The Hydroboration-oxidation of Abietic Acid

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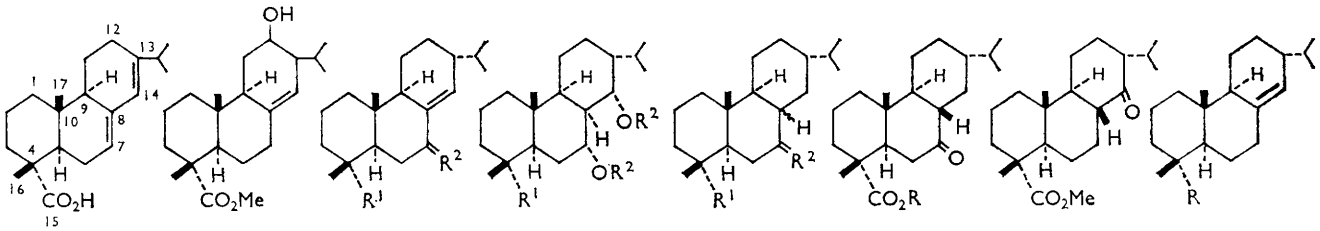
Monohydroboration-oxidation of abietic acid and methyl abietate with both diborane and *t*-2,3-dimethylbutylborane leads to preferential attack on the 7,8-double bond to give 7-hydroxy-8(14)-enes, *e.g.*, (IIIa). Dihydroboration-oxidation with these reagents yields mainly the 7β,14β-dihydroxy derivatives, *e.g.*, (XIXa), with smaller amounts of the 7α,14α-dihydroxy-compounds and a third 7,14-diol of unknown stereochemistry. The dihydroboration reactions are of interest, since it is shown that at least one of the products is derived by migration of the 13,14-double bond of abietic acid to the 8,14-position during hydroboration. Some reactions of the hydroxyabietic acid derivatives are described.

In another investigation [1] an *Alkaligenes* spp. was isolated which would grow on a medium containing abietic acid (I) as its sole carbon source. The transformation products of abietic acid produced by this organism included one believed [1] to be a 7-hydroxydihydroabietic acid and to complete its structural determination authentic 7-hydroxy-derivatives of dihydroabietic acid were required. It seemed likely that such compounds could be prepared if the ring B double bond in abietic acid would undergo selective hydroboration-oxidation.[2] The double bonds in abietic acid are known to differ in reactivity,[3] for example with potassium permanganate the 13,14-bond is attacked preferentially.[4] Similarly it has been reported [5] that abietic acid failed to react during three days with excess of di-isopentylborane. *t*-2,3-Dimethylbutylborane is more reactive than di-isopentylborane and has been reported [10] to be more selective than diborane for the monohydroboration of dienes. Reaction of abietic acid with *t*-2,3-dimethylbutylborane followed by oxidation of the resultant organoborane gave abietinol and a diol (15%), which is shown below to have the structure (IIIa). Subsequently it was found that monohydroboration of abietic acid could be effected more conveniently and in better yield [25% of diol (IIIa)] by one mole of diborane. This reaction also gave a small amount of the triol (IVa) (see below). The position of the secondary hydroxy-group in the diol (IIIa) was fixed by the following reactions. On hydrogenation the diol gave the dihydro-derivative (Va) and, in agreement with its formulation as an allylic alcohol, underwent some hydrogenolysis to tetrahydroabietinol. The half-band widths of the 7-proton signals in the n.m.r. spectra of the diol (IIIa) and its dihydro-derivative (Va) (see Table), establish the equatorial orientation [11] of the secondary hydroxyl group, whilst the marked upfield shift of the 7-proton from the diol to its dihydro-compound confirm the allylic nature of C-7 in the former. The dihydro-derivative (Va) is believed to consist mainly of the



(I) (II) (III) (IV) (V) (VI) (VII) (VIII)

(III) a; R^1 = CH_2OH, R^2 = α-H, β-OH
b; R^1 = CH_2OAc, R^2 = α-H, β-OAc
c; R^1 = CO_2Me, R^2 = α-H, β-OH
d; R^1 = CO_2Me, R^2 = α-OH, β-H

(IV) a; R^1 = CH_2OH, R^2 = H
b; R^1 = CH_2OAc, R^2 = Ac
c; R^1 = CO_2Me, R^2 = H

(V) a; R^1 = CH_2OH, R^2 = α-H, β-OH
b; R^1 = CO_2Me, R^2 = α-H, β-OH
c; R^1 = CO_2Me, R^2 = α-OH, β-H
d; R^1 = CH_2OH, R^2 = α-OH, β-H

(VI) a; R = H
b; R = Me

(VIII) a; R = CH_2OH
b; R = CO_2H

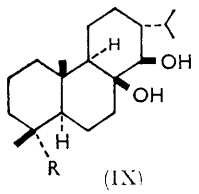
mono-epoxidation of abietic acid yields the 13,14-epoxide. However, the evidence for placing the epoxide function on ring C is not convincing, and it was decided to investigate the monohydroboration-oxidation of abietic acid and its methyl ester in some detail. The results obtained are described here.

Diborane reacts with conjugated dienes to give, after oxidation of the organoborane, either the 1,3- or the 1,4-diol.[6,7] Di-isopentylborane has been shown to be more selective for the monohydroboration of simple dienes [8] and has been used [9] successfully to prepare the mono-ol (II) from methyl levopimarate. However,

[1] B. E. Cross and P. L. Myers, Biochem. J., to be published.
[2] G. Zweifel and H. C. Brown, *Org. Reactions*, 1963, **13**, 1.
[3] J. Simonsen and D. H. R. Barton, 'The Terpenes,' University Press, Cambridge, 1952, vol. III, pp. 382—407.
[4] Ref. 3, pp. 391—396.
[5] B. A. Arbuzov and A. G. Khismatullina, *Izvest. Akad. Nauk S.S.S.R., otdel. Khim. Nauk*, 1961, 1280.
[6] H. C. Brown, 'Hydroboration,' W. A. Benjamin, New York, 1962, p. 209.
[7] M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, 1964, **29**, 1131.
[8] Ref. 6, p. 220.
[9] W. G. Dauben and R. M. Coates, *J. Org. Chem.*, 1963, **28**, 1698.
[10] J. P. Turnbull and J. H. Fried, *Tetrahedron Letters*, 1966, 801.
[11] N. S. Bhacca and D. H. Williams, 'Applications of n.m.r. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 77.

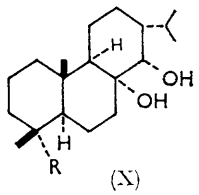
8β-epimer because its n.m.r. spectrum in pyridine * shows strong methyl signals at and above τ 9·04, but only a weak peak at τ 8·97. The latter is probably due to the C-17 methyl group in a small amount of the 8α-epimer, *i.e.*, in a B/C *cis*-fused podocarpane.[12] This conclusion is in agreement with the observation that catalytic reduction of the 8,14-double bond in dihydroabietic acid gives the 8β-compound.[12]

Jones oxidation[14] of the dihydro-compound (Va) yielded the keto-acid (VIa) which is assigned an 8β-podocarpane structure since it is stable to alkali. It failed to give a benzylidene derivative, presumably owing to steric hindrance at C-6. However, the methyl ester (VIb) rapidly gave a dinitrophenylhydrazone, whereas in our hands the 14-keto-ester[12,13] (VII) reacted very slowly † with dinitrophenylhydrazine. These results



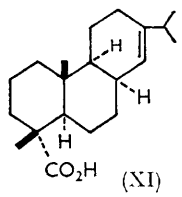
(IX)

(IX) a; R = CO_2H
b; R = CO_2Me

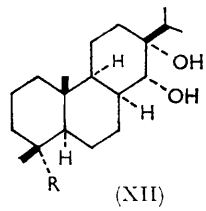


(X)

(X) a; R = CH_2OH
b; R = CO_2H
c; R = CO_2Me

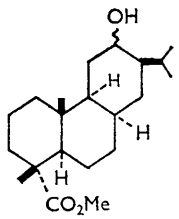


(XI)



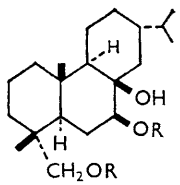
(XII)

(XII) a; R = CH_2OH
b; R = CO_2H



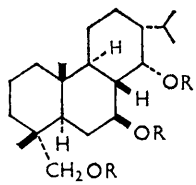
(XIII)

a; 12α – OH
b; 12β – OH



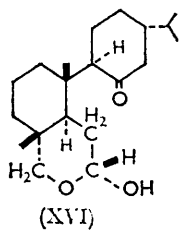
(XIV)

a; R = H
b; R = Ac

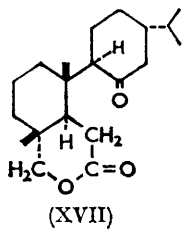


(XV)

a; R = H
b; R = Ac



(XVI)



(XVII)

(*a*) show that the hydroxy-group in the diol (Va) is at C-7 and must therefore be β-oriented and (*b*), suggest that the double bond is at 8,14, *i.e.*, that it has migrated from its original position in abietic acid (see also below). Hence it was important to provide rigorous evidence for the site of the double bond in the diol (IIIa). This has been done by two reaction sequences. In the first of these, the diol was acetylated and the diacetate (IIIb) was hydrogenolysed with lithium in ethylamine to give the dihydroabietinol (VIIIa) together with a small amount of the diol (IIIa). The formation of the mono-ol (VIIIa) showed that the double bond in the diacetate (IIIb) is allylic to the 7-acetoxy-group, whilst the production of the diol (IIIa) established that the double bond in (IIIa) had not migrated during acetylation. On osmylation the dihydroabietinol (VIIIa) gave a triol which was identified as (Xa) by comparison with the sample obtained below from the 13α-isopropyl-8,14-ene (VIIIb).[12,13] Hence the double bond in the dihydroabietinol (VIIIa), and also in the diol (IIIa), must be in the 8,14-position, whilst the isopropyl group must have the α-configuration.

