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"Studies in the Bicyclo(3.2.2)nonane System"

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SUMMARY

Studies in the Bicyclo(3.2.2)nonane System.

Synthetic studies on the bicyclo(3.2.2)nonane system were undertaken with the aim of preparing compounds suitable for conformational and solvolytic studies on this system. Electrolytic decarboxylation of maleic anhydride adducts was used in the preparation of many of these compounds.

In the conformational studies, it has been found that the three carbon bridge in bicyclo(3.2.2)nona-6,8-diene was extremely mobile, the bridge interconverting rapidly between equivalent conformations. Using n.m.r. spectroscopy at low temperatures, attempts to determine the activation energy of this process were unsuccessful, as were attempts on bicyclo(3.2.2) nona-6,8-dien-3-one and bicyclo(3.2.2)nona-6,8-dien-2-one, each of which was also found to have an extremely mobile three carbon bridge. I.R. and n.m.r. studies on ten alcohols and some of their derivatives yielded much information on the conformational preferences of the three carbon bridge in each of these compounds.

In the solvolytic studies, the acetolysis of the tosylates of six of the above alcohols was investigated. The rate of acetolysis of each tosylate was measured. In the series having the tosylate group substituted at C-3, the rate studies showed that, in the unsaturated tosylates, there was no acceleration of

ionisation caused by anchimeric assistance of the double bond. In the series in which the tosylate group was substituted at the C-2 position, the rate studies showed that endo-bicyclo(3.2.2) non-6-en-2-yl tosylate underwent acetolysis slightly faster than bicyclo(3.2.2)nonan-2-yl tosylate. In the series with the tosylate at C-3, the products of acetolysis showed that the only solvolysis processes were elimination or direct substitution of tosylate by acetate. In the series with the tosylate at C-2, the solvolysis processes were found to be rather more complex. Tosylates of exo-bicyclo(3.2.2)non-6-en-2-ol and bicyclo(3.2.2)nona-6,8-dien-2-ol did not form under the usual reaction conditions. Under these conditions, it was shown unambiguously that exo-bicyclo(3.2.2) non-6-en-2-ol underwent the unexpected rearrangement to bicyclo (3.2.2)non-6-en-1-ol. Evidence for bicyclo(3.2.2)nona-6,8-dien-2-ol undergoing rearrangement to bicyclo(3.2.2)nona-6,8-dien-1-ol, under similar conditions, was also obtained.

CONTENTS

STUDIES IN THE BICYCLO(3.2.2)NONANE SYSTEM

INTRODUCTION

In comparison with the copious studies on small, bicyclic systems such as the bicyclo(2.2.1)heptane (1), the bicyclo(2.2.2) octane (2), the bicyclo(3.2.1)octane (3), and the bicyclo(3.3.1) nonane (4) systems, relatively little attention has been paid to the bicyclo(3.2.2)nonane (5) ring system. This possibly has been due to the fact that relatively few methods have been available for the preparation of this bicyclic system, nor has the system exhibited any properties worthy of really extensive study, such as those of the norbornyl (1) system.

The synthesis of the (3.2.2) bicyclic system has been approached in three general, separate ways:

(a) Via cyclohexane derivatives.

(b) Via Diels-Alder and other electrocyclic reactions.

(c) By ring expansion of smaller bicyclic systems.

(a) Via cyclohexane derivatives.

Among the earliest preparations of the general bicyclo (3.2.2)nonane structure was the preparation by Guha [1] of 1,5-dicarbomethoxybicyclo(3.2.2)nona-6,8-dione (6) by treating the disodio salt of succinosuccinic ester (7) with 1,3-dibromopropane. Hydrolysis of the adduct (6) to the corresponding diketo-diacid (8) followed by a Wolff-Kishner reduction gave bicyclo(3.2.2)nonane-1,5-dicarboxylic acid (9). At a later date, Wood and Woo [2] demonstrated

that bis-decarboxylation of the diketo-diacid (8) occurred fairly readily to give bicyclo(3.2.2)nona-6,8-dione (10). The fact that decarboxylation of a bridgehead acid occurs in this system would imply that the bicyclo(3.2.2)nonane system could accommodate bridgehead olefins , sometimes referred to as anti-Bredt olefins. To digress , Wiseman and Chong [3] have also found evidence for bridgehead olefins in recent studies on the (3.2.2) bicyclic system. However , these olefins have proved to be somewhat unstable and cannot be isolated by conventional methods , dimers of the olefins , bicyclo(3.2.2)non-1-ene (11) and bicyclo(3.2.2)non-5-ene (12) , being obtained.

Schaefer [4] has also studied the preparation of bicyclo (3.2.2)nonane type compounds from cyclohexane precursors. It was found that pyrolysis of the cerous salt of 3-(4-carboxycyclohexyl) propionic acid (13) gave bicyclo(3.2.2)nonan-2-one (14) in fair yield , while pyrolysis of an unseparated mixture of the cerous salts of <u>cis</u> and <u>trans</u> isomers of 1,4-cyclohexane diacetic acid (15) gave bicyclo(3.2.2)nonan-3-one (16) in very poor yield.

(b) <u>Via Diels-Alder and other electrocyclic reactions.</u>

The bicyclo(3.2.2) system , in common with other bicyclo (2.2.x) systems (17) , lends itself readily susceptible to synthesis by the extremely useful Diels-Alder reaction. Thus , during the initial studies on this reaction , Alder and Stein [5] reported the

synthesis of bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (18) , prepared from cyclohepta-1,3-diene and maleic anhydride. Subsequent preparations of other members of this bicyclic system soon appeared. Alder and Rickert [6] reported the preparation of 6,7-dicarbomethoxybicyclo(3.2.2)nona-6,8-diene (19) using cyclohepta-1,3-diene once more as the diene moiety and dicarbomethoxyacetylene as the dienophile. Various other bicyclo(3.2.2) nonane type compounds were prepared by varying diene and dienophile , a procedure which did little to further knowledge of this bicyclic system , since it was not considered as a separate entity but rather as merely a product arising from a reaction under study , in this case the Diels-Alder reaction.

Until 1951 , progress in the study of the bicyclo(3.2.2) nonane system was also hindered by a lack of suitable seven-membered cyclic dienes. However , in that year , Nozoe , Seto and Ikemi [7] demonstrated that tropolone (20) reacted readily with maleic anhydride to give bicyclo(3.2.2)nona-3,6-dien-3-ol-2-one-8,9-exo-dicarboxylic acid anhydride (21). Shortly after this , Nozoe , Mukai , Takase and Nagase [8] showed that tropone (22) also reacted fairly readily with maleic anhydride to give bicyclo(3.2.2) nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (23) , although the stereochemistry of the anhydride group was to be established in a later publication [9]. Previously it had been thought

that the troponoid ring system was too aromatic in character to behave as a diene in Diels-Alder reactions but now that the contrary had been demonstrated , several studies concerning the formation of various troponoid adducts were published by Sebe et al. [10] in subsequent years.

The impetus for further study came from the preparation of cyclohepta-3,5-dienone (24) obtained from the base degradation of tropinone methiodide (25) reported by Meinwald, Emerman, Yang and Büchi [11]. Under the conditions of the Diels-Alder reaction, the 3,5-dienone (24) undergoes rearrangement (at about 80°) to the fully conjugated cyclohepta-2,4-dienone (26) which reacts with N-phenylmaleimide to give bicyclo(3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid N-phenylimide (27).

The first synthesis of pure bicyclo(3.2.2)nonane (5), prepared via the Diels-Alder reaction, was reported by Alder, Hartung and Hausmann [12], who reacted cyclohepta-1,3-diene with acrolein to give 8-formylbicyclo(3.2.2)non-6-ene (28). This adduct was catalytically hydrogenated to give 6-formylbicyclo(3.2.2) nonane (29) which was converted to the corresponding enol acetate (30), which in turn was oxidatively cleaved to bicyclo(3.2.2) nonan-6-one (31). Wolff-Kishner reduction of this ketone (31) gave the desired bicyclo(3.2.2)nonane (5).

An interesting variation on the preparation of the

bicyclo(3.2.2)nonane system by means of the Diels-Alder reaction was the addition of an allyl cation to cyclohexa-1,3-diene, a process which the rules of orbital symmetry predict to be a thermally allowed $4_s + 2_s$ cycloaddition. Hoffmann, Joy and Suter [13] successfully prepared 3-methylbicyclo(3.2.2)nona-2,6-diene (32) in 20% yield by this method, from cyclohexa-1,3-diene and 2-methylallyl cation.

A further variation on the electrocyclic type preparations of the bicyclo(3.2.2)nonane system was the preparation by Goldstein and Odell [14] of bicyclo(3.2.2)nona-3,6,8-trien-2-one (33) which was isolated in 40% yield after treatment of the readily available cyclohepta-2,4,6-trienylacetyl chloride (34) with triethylamine, giving the corresponding ketene (35). The ketene (35) then undergoes rearrangement to bicyclo(3.2.2)nona-3,6,8-trien-2-one (33) via the norcaradien-7-yl ketene (36) intermediate.

(c) By ring expansion of smaller bicyclic systems.

The preparation of the (3.2.2) bicyclic system may also be approached by ring expansion of suitably substituted bicyclo(2.2.2) octane and bicyclo(2.2.1)heptane type compounds. In three separate studies, Alder, Krieger and Weiss [15], Alder and Reubke [16], and Endres [17] studied the ring expansion of 2-aminomethylbicyclo(2.2.2) octane (37), prepared by lithium aluminium hydride reduction of the adduct from cyclohexa-1,3-diene and acrylonitrile, followed by catalytic hydrogenation. On treating the 2-aminomethylbicyclo(2.2.2)

octane (37) with nitrous acid, ring expansion occurred via the corresponding diazonium salt. Alder, Krieger and Weiss [15] in the initial study reported the formation of only bicyclo(3.2.2)nonan-2-ol (38). However, in the more comprehensive study of Endres [17], it was reported that, in fact, a mixture of bicyclo(3.3.1)nonan-2-ol (39) (16%), bicyclo(3.2.2)nonan-2-ol (38) (62%), and bicyclo(3.2.2) nonan-3-ol (40) (22%) was obtained.

Another approach to the bicyclo(3.2.2)nonane system involving a substituted bicyclo(2.2.2)octane was reported by Grob, Ohta, Renk and Weiss [18]. Solvolysis of the tosylate of 1-hydroxy-methylbicyclo(2.2.2)octane (41) yielded bicyclo(3.2.2)nonan-1-ol (42). Conversion of this alcohol (42) to 1-chlorobicyclo(3.2.2)nonane (43) with thionyl chloride followed by a sodium in ethanol reduction gave bicyclo(3.2.2)nonane.

Only one preparation of the bicyclo(3.2.2)nonane system from a substituted bicyclo(2.2.1)heptane has so far been reported. Berson and Jones [19], in a study of the oxy-Cope rearrangement, have reported the preparation of bicyclo(3.2.2)non-6-en-2-one (44) in 84% yield by rearrangement of endo-7-vinyl-exo-7-hydroxybicyclo(2.2.1) hept-2-ene (45).

The above three methods, (a), (b), and (c), comprise the main synthetic approaches to the bicyclo(3.2.2)nonane system, and while the examples given are by no means the total synthetic studies

that have been conducted on this system, nevertheless, almost all the other preparations of this bicyclic system involve one or other of these three methods.

However, studies on the (3.2.2) bicyclic system have not been restricted to purely synthetic topics. Stereochemical and conformational aspects of the system have also been considered, providing an interesting comparison with other small, bridged bicycles containing a three carbon atom bridge.

Initial studies on the stereochemistry of the bicyclo(3.2.2) nonane system concerned the stereochemistry of the anhydride or N-phenylimide groups in the adducts with cyclohepta-1,3-diene, which remained unknown, until in 1956, Alder and Mölls [20] showed that in the addition of maleic anhydride to cyclohepta-1,3-diene, the anhydride group of the adduct (18) was in the endo configuration as shown (18). Similarly, Nozoe et al. [9] have found that the stereochemical disposition of the anhydride group in the tropone-maleic anhydride adduct (23) is analogous to that in the cyclohepta-1,3-diene-maleic anhydride adduct (18).

In comparison with bicyclo(3.3.1)nonane type compounds, little study has been conducted on the conformations of compounds of the (3.2.2) series. It may also be interesting to compare the findings of the conformational studies on bicyclo(3.2.1)octanes (3), bicyclo(3.3.1)nonanes (4), bicyclo(3.3.2)decanes (46), and bicyclo

(3.3.3)undecanes (47) with the studies on bicyclo(3.2.2)nonanes (5) so far reported, and with the observations reported later in this study.

Few conformational studies on the bicyclo(3.2.1)octane (3) system have been conducted. However, in n.m.r. studies on the exo- and endo-bicyclo(3.2.1)octan-3-ols [21], (48) and (49) respectively, and on the exo- and endo-bicyclo(3.2.1)oct-6-en-3-ols [22], (50) and (51) respectively, it was proposed that the three carbon bridge was disposed in such a manner that all four alcohols, (48), (49), (50), and (51) existed preferentially in rigid chair conformations with respect to the six-membered ring, irrespective of the exo or endo nature of the hydroxyl group. Contributions of boat conformations to the ground-state populations were found to be negligible even allowing for endo hydroxyl interactions in (49) and (51) when the six-membered ring is in the chair conformation.

In contrast to the (3.2.1) system, the conformational preferences of the bicyclo(3.3.1)nonane (4) system have been studied in detail. Bicyclo(3.3.1)nonane (4) itself can adopt one of three conformations, namely the boat-boat (52), boat-chair (53) or chair-chair (4). Despite a fairly serious transannular interaction between the endo C-3 and C-7 protons, the chair-chair conformation (4) has been found to be preferred both in the crystal and in solution for several bicyclo(3.3.1)nonane (4) derivatives [23]. However, if one

substitutes an endo proton at C-3 or C-7 (or both) by a fairly bulky group, it is frequently found that due to increased transannular interaction the preferred conformation becomes the boat-chair (53). For example, on the basis of equilibration of either exo- or endo-bicyclo(3.3.1)nonan-3-ol, (54) and (55) respectively, with aluminium isopropoxide in isopropanol, Marvell and Knutson [24] obtained mainly the exo isomer (54) (96.9%). The free-energy change for the process, ΔG^{o}, was found to be -2.5 k.cal./mole which is a reasonable approximation of the energy difference between the boat-chair and chair-chair conformations of bicyclo(3.3.1)nonane, and thus this implied that the endo-3-ol (55) prefers to exist in the boat-chair conformation. Also, Fisch, Smallcombe, Gramain, McKervey and Anderson [25] using spin-decoupling and variable temperature n.m.r. techniques, considered a conformational equilibrium to be occurring in endo-bicyclo(3.3.1)nonan-3-ol (55). From the magnitude of the coupling constants it was deduced that the major conformer was the chair-boat form (56), and, on the basis of a facile radical oxidation of the alcohol (55) to the bridged ether, oxaadamantane (57), it was suggested that the minor conformer was the chair-chair form. The presence of (and in some cases preference for) the boat-chair conformer in other 3-endo substituted bicyclo(3.3.1)nonanes has also been the subject of studies by Graham et al. [26]. However, it may be said in summary that it would appear that the preferred conformation of a

bicyclo(3.3.1)nonane depends on the substitution pattern of the actual molecule concerned.

At present there is some dispute concerning a preferred conformation for the bicyclo(3.3.2)decane (46) system. It has been proposed [27] from an n.m.r. study that the preferred conformation of exo-bicyclo(3.3.2)decan-3-ol (58) is the chair-chair as shown, i.e. analogous to the corresponding (3.3.1) alcohol. However, from an electron spin resonance (e.s.r.) study of bicyclo(3.3.2)decane-9,10-semidione (59) at varying temperatures, other investigators [28] have proposed that the preferred conformation of the semidione (59) is the boat-chair as shown, by a comparison with the e.s.r. spectrum of bicyclo(3.2.2)nonane-6,7-semidione (60). It may be that, as with the (3.3.1) system, the preferred conformation of a bicyclo(3.3.2) decane depends on the pattern of substitution.

The next higher analogue in the series, bicyclo(3.3.3)undecane (47), has recently been synthesised [29,30], and a study of its n.m.r. spectrum at 35° has indicated that there is rapid interconversion between the conformations, (47) and (47a). From a study of the temperature dependence of its n.m.r. spectrum, it has been estimated that the free-energy of activation (ΔG^*) for the interconversion process is 11 ± 2 k.cal./mole at -60°.

Little has been reported on the conformational aspects of the (3.2.2) bicyclic system. Russell, Chang and Jefford [31] have

observed that bicyclo(3.2.2)nonane-2,3-semidione (61), prepared by oxidation of bicyclo(3.2.2)nonan-2-one (14), showed magnetic equivalence of the hydrogen atoms at C-4. This was explained in terms of the rapid dynamic interconversion between the two possible conformations, (61) and (61a). In a later publication [28], Russell and Keske prepared bicyclo(3.2.2)nonane-6,7-semidione (60) by oxidation of bicyclo(3.2.2)non-6-ene (62). Studies on the e.s.r. spectrum of this semidione (60) at various temperatures once more indicated rapid interconversion between the two possible conformations, (60) and (60a).

In a similar vein, n.m.r. studies by Jefford, Mahajan and Ramey [32] on 3-bromobicyclo(3.2.2)non-2-ene (63) also indicated, in the opinion of these authors, that the three carbon bridge was rapidly interconverting between the two possible conformations (63) and (63a), causing the observed magnetic equivalence of the allylic protons. The proposition that 3-bromobicyclo(3.2.2)non-2-ene (63) was held in a symmetrical conformation between the two dynamic conformations (63) and (63a) was regarded by Jefford et al. [32] as a much less attractive alternative.

In a further study, which involved synthesis of 6,7-dicarbomethoxybicyclo(3.2.2)nona-2,6,8-triene (64), Bishop and Fleming [33] prepared 6,7-dicarbomethoxybicyclo(3.2.2)nona-6,8-dien-<u>exo</u>-3-ol (65) and the corresponding <u>endo</u>-3-ol (66). From the n.m.r.

spectra, these authors inferred that the three carbon bridges in the two alcohols adopted fixed conformations. However, as shown in this present work, the detection of alternative conformations can only be accomplished by high resolution infra-red spectroscopic studies, a method which was not used by Bishop and Fleming [33].

Further studies on the conformation of the (3.2.2) system have involved a consideration by Hartmann [34] of the differences in steric interaction of the two conformational extremes of bicyclo (3.2.2)non-6-ene, (62) and (62a). It was considered that (62a) would be more favoured since there is less interaction between the C-3 endo hydrogen atom and the trigonally disposed hydrogen atoms at C-6 and C-7 in (62a) than there is between the C-3 exo hydrogen atom and the exo C-8 and C-9 hydrogen atoms in (62). Most of the remaining studies on conformation in the (3.2.2) bicyclic series are concerned with the differences in behaviour of the endo- and exo-bicyclo(3.2.2)nonan-6-ols, (67) and (68) respectively, their relative abundances after equilibration of one or the other, and their relative abundances on reduction of the corresponding 6-ketone (31) by different methods [35]. The exo- and endo-bicyclo(3.2.2) non-6-en-8-ols, (69) and (70) respectively, have also been investigated in a similar manner [35].

As may be seen from the above, very little study on conformational aspects of the (3.2.2) bicyclic system has been conducted.

In part, the aim of this work was to rectify this situation and to increase the knowledge available on the (3.2.2) bicyclic system.

The reactivity and solvolytic characteristics of the (3.2.2) bicyclic system are relatively uninvestigated in comparison with those of the other small, bicyclic systems. "Nonclassical Ions" [36], edited by Bartlett, is an excellent compilation of the important publications in this field and if a general review of solvolysis studies in other bicyclic systems is required, reference should be made to this review.

In the only reported solvolytic study of the bicyclo(3.2.2) nonane system, Schaefer, Endres and Moran [37] investigated the solvolysis of a mixture of exo- and endo-bicyclo(3.2.2)nonan-6-yl-p-nitrobenzenesulphonates, (71) and (72) respectively. The composition of the solvolysis products mixture from (71) and (72) was found to be exo-bicyclo(3.3.1)nonan-2-ol (73) (10%) and, it was believed, exo-bicyclo(4.2.1)nonan-2-ol (74) (90%), both of which can arise from Wagner-Meerwein type shifts of the (3.2.2) compounds, as shown in (71) and (72). In the same publication [37], the acetolysis of bicyclo(3.2.2)nonan-2-yl tosylate (75) was also undertaken. The acetate products of the solvolysis were hydrolysed to the corresponding alcohols and the composition of the mixture identified as bicyclo(3.3.1)nonan-2-ol (39) (32%), bicyclo(3.2.2)nonan-2-ol (38) (52%) and bicyclo(3.2.2)nonan-3-ol (40) (16%).

Solvolytic studies have been conducted on tosylates of 3-hydroxy compounds in the (3.2.1) bicyclic series, providing a comparison with the results obtained in this study. Jefford, Hill and Gunsher [21] prepared and studied the rates and products of acetolysis of the tosylates of exo-bicyclo(3.2.1)octan-3-ol (48) and the corresponding endo alcohol (49). It was found that no skeletal rearrangement occurred in this system under acetolysis conditions, the products obtained being either those of straightforward substitution, i.e. the exo and endo acetates, (76) and (77), or that of elimination, bicyclo(3.2.1)oct-2-ene (78). A subsequent study by LeBel and Maxwell [22] of, among others, the sodium acetate buffered acetolysis of the tosylates of the unsaturated exo-bicyclo(3.2.1)oct-6-en-3-ol (50) and endo-bicyclo(3.2.1)oct-6-en-3-ol (51) showed that there was no participation by the double bond in assisting leaving group departure or in stabilisation of the transition state. In the acetolysis of endo-bicyclo(3.2.1)oct-6-en-3-yl tosylate (79), the major acetolysis products were found to be bicyclo(3.2.1)octa-2,6-diene (80), and the acetates of exo-bicyclo(3.2.1)oct-6-en-3-ol (50) and exo-tricyclo(3.2.1.$0^{2,7}$)octan-6-ol (81), with minor components being the acetates of endo-bicyclo(3.2.1)oct-6-en-3-ol (51), exo-bicyclo (3.2.1)oct-6-en-2-ol (82) and exo-bicyclo(2.2.2)oct-2-en-5-ol (83). In the acetolysis of exo-bicyclo(3.2.1)oct-6-en-3-yl tosylate (84), no exo-bicyclo(3.2.1)oct-6-en-3-yl acetate (85) was formed. The

composition of the product mixture was found to be mainly bicyclo (3.2.1)octa-2,6-diene (80) and endo-bicyclo(3.2.1)oct-6-en-3-yl acetate (86), with smaller amounts of the acetates of exo-tricyclo ($3.2.1.0^{2,7}$)octan-6-ol (81), exo-bicyclo(2.2.2)oct-2-en-5-ol (83) and exo-bicyclo(3.2.1)oct-6-en-2-ol (82). While the products of acetolysis of both exo and endo tosylates, (84) and (79), were similar, it was reported that the product distribution was different in the two solvolyses under study.

Wagner-Meerwein rearrangement studies on the bicyclo(3.2.2) nonane system have been conducted by Hartmann [38], who investigated the deamination of the epimeric 6-aminobicyclo(3.2.2)nonanes, (87) and (88), and the 8-aminobicyclo(3.2.2)non-6-enes, (89) and (90). It was found that such deaminations mainly proceed via stereospecific rearrangements to yield exo alcohols of the bicyclo(3.3.1)nonane or bicyclo(4.2.1)nonane series with high stereospecificity as well as some olefinic material. Thus endo-8-aminobicyclo(3.2.2)non-6-ene (90) upon deamination gave exo-bicyclo(3.3.1)non-3-en-2-ol (91) (89%), while exo-6-aminobicyclo(3.2.2)nonane (88) gave the corresponding saturated (3.3.1) alcohol in 65% yield, the other major product (25%) in this case being exo-bicyclo(3.2.2)nonan-6-ol (68). In contrast, deamination of endo-6-aminobicyclo(3.2.2)nonane (87) gave mainly exo-bicyclo(4.2.1)nonan-2-ol (74) (90%), while exo-8-aminobicyclo (3.2.2)non-6-ene (89) gave only 42% of the corresponding exo-bicyclo

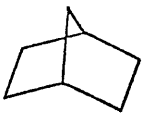
(4.2.1)non-7-en-2-ol (92). In this case, the major product (52%) was found to be tricyclo(4.2.1.$0^{2,8}$)nonan-7-ol (93), arising from homoallylic participation of the double bond in stabilising the carbonium ion (94).

Finally, a mention should be made about bicycloaromaticity [3] with respect to bicyclo(3.2.2)nona-2,6,8-triene (95), its anion (96) and its cation (97). According to Goldstein [39], the anion (96), having 8 π electrons (4n,n=2), should be bicycloaromatic and should be stabilised with respect to a chosen reference compound containing the same number of π electrons. Winstein et al. [40] have recently prepared this anion (96) and have found evidence for electron delocalisation by comparing the proton n.m.r. chemical shifts for the triene (95) and for the corresponding anion (96).

Conversely, the bicyclo(3.2.2)nona-2,6,8-trienyl cation (97) has 6 π electrons (4n+2,n=1), and, according to Goldstein [39], such a bicyclic cation should be antibicycloaromatic, should be destabilised, and should thus be difficult to prepare. In fact, these predictions are borne out by various studies which show that the bicyclo(3.2.2)nona-2,6,8-trienyl cation (97) has a propensity for rearranging to the barbaralyl cation (98). Thus Goldstein and Odell [14] have found that Lewis acids readily converted bicyclo(3.2.2)nona-2,6,8-trien-4-ol (99) to barbaralol (100). The behaviour of this bicyclononatrienyl cation (97) has been investigated further by

both Schleyer et al. [41] and Grutzner and Winstein [42]. However, there is at present some dispute as to whether the bicyclononatrienyl-barbaralyl cationic rearrangement is due to the inherent instability of the bicyclo(3.2.2)nona-2,6,8-trienyl cation (97) [39], or whether it is due to the availability of a low-energy pathway for the conversion [42]. It is agreed, however, that, whatever the cause, the barbaralyl cation (98) is energetically favoured over the bicyclononatrienyl cation (97).

In conclusion, it was considered that little study had been conducted on the (3.2.2) bicyclic system compared with other small, bridged, bicyclic systems. Since furtherance of such study was considered worthwhile, the aim of this investigation was, in short, to extend knowledge of synthetic, conformational, and solvolytic aspects of the bicyclo(3.2.2)nonane system.



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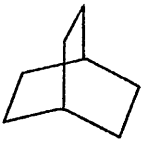

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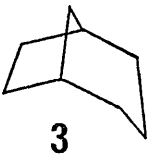

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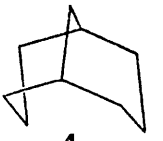

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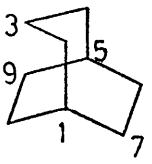

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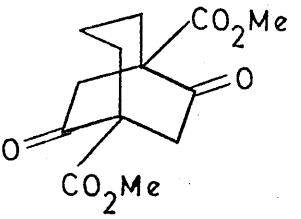

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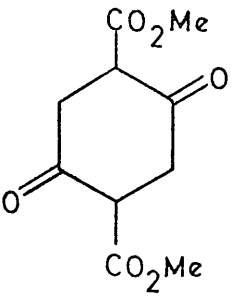

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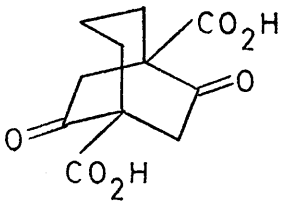

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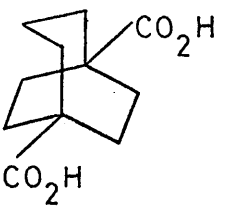

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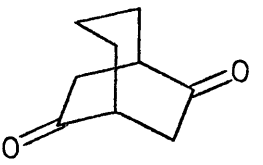

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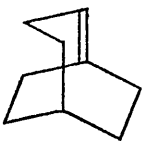

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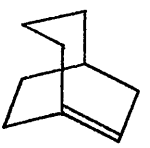

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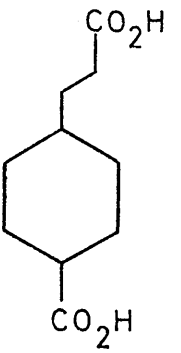

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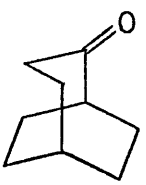

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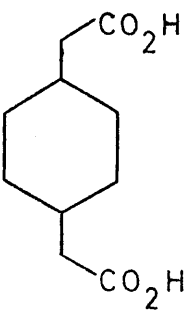

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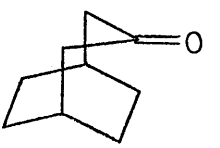

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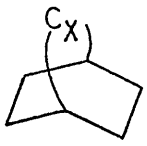

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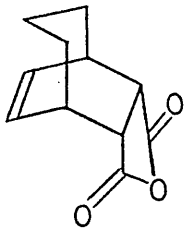

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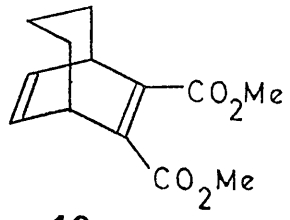

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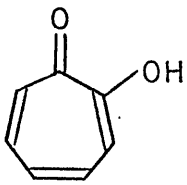

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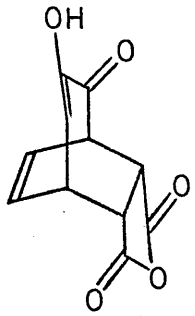

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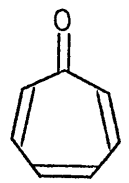

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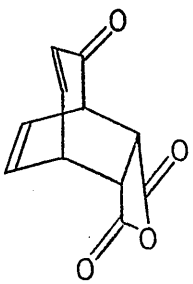

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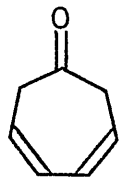

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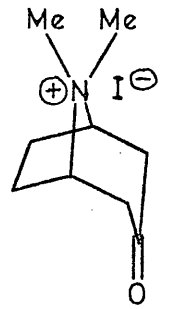

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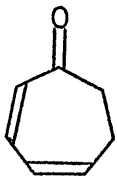

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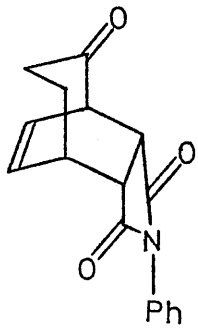

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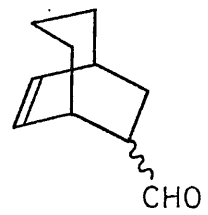

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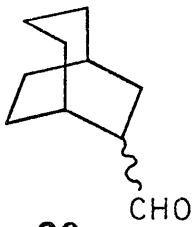

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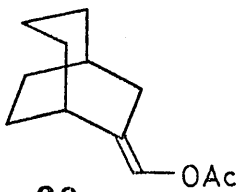

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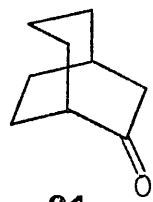

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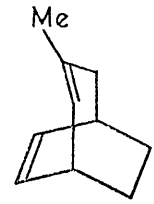

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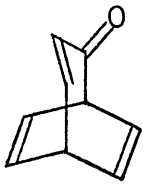

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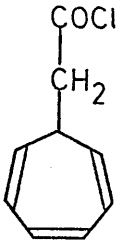

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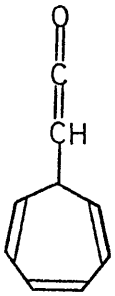

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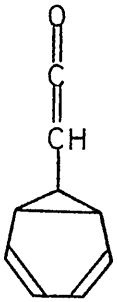

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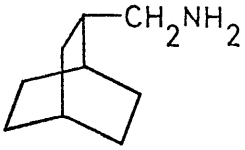

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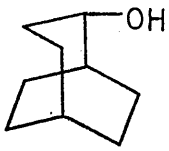

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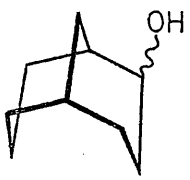

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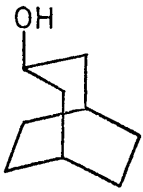

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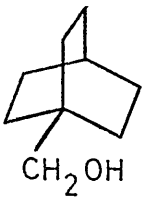

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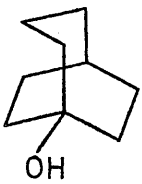

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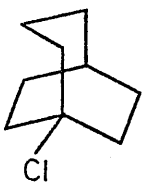

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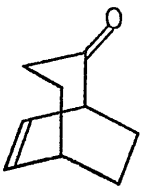

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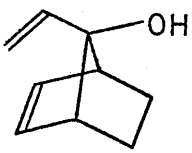

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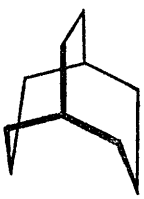

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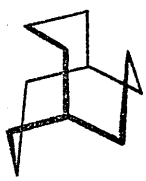

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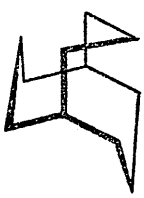

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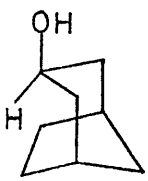

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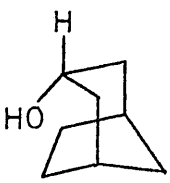

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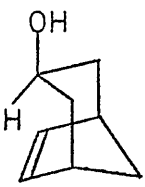

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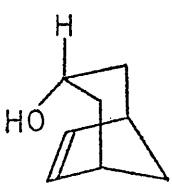

