STUDIES OF SOME PINANE MONOTERPENES

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by

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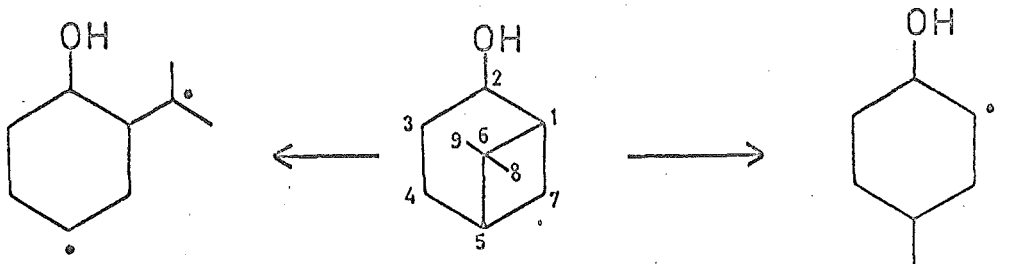
INDEX

ABSTRACT

The pyrolysis of a number of C2, C3 and C4 oxygenated pinanes has been studied. Substituents at C2 or C4 significantly affect the mode of cleavage of the pinane cyclobutane ring. All pyrolysis reactions previously reported proceeded exclusively *via* initial 1,6-bond cleavage. For several compounds in this study an additional reaction path was identified, which involved the initial cleavage of the four membered ring by fission of the 5,6-bond.

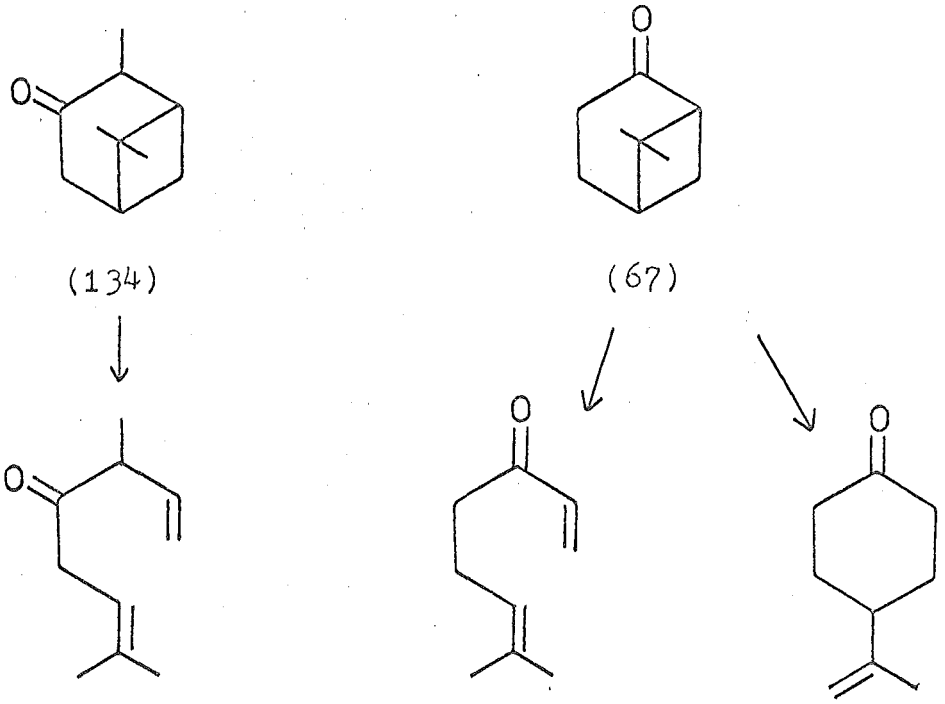


(a) (112) (b)

The relative effectiveness of substituents in inducing initial cleavage at the adjacent C-C bond of the cyclobutane ring (either 1,6- or 5,6-bonds) is in the order C=C > C=O > CH_3 > OH > H.

Substituents also influence the subsequent reactions of the 1,4-diradicals (e.g. (a) and (b)) formed by cleavage of the 1,6- or 5,6-bonds. Isopropenylcyclohexane derivatives

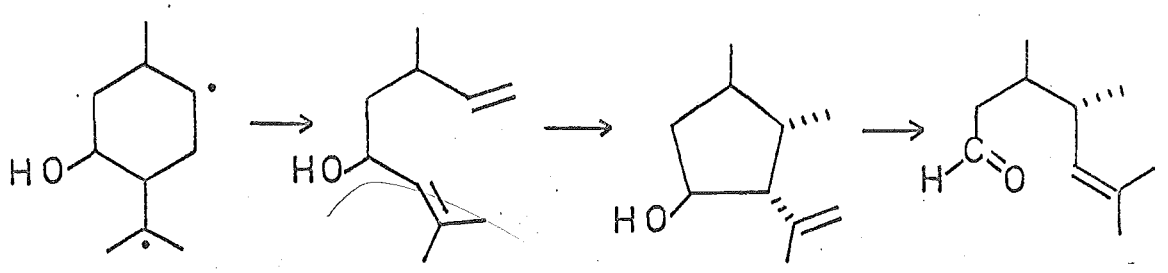
were observed as products only when the pinane substrate contained an sp^2-hybridised centre at C2 or C4, immediately adjacent to the cyclobutane ring.



(134) (67)

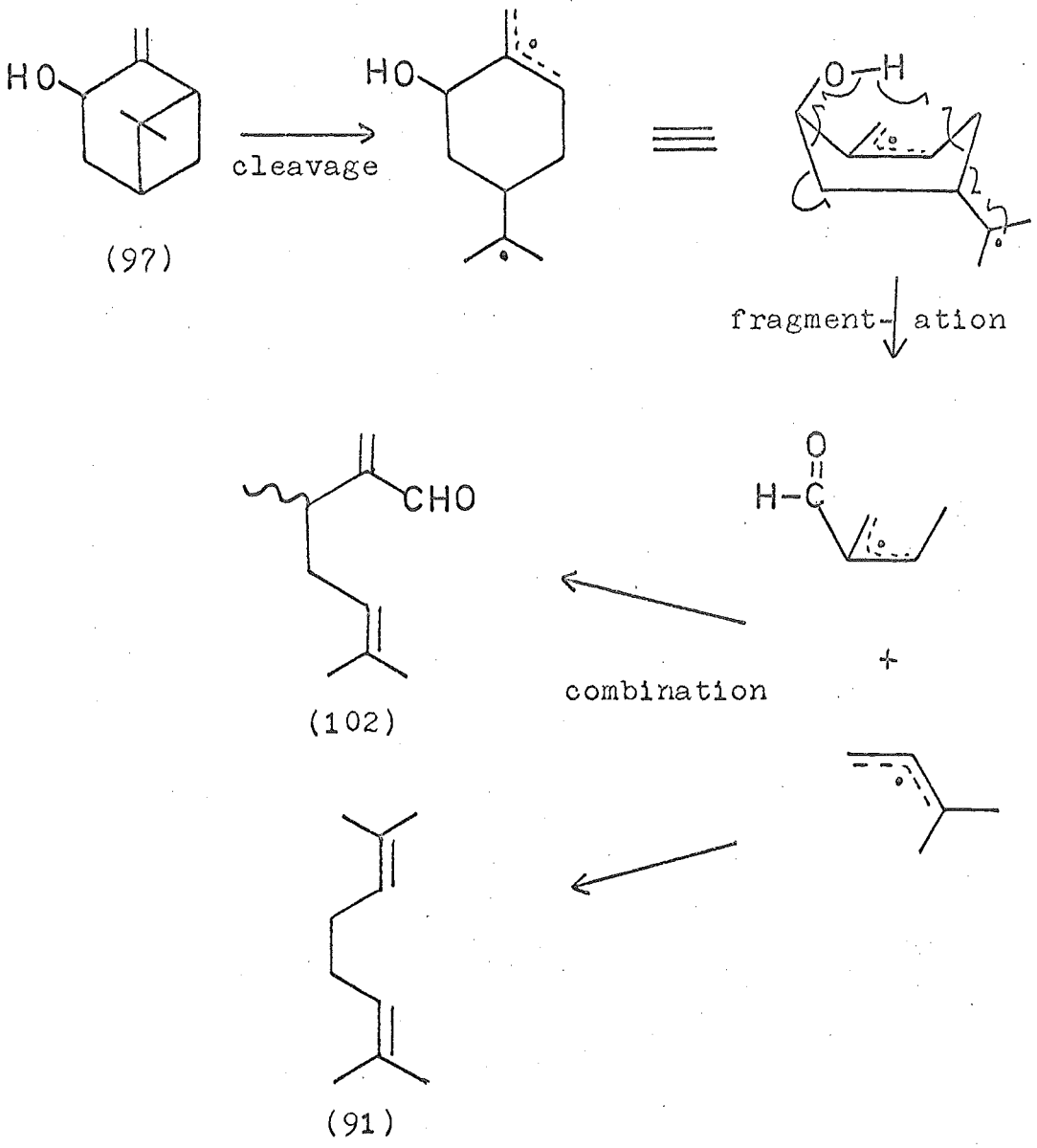
(148) (68) (69)

For pinane derivatives with hydroxyl groups at C2 or C4, an acyclic dienol formed as a primary product may lead to the formation of carbonyl compounds <u>via</u> a 1-hydroxy-2-isopropenyl-cyclopentane derivative.



(142) (143) (138)

In addition, cis-pinocarveol (97), on pyrolysis, undergoes a fragmentation reaction involving the C3 hydroxyl group and leading, after recombination of radicals, to a rearranged aldehyde (102) and a diene (91).



(97)

(102)

(91)

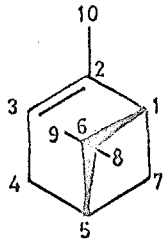
INTRODUCTION

Turpentine

Pinane monoterpenes occur naturally as turpentine which is the mixture of volatile hydrocarbons contained in the wood of coniferous trees. In recent years the Kraft wood pulping process has provided most of the world's turpentine, with current production at 70% of the total 8×10^7 gallon/year. New Zealand's turpentine ($\approx$ 1% of world total) is produced from Pinus radiata, and contains as its main constituents α-pinene (1) and β-pinene (2). New Zealand turpentine contains 65% of β-pinene (the most valuable component commercially) whereas the turpentines of other countries contain only 2-20%.

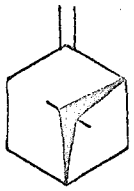
The Pinane Skeleton

The basic pinane nucleus is a bicyclo [3,1,1] heptane with two methyl groups at C6 and one at C2. The most common pinanes, namely α-pinene (1) and β-pinene (2), involve unsaturation at the 2,3 and 2,10 positions. The absolute configurations of (-)α-pinene and (-)β-pinene are as drawn in Fig. 1 where the gem dimethyl group on C6 is closer to the reader than the carbon at C7.



(1)

α-pinene

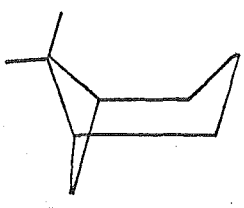


(2)

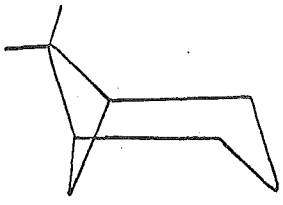
β-pinene

Fig. 1

The pinanes used in this study are of the above absolute configuration. The pinane nucleus is somewhat flexible and can exist in two basic conformations; one with the C3 up, as in Fig. 2a, and the other with C3 down as in Fig. 2b. The energetically most favoured conformation of any particular compound will depend on the substituents on the pinane nucleus. The structures of several pinanes have been determined by x-ray analysis.[1-3]



(a)



(b)

Fig. 2

Thermal Reactions of Pinane Derivatives

Interest in thermal reactions of pinane derivatives began in 1841 when Gay-Lussac and Larivere[5] found that when heated, turpentine produced some oils more volatile, and others less volatile, than the starting turpentine. Twelve years later, Berthelot[6] heated turpentine at 250° for 10 hr in sealed tubes and observed polymerisation accompanied by a change in optical rotation. In 1885, Wallach[7] heated α-pinene at 250-270° and isolated polymers and dipentene (3a). In the same year[8] pinene vapour was passed through an iron tube, almost at red heat, resulting in a gas rich in hydrogen, pentene or pentadiene, as well as aliphatic hydrocarbons.

It was not until 1927 that Smith[9] put Berthelot's observations onto a quantitative basis by measuring the rate of α-pinene racemisation, in the gas and liquid phase, at temperatures up to 237°. From his measurements he calculated the activation energy for pyrolysis of α-pinene to be 44 kcal/mole. This result has subsequently been confirmed.[10]

Conant and Carlson[23] suggested that Smith was not measuring the rate of racemisation of α-pinene, but rather, the rate of rearrangement and that the loss of optical activity was a result of the formation of optically inactive dipentene (3a). Their argument is incorrect, as dipentene

is not the sole product of reaction. It is also significant that α-pinene recovered from pyrolysis at 190-285°[18] has a greatly reduced optical rotation. Although Smith was aware that racemisation was not the only reaction occurring on pyrolysis, he underestimated the extent of the competing rearrangement.

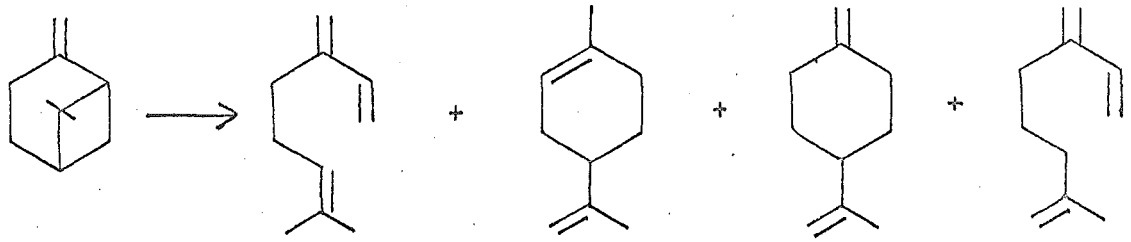
The first significant isolation of the products of α-pinene pyrolysis was made by Dupont[11] in 1935. α-Pinene was passed over copper gauze at 300-350°, resulting in products identified as dipentene (3a), alloocimene (4a) and α- and β-pyronene (5a, 6a). (see Fig. 5, p 8) Seven years later, α-pinene was passed over an electrically heated platinum spiral to produce isoprene (7, 26%). The authors of this work then concluded[12] that it was impossible to transform α-pinene into dipentene. (Most terpene hydrocarbons can be converted into isoprene (7) at high temperatures.[13]). Many other workers[14-25] varied the conditions of pyrolysis in attempts to produce a reaction of industrial applicability. The only other product isolated in this work[24] was the precursor of alloocimine (4a), namely ocimine (8). Some typical results are summarised in Table 1.

Table 1

Products (%) from α-Pinene Pyrolysis

reference	18	21	24	17	25
conditions	190-285°	460°	175°	375°	600°
	25 days -0.5 hr	2 sec	recycled	recycled	16 hr
α-pinene	5-0	10	8	3	14
dipentene (3a)	63-57	36	35	42	18
ocimene (8)	-	-	29	-	33
alloocimine (4a)	4-15	50	28	40	11
dimer of alloocimine	25-19	-	-	-	-
α-pyronene (5a)	1-4	-	-	12	-
β-pyronene (6a)	2-5	-	-		-
polymer	-	4	-	3	24

Early studies[26] of the pyrolysis of β-pinene (2) led to confusion because of the difficulty of obtaining β-pinene free from α-pinene. However, in 1941, pure β-pinene was pyrolysed[27] (at 375°) and the two main products were identified as myrcene (9, 67%), and limonene (3a, 13%). (dipentene ≡ dl limonene). Two minor products of the reaction were not isolated until 1964, namely, 1(7),8-p-menthadiene (10) isolated[28] in 5% yield, and α-myrcene (11), also formed[29] in low yield. (Fig. 3)



(9) myrcene (3a) limonene (10) (11) α-myrcene

Fig. 3

The pyrolysis of β-pinene as a commercial process was first patented in 1950[30], although at this time little was known of the reaction mechanism. At high temperature and short contact time, myrcene (9) is produced from a continuous pyrolysis process in 85% yield. Tonnage quantities of myrcene (9) are used for the production of perfumery compounds such as geraniol (12), nerol (13), linalool (14) and citronellol (15). Large quantities are also used to produce citral (16, 17), which is used as a flavouring agent and also as a precursor in the production of vitamin A. (Fig. 4)

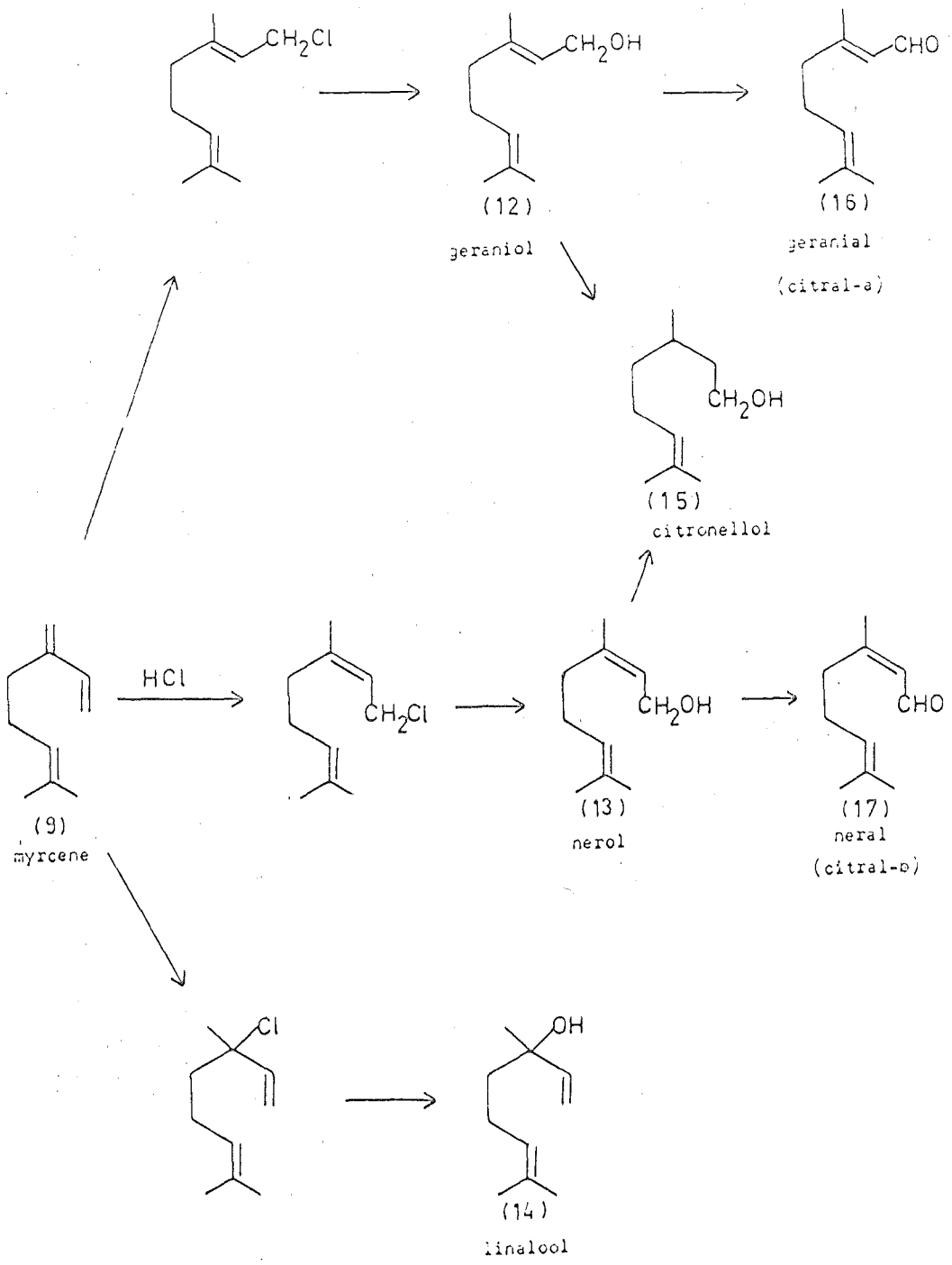
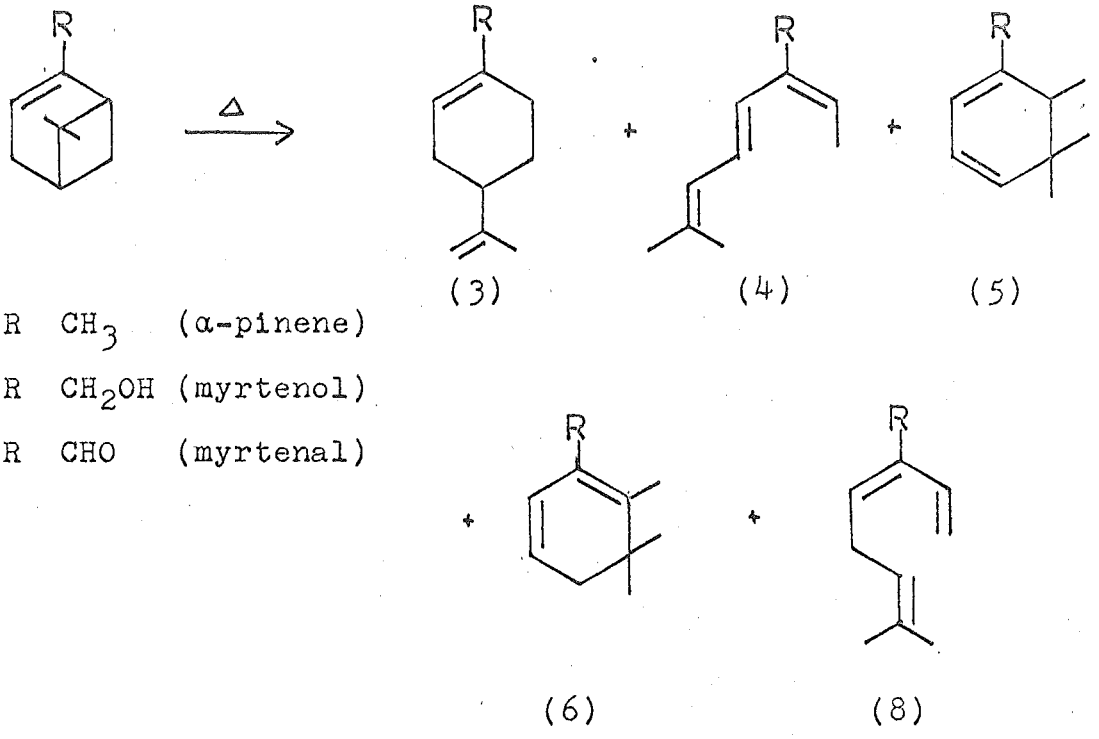

CH2Cl
CH2OH
CHO
(12)
geraniol
(16)
geranial
(citral-a)
CH2OH
(15)
citronellol
HCl
CH2Cl
CH2OH
CHO
(9)
myrcene
(13)
nerol
(17)
neral
(citral-b)
Cl
OH
(14)
linalool

Fig. 4

Many flavouring and perfumery compounds are oxygenated monocyclic and acyclic monoterpenes. The possibility of producing this type of compound by the pyrolysis of oxygenated pinanes has resulted in industrial chemists undertaking these studies. As a result of the limited techniques which were available before 1960, and the industrial rather than academic interest in the pyrolysis of pinanes, some reactions have been incompletely studied and consequently the reaction pathway has not been understood. The compounds which have been pyrolysed in industrial laboratories are all readily produced by various oxidations of α-pinene.



a, R CH_3 (α-pinene)

b, R CH_2OH (myrtenol)

c, R CHO (myrtenal)

Fig. 5

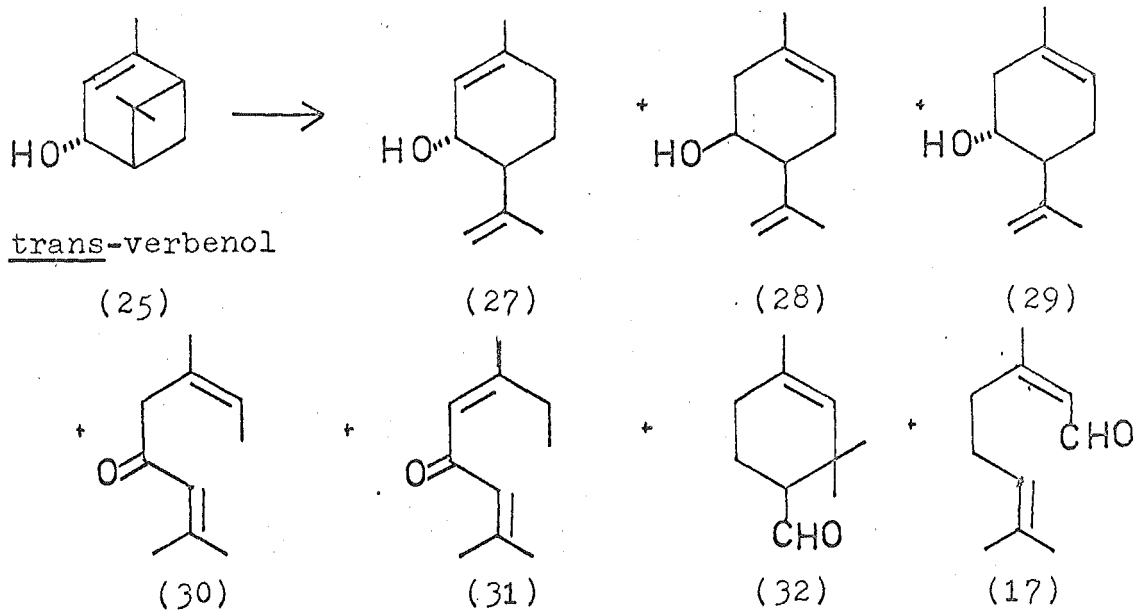
The pyrolysis of C10 derivatives of α-pinene, e.g. myrtenol (18) and myrtenal (19), closely resemble that of α-pinene. Myrtenol (18) passed down an iron pipe at 400° gave[31] perillyl alcohol (3b, 36%), the triene-alcohol (4b, 15%), and α- and β-pyrenol (5b, 6b; 25%). Myrtenal (19), pyrolysed under similar conditions, gave perillyl aldehyde (3c, 31%), the triene-aldehyde (4c, 2%), and α- and β-pyrenal (5c, 6c; 28%). (Fig. 5)

The pyrolysis of a similar compound, nopol (20), in the liquid phase, under pressure for 5 hr at 290°, has been reported[32] to give a mixture of isomeric menthadiene-7-carbinols (21).

α-Pinene-oxide (22) has been pyrolysed[33] in an iron pipe at 200-400° to give a useful perfumery compound trans-carveol (23, 10-2%), pinocamphone (24, 11-57%) and starting material (79-25%).

Pinanes oxygenated at C4 can be produced on an industrial scale by auto-oxidation of α-pinene. Pyrolysis of cis- and trans-verbenol (26, 26) under varying conditions[34-36] gives as products a variety of alcohols, aldehydes and ketones. (Fig. 6) trans-Verbenol (25), heated[34] for 4 hr at 250° in an autoclave, gave trans-isopiperitenol (27), cis- and trans-limonen-5-ol (28, 29) (total 27, 28, 29; 32%), α- and β-pseudotagetone (30, 31; 12.7%) and pseudocyclocitral (32, 16.5%), whereas trans-verbenol (25) passed down an iron pipe at 400° gave[35] limonene alcohols (28, 29; 12.5%), α- and β-pseudotagetone (30, 31; 20%), pseudocyclocitral

(32, 40%) and citral (17, 9%). Similar products were produced[34] by pyrolysis of cis-verbenol (26) in an autoclave.



trans-verbenol (25) (27) (28) (29) (30) (31) (32) (17)

Fig. 6

The pyrolysis of verbenone (33) in an iron pipe at 400° gave[35,36] isopiperitenone (34) and piperitenone (35) (total 47%) as the only identified products. cis-Verbanone (36), pyrolysed in the same manner at 490-510°, gave[37] cis-o-menth-8-en-3-one (37, 22%), conjugated carbonyl compounds (30%) and non-conjugated carbonyl compounds (21%). Similarly, isoverbanol (38), pyrolysed at 450-470°, gave[38] 3,7-dimethyl-1,6-octadien-5-ol (39, 26%), an acyclic aldehyde (19%) and an unidentified alcohol (10%). Recently, the acyclic aldehyde was identified as 3,4,6-trimethyl-5-heptenal (40), by hydrogenation to the known 2,4,5-trimethylheptane (41), although no stereochemistry was specified.

In 1929 Conant and Carlson[42] pyrolysed cis-pinane at 285° and isolated a mixture of isomeric monocyclic compounds and acyclic dienes. The first patent on the reaction was taken out[44] in 1945 when dihydromyrcene (48) was identified in the products. More pyrolysis products were isolated in the early 1950's and identified as 3,7-dimethyl-1,6-octadiene (48, 13%), trans-2,3-dimethyl-4-isopropenylcyclopentane (49, 57%) and cis-2,3-dimethyl-4-isopropenylcyclopentane (50, 19%).[45,46] (Fig. 7)

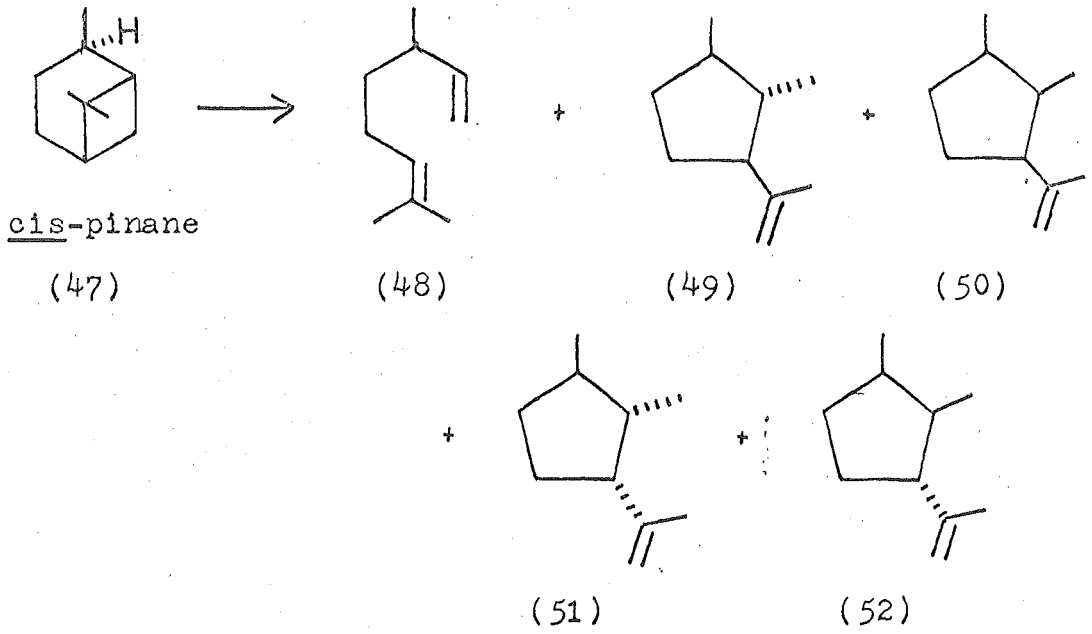


Fig. 7

The reaction was reinvestigated[47] in 1971 when the major product was found to be the cyclopentane (51) and the minor products were proposed as the cyclopentanes, in the relative yields (50) > (49) > (52). (Fig. 7) The stereochemistry of the cyclopentanone (48) was originally established by ozonolysis followed by conversion of the

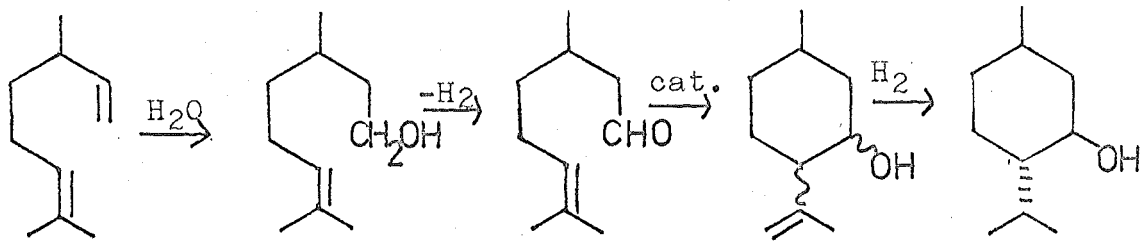
ketone produced to a known hydrocarbon. However, the recent investigation revealed that decomposition of the ozonide with aqueous sodium carbonate and hydrogen peroxide resulted in epimerisation to give structure (a) instead of structure (b). (Fig. 8)

(a) (b)

Fig. 8

A similar error was made[49] in identifying the products of 10-norpinane (53) pyrolysis as 7-methyl-1,6-octadiene (54, 50%) and trans-1-methyl-2-isopropenylcyclopentane (55, 20%), instead[75] of the cis-cyclopentane.

As with β-pinene, the pyrolysis of cis-pinane (47) was utilised commercially before the reaction was fully understood. Under controlled conditions high yields (60-80%) of dihydromyrcene (48) are produced.[50,51] This compound is as versatile as myrcene (9) in its reactions to produce numerous valuable perfumery compounds. (e.g. Fig. 9) Controlled hydration and dehydrogenation convert dihydromyrcene (48) into citronellol (57), and then to citronellal (58). Catalytic ring closure produces a mixture of isopulegol (59) isomers which on hydrogenation give mainly l-menthol (60).



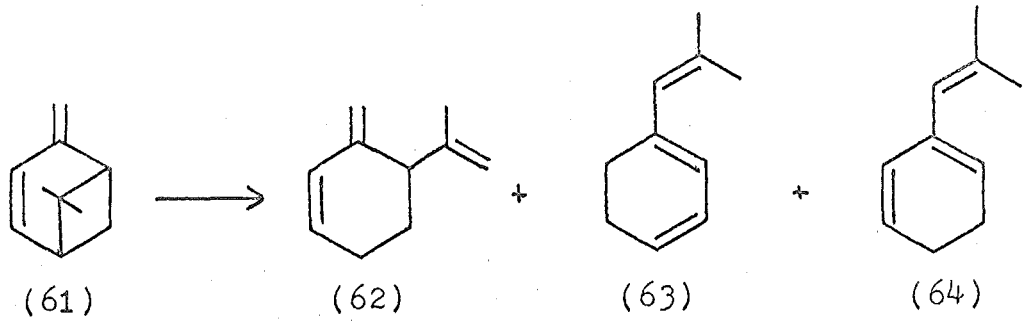
(48) (57) (58) (59) (60)

citronellol l-menthol

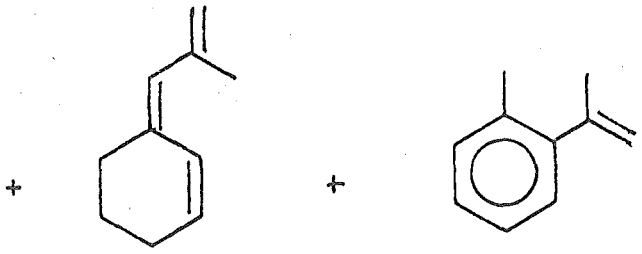
Fig. 9

The other pinane derivatives that have been pyrolysed have been studied in the course of other work. Ohloff and Klein[40] pyrolysed both 10α- and 10β-pinan-2-ol (42, 43) in an attempt to establish the absolute configuration of linalool (44). 10α-Pinan-2-ol (42), after passage though a quartz tube at 600°, gave R-linalool (44, 62%), α-terpineol (46, 13%), a methyl ketone (5%) and 8% unknowns. Apart from slight changes in product yields, the pyrolysis of 10β-pinan-2-ol (43) was similar.

Recently, Ohloff and coworkers[52] pyrolysed verbenene (61) in an attempt to synthesize 1(7),8-o-menthadiene derivatives to assist in assigning absolute configurations to carquejol and other naturally occurring o-menthane derivatives. The products from injecting verbenene (61) into a very hot inlet system on a g.l.c. were identified as 1(7),2,8-o-menthatriene (62, 29%), the trienes (63, 39%; 64, 14%; 65, 9%) and p-isopropenyltoluene (66, trace). (Fig. 10)



(61) (62) (63) (64)



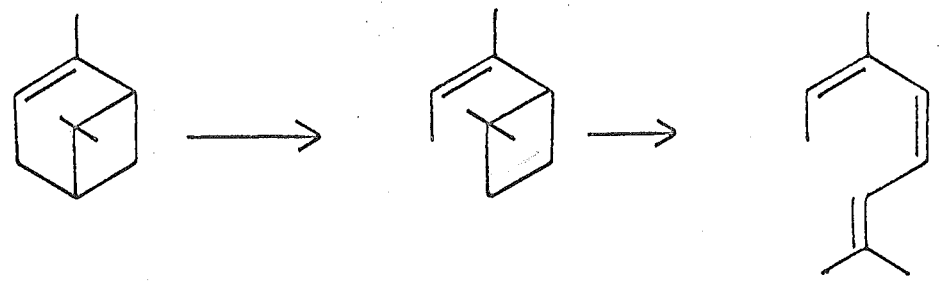
(65) (66)

Fig. 10

Requiring a synthetic route to 7-methyl-1,6-octadien-3-one (68), Mayer and Crandall[53] pyrolysed nopinone (67), hoping that it would parallel β-pinene and produce a high yield of acyclic product. On passing nopinone (67) down a quartz tube at 600°, howevever, only 39% of the dienone (68) was produced, the other products being 4-isopropenylcyclohexanone (69, 27%) and cis- and trans-2-methyl-3-isopropenylcyclopentanone (70, 14%; 71, 5%). (See Fig. 48 p 95)

The Mechanism of α-Pinene Pyrolysis

After Arbusov[14] identified alloocimene (4a) as a product of α-pinene pyrolysis, he proposed[54] a mechanism to explain its formation. (Fig. 11)



α-pinene alloocimine

Fig. 11

However, when Dupont[11] isolated dipentene (3a) and the pyronenes (5a, 6a) as well as alloocimine, he suggested that the pyrolysis occurred by cleavage of two bonds (a) and (b). (Fig. 12)

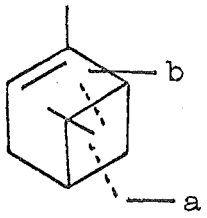


Fig. 12

Cleavage at (a) leads to α- and β-pyronene (5a, 6a), while cleavage at (b) forms dipentene (3a). Cleavage at both (a) and (b) results in the formation of alloocimine (4a). Later he included[55] ocimine (8) in the products formed by cleavage at both (a) and (b), but it is not clear whether this was from theoretical considerations or if he actually isolated the compound.

Pyrolysis of α-pinene is 1st order in α-pinene[56], and the rate is unaffected[57] by the addition of benzoic acid, antioxidants or dipentene. The mechanism is therefore unlikely to involve protonation of the olefin. Similarly, catalysis by peroxides or radical chain reaction initiators does not occur. The most commonly accepted mechanism which fits the kinetic data was proposed by Burwell[58] in 1951. He envisaged the process as involving cleavage of the 1,6 bond to give the diradical (72) which subsequently collapses to the products. (Fig. 13) This mechanism explains the racemisation of α-pinene, the formation of dipentene rather than limonene (3a), and predicted the intermediacy of ocimene (8) in the formation of alloocimine (4a).

Rice and Rice[59] suggested that α-pinene should pyrolyse to form ocimine (8) in 1935, and subsequently they patented a reaction which produced the triene (8).[60]

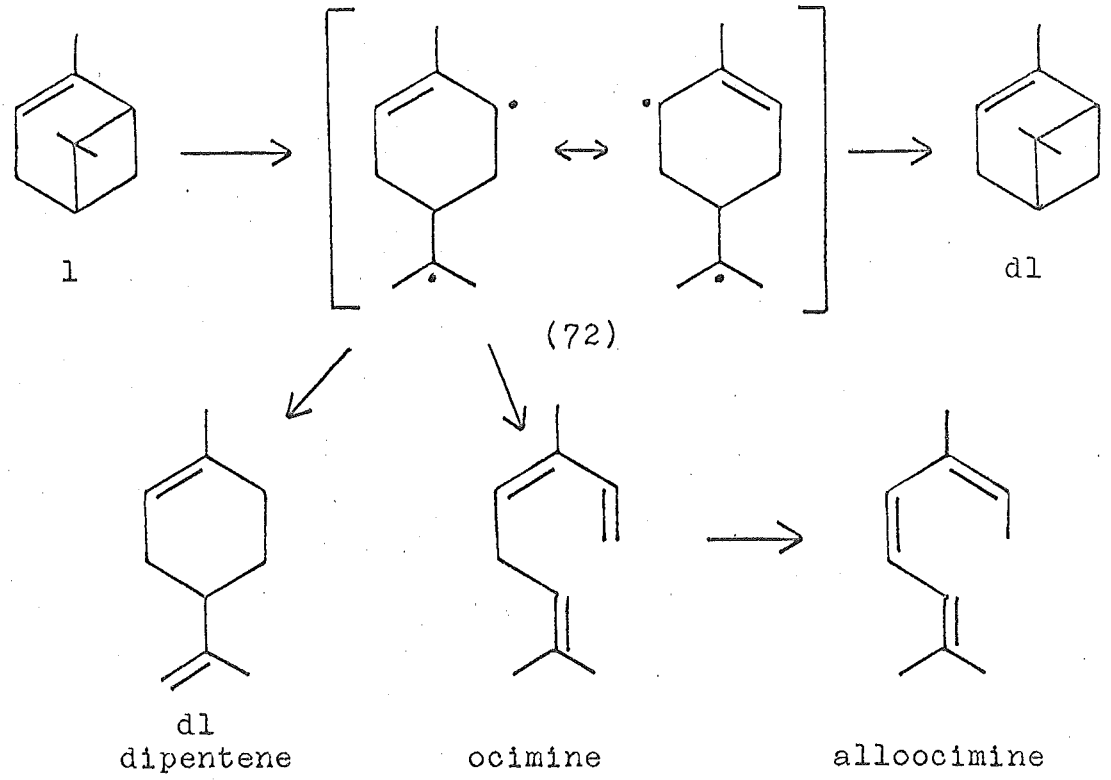
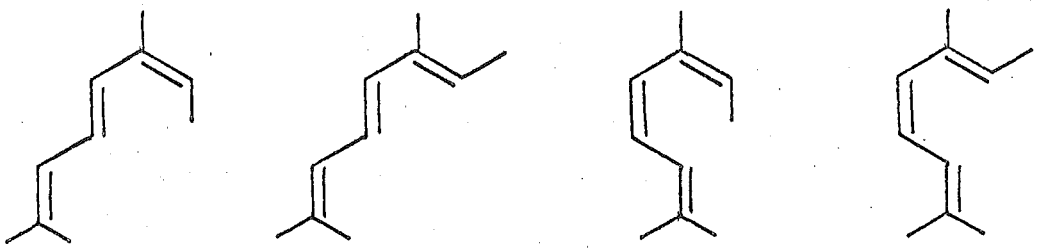


Fig. 13

Two months after Burwell's communication was published, Hunt and Hawkins[61] published a paper in which they predicted that ocimine (8) should be a primary product of α-pinene pyrolysis. (Their paper was received by the publisher nine days before Burwell's communication). By employing a recycling procedure they ensured that only unreacted α-pinene came into contact with the reaction zone and were able to obtain ocimine in 25-37% yield. Ocimine had not been observed in previous high temperature pyrolyses since it has a half-life of only 3 min at 204.5°.

