I

STUDIES ON THE TOTAL SYNTHESIS

OF MONO AND SESQUITERPENES

a thesis presented by

NIGEL BOSWORTH

in partial fulfilment of the requirements

for the award of the degree of

DOCTOR OF PHILOSOPHY

Perkin Laboratory,
Chemistry Department,
Imperial College,
London, S.W.7.

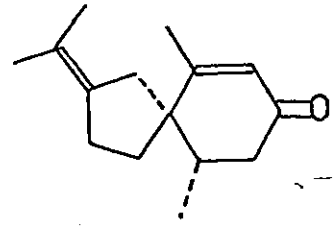
September 1973.

ABSTRACT

The review is divided into two parts. Part I describes the more interesting rearrangements of pinane derivatives described in the literature after 1967. Part II outlines the known methods of formation of spiro [4, 5] decanes (A) related to β-vetivone (B).

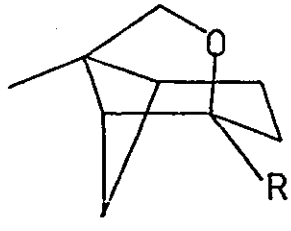


A

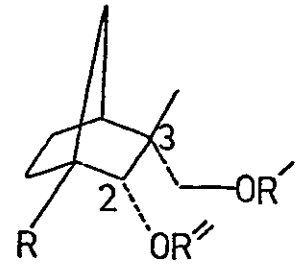


B

The discussion is divided into five parts. Part I describes the rearrangement of pinane-ethers (C) into fenchyl derivatives (D) and discusses the reaction mechanism.

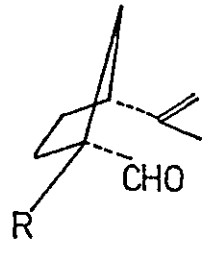


C



D

Part II summarises attempts to cleave the C(2) - C(3) bond in the fenchyl derivatives (D) to give the tetrasubstituted cyclopentane (E).

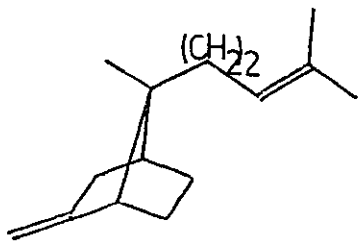


E

Part III shows that bicarbonate anion is a stronger nucleophile than dimethyl sulphoxide.

Part IV describes attempts to find a suitable R group in the ether (C) which would rearrange into the fenchyl derivative (D) and would enable the formation of a spiro [4, 5] decane structure (A). This would be accomplished by cleavage of the C(2) - C(3) bond in compound (D) and subsequent ring formation between the R and aldehyde group in compound (E).

Part V describes the attempted synthesis of γ-γ-dimethyl-allyl-9α-fenchene (F).



F

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to my supervisor, Dr. P.D. Magnus for his helpful encouragement and guidance throughout the course of this work.

Mr. Jones and his staff are thanked for their analytical service, Mrs. Boston for the A-60 n.m.r. spectra, Mr. Jenkins for the HA-100 spectra and Mrs. Lee for the mass spectra.

The technical assistance from Mr. Coleman, Mr. Carter and Mr. Ellis is gratefully acknowledge.

Nigel Bosworth,
Perkin Laboratory

September 1973.

INDEX

		Page
Abstract		ii
Acknowledgements		iv
Review		
Part I	Rearrangements of pinane derivatives.	1
Part II	Synthesis of spiro [4,5] decanes related to vetivone.	25
Discussion		
Part I	Rearrangement of ethers.	44
Part II	Cleavage of the C(2) - C(3) bond in II (Scheme IV).	59
Part III	Bicarbonate as a nucleophile.	64
Part IV	Attempts to find a suitable R group in compound I (Scheme IV).	72
Part V	Attempted synthesis of γ-γ-dimethyl-allyl-9α-fenchene.	88
Experimental		91
References		110

To my Parents

and Yvonne

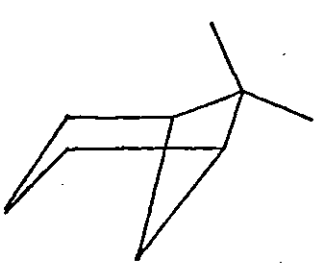
REVIEW PART I

REARRANGEMENTS OF PINANE DERIVATIVES

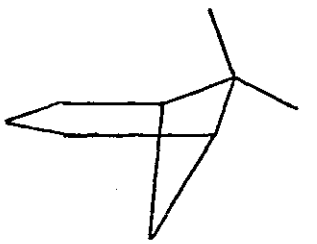
Introduction

This review will describe the more interesting research carried out after 1967 as the work prior to that date has been described[1].

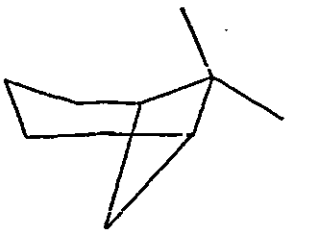
The configurations of most pinane systems are known but little work has been carried out discussing the correlation between conformation and reactivity, although its stereochemistry may ~~give~~ have an important influence on rearrangement. Examination of molecular models and physiochemical data[2-4] suggests the departure of pinane derivatives from the chair conformation (1) towards a planar conformation (2) and may even take up the boat conformation (3).



(1)



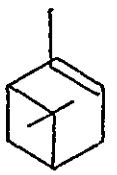
(2)



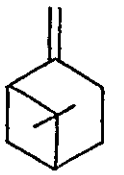
(3)

Thermal rearrangements

The problem of the isomerisation of α- and β-pinene [4,5] has been extensively studied since 1885.

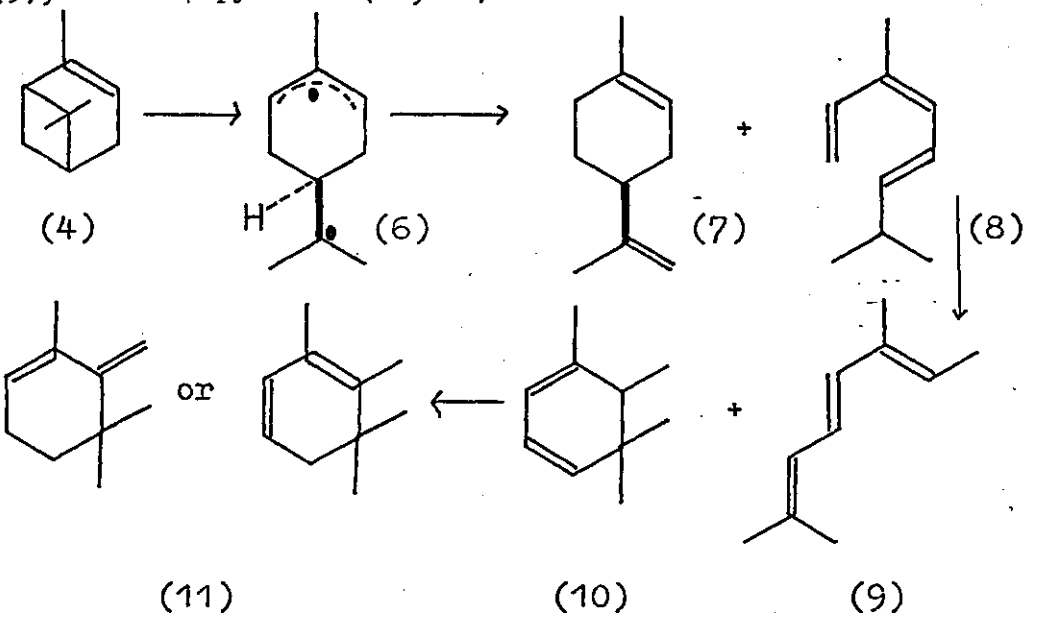


(4)

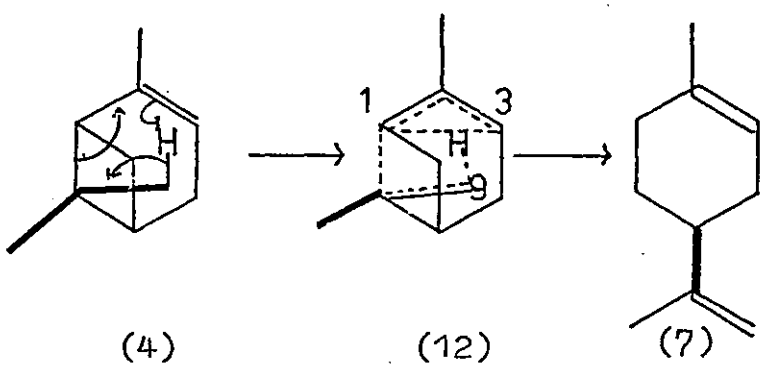


(5)

A mechanism for the thermal isomerisation of α-pinene (4) was suggested by Burwell[5] in 1951. It was postulated that the biradical (6) was produced in the first stage of the reaction and that it was converted into dipentene (7) [dipentene is (±) limonene] or ocimene (8). Ocimene was thought to give as secondary products allo-ocimene (9), α- and β-pyranone (10, 11).



Bochwic and Kapuscinski[6] have put forward a multicentre reaction mechanism:

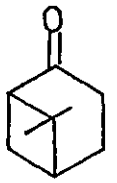


Evidence for the intermediate (12) is obtained from thermodynamic and kinetic data. They state that the reaction is first order unimolecular, not affected by solvent polarity, uninfluenced by catalysts and

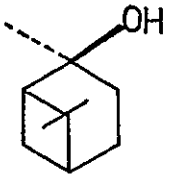
inhibitors of free radical mechanisms. The isomerisation reaction of α-pinene (4) to dipentene (7) is characterised by a negative entropy of activation. These features are characteristic of a multicentre transition state.

To explain the fact that the product is a mixture of (+) and (-) limonene i.e. dipentene the C(9) hydrogen must be transferred in equal proportions to C(1) and C(3). The reason for the equal participation of both isomerisation directions is explained by the increase in entropy of a racemic system as well as the gain in energy when a racemate, and not an optically active system is produced.

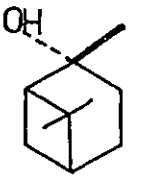
The pyrolysis of various nopinone (13) derivatives have been studied[7-12]. The pyrolysis of the methyl-nopinols (14) and (15) have been reported by Ohloff and Klein[7] to give linalool (16).



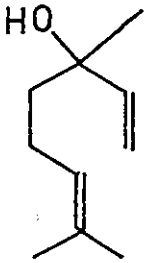
(13)



(14)

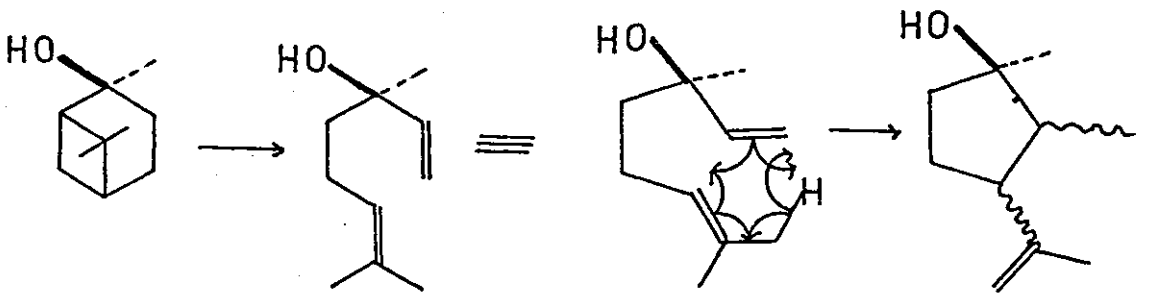


(15)



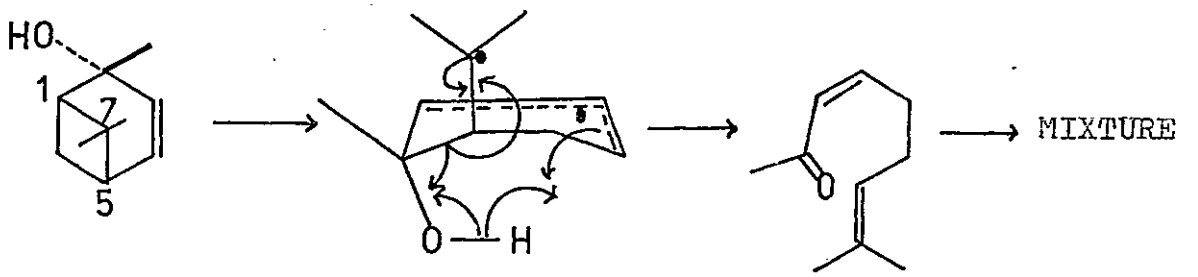
(16)

Coxon, Garland and Hartshorn[8-10] have repeated Ohloff and Klein's work using the same pyrolysis conditions (580°, with a short contact time of *ca.* 0.1s). They showed that linalool (16) is the primary product which decomposes to a mixture of four isomeric hydroxy olefins (17).



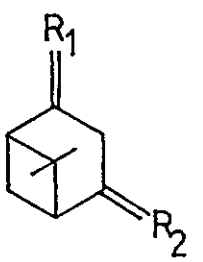
(14) (16) (17)

Coxon et al. have extended the work to investigate the possibility of using substituents to cause either cleavage of the C(1) - C(7) or the C(5) - C(7) bond in the butane ring selectively. The olefin (18) was pyrolysed to give a mixture of six compounds. The primary product



(18) (19) (20)

(20) was shown to be the result of rearrangement of the diradical (19) i.e. the effect of the Δ^3 double bond on the pyrolysis is to activate the C(5) - C(7) bond towards homolysis.



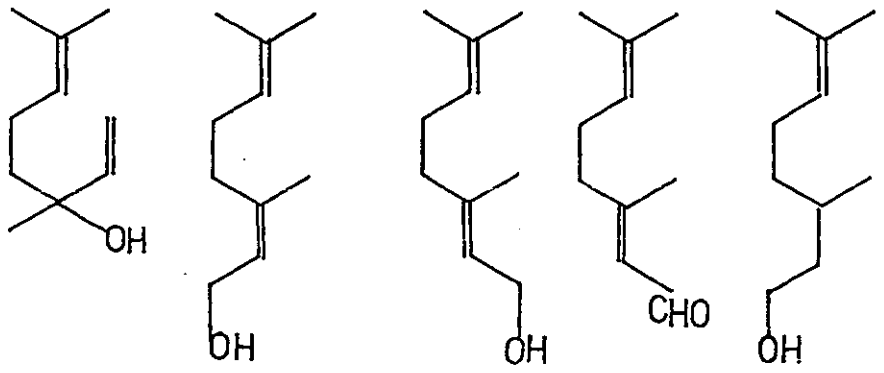
(21)

Various other derivatives (i.e. R^1 and R^2 in (21) are changed) have been pyrolysed and a relative order of effectiveness of substituents in determining which C - C bond of the cyclobutane ring cleaves initially is shown to be: exocyclic methylene > carbonyl > methyl > hydroxyl > hydrogen. At least six compounds are always obtained, usually with not more than 20% of a single component, as the primary products decompose at the temperatures used.

Rearrangement of α- and β- pinene

(a) Catalysis over solids

The formation of acyclic terpenes from pinenes is of great commercial importance[13]. This newer chemistry which was developed during the last decade covers the preparation of important compounds such as linalool (16) nerol (23), geraniol (24) citral (25) and citronellol (26). These compounds were formerly obtained



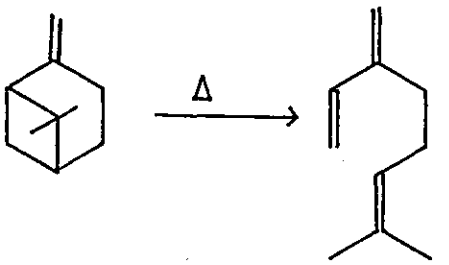
(16) (23) (24) (25) (26)

exclusively by the distillation of essential oils.

In recent years attempts have been made to isomerise the more abundant α-pinene (4) into β-pinene (5). A great many patents have appeared on the subject and a variety of catalysts such as calcium diamine, alkali (KOH) dissolved in dimethyl sulphoxide and metallic sodium. Most of these processes depend on the

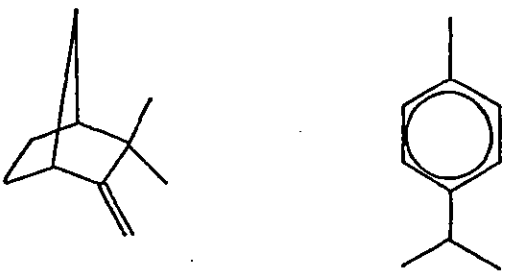
distillation of the small quantity of β-pinene (5) (5%) formed at equilibrium followed by the recycle of α-pinene (4). The high cost of distillation makes the process uneconomic.

β-pinene (5) thus produced is thermally isomerised to myrcene (27) (90%), by heating to 600° for a short contact time. Myrcene is used to prepare nerol (23), geraniol (24) etc.



(5) (27)

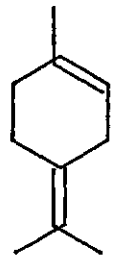
The conversion of β-pinene to dipentene (7), camphene (28) and p-cymene (29) over alumina catalysts has been the subject of extensive study.



(28) (29)

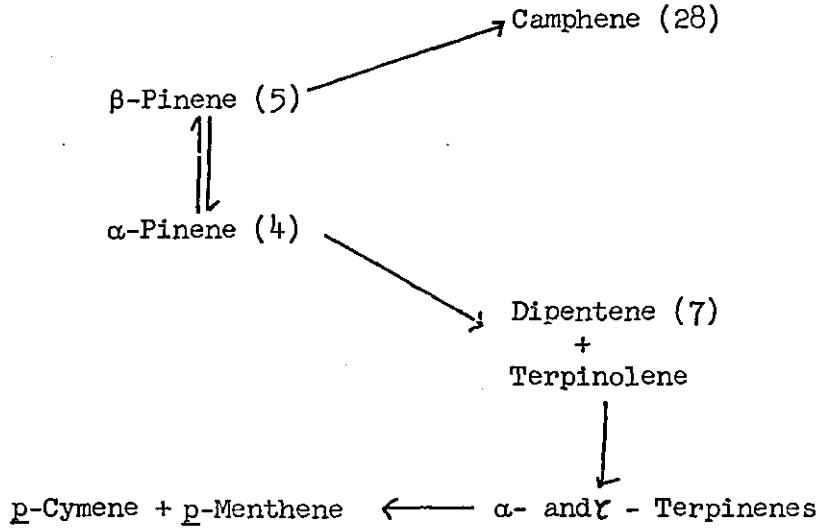
Yeddanapalli[13b] has investigated the reaction while trying to optimise the conditions for the preparation of dipentene (7). Variation of alumina was used to show that at low acid concentrations the main products are α-pinene (4) and camphene (28) and at higher acid strengths the percentage of dipentene (7) and

terpinolene (30) increases. They conclude that α-pinene (4) and camphene (28) are primary products, dipentene (7) and terpinolene



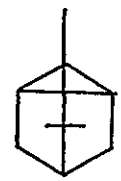
(30)

(30) are secondary products from which tertiary products are formed:



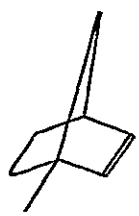
Stanilaus and Yeddanpalli[14] have also carried out distribution studies on the isomerisation of α-pinene in the vapour phase over alumina catalysts of varying acid strength. The primary products are shown to be camphene (28), tricyclene (31), β-pinene (5),

dipentene and terpinolene (30). Product-time studies also show

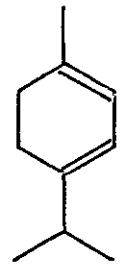


(31)

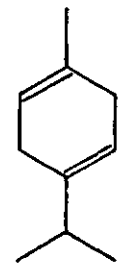
that these compounds are formed initially and decompose to give bornylene (32), α- and ϒ-terpinenes (33, 34) p-cymene (29) and p-menthene (35). The isomerisation is shown to proceed via two



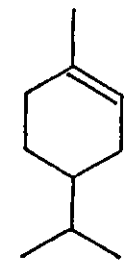
(32)



(33)

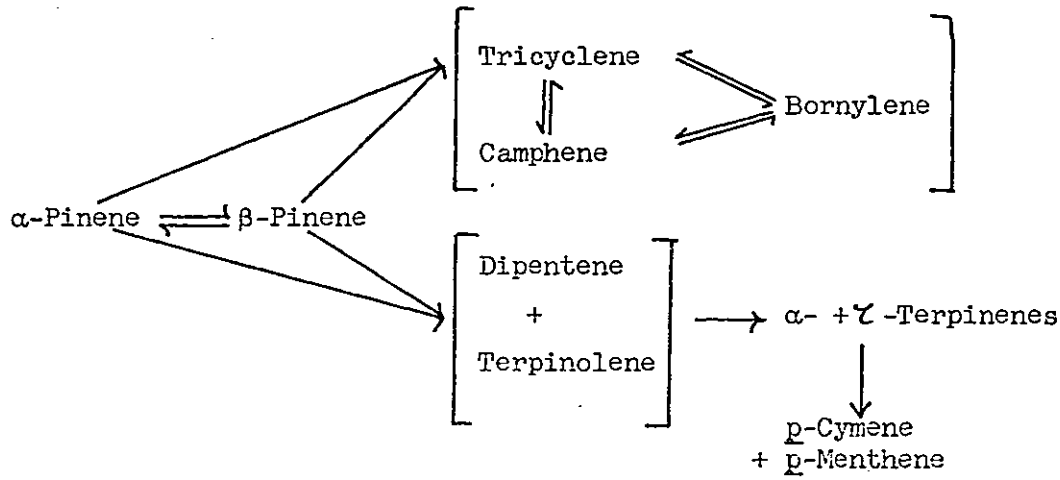


(34)



(35)

parallel paths, one giving the bi- and tricyclic products (camphene (28), β-pinene (5) and tricyclene (31)) and the other giving rise to monocyclic products (dipentene (7), terpinolene (30), α- and ϒ-terpinene (33, 34)).



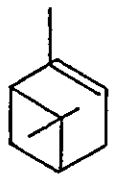
The authors[15] show that chromia-alumina catalyses the conversion of α-pinene (4) to dipentene (7) and terpinolene (30) which are then converted to α- and γ -terpinene (33, 34) and finally p-cymene (29).

Recent work by Brown on the asymmetric synthesis of optically active alcohols has increased the need for a method of obtaining highly optical pure α-pinene (4) as the α-pinene used by Brown was only 93% optically pure. Spanninger and Von Rossenburg[16] have devised a method of converting β-pinene into α-pinene of high optical purity (99%) by heating β-pinene with 20% by weight of iron-pentacarbonyl at 135° for 32 hours.

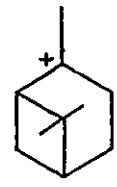
Settine[17] has subsequently published a communication describing a method for the same conversion involving refluxing for 4 hours with 15% by weight of benzoic acid to give a 99% optical yield in quantitative yield.

(b) Action of acids in the liquid phase

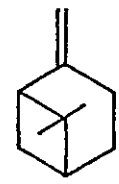
The isomeric α- and β-pinenes (4, 5) are known to react in the presence of acids to give both ring expanded (bornane or fenchane) or ring opened (p-menthane) derivatives. The two isomers would be expected to react via a common carbonium ion (36). Valkanas and



(4)



(36)



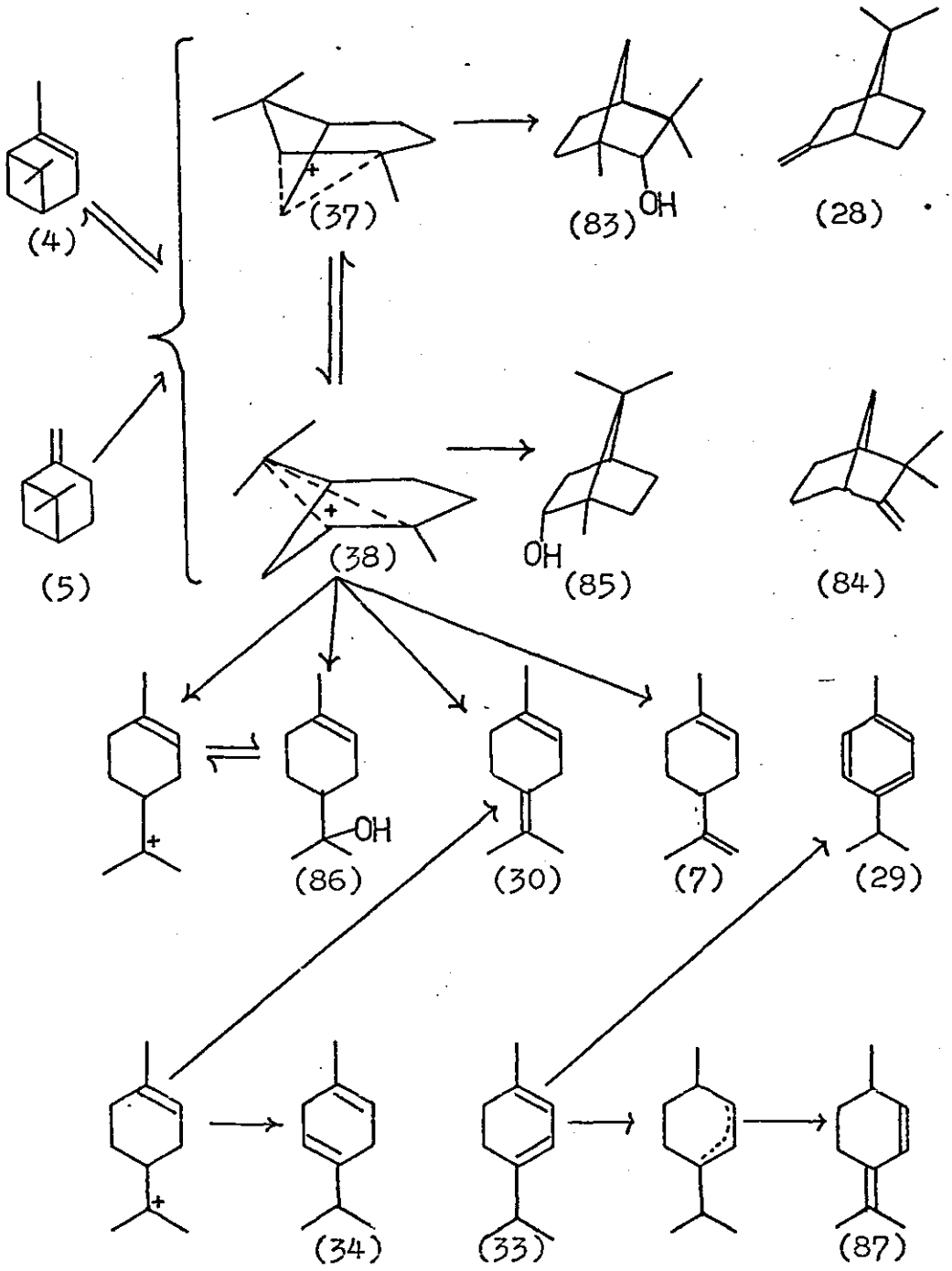
(5)

Iconomou[18] have studied the reaction and have used classical carbonium ion theory to explain the results in terms of carbonium ion (36).

Early workers found that there were quantitative differences in the products obtained from α- and β-pinene, suggesting that there are geometric differences in formally similar ions. Whittaker[19,20] has reinvestigated the reaction both quantitatively and qualitatively using aqueous ionising conditions, showing that the products of the rearrangement of the two olefins are identical in both respects. The theory that there is a common carbonium ion is supported by the fact that α-pinene is formed from β-pinene. The reaction mechanism is depicted in Scheme I. Protonation of the pinenes from the methylene-bridge side gives (38) and from the gem-dimethyl bridge side (37). As the rate of formation of the carbonium ions should vary depending on the pinene system and the product ratios are the same there must be a fast establishment of equilibrium between ions (37) and (38) prior to ion capture.

Whittaker[21] has also investigated the hydration of α- and β-pinene in media of lower dielectric constant. The reaction of the pinenes with perchloric acid in anhydrous acetic acid only gives 2-3% of acetates among the products whereas a similar reaction using sulphuric acid gives 10% acetate after the same time. These results are explained in terms of intimate ion pairs i.e. the acid reacts with the olefin in an undissociated state to give an intimate ion pair in which the counter ion is not strongly nucleophilic. Collapse of the ion pair is then unlikely, and it must either ionise giving a free ion which can yield acetates or eliminate the counter ion withdrawing a proton in a process which is the reverse of the formation of the ion pair. The intimate ion pairs behave differently as the rate of ionisation depends on the counter ion. At lower dielectric constant it is also shown that there is a predominance of

SCHEME 1

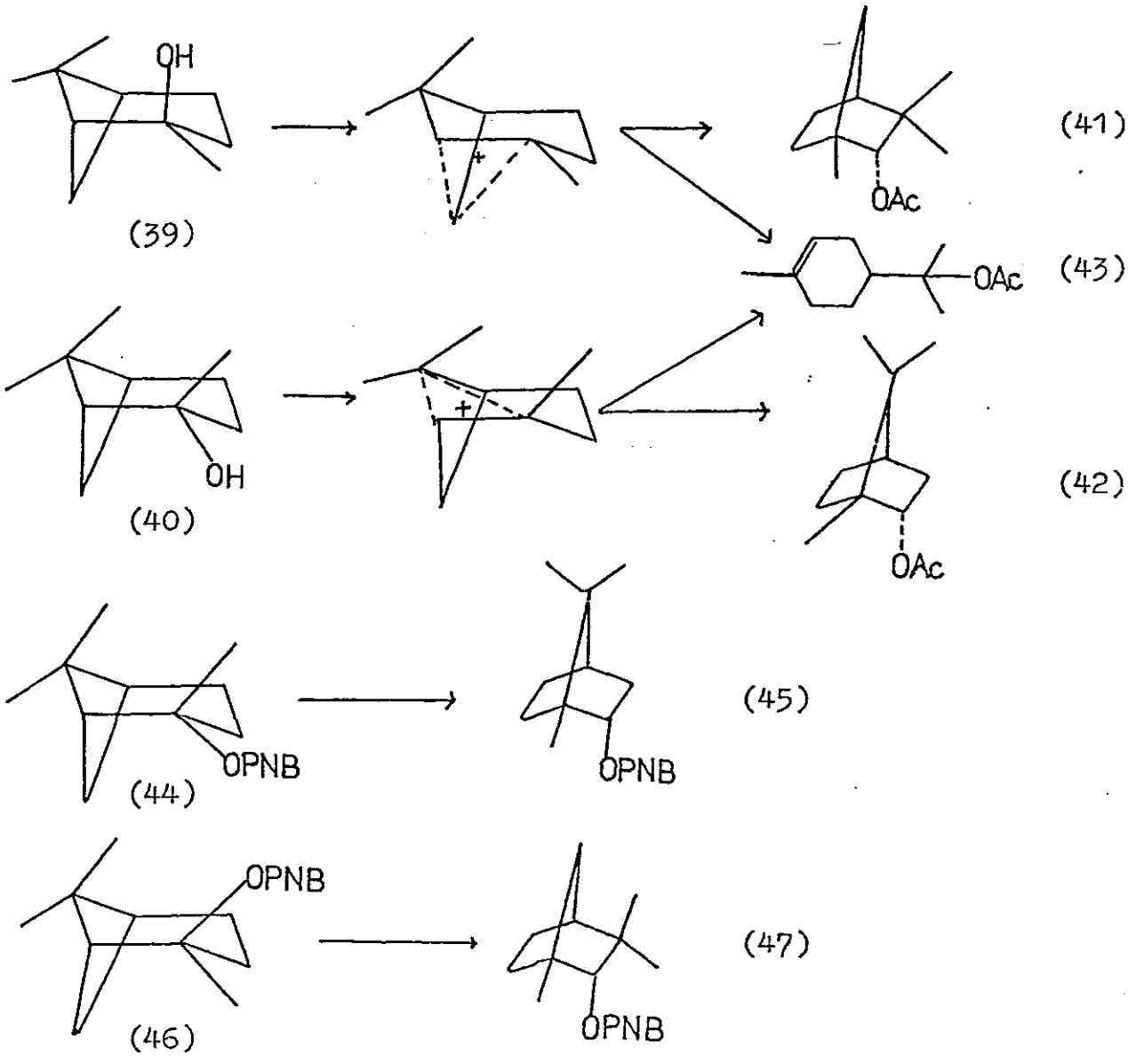


α-Pinene	(4)	Terpinolene	(30)
β-Pinene	(5)	Limonene	(7)
α-Fenchol	(83)	p-Cymene	(29)
α-Fenchene	(84)	γ-Terpinene	(33)
Borneol	(85)	α-Terpinene	(34)
Camphene	(28)	Isoterpinolene	(87)
α-Terpineol	(86)		

elimination over addition of solvent in the absence of a nucleophilic counter ion which may also be explained by the presence of an intimate ion pair.

Rearrangement of pinanols and their derivatives

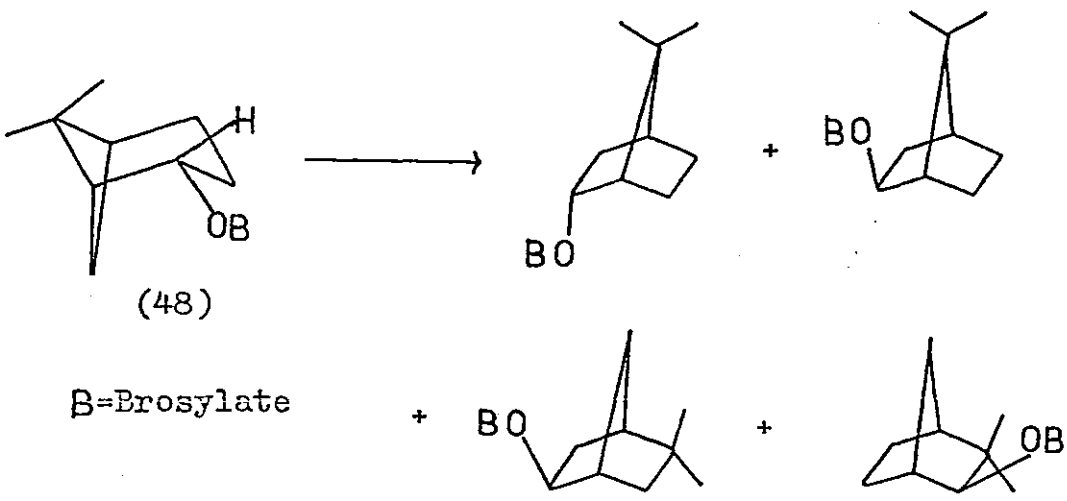
Both trans- and cis-methyl nopinols (39, 40) have been shown by Burrows and Eastman[22] to rearrange when heated with acetic anhydride to form fenchyl acetate (41) and bornyl acetate (42) together with some terpinyl acetate (43) respectively. They postulate the following mechanism:



Abraham[23] has shown that the cis-p-nitrobenzoate (44) rearranges to the bornyl-p-nitrobenzoate (45) while the trans ester rearranges to the α-fenchyl-p-nitrobenzoate (47).

The esters (45, 47) were considered to be formed by internal return from an ion pair, the formation of pure endo- isomers in each case being consistent with the well known formation of the endo-bornyl chloride from pinene hydrochloride.

