AN ABSTRACT OF THE THESIS OF

LOUIS SCERBO for the Ph. D.
(Name) (Degree)

in CHEMISTRY presented on March 27, 1968
(Major) (Date)

Title: THE SYNTHESIS AND CHEMISTRY OF STRAINED BICYCLIC SYSTEMS

Abstract approved [redacted]
Dr. F. Thomas Bond

A facile route to bicyclo(2. 1. 1)hexanes was developed involving the intramolecular photocyclization of 1, 5-hexadien-3-one to bicyclo(2. 1. 1)hexan-2-one. A study of the chemistry of bicyclo-(2. 1. 1)hexan-2-one was undertaken. Deuterium exchange and borohydride reduction demonstrated the strain present in the ketone. Further evidence was obtained from the failure to introduce substituents alpha to the carbonyl group, a usually facile reaction and a necessary step in desired ring contraction studies.

After numerous unsuccessful attempts to introduce a double bond into the bicyclo(2. 1. 1) hexane system, a successful route to the parent bicyclo(2. 1. 1) hexene was achieved. The key step involved dehydrohalogenation of 2-bromobicyclo(2. 1. 1)hexane. Some preliminary studies of the olefin have been carried out and its thermolysis studied.

The Synthesis and Chemistry of Strained Bicyclic Systems

by

Louis Scerbo

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

June 1968

APPROVED:

[redacted]

Assistant Professor of Chemistry

in charge of major

[redacted]

Chairman of the Department of Chemistry

[redacted]

Dean of Graduate School

Date thesis is presented March 29, 1968

Typed by Marion F. Palmateer for Louis Scerbo

ACKNOWLEDGEMENT

The author wishes to express appreciation to Dr. F. Thomas Bond for assistance throughout this study and for his aid in the preparation of this manuscript.

TABLE OF CONTENTS

Page

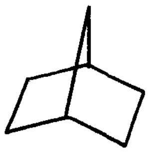
LIST OF TABLES

LIST OF FIGURES

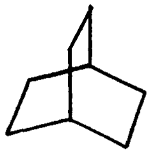
THE SYNTHESIS AND CHEMISTRY OF STRAINED BICYCLIC SYSTEMS

INTRODUCTION

Many contributions to the field of organic chemistry have been derived from the study of rigid bicyclic ring systems. Such study, for the most part, has been concentrated on the bicyclo(2. 2. 1)heptane nucleus 1. The rigid geometry of this system, a 1, 4-bridged boat cyclohexane ring, results in many novel and informative chemical properties (6, 9). Much of the chemistry of 1 can be related to the strain possessed by the system. The effects of strain on the chemistry of 1 can be seen when this system is compared to the relatively strain-free bicyclo(2. 2. 2)octane system 2. Surprisingly, in view of the vast amount of detailed work done on the bicyclo(2. 2. 1)heptanes, very little progress has been made with the bicyclo(2. 1. 1)hexanes 3. The synthesis and chemistry of this bridged cyclopentane (or cyclobutane) is the main subject of this thesis.



1

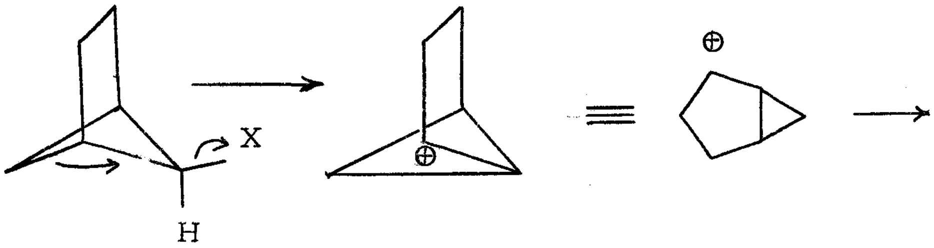


2

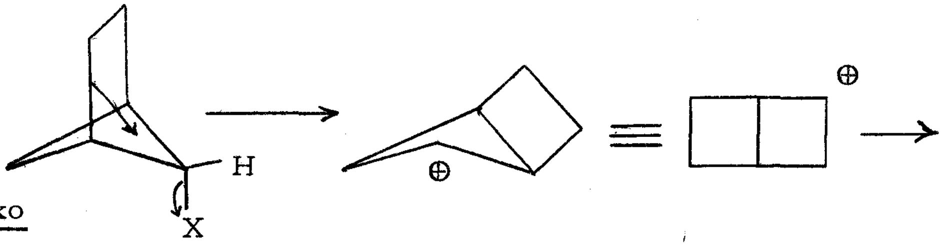
3

The revival of interest in bicyclo(2. 1. 1) hexanes during the past decade (66, 76) is based, in part, by questions which have been brought up in the study of the bicyclo(2. 2. 1)heptanes. One of the biggest problems in dealing with the chemistry of attack at C-2 of bicyclo(2. 2. 1)heptane is that such reactions can occur *via* *exo* or *endo* pathways. The latter of these processes is sterically unfavorable. In comparison, C-2 in 3, lies in a plane of symmetry. Attack from either side of the two-carbon bridge is an equivalent process. Thus the idea of *exo* or *endo* attack does not apply to attack at C-2 (or C-3) in bicyclo(2. 1. 1)hexanes.

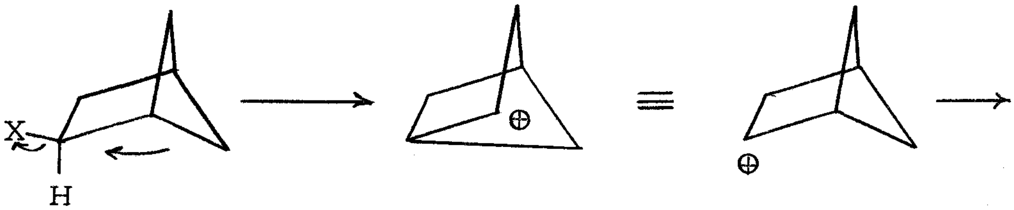
As a direct consequence of the symmetry in 3, however, substitution at the C-5 (or C-6) position can be either *exo* or *endo*, thus allowing the study of the effect of conformation in rigid cyclobutyl ring systems. This is particularly important where participation of adjacent bonds may lead to several types of rearrangements. One may envisage the following possibilities:



endo

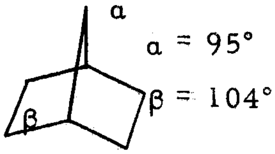


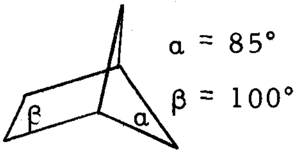
exo

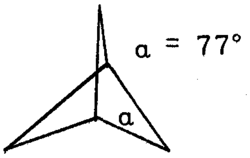


2-substituted

A second important feature of 3 is the increase in internal strain compared to 1. The geometries of these systems, which are represented below, give a qualitative indication of the differences in strain (26, 66).

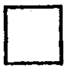
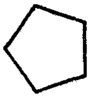
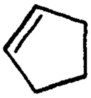
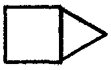
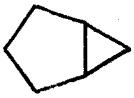




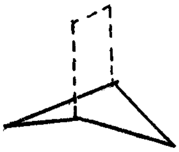


A more quantitative evaluation of the strain energies of bicyclic compounds has not been carried out. However, simple small-ring compounds and their related fused-ring systems have been studied. Some of the results for such simple systems are shown in Table 1 (8).

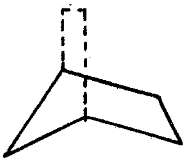
Table 1. Strain energies (S. E.) of selected compounds.

Compound	S. E. (kcal/mole)exp.	S. E. (kcal/mole)calc.
	27. 6	---
	26. 2	---
	6. 3	---
	5. 9	---
	68-69	55. 2
	55. 3	53. 8
	32. 7	33. 9

It can be seen from Table 1 that one can obtain the strain energy of a fused system by a simple summation of the strain energies of its component ring systems (108). The example of bicyclo(1. 1. 0)butane shows that this "additivity" is not only approximate, but fails to hold rigidly for very highly strained fused-ring systems. This is also true for strained bicyclic ring systems. However, direct comparisons between bicyclic systems can be made. When bicyclo(2. 2. 1)heptane 1 is considered as a cyclopentane bridged by two carbons and bicyclo(2. 1. 1)hexane 3 a cyclobutane bridged by two carbons, as shown below, the main difference in strain between the two systems is that between cyclopentane and cyclobutane.



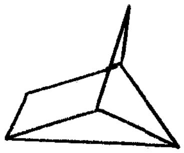
3



1

The data from Table 1 indicate that this value should be about 20 kcal/mole more strain energy for bicyclo(2. 1. 1)hexane. The reported experimental value for the strain energy of bicyclo(2. 2. 1)heptane is 8. 3 kcal/mole. Thus bicyclo(2. 1. 1)hexane would be predicted to have a strain energy of at least 28 kcal/mole.

A final basis for the renewed interest in bicyclo(2. 1. 1)hexanes is that they can be starting points for further synthesis in the area of small-ring bicyclic systems. Again, most of these reactions on bicyclo(2. 1. 1)hexanes parallel reactions which have been studied with the bicyclo(2. 2. 1)heptanes.. Thus, reactions which may lead to such strained systems as tricyclo(2. 2. 0. $0^{2,6}$)hexane 4 and 2-substituted bicyclo(1. 1. 1)pentanes 5 could occur in the bicyclo(2. 2. 1)heptane system. For these reasons and because of the challenge of the synthesis of such highly strained compounds, it was thought interesting and profitable to study the synthesis and reactions of some bicyclo(2. 1. 1)hexanes.



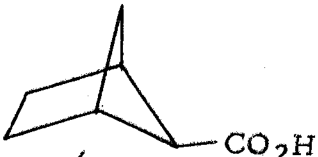
4

5

Bicyclo(2. 1. 1)hexanes

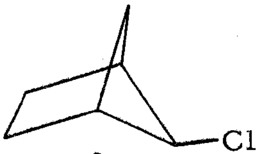
Synthesis

A search of the literature reveals that very little work had been done in the field of bicyclo(2. 1. 1)hexane synthesis before 1960. At this time Wiberg and co-workers reported the synthesis of the simple bicyclo(2. 1. 1)hexane derivatives 6 through 11 (115, 116, 117).



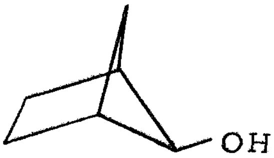
6

7

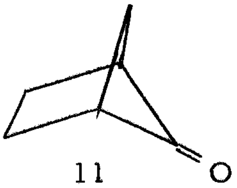


8

9



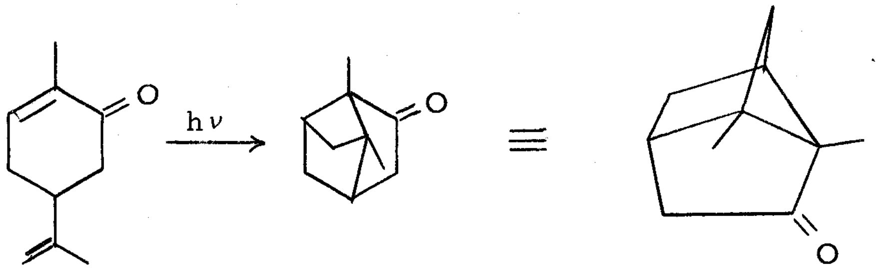
10



11

Concurrently, work was published by Meinwald and co-workers reporting the preparation of similar compounds, usually incorporating methyl substituents on the bridging atoms (C-5). This early work, through 1966, has been well reviewed (76) and only some of the more important points will be summarized here.

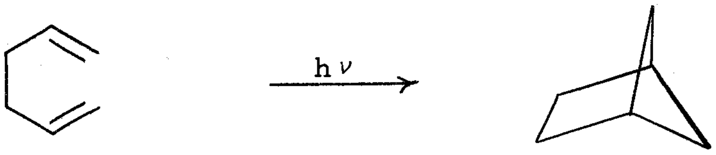
Syntheses of bicyclo(2. 1. 1)hexanes can be divided into three groups according to the general types of reactions used; photocycloadditions, ring contractions, and miscellaneous. The first example of a bicyclo(2. 1. 1)hexane synthesis was also one of the first examples of an intramolecular photocycloaddition reaction (20). In 1908, Ciamician reported that the solar irradiation of carvone 12 gave the tricyclo(3. 3. 0. $0^{2,7}$)octanone 13, a bicyclo(2. 1. 1.)hexane nucleus containing a two-carbon bridge between C-2 and C-5.



12 13

The assigned structure 13 was confirmed by Büchi and Goldman in 1957 (15) and the synthesis improved by Meinwald and Schneider in 1965 (77). Both Meinwald and Schneider (77), and Gibson and Erman (40), studied this reaction in some detail. In the course of their study, Gibson and Erman degraded 13 to some simple methyl substituted bicyclo(2. 1. 1)hexanes.

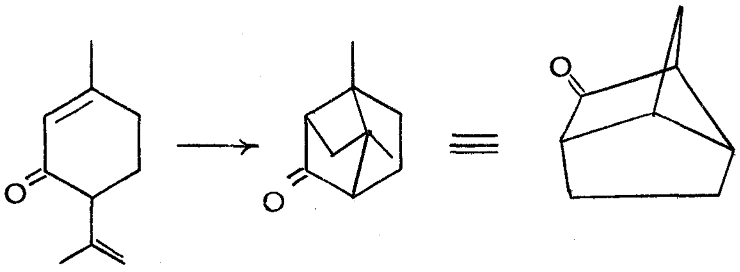
The above reaction is an internal photocycloaddition of one double bond to another in a 1, 5-hexadiene. Srinivasan has shown that mercury-sensitized irradiation of 1, 5-hexadiene itself, 14, leads to the hydrocarbon, bicyclo(2. 1. 1)hexane 3 in low yield (103). Thus the necessary chromophore for bicyclo(2. 1. 1)hexane formation *via*



14 3

photocycloaddition is the 1, 5-hexadiene system.

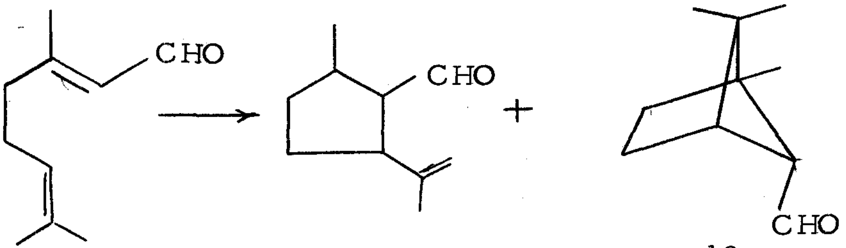
Erman has recently shown that the irradiation of isopiperitenone 15 gives a tricyclic ketone 16 which is very similar to



15 16

carvonecamphor 13 (37). Discussion of this reaction in relation to the carvone-carvonecamphor transformation will be postponed to section VI of this introduction. Again, it is to be noted that a 1, 5-diene is the essential part of the reactant.

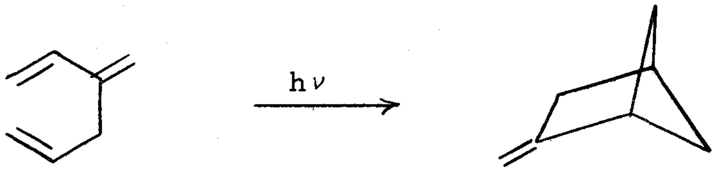
Cookson has also achieved the synthesis of a bicyclo(2. 1. 1)-hexane via a photochemical cycloaddition reaction (22). In his experiment, citral 17 was cyclized by ultraviolet irradiation to a mixture of 2-isopropenyl-5-methylcyclopentane carboxaldehyde 18 and 1, 6, 6, -trimethylbicyclo(2. 1. 1)hexan-endo-2-carboxaldehyde 19. Again a 1, 5-hexadiene system is involved though here the chromophore is external to the diene system. It is most likely that these



17 18 19

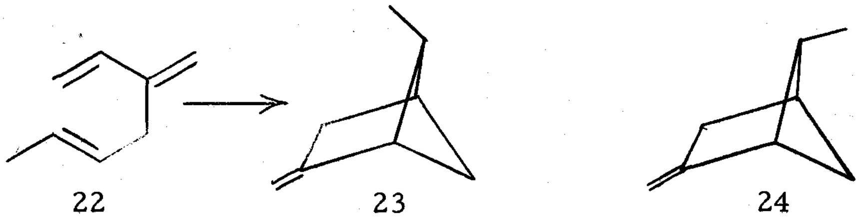
reactions involve the addition of the photoexcited enone to the isolated double bond. The excitable chromophore, however, need not be limited to enones.

Liu (58), Liu and Hammond (59), and de Mayo (19) have all shown that a conjugated diene may undergo photocycloaddition to an isolated double bond. Thus the irradiation of 3-methylene-1, 5-hexadiene 20 leads to the formation of 2-methylenebicyclo(2. 1. 1)-hexane 21.

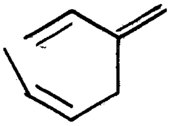


20 21

Irradiation of *trans* -3-methylene-1, 5-heptadiene 22 gave a 6:1 mixture of the two 5-methyl-2-methylenebicyclo(2. 1. 1)hexanes 23 and 24, respectively. The same results are obtained when the isomeric *cis*-triene 25 is irradiated. All the above triene isomerizations



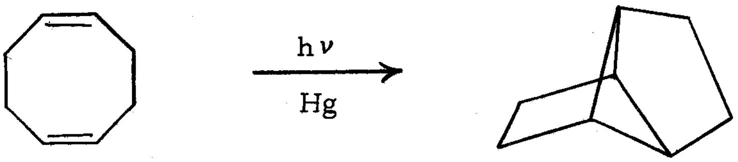
22 23 24



25

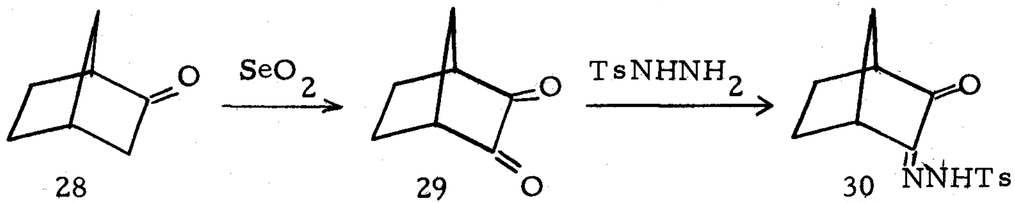
require the presence of a photosensitizer, such as benzophenone. Indeed upon direct irradiation, the major pathway followed leads to a cyclobutene.

One last example of a photocycloaddition reaction which leads to a bicyclo(2. 1. 1)hexane is the mercury-sensitized irradiation of *cis, cis*-octadiene-1, 5 26 to give tricyclo(3. 3. 0. $0^{2,6}$)octane 27. This tricyclic compound incorporates the bicyclo(2. 1. 1)hexane nucleus into its skeleton. At first, only low yields were obtained in this vapor phase reaction (98). Yields were raised considerably when cuprous chloride was used as a catalyst and ether was used as a solvent (5, 99, 100). As discussed later, however, 27 appears to be less strained than the parent bicyclo(2. 1. 1)hexane.

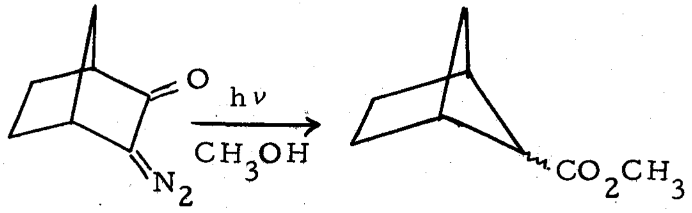


26 27

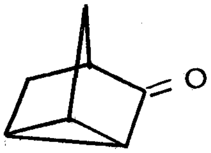
The most common route to substituted bicyclo(2. 1. 1)hexanes has been the ring contraction of appropriate α-diazoketones (76). One typical example of this is the sequence shown below which was used by Wiberg for the synthesis of 5-substituted bicyclo(2. 1. 1)hexanes (116). Compound 32 served as the starting point for the synthesis of other desired compounds.



28 29 30

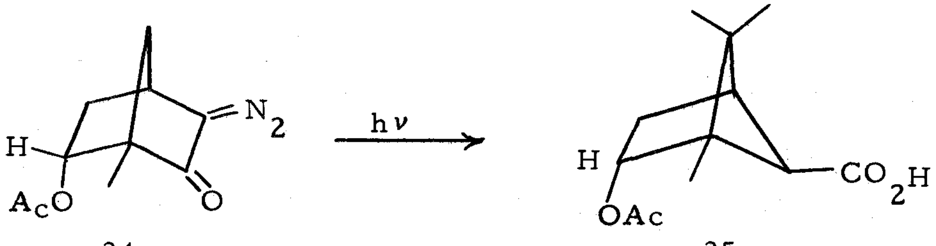


31 32



33

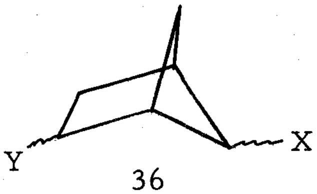
Because of its many steps, this route is plagued by low yields. In addition, one obtains a mixture of isomeric C-5 carboxylates. In this case, the mixture contains predominantly the *endo* isomer. Substitution of a methyl group at C-7 of 28 *syn* to the carbonyl leads to a product mixture in which the *exo* isomer predominates. Another reservation about this reaction sequence is that only C-5 substituted derivatives may be synthesized. It is possible to incorporate other substituents into 28 such as in 34, but there always remains the C-5 carboxylate.



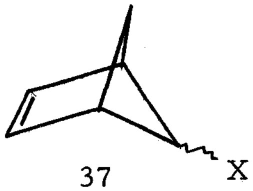
34

35

The existence of a C-5 carboxylate in addition to other substituents is not always a problem. Meinwald and Crandall (68) have made use of the ring contraction of a substituted α-diazonorbornanone to achieve the synthesis of di- and mono-substituted bicyclo(2. 1. 1)-hexanes. Meinwald's immediate goal was a 2, 5-disubstituted bicyclo-(2. 1. 1)hexane 36, which could be converted to either a 2- or a 5-substituted compound, or a 5-substituted bicyclo(2. 1. 1)hexene, 37.



36



37

The reaction sequence which Meinwald and Crandall followed is very similar to the one shown above. This sequence is shown in Figure 1.

The synthesis of 2-substituted bicyclo(2. 1. 1)hexanes was achieved by the decarboxylation of 38 and 39 as shown below. Prior to our study, this lengthy pathway was the only method of obtaining a 2-substituted bicyclo(2. 1. 1)hexane.

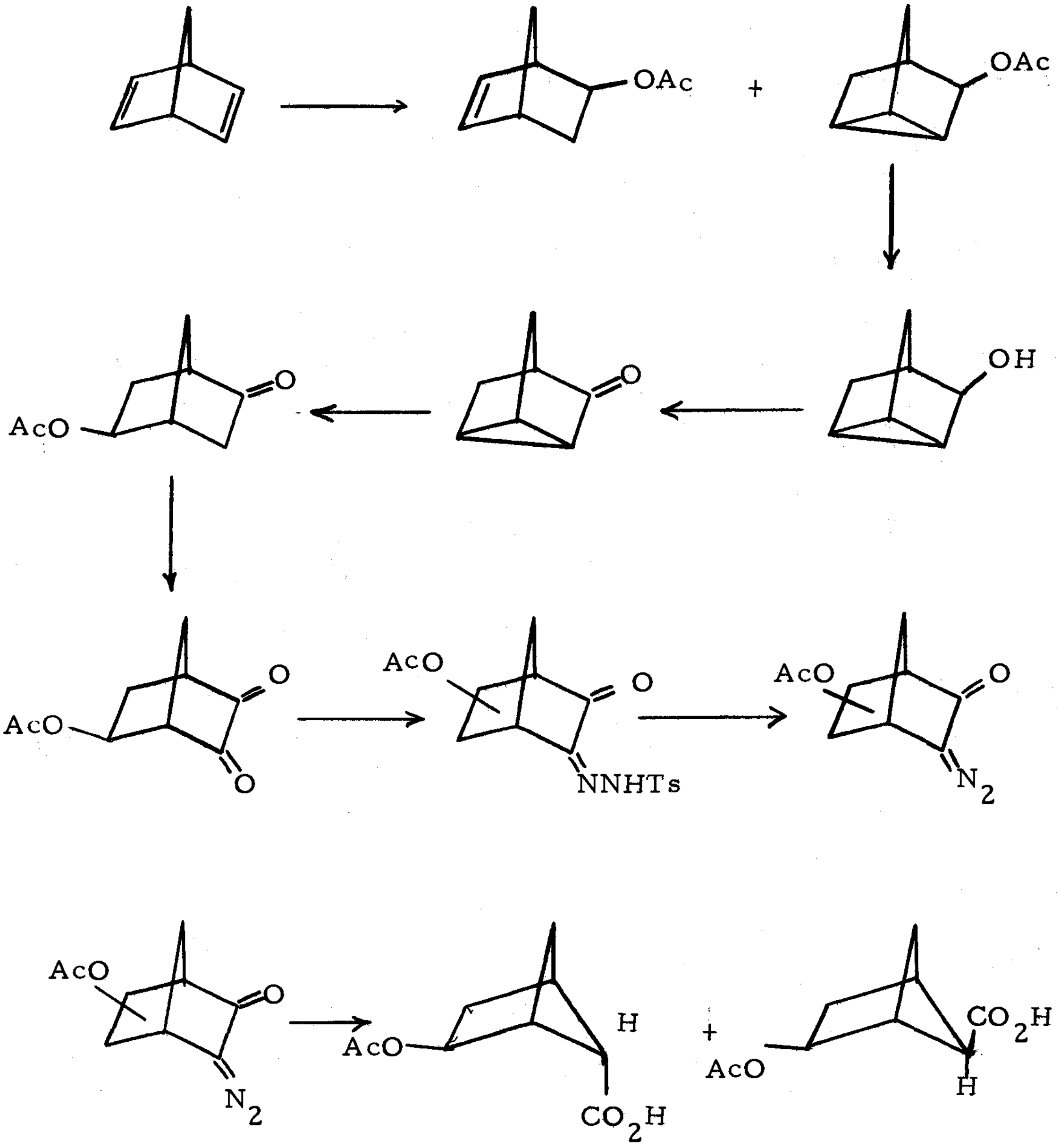
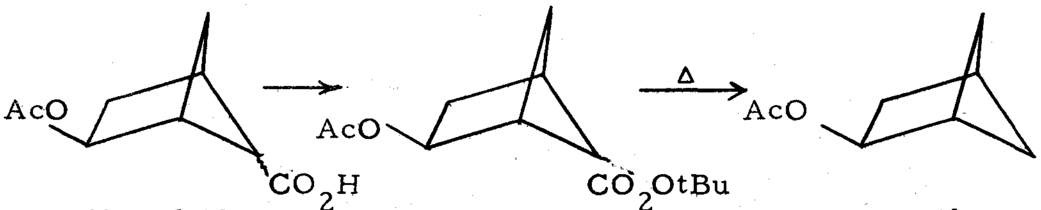
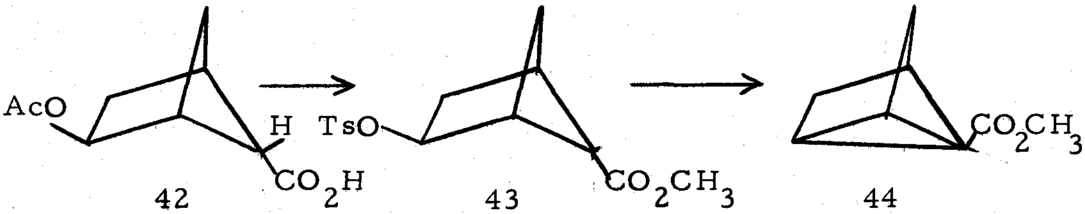


Figure 1. Synthetic route to 2-acetoxybicyclo(2. 1. 1)hexane-5-carboxylic acid.



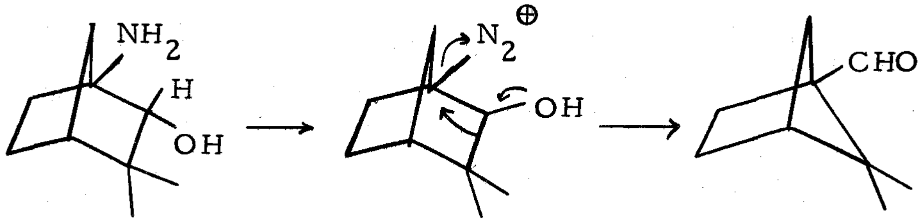
38 and 39 40 41

The second goal which Meinwald had undertaken, the synthesis of a bicyclo(2. 1. 1)hexene 37, was not achieved but some interesting results were obtained. The acetoxy acid 42 was converted to the corresponding tosylate ester 43 and treated with base. Instead of obtaining the desired olefin, an internal displacement occurred yielding the tricyclic ester 44.



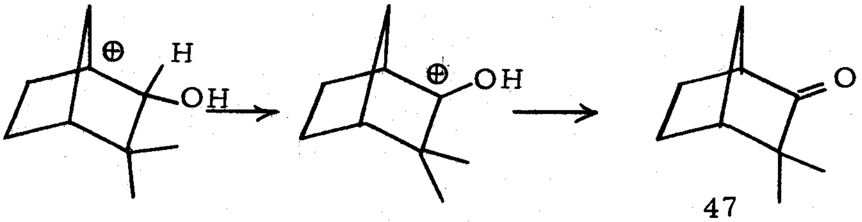
42 43 44

A different type of ring contraction reaction was used by Ebisu and co-workers to give a 1-substituted bicyclo(2. 1. 1)hexane. This scheme involves the deamination of the bridgehead amine 45, which proceeds *via* a semipinacolic rearrangement to give only 5, 5-dimethylbicyclo(2. 1. 1)hexane-1-carboxaldehyde 46 (35). It appears that ring shrinkage is concurrent with loss of nitrogen since no other product was observed. Apparently a 1, 2-hydride shift to give the



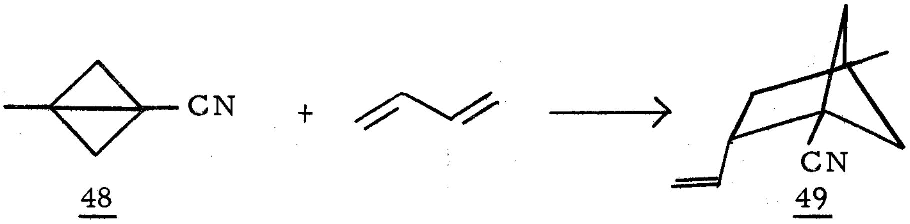
45 46

ketone 47 does not occur. This might be expected if a "free" carbonium ion were involved. Such a bridgehead carbonium ion is not very likely, however.



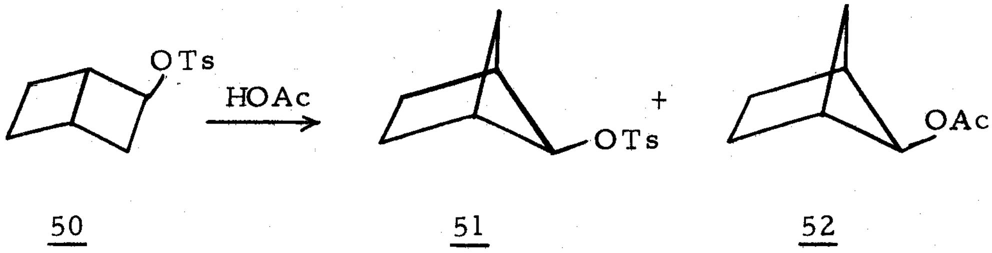
47

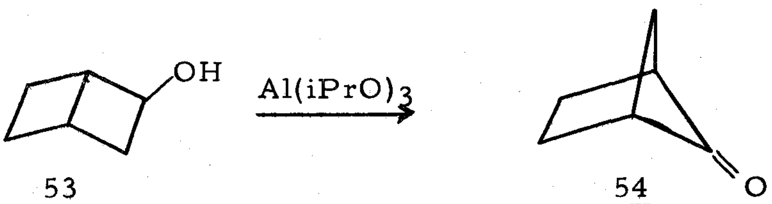
A completely different approach to the synthesis of bicyclo(2. 1. 1)hexanes was developed by Blanchard and Cairncross (16). Their approach is based on thermal cycloaddition reactions of various bicyclo(1. 1. 0)butane derivatives (10). These workers have found that various olefins may be made to undergo cycloaddition reactions with 3-methylbicyclo(1. 1. 0)butanecarbonitrile 48. Thus when 48 was heated at 150° with butadiene in a sealed tube, a 65% yield of a 1:1 adduct was obtained. This adduct was characterized as 2-vinyl-4-methylbicyclo(2. 1. 1)hexanecarbonitrile 49. Of the different olefins used in this study, it was found that those with strong



electron-withdrawing groups gave poorer results than simple olefins. These thermal cycloaddition reactions are of limited general value because high pressure equipment is required, and the starting bicyclobutanes are difficult to prepare.

An interesting, although impractical, route to 5-substituted bicyclo(2. 1. 1)hexanes has been reported by McDonald and Reineke (63, 65). The acetolysis of exo-bicyclo(2. 2. 0)hex-2-yl tosylate 50 leads to a mixture of products, 70% of which was the bicyclo(2. 1. 1)hexanes 51 and 52. The Oppenaurer oxidation of exo-bicyclo(2. 2. 0)hexan-2-ol 53 gives as its major product bicyclo(2. 1. 1)hexan-5-one 54 (64). It is apparent that these reactions are of little synthetic value since the bicyclo(2. 2. 0)hexanes which serve as starting materials are themselves difficult to synthesize.



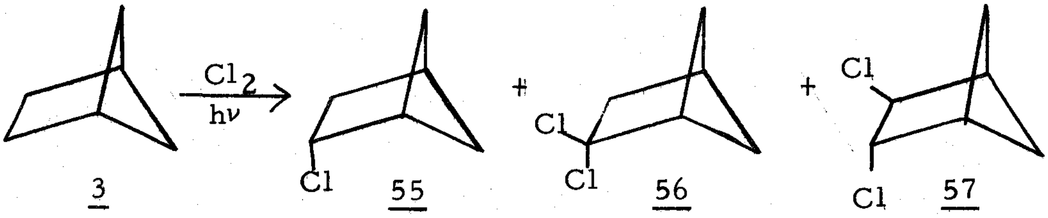


53 54

Chemistry

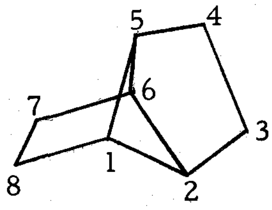
The chemistry of bicyclo(2. 1. 1)hexane derivatives known before 1966 has been well-reviewed and, with the exception of a few important examples, will not be repeated here (76). Some reactions of great theoretical interest are the carbonium ion reactions of bicyclo(2. 1. 1)hexane halides and *p*-toluenesulfonate esters. One of the differences between the bicyclo(2. 1. 1)hexanes and the bicyclo(2. 2. 1)-heptanes is the remarkable reactivity of bridgehead halides and tosylates (115). Although bicyclo(2. 1. 1)hexanes are more strained than bicyclo(2. 2. 1)heptanes, it is found that 1-bromobicyclo(2. 1. 1)-hexane solvolyzes at a rate 10^7 times faster than the corresponding bicycloheptyl derivative. Similar rate enhancements have been noted in the cases of C-5 or C-6 and C-2 substituted bicyclo(2. 1. 1)-hexanes (76).

In connection with his work on the mercury-sensitized isomerization of 1, 5-hexadiene, Srinivasan has conducted some experiments on the chlorination of bicyclo(2. 1. 1)hexane 3. The chlorination of 3 in either the vapor phase, or in solution, or as a pure liquid gave a fair yield of the monochloride 55. Further chlorination gave the two dichlorides 56 and 57 which were derived from 55. These results

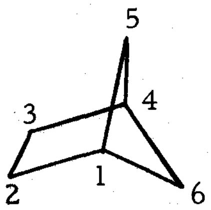


are very similar to those found for the chlorination of bicyclo(2. 2. 1)-heptane where the two-carbon bridges are chlorinated in preference to the bridgehead positions and the one-carbon bridge (103).

The reactions of tricyclo(3. 3. 0. $0^{2,6}$)octane 27 are of considerable interest due to the possible analogy with those of bicyclo-(2. 1. 1)hexane. With this in mind, Meinwald and Kaplan studied methods to introduce functional groups at C-3 (C-3 = C-4 = C-7 = C-8) of 27 (73). With a functional group at C-3, the study of carbonium



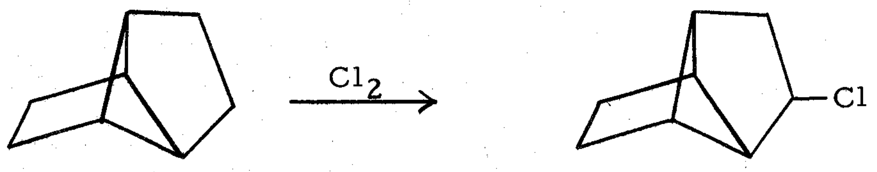
27



3

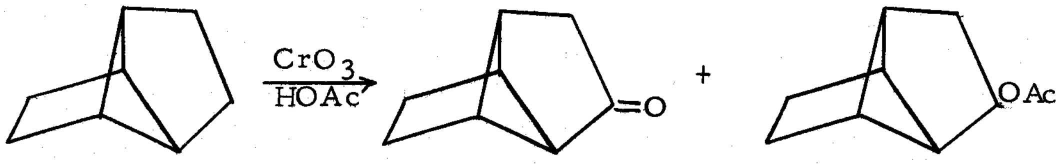
ion reactions analogous to those of 2-substituted bicyclo(2. 1. 1) hexanes is possible.

The liquid phase chlorination of 27 leads only to attack at methylene carbons, i. e., carbons 3, 4, 7, and 8. This is analogous to the chlorination of bicyclo(2. 2. 1)heptane and bicyclo(2. 1. 1)hexane, as mentioned above (103). The only product detected was the 3-chlorotricyclic compound 58. Bromination, however, leads to a complex result.



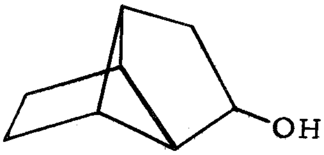
27 58

The oxidation of 27 with chromium trioxide in acetic acid, also believed to be a free radical reaction, gave rise to a 9:1 mixture of the ketone 59 and the acetate 60 in an overall yield of 60%.

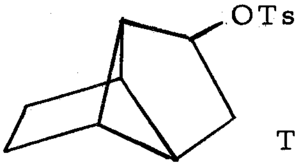


27 59 60

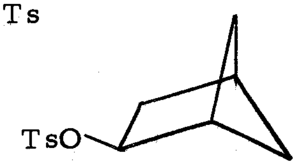
From the ketone 59, it is no problem to reach both the corresponding alcohol 61 and the p-toluenesulfonate ester 62. Acetolysis of the tosylate 62 was found to proceed at a rate 180 times faster than the corresponding bicyclo(2. 1. 1)hex-2-yl tosylate 63. The products of the solvolysis were found to be the unrearranged acetate



61

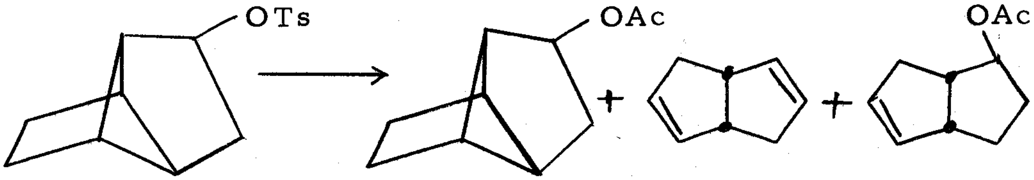


62



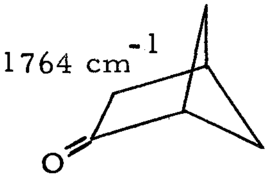
63

60 (40%), bicyclo(3. 3. 0)octa-2, 6-diene 64 (20%), and the bicyclic acetate 65 (17%). The reason for the rate differences between 62

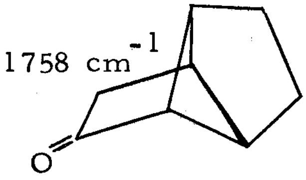


62 60 64 65

and 63 may be related to internal angles at the ionizing carbons. Correlation of the carbonyl stretching frequencies of the corresponding ketones and the included angles lead to calculated angles of 95. 5° for 66 and 98. 5° for 59. This three degree angle difference and the



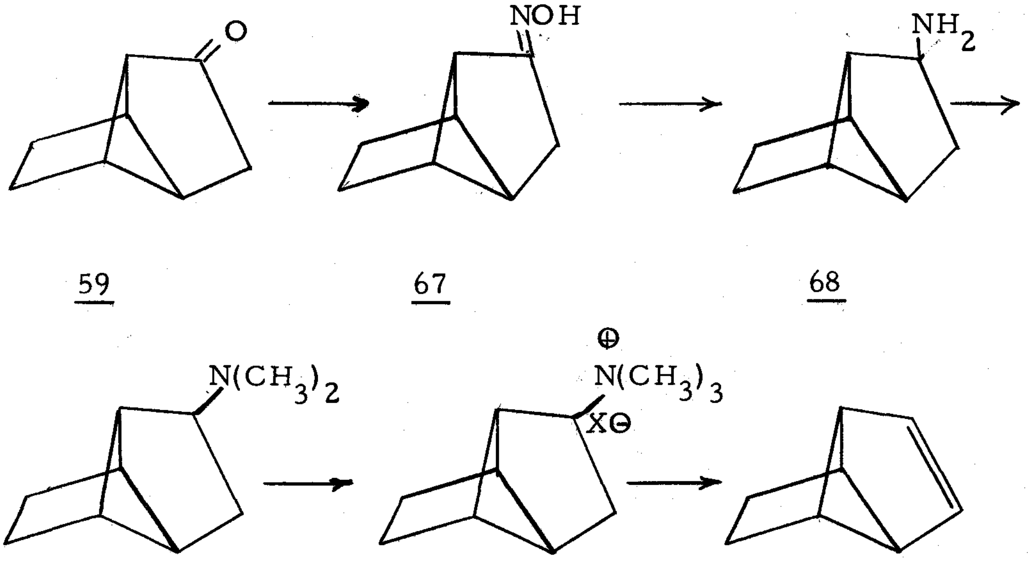
66



59

differences in the structures of the two systems was used as a possible explanation of the rate differences.

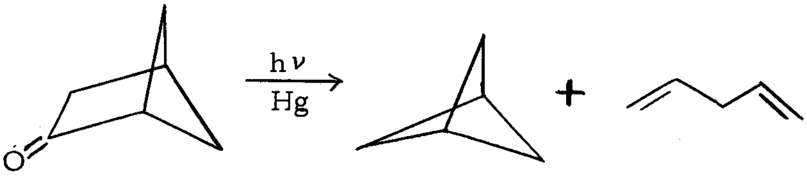
The study of the tricyclo(3. 3. 0. $0^{2,6}$)octene 71 system as a model for bicyclo(2. 1. 1)hexene synthesis was also undertaken by Meinwald. A more detailed discussion of this subject will be postponed to a later section, but a brief indication of the reaction sequence will be given here. The sequence involves both an example of bicyclo(2. 1. 1)hexane chemistry and a standard approach to bicyclic olefins.



59 67 68

69 70 71

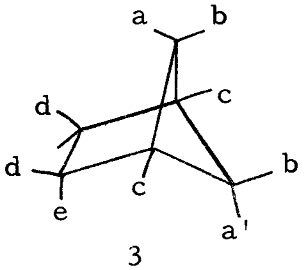
An interesting reaction of bicyclo(2. 1. 1)hexan-2-one 66 is the mercury-sensitized photodecarbonylation to give bicyclo(1. 1. 1)-pentane 72 (78). The success of this reaction, in part, depends on the relatively large amounts of bicyclo(2. 1. 1)hexan-2-one available through a synthetic route described later in the thesis. Using gram quantities of bicyclo(2. 1. 1)hexan-2-one 66, a 13% yield of bicyclo-(1. 1. 1)pentane 72 was obtained. Recycling gives up to 50% conversion of the ketone.