In 1944, Dupont's mechanism for the formation of α- and β-pyronene (5a, 6a) was shown[62] to be incorrect as pyrolysis of alloocimine (4a) at 400° resulted in the formation of α- and β-pyronene (30% and 45%). The structure assigned to β-pyronene (5a) by Dupont has been questioned.[63] It was claimed, from the results of permanganate oxidations, that the β-pyronene of Dupont was actually a mixture of 20% β-pyronene and 30% of another pyronene (73) which contained an exocyclic double bond. Although the interpretation of the chemical evidence does not appear to be at fault, it is difficult to envisage a cyclisation of alloocimine that results in the formation of an exocyclic double bond.

Alloocimine (4a) has four isomeric forms resulting from isomerisation at the 4,5 and 6,7 double bonds. (Fig. 14)



(A) (B) (C) (D)

Fig. 14

The alloocimine from α-pinene pyrolysis has been[64] distilled into two fractions which gave the same adduct with maleic anhydride (m.p. 83-84°), but had slight differences in other physical properties. The structure A (Fig. 14) was assigned to the major fraction and the structure B (Fig. 14) to the minor fraction. In Crowley's[65] summary of the literature

on alloocimine, the structure (A) had maleic anhydride adducts with melting points ranging from 32-40°. The picture is further confused by recent work[66] on the isomerisation of ocimine (8) to alloocimine. Ocimine was heated at 185-190° for 30 min and resulted in a product mixture containing only starting material (43%) and alloocimine (57%), identified as having structure (A). This isomerisation involves a suprafacial [1,5] proton sigmatropic rearrangement,[72] in which two transition states can be drawn. (Fig. 15)

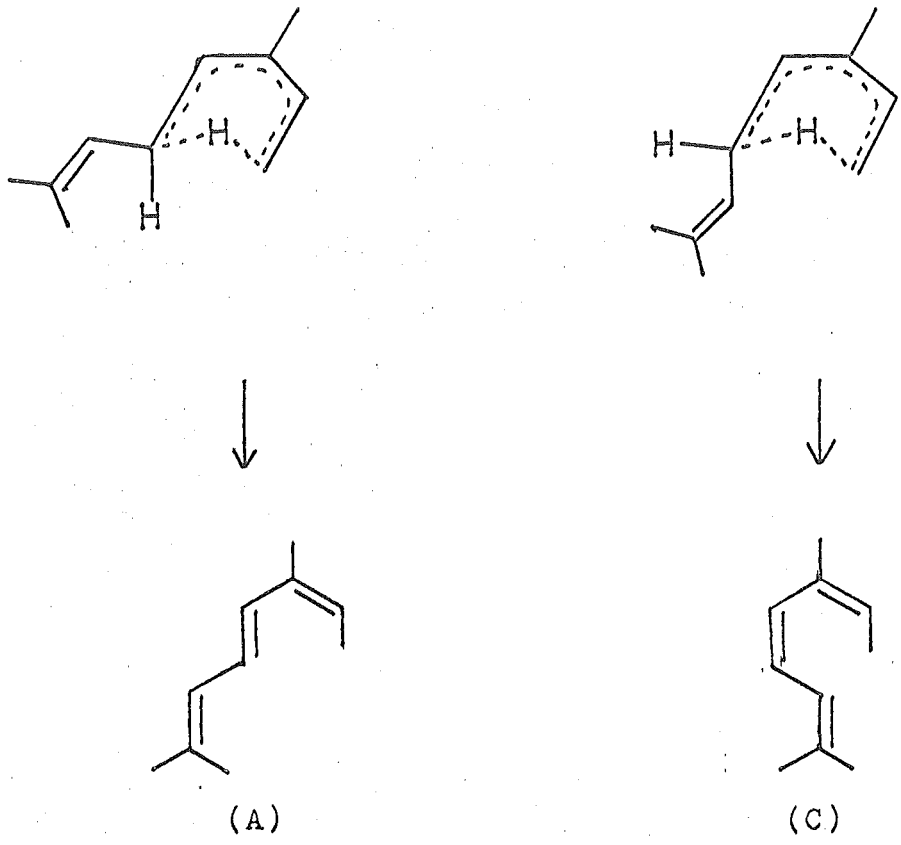


Fig. 15

The ratio of the products of such an isomerisation is a consequence of steric interactions in the transition state and is dependent on the temperature at which the reaction is performed. An increase in the reaction temperature and a reduction of the steric differences between the two transition states will bring the ratio of the products closer to unity. This latter effect is apparent in the cyclisations of dienes (a) and (b)[67]. (Fig. 16)

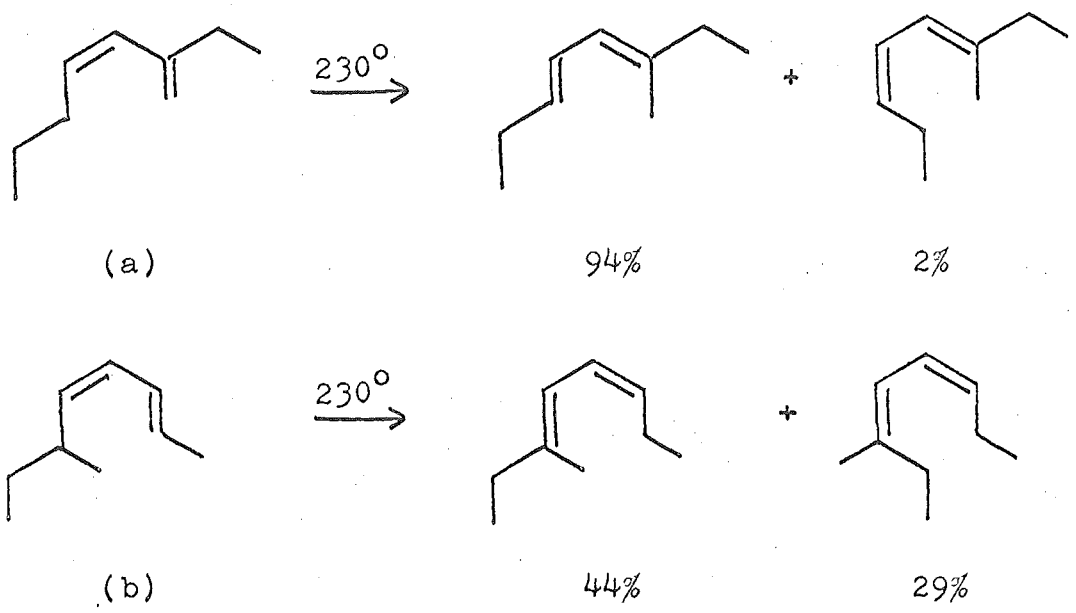


Fig. 16

Compound (b) (Fig. 16) has an extra substituent on the carbon containing the migrating hydrogen, relative to compound (a) (Fig. 16), resulting in a decrease in the difference between the two transition states as evidenced by the loss in stereoselectivity of the reaction. As isomerisation of ocimine (8) at 185-190° forms only alloocimine A (Fig. 15),

the minor alloocimine isomer which forms at much higher temperatures in the pyrolysis of α-pinene should be the isomer C. (Fig. 15)

Although the diradical mechanism is generally accepted, the possibility of concerted electronic reorganisation leading directly to ocimine (8) is a possibility.[68] Such a postulate should be examined in the light of orbital symmetry conservation rules. The concerted cleavage of the four membered ring in a pinane, leading to a 1,6 octadiene, would be an example of a [2 + 2] cycloreversion. Orbital symmetry conservation requires[69] that one of the bonds must be broken in an antarafacial manner and the other in a suprafacial manner. (Fig. 17)

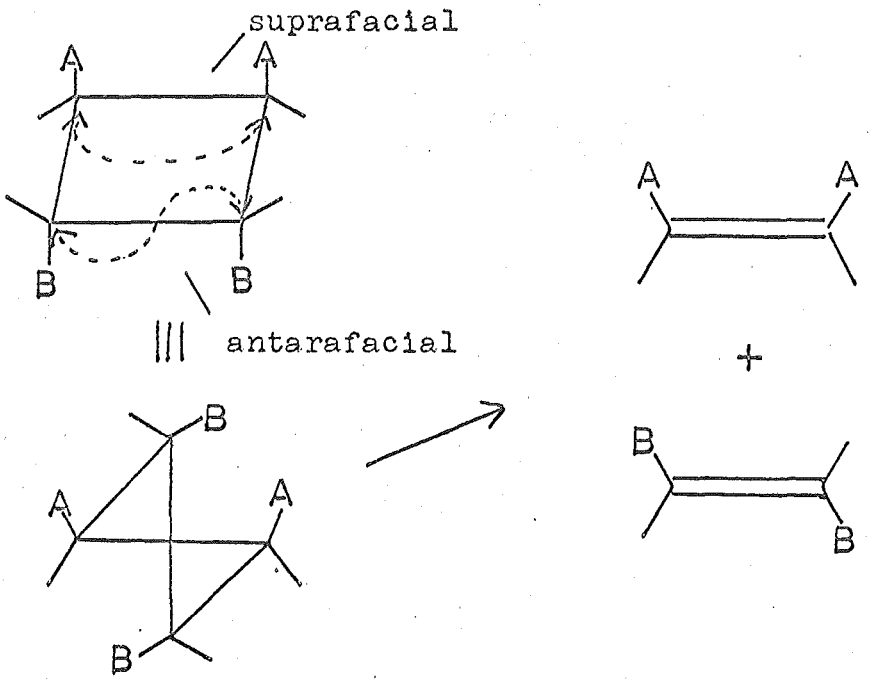
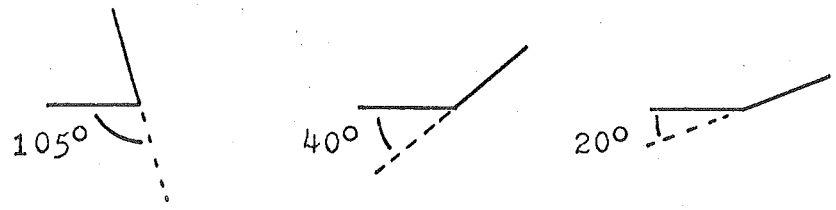


Fig. 17

In the $[2_s + 2_a]$ reaction, the stereochemical requirements of the transition state are severe: the ethylenic components must become orthogonal to each other. A two dimensional projection of cyclobutane with opposite bonds orthogonal shows a distortion from planarity of $\approx 105^{\circ}$. The same projection for pinanes shows a distortion of 35-40° (from crystallographic data),[2] while cyclobutane itself has a 20° distortion.[70] (Fig. 18)



$[2_s + 2_a]$ transition state

pinanes

cyclobutane

Fig. 18

Hoffmann and co-workers,[71] recently stated "there is little reason to believe that in the parent reaction of cyclobutane to two ethylenes there exists any preference for the symmetry-allowed process." Therefore, although there is considerably more distortion in the pinane four membered ring than in cyclobutane itself, the concerted cycloreversion will not contribute significantly to the pyrolysis mechanism.

Recently, a concerted mechanism for the formation of dipentene (3a) from the pyrolysis of α-pinene was proposed,[110] involving a multi-centre transition state. (Fig. 19)

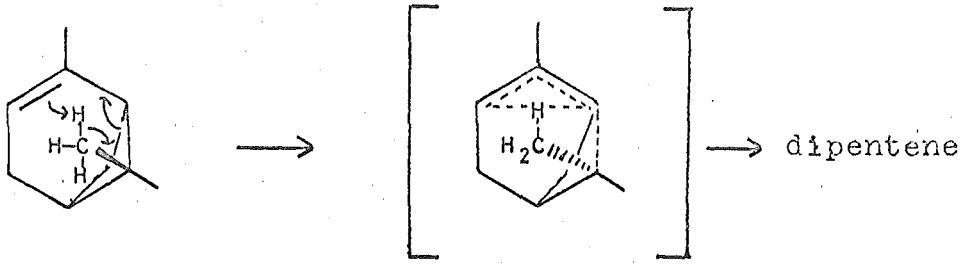


Fig. 19

The mechanism allows for migration of the hydrogen to either the C1 or C3 positions, thus forming dipentene. Migration of the hydrogen to the C1 carbon is a suprafacial concerted [1,3] shift which is thermally forbidden. Therefore, if this mechanism was operating, limonene and not dipentene (3a) would be expected.

The racemisation of α-pinene, which occurs during its pyrolysis, was explained in Burwell's diradical mechanism as a recombination of the tertiary radical with either end of the allylic system. (see Fig. 13 p 17) A sigmatropic shift would also account for the racemisation. Such a suprafacial [1,3] shift must, however, involve inversion at the migrating carbon, with consequent high energy steric interactions. As re-formation of the four membered ring is also a high energy process, the concerted pathway could be expected to compete with radical recombination.

Burwell's[58] diradical mechanism can be usefully applied to pinanes in general, as shown for β-pinene. (Fig. 20)

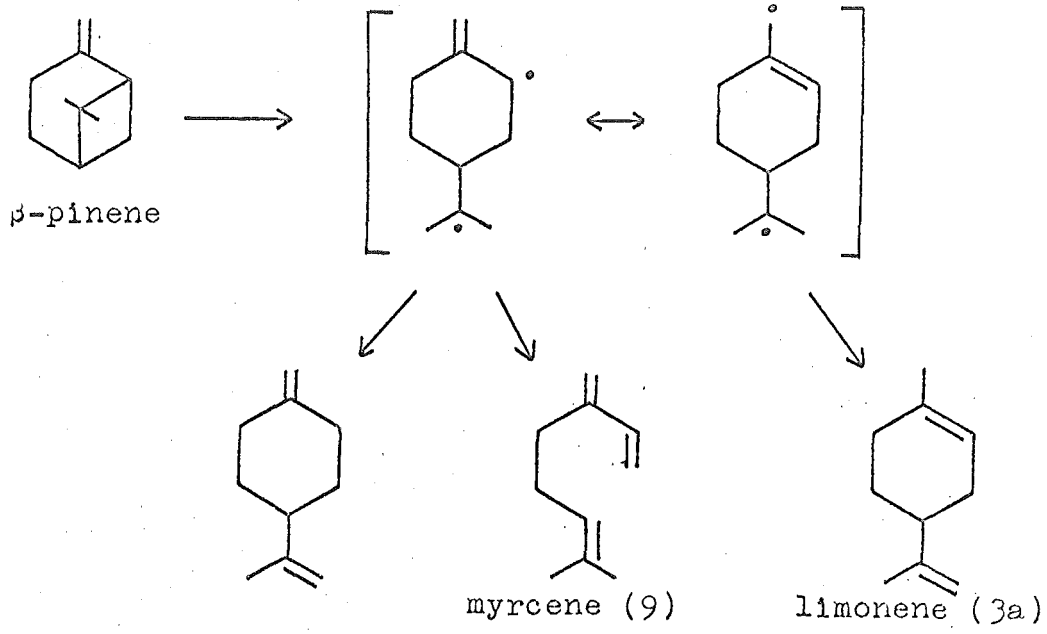


Fig. 20

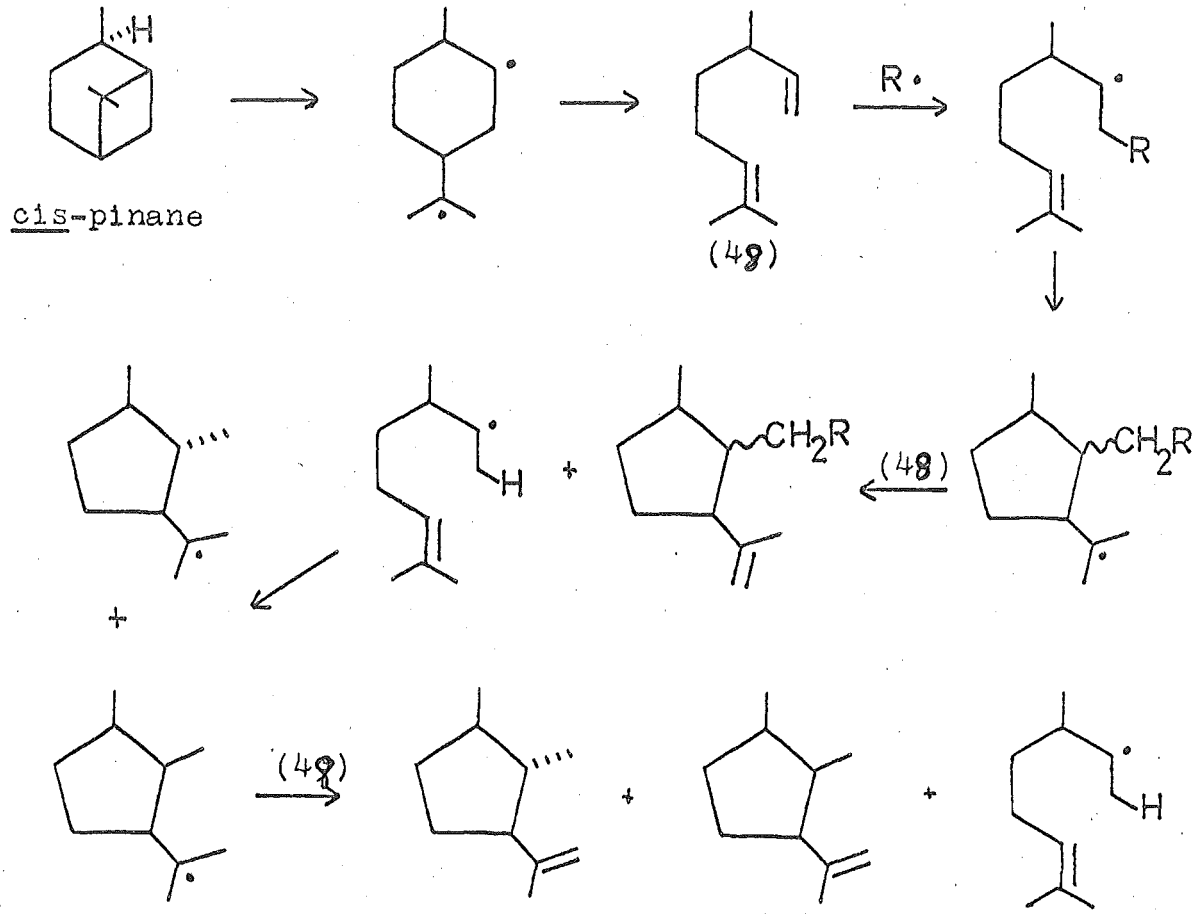


Fig. 21

This diradical mechanism is consistent with the formation[27] of limonene (3a) of high optical purity, and with the formation[29] of 1(7)-8-p-menthadiene (10), a product which was in fact not isolated until 1964, some thirteen years after the mechanism was first suggested.

A radical mechanism was not only proposed[46] for the initial cleavage in the pyrolysis of cis-pinane (47), but also for the subsequent reactions. (Fig. 21)

The mechanism of cyclisation of the diene (49) was disputed[74] by workers who claimed that kinetic data demonstrated the impossibility of a radical chain reaction being involved. They proposed an intramolecular mechanism involving a cyclic transition state. (Fig. 22)

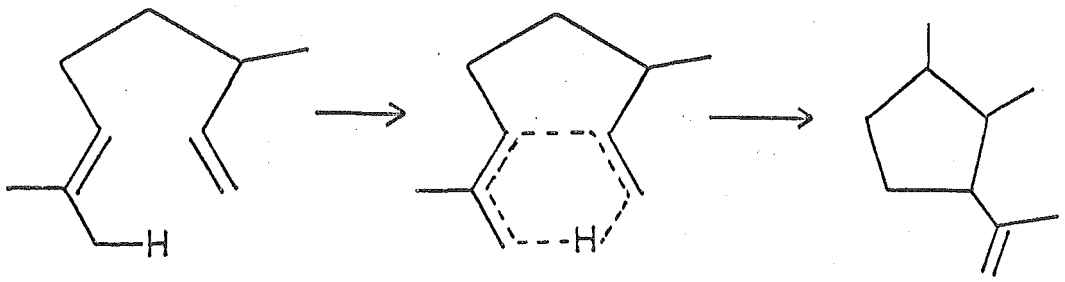


Fig. 22

This type of mechanism was developed by Ohloff and co-workers[48] who argued that, for the cyclisation of linalool (44), (a 1,6-octadiene), there are six transition states possible and they were able to predict the relative favourability of each of these from steric considerations.[48]

DISCUSSION

By the mid 1950's the pyrolysis reactions of α- and β-pinene were well documented. Work since this time has been concentrated on industrial studies of pinane derivatives, pursuing commercially exploitable products.

The present study was undertaken to examine the effects of substituents on the course of the pyrolysis reaction. Substituents might be expected to influence the reaction course by affecting both the direction of cleavage of the four membered ring and the subsequent reaction pathways. Four main types of pinane derivatives were studied, namely oxygenated pinanes containing an endocyclic double bond, oxygenated pinanes containing an exocyclic double bond, pinanols and finally, pinanones.

The Pyrolysis Technique

A variety of procedures have been used to pyrolyse pinane derivatives in the vapour phase. Closed vessels have been used but they are unsatisfactory for large scale reactions and under these conditions polymer formation can become excessive. The pyrolysis reaction has most effectively been carried out in a continuous flow apparatus using low contact times. Continuous systems are usually constructed of pyrex, quartz, or metal, and high temperatures

can readily be achieved using an electrical heating system. The contact time and reaction vessel material usually only affect the ratio of the products formed, but some metals, in particular copper, have a tendency to produce aromatic compounds.

The pyrolysis apparatus used for this work consisted of a stainless steel tube, 2.3 mm in internal diameter, containing a steel rod, 1.6 mm in diameter. The stainless steel tube was housed in a solid steel rod, 50 cm long. This arrangement gave a free space in the reaction chamber of 1.075 cm^2, and a contact time of < 0.1 sec. For example, an injection rate of 250 μl/min at 500° gives a contact time of 0.06 sec. In most cases, to obtain optimum pyrolysis conditions, oxygen free nitrogen was used as a carrier gas with flow rates of 15-30 ml/min. The apparatus was heated in an electrical, tubular oven, equipped with a voltage regulator. The temperature was measured by a thermocouple placed alongside the steel rod in the oven. The injection rate was controlled by using a micrometer syringe. The syringe was equipped with electrical heating facilities for use with crystalline samples. The apparatus is shown schematically in Fig. 23.

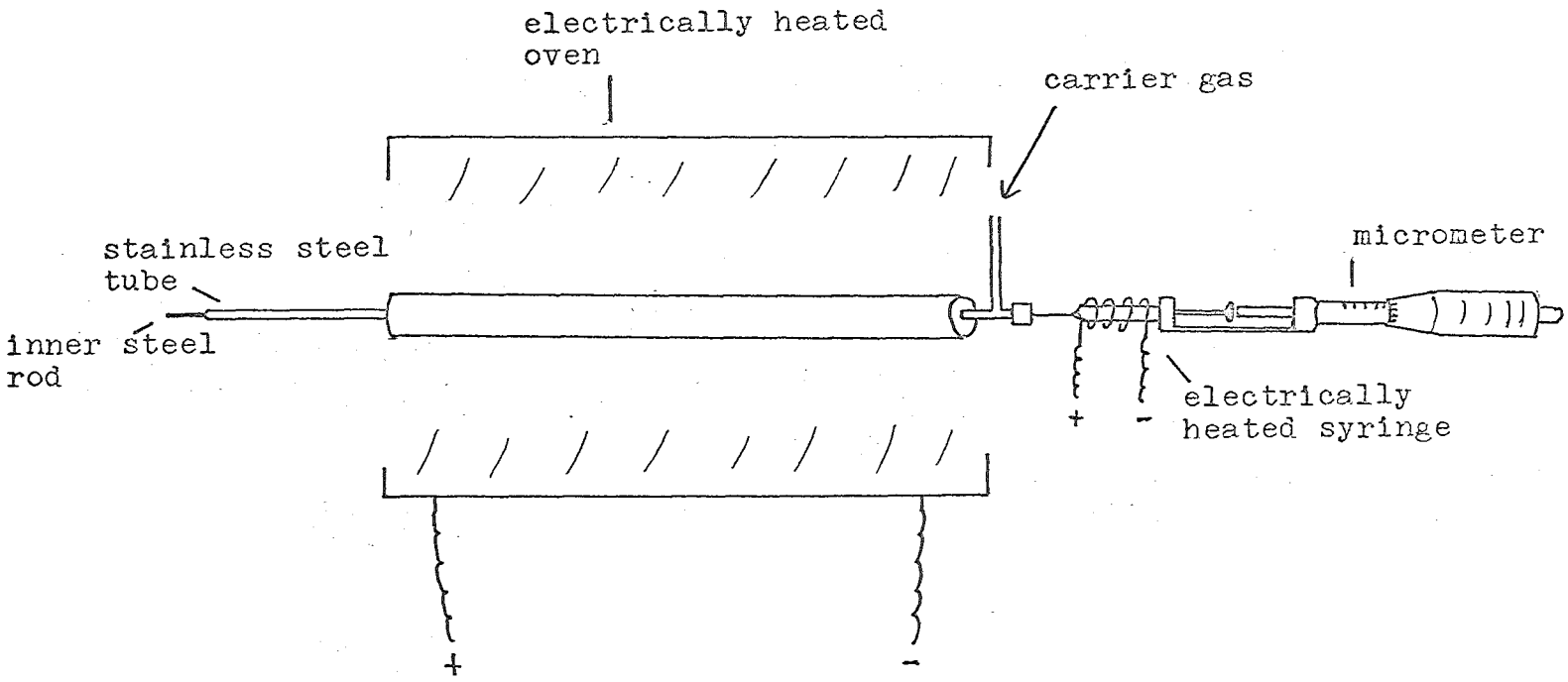

electrically heated
oven
carrier gas
micrometer
stainless steel
tube
inner steel
rod
electrically
heated syringe
+
-
+
-

Fig. 23

Chapter 1

THE PYROLYSIS OF OXYGENATED PINANES CONTAINING AN ENDOCYCLIC DOUBLE BOND

The pinanes studied in this class are derivatives of α-pinene, oxygenated at C3. Compounds such as myrtenol (18) and myrtenal (19) where the oxygen substituent is at C10 have been shown[31] to pyrolyse to products analogous to those obtained from α-pinene. Ring substituted oxygen functions are more likely to have an effect on the pyrolysis and were therefore chosen for this study.

The Pyrolysis of 2-Acetoxy-10-norpin-2-ene (76)

2-Acetoxy-10-norpin-2-ene was prepared by reaction of nopinone (67) with isopropenyl acetate. The enol acetate (76) was pyrolysed at 250 μl/min with a carrier gas flow of 30 ml/min in the temperature range 465-550°, to give a crude product (90%) shown by g.l.c. to consist of nine compounds. Five of these were isolated by fractional distillation and preparative g.l.c. and identified as m-ethyltoluene (86) and the isomeric enol acetates (78, 80, 82 and 83). (Table 2, Fig. 25, p 35)

The enol acetate (78) which was found to be racemic (o.r.d.) had absorptions in its infrared spectrum due to an enol acetate (ν_{max} 1760, 1220 cm^{-1}) and a vinylidene group

(ν_{max} 892 cm^{-1}). The n.m.r. spectrum exhibited the olefinic methyl as a triplet at δ 1.73* coupled (J 1.2 Hz) to the C8 olefinic protons which appeared as a quartet at δ 4.74 (J 1.2 Hz). The C2 olefinic proton appeared as a multiplet (W 12 Hz) at δ 5.38. The structure of the enol acetate (78) was confirmed by its conversion on alumina to 4-isopropenyl-cyclohexanone (69), which was isolated[53,93] from the pyrolysis of nopinone (67).

The enol acetates (82) and (83) displayed diene chromophores in their ultraviolet spectra (λ_{max} 266 nm, ϵ 3700) and (λ_{max} 259.2 nm ϵ 3350) and their structures were consistent with their i.r. and n.m.r. spectra. They were distinguished by the integrals in their n.m.r. spectra, as enol acetate (82) has three olefinic protons, whereas enol acetate (83) only has two. Also, enol acetate (82) has a methyl group on a proton (δ 0.95, J 6.5 Hz) while enol acetate (83) has a methyl on a double bond (δ 1.58).

The enol acetates (82) and (83) were hydrolysed on alumina to the same conjugated ketone (87) (ν_{max} 1685 cm^{-1}; λ_{max} 227.5 nm, ϵ 5960) in which the olefinic protons appeared as doublets of triplets in the n.m.r. spectrum, coupled to each other (J 10.1 Hz) and to the C4 methylene protons (J small). Double irradiation of the C4 protons collapsed the multiplets

*All n.m.r. parameters are in ppm. Multiplets are described by their width at half height ($W_{h/2}$) for well-defined peaks, and by their width (W) for broad peaks of low intensity.

to an AB quartet. The C6 methyl appeared as a doublet at δ 1.05, coupled (J 6.5 Hz) to the C6 proton. The geminal methyl groups appeared at δ 0.90 and 1.06.

The ultraviolet spectrum of the major enol acetate (80), indicated the presence of a conjugated triene (λ_{max} 277.5 nm, ϵ 9200). The n.m.r. spectrum exhibited signals due to three methyls on double bonds, namely the geminal methyl groups at δ 1.78 ($W_{h/2}$ 4.5 Hz) and the C1 methyl which appeared as a doublet at δ 1.79 coupled (J 7.5 Hz) to the C2 proton, a quartet at δ 5.23 (J 7.5 Hz). The configuration of the Δ^4-double bond is apparently cis as demonstrated by the magnitude of the coupling constant, $J_{4,5}$ 10 Hz. However, it is thought, on mechanistic grounds, that this product may have a trans 4,5 double bond. (see p 33)

Hydrolysis on alumina converted the enol acetate (80) into trienone (88). The structure followed from its i.r. (ν_{max} 1670, 963 cm^{-1}), u.v. (λ_{max} 278 nm, ϵ 19,900) and n.m.r. spectra. The ethyl group was apparent from the characteristic quartet at δ 2.56, coupled (J 7.3 Hz) to a triplet at δ 1.10 (J 7.3 Hz). The geminal methyl groups appeared as a doublet at δ 1.89, coupled (J 1.1 Hz) to the C6 proton which was itself coupled (J 11.5 Hz) to the C5 proton, resulting in its appearance as a doublet of septets at δ 5.14. The C5 proton appeared as a quartet at δ 7.46 coupled to the C6 proton and to the C4 proton (J 15.3 Hz), which appeared as a doublet at δ 6.06. The magnitude of

the coupling constant ($J_{4,5}$ 15.3 Hz) demonstrated the trans nature of the double bond.

The isolation of m-ethyltoluene (86) was confirmed[94] by comparison with an authentic sample.

Table 2

Yields (%) of Products from Pyrolysis of 2-Acetoxy-10-norpin-2-ene (76)

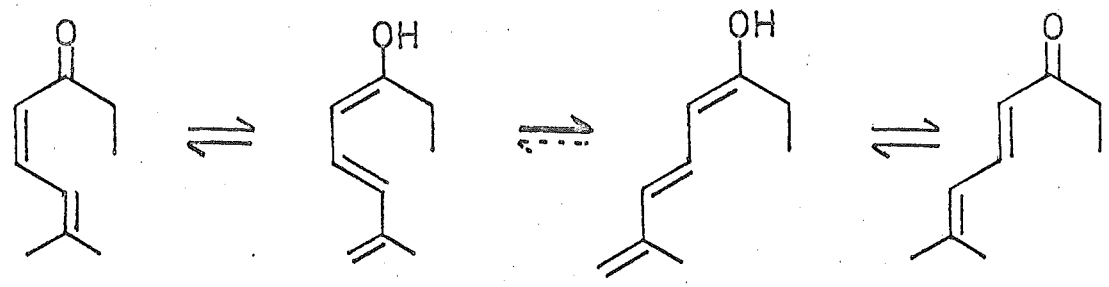
Products	(86)	(80)	(82)	(83)	(78)	(76)	others
465°	6	40	3	4	38	6	3
510°	22	9	4	15	42	1	7
550°	42	2	-	13	38	-	5

As the reaction temperature is increased, the yield of the enol acetate (80) drops markedly while the yield of the benzene derivative (86) shows a comparable increase. (Table 2) The enol acetate (83) has a less dramatic rise in yield with increasing temperature and the isopropenyl-cyclohexene (78) derivative is unaffected. A reaction scheme which rationalizes these results is shown in Fig. 25.

Cleavage of the 1,6 bond in the four membered ring of acetoxy-pinene (76) gives the most stable of the four possible diradicals. The diradical (77) can either undergo a 1,5 hydrogen shift to give enol acetate (78) or collapse to

the enol acetate (79), a compound not isolated. The compound (79) is analogous to the unstable compound ocimine (8), isolated from α-pinene pyrolysis, and can also undergo a suprafacial [1,5] sigmatropic proton shift. As with ocimine (8), two products are possible, namely the cis and trans isomers (81) and (80). As the trans double bond in enol acetate (80) prevents cyclisation from occurring, the cyclic enol acetates (82) and (83) arise solely from the cis enol acetate (81). Also, the trans enol acetate (80) should be produced in greater yield than the cis compound (81), due to steric effects in the transition state. (see p 19) It therefore seems most probable that the acyclic enol acetate (80) isolated has the trans configuration at the disubstituted double bond and has an abnormally low coupling constant. ($J_{4,5}$ 10 Hz)

The hydrolysis product (88) has a trans disubstituted double bond, but as it could have arisen either from the trans enol acetate (80) or from the cis enol acetate (81) by enolisation of the hydrolysis product, it does not prove the stereochemistry of its precursor. (Fig. 24)



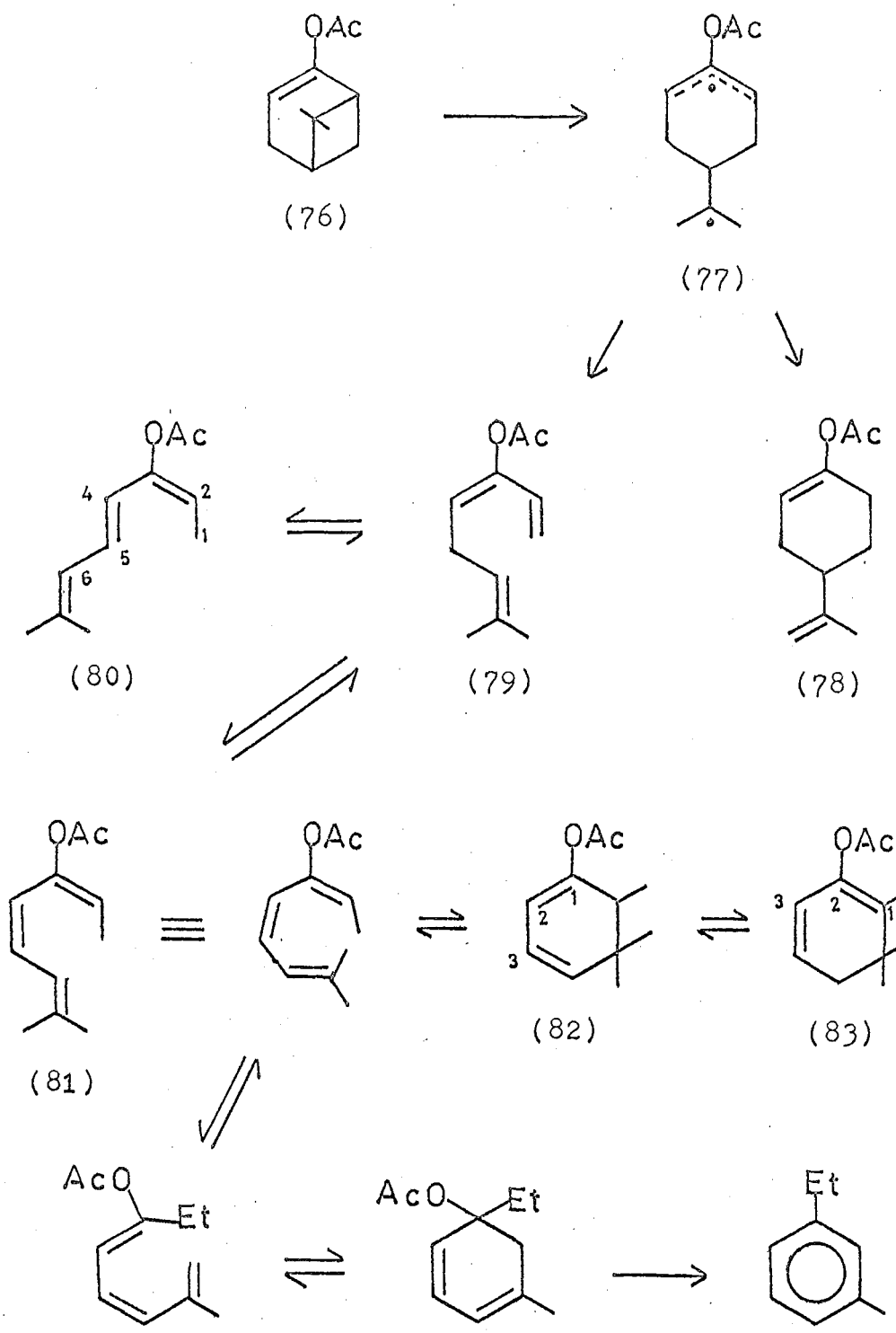
hydrolysis product of enol acetate (81)

(88)

Fig. 24

The enol acetate (81), as well as cyclising to give the enol acetate (82) (which undergoes a [1,5] sigmatropic shift to yield the isomeric enol acetate (83)) can rearrange to compound (84) by an antarafacial [1,7] sigmatropic hydrogen shift. Cyclisation of enol acetate, followed by loss of acetic acid, yields the aromatic product (86).

At low temperatures, the stereospecificity of the initial [1,5] sigmatropic shift to give cis and trans enol acetates (81) and (80), is greatest, and hence the yield of trans enol acetate (80) is high. As the temperature of the pyrolysis is increased, more cis enol acetate (81) is formed. All the pericyclic reactions are reversible, however the loss of acetic acid is not, and the reaction results in a high yield of m-ethyltoluene (86). This latter reaction course is not available to α-pinene, but with this exception, pyrolysis of 2-acetoxy-10-norpin-2-ene (76) parallels that of α-pinene.


OAc
(76)
OAc
(77)
OAc
4
2
1
5
6
(80)
OAc
(79)
OAc
(78)
OAc
OAc
OAc
1
2
3
OAc
3
2
1
(81)
(82)
(83)
AcO
Et
AcO
Et
Et

The Pyrolysis of 2-Hydroxy-10β-pin-3-ene (89)

Oxidation of α-pinene with lead tetraacetate using the method of Whitham,[95] yielded 2-acetoxy-10β-pin-3-ene (90). As hydrolysis of the acetate (90) using aqueous methanol/potassium hydroxide was found to be complicated by rearrangement occurring, the reaction was effected by the use of lithium aluminium hydride which gave pure 2-hydroxy-10β-pin-3-ene (89).

The hydroxy-pinene (89) was pyrolysed at 540° by melting the crystals in the electrically heated syringe and injecting the liquid at 200 μl/min with a carrier gas flow of 15 ml/min. In addition to eleven low boiling compounds (9.5%) and a small amount of starting material (1.5%), six compounds were isolated by fractional distillation and preparative g.l.c. and identified as the diene (91, 7%), the vinyl ketone (92, 3%), the methyl ketone (93, 12%), the conjugated methyl ketones (94, 25%) and (95, 21%), and the inseparable methyl ketones (96a, 96b; 21%). (Fig. 26)

The structure of the diene (91) followed from an infrared band characteristic of a trisubstituted double bond (ν_{max} 833 cm^{-1}), a parent ion in the mass spectrum of M^+ 138, and from its n.m.r. spectrum (four methyls on double bonds at δ 1.68 and 1.60, two protons on the same double bonds at δ 5.13, and four methylene protons at δ 2.00).

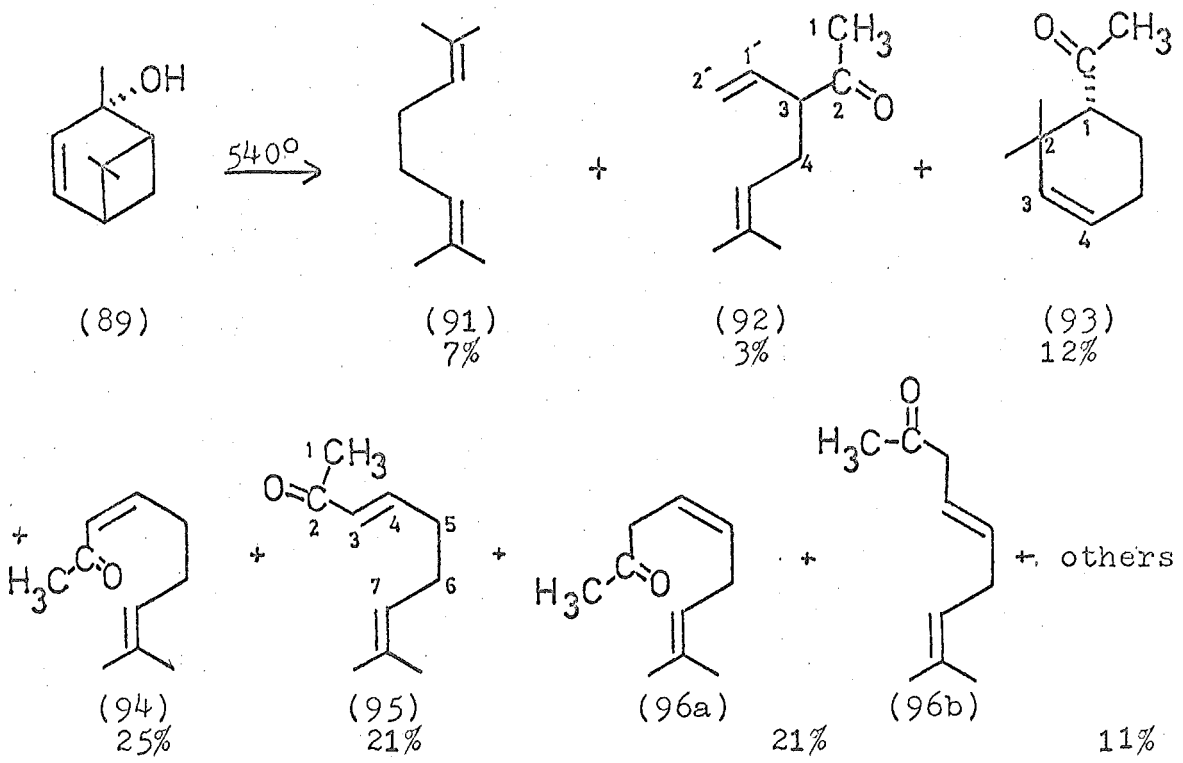


Fig. 26

The extensively rearranged vinyl ketone (92) was isomeric (elemental analysis) with the starting material. Its structure was assigned on the basis of a vinyl group (ν_{max} 999, 920 cm^{-1}), a trisubstituted double bond (ν_{max} 837 cm^{-1}) and a carbonyl group (ν_{max} 1715 cm^{-1}) visible in the i.r. spectrum and from its n.m.r. spectrum. The geminal methyl groups appeared as broad singlets at δ 1.66 and 1.61 ($W_{h/2}$ 3.5 Hz) which were coupled (J small) to the C5 olefinic proton at δ 5.03, itself a broad multiplet (W 14 Hz) coupled to the C4 methylene protons at δ 2.22. The vinyl group protons appeared as a multiplet, δ 5.10-6.12, and the acyl methyl as a singlet at δ 2.12. The C3 proton appeared as a

quartet at δ 3.13, coupled (J 7.5 Hz) to the C1' proton and the protons of the C4 methylene group.

