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THE CHEMISTRY OF SOME STRAINED SYSTEMS
exo-Bicyclo[2.1.1]hex-2-en-5-ol and
exo-anti-Tricyclo[3.1.1.$0^{2,4}$]heptan-6-ol Derivatives

by

© RASTKO VUKOV

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

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FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

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THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance a thesis entitled

THE CHEMISTRY OF SOME STRAINED SYSTEMS

submitted by Rastko Vukov in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

Bicyclo[2.1.1]hexene is a rigid, and highly strained compound. Its unusual geometry suggests that there would be considerable homoallylic participation between the double bond and a carbonium ion centre at C-5. The rigidity of the framework also offers a unique opportunity to study [1,3]sigmatropic rearrangement.

These considerations prompted a synthesis of this skeleton. The first synthesis of a bicyclo[2.1.1]-hex-2-en-5-ol derivative is presented herein. Solvolytic studies of this system, which involved extraordinarily large rate enhancements, show that there is considerable interaction between the double bond and the carbonium ion at C-5. Evidence is presented to show that a non-classical carbonium ion is formed.

Thermolysis of the exo-bicyclo[2.1.1]hex-2-en-5-yl acetate proceeded in a completely stereospecific manner. This reaction represents one of the few known examples of a suprafacial [1,3]sigmatropic rearrangement, which necessarily proceeds with inversion of configuration at the migrating centre.

Introduction of a three-membered ring at the double bond position in the above bicyclic system led to

exo-anti-tricyclo[3.1.1.$0^{2,4}$]heptan-6-ol derivatives. A large rate enhancement was again found in the solvolysis of the corresponding p-nitrobenzoate consistent with homocyclopropyl participation.

Thus, the solvolytic and thermal reactions of the bicyclo[2.1.1]hexene system are entirely consistent with the expected behaviour for these molecules.

ACKNOWLEDGEMENTS

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INTRODUCTION

In recent years considerable effort has been directed towards the investigation of interaction between an incipient carbonium ion and a remote double bond[1] or cyclopropane ring[2]. Among the criteria used to implicate such a participation are solvolytic rate enhancement, stereospecificity of the product formation, and scrambling of isotopic labels in specifically labelled substrates[3]. Although the latter two effects have been observed in a comparatively large number of compounds, very large solvolytic rate enhancements associated with the presence of the double bond or cyclopropane ring in the substrate were reported in very few cases.

In order to gain a better understanding of the requirements necessary for an effective homoallylic and homocyclopropyl participation a study was undertaken in our laboratory. It is advantageous to carry out such studies on systems that are free of conformational flexibility. Because of the rigidity inherent to some bicyclic systems and the proximity of the double bond to the one carbon bridge, bicyclo[2.1.1]hex-2-ene derivatives appeared suitable for this purpose. In addition the inspection of models indicated that this strained system might undergo a [1,3]sigmatropic rearrangement with a carbon atom as a

migrating group. No examples of this type of reaction were known at the time this work was initiated. For these reasons a synthesis of a functionalized bicyclo[2.1.1]-hexene was developed in our laboratory. The homoallylic interaction between the double bond and the incipient carbonium ion was then investigated. Thermolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate was carried out and it indeed effected the carbon [1,3]sigmatropic shift[4]. Finally, a subsequent transformation of the bicyclo[2.1.1]-hexenyl acetate into an exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-ol derivative led to the study of homocyclopropyl participation in this system.

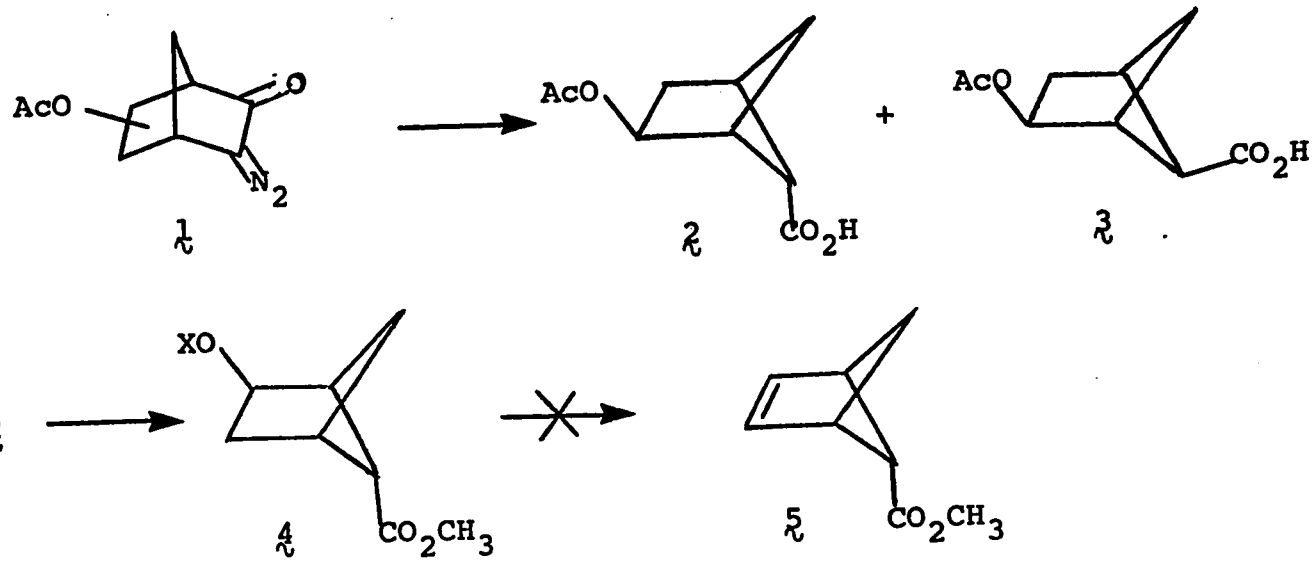
This thesis is divided into three parts. Part one describes synthetic studies; parts two and three deal with solvolysis and thermolysis of the above systems, respectively.

I. SYNTHETIC STUDIES

HISTORICAL:

At the outset of our studies no synthetic method was available for the preparation of bicyclo[2.1.1]hexene derivatives. On the other hand the chemistry of the saturated analogs had been explored to a considerable extent and a number of synthetic routes providing an entry into this highly strained system were well developed[5]. Before presenting our synthetic work, some of the studies, reported to date, on the syntheses of bicyclo[2.1.1]hexenyl derivatives are reviewed.

In 1966 Meinwald and Crandall[6] reported an attempted synthesis of a bicyclo[2.1.1]hexene derivative. Photolysis of an α-diazoketone (1) provided a mixture of two disubstituted bicyclic compounds (2,3), one of which (2) was in turn converted to the corresponding esters (4b-4d). Attempted pyrolytic elimination of acetate (4b), ethyl carbonate (4c), and methyl xanthate (4d) failed to afford the desired unsaturated compound (5). The authors suggested that the reluctance of the esters to undergo elimination was probably due to the strain of the double bond in the expected product (5).

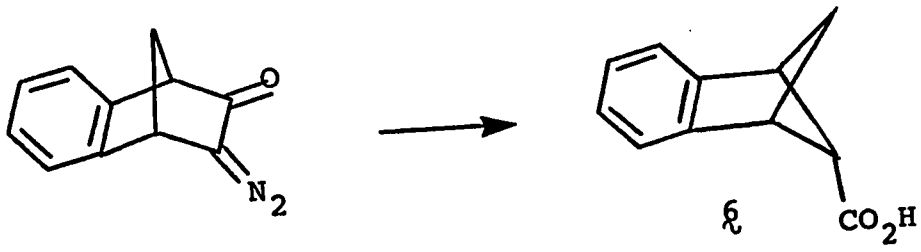


1 → 2 + 3

2 → 4 → ✗ 5

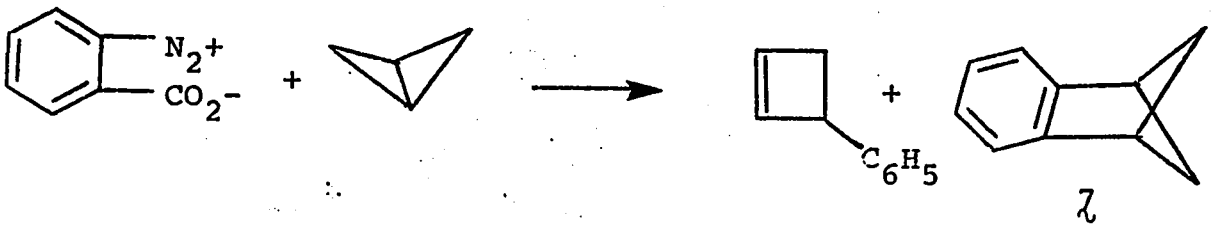
a X=H
b =$COCH_3$
c =CO_2Et
d =$CSSCH_3$

Tanida and Hata[7] in 1966 synthesized a substituted benzbicyclo[2.1.1]hexene (6) utilizing the synthetic scheme shown below.



The parent hydrocarbon (7) was also obtained in the same year by Pomerantz as a minor product of the addi-

tion of benzyne to bicyclobutane[8].



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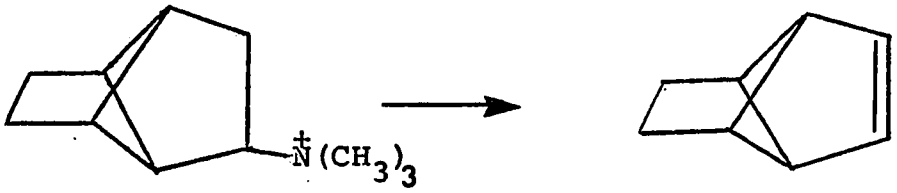
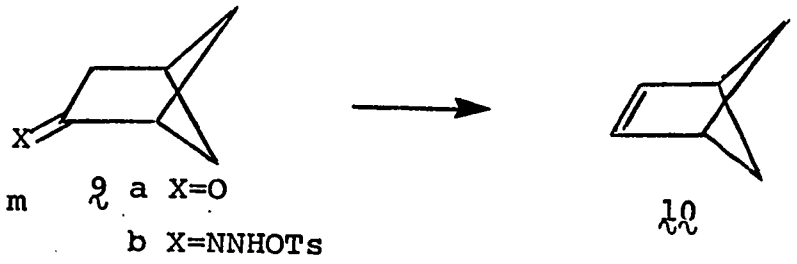
In 1967 Meinwald and Kaplan[9] obtained tricyclo [3.3.0.$0^{2,6}$]oct-3-ene (8), introducing a double bond into the system by the Hofmann elimination reaction.

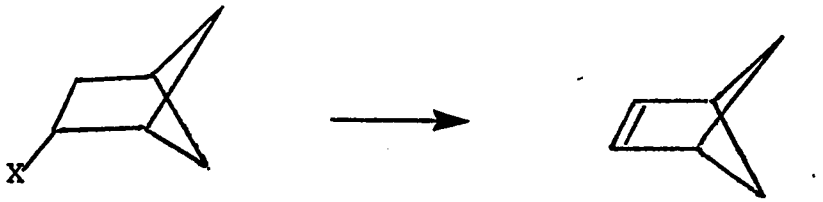


8

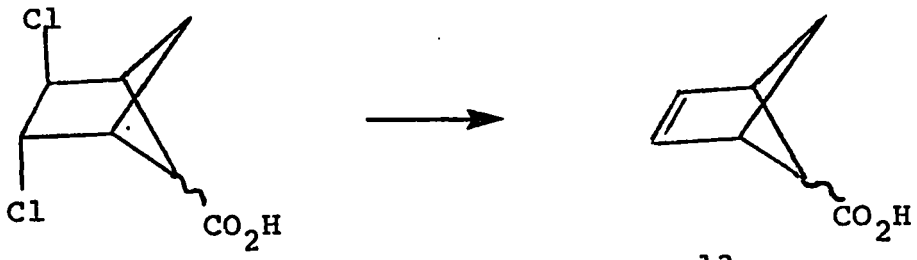
In the following year the same group[10] finally succeeded in synthesizing the parent hydrocarbon (10). The starting point of their synthesis was the bicyclic ketone (9a), prepared according to the method of Bond[11]. They first converted it into the tosylhydrazone (9b) which was then treated with methyllithium to afford the bicyclo-[2.1.1]hex-2-ene (10) in 25% yield.



In 1968 Bond and Scerbo[12] reported another route leading to the same hydrocarbon. The bicyclic ketone (9a) was first reduced to the alcohol (11a), which was subsequently converted to the bromide (11b) and dehydrobrominated.

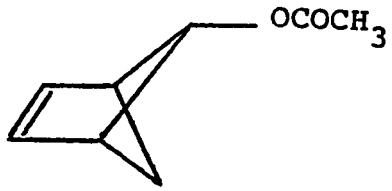


The synthesis of some 5-substituted bicyclo-[2.1.1]hexene derivatives (13) was accomplished in 1968 by Wiberg and Ubersax[13]. They prepared exo- and endo-trans-2,3-dichlorobicyclo[2.1.1]hexyl carboxylates (12) by standard methods. Dehalogenation by magnesium amalgam gave the product in good yield.



12 13

In 1969 the first preparation of a derivative of exo-bicyclo[2.1.1]hex-2-en-5-ol (14) was accomplished in our laboratory[4]. This compound possesses appropriate functional groups for the study of the interaction between the double bond and the incipient carbonium ion. This thesis describes the synthesis of this important compound as well as solvolytic and thermal behaviour of the system.

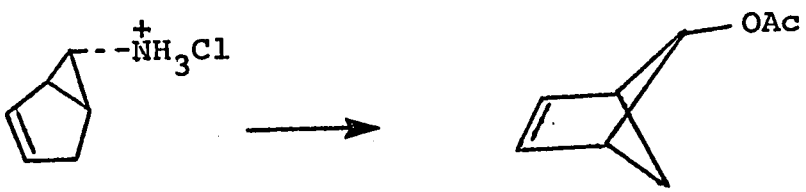


14

In the same year Roth and Friedrich[14] described the synthesis of exo- and endo-5-methylbicyclo[2.1.1]hexenes. They utilized the procedure developed earlier by Meinwald[10].

The most recent synthesis of this system involved

an interesting rearrangement[15]. Deamination of the exo-bicyclo[3.1.0]hex-2-en-6-yl ammonium chloride (15) in glacial acetic acid led to the formation of the exo-bicyclo [2.1.1]hex-2-en-yl acetate (14).

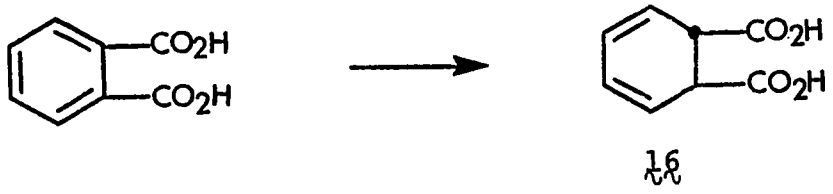


15 14

RESULTS AND DISCUSSION:

Two synthetic approaches to the bicyclo[2.1.1]-hex-2-ene system have been examined in our laboratory. The two schemes had a common feature, which consisted of initial preparation of an appropriately substituted bicyclo[2.2.0]hexyl system and its subsequent transformation into either a bicyclo[2.1.1]hexyl or a bicyclo[2.1.1]-hexenyl derivative. Consequently the initial set of reactions was the same for both approaches.

An easy entry into the bicyclo[2.2.0]hexenyl system was developed by van Tamelen and Papas[16].



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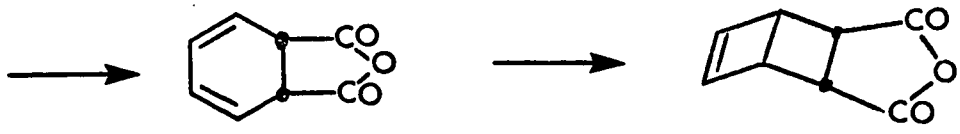
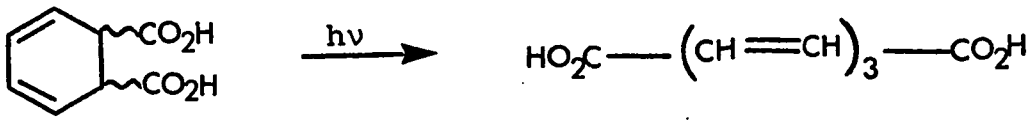


17 18

Utilizing the method of Bayer[16] they obtained trans-1,2-dihydrophthalic acid (16) in high yield by the reduction of o-phthalic acid with sodium amalgam in acetic

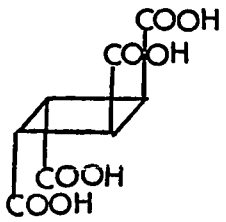
acid. Brief treatment of the trans diacid (16) with hot acetic anhydride effected epimerization and produced cis-1,2-dihydrophthalic anhydride (17) in good yield. The key step leading to the bicyclo[2.2.0]hexene system is the photoisomerization of the cis-1,2-dihydrophthalic anhydride (17). Irradiation of an ethereal solution of the anhydride (17) with a high-pressure mercury lamp using a Vycor filter produced, after purification, the bicyclo[2.2.0]hex-5-ene-2,3-dicarboxylic anhydride (18) in 22% yield.



19

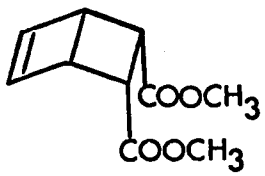
If the photolysis was performed on either cis- or trans-dihydrophthalic acid (19), a complex mixture of ring opened products was obtained. However, if the 1,2 positions in the cyclohexadiene system are bridged by a five membered anhydride, the conrotatory opening of the six membered ring could not compete favorably with the formation of a bicyclic product (18). The structure of the bicyclic anhydride (18) was deduced on the basis of spectral data and chemical transformations. Ozonolysis followed by oxidation transformed the bicyclic anhydride (18) into a known compound, cis,trans,cis-1,2,3,4-cyclobutane

tetracarboxylic acid (20).



20

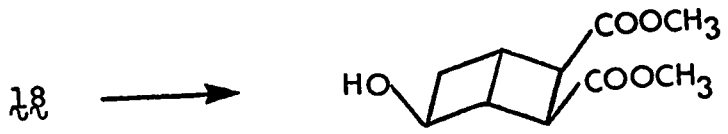
On the assumption that the oxidation reaction does not cause epimerization, this reaction establishes the stereochemistry of the ring fusion as cis, and also the exo orientation of the five membered anhydride ring. The exo orientation of the cis dicarboxylic acid derived from 18 was established by Masamune et al[17]. They found that the half methyl ester and the dimethyl ester of 18 were different from the half methyl ester and the dimethyl ester (21) of the stereoisomer obtained from cyclobutadiene and maleic anhydride.



21

The bicyclic anhydride (18) represented the starting point for our entry into the bicyclo[2.1.1]hexene system. Hydroboration of this material at -15°, followed

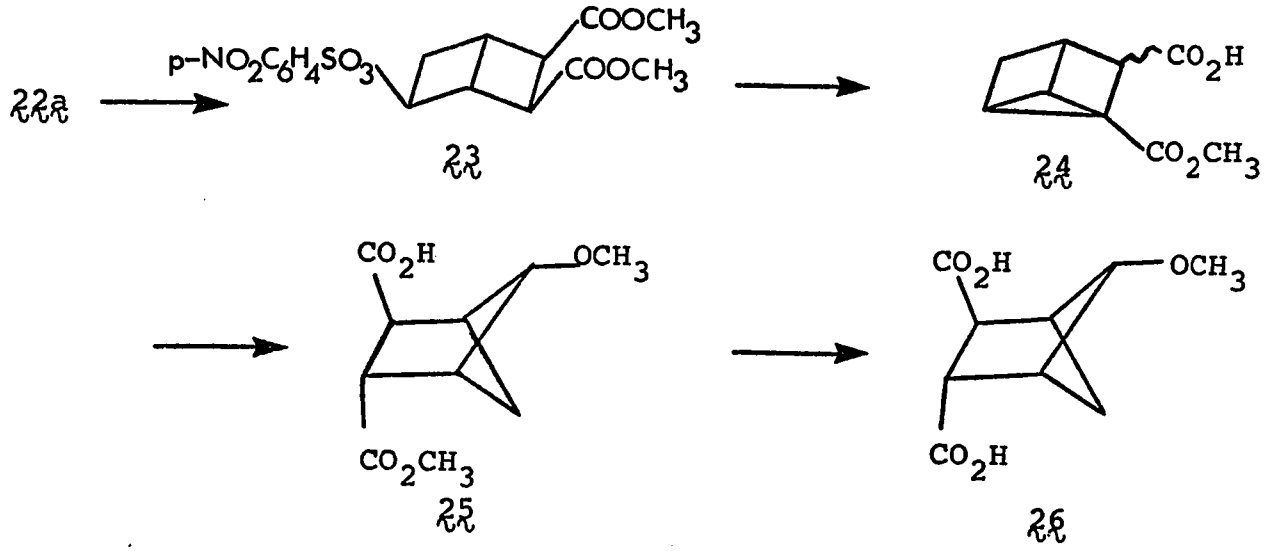
by treatment with alkaline hydrogen peroxide gave <u>exo-</u>-5-hydroxybicyclo [2.2.0] hexan-2,3-dicarboxylic acid (22) in good yield.



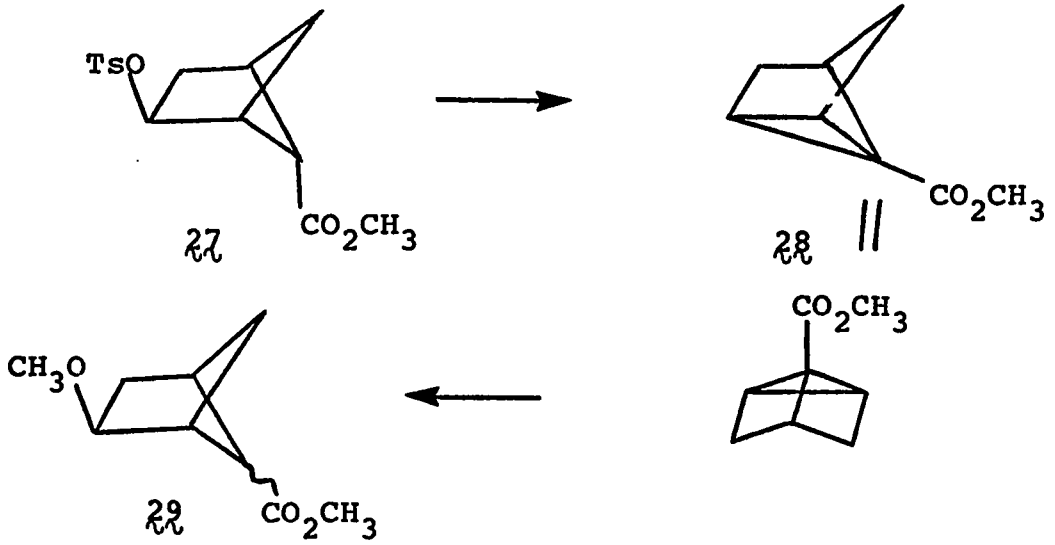
22

The stereochemistry of the substituents in this compound is discussed later.

Up to this point the reaction sequence was identical for both synthetic approaches. The following diagram illustrates the remaining steps of the first synthetic attempt, that was executed by Drs. Caine and Nakatsuka of our laboratory[17].



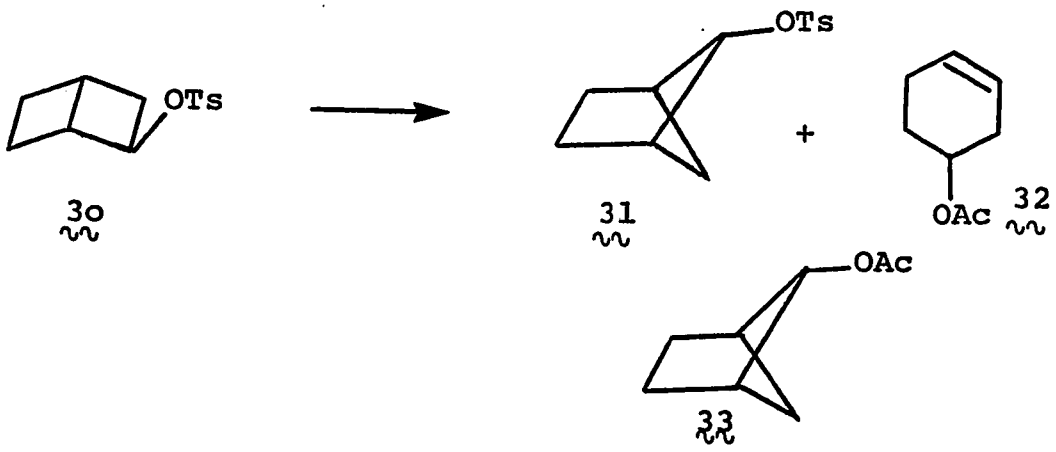
Esterification of the hydroxy diacid (22) with diazomethane, followed by treatment of the resulting dimethyl ester (22a) with p-nitrobenzenesulfonyl chloride and pyridine, afforded the p-nitrobenzenesulfonyloxy dimethyl ester (23). When treated with sodium methoxide in tetrahydrofuran at room temperature, the ester (23) underwent base catalyzed elimination of p-nitrobenzenesulfonic acid to afford the tricyclo[2.2.0.$0^{2,6}$]hexane-2,3-dicarboxylate (24). Prolonged heating of the tricyclic half ester with sodium methoxide in methanol brought about the nucleophilic cyclopropane ring opening, thus producing the exo-5-methoxybicyclo[2.1.1]hexane-2,3-dicarboxylic acid half ester (25). The formation of the tricyclic derivative and its subsequent opening have been described by Meinwald and Crandall[6]. In their study of base promoted elimination of endo-5-carbomethoxybicyclo[2.1.1]hex-anti-2-yl tosylate, they carried out the following reactions.



The treatment of the bicyclic tosylate (27) with base generates a carbanion at C_5, which has proper geometry for an intramolecular displacement of the p-toluenesulfonate, yielding a tricyclic ester (28). The action of sodium methoxide on the tricyclic ester (28) represents a nucleophilic addition to a cyclopropyl conjugated carbonyl system and gives a mixture of two epimeric bicyclic esters (29). The described sequence of reactions proceeded analogously with the trisubstituted bicyclic derivative (23) yielding the trisubstituted bicyclo[2.1.1]hexane derivative (25) that appeared suitable for the introduction of the unsaturation via a bis-decarboxylation reaction. Various decarboxylation reactions were performed on the exo-5-methoxybicyclo[2.1.1]hexane-2,3-dicarboxylate (26) without success. Nor did oxidation with lead tetraacetate in pyridine, with or without ultraviolet light, afford any of the desired unsaturated material. A new method for the alkene synthesis from vicinal dicarboxylic acids was developed in our laboratory[18] specifically for this purpose. It consists of either photolytic or pyrolytic decomposition of di-t-butyl peresters of dicarboxylic acids. Several olefins are produced in good yields. However, when the perester, derived from 26 was subjected to reaction conditions (Δ or $h\nu$) no desired unsaturated compound was

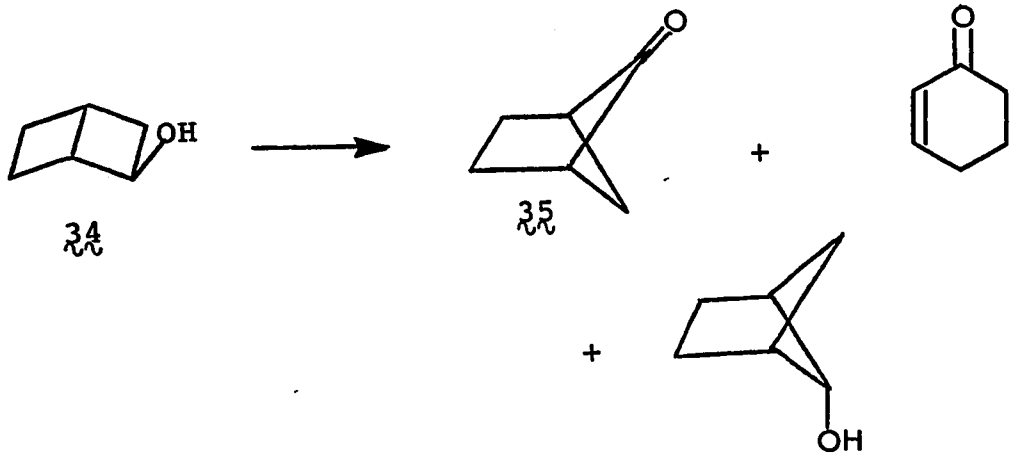
present in reaction products. Finally, the anodic oxidation of dicarboxylic acids was attempted, and likewise failed. Previously Meinwald and Crandall[6] had reported difficulties in introducing a double bond into a bicyclo [2.1.1]hexane derivative. They attributed the failure of the reaction to the strained character of the double bond in the product. The results may be in accord with their observation. At this point the above synthetic approach was abandoned.

At that time some reports appeared that made it increasingly clear that the bicyclo[2.1.1]hexyl or hexenyl cations might represent energy minima on the energy surface connecting some related carbonium ions. McDonald and Reinke[19] described a solvolytic study of exo-bicyclo[2.2.0]hex-2-yl tosylate (30) in acetic acid.



30 31 32 33

The product of ion pair return, exo-bicyclo[2.1.1]hex-5-yl tosylate (31), was formed in 53% yield. The mixture of acetates contained 41% of the acetate having the bicyclo [2.1.1]hexyl (33) skeleton. The predominant formation of the products having the bicyclo[2.1.1]hexyl ring indicates its greater stability, relative to bicyclo[2.2.0]hexyl system, under these reaction conditions. The same authors[20] observed a similar type of rearrangement in the attempted Oppenauer oxidation of exo-bicyclo[2.2.0]hexan-2-ol (34).

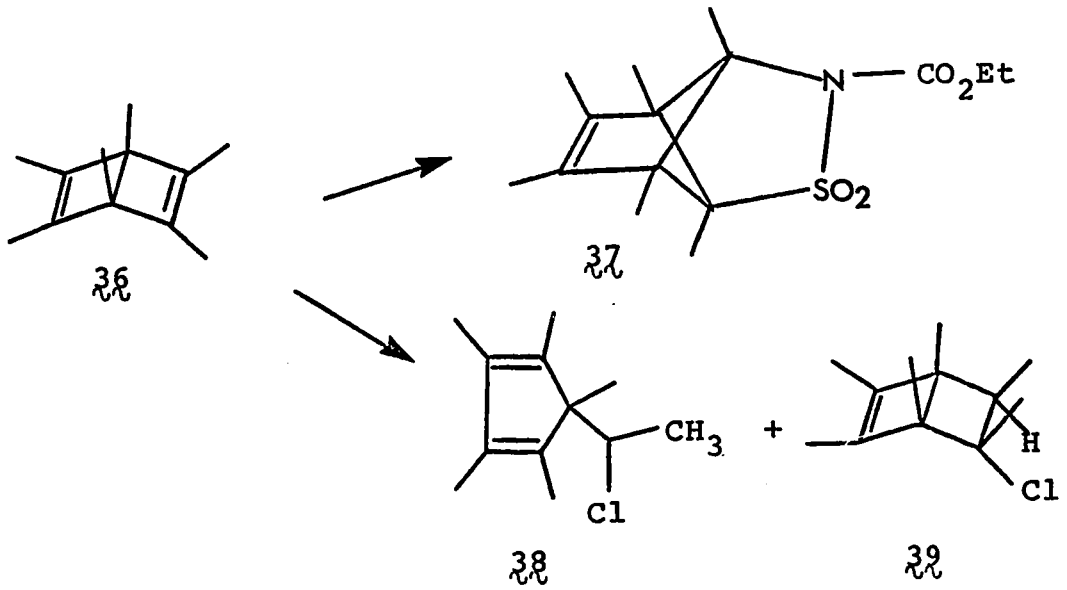


34 35

The major product (∿20%) was identified as the bicyclo [2.1.1]hexan-5-one (35). The other two products were obtained in a low yield (∿1%).

Subsequent reports on the chemistry of hexamethyl Dewar benzene indicated that under certain conditions rearrangements analogous to those observed in the bicyclo-

[2.2.0]hexyl system, take place in the unsaturated system as well. When the hexamethyl Dewar benzene (36) was treated with ethyl-N-sulfocarbamate, a 1:1 adduct (37) was formed[21]. The following structure was proposed on the basis of the NMR spectrum.

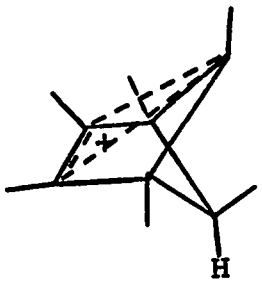


36 37 38 39

However, the treatment of the same starting material with hydrochloric acid produced a different type (38 and 39) of adducts[22].

Paquette and Olah and their coworkers[23] observed directly by NMR, cations derived from either hexamethyl Dewar benzene (36) or hexamethylprismane in fluorosulfonic acid-antimony pentafluoride solution at low temperatures. In either case a mixture of the two cations (40 and 41) was formed (3:1 ratio). The authors assigned the follow-

ing structures to the cations observed.



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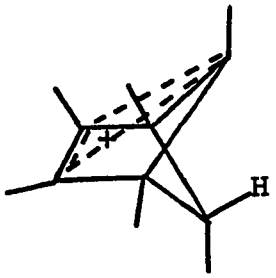
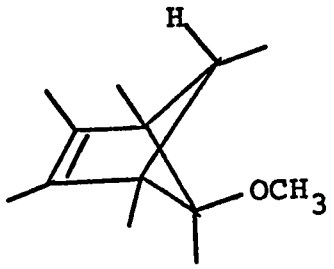


41

The spectra were temperature dependent. This was attributed to the interconversion of the isomeric cations. Additional evidence for the presence of the bicyclo[2.1.1]-hexenyl cations (40 and 41) was obtained by quenching the acidic solution at low temperatures, with excess of sodium methoxide in methanol. A mixture of two ethers was formed. The following structures (42 and 43) were assigned to these compounds on the basis of their NMR spectra.