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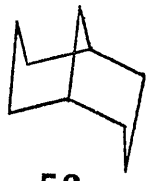

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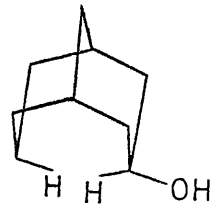

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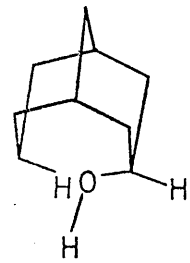

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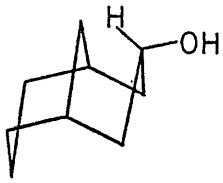

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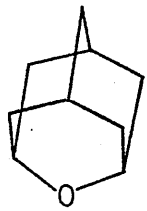

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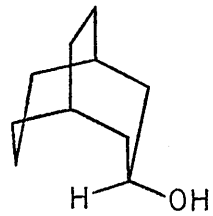

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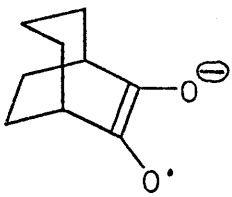

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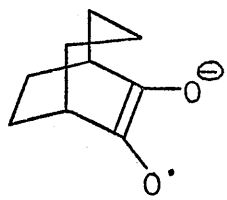

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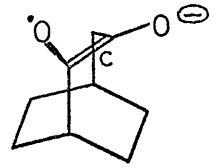

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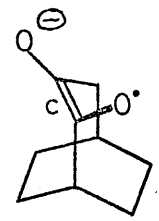

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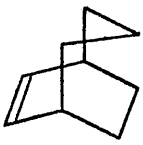

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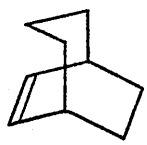

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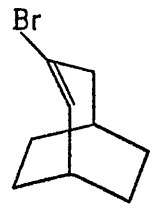

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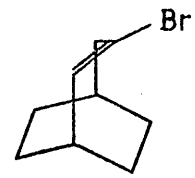

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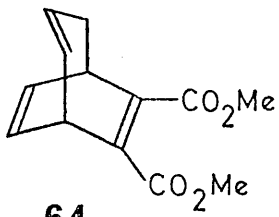

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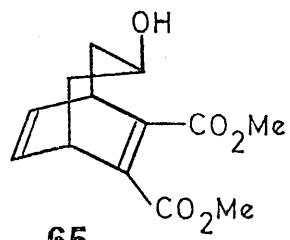

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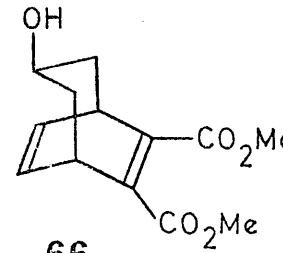

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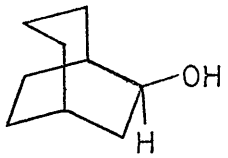

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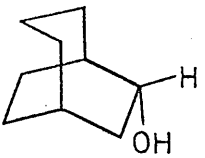

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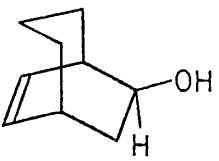

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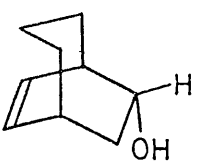

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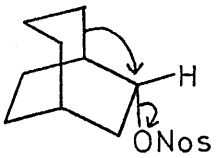

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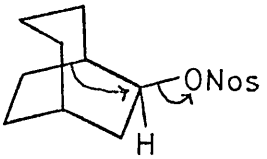

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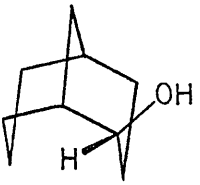

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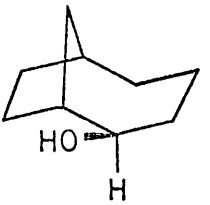

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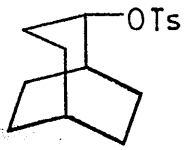

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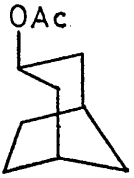

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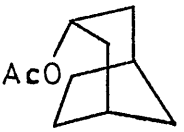

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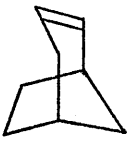

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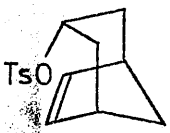

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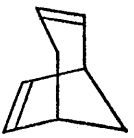

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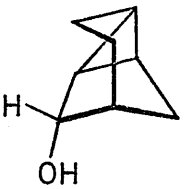

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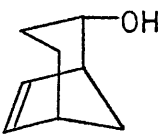

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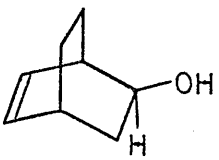

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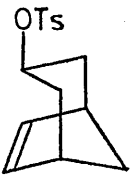

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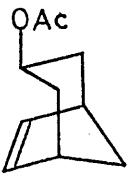

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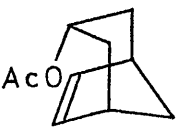

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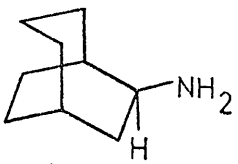

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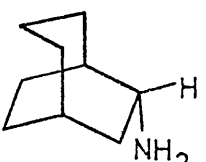

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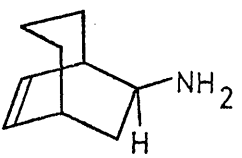

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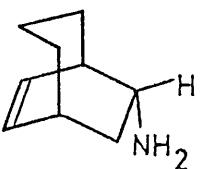

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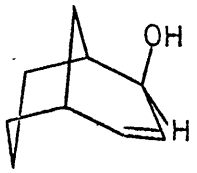

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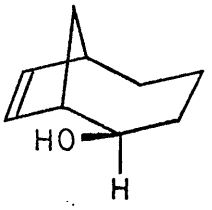

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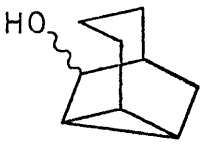

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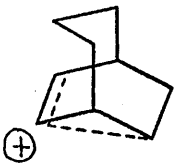

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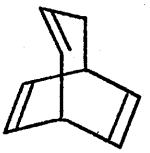

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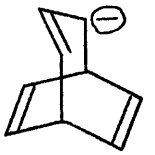

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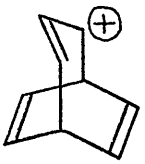

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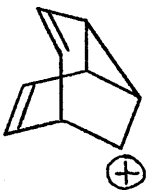

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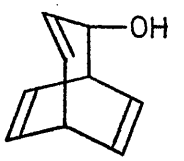

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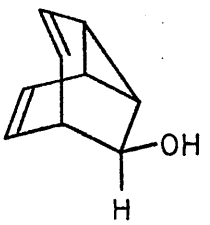

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DISCUSSION

The initial impetus for a detailed study of the bicyclo (3.2.2)nonane system arose from studies by Chalmers [1] on the synthesis of the perhydroazulene structure of β-vetivone (1) proposed by Pfau and Plattner [2]. Several interesting compounds in the bicyclo (3.2.2)nonane system had been prepared and it was decided that a further investigation should be conducted on this system in view of the little attention that it had hitherto received in contrast to other bicyclic systems. The studies reported in this thesis fall into three categories, namely synthetic, conformational, and solvolytic aspects of the (3.2.2) system comprising parts (A), (B), and (C) respectively of this discussion.

(A) Synthetic studies.

A variety of bicyclo(3.2.2)nonane type compounds were required for the conformational and solvolytic studies on the system, as described later in this thesis. These compounds, and their synthesis, were as follows:

It was known [3] that the three carbon bridge in the (3.2.2) bicyclic system was extremely mobile in some cases, the bridge equilibrating rapidly between the two conformations as depicted in Scheme 1. In order to determine the degree of mobility and hence the free energy of activation (ΔG^*) for the process in Scheme 1, it was decided to synthesise bicyclo(3.2.2)nona-6,8-diene (2), 3,3-dimethylbicyclo(3.2.2)nona-6,8-diene (3) and 2,2-dimethylbicyclo(3.2.2)nona-6,8-diene (4). The introduction of the gem-dimethyl groups on the three carbon bridge was to serve a dual purpose; namely, it was hoped that the mass of the methyl groups would reduce the mobility of the bridge and also, the sharp n.m.r. signal for the methyl groups would serve as an excellent means of detection of the point of coalescence of the n.m.r. signals, from which the energy of activation of any conformationally mobile system is determined when using n.m.r. for this purpose.

Bicyclo(3.2.2)nona-6,8-diene (2) was prepared readily by subjecting the Diels-Alder adduct prepared from cyclohepta-1,3-diene and maleic anhydride, i.e. bicyclo(3.2.2)non-6-ene-8,9-endo-dicar-

boxylic acid anhydride (5) [4], to electrolytic bis-decarboxylation [5] giving the desired diene (2). This electrolytic decarboxylation [5], one of several methods [6] available for converting anhydride groupings to olefins, was found to be extremely convenient in that no other reagent, other than the anhydride adduct, was necessary and also from the point of view that the purity of the product was usually fairly high. Two disadvantages were that decarboxylation could be carried out on only 0.005 mole of adduct at a time, and also that in the preparation of the more volatile members of the (3.2.2) bicyclic system, yields tended to be rather low, i.e. about 10-20%. In order to counteract this latter disadvantage, the method as described in the literature [5] was modified slightly by covering the surface of the reaction solution with a layer of 60-80° petrol. This helped to serve as a trap for any volatile products being carried off from the reaction mixture by the carbon dioxide being evolved. By employing this modification, yields were considerably improved. Before using 60-80° petrol in this manner, the yields of bicyclo(3.2.2)nona-6,8-diene (2) prepared by this method were approximately 1%, but with the modification in use it was possible to increase the yield tenfold. The diene (2) was obtained as a very volatile, waxy, colourless solid, so volatile in fact that a satisfactory analysis could not be obtained. However, a mass spectrum, albeit low resolution, gave a molecular ion at the predicted m/e

value of 120, which, coupled with other spectroscopic data (i.r. and n.m.r.), served to indicate that the desired product had been prepared.

The (3.2.2) bicyclic compounds prepared in this study may be grouped into two distinct categories, i.e. those compounds carrying substituents at the C-3 position, and those bearing substituents at the C-2 position. Thus, the intended preparation of the 3,3-dimethyldiene (3) proceeded via intermediates of the C-3 series as shown in Scheme 2, while the intended preparation of the 2,2-dimethyldiene (4) involved intermediates belonging to the C-2 series as shown in Scheme 3.

One of the key reactions in this study was the reaction of 1-benzoyloxycyclohepta-3,5-diene (6) with maleic anhydride which has been investigated by Chalmers [1]. This reaction gave a mixture of three adducts, i.e. exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) (34%), endo-3-benzoyloxybicyclo-(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (8) (11%) and a 2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (9) (18%) the stereochemistry of which at the C-2 position had not been determined previously. It has now been shown, as part of this work, that the benzoate group of this isomer (9) has the endo configuration with respect to the double bond. The determination of the stereochemistry at the C-2 position in the 2-benzoate (9) was obtained by catalytic hydrogenation of the adduct (9), electrol-

ysis of the resulting product (10) and hydrolysis of the 2-benzoyloxybicyclo(3.2.2)non-6-ene (11) thus obtained to give a bicyclo (3.2.2)non-6-en-2-ol (12) which, by g.l.c. and spectroscopic comparison with samples of endo-bicyclo(3.2.2)non-6-en-2-ol (13) and exo-bicyclo(3.2.2)non-6-en-2-ol (14) (see below), was shown to be the exo alcohol (14). Thus, this rendered the stereochemistry of the original adduct as endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15).

The exo-3-benzoate (7), which, like the endo-2-benzoate (15), could be separated pure from the mixture of adducts, was electrolysed (i.e. electrolytically decarboxylated) to give 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16) in 41% yield. The benzoate (16), while having an intensely sweet odour, was not particularly volatile, unlike the parent diene (2).

The benzoate (16), on base hydrolysis, gave the corresponding alcohol, bicyclo(3.2.2)nona-6,8-dien-3-ol (17), which was converted by Jones oxidation to bicyclo(3.2.2)nona-6,8-dien-3-one (18), all three compounds being colourless solids. The oxime (19), prepared from the ketone (18), was obtained as colourless platelets.

3-Methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20) was prepared from the ketone (18) by two separate methods. In the first instance, the dienone (18) was refluxed under dry nitrogen for 4 hrs. in dry tetrahydrofuran with a large excess of a three molar

solution of methyl magnesium chloride in tetrahydrofuran (supplied by Alfa Inorganics). A fairly low yield (24%) of product (20) was obtained, probably due to its volatility combined with the temperature at which the reaction was conducted, i.e. 60°. This Grignard reaction was repeated using a large excess of freshly prepared methyl magnesium iodide in anhydrous diethyl ether as solvent under dry nitrogen as before. The reaction mixture was refluxed for 4 hrs. and then stirred at room temperature for 16 hrs.. 3-Methylbicyclo (3.2.2)nona-6,8-dien-3-ol (20), prepared in this manner, was obtained in 52% yield. Attempts to purify the alcohol (20) by prep. t.l.c. (silica) proved fruitless, since it appeared that the alcohol (20) underwent rearrangement while adsorbed on the silica, giving a less polar compound. A sample of this rearranged compound was obtained, and investigated by i.r. and n.m.r. spectroscopy; the structure (21), containing an ether linkage, was proposed for this compound, since there was no hydroxyl absorption band in the i.r. spectrum, presumed C-O stretching bands being the only outstanding feature of the spectrum. The n.m.r. spectrum could also be fairly satisfactorily interpreted in terms of such a structure (21). Presumably, the rearrangement is being catalysed by the acidic nature of the silica. A similar example of this type of reaction has been reported [7] in the case of endo-bicyclo(3.2.1)oct-6-en-3-yl acetate (22), whereby treatment of this compound with acetic acid containing p-toluene-

sulphonic acid gave the corresponding ether (23). Purification of 3-methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20) was accomplished by prep. t.l.c. using basic t.l.c. alumina (Woelm), under which conditions no rearrangement occurred, giving the alcohol (20) as a colourless oil.

Since yields so far had been somewhat poor and since, by this time, it had been found that the (3.2.2) system was conformationally very mobile (see below), it was decided not to pursue further the synthesis of the 3,3-dimethyldiene (3).

However, several other C-3 substituted compounds were required for the conformational and solvolytic studies on the (3.2.2) system. Therefore, the preparation of bicyclo(3.2.2)nonan-3-ol (24), endo-bicyclo(3.2.2)non-6-en-3-ol (25), exo-bicyclo(3.2.2)non-6-en-3-ol (26) and bicyclo(3.2.2)non-6-en-3-one (27) was undertaken.

Catalytic hydrogenation of the dien-3-ol (17) gave bicyclo (3.2.2)nonan-3-ol (24) which had already been prepared by Schaefer [8] by reduction of the corresponding bicyclo(3.2.2)nonan-3-one (28) which, in its turn, was prepared in low yield by pyrolysis of the cerous salt of cyclohexane-1,4-diacetic acid (29). The melting point of 105-107° reported by Schaefer [8] for the alcohol (24) is at variance with the melting point of 143-145° (corrected) recorded by the author of this work.

Endo-bicyclo(3.2.2)non-6-en-3-ol (25) could be readily

obtained from the exo-3-benzoate (7). Catalytic hydrogenation of the adduct (7) gave endo-3-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (30), electrolysis of which gave endo-3-benzoyloxybicyclo(3.2.2)non-6-ene (31), which was hydrolysed to the desired endo-bicyclo(3.2.2)non-6-en-3-ol (25), obtained as a colourless solid. Jones oxidation of the endo-3-ol (25) gave bicyclo (3.2.2)non-6-en-3-one (27) as a colourless solid.

While the preparation of endo-bicyclo(3.2.2)non-6-en-3-ol (25) was reasonably straightforward, the preparation of exo-bicyclo (3.2.2)non-6-en-3-ol (26) proved a much more troublesome task. An obvious method of preparation was from the endo-3-benzoate adduct (8) by a route analogous to the preparation of the endo-3-ol (25) from the exo-3-benzoate adduct (7) as described above. However, the endo-3-benzoate (8), obtained as a mixture with the endo-2-benzoate (15) (see experimental), was the minor product (11%) from the Diels-Alder reaction concerned. Attempts at obtaining a pure sample of benzoate (8) by means of column chromatography (alumina, acid-washed, Woelm) or prep. t.l.c. (silica) were unsuccessful although the former separation had previously been reported [1].

Consequently, several approaches to the exo-3-ol (26) were studied; these are described in the experimental section. Some of these methods require no further comment here, the reason for their use being self-evident. However, it is felt that some explanation

is required for the employment of some of the approaches to the desired alcohol (26).

An attempted preparation of the exo alcohol (26) involved lithium aluminium hydride reduction of the syn double bond of bicyclo (3.2.2)nona-6,8-dien-3-ol (17). Franzus and Snyder [9] had found that norbornadien-7-ol (32) could be converted readily to exo-norbornen-7-ol (33) by means of lithium aluminium hydride through the intermediacy of the alanate ion (34). The reduction was attempted on bicyclo(3.2.2)nona-6,8-dien-3-ol (17) but was totally unsuccessful. The reason for this lack of success may be that proposed by Franzus and Snyder [9] who stated that very strict steric requirements were necessary for the transition state if the reaction was to be successful. However, in the reaction involving bicyclo(3.2.2)nona-6,8-dien-3-ol (17) these requirements were not met, causing the attempted reduction to be unsuccessful.

Another approach envisaged protection of the C-6 - C-7 double bond in the exo-3-benzoate (7) as the vicinal bromoacetate (35) by way of the corresponding bromohydrin, which would have been prepared by treatment of the exo-3-benzoate (7) with N-bromoacetamide [10]. Electrolysis of the adduct (35) protected in this way would have given the corresponding protected mono-olefinic benzoate (36). Catalytic hydrogenation, hydrolysis, and removal of the protecting group with zinc dust would have yielded exo-bicyclo(3.2.2)

non-6-en-3-ol (26). However, as stated in the experimental section, attempts to prepare the bromohydrin were unsuccessful.

Yet another attempt at preparing the exo-3-ol (26) was prompted by the observation that the catalytic hydrogenation of the olefinic double bond in the exo-3-benzoate adduct (7) was relatively slow, complete reduction taking 24 hrs. using 30% Pd-C at atmospheric pressure. This was possibly due to two steric factors of undetermined importance, which prevented the double bond from being suitably adsorbed on the catalyst surface. The first possible factor was the steric hindrance caused by the endo anhydride group. The second possible factor, it was hoped, was the preferred syn conformation of the three carbon bridge with respect to the double bond, which was also causing steric hindrance to the adsorption of the double bond on the catalyst surface. It was hoped that this steric hindrance to adsorption, and therefore hydrogenation, caused by the three carbon bridge, would also be present in 3-benzoyloxybicyclo (3.2.2)nona-6,8-diene (16) causing a faster rate of hydrogen uptake for the anti double bond, since n.m.r. studies had shown that the three carbon bridge adopted a preferred conformation. However, in small scale experiments (on 0.5 mmole of benzoate) using 5% Pd-C in ethyl acetate, no discernible change in the rate of uptake of hydrogen was observed as the volume corresponding to the saturation of one double bond was reached. Rate of uptake of hydrogen was so

rapid that, by the time the product was isolated, total saturation of both double bonds had occurred, as shown by an n.m.r. spectrum of the product, which exhibited no signals in the olefinic region.

Exo-bicyclo(3.2.2)non-6-en-3-ol (26) was finally prepared in the following manner:

Whereas, in the reaction of 1-benzoyloxycyclohepta-3,5-diene (6) and maleic anhydride, the major adduct, i.e. the exo-3-benzoate (7), could be separated from the reaction mixture in a pure form, the endo-3-benzoate (8) and endo-2-benzoate (15) were difficult to separate [1] (see experimental section). In order to circumnavigate this problem, the mixture of endo adducts, (8) and (15), was catalytically hydrogenated to give the mixture of corresponding reduced adducts, (38) and (39), which was subjected to electrolysis in the normal manner giving a mixture of exo-3-benzoyloxybicyclo(3.2.2)non-6-ene (37) and exo-2-benzoyloxybicyclo(3.2.2) non-6-ene (40) in a respective ratio of 1:3.

The best separation of these isomers for preparative g.l.c. purposes was obtained as follows:

Column: 2% 20M PEG. Temperature: 165°. Gas Flow Rate: 44 ml./min..

	R_t (min.)	Retention Index (R_i)
2-benzoate (40)	21.5	2620
3-benzoate (37)	25.2	2667

In this manner, the isomers were separated efficiently by preparative g.l.c. (although recovery yields were rather low) giving the exo-3-benzoate (37) and exo-2-benzoate (40). This route afforded, after hydrolysis of the benzoate (40), an alternative source of exo-bicyclo(3.2.2)non-6-en-2-ol (14) which was also available by other methods (see later). Because of scarcity of material, the exo-3-benzoate (37) was hydrolysed without further characterisation (after checking for g.l.c. purity) to exo-bicyclo(3.2.2) non-6-en-3-ol (26), which was purified by sublimation and characterised spectroscopically.

Having prepared the above compounds of the C-3 series, their conformational and solvolytic characteristics were then investigated and compared. The results of these further studies are discussed in parts (B) and (C) of this thesis.

Similar synthetic studies were also carried out on the C-2 series. One of the initial aims of the studies on the C-2 series had been the preparation of 2,2-dimethylbicyclo(3.2.2)nona-6,8-diene (4) (Scheme 3) but synthetic problems caused the abandonment of this particular project.

A useful route to several compounds of the C-2 series was via bicyclo(3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid anhydride (41), which was prepared by the Diels-Alder reaction of maleic anhydride and cyclohepta-3,5-dienone (42) [11]. The latter

rearranged to cyclohepta-2,4-dienone (43) prior to reaction.

It was initially felt that electrolysis of such an adduct (41) containing a ketone group, giving the desired bicyclo(3.2.2) nona-6,8-dien-2-one (44), might result in a pinacol type condensation in competition with or complementary to electrolytic decarboxylation. To avoid this, the keto group in the keto anhydride (41) was protected as the ethylene ketal (45) in the initial preparation of the dienone (44). However, a later experiment showed this precaution to be unnecessary, the dienone (44) being obtained from the keto anhydride (41) in 19% yield without protection of the keto group. Bicyclo(3.2.2)nona-6,8-dien-2-one (44), prepared thus, was obtained as a colourless oil.

Treatment of bicyclo(3.2.2)nona-6,8-dien-2-one (44) with a large excess of a commercially available solution of methyl magnesium chloride in dry tetrahydrofuran (Alfa Inorganics) resulted in an almost quantitative yield of 2-methylbicyclo(3.2.2)nona-6,8-dien-2-ol (46), which was to be converted to the 2-methyl-2-bromobicyclo(3.2.2)nona-6,8-diene (47) using triphenylphosphine dibromide [12]. The 2-bromo compound (47) was then in turn to be converted, using lithium dimethyl copper [13], to the ultimately desired 2,2-dimethylbicyclo(3.2.2)nona-6,8-diene (4), which was required for the temperature dependent n.m.r. studies. However, the bromination gave two products in low yield (13% total). This, coupled

with the lack of success in the low temperature n.m.r. studies which had been carried out previously in this study, caused the termination of the proposed preparation of the dimethyldiene (4) at this point.

The remaining compounds required for conformational and solvolytic studies on this system, i.e. bicyclo(3.2.2)nona-6,8-dien-2-ol (48), endo-bicyclo(3.2.2)non-6-en-2-ol (13), exo-bicyclo(3.2.2)non-6-en-2-ol (14) and bicyclo(3.2.2)nonan-2-ol (49), were prepared as described below.

Sodium borohydride reduction of bicyclo(3.2.2)nona-6,8-dien-2-one (44) gave a quantitative yield of bicyclo(3.2.2)nona-6,8-dien-2-ol (48) as a colourless semi-solid. A further method of preparation of this alcohol was by base hydrolysis of 2-benzoyloxybicyclo(3.2.2)nona-6,8-diene (50) obtained from the electrolysis of endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) which was one of the adducts formed in the reaction of maleic anhydride and 1-benzoyloxycyclohepta-3,5-diene (6) [1].

Electrolysis of bicyclo(3.2.2)nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51), prepared from tropone (52) and maleic anhydride [14], did not give the predicted bicyclo(3.2.2)nona-3,6,8-trien-2-one (53) [15], but gave a plethora of products. The major component (obtained in 5% yield) was shown to be a mixture of two ketones in a 70:30 ratio. The major component of the mixture was shown to be bicyclo(3.2.2)nona-6,8-dien-2-one (44) by g.l.c.

and spectroscopic comparison, while the indications were that the minor component was the desired trienone (53). The presence of dienone (44) as a product would suggest that electrolysis of the enone anhydride (51) occurred with partial concomitant reduction of the C-3 - C-4 double bond, presumably by initial electron addition, possibly in a manner akin to that of the Birch reduction.

Catalytic hydrogenation of bicyclo(3.2.2)nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51) gave the desired bicyclo (3.2.2)nonan-2-one-6,7-exo-dicarboxylic acid anhydride (54) [14], which, on electrolysis, gave bicyclo(3.2.2)non-6-en-2-one (55) [16] in 28% yield. Sodium borohydride reduction of this ketone (55) gave a 3:2 mixture of endo-bicyclo(3.2.2)non-6-en-2-ol (13) and exo-bicyclo(3.2.2)non-6-en-2-ol (14) respectively. This indicated that very little selectivity was operative in this reduction, although one might have predicted, in contradiction to the findings, a predominance of the exo alcohol (14), produced by attack of hydride coming in over the less sterically hindering double bond side of the molecule. Separation of these epimers was successfully effected by preparative g.l.c..

In addition, exo-bicyclo(3.2.2)non-6-en-2-ol (14) was also prepared from endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) as described on pps.24-25.

Catalytic hydrogenation (Pd-C in ethyl acetate) of a

mixture of endo- and exo-bicyclo(3.2.2)non-6-en-2-ols, (13) and (14), gave bicyclo(3.2.2)nonan-2-ol (49), which has been prepared by other methods [8].

Solvolytic studies on the (3.2.2) bicyclic system demanded the preparation of the tosylates of the alcohols (13), (17), (24), (25), (26) and (49) by the general method [17] (see experimental for details). Attempts to prepare the tosylates of the exo-6-en-2-ol (14) and the dien-2-ol (48) were unsuccessful and this situation is discussed in section (C) of this discussion.

The preparation of tricyclo(3.3.1.$0^{2,8}$)nonan-9-ol (tetrahydrobarbaralol) (56) [18], one of the solvolysis products, is described in the experimental section of this thesis.

The above comprises the synthetic studies on the bicyclo (3.2.2)nonane system carried out in this thesis. In general, few insuperable synthetic problems were encountered, the main disadvantage being, as stated above, the inadaptability of the electrolysis reaction to large quantities of material, a finding which has been supported by other workers [19].

(B) Conformational studies.

The conformational studies in this work fall into two parts, namely, an investigation of the conformational mobility of the three carbon bridge in the bicyclo(3.2.2)nonane system (Scheme 1) and related studies on the conformational preference or biassing of related 2- and 3-substituted derivatives.

The n.m.r. spectrum of bicyclo(3.2.2)nona-6,8-diene (2) indicated that there was rapid (in the n.m.r. sense) interconversion between the two conformations depicted in Scheme 1. This was deduced from the fact that the C-3 protons appeared as a quintet (J=6 Hz), implying both no geminal coupling and also coupling by four equivalent vicinal protons. Another interesting observation was that, contrary to normal observations, the C-2 and C-4 protons were at higher field than the C-3 protons, although the latter were more distant (through the σ-bond framework) from the deshielding effect of the double bond. However, this unexpected situation may be explained in terms of spatial shielding effects, rather than deshielding effects. The effect of the rapid interconversion in Scheme 1 is such that, in the diene (2), the C-2 and C-4 protons are shielded to some extent by the C-1 - C-7, C-1 - C-8, C-5 - C-6, and C-5 - C-9 bonds, whereas the C-3 protons can only be shielded by the π-electron clouds of the double bonds. However, since this interconversion process is rapid, the n.m.r. spectrum obtained is that of a time aver-

aged structure which has the conformation (57). It will be noted that in this conformation (57) the C-3 protons are distant from any spatial shielding by the π-electron clouds of the double bonds.

The n.m.r. spectrum of bicyclo(3.2.2)nona-6,8-dien-3-one (18) strongly suggested a rapid interconversion between conformers (18) and (18a) due to the isochronous nature of the C-2 (and C-4) protons which appeared as a doublet at 7.63τ ($J_{1,2}$= 3.7 Hz) suggesting no geminal coupling and only vicinal coupling with the bridgehead proton at C-1. Indeed, on irradiation of the signal assigned to the C-1 proton the doublet at 7.63τ collapsed to a singlet. Due to this conformational mobility, the ketone (18) was subjected to low temperature n.m.r. studies.

The n.m.r. spectrum of bicyclo(3.2.2)nona-6,8-dien-2-one (44) also showed that there was rapid conformational interchange of the three carbon bridge, since the C-3 protons appeared as a triplet ($J_{3,4}$= 7 Hz). Had the bridge adopted a fixed conformation, rendering these C-3 protons non-equivalent, a geminal coupling would have been in evidence. Also, the signal would have been further split by the coupling with the C-4 protons, which would also be non-equivalent in a "frozen" conformation. This ketone (44) was also subjected to the low temperature n.m.r. studies discussed below.

Low temperature n.m.r. studies were conducted on bicyclo (3.2.2)nona-6,8-diene (2), bicyclo(3.2.2)nona-6,8-dien-3-one (18),

and bicyclo(3.2.2)nona-6,8-dien-2-one (44), and a series of spectra recorded from +34° to -140°. However, over this range, the spectra remained essentially invariant. Presumably the rate of conformational interchange was becoming slower as the temperature was lowered but this rate of interchange was still too fast for a change in the n.m.r. spectrum to be observed.

Since variation in the line width of an n.m.r. signal always occurs when systems are being studied at various temperatures, methylene chloride was used in these n.m.r. studies as a homogeneity standard. This determined if the line broadening, which occurred as the recording temperature was lowered, was due to the inhomogeneity of the magnetic field or to a genuine change from a mobile to a "frozen" conformation in the molecule under study. Assuming that the signal for the particular proton under investigation will show a shift on passing from the mobile to the "frozen" conformation, this will cause line broadening as the coalescence point is approached, followed by separation into two distinct signals as the "frozen" conformation is attained.

At the coalescence point, it may be shown [20] that the lifetime corresponding to coalescence is

$$2\tau = \frac{\sqrt{2}}{\pi(\nu_A - \nu_B)}$$

where 2τ = lifetime of the system

ν_A = chemical shift of the proton, in hertz, when the proton is in environment A of "frozen" conformation.

ν_B = chemical shift of the proton, again in hertz, when the proton is in environment B of the "frozen" conformation.

The rate of bridge equilibration, k_e, is thus $\frac{1}{2\tau}$.

The Arrhenius equation, which defines the dependence of the rate of change of a chemical system on temperature, is given by

$$k_e = \frac{KkT}{h} . e^{-\frac{\Delta G^*}{RT}}$$

where k_e = the rate of bridge equilibration.

K = frequency factor, set at 1.

k = Boltzmann's constant, i.e. 1.38×10^{-16} erg/ ^oA.

h = Planck's constant, i.e. 6.62×10^{-27} erg second.

T = temperature in degrees absolute (^oA).

ΔG^*= free energy of activation at T concerned.

R = gas constant, i.e. 1.98 cal./degree mole.

$$\text{Now, } k_e = \frac{1}{2\tau} = \frac{\pi(\nu_A - \nu_B)}{\sqrt{2}} = \frac{KkT}{h} . e^{-\frac{\Delta G^*}{RT}}$$

$$\text{Thus, } e^{-\frac{\Delta G^*}{RT}} = \frac{h\pi(\nu_A - \nu_B)}{\sqrt{2}KkT}$$

$$\text{Thus, } -\frac{\Delta G^*}{RT} = \ln \frac{h\pi(\nu_A - \nu_B)}{\sqrt{2}KkT}$$

$$\text{Therefore, } -\Delta G^{*} = 2.303RT.\log_{10}\frac{h\pi(\nu_A-\nu_B)}{\sqrt{2}.KkT}$$

Now, if one makes the assumption for bicyclo(3.2.2)nona-6,8-diene (2) that at least one shift of about 5 Hz would be expected to emerge for slow (n.m.r. sense) exchange, one may calculate that the free energy of activation for the conformational interchange process (ΔG^{*}) at -140° is less than 8 kcal./mole. In bicyclo (3.2.2)nona-6,8-diene (2) there are several such distinct shifts which might be observed on comparing the spectra for the mobile and "frozen" systems, thus reducing, though not eliminating, the possibility of accidental isochrony (or near isochrony).

It would be expected that the free energies of activation for the bridge inversion processes in bicyclo(3.2.2)nona-6,8-dien-3-one (18) and the 2-one (44) would be smaller than that for the diene (2). This was due to the presence of an sp^2 hybridised carbon in the three carbon bridges of the ketones (18) and (44), causing less flexibility and thus effecting smaller free energies of activation and greater conformational mobility than in the case of the diene (2). Since no change with temperature was observed in the n.m.r. spectrum of the diene (2), it was not surprising that the spectra of the ketones (18) and (44) were also invariant over the same temperature range.