Reduction of abietic acid with lithium in liquid ammonia has been shown[12,13] to give the 8,14-ene (VIIIb) containing about 15% of the 13,14-ene (XI). Osmylation of this mixture of acids gave three dihydroxy-acids. One of these acids, which was formed in a yield of about 25%, was identical with an authentic sample of the dihydroxy-acid (XIIb),‡ so that it must be derived from the 13,14-ene (XI). Hence our sample of the 8,14-ene (XI) must have contained at least 25% of the 13,14-ene (XI) (cf. ref. 12). The stereochemistry depicted in (XIIb) is assigned to this dihydroxy-acid because examination of a Dreiding model of the 13,14-ene (XI) shows that approach to the β-face is badly hindered. Osmylation would therefore be expected to take place from the α-side. The C-17 methyl peak in the n.m.r. spectrum of the dihydroxy-acid (XIIb) occurs at τ 8·83 which suggests that in this acid, in contrast to its isomer (Xb) (see above), ring C has a normal, or near normal, chair conformation. If this is so, the coupling constant of the 14-proton (9·5 c./sec.), which is characteristic of an

* The correlation[12] of the C-17 methyl shift with the B/C ring fusion in abietic acid derivatives was based on measurements in deuteriochloroform solution. It is believed that the same general correlation holds for pyridine solutions (see Table). This is illustrated by comparing the spectra of the diols (XIIa) and (XIIb), which are derived from the B/C *cis*-fused 13-ene (XI),[12,13] with that of the diol (XIXb).

† Burgstahler and Marx[13] reported that the 14-keto-ester (VII) failed to form a dinitrophenylhydrazone; cf. ref. 15.

‡ B. E. Cross and P. L. Myers, unpublished work.

[12] J. W. Huffman, T. Kamiya, L. H. Wright, J. J. Schmid, and W. Herz, *J. Org. Chem.*, 1966, **31**, 4128.
[13] A. W. Burgstahler and J. N. Marx, *Tetrahedron Letters*, 1964, 3333.
[14] R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 1953, 457.
[15] W. Herz, A. K. Pinder, and R. N. Mirrington, *J. Org. Chem.*, 1966, **31**, 2257.

axial–axial splitting, supports the α-configuration of the hydroxyl group at C-14 and therefore also at C-13. The other two osmylation products must therefore be the dihydroxy-acids (IXa) and (Xb) and their stereochemistry follows from their n.m.r. spectra. Since osmylation leads to *cis*-diols, the dihydroxy-acid in which the C-14 proton signal appears as a doublet at τ 6·10 with a coupling constant (J = 10 c./sec.) characteristic of an axial–axial splitting clearly has the structure (IXa).

8,14-ene (VIIIb). This is in contrast to epoxidation [12] and hydroboration [12] from which only products resulting from reaction of the β-face have been reported. Reduction of the dihydroxy-acids (Xb) and (XIIb) with diborane gave the triols (Xa) and (XIIa) respectively, whose structures are supported by their n.m.r. spectra.

The chemical shift of the proton at C-9 in these and other hydroxy-derivatives of abietic acid (see Table and

Chemical shift (τ values) of hydrogens; J and $W_{\frac{1}{2}}$ in c./sec

Compound	Solvent	17-H	16-H	15-H	14-H	9-H	7-H	Isopropyl
(IIIa)	Pyridine			6·50dd J = 11·0	3·69	~7·65m	5·68 $W_{\frac{1}{2}}$ = ~20	
(IIIc)	CCl_4	9·26	8·96		4·27		~6·2 $W_{\frac{1}{2}}$ = ~22	~9·13od
(IIId)	CCl_4	9·23	8·87		4·32	~7·6m	5·95 $W_{\frac{1}{2}}$ = 5·5	9·10od
(IVa)	Pyridine	8·94	9·14	6·46dd J = 11·0	6·23 W = ~20	~7·4m	4·86 $W_{\frac{1}{2}}$ = 6·0	9·05d J = 7·0
(IVb)	CCl_4	8·87	9·12	6·35dd J = 11·0	~4·95 $W_{\frac{1}{2}}$ = ~20		5·14 $W_{\frac{1}{2}}$ = 6·0	9·16od J = 6·5
(IVc)	Pyridine	8·97	8·69		~6·2 $W_{\frac{1}{2}}$ = ~20	7·25m	4·91 $W_{\frac{1}{2}}$ = 6·0	9·04d J = 7·0
(Va)	Pyridine			6·57 J = 11·0		~7·7m	~7·37 $W_{\frac{1}{2}}$ = 15	
(Vc)	Pyridine	9·06 or 9·12	8·73			7·4q	6·15 $W_{\frac{1}{2}}$ = 6·0	9·06 or 9·12
(Xb) *	Pyridine	9·02	8·52		6·25d J = 3·0	6·53q		8·94d and 9·01d J = 6·5
(Xc)	$CDCl_3$	9·12	8·76		6·49d J = 2·5	~7·2m		9·06d J = 6·0
(IXa)	Pyridine	8·90	8·58		6·10d J = 10	~7·05m		9·04d J = 7·0
(IXb)	Pyridine	8·98	8·74		6·17d J = 10	~7·05m		9·06d J = 7·0
(IXb)	$CDCl_3$	8·97	8·79		~6·4 $W_{\frac{1}{2}}$ ⩽ 11	~7·45m		9·13od J = 6·0
(XIIb)	Pyridine	8·83	8·63		6·66d J = 9·5	~7·5m		9·02d J = 6·5
(XIVa)	Pyridine	8·70	9·08	6·47dd J = 10·5			6·32 $W_{\frac{1}{2}}$ = 11	9·19d J = 6·0
(XIXb)	Pyridine	9·07	8·63		5·83—6·85 †	~7·45m	5·83—6·85 †	~9·03d J = 7·5
(XIXc)	CCl_4	9·10	8·83		5·8—6·95 †	~7·85m	5·8—6·95 †	9·12d J = 6·5
(XXIb)	CCl_4	~9·13	~9·13	6·31s	6·7 † $W_{\frac{1}{2}}$ = ~17		6·7 † $W_{\frac{1}{2}}$ = ~17	9·23dd J = 6·5

* 100 Mc./sec. spectrum. † 7- and 14-Protons; s, singlet; d, doublet; dd, double doublet; od, overlapping doublet; m, unresolved multiplet; q, quartet.

This is confirmed by the C-17 methyl resonance which is found at low field (τ 8·90) due to 1,3-diaxial deshielding [16] by the 8β-hydroxyl group. The other dihydroxy-acid, in which the C-14 proton occurs at τ 6·25 (J = 3·0 c./sec.), must therefore have structure (Xb). However, since the conformation of ring c in this acid is not a normal chair (see below), its n.m.r. spectrum cannot be used to support this assignment. The formation of the two acids (IXa) and (Xb) in the ratio of one part of the former to four of the latter shows that osmylation takes place preferentially on the α-face of the

Experimental section) deserves comment. For reasons of solubility most n.m.r. spectra have only been measured in pyridine solution when this proton usually appears as an unresolved multiplet τ 7·0—7·5. In some cases, such as the triol (IVa) and the hydroxy-ester (Vc), the 9-proton resonance is seen as an ill-defined quartet. A few of those spectra which have been determined in carbon tetrachloride or deuteriochloroform, for example the dihydroxy-acid (IXb), show the 9-proton resonance but in others it is lost under the methylene envelope.*

[16] K. Tori and E. Kondo, *Tetrahedron Letters*, 1963, 645.

* The 9-proton signal from 13ξ-isopropyl-8ξ-podocarpan-15-oic acid can be seen at τ 7·83 in pyridine but lies under the methylene envelope in carbon tetrachloride solution.

