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SYNTHETIC AND MECHANISTIC STUDIES RELATED TO *cis*- AND *trans*-2-*t*-BUTYL-9-DECALYL CATIONS

A Thesis

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by

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SUMMARY

This thesis is concerned with the generation, by π-route solvolysis, of the isomeric *trans*- and *cis*-2-*t*-butyl-9-decalyl cations, (73) and (74) respectively.

The kinetic and product studies described in Chapter II clearly show that the acetolyses of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl *p*-nitrobenzenesulphonate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)-but-1-yl *p*-nitrobenzenesulphonate (79) both proceed with double bond participation. The rate enhancements, compared with saturated analogues, are *c.* 46 and 8290 respectively. The considerably greater rate enhancement observed in the acetolysis of (79) is explained in terms of the effect of the *t*-butyl group on the side-chain conformations of (79). The acetolyses of (78) and (79) give rise to *c.* 97% and 100% of cyclized products, respectively, obtained from both the *trans*- and *cis*-cations (73) and (74), and include products formed after rearrangement by 1,2-hydride shift of the *cis*-cation (74). The different product distributions obtained in the acetolyses of (78) and (79) are discussed in terms of possible intermediate ion-pairs, with special reference to the locations of the counter-ions and the possible conformations of the cations in the initially-formed intermediate ion-pairs.

Chapter III describes the syntheses of the two unsaturated esters (78) and (79) *via* their parent alcohols 4-(5-*t*-butylcyclohex-1-enyl)butan-1-ol (76) and 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77). Chapter IV describes the syntheses, by unambiguous routes, of the *t*-butyl substituted octahydronaphthalenes (82)-(88), which are the identifiable olefinic products formed in the acetolyses of (78) and (79).

STATEMENT

This thesis contains no material previously submitted for a degree or diploma in any University, and to the best of my knowledge and belief, contains no material previously published or written by another person except where due reference is made in the text.

A.K. Serelis.

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Finally, I wish to thank my wife for her patience, understanding, and sacrifices throughout the course of this work.

CHAPTER I

INTRODUCTION

The effects of substituents on the positions of equilibria and rates of reactions of organic molecules most commonly take the form of electronic effects, transmitted through space or through the carbon skeleton, and steric effects. A substituent may, however, exert its influence by interacting directly with the reaction centre through partial or complete bonding. In such cases the phenomenon is described as neighbouring group participation.[1-6] If the transition state in a rate-determining step is stabilized by such participation, an increased rate of reaction results and the neighbouring group is said to provide anchimeric assistance.[7] The term "intramolecular catalysis" has also been used in this context,[8] but should be strictly applied only to reactions in which the neighbouring group is regenerated in the product. Products with rearranged skeletons, newly formed rings, or possessing stereochemical features inexplicable by the invocation of reaction mechanisms involving normal nucleophilic substitution processes are commonly observed in neighbouring group participation reactions. If neighbouring group participation occurs after the rate-determining step, i.e., in a product forming step, then the structure of the product is affected, but there is no anchimeric assistance.

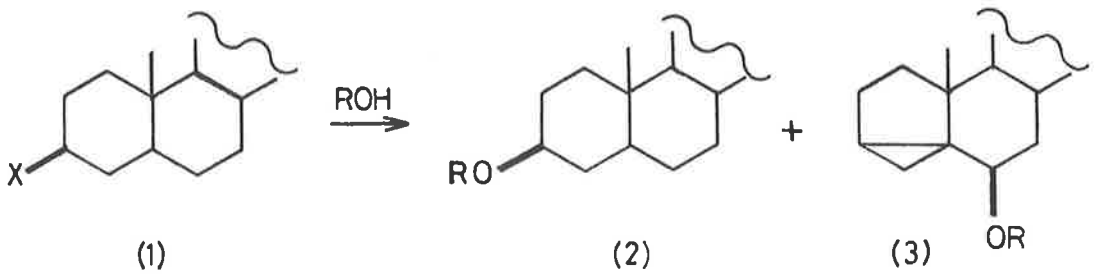
A wide range of functional groups, particularly those possessing lone-pairs of electrons, have been shown to exhibit neighbouring group participation. This includes such classes of functional groups as amides,[9-12] amines,[13-18] ketones,[19-22] carboxylic acids and carboxylate anions,[23-26] esters,[27-30] ethers,[31-37] halides,[38-43] hydroxyl groups,[44-47,335] oximes,[48,49] thioesters,[50-51] and thioethers.[52-57] Participation by metal atoms in organometallic compounds,[58-60] most notably the iron atom of ferrocene derivatives,[61-66,337] has also been observed.

Participation is not, however, restricted to donor groups of the above type. Substitution reactions in which the participating

group is a carbon-carbon bond, for example, have been known for some time. The participating bond may be either a σ-bond or a π-bond.

The earliest examples of participation by carbon-carbon multiple bonds were found in the reactions of allylic[67a,68-71] and benzylic[67b,358] systems. In such cases the participation takes the form of conjugative stabilization of any developing charge in the transition state of the reaction.[5b]

Another type of participation by carbon-carbon π-bonds is observed in systems in which the double bond is in the 3,4-position relative to the leaving group. Behaviour of this type was first noticed by Shoppee[72] in the reactions of 3β-cholesteryl derivatives (1). Shoppee,[72] and later Winstein,[73] found that solvolysis of these derivatives occurred to give products in which the 3β-configuration was retained (2),[72,73] that the corresponding saturated compounds were somewhat less reactive,[73] and that 3α,5-cyclocholestane derivatives (3) could be isolated[73] (fig. I.1). These observations could only be explained in terms of participation of the π-electrons of the 5,6-double bond with the centre of ionization.[72,73,82]



(1) (2) (3)

fig. I.1

Another example of such participation is afforded by the

acetolysis of 4-methylpent-3-enyl tosylate* (4), which proceeds 1200 times faster than that of ethyl tosylate, and yields 2-cyclopropyl-propene (7) as well as 4-methylpent-3-enyl acetate (6)[74] (fig. I.2). Double bond participation is clearly implicated in this reaction, which is postulated as proceeding *via* a carbonium ion** such as (5), in which the positive charge is delocalized over three carbon atoms,[75,76]

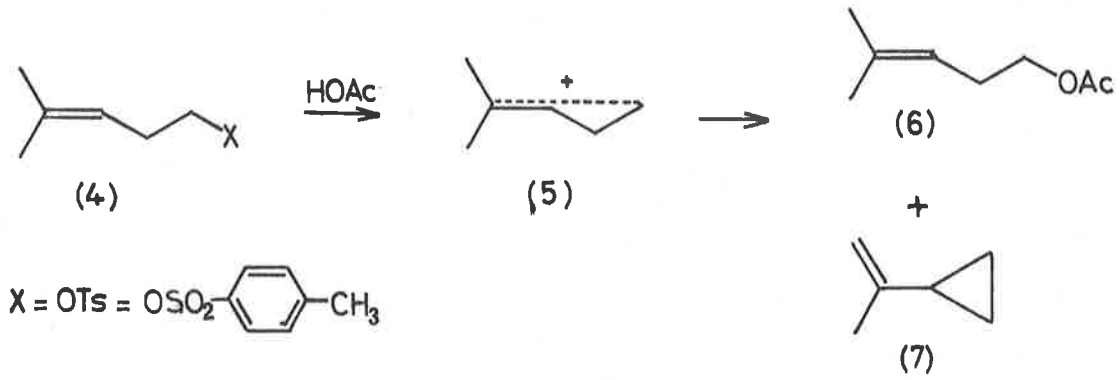


fig. I.2

thus lending considerable stability to the cation.[77] The new bond between C_1 and C_3 is regarded as a σ-type bond formed by p-π overlap[75] (8). The ion (5) has also been considered as an intermediate in the reaction of 4-methylpent-3-enyl chloride (4, X = Cl) with phenol,[91] but, since chloride which is specifically deuterated at C_1 leads to products in which the deuterium label is scrambled over C_1 and C_2, the symmetrical structure (9) is probably a better representation. There has been some discussion, based on theoretical considerations[78] as well as experimental observations that even more extensive delocalization of electrons is involved.[79a]

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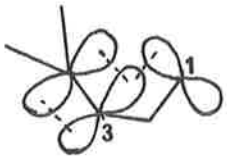
* For convenience in this discussion, the full names of arylsulphonate esters will often be abbreviated to the following common forms: *p*-toluenesulphonate = tosylate, *p*-nitrobenzenesulphonate = nosylate, and *p*-bromobenzenesulphonate = brosylate.

** The nomenclature proposed by Olah[88,89] will be adhered to throughout this discussion.



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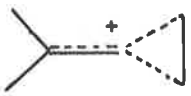
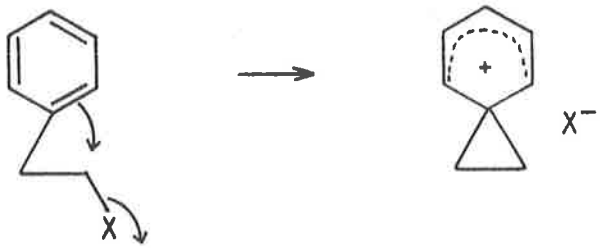


(9)

The general name for interactions of the above type is homoallylic participation, and the intermediate carbonium ions are called homoallyl cations.[67c,72-87,119-123] The related β-phenylethyl systems (10), in which an aryl group participates to form a so-called phenonium ion (11), have also been the subject of many investigations.[4,79d,90]



(10) (11)

It was only relatively recently that participation by more remote double bonds was first observed.[92] Cyclohept-4-enylmethyl brosylate (12) was found to undergo acetolysis 30 times faster than its saturated analogue (which cannot exhibit π-bond participation) forming at least 90% of *endo*-2-bicyclo[3.2.1]octyl acetate (14) (fig. I.3). The bridged carbonium ion (13) was the postulated intermediate in this reaction[92,368] (fig. I.3).

Considerable impetus was given to research in this area when Lawton[93] and Bartlett[94,95] independently reported that 2-cyclopent-3-enylethyl derivatives, (15a)[93] and (15b),[94,95] undergo acetolysis 95 times faster than the analogous saturated compounds and yield *exo*-norbornyl acetate (17) almost exclusively (fig. I.4).

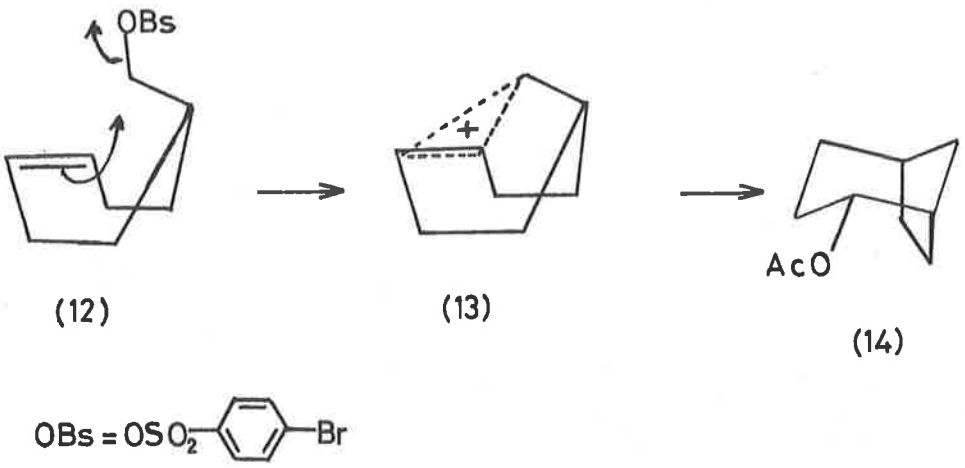


fig. I.3

The importance of these results was that they provided a new route to the norbornyl cation (16), the postulated intermediate, which was the centre of a major controversy which was starting at that time.[96-106] The norbornyl cation (16) had earlier been postulated as the intermediate in the acetolysis of *exo*-2-norbornyl brosylate (18),[103] which proceeds 350 times faster than the acetolysis of the *endo*-isomer (19),[104] and which yields the *exo*-acetate (17) exclusively. The weight of evidence nowadays appears to favour the view that the intermediate cation is actually a pair of classical ions, (20) and (21),

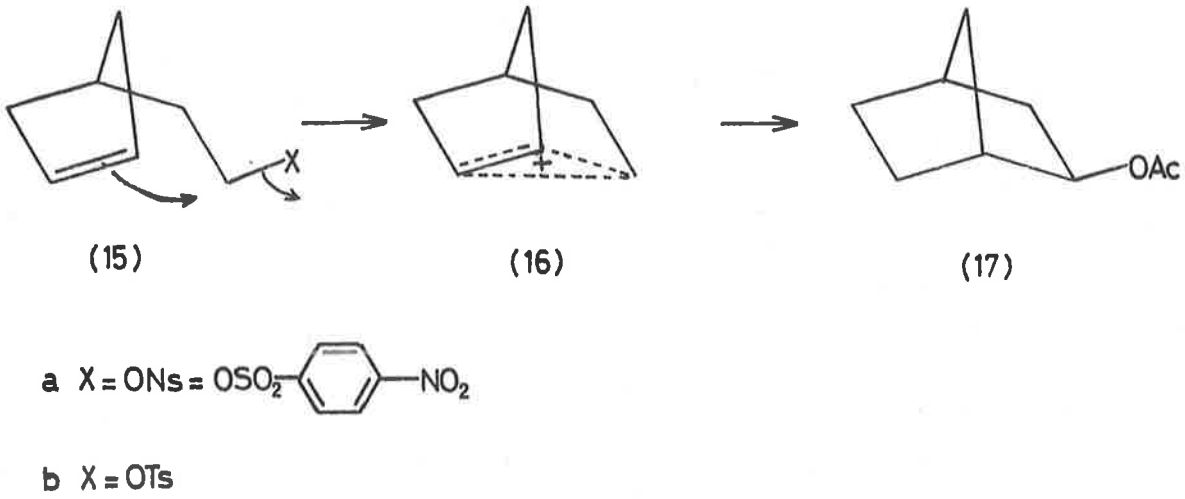
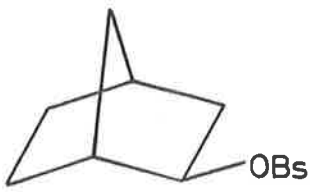


fig. I.4



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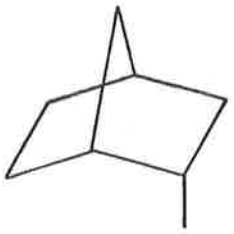
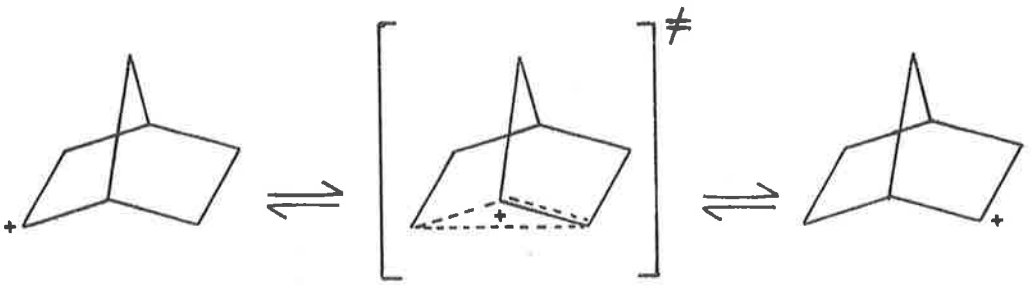


(19)

which undergo a rapid equilibration through a symmetrical transition state resembling (16) (fig. I.5), rather than its being a discrete nonclassical ion in which the positive charge is delocalized. The nature of this enigmatic species is still not fully understood, however, and remains the subject of considerable discussion.[105,338]



(20) (16) (21)

fig. I.5

Winstein has suggested that anchimerically assisted ionizations of substrates in which the neighbouring group contributes π-electrons be called "π-routes to carbonium ions", and that the term "σ-route" be used to designate reactions involving the interaction of σ-electrons with an ionizing centre.[107] Although reactions involving participation by σ-bonds have been widely investigated,[67d,108-116,153,336] because the topic of this thesis is primarily concerned with the generation of carbocations by π-routes, these former will not be discussed except where they have some pertinence as direct alternatives to π-routes.

π-Bond participation in other than allylic and homoallylic systems* has been extensively studied since its discovery by LeNy.[92] Two experimental observations which have been critical in the inference of π-bond participation are (i) a solvolysis rate which is greater than that found for an analogous saturated compound, and (ii) the formation of cyclized products. Application of these criteria to solvolytic studies has shown that anchimeric assistance is increased when the number of electron-donating substituents on the double bond (i.e., the nucleophilicity of the double bond) is increased,[135-137,156-158] and that participation is particularly favourable when the double bond is in the 5,6-position relative to the leaving group.[135-139] With such an arrangement, a cyclic six-centred transition state can be achieved.

The simplest system containing a double bond in the 5,6-position relative to the leaving group is the 5-hexenyl nosylate (22), the solvolytic behaviour of which has been independently reported by Johnson[140] and Bartlett.[141] Both workers found that solvolysis proceeded at approximately twice the rate of the saturated hexyl ester, and that appreciable amounts of cyclized products were formed. This behaviour was in marked contrast to the solvolysis of 4-pentenyl nosylate (23), which was found to proceed at *c.* 0.7 times the rate of its saturated analogue**,[141] and which yielded no detectable cyclized products.[140,141] Further examples of participation by 5,6-double bonds

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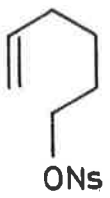
* Participation by the π-electrons of allenes[87,117-123] and acetylenes[124-134] has also been investigated, although nowhere near as widely or intensively as olefinic π-bond participation.

** Rate retardations of similar magnitudes are often observed for the solvolysis of substrates having double bonds in the 4,5-position relative to the leaving group, and are attributed to the adverse inductive effect of the double bond.[138,139,141-143]

are provided by compounds such as (24a), (24c),[139] (24b),[144] (24d), (25),[145] (26), (27a),[138] and (27b),[146] all of which undergo solvolysis at enhanced rates (compared to the corresponding saturated compounds) to yield mainly cyclized products. On the other hand, compounds such as (28a), (29),[138] (28b),[146] and (30)[142] all solvolyze more slowly than their saturated analogues and do not form any cyclized material.

It has been suggested that a symmetrical transition state in which the carbon atom bearing the leaving group is situated over the centre of the participating double bond and in the plane of the π-orbitals is required for cyclization to occur.[135,137,147,148]



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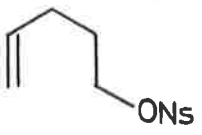

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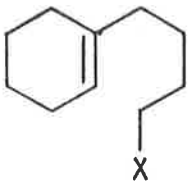
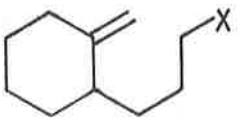


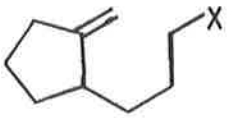
(24)

a X = ONs
b X = OTs
c X = Cl
d X = Br
e X = OH



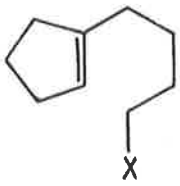
(25)

a X = ONs
b X = Br



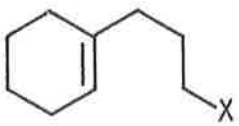
(26)

a X = ONs
b X = Br



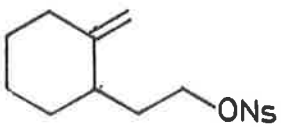
(27)

a X = ONs
b X = OTs



(28)

a X = ONs
b X = OTs



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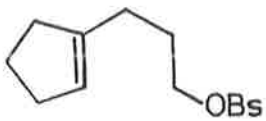


(30)

In compounds such as (23), (28), (29), and (30), where the double bond is in a 4,5-relationship to the leaving group, the spatial separation between the π-bond and the centre of ionization is too great for cyclization to occur *via* a transition state of the required geometry without the addition of considerable strain energy.

There have been examples reported where cyclization of 5,6-unsaturated compounds has been found to result in the formation of 5-membered rings instead of the more usual 6-membered ring. In the acetolyses of 6-methylhept-5-enyl nosylate (31)[149] and 6-phenylhex-5-enyl brosylate (32)[143] (fig. I.6), for example, the increased strain

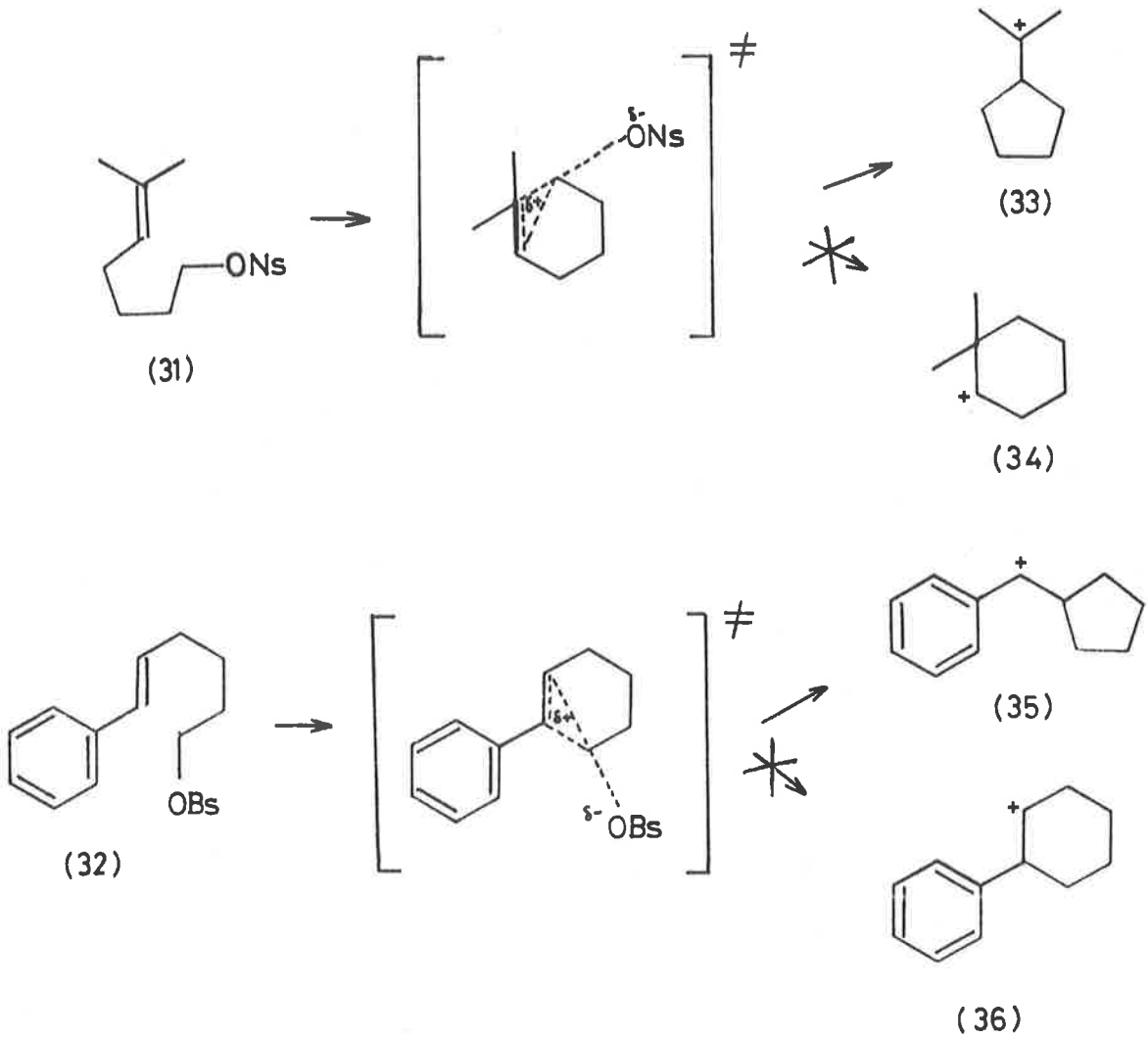
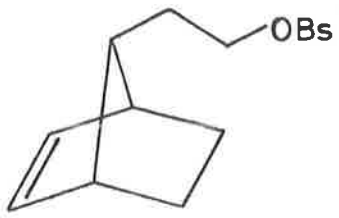


fig. I.6

energy introduced by collapse of the cyclic six-centred transition state to a 5-membered ring is offset by the formation of a more stable carbenium ion than would be obtained by collapse to a 6-membered ring. Thus, in the acetolysis of (31), the tertiary carbenium ion (33) is formed in preference to the thermodynamically less stable secondary carbenium ion (34), and in the acetolysis of (32), the resonance stabilized benzylic carbenium ion (35) is formed rather than the unconjugated carbenium ion (36) (fig. I.6).

Several cases of compounds in which a double bond in a 5,6-relationship to a leaving group failed to exhibit any participation on solvolysis have been reported. Any possibility of double bond participation in the solvolysis of 2-(*anti*-7-norbornenyl)ethyl brosylate (37) is clearly precluded by the geometric arrangement of the double bond and the leaving group, and in fact no participation is observed on acetolysis of this compound.[150] The *syn*-isomer (38), on the other hand, does undergo acetolysis with double bond participation.[150] A more subtle example of a 5,6-unsaturated compound failing to cyclize on solvolysis is afforded by *trans*-3-allylcyclohexyl brosylate (39a) and tosylate (39b).[151] The authors suggest that the complete absence of any π-bond participation in the solvolysis of these compounds can be explained by an unfavourable p- to π-orbital overlap in the transition state of cyclization.[151] (see fig. I.7).



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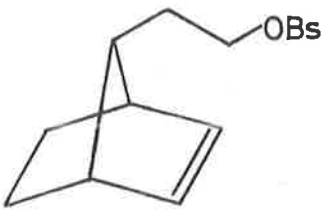

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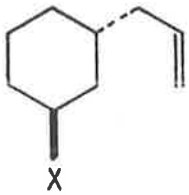
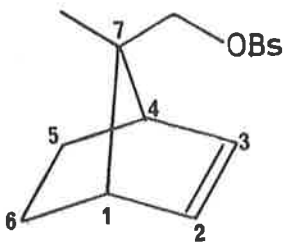


(39) a X = OBs
b X = OTs

Although the absence of participation in solvolytic reactions involving a double bond in a 4,5-position relative to a leaving group is usually quite general, there do exist two examples where such participation has been observed. Acetolysis of the norbornenyl brosylate (40) has been shown to proceed with double bond participation, although at a rate three times slower than that of its saturated analogue, to give a 45% yield of cyclized products.[152] In contrast, the acetolysis of the structurally similar brosylate (41) proceeds, as expected, with no detectable participation by the 4,5-double bond.[154,155] This difference in behaviour has been attributed to the effect of the 7-methyl group of (40) causing subtle distortions in molecular geometry. It was suggested that non-bonded repulsions between the 7-methyl group and the *exo*-hydrogens at C_5 and C_6 decrease the separation between C_8 and the double bond to such an extent that π-bond participation becomes possible.[152]



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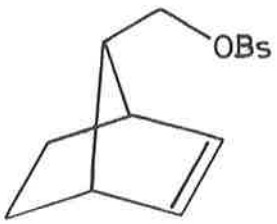

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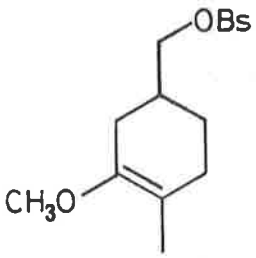

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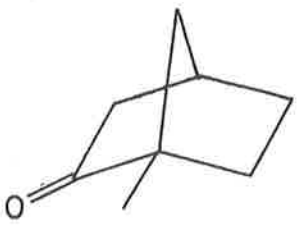
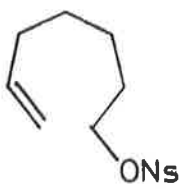


(43)

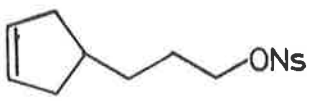
The second example is afforded by the solvolysis of 3-methoxy-4-methylcyclohex-3-enylmethyl brosylate (42) in acetonitrile buffered with triethylamine.[157,158] After acid hydrolysis, the product mixture was found to contain 12% of 1-methylnorcamphor (43). The combined electron-donating effects of the methyl and methoxyl groups provided sufficient enhancement of the nucleophilicity of the double bond to cause solvolytic ring closure in this otherwise unfavourable system. From rate measurements in related compounds,

Felkin and Lion[157,158] have found that methoxy substitution of a double bond increases its nucleophilicity by a factor of 100-200, and that methyl substitution produces a 6-8 fold enhancement.[136,158] Bartlett and Sargent had previously reported that methyl substitution caused rate enhancements of a similar magnitude in the solvolysis of 2-(cyclopent-3-enyl)ethyl derivatives.[135]

Participation by double bonds in a 6,7-position relative to a leaving group has been observed in some systems, but the efficiency of such participation is considerably less than for 5,6-double bond participation. Solvolysis of 6-heptenyl nosylate (44) in 2,2,2-trifluoroethanol, a non-nucleophilic ionizing solvent, yielded 17% of cyclized products.[159] In contrast, solvolysis of the same substrate (44) in the more strongly nucleophilic solvent formic acid proceeded at approximately the same rate as that of 6-hexyl nosylate and gave only 1% of cyclized product.[140] The effect of solvent nucleophilicity has been studied more thoroughly for 5-hexenyl systems,[160] where it was found that the yield of cyclized products could be varied markedly by using solvent mixtures incorporating, with acetic acid, co-solvents of widely differing nucleophilicity and ionizing power.



(44)



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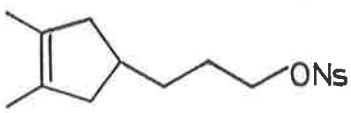
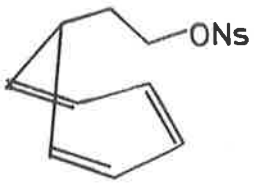


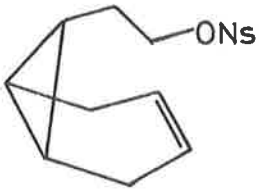
(46)

Studies directed more toward an evaluation of double bond nucleophilicity in terms of substrate-linked factors rather than control of the competing reaction in which the leaving group undergoes direct displacement by an external nucleophile have also been carried

out. Bartlett and co-workers, for example, found that 3-(cyclopent-3-enyl)propyl nosylate (45), underwent acetolysis at the same rate as its saturated analogue and formed no cyclized products.[137] The introduction of two methyl groups, however, increased the nucleophilicity of the double bond sufficiently to enable participation to occur. Thus, 3-(3,4-dimethylcyclopent-3-enyl)propyl nosylate (46) underwent acetolysis 3.2 times faster than its saturated analogue, yielding approximately 60% of cyclized products.[137]



(47)



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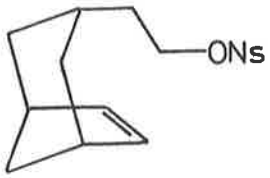
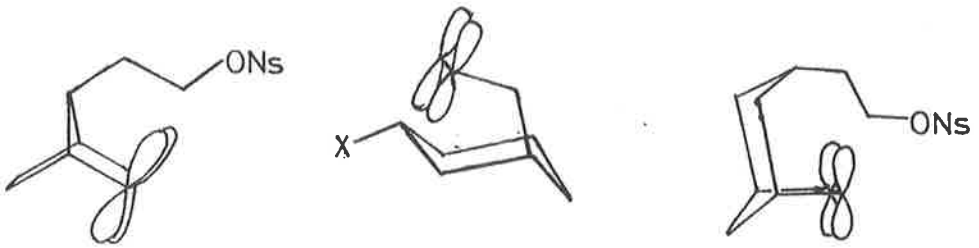


(49)

Sargent and McLaughlin[148] have compared the anchimeric assistance which attends the solvolysis of model compounds such as (15a),[93] and (15b),[94,95] and (38),[150] and have suggested that greater ground state proximity of the double bond to the site of displacement results in increased nucleophilic efficiency for double bond participation.[148] In compounds such as (45),[137] the ground state proximity is even greater, but the impact of this increased proximity is offset by adverse torsional interactions in the transition state for displacement at a primary propyl (45) as opposed to a primary ethyl (15a,b) carbon atom.[148] In support of this contention, the unsaturated nosylates (47),[148] (48),[162] and (49)[161] undergo acetolysis with rate enhancements of 16, 3, and 18, respectively over their respective saturated analogues. Despite the increased 6,7-double bond participation exhibited by these compounds relative to (45), Sargent and McLaughlin consider that the observed magnitudes of the rate enhance-

ments are not in keeping with the ground state proximities of the double bond and the carbon atom bearing the leaving group.[148] They suggest that π-bond participation in the acetolyses of (47), (48), and (49) is retarded by difficulty in achieving colinearity of the π-electron nucleophile, primary carbon, and potential leaving group in the transition state of the reaction.[148] (c.f. the failure of (39a) and (39b) to undergo cyclization during acetolysis.[151]) (fig. I.7).



(37) (39) a X = OBs b X = OTs (49)

fig. I.7

Since the appearance of LeNy's original communication,[92] numerous studies of π-routes to carbenium ions have been reported. Most of the activity has been concerned with (i) establishing the conditions under which double bond participation in unsaturated molecules will occur, (ii) comparing the nature of the products formed by π-routes with those from σ-routes and direct routes, and (iii) using π-routes in synthesis,[125,171-182] particularly in biogenetic-type syntheses of steroid and terpenoid nuclei from acyclic polyenes.[163-171]

One of the most interesting features encountered in the study of carbocations generated by solvolysis is the wide diversity of products which can be obtained from formally identical cations obtained by different π-routes, σ-routes, and direct routes. Solvent capture of the cation can result in the formation of products of sub-

stitution or of elimination. The variation in the proportions of isomeric products of each type is of particular interest because these can vary markedly in a manner which is difficult to predict, or to rationalize with any degree of generality.

Cocivera and Winstein[183] have demonstrated a relationship between ion-pairing and the proportion of elimination products obtained in the solvolysis of *t*-butyl halides. Solvolysis of these substrates in water, a highly dissociating solvent, was found to produce only a small amount (*c.* 5%) of olefin, the yield of which was independent of the nature of the leaving group. In more weakly dissociating solvents (ethanol, acetic acid) the yield of olefin was found not only to increase dramatically (to a maximum of 73% from *t*-butyl chloride in acetic acid), but also to vary quite markedly according to the nature of the counter-ion. The authors concluded that undissociated ion-pairs were involved in the solvolyses carried out in ethanol and acetic acid, but were unwilling to specify whether the proton was removed by a solvent molecule influenced by the counter-ion or by the counter-ion itself.[183]

Skell and Hall have proposed a similar rationale to explain the products of solvolysis of *threo*- and *erythro*-3-deutero-2-butyl tosylates.[184] The extent of deuterium loss was used as a measure of the proportion of olefinic product formed by *cis*-elimination and *trans*-elimination pathways. The former mechanism was found to be favoured by less basic solvents, and the authors suggested that the tosylate counter-ion was probably the base responsible for removal of a proton in these systems. They rejected the idea that the fate of the intermediate carbenium ion was independent of its origin.

Barlett and co-workers investigated the acetolyses of 5-hexenyl (22), cyclohexyl (50), and cyclopentylcarbinyl (51) nosylates,

all of which yielded cyclohexyl derivatives by π-, direct, and σ- routes respectively[141] (fig. I.8). They found that the ratio of

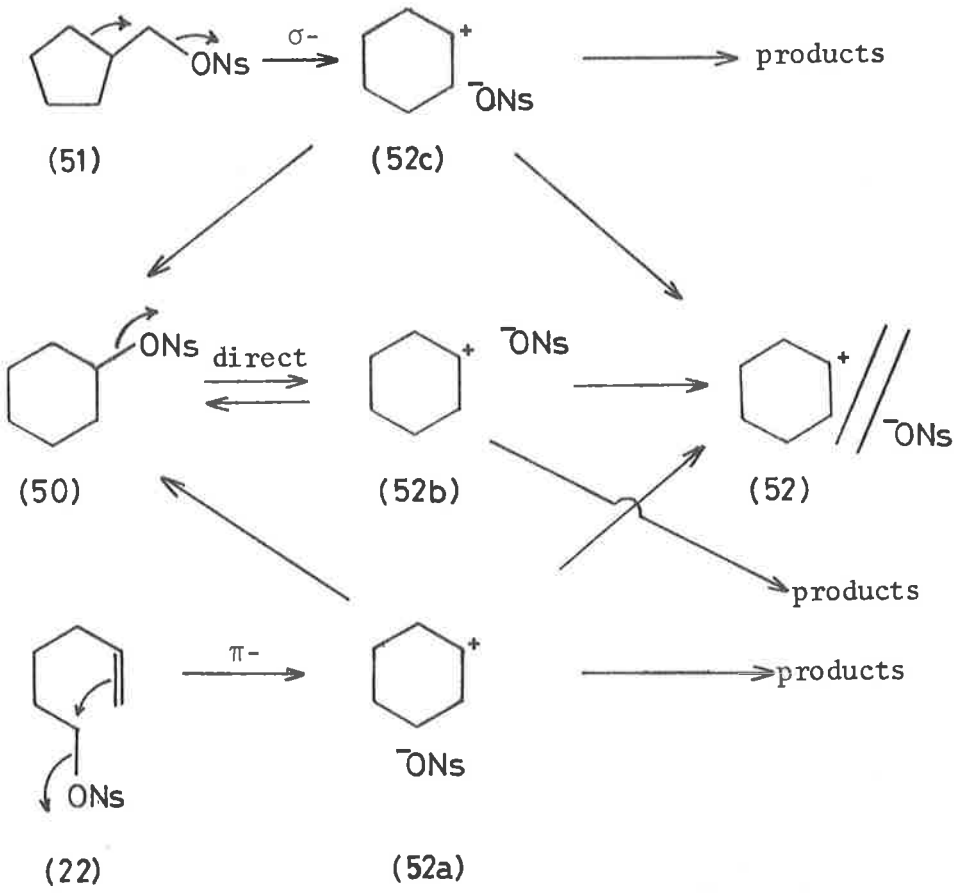


fig. I.8

cyclohexene to cyclohexyl acetate formed from (22), (51), and (50) was 0.4, 3.4, and 6.7 respectively, and concluded that this was not consistent with the intermediacy of a common cationic species. An explanation was proposed in terms of the position of the counter-ion in the intermediate ion-pairs (52a), (52b), and (52c), and of the possibility of internal return in these ion-pairs. The authors suggested that cyclohexyl nosylate (50) underwent simple heterolysis to form the intimate ion-pair (52b) and possibly the solvent separated

ion-pair, or free cyclohexyl cation, (52), and that the products were formed from these in the observed ratio of 6.7. In the case of the ion-pair (52c), obtained *via* the σ-route, the counter-ion is in a good position to undergo internal return to form cyclohexyl nosylate (50), which can then ionize to form (52b). Thus the products from cyclopentylcarbinyl nosylate (51) can arise from any or all of the cations (52), (52b), or (52c) to give the observed olefin:acetate ratio of 3.4. In the ion-pair (52a) obtained from (22) by a π-route, the position of the counter-ion is not ideal for internal return, and the products (olefin:acetate = 0.4) would arise mainly from (52a) or (52).

A comparison of σ-, π-, and direct routes to the cyclopentylphenylcarbinyl cation (35) (fig. I.9) was recently reported by Roman and Closson.[143] Solvolysis of *trans*- and *cis*-6-phenylhex-5-enyl brosylates, (32) and (53) respectively, *trans*-2-phenylcyclohexyl tosylate (55), and a number of cyclopentylphenylcarbinyl derivatives

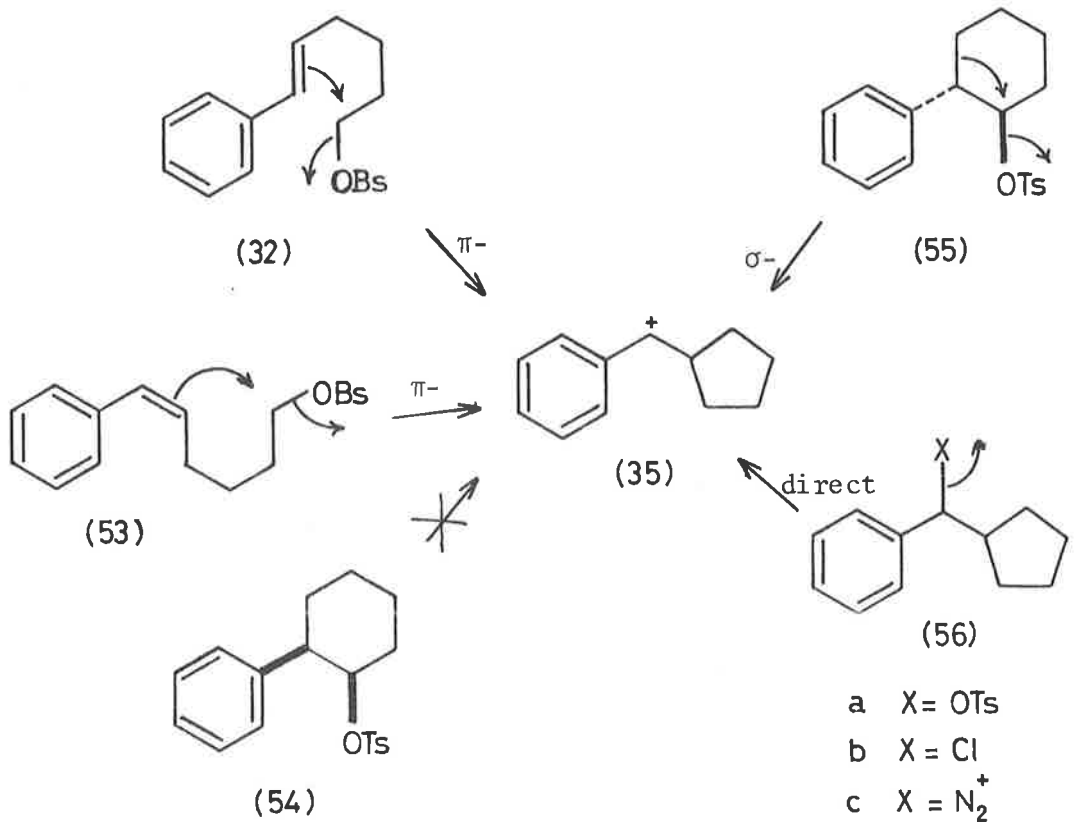


fig. I.9

(56a,b,c) resulted in dissimilar ratios of elimination to substitution products, implying that the intermediate benzylic cation (35) retained a clear "memory" of its route of formation. The authors have suggested that the difference between the product distributions obtained by the different routes could be explained in terms of the relative energetics involved in the different routes. Because of the differences in the relative ground state energies of the respective starting materials, the π-routes would give rise to "hot", or energetic carbenium ions* which are not as selective in their subsequent reactions as the less energetic, or "cool", carbenium ions* obtained by σ-routes and by direct ionization. This postulate was consistent, it was reasoned,[143] with the observation[187] that π-route products were frequently similar to those obtained from σ-route deaminations, which are known to give rise to "hot" carbocations.[188] The variation in the product distributions obtained by the two π-routes was attributed to the sensitivity of the high-energy intermediate carbenium ions to minor conformational and solvation differences.[143]

The 9-decalyl cation (59) has been generated by a wide variety of solvolytic routes (fig. I.10). It is therefore a particularly valuable system in that the effects on product distribution caused by different modes of generation can be compared. In particular, the variation in the yields of the two olefinic products, $\Delta^{1,9}$-octalin (57) and $\Delta^{9,10}$-octalin (58), is a useful probe for studying the intimate mechanism involved in the solvolysis.

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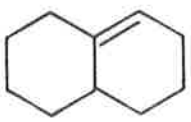
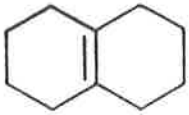
* The difference in energy between "hot" and "cool" carbenium ions, and their subsequent differences in reactivity, has been ascribed mainly to differences in degree of solvation.[185,186,369]



(57)



(58)

The solvolysis of *cis*- and *trans*-9-decalyl derivatives, (60) and (61) respectively, has been examined both in these laboratories[139] and elsewhere.*[144,189] Fort[189] has dismissed the role of ion-pairs in controlling product formation as being relatively unimportant in this system, and has suggested that conformationally non-equivalent carbocations, derived from the isomeric precursors (60b) and (61b) are the product-determining species, but was unwilling to speculate as to their possible shapes. The molecular relaxations which are required to equilibrate these types of systems are known to have rate constants[195-197] of the order of 10^6-10^8 sec^{-1}, while carbenium ion collapse, either by solvent capture or by loss of a proton, is thought to be a diffusion controlled process[189] occurring with a rate constant[198,199] in the range 10^9-10^{11} sec^{-1}. Reaction of the cations with solvent may therefore be expected to be considerably faster than conformational interconversion.[189,359]

Grob, in a preliminary communication,[200] argued along similar lines to Fort,[189] and suggested that *cis*-like (59a) and *trans*-like (59b) conformations of the 9-decalyl cation were involved (fig. I.11). He has since revised this postulate, and now considers that equilibration of the two conformational isomers (59a) and (59b) is possible, and that the product distributions can be adequately explained in terms of unsymmetrically solvated stereoisomeric ion-pairs (59b), obtained

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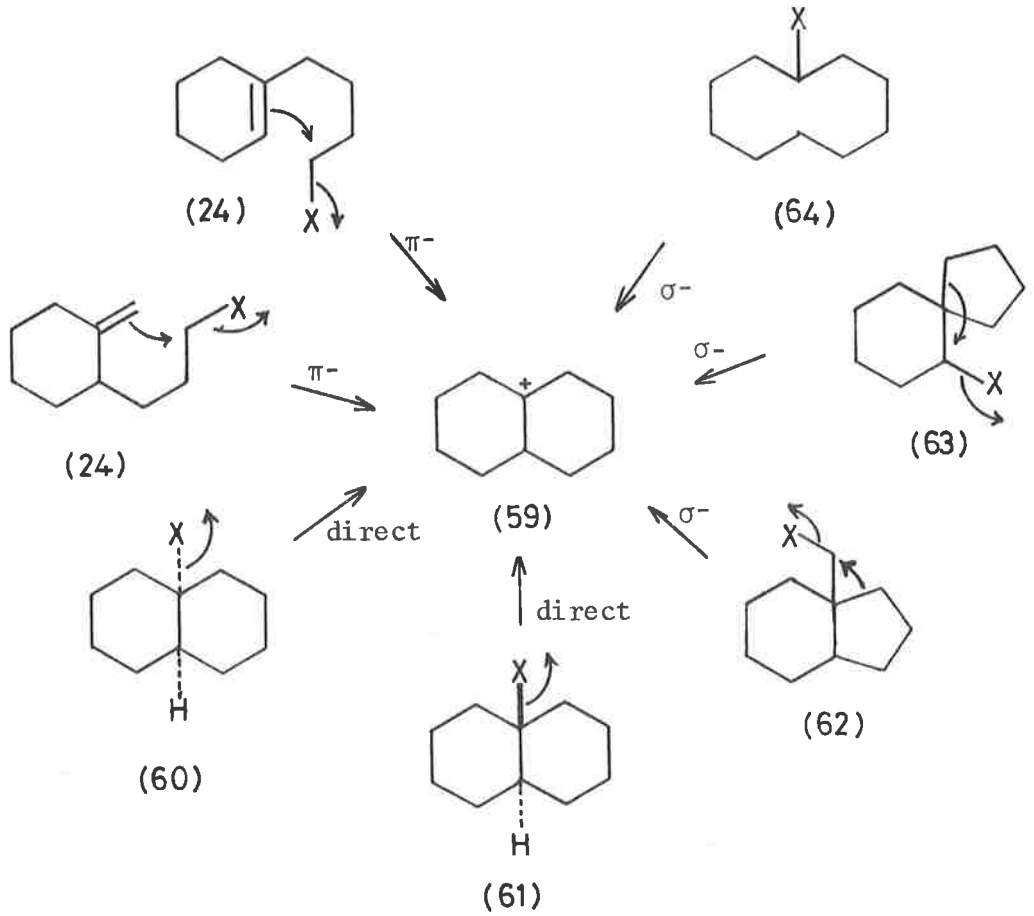
* Olah's investigations[190] on (60d) and (61d), as well as on (64), were carried out in super-acid media and hence do not constitute true solvolytic routes to (59).