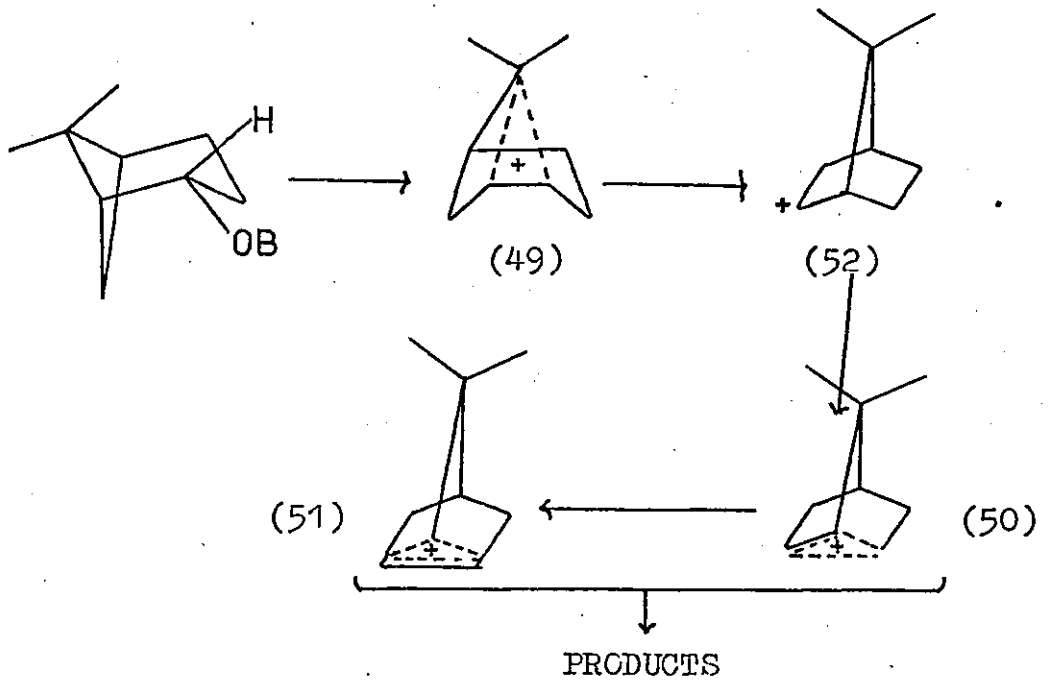
Winstein[24] has shown that the ionisation of nopinyl derivatives is strongly anchimerically assisted. β-Nopinyl brosylate (48) is shown to give the following reaction:



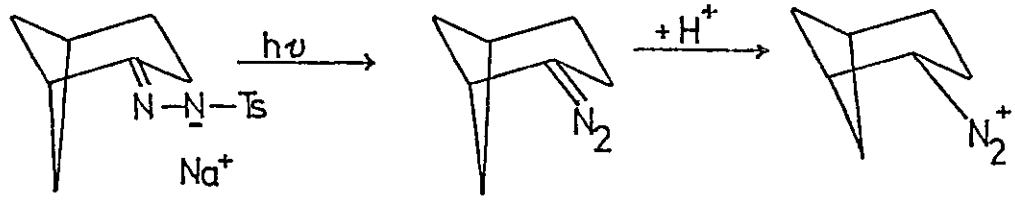
(48)

B=Brosylate

To explain the racemisation that occurs Winstein postulated a reaction scheme involving three non-classical carbonium ions (49, 50, 51) linked by a classical ion (52). Winstein was unable to explain the high ratio of exo- to endo- products.

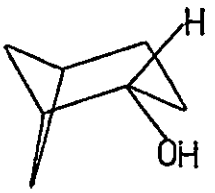


Kirmse[25] has shown that formation of exo- products was unlikely to result from control of the reaction by the leaving group by studying the photolysis of 2-nornopinyl-toluene sulphonyl hydrazone (53). The reaction is believed to proceed via the diazo-compound (54), giving an intermediate in which nitrogen is the leaving group and does not influence the products. The diazo-alkane (54) is sufficiently

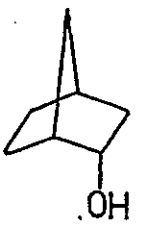


(53) (54)

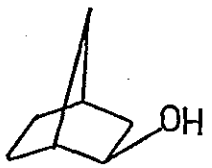
basic for protonation even in the alkaline aqueous on alcoholic solutions used. The deamination procedure also permits variation of the attacking nucleophile and ensures kinetic control. The products are shown to be;



(55)

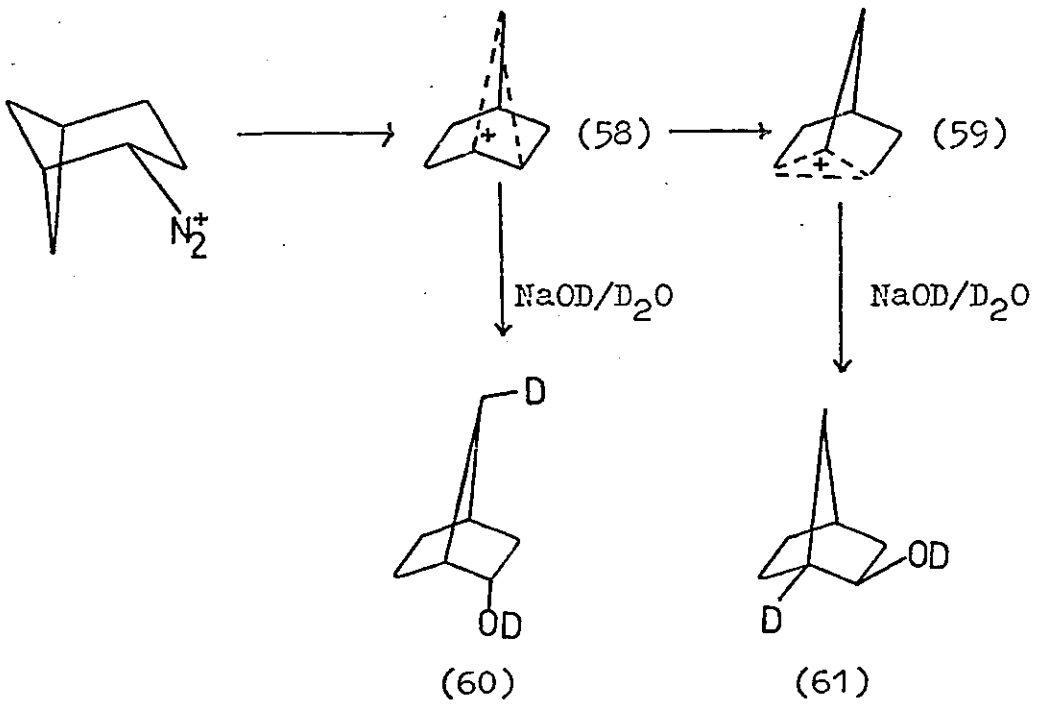


(56)



(57)

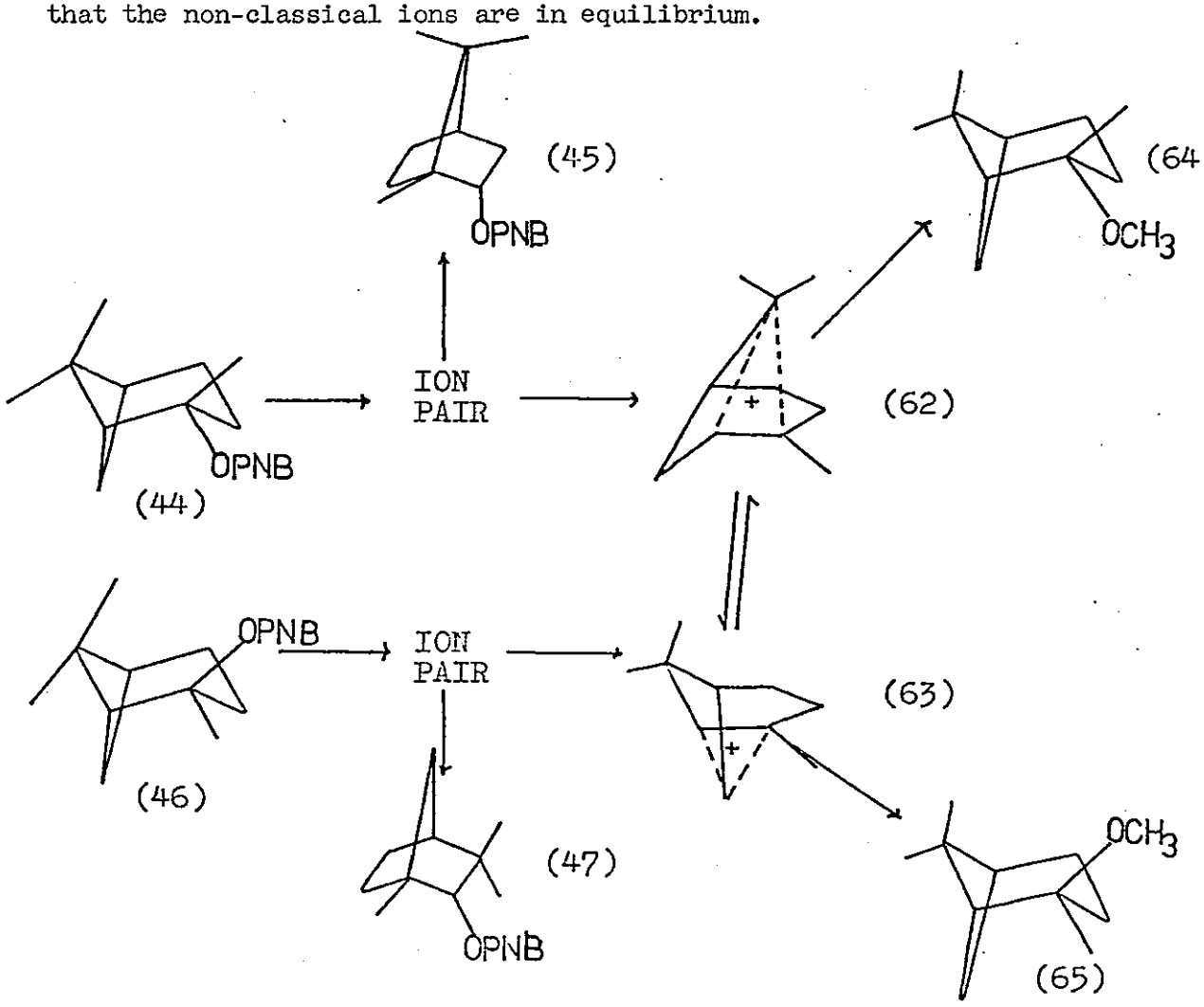
which may be explained by the following mechanism:



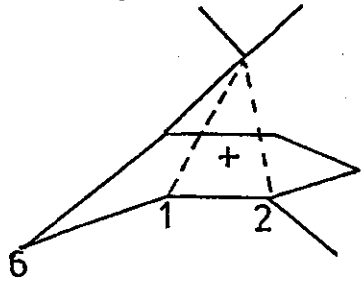
(60) (61)

The endo- compounds are assumed to arise from the non-classical ion (58) and the exo- from the bridged ion (59) which reacts with exo-stereospecificity. Evidence for the ion (58) arises from the reaction in D_2O-DONa-DME when it is shown to give the alcohol (60) i.e. the deuterium is incorporated at the bridge head. Similarly evidence for ion (59) is the preparation of alcohol (61).

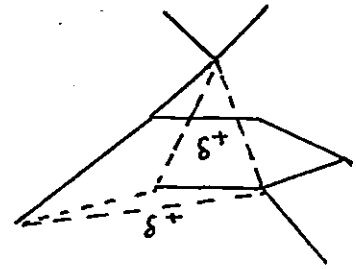
Whittaker[26] has studied the methanolysis of 2-pinanyl-p-nitro-benzoates (44, 46) in the presence of base to give a mixture of products including both cis- and trans-methyl pinanyl ethers (64, 65) from both esters. The p-nitrobenzoates (45, 47) in contrast are shown to be formed stereoselectively as with Abraham. The authors suggest that the explanation is that an intimate ion pair must be formed prior to the formation of the non-classical ions (62, 63) and that the non-classical ions are in equilibrium.



The two extreme forms of the ion (62) are a secondary ion and a tertiary ion. As the methyl group on C-2 provides a stabilisation



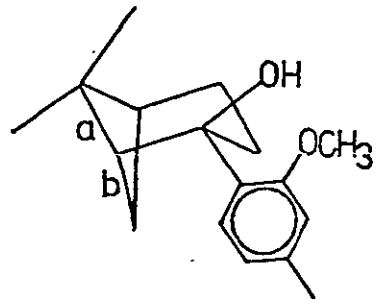
(62)



(66)

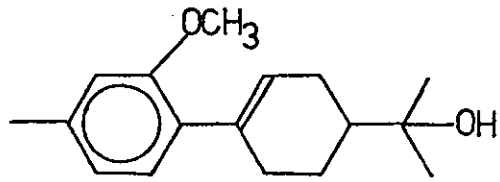
of the latter relative to the former, the charge distribution over the delocalised ion is probably unsymmetrical, the electron deficiency being greater on C-2 than C-1. A migration of the C(1) - C(6) bond would lead to (66) which the authors postulate as the intermediate of ions (62) and (63).

Ramage[27] has attempted to use chromatography over silica to produce stereospecific and selective reactions in the pinane system. The nopinol (67) was chromatographed over silica to give the ring-



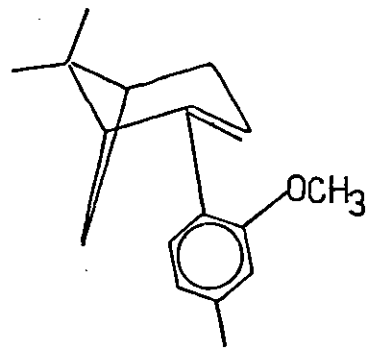
(67)

opened compound (68) (61%) which is formed by selective cleavage of bond (a). Ramage states that bond (b) [cf. (67)] is not coplanar to the OH substituent and that the rearrangement is therefore



(68)

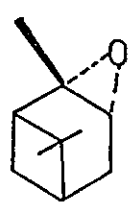
precluded. Chromatography over alumina is found to give the normal dehydration product (69).



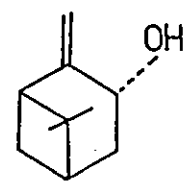
(69)

Oxidations

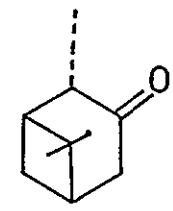
As α-pinene epoxide (70) is readily available its rearrangment has been the subject of intensive research in the hope of finding a cheap route to new flavours and perfumes.



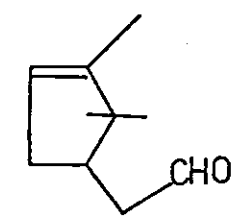
(70)



(71)



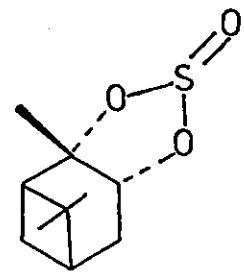
(72)



(73)

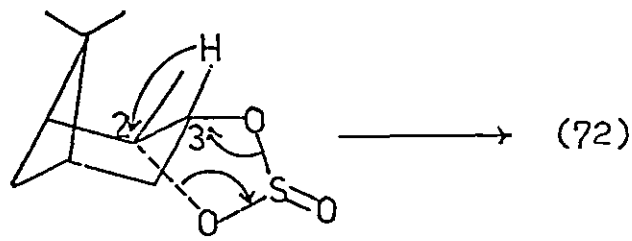
Nigam and Levi[28] have used active alumina to give pinocarveol (71), pinocamphone (72) and camphonelic aldehyde (73) in varying amounts depending on the acidity of the alumina. Similar results have been obtained by other workers[29].

Coxon et al.[30] have pyrolysed the cyclic sulphite (74) to give a



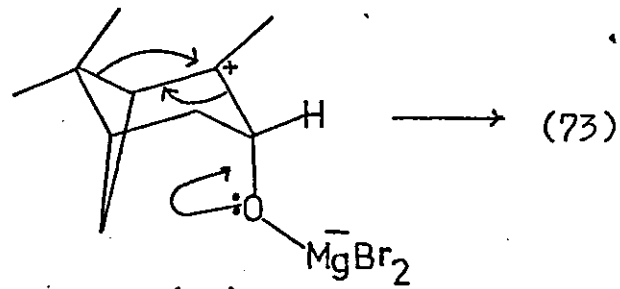
(74)

mixture (98:2) of pinocamphone (72) and camphonelic aldehyde (73) in contrast to the reaction of α-pinene oxide with a Lewis acid e.g. $MgBr_2$ which gives essentially pure aldehyde (73). The reason for the difference in products for the two reactions, both of which involve $C^{2\alpha}$-O bond ionisation is due to the differing conformational constraints imposed on the reacting molecule. The sulphite must be in conformation (75) in which the 3βH is well placed for migration to the 2β-position



(75)

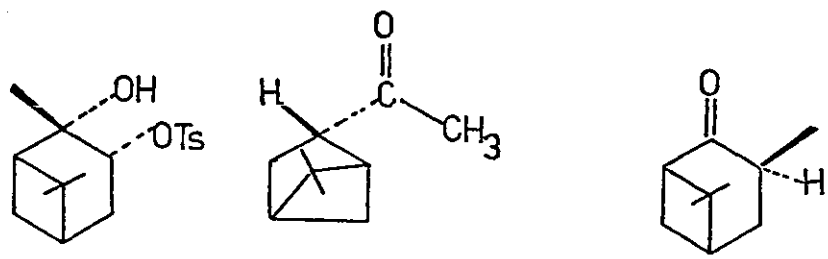
with concerted C^2-O bond cleavage. In contrast to this the most energetically favourable pinane-ring conformation for the -$MgBr_2$ intermediate is (76), as for maximum solvation of the developing C^2 carbonium ion by the departing O atom of the epoxide full charge separation is required.



(76)

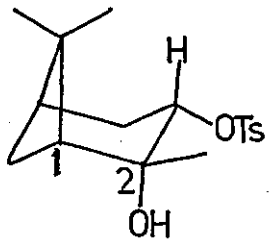
Pinacol type rearrangements.

Hirata[31] has carried out base catalysed rearrangements on α-pinene glycol monotosylates to produce the highly strained bicyclo [2, 1, 1] hexane ring system and has also furnished information regarding the preferred conformations in the pinane ring system (-) cis-α-pineneglycol monotosylate (77). The tosylate was treated with methanolic potassium hydroxide to give the methyl ketone (78) and 3β-methyl nopinone (79). The two mechanisms of formation of

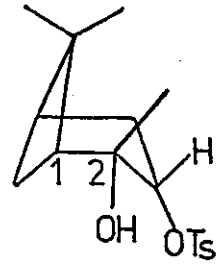


(77) (78) (79)

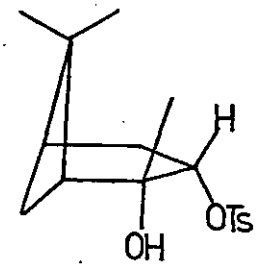
(78) and (79) involve an anticoplanar migration of the 1,2-bond or the methyl group respectively. There are three possible conformations i.e. (80, 81, 82).



(80)



(81)



(82)

Product (78) would be formed from the conformer (80), while the ketone (79) would be formed from conformer (81) as the 1,2-bond and methyl group are respectively anticoplanar. Conformer (82) would lead to equal amounts of (78) and (79). As (78) and (79) are formed in a ratio 50 to 8.5 it is assumed that (80) is the most stable conformation.

REFERENCES TO REVIEW PART I

1. D.V. Banthorpe and D. Whittaker, Quarterly Review, 1966, XX, 3, 373.

2. N. Nakagawa, S. Saito, A. Suzuki and M. Itoh, Tetrahedron Letters, 1967, 1003.

3. (a) A.J. Baretta, C.W. Jefford and B. Waegell, Bull.Soc.Chem. France, 1970, 3899.

   (b) ibid; 3985.

4. Y. Bessiere-Chretien and C. Grison, Bull.Soc.Chem.France, 1971, 1454.

5. R.L. Burwell, J.Amer.Chem.Soc., 1951, 73, 4461.

6. B. Bochwic and J. Kapuscinski, Rocz.Chem., 1967, 41, (10), 1767.

7. G. Ohloff and E.A. Klein, Tetrahedron, 1962, 18, 37.

8. J.M. Coxon, R.P. Garland and M.P. Hartshorn, Aust.J.Chem., 1972, 25, 353.

9. ibid; 947.

10. ibid; 2409.

11. K.K. Schutte-Elte, M. Von Gadola and G. Ohloff, Helv.Chim.Acta., 1971, 54, 1813.

12. C.F. Mayer and J.K. Crandall, J.Org.Chem., 1970, 35, 2688.

13. (a) H.R. Anasari, Flavour Ind. 1970, 1, (4), 252.

(b) P. Ratnasamy, V. Krishnasamy, L.M. Yeddanapalli, Chem.Age. India, 1970, 21, (6), 597.

14. A. Stanilaus and L.M. Yeddanapalli, Can.J.Chem., 1972, 50, (1), 61.

15. ibid; 1972, 50, (1), 113.

16. P.A. Spanninger and J.L. von Rosenberg, J.Org.Chem., 1969, 34 (11), 3658.

17. R.L. Settine J.Org.Chem., 1970, 35, (12), 4266.

18. G. Valkanas and N. Iconomou, Helv.Chim.Acta., 1963, 46, 1089.

19. C.M. Williams and D. Whittaker, Chem.Comm., 1970, 960.

20. C.M. Williams and D. Whittaker, J.Chem.Soc.(B), 1971, 668.

21. C.M. Williams and D. Whittaker, J.Chem.Soc.(B), 1971, 672.

22. W.D. Burrows and R.H. Eastman, J.Amer.Chem.Soc., 1959, 81, 245.

23. (a) N.A. Abraham and M. Vilkas, Bull.Soc.Chim.France, 1960, 1450;

(b) N.A. Abraham and M. Vilkas, Ann.Chim.(France), 1960, 5, 961.

24. S. Winstein and E.C. Friedrich, J.Amer.Chem.Soc., 1964, 86, 2720.

25. W. Kirmse and R. Siegfried, J.Amer.Chem.Soc., 1968, 90, 6564.

26. J.R. Salmon and D. Whittaker, J.Chem.Soc.(B), 1971, 1249.

27. C.R. Hughes, D.F. MacSweeney and R. Ramage, Tetrahedron, 1971, 27, 2247.

28. I.C. Nigam and L. Levi, Can.J.Chem., 1968, 46, (11), 1944.

29. V.S. Joshi, N.P. Damodaran and Dev. Sukh, Tetrahedron, 1968, 24, (17), 5817.

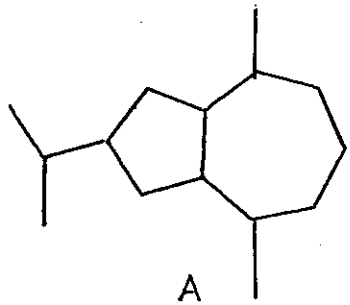
30. J.M. Coxon, E. Danstead, M.P. Hartshorn and K.E. Richards, Tetrahedron, 1969, 25, 3307.

31. T. Hirata and T. Suga, J.Org.Chem., 1971, 36, (3), 412.

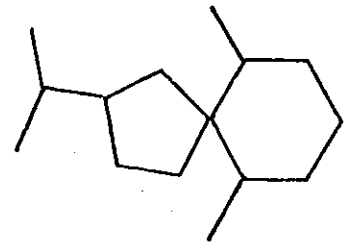
REVIEW PART II

SYNTHESIS OF SPIRO [4, 5] DECANES RELATED TO VETIVONE

Recent synthetic and degradative studies[1,2] have necessitated a structural revision of the entire class of vetivane sesquiterpenes. The previously accepted bicyclo [5.3.0] - decane structure A must be discarded in favour of the spiro [4.5] - decane system B.

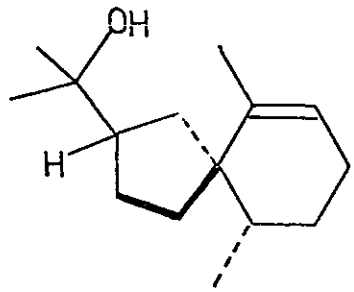


A

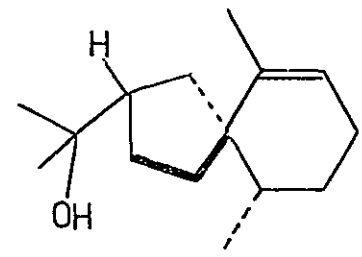


B

This revision creates some intriguing stereochemical problems, particularly with regard to the spiro vetivanes B such as hinesol (1) and epihinesol (agarospirol) (2) (epimeric at the isopropylol group), which possess asymmetric centres in both rings. Solutions to these problems hold important biogenetic implications for this unusual class of terpenes, and at the same time challenge current chemical methodology. Unfortunately the methods available for the synthesis of these systems are limited in that little control is maintained over the developing asymmetric centres.



(1)



(2)

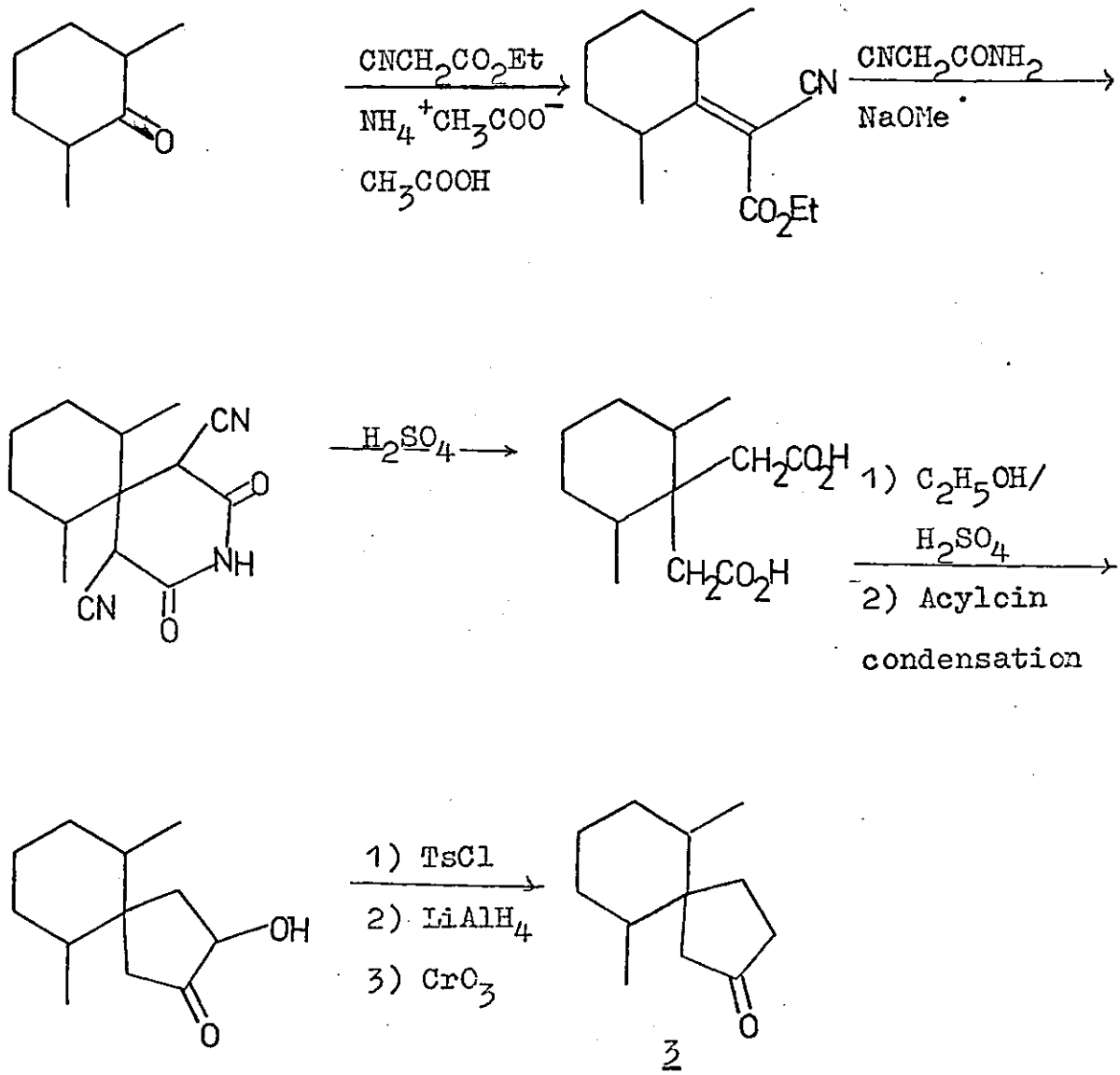
Bhattacharyya[3] made an authentic sample of ketone (3) (Scheme A) to compare with a sample derived from naturally occuring epihinesol (agarospirol). The route used (Scheme A) did not produce a single stereoisomer. However, the synthesis preceded more sophisticated routes that considered in detail the stereochemical problems that are present in the spiro [4.5] -decanes.

Marshall[4] was able by a clever choice of starting material to devise a synthesis of (±)-β-vetivone (7) (Scheme B). Kropp[5] in his investigations on the acid catalysed cleavage of cyclopropyl ketones related to lumisantonin had produced the spiro-cyclopropyl ketone (5). Marshall realised that the compound defines a usable stereochemical relationship of the methyl group relative to the spiro ring system. Kropp obtained the spiro ketone (6) in a low yield as one of the solvolysis products of the tricyclic enone (5), a photochemical rearrangement product of cyclohexadienone (4). The stereochemistry of the spiroketone (6) can be assigned on the basis of the established stereochemistry of the starting dienone (4) and the established relationships in the related santonin-lumisantonin rearrangement.

In his synthesis Marshall produced hinesol (1) and epihinesol (agarospirol) (2) as a 5:3 mixture which were separated by gas chromatography as the acetates. The two epimers were converted into (±)-β-vetivone (7) by a route developed by Yosioka and Kimura[6].

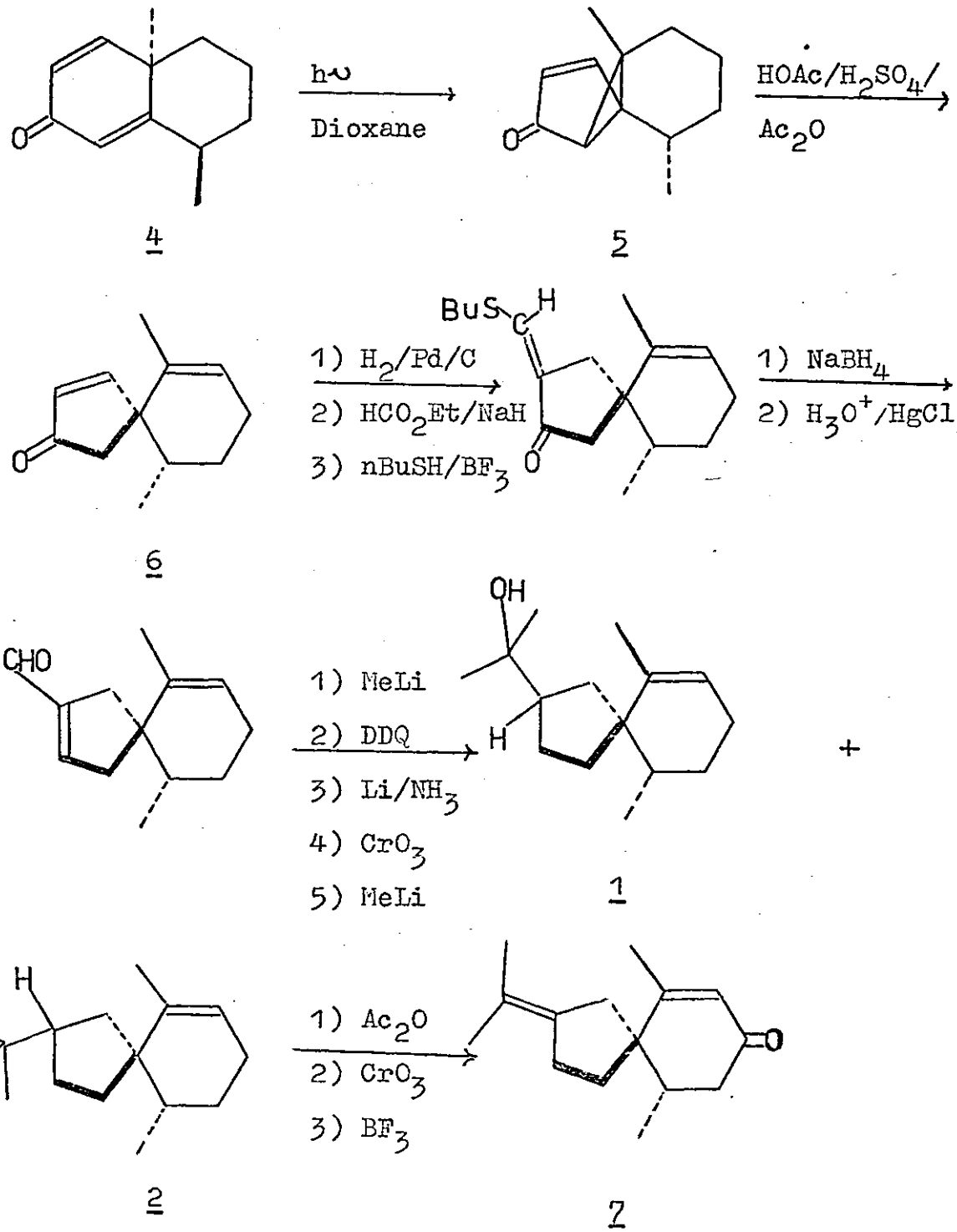
The two alcohols (1) and (2) exhibit nearly identical properties and the stereochemistry of the isopropyl grouping could not be ascertained. Marshall[7] undertook an unequivocal synthesis of the alcohol (1) i.e. hinesol. Marshall's synthesis (Scheme C) takes advantage of the unambiguous stereochemical arrangement of the tricyclic enone (8) to ensure the eventual cis relationship between the C-2 substituent and the C-6 of the spiro system (cf. 12).