66 72

Physical Properties

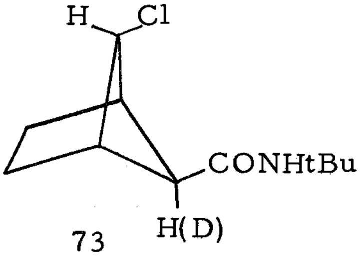
One of the most interesting, and perhaps, most informative physical properties of bicyclo(2. 1. 1)hexane derivatives are their n. m. r. spectra. These spectra can be used in the characterization of substituted bicyclo(2. 1. 1)hexanes and in the study of the geometry of the molecules. For clarity and convenience in the following discussion, the five pairs of identical hydrogens on the parent bicyclo-(2. 1. 1)hexane hydrocarbon will be labeled "a" through "e", as indicated in the following structural formula.



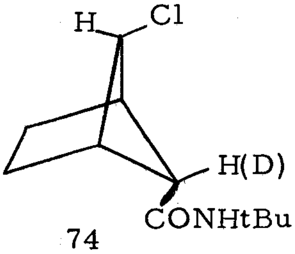
3

One of the most striking observations to be noted in regard to the n. m. r. spectra of bicyclo(2. 1. 1)hexanes is the strong coupling between "a" and a', (74, 117). Other couplings may be explained by use of the Karplus relationship. Inspection of the geometry of the bicyclo(2. 1. 1)hexane molecule reveals that the dihedral angles between a and c, a and b, and b and c are 80°, 120°, and 40° respectively. These correspond to coupling constants of about $J_{ab} = 6 - 9$ cps, $J_{ac} = 0$ cps, and $J_{bc} = 3 - 4$ cps. Proton c should also be coupled to protons d and e with a coupling constant $J = 1 - 2$ cps. There should be no coupling between a and c protons. Theoretically, all the coupling constants are explained. The experimental fact remains that there is a strong coupling between protons a and a'; $J_{aa'} = 6 - 7$ cps. This coupling has been rationalized by the overlapping of the smaller lobes of the a and a' orbitals (74). It is interesting that there is only negligible coupling between b and b' protons which are closer to each other than a and a' protons.

The existence and magnitude of this long-range coupling was first observed by Meinwald and Lewis (74) during their analysis of the spectra of the four chlorocarbamides <u>73</u> and <u>74</u>.

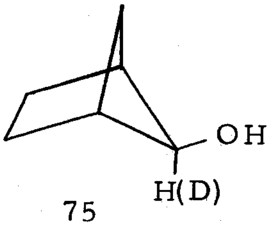


73

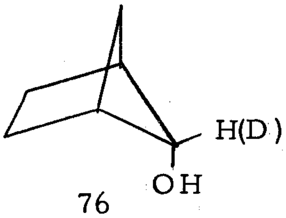


74

In all the spectra the C-5 and/or C-6 protons are easily distinguishable and their coupling constants measurable. Wiberg made similar observations using the isomeric alcohols 75 and 76 as models.



75



76

Although generalizations concerning the chemical shifts of the different types of protons in bicyclo(2. 1. 1)hexanes must be made with caution, the spectrum of the parent compound 3 serves as an example. In the spectrum of 3, the a protons appear as a quartet at 0. 87 ppm. The signal due to the b protons is overlapped with the signals due to the d and e protons and appears at 1. 57 ppm. The bridgehead c protons appear as a multiplet at 2. 49 ppm. The coupling constants are as follows: J_{ab}, 5. 4 cps; $J_{aa'}$, 6. 7 cps; and J_{de}, 1 cps.

The remaining portion of this section consists of a compilation of n. m. r. spectra of selected bicyclo(2. 1. 1)hexane derivatives. In general, the tables consist of chemical shifts for protons a through e and coupling constants. For clarity, the results obtained in this study are included.

In contrast to the n. m. r. data presented, infrared data usually are only informative with respect to the identification of functional groups attached to the bicyclo(2. 1. 1)hexane nucleus. The carbonyl stretching frequencies of substituted bicyclo(2. 1. 1)hexanones, however, are rather characteristic. A summary of some of these carbonyl frequencies is given in Table 3. This choice is motivated both by our own interest in bicyclo(2. 1. 1)hexanones and by the relationship between carbonyl frequencies and the amount of strain in a ring system.

One interesting point to note is that the carbonyl frequency of tricyclo(3. 3. 0. $0^{2,6}$)octan-3-one (1758 cm^{-1}) is lower than that of bicyclo(2. 1. 1)hexan-2-one (1764 cm^{-1}). This is interesting in that it implies the tricyclic ketone is less strained than the bicyclic ketone. Thus reactions which have been accomplished in the tricyclooctane system might be expected to occur with more difficulty in the bicyclo(2. 1. 1)hexane system (73). This has been found to be the case in this work.

Table 2. N.m.r. spectra of bicyclo(2.1.1)hexane derivatives.(1, 2)

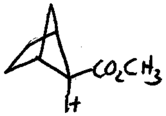
Compound	a	b	a'	b'	c	d, e	Coupling	Ref.
	0.87 q	1.56	0.87 q	1.56	2.49 m	1.58 s	J_{ab} = 5.4 J_{aa} = 6.7	(117)
	1.56 q	1.73 b	1.56 q	1.73 b	2.49 b	1.83 s	---	(117)
	0.89 q	1.52	---	---	1.99	1.52	---	(117)
	1.15 q	1.80 m	1.15 q	1.80 m	2.54 m 2.89 m	2.17 m	J_{aa}=7.0	(58)
	Sharp peaks 0.8 - 2.4				2.52	---	---	(68)
	1.46 d	1.64 b	2.53 d	---	2.69 b	1.86 m	J_{ab}=6.4	(117)

Table 2. Continued.

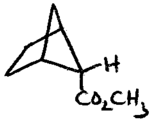
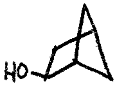
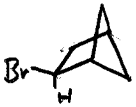
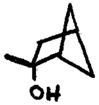
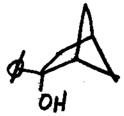
Compound	a	b	a'	b'	c	d, e	Coupling	Ref.
	0.78 q	1.38 b	---	2.14 g	2.70 t	1.47 s	$J_{ab}=6.3$ $J_{bc}=2.9$	(117)
	0.95 q	1.53 m	0.95 q	1.53 m	2.42 q	1.25-2.15m	---	*
	1.60 q	2.20 m	1.60 q	2.20 m	2.80 t	---	$J_{aa'}=7.0$	*
	Complex Multiplets 0.87-2.85				2.62	4.37 m, d	---	*
	1.38 q	1.97 m	1.38 q	1.97	2.42 s	2.82 d	$J_{aa'}=6.5$	*
	1.60 m	2.1-2.5 m	1.60 m	2.1-2.5	1.20 m 3.10 m	1.60 m	---	*

Table 2. Continued.

Compound	a	b	a'	b'	c	d, e	Coupling	Ref.
	1.68 m	1.90 m	1.68 m	2.12	1.15 m 2.70 m	2.42	---	*
	1.08 q	1.60 m	1.08 q	1.60 m	2.0 s, m	2.35 m 3.17	---	*
	1.56 t	2.43 m	1.94 q	---	2.43	2.23	$J_{aa'}=7$	(40)
	2.58 s, b	2.30 d	2.58 s, b	2.30 d	2.58	6.82 t		*, (79)

(1)Chemical shifts in ppm ; TMS internal standard; functional groups not shown.

(2)J in cps.

* Results of this study.

q = quartet; s = singlet, m = multiplet, d = doublet, b = broad

Table 3. Carbonyl stretching frequencies of selected bicyclo(2. 1. 1)-hexanones.

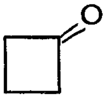
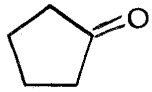
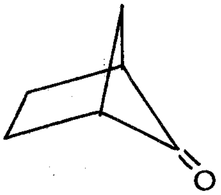
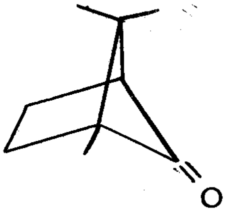
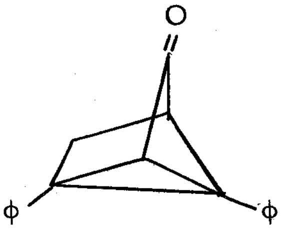
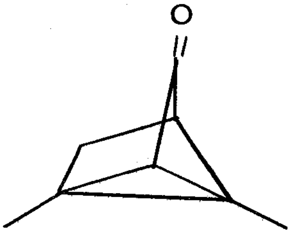
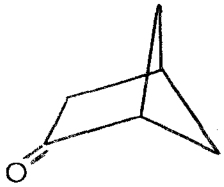
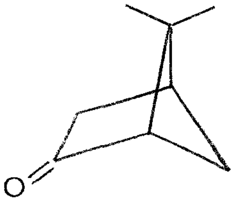
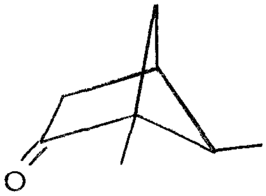
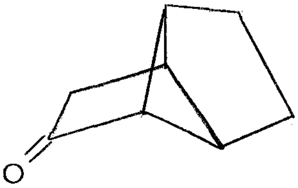
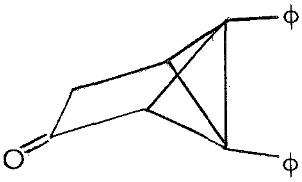
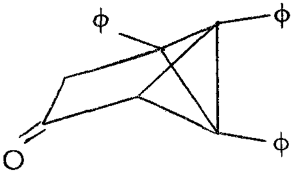
Compound	ν cm^{-1}	Ref.
	1775	(7)
	1740	(7)
	1800	(116, 117)
	1781	(75)
	1786	(60)
	1786, 1768	(29)

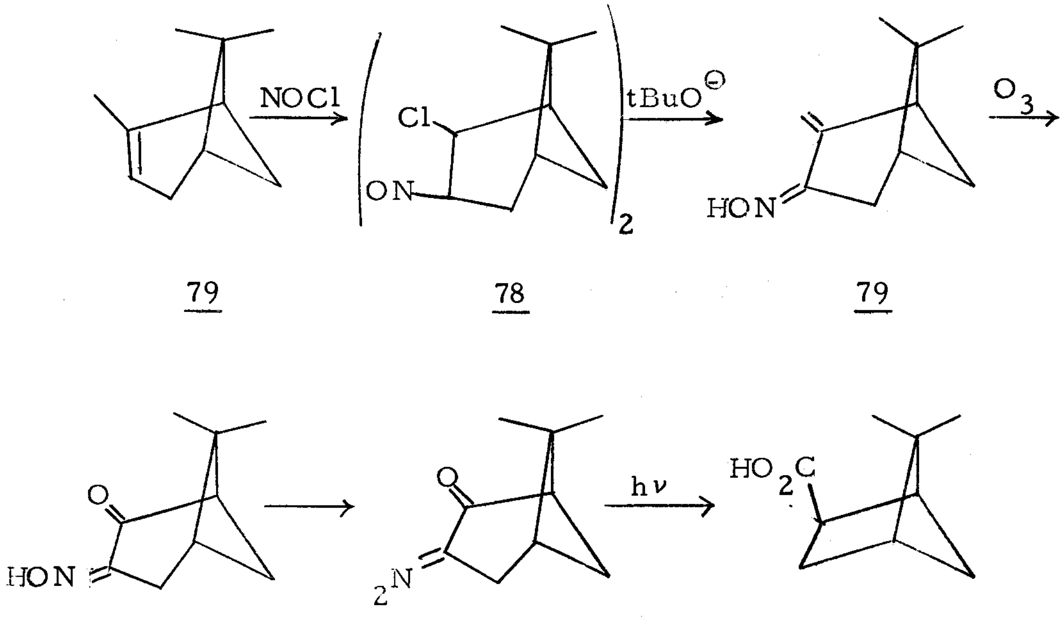
Table 3. Continued.

Compound	ν cm^{-1}	Ref
	1764 (dil. soln.)	
	1764	(72)
	1765	(40)
	1758	(73)
	1745	(61)
	1750	(96)

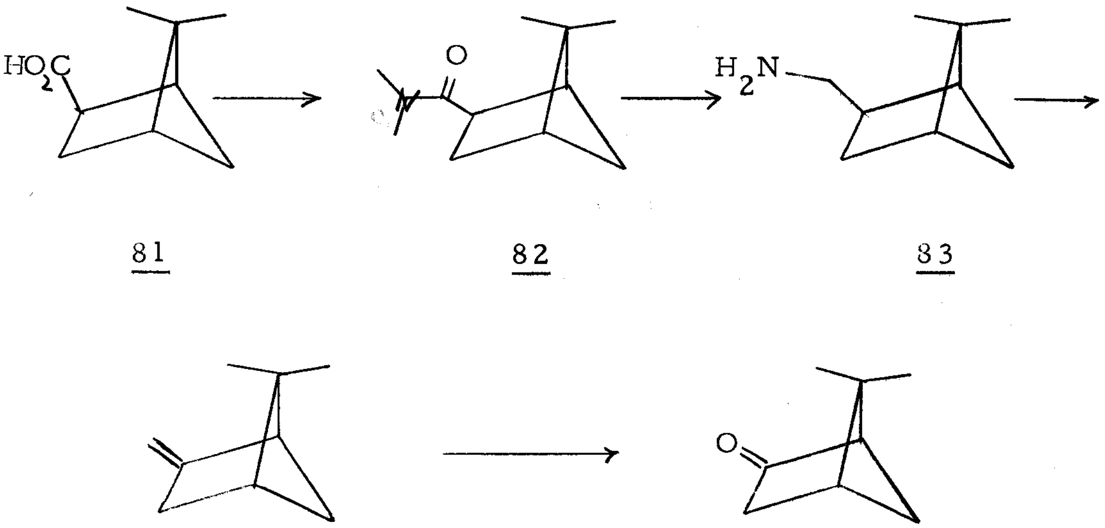
Bicyclo(2. 1. 1)hex-2-yl Compounds

Before leaving the subject of bicyclo(2. 1. 1)hexanes, a discussion of the 2-substituted compounds is relevant since much of this work has been involved in this area. Analogous to the ring contraction reactions which were discussed previously and which led to 5-substituted bicyclo(2. 1. 1)hexanes, the same general scheme of α-diazoketone photolysis has been used to obtain some 2-substituted compounds (76). Meinwald and Gassman have used two interesting routes to obtain various bicyclo(2. 1. 1)hex-2-yl compounds (71, 72).

In the first of these syntheses, α-pinene 77 was treated with nitrosyl chloride to give the nitroso dimer 78 which reacted with potassium t-butoxide to give the oximoölefin 79. This methylene compound was oxidized to the oximoketone 80 and then converted to the corresponding diazoketone. Irradiation of this ketone gave a high yield of 2β-carboxy-5, 5-dimethylbicyclo(2. 1. 1)hexane 81.

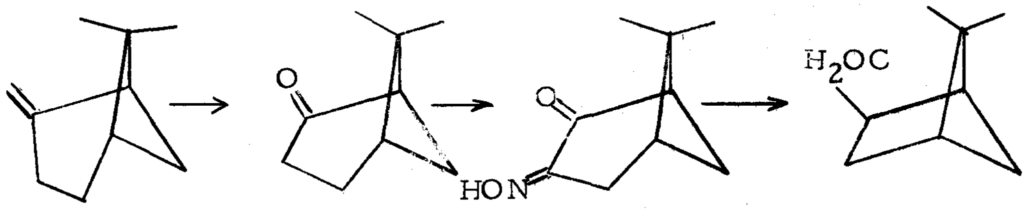


This acid was then converted, by the sequence indicated below, to the bicyclo(2. 1. 1)hexan-2-one 85.

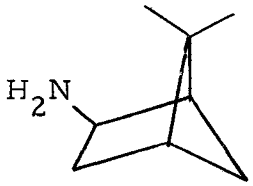


An alternate route to the same ketone has already been mentioned (72).

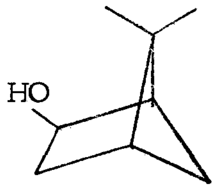
A second route to bicyclo(2.1.1)hex-2-yl compounds involves a sequence similar to the one given above. In this synthesis β-pinene 86 is ozonized to the ketone 87 which is then converted to the oximo-ketone 88 by treatment with strong base and alkylnitrite. The steps to the 2β-acid 81 are now identical to those given above. From 81 the compounds listed below were obtained. Here again, as is the case



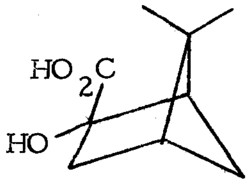
86 87 88 89



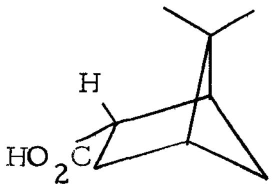
89



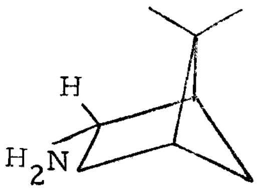
90



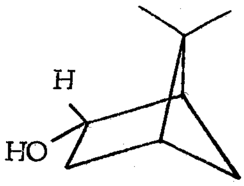
91



92



93

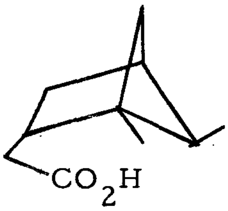


94

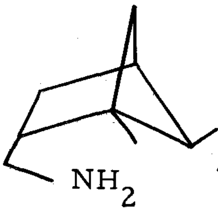
with all α-diazoketone routes, the yield of photolysis product is very low. For instance, the overall yield from α-pinene 77 to 81 was 3.8%. This immediately points to the desirability of a simple route to bicyclo(2.1.1)hex-2-yl compounds, which this thesis reports.

It will be remembered that Srinivasan reported the synthesis of 2-chlorobicyclo(2.1.1)hexane 55 (103). Here the problem is not only separation of the three chlorination products, but also the low yields obtained in the synthesis of the starting bicyclo(2.1.1)hexane. These difficulties do not make this route of great synthetic value, since the monohalide can now be synthesized in fairly large quantities from bicyclo(2.1.1)hexan-2-one.

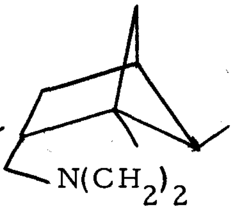
Finally, it should be mentioned that some 2-substituted bicyclo(2.1.1)hexanes can be obtained from degradation of carvonecamphor (40, 77). Some of these degradation products, 95 to 99, are indicated below.



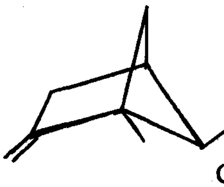
95



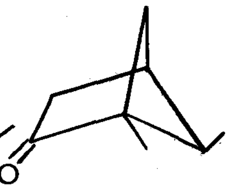
96



97



98



99

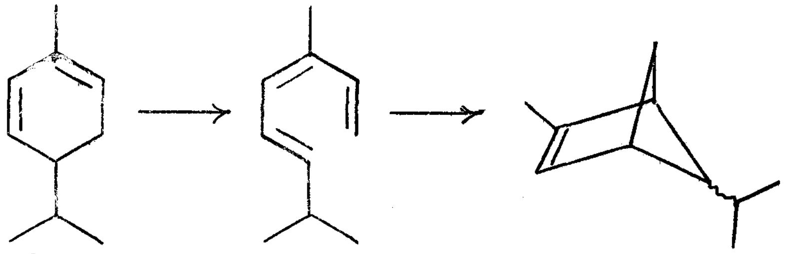
The route from 6-substituted bicyclo(2.2.1)heptane α-diazoketones has also been discussed in a previous section. Again, low yields are the rule and a rule which it seems is hard to break.

Interest in 2-substituted bicyclo(2. 1. 1)hexanes has as its prime motivation, at least within this group, the synthesis of intermediates which can lead to bicyclo(2. 1. 1)hexene. Our endeavors towards this end appear in the discussion section of this thesis. The attempts of other researchers in the field are of interest since they dramatize the difficulties inherent in this problem.

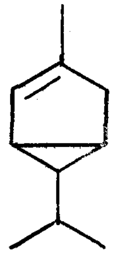
Bicyclo(2. 1. 1)hexenes

Introduction

Prior to the start of this work, no authentic example of a bicyclo(2. 1. 1)hexene had been reported. In 1964, Crowley claimed that irradiation of α-phellandrene 100 led to the formation of the bicyclo(2. 1. 1)hexene 101 *via* the sequence indicated (25). Meinwald has since shown that the product of the irradiation does not have the structure 101, but instead is the bicyclo(3. 1. 0)hexene 102 (70).



100 101

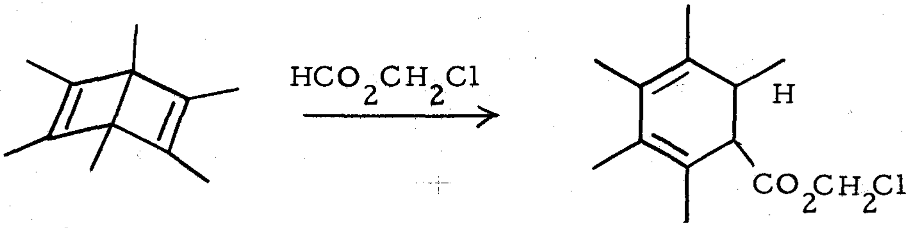


102

This allowed Meinwald to state in 1966, "The synthesis of olefins of this type remains an outstanding problem" (76).

Bicyclo(2. 1. 1)hexene is an interesting compound for several reasons. First, there is the problem of synthesis of such a highly strained olefin. We have already seen in the Introduction that the difference in strain energy between bicyclo(2. 1. 1)hexane and bicyclo-(2. 2. 1)heptane is at least 20 kcal/mole. We can expect at least this difference in strain energy between bicyclo(2. 1. 1)hexene and bicyclo-(2. 2. 1)heptene. This difference can be seen experimentally when syntheses of both olefins are attempted. Norbornene is a relatively easily prepared bicyclic olefin. Bicyclo(2. 1. 1)hexene is not.

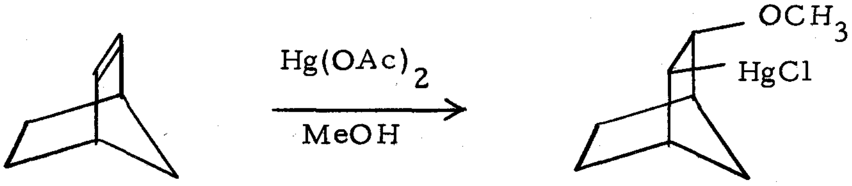
Aside from the synthetic problem, bicyclo(2. 1. 1)hexene is interesting in that it is not only highly strained but symmetrical. This makes it useful in the study of electrophilic additions to strained double bonds. The driving force for addition reactions of this type of olefin is the release of strain energy. For olefins such as bicyclo-(2. 1. 1)hexene, this energy release can be considerable. As an example of the types of electrophilic additions that bicyclo(2. 1. 1)-hexene might undergo, one may consider the reactions of the bicyclo-(2. 2. 0)hexa-2, 4-diene <u>103</u>. Such mild electrophiles as chloromethyl formate and methanol add readily to <u>103</u> to give the substituted



<u>103</u> <u>104</u>

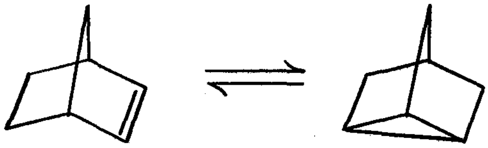
hexadiene 104 (89).

The symmetry of bicyclo(2. 1. 1)hexene would be of great value in the study of electrophilic addition to olefins. For example, oxymercuration normally occurs by a *trans* pathway. In the case of norbornene 105, however, *cis*, *exo*-addition occurs (107). This has been attributed to *endo*-shielding by some workers, a feature which would be lacking in bicyclo(2. 1. 1)hexene.



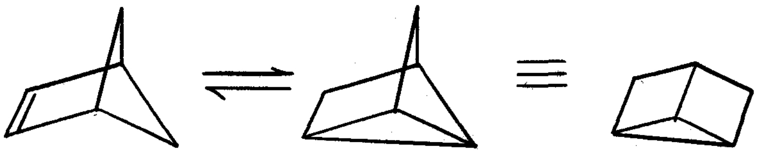
105

The stability of bicyclo(2. 1. 1)hexene would also be an interesting problem. Norbornene 105 is known to equilibrate in the presence of catalyst to nortricyclane 106 (92). At equilibrium, the mixture is found to contain 77% 106 and 23% 105. It would be interesting to



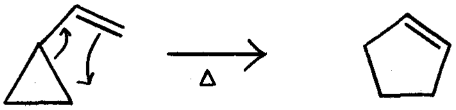
105 106

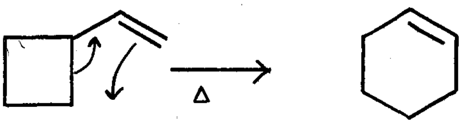
see if a similar result would be obtained with bicyclo(2. 1. 1)hexene. If this were the case, the product would be the known tricyclo-(2. 2. 0. 0^{2,6})hexane 107



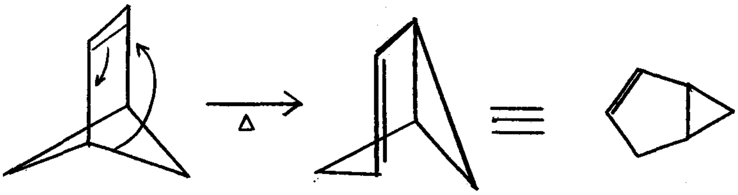
<u>108</u> <u>107</u>

Vinylcyclopropanes and vinylcyclobutanes undergo thermal rearrangement to give cyclopentenes and cyclohexenes, respectively (81).



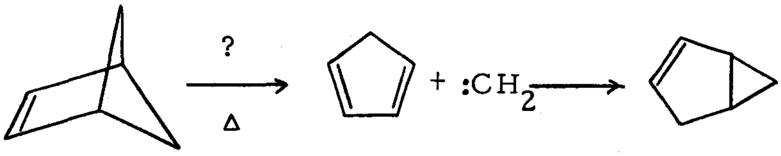


Bicyclo(2. 1. 1)hexene <u>108</u> is a vinylcyclobutane in which the terminus of the vinyl group is also attached to the cyclobutane ring. A thermal rearrangement such as above should also be possible. We have some evidence which indicates that this may be the case.



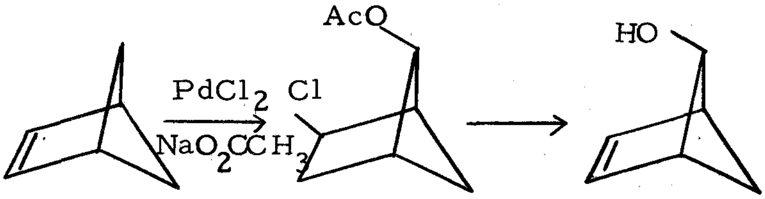
108 109

Bicyclo(2. 1. 1)hexene may also be considered the often sought but never found 1, 4-adduct of methylene and cyclopentadiene. It is possible that upon heating, 108 forms cyclopentadiene and methylene. Recombination in a 1, 2-fashion could also give bicyclo(3. 1. 0)hex-2-ene 109.



108 109

Another interesting aspect of bicyclo(2. 1. 1)hexene is its possible use in further syntheses. For instance, 108 could be converted to a 5-substituted bicyclo(2. 1. 1)hexene *via* a procedure which has been successful with norbornene 105 (8). Compound 110 is a specific example of the type of 5-substituted bicyclo(2. 1. 1)hexene sought by Meinwald and Crandall (68). Finally bicyclo(2. 1. 1)hexene, a strained olefin, should be a good dienophile. Strained olefins, such as cyclopropene act in this manner and give interesting results.



108

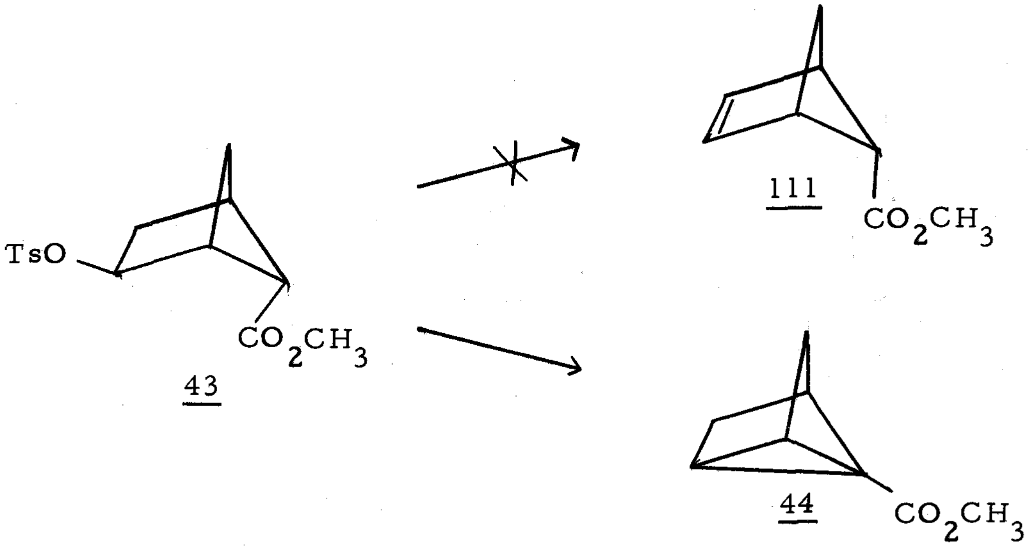
110

The same interesting results can be expected for bicyclo(2. 1. 1)-hexene.

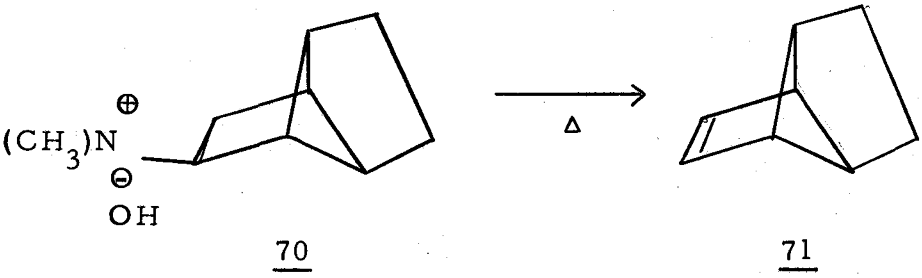
The above discussion gives some inclination why there is so much interest in bicyclo(2. 1. 1)hexene. Many attempts at its synthesis have been and are being made. Some of the more interesting approaches to the problem are summarized in the following section.

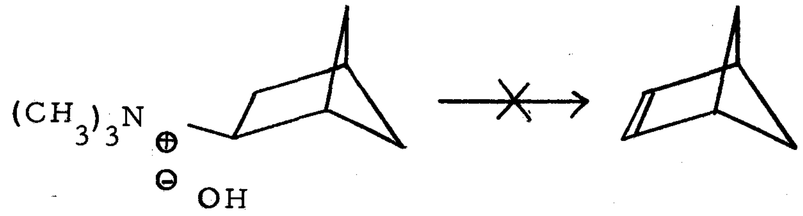
Synthesis

In Section I there was described an attempted synthesis of a bicyclo(2. 1. 1)hexene. The important reaction in the sequence was the base-catalyzed elimination of the tosyl group of 43. The product was not the desired olefin 111, but the tricyclic ester 44, the result of a 1, 3-elimination.

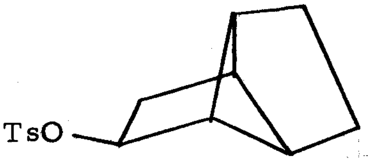


The synthesis scheme leading to tricyclo(3. 3. 0. 0$^{2, 6}$)oct-3-ene 71 was also presented in Section I. The important step in this sequence was the Hofmann elimination reaction shown below. At first glance, this reaction would seem to be a good model for the formation of the analogous bicyclo(2. 1. 1)hexene. More careful thought reveals

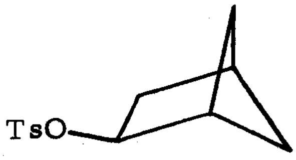




some of the reasons why this reaction does not occur. As was mentioned in Section I, the tosylate 62 solvolyzed 180 times faster than the corresponding bicyclo(2. 1. 1)hex-2-yl tosylate 63. This rate difference implies a more constrained geometry for 63 than for 62.

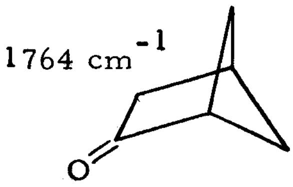


62

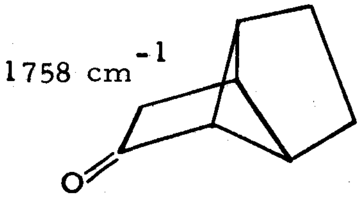


63

This is borne out by the carbonyl stretching frequencies of the corresponding ketones 66 and 59. These two facts lead to the conclusion



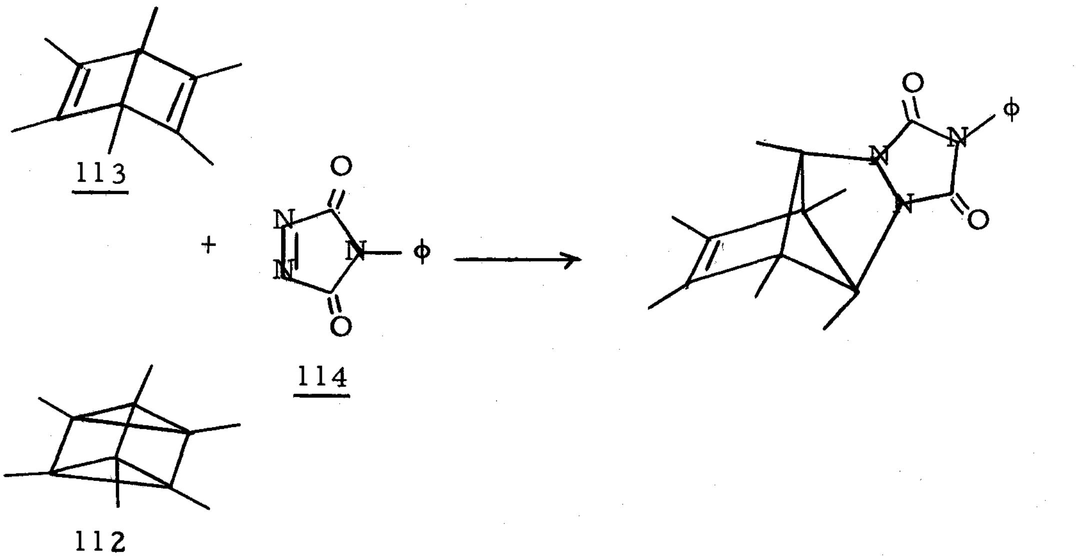
66



59

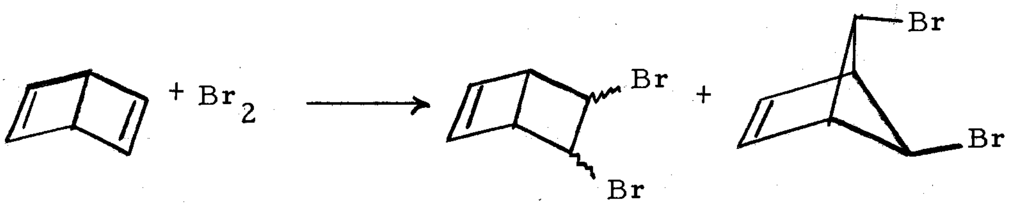
that the tricyclo(3. 3. 0. $0^{2,6}$)octane skeleton is less strained than the bicyclo(2. 1. 1)hexane nucleus. It is apparent that reactions which tend to increase the amount of strain are less likely with bicyclo-(2. 1. 1)hexanes than with the tricyclohexanes. It is not surprising, then, that the Hofmann elimination reaction of 70 leads to olefin while the same reaction fails with the corresponding bicyclo(2.1.1)-hexane derivative. The tricyclic compound 71 exhibits some unusual spectral properties. For instance, the carbon-carbon double bond gives rise to an infrared absorption at 1537 cm^{-1} and an ultraviolet absorption band out to about 250 mμ. These properties are evidently the consequence of the strain in the tricyclic ring system. Bicyclo(2.1.1)hexene would be expected to show similar spectral properties.

An interesting synthesis of what may be called a bicyclo(2.1.1)-hexene has recently been reported by Lemal (56). Treatment of either the prismane 112 or the Dewar benzene 113 with 4-phenyl-1,2,4-triazoline-3,5-dione 114 leads to the adduct 115 by way of the following scheme. Although 115 is a bicyclo(2.1.1)hexene, one would



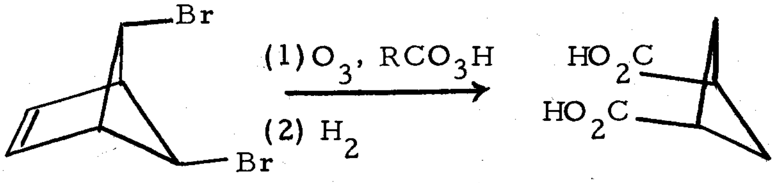
naturally prefer an unsubstituted bicyclohexene.

The existence of a simple substituted bicyclo(2. 1. 1)hexene has been inferred from some data reported by van Tamelen (110). It is believed that bromination of Dewar benzene 116 leads to a mixture of dibromides including a trace of the bicyclo(2. 1. 1)hexene 117.



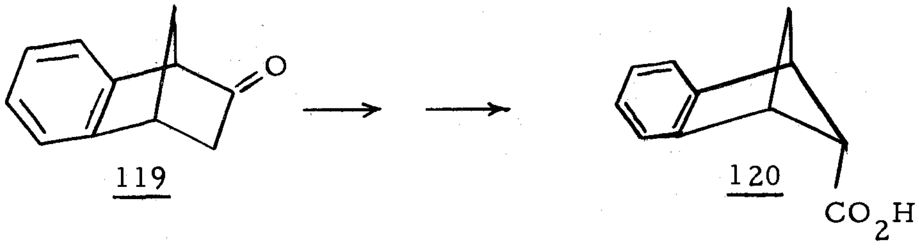
116 117

This belief is based on the recovery of cyclobutane-cis-1, 3-dicarboxylic acid 118 upon ozonolysis of the bromide mixture followed by hydrogenolysis. Structural assignments, however, are still tentative.



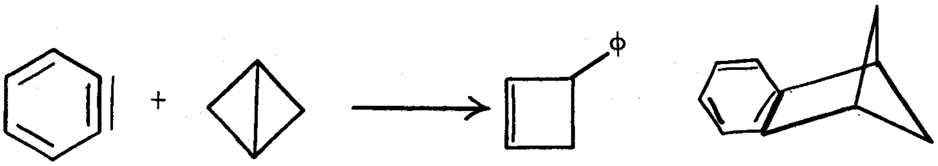
117 118

The last two examples of bicyclo(2. 1. 1)hexene synthesis involve the preparation of benzobicyclo(2. 1. 1)hexenes. Starting with 2-benzonorbornenone 119, Tanida has followed the standard ring contraction route to obtain the benzobicyclo(2. 1. 1)hexene 120 (104).



119 120

The reaction of benzyne with bicyclobutane 121 leads to two products, 3-phenylcyclobutene 122 and benzobicyclo(2. 1. 1)hexene 123 (83). The bicyclo(2. 1. 1)hexene is obtained in about 10% yield.



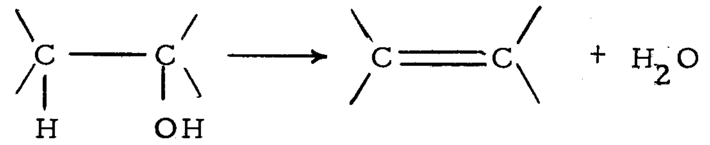
121 122 123

The reaction to give 123 is analogous to the reactions of olefins with bicyclobutanes reported by Cairncross and Blanchard (16) and probably involves the diradical 124.

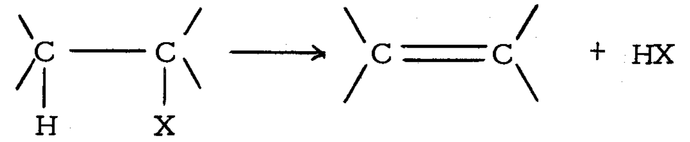
124

General Routes to Olefins

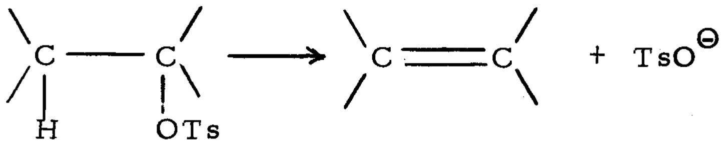
The problem of olefin formation in the bicyclo(2. 1. 1)hexanes seems somewhat surprising when the number of methods available are considered. There are numerous olefin syntheses which have been accomplished. Some of the more common methods are represented in the equations given below (86). With perhaps the exception



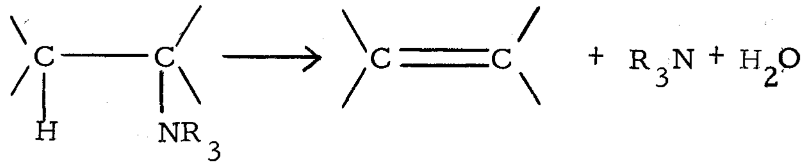
(1)



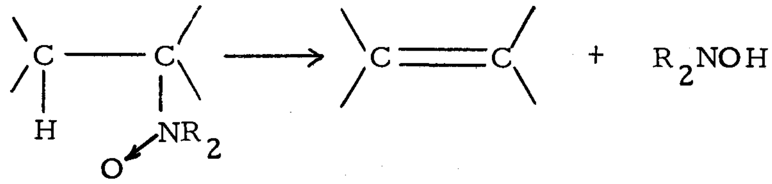
(2)



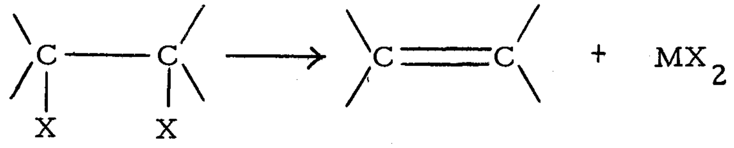
(3)



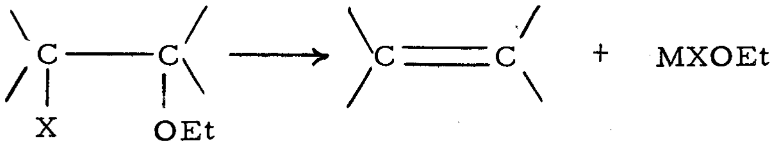
(4)



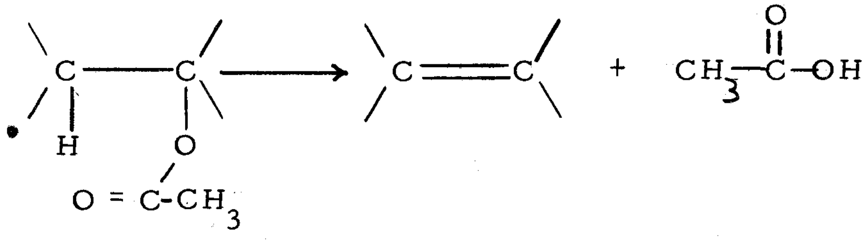
(5)



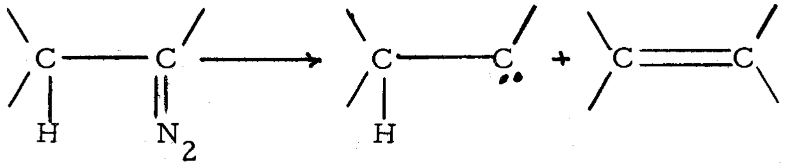
(6)



(7)

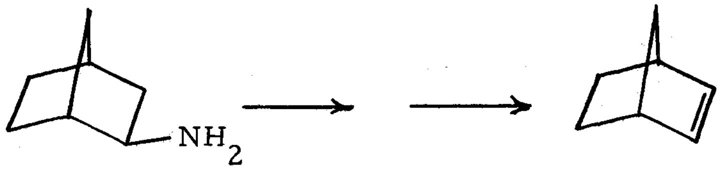


(8)



(9)

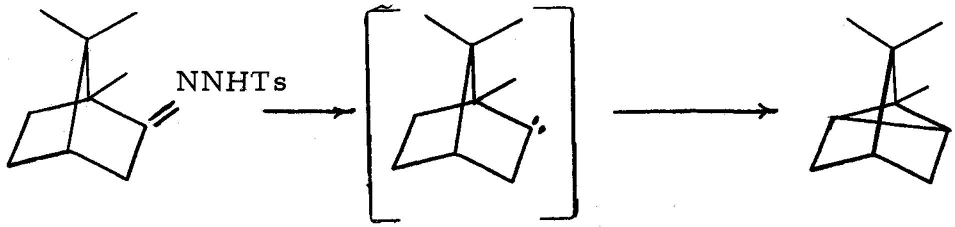
of equations (6) and (7), all the reactions have been used in attempts to obtain bicyclo(2. 1. 1)hexenes or systems related to it. Meinwald made use of the reactions represented by equations (3) and (8) in the unsuccessful synthesis of the bicyclo(2. 1. 1)hexene 111 (68). As might be expected, the Hofmann and the Cope amine oxide pyrolyses, equations (4) and (5), have found wide spread use. The synthesis of tricyclo(3. 3. 0. $0^{2,6}$)oct-3-ene 71 was accomplished *via* the Hofmann reaction (73). It is interesting to note that amine oxide pyrolysis of 125 gave no identifiable product. Norbornene 105 can be obtained



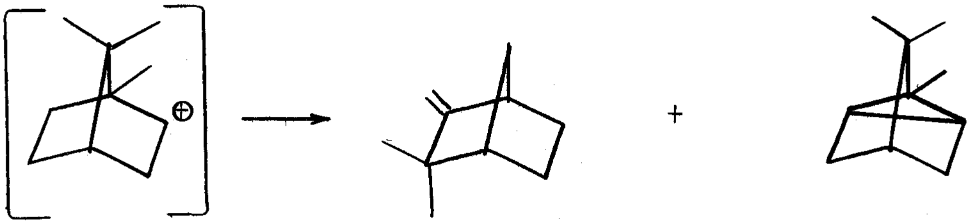
126 105

via the Hofmann elimination of the quaternary ammonium salt of *exo*-2-norbornylamine 126. The same result is obtained from the pyrolysis of the corresponding amine oxide (21, 23, 118). When these two reactions are applied to the corresponding 2-aminobicyclo(2. 1. 1)-hexane derivatives, elimination to the olefin is not observed. A discussion of these reactions will appear later.

