PART I
ACID-CATALYZED REARRANGEMENTS OF CYCLOHEXADIENONE EPOXIDES

PART II
PHOTOCHEMISTRY OF CYCLOHEXADIENONE EPOXIDES

PART III
MISCELLANEOUS

Dissertation for the Degree of Ph. D.
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ENG MU SHIH
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This is to certify that the

thesis entitled

Part I. Acid-Catalyzed Rearrangements of
Cyclohexadienone epoxides
Part II. Photochemistry of Cyclohexadienone Epoxides
Part III. Miscellaneous

presented by

Eng Mu Shih

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of the requirements for

Ph. D. degree in Chemistry

Harold Hart

Major professor

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ABSTRACT

PART I

ACID-CATALYZED REARRANGEMENTS OF CYCLOHEXADIENONE EPOXIDES

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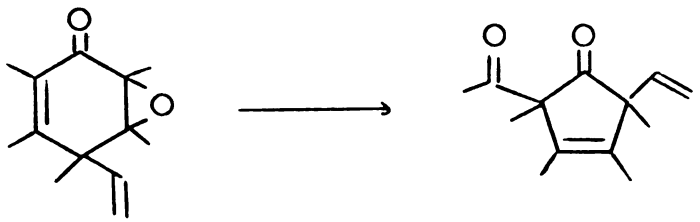
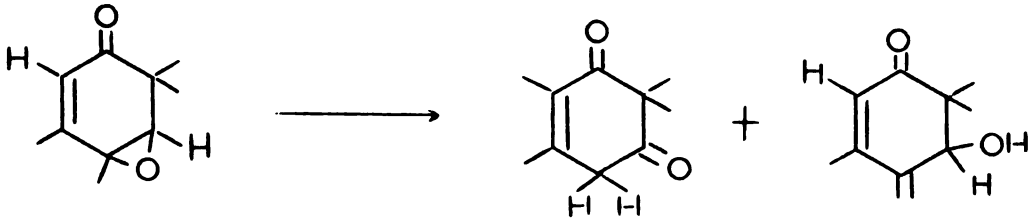
The acid-catalyzed rearrangements of cyclohexadienone epoxides, 38 and 39, are described in Part I of this thesis. The ∝,β-epoxy ketones 38c and 38t (cis and trans-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenones) rearrange in acid exclusively by vinyl migration, in preference to the acetyl and methyl migration observed previously in analogous compounds with a methyl group in place of the 4-vinyl substituent. When the vinyl group and epoxide ring were trans (38t), rearrangement was much faster than with the cis isomer (38c), owing to homoallylic participation during the epoxide ring opening. However the rearrangement

products in both instances were identical, i.e., a 1:4 mixture of cis- and trans-2-acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenones (46c and 46t).

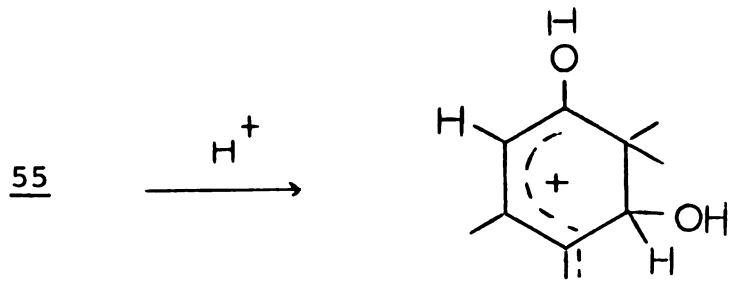


38 c,t 46 c,t

Rearrangement of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone (39) in trifluoroacetic acid (TFA) at room temperature gave 2,3,6,6-tetramethyl-2-cyclohexen-1,5-dione (54, 53%) and 4-methylene-5-hydroxy-3,6,6-trimethyl-2-cyclohexenone (55, 47%). In contrast to permethylated compound 33 (4-methylene-5-hydroxy-2,3,5,6,6-pentamethyl-2-cyclohexenone) 55 underwent no further rearrangement on treatment with TFA, and this was attributed to preferential protonation at the carbonyl oxygen to give the highly delocalized cation R instead of at the hydroxyl group.

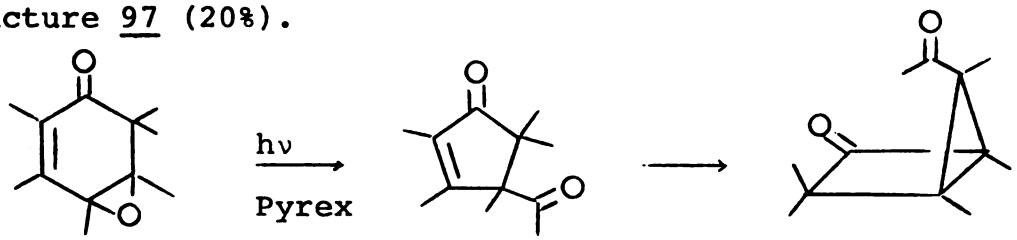


39 54 (53%) 55 (47%)

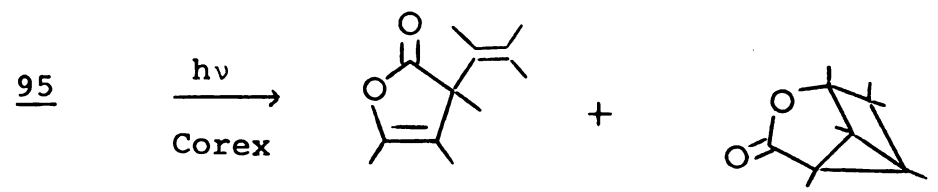


55 R

The photochemistry of cyclohexadienone epoxides, 32 and 39, is described in Part II of this thesis. The UV irradiation of 4,5-epoxy-2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone (32) in ether through a Pyrex filter gave 4-acetyl-2,3,4,5,5-pentamethyl-2-cyclopentenone (36), which rearranged further to bicyclo[2.1.0]pentan-2-one (95). On further irradiation through a Corex filter, compound 95 rearranged to an enol lactone 96 (80%) and a compound which was tentatively assigned structure 97 (20%).



32 36 95



95 96 97

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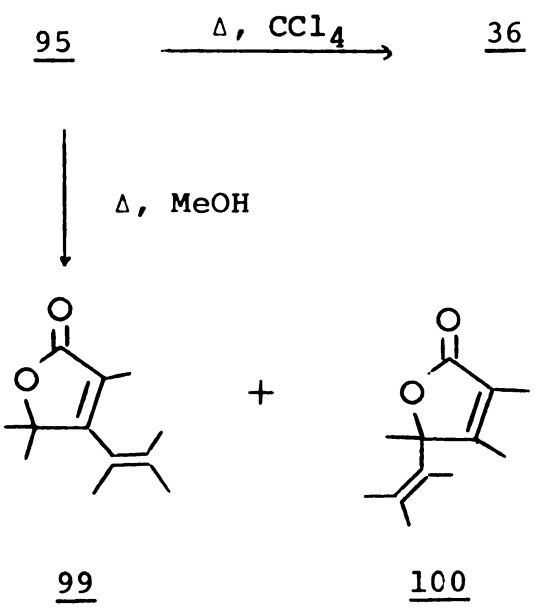
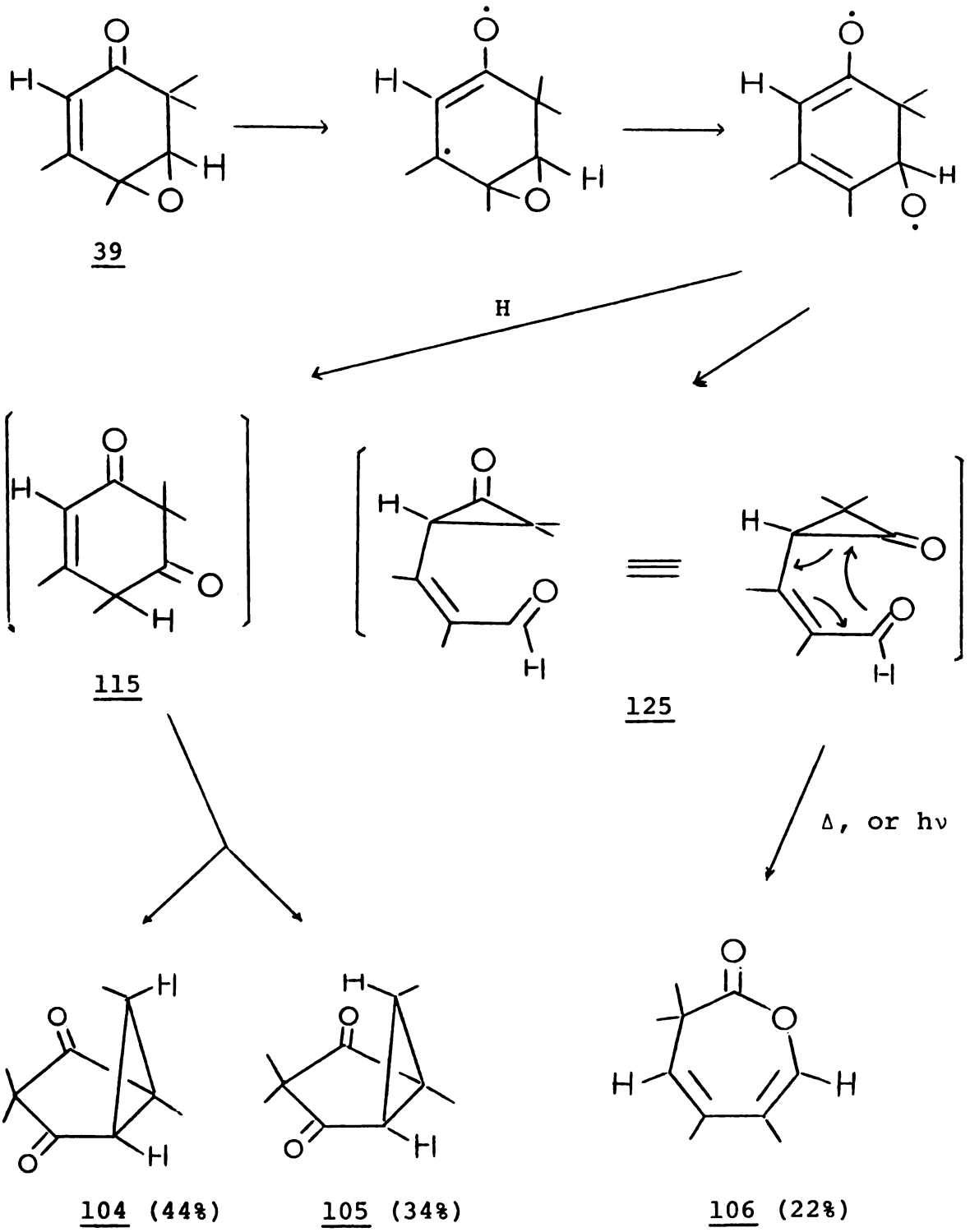
Bicyclopentanone 95 was thermally labile. It reverted slowly to 36 either in the solid state or in a non-polar solvent such as carbon tetrachloride. In methanol, it was converted rapidly to lactones 99 (25%) and 100 (75%). Deuterium-labeling experiments were consistent with the proposed mechanisms for the photorearrangement of 32 and the thermal rearrangement of 95.



Photolysis of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone (39) in ether through Pyrex afforded anti-1,3,3,6-tetramethyl-bicyclo[3.1.0]hexan-2,4-dione (104, 44%), syn-1,3,3,6-tetramethylbicyclo[3.1.0]hexan-2,4-dione (105, 34%) and 4,4,7,7-tetramethyl-2-oxa-cyclohepta-3,5-dien-1-one (106, 22%). Compounds 104 and 105 were shown to originate from the diketone intermediate 115. A new reaction pathway leading to 106 from 39 seems to be operating, via the cyclopropanone intermediate 125. Deuterium-labeling experiments support the proposed mechanism for the photorearrangements of 39.



39

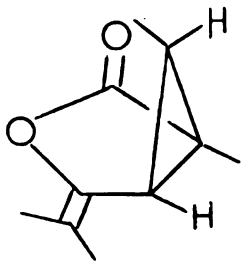
115

125

104 (44%) 105 (34%) 106 (22%)

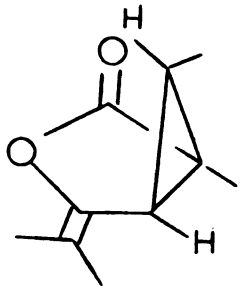
On further irradiation through a Corex filter, 104 rearranged to anti-1,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]-hexan-2-one (107), 105 rearranged to syn-1,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]hexan-2-one (108, 75%) and syn-5,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]-hexan-2-one (109, 25%), 106 gave 2,2,6,7-tetramethyl-4-oxa-bicyclo[3.2.0]hept-6-en-3-one (110).

104 ⟶



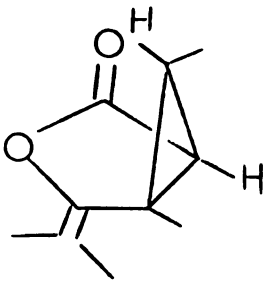
107

105 ⟶



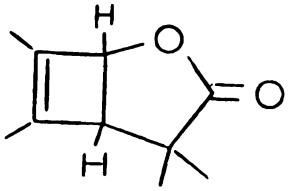
108 (75%)

+



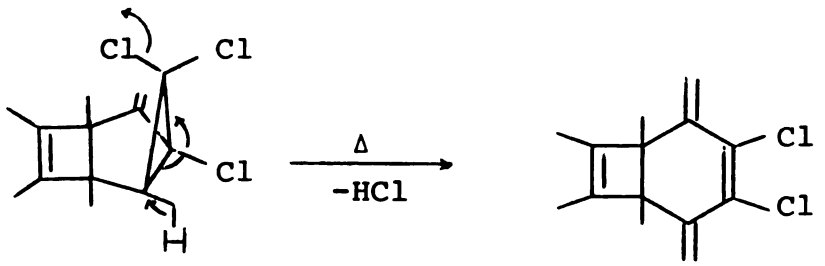
109 (25%)

106 ⟶



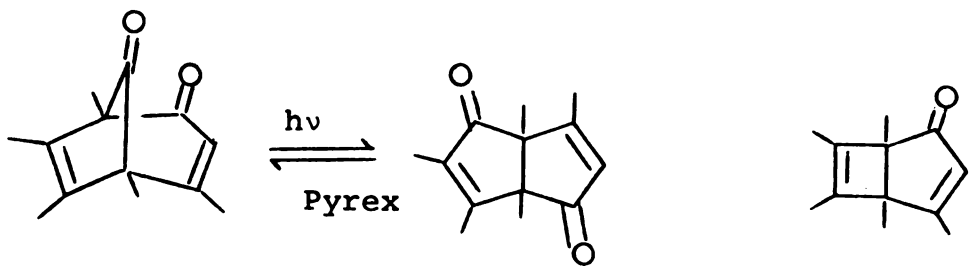
110

Some miscellaneous results are described in Part III of this thesis. The dichlorocarbene adduct of hexamethyldewarbenzene, 134 (3,4,4-trichloro-1,5,6,7,8-pentamethyl-2-methylene-tricyclo[4.2.$0^{3.5}$]oct-7-ene), rearranged to 3,4-dichloro-1,6,7,8-tetramethyl-2,5-dimethylene-bicyclo[4.2.0]-octa-3,7-diene (136) on thermolysis.



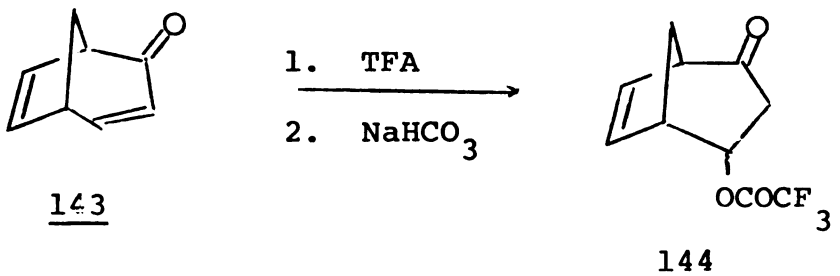
134 136

On irradiation through Pyrex, 1,4,5,6,7-pentamethylbicyclo[3.2.1]octa-3,6-dien-2,8-dione (139) reached a photostationary state with 1,3,4,5,8-pentamethylbicyclo[3.3.0]-octa-3,7-dien-2,6-dione (140). On further irradiation of this equilibrating mixture through Corex, a new photoproduct 141 (1,4,5,6,7-pentamethylbicyclo[3.2.0]hepta-3,6-dien-2-one) was obtained presumably through the decarbonylation of 139.

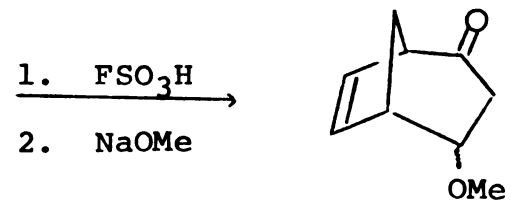


139 (73%) 140 (27%) 141

Treatment of bicyclo[3.2.1]octa-3,6-dien-2-one (143) with trifluoroacetic acid followed by quenching with sodium bicarbonate solution gave 4-trifluoroacetylbicyclo[3.2.1]octa-6-en-2-one (144); treatment of 143 with fluorosulfonic acid followed by quenching with sodium methoxide gave 4-methoxybicyclo[3.2.1]octa-6-en-2-one (145).

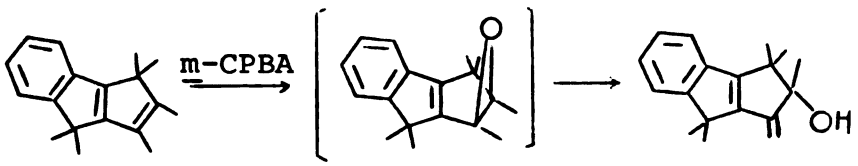


143 144

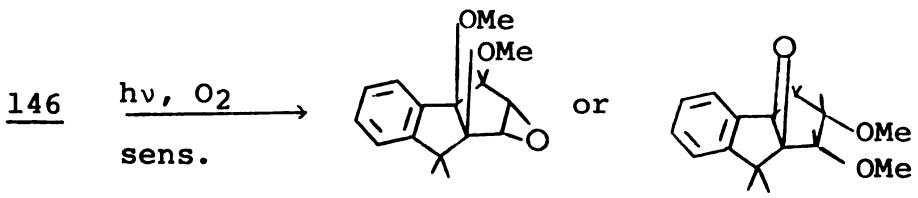


145

Treatment of 1,4-dihydro-1,1,2,3,4,4-hexamethylbenzopentalene (146) with m-chloroperbenzoic acid gave 1,4-dihydro-2-hydroxyl-3-methylene-1,1,2,4,4-pentamethylbenzopentalene (148), presumably through the rearrangement of monoepoxide 147 catalyzed by a trace of acid. Photosensitized oxidation of 146 in methanol led to a methanol adduct, the exact structure of which, represented either as 150a or 150b remained uncertain.

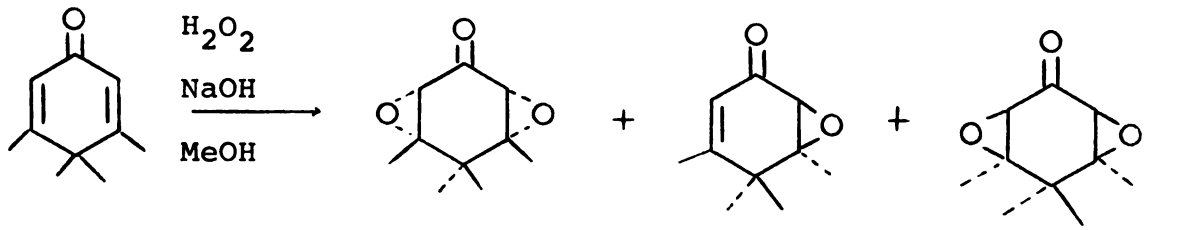


146 147 148



150a 150b

Epoxidation of 3,4,4,5-tetramethyl-2,5-cyclohexadienone (151) with alkali hydrogen peroxide gave monoepoxide 154 (7%) and diepoxides, 153 (5%) and 155 (45%).



151 153 (5%) 154 (7%) 155 (45%)

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MISCELLANEOUS

By

Eng Mu Shih

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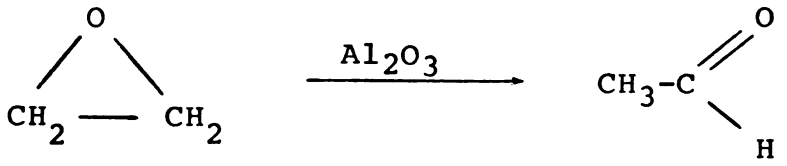
PART I

ACID-CATALYZED REARRANGEMENTS OF CYCLOHEXADIENONE EPOXIDES

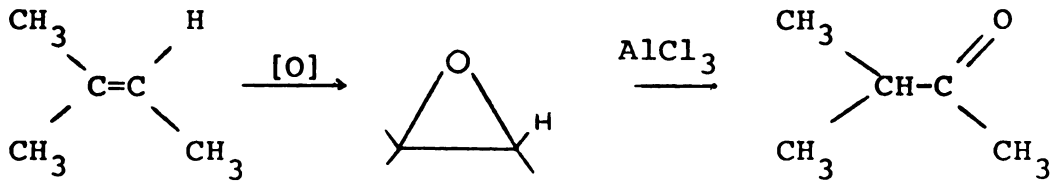
INTRODUCTION

Epoxides can be isomerized to aldehydes, ketones or a mixture of these under acid conditions. Thus etyhlene oxide 1 gives acetaldehyde 2 over aluminum oxide.[1]



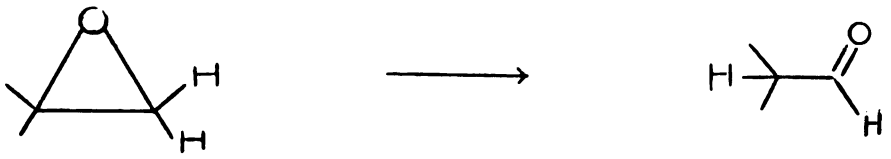
1 2

These acid-catalyzed rearrangements of epoxides are of special interest, since they provide a simple means of converting olefins to carbonyl compounds.[2,3] For example, in the presence of aluminum trichloride, trimethylethylene oxide 4, which can be obtained by epoxidation of trimethylethylene 3, rearranges to methyl isopropyl ketone 5[4]:

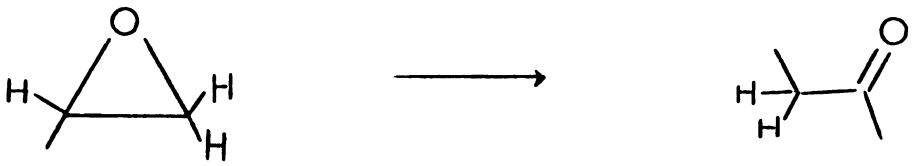


3 4 5

Similarly, isobutylene oxide 6 gives largely isobutyraldehyde 7, and propylene oxide 8 yields propionaldehyde 9.[4]



6 7



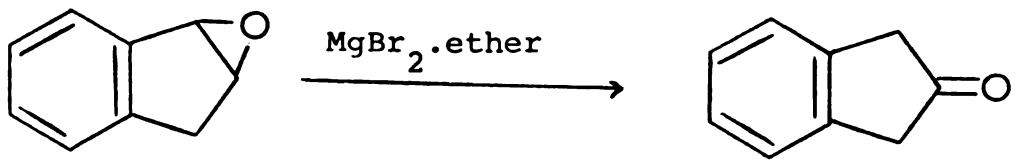
8 9

In general, Lewis acids (i.e., aluminum trichloride, magnesium bromide or boron trifluoride etherate) are used as catalysts, although aqueous mineral acids and non-nucleophilic carboxylic acids such as trifluoroacetic acid may also serve. Rearrangement reactions of this kind become especially useful if one can predict in any particular case what the major product will be. The major product formed from the rearrangement of an epoxide is governed by two main factors: the direction of ring opening, and the relative migratory aptitudes of the different substituents.

The direction of ring opening in acid-catalyzed rearrangements may in general be predicted simply on the basis of the relative ease of ionization of the two carbon-oxygen bonds in question. By analogy with other situations

in organic chemistry, the sequence is expected to be tertiary > secondary > primary for the aliphatic series. The rearrangement of isobutylene oxide 6 to isobutyraldehyde 7 illustrates this rule.

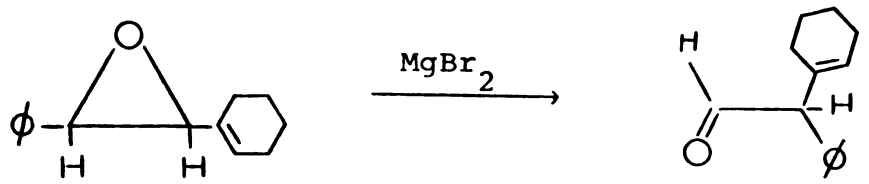
Aryl substituents on epoxides are generally superior to alkyl substituents in enhancing the ease of ionization of the carbon-oxygen bond. The above rule may be generalized to state that, in rearrangements, the carbon-oxygen bond that tends to be broken is the one to the carbon atom substituted to the greatest extent with groups promoting ionization, namely alkyl and aryl. Thus, indene oxide 10 is isomerized to 2-indanone 11 on treatment with magnesium bromide etherate.[5]



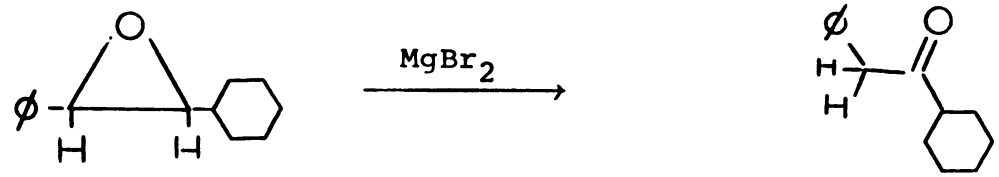
10 11

Vinyl substitution, like phenyl substitution, weakens the adjacent carbon-oxygen bond with respect to ionization, and there are a number of reports of rearrangements of ethylene oxides involving breakage of the bond to a vinyl-substituted rather than a phenyl-substituted carbon atom.[6,7] For example, phenyl cyclohexenyl ethylene oxide 12 is rearranged to phenyl cyclohexenyl acetaldehyde 13[8] in contrast to the cyclohexyl analog 14, which rearranges with

cleavage of the other carbon-oxygen bond to give benzyl cyclohexyl ketone 15.



12 13

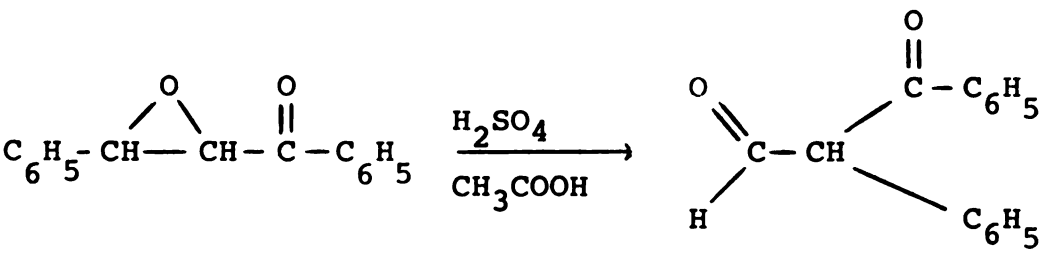


14 15

Once the direction of ring opening has been decided, in epoxide 6, for example, by the preferential formation of a tertiary carbonium ion. There remains a choice between hydrogen migration or alkyl migration. This will normally be decided by the relative migratory aptitudes of the groups, and in general this order is aryl > acyl >H > ethyl > methyl. No rationale for this order of migratory aptitudes has been proposed, since the mechanistic details for this type of rearrangement, which is closely related to the pinacol rearrangement, are not yet clear. Among the few exceptions to this order of migratory aptitudes, are those in which, for steric reasons, hydrogen migrates in preference

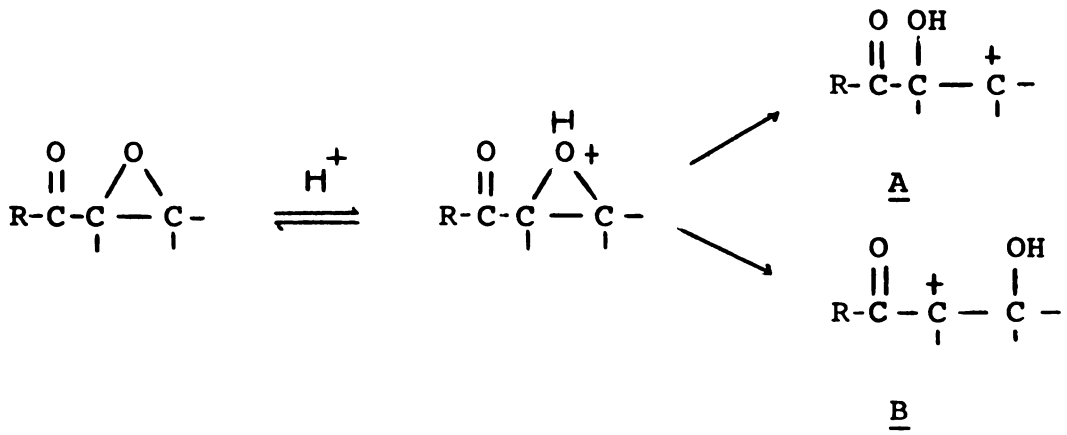
to phenyl.[2]

As with simple epoxides, epoxy ketones also undergo acid-catalyzed ring cleavage with rearrangement, and have served as useful precusors to dicarbonyl compounds. For example, in glacial acetic acid in the presence of sulfuric acid, benzalacetophenone oxide 16 isomerizes to formyl-desoxybenzoin 17.[9]



16 17

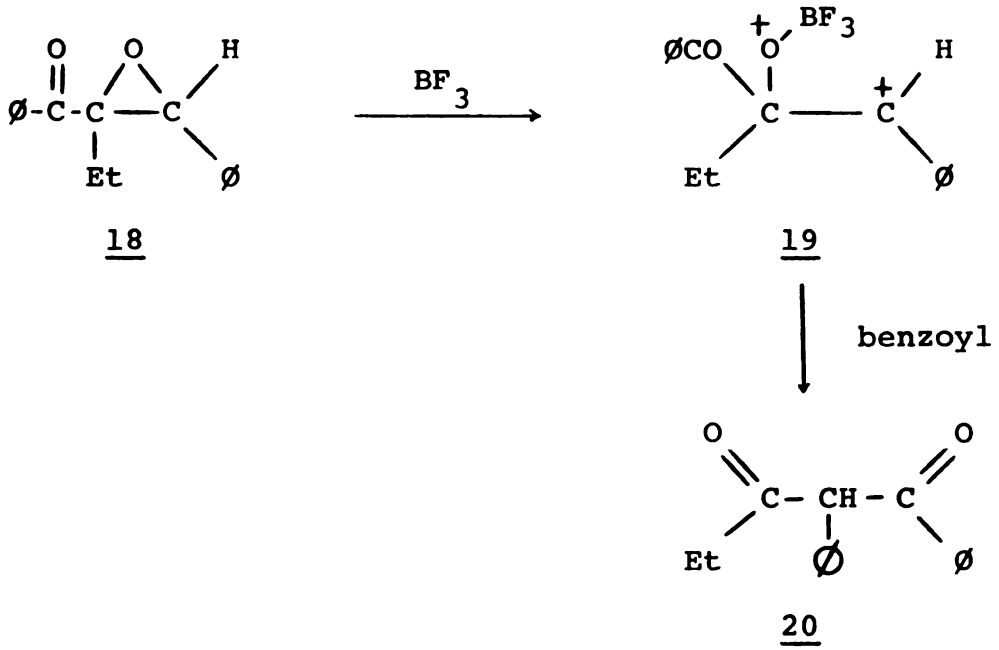
Although the ring opening of ∝,β-epoxyketone under the influence of acids can proceed in two directions, it generally favors the more stable carbonium ion A and the



A

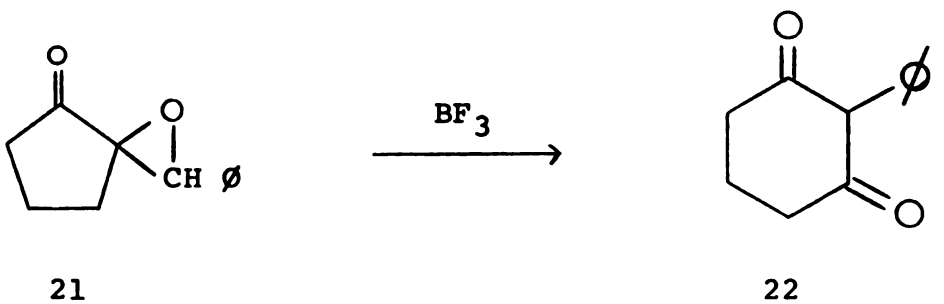
B

observed products depend only on the migratory aptitudes of the groups attached to the epoxide ring. Thus, in the presence of boron trifluoride, α-ethylbenzalacetophenone oxide 18 rearranges, via the intermediate ion 19, to 1,2-diphenyl-1,3-pentanedione 20, the product expected from the preferential benzoyl group migration.[10]

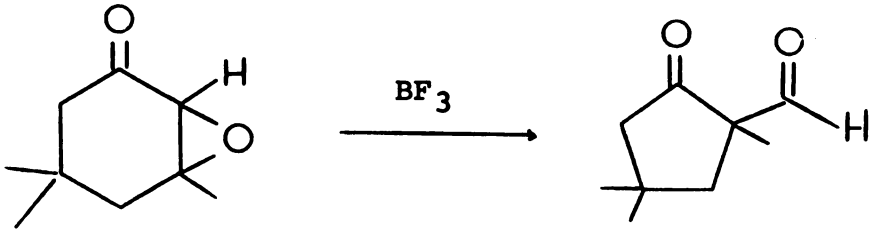


18 19 20

Similarly, 2-benzalcyclopentanone oxide 21 yields diketone 22,[11] and isophorone oxide 23 gives 2-formyl-2,4,4-trimethyl-cyclopentanone 24.[12]



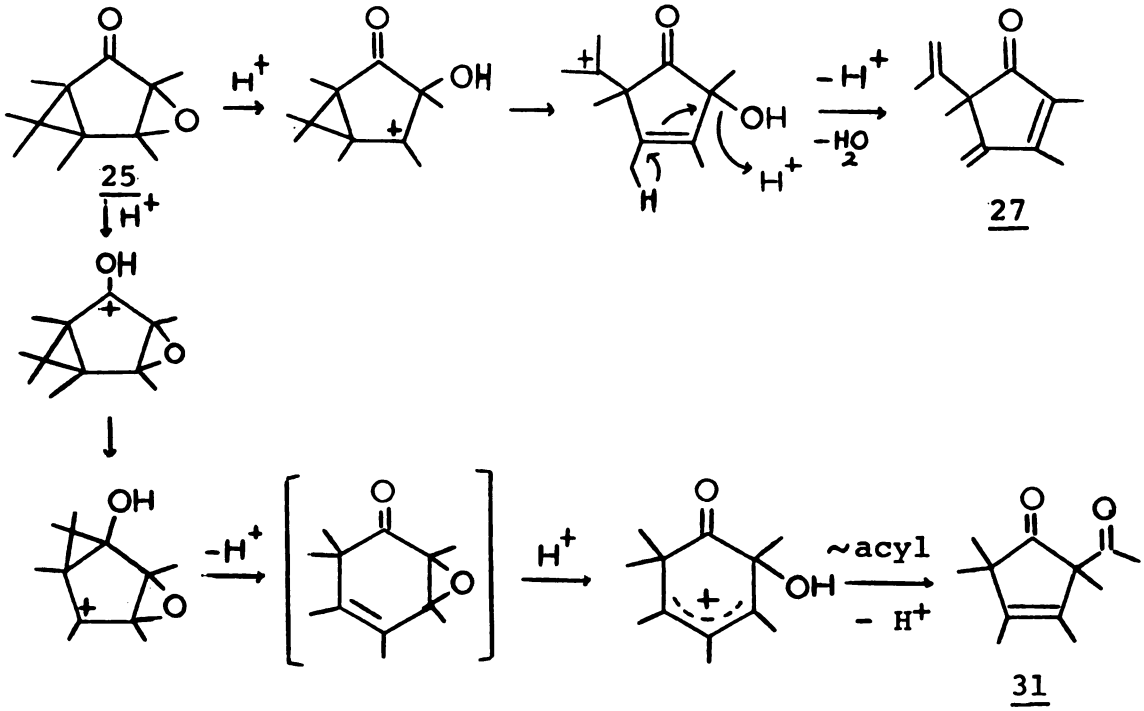
21 22



23 24

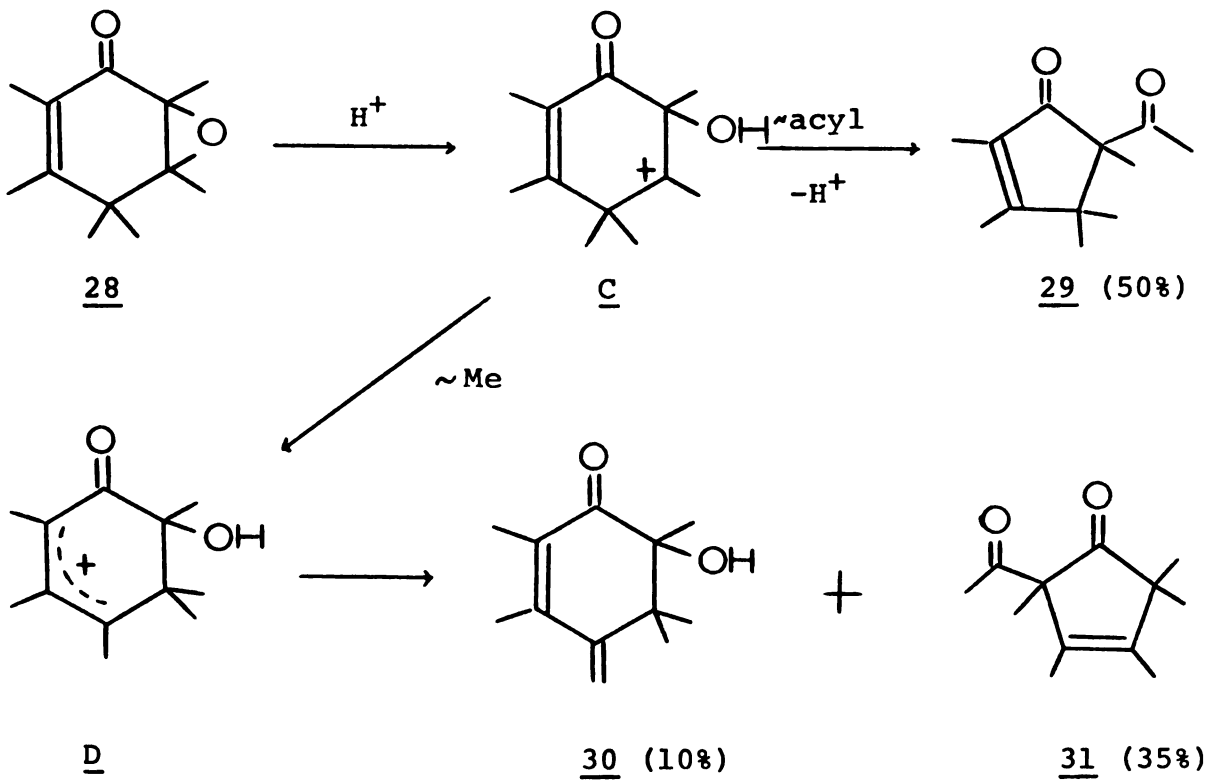
Although the acid-catalyzed rearrangement of epoxyketones is generally initiated by protonation of the epoxy oxygen atom,[13] a competitive protonation at carbonyl oxygen appeared to play a role in the acid-catalyzed rearrangement of 25.[14] This competitive protonation on carbonyl oxygen was necessary to account for the formation of 31, in addition to the expected product 27 (Scheme 1)

Scheme 1



In a recent study,[15] it was shown that acyl and methyl migration compete approximately equally in the acid-catalyzed rearrangement of α,β-epoxyketone 28. Thus on treatment with trifluoroacetic acid, 28 rearranged (Scheme 2) to a nearly equal mixture of 29 and (30 + 31).

