Tetrahedron Vol. 36, pp. 2269 to 2289
Pergamon Press Ltd., 1980. Printed in Great Britain

TETRAHEDRON REPORT NUMBER 91

CHEMISTRY OF ALLENE OXIDES

T. H. Chan* and B. S. Ong†

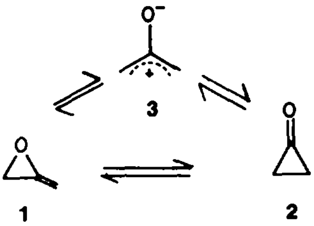
Department of Chemistry, McGill University, Montreal, Quebec, Canada H3A 2K6

(*Received in U.S.A.* 1980)

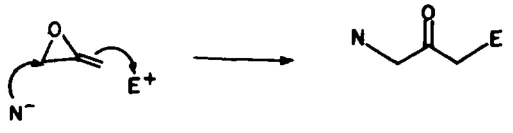
CONTENTS

INTRODUCTION

Allene oxide (1) is a very unusual molecule. It is a member of the valence tautomeric triad—cyclopropanone (2), oxyallyl (3) and allene oxide (Scheme 1). Within its small skeleton, allene oxide encompasses the structural features of an epoxide, a double bond and an enol ether. It is also highly strained. Several quantum mechanical calculations[1-6] have concluded that allene oxide has a higher energy content than cyclopropanone, a molecule already notorious for its instability and reactivity.[7] Accordingly, both cyclopropanone and allene oxide are highly reactive species. They possess unique reactivities and may be expected to undergo reactions at nearly every site on their skeleta. In addition, these systems undergo interconversion ($1 \rightleftharpoons 2$ or $1 \rightleftharpoons 3 \rightleftharpoons 2$), as has been theoretically implicated and experimentally demonstrated, and produces a wealth of complex and interesting chemistry. Synthetically, they may represent useful intermediates of potential significance. With appropriate transformations, cyclopropanones have been converted to a variety of novel carbocyclic and heterocyclic compounds.[7] Similarly, oxyallyls or their metal complexes have been used increasingly in numerous syntheses.[8] Allene oxide, being structurally linked to 2 and 3, should be a useful synthon as well. Thus, reactions at C-1 and C-3 of allene oxide with nucleophiles and electrophiles, respectively, can provide an interesting route to the incorporation of a 3-carbon unit (eqn 1).



Scheme 1.



(1)

The study of the chemistry of allene oxides is a very recent one. It really began in 1968 with the preparation and characterization of the first isolable allene oxide.[9] In the intervening years, new synthetic routes to allene oxides have been developed. Recently a consistent picture concerning their reactivity has emerged. We are beginning to understand the factors controlling their various reactions,

---

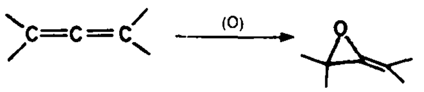
†Present address: Xerox Research Laboratory, Mississauga, Ontario, Canada.

especially the allene oxide-cyclopropanone ($1 \rightleftharpoons 2$) isomerization process. In this review, we shall examine the current status of the chemistry of allene oxides with the hope of stimulating further investigation into this fascinating class of molecules.

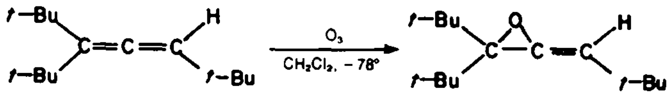
GENERAL APPROACHES TO THE PREPARATION OF ALLENE OXIDES

By dissecting the molecular structure of allene oxide, it is obvious that there are at least three general approaches to its preparation.

(a) The most direct and so far the most generally employed approach is the epoxidation of allenes (eqn 2). The reaction of allene with oxygen (^3P) atoms in the gas phase has been postulated to proceed through allene oxide.[10] Epoxidation of allenes has been accomplished by the use of ozone.[11] Thus treatment of 1, 1, 3-tri-*t*-butylallene (4) with ozone in methylene chloride at −78° affords 5% of 1, 1, 3-tri-*t*-butylallene oxide (5).

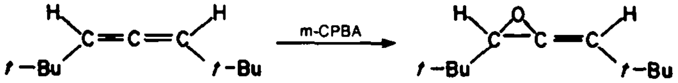


(2)

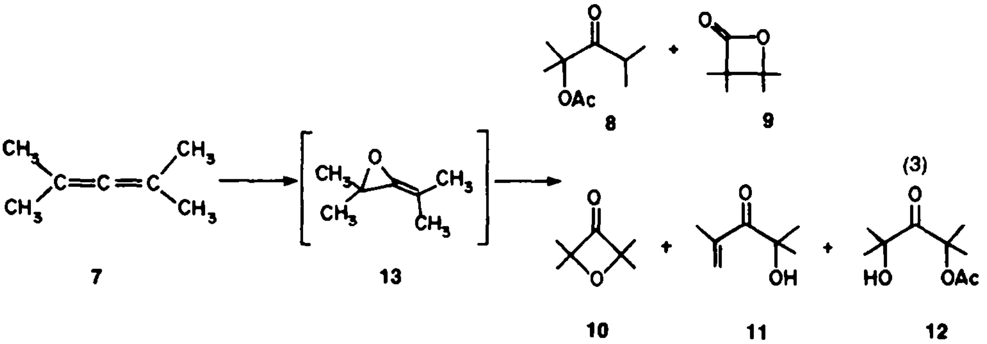


4 5

More conveniently, peracid is used for the epoxidation of allenes. For some allenes bearing bulky substituents, peracid epoxidation can lead to isolable allene oxides. This is the case with 1, 3-di-*t*-butyllallene oxide (6)[9] and 1, 1, 3-tri-*t*-butylallene (5).[12, 13] With allenes having sterically less bulky substituents, peracid epoxidation generally leads to complex mixtures of products. Thus, epoxidation of tetramethylallene (7)[14–16] with peracetic acid affords **8–12** as products, presumably via the allene oxide **13** (eqn 3).[17] Table I summarizes the results of oxidation of various allenes.

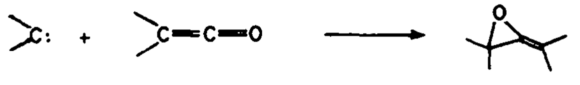


6

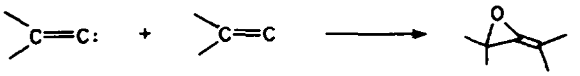


(3)

(b) Relatively little explored is the construction of the allene oxide skeleton by methylene addition to the CO group of ketenes (eqn 4) or by vinylidene addition to aldehydes and ketones (eqn 5). Reactions of diazoalkanes with ketenes give, in general, cyclopropanones. It seems that carbene or carbenoid species attack preferentially the c = c double bond.



(4)



(5)

Table 1. Oxidation of allenes as a method of generating allene oxides

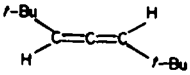
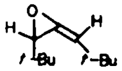
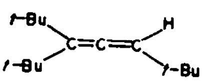
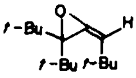
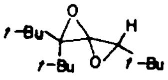
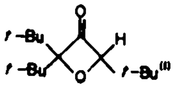
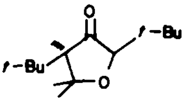
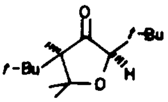
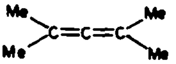
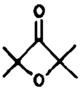
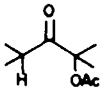
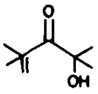
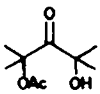
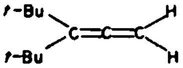
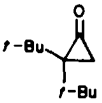
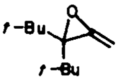
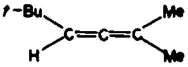
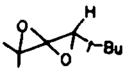
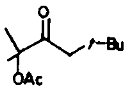
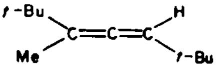
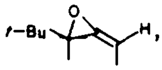
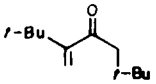
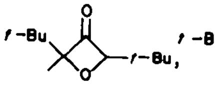
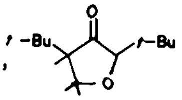
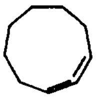
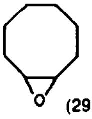
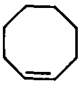
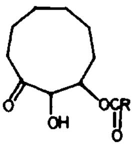
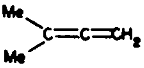
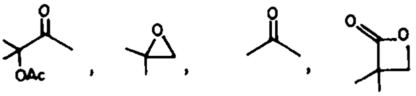
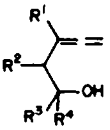
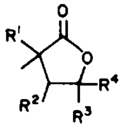
Allene used	Oxidation Conditions	Products (relative amounts)	References
$CH_2{=}C{=}CH_2$	$O(^3P)$ gas phase	CO(57%), C_2H_4 (38%), $CH_2{=}CHCHO$ (1%)	10
	m-CPBA		9
	$O_3/CH_2Cl_2/-78°$	 **5**  **28**	11
	m-CPBA	**5**(10).  **30**	12
	PNPBA	**5**(24), **30**(41), *t*-BuCO*t*-Bu(5),  (20)  (11)	13
	CH_3CO_3H/CH_2CL_2 /Na_2CO_3	, , , 	13, 14
	CH_3CO_3H		13, 15
	PNPBA/ − 30°		13
	CH_3CO_3H	 	13
	PNPBA	, (46)  (6) , (36)  (12)	13

Table 1. (*Contd*)

Allene used	Oxidation Conditions	Products (relative amounts)	Reference
	CH_3CO_3H	 (29),  (11),  (44)	16 27b
 $Me_2C{=}C{=}CH_2$	CH_3CO_3H		16
	H_2O_2/PhCN		27a