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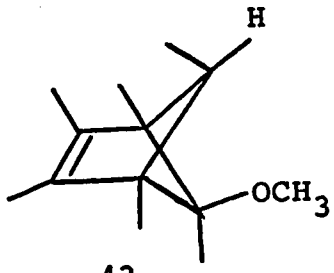
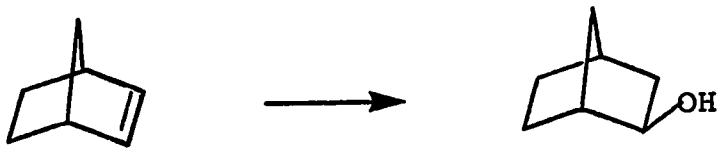


43

All these experimental observations suggested that an entry into the bicyclo[2.1.1]hexenyl system could

be gained by the solvolysis of the appropriate bicyclo-[2.2.0]hexene derivative. This then becomes the key of our second (successful) synthetic approach. As already mentioned, the hydroboration of the bicyclo[2.2.0]hexene-dicarboxylic anhydride (18) followed by the oxidation, afforded the exo-5-hydroxybicyclo[2.2.0]hexan-2,3-dicarboxylic acid (22). The exo configuration of the hydroxy group was assigned by the analogy with the hydroboration of norbornene (44) which gives exo-norborneol (45). Hydro-boration of the bicyclo[2.2.0]hex-2-ene (46) produces the corresponding alcohol (47) in which the hydroxy group is also exo oriented[19].



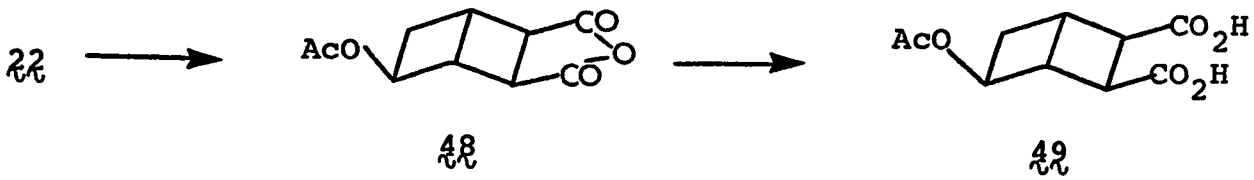
44 45

46 47

The hydroxydicarboxylic acid (22) was converted into its dimethyl ester (22a) by treatment with diazomethane. The following absorptions were observed in the NMR spectrum: τ 5.56 (t, 1 H), 6.12 (s, 1 H), 6.62 (s, 6 H)

and the additional absorptions at 7.05 and 7.53 each integrating for two protons. The triplet absorption at τ 5.56 provides further evidence for the exo orientation of the hydroxyl group, since it has the same multiplicity as that observed in the exo-bicyclo[2.2.0]hexan-2-ol. The endo-bicyclo[2.2.0]hexan-2-ol exhibits greater multiplicity for the absorptions of C-2 methine proton[24]. The NMR spectrum indicates that no epimerization of the carboxyl groups occurred during the hydroboration-oxidation reaction. If epimerization had occurred the methyl protons of the carbomethoxy groups would no longer absorb at the same field positions. The observation that the methyl protons resonate as a sharp singlet at τ 6.62 supports their exo (cis) orientation.

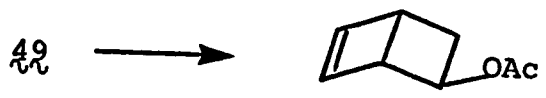
It was found convenient not to purify the hydroxydicarboxylic acid (22), after the hydroboration reaction, but rather to proceed with subsequent steps and effect the purification at a later stage.



Treatment of 22 with acetic anhydride and pyridine, followed by the removal of excess reagents, afforded crude exo-5-acetoxybicyclo[2.2.0]hexane-2,3-dicarboxylic anhydride (48). The NMR data fully support this structure. The IR spectrum exhibited absorptions at 1860 cm^{-1} (w) and 1785 cm^{-1} (s), with a pattern characteristic of a cyclic (5-membered) anhydride, and at 1740 cm^{-1} indicating the presence of an ester group.

Treatment of the acetoxydicarboxylic anhydride 48 with water at 80° followed by chromatography and crystallization provided an acetoxydicarboxylic acid (49) in good yield. The NMR spectrum exhibited all the features expected, and its similarity to that of the corresponding hydroxydimethyl ester (22a) leave no doubt that both the acetoxy and the two carboxyl groups are exo oriented.

Transformation of the acetoxydicarboxylic acid (49) into the exo-bicyclo[2.2.0]hex-5-en-2-yl acetate (50) could be effected in two ways.



50

Initially the oxidative bis-decarboxylation with lead tetraacetate[25] was employed giving product yields of 40%.

Subsequently the decarboxylation was improved using anodic oxidation, according to the procedure of Westberg and Dauben[26]. This method afforded the desired product (50) in 60% isolated yield. The NMR spectrum was in full accord with the expected structure and exhibited the following signals: τ 3.67 (m, 2 H), 5.28 (t, 1 H), 6.67 (m, 2 H), 7.87 (m, 2 H) and 7.99 (s, 3 H).

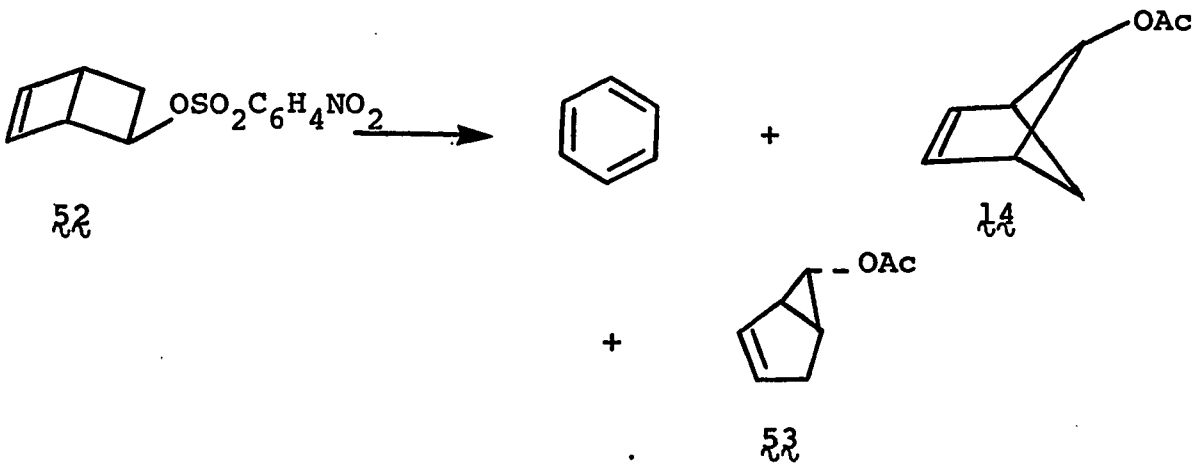
The only modification required at this stage was the replacement of the acetoxy substituent in 50 with some better leaving group. This was achieved by treatment of acetoxybicyclo[2.2.0]hexene (50) with lithium aluminum hydride, or even more conveniently with methylmagnesium iodide. The hydroxy derivative (51) thus obtained was not isolated but the ethereal solution after concentration and drying, was treated directly with p-nitrobenzenesulfonyl chloride and pyridine at 0°.

50 → 51 → 52

The exo-bicyclo[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate (52) was purified by chromatography and crystallization. An NMR spectrum exhibited the following signals: τ 1.65 (q, 4 H), 3.56 (t, 1 H), 3.79 (t, 1 H), 5.17 (t, 1

H), 6.55 (m, 2 H) and 7.78 (t, 2 H). The two olefinic protons of 52 which showed as a broad multiplet in the NMR spectrum of the corresponding acetate 50, have different chemical shifts (τ = 3.56 and 3.79).

Bicyclo[2.2.0]hexenyl p-nitrobenzenesulfonate (52) was solvolyzed in acetic acid[27] containing two equivalents of sodium acetate. It liberated the theoretical amount of p-nitrobenzenesulfonic acid and the first order rate constants were determined (see kinetic part). The product distribution was found to vary with the reaction time.



52 14 53

When the solvolysis was quenched at 50% completion the product mixture consisted of the starting material 52 (50%), benzene (5%), and the two acetates 14 and 53 formed in 32% and 11% yields, respectively. Minor products (~2%) were

also present. However if the reaction time was extended, and the solvolysis carried out for eight half-lives the major product, formed in more than 90% yield, was 53 indicating that the thermal conversion of 14 to 53 was taking place under these reaction conditions. By recycling the starting material 52 the major product 14 could be obtained in ca. 50% combined yield.

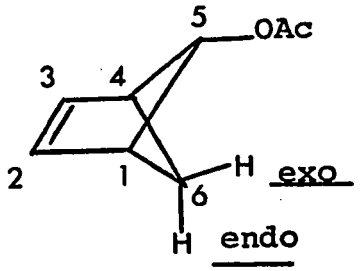
The major solvolysis product 14 was identified as exo-bicyclo[2.1.1]hex-2-en-5-yl acetate, whereas the minor product 53 was shown to be exo-bicyclo[3.1.0]hex-2-en-6-yl acetate. These structural assignments were made on the basis of spectral and chemical evidence. The NMR spectrum of 14 taken in CCl_4 exhibited the following signals: τ 3.27 (t, 2-3 H), 5.31 (d, J = 6.6 Hz, 5-endo-H), 6.76 (m, 6-exo-H), 7.42 (q, 1-,4-H), 7.72 (dd, J = 6.6 and 5.7 Hz, 6-endo-H), and 7.98 (s, acetate).

A number of spectra of bicyclo[2.1.1]hexyl derivatives have been described[28]. Features characteristic of the compounds having an exo oriented substituent are: the long range coupling constant, between the 5-endo and 6-endo protons, and a unique geminal coupling constant between the 6-endo and 6-exo protons. These features are present in the spectrum of the acetate 14. Thus the 5-endo proton exhibits a doublet (long range J = 6.6 Hz) and

6-endo proton appears as a doublet of doublets. It is coupled to the 5-endo proton with a long range coupling constant of 6.6 Hz and to the 6-exo proton with a geminal coupling constant of 5.7 Hz. This interpretation of the NMR spectrum is supported by the results of spin decoupling experiments that are summarized in the following table.

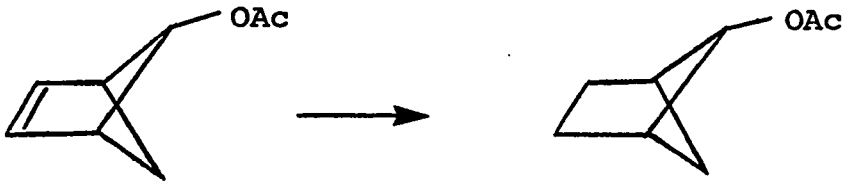
Table 1

Proton Irradiated	Chemical Shift and Multiplicity				
	$H_{1,4}$	$H_{2,3}$	H_5	H_6 endo	H_6 exo
None	7.42q	3.27t	5.31d (J=6.6 Hz)	7.72dd J=6.6 and 5.7 Hz	6.76m
$H_{2,3}$	d	--	--	--	--
$H_{1,4}$	--	s	--	--	--
H_5	--	--	--	d(J=5.7 Hz)	--
H_6 endo	--	--	--	--	t
H_6 exo	--	--	--	d(J=6.6 Hz)	--



All these spectral data are uniquely accommodated by the exo-bicyclo[2.1.1]hex-2-en-5-yl acetate structure.

Finally catalytic hydrogenation of 14, with platinum oxide in methanol, afforded the corresponding dihydro compound (33), which was found to be identical with an authentic sample of exo-bicyclo[2.1.1]hex-5-yl acetate[19]. All these results established the structure and stereochemistry of the major acetolysis product.

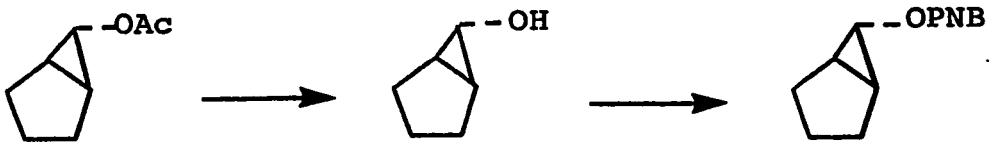


14 33

The structure and stereochemistry of the other acetate product (53) were also determined in a similar way. A sample of the acetate 53 was obtained by carrying out the acetolysis of the bicyclo[2.2.0]hexenyl p-nitrobenzoate (52) for 10 half-lives. At this reaction time 53 becomes the major reaction product (>90%). An NMR spectrum exhibited the following signals: τ 4.2 (m, 1 H), 4.5 (m, 1 H), 6.67 (bs, $W_{\frac{1}{2}}$ = 3 Hz, 1 H), 7.5 (m, 2 H), 7.9 (m, 1 H), 8.0 (s, 3 H) and 8.25 (m, 1 H). The spectrum is indicative of bicyclo[3.1.0]hex-2-en-6-yl acetate

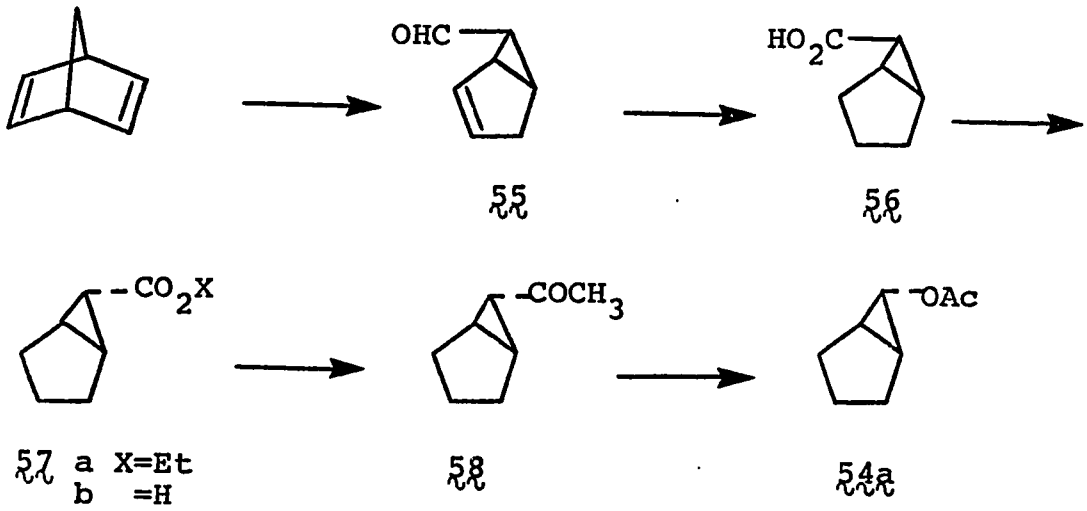
and the stereochemistry of the acetoxy group can be determined by the magnitude of coupling constants of cyclopropane protons[29]. It is known that spin-spin coupling constants of cis protons in the three membered ring are larger than those of the trans protons[30]. The observation that the C_6 hydrogen absorbs at τ 6.67 as a broad singlet ($w_{\frac{1}{2}}$ = 3 Hz) is strongly indicative of the exo configuration of the acetoxy group. This argument was further strengthened by examination of the NMR spectrum of the epimeric endo-bicyclo[3.1.0]hex-2-en-6-yl acetate (62), which was subsequently synthesized. The C_6 proton was found to absorb at τ 6.08 as a triplet with a cis coupling constant of 6.0 Hz.

Catalytic hydrogenation of the exo-bicyclo acetate (53) with Adams catalyst in methyl acetate provided the corresponding dihydro compound (54a). Treatment of 54a with methyllithium gave the 6-hydroxy compound[29] (54b) that was converted into the corresponding p-nitrobenzoate (54c).



54a 54b 54c

The acetate (54a), the hydroxy compound (54b) and the p-nitrobenzoate (54c) were all found to be identical with the corresponding authentic samples, that were prepared in the following manner:



Meinwald and his coworkers[31] have demonstrated that the peracid oxidation of bicyclo[2.2.1]heptadiene gives endo-6-bicyclo[3.1.0]hex-2-enecarboxaldehyde (55). Oxidation with silver nitrate, followed by catalytic hydrogenation provides the corresponding endo-carboxylic acid (56). Esterification of the acid by diazomethane and treatment of the resulting ester with sodium ethoxide in ethanol provides the epimeric exo-6-bicyclo[3.1.0]hex-2-enecarboxylic ester (57a). The ethyl ester was prepared according to the reported procedure and hydrolyzed and the

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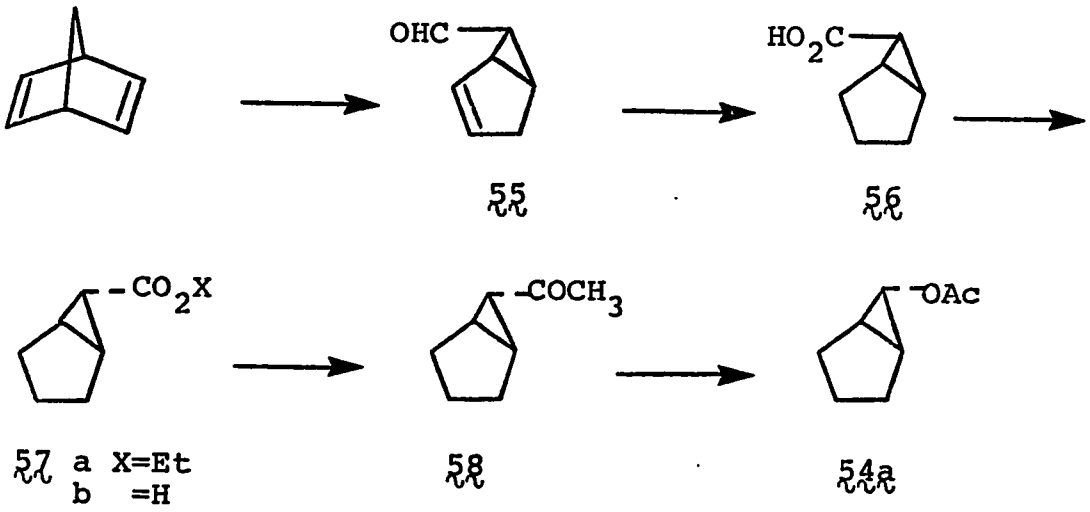

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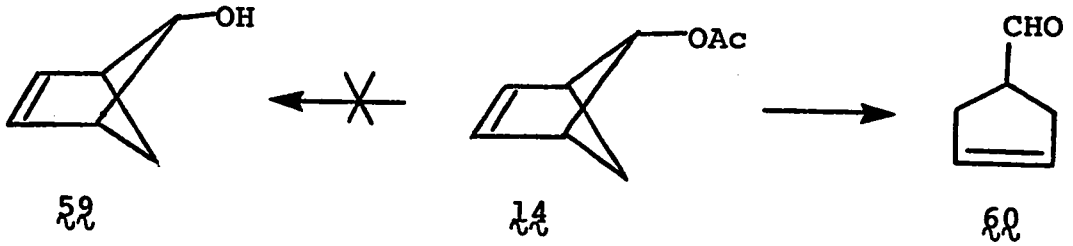
resulting acid (57b) converted into the methyl ketone (58) by treatment with methyllithium. Baeyer-Villiger oxidation[32] of the ketone yielded the exo-bicyclo[3.1.0]hex-6-yl acetate (54a) that was identical with the hydrogenated acetolysis product. The synthetic acetate was converted into the corresponding p-nitrobenzoate by the sequence of reactions already represented (53a - 53c). Identical NMR spectra of the compounds (54a, 54b, 54c) from the two different sources and absence of the melting point depression of the mixture of p-nitrobenzoates (53c) confirm the initial structural assignment.

After the successful preparation of the exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14) our intention was to convert it into a derivative suitable for the solvolytic study. The conversion of the acetate (14) into the corresponding hydroxy derivative (59) was therefore attempted.

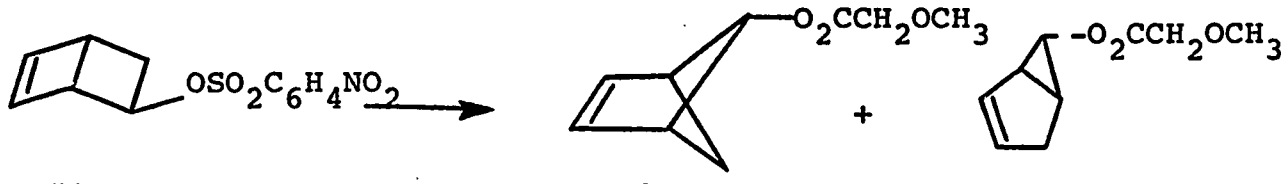


59 14 60

Treatment of the acetate 14 with potassium hydroxide in

methanol or methylmagnesium iodide in ether provided no desired hydroxy derivative (59). In both attempts the formation of Δ^3-cyclopentenecarboxaldehyde (60) was evident, reflecting the extreme instability of the hydroxy compound (59). The structure of the aldehyde was assigned on the basis of its NMR spectrum.

Preliminary experiments indicated that the solvolysis of the exo-bicyclo[2.1.1]hex-2-en-yl acetate in d_4-acetic acid proceeded slowly compared to its transformation into bicyclo[3.1.0]hexenyl acetate (53) and no kinetic data could be obtained for the solvolytic ester exchange reaction. Since the derivative suitable for solvolysis could not be obtained via the corresponding hydroxy compound (59), another approach was examined. The bicyclo-[2.2.0]hexenyl p-nitrobenzenesulfonate (52) was solvolyzed in methoxyacetic acid in the presence of two equivalents of sodium methoxyacetate. At 87° the solvolysis proceeded in a manner similar to the acetolysis of 52 and provided the exo-bicyclo[2.1.1]hex-2-en-5-yl methoxyacetate (61) as a major product.

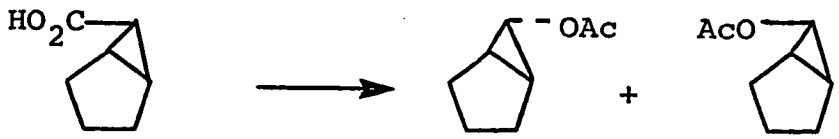


52 61

An NMR spectrum of 61 was very similar to that of 14, except for the signals due to the methoxyacetate group. It was expected that, since the methoxyacetic acid is a stronger acid than the acetic acid, the solvolysis of exo-bicyclo[2.1.1]hexenyl methoxyacetate (61) would proceed at a greater rate than that of the corresponding acetate (14). At the same time the thermolysis rates of the two esters were expected to be of the same order of magnitude, which would allow solvolytic study of the bicyclo[2.1.1]-hexenyl derivative. These expectations were borne out by subsequent experiments which provided the kinetic parameters for the acetolysis of the methoxyacetate (61) (see solvolysis section). The methoxyacetate (61) on acetolysis produced exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14) as the sole solvolysis product. This material was identical with an authentic sample of the bicyclic acetate (14).

In order to investigate fully the mechanism of thermal isomerization of the exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14) into the exo-bicyclo[3.1.0]hex-2-en-6-yl acetate (53) it became desirable to prepare the endo-bicyclo[3.1.0]hex-2-en-6-yl acetate (62). Initially a modification of the synthetic scheme that was utilized for the preparation of exo-bicyclo[3.1.0]hex-6-yl acetate (54a)

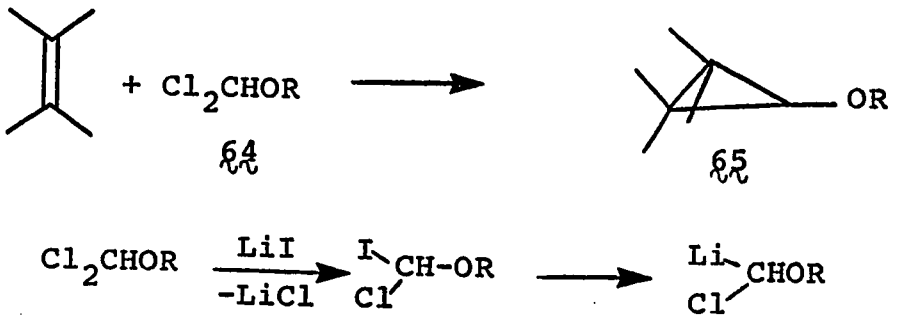
looked promising. Model reactions were therefore performed on the following dihydro compounds:



56 54a 63

The endo-bicyclo[3.1.0]hexane-6-carboxylic acid (56) was prepared as already described (see page 28). Treatment of the carboxylic acid (56) with methyllithium followed by the Baeyer-Villiger oxidation, afforded a mixture of the two acetates (54a, 63). The material obtained was largely epimerized as indicated by the NMR spectrum of the mixture which showed the presence of 64% of exo- (54a) and 36% of endo-bicyclo[3.1.0]hex-6-yl acetate (63). Subsequent reinvestigation showed that the epimerization occurred in the reaction of the carboxylic acid (56) with methyllithium. The formation of the carbanion at C_6 by the action of methyllithium, under equilibrating conditions, could bring about the predominant formation of the thermodynamically more stable exo- isomer (54a). Due to this difficulty, the described sequence was not applied to the unsaturated carboxylic acid (55), but another synthetic approach was sought.

Schöllkopf and his coworkers[29] developed a very useful synthetic method for preparation of cyclopropanols. It consists of the treatment of dichloromethyl ethers (64) with an ethereal solution of methyllithium in the presence of olefinic substrates, to give alkoxycyclopropanes (65) in good yields.

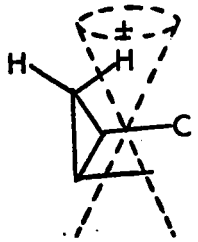


As indicated in the mechanism proposed for the formation of the intermediate the presence of lithium iodide in the reaction mixture is essential. The exact nature of the intermediate involved in this reaction is not quite clear, but it seems likely that the lithium carbenoid complex is involved[33]. By studying the additions to a number of unsymmetrical olefins it was indicated that a subtle interplay of electronic and steric factors in the transition state is responsible for the stereoselectivity of the

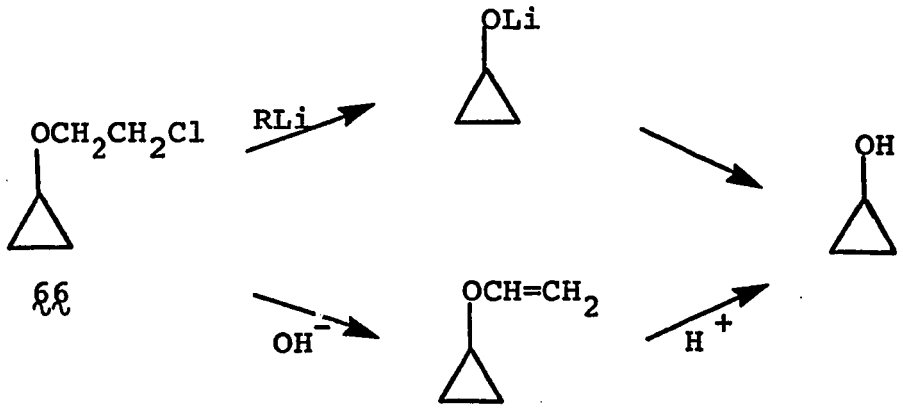
reaction. In the open chain olefins the endo addition to give cis cyclopropanes is always predominant. In cyclic olefins the situation is more complex and depends on factors influencing the stability of the transition state. Thus the "methoxycarbene" gives predominantly syn isomers with cyclopentadiene and cyclooctene, whereas with cyclohexene and cycloheptene anti isomers predominate. The author provided the rationale for this type of behaviour in the following way. In the electrophilic addition of the carbene to the double bond, electronic effects favour the formation of the syn adduct, due to the attractive coulombic interactions between the oxygen of the carbenoid species and the partial positive charges induced on adjacent alkyl groups (cyclopentadiene, open chain olefins, cyclooctene). However, the situation may be reversed by the increasing steric demands of the olefinic substrates, as demonstrated by the predominant formation of anti adducts in some cases (cyclohexene, cycloheptene). Obviously this rationale demands further experimental support.

The configuration of the adducts can easily be established by the examination of coupling constants of the cyclopropane protons ($J_{cis} > J_{trans}$). In addition the configuration can be established on the basis of the observation that the cyclopropyl protons (gem to the substitu-

ent) in the anti isomers absorb at a higher field in the NMR than the corresponding protons in the syn isomers[34]. This is attributed to the fact that the cyclopropyl proton cis to a C-C bond is anisotropically shielded (see the following diagram).

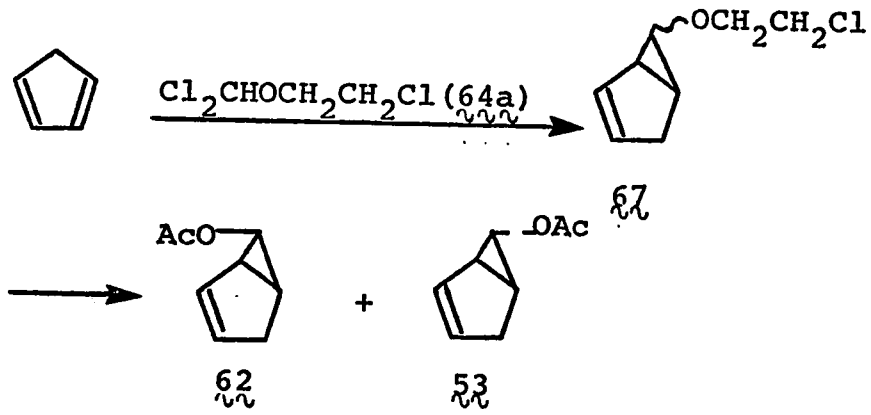


Particularly useful for the preparation of cyclopropanols is the synthesis of the β-chloroethylcyclopropyl ethers (66). These ethers can be transformed to cyclopropanols by treatment with base and acid, or more conveniently with n-butyllithium[34].



66

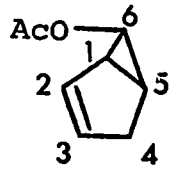
When the dichloromethyl-β-chloroethyl ether (64a) was treated with an excess of methyllithium at 0°, in the presence of cyclopentadiene a mixture of the two adducts was formed. The endo adduct was a predominant product (ca. 2:1). The mixture of the β-chloroethylcyclopropyl ethers (67) was treated with n-butyllithium and the resulting alcohols were acetylated without isolation. The acetate mixture consisted of endo-bicyclo[3.1.0]hex-2-en-6-yl acetate (62) (65%) and the epimeric exo-acetate (53) (35%).



An analytical sample of the endo-acetate (62) was obtained by preparative glpc. The results of spin decoupling experiments are presented in the following Table. The endo-C_6 proton in exo-6-acetoxy[3.1.0]hex-2-ene (53) absorbs at τ 6.67 as a broad singlet ($w_{\frac{1}{2}}$ = 3 Hz), whereas the corres-

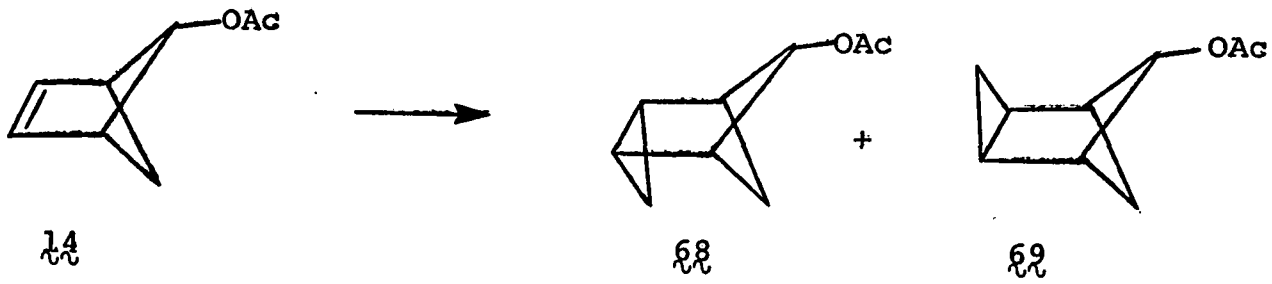
Table 2

Proton Irradiated	Chemical Shift and Multiplicity				
	H_1	$H_{2,3}$	H_4	H_5	H_6
None	7.82m	4.52m	7.52m	8.29m	6.08t J=6.0 Hz
H_6	changed	--	--	changed	--
H_1	--	--	--	--	d
H_5	--	--	--	--	--



ponding exo proton in the isomeric acetate (62) shows a triplet at lower field (τ 6.08, J = 6.6 Hz). This is in accord with the previous observation that in any given pair of cyclopropane derivatives J_{cis} is always larger than J_{trans}.

With the successful synthesis of exo-bicyclo-[2.1.1]hex-2-en-5-yl acetate (14) we turned next to the preparation of the exo-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl acetate isomers (68 and 69).



14 68 69

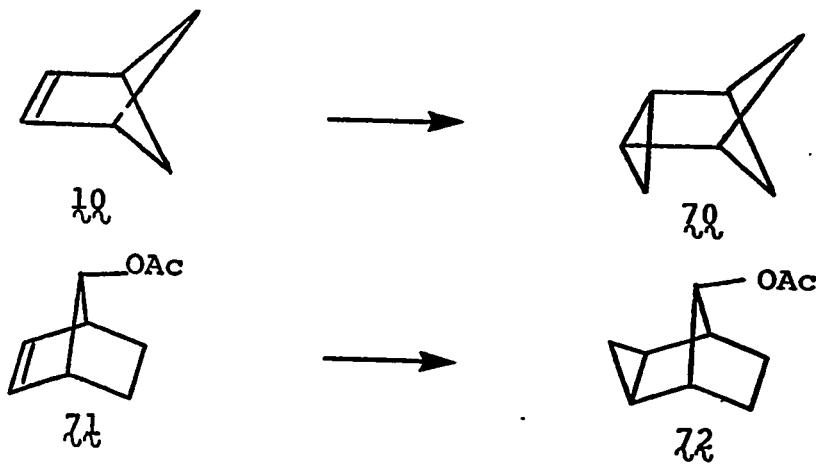
Of particular interest was the anti isomer (68) which has the proper geometry for homocyclopropyl participation[3], which we intended to investigate. The limited supply of the starting material demanded that the cyclopropanation reaction be very efficient. Because of the instability of the exo-bicyclic acetate (14) towards base as well as its thermal instability, the incorporation of a cyclopropane ring to the system had to be carried out under neutral and mild conditions. Therefore a number of model reactions were performed in search for the best reaction conditions.