Scheme 2



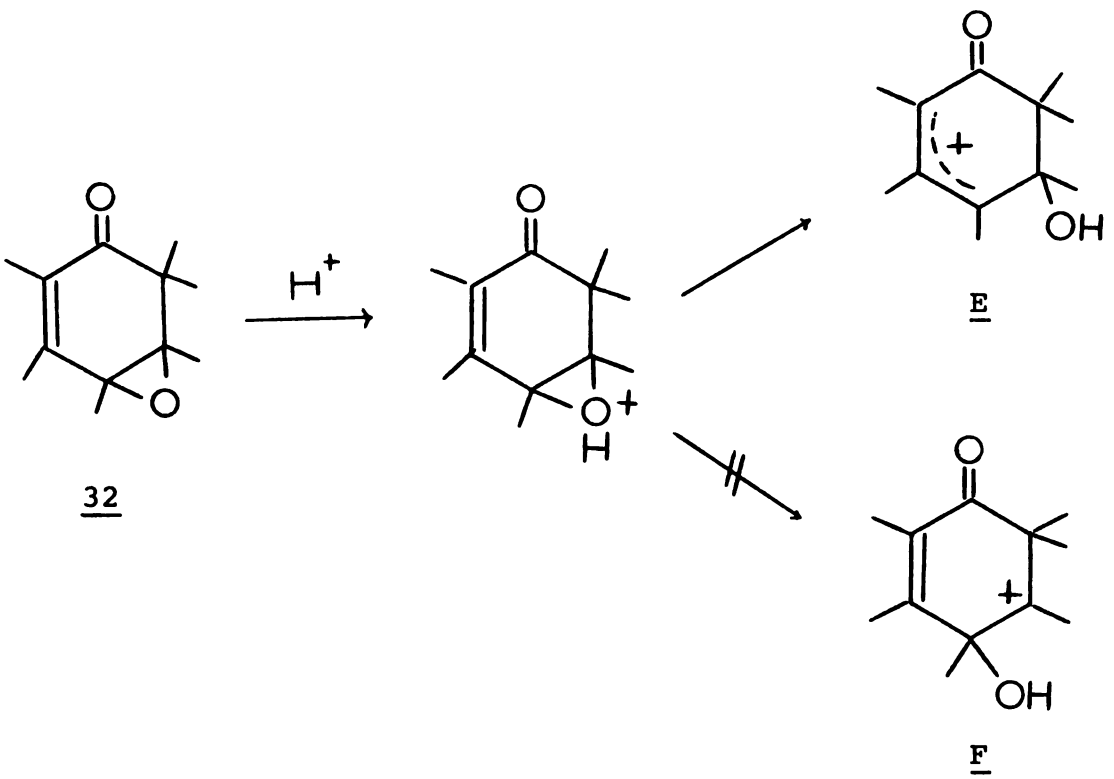
28 C 29 (50%)

D 30 (10%) 31 (35%)

Protonation and ring opening in 28 occurs in such a manner as to place the positive charge remote from carbonyl group, giving ion C. Acyl migration and proton loss affords the major product 29. Methyl migration competes effectively, giving the allylic ion D which may either lose a proton

to give 30 or rearrange by a more complex process, eventually to give 31.

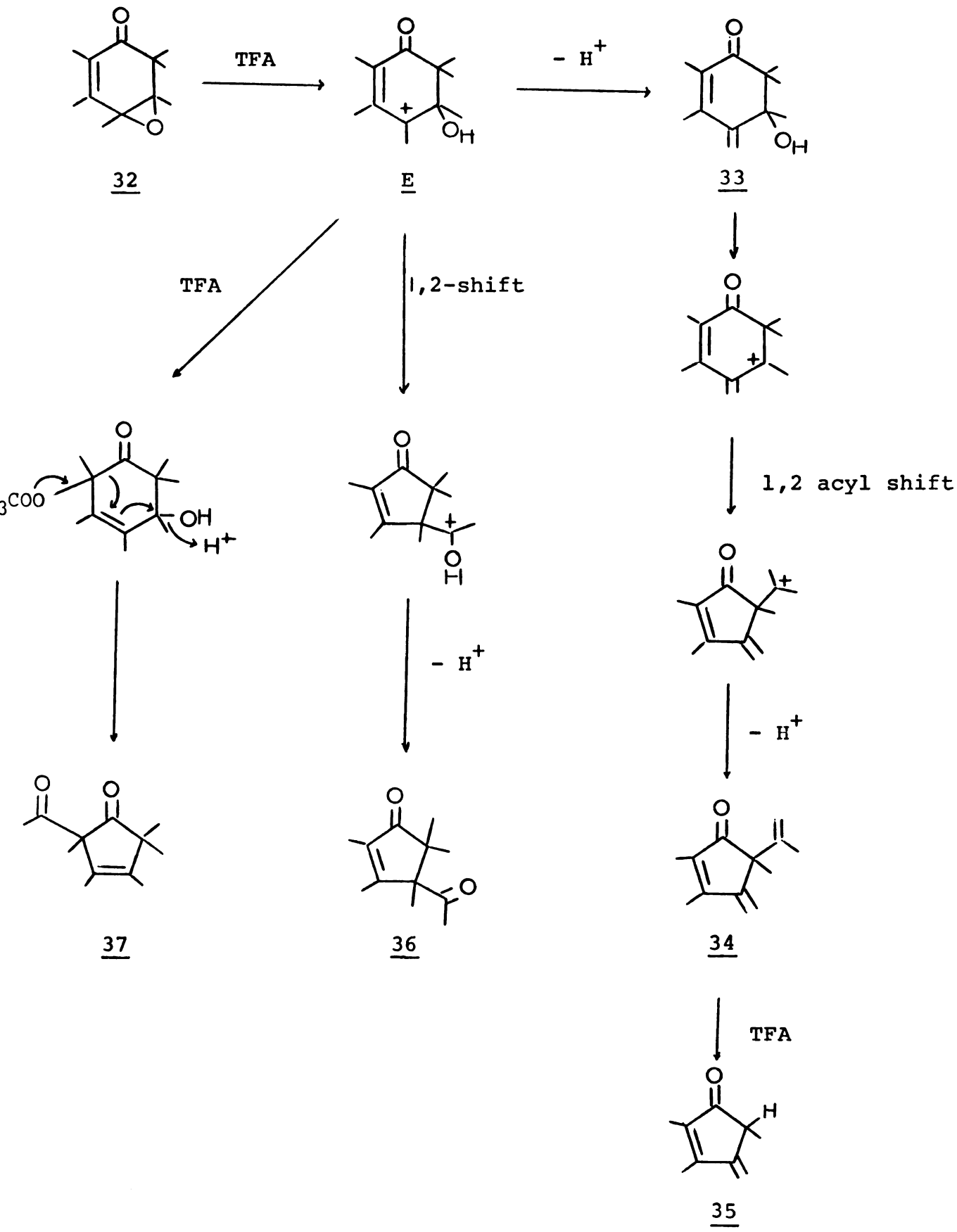
The epoxyketone 32, which is a vinylog of an α,β-epoxyketone, rearranged in acid initially to allylic cation E, not F.[15] Presumably, the conjugative effect is an overriding factor in determining the stability of the resulting carbonium ion.



32 E F

The intermediate E can collapse to 33 by losing a proton (Scheme 3). In neat trifluoroacetic acid, the same intermediate may rearrange by a 1,2-alkyl shift (ring contraction) to give 36 or may, following nucleophilic attack α to the carbonyl group, undergo a ring contraction, leading to 37. The major product 35 may arise from protonation of

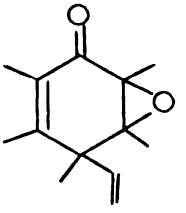
Scheme 3



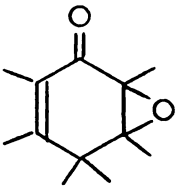
33 followed by a 1,2-acyl shift and deprotonation; product 35 is formed by dealkylation of 34 (Scheme 3). These mechanisms were supported by deuterium labeling experiments.

Only a few examples of dienone epoxide rearrangements have been studied. Although one can, from previous experience, write plausible reaction paths, one's predictive ability as to which path will predominate in any given instance is still rather low. Since the reactions can be synthetically useful, especially for making variously substituted cyclopentenones, it would be helpful to be able to make such predictions with greater accuracy. Therefore it is the purpose of this part of the thesis to examine the manner in which the various methyls groups or other substituents in 28 and 32 determine the mode of the acid-catalyzed rearrangements of cyclohexadienone epoxides.

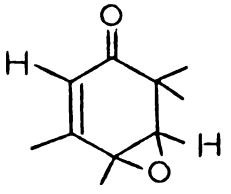
The two cases studied here were 38, which differs from 28 by having a vinyl group at the C-4 position instead of a methyl group, and 39, which differs from 32 by having hydrogens instead of methyls at the C-2 and C-5 positions.



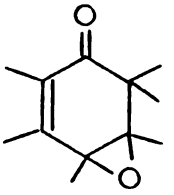
38



28



39

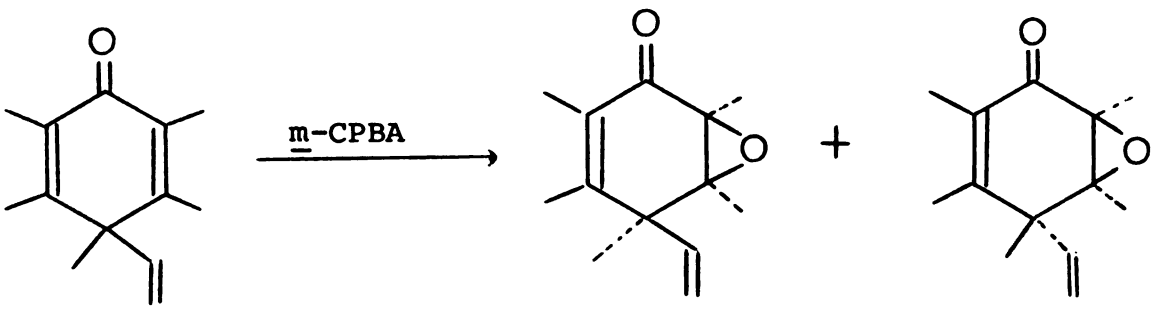


32

RESULTS AND DISCUSSION

1. Acid-Catalyzed Rearrangement of cis- and trans-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenone (38c and 38t)

Treatment of the vinyl cyclohexadienone 40[21] with an equimolar amount of m-chloroperbenzoic acid (m-CPBA) in methylene chloride gave a mixture of two monoepoxides, 38c and 38t, in which the vinyl group and epoxide ring are cis and trans to one another, respectively.

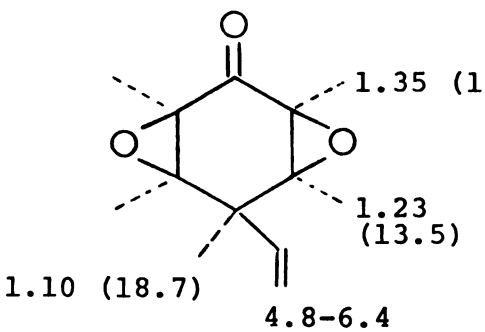


40 38c 38t

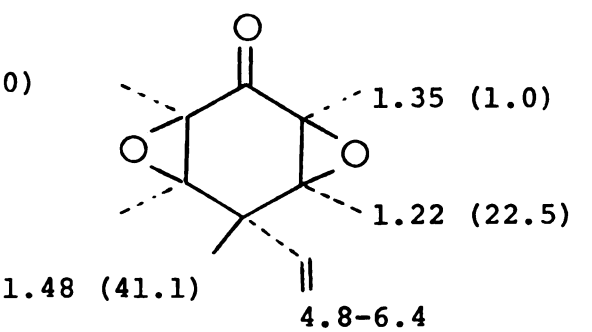
Although it was not possible to separate the two isomers, it was clear from the nmr spectrum of the mixture that epoxidation had occurred exclusively at the α,β-double bond. The area ratio of vinyl protons (multiplet, δ 4.8-6.1) to aliphatic protons (δ 1.1-1.7) was 1:5. With the aid of europium shift

reagent[16] and as a consequence of isolating one of the isomers in pure form (38c; vide infra), it was possible to completely assign the nmr spectrum of each isomer. The ratio of 38c to 38t, as determined by integration of the europium-shifted nmr spectrum, was approximately 3:2.

When excess m-chloroperbenzoic acid was used, di- and tri-epoxides of 40 were formed. The diepoxides were a mixture of 41c and 41t in which the two epoxide rings are cis to one another and either cis or trans to the vinyl group. There was no detectable amount of the isomer with the

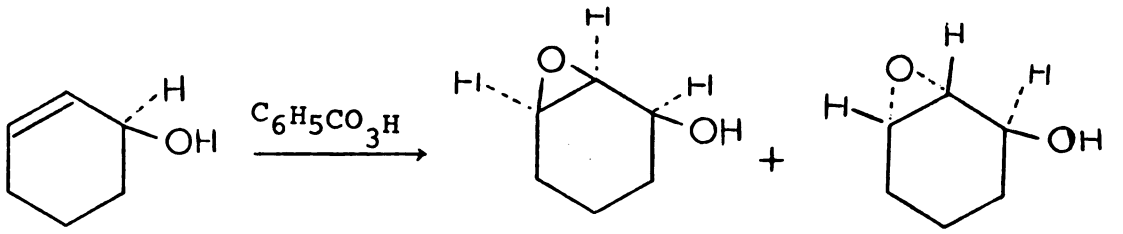


41c



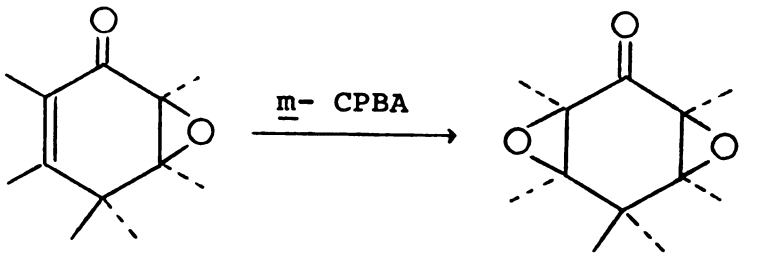
41t

two epoxide rings trans to one another. It is known that the direction of the attack by the peracid in epoxidation may be influenced by nearby polar substituents. Thus, epoxidation of allylic alcohol 42 gave predominantly the cis product 43c.[17]



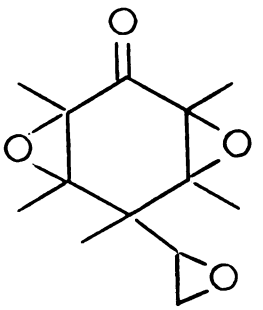
42 43c (91%) 43t (9%)

The directive effect of the hydroxyl group has been suggested to arise because of hydrogen bonding between the hydroxyl group and the attacking peracid. This type of directive effect has also been observed in compound 28 which on epoxidation gave exclusively cis-diepoxide 44.[18]



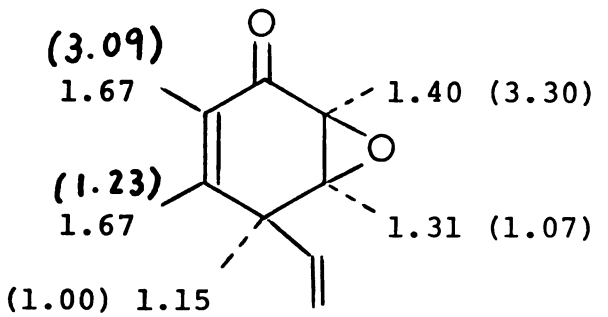
28 44

The configuration of the tri-epoxide 45 is not known, though it seems probable that the two epoxide oxygens on the cyclohexanone ring are cis. Spectral properties of 41 and 45 are given in the experimental section.

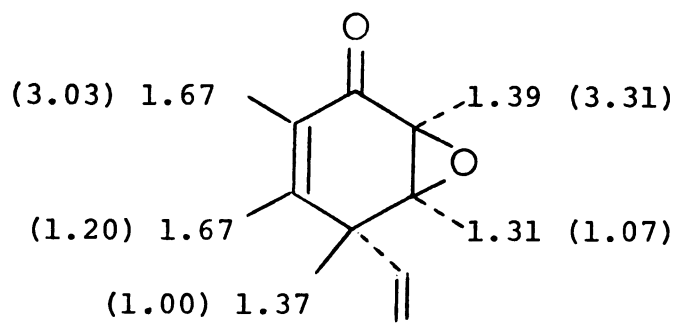


45

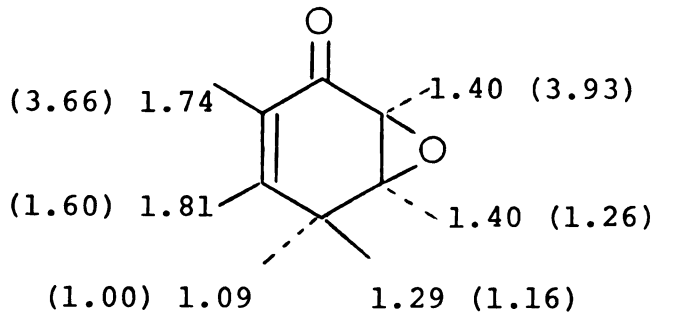
When a methylene chloride solution of the mixture of 38c and 38t was treated with trifluoroacetic acid for 1 hr at room temperature, only one of the two isomers reacted. The unreacted isomer was separated from the rearrangement products by preparative vpc, and was assigned structure 38c. The chemical shifts and europium shift slopes[16] of the five methyl groups are shown on the structural formula. The most striking difference in the nmr spectra of 38c and 38t is the chemical shift of the methyl group at C-4; these signals are 0.22 ppm apart in the two isomers, a result which is consistent with the nmr spectrum of 28.[18]



38c



38t

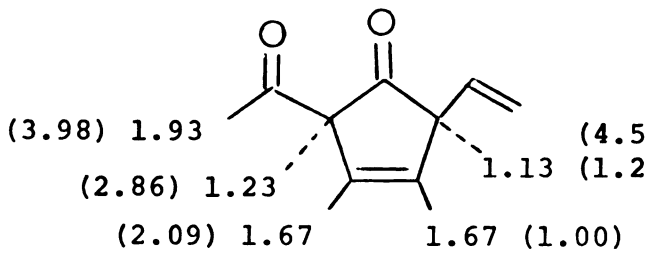


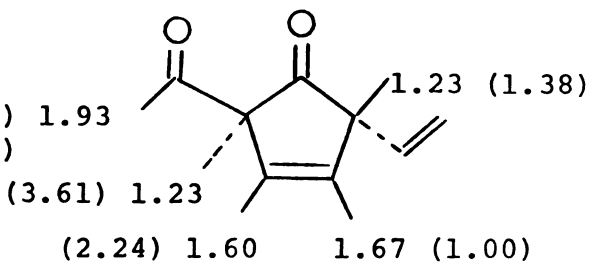
28

The methyl assignments at C-4 in 28 were based on the assumptions that (a) the methyl cis to the electronegative epoxide oxygen should appear at lowest field, and (b) the methyl cis to the epoxide oxygen, a possible coordination site for europium shift reagent, should have a slightly larger europium-shift slope than the methyl trans to the epoxide ring (the main coordination site for europium is

clearly, however, the carbonyl oxygen). On these grounds one can assign structure 38c to the epoxyketone which is recovered from mild treatment of 38c + 38t with trifluoroacetic acid, since its C-4 methyl appears at higher field (thus trans to the epoxide ring) than the C-4 methyl in its isomer. As will be seen, this assignment is consistent with mechanistic rationalizations of the acid-catalyzed rearrangement of 38.

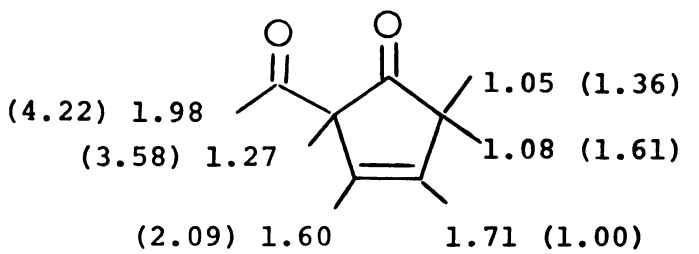
In addition to recovered 38, two rearrangement products were isolated from the mild treatment of 38c + 38t with trifluoroacetic acid. These products were separated by preparative vpc and are assigned structures 46c and 46t (ratio 1:4), in which the methyls at C-2 and C-5 of the cyclopentenone ring are cis and trans, respectively. Each isomer showed two strong carbonyl bands in the infrared (~ 1700, 1740 cm^{-1}) for the acetyl and cyclopentenone carbonyl groups; the uv spectra also showed that neither carbonyl group was conjugated with a carbon-carbon double bond. The nmr spectrum of each isomer showed an acetyl methyl, two allylic methyls, two aliphatic methyls, and three vinyl protons. The mass spectra of 46c and 46t were nearly identical; striking features were a very weak parent peak (m/e 206), a base peak at m/e 164 corresponding to the loss of ketene, and three additional intense peaks for the further loss of 15, 28 and 43 amu. All of the spectra resemble closely the published spectra of 31.[15]





46c

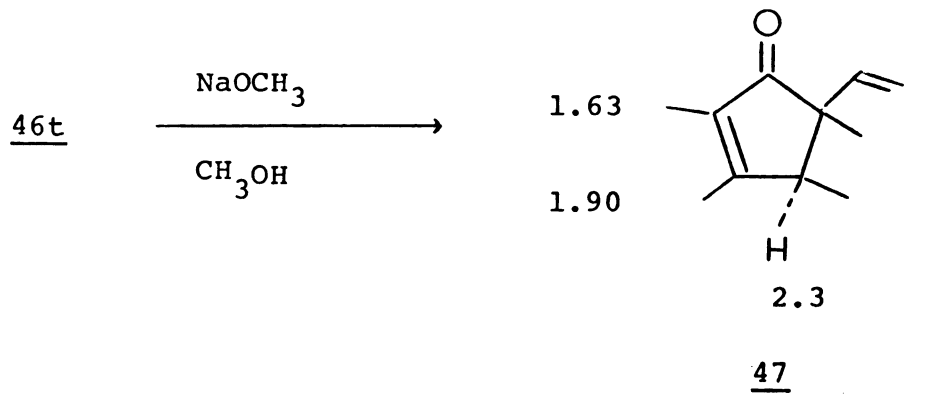
46t



31

The distinction between 46c and 46t is based on different chemical shifts and europium slopes of the C-5 methyl (adjacent to the vinyl substituent). This signal appears at lower field and is affected more by shift reagent when the methyl is cis to the acetyl group at C-2 (i.e., in 46t). Also noteworthy are the lower overall europium shift slopes in 46c compared with 46t, presumably because the large vinyl group cis to the acetyl group in 46c diminished complexation with the shift reagent.

Chemical evidence for the structure of 46 was obtained by base cleavage. The major isomer (46c) was treated with sodium methoxide in methanol at room temperature (12 hrs) to give a mixture of two stereoisomers of a cyclopentenone assigned structure 47. The ir ($\nu_{C=O}$ 1700 cm^{-1}) and uv spectra (λ_{max}^{MeOH} 237 nm, ε 8,800) support the presence of a cyclopentenone moiety, and the nmr spectrum showed two

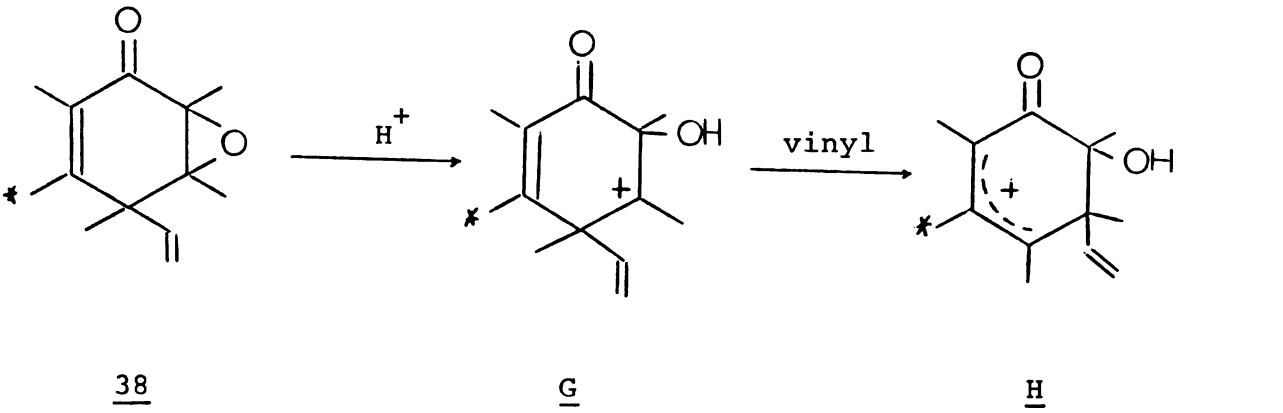


47

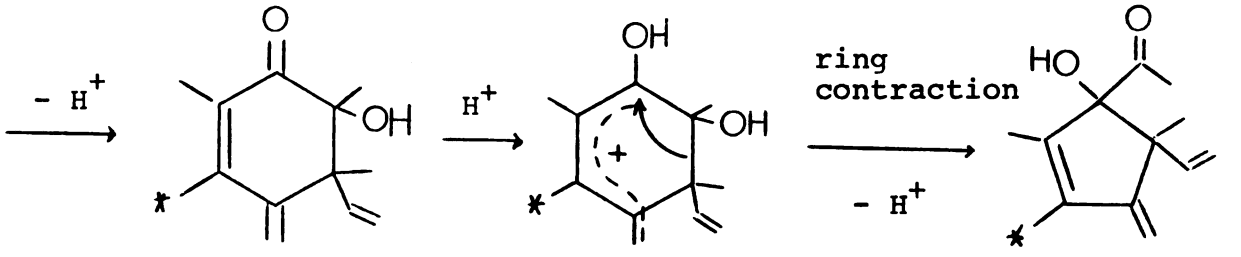
homoallylically coupled methyls (δ 1.63, 1.90, J = 1 Hz), three vinyl protons (δ 4.6-5.8), two aliphatic methyls (approx. δ 1.0) and the methine proton (m, δ2.3). The structure of 47 was further supported by the observation that treatment with $NaOCH_3/CH_3OD$ gave 47-d_4, in which the nmr signals at δ 1.90 and 2.3 were absent, that at δ 1.63 sharpened to a singlet, and the aliphatic methyl signals simplified to sharp singlets.

A plausible mechanism for the formation of 46 from 38 is shown in Scheme 4 (the question of stereochemistry is deferred for later discussion; vide infra).

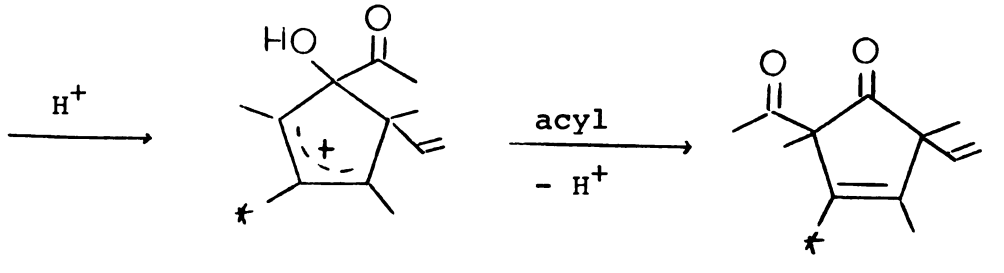
Scheme 4



38 G H

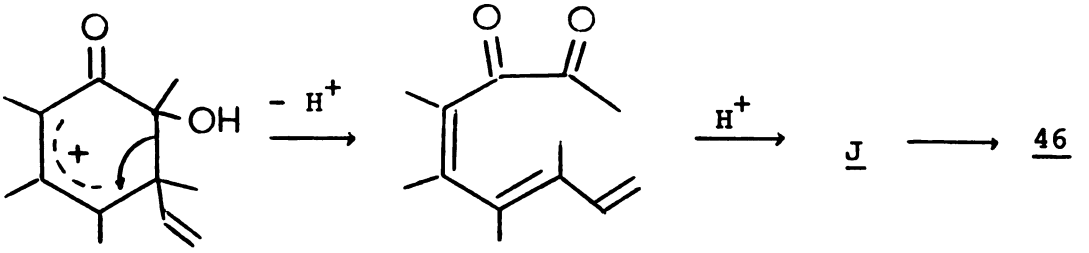


48 I 49



J 46

Protonation of the epoxide oxygen and ring-opening gives ion G (analogous to C from 28, Scheme 2, page 9). Vinyl migration would give the allylic cation H (analogous to D from C, Scheme 2). Proton loss could give 48 (analogous to 30, Scheme 2) which, however, was not observed. Reprotonation, ring contraction (to give 49) and a 1,2-acetyl migration account for the product. Alternatively H could suffer ring opening to 50 which, on protonation and ring closure could lead directly to J, and then 46. These schemes are analogous



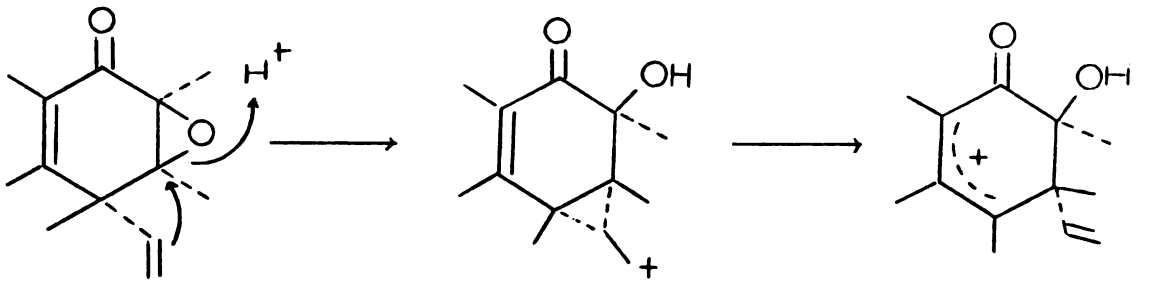
H 50

to the mechanisms established for the formation of 31 from 28.[15]

A labeling experiment was performed to test the reasonableness of Scheme 4. Treatment of 38 (a mixture of cis and trans isomers) with DMSO-d_6 and potassium t-butoxide gave 38* (see Scheme 4) whose nmr spectrum was identical with that of 38 except that the area of the peak at δ 1.67 was reduced by 50% (label at C-5). Treatment of 38* with

TFA at room temperature for 1 hr gave 38c* (signal at δ 1.67 reduced in area by 50%, and sharper than for 38c) and 46t* whose nmr spectrum lacked the signal at δ 1.60 and had a sharpened singlet at δ 1.67. Insufficient 46c* was isolated for spectral examination. These results clearly establish that a vinyl migration occurred during the rearrangement of 38 to 46 (the vinyl group and labeled methyl in 38* are on adjacent carbons, whereas in 46* they are separated by an additional carbon) as outlined in Scheme 4.