The factors governing the chemical shift of the 9-proton are uncertain. This proton appears at particularly low-field in the B/C *cis*-fused 8,14-diols (Xa), (Xb), and (Xc), and in these compounds the explanation may be that rings B and C are distorted so that the 8α-hydroxy-group, and possibly also the 14α-hydroxy-group, deshields the 9-proton. A consequence of such skeletal distortion is that the 9-proton no longer bisects the angle between the 11α- and 11β-protons. Experimental evidence in support of such distortion has been provided by the 100 Mc./sec. n.m.r. spectrum (see Table) of the dihydroxy-acid (Xb) in which the 9-proton signal appears as an ABX quartet at exceptionally low-field (τ 6·53). Double irradiation experiments show that it is coupled with a large coupling constant (10 c./sec.) to a proton at τ 8·34 and with a smaller coupling constant to a proton at τ 8·13. Such coupling constants, which require considerable distortion of ring C, are probably best explained if ring C has a boat conformation which relieves the interactions between the C-17 methyl and the hydrogens at C-12 and C-14 and allows the isopropyl group to become equatorial. Further support for such a conformation is provided by the chemical shift of the C-17 methyl group in the ester (Xc) in which it is found at τ 9·12 in deuteriochloroform solution, *i.e.*, the deshielding effect on the C-17 methyl group normally observed with B/C *cis*-fused podocarpanes [12] is absent. Conformational distortion of ring C has been reported [12] in the 12-hydroxy-compounds (XIIIa) and (XIIIb). However in these derivatives, as in the dihydroxy-acid (XIIa), the isopropyl group is equatorial and less distortion would be expected than in the dihydroxy-acid (Xb) which has an axial isopropyl group. This is borne out by the n.m.r. spectra of the 12-hydroxy-compounds in which the C-17 methyl group remains at low field.[12,17]

The conclusion (see above) that the double bond in the diol (IIIa) is at the 8,14-position has been confirmed as follows. Reaction of the diol (IIIa) with *m*-chloroperbenzoic acid gave a product, assumed to be a mixture of the α- and β-epoxides (two spots on t.l.c.), which was reduced with lithium aluminium hydride giving two triols, m. p. 148—150° and 181—182°. Acetylation of the triol, m. p. 148—150°, gave a diacetate suggesting that the new hydroxy-group is tertiary and this was confirmed by the n.m.r. spectrum of the diacetate which showed only one C*H*·OAc peak at τ ~5·5. This triol reacted with lead tetra-acetate to give a product shown to be the hemi-acetal (XVI) by analytical and spectroscopic data. Thus in the i.r. the hemi-acetal showed a carbonyl band at 1714 and hydroxy-absorption at 3395 cm.$^{-1}$; its n.m.r. spectrum contained a peak at τ 4·28 ($W_{\frac{1}{2}}$ = 4·5 c./sec.) typical of a grouping O–CH–O in which the proton is equatorial [11] and hence the hydroxy-group is assigned the α-configuration. Oxidation of the hemi-acetal with Jones reagent gave the δ-lactone (XVII), $\nu_{max.}$ 1730 cm.$^{-1}$. Hence the triol, m. p. 148—150°, must be a vicinal glycol. It was shown to be the 8β-epimer (XIVa), rather than the 8α-epimer, by its n.m.r. spectrum (see Table) in which the C-17 methyl resonance occurs at τ 8·70, indicating 1,3-diaxial deshielding by an 8β-hydroxy-group.[16] The triol (XIVa) is presumably formed by reduction of the 8β,14β-epoxide. The other triol, m. p. 181—182°, readily gave a triacetate which showed two C*H*·OAc peaks in its n.m.r. spectrum. Of these, the peak at τ 5·76 ($W_{\frac{1}{2}}$ = ~15 c./sec.) is assigned to the proton on C-7, so that the other at τ 4·58 is due to the proton at position 14. This proton must be equatorial because (*a*) its half-band width is only 4 c./sec. and (*b*) it appears at lower field than the peak due to the corresponding proton in related 14-equatorial hydroxy-compounds (see below and Table). The triol, m. p. 181—182°, is provisionally assigned structure (XVa), rather than the alternative 14β-hydroxy-8α-podocarpane structure, because the n.m.r. spectrum of its triacetate (XVb) in carbon tetrachloride solution shows its main methyl resonances at τ 9·14 and 9·17,[12] and only a weak peak at τ 9·03 which is probably half of an isopropyl methyl doublet. Structure (XVa) would be formed by the 1,2-diaxial opening of an 8α,14α-epoxide.

In parallel with the work on monohydroboration of abietic acid described above, the monohydroboration of methyl abietate with *t*-2,3-dimethylbutylborane was examined. With a reaction time of two days two monohydroxy-esters were obtained. One of these was readily shown to be the 7β-hydroxy-compound (IIIc) because on reduction with lithium aluminium hydride it gave the diol (IIIa) described above. Hydrogenation of the hydroxy-ester (IIIc), with Adams catalyst in acetic acid, gave the dihydro-derivative (Vb) and 15—20% of methyl tetrahydroabietate. As in the case of the diol (Va) above, the dihydro-derivative (Vb) is believed to be mainly, or entirely, the 8β-epimer because in its n.m.r. spectrum in carbon tetrachloride the C-17 methyl peak is not found below τ 9·08; a peak at τ 9·03 is probably due to one limb of an isopropyl methyl doublet. Oxidation of the dihydro-ester with Jones reagent afforded the keto-ester (VIb) identical with the specimen prepared above from the diol (IIIa). The other hydroxy-ester was shown by its n.m.r. spectrum (see Table) to contain a secondary axial hydroxy-group and its structure was established as (IIId) by the following reactions. Hydrogenation gave ~15% methyl tetrahydroabietate, by hydrogenolysis, and the dihydro-derivative (Vc) whose n.m.r. spectrum (see Table) confirmed the axial orientation of the hydroxy-group and provided evidence (C-17 methyl at τ ⩾ 9·06 in pyridine) that in all or most of the product rings B/C are *trans*-fused. Oxidation of the dihydro-ester (Vc) with Jones reagent yielded the 7-keto-ester (VIb) identical with the specimens prepared above.

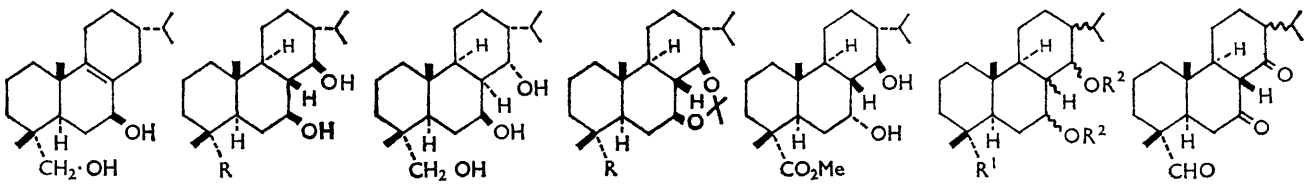
In order to complete our work on the hydroboration-oxidation of abietic acid we examined the products formed when an excess of diborane was used. The major component was a triol, m. p. 138—141°; smaller amounts of two other triols, m. p. 154—155° and 223—224° were also isolated. Since reaction of the diol (IIIa)

[17] W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, *J. Org. Chem.*, 1965, **30**, 3190.

with an excess of diborane followed by oxidative work-up also gave the triol, m. p. 138—141°, as the major product, the latter must have a 7β-hydroxy-group and an α-oriented isopropyl group. The minor product from the hydroboration of the diol (IIIa) was an isomeric diol which, since it showed no olefinic proton signal in its n.m.r. spectrum, is believed to have structure (XVIII). The n.m.r. spectrum of the triol, m. p. 138—141°, contained an AB quartet at τ 6·54 assigned to the C*H*$_2$·OH group, but since this overlapped multiplets due to two C*H*OH groups the configuration at C-14 could not be deduced. However, the isopropylidene derivative of the triol gave an acetate whose n.m.r. spectrum showed the C*H*$_2$·OAc group as a singlet at τ 6·31 and the two C*H*–O protons as broad overlapping multiplets centred at τ 6·7 and of half-band width ~17 c./sec. Hence, both hydroxy-groups are equatorial and since hydroboration-oxidation leads to *cis*-addition of water the triol must, since it is also preparable from the diol (IIIa), have structure (XIXa) or (XX). Structure (XX) may be excluded since the C-17 methyl group in the derivative (XXIb) appears at τ ~9·1, *i.e.*, at a chemical shift typical of a B/C *trans*-fused podocarpane.[12] The triol, m. p. 138—141°, was therefore assigned structure (XIXa). Structure (XIXa) for the triol, m. p. 138—141°, was confirmed by the n.m.r. spectra of some of its derivatives. Oxidation of the isopropylidene derivative (XXIa) to the acid (XXId) *via* the aldehyde (XXIc), and removal of the protecting group gave the dihydroxy-acid (XIXb) whose n.m.r. spectrum (see Table) showed two overlapping C*H*·OH multiplets stretching from τ 5·83 to 6·85. Similarly in the methyl ester (XIXc) (see Table) the C*H*·OH signals formed a broad multiplet extending from τ 5·80 to 6·95, whilst the C-17 protons were at τ 9·10. Hence there can be little doubt that both hydroxy-groups in these compounds are equatorial and that rings B/C are *trans*-fused.