The methyl ketone (93) showed the presence of a carbonyl group (ν_{max} 1712 cm^{-1}) and a cis disubstituted double bond (ν_{max} 737 cm^{-1}) in its i.r. spectrum. The n.m.r. spectrum exhibited the C3 proton as a doublet at δ 5.33 coupled (J 10 Hz) to the C4 proton, itself a doublet of multiplets at δ 5.57 which collapsed to a doublet (J 10 Hz) on double irradiation of the methylene protons. The C1 proton appeared as a multiplet at δ 2.54 (W 19 Hz) while the acyl methyl gave a singlet at δ 2.17. The geminal methyl groups appeared as singlets at δ 1.13 and 0.96.

The dienone (94) was identified as a conjugated ketone by its i.r. (ν_{max} 1697) and u.v. spectra (λ_{max} 228 nm, ϵ 7150). The n.m.r. spectrum exhibited broad singlets at δ 1.68 and 1.62 ($W_{h/2}$ 3.5 Hz) coupled (small J) to the C7 olefinic proton, itself coupled (J 6.5 Hz) to the C8 methylene group resulting in its appearance as a triplet of multiplets at δ 5.14. The acyl methyl gave a sharp singlet at δ 2.18. The cis character of the 3,4 double bond could not be deduced from the n.m.r. spectrum of dienone (94) as the C3 and C4 olefinic protons were superimposed at δ 6.10. The cis stereochemistry is assigned from the band in its i.r. spectrum at ν_{max} 668 cm^{-1} which is a characteristic absorption of a cis C-H wag.[96]

Ketone (95) was also shown to be a conjugated ketone from its i.r. (ν_{max} 1680 cm^{-1}) and u.v. spectra (λ_{max} 223 nm, ϵ 8500). The n.m.r. spectrum showed signals at δ 1.62 and 1.70 ($W_{h/2}$ 3.5 Hz) due to the geminal methyl groups, which were coupled (small J) to the C7 proton, a multiplet (W 21 Hz) centred at δ 5.11. The sharp singlet at δ 2.23 was due to the acyl methyl resonance. The C3 proton appeared at δ 6.08 as a doublet, coupled (J 16 Hz) to the C4 olefinic proton, itself coupled (J 6.5 Hz) to the C5 methylene group resulting in its appearance as a doublet of triplets centred at δ 6.62. The trans stereochemistry of the disubstituted double bond was assigned on the basis of the large vicinal coupling constant,[97] (J 16 Hz) and the band in the i.r. spectrum (ν_{max} 977 cm^{-1}) corresponding to trans C-H wag.[96]

In methyl ketone (96), the disubstituted double bond was assigned the Δ^4 position, since the u.v. spectrum showed no absorption characteristic of a conjugated system. Also, the i.r. spectrum showed the carbonyl group (ν_{max} 1715 cm^{-1}) to be non-conjugated. The n.m.r. spectrum displayed broad singlets at δ 1.63 and 1.70 ($W_{h/2}$ 4.5 Hz), due to the geminal methyl groups. The C7 proton appeared at δ 5.17 as a multiplet (W 22Hz), which collapsed to a triplet on double irradiation of the geminal methyl groups, and to a broad singlet on double irradiation of the C6 methylene. The C6 methylene, also a multiplet at δ 2.73 (W 21 Hz), collapsed to a doublet on double irradiation of the C5 proton. The

C4 and C5 olefinic protons were superimposed at δ 5.57. The acyl methyl appeared as a sharp singlet at δ 2.15, adjacent to a sharp, but less intense signal at δ 2.13. The appearance of these two peaks in the region characteristic for an acyl methyl group, coupled with the fact that the i.r. spectrum shows bands at both 709 cm^{-1} and 968 cm^{-1}, suggests that methyl ketone (96) is an inseparable mixture of cis and trans isomers.

Pyrolysis of the trans conjugated ketone (95) at 540° resulted in its partial conversion to diene (91, 6%), the rearranged ketone (92, 5%), the cis conjugated ketone (94, 9%) and the non-conjugated ketones (95a, 95b; 17%). Similar pyrolysis of the cis conjugated ketone (94) resulted in its partial conversion to the trans conjugated ketone (95, 24%) and the non-conjugated ketones (96a, 96b; 42%). The non-conjugated ketones (95a) and (95b) were unchanged under the reaction conditions.

The only product of the original reaction not observed in these secondary reactions is the ketone (93). A mechanistic pathway consistent with these observations is shown in Fig. 27.

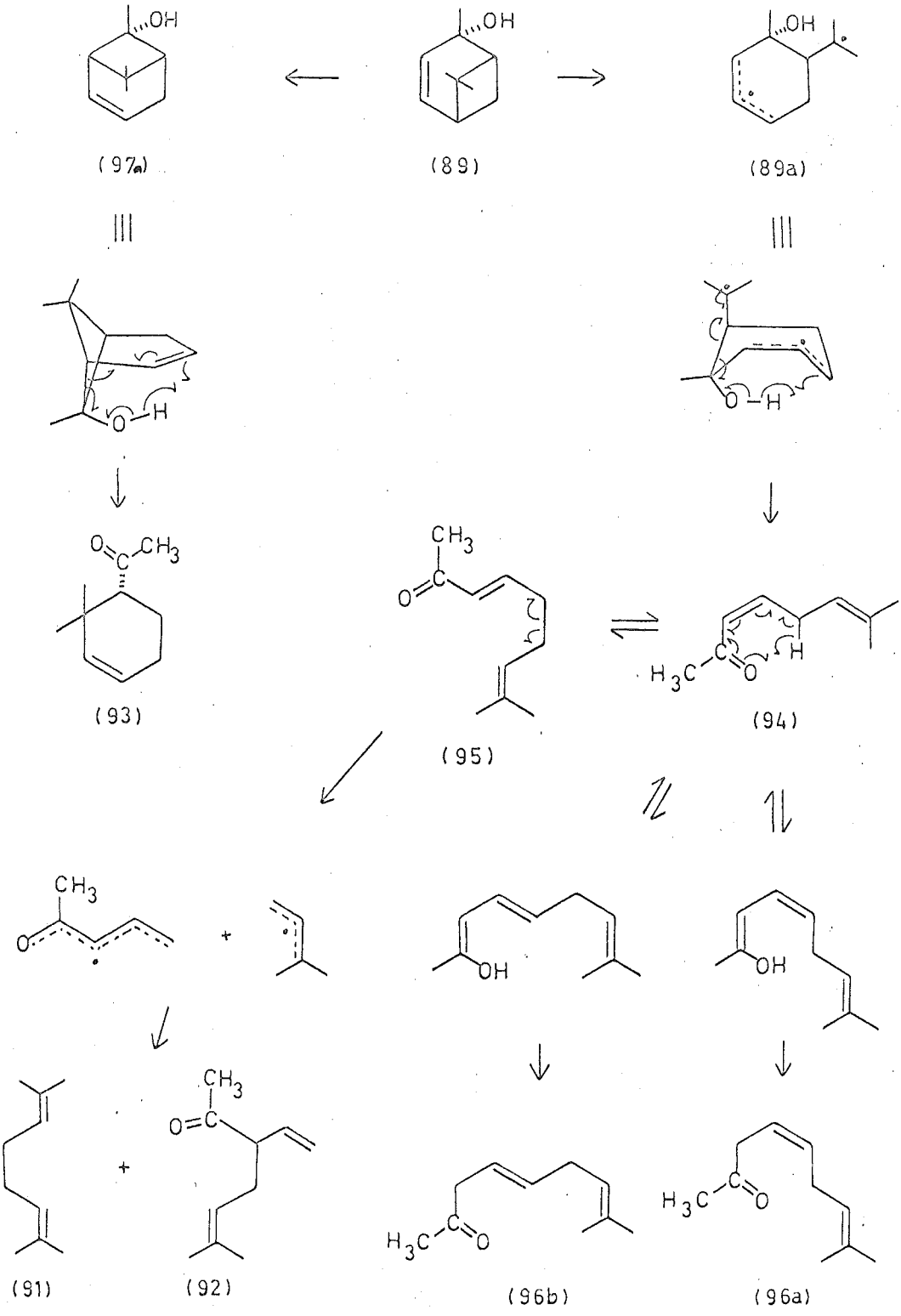

OH
OH
OH
(97a)
(89)
(89a)
O
H
O
H
O
CH3
C
CH3
C
O
H3C
C
O
H
(93)
(95)
(94)
CH3
O
OH
OH
CH3
O=C
H3C
C
O
H3C
C
O
(91)
(92)
(96b)
(96a)

Fig. 27

There are two ways of forming the C7 substituted pinene (97) from the hydroxy-pinene (89). These are recombination of the initially formed diradical (89a) or a [1,3] sigmatropic alkyl shift. The latter process was discussed in connection with the racemisation of α-pinene (see p 23). Assuming that radical recombination produces equal amounts of starting material (89) and pinene (97), then to produce 12% of the ketone (93), 20% of the diradical initially formed must recombine. As the effect of the tertiary alcohol will be to disfavour formation of pinene (97), 20% radical recombination is a conservative figure. Therefore, as at least twice as much radical recombination as [1,3] alkyl shift must occur to produce the same amount of ketone (93), participation of the concerted process cannot be ruled out.

The stereochemistry of the alcohol function in pinene (97) is such that the ketone (93) can be formed directly by a 1,5 hydrogen shift. The [1,5] sigmatropic proton shift in this cis conjugated ketone (94) to form the cis and trans non-conjugated ketones (95a) and (95b) is analogous to the rearrangement of ocimine (8) discussed earlier. (see p 19) Therefore, the trans ketone (95b) can be assigned as the major product. (The relative yield is 2:1 from n.m.r.) The formation of the rearranged ketone (92) from the radical fragments of the trans ketone (96) is substantiated by the isolation of diene (91) a product of dimerisation of the hydrocarbon radical fragment.

Although the formation of the diradical (89a) and the pinene (97) parallel the initial steps in the pyrolysis of α-pinene, the subsequent reaction pathway is dramatically altered by the tertiary alcohol substituent allowing the formation of methyl ketones.

Chapter 2

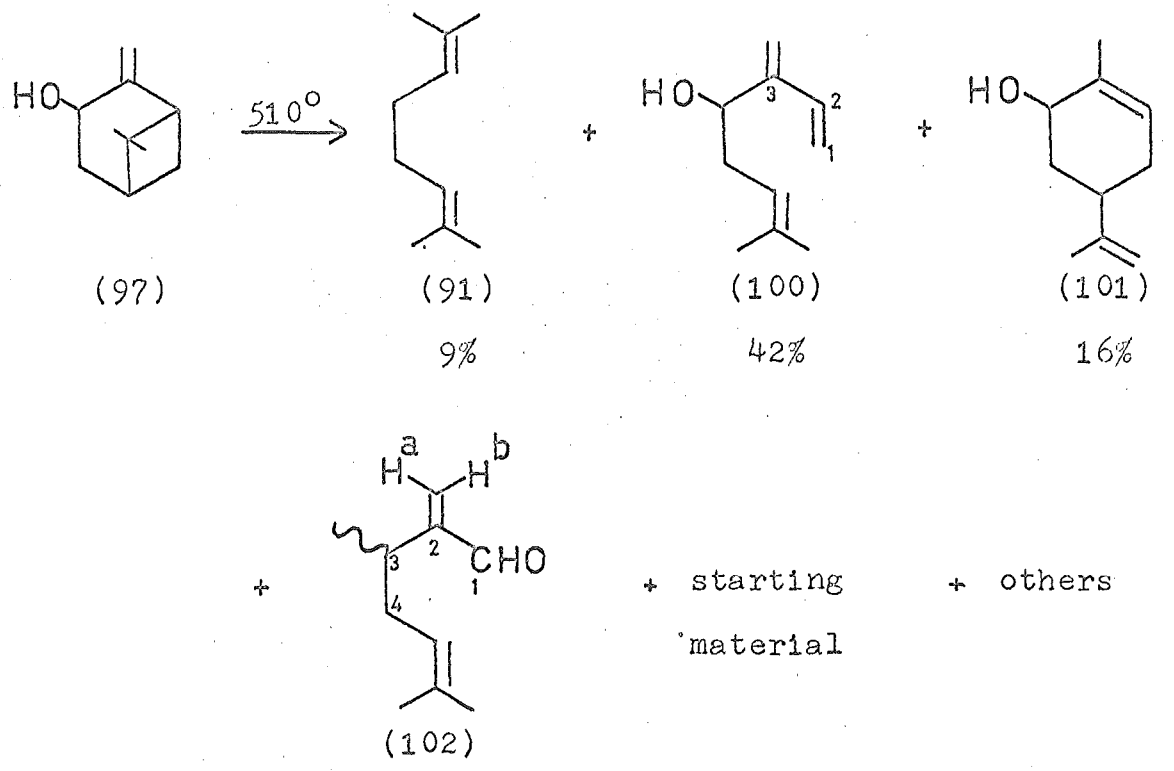
THE PYROLYSIS OF OXYGENATED PINANES CONTAINING AN EXOCYCLIC DOUBLE BOND

The pinanes studied in this class, cis- and trans-pinocarveol (97, 98) and trans-pinocarvyl acetate (106), are derivatives of β-pinene, oxygenated at the C3 position. Although the pyrolysis of β-pinene has been extensively studied, its oxygenated derivatives have been ignored.

The Pyrolysis of cis- and trans-Pinocarveol (97, 98)

trans-Pinocarveol (98) was used as supplied by Ivon Watkins Dow Ltd. Oxidation of trans-pinocarveol by activated manganese dioxide[98] gave a high yield of pinocarvone (99). cis-Pinocarveol (97) was produced[99] by the bromination of pinocarvone followed by debromination and reduction using zinc/acetic acid.

Pyrolysis of cis-pinocarveol at 510° and 250 μl/min, with a carrier gas flow of 15 ml/min, gave a crude product (92%), the major products of which were isolated by fractional distillation, preparative g.l.c. and column chromatography, and identified as the diene (91, 9%), the hydroxy-triene (100, 42%), cis-pinocarveol (97, 3%), cis-carveol (101, 16%) and the rearranged aldehyde (102, 14%). (Fig. 28)



(97) (91) (100) (101) (102)

9% 42% 16% 14% 3% 16%

Fig. 28

The diene (91) had spectra identical to the symmetrical olefin isolated from 2-hydroxy-10β-pin-3-ene (89) pyrolysis. The structure of the hydroxy-triene (100) followed from its u.v. (λ_{max} 225.5 nm, ϵ 9100), and its n.m.r. spectra, which were very similar[29] to those for myrcene (9). The C1, C3' and the C6 olefinic protons appeared as a complex multiplet (δ 4.94-5.51). The C2 vinyl proton appeared as a quartet at δ 6.38, coupled (J 17.6 Hz) to the trans C1 proton and (J 11 Hz) to the cis C1 proton. The position of the C4 proton, δ 4.41, pointed to its being allylic to a double bond as well as being geminal to a hydroxyl group and the nature of the signal, a triplet (J 6 Hz), required that it

be adjacent to two protons. The geminal methyl groups appeared as a singlet at δ 1.65 and a doublet at δ 1.74 (J 1 Hz) resulting from coupling between the C6 proton and the cis methyl group.

cis-Carveol (101) was identified by comparison with an authentic sample, prepared by lithium aluminium hydride reduction of carvone (103).

The structure of the rearranged aldehyde (102) was determined by a consideration of its u.v., i.r. and n.m.r. spectra. The u.v. spectrum showed the presence of a conjugated system (λ_{max} 218.5 nm, ϵ 5694) while the i.r. spectrum exhibited bands characteristic of a conjugated aldehyde (ν_{max} 2720, 1696 cm^{-1}). The n.m.r. spectrum exhibited the aldehyde proton as a singlet at δ 9.55. The methylene proton $C2'_b$ appeared as a doublet at δ 5.98 with a small coupling (J 0.6 Hz) to the $C2'_a$ proton, itself a triplet at δ 6.22, as a result of coupling (J 0.6 Hz) to the C3 protons. The C3 methyl group appeared as a doublet at δ 1.06, coupled (J 6.8 Hz) to the C3 proton, itself coupled to the C4 methylene protons, resulting in its appearance as a sextet at δ 2.76. The C5 olefinic proton resonance at δ 5.05 appeared as a triplet of multiplets due to coupling (J 7.3 Hz) with the C4 methylene protons and a small coupling (J 1 Hz) with the cis geminal methyl, which appeared as a doublet at δ 1.67. The trans geminal methyl appeared as a singlet at δ 1.59.

The pyrolysis of trans-pinocarveol (98) under the same conditions as for cis-pinocarveol (97), gave a crude product

(90%) shown by g.l.c. to consist of thirteen compounds. Six of these were isolated by fractional distillation, preparative g.l.c. and column chromatography and identified as the diene (91, 3.5%), trans-pinocarveol (98, 9.5%), the aldehyde (102, 4.7%), hydroxy-triene (100, 62.2%), trans-isocarveol (104, 6.2%) and trans-carveol (105, 5.2%), by comparison with authentic samples. The hydroxy-triene (100, $[\alpha]_D$ -35°) produced from trans-pinocarveol was enantiomorphic with the hydroxy-triene (100, $[\alpha]_D$ + 36.7°) produced from cis-pinocarveol.

The formation of the hydroxy-trienes (100) and the carveols (101, 103, 104, 105) follows the pattern found in the pyrolysis of β-pinene (see Fig. 3, p 6), but some drastic skeletal rearrangement must have occurred to produce the aldehyde (102).

In an attempt to elucidate the mode of formation of the aldehyde (102), three specifically deuterated cis-pinocarveols were prepared and pyrolysed. Rapid mixing of D_2O and cis-pinocarveol gave O-deuterated cis-pinocarveol (95% D) which on pyrolysis gave the aldehyde (102) with deuterium in the C3 methyl, as indicated by the integral of the n.m.r. signals assigned to this group (≈ 30% reduction). Lithium aluminium deuteride reduction of pinocarvone (99) gave 3-deutero-cis-pinocarveol (> 98% D) which on pyrolysis gave the aldehyde (102), essentially completely deuterated at C1, as shown by the absence of the aldehyde proton in the n.m.r.

spectrum. Base catalysed exchange of pinocarvone in D_2O/ tetrahydrofuran gave 4-deuteropinocarvone (D_1 64%, D_2 15%, after 14 days) which on reduction with lithium aluminium hydride gave 4-deutero-cis-pinocarveol. The aldehyde (102), isolated from pyrolysis of this deuterated cis-pinocarveol, was shown by a consideration of n.m.r. and mass spectra, to be deuterated at C4. The results of these deuterium labelling experiments are summarised in Fig. 29.

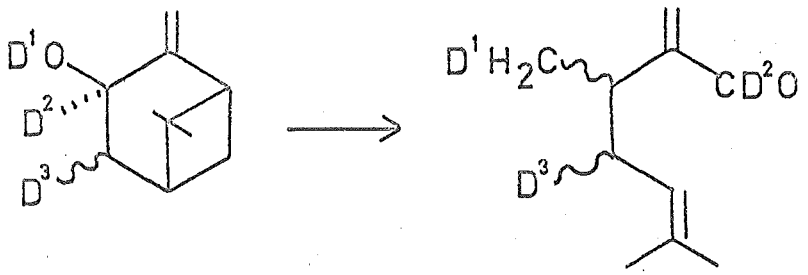


Fig. 29

From the results, a mechanism for the formation of aldehyde (102) was proposed which was consistent with the formation of the diene (91) and the racemic nature of the aldehyde. (Fig. 30)

The hydroxyl proton is able to migrate to the carbon across the ring when the diradical (a) is in a boat conformation. The accompanying electron shifts result in the diradical (a) cleaving into two fragments (c) and (d). Dimerisation of fragment (c) forms the diene (91) while combination of fragments (c) and (d) results in the formation of aldehyde (102).

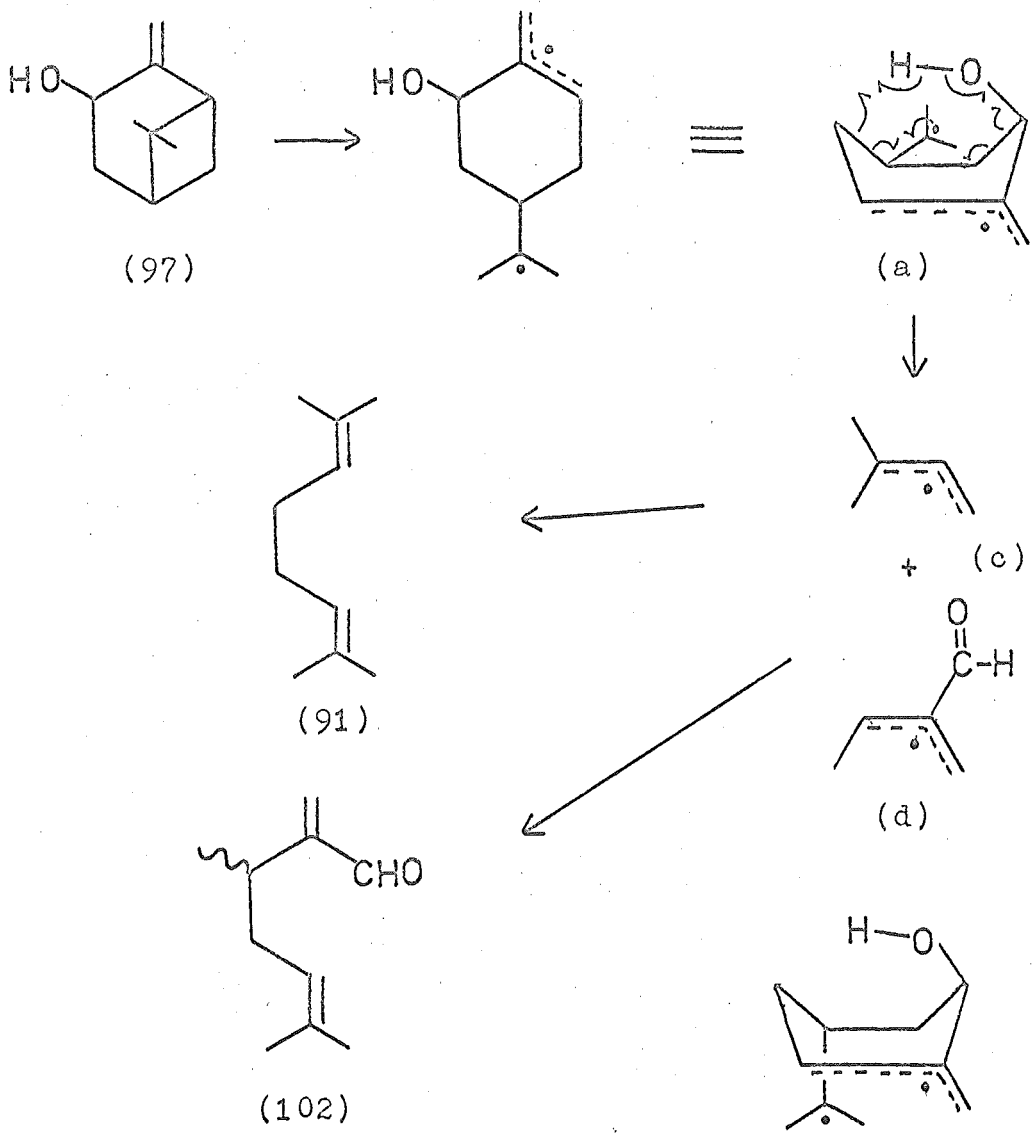


Fig. 30

The difference in the yield of aldehyde (102) from cis-pinocarveol (14%) and trans-pinocarveol (4.7%) can be accounted for by a consideration of the transition state required for aldehyde formation. The transition state formed from cis-pinocarveol (diradical (a), Fig. 30) has the isopropyl radical group equatorial while the transition

state formed from trans-pinocarveol (diradical (b), Fig. 30) has this group in an axial position. Although the energy differences between the two different conformations is small at 510°, diradical (b) must be of higher energy than diradical (a), resulting in a lower yield of aldehyde (102) from trans-pinocarveol.

The Pyrolysis of trans-Pinocarvyl Acetate (106)

trans-Pinocarvyl acetate (106) was prepared by base catalysed acetylation of trans-pinocarveol (98) with acetic anhydride. Pyrolysis of the acetate (106) at 490° at a rate of 250 µl/min with a carrier gas flow of 30 ml/min gave a complex mixture of over thirty compounds. The five major products were isolated by preparative g.l.c. and identified as the trienes (62, 9%) and (63, 11%), perillyl acetate (107, 9%) and the isomeric acetoxy-trienes (108, 27%) and (109, 8%). (Fig. 31, p 54)

The trienes (62) and (63) were identified by comparison with authentic samples and are considered to arise by the initial loss of acetic acid from trans-pinocarvyl acetate to give verbenene (61), which on pyrolysis[52] yields the trienes (62, 63) as the major products.

The i.r. spectrum of perillyl acetate (107) showed the presence of a trisubstituted double bond (ν_{max} 812 cm^{-1}) and a vinylidene double bond (ν_{max} 885 cm^{-1}). The n.m.r. spectrum showed the presence of an isopropenyl group as a methyl

on a double bond at δ 1.72 with small couplings to the olefinic protons at δ 4.68 ($W_{h/2}$ 3 Hz). The proton on the trisubstituted double bond appeared as a broad singlet at δ 5.72 ($W_{h/2}$ 8 Hz), and the methylene protons vicinal to the acetate group appeared as a singlet at δ 4.38. The identification of compound (107) as perillyl acetate was confirmed by its hydrolysis to perillyl alcohol (~~110~~ 36) which is the major product from the pyrolysis of myrtenol (18).[31]

The acetoxy-triene (108) was identified as a myrcene (9)derivative by a consideration of its u.v. and n.m.r. spectra. The u.v. spectrum showed the presence of a diene chromophore (λ_{max}223 nm, ϵ 10,220). In the n.m.r. spectrum the proton geminal to the acetate group and all olefinic protons, except the C2 proton, appeared superimposed as a multiplet at δ 4.95-5.60. The C2 vinyl proton appeared as a quartet at δ 6.36, coupled (J 18 Hz) to the trans C1 proton and (J 11 Hz) to the cis C1 proton. The C5 methylene appeared as a triplet at δ 2.42, coupled (J 7 Hz) to the proton geminal to the acetate group and the C6 olefinic proton. The geminal methyl groups appeared as broad singlets ($W_{h/2}$ 3 Hz) at δ 1.61 and 1.69.

The acetoxy-triene (109) had an intense absorption in the ultraviolet (λ_{max} 278, ϵ 21.000) due to the conjugated triene chromophore. The n.m.r. spectrum exhibited the C2 methyl as a doublet at δ 1.81, coupled (J 7 Hz) to the olefinic proton. This doublet was superimposed on the broad

singlet at δ 1.80 due to the geminal methyl groups. The C3' methylene protons appeared as a singlet ($W_{h/2}$ 3 Hz) at δ 4.66. The C2, C5 and C6 olefinic protons were superimposed in a multiplet (δ 5.42-6.22). The C4 olefinic proton appeared as a doublet at δ 6.38, coupled (J 9 Hz) to the C5 olefinic proton. This is another case where the stereochemistry of the double bond, indicated by the magnitude of the coupling constant, is not consistent with the mechanism of its formation. (c.f. enol acetate (80), p 33) Although the n.m.r. data suggests a cis configuration for the Δ^4-double bond the mechanism involving a suprafacial [1,5] sigmatropic proton shift predicts a trans configuration for the triene (109) isolated. (Fig. 31) A mechanistic scheme for the formation of the products is presented in Fig. 31.

The cleavage of the 1,6 bond in trans-pinocarvyl acetate (106) to form the diradical (111) is competing with elimination of acetic acid to give verbenene (61) which itself pyrolyses as previously described.[52] (p 13) The trienes (62, 63) are produced from verbenene pyrolysis in 68% yield. Therefore, the amount of the trienes isolated from trans-pinocarvyl acetate pyrolysis (20%), is only 68% of the verbenene pyrolysis products present, i.e. verbenene was initially formed from trans-pinocarvyl acetate in 29% yield.

The diradical (111) decomposes in two different ways. The myrcene derivative (108) is produced by the normal mode of collapse of the diradical. Migration of the acetate

from C2 to C7 results in the formation of a diradical analogous to the diradical (72) formed in α-pinene pyrolysis. Decomposition of this diradical forms perillyl acetate (107) on migration of a hydrogen, and the ocimine derivative (110) on cleavage of the bond adjacent to the isopropyl radical group. The acetoxy-trienes (109) and (109a) are formed by a suprafacial [1,5] sigmatropic proton shift in the ocimine derivative (110) giving the <u>trans</u> compound (109) as the major product. (see p 19)

These reactions of β-pinene derivatives parallel closely the pyrolysis of β-pinene itself, however some products are formed which are a consequence of the substituted oxygen function.

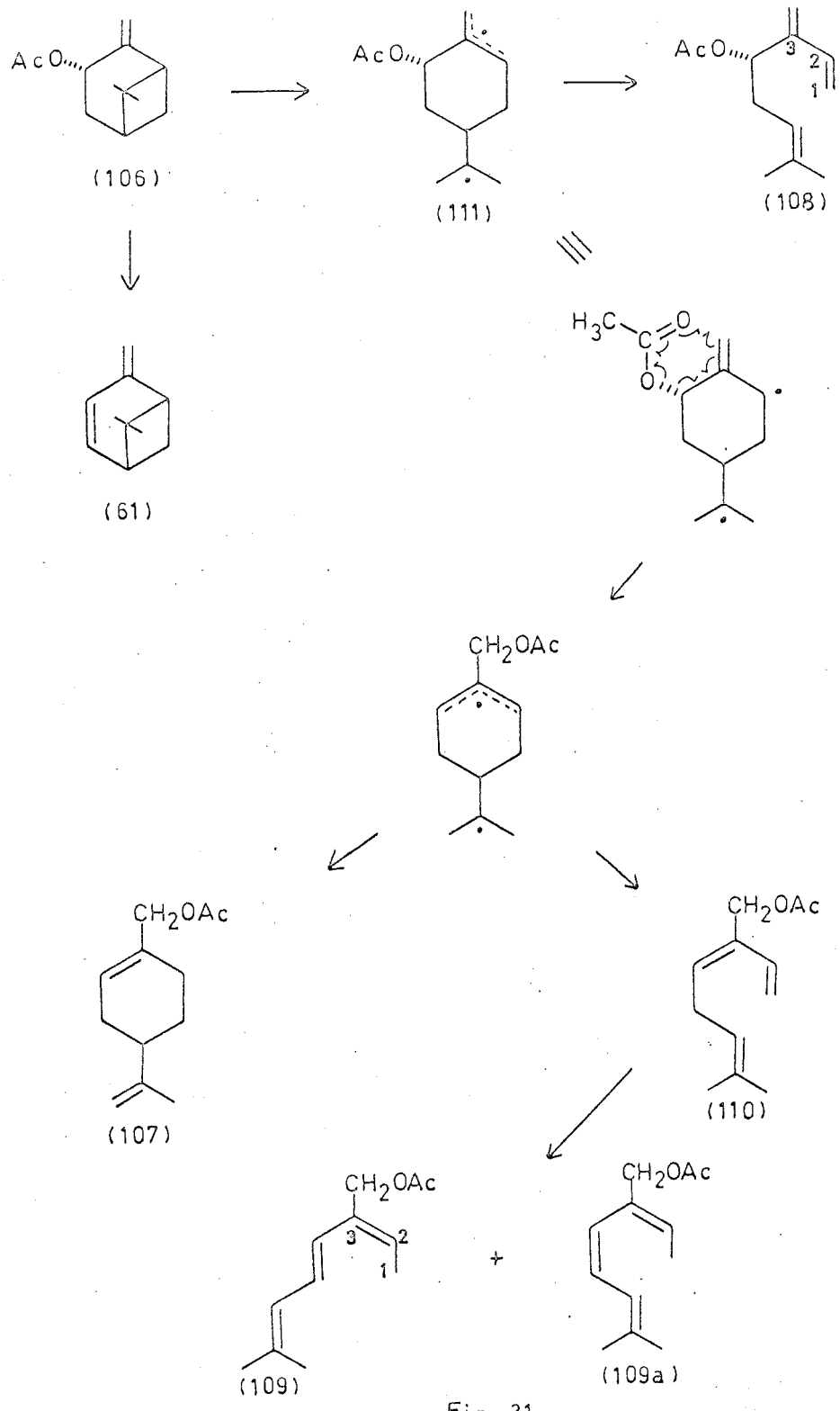

AcO
(106)
AcO
(111)
AcO
3
2
1
(108)
(61)
H3C
C
O
O
CH2OAc
CH2OAc
(107)
CH2OAc
(110)
CH2OAc
3
2
1
(109)
+
CH2OAc
(109a)

Fig. 31

Chapter 3

THE PYROLYSIS OF PINANOLS

In the pyrolysis of pinane derivatives containing a carbon-carbon double bond adjacent to the four membered ring, i.e. derivatives of α- and β-pinene, the cyclobutane cleaved to produce the diradical where the secondary radical is allylic to the double bond. (Fig. 32)

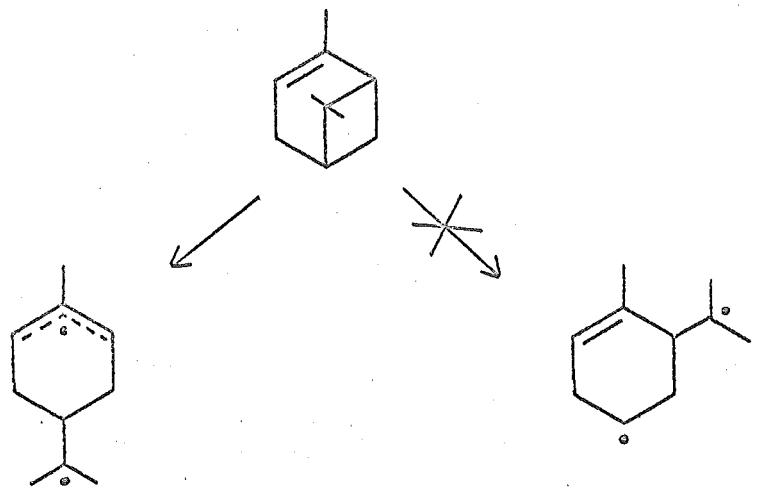


Fig. 32

In saturated pinanes, the energy difference between the two diradicals will not be so great, therefore cleavage of the four membered ring may not be so specific.

Alcohol substituents on saturated pinanes allow pathways to some new products. An unidentified methyl ketone from the pyrolysis of 10α- and 10β-pinan-2-ol (42, 43)[40] and an unknown aldehyde from the pyrolysis of isoverbanol (38)[38] have been reported.

The Pyrolysis of β-Nopinol (112)

Nopinol (112) was prepared[100] by reduction of nopinone (67) with lithium aluminium hydride. The reaction was carried out at low temperature (-70°), increasing the stereoselectivity of the reaction compared with reduction at room temperature.

Nopinol crystals were liquified and injected at 200 μl/min with a carrier gas flow of 15 ml/min, into the pyrolysis tube at 580-630°. In addition to thirteen low boiling compounds and five unknowns, seven major products were formed which were isolated by fractional distillation and preparative g.l.c. and identified as the aldehyde (113), the hydroxy-dienes (114) and (115), and the cyclopentanols (116, 117, 118 and 119). (Fig. 33 and Table 3)

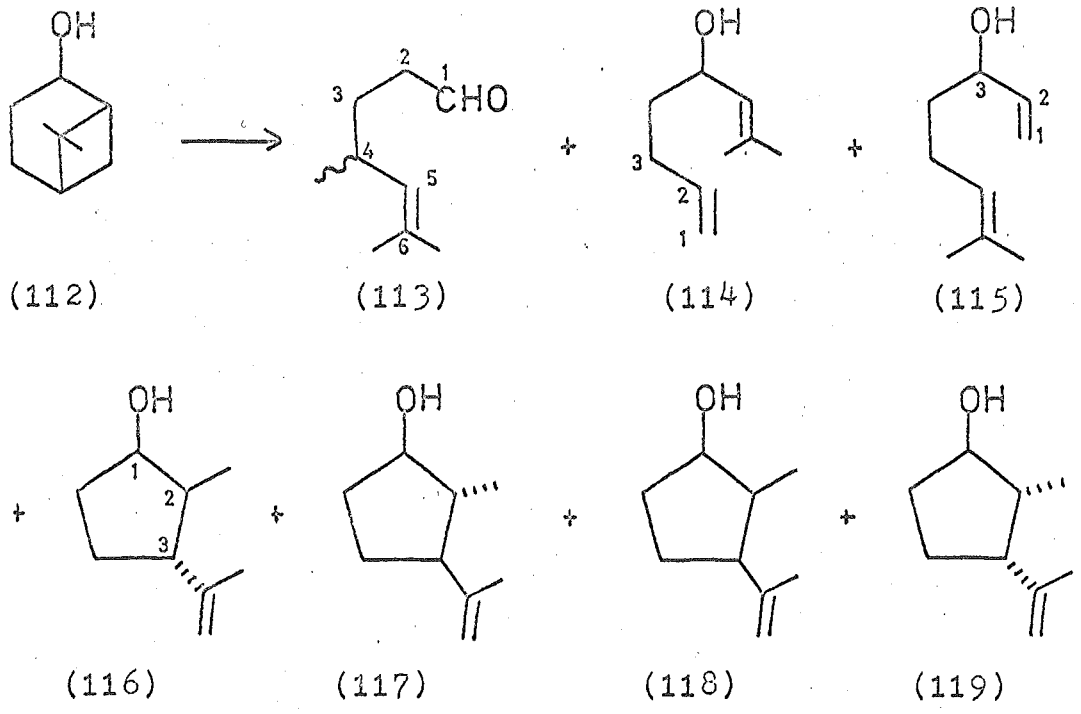


Fig. 33

The structure of the rearranged aldehyde (113) was elucidated from a consideration of its i.r. and n.m.r. spectra. The i.r. spectrum showed the presence of the aldehyde (ν_{max} 1725, 2730 cm^{-1}) and the trisubstituted double bond (ν_{max} 841 cm^{-1}). In the n.m.r. spectrum the aldehyde proton appeared as a triplet at δ 9.75, coupled (J 1.6 Hz) to the C2 methylene protons. The geminal methyl groups appeared as doublets at δ 1.58 and 1.67, coupled (J 1.3 Hz) to the C5 olefinic proton, itself coupled (J 9.5 Hz) to the C4 proton, resulting in its appearance as a doublet of multiplets at δ 4.85. The C4 methyl signal appeared as a doublet at δ 0.95, coupled (J 6.5 Hz) to the C4 proton.

The hydroxy-diene (114) showed bands in its i.r. spectrum characteristic of a trisubstituted double bond (ν_{max} 847 cm^{-1}) and a vinyl group (ν_{max} 911, 922 cm^{-1}). In the n.m.r. spectrum the C1 vinyl protons and the C6 olefinic proton were superimposed at δ 4.78-5.32. The C2 vinyl proton appeared as a multiplet at δ 5.87 due to extensive coupling with the C1 vinyl protons and the C3 methylene protons. The proton geminal to the hydroxyl group was coupled (J 9 Hz) to the C6 olefinic proton and (J=J' 6.5 Hz) to the C4 methylene protons resulting in its appearance as a sextet at δ 4.35. The geminal methyl groups appeared as doublets at δ 1.71 and 1.66, coupled (J 1.3 Hz) to the C6 olefinic proton. The assigned structure of hydroxy-diene (114) was further supported by

oxidation with manganese dioxide to the dienone (155), a compound also isolated from pyrolysis of nopinone (67). (see Fig. 48, p 95)

The i.r. spectrum of the isomeric hydroxy-diene (115) also showed the presence of a vinyl group and a trisubstituted double bond (ν_{max} 931, 991, 841 cm^{-1}). In the n.m.r. spectrum, the C1 vinyl protons and the C6 olefinic proton were again superimposed in a multiplet (δ 4.97-5.42). The geminal methyl groups appeared as broad singlets at δ 1.70 ($W_{h/2}$ 5.5 Hz) and δ 1.63 ($W_{h/2}$ 3.5 Hz), coupled (small J) to the C6 olefinic proton. The C2 vinyl proton appeared as an octet centred at δ 5.93, and coupled (J 17.3 Hz) to the trans C1 proton, the cis C1 proton (J 9.8 Hz) and to the proton geminal to the hydroxyl group (J 5.9 Hz). The CH-OH proton was also coupled (J 5.9 Hz) to the C4 methylene protons resulting in its appearance as a quartet at δ 4.12. The structure of hydroxy-diene (115) was further substantiated by its oxidation with manganese dioxide to dienone (68), a product also isolated from the pyrolysis of nopinone (67). (see Fig. 48, p 95)

The four isomeric cyclopentanols (116-119) were identified by a consideration of their i.r. and n.m.r. spectra, and by the results of further chemical transformations. All the isomers showed the presence of a vinylidene double bond by the band in their i.r. spectra at 888 cm^{-1} for (116) and (117) and 887 cm^{-1} for (118) and (119).

In the n.m.r. spectrum of cyclopentanol (116) the olefinic protons appeared as a multiplet ($W_{h/2}$ 3 Hz) at δ 4.73. The olefinic methyl group signal was split by small couplings (J 1 Hz) with the olefinic protons which resulted in its appearance as a triplet at δ 1.66. The C2 methyl appeared as a doublet at δ 0.95, coupled (J 6.5 Hz) to the C2 proton, while the C1 proton appeared as a triplet at δ 4.12, coupled (J 4 Hz) to the C2 proton and one of the C5 protons. Similarly, in cyclopentanol (117), the olefinic methyl appeared as a triplet at δ 1.68, coupled (J 1 Hz) to the olefinic protons, which appeared as a multiplet ($W_{h/2}$ 3 Hz) at δ 4.73. The C2 methyl appeared as a doublet at δ 0.99, coupled (J 6 Hz) to the C2 proton and the proton geminal to the hydroxyl group appeared as a quartet at δ 3.75, coupled (J 7 Hz) to the C2 proton and both of the C5 protons.

In the n.m.r. spectrum of cyclopentanol (118), the resonance of the olefinic protons appeared as two multiplets ($W_{h/2}$ 5 Hz) at δ 4.81 and 4.68 with small couplings to the olefinic methyl, itself a broad singlet ($W_{h/2}$ 3 Hz) at δ 1.72. The C2 methyl appeared as a doublet at δ 0.70 coupled (J 6.9 Hz) to the C2 proton and the C1 proton appeared as a broad multiplet (W 23 Hz) at δ 4.30. Similarly, in cyclopentanol (119) the olefinic protons appeared as multiplets ($W_{h/2}$ 5 Hz) at δ 4.81 and 4.68, coupled (small J) to the olefinic methyl, itself a broad singlet ($W_{h/2}$ 3.5 Hz) at δ 1.73. The C2 methyl appeared as a doublet at δ 0.64

coupled (J 6.9 Hz) to the C2 proton and the C1 proton appeared as a multiplet (W 13 Hz) at δ 3.98.

