence favoring the 'half-opened' structure has been provided by Kirmse. Kirmse and Jandrella[25] had reported that the decomposition of *exo*-7-norcaranediazonium ion in the presence of sodium bromide yielded *exo*-7-bromo-norcarane as the major product, a result which would be in keeping with the suggestion of Schöllkopf[17] and Schleyer[18] that a half-opened intermediate 19_3 was involved. Moreover, Kirmse and Engbert[26] also reported that the diazotization of isomers **27** and **28** in the presence of sodium bromide yielded their respective bromides with 97–99% retention of configuration (equation 10). This result is comparable to that of Ledlie and coworkers[24] and is consistent with the generation of a 'half-opened' cyclopropyl intermediate,

H₂N, H → ⁺N₂, H →(Br⁻)→ Br, H

(27)

(10)

H, NH₂ → H, N₂⁺ →(Br⁻)→ H, Br

(28)
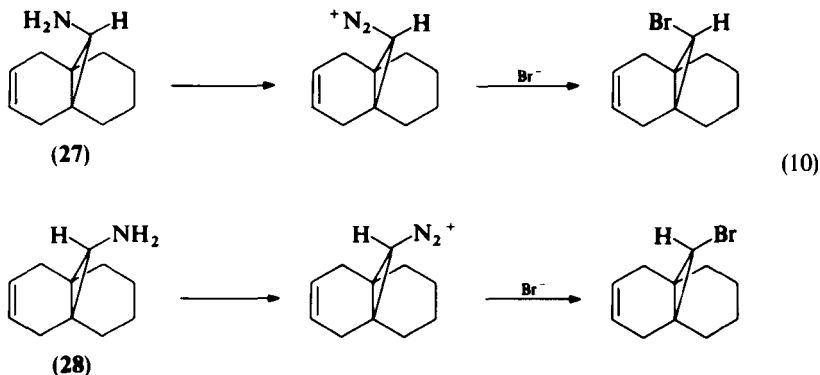
especially when one considers that the usual result from diazonium ion decomposition is that of inversion of configuration, as demonstrated by Kirmse and Arold[27] in the azide capture of the α-phenylethyl cation (74% overall inversion) and by Moss and Schueler[28] who observed an overall 73% net inversion in the lithium azide decomposition of chiral octane-2-diazotate.

Thus, the 'half-opened' cyclopropyl cation, the closed cyclopropyl cation, the cyclopropyl radical and the cyclopropyl anion have the common structural feature in that the empty orbital (cation), half-filled orbital (radical) or filled orbital (anion) all involve pyramidal σ orbitals.

C. Closed Structure

As we have seen, the solvolysis of monocyclic cyclopropyl halides and tosylates leads by a concerted 2π disrotatory electrocyclic ring opening to the corresponding allyl system. Under these circumstances the cyclopropyl cation does not exist as such and is best viewed as an open cation. However, when structural or electronic constraints are placed on the ring so that the 2π electrocyclic ring opening is disfavored, then the cyclopropyl cation can be viewed as a 'half-opened' structure or possibly as a closed structure. How is one to differentiate these latter two possibilities? That is a difficult question to answer. For our purposes we will initially make the arbitrary decision based on kinetics and product analyses. When, for example, as in 16_4, the reaction is slow and the products of the reaction are a mixture of both a closed product with retained configuration and an open allyl product, then we will assume that these products result from a 'half-opened' intermediate. When the product of the reaction is largely, if not entirely, a cyclopropyl derivative of retained configuration, then the intermediate will be viewed as a closed nonplanar cyclopropyl cation.

In an *ab initio* molecular orbital calculation[29] of 1-X-cyclopropyl cations, where X is H, CH₃, NH₂, OH, F, CN and NC, it was found that all the substituents were stabilizing except for CN. The order of stabilization was NH₂ > OH > CH₃ > F ≃ NC. For all substituents with the exception of X = OH and NH₂, the corresponding 2-X-allyl cations are found to be much lower in energy than the isomeric 1-X-cyclopropyl cations. Since there is little or no barrier to ring opening[4b], with the exception of structural constraints leading to 'half-opened' structures (*vide supra*), one would not expect the cyclopropyl cation as such to exist. The only possibility is when X = NH₂ and OH, in which cases the cyclopropyl cation is of lower energy than the corresponding allyl cation[29]. In this connection the 1-dimethylaminocyclopropyl cations[30] have been reported to be observable by NMR spectroscopy. The *ab initio* calculation of Lien and Hopkinson[29a] have

seemingly been substantiated by the observation of the 1-methoxycyclopropyl cation in the gas phase by ion cyclotron resonance. The existence of cyclopropanone itself can also be viewed as an example of the stabilizing effect of oxygen[1c] since the ketone is more stable than the open 2-oxyallyl form (equation 11). If the disrotatory mode of ring opening is

$$\left[\text{(cyclopropanone)} \longleftrightarrow \text{(oxyallyl cation)} \right] \longleftrightarrow \text{(allyl cation, } O^-) \tag{11}$$
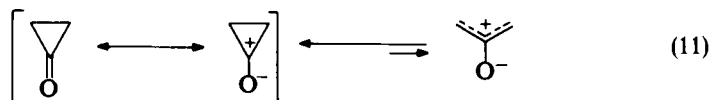
highly unfavorable, would this be a sufficient condition to allow a closed cyclopropyl cation intermediate to be trapped? The work of Pettit[31a], who reported that diazotization of amine **29** yielded the unrearranged chloride **30** (equation 12), has been cited as a possible example. Pettit himself[31a], however, suggests that under the strongly acidic conditions employed by him there occurred an S_Ni reaction leading to formation of **30**.

$$\underset{(\textbf{29})}{\text{NH}_2} \xrightarrow[\text{HCl}]{\text{HONO}} \underset{}{\text{N}_2{}^+\text{Cl}^-} \longrightarrow \underset{(\textbf{30})}{\text{Cl}} \xrightarrow[\text{MeNO}_2]{\text{AgClO}_4} \underset{(\textbf{31})}{\text{ClO}_4{}^-} \tag{12}$$
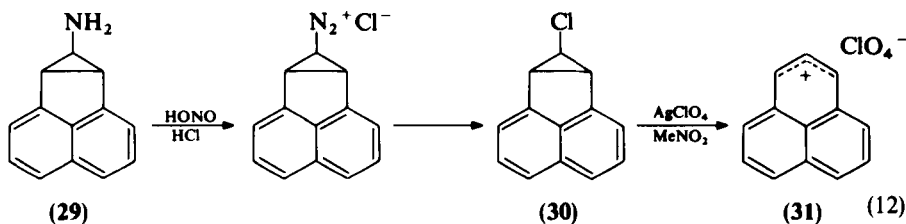
This suggestion was predicated on the observation that the treatment of **30** with silver perchlorate, a reaction known to produce cations, leads to the ring-opened product **31**. An ambiguity still exists, however, since the deamination could be a kinetically controlled reaction between the cyclopropyl cation and chloride ion leading to **30** whereas the reaction of silver perchlorate with **30** is undoubtedly thermodynamically controlled. Dewar and Ganellin[31b] also reported that the deamination of **32** using conditions similar to those of Pettit (strong HCl) gave a 40% yield of unrearranged chloride **33** (equation 13).

$$\underset{(\textbf{32})}{\text{H}\diagdown\text{NH}_2} \xrightarrow[\text{HCl}]{\text{HONO}} \underset{(\textbf{33})}{\text{H}\diagdown\text{Cl}} \tag{13}$$
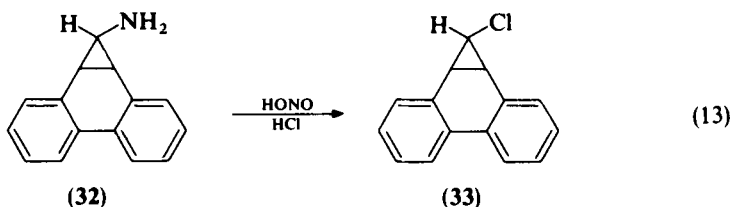
An interesting example is provided by Hart and Martin[32] who confirmed the earlier work of Lipp and Padberg[33] that diazotization of 1-aminonortricyclene (**34**) gave exclusively the unrearranged 1-acetoxynortricyclene (**35**) (equation 14). It should be

$$\underset{(\textbf{34})}{\text{NH}_2} \xrightarrow[\text{HONO}]{\text{AcOH}} \underset{(\textbf{35})}{\text{OAc}} \tag{14}$$
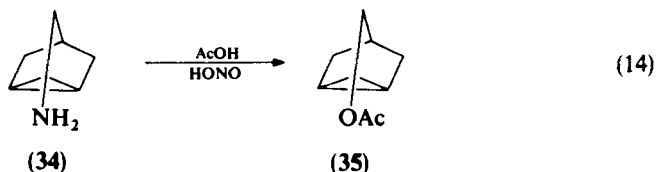
appreciated that if **34** forms a cationic intermediate, then the cyclopropyl cation is at a bridgehead carbon as well. This assures that the intermediate is a fixed nonplanar cyclopropyl cation (**36**), since inversion of the substituents at the cationic carbon atom is not possible. Moreover, electrocyclic ring opening would be energetically unfavorable, since it would lead to a highly strained allyl cation whose double bond is at a bridgehead (equation 15).

(15)

(**36**)
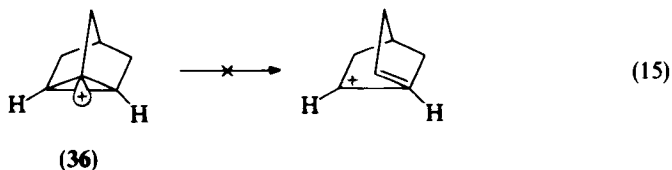
D. Conclusions

The cyclopropyl cation is unique in that one may observe very rapid ring opening to the allyl cation. For many ring-opening reactions the energy of activation is close to zero; thus these intermediates will undergo concerted disrotatory ring opening to the allyl cation when the following conditions are met:

(1) When the allyl cation is more stable than the cyclopropyl cation ($E_a \simeq 0$).
(2) When groups *anti* to the leaving group (X) can rotate outwards without undue strain.
(3) When the α-substituent (Y) is not stabilizing.

If all the above conditions are met, then the cyclopropyl cation does not exist as such but can best be viewed as an open allyl cation (equation 16) since, as the leaving group

Half-open   Open

(16)

Closed
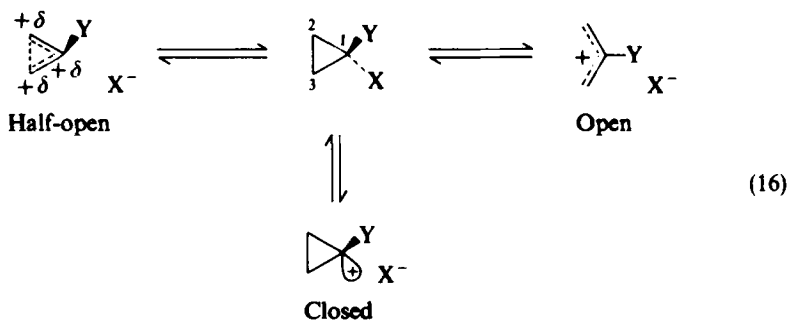
departs and before a full positive charge can develop, disrotatory ring opening occurs and one is well on one's way to the allyl structure. The simplest examples are found in the acetolysis of cyclopropyl tosylate[15b] or halide[19] in acetic acid which yields exclusively allyl acetate and in the diazotization of cyclopropylamine which gives allyl alcohol[34].

At the other end of the spectrum from the open structure is the completely closed structure. The best example is the 1-nortricyclyl cation **36**. Between these two extremes one finds the half-open cyclopropyl cation (equation 16), the sturcture of which will vary with changes in α- and β-substituents. These substituents will affect the extent to which the C-2–C-3 bond is stretched.

Both the closed and half-opened cyclopropyl cations are nonplanar and therefore an inversion barrier should exist (equation 17) as it does for the nonplanar cyclopropyl

$$\sigma \rightleftharpoons \pi \rightleftharpoons \sigma \qquad (17)$$
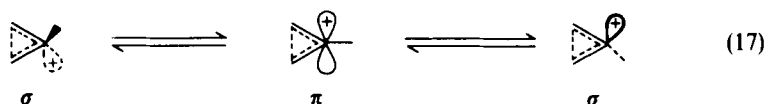
radical and anion. The expected stereochemical consequences would be overall retention of configuration.

III. EFFECTS OF SUBSTITUENTS

A. Leaving Group

1. Halogen and esters

As we have previously discussed, the reactivity of the leaving group (X) depends on its location relative to the other substituents in the ring. Since the disrotatory mode of ring opening is preferred, X should be located *trans* to the substituents in monocyclic systems in order to facilitate reaction. The works of Parham and Yong[35a], Olah and coworkers[35b] and Hausser and Uchic[36], illustrate this point nicely as shown by the rate data for compounds 37–42. The most extensive study is due to Schleyer and coworkers[15a] who

(EtOH; Ag$^+$; 80°C)[35]

(37)	(38)	(39)
$k(s^{-1})$ 2.2 × 10^{-8}	8.2 × 10^{-5}	1.2 × 10^{-6}

(AcOH, NaOAc; 95°C)[36]

(40)	(41)	(42)
$k(s^{-1})$ 3.6 × 10^{-6}	1.2 × 10^{-2}	2.5 × 10^{-4}
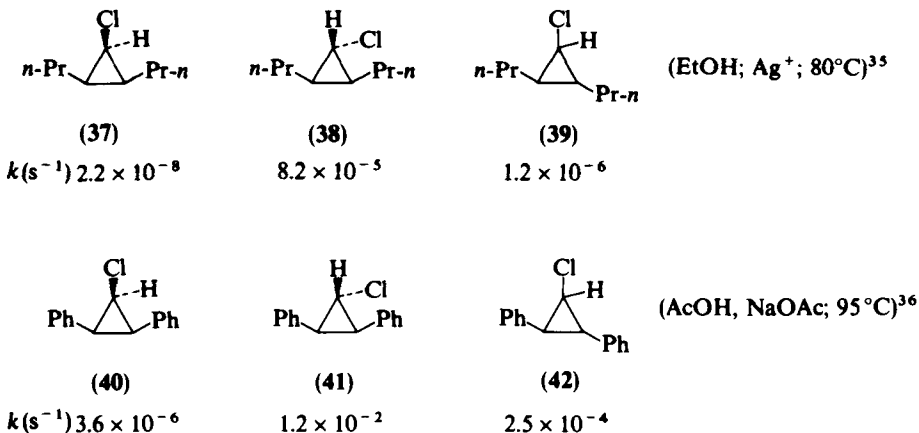
investigated the acetolysis rates of a large number of β-alkyl-substituted cyclopropyl tosylates, bromides and chlorides. In general, the order of reactivity is OTs > Br > Cl. However, there may be a dampening effect in the case of the cyclopropyl system. It can be seen from Table 2 that the relative rate difference between bromide and tosylate is much less than it is in the isopropyl system, although this effect is not observed in the corresponding chloride and bromide. Schleyer and coworkers also demonstrated the influence which the stereochemistry of a β-methyl substituent exerts on the leaving group. As can be seen from Table 3, the order of reactivity is still in general OTs > Br > Cl but the differences among the geometric *cis–cis*, *trans–trans* and *cis–trans* isomers are not as dramatic as those found for the β-propyl and β-phenyl substituents (*vide supra*).

Of the esters of cyclopropanol that are used as leaving groups, the trifluoromethanesulfonate (triflate OTf) is by far the fastest and should be the leaving group of choice

TABLE 2. Effect of the leaving group on the rate of acetolysis at $100\,°C^{15a}$

X	k_{rel}	X	k_{rel}
Cl	1	Cl	1
Br	25	Br	86
OTs	13000	OTs	2310

TABLE 3. Acetolysis rates of the geometric isomers of 2,3-dimethylcyclopropyl systems at $100\,°C^{15a}$

Leaving group	trans–trans k_1 (s^{-1})	cis–cis k_1 (s^{-1})	cis–trans k_1 (s^{-1})
OTs	1.59×10^{-3}	9.0×10^{-8}	1.93×10^{-5}
Br	7.72×10^{-4}	1.28×10^{-7}	1.5×10^{-5}
Cl	2.43×10^{-5}	2.96×10^{-9}	3.18×10^{-7}

TABLE 4. Acetolysis of cyclopropyl esters at $100\,°C^{16}$

X	OTs	ONs^a	ODNs^b	OTf^c
k_1, s^{-1}	4.16×10^{-8}	7.6×10^{-7}	8.6×10^{-6}	4.4×10^{-4}

^{a} p-Nitrobenzenesulfonate.
^{b} 3,5-Dinitrobenzenesulfonate.
^{c} Trifluoromethanesulfonate.

for applications in synthesis. Table 4 lists a number of such esters and the first-order rate constants for their solvolysis (equation 18).

(18)
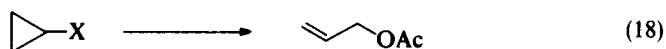
All the above data were obtained from cyclopropyl derivatives which may lead to the open cyclopropyl cationic structure. How will the leaving group be affected when the intermediate involved has the half-opened structure? The results of the acetolysis of the 7-norcaryl system should provide us with the necessary information (Table 5). In this system the *endo* isomers can undergo the favored disrotatory ring opening leading to the open allyl cation, whereas the *exo* isomer leads to the half-opened cyclopropyl cation (equation 19).

endo   *exo*   (19)
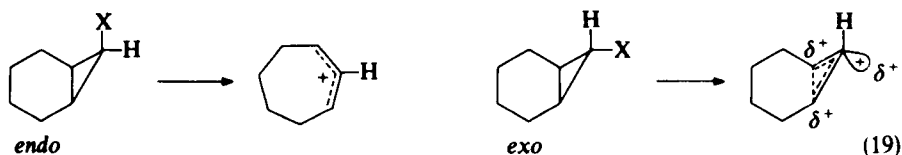
TABLE 5. Relative acetolysis rates at 200 °C for 7-norcaryl isomers[15a]

Leaving group	k_{rel}, exo	k_{rel}, endo
OTs	1^a	1^b
Br	2.7×10^{-3}	1.27
Cl	1.6×10^{-3}	5×10^{-2}
OTf	4000	815

^{a} $k_1 = 2.67 \times 10^{-4}$ s^{-1}.
^{b} $k_1 = 2.52 \times 10^{-2}$ s^{-1}

TABLE 6. Relative acetolysis rates^a of the geometric isomers of 2,3-dimethylcyclopropyl derivatives at 100 °C[15a]

Leaving group	trans–trans	cis–cis	trans–cis
OTs	3.8×10^4	2.2	4.6×10^2
Br	5.0×10^5	82	9.7×10^3
Cl	1.3×10^6	167	2.0×10^4

^{a} Relative to the parent cyclopropyl derivative: cyclopropyl tosylate $k_1 = 4.16 \times 10^{-8}$ s^{-1}; cyclopropyl bromide $k_1 = 1.55 \times 10^{-9}$ s^{-1}; cyclopropyl chloride $k_1 = 1.8 \times 10^{-11}$ s^{-1}.

As might be expected, the solvolysis rate of the *endo* isomer is *ca* 100 times faster than that of the *exo* isomer, since the latter leads to the half-opened cyclopropyl cation rather than to the more stable open allyl cation which results from the solvolysis of the *endo* isomer. The effect of the leaving group for the *endo* isomer shows that it follows the sequence OTs $\leq$ Br > Cl, and for the *exo* isomer the sequence is OTs > > Br $\geq$ Cl. The *endo* sequence is similar to that found in the acetolysis of the *cis,cis*-2,3-dimethylcyclopropyl system (Table 3).

Schleyer and coworkers[15a], in examining the relative solvolysis rates (relative to the parent cyclopropyl) of, *inter alia*, the three geometric isomers of the 2,3-dimethyl-cyclopropyl derivatives (Table 6), found that the magnitude of the alkyl substituent effects is in the order Cl > Br > OTs. They conclude from their extensive studies that the rate enhancement provided by *trans-β*-methyl groups leading to the Cl > Br > OTs sequence is due to electronic effects. For the *cis-β*-substituted system, steric factors play the significant role. It can be seen that the accelerating effect on the chloride solvolysis and less so on the tosylate solvolysis negates the difference between the rates of reaction of the halides and tosylates (the van der Waals radii are Cl > O).

2. Nitrogen

Although no direct comparison with the halogen and ester leaving group is available, nitrogen (N_2) is also a good leaving group. It should be noted that the direct diazotization of amines by nitrous acid is not the preferred mode for generating the diazonium ion intermediates from which nitrogen is extruded to yield the desired cationic intermediate. This was discussed earlier in connection with compounds **29** and **32**. The preferred method is the deacylation of nitrosoamides and this method has been used extensively by Kirmse and Jandrella[25] as well as by others[35] to generate cations. However, care must be taken to assure that one deals with a diazonium ion and not with the diazo compound as

the intermediate. Decomposition of the former leads to cations whereas the latter yields carbenes[27,28,37-39]. This is nicely illustrated[40] using the 7-norcarene-7-diazonium ion (43) generated by deacylation of the nitrosoamide (44). The diazonium ion can lose nitrogen to give the cationic intermediate 45 or, if a strong base is present, it can lose a proton to yield the *diazo* intermediate 46. The *diazo* compound can then lose nitrogen to give a carbene intermediate 47 (equation 20). Fortunately, it is possible to control the reaction conditions so that one is producing solely the diazonium ion intermediate[26,35].

(44)   (43)   (45)

$$-H^+$$

(46)   (47)   (20)
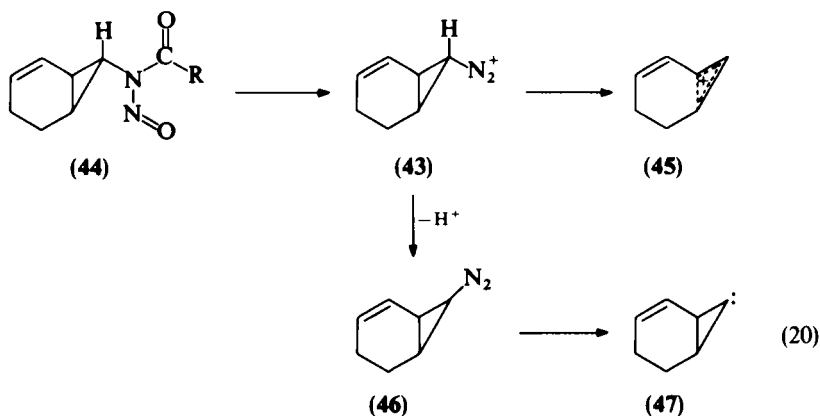
The deamination reactions are usually faster than solvolysis of the halides, requiring only *ca* 0.5 hour for nitrous acid diazotization[31] and about 20 hours for the deacylation of nitrosoamides[28].

3. Dimethylsulfonium salts

Dimethyl sulfide has also been used as a leaving group from dimethylsulfonium salts[41]; the solvolysis is slower than for the chlorides or bromides and higher temperatures are required. Table 7 gives the methanolysis rates for the 1-(methylthio)cyclopropyl derivatives (equation 21). The trimethyl ammonium group has also been used as a leaving group[41b]. Note that the methylthio group stabilizes the cyclopropyl cation and prevents ring opening. We will discuss this in more detail in the following section.

(21)

TABLE 7. Methanolysis rates for 1-(methylthio)cyclopropyl derivatives[41a]

Leaving group (X)	Temperature (°C)	$k \times 10^6$ (s^{-1})
Cl	20	24.9
Br	20	2200
Me$_2$S	48	25.5

B. α-Substituents

1. Introduction

We have discussed the cyclopropyl cation–allyl cation transformation from the viewpoints of stereochemistry and energy differences. Although the addition of stabilizing groups at the β position will increase the difference in energy between the cyclopropyl cation and the allyl cation, adding stabilizing groups to the α position (cf equation 22) should minimize the difference.

$$\text{(22)}$$
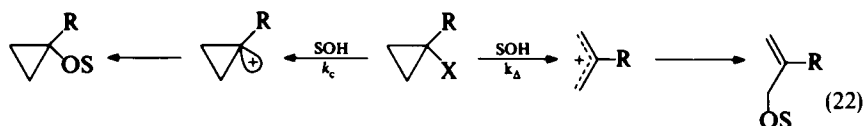
As indicated earlier, Radom, Pople and Schleyer[29b] and more recently Lien and Hopkinson[29a] have performed *ab initio* molecular orbital calculations on the stabilities of α-substituted cyclopropyl cations relative to the corresponding allyl cation. The α-substituents studied were R = H, CH$_3$, NH$_2$, F, CN and NC. Table 8 reports their findings in more detail. Note that only when the substituent is NH$_2$ and possibly OH is the cyclopropyl cation stabilized relative to the allyl cation. The cyano group appears to be the only destabilizing substituent.

TABLE 8. Energies (kcal mol^{-1}) of the 1-R-cyclopropyl cations relative to the 2-R-allyl cations

Substituent (R)	H	Me	NH$_2$	OH	F	CN	NC
6-31G*//3-21G	38.5	19.6	−23.4	1.3	26.3	34.6	20.3

2. Effect on rate of solvolysis

It can be seen from Table 9 that α-substituted cyclopropyl tosylates are much more reactive than the unsubstituted cyclopropyl tosylate (R = H). At 25 °C the acetolysis of α-methylcyclopropyl tosylate is 10^3 times faster than acetolysis of the parent cyclopropyl tosylate. A phenyl group stabilizes the developing positive charge even more to the extent that the cyclopropyl cation can be trapped with the aid of sodium borohydride[42] before it opens to the allyl cation. By comparing an α-phenyl with a cyclopropyl group, we note that the latter is even more effective in stabilizing the positive charge. From Tables 9 and 10 one notes that the decreasing order of stabilization is cyclopropyl > phenyl > vinyl > MeC≡C > i-propyl > H. The effect of stabilizing positive charge on the extent of ring opening to allyl products will be discussed.

3. Effect of α-cyclopropyl on product formation

Landgrebe and Becker[43a] were the first to point out that the presence of a cyclopropyl group in the α position resulted not only in ring opening to the allyl but also yielded the ring-closed product as well. For example, the acetolysis, in the presence of silver acetate, of 1-chloro-1-cyclopropylcyclopropane (**48**) gave a 43% yield of unrearranged 1-acetoxy-1-cyclopropylcyclopropane (**49**).

TABLE 9. Effect of α-substituents on the solvolysis of cyclopropyl derivatives

R	X	Solvent	Temp. (°C)	k_1 (s^{-1})	Ref.
H	OTs	AcOH	25	5.71×10^{-13}	16
	OTs	AcOH	100	4.16×10^{-8}	16
	OTs	80% EtOH	25	4.17×10^{-12}	16
	OTs	50% EtOH	25	3.29×10^{-11}	16
	Br	50% EtOH	130	2.6×10^{-6}	43
	Cl	50% EtOH	95	2.5×10^{-10}	43
Me	Br	50% EtOH	130	1.1×10^{-4}	43
	OTs	AcOH	25	6.16×10^{-10}	16
	OTs	AcOH	100	1.3×10^{-5}	16
i-Pr	OTs	50% EtOH	70	1.83×10^{-5}	44
Ph	OTs	AcOH	50	5.5×10^{-6}	45
	OTs	AcOH	108	1.9×10^{-3}	45
	OTs	50% EtOH	70	8.6×10^{-3}	46
∇	OTs	80% EtOH	25	1.29×10^{-4}	44
	OTs	50% EtOH	70	2.9×10^{-1}	47
	Cl	50% EtOH	95	1.6×10^{-4}	43
C=C	OTs	50% EtOH	70	1.6×10^{-4}	44
Me–C≡C	OTs	50% EtOH	70	1.4×10^{-5}	47
▷–C≡C	OTs	50% EtOH	70	1.9×10^{-3}	47
	Br	50% EtOH	70	1.7×10^{-5}	47
PhC≡C	OTs	50% EtOH	70	8.3×10^{-5}	47
p-MeC$_6$H$_4$C≡C	OTs	50% EtOH	70	6.3×10^{-4}	47
p-MeOC$_6$H$_4$C≡C	OTs	50% EtOH	70	1.3×10^{-2}	48
MeO	Cl	MeOH	38	1.9×10^{-5}	41
MeS	Cl	MeOH	37	2.2×10^{-4}	41
MeO	Me$_2$S$^+$	MeOH	48	2.5×10^{-5}	41
MeS	Me$_2$S$^+$	MeOH	48	1.4×10^{-5}	41
MeS	Br	MeOH	20	2.2×10^{-3}	41

TABLE 10. Relative solvolysis rates of α-substituted cyclopropyl tosylates in 50% EtOH at 70°C

R	i-Pr	MeC≡C	CH$_2$=CH	Ph	∇
Relative rate	1	8	10	470	1600

Under aqueous conditions the only product isolated was **51**, which presumably resulted from a catalyzed opening of **50** via an S_E2 mechanism (equation 23)[49].

$$\tag{23}$$
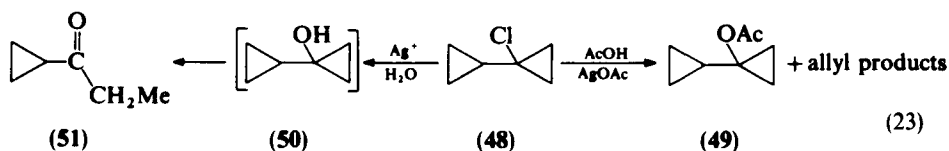
Acetolysis of the tosylate **52** under buffered conditions gave the ring-closed acetate **49** in 24% yield and the ring-opened allyl acetate **53** in 65% yield (equation 24)[44a].

$$(24)$$

(52)   **(49)**   **(53)**
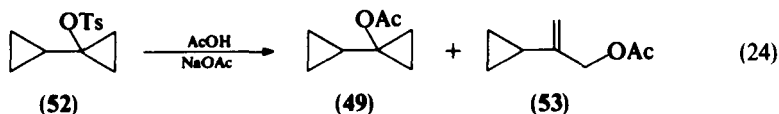
Also, in 50% acetone buffered with calcium carbonate **52** gave 59% of the ring-closed alcohol **50** and 41% of the ring-opened allylic alcohol **54**, a result similar to that of acetolysis. However, when **52** was hydrolyzed in 50% acetone, without the $CaCO_3$, **50** was produced in 63% yield and ketone **51** was isolated in 24% yield (equation 25). Moreover, when the mixture of **50** and **54** was treated with *p*-toluenesulfonic acid in 50% acetone, the mixture of products **50** and **51**, produced in the unbuffered reaction, was obtained, thus showing that the ring-opened allylic alcohol **54** was the precursor of ketone **51** (equation 25).

$$(25)$$
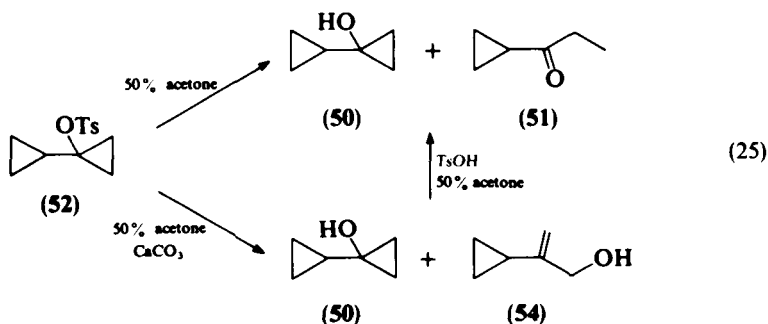
However, if there is an equilibrium between the closed (**55a**) and open (**55b**) cation, then **50** and **54** could be the kinetically controlled reaction products whereas **50** and **51** could be the thermodynamically controlled reaction products (equation 26).

(50)   **(55a)**   **(55b)**   **(54)**

$$(26)$$

(51)
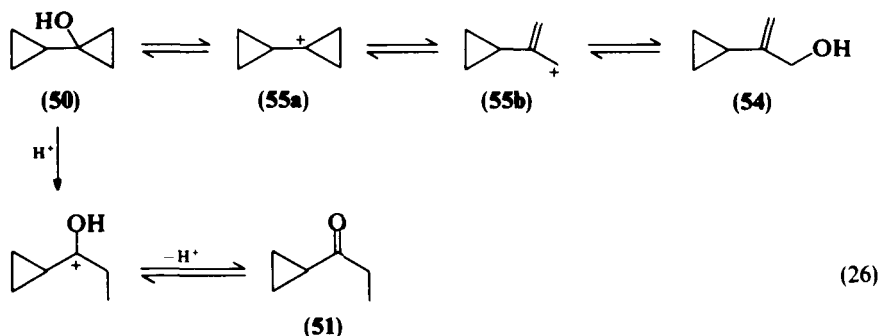
Martin and Landgrebe[43b] showed that in the acetolysis of **52** containing two deuterium atoms on C-2 of the ring substituted by the tosyloxy group, there was no scrambling of the deuterium. The ring substituted by the acetate in **49** also possessed the two deuterium atoms. This eliminates possible degenerate rearrangements of the type depicted in equation 27.

$$ (27) $$
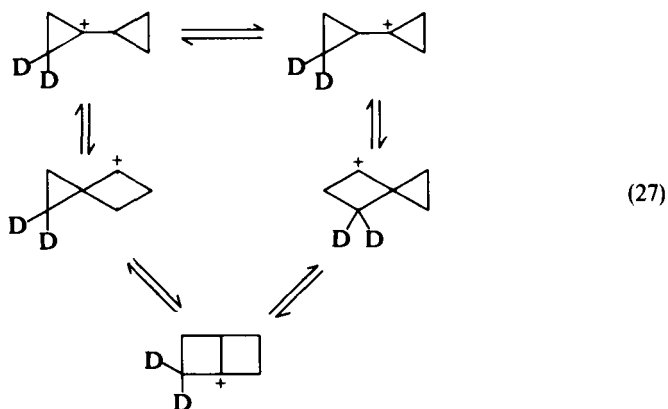
Kirmse and coworkers[41f] have confirmed the conclusions of Martin and Landgrebe[43b]. The decomposition of the E and Z isomers of 1-diazonium-1-cyclopropyl-2-deuterio-cyclopropane in methanol yielded the corresponding methyl ethers with no scrambling of the deuterium (equation 28). The important point is that one can isolate appreciable amounts of closed-ring product.

$$ Z \qquad 9.4\% \qquad 8.9\% \ (50{:}50) \qquad 81.7\% \ (51{:}49) $$

$$ E \qquad 9.2\% \qquad 9.2\% \ (51{:}49) \qquad 81.6\% \ (49{:}51) $$

$$ (28) $$
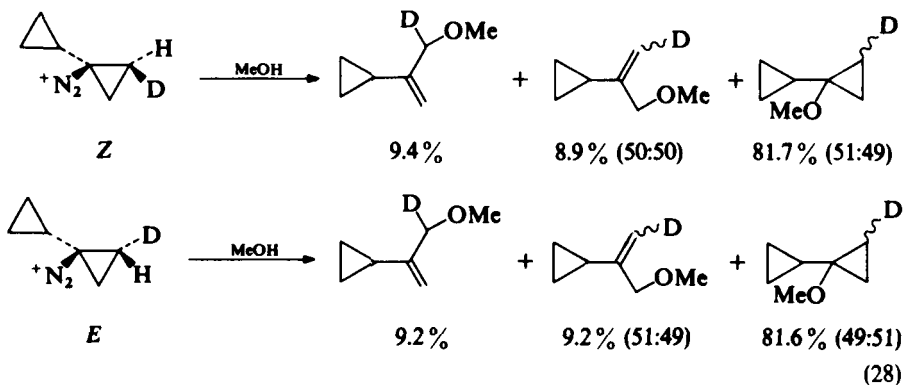
Why does an α-cyclopropyl group stabilize the cyclopropyl cation? Probably due to its ability to withdraw charge, since the cation also becomes a cyclopropyl carbinyl cation which provides extensive charge delocalization due to the well-known behavior of such cations[19,50]. Thus the cyclopropyl group provides an efficient 'vertical' stabilization[51] of the electron-deficient center probably via a bisected intermediate 56[44b] (equation 29).

$$ (56) \qquad (29) $$
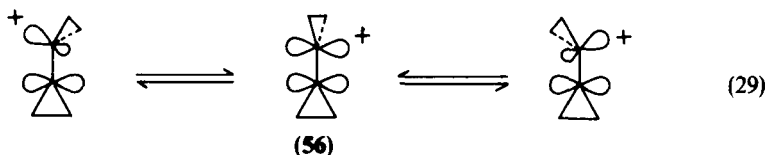
It is this stabilization which forms the basis for understanding the spiropentylcarbinyl cation rearrangement as demonstrated by the elegant study of Gajewski and Oberdier[52].

Migration of C-3 leads to formation of the cyclobutyl cation which is trapped by solvent. This is the well-recognized cyclopropylcarbinyl–cyclobutyl cation rearrangement[1a]. On the other hand, migration of C-2 would and does lead to intermediate **56**, which could then give rise to a mixture of **49** and **53** (equation 30). The

(30)

(49)   **(53)**

48%   11%   23%   12%
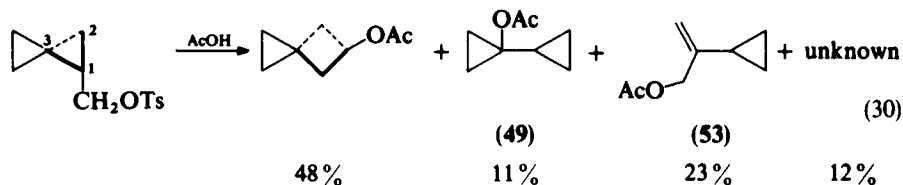
proportion of these two is almost the same as that observed in the acetolysis[44a] of 1-tosyloxy-1-cyclopropylcyclopropane (**52**).

Also in keeping with the stabilized intermediate **56** is the further observation that *both isomers* of the β-methyl substituted spirane give rise to the same product. This would be expected if the planar cation **56** opens in a disrotatory manner (equation 31).

a or b = Me   **(56)**   a = Me
                                                            b = H

(31)
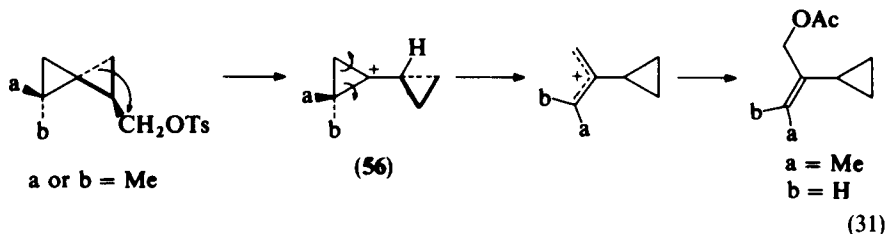
4. α-Phenyl

It can be seen from Table 9 that the α-phenyl group stabilizes the developing positive charge more effectively than an α-methyl or isopropyl group but not as effectively as an α-cyclopropyl group. Schleyer and coworkers[15a] argue that when a phenyl group is directly attached to a center of developing positive charge, the adverse inductive effect is more than compensated by the favorable benzyl-type delocalization and that on this basis an α-phenyl group is better in stabilizing a positive charge than an α-methyl.

The high sensitivity of α-arylcyclopropyl tosylates to the introduction of ring substituents in the solvolysis reaction is due to the fact that the transition state has a structure resembling that of a cyclopropyl cation stabilized by an aryl group and, as we indicated earlier, the ring-closed intermediate has been trapped[42] by sodium borohydride (also *vide infra*). Another argument[45] in favor of the ring-closed intermediate rather than the open allyl type is the weak sensitivity to the introduction of substituents in the aromatic ring in the solvolysis of 2-arylallyl tosylates ($\rho = -0.4$). Of course, if no effective nucleophile is present then **57** goes to the open 2-phenylallyl intermediate (equation 32).

(32)

(57)
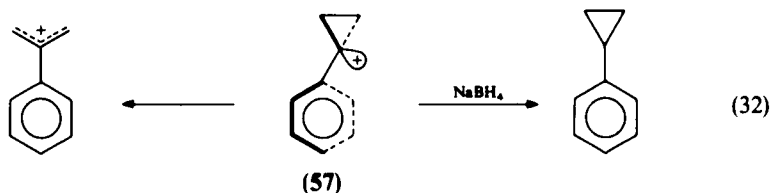
An interesting example of stabilization by an α-phenyl group was provided by de Boer and coworkers[41b] who showed that treatment of the quaternary ammonium salt, depicted below, with methanolic KOH gave a 73% yield of ring-closed product (equation 33).

$$
\left[\text{structure: o-hydroxyphenyl cyclopropyl NMe}_3^+ \right] \text{I}^- \xrightarrow[\text{MeOH}]{-\text{OH}} \cdots \longrightarrow \left[\cdots \longleftrightarrow \cdots \right]
$$

(33)

HO
cyclopropyl
OMe
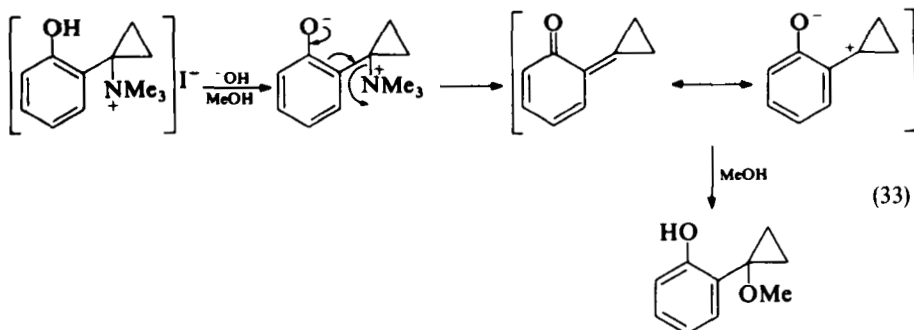
A p-anisyl group also yielded a completely closed product[41c] regardless of the leaving group (equation 34).

$$
\text{(cyclopropane with X and p-OMe-phenyl)} \xrightarrow{\text{MeOH}} \left[\cdots \longleftrightarrow \cdots \text{OMe} \right]
$$
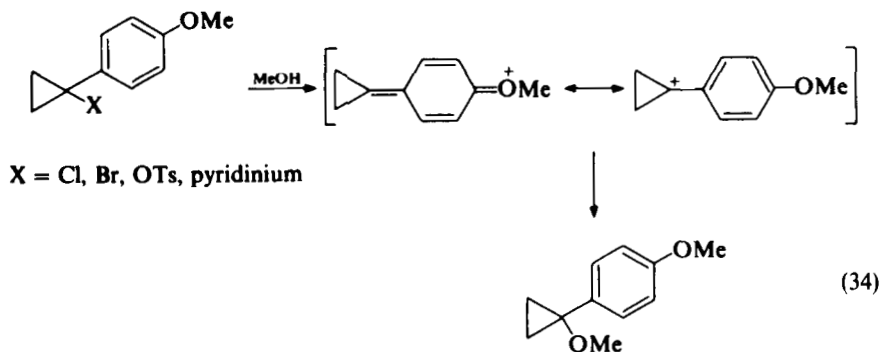
X = Cl, Br, OTs, pyridinium

OMe
(cyclopropane)
OMe

(34)

The cation could also be trapped by added azide, chloride or bromide[41d] ions. When the p-anisyl group is replaced by the less stabilizing p-tolyl group, then a mixture of ring-closed and ring-opened product containing a significantly larger amount of the former is obtained (equation 35)[41d].

$$
\text{(cyclopropane with X and p-Me-phenyl)} \xrightarrow{\text{MeOH}} \text{(product OMe)} + \text{(ring-opened product OMe)}
$$

(35)

X		ratio	
Cl	5	:	3
OTs	10	:	3
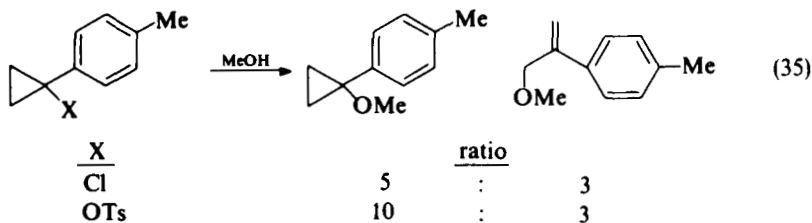
Kirmse and Rode[41e], using the diazonium ion as a leaving group with m-trifluoromethylphenyl, phenyl and p-methoxyphenyl in the 1-position also demonstrated the effectiveness of the p-methoxy group but, under their conditions, the α-phenyl-substituted system already yielded 37.2% of ring-closed product (equation 36).