R^1	R^2	R^3	R^4	Yield of product (%)
Me	H	H	H	80
Me	H	H	Me	80
Me	Me	H	Me	80
Me	H	Me	Me	80
Me	$-(CH_2)_4-$		H	80 (*cis*-isomer)
Me	$-(CH_2)_4-$		H	80 (*trans*-isomer)

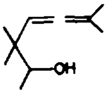
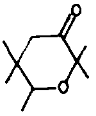
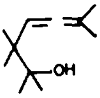
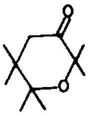
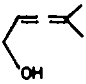
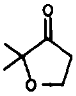
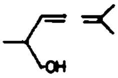
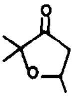
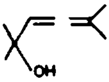
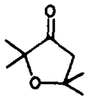
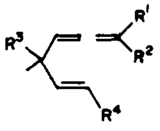
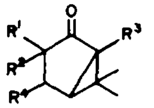
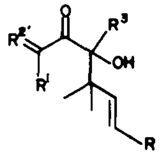
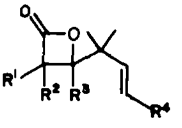
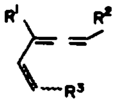
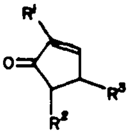
Allene used	Oxidation Conditions	Products (relative amounts)	Reference
	H_2O_2/PhCN	 (60%)	27c
	H_2O_2/PhCN	 (quant)	27c
	H_2O_2/PhCN	 (10%)	27c
	H_2O_2/PhCN	 (60%)	27c
	H_2O_2/PhCN	 (quant)	

Table 1. (*Contd*)

Allene used	Oxidation Conditions	Products (relative amounts)			Reference
	PNPBA				

R^1	R^2	R^3	R^4		Products (relative amounts)		
CH_3	CH_3	H	H	(in CH_2Cl_2)	0%	20%	80%
CH_3	CH_3	H	H	(in CH_3OH)	100%	0%	0%
CH_3	Et	H	H	(in CH_2Cl_2)	50%		50%
CH_3	Et	H	H	(in CH_3OH)	90%		10%
—$(CH_2)_5$—		H	H	(in CH_2Cl_2)	30%	30%	30%
CH_3	Et	H	CH_3	(in CH_2Cl_2)	35%		60%

	PNPBA/ CH_2Cl_2		27d

R^1	R^2	R^3	
CH_3	H	H	60%
C_3H_7	H	H	100%
H	C_3H_7	H	95%
CH_3	H	CH_3	60%

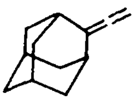
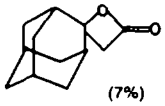
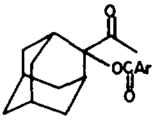
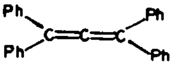
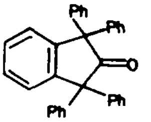
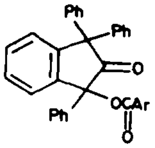
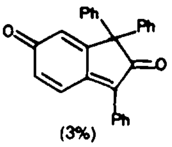
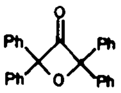
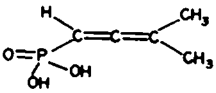
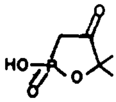
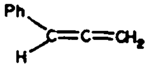
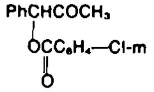
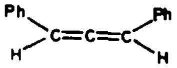
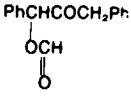
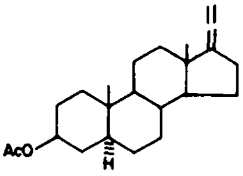
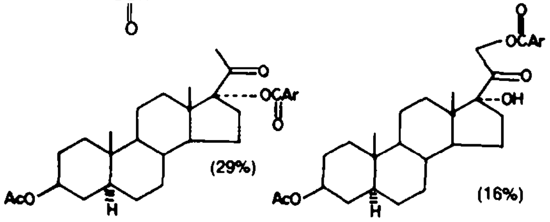
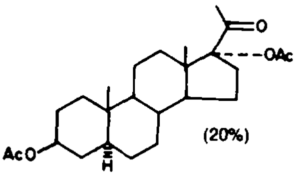
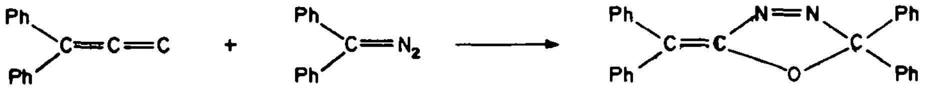
	m-CPBA/ CH_2Cl_2	 (7%)	 (trace)		42
	m-CPBA/ CH_2Cl_2	 (45%)	 (1%)	 $\underset{\underset{O}{\|}}{PhCPh}$ (3%)	43, 45
	m-CPBA/ Na_2CO_3	 (3%)	 (6%)	 $\underset{\underset{O}{\|}}{PhCPh}$ (10%)	
	m-CPBA/ $CHCl_3$				

Table 1. (*Contd*)

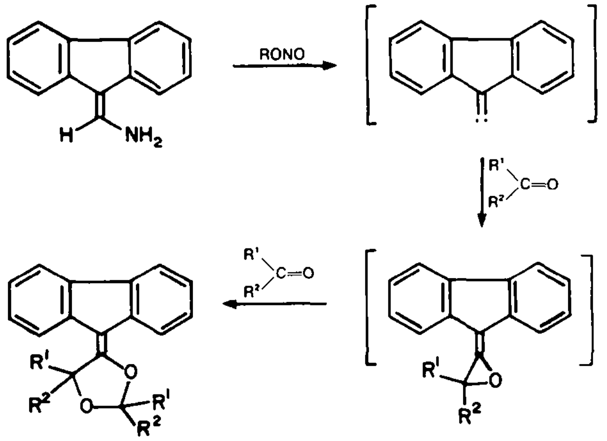
Allene used	Oxidation Conditions	Products (relative amounts)	Reference
	m-CPBA	PhCHO (50%),  $\mathrm{PhCH(OC(=O)C_6H_4\text{—}Cl\text{-}m)COCH_3}$ (9%)	45
	PFA	 $\mathrm{PhCH(OCHO)COCH_2Ph}$	
	m-CPBA	 (29%) (16%)	46
	m-CPBA/ Na_2HPO_4 buffer	compound above (34%)	
	CH_3CO_3H	 (20%)	

An exception is the addition of diphenyldiazomethane to diphenylketene where the oxadiazoline **14** is formed.[18]



14

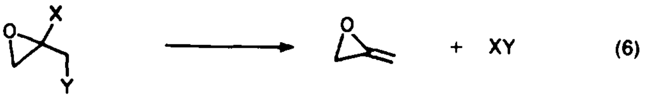
Only one example of a vinyl carbene reaction with a carbonyl compound has been reported.[19] Allene oxide **15** may have been involved as the intermediate (Scheme 2).



15

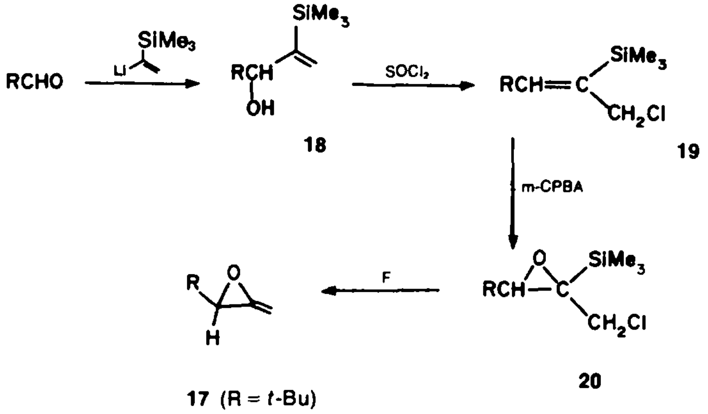
Scheme 2.

(c) Several years ago, we recognized that an alternative approach to allene oxides was to generate the double bond subsequent to the formation of the epoxide ring (eqn 6). What is required is a mild and selective method to effect the elimination of XY from the precursor **16**. Our work in the use of β-functionalized organosilicon compounds as a method of alkene synthesis[20] has led us to examine the use of **16** ($X = R_3Si$, Y = good leaving group) as an entry to allene oxide.[21] We have successfully used



16

this approach to isolate and characterise 1-*t*-butylallene oxide (**17**) according to scheme 3 (R = *t*-butyl).[22]



Scheme 3.

α-Trimethylsilylvinyl lithium reacts with a wide variety of carbonyl compounds to give the β-hydroxyvinylsilane **18** in good yields.[23] Treatment of **18** with thionyl chloride usually afforded a mixture of isomeric chlorides among which the terminal chloride **19** predominates.[23] Epoxidation of the chloride **19** with peracid gave the epoxide **20** as a mixture of geometrical isomers. When the epoxide **20** was stirred with fluoride ion, cleavage of the trimethylsilyl group and the chloride resulted. The allene oxide **17** (R = *t*-Bu) was continuously removed from the reaction mixture by a stream of nitrogen and collected in a cold trap at − 78°.[24]

Other allene oxides with less bulky R groups than *t*-butyl are too reactive to be isolated. They have been generated as transient species by the same procedures.[24, 25] They can react *in situ* with reagents already present in the reaction mixture. In this way, the chemistry of allene oxides can be investigated. Table 2 summarizes the various allene oxides generated by this approach.

It will be of interest to examine other mild and selective method of alkene synthesis which may be compatible with the generation of allene oxides by eqn (6).