24a, X = ONs	(ref. 139)	60,61a, X = Cl	(ref. 139,144)
b, X = OTs	(ref. 144)	b, X = OpNb	(ref. 139.189)
c, X = Cl	(ref. 139)	c, X = OAc	(ref. 139)
d, X = Br	(ref. 145)	d, X = OH	(ref. 190)
25a, X = ONs	(ref. 145)	62 X = OTs	(ref. 191)
b, X = Br	(ref. 145)	63 X = OTs	(ref. 139,143, 194)
		64 X = OH	(ref. 190)

fig. I.10

directly from (61), and (59c), obtained indirectly from (60) by a ring inversion in the initially formed ion-pair (59a) (fig. I.11).[144] The products arising from the cyclization of (24b) were also considered to be controlled by unsymmetrical solvation of the initially formed ion-pair.[144]

Gream has presented more detailed analyses of the products, particularly the olefins (57) and (58), derived from the 9-decalyl cation (59).[139,145] With regard to the acetolysis of *cis*- and *trans*-9-decalyl derivatives, (60) and (61) respectively, Gream has stated[139]

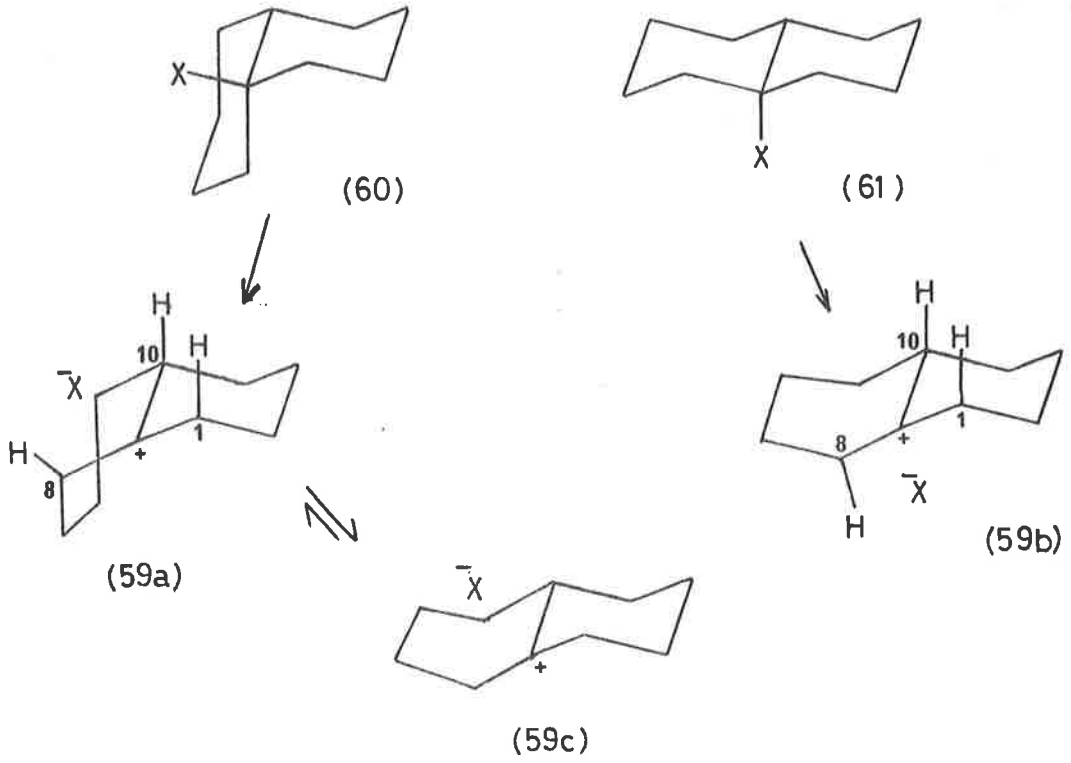


fig. I.11

that his observations in this system are consistent with the formation of two conformational isomers as suggested by Grob[200] and Fort,[189] but considers that the counter-ion plays more than a minor role in determining the nature of the products, acting at least to some extent as the base responsible for removal of a proton to form an olefin. His interpretation of the proportions of olefinic products (57) and (58) in terms of the location of the counter-ion in these and other ion-pairs appears to form a consistent rationale for the mechanism of olefin formation.[139,145]

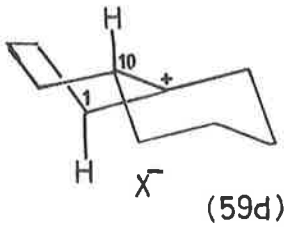
Acetolysis of the *trans*-9-decalyl derivatives (61a) and (61b) gave the two octalins (57) and (58) in the ratios 4.8 and 7.0 respectively.[139] If the cation formed from these derivatives is in fact in the conformation (59b) (fig. I.11), the counter-ion (X^- = Cl^- or $OpNb^-$) is well situated to act as a base in abstracting the hydrogen at C_1 to form $\Delta^{1,9}$-octalin (57), but poorly located to remove the

hydrogen at C_{10}, which is on the opposite side of the molecule, to form $\Delta^{9,10}$-octalin (58). The observed high ratios, 4.8 and 7.0, of (57) to (58) are consistent with this idea. On the other hand, acetolysis of the *cis*-9-decalyl derivatives (60a) and (60b) gave the two octalins (57) and (58) in the ratios 1.09 and 1.12 respectively.[139] The more even product distributions obtained from this system can be rationalized in the same way, as the counter-ion, the hydrogen at C_{10}, and the hydrogen at C_1 (and C_8) are all on the same side of the molecule in the initially formed ion-pair (59a) (fig. I.11). The variation in the ratio of (57) to (58) with the change in leaving group (and hence counter-ion) from chloride to *p*-nitrobenzoate in the *trans*-series (61) is in itself a confirmation of the importance of the counter-ion in the product-determining step.

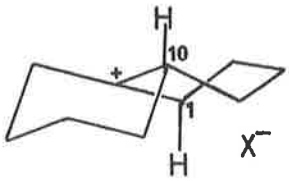
The olefin ratios observed by Grob[144] and by Fort[189] in the solvolyses of *trans*-9-decalyl derivatives (61) differ markedly from those observed by Gream.[139] Grob found that the solvolysis of *cis*- and *trans*-9-chlorodecalin, (60a) and (61a) respectively, in 80% aqueous ethanol gave (57) and (58) in the ratios 1.02 and 0.41 respectively,[144] while Fort found that solvolysis of the corresponding *p*-nitrobenzoates, (60b) and (61b) respectively, in 60% aqueous acetone gave these two olefins in ratios of 1.07 and 1.51 respectively.[189] These results, however, do not necessarily invalidate Gream's hypothesis. Whittaker[201] has shown recently that the counter-ion in intimate ion-pairs plays an important role in cationic reactions of α-pinene and β-pinene in anhydrous acetic acid, whereas in more nucleophilic solvents, such as those containing water, the intimate ion-pair is considerably less important in product formation, if it is formed at all. Also, in an extensive series of investigations, Winstein has shown that ion-pairing is much more important in anhydrous

acetic acid than in solvents containing water.[202]

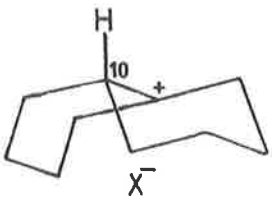
The ratios of olefinic products (57) and (58) obtained when the 9-decalyl cation (59) is generated by π-routes (from derivatives of (24) and (25), fig. I.10) have also been rationalized in terms of the location of the counter-ion in the initially formed intimate ion-pairs.[139,145] In these systems, however, the conformational possibilities for (59) are less clear cut.[139,145] The ratios of (57) to (58) observed on acetolysis of (24a), (24c),(24d), (25a), and (25b) are 2.08, 3.35, 3.25, 1.60, and 4.10 respectively.[139,145] In the four ion-pairs (59d) - (59g) proposed as possible intermediates in the acetolysis of derivatives of (24),[139,145] the counter-ion is on the opposite side of the molecule to the hydrogen atom at C_{10}, removal of which would lead to (58). In two of these ion-pairs, (59d) and (59c), the hydrogen at C_1 on the same side of the molecule is correctly oriented for removal, i.e., parallel to the vacant *p*-orbital of the carbenium ion, but in (59f) and (59g), it is not. It was reasoned[145]



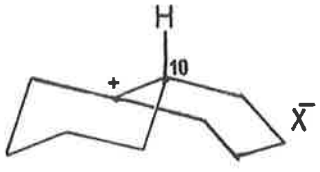
(59d)



(59e)



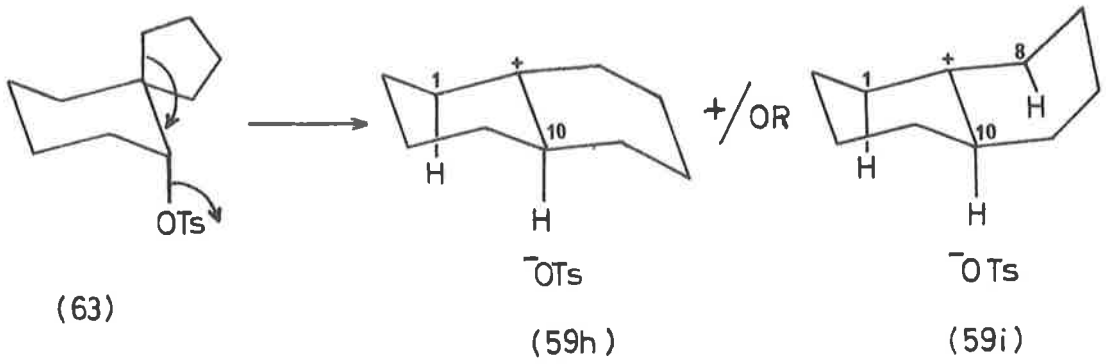
(59f)



(59g)

that the possible ion-pairs which might be obtained by acetolysis of (25a) and (25b) would be very similar to (59d) - (59g) except that the location of the counter-ion would be slightly different. The

preferential formation of $\Delta^{1,9}$-octalin (57) is in all cases in apparent accord with the counter-ion acting as a base, at least to some extent, and removing the more favourably situated hydrogen at C_1 in (59d) and (59e). The similar product ratios obtained from derivatives of (24) and (25) in which the leaving group was the same was held to suggest that similar ion-pair intermediates probably intervene in the acetolysis of these derivatives.[145] Furthermore, the marked differences observed in the product ratios when the leaving group was varied was used as additional evidence that ion-pairs were directly involved, at least in part, in the product forming step.[145] Gream did point out, however, that the formation of considerable quantities of $\Delta^{9,10}$-octalin (58) and *trans*-9-decalyl acetate (61c) from the acetolysis of derivatives of (24) and (25) showed that species and/or factors other than those discussed above are also involved in product formation.[145]



(63) (59h) (59i)

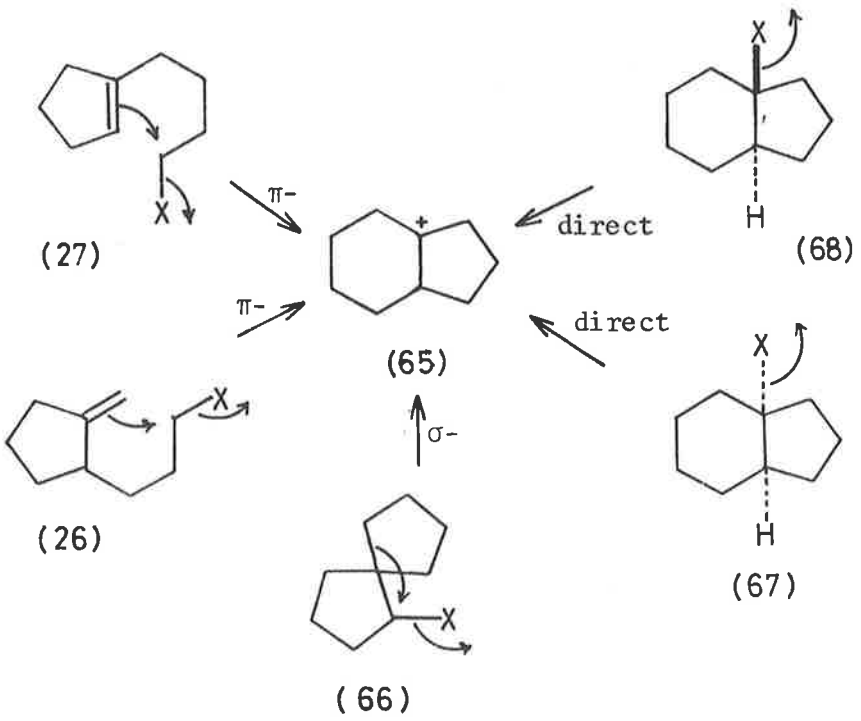
fig. I.12

The acetolysis of spiro[4.5]dec-6-yl tosylate (63) provides yet another example where the products can be conveniently rationalized in terms of at least partial counter-ion control. From this substrate, ion-pairs resembling (59h) and/or (59i) are considered as likely intermediates (fig. I.12).[139] In both of these ion-pairs, the counter-ion is ideally located to remove the hydrogen at C_{10} to form

(58), whereas some movement of the counter-ion would be necessary before it could, if it were indeed the base responsible for olefin formation, remove the hydrogen at C_1 in (59h) or at C_1 or C_8 in (59i) to form (57). The major product would be expected to be $\Delta^{9,10}$-octalin (58) by these considerations, and this has in fact been found to be the case by three independent groups of workers who reported similar ratios of (57) to (58) of 0.35,[139] 0.24,[193] and 0.33.[194]

The generation of the related 8-hydrindanyl cation (65) by a variety of π-, σ-, and direct routes has also been examined (fig. I.13). Although, as Grob has pointed out,[203] the 8-hydrindanyl cation (65) possesses less conformational flexibility than the 9-decalyl cation (59) because of the rigidity of the cyclopentane ring of (65), rationalization of the observed products should still be amenable to the same sorts of considerations as have been applied before. Thus Fort has invoked conformational isomers, in which ion-pairing is probably not important, to explain the products obtained from (67b) and (68b).[189] Grob, on the other hand, has suggested that the products of solvolysis of (27c), (67), and (68) can be satisfactorily explained in terms of unsymmetrical solvation and stereoisomeric ion-pairs,[146] while Gream has again been able to correlate the proportions of olefinic products with the location of the counter-ion in ion-pairs derived from derivatives of (26), (27), (66), (67), and (68).[138]

From the aforegoing discussion it should be apparent that a variety of different factors can and have been considered as having some effect on product formation from carbenium ions. In general, it is most probable that no single factor and/or species can be held to be solely accountable for product formation. The major controlling factor, if indeed there is a single one, can vary, as can the relative weighing of a given combination of factors, according to the gross



26a, X = ONs (ref. 138)
b, X = Br (ref. 138)
27a, X = ONS (ref. 138)
b, X = Br (ref. 138)
c, X = OTs (ref. 146, 203)

66 X = OTs (ref. 193)
67, 68a, X = Cl (ref. 146,203)
b, X = OpNb (ref. 138, 146, 189)

fig. I.13

structure of the carbocation under consideration, the route by which it was generated, the nature of the leaving group, and the solvent system employed. Nowadays, however, it is commonly recognized that reactions of carbenium ions generated by solvolysis must be regarded as reactions of ion-pairs, rather than reactions of free carbenium ions unencumbered by counter-ions.[138,139,141,145,184,201-209,389-392] This is perhaps the only generalization that can be made with any degree of certainty.

To put the topic of this thesis in its proper perspective, it is necessary to re-examine the acetolysis of spiro[4.5]dec-6-yl tosylate (63). Although the major products were those derived from expansion of the cyclopentane ring to form the 9-decalyl cation (59), a small amount of products arising from contraction of the cyclohexane

ring to the 1-cyclopentylcyclopentyl cation (69) and from unassisted ionization to the 6-spiro[4.5]decyl cation (70) were also observed.[139,193,194] (fig. I.14). Since three cations, (59), (69), and (70), were implicated in the solvolysis, the question arose as to whether ionization occurred

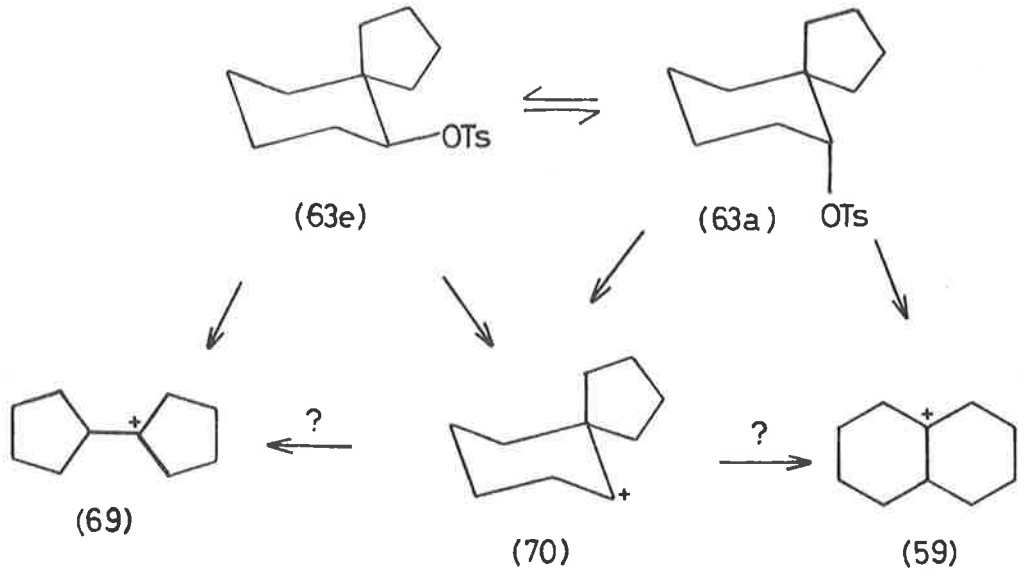


fig. I.14

before bond migration, and whether (70) was therefore a direct progenitor of both (59) and (69) (fig. I.14). In an effort to elucidate the timing of the rearrangement processes, that is, to clarify whether bond migration occurred in concert with or after ionization, and also to study the respective rearrangement processes without the complication of the conformation interconversions which are possible in (63), a study of the acetolyses of the isomeric 9-*t*-butylspiro[4.5]dec-6-yl tosylates (71) and (72) was initiated in these laboratories.*[210]

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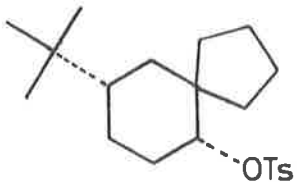
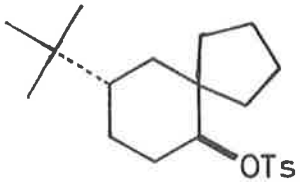
* A less detailed study of the acetolyses of (71) and (72), in which the products were neither completely nor conclusively identified, was subsequently reported by an independent group of workers.[211]



(71)



(72)

The results of kinetic and product studies on the *cis*- and *trans*-spirodecyl tosylates, (71) and (72), clearly indicated that bond migration and ionization were concerted processes in the acetolyses of both of these compounds.[210,356] The products obtained from the acetolyses of (71) and (72) showed that the ring expansions occurred with complete stereospecificity,* a fact which was not evident in the earlier work.[211] This was easily rationalized as a manifestation of the requirement that migrating and leaving groups bear an antiperiplanar arrangement to each other.[213] This condition is satisfied by the chair conformation of the *cis*-tosylate (71), which undergoes ring expansion to form products derived exclusively from the *trans*-2-*t*-butyl-9-decalyl cation (73) (fig. I.15). In the case of the *trans*-tosylate (72), this stereoelectronic requirement for ring expansion cannot be met in the chair conformation (72c) and ring contraction to the cation (75) would be the only possible concerted rearrangement process. However, the formation of only a small amount (*c.* 8%) of products derived from (75) indicated that ring expansion was still the dominant reaction pathway in the acetolysis of (72), and that this must be occurring *via* a boat or twist-boat conformation (72b) in order to

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* At the time, this fact was not conclusively established.[210] It was only at the conclusion of the present work, when stereospecific syntheses of all of the possible products had been achieved, that the stereospecificity of these reactions could be definitely proved.[356]

fulfil the requirement for an antiperiplanar arrangement of migrating and leaving groups (fig. I.15). In this case, the products of ring expansion were derived exclusively from the *cis*-2-*t*—butyl-9-decalyl cation (74) (fig. I.15).

The preponderance of 2-*t*-butyl-$\Delta^{9,10}$-octalin (82) formed in the acetolysis of these derivatives (77% from (71) and 65% from (72)) was in keeping with the observation that in solvolyses of other spiro-compounds (4.g. (63)[139,193,194] and (66)[193]), the formation of tetrasubstituted olefins is preferred. The earlier suggestion that the counter-ion in the initially formed ion-pair was responsible for proton removal[138,139,145] was considered as a likely explanation for this result, since in the ion-pairs (73) and (74) (fig. I.15), the

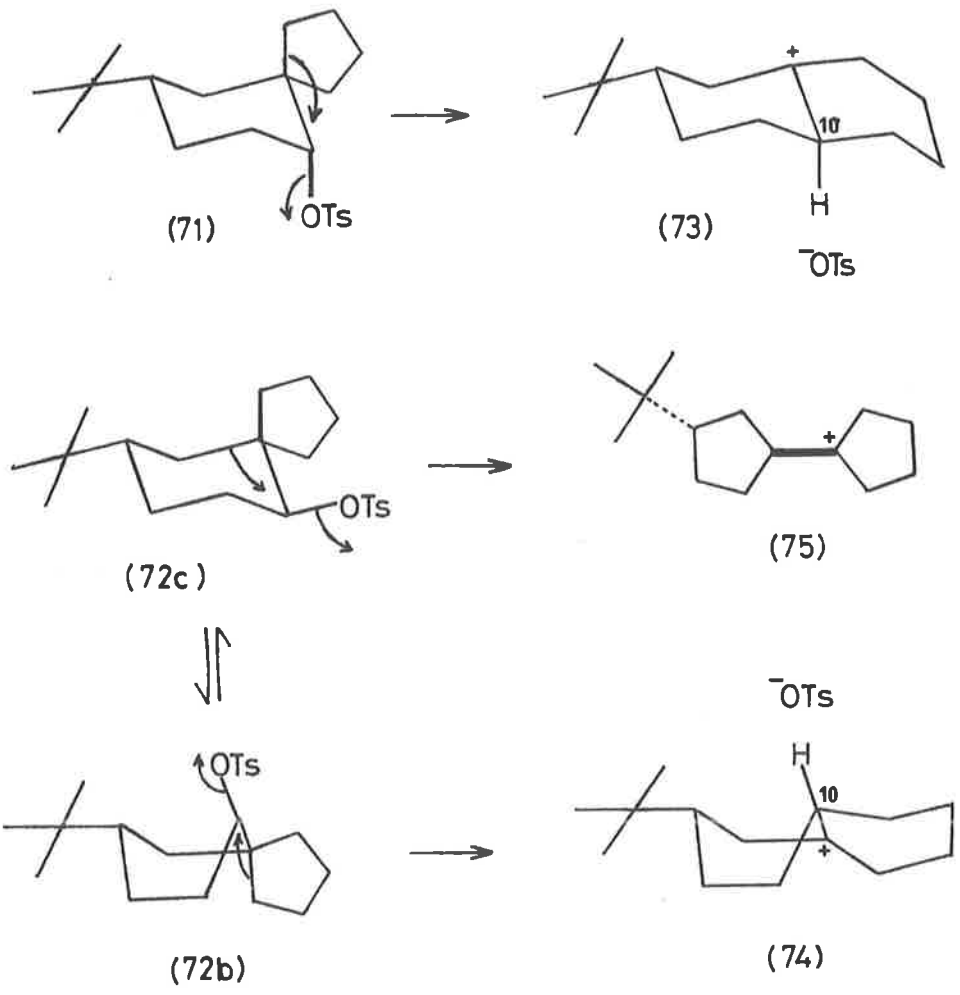
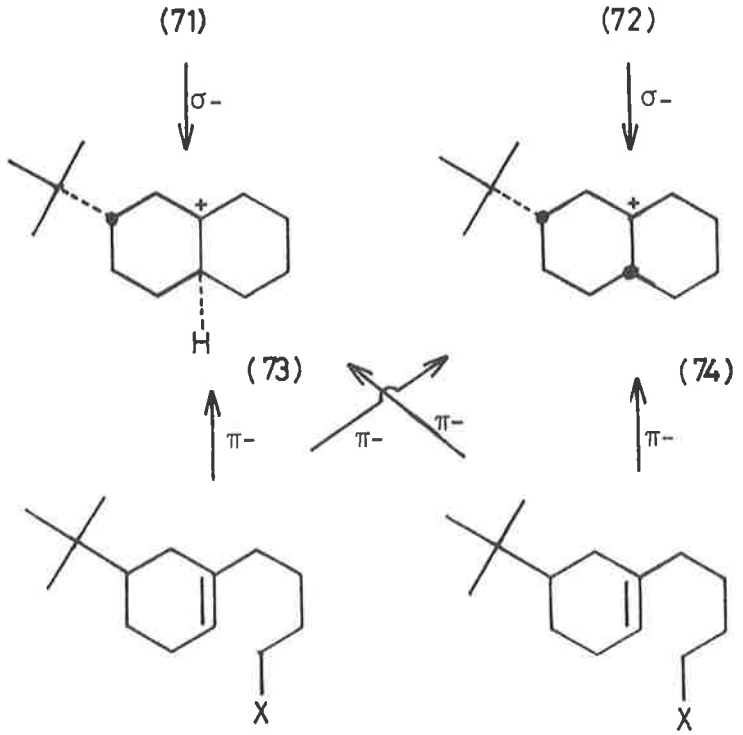


fig. I.15

counter-ion ($^{-}$OTs) is most ideally situated to remove the hydrogen at C_{10} to form 2-*t*-butyl-$\Delta^{9,10}$-octalin (82).[210]

As an extension of Laffer's work,[210] it was decided to generate the *trans*- and *cis*-cations (73) and (74) by π-routes, from the monocyclic precursors (78) and (79) (fig. I.16). Both of the isomeric carbenium ions (73) and (74) would be expected from each of the unsaturated nosylates (78) and (79) (fig. I.16), although not necessarily in equal proportions. It was hoped that the π-route products might provide an interesting and perhaps meaningful comparison with the σ-route products, as had happened in the simpler 9-decalyl (59) (fig. I.10) and 8-hydrindanyl (65) (fig. I.13) systems.



(76) X = OH
(78) X = ONs
(80) X = OAc

(77) X = OH
(79) X = ONs
(81) X = OAc

fig. I.16

The incorporation of the *t*-butyl group into the 9-decalyl cation enables a distinction to be made between the two rings of the

decalin system. Unlike the unsubstituted analogue (59), it is now possible to determine whether proton removal to form $\Delta^{1,9}$-octalins occurs at C_1 or C_8, and perhaps to relate this to the position of the counter-ion in ion-pairs involving (73) and (74).

A second function of the *t*-butyl group is that of a conformational lock.*[212] Although Closson and Gray have provided evidence that π-route solvolyses of 5-hexenyl systems proceed *via* a transition state in which the developing ring is in a chair-like conformation.[214] there are nevertheless a considerable number of possible conformations for the initially formed cation in the generation of a bicyclic system, e.g. (59).[138] The inclusion of a *t*-butyl group should serve to preclude some of the conformations which might normally be possible for the 9-decalyl cation (59), and thereby possibly provide some insight into the importance of conformational effects in reactions of this species.

The results of a kinetic study and a product study of the acetolysis of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl *p*-nitrobenzenesulphonate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)but-1-yl *p*-nitrobenzenesulphonate (79) are presented and discussed in Chapter II of this thesis. The syntheses of these two compounds *via* their parent alcohols (76) and (77) are described in Chapter III.

It was deemed necessary to synthesize by unambiguous routes as many of the expected acetolysis products as possible. The reasons for this are that: (i) it is impossible to interpret the product

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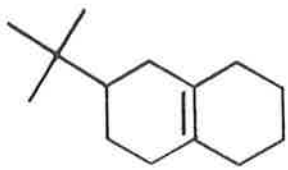
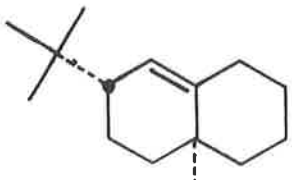
* It has been suggested recently that there are limitations on the use of the *t*-butyl group as a conformation lock.[215] These limitations are said to arise because the *t*-butyl group can distort the ground state geometry of a cyclohexane ring, and because certain transition state geometries can be excluded by steric strain. The significance and applicability of any such limitations in the present system will be considered in the proper context later.

mixtures with any meaning unless the components have been conclusively identified, (ii) gas-liquid chromatographic (g.l.c.) procedures for the identification (by comparison with authentic samples) and quantitative determination of the products had to be developed, and (iii) the stability of the various products to the solvolysis conditions could be verified. The possible olefinic products which can be obtained directly from the cations (73) and (74) are 2-*t*-butyl-1,2,3,4,5,6,7,8-octahydronaphthalene (82), *trans*-7-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (83), *cis*-7-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (84), *trans*-7-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (85), and *cis*-2-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (86).* It is also possible to envisage the formation of four tertiary acetates (89)-(92) by nucleophilic addition of solvent to the cations (73) and



(82)



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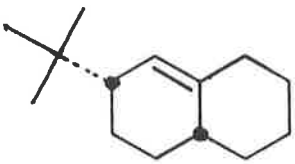

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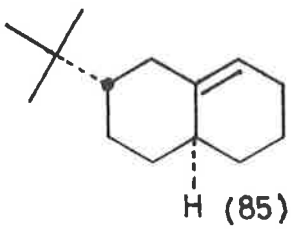

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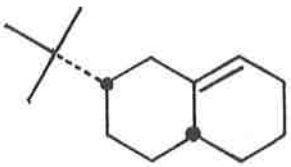

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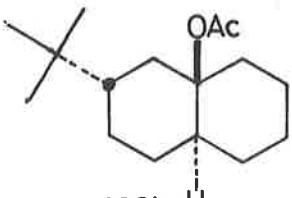
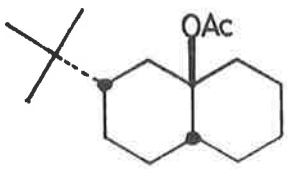


(89)



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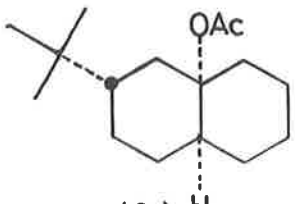

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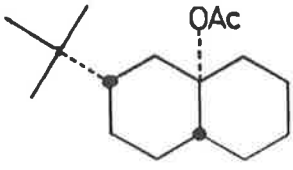

(93)

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* For convenience, these and related compounds will be referred to using the traditional "octalin" nomenclature in the Discussion.

(74). The identification of these acetates was considered to be of only minor significance, incommensurate with the major effort which would be required for their synthesis. No attempt was therefore made to prepare them, except where (89) was fortuitously required as an intermediate in the synthesis of the octalins (83) and (85).

Laffer had previously achieved syntheses of (82) and (85).[210] In the present work, (82) was used as a relay in the synthesis of (83), which also gave (85) as a side product. In Chapter IV, the syntheses of the five olefins (82)-(86) are described.

CHAPTER II

RESULTS AND DISCUSSION

The solvolysis of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl *p*-nitrobenzenesulphonate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)but-1-yl *p*-nitrobenzenesulphonate (79).

The rates of acetolysis of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl nosylate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)but-1-yl nosylate (79) in anhydrous acetic acid containing sodium acetate (0.02M) were determined at a number of different temperatures and the results are shown in Table II.1. For both compounds the reactions were followed for at least three half-lives and good first-order kinetics were observed over this range. In the acetolysis of (78), the solutions were initially 0.01M with respect to ester, and the reaction was followed by titrimetry.[339] The fast rate of acetolysis of (79) at room temperature precluded the use of the titration technique[339] in this case, and kinetic determinations on this ester were therefore performed by following the reaction by ultraviolet spectrophotometry,[137,140] using an initial ester concentration of c. 10^{-4}M.

Since the kinetic criterion for double bond participation is a solvolysis rate which is greater than that of an analogous saturated compound ($k_u/k_s > 1$), the rates of acetolysis of the unsaturated nosylates (78) and (79) are compared with those of their respective saturated analogues (95) and (97) in Table II.2. Although the *t*-butyl substituted compound(s) (98) must strictly be considered as the saturated analogue of (78), it was considered extremely unlikely that the absence of a *t*-butyl group in (95) would cause any significant difference between the rates of S_N2 solvolysis of (95) and (98), and therefore (95), the rates of acetolysis of which had been determined previously,[139] was used for comparison.

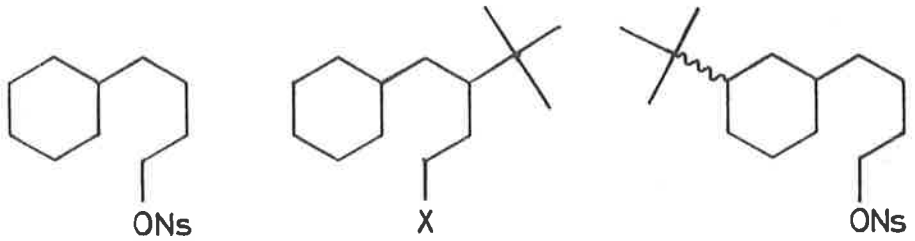
Kinetic determinations (Table II.1, II.2) as well as product studies (see later) clearly show that double bond participation occurs during the acetolysis of both (78) and (79).

Table II.1.

Rates of acetolysis of some *p*-nitrobenzenesulphonate esters.

Substrate	Temp (°C)	$10^5 k$ (sec^{-1})	$\Delta G^{\neq}$ ($kJ\ mol^{-1}$)	$\Delta H^{\neq}$ ($kJ\ mol^{-1}$)	$\Delta S^{\neq}$ ($JK^{-1}mol^{-1}$)
78	100.00	308[A]			
	70.50	23.7, 23.8			
	59.95	8.47, 8.57	107.6[D]	92.4(0.2)[C]	-45.6(0.7)[C]
	51.20	3.44, 3.49			
	25.00	0.172[A]			
79	100.00	42200[A]			
	60.00	1590[A]			
	28.92	68.2, 69.6, 69.7			
	25.00	43.8, 44.0, 44.5	92.1[D]	81.8(0.2)[C]	-34.7(0.8)[C]
	20.98	27.4, 28.3, 2.84			
	16.92	17.1, 17.2, 17.9			
97	100.00	5.06, 5.12			
95[B]	100.00	8.34			
	69.90	0.485			
24a[B]	100.00	347			
	69.90	22.5			
	60.00	8.47	107.9	93.3	-43.9
	51.00	3.14			

[A] By extrapolation. [B] ref. 139. [C] values in parentheses are standard deviations. [D] calculated from $\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq}$.



(95) (96) X = OH (98)

(97) X = ONs

Table II.2.

Comparison of some rates of acetolysis[A]

Temp (°C)	$\frac{k_{78}}{k_{95}}$[B]	$\frac{k_{24a}}{k_{95}}$[C]	$\frac{k_{78}}{k_{24a}}$	$\frac{k_{79}}{k_{97}}$[D]	$\frac{k_{79}}{k_{24a}}$	$\frac{k_{79}}{k_{78}}$
100.0	37	42	0.89	8290	121	137
69.9	46	46	1.00			
60.0			1.03		188	187
51.0			1.07			
25.0						258

[A]Rate constants used in comparisons were obtained from Table II.1, by extrapolation from data in Table II.1, and from ref. 139.
[B]k_u/k_s for (78). [C]k_u/k_s for (24a). [D]k_u/k_s for (79).

It can be seen from Table II.2 that the anchimeric assistance (k_u/k_s) which attends the acetolysis of (78) is of a similar order of magnitude to that observed in the acetolysis of (24a). Although the variation of k_u/k_s with temperature appears to be greater in the case of (78) than of (24a), the values of k_u/k_s at 100° are obtained from extrapolated rate data, and therefore little significance should be attached to this. Similarly, direct comparison of the experimentally determined rate constants for the acetolyses of (78) and (24a) shows a variation which is too slight to be considered

significant.

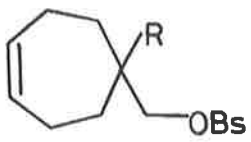
It has been found that the incorporation of an alkyl group at the 4-position of cyclohexene derivatives generally causes a depression in the nucleophilic reactivity of the double bond in intermolecular reactions.[341-344] In this respect, the near-parity in the rates of acetolysis of (78) and (24a) might perhaps be regarded as unusual. However, it should be recognized that the solvolysis of (78) and (24a) involves intramolecular nucleophilic displacement by the double bond, which need not necessarily follow the same patterns of reactivity as intermolecular nucleophilic processes.

In contrast to the not atypical magnitude of the rate enhancement (k_u/k_s = 46 at 69.9°) observed in the acetolysis of (78), the rate enhancement in the rate of acetolysis of 3-*t*-butyl-4-(cyclohex-1-enyl)but-1-yl nosylate (79) compared with its saturated analogue (97) (k_u/k_s = 8290 at 100°) is considerably more dramatic and merits detailed examination.

The favourable influence of appropriate alkyl substitution of an acyclic precursor on both rates and equilibria of cyclization reactions has been known for some time, and is called the Thorpe-Ingold or "*gem*-dialkyl" effect.[271b,273b,345a,346] Rate enhancements achieved by the introduction of alkyl substituents cover a wide range[214,347-351] and can be as high as 5×10^{10} in exceptional circumstances.[348] Allinger and Zalkow have proposed an explanation for this effect in the case of 6-membered ring formation.[346] They suggest that the introduction of an alkyl substituent into an acyclic compound introduces extra gauche interactions in the ground state which are partly relieved on cyclization or on attaining a cyclic transition state. The overall result is that the reactant ground state is raised relative to the product or the transition state, and cycliza-

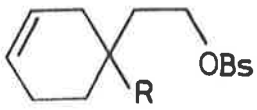
tion is therefore encouraged with regard to both rate and equilibrium.

Examples of the "*gem*-dialkyl" effect in π-route cyclizations are rare. Closson and Gray[214] have found that introduction of methyl groups at the 3- and 4-positions of 5-hexenyl brosylate produces solvolysis rate enhancements of 6.3 and 2.3 respectively, but that a methyl group at the 2-position retards the rate of solvolysis by a factor of 0.8. Chuit also observed that alkyl substitution at the 2-position relative to the leaving group, e.g. in (99)[352] and in (101a) and (101b),[353] caused retardations in solvolysis rates relative to the unsubstituted compounds (12) and (15a), but that a 3-alkyl group, in (100b),[352] enhanced the rate of solvolysis 23-fold. The rate retardations caused by 2-alkyl substitution were explained by Chuit as being due to steric hindrance to ionization,[352,353] whereas the rate acceleration caused by the more remote alkyl group of (100b) was a manifestation of the normal "*gem*-dialkyl" effect.



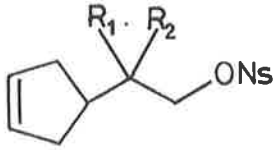
(12) R=H

(99) R=CH_3



(100) a R=H

b R=CH_3



(15a) R_1R_2=H

(101) a R_1=H; R_2=CH_3

b R_1R_2=CH_3

The magnitude of the "*gem*-dialkyl" effect in the acetolysis of 3-*t*-butyl-4-(cyclohex-1-enyl)butyl nosylate (79) can be obtained from a comparison of the rate of acetolysis of (79) with those of (24a) and (78), neither of which possess a substituted side chain (Table II.2).*

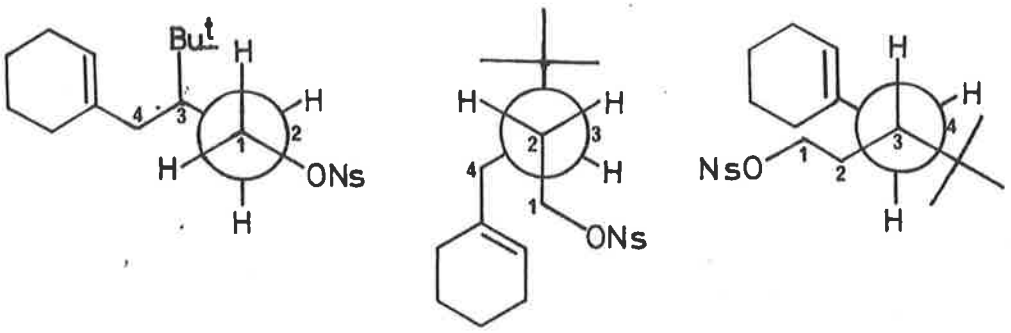
* The ratio k_{79}/k_{24a} provides a more valid comparison, but k_{79}/k_{78} is included because a rate constant at 25° (obtained by extrapolation, Table II.1) is available.

The appropriate rate enhancements of 121 (100^{o}) and 188 (60^{o}), compared to (24a), and 137 (100^{o}), 187 (60^{o}) and 258 (25^{o}), compared to (78), are thus seen to be considerably greater than the rate enhancements found for methyl substitution at the 3-position of 5,6-unsaturated compounds by Chuit[352] and by Closson and Gray.[214] This difference in magnitude is not unreasonable as the much bulkier *t*-butyl group would be expected to have a much greater effect on the possible conformations of the acyclic precursor.

An examination of models reveals that the most favoured (lowest energy) conformation of (79) is one in which the side chain adopts a conformation resembling part of a chair, in which the leaving group (ONs) and the *t*-butyl group occupy "equatorial" positions, and

fig. II.1

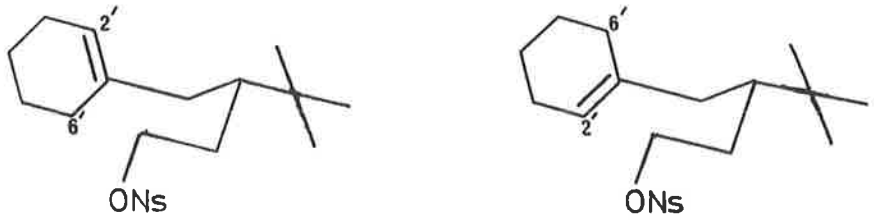
the plane of the cyclohexene ring is approximately perpendicular to the plane defined by C_1, C_2, and C_4 (fig. II.1). The Newman projections (fig. II.2) along the C_1-C_2 bond (A), the C_2-C_3 bond (B), and the C_3-C_4 bond (C) show that in this conformation the bulkiest groups are staggered (antiperiplanar) to each other. Any rotations about the C_2-C_3 bond or the C_3-C_4 bond will introduce gauche interactions involving the *t*-butyl group while rotation about the C_1-C_2 bond will increase gauche interactions with the *p*-nitrobenzenesulphonate group. Rotation through 180^{o} about the C_1,-C_4 will interchange positions 2' and 6' of the cyclohexene ring (fig. II.3). The overall difference between the various non-bonded interactions in these two conformations



A B C

fig. II.2

(fig. II.3, A and B) appears to be marginal and it is not immediately apparent which of these two orientations would be preferred. The two



A B

fig. II.3

conformations represented in fig. II.3 are those of lowest energy with respect to rotation about the $C_{1'}$-C_4 bond. It is significant that in both of these conformations, the cyclohexene double bond and the carbon atom bearing the leaving group are almost ideally situated for double bond participation to occur (see Introduction). Furthermore, if cyclization proceeds *via* a transition state in which the newly formed ring is in a chair conformation,[214] then the transition state for solvolysis of (79) will bear a strong resemblance to either of the above conformations (fig. II.3).

In unsubstituted compounds such as (78) and (24a), the side

chain exists predominantly in an extended (zig-zag) conformation, and energy is required to introduce the gauche interactions which result when the side chain achieves the proper conformation for cyclization. The energy difference between the ground state and the transition state, the activation energy, thus includes this conformational energy. In the case of the *t*-butyl substituted compound (79), the ground state will consist of conformations such as those in fig. II.3 (A and B), in which the gauche interactions which normally result on cyclization are already present, as well as extended (zig-zag) conformations in which gauche interactions are greater than in the folded conformations discussed above. Attainment of the transition state in the cyclization of (79) will therefore result in, respectively, no new gauche interactions or in relief of the gauche interactions already present. Because of the smaller contribution of conformational energy to the overall activation energy of cyclization of (79), as compared with (78) and (24a), the rate of cyclization of (79) is increased. Put another way, the extra gauche interactions which result from the presence of the *t*-butyl group in the side chain of (79) raise its ground state energy relative to that of (78) and (24a), while having little or no effect on the transition state energy.

The steric interactions in (79) discussed above are reflected mainly in a lowered enthalpy of activation[346] for the cyclization of (79) compared with (24a) and (78) (Table II.1). There is, in addition, an entropy effect caused by branching which contributes to the enhanced rate of cyclization of (79). The presence of the *t*-butyl group in (79) imposes a severe restriction on the conformational mobility of the side chain because of the increased energy barriers to internal rotations,[346] and furthermore, a large proportion of the ground state population of (79) is held in a conformation which is well suited for

cyclization (fig. II.3). The loss of rotational entropy on achieving a cyclic transition state is therefore considerably less in the case of (79) than in the unsubstituted analogues (78) and (24a), whose side chains are unrestricted in this way. The differences in the entropies of activation for the acetolyses of (79) and (78) and (24a) reflect, qualitatively at least, the strong ordering effect of the *t*-butyl group in the side chain of (79).

Direct evidence that the *t*-butyl group of (79) exerts a strong ordering effect was obtained from nuclear Overhauser experiments.[354,355] Strong irradiation of the C_1 methylene protons (δ 3.45) of 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77)* caused an increase of *c.* 20% in the intensity of the olefin proton signal (δ5.42). In a control experiment, the nuclear Overhauser enhancement of the olefinic proton (δ5.37) of 4-(5-*t*-butylcyclohex-1-enyl)butan-1-ol (76)* on irradiation of the C_1 methylene protons (δ3.53) was measured under the same conditions and was found to be very much less (< 6%). The strong nuclear Overhauser enhancement observed in the case of (77) indicates that a large proportion of its ground state population, and therefore also of the ground state population of its *p*-nitrobenzenesulphonate ester (79), must exist in conformations similar to those depicted in fig. II.3 in which the olefinic proton and the C_1 methylene protons are in close proximity to one another. The absence of a strong nuclear Overhauser effect in the case of (76) indicates that any such conformational bias in this compound, and therefore in its *p*-nitrobenzenesulphonate ester (78), is much weaker. This clearly supports

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* The parent alcohols (76) and (77) were used rather than the respective *p*-nitrobenzenesulphonate esters (78) and (79) because the latter were not sufficiently soluble in the n.m.r. solvents to give solutions of sufficiently high concentration to allow accurate and reproducible integration of the peak areas.

the earlier contention that the *t*-butyl group in the nosylate (79) exerts a strong ordering effects on the side chain.