SCHEME A

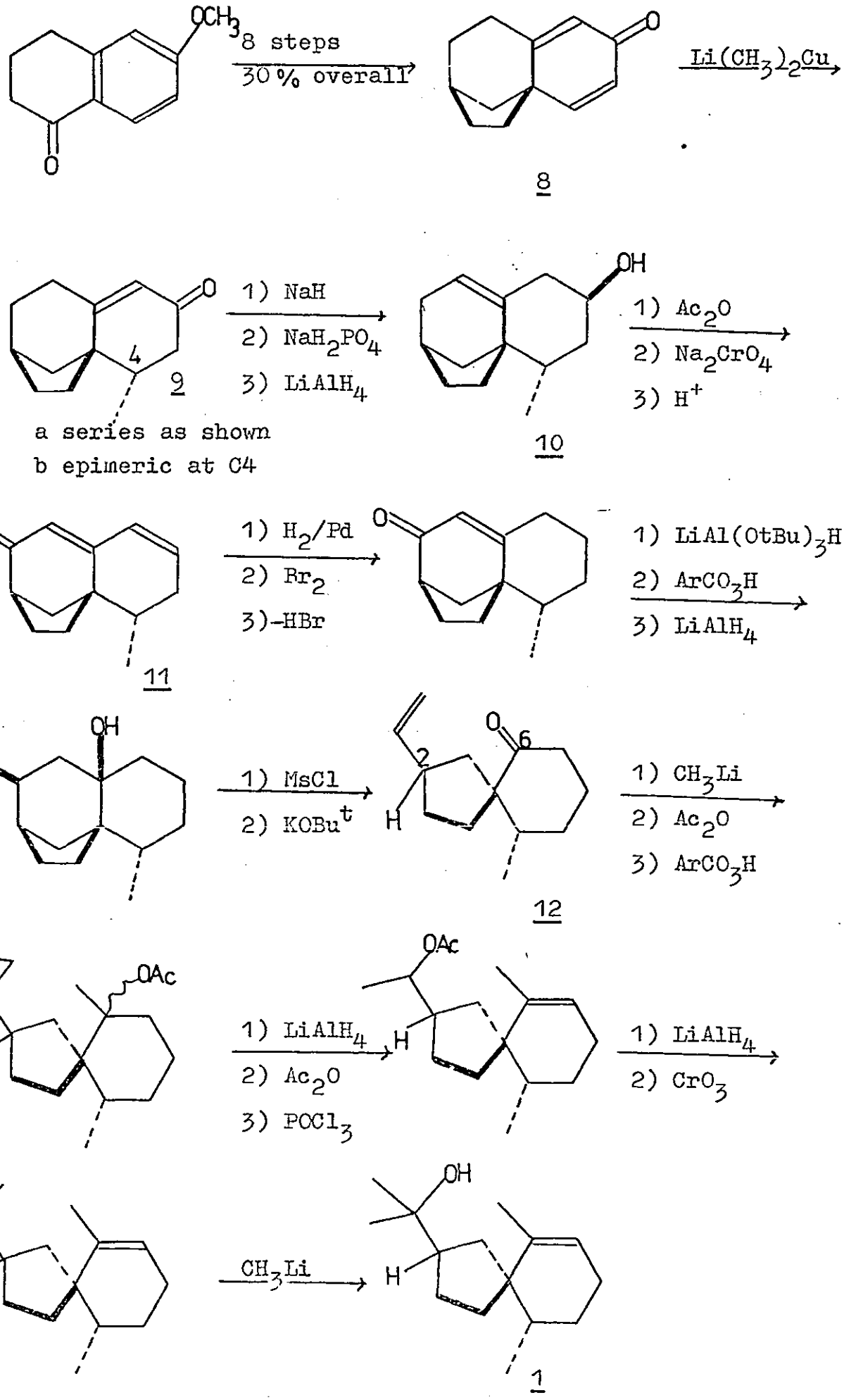

CNCH2CO2Et
NH4+CH3COO−
CH3COOH
CN
CO2Et
CNCH2CONH2
NaOMe
CN
O
NH
CN
O
H2SO4
CH2CO2H
CH2CO2H
1) C2H5OH/
H2SO4
2) Acylcin
condensation
OH
O
1) TsCl
2) LiAlH4
3) CrO3
O

3

SCHEME B


hν
Dioxane
HOAc/H2SO4/
Ac2O
4
5
BuS
H
1) H2/Pd/C
2) HCO2Et/NaH
3) nBuSH/BF3
1) NaBH4
2) H3O+/HgCl2
6
CHO
OH
1) MeLi
2) DDQ
3) Li/NH3
4) CrO3
5) MeLi
H
1
+
OH
H
1) Ac2O
2) CrO3
3) BF3
O
2
7

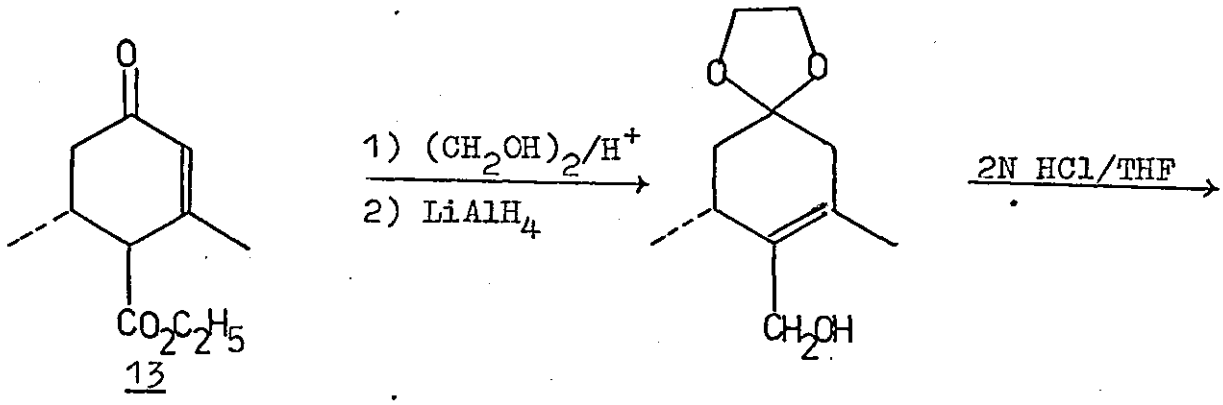
SCHEME C


OCH3
8 steps
30 % overall
O
Li(CH3)2Cu
8
4
9
1) NaH
2) NaH2PO4
3) LiAlH4
a series as shown
b epimeric at C4
OH
1) Ac2O
2) Na2CrO4
3) H+
10
1) H2/Pd
2) Br2
3)-HBr
11
1) LiAl(OtBu)3H
2) ArCO3H
3) LiAlH4
HO
1) MsCl
2) KOBut
2
6
H
1) CH3Li
2) Ac2O
3) ArCO3H
12
OAc
1) LiAlH4
2) Ac2O
3) POCl3
1) LiAlH4
2) CrO3
CH3Li
1

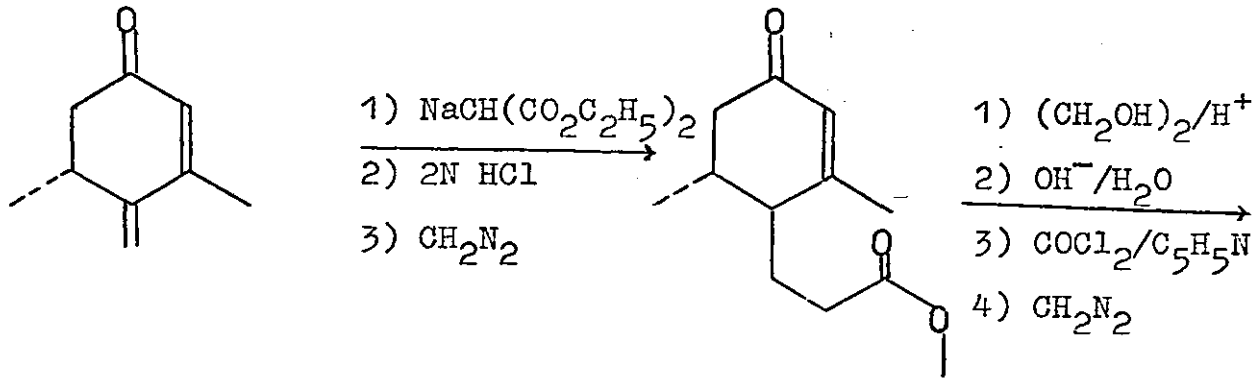
The tricyclic dienone (8) was treated with dimethyl-copper lithium to yield the conjugated ketone (9) as a 1:4 mixture of anti (a series) and syn (b series). The stereochemistry of these adducts was established through single crystal X-ray structure analysis of the p-bromophenylurethane derivative of the homo allylic alcohol (10). The 1:4 mixture of the epimers was separated by preparative gas chromatography of the dienone mixture (11) and the synthesis carried out on (11a) to yield hinesol (1). Application of the scheme to (11b) led to an unsaturated alcohol (1b) whose spectral and chromatographic properties were indistinguishable from those of hinesol (1a). However the derived acetates showed distinctly different gas chromatographic retention times with the acetate from (1a) being identical with authentic hinesol acetate. It is interesting to note that this synthesis of hinesol is based on a twenty-two stage synthesis using (9a) as the starting material and that (9a) is formed in less than twenty-five percent yield.

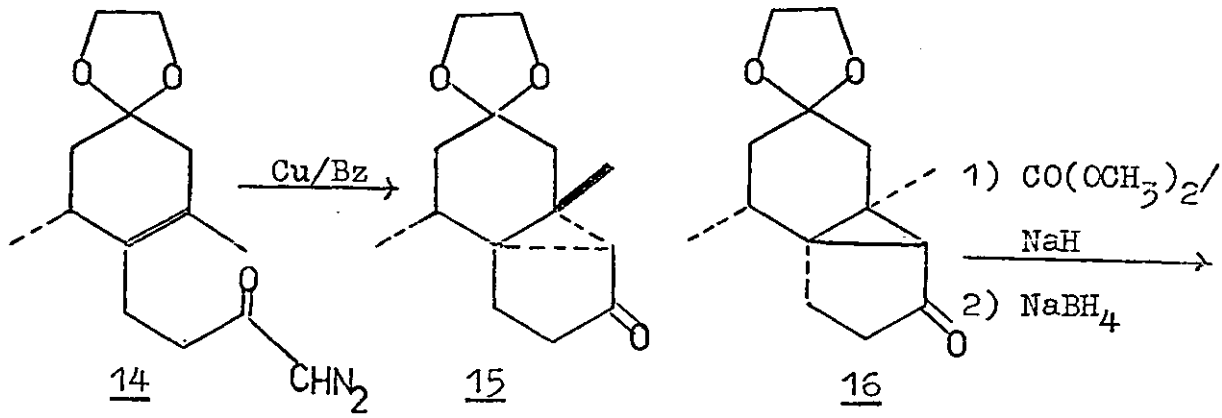
To complement Marshall's work Deslongchamps[8] devised an efficient stereoselective synthesis of (±) epihinesol (2) (Scheme D). This synthesis is based on a clever choice of starting material (13) which is easily prepared in large quantities by condensation of acetaldehyde with ethylacetoacetate followed by resolution of the product to give stereoisomer (13). In the carbene insertion step i.e. the conversion of the diazo ketone (14) to the cyclopropyl compounds (15) and (16) three asymmetric centres are generated and the resulting compound is a mixture of epimers. Deslongchamps carries out the entire synthesis with the mixture as the two extra asymmetric centres are destroyed when the cyclopropyl ring in compound (17) is opened by acid catalysis to yield the spiro ketone (18). The spiro ketone is easily converted into (±) epihinesol (2) which when converted to the acetate was found to have the same g.l.c. retention time as the authentic acetate.

SCHEME D

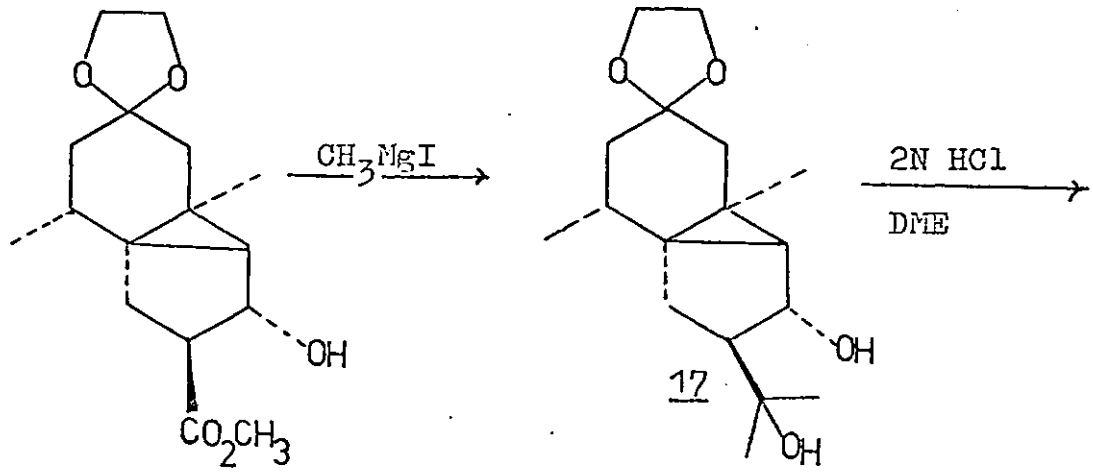


13

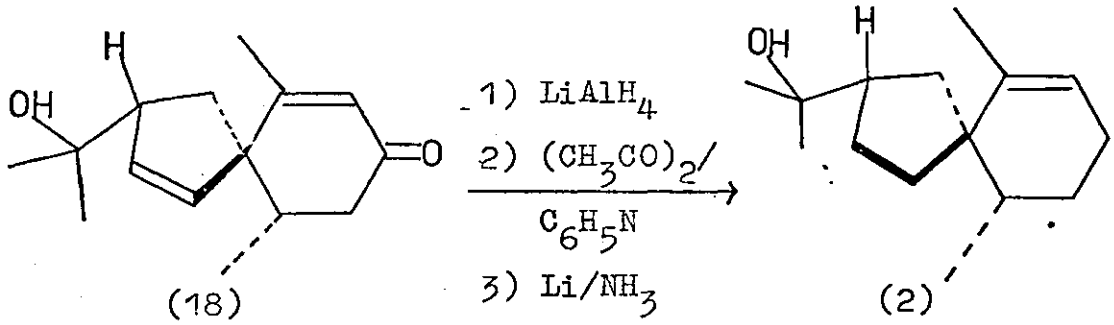




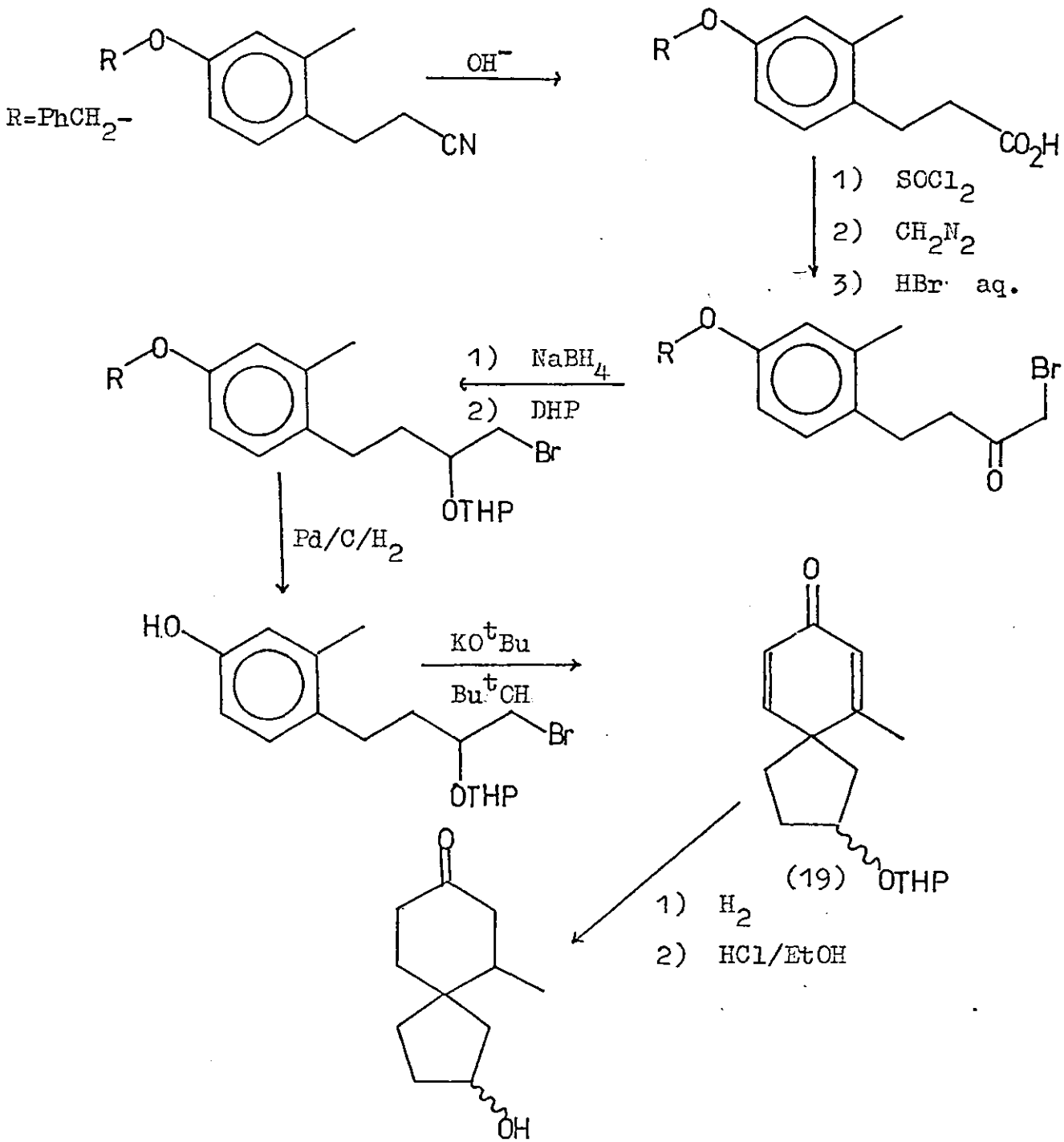
14 15 16



17

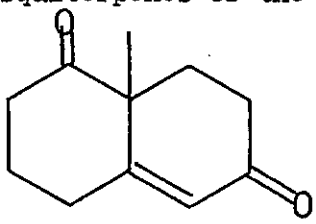

1) $LiAlH_4$
2) $(CH_3CO)_2O$
C_6H_5N
3) Li/NH_3
(18)
(2)

SCHEME E

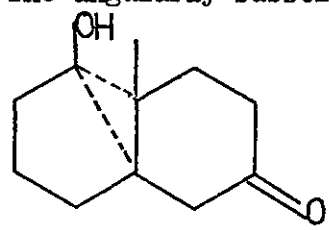

R=$PhCH_2$-
OH^-
CN
CO_2H
1) $SOCl_2$
2) CH_2N_2
3) HBr aq.
1) $NaBH_4$
2) DHP
OTHP
Br
$Pd/C/H_2$
HO
KO^tBu
Bu^tOH
(19)
1) H_2
2) HCl/EtOH
OH

Mukharjii and Gupta[9] used Ar^5 participation of para-tosyl alkyl phenols to synthesise [4, 5] -decanes. They used the reactions depicted in Scheme E. The synthesis described fails to define any of the three asymmetric centres and also attempts to carry out a conjugate addition on the dienone (19) with lithium dimethyl copper failed. Attempted conjugate hydrocyanation also proved unsuccessful. The workers postulate that the cyclopentyl moiety of the spiro dienone hinders the approach of groups at the β-carbon atom from either face of the cyclohexadienone residue.

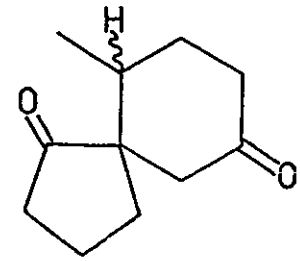
Reusch[10] has published a preliminary communication in which he claims to have produced a remarkably versatile intermediate i.e. (21) which he hopes will provide advantageous new routes for the synthesis of sesquiterpenes of the vetivane class. The angularly substituted



(20)



(21)



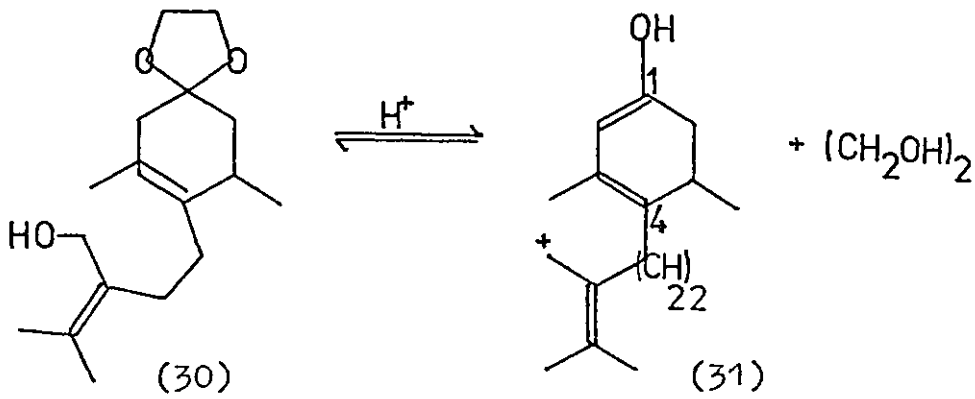
(22)

[4.4.0] dec-1-ene-3,7-dione (20) was converted into the 1 substituted 2-hydroxytricyclo [4.4.0 ^{2,6}] decan-8-one (21) by treatment with lithium in ammonia. The transformation of (21) into 10-methyl spiro [4.5] decan 1,7-dione (22) was accomplished in greater than 75% yield by adding methanol dropwise to a stirred suspension of the sodium salt in benzene. No full paper has yet been published to expand on the work in the short communication.

A group of Japanese workers[11] have used Ar^5 participation of the para-chloro-alkyl phenol (23) to prepare the spiro[4,5] ketone (24) (Scheme F). They say that the ketone (24) is a possible intermediate in the synthesis of hinesol (1), epihinesol (2) and β-vetivone (7). As they obtain an epimeric mixture at C-3 (cf. 24) any synthesis of β-vetivone (7) would involve a separation of a 50:50 mixture prior to or during subsequent reactions. If a synthesis of hinesol (1) or epihinesol (2) was attempted there would be no steric control over the approach of any nucleophile at C-6 (cf. 24) hence the product would be a 50:50 epimeric mixture and would again involve a tedious separation. No further paper has been published concerning this work.

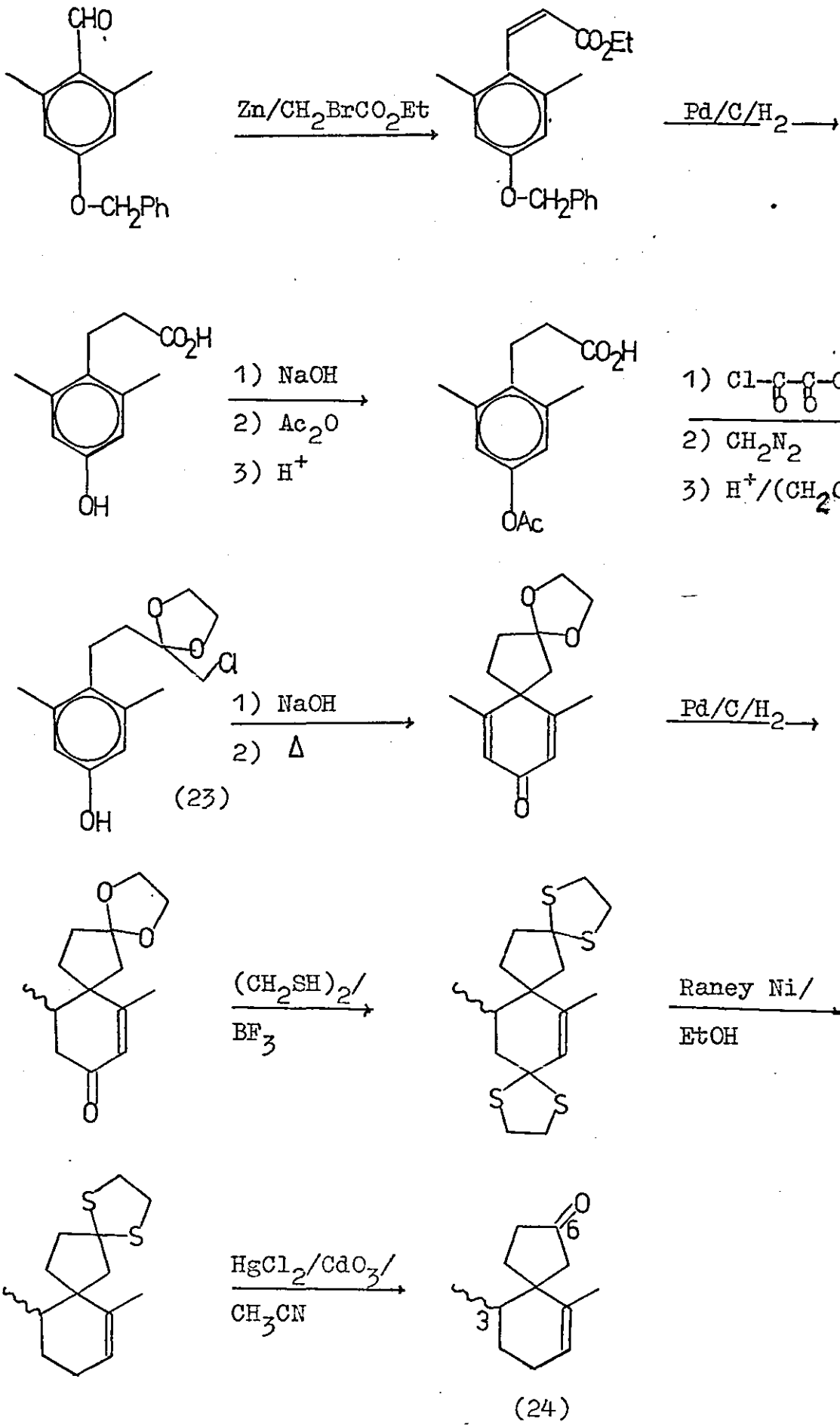
Stork, Danheiser and Ganem[12] have reported a more elegant synthesis of (±) β-vetivone (7) (Scheme G). The lithium enolate of (25) was added to the dichloride (26) to give the six substituted compound (27). The first alkylation involves the allylic chloride. Compound (27) was not isolated but treated with lithium diisopropylamide to give the enolate (28). The enolate ion geometry forces the ring methyl into an axial conformation and then ring formation occurs with the methyl trans to the chloro-alkyl group to give the enol ether (29).

McCurry[13] has used a method based on the cyclisation of the unsaturated allylic alcohol (30) (Scheme H) to synthesise (±) 10-epi-β-vetivone (32). The cyclisation was induced by acid catalysis:

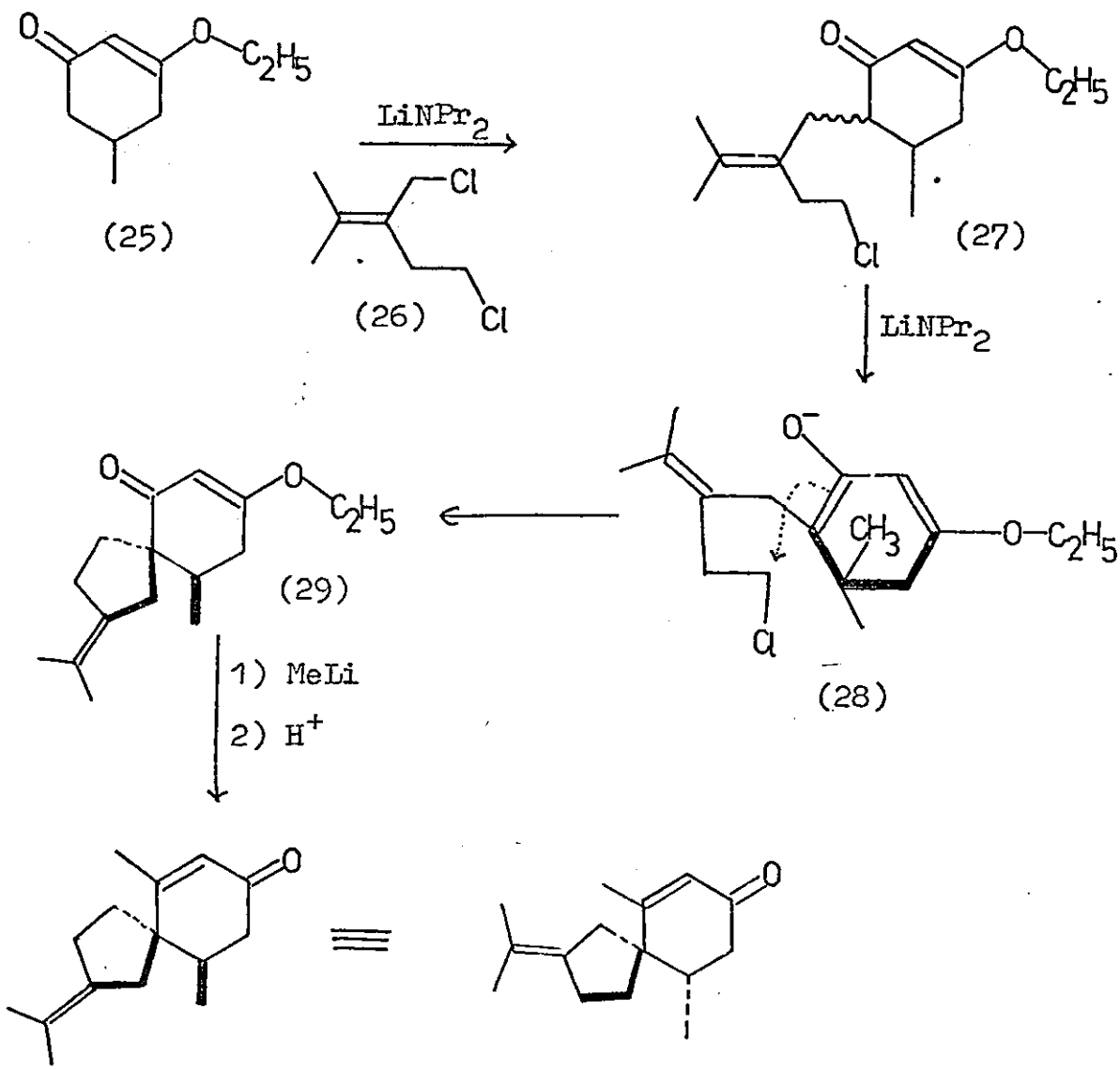


(30) (31)

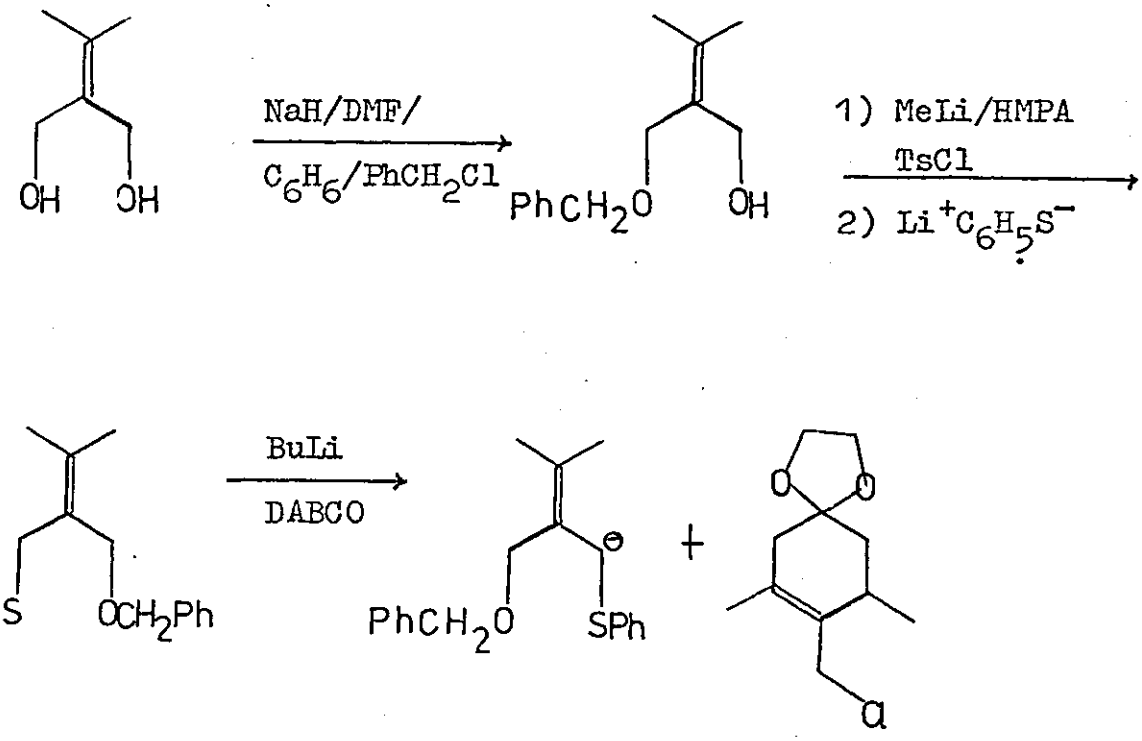
SCHEME F


CHO
O-CH2Ph
Zn/CH2BrCO2Et
CO2Et
O-CH2Ph
Pd/C/H2
CO2H
OH
1) NaOH
2) Ac2O
3) H+
CO2H
OAc
1) Cl-C-C-Cl
O O
2) CH2N2
3) H+/(CH2OH)2
O
O
Cl
OH
(23)
1) NaOH
2) Δ
O
O
O
Pd/C/H2
O
O
O
(CH2SH)2/
BF3
S
S
S
S
Raney Ni/
EtOH
S
S
HgCl2/CdO3/
CH3CN
O
6
3
(24)

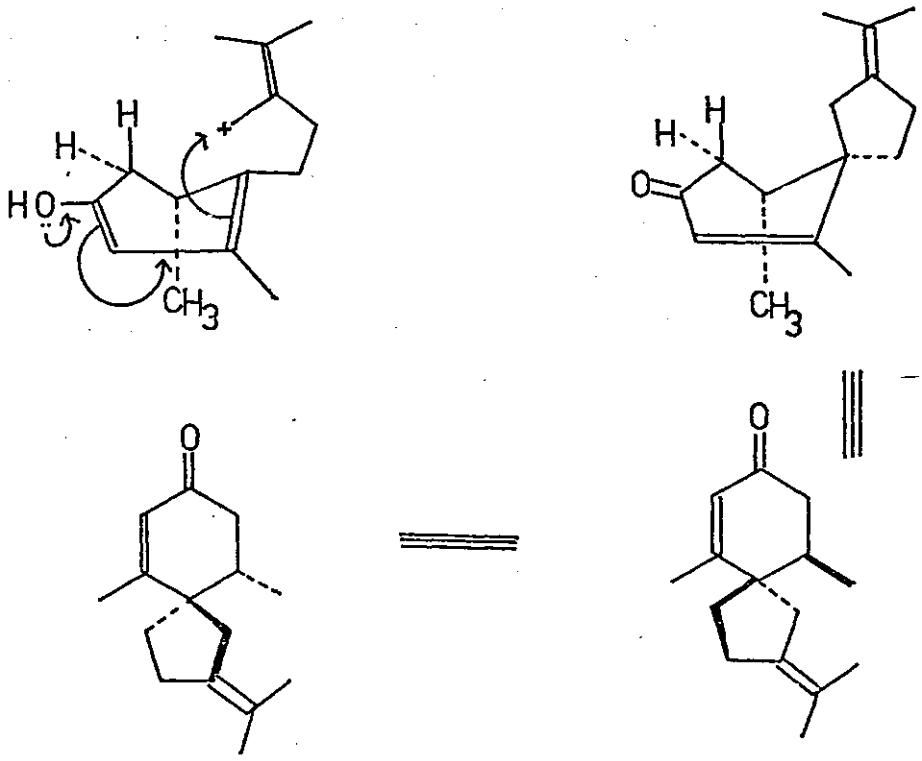
SCHEME G



SCHEME H


NaH/DMF/
C6H6/PhCH2Cl
1) MeLi/HMPA
TsCl
2) Li+C6H5S−
BuLi
DABCO
Li/C2H5NH2
70% H2SO4
(30)
(32)

The 1-alkoxybutadiene system in compound (31) is nucleophilic enough at C-4 to undergo a cyclysation parallel to Ar^5 participation in phenols. As a single epimer is produced the following mechanism is proposed to explain the stereoselectivity of the cyclisation: The

