SOME REACTIONS AT THE C-7 POSITION OF NORBORNENES

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By

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SCOPE AND CONTENTS:

The addition reaction between bicyclo[2.2.1]hept-2-en-7-one and several organolithium reagents was investigated. Saturated alkyllithium reagents, like most Grignard reagents, were shown to add preferentially to the syn-face of the ketone, while unsaturated alkyllithium reagents add preferentially to the anti-face. These results have been rationalized in terms of bimolecular attack by the former reagents and unimolecular attack by the latter reagents.

The 7-t-butylbicyclo[2.2.1]hept-2-en-7-cation was shown to rearrange in mildly acidic media to a cation which lost a proton to yield syn-7-methyl-7-(2'-propenyl)bicyclo[2.2.1]hept-2-ene. The formation of this product can be explained by a Wagner-Meerwein migration which proceeds with retention of configuration about the C-7 cation centre.

A series of 7-R-bicyclo[2.2.1]hept-2-en-7-radicals were allowed to abstract hydrogen from tri-n-butylstannane. When R = CH_3, i-C_3H_7, n-C_4H_9, neopentyl, no stereochemical preference for syn- or anti- abstraction was observed. When R = t-C_4H_9,

a large preference was shown for abstraction to occur on the anti-face, while when R = C_6H_5, syn-abstraction predominated. These observations, in the light of observations of abstraction by the bicyclo[2.2.1]hept-2-en-7-radical, are consistent with homoallylic participation of the double bond at the radical centre of the latter species.

To MAGNIFICAT

(and Debs too)

"What one fool can do another can."

- Sylvanus P. Thompson, F. R. S.

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INTRODUCTION

This thesis records an attempt to explore some of the factors involved in the selectivity of attack on trigonal centres in an unsymmetrical environment. The existing literature on the subject is vast and is not reviewed here. Instead, generalizations are developed as detailed below.

(i) The stereochemistry of nucleophilic addition to ketones is governed by steric and electronic factors of the substrate and is relatively independent of the nature of the nucleophile.

(ii) Wagner-Meerwein migrations and nucleophilic substitution reactions proceed by displacement which inverts the stereochemistry of the carbon bearing the leaving group, when such a group is present in the migration step or rate-determining step, respectively.

(iii) Through-space conjugation of radicals is problematical. In the discussion to follow, extensions to (i) and (iii) and an exception to (ii) are found.

The 2-norbornene skeleton was chosen for this study because of its comparative rigidity. Discussion of steric and electronic effects for this system thus have at least one degree of freedom fixed, or nearly so. Also, as in each of the studies recorded here, homoallylic conjugation plays a

major part, the choice of 2-norbornene with the reaction terminus at C-7 was especially attractive. The 7-norbornenyl cation is one ion for which such non-classical participation is well-established.

Much of the pertinent literature is conveniently divided into reactions of radicals, cations and ketones, and it is under these headings that this introduction continues.

Organolithium Additions to Norbornen-7-one†

The Nature of the Reagent

In 1969, P. D. Bartlett[1] pointed to the complexity of organolithium reactions when he wrote "one must consider a wide range of possibilities for the active participant in any organolithium reaction....", and "....the establishment of the reaction order with respect to each participant is by no means trivial."

It is safe to say that organolithium compounds are electron-deficient oligomers.[2] Evidence for this came from cryoscopy, ebullioscopy, mass spectrometry, X-ray crystallography and ^{7}Li n.m.r. spectra.[3] It is of interest to explore these lines of evidence to show the complexity of the systems.

^{7}Li n.m.r. studies[3] have shown methyllithium to be tetrameric in diethyl ether solution, the four lithium atoms forming a tetrahedron with a methyl group out from the centre of each face. At room temperature, the lithiums exchange rapidly, faster than can be observed with the n.m.r. time scale as reference. Ethyllithium is hexameric in the vapour phase and in freezing benzene, but is tetrameric in the crystal lattice. n-Butyllithium is hexameric in cyclohexane, but is tetrameric in diethyl ether or tetrahydrofuran. Tight complexation of organolithium compounds with several ethers has been observed.[1,4]

---

† Bicyclo[2.2.1]hept-2-en-7-one is referred to as "norbornen-7-one" in the following. Similarly, derivatives of bicyclo[2.2.1]hept-2-ene are described as "norbornenes".

n-Butyllithium is appreciably more strongly etherated than secondary alkyllithiums such as i-propyl- and sec-butyllithium.

The above demonstrates that even in simple systems the structure of organolithium reagents is complex. The effective size and electronic effects of these electron-deficient compounds in complex solvation situations are largely unknown. Qualitative information on this subject is described in the discussion section. In this thesis, care has been taken not to assume anything about the structure of the reagents. Results have been obtained which are consistent with the view that the major structural factor which influences the way in which these reagents react, in the cases studied, is the organic ligand R.

The Mechanism of the Addition Reaction between Organolithium Reagents and Ketones

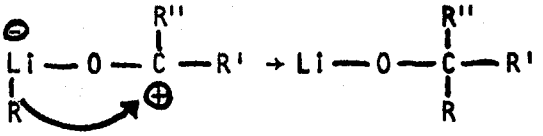
There are comparatively few reports in the literature on the detailed mechanism of this reaction, probably because the addition is so extremely fast.

Whatever equilibrium exists between organolithium aggregates of different sizes and the monomer, any reaction involving the species will be channelled through the entity for which the most favourable mechanism exists. If the preferred oligomer is predominant in the reaction conditions, the reaction will appear to be of first order with respect to organolithium. If a lower aggregate than that predominating is required, the order will be lower; if a higher aggregate, the reaction will appear to be of higher order with respect to RLi. Thus, when n-butyllithium in benzene initiates the polymerization of styrene, the apparent order in n-butyllithium is 1/6.[5] This is in-

terpreted to mean that the effective initiator is n-butyllithium monomer, in a solution where the hexamer predominates.

The role of complexation to available ethers has apparently not been discussed in the literature as a factor to be considered in the reaction of RLi with the carbonyl function. Parallel work, using the ethylenation of RLi (that is, the addition of RLi to ethylene) has been discussed recently by Bartlett.[1] He finds, for a series of primary and secondary alkyllithiums, that ethylenation in diethyl ether is first order in ethylene, fourth order in RLi and (2+n)th order in ether, where n takes values 1 or 2.

With these provisos, let us consider those studies of reactions of RLi with carbonyl compounds that the literature does contain. In 1950, Swain and Kent[6] reacted various aryllithium compounds with 4,4'-disubstituted benzophenones. They found overall second order kinetics for the reaction of phenyllithium with Michler's ketone, 4,4'-di(N,N-dimethylamino)benzophenone. This indicates nothing of the oligomer of phenyllithium involved, but it does imply that no serious complexation occurs between phenyllithium and the NN-dimethylamino groups. The least basic ketone, capable of forming the least stable complex, reacted fastest. The most reactive alkyllithium for such addition is that least effective in ether cleavage and benzene metallation. Of eight possible mechanisms, the only consistent scheme involves a prior equilibrium of ketone and RLi with a complex formed from them, and slow subsequent formation of product, as shown below.



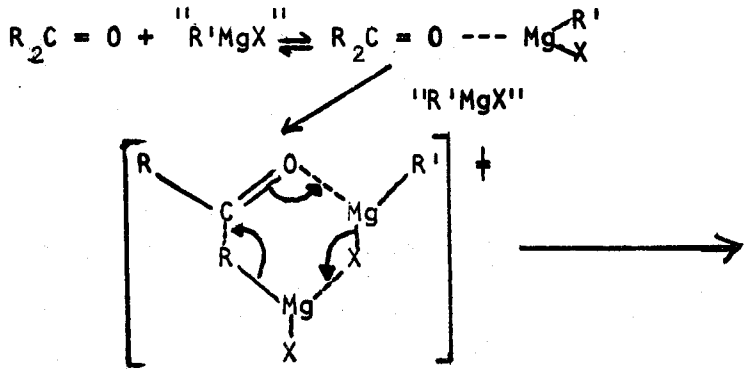
Swain writes full charge separation, giving divalent, negatively charged lithium, in order to emphasize the difference between this intramolecular attack and attack by free RLi. Also, he drew this as a reaction of monomer, but an oligomer would have been equally feasible. The migration of R follows the Wagner-Meerwein reactivity order. This same reaction pathway has been proposed for the reaction of Grignard reagents with nitriles.[7]

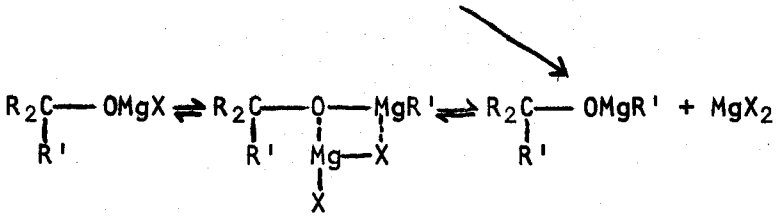
It is valuable to compare this type of complex formation with that proposed for the corresponding addition of Grignard reagents to ketones[7], reference [14]. Here the Wagner-Meerwein order is reversed, the order of migratory aptitude

$$\underline{t}\text{-butyl} > \text{methyl} > \text{phenyl} > \underline{\alpha}\text{-naphthyl}$$

being observed for additions to benzophenone.[7] Benzophenone forms a complex with just equivalent phenylmagnesium bromide, from which it may be recovered intact by mild hydrolysis. An excess of Grignard reagent causes rapid addition to occur. Thus, intermolecular nucleophilic addition occurs using a second reagent molecule; intramolecular migration from a complex, as proposed for organolithium addition, does not occur, or is very slow.

However, considerable controversy has raged on this point. The best explanation of the rather confused kinetic data available appears to be that of Asby,[11] who proposed the scheme below.



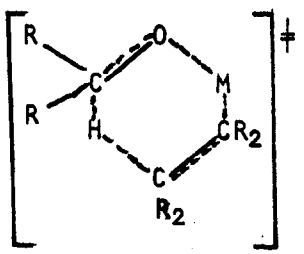


Much of the confusion has arisen from the uncertainty of the structure of the reacting Grignard reagent, but the essential feature of Swain's mechanism, intermolecular nucleophilic attack, remains.

The mechanistic difference between organolithium and Grignard reagents may lie in the relative polarities of the C-M bonds. The R-Li bond is known to be the more polar and in general the reactivity of organometallic compounds of Group I metals far exceeds that of Group II metals such as magnesium. Wittig[8] describes as "at-komplex" the complex formed by association of a nucleophilic centre with an organometallic Lewis acid, and finds that the electronegative organo section of the Lewis acid in such situations becomes more mobile. The R-Li-ketone complex, then, is expected to have a labile R, subject to Wagner-Meerwein-like migrations. The less polar Grignard reagent complexes less strongly with the ketone and intermolecular attack competes effectively with internal migration.

Reduction as a Side Reaction

A mechanistic possibility inherent in Swain's scheme[6] is reduction of the carbonyl moiety,[12] providing a second decomposition path for the "at-komplex". The transition state for this process is represented below.



Several factors determine the amount of reduction relative to addition.

(i) The organometallic compound should have β-hydrogens available,[9] if the favoured six-membered ring transition state is to form. Such hydrogen transfer is exclusively of β-hydrogens, as shown by deuterium tracer experiments by Dunn and Warkentin.[14]

(ii) Steric hindrance of the reagent may lead to relatively more reduction. Whitmore and George[9] reported that i-propyl Grignard reagent reduces di-i-propylketone to the extent of 65%, while when ethyl Grignard reagent was employed, the reduction pathway contributed 21%.

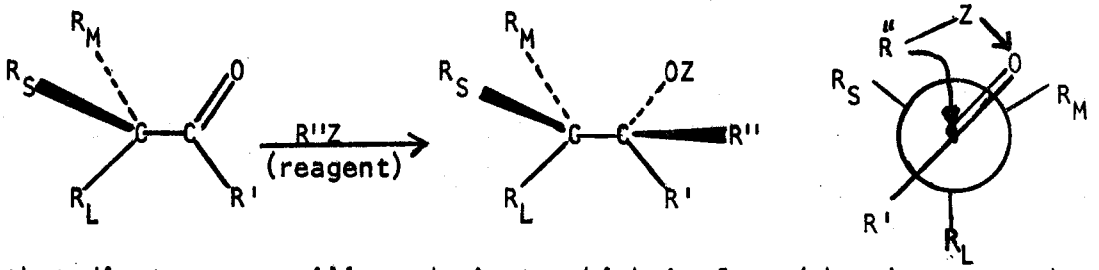
(iii) Complexation of a Grignard reagent enhances addition to a hindered ketone at the expense of reduction.[10] Addition of n-propylmagnesium bromide in diethyl ether to di-i-propylketone was increased from 36% to 70% by premixing the Grignard reagent with 1.5 equivalents of $LiClO_4$ or 1.0 equivalent of tetrabutylammonium bromide. Complexation with the ketone was ruled out by prior mixing of the salt with the ketone; the yield of addition product was not as high in this case.

(iv) Alkyllithium reagents give far less reduction than the corresponding Grignard reagents,[13] reflecting the "R-lability" theory of Wittig.[8] In Grignard reagent-ketone complexes, the anionic character of the substituent is less well developed, allowing more effective competition by the alternative reduction process. Reduction, however, may predominate in RLi reactions where the transition state is highly hindered.

Directive Effects

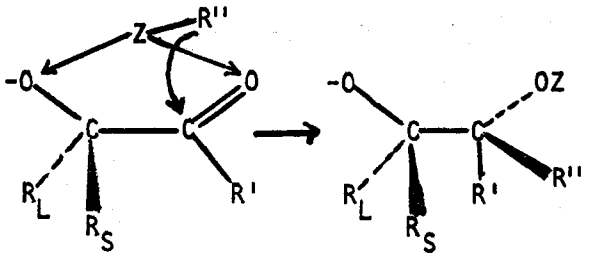
The stereochemical paths of a vast number of 1,2-asymmetric

addition reactions of aldehydes and ketones with organometallic and metal hydride reagents have been correlated using the Cram rule.[15] Assuming kinetic control, for a reaction like the one depicted below,



that diastereomer will predominate which is formed by the approach of the entering group (R'') from the less hindered side of the double bond when the rotational conformation of the C-C bond is such that the double bond is flanked by the two least bulky groups (R_S and R_M) attached to the asymmetric centre.

Cram includes an extension pertinent to the present thesis; if one of the groups on the adjacent chiral centre strongly complexes with the reagent, the rule may not apply. Thus, a cyclic model for steric control is constructed.



This is acceptable for substituents like hydroxy or amino, but Cornforth[16] recognized that for highly polarizable groups like halogen, dipolar interactions may control the stereochemistry, <u>trans</u> coplanar dipoles being at an energy minimum. A note of caution was sounded by Morrison and Mosher in a very recent book on the subject[17] which will be echoed in the results described in this thesis. "[It] has been clearly demonstrated that a change of reagent, temperature, or solvent can bring

about a reversal of the stereochemistry, [and] this obviously represents a complicated situation from which generalizations can be drawn only with great caution....".

Reactions of norbornen-7-one with Grignard Reagents

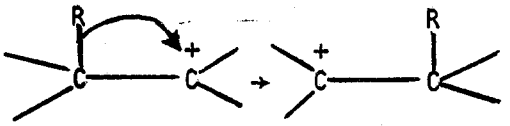
Warkentin[18] reacted a series of Grignard reagents (methyl, ethyl, i-propyl, neopentyl, and t-butyl) with norbornen-7-one and found that, where β-hydrogens were available, reduction, predominantly to norbornen-anti-7-ol, occurred. Those reagents which added did so preferentially to the syn face but reduction was the only process operating for t-butyl Grignard reagent.

The author rationalized the pronounced syn attack preference shown in both addition and reduction by the smaller non-bonded interaction over the etheno bridge (see later), while not discounting the possibility of complexation between the metal and the etheno pi-system.

Migration in 7-Norbornenyl Cations

Wagner-Meerwein Migration:

Details of this well-known reaction have been long known and often reviewed.[19]



Modern analytical methods have been applied to the theoretical analysis of the scheme and it is this facet that is of specific interest to the present work.

Phelan, Jaffe and Orchin[20] used molecular orbital theory to explain the migratory aptitudes of groups undergoing Wagner-Meerwein shifts and showed why the corresponding migrations to radical and anion centres are not observed. Utilizing Bartlett's notion of a non-classical ion as being one in which the ground state has delocalized bonding and electrons,[21] they defined a non-classical species, portrayed below.

which they named as neither transition state nor intermediate. L. C. A. O.'s were constructed and treated by a modified Hückel procedure to yield an energy level diagram which, for the occupancy predicted for the cation, shows considerable stabilization of the bridged species. Less stabilization is predicted for the radical and less still for the anion. Similar calculations for a series of migrations of substituted phenyl groups readily yielded an order of migratory aptitude which corresponded well to that observed in practice.[22]

If such a model is useful for correctly predicting migratory aptitudes and the difference between radical, anion and cation reactions, it may well be that it will prove useful to consider the transition state of the migration to the 7-norbornenyl cation observed in this work as a bridged ion.

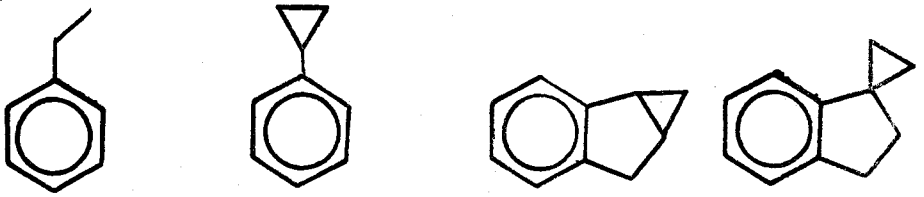
We have, up to this point, described the 1,2-shift as if the cation is always fully formed before migration occurs. However, Winstein[23] found that the presence of a migrating group accelerated the cation forming step. Also migration often occurs stereospecifically trans to the path of the leaving group in cation formation, as in the Beckmann rearrangement. This phenomenon Winstein called "anchimeric assistance". The generality of the observed stereospecificity forms the subject of part of the present work.

Finally, in the latest refinement of this model of 1,2-migrations, Traylor[24] was able to distinguish by spectroscopic methods between two types of anchimeric assistance.

(I) If the nucleophilic neighbouring group moves closer to the incipient cation as the leaving group departs, forming a partial σ bond with this carbon, the assistance thus observed is called ND_1, or internal nucleophilic displacement.

(II) If the neighbouring group assists cation formation without moving, the process is termed vertical, and can be distinguished experimentally from ND_1 processes by comparing the effect of a substituent on reaction rates with the effect on a spectroscopic transition. Vertical participation is common for carbon-metal bonds[24] and strained σ-bonds.[25]

The alignment of these bonds is critical. Schleyer very recently found[26] "hyperconjugative participation by α-methylene groups" in the solvolysis of a series of bridgehead tosylates, which depended on the torsional angle between the leaving group and the hyperconjugating bond. Trans arrangements were preferred. Traylor, in a lecture at McMaster University (1971), described spectroscopic evidence for the same effect. For the series of compounds given below, in which the alignment of the cyclopropyl ring varies, the charge-transfer frequency in the presence of tetracyanoethylene decreased as the cyclopropyl ring became more able to overlap with the aromatic pi-system.



sec^{-1}	24,200	21,300	23,100	20,000

Nucleophilic Capture of Non-Classical Cations

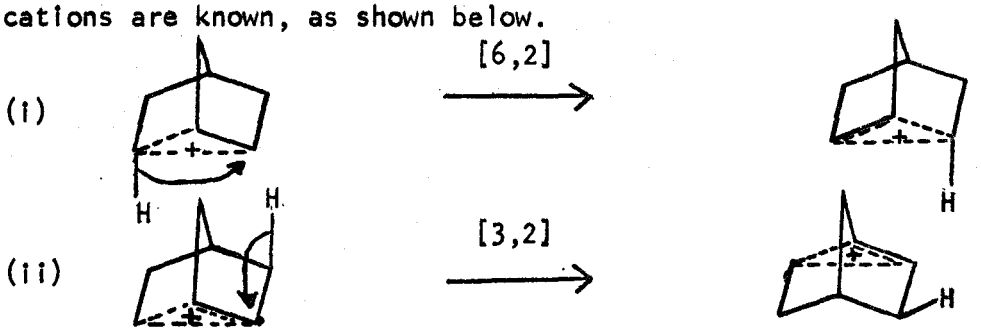
(a) Capture by External Nucleophiles:

A most important mainstay to the justification for assigning non-classical structures to ions such as the 2-norbornyl and 7-norbornenyl cations is the pronounced preference shown for nucleophilic attack anti to the homo-conjugated system.[27,28] This may be envisaged

as being analogous to Walden inversion on bimolecular nucleophilic displacement. The "leaving group" here is the partially-bonded group involved in the 3-centre 2-electron bonding system. The good correlation of rates of solvolysis of para-substituted-7-arylnorbornene-7-nitrobenzoates with σ^+ leads to the conclusion that additional stabilization provided by the aryl group to the 7-cation reduces the relative importance of homoallylic participation.[28]

(b) Intramolecular Capture:

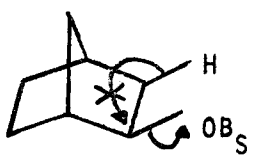
Two broad types of intramolecular capture of 2-norbornyl cations are known, as shown below.

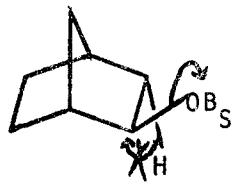


Roberts et al[29] showed that 6,2-shifts occurred in the solvolysis of norbornyl-exo-2-brosylate, where the C-2,3 positions were ^{14}C labelled. Degradation after solvolysis in HCO_2H—$NaHCO_2$ revealed 28.1% of the activity in the C-5,6 positions, providing direct evidence for the migration.

3,2-Shifts were postulated in the same series of reactions. In formolysis of norbornyl-exo-2-brosylate[29] a ^{14}C label at C-2 became nearly statistically distributed. This is consistent with a scrambling process, the essential steps of which are represented above (ii).

However, acetolysis of the same compound does not lead to scrambling indicating a barrier to syn-migration of the exo-3-hydrogen or a barrier to anti-migration of the endo-3-hydrogen, or both, as seen below.

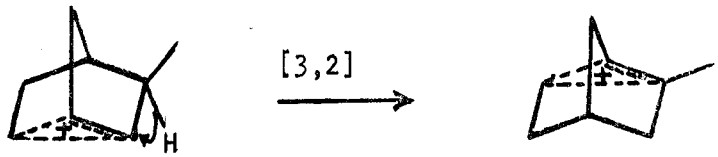




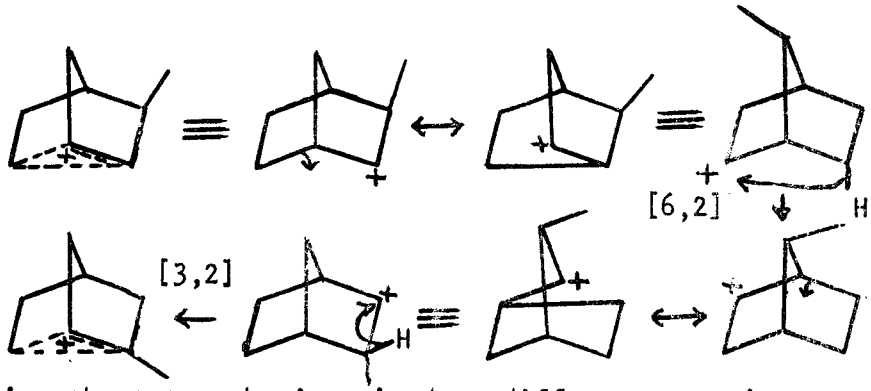
Berson et al[30] showed, by elegant stereochemical arguments, that 6,2-hydrogen shifts are preferred to 2,3-endo migrations. 3-exo-Methyl-2-norbornyl cation may rearrange to the 2-methyl-2-norbornyl cation by either (i) endo-3,2-hydrogen shift, or,

(ii) 6,2-hydrogen shift to the 7-anti-methyl-2-norbornyl cation, which then suffers exo-3,2-hydrogen shift.

(i)



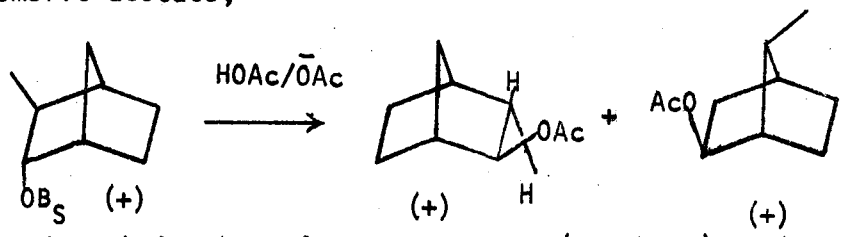
(ii)



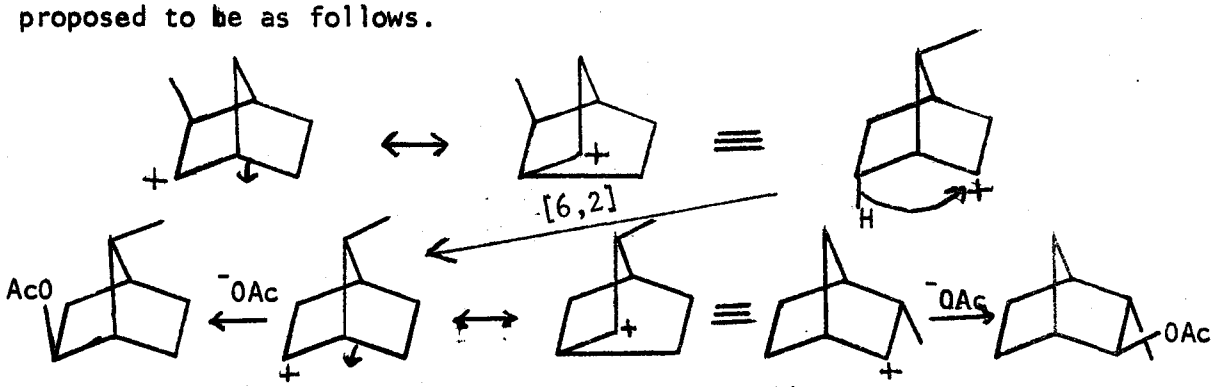
Fortunately, the two mechanisms lead to different enantiomers of the product and by using optically-active reactant, Berson was able to show that the more circuitous route is preferred by a factor of at least 100.

The same author revealed that 6,2-shifts are far faster than either exo- and endo- 3,2 shifts.[30] Acetolysis of 3-exo-methylnorbornyl-

endo-2-brosylate in optically-active form gave the corresponding enantiomeric acetate,



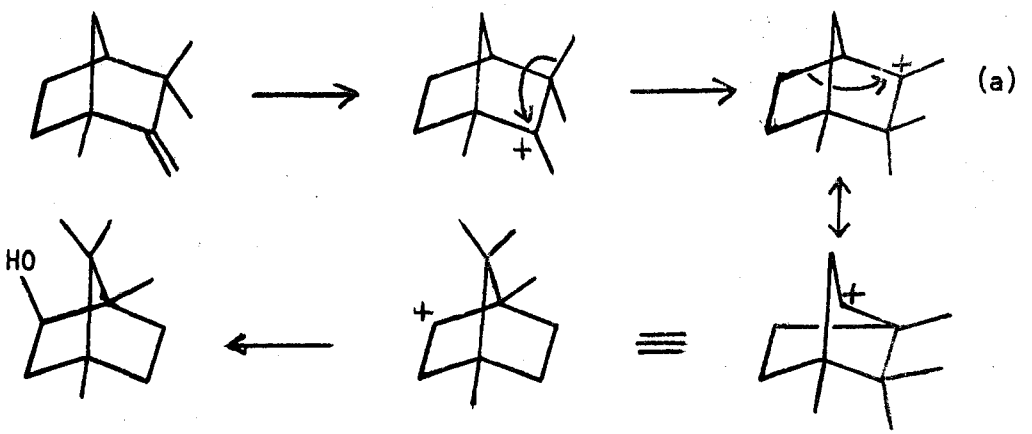
and 7-anti-methylnorbornyl-exo-2-acetate (as above). The mechanism is proposed to be as follows.



3,2-Hydrogen shift would have caused racemization, if the rate of this process had been comparable to that of 6,2-hydrogen migration.

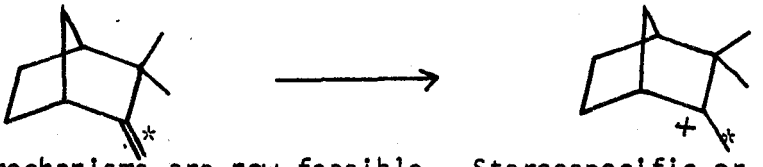
Nametkin Rearrangements:

Nametkin and Brüssoff[31] found an unusual rearrangement of α-methylcamphene, illustrated below[27], ref. p. 156

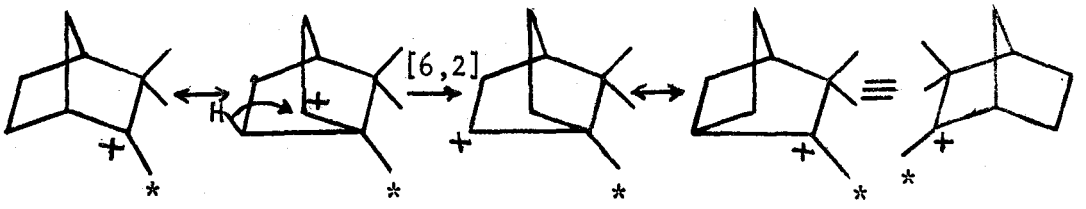


In a manner analogous to that employed for vicinal and 6,2-hydrogen shifts, ^{14}C labelling has been used to firmly establish

the pathway of the Nametkin transformation, at least for the racemization of camphene.[32,33] The initial step is clearly protonation.