Oxidation of cyclopentanols (116) and (117) with chromic acid in ether[82] produced trans-cyclopentanone (71), a compound isolated from the pyrolysis of nopinone (67) (see Fig. 48), demonstrating the trans relationship of the isopropenyl and the methyl groups in cyclopentanols (116) and (117). Similar oxidations of cyclopentanols (118) and (119) produced cis-cyclopentanone (70), establishing the relative stereochemistry of the methyl and isopropenyl groups as cis. Lithium aluminium hydride reduction of trans-cyclopentanone (71) gave cyclopentanol (117), where the hydroxyl group is trans to the C2 methyl group. The identity of this reduction product follows from the known stereochemistry of $LiAlH_4$ reduction of 2-methylcyclopentanone.[101]* In cyclopentanol (119) the C3 proton (δ 2.75) is $\simeq$ 0.5 ppm downfield from the corresponding proton in cyclopentanol (118). This deshielding is a consequence of the 1,3 deshielding effect of the hydroxyl group in a syn relationship with the proton.[102]

As the temperature of the pyrolysis is increased, the yield of the hydroxy-dienes (114) and (115) decreases, while the yield of the aldehyde (113) and cyclopentanols (116-119) increases. In a separate experiment, hydroxy-diene (115) pyrolysed to give only the cyclopentanols (116-119). (Table 3)

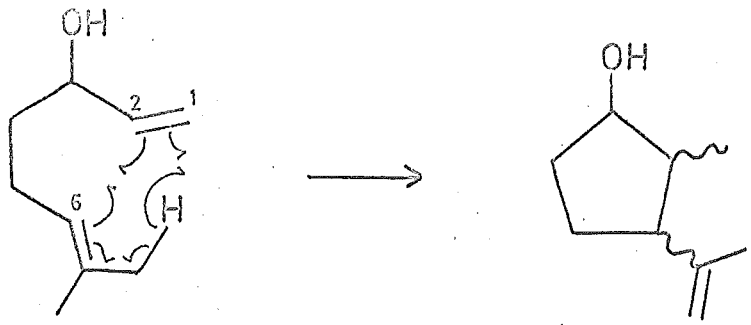
*$LiAlH_4$ reduction of 2-methylcyclopentanone gives trans-2-methyl-cyclopentanol (76%) and cis-2-methylcyclopentanol (24%).

Table 3

Yields (%) of Products from the Pyrolysis of Nopinol (112) and Hydroxy-diene (115)

	Nopinol		Hydroxy-diene (115)
	580°	630°	640°
aldehyde (113)	6	14	-
hydroxy-diene (114)	10	3	-
" " (115)	24	9	27
cyclopentanol (116)	6	7	8
" " (117)	7	10	9
" " (118)	8	14	16
" " (119)	12	20	29
nopinol (112)	4	-	-
others	23	23	11

When a mixture of hydroxy-dienes (114, 26%) and (115, 74%) was pyrolysed at 640°, the reaction products contained aldehyde (113, 9%). Therefore, it appears that the hydroxy-dienes (114) and (115) are the primary products of the reaction; dienol (114) reacting further to produce the aldehyde (113), and dienol (115) cyclising to produce the cyclopentanols (116-119). (Fig. 34)

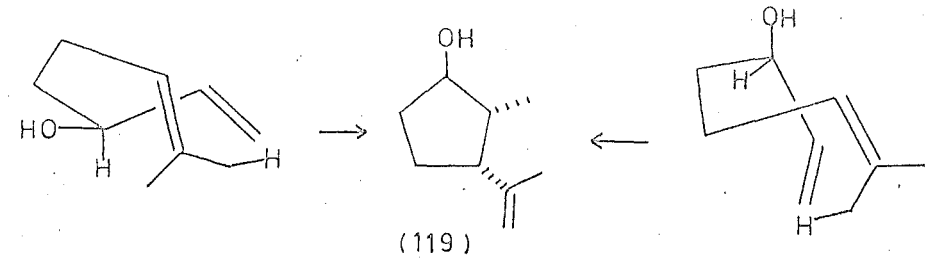


(115) (116-119)

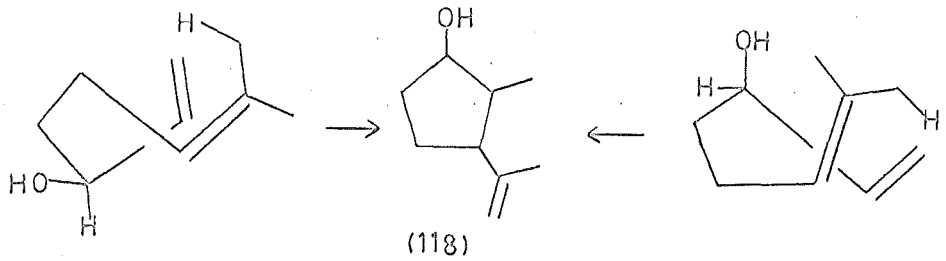
Fig. 34

This cyclisation is an intramolecular version of the ene synthesis.[103] If this reaction is considered in the light of orbital symmetry conservation rules, it is a $[\pi 2 + \pi 2 + \sigma 2]$ cycloaddition reaction and, as an all suprafacial cyclisation, i.e. $[\pi^2{}_s + \pi^2{}_s + \sigma^2{}_s]$ it is a thermally allowed process. In the transition state of the cyclisation of dienol (115), C1 must be close to the migrating hydrogen and C2 and C6 must be within bonding distance.

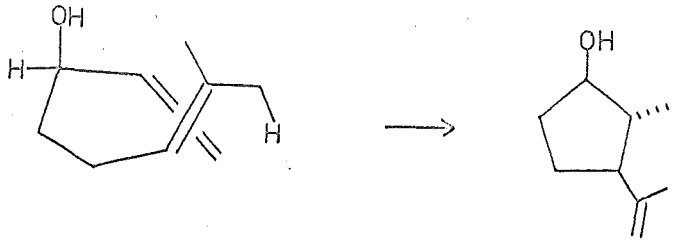
Using Dreiding models, six transition states leading to the four cyclopentanols are possible. (Fig. 36) From an examination of the models ~~of the models~~ of the transition states, the ease of formation of the cyclopentanols should follow the order (119) > (118) > (117) ≈ (116).



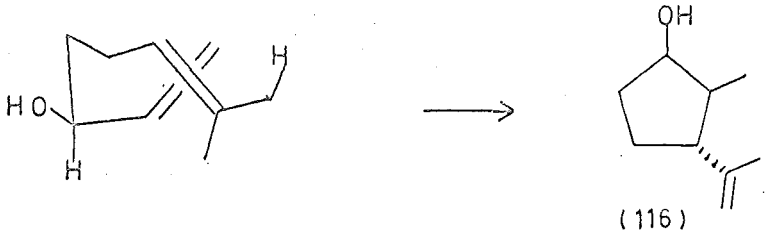
(119)



(118)



(117)



(116)

Fig. 36

When Ohloff and co-workers[48] cyclised R-linalool (44), the yield of the cyclopentanol corresponding to (119), (i.e. a methyl is substituted for the proton geminal to the hydroxyl group) was lower than the cyclopentanol corresponding to (118). As a methyl group has more steric bulk than a hydroxyl group, its steric interactions in the transition state are more severe. Therefore, substitution of a methyl for the proton geminal to the hydroxyl group in dienol (115) changes the relative energies of the transition states and hence the yields.

The rearranged aldehyde (113) is formed from further reaction of hydroxy-diene (114). In order to elucidate the mechanism of the aldehyde's formation, three specifically deuterated nopinols were prepared and pyrolysed. Reduction of nopinone (67) with lithium aluminium deuteride gave 2α-deuteronopinol (> 98% deuterium incorporation by n.m.r.) which on pyrolysis gave the aldehyde (113), without a resonance due to an aldehyde proton in its n.m.r. spectrum. Rapid stirring of nopinol (112) and D_2O exchanged the hydroxyl proton for deuterium (93% D by mass spectra). The aldehyde isolated (65% D by m.s.) from this deuterated nopinol was shown by n.m.r. to be deuterated at C7 and C8 by a 20% reduction in the C6 methyl and C7-H_3 signals. Also, the individual components of the C5 proton resonance were broadened by interaction with the deuterium in the geminal methyl groups. 3-Deuteronopinol was prepared by the base

catalysed deuterolysis of 2-acetoxy-10-norpin-2-ene (76). Pyrolysis of this deuterated nopinol (82% D by m.s.) gave 2-deutero-aldehyde (113, 82% D by m.s.). The aldehyde proton, a triplet in the n.m.r. spectrum of the parent aldehyde (113), appeared as a broad doublet due to the deuterium at C2, and also a reduction in the integral of the methylene region was observed. The results of these deuterium labelling experiments are summarised in Fig. 37.

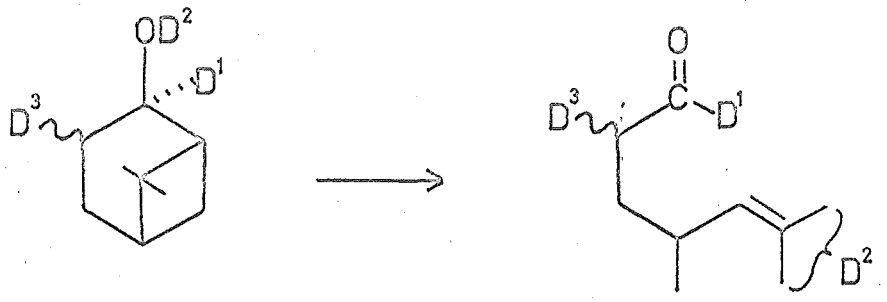
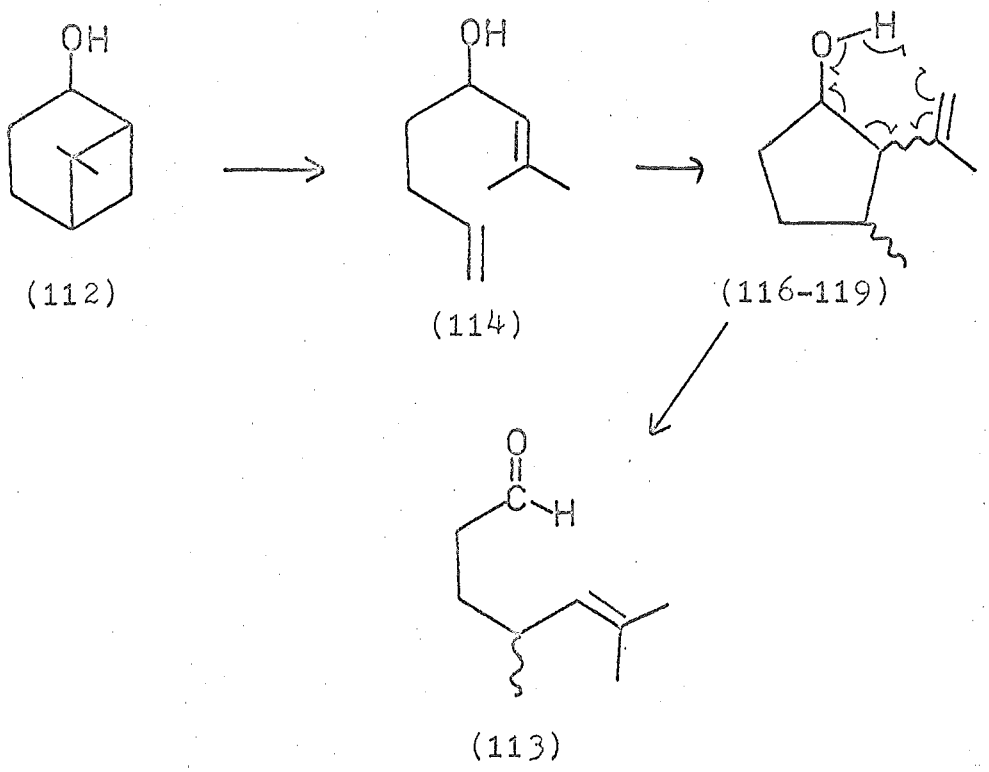


Fig. 37

A mechanism consistent with these results is shown in Fig. 38.



(112) (114) (116-119) (113)

Fig. 38

Although the hydroxyl deuterium migrates specifically to the unsaturated carbon in the cyclopentanol, it is scrambled between the geminal methyl groups in the aldehyde. This is a result of the double bond presenting both faces to the incoming deuterium atom as a consequence of the isopropenyl group rotating so that the double bond is either cis or trans to the C2 proton in the cyclopentanol. (Fig. 39)

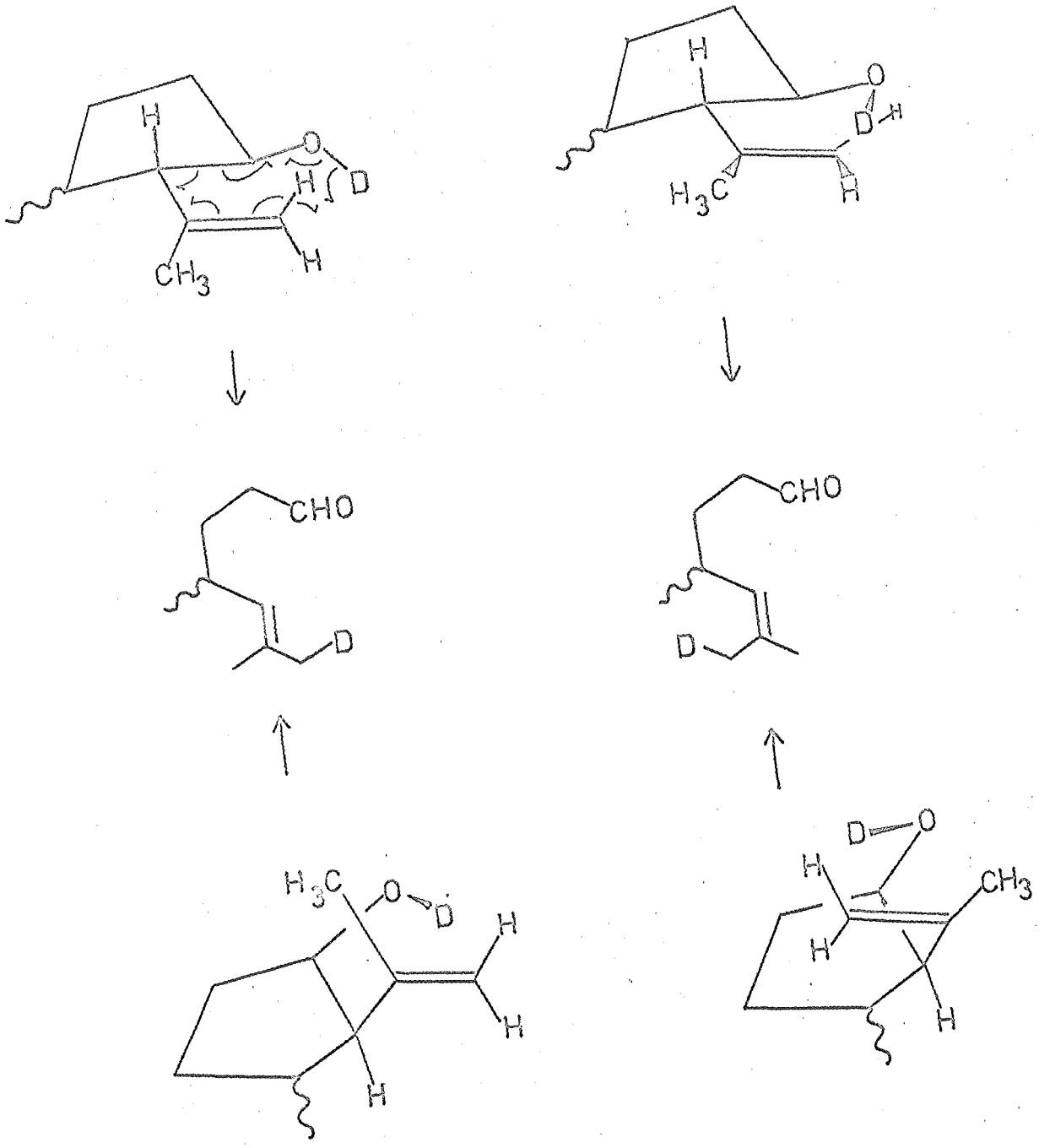


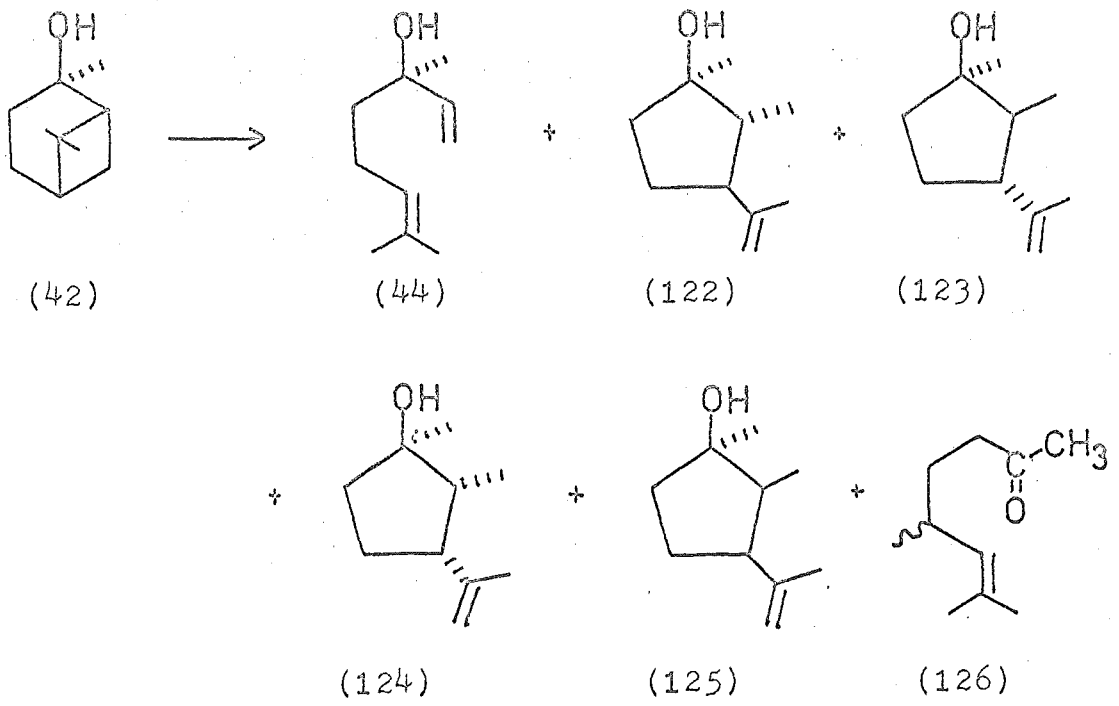
Fig. 39

The Pyrolysis of 10α- and 10β-Pinan-2-ol (42, 43)

Pyrolysis of the pinan-2-ols (42) and (43) has been reported[40] to give linalool (44), α-terpineol (46), a methyl ketone, and an unidentified alcohol. The reaction was therefore reinvestigated to determine the structure of the methyl ketone and to examine the formation of α-terpineol (46).

10α-Pinan-2-ol (42) was prepared by reaction of methyl magnesium iodide on nopinone (67). 10β-Pinan-2-ol (43) has been previously reported[104] as the lithium aluminium hydride reduction product of 2,10-epoxy-10β-pinane (120). A more convenient method[105] was found to be lithium/ethylamine reduction of α-pinene oxide (22) which gave, in addition to isopinocampheol (121, 69%), the required alcohol (43, 31%).

Crystals of 10α-pinan-2-ol (42) were melted and injected at 100 μl/min, with a carrier gas flow of 15 ml/min, into the pyrolysis tube at 580-610°. The crude product (≈ 85%) contained, in addition to eight low boiling compounds and four unknowns in low yield, six major products which were isolated by fractional distillation and preparative g.l.c. and identified as R-linalool (44), the cyclopentanols (122-125), and the methyl ketone (126). (Fig. 40, Table 4) Similar pyrolysis of 10β-pinan-2-ol (43) gave the same (but enantiomeric) major products. (Table 4) No α-terpineol was detected in contrast to the earlier report of Ohloff and Klein.[40]



(42) (44) (122) (123)

(124) (125) (126)

Fig. 40

Linalool (44) was identified by comparison with an authentic sample.

The n.m.r. spectrum of cyclopentanol (122) exhibited the tertiary methyl at δ 1.27 and the adjacent secondary methyl as a doublet at δ 0.87 (J 6.5 Hz). The olefinic methyl appeared at δ 1.67 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons which appeared at δ 4.73 ($W_{h/2}$ 2.5 Hz). Similarly, the cyclopentanol (123) exhibited the tertiary methyl at δ 1.15 and the C2 methyl at δ 0.87 (J 6.5 Hz). The olefinic methyl appeared at δ 1.72 ($W_{h/2}$ 3 Hz) coupled (small J) to the olefinic protons which appeared at δ 4.71 ($W_{h/2}$ 3 Hz).

The cis cyclopentanol (124) exhibited n.m.r. signals at δ 1.28, due to the tertiary methyl, at δ 0.61 (J 7.4 Hz) due to the C2 methyl and at δ 3.07 (W 21 Hz) due to the C3 proton. The olefinic methyl appeared at δ 1.72 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons which appeared at δ 4.08 ($W_{h/2}$ 5 Hz) and δ 4.82 ($W_{h/2}$ 4.5 Hz). Similarly, the cis cyclopentanol (125) exhibited the tertiary methyl at δ 0.78 (J 7.4 Hz) and the C3 proton at δ 2.56 (W 19 Hz). The olefinic methyl appeared at δ 1.73 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons, which appeared at δ 4.72 ($W_{h/2}$ 4 Hz) and δ 4.85 ($W_{h/2}$ 4.5 Hz).

Comparison of the n.m.r. spectra of cyclopentanols (124) and (125) revealed that the C2 methyl signal occurred at lower field (δ 0.78 for (125) compared with δ 0.61 for (128)) for isomer (125), consistent with the cis hydroxyl-C2 methyl stereochemistry. Also, the C3 proton occurred at lower field (δ 3.07 for (124) compared with δ 2.56 for (125)) for isomer (124), consistent with the syn hydroxyl-C3 proton stereochemistry[102].

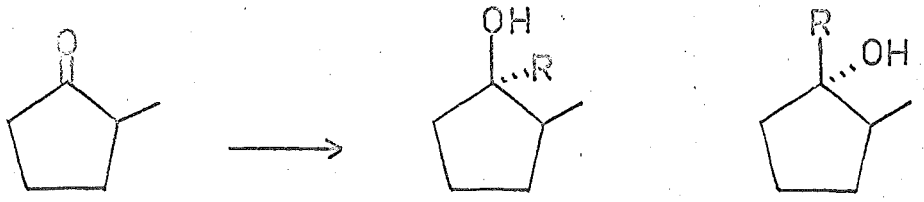
The four cyclopentanols (122-125) were also independently synthesised by the reaction of methyl magnesium iodide on the cyclopentanones (70) and (71). The cis-cyclopentanone (70) gave, on grignard reduction, a mixture (4:96) of cyclopentanols (124) and (125) respectively. The assignment of the C1 stereochemistry from the grignard reaction is based[106] on the preference for the grignard reagent to attack trans to

an α-methyl in a cyclopentanone.* Reaction of the trans-cyclopentanone (71) with methyl magnesium iodide gave a mixture (2:3) of the cyclopentanols (122) and (123) respectively.

The structure of the methyl ketone (126) was assigned by consideration of its i.r. spectrum (ν_{max} 847, 1717 cm^{-1}) and its n.m.r. spectrum. The acyl methyl signal appeared at δ 2.10 as a sharp singlet and the C5 methyl as a doublet at δ 0.93, coupled (J 6.4 Hz) to the C5 proton. The geminal methyl groups appeared as doublets at δ 1.58 (J 1.4 Hz) and δ 1.68 (J 1.2 Hz), coupled to the C6 olefinic proton, itself coupled (J 9 Hz) to the C5 proton resulting in its appearance as a doublet of multiplets at δ 4.84.

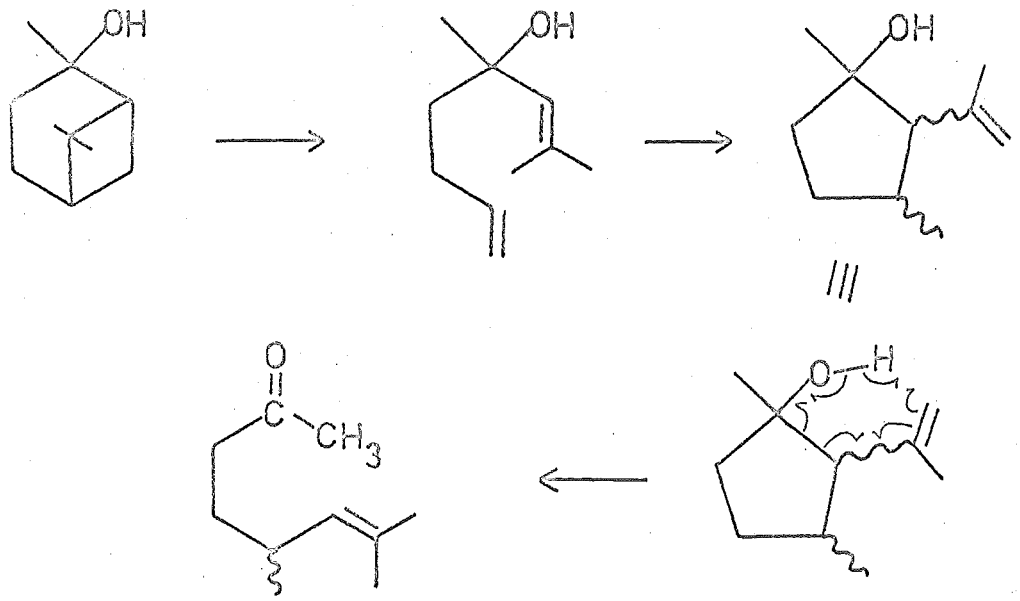
The formation of methyl ketone (126) can be rationalized by employing a mechanism analogous to the one proposed for the formation of aldehyde (113) from the pyrolysis of nopinol (112).

*



EtMgBr	75%	25%
CH_2=CH-MgCl	90%	10%
CH_3Li	70%	30%

This requires the cleavage of the 5,6 bond in the pinan-2-ol and subsequent cyclisation of the hydroxy-diene formed. (Fig.41)



(126)

Fig. 41

Ohloff and Klein[40] assigned to the compound of m.p. 38° the structure of α-terpineol (46, m.p. 36.9°[107]). As there was no trace of α-terpineol it appears that the compound Ohloff and Klein isolated was the cyclopentanol (125, m.p. 38.5-39.5°).

When the temperature is increased in the pyrolysis of 10α-pinan-α-ol (42), an increase in yield of the cyclopentanols (122-125) occurrs with a corresponding decrease in the yield of linalool (44), indicating that the intramolecular ene reaction of linalool is responsible for the formation of the cyclopentanols (122-125). (Table 4)

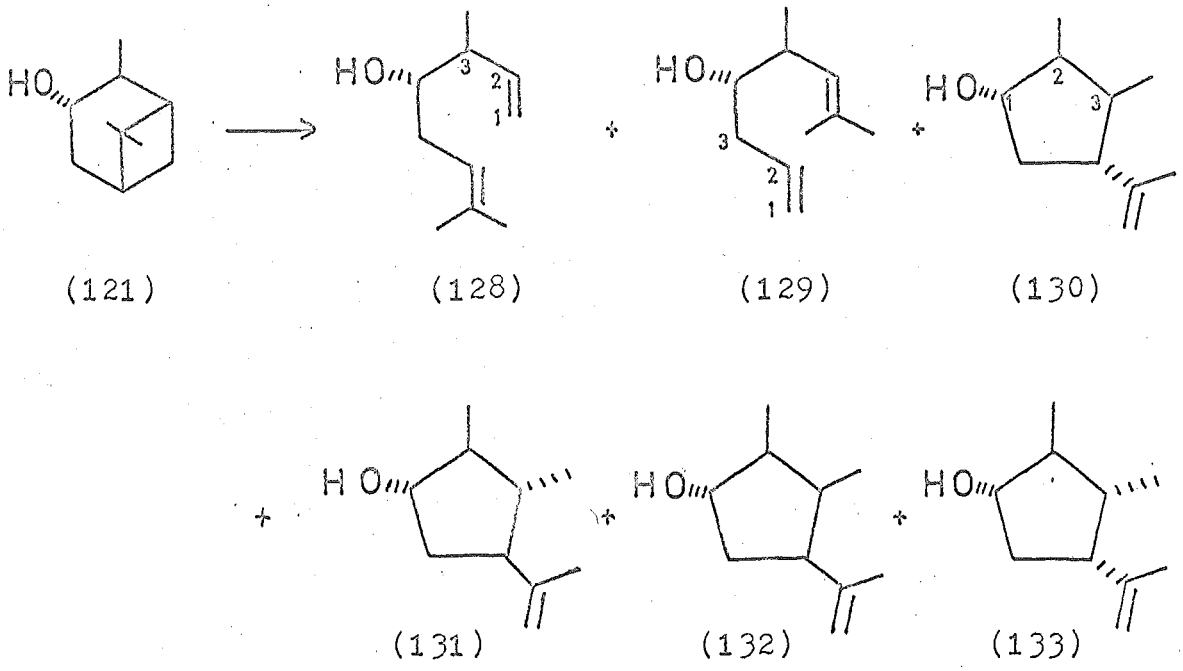
Table 4

Yields (%) of Products from Pyrolysis of 10α-Pinan-2-ol (42), 10β-Pinan-2-ol (43) and R-Linalool (44)

	10α-pinan-2-ol		R-linalool	10β-Pinan-2-ol (43)
Product	580°	610°	610°	580°
linalool (44)	44	17	22	18 (S-linalool)
cyclopentanol (122)	2	4	5	4
(123)	3.5	8	8.5	6
(124)	9	16	20	17
(125)	19	27	31	30
ketone (126)	4.5	10	-	6
others	18	18	13.5	19

The Pyrolysis of Isopinocampheol (121)

Isopinocampheol was prepared[108] by hydroboration of α-pinene, followed by hydrogen peroxide oxidation. Molten isopinocampheol was pyrolysed at 520-600°, with a carrier gas flow of 20 ml/min, at a rate of 200 μl/min. The crude product (≈ 90%) contained a large number of low boiling compounds, starting material, and six major products, which were isolated by fractional distillation and preparative g.l.c. The compounds were identified as the hydroxy-dienes (128) and (129), and the isomeric cyclopentanols (130-133). (Fig. 42, Table 5)



(121) (128) (129) (130) (131) (132) (133)

Fig. 42

The i.r. spectrum of the hydroxy-diene (128) had bands which indicated the presence of a trisubstituted double bond (ν_{max} 834 cm^{-1}) and a vinyl group (ν_{max} 913, 994 cm^{-1}). The n.m.r. spectrum exhibited the C3 methyl signal as a

doublet at δ 1.05, coupled (J 6.8 Hz) to the C3 proton. The geminal methyl group trans to the C6 proton appeared as a singlet at δ 1.64 while the cis geminal methyl group appeared as a doublet at δ 1.73, coupled (J 1.3 Hz) to the C6 olefinic proton, which appeared in a multiplet with the C1 protons (δ 4.88-5.39). The C2 vinyl proton appeared as an octet at δ 5.87, coupled (J 18 Hz) to the trans C1 proton, and (J 9.5, 7.2 Hz) to the cis C1 proton and the C3 proton. The proton geminal to the hydroxyl group appeared as a sextet at δ 3.49, coupled (J 7.5 Hz) to the C3 proton and (J 5.5 Hz) to the C5 methylene protons.

The isomeric hydroxy-diene (129) showed similar structural features in its i.r. spectrum (ν_{max} 843, 914, 987 cm^{-1}) to dienol (128). The n.m.r. spectrum exhibited doublets due to the C5 methyl at δ 1.00, coupled (J 6.5 Hz) to the C5 proton, and due to the geminal methyl groups at δ 1.64 and 1.72, both coupled (J 1.4 Hz) to the C6 olefinic proton. The C1 vinyl protons appeared as multiplets at δ 5.08 ($W_{h/2}$ 4 Hz) and δ 5.23 ($W_{h/2}$ 4.5 Hz). The C2 vinyl proton appeared as a broad multiplet (δ 5.55-6.25) due to extensive coupling with the C1 and C3 protons. The C6 olefinic proton appeared as a doublet of multiplets at δ 4.97, due to coupling (J 5 Hz) with the C5 proton and small couplings with the geminal methyl groups. The proton geminal to the hydroxyl group appeared as an octet, coupled (J 8.9, 6.9, 4 Hz) to the C5 proton and the C3 methylene protons.

In the n.m.r. spectrum of cyclopentanol (130) the C2 and C3 methyls, which appeared as doublets at δ 0.97 (J 7 Hz) and δ 1.05 (J 7 Hz), were not distinguishable. The olefinic methyl appeared as a triplet at δ 1.65 with small couplings (J 1 Hz) to the olefinic protons, which appeared as a multiplet ($W_{h/2}$ 2.5 Hz) at δ 4.73. The proton geminal to the hydroxyl group appeared as a quartet of multiplets at δ 3.78, coupled (J 6 Hz) to the C2 proton and the C5 methylene protons, with small couplings broadening the signals. Similarly, cyclopentanol (131) exhibited n.m.r. signals due to the C2 and C3 methyls at δ 0.83 (J 6.4 Hz) and δ 1.02 (J 5.8 Hz) which could not be assigned. The olefinic methyl appeared as a broad singlet at δ 1.70 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons which appeared at δ 4.65 ($W_{h/2}$ 4 Hz) and δ 4.92 ($W_{h/2}$ 4 Hz). The proton geminal to the hydroxyl group appeared as a quartet at δ 3.72, coupled (J 7.6 Hz) to the C2 proton and the C5 methylene protons.

The cis-cyclopentanol (132) exhibited n.m.r. signals due to the C2 and C3 methyls at δ 0.54 (J 6.8 Hz) and δ 0.98 (J 6.5 Hz). The olefinic methyl appeared at δ 1.73 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons at δ 4.75 ($W_{h/2}$ 4 Hz). The C1 proton appeared at δ 3.33 as a multiplet (W 18 Hz). The major cyclopentanol product (133), exhibited its C2 and C3 methyl signals as doublets at δ 0.83 (J 6.3 Hz) and δ 1.07 (J 5.5 Hz). The olefinic methyl appeared at δ 1.70 ($W_{h/2}$ 3 Hz) with small couplings to the olefinic protons at δ 4.71 ($W_{h/2}$ 4 Hz) and δ 4.82 ($W_{h/2}$ 4.5 Hz). The proton

Table 5

Yield (%) of Products from the Pyrolysis of Isopinocampheol(121) and Hydroxy-diene (128)

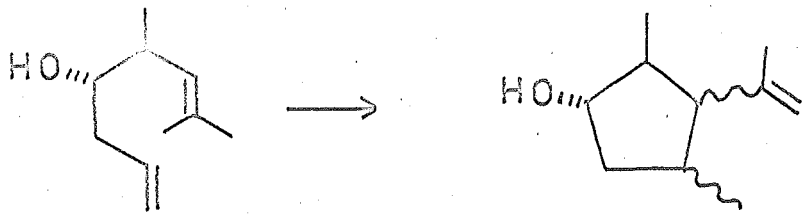
	Isopinocampheol			Hydroxy-diene (128)
Products	520°	580°	600°	590°
dienals				
(128)	28	10	3	13
(129)	3	2	trace	-
cyclopentanols				
(130)	trace	3	4	4
(131)	trace	5	6	4
(132)	5.5	15	17	15
(133)	8	24	26	32
isopinocampheol	48	13	-	-
low boilers	5	18	33	32
others	2.5	10	11	-

geminal to the hydroxyl group appeared as a sextet at δ 3.73 coupled (J 8.8 Hz) to the C2 proton and (J 6.6 Hz) to the C5 methylene protons.

The four cyclopentanols (130-133) were shown to arise from cyclisation of hydroxy-diene (128) by a separate

experiment. (Table 5) The stereochemistry of the cyclopentanols (130-133) was assigned by a comparison of their relative yields with the relative yields of the cyclisation products of the 1,6-octadienes (44) and (115). (see p 73, 61) The assigned stereochemistry of each alcohol was confirmed by chromic acid/ether oxidation to the corresponding cyclopentanone (150-153) formed in the pyrolysis of isopinocamphone (134). (see p 89, Fig. 46)

The hydroxyl group at the C3 position on the saturated pinane ring has had no effect on the pyrolysis reaction at all. The cyclopentanols which have been observed to rearrange, have had the alcohol function adjacent to the isopropenyl group. (see p 66) Neither the cyclopentanols (130-133) isolated, nor the cyclopentanols (of the type in Fig. 43, which were not isolated) arising from the presumed cyclisation of hydroxy-diene (129), have the necessary juxtaposition of groups for aldehyde formation.



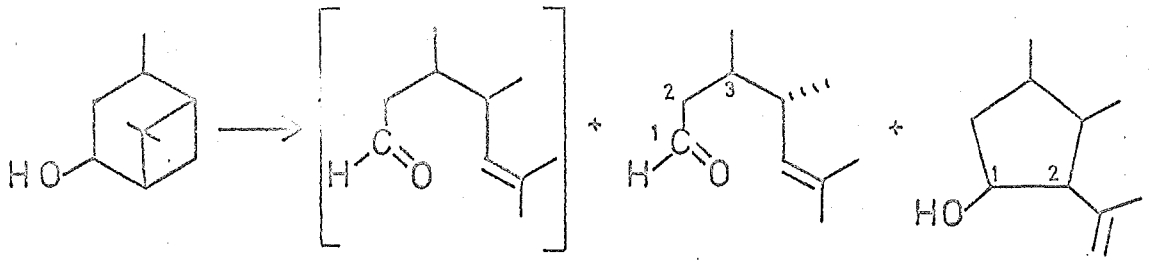
(129)

Fig. 43

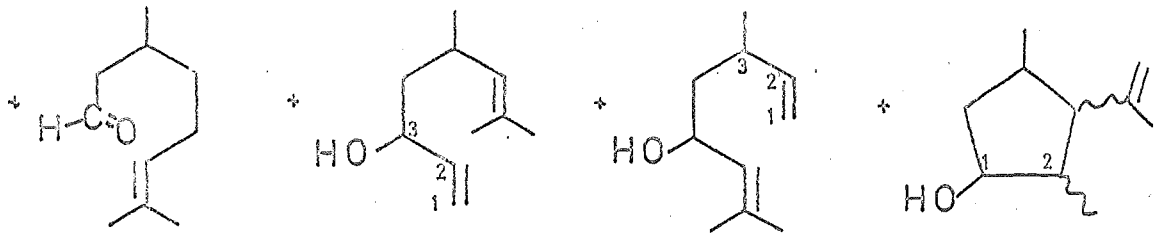
The Pyrolysis of Neo-isoverbanol (135)

Isoverbanol (38) has been pyrolysed by an industrial chemist[38] who identified only the major product of the reaction as the 1,6-octadiene (39). Also isolated, but not identified, was an acyclic aldehyde which was formed in high yield (19%). As isoverbanol (38) can be considered a derivative of nopinol (112), it was thought that the unidentified aldehyde may have been formed in a similar manner to the aldehyde (113). The acyclic aldehyde was later identified[39] as 3,4,6-trimethyl-5-heptenal (40), but its stereochemistry was undefined and its mode of formation unknown.

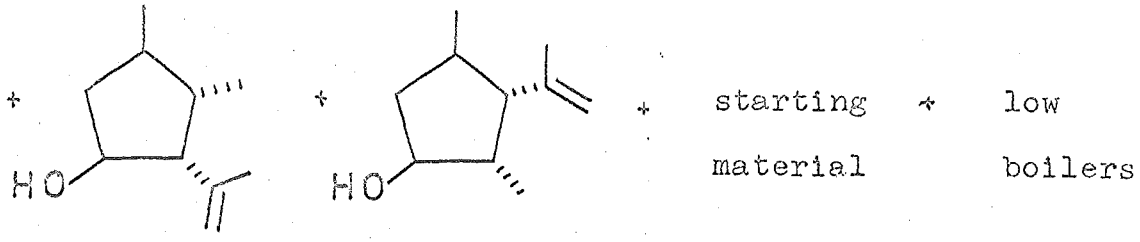
trans-Verbenol (25), prepared by auto-oxidation of α-pinene or lead tetraacetate oxidation of α-pinene, was hydrogenated over platinum dioxide to give a mixture of isoverbanol (38, 91%) and verbanol (136, 9%). As this mixture could not be separated by fractional distillation, it is thought that the previous work (where the same preparation was used) was done using impure isoverbanol. Neo-isoverbanol (135) can be obtained[109] pure from hydrogenation of verbenone (33) over PtO_2 and, as the stereochemistry of the alcohol group does not affect the structure of the aldehyde, the reaction was reinvestigated using this alternative compound.



(135)		(137)	(138)	(139)
	570°	trace	10.5	2
	600°	0.5	18	3



(58)	(141)	(142)	(145)
2.5	7	29.5	8
3	6	21	9



(143)	(144)		
6	6.5	18	9%
7	10	5	17.5%

Fig. 44

Neo-isoverbanol (135) was pyrolysed at 570-600°, at a rate of 300 μl/min, to give a crude product (≈ 90%) which contained, among starting material and low boiling compounds, seven major products, which were isolated by fractional distillation and preparative g.l.c. The compounds were identified from a consideration of their i.r. and n.m.r. spectra as the acyclic aldehyde (138), citronellal (58), the hydroxy-dienes (141) and (142), and the cyclopentanols (139, 143 and 144). (Fig. 44)

The i.r. spectrum of the aldehyde (138) exhibited bands indicating the presence of an aldehyde (ν_{max} 1728, 2720 cm^{-1}) and a trisubstituted double bond (ν_{max} 852 cm^{-1}). The aldehyde proton appeared in the n.m.r. spectrum as a triplet at δ 9.72, coupled (J 1.4 Hz) to the C2 methylene protons. The C3 and C4 methyls appeared as a doublet at δ 0.95, coupled (J 6 Hz) to the C3 and C4 protons respectively. The geminal methyl groups appeared as doublets at δ 1.59 and 1.66, with small couplings (J 1.3 Hz) to the C5 olefinic proton, itself coupled (J 9.5 Hz) to the C4 proton, resulting in its appearance at δ 4.93 as a doublet of multiplets. The relative stereochemistry of the C3 and C4 methyls was established by a separate experiment. (see p 86)

The hydroxy-diene (141) showed bands in its i.r. spectrum which indicated the presence of a vinyl group (ν_{max} 917, 988 cm^{-1}) and a trisubstituted double bond (ν_{max} 838 cm^{-1}). In its n.m.r spectrum, the C1 and C6 protons appeared as a

multplet (δ 4.73-5.38), as did the proton geminal to the hydroxyl group (δ 4.07, W 23 Hz), and the C5 proton (δ 2.63, W 34 Hz). The geminal methyl group trans to the C6 proton appeared as a doublet at δ 1.63 (J 1.1 Hz) while the cis geminal methyl group appeared at δ 1.68, and had a larger coupling (J 1.4 Hz) with the C6 proton. The C5 methyl appeared as a doublet at δ 0.93, coupled (J 6.5 Hz) to the C5 proton. The C2 vinyl proton appeared as an octet at δ 5.88, coupled (J 17.3 Hz) to the trans C1 proton and (J 5.4, 9.8 Hz) to the cis C1 proton and the C3 proton.