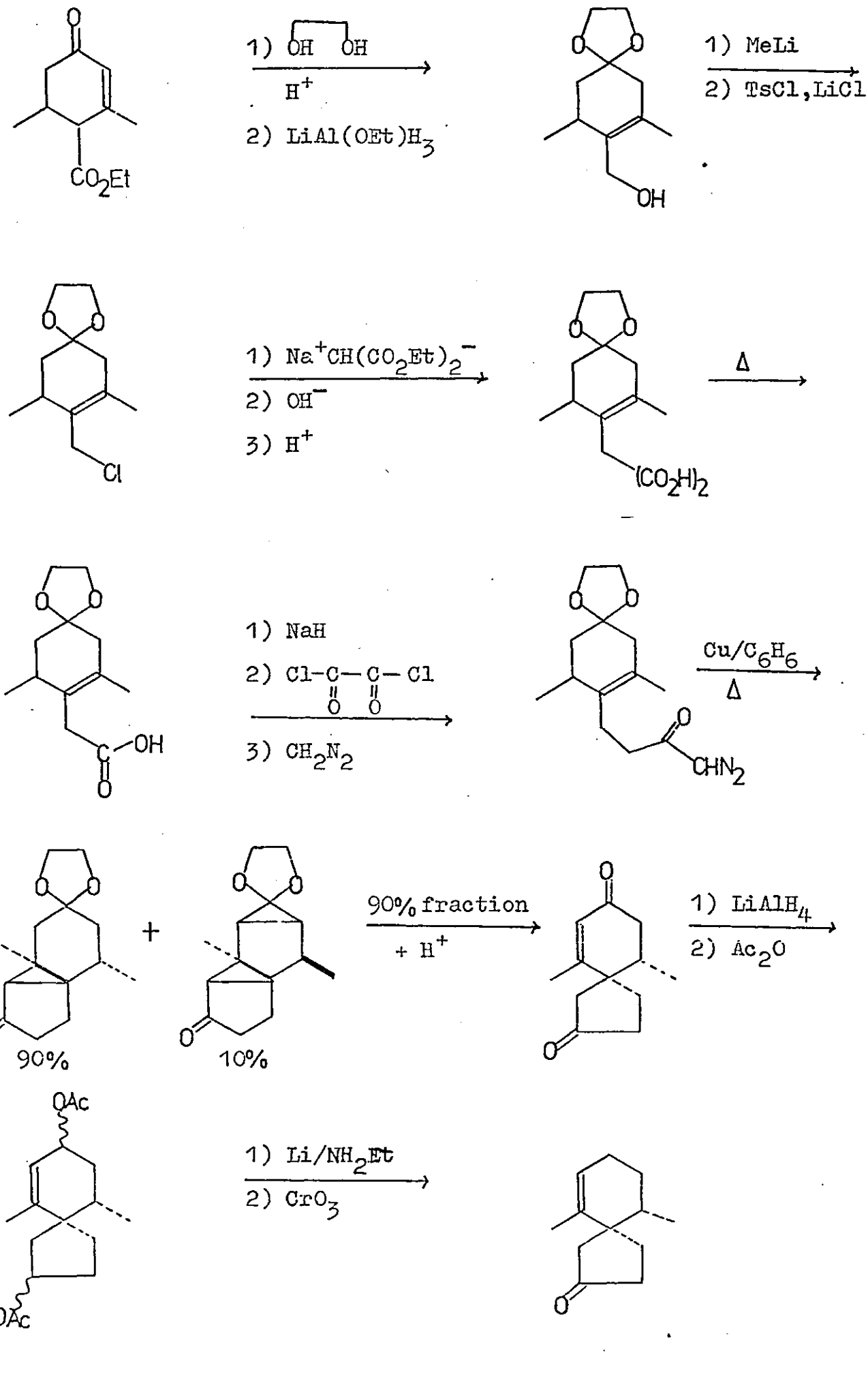


(32)

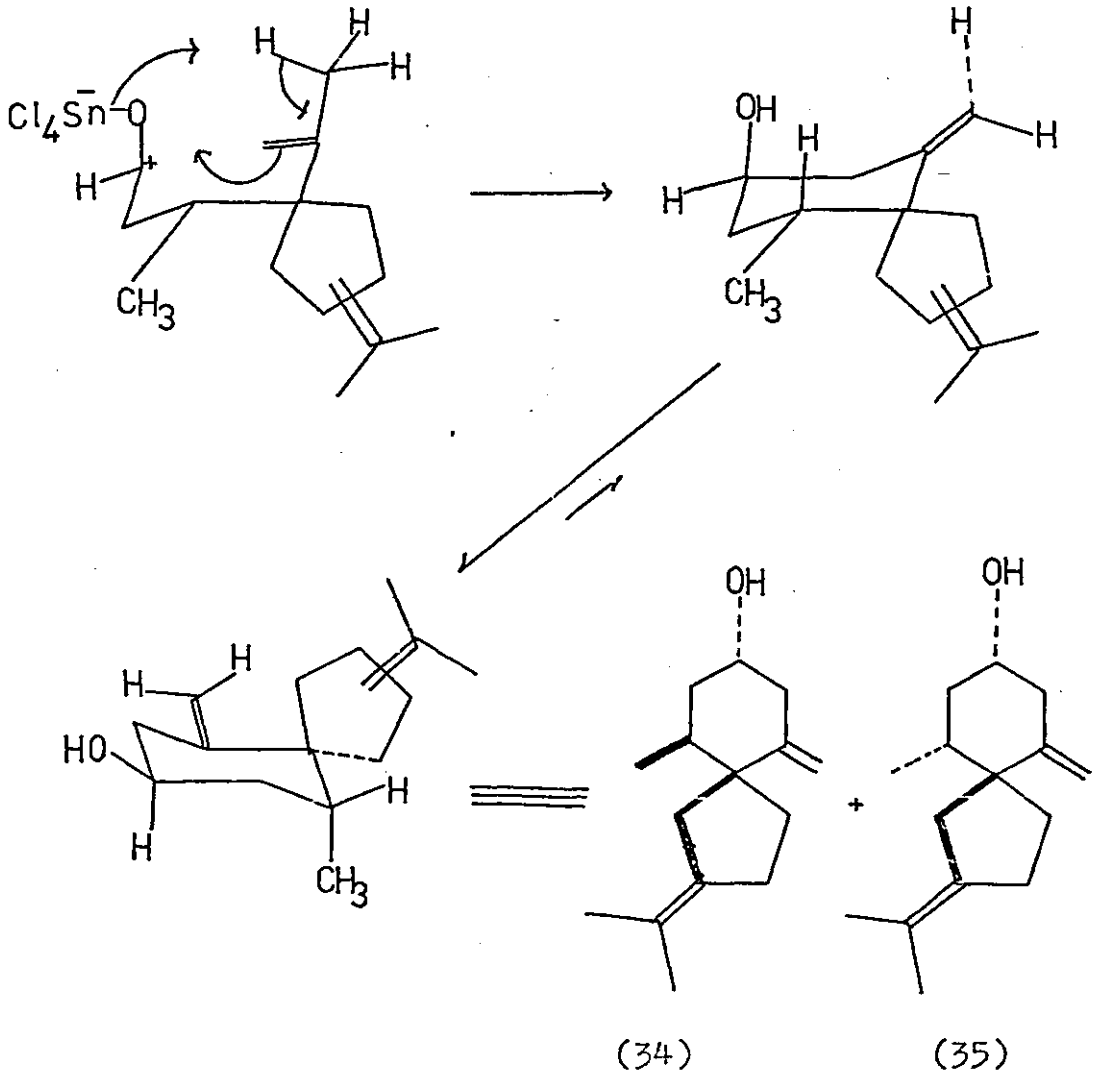
allylic cation approaches the face of the molecule opposite the pseudo axial C-10 methyl group.

McCurry[14] has also devised a synthesis of spiro [4,5] decanes based on a similar route to Deslonchamps's synthesis. McCurry's route (Scheme I) uses the same starting material and both routes employ the same cyclisation step i.e. a ketocarbene insertion but does not give a natural spiro [4,5] decane.

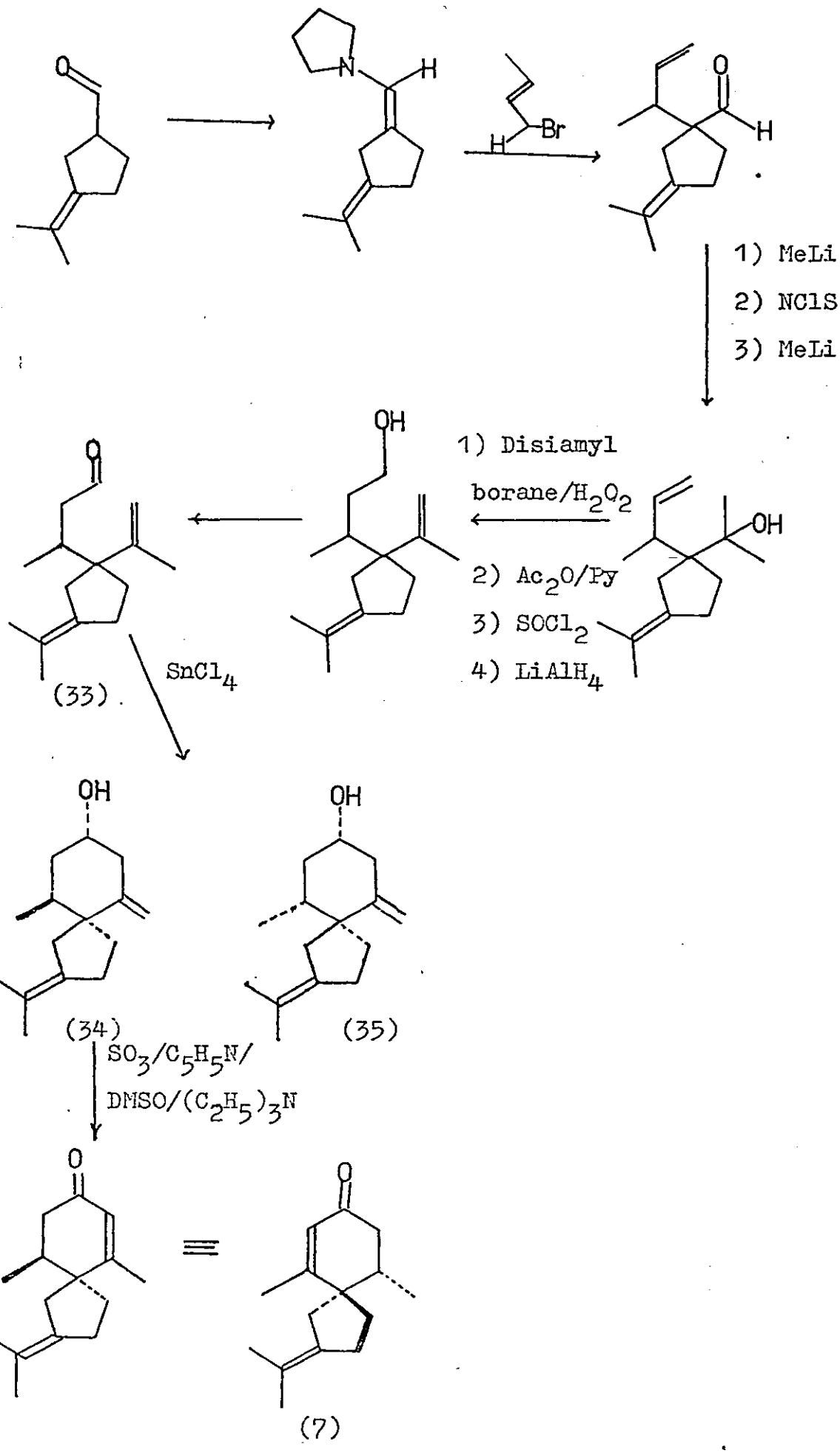
SCHEME I


1) OH OH
H+
2) LiAl(OEt)H3
1) MeLi
2) TsCl,LiCl
1) Na+CH(CO2Et)2−
2) OH−
3) H+
Δ
1) NaH
2) Cl-C(=O)-C(=O)-Cl
3) CH2N2
Cu/C6H6
Δ
90%
10%
90% fraction
+ H+
1) LiAlH4
2) Ac2O
1) Li/NH2Et
2) CrO3

McCurry[15] has devised a synthesis of (±) β-vetivone (7) and (±) 10-epi-β-vetivone (32) based on an aza-Claisen rearrangement (Scheme J). The aldehyde (33) undergoes an acid catalysed Prins cyclisation to give a separable mixture of diasteriomeric alcohols (34) and (35) although there is a possibility of the formation of four diasteriomeric dl pairs. The following mechanism is postulated to account for the stereospecificity of the reaction:



(34) (35)


1) MeLi
2) NClS
3) MeLi
1) Disiamyl borane/H_2O_2
2) Ac_2O/Py
3) $SOCl_2$
4) $LiAlH_4$
$SnCl_4$
(33)
(34)
(35)
SO_3/C_5H_5N/
DMSO/$(C_2H_5)_3N$
(7)

REFERENCES. (TO REVIEW PART II)

1. J.A. Marshall, N.H. Anderson, and P.C. Johnson, J.Amer.Chem.Soc., 1967, 89, 2748.

2. J.A. Marshall and P.C. Johnson, J.Amer.Chem.Soc., 1967, 89, 2750.

3. K.R. Varma, M.L. Maheshwari and S.C. Bhattacharyya, Tetrahedron, 1965, 21, 115.

4. J.A. Marshall and P.C. Johnson, Chem.Comm., 1968, 391.

5. P.J. Kropp, J.Amer.Chem.Soc., 1965, 87, 1615.

6. I. Yosioka and T. Kimura, Chem and Pharm.Bull Japan, 13, 1965, 1430.

7. J.A. Marshall and S.F. Brady, Tetrahedron Letters, 1969, 1387.

8. M. Mongrain, J. Lafontaine, A. Belanger and P. Deslongchamps, Can.J.Chem., 1970, 48, 3273.

9. P.C. Mukharjii and P.K. Sen Gupta, Chem.Ind., 1970, 533.

10. K. Grimm, P.S. Venkataramani and W. Reusch J.Am.Chem.Soc., 1971, 93, 270.

11. A. Ogiso, M. Kurrabayash, H. Nagahori and H. Mishima, Chem.Pharm.Bull., 1970, 18, (6), 1283.

12. G. Stork, R.L. Danheiser and B. Ganem, J.Amer.Chem.Soc., 1973, 95, 3414.

13. P.M. McCurry, Jr., R.K. Singh and S. Link, Tetrahedron Letters, 1973, 1155.

14. P.M. McCurry, Jr., Tetrahedron Letters, 1971, 1845.

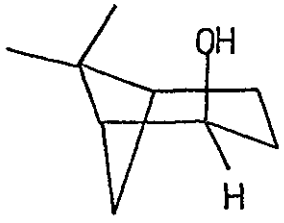
15. P.M. McCurry, Jr., and R.K. Singh, Tetrahedron Letters, 1973, 3325.

DISCUSSION

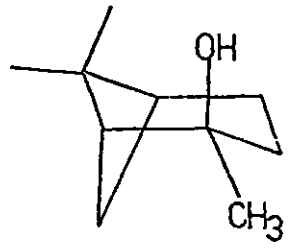
PART I REARRANGEMENT OF ETHERS

Essential oil constituents based on the pinane skeleton represent an extensive series of compounds. The facility with which they are rearranged to other skeletal types has rendered them particularly useful as synthetic precursors. Unfortunately rearrangement of the pinane ring system often produces complex mixtures (see Review). Although interesting from a mechanistic standpoint and to the olfactory senses, the pinanes are not particularly attractive as starting materials for the synthesis of optically pure terpenes.

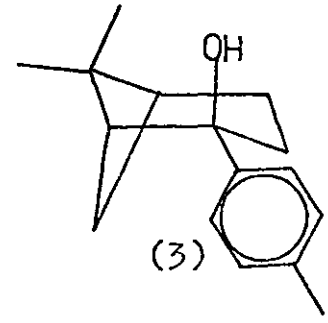
Consider 6,6-dimethylnorpinan-2β-ols* (trans-nopinols) (1), (2) and (3).



(1)

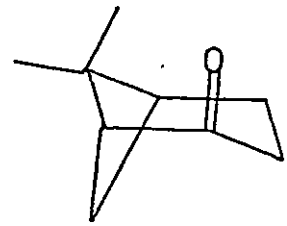


(2)



(3)

These are readily available through nucleophilic addition to nopinone (4); the rearrangement of some of these nopinols has been studied and



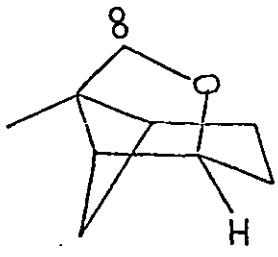
(4)

* The α β notation is used throughout; the isopropylidene bridge is considered to have the β-configuration.

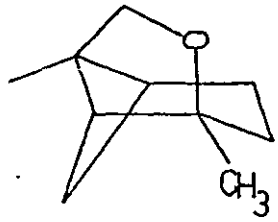
the results are given in Table I. The alcohol (1) benefits from anchimeric assistance in its solvolysis and a mixture of endo- and exo- secondary alcohols results[2,3]. Mere substitution of a methyl group for hydrogen at the position adjacent to the bridgehead, giving pinan-2β-ol (2), produces a striking change in behaviour. Apart from ring opened products, only endo- products are formed[4,5]. In Table I the last example, with the aryl compounds, is in effect a cis-elimination, but is more likely to occur via a benzylic carbonium ion in a non-concerted process[6]. The conformational flexibility of the alcohols (1) and (2) might be implicated in the lack of clean trans-coplanar concerted migration of the 1,7-bond.

It was felt that if the 2-hydroxy-group in the trans- nopinols could be confined to a strictly trans- coplanar relation to the 1,7-bond, a clean rearrangement to the fenchol (1,3,3,-trimethylnorbornan-2-ol) series might result.

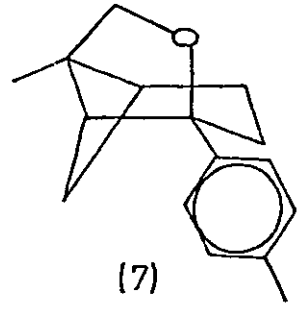
To create a conformationally defined system the 2-hydroxy-group is best incorporated into part of a ring structure. Formation of a carbon-oxygen bond to C-8 leads to the tricyclic 2-8-nopinyl ethers (5), (6) and (7), having the desired conformational requirements.



(5)



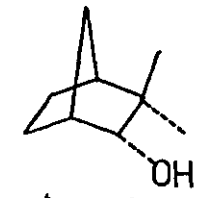
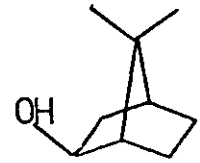
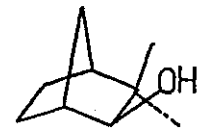
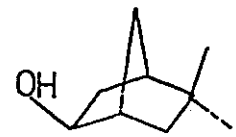
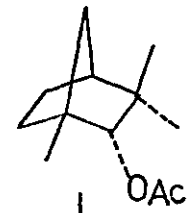
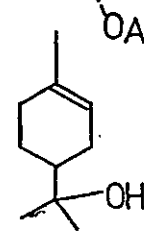
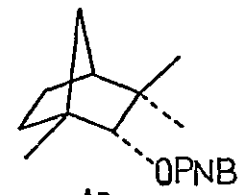
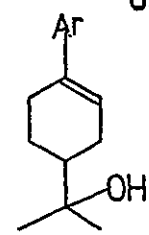
(6)



(7)

6,9-Dimethyl-7-oxatricyclo [4,3,0,$0^{3,9}$] nonane (6)[7,8] was prepared from (-)-pin-2(10)-ene via intramolecular (Br_2-HgO) oxidation of pinan-2β-ol (2). Treatment of the ether (6) in acetonitrile at 20° with acetyl toluene-p-sulphonate[9] did not give the 8-substituted pinane but the 8-substituted fenchol (8).

TABLE I

COMPOUND	PRODUCTS	YIELD%
6,6-Dimethylnorpinan-2β-ol (1)[a]		59
		26
		4
		11
Pinan-2β-ol (2)[b]		40–45
		5–10
		HYDROCARBONS 40–50
Pinan-2β-yl p-nitrobenzoate [c]		25–30
2-Aryl-6,6-dimethylpinan-2β-ol [d]		61

2-Aryl-6,6-dimethylpinan-2β-ol [d] 

. 84

a Refs. 2 and 3; aqueous 70%dioxan-0·099M-$HClO_4$-75°

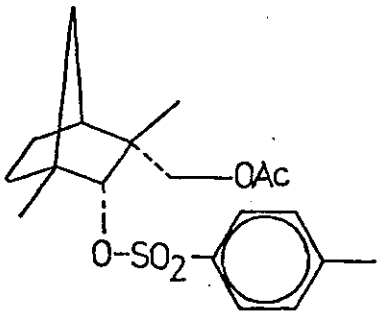
b Ref. 4; acetic anhydride.

c Ref. 5.

d Ref. 6. silica.

e Ref. 6. Woelm I neutral alumina.

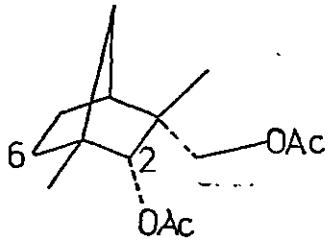
f PNB=p-Nitrobenzoate.



(8)

Its structure was confirmed by n.m.r. spectroscopy and a short sequence of reactions illustrated below.

Similarly, treatment of the pinanyl ether (6) with acetic anhydride and boron trifluoride-ether[10] gave the diacetate (9) (90%). The methylene AB system in the n.m.r. spectrum must arise from a

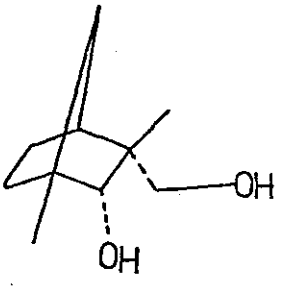


(9)

combination of intrinsic non-equivalence[11] due to the low symmetry (cf. $CH_AH_BU{\cdot}CXYZ$)[12] and unequal conformer population (U.C.P.). It would appear likely that the former effect has precedence in this particular system. The long range 2-6β, 'W' coupling[12,13] (1.5Hz) is in the expected range for a bicyclo-[2,2,1] heptane structure.

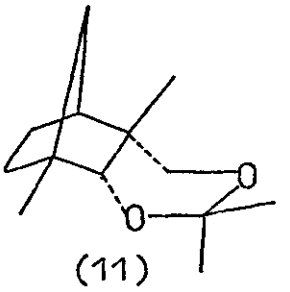
To establish the relative configuration of the two oxygen functions and the stereospecificity of the rearrangement, the following sequence of reactions was carried out. The diacetate (9) was reduced with lithium aluminium hydride in ether to give the diol (10). The

cis-disposition of the two hydroxy-groups was readily demonstrated by



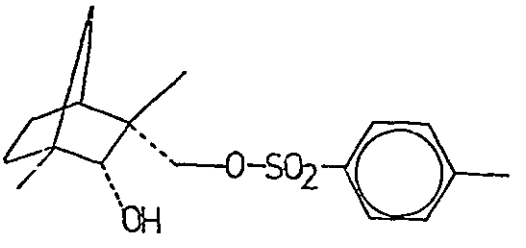
(10)

treatment of the diol (10) with 2,2,-dimethyloxypropane-toluene-p-sulphonic acid to give the acetal (11). Reaction of the diol (10)



(11)

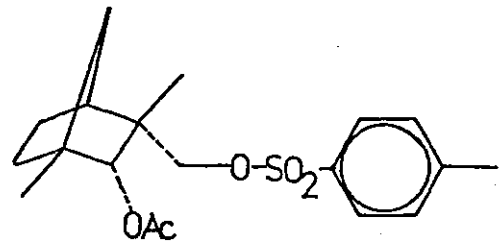
with toluene-p-sulphonyl chloride in pyridine[14] gave the tosylate (12). Acetylation of the tosylate (12) gave the acetate (13) as an unstable



(12)

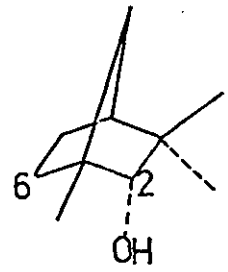
oil [cf.(8)] . Its instability during chromatography on silica gel is readily explained by intramolecular displacement of the primary tosylate[15] by the 2-endo- acetate. Such a displacement is sterically impossible with the 2-tosylate (8).

Reduction of the tosylate (12) with lithium aluminium hydride gave 1,3,3-trimethylnorbornan-2α-ol (α-fenchol) (14) as an impure oil.



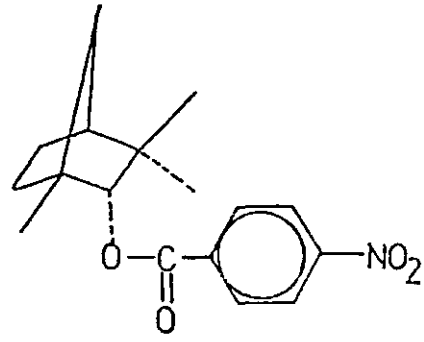
(13)

The τ value for 2-H (6.74) and J_{26} (1.3Hz) are in agreement with the published data[16]. Further characterisation of the alcohol (14) as its p-nitrobenzoate (15) confirmed its structure.

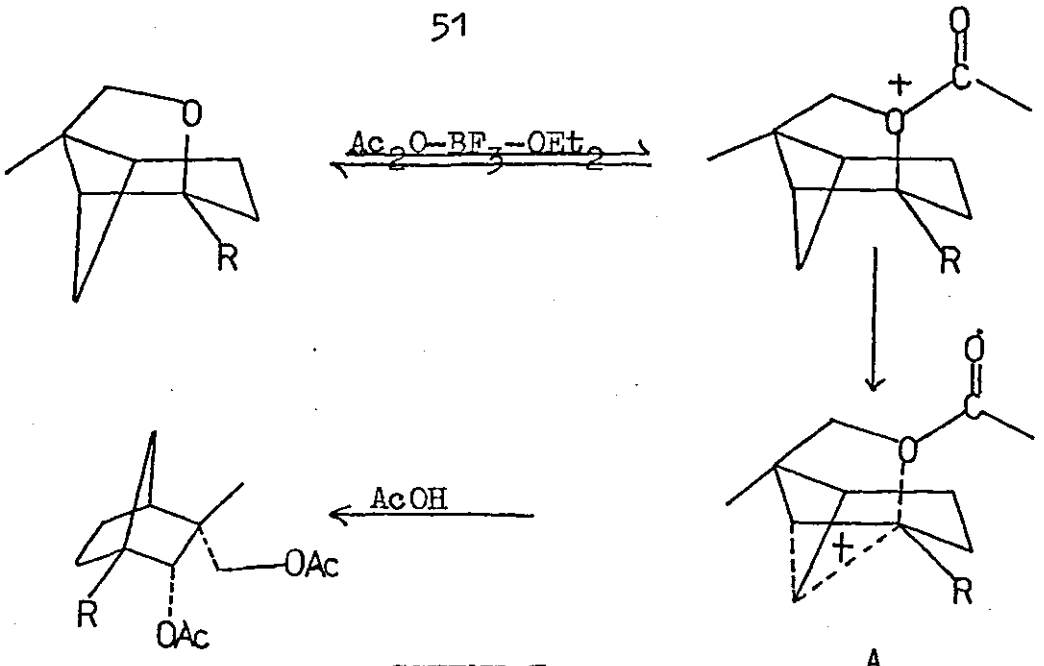


(14)

The remarkably high yield in the rearrangement of the ether (6) to the diacetate (9) compared with the rearrangement of esters from pinan-2β-ol (2) to α-fenchyl esters[4,5] suggests that the mechanism (Scheme I) operates via A as an ion pair, and is completely concerted.



(15)

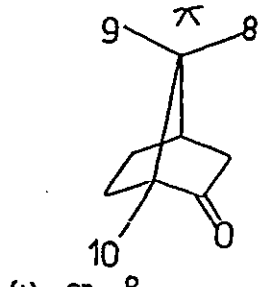


SCHEME I

A

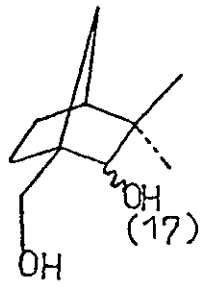
Furthermore, the specific rotations of the fenchol (14) and its p-nitrobenzoate (15) are the highest recorded in the literature[5,17].

The low or 10β-, cis-8 -, and trans-9 substituted bornan-2-one (camphor) derivatives (16) have been described[18] but similar compounds in the fenchane series are virtually unknown. The only reported



(16)

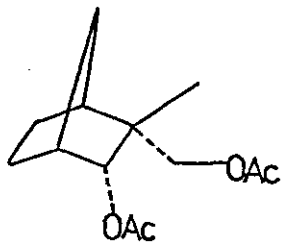
methyl substituted fenchane is Konovalov's 'hydroxyfenchane'[19] whose structure was established as 3,3-dimethylnorbornan-1-yl methanol (10-hydroxyfenchane) (17)[20,21].



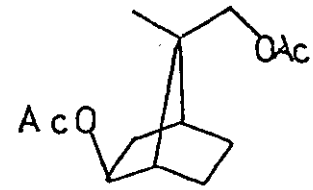
(17)

It would be expected from both Winstein's[2] and Schleyer's[3] study of α- and β-nopinol that the secondary ether (5) would benefit more from anchimeric assistance in its solvolysis than the tertiary ether (6). As a consequence products having the 7,7-dimethylnorbornan-2-ol as well as the 3,3-dimethylnorbornan-2-ol structure may be formed.

9-Methyl-7-oxatricyclo [4,3,0,$0^{3,9}$] nonane[7] (5) (prepared from (-)-pin-2-(10)ene via intramolecular oxidation with bromine-mercury (11) oxide of cis-nopinol[22]) was treated with acetic anhydride-boron trifluoride-ether at 0°. A rapid reaction took place (compared with the rearrangement of the pinyl ether (6) to the acetate (9)) to give two compounds (18) and (19) in the ratio (7:3) (calculated from n.m.r. data). This ratio is independent of the temperature at which the



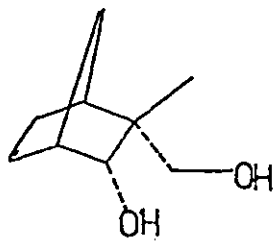
(18)



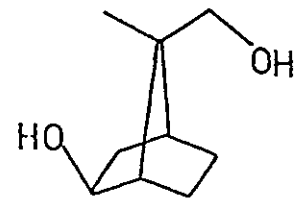
(19)

rearrangement is conducted (from -70 to 20°). The mixture of acetates (18) and (19) could not be separated by the usual techniques (distillation, t.l.c., and g.l.c.). The n.m.r. spectrum indicated the skeletal types present in the mixture.

The mixture of the diacetates (18) and (19) was reduced with lithium aluminium hydride to an inseparable mixture of diols (20) and (21) which were decomposed on silica, alumina, and g.l.c. Benzoylation

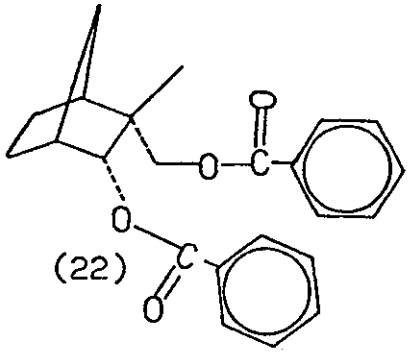


(20)

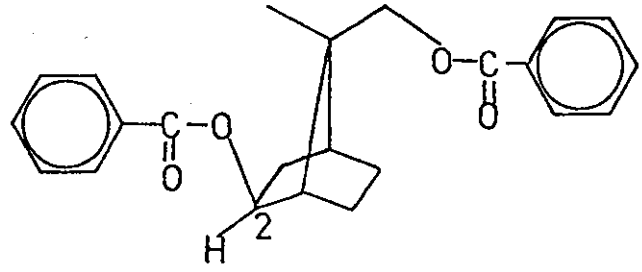


(21)

of the diol mixture (20) and (21) gave two bisbenzoates (22) and (23) that were separable (multiple elution t.l.c.). The n.m.r. spectra of

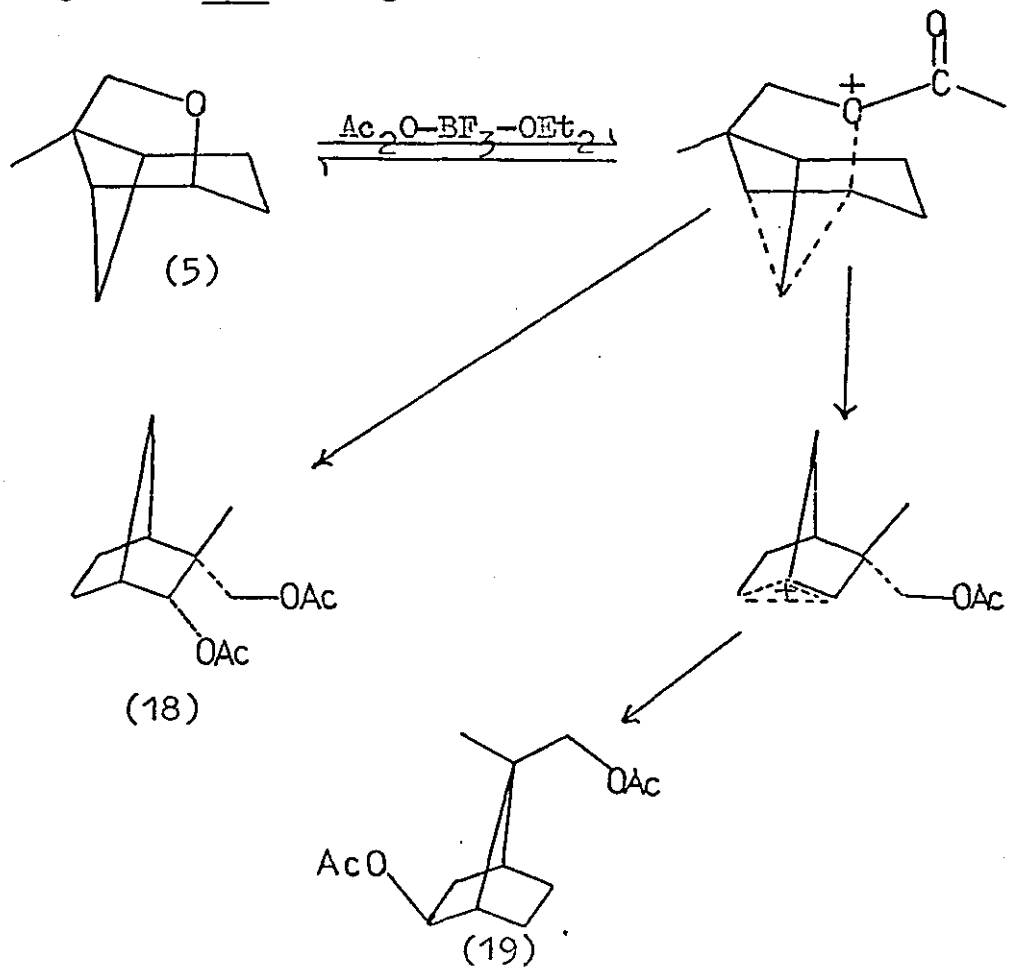


(22)



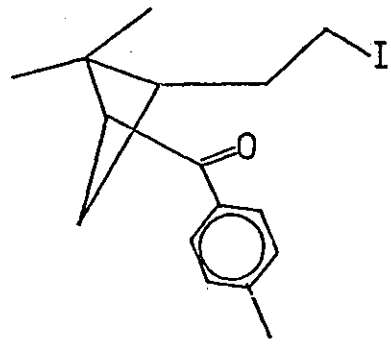
(23)

the two benzoates do not supply sufficient information for unambiguous assignment of the orientation of the 2-proton in (23). On mechanistic grounds (Scheme II), however, it is reasonable that the 2-proton be assigned the endo- configuration.



SCHEME II

(+)-Nopinone (4) was treated with p-tolylmagnesium bromide to give a single alcohol (3). The stereochemistry is assigned as trans on the basis of the usual Grignard additions to nopinone[7] and subsequent transformations. While the bromine-mercury (II) oxide[7,23] procedure was satisfactory for preparing the ethers (5) and (6) from the alcohols (1) and (2) (see experimental section for modifications of Erman's[7] procedure), when applied to the p-tolyl compound (3), a complex mixture of products were formed. With mercury (II) oxide-iodine-hν at -20° [24] the norpinanol (3) was cleanly transformed into two products; the required ether (7) (80%) and the β-fragmentation product (24) (20%).