A recent interesting route to olefins makes use of the β-insertion reaction of carbenes (Equation 10) (49). In rigid bicyclic systems transannular carbon-hydrogen insertion reactions are also possible. Base-catalyzed decomposition of camphor tosylhydrazone 127 in aprotic solvents leads to the tricyclic hydrocarbon 128 (93). In the presence of a proton donor, a cationic mechanism prevails which leads to a mixture of 128 and 129. The formation of camphene 129 is favored by such a process.

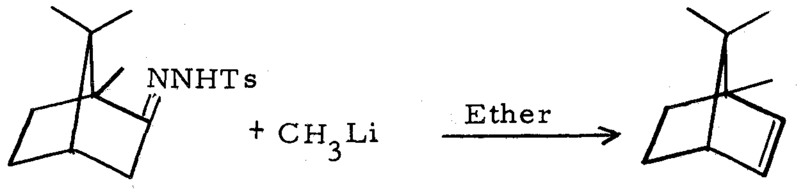


127 128



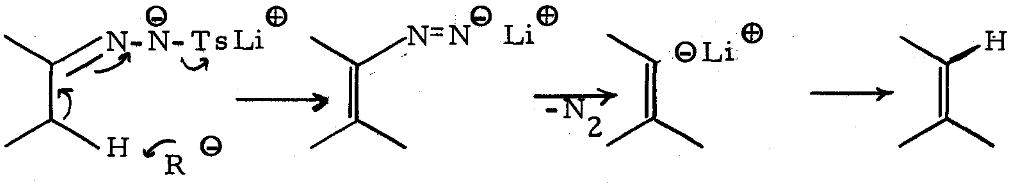
129 128

In 1967, Shapiro reported that treatment of camphor tosylhydrazone 127 with methyllithium in ether at room temperature gave a quantitative yield of 2-bornene 130 (94). It has been proposed that



127 130

this reaction proceeds *via* a carbanion mechanism such as is shown below. This method would be useful in the synthesis of strained bicyclic

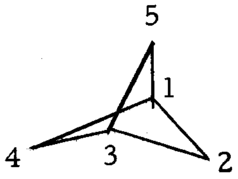


olefins both for the ease of preparation of the starting materials and the mild conditions under which the reaction proceeds.

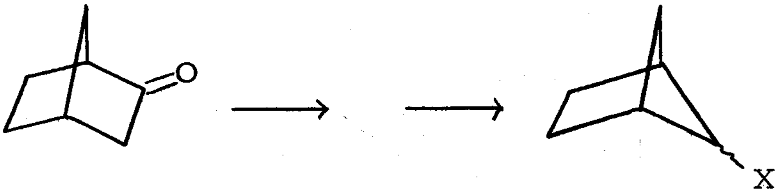
A report of our work in this area appears in the discussion section. However, some comments would be appropriate here. In our attempts to synthesize bicyclo(2. 1. 1)hexene, all the reactions indicated above, except (6), (7), and (8), were tried. Olefin formation was unobserved in all but reaction (2). The failure of these reactions is another indication of the strain associated with the bicyclo(2. 1. 1)-hexene system. When there is a choice between an elimination pathway and some other process, the other process is usually favored. The S_N2 pathway prevails over the E_2 and carbonium ion processes lead to rearrangments or substitutions. It is difficult to see what is so extraordinary about the dehydrohalogenation reaction. Perhaps the rather mild conditions required is the predominant factor.

Bicyclo(1. 1. 1)pentanes

Inspection of the geometry of bicyclo(1. 1. 1)pentane 131 reveals that the internal angles are 77 degrees (66). This bond angle distortion may manifest itself in the form of unusual chemical behavior. As mentioned later, present routes to this most highly strained of all bicyclic systems, are uniformly poor. In particular, there is no route to 2-substituted derivatives available. One potential route to such compounds would be ring contraction of a suitable bicyclo-(2. 1. 1)hexane derivative, assuming the latter were readily available. Thus, following the example (Equation 10) discussed previously for

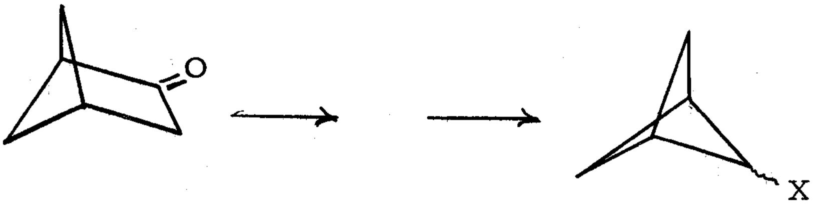


131



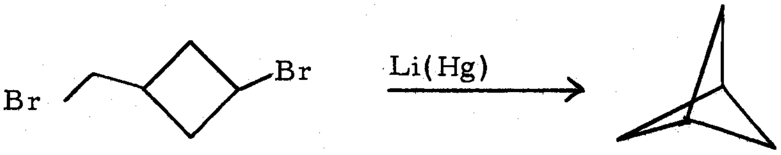
(10)

contracting bicyclo(2. 2. 1)heptanes, one can envisage several routes for contraction of bicyclo(2. 1. 1)hexanes to a bicyclo(1. 1. 1)pentane (Equation 11).

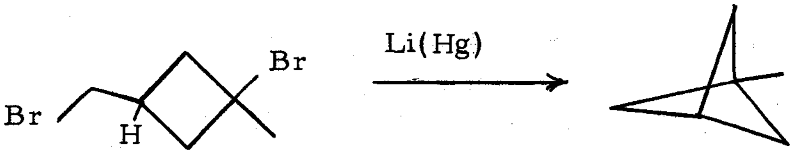


(11)

The synthesis of bicyclo(1. 1. 1)pentane and its 1-methyl derivative was reported by Wiberg in 1966 (113). The reactions utilized are shown below. The yield obtained by this method are very low

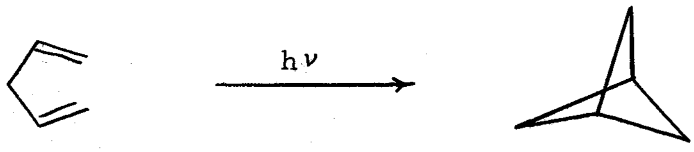


131

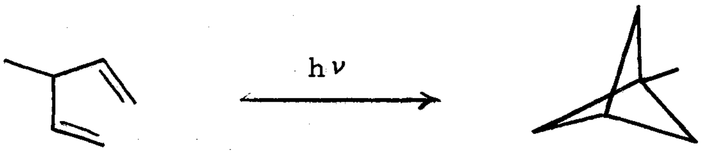


132

(1 - 4%). Similarly, low yields of 131 and 132 are obtained from the mercury-sensitized irradiation of 1, 4-pentadiene 133 and 2-methyl-1, 4-pentadiene 134, respectively (101).



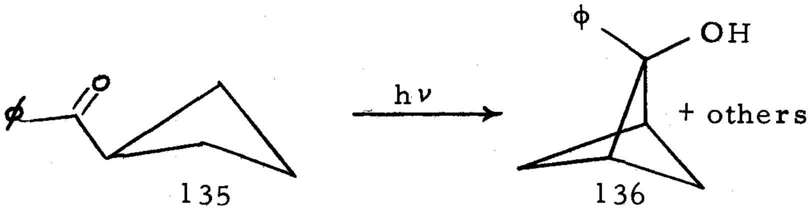
133 131



134 132

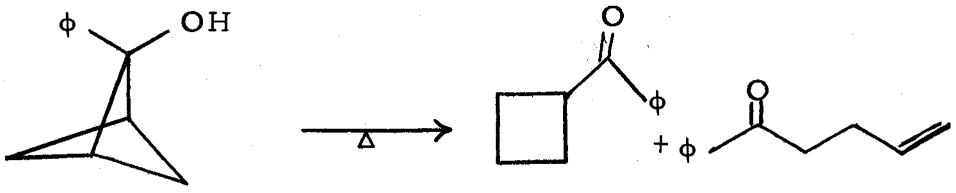
By far, the most practical synthesis of 131 was achieved by Meinwald (78). The mercury-sensitized photodecarbonylation of bicyclo(2. 1. 1)hexan-2-one 66 gives bicyclo(1. 1. 1)pentane in a 13% yield. The study of the chemistry and physical properties of 131 should be facilitated by this synthesis.

The only other synthesis of a bicyclo(1. 1. 1)pentane appeared in late 1967 (82). Padwa reported that irradiation of cyclobutyl phenyl ketone 135 in benzene gave a 38% yield of 2-hydroxy-2-



135 136

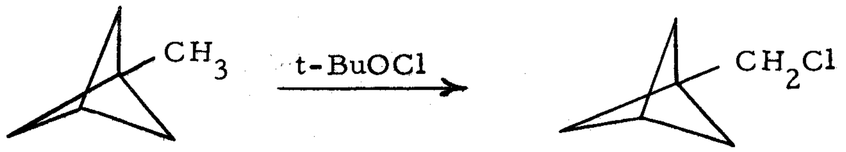
phenylbicyclo(1. 1. 1)pentane 136. Thermolysis of 136 afforded a 2:1 mixture of 135 and 137. Compound 137 is also a product obtained from the irradiation mixture.



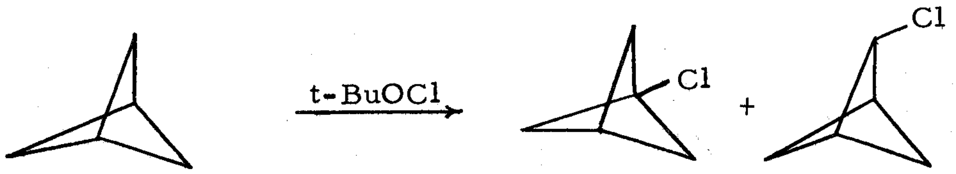
136 135 137

The reactions of bicyclo(1. 1. 1)pentane and its 1-methyl derivative have been limited to their thermolyses and halogenations (113). The thermal isomerization of 131 occurs at 300 degrees giving 1, 4-pentadiene. The rate of rearrangement is about ten times faster than that of bicyclo(2. 1. 1)hexane to 1, 5-hexadiene.

Chlorination of 1-methylbicyclo(1. 1. 1)pentane using *t*-butyl hypochlorite gave a small yield of 1-chloromethylbicyclo(1. 1. 1)-pentane 138. When bicyclo(1. 1. 1)pentane was subjected to the same conditions, a 7:1 mixture of 1-chlorobicyclo(1. 1. 1)pentane 139 and 2-chlorobicyclo(1. 1. 1)pentane 140 was obtained. The formation of the bridgehead chloride as the major product is surprising when the result is compared to that for other bicyclic hydrocarbons, such as norbornane and bicyclo(2. 1. 1)hexane. These compounds give no bridgehead chlorination products.



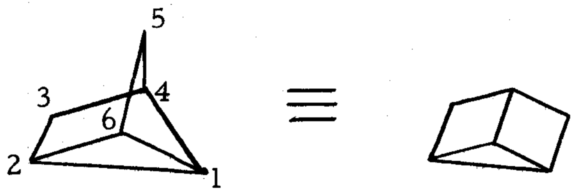
132 138



131 139 140

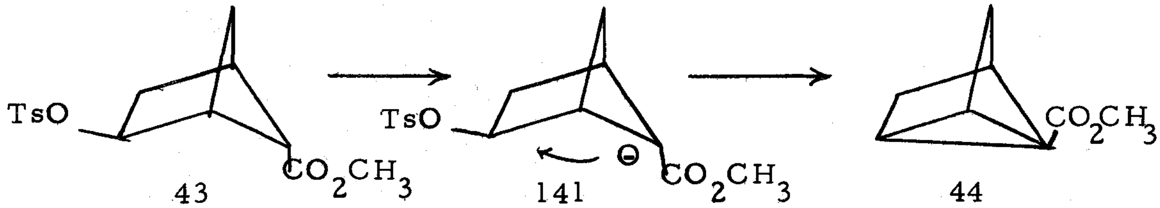
Tricyclo(2. 2. 0. $0^{2,6}$)hexanes

Tricyclo(2. 2. 0. $0^{2,6}$)hexane 4 may be considered a bicyclo-(2. 1. 1)hexane in which C-2 and C-5 are bonded or a 2, 6-bonded bicyclo(2. 2. 0)hexane. The first derivative of 4 obtained was



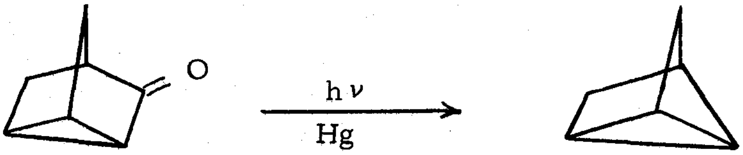
4

synthesized by treatment of the p-toluenesulfonate 43 with potassium t-butoxide (68). The tricyclic ester 44 most rationally arises from the internal displacement of the tosyl group by the enolate anion 141.



43 141 44

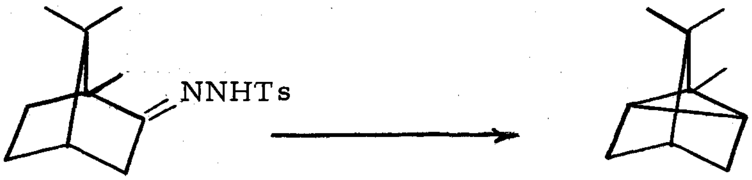
The hydrocarbon 4 has recently been prepared by Lemal and Shin in low yield by means of the mercury-sensitized photodecarbonylation of nortricyclanone 33 (57). The yield of hydrocarbon can



33

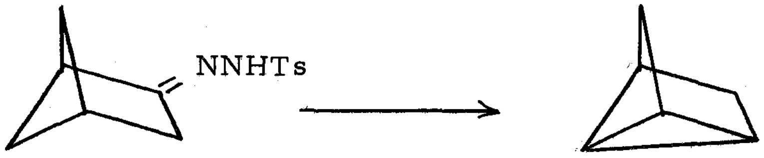
be increased to 36% (at 30% conversion) through use of a "quasi-flow" technique. Aside from hydrogenation studies, no chemistry of 4 was reported.

The use of carbene reactions in the formation of certain tricyclic compounds was mentioned in Section II. The base-catalyzed decomposition of camphor tosylhydrazone 127 in aprotic solvent



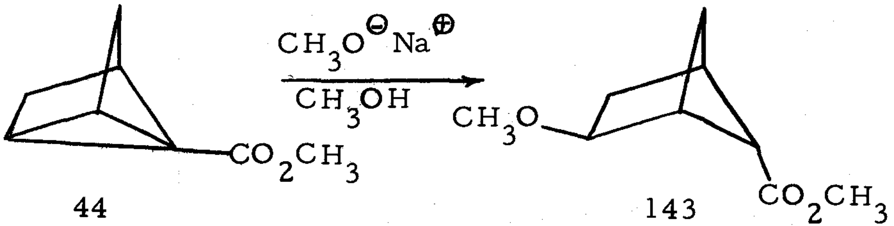
127 128

leads to the tricyclic compound 128 (93). A similar base-catalyzed decomposition of the tosylhydrazone of bicyclo(2. 1. 1)hexan-2-one 142 might lead to 4. A discussion of this reaction will appear later.



142 4

An interesting reaction of 44 was observed (68). Treatment of the tricyclic ester with sodium methoxide in methanol opened the three-membered ring. A mixture of methoxy esters is formed, in which 143 predominates. This is one of the few examples of a Michael addition to a carbon-carbon bond.



44 143

Photocycloadditions

The selective introduction of large amounts of energy by photoirradiation has been frequently used in the synthesis of strained compounds. The relationship between the nature of the excited states of molecules and their chemical behavior is in its infancy. Many of the details of the mechanisms of photoreactions remain unresolved. A few general remarks should be made concerning the language of photochemical processes (41, 55, 109). In the ground state of most molecules, all the electrons are paired and thus in the singlet state, S_g. These electrons are placed in either bonding or non-bonding molecular orbitals, if a heteroatom is involved. When a photon is absorbed, one electron is promoted to an unoccupied orbital of higher energy, an anti-bonding molecular orbital. Since the spin of the electron must be conserved, the excited state will also, initially, be a singlet, S_n. The excited state may be in any of the allowed vibrational levels of the S_n electronic state. The excited molecule usually falls rapidly to the lowest vibrational level of the S_n electronic level. For molecules in the S_n state, where n is greater than one, there is a rapid decay to the S_1 state via a phenomenon called internal conversion, a non-radiative process. The next step depends on the nature of the molecule, the electronic state, and the temperature. The Jablonski diagram in Figure 2 illustrates the various pathways available. A non-radiative process, called intersystem crossing, involves spin inversion to give a triplet excited state, T_n. A radiative emission from S_1 to S_g is termed fluorescence and a similar emission from T_1 to S_g, phosphorescence.

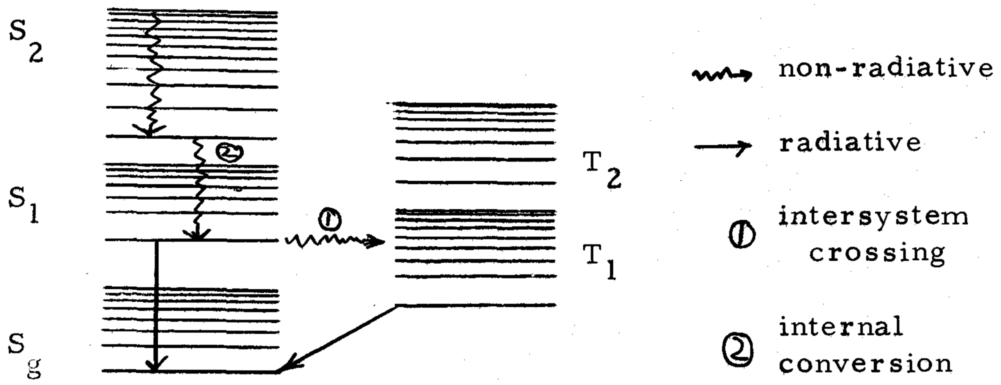
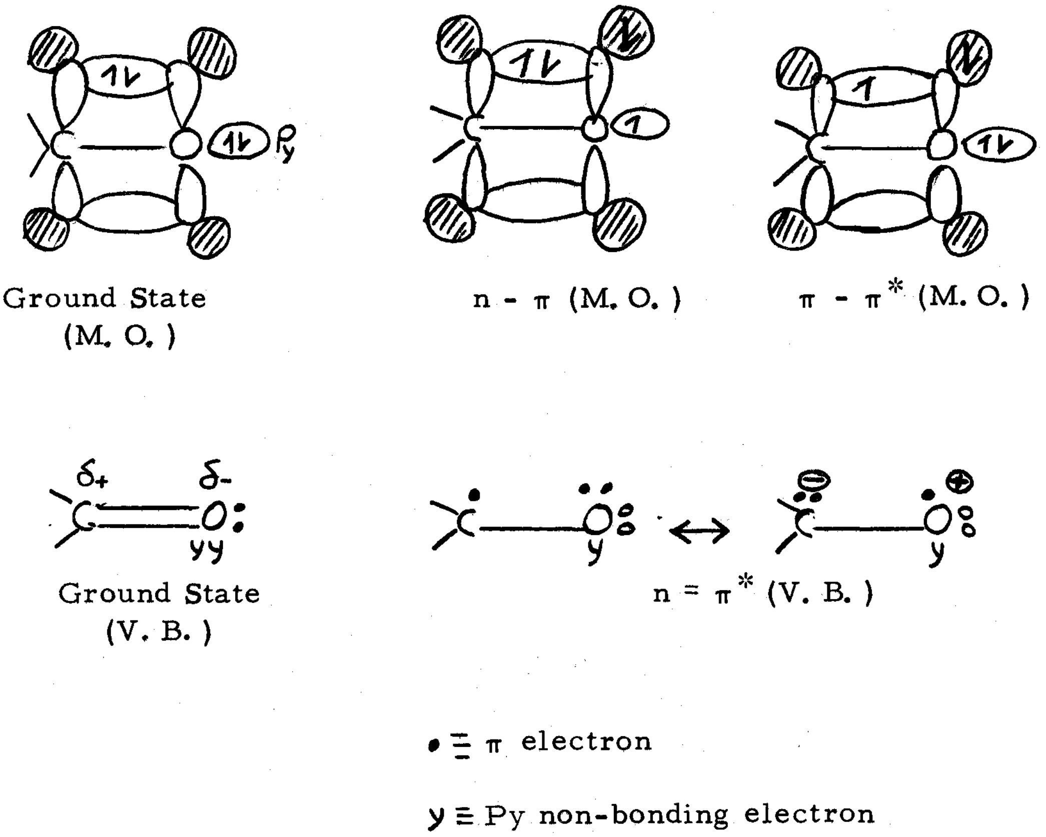


Figure 2. Jablonski Diagram.

In addition to the description of electronic processes in terms of multiplicity, one must consider the types of electronic transitions. In Figure 3 are depicted the molecular orbital and valence bond representations of the $n - \pi^*$ and $\pi - \pi^*$ transitions.

Photocycloaddition reactions have found wide-spread use in the synthesis of various fused and bridged cyclobutanes. The mechanism for such ring formation, although not known in detail, involves the addition of an excited chromophore to an unexcited double bond. These chromophores may be isolated double bonds, conjugated dienes, or conjugated enone systems. The nature of the excited states for these chromophores vary. For olefins, two low-lying excited states are possible, a $\pi - \pi^*$ singlet and a $\pi - \pi^*$ triplet.



Ground State (M. O.)

n - π (M. O.)

π - π* (M. O.)

Ground State (V. B.)

n = π* (V. B.)

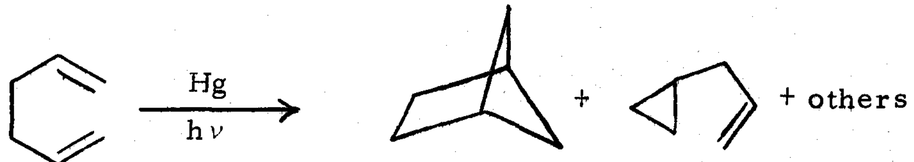
• ≡ π electron

y ≡ Py non-bonding electron

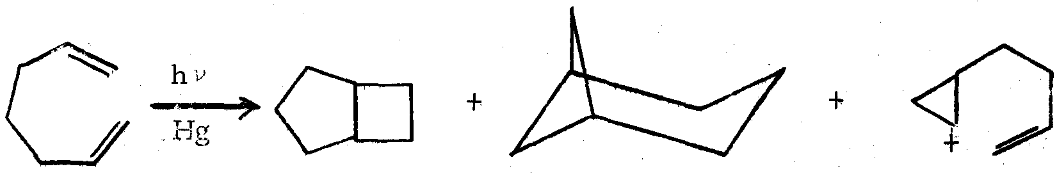
Figure 3. Electronic transitions

For enone systems, four excited states can exist: the π-π* singlet and triplet, and the n-π* singlet and triplet. Since various pathways are open to excitation, the simultaneous existence of several excited states is possible. In this section several examples of photocycloaddition reactions are presented. These will be grouped according to the type of chromophore, i. e., olefin, diene, and enone (27).

Mercury-sensitized isomerization of 1, 5-hexadiene in the vapor phase gave a mixture of bicyclo(2, 1. 1)hexane and allylcyclopropane. Similarly, sensitized irradiation of 1, 6-heptadiene gives a mixture of bicyclo(3. 2. 0)heptane 144, bicyclo(3. 1. 1)heptane 145, 4-cyclopropylpropene 146, and other products. These two reactions illustrate the excitation of one double bond followed by addition to the

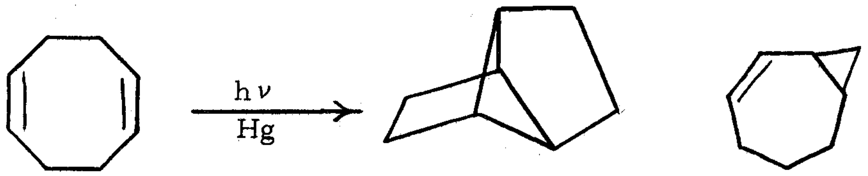


3

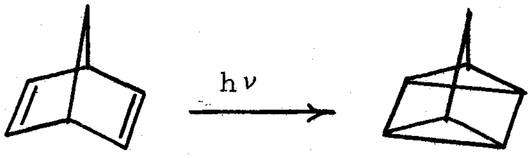


144 145 146

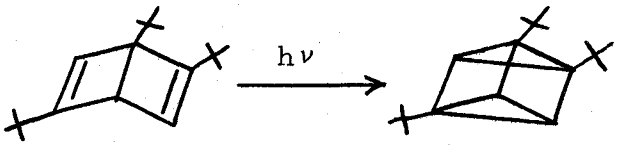
second unexcited double bond. In these cases the excited state is most likely the π-π^* triplet state. Other examples of this type are illustrated in Equations (12) through (15). All of these reactions are of the symmetry allowed (2 + 2) photochemical cycloaddition type.



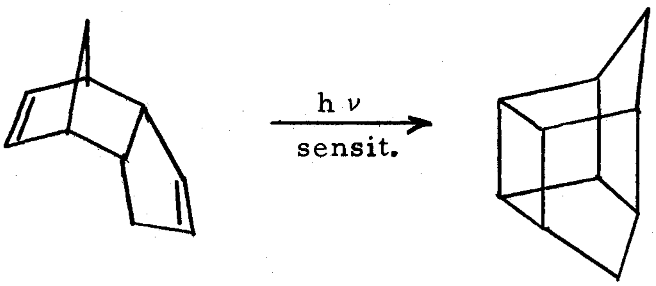
(12)



(13)

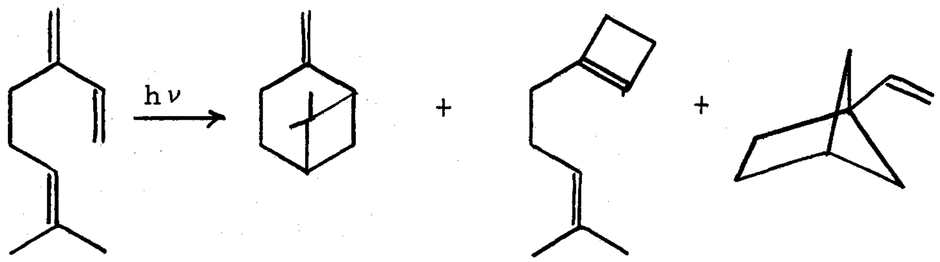


(14)



(15)

Cycloaddition via excitation of dienes can be illustrated by the irradiation of myrcene 147. Direct irradiation of 147 gave a mixture of products shown below. In contrast the triplet photosensitized

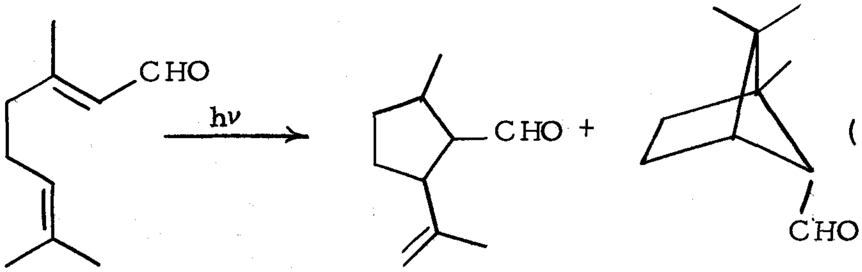


147

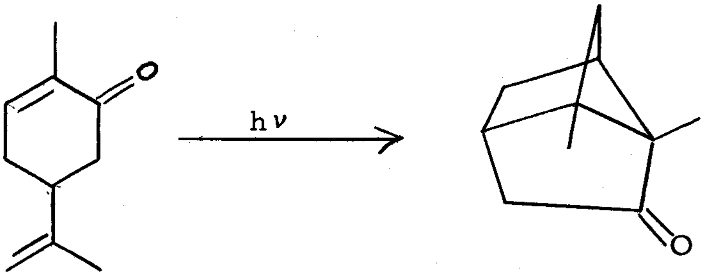
148

reaction of myrcene leads to 148 as the only product. One can surmise that the sensitized reaction proceeds via the $\pi - \pi^*$ triplet excited state while the unsensitized via the $\pi - \pi^*$ singlet state.

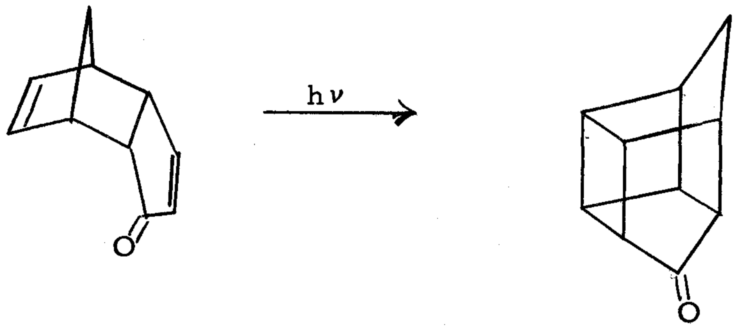
The photochemistry of enone systems will be discussed in more detail in the next section; however, some examples will be given here. These examples are depicted in equations (16) through (19). Generalizations as to the nature of the excited states of these molecules cannot be made at present. However, the $n - \pi^*$ transition is more probable than the $\pi - \pi^*$ transition. The multiplicities of the transition states are less certain.



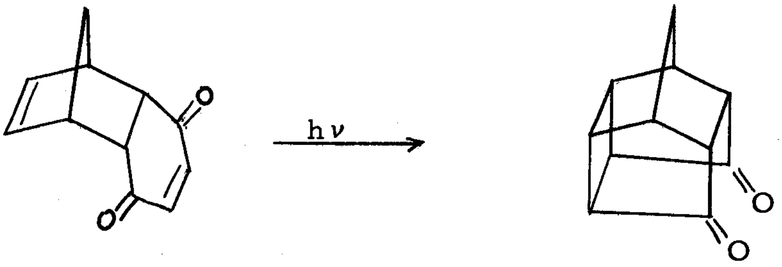
(16)



(17)

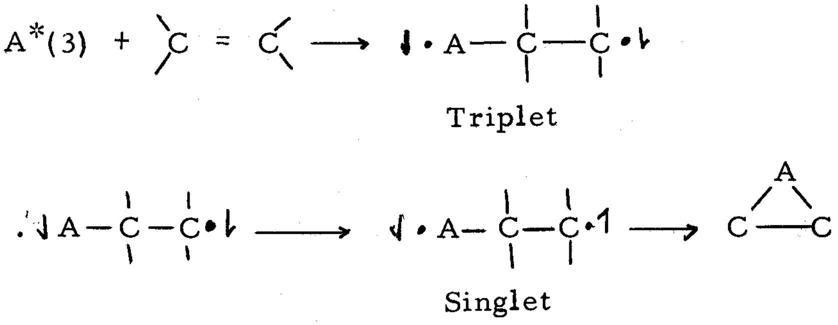


(18)

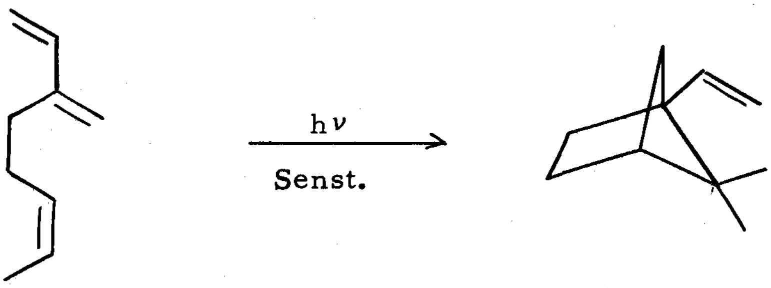


(19)

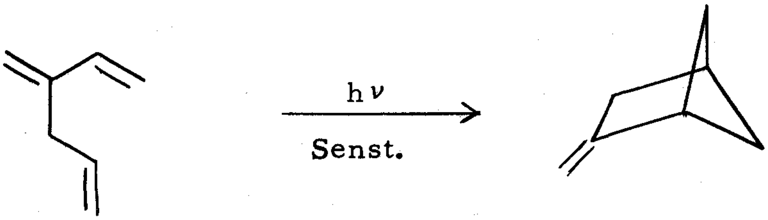
Before entering into a discussion of enone photochemistry, a more detailed look at the photoaddition of dienes to olefins is in order. Photosensitized irradiation of dienes produces the π-π^* triplet excited state. Addition of this triplet to an olefin must produce a triplet intermediate. As a consequence of this, ring closure must be preceded by a step involving spin inversion to a singlet intermediate. These processes are illustrated below.



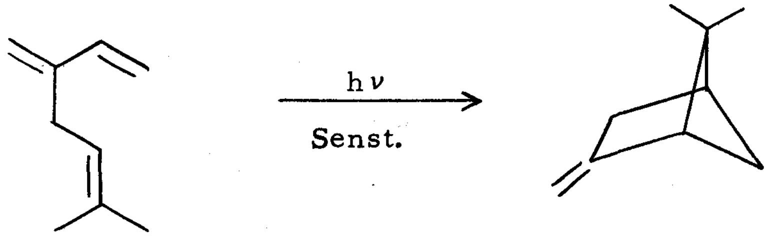
Liu and Hammond have carried out some studies in this area to test the validity of the above mechanism (59). The photocycloaddition reactions of several trienes are represented below, (Equations 20-24)..



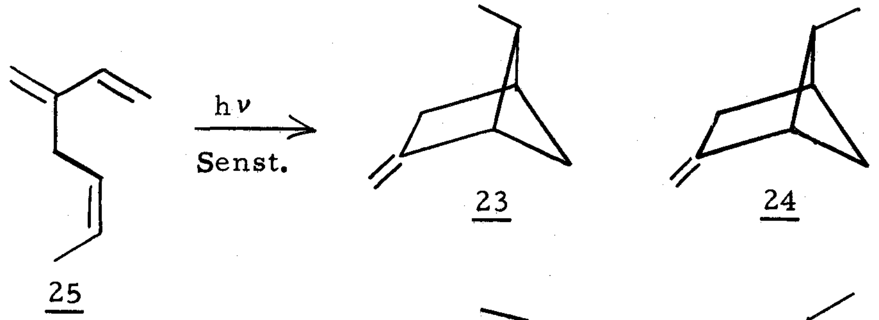
(20)



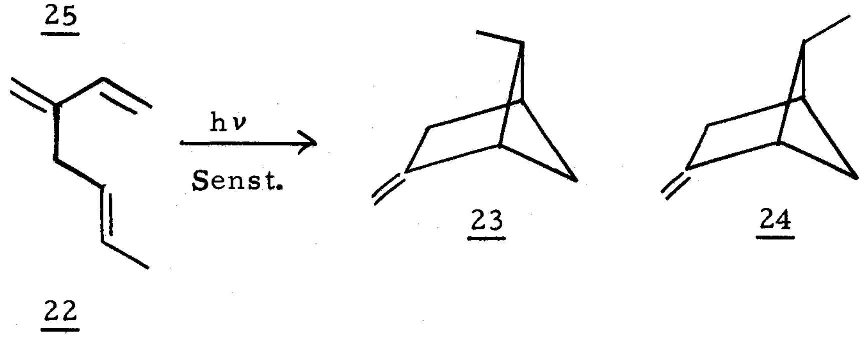
(21)



(22)



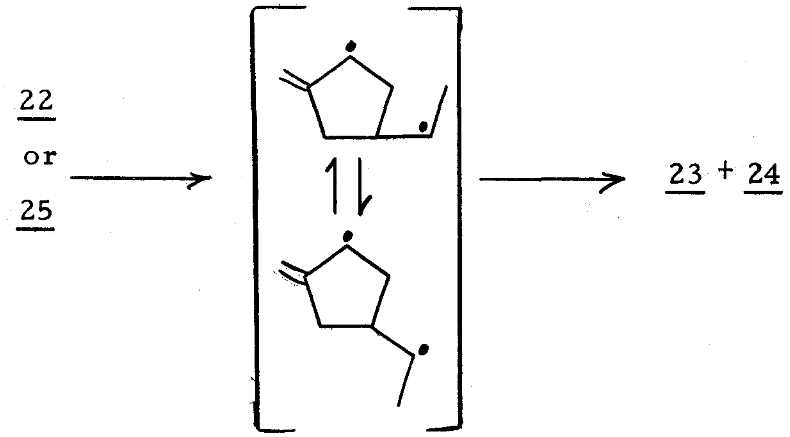
(23)



(24)

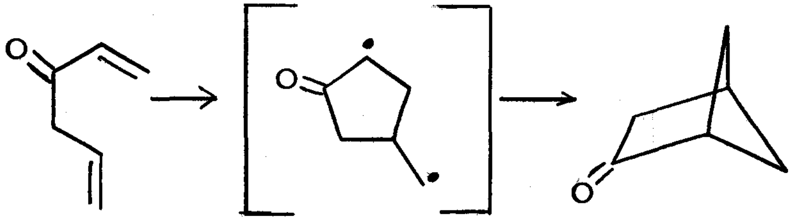
The reactions represented by Equations (23) and (24) result in a product mixture which is independent of the composition of the starting trienes. That is, either 25 or 22 give reaction mixtures of the same composition. In all cases, 23 predominates.

The irradiation of 22 and 25 give some evidence for the existence of a common biradical intermediate.



Therefore, the reaction probably involves initial bond formation between the 1 and 5 positions of the trienes to give a rapidly interconverting pair of isomeric biradicals. Apparently rotation is more rapid than final ring closure.

All the products obtained in the reactions represented above can be derived from such five-membered ring biradicals. In each case a six-membered ring biradical is possible, but products derived from this type of intermediate were not detected. In almost all the examples, six membered ring intermediates would appear to be more stable than those with five-membered rings. This selectivity may be the result of a kinetically controlled initial cyclization. The choice between the two paths is probably determined by geometric considerations. The carbon atoms in the transition state leading to the biradical intermediate must be so arranged in space that five-membered ring formation is more facile. This has application to our own work on the irradiation of 1, 5-hexadien-3-one 149. The product, bicyclo(2. 1. 1)hexan-2-one 66, can be derived from a similar five-membered ring biradical.



149

66

Enone Photochemistry

Non-conjugated unsaturated carbonyl compounds exhibit ultraviolet spectra which are the sum of the absorptions from the ethylene and carbonyl chromophores. The ethylenic absorption occurs in the far ultraviolet and is due to a π-π^* transition. The carbonyl portion of the spectrum consists of two bands. The short-wavelength band is in the far ultraviolet and is not usually observed. This absorption is also attributed to a π-π^* transition. A second low intensity band, due to the promotion of a non-bonding electron on oxygen to the π^* level, appears at long-wavelength.

When the carbonyl group and the double bond are in conjugation a new chromophoric unit is present. The spectrum for this chromophore consists of a band due to an n-π^* transition and an intense π-π^* transition band. Both bands appear at longer wavelength than those for the simple chromophores. The energy level diagram in Figure 4 illustrates the transitions possible for enones.