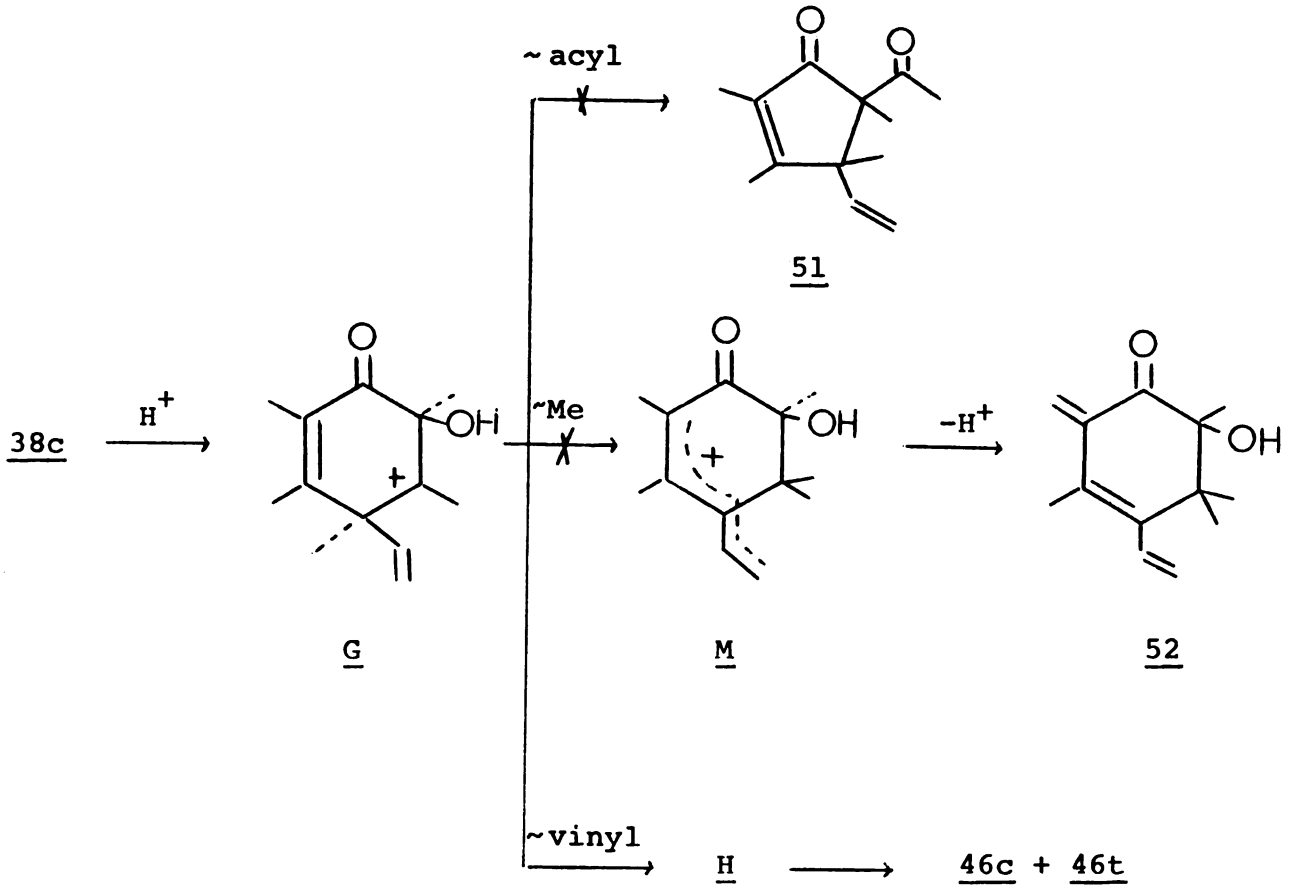
The observation that 38t is rapidly converted by TFA into 46 under conditions where 38c is recovered unchanged strongly suggested that Scheme 4 is oversimplified, and that homoallylic participation occurs in the ring opening of epoxide 38t. That is, the initially formed ion from 38t is not the simple tertiary carbonium ion G but a cyclopropylcarbinyl cation, one contributor of which is shown as structure K. Vinyl migration should give L (corresponds to H in Scheme 4) in which the vinyl and hydroxyl groups are trans. Unfortunately further steps in the mechanistic scheme allow for stereochemical ambiguity and the product is a mixture of 46t and 46c.



38t K L

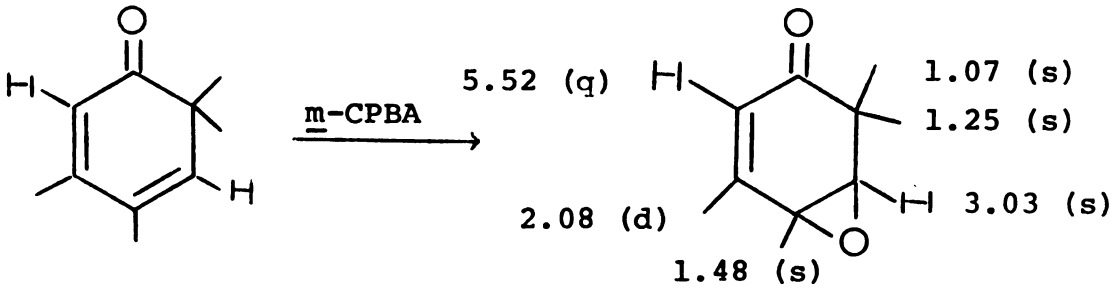
In isomer 38c, where the vinyl and epoxide groups are cis, homoallylic participation in the ionization step is not possible. Consequently, 38c is recovered unchanged under these reaction conditions. It seemed important to determine whether 38c would also rearrange in acid under more forcing conditions. It was found that 38c was inert to TFA at room temperature, even after 12 hrs. However, when the temperature was raised to 60°, 38c did rearrange slowly, reaction being 85% complete in 7.5 hrs. The products were 46c and 46t, identical with those obtained from 38t. It is concluded that both 38c and 38t rearrange exclusively by vinyl migration. They do so, however, by different mechanisms, 38t rearranging with homoallylic participation (via K, L, etc) and 38c rearranging without participation (via G, H, etc)

or with participation but at a later stage (via G, K, L, etc). Even when the reaction occurs without participation, however, acyl or methyl migration are unable to compete with vinyl migration. Thus products such as 51 (which could be formed via acyl migration) or 52 (which could be formed by proton loss from the highly delocalized intermediate cation M) were not observed. One can conclude that vinyl migration is preferred over acyl or methyl migration even when homoallylic participation in the ionization step is not possible.



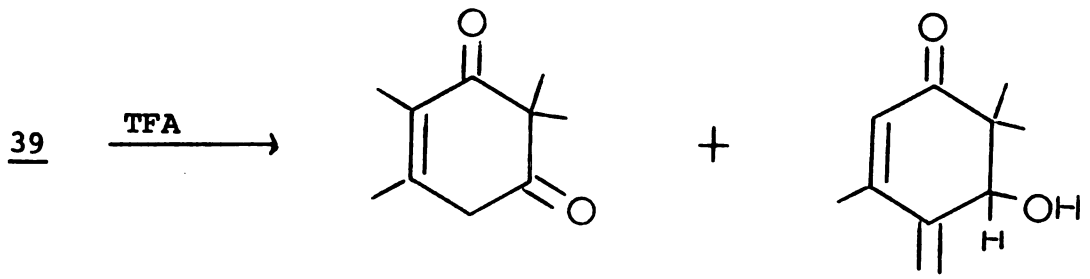
2. Acid-Catalyzed Rearrangement of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone, 39

4,5-Epoxy-3,4,6,6-tetramethyl-2-cyclohexenone (39) was prepared in good yield from the corresponding dienone 53 and m-chloroperbenzoic acid. The properties and structure proof have already been presented.[19]



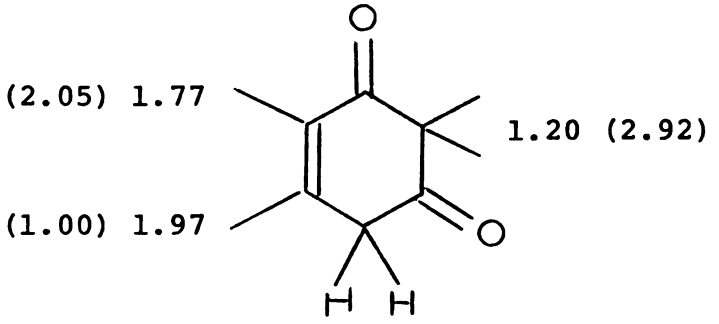
53 39

Treatment of 39 with TFA at room temperature for 1/2 hr gave two isomers which were assigned structures 54 and 55.



54 (53%) 55 (47%)

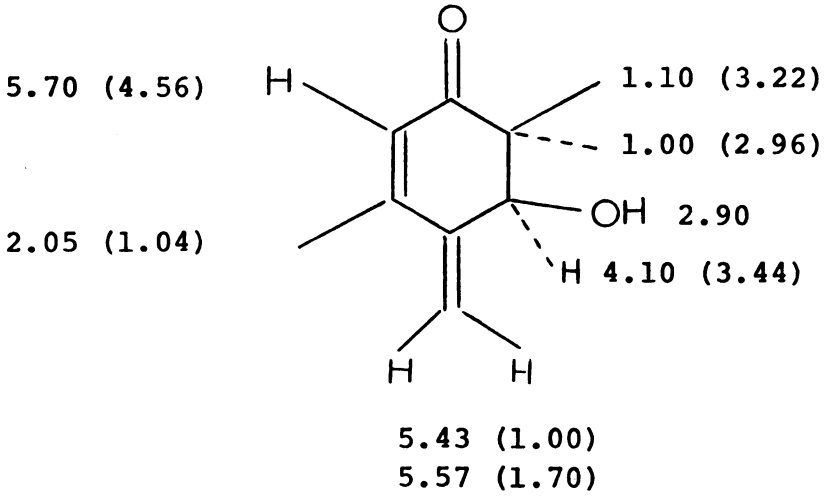
The product structures were established by their spectral properties. The diketone 54 showed two carbonyl absorptions, at 1720 and 1665 cm^{-1}, and strong uv absorption at 245 nm, indicating one conjugated and another non-conjugated carbonyl group in a six-membered ring.[20] The nmr spectrum, which showed two mutually coupled vinyl methyl groups (δ 1.77, 1.97), and europium shift data are consistent with the structure.



54

The compound assigned structure 55 showed a $\nu_{C=O}$ at 1670 cm^{-1} consistent with a conjugated carbonyl group in a six-membered ring; the presence of a hydroxyl group was clear from the ν_{OH} at 3500 cm^{-1} and from the presence of a one-proton peak in the nmr spectrum at δ 2.90 which was removed on D_2O exchange. The nmr spectrum showed three vinyl protons as multiplets (δ 5.43, 5.57, 5.70), one allylically coupled vinyl methyl (δ 2.05) as a doublet with a coupling constant of 2 Hz, and two gem-dimethyls as singlets (δ 1.00, 1.10). The ir spectrum indicated that two of the

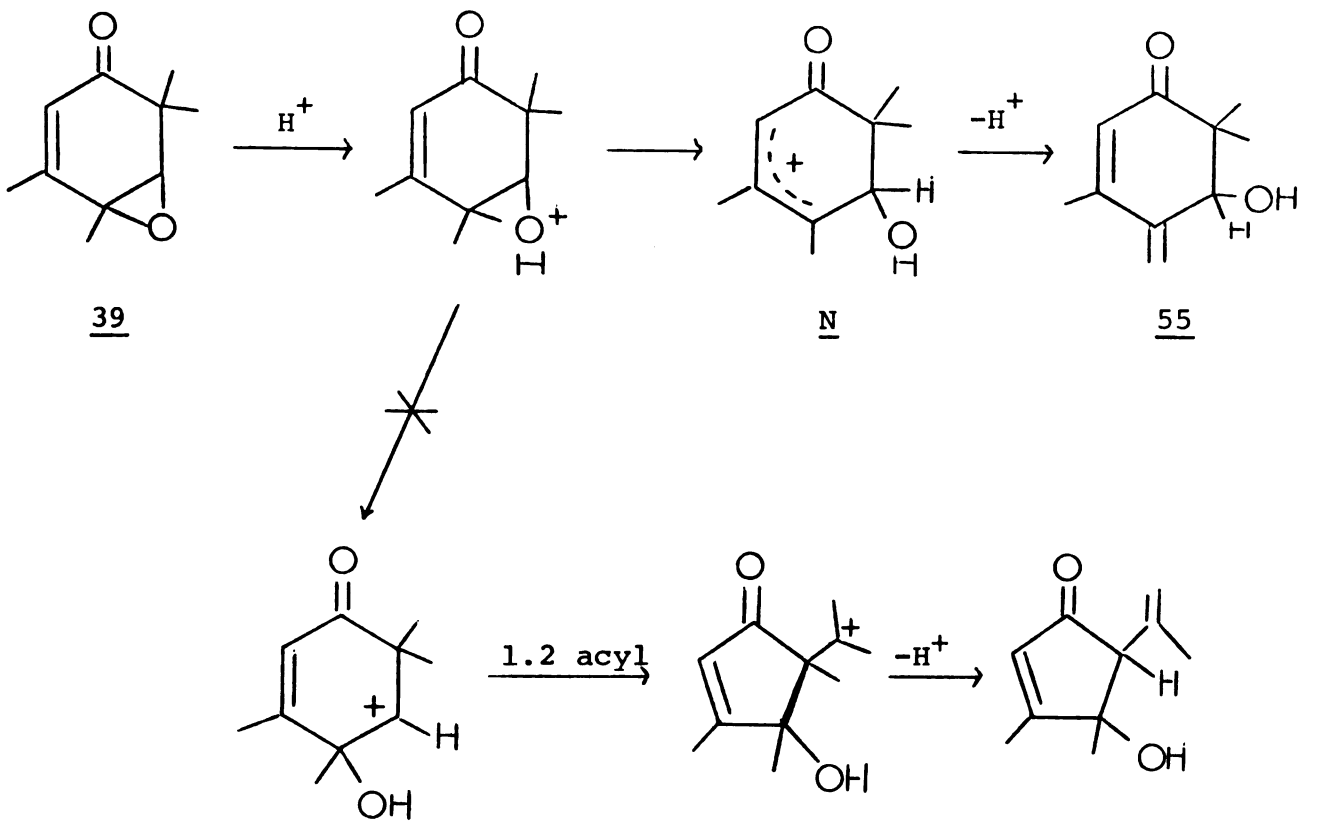
vinyl protons were on a terminal methylene group (930 cm^{-1}) and the uv maximum at 270 nm (ε 16,430) suggested that both double bonds were conjugated with the carbonyl group. Specific assignments within the structure are based on a labeling experiment to be discussed below.



55

Compound 55 is undoubtedly formed from 39 by proton loss from the intermediate cation N (Scheme 5). The alternative ring-opening mode to give O possibly followed by 1,2-acyl shift would lead to structure 56 which is inconsistent with the observed nmr and uv spectra. Ion N is preferred over O because it is tertiary and allylic, and its fate (formation of 55) is entirely analogous to the formation of 33 from 32 via ion E (Scheme 3, page 11).

Scheme 5



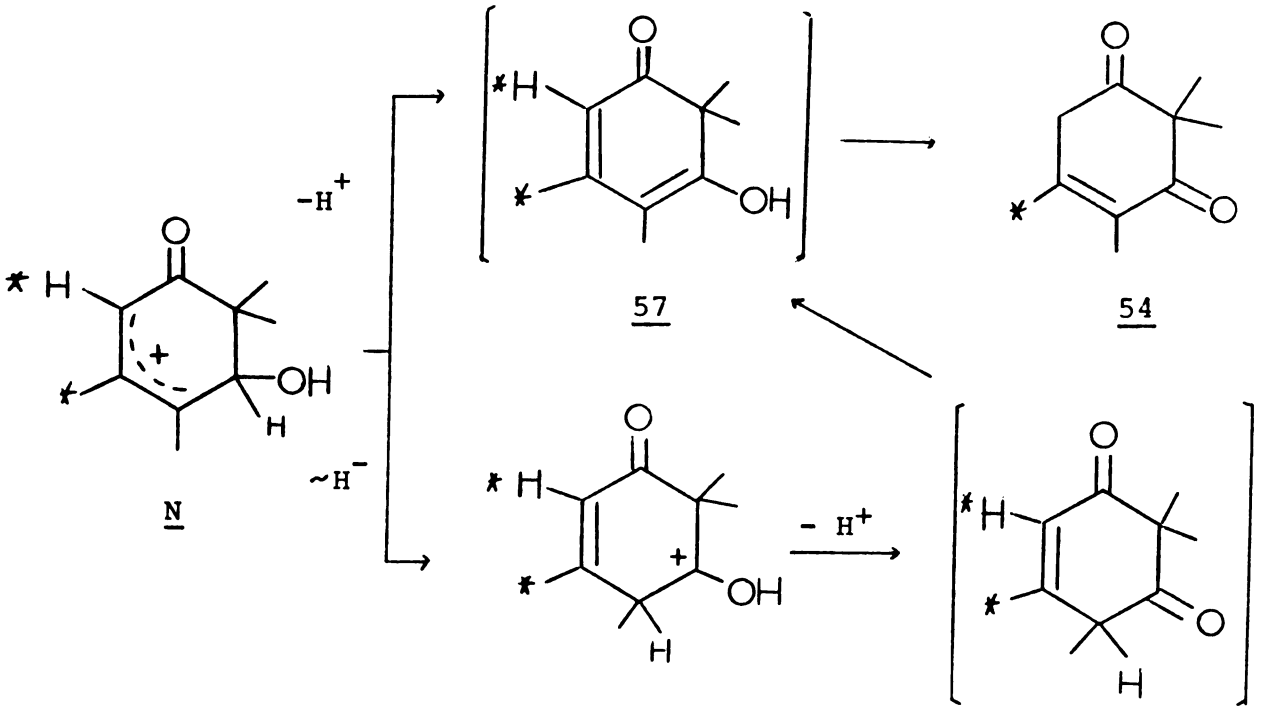
39 N 55

O 56

Possible routes to 54 are shown in Scheme 6. The same intermediate cation N can loss a proton to give 57 which, however, was not observed. Its rapid keto-enol tautomerism accounts for the formation of 54. Alternative processes involve a hydride shift (leading to P), deprotonation (to 58), followed by keto-enol tautomerism (to 54 via 57). The formation of 54 rather than 58 is probably a matter of

thermodynamic control. Compound 54 contains the more stable (Most substituted) double bond; also, any possible unfavorable 1,3-methyl-methyl interactions in 58 are absent in 54.

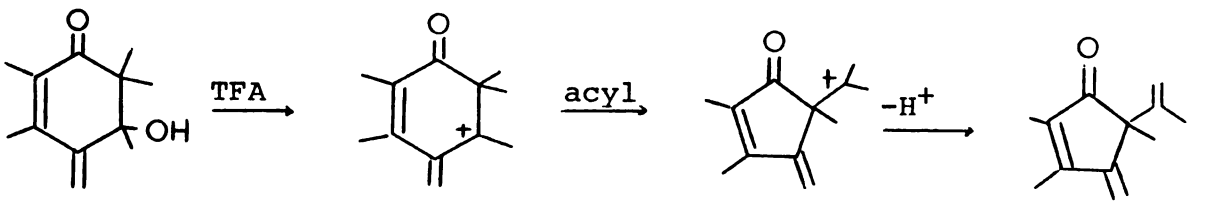
Scheme 6



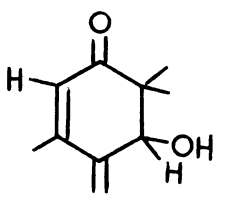
A labeling experiment was performed to test the accuracy of Schemes 5 and 6, and to establish unequivocally the nmr assignments of 55. Treatment of 39 with DMSO-d_6 and potassium t-butoxide gave 39* whose nmr spectrum was identical with that of 39 (see page 26) except that the peaks at δ2.08 and 5.72 were absent (label at C-3 and C-2). Treatment

of 39* with TFA at room temperature for 1/2 hr gave 54* (the signal at δ 1.97 disappeared and the singlet at δ 1.77 sharpened) with one less deuterium labeled atom than 39*, and 55* whose nmr spectrum lacked the signals at δ 2.05 and 5.70 (see pages 27, 28). These results show that no skeletal rearrangement occurred during acid rearrangement of 39 and that 54 was formed via its enol tautomer 57 where hydrogen exchange with solvent was possible.

In contrast to 33, which on protonation rearranged to 34 via a 1,2-acyl shift (Scheme 3, page 11), 55 underwent no further rearrangement on treatment with acid under similar conditions.



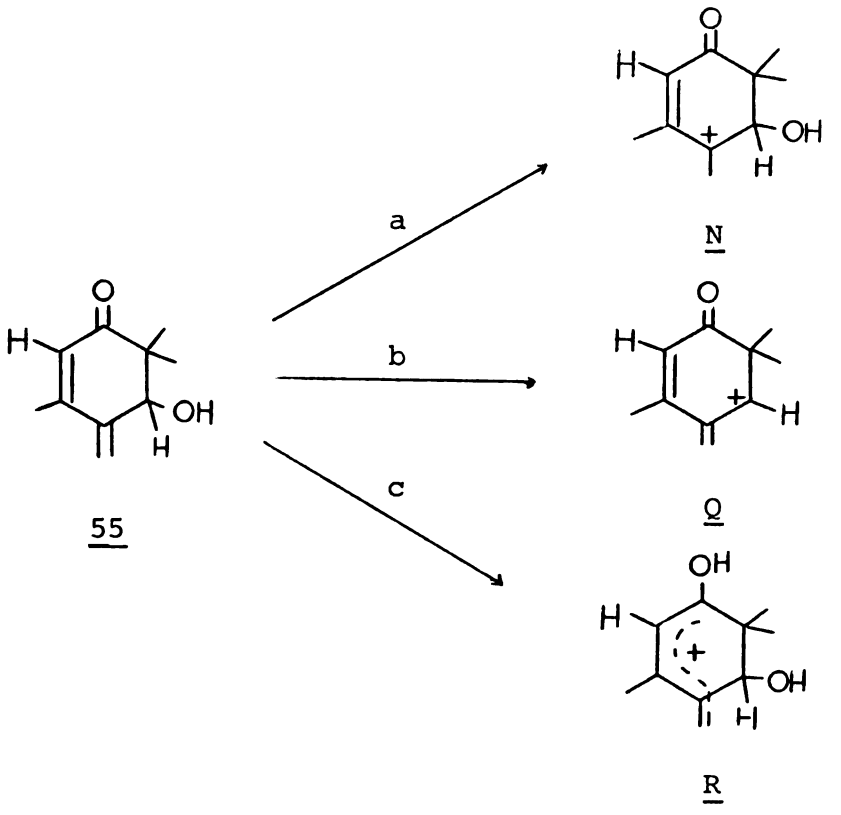
33 34



55

Scheme 7 shows three possible modes for protonation of 55.

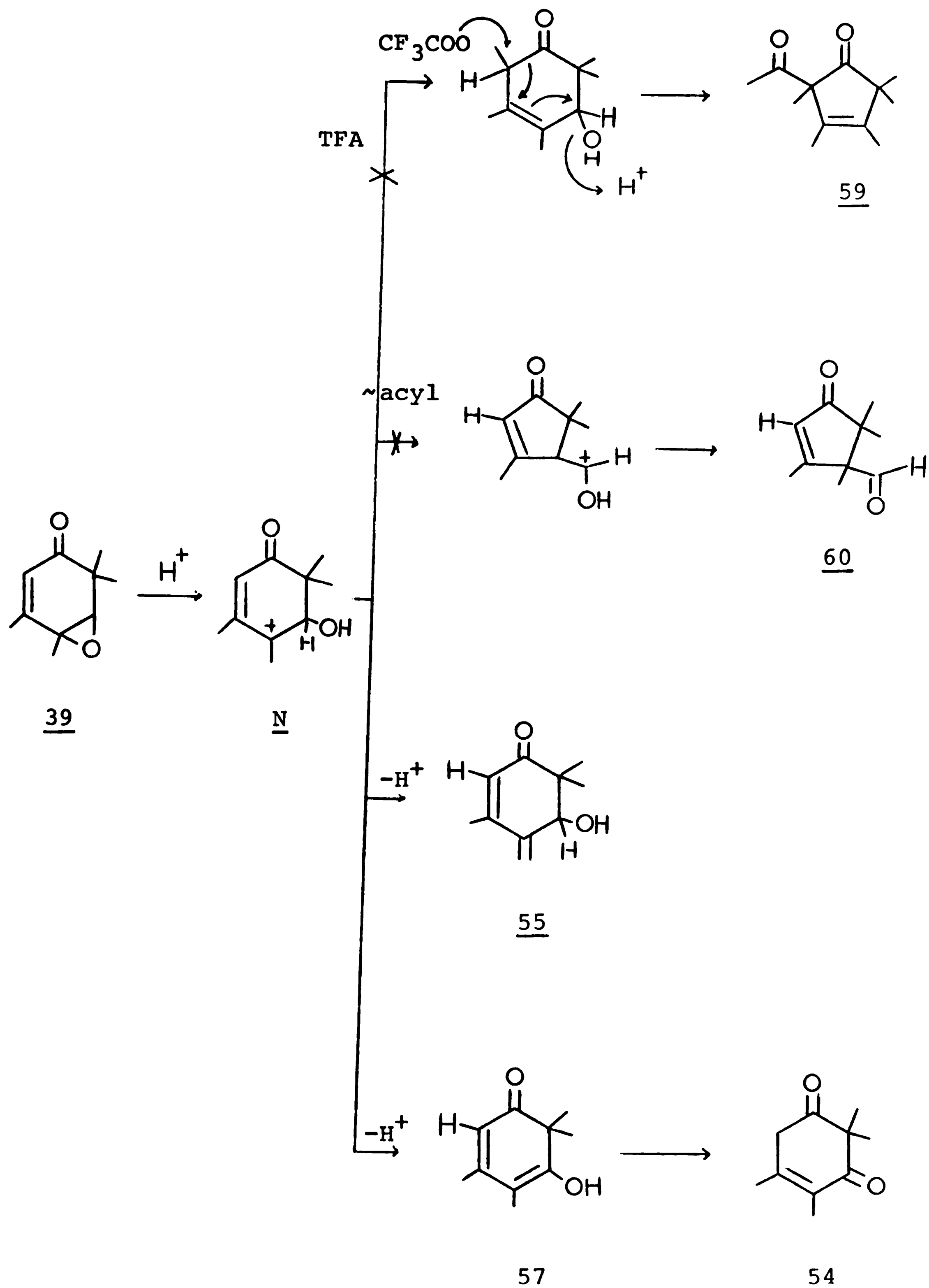
Scheme 7



Pathway a can be eliminated on the basis that if the allylic cation N is formed, it should give 54 and 55 on quenching. But 55 did not rearrange to 54 on treatment with acid. Pathway b is quite unlikely too, since if Q were formed, it is difficult ot understand why it would not undergo a 1,2-acyl shift analogous to that observed for 33. The only other mode of protonation is pathway c involving the highly delocalized intermediate cation R. This highly stabilized cation R may simply be incapable of rearranging under the prescribed experimental conditions, and was

converted back to starting material 55 on quenching. The nmr spectrum of 55 in neat TFA showed two non-equivalent gem-dimethyls at δ 1.27 and 1.30 where each appeared as a singlet, one allylically coupled vinyl methyl at δ 2.20 as a doublet, a one-proton multiplet at δ 4.47, and three vinyl protons at δ 5.82 (m, 2H) and 6.03 (m, 1H). The strongly deshielded absorption at δ 4.47 placed that C-H adjacent to the oxygen atom. These data are consistent with the structure of cation R. Therefore, a new mode of protonation, namely at the carbonyl oxygen, appears to operate on the acid treatment of 55.

In summary, the dienone epoxide 39 rearranges to the highly conjugated systems 54 (via 57) and 55 (via the allylic cation N). In contrast to the permethylated allylic cation E (Scheme 3, page 11), a nucleophilic attack by solvent or a 1,2-alkyl shift cannot compete effectively with a simple proton loss from N to give 54 and 55. Thus, products such as 59 (which could be formed by nucleophilic attack α to the carbonyl group followed by ring contraction) or 60 (which could be formed by a 1,2-alkyl shift followed by a loss of proton) were not observed.



CF3COO
TFA
~acyl
H+
OH
-H+
59
60
39
N
55
57
54

EXPERIMENTAL

1. General Procedures

Analytical gas chromatography (vpc) was carried out on a Varian Aerograph Model 1400 (flame ionization detector), and preparative vpc was performed with a Varian Aerograph Autoprep Model 700 instrument (thermal conductivity detector). Except where otherwise noted, all nmr spectra were measured in $CDCl_3$ or CCl_4 solutions using TMS as an internal standard. The 60 MHz spectra were recorded on a Varian T-60 spectrometer and the 100 MHz spectra were recorded on a Varian HA-100 spectrometer. The small number placed next to protons in the structures in the discussion section are the nmr chemical shifts of those protons relative to tetramethylsilane. The numbers in parentheses beside the chemical shifts are the normalized europium shift numbers. These were obtained by adding small increments of tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione)Eu(III) to the CCl_4 or $CDCl_3$ solution of the compound being investigated. After each addition the nmr spectrum was scanned and the new frequency of each absorption was recorded. The shift for each absorption is the difference between the frequency of the shifted absorption and the original one. The normalized shift

numbers are ratios obtained by dividing the shift of each signal in the spectrum by the shift of the least shifted signal.

Infrared spectra were recorded on a Perkin Elmer 237 grating spectrophotometer and were calibrated against a polystyrene film. Ultraviolet spectra were obtained with a Unicam SP-800 in methanol unless otherwise noted. Mass spectra at 70 eV were obtained from a Hitachi-Perkin Elmer RMU-6 operated by Mrs. Ralph Guile. Melting points were determined with a Thomas-Hoover Melting Point Apparatus and are uncorrected. Analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan, or Clark Microanalytical Laboratories, Urbana, Illinois.

2. Epoxidation of 2,3,4,5,6-pentamethyl-4-vinyl-2,5-cyclohexadienone (40)

To a solution containing 100 mg (0.53 mmol) of 40[21] in 5 ml of methylene chloride was added, at 0°, a solution of m-chloroperbenzoic acid (93.5 mg, 0.54 mmol) in 3 ml of methylene chloride. The reaction, which was followed by nmr, was complete in about 2 hours, during which time m-chlorobenzoic acid precipitated from solution. The solvent was removed by rotary evaporation, petroleum ether (bp 30-60°) was added, and the m-chlorobenzoic acid was removed by filtration. The filtrate was washed with aqueous sodium

bicarbonate, then with saturated sodium chloride, and dried (Na_2SO_4). The solvent was rotary evaporated, and the residue was chromatographed on Florisil (80-100 mesh) using ethyl acetate-hexane (1:4) as eluent. The first fraction was a mixture of the monoepoxides 38c and 38t (43 mg, 88% based on unrecovered dienone). The second fraction was unreacted 40 (55 mg, 55%). The mixture of 38c and 38t had the following properties: ir (neat) 1660 (s), 1625 (w), 1385 (m), 1350 (w), 1030 (w), 885 (w), 685 (w) cm^{-1}; uv (MeOH) λ_{max} 253 nm (ε 12,700), 212 (6,800); nmr (CCl_4) δ 1.15 (s) and 1.31-1.40 (overlapping singlets), combined area 9H, 1.67 (m, 6H), 4.9-6.1 (m, 3H). Europium shift reagent[16], $Eu(fod)_3$, resolved the spectrum and at 100 MHz separate peaks due to the five methyl groups in each stereoisomer were discernible. The area ratios for peaks assigned to 38c and 38t was 3:2. The mass spectrum (70 eV) m/e (rel intensity) of the epoxide mixture was 206 (11), 191 (30), 190 (39), 175 (53), 174 (39), 164 (100), 163 (56), 159 (36), 149 (83), 147 (57), 136 (52), 135 (85), 121 (67), 120 (32), 119 (78), 108 (25), 107 (36), 105 (55), 93 (65), 77 (55), 65 (37).

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80
Found: C, 75.73; H, 8.82

In an effort to decrease the amount of unreacted 40 in the above epoxidation, the ratio of peracid to dienone was increased to 3:1. To a solution containing 100 mg (0.53 mmol) of 40 in 5 ml of methylene chloride was added,

at 0°, a solution of 280 mg (1.62 mmol) of m-chloroperbenzoic acid in 10 ml of methylene chloride. The mixture was stirred at room temperature overnight, then worked up as described above. Chromatography of the crude product over Florisil (80-100 mesh) with ethyl acetate-hexane (1:4) as eluent gave as the first fraction the diepoxides 41c and 41t (58 mg, 50%) and as the second fraction the monoepoxides 38c and 38t (43 mg, 40%). There was no unreacted 40. The diepoxide mixture (2,3;5,6-diepoxy-2,3,4,5,6-pentamethyl-4-vinyl-cyclohexanone) had the following properties: ir (KBr) 1690 (s), 1380 (m), 1100 (m), 950 (m), 870 (w), 680 (w) cm^{-1}; uv (MeOH) λ_{max} 210 nm (ε 2,900); nmr (CCl_4) δ 1.07 (s), 1.20 (overlapping singlets), 1.33 (s), 1.50 (s), area from δ1.07-1.50 (m, 15H), 4.8-6.4 (m, 3H); $Eu(fod)_3$ shift reagent showed that there were two sets of methyl singlets, each with area ratios 1:2:2; for the nmr assignments and europium shift slopes, see structures; the two isomers were present in a 3:2 ratio; mass spectrum (70 eV) m/e (rel intensity) 222 (<1), 179 (18), 165 (13), 151 (49), 137 (70), 125 (23), 124 (24), 109 (100), 93 (34), 91 (30), 81 (34), 79 (37), 77 (31), 67 (35), 55 (29), 53 (54).

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16
Found: C, 70.28; H, 8.21

Repetition of the epoxidation exactly as above but with 374 mg (2.2 mmol) of m-chloroperbenzoic acid and 100 mg (0.53 mmol) of 40 in a total of 20 ml of methylene chloride gave 99 mg (85%) of the diepoxide mixture 41c and 41t and,

as the second fraction from Florisil chromatograph, 10 mg (8%) of triepoxide 45: ir (CCl_4) 1695 (s), 1450 (w), 1375 (m), 1080 (w) cm^{-1}; uv (MeOH) λ_{max}215 nm (ε 6,000); nmr (CCl_4) δ 0.83 (s), 1.4-1.6 (overlapping singlets; total area from δ 0.8-1.7, 15 H), 2.60-3.32 (m, 3H), no vinyl protons; mass spectrum (70 eV) m/e (rel intensity) 238 (1), 195 (13), 167 (77), 164 (33), 163 (28), 153 (50), 149 (100), 147 (33), 137 (73), 135 (65), 133 (43), 125 (86), 123 (86), 121 (36), 119 (44), 109 (70), 107 (94), 105 (55), 97 (28), 95 (26), 93 (52), 91 (97), 84 (20), 81 (45), 79 (80), 77 (64), 67 (60), 65 (39), 55 (63), 53 (75).

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61
Found: C, 65.63; H, 7.59

3. Acid-Catalyzed Rearrangement of cis- and trans-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenone (38c + 38t)

A solution of 38c and 38t (200 mg, 0.97 mmol) in 1 ml of trifluoroacetic acid was stirred at room temperature for 1 hour, then poured into a slurry of aqueous sodium bicarbonate solution and methylene chloride. The organic layer was separated, washed successively with aqueous sodium bicarbonate and saturated aqueous sodium chloride, and dried (Na_2SO_4). Evaporation of the solvent left 186 mg of a light yellow oil which, when subjected to analytical vpc (5' x 0.125 in column, 3% SE-30 on raroporl 30, 100-120 mesh, 125°), showed two peaks corresponding to 46c + 46t

(ret. time 5.5 min, 42%) and unreacted 38c (ret. time 9.5 min, 51%). Preparative vpc (5' x 0.25 in column, 10% SE-30 on chromosorb W, 80-100 mesh, 125°) gave pure cis-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenone 38c: ir (CCl_4) 1660 (s), 1630 (w), 1390 (m), 1250 (m), 935 (w), 880 (s) cm^{-1}; uv (MeOH) λ_{max}250 nm (ε 10,000), 215 (4,830); nmr (CCl_4) see structure, all methyl peaks were sharp singlets except that at δ 1.67 which was slightly broadened; the three vinyl protons appeared as a multiplet, δ 4.8-6.0; mass spectrum (70 eV) m/e (rel intensity) 206 (12), 191 (22), 164 (50), 163 (40), 149 (62), 147 (20), 137 (10), 136 (50), 135 (100), 121 (57), 120 (35), 119 (65), 107 (25), 105 (49), 93 (45), 91 (55), 77 (48), 65 (22). By comparing the nmr spectrum of the mixture of 38c and 38t with that of pure 38c and by plotting the chemical shifts vs. europium shift reagent concentration and extrapolating back to zero shift reagent it was possible to assign the nmr spectrum of 38t (see structure).