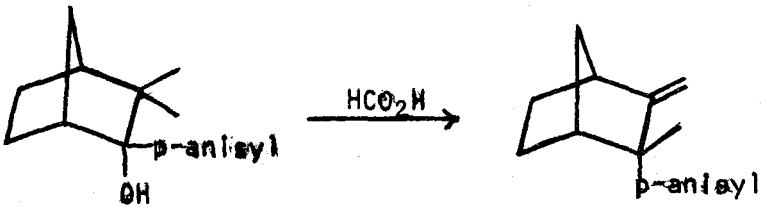


Three mechanisms are now feasible. Stereospecific or non-stereospecific methyl migration from the geminal dimethyl C-2 position would racemize the cation and the third possibility is a 6,2-hydrogen shift, as shown below.



The label was determined by oxidation of the camphene double bond. If stereospecific methyl migration had occurred 50% of the activity would be in the formaldehyde fragment of the oxidation. Non-stereospecific migration would scramble the methyls and the formaldehyde would contain one-third of the activity. The third mechanism involves no methyl rearrangement, and all the activity would remain in the formaldehyde fragment. Thus, the observed 66.3% rearrangement is evidence for methyl migrations, either completely non-specific or specific, this latter case in combination with the 6,2-hydrogen shift. This follows because the latter mechanism converts an endo-methyl group into exo and vice-versa; the label scrambling then becomes equivalent to specific migration.

Bartlett[34] observed that optical activity was preserved in the following transformation.



Clearly, migration of a methyl group has occurred. The optical activity of the product indicates that little or no migration of the p-anisyl group occurs for this process would give racemic alkene. Initial migration of the exo-methyl group followed by elimination explains these results. The second formed cation has an adjacent endo-p-anisyl group. The barrier to migration of endo groups to the norbornyl cation must, thus, be greater than the large difference in migratory aptitude between methyl and p-anisyl.

All the foregoing examples illustrate the preferred stereochemistry of migration to the 2-norbornyl cation. The migration group, as with external nucleophiles, attack the 2 position in an exo fashion, except the [6,2]migrations (see later).

Abstraction Reactions of 7-Norbornenyl Radicals

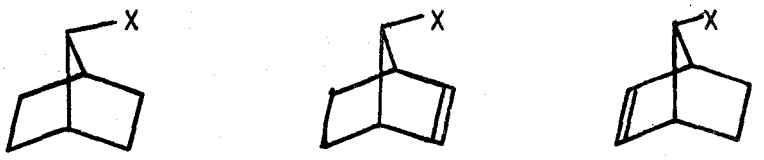
The Search for Non-Classical Free Radicals:

The controversy over the existence of homo-conjugation of any sort (hyperconjugation, homoconjugation of cations), although now largely resolved, has filled the chemical literature, in the past fifteen years, with a plethora of semi-emotional discussions.[35] In many circles the magic of "non-classicality" makes the pulse rate increase. What better bait, then, than the calculations of Howden and Roberts[36] in which, on the basis of simple L. C. A. O. methods, with corrections for angle strain, a negative total energy is predicted for homoallylic radicals, but not for bicyclobutonium radicals. The study was prompted by the observation that cyclopropylcarbinyl, cyclobutyl and allylcarbinyl cations interconvert with "extraordinary ease", but in corresponding radical reactions only allylcarbinyl and cyclopropyl carbinyl species interconvert. The problem with homoconjugation in radical systems was early realized by E. A. C. Lucken, as shown by a comment in a footnote to Dr. Robert's paper.

"The driving-force for the adoption of the 'hypothetical' structures by carbonium ions lies in the electron deficiency of the carbon atom. No such force exists for the corresponding carbanion or or radical, and because of electron repulsion it is probably that radicals and carbanions have classical structures even if they can interconvert by non-classical transition states."

Several kinetic studies on homoallylic systems are available. Rate enhancements as a diagnostic tool must, however, be treated with extreme caution. Consider an example from the better known cation field. The relative solvolysis rates of a series of brosylates are

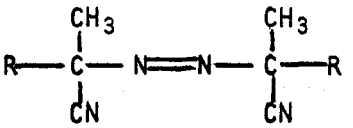
shown below.



Relative rate 1 10^4 10^{11} X = brosylate

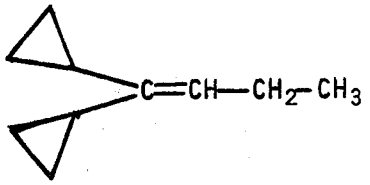
The 10^{11} rate enhancement for 7-anti-norbornenyl brosylate is explicable in terms of homoallylic participation by the double bond. If this compound were unavailable, the rate enhancement observed for the syn isomer might have been similarly explained. Of course, such participation is impossible for the syn isomer, and there is some evidence that participation by the C-4,5 and C-1,6 bonds may cause the acceleration of rate. The rate enhancements observed in corresponding radical reactions are far smaller and are, therefore, likely to be controlled by smaller effects, such as strain relief in the transition state. There is the added danger that partial charge separation may occur in radical reactions. The positive charge may well be homoallylically delocalized in such cases and mislead the observer.

When Overberger[38] heated a series of azo-bis-nitriles the general formula for which is given in the diagram below,



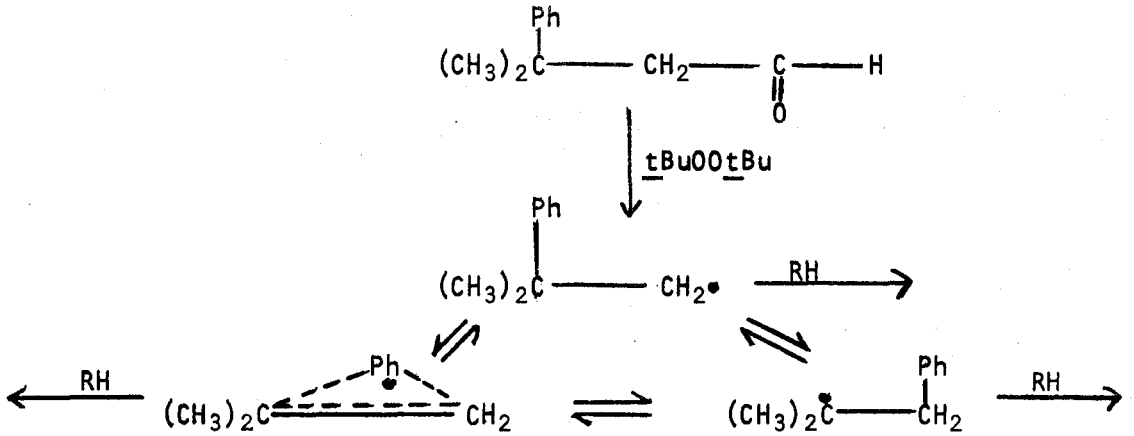
he found a rate enhancement of 20 on changing R from methyl to cyclopropyl. Martin[39] pointed out, however, that the only product recovered with the cyclopropyl rings intact accounted for only 19% yield. This left open the possibility that concerted cleavage of C-N and C-C bonds caused the observed acceleration. Martin[39] did show that

little or no charge polarization occurs in the transition state of the decomposition of azo compounds. The decomposition rate of azo-bis-(tricyclopropyl)methane was 2540 times that of azo-bis-i-butane indicating a stabilizing interaction between the cyclopropyl substituent and the developing radical centre. The product, portrayed below, was obtained in 80% yield.



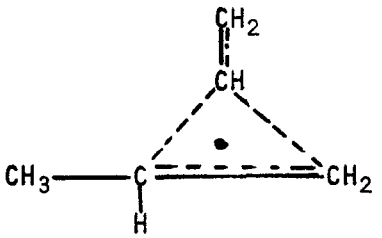
Relief of strain in the transition state would seem to be a likely alternative explanation to the proposed non-classical participation. Martin[39] considered that the strain argument could be eliminated as a cause for the acceleration by the near additive decrease in activation energy on successive substitution of cyclopropyl groups for methyl groups in the hexamethyl compound. Concerted C-N bond cleavage and cyclopropyl opening can involve only one cyclopropyl ring. The linear dependence of the activation energy on the number of rings indicates, however, that all three cyclopropyls are involved.

Product analysis studies have been more extensively applied as a probe for non-classical radicals. Perhaps the most powerful analytical tool employed is a kinetic principle first utilised by Seubold.[40] Using this method he found that, unlike phenyl migration in the neophyl cation, phenyl migration in the neophyl radical did not involve a discrete bridged intermediate.



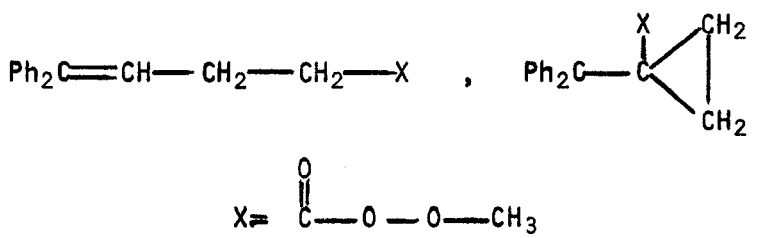
If a cyclic intermediate which could react at either of two sites were important, the ratio of i-butylbenzene to t-butylbenzene products should be independent of the concentration of RH (here the substrate aldehyde). In this case, however, the ratio did change.

When Montgomery and coworkers[41] decarbonylated 3-methyl-4-pentenal, the predominant product was not 3-methylbut-1-ene but rather 1-pentene, and they postulated the intermediacy of the homoconjugated radical below, but rejected the idea when in this case again

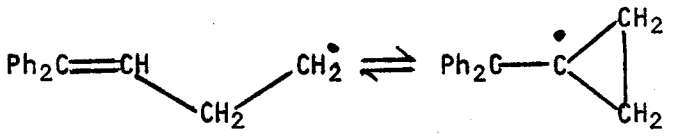


the product composition was dependent on aldehyde concentration. The equilibrating classical radical formulation is thus preferred.

A different interpretation was given by Roberts et al[42] to the results of homolysis of the following unsaturated peresters.

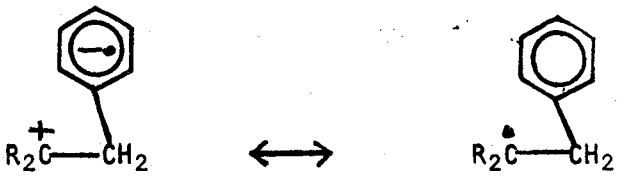


Hydrogen abstraction by either of the corresponding radicals from triethylstannane gave the same product ratio, independent of donor concentration, and deuterated species rapidly equilibrated all the methylene sites. Instead of proposing a single bridged species, Roberts proposed that the process given below was rapid with respect to hydrogen abstraction.



Up to this point we have been concerned with the cyclopropyl carbinyl-allylcarbinyl radical system. There are, however, several other types of radical potentially capable of homoconjugation which have been studied.

Seubold's discussion[40] of the neophyl radical is mentioned above; there is no evidence that a bridged intermediate is involved in the 1,2-phenyl shift observed. A comparison of the migratory aptitudes of various p-substituted aryl groups enabled the author to prepare a Hammett plot. A reaction constant ρ of +1 was considered consistent with polar character in the transition state, as shown below.



1,2-Halogen migrations are well authenticated in radical reactions. Geering[44] proposed a bridged radical to explain the stereospecific trans radical addition of HBr to 1-substituted cyclohexenes. However, Tanner[45] suggested that the specificity observed may be due to equilibrium rather than kinetic control. He found no anchimeric assistance in the

radical halogenation of 1-bromobutene, and considers the existence of a bridged-bromine radical doubtful.

1,2-Alkyl and 1,2-hydrogen migrations have never been shown to occur in radical systems.[43]

The use of e.s.r. has allowed direct observation of free radicals.[46] By this method, for example, cyclopropylmethyl radical, cyclobutyl radical, and allylcarbinyl radical have been separately observable. This is firm evidence that the non-classical equivalent of all three, the bicyclobutonium radical, is a high energy species. These same experiments, however, did reveal that there is some unpaired electron density delocalized over the non-adjacent carbons of the cyclopropylmethyl radical. The CH_2 ring hydrogens have significantly larger coupling constants (1 - 2G) than expected if no spin density were present, even for favourably oriented σ-hydrogens.

The 7-Norbornenyl Radical

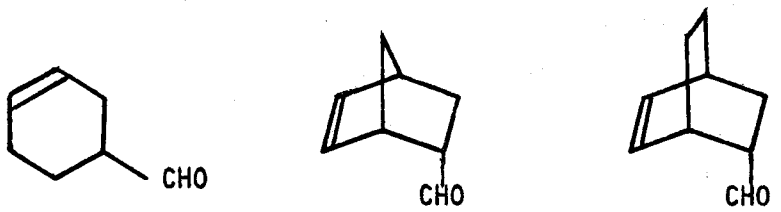
In this section the historical growth of the idea of homoallylic conjugation in the 7-norbornenyl radical is discussed, leading to the best current chemical data. Theoretical predictions by Hoffmann and Santry are compared with this, and the section ends with a consideration of what has been called in two reviews, the "definitive" e.s.r. spectrum, purported to show the classicality of the radical.

Wilt and Lewis[47] prepared several aldehydes for radical decarbonylation. The molecular skeleton was chosen to test for

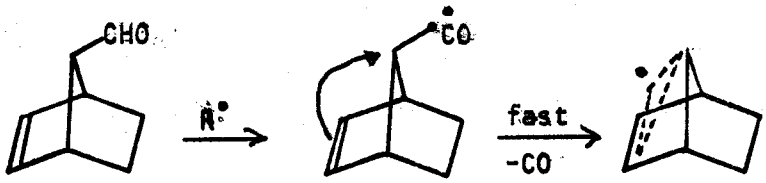
(i) homoallylic rearrangement via classical or non-classical species and

(ii) anchimeric assistance from a suitably located double

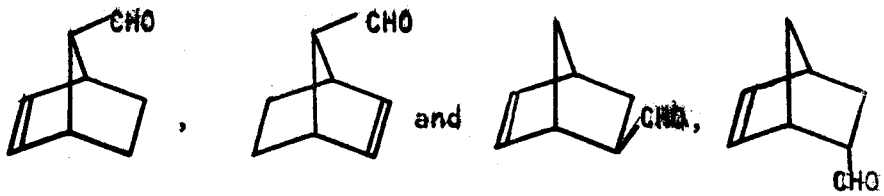
bond. Norbornene-anti-7-aldehyde, when decarbonylated using di-t-butylperoxide initiator gave 2.3% of pure norbornene but 80% of the carbon monoxide expected was evolved. By contrast, the three aldehydes below



gave only 25%, 13% and 19% of the expected CO, respectively; the competing addition reaction to the double bonds dominated. The authors were, thus, led to suggest that the following sequence was in operation.



They also predicted that striking differences in reactivity between the pairs below



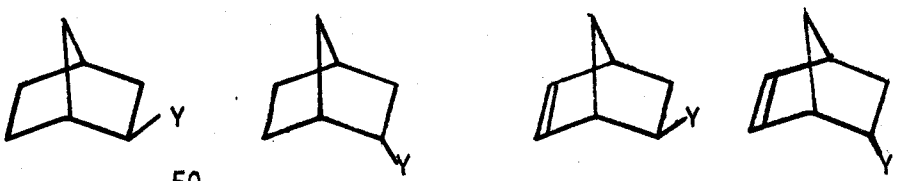
should be observable. While the aldehydes have not been compared, the 7-syn and anti t-butylperesters of norbornene have been prepared and decomposed.[48] If the loss of CO_2 is concerted with the breaking of the O-O bond, the yield of CO_2 from the decomposition should be 100%. The data obtained is presented in the table below.

Perester	CO_2 yield %	Relative rate
7-norbornane	98.3, 96.3	1.00
syn-7-norbornene	48.4	3.08
anti-7-norbornene	98.7, 96.0	2.59

It is thus possible, but not proven, that the saturated perester and the anti-norbornenyl perester decompose in a concerted fashion to the 7-norbornenyl radical. It is also possible from the relative rates of these latter two compounds, that mild anchimeric assistance by the C-2,3 π-bond may be operating. The syn perester apparently cyclized to a lactone.

No significant rate enhancement or rearrangement was observed when the following peresters were found to decompose by a concerted pathway.[49]

$Y = CO_3C(CH_3)_3$



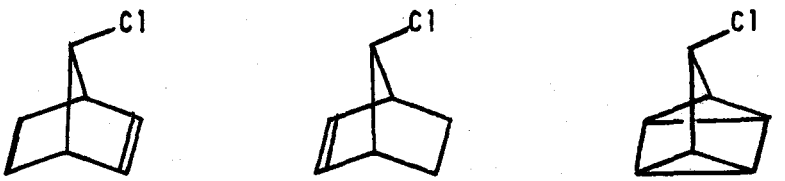
Sanford[50] conducted a number of studies aimed at revealing non-classical radicals in the norbornene series. In the first, he used an original application of polarography. The half-wave potentials of a large selection of halides, primary, secondary, tertiary, benzyl and allyl, when suitably corrected for steric effects, correlate linearly with the corresponding rates of radical reduction (using tri-n-butylstannane). This was taken to be evidence for the radical nature of polarographic reduction of these halides. (It must be noted, however, that excellent correlations of this type are often found between quite unrelated items.)

Major contributions to the rate of homolytic cleavage of C-halogen bonds are the bond angles between other substituents on the carbon atom. Further, a good measure of bond angle changes at a carbon

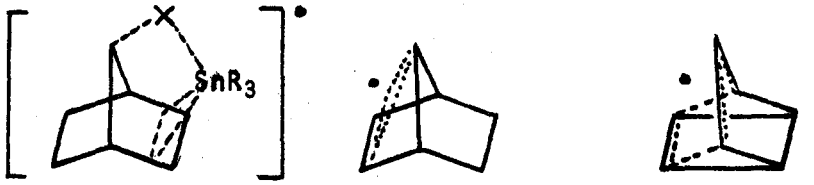
is the stretching frequency of the corresponding carbonyl compound. Thus, when Sanford plotted the half-wave potentials of alkyl halides against the corresponding carbonyl frequencies and a straight line was obtained, he assigned the changes in rate to differences in bond angle at the precursor of the radical centre. However, in a plot on which 7-bromonorbornane, 7-syn-bromonorbornene, and 7-bromonortricyclene correlated well with carbonyl frequency, 7-anti-bromonorbornene lay considerably above the correlation line. Clearly the 7-anti-bromide must be subject to influence other than C-7 bond angle strain, capable of altering the half-wave potential. The effect proposed by Sanford was participation at C-7 by the C-2,3 double bond.

In the second study, Sanford[50] directly compared the relative rate of tri-n-butylstannane reduction of several halides with the corresponding carbonyl frequencies. For the same series of bromides, a linear correlation was again obtained, for all the compounds used, including 7-anti-bromonorbornene. To explain this, Sanford was forced to propose that stannane reduction and polarographic reduction have different transition states. Stannane reduction is then relatively more sensitive to bond angle changes at the reaction site. However, for the reduction of the corresponding chlorides, for which the transition state should be further along the reaction coordinate, marked deviations from linear correlation were observed. Although the linearity was established

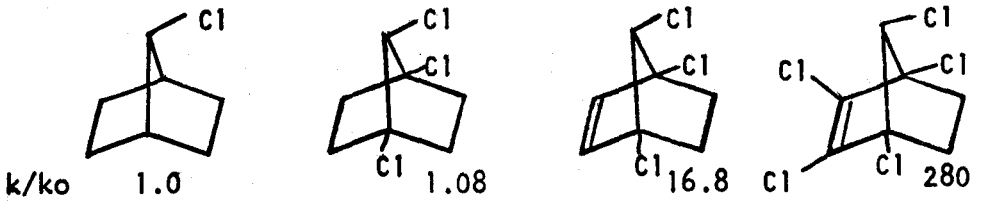
with only three points, it appears clear that the reduction of the compounds below is affected by factors other than bond angle strain.



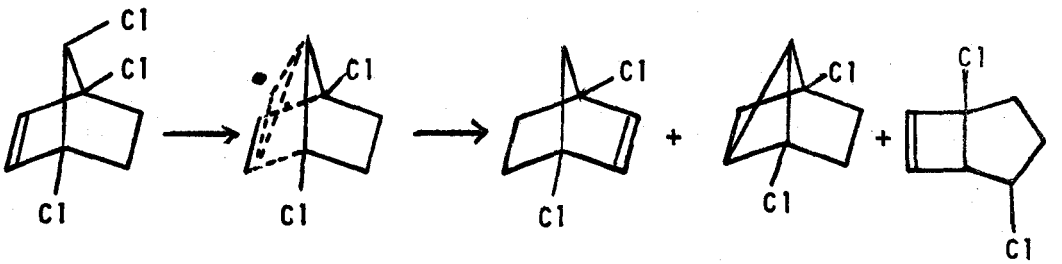
Sanford proposed that non-classical species, given below, lie on the reaction path.



In his third study, Sanford[50] reported the rates of tri-n-butylstannane reduction of a series of polychlorinated norbornyl chlorides and found evidence using product distribution and Seubold's criterion[40] to suggest non-classical intermediates for several of these compounds. Robert's[42] alternative fast equilibration of classical species was not considered. Rates relative to 7-chloronorbornane are given below.

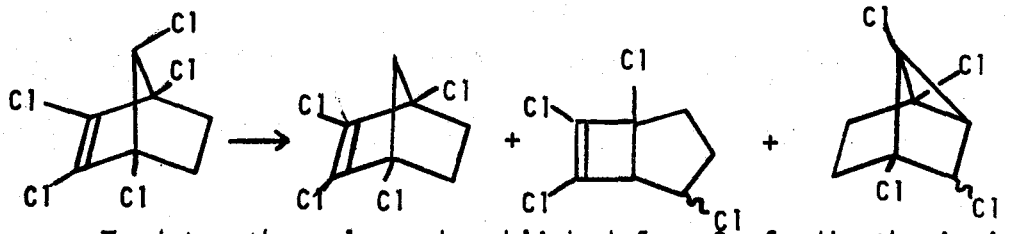


The products of the reduction of 1,4,7-trichloronorbornene are instructive, as can be seen below.



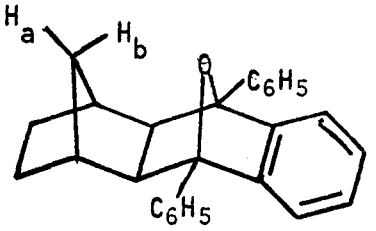
The product distribution was independent of stannane concentration, and taken with the rate enhancement, this can be interpreted as evidence for the delocalized intermediate shown.

By contrast, 1,2,3,4-anti-7-pentachloronorbornene probably reduces via equilibrating radicals, as the products (given below) varied in their distribution with stannane concentration. However, the rate enhancement caused by the halogen substituents indicate that these equilibrating radicals may themselves be non-classical.



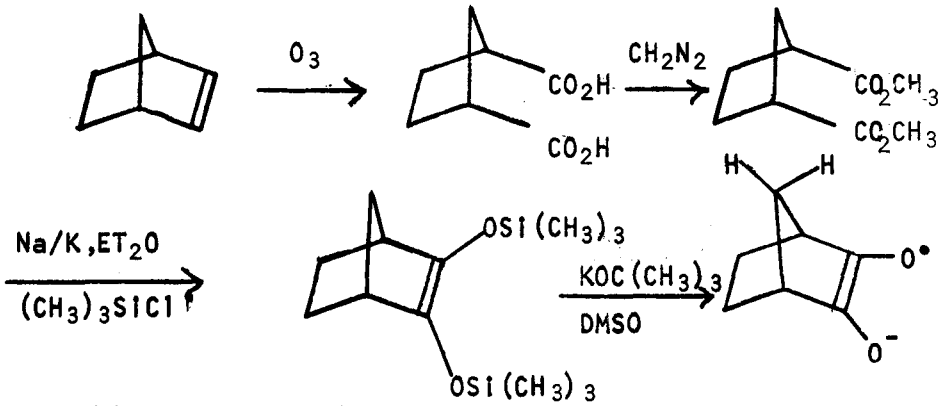
To date, the only work published from Sanford's thesis is the result of a reaction of either syn or anti-7-bromonorbornene with tri-n-butyltindeuteride.[51] While in the original paper and in the thesis[50] the only product reported for the reaction was 7-anti-deuteronorbornene, later work by Cristol and Noreen[52] cast doubt on this. The latter workers unambigously prepared 7-anti-deuteronorbornene by solvolysis of anti-7-norbornenyl p-toluenesulphonate in the presence of lithium aluminium deuteride. They found, on comparison of its p.m.r., spectrum with that of the products of the reduction of the bromide (reproduced in J. Am. Chem. Soc., ref. 51), that reduction almost certainly gave some syn-7-deutero norbornene (some 30%). Sanford and Warkentin (note 15 ref. 52, and unpublished results) confirmed this by two methods. Deuteron magnetic resonance of the norbornene product showed the C-7 H-D signals to be well separated and allowed the ratio to be estimated at 7-anti-D-norbornene:7-syn-D-norbornene = 75:25. A second measure

was obtained from the p.m.r. spectra of the Diels-Alder adducts[53] (see below) prepared from the original samples of 7-deuterionorbornene and 1,3-diphenylisobenzofuran.

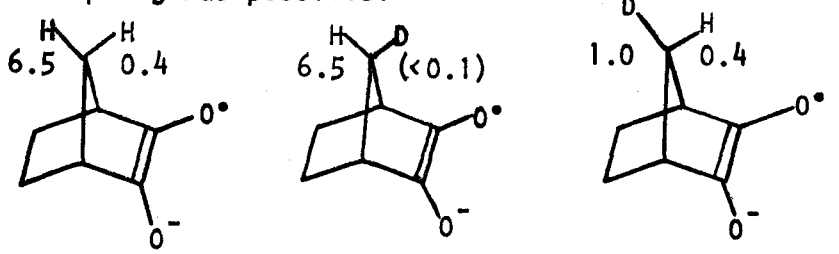


The signal from H_a is well-exposed at δ 0.63, where it can be conveniently integrated; the same ratio was observed.

Still another measure of this ratio was described by Russell and Holland.[54] A mixture of deuteronorbornenes obtained by tri-n-butyltindeuteride reduction of either 7-syn- or 7-anti-bromonorbornene. The conditions of this experiment are not reported; by inference they were the same as used by Sanford and Warkentin.[51] This was converted to a mixture of semidiones by the following series of reactions.



The semidiones produced were analysed by e.s.r., which showed the mixture to be syn-7 and anti-7-deuteronorbornene in which positive assignment of hyperfine coupling was possible.

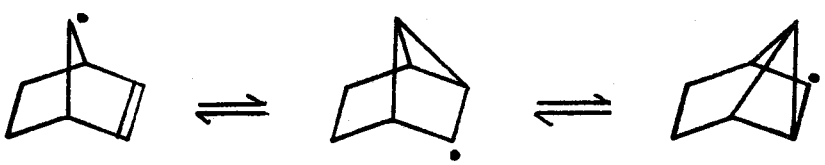


(I) (II)

Comparison of the heights of the wing peaks gave the ratio (i):(ii) = 4.0 ± 0.

Kochi and Krusic[55,p 169] report that the same mixture syn and anti-7-t-butoxynorbornene is formed on photolysis of either syn or anti-7-t-butylperoxy-2-norbornene-7-carboxylate. In this mixture, the anti-ether is favoured by a factor of two, consistent with the selectivity observed in hydrogen transfer from trialkylstannanes. The present author obtained a similar result on photolysing syn-7-iodonorbornene.[56] Depending on the conditions of the irradiation, ratios of anti I : syn I in the 7-iodonorbornene after irradiation varied from 1.2 to 1.7. The two experiments differ in pertinence to the present problem. Perester photolysis is irreversible and the ratio of products observed will mirror kinetic control. In this it corresponds well with abstractions from stannane and indicates a small measure of participation by the double bond. Iodide photolysis, however, must be reversible, since the anti-iodide produced is also excited by the ultraviolet light (254 n.m.) employed. Thus, the product ratio is probably thermodynamically controlled.

Considerable controversy exists over the interpretation of this now well-established stereoselectivity of capture of the 7-norbornenyl radical. Warkentin and Sanford[51] expressed the view that this was clear evidence for the non-classical species. An alternative equilibrating classical radical scheme, given below, requires either a stereoselective reaction of the unhindered C-7 radical or reaction of a cyclopropylcarbinyl

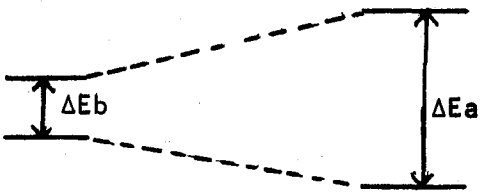


radical at a carbon with little or no radical character. The former possibility was eliminated in the original paper on the basis that a very selective reaction could not be expected from the small steric constraints operating at C-7. Although the complete specificity of capture then thought to occur has now been reduced to a small selectivity by later work, one can still rule out this possibility. Warkentin and Korn[57] have recently shown the syn side to be less hindered. The abstraction clearly cannot then be controlled by steric factors. The alternative reaction of a radical at a centre with little radical character is without precedent.

Russell and Holland[54] took another view. They saw no reason to invoke the non-classical species proposed by Warkentin and Sanford; instead, they suggested that the radical will be non-planar at C-7, the C-7 hydrogen lying syn to the double bond, because of non-bonded interactions. However, the e.s.r. spectrum of the 7-norbornenyl radical[55] is consistent only with C-7 hydrogen lying anti to the double bond (at an angle up to 13°). Cristol and Noreen[52] also disagreed with the non-classical interpretation, apparently because the specificity is small, and similar to that in C-5,6-benzo analogues.