It has been known for a long time that the reaction of olefins with carbenes results in the formation of cyclopropanes. With very reactive carbenes, produced photolytically, insertion and polymerizations compete with the desired addition reactions[35]. This makes such reactions impractical for synthetic purposes. However some carbenoid species possess moderate reactivity and give much higher yields of cyclopropanes. One commonly used

carbenoid source, used in the Simmons-Smith reaction[36], is obtained by reacting methylene iodide with zinc-copper couple. It is thought that the reactive species is bis-(iodomethyl)zinc iodide [$(ICH_2)_2Zn \cdot ZnI_2$]. Although this reagent has been very extensively used, in some cases it has been reported to produce adducts in low yields[37]. A reaction of norbornene with the Simmons-Smith reagent carried out in our laboratory, indicated that a long reaction time at ether reflux temperature was required for the production of the desired methylene adduct in a high yield.

Another more reactive carbenoid species is formed from diazomethane in the presence of copper salts[38]. This reagent has not been as widely used and the mechanism of its action is less well understood. The Pincock and Wells[39] modification of this reaction, which keeps the concentration of diazomethane low at all times, minimizes the danger involved in handling diazomethane. Again norbornene was used as a model substrate and after 10 hours a mixture of the starting material and the product was isolated in essentially quantitative yield. The mixture contained 97% of the tricyclo[3.2.1.$0^{2,4}$]octane, which was identified by its NMR spectrum[40]. When bicyclo[2.1.1]hexene (10) prepared by the method of Meinwald and Uno[10] was exposed to the same reagent, the corresponding tricyclic hydrocarbon

(70) was produced in essentially quantitative yield.



10 70

71 72

The following signals were observed in the NMR spectrum: τ 7.70 (m, 2 H), 8.02 (m, 1 H), 8.30 (m, 1 H), 8.55 - 8.75 (m, 3 H), 8.85 - 9.15 (m, 2 H) and 9.35 (m, 1 H). When the diazomethane was passed through an ethereal solution containing anti-norbornen-7-yl acetate[39] (71) the exo-tricyclo[3.2.1.$0^{2,4}$]oct-8-yl acetate (72) was formed in a good yield. All the products contained the high field multiplets in the NMR spectrum that are characteristic of cyclopropane protons. This method seems to be particularly useful for the cyclopropanation of olefins available only in a limited amount since the generation of diazomethane can be continued until the olefin has been totally consumed.

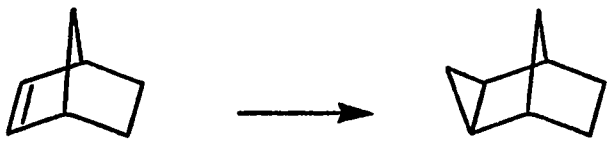
Another method for the preparation of cyclopro-

panes consists of photolysis or pyrolysis of pyrazolines[41]. Some pyrazolines can be prepared by the treatment of corresponding olefins with diazomethane[42], for extended periods of time at 0°. When norbornene was exposed to an excess of diazomethane in an ethereal solution the formation of the corresponding pyrazoline was evident and good yields could be obtained (80% after 100 hours). However, the preliminary experiments showed that the photolysis of the pyrazoline did not produce the desired product cleanly.

Of the methods tested, Pincock's modification of the copper salt-diazomethane reaction was found to be the most suitable for our purpose. Consequently this reaction was applied to a mixture of exo-bicyclo[2.1.1]-hex-2-en-yl acetate (14) and bicyclo[3.1.0]hexenyl acetate (53) in ether. The reaction was monitored by glpc and the generation of the diazomethane was stopped when all of the bicyclo[2.1.1]acetate (14) was consumed (about two hours). In that time the exo-bicyclo[3.1.0]hexenyl acetate (53) did not react to any significant extent. Molecular models indicate that the environment of the double bond in (14) is symmetrical and therefore a mixture containing equal amounts of the two isomers was expected. To our surprise only a single major product of longer retention time (glpc) was formed. Initially it was thought that the

two isomeric tricyclic acetates could not be resolved on the particular gas chromatography column used. However, attempts to resolve the "mixture" on various columns failed. This implied that the methylene addition reaction was proceeding in a highly stereoselective manner.

Reaction of carbenoids with olefins is known to be sensitive to the steric and electronic factors[35b]. Thus the Simmons-Smith reaction of particular allylic and homoallylic alcohols gives products in which the cyclopropyl ring is cis relative to the hydroxy group. It is known that in such cases initial complex formation of the carbenoid with the hydroxyl function occurs which leads to the reagent attacking preferentially on one side. Some other functions, such as methoxy and carbomethoxy, exhibit the same type of directive effect[33]. In other cases, particularly bicyclic and polycyclic olefinic substrates, the stereoselectivity of the reaction has been attributed to steric effects[33]. Thus the addition of the Simmons-Smith reagent[43], as well as CH_2N_2-CuCl, to norbornene produces exclusively the exo-tricyclooctane (73).



73

The absence of the endo adduct indicates very unfavorable steric interactions between the carbenoid and the endo protons on the ethylene bridge in a transition state that would lead to its formation. The situation is somewhat different in the norbornadiene case in which some of the endo adduct is formed[43]. The difference is presumably due to combination of the steric and electronic effects. Acetoxy substituents have been found not to exhibit any electronic directive effects. In fact the Simmons-Smith cyclopropanation of some cyclic allylic acetates has shown that the formation of products which have cyclopropyl ring trans to the acetoxy group[44] takes place. This was attributed to steric hindrance by the acetoxy group to the approach of the carbenoid from the cis side.

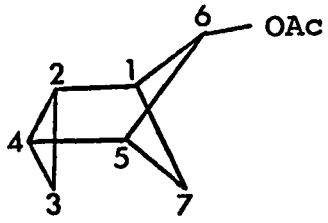
As was already mentioned, models indicate that both sides of the double bond are equally accessible in the exo-bicyclo[2.1.1]hexenyl acetate to the approach of the carbenoid. Since the acetoxy substituent is far removed from the reaction site it cannot provide any steric hindrance to the approach of the reagent. Consequently it was impossible to predict which of the two reaction pathways was preferred. The determination of the stereochemistry of the product is presented below.

An analytical sample of the tricyclic acetate was

separated by preparative glpc. The assignment of signals in the NMR spectrum of the tricyclic acetate (68 or 69) by decoupling techniques is summarized in the following Table.

Table 3

Proton Irradiation	Chemical Shift and Multiplicity					
	$H_{1,5}$	$H_{2,4}$	H_3	H_6	H_7 exo	H_7 endo
None	7.50m	8.72m	8.72m 9.40m	5.45d J=7.8Hz	8.02m	8.72dd J=7.8 and 9Hz
H_7 exo	--	--	--	--	--	dJ=7.8Hz
H_7 endo	--	--	--	s	--	--
H_6	--	--	--	--	--	dJ=9Hz

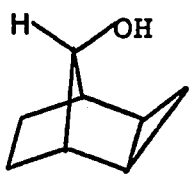


Some characteristic couplings observed in the bicyclo-[2.1.1]hexene were present[28]: C_6 endo proton is coupled to the C_7 endo proton by a long range coupling constant of 7.8 Hz. The geminal coupling constant between the C_7

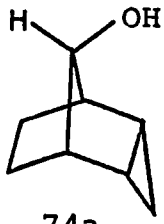
exo and endo protons is 9 Hz. The two methylene cyclopropane protons (3 cis and trans) have different chemical shifts. One appears as part of a three proton multiplet at τ 8.72 whereas the other resonates as a one proton multiplet centered at τ 9.40. The chemical shifts of these two protons have not been rigorously assigned; however, we feel that the trans H_3 should be assigned to the absorption at higher field. A proton in such a position experiences some shielding effect from the cis carbon-carbon bonds[34]. In some cases, when the two protons in question have distinct absorptions, the chemical shift was assigned on the basis of a peak width[45]. The broader signal was assigned the cis configuration which is in accordance with the expected coupling constants. However, in our case this consideration is not possible because one of the methylene cyclopropane absorptions is overlapping with the methine cyclopropane absorptions.

The configuration of the cyclopropane ring (syn or anti to the substituted bridge) could not be conclusively determined from the NMR spectrum. However, the following consideration led us to propose that the cyclopropyl ring was oriented anti to the substituted carbon bridge. The diamagnetic anisotropy of the cyclopropane ring which results in shielding of protons that are positioned above

the ring is a well known phenomenon. Thus Pincock and his coworkers[46] observed this effect in the isomeric endo- (74a) and exo-syn (74b) tricyclo[3.2.1.$0^{2,4}$]octan-8-ols.

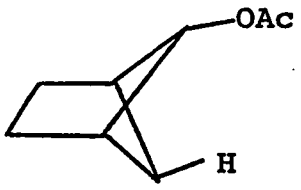


74b

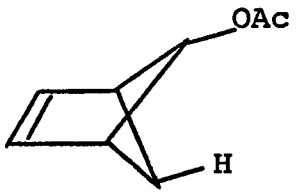


74a

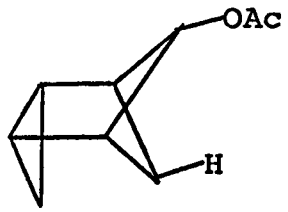
With the cyclopropyl ring exo oriented the bridge hydrogen was ca. 30 Hz farther upfield than in the corresponding endo compound. A similar effect was observed in the methylene adduct of the exo-bicyclo[2.1.1]hexenyl acetate.



33 τ 6.62



τ 6.76



τ 8.02

From the observed spectra of the bicyclo[2.1.1]hexyl derivative (33) it can be seen that the chemical shift of the exo C_6 proton is not considerably affected by the introduction of the double bond in the 2 position. The intro-

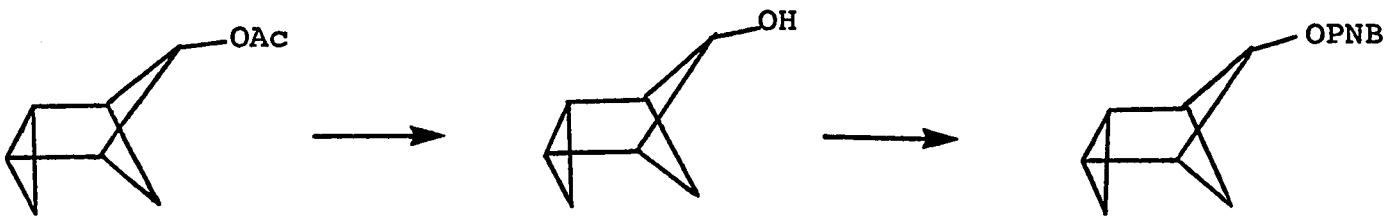
duction of the three membered ring into the molecule shifts the proton in question upfield by approximately 1.2 ppm. The direction of this shift is indicative of the anti orientation of the cyclopropane ring.

Examination of the solvolytic reactivity of the corresponding p-nitrobenzoate provided additional support to the proposed orientation of the three-membered ring. Subsequently an X-ray diffraction study was performed by J. Prudham of this department (under the supervision of Professor M. J. Bennett) on a sample of a tricyclic p-bromobenzoate and has established the orientation of the cyclopropane ring as anti. (See Appendix for X-ray data.)

With the stereochemistry of the cyclopropane ring established, let us consider once more the reason for the stereospecificity of the methylene addition reaction. Directive effects of electronic origin by the acetoxy group are not precedented. On the other hand the acetoxy group is too far removed from the reaction site to offer steric interference. Because of non-bonded interactions between the acetoxy group and the C_6 exo hydrogen atom it is possible that the C_5 bridge of the exo-bicyclo[2.1.1]hexenyl acetate (14) is distorted from "normal" geometry towards the double bond. This would in effect bring the C_5 endo hydrogen into closer proximity to the double bond and thus

could interfere with the approach of the carbenoid reagent from the syn side. Testing this proposal would involve an X-ray study of a crystalline exo-bicyclo[2.1.1]hexene derivative which could not be prepared. Some evidence that the stereospecificity is of steric origin was obtained from the reaction of exo-bicyclo[2.1.1]hexyl acetate (14) with diazomethane at 0°. Diazomethane addition to the double bond would presumably exhibit different electronic interactions than the carbenoid reagent but a single product was formed as indicated by vapour phase chromatography.

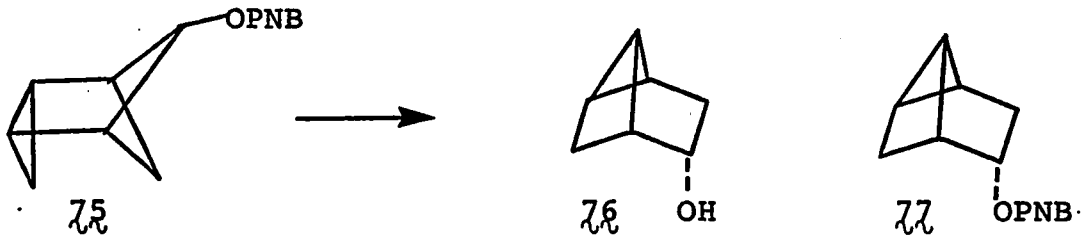
The treatment of an ethereal solution containing a mixture of bicyclo[3.1.0]hexenyl (53) and the tricyclic (68) acetates with methylmagnesium iodide produced a mixture of alcohols. After drying over molecular sieve (4A) the mixture was treated in the usual manner with p-nitrobenzoyl chloride and pyridine.



68 87 75

Chromatography and recrystallization from pentane afforded exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate (75). The IR spectrum exhibited characteristic absorption at 1722 cm^{-1} (ester), 1560 cm^{-1} and 1304 cm^{-1} (nitro group). The following signals were observed in the NMR spectrum: τ 1.75 (m, 4 H), 5.22 (d, 2 H, J = 8 Hz), 7.35 (m, 2 H), 7.90 (m, 1 H), 8.40 - 8.95 (m, 4 H) and 9.41 (m, 1 H). The resonance due to the 7-endo proton in this compound is partially obscured by overlap with the signal due to the three cyclopropyl protons.

The tricyclic p-nitrobenzoate ester (75) solvolyzed in 60% aqueous dioxane with liberation of ca. 0.76 equivalents of p-nitrobenzoic acid. The following products were formed.

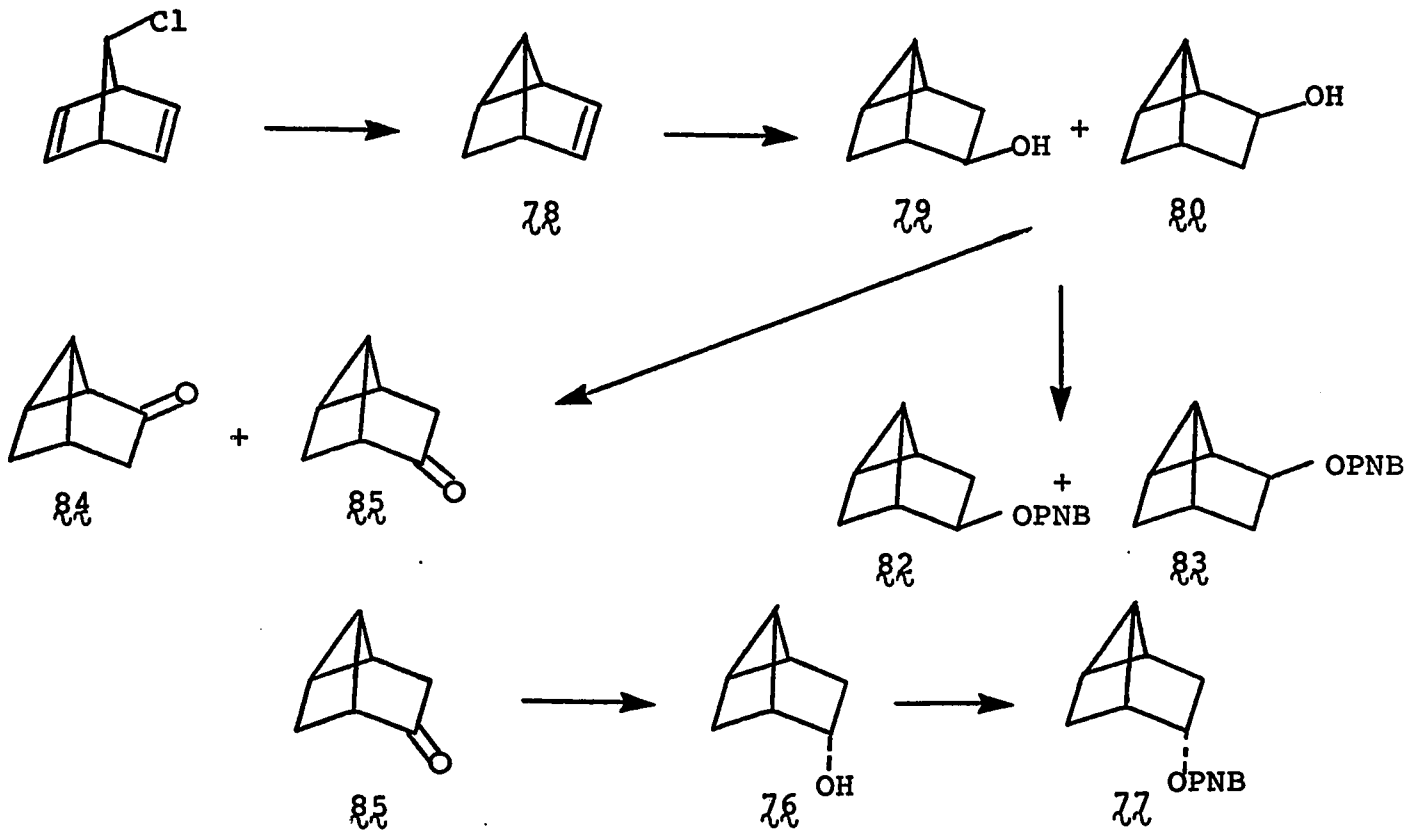


75 76 77

The alcohol (76) was separated by distillation from the solvent and the product of ion pair return (77) and compared with an authentic sample of endo-tricyclo[3.2.0.$0^{2,7}$]

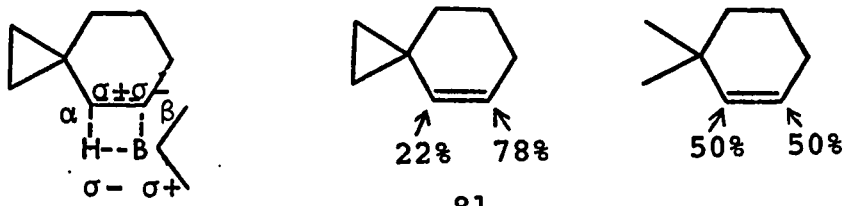
heptan-4-ol. The two were identical in every respect. An NMR spectrum taken in deuterochloroform exhibited the following signals: τ 5.62 (bm, w = 23 Hz, 1 H), 7.50 - 8.60 (m, 8 H) and 8.80 (m, 1 H). The endo orientation of the hydroxyl group is indicated by the similarity of the multiplicity of the C_4 methine proton absorption with those observed in norbornene derivatives with endo oriented substituents[47]. The proof of the stereochemistry of the hydroxyl group follows from the chemical sequence that was used for the preparation of authentic samples (vide infra). That the rearranged tricyclic ester (77) has the same carbon skeleton as the alcohol (76) was apparent from its NMR spectrum, which was identical with the one observed for an authentic sample of endo-tricyclo[3.2.0.$0^{2,7}$]hept-2-yl p-nitrobenzoate.

The authentic samples (76, 77) were prepared by an extension of the synthetic scheme used for the preparation of some tricyclo[3.2.0.$0^{2,7}$]heptane derivatives recently reported[48]. Norbornadien-7-yl chloride was converted into the tricyclic olefin (78) according to the procedure of Brown and Bell[49]. An analytical sample of the tricyclic hydrocarbon was separated by the preparative glpc and it exhibited an NMR spectrum similar to that reported[50].



However, for the subsequent reaction the hydrocarbon (78) was not isolated but was used directly in the hydroboration step. Hydroboration of the tricyclic hydrocarbon followed by the treatment with alkaline hydrogen peroxide afforded a mixture of two alcohols in 74:26 ratio (79, 80). The reason for the regioselectivity of the hydroboration reaction must be of electronic origin since the steric situation for the approach of the reagent to either side

of the double bond is similar. It is thought that the hydroboration reaction proceeds through a polarized transition state in which one of the factors controlling the product distribution is the electron releasing properties of the substituents on the double bond[51].



81

In the case of spiro-2,5-oct-4-ene (81), 78% of the boron attack occurs at the β position[52]. Transition state energy for the formation of such a product is decreased relative to the alternative transition state by the ability of the cyclopropane ring to stabilize an adjacent positive charge. Comparison with hydroboration of the 3,3-dimethylcyclohexene indicates that steric effects do not play an important role in the case of 81. The above argument rationalizes the finding of Lustgarten that exo-tricyclo-[3.2.0.$0^{2,7}$]heptane-4-ol is the major product of the hydroboration reaction. This reaction is expected to produce alcohols with the hydroxy group exo oriented which is

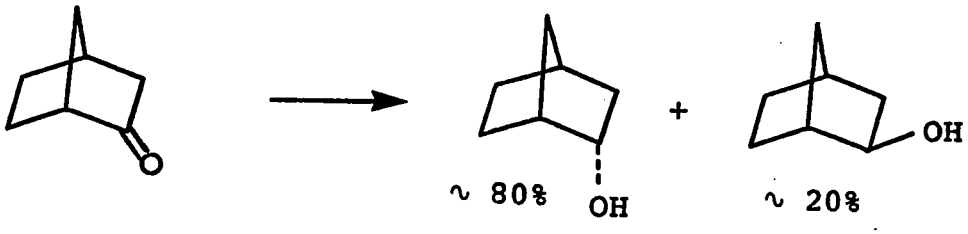
confirmed by the NMR spectrum. Analytical samples were separated by the preparative glpc and both C_3 (80) and C_4 (79) protons were found to exhibit relatively simple multiplicities (τ 5.37 t, 6.08 d) in the NMR. Such absorptions are characteristic of the exo oriented substituents in norbornene derivatives[47].

A portion of the mixture of the two alcohols was treated with p-nitrobenzoyl chloride and pyridine. After chromatography an oily mixture of the two esters was obtained (82, 83). An IR spectrum indicated the presence of an ester group (1715 cm^{-1}) as well as the nitro group (1527 cm^{-1} and 1298 cm^{-1}). The NMR spectrum was similar to the one observed for the mixture of alcohols except for the presence of the aromatic protons and the downfield shift of some absorptions associated with the introduction of an electronegative group into the molecule. The C_3 and C_4 methine protons resonate at 4.47 (t) and 4.95 (d) respectively. Although the two alcohols were separable by preparative glpc it was found convenient to proceed with the oxidation step and effect the separation at that stage. Oxidation with Collins reagent[53] afforded a mixture of two ketones (84, 85). They were separated by column chromatography (silica gel, hexane-benzene). Lustgarten[48] has previously identified the product of the oxidation of the

minor alcohol as tricyclo[3.2.0.$0^{2,7}$]hept-3-one (85) by comparing it with an independently synthesized sample. The major product (84) of the oxidation of the mixture of tricyclic alcohols isolated in this work, had a carbonyl absorption at 1735 cm^{-1} in the IR. The following signals were observed in the NMR: τ 7.35 (m, 5 H), 8.19 (m, 2 H), and 8.43 (q, 1 H).

Reduction of tricyclo[3.2.0.$0^{2,7}$]hept-4-one (84) with sodium borohydride in methanol produced a single product, along with some impurity. The NMR spectrum of the product differed from the one obtained for the exo tricyclic alcohol (79). The C_4 methine proton in the product resonates at τ 5.62 as a broad multiplet ($w_{\frac{1}{2}}$ = 23 Hz).

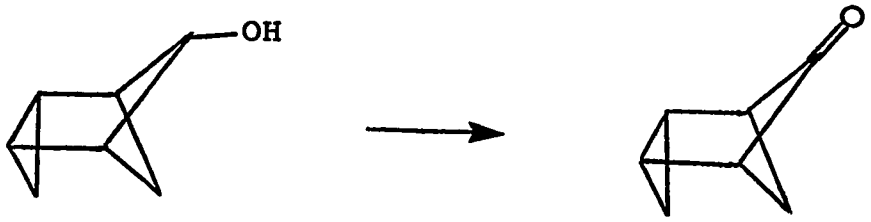
The presence of the exo isomer was not apparent in the NMR spectrum of the product. The exo isomer would be easy to detect in the NMR spectrum since the two types of C_4 methine protons appear at different chemical shifts. The sodium borohydride reduction was expected to proceed stereoselectively. It is known that metal hydride reductions of bicyclic rigid ketones are kinetically controlled[54].



Norbornan-2-one on reduction with sodium borohydride yields predominantly the endo alcohol. This is interpreted as the consequence of steric inhibition for the approach of the reagent from the endo side. Examination of models suggested that the endo approach is even more hindered in the tricyclic ketone (84), which resulted in the exclusive attack of sodium borohydride from the exo side to yield the endo alcohol (76). This synthetic material was compared with the alcoholic fraction of the solvolysis product and the two were found to be identical in every respect. Finally a sample of the endo alcohol (76) was treated with p-nitrobenzoyl chloride and pyridine to afford the corresponding ester (77). An NMR spectrum ($CDCl_3$) exhibited the following signals: τ 1.78 (m, 4 H), 4.70 (m, 1 H, $w_{\frac{1}{2}}$ = 23 Hz), 7.39 (m, 2 H), 7.75 (m, 2 H), 8.08 (m, 1 H), 8.40)m, 2 H), 8.69 (m, 1 H); and was found to be indistinguishable from the spectrum obtained for the product of internal return in the solvolysis of exo-anti p-nitrobenzoate ester (75).

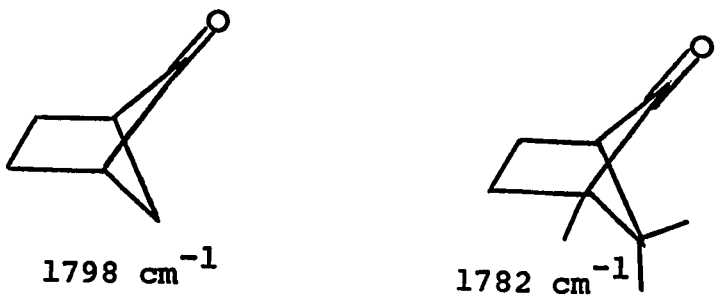
In order to estimate by Foote-Schleyer's method[55] the amount of anchimeric assistance to the ionization in the solvolysis of 75 a sample of the anti-tricyclo[3.1.0.$0^{2,4}$]heptan-6-one was needed. Collins oxidation[53] was therefore carried out on the mixture of alcohols which

contained the exo-anti tricyclic alcohol (87) as a major component. Several attempts resulted in the formation of a mixture of carbonyl compounds containing at least three different types of carbonyl absorptions in the IR spectrum. The desired tricyclic ketone was a very minor product as indicated by the low intensity of the absorption in the 1790 cm^{-1} region.



87 86

However, when the oxidation was effected by aluminum t-butoxide with p-benzoquinone as a hydrogen acceptor[56] in refluxing ether, the desired strained ketone (86) was the major product (strong carbonyl stretch at 1788 cm^{-1}). The carbonyl stretching at 1788 cm^{-1} was in agreement with the corresponding bands in the two related ketones[56, 57].



1798 cm^{-1} 1782 cm^{-1}

The NMR spectrum, except for some absorptions due to impurities, was in complete accord with the proposed structure.

II. STUDIES OF SOLVOLYSIS

HISTORICAL:

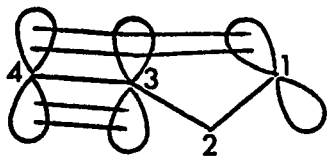
A. Homoallylic Cations

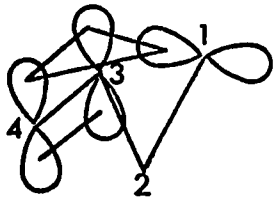
Various explanations have been put forward to account for the difference in the relative rate of formation of carbonium ion intermediates[58], as observed in solvolytic reactions. In some systems the relief of strain present in the ground state may provide the driving force for ionization. Another cause of lower activation energy of carbonium ion formation is resonance stabilization of the intermediate, as in allylic and benzylic cations. Systems in which this type of stabilization is possible have been found to exhibit enhanced rates of solvolysis, when compared with these saturated analogs.

Because of the striking rate enhancement and stereospecificity of product formation observed in some systems in which the above explanations do not apply, yet another mode of stabilization of carbonium ions was proposed: "nonclassical" carbonium ions[3]. These ions are formed by the overlap of the vacant p-orbital at the cationic centre with orbitals on carbon atoms that are not directly bonded to the formal positively charged centre. Orbitals participating in such charge delocalization may be of the σ and π type. In contrast to the resonance sta-

bilization, which is characterized by pure π overlap, the mode of interaction in nonclassical ions is intermediate between σ and π.

Some semi-empirical molecular orbital calculations, which consider 1,3 orbital interaction in homoallylic systems[59], suggest that such cations would be substantially stabilized. Other authors, by applying the same method, have shown that the stabilization would be even greater if both 1,3 and 1,4 interactions are taken into account[60].

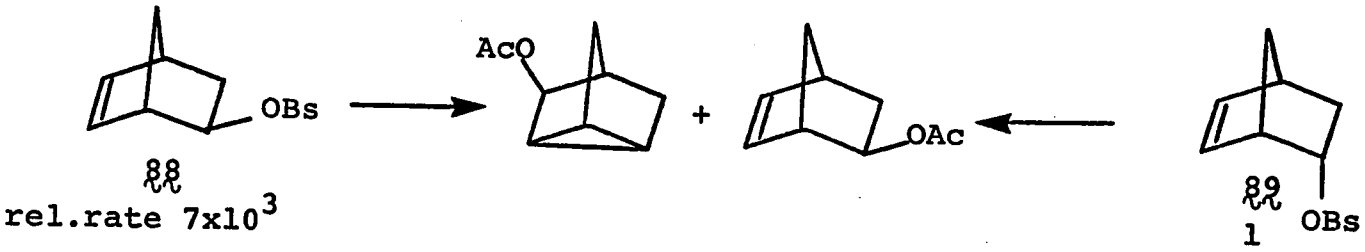




Of the numerous homoallylic systems that have been studied, the bicyclo[2.2.1]heptyl system was found to be particularly interesting. Some of these studies are discussed below.

Study of the rates of acetolysis of exo- and endo-norbornen-2-yl p-bromobenzenesulfonates has shown that the exo isomer (88) solvolyzes 7 x 10^3 times faster than the endo isomer[61] (89). The rate enhancement of the exo

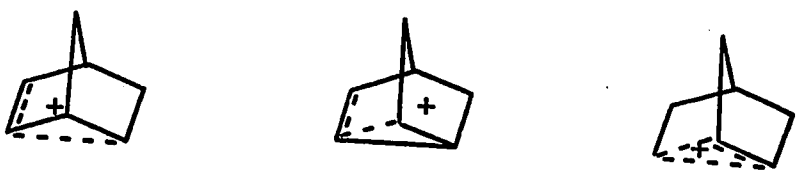
isomer is ascribed to homoallylic assistance during the initial ionization. Due to the unfavorable geometrical relationship between the double bond and the incipient carbonium ion in the endo brosylate such an interaction is prohibited. However, since both isomers give the same product distribution it was suggested that in the case of the endo ester such an interaction would occur subsequent to the rate determining ionization step.



88
rel.rate 7×10^3

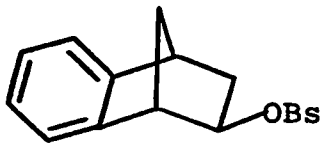
89
1

Subsequent studies on the ^{14}C labelled exo ester (88) indicated that the nonclassical ion (a) cannot fully describe the observed scrambling of the label. Intervention of two additional nonclassical ions was suggested[62].

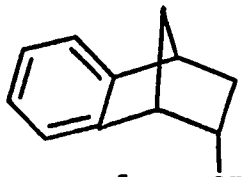


a

Similar exo:endo ratios of solvolytic reactivities were observed in a study of acetolysis of benznorbornen-2-yl p-bromobenzenesulfonates[63].



exo



endo

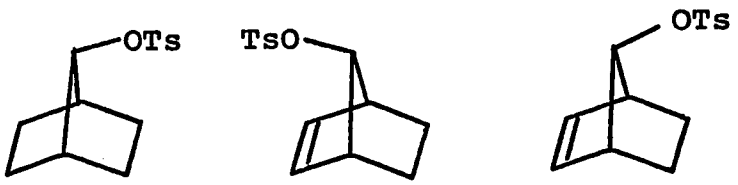
Both compounds gave exo-benznorbornen-2-yl acetate as the sole product. These observations are consistent with homoallylic participation of the aromatic ring, which in this system is similar to the double bond in its ability to assist ionization. The extent of the participation of the benzene ring in ionization can be assessed by observing the effect of substituents on the benzene ring on the solvolytic rate. Tanida studied this effect in the solvolysis of appropriate exo- and endo-benznorbornenyl derivatives. The introduction of a 6-methoxy substituent (homo para * position) accelerates the solvolysis 178 times, whereas the same substituent in the 7 position (homo meta) depresses the rate by a factor of 0.4. The

---

*Denotes that the substituent is in para position to the carbon atom on the aromatic nucleus that is closest to the ester function.

magnitude of the $\frac{k_6\ CH_3O}{k_{6,7}\ (NO_2)_2}$ ratio (1.6×10^7) in the exo series implicates the participation of the aromatic ring in the ionization step. Also the product distribution is substituent-dependent, as demonstrated by the decreasing stereospecificity of the reaction with the introduction (to the aromatic nucleus) of strongly deactivating substituents. In the endo series, the observed ratio is much smaller (230) and the product distribution is not significantly influenced by substituents. These observations indicate the substantial decrease in the anchimeric assistance during the ionization step in the latter series of compounds.