Vpc (5' x 0.125 in column, 5% TCEP (tetracyanoethylated pentaerythritol) on chromosorb W, 80-100 mesh, 125°, FID) resolved the chromatograph of 46c and 46t into two peaks, 46t (80%, ret. time 75 min) and 46c (20%, ret. time 90 min). Preparative vpc (5' x 0.25 in column, 15% TCEP on chromosorb W, 80-100 mesh, 125°) gave each pure isomer: trans-2-acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenone, 46t: ir (CCl_4) 1740 (s), 1710 (s), 1250 (s), 935 (w), 875 (s) cm^{-1}; uv (MeOH) λ_{max}219 nm (ε 2,650), 285 (720); nmr (CCl_4) see structure;

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the peaks at δ 1.60 and 1.67 were mutually coupled quartets, J = 1.5 Hz, other methyl peaks were sharp singlets, and the vinyl protons appeared at δ 4.6-5.8 (m, 3H); mass spectrum (70 eV) m/e (rel intensity) 206 (<1), 164 (100), 149 (63), 136 (54), 135 (29), 121 (73), 119 (28), 105 (30), 91 (26), 77 (19), 66 (27), 65 (23), 44 (36).

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80
Found: C, 75.66; H, 9.03

Cis-2-acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenone, 46c: ir (CCl_4) 1740 (m), 1700 (s), 1250 (s), 875 (s) cm^{-1}; uv (MeOH) λ_{max}218 nm (ε 1,150), 283 (30); nmr (CCl_4) see structure; all peaks were sharp singlets except for the vinyl protons at δ 4.7-5.4 (m, 3H); mass spectrum (70 eV) m/e (rel intensity) 206 (<1), 164 (100), 149 (69), 136 (52), 135 (24), 121 (76), 119 (26), 105 (30), 91 (28), 77 (23), 66 (77), 65 (56). Insufficient 46c was isolated for elemental analysis.

4. Cleavage of 46t with Base

A solution of 46t (26 mg) and sodium methoixde (20 mg) in 3 ml of methanol was stirred at room temperature for 12 hours, then poured into ice-water and extracted with ether. The combined ether layers were washed with saturated sodium chloride and dried (Na_2SO_4). Evaporation of the solvent and analysis of the residue by vpc (5' x 0.125 in column, 3% SE-30 on raroporl 30, 100-120 mesh, 120°) showed that all the 46t was converted to a single product, assigned the structure 2,3,4,5-tetramethyl-5-vinyl-2-cyclopentenone, 47.

Pure 47 was collected by preparative vpc (5' x 0.25 in column, 10% SE-30 on chromosorb W, 80-100 mesh, 120°): ir (CCl_4) 1700 (s), 1650 (w), 1250 (m), 885 (s) cm^{-1}; uv (MeOH) λ_{max} 237 nm (ε 8,820); nmr (CCl_4) δ 1.0-1.2 (m, 6H), 1.63 (q, 3H, J = 1 Hz), 1.90 (q, 3H, J = 1 Hz), 2.3 (m, 1H), 4.6-5.8 (m, 3H); mass spectrum (70 eV) m/e (rel intensity) 164 (85), 149 (100), 135 (49), 121 (60), 119 (20), 105 (38), 93 (30), 91 (29), 79 (25), 77 (23), 67 (25), 65 (15), 53 (26).

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83
Found: C, 80.47; H, 9.92

Treatment of 47 (10 mg) with excess sodium methoxide in CH_3OD for 5 hours at room temperature followed by workup analogous to that used in the preparation of 47 from 46t gave 47-d_4 whose nmr spectrum consisted of two sharp singlets at δ 1.00 and 1.13 (3 H), a sharp singlet at δ 1.63 (3H), and a vinyl proton multiplet at δ 4.6-5.8 (3H).

5. 5-Trideuteromethyl-2,3-epoxy-2,3,4,6-tetramethyl-4-vinyl-5-cyclohexenone, 38*

To a solution containing 145 mg (0.7 mmol) of a mixture of 38c and 38t (as obtained from epoxidation of 40) in 5 ml of dimethylsulfoxide-d_6 was added with stirring and under N_2, 95 mg (0.85 mmol) of potassium t-butoxide. The mixture was stirred at room temperature for 4.5 hours, then quenched with ice-water and extracted with ether. The combined

organic layers were dried (Na_2SO_4) and the solvent evaporated to give a nearly quantitative yield of 38*. The nmr spectrum was identical to that of the starting material, except that the peak at δ 1.67 was decreased in area by 50%.

6. Acid-Catalyzed Rearrangement of 38*

The procedure and workup were as described for the treatment of 38c and 38t with trifluoroacetic acid. The recovered unreacted 38c* had an nmr spectrum identical with that of pure 38c except that the signal at δ 1.67 had sharpened and was reduced in area to only 3H. The major rearrangement product 46t had an nmr spectrum identical with that of pure 46t except that the signal at δ 1.60 was absent, and that at δ 1.67 had sharpened to a singlet. The amount of 46c* collected was insufficient for an nmr spectrum.

7. Acid-Catalyzed Rearrangement of 38c

A solution of pure 38c (22 mg; recovered from the treatment of a mixture of 38c and 38t with trifluoroacetic acid at room temperature for 1 hour) in 0.5 ml of trifluoroacetic acid was allowed to stand at room temperature for 12 hours. There was no change in the nmr spectrum. The solution was then heated at 60° and the nmr spectrum gradually changed. After 7.5 hours the reaction was essentially complete and

the solution was poured into a slurry of aqueous sodium bicarbonate and methylene chloride and worked up (vide supra). Vpc (5' x 0.25 in column, 10% SE-30 on chromosorb W, 80-100 mesh, 135°) gave 15% of recovered 38c and 85% of a mixture (4:1) of 46t and 46c whose spectra (ir, nmr) were identical with those described above.

8. Epoxidation of 3,4,6,6-tetramethyl-2,4-cyclohexadienone 53

To a solution containing 5.0 g (0.033 mol) of 53[22] in 25 ml of methylene chloride was added, at 0°, a solution of m-chloroperbenzoic acid (5.9 g, 0.034 mol) in 50 ml of methylene chloride. The reaction, which was followed by nmr, was complete in about an hour, during which time m-chlorobenzoic acid precipitated from solution. The precipitated m-chlorobenzoic acid was removed by filtration. The solvent of the filtrate was removed by rotary evaporation, and the residue, which consisted essentially of compound 39 and a trace amount of m-chlorobenzoic acid as shown by an nmr spectrum, was chromatographed on a short column of Florisil (80-100 mesh) using ethyl ether as eluent. Compound 39 was obtained in nearly quantitative yield and was identified by comparison of its ir and nmr spectra with those of an authentic sample.[19]

9. Acid-Catalyzed Rearrangement of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone, 39

A solution of 39 (200 mg, 1.21 mmol) in 1 ml of trifluoroacetic acid was stirred at room temperature for 1/2 hour, then poured into a slurry of aqueous sodium bicarbonate solution and methylene chloride. The organic layer was separated, washed successively with aqueous sodium bicarbonate and saturated aqueous sodium chloride, and dried ($MgSO_4$). Evaporation of the solvent left 192 mg of a light yellow oil which, when subjected to analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 175°), showed two peaks corresponding to 54 (retention time 4.5 min, 53%) and 55 (retention time 16 min, 47%). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 180°) gave 2,3,6,6-tetramethyl-2-cyclohexen-1,5-dione (54): ir (CCl_4) 2950 (s), 1720 (s), 1665 (s), 1640 (s), 1390 (m), 1365 (w), 1250 (w), 1165 (w), 1045 (w), 875 (s) cm^{-1}; uv (MeOH) λ_{max}245 nm (ε 7,800); nmr (CCl_4) δ 1.20 (s, 6H), 1.77 (m, 3H), 1.97 (m, 3H), 3.10 (m, 2H); mass spectrum (70 eV) m/e (rel intensity) 167 (5), 166 (39), 123 (11), 97 (8), 96 (100), 70 (9), 68 (37), 66 (28), 53 (16), 44 (9), 43 (13), 42 (15), 41 (36).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.13; H, 8.55

4-Methylene-5-hydroxy-3,6,6-trimethyl-2-cyclohexenone (55): ir (CCl_4) 3500 (br), 3000 (m), 1670 (s), 1595 (w),

1390 (m), 1250 (w), 1170 (w), 1160 (w), 930 (w), 875 (s) cm^{-1}; uv (MeOH) λ_{max}270 nm (ε 16,430); nmr ($CDCl_3$) δ 1.00 (s, 3H), 1.10 (s, 3H), 2.05 (d, 3H, J = 2 Hz), 2.90 (s, 1H, disappeared in the presence of D_2O), 4.10 (m, 1H), 5.43 (m, 1H), 5.57(m,1H),5.70 (m, 1H); mass spectrum (70 eV) m/e (rel intensity) 167 (5), 166 (21), 123 (28), 122 (13), 121 (100), 107 (20), 105 (44), 95 (18), 91 (27), 79 (27), 77 (25), 67 (35), 66 (53), 65 (20), 55 (16), 53 (21), 51 (21).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.17; H, 8.39

10. 2-Deutero-3-trideuteromethyl-4,5-epoxy-4,6,6-trimethyl-2-cyclohexenone, 39*

To a solution containing 500 mg (3.01 mmol) of 39 in 15 ml of dimethyl sulfoxide-d_6 was added with stirring and under N_2, 370 mg (3.30 mmol) of potassium t-butoxide. The mixture was stirred at room temperature for 3 hours, then quenched with ice-water and extracted with ether. The combined organic layers were dried (Na_2SO_4) and the solution was evaporated to give a nearly quantitative yield of 39*. The nmr spectrum was identical to that of the starting material, except that the signals at δ 2.08 and 5.72 had disappeared.

11. Acid Rearrangement of 39*

The procedure and workup were as described for the treatment of 39 with trifluoroacetic acid. The rearrangement product 54* had an nmr spectrum identical with that of 54 except that the signal at δ 1.97 disappeared and that at δ 1.77 had sharpened to a singlet. The other product, 55*, had an nmr spectrum identical with that of 55 except that the signals at δ5.70 and 2.05 were absent.

12. Acid Treatment of 4-methylene-5-hydroxy-3,6,6-trimethyl-2-cyclohexenone, 55

A solution of 55 (100 mg, 0.61 mmol) in 0.5 ml of trifluoroacetic acid was stirred at room temperature, the reaction being monitored by nmr. The nmr spectrum of 55, which remained constant with time, in neat TFA showed: δ 1.27 (s, 3H), 1.30 (s, 3H), 2.20 (d, 3H, J = 2 Hz), 4.47 (m, 1H), 5.82 (m, 2H), and 6.03 (m, 1H). After being stirred at room temperature for 15 hours, the reacti-on mixture was quenched by pouring it into ice and saturated $NaHCO_3$ solution. The mixture was extracted with methylene chloride and worked up as described for the acid rearrangement of 39. The only product (determined by nmr) after 15 hr was unrearranged 55.

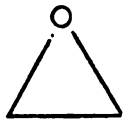
PART II

PHOTOCHEMISTRY OF CYCLOHEXADIENONE EPOXIDES

INTRODUCTION

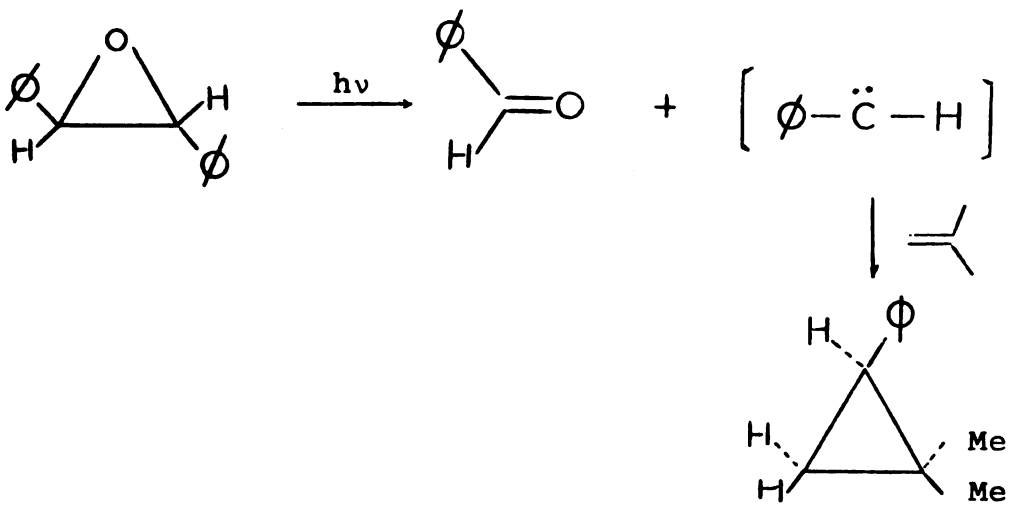
The unusual ground-state reactivity of epoxides has long been recognized and exploited. Only in recent years, has the excited-state chemistry of these inherently strained substrates been intensively explored and the potential synthetic utility of the photoreactions received attention.

Irradiation of the parent compound, ethylene oxide, results in decomposition of the molecule.[23]

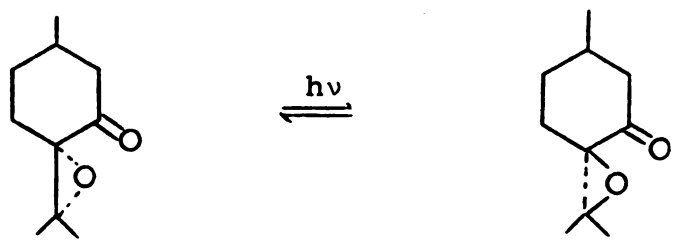


$$\xrightarrow{h\nu} \quad CH_4 + C_2H_6 + H_2 + CO + H_2CO + CH_3CHO$$

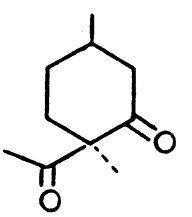
Aryl substituted oxiranes undergo photofragmentation in solution to give arylcarbenes and carbonyl compounds. The arylcarbenes react in alkene solvents to give the corresponding cyclopropanes via addition to the double bond.[24]



Photolysis of α,β-epoxy ketones generally gives β-diketones. Reusch and co-workers[25] observed that α- and β-pulegone oxide, 61 and 62, are interconvertable; the β-diketones 63 are formed at a slower rate photochemically.

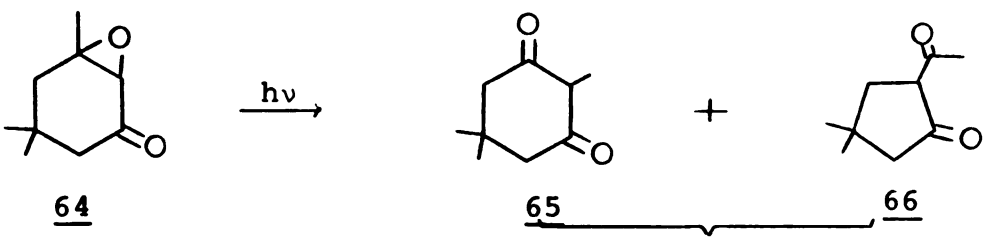


61 62



63

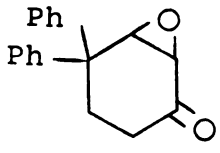
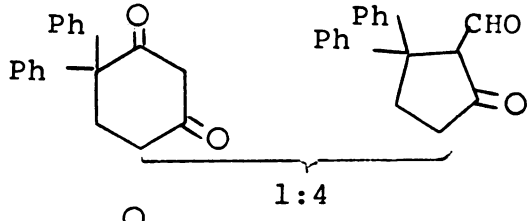
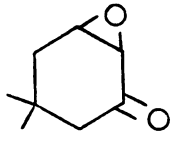
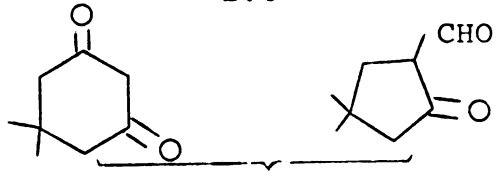
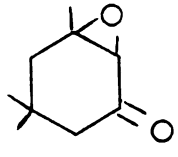
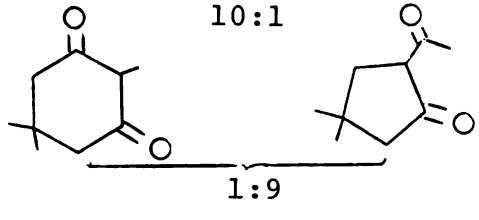
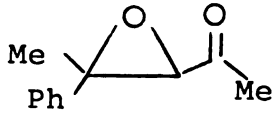
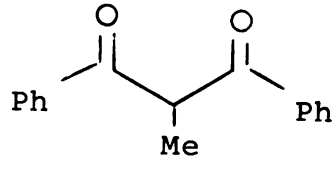
A similar transformation on irradiation of 3,5,5-trimethyl-2,3-epoxycyclohexanone 64 results in a 1:9 mixture of 2,5,5-trimethyl-cyclohexane-1,3-dione 65 and 2-acetyl-4,4-dimethylcyclopentanone 66.



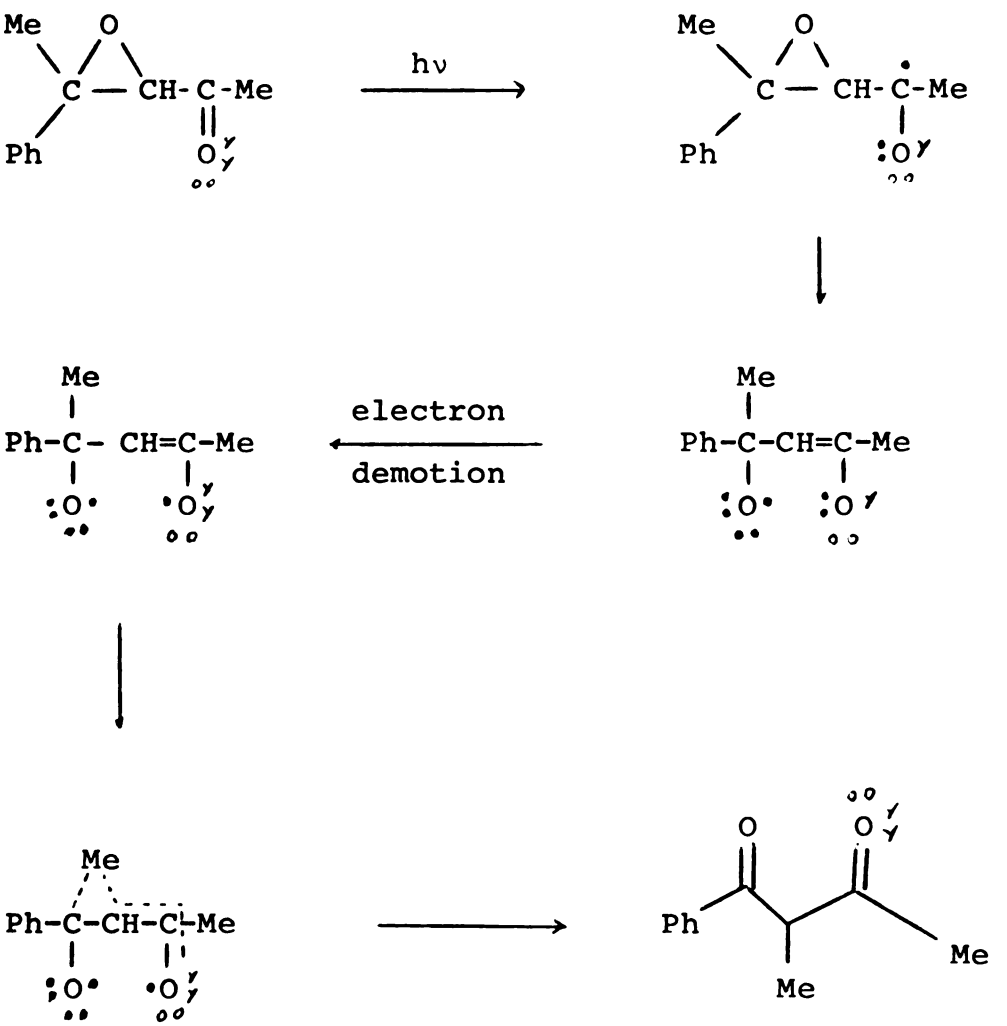
The rearrangement of α,β-epoxyketones involves a characteristic preferential shift of a β-alkyl rather than a β-aryl substituent (see Table I). The following order in migratory aptitude of the β-substituent is based upon the observations described in Table I: benzhydryl and benzyl > hydrogen > methylene > methyl > phenyl.[26]

Zimmerman and co-workers[28] suggested that these rearrangements are initiated by excitation of an electron from a non-bonding orbital situated on the carbonyl oxygen to an antibonding π-orbital. Substituents α to the carbonyl group should be expelled readily by elimination either as anions or as free radical species from the n,π*-excited state. Thus, Zimmerman postulated that the unusual migratory aptitude observed in these systems is in accord with homolytic carbon-oxygen bond fission. Using the "circle,

Table I. Migratory Aptitudes of the β-substituent in the Conversion of the α,β-Epoxyketones to β-Diketones

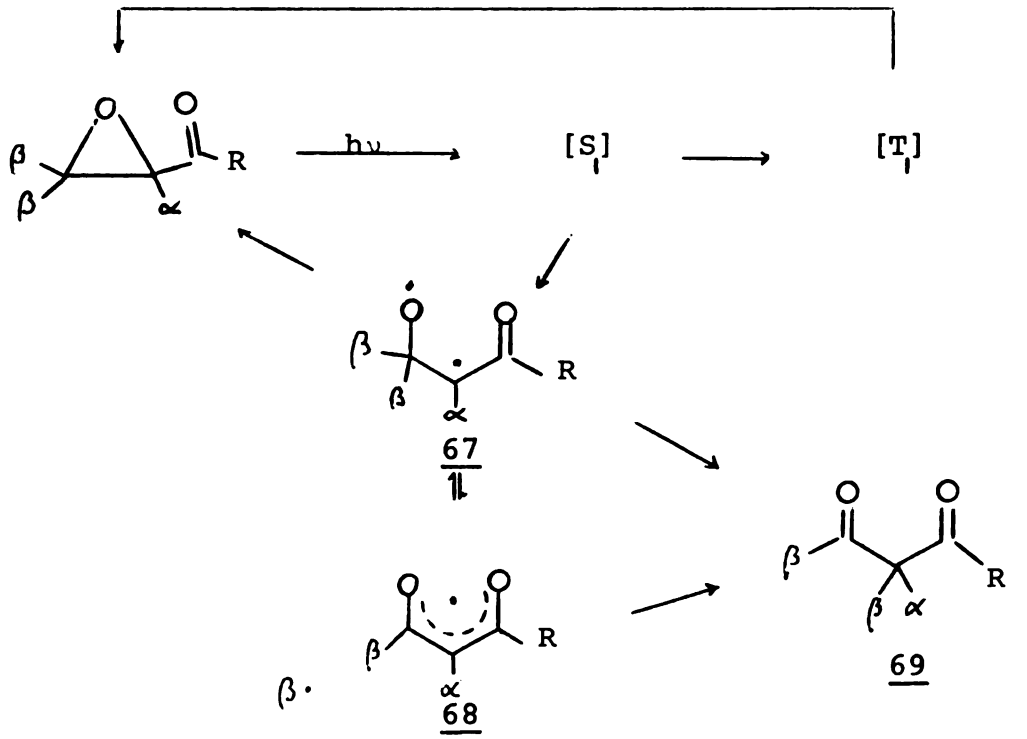
Epoxyketones	Diketones	β-substituents migrating preferentially	Other	Ref.
	 1:4	Ph_2C	H	26
	 10:1	H	CH_2	26
	 1:9	CH_2	Me	26
		Me	Ph	27

dots, y" notation [29] where π electrons are depicted as solid dots, heavily S-weighted electrons as circular dots and P_y electrons as small y's, the suggested mechanism is depicted in the following scheme:



Migration is presumed to occur either by methyl-radical expulsion with intermolecular recombination or by recombination within the solvent cage.

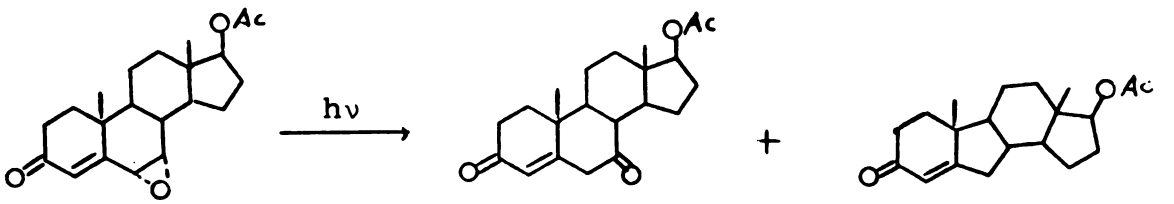
In an elaboration of the mechanism, Markos and Reusch[26] propose the scheme:



A rationalization for the abnormal migration aptitudes has been advanced in which it is suggested that the migrating group has radical character, such as is also observed in the fragmentation mechanism involving the caged radical pair 68. The position of hydrogen in the order of migratory aptitudes, however, militates against a general fragmentation mechanism, since hydrogen atoms are not generally produced in preference to alkyl radicals.[30] These authors, therefore, prefer a single step or synchronous route for rearrangement from 67 to 69.

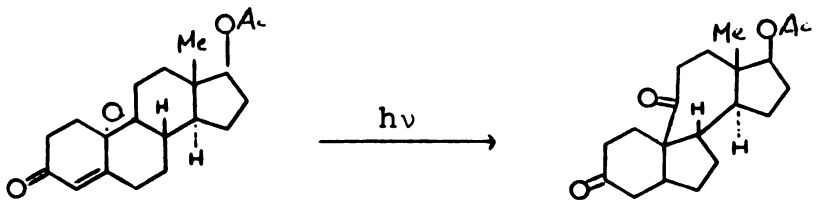
Whereas the photochemistry of α,β-epoxyketones has been studied extensively,[31] there has been very little work done on the photochemistry of vinylogous epoxycarbonyl compound. Most studies in this field were done by two Swiss workers, O, Jeger and K. Schaffner on γ,δ-epoxy-α,β-unsaturated ketosteroids.

Jeger and coworkers[32] noted that 70 isomerized to 71 and 72 upon photolysis.

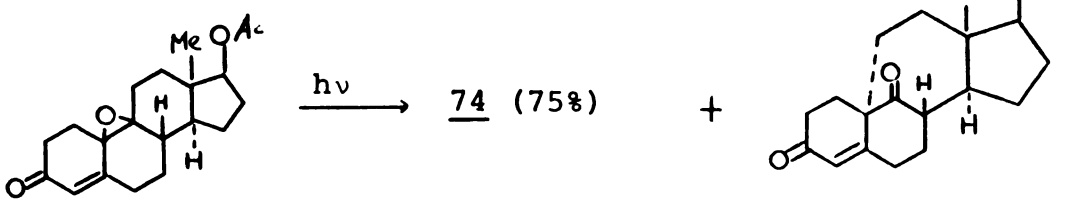


70 71 72

The photochemical rearrangement of the γ,δ-epoxyketones 73 and 75 has also been reported.[33]



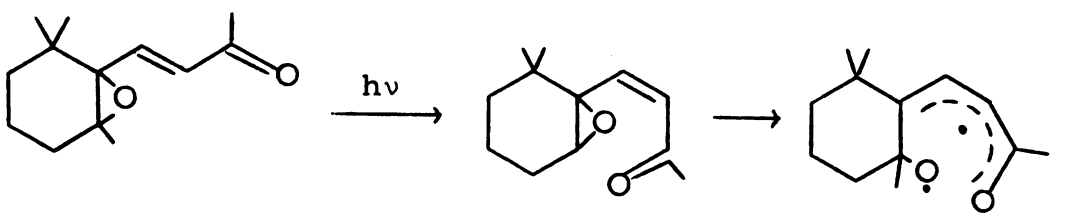
73 74



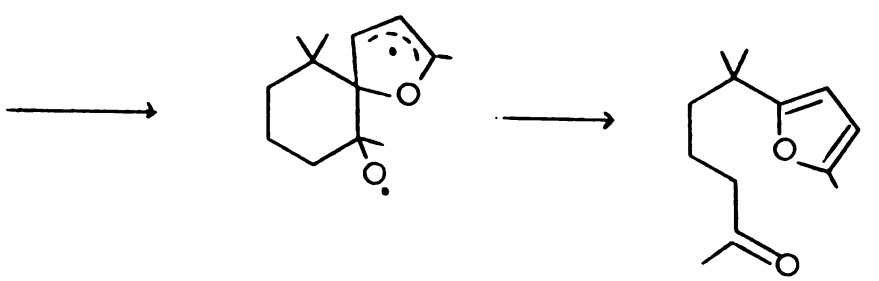
75 76 (25%)

Their results have been used to illustrate to what extent stereoelectronic control due to conformational constraints in alicyclic systems may provide for selective transformations of such α,β-unsaturated-γ,δ-epoxyketones.

Reaction pathways other than $\delta \rightarrow \gamma$ migration become available when the enone group is aliphatic and thus is geometrically less constrained than it is within a cyclic framework. O. Jeger and co-workers[34] studied the conversion of trans-β-ionone epoxide 77 to the furyl ketone 81. They suggested that the trans-cis isomerization of the double bond to 78 and epoxide cleavage to 79 was followed by cyclization between the ketone oxygen and the γ carbon, and 1,4 cleavage of the resulting biradical 80.

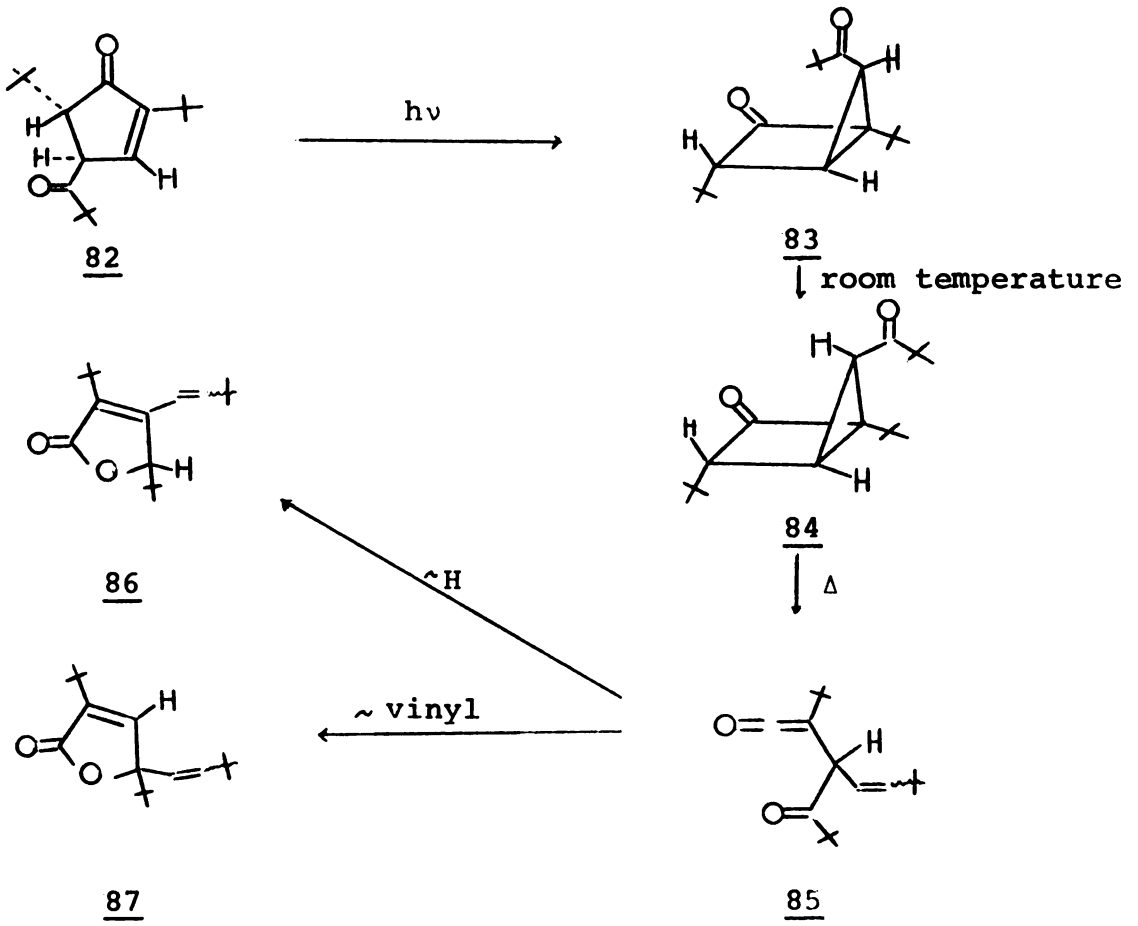


77 78 79



80 81

As a consequence of our research in this field, to be described in this part of the thesis, it is important to also give here a brief account of the photochemical rearrangements of 4-acyl-cyclopentenones and related compounds. In general these compounds rearrange upon irradiation to give bicyclo[2.1.0]pentanones. Matsuura and Ogura[35] and later Plank and Floyd[36] reported the photochemical conversion of trans-2,5-di-t-butyl-4-pivaloylcyclopent-2-enone 82 to the bicyclo[2.1.0]pentanone 83 which isomerized slowly at room temperature to its isomer 84. This in turn rearranged to butenolides 86 and 87 upon thermolysis, possibly via ketene intermediate 85.