(36)

R	% yield	
m-CF$_3$	21.8	78.2
H	37.2	62.8
p-MeO	98.2	1.8
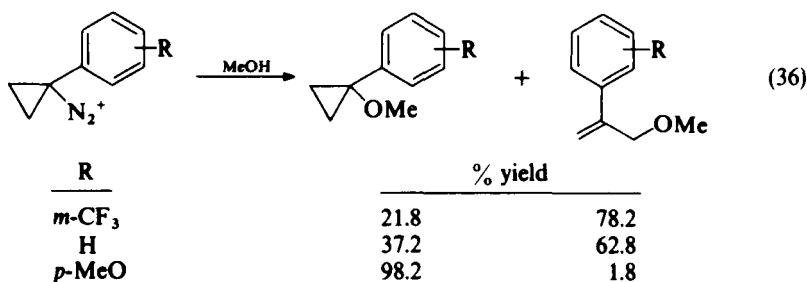
5. α-Vinyl

There is little information on the effect of an α-vinyl substituent. Howell and Jewett[44a] reported that 1-vinylcyclopropyl tosylate solvolyses at 70°C in 50% EtOH at only three times the rate of 1-isopropylcyclopropyl tosylate. Both tosylates are reported to yield open products. As can be seen from Table 9, the solvolysis of the α-phenyl-substituted system is only 40 times faster than that of the α-vinyl-substituted system. It has yet to be determined whether the presence of the vinyl group leads to a cyclopropyl cation intermediate or to a concerted disrotatory ring opening. The low solvolysis rate would suggest that the α-vinyl would behave like the α-phenyl substituent.

α-vinylcyclopropanols have found extensive use in syntheses[53]. They are convenient precursors for cyclobutanones via ring expansion. This subject has been reviewed[1a,53] elsewhere. Of interest is that reaction of the α-vinylcyclopropanols with acid does not involve a cyclopropyl cation formed by protonation of the hydroxyl moiety but instead involves a cyclopropylcarbinyl cation formed by protonation of the double bond. This is consistent with the observed difficulty in breaking a cyclopropyl–oxygen bond even though in this case the hydroxyl group is also allylic (equation 37).

(37)
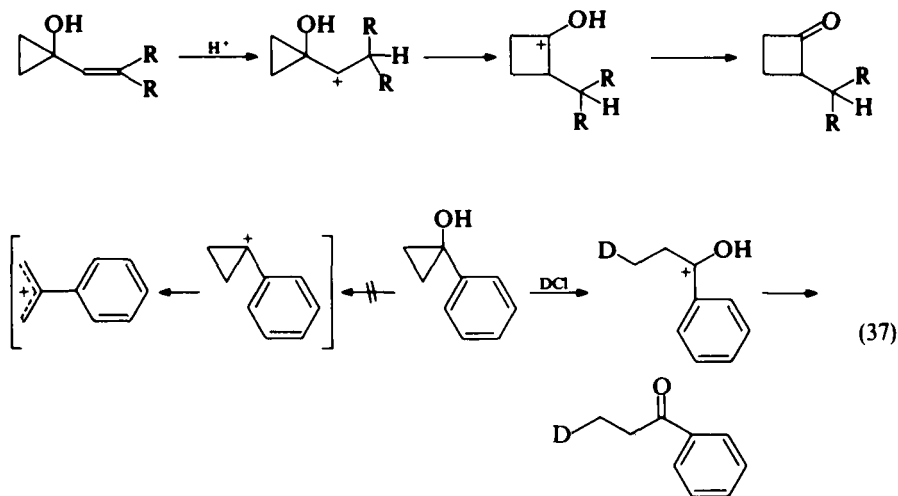
Treatment of cyclopropanols with acids presents an interesting situation. Will the proton react with the hydroxyl group to give an oxonium ion as a leaving group leading to a cyclopropyl cation intermediate, or will the proton react with the nucleophilic

cyclopropane? The answer to this question was provided by DePuy and coworkers[1d,49] who demonstrated that the treatment of α-phenylcyclopropanol with deuterium chloride (1 N) in dioxane–water at 50°C yielded propiophenone containing only a single β-deuterium atom (equation 37).

Moreover, it was shown that (−)-(1S,2R)-1-methyl-2-phenylcyclopropanol (58), when exposed to the identical conditions, gave a 60:40 mixture of (−)-(S)-4-phenylbutanone-2 (59) and 3-phenylbutanone-2 (60). Treatment of the mixture with NaOD racemized 60 and the resultant mixture was chromatographed to give pure (−)-(S)-59 (equation 38).

(−)-(1S,2R)-(58)   (−)-(S)-(59)   (38)

                                                                                                    (60)
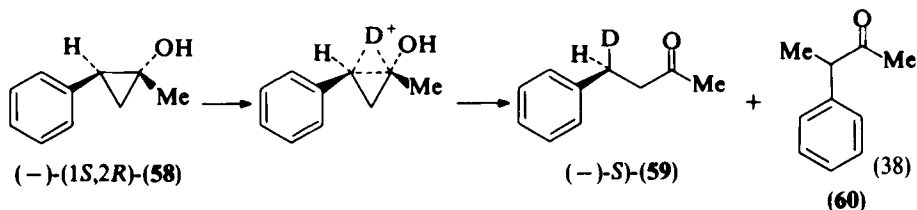
Since the absolute configuration of 58 and 59 had been established, the stereochemistry of the ring-opening reaction is that of retention of configuration. The proposed mechanism[49] is edge deuteriation between C-1–C-2 of the ring. Again, we note that the cyclopropyl–oxygen bond is not broken, but instead it is the ring which is attacked by the proton.

6. α-Ethynyl

As we have seen, vinylcyclopropanol derivatives underwent facile acid-catalyzed rearrangement to cyclobutanones. Ethynylcyclopropanol derivatives, on the other hand, are remarkably stable toward acids. This would be in keeping both with the difficulty in breaking the cyclopropyl–oxygen bond and with the difficulty in breaking the carbon–carbon triple bond, which is known to undergo hydration with difficulty. Thus, heating 1-ethynylcyclopropanol (61) with 0.75 N HCl even with a catalytic amount of mercuric chloride resulted in recovery of 61[54].

(61)
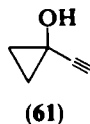
However, the activated acetylene derivative 1-ethoxyethynylcyclopropanol (62) gave, under identical conditions, the hydrated derivative 63 but without ring-opening.

Interestingly enough, the electrophilic Cl$^+$ attacks the ring in what appears to be an S_E2 reaction to yield 64[53]. It has also been reported[54] that Cl$^+$ will attack the triple bond of 62 resulting in rearrangement of the ring and yielding the cyclobutanone derivative 65 (equation 39).

The apparent stability of 1-ethynylcyclopropanols toward acids prompted the investigation by Salaün of the solvolytic behavior of the corresponding tosylates[46–48,53]. Although a double bond in acyclic systems stabilizes an adjacent carbon cationic center, the triple bond has been shown to have a destabilizing effect[55] by a factor of about 10^3. However, it can be seen from Table 9 that 1-propynylcyclopropyl tosylate (66) solvolyzes at a rate that is almost identical to that of the 1-isopropylcyclopropyl tosylate.

(64)   (62)   (63)

(39)

(65)

(66)   (67)   (68)
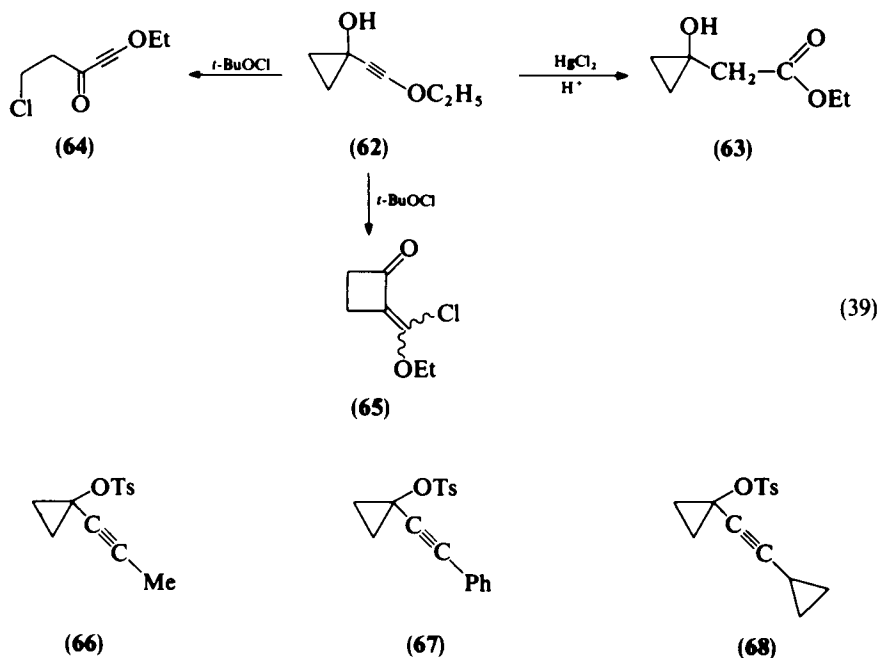
Moreover replacing the methyl group of **66** by a phenyl group to give **67** or by a cyclopropyl group to give **68**, increases the solvolysis rate fivefold for **67** over **66** and by a factor of 10^2 for **68** over **66**. As we have noted before, the cyclopropyl group is superior to a phenyl or vinyl group in stabilizing a positive charge on an adjacent cyclopropyl carbon atom (Table 9). The stabilization is undoubtedly due to the effective delocalization of charge as in **69**.

(69)   R = Me, Ph, ◁
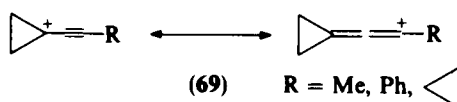
This finds an analogy in the work of Hanack and coworkers[56], who solvolyzed cyclopropylidenebromomethanes and determined the following relative rate of formation of their corresponding cationic intermediates **70–73** at 100 °C in 80% EtOH.

(70)   (71)   (72)   (73)

k_{rel} 1 1×10^3 2.5×10^3 1×10^5
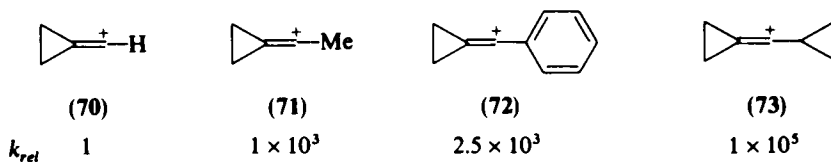
One notes the striking similarity with the relative rates of **66, 67** and **68**. Product analysis also reveals the stabilizing effect of the cyclopropyl group. Cation **70** rearranges to the cyclobutenyl cation, which can react with water to yield cyclobutanone, the product of solvolysis in 60–80% ethanol (equation 40)[56].

$$\triangleright\!\!=\!\!\overset{+}{=}\!-\text{H} \longrightarrow \square_{+} \longrightarrow \square_{\text{OH}} \longrightarrow \square_{\text{O}} \tag{40}$$

(70)
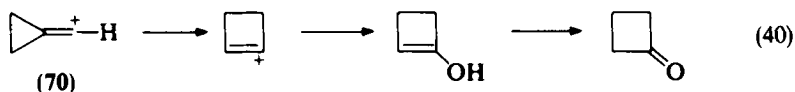
Cation **71** also rearranges to yield a mixture of **74** (35%) and **75** (65%). The latter compound is believed to result from internal return of bromide ion[56] (equation 41).

$$\triangleright\!\!=\!\!\overset{+}{=}\!-\text{Me} \longrightarrow \underset{+}{\square}_{\text{Me}} \xrightarrow{\text{H}_2\text{O}} \underset{\text{O}}{\square}_{\text{Me}}$$

(71)   **(74)**   (41)

$$\downarrow_{\text{Br}^-}$$

$$\underset{\text{Br}}{\square}_{\text{Me}}$$

(75)
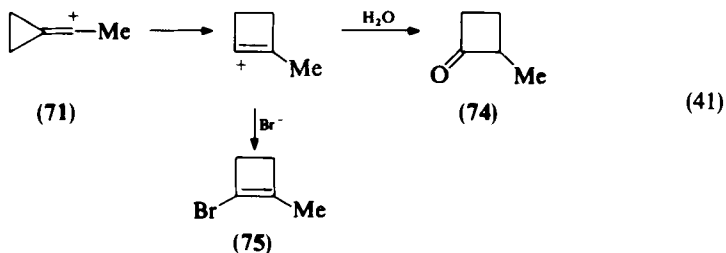
The increased stability of **72** is reflected in the fact that the main product is phenyl cyclopropyl ketone, which is formed by reaction of **72** with water. Of special significance is the observation that **73** gives rise to dicyclopropyl ketone as the only product. These results are in keeping with the postulate that removal of positive charge from the cyclopropyl ring will prevent ring opening.

Analysis of the products **77** and **78** from the solvolysis of **76** (equation 42) reveals a pattern (Table 11)[46-48] identical with that observed for the vinyl systems[56].

$$\overset{\text{OTs}}{\underset{\text{R}}{\triangleright\!\!=}} \xrightarrow[\text{Et}_3\text{N}]{\text{EtOH--H}_2\text{O}} \overset{}{\underset{\text{SO}}{=\!\!\equiv\!-\text{R}}} + \overset{\text{OS}}{\underset{\text{R}}{\triangleright\!\!=}} \tag{42}$$

(76)   **(77)**   **(78)**   S = H, Et
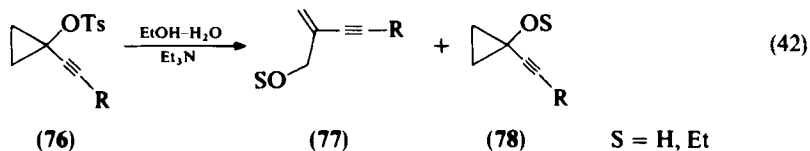
TABLE 11. Product distribution from the solvolysis of substituted 1-ethynylcyclopropyl tosylates in buffered aqueous ethanol[46-48]

R	77 Yield (%)^a	78 Yield (%)^a
Me	90	—
Ph	15	85
p-MeC$_6$H$_4$	5	95
p-MeOC$_6$H$_4$	0	100
$\triangledown$	6	94

^{a} S = H, Et

The product distribution as well as the kinetic data are consistent with delocalization of the positive charge by the adjacent triple bond leading to an intermediate **69**. When **69** can be further delocalized, such as when R = aryl or cyclopropyl, ring opening of the cyclopropyl group is inhibited. However, one must point out that if the aryl and

cyclopropyl group are so strongly stabilizing, then one might expect the reverse reaction, i.e. equation 43, to occur. However, an attempt to carry out this conversion has failed [46].

$$(43)$$
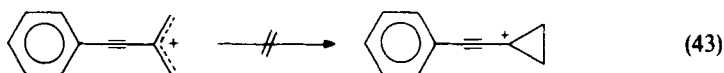
7. α-Alkyl

At 25 °C in acetic acid, 1-methylcyclopropyl tosylate solvolyzes only about 10^3 times faster than cyclopropyl tosylate (Table 9). A much larger acceleration would have been expected if this were an ordinary carbonium ion [16,55]. This decrease in the effect of α-methyl substitution and the increase in the effect of β-methyl substitution (*trans*-2-methylcyclopropyl tosylate solvolyzes *ca* 140-fold faster than cyclopropyl tosylate at 100 °C in EtOH) have been interpreted as being due to internal charge delocalization which is in line with stereospecific ring opening and with considerable progress toward an open allylic cation in the transition state[15b]. A concerted ring opening is also proposed for the solvolysis of 1-isopropylcyclopropyl tosylate[44a] which proceeds only 10^2–10^3 times faster than cyclopropyl tosylate.

A careful product analysis in the decomposition of α-substituted cyclopropyl diazonium ions **79** by Kirmse and coworkers[41f] is summarized in Table 12.

TABLE 12. Product analysis of α-substituted cyclopropyl diazonium ions[41f]

Configuration	R	R'	%	% (E:Z)	% (E:Z)
E	Me	D	47.8	48.1 (85:15)	4.1 (5:95)
Z	Me	D	51.0	43.7 (13:87)	5.3 (96:4)
E	Me	Me	60.1	39.8 (E)	0.09 (28:72)
Z	Me	Me	61.8	35.3 (16:84)	1.9 (96:4)
—	n-Pr	H	83.0	a	5.2
—	i-Pr	H	50.0	b	1.0

[a] An 11% yield of 1-propylidenecyclopropane and a 0.7% yield of 1-(1-methoxypropyl)cyclopropane were also obtained.
[b] A 14.7% yield of isopropylidenecyclopropane and a 34.3% yield of 1-methoxyisopropylcyclopropane were also obtained.

E-1,2-dimethylcyclopropanediazonium ion reacts stereospecifically, and 1-methyl-cyclopropanediazonium ion and *Z*-1,2-dimethylcyclopropanediazonium ion react with similar high stereoselectivity (~85:15). This would be in keeping with a concerted disrotatory ring opening. One should also note that, although the yield is quite small

(0.1–5.2%), the ring-closed product exhibits a high degree of inversion of configuration which implies that some S_N2 reactions have occurred. Of interest is the observation of products from elimination and 1,2-hydrogen shift rearrangements which indicates that a cyclopropyl cationic intermediate is being formed. The 1,2-hydrogen shift gives rise to a more stable cyclopropylcarbinyl system and this rearrangement becomes prominant (34.3% yield) when R = isopropyl (equation 44). There seems to be a gradual transition from a concerted to a stepwise mechanism which seems to depend on the nature and stereochemistry of the alkyl group.

$$\text{equation (44)}$$
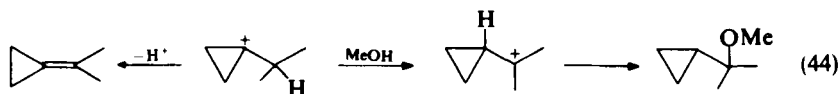
8. α-Halogen

Table 13 contains the rates of solvolysis of a number of mono- and dihalo-cyclopropanes[35]. As expected, the solvolysis rates are in keeping with the Wood-ward–Hoffmann–DePuy electrocyclic disrotatory ring opening. Note that 83 reacts about 10^3 times faster than 82. Of interest is the effect of the second chlorine on the rate of solvolysis. It can be seen, by comparing 80 with 83 and 81 with 84, that the second halogen retards the rate. This is not an unexpected result since the rate-determining step is the ionization of the first halogen, hence the second halogen is expected to inhibit this ionization through an inductive effect.

TABLE 13. First-order rate constants for solvolysis of halocyclopropanes at 80 °C in ethanol in the presence of silver nitrate[35]

	(80)	(81)	(82)	(83)	(84)[55]
k (s^{-1})	1.29×10^{-5}	5.3×10^{-7}	$<2.17 \times 10^{-8}$	8.20×10^{-5}	1.26×10^{-6}

The disrotatory electrocyclic ring opening to the allyl cations has been observed by ^{1}H NMR by Olah and coworkers[35b]. They found that 85 gives rise to 86 and that isomer 87 yielded a mixture of 88 and 86 (equation 45). When X = Cl, 88 comprised 77–99% of the mixture. The formation of 86 from 87 is bound to be due to a side-reaction involving protonation of 87[35b].

$$\text{(85)} \quad \xrightarrow[-117°C]{SbF_5-SO_2ClF} \quad \text{(86)}$$

$$Me \underset{H}{\overset{X\ X}{\triangle}} H \quad \xrightarrow[-117°C]{SbF_5-SO_2ClF} \quad Me\overset{X}{\diagdown\diagup_{+}}\underset{Me}{\diagup} \quad + \quad Me\overset{X}{\diagdown\diagup_{+}}\diagup Me \qquad (45)$$

(87)   (88)   (86)

X = Br, Cl
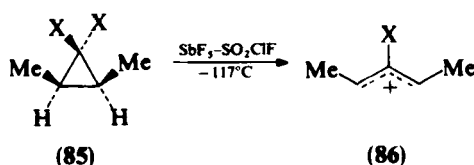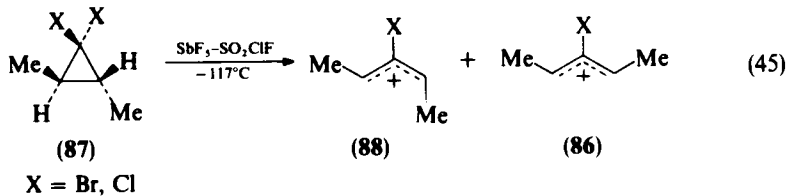
The dihalocyclopropanes are useful synthetic intermediates owing, in part, to their ease of formation by dihalocarbene addition to olefins[39a,b]. As we have previously discussed (Section III.B.2) for the *exo*- and *endo*-bicyclo[n.1.0]alkyl tosylates, the *endo* tosylate can, upon solvolysis, undergo a disrotatory electrocyclic ring opening to yield the *cis,cis*-allyl cation, which then reacts with solvent to give the *cis* olefin (equation 46).

$$(46)$$

(13$_n$)   (14$_n$)   (15$_n$)
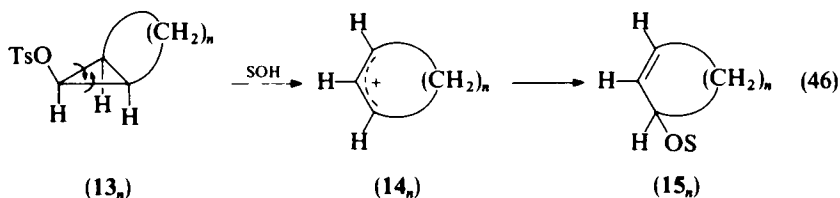
This is formally a ring expansion leading to a *cis* olefin and this type of reaction has found extensive use[39,57]. In theory n can be any whole number for the *endo* tosylate. However, for the *exo* tosylate this is not the case, since solvolysis will lead to a *trans–trans*-allyl cation by a disrotatory ring opening and this intermediate is highly strained.

The intermediate obtained under these conditions is best described as 'half-opened' (see Section III.B.2) when n = 3. However, when n = 4 or larger the intermediate 17$_n$ can exist and reaction of this intermediate with solvent will lead to a strained and reactive olefin 18$_n$ (equation 47) which would be expected to react further with solvent (acetic acid) to give in

$$(47)$$

(16$_n$)   (17$_n$)   (18$_n$)
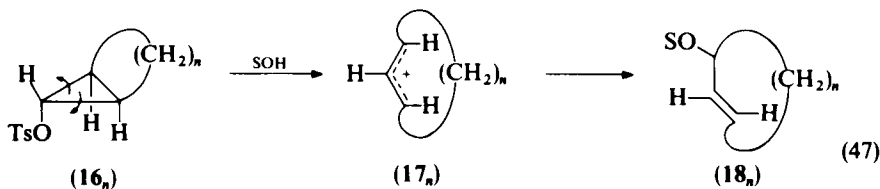
this case a cycloheptyl-1,3-diacetate 22 (equation 7)[20]. Thermal isomerization of a strained *trans* olefin to its *cis* isomer is also possible[58] and care must be taken to control the reaction conditions.

Moreover, it should be noted that the rates of solvolysis of *endo*-bicyclo[n.1.0]alkyl tosylates (giving *cis* isomers) decrease with increasing ring size while the reverse is true for the *exo* series (giving *trans* isomers).

With dihalocarbene adducts of cyclic olefins, where n = 5 or greater, the question arises as to which pathway (a or b in equation 48) is taken by the ring expansion.

There are two equivalent leaving groups, but one is *exo* and the other is *endo* oriented. It was shown that on treatment of 8,8-dibromobicyclo[5.1.0]octane (89a) with silver perchlorate in methanol at 20 °C, a quantitative yield of *trans*-2-bromo-3-methoxycyclooctene (90a) is obtained in five minutes[58](equation 49).

(48)

(89)	(90)	(91)	(49)
(a) X = Y = Br	(a) X = Br	(a) X = Br	
(b) X = Y = Cl	(b) X = Cl	(b) X = H	
(c) X = H, Y = Br	(c) X = H		
(d) X = Br, Y = H			
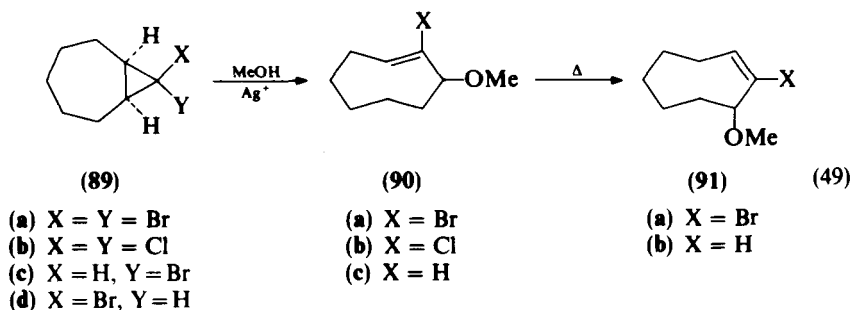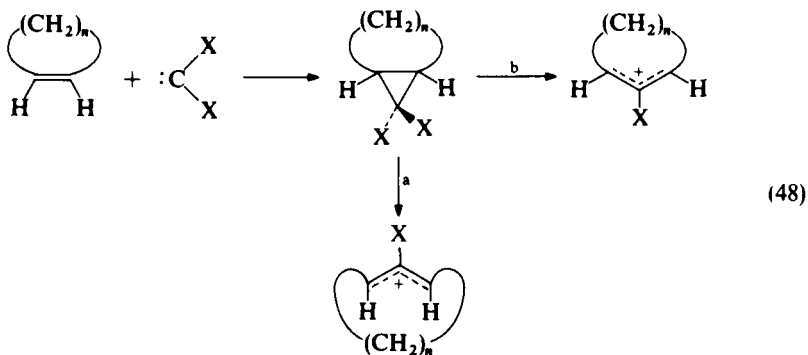
Thus the leaving group is *exo*, as one might expect, and the ring opening gives the *trans–trans* allyl cation which can now be accommodated. It was also demonstrated that heating **90a** converted it to **91a**, the *cis* isomer. The dichloro derivative **89b** behaved in a similar manner to yield **90b**. As anticipated the *exo*-isomer **89c** underwent rapid and quantitative conversion to *trans*-3-methoxycyclooctene (**90c**) whereas the *endo*-isomer **89d** reacted more slowly to yield the *cis*-isomer **91b** (equation 49).

All the above experiments were repeated with the next higher homologue, 9,9-dihalobicyclo[6.1.0]nonane (**92**), and similar results were obtained (equation 50). The mild conditions and excellent yields make this type of ring expansion very attractive.

(50)

(92)
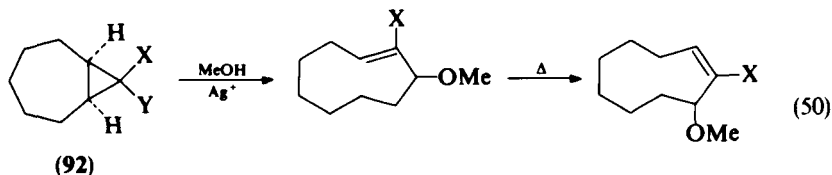
Graefe and Mühlstädt[59a] also showed that silver ion assisted solvolysis of **93** and **95** gave rise to **94** and **96**, respectively. In no case were products found which contained *cis* double bonds (equation 51).

Baird and Reese[59b] also undertook an investigation of the Ag$^+$-catalyzed methanolysis of *exo*-8-bromo (**97a**) and 8,8-dibromobicyclo[5.1.0]oct-2-enes (**97b**) in order to ascertain if double bonds conjugated with the cyclopropyl ring had any effect on the ring-expansion reaction.

(93)   (94)

(51)

(95)   (96)
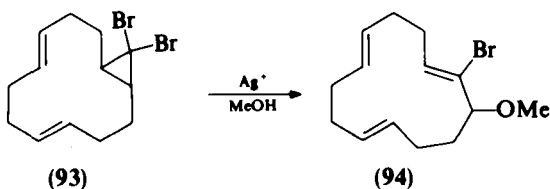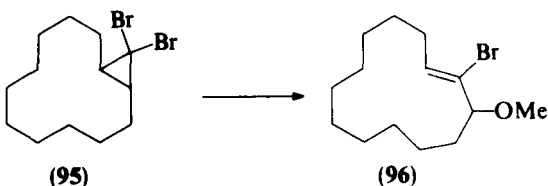
Treatment of *exo*-8-bromobicyclo[5.1.0]oct-2-ene (**97a**) with silver perchlorate in methanol gave a 1:1 mixture of **98a** and **99a** in 91% yield. Assuming the *trans–trans*-allylic cation as an intermediate, the observation of a 1:1 mixture of **98a** and **99a** implies that the solvent attacks both ends of the allylic cation at roughly equal rates. A similar result was obtained when **97b** was treated with silver perchlorate which produced a 1:1 mixture of **98b** and **99b** (equation 52).

(97)   (98)   (99)

(a) X = H   (a) X = H   (a) X = H
(b) X = Br   (b) X = Br   (b) X = Br
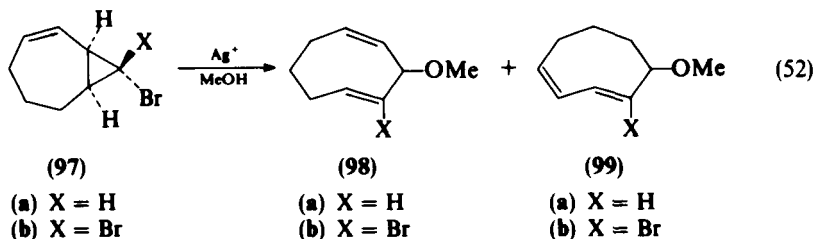
The reaction of *endo*-8-bromobicyclo[5.1.0]oct-2-ene under the same conditions resulted in the formation, as expected, of 5-methoxy-*cis-cis*-cyclooctadiene-1,3 (**100**).

(100)
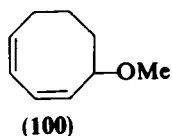
There is also a report [60a] that treatment of **101** with sodium methoxide in methanol yielded a mixture of **102** and **103** (equation 53). It was not clear, however, whether these products were the result of methanolysis or an elimination–addition reaction.

(101)   (102)   (103)

$$CH_2=C\overset{CH(OMe)_2}{\underset{F}{\big|}}$$

via

$$\underset{(101a)}{\underset{F\quad Cl}{\triangle}} \xrightarrow[\text{Pyridine}]{\text{MeOH}}$$

(53a)

cis-(101b)   trans-(101c)
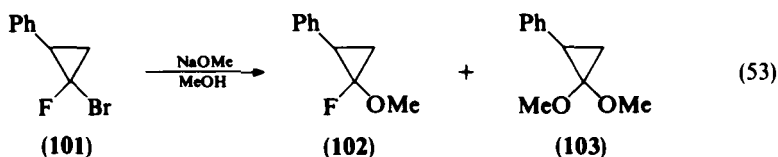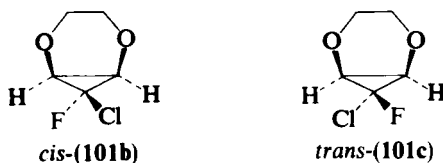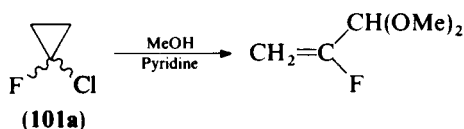
That the latter may be the case is indicated by the work of Molines and Wakselman[60b], who demonstrated that **101a** readily underwent electrocyclic ring opening (equation 53a) and that the cis-isomer **101b** solvolyzed much faster than the trans-isomer **101c**, as predicted by the Woodward–Hoffmann–DePuy rules.

9. α-Oxygen and α-sulfur

As we have discussed previously (see Section III.B.3) ab initio calculations[29] have indicated that oxygen and sulfur substituents attached to the cationic carbon of the cyclopropyl ring will stabilize the cation against ring opening. That this was indeed the case when phenylthio was the substituent was demonstrated by Schöllkopf and coworkers[61] in the methanolysis of, inter alia, 1-phenylthio-1-chloro-2,2-dimethyl-cyclopropane (**104**) which gave a 95% yield of 1-phenylthio-1-methoxy-2,2-dimethyl-cyclopropane (**105**) and a 5% yield of 2-phenylthio-3-methoxy-3-methyl-1-butene (**106**) (equation 54).

$$\text{(104)} \xrightarrow[\text{MeOH/MeO}^-]{80°C} \text{(105) } 95\% + \text{PhS} \cdots \text{(106) } 5\%$$

(54)
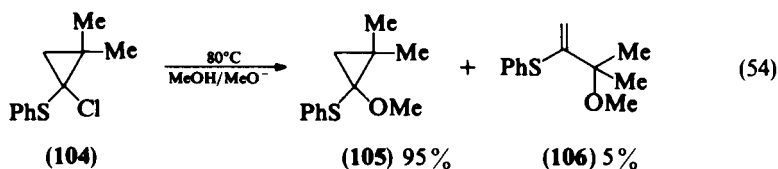
Schöllkopf and coworkers also showed that the pair of epimers **107** and **108** gave rise to an identical ring-closed product **109** although **108** solvolyzed at a rate 96 times faster than that of **107** (equation 55).

(107)   (109)   (108)   (55)
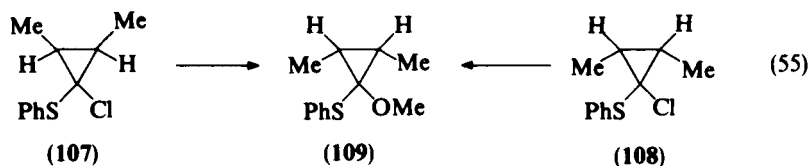
To account for these results they postulated an equilibrium between two 'half-opened' cations **110** in which the methyl groups partially rotate in a synchronous manner and pass through a closed planar cation **111** (equation 56). Attack by solvent would be from the

$$
\underset{(110)}{\text{(structure)}} \rightleftharpoons \underset{(111)}{\text{(structure)}} \rightleftharpoons \underset{(110)}{\text{(structure)}} \tag{56}
$$
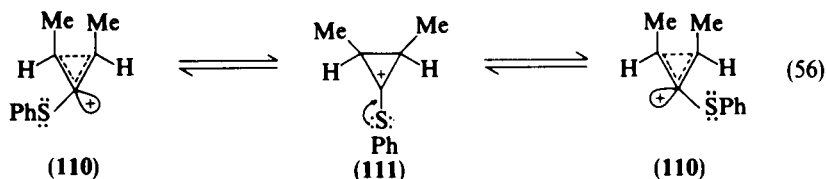
least hindered side. This mechanism accounted for the observed closed product as well as for the modest rate enhancement observed for **108** over its epimer **107**.

In a direct comparison of oxygen vs sulfur as a stabilizing group, it was found[62] that sulfide **112** undergoes methanolysis twelve times faster than the ether **113** (equation 57).

$$
\underset{(112)}{\text{(structure)}} \xrightarrow[100\%]{\text{MeOH, 38°C}} \text{(structure)} \qquad k = 21.9 \times 10^{-5}\,\text{s}^{-1}
$$

$$\tag{57}$$

$$
\underset{(113)}{\text{(structure)}} \xrightarrow[100\%]{\text{MeOH, 38°C}} \text{(structure)} \qquad k = 1.89 \times 10^{-5}\,\text{s}^{-1}
$$
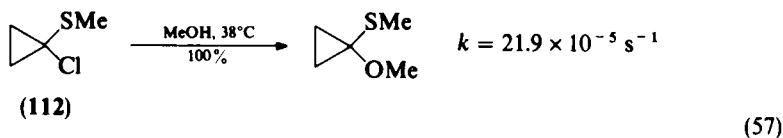
That sulfur stabilizes a cationic center more efficiently is also supported by *ab initio* calculations [63], which show that sulfur is a better π or σ electron donor than oxygen. However, the leaving group appears to exert a remarkable influence[62] which reverses the effect observed for **112** and **113**. Using dimethylsulfonium as a leaving group, the order is reversed and the methoxy derivative **114** is almost twice as reactive as the methylthio derivative **115**. The situation is by no means clear (equation 58)[64].

$$
\underset{\substack{(114)}}{\overset{}{\underset{-\text{SO}_3\text{F}}{\text{(structure)}}}} \xrightarrow[100\%]{\text{MeOH, 65°C}} \text{(structure)} \qquad k_1 = 280 \times 10^{-6}\,\text{s}^{-1}
$$

$$\tag{58}$$

$$
\underset{\substack{(115)}}{\overset{}{\underset{-\text{SO}_3\text{F}}{\text{(structure)}}}} \xrightarrow[100\%]{\text{MeOH, 65°C}} \text{(structure)} \qquad k_1 = 156 \times 10^{-6}\,\text{s}^{-1}
$$
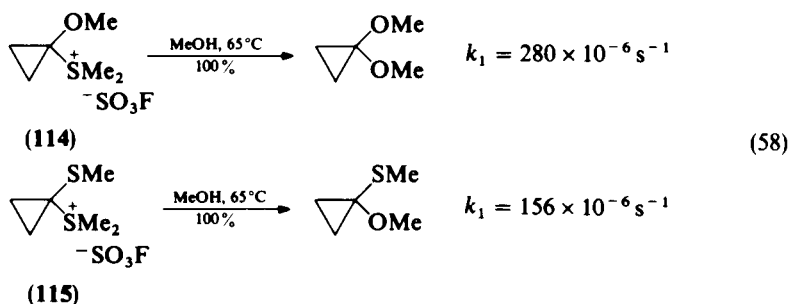
However, it should be emphasized that all the above β-unsubstituted cyclopropane derivatives yield only ring-closed product. Table 14 lists the yield of ring-closed product one observes in both methanolysis and trifluoroethanolysis of a number of 1-halo-cyclopropyl sulfides (equation 59).

$$
\text{(structure)} \xrightarrow{\text{ROH}} \text{(structure)} + \text{(structure)} \tag{59}
$$
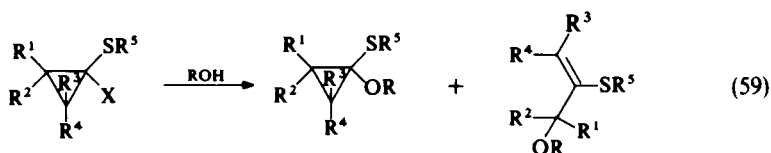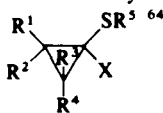
TABLE 14. Amount of ring-closed methanolysis (20°C) and trifluoroethanolysis (0°C) products from 1-halocyclopropyl sulfides

						% yield of ring closed product in	
R¹	R²	R³	R⁴	R⁵	X	MeOH X = OMe	CF₃CH₂OH X = OCH₂CF₃
H	H	H	H	Me	Cl	100	100
H	H	H	H	Ph	Br	100	>95
H	H	H	H	CH₂Ph	Br	100	100
H	H	H	H	(CH₂)₂Ph	Br	100	100
3-Butenyl	H	H	H	Me	Cl	100	50
Me	Me	H	H	Me	Cl	100	22
Me	Me	Me	Me	Me	Cl	80	—
Me	H	Me	H	Me	Br	40	—

For the most part the alkylthiocyclopropyl halides and sulfonium salts undergo nucleophilic displacement without ring opening. Alkyl groups on C-2 and C-3 make the cyclopropyl system more prone to ring opening, especially when located *trans* with respect to the leaving group. This is in keeping with the electrocyclic nature of the ring opening.

The role of solvent is also important and this is dramatically displayed in the solvolysis of 116, where the product of solvolysis goes from complete ring closure (117) in methanol to almost complete ring opening when the very much less nucleophilic trifluoroethanol is used as a solvent (equation 60)[62].

(60)
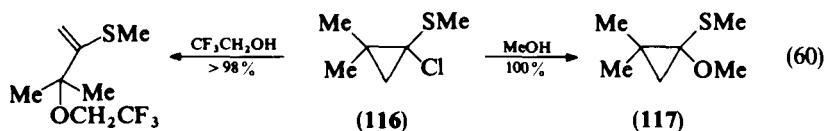
Braun and Seebach [65] have developed an interesting general synthesis of ketones using the chemistry described above (equation 61). A similar sequence (equation 62) can be used for ring expansion.

(61)

(62)
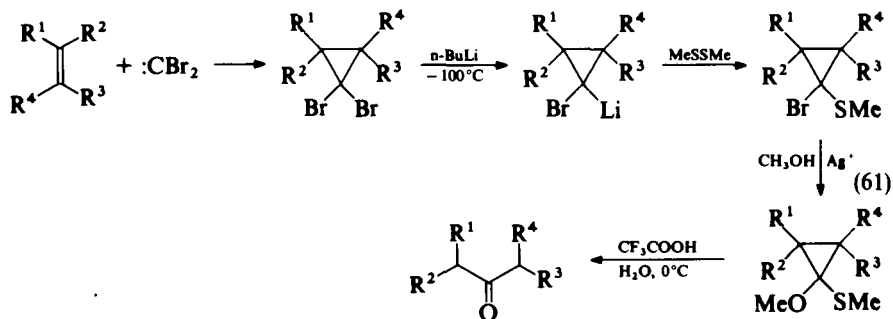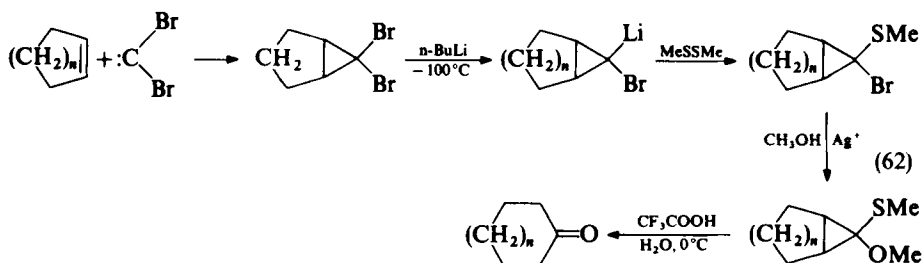
The reaction sequences are all simple, proceed in high yield and do not require further comment. The only weak part of the sequence is the halogen–metal exchange where temperature control is very important and would militate against large-scale reactions as would the use of silver cations. It is also noteworthy that no ring-opened product was observed in any of the reactions of the 1-bromo-1-(methylthio)cyclopropane derivatives with silver ion in methanol to yield the solvolysis product, a 1-methoxy-1-(methylthio)cyclopropane derivative. The opening of the ring is accomplished by use of a strong acid of low nucleophilicity[62] (CF_3COOH) and highly nucleophilic water which is necessary for hydrolysis.