Theoretical Predictions on the 7-Norbornenyl Radical

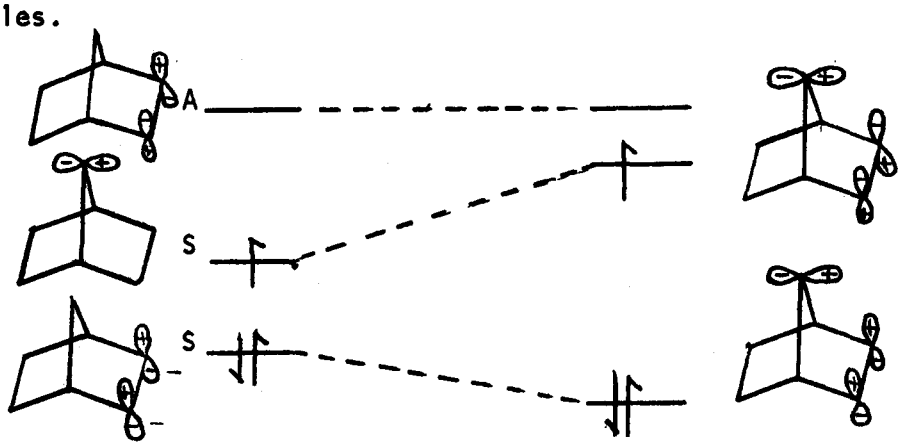
In a refreshingly practical article, R. Hoffmann[58] describes the interaction of orbitals through space and bonds in such systems as the above radical. He begins by specifying an interaction between two orbitals; it is measured by the magnitude of the one-electron energy level splitting after the interaction compared to that splitting in the absence of such interaction.



Interaction = ΔEa - ΔEb.

The consequence of such mixing is calculable by perturbation theory; this directly leads to the well-known "repulsion" result that the lower level is stabilized on interaction and the upper level is destabilized. Also, if two orbitals interact, then the lower energy one of the two mixes into itself the higher energy one in a bonding way, while the higher energy orbital mixes into itself the lower one in an antibonding way.

We may now construct an interaction diagram using the above principles.

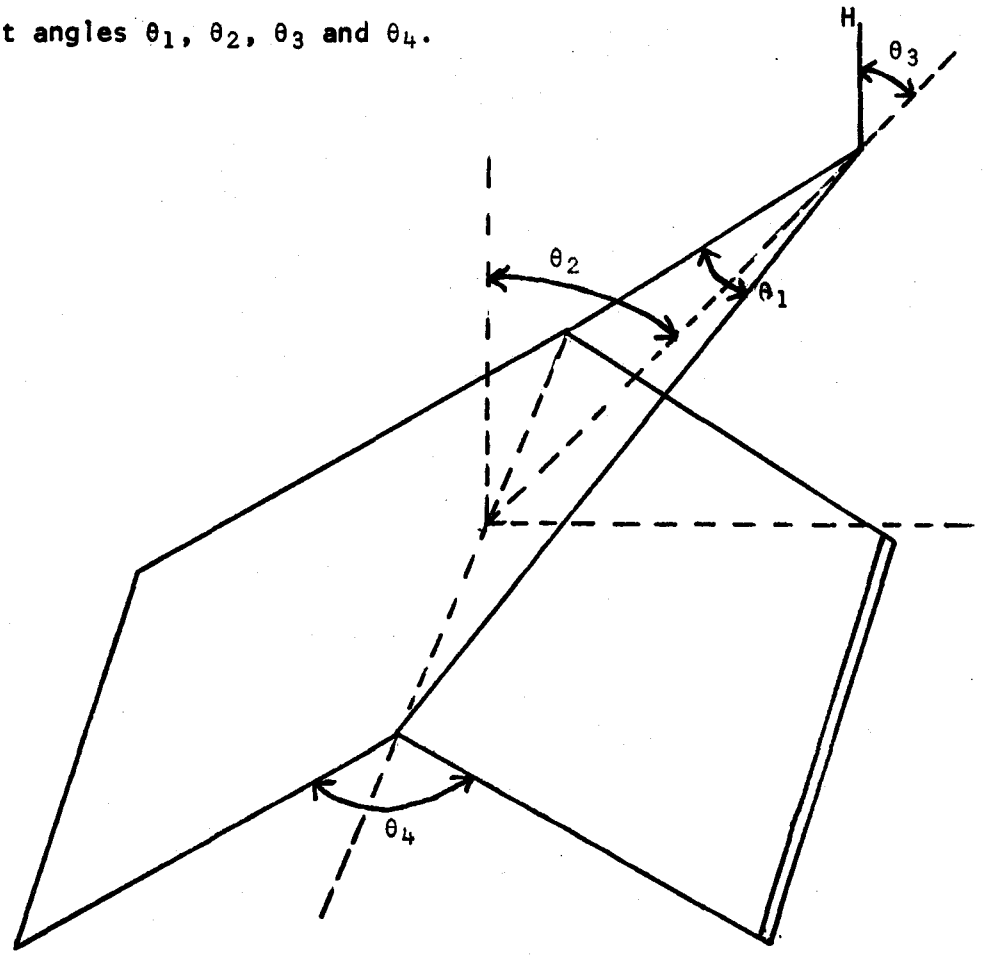


The major symmetry element, the mirror plane, has determined the orbital symmetry and thus, as only states of the same symmetry may mix, the antisymmetric π* C-2,3-orbital remains unchanged. On the other hand, the π orbital mixes with the C-7 p orbital as usual. The π orbital is stabilized, while the radical centre itself is destabilized. Thus, in Hoffmann's words, "stabilization is problematical". From the diagram, it is clear that both electrons of the cation are in the bonding orbital

of the interaction scheme and high stability is predicted.

A more sophisticated treatment was carried out by Ohorodnyk and Santry.[59] The calculations were based on CNDO (complete neglect of differential overlap) approximate self-consistent field molecular orbital theory used in conjunction with the Pople-Nesbet open shell theory.[60] Molecular geometries were calculated using a reduced number of parameters in order to simplify the problem. C-1,7, C-4,7, and C-5,6 bond lengths were set at 1.54°A, C-2,3 at 1.33°A and all C-H bonds were assumed to be 1.09°A; bond angles H-C-H were assumed for C-5,6.

The following table shows the results of solving for the best angles θ_1, θ_2, θ_3 and θ_4.



Theoretical Bond Angles for Norbornene and Its 7-Ions and 7-Radical

Angle	Compound norbornene[a]	7-anion[a]	7-radical[a]	7-cation[a]
θ_1	89	88	95	101
θ_2	- 2	5	55	51
θ_3	53	58	26	12
θ_4	109 [b]	105	113	112

a angle in degrees.

b assumed.

According to this analysis, the significant differences between these three related species lies in the nature of the interaction between C-7 and C-2,3, best envisaged as a three-centre bond. The highest occupied level in the 7-cation is the bonding orbital associated with this three-centred bond. This causes the C-7 carbon to bend towards the double bond until the strain energy balances the energy gain on strengthening the three-centre interaction. The unpaired electron in the 7-radical occupies the lowest anti-bonding orbital of the three-centre bond. The effect of this occupation on the geometry seems to be remarkably small. In fact, the value of θ_2 is increased slightly over that in the cation! Addition of a second electron to the first anti-bonding level to give the 7-anion makes the 3-centre bond antibonding overall and the anion takes a geometry close to that of the parent norbornene.

These calculations contain several informative conclusions about the 7-norbornenyl radical.

(i) The values of 55° for θ_2 and 26° for θ_3 are too large to be consistent with a nonplanar but classical radical.

(ii) There is considerable spin density delocalization. Dr. Santry, in a personal communication, however, warned about putting great reliance on the values calculated for spin density by the CNDO method since one-centre atomic exchange integrals are neglected. These are directly related to the spin-polarization mechanism for isotropic hyperfine interaction in radicals.[55]

(iii) The values of the non-classical stabilization energy for the 7-cation, radical, and anion are respectively, -8, -3, and -1 [Santry[59] defines this quantity as the energy of the ion or radical at equilibrium geometry minus its energy, assuming the geometry of the parent norbornene. A negative value represents stabilization.]

The extreme geometric distortion predicted for the radical, greater than for the cation, may possibly be a function of the assumptions made about bond angles and lengths rather than a true measure of non-classicality. With this caution, it is plain that Santry's calculations support a non-classical structure for the 7-norbornenyl radical.

The E.S.R. Spectrum of the 7-Norbornenyl Radical

In what was potentially the most definitive experiment possible, Kochi and his coworkers[55] prepared t-butyl-peroxy-2-norbornene-7-carboxylate and photolysed it in an e.s.r. probe. From both syn- and anti esters, the 7-norbornenyl radical was obtained and its e.s.r. spectrum was matched with a computed spectrum. This allowed conclusions to be drawn about the structure of the radical.

The most prominent feature of the spectrum is a doublet splitting (10.80 G), clearly due to the only single proton in the molecule, that at C-7. This hyperfine coupling constant qualitatively indicates a large spin density at C-7, in direct contradiction to Santry's prediction.[59] In fairness, the latter readily admits that spin densities are only very approximate when calculated by CNDO methods. Further splitting into three triplets (2.06, 1.54, 1.20 G) cannot be unambiguously assigned without selective deuteration but, by analogy with the spectrum of 7-norbornyl radical, also measured by Kochi,[55] C-2,3 (2.06 g), C-1,4 (1.20 G) and endo C-5,6 (1.54 G) seems a proper assignment.

It is thus clear, even allowing for some uncertainty over the identity of the three triplets observed, that the C-2,3 hydrogens cannot have a splitting of greater than 2.06 G. This is close to the value Kochi and Krusic obtained for the average splitting of C-2,3 endo and exo hydrogens for the saturated 7-norbornyl radical, clearly demanding, in the authors' minds, a classical structure for the 7-norbornenyl radical.

It remains to explain the remarkably low α-coupling constant (10.80G) for the radical compared with 23.9 G for the methyl radical. Kochi[55] observes that such low values have been observed with bent radical centres[62] and concludes that the 7-norbornenyl radical is bent at C-7 with angles $3° < \theta_2 < 13°$, $1° < \theta_3 < 14°$.

By contrast, the 7-norbornyl radical is far less bent at C-7. INDO methods were used to calculate these angles. Pople[63] finds that the INDO method is more accurate for hyperfine coupling constants than the CNDO method employed by Santry.[59]

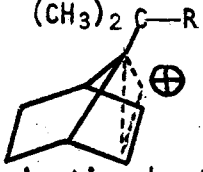
Two criticisms can be made of the interpretation of the e.s.r.

spectrum of the 7-norbornenyl radical described above. It has been shown[57] that the syn face of norbornene is less hindered, but yet the C-7 hydrogen lies possibly 13° to the anti side and attack by tri-n-butylstannane occurs from the anti face preferentially. This is consistent only with a mild participation of the C-2,3 bond with C-7. The second criticism concerns the hyperfine coupling constants of the C-2,3 protons. Expecially as the bridge is bent towards this position, it is likely that the C-2,3 hydrogens are bent down below the plane of the C-1,2,3,4 carbon atoms. Thus, as with the C-7 proton, the coupling constant is lower than it may otherwise have been. To look at it in another way, if participation occurs, the hybridization of C-2,3 becomes more sp^3-like and it is this effect which causes the C-2,3 protons to be in a lower position than in the parent norbornene. This, instead of seeing a large coupling constant for one of the triplets, due to non-classical participation, angle change causes the value to be more "normal".[55] footnote 24

Results and Discussion

sp^2 Hybridization was produced at the C-7 position of bicyclo [2,2.1.]hept-2-ene(norbornene) in three forms, radical, cation, and ketone, and some reactions at these centres were studied. It was hoped that these investigations would answer three questions.

1. How do organolithium reagents react with norbornen-7-one? In particular, what affects the stereochemistry of the addition process?
2. What is the stereochemistry of migration of hydrogen and methyl groups within the non-classical cations below?



R = H, CH_3

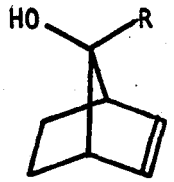
3. Is homoallylic participation by the C-2,3 double bond sufficiently significant to affect product development in the reaction of tri-n-butylstannane with the 7-norbornenyl radical, and its 7-R-substituted analogues (R = methyl, n-butyl, neopentyl, i-propyl, t-butyl, and phenyl)?

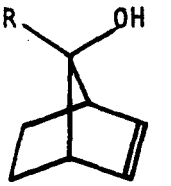
This discussion is in two parts. The first contains the results of studies carried out by the author, together with interpretations, inferences and comparison with related systems. In the second part, the structures of the thirty or so new compounds synthesized for this work are established.

The first system considered is norbornen-7-one and its reactions with organolithium reagents. A representative series of organolithiums (RLi; R = methyl, n-butyl, i-propyl, t-butyl, neopentyl, vinyl, phenyl, and benzhydryl) were allowed to react

with pure norbornen-7-one at temperatures varying from -70° to -78°, in solvents ranging from pure diethyl ether to pure hydrocarbon (pentane or hexane). The main procedure employed was to cool a solution of the ketone and add the reagent. Addition of the reagent to solid ketone and addition of ketone to cooled organolithium solution were tried, but no significant changes occurred.

Both saturated and unsaturated organolithium compounds reacted predominantly by addition to the carbonyl group to give, in near quantitative yield, the two isomeric alcohols below.





In only one case was reduction a significant side reaction. t-Butyllithium in hydrocarbon solvents reacted to give a minimum of 20% total reduction to norbornen-7-ol. Here too, however, addition was a major reaction path. Because of the volatility of norbornen-7-ol, especially the syn-isomer, it is difficult to be accurate in estimates of the stereochemistry of the reduction process, but over a series of experiments, where the method of removal of solvent prior to p.m.r. analysis, was varied, the only reduction product detected was norbornen-anti-7-ol. This compares well with results obtained by Warkentin[18] for Grignard reduction of norbornen-7-one. The lower reduction/addition ratio observed for RLi reaction with ketones compared with Grignard reactions with the same ketones is a general phenomenon[64] and was not studied further.

Product Ratios from Norbornen-7-one and RLi[1]

R of RLi	Ether/ether[2]	Ether/n-hexane[2]	Hydrocarbon/ether[2]	Hydrocarbon/n-hexane[2]
CH_3	1:2.9	1:4.0	1:2.2[3]	1:2.4[3]
CH_3	1:1.9[4]	---	---	---
n-C_4H_9	1:1.0	1:1.1	1:1.0	1:1.0
n-C_4H_9	---	---	1:1.3[5]	---
i-C_3H_7	---	---	---	1:1.1
t-C_4H_9	[6]	[6]	1:6.3	1:2.0
$(CH_3)_3CCH_2$	1:1.6	---	---	---
CH_2=CH	2.4:1	---	---	---
C_6H_5	2.6:1	2.0:1	4.3:1	2.5:1
$(C_6H_5)_2CH$	1:0	---	---	---

(1) The ratios are expressed as syn-7-ol:anti-7-ol. The error involved, estimated from the spread of a minimum of 2 runs, is at least 10% of the stated ratio.

(2) The solvents are given in the order: solvent of RLi/solvent of ketone.

(3) CH_3Li is only partly soluble in n-hexane. Slurries were prepared by adding ethereal CH_3Li to excess n-hexane.

(4) Two equivalents of $BF_3 \cdot (Et_2O)_2$ present. See p. 46.

(5) Ten equivalents of LiOEt present. See p. 46.

(6) t-Butyl addition was observed in variable yield and ratio in these cases. See p. 43.

A summary of the addition results is presented in the table, together with the results of studies on the variation of solvent. Probes such as order of addition and variation of solvent in general proved to be uninformative. In a series of experiments where RLi was added to ketone, the solvents of both ketone and organolithium reagent were varied from diethyl ether to saturated hydrocarbon. Thus, methyllithium, which is commercially available in diethyl ether solutions, was added to the ketone, itself dissolved in diethyl ether or hexane. A similar pair of results was obtained by adding a large excess of n-hexane to the sample of CH_3Li in diethyl ether; this was also reacted with the ketone in the two solvents. Phenyllithium is supplied commercially in benzene-diethyl ether (70:30). The reagent is insoluble in n-hexane and was used undiluted (in benzene-ether 70:30) and also with excess diethyl ether. t-Butyllithium was used in n-pentane and in n-pentane-ether solutions. Vinyllithium in tetrahydrofuran was added to the ketone in diethyl ether. i-Propyllithium in pentane was added to the ketone in n-hexane. Neopentyllithium and benzhydryllithium in diethyl ether were separately added to samples of the ketone in diethyl ether solutions.

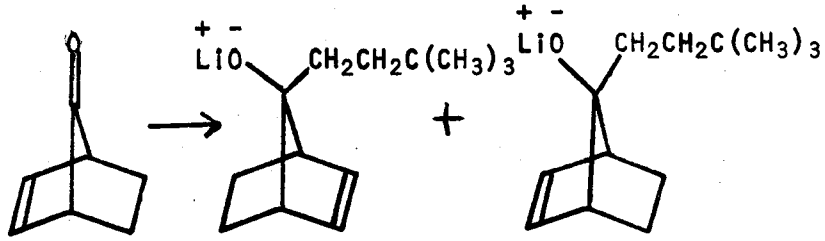
The stereochemical preferences shown by the different organolithium reagents are not likely to be caused by impurities. Two equivalents of $BF_3 \cdot (Et_2O)_2$, for example, altered the syn:anti attack ratio of CH_3Li from 2.9 to 1.9. In the presence of 10 equivalents of LiOEt, addition of n-butyllithium to norbornen-7-one gave an addition ratio of 1.3 in favour of syn attack as compared to 1.0 without LiOEt. Phenyllithium from a new bottle gave the same product ratio as that which had been stored for 3 years.

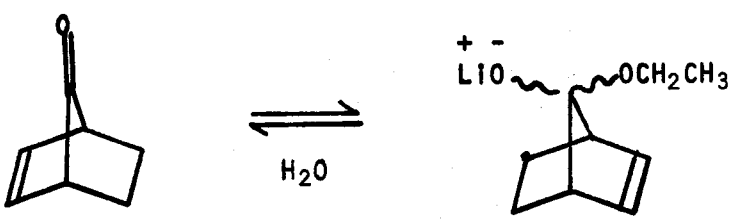
In view of the fact that neither an electrophilic reagent nor a nucleophilic impurity present in copious amount changed the ratios drastically, it is unlikely that unknown impurities in the reagents are responsible for the observed differences.

In all cases except R = t-butyl, the only addition products observed were those where R became a C-7 substituent of the resulting norbornen-7-ol. When t-butyllithium was dissolved in hydrocarbon solvent, normal addition to produce 7-t-butylnorbornen-7-ol (syn and anti) occurred. However, when an excess of t-butyllithium was premixed with diethyl ether at close to room temperature, two other addition products were also observed, shown by i.r., p.m.r.,and elemental analysis to be 7-(3',3'-dimethylbutyl)-norbornen-7-ol (syn and anti in approximately equal amount). Also, addition of t-butyllithium to ether was generally followed, within one minute, by evolution of an odourless, colourless gas. A rationale for these results follows.

(1) $LiC(CH_3)_3 + CH_2(H)-CH_2(OCH_2CH_3) \xrightarrow{k_e} (CH_3)_3CH + H_2C{=}CH_2 + {}^{+}Li{}^{-}OCH_2CH_3$

(2) $LiC(CH_3)_3 + H_2C{=}CH_2 \xrightarrow{k_a} (CH_3)_3C-CH_2-CH_2-Li$

(3) $(CH_3)_3C-CH_2-CH_2Li$ + 

(4) ${}^{+}Li{}^{-}OCH_2CH_3$ + 

There is considerable precedent for the addition of t-butyllithium to ethylene.[65]

Three mechanistic probes were employed to test this mechanism.

(i) If the above scheme is correct, starting ketone should be trapped as hemiketal anion and should be retrievable by hydrolysis. In all experiments this was so, the amount of ketone retrieved decreasing as the relative concentration of RLi increased.

(ii) Ethylene was passed through a pentane solution of t-butyllithium. On allowing the resulting solution to react with norbornen-7-one, 3,3-dimethylbutyl addition products were observed in small yield.

(iii) The mole ratio of t-butyllithium relative to norbornen-7-one was varied from 1 to 10. At a ratio RLi:ketone of 1, no reaction occurred and ketone was retrieved intact. At higher concentrations, the initial mixing of organolithium solution with ether caused a yellow coloration to appear, and a colourless gas to be evolved. When the RLi:ketone ratio was 4, less than 1% reaction occurred, and only 3,3-dimethylbutyl addition could be detected. When the ratio was 8, only 28% ketone remained and both t-butyl, and 3,3-dimethylbutyl addition occurred, in the ratio 1:1.5. 19% Ketone remained when the initial t-butyllithium:norbornen-7-one ratio was 10, and now the t-butyl:3,3-dimethylbutyl addition ratio dropped to 1:31. In addition, at RLi:ketone ratio 10, the extent of t-butyl addition was matched by the amount of reduction of the ketone to norbornen-7-ol.

Points (i) and (ii) are clearly consistent with the proposed mechanism. The concentration studies, however, reveal the system to be more complex. If a steady state is assumed for ethylene, the

following analysis applies.

$$\frac{d}{dt}[C_2H_4] = 0 = ke[\underline{t}\text{-BuLi}][Et_2O] - ka[\underline{t}\text{-BuLi}][C_2H_4]$$

$$\therefore \quad [C_2H_4] = ke\,\frac{[\underline{t}\text{-BuLi}][Et_2O]}{ka[\underline{t}\text{-BuLi}]} = \frac{ke}{ka}\,[Et_2O]$$

Thus, in the steady state, the rate of formation of 3,3-dimethylbutyllithium is given by the equation below.

$$\frac{d}{dt}[\underline{t}\text{-BuCH}_2\text{CH}_2\text{Li}] = ka[C_2H_4][\underline{t}\text{-BuLi}] = \frac{kake}{ka}[Et_2O][\underline{t}\text{-BuLi}] = k'[\underline{t}\text{-BuLi}],$$

since $[Et_2O]$ was held constant.

If the rate is first order in [t-BuLi], the half-life of t-butyllithium must be independent of initial concentration. Thus, if a steady-state exists for ethylene the ratio [t-BuCH$_2$CH$_2$Li]:[t-B-Li] will be constant, independent of initial concentration at any given time before mixing with the ketone. Unless t-butyllithium differs from 3,3-dimethylbutyllithium in the concentration dependence of rate of addition to norbornen-7-one, the ratio of t-butyl to 3,3-dimethylbutyl addition should thus be independent of the relative initial concentration of t-butyllithium and ketone. This is clearly at odds with experiment. Thus, the concentration of ethylene probably does not reach a steady state. It may be that speed of mixing, local temperature, and other macroscopic factors may alter $[C_2H_4]$, and thus the ratio of RLi addition.

One important fact results from the concentration studies. At [t-BuLi]:[ketone] = 1, no reaction occurred, and when this ratio was 4, less than 1% reaction occurred, in the same time and temperature as used with all the experiments. Hemiketal formation does not explain this result completely, since complete termination of the addition reaction did not occur at higher t-butyllithium concentrations.

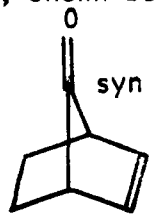
It appears that RLi complexes the ketone before addition can occur.

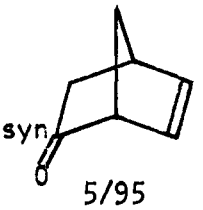
Of most interest is the selectivity observed for addition and the correlation of this with the nature of R. The table (page 41 shows that when R = methyl, i-propyl, t-butyl or neopentyl, anti-ol predominated, while n-butyllithium showed no selectivity at all. For unsaturated organolithium reagents such as vinyl-, phenyl-, and benzhydryllithium, attack on the anti-face to give syn-ol was the major pathway. Contrast this with the uniformly syn attack preference shown by the corresponding Grignard reagents.[18] The present author reacted phenyl Grignard reagent with norbornen-7-one and found attack on the syn-face to be preferred by a factor of 2.8 to 1. Proton magnetic resonance spectra of the crude reaction product were compared with those of the crude products from the addition of phenyllithium to norbornen-7-one. The reversal of the attack ratio could be clearly seen from the resonance signals of the C-2,3 vinyl protons. By way of contrast, the table on page 41 reveals how addition of a strong Lewis acid ($BF_3 \cdot (C_2H_5O)_2$) or a strong base ($LiOC_2H_5$) failed to change the stereochemical preference significantly.

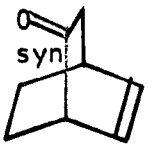
Nucleophilic attack on this ketone has been studied before; the nucleophiles used ranged from sodium borohydride to dimethylsulphoxonium methylide. As one of the purposes for the present work was to probe the mechanism of the reaction, it is pertinent here to discuss the controlling factors proposed by previous workers in the field.

H. C. Brown and J. Muzzio[66] reacted several bicyclic ketones with sodium borohydride in i-propanol, including norbornen-7-one

and norbornan-7-one. The former reacted ten times slower, a fact which Brown and Muzzio attributed to "a decrease in 'I strain' which overcomes the favourable inductive influence of the double bond". It is illuminating to compare the stereochemistry of attack on norbornen-7-one with the stereochemistry of attack on similar bicyclic ketones, shown below.

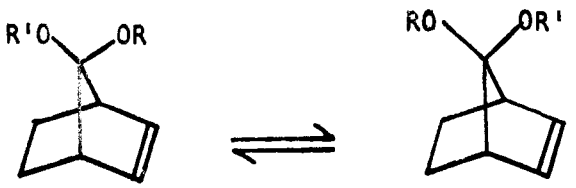






attack
syn/anti 85/15 5/95 18/82

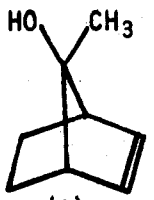
The authors conclude that while steric approach control is important for norbornen-2-one and bicyclo[2.2.2]octan-2-en-5-one, this factor apparently does not affect the reduction of norbornen-7-one. In this treatment, the double bond was assumed to have more steric effect than a saturated two carbon system. However, recent experiments by Korn and Warkentin[57] revealed that the syn-face of norbornen-7-one is the less hindered. They used as a probe equilibration of the system below in which apart from a negligible inductive difference, the only variable was steric hindrance.



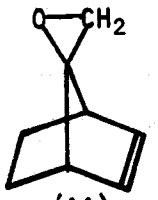
It thus seems more likely that the reactions of $NaBH_4$ with norbornen-7-one and norbornen-2-one are sterically controlled since the syn-face of the 7-ketone and the exo-face of the 2-ketone are less hindered. Bicyclo[2.2.2]octan-2-en-7-one has a more flexible structure and

is presumably more like an acyclic ketone. Thus, to use Brown's own reasoning[66], "product development control" is operating. The syn-ol:$NaBH_4$ complex initially formed is more stable than the anti-ol:$NaBH_4$ complex because the syn-face is less hindered.

R. K. Bly and R. S. Bly[67] observed that methylmagnesium iodide and dimethylsulphoxonium methylide react with norbornen-7-one stereospecifically from the syn side to yield after workup, respectively (I) and (II) below.

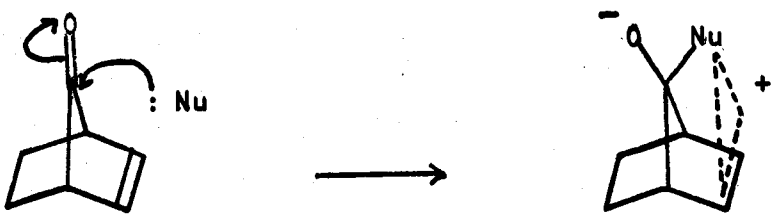


(I)

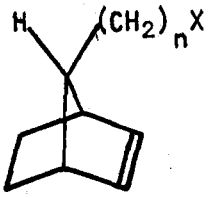


(II)

From their data, the authors could not differentiate between electronic and steric reasons for this specificity but proposed that both were probably important. From inspection of models they concluded that attack from the syn side is less hindered, which agrees with the findings of Korn and Warkentin.[57] They also observed that, as neither nucleophile used by them possesses net charge prior to reaction, coulombic repulsion by the pi-electrons of the double bond is probably not important. However, after the initial attack, dipolar species may be affected by this form of interaction, as visualized below.



The intermediate shown would presumably be more stable than that which would result from anti attack. Later work by R. S. Bly and coworkers[68] has shown, however, that in the solvolysis of compounds such as those given below, acceleration due to homoconjugation of the double bond is not observed when n = 1, but only when n = 2.



If, as seems likely, the intermediate proposed for nucleophilic attack on norbornen-7-one is subject to constraints similar to those of the system shown above (n = 1), it appears that the alternative steric control of the attack is operating.

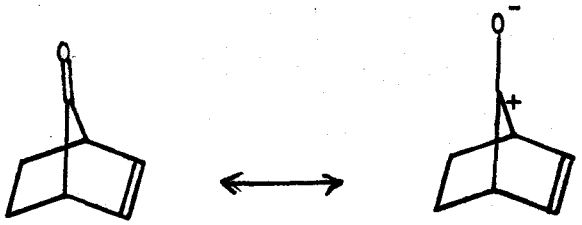
Other work pertinent here is a series of studies by Gassman and coworkers[69], who prepared 7-arylnorbornen-7-ols by the addition of the appropriate aryllithium to norbornen-7-one. Details of the experiments, including the stereochemistry of the addition process, unfortunately have not been published. Dr. Gassman[70] has revealed that 4-trifluoromethylphenyl Grignard reagent adds to norbornen-7-one from the anti face predominantly. This latter reaction is unlike that of any other Grignard reaction with norbornen-7-one. Warkentin[18] found that both addition and reduction occurred on the syn face for all alkyl Grignard reagents used. Experiments reported in this thesis allow rationalization of these observations, as will now be discussed.