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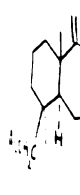
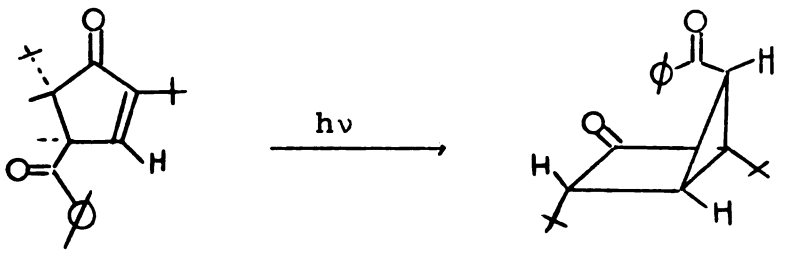


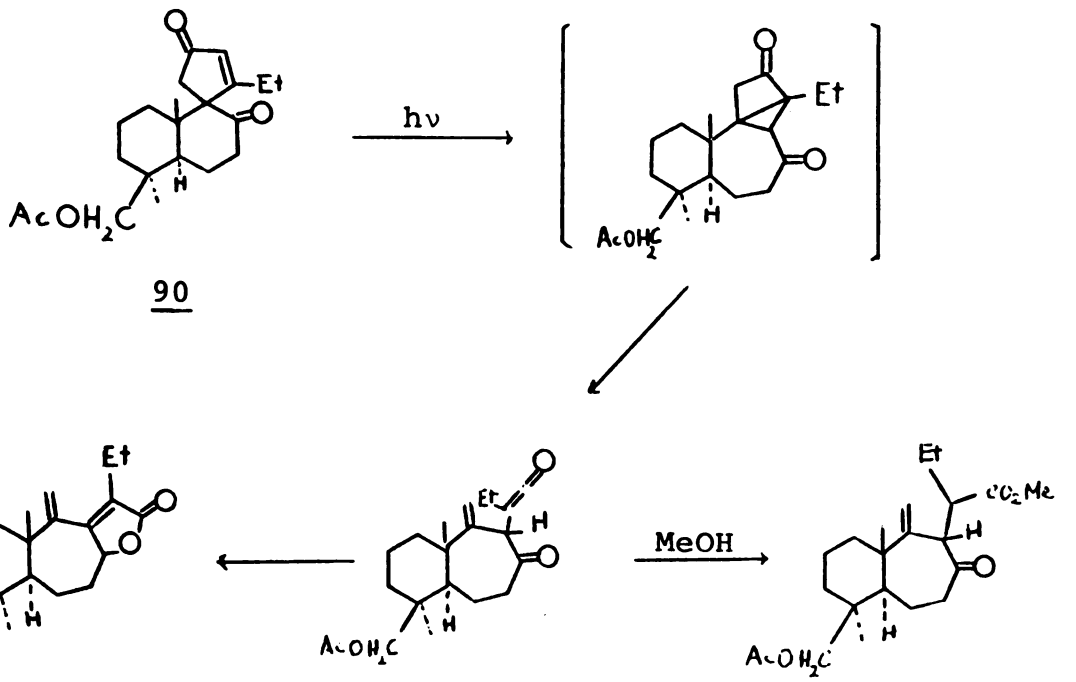
92

Similarly, photolysis of trans-2,5-di-t-butyl-4-benzoylcyclopent-2-enone 88 in methanol gave a quantitative yield of the bicyclo[2.1.0]pentanone 89.[36]



88 89

However, sometimes a bicyclo[2.1.0]pentanone is too thermolabile to be isolated and a butenolide is obtained directly as the result of photolysis. One example is the photochemical rearrangement of spirodiketone 90 to butenolide 92, in which the intermediacy of ketene 91 was established by trapping with methanol to give 93.[37]

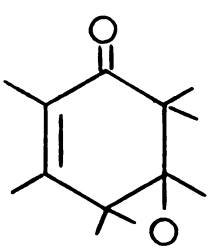


90

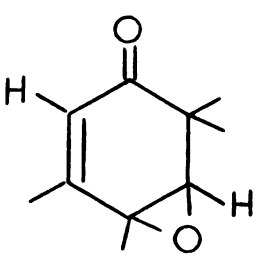
92 91 93

One interesting aspect of these reactions is that both 82 and 88 rearrange to bicyclo[2.1.0]pentanones of identical configuration. This stereospecificity suggests that these rearrangements must involve either a concerted $[\sigma 2_a + \pi 2_a]$ process or must proceed via an oxa-di-π-methane mechanism.

Our purpose of this part of the thesis is to explore reaction pathways and to examine the manner in which the various methyl groups and hydrogens influence the mode of photo-induced rearrangements of cyclohexadienone epoxides 32 and 39. The other purpose is to draw any similarities or dissimilarities between the acid-catalyzed rearrangements as described in Part 1 of this thesis and the photoinduced rearrangements of compounds 32 and 39.



32



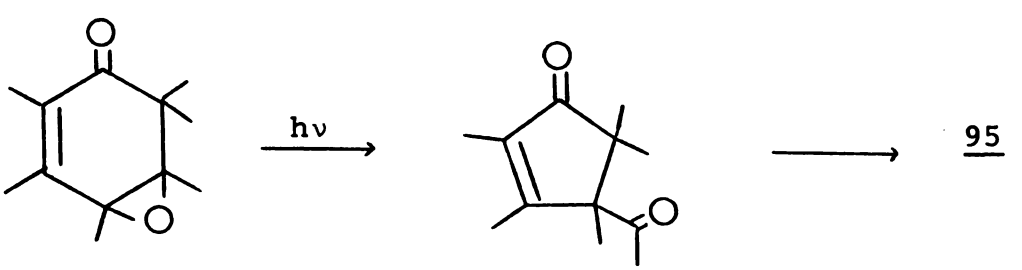
39

RESULTS AND DISCUSSION

1. Photochemistry of 4,5-epoxy-2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone, 32

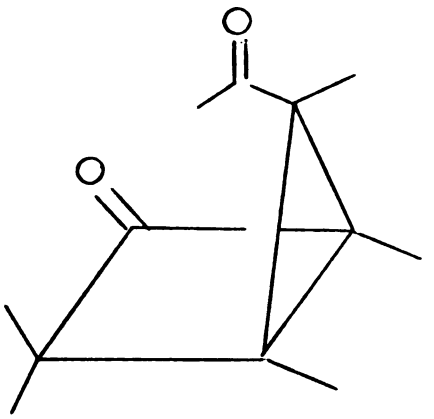
A. Product Structures

Photolysis of 4,5-epoxy-2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone 32[15] in ether through Pyrex was followed by nmr. The nmr signals from 32 began to diminish as the reaction proceeded, while those corresponding to 36 began to rise. Compound 36 is known from the acid-catalyzed rearrangement of 32.[15] As the signals from 36 reached an intensity as high as that of 32, a new set of signals corresponding to another product, 95, began to appear at the expense of both 32 and 36. The total conversion of 32 to 95 required about 16 hrs. Identical results were obtained using a uranium glass filter ($\lambda > 3300$ Å) in the photolysis.



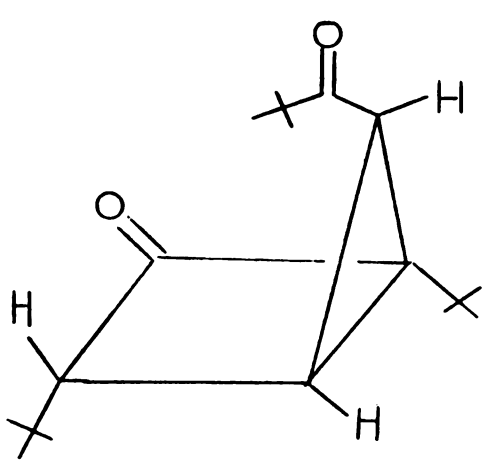
32 36 95

Compound 95 was assigned the structure shown, on the basis



95

of the following spectral data, and on its subsequent reactions. The absence of infrared bands in the region of 1500-1680 cm^{-1} together with the fact that all the methyl signals in the nmr spectrum except the one at δ 2.15 (corresponding to acetyl group) appeared above δ 1.3 and were all singlets indicated that 95 must be a saturated compound. Infrared bands at 1760 and 1710 cm^{-1} are attributed to the cyclobutanone and acetyl absorptions respectively.[20] Infrared bands at 1762 and 1701 cm^{-1} were reported for 5-pivaloyl-1,3-di-t-butylbicyclo[2.1.0]pentan-2-one 83 by Matsuura and Ogura.[35]



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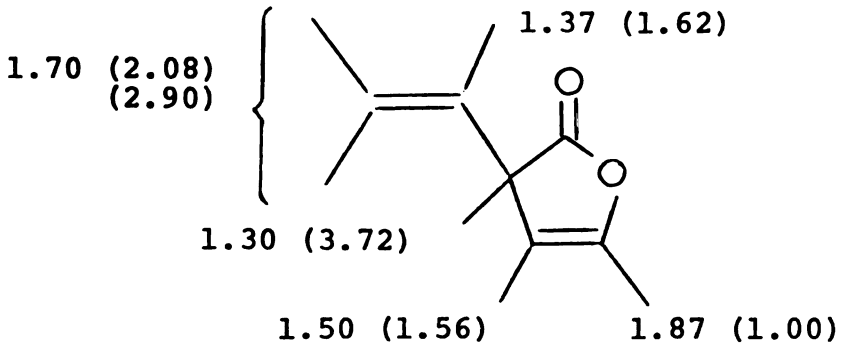
The mass spectrum showed a parent peak at m/e 194 and a base peak at m/e 152 corresponding to a loss of $CH_2=C=O$, presumably from the acetyl group. Due to its thermal lability, to be discussed below, no attempt was made to obtain an elemental analysis of 95. The acetyl group at C_5 was assigned to endo geometry. This is based on the subsequent reactivity of 95 which can be accounted for only if the acetyl group is in the endo position.

Compound 95 was photolabile and rearranged to 96 and 97 on photolysis through a Corex filter. Compound 96 was assigned the structure shown, on the basis of its spectral

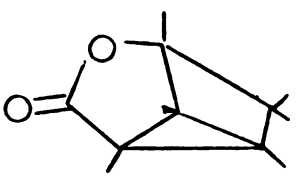


96

properties. The ir absorption at 1790 cm^{-1} is consistent with the structure of five-membered enol lactone;[20] the uv spectrum showed no conjugation within the molecule. The nmr spectrum revealed two homoallylically coupled methyls

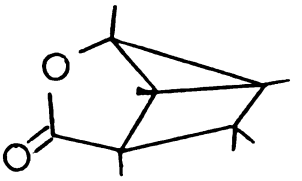
at δ 1.50 and 1.87, and singlets at δ 1.30 (3H), 1.37 (broad, 3H), and 1.70 (6H). The resonance at δ 1.37 is at a rather high field for a vinyl-methyl signal and is possibly affected by the anisotropic effect of the carbonyl group. The mass spectrum showed a base peak at m/e 151 corresponding to a loss of methyl and carbonyl moieties.

Compound 97 was tentatively assigned the structure:



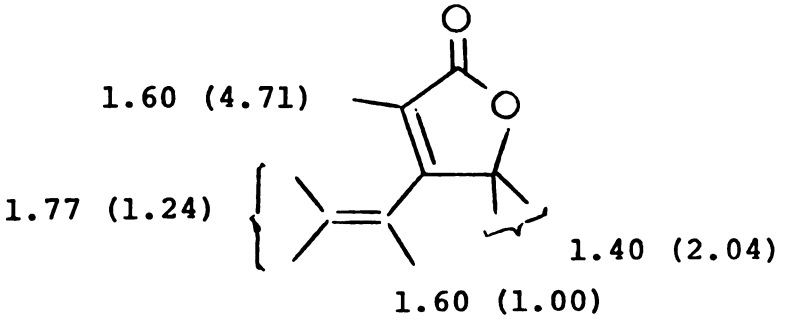
97

The fact that its nmr spectrum showed six singlet methyl signals at or above δ 1.20 and the lack of infrared bands in the region of 1500-1680 cm^{-1} indicate that 97 must be a saturated compound. The ir absorption band at 1760 cm^{-1} suggested a five-membered ring lactone.[20] The uv spectrum showed no conjugation within the molecule. The mass spectrum showed a parent peak at m/e 194 and a base peak at 135 corresponding to the loss of CO_2 and CH_3 moieties. While structure 97 is consistent with the spectral data, it has to be further confirmed by other means such as X-ray analysis or chemical transformations in order to differentiate it from isomeric structures such as 98.



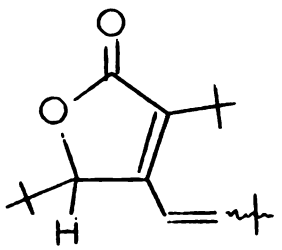
98

Compound 95 was thermally unstable. At room temperature the ir spectrum of freshly prepared 95 showed a well-defined ketene band at 2300 cm^{-1}, besides the frequencies characteristic of 95. The relative intensities of these bands remained constant, even though they did slowly diminish with and were replaced by a new set of signals corresponding mainly to 36. In an attempt to trap this ketene, freshly prepared 95 was treated with a few drops of methanol at room temperature, whereupon it rearranged to a mixture of two new compounds, 99 and 100 (ca. 1:3). Compound 99 was assigned the structure shown:



99

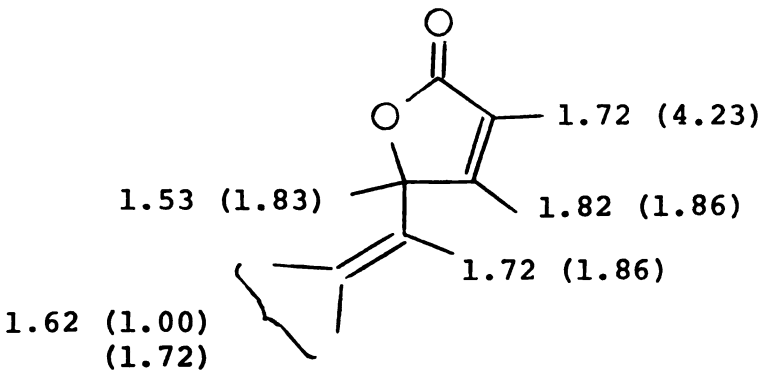
The molecular formula $C_{12}H_{18}O_2$ was confirmed by its mass spectrum (parent peak m/e 194) and elemental analysis. Compound 99 showed infrared bands at 1745 (C=O) and 1700 (C=C) cm^{-1} and uv maxima at 223 nm (ε 2,600) and at 255 nm (ε 1,070) which indicate that 91 is a Δ^1-butenolide with extended conjugation. Infrared bands at 1740 (C=O) and 1669 (C=C) cm^{-1} were reported for lactone 86 by Matsuura and Ogura.[35] In spite of an extended conjugation of the butenolide in 86, it exhibited a normal uv maximum at 215 nm (ε 8,430) for a Δ^1-butenolide and the reason for this was attributed to the non-planarity between the butenolide group and the extended double bond.



86

In its nmr spectrum, compound 99 showed two multiplets at δ 1.60 and 1.77 corresponding to six protons each and a broad six-proton singlet at δ 1.40 which may coupled with other methyls via long-range coupling. The europium shift data are also consistent with the structure.

Compound 100 was assigned the structure shown:

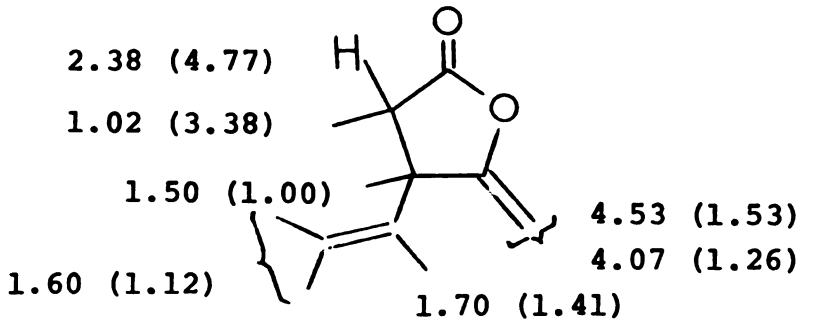


100

That it was isomeric with 95 was shown by mass spectrometry (parent peak m/e 194) and elemental analysis. In the ir region, it showed absorption at 1745 cm^{-1}; its uv spectrum showed λ_{max}230nm (ε 3,100) consistent with the presence of a Δ^{1}-butenolide moiety. The nmr spectrum showed two multiplets at δ 1.62 (6H) and 1.72 (6H), a singlet at δ 1.53 (3H) and a quartet at δ 1.82 which was shown later by a labeling experiment to be coupled to one of the methyls at δ 1.72.

Compound 95 reverted slowly to 36 when allowed to stand in the solid state at -15° for several weeks. When 95 was heated in CCl_4 in a sealed tube at 180° for 3 hrs, it was converted mainly to 36. A minor product 101 was also

isolated by vpc collection. Compound 101 was assigned the structure shown:

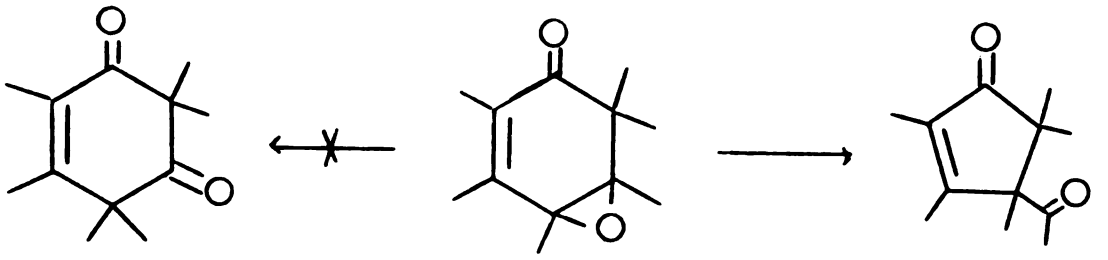


101

That 101 was isomeric with 95 was again shown by mass spectrometry (parent peak m/e 194) and elemental analysis. The ir absorption at 1795 cm^{-1} is consistent with the enol lactone structure;[20] in its nmr spectrum the compound showed the expected resonances: two vinyl protons appeared as doublets at δ 4.07 and 4.53, and are assigned to the exocyclic methylene group; a mutually coupled three proton doublet at δ 1.02 and a methine proton quartet at δ 2.38, the latter having a chemical shift which require that it be α to the carbonyl group;[39] two singlets at δ 1.50 (3H), 1.70 (3H) and a multiplet at δ 1.60 (6H). The mass spectrum showed a base peak at m/e 151 corresponding to the loss of CO and CH_3 moieties.

B. Mechanism

The primary product from the photolysis of 32 through a Pyrex filter was 36. The formation of the 4-acetylcyclopentenone 36 may occur by the cleavage of the C_4-O bond and a shift of C_6 from C_5 to C_4. The preferential ring contraction to 36 rather than methyl migration (to give 102) is consistent with the usual order of migratory aptitudes observed for the photochemical rearrangement of α,β-epoxyketones to β-diketones.[26]



102 32 36

Compound 36 rearranged further on photolysis to 95. This type of photorearrangement was not new and has been reported before by Matsuura and Ogura[35] on photorearrangement of 4-pivaloylcyclopentenone 82 and by Plank and Floyd[36] on 4-benzoylcyclopentenone 88. The mechanism for such stereospecific rearrangement was proposed as either $_{\sigma}2_a + _{\pi}2_a$ concerted process[36] or a stepwise oxa-di-π-methane mechanism.[38]

Compound 95 rearranged to 96 and 97 on photolysis through a Corex filter. The mechanisms leading from 32 to 96 and 97 are quite obvious as shown in Scheme 8. Whether

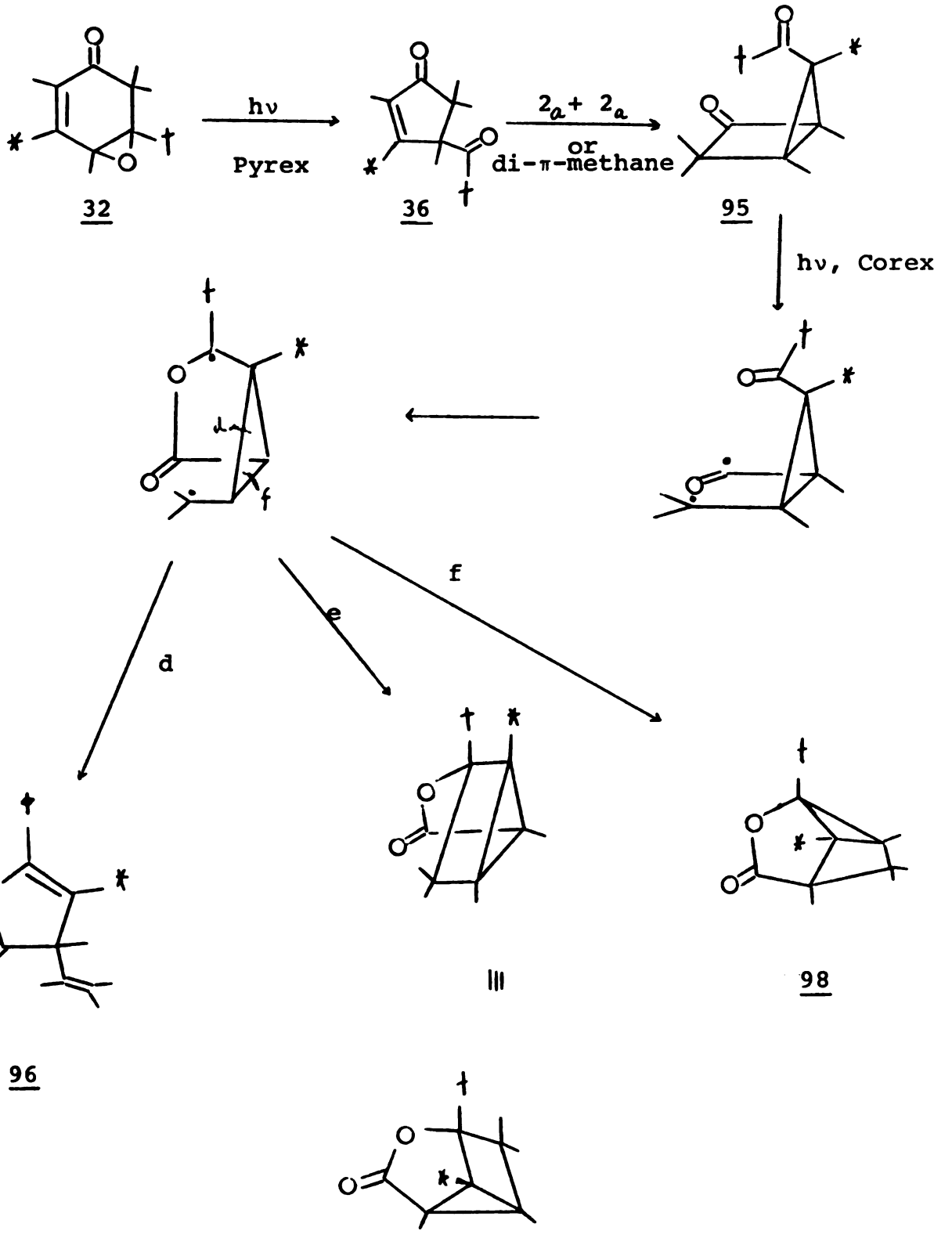
97, formed by recombination process e, or 98, by process f, is the actual photoproduct remains to be seen.

To test the plausibility of the mechanism outlined in Scheme 8, 32 labeled with CD_3 groups in the positions marked * and † (called $32^{*,\dagger}$) was synthesized and irradiated. The nmr spectrum of the primary photoproduct 36 lacked the signal at δ 1.95. When 32 labeled with a CD_3 group only at the position marked * (called 32^{*}) was rearranged, the resulting 36 had an nmr spectrum identical with that of unlabeled 36[15] except that the signal at δ 1.95 was reduced in area by 50% and the band at δ 1.75 sharpened to a singlet.

The final photoproduct 95, which was isolated when 32^{*} was the reactant, lacked the signal at δ 1.23. Starting with $32^{*,\dagger}$, the resulting 95 lacked the δ 1.23 and 2.15 signals. While there was no way of knowing the exact methyl assignments in 95 except for the acetyl group, the label at δ 1.23 was assigned to the C-5 position. This is based on the previous observations[35,36] that bicyclo[2.1.0]pentanone systems were formed stereospecifically from 4-acetyl-cyclopentenone systems, and on the subsequent transformation of 95 which would necessitate that the * label appear at the C-5 position in 95.

Compound 95 rearranged further on photolysis to 96 and possibly 97. When 95^{*} was the reactant, the product 96 lacked the signal at δ 1.50 and the quartet at δ 1.87 was sharpened to a singlet. Starting with $95^{*,\dagger}$, the resulting 96 lacked the signals at both δ 1.50 and 1.87. These label

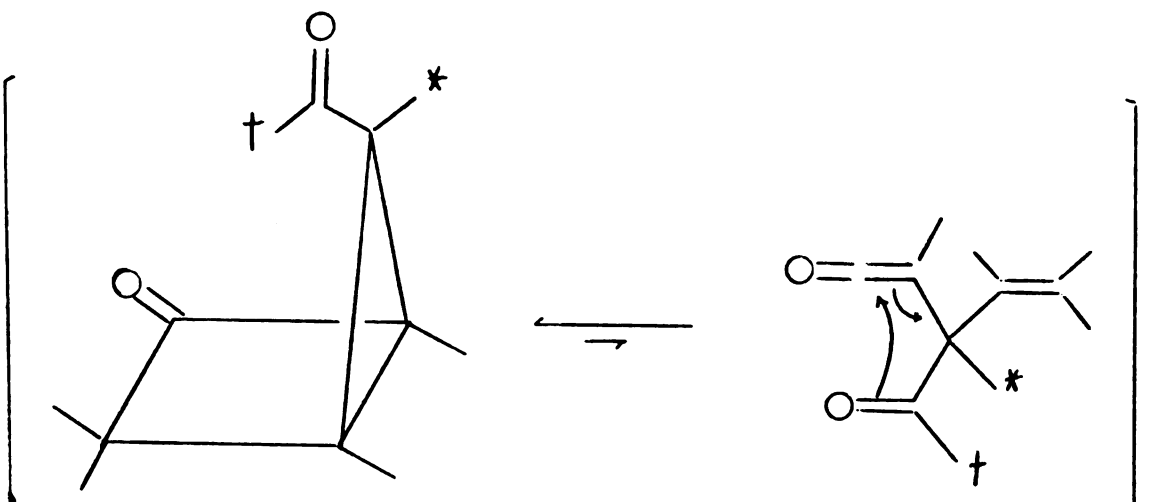
Scheme 8



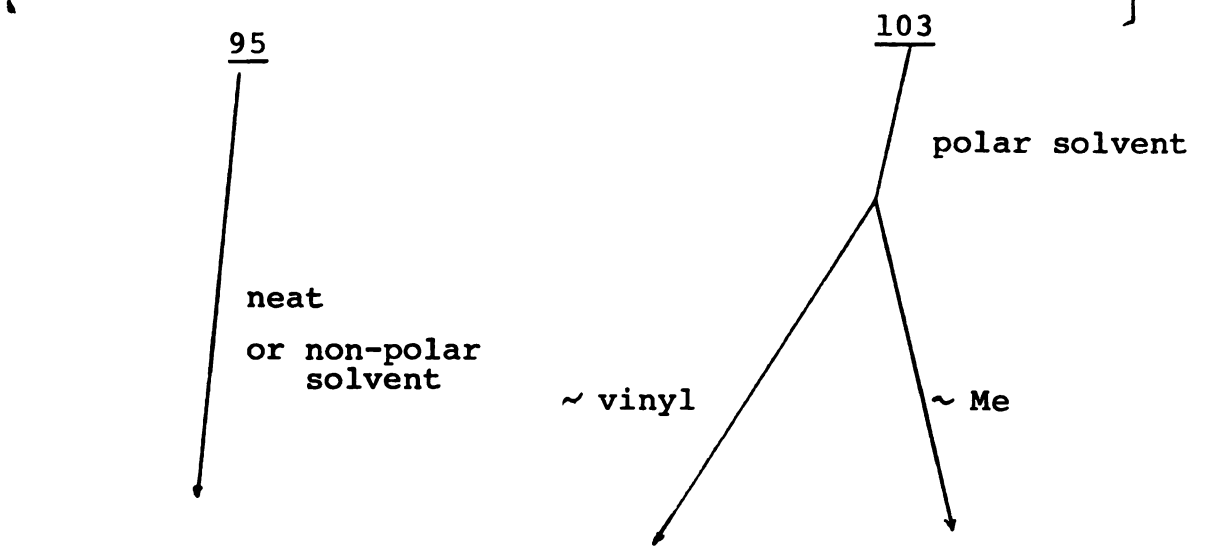
results and the suggested mechanism for the conversion of 95 → 96 are shown in Scheme 8.

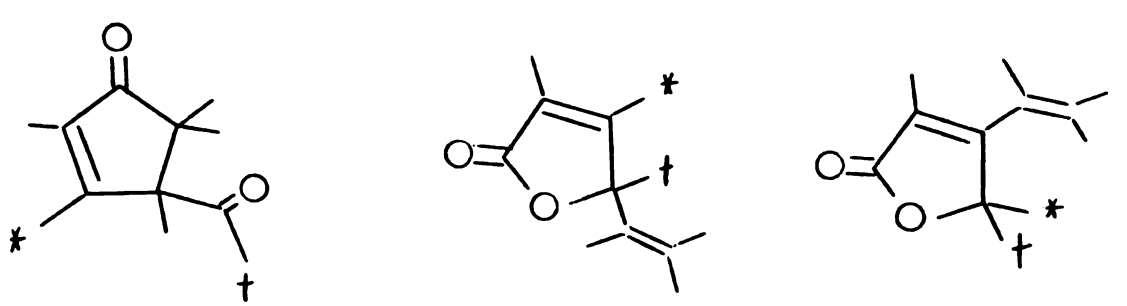
Compound 95 was thermo-labile and rearranged back to 36 either in its solid state or in a non-polar solvent such as CCl_4. At room temperature, the ir spectrum of 95 showed a well-defined ketene band at 2300 cm^{-1}. The relative intensity of this band to the carbonyl absorptions at 1760 and 1710 cm^{-1} remained constant with time. This suggested that 95 might exist in equilibrium with its ring-opened form 103. In an attempt to trap this ketene, 95 was treated with methanol. However, no ketene was trapped; instead two isomeric products 99 and 100 were obtained. A possible mechanism for the thermal transformation of 95 to 99 and 100 is shown in Scheme 9. This type of rearrangement is not new and has been observed before.[35,37] To test the plausibility of the mechansim in Scheme 9, 95 labeled with CD_3 groups in the positions marked * and † (called $95^{*,\dagger}$) was rearranged. The nmr spectrum of the resulting 99 lacked the signal at δ 1.40, and that of 100 lacked the signals at δ 1.53 and 1.82 and the multiplet at δ 1.72 was sharpened to a singlet. When 95 labeled with a CD_3 group only at the position marked * (called 95^{*}) was rearranged, the resulting 99 had an nmr spectrum identical with that of unlabeled 99 except that the area of the peak at δ 1.40 was reduced by 50%; the resulting 100 lacked the signal at δ 1.82 and the multiplet at δ 1.72 was reduced in area by 50% and was sharpened to a singlet. These labeling results fully support the proposed mechanism outlined

Scheme 9



95 103





94 100 99

in Scheme 9. The incapability of methanol to trap ketene is possibly due to the preferred intramolecular reaction over intermolecular addition to methanol. The reasons for the different effect of various solvents on the thermal rearrangement of 95 remain to be determined.

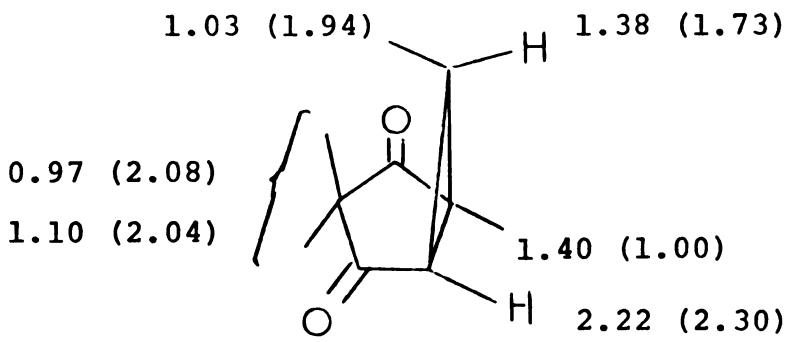
While most of the rearrangements outlined in Schemes 8 and 9 are not new, this work does offer an easy pathway to permethylated bicyclo[2.1.0]pentanones.

2. Photochemistry of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone, 39

A. Product Structures

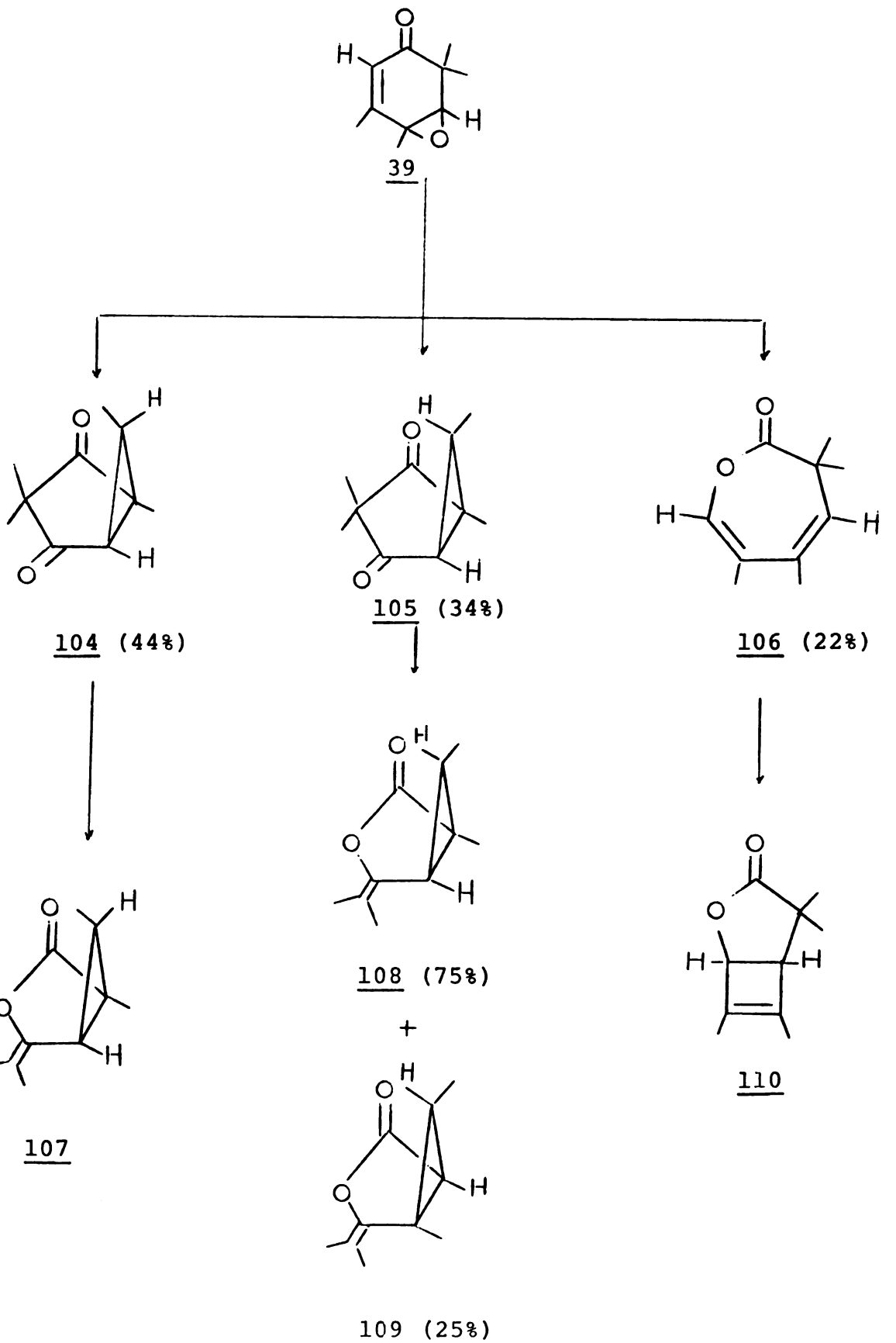
The irradiation of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone 39[19] in ether through Pyrex led to three photoproducts, 104, 105 and 106. Compounds 104 and 105 are photolabile. They rearranged slowly on further irradiation through a Pyrex filter, but much faster through a Corex filter. Compound 104 rearranged to 107, and compound 105 rearranged to 108 and 109. Compound 106 was also photolabile and rearranged to 110 on irradiation through a Corex filter (Scheme 10)

Compound 104 was assigned the structure shown, on the

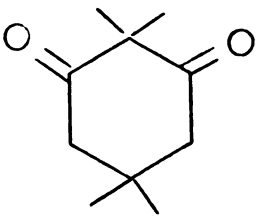


104

Scheme 10



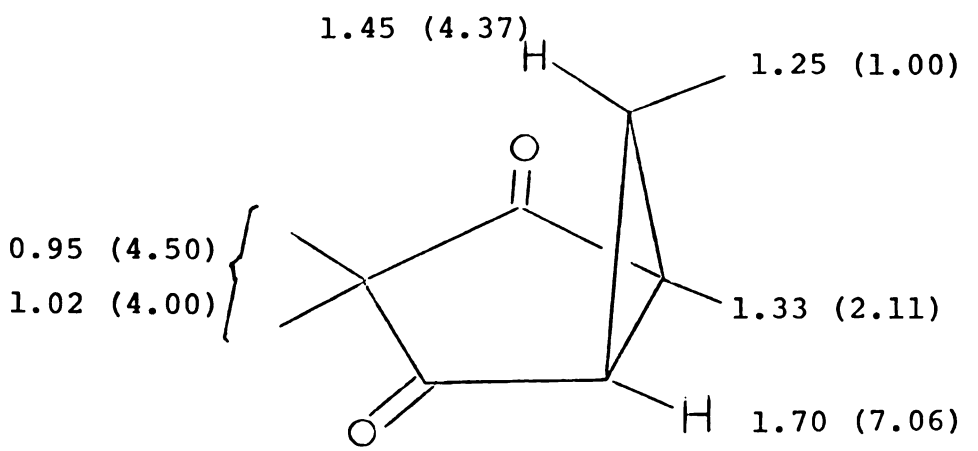
basis of the following spectral data, and on its further photoreaction. The molecular formula $C_{10}H_{14}O_2$ was confirmed by the compound's mass spectrum (parent peak m/e 166) and elemental analysis. The absence of infrared bands in the region of 1500-1680 cm^{-1} and the absence of olefinic hydrogen absorption in the nmr spectrum together with the fact that all the methyl signals appeared at or above δ 1.40 indicated that 104 must be a saturated compound. The uv spectrum possessed only end absorption and the infrared spectrum had carbonyl peaks at 1745 and 1710 cm^{-1}. These two ir absorption bands possibly originate from coupling between the two carbonyl groups. The average value of the two peaks (1727 cm^{-1}) is consistent with the carbonyl absorption characteristic of the bicyclo[3.1.0]hexan-2-one system.[40] Infrared bands at 1688 and 1717 cm^{-1} were reported for 2,2,5,5-tetramethylcyclohexanedione-1,3 111 by Eistert and Geiss.[41]



111

The structural and stereochemical assignments were based on the following nmr data (CCl_4): δ 0.97 (s, 3H), 1.03 (m, 3H), 1.10 (s, 3H), 1.38 (m, 1H), 1.40 (s, 3H) and 2.22 (d, 1H, J = 9 Hz). The magnitude of the coupling implies cis-cyclopropyl vicinal coupling[42] and thus requires that the C_6-methyl group to be endo. The europium shift data are also consistent with the structure. The mass spectrum showed a base peak at m/e 96 corresponding to the loss of a $(CH_3)_2C{=}C{=}O$ moiety.