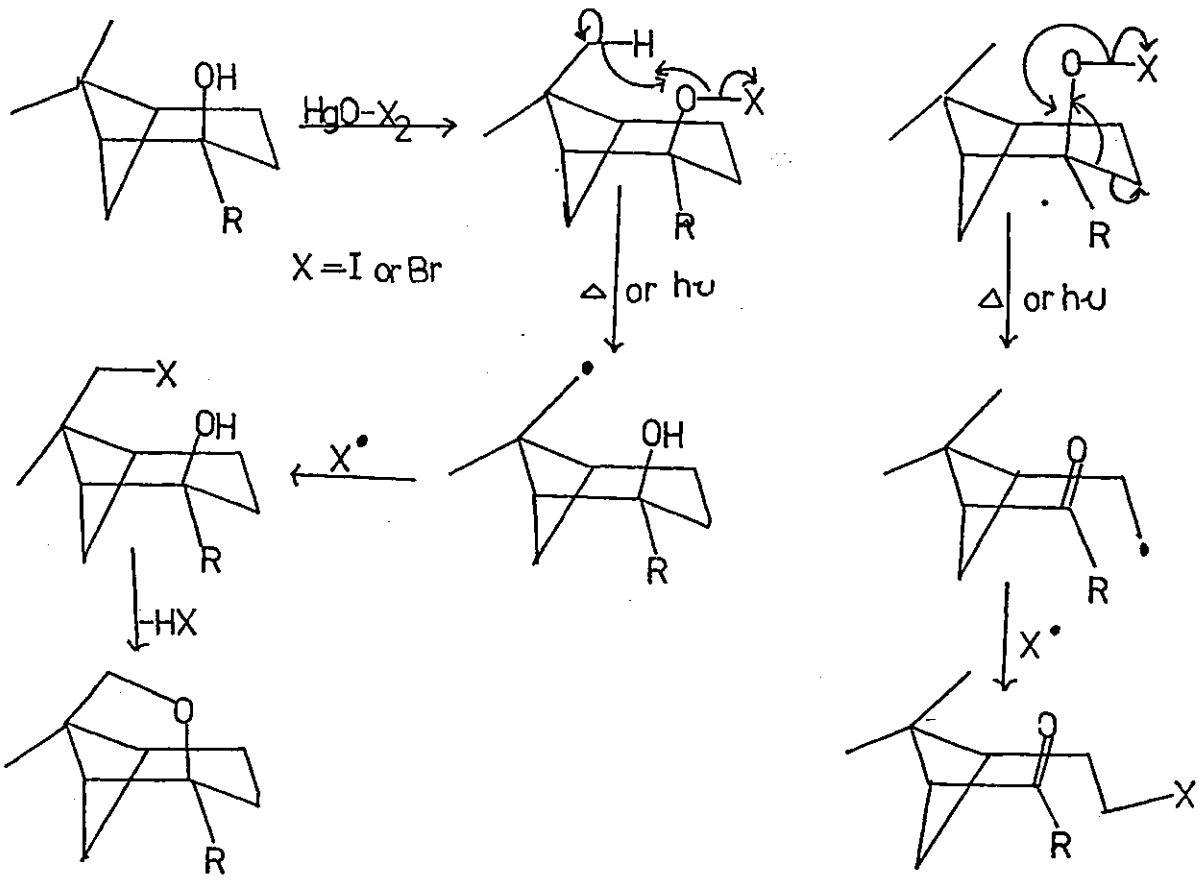


(24)

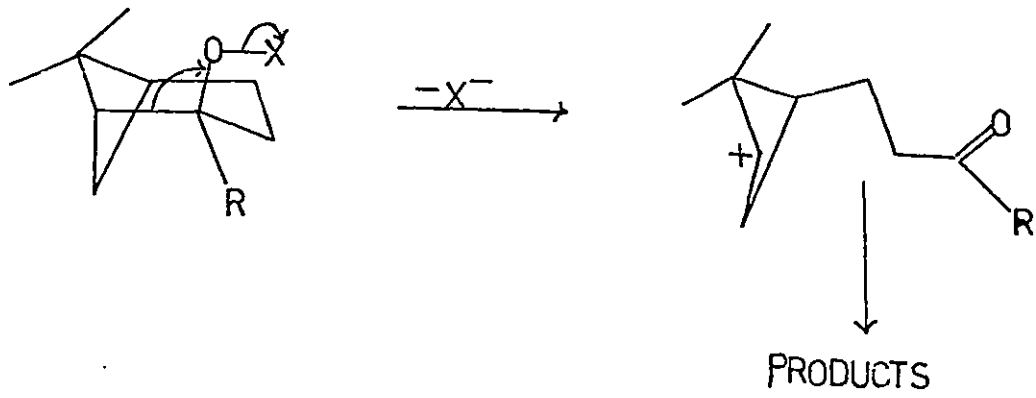
The structure of the crystalline ether (7) followed from its n.m.r. spectrum. Similarly the n.m.r. and i.r. spectra of the cyclobutyl ketone (24) are compatible with the assigned structure.

We found that intramolecular oxidations with both bromine- and iodine-mercury (II) oxide required continuous irradiation (tungsten 750 W lamp) during the whole reaction to achieve reasonable yields of the ethers. This is compatible with a radical process involving homolytic cleavage of hypohalite intermediates. Indeed by-product (24) from the iodine-mercury (II) oxidation is expected if radical intermediates are involved, whereas ionic intermediates would lead to rupture of the cyclobutane ring (Scheme III).

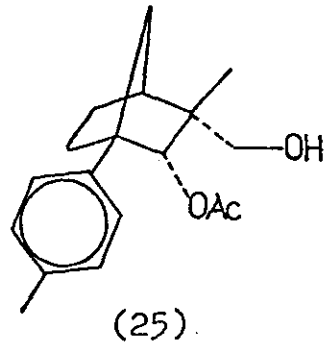
SCHEME III



IF IONIC

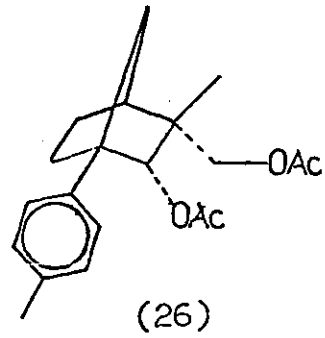


The ether (7) was treated with acetic anhydride-boron trifluoride-ether at 0°. A single crystalline product (25) was isolated in over 90% yield. If the reaction is conducted at 20°, the diacetate (26) is



(25)

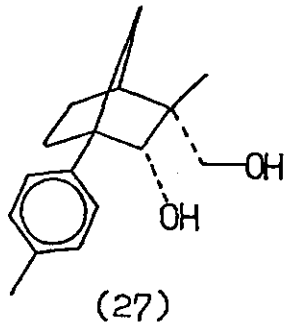
the major product, accompanied by the mono-acetate (25). For convenience the rearrangement was carried out at 0° and worked-up with acetylation (pyridine-Ac_2O).



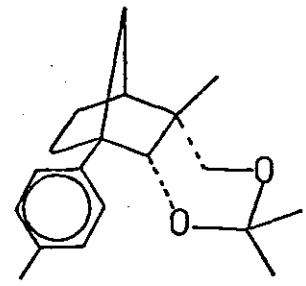
(26)

This expedient enabled the pure crystalline diacetate (26) to be isolated in 90% yield; the by-product (24) was removed during the aqueous work-up, presumably as the pyridinium iodide. The structure of the diacetate (26) was readily deduced from the n.m.r. spectrum (see experimental section). The absence of vinyl protons in the n.m.r. and the styrene absorption in the u.v. spectrum eliminated 2-arylnorpinene- and 1-arylcyclohexene-like structures[6] (see Table I). Treatment of compound (26) with lithium aluminium hydride in tetrahydrofuran gave the diol (27) which readily forms an acetonide (28) thus proving the <u>cis</u> disposition of

the two hydroxy groups.



(27)

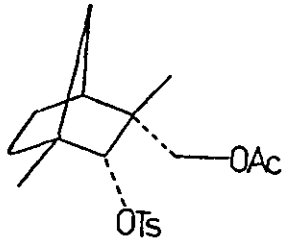


(28)

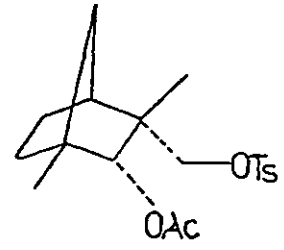
This result is in agreement with the mechanism shown in Scheme I; a clean trans- coplanar migration of the 1,7-bond with concerted C-O cleavage.

Rearrangement of the pinane ring system under carbonium ion conditions usually gives rise to many products[25]. The need to find defined conditions for selective rearrangement has been appreciated by us[1] and others[6]. It appears that when the oxonium-carbonium ion intermediate (Scheme I) is stabilised (R=Me or Ar) high yields of 8-substituted fenchanes result. Whereas when R=H, the higher energy oxonium-carbonium ion is stabilised by anchimeric assistance, leading to the two observed products (18) and (19).

About two years after our initial communication[1a] and nine months after the full paper[1c] a paper appeared[28] that disagrees with certain of our results. It was suggested by Madame Bessiere-Chretien that the structural assignments for (8) and (13) ought to be reversed.

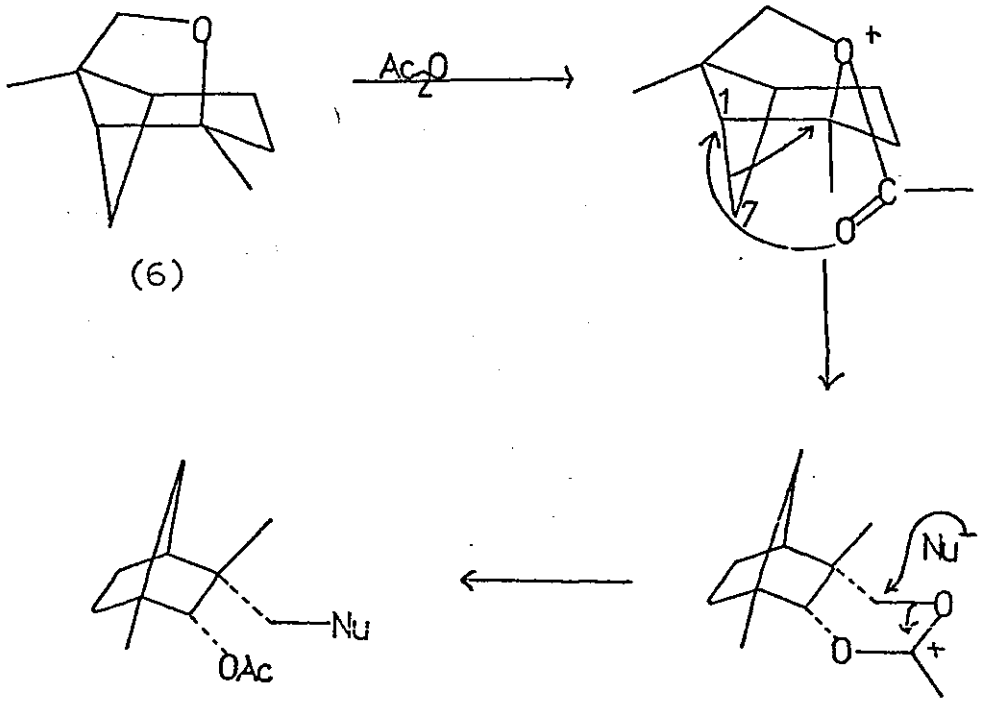


(8)



(13)

Through the collaboration of Dr. A.F. Thomas of Fermenich a sample of (8) prepared by us and a sample prepared by Madam Bessiere Chretien were compared. They are identical in all respects. Consequently the results quoted[28] by Madame Bessiere-Chretien are to be corrected in the near future. The mechanism of rearrangement of (6) to the fenchyl skeleton was written by the French workers as follows:

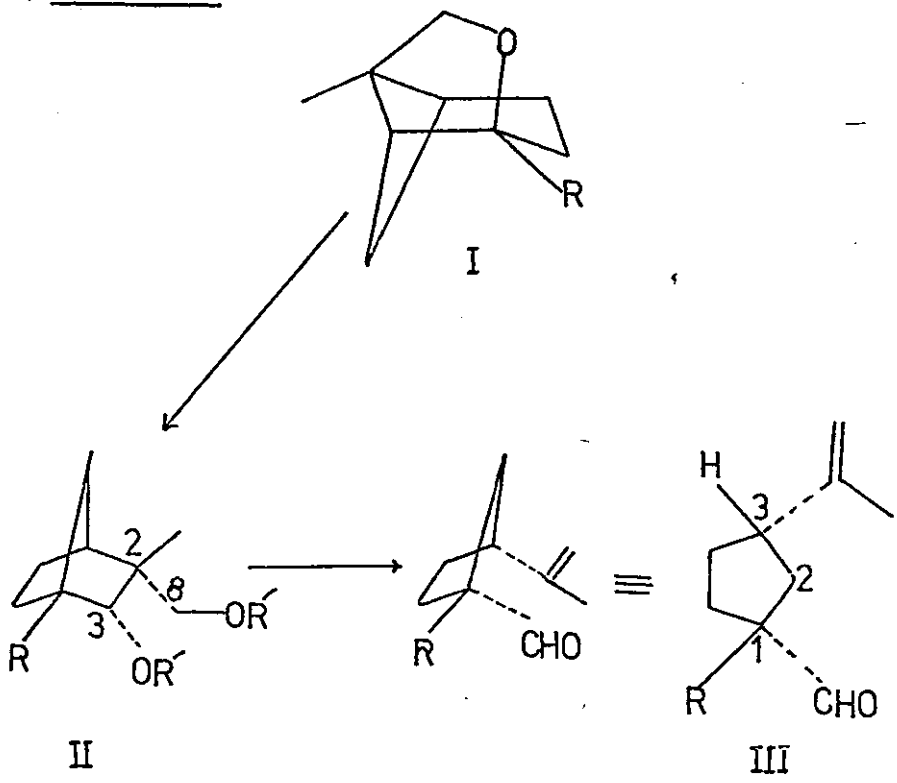


Clearly the acetyl group cannot in fact reach to C-1 to cause migration of the C1-7 bond. Such a mechanism is sterically impossible. Furthermore the nucleophile (Nu) appears at the secondary endo position; a result that militates against an acetoxonium intermediate. The mechanism postulated by us (Scheme I) is consistant with pinane chemistry and agrees with the experimental results.

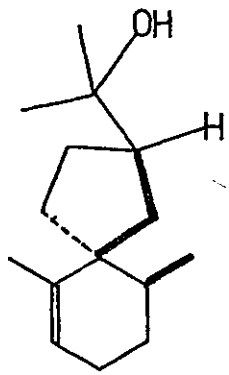
PART II CLEAVAGE OF C(2)-C(3) BOND IN II (SCHEME IV)

The transformation of 7-oxa-tricyclo [4,3,0,$0^{3,9}$] nonanes I (Scheme IV) into 8-substituted 1,3,3-trimethylnorbornane derivatives II is in effect a transformation of a masked 1,4-diol system (tetrahydrofuran derivative) into a 1,3-diol system. The 1,3-diol system may be used in a fragmentation reaction to break the C(2)-C(3) bond in structure (II). The resulting cyclopentane (III) contains two

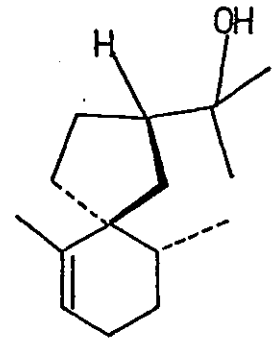
SCHEME IV



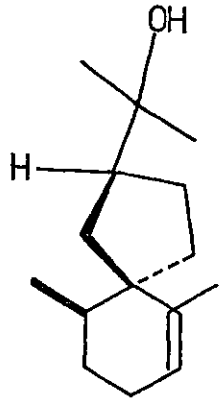
chiral centres of defined absolute configuration derived from (-)-pin-2(10)-ene , the tetrasubstituted centre C-1 being particularly difficult to construct by conventional synthetic methods. Its stereochemical relationships to (-)-hinesol (29), agarospirol (30) and (+)-β-vetivone (32)[29] is as follows. If R in structure (III) (Scheme IV) contained the methyl group attached to an sp^3-hybridised carbon atom and the aldehyde were converted into a methyl group attached to an sp^2 carbon system then the resulting structure (after formation of the cyclohexene



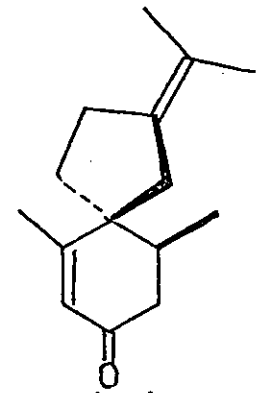
(29)



(30)



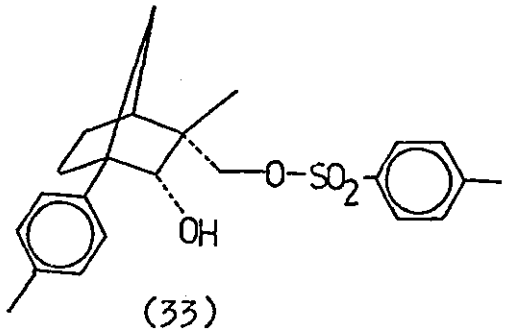
(31)



(32)

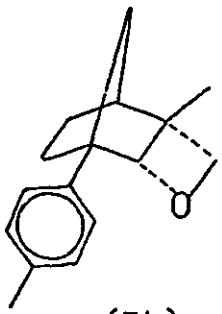
ring) would correspond to (31) which is the mirror image of (-)-hinesol (29). Interchanging the sp^3-methyl and sp^2-methyl groups in (31) gives agarospirol (30), which is epimeric with (-)-hinesol. Conversions of structures (29) and (30) by known procedures would result in (+)-β-vetivone[30] (32). These stereochemical correlations are reversed for the system corresponding to (III) (Scheme IV) derived from (+)-pin-2(10)-ene.

The key transformation for the utilisation of 8-substituted 1,3,3, -trimethylnorbornane (II) (Scheme IV) in the synthesis of spiro [4,5] decanes (29) - (32) is the cleavage of the C(2)-C(3) bond in (II). To study this reaction we chose the tolyl derivative (7) since it rearranges to (25) in 95% yield and all the intermediates in its preparation were crystalline solids. Tosylation of diol (27) gave the primary monotosylate derivative (33) (91%), treatment of which with

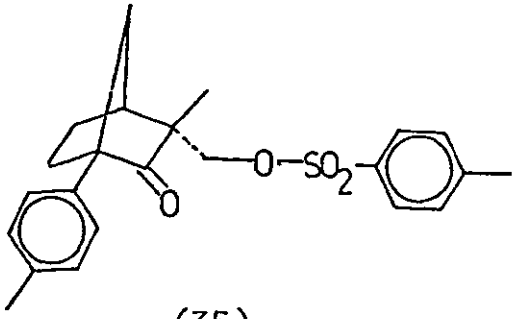


(33)

potassium t-butoxide gave, as expected the oxetan (34) in quantitative yield, thus exemplifying the stereochemical requirements of β-fragmentation[31].



(34)

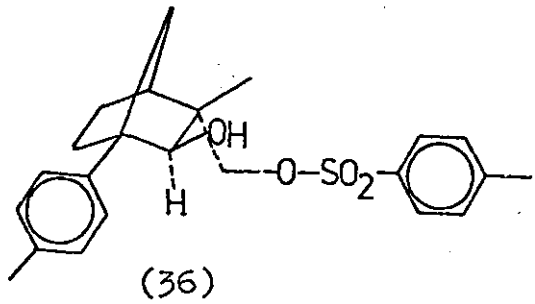


(35)

Oxidation of the tosylate (33) by use of Collins' procedure[32] (CrO_3-pyridine-CH_2Cl_2) gave the ketone (35) (93%) υ max. 1730cm^{-1}.

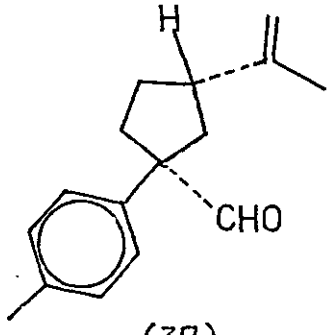
Reduction of the ketone (35) with lithium aluminium hydride reducing agents gave only the starting endo- alcohol (33), whereas use of sodium borohydride in tetrahydrofuran gave a 3:2 mixture of endo- and exo- alcohols as shown by n.m.r. Although this was not satisfactory

as a synthetic step we investigated the β-fragmentation of the exo-alcohol (36).



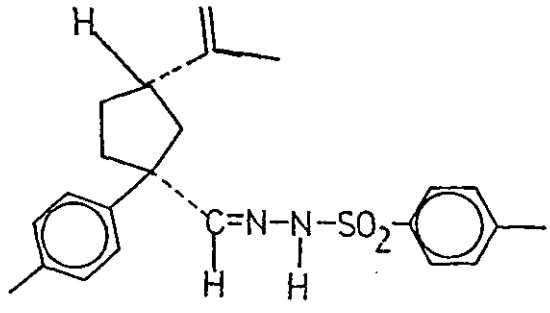
(36)

An inseparable mixture of the exo- and endo- alcohols (36) and (33) was treated with potassium t-butoxide-t-butyl alcohol to give oxetan (34) and the aldehyde (37) in the ratio 3:2 (no other products were formed).



(37)

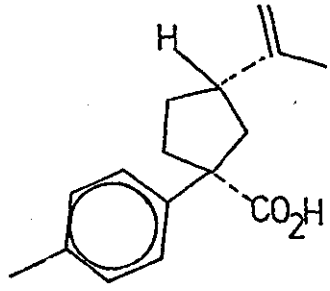
The aldehyde (37) ν max. 1730 and 1650cm^{-1} was isolated and purified as its p-tolylsulphonylhydrazone (38).



(38)

Modified borohydride reducing agents did not improve the ratio of exo- to endo- alcohols, consequently although β-fragmentation of the exo- alcohol (36) is feasible, as a step in a synthesis it is precluded.

The ketotosylate (35) was treated with potassium t-butoxide in dimethyl sulphoxide-water[33] at room temperature, and the isopropenyl acid (39) was isolated as a crystalline compound (⩾98% yield) υmax. 3300, 2800, 1695, 1640 and 900cm^{-1}. No isomerisation of the double



(39)

bond had taken place during the exposure to the strongly basic reaction conditions.

Cleavage of the non-enolisable ketone (35) is thus the method of choice for generating (+)-(1R,3S)-3-isopropenyl-1-p-tolylcyclopentane-1-carboxcylic acid (39). Modification of R in structure (II) (Scheme IV) and subsequent transformations via β-fragmentation appear to offer a simple route to optically active spiro [4,5] decanes (29) - (32) and simpler analogues with no substituents in the cyclohexane ring.

PART III BICARBONATE AS A NUCLEOPHILE

As it was possible to cleave the C(2)-C(3) bond in the exo-alcohol (36) a convenient synthesis of the compound was attempted. The retro-aldol reaction on the endo- alcohol (I) (as shown below) should give the thermodynamically more stable exo- alcohol (II). The aldehyde (II) would be convertable into the ring-opened aldehyde (37) via the route shown.

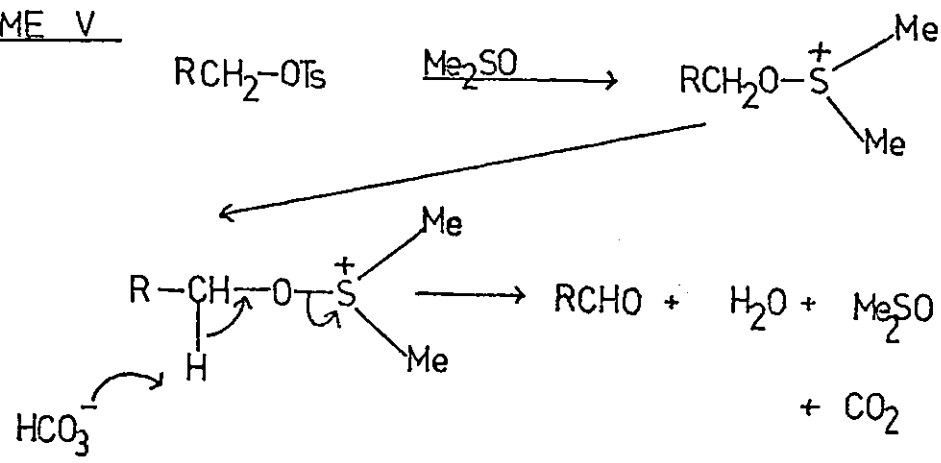
Compound (12) was treated with Me_2SO-$NaHCO_3$ at 100°C to obtain a very clean reaction. The product was isolated in 78% yield and had υ max. 1775cm^{-1}, 8.80(3H,s), 7.70(3H,s), 5.95(2H,ABq,J=11Hz), 6.0 (1H,bs), and 2.9(4H,bs).

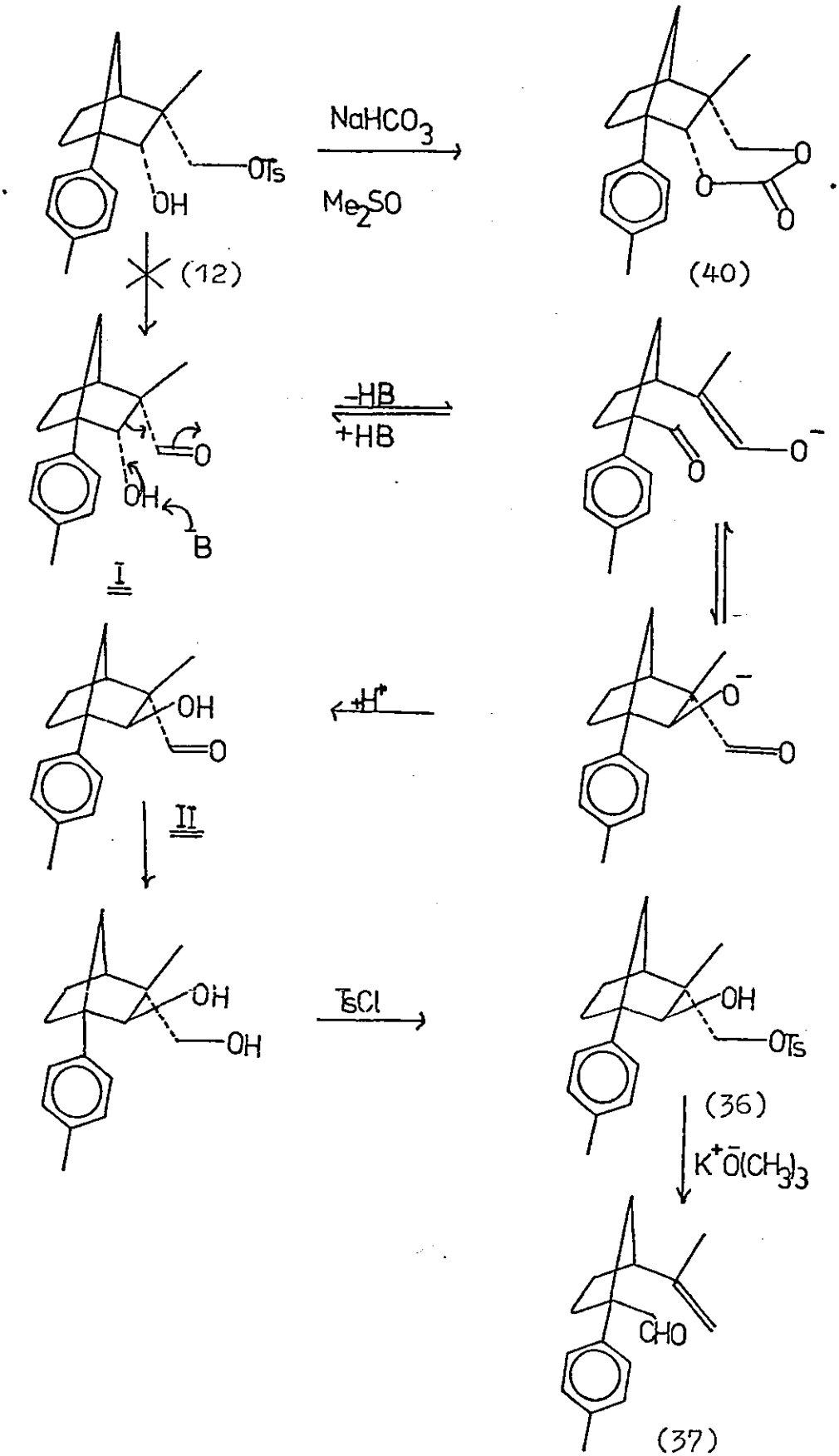
These data is only compatible with the cyclic structure (40) (no aldehyde was produced). This surprising experimental observation was consistently reproducible. To verify the structure of the carbonate (40) the diol (27) was converted into the cyclic carbonate (40) with phosgene-pyridine in toluene. Comparison of their t.l.c., n.m.r., i.r., m.p. and mixed m.p. showed them to be identical.

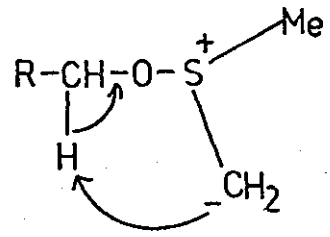
Oxidation of primary and secondary alkyl toluene-p-sulphonates using the Me_2SO-$NaHCO_3$ procedure[34] is thought to utilise the bicarbonate anion as a proton scavenger (Scheme V). The choice of mechanism i.e. path A or B is determined by the group R. The bicarbonate anion is not implicated in any other way presumably because it is thought to be an unlikely nucleophile to displace a primary toluene-p-sulphonate group in an SN.2 reaction[35].

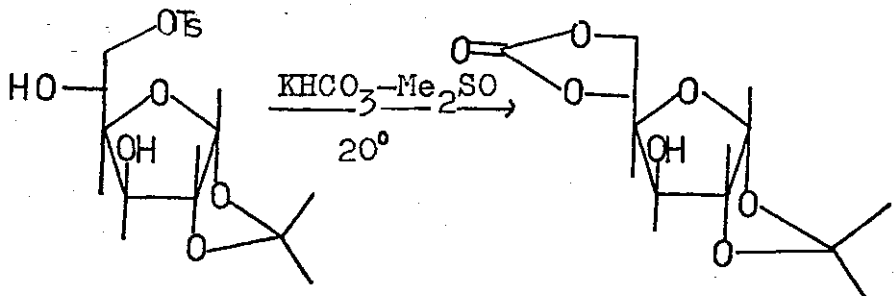
SCHEME V

A




NaHCO3
Me2SO
OTs
OH
(12)
(40)
-HB
+HB
O
OH
B
I
O⁻
+H⁺
II
TsCl
OH
OTs
(36)
K⁺Ō(CH3)3
CHO
(37)

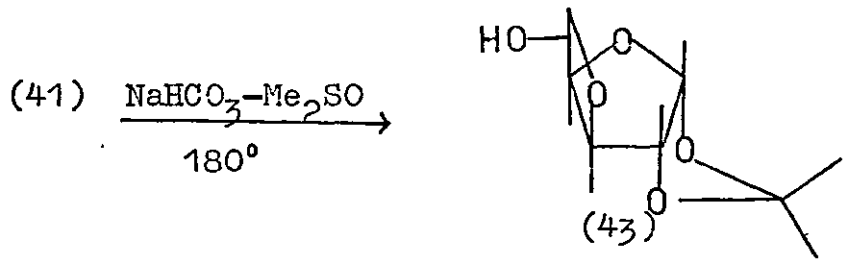




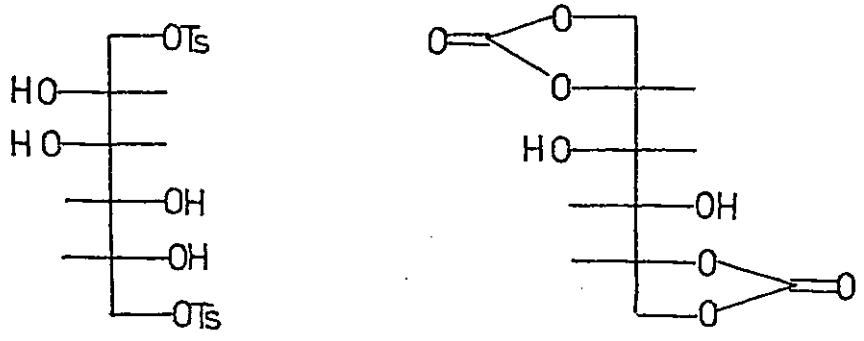
(41) (42)

Two examples of similar displacements are known. Treatment of the glucose derivative (41) with $KHCO_3$-Me_2SO at 20° gave the carbonate (42), whereas $NaHCO_3$-Me_2SO at 180° gave the anhydro derivative (43). Similarly mannitol 1,6 ditosylate (44) on treatment with $KHCO_3$-Me_2SO at 20° gave the bis-carbonate (45)[36].

Dr. R. Gigg is gratefully thanked for bringing this to our attention.



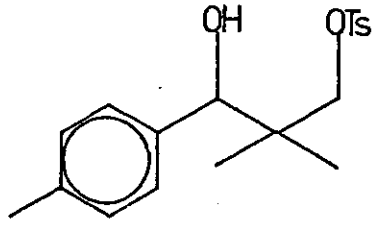
(43)



(44) (45)

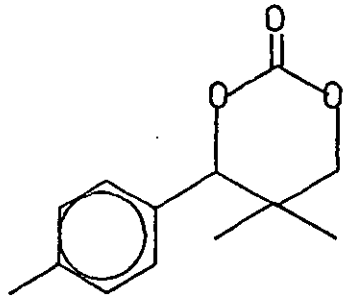
Both these experiments were carried out with the objective of preparing the anhydrosugar and not to oxidise the primary toluene-p-sulphonate group to an aldehyde.

To study the reaction conditions and to gain some insight into the possible mechanism of this reaction the more readily available substrate (46)[37] was used . The tosylate (46) was reacted with $NaHCO_3$-Me_2SO and a number of other systems designed to produce the



(46)

carbonate (47); the results are given in Table II. The formation

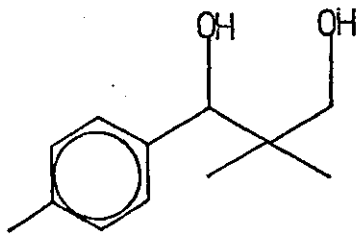


(47)

of the cyclic carbonate is favoured by high temperature (*ca.* 110°) and a brief exposure to the reagents ($NaHCO_3$-Me_2SO). Presumably the decomposition of sodium bicarbonate to sodium hydroxide and carbon dioxide causes hydrolysis of carbonate (46) to diol (48).