From the low temperature n.m.r. studies on the diene (2) and the ketones (18) and (44), the fact emerged that the activation energy for conformational interchange in the (3.2.2) bicyclic system was very small. Of course, the lower the temperature that could be attained, the greater would be the possibility of determining this activation energy. At present, the nature of the signal detector in the n.m.r. spectrometer used is such as to prevent the recording of spectra at temperatures lower than -150°. Since it was necessary, in the (3.2.2) system, to use temperatures lower than -150°, another spectroscopic method (e.s.r.) was investigated. To this end, the oxime of bicyclo(3.2.2)nona-6,8-dien-3-one (18) was prepared. This oxime (19) could be readily converted to the reasonably stable, conformationally mobile iminoxy radical (58) using lead tetraacetate in methylene chloride [21], the process being carried out in situ in the cavity of the e.s.r. spectrometer. The reason for using e.s.r. spectroscopy was that much lower temperatures could be attained, the limitation being the boiling point of the liquefied gas being used as coolant. (For liquid nitrogen, the commonest coolant used, this temperature is -196°). However, various technical factors have prevented the proposed study from being accomplished at present.

The attempt at determining the conformational mobility of the (3.2.2) system having been unsuccessful, studies on the conformational preference or biassing of related 2- and 3-substituted

derivatives were initiated. The remainder of this section of the discussion is concerned with these studies.

It may be useful at the outset to consider the various steric interactions which are experienced in the (3.2.2) system by considering bicyclo(3.2.2)non-6-ene (59). By analogy with the diene (2), one would expect the 6-ene (59) to have high conformational mobility. However, for the purposes of this section of the discussion, only the conformational extremes (59) and (59a) are considered. When the three carbon bridge is in the syn conformation (59), one would expect eclipsing interactions between the exo C-2 and C-4 protons and the exo C-8 and C-9 protons. There will also possibly be some interaction between the electron cloud of the endo C-3 hydrogen atom and the π-cloud of the C-6 - C-7 double bond. When the three carbon bridge adopts the anti conformation (59a), there is a fairly serious steric interaction between the exo C-3 proton and the exo C-8 and C-9 protons. There is possibly also a little interaction between the electron cloud of the double bond and the endo C-2 and C-4 protons. From these considerations, it has been proposed [22] that the syn conformation (59) was the more favoured of the two in the case of bicyclo(3.2.2)non-6-ene (59). However, all the aforementioned interactions in either conformation (59) or (59a) may be lessened by a slight "flattening" of the three carbon bridge as in (60) and (60a). A rise in strain energy in the molecule

would accompany this "flattening", which would reduce the viability of this process. This "flattening" of the three carbon bridge in the (3.2.2) bicyclic system has, in fact, been observed in the solid state in an X-ray diffraction study of exo-p-bromobenzoyloxybicyclo (3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (61) [1,23]. Of course, a substituent-carrying three carbon bridge alters this situation, as will be seen below, although the steric interaction factors play their part in determining the overall conformational bias of a molecule in the bicyclo(3.2.2)nonane system.

Investigations on stereochemistry of epoxidation of the (3.2.2) bicyclic system were conducted on exo-3-benzoyloxybicyclo (3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) and bicyclo (3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5). The stereochemistry of the epoxides formed was readily determined by heating the epoxide in water on a steam bath for several hours [24]. A typical exo epoxide exo anhydride (62) would remain unchanged by this treatment, whereas a typical endo epoxide exo anhydride (63) would be converted to the hydroxy-γ-lactonic acid (64) [24].

The epoxide from the exo-3-benzoate (7), prepared by trifluoroperacetic acid oxidation [25], remained unchanged after treatment in this way, and was thus deemed to have the exo configuration (65). By comparing the result of a similar epoxidation conducted on endo-tricyclo(3.2.2.$0^{2,4}$)non-6-ene-8,9-endo-dicarboxylic acid

anhydride (66), which also gave the exo epoxide (67) [25], it was concluded that the three carbon bridge adopted the syn conformation (7) preferentially in solution. This conclusion was supported by the results of n.m.r. studies conducted previously [1] on the exo-3-benzoate (7). Presumably, the approaching epoxidising reagent, trifluoroperacetic acid, would encounter less steric resistance to approach were it to approach the C-6 - C-7 double bond from the exo face, giving rise to the exo epoxide (65).

In contrast to this, no epoxide of bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) was isolated on treating (5) with trifluoroperacetic acid. The oil, which was obtained, was warmed with water in the normal way, and an infra-red spectrum of the resulting product indicated the presence of a hydroxy lactonic acid. Following methylation with diazomethane, an infra-red spectrum of the methylated product showed absorption bands for hydroxyl (3500 $cm.^{-1}$), ester (1748 $cm.^{-1}$), and lactone (1790 $cm.^{-1}$) groups, although the latter absorption was approximately 10 $cm.^{-1}$ higher than is normal for a typical γ-lactone. The conclusion, drawn from the above, was that the endo epoxide (63) was formed, but then opened under the reaction conditions to give the hydroxy lactonic acid (64) [24]. Unlike the exo-3-benzoate (7), the three carbon bridge in the unsubstituted adduct (5) may be assumed to be undergoing rapid conformational interchange as in bicyclo(3.2.2)nona-6,8-diene (2).

Attack of the epoxidising reagent would then take place from the endo side of the double bond, since the greatest steric hindrance to attack for this molecule would be caused by the anhydride group shielding the exo side of the double bond.

In systems such as bicyclo(2.2.1)hept-2-ene-5,6-endo-dicarboxylic acid anhydride (68), epoxidation in this way gave rise exclusively to the exo epoxide (69) [24], emphasising the steric control of the anhydride group over the stereochemistry of approach of the peracid. Under different reaction conditions, Alder and Mölls [26] prepared the epoxide of bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) to which they assigned the endo configuration (63) for the oxirane ring.

Further conformational studies on this system involved considerable use of n.m.r. and high resolution i.r. spectroscopy. The studies may be divided into those conducted on the C-3 substituted series and those on the corresponding C-2 substituted series. The results obtained from the C-3 series are discussed first, followed by those from the C-2 series. The syntheses of the compounds studied are discussed in part (A) of this discussion.

Whereas the three carbon bridges in bicyclo(3.2.2)nona-6,8-diene (2) and the ketones (18) and (44) were conformationally mobile, as previously discussed, the n.m.r. spectrum of 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16) was interpretable in terms of

an apparently fixed conformation for the three carbon bridge. Thus, the spectrum showed non-equivalence of and therefore geminal coupling between the protons on C-2 (and the equivalent C-4 protons). (See Table II for this and all subsequent n.m.r. spectra).

The spectrum of the benzoate (16) may be interpreted, see diagram (70), thus:

Proton A (7.89τ) appeared as a quintet with a geminal coupling J_{AB}= 12 Hz, and two cis vicinal couplings J_{AM}= 6 Hz, and J_{AX}= 6 Hz. Proton B (8.67τ) appeared as an octet at higher field than proton A due to the combined diamagnetic shielding by the π-electrons of the C-6 - C-7 double bond and by the σ-electrons of the C-1 - C-7 single bond. The eight line signal for proton B may be explained in terms of a geminal coupling J_{BA}= J_{AB}= 12 Hz, a trans vicinal coupling J_{BM}= 10 Hz (characteristically larger than a cis vicinal coupling constant such as J_{AM}) and a small coupling J_{BX}= 1 Hz. The large coupling observed for H_A with H_X and the small coupling of H_B with H_X implied dihedral angles of about 0° and 90°, from application of the Karplus relationship [27], for the angles H_X - C-1 - C-2 - H_A and H_X - C-1 - C-2 - H_B respectively.

The interpretation placed upon the above observations was that the three carbon bridge was not mobile but adopted a predominantly "frozen" configuration. Supporting evidence for this proposition was the observation that the olefinic protons appear in the

n.m.r. spectrum as two sets of equivalent protons on decoupling of the bridgehead protons, implying dissimilar environments for the pairs of protons on different double bonds.

Similarly, the n.m.r. spectrum of endo-3-benzoyloxybicyclo (3.2.2)non-6-ene (31) indicated that the three carbon bridge adopted an apparently "frozen" conformation. However, in the case of the mono-olefinic benzoate (31), the clarity of the pattern of the signals for the C-2 (and C-4) protons was diminished by the superimposition of the signal for the methylene protons on C-8 and C-9.

Extensive conformational studies, using n.m.r. and high resolution i.r. spectroscopy, were also conducted on a number of alcohols, i.e., bicyclo(3.2.2)nona-6,8-dien-3-ol (17), 3-methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20), endo-bicyclo(3.2.2)non-6-en-3-ol (25), exo-bicyclo(3.2.2)non-6-en-3-ol (26), and bicyclo (3.2.2)nonan-3-ol (24).

The n.m.r. spectrum of the dienol (17) was very similar to that of the corresponding benzoate (16) which was discussed above. The relative chemical shifts, splitting patterns and coupling constants for the signals assigned to the C-2 (and C-4) protons of the dienol (17) were similar to those of the C-2 (and C-4) protons of the benzoate (16), suggesting that, like the benzoate (16), the three carbon bridge of the dienol (17) also adopted a "frozen" conformation.

High resolution i.r. studies of the hydroxyl region (in CCl_4 solution) conducted on the dienol (17) (at high dilution to remove any intermolecular hydrogen bonding) showed the presence of intramolecular OH---π-hydrogen bonding (3587 $cm.^{-1}$) which indicated that the dienol (17) existed in solution as a mixture of conformers, (17) and (17a), and implied a degree of conformational mobility in this compound. A rough estimate of conformer population can be deduced by determination of molar absorptivity (ε_a) values and their ratios for free and bonded species. However, this remains purely a qualitative measurement since the molar absorptivity of a bonded hydroxyl (ε_b) tends to be larger than that of a free hydroxyl (ε_f). Also, a measure of the strength of the hydrogen bond may be obtained from the difference in wave number ($\Delta\nu$) between the absorption maxima of the free and bonded hydroxyls. Table III contains a summary of the high resolution i.r. studies conducted on the alcohols of the (3.2.2) bicyclic series discussed in this thesis. The i.r. spectrum of the hydroxyl region for the dienol (17) exhibited free hydroxyl absorption at 3621 $cm.^{-1}$ corresponding to conformation (17), OH---π-bonded absorption at 3587 $cm.^{-1}$ corresponding to the intramolecularly bonded conformer (17a) and an intermediate band situated at 3610 $cm.^{-1}$ which was probably due to rotameric absorption of the free hydroxyl [28] in a molecule having the conformation (17b). Thus, the i.r. spectroscopic information indicated that there was a certain

amount of bridge mobility in the dienol (17). The $\varepsilon_b/\varepsilon_f$ value of 0.143, obtained for this alcohol, indicated a preference on the part of the dienol for conformations (17) and (17b).

The apparent contradiction suggested by comparison of n.m.r. and i.r. spectroscopic evidence may be rationalised by proposing that the lifetime of the hydrogen bonded species (17a) is very short, too short for the signals from its n.m.r. spectrum to give any great contribution to the total spectrum, which arises from the coalescence of the spectra of the individual conformers (17), (17a) and (17b).

Spectroscopic investigation of 3-methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20), by n.m.r., revealed that this alcohol existed in a fixed conformation. However, in contrast to the dienol (17), for which i.r. studies indicated a mixture of conformers to be present, similar studies on 3-methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20) showed a single band in the hydroxyl region of the i.r. spectrum at 3580 $cm.^{-1}$, which indicated, in this case, the exclusive adoption of the hydrogen bonded conformation (20). This preferential conformation must be induced by the unfavourable steric requirements of the methyl group in the alternative conformation (20a), causing the contrast in conformer distribution (in solution) between the dienol (17) and the 3-methyldienol (20).

The n.m.r. spectrum of the 3-methyldienol (20) was also

interpretable in terms of a fixed conformation by reference to the splitting patterns observed for the C-2 (and C-4) protons. A fixed conformation requires non-equivalence of the C-2 (and C-4) protons as was indeed observed for this compound. Thus, see diagram (71), the spectrum was interpreted as follows:

Proton A appeared as a quartet (J_{AB}= 14 Hz, J_{AX}= 6 Hz) centred on 8.01τ, while proton B also appeared as a quartet (J_{BA}= 14 Hz, J_{BX}= 2 Hz), centred at 8.42τ. The fact that H_B was at higher field than H_A was probably due to diamagnetic shielding by the π-electrons of the C-8 - C-9 double bond and by the σ-electrons of the C-1 - C-8 single bond, as in the case of the benzoate (16) discussed above. Again, from application of the Karplus relationship [27], the magnitudes of J_{AX} and J_{BX} implied dihedral angles of about 0° and 90° for H_X - C-1 - C-2 - H_A and H_X - C-1 - C-2 - H_B respectively.

The n.m.r. spectra of the endo- and exo-bicyclo(3.2.2) non-6-en-3-ols, (25) and (26) respectively, were fairly similar. In both cases, the splitting patterns of the signals assigned to the C-2 (and C-4) protons in the alcohols (25) and (26) were similar to those for the equivalent protons in the dienol (17), apart from a slight loss of resolution due to overlapping of the signals for the C-8 and C-9 methylene protons. The evidence from n.m.r. spectroscopy was that the three carbon bridge in each alcohol adopted an

apparently fixed conformation as in the dienol (17).

A comparison of the n.m.r. spectra of the alcohols (25) and (26) was of further interest in that one could determine the shielding effect of the π-electrons of the double bond on the C-2 (and C-4) protons and on the C-3 proton. It was found that the signal for the endo C-2 proton in the endo alcohol (25) was, in fact, 0.06τ downfield relative to the signal for the comparable exo C-2 proton in the exo alcohol (26). Thus, one may reasonably conclude that the π-electrons of the double bond do not greatly contribute (if at all) to the shielding of the endo C-2 proton in the endo alcohol (25), nor probably, by extrapolation, do they contribute greatly to the shielding of similar protons in the benzoates (16) and (31), and in the dienol (17). However, while there is little difference in the chemical shifts of the C-2 protons in the alcohols (25) and (26), the signal for the C-3 proton in the exo alcohol (26) was 0.56τ upfield relative to the signal for the C-3 proton in the endo alcohol (25). This difference in chemical shift between the two C-3 protons showed that the π-electrons had a considerable shielding effect on the C-3 proton of the exo alcohol (26). By implication, it would then appear that the exo alcohol (26) adopted a biassed conformation, with the syn conformer (26) being preferred. Were the bridge "frozen" in the anti conformation (26a), one would not expect the π-electrons to shield the C-3 proton to any extent

whereas considerable shielding was observed, as stated above.

High resolution i.r. spectroscopic studies were also carried out on the endo and exo alcohols (25) and (26). The spectrum of the hydroxyl region of the endo alcohol (25) showed the presence of a free hydroxyl band at 3621 cm.$^{-1}$, and an intramolecularly OH---π-bonded hydroxyl band at 3581 cm.$^{-1}$, with $\varepsilon_b/\varepsilon_f = 0.303$, demonstrating that, in this alcohol, the anti conformer (25) is preferred over the syn conformer (25a) with its concomitant OH---π-hydrogen bond.

Recalling that in the dienol (17) $\varepsilon_b/\varepsilon_f = 0.143$, it may be seen that the endo-3-ol (25) exhibits more intramolecular hydrogen bonding than the dienol (17). This discrepancy may be readily rationalised in terms of steric interaction. In the endo-3-ol (25), when the bridge adopts the anti conformation (25) there is considerable interaction between the C-3 proton and the exo C-8 and C-9 protons, destabilising this conformer to some extent. In the comparable conformation (17) in the dienol, i.e. free hydroxyl, the C-8 and C-9 protons lie in the C-1 - C-8 - C-9 - C-5 plane and, thus, will not interact appreciably with the C-3 proton, the only unfavourable interaction being that between the C-3 proton and the π-electron cloud of the C-8 - C-9 double bond. In both cases, these steric interactions in (17) and (25) could be somewhat relieved by a slight flattening of the three carbon bridge. In any case, it may

be concluded from the $\varepsilon_b/\varepsilon_f$ values for the two alcohols (17) and (25) that, due to greater steric interaction in the anti conformer (25) of the endo-3-ol, this conformer is less favoured than the comparable conformer (17) of the dienol.

A high resolution i.r. spectrum of the exo-3-ol (26) showed the presence only of free hydroxyl absorption at 3622 $cm.^{-1}$ as was expected, thereby verifying the structural assignment.

The high resolution i.r. spectrum of bicyclo(3.2.2)nonan-3-ol (24) showed only free hydroxyl at 3623 $cm.^{-1}$ as might be expected. The n.m.r. spectrum was relatively uninformative due to the isochrony of the methylene protons. However, the presence of a "frozen" conformation for the alcohol (24) was indicated by the (at least) seven-line signal for the C-3 proton at 5.90τ. Schaefer [8] reported this signal as a nine-line A_2B_2X pattern with coupling constants of 5.5 Hz and 11.1 Hz, once more indicative of an immobile conformation for the alcohol (24).

Thus, whereas in the diene (2) and the ketones (18) and (44) the three carbon bridges were very mobile and adopted no preferred conformations, in those C-3 substituted compounds that have been discussed above there was adoption of a preferred conformation, although there was some retention of bridge mobility in every case except that of the 3-methyldienol (20). It may be noted that high resolution i.r. spectroscopy was necessary to detect this bridge

mobility, a technique not used by Fleming in his studies [29], which thus led him to postulate complete immobility of the three carbon bridges in (72) and (73).

Having completed the conformational studies on the C-3 substituted series, the preparation of the corresponding C-2 substituted series was initiated. Due to the greater asymmetry of compounds in the C-2 series, compared with compounds with substitution at C-3, n.m.r. spectroscopy was less useful as a diagnostic tool in determining conformation. Except for the dien-2-one (44), which had an extremely mobile three carbon bridge, it was not possible to detect the existence of any conformer preferences as was usually the case in the C-3 substituted series. In the C-2 substituted series, high resolution i.r. spectroscopy proved most useful in the determination of conformer population.

Studies in the C-2 series were conducted on bicyclo(3.2.2) nona-6,8-dien-2-ol (48), 2-methylbicyclo(3.2.2)nona-6,8-dien-2-ol (46), endo- and exo-bicyclo(3.2.2)non-6-en-2-ol, (13) and (14) respectively, and bicyclo(3.2.2)nonan-2-ol (49).

A high resolution i.r. spectrum of the dien-2-ol (48) revealed the presence of free hydroxyl and OH---π-bonded hydroxyl absorptions at 3621 cm.$^{-1}$ and 3585 cm.$^{-1}$ respectively, once again indicating the presence of a mixture of conformers (48) and (48a) in solution. The small value of $\varepsilon_b/\varepsilon_f$ = 0.285 indicated the preference

of this molecule for that conformation in which OH---π-bonding was not possible, i.e. (48).

The high resolution i.r. spectrum of the 2-methyldien-2-ol (46) exhibited twin bands at 3609 $cm.^{-1}$ (free hydroxyl) and 3585 $cm.^{-1}$ (OH---π-bonded hydroxyl). The $\varepsilon_b/\varepsilon_f$ ratio of 1.10, derived from the spectrum, indicated a 1:1 mixture of conformers (46) and (46a) in this compound when in solution. In contrast to the dien-2-ol (48), in which the non-OH---π-bonded conformer (48) was preferred, this result reflected the severe interaction of the methyl group with the C-6 - C-7 double bond in conformer (46) causing this conformer to be less favoured than the equivalent conformer (48) in the desmethyl dien-2-ol (48).

The value for $\varepsilon_b/\varepsilon_f$ = 0.940 obtained from the high resolution i.r. spectrum of endo-bicyclo(3.2.2)non-6-en-2-ol (13) also indicated an enhancement in the amount of the OH---π-bonded conformer (13a), when compared with the situation found in the dien-2-ol (48). This increased conformational biassing in the endo-2-ol (13) in favour of the anti conformation of the bridge (13a), giving OH---π-bonding, was most probably a result of the interaction of the exo C-2 (and C-4) protons with the exo C-8 (and C-9) protons, an interaction which was present in the alternative syn bridge conformation (13) and which would not be so severe in the dien-2-ol (48) when the three carbon bridge adopted the equivalent conformation (48).

It was not possible to interpret the n.m.r. spectrum of the endo-2-ol (13) in any great detail. However, the olefinic protons appeared as two separate, finely split triplets centred at 3.73τ and 4.02τ, thus showing the effect of the greater proximity of the hydroxyl group in the case of one olefinic proton. In contrast, the olefinic protons in the exo-2-ol (14) appeared as a one signal multiplet at 3.85τ. The n.m.r. spectra of the two alcohols were otherwise uninformative.

The high resolution i.r. spectrum of the exo-2-ol (14), as expected, showed only free hydroxyl absorption at 3621 $cm.^{-1}$, since it was geometrically impossible to form an OH---π-hydrogen bond in this molecule. However, it may be reasonable to assume that when the three carbon bridge adopted the syn conformation (14a), without the stabilising influence of a hydrogen bond and with the steric interaction between the hydroxyl group and the exo C-8 proton, this conformation (14a) would be rendered fairly unfavourable compared with the conformation with the bridge in the anti situation (14). When the bridge adopted the anti conformation (14), there would be little steric interaction between the hydroxyl group, the endo C-2 proton and any other proton in the molecule. Thus, it was proposed that the exo-2-ol (14) adopted a favoured conformation with the three carbon bridge in the anti configuration (14).

The spectroscopic properties of bicyclo(3.2.2)nonan-2-ol (49

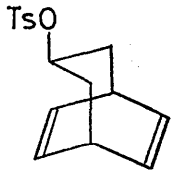
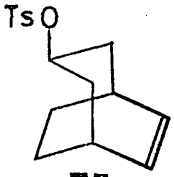
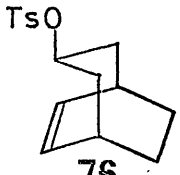
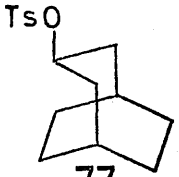
were similar to those of the 3-ol (24) in that they were relatively uninformative from a conformational viewpoint. Thus, the high resolution i.r. spectrum showed only the expected free hydroxyl band at 3622 cm.$^{-1}$.

From the above studies it may be seen that less information was obtained from the C-2 substituted series than was obtained from the C-3 substituted series due to the difficulty of interpreting the n.m.r. spectra of the former series. However, from these studies, a fair amount of information was now available on the conformational effects of substitution at the three carbon bridge in the (3.2.2) bicyclic series.

TABLE A

Acetolysis Rate Constants for the 3-Series of Tosylates.

Temp.: 73.6° (± 0.2°)

Tosylate	No. of runs	k_{av} (sec^{-1} x 10^4)	$k_{relative}$
 74	2	4.68 ± 0.15	1
 75	2	8.37 ± 1.06	1.8
 76	2	23.4 ± 1.1	5.0
 77	3	53.6 ± 1.2	11.4

k_{av} was taken as the average of two runs except for that of (77) which was the average of three runs.

(C) Solvolytic studies.

The alcohols which were prepared for the conformational studies on the bicyclo(3.2.2)nonane system, i.e. (13), (14), (17), (24), (25), (26), (48) and (49), were also required for solvolytic and reactivity studies on their tosylates. Once more, it proved convenient to group the compounds into two series, i.e. the series having the tosylate group at the C-3 position, and the corresponding series with the tosylate group at the C-2 position, henceforth referred to as the 3-series and the 2-series respectively.

The 3-series was comprised of the tosylates of bicyclo (3.2.2)nona-6,8-dien-3-ol (17), endo-bicyclo(3.2.2)non-6-en-3-ol (25), exo-bicyclo(3.2.2)non-6-en-3-ol (26) and bicyclo(3.2.2)nonan-3-ol (24). The tosylates of these alcohols were prepared by the standard method [17] as described in the experimental section and were all colourless solids of low crystallinity.

The i.r. spectra of these tosylates were undistinguished by any features worthy of comment, other than the characteristic tosylate bands at about 1180 $cm.^{-1}$. The n.m.r. spectra were very similar to those of the corresponding alcohols, with similar coupling constants and signal shapes.

The rates of acetolysis of these tosylates were measured as described in Appendix B, and for convenience are tabulated opposite in Table A.

From n.m.r. spectroscopy, the tosylates of the 3-series were regarded as having the preferred conformations shown. In these conformations, it might be expected that the C-6 - C-7 double bond would render some anchimeric assistance to solvolysis in the case of the dienyl tosylate (74) and the exo-6-en-3-yl tosylate (76) as in (78) and (79), thus causing stabilisation of the transition state. If this were the case, then one would have predicted that the rate of acetolysis of the exo-6-en-3-yl tosylate (76) would have been greater than that of the saturated 3-tosylate (77). One would also have predicted that the rate of acetolysis of the dienyl tosylate (74) would have been faster than that of the endo-6-en-3-yl tosylate (75) for similar reasons. In actual fact, the very opposite of these two predictions was observed, the effects having probably arisen from the inductive effects of the double bonds. Thus, it was concluded that there was no stabilisation of the transition state by the C-6 - C-7 double bond in either the dienyl tosylate (74) or the exo-6-en-3-yl tosylate (76). The reason may have been that the C-3 - C-6 (and C-3 - C-7) distance was too large for efficient orbital overlap of the empty orbital on C-3 and the π-electrons of the C-6 - C-7 double bond. Similar results have been obtained recently in studies of the exo- and endo-bicyclo(3.2.1)octan-3-yl tosylates, (80) and (81) [30], and the exo- and endo-bicyclo(3.2.1)oct-6-en-3-yl tosylates, (82) and (83) [7],

Another observation in the (3.2.2) system was that the exo-6-en-3-yl tosylate (76) underwent solvolysis 2.8 times faster than the endo-6-en-3-yl tosylate (75). This ratio was too small to be attributable to assistance to solvolysis by the double bond in the exo tosylate (76). Anchimeric assistance by the double bond had, in any case, been shown to be absent in the acetolysis of the exo tosylate (76) by reason of the solvolysis rates obtained above. A possible explanation of the difference in the rates may be that there was less steric hindrance to attack by the nucleophile in the exo tosylate (76) case, since the olefinic protons were remote from the line of approach of the nucleophile to the reaction site. However, in the endo tosylate (75) case, the exo C-8 and C-9 protons would hinder the approach of the nucleophile, causing a decrease in the rate of acetolysis compared with that of the exo tosylate (76). Thus, this offered a tentative explanation of the discrepancy in the rates of acetolysis of the endo and exo tosylates (75) and (76).

As a continuation of these studies, it was decided to determine the presence, if any, of β-hydrogen participation in the ionisation of the tosylates of the 3-series. For convenience, only bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74) and bicyclo(3.2.2) nonan-3-yl tosylate (77) were selected for study. It was necessary to prepare the 2,2,4,4-tetradeutero analogues of the two tosylates, and a summary of the method employed was as follows:

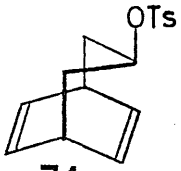
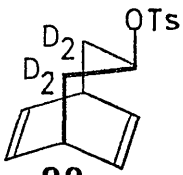
The 3-ones (18) and (28) were converted to the 2,2,4,4-tetradeutero-3-ones (84) and (85) [31], which were reduced to the 2,2,4,4-tetradeutero-3-ols (86) and (87), which in turn were converted to the 2,2,4,4-tetradeutero tosylates (88) and (89). The intermediates in the preparation of the 2,2,4,4-tetradeutero tosylates (88) and (89) were checked by mass spectrometry (n.m.r. spectroscopy in the case of the tosylates) for deuterium content. N.M.R. spectra of the 2,2,4,4-tetradeutero tosylates (88) and (89) showed that, insofar as could be determined, each tosylate molecule contained four deuterium atoms.

It may be shown that a C-D bond is 2.3 kcal./mole stronger than a C-H bond. Thus, in a process such as β-hydrogen participation in solvolysis, where stretching of a C-H bond is involved (90), one might expect that substitution of a hydrogen atom by a deuterium atom at the β-position would lessen this participation and so reduce the rate of solvolysis. In a reaction with a non-linear transition state (such as those under investigation would have) the presence of a β-hydrogen effect gives a typical rate ratio $k_H/k_D = 2.3$ [32] for each hydrogen atom, where k_H is the rate of reaction of the undeuterated species and k_D is the rate of reaction of the deuterated species. In the case of the tosylates (88) and (89) under consideration, the assumption was made for convenience that each β-hydrogen atom could make an equal contribution to stabilisation of the

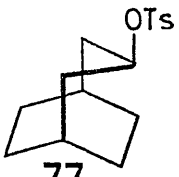
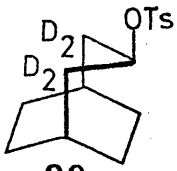
TABLE B

Rates of Acetolysis (Deuterium Labelling Studies).

Temp.: 73.6° (± 0.2°)

Tosylate	No. of runs	k_{av} (sec^{-1} x 10^4)	k_H/k_D
 **74**	2	k_H = 4.68 ± 0.15	
			2.18 ± 0.15
 **88**	2	k_D = 2.15 ± 0.01	

Temp.: 53.7° (± 0.2°)

Tosylate	No. of runs	k_{av} (sec^{-1} x 10^4)	k_H/k_D
 **77**	2	k_H = 12.0 ± 0.8	
			3.10 ± 0.18
 **89**	2	k_D = 3.88 ± 0.16	

transition state irrespective of its stereochemical configuration. Table B shows the results of the rate studies conducted on the tosylates (74), (77), (88) and (89).

For the saturated tosylates (77) and (89), there was a β-d_4 isotope effect, $k_H/k_D = 3.10 \pm 0.18$. Assuming that it was possible for all four deuterium atoms to participate equally in stabilisation regardless of their configuration, i.e. assuming a multiplicity rather than an additivity effect, this isotope effect represented a k_H/k_D ratio per β-deuterium atom of 1.33 ± 0.05. Similarly, in the case of the dien-3-yl tosylates (74) and (88), a β-d_4 isotope effect, $k_H/k_D = 2.18 \pm 0.15$ was obtained. This represented a k_H/k_D ratio per β-deuterium atom of 1.22 ± 0.04.

The values of the kinetic isotope effects per atom, k_H/k_D, obtained in this way, were reasonably close to unity. This inferred that, in the acetolyses of bicyclo(3.2.2)nonan-3-yl tosylate (77) at 53.7° and bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74) at 73.6°, β-hydrogen bridging was not very important in the stabilisation of the rate-determining transition state. By extrapolation, it may be reasonably assumed that it was also not important in the stabilisation of the rate-determining transition states in the acetolyses of the endo- and exo-bicyclo(3.2.2)non-6-en-3-yl tosylates (75) and (76). Thus, in the 3-series of tosylates, neither the olefinic double bonds (in the appropriate cases) nor β-hydrogen bridging

were effective in stabilisation of the rate-determining transition state.

Findings comparable to those above were reported in the recent solvolytic study [7] of the exo- and endo-bicyclo(3.2.1)oct-6-en-3-yl tosylates (82) and (83). However, the (3.2.2) system differed from the (3.2.1) system in that, whereas solvolysis of the (3.2.1) system was accompanied by rearrangement (see introduction, pps. 14-15), solvolysis of the 3-series of the (3.2.2) system occurred with no observed rearrangement of the (3.2.2) skeleton.

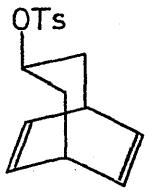
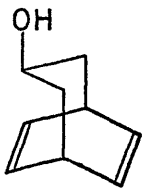
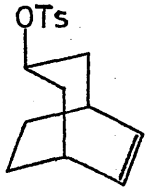
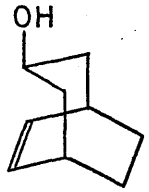
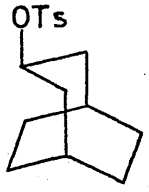
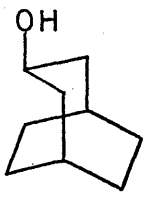
The products of acetolysis of bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74), endo-bicyclo(3.2.2)non-6-en-3-yl tosylate (75) and bicyclo(3.2.2)nonan-3-yl tosylate (77) only were examined, since only a very small amount of exo-bicyclo(3.2.2)non-6-en-3-yl tosylate (76) had been prepared, an amount which was sufficient only for the rate studies.

The acetolyses (on about 30 mg. of tosylate) were conducted as described in the experimental section. The acetate products were hydrolysed to the corresponding alcohols, since the latter were better resolved on analytical g.l.c., which was the main method used for product identification. Identification of the olefins formed in these acetolyses was not attempted, since the handling of very small amounts of the highly volatile olefins of the (3.2.2) series was very difficult. In each case, the acetolyses were conducted at 46°.

TABLE C

Products of Acetolysis of the 3-Series of Tosylates.

Temp.: 46°.

Tosylate	Alcohol obtained (via acetate)
	
74	**17**
	
75	**26**
	
77	**24**

The results are tabulated in Table C, shown opposite.

From the results opposite, it would appear that there was only direct replacement of tosylate by acetate in the 3-series, since no products other than 3-alcohols (and olefins) could be detected by g.l.c.. The replacement of the tosylate group by acetate in the endo-3-tosylate (75) gave the exo-3-acetate (91). After hydrolysis, no endo-3-ol (25) could be detected by high resolution i.r. spectroscopy, so that the acetate formed must have been exclusively the exo-3-acetate (91), indicating complete inversion at C-3 during the acetolysis (accompanied, of course, by competitive elimination processes). However, the mechanism of the above replacement process, giving inversion at C-3, could be either S_N2, or S_N1 with steric hindrance to approach of the acetate on one side of the molecule, caused by the departing tosylate group.