Several reaction pathways are clearly required. Korn and Warkentin[57] have shown by equilibration studies that the syn face of norbornene-7-ketals is less hindered. The addition of saturated

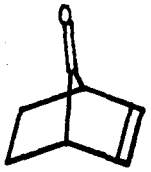
alkyllithium reagents (except n-butyllithium) to norbornen-7-one is consistent with steric control from this source. It is conceivable that the size of oligomeric n-butyllithium renders the attack ratio insensitive to the steric constraints of the substrate. Unsaturated RLi is clearly not directly controlled in its attack by relative steric hindrance of the syn and anti faces. Very recently[71] it was found that phenyllithium and phenyl Grignard reagent react with the same stereochemical preference on addition to 2-methylcyclohexanone. In this case the steric effect of the substrate on these two reagents is the same or else it is compensated for by electronic effects. However, 2-methylcyclohexanone has no obvious polar factors in it and, therefore, addition should be largely sterically controlled. For additions of these two reagents to norbornen-7-one, then, it is reasonable to suggest electronic control of addition.

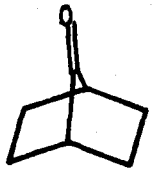
It is possible that repulsive non-bonded interactions may exist between the C-2,3 pi-system of the ketone and the pi-system of the reagent. This may cause the attack to occur preferentially on the anti face, but it is difficult to reconcile this with the fact that all Grignard reagents (including "RMgX", R = C_6H_5, CH_2=CH) attack the syn face preferentially. Similar repulsion would be expected in these cases but is not observed.

On the other hand, it is attractive to consider the possibility of participation by the C-2,3 double bond with the C-7 centre. There exists in the recent literature evidence of interaction between these two centres in the case of the ketone which will now be discussed. To the extent that polar contributors to the structure of norbornen-7-one are important



Hoffmann's treatment of the interaction of non-conjugated pi-systems[58] (see p. 32) would predict considerable interaction. It is generally observed that conjugation to a ketone reduces the frequency of the carbonyl stretching mode in the infrared spectrum. However, when we compare the corresponding norbornen-7-ones, as below,[64] there is clearly little effect.

(1) 1780 cm^{-1} 

 (2) 1773 cm^{-1}

Snyder and Franzus analysed the ultraviolet spectra of the above two compounds in a similar probe.[72] Carbonyl compounds have frequently been taken as models for carbonium ion systems.[64] It was surprising then to find the $n \rightarrow \pi^*$ transition energy for norbornen-7-one higher than that for norbornan-7-one (λ_{max}^{EtOH} = 274, 290 nm, respectively). This appears at first glance to deny interaction of the pi-carbonyl system with the C-2,3 pi-system (and by analogy between the empty bridge p-orbital and ethylene system of the 7-norbornenyl cation!). It is fascinating that simple M. O. calculations predict the observed trend, and are fully consistent with a delocalized system. Although the LCAO-MO method predicts

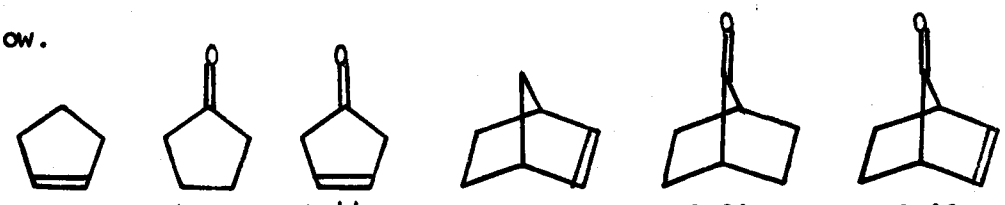
$$(E_{(1)})_{n\rightarrow\pi^*} < (E_{(2)})_{n\rightarrow\pi^*}$$

it also shows that

$$(E_{(1)})_{\pi\rightarrow\pi^*} >> (E_{(2)})_{\pi\rightarrow\pi^*}$$

with the latter approaching the $E_{\pi\rightarrow\pi^*}$ of simple conjugated ketones.

In a third spectroscopic probe, workers at the University of British Columbia studied the photoelectron spectrum of norbornen-7-one.[73] Pertinent ionization potentials (I.P., in eV) are given below.



--	9.25	9.44	--	9.01	9.19
9.18	--	9.98	8.97	--	9.62

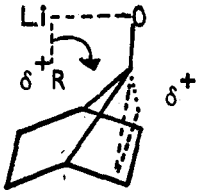
The first I.P. of norbornen-7-one at 9.19 eV is assigned to ionization from the n-orbitals of the ketone oxygen. The shift of 0.18 eV between the unsaturated norbornen-7-one and norbornan-7-one is attributed to the effect of replacing two sp^3 carbons by sp^2 carbons, analogous to the observed difference (0.19 eV) between cyclopentanone and cyclopenten-3-one. The second I.P. of norbornen-7-one (9.62 eV) represents ionization from the C-2,3 π-level. This compares with 8.97 eV for norbornene, giving a stabilization of 0.65 eV for norbornen-7-one. The corresponding difference between cyclopentene and cyclopenten-3-one is 0.80 eV. Previous work[74] shows that replacement of an sp^3 carbon by an sp^2 carbon in a norbornene should increase the I.P. (πcc) by ca. 0.2 eV. Thus, the major effect of the observed difference between the πcc I.P.'s of norbornen-7-one and norbornene is the interaction of the double bond with the carbonyl group.

This same work allows reassessment of the ultraviolet data of Snyder and Franzus,[72] discussed above. On the basis of LCAO MO calculations, a destabilization of the π* orbital of norbornen-7-one

is proposed to explain the anomalous hypsochromic shift on introducing the double bond. Weiler et al,[73] on the contrary, propose that at least part of this shift may be caused by the 0.18 eV stabilization of the n-level of norbornen-7-one relative to that of norbornen-7-one.

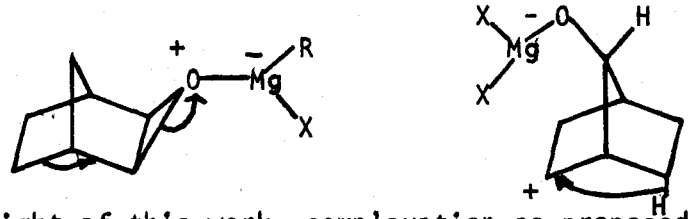
In summary, it appears that there is considerable evidence of interaction of the C-2,3 pi-system with the C-7 carbonyl group. This may have the effect of polarizing the carbonyl more than is normal.

In the presence of a polar R-Li bond, a measure of electrophilic interaction between lithium and carbonyl oxygen may occur before nucleophilic R adds. The observed reaction would then be a nucleophilic attack on the non-classical ion, shown below.



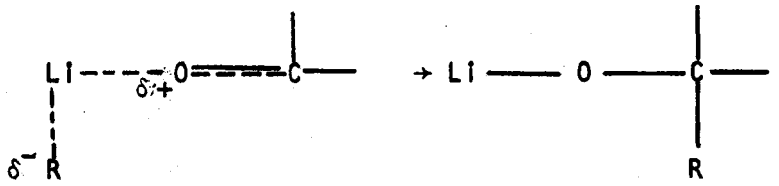
Interaction of C-7 with C-2,3 of norbornen-7-one should cause geometric changes of the same kind as those caused by such bonding in the 7-norbornenyl cation. Consequently, one would expect nucleophilic attack at C-7 of the former to show the same kind of preference; attack should occur on the anti face.[37] Initial electrophilic attack is well established for both Grignard and organolithium reagents.[11,6] For example, consider the complexation of ketones in the presence of a deficient amount of Grignard reagent. The ketone may be retrieved unchanged on hydrolysis, unless more than one equivalent of reagent is present, at which point addition occurs.[7] Very recently Gerteisen and Kleinfelter[75]

found examples for electrophilic reactions by Grignard reagents. The first recorded instances of true Wagner-Meerwein rearrangement and 1,3 hydrogen shifts accompanying a Grignard addition are reported. The critical steps are shown below.



In the light of this work, complexation as proposed in this thesis seems a reasonable suggestion. However, it should be noted that ethers are more basic than ketones.

It remains to explain why saturated alkyllithiums (and Grignard reagents) react with norbornen-7-one to give anti-ol preferentially. The crucial step of the intra-complex addition may be represented as a Wagner-Meerwein-like migration.[6]



For organolithium addition to acyclic ketones, the order of migratory aptitude found in Wagner-Meerwein rearrangements is followed closely.[6] It is thus reasonable that groups such as phenyl, vinyl, and benzhydryl, high in the migratory order, and high in reagent polarity, should react as described above. An extremely polar Grignard reagent, such as p-trifluoromethylphenyl Grignard reagent, reacts similarly on the anti face.[68] In this case, however, the Wagner-Meerwein migratory aptitude is lower than that of unsubstituted phenyl, yet phenyl Grignard reacts on the syn face. There are thus two distinct electronic effects:

(i) the polarity of the R-Li bond, and

(ii) the migratory aptitude.

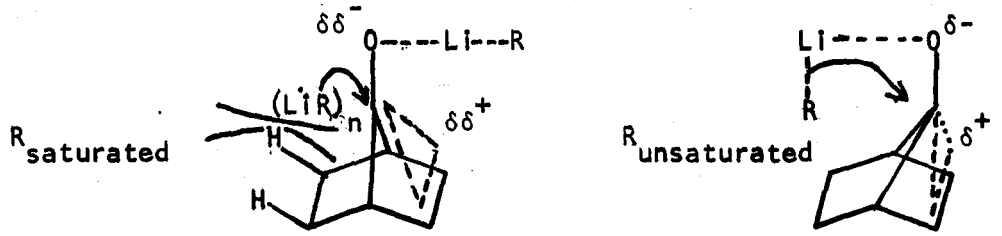
Either effect may dominate.

In cases where bond polarity and migratory aptitude are low, other effects become important. With a lower R-Li or R-Mg bond polarity, less polarization of the ketone carbonyl bond would be expected. Thus, the directional characteristics of the non-classical 7-norbornenyl cation would be less pronounced in the complex. Such is the case for all saturated alkyllithiums and all Grignard reagents (except p-trifluoromethylphenyl Grignard reagent). It is proposed that for these cases, addition occurs bimolecular in reagent, analogous to Grignard additions to acyclic ketones[11] and to organolithium addition to nitriles.[7]

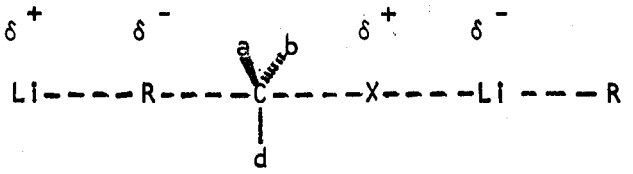
The evidence, other than the circumstantial correlation of bond polarity to reaction path, that has just been discussed, is two-fold. On page 45, the presence of an initial excess of t-butyllithium was shown to be necessary for addition to proceed. This implied an order in reagent greater than one. Further, addition of boron trifluoride etherate changed the syn:anti attack ratio of methyllithium from 2.9:1 to 1.9:1. It appears that the only serious effect that this reagent could have would be to complex the ketone in the initial step, possibly preventing formation of a methyllithium-ketone complex. The incoming Grignard reagent now sees a complex much like that present in the absence of BF_3, but with two differences. BF_3 is monomeric and even with an ether solvation shell, could be smaller than a Grignard oligomer.

Secondly, $BF_3 \cdot ((C_2H_5)_2O)_2$ may well be a stronger Lewis acid than oligomeric Grignard reagent and thus the carbonyl bond will be more polar. Increase of carbonyl bond polarity increases the non-classical participation at C-7 and directs attack more on the anti face. However, as the nucleophile is large and bulky, steric constraints will direct attack, despite the smaller size of the BF_3 complex. The reduction in attack ratio observed with BF_3 present is consistent with these ideas.

It is well to contrast this with the smaller, more labile "intra-complex" nucleophile envisaged for the unimolecular reaction of unsaturated organolithium reagents. In the latter case, the reduced size renders steric parameters relatively less important and attack is controlled more by the directional effect of the homoallylic participation. In pictorial form, the two transition states for anti attack can be represented as shown below.

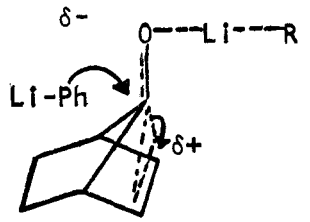


Other workers have attacked a very similar problem in a different fashion. Sommer and Korte[77] found that organolithium compounds such as RLi, R = benzyl, allyl, benzhydryl inverted the stereochemistry of optically active alkyl bromides in a coupling reaction, while simple alkyllithium reagents racemized the asymmetric centres. This they rationalized in terms of an SN2-type mechanism, the transition state of which is shown below.



Such a mechanism is preferred by polar, delocalized (highly nucleophilic) organolithium reagents.

If now in the present case initial complexation with alkyllithium is proposed, the transition state of addition by PhLi is as shown.

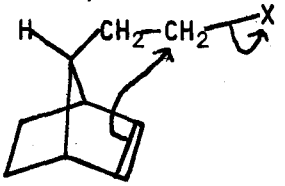


PhLi nucleophile now displaces the delocalized electron density back to the C-2,3 double bond. With less polar RLi (and RMgX), complexation polarizes the carbonyl less and the nucleophilicity of the reagent is lower. Attack on C-7 freely from either side cannot occur as in halide coupling reactions, since there are overiding steric constraints which guide the nucleophile to syn attack.

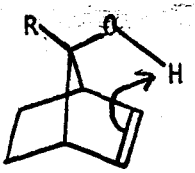
It should be noticed that there are other interpretations possible. The stereochemistry of the addition process can be explained by invoking specific complexation of the organolithium reagent on the less hindered syn face of the ketone. With less polar R-Li and R-Mg bonds, the nucleophilic attack on the carbonyl carbon then occurs in a unimolecular fashion. For more polar, less nucleophilic reagents, such as PhLi, the polarization of the carbonyl bond is greater, causing formation of the non-classical ion discussed above, which favours external nucleophilic attack by a

second RLi oligomer, on the anti face. Alternatively, reagents such as PhLi may complex the anti face simply in order to assist the participation of the C-2,3 double bond and the addition may again be unimolecular. It will be noticed that this scheme is inconsistent with the known mechanisms of Grignard and RLi additions and is inconsistent with some, at least, of the evidence presented above. In particular, there are no examples of unimolecular Grignard reactions, and for t-BuLi at least, the present work shows more than one molecule of reagent is involved.

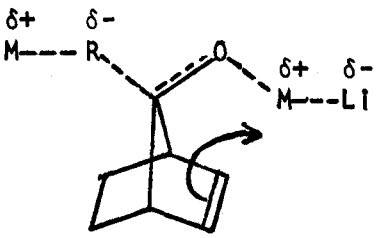
A very different explanation of the specificity of addition suggests itself from the work of Bly[66] who observed that anchimeric assistance was possible in the system below.



Infrared spectroscopic evidence from the present work (see p.93), and work by Bly[68] has shown that strong hydrogen bonding is present in norbornen-7-syn-ols which is clearly analogous to

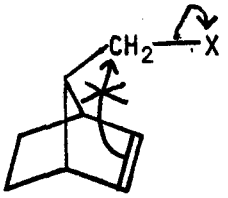


the above. These observations suggest a mode of stabilization for the transition state of anti attack to norbornen-7-one, pictured below.

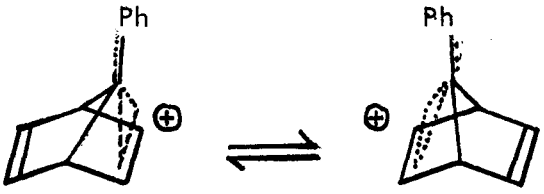


Such stabilization will be favoured by the highly stable, polar organolithium compounds, and Grignard reagents, since the transition state in such a case is later, and is more polar. Participation by the double bond is maximized in this case. For earlier transition states, envisaged for less polar, less stable RLi and Grignard reagents, this effect is small and a steric preference for <u>syn</u> attack takes over.

Repulsion between the developing negative charge on the carbonyl oxygen and the double bond is unlikely since Bly[66] has shown that no interaction occurs in an analogous system. Solvolysis of the compound shown below gave no sign of participation by the double bond.



An objection to this explanation is that not all the strong electronic effects present in the ketone and any transition state drawn are being utilised. Winstein et al[76] have shown that even with a 7-phenyl substituent, the 7-norbornenyl cation is clearly non-classical. For example, 7-phenylnorbornadienyl cation has a $\Delta G^{\pm}$ of <7.6 kcal mole^{-1} for the process below.



The mechanism proposed does not use this information. The Lewis acidity of the reagent must surely tend to concentrate positive charge at C-7, leading to at least partial participation by the

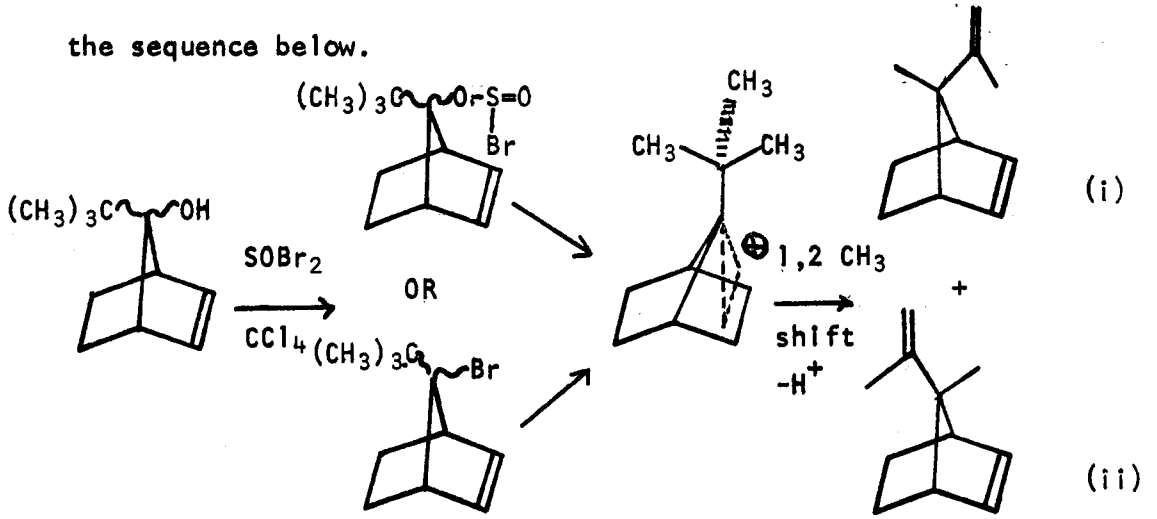
double bond at this centre.

The above rationales of the experimental facts of the addition of nucleophiles to norbornen-7-one may well change with more experimentation. However, the experimental results themselves do force some thought to implications of this work. The impact of such dramatic changes of stereospecificity with relative small changes in reagent on Cram's Rule of Asymmetric Induction is a case in point.

Morrison and Mosher[17] have collected a wide range of data testing the validity of the Cram Rule and the dipolar and cyclic modifications of the Cram Rule. It appears that the effect of a double bond has not been considered as a controlling influence in asymmetric induction. Adjacent groups, such as halogen, amine, and hydroxide, certainly reduce, and in some cases, just invert the specificity expected on the basis of the simple Cram Rule. However, in the present work a double bond, in suitable cases, has caused a complete reversal of addition direction.

Migration in the 7-t-Butylnorbornenyl Cation

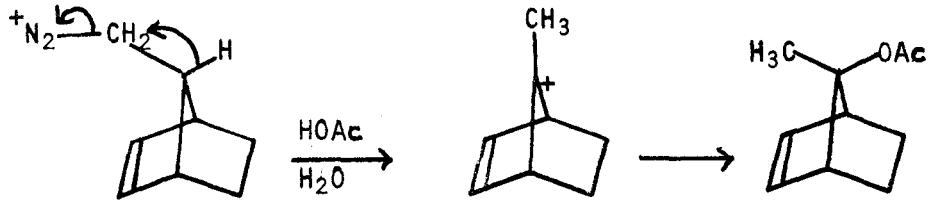
For other work, 7-t-butylnorbornen-7-bromide was needed. Using methods described in the previous section syn and anti-7-t-butylnorbornen-7-ol were prepared and subjected to thionyl bromide bromination in refluxing carbon tetrachloride. From both alcohols, a single diene was formed in high yield, instead of the expected bromides. 7-t-Butylnorbornen-7-anti-bromide (or bromosulphite) could be prepared by carrying out the bromination at room temperature, again in carbon tetrachloride. Treatment of this compound with glacial acetic acid at room temperature gave the same diene. These results can be rationalized as in the sequence below.



Evidence that the cation shown was probably involved was obtained by its generation in SO_2ClF/FSO_3H at low temperature. At -100° p.m.r. analysis revealed that either alcohol produced the same 7-t-butylnorbornenyl cation. At -60°, this cation was observed to rearrange to a second species (50% rearrangement in 60 minutes), which had a spectrum close to that expected for the diene product, 7-methyl-7-(2'-propenyl) norbornene, protonated at C-9. Further evidence was obtained from a relative rate

study of the solvolysis of 7-t-butylnorbornen-syn and anti-7-ol, which is discussed in full below. The anti-ol reacted to form diene far faster than did the syn-ol under identical conditions. This is consistent with anchimeric assistance by the C-2,3 double bond in the solvolysis of the anti-ol. Such behaviour is diagnostic of the existence of the non-classical ion proposed above. Thirdly, methyl migration has clearly occurred in conditions in which only cation or radical reactions are conceivable, and this in itself good evidence for a cation intermediate, since methyl migration in radical reactions are not known.[43]

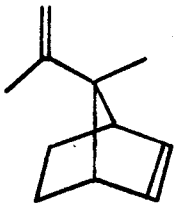
The stereochemistry of the 1,2-methyl migration is of interest. It is well known that external nucleophiles attack the 7-norbornenyl cation on the anti face with high selectivity.[37] For a better example, nucleophilic attack on a 7-alkylsubstituted 7-norbornenyl cation, the work of Berson on memory effects incidentally gave the model required.[78]



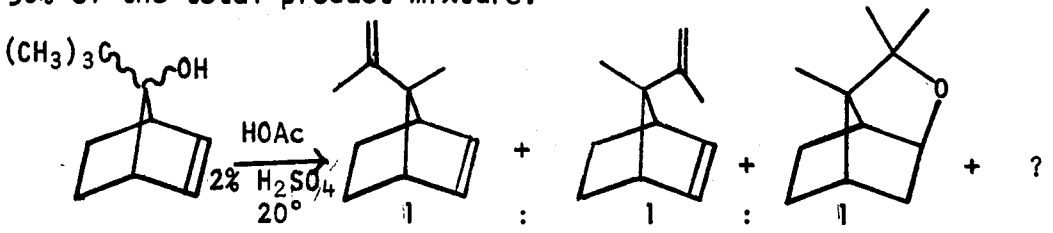
Trapping of the 7-methyl-7-norbornenyl cation in acetic acid gave exclusively 7-anti-acetate, consistent with considerable participation by the C-2,3 double bond.

On this basis we would predict that the diene formed in the reaction of 7-t-butylnorbornen-7-ol with $SOBr_2$ should be exclusively the result of methyl migration anti (ie, structure (i) above). However, it could be shown by nuclear Overhauser effect measurements that this isomer was the minor product (6%)

while the major product (94%) was clearly the result of syn-migration, as below.



Solvolysis of separate samples of 7-t-butylnorbornen-syn-7-ol and 7-t-butylnorbornen-anti-7-ol was now carried out in a variety of conditions to probe this interesting result. In glacial acetic acid containing 2% concentrated sulphuric acid, five products were obtained from either isomer of the alcohol. Three compounds were identified, totally 92% of the product mixture, as shown below. The yield of each was approximately 30% of the total product mixture.

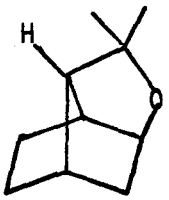


When the concentration of sulphuric acid was increased to 10%, the relative amount of the ether increased to 74% and the total diene yield was 10%. The two unidentified unknowns seen in the previous reaction now totalled 16% of the product mixture.

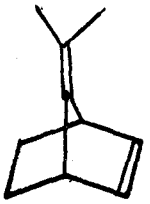
A temperature study was conducted in pure glacial acetic acid. At room temperature, neither alcohol reacted. At 83°, the anti-ol reacted to the extent of 17% in 3 hours to give exclusively diene formed by syn migration, i.e., 7-methyl-anti-7(2'-propenyl)bicyclo[2.2.1]hept-2-ene. At the same temperature, for the same time, the syn-ol was inert. At 108°, the anti-ol has reached a 97/3 mixture of the two dienes after 2 hours, the

major product having the syn methyl group. After 13 days, this ratio dropped to 86/14. After 4 days, only 20% of a sample of syn-ol had reacted, to yield dienes in the ratio (11):(1) = 92:8. This ratio changed in 9 more days to 83:17, essentially the same as that observed for the anti-ol in the same time period. At 170°, a mixture of syn-ol and anti-ol reacted to give 67% total product yield. Of this 71% was the syn-methyl diene, and 8% was its isomer.

Similar Wagner-Meerwein migration using hydrogen as the migrating group was now attempted. In 10% H_2SO_4/HOAc, a mixture of 7-i-propylnorbornen-syn and anti-7-ols gave almost exclusively an ether (below) analogous to that in the t-butyl series,



while in glacial acetic acid at 140°, syn-ol was retrieved, together with a diene product, 7-(2'-propylidene)norbornene.

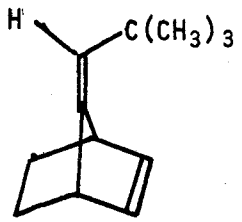


The absence of terminal olefin of the type found in the t-butyl series suggests that

(a) the initial process is proton loss from the 7-cation, i.e., elimination to the non-terminal diene above and,

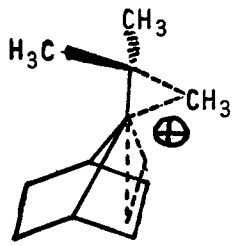
(b) the ether product arises from reprotonation of the diene at C-7, hydroxyl capture and closure.

Treatment of 7-neopentylnorbornen-7-ol (syn-ol:anti-ol = 1:1.57) with thionyl bromide in refluxing carbon tetrachloride gave only one identifiable product, a Δ-7,8 diene analogous to that in the i-propyl series.



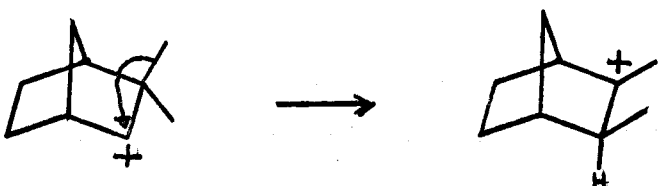
It is unfortunate that these results say nothing about the relative migratory aptitude of hydrogen and methyl, since elimination to the internal olefin (Δ-7,8) is a pathway unavailable to the 7-t-butylnorbornenyl cation.

In the apparent absence of any clear precedent to this migration with retention, a close model was sought for which more information is available. The transition state for the migration must involve delocalization of charge over several carbons.



As in the fully migrated product, all participation by the C-2,3 pi-system is gone, the migration is analogous to a bimolecular nucleophilic substitution. While rarely stated in these terms, external nucleophilic capture of non-classical ions may be regarded as a Walden inversion.

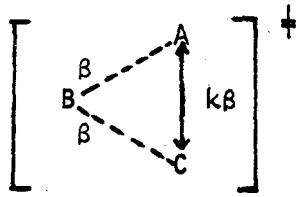
Berson[30] rationalizes the preferred exo-methyl migration to a 2-norbornyl cation in terms which use this concept.



He cites what he calls "strong quantum mechanical reasons for expecting this behaviour". The substitution transition state is a 3-centre problem capable of treatment by simple LCAO calculations. In the ideal case, there will be equal bond integrals (β) between A and B, and between B and C, and a zero integral between A and C for the linear transition state. Thus,

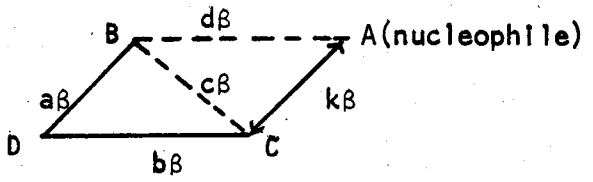
$$[A \overset{\beta}{\text{------}} B \overset{\beta}{\text{------}} C]^{\ddagger}$$

there will be one bonding, one antibonding, and one non-bonding energy level. However, in the transition state for retentive substitution, the A-C integral takes a finite value $k\beta$.



In this case, the energy of the bonding level is lowered relative to that of the linear case, but the non-bonded level is raised to antibonding by a greater amount. Thus, the nucleophilic system (4 electrons) will prefer a linear geometry while the electrophilic system (2 electrons) will prefer the bent geometry. As the author significantly points out, however, "the assumptions of simple LCAO theory are so severe that one should not be surprised if other factors exert a large enough influence to cause occasional contraventions of the predicted behaviour".