The structure of the triol, m. p. 154—155°, followed from some further hydroboration-oxidation reactions. Reaction of methyl abietate with *t*-2,3-dimethylbutylborane for seven days, followed by the usual oxidative work-up, afforded small amounts of the monohydroxy-esters (IIIc) and (IIId) described above. The major product was the dihydroxy-ester (XIXc), previously prepared from the triol (XIXa), but two other dihydroxy-esters, m. p. 165—168° and 174—175°, were also isolated. Lithium aluminium hydride reduction of these two esters gave the triols of m. p. 154—155 and 223—224°, respectively, thus inter-relating the two series of products. Since the dihydroxy-ester, m. p. 165—168°, was also obtained by hydroboration-oxidation of the hydroxy-ester (IIId) it must have structure (IVc) or (XXII). The former was shown to be correct by its n.m.r. spectrum and those of the related triol (IVa), m. p. 154—155°, and triacetate (IVb), in all of which the C-17 methyl resonance appeared at less than τ 9·0 (see Table), *i.e.*, rings B/C are *cis*-fused.[12]

The n.m.r. spectra of the third triol (XXIIIa), m. p. 223—224°, and its triacetate (XXIIIb) and of the related dihydroxy-ester (XXIIIc), m. p. 174—175°, revealed the presence of two secondary hydroxy-groups which must be located at positions 7 and 14. One hydroxy-group must be equatorial since the half-band



(XVIII) (XIX) (XX) (XXI) (XXII) (XXIII) (XXIV)

R
a; CH_2OH
b; CO_2H
c; CO_2Me
d; CH_2OAc

a; R = CH_2OH
b; R = CH_2OAc
c; R = CHO
d; R = CO_2H

	R^1	R^2
a;	CH_2OH	H
b;	CH_2OAc	Ac
c;	CO_2Me	H

width of one of the C*H*OH protons is in the range 15—21 c./sec., whilst the other hydroxy-group is axial ($W\frac{1}{2}$ for CHOH = 5—6 c./sec.). The secondary nature of the hydroxy-groups was confirmed by oxidation of the triol with acetic anhydride in dimethyl sulphoxide[18] to the diketo-aldehyde (XXIV) whose u.v. spectrum [$\lambda_{max.}$ (EtOH) 299 mμ, ε 7400; $\lambda_{max.}$ (EtOH–NaOH) 317 mμ, ε 10,800)] showed it to be a β-diketone. The stereochemistry of these compounds at positions 7, 8, 13, and 14 is uncertain. The peak due to the C-17 methyl group could not be clearly identified in the n.m.r. spectra of the triol and its triacetate. In the spectrum of the dihydroxy-ester (XXIIIc) a strong peak centred at τ 9·04 is believed to contain one overlapping limb of each isopropyl methyl doublet and the C-17 methyl group, but since its chemical shift lies between the values normally found for the C-17 methyl group in *cis*- and *trans*-fused podocarpanes,[12] the stereochemistry at C-8 could not be deduced. Consequently the configurations at positions 7, 13 and 14 are also unknown.

Consideration of the stereochemistry of the triol (IVa) and of the dihydroxy-ester (IVc) is of interest since it shows that migration of the 13,14-double bond of abietic acid occurs during hydroboration. Thus, the triol (IVa) must arise by α-attack on the 7,8-double bond

[18] J. D. Albright and L. Goldman, *J. Amer. Chem. Soc.*, 1965, **87**, 4214.

of abietic acid followed by migration of the 13,14-double bond to the 8,14-position. A second hydroboration from the α-face would then give an organoborane which, after oxidation, would yield the triol (IVa). The triol (XIXa), which is formed in the same reaction mixture as the triol (IVa), could be derived either by β-attack on both double bonds of abietic acid, or by β-attack on the 7,8-double bond followed by migration of the ring c double bond to the 8,14-position and a second hydroboration from the β-side. The same arguments may be applied to the formation of the dihydroxy-esters (IVc) and (XIXc).

EXPERIMENTAL

Column chromatography was carried out on silica gel [Whatman Chromedia SG31 (W. and R. Balston)] and alumina (Woelm neutral alumina, Grade II). For t.l.c. Kieselgel G (Merck) was used. Preparative layer chromatography (p.l.c.) was carried out on Kieselgel G (washed with ethyl acetate) in layers 0·5 mm. thick.

M. p.s were determined on a Kofler block. U.v. spectra and optical rotations were measured in ethanol solution on a Unicam SP 800 spectrometer and a Perkin-Elmer 141 Polarimeter, respectively. Unless otherwise stated, i.r. spectra were obtained as 'Nujol' mulls on a Unicam SP 200 spectrometer and n.m.r. spectra were determined in pyridine solution on a Varian A60 spectrometer with tetramethylsilane as internal standard. Light petroleum had b. p. 60—80°.

Monohydroboration of Abietic Acid.—(a) *With di-isopentylborane.* Abietic acid (1 g.) in tetrahydrofuran (5 ml.) was added to di-isopentylborane [19] (15 mol.) in diglyme (25 ml.) and left to stand at 0° for 3 days. Abietic acid was recovered almost quantitatively.

(b) *With* t-2,3-*dimethylbutylborane.* Boron trifluoride etherate (1·14 g.) was added during 30 min. to sodium borohydride (0·3 g.) and 2,3-dimethylbut-2-ene in diglyme (10 ml.) at 0° under nitrogen. The solution was kept at 0° for 8 hr. Abietic acid (0·8 g.) in tetrahydrofuran (2 ml.) was added and the mixtute left to stand under nitrogen at 0° for 36 hr. Water (0·5 ml.) and 5N-sodium hydroxide (3 ml.) were added, followed by 40% hydrogen peroxide (2 ml., dropwise), keeping the temperature below 40°. The mixture was stirred for 2 hr. at room temperature, acidified to pH 4 and extracted with ether. The extract was washed with water and dried, and the product (790 mg.) recovered and chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (1 : 9) gave abietinol. The fractions eluted with ethyl acetate–light petroleum (1 : 4 and 3 : 7) afforded 7β,15-*dihydroxy*-13α-*isopropylpodocarp*-8(14)-*ene* (IIIa). It crystallised from ethyl acetate–light petroleum as needles (127 mg.), m. p. 143—146°, which contained a small amount of impurity not removable by crystallisation. An analytical sample, purified by p.l.c. in benzene–ethanol (9 : 1), crystallised from ether–light petroleum in needles, m. p. 144—147°, $[\alpha]_D^{24}$ −8° (*c* 0·3) (Found: C, 78·2; H, 11·5. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2%), $\nu_{max.}$ 3400 cm.$^{-1}$, τ 9·1—9·2 (methyls), ~7·65 (multiplet; 9-H), 6·5 (AB quartet; J = 11·0 c./sec.; CH_2·OH), 5·68 (multiplet; $W_{\frac{1}{2}}$ = ~20 c./sec.; CH·OH), 3·69 (1H, broad; 14-H).

The *diacetate* (IIIb), prepared with acetic anhydride in pyridine at room temperature, was a gum which sublimed at 180°(bath)/10^{-3} mm. (Found: C, 73·65; H, 9·6. $C_{24}H_{38}O_4$ requires C, 73·8; H, 9·8%), $\nu_{max.}$ (film) 1735 and 1240 cm.$^{-1}$, τ (CCl_4) 9·19 and 9·13 (methyls), 7·98 and 7·94 (3H singlets; OAc), 6·26 (2H, AB quartet; J = 11 c./sec.; CH_2·OAc), 4·97 (1H multiplet; $W_{\frac{1}{2}}$ = 11 c./sec.; CH·OAc), 4·62 (1H broad; 14-H).

(c) *With one mole of diborane.* Abietic acid (20 g.) in tetrahydrofuran (60 ml.) was added to diborane (1 mol.; prepared from boron trifluoride etherate and sodium borohydride) in diglyme (100 ml.) and left to stand at 0° for 18 hr. After oxidative work-up and recovery as in (b), the product was chromatographed on alumina. Elution with ethyl acetate–light petroleum (1 : 4) gave abietinol (3·46 g.). Ethyl acetate–light petroleum (1 : 1) eluted the diol (IIIa) which crystallised from ether–light petroleum in needles (5·2 g.), m. p. 144—146°, identical with the specimen prepared by method (b). Ethyl acetate–ethanol (1 : 1) eluted 13α-isopropyl-8α-podocarpane-7α,14α,15-triol (IVa) (0·9 g.) which crystallised from ethanol–light petroleum as needles of the *ethanolate*, m. p. 120—130°, resolidifying and remelting 149—151° (Found: C, 71·7; H, 11·3. $C_{20}H_{36}O_3$, C_2H_5OH requires C, 71·4; H, 11·4%), $\nu_{max.}$ 3340 and 3420 (OH) cm.$^{-1}$.

When a solution of the triol in ether was evaporated to dryness and the residue crystallised from ether–light petroleum it formed needles, m. p. 148—150°, of the solvent-free triol, identical (i.r. spectrum) with the specimen prepared below.

When the hydroboration-oxidation reaction mixtures from (b) and (c) were worked up without acidification the same products were obtained.

Hydrogenation of the Diol (IIIa).—The diol (150 mg.) in glacial acetic acid (25 ml.) was hydrogenated in the presence of Adams catalyst (50 mg.) until uptake cease (6 hr.). The solution was filtered, diluted with water, and extracted with ether. The extract was washed with dilute sodium hydroxide solution and water and dried. Recovery, followed by crystallisation from ether–light petroleum, gave 13α-isopropyl-8ξ-podocarpane-7β,15-diol [(Va); mainly 8β-epimer] (113 mg.) as needles, m. p. 166—167° (Found: C, 77·8; H, 11·6. Calc. for $C_{20}H_{36}O_2$: C, 77·9; H, 11·8%), $\nu_{max.}$ 3440 (OH) cm.$^{-1}$, τ 9·12 and 9·04 (methyls), ~7·7 (1H multiplet; 9-H), ~7·37 (1H multiplet; $W_{\frac{1}{2}}$ = 15 c./sec.; CH·OH), 6·57 (2H, AB quartet; J = 11 c./sec.; CH_2·OH).