The products formed in the acetolyses of 4-(5-*t*-butyl-cyclohex-1-enyl)butyl nosylate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)butyl nosylate (79) are listed, in order of increasing retention time, in Table II.3. The high percentage of cyclized products (*c.* 97% from (78) and *c.* 100% from (79)) is in complete accord with the kinetic evidence supporting double bond participation in the rate-determining step. Using the relationship[139] $k_m = k_c + k_u$, where k_m is the measured rate of acetolysis, k_c is the rate of cyclization, and k_u is the rate of unassisted solvolysis, and assuming[141] that $k_u = 0.87\ k_s$, where k_s is the rate of solvolysis of the appropriate saturated analogue, it can be readily calculated that the percentage of uncyclized product (80) obtained from (78) should be near 2%. While the agreement with the experimentally observed value of 2.6% (Table II.3) is not unreasonable, it should be remembered that (98) and not (95) should strictly have been used as the saturated analogue of (78). A similar calculation reveals that *c.* 0.006% of uncyclized acetate (81) should be formed in the acetolysis of (79). In fact, none of the uncyclized acetate (81) could be detected among the products of acetolysis of (79) (Table II.3).

The identities of the olefins (82)-(88), were established by a comparison of g.l.c. properties with independently synthesized compounds (Chapter IV). The two olefins (85) and (86) could not be completely resolved by g.l.c. analysis becaused of the close similarity in their retention times, and therefore small quantities of (86) could not be detected. It was estimated from mixtures of varying concentration that if the g.l.c. peak comprising (85) and (86) contained more than *c.* 20% of (86), then (86) would have been visible as a shoulder on the peak caused by (85). Therefore, although the

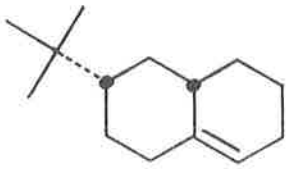
Table II.3.

Products and yields from the acetolyses of (78) and (79)[A].

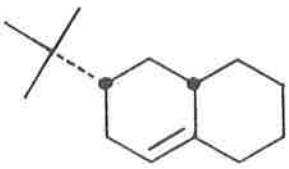
Substrate	(78)	(78)	(79)	(79)	(79)
Time (hr)	33	33	2	33	2
[$LiClO_4$]	-	0.1M	-	-	0.1M
(83)	14.6	11.0	7.4	7.0	5.5
(84)	6.8	5.4	1.8	1.6	2.5
(87)	5.9	2.9	2.3	1.6	1.4
-[B]	2.5	1.9	2.0	1.8	1.7
(88)	6.5	4.1	4.1	4.0	3.7
(85)+(86)[C]	10.7	8.1	29.1	28.5	18.4
(82)	32.3	62.5	37.5	41.8	50.9
(89)	4.6	0.4	4.5	4.3	6.1
(90)+(93)[D]	12.0	0.8	2.4	2.4	4.1
(91)	0.6	0.03	8.0	6.4	5.0
(94)	0.8	0.01	0.8	0.6	0.6
(81)	-	-	-[E]	-[E]	-[E]
(80)	2.6	2.8	-	-	-

[A] Acetolyses were carried out at 60°. Solutions were initially 0.02M in ester and 0.03M in sodium acetate. Yields have been normalized to 100%. [B] Unidentified olefin, see footnote p.49. [C] Major component is (85), see text. [D] See text. [E] None detected.

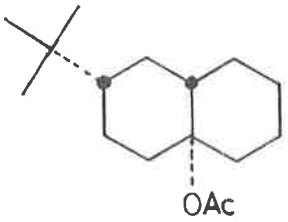
presence or absence of (86) has not been conclusively established, the yield of this olefin (86) from the acetolyses of (78) and (79) can be no higher than 2% and 6% respectively. The identity of the uncyclized acetate (80) and the absence of the uncyclized acetate (81) were also



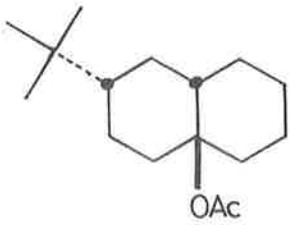
(87)



(88)



(93)



(94)

established from the g.l.c. properties of authentic compounds (Chapter III).

Authentic samples of the cyclic acetates (89) and (93) were synthesized unambiguously (Chapter IV). The identities of the remaining acetates, (90), (91), and (94) were deduced in the following manner. Solvolysis of the *cis*-spirodecyl tosylate (71) gave rise to two acetates,[356] one of which was identified as (89). Since the ring expansion which occurs during the acetolysis of (71) is a stereospecific process, proceeding *via* the intermediate *trans*-cation (73),[210,356] the second of these two acetates must be (91). Comparison by g.l.c. of the products of acetolysis of (71) and of (78) and (79) confirmed that the second of the two acetates (91) formed from (71) was in fact identical to one of the acetates formed from (78) and (79). Acetolysis of the *trans*-spirodecyl tosylate (72) gave rise to only one acetate,[356] and since this reaction is also stereospecific,[210,356] proceeding *via* the *cis*-cation (74), the single acetate which is formed is most likely to be (90).* The acetate (90)

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* The other possibility (92) is considered much less likely on the grounds that its formation would require either that the *t*-butyl group take up an axial position or that the *t*-butyl substituted ring adopt a boat or boat-like conformation.

from the acetolysis of (72) had identical g.l.c. properties with the second of the acetates formed in the acetolysis of (78) and (79). In addition, the acetate (93), obtained by independent synthesis (Chapter IV), showed identical g.l.c. properties to those of (87) under all conditions of analysis, and therefore the individual yields of these two acetates in the product mixtures could not be determined. By elimination, the structure (94) was assigned to the remaining acetate.*

Where possible, the stability of the various products from the acetolyses of (78) and (79) to the reaction conditions was verified. The octalins (82) and (84), when independently subjected to the acetolysis conditions (33 hr at 60° in buffered acetic acid), underwent no detectable isomerization. The octalins (83), (85), and (86) were found to undergo slight isomerization (less than 5%) under these conditions, the main product in each case being the tetrasubstituted olefin (82) (80-90%). After 33 hr at 60°, the acetate (89) was found to have decomposed to the extent of *c.* 4%, forming the octalins (82), (83), and (85) in approximately equal proportions. In addition, when the nosylate (79) was subjected to acetolysis for 33 hr, compared with the normal period of 2 hr for this compound, only a very slight alteration in the product distribution was observed (Table II.3). The possibility that secondary reactions of the initially formed products of acetolysis of (78) and (79) plays a significant role in determining the final product distributions can therefore be disregarded.

Although the presence of the acetates (93) and (94) in the product mixtures obtained from (78) and (79) has not been unequivocally established, the identification of the octalins (87) and (88) is

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* The possibility that this acetate is in fact (92) cannot be completely disregarded. However, see footnote on p.46.

firmly based and demonstrates that 1,2-hydride shifts occur during the solvolysis of (78) and (79) (fig. II.4). The *cis*-stereochemistry of these two octalins, (87) and (88), indicates that they must have arisen from the *cis*-cation (74) by way of the isomeric *cis*-cation (103), formed from (74) by a 1,2-hydride shift between the two bridgehead positions (fig. II.4). If the assignments of the acetate structures are accepted, then the total yields of directly observable products arising from rearrangement of the *cis*-cation (74) in the acetolysis of (78) and (79) is 13% and 7% respectively. The actual extent of rearrangement is likely to be somewhat higher than these figures, since the yield of acetate (93) is unknown, and because some of the tetrasubstituted olefin (82) would almost certainly be formed from the rearranged cation (103). Since the tetrasubstituted olefin (82) can be formed from any of the cations (73), (74), (102), or (103), it is impossible to state with any degree of certainty the extent to which the *cis*-cation (74) undergoes a 1,2-hydride shift before solvent collapse. If the rather drastic assumption that (82) is formed exclusively from the *cis*-cation (74) is made, then the absolute lower limits for the proportion of *cis*-cation (74) which undergoes a 1,2-hydride shift are 23% and 14% in the solvolyses of (78) and (79) respectively. However, if the extent of rearrangement found among the products of defineable stereochemistry can be held to be a reasonable reflection of the overall propensity for rearrangement of the *cis*-cation (74), the extent of 1,2-hydride shift undergone by (74) would be greater than 50%.

The *trans*-cation (73), on the other hand, appears to show no tendency to undergo a 1,2-hydride shift to the cation (102) (fig. II.4). The presence of the unidentified olefin (Table II.3) could be accounted for by such a process, but the evidence linking the

unidentified olefin to the *trans*-cation (73) is tenuous.* In any event, it is clear that the *cis*-cation (74) is much more prone to undergo a 1,2-hydride shift between the bridgehead positions than is the *trans*-cation (73). A possible explanation for this lies in the conformational changes which would accompany such migrations (fig. II.4). It should be noted that the following argument does not constitute an exhaustive analysis of the various conformations possible to the cations (73), (74), (102), and (103), but only those conformations which may be of relevance to an understanding of the driving force behind the rearrangement.

The geometric constraints imposed by the presence of an sp_2 carbon atom at a bridgehead position in a 9-decalyl cation prevent both rings from simultaneously adopting chair conformations : one ring must be in a boat or twist-boat conformation.** In the *cis*-cation (74), ring A*** must be in a boat/twist-boat conformation (fig. II.4)

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* A trace amount of an unidentified olefin, which appears to be identical (by g.l.c. comparison) with the olefin obtained in the present work, was detected in the products of acetolysis of the *cis*-spirodecyl tosylate (71), which solvolyses to give the *trans*-cation (73).[356] Interestingly, only trace amounts of the octalins (87) and (88), formed *via* a 1,2-hydride shift in the *cis*-cation (74), were formed on acetolysis of the *trans*-spirodecyl tosylate (72).[356] Possible reasons for the much lower extent of rearrangement in the *cis*-cation (74) generated by a σ-route from (72) as compared with the π-routes (from (78) and (79)) will be discussed later.

** It is possible to conceive of a half-chair conformation, in which four of the ring atoms are approximately co-planar, as an alternative to a boat or twist-boat. This constitutes a high-energy conformation, however, approximating to the transition state for a chair-boat interconversion,[345b,357] and will therefore be disregarded.

*** For convenience in this and ensuing discussions, the ring bearing the *t*-butyl group will be referred to as ring A, and the unsubstituted ring will be called ring B.

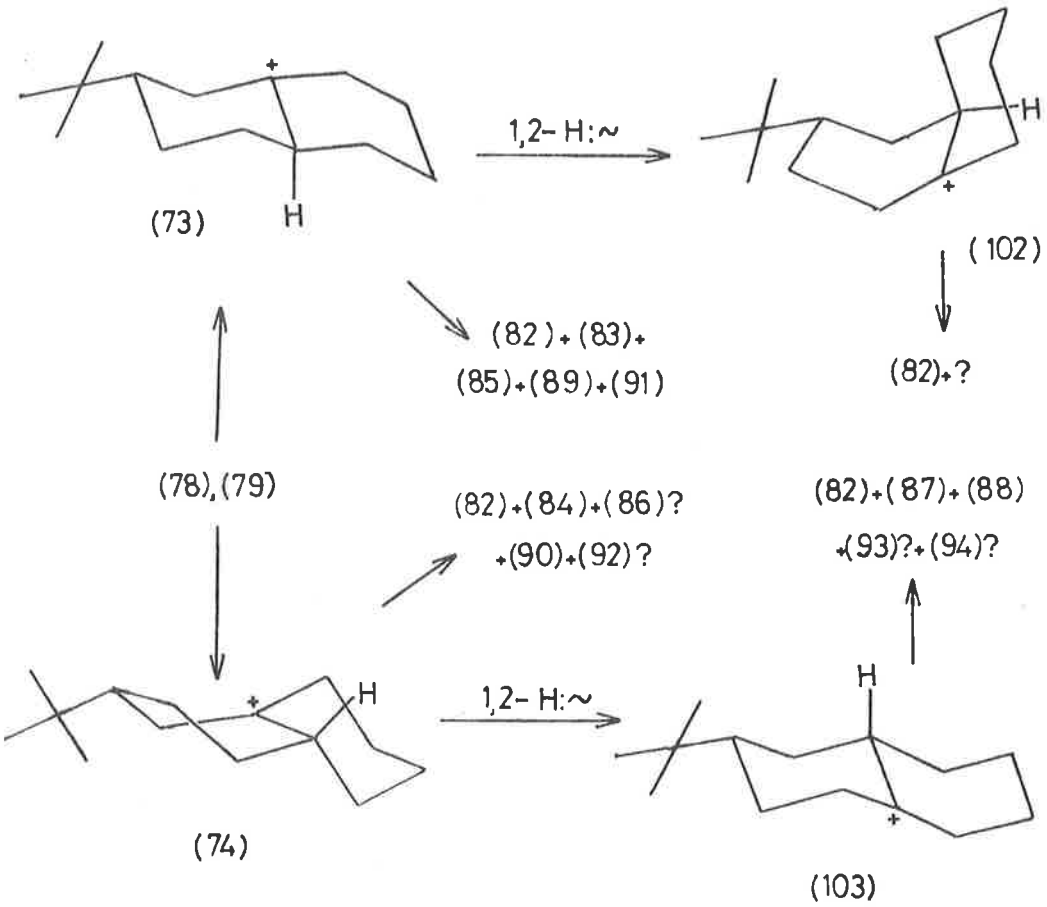


fig. II.4

since a ring A chair conformation would put the *t*-butyl group in an axial position. However, when ring A is in a boat/twist-boat conformation, the *t*-butyl group is eclipsed by a vicinal hydrogen atom. If the *cis*-cation (74) undergoes a 1,2-hydride shift to form (103), ring A can adopt a chair conformation in which the *t*-butyl group is equatorial, with ring B becoming a boat/twist-boat (fig. II.4). The relief of torsional interactions involving the *t*-butyl group in (74) would provide a significant driving force for its rearrangement to (103). In the *trans*-cation (73), however, the above situation is reversed. Ring A can exist in a chair conformation in (73), but a 1,2-hydride shift to form (102) would require that ring A adopt a boat/twist-boat conformation to maintain the *t*-butyl group in an equatorial position (fig. II.4). The resulting increase in torsional strain caused by the *t*-butyl group being in a boat-shaped ring would

cause a 1,2-hydride shift in the *trans*-cation (73) to be energetically less favourable than a corresponding rearrangement in the *cis*-cation (74).

Although 1,2-hydride shifts in solvolytically generated carbenium ions are well known,[108,359-363] the possibility of such processes occurring in the 9-decalyl cation (59) does not appear to have been considered.[139,144,145,189,193,194] Olah and co-workers have recently shown by ^{13}C-n.m.r. spectroscopy that in super-acid media, the 9-decalyl cation (59) exists as a pair of equilibrating carbenium ions undergoing a rapid 1,2-hydride shift between the bridge-head positions.[364] Evidence of this type is only possible because the long carbenium ion lifetimes observed in super-acids permit observation of rearrangements that often do not occur in the presence of stronger nucleophiles.[363b] Equilibration between degenerate cations under solvolysis conditions can only be detected by isotopic labelling techniques or by using asymmetrically substituted precursors. In view of the rearrangement observed in the *cis*-cation (74), the possibility that 1,2-hydride shifts might occur in the parent 9-decalyl cation (59) cannot be ignored.

On acetolysis, the nosylate (78) gives rise to *c.* 31% of products having *trans*-stereochemistry and *c.* 32% of products having *cis*-stereochemistry, whereas (79) cyclizes to give *c.* 49% of *trans*-products and *c.* 11% of *cis*-products (Table II.3). Although the formation of considerable quantities of (82) in both cases leaves much of the stereochemistry of cyclization of (78) and (79) undefined, it seems apparent from the above figures that (78) shows no great preferences for either mode of cyclization (i.e., either to the *trans*-cation (73) or to the *cis*-cation (74)), but that (79) appears to have a marked preference for cyclization to give *trans*-products (i.e.

via the *trans*-cation (73)). An examination of models of (78) reveals no features which would have a strong directing effect to favour attack on either face of the cyclohexene ring. Indeed, studies of the stereochemistry of additions to 4-*t*-butylcyclohexene derivatives show that there is only a slight preference (*cis:trans* less than 2:1) for attack to occur on the same side of the molecule as the *t*-butyl group.[341,365,366]

The apparent preferred *trans*-mode of cyclization of the nosylate (79) is difficult to rationalize. The two conformations of (79) which are most favourable for cyclization were described earlier (fig. II.3, A and B). Of these, conformation A would cyclize to the *cis*-cation (74), and B would give the *trans*-cation (73). However, there does not appear to be any good reason why conformation B should be preferred over conformation A.

It could be argued that the transition state for cyclization to the *cis*-cation (74) would be of higher energy than the transition state for cyclization to the *trans*-cation (73) because the former would involve ring A in a boat/twist-boat conformation rather than ring B. The extra torsional strain associated with a ring A non-chair conformation (see earlier) could cause the *trans*-mode of cyclization to be favoured. Such an argument, however, should be equally applicable to the cyclization of both (78) and (79), the former of which appears to show no greater preference for cyclization to either cation.

As was mentioned in the Introduction, the ratio of $\Delta^{1,9}$-octalin (57) to $\Delta^{9,10}$-octalin (58) has proved useful in the investigation of ionic reactions in which the 9-decalyl cation (59) is the intermediate, and particularly in discussions of the importance of counter-ion location in controlling olefin formation.[138,139,145,210] In the present study, however, the complex array of different $\Delta^{1,9}$-

octalins does not permit the use of a simple ratio of this type as a useful mechanistic probe. A discussion of the products of acetolysis of (78) and (79) in terms of different conformations of the intermediate carbenium ions and of different locations of the counter-ion in the initially formed intimate ion-pairs will nevertheless hinge on differences in yields of the various products obtained from the two substrates (78) and (79).

Although it is not disputed that the acetate anion is a stronger base than the *p*-nitrobenzenesulphonate anion, the importance of the latter as a proton removing base is considered to be due to its often ideal location relative to a suitably oriented hydrogen atom in the initially formed ion-pair.[138,139,145,210] In these discussions, the possibility of olefin formation is considered only when the carbon-hydrogen bond being broken is co-planar, or almost co-planar, with the vacant *p*-orbital of the carbenium ion.[79c]

Some of the ion-pairs initially formed on acetolysis of (78) and (79) are represented in fig. II.5 and fig. II.6. The counter-ion from 4-(5-*t*-butylcyclohex-1-enyl)butyl nosylate (78) is designated by X^-, while Y^- represents the counter ion from 3-*t*-butyl-4-(cyclohex-1-enyl)butyl nosylate (79). Conformations in which the *t*-butyl group is axial or in which one ring is in a half-chair conformation are ignored. Not all of the conformations shown in fig. II.5 and fig. II.6, as well as fig. II.7, are considered to be of equal importance. On the basis of Closson's work,[214] the newly formed ring would be expected to be in a chair conformation. It is conceivable, however, that in the cyclization of (78) to the *trans*-cation (73), the newly formed ring might be forced to adopt a boat/twist-boat conformation in order that the ring bearing the *t*-butyl group (ring A) remain a chair (e.g. (73A, B) in fig. II.5). On the other hand, since ring A

of the *cis*-cation (74) is restricted to a boat/twist-boat conformation, as explained earlier, then the newly formed ring of (74) in the acetolysis of (79) (ring A) must be a boat/twist-boat, and the newly formed ring of (74) in the acetolysis of (78) (ring B) is under no special constraint to adopt other than a chair conformation. It would seem, therefore, that the most important species are those in which one ring is in a chair and the other ring is in a boat/twist-boat conformation, such as (73A-C) (fig. II.5) and (74 A) (fig. II.6). There will of necessity be conformational changes attending the formation of (103) from (74) by a 1,2-hydride shift. On simple thermodynamic grounds it is likely that the important ion-pairs will again be those involving one ring in a chair and the other ring in a non-chair conformation, such as (103A-C) (fig. II.7). However, since the product distributions obtained on acetolysis of (78) and (79) cannot be adequately explained in terms of the more likely ion-pair conformations (73A-C) (fig. II.5), (74 A) (fig. II.6), and (103A-C) (fig. II.7), structures involving both rings in non-chair conformations, (73 D,E) (fig. II.5), (74 B-E) (fig. II.6), and (103 D,E) (fig. II.7) are also taken into consideration.

Considering firstly the *trans*-cation (73) (fig. II.5) from the acetolysis of (78), it can be seen that the counter-ion (X^-), which is in the vicinity of C_5, is rather poorly located to remove the protons at any of C_1, C_8, or C_{10} to form the octalins (83), (85), or (82). In all of the ion-pairs (73A-E), the counter-ion (X^-) is on the opposite side of the molecule to the hydrogens at C_1 and C_{10}, and it is only on the same side as the hydrogen at C_8 in the ion-pairs (73 A) and (73 E). The distance that the counter-ion (X^-) would have to move to abstract any one of these hydrogens, particularly the one at C_1, and to a slightly lesser extent the hydrogens at C_8 and C_{10},

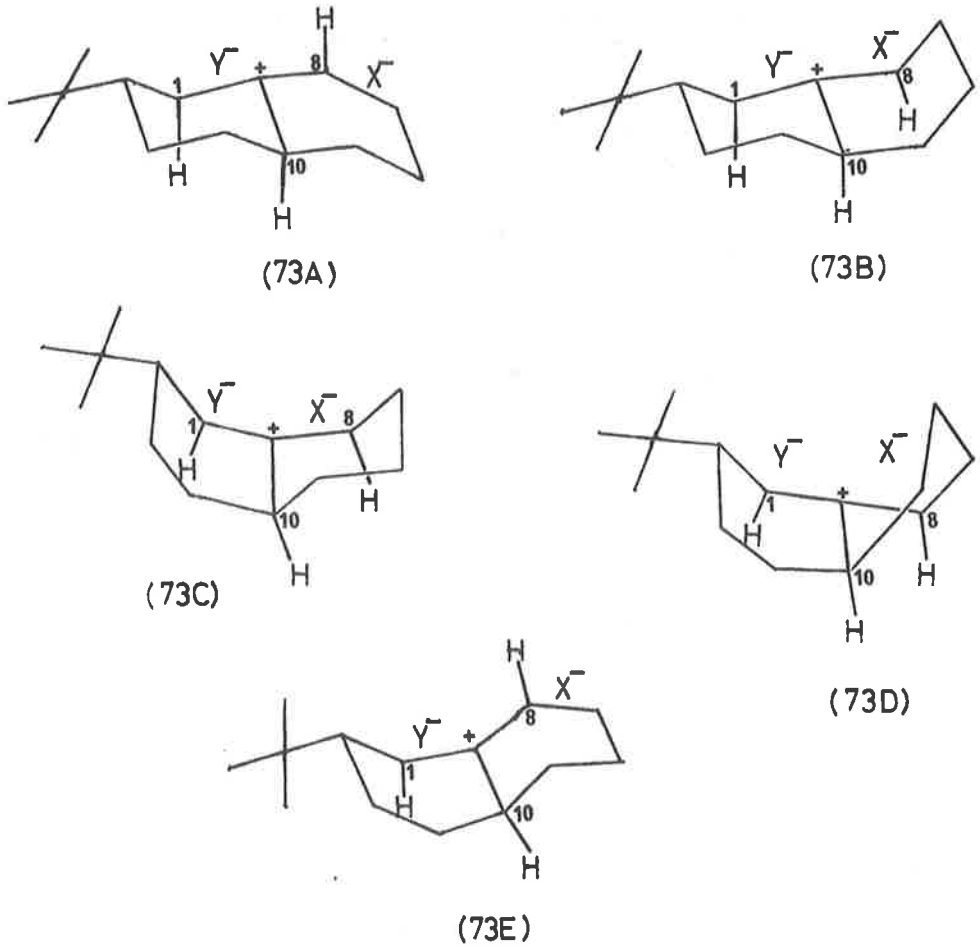


fig. II.5 - Possible ion-pairs from (78) and (79) involving the *trans*-cation (73).

would appear to rule out the likelihood that the counter-ion is acting as a base in these ion-pairs. The fact that more of (83) (14.6%), formed by removal of the hydrogen at C_1, than of (85) (10.7%), formed by loss of the hydrogen at C_8, is obtained in the acetolysis of (78) (Table II.3) is consistent with this view.

The acetolysis of (79), on the other hand, gives only 7.4% of (83) and 29.1% of (85). In the relevant ion-pairs (73A-E), the location of the counter-ion is shown by Y^- (fig. II.5). At first sight, the location of the counter-ion (Y^-) on the same side of the molecule as the axial hydrogen at C_8 in the ion-pairs (78 A) and (78 E) might be linked to the high yield of (85) compared to (83). However,

this high ratio of (85) to (83) must be considered fortuitous since (i) the distance the counter-ion (Y^-) has to move to remove the hydrogen at C_8 to form (85) is too great to reasonably expect such a large difference in yields between (83) and (85), and (ii) in the ion-pairs derived from (78), the counter-ion (X^-) is even closer to the hydrogen at C_8, and therefore the ratio of (85) to (83) would be expected to be even higher, contrary to what is in fact observed.

A rigorous analysis of the role of the counter-ion in the formation of the *cis*-octalins (84) and (86) from the *cis*-cation (74) is not possible because the yields of (86) are not known. Nevertheless, in the ion-pairs involving the *cis*-cation (74) derived from (78) (fig. II.6), the counter-ion (X^-) is again poorly situated to remove any of the hydrogens at C_1, C_8, or C_{10}, except in (74 C) and (74 E), in which the counter-ion (X^-) is at least on the same side of the molecule as the hydrogen at C_8, loss of which would give (86). However, it seems fairly certain that (84) is formed in preference to (86) in the acetolysis of (78). In the ion-pairs (74A-E) (fig. II.6) from the acetolysis of (79), the counter-ion (Y^-) is somewhat better located to remove the hydrogen at C_1 to form (84). However, the yield of this olefin is lower than was obtained in the acetolysis of (78). Again, this behaviour seems irreconcilable with a model in which the counter-ion plays an important role as a base.

One final set of ion-pairs which can be considered are those involving the *cis*-cation (103), which is formed by a 1,2-hydride shift in the *cis*-cation (74) (fig. II.7). In the ion-pairs derived from (78), the counter-ion (X^-) is situated near C_8. If conformations such as (103 A) and (103 E) are important, then the counter-ion (X^-) is ideally located to remove the hydrogen at C_8 to form the octalin (87). In ion-pairs such as (103C-E), however, a slight movement of the counter-

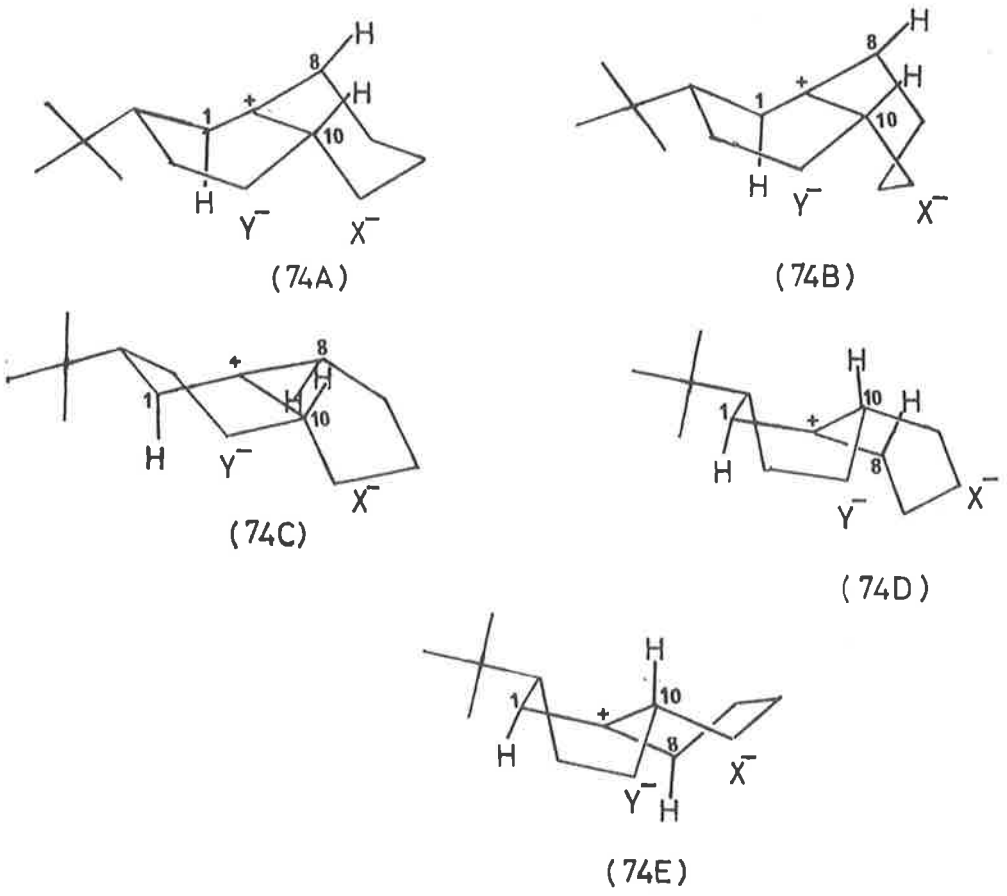


fig. II.6 - Possible ion-pairs from (78) and (79) involving the *cis*-cation (74).

ion (X^-) would put it in a good position to remove the hydrogen at C_1, thereby forming (88). Conformations such as (103A-C) seem, *a priori*, to be the most likely contributors to the chemistry of the cation (103), and on this basis, the formation of (87) and (88) in near-equal amounts in the acetolysis of (78) is not entirely inconsistent with the counter-ion being at least partly responsible, as the proton removing base, for their formation. In the acetolysis of (79), on the other hand, the octalin (88) is formed in preference to (87). This observation can only be consistent with the counter-ion (Y^-) acting as a base if conformations such as (103C-E) are important (fig. II.7). The apparent correlation between the yields of (87) and (88) and the location of the counter-ion in the ion-pairs (103A-E) from

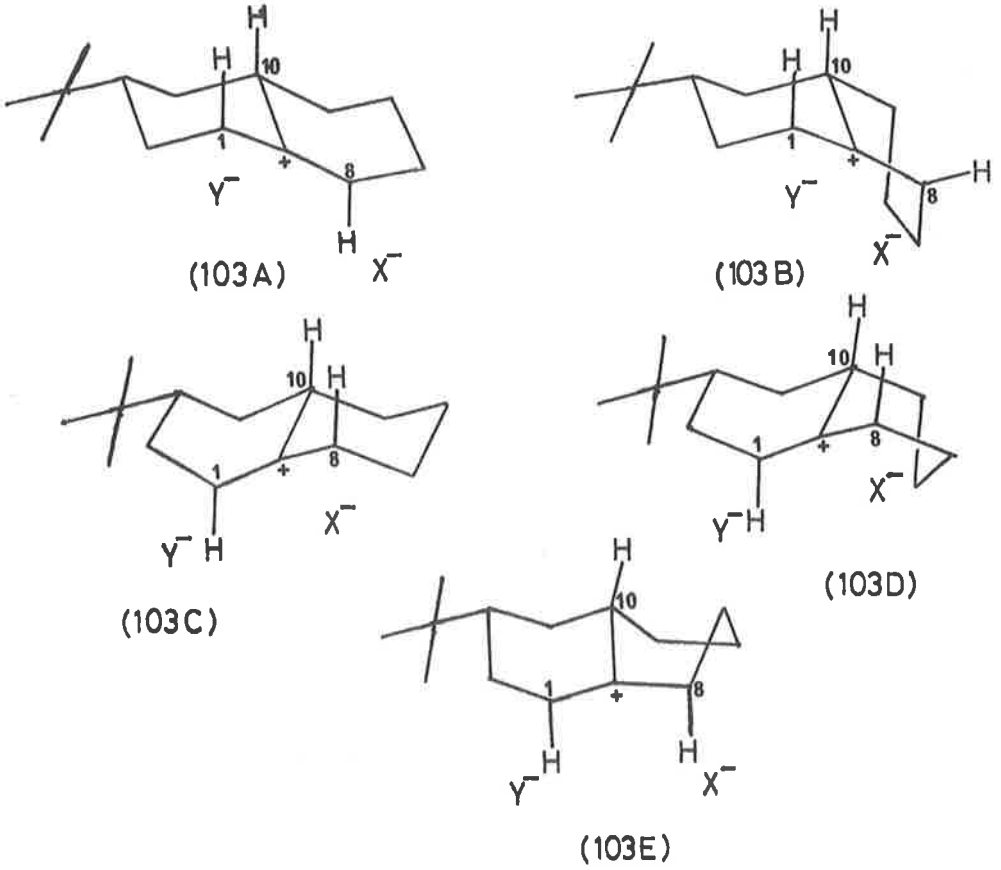
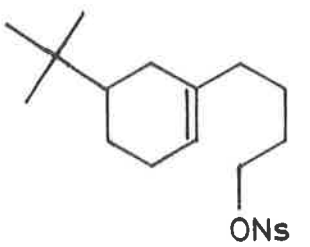


fig. II.7 - Possible ion-pairs in the *cis*-cation (103) formed from (74) by a 1,2-hydride shift.

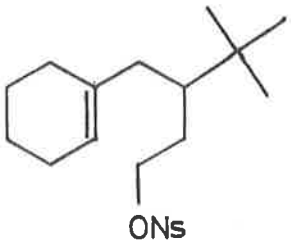
each of the substrates (78) and (79) is therefore not entirely self-consistent, and hence must be viewed with some skepticism.

The overall conclusion which appears to be inescapable is that in the acetolysis of (78) and (79), the role of the counter-ion as the base responsible for olefin formation must be minor, if it is significant at all. This is clear from the lack of correspondence between the position of the counter-ion and the formation of $\Delta^{1,9}$-octalins in the ion-pairs depicted in figs. II.5, II.6, and II.7. In addition, the formation of considerable quantities of the $\Delta^{9,10}$-octalin (82) in the acetolyses of (78) and (79) can by itself be strongly indicative of this conclusion, since the hydrogen at C_{10} which must be removed to form (82) is in all cases on the opposite side of the cation, (73), (74), and (103), to the counter-ion.

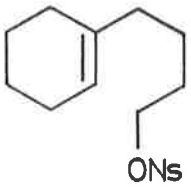
It was mentioned earlier that the ratio of yields of $\Delta^{1,9}$-octalin (57) to $\Delta^{9,10}$-octalin has been useful as a mechanistic probe in studies involving the 9-decalyl cation (59). The ratios of (57) to (58) obtained from the 9-decalyl cation (59) on acetolysis of a number of different substrates are given in fig. II.8 (references in parentheses), together with the analogous ratio of all of the various $\Delta^{1,9}$-octalins (83+84+85+86+87+88+?) to $\Delta^{9,10}$-octalin (82) from the acetolyses of the *t*-butyl substituted substrates (71), (72), (78), and (79).



(78)

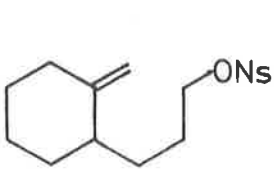


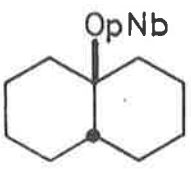
(79)

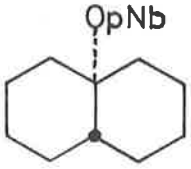


(24a)

$\frac{\Delta^{1,9}}{\Delta^{9,10}}$ = 1.45 1.25 2.08 (139)





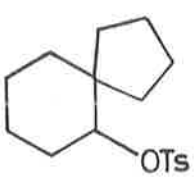


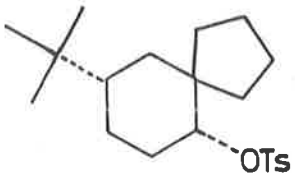
f (25a) (60b) (61b)

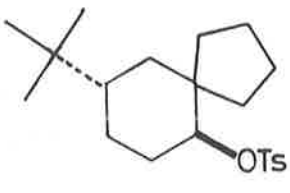
i $\frac{\Delta^{1,9}}{\Delta^{9,10}}$ = 1.59 (145) 1.12 (1.39) 7.1 (139)

g

II.8







(63) (71) (72)

$\frac{\Delta^{1,9}}{\Delta^{9,10}}$ = 0.33 (139) 0.21 (210,356) 0.35 (210,356)

Gream has suggested that on the basis of the similar product distributions obtained on acetolysis of (24a) and (25a) ((57):(58) = 2.08 and 1.59 respectively), similar intermediate cationic species are most likely involved in both cases,[145] and that the preferential formation of $\Delta^{1,9}$-octalin (57) could, at least in part, be explained by the counter-ion acting as a base in the intermediate ion-pairs.[139,145] (See Introduction.) The similarity in the ratios of $\Delta^{1,9}$-octalins to $\Delta^{9,10}$-octalin (82) in the acetolysis products of (78) and (79) (1.45 and 1.25 respectively), however, is fortuitous, since the finer details of the respective product mixtures (Table II.3) definitely establish that there is a considerable difference between the intermediate species. Furthermore, in view of the absence of a demonstrable relationship between the location of the counter-ion in the ion-pairs derived from (78) and (79) and the direction of olefin formation, the similarity between the $\Delta^{1,9}$-octalin to $\Delta^{9,10}$-octalin ratios from (78) and (79), and (24a) and (25a) suggests that the role of the counter-ion in the ion-pairs derived from (24a) and (25a) might not be as important as has been proposed.[139,145] Some of the factors which might be important in causing the slight disparity that is observed in these ratios in the products from (24a), (78), and (79) are the unavailability of certain conformations to the ion-pairs derived from (78) and (79), and distortions in the geometry of the cation, and in the solvation shell caused by the presence of the *t*-butyl group near the cationic centre.

In contrast to the ion-pairs formed during acetolysis of compounds such as (24a), (25a), (78), and (79), in which the counter-ions would have to move some considerable distance before they could abstract a proton to form an olefin (see Introduction, fig. II.5, and fig. II.6), the acetolysis of compounds such as (60b), (61b), (63),

(71), and (72) gives rise to ion-pairs in which the counter-ion is almost ideally located to remove one or more protons (fig. I.11, fig. I.12, and fig. I.15). Indeed, in these latter examples, the product distributions correlate very well with the positions of the counter-ions in the initially formed ion-pairs* (see Introduction). In terms of a general model, it seems that the counter-ion can act as a base to remove a suitably oriented hydrogen atom from the cation to form an olefin when it is ideally situated for this purpose in the initially formed intimate ion-pair (e.g. from substrates such as (60), (61), (63), (71), and (72)), but that this becomes a minor or negligible function of the counter-ion when it has to move any distance to reach the appropriate hydrogen atom. It necessarily follows that if proton abstraction by an ideally situated counter-ion is faster than proton removal by the solvent, which presumably is the dominant elimination mechanism when the counter-ion is not well-positioned to act as a base, then it will also be faster than alternative modes of decomposition of the cation which would normally be important in the absence of strong counter-ion control. This point is well exemplified by several interesting differences between the products obtained by acetolysis of the unsaturated nosylates (78) and (79) and of the *cis*- and *trans*-spirodecyl tosylates (71) and (72).

(i) Acetolysis of (78) and (79) yields *c.* 18% and 16% respectively of cyclized acetates (Table II.3). On the other hand, acetolysis of the spirodecyl tosylates (71) and (72) yields only *c.* 6% and 3%

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* Of particular relevance is the obtention of 2-*t*-butyl-$\Delta^{9,10}$-octalin as the major product in the acetolyses of (71) and (72) (see Introduction and fig. II.8). The high proportion of this product is very well explained by the ideal location of the counter-ion for removal of the hydrogen at C_{10} in the initially formed ion-pairs (fig. I.15), in marked contrast to the products obtained from (78) and (79).

respectively of 9-decalyl acetates.[210,356] In the ion-pairs generated by σ-routes from (71) and (72), capture of the cation by acetate ion cannot compete as effectively with proton loss as in the cations generated by π-routes from (78) and (79), as elimination is a more favourable process because of the location of the counter-ions in the former ion-pairs.

(ii) The *cis*-2-*t*-butyl-9-decalyl cation (74) formed by acetolysis of (78) and (79) readily undergoes a 1,2-hydride shift to form the *cis*-3-*t*-butyl-9-decalyl cation (103), whereas the *cis*-cation (74) obtained by σ-route acetolysis of (72) gives rise to only trace amounts of rearranged products.[356] In the latter case, the hydrogen at C_{10}, because of its proximity to the counter-ion (fig. I.15), is lost much more rapidly than it can migrate.

(iii) The addition of lithium perchlorate, an efficient disruptor of intimate ion-pairs,[367,392] has a marked effect on the product distributions from the acetolysis of (78) and (79) (Table II.3). The effect of lithium perchlorate addition on the products from the acetolyses of (71) and (72), on the other hand, was found to be almost negligible.[210,356] In the latter case, the initially formed ion-pairs would be less susceptible to ion-pair disruption because of the shorter lifetimes involved,* which are again a function of the faster rate of elimination caused by the proximity of the counter-ion to the hydrogen atom at C_{10} (fig. I.15).

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* A dramatic example of the susceptibility of stabilized, and therefore presumably longer-lived carbocations to ion-pair disruption is afforded by the products obtained from the benzylic cation generated by a π-route from *trans*-6-*p*-chlorophenylhex-5-enyl brosylate (c.f. fig. I.9).[143] The addition of lithium perchlorate caused the ratio of cyclized elimination to substitution products to change from 0.12 to 1.86.

In summary, the differences between the products of acetolysis of (78) and (79) cannot be accounted for in terms of the counter-ion being the base responsible for removal of a proton, unlike other systems in which the counter-ion is ideally located for such a purpose. The effect of lithium perchlorate on the respective product distributions does, however, reaffirm that the counter-ion is important at least in the sense that in their reactions, the carbenium ions generated from (78) and (79) must be regarded as ion-pairs rather than free cations, even though the exact role of the counter-ions cannot be defined with any certainty. It is furthermore clear that there are significant differences between the cationic intermediates obtained by acetolysis of (78) and (79). Whether the difference is due to conformational effects or to other factors is not completely obvious. It is possible that differences in solvation of the cations, caused by the different locations of the counter-ion, might have some influence on product formation.

The introduction of the *t*-butyl group has demonstrated that rearrangement can occur prior to solvent collapse in the 9-decalyl cation, and has further complicated the situation by allowing the formation of isomeric cations, (73) and (74). Because of the rearrangement and the formation of isomeric cations, the yield of tetrasubstituted olefin (82) cannot be used as a mechanistic probe since its origin is uncertain.

A study similar to the one described herein, but using *gem*-dimethyl (for example) substituted substrates instead of *t*-butyl substituted compounds would provide complementary, and perhaps more useful, information on the factors influencing the π-route products from the 9-decalyl cation. There would be no stereochemical complications, but 1,2-hydride shifts would still be detectable. The

conformational restrictions imposed by the presence of the *t*-butyl group would be removed or greatly reduced, thus providing a better indication of the importance of hydride shifts in the parent unsubstituted 9-decalyl cation (59). Further work is clearly still needed to resolve the detailed chemistry of the 9-decalyl cation.

CHAPTER III

RESULTS AND DISCUSSION

The synthesis of solvolysis substrates.

Part A - The synthesis of derivatives of 4-(5-*t*-butylcyclohex-1-enyl)butan-1-ol (76).

The route by which 4-(5-*t*-butylcyclohex-1-enyl)butan-1-ol (76) was synthesized is outlined in scheme III.1. The initial strategic problem involved generating an unsymmetrically substituted cyclohexene derivative, e.g. (108), suitable for further elaboration to the required alcohol (76). A very useful general synthesis of α,β-unsaturated carbonyl compounds involves the reduction of the enol ether of a β-dicarbonyl compound, and treatment of the resulting hydroxy enol ether with aqueous acid (fig. III.1).[225] This general approach has been found to be well suited to the preparation of 1-cycloalkene aldehydes from hydroxymethylene ketone derivatives,[219-221] and therefore appeared to be a simple method of obtaining the desired intermediate aldehyde (108).

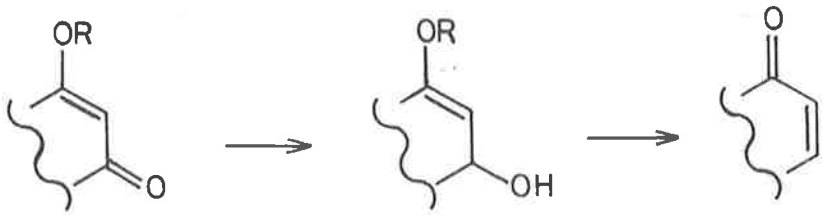
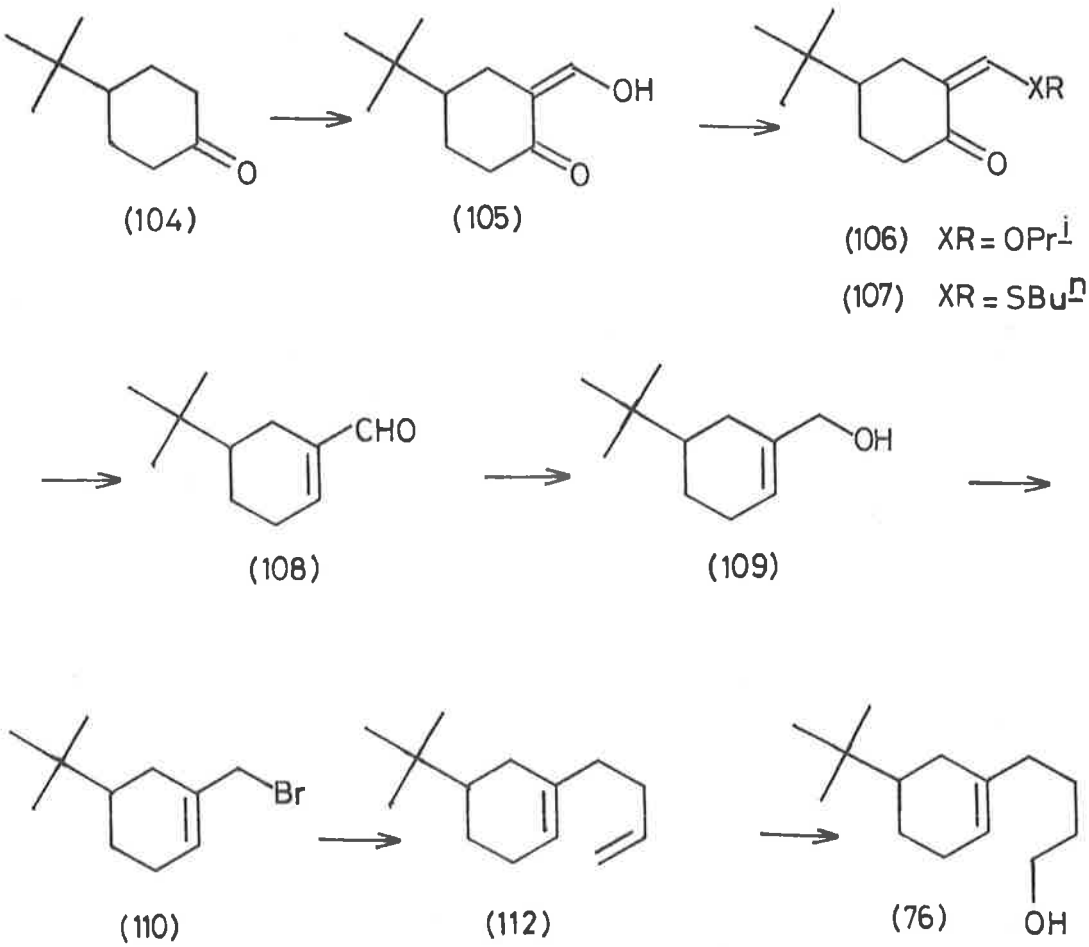


fig. III.1

Reaction of 4-*t*-butylcyclohexanone (104) with ethyl formate, either in benzene solution using sodium methoxide as a base,[216,217] or in ether using sodium hydride as a base,[218] gave the hydroxymethylene ketone (105). The yields for this transformation were consistently higher by the second of these procedures, which was also the more convenient experimentally. The hydroxymethylene ketone (105) was very prone to polymerization and had to be distilled and used



Scheme III.1

immediately.[216]

Formation of the isopropyl enol ether (106) was accomplished by heating the hydroxymethylene ketone (105) with isopropyl alcohol in benzene containing a catalytic amount of *p*-toluenesulphonic acid.[219] The presence of an aldehydic proton resonance (δ 10.10, singlet) in the n.m.r. spectrum of the product of the above reaction indicated that some of the isomeric aldehydic enol ether (114) (*c.* 15%) had also been formed (fig. III.2). When the preparation of the ether (106) was attempted under basic conditions, by treatment of the hydroxymethylene ketone with isopropyl iodide in acetone solution in the presence of potassium carbonate,[216] a similar mixture of the isomeric enol ethers (106) and (114) was obtained. Because of the instability

of these compounds, their separation was not practicable, and therefore subsequent reactions were carried out on the mixture of (106) and (114).