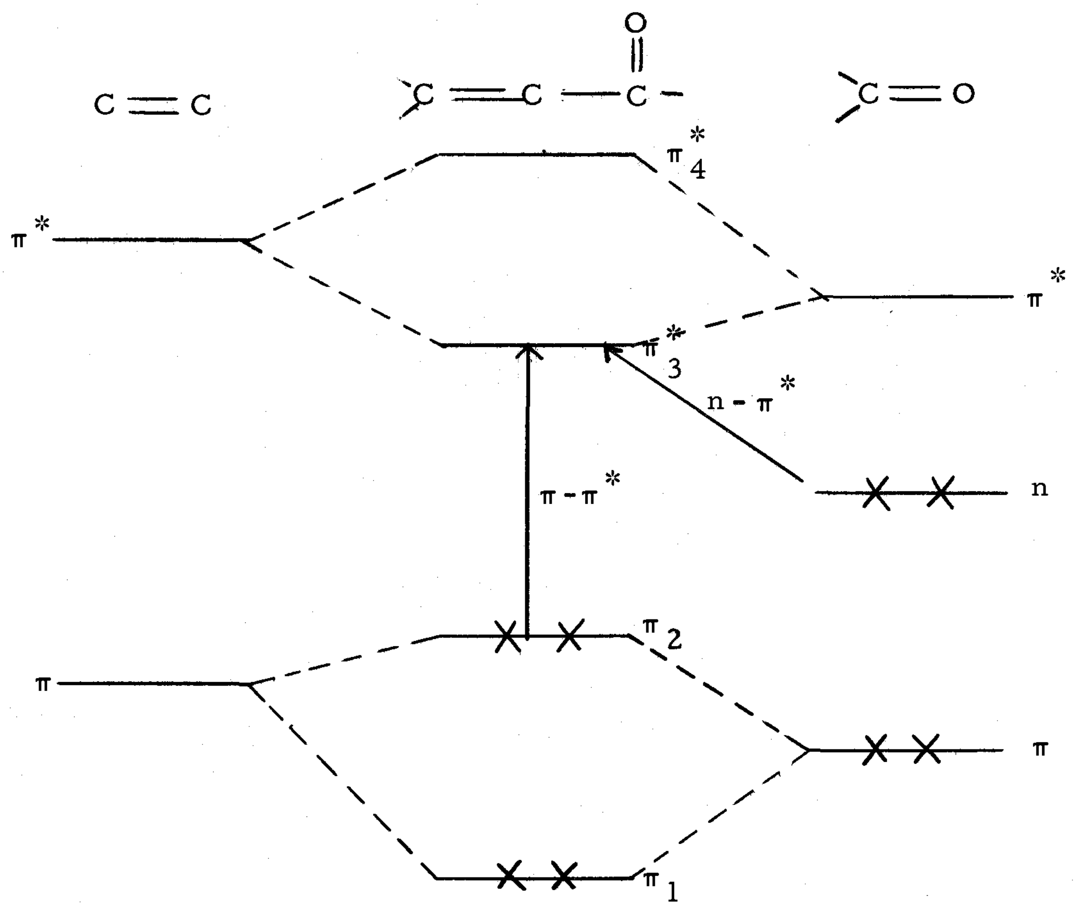
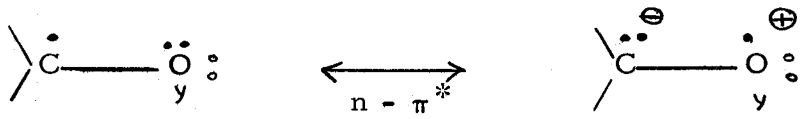
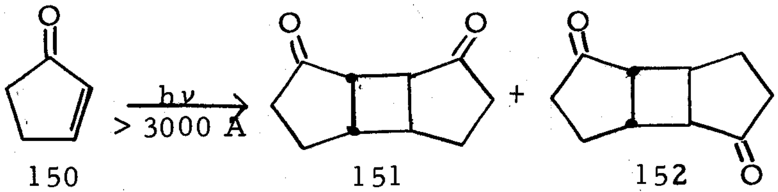


Figure 4. Energy-level diagram for α, β-unsaturated carbonyl compounds (45).

The nature of the $n-\pi^*$ and $\pi-\pi^*$ excited states for carbonyl compounds is given in Figure 3. In the ground state, the carbonyl is polarized so that oxygen carries a partial negative charge and carbon a partial positive charge. The $n-\pi^*$ excited state results from the promotion of a P_y non-bonding electron to an anti-bonding π^* level. The resonance forms for this excited state include one in which oxygen bears a positive charge and carbon a negative charge. This fact has significance in cycloaddition reactions and is used to explain the mode of addition to olefins (31, 45).

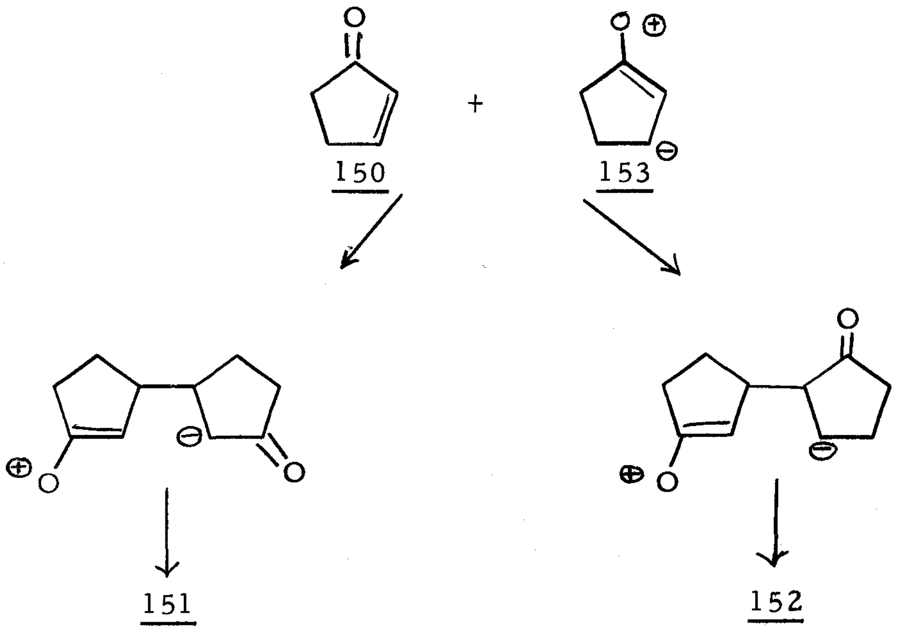


Irradiation of pure cyclopentenone 150, neat or in solution, with wavelengths over 3000 Å produces a high yield of the two dimers 151 and 152, in approximately equal amounts (33). It was first



150 151 152

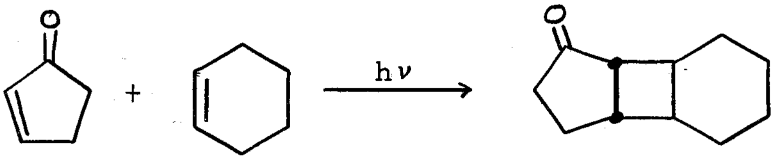
proposed that the reaction proceeds via a n-π* singlet state 153. Eaton stated that if dimerization took place via a two step mechanism, the reaction could be depicted as below (32). Turro has suggested the possibility of two excited states, a singlet and a triplet, participating in the reaction (109). This could be tested by a study of the effect of cyclopentenone concentration on the ratio of 151 to 152. Leermakers has made this study (87). His results indicate that a nonconcerted reaction of some sort is probable, but he does not favor the one proposed by Eaton. Quencher and sensitizer studies suggest that more than one intermediate was involved in the



dimerization. He concluded that at low concentrations a triplet state is operative while at high concentrations of cyclopentenone a singlet state may be involved.

Eaton has recently reported that at high concentrations of quencher, piperylene, the quantum yield for dimerization goes to zero (34). His data seems to rule out the participation of a singlet excited state of cyclopentenone. Eaton explains Leermakers' results as a solvent effect. The character of each reaction solvent is dependent on the concentration of cyclopentenone. Leermakers has since also attributed concentration effects to a solvent effect. He no longer supports his original hypothesis that the singlet state might be important at high cyclopentenone concentration (88).

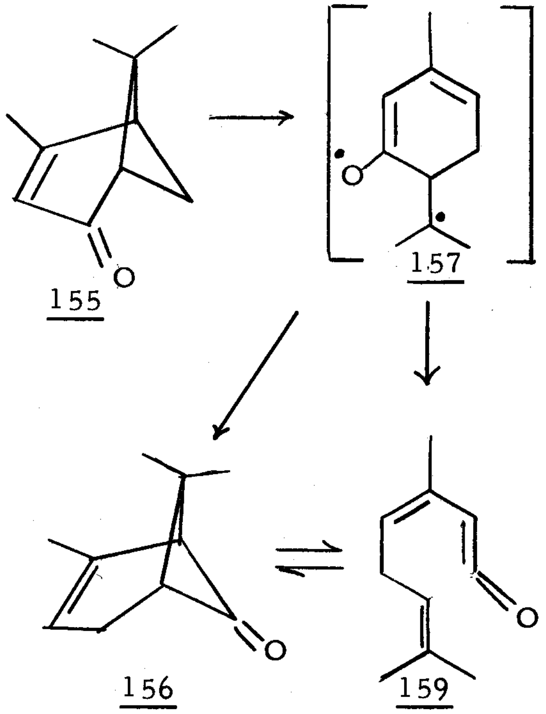
The photoaddition of cyclopentenone to cyclohexene gives the tricyclic olefin 154, analogous to the reaction between cyclopentenone and cyclopentene (32). Addition of benzophenone



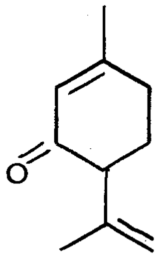
154

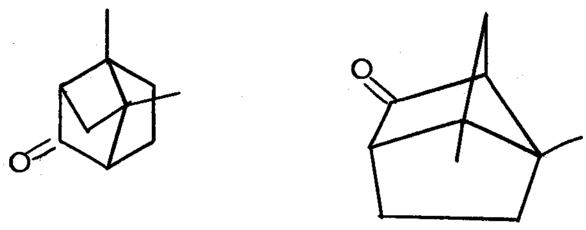
(E_T = 69 kcal/mole) results in no cycloaddition. Irradiation in the presence of high-energy sensitizers of about 73 kcal/mole triplet energy, however, leads to product. Assuming that benzophenone excites cyclopentenone to its lowest triplet state, that state, T_1, cannot be involved in the reaction. The above assumption is based on studies which show that benzophenone does transfer triplet energy to cyclopentenone. If this is true, the reactive species must be cyclopentenone in its T_2 state or a species derived from it.

Irradiation of verbenone 155 under various conditions gives at least 15 products. The main product, chrysanthenone, 156, was obtained in up to 67% yield (37). Each of the major products in the irradiation can be traced to either of two sources. The first source is the primary irradiation scheme indicated below. All of the other products can be derived from the various ketone products of the primary irradiation. This primary irradiation, as can be seen, consists of two pathways, each of which leads to the major product 156.

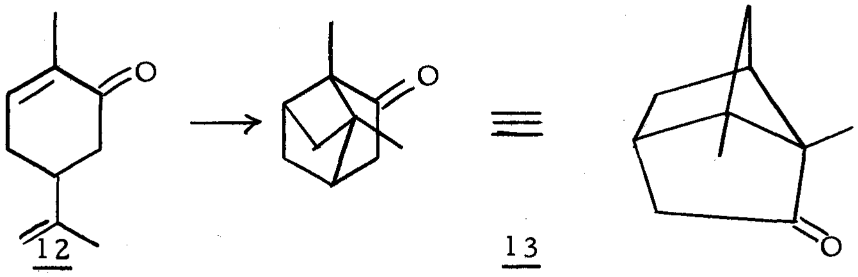


From our point of view, a more interesting reaction is the secondary irradiation. The product of this irradiation is derived from isopiperitone 158. Both 158 and its irradiation product 1, 2-dimethyltricyclo(3. 3. 0. $0^{2,7}$)octan-3-one 160, were isolated from the reaction mixture. Irradiation of pure 158 proved that 160 was


158


160

derived from this ketone. One can immediately recognize the similarity between this reaction and the irradiation of carvone 12 to carvonecamphor 13 (20). The only difference between these irradiations is the mode in which the excited enone system has added to the isolated double bond.

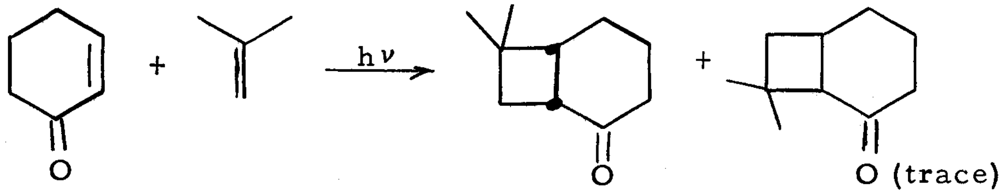


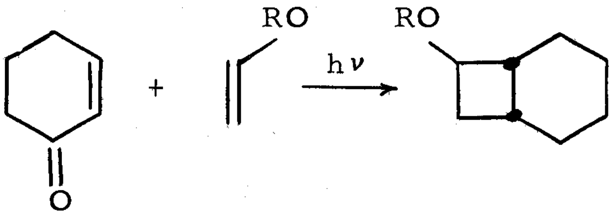
12 13

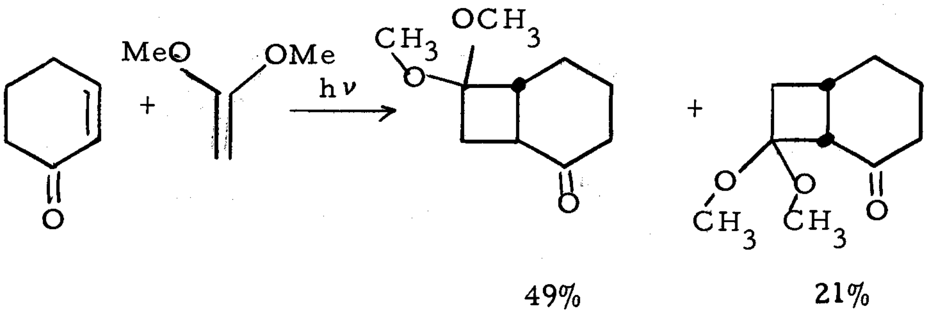
The question of mode of photocycloaddition has arisen in the past. Corey studied the intermolecular photochemical reactions of 2-cyclohexenones with substituted olefins (24). Some of the reactions investigated are represented on the following page. The orientational specificity of these reactions is immediately apparent. The excited enone system reacts with substituted olefins <u>via</u> the same mode of addition. Corey explained this specificity in terms of a complex between the excited ketone and the olefin. The process involved can be described as shown below.

$$\begin{array}{r} K^{*} + 0 \rightleftharpoons (\text{oriented } \pi\text{-complex}) \rightleftharpoons (\text{diradical intermediate}) \\ \downarrow \quad\quad\quad \\ \text{cycloadduct} \quad\quad \end{array}$$

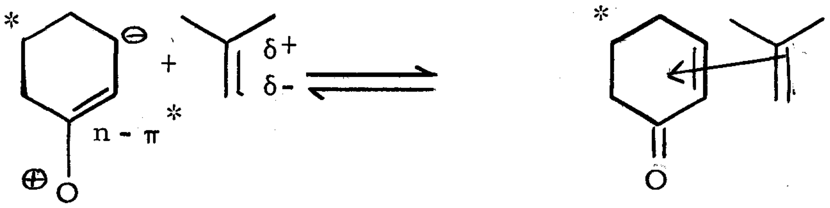
The excited ketone, K^{*}, is most likely an n-π^{*} excited ketone. This excited state for cyclohexenone can be represented by the polar structure 161. This form places a negative charge on the β-carbon.







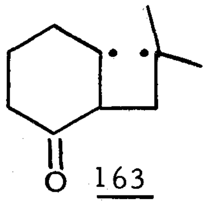
The polarization of the 1, 1-disubstituted olefins used places a partial positive charge on the 1-carbon. The π-complex formed between



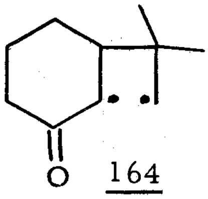
161

162

the excited ketone and the olefin would have the structure 162. Collapse of 162 to a diradical intermediate, 163 or 164, leads to the major products of the reactions.

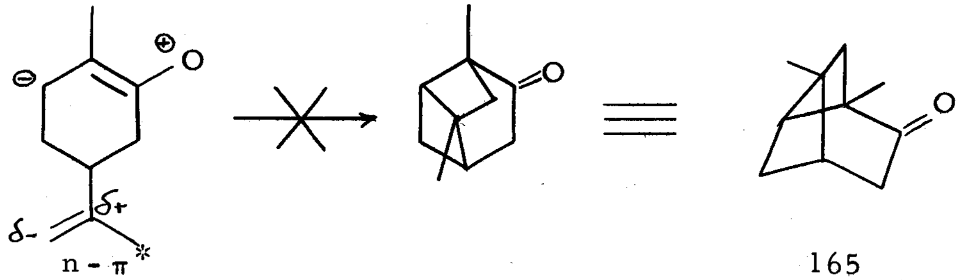


163



164

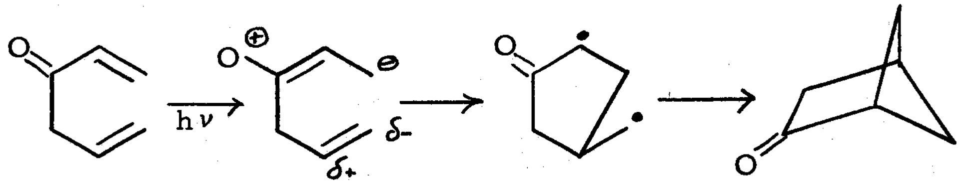
When this approach is applied to the isopiperitenone irradiation, one predicts that the product should have the structure 160, as is found. However, when applied to the carvone-carvonecamphor transformation, the wrong structure is predicted. This is shown in the reaction scheme below. The structure, 165, predicted by Corey's intermediate, is not the structure of carvonecamphor 13.



165

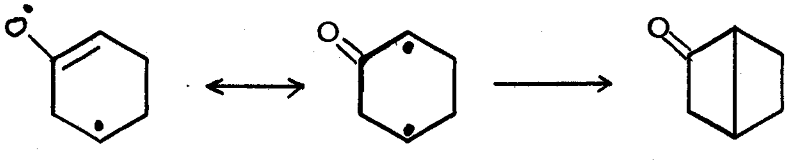
Erman suggests that the production of 13 from 12 and 160 from 158 may reflect the stereochemistry of the interacting π-electron clouds (37). In the case of carvone, it is apparently easier for the disubstituted end of the olefin to reach the α-carbon than to react in the Corey fashion.

Let us see how this discussion applies to the present work. The n-π^* excited state of 1, 5-hexadien-3-one 149 can be represented by structure 168. The Corey mode of addition predicts that

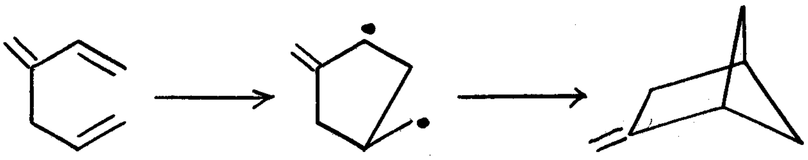


149 168 166 66

a bond should be made between C-1 and C-5 to give an intermediate form 166 (shown as a diradical) which then closes to give bicyclo-(2. 1. 1)hexan-2-one 66. The carvonecamphor mode of cycloaddition would give a biradical intermediate 169. Collapse of this diradical leads to bicyclo(2. 2. 0)hexan-2-one 170. No bicyclo(2.2. 0)hexan-2-one was detected in our irradiations. This is similar to the irradiation of trienes such as 20 where a diradical equivalent to 166 must be involved, as was shown by the stereochemical studies of Liu and Hammond (59).



169 170



20 21

This latter reaction has been shown to involve a $\pi-\pi^*$ triplet state, however, extrapolation of this mechanism to an enone photolysis is quite dangerous.

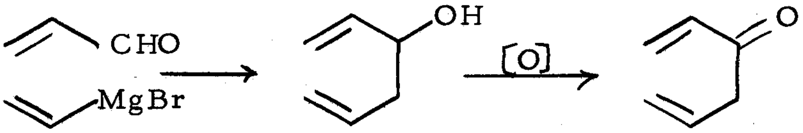
RESULTS AND DISCUSSION

Synthesis of Bicyclo(2.1.1)hexan-2-one

The introduction to this thesis contains many examples of synthetic routes which lead to bicyclo(2.1.1)hexanes. If any generalization could be made about these routes, it would be that the yields are uniformly poor. The development of a facile synthesis of bicyclo(2.1.1)hexanes would open avenues to the study of this highly strained ring system. It was to this end that the work reported in this thesis was initiated.

1, 5-Hexadien-3-one

The method chosen for the synthesis of bicyclo(2.1.1)hexane derivatives features, as its main step, an intramolecular photocycloaddition reaction. As was mentioned in the introduction, several syntheses of bicyclo(2.1.1)hexanes involve photocycloaddition reactions of suitably substituted 1, 5-hexadienes. These dienes vary from the parent 1, 5-hexadiene (103), to 3-methylene-1, 5-hexadiene (58), to 3-keto-1, 5-hexadienes (12). The relative ease of addition of excited enone chromophores to an unexcited olefin immediately suggests the use of a 1, 5-hexadiene which incorporates an enone system into its structure. Hence, a key intermediate in the synthesis of bicyclo(2. 1. 1)hexan-2-one was 1, 5-hexadien-3-one 149, a compound previously reported (48) but not rigorously characterized. An obvious immediate precursor to 149, 1, 5-hexadien-3-ol 171 was conveniently synthesized *via* the reaction of acrolein and allylmagnesium bromide, as developed by Dreyfuss (30). Using this method, consistent yields of 50 - 55% were obtained. The oxidation of 171 to

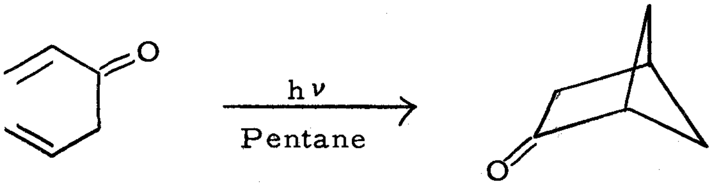


171 149

the desired dienone 149 was accomplished by careful treatment of an acetone solution of the dienol with chromium trioxide (12). Yields of 30-35% were obtained by this method. A slightly different modification of the Jones procedure, as used by Meinwald in the synthesis of nortricyclanone (69), gave similar yields, but a considerable amount of unoxidized alcohol was always present. The first method gave almost complete oxidation. In favor of the Meinwald method was the more rapid isolation procedure. Several other oxidation methods were attempted in the synthesis of 149. Treatment of 171 with manganese dioxide (47), dicyclohexylcarbodiimide in dimethylsulfoxide, or chromium trioxide in pyridine all led to recovery of the starting alcohol without detectable ketone formation. The pure enone 149 is a powerful lachrymator and is quite unstable so that direct irradiation of impure material proved to be the most useful procedure. However, distillation of the crude ketone did give a 35% yield of 1,5-hexadien-3-one, b.p. 30-40^{o}(30 mm). The infrared spectrum of this compound exhibits an absorption band at 1675 cm^{-1} attributed to the α,β-unsaturated carbonyl group. The ultraviolet spectrum shows a maximum at λ_{max}^{EtOH} = 212 mμ (ε = 11,000.). A good n.m.r. spectrum could not be obtained, but a multiplet at 3.5 δ assigned to the alpha-methylene and multiplets between 5.0 - 6.5 δ due to vinyl protons were discernible.

Bicyclo (2.1.1)hexane-2-one

When a solution of 1,5-hexadien-3-one <u>149</u> in pentane was irradiated with a 450 watt Hanovia medium pressure mercury lamp, a photocycloaddition reaction occurred. Irradiation of 30 g of ketone in one liter of pentane takes approximately 30 hours. The reaction time is greatly increased if the polymer, which is formed in the reaction of crude ketone, is not removed from the quartz probe periodically. Irradiation of pure <u>149</u> in pentane eliminates polymer formation. From the irradiation mixture a colorless liquid boiling at 55-58^{o} (20 mm) was obtained in 32% yield from <u>171</u>.



149 66

The infrared spectrum of the irradiation product 66, in carbon tetrachloride, exhibits a band at 1764 cm^{-1} assigned to a strained carbonyl group (see Table 3). No absorption above 205 mμ is seen in the ultraviolet spectrum of this compound. The n.m.r. spectrum of 66 is relatively simple. (See Figure 5). It consists of a quartet centered at 1.60 δ (2 H's, J = 7.0 cps), assigned to the endo C-5 and C-6 protons; a multiplet at 2.10 δ (2 H's), attributed to methylene protons adjacent to the carbonyl; a multiplet centered at 2.20 δ (2 H's), due to the exo C-5 and C-6 protons; and a multiplet at 2.80 δ (2 H's) assigned to the bridgehead hydrogens. See Table 2 for the n.m.r. assignments of similar bicyclo(2.1.1)hexanes.

Deuteration of the ketone 66 gave 3,3-dideuteriobicyclo(2.1.1)-hexan-2-one 172. The n.m.r. spectrum of this compound (Figure 6) is almost identical to that of 66 except that the multiplet at 2.10 δ is absent and the multiplet at 2.80 δ is now a more distinct triplet. This gives added verification to the n.m.r. assignments given above for 66.

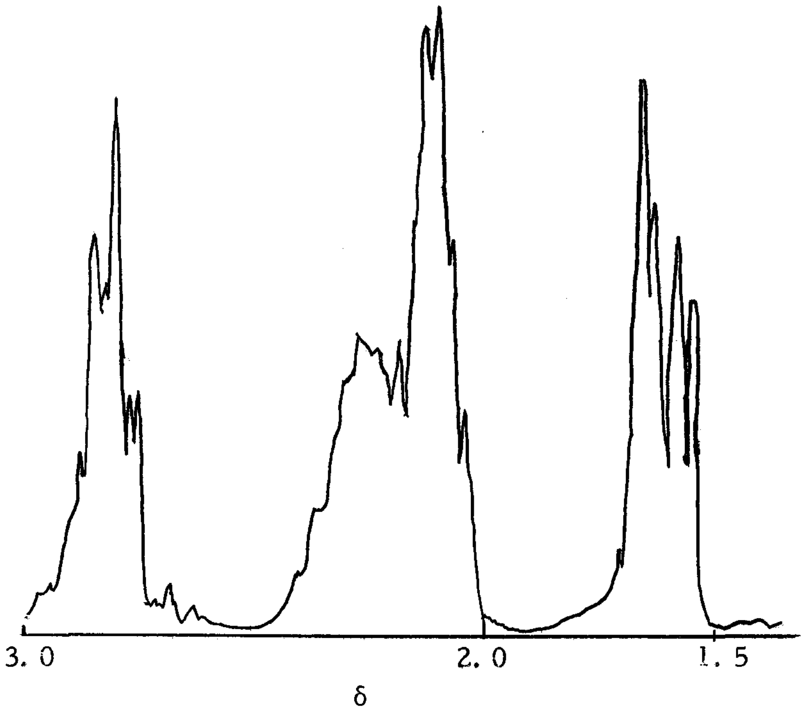


Figure 5. The n. m. r. spectrum of bicyclo(2. 1. 1)hexan-2-one 66.

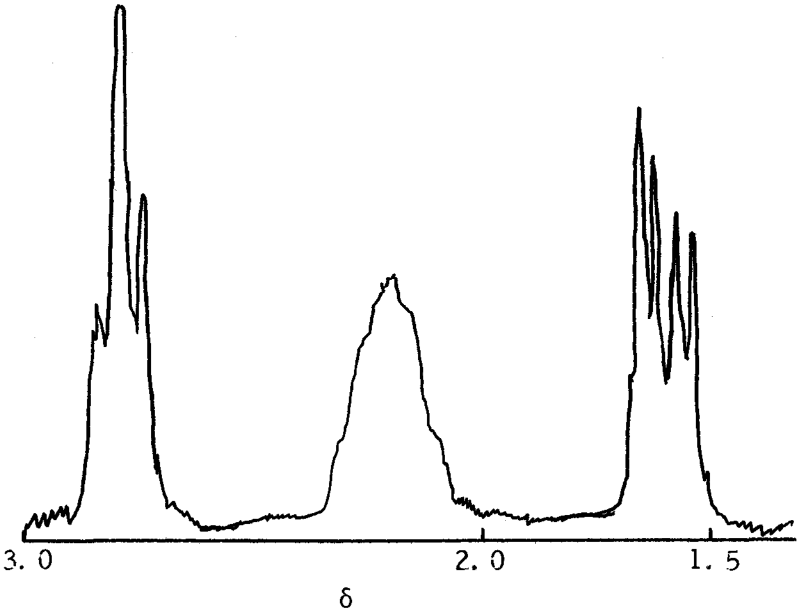
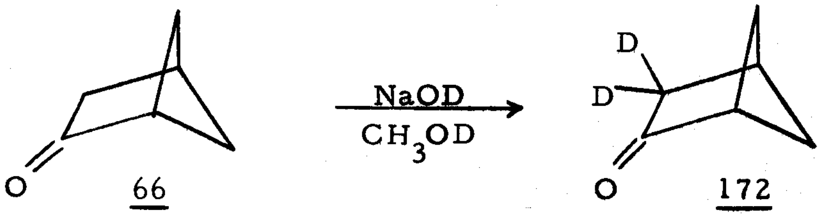
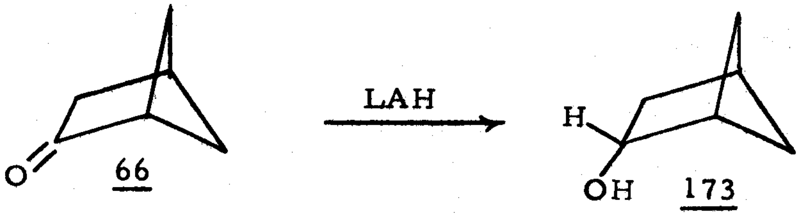


Figure 6. The n. m. r. spectrum of 3, 3-dideuteriobicyclo(2. 1. 1)-hexan-2-one 172.



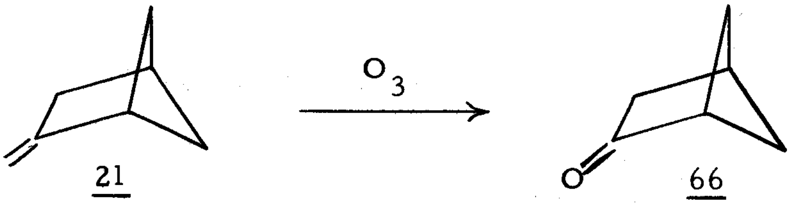
66 172

Reduction of bicyclo(2. 1. 1)hexan-2-one with lithium aluminum hydride in ether gave a 95% yield of a white solid, m. p. 82. 0°-82. 6°. The infrared spectrum of this extremely volatile compound



66 173

shows bands at 3620 and 3300 cm^{-1} attributable to a hydroxyl group. In addition, bands at 1105, 1025, and 990 cm^{-1} are present. The n. m. r. spectrum shows a broad, concentration dependent sextet at 4. 35 δ (2 H's), assigned to the hydrogen on the carbon bearing the hydroxyl group, overlapped by the signal due to the proton on oxygen. Peaks at 0. 95, 1. 53, 1. 25 - 2. 15, and 2. 42 δ showed that the bicyclo(2. 1. 1)hexane skeleton was still intact. The above data are consistent with the structure 173 for bicyclo(2. 1. 1)hexan-2-ol. Spectra of this alcohol were compared with those of an authentic sample and proved to be identical (67). Reoxidation of the alcohol 173 to the ketone 66 proved that no rearrangement had occurred in the reduction. The ketone was also shown to be identical with that



obtained by de Mayo *et al.* (19) from the olefin 21.

Careful examination of the infrared spectrum of the crude product of the irradiation failed to show any carbonyl absorption in the 1780 cm^{-1} region where one would expect to find the carbonyl band of bicyclo(2. 2. 0)hexan-2-one. Apparently cyclization occurs in only one direction, that which parallels the intermolecular examples studied by Corey, *et al.* (24).

Nature of the Photochemical Cyclization

The development of a facile route to bicyclo(2. 1. 1)hexanes and the study of their chemistry was the main purpose of this work. The photochemical cyclization of 1, 5-hexadien-3-one 149 to bicyclo-(2. 1. 1)hexan-2-one 66 is the key step in this route. It is, therefore, useful to examine the nature of such cyclizations. In Figure 7 are listed some other photocycloaddition routes to bicyclo(2. 1. 1)hexanes, most of which were developed after our discovery. Some of the aspects of these cyclizations were discussed in the introduction.

Detailed studies of the mechanism of such intramolecular cyclizations have just recently begun, but are more complicated than

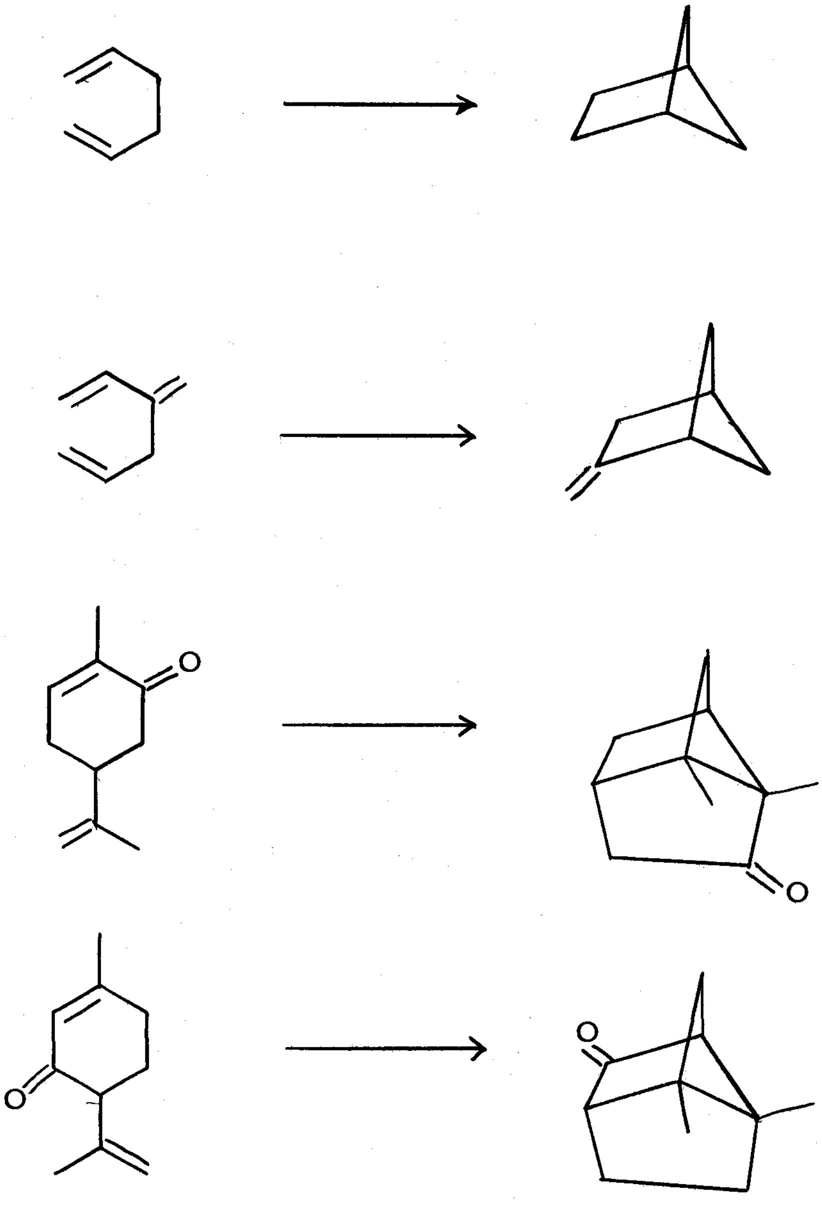
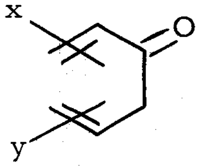
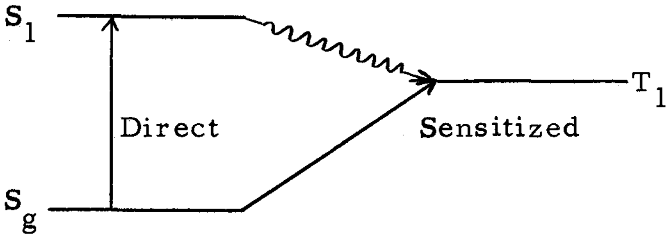


Figure 7. Photochemical cyclization reactions.

similar studies of intermolecular cycloadditions (24). The structure of the olefin cannot be as easily varied as in the case of intermolecular reactions. However, studies are underway on the effect of substituents, X and Y, on the basic 1, 5-hexadien-3-one system. These studies should prove most valuable.

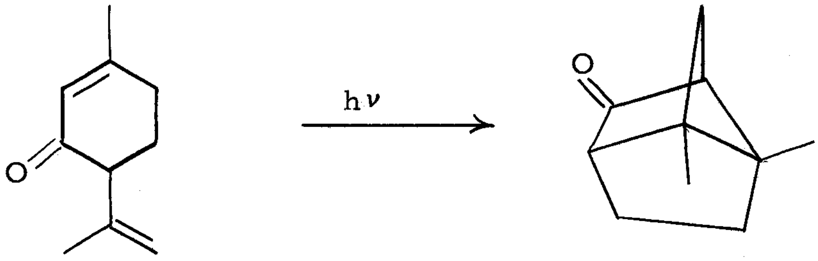


The most important feature of the reactions shown in Figure 7 is that they are sensitized by triplet sensitizers. Such sensitization is usually taken as an indication that a triplet pathway is being followed. In cases where direct irradiation gives the same products as sensitized irradiation, a similar intermediate, shown below as T_1 for convenience, is assumed. Triplet enones have been shown to be



involved in intermolecular dimerizations (28, 32, 33, 34), and are believed to be involved in intermolecular cycloadditions (24). The $n \rightarrow \pi^*$ triplet state is assumed to be involved in these photoreactions, although $\pi-\pi^*$ triplet states must also be considered.

Cyclization of 1, 5-hexadien-3-one 149 to bicyclo(2. 1. 1)hexan-2-one 66 is unique in two ways. First, the reaction was not sensitized by "typical" triplet sensitizers, and second, the reaction was essentially stopped by passage of the ultraviolet light through a Pyrex filter. Irradiation of pure, acetone-free, 149 proceeded at the same rate as unpurified 149. Removal of the impurities, however, greatly reduced polymer formation. Addition of a triplet sensitizer, such as benzophenone (E_T = 69 kcal/mole) or acetone (E_T = 80 kcal/mole) had no effect on the rate. The rate of cyclization was drastically reduced, however, when a Pyrex filter was placed between the light source and the sample. The results of these monitored irradiations are shown in Figure 8 where the ultraviolet absorption at 212 mμ is plotted as a function of time. It is interesting to note that the irradiation of isopiperiteneone 158 in the presence of a Pyrex filter leads to a 35% yield of tricyclic ketone 160, while irradiation in the presence of a Vycor filter apparently did not lead to 160 (37).



158

160

This result implies that excitation to excited states other than the n - π* state does not lead to cyclization of 158.

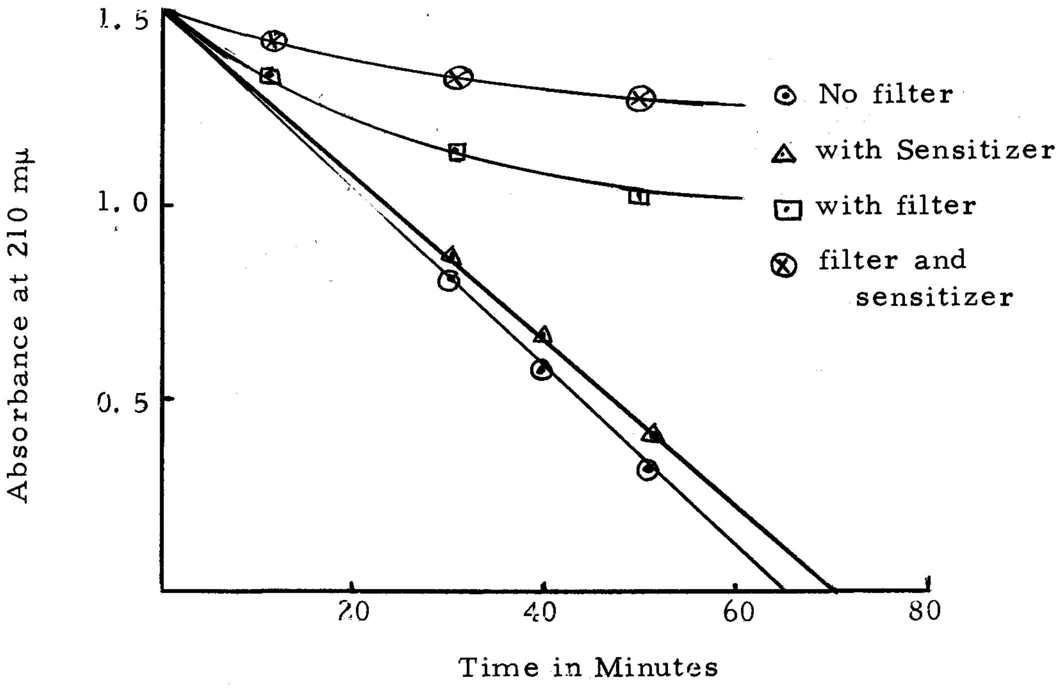
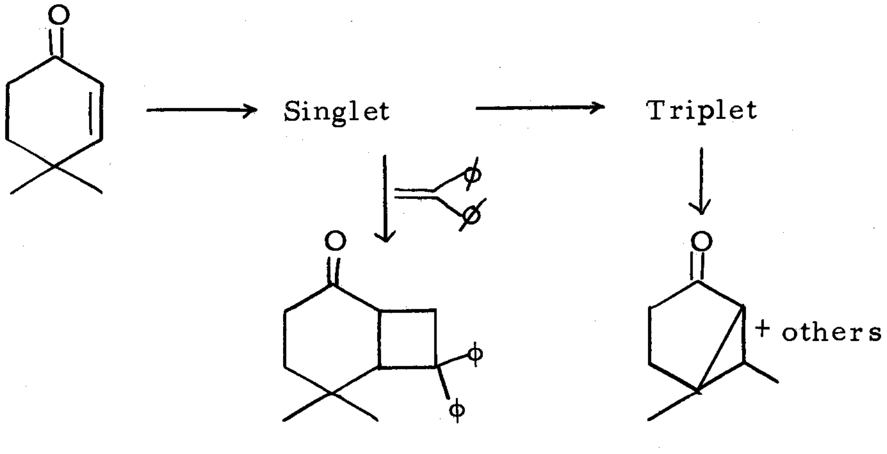


Figure 8. Monitored irradiation of 1, 5-hexadien-3-one.

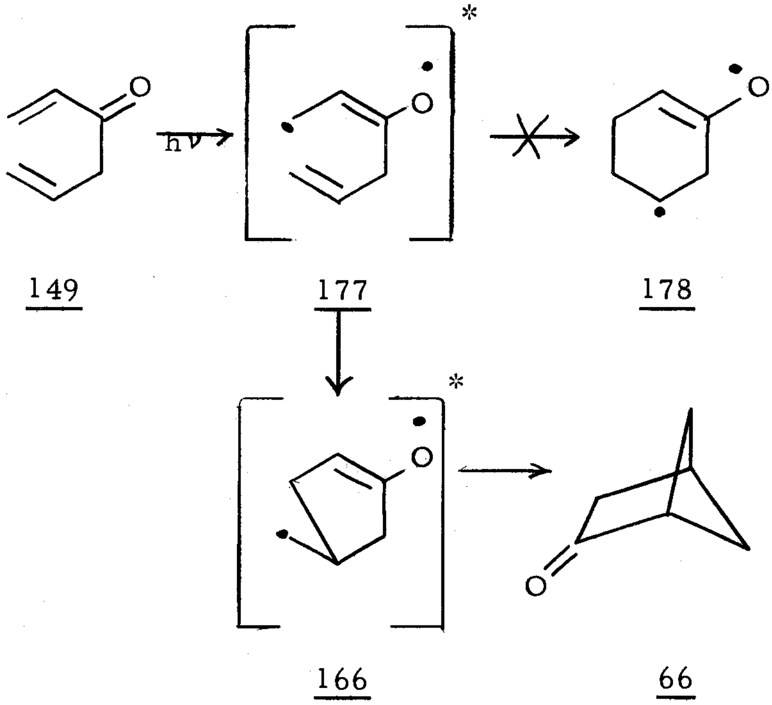
A tentative conclusion can be reached about the nature of the cyclization of 149. It appears that the reaction involves a singlet excited state, presumably π - π* in character. However, possible participation of a high-energy triplet state cannot be ruled out. The reaction of 149, therefore, differs sharply from the otherwise similar cyclization of 3-methylene-1, 5-hexadiene 20. It is conceivable that both singlet and triplet excited enones should add to olefins;

addition in this case is facilitated by the close proximity of the carbon-carbon double bond. In intermolecular reactions a high concentration of olefin should favor trapping the initially formed singlet state prior to intersystem crossing. A striking example is the irradiation of 174 (84), known to give 175 *via* a triplet mechanism. In the presence of 1, 1-diphenylethylene, no rearrangement to 175 was observed and only the cycloaddition product 176 was obtained.