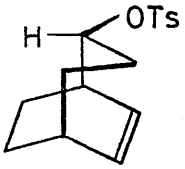
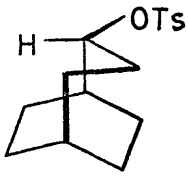
Thus, it may be seen that the 3-series of tosylates underwent solvolysis with no rearrangement to other bicyclic, tricyclic, or even tetracyclic systems, as far as could be detected.

In the 2-series of tosylates, it had been intended to prepare the tosylates of bicyclo(3.2.2)nona-6,8-dien-2-ol (48), endo-bicyclo(3.2.2)non-6-en-2-ol (13), exo-bicyclo(3.2.2)non-6-en-2-ol (14) and bicyclo(3.2.2)nonan-2-ol (49). However, it was not possible to prepare the tosylates of the dien-2-ol (48) or the exo-2-ol (14), as will be discussed below.

TABLE D

Acetolysis Rate Constants for the 2-Series of Tosylates.

Temp.: 73.6° (± 0.2°)

Tosylate	No. of runs	k_{av} (sec^{-1} x 10^4)	$k_{relative}$
 **92**	3	15.4 ± 1.8	2.9
 **93**	2	5.22 ± 0.03	1

The tosylates (92) and (93) [8] of the endo-6-en-2-ol (13) and the saturated 2-ol (49) were prepared by the standard method [17], both tosylates being colourless, microcrystalline solids. As in the case of the 3-series, the i.r. spectra of the tosylates (92) and (93) were not particularly worthy of comment, and the n.m.r. spectra were very similar to those of the corresponding alcohols, with similar signal patterns. The first-order rate constants and relative rate constants for acetolysis of the tosylates (92) and (93) are tabulated opposite in Table D.

Whereas, in the 3-series of tosylates, the unsaturated tosylates (74), (75) and (76) solvolysed slower than the saturated tosylate (77) due to inductive effects, in the 2-series, as is shown, the unsaturated tosylate (92) underwent acetolysis nearly three times faster than the saturated tosylate (93). This rate ratio was extremely small in terms of rate enhancement, and it was unlikely that it arose through anchimeric assistance by the homoallylic double bond assisting ionisation and stabilising the transition state. In the bicyclo(2.2.1)heptane system, for example, exo-norbornen-7-yl tosylate (94) underwent acetolysis 10^{11} times faster than the saturated norborn-7-yl tosylate (95) [33] due to anchimeric assistance to ionisation by the homoallylic double bond in (94), as depicted in (96). Also, in the same system, the endo-norbornen-7-yl tosylate (97) underwent acetolysis 10^{4} times faster than the saturated tosylate

(95) [34], the allylic cation (98) being formed by a C-1 ⇒ C-7 migration of the C-1 - C-6 bond, i.e. a further case of participation by the double bond.

However, whereas participation by the double bond was favoured by the geometry of the exo-norbornen-7-yl tosylate (94), in the (3.2.2) system neither the syn (92) nor the anti (92a) configuration, either of which the endo-2-tosylate (92) could adopt, was particularly favourable for double bond participation in assisting ionisation. By analogy with the endo-norbornen-7-yl tosylate (97) case, assistance to ionisation of endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92) could also have come from a C-1 ⇒ C-2 migration of the C-1 - C-8 single bond. However, the small enhancement in the rate of acetolysis of (92) over that of the saturated 2-tosylate (93) would indicate no participation by either the double bond or the C-1 - C-8 single bond in the case of the endo-2-tosylate (92). The proposition, that homoallylic participation by the double bond was not an important process in the acetolysis of (92), was borne out by the fact that the product from such a process, tetrahydrobarbaralyl acetate (99) identified as the alcohol (56), was a minor product (1.8%) in this acetolysis. The observed small enhancement in the rate of acetolysis of (92) over that of (93) may be merely due to some factor such as ease of departure of the tosylate leaving group.

The products of acetolysis of bicyclo(3.2.2)nonan-2-yl tosylate (93) had already been investigated by Schaefer et al.[8] and are described in the introduction to this study (see p. 13). As in the case of the 3-series, the acetolysis (for product analysis purposes) of endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92) was conducted on approximately 30 mg. of material. The acetate products were hydrolysed to the corresponding alcohols, since these were better resolved on g.l.c., which, once again, was the main method employed for product identification.

In the acetolysis of endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92), g.l.c. examination indicated a mixture of three solvolysis products, i.e. exo-bicyclo(3.2.2)non-6-en-2-ol (14) (93.5%), endo-bicyclo(3.2.2)non-6-en-2-ol (13) (4.7%), and tetrahydrobarbaralol (56) (1.8%). The above three products comprised at least 95% of the total products formed, since very little olefinic material was produced in this acetolysis. The product distribution was one which could reasonably be predicted. The small amount of tetrahydrobarbaralol (56) formed reflected the absence of a large enhancement in the rate of acetolysis of the endo-2-tosylate (92) over that of the saturated tosylate (93), showing that homoallylic participation by the double bond was not very significant in assisting ionisation or in stabilising the transition state in the acetolysis of (92). The large amount of exo-2-ol (14) formed was readily explained in

terms of a simple S_N2 type displacement of tosylate by acetate as in (100). Another possible explanation was attack of acetate at the cyclopropane ring of a tetrahydrobarbaralyl cation, as in (101), which then rearranged to the exo-bicyclo(3.2.2)non-6-en-2-yl acetate (102). Similarly, the small amount of endo-bicyclo(3.2.2)non-6-en-2-ol (13) could have arisen either from S_N1 displacement of tosylate by acetate, as in (103), or from a less favoured mode of attack by acetate on the tetrahydrobarbaralyl cation as in (104). Thus, although homoallylic participation of the double bond in (92), giving the tetrahydrobarbaralyl cation (105) as an intermediate, may not be important in causing rate enhancement, the cation (105) formed in this process may be important as an intermediate in determining the final product distribution. In a slightly different situation, such opening of the cyclopropane ring by acetic acid has been studied [35] for the case of endo-tricyclo(3.2.2.$0^{2,4}$)nonane-6,7-exo-dicarboxylic acid anhydride (106). Treatment of the adduct (106) with sulphuric acid in acetic acid gave a mixture of four products, of which the two major components were exo-5-acetoxymethylbicyclo(2.2.2)octane-2,3-exo-dicarboxylic acid anhydride (107) and exo-2-acetoxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (108), both having arisen from cleavage of the cyclopropane ring of the adduct (106).

Catalytic hydrogenation of the mixture of (13), (14) and

(56) obtained from the solvolysis of the endo-2-tosylate (92), using conditions which did not cleave cyclopropane rings (5% Pd-C in ethyl acetate), should have given a mixture of bicyclo(3.2.2)nonan-2-ol (49) (98.2%) and tetrahydrobarbaralol (56) (1.8%), had the products of solvolysis been correctly assigned. However, catalytic hydrogenation using these conditions gave three products, two of which were identified as bicyclo(3.2.2)nonan-2-ol (49) (34%) and tetrahydrobarbaralol (56) (1.8%). One may then assume that exo-bicyclo(3.2.2) non-6-en-2-ol (14) comprised 29.3% of the original mixture of alcohols from the solvolysis of (92) assuming that there was no bicyclo (3.2.2)non-3-en-2-ol (109) formed, since this also would give bicyclo(3.2.2)nonan-2-ol (49) on catalytic hydrogenation. The third product from the hydrogenation, comprising 64.2% of the mixture, had a smaller retention time than any of the other hydrogenated or unsaturated products. The retention time of the unknown alcohol indicated that it could be tertiary in nature. Further g.l.c. investigation eliminated bicyclo(3.2.2)nonan-1-ol (110) as being the unknown reduced alcohol. Using G.C.M.S., a mass spectrum of the unknown product was obtained. The molecular weight of this compound, obtained from the mass spectrum, was $M^+ = 138$. The most likely formula corresponding to a m/e value of 138 was, in this case, $C_9H_{14}O$, thus indicating the presence of three double bond equivalents (d.b.e.'s) in a molecule of the unknown alcohol. The bicyclic nature

of the endo-2-tosylate (92) accounted for two of these d.b.e.'s. Thus, the presence of a third d.b.e. indicated that the unknown alcohol either had a double bond or was tricyclic. Since this alcohol was obtained after the catalytic hydrogenation of the solvolysis product mixture, it was unlikely that the third d.b.e. was due to a double bond. It was proposed that this alcohol was a tricyclic, tertiary C_9 alcohol, with a possible structure such as (111) or (112).

Several attempts were made to prepare the tosylates of exo-bicyclo(3.2.2)non-6-en-2-ol (14) and bicyclo(3.2.2)nona-6,8-dien-2-ol (48), all of which were unsuccessful and are described in the experimental section of this thesis.

Normally, tosylates of secondary alcohols of the type under study formed over a period of 16 hours, needles of pyridine hydrochloride being obtained, if one employed the general method [17]. On dissolving exo-bicyclo(3.2.2)non-6-en-2-ol (14) in the appropriate amount of dry pyridine, treating the solution with two equivalents of p-toluenesulphonyl chloride, and allowing the mixture to stand in the refrigerator for 16 hours according to the general method [17], no needles of pyridine hydrochloride were observed. Normal work-up of the reaction gave an oil which proved to be a mixture (t.l.c.), no component of which was a tosylate, as evidenced from i.r. spectroscopy. From t.l.c. and i.r. evidence, it appeared also that a considerable amount of alcohol had not reacted. The

alcohol fraction, obtained in 40% yield from the exo-2-ol (14), proved to be a mixture of two components in the ratio 95:5 (g.l.c.). The minor component was identified as starting material, i.e. exo-bicyclo(3.2.2)non-6-en-2-ol (14), while the major component was a hitherto unencountered alcohol. Since its g.l.c. retention time was considerably less than that of the secondary alcohol component, it was felt that the unknown alcohol was tertiary. This proposition was further verified by the fact that Jones oxidation of the mixture oxidised the secondary alcohol (14) to the corresponding ketone (55), which could be separated by t.l.c. from the unchanged unknown alcohol. Thus, a pure sample of the unknown alcohol could be prepared, while simultaneously obtaining very strong evidence for its tertiary nature. Further evidence was obtained from a high resolution, high dilution i.r. spectrum, which showed a nearly symmetrical hydroxyl band at 3613 $cm.^{-1}$, again indicative of a tertiary alcohol. An n.m.r. spectrum showed no carbinol proton, a complex signal (12 H) centred on 8.40τ, and an olefinic signal corresponding to 2 protons, which was a doublet with J = 5 Hz. Apart from emphasising the fact that the unknown compound was a tertiary alcohol, spectroscopic evidence had been relatively uninformative so far.

To simplify the problem somewhat, a small sample of the unknown alcohol was catalytically hydrogenated for g.l.c. purposes.

The saturated alcohol was shown to have g.l.c. retention times (10% PEGA, 125°; 2% 20M PEG, 120°; 1% OV 15, 75°) identical to those of bicyclo(3.2.2)nonan-1-ol (110), prepared by the method of Grob et al.[36].

Thus, it seemed that the unknown alcohol was unexpectedly bicyclo(3.2.2)non-X-en-1-ol where X could be 2 (113), 3 (114), or 6 (115). Considering the simple pattern of the n.m.r. signal for the olefinic protons, implying a certain amount of equivalence, it was felt that X = 2 or 6 was unlikely, since the signal for the olefinic protons in either case would be expected to be quite complex, due to the contrasting environments of the two olefinic protons.

In order that maximum information could be gained from the n.m.r. spectrum, a spectrum of the unknown alcohol (17 mg.) was run in deuterochloroform (approximately 0.4 ml.) in the presence of tris(dipivalomethanato)europium, $Eu(DPM)_3$,[37] (45 mg.). The europium complex has recently been developed and causes a downfield shift of protons in its environment, the nearer the proton to the europium atom, the greater the observed shift.

Examination of the spectrum led to the conclusion that the unknown alcohol was in fact bicyclo(3.2.2)non-6-en-1-ol (115), despite the unexpected shape of the n.m.r. signal for the olefinic protons in the n.m.r. spectrum of the alcohol. A description of

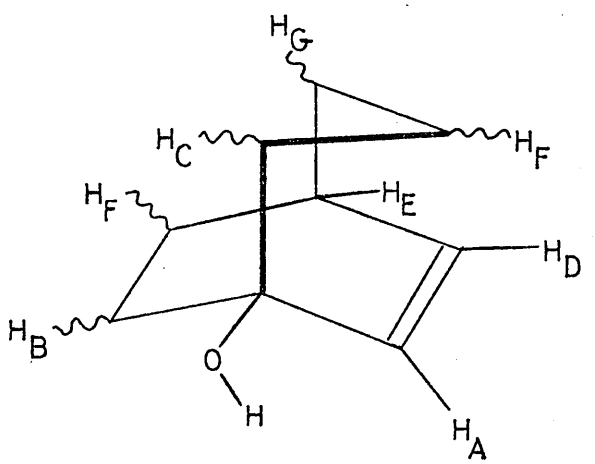
Taking chloroform as the internal standard at 2.73τ, the spectrum was as follows:

Proton	Integration	Chemical Shift (τ)	Description
H_A	1 H	-3.46	d, J = 10
H_B	2 H	+0.37	m
H_C	2 H	+0.92	m
H_D	1 H	+1.80	q, J = 10, 7.5
H_E	1 H	+5.29	m
H_F	4 H	+5.74	m
H_G	2 H	+6.53	m

d = doublet, m = multiplet, q = quartet.

Coupling constants (J) are in hertz (Hz).

The above spectrum and the observations from decoupling studies may be rationalised in terms of the structure of bicyclo (3.2.2)non-6-en-1-ol (115) as shown below.



the spectrum of the alcohol in the presence of the europium complex, with assignations of protons to signals, is shown opposite.

As final and conclusive proof of the structure of the unknown alcohol, the preparation of the novel bicyclo(3.2.2)non-6-en-1-ol (115) from the brosylate of 1-hydroxymethylbicyclo(2.2.2)oct-2-ene (116) was undertaken by a similar method to that of Grob et al. [36] in the preparation of bicyclo(3.2.2)nonan-1-ol (110). As shown in the appropriate diagram, there were two ways in which the unsaturated brosylate (117) could undergo ring expansion, giving either the bicyclo(3.2.2)non-6-en-1-yl cation (118) (Path 1), or the bicyclo(3.2.2)non-3-en-1-yl cation (119) (Path 2), both of which would then be trapped by the solvent (water) to give the corresponding alcohols (115) and (114). However, it was probable that Path 1 would be favoured since, in this pathway, the breaking of an sp^3 carbon - sp^3 carbon bond was involved, whereas Path 2 would involve the breaking of the stronger sp^3 carbon - sp^2 carbon bond. Since the bond-breaking step was most probably the rate-determining step, it was likely that the reaction would proceed more readily and therefore preferentially by Path 1 giving the desired bicyclo(3.2.2)non-6-en-1-ol (115). Similarly, in the bicyclo(2.2.1)heptane system, it was found that solvolysis in aqueous acetone of the tosylate (120) caused rearrangement to give the alcohol (121) by migration of the ethylene bridge, accompanied

by some unrearranged material (122). There was no observed migration of the unsaturated bridge [38].

Bicyclo(3.2.2)non-6-en-1-ol (115), prepared thus, was shown to be homogeneous by g.l.c. (10% PEGA, 125°; 2% 20M PEG, 125°; 1% OV 17, 75°) and t.l.c.. This independently synthesised alcohol (115) was then shown to have spectroscopic (i.r., n.m.r., m.s.) and g.l.c. (conditions as above) properties identical to those of the unknown alcohol, thus showing that the unknown alcohol was, in fact, bicyclo(3.2.2)non-6-en-1-ol (115).

The mechanism of the rearrangement of exo-bicyclo(3.2.2) non-6-en-2-ol (14) to bicyclo(3.2.2)non-6-en-1-ol (115), under tosylation conditions, is not known at present. A simple 1,2-hydride shift (123) may be postulated, although it is difficult to see where the driving force for such a rearrangement should come from. Furthermore, it is not at present known whether the tosylate of the exo-2-ol (14) forms and then rearranges or whether the alcohol (14) itself rearranges, although the absence of pyridine hydrochloride in the reaction mixture would indicate the latter process to be more likely. In short, the mechanism of this rearrangement may either be extremely simple or extremely complicated, and, at present, one may only speculate as to its nature.

On attempting to prepare the tosylate of bicyclo(3.2.2) nona-6,8-dien-2-ol (48) by the general method [17], no needles of

pyridine hydrochloride were deposited as in the case for exo-bicyclo(3.2.2)non-6-en-2-ol (14). Similarly, no tosylate ester was formed, as in the previous case. The oil obtained was purified by t.l.c. and the products with polarity corresponding to alcohols were examined by g.l.c. (10% PEGA, 125°; 2% 20M PEG, 125°; 1% OV 17, 75°), the dien-2-ol (48) (100 mg.) giving 5 mg. of such products. Two products were obtained in a 92:8 ratio, the minor product being bicyclo(3.2.2)nona-6,8-dien-2-ol (48). Catalytic hydrogenation of this mixture of products gave a further mixture in a similar ratio, the minor component being bicyclo(3.2.2)nonan-2-ol (49), while the major component was bicyclo(3.2.2)nonan-1-ol (110). By analogy with the case for exo-bicyclo(3.2.2)non-6-en-2-ol (14), it may therefore be reasonable to assume that the major product formed on attempting to prepare the tosylate of the dien-2-ol (48) was bicyclo(3.2.2)nona-6,8-dien-1-ol (124).

Why these alcohols (14) and (48) should behave in such a manner is rather mysterious. An obvious similarity is that both have a hydroxyl in a configuration exo to a double bond. In the case of the bicyclo(2.2.2)oct-5-en-2-yl tosylates, (125) and (126), it was found that the exo tosylate (125) was much more reactive than the endo tosylate (126), although the exo tosylate (125) apparently formed under the normal conditions [39]. The reason why increased reactivity of this type should prevent the formation of

the tosylates of the exo-2-ol (14) and the dien-2-ol (48) in the case of the bicyclo(3.2.2)nonane system is not known at present and remains open to speculation.

To summarise, whereas, in the 3-series, direct replacement of tosylate by acetate or elimination were the main solvolysis processes, in the 2-series, the solvolytic processes were more diverse, giving rise to a wider range of solvolysis products. Thus, the acetolysis of the saturated 2-tosylate (93) [8] gave the (3.2.2) bicyclic alcohols (24) and (49) as well as some bicyclo (3.3.1)nonan-2-ol (127). Neither the exo-2-ol (14) nor the dien-2-ol (48) formed tosylates under normal preparative conditions [17] but rearranged to give the tertiary alcohols (115) and (124) respectively. The endo-2-tosylate (92) upon acetolysis, followed by hydrolysis and catalytic hydrogenation, gave bicyclo(3.2.2)nonan-2-ol (49), a little tetrahydrobarbaralol (56), and a tertiary, tricyclic alcohol of uncertain structure as the major product. In final contrast, on solvolysis of the bicyclo(3.2.2)nonatrien-2-yl system (128) rearrangement to the barbaralyl system (129) occurred readily [40].

Thus, from the above, it may be seen that there was no apparent pattern arising from the various solvolytic studies conducted on the 2-substituted series of the (3.2.2) bicyclic system, in contrast to that observed for the corresponding 3-series.

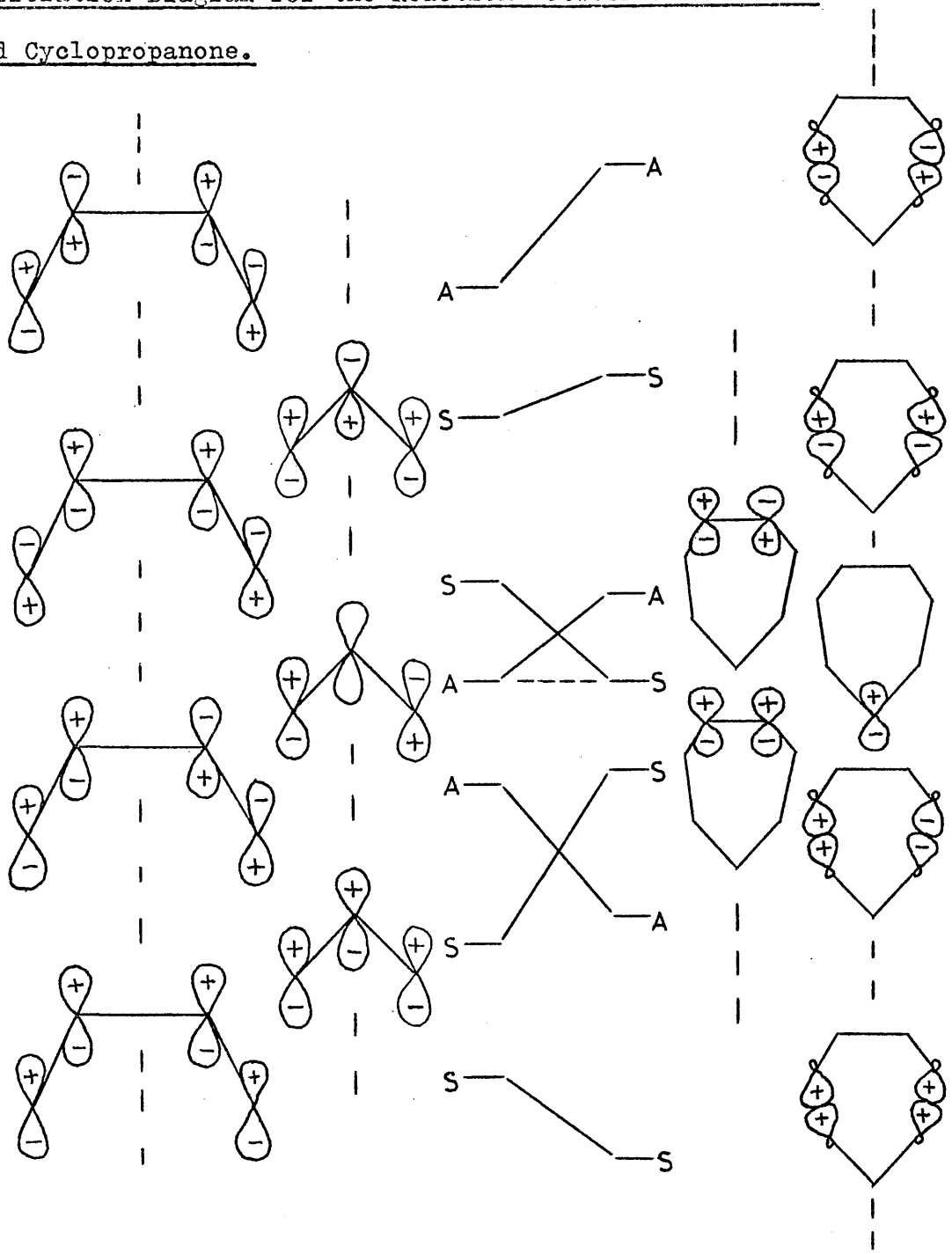
Addendum

Pyrolysis of bicyclo(3.2.2)non-6-en-3-one (27) and bicyclo(3.2.2) nona-6,8-dien-3-one (18).

It is thought probable that cyclopropanones are in equilibrium with an isomeric dipolar species (130). The latter could act as a 2π-electron system and, predictably, could combine with dienes in $_{\pi}4_{s} + _{\pi}2_{s}$ [41] processes. Thus, one might regard bicyclo (3.2.2)non-6-en-3-one (27), prepared by Jones oxidation of the corresponding endo-3-ol (25), as being formed by a $_{\pi}4_{s} + _{\pi}2_{s}$ addition of cyclopropanone to cyclohexadiene. Many reactions of this type have been reported, methylated cyclopropanones having been used [42]. By pyrolysing the ketone (27) it was felt that a cycloreversion could be induced, giving cyclohexadiene which could be identified from its n.m.r. spectrum. After heating the ketone (27) at 270° for 7 days in an evacuated and sealed n.m.r. tube, an investigation of the products by n.m.r. spectroscopy showed cyclohexadiene in fair abundance with a trace of benzene, possibly from dehydrogenation of the cyclohexadiene under the reaction conditions. Similarly, one might regard bicyclo(3.2.2)nona-6,8-dien-3-one (18) as being the result of the addition of cyclopropanone to benzene. In fact, a similar pyrolysis of the dienone (18) gave benzene as the major product.

A correlation diagram may be drawn for these cyclorever-

Correlation Diagram for the Reaction between a cis-Diene and Cyclopropanone.



For convenience, only the reacting orbitals are shown, the cyclopropanone moiety being regarded as (130). The vertical dotted lines represent the respective mirror planes. The horizontal dotted line represents the non-bonding level.

sion processes, the one correlation diagram sufficing for both reactions since the second double bond in the dienone (18) plays no part in the cycloreversion process. For the purposes of the Woodward-Hoffmann predictions, one may regard benzene as a cyclohexatriene with only two of the double bonds being involved in this cycloreversion process. In the correlation diagram, shown opposite, it was noted that each reactant bonding molecular orbital (m.o.) level could correlate with a product bonding m.o. level of like symmetry. A mirror plane (that indicated by the vertical dotted line on the diagram) was selected as the symmetry element to which the m.o.'s were either symmetric (S) or antisymmetric (A). The rules for the construction of such correlation diagrams are given in the Woodward and Hoffmann review on the conservation of orbital symmetry [41]. The correlation diagram under consideration does not prove in any way that the cycloaddition or cycloreversion processes being investigated are concerted, although, in fact, reactions of this type are considered to be concerted. From the information afforded by the correlation diagram, one may only say that, if the reaction is concerted, it should proceed readily under thermal conditions.

EXPERIMENTAL

All melting points, except sealed-tube, were recorded on a Kofler microscope hot-stage and are uncorrected unless otherwise stated. Sealed-tube melting points were recorded on a Gallenkamp melting point apparatus and are also uncorrected unless otherwise stated. Routine infra-red absorption spectra (liquid films and Nujol mulls) were recorded on Unicam S.P.200 or Perkin-Elmer 257 spectrophotometers, while solution infra-red absorption spectra (in carbon tetrachloride) were recorded on either a Perkin-Elmer 257 spectrophotometer or a Unicam S.P.100 double beam spectrophotometer, equipped with an S.P.130 sodium chloride prism grating double monochromator operated under vacuum. High resolution infra-red absorption spectra (at high dilution, i.e. approx. concn. 0.003M, in carbon tetrachloride) were recorded on this latter spectrophotometer. Ultra-violet absorption spectra were recorded on a Unicam S.P.800 spectrophotometer.

Nuclear magnetic resonance (n.m.r.) spectra were obtained on Varian T-60 and HA 100 spectrometers, using approximately 0.3M solutions in deuterochloroform, unless otherwise stated, with tetramethylsilane as internal standard. Coupling constants (J) were measured in hertz (Hz).

Analytical gas-liquid chromatography (g.l.c.) was carried

out on either a Pye Argon Chromatograph equipped with a β-ionisation detector, or a Perkin-Elmer F11 chromatograph equipped with a flame ionisation detector. Preparative gas-liquid chromatography was carried out using a Pye series 105 automatic preparative chromatograph. Thin layer chromatography (t.l.c.) was carried out using silica (Kieselgel G, Merck) for both analytical and preparative (prep. t.l.c.) purposes, using chloroform as eluant, unless otherwise stated.

Mass spectra were recorded on a G.E.C.-A.E.I. M.S.12 spectrometer and coupled gas chromatography-mass spectrometry determinations (G.C.M.S.) were recorded on an L.K.B.900 spectrometer. Figures quoted for molecular and other ions in the mass spectra refer to m/e values. M^+ refers to the molecular ion.

Light petrol refers to the petroleum fraction with boiling range 40-60°.

The seven-membered ring moieties used in the Diels-Alder reactions were prepared as described below.

Tropone (52).

This was prepared, as described in the literature [43], by oxidation of cycloheptatriene with selenium dioxide to yield tropone (52), b.p. 58-60°/0.05 mm., 20% (lit. b.p. 91-92°/4 mm., 25%).

$\nu_{max.}^{cm.^{-1}}$ (film): 1735 (w), 1705 (s) (carbonyl); 1635 (s), 1585 (s), 1522 (m), 1475 (m) (double bonds).

Cyclohepta-1,3-diene.

Cyclohepta-1,3-diene was prepared from cycloheptatriene by lithium-ammonia reduction at -60° as described in the literature [44]. The product was distilled giving a colourless liquid, b.p. 120-121° (lit. b.p. 121-122°/760 mm.).

Cyclohepta-3,5-dienol (131) [11].

Sodium borohydride (14 g.) was slowly added to a vigorously stirred solution of tropone (52) (21 g.) in methanol (500 ml.) and distilled water (70 ml.). Gas evolution occurred immediately. The mixture was stirred vigorously for 2 hrs. and residual hydride was decomposed by the dropwise addition of glacial acetic acid (70 ml.). After neutralisation with sodium carbonate solution, the mixture was

extracted with ether, and the combined ethereal extracts were dried ($MgSO_4$). The ethereal solution was evaporated in vacuo and the resulting yellow oil distilled to give the dienol (131) as a colourless oil (13.2 g., 63%) b.p. 72-73°/25 mm. (lit. b.p. 45-52°/6 mm.).

$\nu_{max.}^{cm.^{-1}}$ (film): 3500-3400 (s) (hydroxyl); 1612 (w) (double bond); 1049 (s), 1015 (s), 670 (s).

1-Benzoyloxycyclohepta-3,5-diene (6) [1].

Cyclohepta-3,5-dienol (131) (13.1 g.) in dry pyridine (120 ml.) was treated with redistilled benzoyl chloride (19.0 g.), added slowly in portions with swirling and cooling in ice. After allowing to stand overnight, the excess acid chloride was hydrolysed with water (20 ml.) and the solution extracted with ether (3x30 ml.). After washing the combined ethereal extracts with dilute sulphuric acid, saturated sodium bicarbonate solution, and brine, the solution was dried (Na_2SO_4), and the ether removed in vacuo. Distillation under reduced pressure afforded the benzoate as a pale yellow oil (20.1 g., 79%) b.p. 120-124°/0.25 mm. (lit. b.p. 99-103°/0.005 mm.).

$\nu_{max.}^{cm.^{-1}}$ (film): 1715 (s) (benzoate); 1600 (w), 1585 (w), 1275 (s), 725 (s).

Cyclohepta-3,5-dienone (42) [11].

A solution of tropone (52) (2.5 g.) in anhydrous ether

(50 ml.) was added dropwise to a vigorously stirred suspension of lithium aluminium hydride (0.71 g.) in anhydrous ether (100 ml.). The mixture was stirred rapidly at room temperature for a further 2 hrs. and was then added gradually to glacial acetic acid (25 ml.) with rapid stirring. After 10 mins. the mixture, which had separated into two layers, was neutralised with aqueous sodium bicarbonate. The layers were separated and the organic layer was washed with a 10% solution of sodium bicarbonate, dried ($MgSO_4$) and concentrated in vacuo. Distillation gave cyclohepta-3,5-dienone (42) as a colourless oil (1.13 g., 45%) b.p. 60-62°/12 mm. (lit. b.p. 40-45°/ 4 mm.).

$\nu_{max.}^{cm.^{-1}}$ (film): 3075 (m) (olefinic protons); 1705 (s) (ketone); 1595 (m), 695 (s) (double bonds).

Heating cyclohepta-3,5-dienone (42) above 70° gave rise to a yellow oil which was presumably the fully conjugated cyclohepta-2,4-dienone (43), the structure of which may be verified by the stereochemistry of the derived Diels-Alder adduct (41) with maleic anhydride.

The various Diels-Alder adducts used in this study were prepared as follows, and the application of stereochemical terms such as exo, endo, etc., to the (3.2.2) bicyclic system is explained in Appendix A.

Bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) [4]

A solution of cycloheptadiene (7.5 g.) and maleic anhydride (8.5 g.) in dry xylene (100 ml.) was heated under reflux for 5 hrs.. The xylene was removed by evaporation and, on cooling the resulting oil at -10°, the product slowly crystallised. The adduct (5) (10.5 g.) was recrystallised from n-hexane as white needles, m.p. 110-111° (lit. m.p. 110-111°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1850 (m), 1825 (m), 1760 (s) (anhydride); 1240 (s), 1083 (s), 725 (m).

Exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) and isomers [1].

A solution of 1-benzoyloxycyclohepta-3,5-diene (6) (19.7 g.), maleic anhydride (11.0 g., purified), and hydroquinone (0.2 g.) in dry xylene (60 ml.) was refluxed under nitrogen with vigorous stirring for 24 hrs.. The solution was allowed to cool to room temperature and then cooled in a freezing mixture at -10° for approximately 30 mins. by which time a white solid had precipitated.

The solid was collected, washed with cold xylene and sucked dry on a water pump. The solid was then dried for several hours at 50° in vacuo and the resulting white powder (9.1 g.) was recrystallised from chloroform/diisopropyl ether to give the pure exo-3-benzoate (7) as colourless platelets (7.9 g., 26%) m.p. 221-223° (lit. m.p. 222-225°). The filtrate from the reaction mixture, on evaporation afforded a gum which had been previously shown [1] to be a mixture of the endo-3-benzoate (8) and a 2-benzoate (9). The endo-3-benzoate (8) was slightly less polar on t.l.c. than the 2-benzoate (9); the two could be separated by either chromatography on an Alumina column (Woelm, acid washed) or by prep. t.l.c. on silica using chloroform/1% formic acid as eluant. Thus the 2-benzoate (9), obtained pure in modest yield, gave platelets, m.p. 152-155° (lit. m.p. 152-155°) on crystallisation from chloroform/diisopropyl ether. [For the determination of the endo stereochemistry of the benzoyloxy group in the 2-benzoate (9) see p.24].

The endo-3-benzoate (8) resisted purification due to the presence of some exo-3-benzoate (7) which had not completely precipitated from the original xylene solution, and also due to the fact that the chromatographic characteristics (other than g.l.c.) of these two benzoates, so far as was studied, were identical.