1-Ethoxycyclopropanol has also become a useful synthetic intermediate since it has become available in large quantity due to a synthesis developed by Ruhlmann[66] starting with ethyl 3-chloropropionate. Treatment of the halo ester with sodium and trimethylsilyl chloride produces 1-trimethylsilyloxy-1-ethoxycyclopropane which, when hydrolyzed by methanol[48], gives the desired alcohol **118** (equation 63).

(63)

(118)
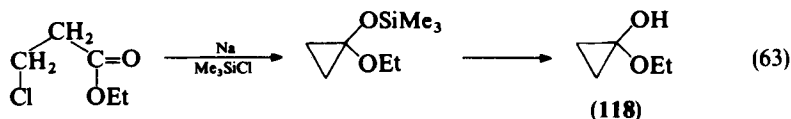
Reaction of **118** with LiCN did not result in displacement of ethoxide to yield the cyanohydrin derivative but instead **118** underwent a cyclopropoxy rearrangement (equation 64)[67].

(64)
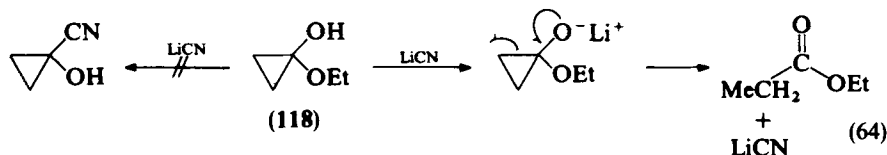
It was also found that exposure of **118** to other lithium reagents such as ethynyllithium and aryllithium did not yield products resulting from nucleophilic displacement[67,68]. However, the reaction of **118** with two equivalents of Grignard reagent did yield the desired nucleophilic displacement[41,68]. Brown and Rao[69] reasoned that lithium reagents could be used as nucleophiles if one converted **118** to the magnesium salt by treatment with methylmagnesium iodide (equation 65).

(65)

(118)
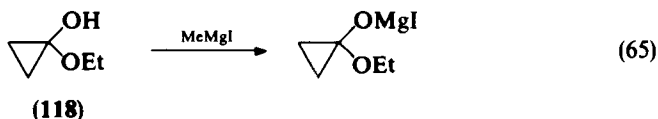
This did indeed turn out to be the case. Salaun[68] has suggested that the more covalent magnesium salt **119** decomposes to yield cyclopropanone, which reacts with nucleophile Nu⁻. Cyclopropanone need not be an intermediate at all. The magnesium can assist in the ionization of the ethoxy group so that **119** becomes the reactive intermediate toward nucleophilic displacement (equation 66). The more ionic lithium intermediate reacts by

$$\begin{array}{c} \text{(equation 66 structure)} \end{array} \qquad (66)$$

(119)
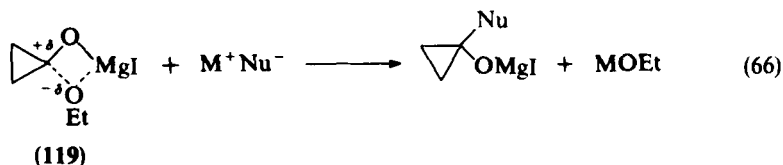
way of the cyclopropoxy rearrangement (*vide supra*). Thus, it has been shown that **119** reacts with nucleophiles such as hydride, LiCN, RLi, RMgX (R = alkyl, aryl, vinyl and ethynyl) and Wittig reagents[68].

Of interest is the observation that 1-acetoxycyclopropanol (**120**) also reacts with a variety of nucleophiles[70]. It has been shown that **120** is strongly intramolecularly hydrogen bonded, which could result in making the acetoxy a good leaving group so that attack by nucleophiles Nu⁻ such as NC⁻, N₃⁻, R₂N⁻, RO⁻ and RS⁻ occurs readily (equation 67).

$$\begin{array}{c} \text{(equation 67 structure)} \end{array} \qquad (67)$$

(120)
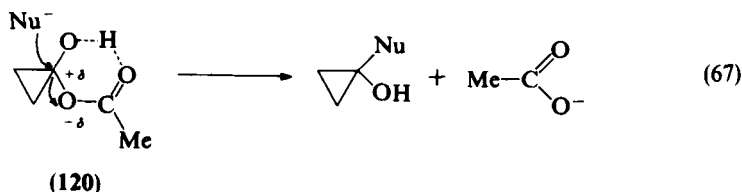
The reaction of 1-ethoxy-1-acetoxycyclopropane with Grignard reagents is likely due to the formation of **119** as an intermediate, which can then react with more Grignard reagent to yield 1-alkylcyclopropanols (equation 68)[67].

$$\begin{array}{c} \text{(equation 68 structure)} \end{array} \qquad (68)$$

(119)
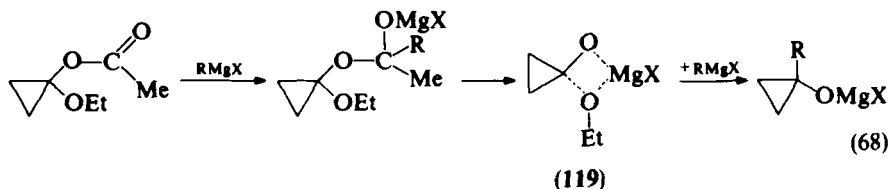
In summary, ether (OR) and thioether (SR) groups are stabilizing substituents for cyclopropyl cationic intermediates which, in general, lead to the formation of ring-closed products.

10. α-Nitrogen

As with cyclopropanone which can be viewed as an oxygen-stabilized cyclopropyl cation, the cyclopropyl iminium salt can be viewed in a similar fashion, so that oxygen and nitrogen both stabilize the closed structures of the cyclopropyl cation.

$$\triangleright\!\!=\!\!O \quad\longleftrightarrow\quad \overset{+}{\triangleright}\!\!-\!\!O^- \qquad\qquad \triangleright\!\!=\!\!\overset{+}{N}\!\!\diagdown \quad\longleftrightarrow\quad \overset{+}{\triangleright}\!\!-\!\!\overset{\cdot\cdot}{N}\!\!\diagdown$$
$$ X^- X^-$$

Szmuszkovicz[71] and coworkers have been able to trap the cyclopropyl iminium intermediate **122**. Treatment of **121** with sodium borohydride yielded **123** possessing the *endo* configuration (equation 69).

(121)   (122)   (123)   (69)
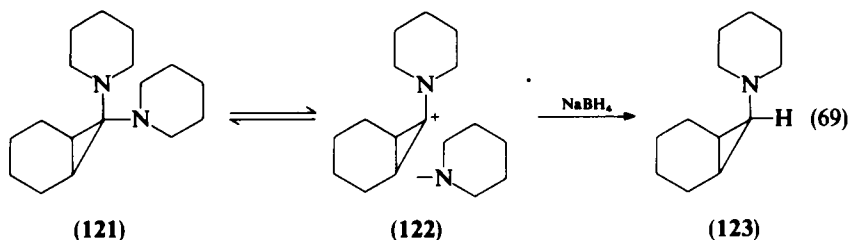
Wasserman and coworkers[54, 72] have shown that the ethyl hemiacetal of cyclopropanone (**118**) reacts readily with aniline at room temperature to yield 1,1-dianilinocyclopropane (**124**) by way of a 1-anilino-1-hydroxycyclopropane (**125**) (equation 70).

(118)   (125)   (124)   (70)
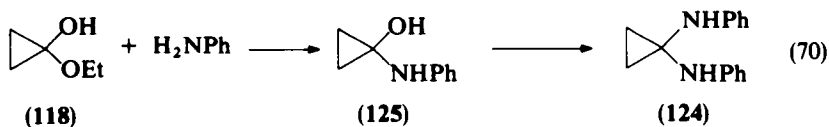
The reaction of **118** with secondary amines such as piperidine gave rise to **126** which, upon treatment with another equivalent of piperidine, yielded **127**. They postulated that **127** was produced from **126** via a cyclopropyl iminium intermediate **128** (equation 71)[72.]

(126)   (128)   (127)   (71)
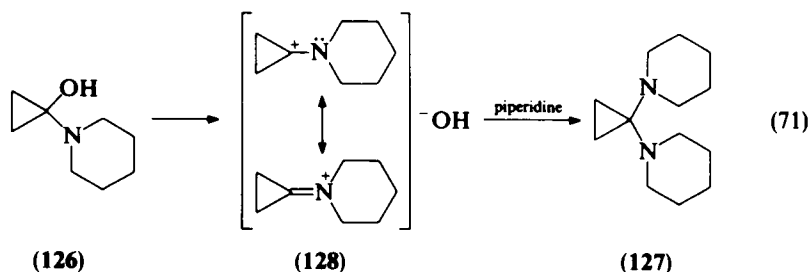
Support for the intermediacy of an iminium ion comes from a ¹H-NMR study. De Boer and coworkers[73] have reported the ¹H-NMR spectrum of *N*,*N*-dimethylcyclopropaniminium fluorosulfonate (**129**) which is generated when 1,1-bis(dimethylamino)cyclopropane is added to a tenfold excess of methylfluorosulfonate at $-78°C$. The ¹H-NMR spectrum of the clear solution, obtained after filtration of the salt, showed two multiplets at $\delta = 3.71$ ppm (6 H) and at 2.26 ppm (4 H) relative to TMS which have been ascribed to **129**. The absorption at $\delta = 3.71$ ppm was shown to consist of 5 lines and at 2.26 ppm to consist of 7 lines. In a double resonance experiment irradiation of either

multiplet caused the other to collapse to a singlet. This then points to a rapidly inverting or a planar ion for **129**.

Consistent with the proposed intermediate **129** is the observation that addition of a methanolic solution of sodium methoxide resulted in the exclusive formation of **130**

(129)   (72)

(130)
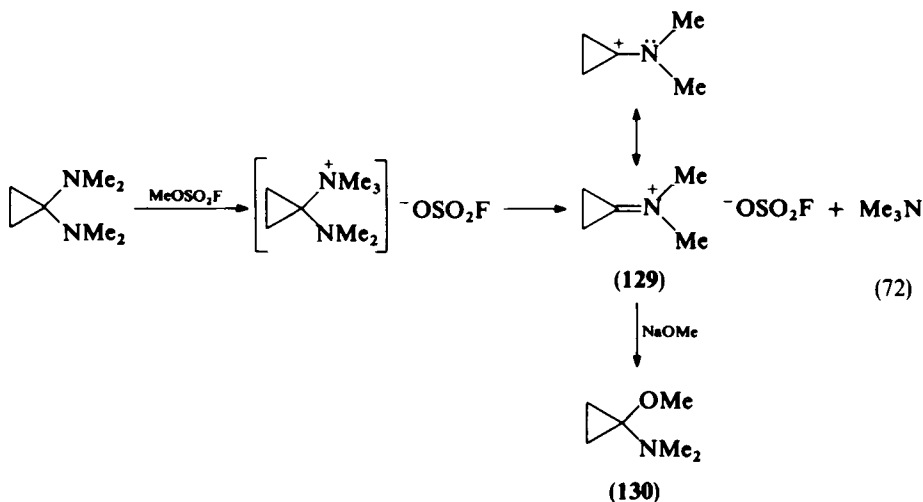
(equation 72). Further chemical evidence[72] was supplied by the reaction of **128** with a nucleophilic eneamine to give **131** (equation 73).

(128)   (73)

(131)
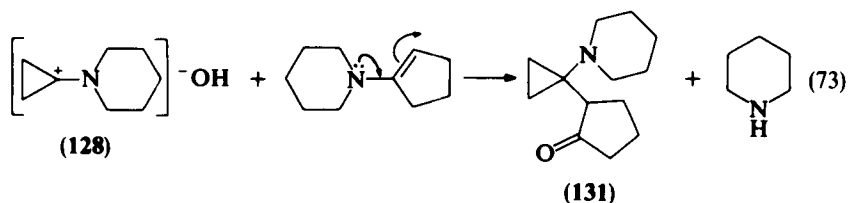
A Mannich reaction, which is believed to proceed via an iminium intermediate, has also been observed (equation 74)[74].

(74)
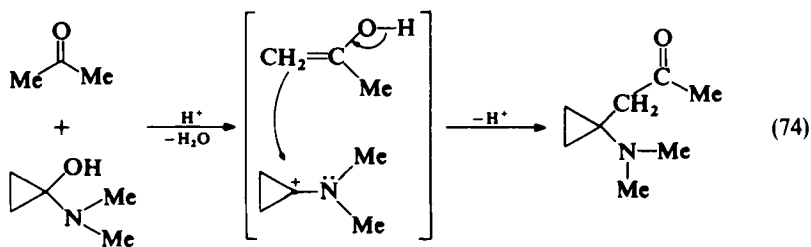
De Boer and coworkers[75] have attempted to explain why in compounds like 1-hydroxy-1-dialkylaminocyclopropane (i.e. **126**) it is the hydroxyl group that is the leaving group rather than the amino group, in spite of the latter group's greater proton affinity.

De Boer suggests that removal of the protonated hydroxyl group is assisted by the donation of the *non*-bonding electron pair on nitrogen which thus avoids serious electron deficiency at the cyclopropyl carbon. This would also explain why mineral acids are poor catalysts, especially in solvents of low polarity and low basicity, since they would completely protonate the amino group and thus deprive it of its electron-donating power.

Ab initio calculations[29] showed that an α-amino substituent bestows greater stability on a cyclopropyl cation than on the corresponding open allyl cation by 23.4 kcal mol^{-1}. This large difference in energy suggests that if one could generate the 2-aminoallyl cation it should readily close to the cyclopropyl cation. Experimentally this is exactly what has been observed (equation 75)[76].

$$\text{(structure)} \quad \longrightarrow \quad \text{(structure)} \qquad (75)$$
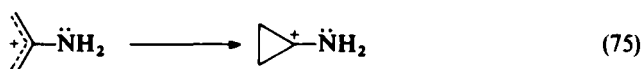
Vilsmaier and coworkers[76], in an elegant study of the reaction of aminovinylsulfonium fluorosulfates with nucleophiles, showed that this leads to the formation of amino-bicyclo[n.1.0]alkanes where $n = 5$–11.

The aminovinylsulfonium fluorosulfates (132) are readily obtained by reaction of succinimidosulfonium fluorosulfate[77] with an appropriate eneamine (equation 76)[78].

$$\text{(structure)} \qquad (76)$$

(132)
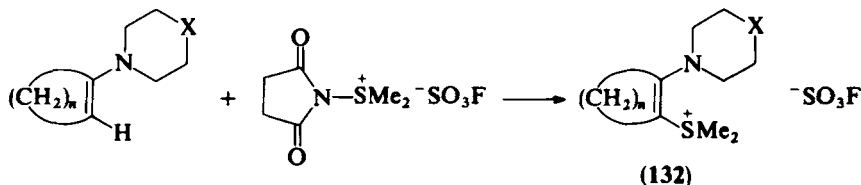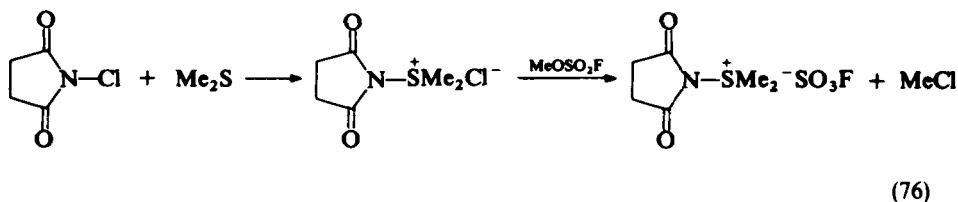
The reaction of 132, i.e. $n = 5$, X = O, with nucleophiles (Nu$^-$) leads to the formation of *endo*-7-morpholino-*exo*-N-bicyclo[4.1.0]heptane 136[76].

The sulfonium salt 132 isomerizes to 133 thereby placing the dimethylsulfonium leaving group in an allylic position which, upon ionization, gives rise to the open allyl cation 134. Ring closure to the energetically more stable cyclopropyl cation 135 and attack by the nucleophile from the least hindered side yields the bicyclic product 136 in isolated yields of 40–80% (equation 77).

Of special interest is the reaction of 136 where Nu = OCH$_3$, which converts it to 137 by reaction with Meldrum's acid. Thus it is the methoxy group which is the leaving group to yield the more stable iminium intermediate 138 (equation 78)[79].

In summary, as predicted by *ab initio* calculations, the amino group, in its ability to reduce the effect of an adjacent positive charge by donating its *non*-bonding electron pair, exerts a powerful stabilizing effect and reduces the tendency toward ring opening of the cyclopropyl moiety to the open allyl cation.

(77)
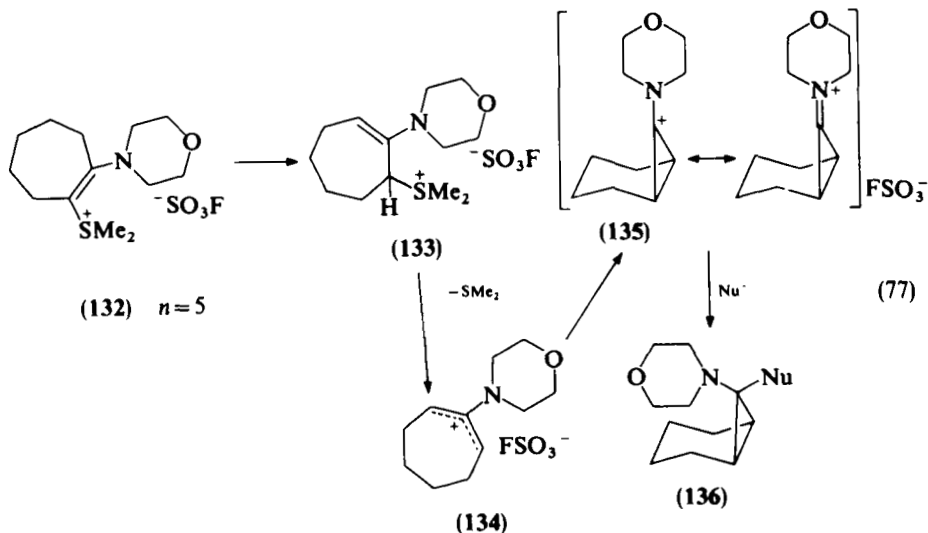
$Nu^- = H^-, RO^-, HO^-, ^-N=C=O,$
$N_3^-, NC^-, Z_2C^-, ^-NHR, ^-CHR^1R^2$ etc. (Z = electron delocalizing groups)

(78)
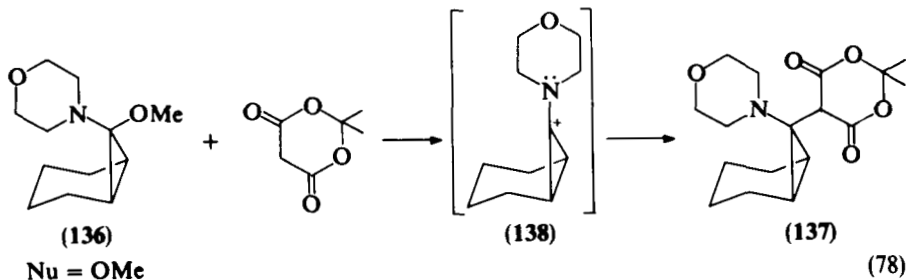
C. β-Substituents

1. Regioselectivity in reactions of open allyl cations

As we have previously discussed, unless constrained, the cyclopropyl cation is best viewed as an open allyl cation. The disrotatory electrocyclic ring opening is stereospecific and produces an allyl cation intermediate which, depending on the geometry of the β-substituent in the ring, will lead to cis or trans olefinic product. Thus, for example, solvolysis of **139** will yield only trans olefin **141** and/or **142** regardless of the side of attack by nucleophilic solvent (SOH) on the allyl cation **140**. Similarly, solvolysis of **146** will yield only cis olefinic products **148** and/or **145**. However, **143** will give rise either to a trans olefin **141** and/or a cis olefin **145** depending on the side of attack by the nucleophilic solvent (SOH) on the open allylic cation **144** (equation 79).

One of the factors which will determine the regioselectivity of attack by the solvent on the open allylic cations **140**, **144** and **147** will be the charge distribution in the cation. If R

(139)   (140) $\xrightarrow{\text{SOH}}$ (141) or (142)

(143)   (144) $\xrightarrow{\text{SOH}}$ (141) or (145)

(79)

(146)   (147) $\xrightarrow{\text{SOH}}$ (148) or (145)
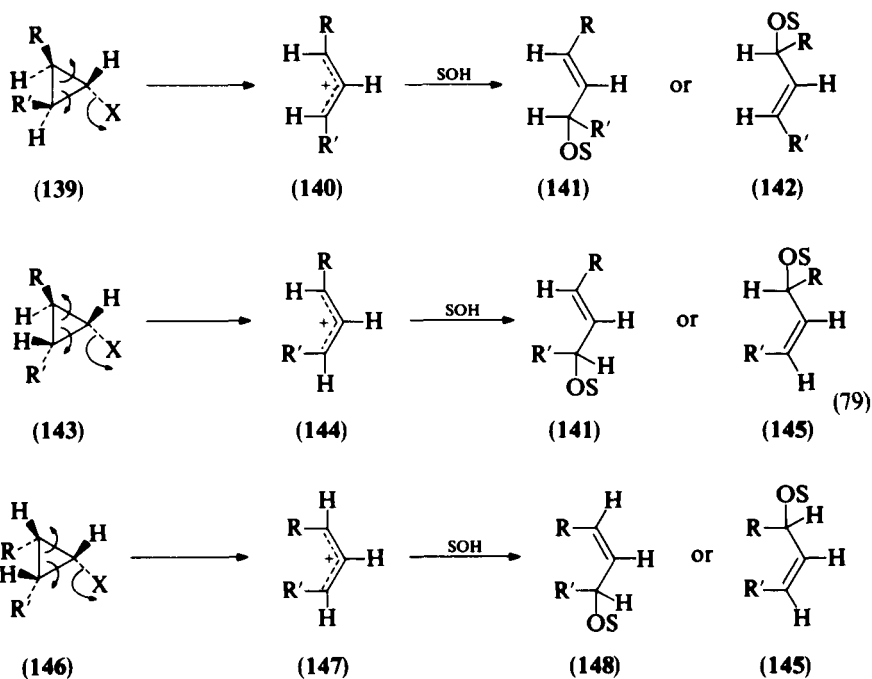
stabilizes a positive charge better than R' then the nucleophile would be expected to attack the carbon attached to R either exclusively or predominantly depending on the extent to which the charge is localized. Parham and Yong[35a] have shown that in the ethanolysis of **139** where R = n-propyl and R' = OEt, the product is exclusively **141** (R = n-propyl, R' = OEt) and none of isomeric **142** is detected. Starting with the isomer **143** (R = n-propyl, R' = OEt) the expected product would again be **141** (R = n-propyl, R' = OEt), and again that is what is found. The ethoxy group stabilizes and localizes the positive charge to a much greater extent than an alkyl group.

Alcoholysis of 1,1-dichloro-2-ethoxycyclopropane (**149**) also yields exclusively the acetal of α-haloacrolein (equation 80)[80].

(149)

(80)
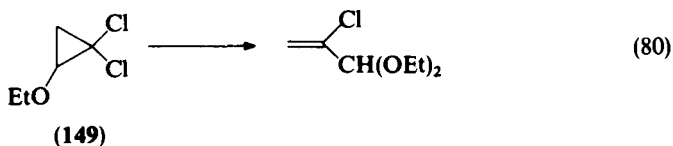
Both cis- and trans-1,1-dichloro-2-ethoxy-3-methylcyclopropane (**150**) give rise to the same product, the diethyl acetal of trans-2-chlorocrotonaldehyde, **151** (equation 81)[80].

trans-(**150**) $\xrightarrow{C_2H_5OH}$ (**151**) $\xleftarrow{C_2H_5OH}$ cis-(**150**)

(81)
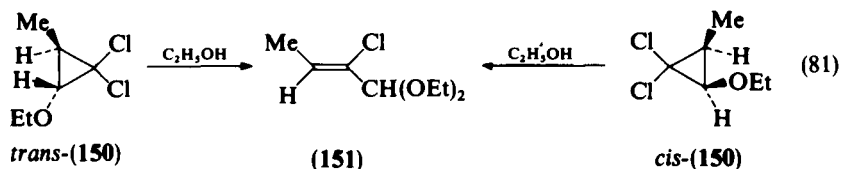
Of interest is the observation that the phenoxy group, as expected, does not stabilize the positive charge as well as the alkoxy group, since acetolysis[81] of 1,1-dibromo-2-phenoxycyclopropane (152) gives rise to a 60:40 mixture of 153 and 154 (equation 82).

$$\text{(82)}$$

(152)   (153)   (154)
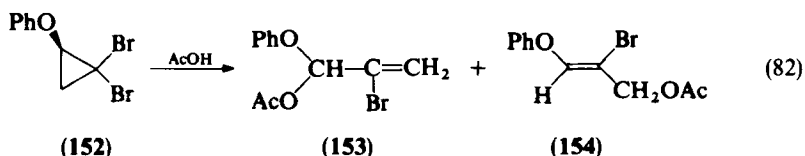
The acetolysis of *cis*- and *trans*-2-fluorocyclopropyl bromides[82] (155) leads to the expected electrocyclic ring-opened allyl cations *cis*-156 and *trans*-156. The attack by solvent leads to the formation of *cis*- and *trans*-157, respectively (equation 83), thus indicating that the fluorine behaves as a destabilizing substituent in 156.

cis-(155)   *cis*-(156)   *cis*-(157)

$$\text{(83)}$$

trans-(155)   *trans*-(156)   *trans*-(157)
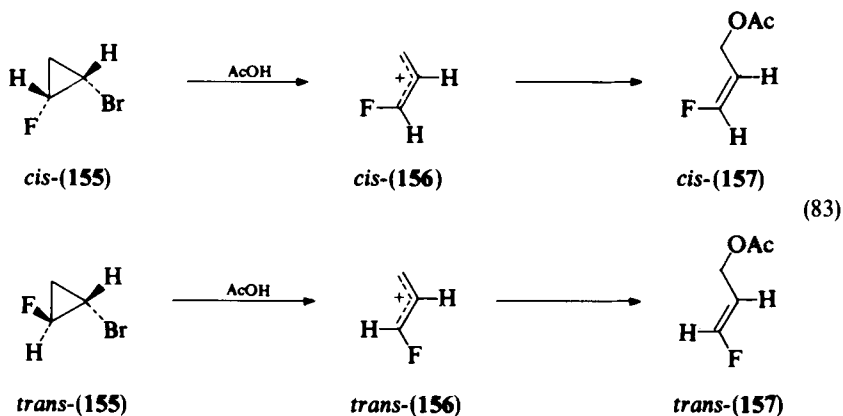
Stabilization of charge also controls in the acetolysis of 1,1-dibromo-2,2-dimethylcyclopropane (158)[83] and in the decomposition of 2-phenylcyclopropyl-diazonium ion (159)[84] (equation 84).

(158)   63%   39%

$$\text{(84)}$$

(159)   65%   25%
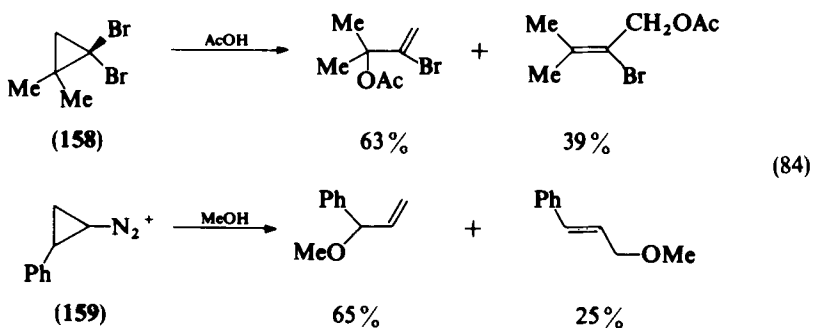
Aksenov and Terent'eva[85] have also shown in the silver-catalyzed methanolysis of 2-aryl-1-bromo-1-fluorocyclopropanes (160) that charge distribution influenced by the aryl group affects the product distribution ratio, and charge localization at the benzylic

carbon always predominates (equation 85). The reactions were performed under kineti-cally controlled conditions (50 °C).

$$\text{(85)}$$
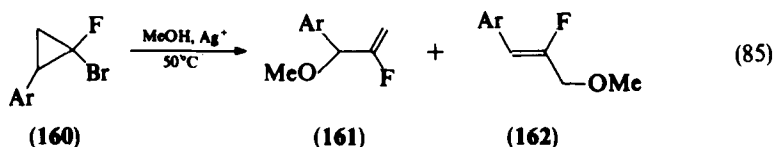
Ar	161/162 ratio
C_6H_5	2.5
$p\text{-MeC}_6H_4$	4.0
$m\text{-MeC}_6H_4$	3.5
$p\text{-BrC}_6H_4$	2.0
$m\text{-BrC}_6H_4$	1.5

However, under thermodynamically controlled conditions (140 °C) in the reaction of **160** (Ar = Ph) the **161/162** ratio changes from 2.5 to 0.048. Unless care is taken to establish kinetic control the products of capture of most aryl-substituted allyl cations reflect thermodynamic control.

It should also be noted that disrotatory ring opening should produce a *cis*-cinnamyl derivative, but none is obtained. Under the conditions of the reaction the *cis*-allyl cation is expected to rapidly convert to the observed *trans*-allyl cation (equation 86).

$$\text{(86)}$$
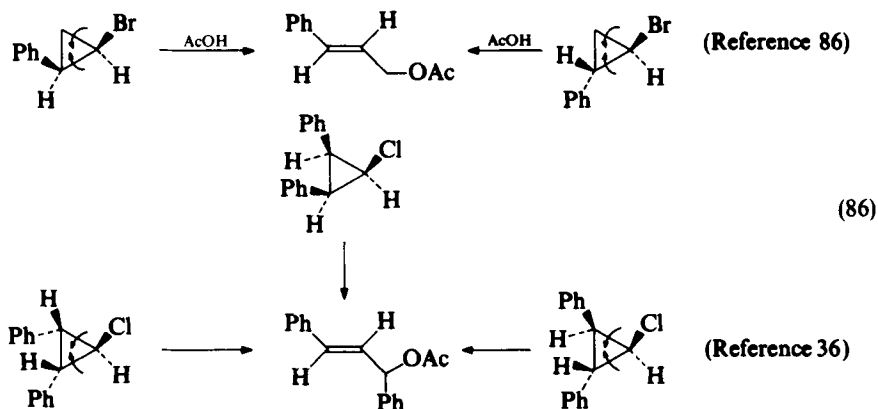
To summarize, in general, unless constrained the solvolyses of cyclopropyl halides or esters proceed by disrotatory electrocyclic ring opening to yield an open allyl cation in which charge distribution will determine at which terminus of the allyl cation the solvent will react. *cis*→*trans* Isomerization of the allyl cation may also occur.

2. Noncyclic substituents (β and β′)

As expected from the synchronous disrotatory pathway for the ring opening of the cyclopropyl cation, β-substituents will in general accelerate the solvolysis of cyclopropane

TABLE 15. Solvolysis rates for β-substituted cyclopropyl derivatives

R	R'	X	$T(°C)$	Solvent	k (s^{-1})
H	H	OTs	100	AcOH	4.6×10^{-8}
Me	H	OTs	100	AcOH	6.3×10^{-6}
H	Me	OTs	100	AcOH	1.0×10^{-7}
Et	H	OTs	100	AcOH	7.5×10^{-6}
H	Et	OTs	100	AcOH	3.4×10^{-7}
i-Pr	H	OTs	100	AcOH	9.6×10^{-6}
H	i-Pr	OTs	100	AcOH	3.3×10^{-7}
t-Bu	H	OTs	100	AcOH	1.4×10^{-5}
H	t-Bu	OTs	100	AcOH	2.1×10^{-7}
$-(CH_2)_3-$		ONs	95	AcOH	2.8×10^{-4}
$-(CH_2)_4-$		ONs	95	AcOH	2.3×10^{-4}
$-(CH_2)_5-$		ONs	95	AcOH	1.2×10^{-4}
$-(CH_2)_6-$		ONs	95	AcOH	2.4×10^{-4}
Me	Me	OTs	100	AcOH	1.9×10^{-5}
Pr	Pr	Br	130	50% EtOH	2.4×10^{-3} [a]
Δ	H	Br	95	50% EtOH	1.0×10^{-3} [a]
H	Δ	Br	95	50% EtOH	3.9×10^{-5} [a]
C=C	H	Br	95	50% EtOH	2.7×10^{-4} [a]
H	C=C	Br	95	50% EtOH	2.5×10^{-5} [a]
Ph	H	Br	119	AcOH	6.3×10^{-5} [b]
H	Ph	Br	119	AcOH	1.5×10^{-5} [b]
Ph	H	OTs	108	AcOH	3.2×10^{-5} [b]
H	Ph	OTs	108	AcOH	2.1×10^{-6} [b]
Ph	Ph	Br	119	AcOH	2.0×10^{-4} [b]
F	H	Br	187	AcOH	4.9×10^{-5} [c]
H	F	Br	187	AcOH	4.6×10^{-6} [c]

[a] J. A. Langrebe and L. W. Becker, *J. Org. Chem.*, **33**, 1193 (1968).
[b] References 45 and 86.
[c] Reference 82.

derivatives with the *trans* β-substituents exerting a greater effect than the *cis* β-substituents. Table 15 shows the effect of a variety of β-substituents on the rate of solvolysis.

It has always been assumed that the reason the *trans* isomer undergoes solvolysis at a rate greater than the *cis* isomer was steric in nature. Dolbier and Phanstiel[82], on the other hand, have concluded on the basis of their results on the solvolysis of *cis*- and *trans*-2-fluorocyclopropyl bromide (155) that electronic effects play the dominant role. It can be seen (Table 15) that the *trans* isomer solvolyzes at a rate $\simeq 10$ times faster than the *cis* isomer; moreover, the ring-opening reaction proceeds with total stereospecificity.

Comparison of the rate data for the 2-fluoro- and 2-methylcyclopropyl bromides is revealing (Table 16). Dolbier and Phanstiel point out that although fluorine is a rate-enhancing substituent, it is not as much so as a β-methyl substituent and that this is what would be expected if the transition state possesses a great deal of allylic cation character. Moreover, one notes that the *trans/cis* ratio is greater for the fluorine substituent than it is for the methyl substituent even though the fluorine substituent, due to its small A value of 0.24 vs 1.8 kcal mol^{-1} for methyl, would exert little if any steric interaction even if it rotated inward rather than outward. Finally, Dolbier and Phanstiel also suggest that the

TABLE 16. Rate data for the solvolysis of 2-R cyclopropyl bromides in AcOH at 100 °C[82]

R	$k \ (\times 10^9 \, \mathrm{s}^{-1})$	k_{rel}	trans/cis
H	1.6	1	
trans-F	22.8	14.25	19
cis-F	1.2	0.75	
trans-Me	981	617	13.8
cis-Me	71.7	44.8	

kinetic results not only indicate a lack of steric effect but are also contrary to thermodynamic considerations. In the methyl system the products obtained seem to correlate with a steric effect in that the *trans* products are more stable than the *cis* products. By contrast, in the fluoro system it is the *cis*-acetate (*cis-157*) which is more stable than the *trans*-acetate (*trans-157*). Based on these observations Dolbier and Phanstiel conclude that the enhanced rates of solvolysis for *trans* vs *cis* β-substituted cyclopropyl derivatives do not derive from steric factors but from electronic effects.

3. Bicyclic (β and β'): monohalogen or ester

This subject, for $n = 2$–6, has been previously discussed in Section II.B under the heading 'half-opened' structure. Of interest are the studies of Creary[42,87] who demonstrated the effect of a neighboring double bond in $163_{3,4}$ and a neighboring cyclopropyl group in 164_3.

exo-(163₃)   exo-(163₄)   exo-(166₃)   exo(165₄)   exo(164₃)
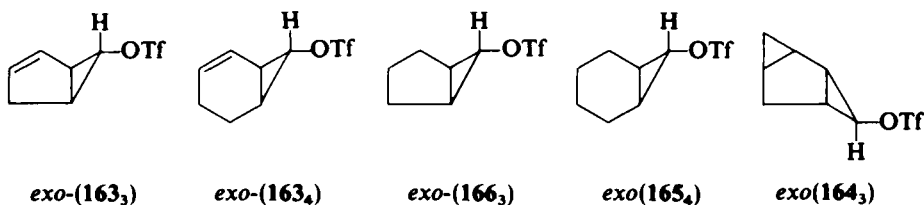
In the nonbicyclic series, both in the β-olefin and β-cyclopropyl substituted cyclopropanes, one observes rate enhancement as is seen for example by comparing acetolysis rates for *cis* and *trans* β-ethylcyclopropyl tosylates in Table 15 with *cis* and *trans* β-vinyl and *cis* and *trans* β-cyclopropyl tosylates. However, as can be seen from

TABLE 17. Rates of acetolysis in AcOH/0.1 M NaOAc[87]

Compound	Temp. (°C)	$k \ (\mathrm{s}^{-1})$
exo-163₃	100	1.56×10^{-5}
exo-163₄	100	1.23×10^{-5}
exo-164₃	160	$6.13 \times 10^{-5 \, a,b}$
exo-165₄	100	5.97×10^{-4}
exo-166₃	100	$1.15 \times 10^{-7 \, b,c}$

[a] Solvent was 60:40 acetone/water.
[b] Rate of *exo-166₃* was 5.67×10^{-4} at 160 °C in 60:40 acetone/water.
[c] Extrapolated value of T. Su, W. F. Sliwinski and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **91**, 5386 (1969).

Table 17, no rate enhancement was observed for *exo*-163$_4$ over its saturated analog *exo*-bicyclo[4.1.0]heptan-7-yl triflate (165$_4$). There was, in fact, a fiftyfold rate retardation. Also, *exo*-164$_3$ underwent acetolysis approximately ten times more slowly than *exo*-bicyclo[3.1.0]hexan-6-yl triflate (166$_3$). Rate enhancement was only observed for 163$_3$, which solvolyzed 136 times faster than 166$_3$.

The only product obtained in the acetolysis of *exo*-163$_3$ is the acetate *exo*-163$_3$-OAc. The suggested mechanism is shown in equation 87.

$$exo\text{-}(163_3) \qquad\qquad (167) \qquad\qquad exo\text{-}(163)_3\text{-OAc} \tag{87}$$
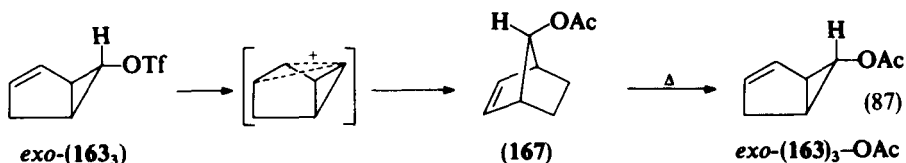
The ease of thermal rearrangement of 167 to *exo*-163$_3$-OAc is well documented[88].

The acetolysis of *exo*-163$_4$ leads to a mixture of two products, *exo*-163$_4$-OAc and *anti*-7-norbornenyl acetate (168), in a ratio of 2.3:1. This result was rationalized in terms of a dual pathway, one leading to a partially opened cyclopropyl cation 169 and another which involves anchimeric participation of the double bond to give 170. The former pathway would result in formation of 163$_4$-OAc with retained configuration in keeping with what would be expected from such a cation, and the latter pathway would yield the *anti*-acetate 168 (equation 88).

$$(169) \qquad exo\text{-}(163_4)\text{-OAc}$$
$$exo\text{-}(163_4) \tag{88}$$
$$(170) \qquad\qquad (168)$$
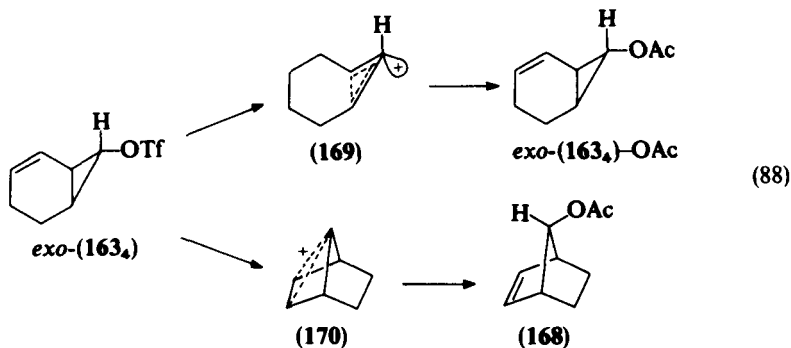
As seen in Table 1 the *exo*-bicyclo[6.1.0]non-9-yl tosylate solvolyzes at about 2900 times as fast as the *endo* tosylate. This is consistent with the intermediacy of a 'half-open' cation as discussed previously. Of interest then was the observation by Boche, Schleyer and coworkers[89] that *endo*-bicyclo[6.1.0]nonatrienyl chloride, *endo*-171, underwent solvolysis at a rate which is ten times faster than that of the *exo* isomer, *exo*-171.

$$exo\text{-}(171) \qquad\qquad (172) \qquad\qquad endo\text{-}(171) \tag{89}$$
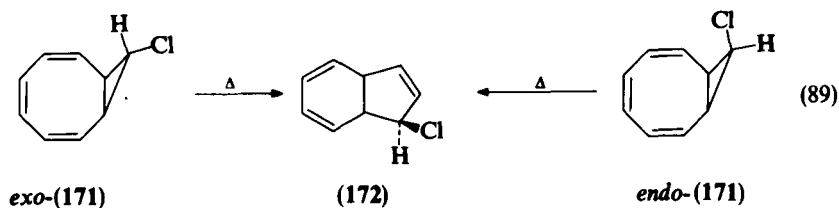
Their thermolysis rates were, however, the same and both *exo-* and *endo-***171** gave the same product, **172** (equation 89). However, studies using deuteriated substrates showed that *exo-* and *endo-***171** react by different mechanisms. Thermolysis of the 9-deuterio derivatives of *exo-***171-d** and *endo-***171-d** resulted in different products, the former giving **172-1d** and the latter **172-2d** (equation 90).

exo(171-d)   (172-1d)   (172-2d)   *endo*-(171-d)

$$(90)$$
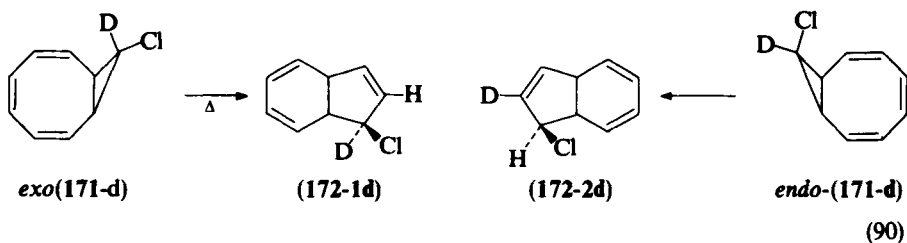
The two mechanisms suggested by Boche, Schleyer and coworkers[89] are as follows: For *endo*–**171** the rate-determining step involves the equilibrium between *endo*–**171** and the ring-closed form of *endo*–**173**. The closed form is an *endo*–bicyclo[2.1.0]pentyl system which should solvolyze very rapidly by a concerted electrocyclic ring opening to yield the open allyl cation, which can then be trapped by solvent or nucleophile depending on whether the conditions are solvolytic or thermal. The solvent or nucleophile will enter from the least hindered side giving **172-2d** and **174-2d** (equation 91).

endo-(171)   *endo*-(173)

(174–2d)   (172–2d)

$$(91)$$
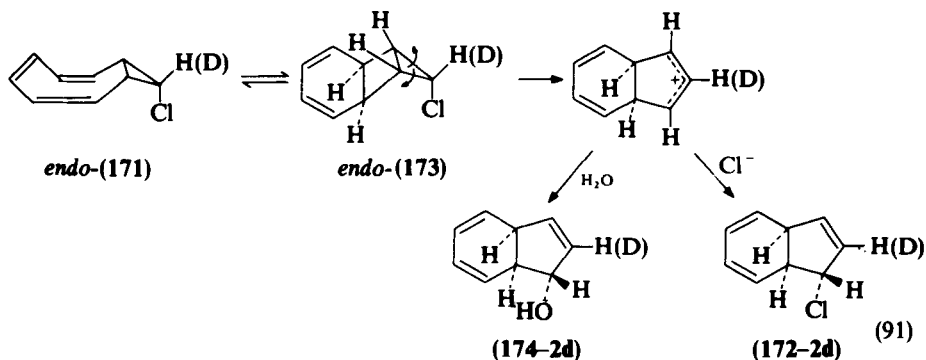
*Exo-***171** would be in equilibrium with the *exo*-isomer of **173**, which is expected to be stable toward ionization and ring opening. Solvolysis of *exo-***171** also gives **174** as the only product, but when *exo-***171-d** is solvolyzed the deuterium is *completely scrambled to all positions*. Boche, Schleyer and coworkers suggest **175** as an intermediate to account for the scrambling via its solvolysis to the cyclononatetraenyl cation which gives 9-hydroxycyclononatetraene. The latter is converted thermally and rapidly to **174**.