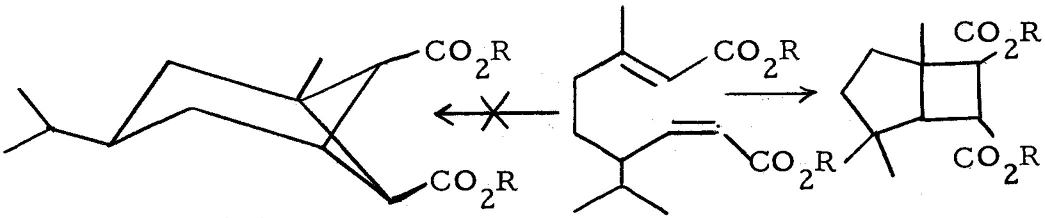


176 175

Regardless of the detailed nature of the excited state, it seems likely that some type of intermediate must be involved. In a manner similar to that used by Liu and Hammond (59) and discussed in the introduction, one can envisage cyclization of the excited enone 177 to either diradical 166 or 178. Formation of 66 can only be explained by the intermediacy of 166. Since 178 contains a more stable

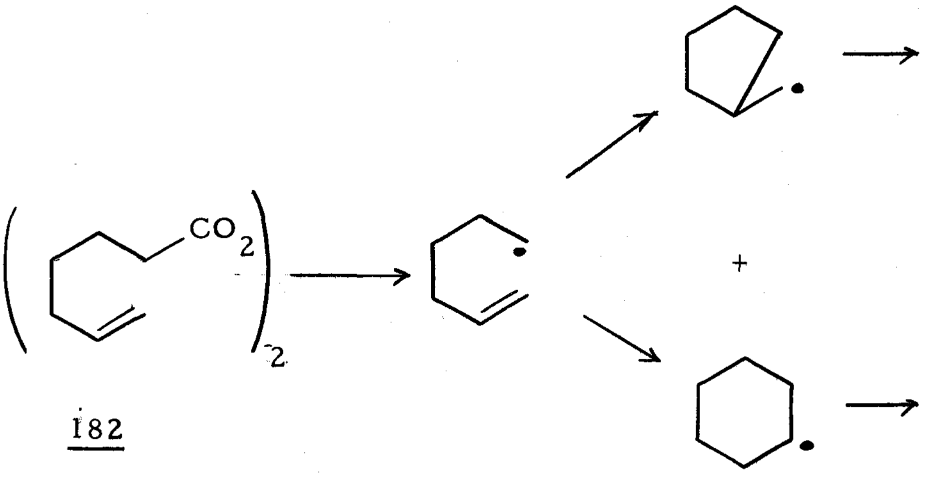


secondary radical, steric proximity must be invoked to explain the formation of 166. Indeed there are many examples of radical closures in which formation of a cyclopentane is more facile than formation of a cyclohexane. Cyclization of the diene and triene in Figure 7 were explained by initial cyclization to a five-membered ring diradical followed by closure to the product (59). Products derived from a possible six-membered ring intermediate appear either only in trace amounts or not at all. Brown (14) has shown that irradiation of 1,6-dienes such as 179 leads only to products 180 which are derived from preferential formation of five-membered ring diradical intermediates.



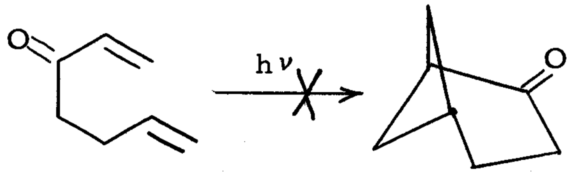
181 179 180

The thermal decomposition of 6-hexenoyl peroxide 182 also leads to products which are derived from five-membered ring intermediates (53). Thus a 36:1 ratio of methylcyclopentane to cyclohexane was obtained from decomposition of 182.

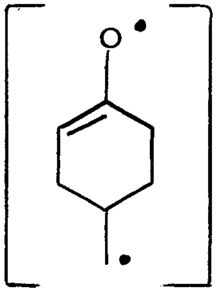


182

This preferential cyclopentane formation is strikingly demonstrated by failure of 183 to close to 184, via 185 (11).

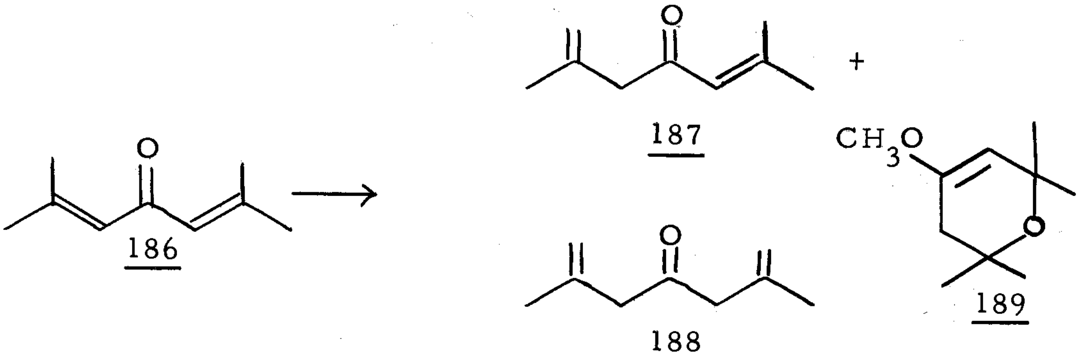


183 184



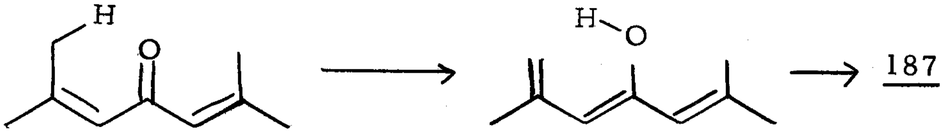
185

Schneider and Meinwald (90) have made the observation that 187 fails to undergo photocycloaddition while our less highly substituted 1, 5-hexadien-3-one is readily converted to bicyclo(2. 1. 1) hexan-2-one. Kropp and Gibson have made a detailed study of the irradiation of phorone, 186, in absolute methanol (51). Under a variety of conditions, it was found that the product mixture contained the two deconjugated ketones 187 and 188 and the pyran 189. The doubly deconjugated ketone 188 always appeared in trace amounts.



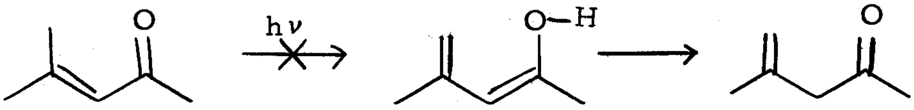
186 187 188 189

Compound 187 can arise by a γ-hydrogen abstraction to give the enol form of 187. This hydrogen abstraction is aided by the



186

preferential s-cis conformation of 186 which places the hydrogen in close proximity to the carbonyl oxygen. Mesityloxide 190 does not undergo a similar photoenolization. Similarly, the photoconversion of 187 to 188 is unfavored. The change from a cross-



190

conjugated chromophore in 187 and 190 apparently causes the n-π* energy level to be raised above the π-π* triplet level. Aromatic carbonyl compounds in the π-π* triplet excited state are not prone to hydrogen transfer reactions. Apparently this can also be applied to aliphatic compounds.

Meinwald (90) has stated the general rule that most simple s-cis-α, β-unsaturated ketones, such as phorone and 187 are unreactive towards cycloaddition reactions when irradiated with light of wavelengths longer than 300 mμ. Ketones in the s-trans-configuration undergo cycloaddition under these conditions. However, 1, 5-hexadien-3-one 149, an s-trans ketone, is also unreactive at wavelengths longer than 300 mμ. Thus s-trans conformations may not be the sole criterion for cycloaddition. Indeed, if s-cis ketones were irradiated at wavelengths below 300 mμ, photocycloaddition might occur.

Utility of Bicyclo(2. 1. 1)hexan-2-one

Our interest in bicyclo(2. 1. 1)hexan-2-one was accentuated by presumably standard sequences which might lead from it to bicyclo(2. 1. 1)hexene 108 and bicyclo(1. 1. 1)pentane-2-carboxylic acid 191. Our interest in these compounds was discussed in the introduction. These schemes, shown in Figures 9 and 10, also represent methods which were attempted. These reactions will, therefore, be discussed in more detail in the discussion of the chemistry of bicyclo(2. 1. 1)-hexan-2-one.

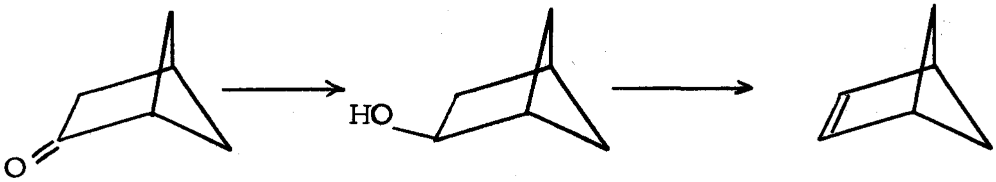


Figure 9. Synthetic routes to bicyclo(2. 1. 1)hexene.

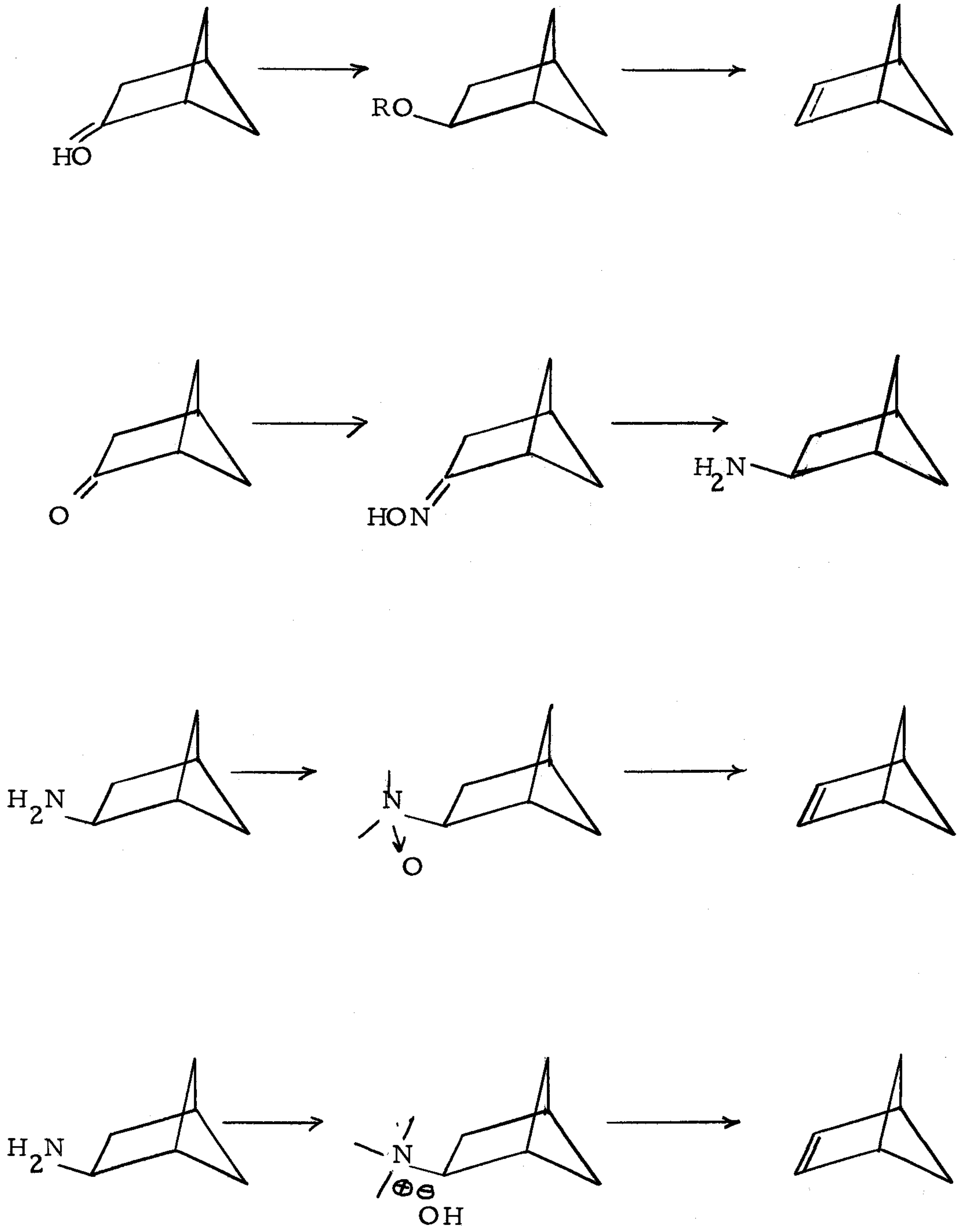


Figure 9. Continued.

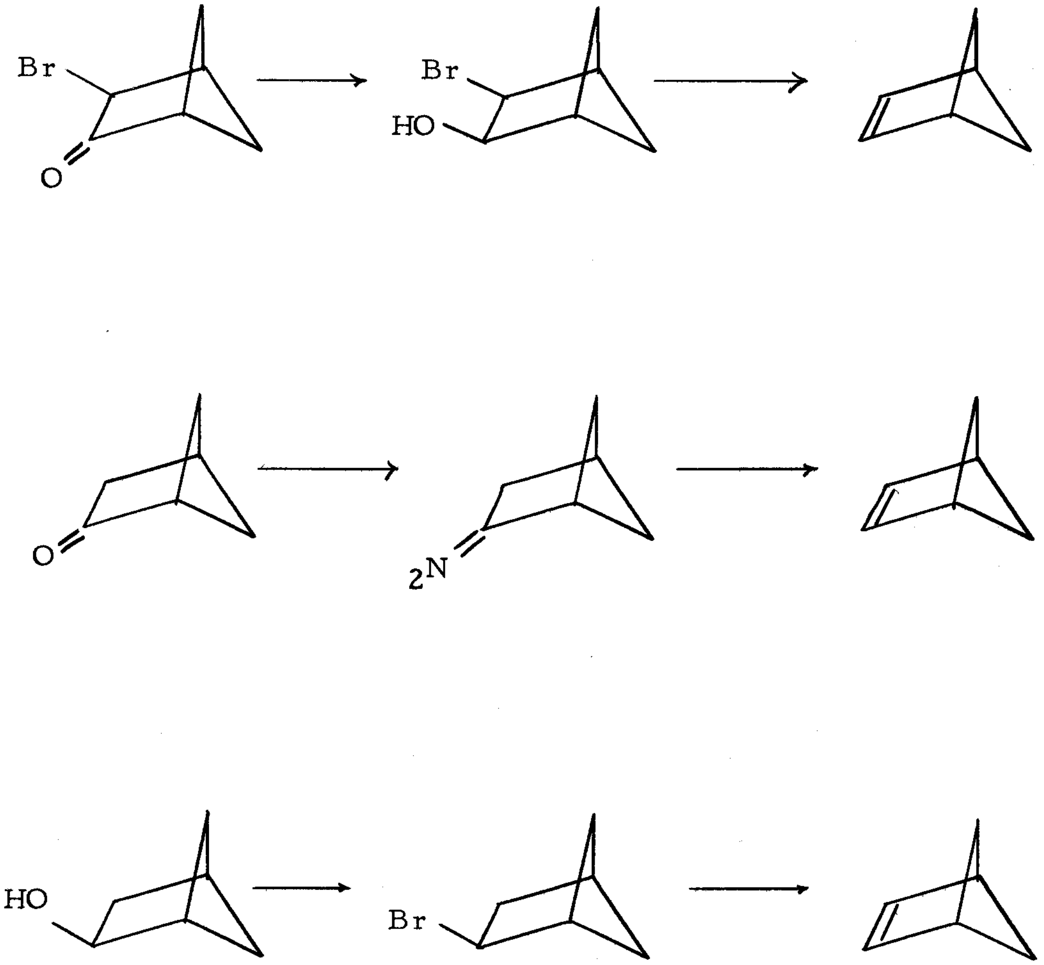


Figure 9. Continued.

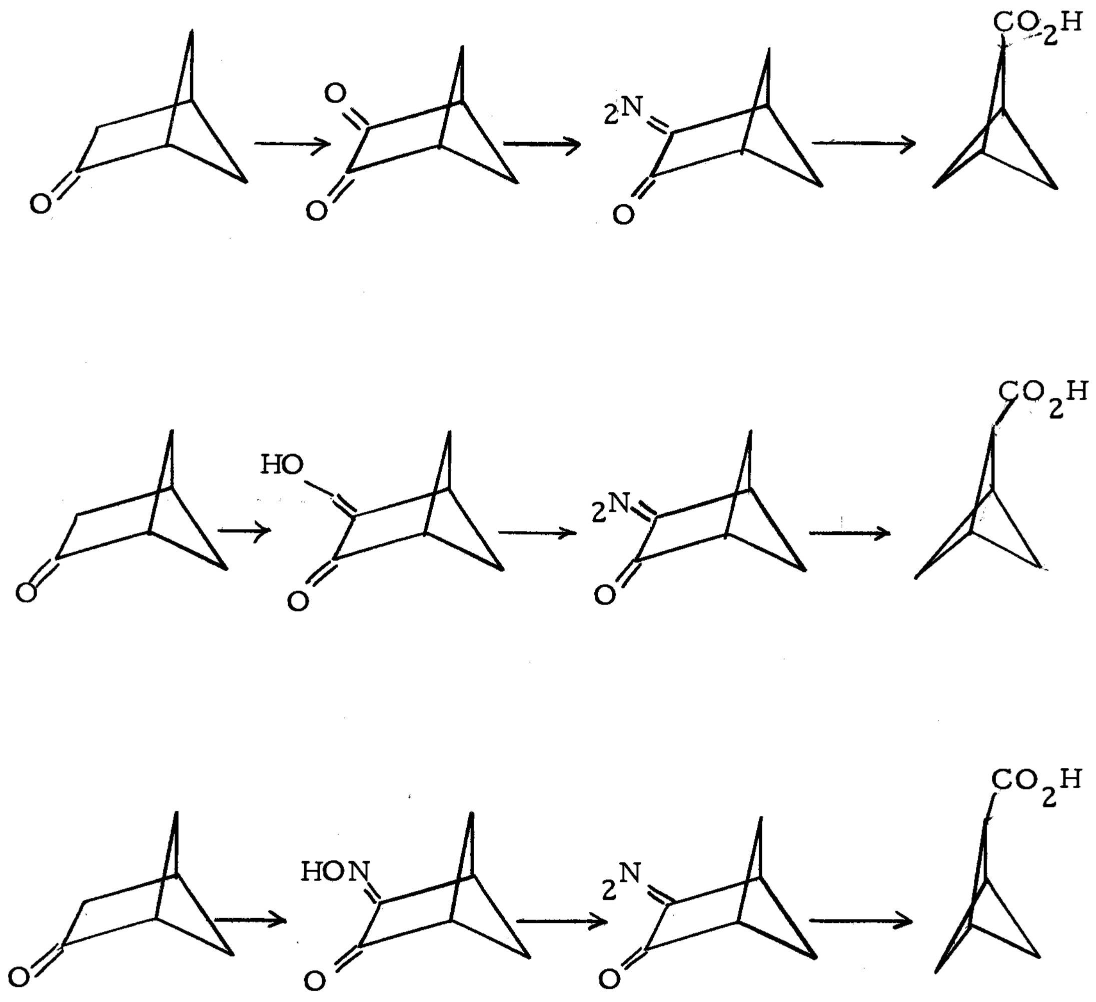
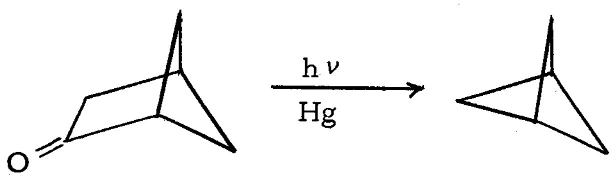


Figure 10. Synthetic routes to bicyclo(1. 1. 1)pentane-2-carboxylic acid.

As mentioned in the introduction, the parent hydrocarbon, 131 was synthesized by the photodecarbonylation of 66.



66

131

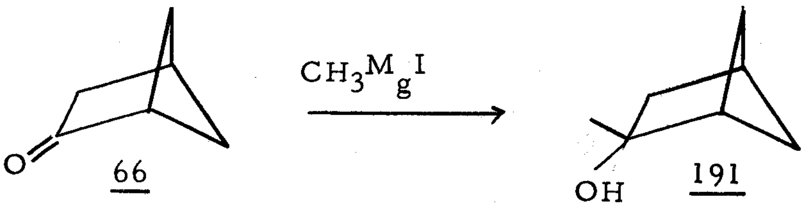
Chemistry of Bicyclo(2. 1. 1)hexan-2-one

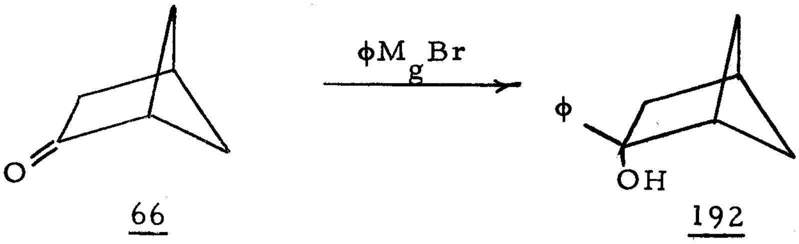
The chemistry of bicyclo(2. 1. 1)hexan-2-one is conveniently divided into two classifications, reactions at C-2 and reactions at C-3. Reactions at C-2 are in many ways similar to those of other bicyclic ketones. On the other hand, reactions at C-3 are greatly affected by internal strain. In general, reactions at C-3 of bicyclo(2. 1. 1)hexan-2-one were extremely more difficult than reactions at corresponding positions in other bicyclic ketones such as norcamphor.

Reactions at C-2

The reactions studied at C-2 of bicyclo(2. 1. 1)hexan-2-one consisted of nucleophilic additons to the carbonyl group. These reactions are rather facile in this system because conversion of an sp^2 carbon to an sp^3 carbon relieves some of the internal angular strain of the bicyclic ketone. Nucleophilic substitution reactions at the carbonyl also appeared to proceed with ease. Oxime and p-toluenesulfonylhydrazone formation occurred under mild conditions in good yields.

The nucleophilic additions of organometallics; such as Grignard reagents are well-known reactions of ketones. The reaction of methylmagnesium iodide with bicyclo(2. 1. 1)hexan-2-one gives high yields of 2-methylbicyclo(2. 1. 1)hexan-2-ol 191. Spectral and analytical data confirm the structural assignment. See Table 2 for the n. m. r. data. Similarly, phenylmagnesium bromide reacted with 66 to give 2-phenylbicyclo(2. 1. 1)hexan-2-ol 192. Again the spectral and analytical data are consistant with the assigned structure.





The reaction of 66 with lithium aluminum hydride has already been discussed in regard to the proof of structure of bicyclo(2. 1. 1)-hexan-2-one 66. The n. m. r. data for this compound and all other compounds discussed in this work is presented in Table 2. The rates of reduction of bicyclic ketones has been used as an indication of the amount of internal strain in a system (13). A comparison of the rates of sodium borohydride reduction of norcamphor and bicyclo(2. 1. 1)-hexan-2-one in isopropanol at 25° was made. The experimental data are plotted in Figure 11.

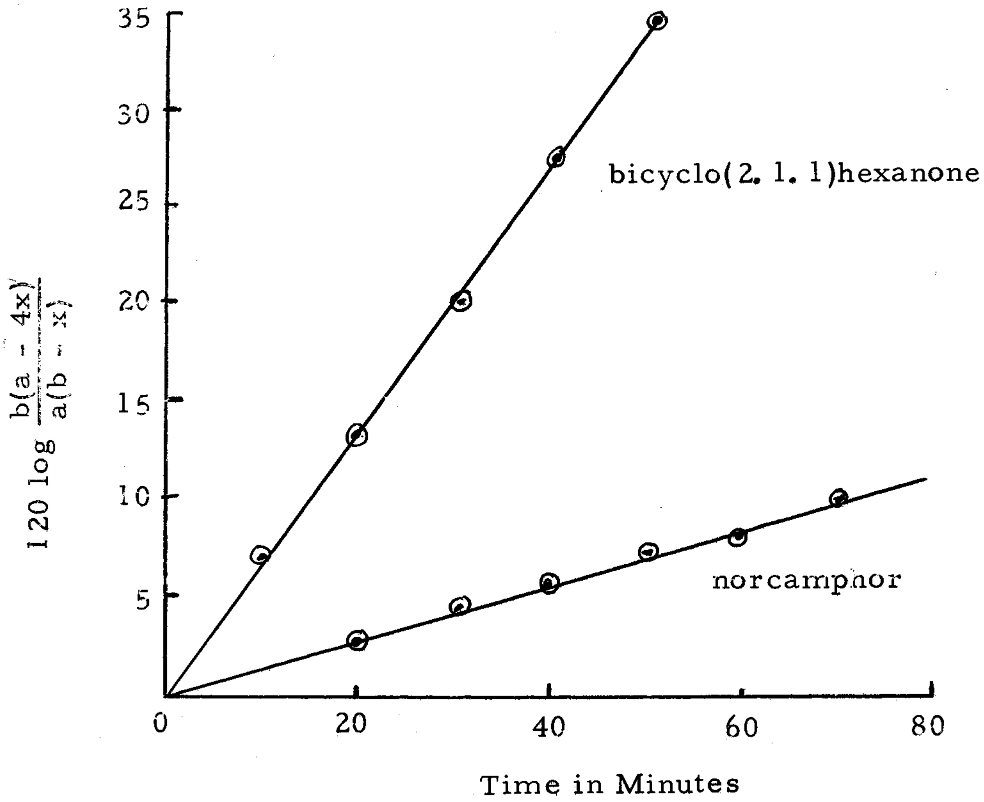
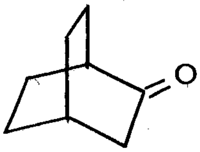
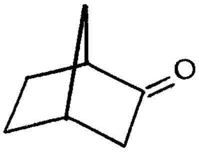
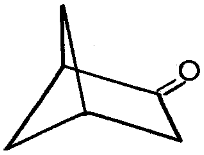
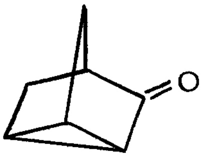


Figure 11. Rates of sodium borohydride reduction of bicyclic ketone.

The rate constant for the reduction of norcamphor is: $k_{NC} = 24.9 \times 10^{-4}$ l/mole-sec while that for bicyclo(2. 1. 1)hexan-2-one is: $k_{BC} = 108.9 \times 10^{-4}$ l/mole-sec. The relative rate obtained from this data, $k_{BC}/k_{NC} = 4.34$, shows that bicyclo(2. 1. 1)hexan-2-one is reduced 4. 34 times faster than norcamphor. This is an indication of the greater internal strain of the bicyclo(2. 1. 1)hexanone system over the bicyclo(2. 2. 1)heptanone system. A comparison with other bicyclic systems is shown in Table 4 (13).

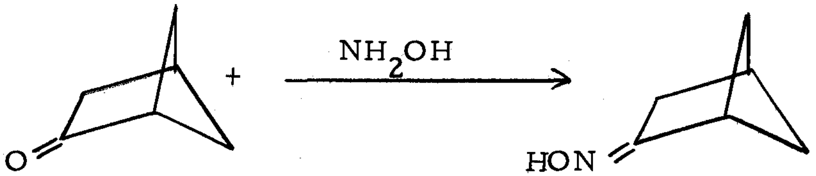
Table 4. Rates of sodium borohydride reductions of bicyclic ketones at 25°.

	k x 10^4 l/mole-sec	k_{rel}
	8.07	1.00
	24.0	2.97
	108.2	13.4
	642.0	79.4

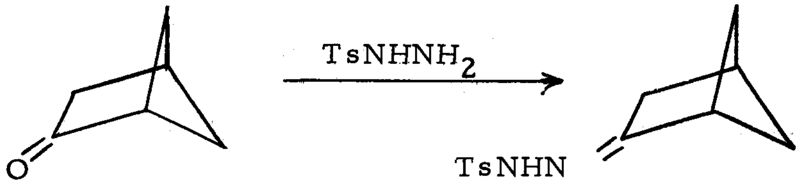
It might be noted that the carbonyl stretching frequencies for the compounds in Table 4 are, in order, 1731, 1751, 1764 and 1762 cm^{-1}. Thus, except for nortricyclanone, carbonyl frequency increases with the relative rate of reduction. Both are indications of the increase in strain on going from bicyclo(2.2.2)octanone to bicyclo(2.1.1)hexan-2-one.

As was mentioned earlier, bicyclo(2.1.1)hexan-2-one <u>66</u>

reacts with hydroxylamine to give a white crystalline solid. Similarly, 66 reacts with *p*-toluenesulfonylhydrazine to give the corresponding tosylhydrazone 194. Both solid derivatives, 193 and 194 exhibit spectral and analytical data with are consistant with the assigned structures. Further transformations at C-2 will be discussed



66 193



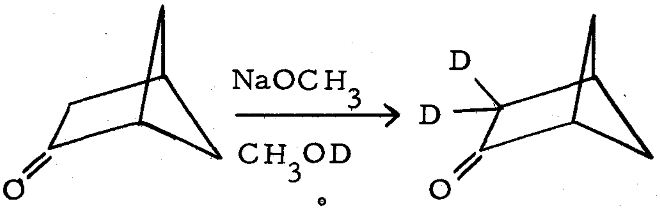
66 194

in relation to their application to the synthesis of bicyclo(2. 1. 1)-hexene.

Reactions at C-3

Removal of a proton at C-3 of bicyclo(2. 1. 1)hexan-2-one leads to the formation of a carbanion which may or may not be stabilized *via* delocalization of the negative charge to the carbonyl oxygen. Such stabilization would involve placing two sp^2 carbons in an already highly-strained ring system. It was found that reactions dependent on the formation of such an enolate anion are indeed very difficult to achieve.

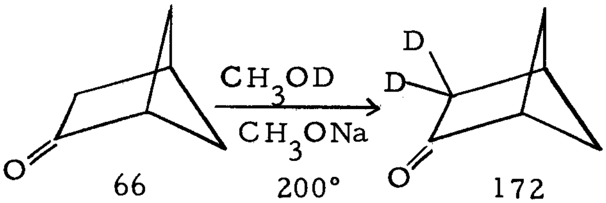
Treatment of bicyclo(2. 1. 1)hexan-2-one 66 with sodium methoxide in deuteriomethanol gave a quantitative yield of the di-deuterated compound 172 (46, 105). The n. m. r. spectrum of this



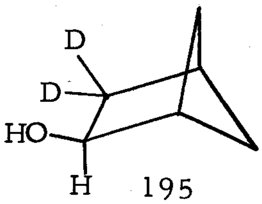
66 100° 172

compound is similar to that of 66 except the peak at 2.10 δ (2 H's) has disappeared. (see Figure 6). The exchange reaction can be carried out in a sealed tube at 100° or at atmospheric pressure.

An interesting reaction occurs when the above exchange is carried out in a sealed tube at 200°. An equimolar mixture of two products is formed. The first product was found to be identical with 172. The second product proved to be an alcohol, as determined by infrared analysis. The infrared spectrum of a solution of the solid alcohol, m. p. 83-84°, shows bands at 3610 and 3330 cm^{-1} due to the hydroxyl group. Bands at 2690 and 2490 cm^{-1} are assigned to oxygen-deuterium stretching. Carbon-deuterium stretching frequencies at 2120, 2200, and 2230 cm^{-1} are also present. The above alcohol was passed through a deactivated alumina column. The infrared spectrum of the solid collected shows that only a hydroxyl group was present. Comparison of the infrared spectra of bicyclo(2. 1. 1)hexan-2-ol and that of the product shows that, except for the carbon-deuterium stretching frequencies, the absorption bands are almost superimposable.. It appears that the deuterated alcohol is 3, 3-dideuteriobicyclo(2. 1. 1)hexan-2-ol 195. This alcohol apparently arises from a Meerwein-Ponndorf-Verley type reduction of the deuterated ketone 172. The n. m. r. spectrum of 195 shows that there is a proton at C-2. There did not appear to be any exchange at the homoenolic position under these conditions.



66 172



195

The kinetics of deuterium exchange on both norcamphor and bicyclo(2. 1. 1)hexan-2-one were carried out at 50°. The reactions were followed by integration of the n. m. r. spectra of samples withdrawn at given time intervals. Rate constants were obtained from plots of gram-atoms of deuterium incorporated versus time. The slope of the tangent of the resultant curves at time equal zero give $k_{NC} = 3.34 \times 10^{-3}$ g-at/mole-sec, for norcamphor, and $k_{BC} = 6.0 \times 10^{-4}$ g-at/mole-sec for bicyclo(2. 1. 1)hexan-2-one (see Figure 12). The relative rate, k_{NC}/k_{BC}, is equal to 5. 57. The rate of deuterium exchange for norcamphor is about six times faster than that for bicyclo(2. 1. 1)hexan-2-one. The carbanion at C-3 of norcamphor must be more easily formed than that at the C-3 position in bicyclo(2. 1. 1)hexan-2-one. This indicates, again, that any reaction which adds strain, such as enolate ion formation, is more difficult in the bicyclo(2. 1. 1)hexane system than in the bicyclo(2. 2. 1)-heptane system. As shown later, bicyclo(2. 1. 1)hexene formation was more difficult than bicyclo(2. 2. 1)hept-2-ene formation. Similarly, reactions involving the enolate anion or a C-3 carbanion are more difficult in bicyclohexanone than in bicycloheptanone.

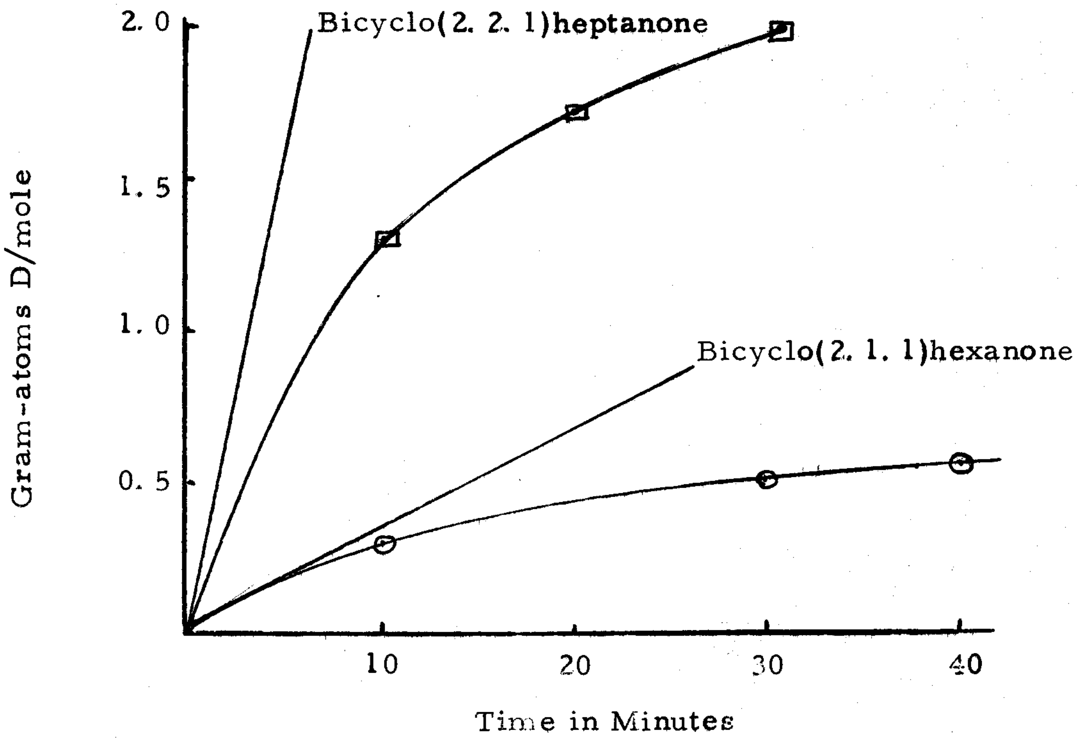
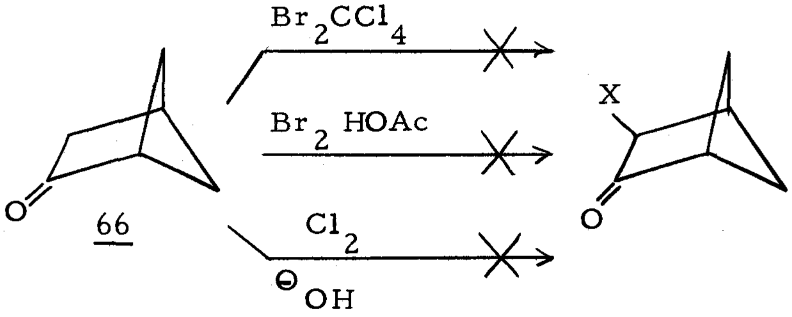
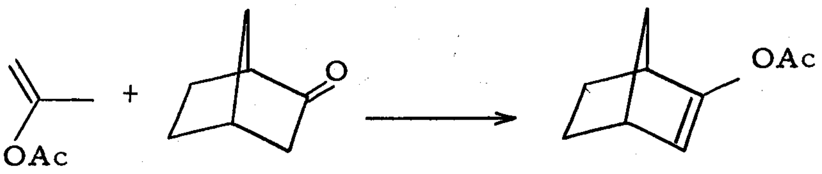


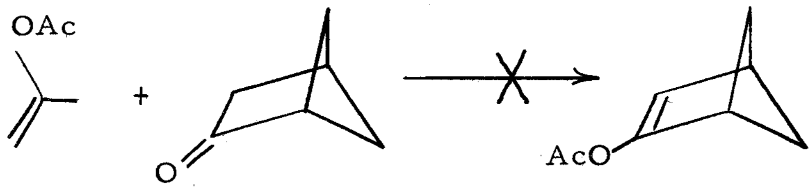
Figure 12. Rates of deuterium exchange for bicyclic ketones.

Under a variety of conditions, all of which achieved the bromination of norcamphor, no bromination of bicyclo(2. 1. 1)hexan-2-one was found to occur.

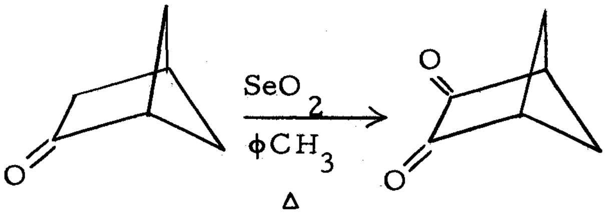


Similarly, the chlorination of 66 resulted only in the recovery of starting ketone. Enol acetylation of 66 also resulted in the complete recovery of starting ketone. Under similar conditions norbornanone was converted to the corresponding 2-acetoxybicyclo(2. 2. 1)hept-2-ene.

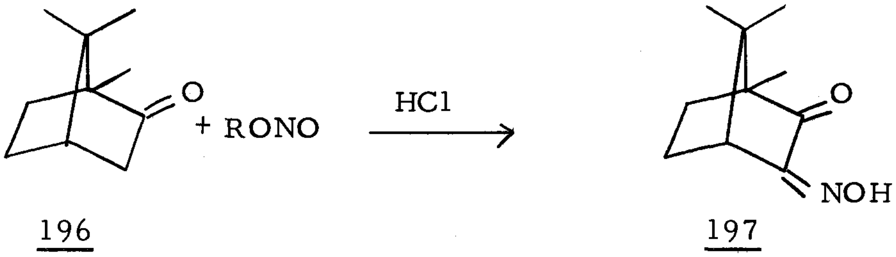




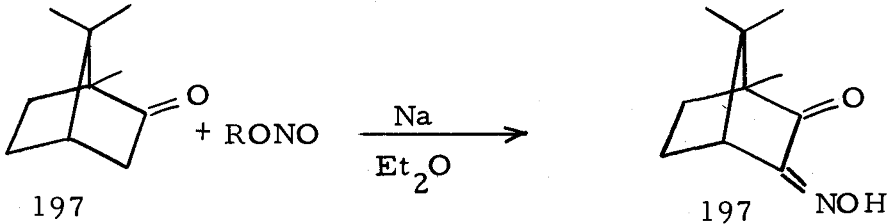
As mentioned in the section devoted to the utility of bicyclo(2.1.1)hexan-2-one, routes leading to the synthesis of bicyclo(1.1.1)pentane-2-carboxylic acid involve reactions at C-3. The first steps in the equations in Figure 10 have either failed or gone in very low yields. Oxidation of bicyclo(2.1.1)hexan-2-one with selenium dioxide in xylene or toluene was tried several times. In general, the procedures consisted of heating a solution of the ketone in an aromatic solvent in the presence of freshly sublimed selenium dioxide. During the course of the reaction water was removed. In all cases no product was isolated. A thick oily resin with an infrared absorption at 1750-1680 cm^{-1} was the only material recovered from the reactions. Similar reactions on the bicyclo(2.2.1)heptan-2-one system are known to proceed in reasonable yields (2, 68, 116).



The formation of α-oximoketones from ketones is usually achieved by the acid or base catalyzed attack of an alkyl nitrite at the alpha carbon (17, 18, 38). Both acid and base catalyzed reactions on camphor 196 were carried out with good results.

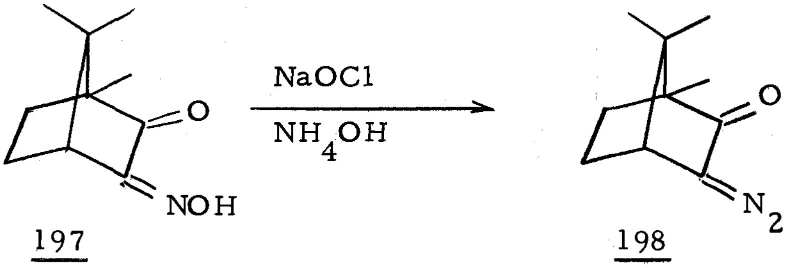


196 197



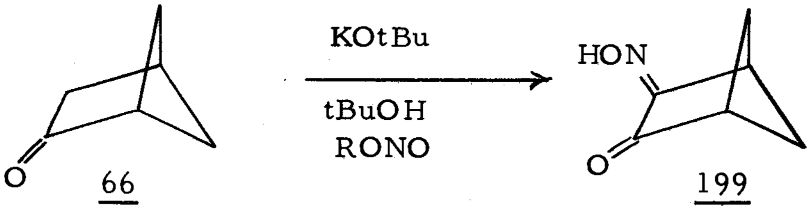
197 197

3-Diazocamphor 198 was obtained in about 30% overall yield from 196.

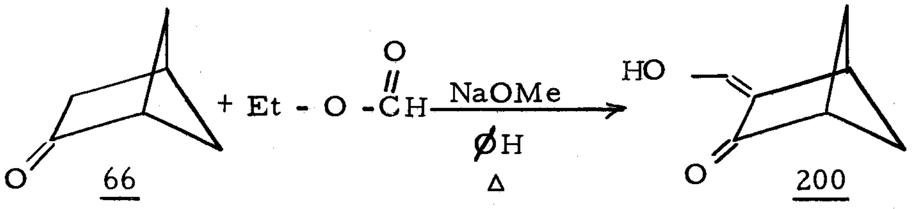


197 198

When bicyclo(2. 1. 1)hexan-2-one was treated in a like manner, no oximoketone was produced. Some encouraging results were obtained when bicyclo(2. 1. 1)hexan-2-one was reacted with a five-fold excess of potassium t-butoxide and an equimolar amount of amyl nitrite at 100° in a sealed tube. The infrared spectrum of the isolated product shows bands at 1550, 1640, 1720 and 3220 cm^{-1}. These data are consistent with an α-oximoketone structure. The oximoketone could not be purified without decomposition, however, and the structural assignment is at best tentative.