In a separate experiment [1], the amount of each isomer formed was determined to be as follows: exo-3-benzoate (7) 34%;

endo-3-benzoate (8) 11%; endo-2-benzoate (15) 18%; total yield, 63%.

G.L.C.

Column: 1% QF 1. Temperature: 210°. Flow rate: 42 ml./min.

Retention time (R_t) in inches.

	exo-3	endo-3	endo-2
R_t	3.94	3.25	4.01

$\nu_{max.}^{cm.^{-1}}$ (mixture) (CCl_4): 1872 (m), 1834 (m), 1784 (s) (anhydride); 1723 (s) (benzoate).

Endo-3-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (30).

Exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) (1.00 g.) dissolved in ethyl acetate (50 ml.) was exhaustively hydrogenated at atmospheric pressure over 30% Pd-C catalyst (200 mg., Engelhard). The reaction mixture was then filtered, the solvent removed in vacuo, and the resulting colourless solid was recrystallised from chloroform/diisopropyl ether to yield the desired product (0.905 g., 90%) m.p. 210-213°.

(Found: C, 68.64; H, 5.73. $C_{18}H_{18}O_5$ requires: C, 68.78; H, 5.77%).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1858 (m), 1772 (s) (anhydride); 1710 (s) (benzoate); 1288 (s), 941 (s), 724 (s).

G.L.C.: See Table I. N.M.R.: See Table II.

Exo-2-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (39).

Endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) (1.1 g.) in ethyl acetate (50 ml.) was hydrogenated as described above over 30% Pd-C (100 mg.). The normal work-up afforded a colourless solid which was recrystallised from chloroform/diisopropyl ether to give the title compound as colourless needles (1.0 g., 90%) m.p. 142-145°.

(Found: C, 68.55; H, 5.73. $C_{18}H_{18}O_5$ requires: C, 68.78; H, 5.77%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1848 (w), 1810 (w), 1765 (s) (anhydride); 1705 (s) (benzoate); 1285 (s), 959 (s), 931 (s).

G.L.C.: Table I. N.M.R.: Table II.

Exo-8,9-epoxy-endo-3-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (65).

Hydrogen peroxide (90%, 0.3 ml.) was added cautiously to a cooled solution of exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) (0.4 g.) in trifluoroacetic acid (2 ml.) according to the method of Fray [25]. After stirring the mixture overnight, water (5 ml.) was added and the resultant white precipitate was filtered, washed with water, dried, and recrystallised from chloroform/diisopropyl ether to give a quantitative yield of the epoxide (65) as fine, colourless, prismatic crystals,

m.p. 228-230°.

(Found: C, 65.85; H, 4.93. $C_{18}H_{16}O_6$ requires: C, 65.85; H, 4.91%.)

$\nu_{max.}^{cm.^{-1}}$ (KBr): 3020-2900 (m); 1855 (m), 1837 (m), 1774 (s) (anhydride) 1710 (s) (benzoate); 1270 (s), 1089 (s), 946 (s), 720 (s).

G.L.C.: Table I. N.M.R.: Table II.

In an attempt to open the oxirane ring [24], a small sample of the epoxide (65) (100 mg.) was warmed at 100° with water (5 ml.) for 3 hrs.. The water was then removed in vacuo and an infra-red spectrum (KBr disc) of the resulting white solid was recorded. The spectrum proved to be identical with the i.r. spectrum (KBr) of the epoxide (65), thus showing that cleavage of the epoxide ring had not occurred under the reaction conditions and inferring [24] that the epoxide ring had the exo configuration as shown (65) (see Discussion p. 44).

Attempted preparation of 8,9-epoxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (63).

Bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) (1.00 g.) was dissolved in trifluoroacetic acid (2 ml.) and the solution treated with hydrogen peroxide (90%, 0.6 ml.). After allowing the solution to stand overnight, water (5 ml.) was added as described [25] in the method of Fray. However, in this instance, no

precipitate formed, and correspondingly, the solution was further quenched with water (15 ml.). The resulting mixture was extracted with chloroform, the combined chloroform extracts washed with sodium carbonate, brine and then dried ($MgSO_4$). Removal of the solvent in vacuo gave an oil (0.55 g., 50%) which resisted crystallisation and slowly solidified to a glass. An infra-red spectrum (KBr) showed a strong hydroxyl absorption at 3420 $cm.^{-1}$ and no carbonyl bands above 1800 $cm.^{-1}$ implying the absence of an anhydride group. The only other intense band was a carbonyl absorption at 1770 $cm.^{-1}$.

A sample of this unknown compound was treated with water at 100° for 3 hrs. as described in the previous epoxidation. On removal of the water, a glass was recovered, the i.r. spectrum (KBr) of which was identical with the spectrum previously described, i.e. hydroxyl band, no anhydride bands. This sample was then dissolved in chloroform and treated with an excess of ethereal diazomethane. An i.r. spectrum (film) of the product showed a diminished hydroxyl absorption at 3500 $cm.^{-1}$ and two bands in the carbonyl region at 1775 $cm.^{-1}$ and 1730 $cm.^{-1}$. A further i.r. spectrum (CCl_4) once more showed two bands in the carbonyl region at 1790 $cm.^{-1}$ and 1748 $cm.^{-1}$.

From this evidence it was deduced (see Discussion p. 45) that the epoxide from bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) was the endo epoxide (63) which opened readily under the reaction conditions [24] to give the hydroxy γ-lactonic

carboxylic acid (64).

Bicyclo(3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid anhydride (41).

Cyclohepta-3,5-dienone (42) (1.1 g.), maleic anhydride (1.0 g.), and hydroquinone (0.1 g.) in dry xylene (40 ml.) were refluxed under nitrogen for 40 hrs.. Under the reaction conditions cyclohepta-3,5-dienone (42) rearranged to cyclohepta-2,4-dienone (43) prior to reaction thus yielding exclusively the 2-keto adduct (41) rather than the 3-keto adduct (132). The reaction mixture was then cooled in a freezing mixture at -10°, whereupon a solid slowly precipitated from the solution. The yield of solid could be increased by the addition of an approximately equal volume of diisopropyl ether to the xylene solution either before or during cooling. The solid was collected, dried, and recrystallised from chloroform/diisopropyl ether giving, after two crystallisations, the title compound as colourless, prismatic crystals (1.1 g., 52.5%) m.p. 156-158°.

(Found: C, 64.19; H, 4.89. $C_{11}H_{10}O_4$ requires: C, 64.06; H, 4.89%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1855 (m), 1770 (s) (anhydride); 1690 (s) (ketone); 1080 (s), 940 (s).

G.L.C.: Table I. N.M.R.: Table II.

2,2-Ethylenedioxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (45).

Bicyclo(3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid anhydride (41) (0.835 g.), ethylene glycol (3.72 g.), p-toluene-sulphonic acid (0.040 g.) and dry benzene (100 ml.) were refluxed with water separation for 12 hrs.. The solvent was then removed in vacuo, chloroform (100 ml.) added, the chloroform washed with 10% sodium carbonate solution, brine, and then dried ($MgSO_4$). Removal of the chloroform in vacuo yielded the desired ketal (45) (0.698 g., 83%). Recrystallisation from acetone/diisopropyl ether gave the ketal as colourless platelets (0.593 g.) m.p. 177.5-178.5°.

(Found: C, 62.43; H, 5.64. $C_{13}H_{14}O_5$ requires: C, 62.37; H, 5.64%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1860 (m), 1835 (m), 1770 (s) (anhydride); 1220 (m), 935 (s), 740 (m).

G.L.C.: Table I. N.M.R.: Table II.

Bicyclo(3.2.2)nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51) [14].

Tropone (52) (10.0 g.), maleic anhydride (15.7 g.), and hydroquinone (0.1 g.) were refluxed in dry xylene (100 ml.) for 4½ hrs.. The mixture was then cooled and allowed to stand at ice temperature for 14 hrs. by which time yellow crystals had separated. These were collected and recrystallised from ethyl acetate to give

the title compound as colourless platelets (12.1 g., 66%) m.p. 181-182.5° (lit. m.p. 181.5-182.5°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1840 (m), 1770 (s) (anhydride); 1665 (s) (ketone); 1270 (s), 1250 (s), 1220 (s), 1080 (s), 945 (s).

Bicyclo(3.2.2)nonan-2-one-6,7-exo-dicarboxylic acid anhydride (54) [14].

Bicyclo(3.2.2)nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51) (3.75 g.) in ethyl acetate (125 ml.) was hydrogenated over 30% Pd-C (0.375 g.). Filtration and evaporation of the solvent gave a white solid which was recrystallised from ethyl acetate giving the desired product as colourless prisms (3.60 g., 96%) m.p. 190-191° (lit. m.p. 191-192°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1862 (m), 1779 (s) (anhydride); 1696 (s) (ketone); 1240 (s), 1220 (s), 1194 (s), 948 (s).

Electrolytic Decarboxylation of Vicinal Dicarboxylic Acid Anhydrides to Olefins [5].

It has been reported [5] that the method described below converts vicinal dicarboxylic acids and their anhydrides to the corresponding olefins more conveniently and in higher yield than the familiar method using lead tetraacetate [45]. The electrolytic method has been applied to the synthesis of the (3.2.2) bicyclic system with some success. The modus operandi of the reaction and its work-up

are independent of the bicyclic reagent and are described below for a general case in order to avoid repetition:

The anhydride (approx. 0.005 mole) was dissolved in 10% aqueous pyridine (100 ml.) and triethylamine (2 ml.) was added. This solution was placed in the reaction vessel (in this case, a wide-mouthed glass jar of suitable dimensions) which was equipped with a stirrer and was cooled in a salt-ice freezing mixture. Due to the volatility of the products, a layer of petrol (60-80°) (approx. 20 ml.),which was immiscible with and less dense than the aqueous pyridine solution, was added to aid the trapping of any volatile material which may have been carried off by the carbon dioxide being evolved during the reaction. This stirred mixture was then electrolysed between two stationary cylindrical platinum wire gauze electrodes at 30-100 volts d.c. with an initial current of 0.8 amp.. Maximum yields were obtained after 5-6 hrs. during which time the cooling mixture was renewed periodically, the current dropped to approximately 0.5 amp., and the pyridine solution darkened. The reaction was worked up by quenching with water (approx. 300 ml.), extracting the resulting mixture with light petrol (or pentane in the case of very volatile products), washing the combined extracts with 5N hydrochloric acid, saturated sodium carbonate, brine and then drying the solvent ($MgSO_4$). Evaporation of the solvent gave the desired product in varying yield (usually inversely proportional to

the volatility of the product), and also, in some cases, in high purity.

(The above entire process will be referred to hereafter as "electrolysis".)

Bicyclo(3.2.2)nona-6,8-diene (2).

Electrolysis of bicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (5) (1.00 g.) gave the desired product (2), after purification by prep. t.l.c. (pentane) and sublimation, as a highly volatile, colourless, waxy solid (75 mg., 13%) m.p.(sealed tube) 84-86°.

(Found: C,82.81; H,9.41. C_9H_{12} requires: C,89.93; H,10.07%.)

The inaccuracy of the analytical figures was due to the extreme volatility of the diene which precluded accurate weighing and transfer to the analyser. A mass spectrum gave a parent ion at m/e 120 which corresponds to the molecular weight for the correct formula, i.e. C_9H_{12}, although, of course, this is not the only such correspondence.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1610 (m), 1283 (m), 1240 (m), 1179 (m), 1065 (s), 909 (s), 859 (s), 765 (s), 712 (s).

Mass spectrum: Major ions at m/e = 120, 105, 92, 91, 78, 65, 51.

G.L.C.: Table I. N.M.R.: Table II.

3-Benzoyloxybicyclo(3.2.2)nona-6,8-diene (16).

Electrolysis of exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) (1.05 g.) gave virtually pure 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16) (0.34 g., 41%) as a pleasant smelling, white, crystalline solid which was purified by prep. t.l.c. and sublimation to give a pure sample, m.p. 75-77.5°.
(Found: C, 80.04; H, 6.91. $C_{16}H_{16}O_2$ requires: C, 79.98; H, 6.71%.)
$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1716 (s) (benzoate); 1272 (s), 1113 (s), 767 (s), 716 (s).
G.L.C.: Table I. N.M.R.: Table II.

Endo-3-benzoyloxybicyclo(3.2.2)non-6-ene (31).

Endo-3-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (30) (500 mg.) was electrolysed in the usual fashion giving, after purification by prep. t.l.c. and sublimation, the desired benzoate (31) as a white, crystalline solid (220 mg., 58%) m.p. 79-82°.
(Found: C, 79.17; H, 7.56. $C_{16}H_{18}O_2$ requires: C, 79.32; H, 7.49%.)
$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1709 (s) (benzoate); 1283 (s), 1117 (s), 721 (s).
G.L.C.: Table I. N.M.R.: Table II.

2-Benzoyloxybicyclo(3.2.2)nona-6,8-diene (50).

Electrolysis of endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-

8,9-endo-dicarboxylic acid anhydride (15) (664 mg.) gave 2-benzoyloxybicyclo(3.2.2)nona-6,8-diene (50) (260 mg., 51.5%) as a colourless oil after purification in the normal manner.

(Found: C, 79.97; H, 6.71. $C_{16}H_{16}O_2$ requires: C, 79.98; H, 6.71%.)

$\nu_{max.}^{cm.^{-1}}$ (film): 1711 (s) (benzoate); 1277 (s), 1116 (s), 723 (s).

G.L.C.: Table I. N.M.R.: Table II.

Exo-2-benzoyloxybicyclo(3.2.2)non-6-ene (40).

Exo-2-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (39) (900 mg.) was electrolysed in the normal manner giving exo-2-benzoyloxybicyclo(3.2.2)non-6-ene (40) (195 mg., 28%) as a colourless oil.

(Found: C, 80.37; H, 7.50. $C_{16}H_{18}O_2$ requires: C, 79.32; H, 7.49%.)

$\nu_{max.}^{cm.^{-1}}$ (film): 1713 (s) (benzoate); 1272 (s), 1114 (s), 712 (s).

G.L.C.: Table I. N.M.R.: Table II.

The inaccurate analytical result obtained for this compound was due to a technical factor. This benzoate (40) was also characterised by its hydrolysis to the previously characterised exo-bicyclo(3.2.2)non-6-en-2-ol (14) (see p. 111).

Bicyclo(3.2.2)nona-6,8-dien-2-one (44).

(a) Via 2,2-ethylenedioxybicyclo(3.2.2)nona-6,8-diene (133).

2,2-Ethylenedioxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarbox-

ylic acid anhydride (45) (0.947 g.) was electrolysed in the normal manner giving the desired ketal (133) (119 mg., 17.4%) as a colourless oil. The ketal (133) could not be obtained completely pure due to its instability towards silica prep. t.l.c., the impurity being the ultimately desired bicyclo(3.2.2)nona-6,8-dien-2-one (44) (as shown by an i.r. spectrum) formed by hydrolysis of the ketal (133) when in contact with the silica. Since the ketal (133) was unstable, it was hydrolysed to the ketone (44) without further attempts at purification.

The ketal (133) (100 mg.) was dissolved in methanol (20 ml.) and 1N hydrochloric acid (20 ml.) and stirred for 1 hr. at room temperature. Water (20 ml.) was then added and the solution extracted with ether. The combined ethereal extracts were washed with 10% sodium bicarbonate solution, brine and then dried (Na_2SO_4). The ether was removed in vacuo giving bicyclo(3.2.2)nona-6,8-dien-2-one (44) (51 mg., 68%) as a colourless oil. The ketone (44) was purified by prep. t.l.c. and then sublimed giving a colourless oil at room temperature, this oil solidifying at 0°. The overall yield of bicyclo(3.2.2)nona-6,8-dien-2-one (44), calculated from bicyclo (3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid anhydride (41), by the above route, was 9.6%.

(b) Via electrolysis of bicyclo(3.2.2)non-6-en-2-one-8,9-endo-dicarboxylic acid anhydride (41).

Electrolysis of the above anhydride (41) (605 mg.) in the normal fashion gave, after prep. t.l.c. and sublimation, bicyclo (3.2.2)nona-6,8-dien-2-one (44) (75 mg., 19%) as a colourless oil. (Found: C, 80.42; H, 7.47. $C_9H_{10}O$ requires: C, 80.56; H, 7.51%.)

$\nu_{max.}^{cm.^{-1}}$ (film): 3095 (m) (olefinic C-H); 1704 (s) (ketone); 1613 (m) (C=C); 1142 (s), 897 (s), 709 (s).

$\lambda_{max.}^{n\text{-hexane}}$: 293 nm. (ε, 110).

G.L.C.: Table I. N.M.R.: Table II.

Bicyclo(3.2.2)non-6-en-2-one (55).

Bicyclo(3.2.2)nonan-2-one-6,7-exo-dicarboxylic acid anhydride (54) (1.30 g.) was electrolysed as described previously to give the desired ketone (55) which was obtained after purification by prep. t.l.c. and sublimation as a colourless, waxy solid (0.24 g., 28%) m.p. (sealed tube) 82-84° (lit.[16] m.p. 89-90°).

(Found: C, 79.16; H, 8.79. $C_9H_{12}O$ requires: C, 79.37; H, 8.88%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3095 (m) (olefinic C-H); 1709 (s) (ketone); 1633 (m) (C=C); 1178 (s), 914 (s), 719 (s).

$\lambda_{max.}^{cyclohexane}$: 296 nm. (ε, 133).

G.L.C.: Table I. N.M.R.: Table II.

Attempted preparation of bicyclo(3.2.2)nona-3,6,8-trien-2-one (53).

Bicyclo(3.2.2)nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51) (1.00 g.) was electrolysed in the usual manner giving a mixture of products which analytical t.l.c. showed to have one major component and many minor ones. This major component (28 mg.) was separated as a colourless oil by prep. t.l.c..

$\nu_{max.}^{cm.^{-1}}$ (film): 1685 (s) (ketone); 1643 (s) (conjugated C=C); 1143 (s), 906 (s), 839 (s), 704 (s).

The i.r. spectrum showed certain similarities to that of bicyclo(3.2.2)nona-6,8-dien-2-one (44). The n.m.r. spectrum of this oil was exceedingly complex. Moreover, a complete n.m.r. spectrum of bicyclo(3.2.2)nona-6,8-dien-2-one (44) could be discerned since it was easily recognisable by the shape and splitting of the signals. Nearly all the remaining signals were in the olefinic region and corresponded fairly closely to the n.m.r. spectrum of bicyclo(3.2.2) nona-3,6,8-trien-2-one (53) described in the literature [15] .

On analytical g.l.c. (Perkin-Elmer F11 chromatograph; 5% QF 1; 40°; nitrogen pressure, 14 lb./in.^{2}) two peaks were observed with retention times of 23.4 mins. and 25.9 mins. in the approximate ratio of 70:30 respectively. By cross injection, it was shown that the major peak had the same retention time as bicyclo(3.2.2)nona-6,8-dien-2-one (44), which, in conjunction with the spectroscopic evidence, suggested strongly that the electrolysis of bicyclo(3.2.2)

nona-3,6-dien-2-one-8,9-exo-dicarboxylic acid anhydride (51) occurred with partial concomitant reduction of the C-3-C-4 double bond to give mainly the dienone (44) in the presence of a minor amount of the desired trienone (53).

Bicyclo(3.2.2)nona-6,8-dien-3-ol (17).

To 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16) (100 mg.) in methanol (10 ml.) was added a solution of potassium hydroxide (0.3 g.) in water (3 ml.) and the solution refluxed for 1 hr.. Brine (15 ml.) was added, the mixture extracted with ether, the combined ether extracts washed with water, brine and then dried ($MgSO_4$). Removal of the solvent in vacuo gave virtually pure bicyclo(3.2.2) nona-6,8-dien-3-ol (17) (45 mg., 80%). Further purification by prep. t.l.c. and sublimation gave this alcohol (17) as a colourless, waxy solid m.p. 54-57°.

(Found: C, 79.14; H, 8.86. $C_9H_{12}O$ requires: C, 79.38; H, 8.89%.)

$\nu_{max.}^{cm.^{-1}}$ (film): 3350 (s) (hydroxyl); 1036 (s), 803 (m), 758 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 3617 (m) (hydroxyl); 1017 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Bicyclo(3.2.2)nona-6,8-dien-3-one (18).

To a stirred solution of bicyclo(3.2.2)nona-6,8-dien-3-ol (17) (45 mg.) in acetone (10 ml.) cooled in ice, Jones reagent was

added dropwise until the orange colouration persisted after which the reaction mixture was stirred for a further 10 mins.. Methanol was then added followed by ice and the mixture was extracted with ether. The combined ethereal extracts were washed with saturated sodium bicarbonate solution followed by brine and then dried ($MgSO_4$). Analytical t.l.c. showed one major component (R_f=0.7 approx.) which was the desired ketone (18) and several minor ones. Prep. t.l.c. followed by sublimation gave bicyclo(3.2.2)nona-6,8-dien-3-one (18) as a volatile, colourless, waxy solid (27 mg., 59%) m.p. 52-55°. (Found: C, 80.40; H, 7.43. $C_9H_{10}O$ requires: C, 80.56; H, 7.51%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1695 (s) (ketone); 1186 (s), 874 (s), 822 (s), 730 (s), 708 (s).

$\lambda_{max.}^{cyclohexane}$: 292 (ε, 22).

G.L.C.: Table I. N.M.R.: Table II.

Bicyclo(3.2.2)nona-6,8-dien-3-one oxime (19).

The oxime (19) was prepared according to the method of Vogel [46] as follows:

To hydroxylamine hydrochloride (0.1 g.) in water (1 ml.) was added a solution of sodium hydroxide (0.1 g.) in water (1 ml.) followed by bicyclo(3.2.2)nona-6,8-dien-3-one (18) (30 mg.). Enough ethanol to give a clear solution was added, and the reaction mixture was refluxed for 15 mins.. On cooling in ice, crystals separated

from this solution. These were filtered, washed with water and crystallised from petrol (60-80°) to afford colourless platelets of the oxime (19) (20 mg., 60%) m.p. 116-117°.

(Found: C, 72.34; H, 7.50; N, 9.07. $C_9H_{11}ON$ requires: C, 72.44; H, 7.43; N, 9.39%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3300 (s) (hydroxyl); 1034 (s), 977 (s), 948 (s), 816 (s), 750 (s).

G.L.C.: Table I. N.M.R.: Table II.

3-Methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20).

(a) To a solution of methyl magnesium iodide, prepared from magnesium (0.86 g.) and methyl iodide (5.11 g.), in dry ether (30 ml.), bicyclo(3.2.2)nona-6,8-dien-3-one (18) (350 mg.) was added slowly with stirring. The resulting mixture was refluxed for 4 hrs. and then stirred at 20° for a further 15 hrs.. Water was then added to destroy the excess Grignard reagent, followed by a little dilute sulphuric acid and the mixture was extracted with ether. The combined ether extracts were washed with saturated sodium carbonate solution, brine, and then dried (Na_2SO_4). Evaporation of the solvent in vacuo afforded the crude alcohol (20) (200 mg., 52%) which was found to be reasonably pure on investigation by analytical t.l.c.. Attempts at purification using silica t.l.c. were unsuccessful since the alcohol (20) appeared to rearrange while in contact with the

adsorbent. The structure of the rearranged product has not been definitely established but i.r. and n.m.r. evidence indicated that it may be the ether (21). Consequently, basic alumina (t.l.c., Woelm) was used in the purification of 3-methylbicyclo(3.2.2)nona-6,8-dien-3-ol (20). Following prep. t.l.c., sublimation gave the pure alcohol (20) as a colourless oil b.p. approx. 100°/4 mm..

(b) To a solution of bicyclo(3.2.2)nona-6,8-dien-3-one (18) (140 mg.) in dry tetrahydrofuran (10 ml.) was added a 3 molar solution of methyl magnesium chloride in tetrahydrofuran (4 ml., Alfa Inorganics) and the mixture refluxed for 4 hrs.. After similar work-up and purification to that described above, 3-methylbicyclo(3.2.2) nona-6,8-dien-3-ol (20) was obtained in only 24% yield.

$\nu_{max.}^{cm.^{-1}}$ (film): 3580 (s) (intramolecularly bonded hydroxyl); 3470 (s) (intermolecularly bonded hydroxyl); 1374 (s), 1110 (s), 1057 (s), 787 (s), 726 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 3581 (s) (intramolecularly bonded hydroxyl); 1381 (s), 1119 (s), 1063 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Due to the volatile nature of the alcohol (20), it was analysed as its 3,5-dinitrobenzoate derivative, which crystallised from ethanol as fine, colourless needles, m.p. 123-124°.

(Found: C, 59.18; H, 4.68; N, 8.08. $C_{17}H_{16}O_6N_2$ requires: C, 59.29; H, 4.68; N, 8.14%.)

An i.r. spectrum of the rearranged product from the alcohol (20) showed no hydroxyl or carbonyl absorption but did exhibit C-O stretching bands. The structure (21) proposed could also be partially rationalised on the basis of the n.m.r. spectrum of the rearranged product.

Bicyclo(3.2.2)nona-6,8-dien-2-ol (48).

(a) To 2-benzoyloxybicyclo(3.2.2)nona-6,8-diene (50) (106 mg.) in methanol (10 ml.), a solution of potassium hydroxide (300 mg.) in water (3 ml.) was added and the mixture refluxed for 1 hr.. Brine (20 ml.) was added, the mixture was extracted with ether, the combined ethereal extracts were washed with water, brine, and then dried ($MgSO_4$). Removal of the solvent in vacuo gave slightly impure bicyclo(3.2.2)nona-6,8-dien-2-ol (48) as a colourless semi-solid (45 mg., 76%). The material could not be purified by prep. t.l.c. (silica) since a small amount of impurity seemed to form from the alcohol (48) each time t.l.c. was attempted. Further attempted purification by sublimation also failed to remove this small amount (approx. 5%) of impurity.

(b) A mixture of sodium borohydride (150 mg.) and bicyclo(3.2.2) nona-6,8-dien-2-one (44) (150 mg.) in methanol (10 ml.) was stirred at room temperature for 1 hr.. Acetic acid (2 ml.) was then added to destroy any excess hydride and the resulting mixture was poured

into saturated sodium bicarbonate solution (30 ml.). The solution was then extracted with ether, and the combined ethereal extracts were washed with water, brine, and then dried (Na_2SO_4). Removal of the solvent in vacuo gave the desired bicyclo(3.2.2)nona-6,8-dien-2-ol (48) (138 mg., 91%) as a colourless semi-solid.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3400 (s) (hydroxyl); 1021 (s), 899 (m), 719 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3617 (m) (hydroxyl); 1018 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Attempted analysis of bicyclo(3.2.2)nona-6,8-dien-2-ol (48) itself proved unsuccessful. It was thus analysed as its 3,5-dinitrobenzoate derivative which was crystallised from ethanol as fine, colourless needles, m.p. 110-113°.

(Found: C, 58.31; H, 4.27; N, 8.36. $C_{16}H_{14}O_6N_2$ requires: C, 58.18; H, 4.27; N, 8.48%.)

2-Methylbicyclo(3.2.2)nona-6,8-dien-2-ol (46).

To bicyclo(3.2.2)nona-6,8-dien-2-one (44) (120 mg.) in dry tetrahydrofuran (10 ml.), a 3 molar solution of methyl magnesium chloride in dry tetrahydrofuran (4 ml.) (supplied by Alfa Inorganics) was added and the reaction mixture was refluxed for 2½ hrs., after which time water (25 ml.) was added to destroy the excess Grignard reagent. The mixture was extracted with ether, the combined ethereal extracts were washed with brine and then dried ($MgSO_4$). Removal of

the solvent in vacuo gave virtually pure 2-methylbicyclo(3.2.2)nona-6,8-dien-2-ol (46). Prep. t.l.c. gave the pure alcohol (46) (128 mg., 95%) which could be further purified by sublimation to give a colourless oil, m.p. 5-10° approx..

(Found: C, 79.86; H, 9.24. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3375 (s) (hydroxyl); 1106 (s), 925 (s), 751 (s), 690 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3601 (m) (free hydroxyl); 3580 (m) (bonded hydroxyl); 1378 (s), 1309 (s), 926 (s), 837 (s), 691 (s), 669 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Attempted preparation of 2-methyl-2-bromobicyclo(3.2.2)nona-6,8-diene (47).

The method employed triphenylphosphine dibromide [12] (134) and was as follows:

Under dry nitrogen, triphenylphosphine (655 mg.) in carbon tetrachloride (20 ml.) was added to a 100 ml. three-necked flask equipped with a stirrer, a pressure equalising dropping funnel, a gas inlet tube and a water condenser. The solution was cooled to below 6° and was then treated gradually, with stirring, with a solution of bromine (400 mg., 0.13 ml.) in carbon tetrachloride (10 ml.). The halogenide, triphenylphosphine dibromide (134), separated from the solution as a flocculent, pale-yellow solid. This was treated

with 2-methylbicyclo(3.2.2)nona-6,8-dien-2-ol (46) (335 mg.) in carbon tetrachloride (10 ml.) and the reaction mixture refluxed for 1½ hrs.. On evaporation of the carbon tetrachloride in vacuo, a white solid (triphenylphosphine oxide) was obtained which was thoroughly washed with cold light petrol. The petrol washings were combined and then removed in vacuo giving a brown oil. The oil was sublimed to remove any remaining phosphorus containing compounds and the resulting colourless oil (150 mg., 32%) was finally purified by prep. t.l.c. giving apparently pure 2-methyl-2-bromobicyclo(3.2.2) nona-6,8-diene (47) (60 mg.). Analytical g.l.c. (1% SE 30; 75°; 47 ml./min.) showed that the supposedly pure product was in fact a mixture of two components in approximately equal amounts with retention times of 16.2 mins. and 18.7 mins.. An infra-red spectrum showed no hydroxyl but was otherwise uninformative as was the n.m.r. spectrum of the mixture.

Due to the poor yield and the fact that the reaction gave two products, it was felt that further study on this line would not prove fruitful.

Endo-bicyclo(3.2.2)non-6-en-2-ol (13) and exo-bicyclo(3.2.2) non-6-en-2-ol (14).

Sodium borohydride (500 mg.) was added slowly to bicyclo (3.2.2)non-6-en-2-one (55) (640 mg.) in methanol (30 ml.) and the

reaction mixture was stirred for 1 hr.. The excess borohydride was destroyed with acetic acid followed by saturated sodium bicarbonate solution to neutralise the excess acetic acid. The aqueous mixture was extracted with ether, the combined ethereal extracts washed with sodium bicarbonate solution, brine, and then dried (Na_2SO_4). Removal of the solvent in vacuo gave a colourless, low-melting solid (631 mg., 93%). Analytical g.l.c. (10% PEGA; 125°) indicated a mixture of two compounds in the ratio 60:40, i.e. the expected endo-bicyclo(3.2.2)non-6-en-2-ol (13) and exo-bicyclo(3.2.2)non-6-en-2-ol (14). Prep. t.l.c. purification of these alcohols was accomplished on silver nitrate impregnated silica but percentage recovery of each component was fairly small (about 20%) since the separation of the bands was not particularly good. From high dilution i.r. studies on these pure samples it was shown that the major component of the mixture was the endo isomer (13) since the i.r. spectrum of this component showed the presence of intramolecular OH---π-hydrogen bonding which is geometrically impossible for the exo isomer (14).

The alcohols were separated most efficiently using preparative g.l.c. with the following conditions:

Column: 2% 20M Carbowax (7 ft.). Temperature: 130°.

Flow Rate: 150 ml./min..

	R_t (mins.)
endo-2-ol (13) :	17.2
exo-2-ol (14) :	20.7

In this manner, a pure sample of each alcohol was obtained:

Endo-bicyclo(3.2.2)non-6-en-2-ol (13).

This alcohol (13) was obtained as a volatile, colourless, crystalline solid, m.p. (sealed tube) 166-168°.

(Found: C, 78.31; H, 10.30. $C_9H_{14}O$ requires: C, 78.21; H, 10.21%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3400 (s) (hydroxyl); 1032 (s), 985 (m), 720 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3622 (m) (free hydroxyl); 3581 (m) (intramolecularly bonded hydroxyl); 1026 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Exo-bicyclo(3.2.2)non-6-en-2-ol (14).

This alcohol (14) was, once again, a volatile, colourless, crystalline solid, m.p. (sealed tube) 150-152°.

(Found: C, 78.16; H, 10.04. $C_9H_{14}O$ requires: C, 78.21; H, 10.21%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3400 (s) (hydroxyl); 1644 (m), 1053 (s), 1032 (s), 998 (s), 718 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3621 (m) (free hydroxyl); 1046 (s), 1022 (s), 991 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

The stereochemistry at C-2 in 2-benzoyloxybicyclo(3.2.2) non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) was hitherto not known. However, catalytic hydrogenation of this adduct to the corresponding nonane (39), followed by electrolysis, and then hydrolysis of the resulting benzoate (40) gave (by g.l.c. and spectroscopic comparison) exo-bicyclo(3.2.2)non-6-en-2-ol (14). From this, it was concluded that 2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) had an endo benzoyloxy group at C-2.

Bicyclo(3.2.2)nonan-2-ol (49).

A mixture of endo- and exo-bicyclo(3.2.2)non-6-en-2-ols, (13) and (14), (210 mg.) in ethyl acetate (15 ml.) was exhaustively hydrogenated over 10% Pd-C (50 mg.). The solution was filtered and the solvent removed in vacuo to give bicyclo(3.2.2)nonan-2-ol (49) (201 mg., 95%). The alcohol (49), after further purification by prep. t.l.c. and sublimation, was obtained as a colourless, crystalline solid, m.p. (sealed tube, corrected) 191-194° (lit.[8] m.p. 186-190°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3400 (s) (hydroxyl); 1033 (s), 999 (m).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Endo-bicyclo(3.2.2)non-6-en-3-ol (25).