(175)
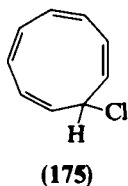
4. Bicyclic (β and β'): geminal dihalides

The geminal dihalides have been extensively studied[1,90] because of their availability and reactivity. They are readily formed by the addition of dihalocarbenes to olefins[57]. Their high reactivity toward solvolysis is due to the fact that they have both *exo* and *endo* halogens available which facilitates electrocyclic disrotatory ring opening when $n = 3,4$ in the *endo* isomers and when $n = 5$, 6, etc. for the *exo* isomers in bicyclo[n.1.0] systems (see Section II.B). We will restrict our coverage to the solvolysis (thermolysis) reactions of representative geminal dihalides which have the bicyclic[n.1.0] structure, where $n = 3,4,5$ and 6 only to illustrate the scope of this ring enlargement sequence or reactions.

a. [3.1.0]. An early example is that of Skell and Sandler[91] who showed that the isomers of the 6,6-dihalo[3.1.0]hexanes (**176**) when treated with aqueous silver nitrate lose, as expected, the *endo* halogen to yield the corresponding halohydrins in a stereospecific manner via a Woodward–Hoffmann–DePuy electrocyclic disrotatory ring opening (equation 92).

$$\text{(92)}$$

(176)
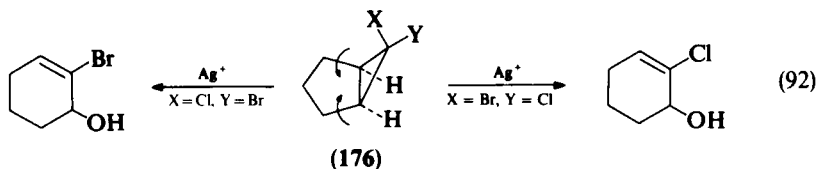
This type of ring expansion has also been applied to the conversion of indene to β-chloronaphthalenes[92], pyrroles to β-chloropyridines[93], indoles to β-chloroquinolines[94] and dihydrofuran to a 5,6-dihydropyran derivative (equation 93)[95].

$$\text{(93)}$$
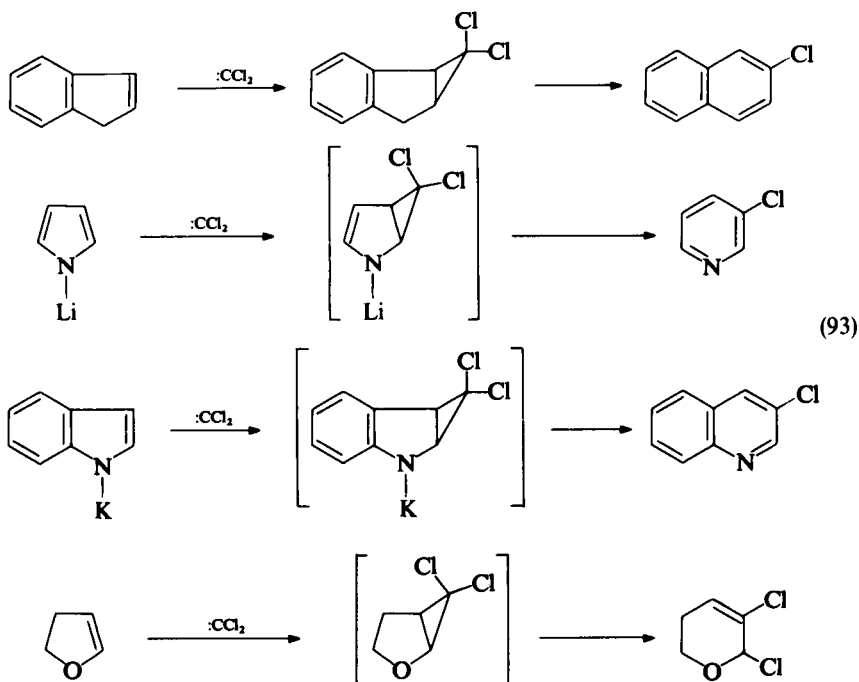
This method of ring expansion was also used by Parham and Rinehart[96] in their syntheses of metacyclophanes 177_n ($n = 8$, 10) (equation 94).

$$(94)$$

$$(177_n)$$
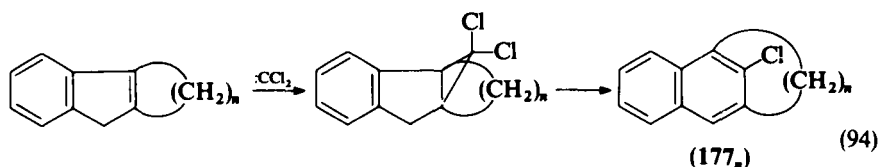
One should exercise caution, however, when proposing mechanisms for ring expansions involving anions adjacent to the three-membered ring such as in the carbene adducts obtained from pyrryl lithium or indenyl potassium. The mechanism of ring expansion for these intermediates may well be different from the usual electrocyclic mechanism.

b. [4.1.0]. Sandler[97] has shown that refluxing a mixture of silver acetate–acetic acid and 7,7-dihalobicyclo[4.1.0]heptane (178), formed from the addition of dihalocarbene to cyclohexene, resulted in the formation of 2-halo-3-acetoxycycloheptene. Heating 178 (X = Br) with silver sulfate and conc. sulfuric acid resulted in the formation of cyclohepten-3-one (equation 95)[98].

$$(95)$$
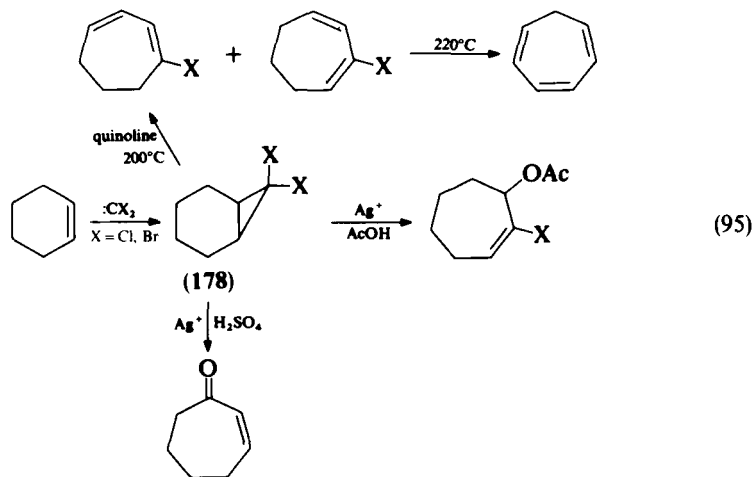
Thermolysis of 178 (X = Br) in quinoline gave a mixture of 2- and 1-bromo-cycloheptadiene-1,3 which, upon further heating at 220 °C, yielded cycloheptatriene (equation 95)[99]. Thus, starting from the same precursor a variety of products can be obtained from the electrocyclic ring-opening reaction. This ring-expansion reaction has also provided an interesting synthesis of tropone (179) (equation 96)[100].

$$(96)$$

$$(179)$$
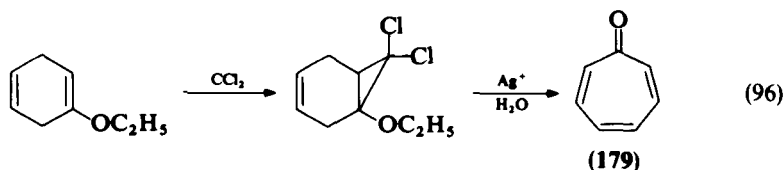
c. [*5.1.0*] *and* [*6.1.0*]. In the [3.1.0] and [4.1.0] systems the *endo* halogen is the preferred leaving group, since disrotatory electrocyclic ring opening leads to a *cis*-allyl intermediate which can be accommodated by the six- and seven-membered ring systems whereas the *trans*-allyl intermediate cannot. However, this is not the case with the [5.1.0] system. Reese and Shaw[58a] showed that treatment of 8,8-dibromobicyclo[5.1.0]octane (**89a**) with silver perchlorate in anhydrous methanol gave a quantitative yield of *trans*-2-bromo-3-methoxycycloctene (**90a**). The eight-membered and higher ring systems can readily accommodate a *trans*-double bond (equation 97).

$$\text{(97)}$$

(89a)   **(90a)**
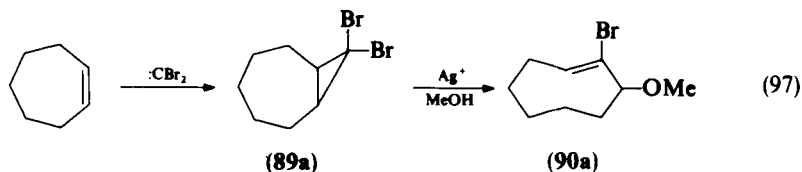
Baird and Reese[101] used this sequence of reactions to prepare a *cis,trans*-1,4-cyclooctadiene (**180**) (equation 98). For other examples of ring expansions to higher homologs see Section III.B.8.

$$\text{(98)}$$

(180)

75%   25%
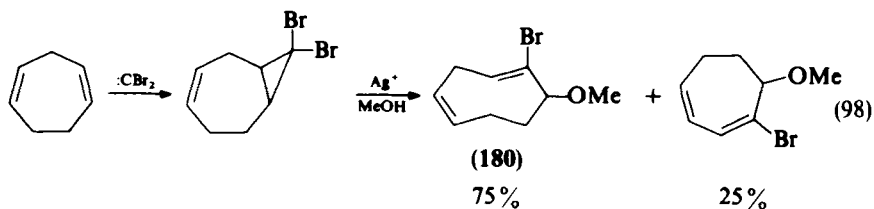
In summary, a general method for ring expansion is provided by the addition of dihalocarbene to a cyclic olefin followed by solvolysis of the adduct to give the next higher homologue via a disrotatory electrocyclic ring opening.

5. Tricyclic (propellanes)[102]

As discussed in Section II.B, the tricyclic [*m.n*.1] system is believed to yield the 'half-opened' cationic intermediate in the electrocyclic ring-opening reaction[23−25]. Attack by nucleophile at position 1 would lead to formation of ring-closed product with retention of configuration, as has been observed[23−25]. If, however, the attack by nucleophile is at position 2 or 3, then the ring-opened bicyclic [*m.n*.1]alk-1-ene possessing a *trans-double bond at the bridgehead* is obtained (equation 99). Whether such a product will be isolable can usually be predicted by Bredt's rule[103].

$$\text{(99)}$$
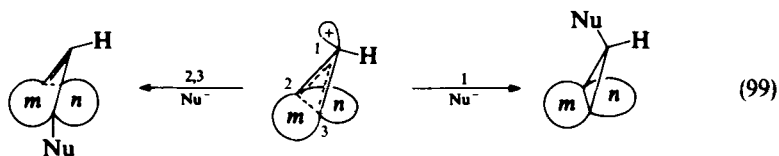
Warner and coworkers[104] found that addition of dichlorocarbene to 3,6-dihydroben-zocyclobutene (**181**) yielded a propellane, 9,9-dichlorotricyclo[3.2.1]non-3-ene (**182**). At 25 °C **182** decomposed to give a dimeric compound **183** whose structure was determined

by X-ray analysis. The structure of **183** implied that **185**, possibly formed via the 'half-opened' intermediate **184**, was the precursor to its formation. Indeed, **185** proved to be a very effective dienophile and was trapped by furan, in a Diels–Alder reaction, to give the adduct **186** (equation 100). It should be appreciated that **185**, although not isolated, is an early example of a bridgehead *trans*-double bond[103] in a seven-membered ring.

(181)   (182)   (184)   (185)

(100)

(186)   (183)
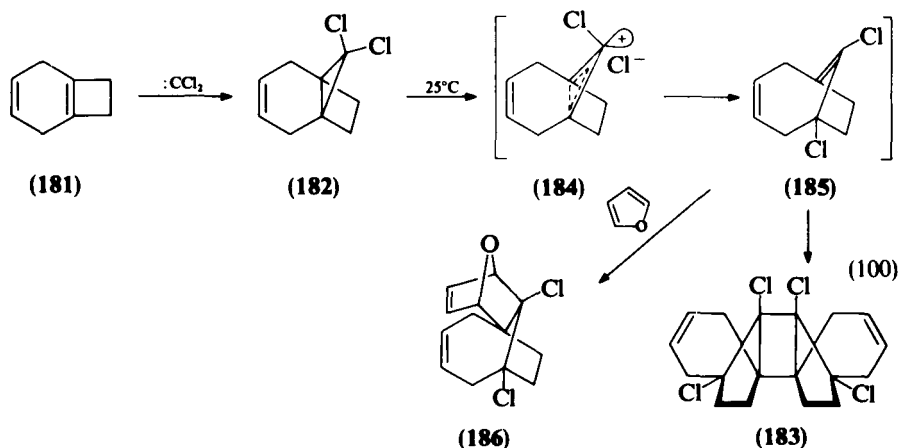
The suggestion of Warner and coworkers was not immediately accepted as evidenced by concurrent publications. Reese and Stebles[105] reported that the silver-ion-promoted solvolysis of 11,11-dibromotricyclo[4.4.1]undecane (**187**) yielded enone **188** as the major product (equation 101) and dismissed a disrotatory ring opening since it would lead to an unfavorable and highly-strained transition state. Ledlie[106] obtained a similar result and both authors postulated a 1,2-carbon shift to account for the formation of **188**.

(187)   (188)
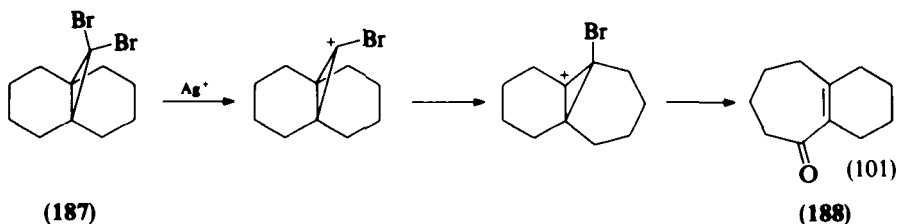
Reese and Stebles[105b] also investigated the silver-assisted solvolysis of 10,10-dibromotricyclo[4.3.1]decane (**189**) and 10,10-dibromotricyclo[4.3.1]dec-3-ene (**190**). The solvolysis of **189** yielded, as the minor component (15%), enone **191**. This result was analogous to the result obtained in the solvolysis of **187**. Besides **191** another product, **192**,

(189)   (191)   (192)
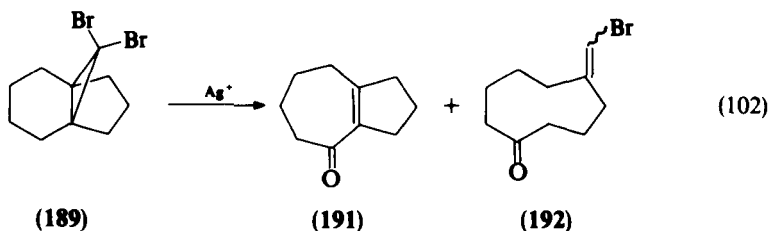
was produced in 50% yield (equation 102). Reese now postulated that **192** resulted from rearrangement of a highly-strained intermediate **193** by acid catalysis (equation 103).

$$(103)$$

(193)
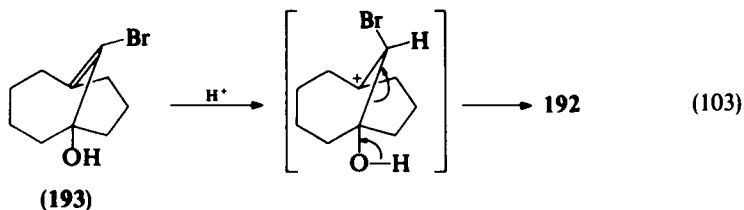
It should be noted that **193** contains a bridgehead *trans*-double bond which is similar to that of **185** proposed by Warner and coworkers earlier[104,107a]. Reese also proposed a highly-strained intermediate **194** as the precursor to **195**. The latter was formed by the silver-ion-catalyzed solvolysis of **190** (equation 104).

$$(104)$$

(190)   **(194)**   **(195)**
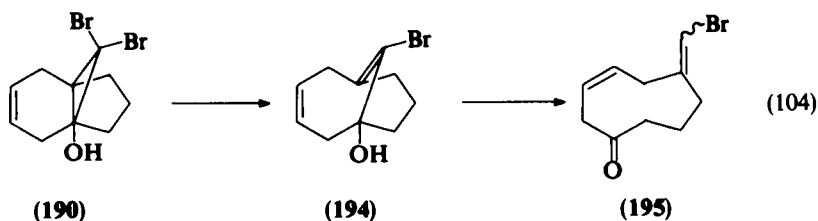
It was apparently agreed that **192** and **195** are formed as a result of disrotatory electrocyclic ring-opening of the three-membered ring, but the question as to the mode of formation of the enones **188** and **191** was still unsettled. Were they formed by a 1,2-carbon shift mechanism or from the same intermediate that led to the formation of **192** and **195** (*vide supra*)?

Warner and Lu[107b] designed a ^{13}C-labelling experiment to answer this question. They reasoned that if one labeled **187** with ^{13}C at C-11, then the 1,2-carbon shift mechanism would lead to the formation of **188** with the label at the carbonyl carbon (equation 105).

(187)

* denotes ^{13}C

(188)

$$(105)$$
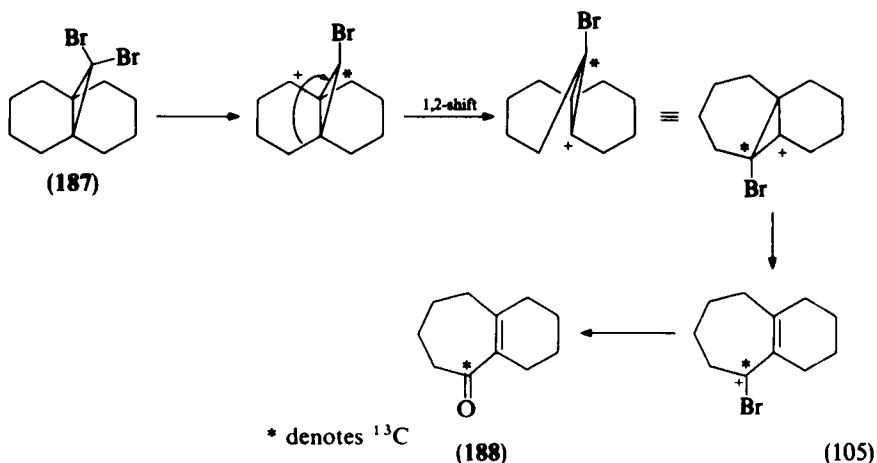
On the other hand if, as proposed by Warner and coworkers[104], solvolysis of **187** leads to a cyclopropyl cation (depicted here as a 'half-opened' cyclopropyl cation) which reacts with solvent to yield a bridgehead *trans*-double-bonded intermediate **196**, further reaction of **196** would lead to a product with the ^{13}C label at the vinyl carbon alpha to the carbonyl carbon (equation 106).

(106)
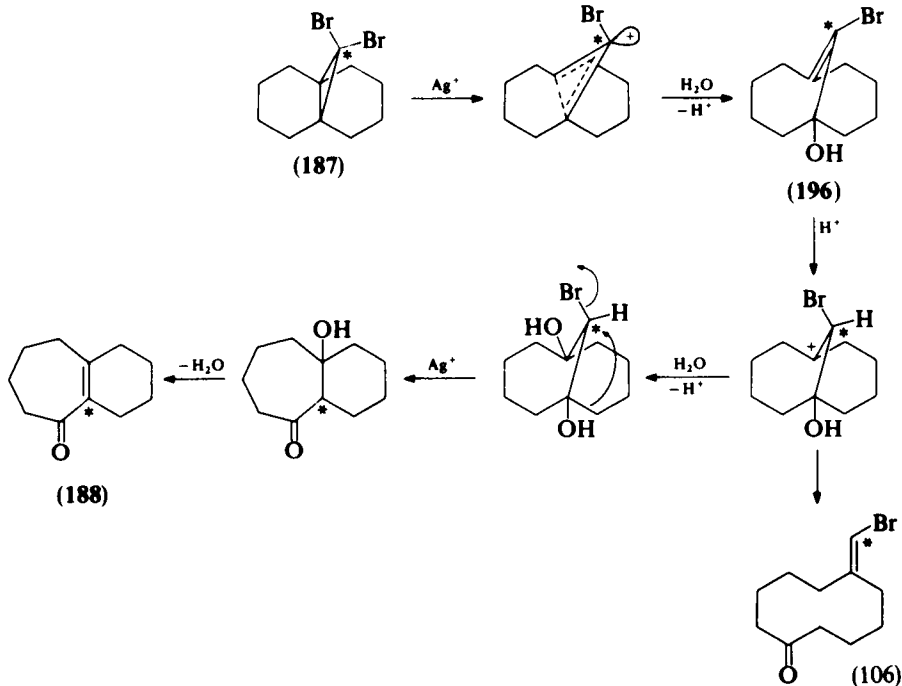
Indeed, all the label was found at C_α to the carbonyl as predicted by the above scheme, which strongly supports the belief that ring opening is the preferred mode.

Reese and Risius[108] as well as Ledlie and coworkers[109] were persuaded by the results of Warner and agreed that a bridgehead *trans*-double-bonded intermediate like **196** was involved in the silver-ion-catalyzed solvolysis of **197, 198, 199, 200** and **201**. Both groups

(107)

(107)
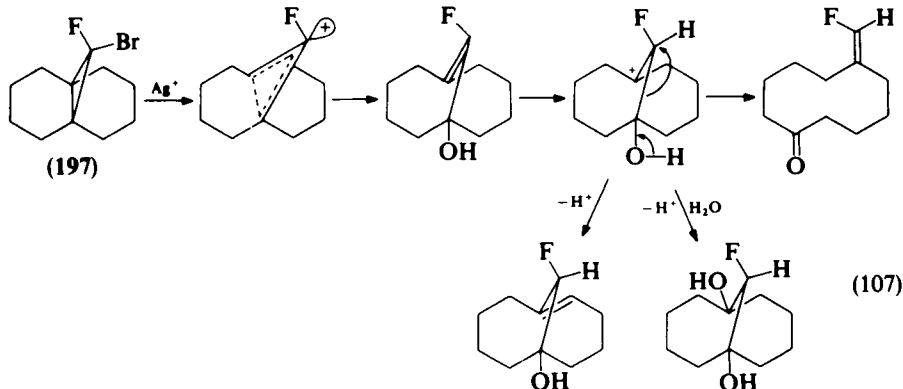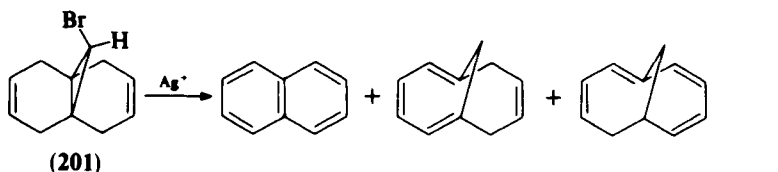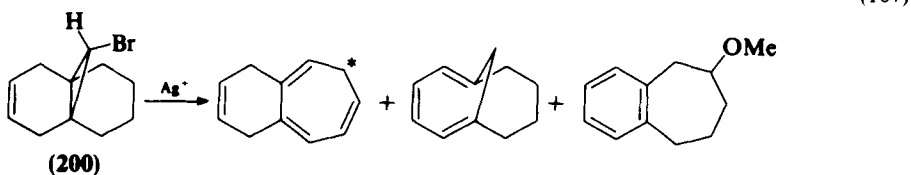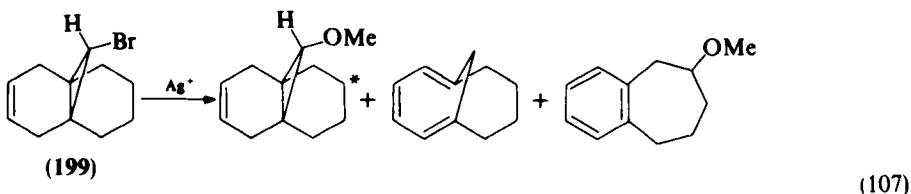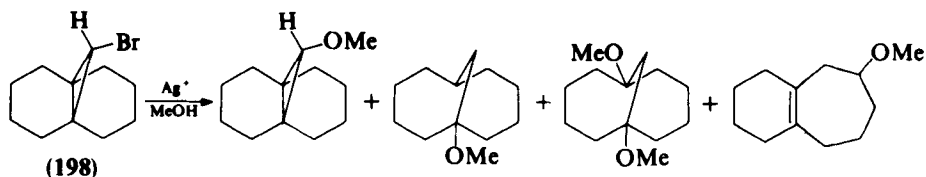
adopted the Warner mechanism in its entirety with the modification by Ledlie, who suggested a 'half-opened' cation instead of the cyclopropyl cation as the initial intermediate in solvolysis. The solvolysis products of 197–201 are shown in equation 107.

Nearly all of the above reaction products can be rationalized by the Warner mechanism[111]. The mode of formation of naphthalene in the solvolysis of 201 has been discussed by Ledlie and coworkers[110] and Warner and coworkers[111]. Structures with * are those corrected by Warner[111].

Having established that a *trans*-double bond at a bridgehead was feasible in rings of ≥ 7, Warner and Lu[112] investigated whether a six-membered ring could also accommodate a *trans*-double bond at the bridgehead. A possible precursor to the six-membered ring is 9,9-dibromotricyclo[3.3.1]nonane (202). Silver-assisted solvolysis of 202 in 90% aqueous acetone gave two major products 203 and 204 in 72% and 14% yield, respectively. These products are believed to result from the 'half-opened' three membered ring cation. Also isolated in minor amounts were compounds 205 and 206 in yields of 1.2% and 2.1%, respectively (equation 108). Only 206 is believed to arise from the

(108)
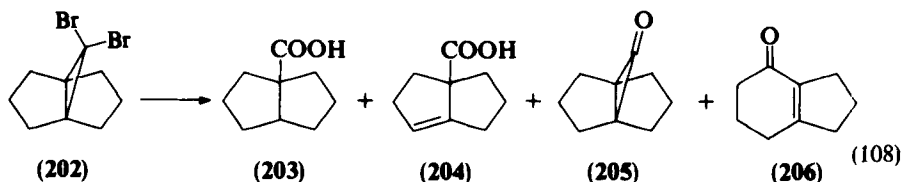
bridgehead *trans*-double-bonded intermediate and, if so, would indicate that this intermediate is a minor component in the reaction and that a six-membered ring does not accommodate a *trans*-double bond at a bridgehead very well.

A scheme (equation 109) has been suggested by Warner and Lu[112] to account for the formation of the observed products.

(109)
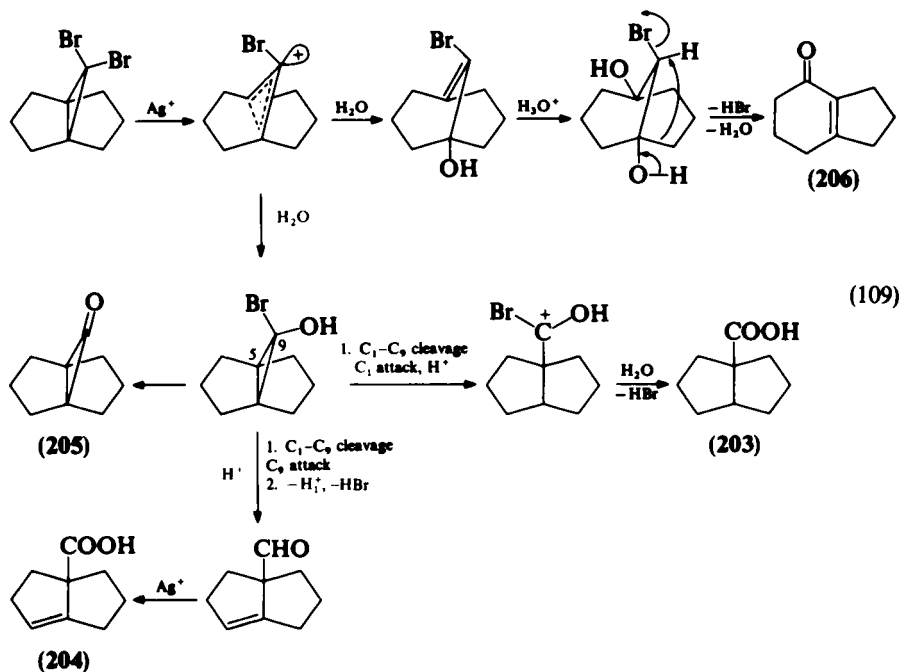
Warner and coworkers have also provided exhaustive and detailed product analyses on the solvolyses of 10,10-dibromotricyclo[4.3.1]decanes[113] as well as other dihalotricyclo[4.4.1]undec-3-enes[111]. They have also demonstrated that epimeric tricyclo[4.4.1]undec-3-enes give diastereomeric bridgehead olefins which retain their configuration (equation 110).

(110)
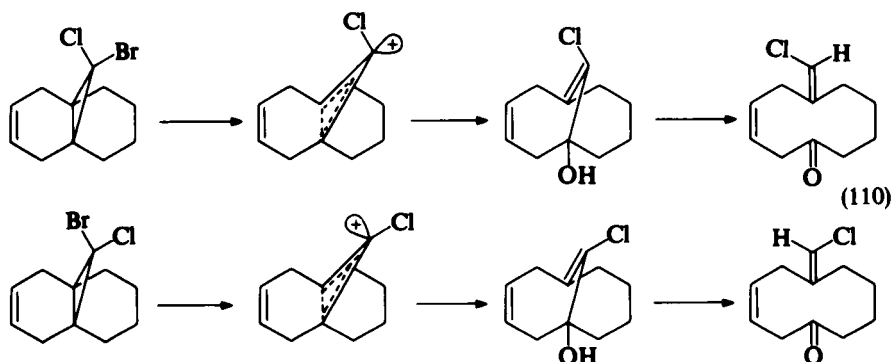
Consistent with this study are deuterium-labelling experiments[114]. Deuterium labeled **207** and **208** have been shown to solvolyze to yield their respective decanone derivatives **207c** and **208c** without scrambling of the deuterium label[114]. The overall specificity observed implies that there is no crossover between the nonplanar 'half-opened' cyclopropyl cations **207a** and **208a** nor is there any between the bridgehead *trans*-double-bonded intermediates **207b** and **208b**. Moreover, it also shows that the rearrangement of **207a** to **207c** and **208a** to **208c** is stereospecific (equation 111).

$$(111)$$
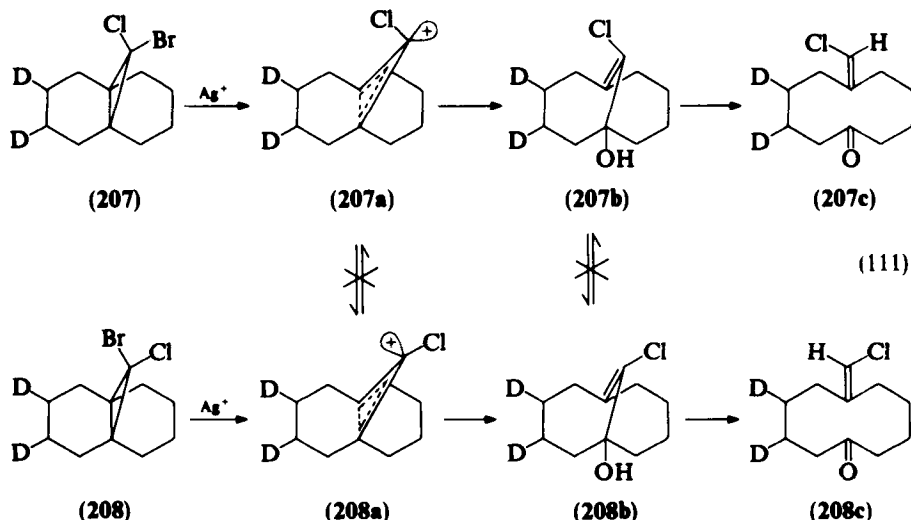
To summarize, the tricyclic [*m.n.*1] systems in which the three-membered ring bears one or more halogens have been shown to solvolyze to yield initially a 'half-opened' cyclopropyl cation, which reacts with solvent to give a bridgehead *trans*-double-bonded intermediate. Both intermediates are formed stereospecifically.

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CHAPTER **4**

Cyclopropyl carbenoids

I. INTRODUCTION

The appellation carbenoid[1] has been given to those intermediates possessing a metal and a halogen on the same carbon atom. Carbenoids are ambiphilic intermediates[2,3], i.e. they can, in their reactivity, behave as nucleophilic or as electrophilic reagents.

Nucleophilic   Electrophilic   Carbene
carbenoid   carbenoid
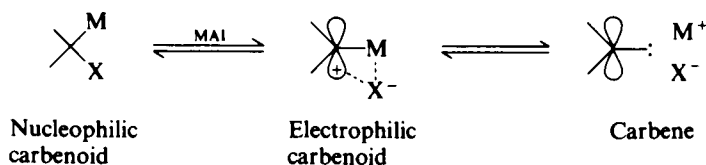
MAI = Metal Assisted Ionization
M = Metal

At very low temperatures, -130 to $-70\,°C$, depending on the other substituents on carbon, carbenoids may behave as nucleophiles whereas at higher temperatures (*ca* -90 to *ca* $-20\,°C$) they may react as electrophiles and at still higher temperature they can convert to carbenes[2a,b].

175

The structure and reactivity of the electrophilic carbenoids will be discussed with emphasis on those carbenoids possessing a cyclopropyl carbon.

II. EVIDENCE FOR CATIONIC NATURE

A. Stereochemistry

Carbenoids are most conveniently prepared by either halogen–metal exchange or by metalation of a suitable organic halide[4]. The former reaction is preferred since halogen–metal exchange can take place at temperatures as low as $-110\,°C$. This gives one

$$\text{Exchange} \quad \underset{X}{\overset{X}{C}} + M{-}R \longrightarrow \underset{X}{\overset{M}{C}} + R{-}X$$

$$\text{Metalation} \quad \underset{H}{\overset{X}{C}} + M^+B^- \longrightarrow \underset{M}{\overset{X}{C}} + B{-}H$$

$$B^- = \text{Base}$$
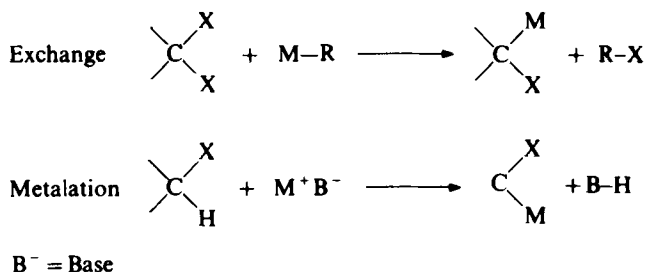
the opportunity to select the type of intermediate that he wants: nucleophilic carbenoid, electrophilic carbenoid or carbene.

Before discussing the cyclopropyl carbenoid attention will be focused on the vinyl carbenoid since it was here that the cationic nature of these intermediates was discovered.

The reaction, in ether, of (S)-(+)-(4-methylcyclohexylidene)bromomethane (1) with t-butyllithium at $-65\,°C$ was shown to yield a stable chiral lithium reagent as evidenced by carbonation to the known (S)-(+)-(4-methylcyclohexylidene)acetic acid[5] (3). In an attempt to increase the yield of the lithium reagent (2), (S)-(+)-1 was treated under Seebach and Neumann's conditions[6] using two equivalents of t-butyllithium at $-90\,°C$, followed by deuteriolysis.

$$(S)\text{-}(+)\text{-}(1) \xrightarrow[-65\,C]{t\text{-BuLi}} (S)\text{-}(2) \xrightarrow{CO_2} (S)\text{-}(+)\text{-}(3)$$
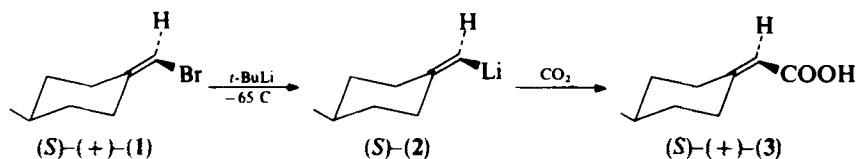
The yield of lithium reagent was not increased as reflected by the isolation of only a 58% yield of (S)-(+)-(4-methylcyclohexylidene)-deuteriomethane (4) and two other products, (R)-(−)-1-(4-methylcyclohexylidene)-1-deuterio-2,2-dimethylpropane (5) and (S)-(−)-1,2-bis(4-methylcyclohexylidene)-2-deuterioethane (6)[7].

(S)-(+)-4 is the major product, which is the result of the usual halogen–metal exchange which proceeds with complete retention of configuration whereas (S)-(−)-5 and (S)-(−)-6 are products derived from carbenoid (S)-7. Of interest to note is that the formation of carbenoid 7, formed by metalation, could be suppressed by carrying out the reaction in tetrahydrofuran rather than in diethyl ether (Table 1). THF favors halogen–metal exchange.

$(S)-(+)-(1)$

2 *t*-BuLi

$(S)-(2)$ + $(S)-(7)$

MeOD

$(S)-(+)-(4)$ + $(S)-(-)-(5)$ + $(S)-(-)-(6)$
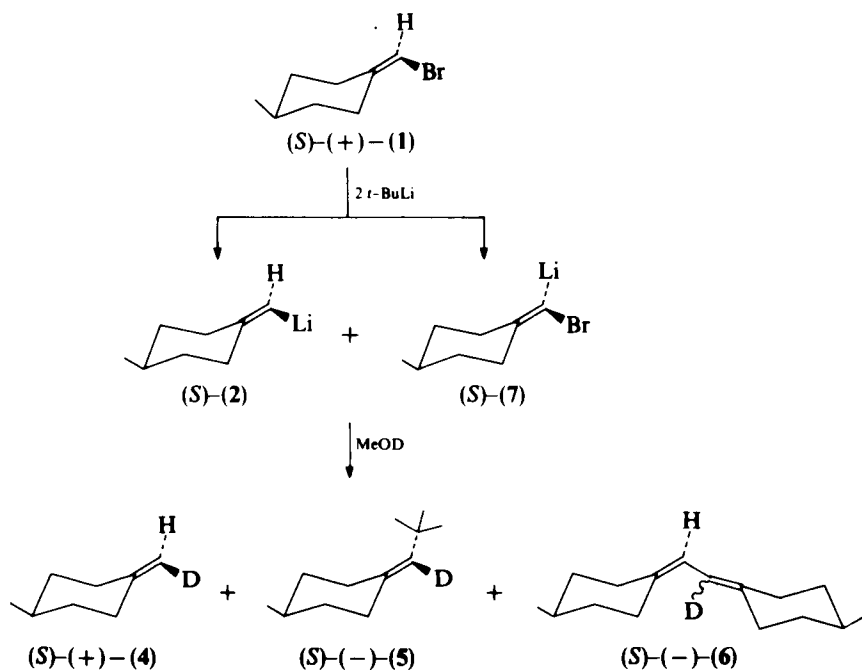
TABLE 1. Reaction of $(S)-(+)-(4$-methylcyclohexylidene) halomethanes with *t*-butyllithium

Halide	Solvent	T(°C)	4 % yield (% o.p.)[a]	5 % yield (% o.p.)[a]	6 % yield (% o.p.)[a]
Br	Et$_2$O	−90	58(100)	17(39)	0.5(50)
Br	THF	−90	90(100)	5(53)	5.0(50)
Cl	Et$_2$O	−95	—	36(31)	
Cl	THF	−95	—	70(39)	

[a] o.p. = optical purity.

The formation of $(S)-(-)-5$ of inverted configuration and *ca* 40% optical purity and of $(S)-(-)-6$ as a 1:1 mixture of diastereomers[8] with *ca* 50% optical purity is significant. The formation of 6 as a 1:1 mixture and of 50% optical purity is obviously the result of the addition of $(S)-2$ to carbene[3a] 8 formed from carbenoid 7. However, chiral 5 with inverted configuration could not have resulted from the addition of *t*-butyllithium to carbene[3a] 8 since this would have resulted in racemic 5.