The isomeric hydroxy-diene (142) had very similar spectra to dienol (141). The i.r. spectrum showed the presence of the vinyl group (ν_{max} 912, 993 cm^{-1}) and the trisubstituted double bond (ν_{max} 833 cm^{-1}). In the n.m.r. spectrum the C1 vinyl protons and the C6 proton appeared as a multiplet (δ 4.81-5.32), as did the C3 proton (δ 2.32, W 34 Hz), but the proton geminal to the hydroxyl group appeared as an octet at δ 4.39, coupled (J 8.8, 5.9 and 7.5 Hz) to the C6 olefinic proton and the C4 methylene protons. The geminal methyl groups appeared as doublets at δ 1.65 and 1.69, both coupled (J 1.5 Hz) to the C6 olefinic proton. The C3 methyl appeared as a doublet at δ 1.00, coupled (J 6.5 Hz) to the C3 proton. The C2 vinyl proton appeared as an octet at δ 5.74, coupled (J 17.4 Hz) to the trans C1 proton, to the cis C1 proton (J 9.6 Hz), and to the C3 proton (J 7.2 Hz). This structural assignment was confirmed by chromic acid/ether oxidation of

the dienol (142) to the dienone (156), a product isolated from the pyrolysis of cis- verbanone (36). (see Fig. 49, p 100)

The n.m.r. spectrum of cyclopentanol (139) exhibited doublets at δ 0.93 (J 5 Hz) and δ 1.07 (J 4 Hz) due to the C3 and C4 methyls which were indistinguishable. The olefinic methyl appeared at δ 1.79 as a doublet, coupled (J 1.3 Hz) to the cis olefinic proton, which appeared as a quartet at δ 5.09 (J 1.5 Hz). The trans olefinic proton appeared as a singlet at δ 4.79 ($W_{h/2}$ 4 Hz), and the proton geminal to the hydroxyl group appeared as a multiplet (W 16 Hz) at δ 4.13.

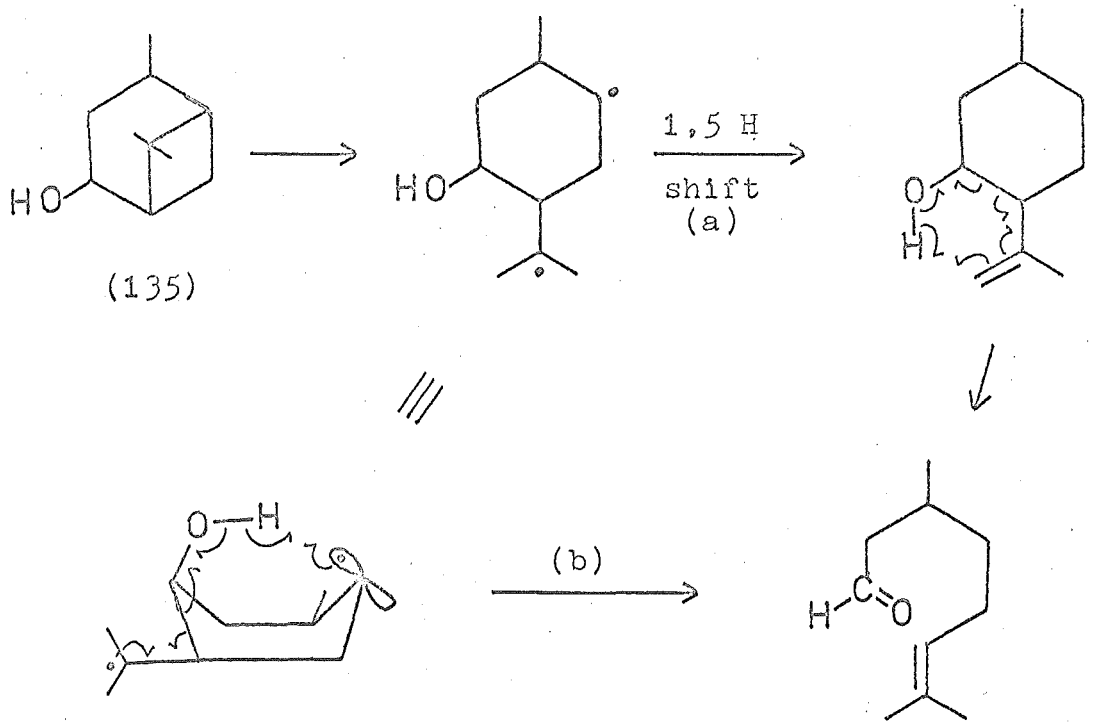
The isomeric cyclopentanol (143) exhibited doublets at δ 0.74 (J 6.7 Hz) and δ 1.07 (J 5.5 Hz) due to the indistinguishable C3 and C4 methyls. The olefinic methyl appeared as a doublet at δ 1.73, coupled (J 1.2 Hz) to the cis olefinic proton, which appeared as a quartet at δ 4.93 (J 1.4 Hz). The trans olefinic proton appeared as a singlet at δ 4.73 ($W_{h/2}$ 3.5 Hz). The proton geminal to the hydroxyl group appeared as a sextet at δ 4.22, coupled (J 7.9, 7.9 and 6.7 Hz) to the C2 proton and the C5 methylene protons. Only two (139 and 143) of the four possible cyclopentanols from hydroxy-diene (142) were formed in isolatable yield. The isopropenyl groups and the adjacent C3 methyls were assigned the cis orientation on the basis of the known preferred modes of cyclisation of 1,6-octadienes. (see p 62)

Similarly, as cyclopentanol (143) is formed in greater yield than cyclopentanol (139), the C3 methyl must be trans to the C4 methyl in the former compound. The structure of cyclopentanol (143) was confirmed by chromic acid/ether oxidation to cyclopentanone (158), a compound isolated from the pyrolysis of cis-verbanone (36). (see p 100)

The n.m.r. spectrum of cyclopentanol (144) exhibited doublets due to the indistinguishable C2 and C4 methyls at δ 0.70 (J 6.7 Hz) and δ 1.03 (J 5.5 Hz). The olefinic methyl appeared as a doublet at δ 1.71, coupled (J 1 Hz) to the cis olefinic proton. The olefinic protons, which could not be distinguished, appeared at δ 4.66 ($W_{h/2}$ 4 Hz) and δ 4.88 ($W_{h/2}$ 4.5 Hz). The proton geminal to the hydroxyl group appeared as a multiplet (W 14 Hz) at δ 3.90. The structure of cyclopentanol (144) was confirmed by chromic acid/ether oxidation to cyclopentanone (159), a product isolated from the pyrolysis of cis-verbanone (36). (see p 100)

The isomeric cyclopentanols (145) could not be obtained pure, but an n.m.r. spectrum of the mixture exhibited signals due to methyls coupled to one proton, methyls on double bonds, geminal olefinic protons, and protons geminal to hydroxyl groups.

The spectra of citronellal (58) were identical to those of an authentic sample, prepared by the chromic acid oxidation of commercial citronellol (57). There are two reasonable mechanisms for the formation of citronellal (58). (Fig. 45)



(135)

Fig. 45

(58)

Mechanism (a) implies that in the pyrolysis of every saturated pinane there should be formed an isopropenylcyclohexane derivative; a process which has not been observed. Mechanism (b) operates only because the hydroxyl group is adjacent to the isopropyl radical group.

Pyroysis of hydroxy-diene (141) at 600° gave the cyclopentanone (144) in high yield (45%), along with the mixture of isomeric cyclopentanols (145, 19%), low boiling compounds (18%) and starting material (18%). Pyrolysis of hydroxy-diene (142) at 600° gave the postulated aldehyde (137, 1%), aldehyde (138, 43%), the cyclopentanols (139, 8%; 143, 6%) along with low boiling compounds (28%) and starting material (14%). Pyrolysis of cyclopentanol (143) at 600° gave

aldehyde (138, 40.5%) along with low boiling compounds (20.5%) and starting material (39%). The stereochemistry of the adjacent methyl groups in the aldehyde (138) is trans as a consequence of the stereochemistry of the C3 and C4 methyls in its precursor, cyclopentanol (143).

The formation of aldehyde (138) from cyclopentanol (143), and its formation from hydroxy-diene (142), confirm the mechanism postulated for the formation of carbonyl compounds from the pyrolysis of pinanols with an alcohol adjacent to a ring junction. (see p 66)

The formation of the isomeric aldehyde (137) was indicated by the presence of a g.l.c. peak with a retention time close to that of aldehyde (138), in the pyrolysis products of neo-isoverbanol. The same compound is formed in 1% yield from the pyrolysis of hydroxy-diene (142). Pyrolysis at 600° of a mixture (83:17) of aldehyde (138) and cyclopentanol (139), gave a mixture (5.5:83:11.5) of the postulated aldehyde (137), aldehyde (138) and cyclopentanol (139).

In all of the pinanols studied, cleavage of both the 1,6 and 5,6 bonds has occurred on pyrolysis. This process has not previously been observed in the pyrolysis of pinanes, presumably due to the difficulty in separating the isomeric

did not report the isolation of 1,6-octadiene (146) (or its cyclisation products) which would be formed by cleavage of the 5,6 bond in cis-pinane (47).

Chapter 4

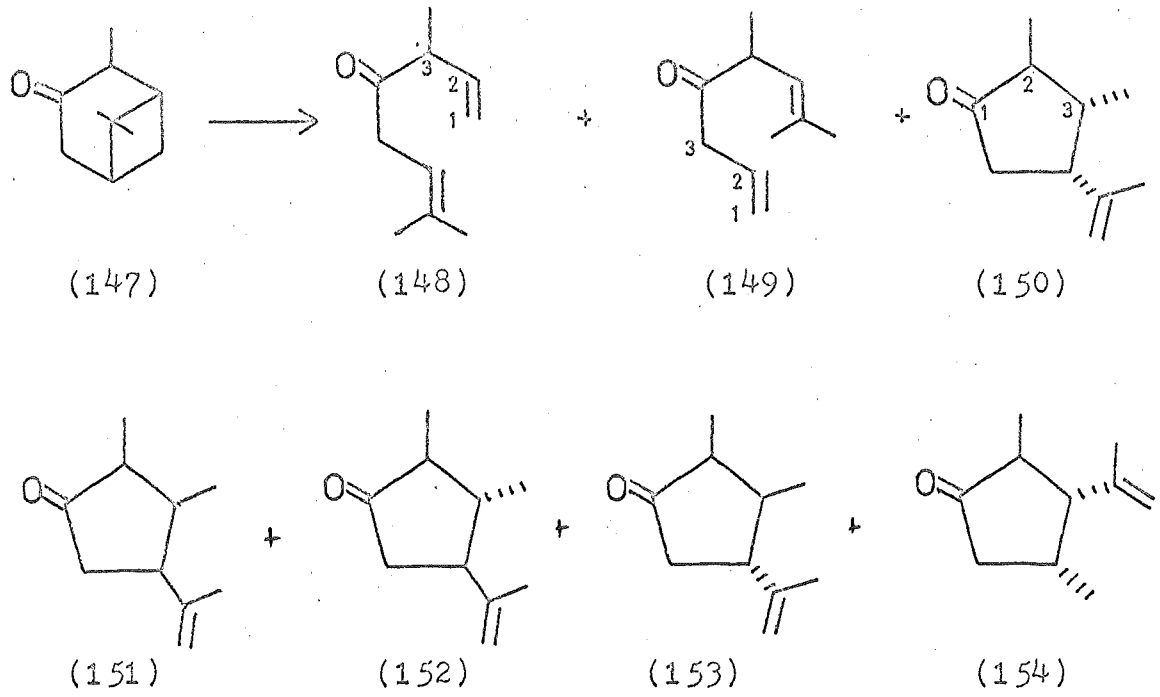
THE PYROLYSIS OF PINANONES

The compounds in this class of pinane studied were isopinocamphone (147), cis-verbanone (36) and nopinone (67). A carbonyl group substituted on the pinane ring could be expected to exert a directing influence on the cleavage of the four membered ring if it is adjacent to a ring junction.

The Pyrolysis of Isopinocamphone (147)

The carbonyl group in isopinocamphone is at the C3 position, i.e. midway between the two ring junctions and therefore cannot influence the relative preference for 1,6 or 5,6 bond cleavage.

Isopinocamphone (147) was prepared by Jones oxidation[108] of isopinocampheol (121) and was pyrolysed at 590-650° at a rate of 300 μl/min with a carrier gas flow of 20 ml/min. The crude product ($\approx$ 90%) contained low boiling compounds, two unidentified compounds in low yield and seven major products which were isolated by fractional distillation and preparative g.l.c. and identified as the dienones (148) and (149), the isomeric cyclopentanones (150-153) and the cyclopentanone (154). (Fig. 46, Table 7)



(147) (148) (149) (150)

(151) (152) (153) (154)

Fig. 46

The i.r. spectrum of dienone (148) had bands which indicated the presence of a vinyl group (ν_{max} 921, 996 cm^{-1}), a trisubstituted double bond (ν_{max} 846 cm^{-1}) and a non-conjugated carbonyl group (ν_{max} 1718 cm^{-1}). In the n.m.r. spectrum the geminal vinyl protons and the C6 olefinic proton appeared as a multiplet (δ 4.97-5.37). The C2 vinyl proton appeared as a septet at δ 5.87, coupled (J 17.5 Hz) to the trans C1 proton, to the cis C1 proton (J 9 Hz) and to the C3 proton (J 8 Hz). The C3 proton was also coupled (J 6.9 Hz) to the C3 methyl, resulting in its appearance as a quintet (three peaks superimposed) at δ 3.27. The C3 methyl appeared as a doublet at δ 1.16 (J 6.9 Hz). The C5 methylene protons appeared as a doublet of multiplets at δ 3.20, the large coupling (J 7 Hz) being with the C6 olefinic proton. The

geminal methyl group cis to the C6 proton appeared as a doublet at δ 1.73 (J 1 Hz) while the trans geminal methyl group appeared as a singlet at δ 1.62 ($W_{h/2}$ 3 Hz).

The i.r. spectrum of the isomeric dienone (149) showed bands due to a vinyl group, a trisubstituted double bond and a non-conjugated carbonyl group (ν_{max} 918, 993, 844, 1719 cm^{-1}). The n.m.r. spectrum exhibited the C1 vinyl protons (δ 4.98-5.28), and the C5 proton (δ 3.45, W $\approx$ 25 Hz), as multiplets. The C2 vinyl proton also appeared as a multiplet (δ 5.58-6.30) due to extensive coupling with the C1 and the C3 protons. The C3 methylene protons appeared as a doublet of multiplets at δ 3.18 due to coupling (J 6.6 Hz) with the C2 proton and another small coupling (J 1.25 Hz). The C5 methyl appeared as a doublet (δ 1.10, J 6.8 Hz) as did the geminal methyl groups (δ 1.69 and 1.72), which were both coupled (J 1.5 Hz) to the C6 olefinic proton, itself coupled (J 8 Hz) to the C5 proton, resulting in its appearance as a doublet of multiplets at δ 5.00.

The four isomeric cyclopentanones (150-153) all had an i.r. band characteristic of a carbonyl group on a five membered ring (ν_{max} 1743, 1742, 1745, 1743 respectively), and all had similar n.m.r. spectra. (Table 6)

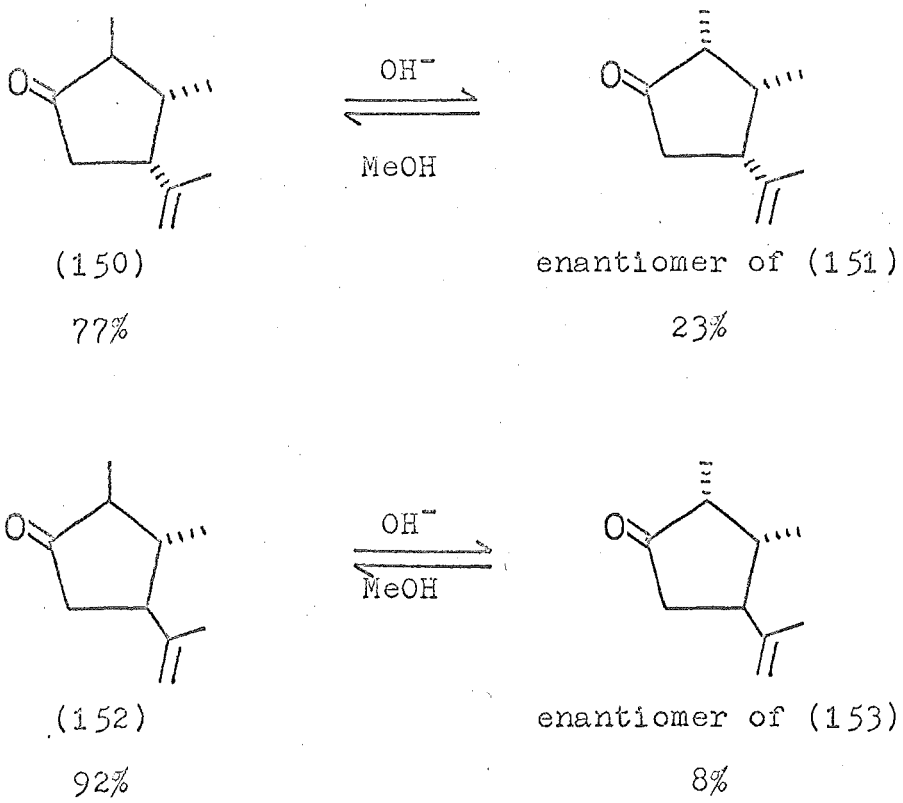
The stereochemistry of the cyclopentanones (150-153) was deduced from the relative yields of the compounds (Table 7) using the results of 1,6-octadiene cyclisations

Table 6

NMR Data for Cyclopentanones (150-153)

	C2 and C3 methyls	olefinic methyls	olefinic protons
(150)	0.95 (J 6.5 Hz) 1.09 (J 7 Hz)	1.78 ($W_{h/2}$ 4 Hz)	4.90 ($W_{h/2}$ 4.5 Hz) 4.67 ($W_{h/2}$ 4.5 Hz)
(151)	0.77 (J 6.5 Hz) 1.03 (J 6.5 Hz)	1.81 ($W_{h/2}$ 3 Hz)	4.95 ($W_{h/2}$ 4 Hz) 4.69 ($W_{h/2}$ 4 Hz)
(152)	1.08 (J 5 Hz) (superimposed)	1.69 (J 1 Hz)	4.86 ($W_{h/2}$ 3 Hz) (superimposed)
(153)	0.80 (J 6.5 Hz) 1.06 (J 7 Hz)	1.78 ($W_{h/2}$ 4 Hz)	5.00 ($W_{h/2}$ 5 Hz) (superimposed)

previously discussed. These assignments were confirmed by the results of base catalysed isomerisations performed on the cyclopentanones. (Fig. 47)



(150) 77%

enantiomer of (151) 23%

(152) 92%

enantiomer of (153) 8%

Fig. 47

In both cases the equilibrium lies towards the cyclopentanone with the least number of adjacent cis substituents.

The i.r. spectrum of cyclopentanone (154) had bands characteristic of a vinylidene group (ν_{max} 894 cm^{-1}) and a carbonyl group on a five membered ring (ν_{max} 1746 cm^{-1}). The n.m.r. spectrum exhibited two doublets at δ 1.03 (J 6 Hz) and δ 0.99 (J 6 Hz) due to the indistinguishable C2 and C4 methyls. The olefinic methyl appeared as a triplet at δ 1.69, coupled (J 1 Hz) to the olefinic protons, which appeared as a multiplet at δ 4.88 ($W_{h/2}$ 6 Hz).

Table 7

Yield (%) of Products from Isopinocamphone (147) and Dienone (148) Pyrolysis

	Isopinocamphone			Dienone (148)
	590°	620°	650°	650°
dienone (148)	17	10	5	11
cyclopentanones				
(150)	27	36	37	39
(151)	12	14	15	16
(152)	2	4.5	7	13
(153)	-	3	4	4
dienone (149)	5	4	3	-
cyclopentanone (154)	1	2	3	-
low boilers	6	18	22	17
unknowns	2	5	4	-
(147)	28	4.5	-	-

From the variation of product yields with temperature (Table 7), it can be seen that the yield of cyclopentanone (154) increases as the yield of dienone (149) decreases. As all the other cyclopentanones (150-153) arise from the cyclisation of dienone (148), the cyclopentanone (154) must be formed by cyclisation of dienone (149) and, as it is the only cyclopentanone of this type present in isolatable yield, it must be the major product of dienone (149) cyclisation and have the stereochemistry assigned.

The Pyrolysis of Nopinone (67)

In the pyrolysis of β-pinene (see p 6), only products resulting from cleavage of the 1,6 bond have been isolated. As nopinone is analogous to β-pinene, a similar preference for this cleavage should be observed on pyrolysis.

Nopinone was prepared by the ozonolysis of β-pinene. Pyrolysis was carried out at 580-630° at a rate of 300 μl/min with no carrier gas flow. The crude product (≃ 90%) contained, in addition to starting material, low boiling compounds and five unknowns, five major products which were isolated by fractional distillation and preparative g.l.c., and identified as the isomeric dienones (68) and (155), the cyclopentanones (70) and (71), and cyclohexanone (69). (Fig. 48)

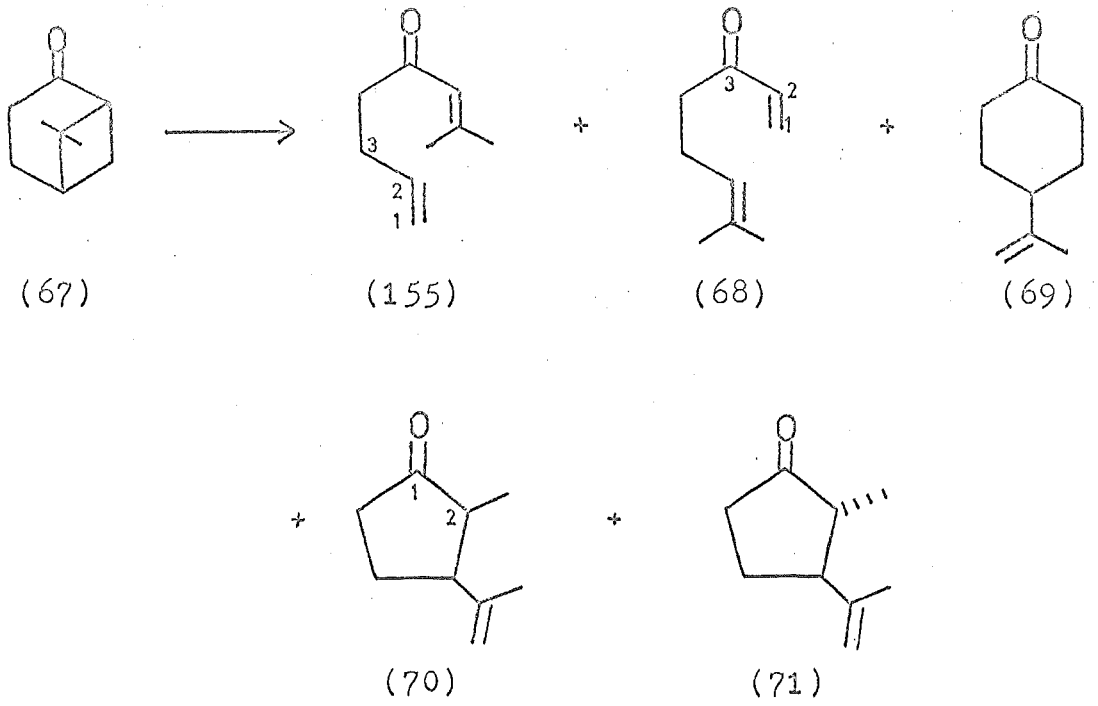


Fig. 48

The conjugated enone chromophore in dienone (68) was indicated by the i.r. (ν_{max} 1688 cm^{-1}) and the u.v. spectra (λ_{max} 215 nm, ϵ 4970). In the n.m.r. spectrum the C1 vinyl protons appeared as a multiplet (δ 6.20-6.42). The C6 olefinic proton also appeared as a multiplet (δ 5.10, W 21 Hz), but double irradiation of the geminal methyl groups removed the small couplings, leaving a triplet due to coupling (J 6 Hz) with the C5 methylene protons. The C2 vinyl proton appeared as a quartet at δ 5.78, coupled (J 8 Hz) to the trans C1 proton and to the cis C1 proton (J 4 Hz). The geminal methyl group cis to the C6 proton appeared at δ 1.68 as a doublet (J 1.2 Hz) while the trans geminal methyl group appeared as a broad singlet at δ 1.63 ($W_{h/2} \approx 4$ Hz).

In the isomeric dienone (155) the i.r. spectrum indicated the presence of a conjugated carbonyl group (ν_{max} 1694 cm^{-1}) and the u.v. spectrum showed that the chromophore had two alkyl substituents on it (λ_{max} 237, ϵ 5000). The n.m.r. spectrum exhibited the geminal methyl group trans to the C6 proton as a doublet at δ 2.15 (J 1.1 Hz), downfield from its characteristic position due to deshielding by the carbonyl group. The other geminal methyl group, cis to the C6 olefinic proton, appeared as a doublet at δ 1.88, also coupled (J 1.1 Hz) to the C6 proton. This resulted in the appearance of the C6 proton as a multiplet at δ 6.08 ($W_{h/2}$ 4.5 Hz). The C1 vinyl protons appeared as a multiplet (δ 4.82-5.28) as did the C2 vinyl proton (δ 5.75, W 25 Hz) due to coupling with the C1 and the C3 protons.

The i.r. spectrum of cyclohexanone (69) had a band characteristic of a carbonyl group on a six membered ring (ν_{max} 1720 cm^{-1}). The n.m.r. spectrum exhibited signals due to eight methylene protons and an isopropenyl group (the methyl as a triplet at δ 1.77, coupled (J 1.1 Hz) to the olefinic protons which appeared at δ 4.78 (J 1.1 Hz) as a quartet).

There are two routes to the cyclohexanone (69): (a) hydrogen transfer in the initially formed diradical from a methyl to C2, and (b) cyclisation of the dienone (68). The latter route became apparent when cyclohexanone (69) was produced as a product of dienone (68) pyrolysis. (Table 8). However, as the cyclisation gave only 8%

cyclohexanone (68) and 61% of the cyclopentanones (70 and 71), less than 4% of the cyclohexanone (68) produced in the pyrolysis of nopinone (67) would have been formed by route (b).

The i.r. spectrum of cis-cyclopentanone (70) had a band characteristic of a carbonyl group on a five membered ring (ν_{max} 1745 cm^{-1}). In the n.m.r. spectrum the olefinic methyl appeared as a broad singlet at δ 1.71 ($W_{h/2}$ 3.5 Hz), with small couplings to the olefinic protons which appeared as multiplets at δ 4.89 and 4.73 (both $W_{h/2}$ 4 Hz). The C2 methyl appeared as a doublet at δ 0.89, coupled (J 7.4 Hz) to the C2 proton, itself coupled (J 7.4 Hz) to the C3 proton, resulting in its appearance as a quintet at δ 2.85.

The trans-cyclopentanone (71) exhibited similar spectral features in the i.r. spectrum (ν_{max} 1745 cm^{-1}) and in the n.m.r. spectrum, where the olefinic methyl appeared at δ 1.76 as a triplet, coupled (J 1 Hz) to the olefinic protons which appeared at δ 4.84 as a multiplet ($W_{h/2}$ 3.5 Hz). The C2 methyl appeared as a doublet at δ 1.05, coupled (J 6 Hz) to the C2 proton, which was located at δ 2.05 by double irradiation experiments.

In the cis-cyclopentanone (70) the C2 proton is forced into the deshielding cone of the carbonyl group, compared to the trans-cyclopentanone (71), as a consequence of the methyl-isopropenyl interaction. This results in the C2 proton, in the cis-ketone (70), appearing 0.80 ppm downfield from the C2 proton in the trans-ketone (71). The stereochemistry of the cyclopentanones (70) and (71) was confirmed by base

Table 8

Yields (%) of Products from Pyrolysis of Nopinone (67) and Dienone (68)

	Nopinone			Dienone (68)
	580°	600°	630°	630°
dienone				
(155)	4	4.5	4.5	-
(68)	33	24.5	16	17
cyclopentanone				
(71)	7	9	11	24
(70)	10	15	17	37
cyclohexanone				
(69)	28	28	27.5	8
low boilers	4	7	13	12
5 unknowns	2	5.5	9.5	2
(67)	12	6.5	1.5	-

catalysed isomerisation of the cis-cyclopentanone (70) to the trans-cyclopentanone (71, 98%). Both cyclopentanones (70 and 71) were produced by cyclisation of the dienone (68), as evidenced by the variation in product composition with temperature, and by a separate experiment, where dienone (68) was pyrolysed. (Table 8)

In the pyrolysis of β-pinene, cleavage of the 1,6 bond was exclusive. The appearance of dienone (155) in the pyrolysis of nopinone indicates that, in this case, some 5,6 bond cleavage is also occurring. There is no substituent at C4 in nopinone which strongly influences the direction of ring cleavage, therefore a carbonyl group must have considerably less influence than an exocyclic double bond in determining the pyrolysis pathway.

After the work on nopinone pyrolysis had been completed, the reaction appeared in the literature.[53] These authors employed a quartz tube and low pressures to effect the pyrolysis, but at 600°, they obtained the same products as above, in approximately the same products as above, in approximately the same relative yield, although they did not isolate the dienone (155).

The Pyrolysis of cis-Verbanone (36)

cis-Verbanone can be considered as a derivative of nopinone (67) where a methyl has been substituted at the C4 position, which is adjacent to a ring junction. In pinane derivatives, which have a tertiary carbon adjacent to one ring junction and a secondary carbon adjacent to the other, (e.g. isopinocamphone (134) and isopinocampheol (121)) the major pyrolysis products have arisen from cleavage of the four membered ring adjacent to the tertiary carbon. Therefore, if, as in nopinone, a secondary carbon can compete

with a carbonyl in influencing the direction of ring opening, then a tertiary carbon should compete more strongly. Therefore, in the pyrolysis of cis-verbanone (36) a larger percentage of products arising from cleavage of the cyclobutane ring adjacent to the methyl substituent should be observed.

Partial hydrogenation over PtO_2 of verbenone (33) resulted in a mixture of cis-verbanone (80%) and neo-isoverbanol (20%). Chromic acid/ether oxidation of the mixture gave cis-verbanone. The previous work done[37] on the pyrolysis of cis-verbanone identified only the main product of the reaction as cis-o-menth-8-en-3-one (37) and reported the remaining products as conjugated and non-conjugated carbonyl compounds.

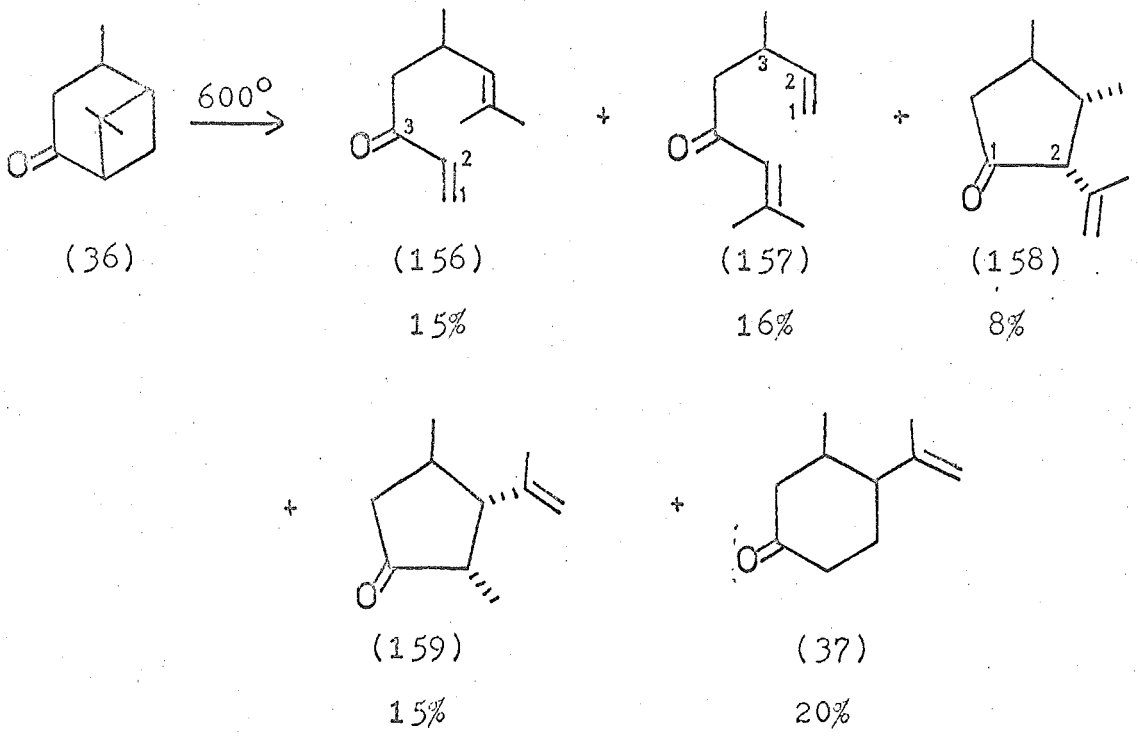


Fig. 49

Pyrolysis of cis-verbanone under the same conditions as for pyrolysis of nopinone (67) gave, at 600°, low boiling compounds (6%), six unidentified compounds (total 9%), starting material (11%) and five major products, isolated by fractional distillation and preparative g.l.c. and identified as the isomeric conjugated dienones (156, 15%) and (157, 16%), the cyclopentanones (158, 8%) and (159, 15%), and cyclohexanone (37, 20%). (Fig. 49)

Dienone (156) was shown to be conjugated, by its i.r. (ν_{max} 1690 cm^{-1}) and u.v. spectra (λ_{max} 208 nm ϵ 9050). In the n.m.r. spectrum the C2 vinyl proton appeared as a quartet at δ 5.77, coupled (J 8.4 Hz) to the trans C1 proton and to the cis C1 proton (J 3.9 Hz). The C1 vinyl protons appeared as a multiplet (δ 6.18-6.41). The geminal methyl groups appeared as doublets at δ 1.63 and 1.64, both coupled (J 1.5 Hz) to the C6 olefinic proton, itself coupled (J 9 Hz) to the C5 proton, resulting in its appearance at δ 4.93 as a doublet of multiplets. The C5 proton appeared as a broad multiplet at δ 2.97 (W 27 Hz) due to coupling with the C5 methyl (a doublet at δ 0.97, J 6.5 Hz), the C6 proton and the C4 methylene protons.

The i.r. spectrum of the isomeric dienone (157) was again characteristic of a conjugated ketone (ν_{max} 1690 cm^{-1}), while the u.v. spectrum demonstrated the substitution of two alkyl groups on the chromophore (λ_{max} 234 nm, ϵ 7460). In the n.m.r. spectrum the C1 vinyl protons appeared as a

multiplet (δ 4.78-5.17). The C2 vinyl proton appeared as an octet at δ 5.80, due to coupling (J 17.9 Hz) with the trans C1 proton and (J 9.8, 6.3 Hz) with the cis C1 proton and the C3 proton. The C6 olefinic proton appeared as a multiplet at δ 6.06 ($W_{h/2}$ 4.5 Hz), due to small couplings with the cis geminal methyl group (a doublet at δ 1.87, J 1.3 Hz) and the trans geminal methyl group which, due to deshielding by the carbonyl group, appeared at δ 2.12 (J 1.1 Hz).

The cyclopentanone (158) had a band in its i.r. spectrum characteristic of a carbonyl group on a five membered ring (ν_{max} 1754 cm^{-1}). The n.m.r. spectrum exhibited the olefinic methyl as a doublet at δ 1.69, coupled (J 1.1 Hz) to the cis olefinic proton which appeared superimposed on the trans olefinic proton at δ 4.90 ($W_{h/2}$ ~5 Hz). The C3 and C4 methyls, which were indistinguishable, appeared as doublets at δ 1.00 (J 6 Hz) and δ 1.05 (J 5 Hz).

The cyclopentanone (159) showed similar structural features in its i.r. (ν_{max} 1744 cm^{-1}) and n.m.r. spectra. The olefinic methyl appeared as a doublet at δ 1.70, coupled (J 1.3 Hz) to the cis olefinic proton which appeared as a quartet at δ 4.96 (J 1.3 Hz). The trans olefinic proton appeared at δ 4.73, as a singlet ($W_{h/2}$ 3.5 Hz). The C2 and C4 methyls, which were indistinguishable, appeared as doublets at δ 0.12 (J 5 Hz) and δ 0.87 (J 7 Hz).

The i.r. spectrum of cyclohexanone (37) showed a band characteristic of a carbonyl group on a six membered ring

(ν_{max} 1715 cm^{-1}). The n.m.r. spectrum exhibited signals due to an isopropenyl group (a methyl at δ 1.79, $W_{h/2}$ 3 Hz, and olefinic protons at δ 4.88 and 4.65, both $W_{h/2}$ 4 Hz), and a methyl geminal to a proton (δ 0.77, J 7 Hz).

The stereochemistry of the cyclopentanones (158) and (159) followed from their mode of formation, as both ketones were the major cyclisation product of the dienones (157) and (156) respectively. Pyrolysis of dienone (156) at 610°, gave cyclopentanone (159, 50.5%), three unidentified compounds (14%), low boiling compounds (12%) and starting material (23.5%). Similarly, the dienone (157), on pyrolysis at 610°, gave cyclopentanone (158, 28%), three unidentified compounds (21%), low boiling compounds (13%) and starting material (38%).

In the pyrolysis of cis-verbanone, large amounts of the diradicals arising from cleavage of both the 1,6 and 5,6 bonds are formed. (Fig. 50) Diradical (structure (b) Fig. 50) decomposes to two primary products, namely dienone (156) and cyclohexanone (37), whereas diradical (structure (a) Fig. 50) decomposes only to dienone (157). (If any of the cyclohexanone (structure (c) Fig. 50) is formed, it is in $<$ 0.5% yield).

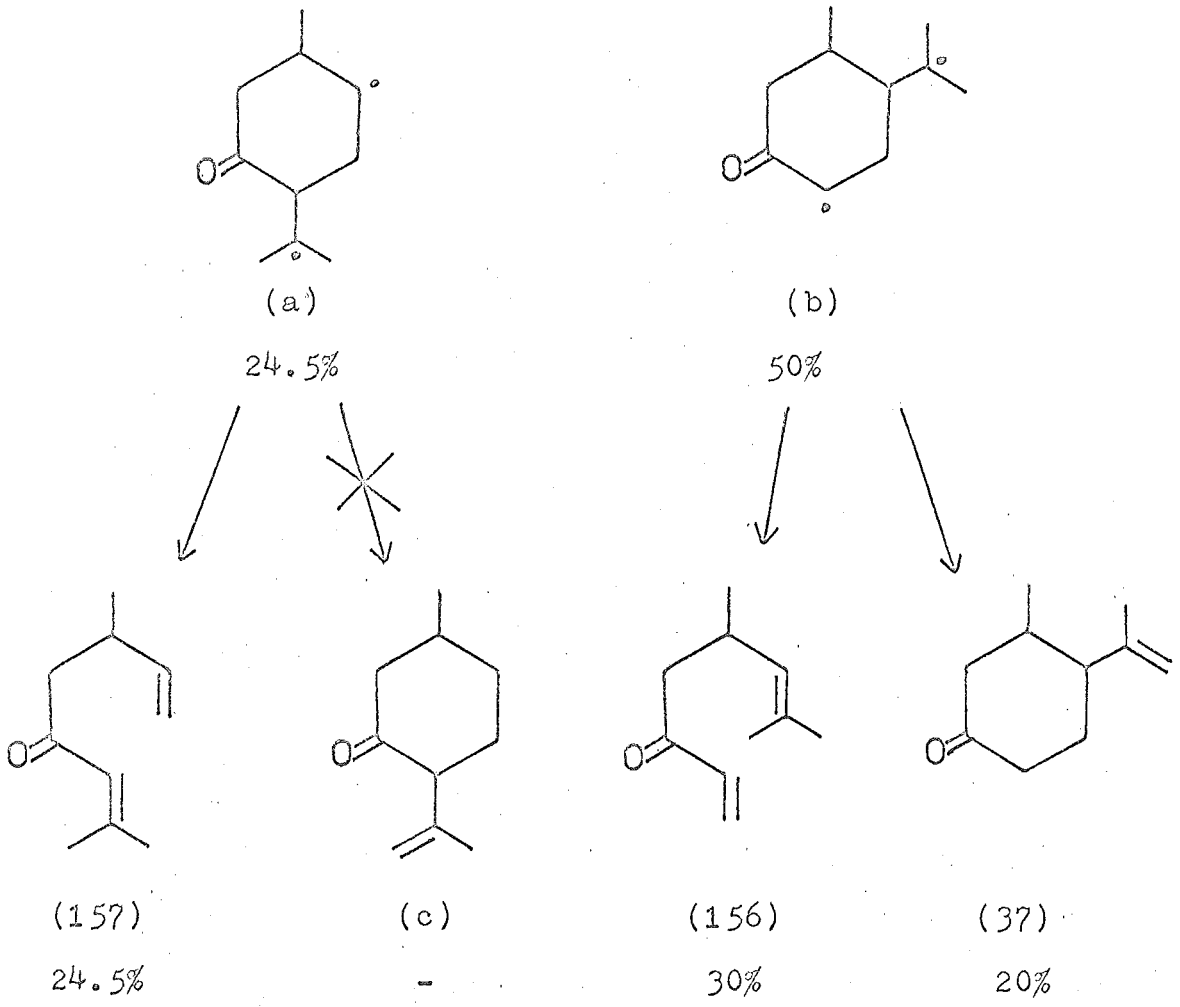


Fig. 50

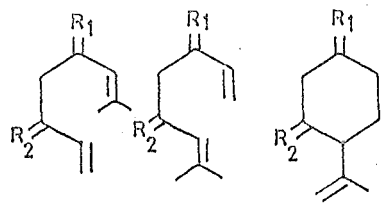
CONCLUSIONS

Substituents on the pinane nucleus have a marked effect on the direction of thermal bond cleavage in the four membered ring. Pyrolysis of a pinane derivative generally results in initial cleavage of the 1,6 or 5,6 bonds to form diradicals, which collapse to give the products. The formation of these products depends on the nature and the position of the substituents on the pinane nucleus.

To determine the amounts of each primary product (1,6-octadienes and isopropenylcyclohexanes) formed in a pyrolysis reaction, secondary products derived by further reaction of the 1,6-octadienes have to be included in the percentages calculated for the dienes. When the relative yields of the primary products are corrected in this manner (Table 9), the relative effects of substituents on the thermal fragmentation of the cyclobutane ring in pinanes can be examined. The major primary acyclic diene is, in each case, labelled as diene (b). The only isopropenylcyclohexane derivative (c) formed in each case studied, arises from the same diradical as does the major diene (b). Therefore, the sum of the diene (b) and the isopropenylcyclohexane (c) (column b + c) compared to the amount of diene (a) is a measure of how the fragmentation of the four membered ring is partitioned between the initial cleavage of the 1,6 and 5,6 bonds.

Table 9

Primary Products of Pinane Pyrolysis Under Optimum Conditions



Pinane		$=R_1$	$=R_2$	SM	(a)	(b)	(c)	(b+c)
Nopinol	(112)	OH H	H H	4	16	57	-	57
10α-pinan-2-ol	(42)	CH_3 OH	H H	-	4	77	-	77
10β-pinan-2-ol	(43)	CH_3 OH	H H	-	6	75	-	75
neo-isoverbanol	(135)	CH_3 H	OH H	18	21	48(3)*	-	51
isopinocampheol	(121)	CH_3 H	H H	13	2	57	-	57
isopinocamphone	(134)	CH_3 H	H H	28	6	58	-	58
nopinone	(67)	C=O	H H	12	4	50	28	78
cis-verbanone	(36)	C=O	CH_3 H	11	24	30	20	50
cis-pinocarveol	(97)	C=C	H H	3	-	42(14)*	16	72
trans-pinocarveol	(98)	C=C	H H	9	-	62(5)*	11	78
trans-pinocarvyl-acetate	(106)	C=C	H H	-	-	27(8)*	9	44

*Minor primary products formed from the same diradical as diene (b).