Endo-3-benzoyloxybicyclo(3,2.2)non-6-ene (31) (80 mg.) was hydrolysed in the usual manner as described previously, giving, after prep. t.l.c. and sublimation, endo-bicyclo(3.2.2)non-6-en-3-ol (25) (35 mg., 77%) as a colourless, crystalline solid, m.p. (sealed tube) 79-80°.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3300 (s) (hydroxyl); 1058 (s), 1034 (s), 786 (m), 730 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3621 (m) (free hydroxyl); 3581 (w) (intramolecularly bonded hydroxyl); 1053 (s), 1027 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Endo-bicyclo(3.2.2)non-6-en-3-ol (25) was analysed as its 3,5-dinitrobenzoate which was crystallised from ethanol giving off-white needles, m.p. 148-150°.

(Found: C, 57.70; H, 4.94; N, 8.39. $C_{16}H_{16}O_6N_2$ requires: C, 57.83; H, 4.85; N, 8.43%.)

Bicyclo(3.2.2)nonan-3-ol (24).

Bicyclo(3.2.2)nona-6,8-dien-3-ol (17) (120 mg.), in ethyl acetate (15 ml.), was exhaustively hydrogenated over 10% Pd-C (40 mg.). The solution was filtered and the ethyl acetate removed in vacuo to give bicyclo(3.2.2)nonan-3-ol (24) (117 mg., 95%) which on further purification by prep. t.l.c. and sublimation gave the alcohol (24)

as a camphoraceous, colourless, crystalline solid, m.p. (sealed tube, corrected) 143-145° (lit.[8] m.p. 105-107°).

(Found: C, 77.12; H, 11.48. $C_9H_{16}O$ requires: C, 77.09; H, 11.50%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3300 (s) (hydroxyl); 1078 (m), 1037 (s).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Bicyclo(3.2.2)non-6-en-3-one (27).

Endo-bicyclo(3.2.2)non-6-en-3-ol (25) (60 mg.), stirred in acetone (15 ml.) at 0°, was treated with Jones reagent until the orange colouration persisted, after which the reaction mixture was stirred for a further 10 mins.. Methanol was added, followed by ice, and the mixture extracted with ether. The combined ether extracts were washed with sodium bicarbonate solution, brine and then dried ($MgSO_4$). Removal of the solvent in vacuo gave a colourless oil which, on purification by prep. t.l.c., gave bicyclo(3.2.2)non-6-en-3-one (27) (36 mg., 61%). Further purification by sublimation gave the ketone (27) as a colourless, waxy solid, m.p. (sealed tube) 94-95°.

(Found: C, 79.14; H, 8.81. $C_9H_{12}O$ requires: C, 79.37; H, 8.88%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1699 (s) (ketone); 1198 (m), 985 (m), 728 (m).

$\lambda_{max.}^{cyclohexane}$: 291 nm. (ε, 25).

G.L.C.: Table I. N.M.R.: Table II.

Attempted preparation of bicyclo(3.2.2)non-6-en-3-one (27) from bicyclo(3.2.2)nona-6,8-dien-3-ol (17).

Bicyclo(3.2.2)nona-6,8-dien-3-ol (17) (60 mg.) was treated with 85% phosphoric acid (2.8 ml.) and just enough methanol to make the mixture homogeneous (approx. 2 ml.) according to the method of Prelog [47]. The mixture was allowed to stand at room temperature for 5 days after which time it was quenched with water (15 ml.) and the resulting mixture extracted with light petrol. The combined petrol extracts were washed with sodium carbonate solution, brine and then dried (Na_2SO_4). Removal of the solvent in vacuo gave an oil which was examined by prep. t.l.c.. Several products had been formed but from a consideration of R_f values only two minor products could possibly be the desired bicyclo(3.2.2)non-6-en-3-one (27). These products were further examined by g.l.c. (5% QF 1; 100°; 54 ml./min.) which showed that neither product was the desired ketone (27). Thus the C-3 - C-6 hydride shift, as in (135), necessary for the conversion of the dienol (17) to the ketone (27), did not occur under these conditions.

Exo-bicyclo(3.2.2)non-6-en-3-ol (26).

(a) Attempted preparation from hydride reduction of bicyclo(3.2.2) nona-6,8-dien-3-ol (17).

Bicyclo(3.2.2)nona-6,8-dien-3-ol (17) (10 mg.) was

stirred with a large excess of lithium aluminium hydride (approx. 40 mg.) in dry ether (5 ml.) at room temperature for 24 hrs.[9]. Examination of the reaction after this time by g.l.c. (10% PEGA; 125°) showed only starting material to be present.

A similar reaction was conducted using refluxing dry tetrahydrofuran (5 ml.) as the reaction milieu. However, after 24 hrs., g.l.c. (same conditions) once more showed only starting material to be present.

(b) Attempted preparation from exo-3-benzoyloxybicyclo(3.2.2) non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) by double bond protection.

An attempt was made to protect the double bond of the exo-3-benzoyloxy adduct (7) as the vic-bromohydrin using N-bromo-acetamide. However, after stirring the benzoate adduct (7) (50 mg.) in 6:1 acetone:water (10 ml.) with a fivefold excess of N-bromo-acetamide for 24 hrs. at room temperature, only starting material was recovered as shown by i.r. spectroscopy.

(c) Attempted preparation by selective catalytic hydrogenation of 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16).

It was hoped that the slowness of the catalytic hydrogenation of the double bond in exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-

8,9-endo-dicarboxylic acid anhydride (7) was partially due to the steric congestion at the catalyst surface caused by the three carbon bridge, thus rendering possible a preferential catalytic hydrogenation of the less hindered double bond in 3-benzoyloxybicyclo(3.2.2) nona-6,8-diene (16). Therefore, 5% Pd-C (50 mg.) in ethyl acetate (10 ml.) was allowed to equilibrate with hydrogen before adding 3-benzoyloxybicyclo(3.2.2)nona-6,8-diene (16) (120 mg.) in ethyl acetate (5 ml.) by means of a dropping-funnel and a two-necked hydrogenation flask. The rate of hydrogen uptake did not change visibly after one equivalent of hydrogen had reacted and by the time the benzoate (136) had been removed from the hydrogen atmosphere reduction of both double bonds had occurred, as shown by an n.m.r. spectrum of the reaction product (136).

(d) Investigation of the hydride reduction of bicyclo(3.2.2) non-6-en-3-one (27).

Lithium aluminium hydride (40 mg.) was added to a stirred solution of bicyclo(3.2.2)non-6-en-3-one (27) (20 mg.) in dry ether (3 ml.). The reaction mixture was stirred for 2 hrs. at room temperature, after which time the excess hydride was destroyed with saturated sodium sulphate solution. The ethereal solution was dried ($MgSO_4$), filtered, and the ether removed in vacuo to give an oil. The two possible endo and exo alcohols, (25) and (26), were found

to be inseparable on a variety of g.l.c. columns (10% PEGA, 2% 20M PEG, 10% 20M PEG, and 5% QF 1) and thus high resolution i.r. spectroscopy was used to estimate the amount of each isomer present in the mixture since there were slight differences in the high resolution i.r. spectra of the two alcohols (25) and (26). In this way, the ratio of endo (25) to exo (26) obtained in this reduction was found to be approximately 1:1.

(e) Investigation of the sodium-ethanol reduction of bicyclo(3.2.2) non-6-en-3-one (27) [48].

Finely divided pieces of sodium (120 mg.) were gradually added to a stirred solution of the ketone (27) (20 mg.) in dry ethanol (3 ml.). Once all the sodium had reacted, iced water (6 ml.) was added and the solution extracted with ether. The combined ethereal extracts were washed with water, brine and then dried ($MgSO_4$). Removal of the ether in vacuo gave an oil which analytical t.l.c. showed to contain approximately 25% starting material. Prep. t.l.c. gave a sample of the mixture of alcohols, (25) and (26), uncontaminated by starting material. Once more, a high resolution i.r. spectrum was employed to determine the endo:exo ratio which was again found to be approximately 1:1.

It may be seen from the above two reductions that there is no selectivity in the reduction of bicyclo(3.2.2)non-6-en-3-one (27).

(f) Attempted S_N2 reaction of sodium acetate on endo-bicyclo(3.2.2) non-6-en-3-yl tosylate (75) [49].

Fused sodium acetate (45 mg.) was added to endo-bicyclo (3.2.2)non-6-en-3-yl tosylate (75) (60 mg.) (see p. 126) in 95% ethanol (5 ml.) and the mixture refluxed for 16 hrs.. The ethanol was removed in vacuo and water (5 ml.) was added. The mixture was extracted with ether and the combined ethereal extracts were dried ($MgSO_4$). On removal of the ether, a colourless oil (8 mg.) was obtained which was shown by analytical t.l.c. (5% chloroform/carbon tetrachloride) to consist apparently of two major components (totalling 90% of the mixture) in the ratio 60:40, the major component having an R_f value of approximately 0.6 while the minor component had an R_f of approximately 0.1. G.L.C. (5% QF 1; gas pressure: 18 lbs./in^2.; temperature programme: 30° increasing to 200° at the rate of 2°/min.) showed three major compounds with R_t (mins.) = 14.2 (50%), 20.4 (35%), and 34.0 (15%).

$\nu_{max.}^{cm.^{-1}}$ (film): 3450 (m) (hydroxyl); 1735 (m), 1725 (m) (acetate); 1096 (s), 732 (s).

The oil, i.e. the reaction product (7 mg.), in dry ether (5 ml.), was stirred for 16 hrs. at room temperature with a large excess of lithium aluminium hydride. After the usual work-up, an oil was obtained, the i.r. spectrum of which showed no absorption in the carbonyl region indicating that all the acetate had been reduced

to alcohol. Investigation by g.l.c. (10% PEGA; 120°; 42 ml./min.) showed the presence of two compounds in equal amounts with R_t (mins.)= 2.6 and 10.6. The slower running component proved to have a retention time exactly similar to endo-bicyclo(3.2.2)non-6-en-3-ol (25). Exo-bicyclo(3.2.2)non-6-en-3-ol (26) has exactly the same g.l.c. characteristics as the endo isomer (25) on all g.l.c. columns investigated, so that this slower running product of the S_N2 reaction may be the desired exo isomer (26). However, the poor yields and impurity of the final product mixture rendered this method of preparing exo-bicyclo(3.2.2)non-6-en-3-ol (26) impracticable.

(g) Exo-bicyclo(3.2.2)non-6-en-3-ol (26) [and exo-bicyclo(3.2.2)non-6-en-2-ol (14)].

The Diels-Alder reaction of 1-benzoyloxycyclohepta-3,5-diene (6) and maleic anhydride gave a mixture of three isomers[1] (see p. 85). Exo-3-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (7) could be separated and obtained pure. However, as already stated above, separation of the remaining isomers, (8) and (15), proved troublesome.

Catalytic hydrogenation of the mixture of residual isomers, (8) and (15), in the usual manner gave the desired mixture of exo-3-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (38) and the corresponding exo-2-benzoate (39). The

combined yields of five electrolyses of this mixture of (38) and (39) gave a mixture of exo-3-benzoyloxybicyclo(3.2.2)non-6-ene (37) and exo-2-benzoyloxybicyclo(3.2.2)non-6-ene (40) as an oil (2.3 g.).

Analytical g.l.c.,

(2% 20M PEG; 165°; 44 ml./min..

	R_t (min.)	Retention Index (R_i)
exo-2-benzoate (40)	21.5	2620
exo-3-benzoate (37)	25.2	2667)

indicated the presence of only these two components in the mixture. Preparative g.l.c. (using the above conditions) of the mixture afforded pure exo-3-benzoyloxybicyclo(3.2.2)non-6-ene (37) (80 mg.) as a colourless, waxy solid and pure exo-2-benzoyloxybicyclo(3.2.2) non-6-ene (40) (350 mg.) as a colourless oil. These compounds were not characterised but were hydrolysed to the corresponding alcohols.

Exo-bicyclo(3.2.2)non-6-en-3-ol (26) (35 mg., 76%) was obtained as a colourless, waxy solid after sublimation, m.p. (sealed tube) 53-54°; exo-bicyclo(3.2.2)non-6-en-2-ol (14) (153 mg., 76%) was obtained as a colourless solid, m.p. (sealed tube) 149-150°, after purification by prep. t.l.c. and sublimation. The exo-2-ol (14) had previously been characterised (see p. 110).

Exo-bicyclo(3.2.2)non-6-en-3-ol (26), due to scarcity of material, was characterised by mass spectrometry and other spectroscopic methods. The exo-3-ol (26) has the formula $C_9H_{14}O$ and thus

has a molecular weight of 138. The major m/e values obtained in the mass spectrum of the exo-3-ol (26) were as follows:

M.S. (m/e) : 138, 120, 105, 95, 91, 80.

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 3620 (s) (free hydroxyl); 1041 (s), 1012 (m).

G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Bicyclo(3.2.2)nonan-3-one (28) [8].

Bicyclo(3.2.2)nonan-3-ol (24) (200 mg.) was subjected to Jones oxidation in the normal manner. Bicyclo(3.2.2)nonan-3-one (28) (160 mg., 80%) (semi-solid) was obtained after the usual work-up and purification by prep. t.l.c..

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1699 (s) (ketone).

General Method for Deuteration of Ketones [31].

The ketone (200 mg., 1.3 mmoles) was dissolved in dioxan (5 ml., spectroscopic grade) and then transferred to a Carius tube. Deuterium oxide (5 ml.) was added, followed by sodium (approx. 20 mg.). After the sodium had reacted, the tube was sealed and maintained at 95° for 14 days. The material was then poured into pentane (100 ml.) and extracted five times with ice-cold water. Drying ($MgSO_4$) of the pentane followed by evaporation in vacuo gave the deuterated ketone.

2,2,4,4-Tetradeuterobicyclo(3.2.2)nonan-3-one (85).

Bicyclo(3.2.2)nonan-3-one (28) (160 mg.) gave only the corresponding 2,2,4,4-tetradeuterobicyclo(3.2.2)nonan-3-one (85) (80 mg., 50%) as a colourless semi-solid.

Comparison of mass spectra:

3-one (28) - major m/e at: 138, 120, 109, 94, 81.

d_4-3-one (85) - major m/e at: 142, 124, 113, 97, 82.

2,2,4,4-Tetradeuterobicyclo(3.2.2)nona-6,8-dien-3-one (84).

Bicyclo(3.2.2)nona-6,8-dien-3-one (18) (120 mg.) gave only the corresponding 2,2,4,4-tetradeuterobicyclo(3.2.2)nona-6,8-dien-3-one (84) (60 mg., 50%) as a colourless semi-solid.

Comparison of mass spectra:

dien-3-one (18) - major m/e at: 134, 116, 105, 91.

d_4-dien-3-one (84) - major m/e at: 138, 120, 108, 93.

Reduction of the tetradeuteroketones (84) and (85) to the corresponding alcohols (86) and (87) respectively.

The ketone was treated with excess lithium aluminium hydride in dry ether at room temperature in the usual manner. The mixture was stirred for 2 hrs., after which time the excess hydride was destroyed with saturated sodium sulphate solution and the ether dried ($MgSO_4$). Filtration and evaporation of the solvent gave the

alcohol in quantitative yield. The material was checked for purity by analytical t.l.c. but was not sublimed.

2,2,4,4-Tetradeuterobicyclo(3.2.2)nonan-3-ol (87).

The title compound was obtained as a colourless, waxy solid, m.p. (sealed tube) 116-120°.

Comparison of the mass spectra of the deuterated and undeuterated alcohols:

3-ol (24) - major m/e at: 140 (v. small), 138, 122, 94.

d_4-3-ol (87) - major m/e at: 144 (v. small), 142, 126, 97.

Infra-red spectroscopic data obtained from the tetradeutero alcohol (87) is shown below:

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3300 (s) (hydroxyl); 2210 (w), 2115 (w) (C-D); 1148 (m), 1018 (s).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3624 (m) (free hydroxyl); 2192 (m), 2100 (m) (C-D); 1147 (s), 1016 (s).

2,2,4,4-Tetradeuterobicyclo(3.2.2)nona-6,8-dien-3-ol (86).

This was obtained as a colourless, waxy solid, m.p. (sealed tube) 48-52°.

$\nu_{max.}^{cm.^{-1}}$ (CCl_4) : 3623 (m) (free hydroxyl); 2205 (m), 2168 (m), 2103 (m) (C-D); 1135 (s), 1026 (s).

N.M.R.: Table II.

Comparison of mass spectra:

dien-3-ol (17) - major m/e at: 136, 117, 92, 91.

d_4-dien-3-ol (86) - major m/e at: 140, 121, 94, 93.

Preparation of Cyclohexyl Tosylate (137).

The following general method [17] for the preparation of p-toluenesulphonate esters (tosylates) was employed:
A solution of cyclohexanol (1.00 g.) in dry pyridine (15 ml.) was cooled to 0° and treated with a one molar excess of p-toluene-sulphonyl chloride. After solution was complete, the flask was stoppered and placed in a refrigerator for 18 hrs., during which time needle-shaped crystals of pyridine hydrochloride formed. The mixture was then poured, with stirring, into ice and water (100 g.), which was then stirred for 30 mins. giving an oil. (In some cases, a solid was obtained at this point, in which case the solid was filtered, washed with water, dried and then recrystallised as described below). This oil was taken up in ether (100 ml.), and the aqueous layer extracted once with ether. The combined ethereal extracts were washed with dilute hydrochloric acid, water and then dried (K_2CO_3/Na_2SO_4). The solvent was evaporated in vacuo at 10° giving an oil which was dissolved in the minimum amount of light petrol at room temperature. The colourless solution was cooled to -75° in a dry ice-acetone bath, whereupon, with scratching, the

tosylate crystallised out as a white solid. The solid was filtered and then dried in vacuo at room temperature to afford cyclohexyl tosylate (137) (1.39 g., 50%) as a colourless, micro-crystalline solid, m.p. 45-46°. This tosylate, and all tosylates in general were stored in the freezing compartment of a refrigerator.

The above procedure will henceforth be denoted by the expression "the general method" of preparation of tosylates.

Bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74).

Prepared by the general method from bicyclo(3.2.2)nona-6,8-dien-3-ol (17), the tosylate (74) was obtained as a colourless, micro-crystalline solid in 66% yield, m.p. 104-106°.

(Found: C, 66.03; H, 6.22. $C_{16}H_{18}SO_3$ requires: C, 66.18; H, 6.25%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1596 (m), 1192 (s), 1173 (s), 954 (s), 913 (s), 830 (s).

N.M.R.: Table II.

2,2,4,4-Tetradeuterobicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (88).

This was obtained in 62% yield from the corresponding alcohol (86) as a colourless, micro-crystalline solid, m.p. 104.5-105.5°.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 2250 (w), 2150 (w) (C-D); 1192 (s), 1174 (s), 899 (s).

The integration of the n.m.r. spectrum (see Table II) of this tosylate (88) showed it to contain four deuterium atoms in the specified positions.

Bicyclo(3.2.2)nonan-3-yl tosylate (77).

This was obtained as a colourless, micro-crystalline solid in 64% yield, m.p. 47-49°.

(Found: C, 65.02; H, 7.34. $C_{16}H_{22}SO_3$ requires: C, 65.28; H, 7.53%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1597 (m), 1179 (s), 953 (s), 909 (s).

N.M.R.: Table II.

2,2,4,4-Tetradeuterobicyclo(3.2.2)nonan-3-yl tosylate (89).

This was obtained as a colourless, micro-crystalline solid in 60% yield, m.p. 47-50°.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 2245 (w), 2145 (w) (C-D); 1179 (s), 963 (s), 922 (s).

The integration of the n.m.r. spectrum (see Table II) of the tosylate (89) showed it to contain four deuterium atoms in the specified positions.

Endo-bicyclo(3.2.2)non-6-en-3-yl tosylate (75).

This was obtained in 64% yield as a colourless, micro-crystalline solid, m.p. 76-78.5°.

(Found: C, 65.64; H, 6.78. $C_{16}H_{20}SO_3$ requires: C, 65.72; H, 6.90%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1598 (m), 1195 (m), 1181 (s), 948 (s), 902 (s).
N.M.R.: Table II.

Exo-bicyclo(3.2.2)non-6-en-3-yl tosylate (76).

The tosylate (76) was obtained in 50% yield as a colourless, micro-crystalline solid, m.p. 58-59°. Due to scarcity of exo-bicyclo(3.2.2)non-6-en-3-ol (26), only a small amount of the tosylate (76) was prepared for measurement and comparison of its rate of acetolysis. It was thus only characterised by its i.r. spectrum, and by the characteristic ultra-violet spectrum of the tosylate group.

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1598 (m), 1357 (s), 1191 (s), 1175 (s), 930 (s).

Endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92).

This tosylate was prepared by the general method, as were all others, and was obtained as a colourless, micro-crystalline solid in 99% yield, m.p. 77-78.5°.
(Found: C, 65.58; H, 6.77. $C_{16}H_{20}SO_3$ requires: C, 65.72; H, 6.90%.)

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1595 (m), 1351 (s), 1189 (s), 1169 (s), 910 (s).
N.M.R.: Table II.

Bicyclo(3.2.2)nonan-2-yl tosylate (93) [8].

Bicyclo(3.2.2)nonan-2-yl tosylate (93) was obtained in

59% yield as a colourless, micro-crystalline solid, m.p. 46-48° (lit. m.p. 46-48°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 1596 (m), 1190 (m), 1171 (s), 910 (s).

N.M.R.: Table II.

Attempted preparation of exo-bicyclo(3.2.2)non-6-en-2-yl tosylate (138).

Exo-bicyclo(3.2.2)non-6-en-2-ol (14) (120 mg.) was subjected to the general procedure for tosylation. No pyridine hydrochloride was deposited as was generally observed. After the usual work-up, an oil (120 mg.) was obtained. The oil was subjected to prep. t.l.c. and the two main bands investigated. The less polar (tosylate?) band on extraction afforded an uncharacterisable oil (which contained no tosylate) which was not further investigated. The more polar band afforded a mixture of two alcohols (48 mg.) in the ratio of 95:5 (as determined by g.l.c.: 10% PEGA, 125°).

The minor component was shown to be identical with exo-bicyclo(3.2.2)non-6-en-2-ol (14) by comparative g.l.c. (10% PEGA, 125°; 2% 20M PEG, 120°; 1% OV 15, 75°). The major component, considered to be a tertiary alcohol from its g.l.c. retention time and its free hydroxyl absorption "frequency" (3613 $cm.^{-1}$), was shown to be identical in all respects (spectroscopically and chromatographically) with bicyclo(3.2.2)non-6-en-1-ol (115) prepared by an independent route.

The mixture of dihydro alcohols, obtained by catalytic hydrogenation (10% Pd-C, ethyl acetate) of the mixture of (14) and (115), was shown to be composed of bicyclo(3.2.2)nonan-2-ol (49) and bicyclo(3.2.2)nonan-1-ol (110) by g.l.c. comparison (same conditions as above).

Bicyclo(3.2.2)nonan-1-ol (110) [36].

The brosylate of 1-hydroxymethylbicyclo(2.2.2)octane (139) (200 mg.) (kindly provided by Dr. D. Morris) and calcium carbonate (120 mg.) in 50% aqueous dioxan (4 ml.) were heated in a sealed tube at 145° for 16 hrs.. The dioxan solution was filtered, water (20 ml.) was added and the solution extracted with pentane (4x25 ml.). The combined extracts were washed twice with water and then dried (Na_2SO_4). Filtration, followed by evaporation of the solvent in vacuo gave pure bicyclo(3.2.2)nonan-1-ol (110) (60 mg., 77%) as a colourless, crystalline solid, m.p. (sealed tube) 193-195° (lit. m.p. 199-201°).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 3609 (m) (hydroxyl); 2936 (s), 1089 (s), 1044 (s).
G.L.C.: Table I. N.M.R.: Table II. High Resolution I.R.: Table III.

Bicyclo(3.2.2)non-6-en-1-ol (115).

By a similar method to that above, the brosylate of 1-hydroxymethylbicyclo(2.2.2)oct-2-ene (116) [36] (170 mg.) (again

kindly provided by Dr. D. Morris) gave bicyclo(3.2.2)non-6-en-1-ol (115) (40 mg., 58%) as a colourless, waxy solid, m.p. (sealed tube) 138-140°.

(Found: C, 78.03; H, 10.22. $C_9H_{14}O$ requires: C, 78.21; H, 10.21%.)

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 3613 (m) (hydroxyl); 3038 (w) (olefinic C-H); 2932 (s) ($-CH_2-$); 1079 (s), 1046 (s).

G.L.C.: Table I . N.M.R.: Table II. High Resolution I.R.: Table III.

Tetrahydrobarbaralol (56) [18,52] .

Tetrahydrobarbaralol (56) was synthesised by the route described in the literature from cyclopentanone (140) via 1-N-pyrrolidylcyclopentene (141) [50] , 2-N-pyrrolidylbicyclo(3.2.1)octan-8-one (142) [51] , and 2-N-methylpyrrolidylbicyclo(3.2.1)octan-8-one iodide (143) [51] . Pyrolysis of the quaternary salt in base gave cyclohept-4-ene-1-carboxylic acid (144) [51] which was converted to the corresponding acid chloride (145) [52] . Treatment of the acid chloride (145) with an ethereal solution of diazomethane containing a few ml. of triethylamine gave the corresponding diazoketone (146) [52] , which on refluxing with copper powder gave tetrahydrobarbaralone (147) [52] , b.p. 85°/0.14 mm. (lit. b.p. 88°/0.15 mm.).

$\nu_{max.}^{cm.^{-1}}$ (CCl_4): 1705 (s) (ketone).

lit. $\nu_{max.}^{cm.^{-1}}$ (CCl_4): 1705 (s).

Tetrahydrobarbaralone (147) was reduced with lithium aluminium hydride in dry ether giving tetrahydrobarbaralol (56) [18], m.p. 182-184° (sublimed) (lit. m.p. 183-184°).

$\nu_{max.}^{cm.^{-1}}$ (Nujol): 3400 (s) (hydroxyl); 1064 (s), 1035 (s), 1018 (s).

G.L.C.: Table I.

Attempted preparations of bicyclo(3.2.2)nona-6,8-dien-2-yl tosylate (148).

(a) The corresponding p-toluenesulphinate (149) was prepared without difficulty [53] from the dien-2-ol (48) and p-toluenesulphinyl chloride (150) [54]. The reported [55] oxidation to the tosylate (148) was undertaken, but investigation of the reaction product by t.l.c. showed the formation of a plethora of polar products. Presumably, the oxidising agent, m-chloroperbenzoic acid, was also epoxidising the double bonds of the bicyclo(3.2.2)nona-6,8-dien-2-ol (48). Opening of these epoxides would give rise to compounds with several hydroxyls which one would expect to have high polarity on t.l.c.. An n.m.r. spectrum of the mixture showed the characteristic pattern of the p-tolyl grouping but showed no olefinic protons.

(b) Generation of the corresponding anion (at 0°) of bicyclo (3.2.2)nona-6,8-dien-2-ol (48) using n-butyllithium, followed by addition of an equivalent amount of p-toluenesulphonyl chloride was also unsuccessful possibly due to the inapplicability of this

method to very small quantities of alcohol, since any excess n-butyl-lithium would give rise to n-butyl tosylate.

(c) Bicyclo(3.2.2)nona-6,8-dien-2-ol (48) (100 mg.) was subjected to the general procedure [17] for tosylation. No pyridine hydrochloride was deposited as was generally observed and after the usual work-up, a quantitative yield of an oil was obtained. The oil was subjected to prep. t.l.c. and the several bands were investigated. The less polar (tosylate?) bands afforded uncharacterisable oils which contained no tosylate. The major polar band afforded a mixture of two alcohols (5 mg.) in the ratio 92:8 (as determined by g.l.c.: 10% PEGA, 125°; 2% 20M PEG, 120°; 1% OV 15, 75°).

The minor component was shown to be identical with bicyclo (3.2.2)nona-6,8-dien-2-ol (48) by comparative g.l.c. (same conditions as above). The major component, considered to be a tertiary alcohol from its g.l.c. retention time, was not identified.

Catalytic hydrogenation (10% Pd-C, ethyl acetate) of the above mixture gave a mixture of tetrahydro compounds which was shown to consist of bicyclo(3.2.2)nonan-2-ol (49) and bicyclo(3.2.2) nonan-1-ol (110) by g.l.c. comparison (same conditions as above). Thus, this provided some evidence that the major component comprising 92% of the original mixture was bicyclo(3.2.2)nona-6,8-dien-1-ol (124).

Acetolysis of Tosylates [56].

A sample of the tosylate (30 mg.) and fused sodium acetate (36 mg.) were dissolved in anhydrous acetic acid (12 ml.) and the solution was kept at 45° for 17 hrs.. The reaction mixture was cooled and poured into water (50 ml.). The solution was then extracted with light petrol, the combined extracts were washed with sodium carbonate solution, brine and then dried ($MgSO_4$). Filtration, followed by evaporation of the solvent gave the olefin-acetate mixture, which was hydrolysed in the manner for benzoates (see previous experimental accounts) to give the olefin-alcohol mixture. This was separated by prep. t.l.c. and the alcohol products examined by g.l.c. (and, in certain cases, by high resolution infra-red spectroscopy).

Acetolyses, by this method, of the tosylates of bicyclo (3.2.2)nonan-3-ol (24), endo-bicyclo(3.2.2)non-6-en-3-ol (25), endo-bicyclo(3.2.2)non-6-en-2-ol (13), and bicyclo(3.2.2)nona-6,8-dien-3-ol (17) were carried out and the products examined and identified. In addition, the rates of acetolysis for all tosylates prepared in this study have been determined. The method and results are given in Appendix B.

Acetolysis of bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74).

Acetolysis of this tosylate in the manner described above followed by hydrolysis and prep. t.l.c. gave the alcohol products

in 22% yield. Analytical g.l.c. (1% OV 15, 75°; 10% PEGA, 125°; 2% 20M PEG, 125°) showed only one alcohol product which, by cross injection, was shown to be bicyclo(3.2.2)nona-6,8-dien-3-ol (17). As further proof, a small sample of this product was catalytically hydrogenated (10% Pd-C, ethyl acetate) giving only bicyclo(3.2.2) nonan-3-ol (24) as shown once again by comparative g.l.c. (same conditions as above).

Acetolysis of bicyclo(3.2.2)nonan-3-yl tosylate (77).

Acetolysis, hydrolysis and prep. t.l.c. in the usual manner gave the alcohol products in 10% yield. Using comparative g.l.c. (same conditions as for previous acetolysis) it was shown that the only alcohol formed was bicyclo(3.2.2)nonan-3-ol (24).

Acetolysis of endo-bicyclo(3.2.2)non-6-en-3-yl tosylate (75).

The acetolysis, hydrolysis and prep. t.l.c. procedure was carried out as before giving a 19% yield of alcohol products. Analytical g.l.c. (1% OV 15, 75°; 5% QF 1, 75°; 10% PEGA, 125°; 2% 20M PEG, 125°) showed only one peak which was either exo-bicyclo (3.2.2)non-6-en-3-ol (26) or the corresponding endo isomer (25), or possibly a mixture of the exo and endo alcohols, (26) and (25), since these two alcohols were found to be inseparable by g.l.c. on all columns investigated. However, there are slight differences

in the high resolution infra-red spectra of the two alcohols and, from a comparison of the infra-red spectra of the exo and endo alcohols, (26) and (25), and the hydrolysed acetolysis product, it was shown that the only alcohol product obtained from this acetolysis (followed by hydrolysis) was exo-bicyclo(3.2.2)non-6-en-3-ol (26).

Acetolysis of endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92).

Acetolysis of this tosylate, followed by hydrolysis and prep. t.l.c. purification of the products gave a 95% yield of alcohol products. Preliminary comparative g.l.c. investigation (1% OV 15, 75°; 10% PEGA, 125°; 2% 20M PEG, 125°) indicated a ternary mixture composed of exo-bicyclo(3.2.2)non-6-en-2-ol (14) (93.5%), endo-bicyclo(3.2.2)non-6-en-2-ol (13) (4.7%), and tetrahydrobarbaralol (56) (1.8%). These findings were also supported by comparative g.l.c. investigation using 2% 20M PEG and 5% QF 1 in conjunction with temperature programming.

Catalytic hydrogenation (5% Pd-C, ethyl acetate) of this mixture gave once more a ternary mixture composed of unchanged tetrahydrobarbaralol (56) (1.8%) (since the cyclopropane ring does not cleave under these conditions [35] as shown by a simple control experiment), bicyclo(3.2.2)nonan-2-ol (49) (34.0%), and an unknown alcohol (64.2%) which, from its g.l.c. retention times

on the usual columns, was presumed to be a tertiary alcohol. Comparative g.l.c. (10% PEGA, 120°) showed that this unknown alcohol was not bicyclo(3.2.2)nonan-1-ol (110).

Using G.C.M.S., a mass spectrum of this unknown alcohol was obtained which showed that the alcohol had one double bond equivalent more (M^+ found-138) than would be expected for a saturated bicyclic alcohol (M^+ expected-140). This would indicate that this unknown alcohol was tricyclic as well as tertiary in nature.

To ensure that the unknown alcohol formed was not merely an artefact, a separate acetolysis, hydrolysis, prep. t.l.c. purification and catalytic hydrogenation were carried out. The same results exactly were obtained.

Pyrolysis of bicyclo(3.2.2)non-6-en-3-one (27).