PHYSICAL AND CHEMICAL PROPERTIES OF ISOLABLE ALLENE OXIDES

At the present time, several allene oxides have been isolated and characterized by spectroscopic means. They have, as a common feature, at least one sterically encumbered *t*-Bu group at the C-1 position. The steric factor, which contributes to their relative lack of reactivity, is precisely the reason which leads to their isolation. Their isolation, nevertheless, indicates that the method of preparation can indeed by used for the generation of other reactive allene oxides. The reactions of these isolable allene oxides can also serve as prototypes to understand the reactions of other transient allene oxides.

(a) *Spectroscopic properties*. The proton NMR spectra of all isolated allene oxides show the expected chemical shifts and multiplicity pattern. The vinyl proton of **6** appears at δ 4.82, not far from the expected chemical shift of the vinyl proton of enol ethers.[9] The two vinyl protons of 1-*t*-butylallene oxide appear as an AB quartet, indicating that the two protons are non-equivalent, one *cis* and the other *trans* to the oxygen.[24] When the vinyl carbon (C-3) is differently substituted, geometrical isomers are

Table 2. Allene Oxides derived from the Silicon method and their reactions with nucleophiles[a]

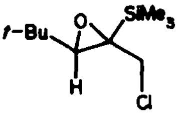
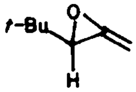
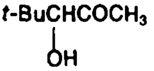
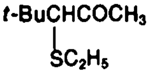
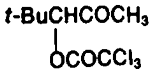
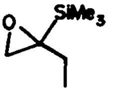
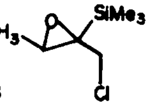
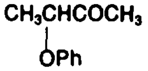
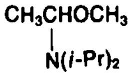
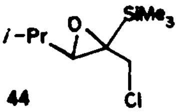
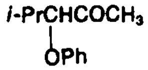
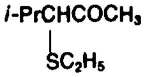
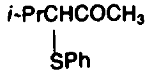
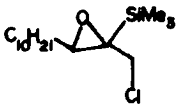
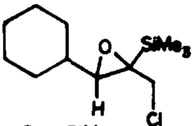
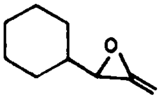
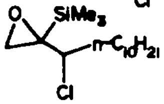
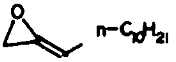
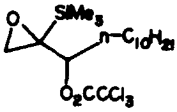
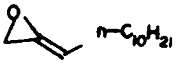
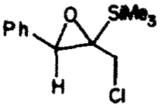
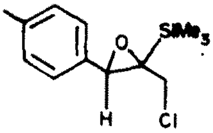
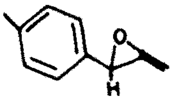
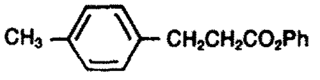
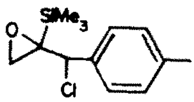
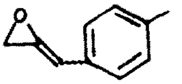
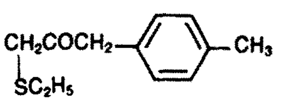
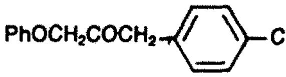
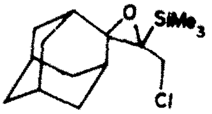
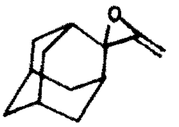
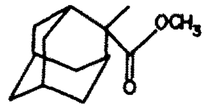
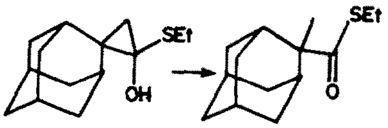
Organosilicon Precursor	Allene oxide generated	Nucleophile used	Product obtained (isolated yield, %)	
		H_2O	 $t\text{-Bu}\underset{\text{OH}}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(68)
		C_2H_5SH	 $t\text{-Bu}\underset{\text{SC}_2\text{H}_5}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(74)
		CCl_3CO_2H	 $t\text{-Bu}\underset{\text{OCOCCl}_3}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(78)
 42		PhOH	$PhOCH_2COCH_3$	(77)
 43		Cl^{-b}	$CH_3CHClCOCH_3$	(50)
		PhOH	 $\text{CH}_3\underset{\text{OPh}}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(78)
		$(i\text{-Pr})_2NH$	 $\text{CH}_3\underset{\text{N}(i\text{-Pr})_2}{\underset{\vert}{\text{C}}}\text{HOCH}_3$	(43)
 44		Cl^{-b}	$i\text{-PrCHClCOCH}_3$	(50)
		PhOH	 $i\text{-Pr}\underset{\text{OPh}}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(73)
		C_2H_5SH	 $i\text{-Pr}\underset{\text{SC}_2\text{H}_5}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	(83)
		PhSH	 $i\text{-Pr}\underset{\text{SPh}}{\underset{\vert}{\text{C}}}\text{HCOCH}_3$	—
 45		Cl^{-b}	$n\text{-C}_{10}\text{H}_{21}\text{CHClCOCH}_3$	(68)
		CH_3OH	$n\text{-C}_{10}\text{h}_{21}\text{CHCOCH}_3$ OCH_3	(60)
46 		Cl^{-b}	$c\text{-C}_6\text{H}_{11}\text{CHClCOCH}_3$	(65)
47 		CH_3OH	$\text{CH}_3\text{OCH}_2\text{COCH}_2n\text{-C}_{10}\text{H}_{21}$	(54)
48 		PhOH	$\text{PhOCH}_2\text{COCH}_2\text{-}n\text{-C}_{10}\text{H}_{21}$	(75)

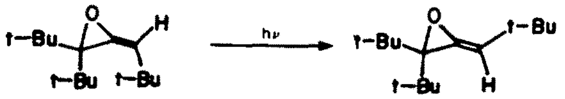
Table 2. (*Contd*)

Organosilicon Precursor	Allene oxide generated	Nucleophile used	Product obtained (isolated yield, %)	
		CH_3OH	$PhCH_2CH_2CO_2CH_3$	(95)
		C_2H_5SH	$PhCH_2CH_2COSPh$	(92)
		$PhNH_2$	$PhCH_2CH_2CONHPh$	(93)
		PhOH		(88)
		C_2H_5SH		(81)
		PhOH		(75)
		CH_3OH		(91)
		C_2H_5SH		

---

[a]. For experimental details, see reference 24. b. After hydrolytic workup.

expected to exist. This was the case for **5**. The isomer obtained by epoxidation of 1, 1, 3-tri-*t*-butylallene was assigned to have the *E*-geometry, assuming peracid approach from the sterically least hindered side, away from the *t*-Bu substituent on the monosubstituted sp^2 carbon.[12, 13] On photolysis, **5** isomerized to a new compound which was assigned as *Z*-allene oxide **21**.[13]



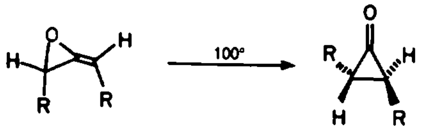
5 **21**

The 13C NMR spectrum of **17** has been examined.[22] It exhibits peaks at 25.9 (CH_3–, q, J_{CH} = 127.3 Hz, 31.9 (*t*-Bu–C–, s), 68.0 (CH–, multiplicity obscured), 70.5 (CH_2–, t, J_{CH} = 167.5 Hz) and 144.3 O–C–, s) ppm, in agreement with the structure.

The IR spectra of all the allene oxides show medium absorption around 1790–1815 cm^{-1} which has been assigned to the stretching of the strained double bond. In addition, a medium to strong band appears at around 930 cm^{-1} which is assigned to the out-of-plane vinyl C–H bending modes.

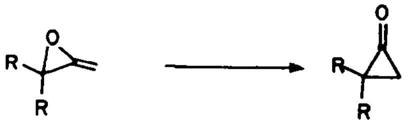
The mass spectra of allene oxides usually show a weak, but discernable molecular-ion peak.

(b) *Thermal isomerization to cyclopropanones.* To date, the most important reaction of allene oxides is the isomerization to the valence tautomeric cyclopropanones. With the well-characterized isolable allene oxides, the experimental results present a conflicting picture. From the work of Camp and Green[9], it was established beyond doubt that 1, 3-di-*t*-butylallene oxide (**6**) isomerized to *trans*-2, 3-di-*t*-butylcyclopropanone (**22**) on heating. The conversion was a relatively slow process, with a half life of 5 hr at 100°, implying an activation barrier of about 40 kcal more or less.



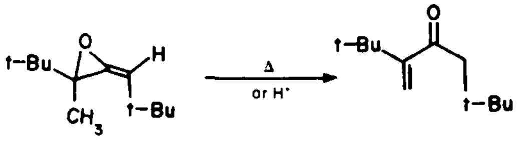
6 (R = *t*-Bu) **22**

On the other hand, 1, 1-di-*t*-butylallene oxide (**23**) isomerized to 2, 2-di-*t*-butylcyclopropanone (**24**) readily at room temperature. The rearrangement process was slower in carbon tetrachloride but the rate was enhanced by the addition of several drops of methanol.[13]



23 (R = *t*-Bu) **24**

For the tri-substituted allene oxides, either 1, 1, 3-tri-*t*-butyl or 1, 3-di-*t*-butyl-1-methylallene oxide (**25**), manifest a reluctance to isomerise to the corresponding cyclopropanones. Pyrolysis of allene oxide **25** at 250° resulted in partial conversion to the ketone **26** with no sign of substituted cyclopropanone. The addition of a trace of acid to **25** also provoked its conversion to 26.[13]

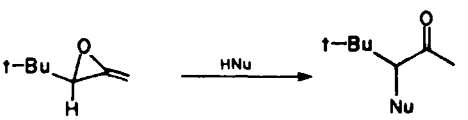


25 **26**

1-*t*-Butylallene oxide (**17**) is stable at 25° for about 1.5 hr but polymerization was observed after 3 hr at room temperature. No evidence of isomerization of **17** to *t*-butylcyclopropanone could be detected either on heating or on treatment with boron trifluoride. In either case, polymer was obtained.[24] The ploymer showed CO absorption in the IR spectrum characteristic of acyclic ketones (*ca* 1710 cm^{-1}). The PMR signals of the ploymer also showed the absence of cyclopropyl protons. It therefore appeared not to have the polycyclopropanone structure.[24]

We shall return to this question of allene oxide-cyclopropanone isomerization later with what we believe to be a unifying explanation.