The relative effectiveness of substituents in inducing cyclobutane ring cleavage at the adjacent ring junction can be estimated by a comparison of the amount of each diradical formed in the presence of the substituents, R_1 and R_2. From the results of nopinol (112) pyrolysis, it can be seen that a hydroxyl group has a greater influence than hydrogen, and from neo-isoverbanol (135), a methyl group has more influence than a hydroxyl group. From the results for cis-verbanone (36) it is evident that a carbonyl group is more effective than a methyl group. Although a carbonyl group has a much greater (but not completely dominant) influence than hydrogen (nopinone (67)), an exocyclic double bond induces cleavage exclusively at the adjacent ring junction when in competition with hydrogen (cis- and trans-pinocarveol (97, 98) and trans-pinocarvyl acetate (106)). Therefore, it appears that in the cleavage of a pinane cyclobutane ring, an exocyclic double bond has a more powerful directing effect than a carbonyl group. From these results the following order of substituent effectiveness can be deduced:

$C{=}C > C{=}O > CH_3 > OH > H.$

The relative influence of exocyclic and endocyclic double bonds can not be assessed from Table 9 since all the pinanes studied that contained a carbon-carbon double bond gave exclusive cleavage of one cyclobutane bond. However, in the pyrolysis of verbenene (61)[52], a comparison can be made, as an exocyclic double bond is adjacent to one of the

ring junctions and an endocyclic double bond adjacent to the other. The pyrolysis products observed (see p 14) arise only from cleavage of the cyclobutane bond adjacent to the endocyclic double bond.

The pinane derivatives studied may be divided into two classes, namely those with an sp^2-hybridised carbon adjacent to a ring junction and those with only sp^3-carbons adjacent to the ring junctions. Only in the former class of pinanes does any isopropenylcyclohexane derivative form on pyrolysis. The reason for this division can be seen in the pyrolysis of cis-verbanone (36).

Pyrolysis of cis-verbanone yields large quantities of the 1,6-octadienes (156) and (157) and the isopropenylcyclohexanone (37). However, there is a notable absence of any isopropenylcyclohexanone derivative formed from the same diradical as dienone (157). (Fig. 50)

To form the dienones (156) and (157), cleavage of the carbon-carbon bond positioned between the tertiary and the secondary radicals must occur. This process occurs most readily when this C-C bond is eclipsed with both of the singly occupied orbitals in the diradical. When the secondary radical in the diradical formed from a pinane is adjacent to carbon atoms which are sp^3-hybridised, the diradical can adopt a conformation in which the C-C bond which is going to cleave, and the radicals, are nearly eclipsed.

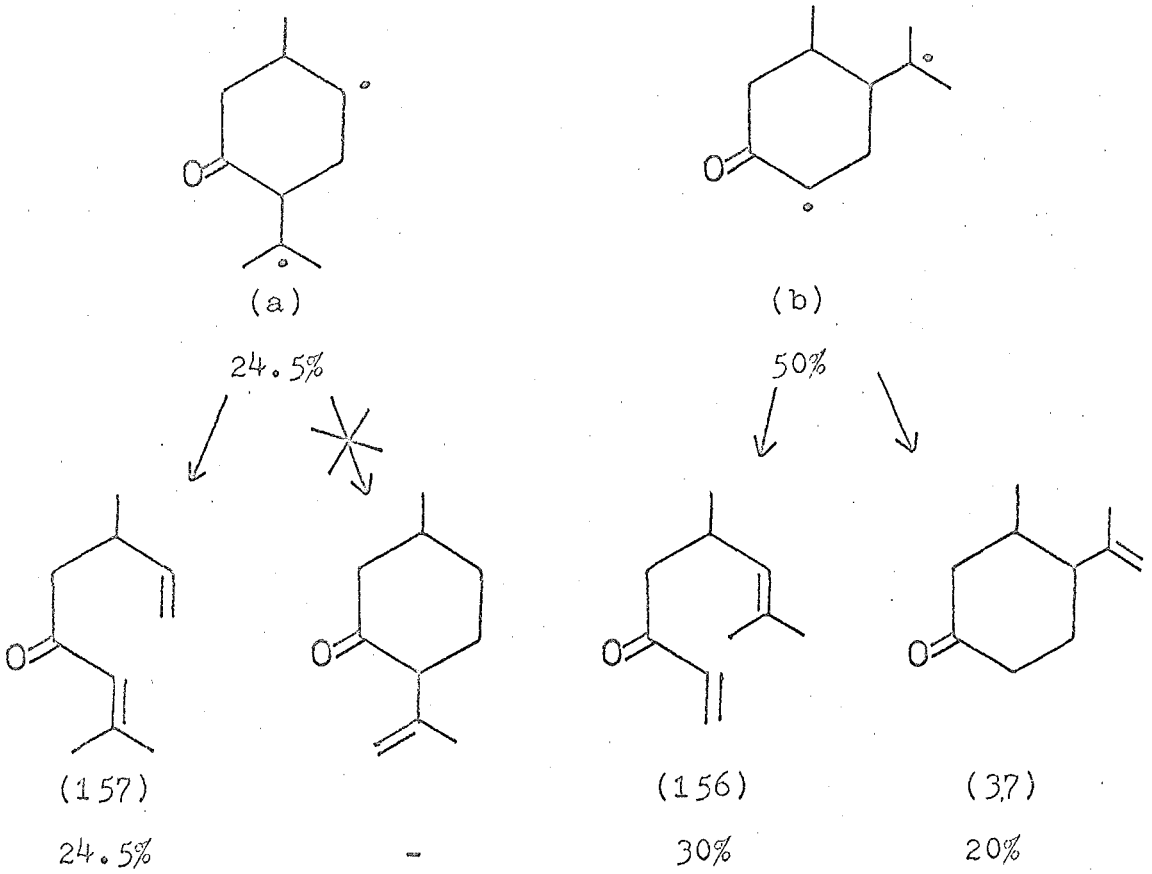


Fig. 50

This situation arises in diradical (a) (Fig. 51), as shown in the Newman projection. However, when a secondary radical is adjacent to a sp^2-hybridised carbon atom, the unpaired electron can be delocalised through the π-system. The stereochemical requirements for the π-delocalisation impose conformational constraints on the system and, consequently, decomposition of the diradical to a 1,6-diene becomes a relatively high energy process. This allows the alternative 1,5 hydrogen transfer from a methyl of the isopropyl radical, to become a competing reaction.

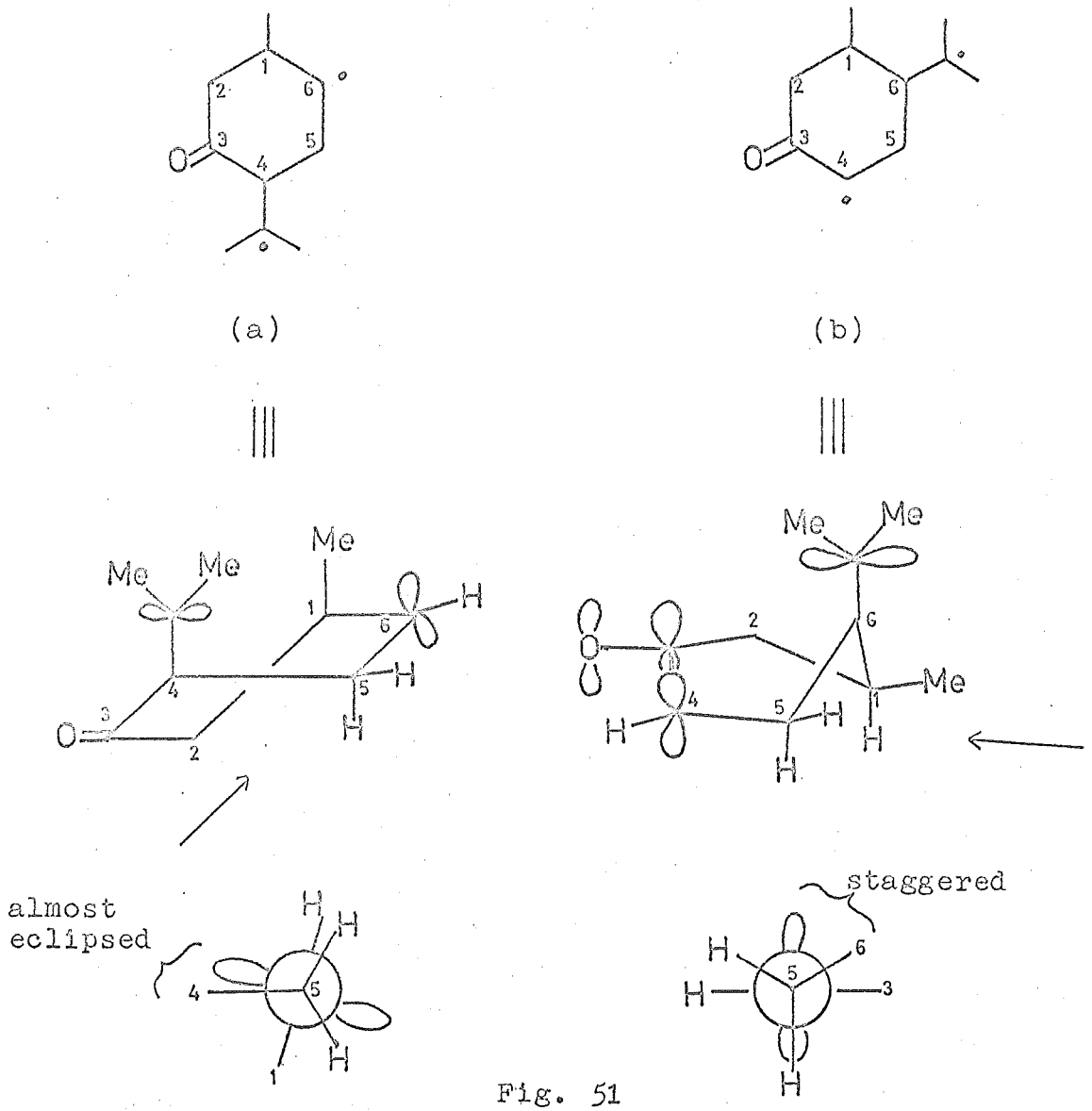


Fig. 51

This situation is illustrated for diene (b) in Fig. 51, where, when the secondary radical is delocalised, the required eclipsing cannot occur, as shown in the Newman projection.

The only compound which does not lead to the expected pattern of primary products is 2-hydroxy-10β-pin-3-ene (89). Although it is the type of pinane which could be expected

to give, on pyrolysis, a 1,6-octadiene and an isopropenylcyclohexane, via diradical (89a) (Fig. 52), this does not occur, since an alternative reaction pathway is possible.

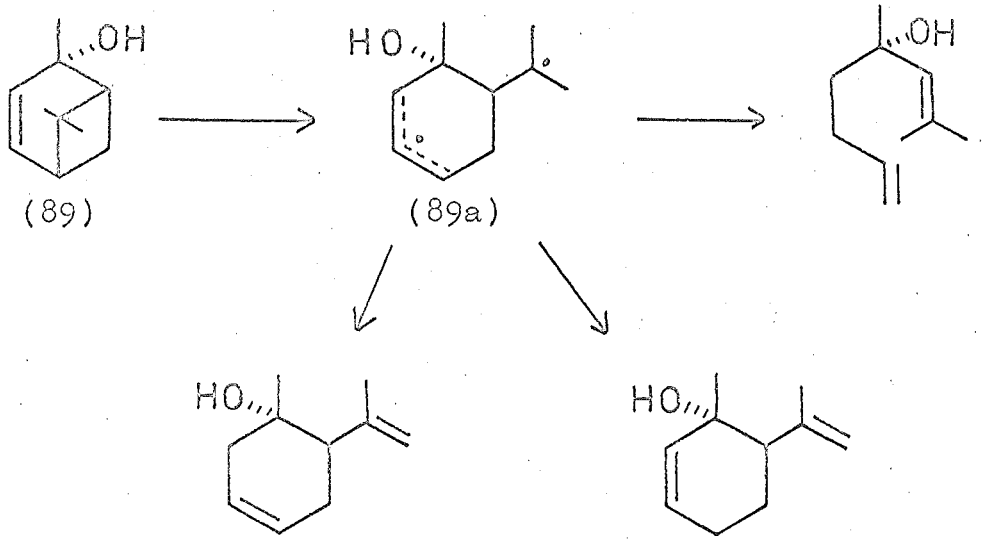
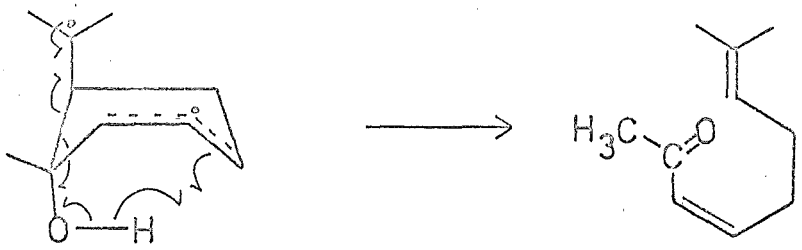


Fig. 52 Expected decomposition pathways of diradical (89a) to primary products.

The diradical (89a) can adopt a conformation in which the tertiary radical, the carbon-oxygen bond and the carbon-carbon bond between these two groups are coplanar. (Fig. 53) This arrangement satisfies the steric requirements for cleavage of the carbon-carbon bond to give the dienone (94), as the major primary reaction product.



(89a) (94)

Fig. 53

In every pinanol where the hydroxyl group is adjacent to the ring junction, a carbonyl compound is observed in the pyrolysis products. These compounds are formed from rearrangement of isopropenylcyclopentanols where the hydroxyl and isopropenyl groups are adjacent. This structural feature arises in the cyclopentanols by cyclisation of only one of the two possible 1,6-octadienols, the other giving a 1,3-hydroxyl-isopropenyl structure. The required dienol is formed when the four membered ring in the pinanol initially cleaves between the gem dimethyl group and the ring junction more remote from the hydroxyl group.

Substituents at C3 on the pinane ring cannot influence the direction of cyclobutane cleavage as the C3 position is equidistant from the two ring junctions. There is no general way in which they affect the formation of secondary products. An effect of a C3 substituent was, however, observed in the pyrolysis of cis- and trans-pinocarveol (97)

and (98). As well as formation of the normal 1,6-octadienol and isopropenylcyclohexanol products, the hydrogen of the hydroxyl group was able to migrate to a carbon on the opposite side of the six membered ring, resulting in fragmentation of the molecule into two radicals which on combination lead to the diene (91) and the aldehyde (102).

APPENDIX A

The Photolysis of Conjugated Pinanes

Verbenone (33) is the only pinane containing a conjugated chromophore which has been photolysed[110-113]. The major product of the photolysis is chrysanthenone (75), a product involving a [1,3] sigmatropic shift.

Verbenene (61) was prepared by the base-catalysed elimination of acetic acid from trans-verbenyl acetate (74). Verbenene (61) was stable to direct photolysis. However, with benzophenone as a sensitizer, triene (62) was formed almost quantitatively.

The u.v. spectrum of triene (62) indicated the presence of a conjugated diene chromophore (λ_{max} 232 nm, ϵ 18,000). In the n.m.r. spectrum the olefinic methyl appeared as a doublet at δ 1.71, coupled (J 1.5 Hz) to the cis isopropenyl olefinic proton, which appeared superimposed on the signal for the trans olefinic proton at δ 4.78 ($W_{h/2}$ 3.5 Hz). The C1' olefinic protons appeared as a multiplet at δ 4.88 ($W_{h/2}$ 4.5 Hz). The proton under the isopropenyl group appeared as a triplet at δ 3.02, coupled (J 6.5 Hz) to the C5 methylene protons. The C2 olefinic proton appeared as a doublet of multiplets at δ 6.17, the large coupling (J 9.5 Hz) being with the C3 olefinic proton which appeared as a multiplet at δ 5.82 (W 21 Hz).

The structure of triene (62) was further substantiated by hydrogenation to a mixture (60:40 by g.l.c.) of o-menthanes. The major product was identified as cis-o-menthane by comparison with an authentic sample[89]. The triene (62) was also identical with the major product isolated[52] from the pyrolysis of verbenene, which appeared in the literature after this photolysis was completed.

4-Methyl-verbenene (161) was prepared by reaction of verbenone (33) with methyl magnesium iodide, followed by careful hydrolysis of the complex. The tertiary alcohol formed by the grignard reaction underwent dehydration during the work up. The diene (161) was extracted with pentane, and was very sensitive to heat, rearranging at $<100^{\circ}$ to 2,4-dimethyl-cumene (163). In the photolysis of the diene (161) in pentane, under the same conditions as for verbenene (61), after 1 hr no further changes occurred in the composition of the reaction mixture, the benzophenone having been converted into benzpinacol. Analysis of the reaction mixture by g.l.c. and preparative g.l.c. showed the presence of starting material (67%) and 2,4-dimethylisopropenylbenzene (162, 33%).

The i.r. spectrum of the aromatic compound (162) showed bands due to the C-H bending of two adjacent hydrogens on a benzene ring (ν_{max} 823 cm^{-1}), due to one hydrogen on a benzene ring (ν_{max} 877 cm^{-1}), and due to a vinylidene group (ν_{max} 897 cm^{-1}). The n.m.r. spectrum exhibited the C2 and

C4 methyl groups as a singlet at δ 2.29. The olefinic methyl appeared as a broad singlet ($W_{h/2}$ 2.5 Hz) at δ 2.01, coupled (small J) to the olefinic protons which appeared as multiplets at δ 5.15 and 4.81 (both $W_{h/2}$ 5 Hz). The aromatic protons appeared as a singlet at δ 6.97.

The aromatic compound (162) contains two hydrogens less than the starting material (161); the benzophenone was correspondingly reduced to benzpinacol.

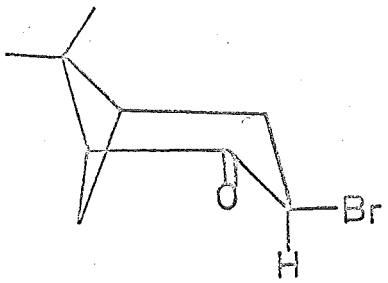
APPENDIX B

The Preparation of Apoverbenone (167)

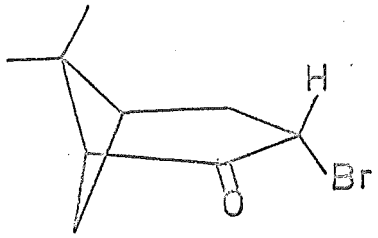
Apoverbenone, which was required for the pyrolysis studies, has been reported[114] to be formed by collidine dehydrobromination of 3β-bromonopinone (164). Direct bromination of nopinone (67) gave, in contrast to previous work[115], a mixture of 3β- and 3α-bromonopinone (164, 165) which could not be smoothly dehydrobrominated with collidine. The formation and attempted dehydrobromination of each bromonopinone was therefore examined.

Bromination of the enol acetate (76), using bromine in carbon tetrachloride, gave 3β-bromonopinone (164). The C3 α- proton n.m.r. resonance of 3β-bromonopinone appeared as a quartet at δ 4.83, coupled (J 11 Hz) to the C4 β- proton and to the C4 α- proton (J 8 Hz). The magnitude of these

coupling constants indicates that, as in the solid phase, the 3β-bromonopinone exists in solution in the "down" conformation with the bromine atom equatorial. (Fig. 54)



(164)



(165)

Fig. 54

Addition of anhydrous sodium carbonate to the bromination system resulted in the conversion of the enol acetate (76) exclusively into 3α-bromonopinone (165). In its n.m.r. spectrum the C3 proton appeared as a quartet at δ 4.68, coupled (J 7.5 Hz) to the C4 β- proton and to the C4 α- proton (J 3.5 Hz). The magnitude of these coupling constants suggests[116] a conformation in which ring carbon atoms 1-5 are essentially coplanar. Although the product (165) of kinetic control epimerized to the product (164) of thermodynamic control when acid was allowed to accumulate during the bromination reaction, the acid catalysed isomerisation of 3α-bromonopinone to 3β-bromonopinone using hydrogen bromide-acetic acid (20%) in carbon tetrachloride was inefficient ($\approx$ 33%) and also gave p-isopropylphenol (166, 30%) and 11

minor components. Lower hydrogen bromide concentration resulted in correspondingly lower conversion of 3α-bromonopinone into the same products.

From the conformations of the ketones (164) and (165) shown in Fig. 54, it can be seen that 3β-bromonopinone cannot undergo an anti-coplanar elimination of hydrogen bromide but 3α-bromonopinone can undergo a syn-planar elimination. Reaction of 3α-bromonopinone with collidine gave apoverbenone (167) in low yield (7%). The other products, besides starting material, were 3β-bromonopinone (50%) and nopinone (13%). Attempted dehydrobromination using lithium carbonate/dimethyl formamide resulted only in partial epimerization at C3. Reaction of 3α-bromonopinone with either sodium methoxide/methanol or potassium t-butoxide/t-butanol, resulted mainly in debromination to nopinone (67).

Some apoverbenone was eventually prepared by lead tetraacetate oxidation of apopinene (169). (Fig. 55) Reaction of nopinone (67) and benzene sulphonylhydrazine gave a high yield of the hydrazone (168). Decomposition of the sodium salt of hydrazone (168) in digol resulted in a mixture of 4-isopropenylcyclohexene (170, 19%) and apopinene (169, 81%). When water was added to the digol, no difference was observed in the course of the reaction. Decomposition of the solid salt gave only apopinene (167).

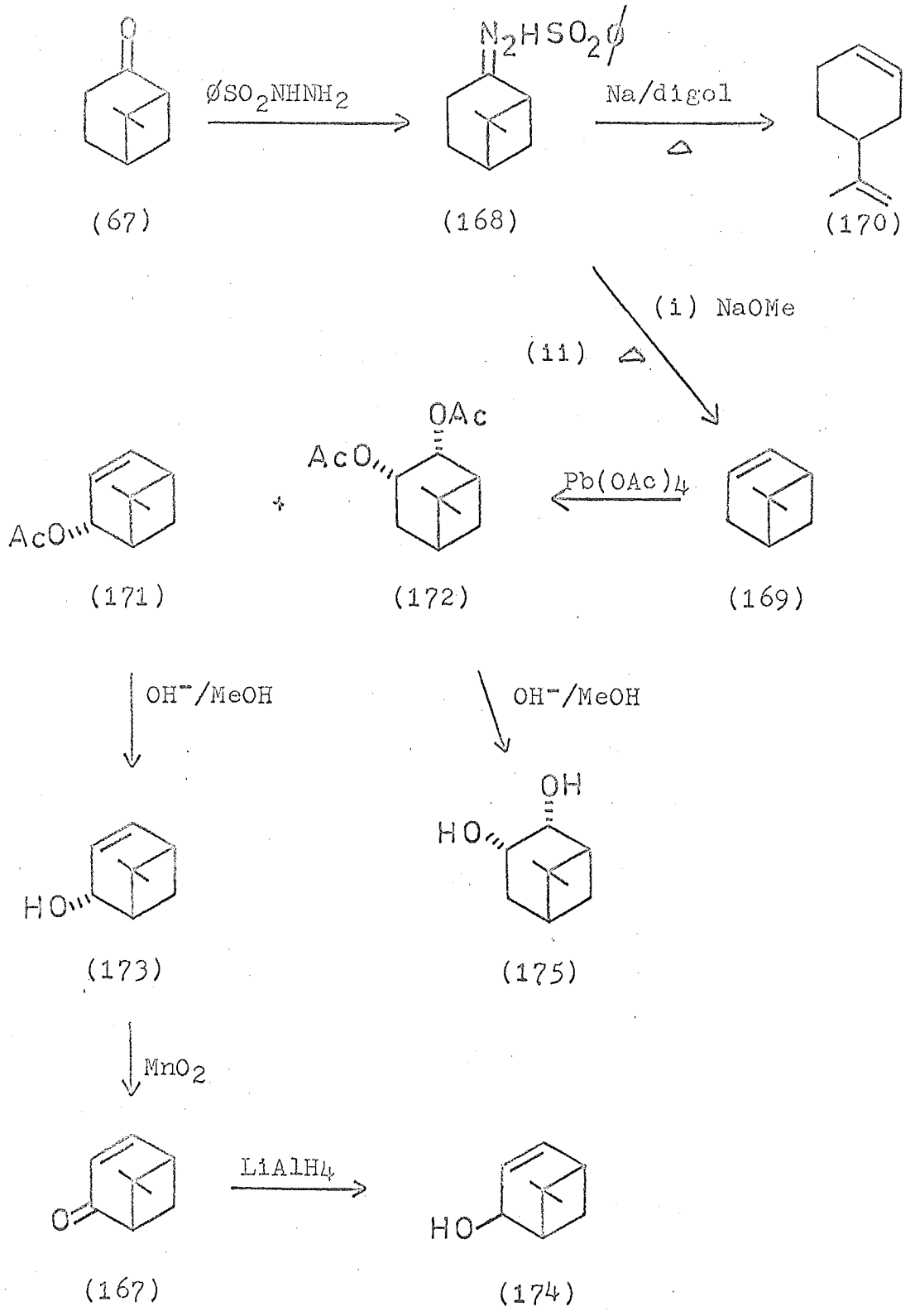

ØSO2NHNH2
N2HSO2Ø
Na/diglol
(67)
(168)
(170)
(i) NaOMe
(ii)
OAc
AcO
Pb(OAc)4
AcO
(171)
(172)
(169)
OH⁻/MeOH
OH⁻/MeOH
OH
HO
HO
(173)
(175)
MnO2
LiAlH4
O
HO
(167)
(174)

Fig. 55

Lead tetraacetate oxidation of apopinene gave (c.f. ref. 86), after distillation, starting material (5%), trans-apoverbenyl acetate (171, 37%) and the diacetate (172, 12%). Hydrolysis of the acetate (171) and the diacetate (172) gave trans-apoverbenol (173) and the diol (175) respectively. Oxidation of trans-apoverbenol (173) with activated manganese dioxide gave apoverbenone (167). Lithium aluminium hydride reduction of apoverbenone gave cis-apoverbenol (174). In the n.m.r. spectrum of cis-apoverbenol (174) the C9 methyl group appeared at δ 1.12 in contrast to δ 0.91 for the C9 methyl resonance in trans-apoverbenol (173). The deshielding of 0.21 ppm of the C9 methyl in cis-apoverbenol is consistent with the syn hydroxyl-methyl stereochemistry.

APPENDIX C

The Mechanism of the Base Catalysed Rearrangement of 2,10-epoxy-10β-pinan-3β-ol (176)

Reaction of both 2,10-epoxy-10β-pinan-3-ols (176) and (178) with sodium hydroxide in aqueous methanol have been reported[117] to give pinocarvone (99) in essentially quantitative yield (> 98% by g.l.c.). The rearrangement of each epoxide (176 and 178) has been determined[104] as approximately

first order in both [epoxide] and [OH^-] . Also the relative rates of rearrangement of epoxide (176):epoxide (178) (10:1) have been[117] rationalized in terms of the relative accessibility of the C3 proton in the epoxides (176 and 178) to attack by hydroxide ion. The mechanistic scheme (Fig. 56) involving slow, irreversible proton abstraction by hydroxide ion, followed by rapid reaction of the carbanion (179), is consistent with the kinetic data.

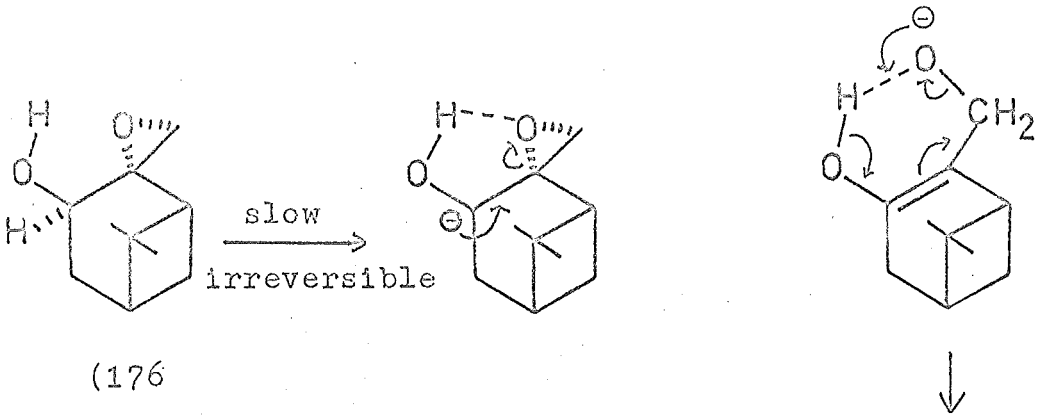


Fig. 56

The cis-pinocarveol (97) deuterated at C3, already prepared in the course of pyrolysis studies, was converted into the corresponding epoxide. Kinetic studies were undertaken to determine whether the loss of the C3 proton is involved in the rate determining step in the rearrangement. A deuterium isotope effect should be observed in the range k_H/k_D = 1-2 as the mechanism proposed is an E1cb elimination[118].

The deuterated epoxide (177) was prepared by m-chloroperoxybenzoic acid epoxidation of C3-deuterated cis-pinocarveol. The optical density readings for the kinetic runs were plotted by the Guggenheim[119] method and gave excellent linear plots. Comparison of the pseudo first order rate constants for the undeuterated (176) and deuterated (177) epoxides, allowed the evaluation of the primary isotope effect, $k_H/k_D = 1.56$ (± 0.04) for the reaction. Furthermore, isolation and examination of unchanged epoxide at ≈50% reaction, showed[120] that no C3-D exchange had occurred, thus excluding reversibility in the initial proton abstraction step.

EXPERIMENTAL

Specific rotation measurements were carried out in chloroform solutions in a 1cm cell. Infrared spectra were recorded on a Shimadzu IR27G spectrophotometer, and are for liquid films for oils and nujol mulls for solids unless otherwise stated. Ultraviolet spectra were recorded on a Shimadzu MPS-50L spectrometer.

NMR spectra were obtained on a Varian A 60 spectrometer for $CDCl_3$ solutions with $CHCl_3$ and TMS as internal standards. NMR parameters were derived by first order analysis and confirmed wherever possible by double irradiation experiments.

Analytical gas chromatography was performed on a MicroTek 2500 ii R using 2% FFAP, Se30 and Carbowax 20M on Aeropak 30, in 1/8" stainless steel columns. Preparative g.l.c. was performed on a Varian Autoprep 705 using 7% FFAP and 20% Se30 on Chromosorb-W 80/100 (DMCS treated, acid washed) in 3/8" aluminium columns.

Fractional distillations were carried out using Nester-Faust annular teflon and spinning band columns.

Alumina (P. Spence, grade H) and silica (Crosfield

Sobsil) was used in column chromatography. Melting points are uncorrected.

Nopinone (67)

β-Pinene (20 g) was dissolved in absolute methanol (180 ml) in a 250 ml vessel fitted with a bubbler tube, and the vessel kept at -70^{0}. Ozone in oxygen generated by a silent discharge apparatus was passed through the solution until the effluent gas gave a strong colouration with moist starch-iodide paper ($\approx$ 30 hrs). The solution was poured into water (1 l) and left for 24 hrs. Extraction with diethyl ether (3 x 100 ml) and subsequent washing with water, gave, after evaporation and fractional distillation, nopinone (14 g). $[\alpha]_D$ +32.4° (c, 1.01); ν_{max} 1715cm^{-1}; λ_{max} 285$_{nm}$ (ϵ 15); c.d. $\Delta\epsilon$ +1.77 (282$_{nm}$), $\Delta\epsilon$ + 0.16 (208); n.m.r. δ 1.33 (C8-H$_3$), 0.85 (C9-H$_3$).

Enol Acetylation of Nopinone (67)

Nopinone (10 g) and toluene-p-sulphonic acid (1 g) in isopropenyl acetate (200 ml) were heated to reflux and the acetone formed in the reaction fractionally distilled from the system through a 12-in. column packed with glass helices. After 5 hr, during which time 30 ml of distillate had been collected, the remaining isopropenyl acetate was removed under reduced pressure. The residue was diluted with ether (400 ml), washed with water, and dried. Fractional

distillation allowed the isolation of 2-acetoxy-10-nor-pin-2-ene (76, 9.4 g), b.p. 72°/4.6 mm; n_D^{20} 1.4689; $[\alpha]_D$ -18.6° (c, 1.05); ν_{max} 1760 cm^{-1}; n.m.r. δ 5.18 ($W_{h/2}$ 6 Hz; C3-H), 2.08 (OAc), 1.31 ($C8\text{-}H_3$), 0.96 ($C9\text{-}H_3$); Found: C, 73.3; H, 9.0. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%).

m-Ethyl toluene (86)

ν_{max} 880, 780 cm^{-1}; n.m.r. δ 7.08 (multiplet, $W_{h/2}$ 30 Hz; aromatic H), 2.77, 1.22 (ethyl), 2.31, identical with an authentic sample.

1-Acetoxy-5,5,6-trimethylcyclohexa-1,3-diene (82)

ν_{max} 1761, 1200 cm^{-1} (enol acetate); λ_{max} (EtOH) 266nm (ϵ 3700); n.m.r. δ 5.87 (multiplet 3H, W 42 Hz; H2, H3, H4), 2.14 (OAc), 1.13, 0.99 (6H, C5 methyls), 0.95 (doublet 3H, J 6.5 Hz; C6 methyl); Found; C, 73.0; H, 8.6. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%.

Hydrolysis of the enol acetate (82, 50 mg) by adsorption on alumina (5 g) and elution with ether after 16 hr gave 5,5,6-trimethylcyclohex-2-enone (87, 40 mg); ν_{max} 1685 cm^{-1}; λmax (EtOH) 227.5 nm (ϵ 5950); n.m.r. δ 6.78 (doublet of triplets 1H, $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 3.5 Hz; H3), 5.96 (doublet of triplets 1H, $J_{2,3}$ 10.1 Hz, $J_{2,4}$ 1.5 Hz; H2), 2.25 (multiplet 3H; H4, H6), 1.06, 0.90 (6H, C5 methyls), 1.05 (doublet 3H, J 6.5 Hz; C6 methyl); Found: C, 77.9; H, 10.0.

$C_9H_{14}O$ requires C, 78.2; H, 10.2%.

2-Acetoxy-1,6,6-trimethylcyclohexa-1,3-diene (83)

ν_{max} 1758, 1200 cm^{-1} (enol acetate); λ_{max} (EtOH) 259.2 nm (ϵ 3350); n.m.r. δ 5.70 (singlet 2H, $W_{h/2}$ 2.5 Hz; H3, H4), 2.16 (OAc), 1.58 (singlet 3H; C1 methyl), 1.02 (singlet 6H; C6 methyls); Found: C, 72.85; H, 8.50. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%.

Hydrolysis of the enol acetate (83) as above gave the conjugated ketone (87).

1-Acetoxy-4-isopropenylcyclohex-1-ene (78)

$[\alpha]_D$ ± 0° (c, 1.01), o.r.d. ϕ_{200} ± 0; ν_{max} 1760, 1220, 892 cm^{-1}; n.m.r. δ 5.83 (multiplet 1H, $W_{h/2}$ 12 Hz; H2), 4.74 (quartet ? 2H; $C=CH_2$), 2.10 (OAc), 1.73 (triplet ? 3H; $C=C-CH_3$). Found: C, 73.1; H, 8.55. $C_{11}H_{16}O$ requires C, 73.3; H, 8.95%.

Hydrolysis of enol acetate (78) as above gave 4-isopropenylcyclohexanone (69); ν_{max} 1720, 890 cm^{-1}; n.m.r. δ 4.78 (quartet ? 2H; $C=CH_2$), 1.77 (triplet ? 3H; $C=C-CH_3$); Found: C, 77.8; H, 10.3. $C_9H_{14}O$ requires C, 78.2; H, 10.2%.

3-Acetoxy-7-methylocta-2,4,6-triene (80)

ν_{max} 1765, 1190 (enol acetate), 1640, 680 cm^{-1}; λ_{max} (EtOH) 277.5 nm (ϵ 9200); n.m.r. δ 6.33 (doublet 1H,

$J_{4,5}$ 10 Hz; H4), 5.93 (multiplet 2H, W 20 Hz; H5, H6), 5.23 (quartet 1H, $J_{2,Me}$ 7.5 Hz; H2), 2.20 (OAc), 1.79 (doublet 3H, $J_{Me,2}$ 7.5 Hz; CH_3), 1.78 (singlet 6H; C7-methyl, C8-H_3); Found: C, 72.9; H, 8.5. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%.

Hydrolysis of the enol acetate (80) as above gave 7-methylocta-(E)4,6-dien-3-one (88); ν_{max} 1670, 963 cm^{-1}; λ_{max} (cyclohexane) 278 nm (ϵ 19,900); n.m.r. δ 7.46 (quartet 1H, $J_{4,5}$ 15.3 Hz; H4); 5.97 (doublet of multiplets 1H, $J_{6,5}$ 11.5 Hz, $J_{6,Me}$ (app.) 1.1 Hz; H6), 2.56 (quartet 2H, $J_{2,Me}$ 7.3 Hz; $H_2$2), 1.89 (doublet ? 6H, $J_{Me,6}$ 1.1 Hz; C7 methyl, C8-H3), 1.10 (triplet 3H, $J_{Me,2}$ 7.3 Hz; C1-H_3); Found: C, 77.8; H 9.85. $C_9H_{14}O$ requires C, 78.2; H, 10.2%.

2-Acetoxy-10β-pin-3-ene (90)

Freshly prepared lead tetraacetate[76] (90 g, dried over P_2O_5), was added during 10 mins to a stirred soln of α-pinene (26 g) and dry benzene (300 ml). The mixture was stirred at 60-65° for 2 hrs, cooled and the resulting lead diacetate filtered. Water was added to the filtrate and the precipitated lead dioxide filtered. Evaporation of the dried benzene soln followed by fractional distillation gave 2α-acetoxy-10β-pin-3-ene (23 g). ν_{max} 700, 1732 cm^{-1}, n.m.r. δ 6.3 (quartet, 1H, $J_{4,3}$ 8.9 Hz, $J_{4,5}$ 5.8 Hz; H4), 6.03

(doublet of multiplets, 1H, $J_{3,4}$ 8.9 Hz, H3), 1.93 (acetate), 1.59 (C2-methyl), 1.37 (C8-H_3), 0.97 (C9-H_3).

2-Hydroxy-10β-pin-3-ene (89)

The acetate (90, 13 g) in dry ether (50 ml) was added to a stirred soln of $LiAlH_4$ (2 g) in dry ether (150 ml) at 0°, over 10 mins. The mixture was stirred for another 15 mins as it came to room temp, then worked up by the careful addition of $Na_2SO_4.10H_2O$ and water. The soln was decanted, dried and evaporated to give 2α-hydroxy-10β-pin-3-ene (9.8 g). m.p. 47-49°, ν_{max} 740, 3390 cm^{-1}, n.m.r. δ 6.28 (quartet of multiplets, 1H, $J_{4,3}$ 9Hz, $J_{4,5}$ 5 Hz; H4), 5.51 (doublet of multiplets, 1H, $J_{3,4}$ 9Hz; H3), 1.36 (C2-methyl), 1.30 (C8-H_3), 0.96 (C9-H_3).

1,7-Dimethyl-2,6-octadiene (91)

ν_{max} 1676, 833 cm^{-1}; n.m.r. δ 5.13 (2H, $W_{h/2}$ 22 Hz, C=CH), 2.00 (4H, $W_{h/2}$ 14 Hz, -CH_2-C=C), 1.68 (singlet, 6H, methyls); identical with an authentic sample[77].

1-Methylketone-2,2-dimethyl-3-cyclohexene (93)

ν_{max} 737, 1712 cm^{-1}, n.m.r. δ 5.57 (doublet of multiplets, 1H, $J_{4,3}$ 10Hz, H4), 5.33 (doublet of multiplets 1H, $J_{3,4}$ 10 Hz, H3), 2.54 (multiplet, 1H, W 19 Hz; H1), 2.17 (CO-CH_3), 1.13, 0.96 (C2-dimethyl). Found: C, 78.56; H, 10.81; $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

3-Vinyl-5-hepten-2-one (92)

ν_{max} 1715, 995, 920, 837 cm^{-1}; n.m.r. δ 6.12-5.10 (multiplet, 3H; C3 vinyl group protons), 5.03 (multiplet, 1H W 14 Hz; H5), 3.13 (quartet, 1H, $J_{3,1'} = J_{3,4a} = J_{3,4b}$ 7.5 Hz; H3), 2.12 (singlet, 3H; CO-CH_3), 1.66, 1.61 (singlets, total 6H, $W_{h/2}$ 3.5 Hz; C6 methyl, C7-H_3). Found: C, 78.5; H, 10.8. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%.

8-Methyl-3Z,7-nonadien-2-one (94)

ν_{max} 1697, 827, 668 cm^{-1}, λ_{max} 228 nm (ϵ 7150); n.m.r. δ 6.10 (multiplet, 2H, W 12 Hz; H1, H2), 5.14 (triplet of multiplets, 1H, $J_{7,6a} = J_{7,6b}$ 6.5 Hz, $J_{7,8\text{-methyl}} = J_{7,C9\text{-}H_3}$ small; H7), 2.65 (multiplet, 2H, W 23 Hz; $H_2$5) 2.18 (singlet, 3H; CO-CH_3), 2.11 ($H_2$6, located by double irradiation experiments), 1.68, 1.63 (singlets, total 6H, $W_{h/2}$ 3.5 Hz; C8 methyl, C9-H_3). Found: C, 78.6; H, 10.9. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%.

8-Methyl-3E,7-nonadien-2-one (95)

ν_{max} 1680, 977, 834 cm^{-1}, λ_{max} 223 nm (ϵ 8500); n.m.r. δ 6.82 (doublet of triplets, 1H, $J_{4,3}$ 16 Hz, $J_{4,5a} = J_{4,5b}$ 6.5 Hz; H4), 6.08 (doublet, 1H, $J_{3,4}$ 16 Hz; H9), 5.11 (multiplet, 1H, W 21 Hz; H7), 2.23 (singlet, 3H; CO-CH_3), 1.70, 1.62 (singlets, total 6H, $W_{h/2}$ 3.5 Hz; C8 methyl, C9-H3). Found: M^+ 152.1195. $C_{10}H_{16}O$ requires 152.1201.

8-Methyl-4Z,7-nonadien-2-one (96a)

ν_{max} 1715, 831, 709 cm^{-1}; n.m.r. δ 5.57 (multiplet, 2H, W 15 Hz; H4,H5, 5.12 (multiplet, 1H, W 22 Hz; H7), 3.17 (multiplet, 2H, W 18 Hz; $H_2$3, 2.73 (multiplet, 2H, W 21 Hz; $H_2$4), 2.13 (singlet, 3H; CO-CH_3), 1.70, 1.63 (singlets, total 6H, $W_{h/2}$ 4.5 Hz; C8 methyl, C9-H_3). Found: C, 78.6; H, 10.8. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%.