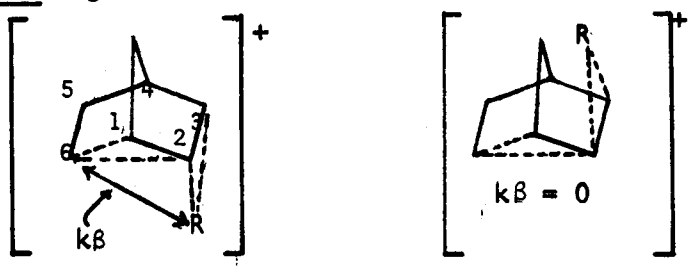
Let us consider the extension of this theory to nucleophilic attack on a non-classical carbonium ion, a four electron-four centre system.



Nucleophile A approaches the three-numbered cycle BDC and attaches to B, while C detaches from B. The inversion mode, corresponding to a linear SN2 reaction would have no A-C interaction ($k\beta = 0$), but retention would have $k\beta > 0$. Simple LCAO calculations[30] again show that the nucleophilic (4-electron) system is always destabilized by inclusion of a front-side interaction ($k\beta > 0$), for "reasonable" variations of parameters, a, b, c, d.

The final extension by Berson[30] is to an intramolecular 1,2-migration within a non-classical ion, the exo-1,2-methyl shift shown on p. 65. This may be treated as a five-centre, 4 electron system.

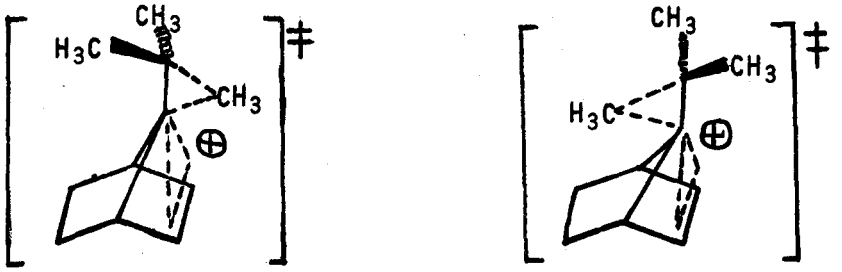
Migration of R on the endo side of the cation will correspond to front-side opening of the C-6, C-1, C-2 mesomeric bridge and will introduce a C-6-R interaction which will be absent in exo migration.



Again LCAO calculations[30] indicate that the exo migration is preferred.

The possible transition states for 1,2-methyl migration

within the 7-t-butylnorbornenyl cation, as shown below, fall into this last category.



If electronic interaction energies, such as calculated by the simple LCAO methods of Berson[30] control the reaction, then indeed an anti migration would be predicted to be the favoured reaction path.

More sophisticated calculations on systems of this type have not yet been reported, apparently. However, such calculations are available for nucleophilic displacement reactions. In the last year, three such studies have been published which will be considered here.

It is convenient to begin by discussing calculations of the SCF type. Fukui[79] defines the interaction energy (ΔW) between two interacting molecular species as the difference between the lowest total energy of the mutually-interacting system of two molecules and the sum of the initial stationary state energies of the two isolated molecules. In general, for weak interactions one may write:

$$\Delta W = E_Q + E_K - D - \pi$$

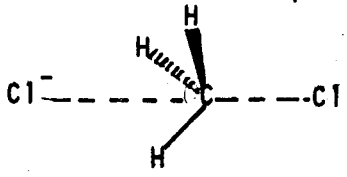
where E_Q is the coulomb interaction energy,

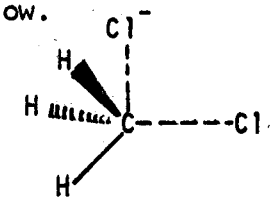
E_K is the exchange interaction energy,

D is the delocalization interaction energy, and

π is the polarization interaction energy.

Using an all-valence-shell-electron, SCF method, Fukui calculates the relative values of all these terms for two transition states possible for the SN2 process, as below.



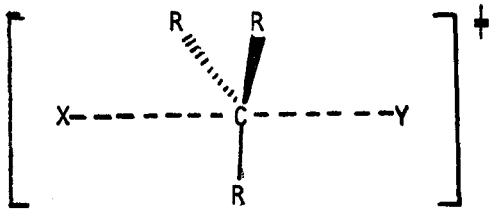


	Inversion mode	Retention mode
E_Q	-0.7876	-0.2594
E_K	1.1641	1.5932
D	1.0525	0.3111
π	0.1762	0.1288
$\Delta\omega$	-0.8522 eV	$\Delta\omega$ +0.8939 eV

The inversion mode is clearly the more likely, although it must be remembered that the fashion in which bond lengths and angles were selected was very arbitrary. It will be noticed that the delocalized energy D is largely responsible for the difference in the stability between the two transition states. This large difference in D is related to the nodal property of the lowest unoccupied M. O. of CH_3Cl which has maximum extension at the backside of the carbon in the direction along the C-Cl axis. The nodal properties and delocalization energies of the 1,2-methyl migration within the 7-t-butylnorbornenyl cation have not been calculated, but geometrical and electronic considerations suggest both properties would be very different from those of Fukui's model compound.

J. P. Lowe[80] in a more extensive treatment of the same problem considers anionic and neutral attack on CH_4 and CH_3F. He finds that on H^- attack on CH_4, charge polarization occurs in concert with bond weakening for the retentive (C_{2v}) mode, but not under the inversive (C_{3v}) mode. Neutral bases have a weaker interaction, but the same effect is observed. A consequence of this bears directly on Fukui's "Frontier Orbital" approach. When a charged base attacks the back side of CH_3F, the major perturbation is charge repulsion, inducing electron density drift to F. Two of the empty M.O.'s of CH_3F can do this, and these calculations show that the M.O. which does carry most of the effect is not that of lowest energy. Consideration of "L.U." orbitals in this case, at least, is of limited usefulness.

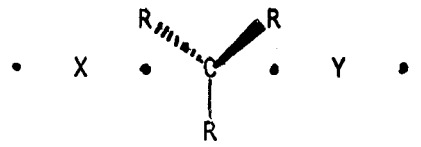
By far, the most unusual of these studies was that of Firestone[81], in which an interesting application of Linnett electronic theory[82] is described. The author claims that the dotted-bond structures normally drawn of transition-states represent our ignorance of their nature and that Linnett theory enables considerably more information to be obtained. A prominent example of a "dotted-bond" transition state is that of the SN2 reaction (below). Two problems



exist immediately for such a formulation according to Firestone. Despite London's prediction[83] that reactions such as XY + Z → X + YZ have vanishingly small activation energies, an activation energy is required. Secondly, there is an implicit expansion of the octet of the central carbon to 10 electrons. Displacement from the hydrogen

molecule implies that 4 electrons are housed in a shell capable of holding 2! The second criticism is not a good one. For a given configuration of atoms, such as in an SN2 transition state, the electrons will arrange so as to minimize energy. Because of repulsions between the atoms, among other things, the energy of this arrangement will be higher than that of reactants or products. Further, because of the concerted nature of the reaction, electron "counts' round each atom have little meaning. The model that Firestone presents, however, loses none of its validity because of the above and will now be discussed in detail, because of its prediction that SN2 (retention) reactions are energetically just feasible.

Firestone proposes a definite structure for the transition state, based on calculations by Bowen[82c,p.75], given below.



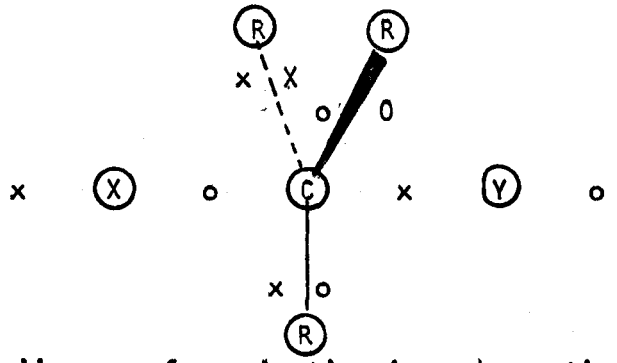
In this structure promotion of electrons to d orbitals is unnecessary and the octet rule remains intact if the habit of pairing electrons whenever possible is abandoned. In this formulation, the number of bonding electrons is kept constant. Activation in such a case would be expected to be zero[83] except for two things.

(1) The 1-electron bond is not necessarily half as strong as the 2-electron bond.

(2) If we define a 2-electron bond as a doubly occupied σ-orbital with a maximum value along the internuclear axis, then sometimes a transformation elsewhere in the molecule causes a displacement of the two spin sets about one of the atoms of the bond, forcing

the bonding electrons apart and off the internuclear line, reducing the bond strength. This contribution to activation, called "L-strain", contributes even although the bonds involved are neither broken nor formed.

Firestone[81] calculates that the bond energies of the three C-R bonds are lowered by L-strain in the transition state by an amount probably more than half the activation energy of many SN2 reactions. The complete Linnett array showing the double tetrahedral quartet of the valence electrons of carbon demonstrates this, as seen below.



When suitable allowance for solvation is made, estimates of L-strain can be surprisingly well equated with the activation energy of SN2 processes, based on an estimated 40° of L-strain.

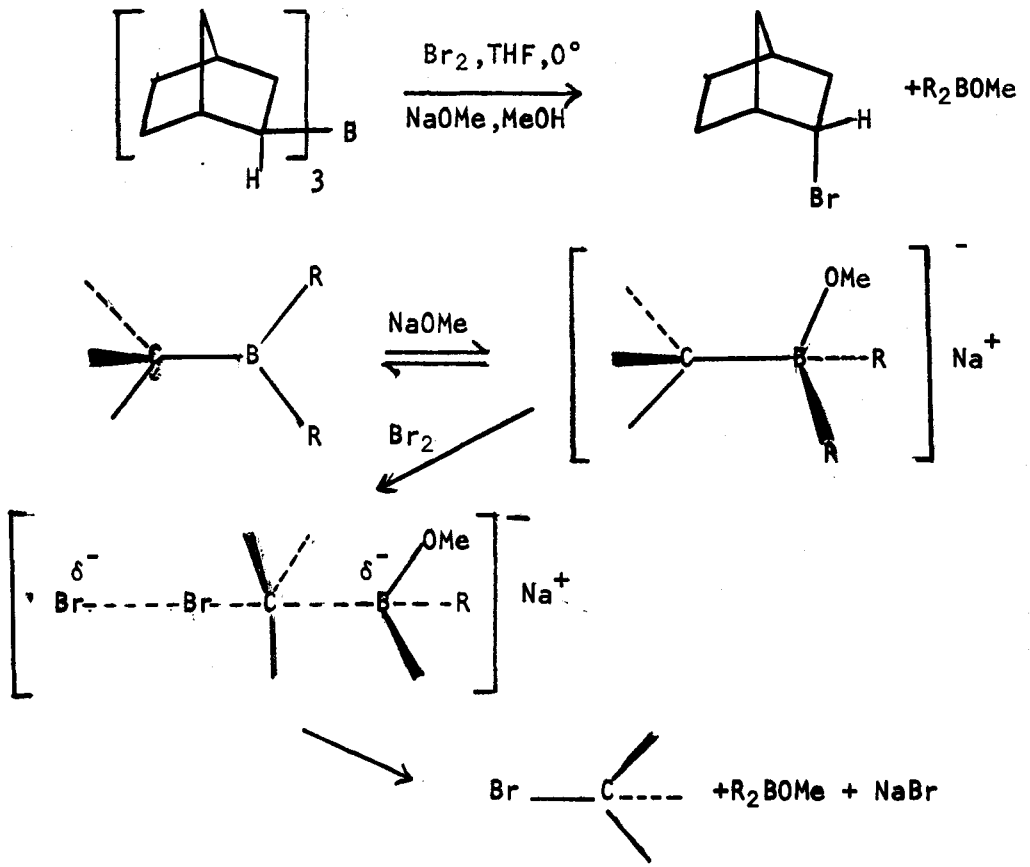
In the C_{2v}, retentive, mode of substitution, the L-strain increases to 70.5°, corresponding to an increase in activation energy over that for inversion of 11 kcals $mol.^{-1}$ for R = H or 16 kcal $mol.^{-1}$ for R = CH_3. Retention then competes very unfavourably with inversion, although it is not altogether forbidden and should indeed be detectable under the proper circumstances.

The concensus of "theoretical" opinion appears to be that the inversion mode is favoured, but retention is not completely eliminated. The barrier quoted of 16 kcal $mol.^{-1}$ against retention may be considerably reduced in a Wagner-Meerwein migration, due to the decreased

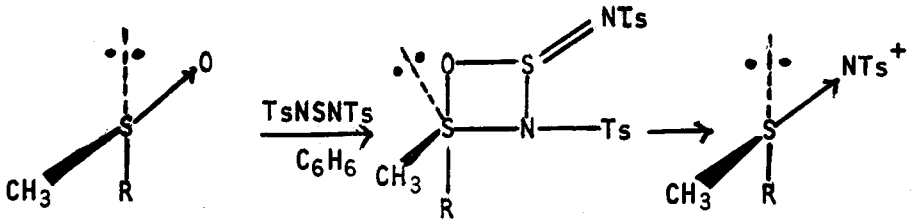
repulsions in a cation, but it is difficult to say more than this using Firestone's approach.

Let us now turn to chemical studies of substitutions and migrations which either appear to proceed with unusual stereochemistry, or, despite being similar to 7-t-butylnorbornenyl cation, react with the normal inversion mode, if at all.

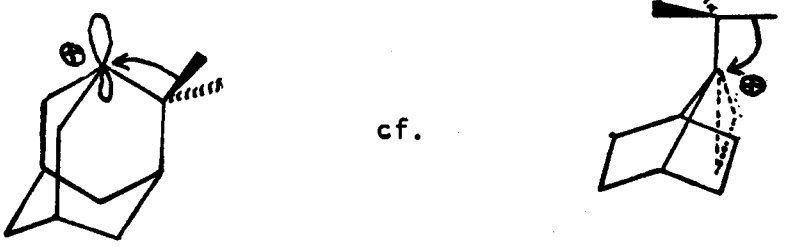
Berson's[30] calculations (p. 65) predicted that inversion on nucleophilic attack and retention on electrophilic attack should be the preferred modes of reaction. These are by no means rigid requirements, as recent studies other than this work, have shown. Brown and Lane, for example, have found an example of electrophilic substitution with inversion.[90b] The reaction of bromine with tri-exo-norbornylborane in methoxide/methanol results in inversion of configuration at carbon to give 75 ± 5% endo-2-bromonorbornane.



As shown in the scheme above, Brown proposes that methoxide complexes with boron, effectively increasing the electron density on carbon, thus enhancing bond scission upon back-side electrophilic attack by bromine. This particular reaction cannot proceed via a four-membered transition state since this would lead to retention, in contrast to other S_E reactions in which inversion is observed.[90b] Nucleophilic substitution with retention has been observed in conditions in which a four-membered transition state is likely. Christensen[91] found that optically active methyl-p-tolyl sulphoxide and methyl butyl sulphoxide react with NN'-bis'(toluene-p-sulphonyl) sulphur di-imide in benzene with complete retention at sulphur.



Possibly the best model for the migration observed in the present work would be the rearrangement of the 2,2-dimethyladamantyl-1-cation.

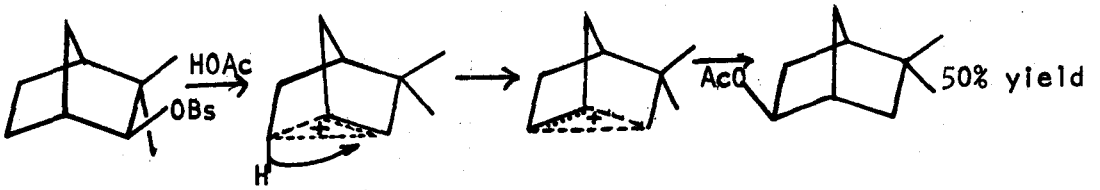


Here, as in the 7-t-butylnorbornenyl cation, the cation centre is non-planar.

Three papers have appeared on this system. In the first, Schleyer[84] reported the solvolysis of the corresponding alcohol and refers to its "abnormal behaviour". He promised a separate paper on the subject, but this has yet to be published. Martin and Ree[85] report no such anomalous behaviour in the solvolysis of the corresponding acetate but tantalized the reader by the statement that the unrearranged acetate is the "predominant product". Schleyer[86] this year withdrew his original suggestion of abnormal behaviour of 2,2-dimethyl-1-adamantyl bromide.

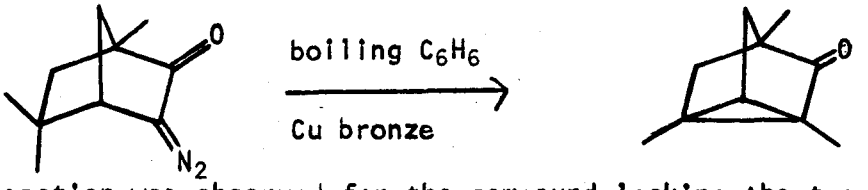
It is unfortunate that the above system is conformationally so locked, since it is likely that this causes migration to be, at the very best, a minor pathway. By comparison with the system studied in this thesis, the incipient migrating methyl is poorly aligned for overlap with the empty p-lobe of the cation. Schleyer[86] found that cyclopropyl substitution of the 1-adamantyl cation gave a rate depression of approximately 10^7 relative to a system containing a non-restricted cyclopropyl substituent alpha to the reaction site. Here too, the alignment of the cyclopropyl group prohibits mesomeric interaction with the cation centre and inductive effects control the rate.

A rather different migration, first established by Berson[30] is more promising. The 6,2-hydrogen shift was reviewed in the introduction (p. 14). Bell and Brown[87] are apparently the only workers to have considered in detail the implications of this migration in terms of the stereochemistry about the site of the leaving group (here brosylate). Quoting work by A. Colter,[88] summarized below,

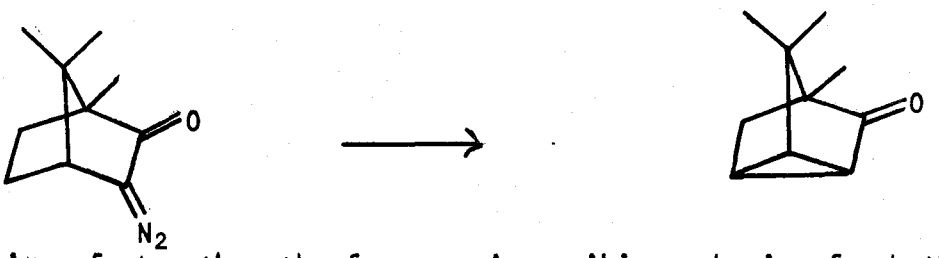


the authors observe that the 6,2-hydrogen shift must be so rapid that it competes with the reaction of the cation with solvent. Brown thought this result very remarkable since it is believed that the hydrogen attacks in the same direction as the bond in the presumed non-classical intermediate. "Normally it is considered that the non-classical structures protects the ion from such attack in the endo direction." To summarize, this appears to be clear precedent for migration within a non-classical ion which proceeds with retention about the site from which the counter anion departed. Further, this process is facile and is often found in reactions of the 2-norbornyl cation.

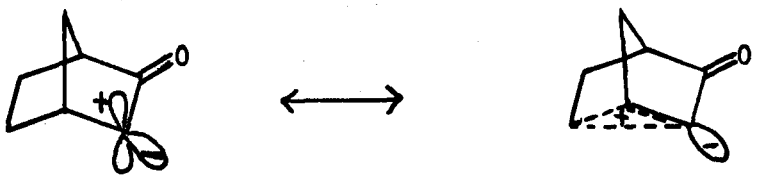
There are no clearly established 6,2-migrations of alkyl groups within cations, which would provide an even better model for migrations within the 7-t-butylnorbornenyl cation. However, a note by Yates and Danishefsky[89] reports work which may be interpreted as involving such a migration. The author thanks Dr. N. H. Werstiuk for drawing his attention to this work. In conditions in which a carbene or carbenoid reaction was likely (see below), a 6,2-methyl migration was observed.



A similar reaction was observed for the compound lacking the two C-6 methyl groups, as below. The latter reaction

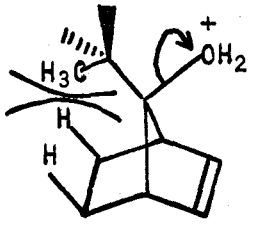


was 1.13 times faster than the former. A possible mechanism for both these processes invokes the presence of a singlet carbene, which for the key species may be represented as below.



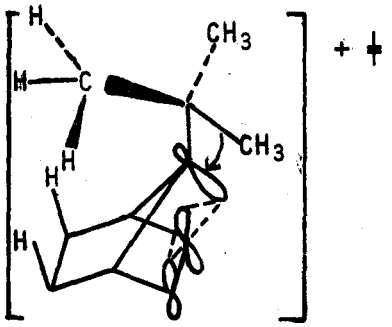
Migration then occurs as for the 6,2-hydrogen shift within the 2-norbornyl cation, again with retention.

We now turn to a mechanistic consideration of the rearrangement of the 7-t-butylnorbornenyl cation. The otherwise uninformative 7-i-propylnorbornenyl cation reaction gives a clue as to why migration in the 7-t-butyl system occurred syn. As with the t-butyl case, it is likely that the free cation lies on the reaction path, since there is a pronounced difference in the rate of disappearance of syn and anti-ol, consistent with anchimeric assistance by the double bond during the solvolysis of the anti-ol. More important, the i-propyl results give strong indication of severe steric strain, manifest in a steric acceleration of solvolysis for the t-butyl compounds. In conditions (glacial HOAc) in which 7-t-butylnorbornen-syn-7-ol reacted, 7-i-propylnorbornen-syn-7-ol remained intact and alcohol, not acetate, was retrieved. A rationale for this is that steric relief in the transition state for formation of the 7-t-butylnorbornenyl cation caused the t-butyl syn-ol to react faster than it otherwise would have done. The large interaction of the t-butyl methyl groups

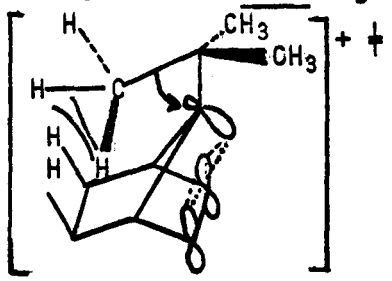


with the exo C-5,6 hydrogens is being at least partly reduced as the cation forms. In the solvolysis of 7-i-propylnorbornen-syn-7-ol, the i-propyl group no doubt favours a much less hindered conformation with the C-8 hydrogen pointing down in a plane directing the C-5,6 bond. Less steric relief accompanies cation formation and the rate drops relative to the t-butyl compound.

This result, and inspection of a model, indicates that the t-butyl system, even in the cation form, is extremely hindered and it is proposed that it is this which controls the stereochemistry of migration. Consider the migration transition state in more detail.



The transition state for syn migration, shown above has the property of good overlap between the C-8 methyl σ-bond and the empty (or nearly empty) p lobe at C-7. Steric interaction between the anti-methyl groups and the endo hydrogens at C-5,6 serve to improve this overlap by forcing the C-7 substituent towards the double bond. Compare this with the transition state for anti migration below.



Now, the migration methyl group sits in a region of large steric interaction, and it may well be that this interaction energy may exceed the 16 kcal mol.$^{-1}$ predicted by Firestone[81] as the electronic barrier to retention.

Inspection of the transition states and the common starting cation allows qualitative estimates of steric relief during the migration to be made. It is clear that the steric strain increases as the migration anti proceeds, since the migrating methyl group passes through the hindered region about the C-5,6 protons. As the methyl group migrates syn the remaining C-8 methyl groups move up and out of the hindered zone. On this basis the activation energy for syn migration should be considerably lower than that for anti migration.

In summary, the 7-t-butylnorbornenyl cation rearranges by a syn-1,2-methyl shift to C-7, despite considerable precedent for nucleophiles to attack anti. Calculations on related systems reveal that the activation energy for this process relative to the normal anti attack is likely to be $\leq$ 16 kcal mol.$^{-1}$. Steric forces in the system are such that it is probably this factor which overcomes the energy barrier.

Hydrogen Abstraction by 7-R-7-Norbornenyl Radicals

A series of 7-R-norbornen-7-bromides, as detailed below, was prepared and submitted to radical reduction. Hydrogen abstraction from tri-n-butylstannane proceeded smoothly at 51°

R	methyl	n-butyl	neopentyl	i-propyl	t-butyl	phenyl
syn-Br	X	X	—	X	—	X
anti-Br	X	—	X	—	X	X
initiation	—	A.I.B.N.	t-BuOOt-Bu	A.I.B.N.	t-BuOOt-Bu	—
	A.I.B.N.		A.I.B.N.			

in n-hexane solution without initiation when R = methyl or phenyl. Azo-bis-isobutyronitrile (A.I.B.N.) was used to initiate the reaction for R = methyl, with no change in product distribution or stereochemistry. With that assurance, A.I.B.N. was used to initiate the reaction for the more hindered cases (R = n-butyl, i-propyl, and neopentyl). This initiation was unsuccessful for R = t-butyl and initiation by di-t-butylperoxide, photolyzed at 310 nm (again at 51°), was used in this case. As a control, similar initiation was used for 7-neopentylnorbornen-anti-7-bromide and no change was observed in product ratio or stereochemistry compared with A.I.B.N. initiation.

The only products identified in a typical yield of 30% were the corresponding 7-R-norbornenes. For two compounds, 7-methylnorbornen-7-bromide and 7-phenylnorbornen-7-bromide, the C-7 stereochemistry of the products was shown to be independent of the C-7 stereochemistry of the starting bromide. It seems probable that in all cases the corresponding 7-R-norbornenyl radical is an intermediate. This is consistent with extensive

studies carried out on the radical reduction of organic halides by Kuivila and coworkers, who proposed the mechanism below,

$$R_3Sn{-}H + Q\cdot \rightarrow R_3Sn\cdot + Q\ H \quad (Q\cdot = \text{initiator})$$

$$R_3Sn\cdot + R'X \rightarrow R_3Sn{-}X + R'\cdot$$

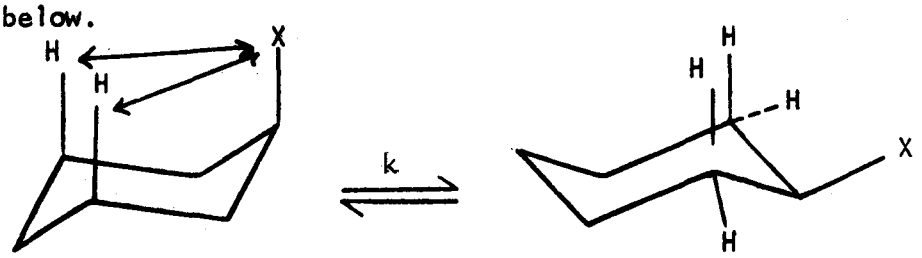
$$R'\cdot + R_3Sn{-}H \rightarrow R_3Sn\cdot + R'{-}H$$

$$2\ R_3Sn\cdot \rightarrow R_3Sn{-}SnR_3$$

$$2\ R'\cdot \rightarrow R'{-}R'$$

and who present good evidence for its validity.[92]

The purpose of the present study was to investigate the stereochemistry of abstraction of hydrogen from the stannane by the 7-R-7-norbornenyl radical. It was suspected that the major effect on the stereochemistry would be the steric bulk of R. As a reference, a system was sought for which good data were available, and in which only steric effects were operating. Such a system is that of the monosubstituted cyclohexanes and their conformational equilibria. Consider the two extreme chair forms of monosubstituted cyclohexanes given below.

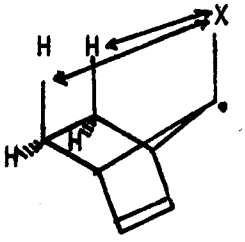


axial equatorial

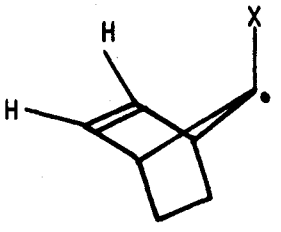
Such cyclohexanes may exist either in the conformation with X axial or in that with X equatorial and these forms are in rapidly-established equilibrium with each other. To a good approximation, the conformers differ in interaction energy in the two 1,3-H-X van der Waals interactions present for the

axial isomer. The four hydrogens adjacent to an equatorial X are considerably further away.

These interactions are surprisingly close to the type of steric interactions present in 7-R-norbornenyl radicals, seen below, drawn[80] as to emphasise this similarity.



"axial"



"equatorial"

Korn and Warkentin (p. 47) have studied the steric interactions present on the syn and anti sides of the norborn-2-ene skeleton and their results indicate that, indeed, the "axial-like" configuration, with a large anti-X, is thermodynamically less favoured than a syn-X compound.

Eliel et al[93] tabulated the positions of the axial X-equatorial X equilibria in terms of $-\Delta G_X^\circ$, the conformational free energy difference between the two forms. These values were directly calculated from the equilibrium constant K, using the relationship $\Delta G_X^\circ = -RT\ln K$. The table below compares the selectivity ratios observed for the abstraction of hydrogen from tri-n-butylstannane by 7-R-norbornenyl radicals in n-hexane at 51° with the values of $-\Delta G_X^\circ$ for each of the substituents R. The graph presents these results in another form.

The attack ratios clearly do not mirror a smooth variation in accord with the size of the substituent alone.