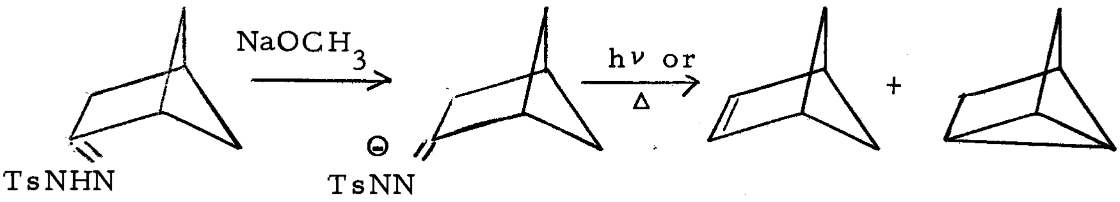
The last route to bicyclo(1.1.1)pentane-2-carboxylic acid involves the synthesis of 3-hydroxymethylenebicyclo(2.1.1)hexan-2-one 200. This compound was synthesized by a base-catalyzed nucleophilic attack of 66 on ethyl formate in benzene (40). A 25% yield of product which is believed to be 200 was obtained. Again purification proved difficult. The following spectral data leads one to the



belief that 200 is the product of the reaction. A maximum at 247 mμ (ε = 10,000) appears in the ultraviolet spectrum. The infrared spectrum consists of bands at 2940, 1725, 1615, 1178 and 860 cm^{-1}. The n.m.r. spectrum is more informative. It consists of multiplets at 1.00 - 2.20 δ, representing the C-5 and C-6 protons; a triplet at 2.41 δ, assigned to the bridgehead hydrogens; a doublet at 4.32 δ possibly due to the vinyl hydrogen; a broad singlet at 5. 05 δ due to the hydroxyl proton and a doublet at 7. 92 δ possibly due to the proton of the aldehyde form of the 3-hydroxymethylene group. On shaking with deuterium oxide the peak at 7. 92 δ collapsed to a singlet and the broad singlet at 5. 05 δ disappeared. A water peak appears at 4. 73 δ. Somewhat similar spectral data was obtained by Gibson and Erman (40) in their synthesis of 1-methyl-3-hydroxymethylenenorcamphor. Although great success toward the synthesis of bicyclo(1. 1. 1)pentane-2-carboxylic acid has not been achieved due to the difficulty in substitution reactions at C-3, it does appear that syntheses towards this end are possible.

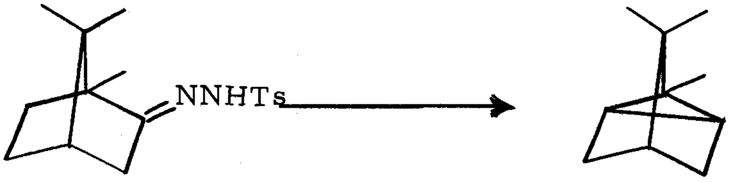
Attempted Synthesis of Tricyclo(2. 2. 0. $0^{2,6}$)hexane

In the introduction, an interest in tricyclo(2. 2. 0. $0^{2,6}$)hexane was expressed. This system is a bicyclo(2. 1. 1)hexane in which C-5 and C-6 are joined. A synthetic route which could have led to either bicyclo(2. 1. 1)hexene or tricyclo(2. 2. 0. $0^{2,6}$)hexane consists of the thermal or photochemical base-catalyzed decomposition of the tosylhydrazone 194.



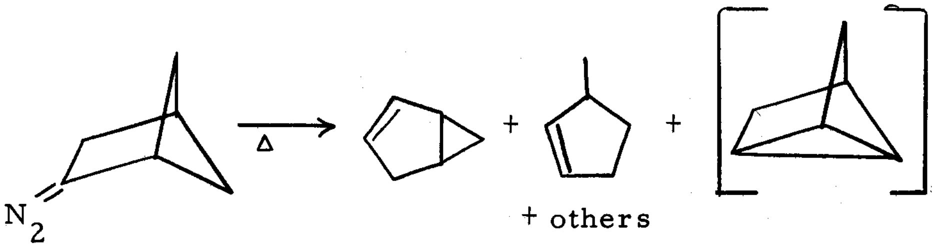
194 201 108 107

This reaction has been studied in the bicyclo(2.2.1)heptane series by Shapiro (93). The base-catalyzed thermal decomposition of camphor tosylhydrazone 127 leads to the tricyclene 128 as the sole



127 128

product under aprotic conditions. The thermal decomposition of 201 gave no bicyclo(2.1.1)hexene, but the existence of the tricyclic compound 107 is still an open question. Although this reaction will be fully discussed in the next section, the known products of the reaction are indicated below. The isolation of a product whose n.m.r. spectrum shows only multiplets at 2.4 - 2.7 δ and 1.65 δ seems to indicate that 107 may be present (57).



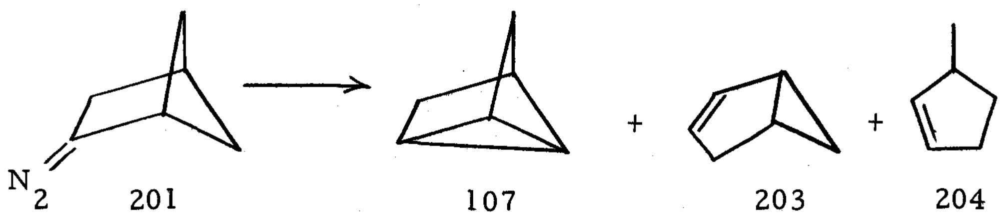
The photochemical decomposition of 201 gives a very low yield of volatiles. An infrared spectrum of the crude product showed the presence of 3-methylcyclopentene but none of the other two major thermal products was detected. It would seem that a more detailed investigation of the photochemical decomposition of 201 might lead to worthwhile results, but the low yield of volatile products would make such a study quite difficult.

Bicyclo(2. 1. 1)hexenes

Interest in bicyclo(2. 1. 1)hexenes was expressed in the introduction. This section is devoted to our efforts toward the synthesis of bicyclo(2. 1. 1)hex-2-ene. Four general approaches were investigated in this study. These include carbene reactions, dehydration of alcohols, pyrolysis of amine derivatives, and dehydrohalogenations. The results of these studies attest to the difficulty of synthesizing bicyclo(2. 1. 1)hexene under all but the mildest conditions.

Carbene Reactions

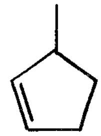
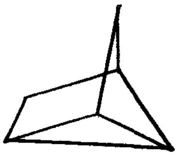
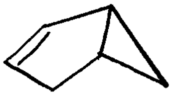
The carbene approach to bicyclo(2. 1. 1)hexene synthesis was briefly discussed in the last section. There we were mainly concerned with the formation of tricyclo(2. 2. 0. $0^{2,6}$)hexane 107. The thermal decomposition of the sodium salt of bicyclo(2. 1. 1)hexan-2-one tosylhydrazone 201 led to the formation of at least five products, three of which were isolated. There is still some question whether the tricyclic compound 107 is really present in the mixture. Bicyclo(2. 1. 1)hex-2-ene 203, a known compound, was identified by comparison of the spectral data with that published in the literature



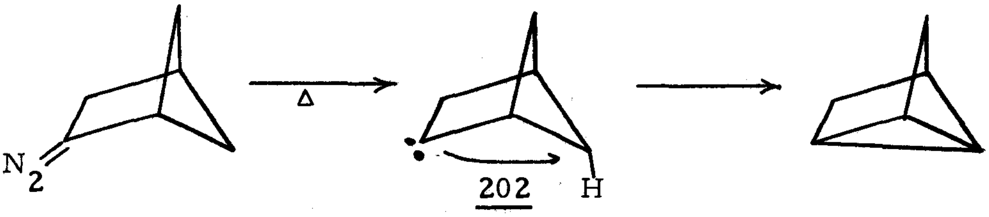
201 107 203 204

(39). Tricyclo(2. 2. 0. $0^{2, 6}$)hexane was tentatively assigned as the structure of 107 on the basis of a weak n. m. r. spectrum which shows multiplets at 1. 65 δ and 2. 4 - 2. 7 δ. This is somewhat consistent with the published n. m. r. data (57). The third component of the reaction mixture, 3-methylcyclopentene, was identified by a combination of mass spectral, n. m. r. and infrared data. The mass spectrum of 204 shows peaks at m/e equal 67 (b), 39, 41, 27, 82 (p), and 81, in order of their intensities. This is in agreement with published mass spectral data for 3-methylcyclopentene (62). The n. m. r. spectrum shows a doublet at 1. 05 δ (3 H's), due to a methyl attached to a methine carbon; multiplets at 1. 70 - 2. 20 δ and 2. 25 - 2. 48 δ (5 H's), assigned to the methine proton and four methylene protons; and a singlet at 5. 58 δ (2 H's) assigned to vinyl protons. The infrared spectrum is also consistent with 3-methylcyclopentene 204. The yields of 204, 107, and 203 were 31. 7, 15. 1, and 51. 0%, respectively. The composition of the mixture, however, is temperature dependent. The thermal stability of these compounds was tested by injection of a sample of the mixture into the injector port of a 15 ft diisodecylphthalate glc column maintained at 28°. The injector temperature was varied from 140 - 325°. Table 5 below shows the effect of temperature on the composition of the mixture.

Table 5. Thermal stability of 107.

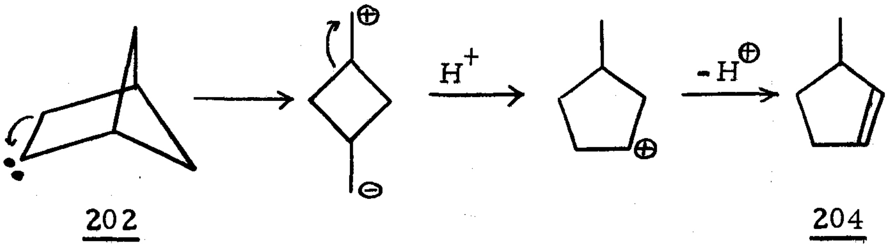
Compound	% Composition at 140°	% Composition at 325°
	31.7	32.3
	15.1	1.5
	51.0	64.6

The amount of 3-methylcyclopentene remains constant, while bicyclo-(3.1.0)hex-2-ene is built up at the expense of what is believed to be tricyclo(2.2.0.$0^{2,6}$)hexane. From this one can state that 203 is not derived from a carbene species, while both 204 and 107 may be. The tricyclic compound 107 and 204 can be arrived at *via* the schemes given below. The tricyclic product arises from the insertion of the carbene into the C-5 hydrogen bond. This, of course, is one of the expected reactions of such a carbene.



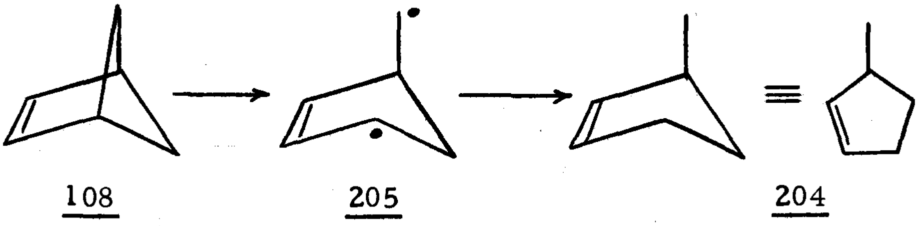
202

A ring opening reaction of the carbene 202 can lead to 3-methylcyclopentene 204.



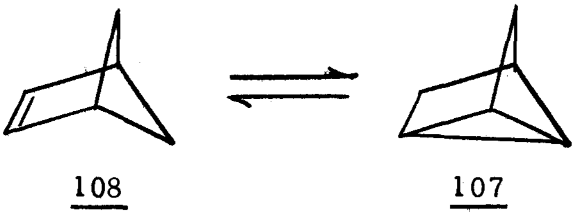
202 204

An alternate route to 204 would involve bicyclo(2. 1. 1)hexene as an intermediate. We shall see why this reaction path is unlikely.



108 205 204

Bicyclo(3. 1. 0)hex-2-ene cannot arise directly from tricyclo-(2. 2. 0. $0^{2,6}$)hexane. However, pathways from bicyclo(2. 1. 1)hexene are possible. A method of interconversion of 108 to 107 must be available.



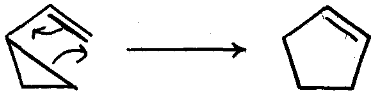
108 107

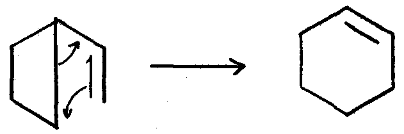
A similar equilibrium is known to exist between nortricyclene 106 and norbornene 105 (92). In this case, however, a catalyst is

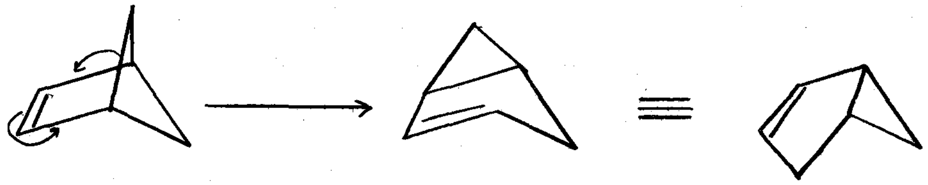
105 106

necessary for the equilibrium to occur. The equilibrium between 105 and 106 is in favor of the tricyclic system. This might also be expected for the bicyclo(2. 1. 1)hexane system. Heat displaces the equilibrium to the right. As soon as bicyclo(2. 1. 1)hexene is formed, it rearranges to 107. No build up of 108 is observed.

Bicyclo(2. 1. 1)hexene can be considered a vinylcyclobutane derivative in which both ends of the vinyl group are attached to the cyclobutane ring. Thermal rearrangements such as indicated below have precedent in rearrangements of vinylcyclopropanes and vinylcyclobutanes (36, 81).







108

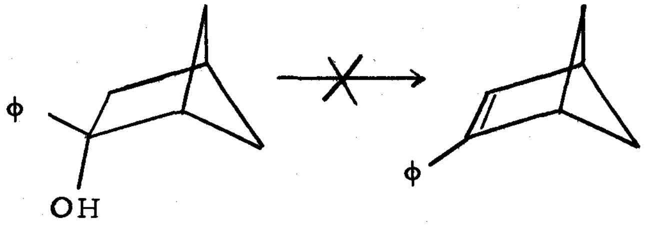
203

Since the reactions of bicyclo(2. 1. 1)hexene 108 are thermal processes, the concentrations of species derived from it should vary with temperature. Such is the case with bicyclo(2. 1. 0)hex-2-ene 203 formation. This is not true for 3-methylcyclopentene 204. Thus bicyclo(2. 1. 1)hexene is probably not the precursor to 204.

In summary, the only products derived directly from the carbene are tricyclo(2. 2. 0. $0^{2,6}$)hexane and 3-methylcyclopentene. Possibly bicyclo(2. 1. 1)hexene was also formed initially but quickly rearranged to bicyclo(3. 1. 0)hexene. Recent work has shown that bicyclo(2. 1. 1)hexene does indeed rearrange to bicyclo(3. 1. 0)hex-2-ene at 180° (11). Ideally experimental conditions should be chosen so that no thermal isomerizations are possible. This was the object of the photolysis of 201. Only very small yields (less than 10%) of volatile material were obtained *via* this method, however. 3-Methylcyclopentene was the only product detected in the reaction mixture. These results, however, are not to be considered conclusive. A more detailed investigation into the photolysis reaction is required.

Alcohol Dehydration

Dehydration of alcohols is a standard route to olefins. These reactions vary from simple dehydrations to pyrolytic elimination of the corresponding acetates, ethyl carbonates, and methyl xanthate esters. When these reactions were applied to 5-substituted bicyclo(2. 1. 1)hexan-2-ol, no formation of olefin was observed (68). This suggested that similar reactions on the parent bicyclo(2. 1. 1)hexan-2-ol might meet with a similar fate. Incorporation of a phenyl ring into the system should, however, aid in the formation of a now conjugated olefin. The required compound, 2-phenylbicyclo(2. 1. 1)-hexan-2-ol 192 was readily available from the reaction of phenylmagnesium bromide with bicyclo(2. 1. 1)hex-2-one. It was decided



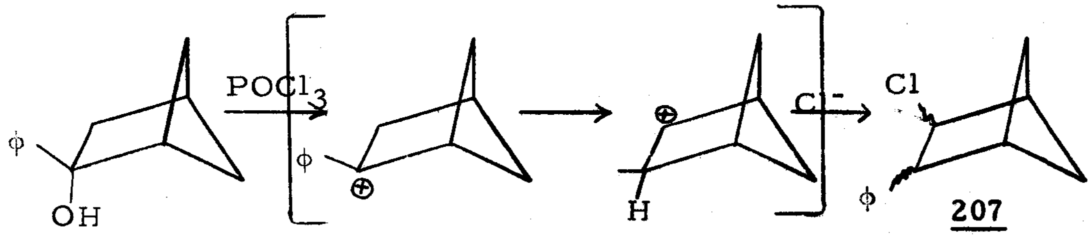
192 206

that simple dehydrations of this tertiary and benzylic alcohol might lead to the desired product 2-phenylbicyclo(2. 1. 1)hex-2-ene <u>206</u>.

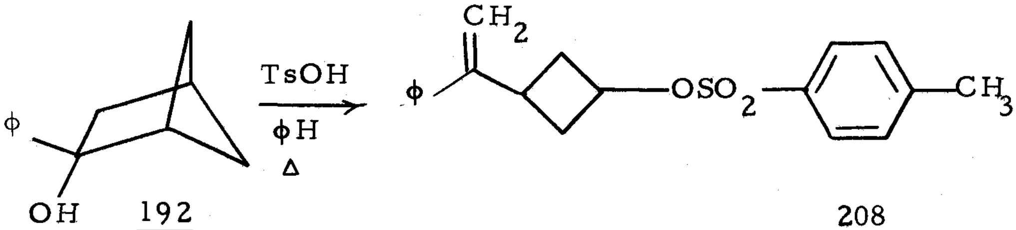
Treatment of the alcohol <u>192</u> with phosphorus oxychloride in pyridine at room temperature did not result in the formation of the olefin <u>206</u>. A gas-liquid chromatograph of the crude product shows that two components were present, A in 54% yield, and B in 36% yield. These two compounds were isolated by collection from a ten foot DEGS column at 190°. Both compounds analyzed correctly for $C_{12}H_{13}Cl$. Obviously a substitution reaction had occurred. The infrared spectra of both A and B are very similar but give no clue as to their structures except that they both contain chlorine and both possess a phenyl ring.

The n. m. r. spectrum of A is most helpful in assigning a structure to the major product. Peaks at 1. 50 - 2. 20 δ (a multiplet, 5 H's) and 2. 15 δ (triplet, 2 H's) are typical of the bicyclo(2. 1. 1)-hexane system. The presence of the phenyl group is indicated by a singlet at 7. 18 δ (5 H's). The fifth proton in the broad multiplet can be assigned to a benzylic proton. Since both bridgehead positions are occupied by protons (2. 15 δ), the chlorine present in the molecule must be attached to a carbon bearing a hydrogen. The remaining doublet at 4. 33 δ (1 H) is attributed to this hydrogen. N. m. r. spectra of 2-bromo- (Table 2), 2-chloro, and 2, 3-dichlorobicyclo-(2. 1. 1)hexanes (103) support these assignments. On the basis of these data one may assign 2-chloro-3-phenylbicyclo(2. 1. 1)hexane 207 as the structure for A.

The structural assignment for component B is not complete. From the n. m. r. data on this compound, it seems likely that this is also a chlorobicyclo(2. 1. 1)hexane. Ring opening rearrangements are, however, possible.



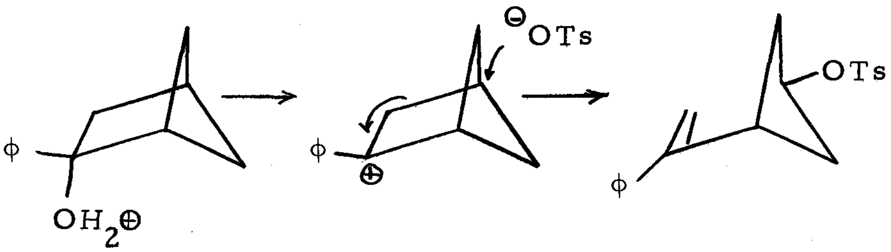
When the p-toluenesulfonic acid catalyzed dehydration of 2-phenylbicyclo(2. 1. 1)hexan-2-ol 192 was attempted, an almost quantitative yield of a solid, m. p. 114-115, was obtained. The infrared spectrum of this compound indicates the presence of a methylene group (890 cm^{-1}). Two maxima in the ultraviolet spectrum, 222 mμ (ϵ = 15, 000) and 257 mμ (ϵ = 7, 000), suggest that this methylene is conjugated to a phenyl ring. Elemental analysis indicates the addition of a tosylate group to 192. The n. m. r. spectrum of this p-toluenesulfonate ester shows a complex multiplet at 6. 9 - 7. 6 δ (11 H's), assigned to nine aromatic protons and two vinyl protons. It is unusual that vinyl protons would appear at such low field. The signal from the vinyl protons of 1-methyl-1-phenylethylene appear at 5.02 and 5.28 δ. Perhaps the vinyl protons in the tosylate ester are somehow deshielded by the toluene aromatic ring. A doublet of doublets at 4.9 δ (1 H) is assigned to the hydrogen on the carbon bearing a tosyl group. The aromatic methyl group appears at 2.48 δ (3 H) and the remainder of the hydrogens appear as a broad multiplet from 1.3 to 2.6 δ. These data are in agreement with the p-toluenesulfonate ester 208.



192

208

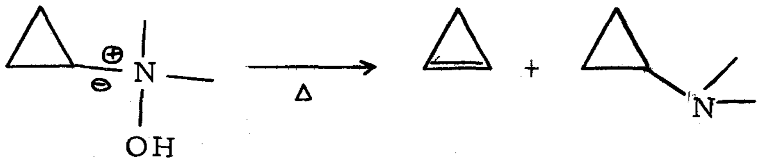
A possible mechanism for the formation of 208 is shown below.



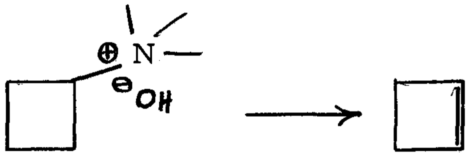
Amine Derivative Reactions

Among the synthetic routes from ketones to olefins, the pyrolysis of amine oxides and quaternary ammonium hydroxides are the most attractive. By such methods various strained olefins have been obtained, some of these are indicated below.

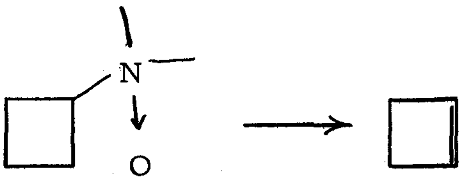
Ref.



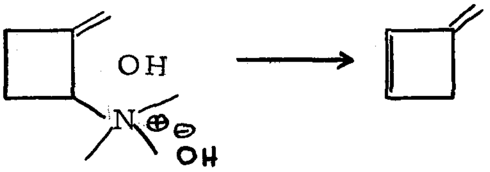
(91)



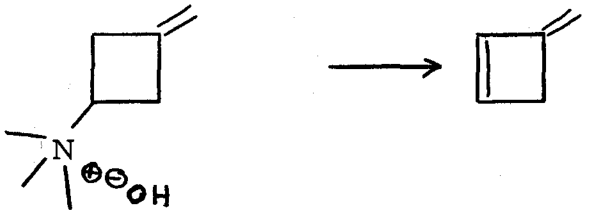
(119)



(85)



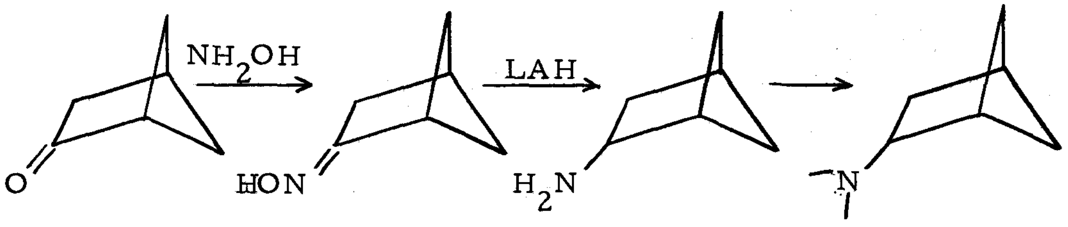
(3)



(43)

Cope and co-workers have made a detailed study of the amine oxide pyrolysis and Hofmann elimination reactions of various bicyclo(2. 2. 1)hept-2-ylamine and 5-aminobicyclo(2. 2. 1)hept-2-ene derivatives (23). The results of this study are summarized in Table 6. In general, the Hofmann reaction always gave the greater yield of olefin. A high preference for the elimination of the *exo*-amine derivative is common to both types of elimination reactions. The smaller yields of olefin from the *endo* isomers can be attributed to the fact that the preferred coplanar orientation in the transition state of these elimination reactions cannot be readily obtained. The *endo* substituents are subject the steric interaction of the two-membered bridge. On the other hand, the *exo* isomers are subjected to the lesser steric requirements of the one-membered bridge. The lower yields of norbornadiene compared to norbornene can be ascribed to the greater strain of the bicyclo(2. 2. 1)hepta-2, 5-diene system.

In general, the route from a ketone to amine derivatives follows the scheme illustrated below for the bicyclo(2. 1. 1)hexyl system.



66 193 209 210

Table 6. Elimination reactions of bicyclo(2.2.1)heptylamine derivatives.

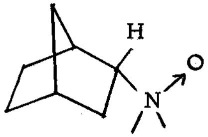
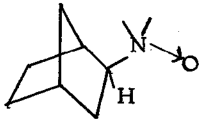
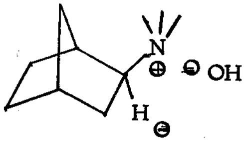
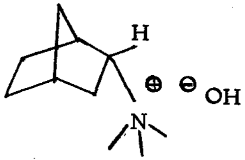
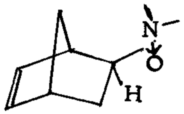
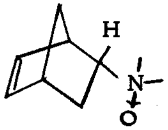
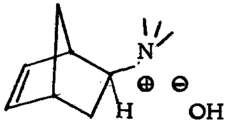
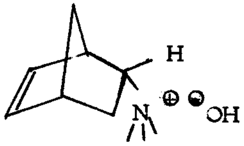
Compound	% Yield of Olefin	% Recovery of Amine*	exo/endo
	2.9	25	22.4
	65.0	4	
	77.0	1	22.0
	3.5	53	

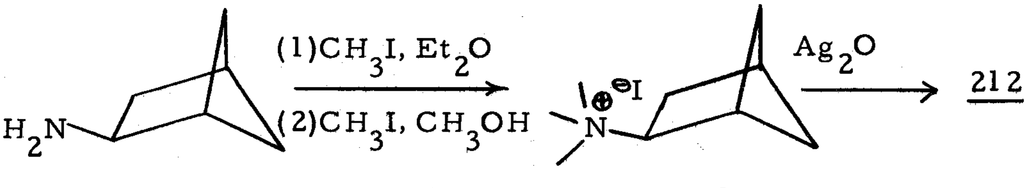
Table 6. (continued)

Compound	% Yield of Olefin	% Recovery of Amine*	exo/ endo
	32. 0	13	22. 9
	1. 4	28	
	58. 0	12	18. 7
	3. 3	51	

---

*Dimethylbicyclo(2. 2. 1)heptylamines.

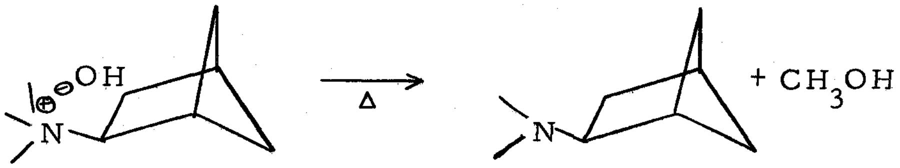
Trimethylbicyclo(2. 1. 1)hex-2-ylammonium iodide 213 was prepared from bicyclo(2. 1. 1)hex-2-ylamine in the usual manner. This involves either methylation of the isolated dimethylamine 210 with methyl iodide, or the exhaustive methylation of the simple amine 209 with methyl iodide. The intermediate quaternary ammonium iodide 213 was converted to the corresponding hydroxide 212 by treatment with silver oxide in methanol.



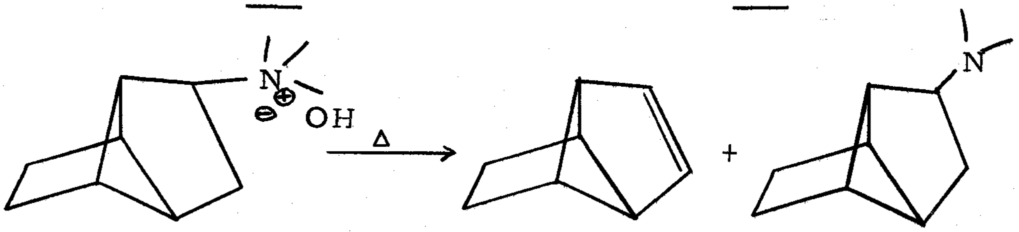
209

213

Pyrolysis of the dried quaternary ammonium hydroxide 212 gave only two products, neither of which was the desired olefin. The first product, methanol, was identified by comparison of retention times on a glc and comparison of infrared spectra. The second product also proved to be a known compound. Infrared and glc comparisons show that this product is N, N-dimethylbicyclo(2. 1. 1)hex-2-ylamine 210. It is apparent that, as is the case with all E_2 elimination reactions, there was competition with the S_N2 reaction. If the elimination pathway is of much higher energy than the substitution pathway, the latter predominates. This is evidently true here. A similar high ratio of substitution to elimination was also observed by Meinwald and Kaplan in the pyrolysis of 70 (73).

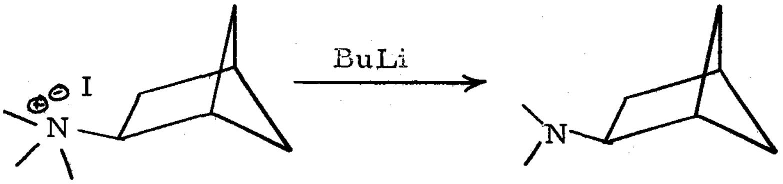


212 210



70 71 214

An E_2 elimination reaction similar to the Hofmann reaction but carried out under milder conditions is the reaction of the quaternary ammonium iodide 213 with butyllithium. This reaction was run at room temperature in ether solvent. The only product isolated from this reaction was again the dimethylbicyclohexylamine 210.

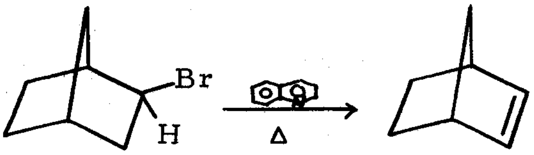


213 210

It should be stated that all the reactions of amine derivatives discussed in this section were first carried out on model compounds. The interconversions of amine derivatives were first tried on both the bicyclo(2. 2. 1)heptyl and cyclohexyl systems. High yields of olefins were obtained from these model elimination reactions. Our work, and that of others (23, 73), indicates that all the above elimination reactions will work on bicyclic systems which are less strained than the bicyclo(2. 1. 1)hexyl system. In the next section, we shall see that when the substitution pathway is blocked, elimination, even in such a highly strained system as ours, is possible.

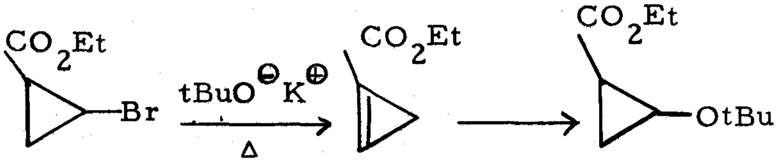
Dehydrohalogenation

Dehydrohalogenation routes to strained ring olefins have not been as common a method of synthesis as elimination reactions of corresponding amine derivatives. However, some of the earliest syntheses of strained bicyclic olefins have involved this method. Both exo-2-bromonorcamphor 215 and exo-2-chloronorcamphor yield bicyclo(2. 2. 1)hept-2-ene 105 on heating with quinoline (1, 50).

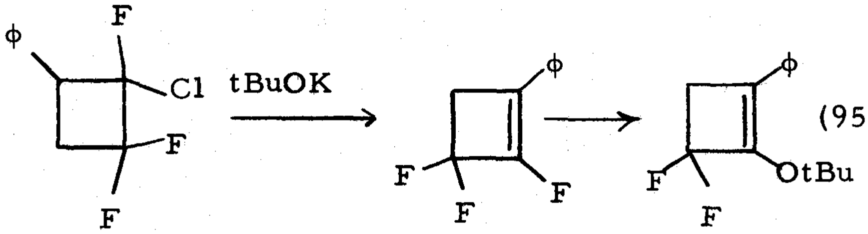


215 105

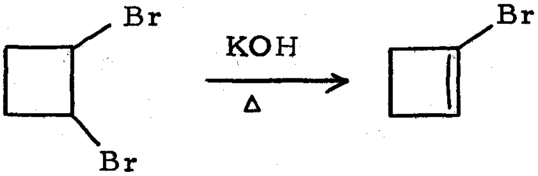
More recent mechanistic studies on this reaction have made use of bases such as potassium t-hexoxide and solvents such as 3-methyl-3-pentanol (52). Dimethylsulfoxide has also come into use as a solvent since it allows for much milder reaction conditions, thus permitting the synthesis of thermally labile olefins. Some other examples of


CO$_2$Et
Br
tBuO$^{\ominus}$K$^{\oplus}$
Δ
CO$_2$Et
CO$_2$Et
OtBu

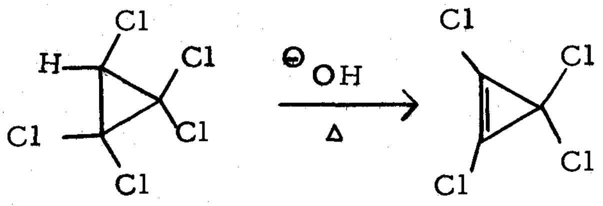
(112)


φ
F
Cl
F
F
tBuOK
φ
F
F
F
φ
F
F
OtBu

(95)


Br
Br
KOH
Δ
Br

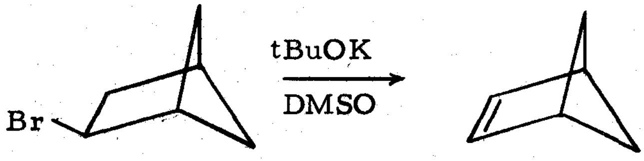
(4)


H
Cl
Cl
Cl
Cl
Cl
$^{\ominus}$OH
Δ
Cl
Cl
Cl
Cl

(106)

olefin syntheses involving the use of dehydrohalogenation procedures are listed above.

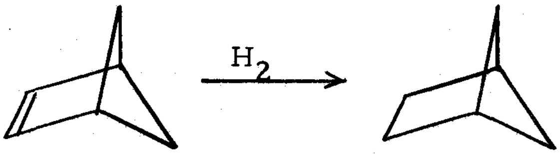
Treatment of 2-bromobicyclo(2. 1. 1)hexane 216 with a six molar excess of potassium t-butoxide in dimethylsulfoxide at 50°, led to a 25% yield of bicyclo(2. 1. 1)hex-2-ene 108.



216 108

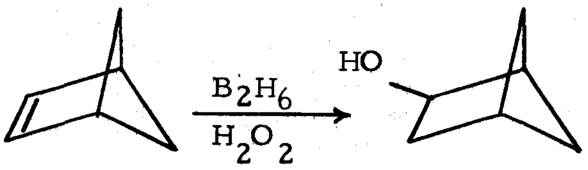
The infrared spectrum of this clear liquid, b. p. 60 - 62°, n_D = 1. 4376, exhibits bands at 662 and 1535 cm^{-1} attributed to vinyl hydrogen and carbon-carbon double bond absorptions, respectively. Other bands are present at 833, 1186, 1234, 1294, and 1425 cm^{-1}. The ultraviolet spectrum of a pentane solution of 108 shows a broad band at λ_{max} = 217 mμ (ϵ = 1115). The n. m. r. spectrum of a carbon tetrachloride solution of 108 shows a multiplet at 6. 62 δ (2H) assigned to the vinyl protons; an unresolved singlet at 2. 38 δ (4 H), due to the exo C-5 and C-6 hydrogens and the bridgehead hydrogens; and an unresolved doublet at 2. 10 δ (2 H) assigned to the endo C-5 and C-6 protons. As this thesis was being written, Meinwald and Uno (79) published a report of the synthesis of 108 via treatment of the p-toluenesulfonylhydrazone 194 with methyllithium at room temperature. Both sets of data are in agreement with each other and are consistent with the structure 108.

The study of the chemistry of bicyclo(2. 1. 1)hexene is still in its preliminary stages but some results have been obtained. The catalytic hydrogenation of 108 led to the known hydrocarbon bicyclo-(2. 1. 1)hexane 3 (11). The n. m. r. spectrum is identical to one reported by Wiberg (117). Competitive hydroboration reactions between equimolar 108 and cyclohexene gave a product ratio of at least 10:1 bicyclo(2. 1. 1)hexan-2-ol to cyclohexanol (11), indicating the greater reactivity of the strained olefin. Bicyclo(2. 1. 1)hex-2-ene was also found to rapidly react with bromine to give what appears to be a mixture of cis and trans-dibromide 217. The n. m. r. spectrum of this mixture shows a broad doublet at 4.5δ(2 H), assigned to the hydrogens on the carbon bearing bromine; sharp multiplets at 1.6 - 2.2δ(4 H), due to the C-5 and C-6 protons (see Figure 13). No rearrangement products such as 2, 5-dibromobicyclo(2. 2. 0)hexane



108

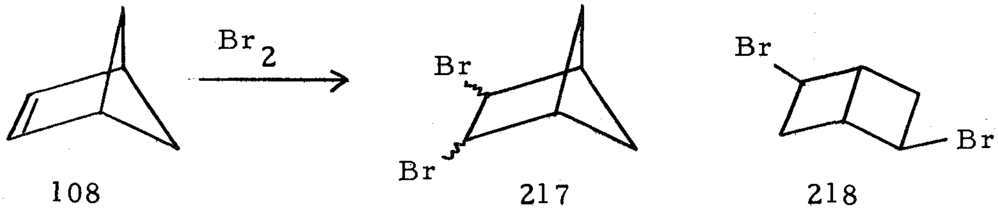
3



108

173

218 was detected.



108 217 218

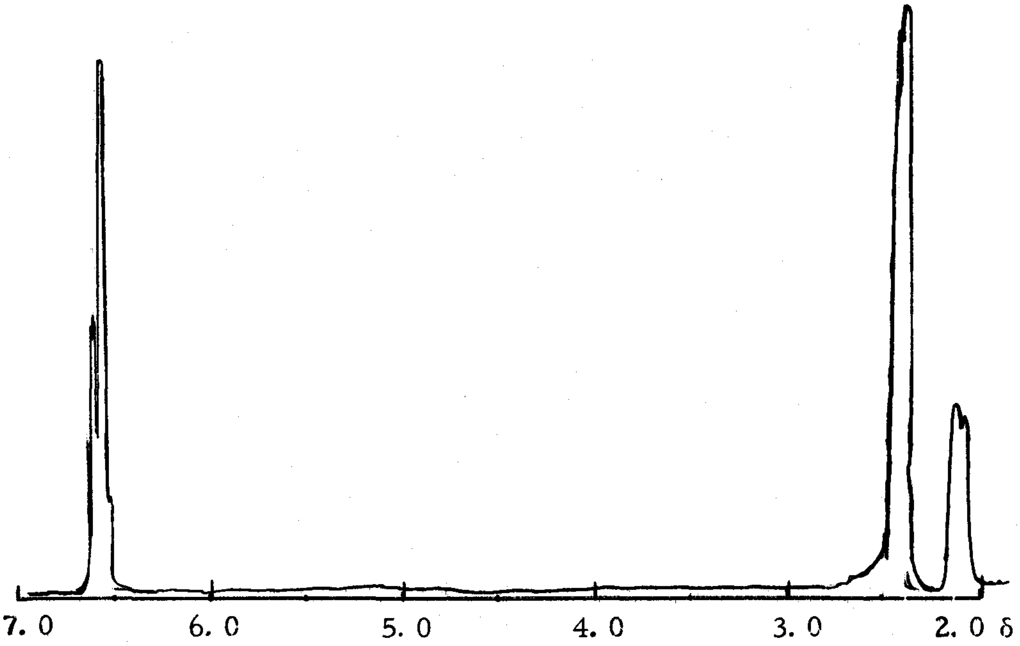


Figure 13. The n. m. r. spectrum of bicyclo(2. 1. 1)hex-2-ene.

Since direct comparison between strained olefins on the basis of chemistry cannot be made at this time, a comparison of spectral data must suffice. In the tables below are compiled pertinent spectral data for some typical strained bicyclic olefins.

Table 7. Selected infrared absorptions of strained olefins.

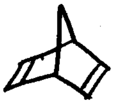
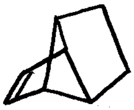
Compound	ν cm^{-1} C = C-H	ν cm^{-1} C = C	Ref.
	715	1568	(92)
	653, 730	1540	
	680	1555	(73)
	662	1535	

Table 8. Vinyl proton n. m. r. chemical shifts of strained olefins (73).

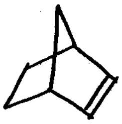
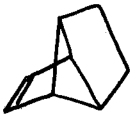
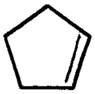
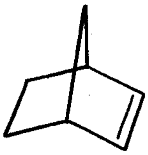
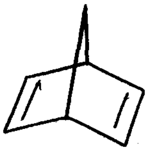
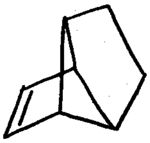
Compound	δ ppm	$J_{H-C=C-H}$ cps
	5.96	6.0
	6.65	5.2
	6.07	5.1
	6.62	5.0

Table 9. Olefinic $^{13}C-H$ coupling constants of strained olefins (73).

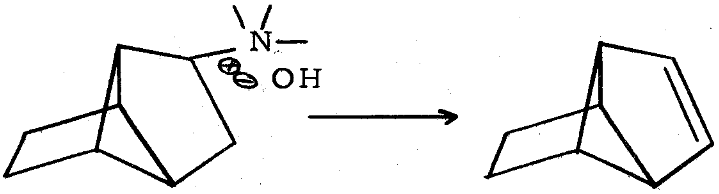
Compound	$J_{^{13}C-H}$ cps	$J_{H-C=C-H}$ cps
	160.5	5.8
	170.0	----
	156.8	11.4
	165.5	6.0
	172.5	5.2
	167 ± 1	5.1
	177 ± 2*	5.0
	220 (54)	----

---

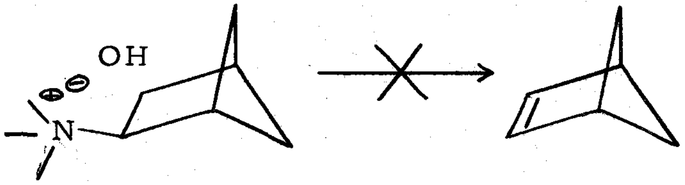
*Recorded on a neat sample on an HR-60 with the assistance of Prof. Robert Fahey, Univ. of Calif., San Diego.

In all the data presented above, definite trends can be seen. There seems to be a decrease in the infrared carbon-carbon double bond stretching frequency with increase in strain of the bicyclic system. Similarly, the chemical shift of vinyl protons also moves to lower fields as the olefin becomes more strained. The best correlation between strain and spectral properties is that indicated in Table 9. Here are given the carbon-13 coupling constants for vinyl protons of typical olefins. It has been found that the magnitudes of these coupling constants vary regularly with the value of the internal C-C-C angle (54), resulting in increasing "s" character to the C-H bond. The coupling constant $J_{^{13}C-H}$ can also be expressed in terms of bond order, i. e., J = 125 cps for sp^3 and J = 250 cps for sp. From Table 9, it can be seen that except for 2, 2-dimethylcyclopropene, bicyclo(2. 1. 1)hex-2-ene vinyl carbon-hydrogen bonds have the most "s" character and the smallest internal C-C-C angles.