8-Methyl-4E,7-nonadien-2-one (96b)

ν_{max} 1715, 968, 831 cm^{-1}; n.m.r. δ 5.57 (multiplet, 2H, W 15 Hz; H4, H5), 5.12 (multiplet, 1H, W 22 Hz; H7), 3.17 (multiplet, 2H, W 18 Hz; $H_2$3), 2.73 (multiplet, 2H, W 21 Hz; $H_2$4). (95a and 95b) identified in admixture).

trans-Pinocarveol (98)

trans-Pinocarveol supplied by Ivon Watkins Dow Ltd, had $[\alpha]_D$ + 59° (c, 1.0), n.m.r. δ 4.99, 4.81 (multiplets, total 2H, $W_{h/2}$ 3 Hz; C=CH_2), 4.42 (doublet, 1H, $J_{3,4a}$ 7 Hz; H3), 1.28 (C8-H_3), 0.64 (C9-H_3).

Pinocarvone (99)

trans-Pinocarveol (98, 17.5 g) was stirred with active manganese dioxide (175 g) in pentane (750 ml) for 24 hrs. The MnO_2 was filtered off using celite and washed well with pentane. Evaporation of the solvent gave pinocarvone (16 g). ν_{max} 1630, 1711 cm^{-1}; n.m.r. δ 5.95, 4.98 (doublets, total

2H, $J_{a,b}$ 1.6 Hz; C=CH_2), 1.39 (C8-H_3), 0.82 (C9-H_3).

cis-Pinocarveol (97)

Bromine (25 g) in acetic acid (45 ml) was added dropwise to a stirred soln of pinocarvone (99, 23 g) in ether (140 ml) at 0-5°. The addition of bromine was stopped at the first sign of colouration of the reaction mixture. Isolation with ether gave a gum, which was redissolved in acetic acid (450 ml). The reaction vessel was immersed in an ice bath, and zinc powder (95 g) was added at such a rate that the temperature did not exceed 10°. The acetic acid was neutralised with an excess of sodium hydroxide soln (6 M). Isolation with ether gave an oil which was fractionally distilled to give cis-pinocarveol (11.8 g); ν_{max} 888, 3425 cm^{-1}; $[\alpha]_D$ -40° (c, 1.0); n.m.r. δ 5.08, 4.76 (multiplets, total 2H, $W_{h/2}$ 4 Hz; C=CH_2), 4.56 (multiplet, 1H, W 16 Hz; H3), 1.26 (C8-H_3), 0.73 (C9-H_3).

R-3-Methylene-7-methyl-1,6-octadien-4-ol (100a)

$[\alpha]_D$ + 36.7° (c, 1.05); ν_{max} 3025 cm^{-1}, λ_{max} (cyclohexane) 225.5 nm (ϵ 9100); n.m.r. δ 6.38 (quartet 1H, $J_{2,1\text{-cis}}$ 11 Hz, $J_{2,1\text{-trans}}$ 17.6 Hz; H2), 4.94-5.51 (multiplet 5H, W 32 Hz; H_21, H_23', H6), 4.41 (triplet 1H, $J_{4,5a}$ $J_{4,5b}$ 6 Hz; H4), 2.33 (multiplet 2H, W 21 Hz; H_25), 1.74 (doublet 3H, $J_{CH_3,6}$ 1 Hz; C8-H_3), 1.65 (singlet 3H; C7 methyl). Found: M^+ 152.1201. $C_{10}H_{16}O$ requires 152.1201.

cis-Carveol (101)

ν_{max} 3550, 888, 810 cm^{-1}; n.m.r. δ 5.47 (1H, $W_{h/2}$ 14 Hz; H2), 4.72 (2H, $W_{h/2}$ 3.5 Hz; $C{=}CH_2$), 4.18 (multiplet, 1H, W 26 Hz; H6), 1.75, 1.72 (total 6H; $C{=}C{-}CH_3$, C2-methyl), identical with an authentic sample.[78]

2-Methylene-3,6-dimethyl-5-heptenal (102)

The crude pyrolysis product (2 g) was adsorbed onto silica (100 g). Elution with 2% ether/pentane gave one fraction containing pure aldehyde (102, 100 mg); ν_{max} 2720, 1696 cm^{-1}; λ_{max} 218.5 nm (ϵ 5700); n.m.r. δ 9.55 (singlet, 1H; H1), 6.22 (triplet, 1H, $J_{a,b} = J_{a,3}$ 0.6 Hz; H_a), 5.98 (doublet, 1H, $J_{b,a}$ 0.6 Hz; H_b), 5.05 (triplet of quartets, 1H, $J_{5,4}$ 7.3 Hz, $J_{5,6\text{-}CH_3}$ 1 Hz; H5), 2.76 (sextet, 1H, $J_{3,Me} = J_{3,4ab}$ 7 Hz; H3), 2.05 (multiplet, 2H; $H_2$4), 1.67 (doublet, 3H, $J_{6\text{-}CH_3,5}$ 1 Hz; C6-CH_3), 1.59 (singlet, 3H; C7-H_3), 1.06 (doublet, 3H, $J_{3\text{-}CH_3,3}$ 6.8 Hz; C3-methyl). Found: M^+ 152.1195. $C_{10}H_{16}O$ requires 152.1201.

S-3-methylene-7-methyl-1,6-octadien-4-ol (100b)

$[\alpha]_D$ -35° (c,1.05), identical in all other respects with the epimeric hydroxy-triene (100a).

trans-Isocarveol (104)

ν_{max} 3380, 890 cm^{-1}, n.m.r. δ 4.82 (2H, $W_{h/2}$ 8 Hz; $H_2$7), 4.71 (2H, $H_2$10), 4.33 (triplet, 1H, $J_{2,3a} = H_{2,3b}$ 3.1 Hz; H2), 1.72 (triplet, 3H, J_{9,H_210} 1 Hz; C9-H_3), identical with

an authentic sample.[79]

trans-Carveol (105)

ν_{max} 3385, 889, 809 cm^{-1}, n.m.r. δ 5.58 (1H, W 13 Hz; H6), 4.73 (2H, $H_2$10), 4.01 (triplet, 1H, $J_{2,3a} = J_{2,3b}$ 3.0 Hz; H2), 1.75, 1.73 (total 6H; C7-H_3, C9-H_3), identical with an authentic sample.[78]

4-Deuteropinocarveol

A solution of pinocarvone (4.5 g) in tetrahydrofuran (20 ml) was added to sodium deuteroxide in deuterium oxide (1.5 ml; 10%) and the mixture stirred for two weeks. Isolation by means of ether gave deuterated pinocarvone shown by mass spectra to be 64% D_1, 15% D_2. Lithium aluminium hydride (3 g) in ether (200 ml) was added over 30 min. to a solution of the deuterated pinocarvone in ether (50 ml), and the mixture stirred at 20° for 1 hour. The crude product, of composition cis-pinocarveol (92%), trans-pinocarveol (8%), was pyrolysed.

3α-Deutero-cis-pinocarveol

To a solution of pinocarvone (5.1 g) in ether (50 ml) was added lithium aluminium deuteride (1 g) in ether (150 ml), and the mixture stirred at 20° for 12 hours. The crude product, isolated by means of ether, was shown (g.l.c.) to contain pinocarvone (39%), trans-pinocarveol (5%) and cis-pinocarveol (56%). 3α-Deutero-cis-pinocarveol (1.9 g), isolated by

chromatography on alumina, gave a n.m.r. spectrum in which the C3-H resonance (δ 4.56) was absent.

3β-Deuteroxy-β-pinene

cis-Pinocarveol (2 g) in dry ether (10 ml) was stirred rapidly for 2 mins with D_2O (3 x 1 ml). Extraction with ether gave the alcohol 95% deuterated (by n.m.r.).

cis-Carveol (101)

Carvone (103, 4.15 g) was stirred in dry ether (100 ml) while $LiAlH_4$ (1 g) in dry ether (30 ml) was added over 15 mins. Stirring was continued for 2 hrs when hydrolysis was carried out by the addition of $Na_2SO_4.10H_2O$, followed by water. The ether soln was decanted and dried. Evaporation of the solvent gave 3.8 g of cis-carveol (85%) and trans-carveol (15%). Preparative g.l.c. gave pure cis- carveol; ν_{max} 810, 888, 3550 cm^{-1}, n.m.r. δ 5.47 (multiplet, 1H, W 14 Hz; H2), 4.72 (multiplet, 2H, $W_{h/2}$ 3.5 Hz; $C=CH_2$), 4.18 (multiplet, 1H, W 26 Hz; H6), 1.75, 1.72 ($C=C-CH_3$, C2-methyl).

trans-Pinocarvyl acetate (106)

trans-Pinocarveol (98), 15 g, in acetic anhydride (30 ml) was brought to reflux when NaOH pellets (500 mg) were slowly and cautiously added. After a further 10 mins the mixture was cooled and poured into ether (200 ml) and stirred with Na_2CO_3 until neutral. The soln. was washed with water and

the ether layer dried. Evaporation of the solvent gave the crude acetate which was fractionally distilled to give trans-pinocarvyl acetate (14.5 g); ν_{max} 905, 1736 cm^{-1}, $[\alpha]_D$ -15° (c, 1.01), n.m.r. δ 5.88 (doublet, 1H, $J_{3,4a}$ 8 Hz; H3), 5.06, 4.88 (quartets ?, total 2H, $W_{h/2}$ 2.5 Hz; $C{=}CH_2$), 2.04 (acetate), 1.29 ($C8\text{-}H_3$), 0.70 ($C9\text{-}H_3$).

1-(2'-methyl-1'-propene)-1,3,Cyclohexadiene (63)

ν_{max} 695 cm^{-1}, n.m.r. δ 5.86 (4H, W 38 Hz; H2, H3, H4, H1'), 2.23 (multiplet, 4H; $H_2$5, $H_2$6), 1.82 (singlet ?, 6H; 2'-methyl, $C3'\text{-}H_3$, identical with an authentic sample.[88]

Perillyl acetate (107)

ν_{max} 1730, 885, 812 cm^{-1}, n.m.r. δ 5.72 (1H, $W_{h/2}$ 8 Hz; H2), 4.68 (2H, $W_{h/2}$ 3 Hz; $C{=}CH_2$), 4.38 (2H, $W_{h/2}$ 3 Hz; $H_2$7), 1.99 (OAc), 1.72 (triplet ?, 3H, J=J' 1 Hz; $C9\text{-}H_3$). Hydrolysis by $LiAlH_4$ gave perillyl alcohol (3b); ν_{max} 3325, 889 cm^{-1}, n.m.r. δ 5.73 (1H, $W_{h/2}$ 3 Hz; H2), 4.73 (2H, $W_{h/2}$ 3 Hz; $C{=}CH_2$), 4.00 (2H, $W_{h/2}$ 3 Hz; $H_2$7), 1.75 (triplet ?, 3H, J=J' 1 Hz; $C9\text{-}H_3$), identical with an authentic sample.[80]

S-4-Acetoxy-7-methyl-3-methylene-1,6-octadiene (108)

$[\alpha]_D$ + 10° (c, 1.01), ν_{max} 1743, 905 cm^{-1}, λ_{max} 223 nm (ϵ 10,220), n.m.r. δ 6.36 (quartet, 1H, $J_{2,1\text{-}cis}$ 11 Hz; $J_{2,1\text{-}trans}$ 18 Hz; H2), 5.23 (6H, W 40 Hz; $H_2$1, $C_3{=}CH_2$,

H4, H6), 2.42 (triplet, 2H; $H_2$5), 2.03 (OAc), 1.69, 1.61 (singlets, total 6H; C7-CH_3, C8-CH_3; Found: M^+ 194.1311. $C_{12}H_{18}O_2$ requires 194.1306.

3'-Acetoxy-7-methyl-2,4,6-octatriene (109)

ν_{max} 960, 1730 cm^{-1}, λ_{max} 278 nm (ϵ 21,000), n.m.r. δ 6.38 (doublet, 1H, $J_{4,5}$ 9 Hz; H4), 5.42-6.22 (multiplet, 3H; H2, H5, H6), 4.66 (singlet, 2H, $W_{h/2}$ 3 Hz; C3'-H_2), 1.98 (acetate), 1.81 (doublet, 3H, $J_{CH_3,2}$ 7 Hz; C1-H_3), 1.80 (singlet, 6H; C7-CH_3, C8-H_3). Found: M^+ 194.1312. $C_{12}H_{18}O_2$ requires 194.1306.

Myrtenol (18)

α-Pinene (136 g) in ethanol (200 ml) was heated under reflux and stirred while selenium dioxide (117 g), (which had previously been dissolved in ethanol (200 ml) by heating), was slowly added over 1 hr. The mixture was then heated under reflux for an additional 5 hr, cooled to room temperature and the metallic selenium filtered off. The filtrate was steam distilled and the distillate extracted with ether. The crude myrtenal (19) was added slowly to a stirred soln of sodium borohydride (25 g) in ethanol (250 ml). After 30 min water (50 ml) was added and the product was extracted with ether. The solvent was dried, evaporated, and distilled to give myrtenol (45 g); ν_{max} 805, 3350 cm^{-1}, n.m.r. δ 5.45 (multiplet, 1H, $W_{h/2}$ 6.5 Hz; H3), 3.95

(multiplet, 2H, $W_{h/2}$ 4 Hz; C2-methylene), 1.29 (C8-H_3), 0.83 (C9-H_3).

Perillyl alcohol (3b)

Myrtenol (18) was pyrolysed at 600° at a rate of 250 l/min, to give a product containing perillyl alcohol (35%), isolated by preparative g.l.c. ν_{max} 889, 3325 cm^{-1}, n.m.r. δ 5.73 (multiplet, 1H, $W_{h/2}$ 7 Hz; H2), 4.73 (singlet ?, 2H, $W_{h/2}$ 3 Hz; $H_2$10), 4.00 (singlet , 2H, $W_{h/2}$ 3 Hz; $H_2$7), 1.75 (triplet, 3H, J=J' 1 Hz; C9-H_3).

Nopinol (112)

To a stirred suspension of $LiAlH_4$ (4 g) in dry ether (100 ml) at -70°, was added dropwise a soln of nopinone (67, 30 g) in dry ether (50 ml). The mixture was stirred for 1/2 hr and then allowed to come to room temperature. The complex, and excess $LiAlH_4$, were hydrolysed by careful addition of $Na_2SO_4.10H_2O$, followed by addition of H_2O. The ether solution was decanted and dried. Evaporation and crystallisation from methanol gave nopinol (26 g) as needles; m.p. 100-101°; $[\alpha]_D$ -10.5° (c, 1.0); ν_{max} 3320 cm^{-1}; n.m.r. δ 4.28 (1H, multiplet, W 20 Hz; H2), 1.22 (C8-H_3), 1.12 (C9-H_3).

4,6-Dimethyl-5-heptenal (113)

ν_{max} 841, 1725, 2730 cm^{-1}; n.m.r. δ 9.75 (1H, triplet,

$J_{1,2ab}$ 1.6 Hz; H1), 4.85 (doublet of multiplets, $J_{5,4}$ 9.5 Hz; H5), 1.67, 1.58 (total 6H, doublets, $J_{CH_3,5}$ 1.3 Hz for both signals; C6-methyl, C7-H_3), 0.95 (3H, doublet $J_{4-CH_3,4}$ 6.5 Hz; C4-methyl). Measured 140.120057, $C_9H_{16}O$ requires 140.120109.

R-7-Methyl-1,6-octadien-5-ol (114)

ν_{max} 847, 911, 992, 3370 cm^{-1}; n.m.r. δ 5.87 (1H, multiplet, W 41 Hz; H2), 4.78-5.32 (3H, multiplet; H6, $H_2$1), 4.35 (1H, sextet, $J_{5,6}$ 9 Hz, $J_{5,4a}$ $J_{5,4b}$ 6.5 Hz; H5), 1.71, 1.66 (total 6H, doublets, $J_{CH_3,6}$ 1.3 Hz for both signals; C7-methyl, C8-H_3). Measured 140.120063, $C_9H_{16}O$ requires 140.120109.

R-7-Methyl-1,6-octadien-3-ol (115)

$[\alpha]_D$ -4° (c, 0.75); ν_{max} 841, 921,991, 3350 cm^{-1}; n.m.r. δ 5.93 (1H, octet, $J_{2,1}$ trans 17.3 Hz, $J_{2,1}$ cis 9.8 Hz, $J_{2,3}$ 5.9 Hz; H2), 4.97-5.42 (3H, multiplet; H6, $H_2$1) 4.12 (1H, quartet, $J_{3,2}$ $J_{3,4ab}$ 5.9 Hz H3), 1.70. 1.63 (total 6H, singlets, $W_{h/2}$ 5.5, 3.5 Hz resp.; C7-methyl, C8-H_3). Found: C, 76.79; H, 11.82; $C_9H_{16}O$ requires: C, 77.09; H, 11.50%.

1R,2S,3R-3-Isopropenyl-2-methyl-cyclopentan-1-ol (116)

ν_{max} 888, 3400 cm^{-1}; n.m.r. δ 4.73 (2H, multiplet, $W_{h/2}$ 3 Hz; C=CH_2), 4.12 (triplet, 1H, $J_{1,2}=J_{1,5a}$ 4 Hz; H1), 1.66 (triplet, 3H, J_{CH_3,CH_2} 1 Hz; C=C-CH_3), 0.95

(doublet, 3H, $J_{CH_3,2}$ 6.5 Hz; C2-methyl). Found: C, 77.18; H, 11.90; $C_9H_{16}O$ requires C, 77.09; H, 11.50%.

1R,2R,3S-3-Isopropenyl-2-methylcyclopentan-1-ol (117)

ν_{max} 888, 3350 cm^{-1}; n.m.r. δ 4.73 (multiplet, 2H, $W_{h/2}$ 3 Hz; $C=CH_2$), 3.75 (quartet, 1H, $J_{1,2}=J_{1,5a}=J_{1,5b}$ 7 Hz; H1), 1.68 (triplet, 3H, J_{CH_3,CH_2} 1 Hz; $C=C-CH_3$), 0.99 (doublet, 3H, $J_{CH_3,2}$ 6 Hz; C2-methyl). Found: C, 77.45; H, 11.85; $C_9H_{16}O$ requires C, 77.09; H, 11.50%.

1R,2R,3R-3-Isopropenyl-2-methylcyclopentan-1-ol (119)

ν_{max} 887, 3375 cm^{-1}; n.m.r. δ 4.81, 4.68 (multiplets, total 2H, $W_{h/2}$ 5 Hz; $C=CH_2$), 3.98 (multiplet, 1H, W 13 Hz; H1), 2.75 (multiplet, 1H, W 24 Hz; H3), 1.73 (singlet ?, 3H, $W_{h/2}$ 3.5 Hz; $C=C-CH_3$), 0.64 (doublet, 3H, $J_{CH_3,2}$ 6.9 Hz; C2-methyl). Measured: 140.119795; $C_9H_{16}O$ requires 140.120109.

1R,2S,3S-3-Isopropenyl-2-methylcyclopentan-1-ol (118)

ν_{max} 887, 3375 cm^{-1}; n.m.r. δ 4.85, 4.70 (multiplets, total 2H, $W_{h/2}$ 5 Hz; $C=CH_2$), 4.30 (multiplet, 1H, W 23 Hz; H1), 1.72 (singlet ?, 3H, $W_{h/2}$ 3 Hz;C $C-CH_3$), 0.70 (doublet, 3H, $J_{CH_3,2}$ 6.9 Hz; C2-methyl). Measured: 140.119791; $C_9H_{16}O$ requires 140.120109.

Oxidation of R-7-Methyl-1,6-octadien-3-ol (115)

The hydroxy-diene (115, 50 mg) in pentane (2 ml) was stirred with active MnO_2 (500 mg) for 24 hrs. Filtration and evaporation gave the dienone (68, 40 mg), identical to an authentic sample.

Oxidation of cyclopentanols

All oxidations of cyclopentanols were carried out on a 50-100 mg scale using the chromic acid/ether method of Brown outlined on p .

Reduction of 3-Isopropenyl-2-methylcyclopentan-1-one (71)

The ketone (71, 30 mg) in dry ether (1 ml) was added to a stirred soln of $LiAlH_4$ (20 mg) in dry ether (3 ml) at -70°. The mixture was allowed to come to room temperature and then worked up with $Na_2SO_4.10H_2O$ and water to give a cyclopentanol (98%) identical (g.l.c., n.m.r.) to 1R,2R,3S-3-isopropenyl-2-methyl-cyclopentan-1-ol (117).

2β-Deuteroxy-10-norpinane

Nopinol (112, 2 g) in dry ether (10 ml) was stirred rapidly for 2 mins with D_2O (3 x 1 ml). Extraction with ether gave the alcohol 93% deuterated (by n.m.r.).

2α-Deutero-nopinol

Nopinone (67, 2 g) in dry ether (10 ml) was added to

a soln of $LiAlD_4$ (500 mg) in dry ether (25 ml) at -70°, over 10 mins. The mixture was stirred for 1/2 hr and then allowed to come to room temperature. Work up in the usual way gave 2α-deutero-nopinol (1.7 g), >98% deuterated (by n.m.r.)

3-Deutero-nopinol

2-Acetoxy-10-norpin-2-ene (76, 2 g) in dry tetrahydrofuran (2 ml) was stirred with D_2O (4 ml) and sodium methoxide (1.5 g) for 2 days. Extraction with ether gave 3-deutero-nopinone (1.5 g) 82% deuterated (by mass spectra). Reduction of 3-deutero-nopinone (1.5 g) with $LiAlH_4$ (400 mg) at -70° as above, gave 3-deuteronopinol (1.2 g).

10α-Pinan-2-ol (42)

Nopinone (67, 30 g) in dry ether (50 ml) was added dropwise to a grignard reagent prepared by the addition of methyl iodide (30 ml) in dry ether (200 ml) to magnesium turnings (10 g). The mixture was heated under reflux for 1 hr and then hydrolysed by the dropwise addition of water. The alcohol was extracted with ether and the crude product adsorbed onto alumina (1000 g). Elution with 2% ether/pentane removed the nopinone impurity, and further elution with 10% ether/pentane gave pure 10α-pinan-2-ol (20 g); m.p. 56-57°; n.m.r. δ 1.26 (C2-methyl), 1.23, (C8-H_3), 1.12 (C9-H_3).

10β-Pinan-2-ol (43)

A soln of α-pinene oxide (22, 60 g) in dry ethylamine (150 ml) was treated portion-wise with lithium (10 g) and the mixture stirred vigorously for 6 hrs. The ethylamine was distilled off and the mixture decomposed with ice and water. The terpene material was extracted with ether, to give 57 g of a mixture of isopinocampheol (121, 69%) and 10β-pinan-2-ol (31%). Pure 10β-pinan-2-ol was obtained by fractional distillation; m.p. 75-76°; n.m.r. δ 1.29 (C2-methyl), 1.24($C8\text{-}H_3$), 0.94 ($C9\text{-}H_3$).

R-Linalool (44)

ν_{max} 3430, 997, 918, 837 cm^{-1}; n.m.r. δ 5.95 (quartet, 1H, $J_{2,1\text{-}cis}$ 10.3 Hz, $J_{2,1\text{-}trans}$ 17.4 Hz; H2), 5.41-4.92 (multiplet, 3H; H_21, H6), 1.68, 1.62 (6H, $W_{h/2}$ 3.5 Hz; $C8\text{-}H_3$, C7-methyl), 1.25 (singlet, 3H; C3-methyl); identical with an authentic sample.

1R,2R,3S-1,2-Dimethyl-3-isopropenylcyclopentan-1-ol (122)

ν_{max} 3470, 1640, 897 cm^{-1}; n.m.r. δ 4.73 (singlet ?, 2H, $W_{h/2}$ 2.5 Hz; $C{=}CH_2$), 1.67 (singlet, 3H, $W_{h/2}$ 3 Hz; $C{=}C\text{-}CH_3$), 1.27 (singlet, 3H; C1-methyl), 0.87 (doublet, 3H, $J_{CH_3,2}$ 6.5 Hz; C2-methyl); identified in admixture with R-linalool (44).

1R,2S,3S-1,2-Dimethyl-3-isopropenylcyclopentan-1-ol (125)

m.p. 38.5-39.5°; ν_{max} 3320, 1647, 885 cm^{-1}; n.m.r. δ 4.85, 4.72 (multiplets, total 2H, $W_{h/2}$ 4 Hz; $C{=}CH_2$), 2.56 (multiplet, 1H, $W_{h/2}$ 19 Hz; H3), 1.90 (H2, located by double irradiatiation experiments), 1.73 (singlet ?, 3H, $W_{h/2}$ 3 Hz; $C{=}C{-}CH_3$), 1.33 (singlet, 3H; C1-methyl), 0.78 (doublet, 3H, $J_{CH_3,2}$ 7.4 Hz; C2-methyl). Found: C, 77.5; H, 11.9. $C_{10}H_{18}O$ requires C 77.9; H, 11.8%.

1R,2S,3R-1,2-Dimethyl-3-isopropenylcyclopentan-1-ol (123)

ν_{max} 3425, 893 cm^{-1}; n.m.r. δ 4.71 (singlet ?, 2H, $W_{h/2}$ 3Hz; $C{=}CH_2$), 1.72 (singlet ?, 3H, $W_{h/2}$ 3 Hz; $C{=}C{-}CH_3$), 1.15 (singlet, 3H; C1-methyl), 0.87 (doublet, 3H, $J_{CH_3,2}$ 6.5 Hz; C2-methyl); identified in admixture with hydroxy-olefin (125).

1R,2R,3R-1,2-Dimethyl-3-isopropenylcyclopentan-1-ol (124)

m.p. 90-91°; ν_{max} 3340, 1648, 885 cm^{-1}; n.m.r. δ 4.82, 4.68 (multiplets, total 2H, $W_{h/2}$ 5 Hz; $C{=}CH_2$), 3.07 (multiplet, 1H, $W_{h/2}$ 21 Hz; H3), 1.92 (H2, located by double irradiation experiments), 1.72 (singlet ?, 3H, $W_{h/2}$ 3 Hz; $C{=}C{-}CH_3$), 1.28 (singlet, 3H, C1-methyl); 0.61 (doublet, 3H, $J_{CH_3,2}$ 7.4 Hz; C2-methyl). Found: C, 77.95; H, 11.8. $C_{10}H_{18}O$ requires C, 77.9; H, 11.8%.

5,7-Dimethyl-6-octen-2-one (126)

ν_{max} 1717, 847 cm^{-1}; n.m.r. δ 4.84 (doublet of multiplets, 1H, $J_{6,7\text{-methyl}} = J_{6,C8\text{-}H_3}$ 1.3 Hz, 9 Hz; H6), 2.37 (H5, located by double irradiation experiments), 2.10 (singlet, 3H; CO-CH_3), 1.68, 1.58 (doublets, total 6H, $J_{CH_3,6}$ 1.3 Hz; C7-methyl, C8-H_3), 0.93 (doublet, 3H, $J_{CH_3,5}$ 6.4 Hz; C5-methyl). Found: C, 77.5; H, 11.9. $C_{10}H_{18}O$ requires C, 77.9; H, 11.8%.

Reaction of the cis-Cyclopentanone (70) with Methyl Magnesium Iodide.

To a solution of the cis-cyclopentanone (70, 200 mg) in dry ether (2 ml) was added dropwise a solution of methyl magnesium iodide (from methyl iodide (0.4 ml) and magnesium (140 mg) in ether (2 ml), and the mixture heated under reflux for 1 hr. The crude product, isolated by means of ether, was shown (g.l.c. and n.m.r.) to consist of a mixture (96:4) of the hydroxy-olefins (125) and (124).

Reaction of the trans-Cyclopentanone (71) with Methyl Magnesium Iodide.

Reaction of the trans-cyclopentanone (71), as above, gave a mixture (2:3) of hydroxy-olefins (122) and (123).

3S,4S-3,7-Dimethyl-1,6-octadien-4-ol (128)

ν_{max} 834, 913, 994, 3440 cm^{-1}, n.m.r. δ 5.87 (octet, 1H,

$J_{2,1\ \underline{trans}}$ 18 Hz, $J_{2,1\ \underline{cis}}$, $J_{2,3}$ 9.5, 7.2 Hz; H2), 4.88-5.39 (multiplet, 3H, $H_2$1, H6), 3.49 (sextet, 1H, $J_{4,3}$ 7.5 Hz, $J_{4,5ab}$ 5.5 Hz; H4), 1.73 (doublet, 3H, $J_{\underline{cis}\text{-}CH_3,6}$ 1.3 Hz; C7-methyl), 1.64 (singlet ?, 3H, $W_{h/2}$ 2.5 Hz; C8-H_3), 1.05 (doublet, 3H, $J_{CH_3,3}$ 6.8 Hz; C3-methyl). Found: C, 77.60; H, 11.80. $C_{10}H_{18}O$ requires, C, 77.87; H, 11.76.

<u>1S,2S,3S,4R-2,3-Dimethyl-4-isopropenylcyclopentan-1-ol</u> (133)

ν_{max} 889, 3360 cm^{-1}; n.m.r. δ 4.82, 4.71 (multiplets, total 2H, $W_{h/2}$ 4.5 Hz; C=CH_2), 3.73 (sextet, 1H, $J_{1,2}$ 8.8 Hz, $J_{1,5ab}$ 6.6 Hz; H1), 1.70 (singlet ?, 3H, $W_{h/2}$ 3 Hz; C=C-CH_3), 1.07 (doublet, 3H, $J_{CH_3,H}$ 5.5 Hz; methyl), 0.83 (doublet, 3H, $J_{CH_3,H}$ 6.3 Hz; methyl). Found: C, 77.49; H, 11.91; $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

<u>1S,2S,3R,4S-2,3-Dimethyl-4-isopropenylcyclopentan-1-ol</u> (132)

ν_{max} 889, 3380 cm^{-1}; n.m.r. δ 4.75 (multiplet, 2H, $W_{h/2}$ 4 Hz; C=CH_2), 3.33 (multiplet, 1H, W 18 Hz; H1), 1.73 (singlet ?, 3H, $W_{h/2}$ 3Hz; C=C-CH_3), 0.98 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; methyl), 0.54 (doublet, 3H, $J_{CH_3,H}$ 6.8 Hz; methyl). Found: C, 77.5; H, 11.79. $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

<u>1S,2S,3S,4S-2,3-Dimethyl-4-isopropenylcyclopentan-1-ol</u> (131)

ν_{max} 889, 3360 cm^{-1}; n.m.r. δ 4.92, 4.65 (multiplets,

total 2H, $W_{h/2}$ 4 Hz; C=CH_2), 3.72 (quartet of multiplets, 1H, $J_{1,2} \simeq J_{1,5ab}$ 7.6 Hz; H1), 1.70 (singlet ? 3H, $W_{h/2}$ 3 Hz; C=C-CH_3), 1.02 (doublet, 3H, $J_{CH_3,H}$ 5.8 Hz; methyl), 0.83 (doublet, 3H, $J_{CH_3,H}$ 6.4 Hz; methyl). Found: C, 77.57; H, 11.84. $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

1S,2S,3R,4R-2,3-Dimethyl-4-isopropenylcyclopentan-1-ol (130)

ν_{max} 890, 3360 cm^{-1}; n.m.r. δ 4.73 (multiplet 2H, $W_{h/2}$ 2.5 Hz; C=CH_2), 3.78 (quartet of multiplets, 1H, $J_{1,2} \simeq J_{1,5ab}$ 6 Hz; H1), 1.65 (triplet, 3H, $J_{CH_3,C=CH_2}$ 1 Hz; C=C-CH_3), 1.05 (doublet, 3H, $J_{CH_3,H}$ 7 Hz; methyl). Found: C, 77.48; H, 11.95. $C_{10}H_{18}O$ requires, C, 77.87; H, 11.76.

4S,5S-5,7-Dimethyl-1,6-octadien-4-ol (129)

ν_{max} 843, 914, 987, 3425 cm^{-1}; n.m.r. δ 5.55-6.25 (multiplet, 1H; H2), 5.23, 5.07 (multiplets, total 2H, $W_{h/2}$ 4 Hz; $H_2$1), 4.97 (doublet of multiplets, 1H, $J_{6,5}$ 5 Hz; H6), 3.42 (octet, 1H, $J_{4,5}$, $J_{4,3a}$, $J_{4,3b}$ 8.9, 6.9, 4 Hz; H4), 1.72, 1.64 (doublets, total 6H, $J_{CH_3,6}$ 1.4 Hz; C7-methyl, C8-H_3), 1.00 (doublet, 3H, $J_{CH_3,5}$ 6.5 Hz; C5-CH_3). Measured: 154.135395. $C_{10}H_{18}O$ requires, 154.135758.

Neo-isoverbanol (135)

Verbenone (33, 20 g) in cyclohexane (40 ml) was stirred with PtO_2 (0.4 g) at room temperature under hydrogen until uptake of H_2 ceased. The soln was filtered and the solvent

removed to give crystalline neo-isoverbanol (19.5 g); m.p. 68-69°; n.m.r. δ 4.25 (multiplet, 1H, W 21 Hz; H4), 1.24 (C8-H_3), 1.20 (C9-H_3), 1.07 (doublet, J 6.5 Hz; C10-H_3).

3R,4S-3,4,6-Trimethyl-5-heptenal (138)

ν_{max} 852, 1728, 2720 cm^{-1}; n.m.r. δ 9.72 (triplet, 1H, $J_{1,2}$ 1.4 Hz; H1), 4.93 (doublet of multiplets, 1H, $J_{5,4}$ 9.5 Hz; H5), 1.66, 1.59 (doublets, total 6H, $J_{CH_3,H}$ 1.3 Hz; C6-methyl, C7-H_3), 0.95 (doublet, 6H, $J_{CH_3,H}$ 6 Hz; C3-methyl). Measured: 154.135395. $C_{10}H_{18}O$ requires 154.135758.

1S,2R,3R,4R-3,4-Dimethyl-2-isopropenylcyclopentan-1-ol (139)

ν_{max} 891, 3490 cm^{-1}; n.m.r. δ 5.09 (quartet, 1H, $J_{C=CH\ cis,CH_3}$ 1.5 Hz; C=C-H_{cis}), 4.79 (singlet ?, 1H, $W_{h/2}$ 4 Hz; C=C-H_{trans}), 4.13 (multiplet, 1H, W 16 Hz; H1), 1.79 (doublet, 3H, $J_{CH_3,C=C-H_{cis}}$ 1.3 Hz; C=C-CH_3), 1.07 (doublet, 3H, $J_{CH_3,H}$ 4 Hz; methyl), 0.93 (doublet, 3H, $J_{CH_3,H}$ 5 Hz; methyl). Found: C, 77.50; H, 11.80. $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

3S,5R-5,7-Dimethyl-1,6-octadien-3-ol (141)

ν_{max} 838, 917, 988, 3370 cm^{-1}; n.m.r. δ 5.88 (octet, 1H, $J_{2,1\ trans}$ 17.3 Hz, $J_{2,1\ cis}$, $J_{2,3}$ 5.4, 9.8 Hz; H2), 4.73-5.68 (multiplet, 3H; $H_2$1, H6), 4.81 (one half of H6 doublet of multiplets observable), 4.07 (multiplet, 1H, W 23 Hz; H3), 2.63 (multiplet, 1H, W 34 Hz; H5), 1.68

(doublet, 3H, $J_{\underline{cis}\text{-}CH_3,6}$ 1.4 Hz; C8-H_3), 1.63 (doublet, 3H, $J_{\underline{trans}\text{-}CH_3,6}$ 1.1 Hz; C7-methyl), 0.93 (doublet, 3H, $J_{CH_3,5}$ 6.5 Hz; C5-methyl). Measured: 154.135394. $C_{10}H_{18}O$ requires 154.135758.

3R,5S-3,7-Dimethyl-1,6-octadien-5-ol (142)

ν_{max} 833,912,993,3370 cm^{-1}; n.m.r. δ 5.74 (octet, 1H, $J_{2,1\ \underline{trans}}$ 17.4 Hz, $J_{2,1\ \underline{cis}}$ 9.6 Hz; H2), 4.81-5.22 (multiplet; $H_2$1, H6), 4.39 (octet, 1H, $J_{5,6}$, $J_{5,4ab}$ 8.8, 5.9, 7.5 Hz; H5), 2.32 (multiplet, 1H, W 34 Hz; H3), 1.69, 1.65 (doublets, total 6H, $J_{CH_3,6}$ 1.5 Hz; C8-H_3, C7-methyl), 1.00 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; C3-methyl). Found: C, 77.58; H, 11.81. $C_{10}H_{18}O$ requires C, 88.87; H, 11.76.

1S,2S,3S,4R-3,4-Dimethyl-2-isopropenylcyclopentan-1-ol (143)

ν_{max} 889, 3380 cm^{-1}; n.m.r. δ 4.93 (quartet, 1H, $J_{C=C-H\ \underline{cis},\ CH_3}$ 1.4 Hz; $C=CH_{\underline{cis}}$), 4.73 (singlet ?, 1H, $W_{h/2}$ 3.5 Hz; $C=CH_{\underline{trans}}$), 4.22 (sextet, 1H, $J_{1,2}$, $J_{1,5ab}$ 7.9, 7.9, 6.7 Hz; H1), 1.73 (doublet, 3H, J_{CH_3,CH_2} 1.2 Hz; $C=C-CH_3$), 1.07 (doublet, 3H, $J_{CH_3,H}$ 5.5 Hz; methyl), 0.74 (doublet, 3H, $J_{CH_3,H}$ 6.7 Hz; methyl). Found: C, 77.49; H, 11.96. $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

1S,2S,3S,4R-2,4-Dimethyl-3-isopropenylcyclopentan-1-ol(144)

ν_{max} 888, 3360 cm^{-1}; n.m.r. δ 4.88, 4.66 (singlets ?, total 2H, $W_{h/2}$ 4.5 Hz; $C=CH_2$), 3.90 (multiplet, 1H, W

14 Hz; H1), 1.71 (doublet, 3H, $J_{CH_3,C=CH_{cis}}$ 1 Hz; C=C-CH_3), 1.03 (doublet, 3H, $J_{CH_3,H}$ 5.5 Hz; methyl), 0.70 (doublet, 3H, $J_{CH_3,H}$ 6.7 Hz; methyl). Found: C, 77.63; H, 11.98. $C_{10}H_{18}O$ requires C, 77.87; H, 11.76.

Citronellal (140)

ν_{max} 830, 1725, 2740 cm^{-1}; n.m.r. δ 9.74 (triplet, 1H, $J_{1,2ab}$ 2.1 Hz; H1), 5.08 (triplet of multiplets, 1H, $J_{6,5ab}$ 7 Hz; H6), 1.68 (doublet, 3H, $J_{CH_3cis,6}$ 1.1 Hz; C7-methyl), 1.61 (singlet ?, 3H, $W_{h/2}$ 3 Hz; C8-H_3), 1.00 (doublet, 3H, $J_{CH_3,3}$ 6.2 Hz; C3-methyl), identical to an authentic sample.

Isopinocampheol (121)

Diborane, generated by the dropwise addition of boron trifluoride diethyl etherate (10 g) onto sodium borohydride (1.62 g) in diethylene glycol dimethyl ether (20 ml) under N_2, was passed into a solution of α-pinene (11 g) in tetrahydrofuran (75 ml) at 0°, by initiating a slow flow of N_2 through the diborane generator. After completion of the addition (2.5 hr), the generator was heated to 70° for 30 min to ensure complete transfer of diborane to the hydroboration flask. This flask was stood for 30 min at room temperature and the excess hydride was destroyed by careful addition of water (10 ml) to the stirred soln. The organoborane was oxidised at 30-50° by adding sodium hydroxide (8.5 ml, 3N) followed by dropwise addition of hydrogen

peroxide (8.5 ml, 30%). The warm reaction mixture was stirred for an additional hour, then extracted with ether, washed with water and dried. Evaporation of the solvent gave solid isopinocampheol (11.5 g); n.m.r. δ 4.05 (multiplet, 1H, W 23 Hz; H3), 1.31 (C8-H_3), 1.13 (doublet, 3H, $J_{CH_3,2}$ 6.8 Hz; C2-methyl).

Isopinocamphone (147)

A soln of isopinocampheol (11 g) in acetone (15 ml), was stirred at 0°, and chromic acid (18 ml, 8N) was added during 45 min. The mixture was stirred for a further 45 min during which time it came to room temperature. The soln was extracted with ether and washed with water. Evaporation of the dried soln gave the crude product. Fractional distillation gave pure isopinocamphone (8.5 g); n.m.r. δ 1.32 (C8-H_3), 1.21 (doublet, 3H, $J_{CH_3,2}$ 7.1 Hz; C2-methyl), 0.88 (C9-H_3).

3S-3,7-Dimethyl-1,6-octadien-4-one (148)

ν_{max} 846, 921, 996, 1718 cm^{-1}; n.m.r. δ 5.87 (septet, 1H, $J_{2,1\ trans}$ 17.5 Hz, $J_{2,1\ cis}$ 9 Hz, $J_{2,3}$ 8 Hz; H2), 4.97-5.37 (multiplet, $H_2$1, H6), 3.27 (quintet, 1H, J_{3,CH_3} 6.8 Hz, $J_{3,2}$ 8 Hz; H3), 3.20 (doublet of multiplets, 2H, $J_{5ab,6}$ 7 Hz; $H_2$5), 1.73 (doublet, 3H, $J_{CH_3,6}$ 1 Hz; C7-methyl), 1.62 (singlet, 3H, $W_{h/2}$ 3 Hz; C8-H_3), 1.16 (doublet, 3H, $J_{CH_3,3}$ 6.9 Hz; C3-methyl). Found: C, 78.96; H, 10.70. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

2S,3R,4R-2,3-Dimethyl-4-isopropenylcyclopentan-1-one (150)

ν_{max} 892, 1743 cm^{-1}; n.m.r. δ 4.90, 4.67 (multiplets, total 2H, $W_{h/2}$ 4.5 Hz; $C{=}CH_2$), 1.78 (singlet ?, 3H, $W_{h/2}$ 4 Hz; $C{=}C{-}CH_3$), 1.09 (doublet, 3H, $J_{CH_3,H}$ 7 Hz; methyl), 0.95 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; methyl). Found: C, 78.91; H, 10.69. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

2S,3S,4S-2,3-Dimethyl-4-isopropenylcyclopentan-1-one (151)

ν_{max} 892, 1742 cm^{-1}; n.m.r. δ 4.95, 4.69 (multiplets, total 2H, $W_{h/2}$ 4 Hz; $C{=}CH_2$), 1.81 (singlet ?, 3H, $W_{h/2}$ 3 Hz; $C{=}C{-}CH_3$), 1.03 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; methyl), 0.77 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; methyl). Found: C, 78.83; H, 10.67. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

2S,3R,4S-2,3-Dimethyl-4-isopropenylcyclopentan-1-one (152)

ν_{max} 893, 1745 cm^{-1}; n.m.r. δ 4.86 (singlet ?, 2H, $W_{h/2}$ 3 Hz; $C{=}CH_2$), 1.69 (triplet, 3H, J_{CH_3,CH_2} 1 Hz; $C{=}C{-}CH_3$), 1.08 (doublet, 6H, $J_{CH_3,H}$ 5 Hz; methyl). Measured: 152.119804. $C_{10}H_{16}O$ requires 152.120109.

2S,3S,4R-2,3-Dimethyl-4-isopropenylcyclopentan-1-one (153)

n.m.r. δ 5.00 (multiplet, 2H, $W_{h/2}$ 5 Hz; $C{=}CH_2$), 1.78 (singlet ?, 3H, $W_{h/2}$ 4 Hz; $C{=}C{-}CH_3$), 1.06 (doublet, 3H, $J_{CH_3,H}$ 7 Hz; methyl), 0.80 (doublet, 3H, $J_{CH_3,H}$ 6.5 Hz; methyl), (identified in admixture with cyclopentanone (154).