TABLE II

SUBSTRATE	REACTION CONDITIONS	PRODUCTS (YIELDS)
(46)	$NaHCO_3$-Me_2SO 60-70° (3h)	(48)
''	'' - '' 100° (0.5h)	(47) 50%
''	'' - '' 100° (1h)	(47)+(48)
''	$KHCO_3$-Me_2SO RT (3 days)	(48)
''	'' - '' 60° (0.5h)	(47) ca. 60
''	'' - '' 110° (0.5h)	(48)
''	K_2CO_3-Me_2SO 100° (15h)	(48)+(47) trace
''	$EtOCO_2^-Na^+$-Me_2SO 100° (0.5h)	(47) 44%
''	NaOH-CO_2-Me_2SO 100° (2h)	complex mixture no (47)
''	NaH-CO_2-Me_2SO 100° (2h)	complex mixture
''	NaOH-CO_2-Me_2SO 100° (6h)	(48)



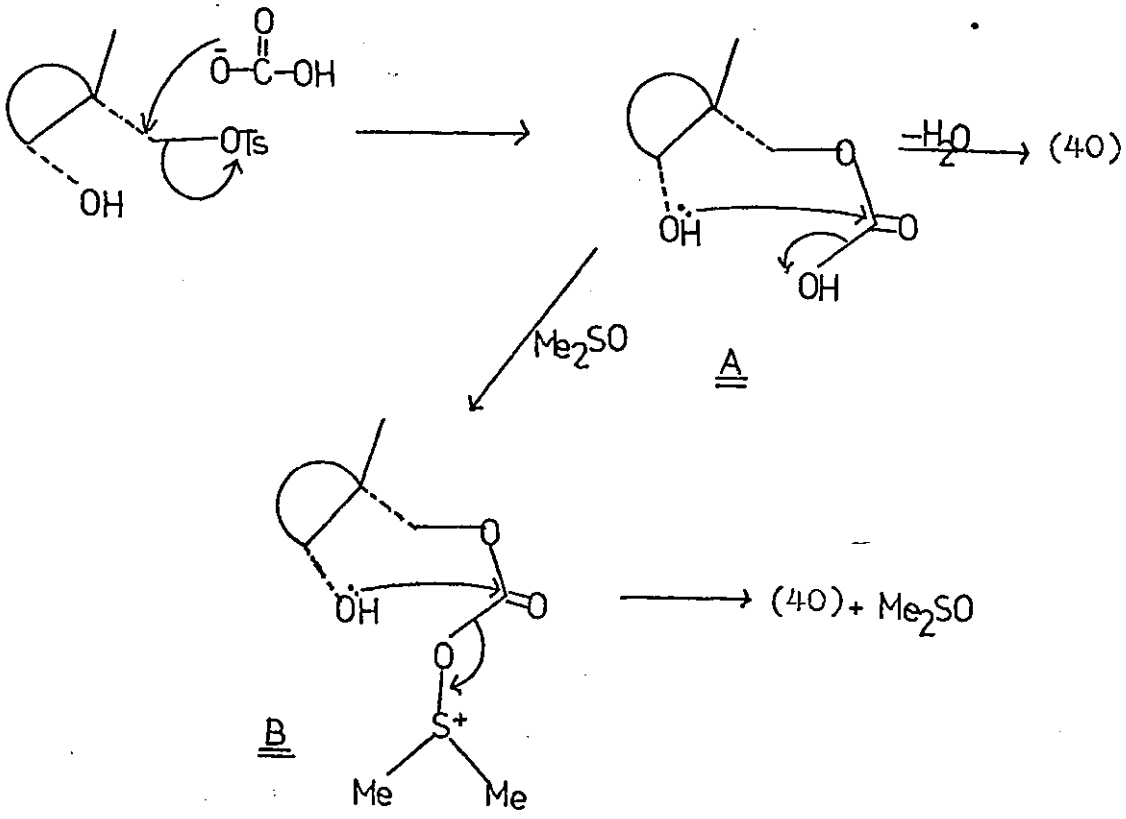
(48)

Displacements in Me_2SO are known to be accelerated. Indeed, neopentyl halides[38] can be converted into nitriles without rearrangement, and Me_2SO enhances the rate of bimolecular nucleophilic displacement of the toluene-p-sulphonates by bromide ion[39]. The nucleophilic constant (n) for bicarbonate anion (3.8) is almost identical to that of bromide anion[40]. The above experiments clearly demonstrate that for the particular substrates (12) and (46) under $NaHCO_3$-Me_2SO conditions, bicarbonate is a better nucleophile than Me_2SO.

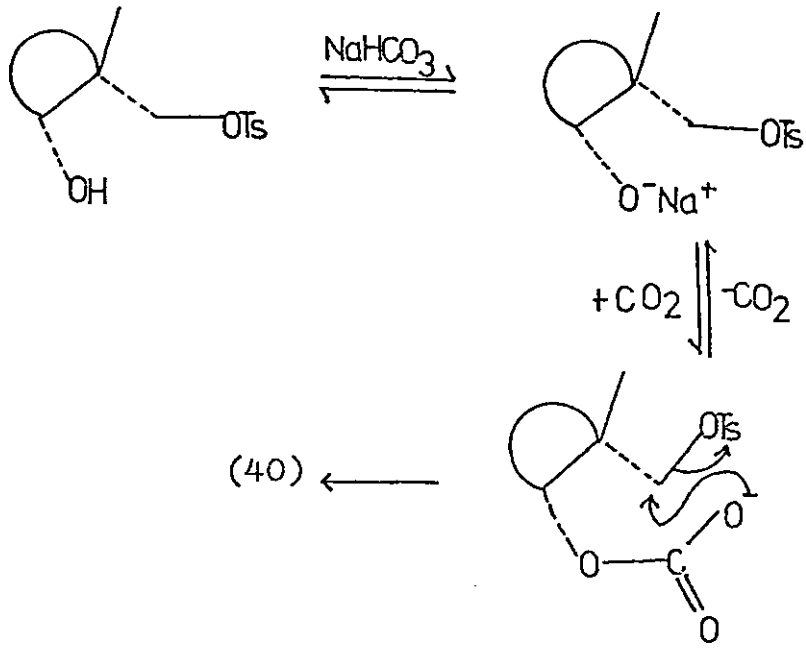
There are two possible mechanisms to account for these results (Scheme VI). The half-ester (A) is ideally constituted for the elimination of water and formation of carbonate (40). Since Me_2SO-$NaHCO_3$ oxidation usually, in the absence of any functional group that can trap intermediates, give carbonyl compounds, it is also possible that (A) also reacts with Me_2SO to give (B). Intermediates of type similar to (B) (without OH) are well known[41] and collapse to an aldehyde, whereas in this particular system it is trapped as the carbonate (40). Whether Me_2SO is implicated or not (in these particular systems), there is no reason to suppose that bicarbonate anion in Me_2SO would be a better nucleophile than Me_2SO itself towards other primary toluene-p-sulphonates. Consequently one is led to the conclusion that for a primary toluene-p-sulphonate, bicarbonate would be a better nucleophile than Me_2SO. The initially formed half-ester

SCHEME VI

PATH A



PATH B



C

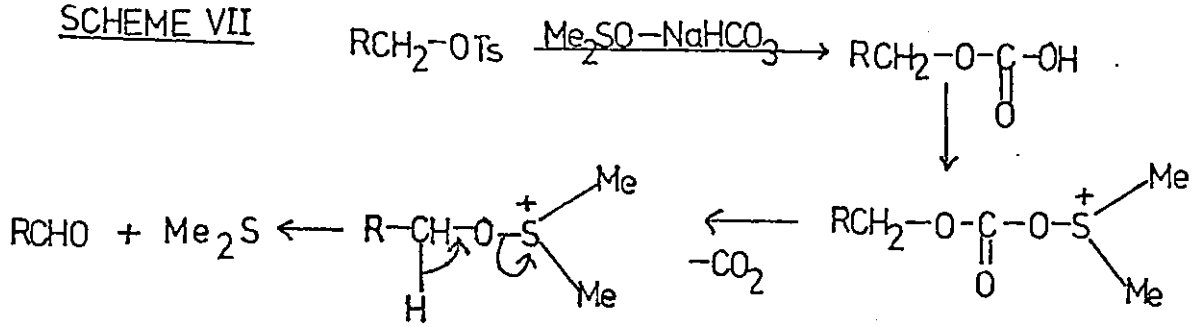
reacts with Me_2SO to produce an intermediate that expels CO_2 and α eliminates to an aldehyde (Scheme VII).

An alternative mechanism (Scheme VI path B), whilst a plausible alternative is less attractive on the following grounds. Any concentration of alkoxide species might be expected to undergo intramolecular oxetan or 1,3-fragmentation reactions rather than intramolecular reaction with CO_2 (see below). Compounds of type (46) are usually made from treatment of an alcohol with NaOH-CO_2[42]. Application of these conditions to (46) (see Table II) gave no carbonate (47), and conditions that avoid the presence of NaOH also failed. The experiment with (46) and $EtOCO_2^-Na^+$ must take place with displacement at the toluene-p-sulphonate group first.

When (12) is treated with $NaHCO_3$ in dimethylformamide or sulpholane the carbonate (40) is formed, (Scheme VI; A) (no other products are present). The reaction is slow (at least 24 hr.) compared with Me_2SO as solvent (0.5hr.). To eliminate the unlikely possibility that an oxetan (34) is an intermediate, (12) was converted to the oxetan (34) (Bu^tOK-Bu^tOH). Exposure of (34) to Me_2SO-$NaHCO_3$ at 100-110° for 15hr. gave no reaction.

Apart from Swains work[40] there is no reference to the nucleophilic properties of bicarbonate anion. It is difficult to avoid the conclusion that bicarbonate anion is an effective nucleophile in Me_2SO for (12) and (46).

SCHEME VII



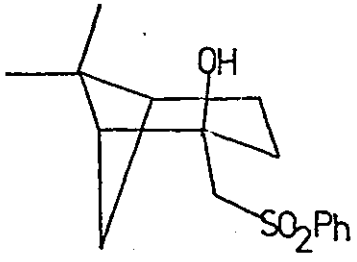
The work with compound (46) was carried out in conjunction with Mr. R.G. Moore.

PART IV ATTEMPTS TO FIND A SUITABLE R GROUP IN COMPOUND I (SCHEME IV)

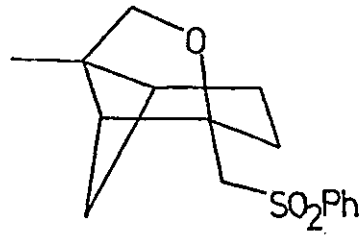
As stated earlier a method of cleaving the C(2)-C(3) bond in the non-enolisable ketone (35) was devised and therefore modification of R in structure (II) (Scheme IV) was the next problem to tackle.

The intriguing chiral properties of the α-sulphonyl carbanion has been a source of much practical and theoretical discussion[43]. The possibility that a methylene group adjacent to a bulky chiral moiety and a sulphonyl group might be asymmetrically alkylated was considered.

The sulphone (50) was prepared by addition of phenyl-sulphonyl methylmagnesium iodide[44] to (+)-nopinone (4) to give the hydroxy-sulphone (49), followed by treatment of (49) with HgO/I_2/hν to give (50) (95%). The hydroxy sulphone (49) could also be prepared from

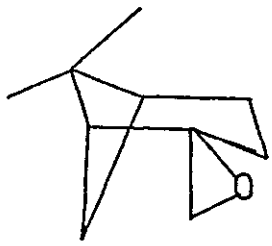


(49)

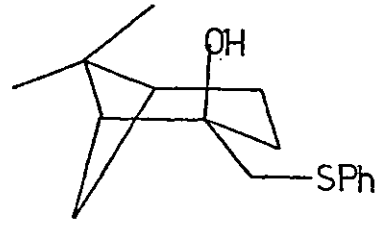


(50)

(+)-nopinone (4) by first of all forming the epoxide[50] (51) (NaH-$Me_3S^+I^-$), followed by opening of the epoxide ring with thiophenoxide ion (K_2CO_3-C_6H_5SH) to give the hydroxy-sulphide (52) and finally oxidising (with m-Cl.$C_6H_5CO_3H$) to the sulphone (49). By use of the

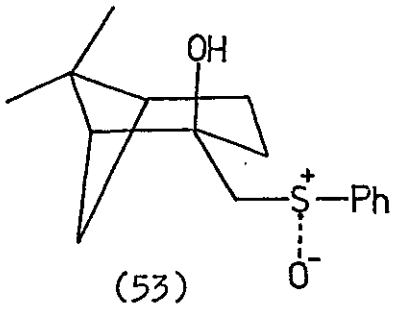


(51)

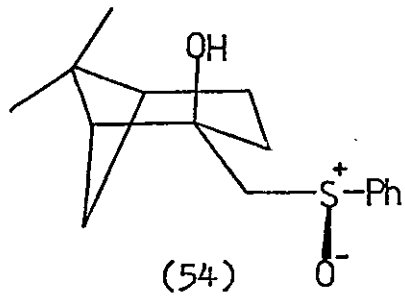


(52)

epoxide method it was possible to prepare the two diastereoisomeric sulphoxides (53) and (54) by use of only one mole of m-Cl.$C_6H_5CO_3H$. (n.m.r. shows a 1:1 ratio).

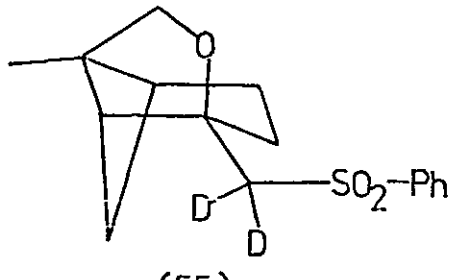


(53)



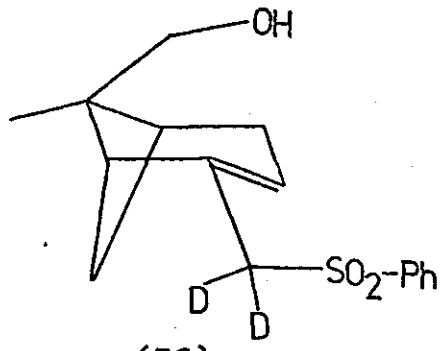
(54)

Treatment of sulphone (50) with n-butyllithium (excess) at -70° in ether, followed by addition of deuterium oxide (at -70°) gave the sulphone (55) (100%). There was no trace of monodeuterated



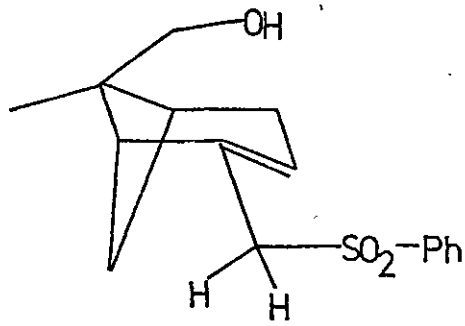
(55)

sulphone (as judged by n.m.r.). The sulphone (55) did not exchange out the deuterium atoms on treatment with aqueous lithium hydroxide, sodium hydroxide, or potassium t-butoxide in t-butanol. All attempts to prepare the monoanion of (50) failed and only mixtures of (50) and (55) were formed. If the dianion of (50) was quenched with deuterium oxide at room temperature the olefin (56) was formed (95%). If the dianion of (50) at -70° was allowed to warm to room temperature, then



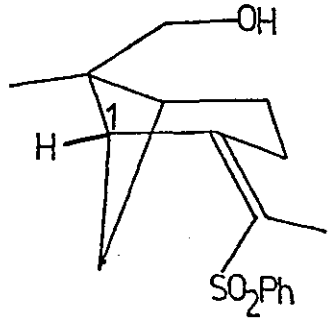
(56)

quenched with water the olefin (57) (95%) was formed.



(57)

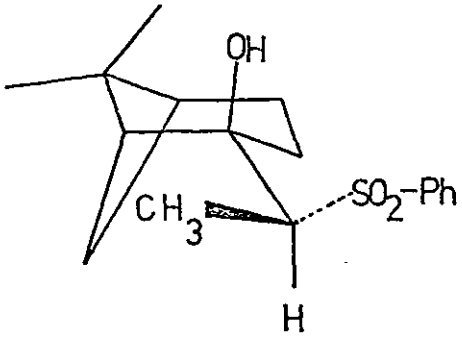
Treatment of the dianion of (50) at -70° with methyl iodide gave no reaction, but on warming the mixture to room temperature the olefin (58) was formed. The assignment of geometrical configuration



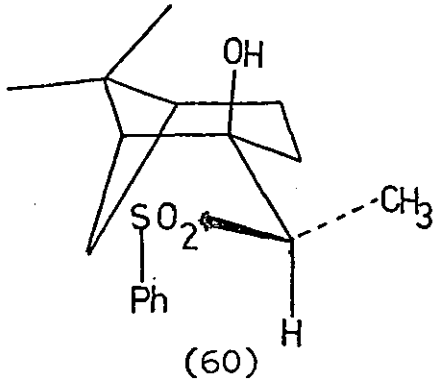
(58)

is based on the i.r. and n.m.r. spectra. The i.r. band at 3475cm^{-1} indicates a hydrogen bonded -OH group, presumably to the sulphonyl group; a situation that can only take place with the geometric configuration (58). The n.m.r. spectrum exhibited a triplet at 6.24 (1H,J=2.5Hz) which can be assigned as the Cl proton if it is deshielded by the phenylsulphonyl group.

(+)-Nopinone (4) was reacted with phenylethylsulphonyl-magnesium iodide to give a mixture of (59) and (60) (arbitarily assigned configuration) in approximately equal proportions (n.m.r. and t.l.c).



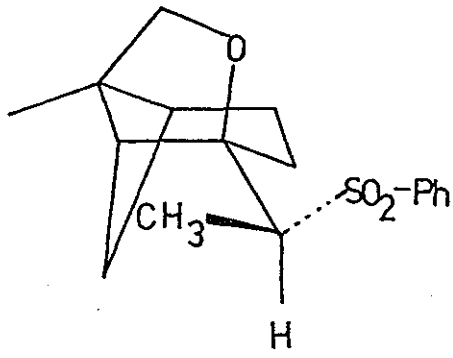
(59)



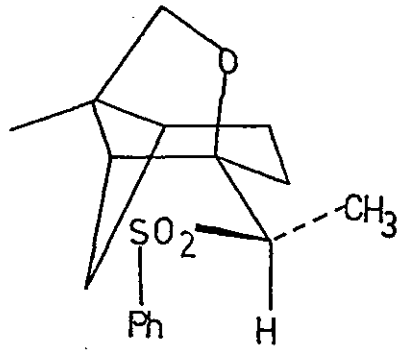
(60)

Intramolecular oxidation ($HgO/I_2/h\upsilon$) of the mixture gave the corresponding ethers (61) and (62). The mixture of (61) and (62) could be separated by p.l.c. Treatment of either (61) or (62) with n-butyllithium in ether at -70° gave the same olefin (58). No isomeric olefin could be detected by n.m.r. on the total product before purification.

Treatment of the olefin (58) with potassium-t-butoxide in t-butanol gave a 1:1 mixture of the cyclic ethers (61) and (62) as the only products. Concerted closure of the alkoxide derived from (58)



(61)

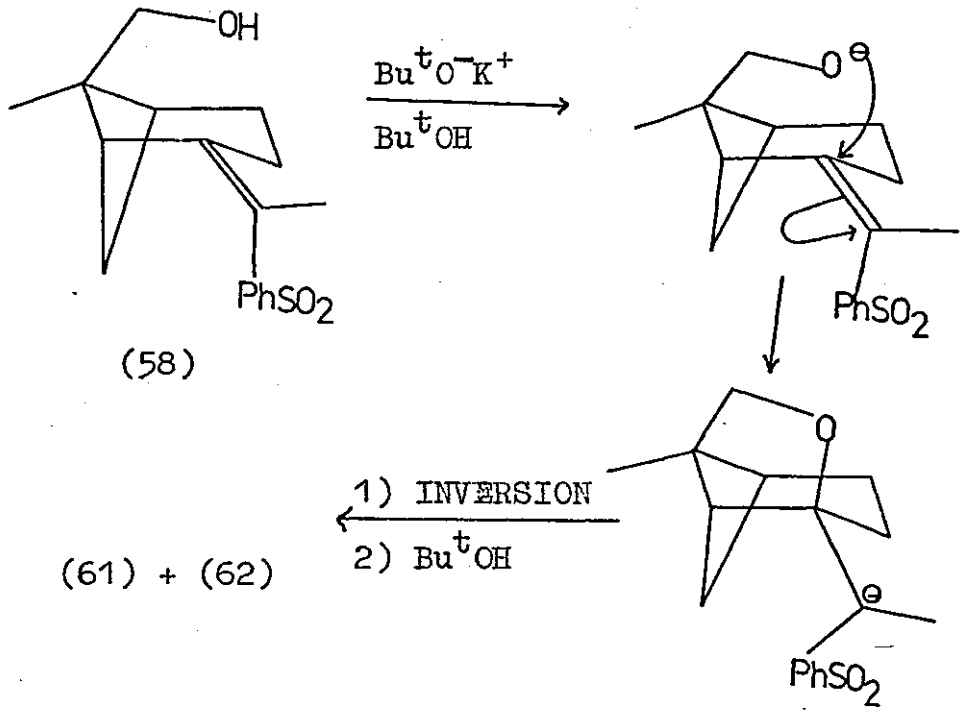


(62)

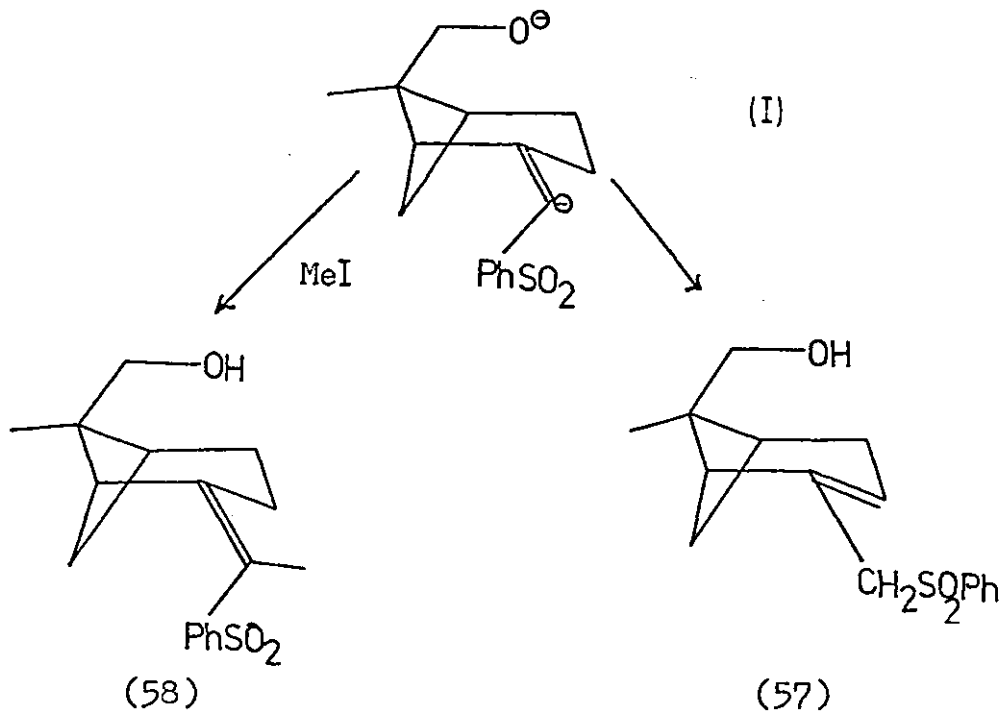
ought to give (62) as the only product. Evidently the ring closure of (58) to (61) and (62) must proceed via an α-sulphonyl carbanion that inverts before it is protonated from the α-face (opposite the gem-dimethyl bridge). (Scheme VIII).

The diastereoisomeric sulphones (61) and (62) undergo irreversible carbanion elimination at -70° either via syn- and anti- processes to give the same olefin (58), or the initially formed carbanion first undergoes inversion in one case, followed by elimination. In general bimolecular elimination processes from diastereoisomeric sulphonate esters leads by trans- elimination to isomeric olefins[48]. A few cases of so-called stereoconvergent eliminations are known[49]. The reverse process, conjugate addition to an α,β-unsaturated sulphone (58) to give both diastereoisomers (61) and (62) must be non-concerted and proceed with α-sulphonyl carbanion inversion. This result implies that the forward process proceeds via α-sulphonyl carbanion inversion rather than syn- and anti- elimination. A distinction hitherto not observed.

SCHEME VIII



SCHEME IX

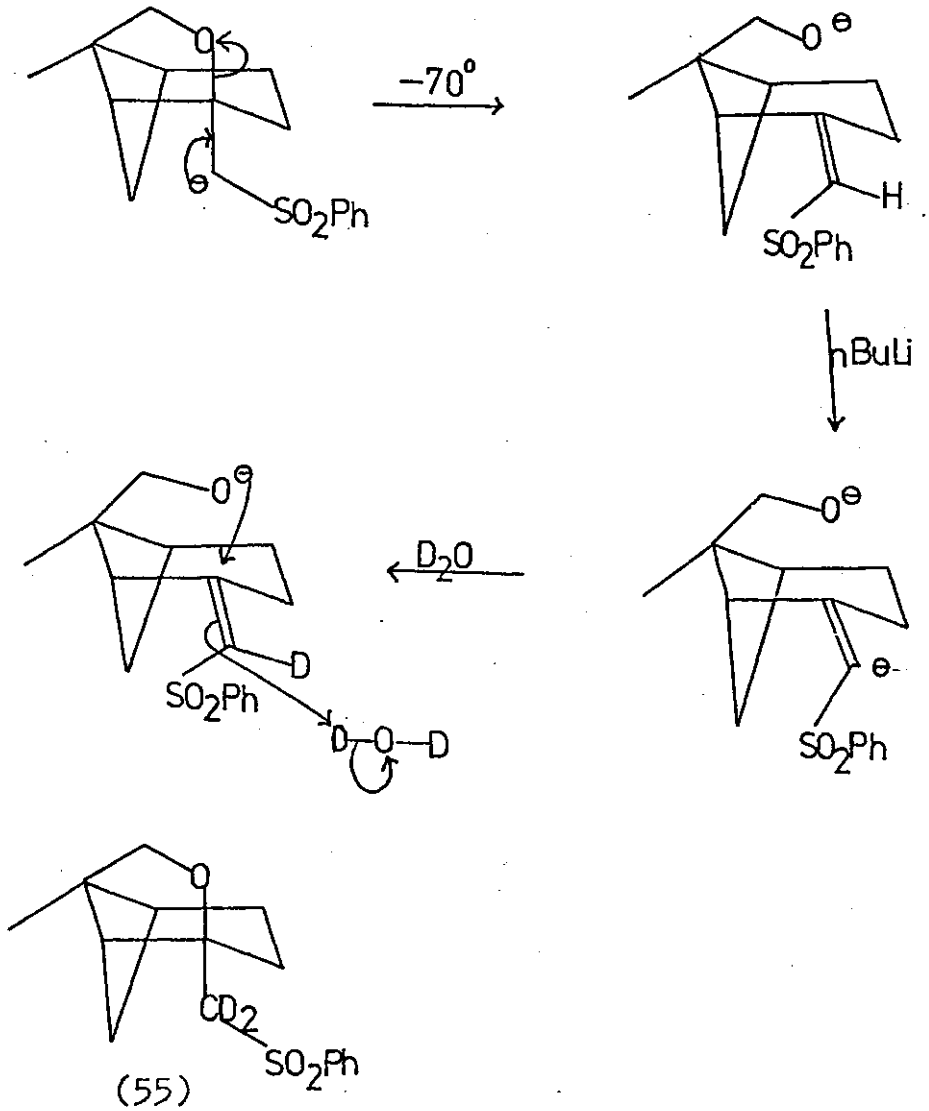


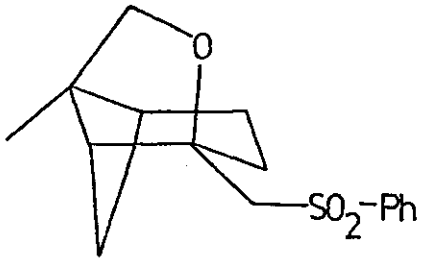
There are a number of reports of 1,1-dianions[45]. The result described for compound (50) can be explained as follows:- (Scheme IX). The dianion remains in the closed ether form at -70°. At room temperature it undergoes irreversible carbanion elimination (ElcB)[46], followed by isomerisation to the β,γ-unsaturated sulphone (57). In the presence of methyliodide the vinylsulphonylcarbanion is trapped to give (58). An alternative explanation is that the monoanion (Scheme X) readily undergoes irreversible ElcB elimination to give the olefin-oxide which reacts with n-butyllithium to give the vinylsulphonylcarbanion. This species on work-up with deuterium oxide gives (55). Whilst there is no diagnostic evidence to distinguish between these two alternatives it is felt that the former picture is more likely. The formation of (56) must involve a 1,1-dianion. Apparently methylation of I (Scheme IX) keeps the substrate in the ring opened form presumably because the lithium alkoxide is not nucleophilic enough to conjugatively add to give (61) and (62). Whereas the potassium alkoxide, being more nucleophilic gives (61) and (62). If I (Scheme IX) were an intermediate at low temperature, subsequently quenched with deuterium oxide to give (55), it must be present as the lithium alkoxide which does not close to give the ether (50). Consequently the formation of a 1,1-dianion of (50) at low temperature rather than the alternative vinylsulphonylcarbanion explanation is favoured. Furthermore if the supposed 1,1-dianion of (50) is allowed to open to the isomeric olefin form by warming to room temperature then cooled to -70° only the olefin (57) is obtained.

It was therefore found to be impossible to alkylate the sulphone (50) as its monoanion or its dianion, due to the ease of the ether cleaving reaction to give the olefin (57).

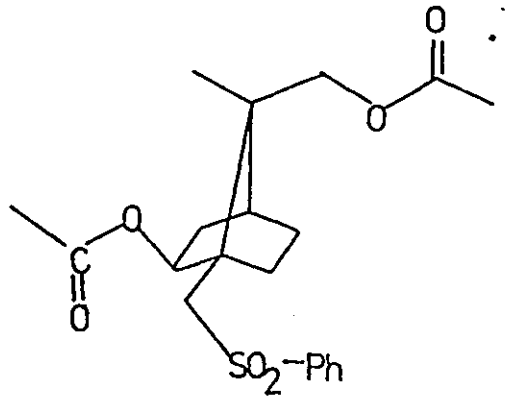
Treatment of the sulphone-ether (50) with acetic anhydride and boron trifluoride-ether gave a mixture of six compounds. The major compound (63) being formed in only twenty five percent yield.

SCHEME X



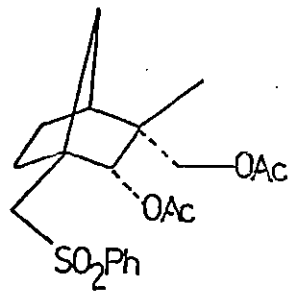


(50)

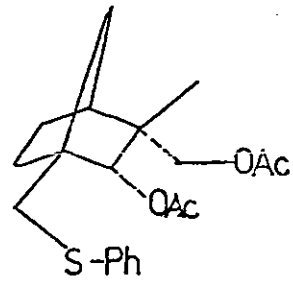


(63)

It seems that the sulphone group must destabilise the intermediate (Scheme II) and gives (63) not the fenchyl derivative (64).



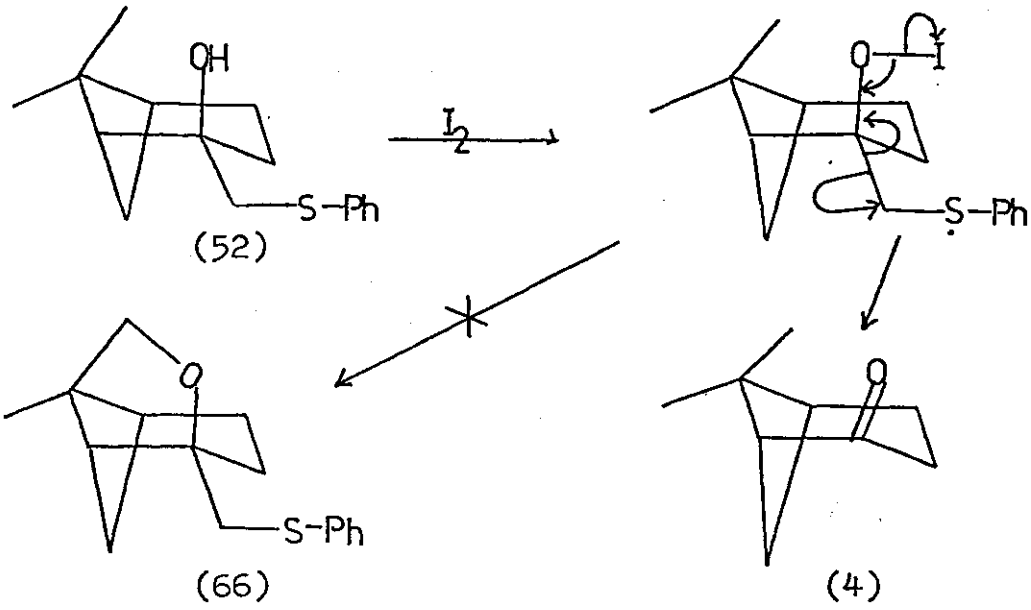
(64)



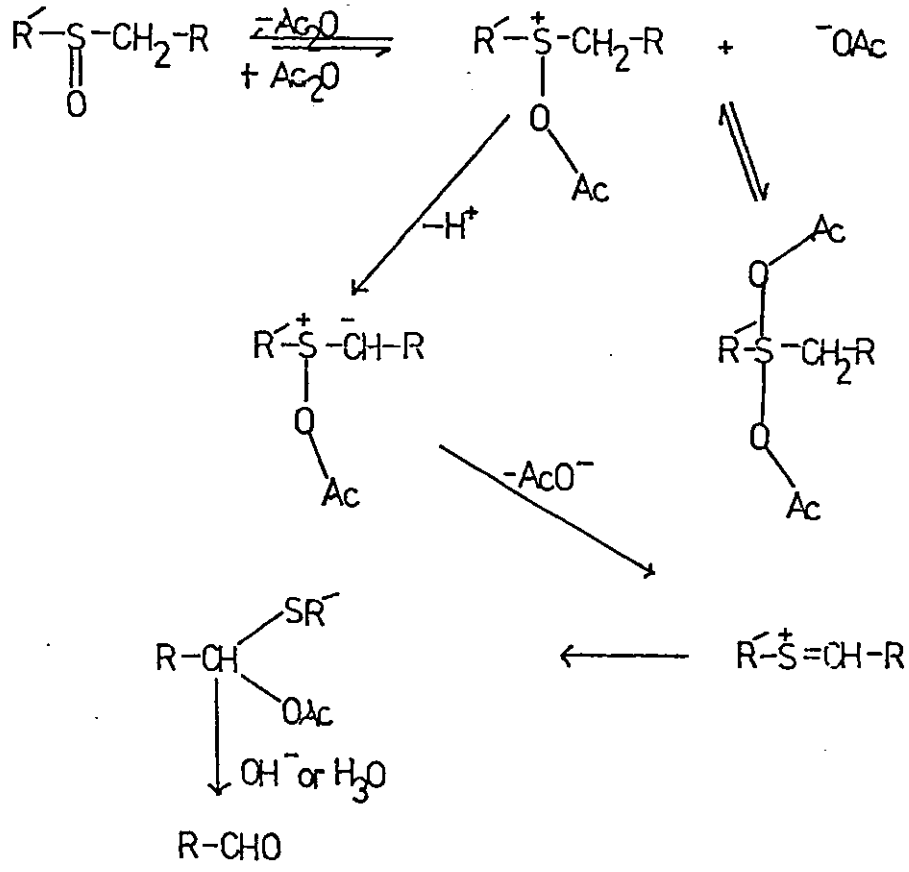
(65)

The sulphone obviously can not be used prior to rearrangement. The preparation of the sulphide (65), which could be oxidised by the usual method to the sulphone (64) was attempted.

The sulphide (52) was subjected to the usual photolysis conditions ($HgO/I_2/h\nu$) but instead of the ether (66) the only product was nopinone (4) formed by an α-fragmentation process.