Bicyclo(3.2.2)non-6-en-3-one (27) (30 mg.) was placed in an n.m.r. sample tube which was then evacuated and sealed. The tube and contents were maintained at 270° in an oven for 7 days after which time the tube was cooled, opened, and an n.m.r. sample prepared in situ with pure carbon tetrachloride.

The n.m.r. spectrum indicated the presence of cyclohexa-1,3-diene [4.17τ (s) and 7.93τ (s)] and also a trace of benzene [2.73τ (s)]. The main product appeared to be polymeric as evidenced by the methylene "mush" from 7.0τ to 9.0τ. No cyclopropane signal

[8.35τ (s) [57]] was observed for cyclopropanone, nor was there any change observed in the spectrum upon the addition of D_2O.

Pyrolysis of bicyclo(3.2.2)nona-6.8-dien-3-one (18).

The above pyrolysis procedure was repeated with bicyclo (3.2.2)nona-6,8-dien-3-one (18). Investigation of the products by n.m.r. showed that benzene [2.73τ (s)] was the major product. The only other products of any consequence were unidentified aromatic compounds.

In the Woodward - Hoffmann terminology, the above two pyrolyses may be regarded as $\pi^4_s + \pi^2_s$ cycloreversions and a molecular orbital correlation diagram, valid for both reactions, may be constructed (see p. 79).

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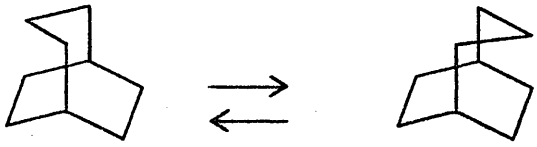

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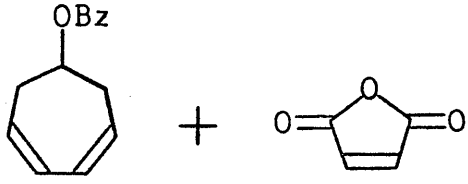

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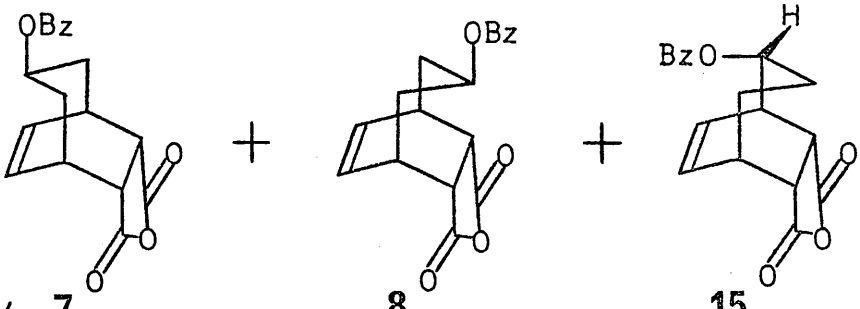

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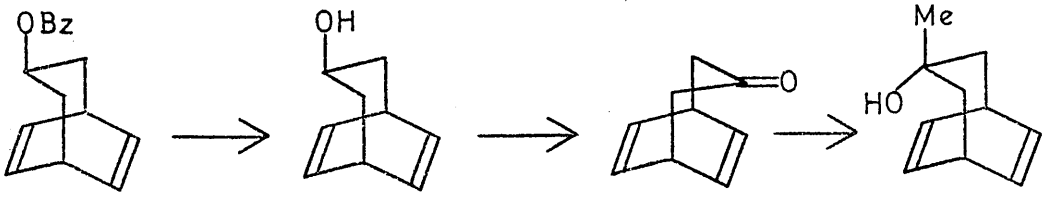

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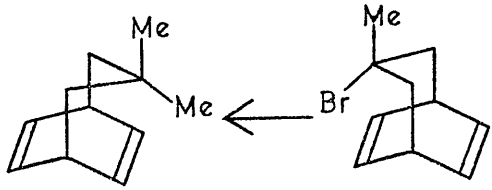

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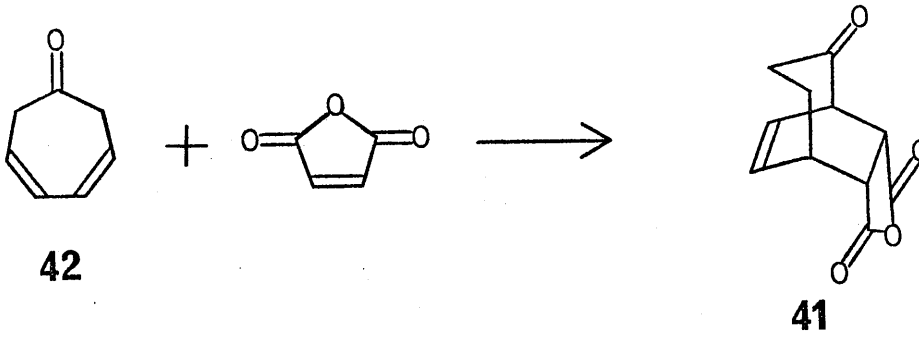

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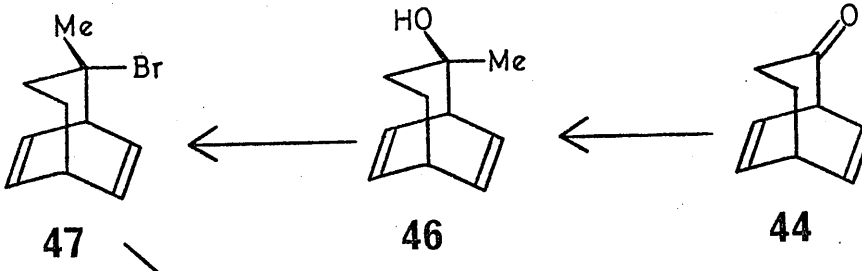

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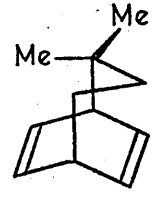

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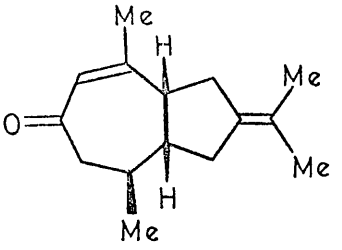

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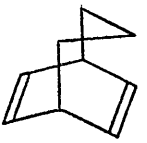

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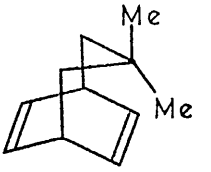

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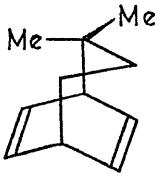

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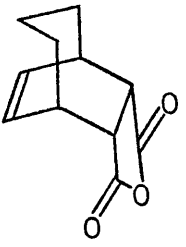

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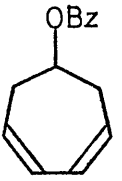

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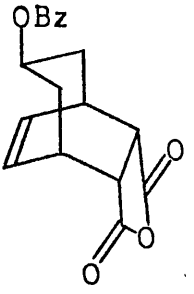

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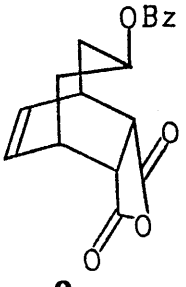

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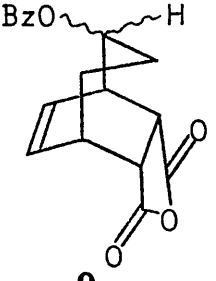

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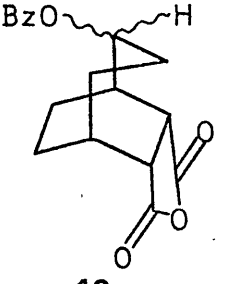

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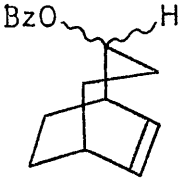

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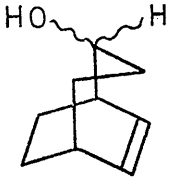

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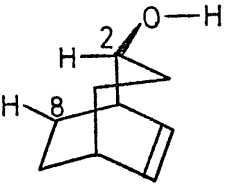

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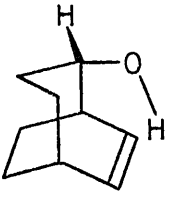

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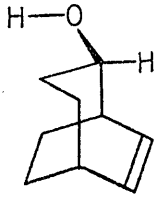

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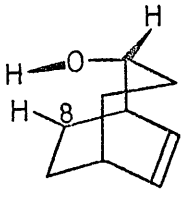

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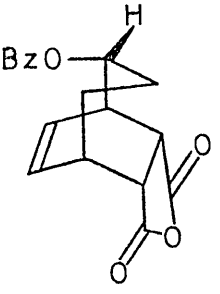

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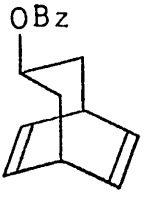

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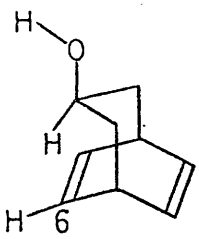

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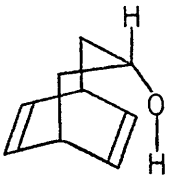

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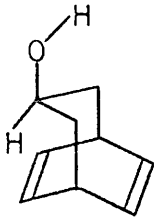

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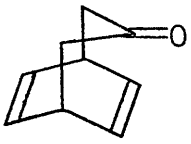

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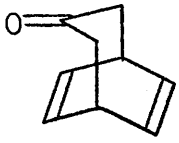

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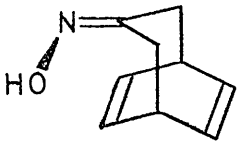

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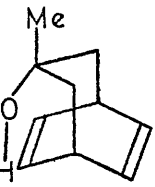
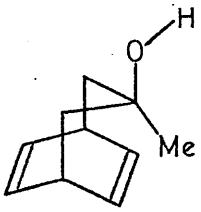


20 cf. **71**



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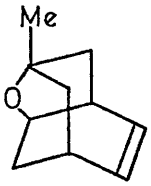

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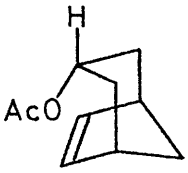

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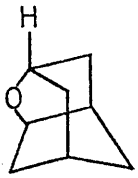

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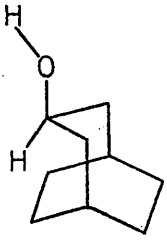

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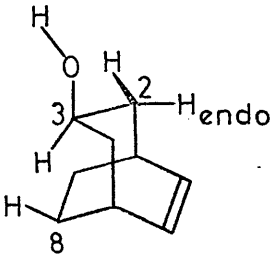

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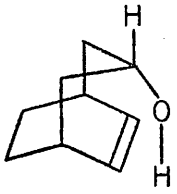

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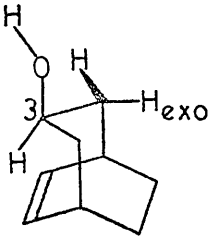

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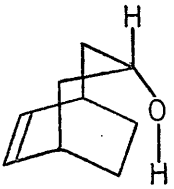

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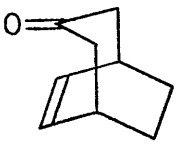

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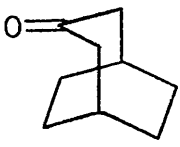

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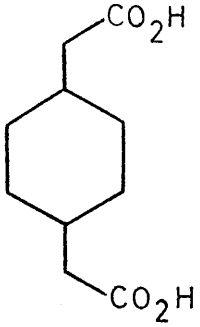

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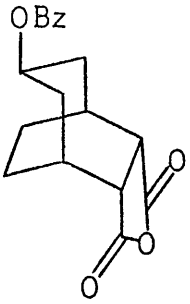

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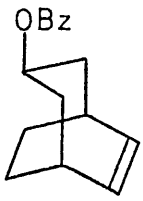

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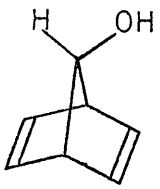

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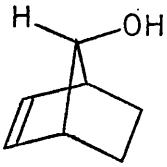

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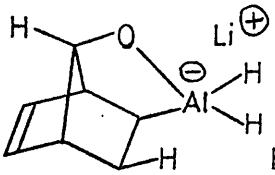

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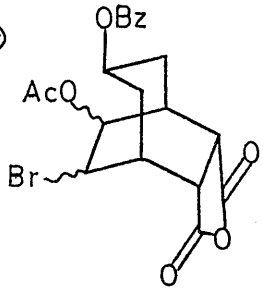

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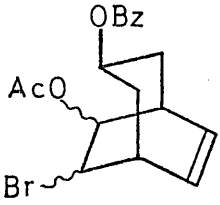

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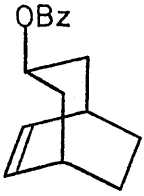

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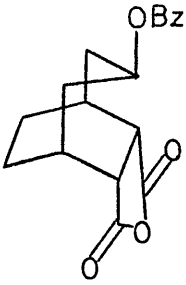

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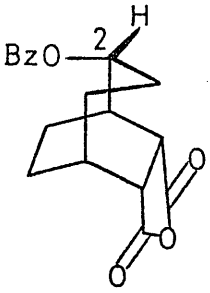

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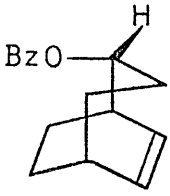

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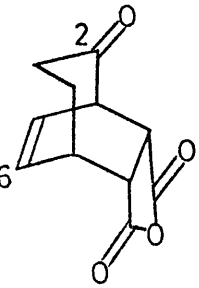

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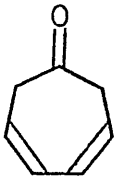

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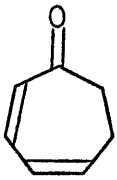

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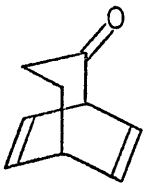

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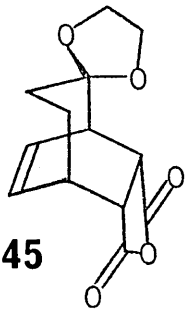

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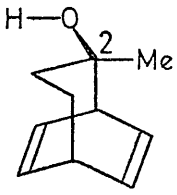

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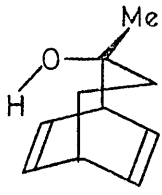

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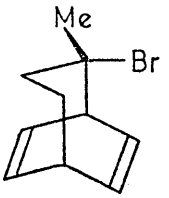

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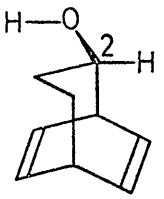

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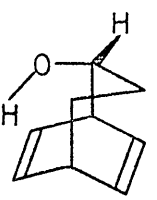

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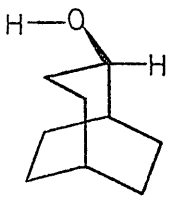

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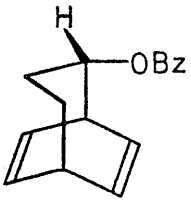

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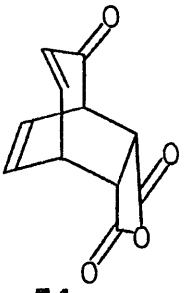

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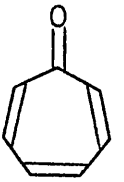

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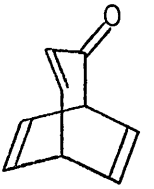

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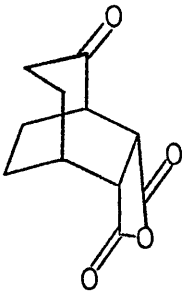

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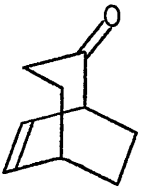

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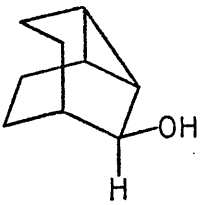

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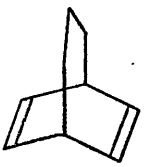

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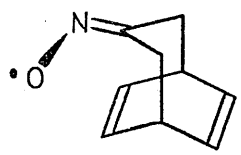

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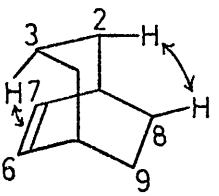

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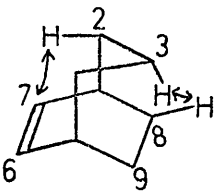

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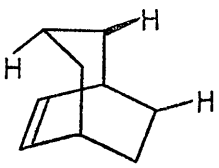

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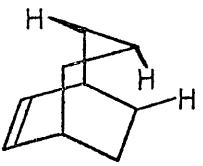

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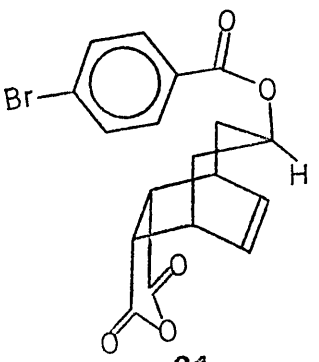

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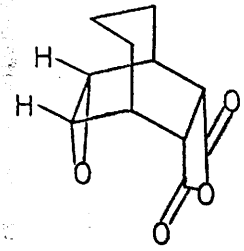

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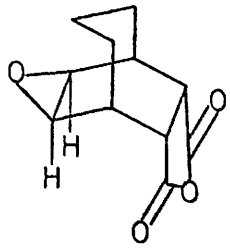

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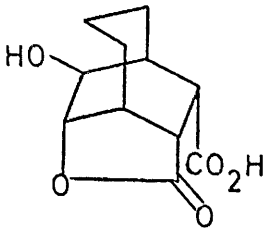

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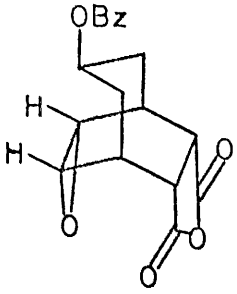

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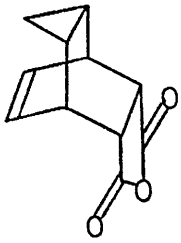

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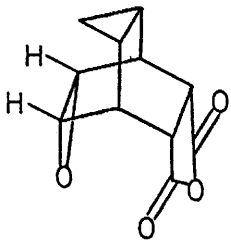

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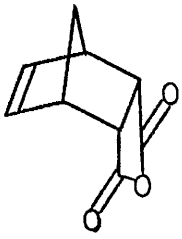

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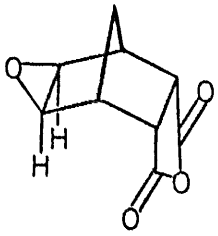

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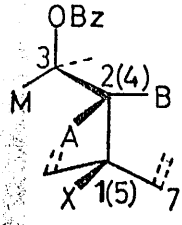

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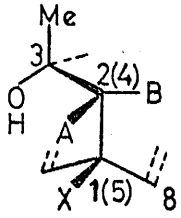

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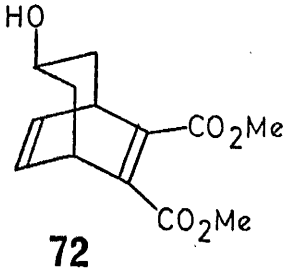

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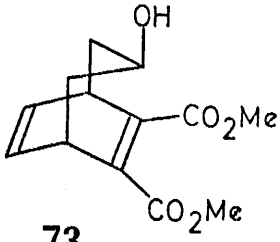

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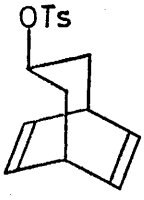

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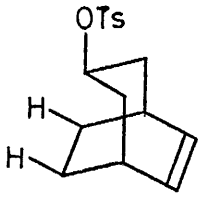

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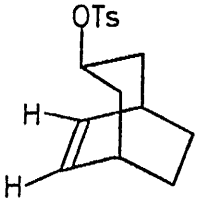

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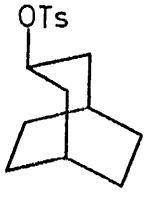

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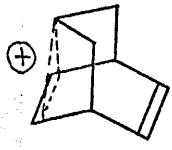

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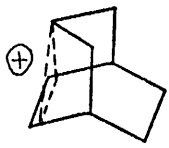

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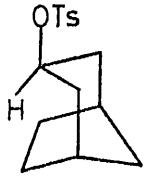

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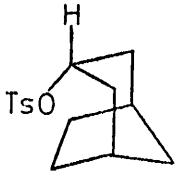

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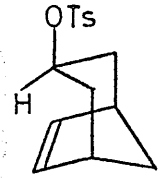

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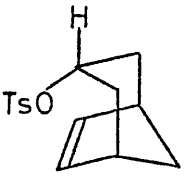

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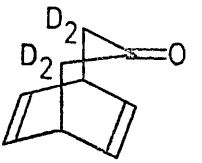

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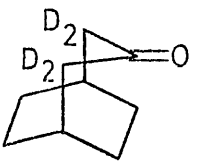

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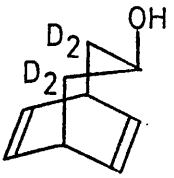

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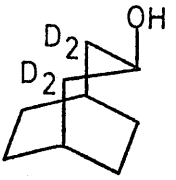

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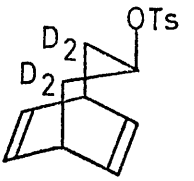

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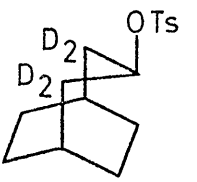

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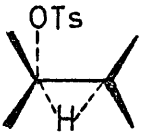

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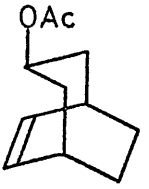

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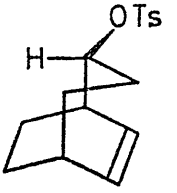

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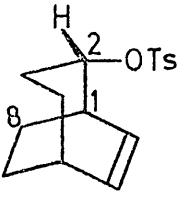

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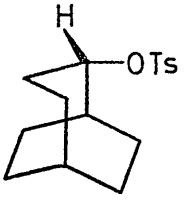

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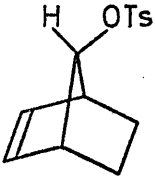

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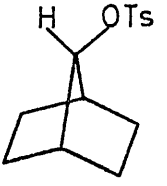

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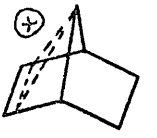

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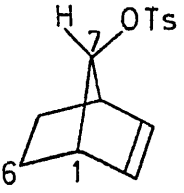

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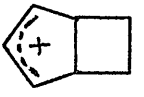

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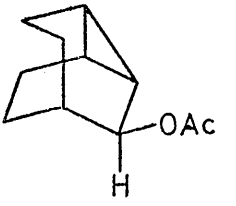

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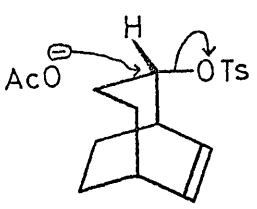

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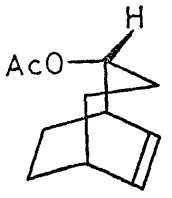

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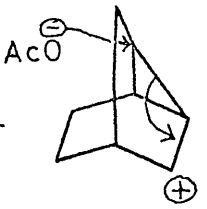

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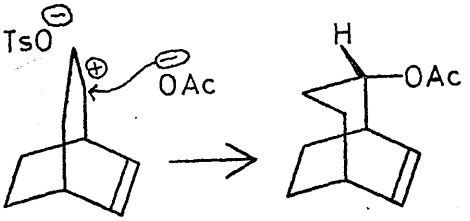

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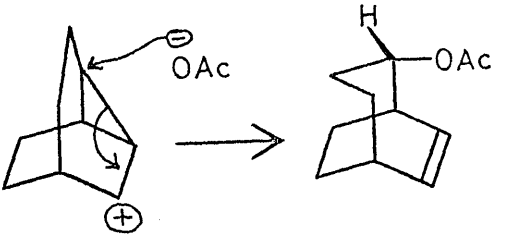

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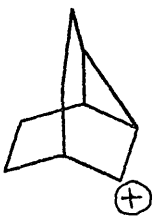

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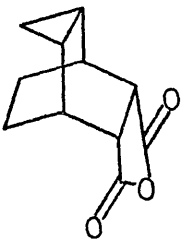

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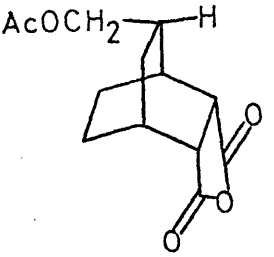

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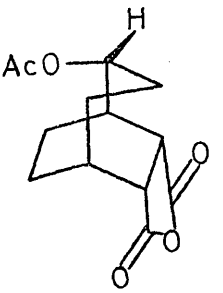

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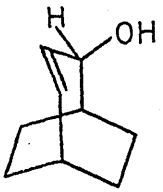

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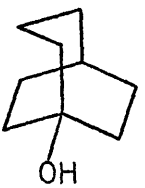

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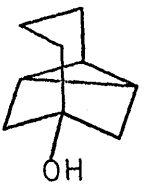

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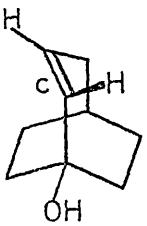

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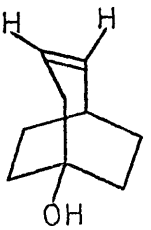

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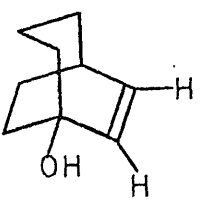

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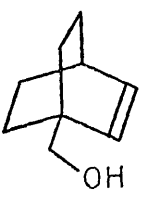

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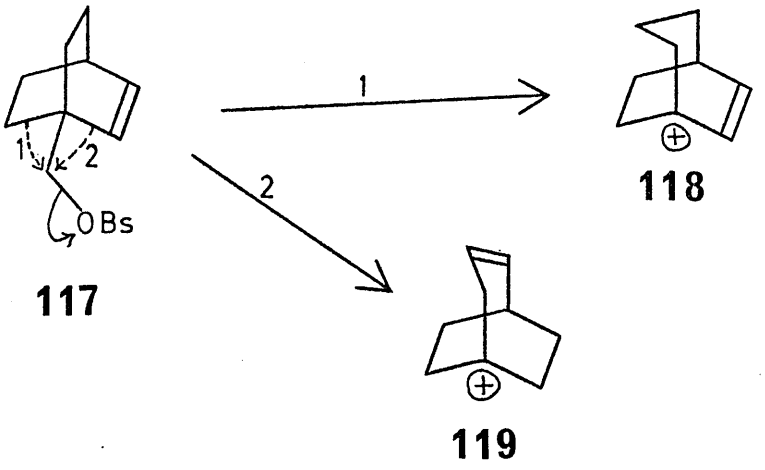
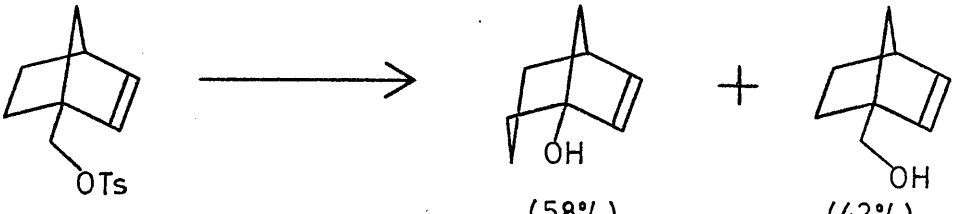
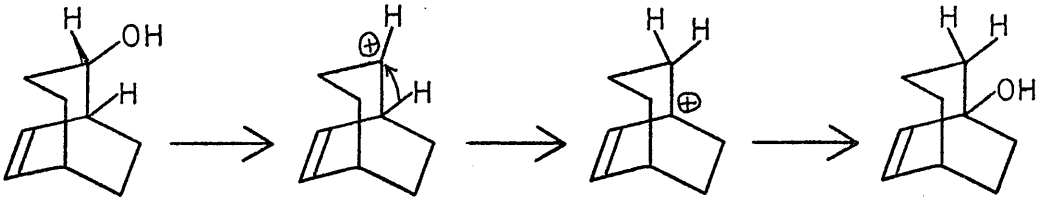


117 **118** **119**



120 **121** (58%) **122** (42%)



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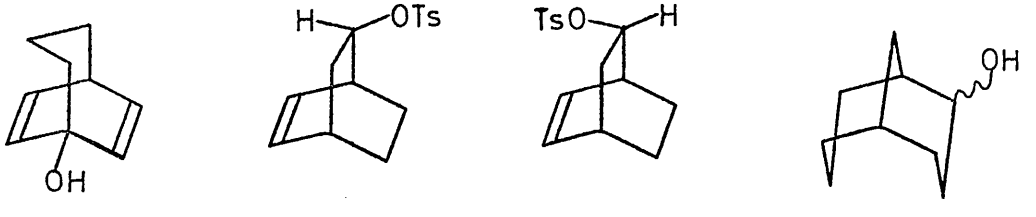
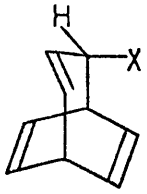


124 **125** **126** **127**



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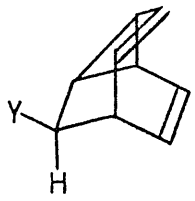

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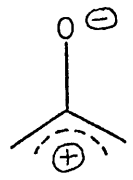

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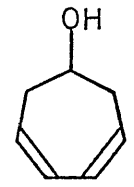

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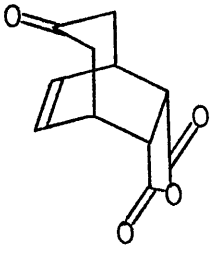

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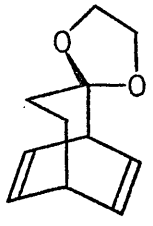

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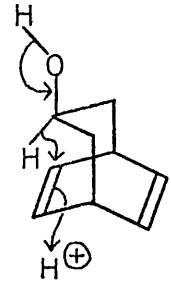
$Br_2.PPh_3$

134



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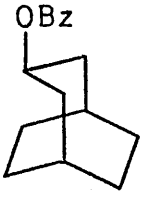

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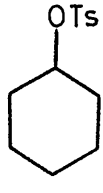

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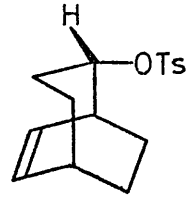

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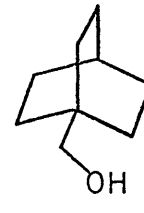

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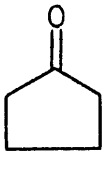

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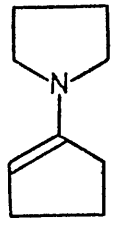

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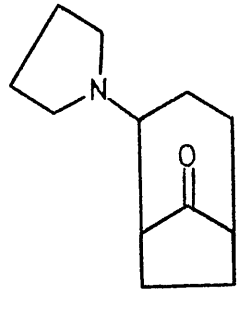

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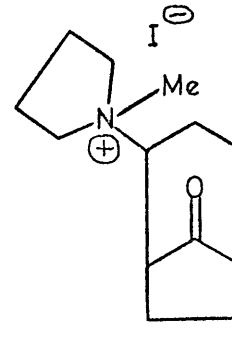

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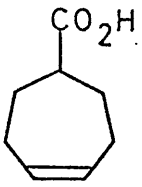

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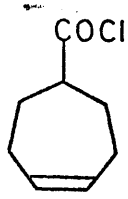

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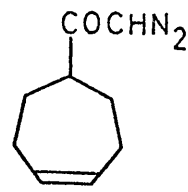

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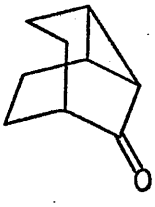

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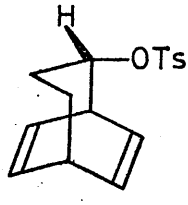

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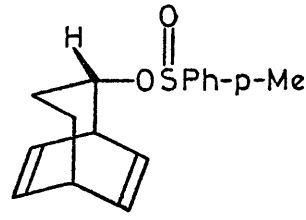

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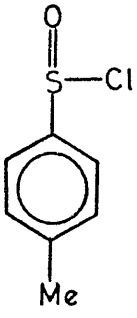

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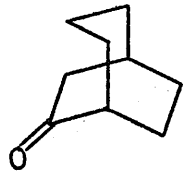

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APPENDIX A

Nomenclature of Bicyclic Compounds.

The nomenclature used in this work is that of the International Union of Pure and Applied Chemistry, as set down by Meinwald and Meinwald [58].

The convention adopted for describing the stereochemistry of substituents is as follows:

(A) If a bicyclic compound contains a double bond, a substituent on an adjacent bridge is described as endo if it lies within the solid angle generated by the bridge to which it is attached and the bridge containing the double bond, and as exo if it lies outwith this angle.

(B) If there is no double bond present, a substituent on a bridge is described as endo if it lies within the solid angle generated by the bridge to which it is attached and the larger of the two remaining bridges, and as exo if it lies outwith this angle.

(C) If there is no double bond present and two of the bridges are the same size, a substituent on the third bridge is described as endo if it lies within the solid angle generated by the bridge to which it is attached and the more heavily substituted of the two remaining bridges, and as exo if it lies outwith this angle.

To describe the stereochemical situation in conformationally mobile or biassed bicyclic systems an extension to these rules

is required:

The stereochemistry of the three carbon bridge in the bicyclo(3.2.2)nonane system is denoted as syn if the apical carbon (C-3) lies within the solid angle generated by the plane through C-1, C-2, C-4 and C-5 and the plane through C-1, C-5, C-6 and C-7, and as anti if it lies outwith this angle, e.g. (59a) represents anti-bicyclo(3.2.2)non-6-ene and (151) represents syn-bicyclo(3.2.2) nonan-6-one.