(c) *Chemical reactions of allene oxides.* 1-*t*-Butylallene oxide (**17**) undergoes reactions with protic nucleophiles (HNu) such as water, thiols and acids to give the addition product ketones **27** in good yields (Scheme 4).[24] In all cases, the reactions are regiospecific in that only products with the nucleophile attached to C-1 have been observed. An S_N2 displacement of the epoxide by the nucleophile at C-1 (eqn 1) can account readily for the products as well as the regiochemistry.

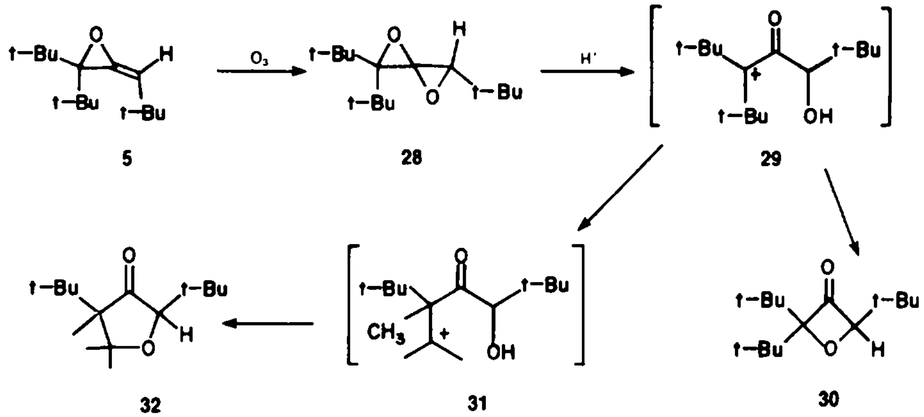


17

27 **a**: Nu = OH
b: Nu = SC_2H_5
c: Nu = CCl_3CO_2—

Scheme 4.

The double bond of allene oxides can be further epoxidized.[13] Thus, reaction of 1, 1, 3-tri-*t*-butylallene oxide (**5**) with ozone gave 2, 5, 5-tri-*t*-butyl-1, 4-diozaspire [2.2] pentane (**28**). The spiro dioxide compound **28** rearranged under acidic conditions to the oxetanone **30** and oxacyclopentanone **32** (Scheme 5). The formation of both **30** and **32** can be adequately explained via the cationic intermediate **29** followed by a Me migration to give **31**.

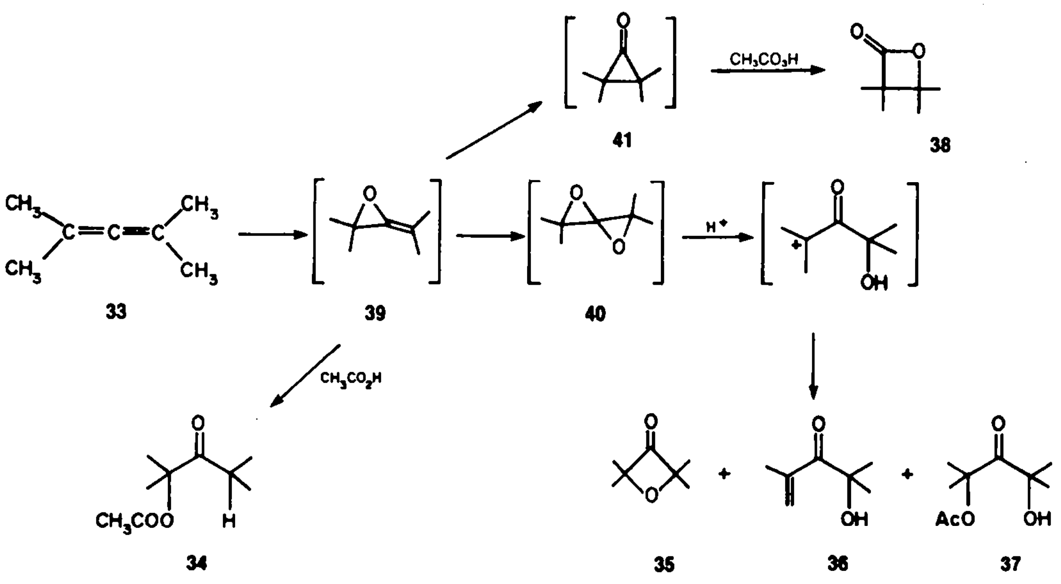


Scheme 5.

GENERATION AND REACTIVITY PATTERN OF TRANSIENT ALLENE OXIDES

The parent allene oxide itself, and other substituted allene oxides with substituent less bulky than a *t*-Bu group have eluded isolation thus far. Their transient existence is inferred from the mode of preparation and the products obtained, by analogy with the isolable allene oxides.

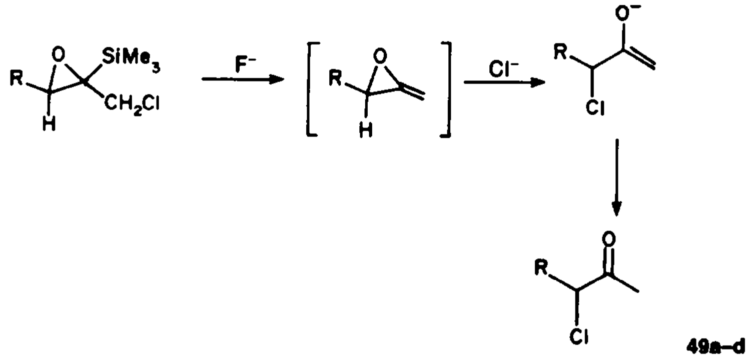
In the oxidation of tetramethylallene (**33**) with peracetic acid, a complex mixture of products was obtained.[13] The products **34**–**38**, were accounted for by the intermediacy of tetramethylallene oxide (**39**) and the reaction of **39** expected under the reaction conditions (Scheme 6).[13] Thus, nucleophilic addition of acetic acid to **39** gave **34**. Further oxidation of allene oxide could yield the spiro dioxide **40**, which under acidic conditions gave rise to compounds **35**, **36** and **37**. Rearrangement of allene oxide **39** to cyclopropanone **41** followed by Baeyer–Villiger oxidation produced the β-lactone **38**. All these reactions have well established precedence from the isolable allene oxides. The products obtained from the oxidation of other allenes can be explained on the same basis (Table 1).



Scheme 6.

It is clear that there are severe limitations to the usefulness of the allene epoxidation route as a general method to generate transient allene oxides. This approach usually results in a complex mixture of products which are inevitably those derived from the acidic and oxidative conditions inherent with the use of peracid.

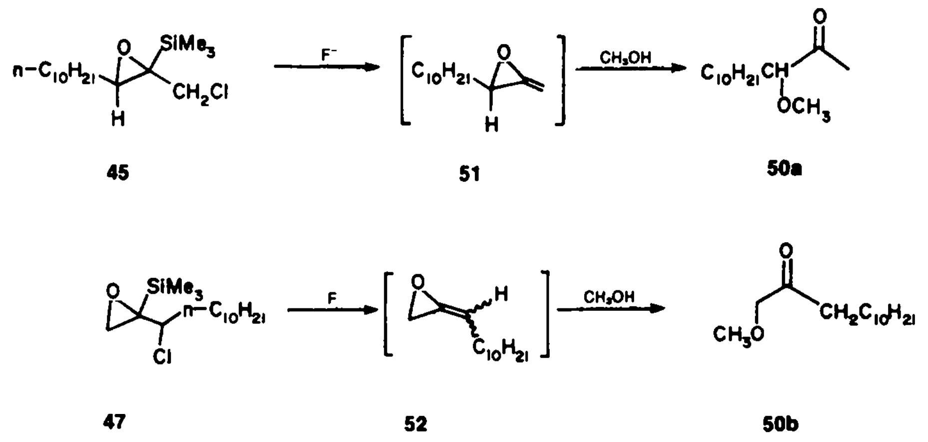
The isolation and characterization 1-*t*-butylallene oxide demonstrates the efficacy of the fluoride ion-promoted β-elimination in the epoxide **16** as an alternative method of generating allene oxides.[24] This method has been applied to the generation of a number of allene oxides where the alkyl group R is sterically less bulky than the *t*-Bu group. The epoxides **42** to **48** were treated with a variety of alkali and tetraalkylammonium fluorides in several polar aprotic solvents (Tables 2 and 3). While the cleavage of the trimethylsilyl-carbon bond occurred readily, in no case was the attempt to isolate the intermediate allene oxide successful. Instead, 3-chloro-2-ketones **49a-d** were obtained in moderate to good yields. These results suggest that the desired β-elimination of trimethylsilyl and chloro functions has occurred, giving the expected allene oxides. Subsequent nucleophilic attack by the chloride ion on the generated allene oxides could then account for the formation of **49a-d** (Scheme 7).



Scheme 7.

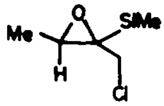
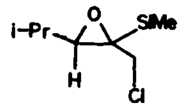
The advantage of this method of generating reactive allene oxides lies in the fact that other reagents can be added to the reaction mixture to trap the allene oxide intermediates. Thus, when the epoxides **42** to **48** are stirred with a slight excess of cesium fluoride in acetonitrile in the presence of threefold excess of a protic nucleophile (HNu), the sole products are the 3-substituted-2-ketones **50** (Table 2).[24] A few brief comments should be made concerning the reagents and solvents. The yields of the products do not vary greatly from one solvent to another (Table 3). In general, the reaction with tetraethylammonium fluoride in dimethyl sulfoxide proceeds at a faster rate. However, cesium fluoride in acetonitrile is more convenient in experimental operation. Potassium fluoride in benzene with 18-crown-6 is also effective.