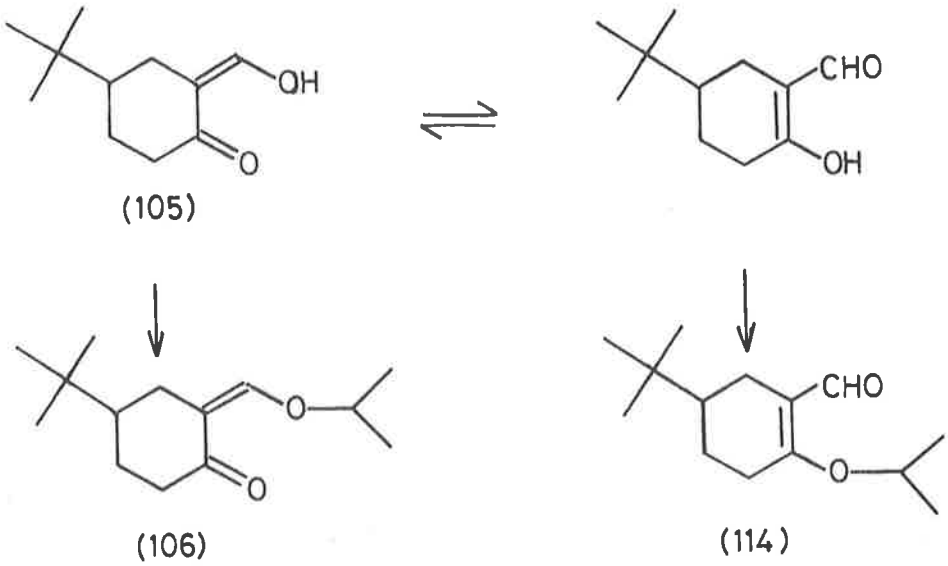


fig. III.2

Reduction of the mixture of (106) and (114) with lithium aluminium hydride, followed by brief treatment with cold dilute sulphuric acid,[219] gave a mixture of six compounds, of which the unsaturated aldehyde (108) was the major component (*c.* 67% by g.l.c. analysis). A pure sample of the aldehyde (108) was obtained by preparative g.l.c., but conventional methods of separation more suited to large scale work (e.g. fractional distillation and column chromatography) were not successful in separating the mixture.* Because of the necessity for large quantities of the aldehyde (108), the *n*-butylthiomethylene ether (107) was examined as a possible alternative intermediate.

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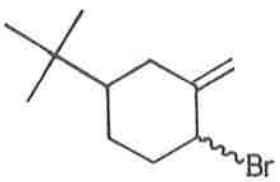
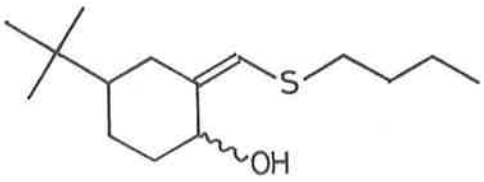
* Reduction of this mixture with sodium borohydride gave an even more complex mixture from which it was not possible to separate the alcohol (109) without considerable difficulty.

The thiomethylene ether (107) was prepared by heating the hydroxymethylene ketone (105) with *n*-butanethiol in benzene in the presence of *p*-toluenesulphonic acid.[220] There were no complicating side reactions in this transformation, and the product (107) had the added advantage of being considerably more stable than the isopropyl enol ether (106). This enabled proof of its homogeneity to be established by g.l.c. analysis and elemental analysis, as well as by n.m.r. spectroscopy. Reduction of the thiomethylene ketone (107) with sodium borohydride in ethanol followed by hydrolysis of the intermediate hydroxythioenol ether (113) with mercuric chloride and cadmium carbonate in aqueous ethanol[221] afforded the unsaturated aldehyde (108) in a homogeneous state. Further reduction of the aldehyde (108) to the allylic alcohol (109) with sodium borohydride posed no problems.



(111)



(113)

Bromination of the allylic alcohol (109) was achieved using phosphorus tribromide and pyridine in benzene.[222] Although allylic rearrangement is a common problem in the halogenation of allylic alcohols,[223] it was hoped that no such difficulty would arise in this case since Piers and co-workers[222] had used this method for the bromination of a structurally similar allylic alcohol (fig. III.3) and had observed no rearranged products. However, two weak resonances in the n.m.r. spectrum of the allylic bromide (110) at δ4.90 and δ4.70 (2:1 respectively by integration) were observed. These were attributed to the methylene protons and to the C_1 proton, respectively, of the

rearranged allylic bromide (111), present as *c.* 15% of the mixture.* That the contaminant was in fact an isomer of the allylic bromide (110) was proved by an elemental analysis of the mixture.

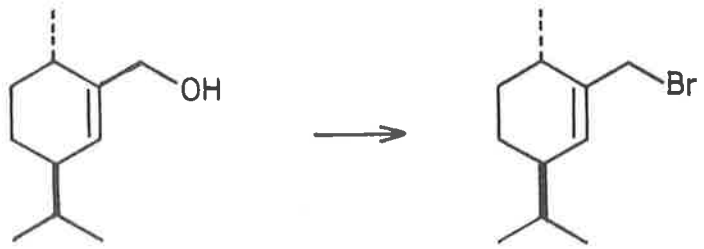


fig. III.3

The formation of two isomers, (110) and (111), in the bromination reaction created no real difficulties however, since in the next step both components of the mixture reacted with allylmagnesium bromide to give 5-*t*-butyl-1-(1-but-3-enyl)cyclohexene (112) as the sole product. The controlling feature of this reaction appears to be the greater steric accessibility of the primary carbon of the allylic system. Thus, the primary allylic bromide (110) undergoes direct coupling in an S_N2-type reaction, while the secondary allylic bromide (111) undergoes coupling with allylic rearrangement in an S_N2'-type reaction to give the same product.

Unaccountably, complete conversion of the bromide mixture to the diene (112) could not be achieved, even when a large excess of allylmagnesium bromide was used, together with a long reaction time and relatively forcing conditions (e.g. refluxing ether). The product

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* G.l.c. analysis could not be used to verify the presence of (111) as a contaminant because the sample underwent extensive decomposition under all conditions of analyses with all columns tried. Thin-layer chromatography was also unsuccessful in resolving the components of the mixture.

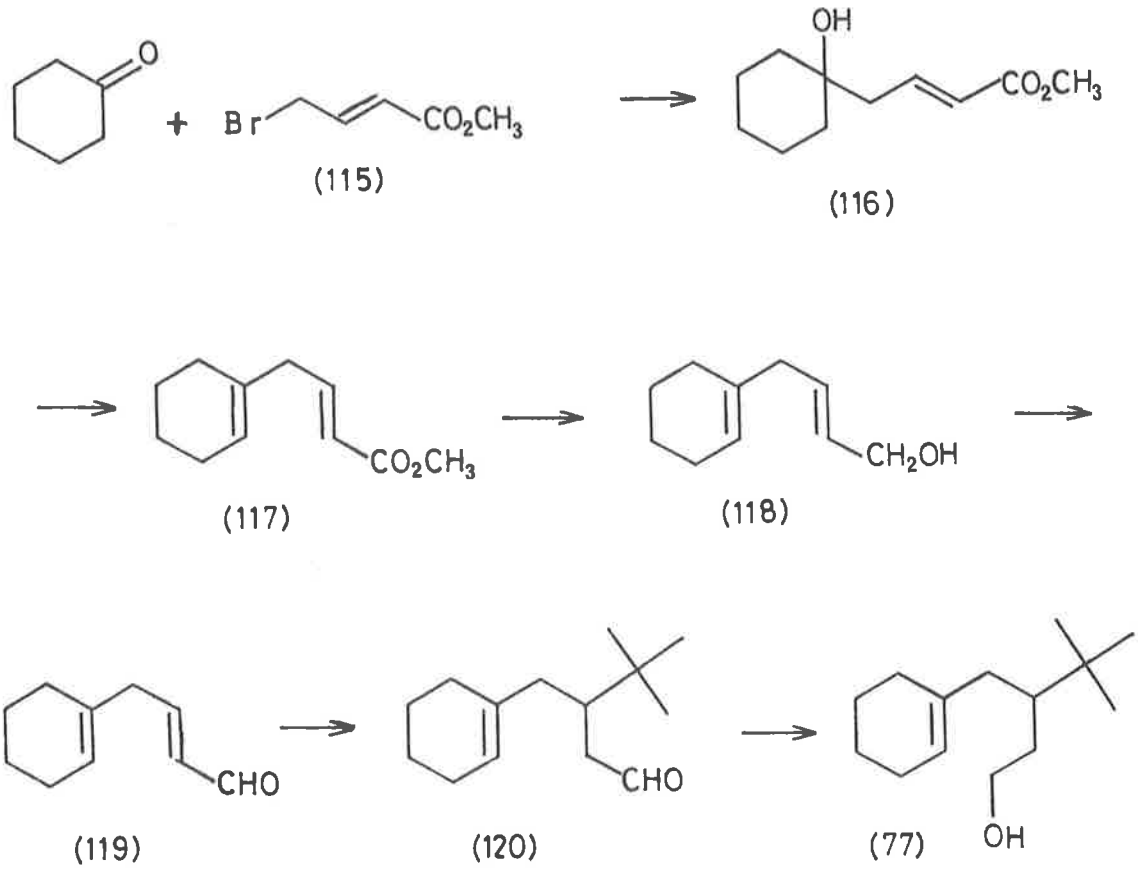
mixture consistently contained *c.* 20% of unchanged bromides (110) and (111). Separation of the diene (112) from starting material could not be achieved by fractional distillation because of a close similarity in boiling points. Chromatography on a column of neutral alumina, however, gave excellent separation.

Hydroboration of the diene (112) with disiamylborane proceeded selectively, as anticipated,[386] at the less substituted double bond to give the required alcohol (76). Separation of the alcohol (76) from unchanged diene (112) was easily achieved by fractional distillation.

The unsaturated alcohol (76) was converted into its acetate (80) and *p*-nitrobenzenesulphonate (78) esters by treatment with acetic anhydride in pyridine[139] and *p*-nitrobenzenesulphonyl chloride in pyridine[261] respectively.

Part B - The synthesis of derivatives of 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77)

The synthesis of 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77) is outlined in scheme III.2. The choice of this particular approach was governed by the availability of the diene ester (117).[224] It was considered that the introduction of the *t*-butyl group to construct the desired carbon skeleton could be simply achieved by the conjugate addition of a *t*-butyl-metal derivative, such as a

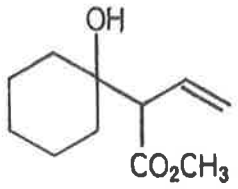


Scheme III.2

t-butylmagnesium halide,[226,227] a *t*-butyl borane,[228] or a *t*-butyl-copperlithium reagent[229,230] to the α,β-unsaturated ester (117) or aldehyde (119).

The Reformatsky reaction of zinc and methyl γ-bromocrotonate

(115) with cyclohexanone in refluxing benzene was found by Drieding and Pratt to give a 30% yield of the hydroxy ester (116).[224] It was thought that the low yield of (116) realized by these workers might be circumvented by following a recent suggestion for improving yields in Reformatsky reactions by minimizing side reactions, and performing the reaction at room temperature.[231] However, when the reaction was carried out at room temperature, a mixture containing *c.* 30% of the required hydroxy ester (116) and *c.* 70% of the "abnormal" product[224] (121) was obtained in 80% yield.



(121)

Drieding and Pratt had previously obtained (121) exclusively when they carried out the above reaction in refluxing ether, but had been undecided as to whether the difference in the course of the reaction was due to the temperature differential in the two cases, or to other properties of the respective solvents.[224] The present finding indicates that it is the reaction temperature which is important. At room temperature, as in the present work, or at the relatively low temperature of refluxing ether,[224] the unconjugated hydroxy ester (121) is formed, *via* the alkoxy zinc intermediate (123), by the kinetically controlled reaction of the alkylzinc species (122) through its more reactive 2-position (fig. III.4). At the temperature of refluxing benzene, however, the initially formed intermediate (123) undergoes rapid equilibration to the thermodynamically more stable conjugated species (124), which gives (116) on work-up (fig. III.4). When the reaction was subsequently performed in benzene at

room temperature to minimize yield-reducing side reactions, but followed by a brief period of heating to achieve equilibration of the zinc alkoxide intermediates (123) and (124) (fig. III.4), methyl (*E*)-4-(1-hydroxycyclohexyl)but-2-enoate (116)* was obtained as the sole product in 75% yield.

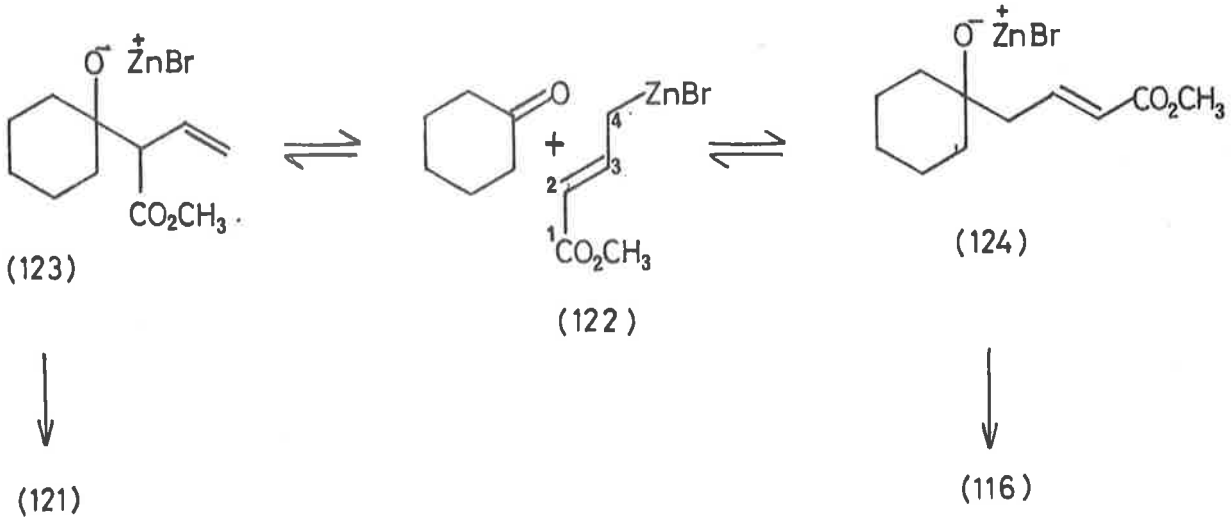


fig. III.4

Dehydration of the hydroxy ester (116) was effected by heating a benzene solution of (116) under reflux in the presence of a catalytic amount of *p*-toluenesulphonic acid.[236] The product of this reaction was invariably a mixture containing predominantly the required diene ester (117) (*c.* 70-88% by g.l.c. analysis), with two minor components, which were most likely[224] the isomeric diene esters (125) and (126). Careful fractional distillation of the mixture eventually gave methyl (*E*)-4-(cyclohex-1-enyl)but-2-enoate (117) of *c.* 98% purity (by g.l.c.) in 38% yield.

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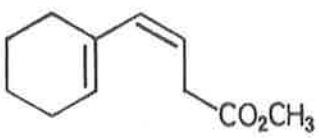
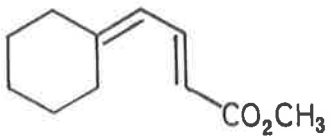
* The double bond in the side chain of (116) and related compounds was assigned the *E*-stereochemistry on the basis of a vicinal coupling constant of 16 Hz in the n.m.r. spectrum of these compounds.[232a] The stereochemistry is not, however, important to the success of the synthesis.

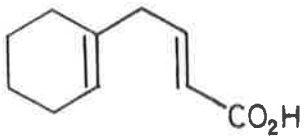
Several other methods for the dehydration of (116) to (117) were also attempted, but were found to be less suitable. Heating a solution of the hydroxy ester (116) in dimethyl sulphoxide with oxalic acid at 110° for 24 hr [233] and heating a solution of (116) in dimethyl sulphoxide under reflux for 24 hr[234] both gave only unchanged starting material. Dehydration could be achieved by heating a two-phase mixture of the alcohol (116) and 6% aqueous oxalic acid under reflux, but the mixture thus obtained contained only *c.* 65% of the required diene ester (117), and *c.* 25% and 10% of two other components, which were assumed to be (125) and (126). Furthermore, under these reaction conditions, hydrolysis of the ester function occurred to give the diene acid (127), which was identified by its spectral properties and by a g.l.c. and spectral comparison of



(125)



(126)



(127)

its methyl ester, prepared by esterification with diazomethane, with an authentic sample of (117).

Reduction of the diene ester (117) with lithium aluminium hydride gave a mixture containing two major components (*c.*73% and 19%). A triplet (J = 6Hz, 2H) at δ3.20 and a lack of olefinic resonances except for a single broad one at δ5.38 (1H) in the n.m.r. spectrum of the mixture indicated that the major component was 4-(cyclohex-1-enyl)butan-1-ol (24e). The minor component was shown by g.l.c. comparison with an authentic sample to be *(E)*-4-(cyclohex-1-enyl)but-2-en-1-ol (118). The concomitant reduction of both the double

bond and the carbonyl group in reductions of α,β-unsaturated carbonyl compounds with lithium aluminium hydride is well established,[237-240] and was not entirely unexpected in this case.

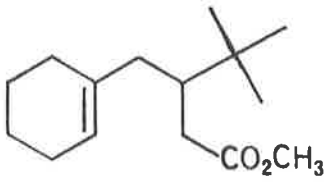
Reduction of the ester (117) with lithium borohydride gave a mixture which contained only *c.*3% of the allylic alcohol (118), *c.* 10% of (24e), and two unidentified major products (*c.*46% and 38%). Infrared and n.m.r. analysis of the mixture revealed that the double bond in the side chain had been almost completely reduced, and that the ester group had only undergone partial reduction.

When reduction of the diene ester (117) was carried out using aluminium hydride, generated by the reaction of lithium aluminium hydride with aluminium chloride,[241] the desired allylic alcohol (118), contaminated with only *c.* 2% (by g.l.c.) of the alcohol (24e), was obtained in good yield. It was found necessary, however, to allow the lithium aluminium hydride and aluminium chloride to stir at room temperature for at least 2 hr before the resulting solution of aluminium hydride could be used. If a shorter time was allowed for the aluminium hydride to form,[241] larger quantities of (24e) were obtained in the product mixture.

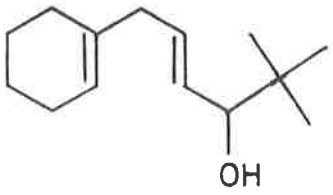
The allylic alcohol (118) was oxidized to the α,β-unsaturated aldehyde (119) with a solution of chromium trioxide-pyridine complex in methylene chloride.[242]

All attempts to prepare methyl 3-*t*-butyl-4-(cyclohex-1-enyl)butanoate (128) by the cuprous chloride or cuprous iodide catalyzed conjugate addition of *t*-butylmagnesium bromide to the diene ester (117) proved unsuccessful. The infrared and n.m.r. spectra of the crude product mixtures showed not only that the double bond in the side chain had been largely removed and that a *t*-butyl group had been introduced, but also that the mixture contained ketonic and hydroxylic

products. Furthermore, the only volatile compound which could be isolated by distillation was unchanged starting material (117). The problem of polymerization in Grignard additions to α,β-unsaturated esters has been observed before, and has been found to be particularly acute with *t*-butylmagnesium halides.[243]



(128)



(129)

When the α,β-unsaturated aldehyde (119) was treated with *t*-butylmagnesium bromide in the presence of either cuprous chloride or cuprous iodide, no reaction was observed and only unchanged starting material (119) was recovered.

The possibility of introducing the *t*-butyl group by conjugate addition using a *t*-butylcopperlithium reagent,[229,230,244-251] was examined next. Although mixed dialkylcopperlithium species are now considered to be the reagents of choice for the conjugate addition of *t*-butyl groups,[246,247,250,251,258] these were almost unknown at the time this work was carried out and hence this study is confined to reactions of di-*t*-butylcopperlithium (130) and its tri-*n*-butylphosphine complex (132).[244,248,249] Di-*t*-butylcopperlithium (130) was prepared at -70° by the reaction of 2 equivalents of *t*-butyllithium* with 1 equivalent of cuprous iodide (eq.1),[244] and its tri-

* Attempts to prepare *t*-butyllithium by the reaction of *t*-butyl chloride or bromide with finely divided lithium (particle size *c.*1 mm) as described by Bartlett and Lefferts[252] were totally unsuccessful. These failures were consistent with the observation that high purity lithium, uncontaminated by at least 1% of sodium, is unreactive toward *t*-butyl halides.[253-256] Attempts to prepare a 1% sodium-lithium alloy by mixing the two metals in a molten state[253] resulted in no amalgamation. A very fine sodium-free lithium dispersion (particle size 10-30μ) was also found to not react with *t*-butyl halides. Ultimately, *t*-butyllithium solution was obtained commercially.

n-butylphosphine complex (132) was prepared (at -70°) from one equivalent of tetrakis[iodo(tri-*n*-butylphosphine)copper(I)] (131)[257] and two equivalents of *t*-butyllithium (eq. 3).[244]

$$2(t\text{-}C_4H_9Li) + CuI \rightarrow \underset{(130)}{(t\text{-}C_4H_9)_2CuLi} + LiI \quad \ldots \quad 1.$$

$$(n\text{-}C_4H_9)_3P + CuI \rightarrow \tfrac{1}{4}\underset{(131)}{[(n\text{-}C_4H_9)_3P.CuI]_4} \quad \ldots \quad 2.$$

$$\tfrac{1}{4}\underset{(131)}{[(n\text{-}C_4H_9)_3P.CuI]_4} + 2(t\text{—}C_4H_9Li) \rightarrow \underset{(132)}{(t\text{-}C_4H_9)_2CuLi.P(n\text{-}C_4H_9)_3} + LiI \quad \ldots \quad 3.$$

The crude product obtained from the reaction of di-*t*-butylcopperlithium (130) and the diene ester (117) showed infrared absorptions at 3400 cm^{-1} and 1705 cm^{-1} and no n.m.r. resonance for a methyl ester. This data is clearly irreconcilable with the required ester (128), and suggests that the reagent had attacked the carbonyl group directly rather than by the expected 1,4-mode of addition. Reaction of the unsaturated aldehyde (119) with this reagent (130) gave a mixture of two products in a 4:1 ratio (by g.l.c.). The spectral data were consistent with the presence of the allylic alcohol (129) as the major product (*c.* 80%) and the desired *t*-butyl substituted aldehyde (120) as the minor component (*c.* 20%).

The preference for 1,2-addition over 1,4-addition to the α,β-unsaturated carbonyl compounds (117) and (119) exhibited by the *t*-butylcopper reagent (130) is at variance with the normal behaviour of dialkyl cuprates.[229,230] It was considered that this inverted preference could be attributed either to the thermal instability which

is particularly severe in the case of tertiary dialkylcuprates,[244,247] or to incomplete or overly slow formation of the reagent (130) under the heterogeneous reaction conditions (eq. 1), resulting in the presence of free *t*-butyllithium. Both of these problems, it was reasoned, could be overcome by replacement of cuprous iodide with its tri-*n*-butylphosphine complex (131). The ether-soluble complex (131) would react much more rapidly with *t*-butyllithium, and the resulting cuprate (132) would be stabilized by virtue of the phosphine ligand[229,230,244] (eq. 3).

It was found that the ligand stabilized cuprate (132) did not react, either by 1,2-addition or by 1,4-addition, with the diene ester (117), but underwent exclusive 1,4-addition to the α,β-unsaturated aldehyde (119) to give 3-*t*-butyl-4-(cyclohex-1-enyl)-butanal (120). This result was more in keeping with the usual behaviour of dialkylcuprates, which normally react with α,β-unsaturated carbonyl substrates exclusively by 1,4-addition, and less readily with esters than with the corresponding aldehydes and ketones.[229,230,258-260]

Isolation of the aldehyde (120) from the crude product mixture was made difficult by the presence of polymeric and organo-copper material, and tri-*n*-butylphosphine. A pure sample of the aldehyde (120) could be obtained by washing the crude product with 20% aqueous ethylenediamine, followed by methyl iodide, which removed most of the unwanted material, and careful chromatography of the remaining mixture on neutral alumina. Reduction of the aldehyde (120) with sodium borohydride then gave 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77). A slightly more convenient procedure involved reduction, with sodium borohydride, of the crude product mixture from the conjugate addition reaction. Isolation of the alcohol (77) by chromatography proved to be easier than a prior separation of the aldehyde

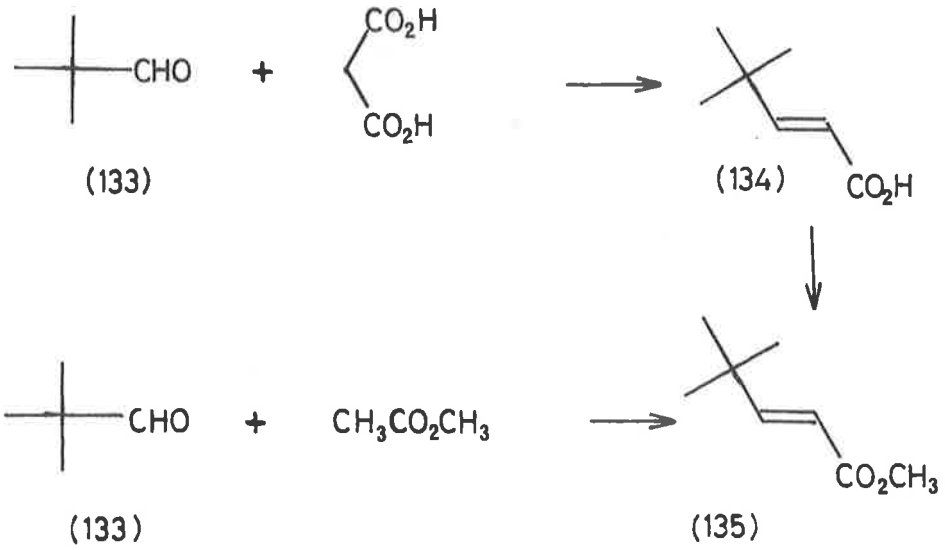
(120) by chromatography.

The alcohol (77) was converted into its required derivatives, the acetate (81) and the *p*-nitrobenzenesulphonate ester (79), by treatment with acetic anhydride in pyridine[139] and *p*-nitrobenzenesulphonyl chloride in pyridine[261] respectively.

Hydrogenation of the unsaturated alcohol (77) to its saturated analogue (96) proved unexpectedly difficult at room temperature and atmospheric pressure. In the presence of a 10% platinum-charcoal catalyst, no hydrogenation occurred even after 5 days. With 5% palladium-carbon or rhodium-carbon catalysts, hydrogenation proceeded slowly to completion (10-14 days), but g.l.c. analysis revealed the formation of two byproducts, one of which (*c.* 10%) was a hydrocarbon possessing a short g.l.c. retention time, presumably formed by hydrogenolysis of (77), and the other of which (*c.* 20%) had g.l.c. properties similar to the 9-decalols (142) and (143) described in Chapter IV. Success was eventually realized by using a 5% rhodium-alumina catalyst. Although hydrogenation was still relatively slow (*c.* 3 days for complete reaction), and relatively large quantities of catalyst were required, the saturated alcohol (96) thus obtained was contaminated with only 2% and 3% respectively of the abovementioned byproducts. The alcohol (96) was converted without purification to its *p*-nitrobenzenesulphonate ester (97) in the usual way.[261]

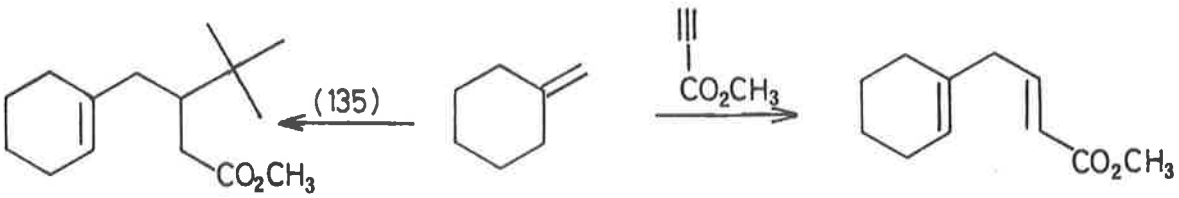
Part C - An unsuccessful electrocylic approach to the synthesis of 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77)

The ene reaction of olefins with highly activated enophiles has been well studied and is a synthetically useful reaction.[262] With relatively unreactive enophiles (e.g. methyl vinyl ketone, acrylic acid esters), however, the ene reaction is of little value, since harsh conditions are required and the yields are usually low.[262-264] Towards the conclusion of the present work, Snider reported that Lewis acid catalysis accelerated the ene reaction of methyl acrylate, methyl vinyl ketone, and acrolein with various olefins to the extent that such reactions could be carried out under very mild conditions.[265] This discovery[265] prompted a brief examination of the possibility that the ene reaction of methylenecyclohexane (136) with methyl 4,4-dimethylpent-2-enoate (135) might provide a facile synthesis of methyl 3-*t*-butyl-4- (cyclohex-1-enyl)butanoate (128) (Scheme III.4), and thence 3-*t*-butyl-4-(cyclohex-1-enyl)butan-1-ol (77).



Scheme III.3

The routes by which the unsaturated ester (135) were synthesized are depicted in Scheme III.3. Attempts to effect the condensation of pivaldehyde (133) with methyl acetate using sodium hydroxide as base were unsuccessful. When potassium *t*-butoxide was used as base, a mixture was obtained from which the major component (*c.* 80%), the required ester (135), was separated by preparative g.l.c. in 13% yield. An alternative synthesis of (135), involving firstly a Doebner condensation[266a] between pivaldehyde (133) and malonic acid, followed by esterification of the resulting acid (134) with diazomethane, did not improve the yield. This method did, however, have the advantage that the intermediate α,β-unsaturated acid (134) could be purified by recrystallization. The overall yield of pure ester (135) obtained by this method was 8%.



(128) (136) (117)

Scheme III.4

Methylenecyclohexane (136) failed to react with methyl 4,4-dimethylpent-2-enoate (135) in the presence of aluminium chloride. After 72 hr in refluxing benzene, unchanged starting material was recovered, and no trace of ene adducts, e.g. (128), could be detected. The extreme bulkiness of the *t*-butyl substituted enophile (135) is the most likely cause of the failure of this reaction, since ene reactions are known to be extremely sensitive to steric effects.[262]

No further attempt was made to find conditions under which methylenecyclohexane (136) and the unsaturated ester (135) might react.

Methylenecyclohexane (136) did, on the other hand, react with methyl propiolate (Scheme III.4) in the presence of aluminium chloride at room temperature. Although the infrared and n.m.r. spectra of the product indicated that the major component was, as expected, methyl *(E)*-4-(cyclohex-1-enyl)but-2-enoate (117), the yield of this reaction was only 20%, and g.l.c. analysis revealed the presence of at least five impurities (totalling *c.* 25%). The relative volatilities, as evinced by their g.l.c. properties, of the components of this mixture suggested that isolation of the major component (117) by distillation would be a simple matter. However, since adequate supplies of the diene ester (117) were already in hand, no attempt at purification, or at optimization of the yield of this reaction, was made.

CHAPTER IV.

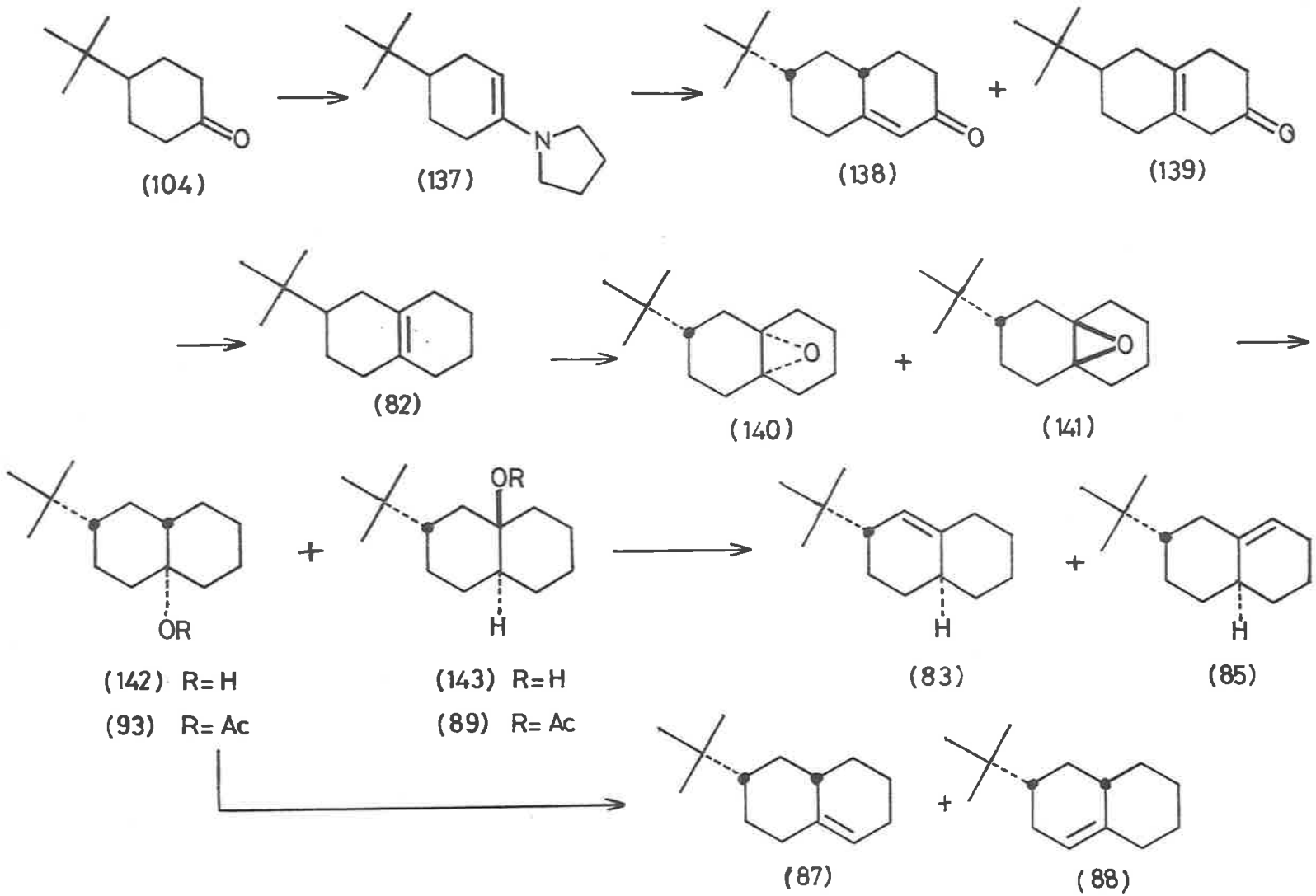
RESULTS AND DISCUSSION

Synthesis of solvolysis products.

Part A - The synthesis of 2-*t*-butyl-1,2,3,4,5,6,7,8-octahydronaphthalene (82), *trans*-7-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (83), and *trans*-2-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (85).

The synthesis of the $\Delta^{9,10}$-octalin (82) and the route by which it was converted to the two *trans*-$\Delta^{1,9}$-octalins (83) and (85) *via* the acetate (89) is outlined in Scheme IV.1. In addition, this route gives access to the two octalins (87) and (88), and the acetate (93), which were unexpected products obtained in the acetolyses of 4-(5-*t*-butylcyclohex-1-enyl)butyl nosylate (78) and 3-*t*-butyl-4-(cyclohex-1-enyl)-butyl nosylate (79) (See Chapter II).

Annelation of the pyrrolidine enamine (137) of 4-*t*-butylcyclohexanone (104) with methyl vinyl ketone according to a published procedure[267] gave a mixture (85:15) of the two octalones (138) and (139). This mixture was reduced with hydrazine and potassium hydroxide in diethylene glycol[268] to a complex mixture of olefinic products, of which 2-*t*-butyl-$\Delta^{9,10}$-octalin (82) was the major component (*c.* 45%). When this olefin (82) was originally synthesized,[210] Laffer separated it directly from the product mixture by preparative g.l.c. In the present work, however, it was found more convenient to isolate the octalin (82) by chromatography on a column of silica gel impregnated with silver nitrate. In addition, it was found that the proportion of $\Delta^{9,10}$-octalin in the mixture could be increased to *c.* 80% by equilibration with boron trifluoride etherate in a 2:1 benzene-sulpholane solvent mixture,[269] thus greatly increasing the overall yield of this sequence. Although the equilibrium concentration of (82) in the mixture was actually found to be greater than 80% (i.e., *c.* 85%), if the equilibration was allowed to proceed beyond this point, a new impurity which could


(104)
(137)
(138)
(139)
(82)
(140)
(141)
OR
OR
H
H
(142) R= H
(93) R= Ac
(143) R=H
(89) R= Ac
(83)
(85)
(87)
(88)

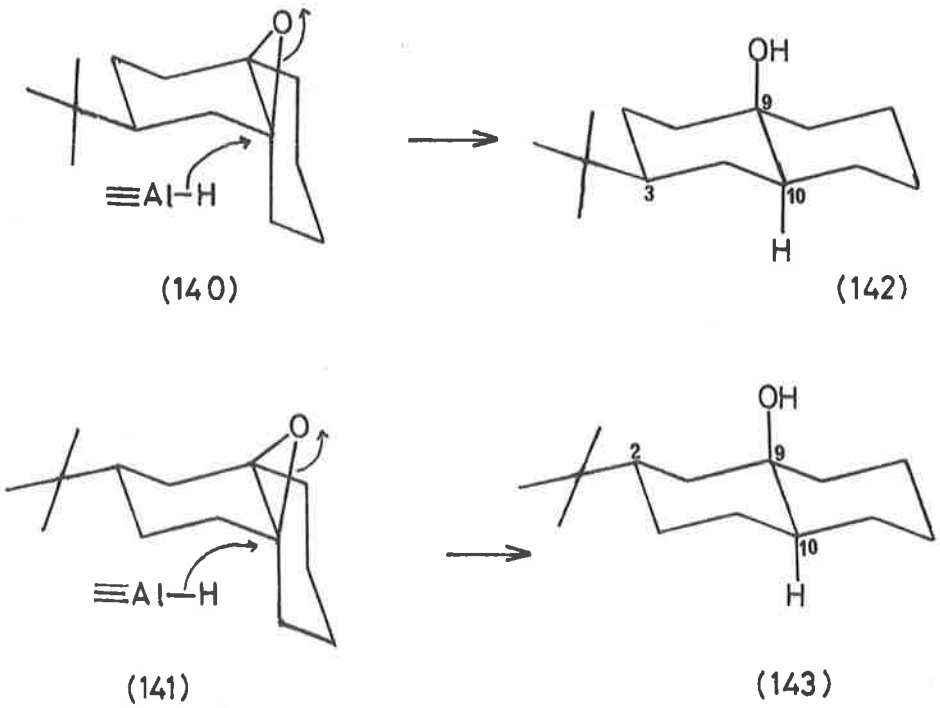
Scheme IV.1

not be separated from the required octalin (82) began to appear. Catalysis of the equilibration by *p*-toluenesulphonic acid in the same solvent system[269] was also examined, but the rate of isomerization was found to be considerably slower than with boron trifluoride etherate, and was accompanied by the formation of a number of new impurities.

Treatment of the octalin (82) with *m*-chloroperbenzoic acid gave an inseparable mixture of the two epoxides (140) and (141) in the ratio 55:45 (by g.l.c. analysis). It was not possible to distinguish between the two isomers at this stage of the synthesis, and structural assignments were only made after the final products from this sequence had been conclusively identified.

In the absence of complicating steric factors, ring opening of cyclohexene oxides by nucleophiles occurs specifically in a *trans*-diaxial manner.[266b,270,271a] This fact is of crucial importance in this synthesis, since it means that *trans*-diaxial ring opening of the epoxide (141) with lithium aluminium hydride will give only the *trans*-fused decalol (143) (fig. IV.1) in which the relative stereochemistry at C_2 and C_{10} is the same as that of the *trans*-octalins (83) and (85). Similarly, *trans*-diaxial ring opening of the epoxide (140) will only give the *trans*-fused decalol (142) (fig. IV.1) in which the relative stereochemistry at C_3 and C_{10} is the same as that of the *cis*-octalins (87) and (88).

When the epoxide mixture, (140) and (141), was treated with lithium aluminium hydride, the two *trans*-fused decalols (142) and (143) were obtained as an inseparable mixture in the ratio 55:45 (by g.l.c.) respectively. The derived acetates, (93) and (89) respectively, formed by acetylation of the decalol mixture with acetyl chloride and N,N-dimethylaniline,[272] could, however, be separated, either by preparative g.l.c. or by careful chromatography on a column of neutral alumina.



(140) (142)

(141) (143)

fig. IV.1

Because of the *trans*-ring fusions of the two acetates (93) and (89), and because acetate pyrolysis involves *cis*-elimination,[273a] only two olefinic products can be formed by pyrolysis of each of these acetates. Thus, pyrolysis of (89) can only give rise to the two octalins (83) and (85), while pyrolysis of (93) can only form (87) and (88).

When the acetate of shorter g.l.c. retention time (also the minor component of the 45:55 acetate mixture) was subjected to flash vacuum pyrolysis, a mixture of two olefins was obtained. The two products were separated by preparative g.l.c., and it was found that the olefin of longer g.l.c. retention time, which was also the major component of the pyrolysis mixture,* had spectral and g.l.c. properties identical with those of an authentic sample of *trans*-7-*t*-butyl-$\Delta^{1,9}$-octalin (85) available from earlier work.[210] In addition, a comparison

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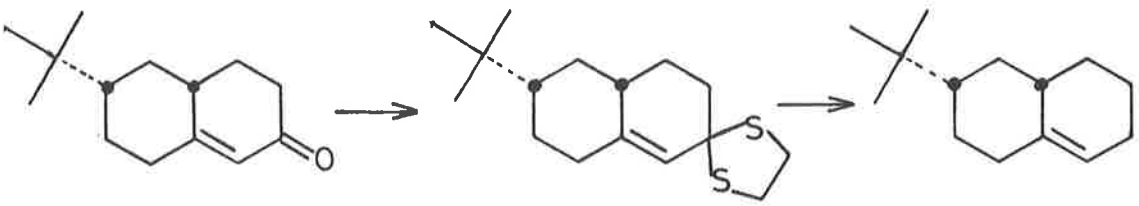
* In two separate experiments the two products were obtained in ratios of 45:55 and 35:65.

of spectral and g.l.c. properties proved that neither of these pyrolysis products was *cis*-6-*t*- butyl-$\Delta^{1,9}$-octalin (87), which had been prepared by an independent route (Scheme IV.2). The second olefin in the pyrolysis product mixture must therefore be *trans*-2-*t*-butyl-$\Delta^{1,9}$-octalin (83), and the acetate precursor is therefore defined as (89). It follows from this identification that the minor components of the decalol and epoxydecalin mixtures were (143) and (141) respectively, and that the major components were (142) and (140) respectively.

The above assignments were confirmed when the acetate of longer g.l.c. retention time (the major component of the 45:55 mixture) was pyrolysed. Again two olefins were obtained (as a 58:42 mixture), but these could not be separated by preparative g.l.c. A comparison of g.l.c. properties with authentic samples, proved that the major component of the mixture (having a shorter g.l.c. retention time) was the *cis*-octalin (87), and that none of the *trans*-octalin (85) was present in the mixture.



(138) (144) (87)

Scheme IV.2

An authentic sample of the octalin (87) was obtained by independent synthesis as outlined in Scheme IV.2. A pure sample of the octalone (138) was obtained by repeated recrystallization of the mixture of (138) and (139) (Scheme IV.1) from hexane[267] at -40°. Treatment of (138) with ethanedithiol in the presence of boron trifluoride etherate[274] effected its conversion into the thioacetal (144),

which on reduction with sodium in liquid ammonia[275] gave the desired octalin (87) as the major component (*c.* 88%, separable by preparative g.l.c.) of a mixture of four compounds.

It is worth mentioning some of the differences in the n.m.r. spectral properties of the two octalins (83) and (85), and of the two acetates (89) and (93). While these differences are by themselves probably insufficient for rigorous and unambiguous identification in the first instance, they are sufficiently characteristic that they can subsequently be used for distinguishing between the possibilities. In the n.m.r. spectrum of the octalin (83), the olefinic proton resonance at δ5.33 had a width at half-height ($W_{\frac{1}{2}}$) of 4 Hz. The corresponding resonance in the spectrum of the octalin (85), which also occurred at δ5.33, had $W_{\frac{1}{2}}$ = 11 Hz. An examination of Drieding models indicates that the dihedral angle in the first compound (83) is approximately 80°, and should therefore give rise to only a small vicinal coupling. In (85), however, the two dihedral angles concerned are *c.* 40° and 90°, and are unchanged, although interconverted, by ring inversion. In this case, the smaller dihedral angle would result in a large vicinal coupling constant which would cause a broadening of the olefinic proton resonance.[232b]

The two acetates (89) and (93) can be differentiated on the basis of the chemical shifts of their respective *t*-butyl groups. The *t*-butyl resonance of (89) occurs at δ0.80, whereas that of (93) is at δ0.84. In the latter case (93), it could be argued that the slight downfield shift relative to (89) is caused by greater deshielding of the *t*-butyl protons by the acetoxy group due to the *cis*-relationship of these two groups.