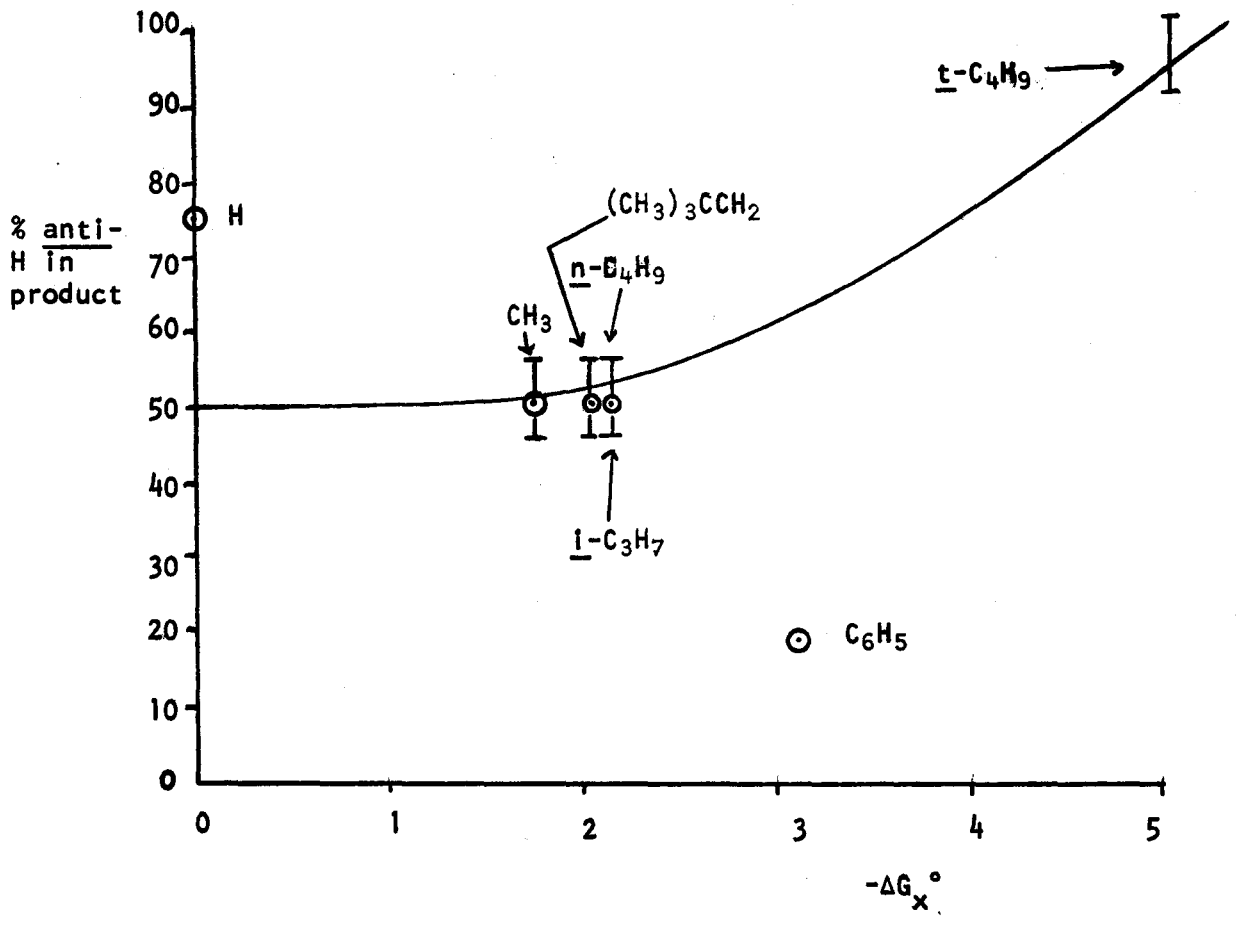
It is difficult to conceive of any effect other than

R	$-\Delta G_x^\circ$	attack, anti/syn	% anti H in product
H	0	3.0[a]	75[a]
CH_3	1.7	1.0, ± 0.1	50 ± 3
n-C_4H_9	2.1	1.0, ± 0.2	50 ± 5
$(CH_3)_3CCH_2$	2.0	1.0, ± 0.2	50 ± 5
i-C_3H_7	2.1	1.0, ± 0.4	50 ± 5
C_6H_5	3.1	0.23, ±0.01	19 ± 0.2
t-C_4H_9	5[b]	> 10	> 90

(a) The attack ratio for R = H is from unpublished work by Warkentin and Sanford and from reference 52.

(b) An approximate value.

Graph of Percentage anti-H in products vs $-\Delta G_x^\circ$



van der Waal's repulsion to be operating when R = CH_3, n-C_4H_9, i-C_3H_7, $(CH_3)_3CCH_2$, or t-C_4H_9. The complete lack of selectivity of attack observed for radicals with R = CH_3, n-C_4H_9, i-C_3H_7, and $(CH_3)_3CCH_2$ is mirrored in the negligible change in the values of ΔG_x° and is fully consistent with the findings of Korn and Warkentin[57] (see p. 47). Equilibration of mixed ketals of norbornen-7-one revealed that the position of the equilibrium is relatively insensitive to the size of the alkoxy substituents at C-7. The maximum value of the equilibrium constant observed was 1.9 when the bulky alkoxy group was 2-pentyl.

Significantly, Korn and Warkentin[57] were not able to prepare the ketal for which R = t-C_4H_9. The value of $-\Delta G_x^\circ$ for this group suggests that steric hindrance prevented ketal formation, even under very forcing conditions. The table above indicates that 7-t-butylnorbornenyl radical abstracted hydrogen on the anti side exclusively, to the limit of p.m.r. detection. A value of $-\Delta G_x^\circ$ of approximately 5 kcal $mole^{-1}$ corresponds to $K = 1.7 \times 10^{-2}$, that is, t-butylcyclohexane exists in the equatorial form exclusively to a very good approximation. The observed attack ratio is thus clearly consistent with steric control of abstraction. The bulky t-butyl group prefers to sit over the less-hindered syn-face.

With such bulky groups at C-7, it might be reasoned that the thermal stability of anti-7-t-butylnorbornene was such that, although formed, this isomer decomposed before detection. However, Baird and Surridge[110] have recently prepared both syn and anti isomers of this compound and report no difficulty in

distilling anti-7-t-butylnorbornene at 130°.

The reaction of 7-phenylnorbornen-7-bromide with tri-n-butylstannane differs from the above because the proposed intermediate, 7-phenylnorbornenyl radical, is benzylic rather than merely tertiary. Clearly, the abstraction by this radical was not controlled by steric factors alone, since the preferred stereochemistry of the resultant norbornene is opposite to that expected if steric control was dominating. To probe the mechanism further, reactions were run at 100° for the bromides (R = CH_3, C_6H_5). The results of this study are shown in the table below.

Abstraction Ratios Anti/Syn on 7-R-norbornenyl Radicals

Temp (°C)	51	100	120
R = phenyl	0.23 ± 0.01	0.32 ± 0.01	—
R = methyl	1.0 ± 0.1	1.0 ± 0.1	1.0[a]

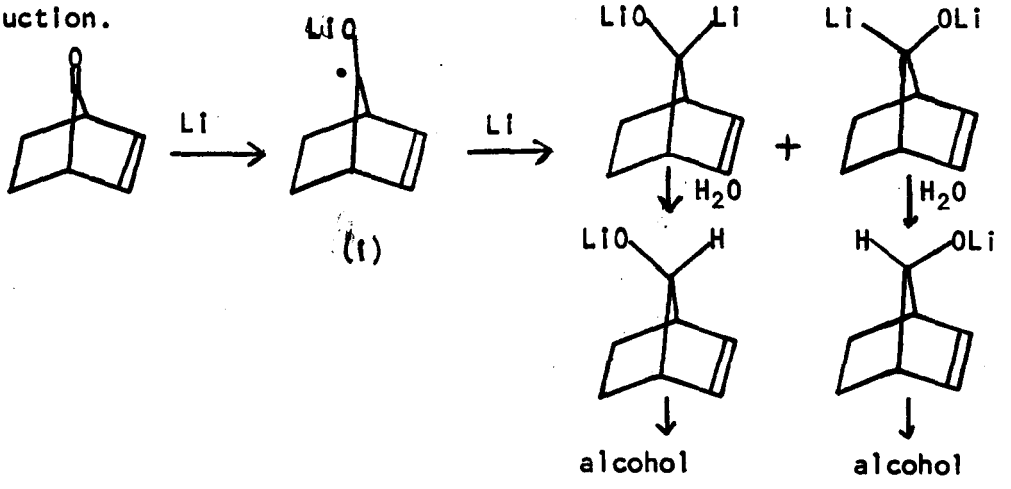
(a) From reference (94).

While it is dangerous to read much into these results, it does appear that there is a definite difference in transition state structure between the two radicals. The complete insensitivity of ratio to temperature change shown by 7-methylnorbornenyl radical may indicate that the entropy of activation for abstraction is zero. This is clearly not the case for the benzylic 7-phenylnorbornenyl radical, which shows a small sensitivity to temperature in its abstraction.

Greater stability would be expected for the phenyl radicals, than for 7-methyl-7-norbornenyl radical. By the

Hammond Postulate, it follows that the transition state for abstraction by 7-phenylnorbornenyl-7-radical will be more product-like. If this implies closer approach by tri-n-butylstannane in the transition state, the reason for the observed selectivity of abstraction becomes clear. The steric effect of the stannane largely dictates the stereochemistry of abstraction, and, as the syn face of the radical is less hindered, reaction occurs there preferentially.

In an apparently unrelated experiment, an example of capture of a 7-norbornenyl radical with stereochemistry of attack similar to that for abstraction by the 7-phenylnorbornenyl radical was revealed. t-Butylbromide and norbornen-7-one were added to lithium pieces in diethyl ether at -70°. In this experiment, unlike similar experiments by Pearce et al,[95] where carbonyl addition was observed, norbornen-7-ol was the only product (50% yield) and the stereochemistry about C-7 favoured the anti-ol by a factor of 4.3:1. It has been previously shown that t-butyllithium gives 80% addition to this ketone with only 20% reduction (p. 43), so that it is unlikely that the mechanism of reduction is the same here. It is possible to suggest a tentative mechanism for the observed reduction.



The intermediate radical (i) is trapped by lithium in a manner which must be subject to the same constraints as an abstraction of a hydrogen by a norbornenyl radical. The stereochemistry of this process is recorded in the products, since the hydrolysis of an alkyllithium is a typical electrophilic substitution, and presumably proceeds with retention. The ratio of the alcohol products indicate the reaction to be occurring preferentially on the syn face, like the abstraction by the 7-phenylnorbornenyl radical. Radical (i) has a stabilizing adjacent oxygen which will have a similar effect to the phenyl substituent of the 7-phenylnorbornenyl radical. A late transition state would again be predicted and the steric effect of the entering lithium atom would dictate a preference for syn attack. Norbornen-anti-7-ol is then the major product.

The remaining radical abstraction in the series is that by the parent 7-norbornenyl radical. It has been discussed above how the syn face of norbornenes is less hindered, and how a bulky group (t-butyl) at C-7 prefers to sit over the syn face of the 7-t-butylnorbornenyl radical. Despite this the stannane prefers to approach the anti face of the unsubstituted 7-norbornenyl radical. On the graph on page 84, the curve through the point for R = H experiences a change in the sign of the gradient compared with the curve through the points where steric control must be operating (R = CH_3, n-C_4H_9, i-C_3H_7, neopentyl, and t-C_4H_9). This is clear evidence that electronic factors are involved in determining the stereospecificity of abstraction by the 7-norbornenyl radical.

One possibility for this electronic interaction is repulsion of the reagent from the double bond. This, however, is inconsistent with the attack ratios obtained when R = CH_3, n-C_4H_9, i-C_3H_7, and neopentyl, for which the same effect would be expected, but it is not observed. In these cases, the larger size of the C-7 substituent (R) could only increase the preference for anti-attack over that observed for R = H, as both the bulk of R and the double bond-reagent repulsion should favour this. In practice, no preference for anti-attack is shown for these four cases.

The best explanation of the attack ratio observed for the unsubstituted 7-norbornenyl radical appears to be that homoallylic participation of the C-2,3 double bond at C-7 directs the reagent to attack preferentially on the anti face. Thus, the calculations of Ohorodnyk and Santry[51] are qualitatively correct and the original suggestion of Warkentin and Sanford[51] stands. The 7-norbornenyl radical is non-classical.

Results and Discussion: Part 2 -- Synthesis and Structural Assignment.

7-R-Norbornen-7-ols

Warkentin[18] found that the title compounds may be prepared by the reaction of suitable Grignard reagents with norbornen-7-one, but reduction was a major side reaction which, in some cases, actually became the major pathway.

Products from Norbornen-7-one and RMgX[18]

	Product distribution (relative %)		
	Addition		Reduction
R of RMgX[a]	*syn*[b]	*anti*[b]	total
CH_3	4	96	--
CH_3CH_2	---	51	49
$(CH_3)_3CH_2$	---	10	90
$(CH_3)_3C$	---	--	100
$(CH_3)_3CCH_2$	---	> 98	1

(a) Grignard reagents are represented here as "RMgX".

(b) Labels (*syn*, *anti*) refer to the hydroxy group.

The alternative synthesis of 7-R-norbornen-7-ols (R = alkyl, aryl) from organolithium reagents has been used to prepare 7-methylnorbornen-7-ol of both *syn* and *anti* configurations,[96] and also a series of 7-arylnorbornen-7-ols.[69a]

For the present study, norbornen-7-one was reacted with four alkyllithium reagents in which the extent of β-branching varied (RLi; R = methyl, *n*-butyl, *i*-propyl, *t*-butyl), with neopentyllithium, 3,3-dimethylbutyllithium, and with three unsaturated organolithium reagents (RLi; R = vinyl, phenyl,

benzhydryl). To a minimum of 81% of a material balance the only products obtained, in general, were the two isomeric 7-R-norbornen-7-ols. t-Butyllithium, which has the maximum number of β-hydrogens, gave less than 20% reduction. In all other cases, reduction was not detected.

The evidence for the structure and, particularly, the stereochemistry about C-7 is discussed in full.

(1) Elemental Analysis:

7-R-Norbornen-7-anti-ols (A) and 7-R-Norbornen-7-syn-ols (B)

	Compound R	%C[a]	%H[a]
A	n-C_4H_9	79.46	10.92
		78.45	10.90
B	n-C_4H_9	79.46	10.92
		79.16	10.90
A	t-C_4H_9	79.46	10.92
		79.50	10.90
B	t-C_4H_9	79.46	10.92
		78.65	10.99
A	t-C_4H_9-CH_2CH_2	80.41	11.34[b]
		80.29	11.79
B	t-C_4H_9-CH_2CH_2	80.41	11.34[b]
		80.27	11.90

(a) Calculated figures in the upper rows; analytical results in the lower rows.

(b) Products of the reaction of t-BuLi, with the ketone in the presence of diethylether (see p. 43).

7-Benzhydrylnorbornen-7-syn-ol did not analyse satisfactorily, probably because of the particularly facile elimination possible. However, high resolution mass spectrometry gave the expected molecular formula ($C_{20}H_{20}O$ requires m/e 276.1514, observed m/e 276.1541). 7-Neopentylnorbornen-7-ol was identified by conversion to the corresponding bromide which is discussed later and fully identified. All other alcohols in the series were known compounds (R = methyl,[96] i-propyl,[18] vinyl,[97] phenyl[69a]).

(ii) P. m. r. Spectra

P.M.R. Spectra of 7-R-Norbornen-7-anti-ols (A) and 7-R-Norbornen-7-syn-ols (B).

	Compound R	H_1	H_2	H_5	H_6	H_R
A	CH_3	2.27	5.92	2.00	0.92	1.25
B	CH_3	2.42	6.12	1.80	0.95	1.13
A	i-C_3H_7	2.43	5.92	1.96	0.92	2.29,0.82[a]
B	i-C_3H_7	2.58	6.14	1.90	0.90	0.92[b]
A	n-C_4H_9	2.34	5.92	--	--	--[c]
B	n-C_4H_9	2.50	6.11	1.80	0.90	1.40
A	t-C_4H_9	2.50	5.82	2.00	1.00	0.90
B	t-C_4H_9	2.75	6.20	2.00	1.00	1.08
A	t-C_4H_9-CH_2	2.53	5.97	2.01	0.98	1.73,1.03
B	t-C_4H_9-CH_2	2.60	6.04	1.80	0.90	1.44,1.00
A	t-C_4H_9-CH_2CH_2	2.33	5.90	--	--	0.80
B	t-C_4H_9-CH_2CH_2	2.49	6.08	1.75	0.92	0.85
A	CH_2=CH	2.40	5.95	2.06	0.92	(d)
B	CH_2=CH	2.62	6.20	1.85	1.00	(e)
A	C_6H_5	2.85	5.82	--	--[c]	7.20
B	C_6H_5	3.16	6.23	--	--[c]	7.32
B	$(C_6H_5)_2CH$[f]	2.49	6.03	2.00	0.90	4.70,7.20

(a) $J_{8,9}$ = 7·0Hz.

(b) $J_{8,9}$ = 6·0Hz.

(c) Blanks indicate that the exact chemical shift could not be obtained because of severe overlap.

(d) The H_8 signal: four lines centred at 6.35δ, J_t = 11 Hz, relative area 1. The H9 signal: complex triplet centred at 5.12δ, J_t = 17, J_c = 11, J_g = 2Hz, relative area 2. These are observed parameters, obtained by 1st order analysis. Relative intensities indicated that the spectrum is of higher order at 60 MHz.

(e) The H_8 signal: four lines centred at 6.02δ, J_t = 15, J_c = 9.5 Hz, relative area 1. The H9 signal: complex triplet, 5.04, 5.26 and 5.50δ, J_t = 15, J_c = 9.5, J_g = 3Hz, relative area 2. The qualification in footnote d also applies here.

(f) 7-benzhydrylnorbornen-anti-7-ol was not formed.

A number of features in the p.m.r. spectra of these alcohols were found entirely consistent within the series studied. The position of the C-1,4 bridgehead protons was diagnostic. Syn-ols (anti-R) gave the lower field absorption. When the hydroxy group was over the C-2,3 vinyl protons, the corresponding vinyl resonance moved to lower field, perhaps because of the deshielding effect of the intramolecular H-bonding (discussed on p. 93). Even in the presence of syn and anti norbornen-7-ol, with their characteristic vinyl (triplet) absorptions, the vinyl triplets of 7-R-norbornen-7-ol could be seen and the syn/anti addition ratio could readily be measured. The "perturbed" triplet reported

to occur in the p.m.r. spectra of 7-R-norbornen-7-ols by Bly[67] could not be seen.

Exo and endo C-5,6 proton resonances were found to vary little from compound to compound. The resonance of the substituent R of the alcohols shows the expected small variations between syn and anti isomers. In general, the C-8 protons (if any) moved to higher field when over the double bond.

(iii) Infra-Red Spectra

Bly and Bly[67] and Erman[96] used the existence of pronounced H-bonding of C-7 syn-hydroxy hydrogens to the C-2,3-vinyl π-systems to assign the stereochemistry of the alcohols. The anti-ols, for all the compounds studied here have a free O-H stretch above 3600 cm^{-1}. All syn-ols, like those of Bly and Bly[67], and Erman[96], exhibited a sharp absorption near 3575 cm^{-1}.

(iv) G.L.P.C. Data

The criteria most often used to assign the stereochemistry of these alcohols are the relative retention times or volumes of syn and anti-ols. This method has been used by Erman[96], Bly[67], Berson[97] and Warkentin[18]. Results obtained here show that this criterion is not sufficient in itself to assign C-7 stereochemistry. In a Carbowax column, of the products of alkyllithium addition to norbornen-7-one, the syn-ol is eluted first, in keeping with the reduction in polarity of this compound caused by intramolecular H-bonding. That the hydroxy group largely determines the elution order and retention time is indicated by the very close retention times for all the 7-R-norbornen-7-ols (R = alkyl, H). De-

composition temperatures were reached in a Carbowax column before 7-phenylnorbornen-7-ol was eluted. An SE30 column allowed separation without decomposition but syn-ol now eluted after anti-ol.

(v) Partial Acetylation

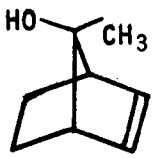
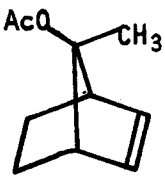
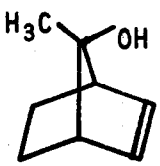
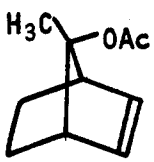
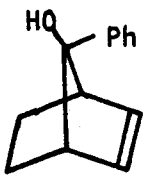
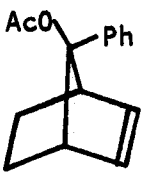
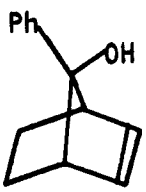
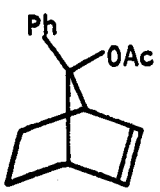
It was reasoned that removal of the intramolecular H-bonding by acetylation of syn-ols should cause a large change in the p.m.r. signals of the C-2,3 vinyl protons, and perhaps also of the C-1,4 bridgehead hydrogens. The best standard of chemical shift to use here was clearly the alcohol itself. Thus, partial acetylation was conducted on separate samples of 7-phenylnorbornen-syn-7-ol and 7-phenylnorbornen-anti-7-ol using acetyl chloride-pyridine in tetrahydrofuran. Erman[96] has prepared the two 7-acetoxy-7-methylnorbornenes by a similar method; the p.m.r. spectra reported for these compounds were compared with those of the phenyl analogues. The pertinent results are summarised in the table following (p.95).

One of the isomers of 7-phenylnorbornen-7-ol has shown a large change in the magnetic environment of the C-2,3 and C-1,4 protons in forming the corresponding acetate. It is clear that this isomer must have a syn-hydroxy group.

(vi) Solvolysis

As is fully described earlier, 7-t-butylnorbornen-7-ol and 7-i-propylnorbornen-7-ol were treated with solutions of acetic acid of various acidities at various temperatures. In both cases, one isomer, assigned anti-ol stereochemistry, solvolyzed faster than the alcohol with syn-ol stereochemistry,

Bridgehead and vinyl shifts of norbornenes[a]

Compound	Bridgehead	Vinyl	Δδ bridgehead[b]	Δδ vinyl[c]
	2.30	5.97		
			0.58	0.02
 [d]	2.88	5.95		
	2.42	6.12		
			0.61	0.12
 [d]	3.03	6.00		
	2.92	5.83		
			0.48	0.00
	3.40	5.83		
	3.16	6.23		
			0.52	0.17
	3.68	6.06		

(a) All numbers are chemical shifts in p.p.m. downfield from T.M.S.

(b) The difference in chemical shift between the bridgehead protons of the acetate and the corresponding alcohol.

(c) The difference in chemical shift between the vinyl protons of the acetate and the corresponding alcohol.

(d) Reference 96.

presumably because of C-2,3 double bond participation. These assignments were consistent with the p.m.r. and i.r. assignments discussed above.

(vii) Bromination

Skattebøl[98] prepared 7-bromo-7-methylnorbornene by reacting 7,7-dibromonorcarene with methyllithium, and assigned the C-7 stereochemistry as syn-Br by the observation that the compound was solvolytically inactive. The anti-bromide would be expected to be solvolytically labile because of the C-2,3 double bond available for homoallylic participation in cation formation. The present author[18] prepared this bromide by treating 7-methylnorbornen-anti-7-ol with thionyl bromide in refluxing carbon tetrachloride, and the p.m.r. of the compound was clearly distinguishable from that reported by Skattebøl[98] for the syn-bromide.

In summary, the C-7 stereochemistry of 7-R-norbornen-7-ols is firmly established for the series R = CH_3, i-C_3H_7, n-C_4H_9, t-C_4H_9, $H_2C{=}CH$, $(CH_3)_3CCH_2$, $(CH_3)_3CCH_2CH_2$, C_6H_5, $(C_6H_5)_2CH$.

Products of 7-t-butylnorbornen-7-ol solvolysis

7-methyl-7-(2'-propenyl)norbornene

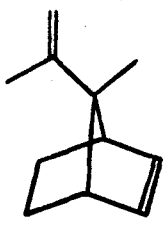
In strongly acidic media, both syn- and anti- isomers of the title compound were formed. Elemental analysis revealed a formula of $(C_{11}H_{16})_n$ for each. The value of n was presumed to be one on the basis of the g.l.p.c. retention time, p.m.r. evidence and chemical properties to be described below. This elemental analysis was separately carried out on two compounds of very close retention time eluted from a freshly prepared Carbowax 20 M column at 118°.

The p.m.r. spectra of the two compounds were remarkably similar, but two areas of difference were observable. On careful study of spectra run at 100 MHz, subtle chemical shift differences, shown in the table below, could be seen.

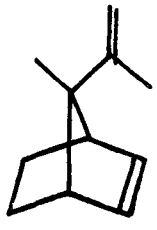
Chemical Shifts of Isomer 1 and 2.

Compound	C-2,3	C-1'	C-1,4	C-7 methyl	C-3'
Isomer 1	5.84,t	4.56	2.56	0.92,s	1.56
Isomer 2	5.95,t	4.64	2.60	1.00,s	1.68

On the basis of the analysis results and p.m.r. evidence, to be discussed below, structures as below are proposed.



Isomer 1



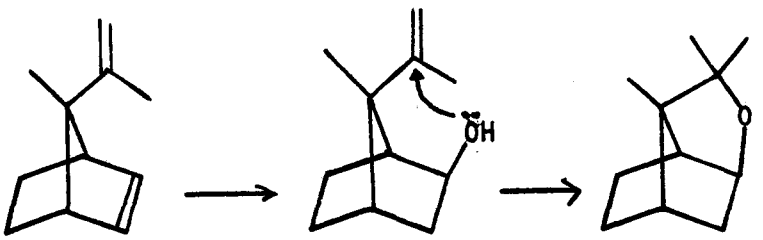
Isomer 2

Chemical evidence for the gross structure is twofold.

(i) It has been previously discussed (p. 61) how it is probable that the 7-t-butylnorbornenyl cation is an intermediate in the solvolysis of 7-t-butylnorbornen-7-ol. The expected rearrangement, if any is to occur, is methyl migration from the t-butyl group. Proton loss from the resulting cation gives 7-methyl-7-(2'-propenyl)norbornene as above.

(ii) Separate samples of isomers 1 and 2 were submitted to solvolytic conditions (acetic acid containing 2% sulphuric acid, 4 hours at room temperature). Each isomer partly converted to the other and also to a third, longer retention time component (a cyclic ether), which will be discussed later.

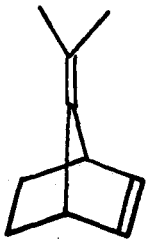
The partial equilibration is in keeping with the nature of the presumably reversible rearrangement proposed. Hydration of the norbornene double bond, and attack of the resulting alcohol on the remaining double bond gives the observed tricyclic ether, as below.

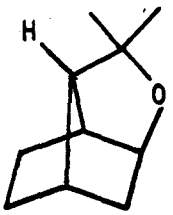


The structure of this ether was inferred from elemental and p.m.r. analysis. The rate of interchange between isomers 1 and 2 is at least comparable to the rate of ether formation, since approximately the same amount of ether formation was

observed from each isomer in identical experiments. In pure glacial acetic acid, where acid catalysis of double bond hydration is subdued compared with that in the $HOAc-H_2SO_4$ mixture, equilibration of the dienes could be observed without measurable formation of the ether.

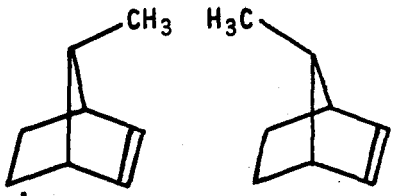
The acidolysis of 7-i-propylnorbornen-7-ol gave two products in conditions specified above (p. 64), the structures of which were inferred by p.m.r. analysis and analogy.





The diene had a p.m.r. spectrum closely related to the analogous diene obtained on solvolysis of 7-neopentylnorbornen-7-ol (p. 65) while the cyclic ether had a p.m.r. spectrum which differed from the analogous compound in the solvolysis of 7-t-butyl-norbornen-7-ol only in that a C-7 proton replaces the C-7 methyl group in the t-butyl series (p. 99).

It was of considerable interest to determine the C-7 stereochemistry of the diene, isomer (1), which predominated in the solvolysis reaction of 7-t-butylnorbornen-7-ol in weakly acidic conditions. The p.m.r. spectra provided a weak clue. The table below shows how the C-7 methyl signal differed between isomers 1 and 2, and compares this with that observed in this work for 7-methylnorbornene.



			isomer 1	isomer 2
C-7 methyl signal (δ)	0.83	0.74	0.92	1.00

In a discussion of the effect of the double bond on the chemical shifts of C-7 hydrogens in 7-substituted norbornenes, Franzus et al[99] show that the 7-syn-proton of norbornene is actually deshielded by the double bond, but when this proton is pushed further towards the double bond by 7-anti substituents, the proton becomes shielded, relative to the 7-anti-proton of norbornene with the same substituent syn. Isomer 1 has such an anti-substituent (2'-propenyl) which may serve to force the syn-methyl group into a shielding region.

That this argument is not sufficient is seen from the fact that there are exceptions to it. For an example, consider the C-7 H chemical shifts of 7-halonorbornenes shown below.

Halogen	C-7 stereochemistry of halogen	Chemical shift of C-7 hydrogen (δ)
Cl[(a)]	syn	3.76
	anti	3.60
Br[(a)]	syn	3.95
	anti	3.85
I[(b)]	syn	3.73
	anti	3.81

(a) From E. Sanford, unpublished results.

(b) Reference (56).

While 7-chloro- and 7-bromonorbornene follow the trends established above, the assignment is reversed for 7-iodonorbornene.

Fortunately, a most unambiguous proof of C-7 stereochemistry was possible for this system. Bell and Saunders[100] correlated the nuclear Overhauser effect (n. O. e.) with the distance(in°A) between the irradiated nucleus and the effected centre. The results of a n.O.e. investigation of 7-methyl-7-(2'-propenyl)norbornene are shown below, together with the results on a suitable model compound.