The reactions of the nucleophiles (HNu) with the intermediate allene oxides are again regiospecific. The regiospecificity is demonstrated by comparing the reactions of the two isomeric epoxides **45** to **47**. Under identical reaction conditions with methanol as the nucleophile, **45** gives only the 3-methoxy-2-ketone **50a**, whereas **47** affords the 1-methoxy-2-ketone **50b** exclusively. The regiospecific nature of the reaction argues convincingly for nucleophilic opening of the epoxide in the isomeric allenes oxides **51** and **52** as the mechanism for this conversion (Scheme 8). Conversely, it also rules out any common species, either the cyclopropanone or the oxyallyl, as the necessary intermediate for these reactions.

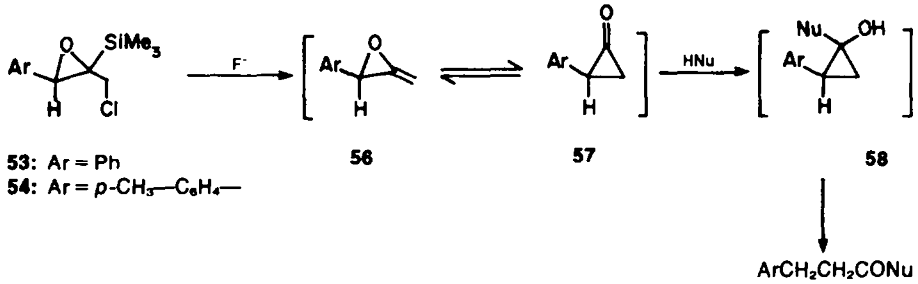


A dramatic change in the course of the reaction occurs when the substituent of the epoxide is an aryl group (**53** and **54**). The epoxides **53** or **54**, on treatment with cesium fluoride in the presence of a protic nucleophile under identical conditions, yield quantitatively a product identified as dihydrocinnamate **55(a-d)**. A

Table 3. Influence of fluoride ion source and solvent on the silicon-method of generating allene oxides[24]

Organosilicon Precursor	Conditions, 25°, 3 days	Nucleophile used	Product (isolated yield)	
	CsF/diglyme	PhOH	$CH_3\underset{\mid\,OPh}{C}H\text{-}COCH_3$	(58)
	CsF/DMSO	PhOH	$CH_3\underset{\mid\,OPH}{C}HCOCH_3$	(61)
	Et_4NF/CH_3CN	PhOH	$CH_3\underset{\mid\,OPh}{C}HCOCH_3$	(75)
	CsF/CH_3CN	PhOH	$CH_3\underset{\mid\,OPh}{C}H\text{-}COCH_3$	(78)
	Et_4NF/glyme	PhOH	$i\text{-}Pr\text{-}\underset{\mid\,OPh}{C}HCOCH_3$	(70)
	Et_4/NF/glyme	C_2H_5SH	$i\text{-}Pr\text{-}\underset{\mid\,SC_2H_5}{C}HCOCH_3$	(74)
	KF/C_6H_6/18-crown-6 (0.5 equiv.)	C_2H_5SH	$i\text{-}Pr\text{-}\underset{\mid\,SC_2H_5}{C}HCOCH_3$	(51)

reasonable pathway for the formation of **55a-d** is through the intermediacy of the allene oxide **56**, which isomerizes to the cyclopropanone **57**, followed by a Favorskii type reaction of the nucleophile with **57** (Scheme 9). The reaction of cyclopropanones with nucleophiles to form the hemiketals of structure **58** (Ar = Ph or p-CH_3-C_6H_4) is well known.[7] The hemiketal can open to give the observed dihydrocinnamate. Indeed, the formation of dihydrocinnamate from phenylcyclopropanone and a nucleophile has been reported previously.[26]



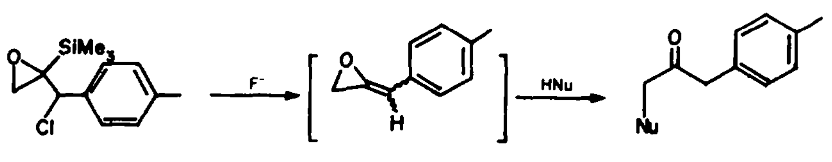
53: Ar = Ph
54: Ar = p-CH_3—C_6H_4—

56 **57** **58**

$ArCH_2CH_2CONu$
55a–d

Scheme 9.

On the other hand, an aryl substitution at C-3 of the epoxide does not lead to the formation of dihydrocinnamate. Reaction of the epoxide **59** with cesium fluoride and a nucleophile yields exclusively the 1-substituted-2-ketone **50c** (Table 2).[24] This is to say, the allene oxide **60** suffers nucleophilic attack faster than its isomerisation to the corresponding cyclopropanone (Scheme 10).



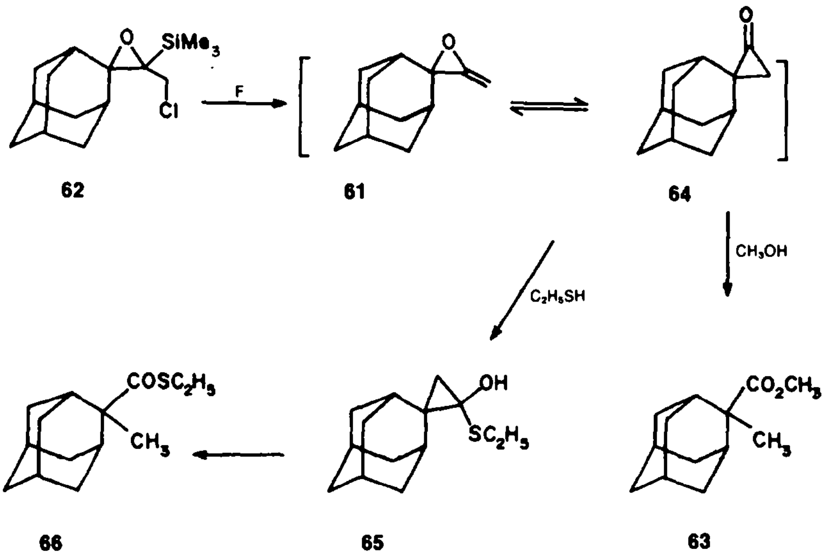
59 **60** **50c**

Scheme 10.

Different again is the fate of 1, 1-disubstituted allene oxides. The compound 3′-methylenespiro [adamantane-2, 2′-oxirane] (**61**) is chosen as the substrate for investigation because the adamantyl skeleton would prevent possible side reaction of double bond formation (e.g. **25**→**26**) or c–c bond migration (e.g. **29**→**32**). When the epoxide **62** is treated with fluoride ion in the presence of methanol, the methyl ester **63** is obtained as the exclusive product in quantitative yield. A reasonable interpretation for the formation of the ester **63** is that the allene oxide **61**, once generated, undergoes a fast isomerization to the cyclopropanone **64**, which on reaction with methanol gives the ester **63** (Scheme 11). Definite proof of the participation of cyclopropanone is obtained when the reaction of **62** with fluoride ion is carried out in the presence of ethanethiol. The hemithioketal **65** is isolated in reasonable purity in 65% yield. On standing at room temperature **65** slowly rearranges to the thiol ester **66**. The rearrangement process is accelerated by heating above 50°.[24]

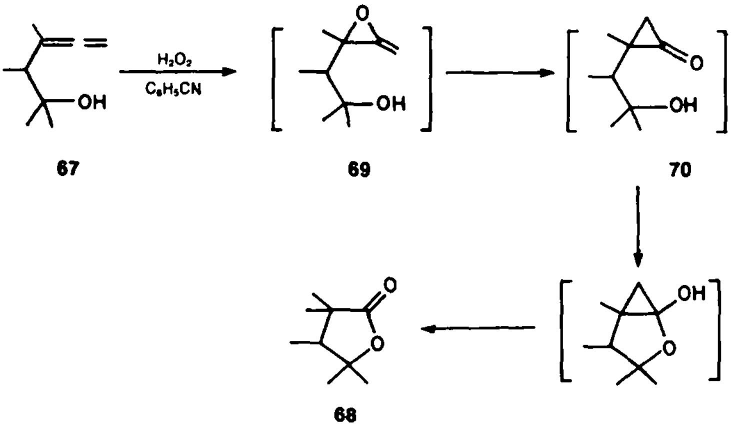
These results, together with the observed isolation of 2, 2-di-*t*-butylcyclopropanone (**24**) from the peracid oxidation of 1, 1-di-*t*-butylallene,[13] suggest that 1, 1-dialkyl substituted allene oxides rearrange with great facility to the corresponding cyclopropanones, even under non-acidic conditions.

Consistent with this conclusion is the epoxidation of the hydroxyallene **67** from which the lactone **68** is isolated as the product.[27] The allene oxide **69** can isomerize rapidly to cyclopropanone **70**. Internal hemiketal formation followed by a Favorskii type reaction gives the lactone as the product (Scheme 12).



Scheme 11.

It appears, therefore, that the nature of the substituent at C-1 of allene oxide has a decisive effect on its fate. When the substituent is either an alkyl group or a hydrogen, the allene oxide suffers nucleophilic attack. When the substituent is sufficiently bulky, as in 1-*t*-butylallene oxide (**17**) or 1, 3-di-*t*-butylallene oxide (**6**), the nucleophilic attack is slow enough so that its isolation is possible. When the substituent at



Scheme 12.