Part B - The synthesis of

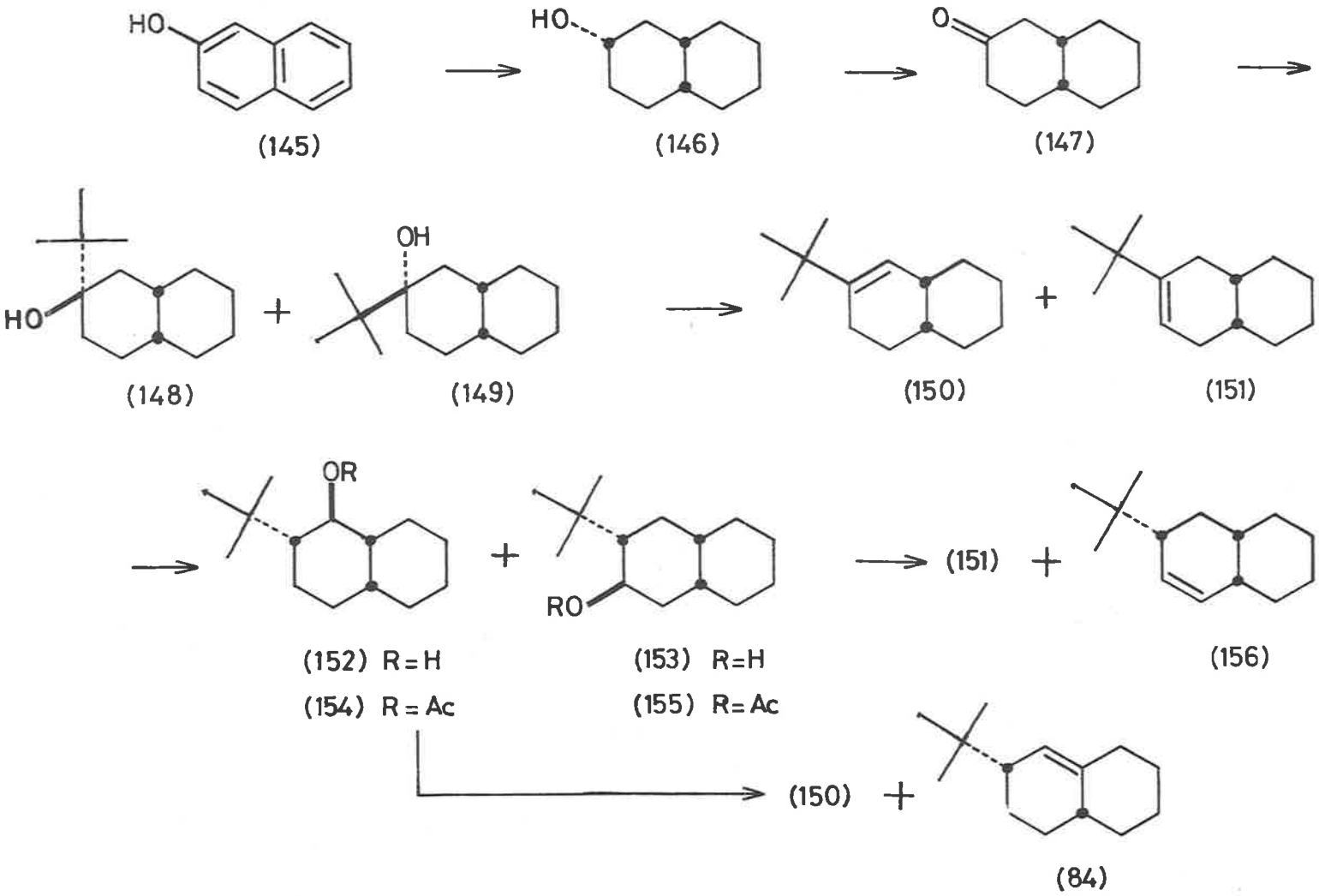
cis-7-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (84).

The synthesis of the *cis*-octalin (84) is outlined in Scheme IV.3.

Hydrogenation of 2-naphthol (145) under 70 atmospheres pressure over a rhodium-alumina catalyst proceeded with high stereospecificity to give predominantly (*c.* 95% by g.l.c.) the *cis,cis*-decalol (146),[276,277] which could be obtained in a pure state by recrystallization of the crude product from hexane. Oxidation of (146) with chromic acid[278] afforded pure *cis*-2-decalone (147).

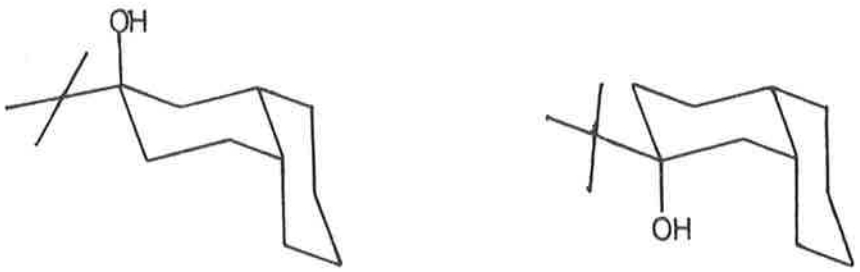
Treatment of the decalone (147) with *t*-butylmagnesium bromide, surprisingly, gave none of the expected tertiary alcohols (148) and (149). Enolization[279b,280] of the ketone (147) appeared to be the main course of the reaction, since unchanged starting material (147) was the major product (39%). In addition, the isolation in 31% yield of epimerically pure *cis,cis*-2-decalol (146) indicated that reduction by the Grignard reagent[279a,281,282] was also occurring. Although there are methods for partially suppressing the enolization[280] and reduction[284,285] pathways in Grignard reactions, it was considered that *t*-butyllithium would constitute a more effective alkylating agent, as alkyllithium reagents do not effect reduction of ketones to any appreciable extent.[283]

Treatment of *cis*-2-decalone (147) with *t*-butyllithium at -70°[283] gave a mixture containing, by g.l.c. analysis, 21% of unchanged starting material (147) and 44% and 35% of the tertiary alcohols (148) and (149) respectively. These two alcohols were distinguished on the basis of their chromatographic behaviour. If these compounds are assumed to exist in conformations in which the *t*-butyl group is


HO
(145)
HO
(146)
O
(147)
HO
(148)
OH
(149)
(150)
(151)
OR
RO
(152) R = H
(154) R = Ac
(153) R = H
(155) R = Ac
(151)
(156)
(150)
(84)

Scheme IV.3

equatorial, then the considerably more crowded hydroxyl group of (149) should be able to bind less effectively with the chromatographic adsorbent than the comparatively more exposed hydroxyl group of (148) (fig. IV.2). The alcohol which was first eluted from a column of neutral alumina was therefore assigned the structure (149), and for the last eluted alcohol was therefore the other isomer (148).*



(148) (149)

fig. IV. 2

Separation of the mixture of alcohols (148) and (149) and the decalone (147) by chromatography was only partially successful. The early and late fractions gave some of the pure alcohols (149) and (148) respectively, but the intermediate fractions, containing the major portions of (148) and (149) were all contaminated with the decalone (147). It seemed likely that removal of the decalone (147) might be facilitated if the alcoholic components (148) and (149) of the mixture were first dehydrated to the octalins (150) and (151).

When the mixture of tertiary alcohols (148) and (149) and the decalone (147) was treated with thionyl chloride in pyridine[286] at 0^{o}, a mixture of the octalins (150) and (151) in the ratio 45:55

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* The O-H stretching absorption in the infrared spectra of the two alcohols lent further support to this assignment. The first-eluted alcohol (149) had a weak but sharp O-H absorption at 3500 cm^{-1}, whereas the last eluted alcohol (148) had a much stronger band at 3430 cm^{-1}. The difference is due to stronger hydrogen bonding by the less sterically crowded hydroxyl group of (148).[292]

respectively,* containing only *c.* 1% of the decalone (147) was obtained. The surprising, although welcome, disappearance of the decalone (147) from the mixture is most likely due to the formation under the reaction conditions and subsequent loss during work-up of some water-soluble or base-soluble derivative of (147). Ketones[288] and other carbonyl compounds[287] can undergo α-chlorosulphination with thionyl chloride in the presence of pyridine. If such a reaction occurred in the case of the decalone (147), the resulting α-ketosulphinyl chloride (156) would be hydrolyzed to the corresponding α-ketosulphinic acid (157) (fig. IV.3), which would be removed during the working-up procedure (see Experimental for details).

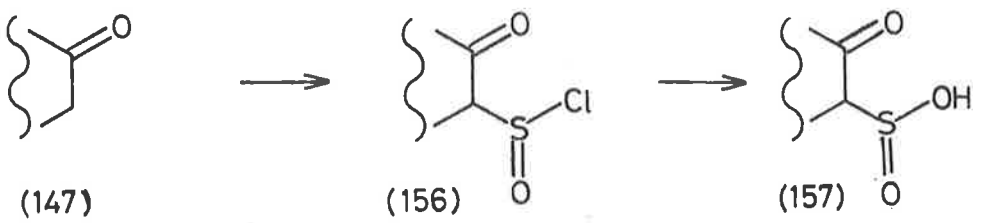

fig. IV.3

Acetophenone has been reported to react with thionyl chloride and pyridine to form a water-soluble pyridinium salt.[290] A similar reaction of the decalone (147) would also account for its disappearance from the reaction mixture, but this appears to be a less likely explanation since this reaction requires slightly more vigorous conditions[290] than were used for the dehydration. Unfortunately time did not permit an investigation of this intriguing observation.

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* Although the two components of the mixture could be separated by preparative g.l.c., it was not possible to distinguish between the structures (150) and (151) directly and unambiguously on the basis of spectral properties. Structural assignments were made by relating the two components of the mixture to later derivatives, the structures of which could be rigorously differentiated.

When each of the alcohols (148) and (149) was separately treated with thionyl chloride and pyridine, the same olefin ratio of 45:55 as was obtained for dehydration of the mixture resulted. If the dehydration was performed by stirring a solution in hexane of the two alcohols (148) and (149) and the decalone (147) with 50% aqueous sulphuric acid.[280] the same olefin ratio was again observed, but the decalone (147) was not lost from the product mixture. It is interesting to note that McMurry used this latter dehydration method in a structurally similar system to effect a completely regiospecific dehydration to a single olefinic product (fig. IV.4).[280] The difference between the regioselectivities observed in these two systems is difficult to rationalize. However, it does serve to further exemplify how subtle differences in molecular geometry can play an important role in the chemistry of $\Delta^{1,2}$- and $\Delta^{2,3}$-octalins.[280,291]

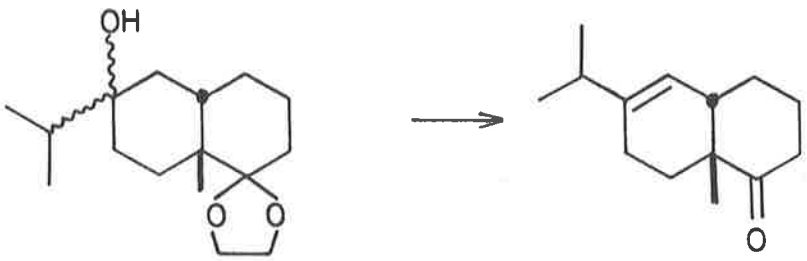


fig. IV.4

An examination of molecular models indicated that the convex face of each of the two *cis*-fused octalins (150) and (151) is the less hindered, and therefore hydroboration should occur at this face to give, after oxidation, the secondary alcohols (152) and (153), respectively, in which the stereochemistry of the desired end-product (84) had been established. The original synthetic strategy required acetylation of the alcohol mixture to form the acetates (154) and (155). Pyrolysis of the acetate mixture would give a mixture of the four

octalins (84), (150), (151), and (156), which would then be separated by preparative g.l.c. Identification of the required octalin would then have been a simple matter, as two of the products, (150) and (151), have already been synthesized, and the remaining pair, (84) and (156), would be readily distinguishable by n.m.r. spectroscopy because of the difference in substitution of the double bond in each. In the event, it was found that only (150) could be isolated from the pyrolysis mixture, and that the other three components, (84), (151), and (156), could only be resolved on capillary g.l.c. columns. To overcome this problem, it was therefore necessary to obtain the acetate (154) in a pure state. Pyrolysis of (154) would then give only (84) and (150), which can be separated by preparative g.l.c.

Hydroboration of the mixture containing 45% of the $\Delta^{1,2}$-octalin (150) and 55% of the $\Delta^{2,3}$-octalin (151) with a solution of diborane in tetrahydrofuran, followed by oxidation with alkaline hydrogen peroxide, gave an unexpectedly complex mixture containing as well as the expected secondary alcohols (152) and (153), the tertiary alcohol (148) and several unidentified minor components (*c.* 1-2%). Furthermore, although the proportion of (153) in the mixture remained approximately constant throughout a number of experiments, the relative yields of (148) and (152) varied quite capriciously even under apparently identical experimental conditions (Table IV.1). From the relative yields in Table IV.1, it is clear that hydroboration of the $\Delta^{2,3}$-octalin (151) proceeds regiospecifically to give the alcohol (153), and that (152) and the tertiary alcohol are both formed from the $\Delta^{1,2}$-octalin (150). A detailed analysis of the various conformational and steric differences between the two octalins (150) and (151) does not reveal any acceptable explanation for this difference in selectivity.

Table IV.1

Relative yields of (148), (152), and (153) from the hydroboration of a 45:55 mixture of (150) and (151)

Product	Relative yields (%)[A]				
(148)	1	4	6	14	22
(152)	45	37	32	31	20
(153)	54	57	56	55	58

A Determined by g.l.c. analysis of the crude product mixture.

The steric environment of the hydroxyl group in the 1-decalol (152) is considerably more crowded than that of the hydroxyl group in the 2-decalol (153) by virtue of its having a second alkyl substituent, the adjacent ring member, as well as the *t*-butyl group flanking it. This property was of considerable importance in distinguishing between these two alcohols. Firstly, the two alcohols could be easily separated by column chromatography. The 1-decalol (152) was eluted more rapidly than the 2-decalol (153) because the more crowded hydroxyl group of (152) could interact less effectively with the adsorbent. Secondly, quite a dramatic difference was seen in the infrared spectra of these two compounds. The 2-decalol (153) showed a strong broad absorption at 3280 cm^{-1}, whereas the 1-decalol (152) showed a somewhat weaker and much sharper band at 3500 cm^{-1}. This difference is easily explained by the considerably reduced intermolecular hydrogen bonding in (152) caused by the greater crowding of the hydroxyl group.[292] Lastly, acetylation of the 2-decalol (153) could be readily effected with acetic anhydride and pyridine at room temperature.[139] The 1-decalol (152), however, was unreactive toward this acetylating system, and its acetate (154) could only be prepared by reaction with

acetyl chloride in N,N-dimethylaniline.[272]

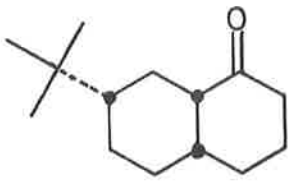
Flash vacuum pyrolysis of the 1-decalyl acetate (154) gave a mixture (31:69 by g.l.c. analysis) of the two octalins (84) and (150), which could be separated by preparative g.l.c. The major component (of shorter g.l.c. retention time) was identified as the $\Delta^{1,2}$-octalin (150) by a comparison of g.l.c. and spectral properties with those of the compound which had been tentatively identified as (150) earlier. The minor component, which had different properties to the two octalins (150) and (151) obtained earlier, was therefore the required $\Delta^{1,9}$-octalin (84). This identification was further supported by some differences between the n.m.r. spectra of the two octalins. The *t*-butyl resonance of (84) occurs at δ0.86, while that of (150) is shifted to lower field (δ1.00) by the greater proximity of the double bond. In addition, the olefinic proton resonance of (84) at δ5.33 has a half-height width ($W_{\frac{1}{2}}$) of 4 Hz, whereas that of (150) has $W_{\frac{1}{2}}$ = 7 Hz. In the $\Delta^{1,9}$-octalin (84), which is a conformationally rigid system, the dihedral angle between the olefinic proton at C_1 and the proton at C_2 is *c.* 90°, and therefore only a small coupling results.[232b] In the case of the $\Delta^{1,2}$-octalin (150), however, conformational inversion is possible, and such a process changes the dihedral angle between the olefinic proton at C_1 and the C_9 bridgehead proton from 30° to 90°. The value of $W_{\frac{1}{2}}$ = 7 Hz therefore represents a population weighted average of the two extreme couplings[232c] and is of necessity larger than the minimum value (4 Hz) which would be observed for a single conformation in which the relevant dihedral angle was 90°.

As a final verification that all structural assignments in this sequence had been made correctly, the acetate to which had been assigned the structure (155) was subjected to flash vacuum pyrolysis. The two products could only be partially resolved by g.l.c., and then

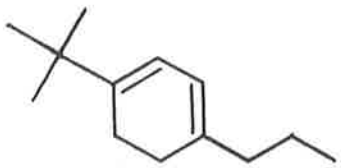
only on a capillary column. The major component (*c.* 80%) had g.l.c. properties identical with those of the octalin (151) prepared earlier, while the minor component (*c.* 20%), of shorter retention time, did not correspond to any of the other octalins which had been prepared in this work. The infrared and n.m.r. spectra of the mixture, when compared with those of the $\Delta^{2,3}$-octalin (151), were also consistent with (151) being the major component. The n.m.r. spectrum showed two olefinic proton resonances at δ5.35 and δ5.58 integrating in the ratio 2:1 respectively, and two *t*-butyl resonances at δ0.99 and δ0.87 integrating in the ratio 4:1 respectively, which indicates that the minor component of the mixture was a disubstituted olefin, and must therefore be (156).

Part C - The synthesis and some reactions of 7-*t*-butyl-3,4,5,6,7,8-hexahydro-1(2H)-naphthalenone (164)

Early approaches to the synthesis of the remaining *cis*-octalin (86) centred on attempts to synthesize the *cis,cis*-1-decalone (158), or some related decalin functionalized at the appropriate 1-position and having the required stereochemistry, as such a system seemed a likely precursor of the desired octalin (86). It seemed likely that the 1-decalone (158) might be readily obtained by hydrogenation of the known $\Delta^{9,10}$-octalone (164). This unsaturated ketone (164) had been previously synthesized by Laffer,[210] albeit with some difficulty and in low yield, by the route outlined in Scheme IV.4. This synthesis was re-examined in an effort to obtain sufficient quantities of the octalone (164) for an investigation of the possibility of converting it to the saturated ketone (158).

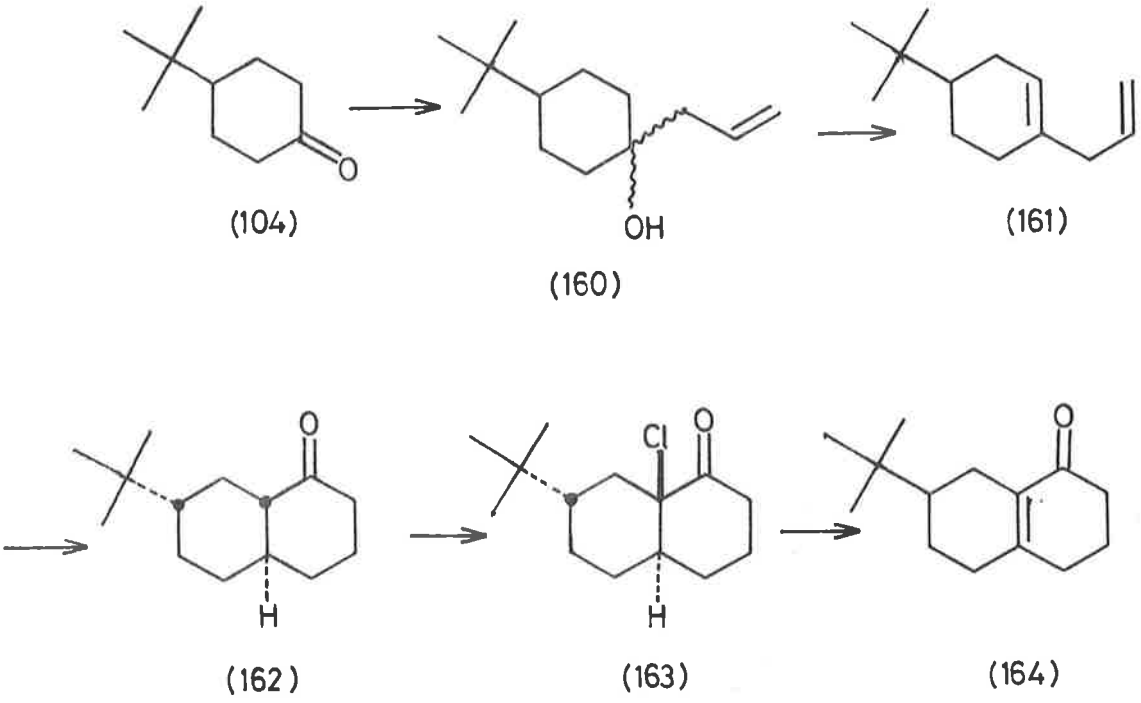


(158)



(159)

The mixture of epimeric tertiary alcohols (160) was obtained from the reaction of 4-*t*-butylcyclohexanone (104) with allylmagnesium bromide. Dehydration of this mixture to the diene (161) with *p*-toluenesulphonic acid in refluxing benzene[236] was found by Laffer to be complicated by a rapid isomerization of (161) to 1-*t*-butyl-4-propyl-1,3-cyclohexadiene (159).[210] He had found it necessary to monitor closely the progress of the reaction by g.l.c. and to terminate it when the first traces of the conjugated diene (159) began



(104) (160) (161)

(162) (163) (164)

Scheme IV.4

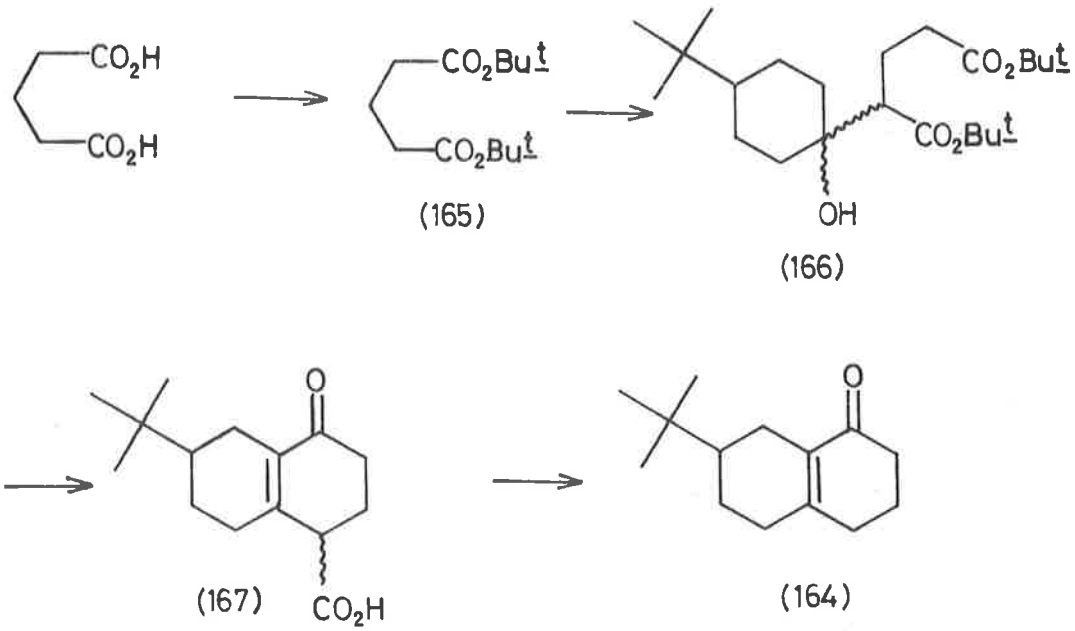
to appear,* then to separate the unconjugated diene (161) from starting material (160) by chromatography, and to recycle the recovered alcohols (160).[210] To circumvent this problem, the dehydration was carried out in boiling 10% aqueous oxalic acid[235] in the hope that isomerization might be minimized in a two-phase reaction system. Indeed, although the dehydration reaction proceeded sluggishly and incompletely, none of the conjugated diene (159) was formed, and the required product (161) could be readily separated from unchanged starting material (160), and from the one minor (*c.* 3%) unidentified by-product that was formed, by column chromatography.

In the earlier work,[210] the carbonylation procedure developed by Brown and Negishi[293,294] was used to convert the unconjugated diene (161) to the *trans*-fused decalone (162). However, the low yield and the

* The isomerization of (161) to (159) only began after an appreciable concentration of (161) had built up in the reaction mixture, and then proceeded fairly rapidly. The two isomeric dienes (159) and (161) could not be separated by column chromatography or fractional distillation.

lack of purity of the product (162) reported by Laffer were discouraging.[210] The milder diene carbonylation reaction reported by Pelter and co-workers[295-298] was therefore attempted, but this method proved to be equally unsatisfactory. Only a 16% yield of volatile material was obtained, and this was shown by g.l.c. to comprise only 80% of the required decalone (162), together with 16% of some unidentified major contaminant and a total of 4% of several minor impurities.

In view of the difficulties thus far encountered and further problems in subsequent steps* of the synthesis described by Laffer,[210] this approach to the $\Delta^{9,10}$-1-octalone (164) was abandoned in favour of the synthesis outlined in Scheme IV.5.[299]



Scheme IV.5

Di-*t*-butyl glutarate (165) was prepared by the acid catalyzed esterification of glutaric acid with isobutene. Treatment of

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* These involved chlorination of the decalone (162) with sulphuryl chloride, and dehydrochlorination of the resulting 9-chlorodecalone (163) to give the enone (164), following procedures described by House and co-workers.[267]

the diester (165) with lithium amide in liquid ammonia generated its lithium enolate, which reacted with 4-*t*-butylcyclohexanone (104) to give the hydroxy diester(s) (166). On being heated at 100° in polyphosphoric acid, the hydroxy diester(s) (166) underwent deisobutylation, dehydration, and cyclization to the keto acid (167). Decarboxylation was effected by heating (167) in aqueous polyphosphoric acid containing acetic acid. The pure enone (164) thus obtained exhibited identical spectral properties to the sample available from earlier work.[210]

Table IV.2

Products from the hydrogenation of (164).

Catalyst, conditions[B]	Products[A] (168)	(162)	(158)
5% Pd-C, EtOH, HCl	2	76	22
5% Rh-C, EtOH, HCl	2	85	13
5% Rh-Al, EtOH, HCl	1	71	28
5% Rh-C, EtOH, neutral	34	41	25
after equilibration[C]	3	79	18
5% Pt-C, EtOH, neutral	49	38	13
after equilibration	5	75	20
Nickel boride P-1,[D] EtOH, HCl	-	-	-

A Yields quoted are relative yields, determined by g.l.c. analysis.

B All hydrogenations were performed at ambient temperature and pressure.

C Equilibration was effected with ethanolic hydrochloric acid.

D Ref. 301, no reaction observed after 72 hr.

Contrary to expectations, hydrogenation of the octalone (164)

gave the *cis,cis*-decalone (158) only as a minor component of a three product mixture (Table IV.2). The identities of the three products were deduced as follows.

An authentic sample of the *trans*-fused decalone (162) was prepared by lithium-ammonia reduction[267,300] of the enone (164). This proved to be identical in all respects with a sample, obtained by preparative g.l.c., of the major product of hydrogenation of (164).

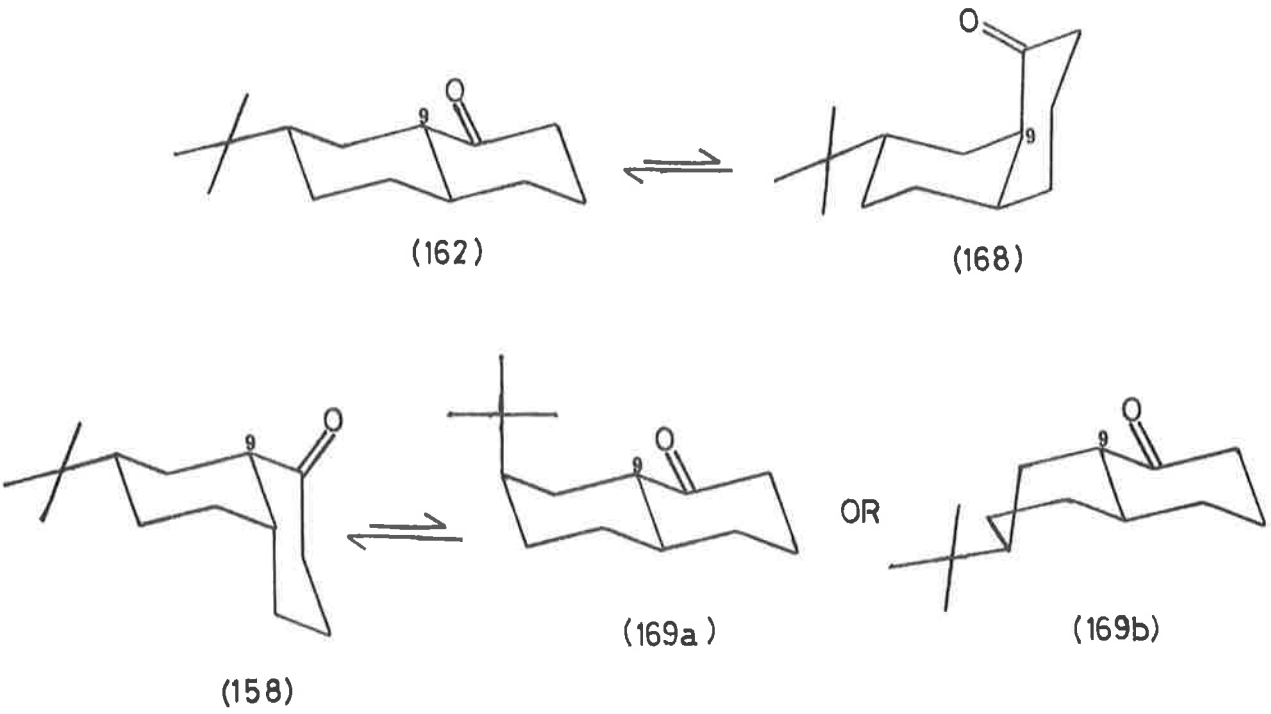

fig. IV.5

The two decalones (162) and (168) are interconvertible by epimerization at C_9 (fig. IV.5), whereas the decalone (158) should be stable under epimerizing conditions, since epimerization at C_9 would require that the *t*-butyl group adopt an axial position (169a), or that the *t*-butyl substituted ring adopt a boat-like conformation (169b), to accommodate the resulting *trans*-ring fusion (fig. IV.5). It can be seen from Table IV.2 that when the hydrogenation of (164) was carried out under epimerizing conditions (in the presence of acid), one of the products (of shortest g.l.c. retention time) was formed in only very small

amounts. Under neutral conditions, more substantial quantities of this compound were formed, but after treatment of the product mixture with acid, the proportion of this isomer was found to have decreased markedly, while the proportion of the decalone (162) increased by an approximately corresponding amount.* The proportion of the third component (of longest g.l.c. retention time) remained approximately unchanged* by the acid catalyzed equilibration. From this behaviour it was deduced that the ketone of shortest g.l.c. retention time was the *trans,cis*-decalone (168), and the ketone of longest g.l.c. retention time was the *cis,cis*-decalone (158). This latter assignment was subsequently confirmed by comparison with an authentic sample of the decalone (158) prepared by a different route (Chapter IV.D).

From the above experiments, it is clear that hydrogenation of the $\Delta^{9,10}$-1-octalone (164) occurs preferentially at the same face of the molecule as bears the *t*-butyl group. Although some of the desired *cis*-fused decalone (158) was formed, the low proportion of this compound in the product mixture and the considerable difficulty involved in separating it by preparative g.l.c. precluded hydrogenation of (164) as a viable method for the synthesis of (158).**

Hutchins and co-workers have found that the reduction of *p*-toluenesulphonylhydrazones of α,β-unsaturated ketones with sodium cyanoborohydride gives alkenes in which the double bond has migrated to the 1,2-position[302,303] (e.g. Scheme IV.6).

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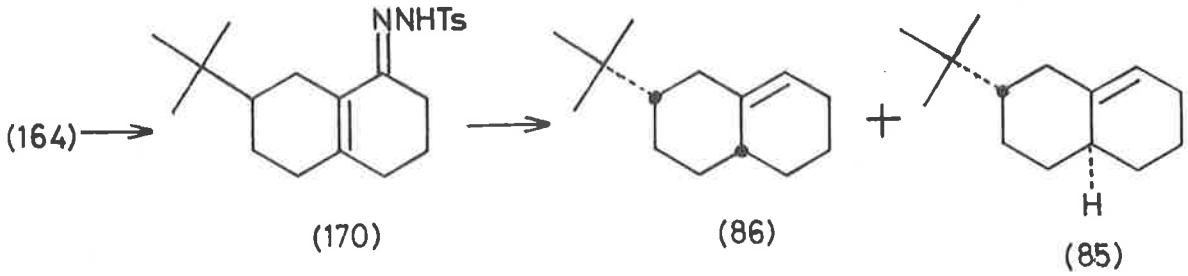
* Within experimental error.

** Some attempts were made to prepare the ethylene acetal and the dienol acetate of (164) as possible intermediates for conversion to (158), but these efforts were unfruitful and will not be discussed.



Scheme IV.6

It was not expected that reduction with sodium cyanoborohydride of the tosylhydrazone (170) of the enone (164) would give exclusively, or even predominantly, the *cis*-octalin (86), as the initial addition of hydride ion at the β-position of the α,β-unsaturated tosylhydrazone (170) should be subject to the same stereochemical factors which governed the direction of hydrogenation of the parent enone (164). Indeed, a mixture of the *cis*- and *trans*-octalins, (86) and (85) respectively, in the ratio 1:3, as well as a third unidentified compound (*c.* 17%) was obtained. Although the two octalins (85) and (86) could not be separated, the g.l.c. properties of the remaining *cis*-octalin (86) were now established. A completely unambiguous synthesis of (86) which allowed its isolation and characterization was nevertheless still deemed desirable.

Part D - The synthesis of

cis-2-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (86).

In contrast to the non-selective hydrogenation of the $\Delta^{9,10}$-1-octalone (164) described earlier (Chapter IV.C), $\Delta^{1,9}$-octalin systems generally undergo hydrogenation with high stereospecificity to give *cis*-fused decalins.[267,280,304,305] In particular, House has reported that hydrogenation of the $\Delta^{1,9}$-2-octalone (138) gives predominantly (*c.* 93%) the *cis,cis*-decalone (171).[267] With the vital stereochemistry already established, it seemed that conversion of (171) to the *cis*-octalin (86) would be relatively straightforward. The successful synthesis of the *cis*-octalin (86) *via* the *cis,cis*-decalone (171) is outlined in Scheme IV.7.

A mixture of the conjugated and unconjugated enones (138) and (139) was prepared as described earlier[267] (Chapter IV.A). House and co-workers obtained the pure enone (138) by recrystallization from hexane at -40° and hydrogenated it over a palladium catalyst in the presence of acid.[267] Under the acidic conditions of the hydrogenation, however, it might be expected that an equilibrium would be rapidly established between (138) and (139), but that the conjugated tri-substituted double bond of (138) would be hydrogenated more rapidly than the unconjugated tetrasubstituted double bond of (139).* Indeed, when a sample of the pure enone (138) was briefly treated with acid the equilibrium mixture (85:15) of (138) and (139) was obtained, and furthermore when the mixture was hydrogenated in the presence of acid, the *cis,cis*-decalone (171) was obtained in a high state of purity (95-100% before distillation). The effort and material loss associated

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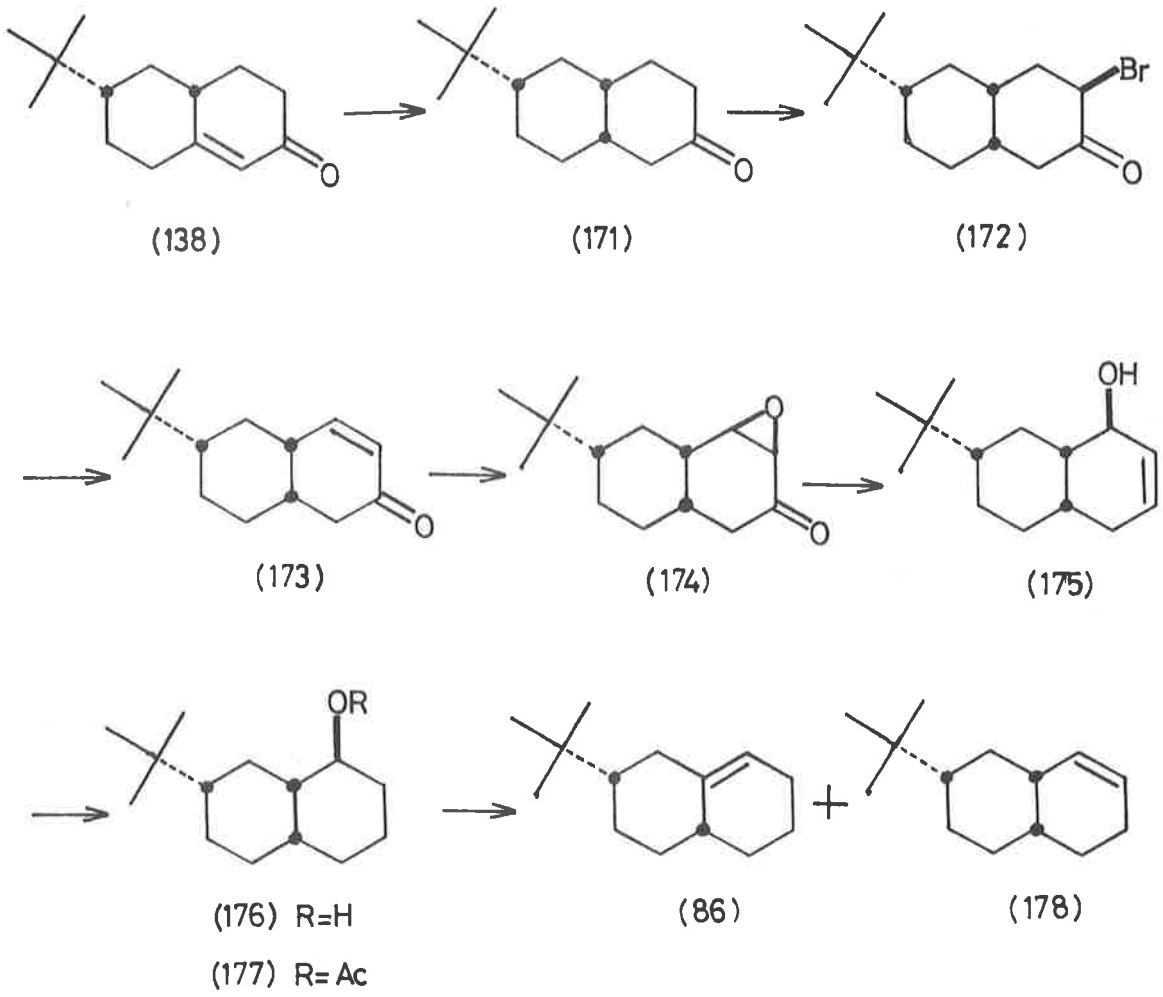
* For an example of the selective hydrogenation of a conjugated trisubstituted enone in the presence of an unconjugated tetrasubstituted double bond, see ref. 306.

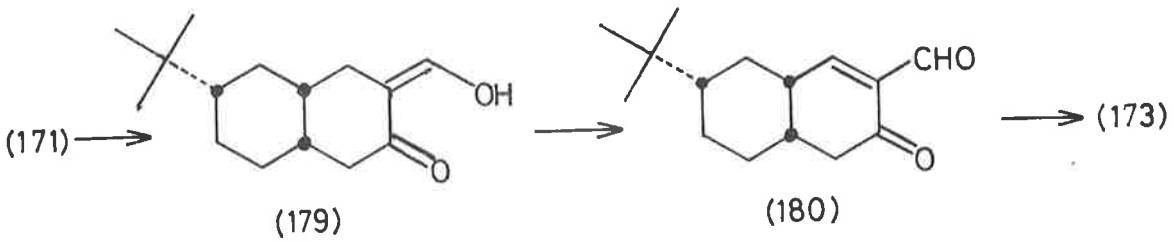
with obtaining the pure enone (138) for this purpose are therefore not necessary.



Scheme IV.7

The original route conceived for conversion of the decalone (171) into the octalone (173) is depicted in Scheme IV.8. Reaction of the decalone (171) with ethyl formate and sodium hydride gave the hydroxymethylene ketone (179), from which the unsaturated keto aldehyde (180) was obtained by dehydrogenation with 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ).[307,308] The n.m.r. spectrum of the latter compound showed an olefinic proton resonance at δ7.61 (1H, doublet, J = 6 Hz) confirming that formylation had occurred, as anticipated, at the more sterically accessible position[217,308,309] (i.e. C_3) of the decalone

(171). Decarbonylation of the keto aldehyde (180) with tris-(triphenylphosphine)rhodium chloride,[307,308,310] however, did not proceed satisfactorily. Only a low yield (*c.* 40%) of volatile material was obtained, and this was shown to be a mixture of the desired octalone (173) (*c.* 60%) and an unidentified compound (*c.* 40%). No attempt was made to separate these two compounds. The inefficiency of this process, combined with the extremely high cost of the rhodium complex rendered this sequence economically unfeasible. The possibility of converting (171) to (173) by a classical bromination-dehydrobromination sequence, i.e., *via* the bromoketone (172) (Scheme IV.7), was therefore examined.



Scheme IV.8

It is well known that the position of bromination of 3-ketosteroids with electrophilic brominating agents is controlled by the preferred direction of enolization of the ketone, which is in turn dependent on the stereochemistry of the A/B ring junction.[266c,291] Thus, *trans*-A/B fused systems give 2-bromoketones and *cis*-A/B fused systems give 4-bromoketones (fig. IV.6). The 2-decalone (171) can be regarded as an analogue of a *cis*-A/B 3-ketosteroid and might therefore be expected to react analogously to form the 1-bromo-2-decalone (181). Under strongly acidic conditions, however, initially formed bromoketones have been known to equilibrate to a thermodynamically more stable product by a process of reversal and rebromination.[266c,311-314]

From an examination of models, it was apparent that the bromine atom of (181) is in a more crowded steric environment than that of (172), and therefore it seemed likely that bromination of (171) under equilibrating conditions would result in the predominant formation of the more stable bromoketone (172).

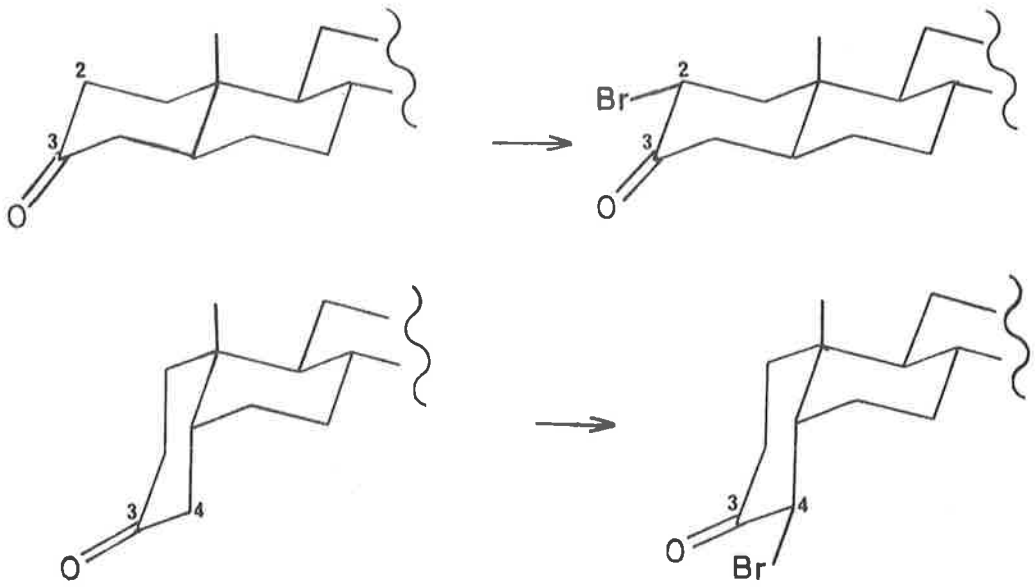


fig. IV.6

When the decalone (171) was allowed to react with bromine in acetic acid containing hydrobromic acid for 24 hr, a crystalline product with a broad melting range was obtained. The n.m.r. spectrum showed a doublet of doublets, the X part of an ABX type spectrum, at δ4.64. The fact that this proton is coupled to two vicinal protons proves that the major product has the bromine atom at C_3. Furthermore, the separation between the two outer lines of this multiplet ($J_{AX} + J_{BX}$ = 19 Hz), which indicates that this proton has an axial orientation,[232d] and the carbonyl stretching absorption at 1720 cm^{-1} (compared with 1705 cm^{-1} for the parent ketone (171)) in the infrared spectrum, which shows that the bromine occupies an equatorial position,[315] both confirm that the 3-bromo-2-decalone (172) has the indicated stereo-

chemistry.

Since the reaction of bromine with ketones under these conditions is subject to thermodynamic control, and because the relative ground state free energies of the various possible products do not appear to be very much higher than that of the most stable product (172), it was considered likely that significant quantities of the 1-bromo-2-decalone (181), as well as dibrominated and unbrominated (171) ketones might be present in the equilibrium mixture.[309,316] The presence of polybrominated ketone(s) was inferred from elemental analysis, which consistently revealed a high bromine content. Neither repeated recrystallization nor chromatography were effective in separating this material from the monobrominated ketone (172).

Dehydrobromination of the bromoketone mixture with calcium carbonate and refluxing N,N-dimethylacetamide[312,317,318] afforded a mixture of the $\Delta^{3,4}$-2-octalone (173) and the $\Delta^{1,9}$-2-octalone (138) in a *c.* 4:1 ratio. A small amount of the decalone (171) (*c.*5%) was detected by g.l.c. analysis, confirming that this compound had indeed been present in the bromination product. The question of whether the appearance of the $\Delta^{1,9}$-2-octalone (138) was due to dehydrobromination of the 1-bromodecalone (181), present as a contaminant of the 3-bromodecalone (172), or whether it arose by elimination from the 3-bromodecalone (172) *via* its enol form[319,320] (172e) (fig. IV.7) was resolved by carrying out the dehydrobromination using a variation[322] of the Mattox-Kendall reaction.[321] Treatment of the bromoketone with semicarbazide hydrochloride in boiling acetic acid, followed by cleavage of the resulting dehydrobrominated semicarbazone with 50% aqueous sulphuric acid in dioxan[322] gave a mixture of the octalones (138) and (173) in the same 1:4 ratio as before. Since there can be no ambiguity about the direction of elimination in this case, the presence of the 1-bromo-

2-decalone (181) as a contaminant of the 3-bromo-2-decalone (172) can be considered as confirmed.