For a further example, catalytic hydrogenation of endo-2-benzoyloxybicyclo(3.2.2)non-6-ene-8,9-endo-dicarboxylic acid anhydride (15) gave exo-2-benzoyloxybicyclo(3.2.2)nonane-6,7-exo-dicarboxylic acid anhydride (39). The reaction involved no change in configuration as would seem apparent, the change in nomenclature arising from application of the rules (A), (B) and (C) above.

APPENDIX B

Rate Measurements

The scarcity of the tosylates studied prompted the use of the spectrometric method of measuring reaction kinetics, as described by Swain and Morgan [59]. This method is dependent upon the differences in molar absorptivity of the tosylate ester and the tosylate anion. At 261 nm., methyl tosylate (in water) has an extinction coefficient of 671 whereas that of tosylate anion is 344. Thus the rate of reaction can be followed by measuring the decrease in absorbance with time. The results obtained for the first order rate constant of the hydrolysis of methyl tosylate by this method have been shown to be in excellent agreement with data obtained by conductometric methods [59].

The application of the same method to solvolytic reactions in buffered acetic acid was found to give consistent results. A modification of the sampling method, as described by Eakin [56], enabled rate measurements to be carried out on extremely small quantities of material. The original method involved taking aliquots from the reaction solution in a thermostated bath and measuring the u.v. absorption. With the equipment now available it was possible to thermostat the u.v. cells inside the spectrometer thus allowing continuous monitoring of the solvolysis reaction.

Acetolysis Procedure

A solution of fused sodium acetate in anhydrous acetic acid (containing 1% acetic anhydride) was allowed to equilibrate in the constant temperature bath, which also thermostated the u.v. cells in the u.v. spectrometer. The reference cell (5.0 mm.) was filled with the buffered acetic acid solution, stoppered, and placed in the reference beam. A sample of the appropriate tosylate (approx. 2.0 mg.) was then placed in the sample cell, the cell filled with buffered acetic acid, and then stoppered. The solution was thoroughly mixed and the cell placed in the sample beam. The region 240 nm. - 300 nm. was then repetitively scanned automatically at preselected time intervals which were varied in accordance with the rates of acetolysis of the tosylates. Scanning was continued until an infinity reading was obtained after an appropriate interval.

Kinetics

The time dependent decrease of optical density at 261 nm. was noted. The percentage of unreacted tosylate (X) was calculated for each reading and the logarithm of the percentage of unreacted tosylate ($\log_{10}$ X) was found to decrease linearly with time, indicating first order kinetics. The initial concentration, i.e. X = 100, was determined by subtracting the infinity reading from the initial

reading. The half-life ($t_{\frac{1}{2}}$) and the first order rate constant (k_1) of each reaction were obtained graphically by means of a plot of $\log_{10} X$ versus time (t); k_{av} is the rate constant obtained by averaging the values of k_1 from the individual runs for each tosylate.

The derivation of the first order rate equation is as follows:

The rate of change of X with time, $-\frac{dX}{dt}$, is proportional to X. This is the condition that a reaction shall have first order kinetics.

Thus, $$-\frac{dX}{dt} = k_1 X$$

Thus, $$-\frac{dX}{X} = k_1 . dt$$

Thus, $$-\int\frac{dX}{X} = k_1 \int dt$$

Thus, $$-\ln X = k_1 t + K$$

where K = integration constant.

Thus, $$-2.303 \log_{10} X = k_1 t + K$$

When $t = 0$, then $X = X_o$, and $K = -2.303 \log_{10} X_o$

Thus, $$k_1 = \frac{2.303(\log_{10} X_o - \log_{10} X)}{t}$$

When the reaction is half complete, i.e. at $t_{\frac{1}{2}}$, then $$X = \frac{X_o}{2}$$

Thus, $$k_1 = \frac{2.303 \log_{10} 2}{t_{\frac{1}{2}}}$$

Thus, $$t_{\frac{1}{2}} = \frac{0.693}{k_1}$$, which is the half-life of the reaction.

Results

The results obtained are shown in the following pages. All the tosylates studied exhibited first order kinetics with respect to acetolysis. In general, the rates of solvolysis were rather slow. The acetolyses were thus studied at 73.6° (estimated ± 0.2°). The acetolysis of bicyclo(3.2.2)nonan-3-yl tosylate (77), which showed the fastest rate of solvolysis, was also studied at 53.7° (± 0.2°) along with the tetradeutero derivative (89).

The results are discussed in section (C) of the Discussion.

Experimental

Solvent

The solvent used in the solvolysis experiments was a 5.14×10^{-3} M solution of fused sodium acetate in "Analar" grade glacial acetic acid (containing 1% added acetic anhydride).

Spectrometer

A Unicam S.P.800 ultra-violet spectrometer was used, the

instrument being equipped with a thermostated cell holder linked to an automatic selection programmer, and capable of thermostating four pairs of u.v. cells when connected to a constant temperature bath. The instrument had facilities for repetitive scanning of a selected region of the spectrum at a preselected time interval (adjustable from 1 min. to 15 mins.).

Acetolysis of bicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (74).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 5.0×10^{-3} M

Time (mins.)	Optical Density (O.D.)	X	$\log_{10} X$
0	1.889	100	2.000
3	1.855	94.4	1.975
6	1.808	86.8	1.939
9	1.761	79.0	1.898
12	1.726	73.3	1.863
15	1.685	66.5	1.823
18	1.646	60.1	1.779
21	1.618	55.5	1.744
24	1.587	50.4	1.702
27	1.560	46.0	1.663
30	1.540	42.6	1.629
33	1.520	39.4	1.596
36	1.500	36.1	1.558
39	1.479	32.7	1.515
42	1.465	30.4	1.483
45	1.450	27.9	1.446
48	1.438	26.0	1.415
51	1.425	23.8	1.377
54	1.410	21.4	1.330
57	1.400	19.7	1.295
60	1.388	17.7	1.248
∞	1.280	0.0	-

From $\log_{10} X$ vs. t, $k_1 = 4.81 \times 10^{-4}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.7×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.421	100	2.000
3	1.374	91.0	1.959
6	1.343	85.0	1.929
9	1.313	79.4	1.900
12	1.279	72.8	1.862
15	1.246	66.4	1.822
18	1.220	61.5	1.789
21	1.191	55.9	1.747
24	1.175	52.8	1.723
27	1.155	48.9	1.689
30	1.135	45.1	1.654
33	1.109	40.2	1.604
36	1.100	38.4	1.584
39	1.085	35.5	1.550
42	1.067	32.1	1.507
45	1.050	28.8	1.459
48	1.035	25.9	1.413
51	1.029	24.8	1.395
∞	0.900	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 4.55 \times 10^{-4}$ sec^{-1}.

From the above, $k_{av} = 4.68 \pm 0.15 \times 10^{-4}$ sec^{-1},

and $t_{\frac{1}{2}} = 24.7 \pm 0.8$ mins..

Acetolysis of 2,2,4,4-tetradeuterobicyclo(3.2.2)nona-6,8-dien-3-yl tosylate (88).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 8 mins. ROTs : 4.2×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.232	100	2.000
8	1.200	89.5	1.952
16	1.179	82.7	1.918
24	1.158	75.8	1.880
32	1.138	69.2	1.840
40	1.112	60.8	1.784
48	1.099	56.5	1.752
56	1.080	50.3	1.702
64	1.061	44.1	1.644
72	1.047	39.5	1.597
80	1.035	35.6	1.551
88	1.023	31.6	1.500
96	1.010	27.4	1.438
∞	0.926	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 2.16 \times 10^{-4}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 8 mins. ROTs : 4.7×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.310	100	2.000
8	1.275	90.0	1.954
16	1.242	80.7	1.907
24	1.210	71.6	1.855
32	1.192	66.5	1.823
40	1.173	61.1	1.786
48	1.155	56.0	1.748
56	1.134	50.0	1.699
64	1.114	44.3	1.646
72	1.100	40.3	1.605
80	1.085	36.1	1.558
88	1.069	31.5	1.498
96	1.059	28.7	1.458
∞	0.958	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 2.14 \times 10^{-4}$ sec^{-1}.

From the above, $k_{av} = 2.15 \pm 0.01 \times 10^{-4}$ sec^{-1},

and $t_{\frac{1}{2}} = 53.7 \pm 0.2$ mins..

Acetolysis of endo-bicyclo(3.2.2)non-6-en-3-yl tosylate (75).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.5×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.460	100	2.000
3	1.397	89.4	1.951
6	1.331	78.2	1.893
9	1.265	67.0	1.826
12	1.206	57.0	1.756
15	1.170	51.0	1.708
18	1.130	44.2	1.645
21	1.099	38.9	1.590
24	1.067	33.5	1.525
27	1.041	29.1	1.464
30	1.020	25.6	1.408
33	1.000	22.2	1.346
36	0.986	19.8	1.297
39	0.971	17.3	1.238
∞	0.869	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 7.62 \times 10^{-4}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.1×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.255	100	2.000
3	1.192	86.5	1.937
6	1.140	75.5	1.878
9	1.086	64.0	1.806
12	1.040	54.2	1.734
15	1.000	45.7	1.660
18	0.962	37.8	1.578
21	0.935	31.9	1.504
24	0.910	26.6	1.425
27	0.891	22.6	1.354
30	0.877	19.6	1.292
33	0.860	16.0	1.204
36	0.847	13.2	1.121
39	0.840	11.7	1.068
∞	0.785	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 9.12 \times 10^{-4}$ sec^{-1}.

From the above, $k_{av} = 8.37 \pm 1.06 \times 10^{-4}$ sec^{-1},

and $t_{\frac{1}{2}} = 13.8 \pm 1.7$ mins..

Acetolysis of exo-bicyclo(3.2.2)non-6-en-3-yl tosylate (76).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 1½ mins. ROTs : 4.7×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.323	100	2.000
1½	1.259	84.4	1.926
3	1.196	69.0	1.839
4½	1.147	57.1	1.757
6	1.101	45.9	1.662
7½	1.067	37.6	1.575
9	1.039	30.7	1.487
10½	1.010	23.6	1.373
12	0.994	19.7	1.295
13½	0.979	16.1	1.207
15	0.965	12.7	1.104
16½	0.955	10.2	1.009
	0.913	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 2.26 \times 10^{-3}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 1½ mins. ROTs : 5.0×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.440	100	2.000
1½	1.361	81.5	1.911
3	1.301	67.4	1.829
4½	1.241	53.4	1.728
6	1.193	42.2	1.625
7½	1.160	34.4	1.537
9	1.129	27.2	1.435
10½	1.102	20.8	1.318
∞	1.013	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 2.42 \times 10^{-3}$ sec^{-1}.

From the above, $k_{av} = 2.34 \pm 0.11 \times 10^{-3}$ sec^{-1},

and $t_{\frac{1}{2}} = 4.9 \pm 0.2$ mins..

Acetolysis of bicyclo(3.2.2)nonan-3-yl tosylate (77).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 5.1×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.523	100	2.000
3	1.229	35.7	1.553
6	1.129	13.8	1.140
9	1.110	9.6	0.982
∞	1.066	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 5.50 \times 10^{-3}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: $1\frac{1}{2}$ mins. ROTs : 2.6×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	0.720	100	2.000
$1\frac{1}{2}$	0.650	58.8	1.769
3	0.609	35.7	1.553
$4\frac{1}{2}$	0.586	21.2	1.326
6	0.574	14.1	1.146
∞	0.550	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 5.30 \times 10^{-3}$ sec^{-1}.

Third run

Temp.: 73.6° ($\pm 0.2^{\circ}$) NaOAc: 5.14×10^{-3} M

Scan Interval: 2 mins. ROTs : 4.6×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.423	100	2.000
2	1.238	62.6	1.797
4	1.080	30.7	1.487
6	0.994	13.3	1.124
8	0.960	6.5	0.813
10	0.945	3.4	0.532
12	0.941	2.6	0.415
∞	0.928	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 5.28 \times 10^{-3}$ sec^{-1}.

From the above, $k_{av} = 5.36 \pm 0.12 \times 10^{-3}$ sec^{-1},

and $t_{\frac{1}{2}} = 2.2 \pm 0.1$ mins..

Acetolysis of bicyclo(3.2.2)nonan-3-yl tosylate (77).

First run

Temp.: 53.7° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 5.1×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.727	100	2.000
3	1.641	80.1	1.904
6	1.580	65.8	1.818
9	1.531	54.4	1.736
12	1.486	43.9	1.643
15	1.448	35.1	1.545
18	1.414	27.2	1.435
21	1.380	19.3	1.286
24	1.364	15.6	1.193
27	1.357	13.9	1.143
∞	1.297	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 1.24 \times 10^{-3}$ sec^{-1}.

Second run

Temp.: 53.7° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 5.0×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.586	100	2.000
3	1.520	86.2	1.936
6	1.453	72.2	1.859
9	1.388	58.6	1.768
12	1.341	48.7	1.688
15	1.300	40.2	1.604
18	1.259	31.6	1.500
21	1.225	24.5	1.389
24	1.198	18.8	1.274
27	1.178	14.6	1.164
30	1.160	10.9	1.037
∞	1.108	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 1.15 \times 10^{-3}$ sec^{-1}.

From the above, $k_{av} = 1.20 \pm 0.08 \times 10^{-3}$ sec^{-1},

and $t_{\frac{1}{2}} = 9.6 \pm 0.6$ mins..

Acetolysis of 2,2,4,4-tetradeuterobicyclo(3.2.2)nonan-3-yl tosylate (89).

First run

Temp.: 53.7° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.9×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.450	100	2.000
3	1.420	93.7	1.972
6	1.390	87.5	1.942
9	1.360	81.2	1.910
12	1.341	77.4	1.889
15	1.320	72.9	1.863
18	1.298	68.3	1.834
21	1.272	62.9	1.799
24	1.250	58.3	1.766
27	1.231	54.4	1.736
30	1.206	49.2	1.692
33	1.195	46.9	1.671
36	1.182	44.1	1.644
39	1.170	41.7	1.620
42	1.159	39.4	1.596
45	1.145	36.4	1.561
48	1.130	33.3	1.522
51	1.119	31.0	1.491
54	1.110	29.2	1.465
∞	0.970	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 3.77 \times 10^{-4}$ sec^{-1}.

Second run

Temp.: 53.7° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.5×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.321	100	2.000
3	1.290	92.8	1.968
6	1.260	85.9	1.934
9	1.237	80.6	1.906
12	1.204	73.0	1.863
15	1.190	69.7	1.843
18	1.171	65.4	1.816
21	1.153	61.2	1.787
24	1.138	57.8	1.762
27	1.119	53.4	1.728
30	1.102	49.5	1.695
33	1.086	45.7	1.660
36	1.071	42.2	1.625
39	1.060	39.7	1.599
42	1.046	36.5	1.562
45	1.032	33.3	1.522
48	1.021	30.7	1.487
51	1.011	28.4	1.453
∞	0.888	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 3.99 \times 10^{-4}$ sec^{-1}.

From the above, $k_{av} = 3.88 \pm 0.16 \times 10^{-4}$ sec^{-1},

and $t_{\frac{1}{2}} = 29.8 \pm 1.2$ mins..

Acetolysis of endo-bicyclo(3.2.2)non-6-en-2-yl tosylate (92).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 15 mins. ROTs : 4.8×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.325	100	2.000
15	1.081	25.4	1.405
30	1.018	6.1	0.785
45	1.004	1.8	0.255
∞	0.998	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 1.53 \times 10^{-3}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 3.4×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.043	100	2.000
3	0.971	80.5	1.906
6	0.906	62.8	1.798
9	0.859	50.0	1.699
12	0.820	39.4	1.596
15	0.791	31.0	1.491
18	0.766	24.4	1.387
21	0.745	19.0	1.278
24	0.726	13.9	1.143
27	0.718	11.7	1.068
30	0.707	8.7	0.940

(cont.)

Time (mins.)	O.D.	X	$\log_{10}$ X
33	0.700	6.8	0.833
36	0.693	4.9	0.690
39	0.689	3.8	0.580
∞	0.675	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 1.36 \times 10^{-3}$ sec^{-1}.

Third run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 5.0×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.786	100	2.000
3	1.671	77.0	1.887
6	1.579	58.6	1.768
9	1.501	43.0	1.634
12	1.435	29.8	1.474
15	1.371	17.0	1.230
18	1.349	12.6	1.100
21	1.335	9.8	0.991
24	1.326	8.0	0.903
27	1.320	6.8	0.832
30	1.309	4.6	0.663
∞	1.286	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 1.73 \times 10^{-3}$ sec^{-1}.

From the above, $k_{av} = 1.54 \pm 0.18 \times 10^{-3}$ sec^{-1},

and $t_{\frac{1}{2}} = 7.5 \pm 0.9$ mins..

Acetolysis of bicyclo(3.2.2)nonan-2-yl tosylate (93).

First run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 3.6×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.113	100	2.000
3	1.087	92.8	1.968
6	1.059	84.9	1.929
9	1.033	77.6	1.890
12	1.006	70.2	1.846
15	0.998	65.1	1.814
18	0.965	58.7	1.769
21	0.948	53.9	1.732
24	0.929	48.6	1.687
27	0.913	44.2	1.645
30	0.900	40.5	1.608
33	0.887	36.9	1.567
36	0.875	33.5	1.525
39	0.862	29.9	1.476
42	0.851	26.8	1.428
45	0.842	24.3	1.386
48	0.834	22.1	1.344
51	0.827	20.1	1.303
54	0.820	18.2	1.260
57	0.814	16.5	1.218
60	0.809	15.1	1.179
∞	0.755	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 5.20 \times 10^{-4}$ sec^{-1}.

Second run

Temp.: 73.6° (± 0.2°) NaOAc: 5.14×10^{-3} M

Scan Interval: 3 mins. ROTs : 4.7×10^{-3} M

Time (mins.)	O.D.	X	$\log_{10}$ X
0	1.422	100	2.000
3	1.385	92.1	1.964
6	1.350	84.6	1.927
9	1.320	78.4	1.894
12	1.288	71.5	1.854
15	1.258	65.1	1.814
18	1.229	58.9	1.770
21	1.200	52.8	1.723
24	1.184	49.4	1.694
27	1.164	45.1	1.654
30	1.146	41.3	1.616
33	1.129	37.7	1.576
36	1.110	33.6	1.526
39	1.100	31.5	1.498
42	1.082	27.7	1.442
45	1.069	24.9	1.396
48	1.060	23.0	1.362
51	1.050	20.8	1.318
54	1.040	18.7	1.272
∞	0.952	0.0	-

From $\log_{10}$ X vs. t, $k_1 = 5.24 \times 10^{-4}$ sec^{-1}.

From the above, $k_{av} = 5.22 \pm 0.03 \times 10^{-4}$ sec^{-1},

and $t_{\frac{1}{2}} = 22.2 \pm 0.1$ mins..

TABLE I

G.L.C. Data

Compound	Column	Temp. (°C)	Press. (lb./in.^{2})	R_t (mins.)
2	2% SE 30	75	16	2.5

Compound	Column	Temp. (°C)	Flow (ml./min.)	R_t (mins.)
19	1% SE 30	125	39	4.9
41	1% QF 1	200	42	7.0
30	"	210	39	35.6
65	"	"	40	109.5
39	"	225	48	9.9
18	5% QF 1	100	24	16.4
27	"	"	39	9.8
44	"	"	30	14.6
55	"	"	53	5.9
16	"	200	43	10.0
31	"	"	39	5.0
40	"	"	38	4.5
45	"	"	66	11.3
50	"	"	39	4.8
13	10% PEGA	125	39	9.3
14	"	"	39	10.6
17	"	"	40	12.6

Table I (cont.)

Compound	Column	Temp. (°C)	Flow (ml./min.)	R_t (mins.)
20	10% PEGA	125	40	5.6
24	"	"	34	9.1
25	"	"	39	9.7
26	"	"	39	9.7
46	"	"	40	7.7
48	"	"	40	11.7
49	"	"	34	8.5
56	"	"	42	9.8
110	"	"	52	5.6
115	"	"	36	8.4

Notes on Tables II and III.

Table II

Protons are recorded as shown below:

H_X ← proton(s) attached to carbon X (includes chemically equivalent protons attached to another carbon).

chemical shift (τ). → X.XX

description of signal (see below). → x

X,X ← coupling constants (Hz), if discernible.

Signal Descriptions

s = singlet	bs = broadened singlet
d = doublet	quin. = quintet
t = triplet	sext. = sextet
q = quartet	ov. = overlapping
m = multiplet	

Table III

$\nu^{cm.^{-1}}_{OH\ app.}$ = observed hydroxyl stretching "frequency".

ε_a = molar absorptivity of the hydroxyl in the alcohol concerned.

$\Delta\nu_{\frac{1}{2}}$ = half band width.

$\varepsilon_b/\varepsilon_f$ = ratio of molar absorptivity of bonded hydroxyl (ε_b) to that of free hydroxyl (ε_f), giving a rough estimate of conformer distribution in the alcohol.

α/β = asymmetry of the absorption band; the nearer to unity is the value, the greater is the symmetry.

TABLE II

N.M.R. Spectra

Compound	H_1	H_{2a}	H_{2s}	H_3	$H_{6,8}$
2	7.16 m	8.68 m		8.31 quin. 6	3.84 q 4.5,3.5
16	6.87 m	7.89 d of t 12,6	8.67 d of q 12,10,1	4.81 m	3.70 2 ov. q 5,3
17	6.83 m	7.95 d of t 13.5,6.5	8.83 d of q 13.5,10,2	6.21 m	3.73 2 ov. q 5,3
18	6.67 m	7.47 d 4		-	3.59 sext. 8.3,6.2,1.3
20	6.81 m	8.01 q 14,6	8.42 q 14,2	-	3.59 2 ov. q 4.5,3
74	6.93 m	8.05 d of t 12,6	8.69 d of q 12,10.5,1	5.40 m	3.80 2 ov. q 4.5,3.5
86	6.92 m	-		6.30 s	3.78 2 t's 3.5
88	6.90 m	-		5.38 s	3.78 2 ov. q 5,3

Table II (cont.)

Compound	H_1	H_{2a}	H_{2s}	H_3	H_6	H_8
30	7.40 m	7.83 normal pattern obscured		4.53 m	6.52 s	8.20 s
31	7.52 m	7.84 d of t 12,6	8.52 t 12	4.43 m	3.74 q 5,3	8.23 s
25	7.53 m	7.95 d of t 12,6	8.74 t 12	5.87 m	3.79 q 5,3	8.33 s
26	7.43 m	8.80 t 12	7.82 d of t 12,6	6.43 m	4.01 q 5,3	8.35 s
27	7.40 m	7.43 s		-	3.68 q 5,3	8.20 d 2
65	6.87 m	7.70 m		4.30 m	6.53 s	6.67 m
75	7.53 m	7.98 d of t 12,6	8.56 t 12	5.03 m	3.83 q 5,3	8.40 s

	H_1	H_2	H_4	H_6
19	6.87 m	7.64 d 4	7.37 d 4	3.70 q 5,3.5

Table II (cont.)

Compound	H_1	H_{2a}	H_{2s}	H_3	$H_{6,8}$
24	8.07 m	7.95 m	8.58 t 12	5.90 m	8.37 s
77	8.18 m	7.60 - 8.60 m		5.10 m	8.37 m
89	8.18 m	-		5.16 s	8.40 m

	$H_{1,5}$	H_2	H_3	H_4	H_{6-9}
46	7.00 m	-	8.30 m	8.47 m	3.73 m
48	6.93 m	6.50 m	8.27 m	8.53 m	3.80 m
49	8.25 m	6.21 m	8.37 m		
93	8.17 m	5.45 m	8.50 m		

	$H_{1,5}$	$H_{3,4}$	$H_{6,7}$	H_8	H_9	$H_{10,11}$
45	6.95 m	8.17 m	3.83 m	6.29 q 9,2	6.65 q 9,2	6.03 s

Table II (cont.)

Compound	H_1	H_2	H_3	H_4	H_5	H_{6-9}
44	6.30 m	-	7.42 t 7	7.95 m	6.83 m	3.69 m
50	6.77 m	5.15 m	7.97 m	8.40 m	7.03 m	3.66 m

	$H_{1,5}$	H_2	$H_{3,4}$	$H_{6,7}$	$H_{8,9}$
13	7.43 m	6.30 m	8.40 m	3.88 m	8.35 t 2
92	7.40 m	5.53 m	8.32 m	3.97 m	8.42 t 2

	$H_{1,5}$	H_2	$H_{3,4}$	$H_{8,9}$	$H_{6,7}$
14	7.70 m	6.33 m	7.90 - 8.43 m		3.85 m
40	7.53 m	5.01 m	7.80 - 8.50 m		3.73 m

	$H_{1,5}$	H_2	$H_{3,4}$	$H_{8,9}$	H_6	H_7
39	7.37 m	4.85 m	7.83 - 8.35 m		6.83 q 10,2	6.57 q 10,2

Table II (cont.)

Compound	H_1	$H_{2,4,9}$	H_8	H_5	H_6	H_7
21	6.79 m	8.00 m	5.20 m	7.07 m	3.86 t 8.5	3.54 q 8.5,6.5
	H_1	H_3	H_4	H_5	$H_{6,7}$	$H_{8,9}$
41	6.40 m	7.37 m	7.86 m	6.65 m	3.66 m	6.40 m
	H_1	H_3	$H_{4,8,9}$	H_5	$H_{6,7}$	
55	6.93 m	7.43 t 7	8.12 m	7.28 m	3.77 m	
	H_{2-9}					
110	8.27 m					
	H_{2-5}	$H_{8,9}$	$H_{6,7}$			
115	8.42 m		3.94 d 5			

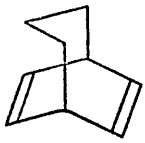
Table II (cont.)

Hydroxyl Proton Resonance Values

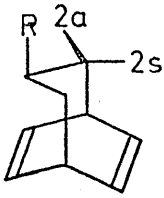
Compound	Chemical Shift	Compound	Chemical Shift
13	8.37 s	46	8.27 s
14	8.54 s	48	8.23 s
17	8.43 s	49	8.40 s
20	6.67 bs	86	8.52 s
24	8.37 s	110	8.59 s
25	8.37 s	115	8.38 s
26	8.71 s	19	1.39 bs

Methyl Group Resonance Values

Compound	Chemical Shift
20	9.02 s
21	8.64 s
46	8.80 s



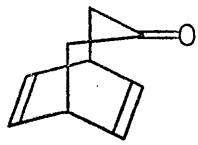
2



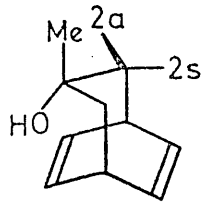
16 R=-OBz

17 R=-OH

74 R=-OTs



18



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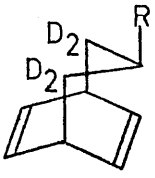
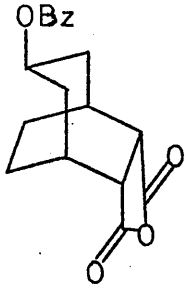


86 R=-OH

88 R=-OTs



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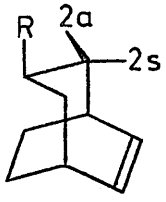
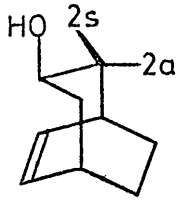


25 R=-OH

31 R=-OBz

75 R=-OTs



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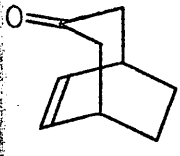

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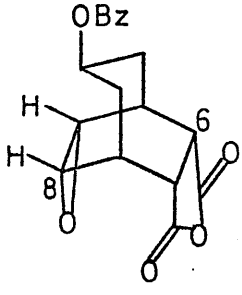

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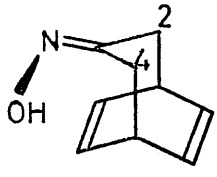

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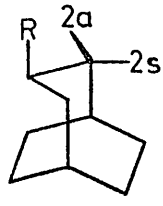
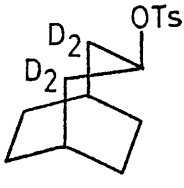


24 R=-OH

77 R=-OTs



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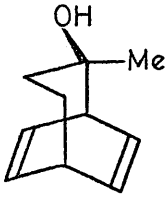

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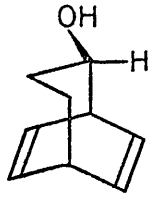

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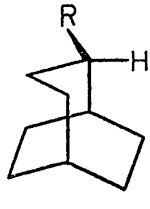
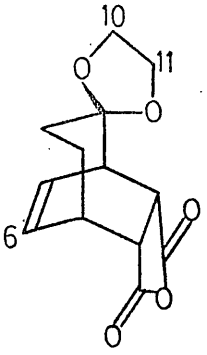


49 R=-OH

93 R=-OTs



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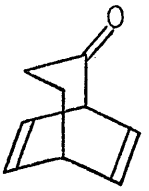

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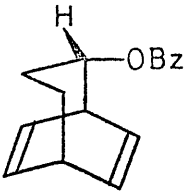

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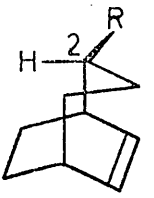
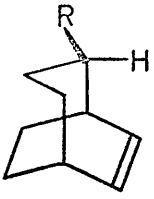


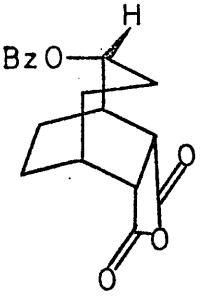
13 R= -OH

92 R= -OTs



14 R= -OH

40 R= -OBz



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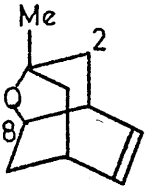

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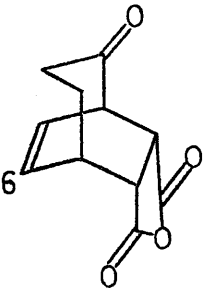

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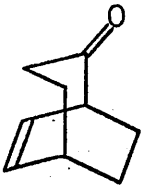

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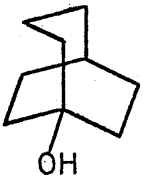

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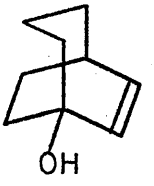

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TABLE III

High Resolution I.R. Spectra

(Spectra were run at a concentration of 0.003M in CCl_4 at 39°).

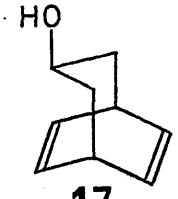
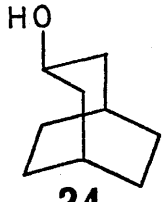
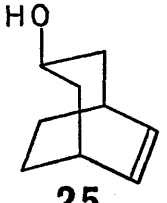
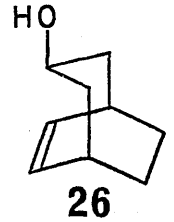
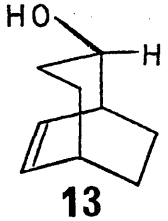
Compound	$\nu_{OH\ app.}^{cm.^{-1}}$	ε_a	$\Delta\nu_{\frac{1}{2}}^{cm.^{-1}}$	$\varepsilon_b/\varepsilon_f$	α/β
 **17**	a) 3621	37.7	29	c/a+b = 0.143	0.61
	b) 3610	28.4			
	c) 3587	9.5	-		-
 **24**	3623	60.0	19	-	0.64
 **25**	a) 3621	43.5	24	0.303	0.46
	b) 3581	13.2	-		-
 **26**	3622	48.1	25	-	0.60
 **13**	a) 3622	28.7	19	0.940	0.58
	b) 3581	27.0	13		0.86

Table III (cont.)

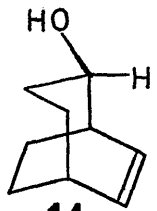
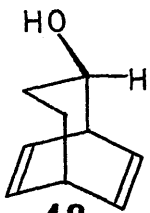
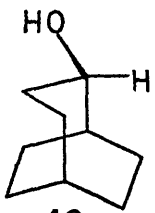
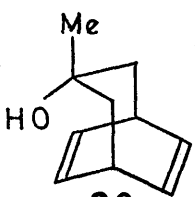
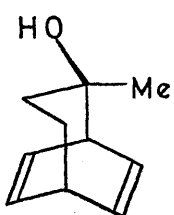
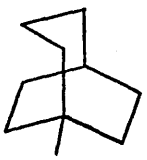
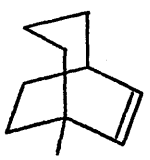
Compound	$\nu_{OH\ app.}^{cm.^{-1}}$	ε_a	$\Delta\nu_{\frac{1}{2}}^{cm.^{-1}}$	$\varepsilon_b/\varepsilon_f$	α/β
 **14**	3621	62.1	16	-	0.78
 **48**	a) 3621 b) 3585	42.0 12.0	31 -	0.285	0.41 -
 **49**	3622	59.9	17	-	0.87
 **20**	3580	90.1	27	∞	1.00
 **46**	a) 3609 b) 3585	30.0 33.0	15 19	1.100	0.75 0.90

Table III (cont.)

Compound	$\nu^{cm.^{-1}}_{OH\ app.}$	ε_a	$\Delta\nu^{cm.^{-1}}_{\frac{1}{2}}$	$\varepsilon_b/\varepsilon_f$	α/β
 **110**	3609	47.2	14	-	1.00
 **115**	3613	56.9	17	-	1.00

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