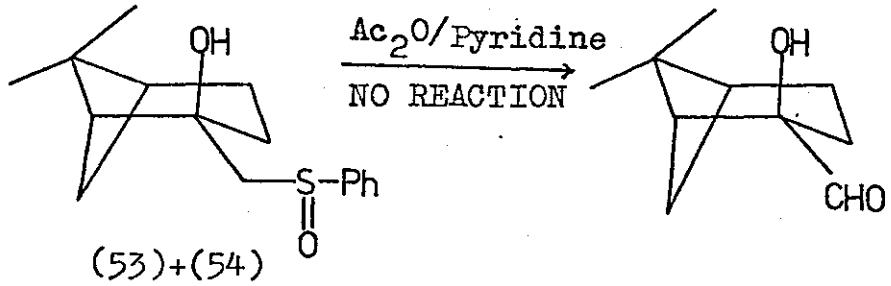


The Pummerer reaction[54] is well known to cleave sulphoxides possessing an α carbon atom bearing a hydrogen atom. The α carbon atom is oxidised and the sulphur atom reduced. It was hoped that

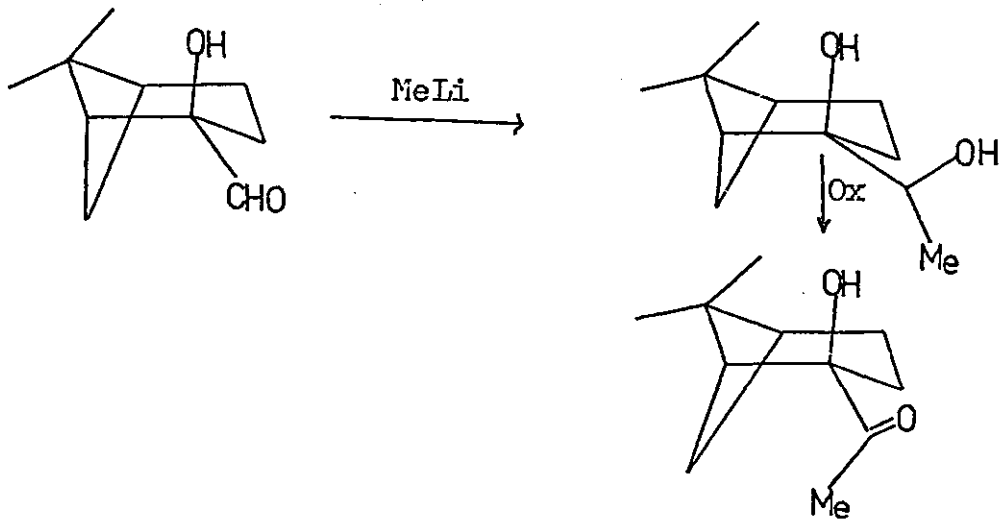


treatment of the sulphoxides (53) and (54) under basic Pummerer[55]

conditions would produce the corresponding aldehyde which could be

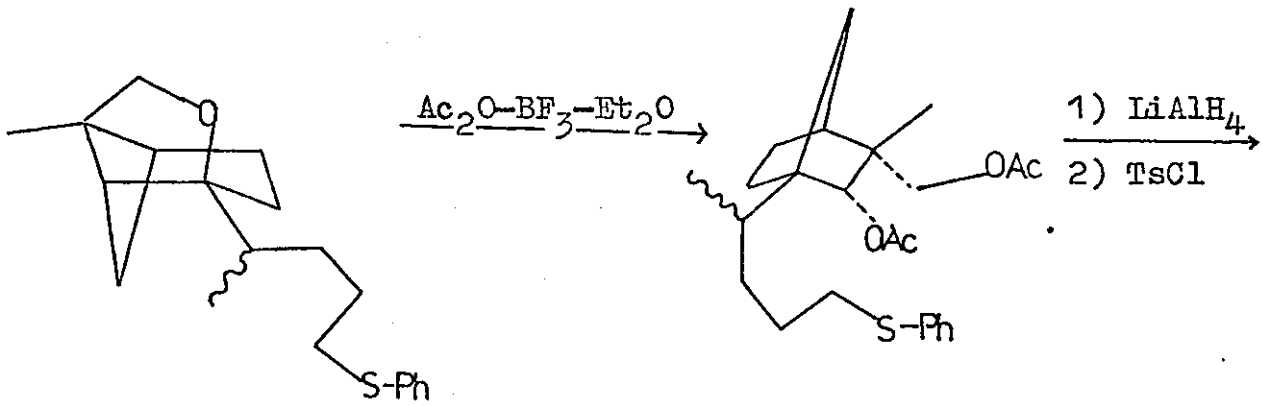


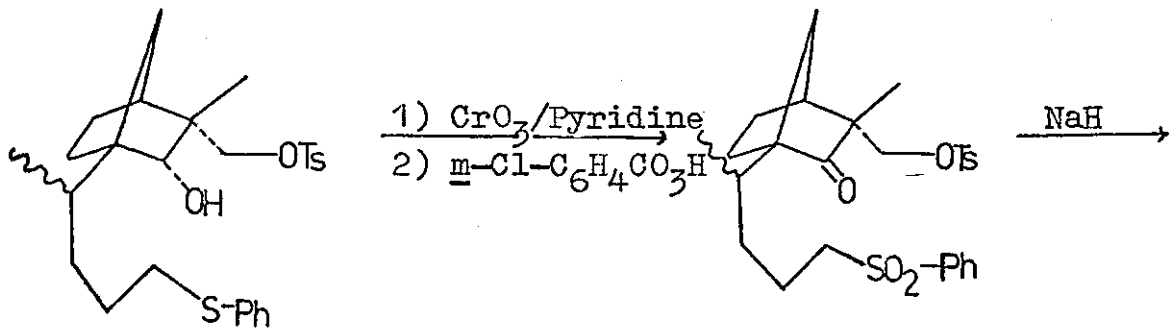
converted to the methyl ketone by treatment with methyl lithium followed by selective oxidation. The methyl ketone would provide a

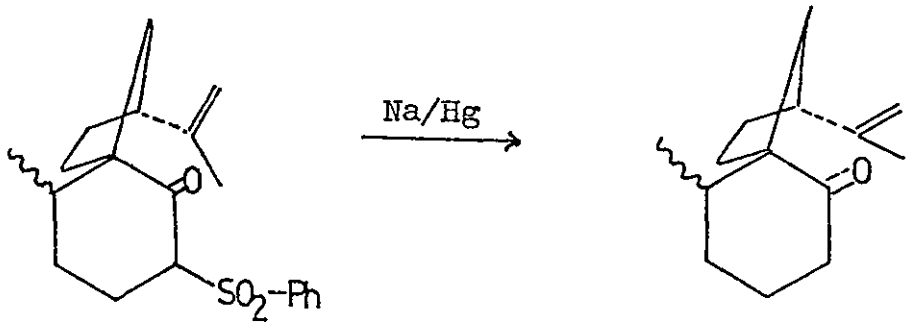


usable R group in structure (I) (Scheme IV) as the Wittig reaction could be used to give a suitably substituted olefin. The sulphoxides were treated with acetic anhydride in pyridine but no reaction occurred under any of the conditions tried.

It was also considered using R=Ph-S-$(CH_2)_3CHCH_3$, structure (I) (Scheme IV), as under the rearrangement conditions this would give (67) which should give the spiro [4,5]-decane system (68) by use of the route shown.

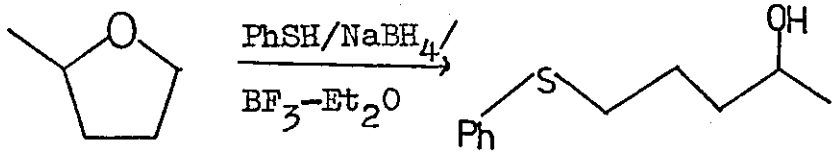

Ac2O-BF3-Et2O
1) LiAlH4
2) TsCl
OAc
OAc
S-Ph
S-Ph


OTs
OH
S-Ph
1) CrO3/Pyridine
2) m-Cl-C6H4CO3H
OTs
O
SO2-Ph
NaH


O
SO2-Ph
Na/Hg
O

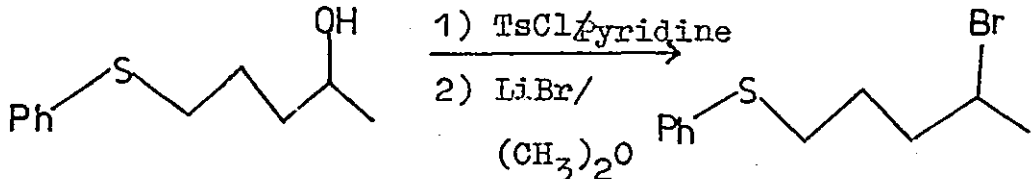
(68)

2-Methyltetrahydrofuran was treated with phenyl thioborane to give 5-phenylmercapto-2-pentanol (69)[51].



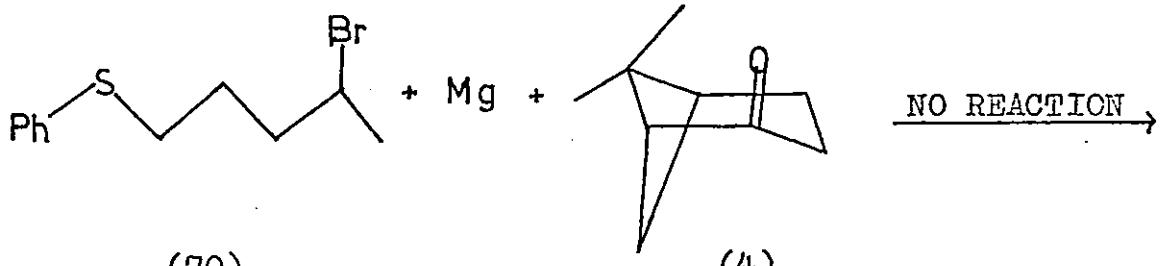
(69)

The alcohol (69) was converted into the bromide (70) by tosylation and bromination. The Grignard reagent derived from (70) was



(69) (70)

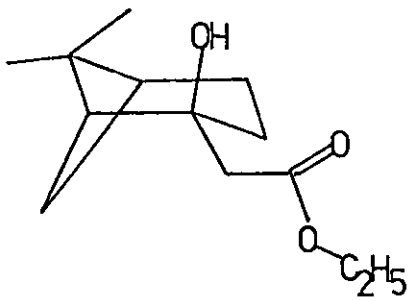
added to nopinone (4) but no reaction occurred under any condition tried.



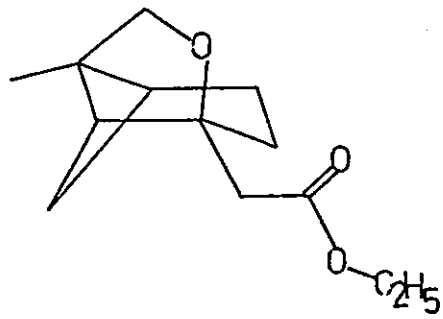
(70) (4)

To test the theory that the Grignard reagent is too hindered, nopinone was treated with isopropyl magnesium bormide. No reaction occurred under any conditions tried with the secondary Grignard. It seems that steric hinderance stops the reaction and therefore this line of approach was discontinued.

The hydroxy ester (71)[7] is known and is convertable into the ether (72). The ether (72) was treated with acetic anhydride-boron trifluoride ether to give a mixture of mono and diacetates which

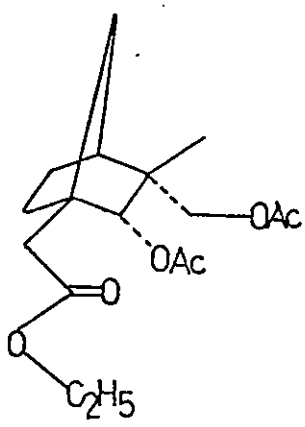


(71)



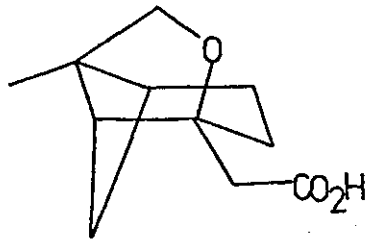
(72)

when acetylated (pyridine-acetic anhydride) gave the rearranged product (73).

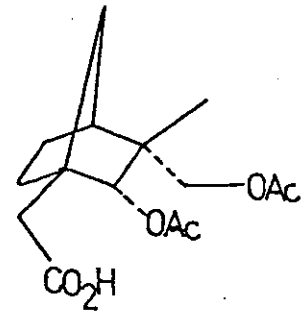


(73)

The ester (72) was hydrolysed under basic conditions ($KOH/CH_3OH/H_2O$) to the acid (74) which when treated with acetic anhydride-boron trifluoride-ether gave the rearranged acid (75).

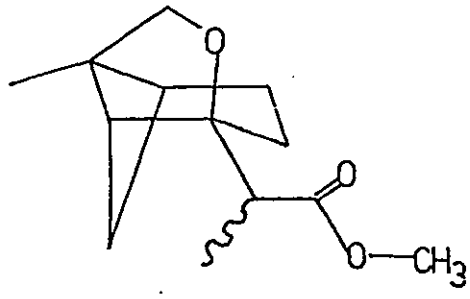


(74)

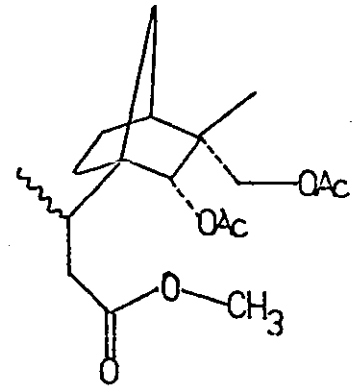


(75)

Having shown that it is possible to rearrange ethers such as (72) it was hoped that ether (76) would undergo rearrangement to the fenchyl derivative (77).

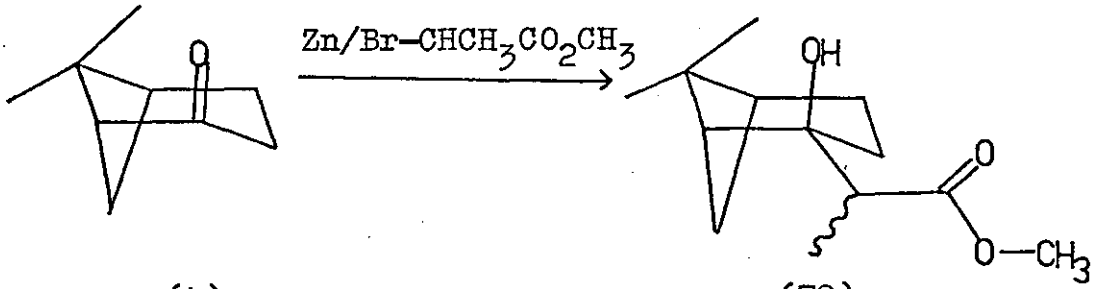


(76)



(77)

To prepare the ether (76) the alcohol (78) was prepared by the Reformatsky reaction between (+)-nopinone (4) and 2-methyl-2-bromo propionicacid methyl ester. The hydroxy ester (78) was photolysed under the usual conditions to give only nopinone (4). It seems that

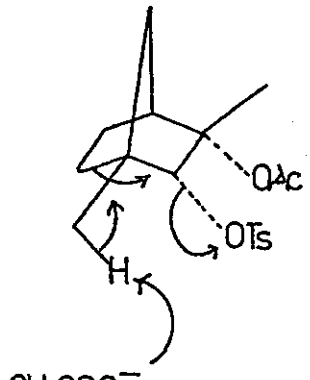


(4) (78)

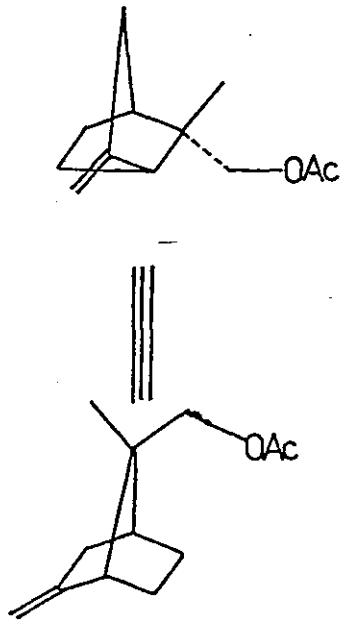
the introduction of the methyl group makes the α-fragmentation process the more favourable one. The methyl group must be added after the rearrangement if this method is to be used as a synthesis of spiro [4,5] decanes.

PART V ATTEMPTED SYNTHESIS OF γ-γ-DIMETHYL-ALLYL-9α-FENCHENE (80)

The rearrangement of the ether (6) with acetyl toluene-p-sulphonate in acetonitrile gave the acetate tosylate (8). The tosylate (8) should on treatment with acetic acid-sodium acetate undergo re-

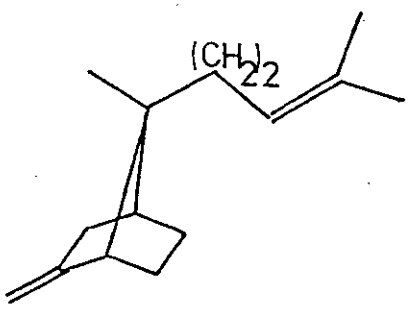


(8)



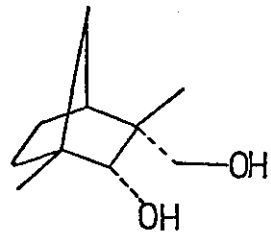
(79)

arrangement to (79) which would be convertable to γ,γ-dimethyl-allyl-9α-fenchene via a short series of reactions.



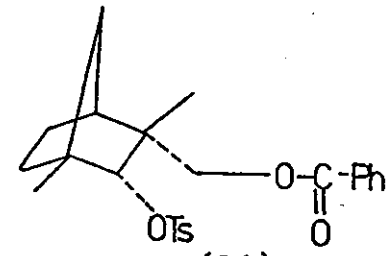
(80)

As the preparation of the acetate-tosylate (8) involves the tedious use of acetyl toluene-p-sulphonate the benzoate-tosylate (81) was prepared from the diol (10) by selective primary monobenzoylation followed by tosylation.



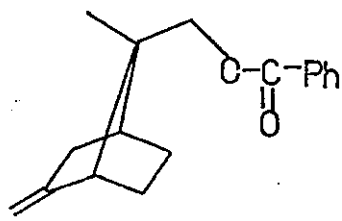
(10)

1) PhCOCl/ Pyridine
2) TsCl/ Pyridine

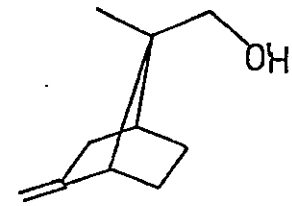


(81)

The benzoate-tosylate (81) was treated with sodium acetate in acetic acid at 100° to yield as the sole product (by n.m.r.) the 9-substituted fenchene (82).

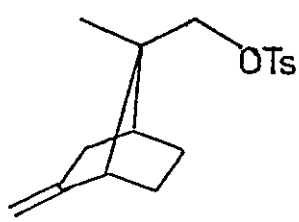


(82)

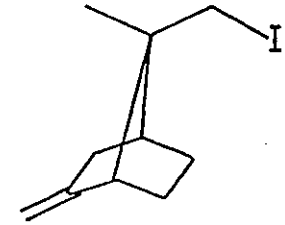


(83)

Reduction of the benzoate (82) with lithium aluminium hydride produced the alcohol (83) which was tosylated with p-toluene-sulphonyl-chloride in pyridine to give the primary tosylate (84).



(84)



(85)

The tosylate (84) was converted into the iodide (85) by reaction with sodium iodide in refluxing acetone. To convert (85) into α,γ-dimethyl-allyl-9α-fenchene (80), the Corey reagent[52a] ($[Ni(CO)_4]$ + $[BrCH_2CH{=}CMe_2]$) seemed to be the method of choice. The iodide (85) was treated with the nickel π allyl complex (derived from $Ni(CO)_4$ and isoamyl bormide) but no reaction occurred. The lack of reaction may be explained by the fact that it was impossible to dry the iodide as the synthesis was carried out on small amounts (which were not distillable).

While we were carrying out this work a paper[28] appeared in the literature, which reports the same synthesis, based on the rearrangement outlined in our preliminary communication[1a]. The authors synthesise α,α-dimethyl-allyl-9α-fenchene (80) from the iodide (85) using the Corey reaction[52] and show that it is identical with a bicyclic hydrocarbon isolated in 1963 (from Valeriana Wallichi by Bhattacharyya et al[53].

EXPERIMENTAL

Unless otherwise stated the following data apply to experiments described in this section. Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. I.R. and u.v. spectra were recorded with a Unicam SP200 and SP800 respectively. Mass spectra were taken with an A.E.I. MS9 double focussing spectrometer. N.m.r. spectra were recorded with Varian A60 and HA100 instruments for solutions in [^{2}H]-chloroform or carbontetrachloride with tetramethylsilane as internal standard. All solvents were purified prior to use by standard techniques. Light petroleum refers to the fraction of b.p. 40-60°.

The following abbreviations refer to the n.m.r. data. s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad.

PINAN-2β-OL[4] (2)

This compound m.p. 57-59°, and $[\alpha]_D^{20}$ -44° (ether), was prepared by ozonolysis[26] of (-)-pin-2(10)-ene and treatment of the resulting (+)-6,6-dimethyl-norpinan-2-one (4) with methylmagnesium bromide.

6,9-DIMETHYL-7-OXATRICYCLO [4,3,0,0^{3,9}] NONANE[7,8] (6)

To a solution of pinan-2β-ol (2) (52g) in carbon tetrachloride (750ml) containing yellow mercury (II) oxide (217g) at 0° was added bromine (19ml) during 1.5h. The stirred mixture was protected from light. After 3h. at 0° the mixture was filtered and the filtrate was irradiated at 0° for 1.25h. with a tungsten lamp (500W; 30cm from the flask). Nitrogen was bubbled through the solution continuously to remove hydrogen bromide. The solution was heated to reflux and after 1h. cooled and washed with aqueous sodium chloride solution. The solution was dried (Na_2SO_4) and evaporated to a straw brown oil.

Distillation gave the pure ether (6) (22g), b.p. 60° at 9mmHg.

1,3-DIMETHYL-2α-p-TOLYLSULPHONYLOXYNORBORNAN-3α-YL-METHYL ACETATE (8)

To a solution of ether (6) (1.0g) in acetonitrile (10ml) at -20° was added acetyl toluene-p-sulphonate (1.7g) in acetonitrile (10ml). After 14h. at room temperature (20°) the mixture was poured into water (50ml) and extracted with light petroleum. The dried (Na_2SO_4) light petroleum layer on evaporation gave a yellow oil (2.0g). The oil was dissolved in light petroleum containing 10% acetone and chromatographed on silica gel plates (60 x 20cm). Elution gave pure acetate-tosylate (8) (80%), m.p. 156-58° (from light petroleum), υmax. 1725 and 1595cm^{-1}, $[\alpha]_D^{25}$ + 54.0 (c 1.9 in chloroform), τ 8.95(3H,s), 8.99(3H,s), 7.95 (3H,s), 6.13(2H,ABq,J=10Hz), 5.48(1H,bs), and 2.48(4H,ABq,J=8Hz). (Found: C, 62.0; H, 7.2. $C_{19}H_{26}O_5S$ requires C, 62.3; H, 7.2%).

2α-ACETOXY-1,3-DIMETHYLNORBORNAN-3α-YL-METHYL ACETATE (9)

The ether (6) (5.0g) in acetic anhydride (100ml) at 0° was treated with boron trifluoride-ether (15ml, 12% soln.). After 48h. at 0°, the mixture was poured into ice-water and extracted with ether (200ml). The extracts were washed with saturated aqueous sodium hydrogen carbonate solution and dried (Na_2SO_4). Evaporation left a dark red oil that slowly crystallised. Sublimation at 100° and 10^{-5}mmHg gave the pure diacetate (9), (90%), m.p. 38-40°, υmax. 2990, 1720, 1385 and 1280cm^{-1}, $[\alpha]_D^{28.5}$ + 36° (c 5.6 in chloroform), τ 8.92(3H,s), 8.95 (3H,s), 7.96(3H,s), 7.98(3H,s), 6.4(2H,ABq,J=6Hz), and 5.45(1H,d,J= 1.5Hz). (Found: C, 66.2; H, 8.7. $C_{14}H_{22}O_4$ requires C, 66.1; H, 8.7%).

2α-HYDROXY-1,3-DIMETHYLNORBORNAN-3α-YL-METHANOL (10)

To the crude diacetate (9) (7.2g) in ether (75ml) was added lithium aluminium hydride (2.5g) in ether (150ml). After 1h. at room temperature the mixture was quenched with ethyl acetate and aqueous ammonium chloride solution. The ether layer was dried (Na_2SO_4) and evaporated to give the diol (10) (3.3g), m.p. 81° (from light petroleum-ether), υ max. ($CHCl_3$) 3525, 3450, 1465, 1075 and 1030cm^{-1}, $[\alpha]_D^{28.5}$ - 21.2° (c 2.8 in chloroform), τ 8.9(6H,s), 6.35(2H,ABq,J=9Hz), and 6.62(1H,s). (Found: C, 70.7; H, 10.6. $C_{10}H_{18}O_2$ requires C, 70.5; H, 10.7%).

2α-HYDROXY-1,3-DIMETHYLNORBORNAN-3α-YL-METHANOL ISOPROYLIDENE ACETAL (11)

To the diol (10) (100mg) in 2,2-dimethoxypropane (5ml) was added a crystal of toluene-p-sulphonic acid monohydrate. After 10 minutes, evaporation and sublimation of the mixture gave the acetal (11) (80%), m.p. 74-76°, υ max. 2950, 1465, 1385, 1230 and 1090cm^{-1}, τ 8.90(3H,s), 8.86(3H,s), 8.75(3H,s), 8.71(3H,s), 6.9(1H,s), and 6.65(2H,ABq,J=6Hz). Mass spectrometry showed a molecular ion at m/e 210 corresponding to $C_{13}H_{22}O_2$.

2α-HYDROXY-1,3-DIMETHYLNORBORNAN-3α-YL-METHYL TOLUENE-p-SULPHONATE (12)

The diol (10) (1.1g) in pyridine (20ml) was treated with toluene-p-sulphonyl chloride (2.65g) at 0°. After 24h. at 0° the mixture was poured into ice-water and extracted with ether. The extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was dissolved in light petroleum and treated with charcoal. The mixture was filtered and the filtrate was cooled to -70°. The tosylate (12) (1.3g) had m.p. 138-139° (from light petroleum), $[\alpha]_D^{28.5}$ + 0.3 (c 0.66 in chloroform), υ max. ($CHCl_3$) 3600, 1600, 1470, 1370, 1100 and 970cm^{-1}, τ 8.98(3H,s), 8.95(3H,s), 7.55(3H,s), 6.65(1H,bs), 6.01(2H,s), 2.42(4H,ABq,J=8Hz), and 8.5(1H,s, exchanged with D_2O). (Found: C, 63.0; H, 7.3. $C_{17}H_{24}O_4S$ requires C, 63.0; H, 7.4%).

1,3-DIMETHYL-3α-p-TOLYLSULPHONYLMETHYLNORBORNAN-2α-YL ACETATE (13)

The hydroxy-tosylate (12) (400mg) in pyridine (20ml) was treated at -20° with acetyl chloride (0.2ml). After 12h. the mixture was worked-up in the usual way to give an oil (80mg) (purified by p.l.c.). The acetate (13) has $[\alpha]_D^{24}$ + 20.59 (c 0.53 in chloroform), υ max. ($CHCl_3$) 1725 and 1602cm^{-1}, τ 8.99(3H,s), 8.94(3H,s), 7.98(3H,s), 7.55 (3H,s), 6.11(2H,ABq,J=9Hz), 5.43(1H,bs), and 2.43(4H,ABq,J=8Hz). Further purification lead to decomposition.

REDUCTION OF THE 2α-HYDROXY-TOSYLATE (12) to 1,3,3-TRIMETHYLNORBORNAN-2α-OL (14)

The 2α-hydroxy-tosylate (12) (200mg) in ether (10ml) was treated with lithium aluminium hydride (120mg). The mixture was heated at reflux for 0.5h. then worked-up in the usual way. The alcohol (14) (65mg) was isolated as an impure oil, υ max. (CCl_4) 3650 and 1220cm^{-1}, $[\alpha]_D^{24}$ + 14.5° (c 0.32 in methanol), τ 9.13(3H,s), 9.04(3H,s), 8.98 (3H,s), and 6.74(1H,d,J=1.3Hz).

1,3,3-TRIMETHYLNORBORNAN-2α-p-NITROBENZOATE (15)

The p-nitrobenzoate (15) was prepared in the usual way, (m.p. 107° (lit.,[5,27] 108-109°), $[\alpha]_D^{24}$ + 17.9 (c 0.66 in CS_2)), and was identical with an authentic sample prepared by the method of Abraham and Vilkas[5].

9-METHYL-7-OXATRICYCLO [4,3,0,$0^{3,9}$] NONANE[7] (5)

Pinan-2α-ol[22] (10g) in pentane (250ml; purified by stirring with conc. H_2SO_4 then 0.3N-$KMnO_4$ in 3N-H_2SO_4, followed by distillation from CaO) containing yellow mercury (II) oxide (22.0g; previously dried at 100°) was treated with a solution of bromine (14.5g) in pentane (50ml), added dropwise over a period of 2h. During the addition, the flask

containing the pinanol was irradiated (tungsten lamp, 500 W) whilst the bromine-pentane solution was protected from light. During the addition and for 1h. afterwards the pentane mixture was kept at reflux under nitrogen. The mercury (II) oxide was filtered off, and the filtrate was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. The resulting oil was passed through a column of neutral alumina (50g) eluting with pentane. Evaporation gave an oil (70%). N.m.r. showed that the ether (5) was sufficiently pure for the next stage.

REARRANGEMENT OF 9-METHYL-7-OXATRICYCLO [4,3,0,$0^{3,9}$] NONANE (5)

The ether (5) (1.0g) in acetic anhydride (20ml) at 0° was treated with boron trifluoride-ether (6ml). After 1h. at 0° the mixture was poured onto ice-water and extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate and water, and dried (K_2CO_3). Evaporation gave an oil (1.5g), distillation of which at 88° and 0.2mmHg did not separate the two components. Neither could the mixture be separated by t.l.c. or g.l.c. υ max. (CCl_4) 1730 and 1250cm^{-1}, τ 8.90(3H,s), 7.9(6H,s), 6.2(2H,ABq,J=9Hz), and 5.5(1H,m) assignable to endo-3α-ACETOXYMETHYL-3-METHYLNORBORNAN-2α-YL ACETATE (18), and τ 8.95(3H,s), 8.04(6H,s), 5.86(2H,s), and 5.0(1H,m), assignable to exo-7-ACETOXY-METHYL-7-METHYLNORBORNAN-2β-YL ACETATE (19). (Found: C, 64.9; H, 8.1. $C_{13}H_{20}O_4$ requires C, 65.0; H, 8.4%). Mass spectrometry of the two-component mixture gave a single molecular ion at m/e 220 corresponding to $C_{13}H_{20}O_4$.

endo-3α-BENZOYLOXYMETHYL-3-METHYLNORBORNAN-2α-YL BENZOATE (22) and exo-7-BENZOYLOXYMETHYL-7-METHYL-NORBORNAN-2β-YL BENZOATE (23)

The mixture of diacetates (18) and (19) (613mg) in ether (20ml) was treated with lithium aluminium hydride (500mg). The mixture was heated at reflux for 5h. and worked-up in the usual way to give the diols (20) and (21), υ max. 3600 and 3400cm^{-1}. All attempts to

separate these by p.l.c., g.l.c. and selective formation of the isopropylidene acetal, borate esters, carbonate, oxalate, p-nitrobenzoates, and cholesteryl carbonate failed. Benzoylation (benzoyl chloride-pyridine) gave a mixture of the two benzoates (22) and (23), which were separated by multiple elution p.l.c. The benzoate (22) had m.p. 98-100° (from light petroleum), ν max. (CCl_4) 1720cm^{-1}, τ 8.8 (3H,s), 5.85(2H,ABq,J=9Hz), 5.1(1H,m), and 1.8-2.7(10H,m). (Found: C, 75.8; H, 6.7. $C_{21}H_{24}O_4$ requires C, 75.8; H, 6.6%), the benzoate (23) had m.p. 98-100° (from light petroleum), ν max (CCl_4) 1720cm^{-1}, 8.8(3H,s), 5.8(2H,s), 5.1(1H,m), and 1.8-2.7(10H,m). (Found: C, 75.6; H, 6.6. $C_{21}H_{24}O_4$ requires C, 75.8; H, 6.6%).

7-7-DIMETHYL-2-p-TOLYLNORPINAN-2β-OL (3)

7,7-Dimethyl-norpinan-2-one (4) (5.2g) was added to a solution of p-tolylmagnesium bormide prepared from p-bromotoluene (6.44g) and magnesium (0.95g) in ether (50ml) . The mixture was heated at reflux for 3.5h. and worked-up by adding a saturated aqueous solution of ammonium chloride. The ether layer was dried (Na_2SO_4) and evaporation gave the alcohol (3) (60%), m.p. 97-99° (from light petroleum-ethyl acetate), ν max. ($CHCl_3$) 3650 and 3550cm^{-1}, $[\alpha]_D^{26}$ - 4.5 (c 0.07 in chloroform), τ 8.75(3H,s), 8.70(3H,s), 8.20(1H,s exchanged by D_2O), 7.7(3H,s), and 2.75(4H,ABq,J=8Hz). (Found: C, 83.6; H, 9.5. $C_{16}H_{22}O$ requires C, 83.4; H, 9.6%).

9-METHYL-6-p-TOLYL-7-OXATRICYCLO [4,3,0,$0^{3,9}$] NONANE (7)

The norpinal (3) (12g) in carbon tetrachloride (200ml) was treated at -20° with mercury (II) oxide (24g). To this stirred mixture was added a solution of iodine (13.25g) in carbon tetrachloride (50ml), protected from light. The iodine solution was added during 1h., whilst the mixture was being irradiated (tungsten lamp, 500 W). After a further 2h. at -20° the mixture was filtered. The solution was washed with aqueous sodium chloride solution, dried (Na_2SO_4), and carbon tetrachloride layer was evaporated. Chromatography over alumina (G3)

(light petroleum) gave the ether (7) (80%), m.p. 84° (from light petroleum), ν max. ($CHCl_3$) 1030 and 985cm^{-1}, $[\alpha]_D^{29}$ + 11.6° (c 0.6 in chloroform), τ 8.65(3H,s), 7.6(3H,s), 6.2(2H,ABq,J=9Hz), and 2.8(4H, ABq,J=6Hz). (Found: C, 83.9; H, 8.7. $C_{16}H_{20}O$ requires C, 84.2; H, 8.8%).

Further elution of the column with light petroleum-benzene (10.1) gave 3-(2-IODOETHYL)-2,2-DIMETHYLCYCLOBUTYL-p-TOLYL KETONE (24) (20%), m.p. 78° (from light petroleum), ν max. ($CHCl_3$) 1660 and 1610cm^{-1}, $[\alpha]_D^{26}$ + 41.2° (c 0.1 in chloroform), τ 9.3(3H,s), 8.7 (3H,s), 7.6(3H,s), 6.85(2H,t,J=7Hz), 6.3(1H,t,J=7Hz), 2.7(2H,d,J=9 Hz), and 2.15(2H,d,J=9Hz). (Found: C, 54.1; H, 6.0. $C_{16}H_{21}IO$ requires C, 53.9; H, 5.9%).

3α-HYDROXYMETHYL-3-METHYL-1-p-TOLYLNORBORNAN-2α-YL ACETATE (25)

The ether (6) (271mg) in acetic anhydride (1ml) and ether (2ml) was treated with boron trifluoride-ether (0.5ml) at 0°. After 1h. work-up in the usual way gave the hydroxy-acetate (25) (314mg), m.p. 108-109° (from light petroleum-ethyl acetate), ν max. ($CHCl_3$) 3550 and 1720cm^{-1}, $[\alpha]_D^{24}$ + 46.8° (c 0.2 in chloroform), τ 8.75(3H,s), 8.0(3H, s), 7.7(3H,s), 6.4(2H,ABq,J=10Hz), 5.25(1H,s), and 2.85(4H,s). (Found: C, 74.8; H, 8.2. $C_{18}H_{24}O_3$ requires C, 75.0; H, 8.4%).

3α-ACETOXYMETHYL-3-METHYL-1-p-TOLYLNORBORNAN-2α-YL ACETATE (26)

Conducting the above experiment at -20° followed by acetylation (Ac_2O-pyridine) gave the diacetate (26) (95%) m.p. 110-112° (from light petroleum-ethyl acetate), ν max. 1720cm^{-1}, $[\alpha]_D^{26}$ + 50.2° (c 0.4 in chloroform), τ 8.8(3H,s), 8.04(3H,s), 8.00(3H,s), 7.6(3H,s), 6.04 (2H,ABq,J=8Hz), 5.28(1H,bs), and 2.98(4H,s). (Found: C, 72.7; H, 7.8. $C_{20}H_{26}O_4$ requires C, 72.7; H, 7.9%).