Compound[a]	Observed n.O.e. (%)[b]
Isomer 1	7[c], 10, 8, 10, (4), 9
Isomer 2	0, 0, 0, 0
7-anti-acetoxy-7-methylnorbornene	5

(a) All compounds employed were of g.l.p.c. purity, dissolved in carbon tetrachloride containing sufficient T.M.S. or chloroform to act as internal lock for the spectrometer.

(b) The general method of determination is described in the experimental section (p.113). The lock was to T.M.S. except where noted.

(c) A chloroform lock signal was used here.

The results of this study are consistent only with a distance of approximately 3°A between the C-7 methyl group and the C-2,3 vinyl protons for isomer 1.

Isomer 1 is thus 7-syn-methyl-7-(2'-propenyl)norbornene

and isomer 2 is assigned the 7-anti-methyl configuration.

7-R-norbornen-7-bromides

The synthesis of 7-syn-methylnorbornen-7-bromide has been achieved by thionyl bromide bromination of the corresponding alcohol.[18] 7-Anti-methylnorbornen-7-bromide was prepared by Skattebøl.[98] These appear to be the only compounds in the series for which the syntheses have been reported.

For the present work, the bromides (R = methyl) were prepared as above. Like Skattebøl,[98] the present author found the syn-bromide predominates in the reaction of methyllithium with 7,7-dibromonorcarene. This could be separated by preparative g.l.p.c. from the anti-bromide also present. Rather than use this procedure as an inefficient method of preparation of 7-syn-methylnorbornen-7-bromide, 7-methylnorbornen-anti-7-ol was brominated in 84% yield to the required compound using thionyl bromide and was purified by either column chromatography or g.l.p.c.

Treatment of 7,7-dibromonorcarene with phenyllithium gave 7-phenylnorbornen-syn-7-bromide which could be purified by recrystallization. Sublimation caused isomerization to 7-phenylnorbornen-anti-7-bromide. The anti-bromide could not be prepared isomerically pure by this method.

7-n-Butylnorbornen-syn-7-bromide and 7-i-propylnorbornen-syn-7-bromide were prepared by similar addition of RLi to 7,7-dibromonorcarene. Both isomers of the bromides were present in the crude reaction products, but the only separation procedure which was at all successful, g.l.p.c., selectively destroyed one isomer in each case, which was assigned the anti-bromide

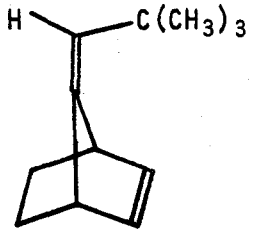
stereochemistry for both R = n-butyl and i-propyl, based on the predicted relatively high solvolytic activity of the anti-bromides.

Addition of t-butyllithium to 7,7-dibromonorcarene gave a crude mixture of syn and anti-7-t-butylnorbornen-7-bromide but no separation procedure could be designed to separate the isomers without extensive decomposition. A most lengthy separation by g.l.p.c. gave the syn-7-bromide (10 mg) sufficient for p.m.r. analysis only. Thionyl bromide bromination of 7-t-butylnorbornen-7-ol (a mixture of syn and anti) gave typically only 7-methyl-7-(2'-propenyl)norbornene, but careful flushing out of the HBr formed with dry nitrogen seemed to reduce the rearrangement to near negligible quantities. The highest purity 7-t-butylnorbornen-7-bromide (90%, 10% diene) was obtained when water was not rigorously excluded from the reaction vessel.

It is interesting that a mixture of syn- and anti-7-t-butylnorbornen-7-ol gave only the one bromide which p.m.r. analysis (to be discussed later) showed to have the anti-Br structure. That this compound was a bromide and not a bromosulphite cannot be rigorously proven, but p.m.r. consistency, analogy with other members of the series, and behaviour in the radical reduction with tri-n-butylstannane, seem consistent with the bromide formulation.

7-Anti-bromo-7-neopentylnorbornene was prepared by bromination of the corresponding alcohol with thionyl bromide in the presence of 1 mole equivalent of triethylamine. Again

high yield (76%) conversion to the anti-bromide occurred from a mixture of syn- and anti-ol. More vigorous treatment ($SOBr_2$, reflux) gave a complex mixture of products from which could be extracted the diene below.



In general, 7-bromo-7-R-norbornene was too unstable to enable meaningful elemental analysis to be carried out, but high resolution mass spectra were consistent with the proposed structures. In every case except R = n-Br, the molecular ion was not observed but the M^+-Br peak was strong. 7-Bromo-7-n-butylnorbornene has a consistent mass spectrum for $C_{11}H_{17}Br$. These results are shown below.

High Resolution Mass Spectra for 7-Bromo-7-R-norbornenes

R	Formula of ion observed		m/e
C_6H_5 [a]	$C_{13}H_{13}$	1) [c]	169.1016
		2) [d]	169.1017
i-C_3H_7	$C_{10}H_{15}$	1)	135.1177
		2)	135.1173
t-C_4H_9 [b]	$C_{11}H_{17}$	1)	149.1321
		2)	149.1330
t-C_4H_9-CH_2	$C_{12}H_{19}$	1)	163.1507
		2)	163.1486
n-C_4H_9	$C_{11}H_{17}{}^{79}Br$	1)	228.0504
		2)	228.0514
	$C_{11}H_{17}{}^{81}Br$	1)	230.0485
		2)	230.0494

(a) A mixture of 7-syn- and 7-anti-bromide.

(b) The anti-bromide.

(c) Observed m/e.

(d) Calculated m/e.

The p.m.r. spectra of all the bromides showed trends which, with the help of the solvolytic and preparative data, allowed assignment of the C-7 stereochemistry.

P.m.r. Spectra of 7-bromo-7-R-norbornenes[a]

R		C-2,3	C-1,4	exo	endo	C-R	
CH_3	1[b]	6.02	2.78	1.80	1.00	1.70	
	2	5.95	2.73	2.30	1.40	1.78	
i-C_3H_7	1	6.08	2.85	1.83	1.0	0.98	J=7Hz
	2						
n-C_4H_9	1	6.06	2.83	--[c]	--[c]	--[c]	
	2						
t-C_4H_9	1	6.03	3.00	--	--	1.01	
	2	5.80	2.90	--	--	1.12	
t-C_4H_9-CH_2	1						
	2	5.95	2.80	--	--	0.95	
C_6H_6	1	6.38	3.67	1.76	1.08	7.44	
	2	5.85	3.32	--	--	7.2	

(a) Chemical shifts expressed as p.p.m. downfield from T.M.S.

(b) 1 refers to the syn-bromide, 2 to the anti-bromide.

(c) A dash indicates that severe overlap prevented the measurement of an accurate chemical shift.

In particular, C-2,3 vinyl triplets were at higher field for

the anti-bromide, as were the C-1,4 multiplets observed for the same isomer. In general, the larger the substituent R at C-7, the larger the difference in the C-1,4 resonance between syn and anti isomers.

A measurement of the n.O.e. of the t-butyl group on the C-2,3 vinyl signal provided further evidence for the C-7 stereochemistry of 7-t-butylnorbornen-anti-7-bromide. A value of 7% was recorded, consistent with a syn placement of the t-butyl group.

7-R-norbornenes

The synthetic method used here was described earlier (p. 80). The discussion is thus restricted to structural proof. As with the bromides, high resolution mass spectrometry was employed to find the molecular formula in each case, as summarised below.

High Resolution Mass Spectra of 7-R-Norbornenes

R[a]	Ion observed		m/e
C_6H_5	$C_{13}H_{14}$	1)[b]	170.1111
		2)[c]	170.1095
i-C_3H_7	$C_{10}H_{16}$	1)	136.1230
		2)	136.1251
n-C_4H_9	$C_{11}H_{18}$	1)	150.1418
		2)	150.1408
t-C_4H_9		known compound[110]	
t-C_4H_9-CH_2	$C_{12}H_{20}$	1)	164.1581
		2)	164.1564

(a) Mixtures of syn-, anti-7-R-norbornenes except for R = t-C_4H_9, where only the syn-isomer was present.

(b) Observed m/e.

(c) Calculated m/e.

Unambiguous assignment of structure was possible using 100 MHz p.m.r. spectra. The appropriate data is summarised in the table below.

P.m.r. Spectra of 7-R-Norbornenes[a]

R	C-2,3		C-1,4		R		C-7[c]	
	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
CH_3	5.77	5.94	2.46	2.36	0.83[b]	0.74[b]		
i-C_3H_7	5.80	6.00	2.66	2.55	0.79 (J=7)	0.75 (J=7)		
n-C_4H_9	5.78	6.00	2.56	2.45	1.14[b]	0.86[b]		
t-C_4H_9	5.72	--	2.70	--	0.77	--		
t-C_4H_9-CH_2	5.81	6.00	2.60	2.42	0.83[b]	0.87[b]		
C_6H_5	5.87	6.06	3.03	3.03	6.96	7.04	2.80	2.70

(a) Expressed as p.p.m. downfield shift from T.M.S. measured on a Varian HA100 Spectrometer. (1) ≡ syn-R. (2) ≡ anti-R.

(b) The syn:anti assignment of these peaks is based on analogy with R = i-C_3H_7.

(c) The C-7 H was assigned only for R = C_6H_5. In every other case, this peak was observed by endo and exo C-5,6 proton resonances.

The most important feature for structural assignment was the fine coupling observed in the C-2,3 vinyl signals when there was an anti-C-7 hydrogen. Franzus et al[99] observed

such coupling in the spectrum of norbornene (J = 0.5 Hz) and assigned it using selective deuteration. In every case in the present work, the upfield vinyl resonance was split with J = 0.5 Hz. This was shown, for R = C_6H_6, to be due to the 7-anti-proton. Saturation of the anti-C-7 proton resonance in the spectrum of 7-syn-phenylnorbornene by external irradiation completely removed the fine coupling visible in the C-2,3 resonance. Similar treatment of 7-anti-phenylnorbornene gave a C-2,3 triplet which was entirely superimposable upon the triplet present in the absence of the saturating field. The assignment of the C-7 stereochemistry of the 7-phenylnorbornenes is thus complete. The stereochemistry of the other 7-R-norbornenes follows on analogy with norbornenes[99] and 7-phenylnorbornene.

An alternative synthesis of 7-phenylnorbornene was found possible, using the method of Johnson, Blizzard and Carhart.[101] 7-Bromo-7-phenylnorbornene (syn-Br:anti-Br = 4:1) was treated with lithium aliminiumhydride in refluxing tetrahydrofuran and gave, in 98% yield, 7-phenylnorbornene (syn-C_6H_5: anti-C_6H_5 = 1:3.24). Catalytic hydrogenation (5% Pd on charcoal, methanol, atmospheric pressure, 3.5 hours) of 7-phenylnorboenene gave 7-phenylnorbornane which was identified by its p.m.r. spectrum. The C-2,3 vinyl signal disappeared and the high field multiplet increased in total integral. This contrasts with the results of Roberts[94] who submitted 7-methylnorbornene to identical catalytic hydrogenation and found no reduction occurred even after 15 hours. Adam's

catalyst (PtO_2) was required to hydrogenate this methyl compound. The present author treated 7-*syn*-bromo-7-*n*-butylnorbornene with lithium aluminium hydride but retrieved only unreacted starting material. Presumably the 7-phenylnorbornen-7-bromide was reduced via the readily-formed benzylic cation.

EXPERIMENTAL

General:

(a) Instruments Employed

(i) Infra-red spectra were measured on Perkin-Elmer 337 or 521 or Beckman I. R. 5 spectrometers.

(ii) Most proton-magnetic resonance (p.m.r.) spectra were measured on a Varian Associates T60 spectrometer. The use of a HA100 instrument is specified in the text. All p.m.r. data are expressed as parts-per-million downfield from tetramethylsilane (T.M.S.) as primary internal reference. In some cases, specifically mentioned in the text, secondary standards such as internal methylene chloride or chloroform were employed. Proton magnetic resonance data are expressed as: position, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), proton integration, coupling constant (J, Hz), and assignment.

(iii) Both preparative and analytical gas-liquid partition-chromatography (g.l.p.c.) was carried out on a Varian Aerograph A90-P3 instrument, fitted with a thermal conductivity detector. Helium (dry, Canadian Helium Limited) was the only carrier gas used. Quantitative product ratios from g.l.p.c. analyses were obtained by simple triangulation; in all cases base line drift was not tolerated.

(iv) A Thomas Hoover Capillary melting point apparatus was used for melting point determinations. Calibration to accurate standards (supplied by Arthur H. Thomas Co.) may be assumed throughout.

(v) The constant-temperature bath employed was of approximately 5ℓ capacity, filled with mineral oil. The temperature was controlled by a mercury contact thermostat attached to a "Fisher" transistor relay to ± 0.2°C. Heating was provided by a 100 watt immersion heater.

(vi) High resolution mass spectra were obtained on a Consolidated Electrodynamics Inc. Model 21-110b instrument. The author thanks Professor D. B. McLean and his group for running these spectra.

(vii) Elemental analyses were by Chemalytics Incorporated, Tempe, Arizona, U. S. A.

(viii) Photolyses were carried out in flat-faced quartz cells fitted with integral waterchambers, through which was passed water at 51 ± 0.1°C, from a Haake constant temperature bath. Radiation was supplied by a Bausch and Lomb high pressure mercury lamp and was passed through a monochromator to give a narrow beam at 310 nm.

Miscellaneous:

(i) Light petroleum (20-40°) was fractionated before use through a 30 cm Vigreux column, the 30-42° cut being collected.

(ii) Anhydrous potassium carbonate or anhydrous magnesium sulphate was used to dry all organic materials prepared.

(iii) Samples for nuclear Overhauser effect (n.O.e.) studies were prepared as follows. The compound, together with an excess of T.M.S. (for internal lock purposes) was dissolved in carbon tetrachloride and filtered through fine sintered glass directly into a carefully cleaned n.m.r. tube fitted with a ground glass adaptor suitable for attachment to a vacuum line. The sample was degassed down to less than 5 microns no fewer than five times before sealing.

5,5-Dimethoxy-1,2,3,4,-tetrachlorocyclopentadiene

Hexachlorocyclopentadiene (172.0 g, 0.60 mole), in methanol (500 ml), was stirred under a reflux condenser at room temperature and potassium hydroxide (84.0 g, 1.50 mole) in methanol (400 ml) was added dropwise over 2 hours, the temperature not rising above 50°. The yellow solution, containing solid potassium chloride was stirred for a further 12 hours before it was transferred to a separatory funnel. Most of the product settled to the bottom; the rest was extracted out with diethyl ether. The combined organic layers were water washed, dried and the light solvents were removed: distillation at low pressure yielded the title compound as a light yellow oil (114.9 g, 72.6%, b.p. 138-140°/38 mm, lit,[102] 108-110°/11 mm).

p.m.r.: δ 3.40, s, C-5 methoxy.

g.l.p.c.: Carbowax 20 m, 20%, on Chromosorb 60/80 mesh, 5' x 1/4", 157°, 52 ml.min^{-1}, 5.3 min.

7,7-Dimethoxy-1,2,3,4,-tetrachlorobicyclo[2.2.1]hept-2-ene

5,5-Dimethoxy-1,2,3,4,-tetrachlorocyclopentadiene was placed in a 30 cm x 4 cm pyrex tube fitted with a fine sintered glass gas bubbler and an outlet hole. The bottom half of the tube was heated to 180 - 190° and ethylene (Matheson, 99.5% purity) was passed through the solution until p.m.r. analysis revealed greater than 95% conversion to product (approximately 10 h, depending on flow rate). Vacuum distillation yielded the title compound as a near colourless oil,

b.p. 100-101/1.34 mm, lit,[103] 72-81°/0.10 mm.

p.m.r.: δ 3.60, s, 3, C-7 methoxy; δ 3.51, s, 3, C-7 methoxy; δ 2.30, m, 2, C-5,6 exo; δ 1.80, m, 2, C-5,6 endo.

g.l.p.c.: SE30 15% on Chromosorb 60/80, 5' x 1/4", 143°, 66 ml.min^{-1}, 20 min.

7,7-Dimethoxybicyclo[2.2.1]hept-2-ene

7,7-Dimethoxy-1,2,3,4,-tetrachlorobicyclo[2.2.1] hept-2-ene (32.0 g, 0.11 mole) and t-butanol (Fisher, 90 g, 1.22 mole) were dissolved in tetrahydrofuran (Fisher, 525 ml) in a 2ℓ, 3-necked flask fitted with an efficient condenser, a magnetic stirrer and a source of dry nitrogen. Sodium (Fisher, 60 g, 2.6 g atom), finely chopped into pieces less than 0.5 cc in volume, was added over 2 hours, external heating being controlled to maintain gentle reflux. After 8 hours, the dark mixture was cooled and decanted off the excess sodium, which congealed into a single lump. Methanol (100 ml) was added to decompose any sodium left in the solution. Careful extraction into petroleum ether, followed by water wash, concentration, drying and evaporation, gave an orange oil which, on vacuum distillation, yielded 7,7-dimethoxybicyclo[2.2.1] hept-2-ene as a colourless oil, 8.2 g, 49%, b.p. 68-70°/28mm, lit,[103] 70-78°/30 mm.

p.m.r.: δ 6.03, t, 2, C-2,3, vinyl; δ 3.11, s, 3, C-7 methoxy; δ 3.02, s, 3, C-7 methoxy; δ 2.67, m, 2, C-1,4 bridgehead; δ 1.77, m, 2, C-5,6 exo;

δ 0.80, m, 2, C-5,6 endo.

g.l.p.c.: SE30, 15% on Chromosorb 60/80, 5' x 1/4", 128°, 66 ml.min^{-1}, 6.1 min.

Bicyclo[2.2.1]hept-2-en-7-one[104]

5,5-Dimethoxybicyclo[2.2.1]hept-2-ene (6.0 g) was added to aqueous sulphuric acid (5%, 500 ml) and vigorously stirred for 2 h. at room temperature. Extraction into petroleum ether (30-42°), drying and removal of solvent gave a quantitative yield of bicyclo[2.2.1]hept-2-en -7-one, of sufficient purity for all purposes. Vacuum distillation yields a very light yellow oil, b.p. 64-8°/40-45 mm, lit[103] 66-70°/34 mm. On standing at 0°C, this coloration disappears.

p.m.r.: δ 6.46, t, 2, C-2,3 vinyl; δ 2.75, m, 2, C-1,4 bridgehead; δ 2.00, m, 2, C-5,6 exo; δ 1.08, m, 2, C-5,6 endo.

g.l.p.c.: Carbowax 20 M, 15%, on Chromosorb, 20/80 mesh 10' x 1/4", 143°, 80 ml.min^{-1}, 4.8 min.

Organolithium addition to bicyclo[2.2.1]hept-2-en-7-one

(a) General procedure

The following description is typical of all experiments. n-Butyllithium (1.6 M in n-hexane, 2.0 ml, 3.2 mmole) was dissolved in diethylether (sodium dried, 5.0 ml) at room temperature in a dry, pressure-equalizing dropping funnel topped by a plug of dried cotton wool. Below this, at -75°, bicyclo [2.2.1]hept-2-en-7-one (50 mg, 0.46 mmole) was dissolved in

n-hexane (5.0 ml) and stirred magnetically. The n-butyllithium solution was added dropwise to the ketone solution over 2 minutes and the resulting mixture was stirred for a further 15 minutes. The reaction was quenched by pouring onto water (room temperature, approximately 75 ml). The diethylether layer was separated, washed twice with water (2 x 75 ml) and dried before concentrating with a rotary evaporator. Product ratios were acceptable only if the last traces of diethylether ware not removed, as the products are quite volatile.

In a similar experiment employing methyllithium in diethylether (the addition products of which were the most volatile encountered) and bicyclo[2.2.1]hept-2-en-7-one (1.06 g, 9.82 mmole) in n-hexane, the yield of ether-free 7-methyl-bicyclo[2.2.1]hept-2-en-7-ols was 0.98 g (81%). An analogous experiment using t-butyllithium gave both addition and reduction of the ketone; on a 1.0 g scale, the yield of crude, based on addition, was 82%.

In all other cases, the yields were higher.

The results of these studies are tabulated on p. 41.

(b) Order of addition

In a series of experiments, ketone solutions were added to organolithium solutions. The following is typical. Bicyclo[2.2.1]hept-2-en-7-one (0.135 g, 1.25 mmole) in diethylether (sodium-dried, 6.0 ml) and t-butyllithium (2.2 M, in pentane, 2.0 ml, 4.4 mmole) were cooled separately in stoppered flasks to -74°. The ketone solution was quickly added

to the organolithium reagent and the mixture was stirred (at -74°) for 2 h. in anhydrous conditions. Work-up as before yielded 7-t-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene as a colourless oil (0.219 g).

(c) Temperature control

In all cases dry-ice-acetone baths were used. An alcohol thermometer immersed in the bath adjacent to the reaction vessel recorded the temperature. All solutions were immersed in the bath for at least 10 min to ensure equilibration.

(d) Standardisation of organolithium reagents

Vinyllithium, methyllithium, t-butyllithium and phenyllithium were supplied by Alpha Inorganics Inc. n-Butyllithium was a product of Foote Mineral Co. Limited.

The concentration of the reagents was regularly checked by titration against hydrochloric acid (aqueous, 2.44 M) using phenolphthalein as indicator. This analysis relies on the insolubility of lithium hydroxide in the solvents present. When the measured concentration was less than 50% of the rated strength, the reagent was not used.

(e) Solvent studies

The solvents of both ketone and organolithium reagent were varied from diethyl ether to saturated hydrocarbon. Thus, for example, methyllithium, which is commercially available in diethyl ether solution, was added to the ketone, itself dissolved in diethyl ether or n-hexane. A similar pair of results was obtained by adding a large excess of n-hexane to the sample

of methyllithium in diethyl ether; this was also reacted with the ketone in the two solvents. Phenyllithium is supplied commercially in benzene-diethyl ether (70:30). The reagent is insoluble in n-hexane and was used undiluted (in benzene-diethyl ether 70:30) and also with excess diethyl ether. t-Butyllithium was used in n-pentane and in n-pentane-ether solutions. n-Butyllithium was used in hexane and in ether-hexane solutions.

Syn-7-acetoxy-7-phenylbicyclo[2.2.1]hept-2-ene

To a mixture of syn-7-hydroxy-7-phenylbicyclo[2.2.1] hept-2-ene (48.2 mg, 0.26 mmole) pyridine (A.R., 0.13 ml, 1.6 mmole) and tetrahydrofuran (10.0 ml), acetyl chloride (0.10 ml, 2.0 mmole) was added dropwise. After refluxing for 3 h. in anhydrous conditions, the mixture was repeatedly extracted with water in the presence of diethyl ether; the ether layer was dried, and the solvent was removed to give a white crystalline solid (44 mg). P.m.r. analysis indicated partial conversion to the required acetate.

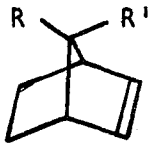
Anti-7-acetoxy-7-phenylbicyclo[2.2.1]hept-2-ene

To a mixture of anti-7-hydroxy-7-phenylbicyclo[2.2.1] hept-2-ene (0.115 g, 0.618 mmole) and pyridine (A.R., 0.25 ml, 3.1 mmole) in diethyl ether (sodium dried, 5 ml) was added to acetyl chloride (0.151 ml, 3.0 mmole). After stirring at room temperature for 18 h., the pyridinium hydrochloride was filtered off and washed with diethyl ether. The combined ethereal solution was water washed, dried, and the solvent was

removed to yield a light yellow oil (0.096 g). P.m.r. analysis revealed that the reaction had proceeded to 62% of completion, sufficient for the required spectral comparison with the corresponding alcohol.

7-(3',3'-Dimethylbutyl)-7-hydroxybicyclo[2.2.1]hept-2-ene

Samples of bicyclo[2.2.1]hept-2-en-7-one (50 mg, 0.46 mmole) were dissolved in diethyl ether (sodium dried, 5.0 m) in small round-bottomed flasks fitted with pressure-compensating dropping funnels topped by plugs of heat-dried cottom wool. Varying quantities of t-butyllithium (in pentane, 2.34 M) were syringed onto 5 ml aliquots of diethylether placed in the dropping funnels. After approximately one minute, when the solutions appeared homogeneous, the alkyllithium reagent was added to the lower, ketone solutions, the latter being cooled to -78° with an acetone-dryice bath, and the mixtures were stirred for 15 min. After normal work-up g.l.p.c. analysis (Carbowax 20 M, 20%, on Chromosorb W, 20/60, 10' x 1/4", 143°, 80 ml.min^{-1}) showed the following.



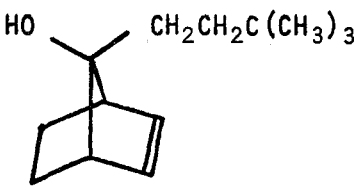
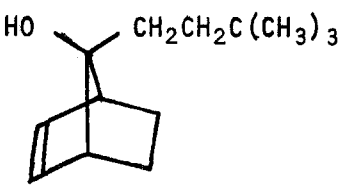
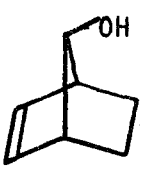
		Number of mole equivalents of t-BuLi			
R	R'	1.0	4.0	8.0	10
OH	$(CH_3)_3CCH_2CH_2$	--(a)	trace(a)	15.4(a)	13.7(a)
$(CH_3)_3CCH_2CH_2$	OH	--	trace	23.6	61.7
OH	$(CH_3)_3C$	--	--	24.2	1.8
$(CH_3)_3C$	OH	--	--	8.5	0.6
OH	H	--	trace	trace	1.2
H	OH	--	--	trace	0.7
C-7-ketone		100	100	28.3	19.6

(a) % of total trace area.

The reaction of t-butyllithium with bicyclo[2.2.1]hept-2-en-7-one in the presence of ethylene

t-Butyllithium (in pentane, 2.43 M, 4.0 ml, 9.7 mmole) was places in a small pressure-compensating dropping funnel fitted with a cottom wool plug. Dry ethylene was bubbled through through the solution for 15 min. at room temperature. The mixture was then allowed to pass through the funnel into a flask cooled to -77°, containing a stirred mixture of bicyclo[2.2.1]hept-2-en-7-one (100 mg, 0.93 mmole) and n-hexane (20.0 ml), where it stayed for 30 min. Normal work-up gave syn- and anti-7-t-butyl-7-hydroxybicyclo [2.2.1]hept-2-ene (syn-ol:anti-ol 1:2.3, 89%). Minor products were also observed by g.l.p.c. (Carbowax 20M, 20%, on Chromosorb W, 20/60, 10' x 1/4", 143°, 80 ml.min^{-1}).

Minor Products

Compound	Percentage	Retention time (in)
	2	21
	1	15
Unknown	5	29.5
Unknown	2	31.5
	1	10.5

The reaction of phenyl Grignard reagent with bicyclo[2.2.1]hept-2-en-7-one

Dry bromobenzene (7.60 g, 46.0 mmole) was added through a serum cap to a stirred mixture of heat-dried, Grignard-grade magnesium turnings (Shawinigan, 2.0 g, 0.082 g-atom) in sodium-dried diethyl ether (25 ml) under a N_2 atmosphere. The reaction was initiated with gentle heating, and after 1 h. reflux the solution was brown in colour. Bicyclo[2.2.1]hept-2-en-7-one (0.50 g, 4.6 mmole) was added dropwise and the mixture was held at reflux temperature for 1 h. before pouring onto saturated awueous NH_4Cl solution. This hydrolysis was highly exothermic, indicating the presence of excess Grignard reagent. Drying the ether layer and removal of solvent left a yellow oil (1.0 g.). This was shown to contain anti-7-hydroxy-7-phenylbicyclo[2.2.1]hept-2-ene (44 parts) and 7-phenyl-syn-7-hydroxybicyclo[2.2.1]hept-2-ene (16 parts) (70% yield) by spectral and g.l.p.c. comparison with authentic samples. The third product, biphenyl, was identified from its p.m.r. spectrum and m.p. (70-71°, lit[104] 70°).

7-Hydroxy-7-vinylbicyclo[2.2.1]hept-2-ene

Bicyclo[2.2.1]hept-2-en-7-one (0.25 g, 2.3 mmole) was dissolved in diethyl ether (sodium dried, 25 ml) and cooled to -78°. Vinyllithium (2.0 M in tetrahydrofuran, 7.7 ml, 23 mmole) was added dropwise over 2 min. and the mixture was stirred for 1 h. before working-up as usual. The product was a yellow oil (1.41 g) which contained tetrahydrofuran, syn-7-hydroxy-

7-vinylbicyclo[2.2.1]hept-2-ene (2.55 parts) and anti-7-hydroxy-7-vinylbicyclo[2.2.1]hept-2-ene (1 part, m.p., 56-56.5°, lit[97] 58.2-59.8°).

g.l.p.c.: Carbowax 20 M, 15% on Chromosorb W, 60/80 mesh, 10' x 1/4", 150°, 37 ml.min^{-1}, syn-ol 16.2 min., anti-ol 18.0 min.

Neopentyllithium[105]

Neopentylchloride (3.0 g, 0.028 mol, dried over K_2CO_3) in petroleum ether (b.p. 30-42°, dried over K_2CO_3, 20 ml) was added dropwise to lithium (Alpha Inorganics, "Ventrol", freshly cut ribbon, 0.42 g, 0.06 g. aton) into 35 ml stirred, refluxing, dry petroleum ether. After refluxing for 12 h., the purple solution was cooled and the supernatant liquid was titrated against 2.42 M HCl, and was found to be 0.39 M base (49% yield).