Vinyl chlorides do not undergo halogen–metal exchange at any appreciable rate but they undergo metalation readily. Thus their use would result in elimination of products 4 and 6 and increase the yield of 5. It can be seen from Table 1 that this is precisely what has occurred.

(S)-(2)   8

| MeOD

(S)   (S)   (S)   (R)

(S)-(−)(6)   "meso"-(6)
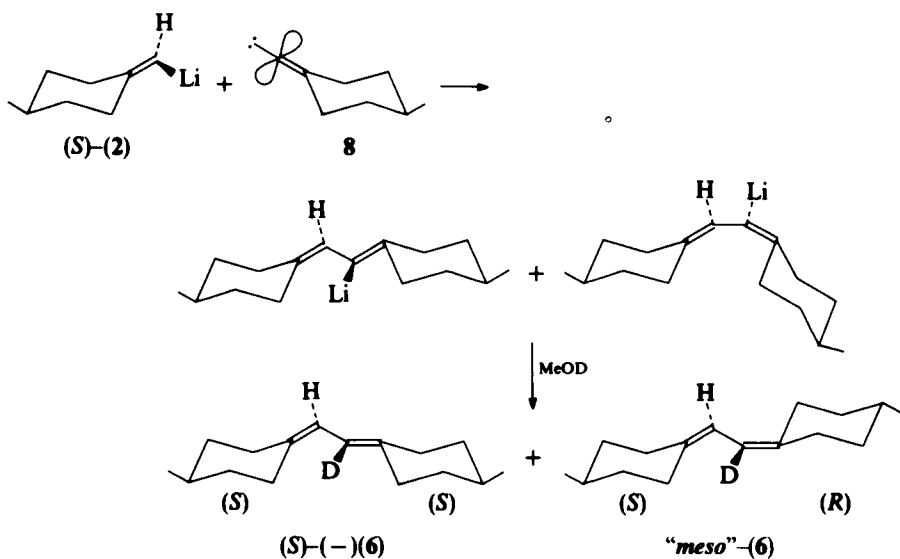
The mechanism postulated[7] for the formation of 5 is shown in Scheme 1.

Nu = Nucleophile

SCHEME 1   (±)
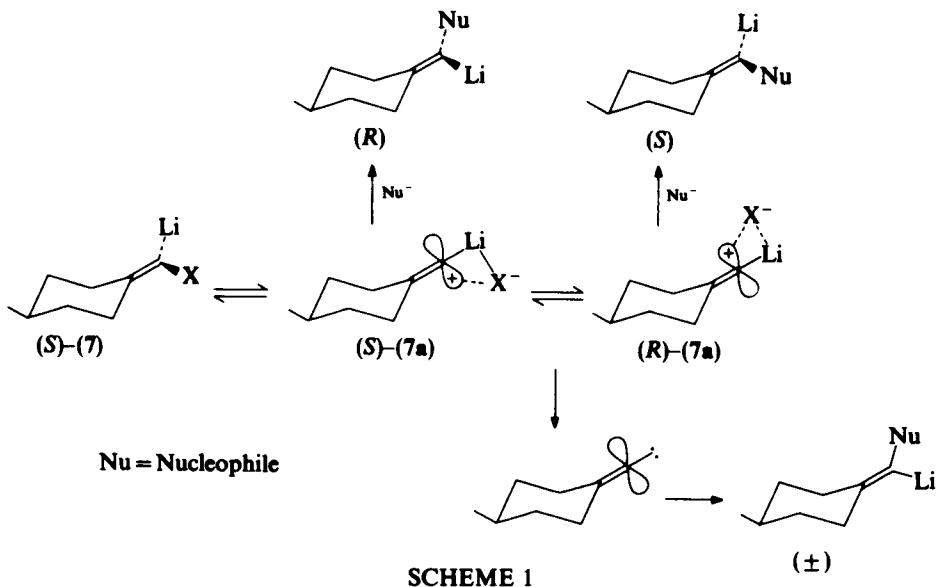
Ordinarily vinyl halides such as 1 are very slow to ionize and therefore do not undergo S_N1 reactions at an appreciable rate. However, when the proton is replaced by a lithium atom such as in carbenoid 7, then even at −70 and −90 °C there is a weakening of the carbon–halogen bond (*vide infra*) and ionization occurs. This results in generating a positive charge in a p orbital on carbon to produce a tight ion pair. The ionization of the halogen is facilitated by coordination with the lithium and this process has been referred

to as 'Metal Assisted Ionization' (MAI)[7]. The departing halide would block one enantioface of the substrate in the still chiral tight ion pair so that the nucleophile, i.e. *t*-butyllithium, would attack from the opposite side leading to inversion of configuration. The racemization that is observed in **5** could be due to either carbene formation (**8**) followed by addition of *t*-butyllithium or to the lithium atom in the tight ion pair behaving as a pivotal point about which the halogen can migrate from one face to the other [(*S*)-**7a**→(*R*)-**7a**]. The stereochemistry observed, partial racemization and overall inversion of configuration, is typical of a solvolysis reaction involving a chiral substrate[9].

The cationic nature of carbenoids is also demonstrated in the Fritsch–Buttenberg–Wiechell rearrangement[2a, 10] where electron-donating groups (X) in the *para* position of the migrating aryl group facilitate the rearrangement and electron-withdrawing groups retard it (reactivity order of X = Cl < H < Me < OMe). The rearrangement has also been shown to be stereospecific in that the migrating group in general prefers to be *trans* to the leaving halogen[2a].
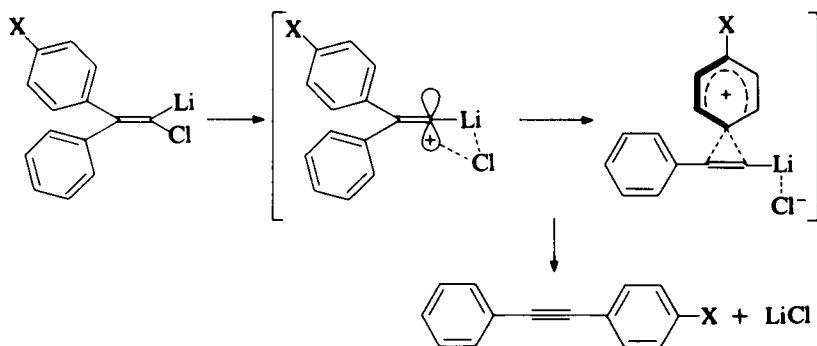
Further stereochemical evidence for carbenoids behaving as cationic intermediates is found in the reaction of (*S*)-(+)-1-chloro-2,2-diphenylcyclopropane (**9**) with n-butyllithium. Here, again, the halide **9** is also unreactive toward solvolysis[11] being at least 10⁶ times slower than, for example, cyclohexyl chloride. The cyclopropyl system provides an additional probe in that the cyclopropyl cation undergoes electrocyclic ring opening, and therefore if carbenoids are to be viewed as cationic intermediates one should observe ring-opened reaction products and this is precisely what is observed[12a].
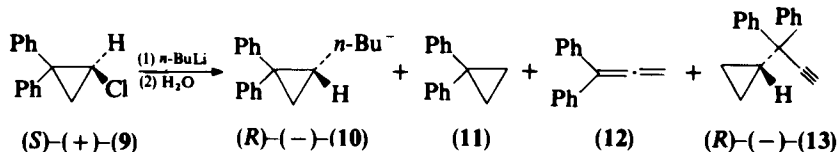
Treatment of (*S*)-(+)-**9** with two equivalents of n-butyllithium at −25 °C in THF resulted in the formation of (*R*)-(−)-**10** in 20% yield and with an optical purity of 51%. Note that the configuration of **10** is inverted[12b]. The formation of **11** in 9% yield is due either to a small amount of halogen–metal exchange or to hydride abstraction from n-BuLi coordinated to **15**. The products **10, 12** and **13** are the result of metalation to give carbenoid (*S*)-**14**, which undergoes metal-assisted ionization to the tight ion pair (*S*)-**15**. This intermediate is best viewed as either a half-opened or closed structure (see Chapter 3). The nucleophile, n-butyllithium, attacks the intermediate from either face with inversion predominating. When the σ orbital containing the positive charge becomes a p orbital,
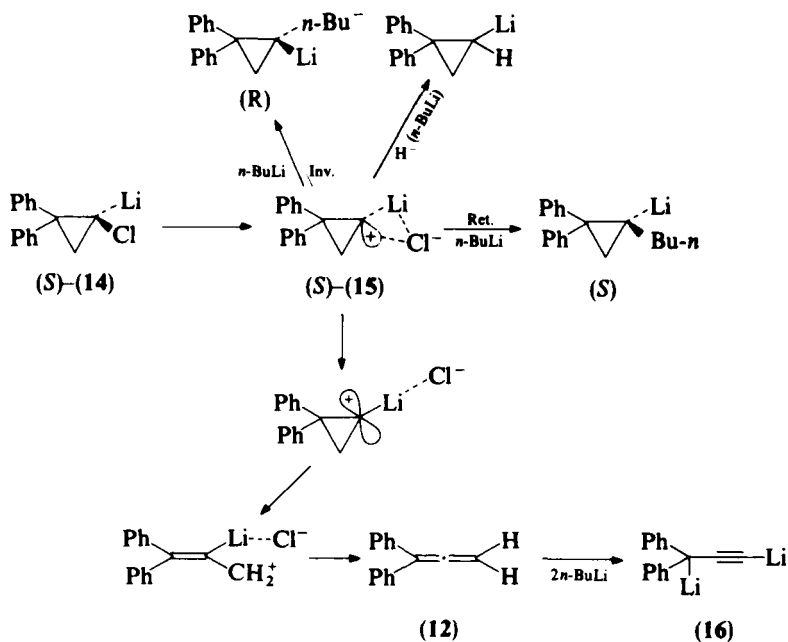
electrocyclic ring opening occurs to yield the open allyl cation, which is converted to allene 12. The allene in the presence of lithium reagents is readily converted to 16. The major product (*ca* 50%) R-(−)-13 is the result of inversion by nucleophilic 16 on (S)-15 in the same manner as does n-butyllithium.

Negishi and coworkers[12c] have also observed that the reaction of 1-bromo-2-methyl-2-phenylcyclopropyllithium with Cp_2ZrCl (*n*-octyl) at − 78 °C resulted in the formation of 1-n-octyl-2-methyl-2-phenylcyclopropane. This reaction probably also proceeds by attack of nucleophile on a carbenoid analogous to that represented by 15.

B. ¹³C NMR

Seebach and coworkers[13] have provided ¹³C NMR evidence for the electron-deficient nature of the carbenoid carbon. Table 2 shows the effect of replacing the proton on the halogen-bearing carbon by a lithium atom. One observes, at − 100 °C, a large amount of deshielding with a $\Delta\delta$(H, Li) on the order of 50–60 ppm for the cyclopropyl carbon and 65–100 ppm for the vinyl carbon. These results are consistent with the view that replacing the proton by a lithium atom causes a weakening of the C–Br bond and decreasing the electron density about the carbon atoms leading to structures like 7a and 15. These structures have also been proposed by Köbrich and coworkers[2a] and Seebach and coworkers[13b].

C. *Ab Initio* Calculations

Schleyer, Houk and coworkers[14] have reported calculations on the geometry and energy for carbenoid intermediates. Their results on CH_2LiX (X = F, Cl) are shown below and one notes that the structures are similar to those discussed earlier. The replacement of a proton by a lithium atom in tetrahedrally hybridized CH_3X (X = F, Cl) to give the

TABLE 2. ^{13}C-NMR spectra of lithium carbenoids in THF[13]

Compound	δ(ppm)	Carbenoid	δ(ppm)	$\Delta\delta$(H,Li) (ppm)
bicyclo[n.1.0] cyclopropane with H, Br	25.8	bicyclo[n.1.0] cyclopropane with Li, Br	87.8	62.0
bicyclo cyclopropane with Br, H	34.7	bicyclo cyclopropane with Br, Li	90.7	56.0
bicyclooctane cyclopropane with Br, H	24.4	bicyclooctane cyclopropane with Br, Li	79.9	55.5
dihydronaphthalene cyclopropane with H, Cl	43.5	dihydronaphthalene cyclopropane with Li, Cl	86.0	42.5
dihydronaphthalene cyclopropane with H, Br	36.4	dihydronaphthalene cyclopropane with Li, Br	102.7	66.3
Ph, H / H, Br cyclopropane	23.0	Ph, Li / H, Br cyclopropane	76.8	53.8
Ph, Br / H, H cyclopropane	25.5	Ph, Br / H, Li cyclopropane	80.9	55.4
H, Cl / Cl, H ethylene	121.3	H, Cl / Cl, Li ethylene	189.4	68.1
cyclohexylidene with H, Br	99.2	cyclohexylidene with Li, Br	200.8	101.6
t-Bu-cyclohexylidene with H, Br	121.8	t-Bu-cyclohexylidene with Li, Br	187.2	65.4

carbenoid $LiCH_2X$ (X = F, Cl) results in the bridged structure as the most stable one. These workers view these structures as being tight ion pairs $(LiCH_2)^+ X^-$, which would be consistent with the electrophilic character of the carbenoids. The geometry of a trigonally hybridized carbenoid such as 1-lithio-1-fluoroethylene corresponds in structure to the
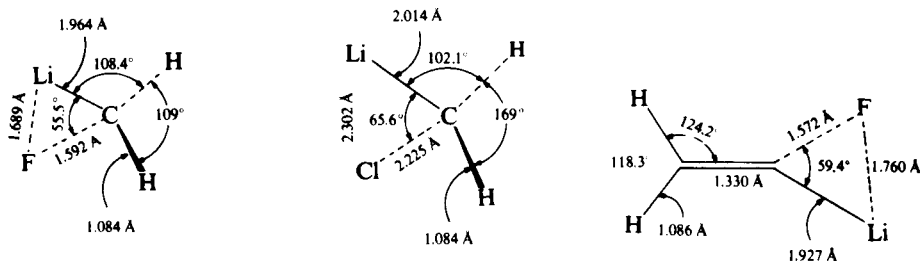
tetrahedrally hybridized carbenoids[15]. With the understanding that these structures were generated by the use of 'gas-phase' calculations (unsolvated species), the calculations agree with what would be expected for carbenoid intermediates that possess electrophilic character and are consistent with the stereochemical results observed in their reactions.

III. REACTIONS OF CARBENOIDS

A. Rearrangement to Allenes[16]

Doering and La Flamme[17a] made the original observation that geminal cyclopropyl dihalides when treated with sodium or magnesium metal yield allenes in good yield. They suggested that the two-step sequence of addition of dibromocarbene to an olefin followed by reaction of the adduct with magnesium or sodium metal might represent a general method to increase the chain length by one carbon atom. Logan[18] showed that
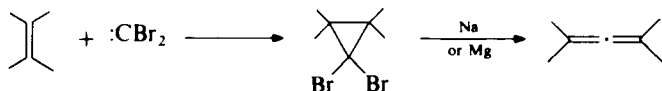
dichlorides and Grignard reagents also react to yield allenes. Moore and coworkers[17b, 19a] and Skattebøl[20] extended this reaction to include the use of alkyllithium reagents instead of Grignard reagents or metals. The yields of allenes were in general improved. Table 3 lists a number of substituted geminal dihalides that have been converted to allenes in good yields.

As expected cyclic allenes, C_9 and higher, are also amenable to preparation by this method[16]. Cyclonona-1,2-diene was prepared in 93% yield[19, 20] and cyclodeca-1,2-diene in *ca* 80% yield[19]. Skattebøl[20] has also prepared cyclic diallenes by converting 17$_n$ ($n=2,5$) to the corresponding diallene 18$_n$ ($n=2,5$) in moderate yield.

The stereochemistry of this reaction has been investigated by Moore and Bach[25]. The addition of dibromocarbene to *trans*-(S)-(+)-cyclooctene (19) gave the desired starting material (1R,8R)-(−)-20. Treatment of (1R,8R)-(−)-20 with methyllithium at −78 °C yielded the cyclic allene (S)-(−)-21 with approximately 95% optical purity. The absolute configuration of 21 had been established previously[26]. The ring opening has occurred by either a conrotatory mode of the *trans*-methylene groups or a monorotatory opening.

(17$_n$)   (18$_n$)
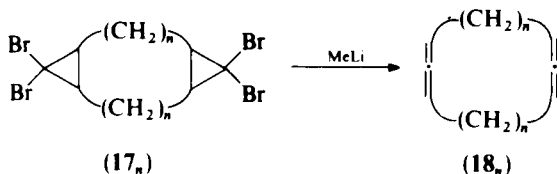
TABLE 3. Conversion of substituted geminal cyclopropyl halides to allenes

R¹	R²	R³	R⁴	X	M, RM	Allene, % yield	Ref.
Me	H	Me	H	Br	Mg	10	17a
Me	H	Me	H	Br	Na/Al₂O₃	44	17a
n-Pr	H	H	H	Br	Na/Al₂O₃	64	17a
n-Pr	H	H	H	Br	Mg	34	17a
n-decyl	H	H	H	Cl	EtMgBr	44	18
n-octyl	H	H	H	Br	MeLi	68	19c
Δ³-butenyl	H	H	H	Br	MeLi	72	20
t-Bu	H	H	H	Br	MeLi	56	21
t-Bu	Me	H	H	Br	MeLi	42	23
n-Pr	H	Me	H	Br	MeLi	88	19c
Me	Me	Me	H	Br	MeLi	69	20
Me	Me	Me	Me	Br	MeLi	73	20
Ph	H	H	H	Br	MeLi	82	20
Ph	Ph	H	H	Br	MeLi	43	20
–CH₂-CH₂–		–CH₂-CH₂–		Br	MeLi	86	22
–CH₂-CH₂–		H	H	Br	PhLi	a	24
t-Bu	H	Me	H	Br	MeLi	a	23
t-Bu	H	H	Me	Br	MeLi	a	23
Ph	Me	H	H	Br	MeLi	a	23
Ph	i-Pr	H	H	Br	MeLi	a	23

* Only product isolated.

A similar but less stereospecific result is obtained in the decomposition of the diazo intermediate (1R,8R)-**22**. Whether the allene (S)-(−)-**21** derives from a carbene intermediate generated by the decomposition of (1R,8R)-**22** or from a carbenoid precursor

(S)-(+)-(19)   (1R,8R)-(−)-(20)   (S)-(−)-(21)   (1R,8R)-(22)
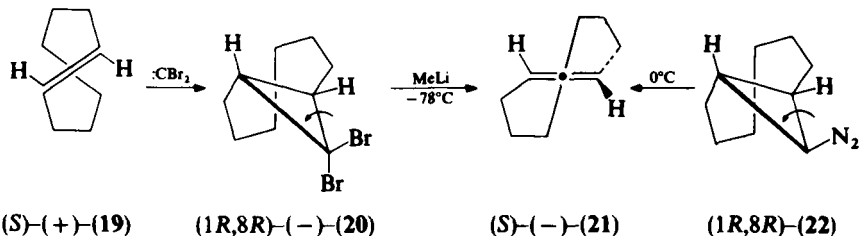
obtained by treating (1R,8R)-(−)-**20** with methyllithium, the ring opening is opposite to that observed by Jones and coworkers[16c] in their monocyclic systems (R = Me,Ph).
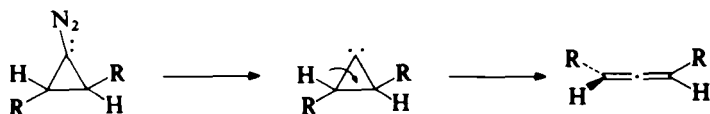
It is believed that the difference between the bicyclic and monocyclic carbene or carbenoid systems is due to the accommodation of torsional strain in the bicyclic system, caused by the *trans* fusion of the ring, which becomes more important than the steric effects that seem to control the opening of the monocyclic ring system. The mechanism of this reaction is not completely understood but it is clear that any mechanism proposed must not involve a planar intermediate.

The singlet cyclopropylidene-to-allene rearrangement has received a great deal of theoretical investigation[27-29]. The MINDO/2 method[27] concluded that the opening was nonrotatory and that the rotation of the groups occurred only after the transition structure has been passed. Using the INDO method Dillon and Underwood[28] found the rearrangement to occur by an initial disrotatory motion followed by the reversal of one of the methylene groups until an unsymmetrical transition structure with a C–C–C bond angle of *ca* 96° is obtained. From this structure the reaction proceeds by a conrotatory motion to yield allene. Pasto and coworkers[29] deduced from their *ab initio* studies a mechanism that was similar but not identical to the one proposed by Dillon and Underwood[28]. They argued that the reaction proceeds initially by a disrotatory motion almost to the transition state where the C–C–C bond angle is somewhere between 90° and 94.5°. At this point a rapid change occurs from the disrotatory structure to a monorotated structure which is then converted to allene.
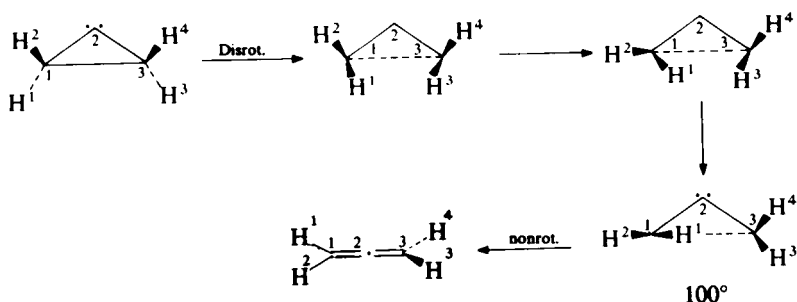
Rauk and coworkers[30], using analytical gradient techniques to create stationary points on the potential hypersurfaces which have been rigorously characterized through vibrational analysis, confirmed the mechanism proposed by the Pasto group[29] and by Dillon and Underwood[28]. Ruedenberg and coworkers[31] in a more complete examination of the energy surface found that the transition state was bifurcated and that on the downhill path from the transition state to the product, *ca* 95° on, 'the two CH_2 groups can rotate freely in a synchronized cogwheellike fashion'. Hence, since any stage of this free internal motion leads to a staggered allene; there does not exist a unique single reaction pathway from the transition state to the product. However, the stereoisomerism observed requires a concerted twisting and bending.

The investigation of 2,3-dimethylcyclopropylidene showed, in agreement with experiment[16c], that the *cis* isomer is nonstereospecific and the *trans* isomer is stereospecific in that, after bifurcation, the preferred branch corresponds to that conrotatory motion which places a hydrogen rather than a methyl group close to the C–C–C ring. Thus, steric effects play an important role. These same workers also provided evidence that dipolar attraction can also be a significant factor.

Some interesting and unusual rearrangements are depicted below. The reaction of **23** with methyllithium resulted in the formation of indene (**24**). This conversion is believed to proceed by the initial formation of allene intermediate which undergoes ring closure followed by a 1,5-sigmatropic rearrangement[32]. A similar[32b] sequence of reactions is involved in the conversion of **25** to **26**.

(23)   (24)

(25)   (26)
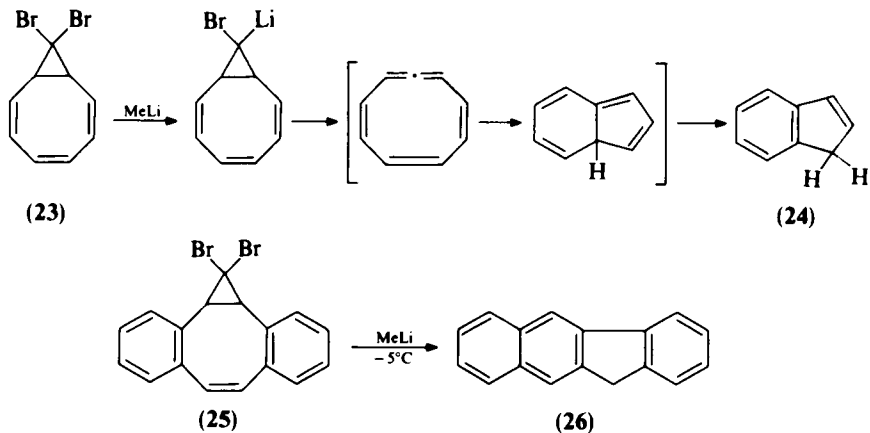
A cyclic cumulene (27) has also been prepared by the carbenoid–allene rearrangement sequence[33a].

(27)
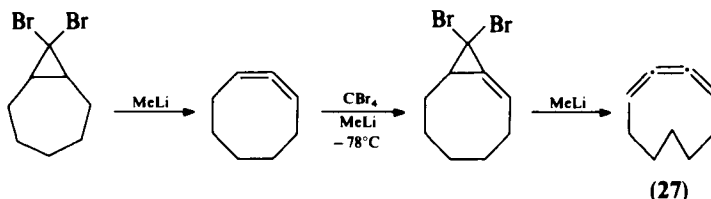
Although one cannot be certain whether carbenoids are the reactive intermediates, the use of ultrasonic radiation for the reaction of *gem*-dihalocyclopropanes with either sodium, lithium or magnesium metal holds promise as being a convenient method to produce allenes[33b]. The reaction is over in minutes and the yields are very good (Table 4).

B. Insertion into C–H Bonds

Goldstein and Dolbier[34] had established, early in 1965, that the intermediate involved in the intramolecular insertion reaction of α-haloneopentyllithium was the carbenoid itself and not a carbene. This section will deal with the insertion reactions of such carbenoids.

X = Cl, Br, I
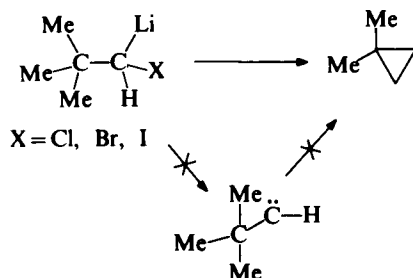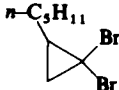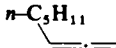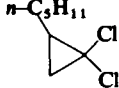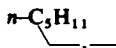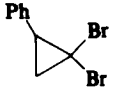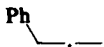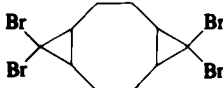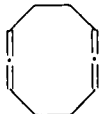
TABLE 4. Reaction of *gem*-dihalocyclopropanes with metals under ultrasonic radiation[33b]

gem-Dihalide	Metal	Irradiation time (min)	Product	Yield (%)
n-C₅H₁₁, Br, Br	Li	10	n-C₅H₁₁	81
	Mg	10		87
n-C₅H₁₁, Cl, Cl	Na	5	n-C₅H₁₁	68
Ph, Br, Br	Mg	10	Ph	76
Br, Br, Br, Br	Li	20		63

Similarly, if the cyclopropane ring is heavily substituted, then the reaction of *gem*-dihalides with methyllithium does not result in allene formation but instead an intra-molecular carbenoid insertion into a C–H bond is observed. Hence the reactions of **28** and **29** with methyllithium yield the bicyclobutanes **30** and **31**, respectively[35]. Of interest is the
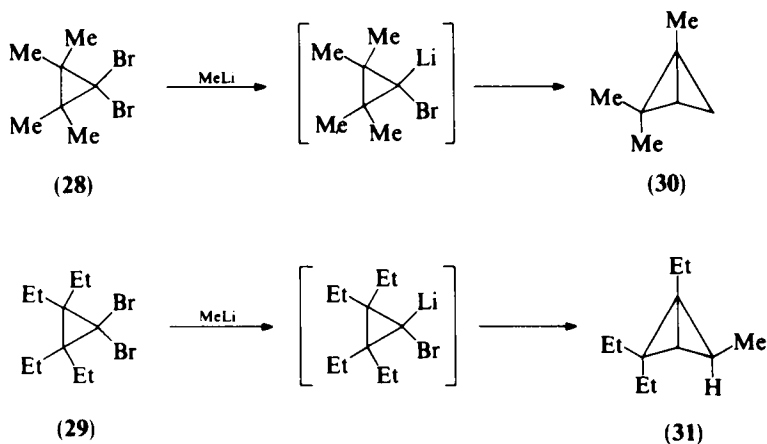
observation that in **32** the insertion occurs almost exclusively (> 87%) in the CH₂ group of the ethyl rather than in the methyl groups[35c]. In general, excluding electronic, conformational and unusual steric effects[19b], carbenoids show a 3° > 2° > 1° order for insertion into a C–H bond[19a].

(32)

For the most part, *monocyclic* cyclopropanes that are mono- or disubstituted will not yield insertion products but instead will ring-open to yield allenes (*vide supra*). This is understandable, since electrocyclic ring-opening should be sterically retarded in the tetra-substituted cyclopropanes thus permitting other possible reactions to occur, such as insertion. Other factors that will determine the extent of allene formation *vs* insertion will be steric interactions such as in the case of 33, where the *t*-butyl group causes an increase in the angle (α) which places the methyl group closer to the carbenoid center and gives rise to a 42% yield of bicyclobutane 34 and only a 28% yield of the allene 34a[36].

(33)   (34)   (34a)
                        42%   28%

Nonbonding electron pairs on heteroatoms can play a significant role in stabilizing the carbenoid and in this manner suppress allene formation[2d]. This may account for the observation that 35 yields the insertion product 36 rather than allene[37].

(35)   (36)

A similar example has been provided by Fraser-Reid and coworkers[38] who showed the effect of an additional oxygen atom and a phenyl group.

An amino nitrogen, e.g. *N*-benzyl, will also exhibit stabilization as exemplified by the reaction of 37 with n-butyllithium to yield 38[39a]. The amide function of 39 appears to behave as a stabilizing group as well giving 40[39b].

(37)   (38)

(39)   (40)

Nonbonding electron pairs play an important role in that they can either direct (kinetic) the halogen–metal exchange or cause equilibration of the carbenoid epimers (thermo-dynamic) formed by halogen–metal exchange to be that epimer in which the lithium atom is *syn* to the atom bearing the n electrons. Besides the examples illustrated above Nozaki and coworkers[39c] (equations 1 and 2) and Taylor and coworkers[39d] (equations 3 and 4) have provided further experimental verification. It should be appreciated that ordinarily halogen–metal exchange would be expected to occur from the least hindered *exo* side.

(1)

(2)

(3)

X = Cl, Br

(4)

X = Cl, Br
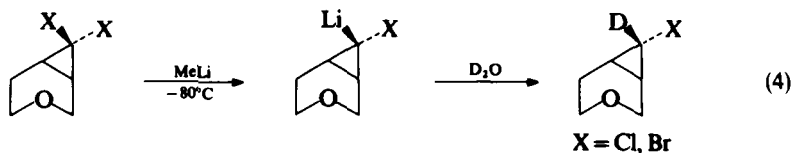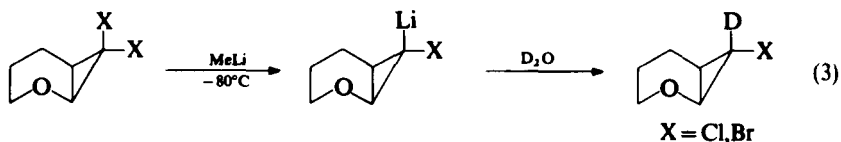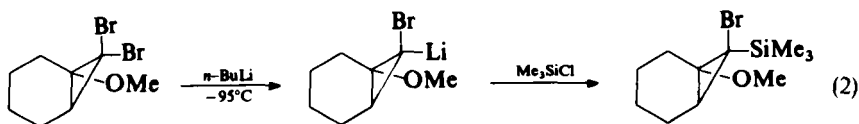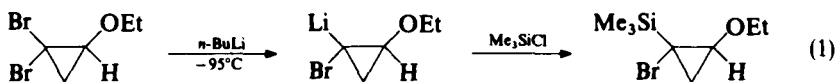
An alkoxide group is an excellent hydride source which can promote insertion by a neighboring carbenoid. This was demonstrated by Skattebøl and coworkers[40] in an elegant manner. The reaction of **41** with an excess of methyllithium in ether at −55 to −75 °C resulted in the formation of allene **42** (30%) and the cyclopropyl carbinol **43** (15%). The formation of **43** is of interest. Skattebøl reasoned that **43** was formed by the insertion of carbenoid into the C–H bond adjacent to the oxygen function to give the bicyclobutane derivative **44**. Rearrangement of **44** *via* cyclopropoxide rearrangement[41]

(41)   (42)   (43)
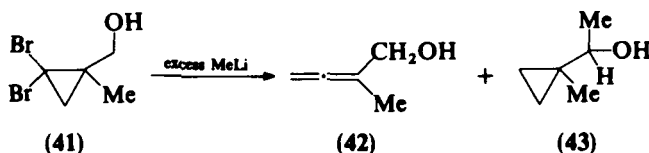
would lead to the formation of aldehyde **45**, which in turn would react with excess methyllithium to produce **43**. Supportive evidence for the reaction scheme was provided by treating the deuteriated alcohol **46** under identical conditions to yield alcohol **47** with the labelling in complete agreement with the mechanism proposed.

(44) (45) (43)

(46) (47)
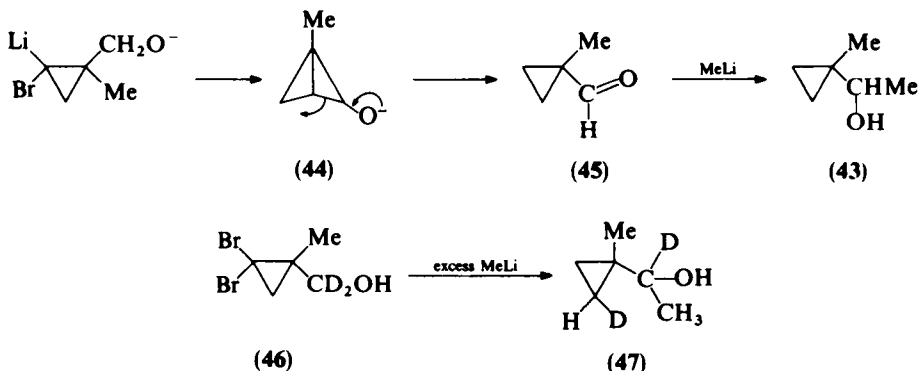
The effectiveness of alkoxides as a source of hydride has been further demonstrated by the work of Oku and coworkers[42] who used alkoxides as a trap for carbenoids in an *intermolecular* reaction. They showed that a hydride abstraction–recombination mechanism rather than a concerted insertion mechanism obtains in the reaction of norcaranylidene carbenoid with alkoxides. This conclusion was based on the preferential *endo* stereoselectivity observed in the carbenic carbon of the insertion products. Thus, when **48** was treated with methyllithium in ether at 0 °C in the presence of either potassium benzyl oxide, 2-phenethyl oxides or cyclohexyl oxide, the yield of *endo* product **49** was 85%, 93% and 100%, respectively. A concerted insertion mechanism would be expected to yield *exo* product by the approach of the alkoxide from the least hindered *exo* face. That hydride abstraction is such a common reaction of carbenoids further strengthens the view that carbenoids should be considered as cationic intermediates[12, 15].

(48)

endo-(49)
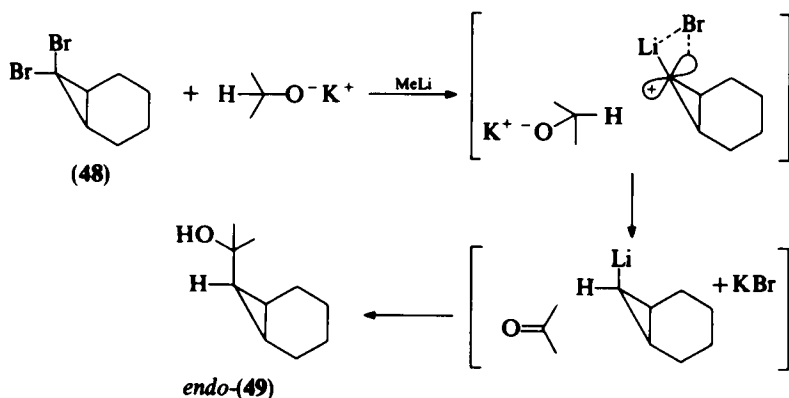
In this mechanism, as expected, the *exo* bromide undergoes halogen–metal exchange to yield the carbenoid and the hydride is abstracted from the less hindered *exo* face to give rise to a configurationally stable[5] *endo* cyclopropyllithium reagent. The lithium reagent

can then condense with the carbonyl derivative, which had been formed from the alkoxide by the abstraction of hydride, to yield *endo* **49**.

Electronic effects are also shown by molecules possessing geminal aryl groups. Since two aryl groups can strongly stabilize a positive charge, those molecules possessing this moiety will tend to increase the extent of C_2–C_3 bond breaking in the transition state and hence undergo ring opening, which will then result in allene formation. This effect accounts nicely for the observation that **50** yields 27% allene whereas **51** yields no allene and that **52** gives allene exclusively[35d]. Further support is found in the observation that
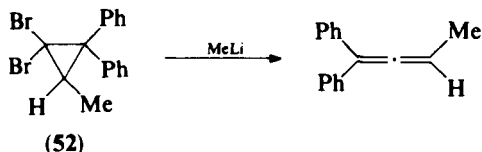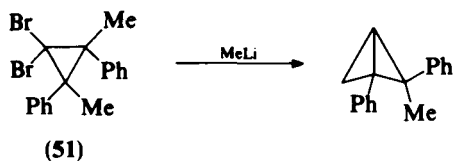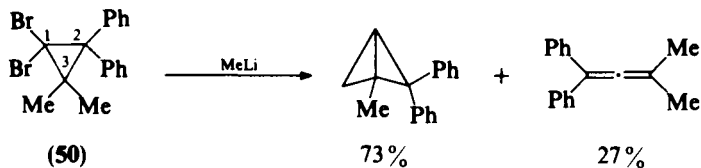
replacing the phenyl groups in **50** by *p*-anisyl groups (An) in **53** leads to an increase in the yield of allene[35d].
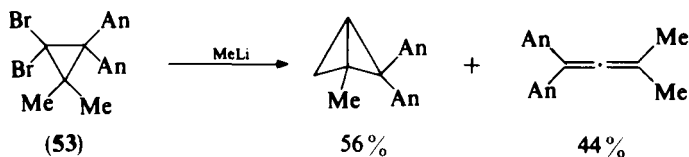
In bicyclic systems [*n*.1.0] where *n* > 5, one can isolate cyclic allenes in reasonable yields (*vide supra*). When *n* = 5 (**54**) one obtains[43], *inter alia*, not only the dimer **55** of the cyclic allene but also the insertion product **56**. When *n* = 4 (**57** and **58**) one no longer observes
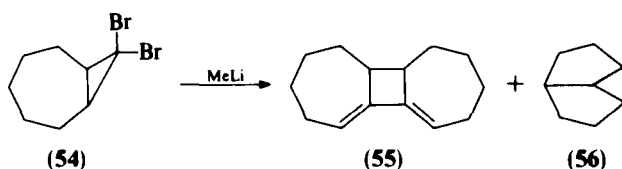
any allene formation, but the yield of insertion product is increased[44]. Here again in **58**, one observes[45] the preference for a CH_2 (2°) group over the methyl (1°) group for insertion.

(57)   37%   1.6%

(58)   40%   60%
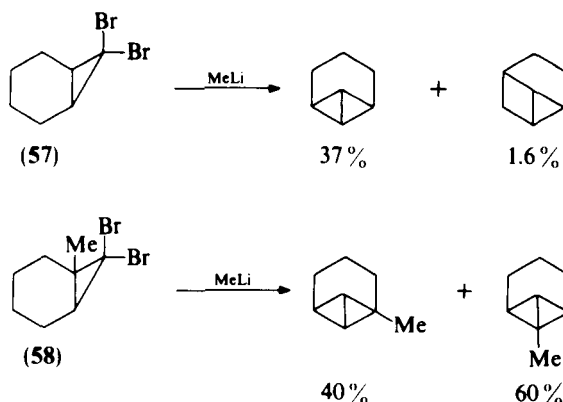
Conformational effects also play a significant role in the C–H insertion by carbenoids[2d]. This has been demonstrated by the work of Paquette and coworkers[46] on the reaction of **59** with methyllithium to yield **60** and **61** in relative yields of 23 and 77%, respectively. This result requires that the carbenoid undergoes C–H bond insertion via

(59)   (60)   (61)
                              23%   77%
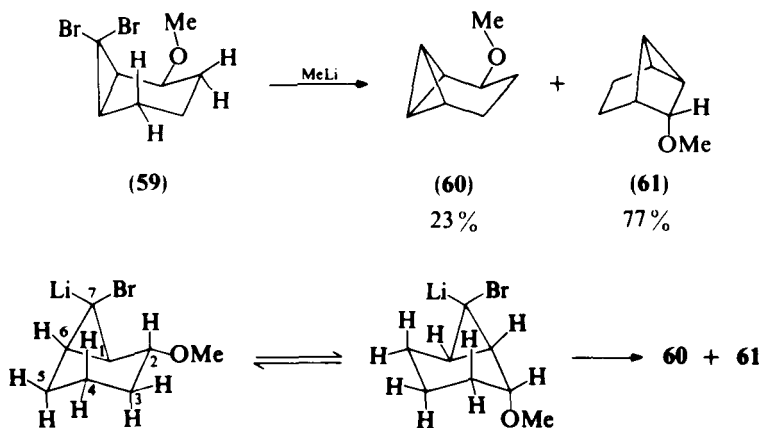
that conformation in which the 2-methoxy substituent is axially disposed. Paquette argues that the electronic effect of the 2-methoxyl group is to offset electron deficiency at C_3 and to deter attack at the geminal C–H at C-2 because of its electronegativity influence on the bond nucleophilicity. He proposes that the C–H reactivity at C-3 is enhanced by the axial methoxyl substituent providing 'backside' assistance.

Cory and coworkers[47] applied the carbon atom insertion to an elegant synthesis of ishwarane (**62**). It had been previously observed[47, 48] that in conformationally mobile systems such as **63** treatment with methyllithium at − 10 °C yielded insertion products **64** and **65** in yields at 21% and 33%, respectively. However, it was felt that in a more rigid

(63)   (64)   (65)

                21%   33%
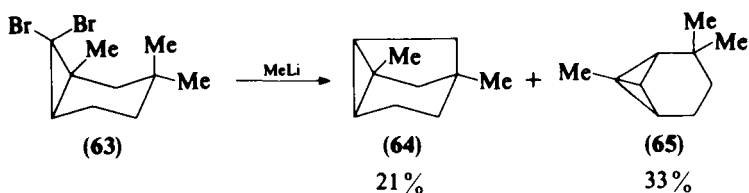
system containing a *cis* axial methyl group as in **66**, that insertion into the methyl group might take preference over insertion into a ring CH_2. Indeed, ishwarane (**62**) was obtained

(66)   (62)
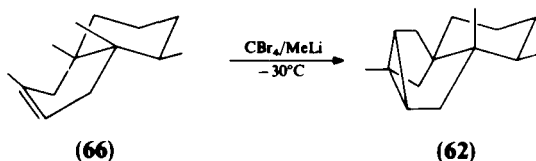
in 20% yield by treating **66** with carbon tetrabromide and methyllithium at $-30\,^{\circ}C$ in a one-pot reaction[47]. Another good example of stereochemical control is provided by the reaction of **67** to give **68** and not **69**[49].