Chromatography of the mother-liquors from (Va) on alumina and elution with ethyl acetate–light petroleum (1 : 9) gave tetrahydroabietinol, identified by its i.r. spectrum.

13α-*Isopropyl*-7-*oxo*-8β-*podocarpan*-15-*oic Acid* (VIa).—The diol (Va) (100 mg.) in acetone (40 ml.) at 0° was treated with the 8N-chromium trioxide reagent [14] (0·5 ml.) for 90 min. Methanol was added, the solution was concentrated *in vacuo*, the residue was taken up in ether, and the ether layer was washed with 2N-sodium hydroxide solution. The alkaline solution was acidified with dilute hydrochloric acid and the product recovered in ether. It crystallised from ether–light petroleum as needles (81 mg.) of the *keto-acid* (VIa), m. p. 215—217°, $[\alpha]_D^{25}$ −17° (*c* 0·39) (Found: C, 75·1; H, 9·95. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·1%), $\nu_{max.}$ ($CHBr_3$) (Perkin-Elmer 125 Spectrometer) 2640 (OH of CO_2H) and 1694 (C=O) cm.$^{-1}$, τ 9·16 (6H overlapping doublets; J = 5·5 c./sec.; isopropyl), 8·92 (3H singlet;

[19] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 1961, **83**, 1241.

17-methyl), 8·62 (3H singlet; 16-methyl). The mother-liquors from the keto-acid (VIa) gave prisms (10 mg.), m. p. 208—212°, with an i.r. spectrum in $CHBr_3$ slightly different from that of the keto-acid (VIa).

The keto-acid (45 mg.) in ethanol (20 ml.) was recovered (44 mg.) after treatment with potassium hydroxide (40 mg.) for 24 hr.; it (40 mg.) failed to react with potassium hydroxide (40 mg.) and benzaldehyde (25 mg.) in ethanol (20 ml.) during 72 hr. at room temperature.

The methyl ester (VIb), prepared with ethereal diazomethane, was a gum, $[\alpha]_D^{23}$ −22° (*c* 0·6), identical (i.r. spectrum) with the specimen prepared below by oxidation of the hydroxy-ester (Vc). When treated with 3 ml. of a solution of 2,4-dinitrophenylhydrazine (0·7 g.) in methanol (30 ml.) and concentrated sulphuric acid (2 ml.), the ester (70 mg.) in methanol (10 ml.) gave a precipitate of the 2,4-*dinitrophenylhydrazone* in 5 min. The derivative crystallised from methanol in yellow needles, m. p. 178—179° (Found: C, 63·0; H, 7·4; N, 10·5. $C_{27}H_{40}N_4O_6$ requires C, 63·0; H, 7·4; N, 10·9%), $\nu_{max.}$ 1715 (ester) cm.$^{-1}$.

2,4-*Dinitrophenylhydrazone of Methyl* 13α-*Isopropyl*-14-*oxo*-8β-*podocarpan*-15-*oate*.—The keto-ester [13,15] (VII) (40 mg.) was treated with 2,4-dinitrophenylhydrazine as in the preceding experiment except that the reaction mixture was left for 14 days. Water was added and the product was recovered in ether and crystallised from ethanol–water to give the 2,4-*dinitrophenylhydrazone* (22 mg.) as orange needles, m. p. 204—206° (Found: C, 62·75; H, 7·35. $C_{27}H_{40}N_4O_6$ requires C, 63·0; H, 7·4%), $\nu_{max.}$ 1712 (ester) cm.$^{-1}$.

Hydrogenolysis of the Diacetate (IIIb).—The diacetate (300 mg.) was added to a stirred solution of lithium (200 mg.) in anhydrous ethylamine (50 ml.) at room temperature, stirring was continued for 75 min., and ammonium chloride was added. The ethylamine was evaporated under reduced pressure, the residue was dissolved in water, and the product (232 mg.) was recovered in ether and chromatographed on alumina (Grade V). Elution with ether–light petroleum (1 : 4) gave 15-hydroxy-13α-isopropylpodocarp-8(14)-ene (VIIIa) as a gum (145 mg.) which sublimed at 180°(bath)/10^{-3} mm. but failed to give satisfactory analyses, $\nu_{max.}$ (film) 3400 (OH) and 1655 (C=C) cm.$^{-1}$, τ (CCl_4) 9·1—9·24 (methyls), ~7·85 (1H multiplet; 9-H), 6·86 (2H, AB quartet; *J* = 11 c./sec.; CH_2·OH), 4·76 (1H broad; 14-H). The alcohol (VIIIa) was characterised as its *acetate*, prepared with acetic anhydride in pyridine, which sublimed at 170°(bath)/10^{-3} mm. as a gum. (Found: C, 79·95; H, 10·9. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9%), $\nu_{max.}$ (film) 1740 and 1240 (acetate) cm.$^{-1}$.

Elution of the column with ethyl acetate afforded the diol (IIIa), m. p. 144—147°, identified by its i.r. spectrum.

Reaction of the 8(14)-*Ene* (VIIIa) *with Osmium Tetroxide*.—The 8(14)-ene (100 mg.) in pyridine (1 ml.) was treated with osmium tetroxide (120 mg.) for 72 hr. Water (15 ml.), pyridine (17 ml.), and sodium metabisulphite (1 g.) were added and the solution shaken for 30 min. Recovery in ether gave a gum (102 mg.) which was chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (3 : 7) gave 13α-*isopropyl*-8α-*podocarpane*-8α,14α,15-*triol* (Xa) which crystallised from ethyl acetate–light petroleum as prisms (35 mg.), m. p. 110—113°, $[\alpha]_D^{26}$ −48° (*c* 0·3) (Found: C, 73·7; H, 10·95. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3470 (OH) cm.$^{-1}$, τ 9·02, 8·97, 8·92, and 8·86 (singlets; methyls), 7·1 (1H multiplet; 9-H), 6·47 (AB quartet; *J* = 10 c./sec.; CH_2·OH), 6·22 (doublet; *J* = 3 c./sec.; CH·OH). It was identical (i.r. spectrum) with the specimen prepared below from the acid [12,13] (VIIIb).

Reaction of 13α-*Isopropylpodocarp*-8(14)-*en*-15-*oic Acid* (VIIIb)* *with Osmium Tetroxide*.—The acid (1 g.) in pyridine (5 ml.) was treated with osmium tetroxide (1·1 g.) for 72 hr. Water (30 ml.), pyridine (30 ml.), and sodium metabisulphite (2 g.) were added and the solution was shaken for 2 hr. The product was extracted into ether and the extract was washed with dilute hydrochloric acid and water and dried. Recovery gave a gum which was chromatographed on silica gel. Elution with ethyl acetate–light petroleum (2 : 3) yielded 13α,14α-*dihydroxy*-13β-*isopropyl*-8α-*podocarpan*-15-*oic acid* (XIIb) which crystallised from ether–light petroleum as needles (248 mg.), m. p. 186—188°, $[\alpha]_D^{24}$ −19° (*c* 0·35) (Found: C, 70·85; H, 10·15. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%), $\nu_{max.}$ 3480 (OH), 2670 and 1673 (CO_2H) cm.$^{-1}$.

Elution with ethyl acetate–light petroleum (1 : 1) afforded 8α,14α-*dihydroxy*-13α-*isopropyl*-8α-*podocarpan*-15-*oic acid* (Xb) which crystallised from ether–light petroleum (b. p. 40—60°) as needles (403 mg.), m. p. 151—154°, $[\alpha]_D^{24}$ −39·5° (*c* 0·37) (Found: C, 71·0; H, 10·0. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%), $\nu_{max.}$ 3500 (OH), 2650 and 1690 (CO_2H) cm.$^{-1}$.

The *methyl ester* (Xc), prepared with ethereal diazomethane, crystallised from ether–light petroleum as needles, m. p. 148—149° (Found: C, 71·2; H, 10·2. $C_{21}H_{36}O_4$ requires C, 71·55; H, 10·3%), $\nu_{max.}$ 3570, 3420 (OH), and 1720 (CO_2Me) cm.$^{-1}$.

Ethanol–ethyl acetate (1 : 9) eluted a fraction which crystallised from ether–light petroleum in needles (110 mg.) of 8β,14β-*dihydroxy*-13α-*isopropyl*-8β-*podocarpan*-15-*oic acid* (IXa), m. p. 229—232°, $[\alpha]_D^{24}$ −17° (*c* 0·34) (Found: C, 70·75; H, 10·05. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%), $\nu_{max.}$ 3490 (OH) and 1673 cm.$^{-1}$.