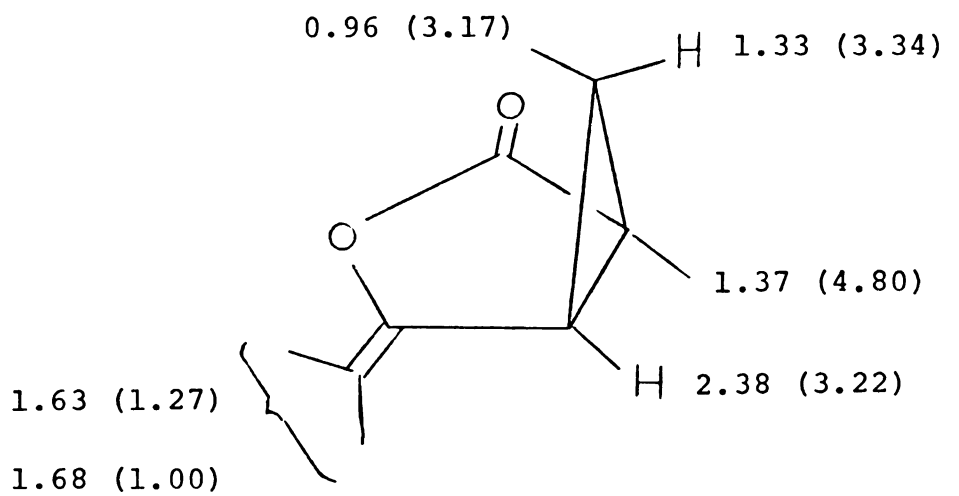
Compound 105 had nearly identical mass, ir and uv spectra with those of 104, strongly suggesting that compound 105 was structurally and stereochemically isomeric with compound 104. Its structure and stereochemical assignments shown were based on the following nmr (CCl_4) data:



105

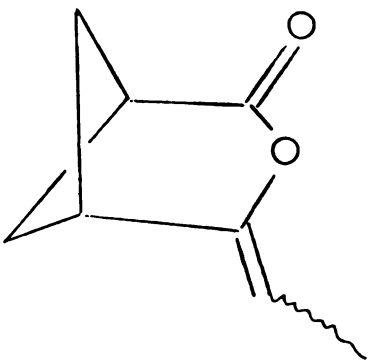
δ 0.95 (s, 3H), 1.02 (s, 3H), 1.25 (m, 3H), 1.33 (s, 3H), 1.45 (m, 1H) and 1.70 (d, 1H, J = 2 Hz). The small coupling constant for the methine protons implies trans-cyclopropyl vicinal coupling[42] and thus requires that the C_6-methyl group be exo. The europium shift data are also consistent with the structure.

Compound 107 was assigned the structure shown, on the



107

basis of the following spectral data. The molecula $C_{10}H_{14}O_2$ was confirmed by the compound's mass spectrum (parent peak m/e 166) and elemental analysis. In the ir spectrum, it showed absorptions at 1780 (C=O) and 1710 (C=C) cm^{-1}, and its uv spectrum showed λ_{max} 230 nm (ε 3,320) consistent with the enol lactone structure.[20] Infrared bands at 1783 and 1698 cm^{-1} were reported for enol lactone 112 by Gibson.[43]

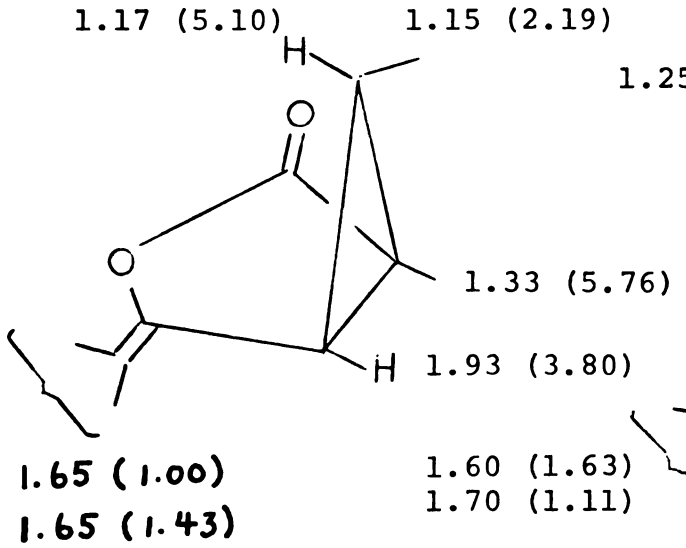


112

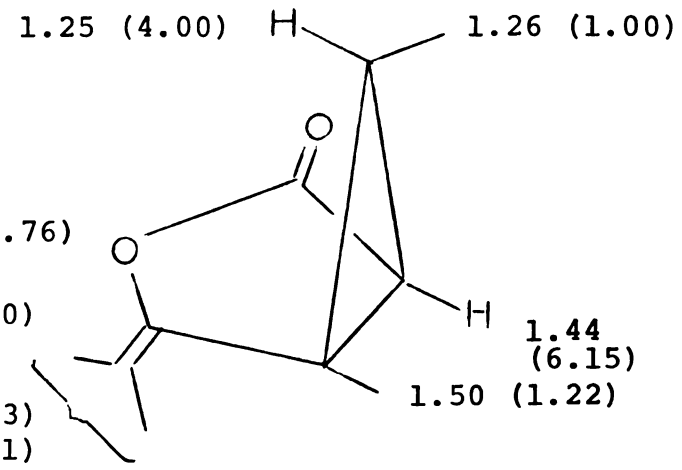
The slightly lower frequency of the carbonyl band in 107 could be due to partial conjugation of the carbonyl group with the adjacent cyclopropane ring. The stereochemical assignments were based on the following nmr data (CCl_4): δ 0.96 (m, 3H), 1.33 (m, 1H), 1.37 (s, 3H), 1.63 (s, 3H), 1.68 (s, 3H) and 2.38 (d, 1H, J = 7 Hz). The magnitude of the coupling constant implies cis-cyclopropyl vicinal coupling[42] and thus requires that the C_6-methyl group be endo. The mass spectrum showed a base peak at m/e 96. It is interesting that the mass spectra of 104 and 107 are nearly identical, suggesting that a similar rearrangement may occur on electron impact. Specific assignments within the structure are based on the europium shift data and comparison with compound 114 (vide infra).

Compounds 108 and 109 had nearly identical mass, ir and uv spectra with those of 107 which strongly suggested that they were structurally and stereochemically isomeric

with compound 107. Their structures and stereochemical assignments shown were based on their nmr data (CCl_4) and



108

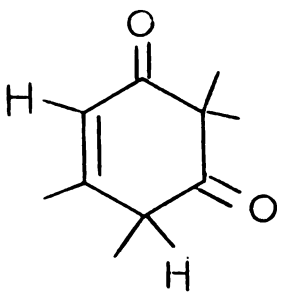


109

the results of labeling experiments to be discussed below. Compound 108 had: δ 1.15 (broad singlet, 3H), 1.33 (s, 3H), 1.17 (m, 1H), 1.65 (s, 6H) and 1.93 (broad singlet, 1H); compound 109 had: δ 1.25 (m, 1H), 1.26 (m, 3H), 1.44 (d, 1H, J = 3 Hz), 1.50 (s, 3H), 1.60 (s, 3H) and 1.70 (s, 3H). The magnitude of the coupling constant between the hydrogen at ring juncture and the C_6-H implies cis-cyclopropyl vicinal coupling[42] and thus requires that the C_6-methyl group be exo. The positions of the methyl groups at the ring junctures were assigned based on the europium shift data and by

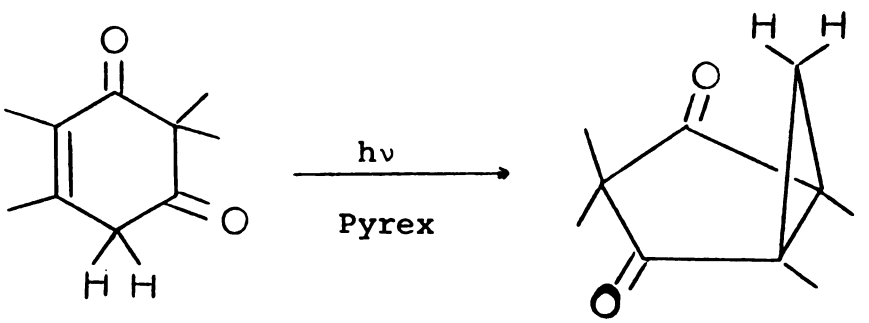
comparison with the model compound 114 (vide infra).

Since the diketone 115, which was not isolated, was suspected to be the precusor of compounds 104 and 105 in the photolysis of 39, compound 54, an analog of diketone 115,



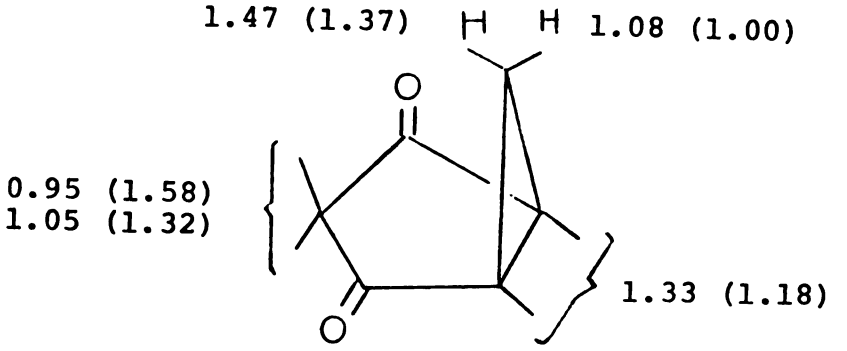
115

was subjected to photolysis under similar conditions. Compound 54 was obtained from the acid-catalyzed rearrangement of epoxyketone 39 (see Part I). On photolysis through a Pyrex filter, compound 54 rearranged to 113.



54 113

Compound 113 was assigned the structure shown, on the

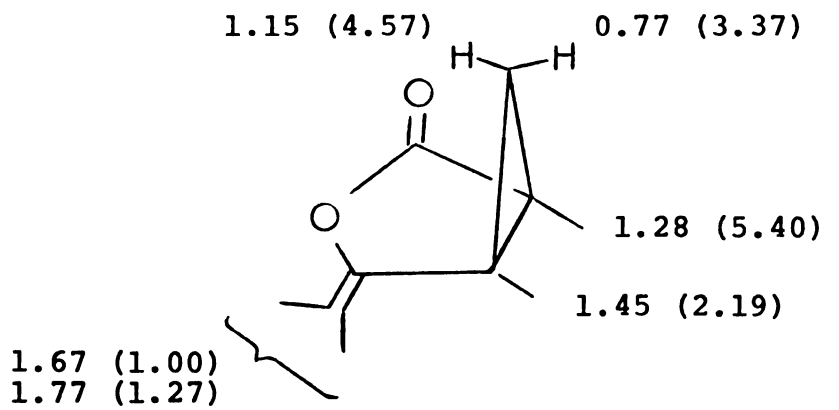


113

basis of the following spectral data, and on its subsequent reaction. Molecular formula $C_{10}H_{14}O_2$ was confirmed by the compound's mass spectrum (parent peak m/e 166) and elemental analysis. It had nearly identical ir and uv spectra with those of 104 and 105. The symmetrical structure of the molecule was suggested by the presence of two equivalent methyls at the ring junctures as revealed by its nmr spectrum and was later further confirmed by a labeling experiment (see experimental section). Besides the two equivalent methyls at δ 1.33 (s, 6H), the nmr spectrum showed two three-proton singlets at δ 0.95, 1.05 and two one-proton doublets at δ 1.08, 1.47 with a coupling constant of 5 Hz. The assignments for the methylene bridge protons were based on the europium shift data, since the proton on the same face of the carbonyl moieties (endo-H) should be shifted

downfield at a faster rate than the exo-H. The downfield chemical shift of the endo bridged methylene proton at δ 1.47 as compared with exo methylene proton at δ 1.08 is attributable to the anisoptropic deshielding effect of the carbonyl moieties. The mass spectrum showed a base peak at m/e 96 corresponding to the loss of a $(CH_3)_2C{=}C{=}O$ moiety.

Compound 113 was photolabile and rearranged to 114 on irradiation through a Corex filter. Compound 114 was assigned the structure shown, on the basis of its spectral

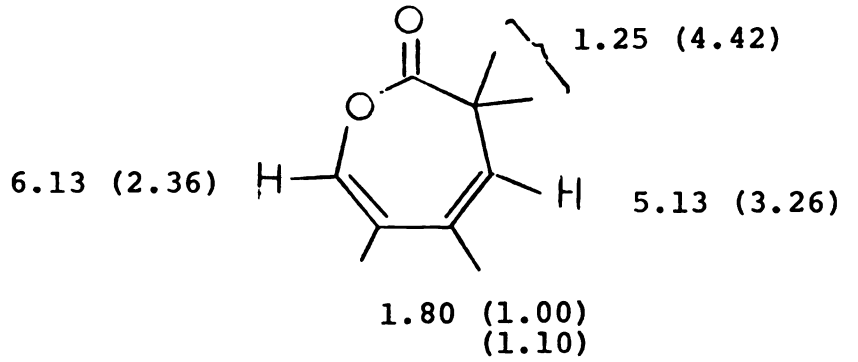


114

properties. The molecular formula $C_{10}H_{14}O_2$ was again confirmed by the mass spectrum (parent peak m/e 166) and elemental analysis. Compound 114 had nearly identical ir and uv spectra with those of 107, 108 and 109. Its nmr spectrum showed two three-proton singlets at δ 1.28 and 1.45 and two one-proton doublets at δ 0.77 and 1.15 with a coupling

constant of 4 Hz. The assignments for the methylene protons were made by applying the same arguments as were used with compound 113. The assignments for the ring-junctured methyls were based on europium shift data. Assuming that the shift reagent coordinates at the carbonyl group,[44] the methyl group at δ 1.28 which has the larger europium shift is assigned to the position next to the carbonyl group. The mass spectrum of 114 showed a base peak at m/e 96 and had a fragmentation pattern very similar to that of 113.

Compound 106 was assigned the structure shown, on the

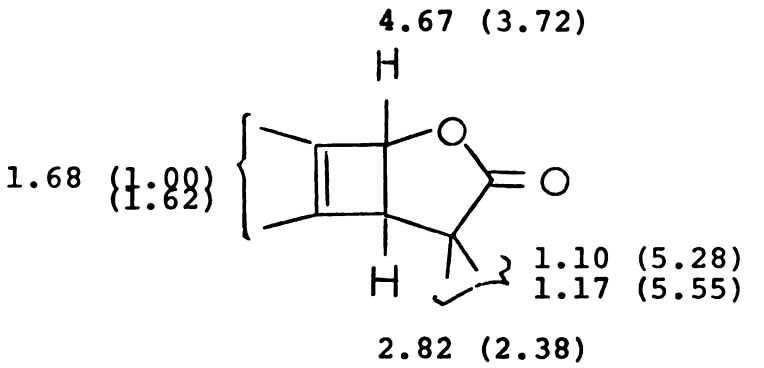


106

basis of the following spectral data, and on its subsequent reaction. The molecular formula $C_{10}H_{14}O_2$ was confirmed by the mass spectrum (parent peak m/e 166) and elemental analysis. The presence of two equivalent gem-dimethyls

as revealed by its nmr spectrum suggested that compound 106 possessed a plane of symmetry, or readily passed through such a conformation. Besides the two equivalent gem-dimethyls at δ 1.25, the nmr spectrum showed two vinyl-methyls centered at δ 1.80 as a multiplet and two vinyl hydrogens at δ 5.13 and 6.13 where each appeared as a broad singlet. Homoallylic coupling between the C_3-H and the C_4-methyl was revealed by a labeling experiment (see experimental section). The uv spectrum showed a maximum at 240 nm (ε 3,225) which indicates that compound 106 has a diene moiety. A uv maximum at 248 nm (log ε 3.87) was reported for 1,3-cycloheptadiene by Pesch and Friess.[45] The ir absorption at 1745 cm^{-1} showed that there is no conjugation between the carbonyl group and the diene moiety. The mass spectrum showed a base peak at m/e 123 corresponding to the loss of methyl and carbonyl moieties. The exact disposition of vinyl hydrogens and methyls on the diene moiety is based on their chemical shifts, europium shift data, on the structure of the photoproduct 110 (vide infra) from 106, and on the labeling experiment to be discussed below.

Compound 110 was assigned the structure shown on the basis of its spectral properties. That it was isomeric with 106 was shown by mass spectrometry (parent peak m/e 166)

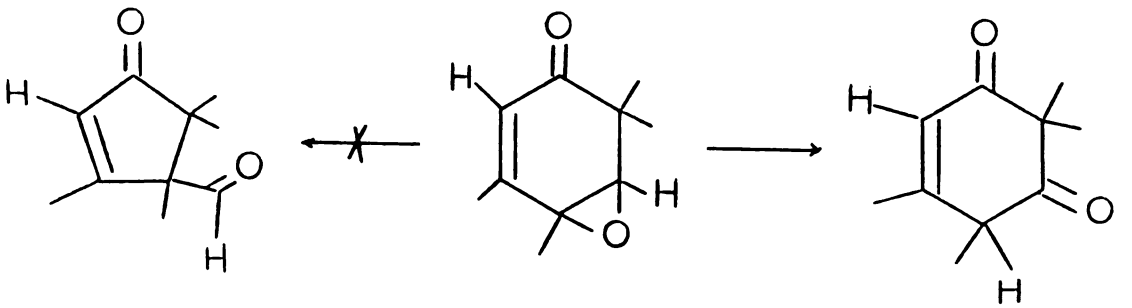


110

and elemental analysis. In the ir region, it showed absorption at 1780 cm^{-1} consistent with a γ-lactone structure.[20] The uv spectrum showed no conjugation within the molecule. In its nmr spectrum the compound showed two aliphatic methyls at δ 1.10 and 1.17 where each appeared as a singlet, two vinyl methyls at δ 1.68 which happened to have the same chemical shift and appeared as a singlet, a one-proton multiplet at δ 2.82 and a one-proton doublet at δ 4.67 with a coupling constant of 4 Hz. The homoallylic coupling between the two vinyl methyls was revealed by spreading the signal at δ 1.68 into two multiplets using europium shift reagent. The strongly deshielded absorption at δ 4.67 placed that C-H adjacent to the oxygen atom.[39] The mass spectrum showed a base peak at m/e 123 corresponding to the loss of methyl and carbonyl moieties.

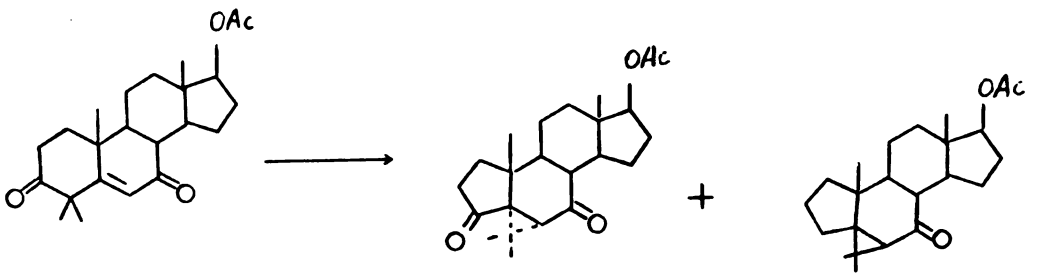
B. Mechanism

The photolysis of compound 39 in anhydrous ether through a Pyrex filter resulted in the formation of 104, 105 and 106. Since the photochemistry of either α,β-epoxyketones or vinylogous epoxyketones generally leads to β-diketones,[42,43,44] compound 115 was suspected to be involved as an intermediate in the photorearrangement of 39. Though no direct evidence could be obtained for the formation of 115 during the course of the irradiations, support for the presence of 115 was provided by the observation that compound 54, a structural analog of 115, rearranged on photolysis to 113 which is analogous to 104 and 105. Compound 113 rearranged further on photolysis to 114 which is analogous to 107, 108 and 109. The formation of 115 from the photorearrangement of 39 may occur by the cleavage of the C_4-O bond and a hydrogen migration from C_5 to C_4. The preferential hydrogen migration to give 115 rather than ring contraction to give 116 is



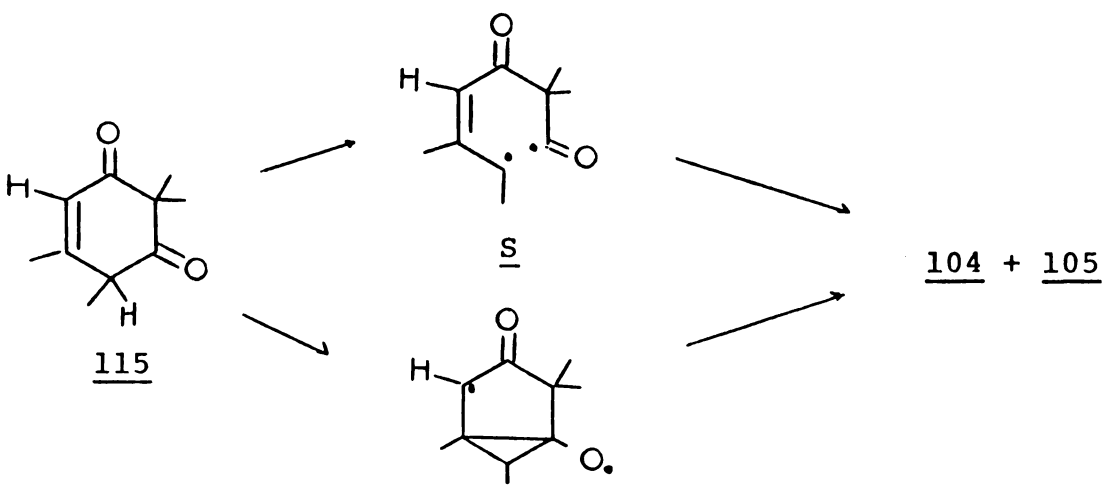
116 39 115

consistent with the usual order of migratory aptitude observed for the photochemical rearrangement of α,β-epoxy-ketones to β-diketones.[26] Assuming that 115 is an intermediate, three possible mechanisms can be envisioned for the rearrangement of 115 → 104 + 105 as were proposed by Saboz[46] for the photorearrangement of 117 → 118 + 119.



117 118 119

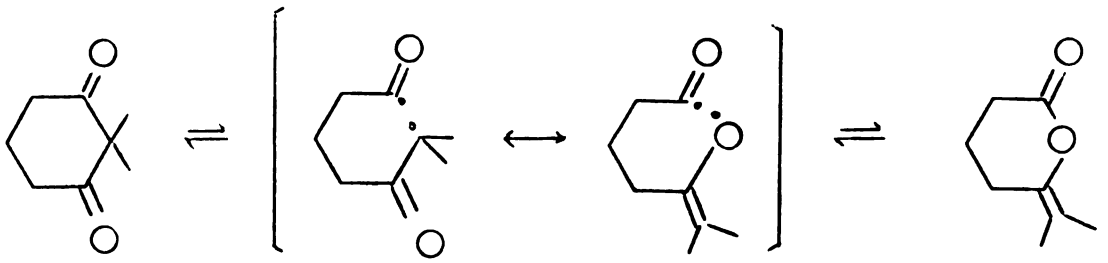
These are: 1) a step by step process through diradicals S; 2) a step by step process through diradical T (i.e., an oxa-di-π-methane rearrangement); 3) or a concerted $_{\sigma}2_{a} + _{\pi}2_{a}$ cycloaddition reaction.



115 S 104 + 105

T

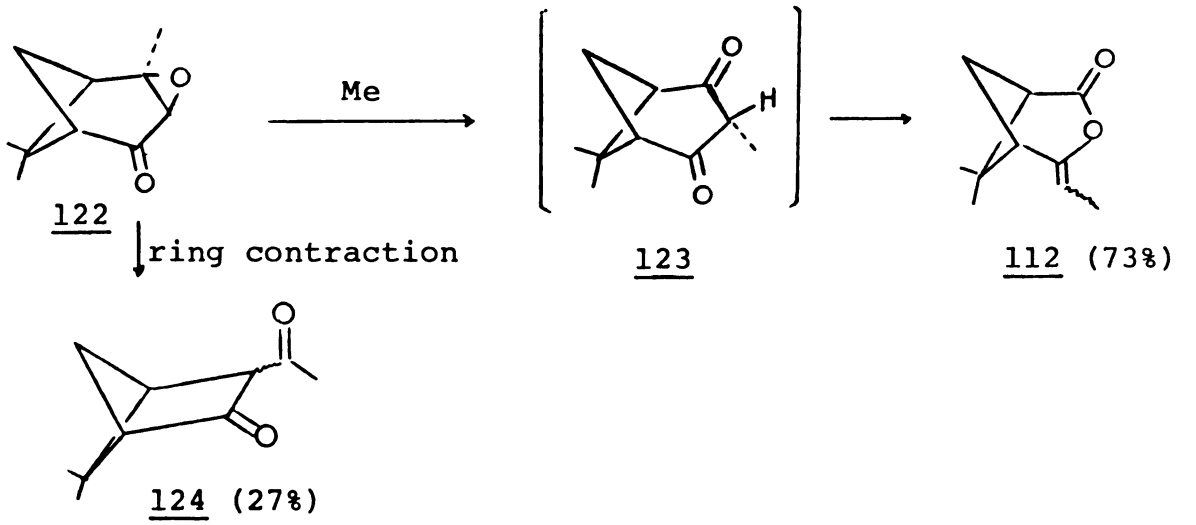
Compound 104 rearranged further on photolysis to 107, and 105 rearranged to 108 and 109. The photochemical rearrangement of non-enolizable β-diketones is known to give predominantly enol lactones with an exocyclic olefinic double bond. For example, Nozaki and coworkers[47] reported that 2,2-dimethyl-1,3-cyclohexanedione 120 afforded exclusively the exocyclic enol δ-lactone 121 on photolysis.



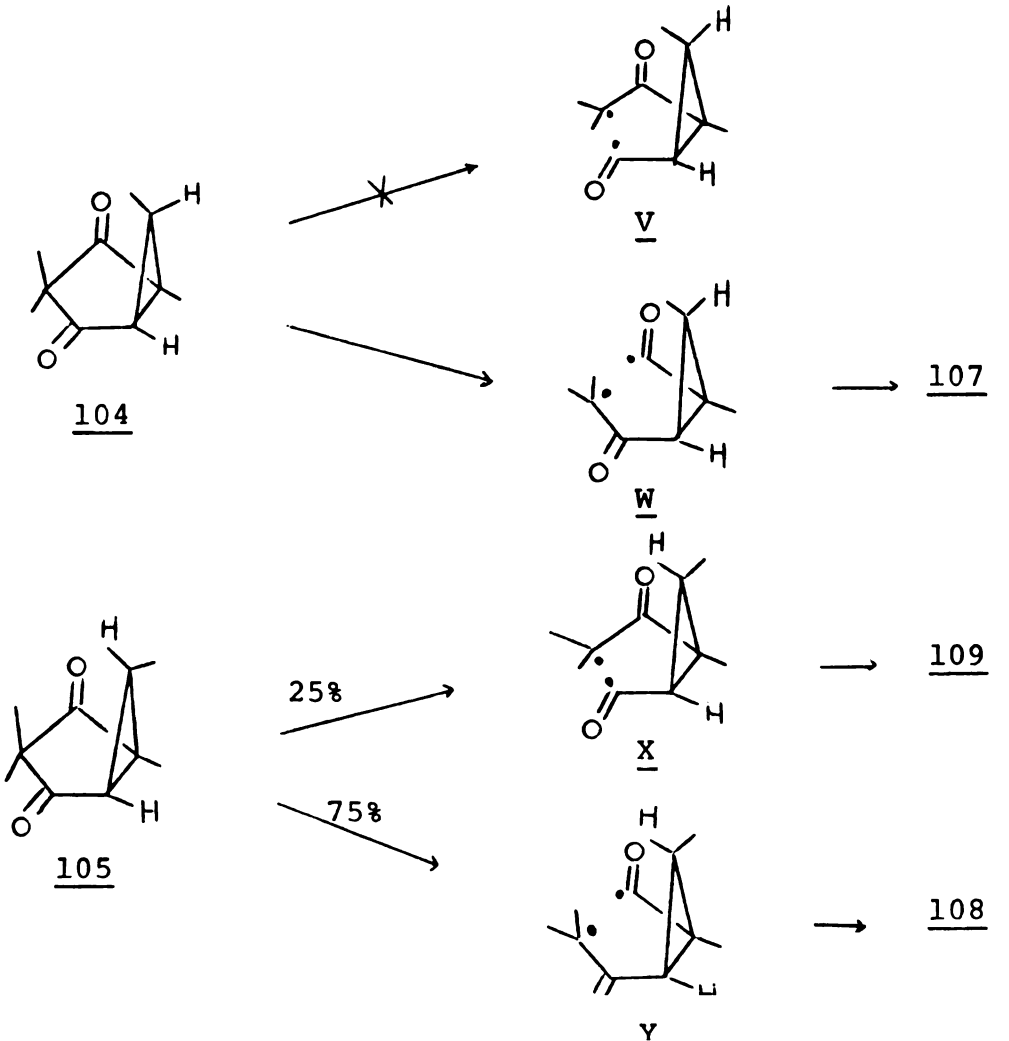
120 U 121

The mechanism for the formation of the enol lactone was proposed as follows: photoexicitation of 120 results in α-fission giving diradical U, which recyclizes to the enol lactone 121.

A recent paper by Gibson[43] on the photochemistry of (-)-trans-verbenone epoxide 122 reported a similar type of rearrangement, even though the proposed intermediate 123 for the formation of 112 was too photolabile to be isolated.



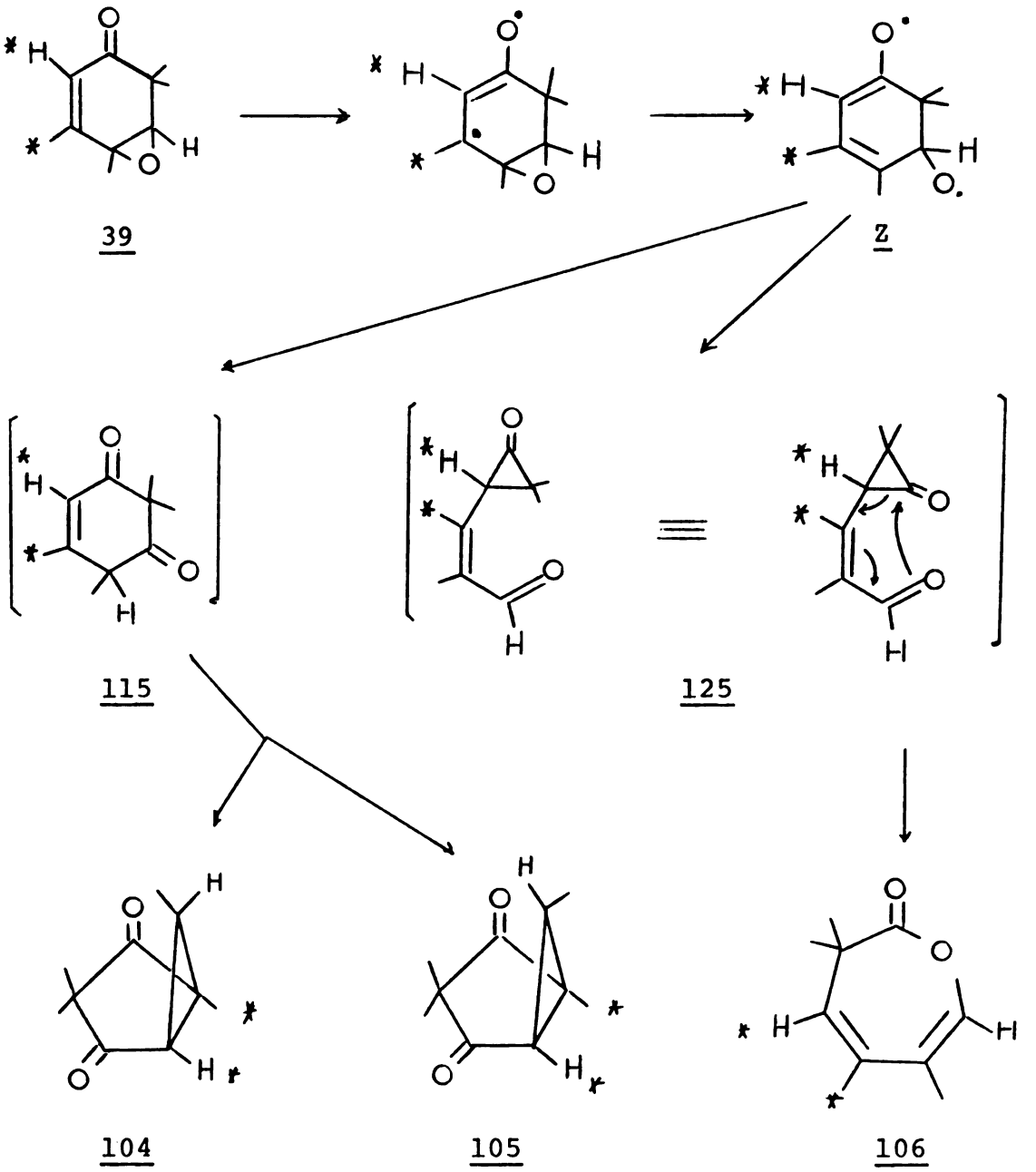
Compounds 104 and 105 which are unsymmetrical diketones could, on photoexcitation, undergo ∝-fission in either direction to generate diradicals V, W and X, Y respectively. Our



data showed that the preferential α-fission is in the direction which would generate more stabilized diradicals W and Y.