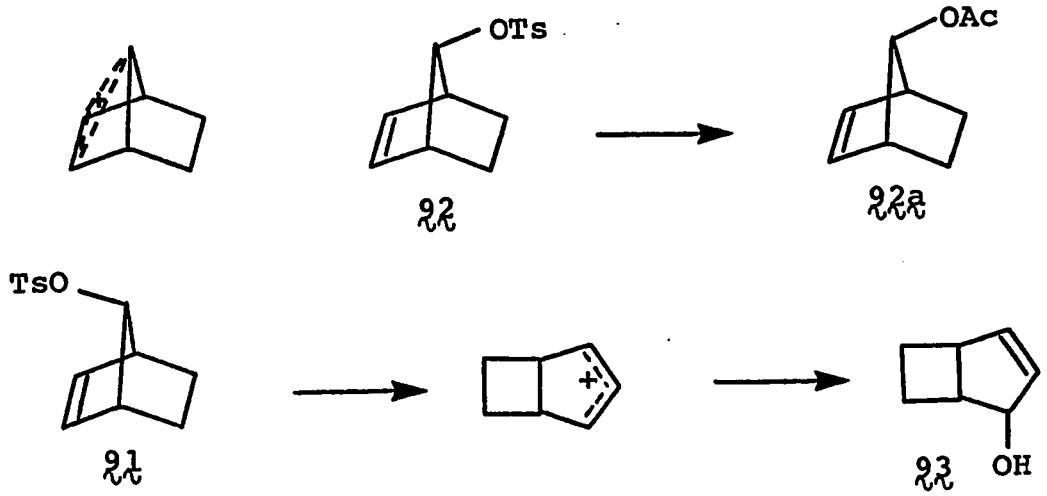
Rate enhancement is particularly pronounced in the anti-norbornen-7-yl system[64]. Solvolysis of the tosylate (92) in acetic acid is 10^{11} times faster than that of its saturated analog (90). The syn isomer (91) shows an enhancement of only 10^4.



90 91 92

rel.rate 1 10^4 10^{11}

The large rate increase was explained on the basis of symmetrical participation of the double bond in the rate determining step. In the syn isomer the position of the double bond relative to the substituent is unfavorable for homoallylic participation, but instead, assistance by the σ electron pair of the C_4 - C_5 single bond may be envisaged[65]. Such a process would produce an allylic carbonium ion and thus account for the observed rate increase.

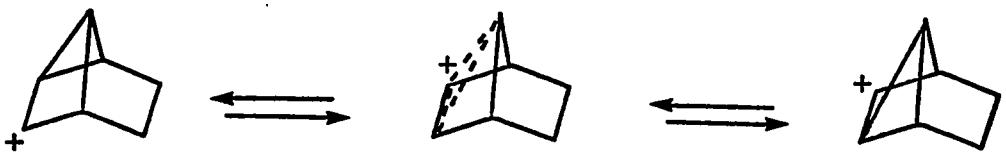


The only product in the acetolysis of the anti ester (92), was the acetate of retained configuration (92a), supporting the concept of homoallylic participation. The product of the basic hydrolysis of the syn ester (91) was a rearranged alcohol (93).

The ability of the double bond to homoconjugate

with a developing carbonium ion was firmly established. However, the nature of the intermediate became a subject of lively controversy.

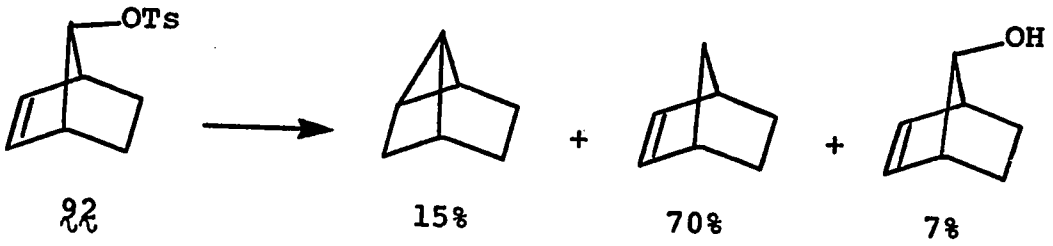
The main opponent of the symmetric participation of the π electrons of the double bond in the anti-norbornen-7-yl system has been H. C. Brown[66]. In contrast to Winstein's proposal of a "nonclassical" ion, Brown suggested that the result observed can be accommodated on the basis of a pair of rapidly equilibrating classical carbonium ions, in which case the nonclassical ion would represent the transition state for the equilibration.



It was difficult to devise experiments that would distinguish between the two proposals.

When the solvolysis of the anti-norbornen-7-yl (92) tosylate was carried out under reductive conditions, with sodium borohydride in aqueous diglyme, a mixture of bicyclic and tricyclic compounds was obtained, indicating that the hydride might have trapped the classical ions

shown above[67].

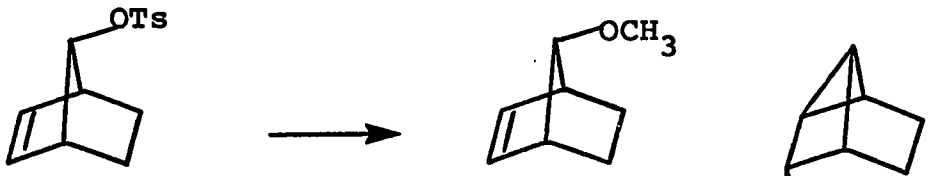


Brown found it difficult to rationalize this result on the basis of the nonclassical carbonium ion proposed by Winstein. He further proposed that the tricyclic compounds might be formed as the kinetically controlled products in the non-reductive solvolysis of anti-norbornen-7-yl tosylate. They are, however, not observed because of their instability in the reaction medium.

Winstein[68] demonstrated that in 50% aqueous acetone in the presence of $NaHCO_3$, the solvolysis of anti-norbornen-7-yl tosylate proceeds in a completely stereospecific manner giving anti-norbornen-7-ol (92b). At that time, the tricyclo[3.2.0.$0^{2,7}$]heptan-6-ol derivative (94) was not available but Winstein felt it would be stable under these reaction conditions. Winstein and coworkers argued that the presence of a classical carbonium ion at C_7 appeared to be excluded by the high rate of solvolysis and the lack of leakage into the syn-norbornen-7-yl deri-

vative. Accordingly the reaction with water exclusively at C_7 and the reaction with $NaBH_4$ predominantly at the same center in the reductive solvolysis of anti-norbornen-7-yl tosylate are difficult to rationalize on the basis of the equilibrating classical ions. The reduction of anti-norbornen-7-yl tosylate with $NaBH_4$ in dry diglyme gives a tricyclic hydrocarbon (94) in high yield. These observations are explained on the basis of a nonclassical intermediate in which the ratio of C_2:C_7 reactivity is dependent on the nature of the nucleophile.

Winstein's[69] study of the methanolysis of anti-norbornen-7-yl tosylate demonstrated striking changes in product composition with increasing sodium methoxide concentration.



92 92c 95

$[CH_3ONa]$	%	%
0	100	0
0.20	93.6	6.4
1.93	65.3	34.7
3.98	48.5	51.5

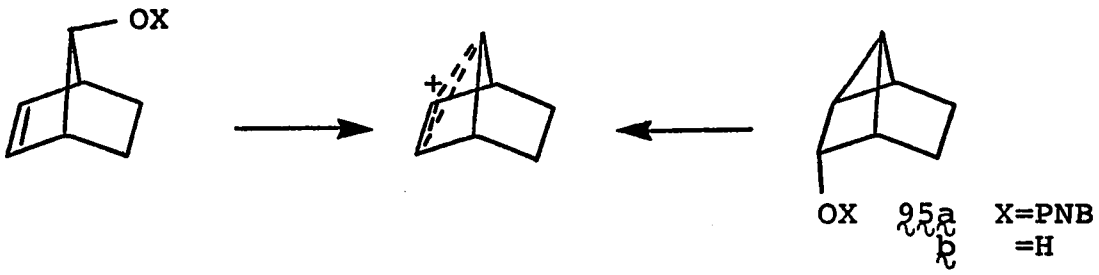
These data made it obvious that the presence of sodium methoxide was responsible for the formation of the tri-

cyclic ether (95).

When the tosylate (92) was solvolyzed in methanol buffered with NaOAc-AcOH, methyl anti-norbornen-7-yl ether (92c) was formed in 97.7% yield, along with 0.3% of a tricyclic ether (95). Synthetic tricyclic ether was found to be completely stable under those reaction conditions. Thus kinetic control gives a C_2:C_7 reactivity ratio of ∿300.

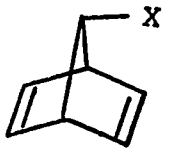
The stereospecificity of the tricyclic ether (95) formation in the methanolysis of anti-norbornen-7-yl tosylate in the presence of methoxide ion was used as an additional argument in favor of a nonclassical structure for the intermediate[70]. Most of the additions to the norbornene system occur from the exo side. If classical ions were intermediates, a mixture of exo and endo, with exo product predominating, would be expected. The tricyclic ether (95) formed was found to be (>97%) pure endo isomer, which indicated the involvement of a nonclassical intermediate. When the tricyclic ester (95a) became available it was demonstrated that the kinetically controlled product of its solvolysis is anti-norbornen-7-ol[71]. Although the tricyclic alcohol (95b) was shown to be stable under solvolysis conditions it was not observed in the solvolysis products. The authors felt that both the σ and the π

route lead to the same intermediate, which is best described as a nonclassical ion.



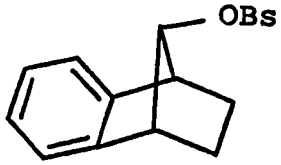
The norbornadien-7-yl system (96) has also been extensively studied and it largely parallels the behaviour of the anti-norbornen-7-yl system[72, 50] (92). Substituted norbornadien-7-yl derivatives were shown to solvolyze 10^{14} times faster than the corresponding norborn-7-yl derivatives (90). The additional solvolytic rate enhancement (10^3) of this system, over that of anti-norbornen-7-yl (92) was ascribed to either a "ground-transition" state effect or to extra charge delocalization in the transition state. The proposal that a syn double bond participates extensively in charge delocalization was eliminated when the NMR spectrum of norbornadienyl cation was observed[73]. The presence of two nonequivalent groups of olefinic protons was most compatible with a nonclassical ion formed by participation of only the anti double bond. Treatment

of norbornadien-7-yl chloride with sodium methoxide in methanol, or $LiAlH_4$ in ether, yields a mixture of bicyclic and tricyclic compounds[74].

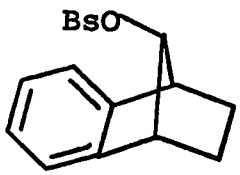


96

Some additional evidence for the homoallylic interaction was obtained in a study of the acetolysis of syn and anti benznorbornen-9-yl brosylates[75]. In this system the benzene ring is less effective than a double bond in assisting ionization. anti-Benznorbornen-9-yl brosylate (97) solvolyzes 10^5 faster than a norborn-7-yl (90) derivative. Respective acceleration for the syn ester (98) is 10^2. The mode of product formation is quite analogous to that observed in the norbornen-7-yl derivative.



97

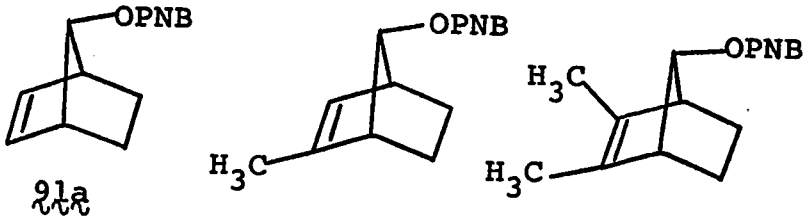


98

The introduction of a methoxy group at the 4 position of the anti ester (97) increases the rate by a factor of 53. Introduction of the electron withdrawing nitro group to the same position reduces the solvolytic rate by a factor of 10^4. The magnitude of these effects, as represented by the $\frac{k\ CH_3O}{k\ NO_2}$ ratio of 386,000, is far too large to be explained by simple electrostatic interactions. In contrast, these effects in the syn series (98) were of a much smaller order of magnitude. These results are consistent with the presence of homoallylic interactions in the anti series, whereas in the syn series, such interactions are absent due to the lack of proper geometry. Additional information about the nature of the intermediate was obtained by measuring the rates of solvolyses of 4,5-disubstituted brosylates. The observation that the acceleration effect of the second methoxy group introduced is of the same magnitude as that of the first one, is interpreted as strong support for a symmetrical nonclassical intermediate.

Gassman and Paton[76] have studied the effect of methyl substituents at the 2,3 positions on the rate of solvolysis of anti-norbornen-7-yl p-nitrobenzoate (91a). This approach was described as being possibly the best means of determining the nature of the transition state in

an ionization reaction[77].



91a
rel.rate 1

13.3

148

Reactions proceeding through symmetrical transition states are expected to exhibit cumulative substituent effects. Each successive substituent affects the reaction rate by approximately the same factor. Such effects have been observed in epoxidation and ionic bromination reactions of olefins. A different effect is exhibited by reactions that are known to proceed through classical carbonium ion intermediates, such as acid catalyzed hydration of olefins. For example, isobutylene reacts 10^3 times faster than propylene in such a reaction. However introduction of an additional methyl group on the less substituted end of the double bond produces no further increase in the reaction rate. Introduction of the first methyl group to the double bond in the anti-norbornen-7-yl p-nitrobenzoate (91a) increases the rate of solvolysis by a factor of 13.3. The second methyl group caused an additional 11.1 fold

increase in the reaction rate.

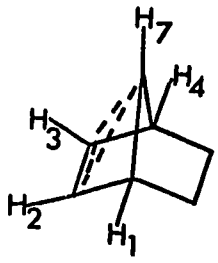
	Relative Rate of Hydration
CH_3 CH_3 >C=CH_2	1000
CH_3-CH=CH_2	1
CH_3-CH=CH-CH_3	0.7

The authors felt that such a result is most consistent with the formation of a symmetrical delocalized norbornen-7-yl cation.

All the evidence presented so far supporting the nonclassical nature of the intermediate involved in solvolyses of the anti-norbornen-7-yl system is based on kinetic results and examination of reaction products and their stereochemistry. Physical methods[78] have also been used extensively for the direct observation of carbonium ion intermediates. Although conditions under which carbonium ions can be observed are very different from those in which such species have been postulated and although the lifetimes of cations are much longer under these conditions, such studies provide valuable information.

Winstein and coworkers[70] studied spectra of norbornenyl cations derived either from anti-norbornen-7-ol

or a tricyclic ether (95) in a strongly acidic medium.



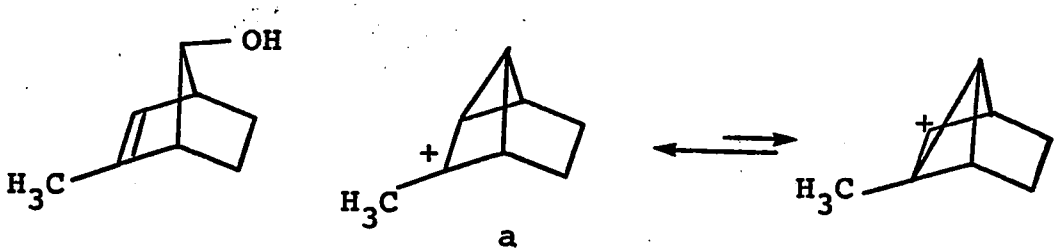
H_1 and H_4 τ 5.76 (m)

H_2 and H_3 τ 2.93

H_7 τ 6.76 (m)

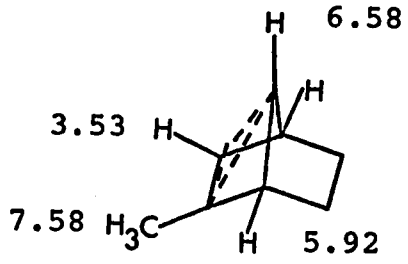
The spectra showed that the positive charge is delocalized and mostly concentrated at C_2 and C_3, which is consistent with the nonclassical ion. However the spectra observed did not exclude equilibrating classical ions. Deno interpreted the high field position of the C_7 hydrogen in a related norbornadienyl cation as evidence for a classical cation[79].

Much more compelling evidence in favour of the symmetrical nonclassical intermediate is obtained when the equivalence of the vinyl positions is destroyed by the introduction of a methyl substituent, as shown in the following scheme[80].



a

If equilibrating classical ions were involved, the tertiary carbonium ion (a) should be predominant, and the NMR spectrum should correspond to that species. Spectra of a number of cyclopropyl carbinyl cations are known and the chemical shifts of the cyclopropyl protons (α and β) are at relatively high fields (τ 7-8). The chemical shifts of protons in 2-methylnorbornenyl cation are shown below.



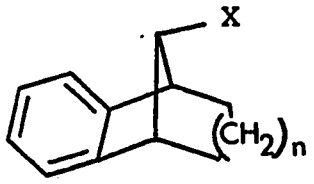
The position of the C_3 proton absorption is almost 3 ppm lower than expected for a cyclopropyl carbinyl cation. Clearly this is incompatible with the involvement of classical ions, and presents another strong argument in favour of the nonclassical bridged structure.

In summary, much compelling evidence in favour of a nonclassical intermediate in the anti-norbornen-7-yl system has been accumulated, firmly supporting the original proposal of Winstein[78b]. Recent studies by Olah[78b] of long-lived carbonium ions utilizing various physical methods have shown that the classical and nonclassical

carbonium ions are distinguishable. With these developments, the whole controversy that has provided much of the impetus for research in this area of organic chemistry may be resolved.

The distance between the developing carbonium ion and the participating π system should have a profound influence on the effectiveness of homoallylic participation. The magnitude of this effect must necessarily be studied in conjunction with other factors that influence the stability of carbonium ions. Tanida[81] has studied the solvolysis of a homologous series of benzbicyclo[2.1.n] brosylates (n = 1-4). Relative rates are shown in Table 4.

Table 4



n	rel.rate
1	32
2	1
3	4.8×10^{-3}
4	1.2×10^{-5}

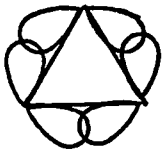
The first three esters (n = 1-3) gave as the sole product the acetates of retained configuration (quantitative yield) whereas the ester that had the lowest rate of acetolysis yielded some product of inverted configuration. With the

increasing number of carbon atoms (n) in the bridge, C-C bond angles at the reaction sites become progressively larger. Considering only this effect, one would expect the acetolysis rate to increase with the lengthening of the bridge, since the increased bond angle at the reaction site facilitates formation of an sp^2 hybridized carbonium ion. However, the observed trend of relative rates is reversed. The observed rate decrease with the increasing number of carbon atoms in the bridge is caused by the progressively increasing distance between the reaction site and the participating aromatic nucleus, which renders homoallylic assistance less effective. Thus the effect of increased bond angle at the reaction site, which may play an important role in other substrates, is in this system overwhelmed by homoallylic participation.

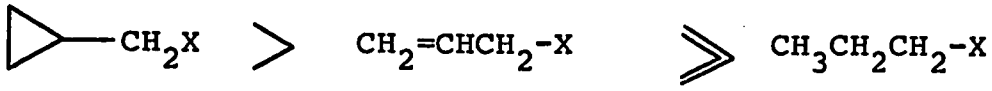
B. Cyclopropyl Participation

It has been known for a long time that the chemical reactivity of the cyclopropane ring differs from that of other saturated compounds. Often cyclopropanes undergo addition, rather than substitution reactions, which suggests the presence of greater p-character in cyclopropane C-C bonds[88]. Spectral studies have indicated that the cyclopropyl ring exhibits conjugation effects that are intermediate between saturated compounds and olefins[89, 92].

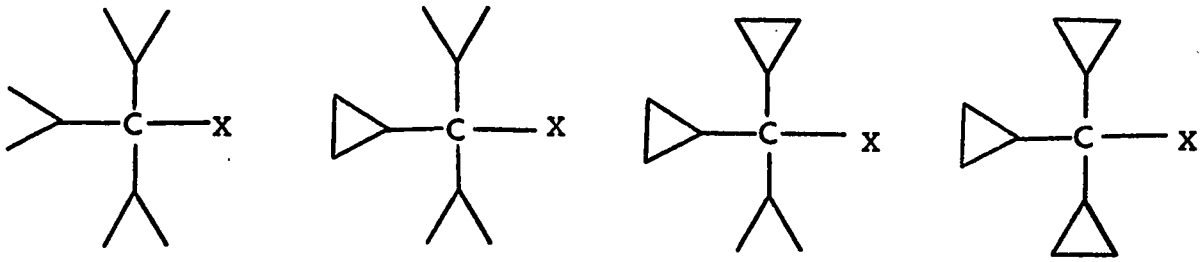
These observations, along with the results of other physical measurements, led to various models of bonding in cyclopropane[89]. According to the "bent bond" model, the hybrid orbitals (s and p) which form the ring system, do not lie along the sides of a triangle, but are spread to 106°.



The degree of participation of s and p orbitals in forming hybrid annular bonds differs in various models. The currently accepted description for the bonding is the formation of C-C bonds by overlap of sp^5 hybridized orbitals and sp^2 hybridization in the CH_2 bonds[90]. This description was experimentally supported by studies of C^{13} coupling constants in some cyclopropanes[91]. In analogy to the double bond, the cyclopropyl ring interacts strongly with a carbonium ion centre and participates in its stabilization. In fact it has been observed that the solvolysis of cyclopropyl carbinyl derivatives proceeds at a greater rate than that of corresponding allylic compounds[92].



The ability of a three member ring to participate in the stabilization of an adjacent positive charge is demonstrated in the following example:



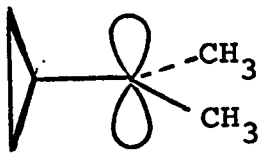
rel.rate 1 250 23.5×10^3 $\sim 25 \times 10^6$

It can be seen that introduction of each successive cyclopropane ring makes an approximately equal contribution to the stabilization of the carbonium ion. The effectiveness of the participation of all three cyclopropyl rings in the solvolysis of tricyclopropylcarbinyl benzoate is demonstrated by the observation that it solvolyzes appreciably faster than triphenylmethyl benzoate[92].

In 1962 Deno[93] observed the tricyclopropylcar-

bonium ion by NMR spectroscopy. That all three cyclopropane rings are participating in the stabilization of the positive charge was confirmed by the NMR spectrum which consisted of a single sharp line in sulfuric acid.

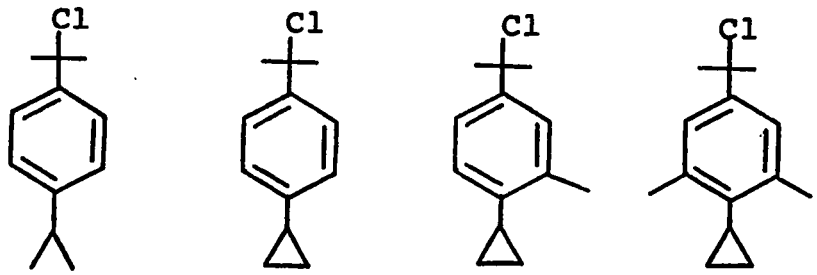
The maximum interaction between a cyclopropyl ring and an adjacent carbonium ion occurs when the plane of the ring is parallel to the p orbital of the carbonium ion. This follows from the NMR spectrum of cyclopropyldimethyl cation in which the two methyl groups are not equivalent[94]. In the bisected form postulated, the methyl group that absorbs at a higher field is <u>syn</u> to the three-membered ring and thus is anisotropically shielded.



Recently the barrier for the rotation was measured by a double resonance technique and was found to be 13.7 kcal/mol[95].

The ultraviolet spectra of several cyclopropyl carbonium ions have been examined and the results indicate the presence of extensive charge delocalization[96].

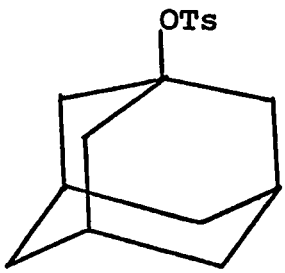
The existence of a preferred conformation of a cyclopropyl ring for stabilization of a carbonium ion was demonstrated in a study of t-cumylchloride derivatives[97].

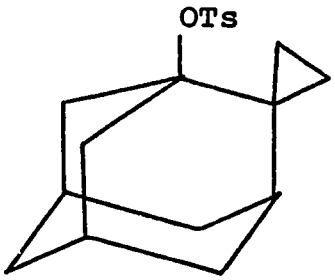


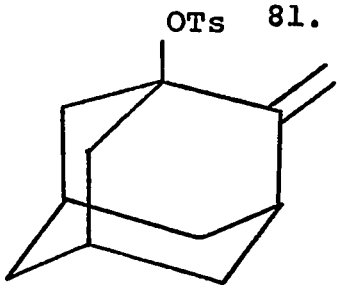
rel.rate 17.8 157 86 9

Introduction of methyl groups ortho to the cyclopropyl ring prevents it from attaining the bissected geometry necessary for stabilization, thus making it even less electron-releasing than the isopropyl group.

When the cyclopropyl ring does not have rotational freedom and is frozen in the unfavoured 90° twist geometry, its conjugative stabilization of an adjacent carbonium ion becomes negligible[98]. The same effect is observed with an adjacent vinyl group that cannot achieve coplanarity with the developing carbonium ion as shown by the relative solvolysis rates of the esters presented in the following scheme.





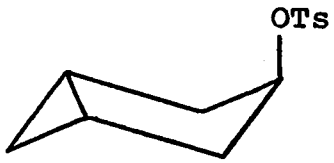


rel.rate 1.1×10^4 73 1

Participation of the cyclopropane ring in the stabilization of the positive charge may give rise to either cyclopropylcarbinyl or homocyclopropylcarbinyl rearrangements[99]. Cyclopropylcarbinyl rearrangements[100] have been extensively studied and are not of major concern in this thesis.

Several examples of homocyclopropyl rearrangements have been described. The first case of homoallylic participation of a cyclopropane ring was described by Winstein and his coworkers[101]. They studied extensively the solvolysis of cis- and trans-bicyclo[3.1.0]hex-3-yl tosylates.

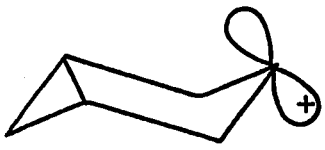
99



100

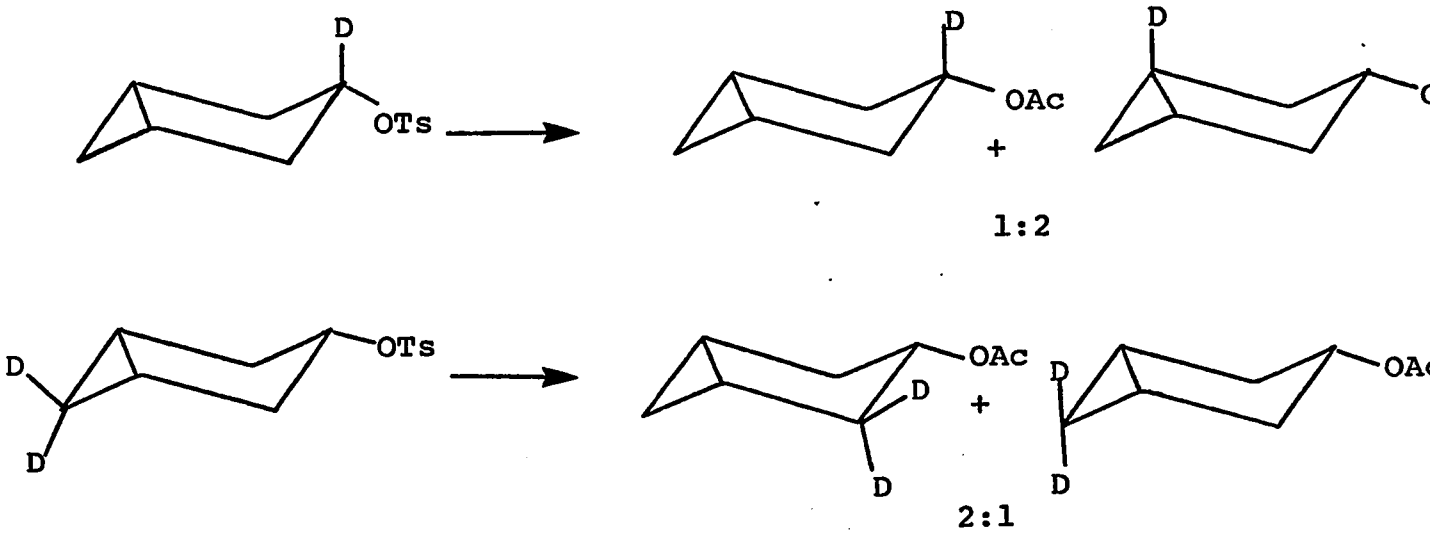
The cis tosylate (99) solvolyzes in acetic acid 35 times faster than its epimer, and yields almost exclusively (99%) the acetate of retained configuration. On the other hand the slower trans isomer (100) gives, besides cis-bicyclo[3.1.0.]hex-3-yl acetate, a mixture of acetates and a considerable quantity of unsaturated compounds (33%). In the acetolysis of the cis tosylate with addition of $LiClO_4$ a "special salt" effect (associated only with relatively stable intermediates) was observed. The trans isomer did not exhibit the special salt effect. The authors interpreted the behaviour of the cis ester in terms of cyclopropyl assisted ionization, to give the tris-homocyclopropenyl cation (101). This ion is a symmetrical analog of the cyclopropenyl cation and is considered to be a homoaromatic species. The solvolysis of the trans ester was described as non-assisted ionization proceeding through a classical carbonium ion (102).

101



102

These arguments were further strengthened by solvolysis studies on C_6 and C_3 deuterium labelled cis-bicyclo[3.1.0]-hex-3-yl tosylates.



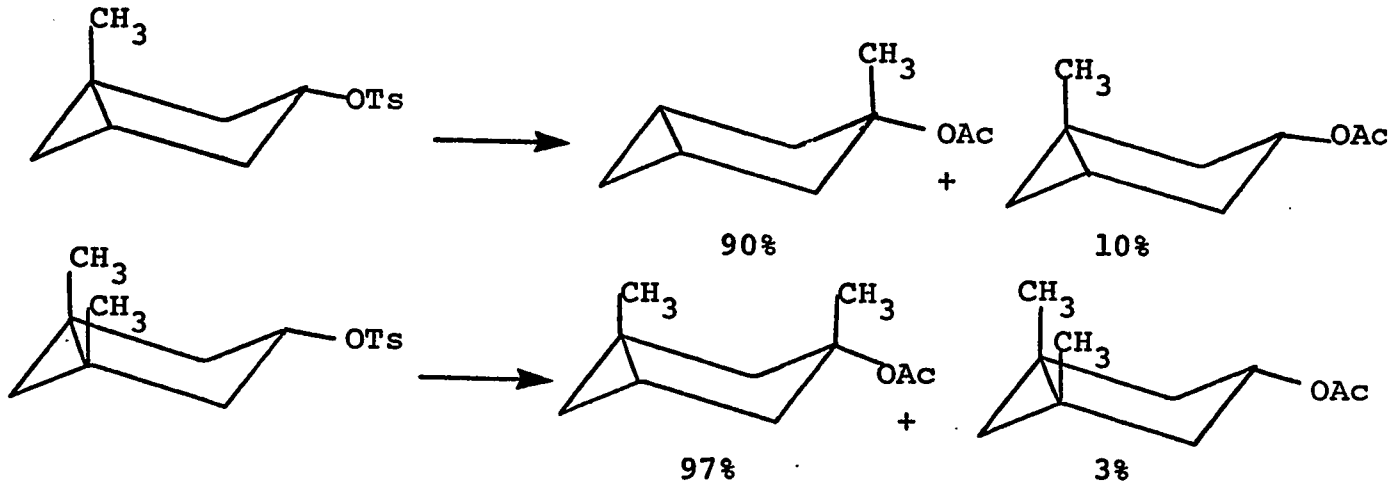
As shown in the above scheme the deuterium atoms were statistically scrambled in the reaction products in accordance with the proposed intermediate. It was conceivable that the observed scrambling could result from rapid interconversion of classical carbonium ions. This possibility was ruled out by the absence of any significant deuterium scramlbing in the cis-bicyclo[3.1.0]hexyl acetate isolated as a product of solvolysis of the deuterium labelled trans ester.

Corey and Uda[102] tested Winstein's proposal by studying the acetolysis of 1,5-diphenyl-bicyclo[3.1.0.]-

hex-3-yl tosylate. Their approach was based on the assumption that in the case of involvement of a tris homocyclopropenyl cation, the introduction of 1,5-diphenyl substituents should produce a marked solvolytic rate increase relative to the parent system. However a small rate retarding effect was observed which, according to the authors, is not consistent with formation of the nonclassical intermediate. Rearranged products were characterized and although no detailed mechanism was proposed the authors preferred a variation of a classical type intermediate. Other authors felt that the rate retardation caused by the introduction of phenyl groups was not very meaningful, since their effects on rate are complicated by opposing inductive and resonance effects[101]. The steric effect of phenyl groups should also be taken into account as pointed out by Winstein. The relatively small rate enhancement observed in the cis ester (95) can be explained; the chair form, which is required for the formation of the nonclassical ion, is not the most stable conformation in this system. Because of the nonbonded interactions in the diphenyl derivatives, the chair form is even less readily attained, which favours ionization through a classical, boat shaped intermediate.

Since the electronic effects of alkyl groups are

less complex, a number of mono- and di-alkyl substituted cis-bicyclo[3.1.0]hex-3-yl tosylates were studied under solvolytic conditions[3]. The stereochemistry of product formation and rate enhancement are consistent with the proposed nonclassical intermediate, although the rate enhancements are lower than expected.

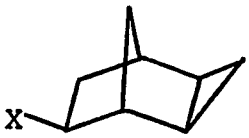


Some direct observations of the bicyclo[3.1.0]hexenyl cation by NMR spectroscopy appear to support its non-classical nature[103].

Studies on rigid polycyclic substrates eliminate uncertainties associated with conformation flexibility. A number of such systems were studied, which led to recognition of the favoured geometry for homoallylic participa-

tion of the cyclopropane ring.

Solvolyses of isomeric tricyclo[3.2.1.$0^{2,4}$]oct-6-yl brosylates were studied by two independent groups of workers[104]. The major product in each case is the exo-exo acetate (103).