(69)   (67)   (68)
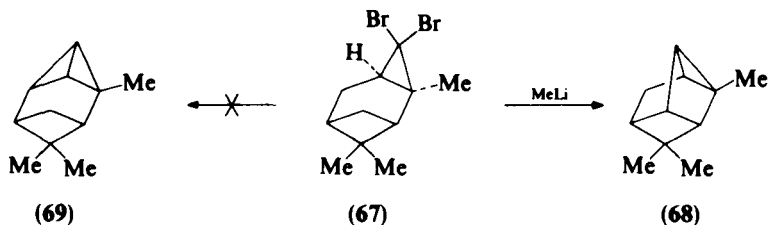
The stereochemistry at the carbenoid carbon may also be important. Taylor and coworkers[50a] investigated the reaction of the epimeric **70** and **71** with methyllithium to yield the epimeric carbenoids **72** and **73**. It can be seen that the two epimeric carbenoids

(70)   (72)   (74) 92%

(71)   (73)   (75) 27%

(76)   61%
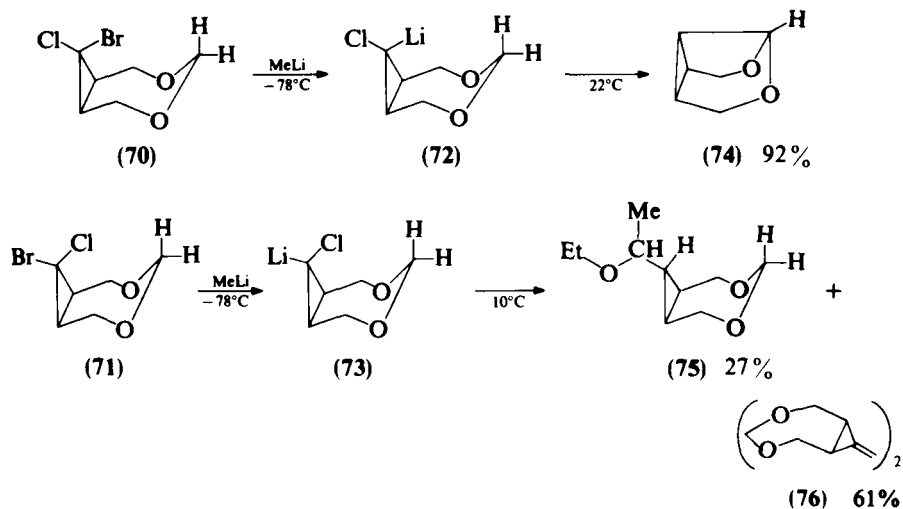
react to give different products; **72** produces the intramolecular insertion product **74** in 92% yield and **73** leads to an intermolecular insertion reaction product with the diethyl ether solvent (**75**) and to a dimeric product **76** which presumably is due to carbene formation. It should also be noted that the intermolecular insertion reaction in this case is stereospecific to yield *exo* product. Oku and coworkers[42] have also observed *exo* products resulting from insertion by carbenoids into ether solvent during their studies on hydride abstraction from alkoxides. The latter reaction (*vide supra*) is a two-step reaction involving a hydride abstraction–recombination mechanism whereas the ether insertion appears to involve a concerted mechanism via transition state **77**. The insertion into ether solvents by carbenoids with retention of configuration has been observed by a number of workers[12b, 44].
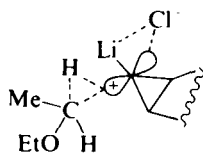
(77)

The study by Paquette and coworkers[50b] on the carbenoids derived from tricyclic (*m.n.*1)propellanes is informative and suggests that π bonds may also stabilize carbenoid intermediates. Equations 5–10 describe the carbenoids formed and the insertion products derived from them.

The result shown in equation 5 is understandable on the basis that in intermediate **b** the axial C_α–H protons of the five-membered ring are not only closer to the carbenoid center

(5)

(6)

(7)

$$(8)$$

$$(9)$$

$$(10)$$
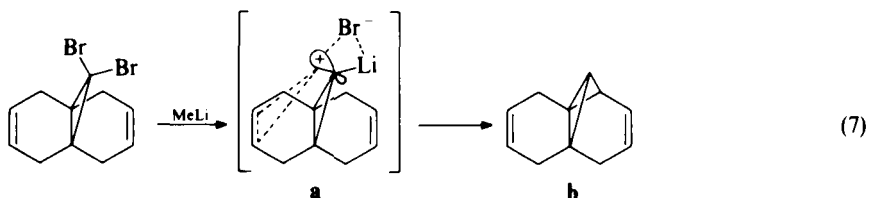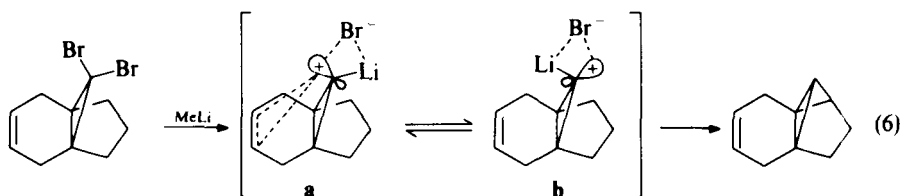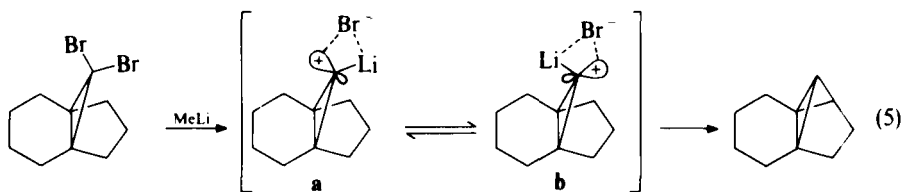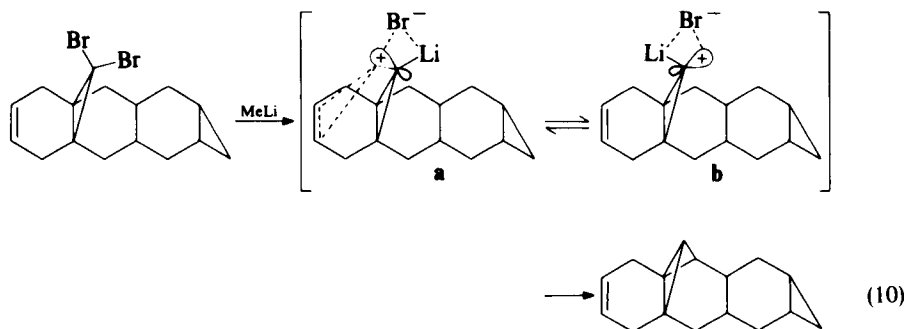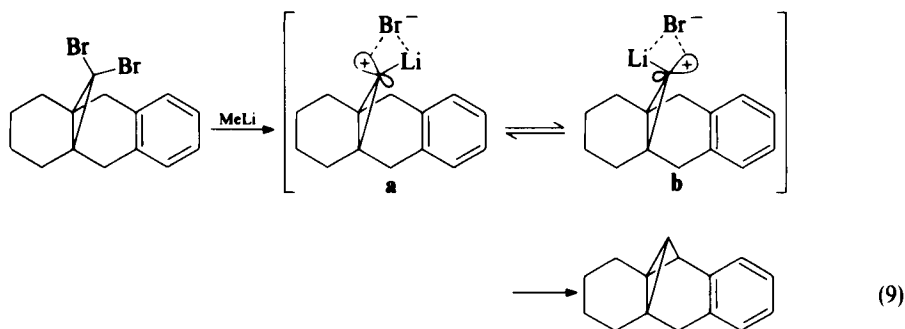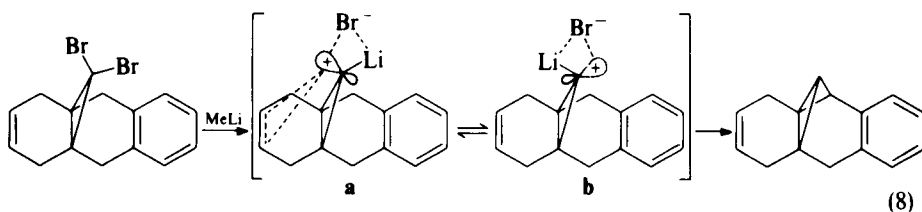
but are better oriented for overlap with the vacant orbital, therefore making intermediate **b** a better candidate than intermediate **a** for the insertion reaction.

In equation 6 we note that intermediate **b** has the same advantage as the intermediate **b** of equation 5, but in this case intermediate **a** is delocalized by interacting with the π system of the six-membered ring; hence intermediate **a** is much less reactive toward insertion than intermediate **b** (**b** ≫ **a**). The result in equation 7 shows that, despite delocalization, insertion can still occur.

In equation 8 intermediate **a** is better delocalized than intermediate **b** with the result that insertion into the benzylic C–H bond (**b** > **a**) occurs.

In equation 9 the choice between intermediate **a** and **b** favors **b** due to flattening of the ring, caused by the phenyl group which places the C–H protons closer to the reaction center.

In equation 10 the effect of the cyclopropyl ring is to flatten the six-membered ring making its C_α–H bond more available for insertion, so the intermediate **b** will be favored over intermediate **a** in which overlap with the π system has occurred (**b** ≫ **a**).

The order of reactivity based on the above rationale is
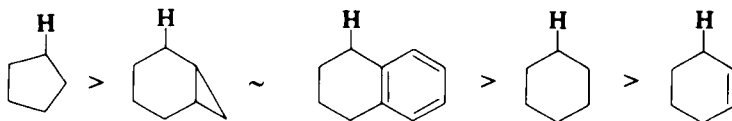
C. Skatteböl Rearrangement

In 1962 Skattebӧl[51a] published the seminal paper on the reaction which now bears his name. Initially he was continuing his investigation on the conversion of 1,1-dibromocyc-lopropanes by alkyllithium reagents to allenes. However, in the reaction of **78** with methyllithium at $-78\,°C$ he obtained not only the expected allene but also an equal amount of **79**[51b]. This provided the first example of an intramolecular addition of a

(78)   (79)
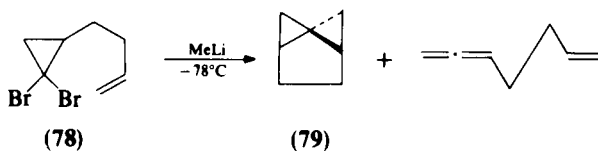
carbenoid to a double bond[51c]. Extension of the reaction to a higher homologue **80** and to a lower homologue **81** produced the following results:

(80)   13%   87%

(81)
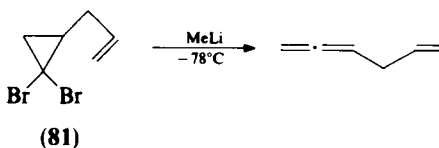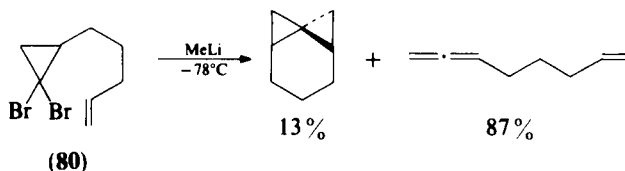
When the vinyl group was directly attached to the cyclopropyl ring as in **82** and **83** a rearrangement occurred to yield a cyclopentadiene.

(82)   14%   86%

(83)   5%   95%
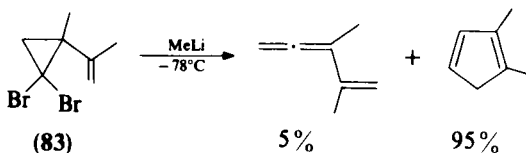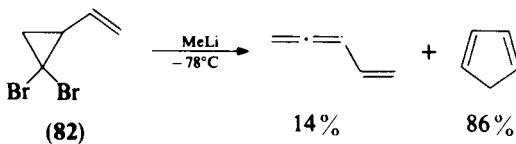
The effect of substitution on the rearrangement has been investigated by Holm and Skatteböl[52]. The results of this study are summarized in Table 5.

(86)

(87)   (88)

(89)   (90)
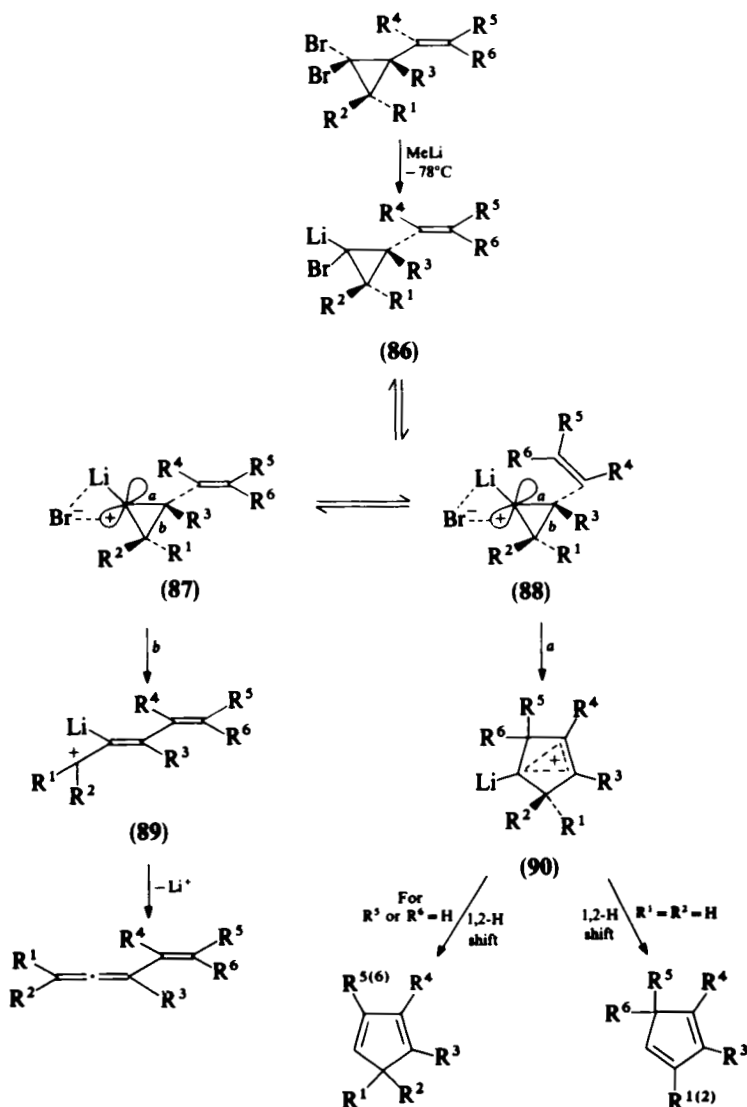
The reaction of substituted *gem*-dibromocyclopropanes with methyllithium at $-75\,°C$ leads to the formation of carbenoid **86** by halogen–metal exchange. Metal-assisted ionization (MAI) occurs to yield **87** as the reactive intermediate, which is in equilibrium with its rotamer **88**.

Whether one obtains rearrangement to allene or cyclopentadiene does not seem to be due to differences in activation energy, since calculation by Brinker and coworkers[53] have shown that for either pathway the activation energy is *ca* $13\,kcal\,mol^{-1}$. What then

TABLE 5. Products from reaction of alkenyl-*gem*-dibromocyclopropanes and methyllithium at −78°C
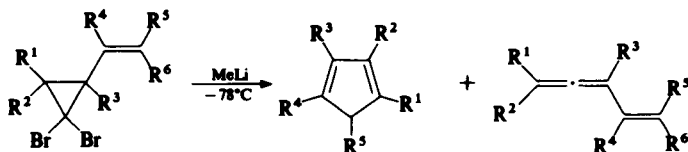
Entry	R^1	R^2	R^3	R^4	R^5	R^6	Isomeric 1,3-cyclopentadienes (%)	Allene (%)
1	H	H	H	H	H	H	(89)	(11)
2	Me	H	H	H	H	H	—	(100)
3	H	Me	H	H	H	H	2-methyl (68)	(32)
4	H	H	Me	H	H	H	2- and 1-methyl (99)	(1)
5	H	H	H	Me	H	H	2- and 1-methyl (96)	(4)
6	H	H	H	H	Me	H	2-methyl (87)	(13)
7	H	H	H	H	H	Me	—	(100)
8	Me	H	H	H	H	Me	—	(100)
9	H	Me	H	H	Me	H	2,5-dimethyl (68)	(32)
10	H	H	Me	Me	H	H	1,2-dimethyl (99)	(1)
11	Me	Me	H	H	H	H	—	(100)
12	H	H	H	H	Me	Me	—	(100)
13	Me	Me	Me	H	H	H	*a*	
14	H	Me	H	H	Me	Me	—	(100)
15	H	H	Me	H	Me	Me	2,5,5-trimethyl (85)	(15)
16	Me	Me	H	H	Me	Me	—	(100)
17	H	H	H	−(CH$_2$)$_4$−		H	**84** (83); **85**(17)^b	
18	H	−(CH$_2$)$_4$−		H	H	H	**84** (83); **85** (17)^b	
19	Ph	H	H	H	H	H	—	(100)
20	H	Ph	H	H	H	H	—	(100)
21	H	H	Ph	H	H	H	1-phenyl (93)	(7)
22	H	H	H	Ph	H	H	1-phenyl (78)	(22)
23	H	H	H	H	Ph	H	2-phenyl (71)	(29)
24	H	H	H	H	H	Ph	—	(100)

^{a} Complex mixture containing, *inter alia*, isomeric bicyclo[1.1.0]butanes.
^{b}

84   **85**
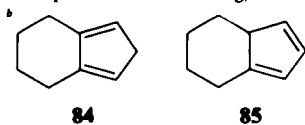
determines the pathway? It would seem that the rotamer equilibrium could perhaps account for the direction that the reaction takes. For example, as seen in Table 5, when substitution by methyl groups is as in entries 2,7,8,11,12,14 and 16, as well as substitution by the phenyl group as in 24, one obtains exclusively allene. In each of these cases, where one obtains exclusively allene, one notes that R^1 = Me or R^6 = Me, Ph or both R^1 and R^6 = Me. In those cases where steric interactions would not favor **88** (*s-cis* conformation) the equilibrium is shifted toward **87** (*s-trans*); one obtains exclusively a vinyl allene.

Another interesting steric interaction is the buttressing effect of a methyl or phenyl group in R^3 (entries 4,10,13,15 and 21). This results in an increased yield of cyclopenta-diene formation relative to the completely unsubstituted compound (entry 1). A phenyl

group in R^2 may also be exerting an electronic effect, since breaking bond b would result in a delocalized intermediate **89**.

The effect of conformation s-cis or s-trans is best illustrated by the work of Reinarz and Fonken[54] using systems in which the s-cis **91** and s-trans **92** are fixed. Since the distal carbon of the double bond is available in s-cis **91** one obtains only the cyclopentadiene **93**, the Skatteböl rearrangement product. On the other hand, in the s-trans **92**, where the distal carbon is not available, only the allene **94** is produced.
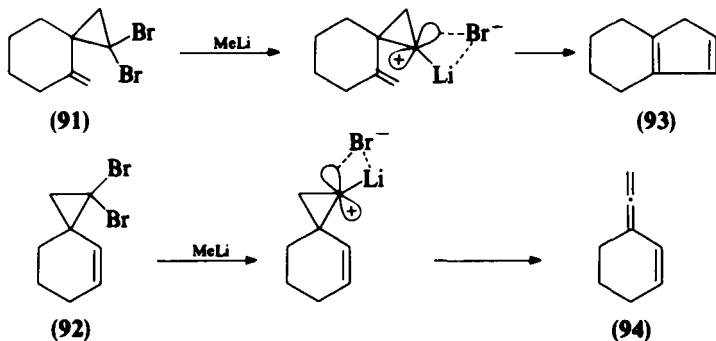
It should also be appreciated that different bonds in the three-membered ring are broken when the reaction proceeds to give either vinyl allene or cyclopentadiene. In the latter case, the Skatteböl rearrangement, it is bond a (**88** to **90**) that is broken and in the former case (**87** to **89**) it is bond b that is broken. In the rearrangement to vinyl allene it is clear from product analyses that bond b is broken, but in the Skatteböl rearrangement the decision is not obvious.
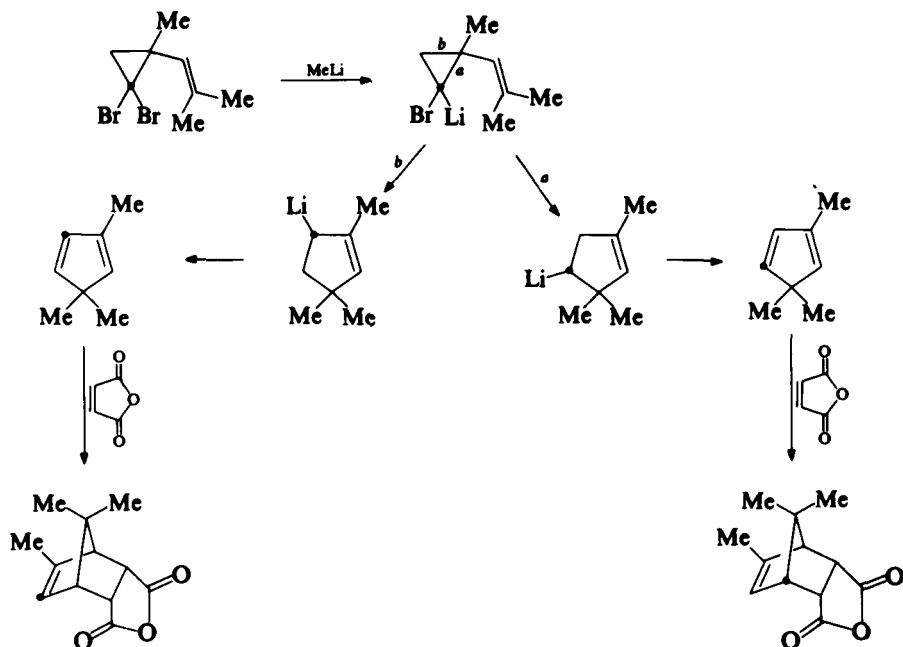
Proof that the rearrangement proceeded by the breaking of bond a was provided by Holm and Skatteböl[55] in a labelling experiment using ^{13}C-NMR analysis. The results clearly showed that the bond broken was a and not b, since all the label was found at C-1, the bridgehead carbon. Baird and Jeffries[56], via labelling experiments with ^{13}C, also supported an intermediate such as 90 for the Skatteböl rearrangement as did the rearrangement of double-labelled trans-1,2-bis(2,2-dibromocyclopropyl)ethene to yield, inter alia, 1,4-dihydropentalene[57].

Further examples of the Skatteböl rearrangement have appeared. Brinker and Fleischhauer[57] have demonstrated the effect of a diene moiety on the rearrangement. The

(95)
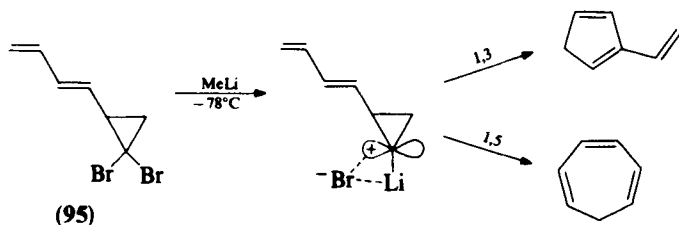
question here is whether one will obtain a 1,3 or 1,5 interaction of the carbenoid center with the 1,3-diene. The reaction of 95 with methyllithium at 0 °C yielded a mixture of cyclopentadienes 96 and 97 (52%) and the allenyl diene 98 (48%) whose configuration is trans at C_4–C_5. However, when the cis isomer 99 was treated with methyllithium at

(96)   **(97)**   **(98)**
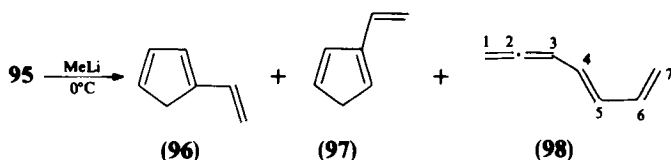
-78 °C a 1,5 interaction was obtained to yield 102 as well as formation of a dienyl allene 100 (cis configuration C_4–C_5) which undergoes electrocyclic ring closure to 101.

(100)   **(101)**

(99)

(102)
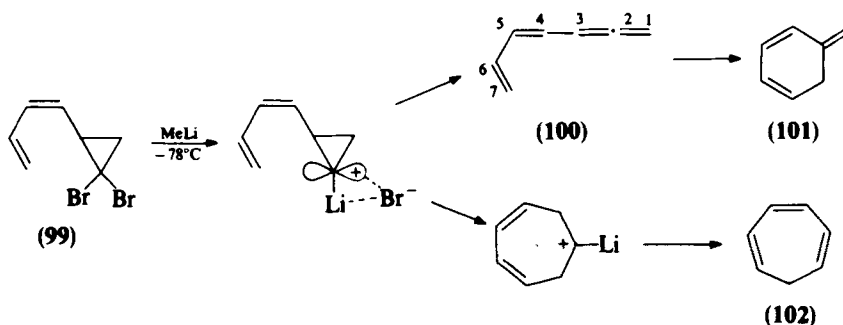
An interesting observation was made by Skatteböl and reported in his 1967 publication[51]. He reported that 103, when treated with methyllithium at -78 °C, gave an 80% yield of 104.

Moss and Jones[16b] speculated as to a mechanism for this conversion which, in light of current information[7, 12, 58], is essentially correct. Halogen–metal exchange leads to

(103)   (104)

(103)   (105a)   (105b)   (105c)

(104)   (106)
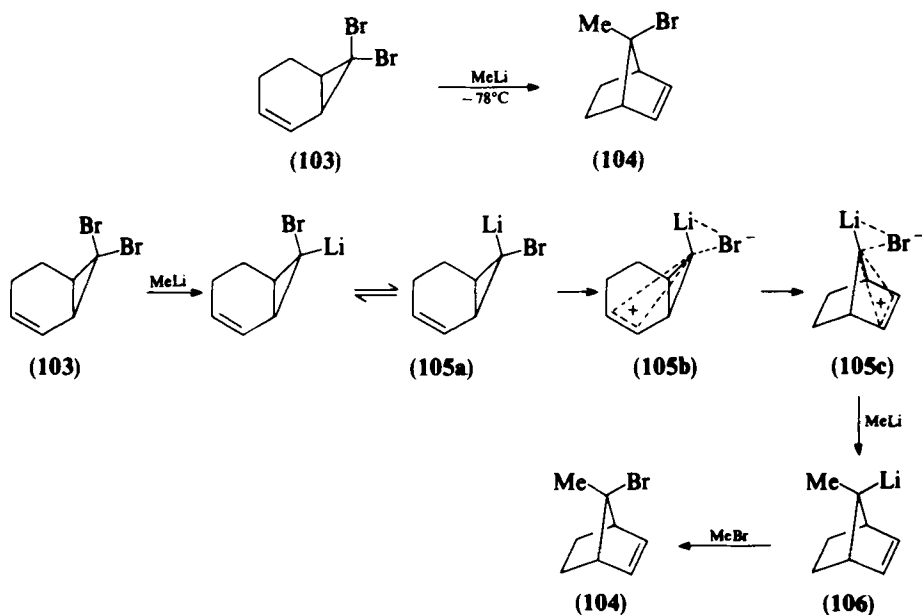
carbenoid **105a**, which can then undergo metal-assisted ionization (MAI)[7, 12] with backside neighboring group participation of the π bond to give **105b** which proceeds by a 1,3-migration to yield **105c**. Nucleophilic attack by methyllithium[7, 12, 47] on **105c** leads to the formation of **106**, which undergoes halogen–metal exchange with the methyl bromide[58] that had been formed *in situ*.

Paquette and coworkers[59] have used the Skatteböl rearrangement to synthesize, *inter alia*, a chiral optically pure annulated cyclopentadiene **107** starting with (1R)-(+)-camphor.

(1R)-(+)

(107)
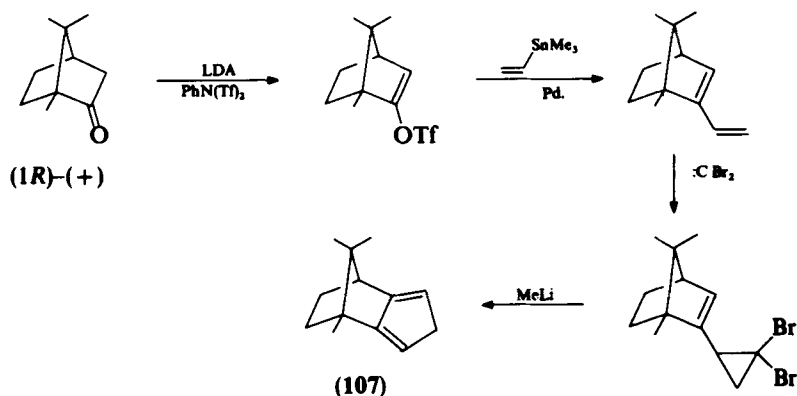
The rearrangement has also been extended to an imine derivative **108**, which has been converted to a pyrrole derivative[60].

(108)
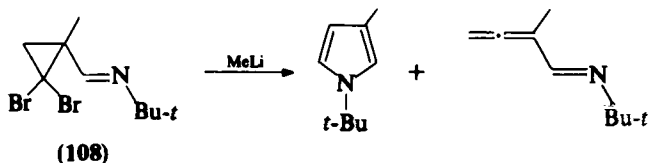
D. Effect of Temperature

As indicated in the introduction, the nature of the intermediate cyclopropyl carbenoids is temperature dependent. This is reflected in the type of reactions the carbenoids will undergo. For example, Loozen and coworkers[61] showed that **109** at −70 to −105 °C undergoes halogen–metal exchange with n-butyllithium to yield a carbenoid, which is stable at these temperatures and can be trapped by methyl iodide according to the method of Nozaki and coworkers[3f]. At this temperature the carbenoid behaves like an anion. At

(109)

(110)   **(111)**
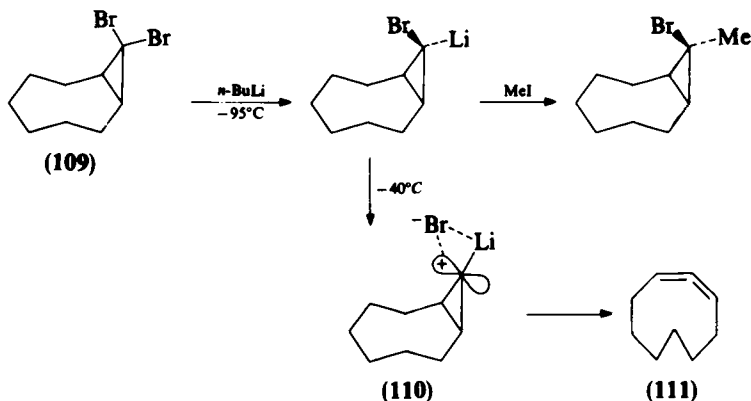
−40 °C, however, the carbenoid is converted to allene **111**, presumably via carbenoid **110**. At this temperature the carbenoid behaves like a cation.

Baird and Baxter[39b], in their investigation of a stabilized carbenoid **113** formed by treating **112** with methyllithium at −60 °C, showed that at this temperature only

(112)   **(113)**   **(114)**   **(115)**   **(116)**

(117)   **(118)**   **(119)**
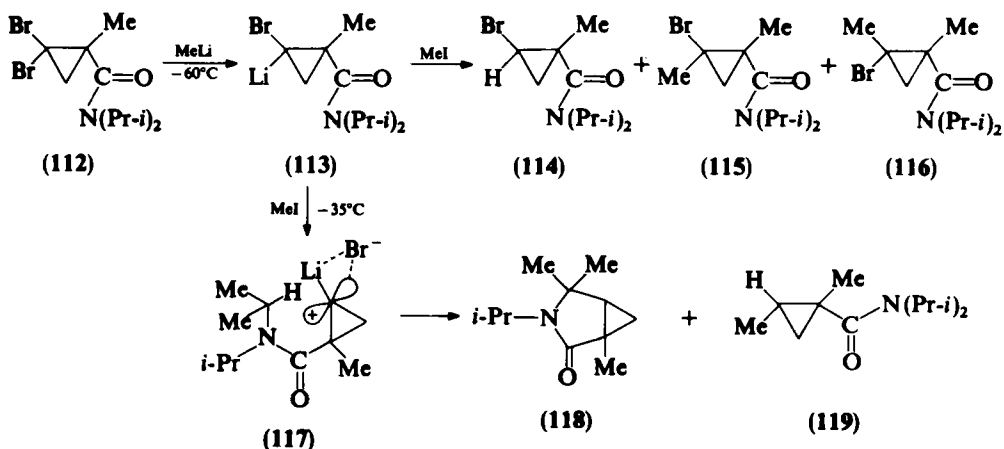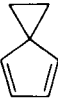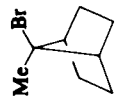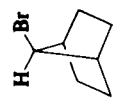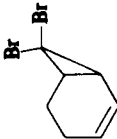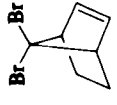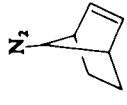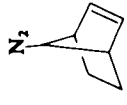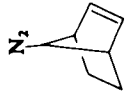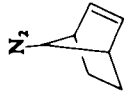
TABLE 6. Product distribution (% yield) from decomposition of various substrates[53]

Entry	Substrate	T(°C)	Conditions			Br H Me	Me Br	H Br
1		0	MeLi, ether	0.5	0.5	1.0	93	—
2		100	'MeLi tube'	25.1	4.8	10.5	14.7	—
3		0	MeLi, ether	0.5	1	—	93.5	—
4		100	'MeLi tube'	47.5	12.6	—	6.6	20.5
5		180		56	10	—	—	—
6		275		51	4.9	—	—	—

carbenoid **113** was formed. Quenching with methyl iodide yielded **114**, **115** and **116**, products derived from an anionic carbenoid. Again, at $-35\,^{\circ}\text{C}$ with another equivalent of methyl iodide one obtains, *inter alia*, products from carbenoid **117** which leads to insertion product **118** and alkylated product **119**. The products are derived from a cationic carbenoid. The alkylated product **119** results from reaction of **117** with *n*-butyllithium.

As we have seen, the Skattebøl rearrangement of **82** with methyllithium at $-78\,^{\circ}\text{C}$ yields cyclopentadiene and vinylallene in a 6:1 ratio. Brinker and Ritzer[53a], using their

(82)   14%   86%
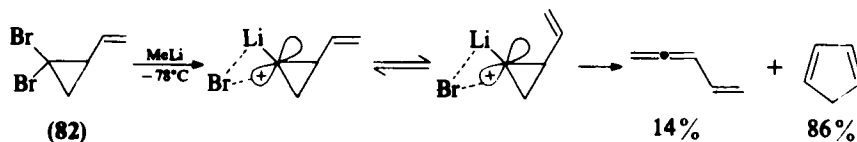
'MeLi tube' techniques which generates carbenes from *gem*-dibromides, found that at the isokinetic temperature, *ca* 30 °C, the ratio is 1:1. This implies that product formation from a carbenoid intermediate is more selective than from a free carbene, which one might anticipate to be formed at the higher temperatures.

It is apparent from Table 6 (entries 2, 3, 5 and 6) that the 'MeLi tube' produces products which are comparable to those obtained from the Bamford–Stevens reaction. There is little doubt that the latter reaction involves carbene intermediates[16a] and this is the basis of Brinker and Ritzer's[53a] conclusion that carbenes are the intermediates that are generated from the reaction of *gem*-dibromides with the 'MeLi tube'. By contrast, note the product distribution in entries 1, 2 and 3, 4. The use of methyllithium in solution gives rise to an entirely different product (*vide supra*) as shown in the conversion of **105b** and **105c**, and moreover the results are the same whether the reaction is performed at -78 or at $0\,^{\circ}\text{C}$.

For each type of carbenoid (electrophilic or nucleophilic) there will be a temperature range at which it will exist, and this range will undoubtedly also be dependent on the substituents attached to the carbenoid carbon and the solvent used for the reaction.

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CHAPTER **5**

Cyclopropane cation radicals

I. INTRODUCTION

Cyclopropane cation radicals and isomerization/dissociation processes of ionized cyclopropanes have been treated extensively in a chapter, 'The chemistry of ionized cyclopropanes in the gas phase', by H. Schwarz in *The Chemistry of the Cyclopropyl Group*[1]. The cyclopropane cation radicals have been prepared by conventional mass spectrometry (MS), gas phase radiolysis, ion cyclotron resonance (ICR) spectroscopy, photodissociation, collision activation (CA) mass spectrometry and field ionization kinetics (FIK). It has been emphasized that these investigations are ideally suited for comparison with theoretical studies, since they are executed on isolated molecules, i.e. in the absence of solvents or counterions. The literature has been covered up to 1986.

   The purpose of this chapter is to summarize the following topics: (1) recent results of theoretical studies of cyclopropane cation radicals; (2) recent investigations of cyclopropane cation radicals in the gas phase; (3) investigations of C_3H_6 cation radical species

in rigid systems; (4) investigations of cyclopropane cation radicals prepared by photo-oxidation and (5) investigations on cyclopropane cation radicals prepared by chemical oxidants.

A comparison of gas phase with solution and condensed-phase studies is of special interest, because in the Addenda of Reference 1 a series of recent papers is cited which 'stress that the structural changes of ionized cyclopropane in both the gas phase and in condensed phase are entirely analogous'[1, 2]. There are, however, conflicting opinions in the literature concerning this point.

II. THEORETICAL STUDIES OF THE CYCLOPROPANE CATION RADICAL AND THE $C_3H_6^{+\bullet}$ POTENTIAL SURFACE

Earlier work along these lines has been published by Haselbach[3], Rowland[4], Collins and Gallup[5] and Wayner, Boyd and Arnold[6]. A recent publication on the cyclopropane cation radical $1^{+\bullet}$ by Borden and coworkers[7] deals, first, with its ring opening to the propene cation radical $3^{+\bullet}$. Second, it is found that the trimethylene cation radical $2^{+\bullet}$ is not a stable intermediate. This publication is discussed in more detail here because there is an ongoing discussion about the existence of $2^{+\bullet}$.

$$(1^{+\bullet}) \qquad (2^{+\bullet}) \qquad (3^{+\bullet})$$
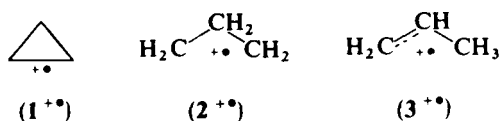
Table 1 lists UHF (unrestricted Hartree–Fock)/6-31G* and MP2 (second-order Møller–Plesset; inclusion of electron correlation)/6-31G* energies (kcal mol^{-1}) of $1^{+\bullet}$, various conformations of $2^{+\bullet}$ and two transition states ($C_2^{+\bullet}$TS, conrotatory ring opening $1^{+\bullet} \rightarrow 2^{+\bullet}$ and $C_1^{+\bullet}$TS, ring opening accompanied by hydrogen migration $1^{+\bullet} \rightarrow 3^{+\bullet}$).

The geometry of the propene cation radical $3^{+\bullet}$, optimized by 6-31G UHF calculations in C_s symmetry, is the lowest energy point found on the $C_3H_6^{+\bullet}$ potential surface.*

TABLE 1. UHF/6-31G* and MP2/6-31G* energies (kcal mol^{-1}) relative to the propene cation radical $3^{+\bullet}$ [7]

Cation radical	UHF/6-31G*	MP2/6-31G*
$3^{+\bullet}$	0^a	0^b
$1^{+\bullet}$ (90, 90)^c	15.3	9.8
$2^{+\bullet}$ (C_{2v}) (0, 0)$^{c, e}$	42.1	31.5
$2^{+\bullet}$ (C_s) (0, 0)$^{c, e}$	35.6	37.6
$2^{+\bullet}$ ($^2A'$) (0, 90)^c	35.5	39.1
$2^{+\bullet}$ ($^2A''$) (0, 90)^c	37.3	38.4
$2^{+\bullet}$ (C_s') (7, -7)^c	37.3	29.6
$C_2^{+\bullet}$TS (33, 33)^c	44.8	34.5^d
$C_1^{+\bullet}$TS (40, -87)^c	36.1	39.5

^{a} $E = -116.7734$ hartrees.
^{b} $E = -117.1122$ hartrees.
^{c} Dihedral angles between the planes of each of the terminal methylene groups and that of the three carbon atoms.
^{d} The MP2/6-31G* optimized geometry for the $C_2^{+\bullet}$ transition state has the same energy.
^{e} The most stable geometry of $2^{+\bullet}$ should have C_{2v} symmetry; for details, see Reference 7.

The geometry of $1^{+\bullet}$ in which one C–C ring bond is much longer than the other two has been previously optimized at the UHF/6-31G* level[8]. A UHF vibrational analysis for $1^{+\bullet}$ at this geometry shows that all the frequencies are positive, indicating that $1^{+\bullet}$ is a true local minimum on the $C_3H_6^{+\bullet}$ potential surface. The rearrangement $1^{+\bullet} \rightarrow 3^{+\bullet}$ is exothermic by 9.8 kcal mol^{-1} at the MP2 level, which increases to 10.3 kcal mol^{-1} after correction for zero-point energy differences. The experimental value is slightly less than 13 kcal mol^{-1} [9].

As far as the *trimethylene cation radical* $2^{+\bullet}$ is concerned, a 6-31G* UHF vibrational analysis was performed at the 6-31G* optimized C_{2v} (0, 0) geometry (which is the preferred one when sufficient electron correlation is included; see Table 1). As was the case with a 3-21G vibrational analysis, performed at the 3-21G optimized C_s geometry of $2^{+\bullet}$ [10], the 6-31G* vibrational analysis showed one imaginary and one low frequency. A similar situation was found in the cases of the $^2A'$ (0, 90) and $^2A''$ (0, 90) geometries of $2^{+\bullet}$, which clearly shows that $2^{+\bullet}$ is not a stable intermediate. The energy difference between $2^{+\bullet}$ in the (C_{2v}) (0, 0) geometry (31.5 kcal mol^{-1}) and $1^{+\bullet}$ (90, 90) (9.8 kcal mol^{-1}) of 21.7 kcal mol^{-1} is of practical importance: it rules out the irreversible opening of $1^{+\bullet}$ to $2^{+\bullet}$ which has been claimed to occur in $CF_2ClCFCl_2$ matrices[11], except that there is a very strong, stabilizing interaction between a nucleophile and the carbocationic methylene group. We will return to this point in Section IV.

The MP2 value of 21.7 kcal mol^{-1} for the energy difference between $1^{+\bullet}$ and the (0, 0) geometry of $2^{+\bullet}$ becomes 18.9 kcal mol^{-1} after correction for the computed difference in the zero-point vibrational energies. A thermocycle yields an estimated energy difference between $1^{+\bullet}$ and $2^{+\bullet}$ of 19.0 kcal mol^{-1}, an agreement which was regarded as 'fortuitous'[7].