3α-HYDROXYMETHYL-3-METHYL-1-p-TOLYLNORBORNAN-2α-OL (27)

The diacetate (26) (1.17g) in dry tetrahydrofuran (20ml) was treated with lithium aluminium hydride (0.4g). The mixture was heated at reflux for 0.5h. and quenched with ether-water-ammonium chloride. The ether layer was dried (Na_2SO_4) and evaporated to yield the diol (27), m.p. 109-112° (from light petroleum-ethyl acetate) max. ($CHCl_3$) 3500cm^{-1}, τ8.85(3H,s), 7.7(3H,s), 6.30(2H,ABq,J=11Hz), 7.1(1H,s), and 2.8(4H,s). (Found: C, 77.8; H, 9.0. $C_{16}H_{22}O_2$ requires C, 78.0; H, 9.0%).

OO'-ISOPROPYLIDENE-3α-HYDROXYMETHYL-3-METHYL-1-p-TOLYLNORBORNAN-2α-OL (28)

Treatment of the diol (27) (50mg) in acetone (5ml) with a trace of anhydrous copper (II) sulphate gave the isopropylidene derivative (28), b.p. 70° at 5 x 10^{-3}mmHg, υ max. 1390, 1230 and 1100cm^{-1}, $[\alpha]_D^{28}$ + 39.9° (c 0.12 in $CHCl_3$), τ 8.6(3H,s), 8.4(3H,s), 8.35(3H,s), 7.65 (3H,s), 6.4(2H,ABq,J=11Hz), 6.45(1H,s), and 2.8(2H,A_2B_2q,J=8Hz). (Found: C, 79.6; H, 9.0) $C_{19}H_{26}O_2$ requires C, 79.7; H, 9.2%).

2α-HYDROXY-3-METHYL-1-p-TOLYLNORBORNAN-3α-YL-METHYL TOLUENE-p-SULPHONATE (33)

The diol (27) (0.5g) in pyridine (10ml) at -20° was treated with toluene-p-sulphonyl chloride (0.8g) in pyridine (10ml). After 48h. at -5° the mixture was poured into water and extracted with ether. The extract was washed with 3N hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water. The dried (Na_2SO_4) extract was evaporated to give the tosylate (33) (0.74g, 91%), m.p. 114-115° (from light petroleum-ether), $[\alpha]_D^{28}$ + 34.4 (c 0.08 in $CHCl_3$), υ max. ($CHCl_3$) 1600, 1360 and 980cm^{-1}, τ 8.8(3H,s), 7.8(3H,s), 7.55(3H,s), 7.5(1H,s, exchanged by D_2O), 6.45(1H,d,J=4Hz), 5.95(2H,ABq,J=10Hz), 2.85(4H,s), and 2.4(4H, A_2B_2q,J=9Hz). (Found: C, 68.8; H, 7.0; S, 8.2. $C_{23}H_{28}O_4S$ requires C, 69.0; H, 7.0; S, 8.0%).

TREATMENT OF THE TOSYLATE (33) WITH POTASSIUM t-BUTOXIDE IN t-BUTYL ALCOHOL

The tosylate (33) (50mg) in t-butyl alcohol (3ml) under nitrogen was treated with potassium t-butoxide (50mg). After 0.5h. at reflux the mixture was poured into water and extracted with chloroform. Evaporation of the dried (Na_2SO_4) extract and distillation of the residue (50° at 10^{-3}mmHg) gave 5-METHYL-1-p-TOLYL-3-OXATRICYCLO [4,2, $1,0^{2,5}$] NONANE (34), (98%), m.p. 43°, α^{28} + 15.9° (c 0.10 in $CHCl_3$), max. 970cm^{-1}, 8.72(3H,s), 7.80(3H,s), 5.54(2H,ABq,J=7Hz), 5.54(1H,s) and 2.85(4H,s). (Found: C, 84.2; H, 9.2. $C_{16}H_{20}O$ requires C, 84.2; H, 8.8%).

3-METHYL-2-OXO-1-p-TOLYLNORBORNAN-3α-YL-METHYL TOLUENE-p-SULPHONATE (35).

To chromium trioxide (0.6g) in dichloromethane (16ml) was added pyridine (0.95g). After 15 minutes at room temperature the monotosylate (33) (0.425g) in dichloromethane (5ml) was added. The dichloromethane was decanted after 15 minutes and the residue washed with ether (2 x 15ml). The combined organic solutions were washed with aqueous 3N-sodium hydroxide (10ml), 2N-hydrochloric acid (10ml). saturated aqueous sodium hydrogen carbonate (10ml), and aqueous sodium chloride (10ml). The dried (K_2CO_3-Na_2SO_4) extract was evaporated to give the ketone (35) (0.393g, 93%), m.p. 101-104° (from ether-hexane), $[\alpha]_D^{28}$ - 66.3° (c 0.06 in $CHCl_3$), υ max. 1730, 1380 and 990cm^{-1}, τ 8.85(3H,s), 7.7(3H,s), 7.55(3H,s), 5.97(2H,ABq,J=10Hz), 2.85(4H,s), and 2.4(4H, A_2B_2q,J=9Hz). (Found: C, 69.3; H, 6.7; S, 8.1. $C_{23}H_{26}O_4S$ requires C, 69.3; H, 6.6; S, 8.0%).

REDUCTION OF KETO-TOSYLATE (35) WITH SODIUM BOROHYDRIDE

The keto-tosylate (35) (300mg) in dry tetrahydrofuran (20ml) was treated with sodium borohydride (150mg) in methanol (2ml). After 4h. at 0° work-up with dilute hydrochloric acid and extraction with ether (25ml) gave a mixture (296mg) of the epimeric alcohols (33) and (36), (tertiary Me) 8.8 and 8.9τ(ratio 3:2).

β-FRAGMENTATION OF ALCOHOLS (33) AND (36)

The mixture of alcohols (33) and (36) (296mg) in t-butyl alcohol (20ml) under nitrogen was treated with potassium t-butoxide (300mg). After 0.5h. at reflux the mixture was worked-up in the usual way. Two products were formed, (34) and (37) in the ratio 3:2, νmax. 1730, 1650 and 970cm^{-1}, τ for (37) 8.3(3H,d,J=1Hz), 7.7(3H,s), 5.35(2H,m), 2.95 (4H,s) and 0.7(1H,s).

3-ISOPROPENYL-1-p-TOLYLCYCLOPENTANE-1-CARBALDEHYDE-p-TOLYLSULPHONYL-HYDRAZONE (38)

Treatment of the mixture from the above experiment with toluene-p-sulphonylhydrazide (100mg) in tetrahydrofuran (5ml) gave the p-tolylsulphonylhydrazone (38) as an oil (purified by p.l.c.), νmax. 3200, 1645, 1380, 1160 and 890cm^{-1}, τ8.74(3H,s), 7.9(3H,bs), 7.7(3H,s), 5.5 (2H,m), 3.2(4H,s), 2.75(4H,A_2B_2q,J=9Hz), 3.0(1H,s) and 1.7(1H,s), m/e 212(M^+-184; loss of toluene-p-sulphonylhydrazide residue) and 184 (no M^+).

(+)-(1R,3S)-3-ISOPROPENYL-1-p-TOLYLCYCLOPENTANE-1-CARBOXCYLIC ACID (39)

The keto tosylate (35) (300mg) in dimethyl sulphoxide (5ml) under nitrogen at room temperature was treated with potassium t-butoxide (0.8g) and water (0.360g). After 2h. the mixture was poured into water (30ml). Acidification with 6N-hydrochloric acid (5ml) and extraction

with chloroform (2 x 15ml), drying (Na_2SO_4), and evaporation gave the acid (39), purified by short column distillation at 100° and 10^{-5}mmHg (98% yield); m.p. 57°, $[\alpha]_D^{28}$ + 10.7° (c 0.07 in $CHCl_3$), υmax. 1695, 1640, 900 and 3300-2800cm^{-1}, τ8.35(3H,s), 7.8(3H,s), 5.4(2H, bd,J=5Hz), 2.95(4H,A_2B_2q,J=7Hz), and 0.1(1H,bs, exchanged by D_2O). (Found: C, 78.4; H, 8.0. $C_{16}H_{20}O_2$ requires C, 78.7; H, 8.3%).

REACTION OF 2α-HYDROXY-3-METHYL-1-p-TOLYLNORBORNAN-3-YL-METHYL TOLUENE-p-SULPHONATE (12) WITH $NaHCO_3$ - Me_2SO

The hydroxytosylate (12) in dimethylsulphoxide (1ml) containing sodium bicarbonate (40mg) was heated to 100-110° for 0.5h. The mixture was cooled, poured into ether and washed with saturated aqueous sodium bicarbonate and water. Evaporation of the dried (Na_2SO_4) ether layer gave the carbonate (40) (78%), m.p. 104° (from benzene-light petroleum), $[\alpha]_D^{28}$ + 87.6° (c 0.7 in $CHCl_3$). (Found: C, 74.9; H, 7.4; $C_{17}H_{20}O_3$ requires C, 75.0; H, 7.4%).

PREPARATION OF AUTHENTIC CARBONATE (40)

The diol (27) (50mg) in pyridine (1ml) was treated with phosgene in toluene (12% soln. 2eq.) at 0° overnight. Work-up in the usual way gave the carbonate (40) (80%), m.p. 104°.

REACTIONS OF 1-PHENYL-2,2-DIMETHYL-1,3-DIHYDROPROPANE 3-TOLUENE-p-SULPHONATE (46) WITH $NaHCO_3$

General procedure:- The tosylate (0.5g) in Me_2SO (10ml) containing excess $NaHCO_3$ (0.5g) is heated and the reaction is monitered by t.l.c. (Table II). Similar conditions are used for all experiments given in the Table. The carbonate (47), isolated in the usual way had m.p. 105-106° (from light petroleum), υmax. 1760, 1720cm^{-1}, τ9.04(3H, s), 9.01(3H,s), 5.83(2H,ABq,J=11Hz), 4.76(1H,s), 2.6(5H,bs). (Found: C, 69.6; H, 7.0; $C_{12}H_{14}O_3$ requires C, 69.6; H, 6.8%).

7,7-DIMETHYL-2-METHYLPHENYLSULPHONYLNORPINAN-2β-OL (49)

To a suspension of phenylsulphonylmethylmagnesium iodide[44] (prepared from magnesium (0.87g) methyliodide (5.55g) and phenylmethylsulphone (6.15g) in ether (30ml) and benzene (100ml) refluxed for 2h.) was added (+)-nopinone (4) (5.0g) in benzene (10ml). After stirring overnight the mixture was poured into saturated aqueous ammonium chloride solution. The benzene layer was dried (Na_2SO_4) and evaporated to give the hydroxysulphone (49) (70%), m.p. 101-103° (from light petroleum), $[\alpha]_D^{24}$ + 27.1° (c 2.4 in chloroform) υ max. 3500, 1320, 1170cm^{-1}, τ 8.9(3H,s), 8.75(3H,s), 6.6(2H,s), 2.3(5H,m), 4.45(1H,bs, exchanged by D_2O). (Found: C, 65.1; H, 7.4; S, 10.9; $C_{17}H_{22}O_3S$ requires C, 65.3; H, 7.5; S, 10.9%).

9-METHYL-6-METHYLPHENYLSULPHONYL-7-OXATRICYCLO [4,3,0,$0^{3,9}$] NONANE (50)

The hydroxysulphone (49) (2.0g) in carbontetrachloride (20ml) was treated with mercury (II) oxide (5g) and iodine (3.52g). The mixture was stirred and irradiated (tungsten lamp, 500 W) for 2h. at room temperature under nitrogen. After filtering, the solution was washed with aqueous sodium metabisulphite solution, aqueous sodium chloride solution and dried (Na_2SO_4). Evaporation gave the sulphone (50) (95%), m.p. 104° (from hexane-ether), $[\alpha]_D^{24}$ - 100° (c 0.7 in chloroform) υ max. 1340, 1170cm^{-1}. λ_{max}^{EtOH} 272, 265, 258 and 253nm (ε, 1770, 940, 660 and 410 respectively), τ 8.7(3H,s), 6.55(2H,bs), 6.5 (2H,ABq,J=9Hz), 2.3(5H,m). (Found: C, 65.9; H, 6.8; S, 11.0; $C_{17}H_{20}O_3S$ requires C, 65.7; H, 6.9; S, 11.0%).

7,7-DIMETHYL-2-METHYLPHENYLSULPHYLNORPINAN-2β-OL (49) FROM THE EPOXIDE (51)

The epoxide (51) (15.2g) in acetone (50ml) was added to thiophenol (11.0g) and potassium carbonate (20g) and refluxed for 17h.

After evaporation of the acetone the alcohol (49) was extracted into dichloromethane, dried (Na_2SO_4) and evaporated to yield an oil (n.m.r. indicates (49) is the only product). The compound was purified by distillation (90°, 10^{-2}mmHg) or p.l.c., υ max. 3450 and 1585cm^{-1}, τ8.90(3H,s), 8.80(3H,s), 6.70(2H,ABq,J=15Hz), 2.7(5H,m) and 7.7(1H,s, exchangable with D_2O). (Found: C, 72.97; H, 8.38, S, 11.98. $C_{17}H_{22}O_5$ requires C, 73.25; H, 8.45, S, 12.2%).

7,7-DIMETHYL-2-METHYLPHENYLSULPHOXYLNORPINAN-2β-OLS (53) and (54)

To the sulphide (52) (1.0g) in dichloromethane (20ml) was added slowly meta-chloroperbenzoic acid (0.7g). After 0.5h. at room temperature the solution was washed with saturated aqueous sodium bicarbonate, dried (Na_2SO_4) and evaporated to give the sulphoxides (53) and (54) (94%), m.p. 110-111° (from light petroleum), υmax. 3400, 1585 and 1050cm^{-1}, τ 8.95(6H,s), 8.78(3H,s), 8.85(3H,s), 7.18(2H,s), 7.08 (2H,s) and 2.5(10H,m), (n.m.r. shows a 1:1 ratio of (53) and (54)). (Found: C, 68.82; H, 7.96; S, 11.39. $C_{17}H_{22}O_2S$ requires C, 69.04; H, 7.97; S, 11.49%).

7,7-DIMETHYL-2-METHYLPHENYLSULPHONYLNORPINAN-2β-OL (49) FROM SULPHIDE (52)

To the sulphide (52) (1.0g) in dichloromethane (20ml) was added slowly meta-chloroperbenzoic acid (1.4g). After 0.5h. at room temperature the solution was washed with saturated aqueous sodium bicarbonate, dried (Na_2SO_4) and evaporated. Recrystallisation from light petroleum gave the hydroxy-sulphone (49) (>90%).

REACTIONS OF 9-METHYL-6-METHYLPHENYLSULPHONYL-7-OXATRICYCLO [4,3,0, $0^{3,9}$] NONANE (50) WITH n-BUTYLLITHIUM

The sulphone (50) (100mg) in ether (5ml) at -70° was treated with excess n-butyllithium (3ml 2M) at -70°. After 0.5h. at -70° the reaction was quenched with deuterium oxide. The sulphone (55) (100mg) was isolated in the usual way. M^+294 m/e. ,τ8.7(3H,s), 6.5(2H,ABq,J=9Hz), 2.3(5H,m).

The sulphone (50) (120mg) in ether (5ml) at -70° was treated with excess n-butyllithium (6ml 2M) at -70°. The mixture was allowed to warm to room temperature and quenched with water. The olefin (57) (120mg), was isolated in the usual way. It had m.p. 75° (from light petroleum),νmax. 3500, 1585cm^{-1},$\lambda_{max.}^{EtOH}$ 272, 265 and 258nm (ε, 760, 1000 and 1000 respectively). τ, 8.6(3H,s), 6.5(2H, ABq,J=11Hz), 6.15(2H,bs), 4.4(1H,m), 2.3(5H,m). (Found: C, 65.6; H, 7.2; S, 11.0; $C_{17}H_{20}O_3S$ requires C, 65.7; H, 6.9; S, 11.0%).

Similarly if the above reaction was quenched with deuterium oxide the olefin (56) was formed M^+294 m/e, absence of signal at 6.15 in n.m.r.

The sulphone (50) (100mg) in ether (5ml) at -70° was treated with n-butyllithium (3ml 2M) at -70°. Methyl iodide (200mg) was added to the mixture and the solution left overnight at room temperature (no reaction took place at -70° to 0°). Work-up in the usual way gave the olefin (58) (70%), m.p. 134-135° (from hexane-ethylacetate), $[\alpha]_D^{24}$ + 252° (c 0.4 in chloroform),ν max. 3475, 1610cm^{-1} $\lambda_{max.}^{EtOH}$ 272 and 267nm (ε, 750 and 1200 respectively). τ, 8.64(3H,s), 8.02(3H,s), 6.8(2H, ABq,J=5.5Hz), 6.24(1H,t,J=2.5Hz), 2.5(5H,m). (Found: C, 66.6; H, 7.1; S, 10.2; $C_{18}H_{22}O_3S$ requires C, 66.7; H, 7.3; S, 10.4%).

7,7-DIMETHYL-2-(1'-ETHYLPHENYLSULPHONYL)-NORPINAN-2β-OLS (59) AND (60)

To a solution of ethylphenylsulphonyl magnesium iodide in ether was added (+)-nopinone (3.0g) in benzene (100ml). The mixture was heated at 70° for 4h. then worked-up in the usual way to give an oil consisting of a mixture of the hydroxysulphones (59) and (60) (3.5g) υmax. 3500cm^{-1}. (Found: C, 66.4; H, 7.6; S, 10.2; $C_{18}H_{24}O_3S$ requires C, 66.2; H, 7.8; S, 10.4%).

9-METHYL-6-(1'-ETHYLPHENYLSULPHONYL)-7-OXATRICYCLO [4,3,0,0^{3,9}] NONANES (61) AND (62)

Treatment of the mixture of (59) and (60) (3.23g) in carbontetrachloride (40ml) with mercuric oxide (10g), iodine (6g) followed by irradiation for 17h. gave the sulphones (61) and (62) (2.5g), oil, υmax. 1330 and 1175cm^{-1}. τ (less polar constituents) 8.75(3H,s), 8.63(3H,d,J=7.5Hz), 6.55(2H,ABq,J=8.5Hz), 6.6(1H,q,J=7.55Hz), 2.3(5H,m), (more polar constituent), 8.7(3H,s), 8.75(3H,d,J=7Hz), 6.4(2H,ABq, J=8.5Hz), 6.65(1H,q,J=7Hz), 2.3(5H,m). (Found: C, 66.6; H, 7.1; S, 10.4; $C_{18}H_{22}O_3S$ requires C, 66.7; H, 7.3; S, 10.4%).

7-OXATRICYCLO [4,3,0,0^{3,9}] NONANES (61) AND (62) WITH n-BUTYLLITHIUM

The two diastereoisomers (61) and (62) (60mg) were separately treated with excess n-butyllithium at -70° and quenched with deuterium oxide. Work-up by extraction with ether and washing gave the olefin (58) (55mg) from both (61) and (62), identical in all respects with an authentic sample (t.l.c., i.r. etc.)

TREATMENT OF OLEFIN (58) WITH POTASSIUM t-BUTOXIDE

Treatment of the olefin (58) (20mg) in t-butanol (5ml) with potassium t-butoxide (50mg) at 30° gave rapidly (5 minutes) a 1:1 mixture of (61) and (62) (100%).

REACTION OF 9-METHYL-6-METHYLPHENYLSULPHONYL-7-OXATRICYCLO [4,3,0,$0^{3,9}$] NONANE (50) WITH BORON TRIFLUORIDE-ETHER

The ether (50) (200mg) in acetic anhydride (5ml) at -70° was treated with boron trifluoride-ether (3ml). The solution was allowed to warm to room temperature before pouring into ice-water and extracting with ether. The extracts were washed with aqueous sodium hydrogen carbonate, water and dried (K_2CO_3-Na_2SO_4). Evaporation gave an oil which was composed of six compounds. P.l.c. gave the sulphone (63) (50mg) as an oil with υmax. 1715cm^{-1}, τ8.90(3H,s), 8.05(3H,s), 7.95(3H,s), 6.55(2H,ABq,J=15Hz) and 6.1(2H,s). Could not crystallise or produce an analytical sample.

5-PHENYLMERCAPTO-2-PENTANOL (69)

This compound had only been prepared in small amounts and yields determined by g.l.c.

Thiophenol (16.5g) was added to 2-methyltetrahydrofuran, followed by sodium borohydride (3.55g). After 0.5h. at room temperature boron trifluoride-ether (10.62g) was added. The solution was left overnight before adding sodium hydroxide (6.76g) in water (50ml). The solution was extracted with ether (50ml), dried (Na_2SO_4) (37.5%) (0.2mmHg 123-5°). The n.m.r. agrees with the literature.

5-PHENYLMERCAPTO-2-PENTYL BROMIDE (70)

To the alcohol (69) (2.5g) in pyridine (10ml) was added toluene-p-sulphonyl chloride (3g) also in pyridine (10ml). After 5h. at room temperature the solution was worked-up as usual to give the tosylate derivative of the alcohol (2g) (69).

The tosylate (2g) was refluxed in acetone (20ml) with lithium bromide (2g). After 15h. at reflux the acetone was evaporated. The residue was dissolved into a water-ether mixture. The ether layer was separated, dried (Na_2SO_4) and evaporated to yield a distillable oil (1.5g) (0.1mmHg, 120°). τ 8.34(3H,d,J=7Hz), 7.1(2H,t,J=6Hz), 6.0(1H,bm) and 2.75(5H,m).

REARRANGEMENT OF ESTER (72) TO ESTER (73)

To the ether (72) (257mg) in acetic anhydride (1ml) was added boron trifluoride-ether (0.5ml) at 0°. After 3h. the solution was poured into water (15ml) before working-up in the usual way to give an oil (287mg) of a mixture of mono- and diacetates. The mixture was added to pyridine (5ml) and acetic anhydride (5ml). After 17h. the reaction was worked-up in the usual way to give a distillable oil (0.007mmHg, 100°) which was found to be mainly the diacetate (73) but was not analytically pure.

REARRANGEMENT OF THE ACID (74) UNDER ACETIC ANHYDRIDE-BORON TRIFLUORIDE-ETHER CONDITIONS

To the acid (116mg) (74) in acetic anhydride (2ml) was added boron trifluoride-ether (0.5ml) at 0°. The solution was kept at 0° for 17h. before working-up in the usual way. The product acid had n.m.r. signals at τ8.85(3H,s), 7.95(6H,s), 7.65(2H,s), 4.1(2H,ABq, J=10hz) and 1.7 (1H,bs, exchangable by D_2O). The reaction appears to be 'one spot' but could not purify the product to analytical purity.

1,3-DIMETHYL-2α-p-TOLYLSULPHONYLOXYNORBORNAN-3α-YL-BENZOATE (81)

Benzoyl chloride (2.7g) in pyridine (20ml) was added to the diol (10) (3.25g) in pyridine (20ml) dropwise over a period of 0.5h. at 0°. After 1h. p-toluene sulphonyl chloride (15g) was added and the solution heated to 90° for 40h. before working-up in the usual way to give the benzoate-tosylate (81) (3.7g) (55%) m.p. 159° (from ether-hexane), υmax. 1710 and 1600cm^{-1}, τ 9.15(3H,s), 8.88(3H,s), 7.64(3H,s), 5.77(1H,bs), 5.95(2H,ABq,J=11Hz) and 2.4(9H,m). (Found: C, 67.1; H, 6.7; S, 7.4; $C_{24}H_{28}O_5S$ requires C, 67.3; H, 6.6; S, 7.5%).

BENZOYLOXY-9α-FENCHENE (82)

The benzoate-tosylate (81) (1g) was added to sodium acetate (3g) and acetic acid (20ml). After heating to 90° for 24h. the solution was cooled and added to water, extracted with ether (40ml) dried (Na_2SO_4) and evaporated to give the fenchene as a distillable oil (0.56g) (94%) (0.01mmHg, 100°) and had υmax. (CCl_4) 1715, 1660, 1600 and 900cm^{-1}, τ8.88(3H,s), 5.65(2H,s), 5.3(1H,bs), 5.1(1H,bs) and 2.3(5H,m). (Found: C, 79.5, H, 7.8. $C_{17}H_{20}O_2$ requires C, 79.5, H, 7.9%).

HYDROXY-9α-FENCHENE (83)

Lithium aluminium hydride (0.5g) was added to the benzoate (0.6525g) in ether (10ml). After refluxing for 0.5h. the solution was worked-up in the usual way to give the alcohol as an oil with n.m.r. τ 8.98(3H,s), 6.4(2H,s), 5.35(1H,s) and 5.15(1H,bs) which agrees with the literature[28].

TOSYLATE OF HYDROXY-9α-FENCHENE (84)

The alcohol (83) (380mg) was dissolved in pyridine (10ml) and toluene-p-sulphonyl chloride (1g) was added at room temperature. The product was worked-up in the usual way after 5h. to give an oil (380mg) (50%) after p.l.c. with n.m.r. τ 8.85(3H,s), 7.55(3H,s), 6.0(2H,s), 5.3(1H,bs), 5.15(1H,bs) and 2.4(4H,A_2B_2q,J=8) which agrees with the literature[28].

IODO-9α-FENCHENE (85)

The tosylate (84) (0.3g) was added to sodium iodide (0.5g) in acetone (20ml). After 17h. at reflux the reaction was cooled and evaporated. The residue was dissolved in water-ether. After separation the ether layer was washed with saturated aqueous sodium bicarbonate, dried (Na_2SO_4) evaporated to yield an oil (0.25g) after p.l.c. which had n.m.r. τ(CCl_4) 8.9(3H,s), 6.75(2H,s), 4.45(1H,bs) and 5.2(1H,bs) which agrees with the literature[28].

REFERENCES

1. (a) N. Bosworth and P.D. Magnus, J.C.S. Chem.Comm., 1971, 618;

   (b) N. Bosworth and P.D. Magnus, J.C.S. Chem.Comm., 1972, 257;

   (c) N. Bosworth and P.D. Magnus, J.C.S. Perkin I, 1972, 943;

   (d) N. Bosworth and P.D. Magnus, J.C.S. Perkin I, 1973; 76.

2. E.C. Friedrich and S. Winstein, J.Amer.Chem.Soc., 1964, 86, 2721.

3. P. von R. Schleyer, W.E. Watts and C. Cupas, J.Amer.Chem.Soc., 1964, 86, 2722.

4. W.D. Burrows and R.H. Eastman, J.Amer.Chem.Soc., 1959, 81, 245.

5. N.A. Abraham and M. Vilkas,

   (a) Bull.Soc.Chim.France, 1960, 1450;

   (b) Ann.Chim. (France), 1960, 5, 961.

6. C.R. Hughes, D.F. MacSweeney and R. Ramage, Tetrahedron, 1971, 27, 2247.

7. T.W. Gibson and W.F. Ermann, J.Amer.Chem.Soc., 1969, 91, 4771.

8. A.G. Hortmann and R.E. Youngstrom, J.Org.Chem., 1969, 34, 3392.

9. M.H. Karger and Y. Mazur, J.Amer.Chem.Soc., 1968, 90, 3878.

10. (a) C.R. Naraganan and K.N. Iyer, J.Org.Chem., 1965, 30, 1734;

(b) R.D. Youssefyeh and Y. Mazur, Tetrahedron Letters, 1962, 1287.

11. H.S. Gutowsky, J.Chem.Phys., 1962, 37, 2196.

12. L.M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry', 2nd edn., Perganmon, pp. 372 and 334.

13. M.J. Barfield, J.Chem.Phys., 1964, 41, 3825.

14. A.J. Aasen and C.C.J. Culvenor, J.Org.Chem., 1969, 34, 4143.

15. (a) Pl. A. Plattner and W. Long, Helv.Chim.Acta., 1944, 27, 1872;

(b) D.K. Fukushima, N.S. Leeds, H.L. Bradlow, T.H. Kritchevsky, M.B. Stokem and T.F. Gallagher, J.Biol.Chem., 1955, 212, 449;

(c) D. Taub, R.D. Hoffsommer and N.L. Wendler, J.Amer.Chem.Soc., 1959, 81, 3291.

16. (a) J.I. Mosher, Mol.Phys., 1963, 6, 93;

(b) A. Coulombeau and A. Rassat, Bull.Soc.Chim.France, 1965, 3338.

17. 'Rodd's Chemistry of Carbon Compounds', ed. S. Coffey, vol. II, 2nd edn., Part C, p. 240.

18. (a) J.L. Simonsen and L.N. Owen 'The Terpenes', vol. II, 2nd edn., p. 386;

(b) ref. 17, p. 207;

(c) T. Hasselstrom, J.Amer.Chem.Soc., 1931, 53, 1097;

(d) E.J. Corey, M. Ohno, S.W. Chow and R.A. Scherrer, J.Amer. Chem.Soc., 1959, 81, 6305;

(e) E.J. Corey, S.W. Chow and R.A. Scherrer, J.Amer.Chem.Soc., 1957, 79, 5773;

(f) F. Dallacker, K. Ulrichs and M. Lipp, Annalen, 1963, 667 50.

19. S.S. Nametkin and V.A. Khokhrjakova, J.Russ.Phys.Chem.Soc., 1915, 47, 1611.

20. G. Komppa and A. Klami, Ber., 1935, 68B, 2001.

21. T. Kuusinen, Ann.Acad.Sci.Fennicae.Ser.AII, 1956, 69, 55 (Chem. Abs., 1957, 51, 4317).

22. S. Winstein and N.J. Holness, J.Amer.Chem.Soc., 1955, 77, 3054.

23. R.A. Sneen and N.P. Metheny, J.Amer.Chem.Soc., 1964, 86, 5503.

24. M. Akhtar and D.H.R. Barton, J.Amer.Chem.Soc., 1964, 86, 1528.

25. J.A. Berson, 'Molecular Rearrangements I', ed. P. de Mayo, Interscience, New York, 1963, p. 111.

26. J. Meinwald and P.G. Gassman, J.Amer.Chem.Soc., 1960, 82, 5445.

27. J. Kenyon and H.E.M. Priston, J.Chem.Soc., 1925, 1472.

28. C. Grison and Y. Bessiere-Chretien, Bull.Soc.Chim.France, 1972, 12, 4570.

29. Leading references to this series of sesquiterpenes are;

(a) J.A. Marshall and S.F. Brady, J.Org.Chem., 1970, 35, 4068;

(b) J.A. Marshall and S.F. Brady, Tetrahedron Letters, 1969, 1387;

(c) J.A. Marshall and P.C. Johnson, Chem.Comm., 1968, 391;

(d) I. Yosioka and T. Kimura, Chem. and Pharm.Bull. (Japan), 1965, 13, 1430;

(e) W.Z. Chow, O. Motl and G. Sorm, Coll.Czech.Chem.Comm., 1962, 27, 1914;

(f) M. Mongrain, J. Lafontaine, A. Belanger and P. Deslongchamps, Canad.J.Chem., 1970, 48, 3273.

30. 'The Terpenes', vol. III, 2nd edn., ed. J. Simonsen and D.H.R. Barton, Cambridge University Press, 1952, p. 224.

31. (a) C.A. Grob and P.W. Schiess, Angew.Chem.Internat.Edn., 1967, 1, 6;

(b) C.A. Grob, Angew.Chem.Internat.Edn., 1969, 8, 535.

32. J.C. Collins, W.W. Hess and F.J. Frank, Tetrahedron Letters, 1968, 3363.

33. P.G. Gassman and F.V. Zalar, Tetrahedron Letters, 3031, 3251.

34. W.W. Epstein and F.W. Sweat, Chem.Rev., 1967, 67, 247.

35. (a) N. Kornblum, W.J. Jones and G.J. Anderson, J.Amer.Chem.Soc., 1959, 81, 4113;

(b) H.H. Nace and J.J. Monagle, J.Org.Chem., 1959, 24, 1792;

(c) J.M. Tien and I.M. Hunsberger, Chem. and Ind., 1959, 88;

(d) K. Torsell, Acta.Chem.Scand., 1967, 21, 1.

36. G. Hanisch and G. Henseke, Ber., 1967, 100, 3225.

37. (a) F. Nerdel and U. Kretzschmar, Ann., 1965, 688, 61;

(b) K. Kulka, O. Hansen and R. Joseph. Fritzsche Dodge and Olcott New York.

38. L. Friedman and H. Shechter, J.Org.Chem., 1960, 25, 877.

39. J. Cason and J.S. Correia, J.Org.Chem., 1961, 26, 3645.

40. C.G. Swain and C.B. Scott, J.Amer.Chem.Soc., 1965, 75, 141.

41. D.H.R. Barton, B.J. Garner and R.H. Wightman, J.Chem.Soc., 1964, 1855.

42. (a) J.I. Jones, Chem.Ind., 1958, 228;

(b) J. Thamsen, Acta.Chem.Scand., 1956, 10, 1165;

(c) A. Jensen, E. Jorgensen and C. Faurhott, Acta.Chem.Scand., 1952, 6, 1036.

43. (a) D.J. Cram, 'Fundamentals of Carbanion Chemistry', Academic Press, New York, 1965;

(b) S. Wolfe, A. Rank, I.G. Csizmadia, J.Amer.Chem.Soc., 1969, 91, 1567 and references sited therein;

(c) D.J. Cram, R.D. Trepka and P. St. Janiak, J.Amer.Chem.Soc., 1966, 88, 2749;

(d) E.J. Corey, T.H. Lowry, Tetrahedron Letters, 1965, 13, 793 and 803;

(e) E.J. Corey, H. Konig and T.H. Lowry, Tetrahedron Letters, 1962, 12, 515.

44. (a) L. Field, J.Amer.Chem.Soc., 1952, 74, 3919;

(b) W.M. Ziegler and R. Conner, J.Amer.Chem.Soc., 1940, 62, 2596.

45. (a) W.E. Truce and L.W. Christansen, Chem.Comm., 1971, 588;

(b) E.M. Kaiser and C.R. Hauser, J.Amer.Chem.Soc., 1966, 88, 2348;

(c) E.M. Kaiser and C.R. Hauser, Tetrahedron Letters, 1967, 3341;

(d) E.M. Kaiser, L.E. Solter, R.A. Schwarz, R.D. Beard and C.R. Hauser, J.Amer.Chem.Soc., 1971, 93, 4237.

46. F.G. Bordwell, M.M. Vestling and K.C. Lee, J.Amer.Chem.Soc., 1970, 92, 5950.

47. C.J.M. Stirling, J.Chem.Soc., 1964, 5863.

48. S.J. Cristol and R.S. Bly,Jun., J.Amer.Chem.Soc., 1960, 82, 142.

49. S.J. Cristol and P. Pappas, J.Org.Chem., 1963, 28, 2066.

50. J.M. Coxon, E. Dansted, M.P. Hartshorn and K.E. Richards, Tetrahedron, 1968, 24, 1193.

51. D.J. Pasto, C.C. Cumbo and P. Balasubramaniyan, J.Amer.Chem.Soc., 1966, 88, 2187.

52. E.J. Corey and M.F. Semmelhack, J.Amer.Chem.Soc., 1967, 89, 2756.

53. K.S. Kulkarni, S.K. Paknikar, A.S. Vaidya, G.R. Kelkar, R.B. Bates and S.C. Bhattacharyya, Tetrahedron Letters, 1963, 505.

54. C.R. Johnson and J.C. Sharp, Quart.Report Sulphur Chem., 1961, 4, 1.

55. T. Matsumoto, H. Shirahama, A. Ichihara, H. Shin, S. Kagawa, F. Sakan and K. Migano, Tetrahedron Letters, 1971, 23, 2049.