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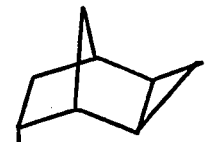
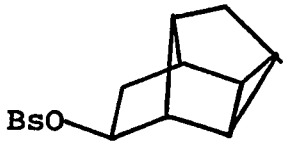
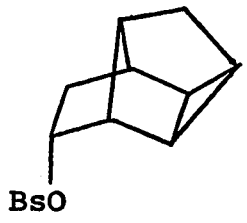


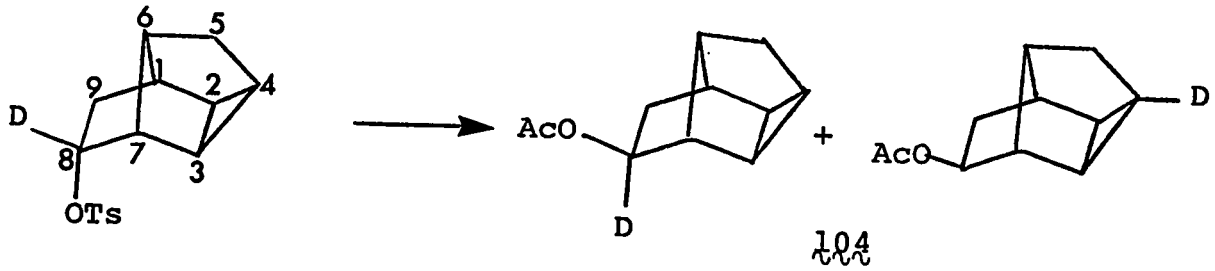
The observed rate accelerations were very modest, as is evident from the four fold increase in the $\frac{k\ exo}{k\ endo}$ ratio over the normal value. Weak participation of the cyclopropane ring was suggested as a possible explanation.

A study on a related tetracyclo[3.3.$0^{2,4}$.$0^{3,7}$]-non-8-yl system was described by Freeman and Bolls[105].



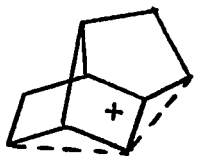


Both brosylates on acetolysis produce the same exo acetate (104). Rate enhancements were observed for both isomers with the exo isomer having the greater enhancement. Acetolysis of the deuterium labelled brosylate produced the exo acetate in which the deuterium was equally distributed between the C_8 and C_4 in the cyclopropyl ring.



104

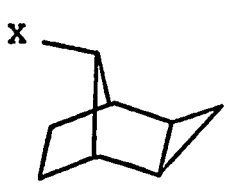
These observations are best explained in terms of a nonclassical carbonium ion, which is formed by cyclopropyl participation in which carbons 8 and 4 become equivalent.



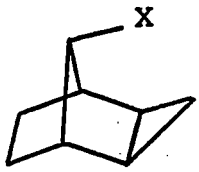
The cation was directly observed by NMR spectroscopy when the parent alcohol was treated with fluorosulfonic acid at low temperature.

A solvolytic study of isomeric tricyclo[3.2.1.$0^{2,4}$]-

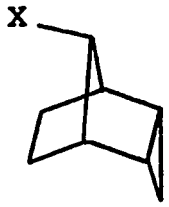
octan-8-ol derivatives was particularly informative[106]. The isomeric esters possess four different arrangements of the cyclopropane ring relative to the C_8 leaving group. Since these are rigid structures, direct comparison of relative rates is possible.



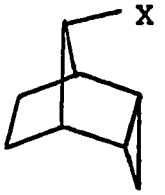
exo-anti



exo-syn



endo-anti

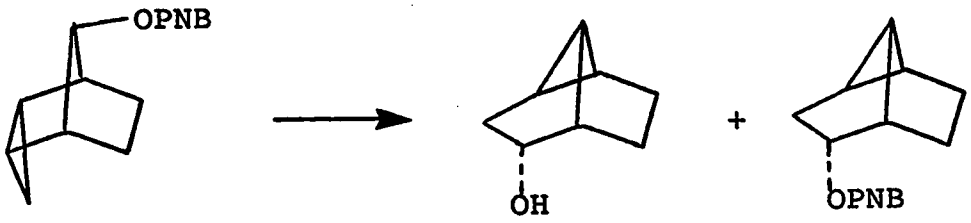


endo-syn

re.rate	1	10^4 [106]	10^{14} [105]	10

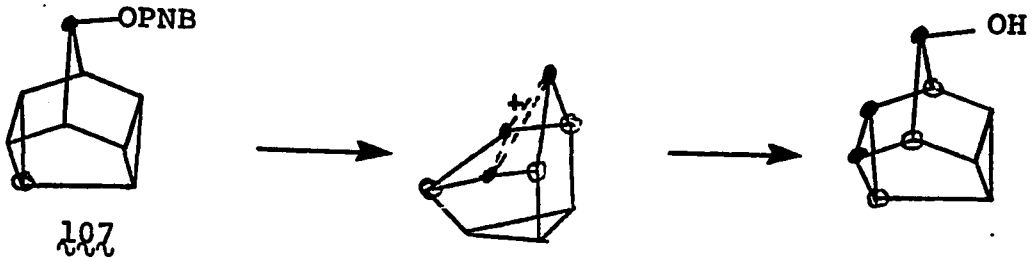
Although the endo-anti and endo-syn esters have essentially identical steric and angular environments around the reaction site, their rates of solvolysis differ by a factor of 10^{13}. Such a tremendous rate acceleration of the endo-anti ester (105) is explained by backside participation of the cyclopropane ring during the ionization step. The geometric relationship optimal for cyclopropane participation is different from the one described for a cyclopropyl carbinyl derivatives. It is analogous to the type of interaction involved in the homoallylic participation of a double bond and can be visualized as a σ type overlap of the sp^5 orbitals of the ring with the develop-

ing p orbital of the carbonium ion. The cyclopropane ring in this particular system is even more effective than the double bond in homoallylic stabilization of a carbonium ion ($\frac{k\ \underline{endo}\text{-}\underline{anti}}{k\ \underline{anti}\text{-norbornen-7-yl}} = 10^3$). It was also suggested that the release of strain involved in the ground state may be partly responsible for the rate enhancement observed for the <u>exo-anti</u> ester (105), as shown in the diagram. The geometric arrangement that allows backside edge participation of the cyclopropane ring is unique in the amount of anchimeric assistance provided. Other esters that are suitable for "face" cyclopropane participation have little or no acceleration at all. The exception is the <u>exo-syn</u> (106) ester in which a 10^4 rate enhancement was observed; however, it is thought to be of different origin. This acceleration may be largely due to non-bonded interactions or, in analogy with <u>syn</u>-norbornen-7-yl system, the σ electron pair from the $C_1 - C_7$ bond may be participating in the ionization step to give a cyclopropyl carbinyl cation. The solvolysis of the <u>exo-anti</u> p-nitrobenzoate (105) yielded two rearranged compounds that had an identical carbon skeleton. The extremely high rate of solvolysis, the presence of ion pair return, and the stereospecificity of the product formation all implicate the involvement of the <u>tris</u> homocyclopropenyl intermediate.



105

Recently a study of a related pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]non-9-yl system (107) was reported[2]. This structure is capable of three-fold degeneracy. In addition, participation of the syn cyclopropane ring would lead to complete degeneracy of all ring carbon atoms. The solvolytic rate of the corresponding p-nitrobenzoate was found to be just eighty times slower than that of the tricyclic ester (105). The large rate enhancement cannot be attributed to relief of strain, since the reaction product contains the same pentacyclic carbon skeleton. The extent of carbon atom degeneracy was determined by studies of C_9 and C_4 deuterium labelled compounds, using ^2H and ^1H NMR spectroscopy. The experimental observations are compatible with the threefold symmetric tris homocyclopropenyl cation, in which carbons 9, 3 and 2 and alternately 1, 8 and 4 become equivalent. Only the anti cyclopropane ring participates in the stabilization of the carbonium ion as demonstrated by the absence of more extensive carbon scrambling.



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This example illustrates the uniqueness of the geometric relationship required for extensive homocyclopropyl participation in ionization.

RESULTS AND DISCUSSION:

Solvolysis of exo-bicyclo[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate

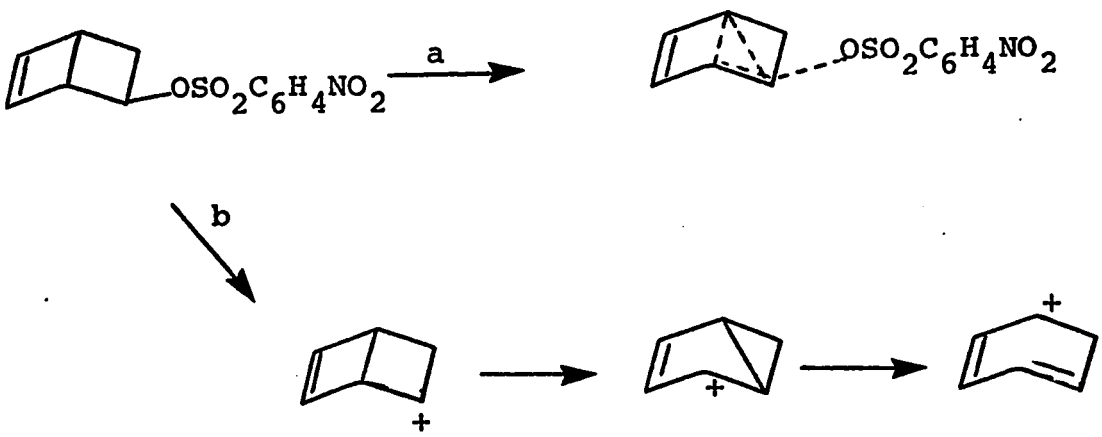
After the successful preparation of exo-bicyclo-[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate (52) a study of its solvolytic behaviour was undertaken. In acetic acid containing two equivalents of sodium acetate, the ester solvolyzed with liberation of the theoretical amount of p-nitrobenzenesulfonic acid with a first order rate constant $k = 6.07 \times 10 \text{ sec}^{-1}$ at 89.7°. As already described (Part one) the product distribution varied with the length of reaction time, indicating that the thermal isomerization of the primary solvolytic product exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14) to exo-bicyclo[3.1.0]hex-2-en-6-yl acetate (53) was taking place under the reaction conditions. The structural proof for the products has been presented in Part one of this thesis.

Considering the structural features of the bicyclo[2.2.0]hexenyl sulfonate ester (52) several solvolysis pathways leading to a number of products can be considered. These products could be formed in a mixture, or any of them could be formed exclusively depending on the energetics of the respective pathways.

temperatures in the presence of silica-alumina catalyst give the same equilibrium mixture consisting of 77% of nortricyclene and 23% of norbornene[82]. The tricyclic products of the above type were not observed in electrophilic addition reaction on bicyclo[2.2.0]hexadiene[83] .

The total absence of products that would be generated *via* pathway A in the solvolysis of 52 indicates availability of energetically more favourable reaction routes.

B. *A priori*, two possible routes can be visualized for the formation of benzene in the solvolysis of *exo*-bicyclo-[2.2.0]hexen-2-yl ester.



De Puy[126] has considered the solvolysis of cyclobutyl esters as being analogous to the solvolysis of the corres-

ponding cyclopropyl derivatives, suggesting that if cyclobutanes are viewed as homocyclopropanes, the solvolysis of their appropriate derivatives may be subject to the Woodward-Hoffmann rules[84]. Thus, if the ring opening occurs simultaneously with the departure of the leaving group, the substituents cis to the leaving group rotate inward, enabling orbitals of the participating σ bond to interact with the back side of the developing carbonium ion. Similarly, with substituents that are trans to the departing group, outward rotation is predicted.

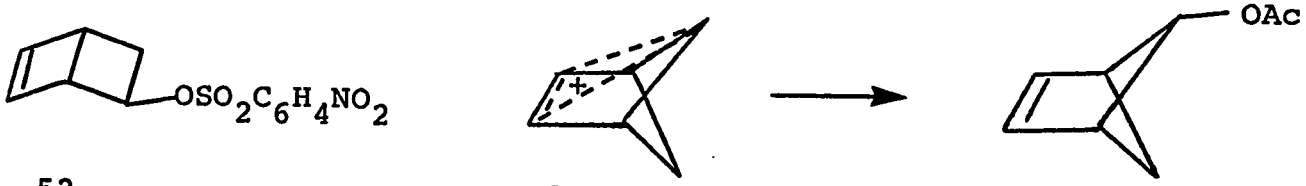
The above considerations have been successfully utilized as the explanation of the difference in solvolytic reactivity between the two isomeric bicyclo[2.1.0]pent-2-yl esters[113].

Extension of the above discussion to the solvolysis of the exo-bicyclo[2.2.0]hexen-2-ol derivative implies that the required mode of rotation in this ester would lead to a considerable increase in strain energy. For this reason, the concerted pathway (a) that would lead to the formation of benzene becomes unimportant relative to the participation of the C_1 - C_2 bond (path C) in the initial dissociation. On the other hand, in the solvolysis of the epimeric endo derivative, the concerted pathway involving the participation of the C_1 - C_4 electron pair

should play a more important role. The required outward mode of rotation would lead to a decrease in strain energy and consequently essentially quantitative formation of benzene can be expected.

An alternative, stepwise process (C) is most likely responsible for the formation of the small amount of benzene observed in the solvolysis of the exo-bicyclo [2.1.0]hexen-2-yl ester. A "cyclobutane-cyclopropylcarbinyl-homoallyl" type of rearrangement would result in the formation of cyclohexadienyl cation. A loss of proton would then result in aromatization.

C. The solvolysis of the exo-bicyclo[2.2.0]hexenyl p-nitrobenzene sulfonate (52) is best described as proceeding largely through an anchimerically assisted ionization step.



52 108 14

Participation of the C_1 - C_6 electron pair could lead either to the formation of the stable bis-homocyclopropenyl cation

or the exo-bicyclo[2.1.1]hexen-5-yl p-nitrobenzenesulfonate derived from ion-pair return. In the latter case the solvolysis of this ester would then give rise to the same stable cation (108). Reaction of this cation with solvent produces the observed bicyclo[2.1.1]hexenyl acetate (14). Although a comparative solvolytic study has not been done, some rate acceleration should be observed for the unsaturated ester (52) relative to its saturated analog.

As mentioned previously, solvolysis of exo-bicyclo[2.2.0]hexenyl p-nitrobenzenesulfonate ester (52) in methoxyacetic acid proceeded in much the same manner as in acetic acid. The exo-bicyclo[2.1.1]hexen-5-yl methoxyacetate (61) was produced as the sole solvolytic product. The first order rate constant obtained for this reaction was $k = 8.24 \times 10^{-5} sec^{-1}$ at 80.0°.

Solvolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl methoxyacetate

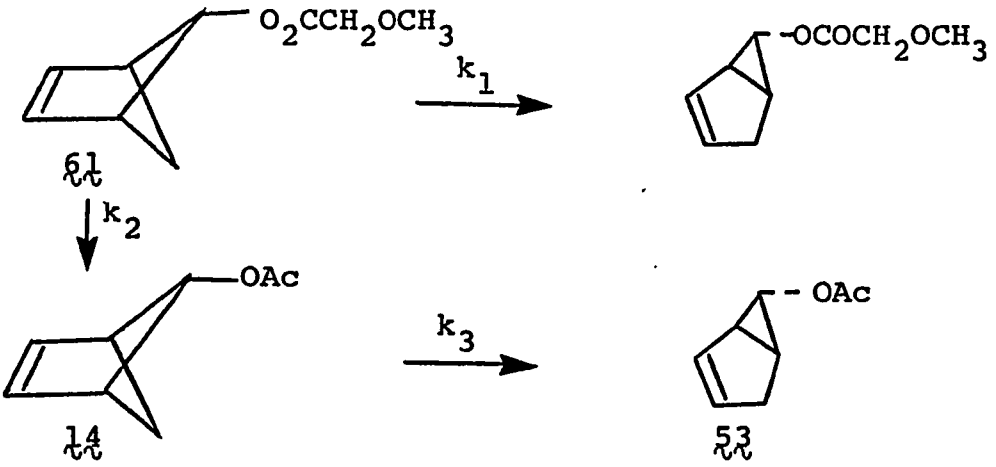
There was some difficulty in preparing an exo-bicyclo[2.1.1]hexen-5-yl derivative suitable for solvolysis. A few attempts to obtain the corresponding hydroxy compound (59) resulted in the formation of Δ^3-cyclopentencarboxaldehyde (60), indicating the instability of the desired alcohol. Therefore we were unable to obtain derivatives commonly used for solvolytic studies (p-nitrobenzo-

ate, tosylate, etc.). Also attempted solvolysis of the exo-bicyclo[2.1.1]hexen-5-yl acetate (14) in acetic acid-d_4 indicated that solvolytic ester exchange proceeded slowly compared to thermolysis of the starting acetate. For this reason we were unable to obtain kinetic data for that solvolysis reaction.

A different approach that proved successful was the preparation of exo-bicyclo[2.1.1]hexen-5-yl methoxyacetate (61) and examination of its solvolytic reactivity. Since methoxyacetic acid (pKa = 3.52) is a stronger acid than acetic acid (pKa = 4.75), the acetolysis of the corresponding methoxyacetate (61) should proceed at a greater rate than that of exo-bicyclo[2.1.1]-hexenyl acetate (14). At the same time the rates of thermolysis for the two esters were expected to be of the same order of magnitude which would enable us to obtain the desired kinetic parameters. The exo-bicyclo[2.1.1]hexen-5-yl methoxyacetate was solvolyzed in acetic acid; the reaction progress was monitored by measuring its disappearance against an internal standard by glpc. The methoxyacetic ester (61) underwent two parallel first-order reactions, yielding exo-bicyclo[2.1.1]hexen-5-yl acetate (14) and exo-bicyclo[3.1.0]hex-2-en-6-yl methoxyacetate.

Structural proof for these two products are des-

cribed in Part one of this thesis. The reaction sequence and appropriate rate constants are shown in the following scheme.



The rate of formation of the acetate (14) was determined in an indirect manner because direct determination of k_2 requires the measurement of two glpc peak areas; different detector sensitivities increase the magnitude of error involved in the determination. The following reaction parameters were obtained:

$$(k_1 + k_2)_{75.5°} = 4.03 \times 10^{-5} sec^{-1}$$
$$(k_1 + k_2)_{96.0°} = 3.17 \times 10^{-4} sec^{-1}$$
$$(k_1)_{75.5°} = 3.81 \times 10^{-6} sec^{-1}$$
$$(k_1)_{96.0°} = 5.07 \times 10^{-5} sec^{-1}$$

The rate of solvolysis (k_2) of the methoxyacetate ester (61) was then obtained as the difference between the total rate of disappearance ($k_1 + k_2$) of the starting material and the rate of its thermolysis (k_1). Thus the rate of formation of exo-bicyclo[2.1.1]hexenyl acetate (14) is:

$$k_2 = (k_1 + k_2) - k_1$$

$$(k_2)_{75.5°} = (3.65 \pm 0.14) \times 10^{-5} sec^{-1}$$

$$(k_2)_{96.0°} = (2.66 \pm 0.10) \times 10^{-4} sec^{-1}$$

$$\Delta H^{\dagger} = 24 \text{ kcal/mol}$$

$$\Delta S^{\dagger} = -10 \text{ eu}$$

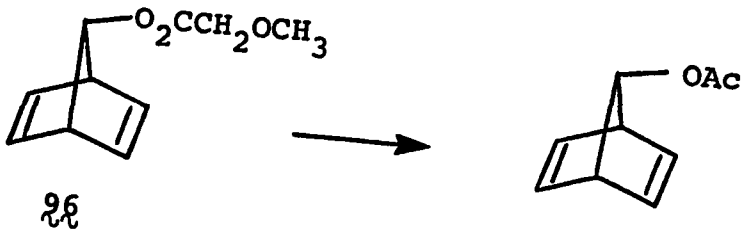
The extrapolated rate of acetolysis of methoxyacetate (61) at 25° is:

$$k_{25°} = 9 \times 10^{-8} sec^{-1}$$

The ratio of the rate of formation (k_2) of the exo-bicyclo[2.1.1]hexen-5-yl acetate (14) to the rate of its thermolysis (k_3) was 3-5. Formation of the exo-bicyclo[3.1.0]hexen-6-yl acetate (53) was evident during this solvolysis reaction.

In order to compare the solvolytic reactivity of the methoxyacetate (61) with those of other similar systems norbornadien-7-yl methoxyacetate (96) was prepared.

Acetolysis of this compound (96), quantitatively gave the



96

corresponding acetate. This reaction was also followed by glpc, which provided the following kinetic parameters:

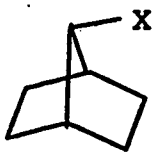
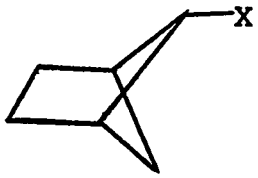
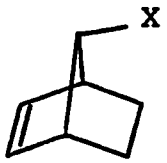
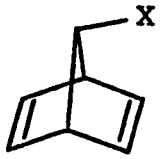
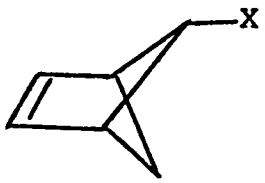
$$k_{75.5°} = (1.12 \pm 0.03) \times 10^{-5} sec^{-1}$$
$$k_{96.0°} = (8.70 \pm 0.22) \times 10^{-5} sec^{-1}$$
$$\Delta H^{\dagger} = 25 \text{ kcal/mol}$$
$$\Delta S^{\dagger} = -10 \text{ eu}$$

The extrapolated rate constant at 25° was calculated to be:

$$k_{25°} = 2 \times 10^{-8} sec^{-1}$$

Thus acetolysis of <u>exo</u>-bicyclo[2.1.1]hexen-5-yl methoxyacetate (61) is approximately five times faster than that of the corresponding norbornadien-7-yl derivative. Relative solvolytic rates of some representative esters at 25° are given in the following table.

Table 5

	Relative rate	Reference
	1	86
	10^5	85
	10^{11}*	64
	10^{14}	86
	5×10^{14}	this work (4)

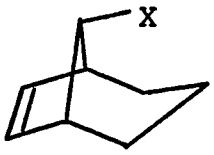
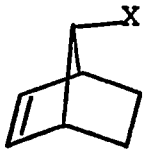
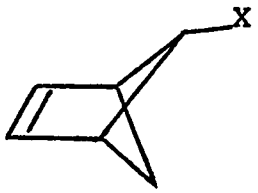
*The hydrolysis rate of anti-norbornen-7-yl chloride in 80% aqueous acetone was compared with that of norbornadien-7-yl chloride. The relative rates of a given pair of p-toluenesulfonates is assumed to be the same as those of the chlorides and methoxyacetates.

In comparing the solvolytic behaviour of the bicyclo[2.1.1]-hexene and anti-norbornen-7-yl systems, the additional anchimeric assistance observed for the former is undoubtedly due to the shorter distance between the double bond and the formal cationic center. Again in this study it is apparent that the effect of the bond angle at the reaction site plays a minor role in systems possessing favourable geometry for homoallylic participation. Thus, although the bond angle (C_1 - C_5 - C_4) in bicyclo[2.1.1]-hexene derivative is undoubtedly smaller than the corresponding angle (C_1 - C_7 - C_4) in norbornenyl systems the former system exhibits ca. 5×10^3 greater solvolytic reactivity[87].

Alternatively, as was done in a recent study[1], the relative solvolytic rates of unsaturated esters and their saturated analogs can be used as an indication of the amount of anchimeric assistance observed for a particular system. However before such a comparison is undertaken, the choice of a saturated ester as a model has to be made carefully. The solvolysis of exo-bicyclo-[2.1.1]hex-5-yl tosylate (31) has been studied and it was shown that the saturated ester itself undergoes anchimerically assisted solvolysis. An extrapolated value for the acetolysis rate constant for this ester at 25° is

$k = 2.24 \times 10^{-11} sec^{-1}$. However, the unassisted rate for this system as calculated by the Foote-Schleyer equation should be $k = 2 \times 10^{-18} sec^{-1}$. Therefore the solvolysis of exo-bicyclo[2.1.1]hex-5-yl tosylate is anchimerically assisted by a factor of ca. 1×10^{7}. If the calculated rate is used as the unassisted model the following ratios are obtained.

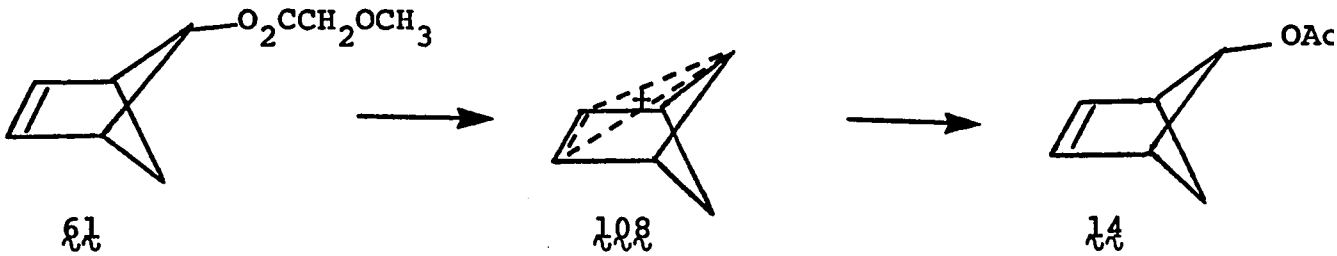
Table 6

	k_{unsat}/k_{sat}	Reference
	1.9×10^{5}	1
	1.0×10^{11}	64
	5.0×10^{16}	4

The above results demonstrate the influence of the distance between the double bond and the developing carbonium ion center on the rate of solvolysis of representative esters. Shortening of the saturated bridge, in the above bicyclo[n.2.1]derivatives, brings the potential cationic center closer to the site of unsaturation. This enables more effective homoallylic participation, which is reflected by greatly enhanced solvolytic rates. Even in the endo-bicyclo[3.2.1]oct-8-yl system, which exhibits the least anchimeric assistance of the examples presented, the delocalization of the charge in the intermediate seems substantial, as demonstrated by the retained configuration in the solvolysis product.

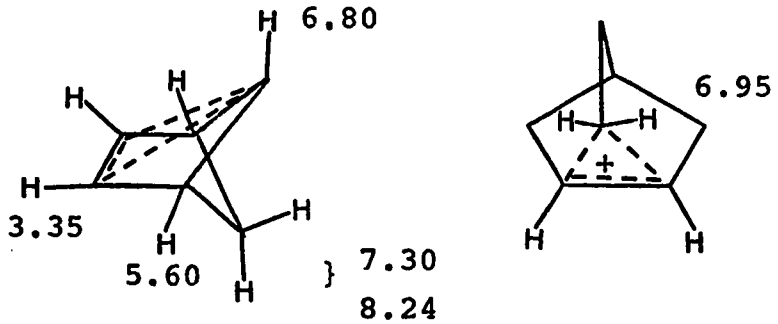
The extremely high rate enhancement observed in the exo-bicyclo[2.1.1]hex-2-en-5-yl system indicates the involvement of a very stable nonclassical type of intermediate. This is further confirmed by the exclusive formation of the product of retained structure and configuration. Thus the acetolysis of the exo-bicyclo[2.1.1]hexenyl methoxyacetate is best described as proceeding through a bis-homocyclopropenyl type of intermediate. This intermediate was directly observed by NMR spectroscopy. A solution of exo-bicyclo[2.1.1]hexenyl acetate (14) in methylene chloride was transferred into fluorosulfonic acid under

vacuum at liquid nitrogen temperature. The solution was mixed at -60°, giving a bright orange color in the lower layer[70].



61 108 14

The NMR spectrum, using methylene chloride as an internal standard, exhibited the following signals: τ 3.35 (unresolved d, 2H), 5.60 (unresolved d, 2H), 6.80 (dt, 1H), 7.30 (overlap of d and s, 1H and 3H) and 8.24 (dd, 1H). Irradiation at either τ 6.80 or 7.30 collapsed the signal at τ 8.24 into a doublet.



The NMR signals of the bicyclo[2.1.1]hexenyl cation have been assigned as shown on the above diagram[80]. This spec-

trum is quite similar to those recorded for some other nonclassical cationic species (see page 73 and the above diagram for norbornyl cation). In these ions, the chemical shifts of protons attached to the bridging carbon atom are at a quite high field. This is thought to be due to the charge delocalization involving $C_{2,3}$ and the rehybridization of the carbon atom in question[80]. As seen from these spectra, the "olefinic" protons in different cations resonate at approximately the same, low field region.

In conclusion, solvolytic study of the bicyclo-[2.1.1]hexene system provides an additional example of homoallylic participation. Due to the favourable geometric relationship between the double bond and the potential cationic center a uniquely large anchimeric assistance to ionization was observed in this system.

Solvolysis of exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate

After successfully completing the synthesis of the exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate (75) a study of its solvolytic reactivity was undertaken. The products and their structural proofs are described in the first chapter of this thesis. The ester (75) solvolyzed in 60% aqueous dioxane with liberation of 0.76 equivalent of p-nitrobenzoic acid. The progress of the reac-

tion was followed by titrating the liberated acid against a standard solution of sodium hydroxide in 60% aqueous dioxane using phenolphthalein. The rate constants were corrected for the amount of internal return and provided the following activation parameters:

$$k_{121.56} = (1.30 \pm 0.08) \times 10^{-4} sec^{-1}$$
$$k_{101.55} = (2.66 \pm 0.13) \times 10^{-5} sec^{-1}$$
$$\Delta H^{\dagger} = 22.5 \pm 1.8 \text{ kcal/mol}$$
$$\Delta S^{\dagger} = -19.8 \pm 4.6 \text{ eu}$$

These data give an extrapolated rate constant for the solvolysis of the tricyclic ester at 25°:

$$k_{25} = 7.82 \times 10^{-9} sec^{-1}$$

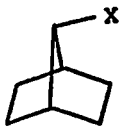
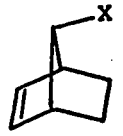
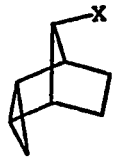
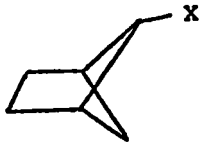
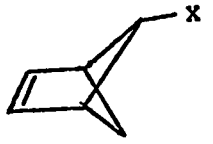
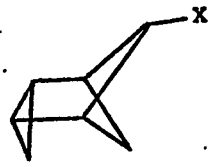
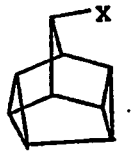
Recently reported[107] reaction parameters for the solvolysis of the anti-norbornen-7-yl p-nitrobenzoate (92d) in the same solvent system give an extrapolated rate constant at 25°:

$$k_{25} = 7.78 \times 10^{-11} sec^{-1}$$

Thus the solvolysis of the tricyclic ester (75) proceeds about a hundred times faster than that of the corresponding anti-norbornen-7-yl derivative (92d). Rates of solvolysis of some representative esters are given in the

following table.

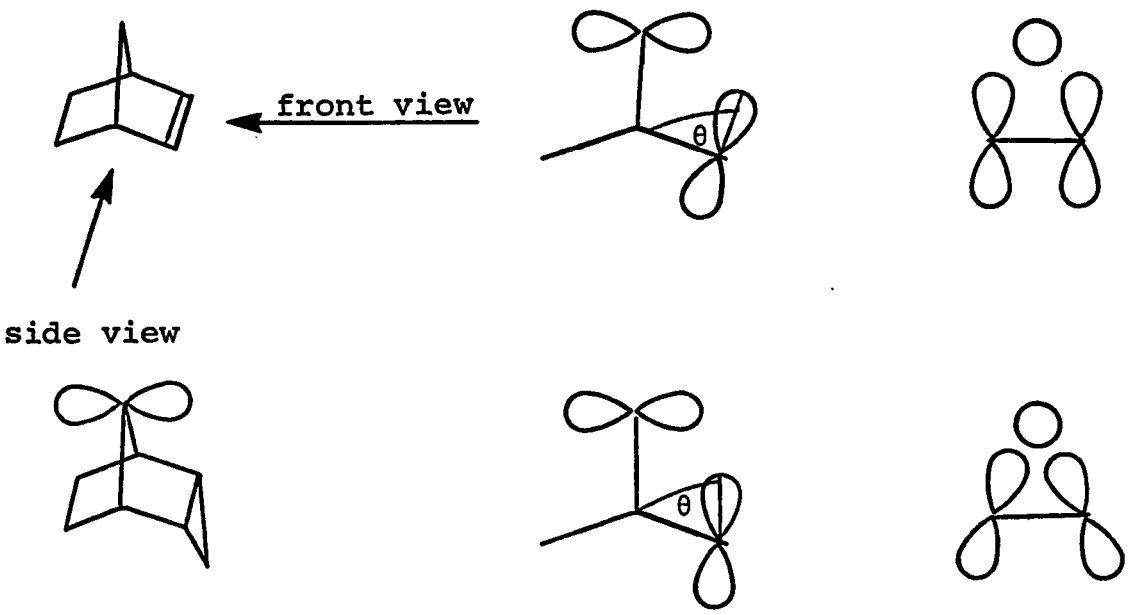
Table 7

	relative rate	reference
	1	72
	10^{11}	72
	10^{14}	106,107
	10^{5} (10^{-2})*	85
	5×10^{14}	4
	10^{13}	this work
	10^{12}	2

*The relative rate in parentheses is the unassisted rate as calculated by the Foote-Schleyer equation.

Besides demonstrating the ability of the double bond and cyclopropane ring to greatly enhance solvolytic reactivities, this above table allows additional comparisons. The rate acceleration observed for the anti-norbornen-7-yl system (92d) is 10^{11} relative to the corresponding saturated compound. The related exo-anti-tricyclo-[3.2.1.$0^{2,4}$]oct-8-yl derivative (105) exhibits an additional thousand-fold rate acceleration when compared with the unsaturated ester (92d). The additional rate acceleration may be rationalized in the following terms[106, 108]: examination of models indicates that the participating orbitals of the tricyclic ester are disposed more favourably towards the incipient carbonium ion than are the corresponding orbitals in the unsaturated ester. This effect is illustrated in the following scheme which depicts both side and front views of the two systems. Angle θ of the tricyclic derivative (105) is less than the corresponding angle in the anti-norbornen-7-yl derivative (92d). The front view diagram shows that the participating cyclopropyl orbitals are oriented in such a way as to allow more effective interaction than are the p orbitals of the double bond. Both of these effects, it was suggested by authors, lead to more effective orbital interaction and may in part account for the additional anchimeric assis-

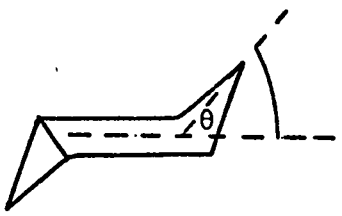
tance.