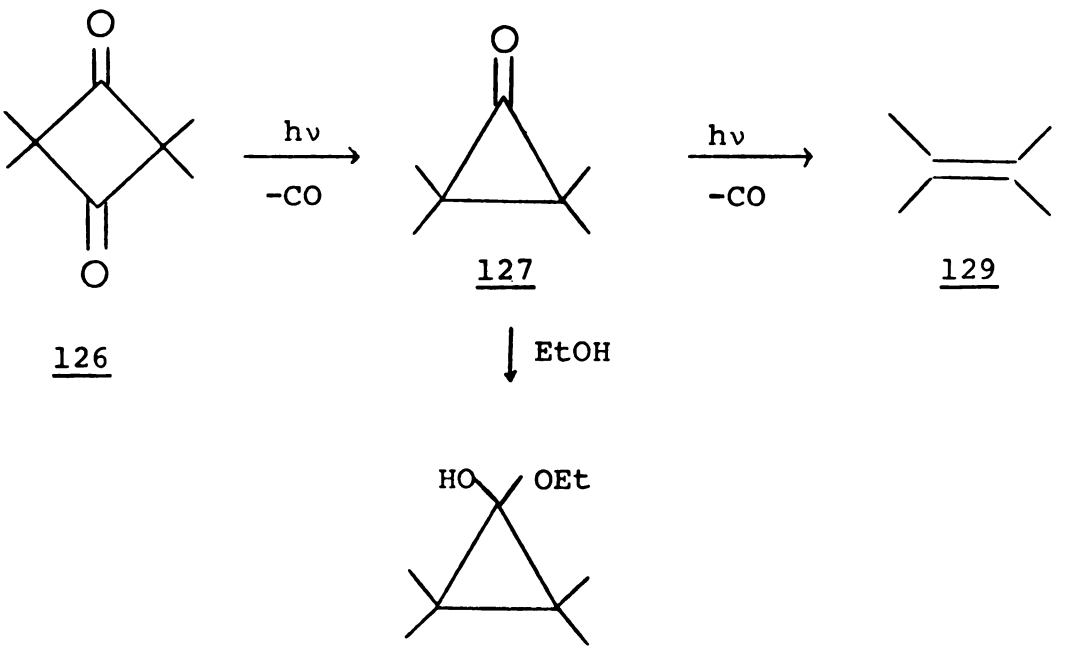
Possible routes to 104-106, consistent with the labeling results, are shown in Scheme 11. Experiments were

Scheme 11



done with tetradeuterio-epoxyketone 39* (see Part I). The mechanisms leading from 39 to 104, 105 are fairly obvious, but the mechanism leading from 39 to 106 is less obvious. The possibility that the intermediate 115 was involved in the primary process leading to 106 was ruled out by our control experiment starting with 54, since compound 54 afforded exclusively 113 on photolysis. It is found that four processes suffice to rationalize the transformation of 39 to 106: (1) $n-\pi^*$ excitation, (2) a bond scission process involving the C_4-O bond to give Z, (3) some rebonding processes followed by π-electron demotion to give the cyclopropanone intermediate 125, and (4) ground state (or possibly excited state) transformation of 125 to the observed product 106.

In an effort to detect the transient formation of the cyclopropanone intermediate 125, the irradiation of vinyl epoxyketone 39 was carried out using absolute methanol as solvent. Previous work on the photochemistry of tetramethylcyclobutanedione 126 has shown that the corresponding cyclopropanone intermediate 127 can be trapped by reacting with ethanol to form tetramethylcyclopropanone ethyl hemiketal 128.[48]



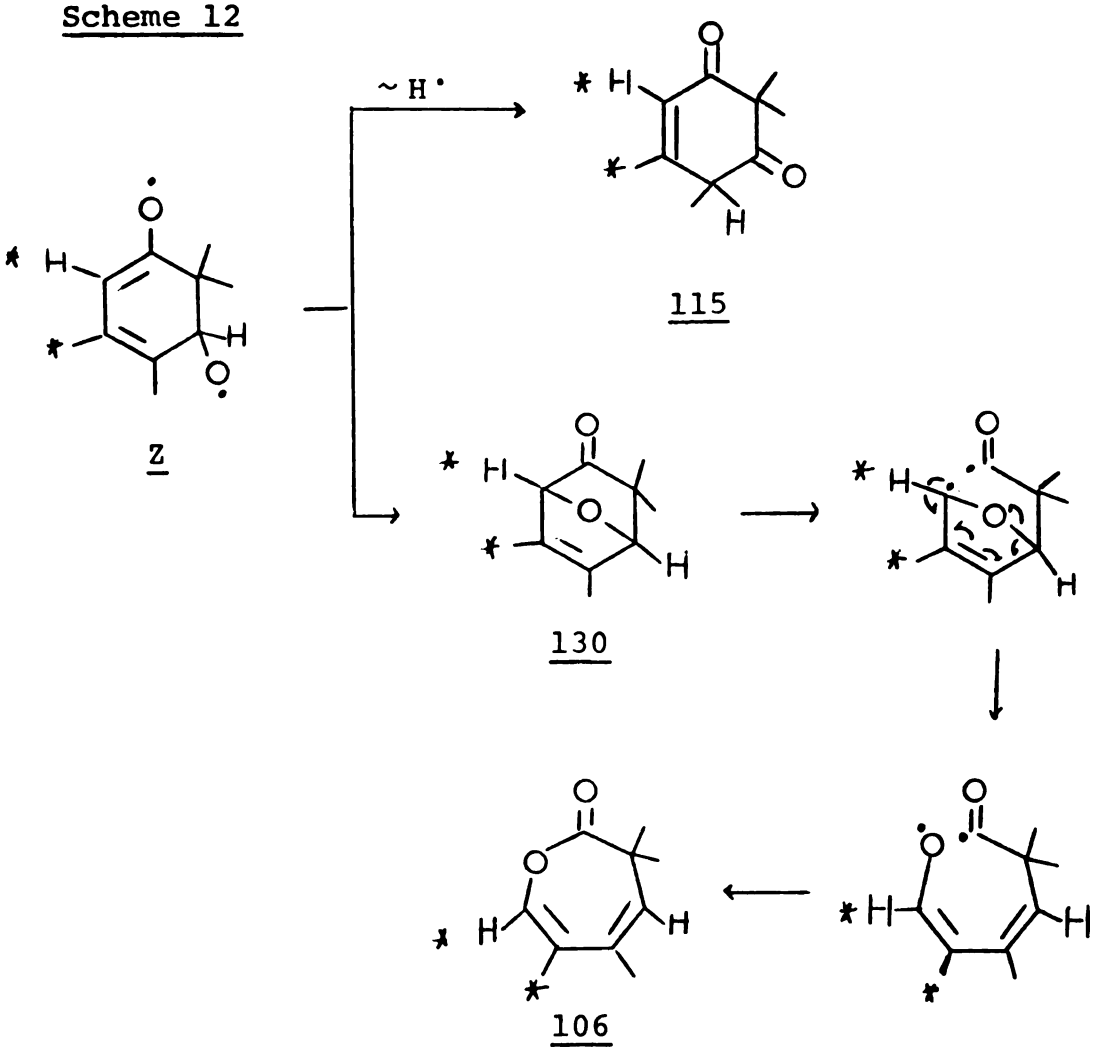
126 127 129

128

However, we could obtain no evidence for the formation of 125 under these conditions, and identical results were obtained as when ether was used as the solvent. The inability to trap the cyclopropanone intermediate with methanol shows that, if 125 is indeed an intermediate in the process, its intramolecular reaction to 106 must be very rapid with respect to the intermolecular addition of methanol.

Another mechanism which, although reasonable, is definitely excluded by the labeling experiment, is outlined in Scheme 12. Intermediate Z (from Scheme 11) may either under a hydrogen shift to give 115 or may undergo some rebonding processes to give the intermediate bicyclic ketone 130. Excited state transformation of 130 could lead to 106.

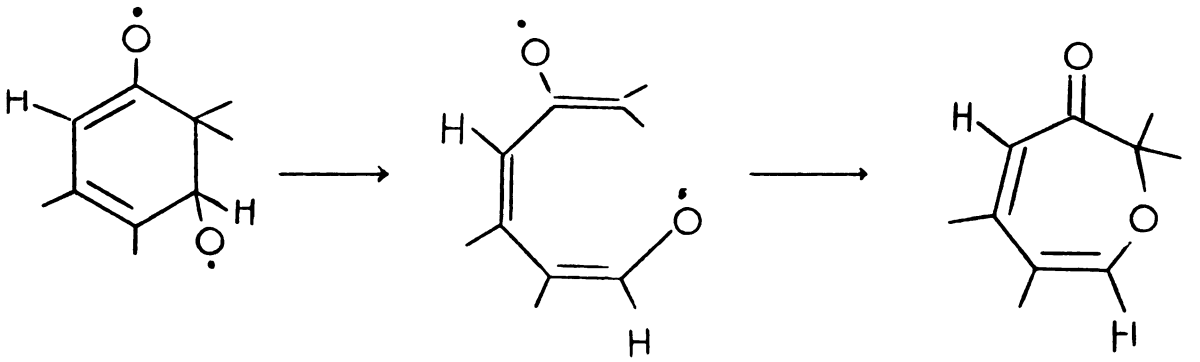
Scheme 12



However, had this mechanism been operating, the product 106 would have contained labels at the C_3 and C_4 positions instead of at the C_5 and C_6 positions as observed.

The alternative ring-opening mode from the intermediate Z to give Z' would lead to structure 131 (Scheme 13), which is also reasonably consistent with the observed nmr spectrum and the labeling results, but which is inconsistent with the uv and ir data.

Scheme 13



Z Z' 131

In summary, the dienone epoxide 39 rearranges mainly via the diketone intermediate 115. A new reaction pathway leading to 106 seems to be operating via the cyclopropanone intermediate 125.

EXPERIMENTAL

1. General Procedures

Except where otherwise noted, all nmr spectra were measured in $CDCl_3$ or CCl_4 solutions using TMS as an internal standard. The 60 MHz spectra were recorded on a Varian T-60 spectrometer and the 100 MHz spectra were recorded on a Varian HA-100 spectrometer. Infrared spectra were recorded on a Perkin Elmer 237 grating spectrophotometer and were calibrated against a polystyrene film. Ultraviolet spectra were obtained with a Unicam SP-800 in 95% ethanol, unless otherwise noted. Mass spectra were obtained from a Hitachi-Perkin Elmer RMU-6 operated by Mrs. Ralph Guile. Melting points were determined with a Thomas-Hoover Melting Point Apparatus and are uncorrected. Varian Aerograph gas chromatographs were used. Analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan.

2. Photolysis of 4,5-epoxy-2,3,4,5,6,6-hexamethyl-2,4-cyclohexadienone, 32

A degassed solution of 50 mg (0.26 mmol) of 32 in 25 ml of anhydrous ether was irradiated through Pyrex with

a 450 W Hanovia lamp at 0°. The photolysis was followed by nmr spectroscopy. The nmr signals from 32 began to diminish as the reaction proceeded, while those corresponding to 36[15] began to rise. As the signals from 36 reached a intensity as high as that of 32, a new set of signals from 95 began to rise at the expense of both 32 and 36. The total conversion from 32 to 95 took about 16 hours.

Recrystallization from petroleum ether (bp 30-60°) gave a solid mass of bicyclo[2.1.0]pentan-2-one, 95 (45 mg, 90%): ir (CCl_4) 3000 (m), 1760 (s), 1710 (s), 1470 (w), 1400 (w), 1370 (w), 1230 (w) cm^{-1}; uv (MeOH) λ_{max} 225 nm (ε 2,590); nmr (CCl_4) δ 0.77 (s, 3H), 1.07 (s, 3H), 1.18 (s, 3H), 1.23 (s, 3H), 2.15 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 195 (3), 194 (20), 179 (9), 153 (13), 152 (100), 151 (31), 150 (9), 137 (56), 123 (48), 108 (54), 93 (28), 91 (28), 91 (18), 81 (34), 79 (13). Due to its thermal instability, no attempt was made to obtain its elemental analysis.

3. Photolysis of 4,5-epoxy-3-trideuteriomethyl-2,4,5,6,6-pentamethyl-2,4-cyclohexadienone, 32*

The procedure and workup were as described for the irradiation of 32. The initial rearrangement product 36* had an nmr spectrum identical with that of 36[15] except that the signal at δ 1.95 disappeared and the quartet at δ 1.75 sharpened to a singlet. The final product 95* had an nmr

spectrum identical with that of 95 except that the signal at δ 1.23 disappeared.

4. Photolysis of 4,5-epoxy-3,5-bis(trideuteriomethyl)-2,4,6,6-tetramethyl-2,4-cyclohexadienone, 32*,†

The procedure and workup were as described for the irradiation of 32. The initial rearranged product 36*,† had an nmr spectrum identical with that of 36* except that the signal at δ 1.95 was absent. The final product 95*,† was identical with that of 95* except that the signal at δ 2.15 disappeared.

5. Photolysis of Bicyclopentanone, 95

A degassed solution of 100 mg (0.52 mmol) of 95 in 30 ml of anhydrous ether was irradiated through Corex with a 450 W Hanovia lamp at 0°. The photolysis was followed by nmr. The reaction went to completion in about 12 hrs. Analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 165°) showed two components: 96 (79.6%, ret. time 5 min) and 97 (20.4%, 7 min). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 145°) gave lactone 96: ir (CCl_4) 2960 (w), 2910 (m), 2850 (w), 1790 (s), 1700 (w), 1450 (m), 1385 (m), 1370 (w), 1365 (w), 1290 (w), 1275 (w), 1225 (m), 1030 (s), 980 (m), 930 (w) cm^{-1};

uv (EtOH) only end absorption; nmr (CCl_4) δ 1.30 (s, 3H), 1.37 (broad singlet, 3H), 1.50 (q, 3H), 1.70 (s, 6H), 1.87 (q, 3H); mass spectrum (70 eV) m/e (rel intensity) 194 (13), 179 (6), 151 (100), 126 (21), 123 (35), 81 (26), 67 (14), 55 (15), 53 (19).

Anal. Calcd. for $C_{12}H_{12}D_6O_2$: C, 71.94
Found: C, 72.00

Lactone 97: mp 104-106°; ir (CCl_4) 2950 (m), 2920 (m), 2850 (m), 1760 (s), 1460 (w), 1380 (m), 1300 (m), 1050 (m), 950 (m) cm^{-1}; uv (EtOH) λ_{max} 220 nm (ε 890); nmr (CCl_4) δ 0.70 (s, 3H), 1.03 (s, 3H), 1.12 (s, 6H), 1.17 (s, 3H), 1.20 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 194 (2), 179 (2), 155 (55), 135 (100), 120 (16), 119 (42), 107 (19), 104 (22), 93 (21), 91 (27), 44 (60), 43 (25), 41 (24), 39 (20).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34
Found: C, 74.22; H, 9.36

6. Photolysis of Bicyclopentanone, 95*

The procedure and workup were as described for the irradiation of 95. The rearranged product 96* had an nmr spectrum identical with that of 96 except that the signal at δ 1.50 disappeared and the quartet at δ 1.87 sharpened to a singlet; 97* was identical with that of 97 except that the signal at δ 1.17 disappeared.

7. Photolysis of Bicyclopentanone, 95*,†

The procedure and workup were as described for the irradiation of 95. The rearranged product 96*,† had an nmr spectrum identical with that of 96 except that the signals at δ 1.87 and 1.50 disappeared; 97*,† was identical with that of 97 except that the signals at δ 1.17 and 1.20 were absent.

8. Thermal Reaction of Bicyclopentanone, 95

a). in Methanol:

When compound 95 was treated with a few drops of methanol, it rearranged to a mixture of 99 and 100 (ca. 1:3 as determined by nmr spectrum). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 170°) gave lactone 99 (ret time 25 min): ir (CCl_4) 2950 (w), 1745 (s), 1700 (m), 1460 (w), 1380 (w), 1280 (m), 1080 (m), 980 (m) cm^{-1}; uv (MeOH) λ_{max} 223 nm (ε 2,600), 255 (1,070); nmr (CCl_4) δ 1.77 (m, 6H), 1.60 (m, 6H), 1.40 (broad singlet, 6H); mass spectrum (70 eV) m/e (rel intensity) 195 (11), 194 (78), 179 (14), 151 (20), 136 (23), 123 (12), 109 (36), 108 (78), 107 (14), 93 (100), 91 (28), 77 (25), 65 (13), 53 (20).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34
Found: C, 74.27; H, 9.50

Lactone 100 (ret time 45 min): ir (CCl_4) 2950 (w), 1745 (s), 1450 (w), 1390 (w), 1330 (w), 1260 (w), 1130 (w) 1090 (w) cm^{-1}; uv (MeOH) λ_{max}230 nm (ε 3,100); nmr (CCl_4) δ 1.53 (s, 3H), 1.62 (m, 6H), 1.72 (m, 6H), 1.82 (q, 3H); mass spectrum (70 eV) m/e (rel intensity) 194 (25), 179 (32), 151 (36), 150 (28), 149 (100), 137 (10), 136 (7), 135 (29), 134 (14), 133 (18), 126 (53), 125 (48), 123 (43), 119 (15), 109 (11), 107 (10), 97 (16), 93 (10), 91 (14), 81 (20).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34
Found: C, 74.20; H, 9.47

b). in CCl_4

When compound 95 (40 mg, 0.21 mmol) in 0.5 ml CCl_4 was heated in a sealed tube at 180° for 3 hrs, it transformed into a mixture of 101 and 36 (ca. 1:9 as determined by nmr spectrum). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 160°) gave diketone 36[15] (ret time 45 min) and lactone 101 (ret time 35 min). Lactone 101 had: ir (CCl_4) 2950 (w), 1795 (s), 1695 (w), 1660 (m), 1460 (m), 1390 (w), 1250 (w), 1200 (w), 1130 (w), 1080 (w), 1050 (m), 990 (w), 860 (w) cm^{-1}; uv (MeOH) λ_{max} 225 nm (ε 1,310); nmr (CCl_4) δ 1.02 (d, 3H, J = 7 cps), 1.50 (s, 3H), 1.60 (m, 6H), 1.70 (s, 3H), 2.38 (q, 1H, J = 7 cps), 4.07 (d, 1H, J = 2 cps), 4.53 (d, 1H, J = 2 cps); mass spectrum (70 eV) m/e (rel intensity) 194 (32), 179 (32), 152 (23), 151 (100), 137 (29), 136 (15), 133 (25), 123 (13), 121 (10), 109 (20), 107 (10), 91 (14), 81 (12), 79 (12), 77 (14).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34
Found: C, 74.15; H, 9.34

c). Neat

When compound 95 was allowed to stand in the crystalline state at -15° for several eeeks, it reverted slowly to 36.

9. Thermal Reaction of Bicyclopentanone 95*

a). in Methanol:

The procedure and workup were as described for the unlabeled 95. The rearranged product 99* had an nmr spectrum identical with that of 99 except that the area of peak at δ 1.40 was reduced by 50%; 100* was identical with that of 100 except that the signal at δ 1.82 disappeared and the multiplet at δ 1.72 sharpened to a singlet.

b). in CCl_4

The procedure and workup were described for unlabeled 95. The rearranged product 101* had an nmr spectrum identical with that of 101 except that the signal at δ 1.50 disappeared; 36* was identical with that of 36[15] except that the signal at δ 1.95 disappeared and that at δ 1.75 sharpened to a singlet.

10. Thermal Reaction of Bicyclopentanone 95*,†

a). in Methanol:

The procedure and workup were as described for unlabeled 95. The rearranged product 99*,† had an nmr identical with that of 99 except that the signal at δ 1.40 disappeared; 100*,† was identical with that of 100* except that the signal at δ 1.53 disappeared.

b). in CCl_4:

The procedure and workup were as described for the unlabeled 95. The rearranged product 101*† had an nmr identical with that of 101* except that the signals at at δ 4.07 and 4.53 nearly disappeared; 36*,† was identical with that of 36* except that the signal at δ 1.95 disappeared.

11. Photolysis of 4,5-epoxy-3,4,6,6-tetramethyl-2-cyclohexenone, 39

A degassed solution containing 300 mg (1.81 mmol) of 39 in 30 ml of anhydrous ether was irradiated through Pyrex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 140°). The reaction was complete in about 8 hrs. Vpc showed three compounds: 104 (44%, ret time 8.5 min), 105 (34%, 12.5 min), and 106 (22%, 16.5 min). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 150°) gave anti-1,3,3,6-tetramethyl-bicyclo[3.1.0]hexan-2,4-dione 104: Ir (CCl_4) 3000 (m), 1745 (w), 1710 (s), 1465 (w), 1385 (w), 1300 (w), 1140 (w) cm^{-1}; uv (MeOH) λ_{max}215 nm (ε 2,590); nmr (CCl_4) δ 0.97 (s, 3H), 1.03 (m, 3H), 1.10 (s, 3H), 1.40 (s, 3H), 1.38 (m, 1H), 2.22 (d, 1H, J = 9 Hz); mass spectrum (70 eV) m/e (rel intensity) 167 (9), 166 (77), 151 (29), 138 (14), 124 (15), 123 (55), 107 (20), 105 (10), 96 (100), 95 (27), 91 (17), 81 (19), 70 (23), 68 (64), 67 (65), 53 (38).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49

Found: C, 72.28; H, 8.49

syn-1,3,3,6-Tetramethylbicyclo[3.1.0]hexan-2,4-dione 105: ir (CCl_4) 3000 (m), 1740 (m), 1705 (s), 1465 (w), 1390 (w), 1280 (m), 1130 (w), 1095 (m) cm^{-1}; uv (MeOH) λ_{max}225 nm (ε 1,240); nmr (CCl_4) δ0.95 (s, 3H), 1.02 (s, 3H),

1.25 (m, 3H), 1.33 (s, 3H), 1.45 (m, 1H), 1.70 (d, 1H, $\underline{J}$ = 2 Hz); mass spectrum (70 eV) m/e (rel intensity) 167 (9), 166 (58), 151 (19), 149 (16), 138 (18), 124 (20), 123 (59), 107 (28), 105 (15), 97 (10), 96 (100), 95 (35), 91 (20), 81 (20), 78 (17), 76 (11), 70 (20), 68 (78), 67 (83), 55 (21), 53 (58), 51 (15).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.25; H, 8.37

12. Photolysis of 39*

The procedure and workup was as described for the irradiation of 39. The rearranged product 104* had an nmr spectrum identical with that of 104 except that the signals at δ 1.40 and 2.22 disappeared; 105* was identical with that of 105 except that the signals at δ 1.33 and 1.70 disappeared; 106* was identical with that of 106 except that the signal at δ 5.13 disappeared and the area of the peak at δ 1.80 was reduced by 50% and was simplified to a doublet.

13. Photolysis of anti-1,3,3,6-tetramethylbicyclo[3.1.0]-hexan-2,4-dione, 104

A degassed solution containing 100 mg (0.60 mmol) of 104 in 10 ml of anhydrous ether was irradiated through

Corex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 140°). As the reaction proceeded, the peak with a retantion time of 8.5 min (corresponding to 104) decreased in area and a product peak appeared at 10.5 min. After 1.5 hr, the reaction was complete and the product, anti-1,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]hexan-2-one 107 was collected by preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb w, 80/100, 170°): ir (CCl_4) 3000 (m), 1780 (s), 1710 (m), 1450 (w), 1305 (w), 1140 (w), 1100 (m), 1050 (m), 970 (w), 870 (m) cm^{-1}; uv (MeOH) λ_{max}230 nm (ϵ 3,320); nmr (CCl_4) δ 0.96 (m, 3H), 1.33 (m, 1H), 1.37 (s, 3H), 1.63 (s, 3H), 1.68 (s, 3H), 2.38 (d, 1H, J = 7 Hz); mass spectrum (70 eV) m/e (rel intensity) 167 (5), 166 (46), 151 (29), 148 (13), 138 (19), 124 (22), 123 (76), 107 (20), 105 (15), 96 (100), 95 (29), 91 (21), 68 (41), 66 (50), 55 (22), 53 (21).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.27; H, 8.46

14. Photolysis of 104*

The procedure and work-up was as described for the irradiation of 104. The rearranged product 107* had an nmr spectrum identical with that of 107 except that the signals at δ 1.37 and 2.38 were absent.

15. Photolysis of syn-1,3,5,6-tetramethylbicyclo[3.1.0]-hexan-2,4-dione, 105

A degassed solution containing 100 mg (0.60 mmol) of 105 in 10 ml of anhydrous ether was irradiated through Corex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 140°). As the reaction proceeded, the peak with a retention time of 12.5 min (corresponding to 105) decreased in area and two product peaks appeared with retention times of 17.0 and 28.5 min in the ratio of 3:1. After 1.5 hr the reaction was complete. Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 170°) gave a major component, syn-1,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]hexan-2-one 108: ir (CCl_4) 3000 (m), 1780 (s), 1715 (m), 1450 (w), 1290 (w), 1140 (w), 1060 (m) cm^{-1}; uv (MeOH) λ_{max}235 nm (ε 2,400); nmr (CCl_4) δ 1.15 (broad singlet, 3H), 1.33 (s, 3H), 1.17 (m, 1H), 1.65 (s, 6H), 1.93 (broad singlet, 1H); mass spectrum (70 eV) m/e (rel intensity) 167 (5), 166 (39), 151 (20), 138 (14), 124 (22), 123 (68), 107 (25), 96 (100), 95 (30), 91 (26), 79 (20), 68 (52), 67 (71), 55 (31), 53 (55).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49

Found: C, 72.24; H, 8.57

The minor component was syn-5,6-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]hexan-2-one 109: ir (CCl_4)

2980 (w), 2940 (w), 1785 (s), 1700 (m), 1460 (w), 1280 (m), 1250 (w), 1180 (m), 1140 (w), 1080 (w), 975 (w), 890 (w) cm^{-1}; uv (MeOH) λ_{max} 235 nm (ε 6,150); nmr (CCl_4) δ 1.25 (m, 1H), 1.26 (m, 3H), 1.44 (d, 1H, J = 3 Hz), 1.50 (s, 3H), 1.60 (s, 3H), 1.70 (s, 3H); mass spectrum (70 eV) m/e (rel intensity) 167 (12), 166 (100), 151 (40), 138 (13), 124 (15), 123 (49), 107 (27), 97 (14), 96 (52), 95 (27), 91 (27), 81 (16), 79 (19), 70 (30), 69 (20), 68 (48), 67 (45), 55 (16), 53 (27), 51 (8). Insufficient 109 was isolated for elemental analysis.

16. Photolysis of 105*

The procedure and workup was as described for the irradiation of 105. The rearranged product 108* had an nmr spectrum identical with that of 108 except that the signals at δ 1.33 and 1.93 were absent. The amount isolated for the other rearranged product 109* was not enough for nmr spectral measurement.

17. Photolysis of 4,5,7,7-tetramethyl-2-oxa-cyclohepta-3,5-dien-1-one, 106

A degassed solution containing 100 mg (0.60 mmol) of 106 in 10 ml of anhydrous ether was irradiated through Corex with a 450 W Hanovia lamp. The photolysis was

followed by analytical vpc (5' x o.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 135°). As the reaction proceeded, the peak with a retention time of 12.5 min (corresponding to 106) decreased in area and a product peak appeared at 6 min. After 2 hr the reaction was complete and the product, 2,2,6,7-tetramethyl-4-oxa-bicyclo[3.2.0]-hept-6-en-3-one 110 was collected by preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 180°): ir (CCl_4) 2960 (m), 2920 (w), 1780 (s), 1385 (w), 1330 (w), 1250 (w), 1160 (m), 1100 (s), 1060 (m), 1050 (m), 875 (s) cm^{-1}; uv (MeOH) λ_{max}210 nm (ε 830); nmr (CCl_4) δ 1.10 (s, 3H), 1.17 (s, 3H), 1.68 (s, 6H), 2.82 (m, 1H), 4.67 (d, 1H, J = 4 Hz); mass spectrum (70 eV) m/e (rel intensity) 166 (4), 148 (40), 123 (100), 109 (18), 107 (32), 91 (28), 79 (22), 77 (13), 67 (22), 55 (19), 53 (16). Insufficient 110 was isolated for elemental analysis.

18. Photolysis of 106*

The procedure and workup was as described for the irradiation of 106. The rearranged product 110* had an nmr spectrum identical with that of 110 except that the signal at δ 2.82 disappeared and the area of the peak at δ 1.68 was reduced in area by 50%.

19. Photolysis of 2,3,6,6-tetramethyl-2-cyclohexen-1,5-dione, 54

A degassed solution containing 200 mg of 54 in 15 ml of anhydrous ether was irradiated through Pyrex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP in chromosorb W, AW-DMCS 80/100, 160°). As the reaction proceeded, the peak with a retention time of 7.0 min (corresponding to 54) decreased in area and a product peak appeared at 2.0 min. After 3 hr the reaction was complete and the product, 1,3,3,5-tetramethyl-bicyclo[3.1.0]hexan-2,4-dione 113 was collected by preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 170°): ir (CCl_4) 3000 (m), 1750 (m), 1710 (s), 1470 (w), 1390 (w), 1290 (m), 1070 (m) cm^{-1}; uv (MeOH) λ_{max}225 nm (ε 1,190); nmr (CCl_4) δ 0.95 (s, 3H), 1.05 (s, 3H), 1.33 (s, 6H), 1.08 (d, 1H, J = 5 Hz), 1.47 (d, 1H, J = 5 Hz); mass spectrum (70 eV) m/e (rel intensity) 167 (4), 166 (38), 151 (10), 124 (20), 123 (53), 97 (7), 96 (100), 95 (14), 68 (38), 67 (35), 53 (15).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.23; H, 8.57

20. Photolysis of 54*

The procedure and workup was as described for the irradiation of 54. The rearrangement puoduct 113* had an nmr spectrum identical with that of 113 except that the area of the peak at δ 1.33 was reduced in area by 50%.

21. Photolysis of 1,3,3,5-tetramethylbicyclo[3.1.0]hexan-2,4-dione, 113

A degassed solution containing 100 mg (0.60 mmol) of 113 in 10 ml of anhydrous ether was irradiated through Corex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 160°). As the reaction proceeded, the peak with a retention time of 7.0 min (corresponding to 113) decreased in area and a product peak appeared at 16 min. After 1 hr the reaction was complete and the product, 1,5-dimethyl-4-isopropylidene-3-oxa-bicyclo[3.1.0]hexan-2-one 114, was collected by preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 170°): ir (CCl_4) 3000 (m), 1780 (s), 1700 (m), 1350 (w), 1300 (w), 1135 (w), 1150 (w), 1070 (m), 1030 (m) cm^{-1}; uv (MeOH) λ_{max}235 nm (ε 3,780); nmr (CCl_4) δ 0.77 (d, 1H, J = 4 Hz), 1.15 (d, 1H, J = 4 Hz), 1.28 (s, 3H), 1.45 (s, 3H), 1.67 (s, 3H), 1.77 (s, 3H); mass spectrum (70 eV) m/e (rel intensity)

167 (4), 166 (34), 151 (10), 124 (21), 123 (58), 97 (7), 96 (100), 95 (16), 69 (10), 68 (35), 67 (33), 53 (15).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49
Found: C, 72.04; H, 8.34

22. Photolysis of 113*

The procedure and work-up was asdescribed for the irradiation of 113. The rearrangement product 114* had an nmr spectrum identical with that of 114 except that the areas of the peaks at δ 1.28 and 1.45 were reduced in area by 50%.

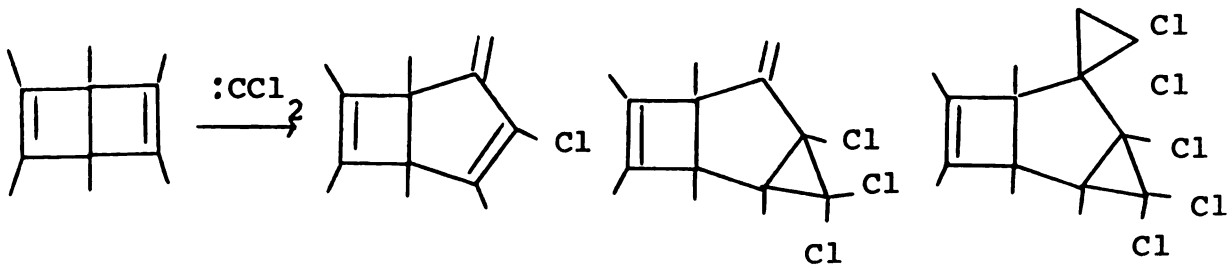
PART III

MISCELLANEOUS

RESULTS

1. Thermal Rearrangements of some of the Dichlorocarbene Adducts of Hexamethyldewarbenzene

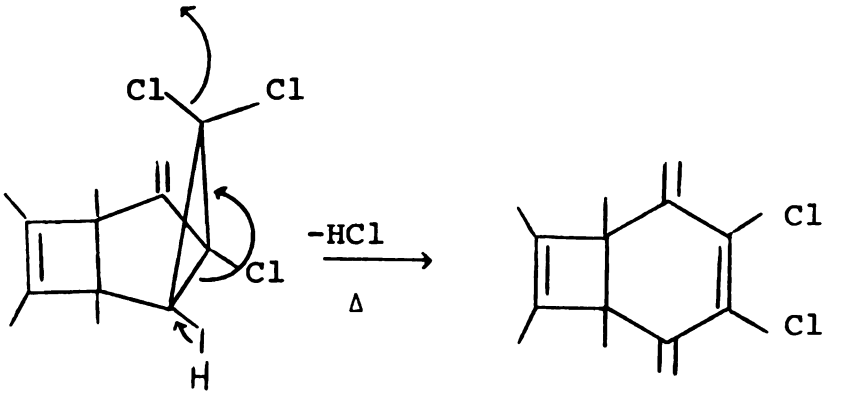
It was reported[49] that dichlorocarbene gives three adducts with hexamethyldewarbenzene 132; the structures were formulated as 133, 134 and 135.



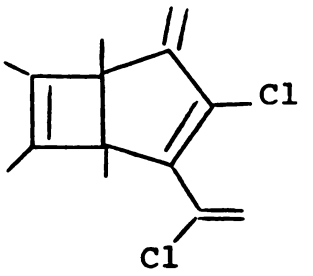
132 133 134 135

In the process of separating 133 from 134 and 135 by vacuum distillation, compounds 136 and 137 (in the ratio 1:3) were obtained as the high boiling fraction (120°-130° at 0.1 mm), besides 133 as the low boiling fraction (80-87° at 0.1 mm). Compound 136 was shown to arise from the thermal rearrangement of 134 by losing a molecule of HCl. The

origin of 137 remains unknown.



134 136

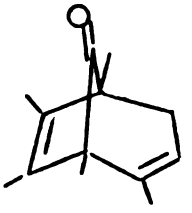


137

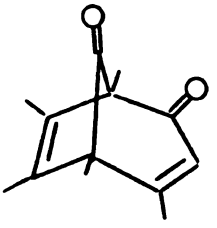
2. Photoisomerization of 1,4,5,6,7-pentamethylbicyclo[3.2.1]-octa-3,6-dien-2,8-dione, 139

Allylic oxidation of 1,2,5,6,7-pentamethylbicyclo[3.2.1]-octa-2,6-dien-8-one 138[21] with chromium trioxide-pyridine complex gave the corresponding dione 139 in moderate yield (ca. 40%). On irradiation through Pyrex, 139 reached a photostationary state with 140. On further irradiation of this equilibrating mixture through Corex, a new photoproduct 141 was obtained,[53] presumably through the decarbonylation of 139. Compound 141 was photolabile and rearranged slowly

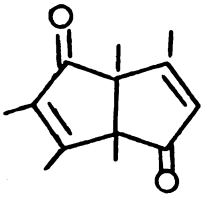
to a ketene which was tentatively assigned the structure 142.