From our point of view the most interesting comparison can be made between bicyclo(2. 1. 1)hexene <u>108</u> and tricyclo(3. 3. 0. $0^{2,6}$)-oct-3-ene <u>71</u>. Spectral data all seems to indicate that <u>108</u> is more strained than <u>71</u>. One would predict that reactions which increase strain would be more difficult to achieve for <u>108</u> than for <u>71</u>. As was discussed previously, this is the case. Specifically, the Hofmann elimination reaction of <u>70</u> to <u>71</u> proceeded in 30% yield, while the same reaction failed to occur with the corresponding bicyclo(2. 1. 1)hexane quaternary ammonium hydroxide.

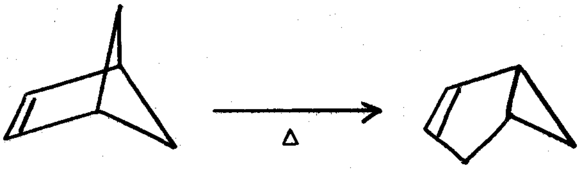


70 71



The n. m. r. data in Table 9 are in agreement with data shown in Table 3 which lists carbonyl frequencies for various bicyclo(2. 1. 1)hexanes. The frequency for tricyclo(3. 3. 0. $0^{2,6}$)octan-3-one (1758 cm^{-1}) is lower than that for bicyclo(2. 1. 1)hexan-2-one (1764 cm^{-1}). This again indicates that the tricyclic system is less strained than the bicyclo(2. 1. 1)hexane system.

Finally, it is of interest to note that the possible rearrangement of 108 to 203 is a reality. When a sample of 108 was heated in a



108 203

sealed tube at 180° for 25 minutes, the infrared spectrum and gas chromatogram of the product indicated that greater than 80% conversion to 203 had occurred (11). Preliminary electrophilic addition studies look equally promising and it would appear that the chemistry of 108 will more than justify the great efforts expended in its synthesis. In this light, it is important to note that the dehydrobromination route developed in this thesis allows isolation of 108 by distillation, a presumably more convenient route than preparative gas chromatography employed by Meinwald and Uno (79).

EXPERIMENTAL

All melting points were recorded on a Büchi melting point apparatus and are uncorrected. Proton n. m. r. spectra were run in carbon tetrachloride or deuterochloroform and are reported as parts per million from the internal standard tetramethylsilane. Infrared absorption spectra were determined using a Beckman IR-8 spectrophotometer. The gas chromatograms were taken on the Aerograph A-90-P using helium as the carrier gas. Type of column and temperature setting are specified in each case.

1, 5-Hexadien-3-ol 171

A solution of five grams of allyl bromide and a few crystals of iodine in 600 mℓ of dry ether was added to 141 g (5. 8 g-at) of magnesium turnings in a flame-dried, nitrogen-flushed 5-ℓ three-necked flask. After the reaction was initiated, a solution of the remainder of the 605 g (5. 0 moles) of allyl bromide, 600 g, and 224. 0 g (4. 0 moles) of freshly distilled acrolein in 1500 mℓ of dry ether was added dropwise at such a rate as to maintain a gentle reflux while the reaction flask was cooled in an ice bath. After the addition of allyl bromide and acrolein was complete, the resulting mixture was heated under relux for two hours. The reaction mixture was allowed to cool and then poured onto approximately 800 g of ice and 400 g of ammonium chloride. The resulting magnesium salts were filtered and washed with ether. The filtrate was continuously extracted with ether for two days. The ether solutions were combined, washed with 10% sodium bicarbonate solution, and then saturated salt solution. The ether solution was then dried over magnesium sulfate. The solvent was removed under reduced pressure. The crude product was distilled to give a clear liquid which boiled at 44-45° (11 mm), (30); yield 187. 5 g (48. 8%). The product was found to be greater than 99% pure according to glc analysis (10 ft diethylene glycol succinate column, 90°, 60 mℓ per min flow rate).

1, 5-Hexadien-3-one 149

In a 5-ℓ three-necked flask, equipped with a mechanical stirrer, dropping funnel, and immersion thermometer, was placed a solution of 76. 4 g (0. 78 mole, 89. 5 mℓ) of 1, 5-hexadien-3-ol in 4 ℓ of acetone (distilled from potassium permanganate). The solution was cooled in an ice bath until a temperature of 0-5° was reached. To this rapidly stirred, cooled solution was added 220 mℓ (1. 1 equivalents) of 2. 6 M Jones reagent (260 g chromium trioxide, 230 mℓ concentrated sufuric acid, diluted to 1 ℓ with distilled water). The addition was continued over a period of 45 - 50 minutes, maintaining the reaction mixture at a temperature of 0 - 5° by adjustment of the rate of addition. After the addition was complete, the reaction mixture was allowed to stir for 30 additional minutes, after which, 100 mℓ of methanol was added.

The following workup procedure was devised to insure complete extraction of the ketone into ether in a minimum amount of time. It suffered from the disadvantage that a large amount of acetone and water was also extracted. One liter of the reaction mixture was poured into a 4 ℓ beaker containing 1 kg of ice and 15 g of sodium chloride. The pH of this solution was immediately adjusted to pH 6 - 7 by addition of 10% sodium bicarbonate solution. The remainder of the reaction mixture was cooled in an ice-water bath. The neutralized solution was extracted once with 400 mℓ of ether, or as much ether as was needed to cause a separation of the aqueous layer. The ether solution was saved, while to the aqueous layer was added another liter of the reaction mixture. The resulting solution was neutralized and extracted as before. This procedure was repeated until all the reaction mixture was extracted with ether. The remaining aqueous layer was then extracted with four 200 mℓ portions of ether. The combined ether layers were washed with three 20 mℓ portions of saturated sodium chloride solution and two 20 mℓ portions of water. The aqueous washings were then extracted twice with 200 mℓ portions of ether and the ether washed as above.

The combined ether extracts (ca 8 ℓ) were partially dried over 400 g of magnesium sulfate. The solvent was then removed on a rotary evaporator. The temperature of the water bath was kept below 15° and the aspirator pressure at 33 mm. to prevent loss of the ketone product. The volume was constantly maintained at a level to account for the presence of a large amount of water. By this method the removal of the ether took approximately 20 hours. To the resultant 500 mℓ of solution was added enough reagent pentane to cause a separation of the aqueous layer. The pentane layer was separated and the water layer was extracted ten times with 100 mℓ portions of pentane. The combined pentane layers were washed twice with 25 mℓ portions of saturated salt solution and then dried over magnesium sulfate.

The 1, 5-hexadien-3-one-pentane solution was then either used directly for subsequent photochemical reactions, or the solvent was removed and the crude ketone distilled. Distillation of the crude product gave 26. 7 g (35%) of 1, 5-hexadien-3-one, b. p. 30° - 40° (30 mm), λ_{max} = 212 mμ (ϵ = 11, 000). The infrared absorption band attributed to the α,β -unsaturated ketone appears at 1675 cm^{-1} (48).

Bicyclo(2. 1. 1)hexan-2-one 66

A solution of 26. 7 g (0. 28 mole) of crude 1, 5-hexadien-3-one (based on glc analysis of crude oxidation product) in 1. 2 ℓ of olefin-free pentane was placed in the sample chamber of an immersion-type irradiation apparatus. Into this solution was placed the water-cooled quartz immersion probe containing a 450 watt Hanovia medium pressure mercury lamp. The solution was irradiated for 72 hours under a nitrogen atmosphere. Every 12 hours the lamp was shut off in order to remove polymer from the sides of the quartz probe. The photochemical reaction was followed by several means. The course of the reaction was followed by the disappearance in the ultraviolet of the absorption band at 212 mμ, or the disappearance of the infrared carbonyl absorption at 1675 cm^{-1} and the appearance of an absorption at 1760 cm^{-1}. The reaction was also followed by analysis of aliquot samples in a glc (10 ft DEGS column at 90°). By all of these methods, it was found that the reaction was complete after 72 hours.

The irradiation solution was redried over magnesium sulfate and the pentane removed by distillation through a 25 cm column packed with glass helices. The residue was distilled under reduced pressure to give a product which was pure by glc analysis (98%). The pure product, a colorless liquid boiling at 55 - 58° (20 mm), amounted to 24. 1 g (89. 8%) or a 32. 2% yield from 1, 5-hexadien-3-ol.

The infrared spectrum of the product exhibits a band at 1764 cm^{-1} attributed to the carbonyl group, the ultraviolet spectrum only shows end absorption. The n. m. r. spectrum, (see Figure 5), shows a quartet centered at 1. 60 δ (2 H), a doublet further split at 2. 10 δ (2 H), a multiplet centered at 2. 22 δ (2 H) and a triplet with additional splitting at 2.80 δ (2 H). See Table 2 for the assignments for these absorptions.

Monitored Irradiations of 1,5-Hexadien-3-one

A solution of 5 g of 1,5-hexadien-3-one in one liter of olefin-free pentane was prepared. Approximately 170 mℓ of this solution was irradiated with a 450 watt Hanovia medium pressure mercury lamp. The course of the reaction was followed in the ultraviolet. Aliquots (0.5 mℓ) were removed at regular interval and diluted with pentane to a volume of 100 mℓ. The ultraviolet absorption at 212 mμ was monitored as a function of time. The reaction was found to be complete within two hours.

To another 170 mℓ portion of the ketone solution was added 3 mg of benzophenone. The irradiation was carried out as before with no appreciable difference in the rate of disappearance of the α, β-unsaturated ketone chromophore.

The experiment was repeated on another 170 mℓ portion of ketone solution. In this case, a Pyrex filter was placed around the Hanovia lamp. The reaction proceeded at a greatly diminished rate although a complete suppression of the reaction was not observed. The minimal reaction was due, most probably, to leakage around the cylindrical filter. The filter was removed and the irradiation re-initiated. The reaction again reached a rate comparable to that of the original unfiltered irradiation.

The irradiation of 170 mℓ of ketone solution which contained 3 mg of benzophenone was carried out using a Pyrex filter. It was found that the reaction was quenched to the same extent as the unsensitized filtered irradiation. Again on removal of the filter, the rate increased to its normal value. These data are plotted in Figure 8.

Irradiation of 1, 5-Hexadien-3-ol

A solution of 4.9 g (0.05 mole) of 1, 5-hexadien-3-ol was dissolved in 1.2 ℓ of purified acetone. The alcohol solution was irradiated with a medium pressure Hanovia lamp for eight hours. Samples were taken every two hours and the acetone removed on a rotary evaporator. Glc analysis on a 10 ft DEGS column at 90° revealed that no ring closure had occurred. A quantitative recovery of 1, 5-hexadien-3-ol was obtained.

Sensitized Irradiation of 1, 5-Hexadien-3-ol

The irradiation of a solution of 10.5 g (0.171 mole) of 1, 5-hexadien-3-ol and 2.1 g of acetophenone in 1.2 ℓ of dry ether was carried out for 36 hours using a medium pressure Hanovia lamp. The reaction was followed by glc analysis of aliquot samples (5 ft DEGS column at 90°). No trace of bicyclo(2.1.1)hexan-2-ol was detected. Aside from some polymers, only starting alcohol and acetophenone were recovered.

Bicyclo(2. 1. 1)hexan-2-ol 173

To one liter of diethyl ether distilled from lithium aluminum hydride was added 10. 0 g (0. 264 mole) of lithium aluminum hydride. The suspension was stirred rapidly at room temperature while 20. 0 g (0. 22 mole) of bicyclo(2. 1. 1)hexan-2-one in 500 mℓ of dry ether was added at a rate so as to maintain a gentle reflux. After the addition had been complete, the reaction mixture was heated under reflux for 60 hours. The mixture was allowed to cool and settle. Most of the ether was then decanted. The remaining material was poured onto 2 ℓ of ice and 300 g of potassium sodium tartrate. The resulting aqueous solution was then continuously extracted with ether. The combined ether solutions were washed with dilute hydrochloric acid and then with saturated salt solution until the water layer was neutral. The solvent was removed by distillation through a 25 cm vigreux column to give 25. 48 g of crude product. Analysis by glc showed the product to be 85. 8% bicyclo(2. 1. 1)hexan-2-ol. The crude oil was sublimed at aspirator pressure (14 mm) to give 20. 8 g (95. 5%) of a white solid, m. p. 82. 0 - 82. 6°. The infrared spectrum of a solution of the alcohol in carbon tetrachloride shows bands at 3620 and 3300 cm^{-1}, attributable to the hydroxyl group, in addition to bands at 1105, 1025, and 990 cm^{-1}. The n.m.r. spectrum shows a broad, concentration dependent sextet at 4.35 (2 H), assigned to the hydrogen on the carbon bearing the hydroxyl and the hydrogen on the oxygen. The spectrum also shows the normal bicyclo(2.1.1)hexyl absorptions at 0.95, 1.53, 1.25 - 2.15 and 2.42 δ assigned to the endo C-5 and C-6 protons, the exo C-5 and C-6 protons, the hydrogens on the alpha carbon, and the bridgehead hydrogens, respectively. These spectral data were compared to those of authentic samples (67) and proved to be identical.

Bicyclo(2.1.1)hexan-2-one p-Toluenesulfonylhydrazone 194

A minimum amount (10 mℓ) of methanol was used to dissolve 4.47 g (0.024 mole) of p-toluenesulfonylhydrazine. The resulting solution was mixed with a solution of 2.30 g (0.024 mole) of bicyclo(2.1.1)hexan-2-one in 10 mℓ of methanol. The clear solution was allowed to stir overnight at room temperature. A white solid started to precipitate after 20 minutes. The solid was filtered and washed with cold methanol. The mother liquors were concentrated to give a second crop of crystals. The white solid was recrystallized from methanol to give 4.75 g (78.3%) of product, m.p. 185.5-186.0°

Anal. Calcd. for $C_{13}H_{16}N_2SO_2$: C, 59.08; H, 6.10; N, 10.60

Found : C, 58.89; H, 6.18; N, 10.54

The infrared spectrum of a chloroform solution of the tosylhydrazone shows an intense band at 1160 cm^{-1} assigned to a sulfur-oxygen bond absorption of the sulfonyl group.

2-Oximobicyclo(2. 1. 1)hexane 193

A mixture of 20. 0 g (0. 208 mole) of bicyclo(2. 1. 1)hexan-2-one, 20. 0 g (0. 288 mole) of hydroxylamine hydrochloride and 20 mℓ of pyridine in 200 mℓ of ethanol was heated under reflux on a steam bath for two hours. The ethanol was removed on a rotary evaporator, and the residue treated with 200 mℓ of water. The water solution was extracted with ether to give, after evaporation of the solvent, 20. 1 g (87. 1%) of crude oxime. The yellow oil was recrystallized from hexane-benzene (or sublimed directly) to give 18. 5 g (80. 0%) of white crystalline oxime, m. p. 54. 0 - 54. 5°.

The infrared spectrum of 2-oximobicyclo(2. 1. 1)hexane exhibits bands at 3250 cm^{-1} assigned to the hydroxyl group and 1700 cm^{-1} attributable to the carbon-nitrogen double bond. Strong bands also appear at 1425, 1210, 1045, 945 and 918 cm^{-1}. The n. m. r. spectrum (see Table 2) shows a pattern which is very characteristic of the bicyclo(2. 1. 1)hexane system. The spectrum consists of a quartet at 1.38 δ due to the endo C-5 and C-6 hydrogens; a multiplet at 1.97 δ, assigned to the corresponding exo protons; a singlet with slight coupling at 2.42 δ, attributed to the bridgehead hydrogens; and a doublet of multiplets centered at 2.82 δ, due to the alpha methylene hydrogens.

2-Aminobicyclo(2.1.1)hexane 209

A suspension of 18.9 g (0.50 mole) of lithium aluminum hydride in anhydrous ethyl ether was treated with a solution of 13.0 g (0.117 mole) of 2-oximobicyclo(2.1.1)hexane in 250 mℓ of dry ether. The oxime solution was added dropwise to the lithium aluminum hydride suspension during the period of one hour. The reaction mixture was then heated under reflux for 48 hours, cooled to 0° in an ice bath, and treated with 100 mℓ of methanol. The reaction mixture was poured onto saturated potassium sodium tartrate solution. The salts were filtered and washed with ether and the water layer extracted with ether continuously for 24 hours. The combined ether fractions were washed with saturated sodium chloride solution and dried over anhydrous potassium carbonate. Evaporation of the solvent yielded 11.3 g of crude product which was distilled under reduced pressure to give 9.8 g (86.4%) of liquid amine, b.p. 34 - 35° (17 mm).

The infrared spectrum of bicyclo(2.1.1)hex-2-ylamine shows a doublet at 3310 and 3315 cm^{-1} characteristic of nitrogen-hydrogen stretching frequencies in amines. The n. m. r. spectrum shows a resonance at 3. 50 δ (doublet of multiplets) assigned to the C-2 hydrogen in addition to multiplets at 1. 08, 1. 60, 2. 00 and 2. 35 δ all representing two hydrogens each (see Table 2).

Anal. Calcd. for $C_6H_{11}N$: C, 74. 23; H, 11. 34; N, 14. 43
Found : C, 73. 98; H, 11. 32; N, 14. 12.

N, N-Dimethyl-2-aminobicyclo(2. 1. 1)hexane 210

To 9. 7 g (0. 10 mole) of 2-aminobicyclo(2. 1. 1)hexane was added with cooling 7. 5 mℓ of aqueous formaldehyde (37%), followed by the slow addition of 7. 0 mℓ of 97% formic acid. The resulting mixture was heated in an oil bath at 95° for 12 hours. The temperature was then raised to reflux and held there for four additional hours. The reaction mixture was cooled, made strongly basic with 6 N potassium hydroxide and extracted with pentane. The pentane solution was then washed with an excess of 1 N potassium hydroxide. The pentane solution was now extracted with 1 N hydrochloric acid and the acidic extracts combined and reextracted with pentane. The addition of 6 N potassium hydroxide to the aqueous layer to pH 10 was followed by a final extraction with pentane. The resulting pentane solution was dried over anhydrous potassium carbonate. The solvent was removed by distillation at atmospheric pressure and the residue distilled at reduced pressure. The clear liquid, b.p. 42 - 43° (11 mm) amounted to 6.41 g (51.3%).

Constants for this tertiary amine are: infrared spectrum: 2960, 2870, 2800, 2780, 1460, 1320 and 1030 cm^{-1}; n.m.r. spectrum: a sharp singlet at 2.18 δ ($N-CH_3$) in addition to broad multiplets from 2.6 to 1.0 δ. A less involved preparation of N,N-dimethyl-2-aminobicyclo(2.1.1)hexane appears later.

Anal. Calcd. for $C_8H_{15}N$: C, 76.80; H, 12.00; N, 11.20.

Found: C, 76.98; H, 12.03; N, 10.92.

N,N-Dimethylbicyclo(2.1.1)hex-2-ylamine Oxide 211

Treatment of a solution of 6.41 g (0.05 mole) of dimethylbicyclo(2.1.1)hex-2-ylamine in 15 mℓ of anhydrous methanol with 10.0 mℓ of 30% hydrogen peroxide was followed by an eight hour period of constant stirring at room temperature. After this period of time, an additional 7.7 mℓ of hydrogen peroxide was added. The mixture was then stirred for 16 additional hours. To the resulting solution was added a small amount (1 - 2 mg) of platinum black. After stirring at room temperature for 24 hours, the solution was filtered, the methanol evaporated and the solid residue dried to constant weight at a pressure of 0.05 mm of mercury. A yield of 6.63 g (93.3%) of white solid which melted at 82 - 84°, was thus obtained. This solid decomposed with a temperature range of 135 - 140°.

N, N, N-Trimethylbicyclo(2. 1. 1)hex-2-ylammonium Hydroxide 212

Six grams of dimethylbicyclo (2. 1. 1)hex-2-ylamine (0. 048 mole) was treated with one equivalent of methyl iodide in 100 mℓ of anhydrous ether. The reaction mixture was stirred overnight during which time a white precipitate was formed. The solvent was removed under reduced pressure and the resulting solid dried to a constant weight with a vacuum pump. In this manner, 12. 3 g (95%) of quaternary ammonium iodide was obtained. To this solid was added 100 mℓ of aqueous methanol and two equivalents of fresh silver oxide, prepared from 16. 38 g of silver nitrate in 55 mℓ of water and 38. 5 g of sodium hydroxide in 20. 4 mℓ of water. The solid oxide was filtered and washed with water until the washings were neutral. The solid was partially dried (moist) and added to the methanol solution of the quaternary ammonium iodide. The mixture was stirred for 24 hours, filtered and the filtrate evaporated to give 6. 58 g (85%) of yellow oil which was used as such in subsequent experiments.

N, N, N, -Trimethylbicyclo(2. 1. 1)hex-2-ylammonium Iodide 213

To a solution of 2-aminobicyclo(2. 1. 1)hexane in 100 mℓ of anhydrous diethyl ether was added 20. 1 g (0. 142 mole) of methyl iodide. After stirring at room temperature for 48 hours, the solvent was removed on a rotary evaporator giving a yellow oil whose infrared spectrum was identical to that of dimethylbicyclo(2. 1. 1)hex-2-ylamine prepared as described above. The crude tertiary amine amounted to 7. 5 g (96. 7%). Thirty grams of sodium carbonate, 100 mℓ of methanol and 35 mℓ of methyl iodide was added to the dimethylbicyclohexylamine. This mixture was then stirred and heated under reflux for three days. The solvent and any excess methyl iodide was removed under vacuum and the resulting white solid was partially extracted into chloroform, leaving sodium carbonate as a residue. The chloroform solvent was evaporated to give 16. 4 g (98%) of a cream colored solid. After recrystallization from ethanol-ether, 12. 0 g (71. 9%) of solid product was obtained. An infrared spectrum of a nujol mull of this product shows rather indistinct bands in the fingerprint region. Results from elemental analysis are also rather inconclusive, but it can safely be assumed that this white solid was the desired trimethylbicyclo(2. 1. 1)hex-2-ylammonium iodide.

N, N-Dimethylcyclohexylamine 219

One mole (99. 0 g) of cyclohexylamine, cooled in an ice bath, was treated with 75 mℓ of aqueous formaldehyde, added dropwise over a period of 30 minutes. This was followed by the slow addition of 70 mℓ of 97% formic acid. The mixture tended to solidify at ice bath temperature so good stirring was necessary. After the addition of formic acid was complete, the mixture was heated at 95° for 12 hours, after which, the temperature was raised and the mixture heated under reflux for eight additional hours. The cooled reaction mixture was made strongly basic with 6 N potassium hydroxide and extracted with five 50 mℓ portions of pentane. The combined pentane layers were washed with three 20 mℓ portions of 1 N potassium hydroxide, then extracted with an excess of 1 N hydrochloric acid. The resulting aqueous layer was then extracted with three 20 mℓ portions of pentane. The aqueous layer was again made strongly basic with 6 N potassium hydroxide and reextracted with five 50 mℓ portions of pentane. The pentane solution was dried over sodium carbonate and the solvent removed on a rotary evaporator. The residue was distilled at reduced pressure to give 42.8 g (33.7%) of dimethylcyclohexylamine b. p. 51 - 54° (14 mm).

Cyclohexene from Trimethylcyclohexylammonium Iodide

A solution of 12.7 g (0.10 mole) of dimethylcyclohexylamine in 150 mℓ of anhydrous diethyl ether was treated with 14.2 g (0.10 mole) of methyl iodide, and allowed to stir at room temperature for 48 hours. To the resulting suspension was added 140 mℓ of 0.97 M butyllithium (0.136 mole). After stirring, under a nitrogen atmosphere for 72 hours at room temperature, the suspension became cream colored. Throughout the reaction large quantities of gas were evolved. At the end of the reaction period, 200 mℓ of water and 150 mℓ of 5% hydrochloric acid was added. The ether portion of the reaction mixture was washed with three 20 mℓ portions of water and two 20 mℓ portions of saturated sodium chloride solution and dried over magnesium sulfate. The solvent was removed by distillation through a 25 cm packed column. Analysis of the residue by glc showed identical retention times to authentic cyclohexene samples. The residue was distilled to give 4. 37 g (53. 6%) of clear liquid, b. p. 82 - 85°, whose infrared spectrum was identical to that of cyclohexene.

Pyrolysis of Trimethylcyclohexylammonium Hydroxide

Into 100 mℓ of anhydrous ether was placed 12. 7 g (0. 10 mole) of dimethylcyclohexylamine and 14. 2 g (0. 10 mole) of methyl iodide. The resulting solution was stirred overnight at room temperature, during which time a white precipitate formed. The solvent was evaporated to yield 15. 9 g (94. 2%) of white solid. This solid was dissolved in 100 mℓ of 50% aqueous methanol and treated with two equivalents (46. 4 g) of freshly prepared silver oxide. (See above). After stirring at room temperature for 12 hours the mixture was filtered and the solvent removed to give 14. 4 g (90%) of yellow solid. This solid was dried to constant weight then pyrolyzed at reduced pressure (13 mm) at 120°, the volatile products being trapped in a

Dry Ice-acetone trap. The liquid recovered from the cold trap was analyzed by glc and found to be one component (99%) whose retention time was identical to that of cyclohexene. The yield of cyclohexene was 6.97 g (85%). The infrared spectrum of the product was also identical that that of authentic cyclohexene.

N, N-Dimethylcyclohexylamine Oxide 220

A solution of 22.4 g (0.176 mole) of N, N-dimethylcyclohexylamine in 45 mℓ of anhydrous methanol was cooled in an ice bath. To this cooled, rapidly stirred solution, was slowly (one hour) added 50.6 mℓ of 30% hydrogen peroxide. After eight hours of constant stirring at room temperature, an additional 8.5 mℓ (total 59.1 mℓ) of hydrogen peroxide was added. The solution was stirred for 16 hours, after which, a trace (1 mg) of platinum black was added and the suspension stirred at room temperature for 24 hours. The solution was filtered and the solvent removed *in vacuo*. The residue was dried at 0.05 mm pressure to a constant weight to give 22.0 g (81.7%) of a yellow oil which was used immediately without further purification.

Pyrolysis of N, N-Dimethylcyclohexylamine Oxide

Ten grams of crude dimethylcyclohexylamine oxide (0.07 mole) was placed in a 50 mℓ pear-shaped flask, attached by a short path glass tube to two traps which were connected in series to a water aspirator. The traps were placed in a Dry Ice-acetone bath and the system evacuated to 15 mm pressure. The flask containing the amine oxide was lowered into a preheated (120°) oil bath. Within a minute or two, liquid was visible (after cooling) in the connector tube. Heating was continued until the residue in the reaction flask melted and began to char. The liquids in the two traps were collected and dried over magnesium sulfate. Glc analysis of the contents of both traps (10 ft DEGS, 90°) showed that the first trap contained 5.0 g of liquid which was 87% cyclohexene. The second trap (1.1 g) analyzed for 61% cyclohexene. The total yield of cyclohexene was 5.02 g (87.3%). Comparison of the infrared spectra of the samples collected from the glc and an authentic cyclohexene sample show that they were identical. The residue left in the reaction flask (4.0 g) accounted for 78.3% of the theoretical. The volatile impurities which were found in the traps with cyclohexene were not identified.

Pyrolysis of N, N,-Dimethylbicyclo(2.1.1)hex-2-ylamine Oxide

Pyrolysis of 6.6 g (0.046 mole) of amine oxide 211 was accomplished by heating in a round-bottom flask equipped with a nitrogen inlet and connected through a short path system to two traps, in series, cooled in Dry Ice-acetone. The pressure was reduced to 12 mm, and the flask placed in an oil bath maintained at 135°. No volatile material was collected in the traps, although the amine oxide appeared to undergo some decomposition. The bath was slowly heated to 155°. The amine oxide in the flask appeared decomposed, but only a trace of volatile material was recovered from the traps. The n. m. r. spectrum of this liquid does not show absorptions in the olefinic region or any other absorptions indicative of the bicyclo-(2. 1. 1)hexane system. The residue in the round-bottom flask was a dark brown unidentified resin.

Pyrolysis of Trimethylbicyclo(2. 1. 1)hex-2-ylammonium Hydroxide

The crude yellow oily trimethylbicyclo(2. 1. 1)hex-2-ylammonium hydroxide, **212**, prepared above, was placed in a round-bottom flask connected *via* wide-bore glass tubing to two traps in series. The traps were cooled in Dry Ice-acetone. The pressure of the system was reduced to 13 mm and the flask heated gradually in an oil bath until the temperature of 120° was reached. Almost all the material in the flask decomposed and was collected in the traps. Analysis of the material collected in the traps showed that no olefin had been formed. The only products detected were traces of methanol and the major component dimethylbicyclo(2. 1. 1)hex-2-ylamine, identified by comparison with authentic material. A 40% recovery of dimethylbicyclo(2. 1. 1)hex-2-ylamine was obtained for the pyrolysis reaction.

Reaction of Trimethylbicyclo(2.1.1)hex-2-ylammonium Iodide with Butyllithium

To 250 mℓ of dry ether was added 12.0 g (0.045 mole) of the dry trimethylbicyclohexylammonium iodide prepared above. This suspension was stirred under nitrogen in a flask equipped with a Dry Ice condenser in series with a trap immersed in a Dry Ice-acetone bath. After flushing the system with nitrogen, 60 mℓ of 0.97 M (0.054 mole) butyllithium was added to the quaternary ammonium iodide suspension. The reaction mixture was then stirred at room temperature for 48 hours. Excess butyllithium was destroyed by the addition of 100 mℓ of water and 75 mℓ of 5% hydrochloric acid. The resulting aqueous layer was separated and extracted with ether. This ether extract was combined with the original ether layer and consecutively washed with three 20 mℓ portions of water and saturated salt solution and dried over magnesium sulfate.

The aqueous layer was made basic with 5% sodium hydroxide solution and treated as above. In both cases, the ether was removed by distillation through a 25 cm packed column. No residue was obtained after the distillation of the ether from the latter extraction. An infrared spectrum of the residue from the former extraction shows the absence of any bands attributable to an olefin. The spectrum, however, resembled that of dimethylbicyclo(2. 1. 1)hex-2-ylamine. This was confirmed by an n. m. r. spectrum of a sample collected from a 10 ft DEGS column at 90°. The spectrum is identical to that of an authentic sample. The only other product was not completely identified but appeared to be an aliphatic hydrocarbon. In all, approximately 35% of the theoretical dimethylbicyclo(2. 1. 1)-hex-2-ylamine was accounted for. Unreacted trimethylbicyclo(2. 1. 1)-hex-2-ylammonium iodide presumable accounts for the remainder of the material. This was, however, not recovered.

3-Oximocamphor 197

Freshly cut sodium metal, 8. 5 g (0. 343 g-at), was placed in 500 mℓ of anhydrous ether. To this was slowly added 54. 0 g (0. 355 mole) of camphor. After the camphor had completely dissolved (one hour), 45. 0 g (0. 384 mole) of freshly prepared amyl nitrite was slowly added over a period of 45 minutes. (Note: The solution foamed vigorously upon addition of the amyl nitrite. This was controlled by cooling and very rapid stirring). After the addition of amyl nitrite was complete, the red-brown product mixture was cooled in an ice bath for two hours, then enough water and ice was added to cause a separation of layers. After removal of the aqueous layer, the ether layer was washed twice with 25 mℓ portions of water. The combined water layers were extracted with three 15 mℓ portions of ether to remove any borneol and unreacted camphor. Any excess ether was evaporated from the water solution and the solution then brought to pH 6 with dilute hydrochloric acid. The resulting aqueous solution was then extracted with four 50 mℓ portions of ether. The ether solution was washed with three 20 mℓ portions of saturated bicarbonate, saturated salt and saturated ammonium chloride solution and dried over magnesium sulfate. The solvent was evaporated to give 23.44 g (35.6%) of yellow solid, m.p. 108 - 112°. This was recrystallized from benzene-hexane to give 20.4 g (31.0%) of 3-oximocamphor, m.p. 112 - 114°.(anti-oxime, m.p. 114°) (38). The infrared spectrum of the product shows bands at 1760 cm^{-1} due to the carbonyl group, 1720 cm^{-1} due to the nitrogen-carbon double bond and 3300 cm^{-1} attributable to the hydroxyl group.

When the same procedure was used on bicyclo(2.1.1)hexan-2-one, none of the corresponding 3-oximobicyclo(2.1.1)hexan-2-one was detected.

3-Diazocamphor 198

In a minimum amount of 14 M sodium hydroxide (10 - 15 mℓ) was dissolved 16.4 g (0.087 mole) of finely ground 3-oximocamphor. The volume was brought up to 800 mℓ with distilled water. The solution was cooled to 0°, 32.8 mℓ of 15 M ammonium hydroxide added, followed by the dropwise addition of 386 mℓ of 5.25% sodium hypochlorite solution (Chlorox) over the period of an hour. The solution was stirred at 0° for 30 minutes. The reaction mixture was then extracted with low-boiling petroleum ether by stirring vigorously with three 500 mℓ portions of solvent for 2, 2 and 12 hour periods, respectively. The combined extracts were dried over magnesium sulfate and the solvent then evaporated to give 11. 3 g (72. 0%) of crude product. The crude solid was recrystallized from petroleum ether to give 10. 8 g (68. 8%) of 3-diazocamphor, m. p. 73 - 74°. The infrared spectrum of the yellow solid shows bands at 2080 cm^{-1} assigned to the diazo group and 1695 cm^{-1} attributable to the carbonyl group.

3-Oximobicyclo(2. 1. 1)hexan-2-one 199

In a 20 mℓ Pyrex tube was placed 0. 96 g (0. 01 mole) of bicyclo-(2. 1. 1)hexan-2-one, 6. 72 g (0. 06 mole) of potassium t-butoxide and 1. 76 g (0. 015 mole) of amyl nitrite. The volume was brought up to about 10 mℓ with anhydrous t-butanol and the tube sealed. At the same time a similar tube was treated in the same manner except no ketone was added. Both tubes were placed in an oil bath heated at 105° for 24 hours. The contents of the tubes were cooled and poured onto 100 mℓ of water and extracted with ether. The aqueous layers were then acidified with dilute hydrochloric acid and again extracted with three 20 mℓ portions of ether. After washing with saturated salt solution and drying over magnesium sulfate, the ether solvent was removed to give 0.95 g of thick oil (76%). No product was isolated from the blank tube. The infrared spectrum of this crude product shows bands at 1550, 1640, 1720 and 3220 cm^{-1}. These can be assigned to the carbon-nitrogen double bond, the carbonyl, and the hydrogen bonded hydroxyl group, respectively. The n. m. r. spectrum consists of a multiplet from 1.50 to 2.60 δ, a doublet at 1.26 δ, a singlet at 1.14 δ, and doublet at 1.00 δ. Undoubtedly, the sample is impure, but all attempts at purification have resulted in the decomposition of the product. Distillation at 0.05 mm pressure and oil bath temperatures of up to 190° resulted in the formation of a black tar and no distillate.

Attempted Selenium Dioxide Oxidation of Bicyclo(2.1.1)hexan-2-one

A mixture of 4.8 g (0.05 mole) of bicyclo(2.1.1)hexan-2-one and 5.65 g (0.05 mole) of freshly sublimed selenium dioxide in 60 mℓ of dry toluene was placed in a 100 mℓ round-bottom flask equipped with a Stark separator. This mixture was heated under reflux for two days. During that period of time 1 mℓ of water was collected in the Stark separator. Most of the toluene was then removed by distillation at reduced pressure. The cooled residue was diluted with ether and selenium metal collected by filtration. The ether solvent was removed to give 2.4 g (43.7%) of brown oil. All attempts at distillation and sublimation at pressures as low as 0.05 mm and oil bath temperatures as high as 200°, failed. Only charred material was recovered. An infrared spectrum of the crude product shows a broad carbonyl band, actually three peaks, between 1750 and 1680 cm^{-1}. Similar reactions carried out using xylene as the solvent also gave the same crude product as above.

3-Hydroxymethylenebicyclo(2.1.1)hexan-2-one 200

A slurry of 10.8 g (0.20 mole) of sodium methoxide in 205 mℓ of anhydrous benzene was cooled in an ice bath. To this cooled mixture was added, with stirring, a mixture of 19.2 g (0.20 mole) of bicyclo(2.1.1)hexan-2-one and 27.4 g (0.37 mole) of ethyl formate. After the addition was complete, the ice bath was removed and replaced by an oil bath which was heated to 60°. The reaction mixture was stirred under a nitrogen atmosphere for 60 hours. After cooling to room temperature, the reaction product was extracted with ten 20 mℓ portions of 1 N potassium hydroxide. The aqueous layer was then acidified with 5% hydrochloric acid. This aqueous layer was continuously extracted with 1 ℓ of ether for eight hours. The ether layer was washed with three 20 mℓ portions of 10% sodium bicarbonate solution and three 20 mℓ portions of saturated sodium chloride solution. After drying the ether solution over magnesium sulfate, the solvent was removed in vacuo to give 7.10 g (28.6%) of crude product. Analysis of the crude product on a 10 ft DEGS column at 150° indicated the presence of two overlapping peaks representing about 95% of the crude product. These peaks were not separable under several conditions. Collection of these two compounds together was achieved.

The infrared spectrum of the glc collected compounds shows bands at 3330, 2940, 1725, 1690, 1616, 1178 and 860 cm^{-1}. The ultraviolet spectrum shows a maximum at 247 mμ (ϵ = 10,000). In the n.m.r. spectrum of these two compounds, there appear: a doublet at 7.92 δ, a broad singlet at 5.05 δ, a doublet at 4.32 δ, a triplet at 2.41 δ, and multiplets at 1.00 to 2.20 δ. On shaking the n.m.r. sample with deuterium oxide, the doublet at 7.92 δ collapsed to a singlet and the singlet at 5.05 δ disappeared. A water singlet appears at 4.73 δ.

Purification of the crude product led to decomposition. Distillation at 0.05 mm and oil bath temperatures up to 200° only caused the charring of the product without the appearance of a distillate. In spite of this, the spectral data appears consistent with that expected for 3-hydroxymethylenebicyclo(2.1.1)hexan-2-one (40).

Attempted Enol Acetylation of Bicyclo(2. 1. 1)hexan-2-one

A solution of 8. 0 g (0. 083 mole) of bicyclo(2. 1. 1)hexan-2-one and two drops of concentrated sulfuric acid in 60 mℓ of isopropenyl acetate was heated under reflux for 80 hours. At appropriate time intervals, the reflux condenser was replaced by a distillation head and material was distilled until a temperature of 98° was reached. The distillate was then analyzed on a 10 ft tricresylphosphate glc column maintained at 85°. Analysis showed acetone formation throughout the reaction. Analysis of the contents of the reaction flask on a 10 ft DEGS column at 100° showed only the presence of starting ketone, isopropenyl acetate and some acetone. The starting bicyclo(2. 1. 1)hexan-2-one was recovered by distillation of the reaction mixture through a 25 cm packed column.

3-Bromonorcamphor 222

To a solution of 5. 0 g (0. 044 mole) of norcamphor in 100 mℓ of carbon tetrachloride heated under reflux was added a solution of 7. 30 g (0. 046 mole) of bromine in 30 mℓ of carbon tetrachloride. The bromine solution was added in small portions, several minutes after the addition of each portion, the bromine color disappeared. The last third of the bromine addition took longer to decolorize. In all, the addition and disappearance of bromine took three hours. The carbon tetrachloride was distilled through a packed column and the residue taken up in ether. The ether was washed with water, 10% sodium bicarbonate and saturated salt solutions. The solution was then dried over magnesium sulfate and the solvent evaporated to give 7.34 g (87.3%) of product.

The physical constants for the product are: $\lambda_{max} = 312$ mμ ($\epsilon = 78$)[lit. 312 mμ (84)]: infrared carbonyl band at 1750 cm^{-1} (norcamphor, 1740 cm^{-1}); n.m.r. spectrum, sharp doublet at 3.73 due to the hydrogen of the carbon bearing bromine; b.p. 123 - 128° (20 mm)[lit. b.p. 126-128° (23 mm)].

Attempted Chlorination of Bicyclo(2.1.1)hexan-2-one

Through a vigorously stirred mixture of 2.94 g (0.031 mole) of bicyclo(2.1.1)hexan-2-one and water was bubbled enough chlorine gas to saturate the solution (one minute at 1 mℓ per minute flow rate). This was done while the reaction flask was submerged in an ice bath. Chlorine was then bubbled in until the ketone, which floats on water, was converted to a yellow liquid, which sank to the bottom when the stirring was ceased. This liquid was separated and the aqueous layer extracted with ether. The ether layer was washed with water and saturated salt solution and dried over magnesium sulfate. A glc comparison, along with infrared comparisons indicate that a quantitative recovery of starting bicyclo(2.1.1)hexan-2-one was accomplished. Under these same conditions, cyclohexanone is readily converted to 2-chlorocyclohexanone.

Attempted Bromination of Bicyclo(2.1.1)hexan-2-one

To a boiling solution of 3.49 g (0.036 mole) of bicyclo(2.1.1)-hexan-2-one in 100 mℓ of carbon tetrachloride was added a solution of 5.75 g (2 mℓ, 0.0364 mole) of bromine in 30 mℓ of carbon tetrachloride. No color change was noticed after the addition of bromine. The reaction mixture was heated under reflux for 24 hours, with no appreciable loss of bromine color. The solvent was distilled through a 25 cm packed column, the residue taken up in ether and washed with water, 10% sodium thiosulfate and saturated sodium chloride solution. The ether solution was dried over magnesium sulfate. After evaporation of the solvent, 4.50 g (72.7%) of crude product was obtained. Comparison of the spectral and glc properties of the product indicated that it was unreacted bicyclo(2.1.1)hexan-2-one. This reaction was repeated with an equivalent of glacial acetic acid as a catalyst. Again, only starting ketone was isolated.

3,3-Dideuterionorcamphor 221

A mixture of 0.4 g (0.0036 mole) of norcamphor and 6.0 mℓ of a solution of deuterium oxide (12.0 mℓ), methanol-O-d (2.8 mℓ) and sodium methoxide (2.96 g) was placed in a 10 mℓ ampoule and sealed. The sealed tube was then placed in an oil bath maintained at 100° for 20 hours. After cooling, the contents of the tube was extracted with four 10 mℓ portions of ether. The ether layer was washed three times with small amounts of deuterium oxide, then dried over magnesium sulfate. The solvent was removed by distillation through a 15 cm packed column and the residue was sublimed at 15 mm pressure, to give 0.38 g (95%) of white solid. The infrared spectrum of the product shows bands at 2130, 2180 and 2220 cm^{-1} attributable to carbon-deuterium stretching frequencies. The disappearance of the 1410 cm^{-1} band indicates that complete deuteration had occurred. This was confirmed by the n.m.r. spectrum which shows the absence of a signal at 1.75 δ (2 H) assigned to the protons alpha to the carbonyl. The above experiment was repeated at 200° to again give the same dideuterionorcamphor.

3,3-Dideuteriobicyclo(2.1.1)hexan-2-one 172

To 0.4 g (0.0042 mole) of bicyclo(2.1.1)hexan-2-one was added 6.0 mℓ of a solution prepared from 12.0 mℓ of deuterium oxide, 2.8 mℓ of methanol-O-d and 2.96 g of sodium methoxide. This mixture was placed in a tube and the tube sealed. The sealed tube was placed in an oil bath kept at 100° for 28 hours. After cooling, the reaction product was extracted with three small portions of deuterium oxide and dried. The ether was removed by distillation through a 15 cm packed column to give 0.25 g (62.5%) of product. The ketone was collected from a glc (10 ft DEGS, 90°). The infrared spectrum shows bands at 2235, 2190 and 2130 cm^{-1} attributable to carbon-deuterium stretches; the absence of a band at 1410 cm^{-1} indicates dideuteration. The n.m.r. spectrum of the deuteriocompound (see Figure 6) shows the loss of a peak at 2.10 δ (2 H) and total integration representing six protons.