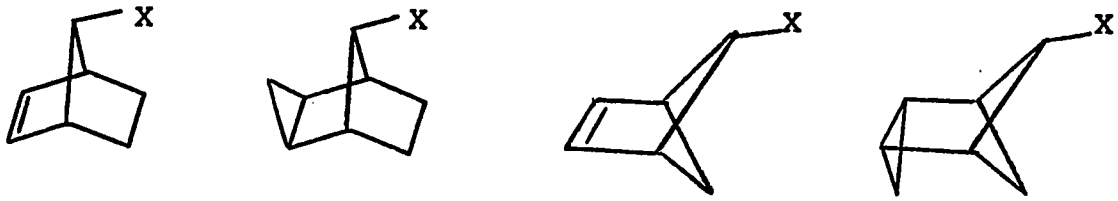
In comparison, the pentacyclononyl p-nitrobenzoate (107) solvolyzes some 80 times slower than the tricyclooctyl ester (105) or about 10 times faster than the corresponding anti-norbornen-7-yl derivative. The smaller rate acceleration (10^1) observed for the pentacyclic ester (107) compared with the tricyclic ester (10^3) was discussed in terms of extra strain release in the transition state of the tricyclic p-nitrobenzoate (105). The tricyclic compound rearranges to a less strained structure while the pentacyclic ester yields product of retained carbon skeleton. In addition, the change in the

orientation of the cyclopropane ring was considered. It was suggested that due to the incorporation of the cyclopropane into this polycyclic ring system it might become less favourably oriented towards the potential cationic center.

In analogy to the relative reactivities described above (in particular, those of 105 and 92d) one would expect that the exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl (75) derivative would exhibit greater solvolytic reactivity (ca. 10^3) than the appropriately substituted bicyclo-[2.1.1]hexene system. Contrary to this expectation, a slight rate retarding effect (ca. 10) was observed. Consideration of some dihedral angles in models of these compounds did not reveal the origin of this discrepancy. Some theoretical calculations[109] have indicated that the amount of stabilization of the tris-homocyclopropenyl cation is dependent on the angle by which the C_3 is raised above the plane of the molecule. It was also predicted that the maximum stabilization would occur if the C_3 is raised about 80° towards the chair form.



The X-ray data are available for the anti-norbornen-7-yl[110a] (a) and syn-tricyclo[3.2.1.$0^{2,4}$]oct-8-yl system[110b] (b) and they reveal that the angles under consideration are ca. 56°. By comparison of molecular models it was concluded that the angle in the bicyclo[2.1.1]hexene derivative (c) has a similar value. The X-ray data obtained in this study for the exo-anti tricyclo heptyl (d) system reveal that the pertinent dihedral angle is ca. 76°



a b c d

which gives rise to the prediction that the tricyclo[3.1.1.$0^{2,4}$]heptyl derivative (d) should exhibit the largest solvolytic reactivity of the systems under consideration. The reason for this discrepancy is obscure at this time and therefore any further discussion would necessarily be of highly speculative nature.

Another way of estimating the amount of anchimeric assistance to ionization in solvolytic reactions is the semi-empirical method devised by Foote and Schleyer[55] that has been mentioned several times. By this method the

unassisted solvolytic rate can be calculated by taking into account the bond angle strain, torsional strain, nonbonded strain and inductive effects. The amount of anchimeric assistance is then obtained as the ratio between the observed rate (relative to that of cyclohexyl tosylate) and the calculated rate. The following equation correlates the carbonyl stretching frequency of the ketone with the rate of solvolysis of the corresponding secondary tosyl ester in acetic acid at 25°.

$$\log_{\text{rel. rate}} = (1715 - \nu_{CO}\ \text{cm}^{-1})/8$$

The effect of torsional strain can likewise be estimated from the expression:

$$1.32\Sigma(1 + \cos 3\phi_i)$$

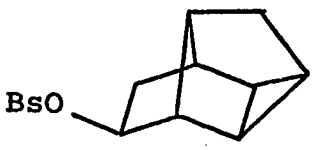
This term considers the effect of the dihedral angle between groups around the reaction site. The effect of nonbonded interactions is assessed by the (GS - TS) term. Finally, when electronegative groups are present in the molecule, an empirical correction for their inductive effect is employed. The appropriate values for the last two terms are available in the literature. The equation that relates all these terms with the relative rate is given below.

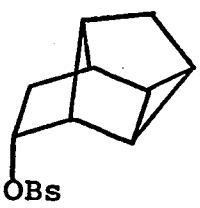
$$\log k_{rel} = (1715 - \nu_{co})/8 + 1.32\ (1 + \cos 3\phi_i) +$$

$$+ (GS - TS)/1.36 + \text{Inductive Term}$$

This equation was successfully employed for calculation of relative rates of solvolysis for numerous tosyl esters in acetic acid at 25°. If the method is to be applied to esters other than tosylates then an estimate of the solvolytic rate for the corresponding tosylate must be made. For the solvolysis of a p-nitrobenzoate in some common solvents this estimate can be achieved by multiplying by a factor of 10^7 the solvolytic rate of the p-nitrobenzoate[111] (25°). The value thus obtained represents the estimated rate of solvolysis of a given tosylate in a particular solvent system. By utilizing appropriate factors available in the literature[112] the above rate can then be converted into an estimated rate in acetic acid. The results of the application of the Foote-Schleyer equation to some pertinent systems are given in the following table.

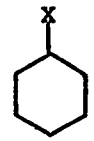
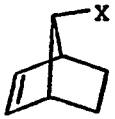
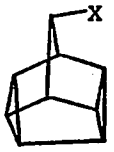
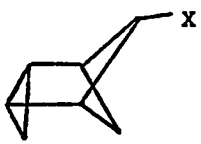
Identical treatment of some other systems provided the following values[105].





Log. anch. assistance	5.9	3.7

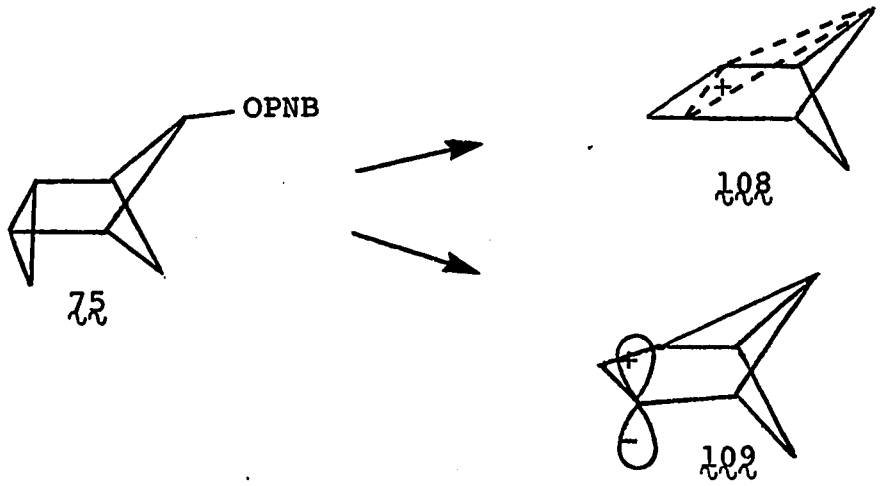
Table 8

System	$\bar{\nu}$ of Ketone (cm^{-1})	ϕ Degree	GS-TS	Inductive	log. $k_{rel.}$ rate		log. Anch. Assistance	Ref.
					Calc.	Observed		
	1716	60,60	0	0	-0.1	0	0.1	55
	1773	60,60	0.4	0	-7.0	-7.0	0	55
	1780	60,60	0.3	-0.9	-8.8	+4.11	12.9	55
	1760	60,60	0.4	-0.5	-5.8	+6.7	12.5	108
	1770	60,60	0.4	-1	-7.57	+4.7	12.3	2
	1788	0,60	0.4	-0.5	-9.3	+5.9	15.2	This Work

Comparison of the above two compounds with the last three esters in the table clearly indicates that the amount of anchimeric assistance greatly depends on the relative configuration of the participating cyclopropane ring and the leaving group. It is interesting to note that according to the results of the applications of the Foote-Schleyer equation to the above compounds, the exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl system (75) exhibits the largest amount of anchimeric assistance. Since the ketone corresponding to the bicyclo[2.1.1]hexene skeleton is not known, it is not possible to apply the above calculation to that system. Regardless of the relative reactivities of the unsaturated esters and their counterparts containing a cyclopropane ring the characteristic feature emerging from these studies is a tremendous anchimeric assistance observed for derivatives possessing either of these functionalities in proper geometry relative to the departing group.

All the evidence accumulated in this study indicates that the solvolysis of exo-anti-tricyclo[3.1.1.$0^{2,4}$]-hept-6-yl p-nitrobenzoate (75) proceeds through a nonclassical type of intermediate. Carbonium ion formation begins by equal contribution of cyclopropyl orbitals from C_2 and C_4 which can lead to the formation of two possible inter-

mediates[106]. If equal contribution continues, a cyclopropenyl type of intermediate is formed. Alternatively the contribution from one of the atoms can predominate, thus leading to the formation of a classical intermediate (109).



The two types of intermediates under consideration would lead to different stereoselectivity of product formation. Therefore the product analysis study is indicative of the type of intermediate involved. As already indicated the endo-tricyclo[3.2.0.0^{2,7}]heptyl alcohol (76) and the corresponding p-nitrobenzoate (77) were the exclusive products of solvolysis of exo-anti-tricyclo[3.1.1.0^{2,4}]heptyl p-nitrobenzoate. A control experiment indicated that the isomeric exo-tricyclo[3.2.0.0^{2,7}]heptan-4-ol (79) survives the reaction conditions. The exo-anti-tricyclo-

[3.1.1.$0^{2,4}$]heptan-6-ol (87) was likewise tested and found to rearrange slowly into a single product, which was tentatively identified as Δ^3-cyclohexenecarboxaldehyde (coinjection with an authentic sample, mass spectral comparison). However neither exo-anti-tricyclo[3.1.1.$0^{2,4}$]heptan-6-ol nor Δ^3-cyclohexenecarboxaldehyde was present in the solvolysis product.

The exclusive formation of rearranged products indicates extensive delocalization of positive charge from C_7 to C_2 and C_4 in the intermediate. The presence of ca. 26% of the ion pair return product implicates the involvement of a relatively stable cationic species.

The high stereoselectivity of the product formation provides similar and more compelling evidence. The related tricyclo[3.2.0.$0^{2,7}$]heptan-4-one (84) on reduction with sodium borohydride yields exclusively the product of exo attack. In contrast endo attack is the exclusive mode of approach by nucleophilic species to the corresponding cation under solvolytic conditions. This is consistent with an electronic effect which shields the exo side and directs the approaching nucleophile to the sterically more hindered endo side.

Accelerated rates of solvolysis, lack of extensive rearrangement and the stereospecific formation of

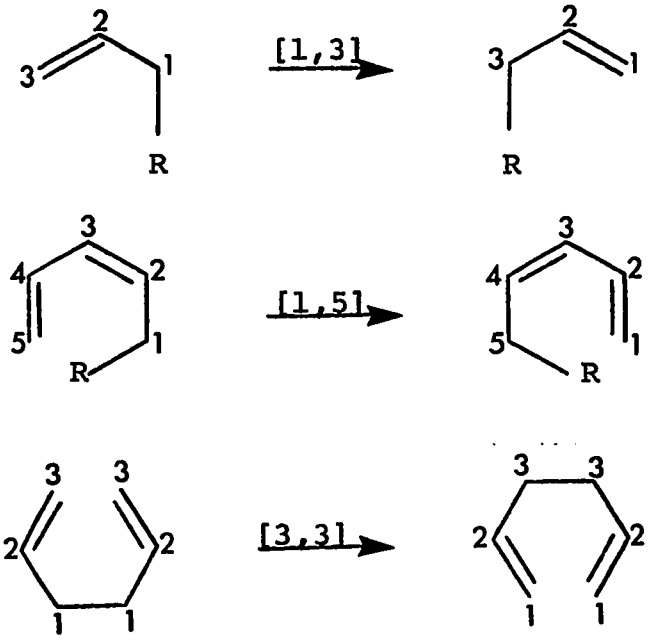
products have all been taken as evidence for the formation of a tris-homocyclopropenyl cation. In one case the formation of the ion-pair return product was interpreted as being indicative of the presence of a relatively long lived cation[106]. According to these criteria the solvolysis of the exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate proceeds via a nonclassical intermediate.

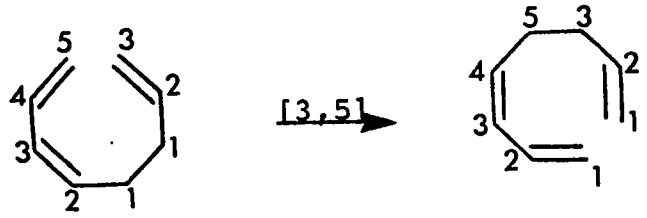
III. STUDY OF THERMOLYSIS

HISTORICAL:

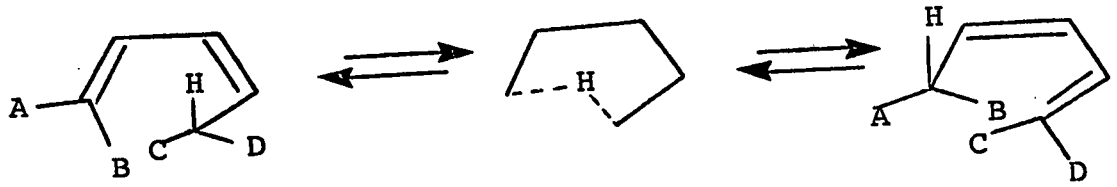
Sigmatropic Reactions

A sigmatropic reaction of order [i, j] is defined as "the migration of a σ-bond, flanked by one or more π-electron systems, to a new position whose termini are i-1 and j-1 atoms removed from the original bonded loci, in an uncatalyzed intramolecular process."[84] Some generalized illustrations of sigmatropic reactions are shown below.

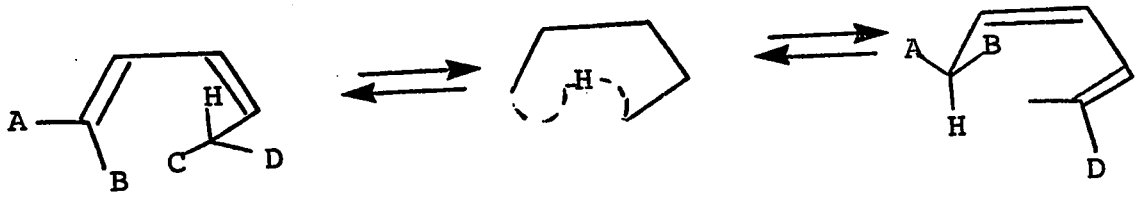




As illustrated for the [1, 5] hydrogen migration there are two topologically distinct ways of effecting this migration,



suprafacial



antarafacial

In the suprafacial process, the hydrogen interacts at all times with the same face of the π system. In the antarafacial process the migrating atom passes from the top face of one carbon to the bottom face of another.

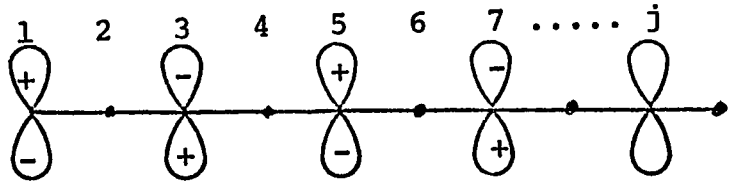
The transition states for thermally induced reaction may be considered as consisting of interaction

between a hydrogen atom and the highest occupied molecular orbital of a radical, containing $2k + 3\pi$ electrons. This is illustrated on the [i, j] sigmatropic migration within the all cis polyolefinic framework.

$$R_2\overset{1}{C}=\overset{2}{C}H-(CH=CH)_k-\overset{j}{C}HR_2 \longrightarrow R\overset{1}{C}H(CH=CH)_kCH=CH_2$$

A B

The highest occupied molecular orbital has the form shown:



In order to maintain positive overlap between the highest occupied orbital of the olefinic system and the hydrogen orbital, the isomerization of A → B must occur thermally by a suprafacial path when k is odd, and antarafacially when k is 0 or even. For transformation involving the excited states, the important consideration is the interaction between the lowest unoccupied orbital of the polyenic chain and the hydrogen atom orbital. Thus the selection rule is precisely reversed, as compared with that

for the ground states. The selection rules for sigmatropic changes of the order [1, j] for j < 7 are summarized in the following table.

Table 9

Selection Rules for a Sigmatropic Change of the Order [1, j]

[1, j]	Thermal	Excited State
[1, 3]	Antarafacial	Suprafacial
[1, 5]	Suprafacial	Antarafacial
[1, 7]	Antarafacial	Suprafacial

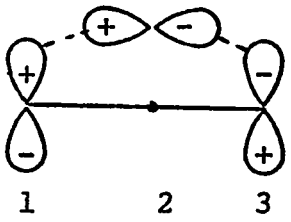
For sigmatropic changes of order [i, j] in which both i and j are greater than 1, the appropriate selection rules have also been derived[84].

Sigmatropic reactions that violate these selection rules may be taking place through multi-step process; these are expected to proceed through higher energetic barriers than concerted reactions.

The nature of the orbital binding the connecting atom of the migrating group R to the unsaturated system plays a very important role[84, 114] and therefore must be specified. If and only if the orbital involved is symmetrical (s-orbital) or one lobe of an unsymmetrical orbi-

tal (p-orbital), then the rules summarized in the above table apply. In such a case a sigmatropic reaction occurs with retention of configuration at the migrating atom. However, if the migrating atom uses both lobes of an unsymmetrical orbital (p-orbital) during the reaction, then the rules summarized in the table are precisely reversed (thermally induced [1, 3] migration is suprafacial etc.). In addition, since the migrating group uses the opposite faces of its connecting atom in the transition state, such a process occurs with inversion of configuration at the atom under consideration. The above discussion is illustrated in the following scheme by the example of the [1, 3] sigmatropic migration.

[1, 3] antarafacial sigmatropic shift. R uses a symmetrical or one lobe of an unsymmetrical orbital (retention).



[1, 3] suprafacial shift with inversion of configuration. R uses both lobes of an unsymmetrical orbital.

In order that the orbital symmetry rules be applicable, the unsaturated system under consideration must retain approximate coplanarity in the transition state. If a potential reaction were to involve distortion of the carbon framework to the extent that overlap within the π-system is impaired, then such a symmetry allowed process would be rendered difficult or impossible. This may explain why no examples of thermal [1, 3] hydrogen shifts have been found. For the same reason antarafacial processes are impossible for transformations within small or medium size rings. Thus, the study of [1, 3] sigmatropic shifts is practically restricted to the suprafacial processes.

Of primary concern in this thesis are thermally induced [1, 3] sigmatropic reactions.

Whether or not the particular sigmatropic rearrangement is proceeding via a concerted or stepwise path-

way can be tested experimentally in one of the following ways:

a) by determining the stereochemistry of the products and comparing it with the geometry predicted by the selection rule: a reaction proceeding via a concerted mechanism necessarily must yield products of the predicted stereochemistry.

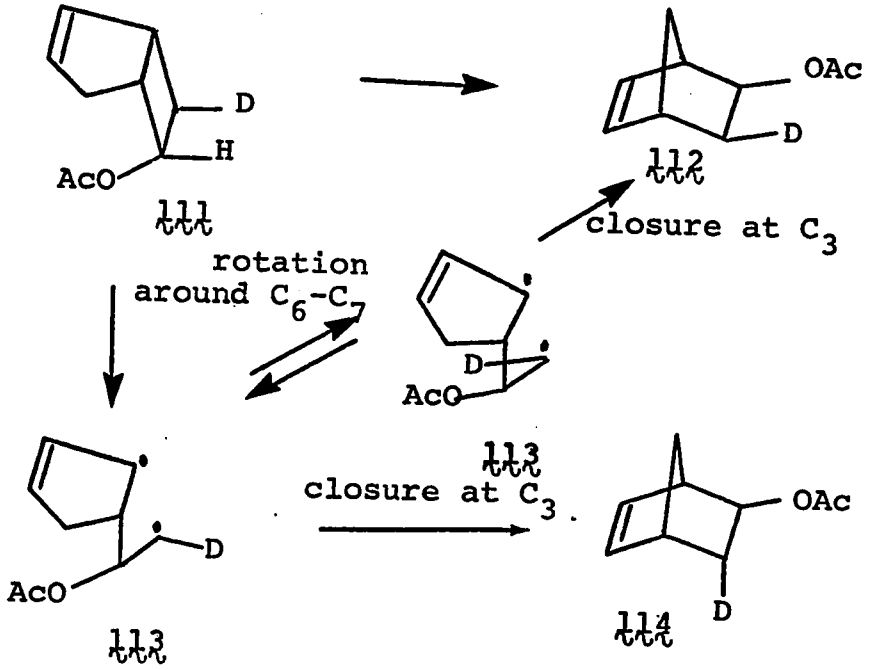
b) by determining the kinetic parameters and comparing them with those that were estimated on the basis of the transition state method calculation. These estimates are specific to the free radical pathway and concerted reactions are implicated when the observed value for energy of activation and a frequency factor are significantly lower than the predicted ones.

c) by obtaining direct evidence for the presence of radical intermediates.

In 1968 Berson and Nelson[114] studied thermal isomerization of specifically labelled exo-7-d-bicyclo-[3.2.0]-2-hepten-endo-6-yl acetate (111) to norbornyl acetate. Since antarafacial migration is improbable in small and medium sized rings, only two alternative pathways appeared feasible:

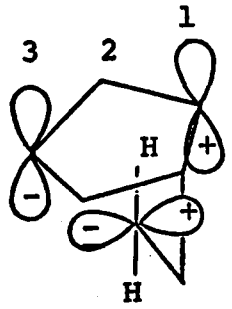
a) [1, 3] suprafacial sigmatropic shift with inversion at the migrating center, or

b) a stepwise process that would lead either to randomization (if free rotation around C_6 - C_7 is faster than the reclosure of the C_1 - C_3 bond) or retention (if the situation is reversed) of stereochemistry at the migrating carbon atom.



Pyrolysis of 111 was quenched at 6-30% completion (because of competing reactions) and the exo-norbornen-2-yl acetate (112) was shown to contain at least 95% of deuterium in a cis position to the acetate group. Thus the rearrangement proceeded in a stereospecific manner with inversion of configuration at the migrating centre. The following transi-

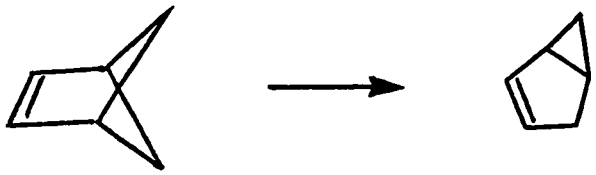
tion state was proposed.



If the 3-5% of the endo-3-d isomer (114) that were found in the pyrolysis product were formed via a stepwise process involving a diradical intermediate (115), the activation energy for such a process is only 2.5 kcal/mole higher than that of the concerted process.

In the transition state (113) the migrating carbon and its two substituents lie in a plane perpendicular to the five member ring. By the attachment of a bulkier group to the endo C_7 position, (according to the authors) the steric interactions in the transition state would probably become so severe that the stepwise process might be dominant in the reaction. This assumption was verified in their subsequent study[116] of the endo-bicyclo[3.2.0]hept-2-ene-6-yl acetate having a methyl group in the endo and exo C_7 position.

In 1969 Frey et al[117] reported a study of the thermal gas phase isomerization of bicyclo[2.1.1]hex-2-ene (10).



10

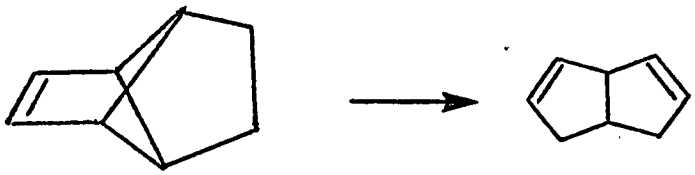
The reaction was found to proceed quantitatively and for the temperature range of 149-190° the first order rate constants were found to fit the Arrhenius equation:

$$k = 10^{13.95 \pm 0.07} \exp(-35.170 \pm 140/RT)\,sec^{-1}$$

There are no methods available for estimating the activation energy for the concerted process. The frequency factor however, can be estimated and the predicted value is $A = 10^{14}$. On the other hand both E_a and A can be estimated for a stepwise process using the method developed by Benson and O'Neal[118]. This calculation predicts an energy of activation of 36.4 kcal/mole and a frequency factor of $10^{14.7}$. The close agreement between the value of the A factor predicted for a concerted process and the observed value led the authors to conclude that a stepwise process does not play a major role in this reaction. The comparison of the estimated energy of activation (36.4 kcal/mole) with the observed one (35.17 kcal/mole) seems to suggest that the energetic stabilization of a concerted transition state in this case is not very sub-

stantial.

The same authors[117] studied the thermal isomerization of tricyclo[3.3.0.$0^{2,6}$]oct-3-ene (115). This reaction must proceed through a radical dissociation-hydrogen migration process since the presence of the extra ring makes a concerted reaction impossible.



115

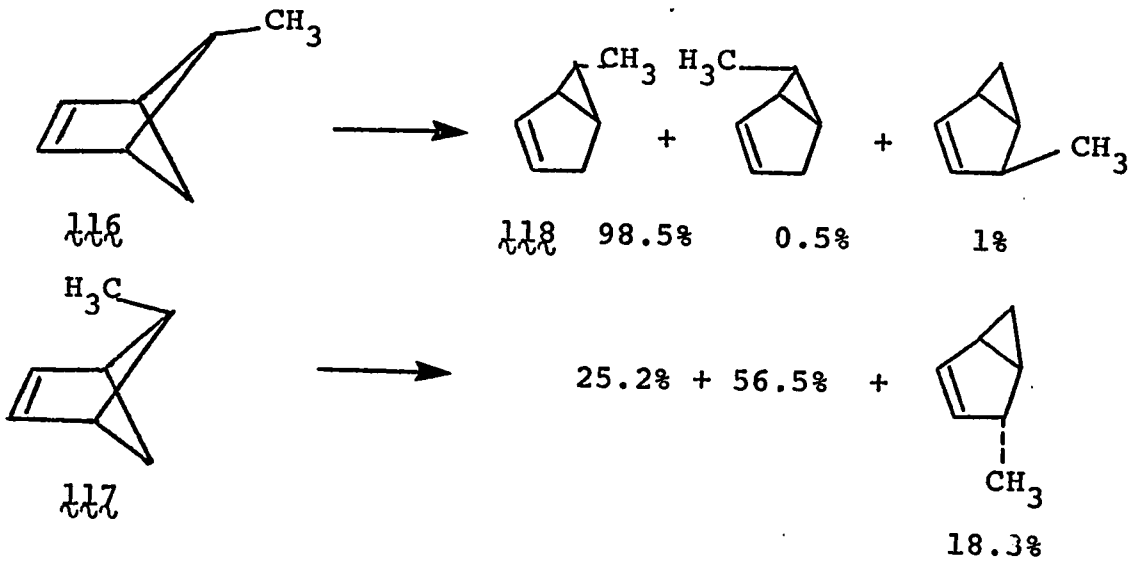
First order rate constants were found to fit the Arrhenius equation

$$k = 10^{14.35 \pm 0.06}{}_{exp}(-35.2000 \pm 130/RT)_{sec^{-1}}$$

The comparison of activation energy observed for 115 with that observed for bicyclo[2.1.1]hex-2-ene (10) is not very meaningful. The extra strain present in the tricyclic compound (115) probably lowers the activation energy required for a diradical process. The estimated value of the A factor for a concerted process is $10^{14.0}$ (assuming that $\Delta S^{\dagger} = 0$). The observed value of the A factor is $10^{14.35}$ corresponding to a slightly positive entropy of activation, which is reasonable for a diradical intermediate.

We reported in 1969 a study of the thermolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate[4] (14).

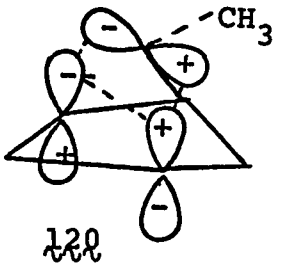
Later in the same year Roth and Friedrich[119] described the thermal behaviour of epimeric 5-methylbicyclo[2.1.1]hex-2-enes. The two epimers underwent thermolysis at different rates (endo isomer being ten times slower) yielding the following products.



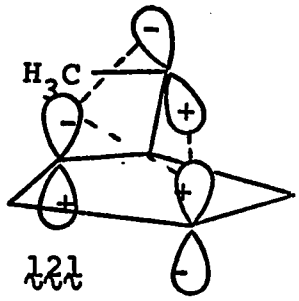
The rearrangement of 116 proceeds in a stereospecific manner giving the product (118) of inversion of configuration at the migrating C_5 centre. The rearrangement of 117 is less stereospecific; however, the product formed by inversion of configuration (119) is still predominant.

The difference in stereospecificity and the rate of reaction of the two compounds (116, 117) was explained

in the following manner:



120



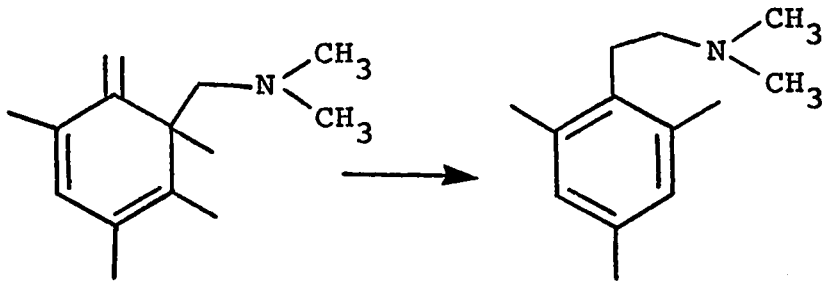
121

The exo methyl isomer (116) rearranges through a transition state (120) in which the methyl group is positioned outside the ring. In contrast, the endo methyl compound (117) proceeds through the transition state (121) in which the methyl group is positioned over the ring and therefore suffers strong nonbonded interactions. As a consequence the distance between the methyl group and the ring is increased, resulting in less effective orbital overlap and thus making the stepwise process competitive, resulting in a decreased rate of rearrangement. Likewise the tendency for the less substituted methylene bridge to migrate is increased.

Baldwin and Brown[120], in a study of a thermal isomerization of the exo-methylenecyclohexadienamine were able to obtain direct evidence for the involvement of a radical dissociation-recombination mechanism. When the rearrangement (122 → 123) was carried out between 120-170° in the probe of an NMR spectrometer emission and

enhanced absorption were observed in the NMR signals of the protons directly attached to the carbon atoms involved in the rebonding process. Observation of chemically induced dynamic nuclear polarization strongly suggests that the reaction is proceeding via a diradical mechanism.

Testing of the mechanism of sigmatropic reactions by following the degree of their stereospecificity has been the most successful of the methods employed. The other two methods are not particularly decisive but they do provide an insight into the mechanism operating. The drawback of the method employing estimation of activation parameters is that in some cases the difference between predicted and observed values are not large enough as to implicate clearly one mechanistic possibility. On the other hand the CIDNP[121] phenomenon is necessarily time-dependent and therefore its absence does not exclude an extremely short-lived diradical intermediate.

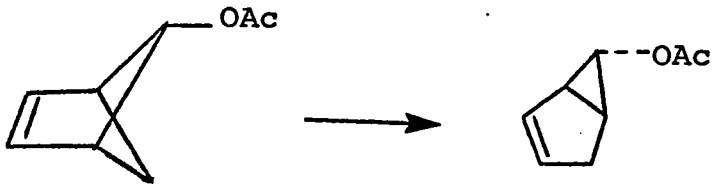


122 123

RESULTS AND DISCUSSION:

Thermolysis of exo-Bicyclo[2.1.1]hex-2-en-5-yl Acetate

From studies of the products, it was suspected that the thermal conversion of exo-bicyclo[2.1.1]hexen-5-yl acetate (14) to exo-bicyclo[3.1.0]hexen-6-yl acetate (53) was taking place during the solvolysis of bicyclo-[2.2.0]hexenyl p-nitrobenzenesulfonate (52).



14 53

The distribution of acetate products (14 and 53) varied with the reaction time and 53 became the major product (>90%) after ten solvolytic half lives. The structural proof for the exo-bicyclo[3.1.0]hexen-6-yl acetate is presented in Part one of this thesis.

The isomerization of 14 was studied in n-dodecane, by monitoring (glpc) the disappearance of the starting material against an internal standard. The isomerization was first order and provided the following kinetic parameters.

$$k_{85.1} = (3.39 \pm 0.10) \times 10^{-5} sec^{-1}$$

$$k_{105.1} = (2.78 \pm 0.07) \times 10^{-4} sec^{-1}$$
$$\Delta H^{\dagger} = 27.5 \text{ kcal/mol}$$
$$\Delta S^{\dagger} = -2 \text{ eu}$$

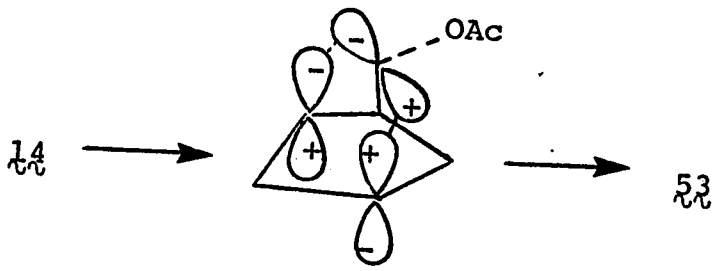
The rate of isomerization was also measured in acetic acid.

$$k_{90.4} = (4.25 \pm 0.11) \times 10^{-5} sec^{-1}$$
$$k_{110.0} = (3.60 \pm 0.10) \times 10^{-4} sec^{-1}$$
$$\Delta H^{\dagger} = 29 \text{ kcal/mol}$$
$$\Delta S^{\dagger} = 2 \text{ eu}$$

The insignificance of the rate difference ($k \frac{\text{n - dodecane}}{\text{acetic acid}} = 1.5$) rules out the possibility that this process is of an ionic nature.