138

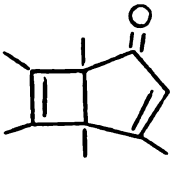


hν
Pyrex

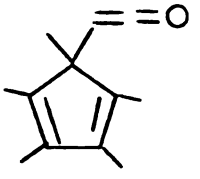


139 (73%) 140 (27%)

Corex



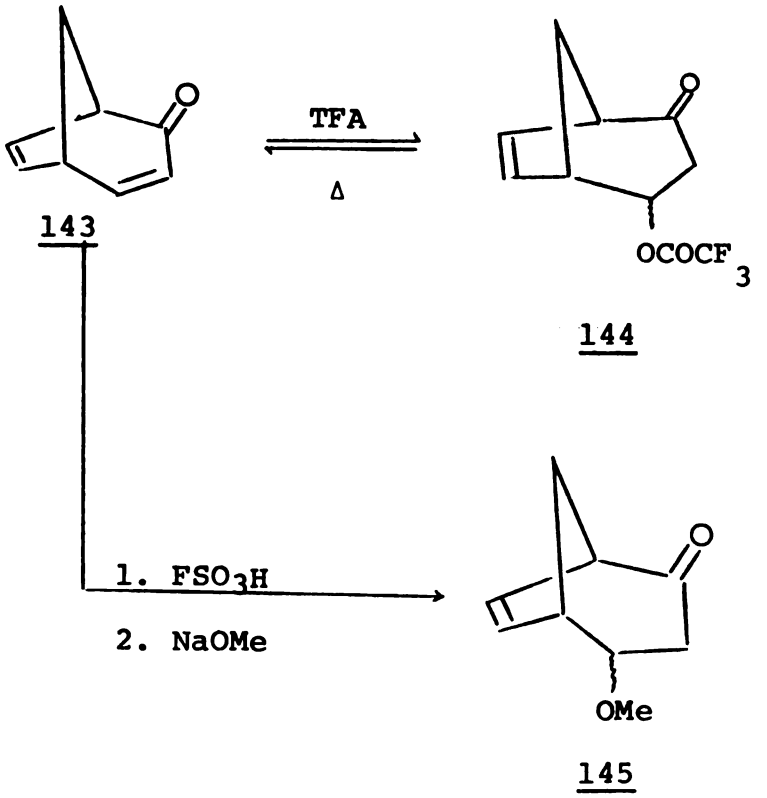
141



142

3. Acid Treatment of Bicyclo[3.2.1]octa-3,6-dien-2-one, 143

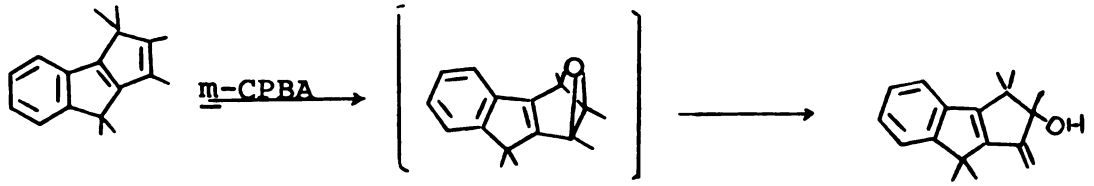
Treatment of 143[50] with trifluoroacetic acid (TFA) at room temperature gave 144; treatment of 143 with fluorosulfonic acid (FSO_3H) at room temperature followed by quenching with sodium methoxide gave 145. The structure of 144 was confirmed by the fact that it reverted to 143 at high temperature on an SE-30 column by eliminating a molecule of trifluoroacetic acid. The structure of 145 was confirmed by independent synthesis via a Michael addition of methanol to 143.



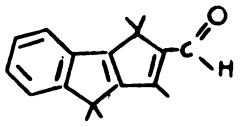
143 144 145

4. Epoxidation and Photosensitized Oxidation of 1,4-dihydro-1,1,2,3,4,4-hexamethylbenzopentalene, 146

Treatment of 146[51] with m-chloroperbenzoic acid (m-CPBA) gave 148, presumbly through the rearrangement of monoepoxide 147 catalyzed by a trace of acid. When the reaction mixture was chromatographed over neutral alumina, a minor product 149 was isolated besides 148. The origin of 149 remains unknown.

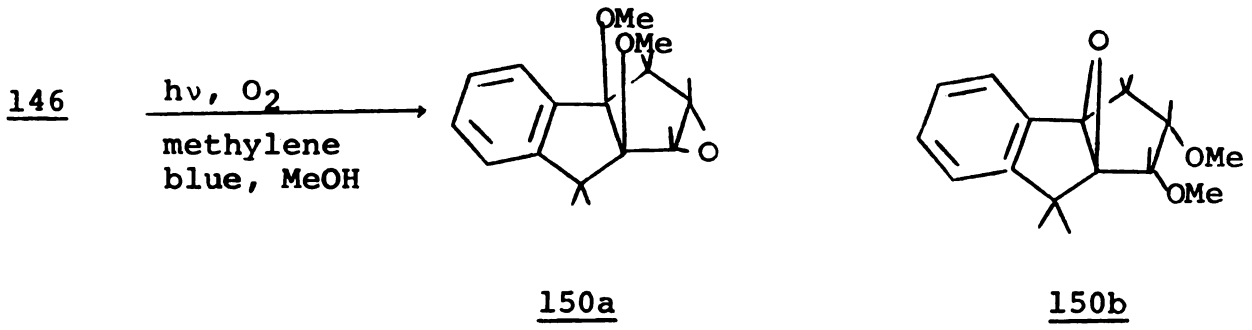


146 147 148 (85%)



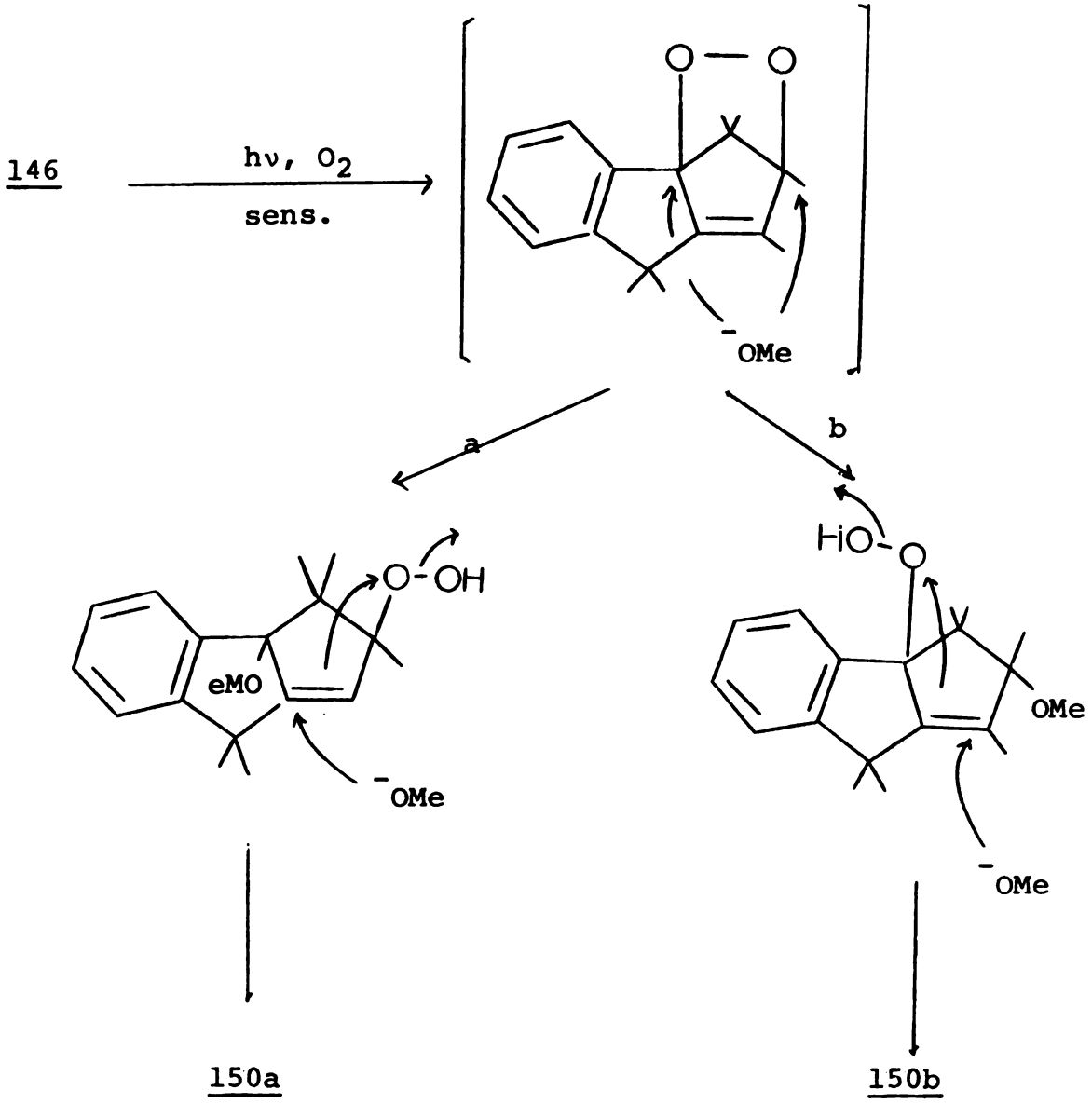
149 (5%)

Photosensitized oxidation of 146 in methanol led to a compound, the exact structure of which, represented either as 150a or 150b, remains uncertain. Possible routes to 150a and 150b are shown in Scheme 14.



150a 150b

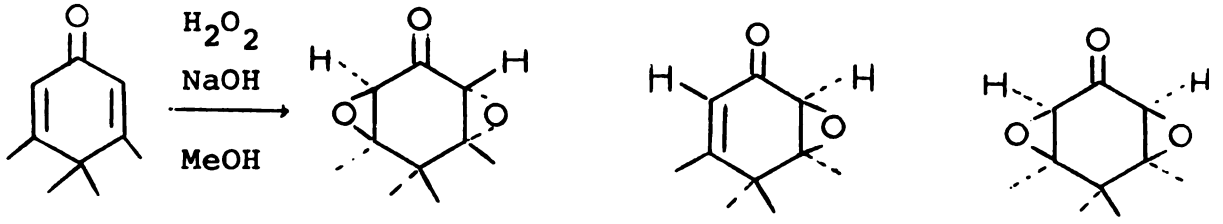
Scheme 14



150a 150b

5. Epoxidation of 3,4,4,5-tetramethyl-2,5-cyclohexadienone, 151

The reaction of 151[54] with m-chloroperbenzoic acid led to no epoxidation of the double bond. Epoxidation with alkaline hydrogen peroxide gave 152 (43%), 153 (5%), 154 (7%) and 155 (45%). Compound 152 decomposed on preparative vpc column, and its structure remains to be determined.



151 153 (5%) 154 (7%) 155 (45%)

EXPERIMENTAL

1. Vacuum Distillation of the Dichlorocarbene Adducts of Hexamethyldewarbenzene

A mixture of compounds 136 and 137 was obtained in the vacuum distillation of dichlorocarbene adducts of hexamethyldewarbenzene[49] at 120-130° (0.1 mm), besides the expected 133 at 80-87° (0.1 mm). Analytical vpc (5' x 0.125 in column, 3% SE-30 on chromosorb W, 80/100, 150°) of the mixture showed a major component 137 (75%, retention time 2.5 min) and a minor component 126 (25%, retention time 3.5 min). Preparative vpc (5' x 0.25 in column, 10% SE-30 on chromosorb W, 80-100 mesh, 165°) gave 137: ir (CCl_4) 2960 (m), 1580 (w), 1450 (w), 1380 (w), 1250 (m), 880 (s) cm^{-1}; uv (MeOH) λ_{max} 265 nm (ε 8,500); nmr (CCl_4) δ 1.15 (s, 3H), 1.18 (s, 3H), 1.50 (q, 3H), 1.60 (q, 3H), 4.53 (s, 1H), 5.17 (s, 1H), 5.40 (d, 1H, J = 1 Hz), 5.53 (d, 1H, J = 1 Hz); mass spectrum (70 eV) m/e (rel intensity) 258 (6), 256 (31), 254 (47), 241 (16), 239 (24), 221 (36), 220 (20), 219 (100), 206 (19), 205 (18), 204 (60), 203 (22), 202 (33), 200 (50), 189 (22), 184 (50), 183 (38), 169 (60), 167 (44), 164 (90), 156 (35), 155 (30), 154 (98), 153 (56), 152 (46), 141 (35), 139 (33), 129 (71), 128 (90),

127 (42), 115 (80), 91 (35), 77 (60), 75 (37), 65 (36), 63 (48), 53 (35), 51 (68), 39 (76); Cmr ($CDCl_3$)[52] 151.57 (t), 146.23 (m), 144.92 (m), 144.66 (s), 140.93 (s), 132.71 (s), 118.94 (t), 106.64 (t), 59.91 (s), 54.49 (s), 16.44 (q), 13.81 (q), 11.00 (q), 7.05 (q) ppm.

Anal. Calcd. for $C_{14}H_{16}Cl_2$: C, 65.94; H, 6.32
Found: C, 65.63; H, 6.50

The minor component 136 had: ir (CCl_4) 2960 (m), 1440 (w), 1250 (m), 950 (w), 880 (s) cm^{-1}; uv (MeOH) λ_{max}273 nm (ε 15,900); nmr (CCl_4) δ 1.23 (s, 6H), 1.37 (s, 6H), 5.10 (s, 2H), 5.53 (s, 2H); mass spectrum (70 eV) m/e (rel intensity) 258 (1), 256 (7), 254 (11), 241 (41), 239 (64), 226 (20), 224 (30), 221 (24), 220 (15), 219 (70), 218 (13), 206 (35), 205 (30), 204 (100), 203 (40), 191 (10), 189 (25), 169 (34), 167 (12), 153 (30), 152 (30), 141 (13), 129 (22), 128 (35), 127 (19), 115 (36), 77 (29), 63 (22), 51 (29), 39 (34).

2. Thermal Rearrangement of 134

A solution of 134 (50 mg, 0.17 mmol) in 0.5 ml carbon tetrachloride was sealed in an nmr tube and heated in an oil bath maintained at 120°. The reaction, monitored by nmr, went to completion in about an hour. Analytical vpc (5' x 0.125 in column, 3% SE-30 on chromosorb W, 80/100, 150°) showed nearly quantitative conversion of 134 to 136.

3. Allylic Oxidation of 1,2,5,6,7-pentamethylbicyclo[3.2.1]-octa-2,6-dien-9-one, 138[21]

To a slightly cooled solution of 4.75 g (0.06 mol) of anhydrous pyridine in 80 ml of methylene chloride was added 3.0 g (0.03 mol) of chromium trioxide, and the mixture was allowed to stir at room temperature for 45 min under nitrogen. A solution of 510 mg (2.7 mmol) of 138 in a small amount of methylene chloride was added and the mixture was allowed to stir for 24 hrs at room temperature. The solution was decanted, the residue was rinsed with petroleum ether (bp 30-60°), and the combined organic phase was washed in succession with saturated sodium bicarbonate solution, 2 N hydrochloric acid, saturated sodium bicarbonate, and saturated salt solution. The organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure, and the residual oil, when subjected to analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, Aw-DMCS 80/100, 180°) showed a major peak corresponding to 139 (retention time 9.0 min) and several not very well resolved peaks with shorter retention times. Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 200°) gave 139: 224 mg (40% yield); ir (CCl_4) 3000 (m), 1770 (s), 1660 (m), 1450 (w), 1390 (w), 1250 (m), 880 (s) cm^{-1}; uv (MeOH) λ_{max}235 nm (ε 2,540), 262 (2,500); nmr (CCl_4) δ1.20 (s, 3H), 1.27 (s, 3H), 1.58 (q, 3H, J = 1 Hz),

1.68 (q, 3H, J = 1 Hz), 1.97 (d, 3H, J = 1 Hz), 5.53 (m, 1H); mass spectrum (70 eV) m/e (rel intensity) 204 (44), 189 (33), 176 (28), 161 (37), 134 (13), 133 (100), 105 (23), 91 (33), 79 (16), 78 (8), 77 (28).

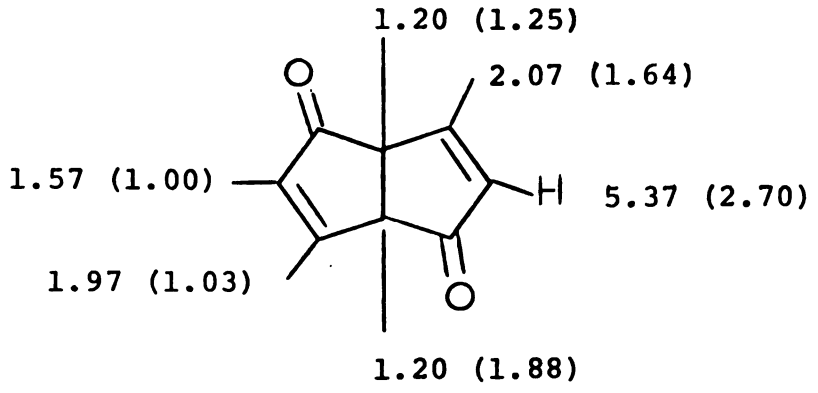
Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90
Found: C, 76.31; H, 8.04

4. Irradiation of 1,4,5,6,7-pentamethylbicyclo[3.2.1]-octa-3,6-dien-2,8-dione, 139

A degassed solution containing 100 mg (0.49 mmol) of 139 in 20 ml of anhydrous ether was irradiated through Pyrex with a 450 W Hanovia lamp. The photolysis was followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 190°). The reaction reached a photostationary state in about 2 hr. Vpc showed 2 peaks corresponding to 139 (retention time 6.2 min, 73%) and 140 (retention time 4.5 min, 27%). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 200°) gave 1,3,4,5,8-pentamethylbicyclo[3.3.0]octa-3,7-dien-2,6-dione, 140: ir (CCl_4) 1700 (s), 1650 (w), 1620 (w), 1445 (w), 1390 (w), 1250 (m), 880 (s) cm^{-1}; uv (MeOH) λ_{max}235 nm (ε 13,400), 335 (730); nmr (CCl_4) δ 1.20 (m, 6H), 1.57 (q, 3H, J = 1 Hz), 1.97 (q, 3H, J = 1 Hz), 2.07 (d, 3H, J = 2 Hz), 5.37 (m, 1H); europium shift data (see structure);

mass spectrum (70 eV) m/e (rel intensity) 205 (15), 204 (100), 189 (68), 176 (55), 161 (48), 123 (85), 105 (16), 91 (27), 79 (12), 77 (22), 65 (12).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90
Found: C, 76.34; H, 7.90



140

If the photolysis was continued through Corex after reaching photostationary state, the peaks corresponding to 139 (retention time 6.2 min) and 140 (retention time 4.5 min) began to decrease in areas and a new product peak appeared at 1.5 min when followed by analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 190°). After 1.5 hr, the reaction was nearly complete and the product 141 was collected by preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 160°). Compound 141 had spectra data identical with that of the known compound.[53]

Compound 141 was photolabile and rearranged slowly

on further irradiation through Corex presumbly to compound 142 as indicated by the appearance of the ir absorption band at 2102 cm^{-1}. No attempts were made to isolate this compound.

5. Irradiation of 1,3,4,5,8-pentamethylbicyclo[3.3.0]-octa-3,7-dien-2,6-dione, 140

The procedure and workup were as described for the irradiation of 139. Identical results were obtained as in the irradiation of 139.

6. Treatment of Bicyclo[3.2.1]octa-3,6-dien-2-one (143) with Trifluoroacetic Acid

A solution of 50 mg (0.42 mmol) of 143[50] in 0.3 ml of ice-cold trifluoroacetic acid was stirred at room temperature, the reaction being monitored by nmr. It went to completion in about 4 hr and was quenched by pouring the mixture into ice and saturated $NaHCO_3$ solution. The product was extracted with methylene chloride and washed with saturated NaCl solution and dried (Na_2SO_4). An nmr spectrum of the crude product showed no starting material. However, vpc analysis (5' x 0.125 in column, 3% SE-30 on chromosorb W, 80/100, 100°) showed three compounds: starting material 143 (15%, ret time 6.3 min),

144a (21%, ret time 7.5 min), and 144b (64%, ret time 8.0 min). The ratio of these three compounds depended on the column temperature. At higher column temperatures, the peaks corresponding to 144a and 144b decreased in areas, while that corresponding to 143 increased in its area. The mixture of 144a and 144b, which could not be separated easily without much decomposition on vpc, was collected by preparative vpc (5' x 0.25 in column, 10% Se-30 on chromosorb W, 80/100, 135°): ir (neat) 2960 (w), 1780 (s), 1720 (s), 1460 (w), 1420 (w), 1350 (w), 1220 (s), 1160 (s) cm^{-1}; nmr ($CDCl_3$) δ 2.3-3.4 (m, 6H), 5.35 (m, 1H), 6.2-6.4 (m, 2H); mass spectrum (70 eV) m/e (rel intensity) 234 (3), 196 (3), 153 (4), 138 (8), 120 (51), 95 (14), 93 (12), 92 (41), 91 (94), 79 (25), 78 (38), 77 (15), 69 (30), 67 (28), 66 (100), 65 (28), 55 (23).

7. Treatment of Bicyclo[3.2.1]octa-3,6-dien-2-one (143) with Fluorosulfonic Acid

To a solution of 50 mg (0.42 mmol) of 143[50] in CH_2Cl_2 (0.4 ml) was added fluorosulfonic acid (0.1 ml) at -78°. The mixture was slowly warmed to room temperature and stirred for 1 hr. The reaction was quenched by pouring the mixture into methanol and NaOMe solution at -78°. The methanol was evaporated, water was added to the residue, and the product was extracted with CH_2Cl_2 and washed with saturated NaCl

solution and dried (Na_2SO_4). Vpc analysis (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS 80/100, 155°) of the crude product showed nearly exclusive formation of 145 (ret time 24 min). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80/100, 120°) gave 145: ir (neat) 2960 (s), 1713 (s), 1460 (w), 1415 (w), 1170 (w), 1230 (m), 1100 (s), 1040 (w), 1010 (w), 980 (w), 940 (w), 920 (w), 750 (s) cm^{-1}; uv (MeOH) λ_{max}290 nm (ε 150); nmr (CCl_4) δ 1.6-3.3 (m, 6H), 3.33 (s, 3H), 3.60 (m, 1H), 6.20 (m, 2H); mass spectrum (70 eV) m/e (rel intensity) 152 (2), 120 (14), 110 (9), 92 (15), 91 (33), 79 (16), 78 (12), 74 (39), 67 (15), 66 (100), 65 (15), 58 (11), 45 (14).

8. Michael Addition of Methanol to 143

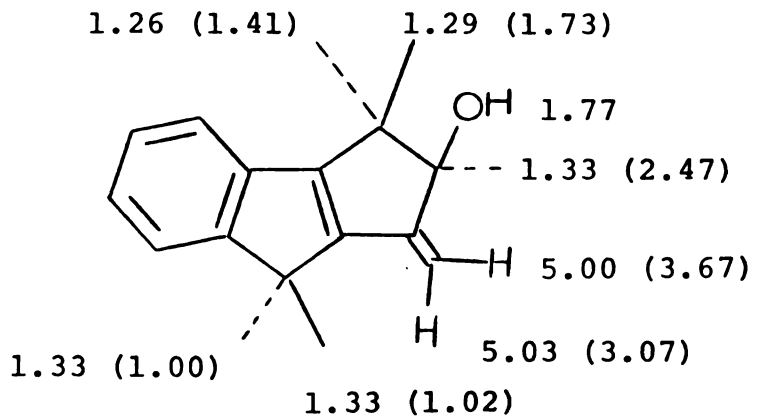
To a solution of 143[50] (50 mg, 0.42 mmol) in methanol was added 23 mg (0.43 mmol) of NaOMe, and the mixture was allowed to reflux for 14 hrs. The methanol was evaporated, water was added to the residue, and the product was extracted with CH_2Cl_2, and washed with saturated NaCl solution and dried (Na_2SO_4). Evaporation of the solvent gave a quantitative yield of 145.

9. Epoxidation of 1,4-dihydro-1,1,2,3,4,4-hexamethylbenzopentalene, 146

To a solution of 146[51] (190 mg, 0.80 mmol) in 5 ml of

methylene chloride was added, at 0°, a solution of 150 mg (0.87 mmol) of m-chloroperbenzoic acid in 2 ml of methylene chloride. The mixture was stirred for 1 hr at room temperature during which time m-chlorobenzoic acid precipitated from solution. The solvent was evaporated, petroleum ether (bp 30-60°) was added to the residue, and m-chlorobenzoic acid was removed by filtration. Evaporation of the solvent from the filtrate left a brown oil; an nmr spectrum of the crude material showed it to be > 90% 148. The crude product was chromatographed on Alumina (80-200 mesh) using 20% EtOAc/hexane as eluent, to give 173 mg (0.68 mmol, 85%) of 148 and 10 mg (0.04 mmol, 5%) of 149. Compound 148 had mp 89-90°; ir (KBr) 3400 (s), 2950 (s), 1620 (m), 1460 (m), 1370 (m), 1300 (w), 1180 (m), 1140 (m), 1080 (s), 1000 (w), 950 (m), 860 (s), 790 (w), 750 (s) cm^{-1}; uv (MeOH) λ_{max} 320 nm (shoulder, ε 8,180), 300 nm (ε 10,200), 290 nm (shoulder, ε 8,500), 243 nm (shoulder, ε 5,670), 235 nm (ε 6,820), 230 nm (shoulder, ε 5,700); nmr ($CDCl_3$) δ 1.33 (m, 15H), 1.77 (s, 1H, disappeared with D_2O), 5.03 (d, 2H, J = 2 Hz), 7.26 (m, 4H); europium shift data (see structure); mass spectrum (70 eV) m/e (rel intensity) 255 (13), 154 (53), 240 (20), 239 (92), 238 (23), 237 (17), 236 (59), 224 (27), 223 (32), 222 (24), 221 (100), 211 (15), 209 (12), 208 (17), 207 (19), 206 (55), 197 (15), 191 (29), 190 (14), 189 (15), 181 (14), 179 (15), 178 (20), 169 (15), 165 (27), 152 (12), 103 (12), 89 (18).

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72
Found: C, 85.05; H, 8.72



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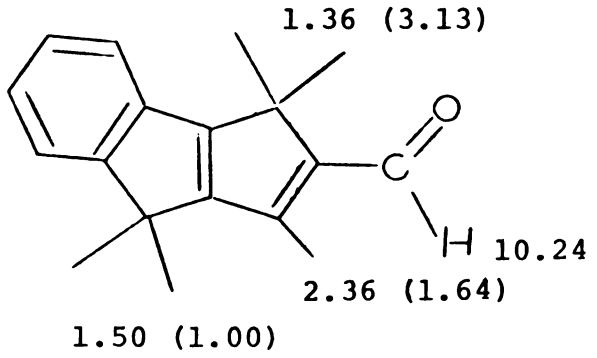
Compound 149 had mp 188-189°; ir (KBr) 2960 (m), 2860 (m), 1660 (s), 1540 (w), 1460 (s), 1400 (m), 1370 (m), 1200 (w), 840 (m), 760 (s), 720 (m) cm^{-1}; uv (ether) λ_{max}345 nm (ε 4,280), 307 nm (shoulder, ε 18,820), 295 nm (ε 11,100), 288 nm (shoulder, ε 10,600); nmr ($CDCl_3$) δ 1.36 (s, 6H), 1.50 (s, 6H), 2.36 (s, 3H), 7.30 (m, 4H), 10.24 (s, 1H); europium shift data (see structure); mass spectrum (70 eV) m/e (rel intensity) 253 (26), 252 (100), 237 (45), 224 (12), 223 (29), 222 (22), 210 (14), 209 (67), 208 (17), 195 (10), 194 (30), 193 (22), 191 (12), 189 (10), 181 (11), 179 (31), 178 (39), 165 (15), 111 (11), 89 (13).

Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99
Found: C, 85.73; H, 7.96



149

10. Photosensitized Oxidation of 1,4-dihydro-1,1,2,3,4,4-hexamethylbenzopentalene, 146

A solution of 146[51] (147 mg, 0.62 mmol) in 25 ml MeOH through which oxygen was bubbling was irradiated with a 150 W Tungsten lamp in the presence of a catalytic amount of methylene blue. The photolysis was stopped after 6 hr. The methylene blue was removed on a short column of Florisil. The crude product was recrystallized from methanol to give a compound either as 150a or 150b: 136 mg (70% yield); mp 150-151°; ir (KBr) 2990 (s), 1490 (m), 1460 (m), 1440 (m), 1380 (m), 1360 (w), 1320 (w), 1305 (m), 1260 (m), 1240 (w), 1200 (w), 1160 (m), 1150 (m), 1130 (m), 1100 (s), 1070 (m), 1050 (s), 990 (s), 970 (m), 930 (s),

900 (m), 770 (m) cm^{-1}; uv (MeOH) λ_{max}210 nm (ε 4,740); nmr (CCl_4) δ 0.93 (s, 3H), 1.37 (s, 3H), 1.40 (s, 3H), 1.49 (s, 3H), 1.52 (s, 3H), 1.87 (s, 3H), 2.97 (s, 3H), 3.30 (s, 3H), 7.00 (m, 4H); mass spectrum (70 eV) m/e (rel intensity) 316 (25), 301 (33), 285 (28), 284 (42), 270 (23), 269 (100), 254 (19), 253 (44), 241 (13), 240 (12), 239 (49), 238 (23), 237 (24), 225 (20), 224 (45), 223 (35), 222 (15), 211 (13), 210 (14), 209 (31), 195 (16), 171 (12), 169 (15), 165 (25), 157 (18), 129 (14), 128 (17).

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92
Found: C, 75.84; H, 9.01

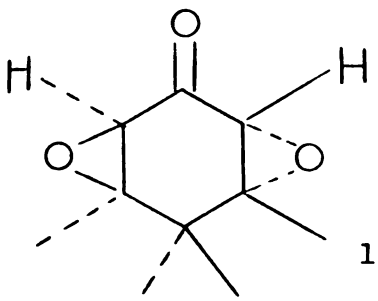
11. Epoxidation of 3,4,4,5-tetramethyl-2,5-cyclohexahexadienone (151) with m-chloroperbenzoic acid

To a solution containing 200 mg (1.33 mmol) of 151[54] in 10 ml of methylene chloride was added, at 0°, a solution of m-chloroperbenzoic acid (240 mg, 1.40 mmol) in 5 ml of methylene chloride. The reaction mixture showed no sign of reaction (nmr) after being stirred overnight at room temperature. After the usual workup as in the epoxidation of 53 (see page 36), 151 was recovered in quantitative yield.

12. Epoxidation of 3,4,4,5-tetramethyl-2,5-cyclohexadienone (151) with alkali hydrogen peroxide

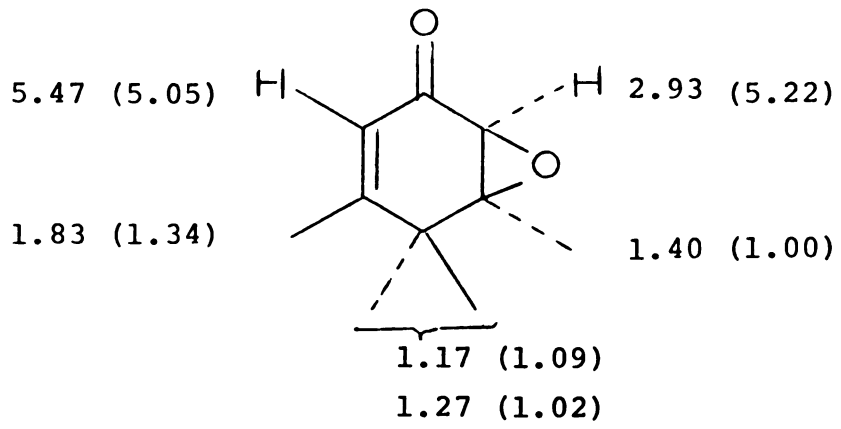
To a solution of 1.86 g (0.012 mol) of 151[54] and 12 ml

(0.12 mol) of 30% aqueous hydrogen peroxide in 30 ml of methanol cooled to 15° was added dropwise and with stirring 7 ml (0.014 mol) of 2 N aqueous sodium hydroxide. After being stirred at room temperature for 4 hrs, the reaction mixture was diluted with water and extracted with ether. The ether extracts were washed with saturated salt solution and dried ($MgSO_4$). Evaporation of the solvent left 0.975 g of an oil which, when subjected to analytical vpc (5' x 0.125 in column, 10% FFAP on chromosorb W, AW-DMCS, 80/100, 143°) showed four components: 152 (43%, ret time 3.2 min), 153 (5%, 4.5 min), 154 (7%, 7.5 min), and 155 (45%, 9.5 min). Preparative vpc (5' x 0.25 in column, 10% FFAP on chromosorb W, 80-100 mesh, 180°) gave trans-2,3:5,6-diepoxy-3,4,4,5-tetramethylcyclohexanone 153: ir (CCl_4) 3000 (m), 1720 (s), 1480 (w), 1400 (w), 1320 (w), 1295 (w), 905 (m) cm^{-1}; uv (MeOH) λ_{max} 215 nm (ε 580); nmr (CCl_4) δ 1.20 (s, 6H), 1.28 (s, 6H), 2.83 (s, 2H); europium shift data (see structure); mass spectrum (70 eV) m/e (rel intensity) 182 (1), 167 (2), 153 (4), 150 (5), 139 (11), 135 (7), 126 (8), 125 (100), 123 (9), 110 (11), 107 (14), 97 (15), 91 (12), 83 (12), 79 (14), 77 (10), 69 (26), 67 (21), 55 (77), 53 (20).



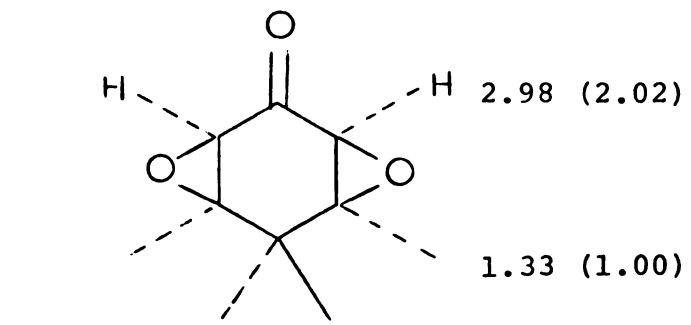
153

5,6-Epoxy-3,4,4,5-tetramethyl-2-cyclohexenone 154: ir (CCl_4) 3020 (w), 2990 (w), 1670 (s), 1470 (w), 1430 (w), 1370 (w), 1250 (s), 870 (s) cm^{-1}; uv (MeOH) λ_{max} 245 nm (ε 5,100); nmr (CCl_4) δ 1.17 (s, 3H), 1.27 (s, 3H), 1.40 (s, 3H), 1.83 (d, 3H, J = 2 Hz), 2.93 (s, 1H), 5.47 (d, 1H, J = 2 Hz); europium shift data (see structure); mass spectrum (70 eV) m/e (rel intensity) 166 (3), 151 (56), 150 (21), 149 (4), 138 (59), 137 (12), 135 (25), 123 (62), 109 (73), 107 (25), 105 (11), 95 (18), 93 (11), 91 (23), 81 (30), 79 (25), 77 (22), 69 (16), 67 (100), 65 (15), 55 (40), 53 (28), 51 (16).



154

Cis-2,3:5,6-diepoxy-3,4,4,5-tetramethylcyclohexanone 155: ir (CCl_4) 3020 (m), 2980 (w), 1700 (s), 1470 (w), 1430 (w), 1405 (w), 1380 (w), 1305 (w), 1270 (w), 1075 (w) cm^{-1}; uv (MeOH) λ_{max}215 nm (ϵ 990), 233 nm (ϵ 990); nmr (CCl_4) δ 1.15 (s, 3H), 1.33 (s, 6H), 1.37 (s, 3H), 2.98 (s, 2H); europium shift data (see structure); mass spectrum (70 eV) m/e (rel intensity) 182 (3), 167 (4), 151 (5), 150 (10), 139 (8), 138 (8), 135 (13), 126 (10), 125 (100), 123 (12), 111 (13), 109 (13), 107 (27), 97 (15), 95 (10), 91 (21), 83 (14), 81 (18), 79 (20), 77 (16), 69 (28), 67 (33), 65 (11), 57 (14), 55 (84), 53 (31).



155

Compound 152,which decomposed on the preparative vpc column, was not collected.

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