7-(2',2'-Dimethylpropyl)-7-hydroxybicyclo[2.2.1]hept-2-ene

Bicyclo[2.2.1]hept-2-en-7-one (0.50 g, 0.46 mmole) in diethyl ether (sodium dried, 20 ml) was cooled to -78° and stirred. Neopentyllithium (in petroleum ether as above, 0.39 M, 50 ml, 1.9 mmole) was added over 30 sec. through a dry filter pad of glass wool under suction. The purple mixture was stirred for 1 h. before normal work-up, which yielded a colourless oil (1.20 g). This contained more than 0.40 g of unreacted neopentylchloride and the residue was 7-(2',2'-dimethylpropyl)-7-hydroxybicyclo[2.2.1]hept-2-ene (syn-ol: anti-ol = 1:1.57).

g.l.p.c.: (a) SE30 15% on Chromosorb W, 60/80 mesh, 5' x 1/4", 150°, 50 ml.min^{-1}, 10.0 min (both isomers).

(b) Carbowax 20M, 20% on Chromosorb W, 60-80 mesh, 5' x 1/4", 180°, 120 $ml.min^{-1}$, 120 min, with isomers 2 minutes apart.

Benzhydryllithium [106]

Benzhydrylchloride (10.0 g, 0.0625 mole), lithium pieces (1 cm^3, 0.88 g, 0.13 mole) and tetrahydrofuran (freshly distilled from lithium aluminium hydride, 30 ml) were stirred in anhydrous conditions at room temperature. After 42 h., a deep wine-red coloration was evident. The mixture was stirred for a further 18 h. before titration against 2.42 M HCl, which showed the base strength to be 1.06 M. The yield of benzhydryllithium was thus 51%.

Syn-7-(diphenylmethyl)-7-hydroxy bicyclo[2.2.1]hept-2-ene

Bicyclo[2.2.1]hept-2-en-7-one (1.0 g, 9.3 mmole) in diethylether (sodium dried, 5.0 ml) was added dropwise to a stirred solution of benzhydryllithium (1.06 M) in tetrahydrofuran (15 ml, 15 mmole) and diethylether (10 ml) at a temperature less than 10°. After 5 min. the deep red coloration was replaced by a dull salmon-pink. The mixture was stirred for 90 min. before pouring onto a mixture of water and petroleum ether (30-42°). Repeated water extraction, drying and removal of solvent under vacuum yielded 2.77 g of white crystals. Recrystallization from methanol gave a white crystalline solid (0.5 g), shown by p.m.r. to be syn-tetraphenylethane, m.p. 195-197°, lit[104] 212.5° (δ 7.0, s, 20; δ 4.65, s, 2). The

filtrate was retained and the solvent removed to yield essentially pure syn-7-(diphenylmethyl)-7-hydroxybicyclo[2.2.1]hept-2-ene in quantitative yield, which was sublimed (120°, 20 μ) to give waxy, white crystals, m.p. 63-65°.

Effect of sodium ethoxide

n-Butyllithium (1.78 M in hexane, 5.2 ml, 9.3 mmole) was added to ethanol (absolute, 0.43 g, 9.3 mmole) in diethyl-ether (10 ml) at -78°. The mixture was stirred for 5 min. before bicyclo[2.2.1]hept-2-en-7-one (100 mg, 0.93 mmole) was added followed, after 5 min., by n-butyllithium (5.2 ml, 9.3 mmole). After 15 min. of stirring at -78°, the mixture was worked-up as usual, resulting in a colourless oil (0.090 g, 63%). Analysis by g.l.p.c. showed this to consist of starting ketone (7%) and 7-n-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene in the ratio 1:3 (anti-ol:syn-ol).

Effect of boron trifluoride

To bicyclo[2.2.1]hept-2-en-7-one (50 mg, 0.46 mmole) in dry diethyl ether (10 ml) was added freshly distilled boron trifluoride etherate (144 mg, 1.01 mmole) and the solution was stirred for 5 min. at 22° before it was cooled to -70°. Methyllithium (1.83 M in ether, 2.6 ml, 4.6 mmole) was added during 3 min. Normal work-up gave a colourless oil (60 mg) which crystallised on standing. Analysis by g.l.p.c. showed that the ratio, anti-ol:syn-ol, of 7-hydroxy-7-methylbicyclo [2.2.1]hept-2-ene was 1.9.

Protonation of 7-t-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene

SO_2ClF (0.1 ml) was condensed into an n.m.r. tube precooled to -120° (approximately). Freshly distilled FSO_3H (0.2 ml) was slowly and carefully pipetted into the bottom of the tube and the substances were intimately mixed. 7-Hydroxy-7-butylbicyclo[2.2.1]hept-2-ene (syn-ol:anti-ol = 1:2.4; 30 mg), dissolved in a trace of CH_2Cl_2, was added dropwise with mixing. The clear orange solution was placed in a precooled n.m.r. probe (Varian A60) and the spectrum was recorded, using methylene chloride as internal reference (δ = 5.30).

Results (1) -100°: Viscosity broadening reduced resolution; δ 7.33, 2 protons, C-2,3 vinyl; δ 4.20, 2 protons, C-1,4 bridgehead; δ 2.7-1.7, 9 protons; δ 1.17, 10 protons, C-8, t-butyl.

A high integral for the high field region indicated some polymerization.

(2) -60°: Considerably better resolution was possible at this temperature;

(a) δ 7.25 (t), 4.16 (m), 1.16 (s); and,

(b) δ 7.66 (d), 3.50 (m), 1.53 (s), 1.45 (s).

After 30 min. at -60°, the ratio a:b = 1.0. After 60 min. the ratio was 0.4 and after 90 min. it was less than 0.05. With time, the high field methylene envelope increased relative to other signals in the spectrum.

7-Methyl-7-(2'-propenyl)bicyclo[2.2.1]hept-2-ene

7-t-Butyl-7-hydroxybicyclo[2.2.1]hept-2-ene (syn-ol:

anti-ol = 1:1.8, 0.470 g, 3.01 mmole) in carbon tetrachloride (2 ml) was added to a stirred mixture of $SOBr_2$ (0.5 ml, 1.35 g, 6.50 mmole) in carbon tetrachloride (15 ml). After refluxing in the dark in anhydrous conditions for 2.5 h., the mixture was poured onto 150 ml water. The organic layer was water-washed, dried and the solvent was removed to give a yellow oil (0.357 g, 84%) containing only syn-7-methyl-7-(2'-propenyl)bicyclo [2.2.1]hept-2-ene (79%), and the anti-methyl isomer (5%).

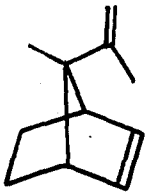
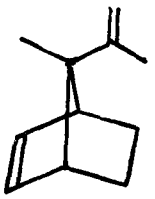
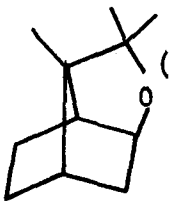
g.l.p.c.: Carbowax 20 M, 15% on Chromosorb W, 60-80 mesh, 10' x 1/4", 118°, 52 $ml.min^{-1}$, syn-methyl: 8.0 min, anti-methyl: 6.5 min.

The reaction of 7-t-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene with acetic acid containing 2% sulphuric acid

(a) 7-t-Butyl-anti-7-hydroxybicyclo[2.2.1]hept-2-ene (117.8 mg, 0.795 mmole) was dissolved in glacial acetic acid containing exactly 2% by volume concentrated (95.5% minimum) sulphuric acid (50 ml total) at 22.5°. An orange coloration was apparent after 1 min. After stirring for 6 h. the mixture was poured onto 75 ml of water. This was extracted with petroleum ether (b.p. 30-42°, 20 ml). The aqueous layer was just neutralised with aqueous $NaHCO_3$ solution and reextracted with petroleum ether. The combined organic layers were washed with $NaHCO_3$ solution and water, dried and concentrated to give a sweet-smelling yellow oil (92.7 mg) which contained a trace of petroleum ether in addition to products of the reaction.

(b) An exactly similar reaction using 7-t-butyl-syn-

7-hydroxy bicyclo[2.2.1]hept-2-ene (58.6 mg) gave the same yellow oil (52.1 mg). Analysis by g.l.p.c. (Carbowax 20M, 15% on Chromosorb W, 60-80 mesh, 10' x 1/4", 118°, 52 $ml.min^{-1}$) showed the composition to be that given in the following table.

Compound	Percentage[a]	Relative Retention Time
Unknown	7	0.25
 (b)	31	0.31
 (b)	28	0.38
Unknown	27	0.51
 (c)	33	1.0

(a) The same precentages were obtained from both <u>syn</u>- and <u>anti</u>-ol.

(b) analysis $C_{11}H_{16}$ requires C: 89.19%; H: 10.81%.

found (a) <u>syn</u>-methyl C: 89.31%; H: 10.93%

(b) <u>anti</u>-methyl C: 88.74%; H: 10.80%.

(c) g.l.p.c.: 21.1 mm retention time.

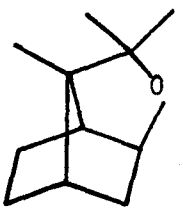
p.m.r.: (HA100 spectrometer), δ 3.86, t, 1, C-3; δ 1.14; δ 1.04; δ 0.96, s, C-8,9,9.

analysis $C_{11}H_{18}O$ requires C: 79.53%; H: 10.85%

found C: 79.87%; H: 10.04%

The reaction of 7-t-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene with acetic acid containing 10% sulphuric acid

7-t-Butyl-7-hydroxybicyclo[2.2.1]hept-2-ene (syn-ol: anti-ol = 1:1, 0.660 g, 1.08 mmole) was dissolved in glacial acetic acid containing 10% by volume of sulphuric acid (95.5% minimum) (total 10 ml). The mixture, which went black in 5 min., was left in dry conditions for 3 h. at 22.5°. After extraction with petroleum ether, the solution was neutralized with Na_2CO_3, washed with water, dried and concentrated to give an oil (77 mg) with the following composition.

Compound	Percentage	Relative Retention Time[a]
Unknown	15.2	0.39
Dienes[b]	9.8	0.52
Unknown	11.0	0.63
	73.5	1.00

(a) The column employed was SE30, 20%, on Chromosorb W, 60/80 mesh, 5' x 1/4", 125°, 42 ml.min^{-1}.

(b) Injection on a Carbowax column revealed a roughly 1:1 mixture of the two dienes (7-methyl-7-(2'-propenyl)bicyclo[2.2.1]hept-2-ene).

The reaction of 7-t-butyl-7-hydroxybicyclo[2.2.1]hept-2-ene with acetic acid alone

(a) Room Temperature:

The alcohol (syn-ol:anti-ol = 1:1, 200 mg) was treated with glacial acetic acid (10 ml) for 20 h. at room temperature. After 1 h. and at the end of 20 h., no reaction (p.m.r.) had occurred.

(b) 83°:

(i) 7-t-Butyl-syn-7-hydroxy bicyclo[2.2.1]hept-2-ene (11.5 mg) and glacial acetic acid (0.50 ml) were sealed in an evacuated tube which was immersed in a bath set at 83.0° for 3 h. The material was then poured onto water, extracted twice with petroleum ether (b.p. 30-42°), washed with aqueous Na_2CO_3, dried and concentrated to reveal a colourless oil (11.2 mg) which by g.l.p.c. contained only starting material.

(ii) 7-t-Butyl-anti-7-hydroxy bicyclo[2.2.1]hept-2-ene (7.2 mg) and glacial acetic acid (0.50 ml) were heated as above to 83° for 3 h. Work-up gave a colourless oil (7.4 mg), which by g.l.p.c. (Carbowax, 120°) contained starting material (83%) and 7-methyl-anti-7(2'-propenyl)bicyclo[2.2.1]hept-2-ene (17%).

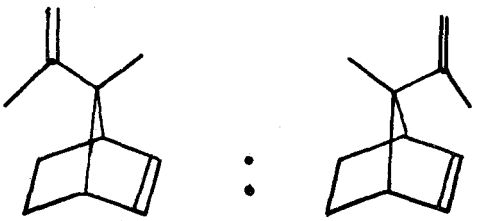
(c) 140°:

The alcohol (syn-ol:anti-ol = 1:1, 200 mg) was added to 10 ml glacial acetic acid in a thick-walled tube. After sealing under vacuum, the solution was heated for 2 h. at 140 ± 5°. Clean conversion to 7-methyl-7(2'-propenyl)bicyclo [2.2.1]hept-2-ene occurred (syn-methyl:anti-methyl = 3.6:1).

(d) 108° Equilibration Studies:

The same procedure was employed as at 140°.

Time	2 h.	4 days	13 days
syn-ol	N. R.	92:8[b]	83:17[a]
anti-ol	97:3		86:14

(a) Ratio is 

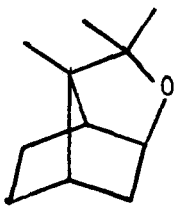
(b) Material analysed contained 80% unchanged starting material.

The reaction of 7-i-propyl-7-hydroxy bicyclo[2.2.1]hept-2-ene with acid

(a) The title alcohol (syn-ol:anti-ol = 1:1.1, 0.34 g) was added to a mixture of glacial acetic acid (50 ml) and 95.5% sulphuric acid (1.0 ml) and the brown solution was stirred for 4 h. Work-up gave an orange oil (0.20 g) which g.l.p.c. analysis (Carbowax 20 M, 10' x 1/4", 120°, 47 m/min^{-1}) revealed to contain:

(i) An unknown, 18%, retention time 5.4 min.

(ii) Ether of structure below, 45.7%, 13.7 min.



			m/e
mass spectrum:	$C_{10}H_{16}O$.	M^+	152
		$M^+-CH_3^\circ$	137
		$M^+-C_3H_7^\circ$	109

p.m.r.: δ 1.10, s, 3, C-8 methyl; δ 1.16, s, 3, C-8 methyl; δ 0.8-2.0, 6, methylene; δ 2.20, m, 1, C-1 or 4 bridgehead; δ 2.40, m, 1, C-1 or 4 bridgehead; δ 3.90, t, 1, proton adjacent to oxygen.

i.r.: 990 cm^{-1}, of oxetane 990 cm^{-1}.

(iii) Syn-7-hydroxy-7-i-propylbicyclo[2.2.1]hept-2-ene, 36.3%, 18.2 mm retention time.

(b) The title alcohol (syn-ol:anti-ol = 1:1.1, 400 mg) and glacial acetic acid (2.0 ml) were sealed under vacuum in a glass tube and heated for 2 h. at 151°. Work-up revealed unreacted syn-ol and 7-(2'-propylidene)bicyclo[2.2.1]hept-2-ene in equal quantities.

Diene: p.m.r.: δ 1.50, s, 6, CH_3; δ 6.10, 5, 2, C-2,3 vinyl; δ 3.20, pentuplet, 2, C-1,4 bridgehead; δ 0.95, m, 2, endo-C-5,6; δ 1.60, m, 2, exo-C-5,6.

Thionyl bromide

HBr gas was passed through $SOCl_2$ to produce $SOBr_2$ as a light yellow liquid (b.p. 49°/23 mm, lit[107] 48°/20 mm). This kept well in anhydrous conditions at 0° for up to 3 months, after which time redistillation was necessary.

Tri-n-butyl stannane

Treatment of tri-n-butyltin chloride (Aldrich) with $LiAlH_4$ by Kuivila's procedure[108] gave the hydride as a clear colourless liquid in 53% yield (b.p. 131-2°/7 mm).

Tri-n-butyl stannane keeps well in anhydrous cool conditions, but over a period of 6 months, a white precipitate accumulated. This could be removed by fractional vacuum distillation. The precipitate did not accumulate if the stannane was kept under N_2.

7,7-Dibromobicyclo[4.1.0]hept-2-ene[109]

Cyclohexa-1,3-diene (Aldrich, p.m.r., pure, fresh, 12.5 g, 0.156 mole) was mixed with bromoform (Matheson, Coleman and Bell, 39.7 g, 0.155 mole) and t-butanol (25 ml). The mixture was stirred in anhydrous conditions and cooled to 0-3° before a ketone solution of potassium t-butoxide in t-butanol (1 M, 250 ml) was added over 9 h. After 200 ml of base had been added, freezing occurred. The temperature was raised to 14° to melt the solid and addition continued. An equal volume of water, saturated with NaCl, was added and the upper layer was collected. The aqueous layer was several times extracted with petroleum ether and the combined organic layers were extracted twice

with 150 ml portions of saturated aqueous NaCl solutions before drying and removal of solvent. A light yellow oil (28.2 g, 72%), contained (p.m.r.) greater than 90% of the title compound. Vacuum distillation gave 7,7-dibromobicyclo[4.1.0] hept-2-ene in 46% yield (b.p. 75°/1.65 mm).

p.m.r.: (a) cyclohexa-1,3-diene: δ 2.1, sharp multiplet, 4; δ 5.68, sharp multiplet, 4.

(b) 7,7-dibromobicyclo[4.1.0]hept-2-ene: δ 1.97, sharp multiplet, 6; δ 5.82, sharp multiplet, 2.

Syn-7-bromo-7-methylbicyclo[2.2.1]hept-2-ene[98]

7,7-Dibromobicyclo[4.1.0]hept-2-ene (1.63 g, 0.65 mmole) was dissolved in sodium-dried diethyl ether (5.0 ml) and cooled to -78°. Methyllithium (2.07 M, in diethyl ether, 3.4 ml, 1.08 mmole) was added over 2 min. and the mixture was stirred for 1 h. The solution was added to excess water and the organic materials were extracted with petroleum ether, washed with water, dried and concentrated to give an oil (0.94 g).

Analysis by p.m.r. showed 50% reaction with the bromides appearing in the ratio reported by Skattebøl[98] (syn-Br: anti-Br = 72:23). Repetition of the above, using 2.0 g of norcarene and the same amount of methyllithium gave 1.26 g of product.

The above products were combined, dissolved in diethyl-ether (10 ml) and methyllithium (as above, 5.0 ml) was added at -70°. After stirring for an hour, normal work-up gave a

light yellow oil (1.75 g, 65%) which by p.m.r. was nearly pure syn-7-bromo-7-methylbicyclo[2.2.1]hept-2-ene.

G.l.p.c. (SE30, 20% on 60/80 Chromosorb W, 5' x 1/4", 148°, 3 ml.min^{-1}, 8.4 min.) gave pure syn bromide (m.p. 46-48°, lit[98] 49-50°)

Anti-7-bromo-7-methylbicyclo[2.2.1]hept-2-ene

Anti-7-bromo-7-methylbicyclo[2.2.1]hept-2-ene was prepared by the method of Warkentin[18] in 87% yield. The crude material was greater than 95% pure after rather prolonged removal of solvent in the final step; this removal of the trace of syn-ol, the more volatile isomer.

The above alcohol (0.495 g, 3.99 mmole), triethylamine (Eastern, fresh, colourless, 555 µl, 4.5 mmole) and carbon tetrachloride (30 ml) were stirred at room temperature in anhydrous conditions. Thionyl bromide (333 µl, 4.3 mmole) was added all at once and the mixture was stirred for 30 min. The mixture was poured onto a large excess of water, washed, dried, and concentrated to yield a light orange oil (0.664 g, 84.5%) which was pure anti-7-bromo-7-methylbicyclo[2.2.1]hept-2-ene by p.m.r., isomeric with the known syn-bromide.[98] The orange coloration was removed by column chromatography (Fisher Neutral Alumina, 19 ml, petroleum ether eluent).

g.l.p.c.: Carbowax 20 M, 15% on Chromosorb W, 60/80, 5' x 1/4", 145°C, 30 ml. min.$^{-1}$, 2.8 min.

7-Bromo-7-phenylbicyclo[2.2.1]hept-2-ene

7,7-Dibromobicyclo[4.1.0]hept-2-ene (2.00 g, 7.95 mmole) was dissolved in diethyl ether (sodium-dried, 10.0 ml) and cooled to -78°. Over 3 min., phenyllithium (in benzene 3: diethyl ether 1, 2.3 M, 7.0 ml, 16 mmole) was added and the mixture was stirred for 90 min. Work-up as before gave a yellow oil (2.60 g) containing (by p.m.r.), (a) syn-7-bromo-7-phenylbicyclo[2.2.1]hept-2-ene (70%) and (b) biphenyl (30%). Purification was possible by recrystallization from petroleum ether, giving white needles of syn-bromide (m.p. 64-7°).

Sublimation of the crude allowed separation of the bromide also, but considerable isomerization occurred giving a pure mixture of the two 7-bromides. Increase in the temperature of sublimation caused more of the syn-bromide to isomerise to the anti-bromide.

Syn-7-bromo-7-n-butylbicyclo[2.2.1]hept-2-ene

7,7-Dibromobicyclo[4.1.0]hept-2-ene (2.00 g, 7.95 mmole) in diethyl ether (sodium-dried, 10.0 ml)was cooled to -78° in anhydrous conditions and n-butyllithium in hexane (1.78 M, 9.0 ml, 16 mmole) was added over 5 min. After stirring for 90 min., the mixture was poured onto water and normal work-up gave a light yellow oil (1.24 g) which, by p.m.r., contained the title compound and its anti-bromo isomer (ratio 2:1, respectively) (80%), unchanged starting material (20%) and traces of unidentifiable products.

On most columns, g.l.p.c. analysis gave unidentifiable products. However, on a SE30 column (20%, on Chromosorb W, 60/80 mesh, 5' x 1/4", 166°, 50 ml.min^{-1}, 5.3 min.) the syn-bromide was pure. The anti-bromide could not be obtained isomerically pure.

Syn-7-bromo-7-i-propylbicyclo[2.2.1]hept-2-ene

(a) 2-Bromopropane (2.7 g, 22 mmole) and 7,7-dibromobicyclo[3.1.0]hept-2-ene (2.0 g, 7.0 mmole) were dissolved in diethyl ether (sodium-dried, 10 ml) and added over 10 min. to finely chopped lithium pieces (1.0 g) stirred in diethyl ether (sodium-dried, 25 ml, cooled to -25°). A green coloration developed after 10 minutes. After 2 h. at -30°, the mixture was poured onto water (75 ml) saturated with sodium chloride. The aqueous layer was reextracted four times with petroleum ether and combined organic material was water washed, dried and the solvent was removed under vacuum to yield a yellow oil (1.25 g) which by p.m.r. contained the title compound (syn-Br:anti-Br = 60:40).

The only successful separation procedure found was g.l.p.c. which allowed the syn-bromide to be isolated (m.p. 70-73°).

g.l.p.c.: SE30, 15% on Chromosorb, 60/80, 5' x 1/4", 145°, 118 ml.min^{-1}, 6.0 min.

(b) 7,7-Dibromobicyclo[2.2.1]hept-2-ene (1.0 g, 3.9 mmole) was dissolved in diethyl ether (sodium-dried, 10 ml) and cooled to -78°. Isopropyllithium (1,85 M in pentane, 15.6 mmole,

8.45 ml) was added over 2.5 min. and the mixture was stirred for 90 min., before pouring onto water and working-up as before. The required bromides (syn-Br:anti-Br = 63:27) were obtained as a light yellow oil (0.692 g, 81%). G.l.p.c. as before yielded syn-7-bromo-7-isopropylbicyclo[2.2.1]hept-2-ene. A second peak of longer retention time was shown by p.m.r. to contain a mixture of unknown compounds, and was not analysed further.

Anti-7-bromo-7-t-butylbicyclo[2.2.1]hept-2-ene

(a) Finely chopped lithium (1.5 g) in diethyl ether (sodium-dried, 25 ml) was stirred at -20° and a mixture of t-butyl-bromide (1.10 g, 8.05 mmole) and dibromobicyclo[4.1.0]hept-2-ene (2.0 g, 7.9 mmole) in diethyl ether (sodium-dried, 10 ml) was added dropwise over 15 minutes. After stirring for 13 h., the temperature being allowed to slowly rise to 22°, the mixture was poured onto water and worked-up as before to yield 0.80 g of yellow oil. Analysis by p.m.r. showed the product to be a complex mixture, with dominant norbornen-like features (δ 6.18, t, 2; δ 3.10, m, 2), but with no sign of a retained t-butyl group.

(b) The reaction was repeated using three times the amount of t-butylbromide and a reaction time of 2 h. at -20°. At one stage the temperature inadvertently rose to near room temperature; an immediate temperature increase refluxed the ether vigorously. The reaction subsided on rapid recooling. The dark solution, worked-up as before, gave a pungent oil (1.10 g) containing the required bromides in the ratio syn-Br:anti-Br = 50:40

by p.m.r. However, chromatography (both column and g.l.p.c.) gave no recognisable product.

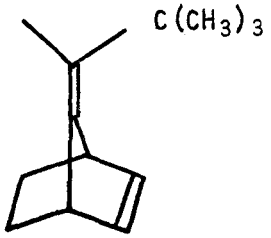
(c) 7,7-Dibromobicyclo[2.2.1]hept-2-ene (1.0 g, 3.0 mmole) in dry petroleum ether (b.p. 30-42°) was cooled to -78° and with stirring, t-butyllithium (2.34 M, in n-pentane, 6.7 ml, 15.6 mmole) was added dropwise over 1.5 min. After stirring for 90 min., the mixture was poured onto water and worked-up as before to yield a yellow oil (0.684 g.). Column chromatography proved unsuccessful in separating the components of the complex mixture resulting. G.l.p.c. (SE30, 15% on Chromosorb W, 5' x 1/4", 85 ml.min^{-1}, 162°) showed many components; a peak collected at retention time 8.8 min. (< 20% of the total product) showed the characteristic p.m.r. spectrum of 7-t-butylbicyclo[2.2.1]hept-2-ene-syn-7-bromide. This yield was judged of insufficient magnitude to warrant pursuing this synthesis further. Injection of quantities greater than 20 µl of 50% solution reduced the resolution to an unacceptable level.

(d) 7-t-Butyl-7-hydroxybicyclo[2.2.1]hept-2-ene (syn-OH: anti-OH = 1:6, 58.0 mg, 0.372 mmole) was dissolved in CCl_4 (6.0 ml) and thionyl bromide (286 µl, 3.72 mmole) was added. The mixture was stirred at room temperature for 2.5 h. under a reflux condensor through which ice-water was passed. Dry nitrogen was bubbled through the solution to flush out HBr throughout the reaction time. The resulting yellow solution was poured onto aqueous K_2CO_3, dried, and the solvent was removed to yield anti-7-bromo-7-t-butylbicyclo[2.2.1]hept-2-ene (70.1 mg) which, by p.m.r. was at least 95% pure.

Anti-7-bromo-7-neopentylbicyclo[2.2.1]hept-2-ene

(a) 7-Hydroxy-7-neopentylbicyclo[2.2.1]hept-2-ene (syn-ol: anti-ol = 1:1.57) (0.380 g, 2.11 mmole), thionyl bromide (freshly distilled, 176 µl, 2.28 mmole) triethylamine (294 µl, 2.38 mmole) and carbon tetrachloride (25 ml) were stirred at room temperature for 15 minutes. Normal work-up gave an oil (0.390 g, 76%) which p.m.r. analysis showed to be pure title compound. The compound was solvolytically sufficiently active to hydrolyse on a column of Fisher Neutral Alumina.

G.l.p.c. purification yielded a diene probably of the structure below, produced by dehydrobromination of the bromide.



Elemental analysis $C_{13}H_{20}$ requires 88.90% C; 11.10% H.

found 88.33% C; 10.78% H.

The reaction of lithium with bicyclo[2.2.1]hept-2-en-7-one

t-Butylbromide (4.1 g, 30.0 mmole), bicyclo[2.2.1]hept-2-7-one (1.0 g, 9.3 mmole) and sodium dried diethyl ether (10 ml) were added over 20 min. to a stirred mixture of lithium (finely cut, 0.5 g, 71 mmole) and sodium dried diethyl ether (25 ml), the latter being kept at less than -70°. The solution was allowed to warm to room temperature; after 3 h. a green colour was evident; just before work-up (24 h.) the colour was orange. Normal work-up gave yellow oil (0.46 g) containing less than 10% of addition product. Analysis by g.l.p.c. showed that

the only products were anti-7-hydroxybicyclo[2.2.1]hept-2-ene (81%) and syn-7-hydroxybicyclo[2.2.1]hept-2-ene (19%).

g.l.p.c.: Carbowax 20 M, 15% on Chromosorb, 60-80 mesh, 10' x 1/4", 165°, 55 ml.min^{-1}, anti-ol 7.3 min., syn-ol 5.1 min.

Hydrogen abstraction from tri-n-butylstannane by 7-R-bicyclo[2.2.1]hept-2-en-7-radicals

In cases (R-methyl, phenyl) where no initiation was required, stannane and 7-R-bicyclo[2.2.1]hept-2-en-7-bromide (ratio 1.10:1, respectively) were dissolved in excess spectroscopic grade n-hexane, sealed in glass under vacuum and placed for 1 week in a constant temperature bath (T = 51 ± 0.1°). The crude mixture was analysed by p.m.r., concentrated, and analysed by g.l.p.c. The total 7-R-bicyclo[2.2.1]hept-2-ene fraction was collected from the chromatograph and again subjected to p.m.r. analysis. There was no change in the syn:anti ratio in any case.

Azobis-isobutyronitrile (AIBN) initiator was employed for R = methyl, n-butyl, neopentyl, and i-propyl. A mixture of between 5 and 10 mg of AIBN to 30 mg of substrate was treated as above with tri-n-butylstannane.

Irratiation of di-t-butylperoxide at 310 nm for 3 h. in the presence of 7-R-bicyclo[2.2.1]hept-2-en-7-bromide (R = t-butyl, n-butyl, i-propyl and neopentyl) and tri-n-butylstannane provided the third method of production of the corresponding radicals. The stereochemistry of the 7-R-bicyclo[2.2.1]hept-2-enes obtained were shown to be insensitive of the concentration of either

initiator or stannane present, provided the stannane:bromide ratio exceeded one.

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