As previously noted during the entire course of the thermal isomerization of exo-bicyclo[2.1.1]hexenyl acetate (14) only the formation of exo-bicyclo[3.1.0]hexenyl acetate (53) was observed. No endo-bicyclo[3.1.0]-hexenyl acetate (62) was formed. When this latter compound (62) was subjected to the thermolysis conditions it was recovered unchanged after a reaction time in which the thermolysis of 14 would have been essentially complete. This control experiment demonstrated that the endo acetate (62) was not involved in the thermolysis of the exo-bicyclo-[2.1.1]hexenyl acetate (14). Indeed the observed stereospecificity indicates that the rearrangement is a supra-

facial [1, 3] sigmatropic migration proceeding with inversion of configuration at the migrating centre. Formation of exo-bicyclo[3.1.0]hexen-6-yl acetate (53) would occur through the following transition state, which is in accord with the principles of orbital symmetry conservation[84].



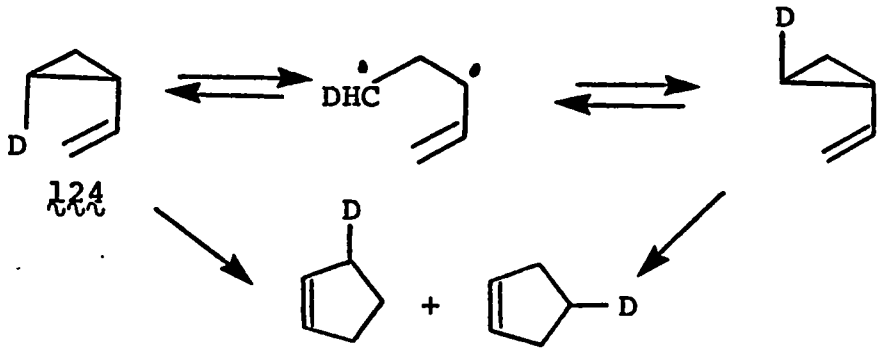
14 → 53

Although the kinetic parameters obtained are the first for this type of reaction, the lack of any suitable model for comparison precludes these data from being particularly revealing.

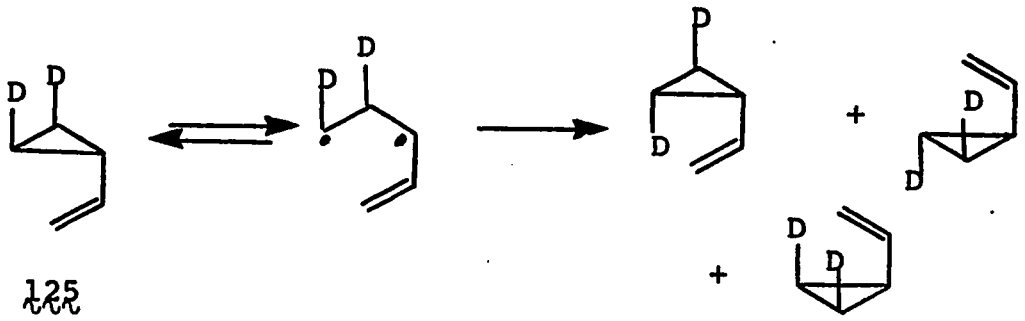
The above thermal isomerization is a reverse of the well-known vinylcyclopropane-cyclopentene rearrangement. Since the vinylcyclopropane-cyclopentene rearrangement is exothermic the reverse process is only rarely observed[122]. In bicyclo[2.1.1]hexene the strain of the system makes such a process possible.

The rearrangement of vinylcyclopropanes has been extensively studied and was shown to almost certainly proceed via diradical intermediates. Willcot[123] has shown that in the thermolysis of specifically deuterium labelled

vinylcyclopropane the loss of stereospecificity of the labelled site occurs at least five times faster than its rearrangement to cyclopentene. These results were explained on the basis of a diradical intermediate.



The thermolysis of cis-2,3-dideuterio-vinylcyclopropane (125), studied by the same group provides some additional evidence for the intervention of a diradical intermediate. A 2:1 mixture of trans- and cis-2,3-dideuterio vinylcyclopropane was produced. This scrambling of the label is indicative of a diradical in which free rotation around C - C bonds is rapid relative to the rate of ring closure:



125

However, the question of whether or not this radical is involved in the vinylcyclopropane-cyclopentene rearrangement has not been established. The present studies clearly demonstrate that at least the thermal conversion of 14 to 53 proceeds in a concerted manner. Stereospecificity was also observed in the thermolysis of exo-5-methyl bicyclo[2.1.1]hexene[119]. Some evidence has been presented that the isomerization of the parent hydrocarbon proceeds in a concerted manner[117]. However undoubtedly the presence of substituents on the system undergoing rearrangement may profoundly influence the course of the reaction; extrapolation from the substituted molecules to the parent compound is not possible. Therefore a study of the thermal isomerization of a specifically deuterium labelled bicyclo[2.1.1]hexene (10) would be warranted. After such a study has been completed, one can define the role of

the diradical in the vinylcyclopropane-cyclopentene rearrangement with a high degree of confidence.

IV. EXPERIMENTAL

All melting points and boiling points are uncorrected.

The IR spectra were obtained on a Perkin-Elmer model 21 and 257 infrared spectrophotometers.

Proton NMR spectra were measured with Varian Associates A-60 and HA-100 spectrometers.

The mass spectra were obtained on A.E.I. MS-2, MS-9 and MS-12 mass spectrometers.

Three glpc chromatographs were employed in this work (column packing material is specified in each particular case): F&M 5750 research chromatograph, H P 7620 A research chromatograph, (both of which were equipped with 6 ft x 3/16 in columns) and an F&M model 700 gas chromatograph (preparative) equipped with 10 ft x 1/4 in columns.

In all cases when the compound was distilled but no boiling point is reported a "cold finger" apparatus[125] was employed. It consisted of a cylindrical flask with a spiral-path cooling jacket between the pot and the tray. A temperature-controlled coolant was circulated through the jacket. By varying the vacuum and the temperature of the system a very effective separation of a number of compounds from solvent could be achieved. In the case of very small quantities of compound the distillate was washed out

of the cold finger with appropriate solvent and directly subjected to NMR analysis.

Preparation of trans-1,2-dihydrophthalic acid[16] (16)

A 5 l. three-necked flask equipped with a mechanical stirrer was charged with a solution of phthalic acid (188 g, 1.13 mole) and sodium acetate (270 g) in water (1700 ml). This solution was cooled in an ice bath and 3% sodium amalgam (3008 g) was added in 100 g portions over a 5 hour period. Immediately following the addition of each portion, 50% aqueous acetic acid (15-20 ml, 750 ml total) was introduced. The temperature of the solution was kept between 8-11°. Stirring was continued for an additional hour and the mixture was decanted from the mercury, then filtered. After acidification by 20% sulfuric acid (to pH ∿1), the solution was stored in an ice bath until precipitation was complete. The solid was collected in a Buchner funnel, washed with cold water (3 l.), and then dried under reduced pressure (90°, 20mm) to afford 155 g (84%) of 16, mp 203-207 (lit.[24] mp 207-214). NMR spectrum (acetone-d_6): τ 4.06 (s, 4H), 6.28 (s, 2H).

Preparation of cis-1,2-dihydrophthalic acid anhydride (17)

Acetic anhydride (800 ml) was heated to 105° in a three-necked flask equipped with a reflux condenser and

a mechanical stirrer. To this flask was then added 16 (155 g, 0.92 mole). The mixture was heated at 105° with vigorous stirring for 15 minutes, after which time all of the solid had dissolved. The bulk of the acetic anhydride was removed in vacuo (40°/20 mm). Residual acetic anhydride was removed by stirring the solid residue with xylene, which was then removed in vacuo. After washing with Skelly B, the solid was further purified by sublimation (80°/0.1 mm) to afford 110 g (79%) of 17, mp 102-106° (lit. mp 111-113°). NMR spectrum ($CDCl_3$): τ 3.70-4.36 (m, 4H), 5.99 (m, 2H). The sublimed anhydride was used in the subsequent step without further purification.

Preparation of bicyclo[2.2.0]hex-5-ene-2,3-dicarboxylic anhydride[16] (18)

A solution of 17 (5 g, 33 mmole) in anhydrous ether (1800 ml) was photolyzed under a nitrogen atmosphere using a 450W mercury lamp (Hanovia type), which was immersed in the solution in a water cooled quartz well containing a Vycor filter. The solution was stirred magnetically and photolyzed for twenty hours. The quartz well was removed every four hours and wiped free of yellow deposit, which blocked the effective irradiation (done 3-4 times). Ether was then removed in vacuo and the residue chromatographed (silicic acid-chloroform). Sublima-

tion (65-70°/0.1 mm) provided 1.52 g (30%) of 18. After recrystallization from Skelly B/ether it had a mp 159-162° (lit.[24] mp 160-164°). NMR spectrum ($CDCl_3$): τ 3.55 (m, 2H), 6.34 (m, 2H), 6.62 (m, 2H).

Preparation of exo-5-hydroxybicyclo[2.2.0]hexan-2,3-dicarboxylic acid (22)

A solution of 18 (4.1 g, 27.3 mmole) in dry tetrahydrofuran (80 ml) was placed in a 500 ml round bottom flask, equipped with nitrogen inlet and a magnetic stirrer. The flask was cooled to -15°. Diborane solution in tetrahydrofuran (1.3 M, 13.4 ml) was then added over a period of 15 minutes. After addition was complete, the flask was kept at -15° for two hours. Excess hydride was decomposed by the addition of aqueous tetrahydrofuran (40 ml, 1:1). The organo-borane was oxidized at 60° by the addition of 3 N sodium hydroxide (40 ml), followed by dropwise addition of 30% hydrogen peroxide (16 ml). The mixture was heated for another two hours at 60°, then cooled to 0°, and acidified with dilute hydrochloric acid to pH ∿1. The tetrahydrofuran was removed in vacuo and the acidic aqueous layer was continuously extracted with ether for twenty-four hours. After removal of the solvent the residue was dried by repeated evaporation with benzene (3 x 100 ml).

Crude 22 (5.3 g) was obtained as a white solid. NMR spectrum of the corresponding dimethyl ester exhibited the following signals ($CDCl_3$): τ 5.55 (t, 1H), 6.12 (s, 1H), 6.32 (s, 6H), 6.60 (m, 2H), 7.05 (m, 2H), 7.53 (m, 2H).

Preparation of exo-5-acetoxybicyclo[2.2.0]hexan-2,3-dicarboxylic anhydride (48)

The crude 22 (24 g, 0.129 mole) was stirred with pyridine (10 ml) and acetic anhydride (100 ml) at 45° for twelve hours in an inert atmosphere. The bulk of the solvent was removed in vacuo. The residual acetic anhydride was removed by stirring the residue with xylene (3 x 100 ml) which was then removed under reduced pressure to yield 34 g of crude 48. NMR spectrum ($CDCl_3$): τ 3.80 (t, 1H), 6.30-7.60 (m, 6H), 7.96 (s, 3H). IR spectrum ν_{max} 1860 cm^{-1} (m), 1785 cm^{-1} (s), 1740 cm^{-1} (s).

Preparation of exo-5-acetoxybicyclo[2.2.0]hexan-2,3-dicarboxylic acid (49)

The crude 48 (34 g) was stirred in water (100 ml) at 80° for two hours. The water was removed under reduced pressure and the residual solid dried by repeated evaporation with benzene (3 x 100 ml). Chromatography of the resultant solid (silicic acid, 4% methanol in chloroform) followed by crystallization from chloroform-ether

afforded 12.4 g of 49, mp 182-183.5°. NMR spectrum (acetone-d_6): τ 3.94 (bs, 2H), 4.78 (t, 1H), 6.40 (m, 2H), 6.97 (m, 2H), 7.39 (m, 2H), 7.98 (s, 3H).

Preparation of exo-bicyclo[2.2.0]hex-5-en-2yl acetate (50)

A solution of 49 (1 g, 4.4 mmole) in water (9 ml) containing triethylamine (1.4 ml) was added to pyridine (97 ml) in an electrolysis cell[26]. The cell was cooled externally with an ice bath to maintain an internal temperature of about 20°. The solution was electrolyzed with an internal current of 0.8 A (DC) which, over a period of eight hours, decreased to less than 0.2 A at which point the electrolysis was discontinued. The reaction mixture was diluted with water (150 ml) then continuously extracted with pentane for twenty hours. The pentane extract was washed with cold 2 N hydrochloric acid (3 x 50 ml), 5% aqueous sodium bicarbonate solution (3 x 50 ml) and brine (2 x 80 ml). The solution was dried (anhyd. Na_2SO_4) and concentrated to ca. 5 ml by distillation through a spinning band column. Fractionation of the resultant residue under reduced pressure afforded 0.358 mg (59%) of 50. NMR spectrum (CCl_4): τ 3.67 (m, 2H), 5.28 (t, 1H), 6.67 (m, 2H), 7.87 (m, 2H), 7.99 (s, 3H). Mass spectrum m/e = 78.

Preparation of exo-bicyclo[2.2.0]hex-5-en-2-ol (51)

To a magnetically stirred solution of methylmagnesium iodide (1.32 M, 27 ml, 36 mmole) in ether, cooled to 0°, was added dropwise an ethereal solution of 50 (500 mg, 3.6 mmole). The reaction mixture was stirred for two hours at room temperature and after cooling in an ice bath a saturated aqueous solution of ammonium chloride (20 ml), was added dropwise. The aqueous layer was extracted with ether (3 x 50 ml) and the combined ethereal extracts were washed with brine (2 x 40 ml) and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 5 ml and further dried over activated molecular sieve (4A). Glpc analysis (UCW-98, at 100°C) showed the presence of a single product. Mass spectrum m/e = 96. The above solution was used directly in the subsequent step.

Preparation of exo-bicyclo[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate 52

A dry ethereal solution of 50 (ca. 3.6 mmole) and dry pyridine (3 ml), cooled in an ice bath, was treated with p-nitrobenzenesulfonyl chloride (1.5 g). The solution was stirred for two hours and an additional portion of p-nitrobenzenesulfonyl chloride (1.2 g, was added. After standing the reaction mixture in the

refrigerator for 38 hours a third portion of p-nitrobenzenesulfonyl chloride (2 g) was added. When all of the alcohol had been consumed (total 66 hours) the solution was poured into ice-water (100 ml) and the mixture was stirred at 0° for thirty minutes. The resulting solid, collected by suction filtration, was dissolved in chloroform and dried (anhyd. Na_2SO_4). Removal of solvent followed by chromatography (silicic acid, chloroform and recrystallization from pentane-ethyl acetate afforded 0.75 g (74%) of 52, mp 73-74°. NMR spectrum ($CDCl_3$): τ 1.65 (q, 4H), 3.56 (t, 1H), 3.79 (t, 1H), 5.17 (t, 1H), 6.55 (m, 2H), 7.78 (t, 2H).

Preparation of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14)

Bicyclic ester 52 (600 mg, 2.13 mmole), anhydrous sodium acetate (330 mg, 4.0 mmole) and glacial acetic acid (6 ml) were placed in a pyrex test tube, sealed and heated in an oil bath at 90 ± 2° for four hours. After cooling, the tube was opened and the contents poured into ice-water (50 ml). The aqueous layer was extracted with ether (3 x 40 ml), and the combined ethereal layer was washed with water (3 x 20 ml), cold 2 N hydrochloric acid (3 x 20 ml, cold 5% sodium bicarbonate solution (3 x 20 ml), and brine. After drying (anhyd. Na_2SO_4), the ethereal solution was

concentrated to ca. 5 ml and the residue fractionated under reduced pressure to afford 110 mg (75%) of a mixture of two acetates in a 3:1 ratio. The more abundant product that exhibited shorter glpc retention time (UCW-98, ct 100°) was shown to be 14. The product with longer retention time was identified as 53. The residue was unchanged starting material (ca. 300 mg). An analytical sample of the acetate 14 was obtained by preparative glpc (UCW-98, 10 foot ct 100°). NMR spectrum of 14 (CCl_4): τ 3.27 (t, 2H), 5.31 (d, 1H, J = 6.6 Hz) 6.76 (m, 1H), 7.42 (q, 2H), 7.72 (dd, 1H, J = 6.6 Hz and 5.7 Hz), and 7.98 (s, 3H). Mass spectrum m/e = 110.

Catalytic hydrogenation of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14)

A solution of 14 (ca. 10 mg, 0.07 mmole) in methanol (4 ml) was hydrogenated in the presence of platinum oxide (100 mg), prereduced with hydrogen. After five hours at ambient temperature the hydrogenation was discontinued, the catalyst filtered off and the solution fractionated, to give 33. NMR spectrum ($CDCl_3$): τ 5.77 (d, 1H, J = 7.2 Hz), 6.62 (m, H_1), 7.53 (m, 2H), 8.02 (s, 3H), 8.41 (s, 4H), 8.77 (t, 1H, J = 7 Hz).

Preparation of exo-bicyclo[3.1.0]hex-2-en-5-yl acetate (53)

A solution of 52 (400 mg, 1.42 mmole) and sodium acetate (200 mg, 2.43 mmole) in acetic acid (4 ml) was placed in a reaction tube. After sealing, the tube was heated in an oil bath at 100° for 14.5 hours, then cooled and analyzed as follows. The contents were diluted with ether (80 ml) and the organic layer was washed with cold water (40 ml) 5% aqueous sodium bicarbonate solution (2 x 30 ml), water (2 x 20 ml) and brine. After drying (anhyd. Na_2SO_4 and molecular sieve 4A) the solution was concentrated to ca. 2 ml by distillation through a spinning band column. Fractionation of the residue afforded ca. 100 mg (51%) of 53. NMR spectrum ($CDCl_3$): τ 4.25 (m, 1H), 5.47 (m, 1H), 6.67 (bs, $W_{1/2}$ = 3.5 Hz, 1H), 7.53 (m, 2H), 7.95 (m, 1H), 8.05 (s, 3H) and 8.30 (m, 1H).

Catalytic Hydrogenation of exo-bicyclo[3.1.0]hex-2-en-6-yl acetate (53)

Platinum oxide (35 mg) was suspended in methyl acetate (10 ml) and reduced with hydrogen over a period of 15 hours. A solution of 53 (90 mg, 0.65 mmole) in methyl acetate (3 ml) was then added and the reaction continued for an additional four hours. The catalyst was filtered

off and the solution concentrated to ca. 2 ml. Fractionation of the residue afforded 67 mg (73%) of 54a. NMR spectrum (THF-d_8): τ 6.30 (b.s., 1H), 8.00-8.70 (m, 11H).

Preparation of exo-bicyclo[3.1.0]hexan-6-ol (54b)

A solution of 54a (80 mg, 0.57 mmole) in anhydrous ether was treated with methyllithium (1.6 M in ether, 2 ml, 3.2 mmole) at 0° under an inert atmosphere. The reaction mixture was stirred at room temperature for 2 hours and then transferred to a separatory funnel and added dropwise to an aqueous solution of boric acid (1.5 g, 20 ml). The aqueous layer was extracted with ether (2 x 30 ml) and the combined ethereal extracts were washed with brine (2 x 20 ml) and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 2.5 ml and further dried over molecular sieve (4A). This ethereal solution of the bicyclic alcohol (56b) was used directly in the subsequent step.

Preparation of exo-bicyclo[3.1.0]hexan-6-yl p-nitrobenzoate (54c)

An ethereal solution of 56b (ca. 0.57, mmole) was cooled in an ice bath and pyridine (1 ml) and p-nitrobenzoyl chloride (300 mg, 1.49 mmole) were added with stirring. The reaction mixture was stirred at 0° for 30

minutes and then poured into ice-water (25 ml). The aqueous layer was extracted with ether (3 x 30 ml) and the combined ethereal layer was then washed with water (2 x 5 ml), 2N hydrochloric acid (2 x 5 ml), water (2 x 5 ml) saturated aqueous sodium bicarbonate (3 x 5 ml), and brine. After drying the ether was evaporated to yield 170 mg of yellowish solid. Chromatography (silicic acid, chloroform) followed by recrystallization from 95% ethanol afforded 54c, mp 86-87°. NMR spectrum ($CDCl_3$): τ 1.82 (m, 4H), 5.94 (b.s., 7H), 7.90-8.55 (m, 8H).

An authentic sample of 54b was likewise converted into the corresponding p-nitrobenzoate ester. The acetate 54a (100 mg, 0.72 mmole) was treated with methyllithium (1.6 M, 2.1 ml, 3.36 mmole) to yield the alcohol which was in turn treated with p-nitrobenzoyl chloride (310 mg, 1.54 mmole) in the presence of pyridine (2 ml). The resulting crude ester 54c (200 mg) after chromatography and recrystallization from 95% ethanol had a mp 86.5-87.5°.

Preparation of endo-bicyclo[3.1.0]hex-2-en-6-carboxaldehyde (55)

This compound was prepared according to the procedure described in the literature[31].

Preparation of endo-bicyclo[3.1.0]hex-2-en-6-carboxylic acid[31] (56)

Oxidation of 55 with silver nitrate provided 56 in good yield.

Hydrogenation of endo-bicyclo[3.1.0]hex-2-en-6-carboxylic acid (56)

Hydrogenation was effected according to the literature procedure[31].

Epimerization of endo-bicyclo[3.1.0]hexan-6-carboxylic acid methyl ester (57a)

An ethereal solution of 56 was esterified by treatment with diazomethane. The resulting methyl ester (57a) was epimerized according to the procedure of Meinwald et al[31].

Preparation of methyl exo-bicyclo[3.1.0]hex-6-yl ketone (58)

A solution of 57b (1.0 g, 7.9 mmole) in anhydrous tetrahydrofuran was treated with methyllithium (1.7 M, 10.5 ml, 7.8 mmole, in ether). The methyllithium solution was added over a period of 30 minutes at such a rate as to maintain gentle reflux of the solution. The reaction mixture was then stirred for one hour at ambient temperature

and then 10 ml of a saturated aqueous solution of ammonium chloride was added dropwise. The aqueous layer was extracted with ether (3 x 20 ml) and the combined organic layer was washed with aqueous ammonium chloride solution (15 ml), 5% aqueous sodium bicarbonate (10 ml), and brine. After drying (anhyd. Na_2SO_4) solvents were removed and the resulting residue distilled to afford 680 mg (69%) of 58. IR spectrum showed ν_{max} 1695 cm^{-1}.

Preparation of exo-bicyclo[3.1.0]hex-6-yl acetate[32] (54a)

To a suspension of 90% hydrogen peroxide (0.85 ml) in methylene chloride was added dropwise trifluoroacetic acid anhydride (5.2 ml) at 0° over a period of 20 minutes. The mixture was kept at 0° for an additional twenty minutes.

One-half of the above mixture was added to the solution of 58 (498 mg, 4.01 mmole) in methylene chloride (20 ml) containing anhydrous disodium phosphate (13 g), with vigorous stirring over a period of twenty minutes. The reaction mixture was then refluxed for forty minutes and cooled to room temperature. Water (10 ml) was added and the aqueous layer was extracted with methylene chloride (4 x 30 ml). The organic layer was washed with 5% aqueous sodium bicarbonate solution (2 x 15 ml), aqueous

sodium bisulfate solution (3 x 10 ml), water and brine. After drying (anhyd. Na_2SO_4), the solution was concentrated to ca. 4-5 ml and fractionated to afford 380 mg (67%) of 54a. NMR spectrum (CCl_4): τ 6.30 (b.s., 1H), 8.00-8.70 (m, 11H). IR ν_{max} 1732 cm^{-1}.

Hydrolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14)

An ethereal solution of a mixture of acetates 14 and 53 (ca. 100 mg) was treated with 0.1 N methanolic sodium hydroxide (2 ml) with stirring at ambient temperature. After twelve hours the reaction mixture was diluted with ether (75 ml) and was then washed with water (25 ml x 2) and brine (25 ml). The solution was dried and concentrated to 3 ml by distillation through a spinning band column. The residue was fractionated to give 60. NMR spectrum ($CDCl_3$): τ 0.22 (d, 1H, J = 2.2 Hz), 4.24 (s, 2H), 6.92 (m, 1H), 7.20-7.45 (m, 4H).

Attempted preparation of exo-bicyclo[2.1.1]hex-2-en-5-ol (59)

A solution of the acetate 14 (ca. 15 mg, 0.1 mmole) in ether was treated with an ethereal solution of methyl magnesium iodide (1.2 M, 1 ml, 1.2 mmole) at 0° in an inert atmosphere. The reaction mixture was stirred for one hour at room temperature and water (4 drops) was added.

The aqueous layer was extracted with ether and the combined ethereal layer washed with water and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 3 ml and the resulting solution fractionated. The product exhibited an NMR spectrum characteristic of 60.

Preparation of exo-bicyclo[2.1.1]hex-2-en-5-yl methoxyacetate (61)

A solution of 52 (725 mg) and sodium methoxyacetate (440 g) in methoxyacetic acid (3 ml) was placed in a reaction tube. After sealing, the tube was heated in an oil bath at 87° for one hour, then cooled and opened. The contents were diluted with ether (150 ml), and the organic layer was washed with aqueous sodium bicarbonate solution (4 x 40 ml), water and brine. After drying (anhyd. Na_2SO_4) the solution was concentrated by distillation through a spinning band column and fractionated to give 170 mg of 61. NMR spectrum ($CDCl_3$): τ 3.25 (t, 2H) 5.10 (d, 1H, J = 6.8 Hz), 5.91 (s, 2H), 6.52 (s, 3H), 6.73 (m, 1H), 7.34 (q, 2H) and 7.67 (dd, 1H, J = 6.8 and 5.7 Hz).

Preparation of endo-bicyclo[3.1.0]hexan-6-yl acetate (63)

To a solution of 56 (1.00 g, 7.9 mmole) in anhydrous tetrahydrofuran (25 ml) and ether (15 ml) was added

ethereal methyllithium (1.6 M, 10.7 ml, 17.1 mmole) over a period of twenty-five minutes. The reaction mixture was stirred for one hour at room temperature and then worked up in a manner similar to that described for the preparation of the exo bicyclic ketone (58). After concentration, the solution was fractionated to yield 250 mg (25%) of a mixture of methyl, exo-bicyclo[3.1.0]hex-6-yl and endo-bicyclo[3.1.0]hex-6-yl ketones. The above mixture (250 mg, 2.01 mmole) was oxidized in a manner similar to that described for 58. After work up and fractionation a mixture consisting of 54a (72%) and 63 (28%) was obtained. NMR spectrum (CCl_4): τ 6.30 (s, 0.72H), 6.45 (s, 0.28H), 7.80-8.80 (m, 11H).

Preparation of β-chloroethyl formate[29]

A solution of ethylenechlorohydrin (160 g, 2 mole) in benzene (500 ml) was added to 80% formic acid (115 g, 2 mole). After adding p-toluenesulfonic acid (2 g) the mixture was refluxed under a Dean-Stark apparatus, until no more water-benzene azeotrope was formed. After neutralizing by the addition of sodium bicarbonate, the reaction mixture was distilled to give 152 g (70%) of a fraction boiling at 129-133°. This was redistilled through a spinning band column to afford β-chloroethyl formate. NMR spectrum ($CDCl_3$): τ 1.82 (s, 1H), 5.92 (m, 4H),

IR spectrum ν_{max} 1740 cm^{-1}.

Preparation of dichloromethyl β-chloroethyl ether[29] (64a)

β-chloroethylformate (26 g, 0.24 mole) was treated with phosphorus pentachloride (46.8 g, 0.22 mole), added in small portions at 0°. After the initial evolution of heat and dissolution of the phosphorus pentachloride, the reaction mixture was stirred at room temperature for two hours. Fractional distillation of the reaction mixture yielded 384 g (98%) of the dichloromethyl β-chloroethyl ether, bp 106-110/110 mm. NMR spectrum ($CDCl_3$): τ 2.67 (s, 1H), 6.03 (m, 4H).

Preparation of β-chloroethyl bicyclo[3.1.0]hex-2-en-6-yl ethers[29] (67)

To a mixture of freshly distilled cyclopentadiene (260 ml) and 64a (32.5 g, 0.20 mole), cooled to -7°, was added dropwise an ethereal solution of methyllithium (0.8 M, 400 ml), over a period of three hours. Excess methyllithium was then quenched by the addition of wet ether (100 ml) followed by water (150 ml). The aqueous layer was extracted with ether and the combined ethereal extracts were washed with water and concentrated in vacuo. The residue was diluted with hexane and dried (anhyd. Na_2SO_4, then molecular sieve 4A). The solvents were distilled

off and the residue fractionated to give 29.5 g (92%) of a mixture of endo- (67%) and exo- (33%) 67, bp 80-88°/13 mm. NMR spectrum ($CDCl_3$): τ 3.95-4.45 (m, 2H), 6.18-6.55 (m, 5H), 7.10-7.62 (m, 2H), 7.75-8.70 (m, 2H).

Preparation of exo- and endo-bicyclo[3.1.0]hex-2-en-6-ols[29]

To an ethereal solution of 67 (10 g, 62 mmole) in hexane, was added dropwise a solution of n-buthyllithium (92 ml, 2.25 M), over a period of two hours at room temperature. After the addition was complete the reaction mixture gave a positive Gilman test. The excess of n-butyllithium was quenched by the addition of an aqueous solution of boric acid. The aqueous layer was extracted with ether (3 x 50 ml) and the extract washed with brine and dried (anhyd. Na_2SO_4, then molecular sieve 4A). This solution was concentrated to ca. 20 ml by distillation through a spinning band column and used directly in the subsequent step.

Preparation of exo- and endo-bicyclo[3.1.0]hex-2-en-6-yl acetates (53, 62)

To a solution of exo- and endo-bicyclo[3.1.0]-hex-2-en-6-ols (ca. 62 mmole) in hexane was added dry pyridine (5 ml) and acetic anhydride (50 ml). The mixture

was stirred for twelve hours at room temperature. After the addition of methanol (100 ml) the solution was heated at 50° for one hour. The reaction mixture was cooled and poured into ice-water (50 ml) and the aqueous layer was extracted with hexane (2 x 50 ml). The organic layer was washed with water, 5% aqueous sodium bicarbonate solution (3 x 50 ml) and brine. After drying (anhyd. Na_2SO_4) the solution was concentrated to ca. 10 ml. The residue was fractionated under reduced pressure to afford 2.11 g (42%) of a mixture of 53 (35%) and 62 (65%).

An analytical sample of 62 was obtained by preparative glpc (10 ft. ββ'-oxidopropionitrile column 15% on firebrick, ct 85°). NMR spectrum ($CDCl_3$): τ 4.52 (m, 2H), 6.08 (t, 1H, J = 6.0 Hz), 7.52 (m, 2H), 7.82 (m, 1H), 8.17 (s, 3H), 8.29 (m, 1H).

Preparation of exo-anti-bicyclo[3.1.1.$0^{2,4}$]hept-6-yl acetate (68)

To a magnetically stirred cold (0°) mixture of potassium hydroxide solution (100 ml, 50%) and ether (150 ml) in a 250 ml flask (without ground joints), was added N-nitrosomethylurea in ca. 1 g portions every hour[39]. A nitrogen stream (70 ml/min) bubbled through the solution, swept the generated diazomethane first through a drying

tube (potassium hydroxide and soda lime) and then into a cold magnetically stirred ethereal (50 ml) solution of the acetates 14 and 53 (330 mg, 2.39 mmole) containing suspended cuprous chloride (500 mg). The progress of the reaction was followed by glpc (UCW-98, ct 100°). In two hours all of 14 had been converted into a single product. The reaction mixture was filtered through celite and concentrated to ca. 5 ml. Fractionation of the residue under reduced pressure afforded 330 mg (90%) of a mixture of 53 and 68. An analytical sample of 68 was obtained by preparative glpc (10 foot SE-30 column, ct 130°). NMR spectrum ($CDCl_3$): τ 5.45 (d, 1H, J = 7.8 Hz), 7.50 (m, 2H), 7.92 (s, 3H), 8.02 (m, 1H), 8.72 (m, 3H), 8.95 (dd, 1H, J = 7.8 and 9 Hz), 9.46 (m, 1H). The tricyclic acetate showed as a single peak in the glpc trace on the following columns: UCW-98, ββ'-oxidopropionitrile, reoplex, squalene, carbowax and diisodecyl phthalate.

By this method, the following olefins have been converted into corresponding compounds containing a cyclopropane ring:

Bicyclo[2.1.1]hexene (10): The starting olefin was prepared by the method of Meinwald and treated with diazomethane in the presence of cuprous chloride. After the

work up an analytical sample was obtained by preparative glpc (10 foot, SE-30 column, ct 35°). NMR spectrum ($CDCl_3$): τ 7.70 (m, 2H), 8.30 (m, 1H), 8.75 (m, 1H), 8.55-8.75 (m, 3H), 8.85-9.15 (m, 2H), 9.35 (m, 1H). Mass spectrum m/e = 92.

Norbornene: Commercially available norbornene was exposed to the reaction conditions similar to that described for 14, to afford tricyclo[3.2.1.$0^{2,4}$]octane. NMR spectrum ($CDCl_3$): τ 7.82 (m, 2H), 8.50-9.10 (m, 5H), 9.10-9.50 (m, 2H), 9.55-10.35 (m, 2H).

anti-norbornen-7-yl acetate (71): The starting material was prepared by diimide reduction of norbornadien-7-yl acetate. The anti-norbornen-7-yl acetate was converted, as described above to 72. NMR spectrum ($CDCl_3$): τ 5.57 (m, 1H), 7.67 (m, 2H), 8.02 (s, 3H), 8.15-8.75 (m, 4H), 9.00-9.40 (m, 3H), 9.75-10.10 (m, 1H).