C-1 is an aryl group, the allene oxide isomerizes first to a cyclopropanone before nucleophilic attack. Finally, when C-1 is disubstituted, as in **61** or **23**, the allene oxide also isomerises relatively quickly to the corresponding cyclopropanone.

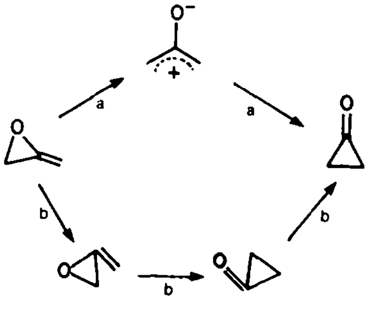
MECHANISM OF THE ALLENE OXIDE-CYCLOPROPANONE ISOMERISATION PROCESS

We can now attempt to rationalize the observation concerning the allene oxide-cyclopropanone isomerization process. There are two aspects to the tautomerization problem indicated by Scheme 1: one is the relative stability of these structures and the other is the mechanism of the isomerization process.

Several quantum mechanical computations[1-6] on the energies of allene oxide, cyclopropanone and the zwitterionic oxyallyl species have appeared in the past decade or so. The computed results differ widely, but they do generally agree (except those of the extended Huckel method[1]) that oxyallyl is the highest-energy form, and cyclopropanone, the lowest-energy species (Table 4). Recently, Liberles *et al.*[3,4] have carried out several MINDO and INDO calculations on substituted cyclopropanones and oxyallyls. Both methods indicate that the energy differences between these species are quite dependent on the nature of the substituents.

Experimentally, there is no doubt from various spectroscopic studies[9] that cyclopropanone has the closed structure indicated by **2**. The isolation of 1-*t*-butyl, 1, 3-di-*t*-butyl, and 1, 1, 3-tri-*t*-butylallene oxides suggests that **1** is also a viable species. Most of the theoretical calculations (excepting EHM[1]) are then consonant with the experimental facts in predicting the oxyallyl structure (**3**) being the highest-energy form among the valence tautomeric triad (Scheme 1).

There is the further question concerning the mechanism of the allene oxide-cyclopropanone isomerization process. The crux of the question is whether oxyallyl (**3**) is involved as an intermediate in the isomerization or not. Most of the calculations[2-6] suggest that the high energy content of **3** does not justify its participation as an intermediate or transition state in the reactions of allene oxide or cyclopropanone. The latest CNDO/2 computations[6] which map the energy surface for the allene oxide-oxyallyl-cyclopropanone system indicate that the allene oxide-cyclopropanone isomerization process involving an oxyallyl intermediate or transition state is energetically very unlikely (Scheme 13, path a). Instead, a novel pathway involving bending of the molecule has been suggested (Scheme 13, path b). The argument for this hypothesis is that bending of molecule requires less energy than bond stretching, and even though the oxyallyl form may be resonance-stabilized, the stabilization energy gained is insufficient to compensate for the destabilization due to bond breakage.[6]



Scheme 13.

Such a hypothesis is, however, not consistent with experimental evidence. The observation that the substituent at C-1 of an allene oxide has a decisive effect on its rate of isomerization to a cyclopropanone does not appear to be compatible with a mechanism based solely on the bending of the

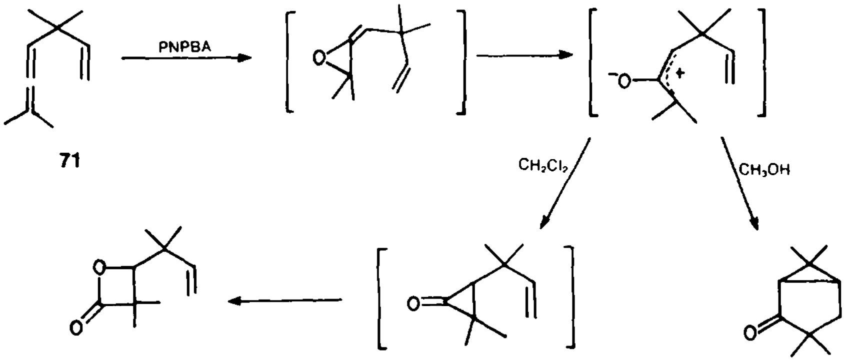
Table 4. The calculated energies of allene oxide, oxyallyl and cyclopropanone (kcal/mole)

Method	Allene oxide	Oxyallyl	Cyclopropanone	Reference
Extended Huckel method	−2	−23	0	1
INDO	6	232	0	3,4,5
MINDO/2	—	78	0	2
ab initio SCF	21	83	0	3
CNDO/2	~0	~240	0	6

molecule as outlined by path b in Scheme 13. A reasonable interpretation of the substituent effect is that, in the allene oxide-cyclopropanone isomerization process, the rate-determining step must involve rupture of C-1 oxygen bond with considerable charge developing at C-1. An oxyallyl intermediate, as outlined by path a, (Scheme 13), would be in agreement with such a substituent effect.

An obligatory oxyallyl intermediate can explain satisfactorily the reactivity pattern observed for all allene oxides thus far. For allene oxide itself, or monoalkyl-substituted ones, the kinetic barrier to the isomerization is relatively high; the allene oxides suffer nucleophilic attack or polymerization more readily. If the substituent is bulky, so that the bimolecular nucleophilic substitution reaction is slowed down, as in the case of 1-*t*-butyl or 1, 3-di-*t*-butyl, the allene oxides can be isolated. For 1, 3-di-*t*-butylallene oxide (**6**), reaction with external reagent is so slow that isomerization to 2, 3-di-*t*-butylcyclopropanone can be observed upon heating. This establishes the cyclopropanone form to be more stable than the allene oxide for this case. For aryl-substituted or disubstituted allene oxides, the rate of isomerization to cyclopropanone is faster than the attack of nucleophile, and they undergo reactions characteristic of the cyclopropanones. Finally, 1, 1, 3-tri-*t*-butylallene oxide most likely owes its stability to a steric factor as originally suggested.[12]

An obligatory oxyallyl intermediate also explains the rather substantial solvent effect on the rate of isomerization of 1, 1-di-*t*-butylallene oxide (**23**) to 2, 2-di-*t*-butylcyclopropanone (**24**). A similar solvent effect has also been observed in the epoxidation of the vinylallene **71**. The product distribution depends dramatically on the solvent used for the reaction: An oxyallyl intermediate has been invoked to account for this observation (Scheme 14).[27b]



Scheme 14.

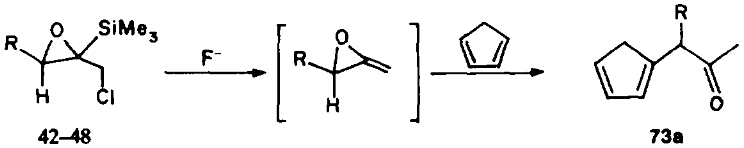
The discrepancy between experimental conclusion and theoretical calculation cast some doubts on the validity of using CNDO/2 method for mechanistic prediction of small-ring compounds. In a recent comparison of various molecular orbital computational methods, it is pointed out that CNDO/2 method increases computational speed often at the sacrifice of accuracy.[28, 29] This is then one of those situations. It is also clear that experimental verification must remain the final arbiter of theoretical calculations.

SYNTHETIC POTENTIAL OF ALLENE OXIDES

Allene oxides, being extremely reactive molecules, have considerable potential as intermediates in synthesis. Particularly useful is the possibility that allene oxide can react both with carbon nucleophiles and carbon electrophiles (eqn 1). The development of the organosilicon method of generating allene oxides (eqn 6) allows some of these potential reactions to be examined.

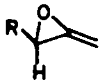
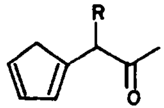
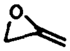
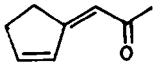
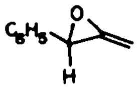
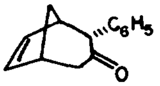
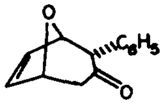
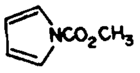
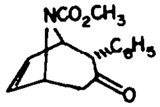
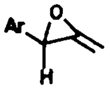
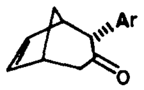
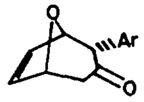
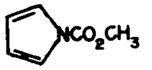
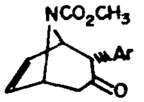
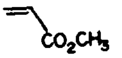
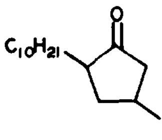
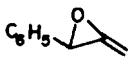
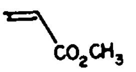
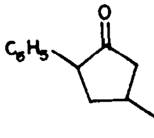
Reaction of allene oxides with cyclopentadiene and related heterocyclopentadienes

Alkyl-substituted allene oxides (**42–48**), when generated the presence of cyclopentadiene, afford the substitution products **72a-d** (Scheme 15) in moderate yields (Table 5).[30] With the parent allene oxide,

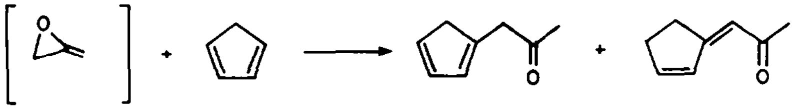


Scheme 15.