The *methyl ester* (IXb), prepared with ethereal diazomethane, crystallised from ether–light petroleum as needles, m. p. 148—150° (Found: C, 71·85; H, 10·4. $C_{21}H_{36}O_4$ requires C, 71·55; H, 10·3%), $\nu_{max.}$ 3450 and 1725 cm.$^{-1}$.

13β-*Isopropyl*-8α-*podocarpane*-13α,14α,15-*triol* (XIIa).—The acid (XIIb) (150 mg.) in tetrahydrofuran (20 ml.) was reduced with diborane (1·1 mol.) in diglyme (10 ml.) at 0° under nitrogen for 24 hr. After addition of water the product was recovered in ether; it crystallised from ethyl acetate–light petroleum as prisms (107 mg.) 13β-*isopropyl*-*podocarpane*-13α,14α,15-*triol* (XIIa), m. p. 185—187°, $[\alpha]_D^{24}$ −15·5° (*c* 0·5) (Found: C, 74·1; H, 11·15. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3370 (OH) cm.$^{-1}$, τ 9·16, 9·06, and 8·96 (singlets, isopropyl and 16-methyl), 8·83 (singlet; 17-methyl), 7·4 (multiplet; 9-H), 6·66 (doublet; *J* = 9·0 c./sec.; CHOH), 6·53 (AB quartet; *J* = 10·5 c./sec.; CH_2OH).

13α-*Isopropyl*-8β-*podocarpane*-8α,14α,15-*triol* (Xa).—The acid (Xb) (100 mg.) was reduced as in the preceding experiment. The product crystallised from ethyl acetate–light petroleum in prisms (66 mg.) of the triol (Xa), m. p. 111—114°, identical with the specimen prepared above from the 8,14-ene (VIIIa).

Epoxidation of 13α-*Isopropylpodocarp*-8(14)-*ene*-7β,15-*diol* (IIIa).—The diol (1·6 g.) and *m*-chloroperbenzoic acid (1·3 g.) in chloroform (50 ml.) were stirred for 2 hr. and then

* This acid contains 15% of the isomer (XI).[12,13]

the solution was washed with 2N-sodium hydroxide solution and water and dried. Recovery gave a gum (1·63 g.) which was shown by t.l.c. (15% ethanol in benzene) to be a mixture of two compounds of almost identical R_F.

Reduction of the Epoxides with Lithium Aluminium Hydride.—The above mixture of epoxides (1·63 g.) in dry tetrahydrofuran (50 ml.) was added slowly to a suspension of lithium aluminium hydride (1·9 g.) in tetrahydrofuran (50 ml.) at 0°. The mixture was stirred at room temperature for 30 min., refluxed for 2 hr., and cooled and ethyl acetate and water were added. The mixture was acidified (pH 2) with dilute sulphuric acid and the product was recovered in ether and chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (3 : 7) gave 13α-*isopropyl*-8β-*podocarpane*-7β,8β,15-*triol* (XIVa) which crystallised from ether–light petroleum as needles (490 mg.), m. p. 148—150°, $[\alpha]_D^{24}$ +8° (*c* 0·5) (Found: C, 74·0; H, 11·15. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3485 and 3360 cm.$^{-1}$.

The *diacetate* (XIVb) was prepared by treating the triol (70 mg.) with acetic anhydride (1 ml.) in pyridine (2 ml.) for 72 hr. After purification by p.l.c. [in ethanol–benzene (1 : 9)] and sublimation at 170°(bath)/10^{-4} mm. it was a gum (Found: C, 70·2; H, 10·4. $C_{24}H_{40}O_5$ requires C, 70·55; H, 9·9%), $\nu_{max.}$ 3575 (OH), 1738 and 1722 (C=O) cm.$^{-1}$, τ (CCl_4) 9·15 and 9·02 (methyls), 7·98 (6H singlet; OAc), 6·33 (2H, AB quartet; J = 11·5 c./sec.; CH_2·OAc), 5·53 (1H multiplet; $W_{\frac{1}{2}}$ = 12 c./sec.; CH·OAc).

Ethanol–ethyl acetate (1 : 1) eluted 13α-*isopropyl*-8β-*podocarpane*-7β,14α,15-*triol* (XVa) which crystallised from ethyl acetate–light petroleum as needles (324 mg.), m. p. 181—182°, $[\alpha]_D^{24}$ −11° (*c* 0·54) (Found: C, 74·15; H, 11·2. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3610 and 3330 (OH) cm.$^{-1}$.

The *triacetate* (XVb) was prepared as above and chromatographed on alumina. It was eluted with ether–light petroleum (3 : 7) and after sublimation at 160°(bath)/5 × 10^{-4} mm. had m. p. 105—107° (Found: C, 69·2; H, 9·35. $C_{26}H_{42}O_6$ requires C, 69·3; H, 9·4%), $\nu_{max.}$ 1740 and 1728 cm.$^{-1}$, τ (CCl_4) 9·16, 9·13, and 9·03 (methyls), 8·07, 8·03, and 8·01 (singlets; OAc), 6·32 (2H, AB quartet; J = 11·0 c./sec.; CH_2·OAc), 5·76 (1H multiplet; $W_{\frac{1}{2}}$ = ~15 c./sec.; CH·OAc at 7), 4·58 (1H broad singlet; $W_{\frac{1}{2}}$ = 4·5 c./sec.; CH·OAc at 14).

Oxidation of the Triol (XIVa) *with Lead Tetra-acetate.*—Lead tetra-acetate (260 mg.) was added to the triol (130 mg.) in pyridine (15 ml.) and the solution was stirred for 15 min. and left to stand for 24 hr. The solution was diluted with water and the product recovered in ether and chromatographed on silica gel. Elution with ether–light petroleum (1 : 4 and 3 : 7) gave the *keto-hemiacetal* (XVI) which crystallised from ether–light petroleum (b. p. 40—60°) as needles (118 mg.), m. p. 144—147° (Found: C, 74·3; H, 10·45. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·6%), $\nu_{max.}$ 3395 (OH) and 1714 (C=O) cm.$^{-1}$, τ 9·23 (6H doublet; J = 5·5 c./sec.; isopropyl), 8·83 and 8·76 (singlets; methyls), 6·43 (2H, AB quartet; J = 10·5 c./sec.; CH_2·O), 4·28 (broad singlet; $W_{\frac{1}{2}}$ = 4·5 c./sec.; O–CH–O).

Oxidation of the Keto-hemiacetal (XVI).—The hemiacetal (69 mg.) in acetone (50 ml.) was treated with the 8N-chromium trioxide reagent (0·2 ml.) for 4 min. at 0°. The product, isolated in the usual manner (see above), crystallised from ether–light petroleum to give the δ-*lactone* (XVII) as needles (65 mg.), m. p. 130—132° (Found: C, 74·75; H, 10·25. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·1%), $\nu_{max.}$ 1730 (δ-lactone C=O), 1706 (cyclohexanone) cm.$^{-1}$, τ ($CDCl_3$) 9·17, 9·08, 8·95, and 8·86 (singlets; methyls), 6·17 (singlet; CH_2·O·).

Hydroboration of Methyl Abietate with t-2,3-*Dimethylbutylborane during Two Days.*—Methyl abietate (2 g.) was treated with *t*-2,3-dimethylbutylborane (3 mol.) for 2 days at 0° and the product was subjected to oxidative work-up as described above for abietic acid. The resultant gum was chromatographed on alumina. Elution with ether–light petroleum (1 : 9) gave methyl abietate (505 mg.). Ether–light petroleum (3 : 7 and 7 : 13) eluted methyl 7β-hydroxy-13α-isopropylpodocarp-8(14)-en-15-oate (IIIc) which was an intractable gum (515 mg.), $\nu_{max.}$ (film) 3490 and 1722 cm.$^{-1}$.

Elution with ether–light petroleum (9 : 11) yielded methyl 7α-hydroxy-13α-isopropylpodocarp-8(14)-en-15-oate (IIId) as a gum (318 mg.), $\nu_{max.}$ 3500 and 1722 cm.$^{-1}$.

Attempts to prepare crystalline 3,5-dinitrobenzoates from both of the hydroxy-esters were unsuccessful.

Lithium Aluminium Hydride Reduction of the Hydroxy-ester (IIIc).—The ester (40 mg.) in tetrahydrofuran (20 ml.) was treated with lithium aluminium hydride (0·2 g.) for 2 hr. under reflux. The product, isolated in the usual way, crystallised from ether–light petroleum as needles of the diol (IIIa), m. p. 143—146°, identical (i.r. spectrum) with the specimen prepared above from abietic acid.

Hydrogenation of the Hydroxy-ester (IIIc).—The ester (350 mg.) in glacial acetic acid (125 ml.) was hydrogenated in the presence of Adams catalyst (150 mg.; previously reduced in hydrogen) until uptake was complete (1·2 mol.). The catalyst was filtered off, the solution was diluted with water, and the product extracted into ether. The ethereal extract was washed with 2N-sodium hydroxide solution and water and dried and the recovered residue was chromatographed on alumina. Elution with ether–light petroleum (1 : 9) afforded methyl tetrahydroabietate (57 mg.) identified by its i.r. and n.m.r. spectra. Ether–light petroleum (1 : 3) eluted *methyl* 7β-*hydroxy*-13α-*isopropyl*-8ξ-*podocarpan*-15-*oate* [(Vb); mainly 8β-epimer] (232 mg.) which sublimed at 150°(bath)/10^{-4} mm. (Found: C, 74·5; H, 10·7. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%), $\nu_{max.}$ (film) 3510 and 1716 cm.$^{-1}$, τ (CCl_4) 9·17, 9·14, 9·08, 9·03 (singlets; methyls), 8·84 (singlet; 16-methyl), 6·93 (multiplet; $W_{\frac{1}{2}}$ = 15 c./sec.; CH·OH), 6·37 (singlet; CO_2Me). It crystallised from light petroleum (b. p. 30—40°) at −40° with m. p. 67—73°.