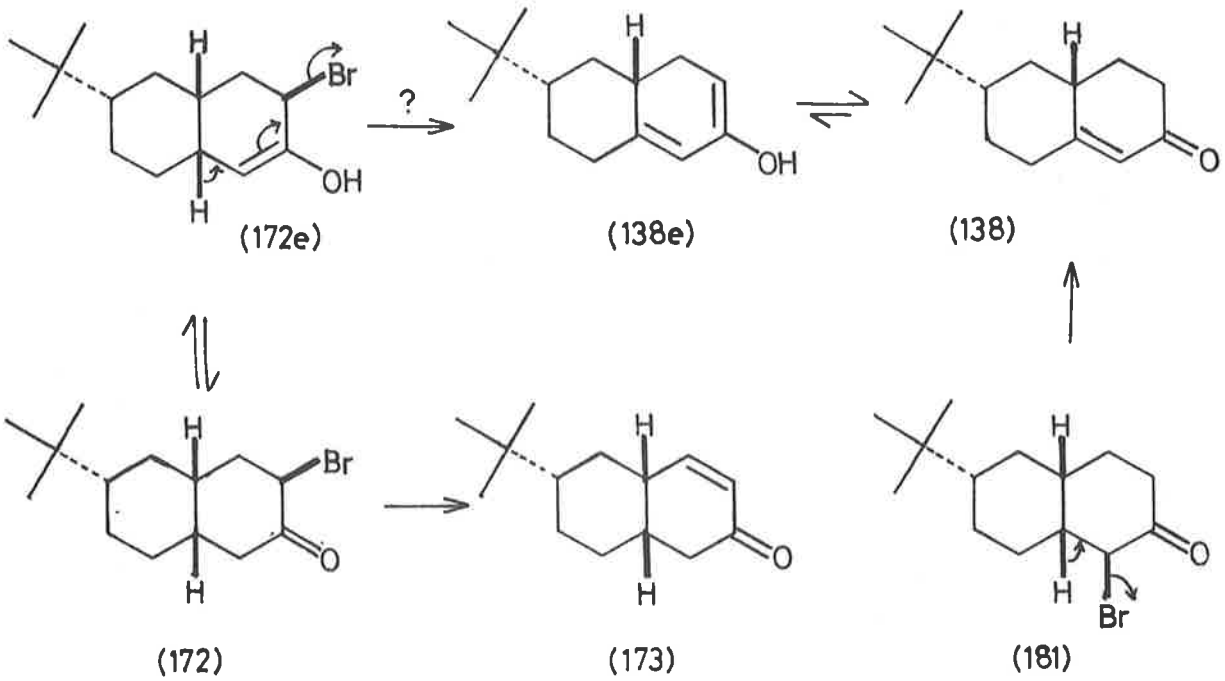


fig. IV.7

Whereas the complete separation of the two bromoketones (172) and (181) appeared to be very difficult, if indeed at all possible, and the separation of the two octalones (138) and (173) by column chromatography was relatively easy, it was deemed more convenient to carry out the dehydrobromination on the mixture of bromoketones and to separate the mixture of products. Although the very poor yield of $\Delta^{3,4}$-2-octalone (173) (*c.* 10% from (171)) obtained by this method was disappointing, this route was nevertheless superior to the previous method (Scheme IV.8) in terms of both economy and applicability to large scale work.*

When the enone (173) was treated with an excess of alkaline hydrogen peroxide in methanol at room temperature,[266d] the epoxy

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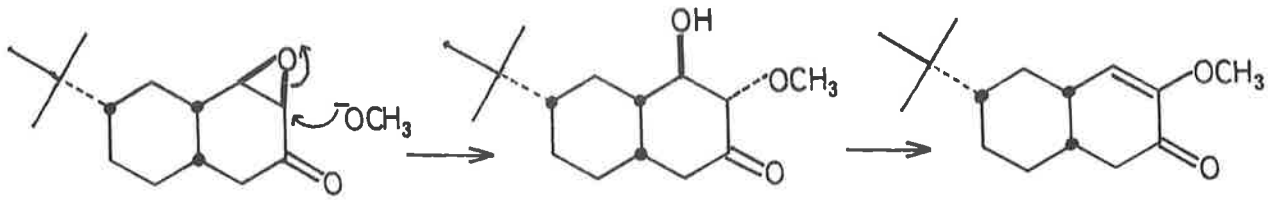
* A new and apparently superior general route to $\Delta^{3,4}$-2-octalones of this type has recently been published.[323]

ketone (174) was obtained in only low yield (*c.* 10-30%) together with a crystalline by-product possessing acidic properties, which suggested that further oxidation of the epoxy ketone was occurring under these conditions. In an attempt to overcome this problem, the epoxidation was performed at low temperature (0-5°) using only a slight excess of hydrogen peroxide. These measures only marginally improved the yield of epoxy ketone (174), however, and a new by-product whose spectral properties (n.m.r. resonances at δ5.74 (doublet, J = 5 Hz, 1H) and δ3.53 (singlet, 3H), and strong infrared absorptions at 1695 and 1625 cm^{-1}) were consistent with the structure (182), could be isolated from the reaction by chromatography.



(174) (182)

fig. IV.8

The formation of the 3-methoxyenone (182) can be rationalized in outline by the series of reactions shown in fig. IV.8. The conversion of α,β-epoxy ketones to α-heteroalkyl enones by reaction with protic nucleophilic solvents in the presence of base is a well-established reaction.[324-327] However, the conditions required for such transformations are generally much harsher than those required for the formation of the respective α,β-epoxy ketones, and as a consequence, the epoxidation of enones is generally not complicated by side reactions of the above type. The occurrence of such a reaction in the present case was most puzzling, but its method of prevention was obvious. When the epoxidation of the enone (173) with alkaline hydrogen peroxide

was carried out in a non-nucleophilic solvent system, a 4:1 mixture of dioxan and dimethoxyethane,* the epoxy ketone (174) was obtained exclusively and in excellent yield.

Reaction of the epoxy ketone (174) with hydrazine in the presence of a trace of acetic acid[329,330] gave the allylic alcohol (175). Hydrogenation of (175) over a rhodium-alumina catalyst gave a mixture of three decalols (86%, 9%, and 5% by g.l.c. analysis), which, on oxidation with Jones' reagent,[331] gave a mixture containing only the two decalones (171) (14%) and (158) (86%). These observations are readily explained by a rearrangement of the allylic alcohol (175) to the mixture of epimeric alcohols (183) on the catalyst surface, followed by hydrogenation to the saturated alcohols (184), which on oxidation gives a single ketone (171) (fig. IV.9). A similar rearrangement had been reported[332] as being caused by traces of acid on the catalyst surface, and could be suppressed by the addition of alkali-metal salts to the reaction mixture. In the present example however, it was found necessary to stir the catalyst with a methanolic solution of sodium hydroxide before adding the unsaturated alcohol (175) and commencing the hydrogenation. When this precaution was observed, hydrogenation of (175) gave the decalol (176) in a pure state, and oxidation of (176) gave the 1-decalone (158) uncontaminated by any of its isomer (171).

The axial orientation of the hydroxyl group in (176) was confirmed by the half-height width ($W_{\frac{1}{2}}$) of 8 Hz of the C_1 proton

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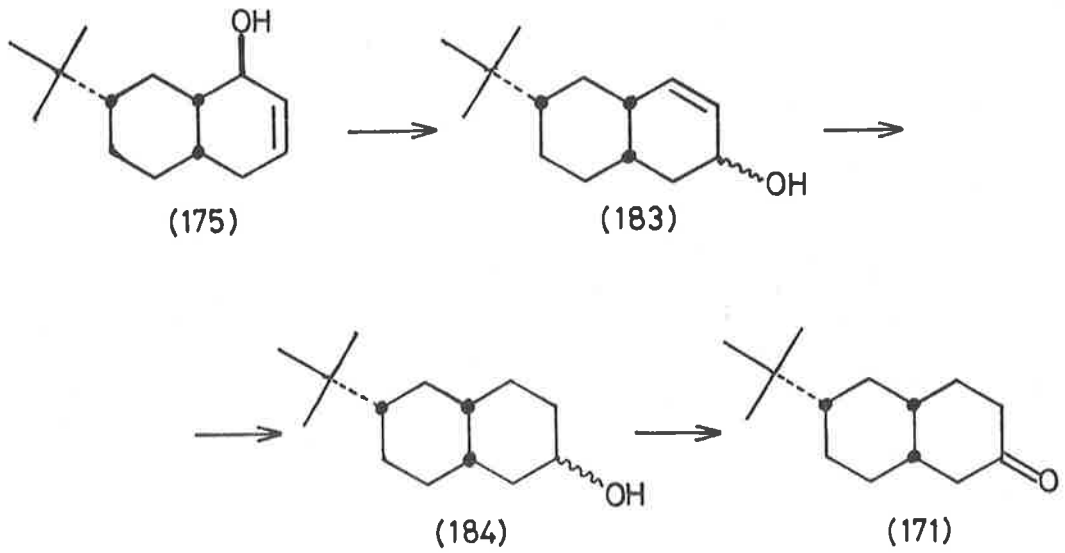
* Precedent exists for the use of dioxan as a solvent for epoxidations with alkaline hydrogen peroxide.[328] In the present case, the addition of dimethoxyethane was necessary to prevent the reaction mixture from solidifying, since the required reaction temperature (0-5°) was below the freezing point of dioxan (11°).



(175) (183) (184) (171)

fig. IV.9

resonance in the n.m.r. spectrum of (176), since a $W_{\frac{1}{2}}$ value of less than 12 Hz is characteristic of an equatorial proton.[232e] Since the reaction of α,β-epoxy ketones with hydrazine is known to proceed with retention of configuration,[318,333, 334] the stereochemistries of the allylic alcohol (175) and of the epoxy ketone (174) are confirmed as being as shown. Attack of peroxide ion on the less hindered convex face of the octalone (173) would be expected to give the epoxy ketone with the designated stereochemistry (174), but this could not be confirmed directly from the observed n.m.r. spectral properties of (174).

The fortuitous generation of a *cis*-relationship between the oxygen substituent at C_1 and the angular hydrogen at C_9 of the above-mentioned derivatives was used to prepare the *cis*-octalin (86) by a *cis*-elimination process. Pyrolysis of the acetate (177), prepared by treatment of (176) with acetic anhydride and pyridine, gave a mixture of the two octalins (86) and (178) in a 36:64 ratio. The two octalins were partially separated by chromatography on a column of silica gel

impregnated with silver nitrate, and the octalin (86) was obtained in a homogeneous state after further purification by preparative g.l.c.* The n.m.r. spectral properties of the octalins (86) (δ5.33, 1H) and (178) (δ5.58, 2H) enabled them to be readily distinguished.

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* It is interesting to note that the *t*-butyl substituted ring of the *cis*-octalin (86) is constrained to adopt a boat or twist-boat conformation in order for the *t*-butyl group to remain in an equatorial position (c.f. discussions on the conformations of the *cis*-cation (74) in Chapter II). While it might be expected that the increased strain which would result from the enforced boat/twist-boat conformation should have some effect on the chemical reactivity and stability of (86), it was, nevertheless, found to be relatively stable under the conditions of acetolysis of the unsaturated nosylates (78) and (79) (Chapter II).

CHAPTER V.

EXPERIMENTAL

GENERAL:

Infrared spectra were determined as liquid films, unless stated otherwise, with a Unicam SP200 or a Jasco IRA-1 grating infrared spectrophotometer, using the 1603 cm^{-1} band of polystyrene as a reference. The characteristics of the infrared bands are expressed in the text as follows: s, strong; m, medium; w, weak; sh, shoulder; b, broad.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian T60 spectrometer operating at 60 MHz, using tetramethylsilane as an internal reference. All spectra were determined in carbon tetrachloride unless stated otherwise.

Mass spectra were recorded with a Hitachi Perkin-Elmer RMU-6D double focusing mass spectrometer operating at 60 eV. Spectral data are quoted as major fragments with relative abundances in parentheses.

Melting points were measured using a Kofler hot-stage melting point apparatus and are uncorrected.

Microanalyses were performed by the Australian microanalytical service, Melbourne.

Gas-liquid chromatographic (g.l.c.) analyses were carried out using a Perkin-Elmer 881 gas chromatograph fitted with a Perkin-Elmer 194B printing integrator. Preparative g.l.c. was carried out with an Aerograph A-700 or A-705 instrument. All instruments were equipped with flame ionization detectors and nitrogen was used as the carrier gas. The following columns were used:

A. 1.5% NPGS and 1.5% XE-60 on Varaport 30 (100/120), 3.0 m x 3.0 mm.

B. 5% Carbowax 20M on Gaschrom P (80/100) which had been treated with cold 10% aqueous sodium hydroxide for 10 min,

washed thoroughly with distilled water, and dried at 130° for 15 hr, 3.0 m x 2.0 mm.

C. 5% Apiezon M on Varaport 30 (100/120), 3.6 m x 2.0 mm.

D. 5% FFAP on Varaport 30 (100/120), 3.6 m x 2.0 mm.

E. 10% Carbowax 20M on Chromosorb W (80/100), treated as for column B, 3.6 m x 2.0 mm.

F. 5% XE-60 on Aeropak 30 (100/120), 6.0 m x 3.0 mm.

G. 5% Ucon on Varaport 30 (100/120), 3.6, x 2.0 mm.

H. 0.75% FFAP on Chromosorb W (80/100), 6.0 m x 3.0 mm.

I. 20% BDS on Gaschrom P (60/80), 1.5 m x 9.0 mm.

J. 15% FFAP on Chromosorb A (40/60), base washed (as for column B) to pH 8, 2.4 m x 6.3 mm.

K. 25% FFAP on Chromosorb A (40/60), treated as for column J, 5.0 m x 7.0 mm.

L. 30% FFAP on Chromosorb A (40/60), 3.0 m x 9.0 mm.

M. OV-101, capillary, 100 m x 0.254 mm.

N. Apiezon L, capillary, 100 m x 0.508 mm.

Columns B-E, G,J, and K were constructed of pyrex glass, A,F,H,M, and N of stainless steel, and I and L of aluminium. The carrier gas (nitrogen) flow rate was 30 ml/min for the analytical columns A-H, *c.* 100 ml/min for the preparative columns I-L, and *c.* 1 ml/min for the capillary columns M and N.

Column chromatography was carried out on Spence neutral alumina, unless specifically stated otherwise, and using dry redistilled solvents. Silica impregnated with silver nitrate was prepared by mixing a solution of silver nitrate (100 g) in acetonitrile (200 ml), which had been diluted with ethanol (200 ml) with sorbsil (300 g), and then removing the solvent from the resulting slurry under reduced pressure with constant agitation. The resulting silver nitrate

impregnated silica was further dried under reduced pressure (0.1 torr), then activated at 110° for 24 hr before use.

All organic extracts were dried over anhydrous magnesium sulphate, unless stated otherwise. Redistilled solvents were used for all extractions.

In this text, light petroleum refers to the fraction of b.p. 55-65°.

The commonly used anhydrous solvents were purified as follows. Ether was dried over calcium chloride granules for 48 hr, distilled from phosphorus pentoxide, and stored over sodium wire. Benzene was dried by refluxing over a water separator until no more water was collected, then distilled and stored over sodium wire. Light petroleum and hexane of sufficient dryness were obtained by distillation. Pyridine was heated under reflux over potassium hydroxide pellets for 24 hr, then distilled from fresh potassium hydroxide and stored over 4 Å molecular sieves. Reagent grade tetrahydrofuran was distilled from lithium aluminium hydride immediately before use. Chloroform and methylene chloride were distilled from phosphorus pentoxide. Acetic anhydride was distilled from calcium carbide. Liquid ammonia was distilled from sodium, at room temperature, directly into the reaction vessel immediately before use. Dioxan was purified and dried as described by Hess and Frahm[374,382c] and stored over sodium wire.

Work described in Chapter II.

Kinetic Studies.

Acetic acid: A.R. grade acetic acid was heated under reflux in the presence of potassium permanganate. The acid was distilled and the fraction of b.p. 117-118°, to which acetic anhydride (*c.* 2% by volume) was added, was heated under reflux for 24 hr, and then redistilled through a 50 cm Fenske column equipped with a Human head. The fraction b.p. 117.5-118° was collected and stored, after the addition of *c.* 1% by volume of acetic anhydride, under a nitrogen atmosphere.

Acetic anhydride: A.R. grade acetic anhydride was heated under reflux over calcium carbide for 5 days, then distilled through a 20 cm column packed with glass helices. The fraction b.p. 139-140° was collected and stored under nitrogen.

Anhydrous sodium acetate: A.R. grade anhydrous sodium acetate was heated at 125°/1.0 torr for 24 hr.

Sodium acetate-acetic acid: For rate measurements, a solution of sodium acetate (*c.* 0.02 M) was prepared by dissolving anhydrous sodium acetate in anhydrous acetic acid containing *c.* 1% acetic anhydride by volume. The solution was standardized against perchloric acid using bromophenol blue (saturated solution in acetic acid, 5 drops) as the indicator.

Standard perchloric acid: A solution of perchloric acid (*c.* 0.01 M) in acetic acid (containing *c.* 1% acetic anhydride by volume) was prepared according to the procedure of Moriarty and D'Silva.[339] The perchloric acid solution was standardized against a freshly-prepared solution of potassium hydrogen phthalate (A.R.) in acetic acid using bromophenol blue as indicator.

Kinetic determinations: The acetolyses of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl nosylate (78) and 3-*t*-butyl-4-cyclohexylbut-1-yl nosylate (97) were carried out using the ampoule technique and the rates were measured titrimetrically.[339]

In a typical run, an accurately weighed sample of the nosylate (*c.* 198 mg, to give a *c.* 0.01M solution) was dissolved in the standard sodium acetate-acetic acid solution (50 ml). The solution was transferred to a burette and aliquots (*c.* 5.5 ml) were sealed under a nitrogen atmosphere in nine pyrex glass ampoules. The ampoules were immersed simultaneously in a constant temperature bath (± 0.05°) and allowed to attain thermal equilibrium (10-15 min). At the end of this time, the first ampoule was removed from the bath and placed in a dry-ice/acetone bath to quench the reaction. The time of removal of this ampoule was taken as "zero" time. The ampoule was brought to room temperature and opened; an aliquot (*c.* 5.0 ml, withdrawn with a consant volume pipette whose exact capacity had been previously determined) of the solution was titrated against the standard perchloric acid solution (see above) using bromophenol blue as indicator. The remaining ampoules were removed after the appropriate intervals of time and treated in a similar manner. The first order rate constants were determined graphically by measuring the slope of plots of $\log[(V_t-V_\infty)/V_o-V_\infty)]$ against time, where V_t is the value of the titre at time t, V_∞ is the value of the "infinity" titre (i.e. at *c.*10 half-lives), and V_o is the value of the titre at "zero" time. First-order plots (i.e. straight lines) were obtained for 80-90% reaction (*c.* 3 half-lives). The experimental values (of k) deviated from the mean by less than 0.8%, and the "infinity" titres were reproducible to within 2% of the theoretical value.

The acetolysis of 3-*t*-butyl-4-(cyclohex-1-enyl)but-1-yl nosylate (79) was followed spectrophotometrically[340] by monitoring the decrease in ultaviolet absorption of a cyclohexane solution of the nosylate (λ_{max} = 250 nm).[137]

In a typical run, a sample of the nosylate (2-3 mg) was dissolved as rapidly as possible in the standard sodium acetate-acetic acid solution (50 ml), which had been pre-equilibrated at the desired temperature. The solution, in a stoppered flask, was immersed in a constant temperature bath (± 0.01°) and allowed to attain thermal equilibrium (4-5 min). At the end of this time, an aliquot (*c.* 5.0 ml) of the solution was withdrawn (using a constant volume pipette) and drained as rapidly as possible into a 25 ml separating funnel* containing distilled water (10 ml, constant volume pipette) and spectroscopic grade cyclohexane (5 ml, constant volume pipette). The time of quenching of this aliquot was taken as "zero" time. The separating funnel was shaken vigorously for 1 min, then allowed to stand for 2 min. The aqueous layer was removed and a portion of the cyclohexane layer was transferred to a teflon-stoppered, 1-cm quartz U.V. cell. The absorbance of the solution was measured at 250 nm against pure cyclohexane using a Gilford model 2000 multiple sample absorbance recorder with a Beckmann DU monochromator. Further aliquots were removed at appropriate intervals and treated as far as possible in exactly the same manner. The first order rate constants were determined graphically by measuring the slope of plots of $\log[(A_t-A_\infty)/(A_0-A_\infty)]$

---

* For the first sample of each kinetic run, the separating funnel was pre-wetted with a mixture of cyclohexane (5 ml), distilled water (10 ml), and acetic acid (5 ml), then rinsed with cyclohexane. For succeeding samples, the separating funnel was merely rinsed with cyclohexane.

against time, where A_t is the absorbance at time t, A_∞ is the value of the absorbance at "infinite" time (i.e. after 10 half-lives), and A_o is the absorbance at "zero" time. Good first-order plots (i.e. straight lines) were obtained over the entire extent of reaction which was examined (up to 93% reaction, or 4 half-lives). The experimental values (of k) deviated from the mean by less than 3%, and the "infinity" absorbances deviated from the mean by less than 2.5%.

In the first instance, the activation parameters $\Delta H^{\neq}$ and $\Delta S^{\neq}$ were calculated from the Arrhenius equation:

$$k = (KT/h) \exp(-\Delta H^{\neq}/RT) \exp(\Delta S^{\neq}/R)$$

where k is the first-order rate constant at the temperature T, K is the Boltzmann constant, h is Planck's constant, and R is the gas constant. Values of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ and their standard deviations, as well as extrapolated values of rate constants, listed in Table IV.1, were determined on a CDC 6400 computer by use of QCPE Program No. 79.

Product Studies:

An accurately weighed sample of the nosylate (*c.* 40 mg, to give a *c.*0.02M solution was dissolved in 5 ml of a solution of sodium acetate (*c.* 0.03M) in acetic acid containing 1% by volume of acetic anhydride. The solution was gently but thoroughly flushed with nitrogen, then sealed under a nitrogen atmosphere in an ampoule and heated at 60° for the periods shown in Table II.3. After the ampoule had been cooled in ice, the contents were quantitatively transferred, with the aid of ether, to a separating funnel containing ice-cold water (100 ml). An accurately weighed sample of the internal standard, 1,7-dimethylnaphthalene (8-10 mg) was then added to the contents of the separating funnel with the aid of more ether (total ether 100 ml).

The aqueous layer was separated and the ether extract was washed with successive ice-cold portions of water (100 ml), 5% sodium bicarbonate solution (2 x 75 ml), and water (100 ml), and dried. The solution was then carefully concentrated by distilling almost all of the ether through a column (20 cm) packed with glass helices, whilst maintaining the bath temperature at 45-50°. When the temperature at the head of the column dropped below the boiling point of ether (34.5°), the heating bath was removed and the distillation flask was cooled in ice to facilitate drainage of solvent held in the column. The final concentrate (2-3 ml) was analysed by g.l.c. as follows:

(a) Qualitative analyses: Qualitative identifications were made initially by comparing the retention times of the components with those of authentic samples, and then by the technique of peak enhancement ("spiking"). Columns N (190°) and E (180°) were used for this purpose.

(b) Quantitative analyses: In order to estimate the absolute yield of products, the responses (to the detector in the g.l.c. apparatus) of the authentic compounds (where available) with respect to the internal standard were determinated (in triplicate). Accurately weighed samples of the compound (*c.* 8 mg for olefins and 12 mg for acetates) and the internal standard (5-13 mg) were mixed and dissolved in light petroleum (*c.* 1.5 ml). The various solutions were then analysed by g.l.c., using column F (180°) for the olefins, and column E (see below) for the acetates. The peak areas were determined by integration. The response ratio $R = a_c w_s / a_s w_c$ could then be calculated, where a_c and w_c are the peak area and the weight, respectively, of the compound, and a_s and w_s are the peak area and weight, respectively, of the internal standard. Each response ratio is the average of at least

4 determinations on each of 3 mixtures of compound and internal standard. The response ratios are listed in Table V.1. Where the response ratio of a compound could not be determined directly, the average response ratio of the other compounds of its type (i.e. olefin or acetate) was assumed.

Quantitative analyses of olefinic products were carried out using column N (190^{o}). Acetate analyses were performed on column E. The acetates from the acetolysis of (79) were analysed at 150^{o}, and the acetates from the acetolysis of (78) were analyzed at 160^{o} for 20 min, followed by temperature programming up to 190^{o} at 48^{o}/min to elute the uncyclized acetate (80). The peak areas were determined by a combination of integration and triangulation (where peaks were incompletely resolved) and then the percentage yields of each of the products were determined. Each product analysis was the average of 3 g.l.c. determinations and was carried out in triplicate. 1,7-Dimethylnaphthalene proved unsatisfactory as an internal standard because it exhibited "tailing" on capillary g.l.c. columns, which were essential for successful olefin analysis. The peak area of the internal standard could therefore not be measured accurately or reproducibly, with the result that the experimentally determined olefin yields varied* over the range 85-125%. The problem of "tailing" did not arise in the acetate analyses, and consequently reproducible acetate yields (± 0.2%) were consistently obtained. The olefin yields have been normalized after allowing for the acetate yields (Table II.3).

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* For this reason, the olefin response ratios were not measured using a capillary column (see earlier). It should be noted that the determination of the relative proportions of the olefins in the product mixtures is not affected by an inability to accurately measure the internal standard peak area.

Table V.1

Response ratios and g.l.c. retention times of products of acetolysis of (78) and (79)

Product	Response Ratio[C]	Retention time (min.sec.)[D]
Olefins.		
(83)	0.87	47.35
(84)	0.98	48.11
(87)	0.95[B]	51.27
-[A]	0.95[B]	51.53
(88)	0.95[B]	52.27
(85)	0.99	52.52
(86)	0.95[B]	53.10
(82)	0.95	53.41
Acetates.		
(89)	0.63	12.40 (15.50)
(90)	0.64[B]	14.50 (19.00)
(93)	0.64	14.50 (19.00)
(91)	0.64[B]	17.50 (22.45)
(94)	0.64[B]	19.30 (24.20)
(81)	0.56	- (25.00)
(80)	0.55	24.30 (-)

A Unidentified olefin, see Chapter II.

B Assumed value, see text.

C With respect to 1,7-dimethylnaphthalene.

D Typical values whose absolute magnitudes may vary slightly. For the acetates, the first figure is the retention time found under the conditions used for the analysis of the acetates from (78), and the figures in parentheses refer to the conditions used for analysis of the acetates from (79) (see text).

Work described in Chapter III.

Part A.

4-t-Butylcyclohexanone (104):

Initially, the chromic acid oxidation method developed by Brown, Garg, and Liu (Procedure B)[278] was used to convert 4-*t*-butylcyclohexanol to 4-*t*-butylcyclohexanone (104) b.p. 113-114°/18 torr (lit.[212] 90-92°/9 torr). In later work, commercial grade (Merck) 4-*t*-butylcyclohexanone was used.

4-t-Butyl-2-hydroxymethylenecyclohexanone (105):

(i) A solution of 4-*t*-butylcyclohexanone (104) (3.08 g, 20 mmol) and dry ethyl formate[371a] (2.96 g, 40 mmol) in dry benzene (40 ml) was added under nitrogen to a stirred, ice-cooled suspension of sodium methoxide[216] (2.24 g, 40 mmol), in benzene (30 ml). The resulting mixture was stirred at room temperature for 20 hr, then poured into ice water (100 ml). The benzene layer was separated and extracted with cold 10% aqueous sodium hydroxide (3 x 50 ml). The combined alkaline extracts were washed with ether (50 ml), acidified with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ether (3 x 100 ml). The ether extracts were combined and washed with 5% aqueous sodium bicarbonate (50 ml), water (50 ml), dried, and evaporated to give an orange oil (3.13 g, 84%). Distillation afforded *4-t-butyl-2-hydroxymethylenecyclohexanone* (105) as a faintly yellow oil (1.62 g, 44%) b.p. 82°/0.7 torr which crystallized on cooling. ν_{max} (nujol) 2920s, 1640s, 1590s, 1400m, 1370s, 1180s, and 900b cm^{-1}; n.m.r.: δ14.15 (1H, broad, exchanges with D_2O, =CH-O<u>H</u>), 10.35 (1H, singlet, =C<u>H</u>-OH), 0.93 (9H, singlet, *t*-butyl), and 2.7-1.0 (complex, other H); mass spectrum: m/e 182 (32, M^+ for $C_{11}H_{18}O_2$), 125 (52), 111 (39), 98 (36), 57 (100), and 41 (43). A satisfactory analysis could not be obtained (see Discussion).

(ii) A suspension of sodium hydride (2.40 g, 0.10 mol; as 4.8 g of a 50% dispersion in mineral oil) in dry ether (100 ml) containing ethanol (0.5 ml) was cooled to 0^{o} and placed under a nitrogen atmosphere. A solution of 4-*t*-butylcyclohexanone (104) (15.4 g, 0.10 mol) and ethyl formate (14.8 g, 0.20 mol) in ether (150 ml) was then added dropwise over a period of 0.5 hr. The resulting mixture was stirred at room temperature for 6 hr and allowed to stand at room temperature for a further 11 hr, after which time ethanol (20 ml) was added and stirring was resumed for 1 hr. Water (40 ml) was added and the ensuing mixture was thoroughly mixed. The organic layer was separated and washed with water (20 ml). The aqueous layers were combined, washed with ether (20 ml), acidified with dilute hydrochloric acid and extracted with ether (2 x 60 ml). The combined ether extracts were washed with saturated brine (50 ml), dried, and evaporated to give an orange oil (15.6 g, 84%). The spectral properties of the hydroxymethylene ketone (105) obtained in this way were identical to those described above.

4-t-Butyl-2-isopropoxymethylenecyclohexanone (106):

(i) A solution of the hydroxymethyleneketone (105) (1.30 g, 7.0 mmol) and isopropyl alcohol (10 ml) in benzene (40 ml) containing *p*-toluenesulphonic acid (50 mg) was heated under reflux in an apparatus equipped with a water separator until no more water was being evolved. The resulting solution was washed with 10% sodium hydroxide saturated with sodium chloride (3 x 30 ml), then with water until the aqueous washings were neutral to litmus, dried (sodium sulphate), and evaporated to give an orange oil (1.55 g, 95%). Distillation gave *4-t-butyl-2-isopropoxymethylenecyclohexanone* (106) as a colourless oil (0.64 g, 39%) b.p. $102\text{-}104^{o}/0.6$ torr which rapidly turned yellow and crystallized. ν_{max} (nujol) : 2920s, 1665s, 1580s, 1400m, 1370m, 1220s, 1105s, and 990m cm^{-1}; n.m.r. : δ10.10 (singlet, -C<u>H</u>=O, see Discussion), 7.23 (1H,

doublet, J = 2 Hz, =C<u>H</u>-O), 4.20 (1H, heptet, J = 6 Hz, -O-C<u>H</u>$(CH_3)_2$), 1.33 (6H, doublet, J = 6 Hz, -CH($C\underline{H}_3$)$_2$), 0.93 (9H, singlet, *t*-butyl), and 2.9-1.4 (complex, other H); mass spectrum: m/e 224 (2, M^+ for $C_{14}H_{24}O_2$), 57 (100), 45 (75), 44 (48), 43 (44), and 41 (46). A satisfactory elemental analysis could not be obtained (see Discussion).

(ii) A solution of the hydroxymethylene ketone (105) (14.0 g, 75 mmol) in dry acetone (30 ml) was added portionwise to a stirred suspension of anhydrous potassium carbonate (17.0 g, 120 mmol) in dry acetone (70 ml). Isopropyl iodide was added, and the resulting mixture was stirred at room temperature under a nitrogen atmosphere for 48 hr, then heated under reflux for 44 hr. The cooled reaction mixture was filtered under reduced pressure and the residue was washed with a little ether. The filtrate was concentrated under reduced pressure, and the residue was dissolved in ether (100 ml). The ethereal solution was washed with 5% sodium hydroxide (2 x 50 ml), water (50 ml), saturated brine (50 ml), dried (potassium carbonate), and evaporated to give an orange oil (13.64 g, 81%) whose properties were identical to those of the enol ether (106) described above.

4-t-Butyl-2-n-butylthiomethylenecyclohexanone (107):

A solution of the hydroxymethyleneketone (105) (134.0 g, 0.72 mol) and *n*-butanethiol (90.0 g, 1.0 mole) in benzene (500 ml) containing *p*-toluenesulphonic acid (1.0 g) was heated under reflux in a flask fitted with a Dean-Stark water separator until the theoretical amount of water (13 ml) had been collected. The cooled solution was washed with 10% sodium hydroxide solution (2 x 100 ml), saturated brine (100 ml), dried, and evaporated to give a black oil. Distillation afforded *4-t-butyl-2-n-butylthiomethylenecyclohexanone* (107) as a yellow oil (134.5 g, 74%) b.p. 157-161°/0.5 torr, which was homogeneous

by g.l.c. analysis (A, 170°) (Found: C, 71.1; H, 10.6; S, 12.3. $C_{15}H_{26}OS$ requires C,70.8; H, 10.3; S, 12.6%). ν_{max} 2950s, 1685s, 1555s, 1470m, 1400w, 1370m, 1310s, 845s, and 820s cm^{-1}; n.m.r. : δ7.33 (1H, doublet, J = 2 Hz, =C<u>H</u>-S), 2.85 (2H, triplet, J = 7Hz, -SC<u>H</u>$_2$-), 0.96 (9H, singlet, *t*-butyl), and 2.9-1.2 (complex, other H); mass spectrum: m/e 254 (16, $M^{+\cdot}$ for $C_{15}H_{26}OS$), 198 (14), 197 (100), 57 (26), 55 (11), and 41 (18).

5-t-Butylcyclohex-1-enecarbaldehyde (108):

(i) A solution of the isopropoxymethylene ketone (106) (33.2 g, 0.15 mol) in dry ether (400 ml) was slowly added to a stirred suspension of lithium aluminium hydride (5.70 g, 0.15 mol) in ether (100 ml). The resulting mixture was heated under reflux for 0.5 hr, then cooled in ice. The product and excess of hydride were decomposed in the usual way* and the inorganic salts were removed by filtration. The filtrate was washed with cold 10% aqueous sulphuric acid (250 ml), 5% sodium bicarbonate solution (200 ml), water (150 ml), dried, evaporated, and distilled to give a colourless oil (19.8 g, 79%) b.p. 80-82°/1.2 torr. Analysis by g.l.c. (B, 140°) revealed the presence of 6 compounds. A pure sample of *5-t-butylcyclohex-1-enecarbaldehyde* (108), the major component (*c.* 67%) of this mixture, was obtained by preparative g.l.c. (I, 150°) (Found: C, 79.2; H, 11.3. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%). ν_{max} (nujol) 2920s, 2690w, 1685s, 1640m, 1400w, 1370m, 1180m, and 1155m cm^{-1}; n.m.r. : δ9.43 (1H, singlet, -C<u>H</u>O), 6.72 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, C=C<u>H</u>-), 0.92 (9H, singlet, *t*-butyl), and 2.8-1.0 (complex, other H); mass spectrum: m/e 166 (19, $M^{+\cdot}$ for $C_{11}H_{18}O$), 110 (68), 95 (22), 81 (30), 57 (100), and 41 (37).

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* This refers to a standard procedure[372] which was adopted for all reductions involving lithium aluminium hydride. For every x g of lithium aluminium hydride used, the reaction mixture was treated with the sequential dropwise addition of water (x ml), 15% sodium hydroxide solution (x ml), and more water (3x ml).

(ii) A solution of the *n*-butylthiomethylene ketone (107) (133 g, 0.52mol) in ethanol (500 ml) was added slowly to an ice-cooled stirred suspension of sodium borohydride (30.4 g, 0.80 mol) in ethanol (500 ml). After complete addition, the reaction mixture was stirred at 0^{o} for 2 hr then at room temperature for 3 hr. The ethanol was removed by evaporation at reduced pressure, and the residue was diluted with water (500 ml) and extracted with ether (2 x 250 ml). The combined ether extracts were washed with water (2 x 250 ml), saturated brine (250 ml) and evaporated. The oily residue was dissolved in 95% aqueous ethanol (500 ml) and the solution was added to a suspension of cadmium carbonate (89.7 g, 0.52 mol) and mercuric chloride (141.3 g, 0.52 mol) in 95% aqueous ethanol (1000 ml) containing water (150 ml). After the resulting mixture had been stirred and heated under reflux for 0.5 hr, it was cooled and filtered under reduced pressure. The residue was washed with a little ether and the washings were combined with the filtrate and evaporated. The residue from evaporation was diluted with water and benzene (250 ml each) and filtered again. The aqueous layer was separated and extracted with benzene, and the combined organic layers were washed with water (200 ml), saturated brine (100 ml), dried, and evaporated to yield a red oil. Distillation gave the aldehyde (108) (66.2 g, 76%) b.p. $68\text{-}70^{o}/0.6$ torr as a colourless oil which crystallized on standing. G.l.c. analysis (B, 140^{o}) revealed the presence of less than 1% of impurities. The spectral properties of the aldehyde obtained by this method were identical to those described above.

5-t-Butylcyclohex-1-enylmethanol (109):

A solution of the aldehyde (108) (66.3 g, 0.40 mol) in ethanol (400 ml) was added slowly to an ice-cooled stirred suspension of sodium borohydride (30.4 g, 0.80 mol) in ethanol (500 ml). After

the addition had been completed, the mixture was stirred at ice temperature for 2 hr, then at room temperature for 3 hr. The solvent was removed *in vacuo* and the residue was treated with water (500 ml) and extracted with ether (2 x 250 ml). The combined ether extracts were washed with water (2 x 250 ml), saturated brine (150 ml), dried, and evaporated. Distillation yielded *5-t-butylcyclohex-1-enylmethanol* (109) as a colourless oil (55.1 g, 82%) b.p. 93-95°/1.3 torr which was homogeneous by g.l.c. analysis (B, 140°; H, 120°) (Found: C, 78.3; H, 11.8. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%). ν_{max} 3340 bs, 2950 s, 1670w, 1400m, 1370s, and 1020s cm^{-1}; n.m.r. : δ5.63 (H, broad, $w_{\frac{1}{2}}$ = 10 Hz, =C<u>H</u>-), 3.87 (2H, broad singlet, C<u>H</u>$_2$-OH), 3.30 (1H, broad, exchanges with D_2O, -O<u>H</u>), 0.90 (9H, singlet, *t*-butyl), and 2.3-1.0 (complex, other H); mass spectrum: m/e 168 (9, M^+ for $C_{11}H_{20}O$), 79 (35), 57 (100), 44 (42), 41 (36), and 28 (94).

1-Bromomethyl-5-t-butylcyclohexene (110):

A stirred solution of the allylic alcohol (109) (33.6 g, 0.20 mol) in dry benzene (400 ml) containing pyridine (6.72 ml)* was cooled in an ice-bath and treated with the dropwise addition of a solution of phosphorus tribromide (27.1 g, 0.10 mol) in dry benzene (100 ml). After the addition had been completed, the resulting mixture was stirred for 1 hr at ice temperature, then filtered. The filtrate was washed with water (200 ml), 5% sodium bicarbonate solution (200 ml), water (200 ml), saturated brine (200 ml), dried and evaporated to give a yellow oil (42.3 g, 93%). Distillation afforded the mixture of isomeric bromides (110) and (111) (see Discussion) as a colourless oil (35.6 g, 83%) b.p. 75-77°/0.2 torr (Found: C, 57.3; H, 8.2; Br, 34.4 $C_{11}H_{19}Br$ requires C, 57.2; H, 8.3; Br, 34.6%). A pure sample of *1-bromomethyl-5-t-butylcyclohexene* (110) for spectro-

* The amount of pyridine used in this reaction was found to be crucial. An excess was found to cause side reactions, leading to a complex product mixture.

scopic characterization was obtained in the following manner. A portion of the bromide mixture was distilled through a short fractionating column and the distillate was collected as two approximately equal portions of b.p. 64-66°/0.1 torr and 66-67°/0.1 torr. The second fraction was redistilled and the final few drops of distillate were collected separately and shown by n.m.r. to be the pure bromide (110). ν_{max}, 3010 wsh, 2940s, 1660w, 1400w, 1370s, and 1205s cm^{-1}; n.m.r. : δ5.82 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, =C<u>H</u>-), 3.85 (2H, singlet, -C<u>H</u>$_2$Br), 0.90 (9H, singlet, *t*-butyl), and 2.4-0.8 (complex, other H); mass spectrum: m/e 232 (5, $M^{\cdot+}$ for $C_{11}H_{19}Br^{81}$), 230 (5, $M^{\cdot+}$ for $C_{11}H_{19}Br^{79}$), 151 (20), 95 (100), 57 (91), and 41 (27).

5-t-Butyl-1-(1-but-3-enyl)cyclohexene (112):

A solution of allylmagnesium bromide in ether (100 ml) was prepared from freshly-distilled allyl bromide (36.3 g, 0.30 mol) and magnesium turnings (7.29 g, 0.30 g.atom). Unchanged magnesium was removed by filtration through a plug of dry glass wool, and to the resulting clear Grignard reagent solution was added, with stirring, a solution of the allylic bromides (110) and (111) (34.6 g, 0.15 mol) in dry ether (100 ml). The resulting solution was stirred and heated under reflux under a nitrogen atmosphere for 12 hr, cooled, and treated with the dropwise addition of a mixture of water (50 ml) and acetic acid (20 ml). The aqueous layer was separated and extracted with ether (100 ml). The combined organic layers were washed with water (100 ml), 5% aqueous sodium bicarbonate (3 x 100 ml), saturated brine (100 ml), dried, and evaporated to give a yellow oil. Chromatography on a column of neutral alumina (800 g) using light petroleum as eluent gave *5-t-butyl-1-(1-but-3-enyl)cyclohexene* (112) as a colourless oil (23.8 g, 83%) which was homogeneous by g.l.c. analysis (C, 170°). A small sample was distilled, b.p. 129-130°/18 torr, for microanalysis

(Found: C, 87.0; H, 12.7. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3050 wsh, 2920s, 1640m, 1400m, 1370s, and 915s cm^{-1}; n.m.r. : δ6.17-5.54 (1H, complex, -C<u>H</u>=CH_2), 5.38 (1H, broad, $w_{\frac{1}{2}}$ = 11 Hz, ring =C<u>H</u>-), 5.20-4.73 (2H, complex, =C<u>H_2</u>), 0.88 (9H, singlet, *t*-butyl), and 2.4-1.0 (complex, other H); mass spectrum: m/e 192 (1, M^+ for $C_{14}H_{24}$), 135 (31), 95 (23), 93 (20), 79 (21), 67 (23), 57 (100), and 41 (34).

4-(5-t-Butylcyclohex-1-enyl)butan-1-ol (76):

A solution of disiamylborane (88 mmol) was prepared from 2-methylbut-2-ene (12.5 g, 176 mmol), sodium borohydride (2.53 g, 67 mmol), and boron trifluoride etherate (12.53 g, 88 mmol) in dry diglyme (15 ml) according to the procedure of Brown and Zweifel.[386] This solution was added dropwise with stirring to an ice-cooled solution of the diene (112) (15.36 g, 80 mmol) in dry diglyme (15 ml) under a nitrogen atmosphere. The resulting solution was stirred for 2 hr at 0°, after which water (15 ml) was cautiously added, followed by 15% sodium hydroxide solution (40 ml) and 30% hydrogen peroxide (40 ml). The reaction mixture was stirred for 8 hr at ambient temperature, then diluted with ether (200 ml). The aqueous lower layer was separated and extracted with a further portion of ether (200 ml). The combined ether layers were washed with water (4 x 200 ml), dried, and evaporated to give a colourless oil. Fractional distillation gave unchanged starting material (2.78 g) b.p. 63-65°/0.5 torr and *4-(5-t-butylcyclohex-1-enyl)butan-1-ol* (76) as a colourless oil (8.18 g, 59% based on unrecovered starting material) b.p. 109-116°/0.5 torr. G.l.c. analysis (D, 190°) revealed the present of *c.* 5% of impurities. A homogeneous sample was prepared by preparative thin-layer chromatography (silica, developed with 50% ether-light petroleum) followed by evaporative distillation. (Found: C, 80.2; H, 12.3. $C_{14}H_{26}O$ requires

C, 79.9; H, 12.5%). ν_{max} 3450 sb, 2930s, 1670w, 1400m, 1370s, and 1065s cm^{-1}; n.m.r. : δ5.37 (1H, broad, $w_{\frac{1}{2}}$ = 10 Hz, =C<u>H</u>-), 3.53 (2H, poorly resolved triplet, J = 6Hz, -C<u>H</u>$_2$-OH), 3.00 (variable, 1H, sharp - broad singlet, -O<u>H</u>), 0.86 (9H, singlet, *t*-butyl), and 2.3-0.8 (complex, other H); mass spectrum: m/e 210 (2, M^+ for $C_{14}H_{26}O$), 153 (21), 135 (100), 93 (34), 81 (23), 79 (30), 67 (30), 57 (47), and 41 (24).

4-(5-t-butylcyclohex-1-enyl)but-1-yl p-*nitrobenzenesulphonate (78):*

p-Nitrobenzenesulphonyl chloride (4.44 g, 20 mmol) was added slowly to a stirred, ice-cooled solution of the alcohol (76) (3.15 g, 15 mmol) in dry pyridine (30 ml). After it had been stirred at 0° for 0.75 hr, the reaction mixture was treated with water (1.5 ml), and allowed to stir for a further 10 min. The resulting solution was poured into water (300 ml) and extracted with ether (300 ml). The ether extract was washed with water (300 ml), 10% sulphuric acid (2 x 150 ml), 5% sodium bicarbonate solution (2 x 150 ml), saturated brine (150 ml), dried, and evaporated to give a yellow oil (4.39 g, 74%) which crystallized on standing. Recrystallization to constant melting point from ether-light petroleum at -5° gave *4-(5-t-butylcyclohex-1-enyl)but-1-yl* p-*nitrobenzenesulphonate* (78) as fine white prisms (1.77 g, 29%) m.p. 60-63° (Found: C, 60.9; H, 7.4; N, 3.9. $C_{20}H_{29}NO_5S$ requires C, 60.7; H, 7.4; N, 3.5%). ν_{max} (nujol) 3140w, 2960s, 1675w, 1610m, 1550s, 1400m, 1370s, 1310m, 1175s, 955s, and 935s cm^{-1}; n.m.r.: δ8.6-8.0 (4H, AA'BB' system centred at δ8.41 and δ8.11, $J_{AB'} = J_{BA'}$ = 9 Hz, $J_{AA'} = J_{BB'}$ = *c.* 1.5 Hz, aromatic H), 5.33 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, =C<u>H</u>-), 4.13 (2H, triplet, J = 6 Hz, -C<u>H</u>$_2$-ONs), 0.87 (9H, singlet, *t*-butyl), and 2.2-1.0 (complex, other H).