Table 5. Reactions of allene oxides generated by the silicon method with alkenes[30, 31]

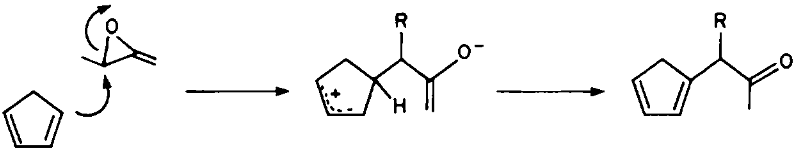
Allene oxide generated	Alkene used	Product (isolated yield %)
 R = Me R = i-Pr R = n-$C_{10}H_{21}$ R = cyclohexyl		 (30) (48) (46) (43)
		 (24)
		 (66)
		 (65)
		 (49)
 Ar = p-CH_3—C_6H_4—		 (72)
		 (68)
		 (47)
		 (27)
		 (15)

reaction with cyclopentadiene under identical conditions affords 73a and 73b.



73a 73b

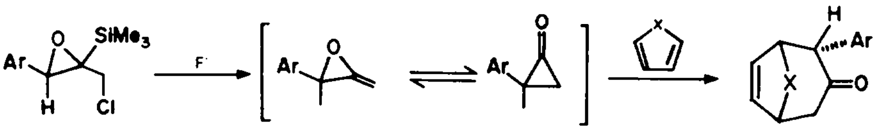
On the basis of the electrophilic character of allene oxide, a mechanism involving an initial nucleophilic attack on the allene oxide by cyclopentadiene can be proposed. This results in the formation of a zwitterion of structure **74** as depicted in Scheme 16. Subsequent intramolecular proton transfer could lead eventually to **72**. When R is hydrogen, rearrangement to the more conjugated system **73b** can occur under the reaction conditions. The proposed mechanism (Scheme 16) is consistent with the regiospecific nature of the reaction; in all cases, α-substituted ketones are obtained.



74

Scheme 16.

No reactions are observed between the alkyl-substituted allene oxides and furan or N-carbomethoxypyrrole; only 3-chloro-2-ketone is isolated from the reaction mixture in each case (Scheme 7). On the other hand, generation of aryl-substituted allene oxides under identical conditions in the presence of cyclopentadiene give exclusively the cycloadduct **75**. The formation of **75** is in agreement with a prior rearrangement of the aryl-substituted allene oxides to the cyclopropanones (Scheme 17).[21, 30]



Scheme 17.

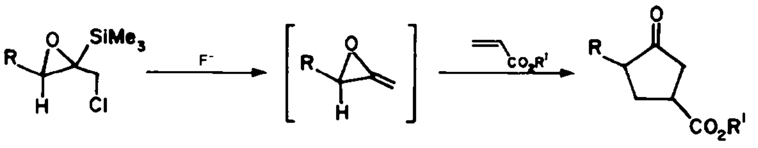
75 X = CH_2, O or NCO_2CH_3

Cycloaddition of cyclopropanones with conjugated dienes has been widely studied.[7] It represents a reaction of growing synthetic importance because it provides a facile entry to 7-membered rings.

Similar cycloadducts (X = O or $N-\overset{O}{\overset{\|}{C}}-OMe$) were formed when the aryl-substituted allene oxides are generated in the presence of furan or N-carbomethoxypyrrole (Table 5). This reaction can therefore be used for the synthesis of the tropane skeleton as well as the 8-oxabicyclo [3.2.1] octyl system.

Reactions of allene oxide with acrylic esters[31]

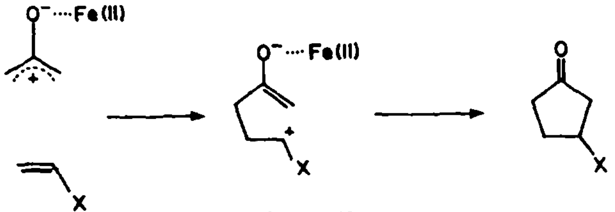
When allene oxides were generated by the silicon method in the presence of styrene, vinyl ethers or vinyl acetate, only α-chloroketones **49** (Scheme 7) resulted from the attack of the chloride ion on the allene oxide are obtained. However, preliminary investigation indicates that allene oxides do cycloadd to alkyl acrylates. Thus, when the epoxides **45** and **53** were treated with fluoride ion in the presence of excess alkyl acrylate, cyclopentanones have been observed. The cycloaddition is regiospecific, affording in each case a 2, 4-disubstituted cyclopentanone derivatives **76(a-b)** in moderate yields (Scheme 18).



Scheme 18.

76a, b

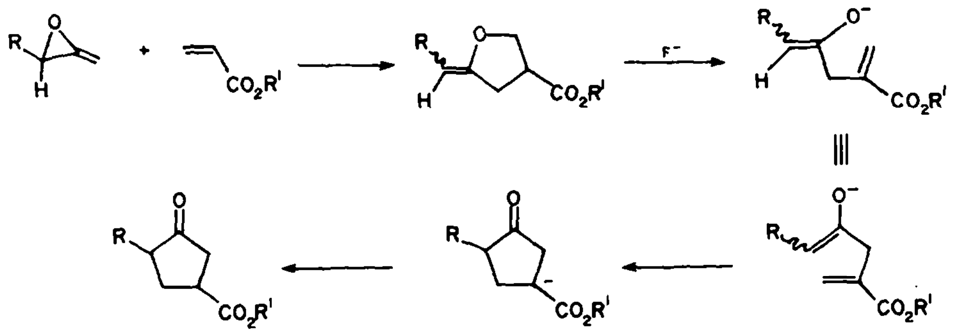
The regiospecific formation of the 2, 4-disubstituted cyclopentanone **76** poses an interesting mechanistic question. Recently, cycloaddition of reactive oxyallyl-Fe(II) intermediates with styrene[32] and enamines[33] was reported and the cycloaddition was explained in terms of a stepwise mechanism involving a zwitterionic intermediate (Scheme 19). Such a mechanism can be ruled out for the reaction of reactive allene oxides with acrylates in view of the lack of cycloadduct with the electron-rich enamines



Scheme 19.

or vinyl ethers. An alternative mechanism, involving nucleophilic attack of the olefin on C-1 of the generated allene oxide, would lead to the unobserved 2, 3-disubstituted regioisomer. The same regioisomer would be expected if the attack is initiated by C-3 of the allene oxide on the electron deficient olefins.

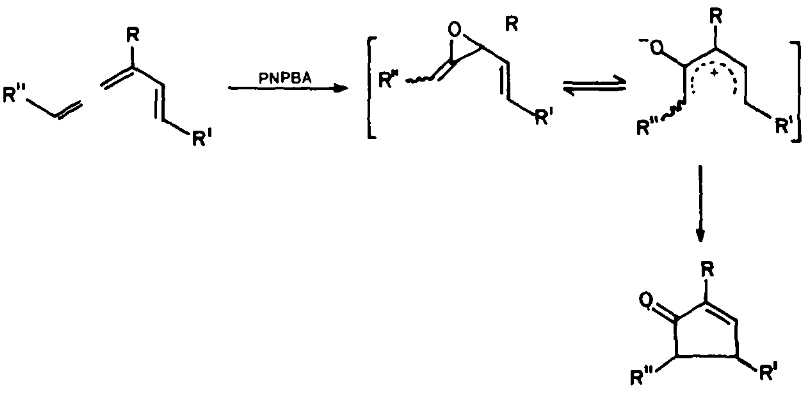
Consistent with the knowledge we gained from our studies on the properties of allene oxides, the following mechanism may be proposed. It involves an initial cycloadduct formation of the acrylate with allene oxide by breaking of the C_2–O bond (Scheme 20). Such a cycloaddition has been previously suggested (Scheme 2)[19] and is a symmetry allowed $s4\pi + s2\pi$ reaction. An oxyallyl intermediate may intercede in the first step.



Scheme 20.

Intramolecular trapping of allene oxides

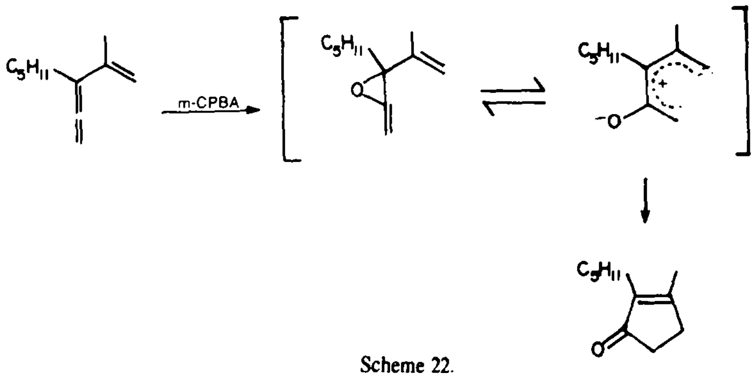
A useful application of allene oxides in synthesis is to trap the reactive allene oxide intramolecularly by another functional group. Using such an approach, 1, 2-oxaphospholanes,[44] γ-lactones[27] (Scheme 12), bicyclo [3.1.0.] hexane-2-ones[27] (Scheme 14) and cyclopentenones[27] (Scheme 21) can be prepared.



Scheme 21.