Pathway $2^{+\bullet} \rightarrow 3^{+\bullet}$. The (0, 0) geometry has an imaginary frequency for a disrotatory motion that positions a hydrogen at the central carbon for migration to one of the equivalent terminal carbons. This vibrational coordinate reduces the molecular symmetry from C_{2v} to C_s with the symmetry plane perpendicular to that of the three carbons. Following this coordinate, a C_s energy minimum is located. The energy of this stationary point (C_s'; 37.3 and 29.6 kcal mol^{-1}, respectively; see Table 1) is lower than that of the (0, 0) geometry of $2^{+\bullet}$. However, like the (0, 0) geometry the C_s' geometry, too, is not a UHF energy minimum but a saddle point. The vibrational mode corresponds to migration of the properly oriented hydrogen toward one of the terminal carbon atoms. UHF calculations indicate that the energy decreases monotonically toward $3^{+\bullet}$. Thus, on this level, there is no barrier to the conversion of $2^{+\bullet}$ to $3^{+\bullet}$. MP2 and MP3 calculations led to a similar result: 0.2 kcal mol^{-1} is an upper limit to the barrier for the hydrogen migration. However, this value is so small that the possible existence of this minimum on the $C_3H_6^{+\bullet}$ potential surface has no chemical significance. Again, the trimethylene cation radical $2^{+\bullet}$ is not an intermediate.

Pathway $1^{+\bullet} \rightarrow 2^{+\bullet}$. As noted earlier, the conrotatory opening of $1^{+\bullet}$ to $2^{+\bullet}$ is allowed by orbital symmetry. At the energy maximum ($C_2^{+\bullet}TS$) the methylene groups have rotated 57° to transform $1^{+\bullet}$ into the (0, 0) geometry of $2^{+\bullet}$ (UHF/6-31G*). The energy is about 3 kcal mol^{-1} above that of the (0, 0) geometry of $2^{+\bullet}$. However, a UHF vibrational analysis found that the $C_2^{+\bullet}TS$ has two imaginary frequencies and is thus not a true transition state (at least at the UHF level).

Pathway $1^{+\bullet} \rightarrow 3^{+\bullet}$. The isomerization of the cyclopropane $1^{+\bullet}$ to the propene cation radical $3^{+\bullet}$ could, in principle, proceed by conrotatory opening of $1^{+\bullet}$ to the trimethylene cation radical $2^{+\bullet}$, followed by hydrogen migration. However, as shown above, the C_2 pathway is not a transition state.

A transition state with C_1 symmetry ($C_1^{+\bullet}TS$), where hydrogen migration accompanies ring opening, instead, was located. As shown in Table 1, at the UHF level $C_1^{+\bullet}TS$ lies 8.7 kcal mol^{-1} below the maximum along the C_2 conrotatory path for ring opening

$(C_2^{+\bullet}TS)$. However, with the inclusion of electron correlation at the MP2 level, the energies are reversed, with the $C_2^{+\bullet}TS$ geometry now 5.0 kcal mol^{-1} below the $C_1^{+\bullet}TS$ geometry. The lowest energy pathway that connects $1^{+\bullet}$ to $3^{+\bullet}$ thus involves conrotatory ring opening of $1^{+\bullet}$ and passage over a C_2 transition state, followed by hydrogen migration to form $3^{+\bullet}$.

In summary, from the most recent calculations of Du, Hrovat and Borden[7] on the $C_3H_6^{+\bullet}$ potential surface, the following results evolve: (1) the propene cation radical $3^{+\bullet}$ is more stable by 10.3 kcal mol^{-1} than the cyclopropane radical cation $1^{+\bullet}$; (2) the formation of a trimethylene cation radical $2^{+\bullet}$ is strongly endothermic [$2^{+\bullet}$ ($C_{2v}/0, 0$) lies 21.7 kcal mol^{-1} above $1^{+\bullet}$ and 31.5 kcal mol^{-1} above $3^{+\bullet}$]; (3) most importantly, all the trimethylene cation radical conformations $2^{+\bullet}$ calculated are not stable intermediates in a chemically significant sense.

It is interesting to compare the results of these calculations with the results of experimental investigations (having in mind a famous chemist's saying: 'Nobody believes in the results of calculations, except the author; everybody believes in experimental results, except the author').

III. C_3H_6 CATION RADICAL SPECIES IN THE GAS PHASE

Sack, Miller and Gross have addressed the ring opening of gas-phase cyclopropane cation radicals in a recent publication[2], although this reaction has been studied extensively before[1, 2]. In their opinion, however, it is still imperfectly understood because of 'conflicting interpretations'[2].

Since it is not possible to distinguish between cyclopropane and propene on the basis of the conventional mass spectra, it has been necessary to turn to other tools in order to better characterize the ions. The first *reactivity comparison* of the C_3H_6 cation radicals formed from cyclopropane and propene were made by Ausloos and Lias[12] and Sieck and Futrell[13]. The first direct evidence for the intact cyclopropane cation radical $1^{+\bullet}$ was based on its reactivity with NH_3 to form $CH_2NH_2^+$ [14, 15] and the distonic ion $^\bullet CH_2NH_2^+$ [15].

Propene cation radicals $3^{+\bullet}$ react exclusively by transferring a proton to NH_3 [16]. The reaction of cyclopropane cation radicals $1^{+\bullet}$ with NH_3 is energy dependent: ions formed near the ionization threshold remain cyclic, whereas at higher ionizing energies a significant fraction of the ions exhibit propene-like reactivity. Lias and Buckley[17] found that there is an onset of 1.3–1.6 eV before the cyclopropane-derived $C_3H_6^{+\bullet}$ ions begin to react by H$^+$ transfer.

Also, distinctive features are produced when the ions are subjected to collisional ionization. The differences in the spectra of doubly charged product ions are independent of ionizing energy over the range of 17 to 70 eV. Thus, the barrier for isomerization of cyclopropane $1^{+\bullet}$ to propene $3^{+\bullet}$ cation radical was interpreted to be higher in energy (> 1.6 eV) than the threshold for H$^\bullet$ loss[18]. No evidence could be found for a trimethylene cation radical $2^{+\bullet}$.

Because of these earlier results, Gross and coworkers[2] searched for the existence of the trimethylene cation radical $2^{+\bullet}$ by the following means. First, collisional ionization spectra of $C_3H_6^{+\bullet}$ ions formed at lower ionization energy than previously used were obtained, in order to see if changes are apparent near the isomerization threshold. Second, different ion–molecule reactions were devised for measuring the reactivities of $1^{+\bullet}$ and $3^{+\bullet}$ as a function of internal energy, which has been useful for determining structures of gas-phase ions.

From *collisional ionization mass spectrometry* the authors concluded that as the internal energy of the cyclopropane cation radical $1^{+\bullet}$ is increased, the ion does not isomerize to propene cation radical $3^{+\bullet}$ but to some other structure, 'possibly $2^{+\bullet}$'[2]. They pointed out,

however, that 'exact structural assignments are difficult to make because only relatively uninformative fragments are observed'. Therefore, measurements of reactivity in specific ion–molecule reactions were also undertaken.

In the *reaction with NH_3* the protonation of NH_3 became the more favored pathway as ionization energy was increased, as previously reported[16, 17]. Furthermore, charge exchange by $CS_2^{+\bullet}$ produced exclusively the cyclic ions in accord with Reference 17.

From the *reaction with propene-d_6* it was concluded that a significant portion of $C_3H_6^{+\bullet}$ ions formed above 15 eV exhibit chemical properties that are clearly different than those of either propene ($3^{+\bullet}$) or ground-state cyclopropane ($1^{+\bullet}$) radical cations. The cyclopropane radical cation $1^{+\bullet}$ does not isomerize to the propene structure to any appreciable extent. The differences in the product ion abundances depend markedly on the internal excitation of $1^{+\bullet}$ and $3^{+\bullet}$. The authors' interpretation is that 'the reactivity trends exhibited by cyclopropane cation radicals can be accounted for by involving ring opening to give the trimethylene cation radical $2^{+\bullet}$'[2].

As far as the structure of the cyclopropane cation radical is concerned, 'the only consistent explanation for the results presented here and elsewhere[19] is that the cyclopropane cation radical $1^{+\bullet}$ undergoes bond stretching with increases in internal energy to yield eventually an acyclic trimethylene cation radical $2^{+\bullet}$. The trimethylene cation radical $2^{+\bullet}$ is simply 'a high-energy form of the cyclopropane cation radical $1^{+\bullet}$'[2].

From the calculations discussed in Section II it was concluded that $2^{+\bullet}$ is not an intermediate in a chemically significant sense'[7]. A common denominator for the gas-phase experiments[2] and the calculations[7] could thus be that 'activated cyclopropane cation radical $1^{+\bullet}$ (in other words, the trimethylene cation radical $2^{+\bullet}$) is not a unique chemical species existing on a separate minimum on a potential surface but rather a vibrationally excited form of $1^{+\bullet}$ with an enlarged C–C–C bond angle'[2, 7].

IV. CYCLOPROPANE CATION RADICAL SPECIES IN RIGID SYSTEMS

Iwasaki and coworkers studied the cyclopropane cation radical in different matrices at low temperatures by ESR[11a]. (It may be worth pointing out that the ESR spectra strictly reveal only the presence of an unpaired species and its interaction with certain nuclei.) The spectra in SbF_5 and $CFCl_2CF_2Cl$, respectively, at 4.2 K consist of 5 × 3 lines with 12.5 and 21.0 G couplings to four and two equivalent protons, respectively. The result is explained by means of the degenerate cyclopropane Walsh orbitals $3e'$, the symmetrical ψs and the

(ψs) (ψa)

$(6a_1)$ $(3b_1)$
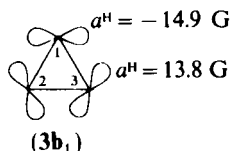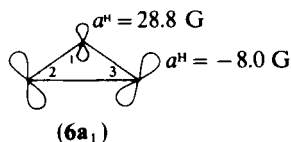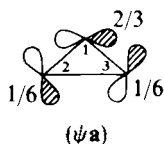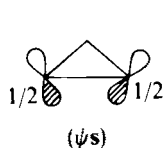
unsymmetrical ψa, which are transformed into the cyclopropane cation radical orbitals $6a_1$ and $3b_1$, respectively. The isotropic hyperfine coupling constants in the unpaired orbitals $6a_1$ and $3b_1$ shown in the structures are the result of INDO MO calculations.

If the symmetrical ψs contains an unpaired electron after loss of an electron, the zeroth-order wave function suggests a spin density of 1/2 on both C2 and C3, providing a reasonable explanation for the observation of four equivalent α-protons at C2 and C3 as well as the two equivalent β-protons at C1. The observed 12.5 G splitting is consistent with a spin density of about a half, whereas the 21.0 G splitting is reasonable for the β-protons with a 60° conformation, if the contributions of both the C2 and C3 atoms are taken into consideration.

When ψs becomes the singly occupied orbital, the C2–C3 bond is elongated and the other bonds are shortened because such deformations reduce the bonding nature of ψs and the antibonding nature of ψa. This is in agreement with INDO calculations and connected with a symmetry reduction from D_{3h} to C_{2v}.

At higher temperatures (77 K) the ESR signals both in SbF_5 and $CFCl_2CF_2Cl$ narrow markedly, suggesting the onset of a dynamic Jahn–Teller effect which averages the positive and negative hyperfine coupling constants. It is, however, mentioned that distortions by matrix perturbation could also be responsible for the observed effect. In a $CFCl_3$ matrix, similar observations are made as in the other matrices. Earlier, Shida and Takemura have studied cyclo-$C_3H_6^{+\bullet}$ in $CFCl_3$ at 77 K[20]. They interpreted the unresolvable single-line spectrum also in terms of averaging by dynamic Jahn–Teller effects.

A closed cyclopropane and an open tetramethylated cation radical species have been reported by Williams and coworkers[21] The cyclopropane cation radical structure $4^{+\bullet}$ is

$(4^{+\bullet})$
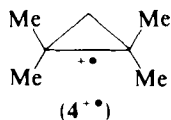
deduced from ESR hyperfine coupling constants in $CF_2ClCFCl_2$, $CFCl_3$ and CF_3CCl_3 matrices at 77 K. If the $CF_2ClCFCl_2$ matrix is warmed above 110 K, a new ESR spectrum is observed, and the ESR parameters are assigned to the orthogonal distonic[15] structure $5^{+\bullet}$.

$(5^{+\bullet})$
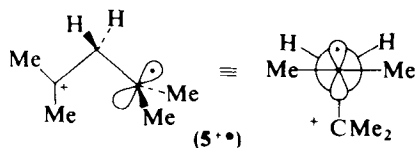
ESR studies on the ring opening of several other cyclopropane cation radicals in freon matrices are reported by Qin and Williams[22]. Among the cyclopropane cation radicals studied are $1^{+\bullet}$, $6^{+\bullet}$, $7^{+\bullet}$, $8^{+\bullet}$ and again $4^{+\bullet}$. The weakened bond is always the most highly substituted C–C bond in the three-membered ring.

$(1^{+\bullet})$ $(6^{+\bullet})$ $(7^{+\bullet})$

$(8^{+\bullet})$ $(4^{+\bullet})$
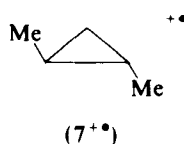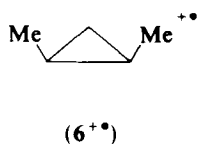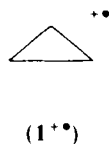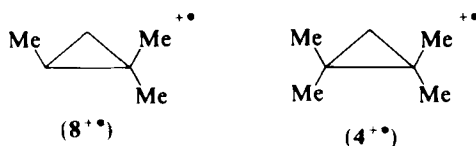
Open 'orthogonal' structures have been found in the cases of $2^{+\bullet}$, $9^{+\bullet}$, $10^{+\bullet}$, $11^{+\bullet}$ and $5^{+\bullet}$. The ring-opened species are of special interest given that the high-level theoretical

$(2^{+\bullet})$ $(9^{+\bullet})$ $(10^{+\bullet})$

$(11^{+\bullet})$ $(5^{+\bullet})$
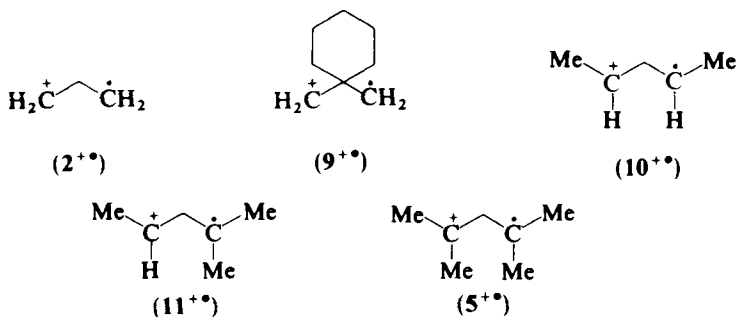
calculations discussed in Section II[7] and those of Arnold and coworkers[6] deny their existence. Furthermore, as shown in Section III on C_3H_6 cation radicals in the gas phase, clear evidence for the existence of a trimethylene cation radical species is lacking.

As far as the different freons and the cation radical ring-opening reactions are concerned, one observes a strong matrix effect. The $CFCl_2CF_2Cl$ matrix allows this reaction to occur with particular ease in comparison with matrices of other halocarbons, especially those containing the CCl_3 group. It is thus concluded 'that the matrix can play a very significant role in monorotatory processes which lead to the partial or complete breaking of a one-electron bond'[22]. The calculations[6, 7] do not lend support to an orthogonal ring-opened form of the cyclopropane cation radical—a (90, 0) structure is predicted to be metastable. This, however, applies only to the *gas phase*, since solvent interactions have not been considered in the calculations. Thus, if one keeps in mind the *specific matrix interactions* mentioned above, there is no underlying conflict between theory and the matrix experiments on the question of the existence of a trimethylene cation radical species.

The stability of the ring-opened form of cyclopropane cation radicals has been explained in different ways. It has been suggested that the carbocation center is strongly bonded to a suitable nucleophile, which could be either the chloride ion (Arnold[6]) produced as a result of dissociative electron attachment to the matrix, or a solvent molecule[23]. Symons[23] proposed for the unsubstituted ring-opened cyclopropane cation radical an adduct structure of the type $12^{+\bullet}$. In the case of the tetramethyl derivative $5^{+\bullet}$ Symons concluded that 'the alternative orthogonal structure may well be correct'[23]. There is no ESR evidence for halogen bonding at the γ carbon[22].

$$H_2\overset{+}{C}\text{–}CH_2\text{–}CH_2\text{–}\overset{+}{C}lCFCl\text{–}CF_2Cl$$

$(12^{+\bullet})$
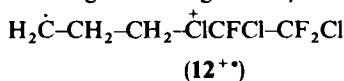
In contrast to the above-mentioned interpretations of the matrix effect, Qin and Williams[22] assume a *solvent* rather than a chloride or chlorine atom ligand *effect*. The driving force for the ring-opening reactions should be the greater solvation energy of the carbocation moiety in the localized than in the ring-closed species. In other words, a

strong specific solvation effect can overcome the difficulties associated with the high energy calculated for the (90, 0) ring-opened cation radical. In terms of solvation effect, the specific effectiveness of $CFCl_2CF_2Cl$ in facilitating the ring-opening reaction could well be due to the greater plasticity of this matrix in the temperature range of interest[22].

In summary, the gas phase and the matrix chemistry of cyclopropane and trimethylene cation radicals seem to be different stories. Similarly, the 'gas-phase' calculations have only little to do with what goes on in the matrix. This is not surprising at all: the properties of cations and anions in the gas phase are often very different from those in condensed phases. A similar situation prevails here, too. Besides, the real nature of trimethylene cation radicals in a matrix awaits further confirmation.

V. CYCLOPROPANE CATION RADICAL SPECIES IN FLUID SOLUTION

A. Photoinduced Electron Transfer (PIET)

H. D. Roth, a pioneer in the field of cyclopropane cation radicals, published a review article on organic cation radicals in solution in 1987[24a]. In the following we will concentrate on the methods successfully used by him and others to study such species.

Since cation radicals studied by the matrix isolation technique and ESR spectroscopy (see Section IV) are very often prepared by means of the energy-rich γ- or X-irradiation, and since the dissipation of excess energy in rigid matrices is normally rather slow, there are drawbacks to this method. Also, the application of the ESR experiment is usually limited to species with lifetimes well above the millisecond range. Thus, a milder method of generation and a faster method of observation would be useful.

A mild and versatile method for the generation of radical cation–radical anion pairs in solution is based on photoinduced electron transfer (PIET). This method utilizes the fact that the oxidation power of an acceptor A and the reductive potential of a donor D are substantially enhanced by photooxidation. The resulting pairs have limited lifetimes, since they readily undergo intersystem crossing (isc) and recombination.

$$A \xrightarrow{h\nu} {}^1A^* \xrightarrow{isc} {}^3A^*$$

$$^3A^* + D \longrightarrow \overline{^3A^{\cdot\cdot}D^{+\cdot}}$$

$$\overline{^3A^{\cdot\cdot}D^{+\cdot}} \rightleftharpoons \overline{^1A^{\cdot\cdot}D^{+\cdot}}$$

$$\overline{^1A^{\cdot\cdot}D^{+\cdot}} \longrightarrow A + D$$
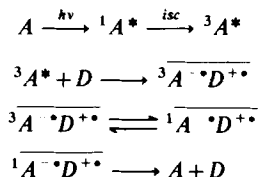
Singlet excited state electron acceptors are likewise used as organic photooxidants.

B. The CIDNP Method

Chemically induced dynamic nuclear polarization (CIDNP) is based on transient enhanced NMR signals, in absorption or emission, shown by some diamagnetic products of radical reactions. The signals can be related to ^1H hyperfine couplings which reveal structural features of the intermediates. The generation of nuclear spin polarization effects requires radical (ion) pairs with lifetimes in the nanosecond range. This time scale is sufficient to allow the intermediates to dissipate excess energy. Thus, the CIDNP results can be expected to reflect the equilibrium geometry of the intermediates. This method has been successfully applied to the investigations of cyclopropane cation radicals.

C. Cyclopropane Cation Radicals

The photoinduced electron-transfer from trans-1,2-diphenylcyclopropane to chloranil was studied by Roth and Schilling in 1980[24b]. It is concluded that the intermediate should

have the structure **13**⁺˙ in which the one-electron bond is 'broken or weakened'. The alternative open structure **14**⁺˙ should provide a ready pathway for isomerization, since it could collapse to either the *cis* or the *trans* geometrical isomer which is not observed. A closed cation radical species is also excluded.

(**13**⁺˙)   (**14**⁺˙)

In the presence of 1,4-dicyanonaphthalene as electron acceptor, *cis*-1,2-diphenyl-cyclopropane is observed, too. Electron-transfer quenching of the excited-singlet acceptor generates the open **13**⁺˙ paired with the acceptor anion radical. The reactant *trans*-1,2-diphenylcyclopropane is regenerated by geminate electron return in singlet pairs, whereas the rearranged *cis*-1,2-diphenylcyclopropane is formed via triplet recombination yielding a triplet state with orthogonal p orbitals (³**15**-*Z* or ³**15**-*E*). These diradicals can decay to either *cis*- or *trans*-1,2-diphenylcyclopropane.

(³**15**)-*Z*   (³**15**)-*E*
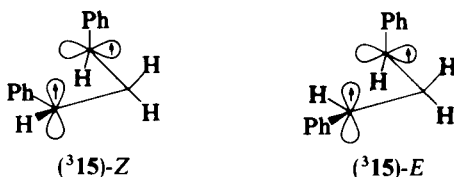
Wong and Arnold have also studied the 1,3-diphenylcyclopropane system[25]. They explained their results with a triplet recombination mechanism of the resulting radical ion pair. The results of Roth and Schilling are compatible with those of Wong and Arnold.

Roth and Schilling extended their investigations to the alkyl-substituted cyclopropanes **16–23**[24c]. CIDNP effects have been observed for the tri- and tetrasubstituted cyclopropanes **16, 17, 21** and **22**; on the other hand, the disubstituted **18, 19, 20** and **23** failed to give rise to any spin polarization effects. In the case of the trisubstituted **17** the intermediate could be unambiguously identified as **17**⁺˙ with the most highly substituted bond being 'weakened or broken'[24c].

	R^1	R^2	R^3	R^4
16	Me	Me	Me	Me
17	Me	Me	Me	H
18	Me	Me	H	H
19	Me	H	H	Me
20	Me	H	Me	H
21	$-CH_2-CH=CH-CH_2-$	$-CH_2-CH=CH-CH_2-$		
22	$-CH_2-CH=CH-CH_2-$		Me	Me
23	$-CH_2-CH=CH-CH_2-$		H	H

(21)   (22)

(17$^{+\bullet}$) π-(17$^{+\bullet}$)
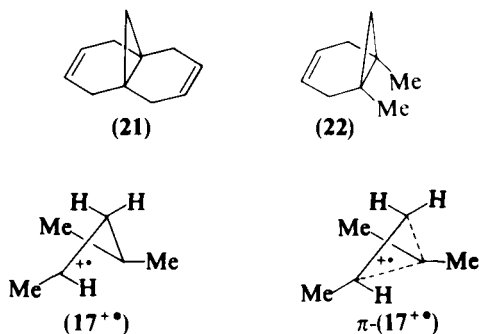
The alternative π-complex type structure π-17$^{+\bullet}$ is excluded. Interestingly, the lowest transition in the photoelectron spectrum of cyclopropane has been assigned to the ionization from the unsymmetrical orbital ψ_a (see Section IV)[26]. However, this conclusion does not necessarily have any bearing on the structure of the cation radical in solution. Photoelectron spectra do reflect the energy difference of vertical transitions and do not reflect the energy difference between states.

Accordingly, the irradiation of chloranil in acetone solutions in the presence of 17 leads to a trimethylene cation radical species 17$^{+\bullet}$ which should be stabilized by *solvation effects*. Similar results were obtained in analogous reactions of 16, 22 and 23. The situation in *solution* thus seems to be similar to that in *rigid systems* (matrices) (compare Section IV).

Additional significant information about the intermediate cation radicals is provided by the complete absence of any olefinic polarization for the bicyclic cyclopropane derivative 22 and the tricyclic 21. This observation eliminates any participation of the olefinic groups and identifies the tetraalkyl-substituted cyclopropane moieties as the effective electron donors in these bifunctional substrates rather than the disubstituted olefin.

The [2.3]benzo[5.6]methanonorbornene system 24 was also subjected to CIDNP investigations[24d]. The results are compatible either with a homohyperconjugative

(24)   (24$^{+\bullet}$) π-(24$^{+\bullet}$)
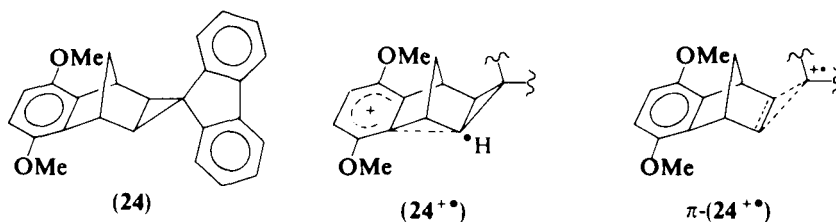
interaction (24$^{+\bullet}$) or with a delocalization of spin onto the quarternary cyclopropane carbon, corresponding to the π-complex type structure π-24$^{+\bullet}$. The experimental data, however, do not allow one to distinguish between the two alternatives.

In the case of the benzonorcaradiene 25[24d] the CIDNP results indicate that the structure of the benzonorcaradiene cation radical is best described as a resonance hybrid of several structures, including the π-complex type structure π-25$^{+\bullet}$ derived from the unsymmetrical 3e′ Walsh orbital ψ_a (see Section IV). The stability of this structure is ascribed to the aromaticity of the ten-carbon part attached to the methylene cation radical in a π-type fashion.

H H

H H
+ •

(25)

π-(25⁺•)
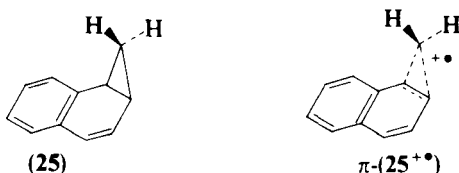
Other cyclopropanes studied are the bismethano-paracyclophane **26** and the [9:10]methanoacenaphthene **27**[24d].

(26)

(27)
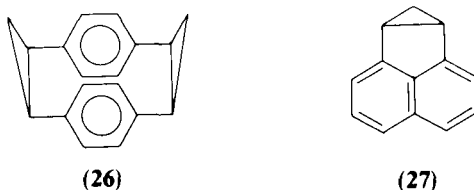
Bicyclobutanes are a special class of cyclopropanes. The HOMO of the bicyclobutane is bonding primarily in the transannular bond whereas the next lower MOs are bonding in the perimeter bonds. Tricyclo[4.1.0.0^{2,7}]heptane **28** can be transformed by PIET into the cation radical. Trapping experiments of Gassman and coworkers have provided evidence for structure **28**⁺•[27a], which was confirmed by CIDNP investigations[24c].

(28)

+ •

(28⁺•)

Gassman and coworkers were the first to demonstrate that a wide variety of highly strained polycyclic hydrocarbons, including 15 bicyclo[1.1.0]butanes[27b, c], have sufficiently high energy HOMOs that they were readily oxidized to cation radicals[27d, c]. The reaction of 1,2,2-trimethylbicyclo[1.1.0]butane with excited-state 1-cyanonaphthalene and trapping of the intermediate cation radical were described by Gassman and Carrol[27f].

In a recent paper by Gerson, Qin and Ess the structure of the parent bicyclo-[1.1.0]butane cation radical has been investigated[28]. While the flop angle α in bicyclo-[1.1.0]butane **29** amounts to 121.7°, the same angle in the cation radical **29**⁺• calculated by

121.7°

1.497 Å

(29)

132.2°

1.786 Å

(29⁺•)

• 180°

2.04 2.10Å

(30••)
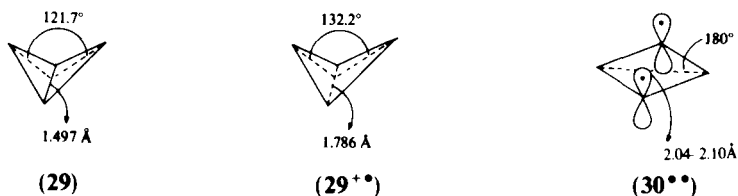
MNDO to be 132.2°, is much closer to that in **29** than to that in the planar cyclobutane-1,3-diyl **30**•• ($\alpha = 180°$). Again, the electron is expelled from the transannular CC bond[26c] and this is accompanied by a lengthening of this bond. The bond distance in **29**⁺• (MNDO: 1.786 Å) lies midway between those of **29** (1.497 Å) and **30**•• (UHF-MNDO: 2.04 Å; *ab initio*: 2.10 Å).

Benzvalene **31** and naphthvalene, on the other hand, form cation radicals like **31**⁺˙ in which the spin density is located largely in the unsaturated part of the molecule[24f].

(31)	**(31⁺˙)**

D. Cation Radicals with Homoaromatic Structures

Roth and Abelt investigated a series of bridged bicyclo[5.1.0]octa-2,5-dienes (**32–40**) with respect to the structure of their cation radicals[24g]. Compounds **32–40** have double-well potentials and undergo rapid degenerate Cope rearrangements, which may be fast

	X			X
32	CH_2		**37**	$C=CH-C_3H_7$
33	$C=O$		**38**	$C=CH-Cl$
34	$COCH_2CH_2O$		**39**	$C=CH-CN$
35	$C=CH_2$		**40**	—
36	$C=CHCH_3$			

even at $-150\,°C$. To date no conclusive evidence has been reported for a bridged bicyclooctadiene system with a single bis-homoaromatic energy minimum (**41**).

The cation radicals of **32–40**, prepared by photoinduced electron transfer to strong acceptors (chloranil, fluoranil) in solution, however, show a different behavior. Chemically induced dynamic nuclear polarization effects observed during the reactions of the simple bridged systems **32**, **33**, **34** and **40** indicate that the corresponding intermediate cation radicals **32**⁺˙, **33**⁺˙, **34**⁺˙ and **40**⁺˙ have the bis-homoaromatic structure **42**⁺˙ [at least on the time scale of the CIDNP experiment ($\leqslant 10^{-8}$ s)]. These are the first homoaromatic *cation radicals* of any structure type (mono- and bis-homoaromatic cations are of course well documented classes of compounds[29]). The spin density distribution in **42**⁺˙ reflects the coefficients of the HOMO of a bis-homoaromatic structure (**43**).

(41)	**(42⁺˙)**
(43)	**(44⁺˙)**
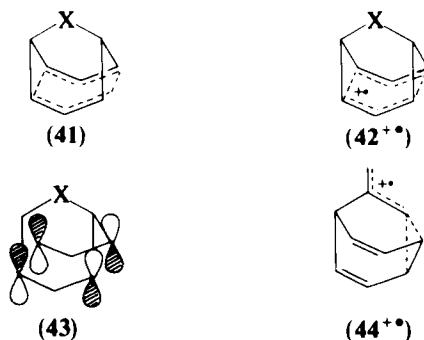
Introduction of (substituted) *exo*-methylene groups as bridging units (**35–39**) leads to a composite structure type with contributions from the bis-homoaromatic structure **42**⁺• and/or a vinylcyclopropane-type structure **44**⁺•. Very recently the cation radical **40**⁺• has been characterized by ESR (S. Dai, J. T. Wang and F. Williams, *J. Am. Chem. Soc.*, 112, 2835, 2837 (1990)).

E. Rearrangements of Cyclopropane Cation Radicals

Since its discovery by Hogeveen and Volger[30] and Gassman and coworkers[27g] in the late sixties, the catalytic conversion of quadricyclane(s) **45** to norbornadiene(s) **46** has attracted considerable attention because of its potential as a possible compound of a solar-energy storage cell[31].
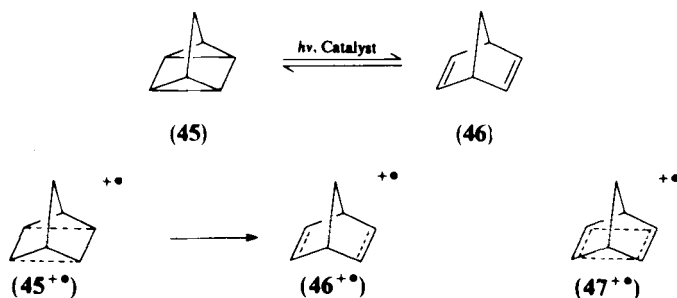
One of the possibilities for transferring **45** into **46** with release of 23–27 kcal mol⁻¹ [32] is an electron transfer catalyzed reaction via the corresponding cation radicals **45**⁺• and **46**⁺•, respectively. The study of electron donor–acceptor systems in solution has shed light also on this reaction[24a]. While other methods have failed to provide evidence for more than one cation radical on the energy surface of **45**⁺• and **46**⁺•, CIDNP results dispelled any notion of a single minimum **47**⁺• and furnished clear-cut evidence for two distinctive transients, each corresponding to one of the precursors. These studies also showed that **46**⁺• has no tendency to rearrange to **45**⁺•, whereas **45**⁺• rearranges to **46**⁺•, though on a slower time scale than that of intersystem crossing and recombination[24b]. These results are in keeping with the substantial energy difference and a non-negligible barrier between the isomeric cation radicals **45**⁺• and **46**⁺•.

Gassman and Hershberger have recently disclosed an electrochemical 'switch' for starting and stopping the energy-releasing conversion of **45** to **46**[27h]. This was made possible through the use of a triarylamine ⇌ triarylaminium cation radical pair.
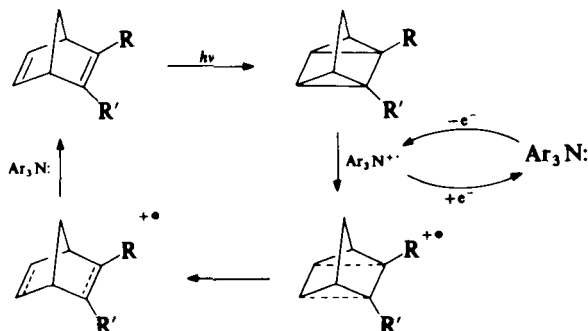
In the case of the parent system (R = R′ = H) tris(p-tolyl)aminium cation radical was used as the oxidizing catalyst. The aminium cation radical was prepared at an electrode. When the applied current was removed, the conversion of quadricyclane to norbornadiene slowed quickly. When tris(p-bromophenyl)amine was used as the carrier, the conversion could be stopped instantly through the application of a cathodic potential and restarted through the use of an anodic potential. It is stressed, however, that while the chemical efficiency approaches 100%, *it is not* 100%. Thus, more work is necessary even before this concept could be utilized in a practical solar-energy storage cell.

The cation radicals of benzvalene and naphthvalene (**48⁺•**) undergo ring-opening reactions to the corresponding benzenoid aromatics[24i] (e.g. **48⁺•→49⁺•**).

(**48⁺•**)   (**49⁺•**)
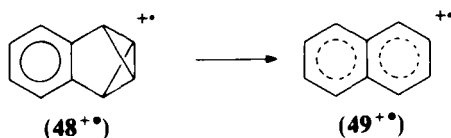
These rearrangements must have appreciable activation energies since they can be suppressed at −40 °C[24i]. Other bicyclobutane derivatives, e.g. **50**, undergo electron-transfer-induced rearrangements to cyclobutene derivatives[27i].

(**50⁺•**)   (**51⁺•**)   (**52⁺•**)
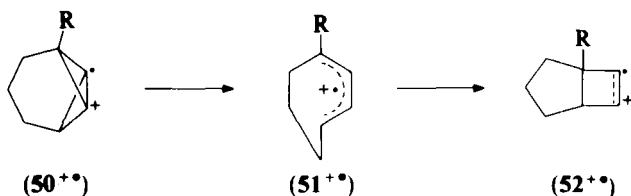
At the moment it is not clear whether this reaction follows a pathway analogous to the thermal reaction: conrotatory cycloreversion **50⁺•→51⁺•**[24a] followed by conrotatory ring closure to give **52⁺•**.

Bicyclo[6.1.0]nonatriene **53** and its derivatives are among the most thoroughly investigated hydrocarbon systems. A multiplicity of thermal and photochemical rearrangements has been documented[33].

(**53**)   (a) R, R′ =

                           (b) R = R′ = Ph
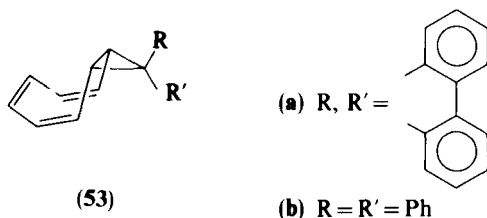
A recent publication[34] reports on the structure and rearrangements of the bicyclononatrienes **53a** and **53b** under electron transfer conditions. 9,10-Dicyanoanthracene (DCA) sensitized irradiation of **53a** at wavelengths > 370 nm resulted in the formation of **54a** as the major product (47%) together with smaller yields of **55a** (16%) and **56a** (6%), whereas the analogous irradiation of **53b** gave **55b** as a sole product. Direct photolysis of **53a** leads only to **55a** and **56a**; no **54a** is formed.

(54) **(55)** **(56)**

(a) R, R' = [biphenyl structure] (b) R = R' = Ph
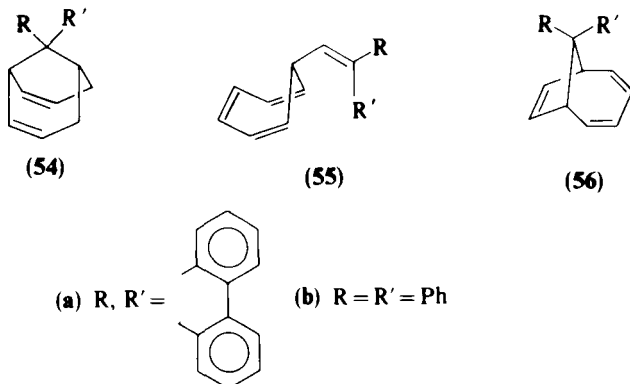
In the DCA-sensitized reaction the formation of **54a** is favored in polar solvents such as acetonitrile, whereas the formation of **55a** and **56a** is not strongly affected by solvent polarity. The intriguing effect of solvent polarity on product distribution is ascribed to the involvement of two different intermediates with different degrees of charge separation. In polar media, a solvent-separated radical ion pair is involved to give **54a**; in nonpolar solvents an exciplex is suggested that would produce **55a** and **56a**.

Concerning the nature of the intermediate which gives **54a**, the CIDNP effects rule out **53⁺˙**. On the other hand, the singly linked species **57⁺˙** is an attractive candidate to

(53⁺˙) **(57⁺˙)**
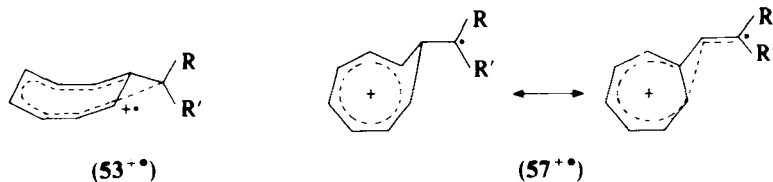
explain the rearrangement. However, the results are not sufficient to identify the intermediate.

The difference between **53a** and **53b** 'can be explained probably because of relative larger steric hindrance'.

Similar skeletal rearrangements were observed when the electron donor–acceptor (EDA) complex of **53a** with tetracyanoethylene (TCNE) was irradiated. This is of special interest because of the electron transfer observed in cycloaddition reactions involving cyclopropyl species and TCNE (see Section VI).

Cyclopropane stereomutations catalyzed by one-electron oxidants have been reported recently by Dinnocenzo and Schmittel[35]. When cis-1-p-anisyl-2-vinylcyclopropane (**58**) was treated with 5–10 mol% of (p-BrC₆H₄)₃N⁺˙SbF₆⁻ in methylene chloride at −78 °C or in acetonitrile at −40 °C, 84% and 88% respectively of the trans isomer **59** have been formed.

p-MeOC₆H₄

H H

(58)

5–10 mol % (p-BrC₆H₄)₃N⁺˙SbF₆⁻

CH₂Cl₂, −78°C, 84%

H

p-MeOC₆H₄ H

(59)
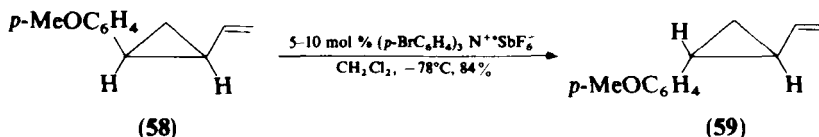
The reaction was similarly catalyzed by $O_2^{+\bullet}SbF_6^-$ (48% yield). The isomerization half-life at $-90\,°C$ in CH_2Cl_2 with 10 mol% $(p\text{-}BrC_6H_4)_3N^{+\bullet}SbF_6^-$ was ca 10 min. A comparison with the extrapolated *thermal cis→trans* rearrangement rate of 1-phenyl-2-vinylcyclopropane $(t_{1/2(-90°C)}$ ca 10^{25} min) reveals that the $(p\text{-}BrC_6H_4)_3N^{+\bullet}SbF_6^-$-catalyzed reaction is accelerated by a factor of ca 10^{24}! For the catalyzed reaction, a cation radical chain mechanism is proposed.

$$cis\text{-}\mathbf{58} + (p\text{-}BrC_6H_4)_3N^{+\bullet}SbF_6^- \quad (O_2^{+\bullet}SbF_6^-)$$

$$\longrightarrow (p\text{-}BrC_6H_4)_3N\colon (O_2)$$

$$cis\text{-}\mathbf{58} \longrightarrow cis\text{-}\mathbf{58}^{+\bullet}$$

$$trans\text{-}\mathbf{59} \longleftarrow trans\text{-}\mathbf{59}^{+\bullet}$$
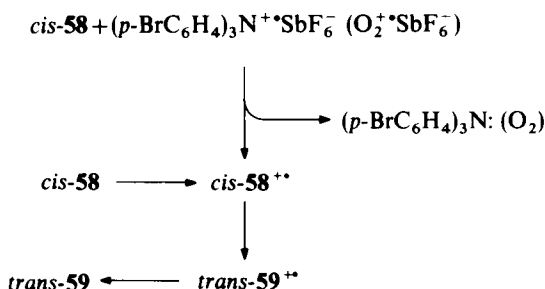
Excluded from this mechanism is the trimethylene biradical. The one-electron reduction of intermediate cyclopropane cation radicals by the strongest available reductant, $(p\text{-}BrC_6H_4)_3N$, does not provide enough energy to populate the biradical.

The specifically deuteriated *cis* cyclopropane **60** was synthesized in order to distinguish between the three mechanistic possibilities of the stereomutation reactions, i.e. (1) one-center rotation at C1, (2) deprotonation/reprotonation at C1 and (3) two-center rotation via a 'ring-opened cyclopropane cation radical **(64$^{+\bullet}$)**'.