Methyl 13α-*Isopropyl*-7-*oxo*-8β-*podocarpan*-15-*oate* (VIb).—The hydroxy-ester (Vb) (190 mg.) in acetone (50 ml.) was treated with the 8N-chromium trioxide reagent (0·3 ml.) at 0° for 10 min. The product was isolated in the usual manner and chromatographed on alumina. The *keto-ester* was eluted with ether–light petroleum (1 : 9) and sublimed at 175°(bath)/10^{-3} mm., $[\alpha]_D^{23}$ −22° (*c* 0·6) (Found: C, 75·85; H, 10·2. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·2%), $\nu_{max.}$ (film) 1718 (ester) and 1708 (cyclohexanone) cm.$^{-1}$, τ (CCl_4) 9·13 (doublet; J = 5·5 c./sec.; isopropyl), 8·94 (singlet; 17-methyl), 8·82 (singlet; 16-methyl), 6·32 (singlet; CO_2Me). It was identical (i.r. spectrum) with the specimen prepared above from the diol (Va).

Treatment of the keto-ester (VIb) in ethanol with benzaldehyde and potassium hydroxide at 40° during two days afforded only the keto-acid (VIa).

Hydrogenation of the Hydroxy-ester (IIId).—The ester (220 mg.), when hydrogenated under the conditions used for the 7β-epimer (see above), took up 1·27 mol. of hydrogen. Chromatography of the product on alumina and elution with ethyl acetate–light petroleum (1 : 9) gave methyl

tetrahydroabietate (40 mg.). Elution with ethyl acetate–light petroleum (1 : 4) afforded methyl 7α-hydroxy-13α-isopropyl-8ξ-podocarpan-15-oate [(Vc); mainly 8β-epimer] which crystallised from ether–light petroleum as prisms (140 mg.), m. p. 133—134° (Found: C, 74·75; H, 10·7. Calc. for $C_{21}H_{36}O_3$: C, 74·95; H, 10·8%), $\nu_{max.}$ 3600 and 1700 cm.$^{-1}$.

Oxidation of the Hydroxy-ester (IIId).—The ester (100 mg.) was oxidised with the 8N-chromium trioxide reagent (0·2 ml.) and the product was isolated and purified in the manner described for the 7β-hydroxy-ester. The keto-ester (VIb) obtained (80 mg.) had $[\alpha]_D^{23}$ −22° (*c* 0·75) and was identical (i.r. and n.m.r. spectra) with the specimens obtained above from the diol (Va) and the 7β-hydroxy-ester (Vb).

13α-*Isopropyl*-8ξ-*podocarpan*-7α,15-*diol* (Vd).—Lithium aluminium hydride (250 mg.) was added to the ester (Vc) (40 mg.) in tetrahydrofuran (25 ml.) and the mixture was refluxed for 2 hr. Ethyl acetate was added and the solution was acidified to pH 4. Recovery gave the diol [(Vd); mainly 8β-epimer] which crystallised from ether–light petroleum as prisms, m. p. 156—159° (Found: C, 77·3; H, 11·4. Calc. for $C_{20}H_{36}O_2$: C, 77·9; H, 11·8%), $\nu_{max.}$ 3400 cm.$^{-1}$, τ 9·10 and 9·06 (methyls), 6·52 (AB quartet; J = 11 c./sec.; CH_2·OH), 6·06 (multiplet; $W_{\frac{1}{2}}$ = 7·0 c./sec.; CH·OH).

Reaction of Abietic Acid with Excess of Diborane.—Boron trifluoride (9·4 g.) was added during 30 min. to a stirred solution of sodium borohydride (2 g.) in diglyme (50 ml.) at 0° under a static pressure of nitrogen. Abietic acid (5 g.) in tetrahydrofuran (15 ml.) was then added dropwise during 15 min. and the resultant solution was left to stand for 36 hr. at 0—5°. Water (5—10 ml.) and 5N-sodium hydroxide solution (15 ml.) were added, followed by 40% hydrogen peroxide (15 ml., dropwise) keeping the temperature below 40°. The mixture was stirred for 2 hr., acidified to pH 2 with dilute hydrochloric acid and extracted with ether. The combined ethereal layers were washed with water and evaporated *in vacuo* and the product was chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (1 : 4 and 3 : 7) gave 13α-*isopropyl*-8β-*podocarpane*-7β,14β,15-*triol* (XIXa) which crystallised from ether–light petroleum as needles (2·7 g.), m. p. 138—141°, $[\alpha]_D^{24}$ +20·5° (*c* 0·17) (Found: C, 74·5; H, 11·15. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3270 cm.$^{-1}$, τ 9·14, 9·07, and 8·97 (singlets; methyls), ~7·55 (multiplet; 9-H), 6·54 (AB quartet; J = 11 c./sec.; CH_2·OH), ~6·2 (multiplet; $W_{\frac{1}{2}}$ = ~20 c./sec.; CH·OH).

Ethyl acetate eluted 13ξ-*isopropyl*-8ξ-*podocarpane*-7ξ,14ξ,15-*triol* (XXIIIa) which crystallised from ethyl acetate–light petroleum in needles (550 mg.), m. p. 223—224°, $[\alpha]_D^{24}$ +19° (*c* 0·2) (Found: C, 74·15; H, 11·2. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3580, 3320, and 3220 cm.$^{-1}$, τ 9·09, 9·03, 8·97, and 8·93 (singlets; methyls), 6·53 (2H, AB quartet; J = 10·5 c./sec.; CH_2·OH), 5·7 (1H multiplet; $W_{\frac{1}{2}}$ = 15 c./sec.; CH·OH), 5·12 (1H broad singlet; $W_{\frac{1}{2}}$ = 5 c./sec.; CH·OH).

The triol (XXIIIa) was recovered after treatment with anhydrous copper sulphate in acetone for 24 hr.

On standing, the combined mother-liquors from the triols (XIXa) and (XXIIIa) deposited crystals of 13α-*isopropyl*-8α-*podocarpane*-7α,14α,15-*triol* (IVa) which crystallised from ether–light petroleum as needles (112 mg.), m. p. 154—155°, $[\alpha]_D^{26}$ −9° (*c* 0·3) (Found: C, 73·8; H, 11·1. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%), $\nu_{max.}$ 3380 cm.$^{-1}$.

The isopropylidene derivative (XXIa) of the triol (XIXa) was prepared by treating the triol in acetone with anhydrous copper sulphate at room temperature for 18 hr. It was a gum, $\nu_{max.}$ (film) 3480 cm.$^{-1}$, τ (in CCl_4) 9·22 (overlapping doublets; J = 7 c./sec.; isopropyl), 9·24 and 9·09 (16- and 17-methyls), 8·70 and 8·57 (singlets; isopropylidene methyls), 6·87 (AB quartet; J = 10 c./sec.; CH_2·OH), 6·6 (multiplet; $W_{\frac{1}{2}}$ = ~22 c./sec.; 2 CH·O·). Its *3,5-dinitrobenzoate* crystallised from ethanol in needles, m. p. 179—181° (Found: C, 64·7; H, 7·35. $C_{30}H_{42}N_2O_8$ requires C, 64·5; H, 7·6%). The *acetate* (XXIb) of the isopropylidene derivative (XXIa), prepared with acetic anhydride in pyridine, was purified by p.l.c. in ethanol–benzene (1 : 19) followed by sublimation at 170°(bath)/10^{-3} mm. It had m. p. 91—93° (Found: C, 73·75; H, 10·35. $C_{25}H_{42}O_4$ requires C, 73·85; H, 10·4%), $\nu_{max.}$ 1740 and 1245 (acetate) cm.$^{-1}$.

The *triacetate* (XXIIIb) of the triol (XXIIIa), prepared with acetic anhydride in pyridine, was eluted from alumina with ether–light petroleum (2 : 3). It sublimed at 170°(bath)/10^{-4} mm. as crystals, m. p. 102—107° (Found: C, 68·9; H, 9·15. $C_{26}H_{42}O_6$ requires C, 69·3; H, 9·4%), τ (CCl_4) 9·16, 9·00, and 9·06 (singlets; methyls), 8·07, 8·04, and 8·00 (singlets; OAc), 6·31 (2H, AB quartet; J = 11 c./sec.; CH_2·OAc), ~5·51 (1H multiplet; $W_{\frac{1}{2}}$ = ~21 c./sec.; CH·OAc), 4·85 (1H broad singlet; $W_{\frac{1}{2}}$ = 6·0 c./sec.; CH·OAc).