2S,3R,4S-2,4-Dimethyl-3-isopropenylcyclopentan-1-one (154)

ν_{max} 894, 1746 cm^{-1}; n.m.r. δ 4.88 (multiplet, 2H, $W_{h/2}$ 6 Hz; C=CH_2), 1.69 (triplet, 3H, J_{CH_3,CH_2} 1 Hz; C=C-CH_3), 1.03 (doublet, 3H, $J_{CH_3,H}$ 6 Hz; methyl), 0.99 (doublet, 3H, $J_{CH_3,H}$ 6 Hz; methyl). Found: C, 78.71; H, 10.83. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

5S-5,7-Dimethyl-1,6-octadien-4-one (149)

ν_{max} 844, 918, 993, 1719 cm^{-1}; n.m.r. δ 5.58-6.30 (multiplet, 1H, H2), 4.98-5.28 (multiplet, 2H, $H_2$1), 5.00 (doublet of multiplets, 1H, $J_{6,5}$ 8 Hz; H6), 3.45 (multiplet, 1H, W 25 Hz; H5), 3.18 (doublet of multiplets, 2H, $J_{3ab,2}$ 6.6 Hz, J' 1.25 Hz; $H_2$3), 1.69, 1.72 (doublets, total 6H, $J_{CH_3,6}$ 1.5 Hz; C8-H_3, C7-methyl), 1.10 (doublet, 3H, $J_{CH_3,5}$ 6.8 Hz; C5-methyl). Measured: 152.119824. $C_{10}H_{16}O$ requires 152.120109.

Base catalysed isomerisations of cyclopentanones.

Cyclopentanone (100 mg) in aqueous methanol (1 ml, 20:1) containing sodium hydroxide (100 mg) was shaken until the ketones came to equilibrium, when the yields of products was determined (g.l.c.).

trans-Verbenyl acetate (74)

Lead tetra-acetate (210 g), (humidified with 10-15% acetic acid), was added during 15 mins to a stirred soln of

freshly distilled α-pinene (64 g) and dry benzene (700 ml) maintained at 60-65°. The mixture was stirred at 60-65° for 2 hrs, cooled, and the resulting lead diacetate filtered. Water was added to the filtrate and the precipitated lead dioxide filtered. Evaporation of the dried benzene soln followed by fractional distillation gave verbenyl acetate (38 g); ν_{max} 1235, 1738 cm^{-1}; n.m.r. δ 5.33 (multiplet, total 2H, $W_{h/2}$ 4 Hz; H3, H4), 2.02 (acetate), 1.74 (C2-methyl), 1.35 (C8-H_3), 0.93 (C9-H_3).

trans-Verbenol (25)

trans-Verbenyl acetate (15 g) and potassium hydroxide (5 g) were stirred in aqueous methanol (50 ml, 15:1) for 5 mins. Extraction with ether followed by evaporation and distillation gave trans-verbenol (11 g); ν_{max} 824, 3379 cm^{-1}; n.m.r. δ 5.35 (multiplet, 1H, $W_{h/2}$ 5.5 Hz; H3), 4.29 (multiplet, 1H, $W_{h/2}$ 6.5 Hz; H4), 1.72 (doublet, 3H, $J_{CH_3,3}$ 1.5 Hz; C2-methyl), 1.33 (C8-H_3), 0.87 (C9-H_3).

Verbenone (33)

(a) trans-Verbenol (11 g) and active manganese dioxide (100 g) were refluxed in dry benzene (400 ml) for 45 mins. The mixture was filtered using celite, and the MnO_2 washed well with pentane. Evaporation of the solvent and distillation gave verbenone (9 g); ν_{max} 864, 1683 cm^{-1}; $[\alpha]_D$ -231° (c, 1.04); n.m.r. δ 5.73 (quartet, 1H, J_{3,CH_3}

1.5 Hz; H3), 2.01 (doublet, 3H, $J_{CH_3,3}$ 1.5 Hz; C2-methyl), 1.50 ($C8\text{-}H_3$).

(b) α-pinene (500 g) was kept at 80° for 100 hrs while air was bubbled through at ≈ 100 ml/min. Steam distillation reduced the hydroperoxides formed, and separated the volatiles from the residue. The crude verbenone/verbenol mixture was stirred at 0° in acetic acid (100 ml) while sodium dichromate (40 g) in acetic acid (100 ml) was added dropwise. After completion of the addition the mixture was stirred for 30 min. The mixture was poured into water and extracted with ether. After neutralization over sodium carbonate the soln was dried and the solvent evaporated. Fractional distillation gave verbenone (40 g).

cis-Verbanone (36)

Verbenone (19 g) in cyclohexane (40 ml) was stirred with PtO_2 (0.2 g) at room temperature under hydrogen until the uptake of H_2 slowed markedly. Filtration of the soln and removal of the cyclohexane gave an oil, 80% cis-verbanone and 20% neo-iso verbanol (135) (by g.l.c.) The mixture (19 g) was chilled in ether (50 ml) to 0°. Chilled chromic acid soln[82] (25 ml) was added over 5 mins. Then another 25 ml of chilled acid soln was added over 5 mins. Stirring was continued for 5 min, then the upper layer allowed to separate. The aqueous layer was extracted with ether (2 x 25 ml), and the combined ether extracts were washed with

sodium carbonate soln (5%), then with water. The soln was dried and the solvent removed to give crude cis-verbanone (18 g). Distillation gave pure cis-verbanone (15 g); n.m.r. δ 1.34 (C8-H_3), 1.17 (doublet, 3H, $J_{CH_3,2}$ 6.5 Hz; C2-methyl), 1.00 (C9-H_3).

5R-5,7-Dimethyl-1,6-octadien-3-one (156)

ν_{max} 840, 1690 cm^{-1}; λ_{max} (cyclohexane) 208 nm (ϵ 9050); n.m.r. δ 6.18-6.41 (multiplet, 2H; $H_2$1), 5.77 (quartet, 1H, $J_{2,1\ trans}$ 8.4 Hz, $J_{2,1\ cis}$ 3.9 Hz; H2), 4.93 (doublet of multiplets, 1H, $J_{6,5}$ 9 Hz; H6), 2.97 (multiplet, 1H, W 27 Hz; H5), 1.64, 1.63(doublets, total 6H, $J_{CH_3,6}$ 1.5 Hz; C7-methyl, C8-H_3), 0.97 (doublet, 3H, $J_{CH_3,5}$ 6.5 Hz; C5-methyl). Measured: 152.119811. $C_{10}H_{16}O$ requires 152.120109.

3R-3,7-Dimethyl-1,6-octadien-5-one (157)

ν_{max} 914, 995, 1690 cm^{-1}; λ_{max} (cyclohexane) 234 nm (ϵ 7460); n.m.r. δ 6.06 (multiplet, 1H, $W_{h/2}$ 4.5 Hz; H6), 5.80 (octet, 1H, $J_{2,1\ trans}$ 17.9 Hz, $J_{2,1\ cis}$, $J_{2,3}$ 6.3, 9.8 Hz; H2), 4.78-5.17 (multiplet 2H; $H_2$1), 2.12 (doublet, 3H, $J_{trans\text{-}CH_3,6}$ 1.1 Hz; C7-methyl), 1.87 (doublet, 3H, $J_{cis\text{-}CH_3,6}$ 1.3 Hz; C8-H_3), 1.02 (doublet, 3H, $J_{CH_3,3}$ 6.5 Hz; C3-methyl). Found: C, 98.50; H, 10.93. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

2S,3S,4R-3,4-Dimethyl-2-isopropenylcyclopentan-1-one (158)

ν_{max} 893, 1754 cm^{-1}; n.m.r. δ 4.90 (multiplet, 2H, $W_{h/2}$ 6.5 Hz; C=CH_2), 1.69 (doublet, 3H, $J_{CH_3,C=CH\ cis}$ 1.1 Hz; C=C-CH_3), 1.05 (doublet, 3H, $J_{CH_3,H}$ 5 Hz; methyl), 1.00 (doublet, 3H, $J_{CH_3,H}$ 6 Hz; methyl). Found: C, 78.56; H, 10.85. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

2S,3S,4R-2,4-Dimethyl-3-isopropenylcyclopentan-1-one (159)

ν_{max} 894, 1744 cm^{-1}; n.m.r. δ 4.96 (quartet, 1H, $J_{C=CH_{cis},CH_3}$ 1.3 Hz; C=CH_{cis}), 4.73 (singlet ?, 1H, $W_{h/2}$ 3.5 Hz; C=CH_{trans}), 1.70 (doublet, 3H, $J_{CH_3,C=CH_{cis}}$ 1.3 Hz; C=C-CH_3), 1.12 (doublet, 3H, $J_{CH_3,H}$ 5 Hz; methyl), 0.87 (doublet, 3H, $J_{CH_3,H}$ 7 Hz; methyl). Found: C, 78.62; H, 10.42. $C_{10}H_{16}O$ requires C, 78.90; H, 10.59.

3R,4S-3-Methyl-4-isopropenylcyclohexan-1-one (37)

ν_{max} 892, 1715 cm^{-1}; n.m.r. δ 4.88, 4.65 (multiplets, total 2H, $W_{h/2}$ 4 Hz; C=CH_2), 1.79 (singlet ?, 3H, $W_{h/2}$ 3 Hz; C=C-CH_3), 0.77 (doublet, 3H, $J_{CH_3,3}$ 7 Hz; C3-methyl).

7-Methyl-1,6-octadien-5-one (155)

ν_{max} 808, 914, 1694 cm^{-1}; λ_{max} (cyclohexane) 237 (ϵ 5000); n.m.r. δ 6.08 (multiplet, 1H, $W_{h/2}$ 4.5 Hz; H6), 5.75 (multiplet, 1H, W 2.5 Hz; H2), 4.82-5.24 (multiplet, 2H; H_21), 2.15 (doublet, 3H, $J_{trans\text{-}CH_3,6}$ 1.1 Hz; C7-methyl), 1.88 (doublet, 3H, $J_{cis\text{-}CH_3,6}$ 1.1 Hz; C8-H_3). Found: C, 78.59; H, 10.51. $C_9H_{14}O$ requires 78.21; H, 10.21.

7-Methyl-1,6-octadien-3-one (68)

ν_{max} 830, 1688 cm^{-1}; λ_{max} (cyclohexane) 215 (ϵ 4970); n.m.r. δ 6.20-6.42 (multiplet; $H_2$1), 5.78 (quartet, 1H, $J_{2,1\ cis}$ 4 Hz, $J_{2,1\ trans}$ 8 Hz; H2), 5.10 (multiplet, 1H, W 21 Hz; H6), 1.68 (doublet, 3H, $J_{cis\text{-}CH_3,6}$ 1.2 Hz; C8-H_3), 1.63 (singlet, 3H, $W_{h/2}$ 4 Hz; C7-methyl).

trans-2-Methyl-3-isopropenylcyclopentan-1-one (71)

ν_{max} 893, 1745 cm^{-1}; n.m.r. δ 4.84 (multiplet, 2H, $W_{h/2}$ 3.5 Hz; C=CH_2), 1.76 (triplet, 3H, J_{CH_3,CH_2} 1 Hz; C=C-CH_3), 1.05 (doublet, 3H, $J_{CH_3,2}$ 6 Hz; C2-methyl).

cis-2-Methyl-3-isopropenylcyclopentan-1-one (70)

ν_{max} 898, 1745 cm^{-1}; n.m.r. δ 4.89, 4.73 (multiplets, total 2H, $W_{h/2}$ 4 Hz; C=CH_2), 2.85 (quintet, 1H, J_{2,CH_3} $J_{2,3}$ 7.4 Hz; H2), 1.71 (singlet ?, 3H, $W_{h/2}$ 3.5 Hz; C=C-CH_3), 0.89 (doublet, 3H, $J_{CH_3,2}$ 7.4 Hz; C2-methyl).

4-Isopropenylcyclohexan-1-one (69)

ν_{max} 890, 1720 cm^{-1}; n.m.r. δ 4.78 (quartet, 2H, J_{CH_2,CH_3} 1.1 Hz; C=CH_2), 1.77 (triplet, 3H, J_{CH_3,CH_2} 1.1 Hz; C=C-CH_3).

Verbenene (61)

trans-Verbenyl acetate (74, 10 g) was refluxed in acetic anhydride (25 ml) containing potassium hydroxide (3 g) for 2 hrs. The mixture was poured into water and extracted with

ether. After neutralizing and drying, the solvent was evaporated. The crude product was distilled to give pure verbenene (7 g); $[\alpha]_D$ + 98° (c, 1.08); ν_{max} 888 cm^{-1}; n.m.r. δ 6.30 (quartet, 1H, $J_{4,3}$ 8.5 Hz, $J_{4,5}$ 5.5 Hz; H4), 6.03 (doublet, 1H, $J_{3,4}$ 8.5 Hz; H3), 4.67 (singlet, 2H, $W_{h/2}$ 2 Hz; C2-methylene), 1.39 (C8-H_3), 0.87 (C9-H_3).

Photolysis of Verbenene

Verbenene (4 g) and benzophenone (1 g) in pentane (500 ml), were irradiated under nitrogen for 20 hrs using a Hanovia 450W 7936A lamp and a pyrex filter, to give a 90% conversion to o-1,(7),2,8-menthatriene (62) which was purified by preparative g.l.c; $[\alpha]_D$ + 5° (c, 1.5); ν_{max} 888, 1648 cm^{-1}; λ_{max} (cyclohexane) 232 nm (ϵ 18,000); n.m.r. δ 6.17 (doublet of multiplets, 1H, $J_{2,3}$ 9.5 Hz; H2), 5.82 (multiplet, 1H, W 21 Hz; C1-methylene), 4.78 (multiplet, 2H, $W_{h/2}$ 3.5 Hz; C8-methylene), 3.02 (triplet, 1H, $J_{6,5ab}$ 6.5 Hz; H6), 1.71 (doublet, 3H, $J_{CH_3,C=CH\ cis}$ 1.5 Hz; C8-methyl), identical to an authentic sample.

Hydrogenation of o-1(7),2,8-menthatriene (62)

The triene (62, 450 mg) in ethanol (10 ml) was stirred with 10% palladium on charcoal (50 mg) under hydrogen for 7 hrs when uptake of H_2 ceased. Filtration and evaporation gave an oil consisting of two components (60:40 by g.l.c.). The major product was isolated by preparative g.l.c. and

identified as trans-o-menthane (160); ν_{max} 1372, 1379, 1389, 2857, 2874, 2924, 2959 cm^{-1}; n.m.r. δ (CCl_4) 0.73, 0.85 (doublets, total 6H, $J_{CH_3,H}$ 7 Hz; isopropyl methyls), 0.88 (doublet, 3H, $J_{CH_3,H}$ 8 Hz; methyl), identical to an authentic sample.[89]

4-Methylverbenene (161)

Methyl iodide (16 g) in dry ether (60 ml) was added to magnesium turnings (2.8 g) in a dry flask, flushed with nitrogen. The mixture was refluxed for 45 mins to complete the formation of the grignard reagent. Verbenone (4 g) in dry ether (60 ml) was added cautiously to the grignard reagent and the mixture was refluxed for 1 hr. The complex was then hydrolysed by the careful dropwise addition of water. The product was extracted with pentane (500 ml), washed with water and dried. The solvent was carefully evaporated from a 25 ml portion of the soln and spectra were run immediately; $[\alpha]_D$ -5.6° (c, 0.9); ν_{max} 871 cm^{-1}; n.m.r. δ 5.72 (multiplet, 1H, $W_{h/2}$ 5 Hz; H3), 4.50 (singlet ?, 2H, $W_{h/2}$ 2.5 Hz; C2-methylene), 1.77 (C4-methyl), 1.34 (C8-H_3), 0.80 (C9-H_3), identical to an authentic sample.[90]

Photolysis of 4-Methylverbenene (161)

4-Methylverbenene ($\approx$ 3.8 g) in pentane soln direct from the grignard reaction, and benzophenone (2 g) were irradiated under the same conditions as above for verbenene. After

1 hr the reaction vessel was lined with precipitated benzophenone pinacol and photolysis of the diene (161) ceased. Analysis by g.l.c. and preparative g.l.c. showed the product to consist of 4-methylverbenene (67%) and 2,4-dimethyl-isopropenylbenzene (162, 33%); ν_{max} 823, 877, 897 cm^{-1}; n.m.r. δ 6.97 (singlet, 3H, $W_{h/2}$ 1.5 Hz; aromatic protons), 5.15, 4.81 (multiplets, total 2H, $W_{h/2}$ 5 Hz; $C{=}CH_2$), 2.29 (singlet, 6H; methyls), 2.01 (multiplet, 3H, $W_{h/2}$ 2.5 Hz; $C{=}C{-}CH_3$), (lit. 92).

2,4-Dimethylcumene (163)

ν_{max} 817, 876 cm^{-1}; n.m.r. δ 7.08 (multiplet, 3H, W 24 Hz; aromatic protons), 3.12 (septet, 1H, $J_{H,\text{isopropyl methyls}}$ 7 Hz; isopropyl H), 2.28 (singlet, 6H; methyls), 1.20 (doublet, 6H, $J_{\text{isopropyl methyls},H}$ 7 Hz; isopropyl methyls), (lit. 91).

3β-Bromonopinone (164)

Bromine (0.15 ml; 1.07 mole) in carbon tetrachloride (2 ml) was added over 5 mins to a stirred soln of 500 mg of 2-acetoxy-10-norpin-2-ene (76) in carbon tetrachloride (2.5 ml) at 0°, and the resulting soln was kept at 0° for a further 5 mins. Isolation of the terpene material by means of ether, and crystallization from methanol gave 3β-bromonopinone (448 mg); m.p. 109.5-110.5°; $[\alpha]_D$ + 19° (c, 1.06); ν_{max} (CCl_4) 1734 cm^{-1}; λ_{max} 291 nm (ϵ 55);

c.d. $\Delta\epsilon$ +3.14 (287 nm), $\Delta\epsilon$ -1.5 (216 nm); n.m.r. δ 4.83 (C3-H), 1.38 (C8-H_3), 0.88 (C9-H_3).

3α-Bromonopinone (165)

Bromine (0.3 ml; 1.07 mole) in carbon tetrachloride (4 ml) was added over 5 mins to a stirred suspension of sodium carbonate (1 g; anhydrous) in a solution of 2-acetoxy-10-norpin-2-ene (76, 1.05 g) in carbon tetrachloride (4 ml) at 0°, and the resulting suspension kept at 0° for a further 5 mins. Isolation, as above, and crystallization from methanol gave 3α-bromonopinone (990 mg); m.p. 69.5-70.0°; $[\alpha]_D$ + 146° (c, 1.05); ν_{max} (CCl_4) 1730 cm^{-1}; λ_{max} 313 nm (ϵ 81); c.d. $\Delta\epsilon$ + 1.30 (312 nm), $\Delta\epsilon$ -0.97 (230 nm); n.m.r. δ 4.48 (C3-H), 1.38 (C8-H_3), 0.84 (C9-H_3). Found: C, 49.7; H, 6.05; Br, 37.4. $C_9H_{13}BrO$ requires C, 49.8; H, 6.0; Br, 36.8%.

Hydrogen Bromide Catalysed Reaction of 3α-Bromonopinone (165)

3α-Bromonopinone (2 g) in carbon tetrachloride (10 ml) was shaken with hydrogen bromide/acetic acid (2 ml; 50 w/v) for 10 mins. The crude product, isolated by means of ether, was shown by g.l.c. to consist of two major components, 3β-bromonopinone (164, 33%) and p-isopropyl phenol (166, 31%), and 11 minor components (total 36%). The p-isopropylphenol (166) was isolated by preparative g.l.c.; ν_{max} 3310, 830 cm^{-1} (1,4-disubstituted benzene); n.m.r. δ 7.08 (doublet,

2H, J 8.5 Hz; aromatic H), 6.75 (doublet, 2H, J 8.5 Hz; aromatic H), 2.83 (septet, 1H, J 6.8 Hz; isopropyl H), 1.20 (doublet, 6H, J 6.8 Hz; $-(CH_3)_2$), (lit. 83); ν_{max} 3310, 830 cm^{-1}.

Attempted Dehydrobromination of 3α-Bromonopinone (165)

(i) The ketone (165, 400 mg) was added to a suspension of lithium carbonate (500 mg) in dry dimethylformamide (5 ml) at 153°, and the mixture heated under reflux for 2 hrs. The crude product, isolated by means of ether, was shown (g.l.c.) to be a mixture (1:1) of the 3α- and 3β-bromonopinones (165 and 164).

(ii) A solution of the ketone (165, 200 mg) in collidine (2.5 ml) was heated under reflux for 8 hrs. The crude product, isolated by means of ether, was shown (g.l.c.) to consist of 3β-bromonopinone (164, 50%), 3α-bromonopinone (165, 30%), nopinone (67, 13%), and apoverbenone (167, 7%).

(iii) The ketone (165, 480 mg) was added to methanol (10 ml) containing sodium methoxide (1.5 g), and the mixture heated under reflux for 3 hrs. The crude product, isolated by means of ether, was shown (g.l.c.) to consist of nopinone (67, 78%), 3α-bromonopinone (165, 19%), and 3β-bromonopinone (164, 3%).

(iv) Reaction at reflux of the ketone (165, 400 mg) with potassium t-butoxide in t-butanol for 15 mins, gave a crude product shown (g.l.c.) to be essentially pure nopinone (67).

The Benzene-sulphonylhydrazone of Nopinone (168)

Nopinone (5 g) was added to a mixture of benzene-sulphonylhydrazine (6.23 g, 1 mole) and p-toluenesulphonic acid (50 mg) in warm absolute methanol (10 ml). The solution was warmed at 60° for 10 mins, then left for 10 mins when crystallisation was induced. After standing in an ice bath the crystals were collected and washed briefly with cold petroleum ether. Recrystallisation from methanol gave the hydrazone (168, 9.1 g), as needles; m.p. 133-135°; $[\alpha]_D$ + 32°(c, 1.0); ν_{max} 1020 (S=O), 1450 (C=N), 3245 cm^{-1} (N-H); n.m.r. δ 8.12-7.43 (multiplet, 6H; aromatic protons); 1.21 (C8-H_3), 0.62 (C9-H_3). Found: C, 61.33; H, 6.65; N, 9.26; S, 10.64. $C_{15}H_{20}N_2SO_2$ requires C, 61.62; H, 6.89; N, 9.58; S, 10.97%.

Decomposition of the Hydrazone (168)

(i) The hydrazone (168, 3.3 g) was dissolved in a minimum amount of absolute methanol ($\approx$ 4 ml) and to this soln was added NaOMe (700 mg, 1.15 mole). The contents of the flask were warmed until all the solid was dissolved and then the methanol was removed at reduced pressure. The sodium salt of the sulphonyl hydrazone was heated in an oil bath to 170°. No further decomposition was observed after 5 mins. The products of decomposition were removed under reduced pressure as they were formed, and collected in a dry ice/acetone trap. Isolation of the product from the

small amount of methanol in the trap gave apopinene (169, 970 mg, 70%), (lit. 84); ν_{max} 721 cm^{-1}; n.m.r. δ 6.15 (multiplet, 1H, W 22 Hz; H2), 5.54 (doublet of multiplets, 1H, $J_{2,3}$ 9 Hz; H3), 1.28 ($C8\text{-}H_3$), 0.90 ($C9\text{-}H_3$).

(iia) The hydrazone (168, 2.5 g) was added to a soln of sodium metal (750 mg) in digol (20 ml) and stirred in an oil bath at 170°. The top of the condensor was connected to a tube immersed in water so that N_2 evolution could be observed. When no more N_2 was evolved (2.5 hrs) the product was isolated with pentane. The crude product (816 mg, 78%) was separated by preparative g.l.c. into apopinene (169, 81%) and 4-isopropenylcyclohexene (170, 19%), (lit 85); ν_{max} 889, 725 cm^{-1}; n.m.r. δ 5.70 (multiplet, 2H, $W_{h/2}$ 3.5 Hz; H1,H2), 4.72 (quartet ?, 2H, $W_{h/2}$ 2.5 Hz; $C{=}CH_2$), 1.74 (triplet, 3H, J_{CH_3,CH_2} 1.1 Hz; methyl).

(iib) The hydrazone (168, 900 mg) was added to a soln of NaOH (1 g) in water/digol (1:6, 20 ml) and stirred in an oil bath at 160°. The reaction was followed as in (iia). The crude product was found by g.l.c. analysis to be apopinene (169, 81.5%) and 4-isopropenylcyclohexene (170, 18.5%).

Lead tetraacetate Oxidation of Apopinene (169)

Apopinene (10 g) in dry benzene (150 ml) was stirred while lead tetraacetate was added over 15 mins. The mixture was refluxed for 3 hrs, then cooled. Stirring was

continued overnight. The mixture was filtered to remove the lead diacetate formed and then water was added to the filtrate to precipitate any lead dioxide formed. The filtered, neutralized, dried benzene soln was evaporated and the residue fractionally distilled to give apopinene (500 mg), trans-apoverbenyl acetate (171, 5 g), (lit. 86); $[\alpha]_D$ + 75.9° (c, 1.08); ν_{max} 732, 1238, 1720 cm^{-1}; n.m.r. δ 6.45 (multiplet, 1H, W 18 Hz; H2), 5.62 (doublet of multiplets, 1H, $J_{3,2}$ 10 Hz; H3), 5.40 (multiplet, 1H, $W_{h/2}$ 6 Hz; H4), 2.03 (3H; acetate), 1.35 (C8-H_3), 0.97 (C9-H_3); and 2α,3α-diacetoxy-6,6-dimethylnorpinane (172, 2.1 g), (lit. 86); $[\alpha]_D$ -17.1° (c, 1.2); ν_{max} 1242, 1720 cm^{-1}; n.m.r. δ 5.21 (multiplet, 2H, W 25 Hz; H2, H3), 2.06 (3H; acetate), 2.01 (3H; acetate), 1.26 (C8-H_3), 0.98 (C9-H_3).

trans-Apoverbenol (173)

Apoverbenyl acetate (171, 4 g) was placed in a soln of KOH (1.5 g) in aqueous methanol (15 ml, 15:1). Analysis by g.l.c. showed that the acetate was quantitatively hydrolysed within 5 mins. Isolation with ether gave trans-apoverbenol (3 g); (lit. 86); $[\alpha]_D$ + 71.4° (c, 0.3); ν_{max} 726, 3335 cm^{-1}; n.m.r. δ 6.33 (multiplet, 1H, W 18.5 Hz; H2), 5.64 (doublet of multiplets, 1H, $J_{3,2}$ 9 Hz; H3), 4.33 (multiplet, 1H, $W_{h/2}$ 7.5 Hz; H4) 1.34 (C8-H_3), 0.91(C9-H_3).

Apoverbenone (167)

trans-Apoverbenol (173, 2.85 g) and activated MnO_2 (30 g) were refluxed in dry benzene (125 ml) for 45 mins. The MnO_2 was filtered off using celite, and washed well with ether. Removal of the solvent gave apoverbenone (2.54 g), (lit. 86,87); $[\alpha]_D$ + 129.2° (c, 1.12); ν_{max} 728, 1694 cm^{-1}; n.m.r. δ 7.53 (quartet, 1H, $J_{2,3}$ 9 Hz, $J_{2,1}$ 6 Hz; H2), 5.94 (doublet of triplets, 1H, $J_{3,2}$ 9 Hz, J' 1.4 Hz; H3), 1.52 (C8-H_3), 1.04 (C9-H_3).

cis-Apoverbenol (174)

Apoverbenone (167, 100 mg) in dry ether (2 ml) was added dropwise to $LiAlH_4$ (50 mg) in dry ether (2 ml) at room temperature. The solution was stirred for 30 mins when hydrolysis with $Na_2SO_4.10H_2O$ was carried out. The soln was decanted, dried and evaporated to give a crude product analysed by g.l.c. as cis-apoverbenol (98%) and trans-apoverbenol (173, 2%). Crystallisation from pentane gave cis-apoverbenol (95 mg); m.p. 86-86.5°; $[\alpha]_D$ -9.2° (c, 0.67); ν_{max} 738, 3288 cm^{-1}; n.m.r. δ 6.33 (quartet of multiplets, 1H, $J_{2,3}$ 9 Hz; H2), 5.69 (doublet of quartets, 1H, $J_{3,2}$ 9 Hz, J' 2 Hz, J" 1.5 Hz; H3), 4.53 (multiplet, 1H, $W_{h/2}$ 6 Hz; H4), 1.36 (C8-H_3), 1.12 (C9-H_3).

6,6-Dimethylnorpinan-2α,3α-diol (175)

Aqueous methanol (1.5 ml, 15:1) containing KOH (75 mg) was added to the diacetate (172, 200 mg). The mixture was

briefly stirred then isolated with ether to give the crude diol (175, 110 mg); ν_{max} 3325 cm^{-1}; n.m.r. δ 3.98 (multiplet, 4H, $W_{h/2}$ 6 Hz; H2,H3, C2-OH, C3-OH), 1.23 (C8-H_3), 0.87 (C9-H_3).

2,(10)-Epoxy-10β-pinan-3β-ol (176)

cis-Pinocarveol (97, 340 mg) was added to an ice cold soln of m-chloroperoxybenzoic acid (1 g) in ether (12 ml). The mixture was kept at 4° for 48 hrs and then washed quickly with cold sodium hydroxide soln (1 M) until the washings no longer coloured starch-iodide paper. Evaporation of the solvent gave 2,10-epoxy-10β-pinan-3β-ol (340 mg); n.m.r. δ (CCl_4) 4.23 (triplet, 1H, $J_{3,4ab}$ 8.5 Hz; H3), 3.23, 2.40 (AB quartet, 2H, J_{AB} 5 Hz; $C^{O}\!\!\diagdown\!\!CH_2$), 1.26 (C8-$H_3$), 0.92 (C9-$H_3$).

3α-Deutero-2(10)-pinen-3β-ol

A soln of pinocarvone (99, 5.1 g) in dry ether (50 ml) was added dropwise to a stirred suspension of $LiAlD_4$ (1 g) in dry ether (150 ml). The mixture was stirred at 20° for 16 hrs. Isolation with ether gave a crude product shown (g.l.c.) to contain pinocarvone (39%), trans-pinocarveol (4%), and cis-pinocarveol (57%). The mixture was adsorbed onto alumina (250 g). Elution with pentane/ether (3:1) gave fractions containing pinocarvone. Elution with ether gave pure (g.l.c.) 3α-deutero-2(10)-pinen-3β-ol (1.9 g);

ν_{max} 888, 3425 cm^{-1}; n.m.r. δ 5.08, 4.76 ($C=CH_2$), 1.26 ($C8-H_3$), 0.73 ($C9-H_3$).

3α-Deutero-2(10)-epoxy-10β-pinan-3β-ol (177)

3α-Deutero-2(10)-pinen-3β-ol (260 mg) was added to an ice cold soln of m-chloroperoxybenzoic acid (1 g) in ether (12 ml). The mixture was kept at 4° for 2 days. Isolation with ether gave the deuterated epoxide (177, 280 mg) pure by g.l.c.; n.m.r. δ (CCl_4), 3.23, 2.40 (AB quartet, 2H, J_{AB} 5 Hz; $C\overset{O}{-}CH_2$), 0.92 ($C9-H_3$), deuterium content > 98% by n.m.r.

Kinetics

The reactions were studied at 60° for H_2O/MeOH solns (10:1) with $[OH^-]$ in the range 0.06-0.50 M and [epoxide] 3×10^{-4} M. The rate of formation of pinocarvone was recorded by measuring the optical density of reaction mixtures at 252 nm, the absorption maximum for pinocarvone.

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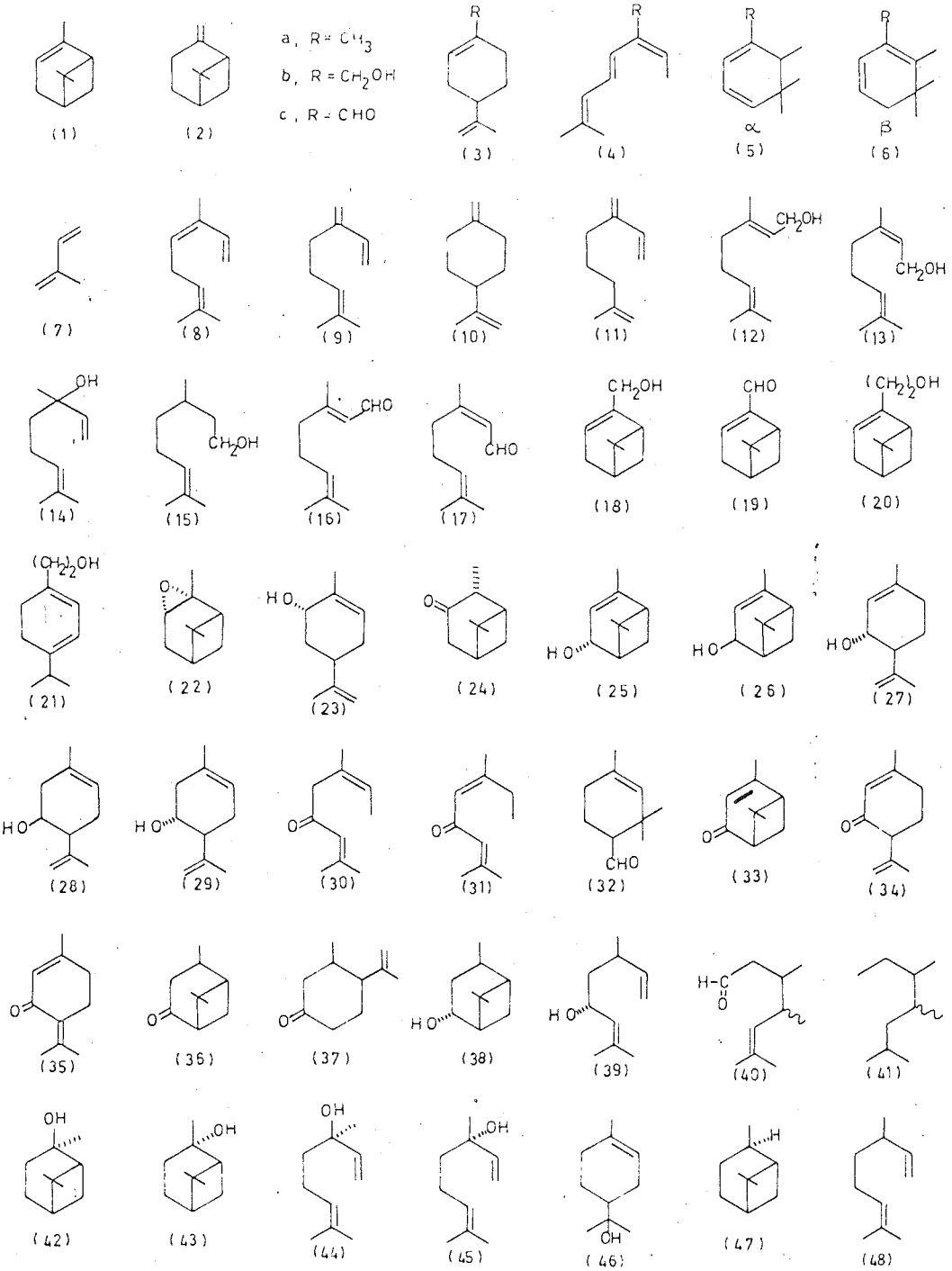
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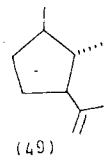
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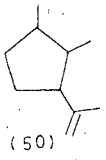
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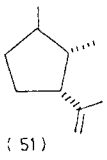
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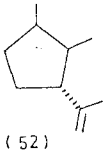
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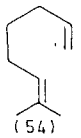
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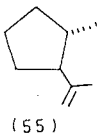
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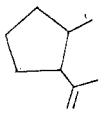
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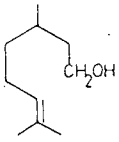
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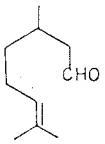
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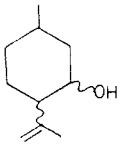
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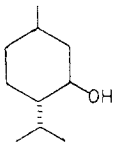
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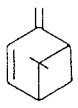
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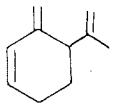
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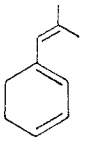
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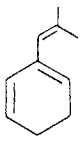
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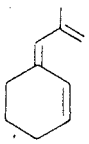
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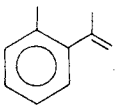
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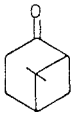
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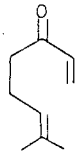
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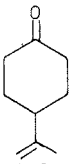
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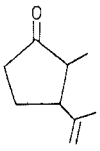
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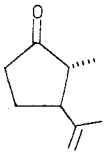
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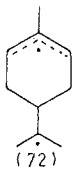
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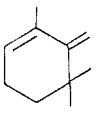
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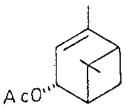
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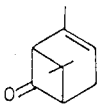
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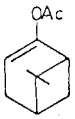
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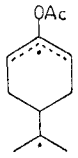
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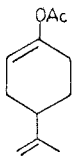
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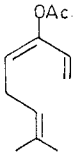
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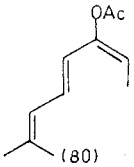
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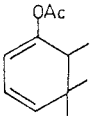
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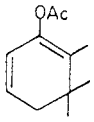
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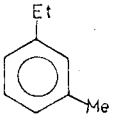
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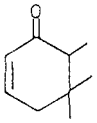
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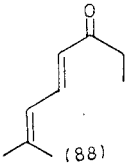
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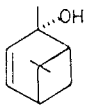
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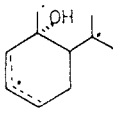
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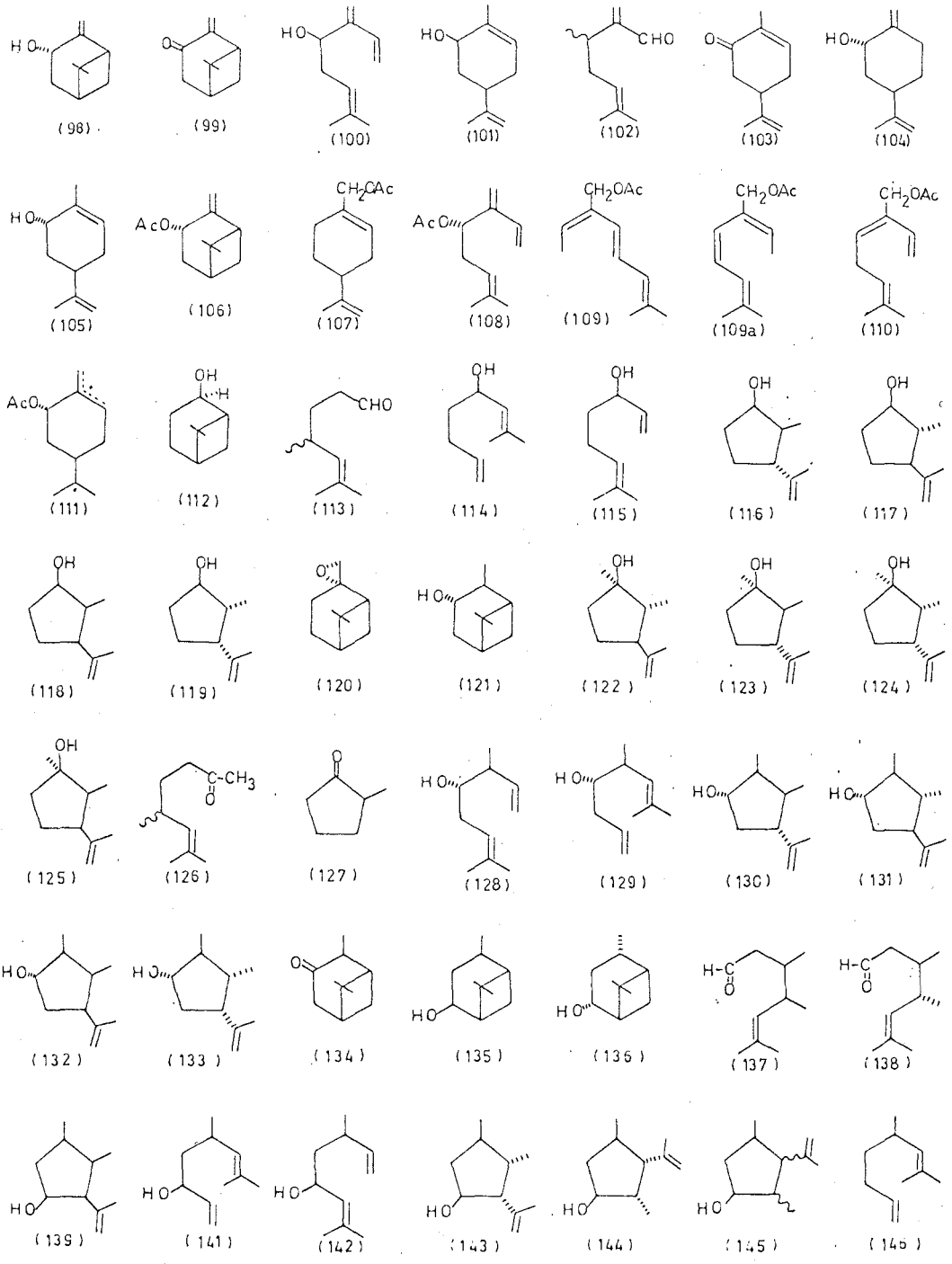
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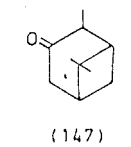
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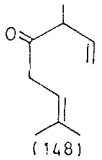
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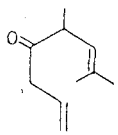
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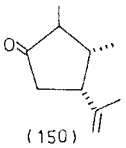
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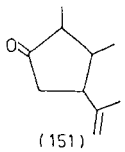
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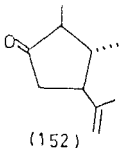
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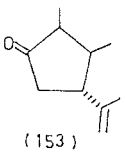
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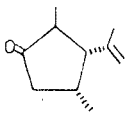
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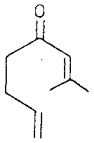
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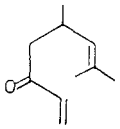
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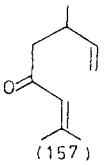
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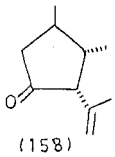
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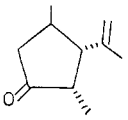
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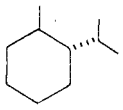
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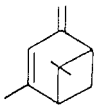
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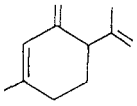
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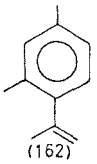
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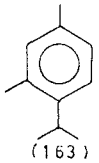
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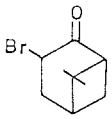
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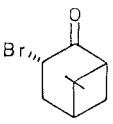
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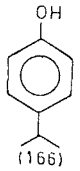
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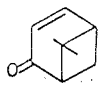
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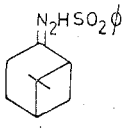
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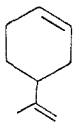
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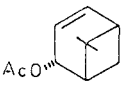
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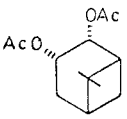
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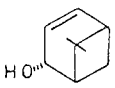
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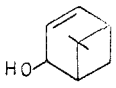
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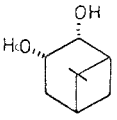
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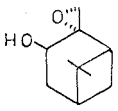
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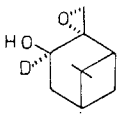
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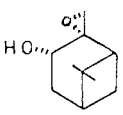
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