(60)

(61)

(62)

(63)

(64$^{+\bullet}$)

$R = p\text{-}MeOC_6H_4$
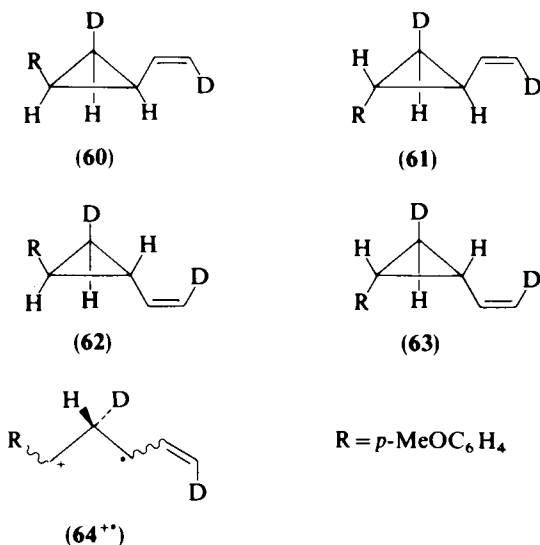
The one-center rotation and the deprotonation/reprotonation mechanisms predict that isomerization will produce a single *trans* isotopomer, **61**. In contrast, the two-center rotation mechanism predicts that a mixture of the two *trans* isotopomers **61** and **62** is formed. In practice, nearly equal amounts of **61** (48%) and **62** (52%) have been found, thus

excluding the one-center rotation and the deprotonation/reprotonation mechanism. A correlated two-center rotation, a subset of the two-center rotation mechanism, is also excluded: it would only permit the interconversion of the two *cis* isotopomers **60** and **63**. Thus, only the two-center uncorrelated rotation route remains. This suggests that the 'ring-opened cyclopropane cation radical **64**$^{+•}$ is an intermediate on the potential energy surface of isomerization, rather than a transition state'[35].

From this study it is apparent that the isomerization mechanism for cyclopropanes using one-electron *chemical* oxidants can differ from that using *photochemical* oxidants. The inability of the open 1,2-*trans*-diphenylcyclopropane cation radical **13**$^{+•}$ (see Section V. C.) to isomerize is likely dictated by the relative rates of back electron transfer to isomerization.

Why is cyclopentene (**67**) formation *not* observed in the reactions of *cis*-**58** and/or *trans*-**59** with (p-BrC$_6$H$_4$)$_3$N$^{+•}$ (or O$_2^{+•}$) SbF$_6^-$? Why does the corresponding trimethylene cation radical **65**$^{+•}$ not form the cyclopentene cation radical **66**$^{+•}$?

s-*trans*-(**65**$^{+•}$)   s-*cis*-(**65**$^{+•}$)

(**67**)   (**66**$^{+•}$)

R = p-MeOC$_6$H$_4$
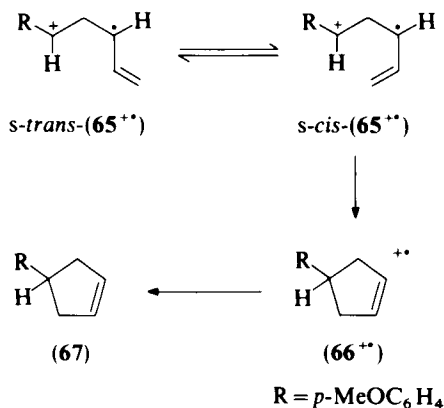
Dinnocenzo and Conlon[36] discussed three reasons: (1) only s-*trans*-**65**$^{+•}$ is formed which is incapable of forming the cyclopentene cation radical **66**$^{+•}$; (2) s-*cis*-**65**$^{+•}$ does not close for stereoelectronic reasons since the ring closure is a disfavored 5-Endo-Trig reaction in Baldwin's nomenclature[37]; (3) the ring-closure reaction does not occur for thermodynamic reasons: **66**$^{+•}$ js less stable than the cyclopropane cation radicals *cis*-**58**$^{+•}$ and *trans*-**59**$^{+•}$, respectively.

Apparently, the first hypothesis is correct. Reaction of the bicyclic **68** with (p-BrC$_6$H$_4$)$_3$N$^{+•}$SbF$_6^-$ led to **69** in 86% yield within 5 min at 22°C.

(**68**)   (**69**)

R = p-MeOC$_6$H$_4$
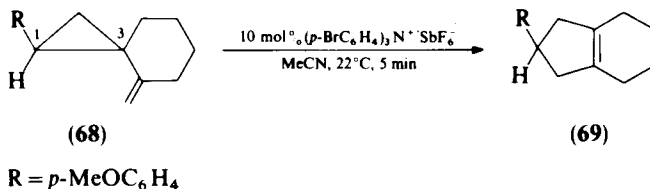
The activation barrier for the cation radical isomerization is low compared to that of neutral vinylcyclopropanes. The thermal isomerization half-life **68**→**69** is *ca* 46 min at 211 °C; using an activation entropy of −0.35 eu for the ring expansion[38] provides a half-life of 3 × 10^{12} min at 22 °C. The difference is explained satisfyingly by the strength of the

C1-C3 bond in **68** versus that in its cation radical. Thermodynamic cycle calculations[36] predict that the C1–C3 bond energy will be lowered by *ca* 25 kcal mol^{-1} upon removal of an electron. These cation radical rearrangements are somewhat reminiscent of the Skatteböl rearrangement, see Chapter 4.III.C.

Dinnocenzo and Conlon[36] also showed that it is not only the conformationally rigid vinylcyclopropane **68** which rearranges. Similarly, the vinylcyclopropanes **70** and **71** rearrange to the vinylcyclopentene **72** under aminium ion catalysis.

(70)   (71)   (72)

R = *p*-MeOC$_6$H$_4$
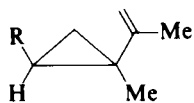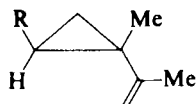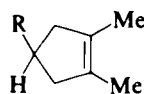
The detailed mechanisms of the aminium catalyzed ring expansion of **68**, **70** and **71** remain uncertain, although there are two clear alternatives: (1) stepwise isomerization via trimethylene cation radical intermediates or (2) concerted isomerization via odd-electron pericyclic transition states[39]. Less clear is why **70** and **71** ring-expand smoothly under aminium ion catalysis but *cis*-**58** and *trans*-**59** do not. Perhaps, as in the Skatteböl rearrangement, the difference is due to a buttressing effect, see Chapter 4.III.C.

In a further study Dinnocenzo and Conlon differentiated between the two mechanistic alternatives[40] outlined above. The catalytic rearrangement of *trans*-**73** and *cis*-1-*p*-anisyl-2-(*E*-2-buten-2-yl)-2-methylcyclopropane (**74**) with either (*p*-ClC$_6$H$_4$)$_3$N$^{+\bullet}$ SbF$_6^-$ or Fe(1, 10-phenanthroline)$_3^{3+}$ (PF$_6^-$)$_3$, or the excited state of 1,4-dicyanonaphthalene, provided *trans*-**75** and 4-*p*-anisyl-1,2,3-trimethylcyclopentene (**76**) in a 6:1 ratio. The isomerization

(73)   (74)

(75)   (76)   R = *p*-MeOC$_6$H$_4$
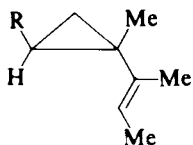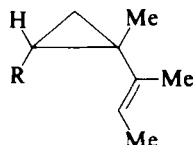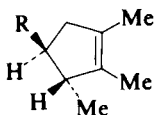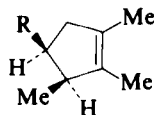
73⇌**74** does not successfully compete with the formation of **75** and **76**. These stereo-chemical results are most consistent with a stepwise, cation radical mechanism for ring expansion.

One-electron oxidation can also change the formal periselectivity of vinylcyclopropane rearrangements. Thus, while all the three catalytic oxidants described above convert *trans*-1-*p*-anisyl-1,2-dimethyl-2-isopropenylcyclopropane (**77**) to 4-*p*-anisyl-1,2,4-trimethylcyclopentene (**78**), thermolysis of **77** instead provides only 2-*p*-anisyl-4,5-dimethyl-hexa-1,4 -diene (**79**).

(77)   (78)   (79)

$$R = p\text{-MeOC}_6\text{H}_4$$
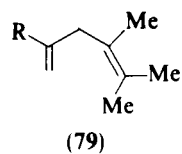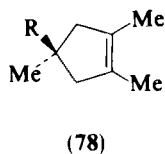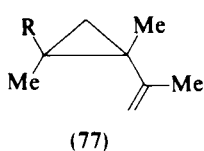
Finally, an interesting cyclopropane isomerization has been reported by Dinnocenzo and Schmittel[41a]. When the *cis*-cyclopropane **80** was dissolved in oxygenated CF_3CO_2D at room temperature, a deep purple color immediately developed. After 15 min **80** was consumed and the *trans* isomer **81** was formed (50%).

(80)   (81)

$$R = p\text{-MeOC}_6\text{H}_4$$
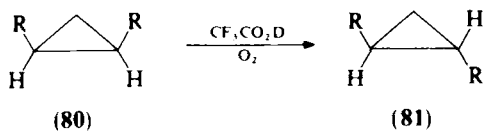
Only rigorous elimination of dioxygen O_2 suppressed the isomerization rate dramatically. Further investigations are not consistent with a proton catalyzed reaction. The conclusion concerning the reaction mechanism is that 'it likely involves a substrate-dioxygen charge-transfer complex, although the mechanism is not completely understood'. The authors indicate that Lewis acid promoted reactions could also involve electron transfer since many Lewis acids (e.g. $SbCl_5$, $AlCl_3$ and BF_3) are known to promote one-electron oxidation.

Cyclopropane and trimethylene cation radicals supposedly are involved in the chloranil (CA) sensitized rearrangement of the spiropentanes **82** to the methylenecyclo-butanes **87** and **89**, respectively[42].

(82)   (83⁺•) CA⁻•   (84⁺•)CA⁻•   (85⁺•)   + CA⁻•

(91)   (90)   (88⁺•)   (86⁺•)

$$R = p\text{-MeOC}_6\text{H}_4, \ p\text{-MeC}_6\text{H}_4, \ \text{Ph}$$

(89)   (87)
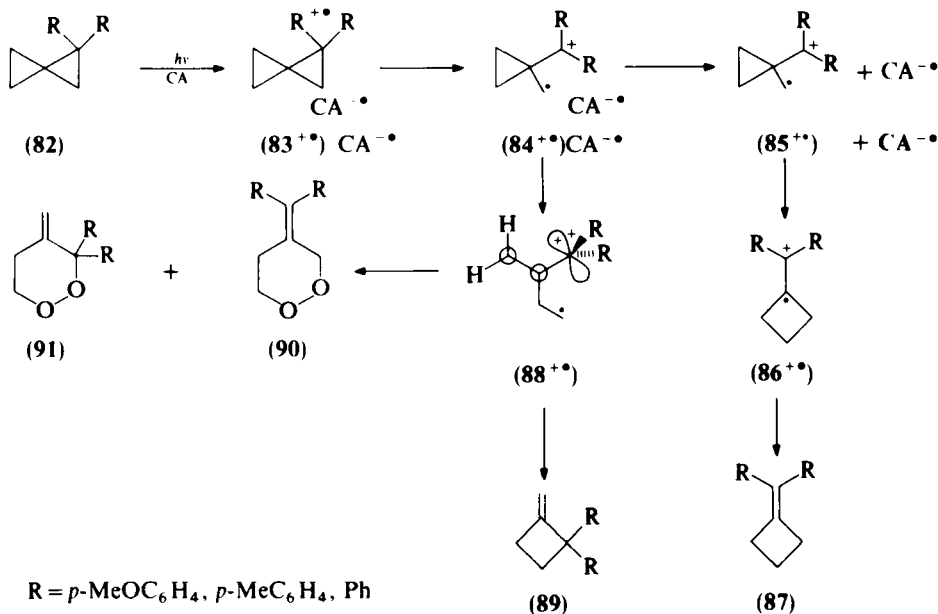
If one assumes that the peripheral 1,3-cation radical **85** [+•] forms **87** whereas the twisted 1,4-cation radical **88** [+•] preferentially gives **89**, then the single electron-transfer induced spiropentane **82**→methylene cyclobutane **87, 89** rearrangement can be explained as follows: the initially formed radical ion pair **83** [+•]CA [−•] is converted to the ring-opened radical ion pair **84** [+•]CA [−•]; in the polar acetonitrile **84** [+•]CA [−•] efficiently separates into the free radical cation **85** [+•] which rearranges to **86** [+•] and gives **87**, whereas in the less polar solvent benzene **84** [+•]CA [−•] rearranges to **88** [+•] to form **89**. Interestingly, the intermediate 1,4-cation radical was trapped by O_2 in a cycloaddition finally to give the cycloadducts **90** and **91**.

VI. CYCLOADDITIONS OF CYCLOPROPANES WITH HIGHLY ACCEPTOR SUBSTITUTED OLEFINS VIA ELECTRON TRANSFER

In 1970, Martini and Kampmeier reported that 1,1-diphenylcyclopropane **(92)** reacts with TCNE in benzene at 125 °C to give, in addition to the acyclic adduct **93**, 3,3-diphenylcyclopentane-1,1,2,2-tetracarbonitrile **(94)** [43].
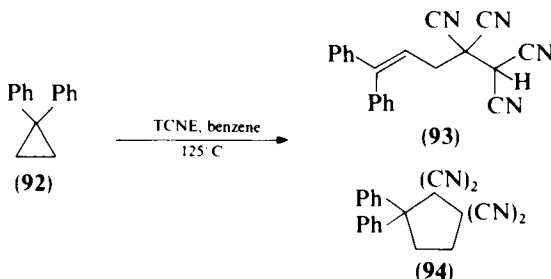
The formation of the cyclopentane derivative **94** is of particular interest since a strained cyclopropane σ-bond is involved in the cycloaddition, and a five-membered ring is constructed in a single operation. Since then several groups have demonstrated the formation of a cyclopentanes in the reactions of certain cyclopropanes with olefins.

Nishida and coworkers treated the cyclopropane-substituted olefins **95** with TCNE and observed the formation of the cyclopentane cycloadducts **96** [44]. The reaction was
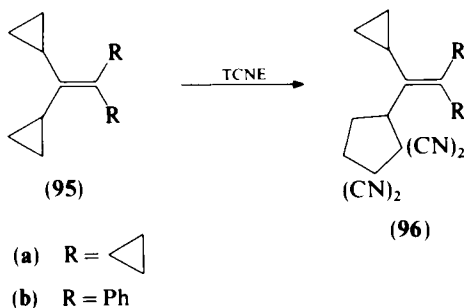
explained with an initial electron transfer to give **97** [+•] and then **98** [+•], which reacted with the anion radical TCNE [−•] to give **96**. This reaction is in strong contrast to the ready 2 + 2 cycloaddition reactions very often observed in the reactions of electron-rich olefins with TCNE [45].

$$\left[\begin{array}{c} \triangle \\ \overset{\cdot}{C}-\overset{+}{C}\overset{\diagup R}{\diagdown R} \\ \triangle \end{array}\right] \longrightarrow \left[\begin{array}{c} \triangle \\ \underset{H_2C\diagdown}{HC}\overset{+}{\underset{\diagdown CH_2}{C=C}}\overset{\diagup R}{\diagdown R} \end{array}\right]$$

<center>(97^{+•})</center>

<center>(98^{+•})</center>
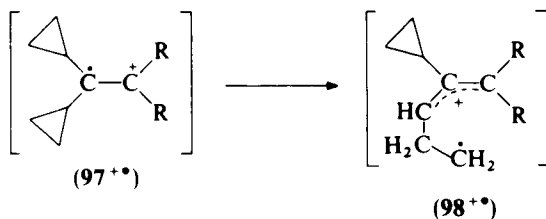
No mechanistic details or suggestions have been given for the reactions of cyclopropan-one acetals **99** with TCNE which also led to cyclopentanes (**100**)[46].

<center>
RO OR   TCNE   (CN)$_2$
</center>

$$\underset{R'}{\overset{RO\diagup\diagdown OR}{\triangle}} \xrightarrow{\text{TCNE}} R'\diagdown\overset{(CN)_2}{\underset{(OR)_2}{\bigcirc}}(CN)_2$$

<center>(99)   (100)</center>
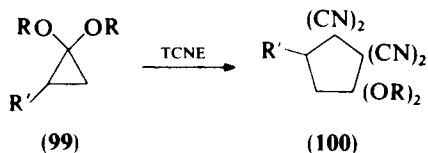
A rather selective cycloaddition of TCNE was observed in the reaction with the substituted cyclopropanone acetal **101** leading only to **102** and **103**[47]. This reaction was

$$\underset{(101)}{\overset{Me}{\underset{Me}{\overset{Me}{\diagup}}}\diagdown\underset{OMe}{\overset{SMe}{}}} \xrightarrow[\text{2 weeks, 80 C}]{\text{TCNE, CH}_2\text{Cl}_2} \underset{(102)}{\overset{Me}{\underset{Me}{\cdots}}\overset{(CN)_2}{\underset{OMe}{SMe}(CN)_2}} + \underset{(103)}{\overset{Me}{\cdots}\overset{(CN)_2}{\underset{SMe}{MeOMe}(CN)_2}}$$
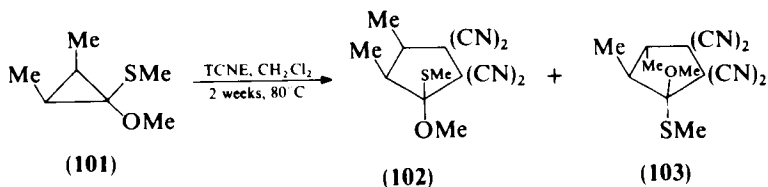
suggested to occur in a symmetry-allowed [π2s + σ2a] pathway (which is rather unlikely the case). Irradiation of a methylene chloride solution of **101** and TCNE strongly accelerated the reaction, which is terminated after 10 h at 0 °C. It was proposed that the photochemical process probably involves radical ions as intermediates in which the stereospecificity is largely lost.

Electron transfer photochemistry of aromatic imides and phenylcyclopropane **104** leading to radical anion–radical cation cycloaddition was described by Mazzocchi and coworkers[48]. When **104** was reacted with *N*-methylphthalimide (**105**) in methanol, the ether **106** and the hydroxylactam **107** were formed. This establishes that an electron

<center>Ph⌒⌒OMe +</center>

<center>(106)</center>

$$\underset{(104)}{Ph\diagup\triangle} + \underset{(105)}{\overset{O}{\underset{O}{\bigcirc\hspace{-2mm}N-Me}}} \xrightarrow[\text{MeOH}]{h\nu}$$

<center>
Ph
HO⌒⌒⌒OMe
N—Me
O
</center>

<center>(107)</center>
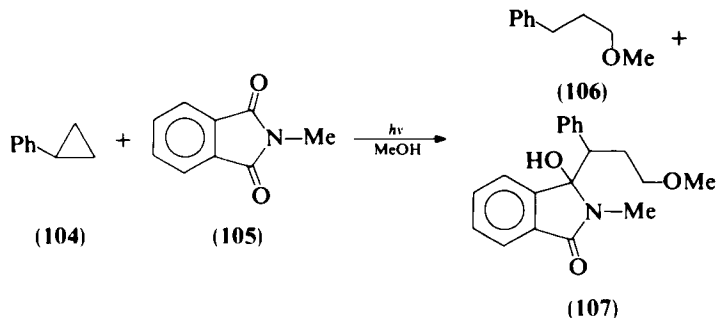
transfer process has taken place and that **105** (or **105⁻•**) cannot compete as a nucleophile with methanol for the cation radical **104⁺•**. Very recently, Dinnocenzo and coworkers[41b]
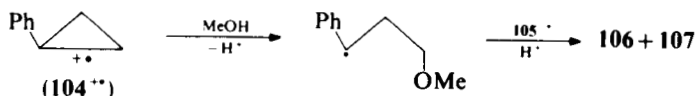
have shown with suitably substituted cyclopropane cation radicals that nucleophiles (like methanol) add with inversion of configuration. However, when **104** and **105** were irradiated in acetonitrile the reaction gave two isomeric products **108a** and **108b**, each in 11% yield. The formation of **108** was suggested to occur via a photochemically generated radical anion/radical cation pair undergoing cycloaddition.

(a)   X = H, Y = Ph
(b)   X = Ph, Y = H

(108)
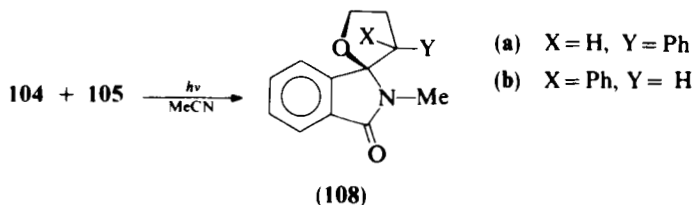
Mizuno, Otsuji and coworkers reported on the photooxygenation of 1,2-diarylcyclo-propanes via electron transfer[49]. When they reacted the cyclopropanes **109a–g** with dioxygen and a catalytic amount of 9,10-dicyanoanthracene (DCA) in acetonitrile in the presence of light (high-pressure mercury lamp filtered through an aqueous NH_3–$CuSO_4$ filter), they isolated the 1,2-dioxolanes **110a–g** and **111a–g** in excellent yields (>90%).

(109 a–g)   (110 a–g)   (111 a–g)

	Ar	Ar'
(a)	$4\text{-}Me_2NC_6H_4$	$4\text{-}MeOC_6H_4$
(b)	$4\text{-}Me_2NC_6H_4$	Ph
(c)	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4$
(d)	$3,4\text{-}(MeO)_2C_6H_3$	$3,4\text{-}(MeO)_2C_6H_3$
(e)	$4\text{-}MeOC_6H_4$	$4\text{-}MeC_6H_4$
(f)	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$
(g)	$4\text{-}MeOC_6H_4$	Ph
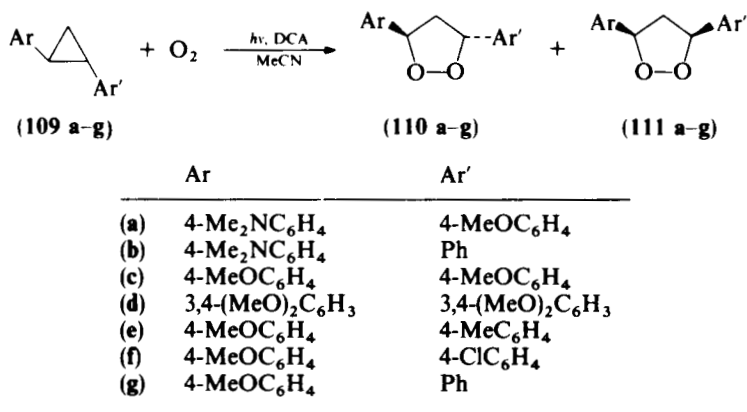
From other investigations (DCA-sensitized photooxygenation of 1,2-diarylcyclopro-panes in the presence of aromatic hydrocarbons like phenanthrene; pyrene-sensitized photooxygenation of **109c** in the presence of 1,4-dicyanobenzene; solvent effects on the DCA-sensitized photooxygenation of **109c**; photooxygenation in the presence of metal salts; fluorescence quenching and redox properties) and the observation of a fast *trans* ⇌ *cis* equilibrium of **109**, they invoked the following mechanism.

The DCA-sensitized photooxygenation of **109a–g** is initiated by a one-electron transfer from **109** to ¹DCA* to give **109⁺•** as the reactive species (primary process). There is no discussion of the structure of **109⁺•** ('closed, half-open, open') in this work.

For the oxygenation two pathways are discussed. The first mechanism involves the reaction between $109^{+\bullet}$ and $O_2^{-\bullet}$ that can be generated by electron transfer from $DCA^{-\bullet}$

$$DCA^{-\bullet} + {}^3O_2 \longrightarrow DCA + {}^3O_2^{-\bullet}$$

$$109^{+\bullet} + {}^3O_2^{-\bullet} \longrightarrow 110 + 111$$
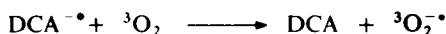
to ${}^3O_2$. The second mechanism involves the hole transfer from the three-membered ring species to the intermediate which is generated by the reaction between $109^{+\bullet}$ and ${}^3O_2$.
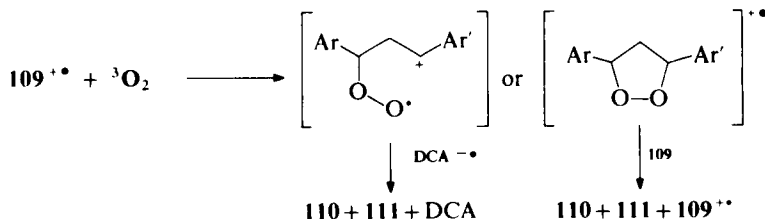
Singlet oxygen is not involved as a principal reactive species in the DCA-sensitized photooxygenation[50].

A study of the irradiation of the donor–acceptor complexes of 1,1,2,2-tetraarylcyclopropanes 112a–f with TCNE under aerated conditions involving oxygenation to give 113a–f was published by Miyashi and coworkers[51]. The yields of 113 increased as the
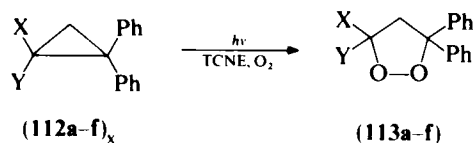
	X	Y
(a)	$p\text{-MeOC}_6\text{H}_4$	$p\text{-MeOC}_6\text{H}_4$
(b)	$p\text{-MeOC}_6\text{H}_4$	$p\text{-MeC}_6\text{H}_4$
(c)	$p\text{-MeOC}_6\text{H}_4$	Ph
(d)	$p\text{-MeOC}_6\text{H}_4$	$p\text{-ClC}_6\text{H}_4$
(e)	$p\text{-MeC}_6\text{H}_4$	$p\text{-MeC}_6\text{H}_4$
(f)	Ph	Ph

solvent polarity and the electron-donating power of 112 increased. The amount of TCNE did not significantly change the yields of oxygenation which indicates its role as a catalyst. In the reaction of the *cis* isomer 114 a photostationary mixture of 114 and its *trans* isomer 115 was observed to precede the formation of the *cis* and *trans* cycloadducts 116 and 117.

The mechanism of the TCNE-catalyzed *cis/trans* isomerization and adduct formation is discussed in the following manner. First, the radical ion pair [cyclopropane$^{+\bullet}$TCNE$^{-\bullet}$] is formed. In the more polar solvents and with the more electron-donating substituents dissociation of [cyclopropane$^{+\bullet}$TCNE$^{-\bullet}$] to cyclopropane$^{+\bullet}$ followed by ring cleavage

(114)   (115)

(116)   (117)
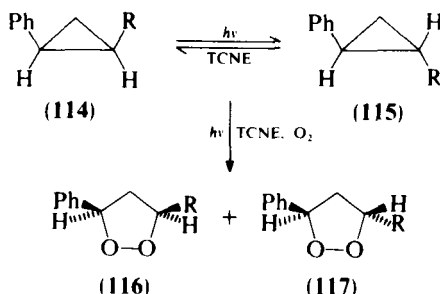
to trimethylene$^{+\bullet}$ should occur. Another possibility is the cage cleavage of [cyclopropane$^{+\bullet}$TCNE$^{-\bullet}$] to [trimethylene$^{+\bullet}$TCNE$^{-\bullet}$], which is less sensitive to solvent polarity. The solvent-mediated former process, and consequent oxygenation, thus exclusively occur in the more polar solvent through trimethylene$^{+\bullet}$. The dissociation of [trimethylene$^{+\bullet}$TCNE$^{-\bullet}$] can also generate trimethylene$^{+\bullet}$, but this process is assumed to be less important as compared with the primary dissociation pathway. It is of interest that in the case of several methylenecyclopropanes, oxiranes and aziridines, cage coupling of [ring-opened$^{+\bullet}$TCNE$^{-\bullet}$] to give TCNE cycloadducts of the type 118 is observed besides the oxygenation reactions[51]. The observation that oxygenations of 112a–e are

$$X = C = CH_2, O, N$$
$$R^1 - R^4 = aryl \ and \ H$$

(118)
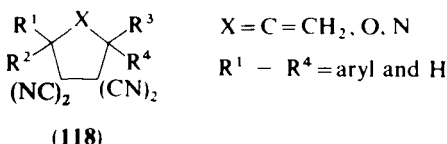
also catalyzed by tris(p-bromophenyl)$_3$aminium hexachloroantimonate in the dark[52] can be taken as further evidence for the mechanism discussed above. It should also be mentioned that the photoexcitation of the complex [112f·TCNE] was first reported by Arnold and coworkers[53], and that Schaap and coworkers had reported on the dicyano-anthracene-biphenyl-cosensitized electron-transfer photooxidation of 112f to give 113f[50a,b].

In summarizing the results discussed so far, it seems that trimethylene cation radicals, formed via *photosensitized* electron transfer from the corresponding cyclopro-panes, can undergo cycloaddition reactions to give five-membered ring cycloadducts. Is there also a *thermal* electron-transfer reaction to start a cycloaddition of this sort?

The thermal reaction of 119a and TCNE to give 120a was studied by Nishida, Tsuji and coworkers[54a].

(119)   (120)

(a) R = —◁

(b) R = Me
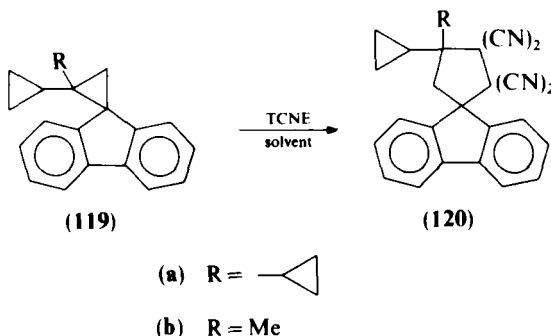
On mixing **119a** and TCNE, a colored solution was formed which faded shortly afterwards. The time required to give the colorless solution depended on the polarity of the solvent used: less than 1 s in MeCN or $MeNO_2$; 1–2 s in acetone; ca 30 s in CH_2Cl_2; ca 24 min in ethyl acetate; 1.5 h in benzene. The reaction of **119b** with TCNE proceeded slowly (overnight in CH_2Cl_2) but analogously to give **120b**. In contrast, the related 1,1-dicyclopropyl-2,2-diphenylcyclopropane **121** was practically unreactive with TCNE under similar reaction conditions and only a 'trace amount' of **122** was found in CH_3CN after 20 h. The 2,2-dicyclopropylvinyl derivative **123**, on the other hand, reacted very
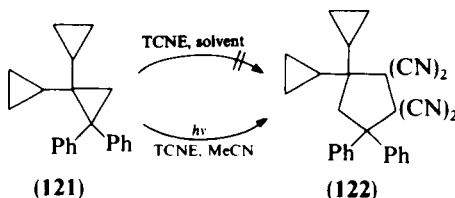
readily with TCNE to give **124**. In contrast, **125** produced two adducts, **126** and **127**, in its slow reaction with TCNE.
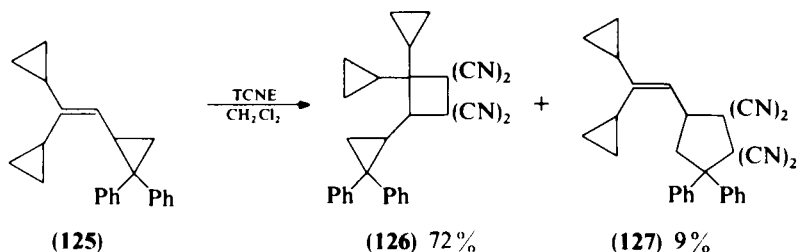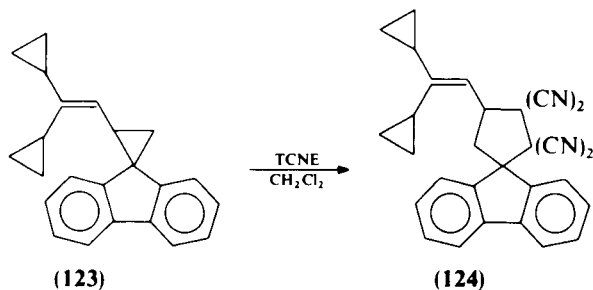
Since **123** and **125** are *tri*-substituted olefins, $[\pi2 + \pi2]$ cycloadditions via zwitterionic intermediates might take place[45, 55]. This was indeed the case in the reaction of **125**, but **123** produced exclusively **124**. Here, the effect of the fluorene moiety was observed for a second time: the marked difference between **119a** and **121**, as well as between **123** and **125**, is evidently due to the presence or absence of the fluorene part. According to Scott, Houk, Paddon-Row and coworkers[55], an electron transfer is favored thermodynamically when the difference between the ionization potential (IP) of the donor and the electron affinity

(EA) of the acceptor is less than 4–5 eV. Thus, since the IP of spiro[cyclopropane-1,9′-[9H]fluorene] (IP^v = 7.84 eV) is substantially lower than that of 1,1-diphenylcyclopropane (IP^v = 8.48 eV) it was proposed that the electron transfer from the substrate to TCNE (EA = 2.8–2.9 eV) might readily occur in the reactions of 119 and 123 but not in the reaction of 121; 125 apparently shows some electron transfer.

$$119 \ + \ TCNE \ \rightleftharpoons \ [119^{+\cdot}TCNE^{-\cdot}] \ \rightleftharpoons \ \longrightarrow \ 120$$
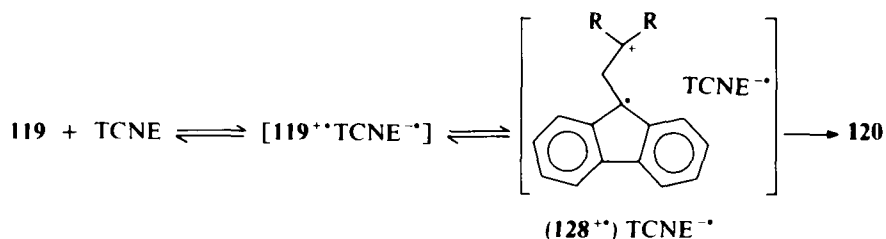
(128^{++}) TCNE$^{-\cdot}$

The resultant closed radical cation, e.g. 119$^{+\cdot}$ TCNE$^{-\cdot}$, will open its cyclopropane ring to give 128^{++} TCNE$^{-\cdot}$ when the three-membered ring carries good cation-stabilizing groups. The trimethylene cation radical 128$^{+\cdot}$ will then react with nearby TCNE$^{-\cdot}$ to give 120. The single electron-transfer is the rate-controlling step[54b].

It is not surprising that the *thermally* very low reactive 121 reacted with TCNE under *illumination* with a halogen lamp (42% conversion at 12 °C in MeCN after 4 h) to give 122. The charge-transfer complex (λ_{max} = 363 nm) might be excited by illumination and the resultant excited state would collapse to an ion radical pair similar to [119$^{+\cdot}$TCNE$^{-\cdot}$] which will undergo subsequent transformations.

In addition to the reactions with TCNE, Nishida and coworkers studied the ring-opening dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) of some cyclopropanes activated by a spiro-linked fluorene[56].

(119b) R^1 = Me, R^2 = △

(129)   R^1 = R^2 = Me

130

(131)

130,131 (a) R = △

(b) R = Me
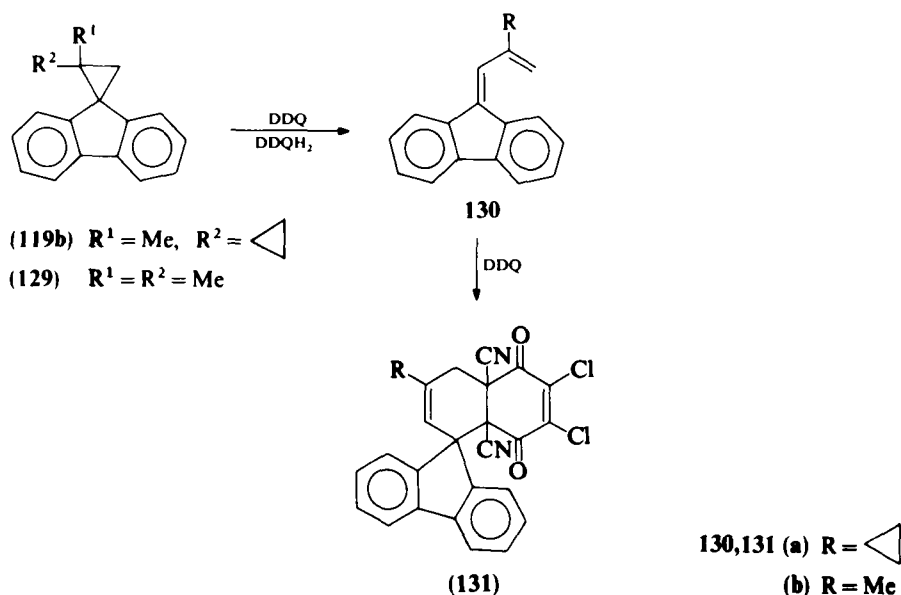
When a 1:2 molar equivalent mixture of **129** and DDQ was refluxed in benzene for 12 h, **131b** was isolated in 78% yield. **131b** is the cycloadduct of the diene **130b** with DDQ as shown by independent synthesis. The reaction with **119b** to give **131a** via **130a** took place even at room temperature. In contrast, the diphenyl derivatives **132** were not dehydrogenated thermally to give the corresponding dienes **133** and subsequently the cycloadducts **134**.

(132)

(a) R¹ = Me, R² = △

(b) R¹ = R² = Me

(133)

(134)

(a) R = △

(b) R = Me
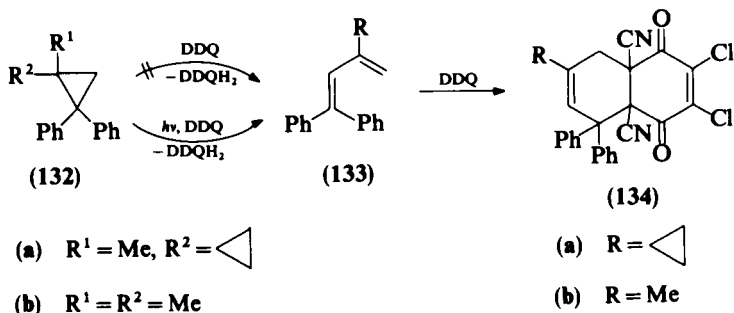
On the other hand, photochemical dehydrogenation of **132a, b** led to the adducts **134a, b**. In the case of **132a**, 8% of the diene **133a** was obtained in addition.

The intermediate in the quinone dehydrogenations was also trapped with methanol. Thus, when **119b** reacted with DDQ in benzene–methanol solutions at room temperature, **135** and **136** were isolated.

(135) 24%

(136) 62%
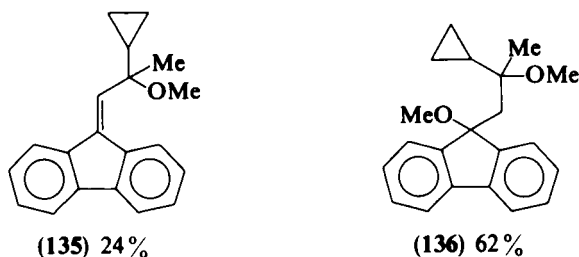
In both reaction types, the cycloadditions with TCNE and the dehydrogenation reactions with DDQ, it is apparent that electronic matching is essential for ready *thermal* reactions. It has been demonstrated that the reactions are practically limited to occur between *gem*-dialkyl substituted, spiro-activated cyclopropanes, and a strongly acceptor olefin, such as TCNE and DDQ. On the basis of electrochemical data, the authors suggested that the substrate should be oxidized in contact with the acceptor and that the radical cation is a key intermediate in the consecutive transformations. The fact that methanol totally quenched both DDQ dehydrogenations and TCNE cycloadditions suggests that the polar nature of the intermediate(s) is common to both reactions. The reaction scheme of the DDQ reactions is shown.

It is not clear from the investigations whether the cation radicals **137a** or **b** are 'closed, half-open or open' in nature. From the recent work of Dinnocenzo and coworkers, however, it seems rather likely that they are ring-closed[41b]. Deprotonation of **137⁺·** by DDQ⁻· should be a facile reaction since cation radicals are known to have high acidity. The oxidation of **138·** to **139⁺** may raise some questions. The fact that **136** was formed as

(a) $R = \triangleleft$

(b) $R = Me$
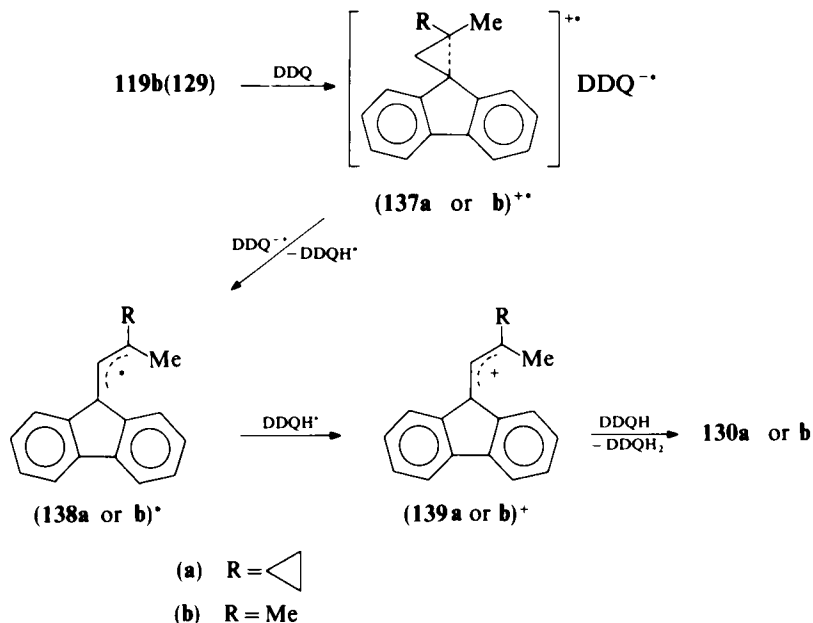
the major product in the methanol trapping experiments suggests that formation of the 9-fluorenyl cation is possible. Deprotonation of 139^+ leads to the dienes 130 which, with the second equivalent of DDQ, finally give the cycloadducts 134.

To briefly summarize this chapter, there is evidence that cyclopropane and trimethylene cation radicals are formed in solution and in freon matrices. For the formation of trimethylene cation radicals, solvation is energetically very important. 'Gas phase' calculations show clearly that the trimethylene cation radical is not a stable intermediate, which seems to be corroborated by mass-spectroscopic investigations. Within the last five to ten years an increasing number of applications of cyclopropane(trimethylene) cation radicals for synthetic purpose has been observed.

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Author index

This author index is designed to enable the reader to locate an author's name and work with the aid of the reference numbers appearing in the text. The page numbers are printed in normal type in ascending numerical order, followed by the reference numbers in parentheses. The numbers in *italics* refer to the pages on which the references are actually listed.

237

Subject index