4-(5-t-Butylcyclohex-1-enyl)but-1-yl acetate (80):

A solution of the alcohol (78) (280 mg, 1.33 mmol) in acetic anhydride (4 ml) and pyridine (4 ml) was stirred at room temperature for 40 hr, then diluted with water (50 ml) and extracted with light petroleum (3 x 20 ml). The combined organic extracts were washed with water (25 ml), 5% hydrochloric acid (2 x 25 ml), 5% sodium bicarbonate solution (2 x 25 ml), dried, and evaporated. The oily residue was distilled to give *4-(5-t-butylcyclohex-1-enyl)but-1-yl acetate* (80) as a colourless oil (280 mg, 84%), b.p. 95-105° (block)/ 0.3 torr, which was homogeneous by g.l.c. analysis (B, 180°) (Found: C, 76.4; H, 11.2. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 3010 wsh, 2920s, 1725s, 1670w, 1400m, 1370s, 1240sb, and 1045s cm^{-1}; n.m.r. : δ5.33 (1H, broad, $w_{\frac{1}{2}}$ = 10 Hz, =C<u>H</u>-), 3.99 (2H, triplet, J = 6 Hz, -C<u>H</u>$_2$-OAc), 1.98 (3H, singlet, -OCOC<u>H</u>$_3$), 0.87 (9H, singlet, *t*-butyl), and 2.2-1.0 (complex, other H); mass spectrum: m/e 252 (0.2, M^+ for $C_{16}H_{28}O_2$), 136 (39), 135 (100), 93 (34), 79 (31), 57 (79), and 43 (35).

<u>Part B.</u>

Methyl crotonate:

Esterification of crude commercial crotonic acid with methanol in the presence of sulphuric acid was carried out as described by Vogel[371b] to give methyl crotonate (b.p. 118-121°; lit.[371b] 118-120°) as a colourless liquid in 64% yield.

Methyl γ-bromocrotonate (115):

A mixture of freshly-recrystallized[382b] N-bromosuccinimide (178 g, 1.0 mol), azobisisobutyronitrile (0.33 g, 2.0 mmol), and a solution of methyl crotonate (150 g, 1.5 mole) in carbon tetrachloride (300 ml) was raised slowly to its boiling point and heated under gentle

reflux until all the solid material had risen to the top of the reaction flask (*c.* 1-3 hr). The cooled mixture was filtered and the residue was washed with a little ether. The filtrate was concentrated and the residue was distilled to give unchanged methyl crotonate (28.7 g) b.p. 34-36°/12 torr and methyl γ-bromocrotonate as a faintly yellow liquid (149 g, 83% based on NBS) b.p. 90-94°/12 torr (lit.[373] 83-85°/13 torr).

Methyl (E)-4-(1-hydroxycyclohexyl)but-2-enoate (116):

A solution of methyl γ-bromocrotonate (115) (107.4 g, 0.60 mol) in dry benzene (200 ml) was added dropwise with stirring to a flask containing zinc wool (38.3 g, 0.60 g.atom), a crystal of iodine, and a solution of cyclohexanone (58.8 g, 0.60 mol) in benzene (200 ml) under a nitrogen atmosphere. Stirring was continued at room temperature until all the zinc had dissolved (2-7 days). The resulting solution was heated under reflux for 1.5 hr, cooled, and treated with concentrated ammonium hydroxide (300 ml) and water (200 ml). The aqueous layer was separated and extracted with ether (3 x 150 ml). The combined organic layers were washed with water (300 ml), dried, and evaporated to give a yellow oil (86.4 g, 73%). Distillation gave methyl *(E)*-4-(1-hydroxycyclohexyl)but-2-enoate (116) as a viscous colourless oil (73.1 g, 62%) b.p. 99-104°/0.3 torr (lit.[224] 96-104°/0.25 torr).

Methyl (E)-4-(cyclohex-1-enyl)but-2-enoate (117):

A solution of the hydroxy ester (116) (93.6 g, 0.47 mol) and *p*-toluenesulphonic acid (5.0 g) in benzene (600 ml) was heated under reflux in a flask fitted with a Dean-Stark water separator until no more water collected (*c.* 60 hr). The cooled solution was washed with water (200 ml), 5% sodium bicarbonate solution (200 ml), saturated

brine (200 ml), dried, and evaporated to give a red oil (85.1 g, 100%), which was shown by g.l.c. (B, 150°) to consist of the required diene ester (117) (*c.* 70%) and two minor components (see Discussion). Distillation through a 50 cm electrically heated column packed with glass helices and fitted with a Human still head gave three fractions, b.p. 85-87°/0.8 torr (37.2 g) containing 91% of (117), b.p. 87-92°/0.8 torr (5.2 g) containing 66% of (117), and b.p. 92-94°/0.8 torr (7.2 g) containing 11% of (117). The first fraction was redistilled under the same conditions and the distillate b.p. 87°/0.8 torr (lit.[224] 120°/1.0 torr) was arbitrarily collected in four portions. The first two fractions were pure methyl *(E)*-4-(cyclohex-1-enyl)but-2-enoate (117) (13.8 g, 16%). Combination of all four portions gave the diene ester (117) (32.1 g, 38%) of 98% purity.

(E)-*4-(Cyclohex-1-enyl)but-2-en-1-ol (118):*

To a stirred, ice-cooled suspension of lithium aluminium hydride (1.14 g, 30 mmol) in dry ether (50 ml) was added, portionwise, aluminium chloride (1.33 g, 10 mmol). The resulting mixture was allowed to warm to room temperature, at which it was stirred for 2 hr. At the end of this period, the solution of aluminium hydride[241] (40 mmol) was cooled again to 0° and treated with the dropwise addition of a solution of the pure diene-ester (117) (4.00 g, 22.2 mmol) in dry ether (20 ml). After the reaction mixture had been stirred at room temperature for 3 hr, the excess hydride was decomposed in the usual way (see p.128). The resulting mixture was filtered and the residue was washed with a little light petroleum. The combined organic solutions were washed with water (100 ml), dried, and evaporated to give a colourless oil (3.18 g, 94%), which was shown to be of 98% purity by g.l.c. analysis (B, 160°). A homogeneous sample of (E)-*4-*

(cyclohex-1-enyl)but-2-en-1-ol (118) was obtained by preparative g.l.c. (J, 190°) followed by distillation b.p. 85°/0.3 torr. (Found: C, 78.6; H, 10.3. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%). ν_{max} 3300sb, 3010sh, 2920s, 1665w, 1450m, 1100m, 1090m, 1005s, and 980s cm^{-1}; n.m.r. : δ6.3 - 5.3 (3H, complex, vinyl H), 3.97 (2H, unresolved - approximating to singlet, -$\underline{CH_2}$-O), 3.70 (1H, singlet, exchanges with D_2O, -O$\underline{H}$), 2.60 (2H, unresolved - approximating to broad singlet, =$\overset{|}{C}$-$\underline{CH_2}$-CH=), and 2.3-1.3 (complex, other H); mass spectrum: m/e 152 (31, M^{+} for $C_{10}H_{16}O$), 121 (55), 93 (48), 91 (51), 81 (100), 79 (75), and 67 (35).

(E)-*4-(Cyclohex-1-enyl)but-2-enal (119)*:

Anhydrous chromium trioxide (19.8 g, 198 mmol) was added to a mechanically stirred solution of pyridine (31.4 g, 396 mmol) in methylene chloride* (400 ml). After the resulting deep burgundy solution had been stirred at room temperature for 0.5 hr, a solution of the allylic alcohol (118) (5.02 g, 33 mmol) in methylene chloride* (50 ml) was added all in one portion. After the reaction mixture had been stirred for 0.5 hr at room temperature, the supernatant liquid was decanted from the solid residue, which was then washed with ether (600 ml). The organic solutions were combined and washed with 5% aqueous sodium hydroxide (3 x 300 ml), water (300 ml), 5% hydrochloric acid (2 x 300 ml), 5% sodium bicarbonate solution (2 x 300 ml), saturated brine (300 ml), dried, and evaporated to give a yellow oil (4.70 g, 94%). Distillation afforded (E)-*4-(cyclohex-1-enyl)but-2-enal* (119)

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* Purification of the methylene chloride as described by Ratcliffe and Rodehorst[242] was essential to the success of this oxidation.

as a colourless oil (4.70 g, 60%), b.p. 68-70°/0.4 torr, which was shown to be homogeneous by g.l.c. analysis (B, 160°). (Found: C, 80.1; H, 9.3. $C_{10}H_{14}O$ requires C, 80.0; H, 9.4%). ν_{max} 3020sh, 2920s, 2720m, 1690s, 1630s, 1450m, 1120s, and 990s cm^{-1}; n.m.r. : δ9.50 (1H, doublet, J = 7 Hz, -CHO), 6.77 (1H, doublet (J = 16 Hz) of triplets (J = 7Hz), $-CH_2-CH=$), 6.05 (1H, doublet (J = 16 Hz) of doublets (J = 7 Hz) with triplet fine structure (J ∿ 1 Hz), =CH-CHO), 5.52 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, ring =CH-), 2.93 (2H, doublet (J = 7 Hz) with doublet fine structure (J ∿ 1 Hz), $= \overset{|}{C}-CH_2-CH=$), and 2.3-1.3 (complex, other H); mass spectrum: m/e 150 (22, M^+ for $C_{10}H_{14}O$), 121 (36), 107 (35), 91 (47), 81 (100), and 79 (64).

Standardization of t-*butyllithium:*

t-Butyllithium (Fluka, *c.* 2M) was standardized by titration at -10° and under a nitrogen atmosphere against a standard solution of 2-propanol in toluene (1.00 M) using a solution of 9,10-phenanthroline in toluene (0.1%, 5 drops) as indicator. The method is based on the procedure described by Ellison and co-workers.[370]

3-t-Butyl-4-(cyclohex-1-enyl)butanal (120):

Tetrakis[iodo(tri-*n*-butylphosphine)copper (I)] (131) m.p. 76° (lit.[257] 75°) was prepared in 52% yield from cuprous iodide and tri-*n*-butylphosphine by a standard method.[257]

To a stirred solution of the tri-*n*-butylphosphinecopper (I) iodide complex (131) (4.68 g, 11.9 mmol) in dry ether (40 ml) at -70° and under a nitrogen atmosphere was added *t*-butyllithium (22.7 mmol) as a solution in pentane (2.7M, 8.4 ml). After the resulting yellow solution had been stirred for 0.5 hr at -70°, it was treated with the dropwise addition of a solution of the unsaturated aldehyde (119) (1.05 g, 7.0 mmol) in dry ether (10 ml), whereupon the solution turned

a deep blood-red colour. This solution was stirred at -70° for 3 hr, then allowed to warm to -30° over a period of 1 hr. The resulting pale orange solution was poured, with vigorous stirring, into 10% sulphuric acid (100 ml). The organic layer was separated and diluted with light petroleum (50 ml), then washed with water (100 ml), 20% aqueous ethylene diamine (3 x 40 ml), water (40 ml), 10% hydrochloric acid (2 x 40 ml), 5% sodium bicarbonate solution (40 ml), dried, and evaporated to give a yellow oil (2.6 g). Chromatography on neutral alumina (52 g) gave, on elution with light petroleum, unidentified hydrocarbons contaminated with some of the required aldehyde (120), (1.10 g) followed by pure aldehyde (120) (0.55 g). The early fractions were rechromatographed on alumina (110 g), giving a further 150 mg of the pure aldehyde (120). Distillation of the combined eluates gave *3-t-butyl-4-(cyclohex-1-enyl)butanal* (120) as a colourless oil (0.65 g, 45%) b.p. 75-80° (block)/0.3 torr, which was *c.* 99% pure by g.l.c. analysis (B, 160°). (Found: C, 80.6; H, 11.2. $C_{14}H_{24}O$ requires C, 80.7; H, 11.6%). ν_{max} 2930s, 2700m, 1720s, 1400m, 1370m, 1225m, 1090m, and 915w cm^{-1}; n.m.r. : δ9.65 (1H, triplet, J ∿ 1.5 Hz, -C<u>H</u>O), 5.40 (1H, broad, $w_{\frac{1}{2}}$ = 7 Hz, =C<u>H</u>-), 0.88 (9H, singlet, *t*-butyl), and 2.4-1.0 (complex, other H); mass spectrum: m/e 208 (2, M^{+} for $C_{14}H_{24}O$), 164 (58), 149 (100), 133 (70), 121 (50), 95 (64), 91 (54), 81 (59), 67 (59), 57 (91), and 41 (79).

3-t-Butyl-4-(cyclohex-1-enyl)butan-1-ol (77):

(i) The diene-aldehyde (119) (3.88 g, 25.9 mmol) was allowed to react with the organocopper reagent from *t*-butyllithium (2.5M in pentane, 33.3 ml, 83.3 mmole) and the tri-*n*-butylphosphinecopper (I) iodide complex (131) (17.3 g, 44.0 mmol) as described above. The reaction mixture was poured into 10% sulphuric acid (150 ml) with stirring, and the organic layer was separated, diluted with light petroleum (50 ml),

and washed with 10% sulphuric acid (150 ml), water (150 ml), 5% sodium bicarbonate solution (100 ml), saturated brine (100 ml), dried, and evaporated. The brown oily residue (13.4 g), containing the aldehyde (120) (*c.* 5.4 g), was added to a stirred, ice-cooled solution of sodium borohydride (2.60 g, 68 mmol) in ethanol (100 ml). The reaction mixture was stirred at ice-temperature for 2.5 hr, then concentrated under reduced pressure. The brown gummy residue was taken up in ether-light petroleum (1:1, 150 ml), and the organic solution was washed with water (3 x 100 ml), dried, and evaporated. The residual black oil (10 g) was chromatographed on neutral alumina (200 g). Elution with light petroleum and 10% ether-light petroleum gave unwanted material, and further elution with 20% ether-light petroleum gave, after distillation, *3-t-butyl-4-(cyclohex-1-enyl)butan-1-ol* (77) as a colourless oil (3.22 g, 59%) b.p. 90-95°/0.4 torr, homogeneous by g.l.c. analysis (D, 190°; B, 170°). (Found: C, 79.8; H, 12.2. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} 3300bs, 2900s, 1660w, 1400m, 1370s, 1040s, and 915m cm^{-1}; n.m.r. : δ5.42 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, =C<u>H</u>-), 3.45 (2H, triplet, J = 7 Hz, -C<u>H</u>$_2$-OH), 0.88 (9H, singlet, *t*-butyl), and 2.4-1.2 (complex, other H); mass spectrum: m/e 210 (3, M^+ for $C_{14}H_{26}O$), 153 (41), 97 (42), 69 (41), 67 (48), 57 (66), 55 (100), and 41 (65).

(ii) To a stirred, ice-cooled solution of sodium borohydride (190 mg, 5.0 mmol) in ethanol (10 ml), was slowly added a solution of the pure aldehyde (120) (416 mg, 2.0 mmol) in ethanol (3 ml). The resulting solution was stirred at 0° for 2.5 hr, after which time the ethanol was removed under reduced pressure, and the residue was partitioned between water (40 ml) and a 1:1 mixture of ether and light petroleum (40 ml). The organic layer was separated, washed with water (2 x 40 ml), and dried. Removal of the solvent left the alcohol (77)

as a colourless oil (420 mg, 100%) identical in all respects with that obtained as described above.

3-t-Butyl-4-(cyclohex-1-enyl)but-1-yl p-*nitrobenzenesulphonate (79):*

p-Nitrobenzenesulphonyl chloride (2.77 g, 12.5 mmol) was added to a stirred ice-chilled solution of the alcohol (77) (2.10 g, 10 mmol) in dry pyridine (20 ml). After being stirred at 0^{o} for 1.25 hr, the reaction mixture was treated with water (1.0 ml) and allowed to stir for a further 10 min. The resulting solution was poured into water (200 ml) and extracted with ether (250 ml). The ether extract was washed with water (150 ml), 10% sulphuric acid (2 x 100 ml), 5% sodium bicarbonate solution (150 ml), saturated brine (200 ml), dried, and evaporated to give a pale yellow solid (3.15 g, 80%). Recrystallization to constant melting point from ether-light petroleum at -5^{o} gave *3-t-butyl-4-(cyclohex-1-enyl)but-1-yl* p-*nitrobenzenesulphonate* (79) as off-white platelets (1.24 g, 31%) m.p. 61-62°. (Found: C, 61.0; H, 7.5; N, 3.7. $C_{20}H_{29}NO_5S$ requires C, 60.7; H, 7.4; N, 3.5%). ν_{max} (nujol) 3130m, 2960s, 1670w, 1610m, 1540s, 1400m, 1365s, 1350s, 1180s, 940s, and 860s, cm^{-1}; n.m.r. δ 8.6 - 7.9 (4H, AA'BB' system centred at δ8.39 and δ8.07, $J_{AB'} = J_{BA'} = 9$ Hz, $J_{AA'} = J_{BB'} = c.1.5$ Hz, aromatic H), 5.38 (1H, broad, $w_{\frac{1}{2}} = 8$ Hz, =C<u>H</u>-), 4.02 (2H, complex, -C<u>H</u>$_2$-O-), 0.86 (9H, singlet, *t*-butyl), and 2.2 - 1.1 (complex, other H).

3-t-Butyl-4-(cyclohex-1-enyl)but-1-yl acetate (81):

The alcohol (77) (105 mg, 0.50 mmol) was acetylated with acetic anhydride (1.5 ml) and pyridine (1.5 ml) by the method described for the preparation of 4-(5-*t*-butylcyclohex-1-enyl)but-1-yl acetate (80). After distillation, *3-t-butyl-4-(cyclohex-1-enyl)but-1-yl acetate* (81) was obtained as a colourless oil (89 mg, 71%) b.p. 75-80°(block)/

0.4 torr, which was homogeneous by g.l.c. analysis (B, 160°) (Found: C, 76.5; H, 11.1. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2930s, 1735s, 1660w, 1400m, 1375s, 1240sb, 1040s, and 810m cm^{-1}; n.m.r. : δ5.43 (1H, broad, $w_{\frac{1}{2}}$ = 8 Hz, =C<u>H</u>-), 3.90 (2H, poorly resolved triplet, J ∿ 7 Hz, -C<u>H</u>$_2$-OAc), 1.95 (3H, singlet, -OCOC<u>H</u>$_3$), 0.88 (9H, singlet, *t*-butyl), and 2.2 - 1.2 (complex, other H); mass spectrum: m/e 252 (0.5, M^+ for $C_{16}H_{28}O_2$), 136 (32), 135 (100), 67 (24), 57 (32), 55 (48), 43 (43), and 41 (25).

3-t-Butyl-4-cyclohexylbutan-1-ol (96):

A solution of the unsaturated alcohol (77) (630 mg, 3.0 mmol) in ethanol (20 ml) was hydrogenated over a 5% rhodium-alumina catalyst (300 mg) at room temperature and atmospheric pressure until the uptake of hydrogen had ceased (*c.* 72 hr). The reaction mixture was filtered through celite and evaporated. The residue was dissolved in light petroleum (40 ml), washed with water (40 ml), dried, and evaporated to give *3-t-butyl-4-cyclohexylbutan-1-ol* (96) as a colourless oil (580 mg, 91%), which was not purified further. G.l.c. analysis (D, 180°) revealed the presence of only 5% of impurities (see Discussion), and the absence of any unchanged starting material. ν_{max}, 3400sb, 2960s, 1450m, 1400m, 1370m, and 1050m cm^{-1}; n.m.r. : δ3.50 (2H, triplet, J = 7 Hz, -C<u>H</u>$_2$-O), 2.95 (1H, singlet, exchanges with D_2O, -O<u>H</u>) 0.86 (9H, singlet, *t*-butyl), and 2.1 - 0.7 (complex, other H).

3-t-Butyl-4-cyclohexylbut-1-yl p-nitrobenzenesulphonate (97):

Treatment of the crude alcohol (96) (530 mg, 2.5 mmol) with *p*-nitrobenzenesulphonyl chloride (1.11 g, 4.0 mmole) and pyridine (6 ml) in the manner described for the unsaturated analogue (77) gave the saturated nosylate (97) as a pale yellow solid (960 mg, 97%). Recrystallization to constant melting point from ether-light petroleum at -5°

gave *3-t-butyl-4-cyclohexylbut-1-yl* p-*nitrobenzenesulphonate* (97) as fine white needles (580 mg, 59%) m.p. 95-96°. (Found: C, 60.3; H, 7.7; N, 3.5. $C_{20}H_{31}NO_5S$ requires C, 60.4; H, 7.9; N, 3.5%). ν_{max} (nujol) 3120m, 2960s, 1600w, 1530s, 1395m, 1365s, 1345s, 1180s, and 945s cm^{-1}; n.m.r. ($CDCl_3$): δ8.6 - 8.0 (4H, AA'BB' system centred on δ8.43 and δ8.15, $J_{AB'} = J_{A'B} = 9$ Hz, $J_{AA'} = J_{BB'} \sim 1.5$ Hz, aromatic H), 4.17 (2H, triplet, J = 8 Hz, $-CH_2-O$), 0.80 (9H, singlet, *t*-butyl), and 2.1 - 0.7 (complex, other H).

Part C:

Methylenecyclohexane (136):

A mixture of methyltriphenylphosphonium iodide (80.8 g, 0.20 mol) and potassium *t*-butoxide (22.4 g, 0.20 mol) under a nitrogen atmosphere was cooled to 0° and dry ether (250 ml) was added to it. After the resulting slurry had been stirred at ice temperature for 2.5 hr, a solution of cyclohexanone (19.6 g, 0.20 mmol) in dry ether (40 ml), was slowly added over a period of 4 hr. The reaction mixture was then stirred for 15 hr at room temperature, followed by 6 hr under reflux. The cooled reaction mixture was washed with water (3 x 600 ml), diluted with an equal volume of pentane, washed with more water (500 ml), and dried. The resulting solution was carefully fractionated through a 15 cm column packed with glass helices, and methylenecyclohexane was collected as the fraction b.p. 99.5 - 100° (lit.[375] 102-103° (4.77 g, 25%).

Methyl propiolate:

Esterification of propiolic acid with methanol in the presence of sulphuric acid as described by James and Fanta[376] gave a 25%

yield of methyl propiolate b.p. 100.5-101.5° (lit.[377] 102°).

The ene reaction between methylenecyclohexane and methyl propiolate:

To an ice-cooled solution of methyl propiolate (462 mg, 5.5 mmol) in dry benzene (3 ml) was added aluminium chloride (67 mg, 0.5 mmol) and methylenecyclohexane (480 mg, 5.0 mmol). After stirring at room temperature for 42 hr, the reaction mixture was diluted with light petroleum (20 ml), then washed with water (20 ml), 10% sulphuric acid (20 ml), 5% sodium bicarbonate solution (20 ml), dried, and evaporated to give a colourless oil (200 mg, 22%). G.l.c. analysis (B, 160°) of the product indicated the presence of one major component (*c.* 75%), which was identified as methyl *(E)*-4-(cyclohex-1-enyl)but-2-enoate (117) on the basis of its spectral and g.l.c. properties. The mixture was not investigated further.

4,4-Dimethylpent-2-enoic acid (134):

To a sitrred, ice-cooled solution of malonic acid (46.8 g, 0.45 mol) in pyridine (75 ml), containing piperidine (6 ml), was added pivaldehyde (133) (25.8 g, 0.30 mol). The resulting mixture was stirred at room temperature for 12 hr, then stirred and heated under reflux for 6 hr. The cooled solution was diluted with water (750 ml) and extracted with ether (400 ml). The ether layer was washed with water (2 x 600 ml), 10% hydrochloric acid (2 x 300 ml), water (600 ml), saturated brine (200 ml), dried, and carefully evaporated to give a yellow oil (4.52 g, 12%) which crystallized on cooling. Recrystallization from pentane gave 4,4-dimethylpent-2-enoic acid (134) as white needles (3.33 g, 9%), m.p. 58-60° (lit.[378] 59°).

Methyl 4,4-dimethylpent-2-enoate (135):

(i) A mixture of pivaldehyde (133) (8.6 g, 0.10 mol) and methyl acetate (11.1 g, 0.15 mol) was added slowly to a vigorously stirred suspension of potassium *t*-butoxide (12.3 g, 0.11 mmole) in dry hexane (30 ml). The resulting mixture was stirred for 7 hr at room temperature, after which water (50 ml) was carefully added to it. The organic layer was separated, washed with water (50 ml), saturated brine (50 ml), dried, and carefully evaporated to leave a yellow oil (3.3 g, 23%). Purification by preparative g.l.c. (J, 120°) gave a homogeneous (B, 100°) sample of methyl 4,4-dimethylpent-2-enoate (135) as a colourless oil (1.6 g, 13%) b.p. 118-120°/350 torr (lit.[379] 50-60°/14 torr).

(ii) An ethereal solution of diazomethane[380] was added dropwise to a stirred, ice-cooled solution of 4,4-dimethylpent-2-enoic acid (134) (3.33 g, 26 mmol) in ether (15 ml) until the yellow colour just persisted. The resulting solution was concentrated to half its volume on a warm water-bath, filtered, and carefully evaporated to leave a pale yellow oil (2.90 g, 79%) which was identical in all respects to the ester (135) obtained as described above.

Work described in Chapter IV.

Part A.

4-t-Butyl-1-pyrrolidinocyclohexene (137):

A solution of 4-*t*-butylcyclohexanone (104) (154 g, 1.00 mol) and pyrrolidine (107 g, 1.5 mol) in benzene (400 ml) was heated under reflux under an atmosphere of nitrogen in a flask fitted with a water separator. When the evolution of water had ceased, the solution was cooled and the solvent was removed under reduced pressure. Distillation of the residue gave 4-*t*-butyl-1-pyrrolidinocyclohexene (137) as a colourless oil (197 g, 95%) b.p. 109-112°/0.4 torr (lit.[381] 117-119°/0.35 torr) which was used immediately in the next step.

cis-6-t-Butyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenone (138):

Reaction of the enamine (137) (197 g, 0.95 mol) with freshly-purified methyl vinyl ketone[382a] (77 g, 1.10 mol) in the manner described by House and co-workers[267] gave a mixture of *cis*-6-*t*-butyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenone (138) and 6-*t*-butyl-3,4,5,6,7,8-hexahydro-2(1H)-naphthalenone (139) as a colourless oil (118 g, 60%) b.p. 105-108°/0.05 torr (lit.[267] 110-115°/0.05 torr). G.l.c. analysis (G, 200°; B, 190°) showed that the mixture contained *c.* 85% of (138), *c.* 15% of (139), and less than 2% of 4-*t*-butylcyclohexanone (104). Six recrystallizations from hexane at -40° gave a sample of the conjugated ketone (138) of *c.* 99% purity (B, 190°) m.p. 25-27° (lit.[267] 27.5-29°).

2-t-Butyl-1,2,3,4,5,6,7,8-octahydronaphthalene (82):

Potassium hydroxide (39.0 g, 0.70 mol) was added to a solution of a mixture of the two ketones (138) and (139) (51.5 g, 0.25 mol, prepared as described above) and hydrazine hydrate (100%, 30 ml) in diethylene glycol (500 ml). The mixture was stirred and heated at *c.*

170° for 2 hr, after which water and excess of hydrazine hydrate were removed by distillation (bath temperature 170°). The remaining solution was heated and stirred at 180° for a further 3 hr, then cooled, recombined with the distillate, and diluted with water (1000 ml). The resulting mixture was extracted with light petroleum (3 x 200 ml), and the combined organic extracts were washed with water (4 x 700 ml), dried, and concentrated to give a dark brown oil (45.2 g). Chromatography on a column of neutral alumina (500 g, elution with light petroleum) gave a yellow oil (31.2 g, 65%), which was shown by g.l.c. analysis (C, 180°) to be a mixture of at least six components, of which the major one (*c.*45%) was the required tetrasubstituted olefin (82).

A solution of the olefin mixture (31.2 g, 0.16 mol) and boron trifluoride etherate (33.4 g, 0.24 mol) in benzene (300 ml) and sulpholane (600 ml) was stirred at room temperature for 77 hr. At the end of this period, water (150 ml) was added to the solution, followed by light petroleum (200 ml). The lower layer was separated and extracted with light petroleum (2 x 200 ml). The combined organic layers were washed with water (4 x 250 ml), saturated brine (250 ml), dried, and concentrated to give a yellow oil (31.2 g, 100%) which was shown by g.l.c. (C, 180°) to contain *c.* 82% of (82). Chromatography on silica gel impregnated with silver nitrate (800 g, elution with light petroleum, monitored by g.l.c. - C, 180°) gave *2-t-butyl-1,2,3,4,5,6,7,8-octahydronaphthalene* (82) as a colourless oil (17.2 g, 55%, 36% based on (138) and (139)) b.p. 130°/8 torr. (Found: C, 87.1; H, 12.4. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 2920s, 1480m, 1450m, 1400m, and 1370s cm^{-1}; n.m.r. : δ0.87 (*c.* 9H, singlet, *t*-butyl) and 1.0 - 2.0 (*c.* 15H, complex, other H); mass spectrum : m/e 192 (11, M^{+} for $C_{14}H_{24}$), 135 (100), 93 (57), 91 (31), 79 (47), and 67 (74).

2α-t-Butyl-4aα,8aα-epoxy-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene (140) and 2β-t-butyl-4aα,8aα-epoxy-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene (141):

A solution of *m*-chloroperbenzoic acid (17.3 g, 100 mmol, as 20.3 g of an 85% mixture with *m*-chlorobenzoic acid) in methylene chloride (300 ml) was added slowly to a stirred, ice-cooled solution of the octalin (82) (15.4 g, 80 mmol) in methylene chloride (50 ml). The resulting solution was stirred at room temperature for 1.5 hr, then washed with water (400 ml), 5% sodium bicarbonate solution (3 x 300 ml), dried (potassium carbonate), and concentrated to a colourless oil (16.1 g, 97%) b.p. 101-102°/1.5 torr. G.l.c. analysis (D, 160°, 125°) indicated that *2α-t-butyl-4aα,8aα-epoxy-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene* (140) and *2β-t-butyl-4aα,8aα-epoxy-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene* (141) were present in the ratio *c.*55:45, and were free of impurities. (Found: C, 80.8; H, 11.4. $C_{14}H_{24}O$ requires C, 80.7; H, 11.6%). ν_{max} 2930s, 1400m, 1370s, 1180m, 970m, 845m, and 695m cm^{-1}; n.m.r. : δ0.84 (*c.* 9H, singlet, *t*-butyl) and 2.2-1.0 (*c.* 15H, complex, other H); mass spectrum : m/e 208 (5, M^{+} for $C_{14}H_{24}O$), 151 (31), 134 (41), 133 (22), 111 (100), 91 (27), 81 (24), 67 (30), 57 (35), and 41 (21).

2α-t-Butyl-1,2,3,4,5,6,7,8aβ-octahydro-4aα(2H)-naphthalenol (142) and 3β-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenol (143):

A solution of the epoxide mixture, (140) and (141), (16.6 g, 80 mmol) in dry ether (300 ml) was added to a stirred suspension of lithium aluminium hydride (7.60 g, 0.20 mol) in dry ether (100 ml). The resulting mixture was stirred and heated under reflux for 70 hr, cooled in an ice-bath, and treated with water and aqueous sodium hydroxide in the usual way. The resulting mixture was filtered, and the filtrate was washed with water (250 ml), saturated brine (250 ml),

dried, and evaporated to give a white oil which crystallized on cooling. Distillation afforded *2α-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenol* (142) and *3β-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenol* (143) as a white crystalline mass (14.9 g, 90%) b.p. 100-105°/0.5 torr, m.p. 33-41°. G.l.c. analysis (D, 180°, 150°) indicated that (142) and (143) were present as a *c.* 55:45 mixture, and were free of impurities. (Found: C, 80.0; H, 12.7. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} (nujol) 3450sb, 2920s, 1450m, 1400m, 1370m, 980m, and 965s cm^{-1}; n.m.r. : δ0.85 (*c.* 9H, singlet, *t*-butyl) and 2.0-1.0 (*c.* 17H, complex, other H); mass spectrum: m/e 210 (40, M^+ for $C_{14}H_{26}O$), 111 (100), 98 (36), 69 (35), 67 (44), 57 (77), 55 (53), and 41 (52).

2α-t-Butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenyl acetate (93) and 3β-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenyl acetate (89):

To a stirred, ice-cooled solution of the alcohol mixture, (142) and (143) (12.6 g, 60 mmol) in N,N-dimethylaniline (35 ml) was added acetyl chloride (10 ml). The resulting solution was stirred at room temperature for 1 hr, then heated on a steam-bath for 4 hr. After cooling, the solution was poured into ice water (300 ml) and extracted with light petroleum (2 x 100 ml). The combined organic extracts were washed with water (150 ml), 10% hydrochloric acid (2 x 150 ml), 5% sodium bicarbonate solution (150 ml), dried, and evaporated to give a yellow oil (14.9 g, 98%), which was shown by g.l.c. (B, 150°) to be a 55:45 mixture of the two acetates (93) and (89), contaminated with *c.* 5% of volatile impurities. Although the two acetates could be separated by preparative g.l.c. (J, 160°), some decomposition occurred, leading to contamination of the acetates with

olefinic material. Pure samples of each acetate were obtained by chromatography of the mixture (in 3.0 g portions) on neutral alumina (300 g), using light petroleum as eluent, and monitoring the separation by g.l.c. (B, 160°). The acetate (89) was eluted first, followed by a mixture of (89) and (93). When this mixture was rechromatographed under the same conditions, a mixture of (89) and (93) was eluted first, followed by pure (93). In this way, pure *3β-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenyl acetate* (89) was obtained as a colourless oil (2.65 g, 17%) b.p. 80-85° (block)/0.05 torr (Found: C, 76.4; H, 11.1. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2920s, 1725s, 1455s, 1400m, 1370s, 1240s, 1020s, and 970s cm^{-1}; n.m.r. : δ1.98 (3H, singlet, $-OCOCH_3$), 0.80 (9H, singlet, *t*-butyl), 3.0-2.4 (2H, complex, other H), and 2.0-0.7 (complex, other H); mass spectrum: m/e 192 (4, M^+ -60 for $C_{16}H_{28}O_2$), 136 (26), 135 (100), 134 (21), 67 (36), 57 (37), 55 (27), 43 (29), and 41 (28), and *3α-t-butyl-1,3,4,5,6,7,8,8aβ-octahydro-4aα(2H)-naphthalenyl acetate* (93) was obtained as a colourless oil (1.27 g, 9%) b.p. 95-100° (block)/0.15 torr (Found: C, 76.5; H, 11.1. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2920s, 1725s, 1455s, 1400m, 1370s, 1240s, 1020s, 980s, and 960s cm^{-1}; n.m.r. : δ1.97 (3H, singlet, $-OCOCH_3$), 0.84 (9H, singlet, *t*-butyl), 3.0-2.5 (2H, complex, other H), and 1.9-0.7 (complex, other H); mass spectrum: m/e 192 (50, M^+ -60 for $C_{16}H_{28}O_2$), 136 (36), 135 (100), 134 (16), 93 (13), 67 (11), and 57 (16). In addition, a 27:73 mixture of (89) and (93) (6.33 g, 42%) was recovered.

trans-7-t-Butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (83) and trans-2-t-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (85):

The acetate (89) (2.30 g, 9.1 mmol) was slowly distilled under reduced pressure (0.3 torr) through a Vycor tube (50 cm x 2.5 cm) packed with silica beads and heated at 525°, and the pyrolysate was

collected in a trap cooled to -70°. The condensed material was rinsed out of the trap and the column with light petroleum, and the washings were washed with 5% sodium bicarbonate solution, dried, and evaporated to give a yellow oil (1.59 g, 91%). G.l.c. analysis (C, 180°) indicated that (83) and (85) were present in the ratio 35:65, together with *c.* 7% of several minor impurities. Separation by preparative g.l.c. (K, 190°) afforded trans-*7-t-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene* (83) as a colourless oil (290 mg, 17%) b.p. 108-112° (block)/16 torr, homogeneous by g.l.c. (C, 180°) (Found: C, 87.7; H, 12.7. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3060w, 2950s, 1665w, 1395m, 1365s, 975m, and 845m cm^{-1}; n.m.r. : δ5.33 (1H, broad, $w_{\frac{1}{2}}$ = 4 Hz, =C<u>H</u>-), 0.85 (9H, singlet, *t*-butyl), and 2.3-0.8 (complex, other H); mass spectrum: m/e 192 (7, M^{+} for $C_{14}H_{24}$), 136 (20), 135 (100), 134 (17), 93 (16), 91 (11), and 67 (23), and *trans*-2-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (85) also as a colourless oil (570 mg, 33%) b.p. 105-110° (block)/16 torr (lit.[210] 110°/4 torr) which was homogeneous by g.l.c. (C, 180°). The spectral properties of the octalin (85) were identical to those exhibited by the octalin (85) prepared by Laffer.[210]

cis-*3-t-Butyl-7,7-(ethane-1,2-dithio)—1,2,3,4,4a,5,6,7-octahydronaphthalene (144):*

Boron trifluoride etherate (0.75 ml) was added to an ice-cooled mixture of the pure octalone (138) (2.06 g, 10 mmol) and 1,2-ethanedithiol (1.5 ml). The resulting mixture was allowed to stand at room temperature, with occasional shaking, for 0.5 hr. Addition of methanol (10 ml) caused the separation of a colourless oil which crystallized on cooling to 0°. The white crystalline solid (2.72 g, 92%) m.p. 62-64° was collected and washed with a little methanol. Recrystallization from methanol gave cis-*3-t-butyl-7,7-(ethane-1,2-*

dithio)-1,2,3,4,4a,5,6,7-octahydronaphthalene (144) as white prisms (2.00 g, 71%) m.p. 71.5-72.5°. One further recrystallization from methanol gave a sample m.p. 74° for elemental analysis (Found: C, 68.0; H, 9.5. $C_{16}H_{26}S_2$ requires C, 68.0; H, 9.3%). ν_{max} (nujol) 3030w, 1650w, 1400w.sh, 1385w, 1370m, 930m, and 850 m cm^{-1}; n.m.r. : δ5.49 (1H, broad singlet, $w_{\frac{1}{2}}$ = 4Hz, =C<u>H</u>-), 3.27 (4H, singlet, -SC<u>H</u>$_2$C<u>H</u>$_2$S-), 0.85 (9H, singlet, *t*-butyl), and 2.3-0.7 (complex, other H); mass spectrum: m/e 282 (19, M^+ for $C_{16}H_{26}S_2$), 254 (23), 222 (24), 105 (21), 91 (46), 61 (21), 57 (100), 55 (24), and 41 (39).

cis-*3*-t-*Butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (87):*

Sodium (1.0 g) was added in small pieces to a suspension of the thioacetal (144) (560 mg, 2 mmol) in dry ether (5 ml) and liquid ammonia (100 ml). The reaction mixture was stirred for 2 min after the addition had been completed, then treated with the dropwise addition of ethanol until the blue colour was dispelled. The ammonia was allowed to evaporate and the residue was diluted with water (100 ml) and extracted with light petroleum (3 x 50 ml). The combined organic extracts were washed with water (100 ml), saturated brine (100 ml), dried, and evaporated. Distillation gave a malodorous colourless oil (320 mg, 84%) b.p. 130-135° (block)/11 torr, which was shown by g.l.c. (C, 180°) to consist of one major component (87) (*c.* 89%) and three minor impurities (total *c.* 11%). Preparative g.l.c. afforded a homogeneous sample of cis-*3*-t-*butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene* (87) (Found: C, 87.7; H, 12.4. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3020 w.sh, 2920s, 1665w, 1400m, 1370s, 1240m, 980m, and 810 cm^{-1}; n.m.r. : δ5.30 (1H, broad, $w_{\frac{1}{2}}$ = 11 Hz, =C<u>H</u>-), 0.84 (9H, singlet, *t*-butyl), and 2.1-0.6 (complex, other H); mass spectrum: m/e 192 (20, M^+ for $C_{14}H_{24}$), 136 (27),

135 (100), 93 (24), 79 (20), 67 (17), and 57 (15).

Pyrolysis of the acetate (93):

The acetate (93) (230 mg, 0.92 mmol) was subjected to flash vacuum pyrolysis under the same conditions as were used for the acetate (89). A colourless oil (130 mg, 74%) was obtained, and was shown by g.l.c. (C, 170°) to consist of two components in the ratio 58:42. Comparison (C, 150°; G, 170°) with an authentic sample indicated that the major component was *cis*-3-*t*-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (87), and therefore the minor component must be cis-6-t-*butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene* (88). The two components of the mixture could not be separated by preparative g.l.c.

Part B.

1,2,3,4,4aβ,5,6,7,8,8aβ-Decahydro-2α-naphthalenol (146):

A solution of 2-naphthol (145) (108 g, 0.75 mole) in ethanol (700 ml) was hydrogenated in a Baskerville-Lindsay high pressure hydrogenation apparatus under a pressure of 70 atmospheres at room temperature and in the presence of a 5% rhodium-alumina catalyst (11.0 g) for 5 days. The resulting mixture was filtered through celite and the filtrate was evaporated to give a pink oil which crystallized on cooling (115.7 g, 100%). G.l.c. analysis (B, 150°) showed the decalol (146) to be of greater than 94% purity. Two recrystallizations from hexane gave 1,2,3,4,4aβ5,6,7,8,8aβ-decahydro-2α-naphthalenol (146) as white platelets (75 g, 65%), m.p. 102-103° (lit.[387] 105°), which were homogeneous by g.l.c. analysis (B, 150°).

cis-*3,4,5a,5,6,7,8,8a-Octahydro-2(1H)-naphthalenone (147):*

Oxidation of an ethereal solution of the decalol (146) (24.6 g,

0.16 mol) with a 100% excess of chromic acid according to the general procedure developed by Brown *et al.* (Procedure B)[278] gave *cis*-3,4,4a,5,6,7,8,8a-octahydro-2(1H)-naphthalenone (147) as a colourless oil (21.3 g, 88%) b.p. 120-121°/10 torr (lit.[388] 77-79°/2 torr).

2β-t-Butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-2α-naphthalenol (148) and 2β-t-butyl-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2α-naphthalenol (149):

A solution of the decalone (147) (7.60 g, 50 mmol) in dry hexane (50 ml) was added dropwise to a stirred solution of *t*-butyllithium in pentane (2.6M, 20.0 ml, 52 mmol) at -70° under a nitrogen atmosphere. After the addition had been completed, the reaction was allowed to warm to room temperature and stirred for 1 hr, after which it was hydrolyzed by the careful dropwise addition of water (10 ml). More water (40 ml) was added, followed by solid potassium carbonate (10 g). After the mixture had been stirred for 10 min, the organic layer was separated, washed with water (50 ml), dried, and evaporated to give a colourless oil (9.02 g). G.l.c. analysis (C, 200°) indicated the presence of 22% of unchanged starting material (147) and 43% and 35% each of (148) and (149) respectively. The mixture was chromatographed on a column of neutral alumina (360 g). Elution* with light petroleum afforded *2β-t-butyl-1,2,3,4,4aβ,5,6,7,8,8aβ-decahydro-2α-naphthalenol (149)* as a white solid (2.05 g, 20%) m.p. 94-97°, which was homogeneous by g.l.c. analysis (C, 200°). Two recrystallizations from hexane gave white prisms m.p. 95.5-97° (Found: C, 79.7; H, 12.3. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} (nujol) 3500m.sharp, 2920s, 1390w.sh, 1370m, and 827m cm^{-1}; n.m.r. ($CDCl_3$): δ0.88 (*c.* 9H, singlet, *t*-butyl) and 2.2-0.9 (*c.* 17H, complex, other H); mass

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* Monitored by g.l.c. (C, 210°).

spectrum: m/e 210 (0.09, M^+ for $C_{14}H_{26}O$), 153 (100), 135(44), 95 (25), 67 (17), 43 (19), and 41 (17). Further elution gave (149) contaminated with starting material (147), followed by a mixture of (148) and starting material (147). After all the starting material (147) had passed through the column, pure *2β-t-butyl-1,2,3,4,4aα,5,6,7,8,8aα-octahydro-2α-naphthalenol* (148) was eluted with 1% ether-light petroleum as a colourless oil (1.29 g, 12%) b.p. 95-100° (block)/0.3 torr which crystallized after distillation, m.p. 62-64° (Found: C, 80.3; H, 12.5. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} (nujol) 3430s.sharp, 2900s, 1400s.sh, 1380s, 1370s, 995s, and 910s cm^{-1}; n.m.r. : δ0.92 (*c.* 9H, singlet, *t*-butyl) and 2.2-0.9 (*c.* 17H, complex, other H); mass spectrum: m/e 210 (0.19, M^+ for $C_{14}H_{26}O$), 153 (100), 135 (55), 95 (25), 67 (22), 57 (18), 43 (20), and 41 (20).

cis-*7-t-Butyl-1,2,3,4,4a,5,6,8a-octahydronaphthalene (150)* and cis-*6-t-butyl-1,2,3,4,4a,5,8,8a-octahydronaphthalene (151)*:

(i) A stirred solution of the decalol (149) (1.59 g, 7.58 mmol) in dry pyridine (20 ml) was cooled in ice and treated with the dropwise addition of freshly-purified[371c] thionyl chloride (7 ml). The resulting solution was stirred at ice temperature for 3 hr, then added slowly and with stirring to ice water (200 ml) and extracted with light petroleum (2 x 50 ml). The combined organic extracts were washed with water (250 ml), 10% hydrochloric acid (2 x 200 ml), 5% sodium bicarbonate solution (100 ml), dried, and evaporated to give a yellow oil (1.38 g, 100%). Analysis by g.l.c. (C, 180°, E, 110°) indicated that the octalins (150) and (151) were present as a 44:56 mixture, which was free of impurities.

(ii) In a similar manner, the decalol (148) (1.00 g, 4.75 mmol) was dehydrated with thionyl chloride (5 ml) and pyridine (10 ml) to

give a 44:56 mixture of the two octalins (150) and (151) only (C, 180°) as a yellow oil (0.93 g, 100%).

(iii) Under the same conditions as described above, a mixture of the two decalols (148) (43%) and (149) (35%) containing the decalone (147) (22%) (11.30 g) was dehydrated with thionyl chloride (30 ml) and pyridine (100 ml) to give a 44:56 mixture of the two octalins (150) and (151) as a yellow oil (8.10 g) b.p. 120-122°/11 torr, containing *c.* 1% of the decalone (147). Separation by preparative g.l.c. (K, 185°) gave pure (C, 180°) samples of cis-*7*-t-*butyl*-*1,2,3,4,4a,5,6,8a*-*octahydronaphthalene* (150). (Found: C, 87.3; H, 12.4. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 2920s, 1645w, 1450s, 1395m, 1365s, 875m, and 830m cm^{-1}; n.m.r. : δ5.27 (1H, broad, $w_{\frac{1}{2}}$ = 6Hz, =C<u>H</u>-), 1.00 (9H, singlet, *t*-butyl), and 2.3-1.0 (complex, other H); mass spectrum: m/e 192 (5, M^{+} for $C_{14}H_{24}$), 136 (23), 135 (100), 134 (16), 93 (22), 79 (17), 67 (25), 57 (15), and 41 (21), and cis-*6*-t-*butyl*-*1,2,3,4,4a,5,8,8a*-*octahydronaphthalene* (151) (Found: C, 87.0; H, 12.8. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3020w,sh, 2900s, 1650w, 1455s, 1395m, 1365s, and 810m cm^{-1}; n.m.r. : δ5.32 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, =C<u>H</u>-), 0.99 (9H, singlet, *t*-butyl), and 2.2-1.1 (complex, other H); mass spectrum: m/e 192 (10, M^{+} for $C_{14}H_{24}$), 136 (25), 135 (23), 95 (32), 93 (20), 81 (25), 79 (24), 67 (41), 57 (100), 55 (25), and 41 (43).