Treatment of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14) with diazomethane[42]

An ethereal solution of 14 (ca. 40 mg) was treated with a ten fold excess of diazomethane at 0° over a period of two weeks. Reaction was monitored by glpc and the formation of a single major product was evident. At-

tempted chromatographic purification of the reaction mixture resulted in decomposition of the product.

Preparation of exo-anti-tricyclo[3.1.1.$0^{2,4}$]heptan-6-ol (87)

To a magnetically stirred solution of methyl magnesium iodide (1.5 M, 18 mol) in ether, cooled in an ice bath, was added dropwise an ethereal solution of 68 and 53 (ca. 2.47 mmole). The mixture was stirred for one hour at room temperature, then cooled in an ice bath and hydrolyzed by dropwise addition of a saturated aqueous ammonium chloride solution (10 ml). The aqueous layer was extracted with ether (3 x 10 ml), and the combined ethereal extracts were washed with brine (10 ml) and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 5 ml and further dried over molecular sieve (4A). (In most instances the resulting dry ethereal solution was used directly in the subsequent step). Fractionation of the resulting residue under reduced pressure afforded 250 mg (92%) of a mixture of 53 and 87 (68%).

Preparation of exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate (75)

To a solution of 87 (ca. 1.3 mmole) in anhydrous ether, cooled in an ice bath, was added dry pyridine (2 ml)

and p-nitrobenzoyl chloride (400 mg, 2.16 mmole). The solution was stirred for one hour and then stored in the refrigerator overnight. The mixture was then poured into ice-water (60 ml) and stirred for thirty minutes in an ice bath. The resulting solid was filtered off and the aqueous layer was extracted with chloroform (3 x 20 ml) which was then washed with water (2 x 10 ml). The filtered solid was dissolved in chloroform and combined with the chloroform extract and dried (anhyd. Na_2SO_4). The solvent was evaporated to give 599 mg of crude 75. Chromatography of the crude ester (silicic acid, 3% ether in pentane), followed by crystallization from pentane afforded 300 mg (80%) of pure material mp 82-83°. NMR spectrum ($CDCl_3$): τ 1.75 (m, 4H), 5.22 (d, 1H, J = 8 Hz), 7.35 (m, 2H), 7.90 (m, 1H), 8.40-8.95 (m, 4H), 9.41 (m, 1H). IR spectrum: ν_{max} 1717 cm^{-1} (ester), 1556 and 1299 cm^{-1} (nitro group). Anal. calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. found: C, 64.92; H, 5.23, N, 5.67.

Preparation of exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-bromobenzoate (110)

To a solution of 87 (ca. 90 mg, 0.81 mmole) in anhydrous ether, cooled in an ice bath, was added dry pyridine (1.2 ml) and p-bromobenzoyl chloride (178 mg, 0.81

mmole). The reaction mixture was stirred at 0° for one hour and then stored overnight in the refirgerator. The mixture was poured into ice-water (40 ml) and stirred for 30 minutes in an ice bath. The resulting solid was filtered off and then dissolved in chloroform and dried (anhyd. Na_2SO_4). The solvent was removed in vacuo to yield 319 mg of crude 110. Chromatography of the crude ester (silicic acid, 2% ether in pentane) followed by recrystallization from pentane-ether afforded 70 mg (30%) of white crystals, mp 61-63°. NMR spectrum ($CDCl_3$): τ 2.50 (q, 4H), 5.37 (d, 1H, J = 7.2 Hz), 7.49 (m, 2H), 8.02 (m, 1H) 8.60-9.27 (m, 4H), 9.42 (m, 1H). IR spectrum: ν_{max} 1712 cm^{-1}.

Solvolysis of exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-6-yl p-nitrobenzoate (75)

A solution of 75 (100 mg, 0.38 mmole) in 60% aqueous dioxane (30 ml) was placed in a reaction tube, degassed on a high vacuum line, and sealed. The tube was immersed in an oil bath at 121.5° and heated for twenty hours. The tube was opened and the contents were diluted with pentane (200 ml). The organic layer was washed with water (3 x 100 ml), aqueous sodium bicarbonate solution (3 x 30 ml), and brine. The solution was

dried (anhyd. Na_2SO_4), concentrated by distillation through a spinning band column and distilled under reduced pressure. The distillation residue was recrystallized from pentane to give 20 mg (20%) of a solid, that had an NMR spectrum identical to synthetic 75.

The distillate was washed out of the tray with $CDCl_3$. NMR spectrum was identical with the one of synthetic 76. Mass spectrum m/e = 110. The average yield of 75 was ca. 90% as determined by glpc (internal standard) at two solvolytic half-lives.

Preparation of tricyclo[3.2.0.$0^{2,7}$]hept-4-ene (78)

In a stirred flask, at 50° were placed sodium borohydride (15 g, 0.39 mole), diglyme (65 ml), and water (35 ml). Norbornadien-7-yl chloride (5 g, 39 mmole) was added dropwise and the reaction mixture stirred for two hours. The aqueous layer was extracted with pentane (3 x 50 ml) and the combined organic extracts were washed with water (2 x 30 ml) and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 50 ml by a distillation through a spinning band column and used without further isolation of the hydrocarbon. Glpc (UCW-98, ct room temperature) analysis showed the presence of 78 (86%) and norbornadiene (14%). An analytical sample of the tri-

cyclic hydrocarbon was obtained by preparative glpc (4 foot silicon rubber gum, ct 40°). NMR spectrum ($CDCl_3$): τ 4.10 (m, 2H), 7.22 (m, 2H), 7.87 (m, 1H), 8.23 (m, 1H), 9.49 (q, 1H). Mass spectrum m/e = 92

Preparation of exo-tricyclo[3.2.0.$0^{2,7}$]heptan-4-ol (79) and exo-tricyclo[3.2.0.$0^{2,7}$]heptan-3-ol[48] (80)

An anhydrous solution of 78 (ca. 33 mmole) in pentane (50 ml) was diluted with dry tetrahydrofuran (100 ml) and placed into a flask immersed in an ice bath. A solution of diborane in tetrahydrofuran (1 M, 30 ml, 30 mmole) was added dropwise and the reaction mixture stirred for one hour at room temperature. An aqueous solution of sodium hydroxide 13 N, 20 ml) and 30% hydrogen peroxide (30%, 20 ml) was then added and the mixture was refluxed for one hour. The aqueous layer was extracted with ether (3 x 70 ml) and the combined organic layers were washed with brine and dried (anhyd. Na_2SO_4). The solution was concentrated to ca. 10 ml and the residue fractionated to afford 3.1 g (86%) of a mixture of 79 (74%) and 80 (26%). Analytical samples of the two alcohols were separated by preparative glpc (10 foot Carbowax column, ct 130°). NMR spectrum of 79 ($CDCl_3$): τ 6.08 (d, 1H), 7.45-8.15 (m, 6H), 8.50 (m, 2H), 9.15 (q, 1H). NMR spectrum of 80 ($CDCl_3$):

τ 5.37 (t, 1H), 7.32-8.38 (m, 6H), 8.50 (m, 2H), 9.05 (m, 1H). Mass spectra m/e = 110.

Preparation of exo-tricyclo[3.2.0.$0^{2,7}$]hept-4-yl (82) and exo-tricyclo[3.2.0.$0^{2,7}$]hept-3-yl (83) p-nitrobenzoates

A mixture of 79 and 80 was converted into the corresponding p-nitrobenzoates (82 and 83) in a manner similar to that described for the preparation of 75. No separation was attempted on the oily product mixture. NMR spectrum ($CDCl_3$): τ 1.76 (m, 4H), 4.47 (t, 0.73H), 4.95 (d, 0.27H) and 7.3-9.1 (m, 8H). IR spectrum ν_{max} 1715 cm^{-1}, 1527 cm^{-1}, and 1298 cm^{-1}.

Preparation of tricyclo[3.2.0.$0^{2,7}$]hept-4-one (84) and tricyclo[3.2.0.$0^{2,7}$]hept-3-one (85)

Chromium trioxide (30 g, 0.27 mole) was added to a magnetically stirred solution of dry pyridine (50 g) in methylene chloride[53] (50 ml). The resultant burgundy solution was stirred for 15 minutes at room temperature. After this period a solution of 79 and 80 in methylene chloride (5.1 g, 46 mmole) was added in one portion. After stirring for an additional 15 minutes the solution was decanted from the residue, which was washed with ether (3 x 50 ml).

The combined organic layers were washed with 5% aqueous sodium hydroxide solution (3 x 100 ml), 5% hydrochloric acid (100 ml), 5% sodium bicarbonate solution (3 x 50 ml) and brine. After drying (anhyd. Na_2SO_4) the solution was concentrated to ca. 10 ml and the residue was fractionated under reduced pressure to give 3.1 g (60%) of a mixture of 84 and 85. 3.1 g of this mixture was chromatographed (silica gel, hexane-benzene) to give 700 mg of pure 84. NMR spectrum ($CDCl_3$): τ 7.35 (m, 5H), 8.19 (m, 2H), 8.43 (q, 2H). IR spectrum ν_{max} 1735 cm^{-1}.

Preparation of endo-tricyclo[3.2.0.$0^{2,7}$]heptan-7-ol (76)

To a methanolic solution of 84 (650 mg, 6.01 mmole) at room temperature was added sodium borohydride (600 mg, 15.7 mmole) in methanol (10 ml). The reaction mixture was stirred for 20 minutes and then refluxed for an additional 10 minutes. Aqueous sodium hydroxide solution (3%, 50 ml) was added and the aqueous layer was extracted with ether (3 x 30 ml). The organic layer was washed with brine and dried (anhyd. Na_2SO_4), then concentrated to ca. 5 ml. Fractionation of the residue under reduced pressure afforded 607 mg (91%) of 76. NMR spectrum ($CDCl_3$): τ 5.62 (m, $w_{1/2}$ = 23 Hz, 1H), 7.50-8.60 (m, 8H), 8.80 (m, 1H). Mass spectrum m/e = 110.

Preparation of endo-tricyclo[3.2.0.$0^{2,7}$]hept-4-yl p nitrobenzoate (77)

A sample of 76 was converted into the corresponding p-nitrobenzoate 77 in a manner similar to that described for the preparation of 75. After chromatography (silicic acid, 5% ether-hexane) and recrystallization from pentane, 77 had a mp 86.5-88°. NMR spectrum ($CDCl_3$): τ 1.78 (m, 4H), 4.70 (m, $w_{1/2}$ = 23 Hz, 1H), 7.39 (m, 2H), 7.75 (m, 2H), 8.08 (m, 1H), 8.40 (m, 2H) and 8.69 (m, 1H). IR spectrum ν_{max} 1717 cm^{-1}, 1527 cm^{-1}, and 1343 cm^{-1}. Analysis: $C_{14}H_{13}NO_4$ Calc. C 64.86%, H 5.05%, N 5.40%
Found. C 64.59%, H 4.85%, N 5.66%

Preparation of exo-tricyclo[3.1.1.$0^{2,4}$]heptan-6-one (87)

To a dry ethereal solution of 87 (40 mg, 0.36 mmole) was added p-benzoquinone[56] (235 mg, 2.3 mmole) and aluminium t-butoxide (140 mg, 0.5 mmole). The mixture was refluxed for 17 hours under an inert atmosphere. The mixture was filtered through celite and washed with 2 N hydrochloric acid (2 x 5 ml), 5% sodium hydroxide (2 x 5 ml) and brine. After drying (anhyd. Na_2SO_4) the solution was concentrated by distillation through a spinning band column and fractionated under reduced pressure to afford 87. NMR spectrum (CCl_4): τ 6.97 (m, 2H), 8.85 (m, 3H),

9.15 (m, 2H) and 9.42 (m, 1H). IR spectrum ν_{max} 1788 cm^{-1}.

Kinetic Studies

The kinetic studies of 52 and 75 were carried out in a manner similar to that described in the literature[19,92].

In all kinetic runs temperature control of the oil bath used was accurate to at least 0.03°.

Acetolysis of exo-bicyclo[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate (52)

A solution of 52 (68.0 mg, 0.24 mmole) in acetic acid (25 ml) that contained an excess of sodium acetate was prepared. Two milliliter aliquots of this solution were placed into ten reaction tubes which were then sealed and immersed in a constant temperature oil bath at 89.7°. Tubes were withdrawn periodically and after cooling in an ice bath opened and analyzed. Excess sodium acetate was titrated against a standard solution of p-toluenesulfonic acid in acetic acid. A saturated solution of p-naphthol benzene in acetic acid was used as an indicator. The p-nitrobenzenesulfonic acid liberated essentially equalled the theoretical amount expected with the first order rate constant $k = 6.07 \times 10^{-5} sec^{-1}$.

Solvolysis of exo-bicyclo[2.2.0]hex-5-en-2-yl p-nitrobenzenesulfonate (52) in methoxyacetic acid

A solution of 52 (29 mg, 0.10 mmole) in methoxy acetic acid (5 ml) that contained an excess of sodium methoxyacetate was prepared. A one milliliter portion of this solution was placed in a reaction tube then sealed and immersed in a constant temperature oil bath at 80°. After two hours the tube was cooled and analyzed as follows. The contents were diluted with ether (5 ml) and a 2 ml portion of a standard solution of p-toluenesulfonic acid (0.0392 M) in acetic acid was added. The excess acid was titrated against a standard solution of sodium acetate in acetic acid (0.0102 M) in the presence of bromocresol green indicator. The first order rate constant for this reaction was found to be $k = 8.24 \times 10^{-5} sec^{-1}$ ($\tau_{1/2}$ = 2.33 hours).

Acetolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl methoxyacetate (61)

A solution of 61 (60 mg, 0.36 mmole) and cis-decahydronaphthalene (internal standard) in anhydrous acetic acid (1 ml) containing sodium acetate (70 mg in 2 ml) was prepared. The solution was divided among ten reaction tubes which, after sealing, were immersed in a constant temperature oil bath kept at 75.5°. The reaction

tubes were withdrawn at appropriate times and the reaction quenched by cooling them in an ice bath. The samples thus obtained were analyzed by glpc. Integration of the peaks was carried out with a planimeter. The decrease of the starting material was measured against the standard. The kinetic parameters obtained for this reaction are summarized on page 99. Another kinetic run was performed at 96.0°, in an identical manner. These results are shown on the same page.

Acetolysis of norbornadien-7-yl methoxyacetate

The norbornadienyl methoxyacetate (65 mg) and n-dodecane (6 μl) were dissolved in anhydrous acetic acid (1 ml) containing sodium acetate (35 mg, 0.43 mmole). The solution was divided among ten reaction tubes which were then sealed and immersed in an isothermal oil bath at 75.5°. Sample tubes were withdrawn at appropriate time intervals, cooled in an ice bath and then opened. The disappearance of the starting material was measured against the standard by glpc.

Another kinetic run was carried out on a similar sample at 96.0° in an identical manner. The kinetic results are presented on page 101.

Solvolysis of exo-anti-tricyclo[3.1.1.$0^{2,4}$]hept-7-yl p-nitrobenzoate (75)

A solution of 75 (115 mg) in 60% aqueous dioxane (25 ml) was divided among seven reaction tubes. Tubes were degassed on a high vacuum system, sealed and immersed in a constant temperature oil bath. Samples were withdrawn at appropriate times, cooled and then opened. One milliliter aliquots were withdrawn and the liberated p-nitrobenzoic acid was titrated against standard sodium hydroxide solution in 60% dioxane in the presence of phenolphthalein indicator. Kinetic parameters thus determined are presented on page 108. Rate constants are corrected for internal return and are average values of two independent runs.

Thermolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14)

A solution of 14 (25.6 mg) and cis-decalin (6 mg) in acetic acid (400 mg) was distributed among ten reaction tubes. Tubes were sealed and placed into a constant temperature oil bath at 110.0°. Samples were withdrawn at appropriate times and the decrease of starting material measured against the standard, by glpc.

Another kinetic run was performed at 90.4° in the same manner. Kinetic parameters obtained for those

reactions are given on page 136.

Thermolysis of exo-bicyclo[2.1.1]hex-2-en-5-yl acetate (14)

A solution of 14 (21.6 g) in n-dodecane (1 ml) which contained cis-decalin (7.1 mg) as an internal standard was prepared. This solution was partitioned between ten tubes. After sealing the tubes were immersed in a constant temprature oil bath at 105.1°. Tubes were withdrawn at appropriate times and the contents analyzed by glpc. The kinetic parameters obtained are presented on page 136. Another kinetic run was performed in a similar manner at 85.1°. (see page 135 for kinetic parameters).

REFERENCES

1. B. A. Hess, Jr., J. Amer. Chem. Soc., 93, 1000 (1971).
2. R. M. Coates and J. L. Kirkpatrick, ibid., 92, 4883 (1970).
3. S. Winstein, Quart. Rev., 23, 141 (1969).
4. S. Masamune, S. Takada, N. Nakatsuka, R. Vukov, E. N. Cain, J. Amer. Chem. Soc., 91, 4322 (1969).
5. J. Meinwald and Y. C. Meinwald, Advan. Alicyclic. Chem., 1, 1 (1966).
6. J. Meinwald and J. K. Crandall, J. Amer. Chem. Soc., 88, 1292 (1966).
7. H. Tanida and Y. Hata, ibid., 88, 4289 (1966).
8. M. Pomerantz, ibid., 88, 5349 (1966).
9. J. Meinwald and B. E. Kaplan, ibid., 89, 2611 (1967).
10. J. Meinwald and F. Uno, ibid., 90, 800 (1968).
11. F. T. Bond, H. L. Jones and L. Scerbo, Tetrahedron Lett., 4685 (1965).
12. F. T. Bond and L. Scerbo, ibid., 2789 (1968).
13. K. B. Wiberg and R. W. Ubersax, ibid., 3063 (1968).
14. W. R. Roth and A. Friedrich, ibid., 2607 (1969).
15. W. Kirmse and F. Scheidt, Angew. Chem. In. Ed., 10, 263 (1971).
16. (a) E. E. van Tamelen, S. P. Pappas and K. L. Kirk, J. Amer. Chem. Soc., 93, 6092 (1971).

(b) A. Bayer, Ann., 269, 145 (1892).

17. S. Masamune, unpublished results.

18. E. N. Cain, R. Vukov and S. Masamune, Chem. Commun., 98 (1969).

19. R. N. McDonald and C. E. Reineke, J. Org. Chem., 32, 1878 (1967).

20. R. N. McDonald and C. E. Reineke, Tetrahedron Lett., 2739 (1966).

21. L. A. Paquette, ibid., 2133 (1968).

22. L. Q. Paquette and G. R. Krow, ibid., 2139 (1968).

23. L. A. Paquette, G. R. Krow, J. M. Bollinger and G. A. Olah, J. Amer. Chem. Soc., 90, 7147 (1968).

24. R. N. McDonald and C. E. Reineke, J. Org. Chem., 32, 1888 (1967).

25. C. A. Grob, M. Ohta and A. Weiss, Angew. Chem., 70, 343 (1958).

26. H. H. Westberg and H. J. Dauben, Jr., Tetrahedron Lett., 5123 (1968).

27. S. Masamune, E. N. Cain, R. Vukov, S. Takada and N. Nakatsuka, Chem. Commun., 243 (1969).

28. K. B. Wiberg, B. R. Lowry and B. J. Nist, J. Amer. Chem. Soc., 84, 1594 (1962).

29. U. Schöllkopf, J. Paust, A. Al-Azrak and H. Schumacher, Chem. Ber., 99, 3391 (1966).

30. L. M. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry. Pergamon Press, 1969, pp. 286.

31. J. Meinwald, S. S. Labana and M. S. Chadha, J. Amer. Chem. Soc., 85, 582 (1963).

32. W. D. Emmons and G. B. Lucas, ibid., 77, 2287 (1955).

33. R. A. Moss, Selective Organic Transformations, Volume 1, p. 35. B. S. Thyagarajan (editor), Wiley-Interscience, 1970.

34. U. Schöllkopf, Angew. Chem. In. Ed., 7, 588 (1968).

35. (a) J. Hine, Divalent Carbon, Ronald Press Co., New York, 1964,

(b) W. Kirmse, Carbene Chemistry, Academic Press, IInd ed., Vol. I, 1971.

36. (a) H. E. Simmons and R. D. Smith, J. Amer. Chem. Soc., 81, 4256 (1959).

(b) Org. Syn., 41, 72 (1961).

37. A. C. Cope, S. Moon, C. H. Park and G. L. Woo, J. Amer. Chem. Soc., 84, 4865 (1962).

38. W. von E. Doering and W. R. Roth, Tetrahedron, 19, 715 (1963).

39. R. E. Pincock and J. I. Wells, J. Org. Chem., 29, 965 (1964).

40. R. S. Boikess and S. Winstein, J. Amer. Chem. Soc., 85, 344 (1963).

41. R. J. Crawford and A. Mishra, ibid., 88, 3963 (1966).

42. D. Cameron, Ph.D. Thesis, University of Alberta, 1967.

43. H. E. Simmons, E. P. Blanchard and R. D. Smith, J. Amer. Chem. Soc., 86, 1347 (1964).

44. A. C. Cope, S. Moon and P. E. Peterson, J. Amer. Chem. Soc., 84, 1935 (1962).

45. J. S. Haywood-Farmer and R. E. Pincock, ibid., 91, 3020 (1969).

46. J. S. Haywood-Farmer, R. E. Pincock and J. F. Wells, Tetrahedron, 22, 2007 (1966).

47. J. C. Davis and T. V. Van Auken, J. Amer. Chem. Soc., 87, 3900 (1965).

48. R. K. Lustgarten, ibid., 93, 1275 (1971).

49. H. C. Brown and H. Bell, ibid., 85, 2324 (1963).

50. P. R. Story, ibid., 83, 3347 (1961).

51. H. C. Brown, "Hydroboration", W. A. Benjamin, Inc., New York, 1962.

52. S. Nishida, I. Moritani, K. Ito and K. Sakai, J. Org. Chem., 32, 939 (1967).

53. R. Ratcliffe and R. Rodehorst, ibid., 35, 4000 (1970).

54. S. Yamada and K. Koga, Selective Organic Transformations, Chapter 1, B. S. Thyagarajan (editor), Wiley-Interscience, 1970,New York.

55. (a) C. S. Foote, J. Amer. Chem. Soc., 86, 1853 (1964),

(b) P. von R. Schleyer, ibid., 86, 1854 (1964).

56. K. B. Wiberg, B. R. Lowry and T. H. Colby, ibid., 83, 3998 (1961).

57. J. Meinwald, A. Lewis and P. G. Gassman, ibid., 84, 977 (1962).

58. M. Hanack and H. J. Schneider, Angew. Chem. In. Ed., 6, 666 (1967).

59. M. Simmonetta and S. Winstein, J. Amer. Chem. Soc., 18 (1954).

60. W. G. Woods, R. A. Carboni and J. D. Roberts, ibid., 78, 5653 (1956).

61. S. Winstein, H. M. Walborsky and K. Schreiber, J. Amer. Chem. Soc., 72, 5795 (1950).

62. J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., ibid., 77, 3034 (1955).

63. H. Tanida, T. Irie and T. Tsushima, ibid., 92, 3404 (1970).

64. S. Winstein, M. Shatavsky, C. Norton, R. B. Woodward, ibid., 77, 4183 (1955).

65. S. Winstein and E. T. Stafford, ibid., 79, 505 (1957).

66. H. C. Brown, K. J. Morgan and F. J. Chloupek, ibid., 87, 2137 (1965).

67. H. C. Brown and H. M. Bell, ibid., 85, 2324 (1963).

68. S. Winstein, A. H. Lewin and K. C. Pande, ibid., 85, 2324 (1963).

69. A. Diaz, M. Brookhart and S. Winstein, ibid., 88, 3133 (1966).

70. M. Brookhart, A. Diaz and S. Winstein, ibid., 88, 3135 (1966).

71. J. Lhomme, A. Diaz and S. Winstein, ibid., 91, 1548 (1969).

72. S. Winstein, C. Ordronneau, ibid., 82, 2084 (1960).

73. P. R. Story and M. Saunders, ibid., 82, 6199 (1960).

74. H. Tanida, T. Tsuji and T. Irie, ibid., 88, 864 (1966).

75. H. Tanida, Accounts of Chem. Res., Vol 1, 239 (1968).

76. P. G. Gassman and D. S. Patton, J. Amer. Chem. Soc., 91, 2160 (1969).

77. P. D. Bartlett and G. D. Sargent, ibid., 87, 1297 (1965).

78. (a) G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras and C. Y. Lui, ibid., 92, 4627 (1970).
(b) G. A. Olah, ibid., 94, 808 (1972).

79. N. C. Deno, Prog. Phys. Org. Chem., 2, 129 (1964).

80. P. K. Lustgarten, M. Brookhart, S. Winstein, P. G. Gassman, D. S. Patton, H. C. Richey and J. D. Nichols, Tetrahedron Lett., 1699 (1970).

81. (a) Y. Hata and H. Tanida, J. Amer. Chem. Soc., 91, 1170 (1969).
(b) H. Tanida and T. Irie, J. Org. Chem., 36, 2777 (1971).

82. P. von R. Schleyer, J. Amer. Chem. Soc., 80, 1700 (1958).

83. E. E. van Tamelen and D. Carty, ibid., 93, 6102 (1971).

84. R. B. Woodward and R. Hoffman, "The conservation of orbital symmetry", Academic Press Inc., 1970,New York.

85. K. Wiberg and R. Fenoglio, Tetrahedron Lett., 1273 (1963).

86. S. Winstein and C. Ordronneau, J. Amer. Chem. Soc., 82, 2084 (1960).

87. P. D. Bartlett and W. P. Giddings, ibid., 82, 1240 (1960).

88. M. Yu Lukina , Russ. Chem. Rev., 31, 419 (1962).

89. W. A. Bernett, J. Chem. Ed., 44, 17 (1967).

90. M. Randić and Z. Maksić, Theoretica Chim. Acta, 3, 59 (1965).

91. J. D. Roberts and F. J. Weigert, J. Amer. Chem. Soc., 89, 5962 (1967).

92. (a) H. Hart and J. M. Sandri, ibid., 81, 320 (1959), (b) H. Hart and P. A. Law, ibid., 86, 1959 (1964).

93. N. C. Deno, H. G. Richey, Jr., J. S. Liu, J. D. Hodge, J. J. Honser and M. J. Wisotsky, ibid., 84, 2016 (1962).

94. C. U. Pittman, Jr., and G. A. Olah, ibid., 87, 2998, 5123 (1965).

95. D. S. Kabakoff, E. Namanworth, ibid., 92, 3234 (1970).

96. G. A. Olah, C. U. Pittman and M. C. R. Symons, Chapter 5 "Carbonium Ions" Vol. I, Olah and Schleyer, Interscience, 1968,New York.

97. H. C. Brown and J. D. Cleveland, J. Amer. Chem. Soc., 88, 2051 (1966).

98. J. C. Martin, B. R. Ree, ibid., 91, 5882 (1969).

99. R. E. Leone and P. von R. Schleyer, Angew. Chem. In. Ed., Vol. 9, 860 (1970).

100. K. B. Wiberg, B. A. Hess, Jr., and A. J. Ashe "Carbonium Ions", G. A. Olah and P. V. R. Schleyer, Ed., Vol. III, Interscience,New York (in press).

101. S. Winstein, E. C. Friedrich, R. Baker and Y. Lin, Tetrahedron, (1966), Suppl. 8, Part II, 621 and the references cited therein.

102. E. J. Corey and H. Uda, J. Amer. Chem. Soc., 85, 1788 (1963).

103. G. A. Olah and W. S. Toglyesi, Abstr. of papers, p. 57, 18th International Congress of Pure and Applied Chemistry, Montreal, August, 1961.

104. (a) K. B. Wiberg and G. R. Wenzinger, J. Org. Chem., 30, 2278 (1965).

(b) A. K. Colter and R. C. Musso, ibid., 30, 2462 (1965).

105. P. K. Freeman and D. M. Balls, Tetrahedron Lett., 437 (1967).

106. J. S. Haywood-Farmer and R. E. Pincock, J. Amer. Chem. Soc., 91, 3020 (1969) and the references cited therein.

107. H. Tanida, T. Tsuji, T. Irie, ibid., 89, 1953 (1967).

108. J. S. Haywood-Farmer, Ph.D. Dissertation, University of British Columbia, 1967.

109. R. Hoffmann, Tetrahedron Lett., 3819 (1965).

110. (a) A. C. Macdonald and J. Trotter, Acta Cryst., 19, 456 (1965),

(b) A. C. Macdonald and J. Trotter, ibid., 18, 243 (1965).

111. S. Masamune, K. Fukumoto, Y. Yasunari and D. Darwish, Tetrahedron Lett., 193 (1966).

112. For example, S. Winstein, A. H. Fainberg and E. Grunwald, J. Amer. Chem. Soc., 79, 4146 (1957).

113. K. B. Wiberg, V. Z. Williams, Jr., and E. Friedrich, ibid., 92, 564 (1970).

114. J. A. Berson, Accounts of Chem. Research, Vol. 1, 152 (1968).

115. J. A. Berson and G. L. Nelson, J. Amer. Chem. Soc., 89, 5503 (1967).

116. J. A. Berson and G. L. Nelson, ibid., 92, 1096 (1970).

117. (a) H. M. Frey, R. G. Hopkins and H. E. O'Neal, Chem. Commun., 1069 (1969),
(b) H. M. Frey and R. G. Hopkins, J. Chem. Soc., (B), 1410 (1970).

118. H. E. O'Neal and S. W. Benson, Int. Journal of Chemical Kinetics, Vol. II, 423 (1970).

119. W. R. Roth and A. Friedrich, Tetrahedron Lett., 2607 (1969).

120. J. E. Baldwin and J. E. Brown, J. Amer. Chem. Soc., 91, 3647 (1969).

121. H. Fischer, topics in Current Chemistry, 24, 1 (1971) Springer-Verlag.

122. W. von E. Doering and E. K. G. Schmidt, Tetrahedron, 27, 2005 (1971).

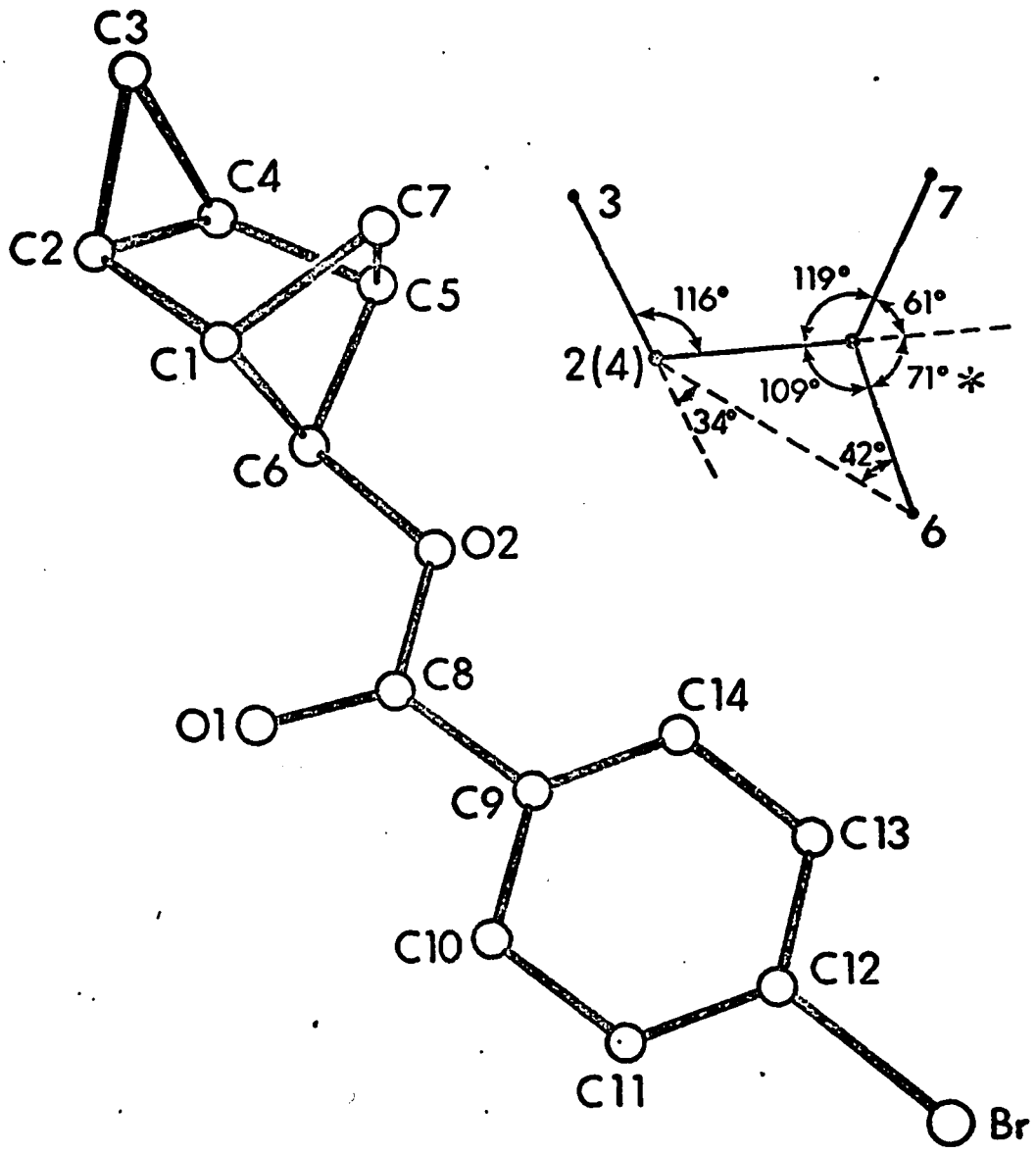
123. M. R. Willcott and V. H. Cargle, J. Amer. Chem. Soc., 89, 723 (1967).

124. M. R. Willcott III, and V. H. Cargle, ibid., 91, 4310 (1969).

125. K. Hojo, R. T. Seidner and S. Masamune, ibid., 92, 6641 (1970).

126. C.H.DePuy, Accounts Chem.Res.,1, 33 (1968)

APPENDIX


C3
C4
C7
C2
C5
C1
C6
O2
C8
O1
C14
C9
C13
C10
C12
C11
Br
3
7
116°
119°
61°
2(4)
109°
71° *
34°
42°
6