The *triacetate* (IVb) of the triol (IVa), prepared in the usual way, was eluted from alumina with ethyl acetate–light petroleum (2 : 3). It sublimed at 170°(bath)/10^{-4} mm. as a gum (Found: C, 69·3; H, 9·35. $C_{26}H_{42}O_6$ requires C, 69·3; H, 9·4%), $\nu_{max.}$ (film) 1740 cm.$^{-1}$.

Hydroboration of 7β,15-*Dihydroxy*-13α-*isopropylpodocarp*-8(14)-*ene* (IIIa).—The diol (1 g.) was treated with excess diborane in the usual way and the product, after oxidative work-up, was chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (1 : 4) afforded 7β-*hydroxy*-13α-*isopropylpodocarp*-8-*ene* (XVIII) which crystallised from ethyl acetate–light petroleum as needles (55 mg.), m. p. 160—162° (Found: C, 78·5; H, 11·5. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2%), $\nu_{max.}$ 3480 (OH) cm.$^{-1}$.

Elution with ethyl acetate–light petroleum (3 : 7) gave 13α-isopropyl-8β-podocarpane-7β,14β,15-triol (XIXa) (540 mg.) which crystallised from ether–light petroleum as needles, m. p. 134—137°, identical (i.r. spectrum) with the specimen prepared above from abietic acid.

Preparation of the Acid (XXId).—The isopropylidene derivative (XXIa) (160 mg.) in acetone (50 ml.) was oxidised at 0° with the 8N-chromium trioxide reagent (0·15 ml.). The product, isolated in the usual way, was the aldehyde (XXIc) as a semi-solid (148 mg.), $\nu_{max.}$ 2690 and 1722 (CHO) cm.$^{-1}$, τ (CCl_4) 9·08 (overlapping doublets; J = 7 c./sec.; isopropyl), 9·08 (singlet; 17-methyl), 8·76 (singlet; 16-methyl), 8·76 and 8·63 (isopropylidene methyls), 6·54 (multiplet; 2 CH·O·), 0·91 (singlet; CHO). Potassium permanganate (70 mg.) in acetone (15 ml.) was added to the aldehyde (145 mg.) in acetone (25 ml.) and the mixture was left with occasional shaking for 1 hr. The solvent was removed *in vacuo* and sodium metabisulphite solution was added, followed by dilute hydrochloric acid to pH 4—5. The solution was extracted with ether and the combined ether extracts were extracted with 2N-sodium hydroxide solution. The alkaline layer was acidified and the product recovered in ether and chromatographed on silica gel. Elution with ether–light petroleum (1 : 4) gave the *acid*

(XXId) which crystallised from acetone in prisms (92 mg.), m. p. 220—222° (Found: C, 72·95; H, 10·05. $C_{23}H_{38}O_4$ requires C, 73·0; H, 10·1%), $\nu_{max.}$ 2660 and 1687 cm.$^{-1}$, τ (CCl_4) 9·22 (overlapping doublets; J = 7 c./sec.; isopropyl), 9·08 (singlet; 17-methyl), 8·81 (singlet; 16-methyl), 8·73 and 8·56 (singlets; isopropylidene methyls), 6·6 (multiplet; $W_{\frac{1}{2}}$ = ~23 c./sec.; 2 CH·O·).

7β,14β,-Dihydroxy-13α-isopropyl-8β-podocarpan-15-oic Acid (XIXb).—The isopropylidene derivative (XXId) (74 mg.) in 70% acetic acid (40 ml.) was heated at 75° for 4 hr. The solution was adjusted to pH 6 with sodium hydrogen carbonate solution and the product was recovered in ether. Chromatography on silica gel and elution with ether–light petroleum (1 : 1) gave the *acid* (XIXb) which crystallised from ether–light petroleum as prisms (37 mg.), m. p. 260—262° (Found: C, 70·6; H, 9·8. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%), $\nu_{max.}$ 3370 (OH) and 2650 and 1690 (CO_2H) cm.$^{-1}$.

The *methyl ester* (XIXc), prepared with ethereal diazomethane, was a gum which sublimed at 170°(bath)/5 × 10^{-3} mm., $[\alpha]_D^{26}$ −14° (*c* 0·34) (Found: C, 71·1; H, 10·2. $C_{21}H_{36}O_4$ requires C, 71·55; H, 10·3%), $\nu_{max.}$ 3425 (OH) and 1723 (ester) cm.$^{-1}$. It was identical (i.r. spectrum) with the ester prepared below by hydroboration-oxidation of methyl abietate.

Oxidation of the Triol (XXIIIa).—The triol (200 mg.) was added to acetic anhydride (6·4 ml.) and dimethyl sulphoxide (9·6 ml.) and left to stand for 24 hr. The solution was extracted with ether and the extract washed with sodium hydroxide solution and water and dried. Recovery gave a gum which was chromatographed on silica gel. Elution with ether–light petroleum (1 : 9) gave *13ξ-isopropyl-7,14-dioxo-8β-podocarpan-15-al* (XXIV) which crystallised from ether–light petroleum in needles (22 mg.), m. p. 155—157° (Found: C, 75·0; H, 9·25. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%), $\nu_{max.}$ (Perkin-Elmer 125 spectrometer) 3480 (OH) 2700 and 1720 (CHO), 1708 (C=O), and 1590 (C=C) cm.$^{-1}$ (in $CHBr_3$) 2690 and 1720 (CHO), 1708 (C=O), and 1585 (C=C) cm.$^{-1}$, $\lambda_{max.}$ 299 mμ (ε 7400), $\lambda_{max.}$ (EtOH–NaOH) 317 mμ (ε 10,800).

Hydroboration of Methyl Abietate with t-*2,3-Dimethylbutylborane during Seven Days*.—Methyl abietate (3·4 g.) was treated with *t*-2,3-dimethylbutylborane (5·6 mol.), as described, for 7 days. After oxidative work-up (see above) the product was chromatographed on alumina. Elution with ether–light petroleum (2 : 3 and then 11 : 9) gave firstly the 7β-hydroxy-ester (Vb) (212 mg.) and then the 7α-hydroxy-ester (Vc) (206 mg.); they were identified by their i.r. spectra. The column was then stripped with ethyl acetate and the residue (3·0 g.) rechromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (1 : 4) gave methyl 7β,14β-dihydroxy-13α-isopropyl-8β-podocarpan-15-oate (XIXc) as a gum (1·22 g.) which was identical (i.r. spectrum and optical rotation) with the specimen prepared above.

Ethyl acetate–light petroleum (2 : 3) eluted *methyl 7ξ,14ξ-dihydroxy-13ξ-isopropyl-8ξ-podocarpan-15-oate* (XXIIIc) (192 mg.) which crystallised from ether–light petroleum in rosettes of needles, m. p. 174—175°, $[\alpha]_D^{24}$ +20° (*c* 0·46) (Found: C, 71·7; H, 10·25. $C_{21}H_{36}O_4$ requires C, 71·55; H, 10·3%), $\nu_{max.}$ 3430 (OH) and 1725 (ester) cm.$^{-1}$, τ 9·12, 9·04, and 8·94 (singlets; methyls), 8·69 (3H singlet; 16-methyl), 6·45 (singlet; CO_2Me), 5·63 (1H multiplet; $W_{\frac{1}{2}}$ = ~15 c./sec.; CH·OH), 5·10 (1H multiplet; $W_{\frac{1}{2}}$ = 5·0 c./sec.; CH·OH).

Elution with ethyl acetate afforded *methyl 7α,14α-dihydroxy-13α-isopropyl-8α-podocarpan-15-oate* (IVc) (270 mg.) which crystallised from ether–light petroleum in needles, m. p. 165—168°, $[\alpha]_D^{24}$ −13° (*c* 0·42) (Found: C, 71·2: H, 10·25. $C_{21}H_{36}O_4$ requires C, 71·55; H, 10·3%), $\nu_{max.}$ 3550 (OH) and 1700 (ester) cm.$^{-1}$.

Lithium Aluminium Hydride Reduction of the Dihydroxy-esters (XXIIIc) *and* (IVc).—The ester in tetrahydrofuran (50 ml.) was treated with lithium aluminium hydride (0·2 g.) for 2 hr. under reflux. The products were isolated in the usual manner.

(*a*) The dihydroxy-ester (XXIIIc) (100 mg.) gave the triol (XXIIIa) which crystallised from ethyl acetate–light petroleum as needles (76 mg.), m. p. 223—224°, identical (i.r. spectrum) with the specimen prepared above from abietic acid.

(*b*) The dihydroxy-ester (IVc) (90 mg.) gave the triol (IVa) which crystallised from ethanol–light petroleum as needles (72 mg.), m. p. 149—151°, identical (i.r. spectrum) with the specimen prepared from abietic acid.

Hydroboration of the Hydroxy-ester (IIId).—The ester (250 mg.) was treated with excess diborane in the usual way for 24 hr. After oxidative work-up the product was chromatographed on alumina (Grade V). Elution with ethyl acetate–light petroleum (1 : 4) gave starting material (150 mg.) identified by its n.m.r. spectrum. Ethyl acetate eluted the dihydroxy-ester (IVc) (48 mg.), m. p. 164—167°, identical (i.r. spectrum) with that prepared above from methyl abietate.

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