The mechanism which is proposed for the formation of cyclopentanones is particularly intriguing and illustrate the potential of allene oxides as synthetic intermediates. An interesting synthesis of dihydrojasmone based on the intramolecular trapping of allene oxide intermediate has recently been reported (Scheme 22).[46,49]

Judging from the above reactions, it is clear that allene oxides can be useful as a 3-carbon unit in the construction of carbocyclic rings. In view of the reactivity of allene oxides, other interesting and useful

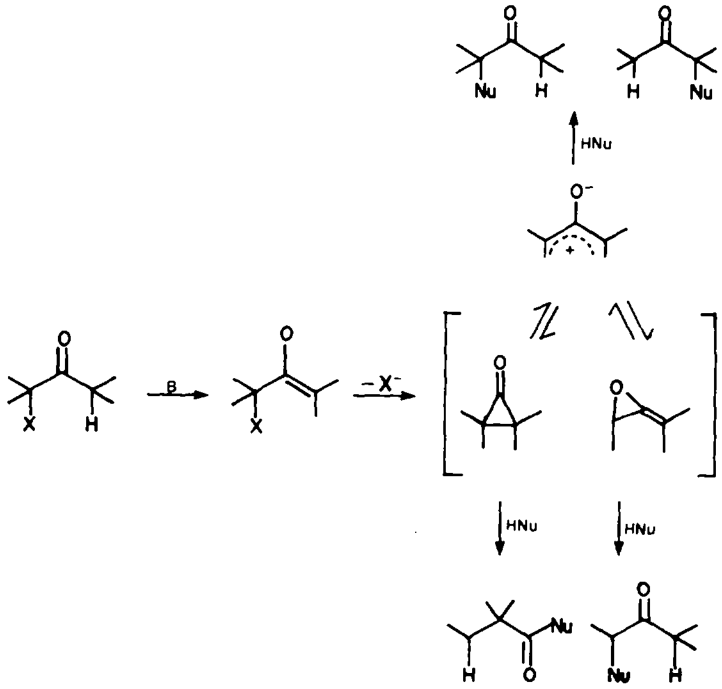


Scheme 22.

reactions will undoubtedly be found. It will be a fertile area of research especially if new methodology to generate the reactive allene oxides can be developed.

ALLENE OXIDE AND THE MECHANISM OF FAVORSKII REARRANGEMENT

The formation of cyclopropanone intermediates in certain Favorskii rearrangements has been elegantly demonstrated by the labelling experiment of Loftfield[34] and the stereochemical study of Stork and Borowitz.[35] Intermediates other than cyclopropanone must, however, be involved in order to account fully for the products of α-halo ketones under basic conditions. Oxyallyl[36] and allene oxide[37,38] are some of the obvious candidates. Both have previously been proposed even though allene oxide was considered merely as a delocalised structure of cyclopropanone. Recent efforts to generate stable oxyallyl have not yet met with success.[39,40] The chemistry of allene oxides outlined in this review suggests the following points to be relevant to the mechanism of Favorskii rearrangement: (1) allene oxide has sufficient stability to be considered as an independent species in its own right, (2) Favorskii type products can indeed be obtained from allene oxides, e.g. **56**→**55** or **61**→**63** and (3) reactions of allene oxides with protic nucleophiles give α-substituted ketones (Scheme 4). The same products often observed in the reaction of α-halo ketones under Favorskii conditions. A generalised mechanism for the Favorskii rearrangement can therefore be proposed (Scheme 23).[41] The relative distribution of various products depends then on the structure of the substrate, the polarity of the solvent and the nucleophile, involving an interplay between the three valence tautomers, cyclopropanone, oxyallyl, and allene oxide.



Scheme 23.

Acknowledgements—We are grateful to Drs. M.P. Li and W. Mychajlowskij for the initial work on the silicon route to allene oxide. We thank Prof. D.N. Harpp and J.P. Snyder for helpful discussion.

REFERENCES

[1] R. Hoffman, *J. Am. Chem. Soc.* **90**, 1476 (1968).

[2] N. Bodor, M. J. S. Dewar, A. Harget and E. Haselback, *Ibid.* **92**, 3854 (1970).

[3] A. Liberles, A. Greenberg and A. Zesk, *Ibid.*, **94**, 8685 (1972).

[4] A. Liberles, S. Kang and A. Greenberg, *J. Org. Chem.* **38**, 1922 (1973).

[5] J. F. Olsen, S. Kang and L. Burnelle, *J. Mol. Struct.* **9**, 305 (1971).

[6] M. E. Zandler, C. E. Choc and K. K. Johnson, *J. Am. Chem. Soc.* **96**, 3317 (1976).

[7] For a review, see N. J. Turro, *Acc. Chem. Res.* **2**, 25 (1969).

[8] See R. Noyori, Y. Hayakawa, H. Takaya, S. Murai, R. Kobayashi and N. Sonoda, *J. Am. Chem. Soc.* **100**, 1759 (1978) and ref. cited.

[9] R. O. Camp and F. D. Greene, *Ibid.* **90**, 7349 (1968). See also F. D. Greene, R. L. Camp, L. Kim, J. Pazos, D. B. Sclove and C. J. Wilberson, *Proc. Internat. Congr. Pure Appl. Chem.* **2**, 325 (1971).

[10] J. J. Havel, *J. Am. Chem. Soc.* **96**, 530 (1974).

[11] J. K. Crandall and W. W. Conover, *J. Chem. Soc.* Chem. Comm. 340 (1973).

[12] J. K. Crandall and W. H. Machleder, *J. Heterocyclic Chem.* **6**, 777 (1969).

[13] J. K. Crandall, W. W. Conover, J. B. Komin and W. H. Machleder, *J. Org. Chem.* **39**, 1723 (1974).

[14] J. K. Crandall and W. H. Machleder, *Tetrahedron Letters* 6037 (1966).

[15] J. K. Crandall, W. H. Machleder and M. J. Thomas, *J. Am. Chem. Soc.* **90**, 7346 (1968).

[16] J. K. Crandall, W. H. Machleder and S. A. Sojka, *J. Org. Chem.* **38**, 1149 (1973).

[17] The preparation of tetramethylallene oxide has been claimed and later retracted: H. M. R. Hoffman and R. H. Smithers, *Angew. Chem. Int. Ed. Engl.* **9**, 71 (1970); H. M. R. Hoffman, K. E. Clemens, E. A. Schmidt and R. H. Smithers, *J. Am. Chem. Soc.* **94**, 3201 (1972).

[18] W. Kirmse, *Chem. Ber.* **93**, 2357 (1960).

[19] Y. N. Kuo and M. J. Nye, *Can. J. Chem.* **51**, 1995 (1973).

[20] T. H. Chan, *Acc. Chem. Res.* **10**, 442 (1977).

[21] T. H. Chan, M. P. Li, W. Mychajlowskij and D. N. Harpp, *Tetrahedron Letters* 3511 (1974).

[22] T. H. Chan, B. S. Ong and W. Mychajlowskij, *Ibid.* 3253 (1976).

[23] T. H. Chan, W. Mychajlowskij, B. S. Ong and D. N. Harpp, *J. Org. Chem.* **43**, 1526 (1978).

[24] T. H. Chan and B. S. Ong, *Ibid.* **43**, 2994 (1978).

[25] B. S. Ong and T. H. Chan, *Tetrahedron Letters* 3257 (1976).

[26] S. E. Schaafsma, H. Steinberg and T. J. DeBoer, *Rec. Tra. Chim. Pays-Bas* **85**, 1170 (1966).

[27] [a] M. Bertrand, J. P. Duclere, G. Gil, J. Grimaldi and P. Sylvestre-Panthet, *Tetrahedron Letters* 3305 (1976); [b] J. Grimaldi, M. Malacria and M. Bertrand, *Ibid.* 275 (1974); *Bull Soc. Chim. Fr.* 1925 (1975); [c] J. Grimaldi and M. Bertrand, *Tetrahedron Letters* 3269 (1969); *Bull Soc. Chem. Fr.* 957 (1971); [d] M. Bertrand, J. P. Dulcere, G. Gill, J. Grimaldi and P. Sylvestre-Panthet, *Tetrahedron Letters* 1507 (1976).

[28] T. A. Halgren, D. A. Kleier, J. H. Hall, L. D. Brown and W. N. Lipscomb, *J. Am. Chem. Soc.* **100**, 6595 (1978).

[29] We have been informed by Prof. J. P. Snyder that calculations using PRDDO method indicate that oxyallyl may have an open shell birdical singlet structure as the ground state. We are grateful to Prof. Snyder for this information prior to the publication of his work.

[30] B. S. Ong and T. H. Chan, *Heterocycles* **7**, 913 (1977).

[31] T. H. Chan and B. S. Ong, to be published.

[32] Y. Hayakawa, K. Yokoyama and R. Noyori, *J. Am. Chem. Soc.* **100**, 1791 (1978).

[33] Y. Hayakawa, K. Yokoyama and R. Noyori, *Ibid.* **100**, 1799 (1978).

[34] R. B. Loftfield, *Ibid.* **73**, 4707 (1951).

[35] G. Stork and I. J. Borowitz, *Ibid.* **82**, 4307 (1960).

[36] J. G. Aston and J. D. Newkirk, *Ibid.* **73**, 3900 (1951).

[37] H. O. House and W. F. Gilmore, *Ibid.* **83**, 3980 (1961).

[38] A. W. Fort, *Ibid.* **84**, 2620, 2625, 4979 (1962).

[39] D. Mitchell, J. H. Eilert and N. L. Bauld, *Tetrahedron Letters* 2865 (1979).

[40] A. S. Kende, R. Greenhouse and J. A. Hill, *Ibid.* 2867 (1979).

[41] For consideration of other mechanisms, see A. S. Kende, *Organic Reactions* **11**, 261 (1960).

[42] T. Sasaki, S. Eguchi and Y. Hirako, *Tetrahedron Letters* 541 (1976).

[43] A. Oku, K. Shimada and F. Mashio, *Bull. Chem. Soc. Japan* **46**, 275 (1973).

[44] R. S. Macomber, *J. Org. Chem.* **43**, 1832 (1978).

[45] T. Greibokk and L. Skattebøl, *Acta Chem. Scand.* **27**, 1421 (1973).

[46] M. L. Ronmestant, M. Malacria and J. Goré, *Synthesis* 755 (1976).

[47] M. Biollaz, W. Haefliger, E. Vedarde, P. Crabbe and J. H. Fried, *J. Chem. Soc. Chem. Comm.* 1322 (1971).

[48] P. Kolsaker and S. Børresen, *Acta Chem. Scand.* **33B**, 133 (1979).

[49] M. Malacria and J. Goré, *J. Org. Chem.* **44**, 885 (1979).