(iv) A solution of the above-described mixture of decalols (150) and (151) and decalone (147) (0.33 g) in hexane (10 ml) was stirred with 50% aqueous sulphuric (10 ml) for 3 hr at room temperature. The hexane layer was separated, washed with 5% sodium bicarbonate solution (2 x 30 ml), and dried. G.l.c. analysis (C, 180°, 200°) revealed the presence of *c.* 25% of the decalone (147) and *c.* 30% and 40% respectively

of the two octalins (150) and (151), and indicated the complete disappearance of the decalols (148) and (149).

2β-t-Butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenol (152) and 3β-t-butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-2α-naphthalenol (153):

To a stirred, ice-cooled solution of diborane in tetrahydrofuran (2.0M, 18.2 ml, 36.4 mmol) under a nitrogen atmosphere was added a solution of the mixture of octalins (150) and (151) (7.0 g, 36.4 mmol) in tetrahydrofuran (60 ml). After the reaction had been stirred at ice temperature for 1.5 hr followed by room temperature for 1 hr, water (2 ml) was slowly added to it, followed by 3N sodium hydroxide solution (30 ml) and 30% hydrogen peroxide (30 ml). The resulting mixture was stirred at ambient temperature for 1.5 hr, then diluted with ether (250 ml). The organic layer was separated, diluted again with light petroleum (100 ml), and washed with water (3 x 200 ml), saturated brine (200 ml), dried, and evaporated to give a yellow oil (6.83 g) which crystallized on cooling. G.l.c. analysis (D, 180°) indicated the presence of the decalols (148), (152), and (153) in the ratio 4:37:57 (see, however, Table IV.1), as well as *c.* 1% of an unidentified compound and *c.* 15% of unchanged starting material. The mixture was chromatographed* in portions of 2.3 g on a column of neutral alumina (230 g). Unchanged starting material (150) and (151) (0.90 g) was eluted first (light petroleum), followed by pure 1-decalol (152) (25% methylene dichloride-light petroleum) as a white solid (1.52 g, 23% based on unrecovered starting material), m.p. 117-120° (sealed tube). Two recrystallizations from hexane afforded 2β-t-*butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenol* (152) as fine white needles, m.p. 121-122° (sealed tube) (Found: C, 80.3;

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* Monitored by g.l.c. (D, 180°).

H, 12.3. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} (nujol) 3500s. sharp, 2960s, 1390m.sh, 1375s, 1365s, and 1020s cm^{-1}; n.m.r. ($CDCl_3$) : δ3.80 (1H, X part of ABX spectrum approximating to doublet of doublets, $J_{AX} + J_{BX} \sim 24$ Hz, axial H, -C<u>H</u>(OH)-), 1.00 (9H, singlet, *t*-butyl), and 2.2-0.8 (complex, other H); mass spectrum: m/e 210 (4, M^+ for $C_{14}H_{26}O$), 136 (30), 135 (100), 134 (54), 121 (77), 95 (31), 93 (30), 81 (41), 67 (40), 57 (87), 55 (34), and 41 (67). Further elution gave a mixture (3.0 g) containing 83% of the 2-decalol (153). Recrystallization from hexane gave pure 3β-t-*butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-2α-naphthalenol* (153) as fine white cubes (2.10 g, 31% based on unrecovered starting material) m.p. 100°. Two further recrystallizations gave m.p. 101° (Found: C, 80.2; H, 12.5. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} (nujol) 3280 sb, 2960s, 1390m, 1380m, 1360m, 1045s, 1040s, and 1020s cm^{-1}; n.m.r. ($CDCl_3$): δ3.75 (1H, broad, $w_{\frac{1}{2}}$ = 23 Hz, axial H, C<u>H</u>(OH)-), 1.00 (9H, singlet, *t*-butyl), and 2.0-0.8 (complex, other H); mass spectrum: m/e 210 (0.2, M^+ for $C_{14}H_{26}O$), 136 (100), 135 (51), 134 (40), 121 (44), 95 (44), 93 (40), 81 (62), 79 (43), 67 (57), 57 (80), 55 (49), and 41 (68).

2β-t—Butyl—1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenyl acetate (154):

Acetylation of the decalol (152) (1.40 g, 6.67 mmol) with acetyl chloride (5 ml) and N,N-dimethylaniline (15 ml) in the manner described for the mixture of decalols (89) and (93) gave the acetate (154) as a yellow oil (1.68 g, 100%). G.l.c. analysis (B, 160°) indicated that the only contaminants were *c.* 2% of olefinic material, which were easily removed by chromatography on neutral alumina. Distillation of a small portion gave 2β-t-*butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenyl acetate* (154) as a colourless oil b.p.

105-110° (block)/0.5 torr, which was homogeneous by g.l.c. analysis (B, 160°) (Found: C, 76.4; H, 11.4. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2920s, 1725s, 1460s, 1400m, 1375s, 1250sb, and 1030s cm^{-1}; n.m.r. : δ5.15 (1H, X part of ABX spectrum, approximating to triplet, $J_{AX} + J_{BX} \sim 20$ Hz, axial H, -C<u>H</u>(OAc)-), 1.97 (3H, singlet, -OCOC<u>H</u>$_3$), 0.88 (9H, singlet, *t*-butyl), and 1.9-1.1 (complex, other H); mass spectrum: m/e 192 (3, M^+ -60 for $C_{16}H_{38}O_2$), 136 (25), 135 (100), 134 (49), 95 (25), 94 (27), 57 (50), 43 (45), and 41 (28).

3β-t-Butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-2α-naphthalenyl acetate (155):

A solution of the 2-decalol (153) (1.05 g, 5.0 mmol) in pyridine (10 ml) and acetic anhydride (10 ml) was stirred at room temperature for 72 hr. The solution was diluted with water (100 ml), and after 1 hr, the resulting mixture was extracted with light petroleum (2 x 40 ml). The combined organic extracts were washed with water (100 ml), 10% hydrochloric acid (2 x 100 ml), 5% sodium bicarbonate solution (2 x 75 ml), dried, and evaporated to give a colourless oil (1.14 g, 95%). G.l.c. analysis (B, 170°) revealed the presence of *c.* 4% of impurities. A small sample was distilled to give *3β-t-butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-2α-naphthalenyl acetate* (155) as a colourless oil b.p. 75-80° (block)/0.4 torr, of *c.* 98% purity (B, 170°) (Found: C, 76.5; H, 11.1. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2920s, 1725s, 1450m, 1400m.sh, 1375s, 1240sb, and 1025s cm^{-1}; n.m.r. : δ4.85 (1H, complex multiplet, separation between outer lines = 24 Hz, acial H, -C<u>H</u>(OAc)-), 1.93 (3H, singlet, -OCOC<u>H</u>$_3$), 0.89 (9H, singlet, *t*-butyl), and 2.2-1.1 (complex, other H); mass spectrum: m/e 192 (0.9, M^+ -60 for $C_{16}H_{28}O_2$), 137 (26), 136 (94), 135 (24), 121 (21), 95 (22), 94 (23), 81 (22), 58 (100), 43 (50), and 41 (20).

cis-7-t-Butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (84):

The acetate (154) (810 mg, 3.2 mmol) was subjected to flash vacuum pyrolysis under the same conditions as were used for the acetate (89). A colourless oil (560 mg, 91%) was obtained and was shown by g.l.c. (N, 190°) to consist of the octalins (150) and (84) in the ratio 69:31, contaminated with *c.* 1-2% of (151).* Separation by preparative g.l.c. (K, 150°) gave (150) as a colourless oil (340 mg, 55%), identical in all respects with the sample obtained earlier, and *cis-7-t-butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene* (84), contaminated with *c.* 5% of (151) (N, 190°; E, 110°), as a colourless oil (160 mg, 26%) b.p. 105-110° (block)/18 torr (Found: C, 85.7; H, 12.3. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%. ν_{max} 3050w, 2950s, 1665w, 1440s, 1390m, 1360s, 970m, and 840s cm^{-1}; n.m.r. : δ5.33 (1H, broad, $w_{\frac{1}{2}}$ = 4 Hz, =C<u>H</u>-), 0.87 (9H, singlet, *t*-butyl), and 2.3-1.2 (complex, other H); mass spectrum: m/e 192 (9, M^{+} for $C_{14}H_{24}$), 136 (24), 135 (100), 134 (16), 93 (24), 91 (14), 79 (11), 67 (34), 57 (12), and 41 (15).

Pyrolysis of the acetate (155):

The acetate (155) (1.00 g, 3.97 mmol) was pyrolysed under the same conditions as were used for the pyrolysis of the acetate (89). A yellow oil (760 mg, 100%) was obtained which appeared according to g.l.c. analysis (C, 190°) to contain one major component (*c.* 90%). This major peak was collected by preparative g.l.c. (K, 180°) and was shown by analysis on a capillary g.l.c. column (M, 160°) to consist of a mixture of two compounds in the ratio 4:1. The major component was shown by g.l.c. and spectral properties to be the octalin (151), and the minor component must therefore be *6α-t-butyl-1,2,3,4,4aβ,5,6,8aβ-*

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* This compound was invariably obtained as a contaminant in the products of pyrolysis of (154). Since (154), and its precursor (152), were both homogeneous, the most likely explanation for the presence of (151) is that it arises by isomerization of (150) under the reaction conditions.

octahydronaphthalene (156) (see Discussion).

Part C.

1-Allyl-4-t-butylcyclohexanol (160):

A solution of allylmagnesium bromide, from allyl bromide (121 g, 1.0 mol) and magnesium turnings (24.3 g, 1.0 g.atom), in ether (200 ml) was cooled to 0° and treated, with stirring, with the dropwise addition of a solution of 4-*t*-butylcyclohexanone (104) (77.0 g, 0.50 mol) in dry ether (250 ml). The resulting solution was stirred at room temperature overnight (17 hr), then cooled in ice and treated with the dropwise addition of water (50 ml), followed by 50% aqueous acetic acid (300 ml). The aqueous layer was separated and extracted with light petroleum (2 x 150 ml). The combined organic layers were washed with water (2 x 150 ml), 5% sodium bicarbonate solution (2 x 150 ml), dried, and concentrated. Distillation afforded a *c.*51:49 mixture of the *cis*- and *trans*-isomers of 1-allyl-4-*t*-butylcyclohexanol (160), contaminated with 1% of 4-*t*-butylcyclohexanone (104), as a colourless, viscous oil (93.3 g, 95%) b.p. 129-133°/12 torr (lit.[383] 73-75°/0.2 torr.

1-Allyl-4-t-butylcyclohexene (161):

A mixture of the isomeric 1-allyl-4-*t*-butylcyclohexanols (160) (83 g, 0.42 mol) and 10% aqueous oxalic acid (600 ml) was heated under reflux under a nitrogen atmosphere for 250 hr.* The cooled reaction mixture was extracted with light petroleum (2 x 200 ml), and

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* It was in fact found, by monitoring the progress of the reaction by g.l.c. (C, 170°), that 71% conversion to the diene (161) had occurred after 75 hr, and that further reaction proceeded extremely sluggishly.

the combined organic extracts were washed with 5% sodium bicarbonate solution (200 ml), dried, and concentrated to a yellow oil (76.7 g). Analysis by g.l.c. (C, 170°) showed that the product consisted of the required diene (161)(81%)* unchanged starting material (14%) and an unidentified compound (5%). The product was chromatographed in 20 g portions on neutral alumina (1000 g, Woelm, activity I) and elution (with light petroleum) was monitored by g.l.c. (C, 170°). The fractions containing pure diene (101) (eluted first) were combined, concentrated, and distilled, giving 1-allyl-4-*t*-butylcyclohexene (161) as a colourless liquid (42.7 g, 57%) b.p. 110-112°/13 torr (lit.[210] 91-92°/6.8 torr.

7α-t-Butyl-3,4,4aα,5,6,7,8,8aβ-octahydro-1(2H)-naphthalenone (162):

(i) A solution of 2,3-dimethylbut-2-ene (460 mg, 5.5 mmol) in tetrahydrofuran (10 ml) was added to a stirred, ice-cooled solution of diborane in tetrahydrofuran (1.0M, 5.0 ml, 5.0 mmol) under a nitrogen atmosphere. The resulting solution was allowed to stir for 1 hr at room temperature, then treated with the dropwise addition, over a period of 1.5 hr, of a solution of the diene (161) (890 mg, 5.0 mmol) in tetrahydrofuran (15). After the resulting solution had been stirred for 15 hr at room temperature, powdered sodium cyanide (300 mg, 6.0 mmol) was added to it. The resulting suspension was stirred for 4.5 hr at room temperature, then cooled to -70° and treated with trifluoroacetic anhydride (1.07 ml, 1.60 g, 8.0 mmol). The resulting mixture was warmed slowly to room temperature, at which it was stirred for 1.5 hr. 3M Sodium acetate solution (5 ml) was then added, followed by 30% hydrogen peroxide (5 ml). The resulting mixture was stirred at 40-60°

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* It was in fact found, by monitoring the progress of the reaction by g.l.c. (C, 170°), that 71% conversion to the diene (161) had occurred after 75 hr, and that further reaction proceeded extremely sluggishly.

for 1.5 hr, then saturated with potassium carbonate and extracted with light petroleum (100 ml). The organic extract was washed with saturated brine (100 ml), dried, and evaporated. Distillation of the residue gave a colourless viscous oil (300 mg, 29%) b.p. 100-110° (block)/0.3 torr, which was shown by g.l.c. (D, 190°) to consist of two major components (81% and 16%) and several minor contaminants (total 3%). The major component was shown to be 7α-*t*-butyl-3,4,4aα,5,6,7,8,8aβ-octahydro-1(2H)-naphthalenone (162) by comparison with an authentic sample.

(ii) Dry liquid ammonia (250 ml) was added to a solution of the octalone (164) (4.12 g, 20 mmol) and *t*-butyl alcohol (4.44 g, 60 mmol) in dry tetrahydrofuran (40 ml). Lithium (560 mg, 80 mg.atom) was added piecewise and the resulting solution was stirred under reflux for 1 hr. Water (6 ml) was carefully added to destroy the excess of lithium, and the ammonia was allowed to evaporate. The residue was taken up in ether (100 ml) and washed with water (50 ml), followed by saturated brine (50 ml). The ether was evaporated and the residual yellow oil was taken up in acetone (15 ml) and oxidized with Jones' reagent.[331] The reaction mixture was diluted with water (150 ml) and extracted with ether (2 x 50 ml). The combined ether extracts were washed with 5% sodium bicarbonate solution (100 ml), saturated brine (100 ml), dried, and evaporated to give a yellow oil (3.96 g, 95%), which crystallized from hexane as white needles (2.57 g, 56%) m.p. 58-64°. G.l.c. analysis (D, 190°) revealed the presence of 4% of some impurity (possibly (168)). Two further recrystallizations from hexane gave pure 7α-*t*-butyl-3,4,4aα,5,6,7,8,8aβ-octahydro-1(2H)-naphthalenone (162) m.p. 69-71° (lit.[210] 69.5-70.5°).

Di-t-butyl glutarate (165):

The following procedure is based on a preparation of di-*t*-butyl malonate.[384]

A pressure bottle was cooled to below -30° and charged with ether (30 ml), glutaric acid (13.2 g, 0.10 mol), concentrated sulphuric acid (0.5 ml), and liquified isobutylene (30 ml). A rubber stopper was securely clamped into place and the bottle was shaken at room temperature until all the glutaric acid had dissolved (*c.* 40 hr). The bottle was cooled to below -30°, carefully opened, and the contents were poured into a separating funnel containing ice-cold 15% sodium hydroxide solution (100 ml). After careful shaking, the aqueous layer was separated and extracted with light petroleum (2 x 15 ml). The combined organic layers were washed with 5% sodium bicarbonate solution (50 ml), saturated brine (50 ml), dried, (potassium carbonate), and concentrated. Distillation* afforded di-*t*-butyl glutarate (165) as a colourless oil (11.2 g, 46%) b.p. 94.5-95.5°/0.8 torr (lit.[385] 96-97°/3 torr).

6-t-Butyl-1,2,3,4,5,6,7,8-octahydro-4-oxo-1-naphthalene carboxylic acid (167):

A small piece of lithium was added to stirred liquid ammonia (400 ml). After the appearance of the blue colour, a few crystals of ferric nitrate were added, followed by more lithium metal until 2.08 g (0.30 g.atom) had been added. When the blue colour had been discharged, a solution of di-*t*-butyl glutarate (165) (45.6 g, 0.19 mol) in dry

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* Some decomposition to glutaric acid and isobutylene invariably accompanied distillation, even when base-washed apparatus was used. Since decomposition started some time after the start of the distillation, but was thereafter autocatalytic, the problem was particularly severe with large scale preparations, in which long distillation times were required.

ether (70 ml) was added over a period of 4 min. The resulting solution was stirred for 2 min, and a solution of 4-*t*-butylcyclohexanone (104) (28.8 g, 0.19 mol) in ether (150 ml) was added over a period of 4 min. The reaction mixture was stirred for 1.5 hr, then decomposed by the slow addition of solid ammonium chloride (17.0 g, 0.32 mol). After more ether (200 ml) had been added, a hot water-bath was applied and the ammonia was distilled off at ether reflux. The remaining mixture was cooled in an ice-bath and water (150 ml) was added to it, slowly at first. The aqueous layer was separated and extracted with ether (100 ml). The ether layers were combined and washed with 5% hydrochloric acid (150 ml), 5% sodium bicarbonate solution (2 x 150 ml), saturated brine (250 ml), dried (sodium sulphate), and evaporated. Unchanged di-*t*-butyl glutarate (165) and 4-*t*-butylcyclohexanone (104) were removed by distillation at 180° (bath temperature)/0.3 torr, leaving the hydroxy diester (166) as an involatile viscous red oil (49.6 g, 66%). The pot residue (166) was transferred to an Erlenmeyer flask and blended with polyphosphoric acid (85%, 200 ml). The mixture was heated on a steam-bath for 2 hr, cooled, carefully diluted with ice (200 g) and water (150 ml), and extracted with a 1:1 mixture of ether and methylene chloride (4 x 200 ml). The combined extracts were washed with water (2 x 200 ml) and extracted with 5% sodium bicarbonate solution (6 x 75 ml). The alkaline extracts were combined, washed with light petroleum (2 x 100 ml), and acidified with concentrated hydrochloric acid. The resulting mixture was extracted with ether (3 x 100 ml), and the combined ether extracts were washed with water (150 ml), saturated brine (150 ml), dried, and evaporated to give a honey-brown glass (13.7 g, 29% from di-*t*-butyl glutarate). A small portion was crystallized (decolourizing charcoal) from ether-hexane to give off-white prisms m.p. 123-125°. Recrystallization to

constant m.p. (ether-hexane) gave *6-t-butyl-1,2,3,4,5,6,7,8-octahydro-4-oxo-1-naphthalene carboxylic acid* (167) as white prisms, m.p. 126-128° (Found: C, 72.1; H, 9.0. $C_{15}H_{22}O_3$ requires C, 72.0; H, 8.9%). ν_{max} (nujol) 3300-2400b, 2920s, 2730m.sh, 2600m, 1715s, 1625s, 1400m, 1370m, 1280s, 1245s, and 1165s cm^{-1}; n.m.r. : δ10.75 (1H, broad singlet, exchanges with D_2O, $-CO_2\underline{H}$), 3.17 (1H, broad, $w_{\frac{1}{2}}$ = 11 Hz, $-C\underline{H}(CO_2H)-$), 0.92 (9H, singlet, *t*-butyl), and 2.9-1.0 (complex, other H); mass spectrum: m/e 250 (78, M^+ for $C_{15}H_{22}O_3$), 194 (53), 149 (71), 147 (83), 129 (43), 107 (40), 91 (72), 57 (100), and 41 (43).

7-t-Butyl-3,4,5,6,7,8-hexahydro-1(2H)-naphthalenone (164):

A mixture of the crude keto acid (167) (12.5 g, 50 mmole) and a solution of polyphosphoric acid (40 ml) and acetic acid (60 ml) in water (250 ml) was heated under reflux for 24 hr. Ammonium sulphate (80 g) and sufficient sodium chloride to saturate the aqueous layer were added to the cooled reaction mixture, which was then extracted with ether (4 x 75 ml). The combined ether extracts were washed with water (2 x 150 ml), 5% sodium bicarbonate solution (4 x 100 ml), saturated brine (100 ml), dried, concentrated, and distilled to give 7-*t*-butyl-3,4,5,6,7,8-hexahydro-1(2H)-naphthalenone (164) as a pale yellow oil (5.9 g, 57%) b.p. 92-94°/0.1 torr (lit.[210] 110-115°/0.2 torr), which was homogeneous by g.l.c. (D, 190°; C, 230°).

Hydrogenation of the enone (164):

All hydrogenations were carried out at room temperature and atmospheric pressure in ethanol solution. A typical experiment is described below.

A solution of the α,β-unsaturated ketone (164) (103 mg, 0.5 mmol) in ethanol (5 ml) containing 3M hydrochloric acid (0.5 ml) was hydrogenated at ambient temperature and pressure in the presence of

c. 10 mg of the appropriate catalyst (Table IV.2). When the theoretical amount of hydrogen (11 ml) had been taken up, the hydrogen atmosphere was removed and the reaction mixture was stirred for a further 3 hr. The catalyst was removed by filtration through celite and the filtrate was evaporated and the residue was taken up in light petroleum (20 ml). The resulting solution was washed with 5% sodium bicarbonate solution (20 ml), dried, and evaporated, and the product was analysed by g.l.c. (D, 190^{o}) (Table IV.2).

Hydrogenations under neutral conditions were performed in a similar manner, but with no acid present. When the theoretical amount of hydrogen (11 ml) had been taken up, the catalyst was removed by filtration and the filtrate was analysed by g.l.c. (D, 190^{o}). To effect equilibration of the products obtained under these conditions, 3M hydrochloric acid (0.5 ml) was added to a solution of the products of hydrogenation in ethanol (5 ml), and the resulting solution was stirred at room temperature for 3 hr. At the end of this time, the solution was concentrated, and the residue was taken up in light petroleum (20 ml), washed with 5% sodium bicarbonate solution (20 ml), dried, and evaporated. The residue was analysed by g.l.c. (D, 190^{o}).

The product mixtures from a number of experiments were combined and the major component was separated by preparative g.l.c. (L, 240^{o}). The spectral and g.l.c. properties were identical with those of the *trans*-fused decalone (162) obtained by lithium-ammonia reduction of the octalone (164) and from earlier work.[210] In addition, recrystallization from hexane gave white needles, m.p. and mixed m.p. 69-70^{o} (lit.[210] 69.5-70.5^{o}).

7-t-Butyl-3,4,5,6,7,8-hexahydro-1(2H)-naphthalenone p-toluenesulphonylhydrazone (170):

A solution of the octalone (164) (1.35 g, 6.55 mmol) and *p*-toluenesulphonohydrazide (1.34 g, 7.20 mmol) in ethanol (1.5 ml) was heated under reflux for 12 hr. On cooling the solution to room temperature, the tosylhydrazone (170) crystallized as yellow prisms (1.73 g, 71%) m.p. 142-144°. Recrystallization to constant melting point afforded *7-t-butyl-3,4,5,6,7,8-hexahydro-1(2H)-naphthalenone p-toluenesulphonylhydrazone (170)* as white prisms m.p. 148-151°. (Found: C, 67.2; H, 8.0; N, 7.6. $C_{21}H_{30}N_2O_2S$ requires C, 67.3; H, 8.1, N, 7.5%). ν_{max} (nujol) 3190s sharp, 2910s, 1640w, 1600w, 1405s, 1345s, 1165s, and 815s cm^{-1}; n.m.r. ($CDCl_3$) : δ8.1-7.1 (4H, AA'BB' system centred on 7.94 and 7.31, $J_{AB} = J_{A'B'} = 8$ Hz, $J_{AA'} = J_{BB'} \sim 1.5$ Hz, aromatic H), 6.6 (1H, broad, exchanges with D_2O, =NN<u>H</u>-Ts), 2.43 (3H, singlet, Ar<u>CH</u>$_3$), 0.92 (9H, singlet, *t*-butyl), and 2.4-1.2 (complex, other H).

Reaction of (170) with sodium cyanoborohydride:

A few small crystals of bromocresol green were added to a solution of the tosylhydrazone (170) (374 mg, 1 mmol), in a 1:1 mixture of dimethylformamide and sulpholane (5 ml). The pH of the solution was adjusted to *c.* 3.8 by adding concentrated hydrochloric acid until the green solution became tan coloured. The solution was then stirred and heated at 110° for 3 hr, during which time the pH was maintained at below 3.8 by adding concentrated hydrochloric acid as required. After cooling, the solution was diluted with water (25 ml) and extracted with light petroleum (2 x 20 ml). The combined extracts were washed with water (3 x 40 ml), dried, evaporated, and distilled to give a colourless oil (154 mg, 80%) b.p. 120-130° (block)/20 torr. G.l.c. analysis (N, 180°) revealed the presence of three compounds.

Comparison of g.l.c. properties with authentic samples indicated that the major component (62%) was the *trans*-octalin (85), and that of the other two components (19% each), the one with a g.l.c. retention time nearly identical to that of (85) was the *cis*-octalin (86). The third component was not identified.

Part D.

6α—t—Butyl-3,4,4aβ,5,6,7,8,8aβ-octahydro-2(1H)-naphthalenone (171):

A solution of the mixture of octalones (138) and (139) (103 g, 0.50 mol) in ethanol (500 ml) containing 3M hydrochloric acid (50 ml) was hydrogenated at atmospheric pressure and room temperature in the presence of a 5% palladium-carbon catalyst (10.3 g). The progress of the reaction was monitored by g.l.c. in the following manner. Aliquots (*c.* 0.5 ml) of the reaction mixture were withdrawn at intervals by syringe, diluted with light petroleum (*c.* 1.5 ml), and shaken briefly with powdered anhydrous potassium carbonate. After centrifugation, the supernatant liquid was analysed by g.l.c. (D, 190°). When starting material had been totally consumed* (*c.* 40 hr), the catalyst was removed by filtration through celite and the filtrate was concentrated under reduced pressure. The concentrate was diluted with light petroleum (400 ml) and the aqueous layer was removed. The organic phase was washed with water (300 ml), 5% sodium bicarbonate solution (200 ml), dried, and evaporated. Distillation of the residue afforded 6α-*t*-butyl-3,4,4aβ,5,6,7,8,8aβ-octahydro-2(1H)-naphthalenone (171) as a colourless oil (88.2 g, 85%) b.p. 100-101°/0.2 torr (lit.[267] 79°/0.12 torr) which contained, according to g.l.c. analysis (B, 170°; D, 190°; G, 200°; H, 150°), less than 0.5% of a single impurity.

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* At this stage, g.l.c. analysis indicated the presence of only one unidentified contaminant (*c.* 4%) of the decalone (171).

6α-t-Butyl-3-hydroxymethylene-3,4,4aβ,5,6,7,8,8aβ-octahydro-2(1H)-naphthalenone (179):

A suspension of sodium hydride (0.57 g, 24 mmol - as 1.14 g of a 50% dispersion in mineral oil) in dry ether (15 ml) was cooled in ice and placed under a nitrogen atmosphere. Into this stirred suspension was dropped a solution of the ketone (171) (4.16 g, 20 mmol) and ethyl formate (4.44 g, 60 mmol) in ether (30 ml) containing several drops of ethanol. The resulting mixture was stirred at room temperature for 20 hr, after which time ethanol (6 ml) was added. After stirring for a further 1 hr, the mixture was treated with water (30 ml), and stirred until the solid cake had dissolved. The ether layer was separated and extracted with 5% sodium hydroxide solution (2 x 50 ml). The combined aqueous layers were washed with light petroleum (2 x 30 ml), acidified with concentrated hydrochloric acid, and extracted with ether (2 x 40 ml). The combined ether extracts were washed with water (50 ml), 5% sodium bicarbonate solution (50 ml), saturated brine (50 ml), dried, and evaporated to give a yellow crystalline solid (3.30 g, 70%). Recrystallization from hexane gave *6α-t-butyl-3-hydroxymethylene-3,4,4aβ,5,6,7,8,8aβ-octahydro-2(1H)-naphthalenone* (179) as white needles (2.00 g, 42%) m.p. 94-95°. Two further recrystallizations from hexane did not alter the melting point (Found: C, 76.0; H, 10.3. $C_{15}H_{24}O_2$ requires C, 76.2; H, 10.2%). ν_{max} (nujol) 2910s, 1645s, 1590sb, 1385s, 1370s, 1170s, 875s, and 775s cm^{-1}; n.m.r. : δ14.3 (1H, broad, exchanges with D_2O, -OH), 8.64 (1H, singlet, =CHOH), 0.87 (9H, singlet, *t*-butyl), and 2.9-1.0 (complex, other H); mass spectrum: m/e 236 (100, M^+ for $C_{15}H_{24}O_2$), 180 (46), 123 (50), 95 (30), 81 (36), 79 (34), 67 (30), 57 (84), 55 (30), and 41 (35).

7α-t-Butyl-3,4,4aβ,5,6,7,8,8aβ-octahydro-3-oxo-2-naphthalenecarbaldehyde (180):

A solution of the hydroxymethylene ketone (179) (572 mg, 2.0 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (545 mg, 2.4 mmol) in sodium dried dioxan (30 ml) was stirred at room temperature and under a nitrogen atmosphere for 2 hr. The reaction mixture was diluted with methylene chloride (50 ml) and filtered through a short column of neutral alumina (6 g), which was then washed with more methylene chloride (50 ml). The combined eluates were evaporated and the residue was taken up in light petroleum (40 ml), washed with water (6 x 50 ml), dried, and evaporated to give *7α-t-butyl-3,4,4aβ,5,6,7,8,8aβ-octahydro-3-oxo-2-naphthalenecarbaldehyde* (180) as a yellow oil (210 mg, 45%). ν_{max} 2920s, 2720w, 2660w, 1720s.sh, 1690s, 1680s, 1610s, 1370s, 1240s, 810m, and 755m cm^{-1}; n.m.r. : δ10.02 (1H, singlet, -CH=O), 7.60 (1H, doublet, J = 5 Hz, -CH=C), 0.88 (9H, singlet, *t*-butyl), and 2.8-0.7 (complex, other H). Because of its instability and tendency to undergo rapid polymerization, the keto aldehyde (180) was used in the next step without further purification, and was not characterized other than spectroscopically.

Decarbonylation of (180):

A solution of the keto aldehyde (210 mg, 0.90 mmol) and tris-(triphenylphosphine)rhodium chloride (925 mg, 1.0 mmol) in dry benzene (10 ml) was heated under reflux under a nitrogen atmosphere for 4 hr. The cooled reaction mixture was filtered and evaporated. The residue was thoroughly washed with ethanol (50 ml), and the resulting ethanol solution was filtered and evaporated. Distillation of the residue gave a pale yellow oil (83 mg, 40%), b.p. 120-130° (block)/ 0.3 torr which was shown by g.l.c. (B, 190°) to be a 60:40 mixture of

two compounds. The spectral properties of the mixture were consistent with the major component being the ocatalone (173) (see later).

3α-Bromo-6β-t-butyl-3,4,4aα,5,6,7,8,8aα-octahydro-2(1H)-naphthalenone (172):

A solution of bromine (16.0 g, 0.10 mol) in acetic acid (100 ml) was added slowly to a stirred solution of the decalone (171) (20.8 g, 0.10 mol) in acetic acid (50 ml). After it had been stirred at room temperature for 24 hr*, the resulting solution was diluted with water (1500 ml) and extracted with ether (2 x 300 ml). The combined ether extracts were washed with water (2 x 1000 ml), 5% sodium bicarbonate solution (400 ml), saturated brine (400 ml), dried, and evaporated to give a pale brown oil (27.5 g, 96%). Crystallization from hexane gave impure (see Discussion) *3α-bromo-6β-t-butyl-3,4,4aα,5,6,7,8,8aα-octahydro-2(1H)-naphthalenone (172)* as white needles (16.7 g, 58%) m.p. 78-87°. ν_{max} (nujol) 2920s, 1720s, 1400m, 1380s, 1370s, 1065m, and 820m cm^{-1}; n.m.r. : δ4.64 (1H, X part of ABX spectrum, approximating to doublet of doublets, $J_{AX} + J_{BX} = 19$ Hz, axial H, -CHBr-), 0.90 (9H, singlet, *t*-butyl), and 2.7-1.0 (complex, other H); mass spectrum : m/e 288 (1, M^{+} for $C_{14}H_{23}Br^{81}O$), 2.86 (1, M^{+} for $C_{14}H_{28}Br^{79}O$), 232 (10), 230 (11), 151 (23), 150 (17), 96 (11), 57 (100), 56 (11), 55 (15), and 41 (19). A satisfactory analysis could not be obtained (see Discussion).

6α-t-Butyl-4aβ,5,6,7,8,8aβ-hexahydro-2(1H)-naphthalenone (173):

(i) A solution of the impure bromoketone (172) (24.6 g, 85.5 mmol) in N,N-dimethylacetamide (200 ml) was stirred and heated under

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* Control experiments showed that in fact 1 hr was sufficient time for the equilibrium to be established (see Discussion).

reflux with calcium carbonate (30.0 g, 0.30 mmol) under a nitrogen atmosphere for 1 hr. The cooled reaction mixture was diluted with water (1000 ml) and light petroleum (300 ml), and the excess of calcium carbonate was decomposed with dilute hydrochloric acid. The aqueous layer was separated and extracted with light petroleum (300 ml). The combined organic layers were washed with water (2 x 1000 ml), 10% sodium hydroxide (2 x 500 ml), water (1000 ml), dried, and evaporated to give a yellow oil (8.81 g), which was shown by g.l.c. (B, 190°) to consist of 5% of the decalone (171), and 20% and 75% of the octalones (138) and (173) respectively. The mixture was chromatographed in 3 g portions on neutral alumina (400 g). Elution with 5% ether-light petroleum (monitored by g.l.c. -B, 190°) gave firstly a mixture of (171) and (173), followed by pure (173), then (173) contaminated by (138). The early and late impure fractions were combined and rechromatographed under the same conditions. In this way, pure *6α-t-butyl-4aβ,5,6,7,8,8aβ-hexahydro-2(1H)-naphthalenone* (173) was obtained as a colourless oil (4.20 g, 24%) b.p. 92-94°/0.1 torr (Found: C,81.7; H, 10.8. $C_{14}H_{22}O$ requires C, 81.5; H, 10.8%). ν_{max} 2920s, 1680s, 1615m, 1395s, 1370s, 1240s, 790s, and 780s cm^{-1}; n.m.r. : δ6.84 (1H, doublet of doublets, $J_{4,4a}$ = 5 Hz, $J_{3,4}$ = 10 Hz, -CH=C<u>H</u>-C=O), 5.83 (1H, doublet, $J_{3,4}$ = 10 Hz, -CH=C<u>H</u>-C=O), 0.88 (9H, singlet, *t*-butyl), and 2.6-0.8 (complex, other H); mass spectrum : m/e 206 (M^+ for $C_{14}H_{22}O$), 177 (43), 149 (24), 108 (17), 95 (22), 57 (43), 43 (23), 41 (100), and 39 (23).

(ii) A solution of the impure bromoketone (172) (574 mg, 2 mmol) and semicarbazide hydrochloride (245 mg, 2.2mmol) in acetic acid was gently boiled in an open flask for 6 min. The cooled solution was diluted with water (25 ml) and extracted with ether (20 ml). The ether extract was washed with water (2 x 40 ml) and evaporated to give a semicrystalline orange solid (410 mg). This material was dissolved in

dioxan (10 ml) and treated with the slow addition of 50% sulphuric acid (10 ml), with ice cooling. The resulting mixture was poured into water (100 ml), and extracted with light petroleum (2 x 50 ml). The combined extracts were washed with water (4 x 100 ml), 5% sodium bicarbonate solution (50 ml), dried, and evaporated to give a yellow oil (200 mg, 48%). The spectral properties of this product, as well as g.l.c. analysis (B, 190°) indicated that it had the same composition as the crude product from part (i).

6β-t-Butyl-3α,4α-epoxy-3,4,4aα,5,6,7,8,8aα-octahydro-2(1H)-naphthalenone (174):

A 5% sodium hydroxide solution (4.0 ml, *c.* 5.0 mmol) was added dropwise to a stirred, ice-cooled solution of the enone (173) (4.12 g, 20.0 mmol) in dioxan (40 ml) and dimethoxyethane (10 ml) containing 30% hydrogen peroxide (2.06 ml, 24.0 mmol). The resulting mixture was stirred at 0-5° until g.l.c. analysis (B, 190°) indicated that all of the starting material (173) had been consumed (*c.* 24 hr). The reaction mixture was diluted with water (500 ml) and extracted with light petroleum (3 x 100 ml). The combined organic extracts were washed with water (5 x 500 ml), dried (sodium sulphate), and evaporated to give a mass of white crystals (4.40 g, 99%) m.p. 60-65°, which were homogeneous by g.l.c. analysis (B, 190°). Recrystallization of a portion from hexane afforded *6β-t-butyl-3α,4α-epoxy-3,4,4aα,5,6,7,8,8aα-octahydro-2(1H)-naphthalenone* (174) as white needles of m.p. 70-71°. Two further recrystallizations (hexane) did not alter the melting point (Found: C, 75.7; H, 9.9. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%). ν_{max} (nujol) 2920s, 1700s, 1385s.sh, 1370s, 1050m, 1030m, 945m, 850s. sh, 845s, and 810m cm^{-1}; n.m.r. : δ3.30 (1H, doublet of doublets, $J_{3,4}$ = 4.0 Hz, $J_{4,4a}$ = 2.8 Hz, -CH(O)CH-C=O), 3.07 (1H, doublet,

$J_{3,4}$ = 4.0 Hz, -CH(O)CH-C=O), 0.87 (9H, singlet, *t*-butyl), and 2.6-0.8 (complex, other H); mass spectrum : m/e 222 (7, M^+ for $C_{14}H_{22}O_2$), 166 (52), 149 (53), 137 (31), 124 (21), 123 (33), 120 (26), 95 (24), 84 (21), 81 (22), and 57 (100).

7β-t-Butyl-1,4,4aα,5,6,7,8,8aα-octahydro-1α-naphthalenol (175):

Hydrazine hydrate (100%, 3.15 g, 60 mmol) was added to a stirred, ice-cooled solution of the epoxy ketone (174) (4.44 g, 20.0 mmol) in methanol (50 ml). The resulting yellow solution was treated with the dropwise addition of acetic acid (240 mg, 4.0 mmol), after which it was allowed to warm to room temperature. After it had been stirred for a total of 2 hr, the solution was concentrated to a small volume (*c.* 15 ml), diluted with water (150 ml), and extracted with light petroleum (3 x 50 ml). The combined extracts were washed with 5% sodium bicarbonate solution (100 ml), water (200 ml), dried, and evaporated to give an orange oil (4.16 g, 100%). Filtration through a column of neutral alumina (50 g, elution with light petroleum) gave a pale yellow oil, homogeneous by g.l.c. (B, 190°), which slowly crystallized on standing. Recrystallization from hexane gave *7β-t-1,4,4aα,5,6,7,8,8aα-octahydro-1α-naphthalenol* (175) as fine white needles (3.15 g, 75%), m.p. 79-81°. Two further recrystallizations (hexane) gave m.p. 82° (Found: C, 81.0; H, 11.5. $C_{14}H_{24}O$ requires C, 80.7; H, 11.6%). ν_{max} (nujol) 3300sb, 3000w,sh, 1645w, 1395w, 1375 m.sh, 1370m, 1010s, and 990s cm^{-1}; n.m.r. : δ5.77 (2H, broad, $w_{\frac{1}{2}}$ = 6 Hz, -CH=CH-), 3.63 (1H, broad, $w_{\frac{1}{2}}$ = 8 Hz, -CH(OH)-CH=), 3.3 (1H, variable, exchanges with D_2O, -OH), 0.85 (9H, singlet, *t*-butyl), and 2.3-0.9 (complex, other H); mass spectrum: m/e 208 (12, M^+ for $C_{14}H_{24}O$), 92 (21), 91 (46), 84 (49), 70 (100), 57 (80), 55 (21), 44 (26), and 41 (36).

7β-t-Butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenol (176):

The hydrogenation catalyst, 5% rhodium-on-alumina (620 mg), was stirred with a solution of sodium hydroxide (1.9 g) in methanol (40 ml) for 1 hr before use. To this suspension was added a solution of the allylic alcohol (175) (3.11 g, 14.9 mmol) in methanol (100 ml), and the resulting mixture was stirred at room temperature under a hydrogen atmosphere until hydrogen uptake ceased. After filtration through a pad of celite, the methanol solution was concentrated and the residue was taken up in light petroleum (100 ml). The solution was washed with water (100 ml), dried, and evaporated to give a viscous yellow oil (3.15 g, 100%), which was shown to be homogeneous by g.l.c. analysis (B, 180°; D, 190°). Distillation of a small portion gave pure *7β-t-butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenol* (176) as a colourless oil b.p. 100-110° (block)/1.5 torr (Found: C, 80.0; H, 12.4. $C_{14}H_{26}O$ requires C, 79.9; H, 12.5%). ν_{max} 3300sb, 2900s, 1400s, 1370s, 1130s, 995s, 975s, 965s, and 870m cm^{-1}; n.m.r. : δ3.67 (1H, broad, $w_{\frac{1}{2}}$ = 6 Hz, equatorial H, -CH(OH)-), 3.0 (1H, variable, exchanges with D_2O, -OH), 0.84 (9H, singlet, *t*-butyl), and 2.2-0.9 (complex, other H); mass spectrum : m/e 210 (1, M^+ for $C_{14}H_{26}O$), 137 (55), 136 (100), 135 (59), 94 (44), 67 (33), 57 (66), and 41 (30).

7α-t-Butyl—3,4,4aβ,5,6,7,8,8aβ-octahydro-1(2H)-naphthalenone (158):

A solution of the decalol (176) (280 mg, 1.33 mmol) in acetone (5 ml) was oxidized with an excess of Jones' reagent[331] at room temperature for 5 min, then poured into water (50 ml) and extracted with light petroleum (2 x 20 ml). The combined extracts were washed with water (40 ml), 5% sodium bicarbonate solution (40 ml), dried, and evaporated. Distillation of the oily residue gave *7α-t-butyl-3,4,4aβ,5,6,7,8,8aβ-octahydro-1(2H)-naphthalenone* (158) as a

colourless oil (190 mg, 68%) b.p. 95-100° (block)/0.3 torr which was homogeneous by g.l.c. (B, 170°) (Found: C, 80.8; H, 11.9. $C_{14}H_{24}O$ requires C, 80.7; H, 11.6%). ν_{max} 2920s, 1700s, 1400w, 1370m, and 1225m cm^{-1}; n.m.r. : δ0.87 (singlet, *t*-butyl) and 2.5-1.0 (complex, other H); mass spectrum: m/e 208 (14, M^{+} for $C_{14}H_{24}O$), 153 (23), 152 (46), 110 (58), 97 (100), 91 (18), 81 (15), 67 (22), 57 (58), 55 (20), and 41 (34).

7β-t-Butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenyl acetate (177):

A solution of the decalol (176) (1.17 g, 5.56 mmol) in pyridine (10 ml) and acetic anhydride (10 ml) was stirred at room temperature for 41 hr, then poured into water (100 ml). After 1 hr, the resulting mixture was extracted with light petroleum (2 x 30 ml). The extracts were combined and washed with water (100 ml), 10% hydrochloric acid (2 x 50 ml), 5% sodium bicarbonate solution (50 ml), dried, and evaporated to yield a yellow oil (1.39 g, 99%), which was shown to be homogeneous by g.l.c. analysis (B, 180°). Distillation of a small portion gave pure *7β-t-butyl-1,2,3,4,4aα,5,6,7,8,8aα-decahydro-1α-naphthalenyl acetate* (177) as a colourless oil b.p. 100-105° (block)/0.3 torr which crystallized on standing, m.p. 46-47° (Found: C, 76.2; H, 11.1. $C_{16}H_{28}O_2$ requires C, 76.1; H, 11.2%). ν_{max} 2920s, 1730s, 1395w, 1380m.sh, 1370s, 1240sb, and 955 m cm^{-1}; n.m.r. : δ4.72 (1H, broad, $w_{\frac{1}{2}}$ = 6 Hz, equatorial H, -C<u>H</u>(OAc)-), 1.98 (3H, singlet, -OCOC<u>H</u>$_3$), 0.86 (9H, singlet, *t*-butyl), and 2.1-0.9 (complex, other H); mass spectrum : m/e 192 (52, M^{+} -60 for $C_{16}H_{28}O_2$), 136 (42), 135 (100), 121 (22), 94 (28), 67 (22), 57 (46), 43 (36), and 41 (22).

cis-2-t-*Butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene (86):*

The acetate (177) (1.26 g, 5.0 mmol) was subjected to flash

vacuum pyrolysis under the same conditions as were used for the acetate (89). A yellow oil (660 mg, 69%) was obtained and was shown by g.l.c. (C, 190°) to consist of the octalins (86) and (178) in a 36:64 ratio (*c.* 92%), together with *c.* 8% of unidentified minor impurities. The product was chromatographed on silica impregnated with silver nitrate (80 g). Elution with light petroleum (monitored by g.l.c. -C, 190°) gave (86) (*c.* 93% pure) followed by (178) (*c.* 93% pure). Purification of both compounds by preparative g.l.c. (K, 190°) gave cis-*2*-t-*butyl-1,2,3,4,4a,5,6,7-octahydronaphthalene* (86) of *c.* 98% purity as a colourless oil (187 mg, 19%) b.p. 110-113° (block)/13 torr (Found: C, 87.5; H, 12.5. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3050w.sh, 2920s, 1660w, 1390m, 1360s, 985w, and 790w cm^{-1}; n.m.r. : δ5.35 (1H, broad, $w_{\frac{1}{2}}$ = 9 Hz, =C<u>H</u>-), 0.87 (9H, singlet, *t*-butyl), and 2.3-1.0 (complex, other H); mass spectrum : m/e 192 (17, M^{+} for $C_{14}H_{24}$), 136 (24), 135 (100), 93 (45), 91 (21), 81 (22), 79 (42), 67 (62), 57 (70), 55(30), and 41 (64), and *2α-t-butyl-1,2,3,4,4aβ,5,6,8aβ-octahydronaphthalene* (178) as a homogeneous colourless oil (218 mg, 23%) b.p. 106-110° (block)/12 torr (Found: C, 86.9; H, 12.3. $C_{14}H_{24}$ requires C, 87.4; H, 12.6%). ν_{max} 3030s, 2920s, 1650m, 1390s, 1360s, 805m, 710s, and 690s cm^{-1}; n.m.r. : δ5.58 (2H, broad, $w_{\frac{1}{2}}$ = 5 Hz, -C<u>H</u>=C<u>H</u>-), 0.85 (9H, singlet, *t*-butyl), and 2.3-0.7 (complex, other H); mass spectrum : m/e 192 (6, M^{+} for $C_{14}H_{24}$), 135 (35), 93 (40), 91 (23), 81 (28), 80 (25), 79 (64), 77 (29), 67 (72), 57 (100), 55 (30), and 41 (66).

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