High Temperature Deuterium Exchange on Bicyclo(2.1.1)hexan-2-one

A mixture of 0.20 g (0.0021 mole) of bicyclo(2.1.1)hexan-2-one and 3 mℓ of sodium deuteroxide, prepared as above, was heated in a sealed tube at 200° for 35 hours. The cooled contents of the tube was extracted with ether and the products isolated as above. The reaction product consisted of two components. Isolation of both components showed that one compound has spectral characteristics which are identical with 3,3-dideuteriobicyclo(2.1.1)hexan-2-one. The second product proved to be an alcohol, as determined by infrared analysis. The infrared spectrum of the solid alcohol shows bands at 3610 and 3330 cm^{-1}, due to the hydroxyl group; 2690 and 2490 cm^{-1} attributable to a deuteroxyl group; 2120, 2200, and 2230 cm^{-1} attributable to carbon-deuterium stretches. The above alcohol was passed through a deactivated alumina column to give a compound with a non-deuterated hydroxyl group, as seen in the infrared spectrum. The product collected from the glc was a white solid, m. p. 83 - 84°. A mixed melting point determination with bicyclo(2. 1. 1)-hexan-2-ol showed no depression in the melting point. Comparison of the infrared spectrum of the product with that of bicyclo(2. 1. 1)-hexan-2-ol shows that, except for the carbon-deuterium stretching frequencies, the other bands are almost superimposable. Thus it appears that the deuterated alcohol is 3, 3-dideuteriobicyclo(2. 1. 1)-hexan-2-ol, derived by a Meerwein-Ponndorf-Verley type reduction of the deuterated ketone. The n. m. r. spectrum shows the expected absorptions for this compound. The proton at C-2 appears at 4. 25 δ.

2-Methylbicyclo(2. 1. 1)hexan-2-ol 191

A solution of methylmagnesium iodide in anhydrous ether was prepared from 1. 58 g (0. 066 g-at) of magnesium turnings in 100 mℓ of ether to which was added 8. 52 g (0. 06 mole) of methyl iodide. The methylmagnesium iodide solution was then treated with a solution of 4. 8 g (0. 05 mole) of bicyclo(2. 1. 1)hexan-2-one in 50 mℓ of anhydrous ether. After completion of the addition of ketone, the reaction mixture was stirred for four hours under reflux, then cooled and poured onto an ice-ammonium chloride mixture. The inorganic salts were filtered and washed with ether and the aqueous layer extracted with additional ether. The combined ether extractions were washed, dried and evaporated to give 4.8 g (85%) of oily material which distilled at 145 - 150°. The purified yield amounted to 4.2 g (75%). An analytical sample collected from a glc (10 ft DEGS, 110°) shows bands in the infrared at 3390, 2900, 2800, 1390, 1220, 1025, 934, 900 and 848 cm^{-1}. The n.m.r. spectrum of the compound consists of: a singlet at 1.40 δ (3 H), due to the methyl group; a narrow multiplet at 1.60 δ (4 H), assigned to the alpha methylene hydrogens and the endo C-5 and C-6 hydrogens; a broad multiplet at 2.1 - 2.5 δ (2 H) assigned to the exo C-5 and C-6 hydrogens; a multiplet at 3.1 δ due to the C-4 bridgehead hydrogen and a multiplet at 1.20 δ due to the C-1 bridgehead proton.

Anal. Calcd. for $C_7H_{12}O$: C, 75.0; H, 10.72.

Found : C, 75.0; H, 10.90.

2-Phenylbicyclo(2.1.1)hexan-2-ol 192

To a flask containing 1.58 g (0.066 mole) of magnesium turnings and a crystal of iodine in 20 mℓ of anhydrous ether was added 9.41 g (0.060 mole) of bromobenzene in 75 mℓ of ether. After the addition of bromobenzene was complete, the reaction was heated under reflux for one hour, then cooled. A solution of 4.80 g (0.05 mole) of bicyclo(2.1.1)hexan-2-one in 50 mℓ of ether was added slowly to the phenylmagnesium bromide solution. During the addition, the solution became cloudy and a precipitate was formed. The reaction mixture was heated under reflux for 12 hours, cooled, and worked up in the usual manner. Distillation of the crude alcohol, b.p. 78 - 80° (0.30 mm) gave 6.33 g (72.8%) of product which was pure by glc analysis (10 ft DEGS, 110°). The infrared spectrum of the product shows the following bands: 3400, 3050, 3010, 3000, 2940, 2860, 1100, 1015, 990, 910, 870, 755, 732, 692 and 645 cm^{-1}. The n.m.r. spectrum shows the following absorptions: a multiplet at 7.28 (5 H), multiplets centered at 2.66 (1 H), 2.42 (2 H), 212 (1 H), 1.92 (1 H), 1.69 (3 H) and a broad multiplet centered at 1.15 δ (1 H). See Table 2 for assignments of f these absorptions.

<u>Anal</u>. Calcd. for $C_{12}H_{14}O$: C, 82.80; H, 8.06.

Found: C, 82.94; H, 8.11.

Attempted Dehydration of 2-Methylbicyclo(2.1.1)hexan-2-ol

To 4.12 g (0.028 mole) of phosphorus oxychloride in 25 mℓ of anhydrous pyridine was added 1.12 g (0.01 mole) of 2-methylbicyclo(2.1.1)hexan-2-ol in 5 mℓ of pyridine. After stirring at room temperature for 60 hours, the reaction mixture was cooled and then hydrolyzed with an ice-water mixture. The hydrolyzed reaction mixture was extracted with three 15 mℓ portions of ether. The ether layers were washed and then dried over magnesium sulfate. Evaporation of the solvent resulted in the recovery of 1.02 g (91%) of the starting alcohol, as shown by infrared and glc comparisons. The reaction was repeated at 50°. Again only starting alcohol was recovered (90%).

Reaction of 2-Phenylbicyclo(2. 1. 1)hexan-2-ol with Phosphorus Oxychloride

A mixture of 1. 74 g (0. 01 mole) of 2-phenylbicyclo(2. 1. 1)-hexan-2-ol and 4. 12 g (0. 028 mole) of phosphorus oxychloride in 25 mℓ of dry pyridine was allowed to stand at room temperature for 24 hours. The reaction mixture was then cooled and hydrolyzed with an ice-water mixture. After extraction with ether, the combined ether extracts were washed with three 20 mℓ portions of dilute hydrochloric acid and three 20 mℓ portions of saturated salt solution. The washed ether extract was dried over magnesium sulfate and the solvent removed by distillation through a short (25 cm) packed column. An infrared spectrum of the crude mixture shows the absence of any hydroxyl band. Analysis of the crude product on a 10 ft DEGS column maintained at 190° showed a mixture of two products A and B in the ratio of 3 to 2. This corresponds to a yield of 56% for A and 36% for B. The remaining 8% of the crude product was not identified.

The infrared spectrum of a collected sample of A shows absorption bands at 690 and 760 cm^{-1} attributed to the phenyl hydrogens. The ultraviolet spectrum exhibits a maximum at 253 mμ (ϵ = 13, 000). The n. m. r. spectrum consists of a singlet at 7. 18 δ (5 H), arising from aromatic proton absorption; a doublet at 4.33 δ (1 H), a triplet at 2.15 δ (2 H), attributed to the bridgehead protons; and a multiplet from 1.50 - 2.20 δ (5 H), attributed to the C-5 and C-6 protons plus a benzylic proton. The peak at 4.33 δ is assigned to a proton on a carbon bearing chlorine. The compound analyzed correctly for $C_{12}H_{13}Cl$. From these data the structure of A was assigned as 2-chloro-3-phenylbicyclo(2.1.1)hexane.

Compound B exhibited an infrared spectrum similar to compound A. The only difference is the absence of the peak at 710 cm^{-1}. The n.m.r. spectrum consists of a multiplet at 7.24 δ (5 H), assigned to aromatic protons; a singlet at 6.02 δ (1 H); a multiplet at 3.50 δ (2 H) and a multiplet at 1.7 - 3.0 δ (5 H). The analysis data given below indicates that this may also be a chlorobicyclo(2.1.1)hexane, but the structural assignment is not complete.

Anal. Calcd. for $C_{12}H_{13}Cl$: C, 74.81; H, 6.75; Cl, 18.44.
Found : C, 74.91; H, 6.61; Cl, 18.52.

Reaction of 2-Phenylbicyclo(2.1.1)hexan-2-ol with p-Toluenesulfonic Acid

A mixture of 1.74 g (0.01 mole) of 2-phenylbicyclo(2.1.1)-hexan-2-ol and 1.56 g (0.01 mole) of p-toluenesulfonic acid in 100 mℓ of dry benzene was heated under reflux for 16 hours. During this time water was continuously removed by means of a Stark separator.

The trap was removed and the solvent distilled. The residue was taken up in 100 mℓ of ether and the ether solution washed with three 10 mℓ portions of saturated sodium bicarbonate solution and three 10 mℓ portions of saturated sodium chloride solution. After drying the solution over magnesium sulfate, the solvent was removed under reduced pressure to give a cream colored solid. This impure material, m.p. 82 - 88° was recrystallized from hexane-acetone to give 1.53 g (98%) of white crystals, m.p. 114-115°.

The infrared spectrum of a solution of the product in chloroform shows peaks at 1385, 1190 and 1180 and typical aromatic absorptions, indicating the presence of a toluenesulfonyl group. The ultraviolet spectrum exhibits two maxima, one at 257 mμ (ϵ = 7000) and the other at 222 mμ (ϵ = 15, 000). The n. m. r. spectrum shows a complex multiplet from 6.9 to 7.8 δ (11 H), a doublet of doublets at 2.4 δ (1 H), and multiplet from 1.0 to 2.0 δ (8 H).

Anal. Calcd. for $C_{20}H_{19}O_3S$: C, 69.59; H, 6.10.

Found : C, 69.30; H, 5.95.

The above data are consistant with the structure 1-phenyl-1-(3-cyclobutanol)-ethylene p-toluenesulfonate.

Thermal Decomposition of the Sodium Salt of Bicyclo(2.1.1)hexan-2-one Tosylhydrazone

A solution of 12.0 g (0.045 mole) of bicyclo(2.1.1)hexan-2-one tosylhydrazone in about 10 mℓ of dry methanol was added to a solution of 1.05 g (0.045 g-at) of sodium metal in 50 mℓ of anhydrous methanol. After stirring for several minutes, the solvent is removed *in vacuo*. The semi-dried material was broken up with a spatula and redried at 1 mm pressure for ten hours. The hard cake was broken up several times during the drying period. To the flask containing the powdered tosylhydrazone salt was added 36 g of Celite 545, which had previously been washed with pentane and dried at 110° for 12 hours. The flask containing the mixture of Celite and tosylhydrazone salt was attached to three traps in series by wide-bore glass connectors. The first two traps were cooled in Dry Ice-acetone baths. The last trap was cooled in liquid nitrogen. The pressure was reduced to 13 mm and the reaction flask heated to 120° to remove any residual methanol. The temperature was then raised to 175° and maintained at that temperature for an hour, or as long as volatile material was given off. Yellow liquid was collected in the first two traps. Nothing was detected in the third trap. The yield of volatile material was 1.30 g or 36% based on conversion to C_6H_8. This volatile material was analyzed on a 15 ft, 15% diisodecylphthalate column at 65°. The reaction mixture consisted of five major products: A, 2%; B, 42%; C, 7%; D, 40%; and E, 9%. Compounds B, C, and D were collected from the glc column. Their proofs of structures are given below.

Compound D. The n. m. r. spectrum of D consists of a quartet at - 0. 19 δ (1 H), a sextet at 0. 78 δ (1 H), a broad multiplet centered at 1. 68 δ (2 H), a multiplet at 2. 40 δ (2 H), and a doublet of quartets centered at 5. 60 δ (2 H). The infrared spectrum shows bands at 3080, 1595, 1021 and 711 cm^{-1}. Both these pieces of spectral data are in agreement with the data published for bicyclo-(3. 1. 0)hex-2-3ne (39).

Compound B. The n. m. r. spectrum of B shows a doublet at 1. 05 δ (3 H), multiplets at 1. 70 - 2. 25 δ (2 H) and 2. 25 - 2. 48 δ (3 H) and a singlet at 5. 58 δ (2 H). The important bands in the infrared spectrum are those at 3070, 2860, 1615, 1540, 1430, 1370 and 666 cm^{-1}. The mass spectrum of B shows a parent peak at m/e 82, a base peak at 67 and other intense peaks at 39, 41, 27 and 81. These data are consistent with that of 3-methylcyclopentene (62).

The only other component collected was compound C. The weak n. m. r. spectrum of this compound consists of multiplets at 2. 4 - 2. 7 δ and 1. 65 δ. No integration of the spectrum was obtained. These data are similar to that published for tricyclo(2. 2. 0. $0^{2,6}$)-hexane (57), i. e., multiplets at 1. 5 - 1. 8 δ and 2. 8 - 3. 0, but no definite structural assignment can be made at this time.

A sample of the reaction mixture above was injected into a 15 ft 10% diisodecylphthalate column maintained at 28°. Two different injector temperatures were used to test the thermal stability of components D, C, and B. The results are shown in the table below.

Compound	% Composition at	
	140°	325°
A	2.1	2.1
B	31.7	32.3
C	15.1	1.5
D	51.0	64.4

Kinetics of Base-Catalyzed Deuterium Exchange Reactions of Bicyclo(2.1.1)hexan-2-one

A stock base solution was prepared from 120 mℓ of deuterium oxide, 28 mℓ of deuteriomethanol, and 29.6 g of sodium methoxide. A 125 mℓ portion of this base solution was placed in the reaction flask and immersed in a constant temperature bath at 50.0 ± 1°. To this solution was added 2.4 g (0.025 mole) of bicyclo(2.1.1)hexan-2-one. Ten mℓ aliquots were removed at ten minute intervals. These aliquots were extracted with ether and washed with deuterium oxide and the ether solution dried over magnesium sulfate. The ether was removed. The sample was then purified by collection from a 10 ft DEGS column at 90° or used in the impure state. After all samples were prepared, an n. m. r. spectrum of each sample was taken. The number of deuterium atoms per molecule of ketone was determined from the integration of the band (2. 08 δ) due to the protons alpha to the carbonyl of the ketone. The signal due to the bridgehead protons (2. 80 δ) was used as the internal standard. The gram-atoms of deuterium per mole was plotted against time. The initial rates were determined from the slope of the tangent to the curve at time equal zero (see Figure 12).

The same procedure was repeated using 2. 75 g (0. 025 mole) of norcamphor. The rate constants calculated from the data are: norcamphor, $k_{NC} = 3.34 \times 10^{-3}$ g - at/mole-sec. ; and bicyclo(2. 1. 1)-hexan-2-one, $k_{BC} = 6.0 \times 10^{-4}$ g-at/mole-sec. The relative rate of exchange, k_{NC}/k_{BC}, equals 5. 57. The samples collected from the glc showed no signs of exchange on the column.

Kinetics of the Sodium Borohydride Reduction of Bicyclo(2. 1. 1)hexan-2-one

To a 250 mℓ volumetic flask immersed in a constant temperature bath at 25. 0 ± 1° was added 100 mℓ of 0. 04 M sodium borohydride solution. This solution was prepared by dissolving 1. 5438 g of commercial grade (98%) sodium borohydride in enough dry isopropanol to make one liter of solution. To the above 100 mℓ of this solution was added 100 mℓ of 0. 16 M bicyclo(2. 1. 1)hexan-2-one in isopropanol at 25°. The initial concentration of the reactants were thus 0.08 M in ketone and 0.02 M in sodium borohydride. At intervals, 10 mℓ aliquots of the mixture were withdrawn and added to 50 mℓ of 0.1 N potassium iodate solution containing 2 g of potassium iodide. To this mixture was then added 10 mℓ of 5 N sulfuric acid. The iodine liberated was titrated with 0.1 N sodium thiosulfate.

A plot of time against the expression

$$\frac{2.303}{a - 4b} \log \frac{b(a - 4x)}{a(b - x)}$$

gives a line whose slope equals the rate constant for the reaction. In the above expression, a is the initial concentration of ketone, b, the initial concentration of sodium borohydride and x, the amount of sodium borohydride reacted in time, t. The average rate constant for the sodium borohydride reduction of bicyclo(2.1.1)hexan-2-one is 108.95×10^{-4} ℓ-mole^{-1}-sec^{-1} (see Figure 11).

Similarly, the kinetics of the sodium borohydride reduction of norcamphor were determined. The average rate constant is 24.9×10^{-4} ℓ-mole^{-1}sec^{-1}, in good agreement with the literature value, 24.0×10^{-4} ℓ-mole^{-1}-sec^{-1} (13). The relative rate of borohydride reductions of the two ketones is $k_{BC}/k_{NC} = 4.34$.

2-Bromobicyclo(2.1.1)hexane 216

To a mixture of 100.3 g (0.37 mole) of phosphorus tribromide and 1 mℓ of anhydrous pyridine, cooled in an ice bath, was added 9.8 g (0.10 mole) bicyclo(2.1.1)hexan-2-ol and 1.5 g of dry pyridine. After the addition was complete, the reaction was gradually allowed to come to room temperature. After stirring at room temperature for 48 hours, the reaction mixture was hydrolyzed with an ice-water mixture. The resultant mixture was extracted with three 50 mℓ portions of ether. The ether was washed with sodium bicarbonate solution and saturated salt solution, and dried over magnesium sulfate. Evaporation of the solvent yielded 15.9 g (98%) of crude product which consisted of two components. Unreacted alcohol accounted for 15% of the product, the remainder (85%) was crude bromide. The crude product was distilled under reduced pressure to give 12.5 g (77.8%) of 2-bromobicyclo(2.1.1)hexane, b.p. 55 - 60° at 20 mm.

No band due to hydroxyl absorption appeared in the infrared spectrum. The n.m.r. spectrum of 2-bromobicyclo(2.1.1)hexane is very similar to that of bicyclo(2.1.1)hexan-2-ol except that a doublet of sextets appears at 4.30 δ. This absorption is assigned to the proton at C-2 (see Table 2).

Anal. Calcd. for C_6H_9Br : C, 44.87; H, 5.77; Br, 49.68.

Found : C, 44.75; H, 5.59; Br, 49.64.

Bicyclo(2.1.1)hex-2-ene 108

To a mixture of 325 g (2.9 moles) of potassium t-butoxide in 1.5 ℓ of anhydrous dimethylsulfoxide was added 36.5 g (0.227 mole) of 2-bromobicyclo(2.1.1)hexane in 250 mℓ of dry dimethylsulfoxide. During the addition, the temperature was a constant 25°. After two hours stirring at 25°, the temperature of the reaction mixture was raised to 50°. The reaction was stirred for an additional 48 hours under a nitrogen atmosphere. The exit tube of the nitrogen purge system was connected to a Dry Ice trap. During the reaction only very minute amounts of liquid were detected in the trap. This liquid proved to be dimethylsulfoxide. After cooling, the reaction mixture was poured onto 1 ℓ of ice and extracted with eight 25 mℓ portions of cyclooctane. It was evident that most of the t-butanol formed in the hydrolysis of the reaction mixture was present in the organic layer. The cyclooctane solution was then washed with two 15 mℓ portions of 5% hydrochloric acid solution and five 15 mℓ portions of water. This solution was dried over magnesium sulfate, filtered and distilled through a spinning band column. The pot temperature never exceeded 110°, the column and head temperatures were always kept within a degree of each other. Five fractions were collected. The boiling points range from 60 - 87°. Fractions 1, 2, and 3 contained large amounts of volatile material which was neither cyclooctane nor t-butanol, as determined by glc analysis on a 15 ft 15% diisodecylphthalate column at 95°. The combined yield of volatile compound amounted to 4.5 g (24.8%). Since fraction 1 represented an 85% pure sample, all collections from the glc were achieved from it. The material obtained via glc collections is a clear liquid, b.p. 60 - 62°, $n_D = 1.4376$. The n.m.r. spectrum (see Figure 13) of a carbon tetrachloride solution of this liquid shows a multiplet at 6.62 δ (2 H), assigned to vinyl protons; an unresolved singlet at 2.38 δ (4 H), due to the exo C-5 and C-6 protons and the bridgehead hydrogens; and an unresolved doublet at 2.10 δ (2 H) assigned to the endo C-5 and C-6 protons. The infrared spectrum exhibits bands at 662 cm^{-1}, vinyl carbon-hydrogen absorption and 1535 cm^{-1}, carbon-carbon double bond absorption. In addition bands at 833, 1186, 1234, 1294, and 1425 cm^{-1} are present. The ultraviolet spectrum of a pentane solution of the product consists of a broad band at $\lambda_{max} = 217$ mμ ($\epsilon = 1115$). These data are all consistent with the structure bicyclo(2.1.1)hex-2-ene.

Anal. Calcd. for C_6H_8 : C, 89.94; H, 10.06.

Found : C, 89.62; H, 10.18.

BIBLIOGRAPHY

1. Alder, Kurt and Hans Ferdinand Rickert. Zur Kenntis der Dien-synthese. XI. Über die Dien-synthese mit vinylestern und halogenierten Äthylenen. Einfache Wege in die Norcampherreihen. Justus Liebigs Annalen der Chemie 543:1-27. 1939.

2. Alder, Kurt et al. Über des Nortricyclen. Darstellung und spektroscopisches Verhalten einiger Homologen des Campherchinons. Justus Liebigs Annalen der Chemie 593:23-35. 1955.

3. Appelquist, Douglas E. and John D. Roberts. Small-ring compounds. XV. Methylenecyclobutene and related substances. Journal of the American Chemical Society 78:4012-4022. 1956.

4. Avram, Margaretè, Costin D. Nenitzescu and Elsie Marica. Untersuchungen in der Cyclobutanreihe. II. Zur Kenntis des Cyclobutadiens. Chemische Berichte 90:1857-1868. 1957.

5. Baldwin, John E. and Richard H. Greeley. Cycloadditions. IV. Mechanism of the photoisomerization of cis, cis-1, 5-cyclooctadiene to tricyclo(3. 3. 0. $0^{2,6}$)octane. Journal of the American Chemical Society 87:4514-4516. 1965.

6. Bartlett, Paul D. Non-classical ions. New York, W. A. Benjamin, 1965. 533 p.

7. Belamy, L. J. The infrared spectra of complex molecules. London, Methuen, 1958. 408 p.

8. Benson, Sid. Stanford Research Institute. Personal communication. Stanford. September, 1967.

9. Berson, Jerome. Carbonium ion rearrangements in bridged bicyclic systems. In: Molecular rearrangements, ed by Paul de Mayo. Vol. 1. New York, Interscience, 1963, p. 111-231.

10. Blanchard, E. P., Jr. and A. Cairncross. Bicyclo(1. 1. 0)-butane chemistry. I. The synthesis and reactions of 3-methylbicyclo(1. 1. 0)butanecarbonitriles. Journal of the American Chemical Society 88:487-495. 1966.

11. Bond, F. Thomas, Assistant Professor, Department of Chemistry, University of California. Unpublished observations. San Diego, February, 1968.

12. Bond, F. Thomas, Harold L. Jones and Louis Scerbo. A facile synthesis of bicyclo(2. 1. 1)hexan-2-one. Tetrahedron Letters, 1965, 4685-4686.

13. Brown, Herbert C. and John Muzzio. Rates of reaction of sodium borohydride with bicyclic ketones. Steric approach control and steric departure control in the reactions of rigid bicyclic systems. Journal of the American Chemical Society 88:2811-2822. 1966.

14. Brown, Morris. The photolysis of some 1, 6-dienes. Total synthesis of (±)-α-bourbonene. Journal of Organic Chemistry 33:162-166. 1968.

15. Buchi, G. and I. M. Goldman. Photochemical reaction. VII. The intramolecular cyclization of carvone to carvonecamphor. Journal of the American Chemical Society 79:4741-4748. 1957.

16. Cairncross, A. and E. P. Blanchard, Jr. Bicyclo(1. 1. 0)butane chemistry. II. Cycloaddition reactions of 3-methylbicyclo-(1. 1. 0)butanecarbonitriles. The formation of bicyclo(2. 1. 1)-hexanes. Journal of the American Chemical Society 88:496-504. 1966.

17. Cava, M. P., R. L. Little and D. R. Napier. Condensed cyclobutane aromatic systems. V. The synthesis of some α-diazoindanones. Ring contractions in the indane series. Journal of the American Chemical Society 80:2257-2263. 1958.

18. Cava, M. P. and B. R. Vogt. Steroids IV. A synthetic route to A-bisnorsteroids. Journal of Organic Chemistry 30:3775-3780. 1965.

19. Charlton, J. L., P. de Mayo and Lars Skattebøl. 2-Methylene-(2. 1. 1)bicyclohexane. Tetrahedron Letters, 1965, p. 4679-4683.

20. Ciamician, Giacomo and P. Silber. Chemische lichtwirkungen. Berichte den Deutschen Chemischen Gesellschaft 41:1928-1935. 1908.

21. Coke, James L. and Manning P. Cooke, Jr. Elimination reactions. II. Hofmann elimination in bicyclic compounds. Journal of the American Chemical Society 89:6701-6704. 1967.

22. Cookson, R. C. *et al.* The photochemistry of citral. Tetrahedron 19:1995-2007. 1963.

23. Cope, Arthur C., Engelbert Ciganek and Norman A. Le Bel. Amine oxides. VI. The formation of 2, 5-norbornadiene and 2-norbornene from 5-dimethylamino-2-norbornene and 2-dimethylaminonorbornane. Journal of the American Chemical Society 81:2799-2804. 1959.

24. Corey, E. J. *et al.* A study of the photochemical reactions of 2-cyclohexenones with substituted olefins. Journal of the American Chemical Society 86:5570-5583. 1964.

25. Crowley, Kevin J. Synthesis of a bicyclo(2. 1. 1)hexene. Journal of the American Chemical Society 86:5692-5693. 1964.

26. Dallinga, G. and Miss L. H. Toneman. Electron diffraction by gases. The molecular structure of bicyclo(2. 1. 1)hexane. Recueil des Travaux Chimique des Pays-bas 86:171-186. 1967.

27. Dilling, Wendell, L. Intramolecular photochemical cycloaddition reactions of nonconjugated olefins. Chemical Reviews 66:373-393. 1966.

28. de Mayo, Paul., J. P. Pete and M. Tchir. Cyclopentenone photocycloaddition. A reaction from a higher triplet state. Journal of the American Chemical Society 89:5712-5713. 1967.

29. Doering, W. von E. and Martin Pomerantz. 2, 4-dimethyltricyclo(1. 1. 1. $0^{2,4}$)pentan-5-one. Tetrahedron Letters, 1964, p. 961-966.

30. Dreyfuss, M. Peter. A convenient method for utilizing allyl Grignard reagent. Journal of Organic Chemistry 28:3269-3272. 1963.

31. Dyer, John R. Applications of absorption spectroscopy of organic compounds. Englewood Cliffs, Prentice-Hall, 1965. 147 p.

32. Eaton, Philip E. On the mechanism of the photodimerization of cyclopentenone. Journal of the American Chemical Society 84:2454-2455. 1962.

33. Eaton, Philip E. The tricyclo(5. 3. 0. $0^{2,6}$)decane system. The photodimers of cyclopentenone. Journal of the American Chemical Society 84:2344-2348. 1962.

34. Eaton, Philip E. and William S. Hurt. Photodimerization of cyclopentenone. Singlet or triplet? Journal of the American Chemical Society 88:5038-5039. 1966.

35. Ebisu, Kikuye et al. A synthesis of 5, 5-dimethylbicyclo(2. 1. 1)-hexane-1-carboxaldehyde. Journal of the American Chemical Society 88:1995-1998. 1966.

36. Ellis, R. J. and H. M. Frey. Thermal decomposition of isopropenylcyclobutane. Transactions of the Faraday Society 59: 2076-2079. 1963.

37. Erman, William F. Photochemical transformations of unsaturated bicyclic ketones. Verbenone and its photodynamic products of ultraviolet irradiation. Journal of the American Chemical Society 89:3828-3841. 1967.

38. Forster, Martin O. and K. A. N. Roa. Studies in the camphane series. Part XLI. The unstable modification of isonitrosocamphor. Journal of the Chemical Society, 1926, p. 2670-2675.

39. Freeman, Peter K., Marvin F. Grostic and Floyd A. Raymond. Reactive intermediates in the bicyclo(3. 1. 0)hexyl and bicyclo-(3. 1. 0)hexylidene systems. I. The acid catalyzed addition of methanol and acetic acid to bicyclo(3. 1. 0)hexene-2. Journal of Organic Chemistry 30:771-777. 1965.

40. Gibson, Thomas and William F. Erman. The structures of the photolysis products of carvonecamphor. Journal of Organic Chemistry 31:3028-3032. 1966.

41. Hammond, George S. and Nicholas J. Turro. Organic photochemistry. The study of photochemical reactions provide information on the excited states of molecules. Science 142: 1541-1553. 1963.

42. Horne, Deane A. Unpublished research on the synthesis of bicyclo(2. 1. 1)hexanes. Corvallis, Oregon State University, Department of Chemistry, 1968.

43. Howton, David R. and Edwin R. Buchman. The thermal decomposition of (2-methylenecyclobutyl)-trimethylammonium hydroxide. Journal of the American Chemical Society 78:4011-4012. 1956.

44. Jackman, L. M. Applications of nuclear magnetic resonance spectroscopy in organic chemistry. New York, MacMillan, 1959. 130 p.

45. Jaffé, H. H. and Milton Orchin. Theory and applications of ultraviolet spectroscopy. New York, John Wiley and Sons, 1962. 609 p.

46. Jerkunica, J. M., S. Borcic and D. E. Sunko. Base catalyzed deuteration of norcamphor and dehydronorcamphor. Tetrahedron Letters, 1955, p. 4465-4467.

47. Jones, Harold L. Unpublished research as an undergraduate honors research participant. Corvallis, Oregon State University, Department of Chemistry, 1965.

48. Jones, N., H. T. Taylor and E. Rudd. Aliphatic Friedel-Crafts reactions. IV. Preparation of divinyl ketones. Journal of the Chemical Society, 1961, p. 1345-1347.

49. Kirmse, Wolfgang. Carbene chemistry. New York, Academic Press, 1964. 302 p.

50. Komppa, Gust. and Siegfried Beckmann. Über die Norcamphergruppe. I. Justus Liebigs Annalen der Chemie 512:172-185. 1934.

51. Kropp, P. J. and T. W. Gibson. A cyclic product from phorone. Journal of the Chemical Society, C 1967, p. 143-145.

52. Kwart, H., T. Takeshita and J. L. Nyce. Deuterium tracer studies on the elimination reactions of norbornyl tosylate and bromide. XI. Journal of the American Chemical Society 86: 2606-2611. 1964.

53. Lamb, Robert C., Paul Wayne Ayers and Myron K. Toney. Organic peroxides. II. The mechanism of the thermal decomposition of 6-heptenoyl peroxide in toluene. The rearrangement of the 5-hexenyl radical. Journal of the American Chemical Society 85:3483-3486. 1963.

54. Laszlo, Pierre and Paul von Ragué Schleyer. Analysis of the nuclear magnetic resonance spectra of norbornene derivatives. Journal of the American Chemical Society 86:1171-1179. 1964.

55. Leermakers, Peter A. and George F. Vesley. Organic photochemistry and the excited state. Journal of Chemical Education 41:535-541. 1964.

56. Lemal, David M. and Jerrold P. Lokensgard. Hexamethylprismane. Journal of the American Chemical Society 88:5934-5935. 1966.

57. Lemal, David M. and Kyung S. Shim. Tricyclo(2. 2. 0. $0^{2,6}$)-hexane. Journal of the American Chemical Society 86:1550-1553. 1964.

58. Liu, Robert S. H. 2-Methylenebicyclo(2. 1. 1)hexanes. A nonstereospecific photosensitized, cyclization reaction of trienes. Tetrahedron Letters, 1966, p. 2159-2165.

59. Liu, Robert S. H.,. and George S. Hammond. Photosensitized internal addition of dienes to olefins. Journal of the American Chemical Society 86:4936-4944. 1964.

60. Masamume, Satoru. Strained ring systems. I. The tricyclo-(1. 1. 1. $0^{4,5}$)pentane system. Journal of the American Chemical Society 86:735-736. 1964.

61. Masamume, Satoru. Strained systems. III. Bond cleavage reactions of tricyclo(1. 1. 1. $0^{4,5}$)pentane and tricyclo(2. 1. 1. $0^{5,6}$)-hexane systems. Tetrahedron Letters, 1965, p. 945-951.

62. American Petroleum Institute. Mass spectral data. College Station, Texas, Texas Agriculture and Mechanics University, 1965. 1 p. (Research Project 44)

63. McDonald, Richard N. and Charles E. Reineke. Strained ring systems. IV. The synthesis and solvolysis of *exo*-bicyclo-(2. 2. 0)hex-2-yl tosylate. Journal of Organic Chemistry 32:1878-1887. 1967.

64. McDonald, Richard N. and Charles E. Reineke. Strained ring systems. V. The synthesis of bicyclo(2. 2. 0)hexan-2-one and *endo*-bicyclo(2. 2. 0)hexan-2-ol. Journal of Organic Chemistry *32*:1888-1893. 1967.

65. McDonald, Richard N. and Charles E. Reineke. The synthesis and acetolysis of *exo*-bicyclo(2. 2. 0)hex-2-yl tosylate. Journal of the American Chemical Society 87:3020-3021. 1965.

66. Meinwald, J. Highly strained bicyclic systems: The bicyclo-(2. 1. 1)hexanes. Record of Chemical Progress 22:39-57. 1961.

67. Meinwald, J. Professor, Department of Chemistry, Cornell University. Personal communication. Ithaca, N. Y. May, 1966.

68. Meinwald, J. and L. K. Crandall. Highly strained bicyclic systems. XI. Synthesis of 2-bicyclo(2. 1. 1)hexanol and tricyclo-(2. 2. 0. $0^{2,6}$)hexane-1-carboxylic acid. Journal of the American Chemical Society 88:1292-1301. 1966.

69. Meinwald, J., J. K. Crandall and W. E. Hymans. Nortricyclanone (tricyclo(2. 2. 1. $0^{2,6}$)heptan-3-one). Organic Synthesis 45:77-79. 1965.

70. Meinwald, J., Albrecht Eckell and Karen L. Erikson. The photoisomerization of α-phellandrene. A structural assignment. Journal of the American Chemical Society 87:3532-3534. 1965.

71. Meinwald, J. and Paul G. Gassman. Highly strained bicyclic systems. I. The synthesis of some bicyclo(2. 1. 1)hexanes of known stereochemistry. Journal of the American Chemical Society 82:2857-2863. 1960.

72. Meinwald, J. and P. G. Gassman. Highly strained bicyclic systems. II. The synthesis of optically active 2α- and 2β-amino and hydroxy bicyclo(2. 1. 1)hexanes. Journal of the American Chemical Society 82:5445-5450. 1960.

73. Meinwald, J. and Bruce Emil Kaplan. Synthesis and reactions of 3-substituted tricyclo(3. 3. 0. $0^{2,6}$)octanes and of tricyclo-(3. 3. 0. $0^{2,6}$)oct-3-ene. Journal of the American Chemical Society 89:2611-2618. 1967.

74. Meinwald, J. and Arthur Lewis. Long-range spin-spin couplings in the nuclear magnetic resonance spectra of bicyclo(2. 1. 1)-hexanes. Journal of the American Chemical Society 83:2769-2770. 1961.

75. Meinwald, J., A. Lewis and P. G. Gassman. Highly strained bicyclic systems. VI. Reactions of 1, 5, 5-trimethylbicyclo-(2. 1. 1)hexane-6-carboxylic acid and the synthesis of bicyclo-(2. 1. 1)hexyl analogs of borneol and isoborneol. Journal of the American Chemical Society 84:944-983. 1962.

76. Meinwald, J. and Yvonne C. Meinwald. Bicyclo(n. 1. 1)alkanes and related tricyclic compounds. In: Advances in alicyclic chemistry, ed. by H. Hart and G. J. Karabatsos. Vol. 1. New York, Academic Press, 1966. p. 3-51.

77. Meinwald, J., Ronald A. Schneider and Alan F. Thomas. Stereospecific hydrogen transfer in the photolysis of carvone-camphor. Journal of the American Chemical Society 89:70-72. 1967.

78. Meinwald, J., William Szkrybalo and Donald R. Dimmel. Bicyclo(1. 1. 1)pentane from mercury sensitized and unsensitized gas phase photolysis of bicyclo(2. 1. 1)hexan-2-one. Tetrahedron Letters, 1967. p. 731-733.

79. Meinwald, J. and Fumio Uno. The synthesis of bicyclo(2. 1. 1)-hex-2-ene. Journal of the American Chemical Society 90:800. 1968.

80. Meinwald, J. et al. Highly strained bicyclic systems. X. The chemistry of 6-substituted exo-5-chlorobicyclo(2. 1. 1)hexanes. Journal of Organic Chemistry 29:3469-3473. 1964.

81. Overberger, C. G. and A. E. Borchert. Novel thermal rearrangements accompanying acetate pyrolysis in small ring systems. Journal of the American Chemical Society 82:1007-1008. 1960.

82. Padwa, Albert and Edward Alexander. Photochemical transformation of a substituted bicyclo(1. 1. 1)pentane. Journal of the American Chemical Society 89:6376-6377. 1967.

83. Pomerantz, Martin. The electronic structure and reactivity of small-ring compounds. II. The reaction of bicyclobutane with benzyne. Journal of the American Chemical Society 88:5349-5350. 1966.

84. Rettig, T. A. The photochemistry of some 2-cyclohexenones. Ph. D. thesis, Ames, Iowa State University, 1966. 246 numb. leaves.

85. Roberts, J. D. and Charles W. Sauer. Small-ring compounds. III. Synthesis of cyclobutanone, cyclobutanol, cyclobutene and cyclobutane. Journal of the American Chemical Society 71: 3925-3929. 1949.

86. Royals, E. Earl. Advanced organic chemistry. Englewood Cliffs, Prentice-Hall, 1954. 846 p.

87. Ruhen, James L. and Peter A. Leermakers. On the photodimerization of cyclopentenone. Journal of the American Chemical Society 88:5671-5672. 1966.

88. Ruhen, James L. and Peter A. Leermakers. Photochemistry of cyclopentenone in various media. Journal of the American Chemical Society 89:4944-4948. 1967.

89. Schafer, W. and H. Hellman. Hexamethyl(Dewar benzene) (hexamethylbicyclo(2. 2. 0)hexa-2, 5-diene). Angewandte Chemie, International ed. in English, 6:518-525. 1967.

90. Schneider, Ronald A., and J. Meinwald. Photochemical reactions of α, β-unsaturated carbonyl compounds with olefins. Journal of the American Chemical Society 89:2023-2332. 1967.

91. Schlatter, Maurice J. The preparation of cyclopropene. Journal of the American Chemical Society 63:1733-1737. 1941.

92. Schleyer, Paul von Ragué. The relative stability of bridged hydrocarbons. Norbornene and tricyclene. Journal of the American Chemical Society 80:1700-1704. 1958.

93. Shapiro, Robert H., J. H. Duncan and J. C. Clopton. The effect of base concentration and solvent polarity on the base-catalyzed decomposition and camphor tosylhydrazone under aprotic conditions. Journal of the American Chemical Society 89:1442-1446. 1967.

94. Shapiro, Robert H. and Marsha J. Heath. Tosylhydrazones. V. Reaction of tosylhydrazones with alkyllithium reagents. A new olefin synthesis. Journal of the American Chemical Society 89:5734-5735. 1967.

95. Silversmith, Ernest F. and J. D. Roberts. Small-ring compounds. XVII. 2-Hydroxy-3-phenyl-2-cyclobutenone and related substances. Journal of the American Chemical Society 80:4083-4088. 1958.

96. Small, Audrey. Rearrangements of 1-(1, 2, 3-triphenylcyclopropenyl)-3-diazopropan-2-one. Journal of the American Chemical Society 86:2091-2092. 1964.

97. Srinivasan, R. Mercury photosensitized decomposition of norcamphor and d-camphor. Journal of the American Chemical Society 83:4923-4927. 1961.

98. Srinivasan, R. Mercury photosensitized isomerization of 1, 5-cyclooctadiene to tricyclo(3. 3. 0. $0^{2,6}$)octane. Journal of the American Chemical Society 85:819-820. 1963.

99. Srinivasan, R. Photochemical transformations of 1, 5-cyclooctadiene. Journal of the American Chemical Society 86:3318-3321. 1964.

100. Srinivasan, R. The use of π-complex of an olefin as a photochemical catalyst. Journal of the American Chemical Society 85:3048-3049. 1963.

101. Srinivasan, R. and Karen Hill Carlough. Mercury ($^3P_1$) photosensitized internal cycloaddition reactions in 1, 4-, 1, 5-, and 1, 6-dienes. Journal of the American Chemical Society 89: 4932-4936. 1967.

102. Srinivasan, R. and A. A. Levi. Kinetics of the thermal isomerization of bicyclo(2. 1. 1)hexane. Journal of the American Chemical Society 85:3363-3365. 1963.

103. Srinivasan, R. and F. I. Sonntag. Bicyclo(2. 1. 1)hexane. Preparation and photochlorination. Journal of the American Chemical Society 89:407-410. 1967.

104. Tanida, Hiroshi and Yoshiteru Hata. A benzobicyclo(2. 1. 1)-hexene. Journal of the American Chemical Society 88:4289-4290. 1966.

105. Thomas, A. F. and B. Willhelm. A peculiarity in the deuteration of certain bicyclo(2. 2. 1)heptanones. Tetrahedron Letters, 1955, p. 1309-1311.

106. Tobey, Stephen W. and Robert West. Pentachlorocyclopropane. Journal of the American Chemical Society 88:2478-2481. 1966.

107. Traylor, T. G. and A. W. Baker. The oxymercuration of olefins. I. A general method for determination of the stereochemistry of oxymercuration. Journal of the American Chemical Society 85:2746-2752. 1963.

108. Turner, Richard B. et al. Strain in 1, 3-dimethylbicyclo(1. 1. 0)-butane. Tetrahedron Letters, 1965, p. 997-1002.

109. Turro, Nicholas J. Molecular photochemistry. New York, W. A. Benjamin, 1965. 286 p.

110. Van Tamelen, E. E. and D. Corty. Nonaromatization reactions of bicyclo(2. 2. 0)hexa-2, 5-diene. Journal of the American Chemical Society 89:3292-3293. 1967.

111. Viehe, H. G. et al. Valence bond isomers of (substituted) benzene. Simultaneous formation of substituted tetracyclohexane, tricyclohexene and bicyclohexadiene by spontaneous trimerization of t-butylfluoroacetylene. Angewandte Chemie, International ed. in English, 3:755756. 1964.

112. Wiberg, Kenneth B., Robert K. Barnes and Jerry Albin. Cyclopropene. I. The reaction of 2-bromocyclopropanecarboxylates with potassium t-butoxide. Journal of the American Chemical Society 79:4994-4999. 1957.

113. Wiberg, K. B. and Daniel S. Connor. Bicyclo(1. 1. 1)pentane. Journal of the American Chemical Society 88:4437-4441. 1966.

114. Wiberg, K. B. and Richard Fenoglio. On the acetolysis of exo- and endo-bicyclo(2. 1. 1)hex-5-yl tosylates. Tetrahedron Letters, 1963, p. 1273-1275.

115. Wiberg, K. B. and Betty R. Lowry. Strained small ring compounds: Bridgehead substituted bicyclo(2. 1. 1)hexanes. Journal of the American Chemical Society 85:3188-3193. 1963.

116. Wiberg, K. B., Betty R. Lowry and Thomas H. Colby. Bicyclo(2. 1. 1)hexane derivatives. Journal of the American Chemical Society 83:3998-4006. 1961.

117. Wiberg, K. B., Betty R. Lowry and Bernard J. Nist. N. m. r. spectra of bicyclo(2. 1. 1)hexane derivatives. Journal of the American Chemical Society 84:1594-1597. 1962.

118. Wilcox, Charles F. and Goerge C. Whitney. The preparation of bicyclo(2. 2. 1)hepta-2, 5-diene-7-spiro-1'-cyclopentane. Journal of Organic Chemistry 32:3348-3351. 1967.

119. Willstatter, Richard and James Bruce. Zur Kenntis der Cyclobutanreihe. Berichte den Deutschen Chemischen Gesellschaft 40:3979-3999. 1907.