

## Diterpenes. Part X.<sup>1</sup> Some Transformations of Phyllocladene and Iso-phyllocladene

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The products from, and the effect of solvent on the ring-opening of 15 $\alpha$ ,16-epoxyphyllocladane (1) and of 16,17-epoxyphyllocladane (17) with boron trifluoride have been examined. The action of other Lewis acids has also been investigated. Treatment of 15 $\alpha$ ,16-epoxykaurane (21) with boron trifluoride-ether complex results in rearrangement, giving atisiran-15-one (25).

Photo-oxygenation of phyllocladene (6) and isophyllocladene (19) has been studied; a minor product from the latter reaction is 15 $\alpha$ ,16-epoxyphyllocladan-17-ol (2).

INTERCONVERSIONS and rearrangements of tri-, tetra-, and penta-cyclic diterpenes have been studied extensively in recent years, both as a means of establishing structural inter-relationships and as a model for biosynthetic pathways. A Glasgow group<sup>2</sup> has reported the acid-catalysed conversion of the hydrocarbons hibaene, trachylobane, and kaurene into mixtures of atisirene, isoatisirene, kaurene, and isokaurene; atisirene and isoatisirene are themselves converted into the same equilibrium mixture. The same group has also studied the solvolysis of the toluene-*p*-sulphonates of *exo*- and *endo*-17-norkauran- and -17-norphyllocladan-16-ols,<sup>3</sup> and Japanese<sup>4</sup> and Indian<sup>5</sup> workers have studied the acid-catalysed isomerisation of hibaene  $\alpha$ -epoxide and the isomerisation of related hydrocarbons. In all cases the transformations can be rationalised by postulating 1,2-alkyl and -hydride shifts and, less frequently, 1,3-hydride shifts. Relative yields can be rationalised on the basis of the known order of stability of alkyl carbonium ions, the lowered stability of a cyclopentyl carbonium ion relative to that of a cyclohexyl carbonium ion, and the generally observed preference for alkyl shifts relative to hydride shifts.

In a preliminary communication<sup>6</sup> two of us reported the reaction of 15 $\alpha$ ,16-epoxyphyllocladane (1) with boron trifluoride-ether complex to give 16-epiphylllocladan-15-one (3)<sup>7</sup> and, in 29% yield, a new ketone which was assigned the structure (10). We now report details of our structural assignment and of a subsequent study of the effect of solvent on the rearrangement. A recent paper<sup>8</sup> has confirmed the constitution and stereochemistry of neoatisiran-15-one (10) by a synthesis of its enantiomer from (–)-neoatisirene (12).

The new ketone, C<sub>20</sub>H<sub>32</sub>O, showed i.r. absorption at 1714 cm<sup>-1</sup> (cyclohexanone), showed a negative Cotton effect curve, and gave an n.m.r. spectrum in accord with the proposed structure. In particular, a doublet at  $\delta$  1.08 p.p.m. due to the C-16 methyl group collapsed to a singlet on irradiation at  $\delta$  2.00 p.p.m. Treatment of the

ketone with sodium methoxide-methan-[<sup>2</sup>H]ol gave a ketone, which contained one atom of deuterium as shown by the mass spectrum, and which showed its C-16 methyl n.m.r. signal as a broad singlet. The hindered nature of the carbonyl group was indicated by the failure of the compound to form an ethylene acetal, an oxime, or a *p*-tolylsulphonylhydrazone, even under forcing conditions. Treatment with sulphuryl chloride gave a chloro-derivative, but no reaction occurred with bromine in acetic acid or with pyridinium bromide perbromide.

Reduction of neoatisiran-15-one with lithium aluminium hydride afforded a good yield of a single alcohol, m.p. 156–158°, which was formulated as neoatisiran-15 $\beta$ -ol (11), since attack on the hindered ketone would be expected to occur from the  $\alpha$ -face. The assignment was supported by the n.m.r. spectrum, in which the C-10 methyl signal appeared downfield from the position which it occupied in the ketone, and by the i.r. spectrum, which showed a strong band at 3628 cm<sup>-1</sup> due to non-bonded OH stretching, and a weak broad band at 3480 cm<sup>-1</sup> due to a hydrogen-bonded species.

In an attempt to convert it into the known (+)-neoatisirene (13) or (+)-isoneoatisirene (14)<sup>9</sup> by dehydration, the alcohol (11) was treated with thionyl chloride in pyridine. This afforded an alkene, C<sub>20</sub>H<sub>32</sub>, m.p. 104–105°, which was formulated as compound (15) from its spectral parameters. Since our isolation of this compound it has also been obtained in a similar manner by McCrindle and his co-workers<sup>8</sup> who have assigned the same structure and have rationalised its formation. Treatment of neoatisiran-15 $\beta$ -ol with boron trifluoride-ether complex in acetic acid also afforded the alkene (15), but, in addition, gave a further compound which is probably the isomer (16) formed by acid-catalysed isomerisation.<sup>8</sup> The alkene (15) was also formed when, in an attempt to form a heavy-atom derivative for X-ray analysis, neoatisiran-15 $\beta$ -ol was treated with bromoacetyl bromide. In this case, the alkene probably arises by an alkyl-oxygen cleavage of a bromoacetyl

<sup>1</sup> Part IX, L. H. Briggs, R. C. Cambie, P. S. Rutledge, and D. W. Stanton, *J. Chem. Soc.*, 1965, 6212.

<sup>2</sup> R. A. Appleton, A. J. McAlees, A. McCormick, R. McCrindle, and R. D. H. Murray, *J. Chem. Soc. (C)*, 1966, 2319; see also, R. A. Appleton, J. C. Fairlie, R. McCrindle, and W. Parker, *J. Chem. Soc. (C)*, 1968, 1716.

<sup>3</sup> R. A. Appleton, P. A. Gunn, and R. McCrindle, *J. Chem. Soc. (C)*, 1970, 1148.

<sup>4</sup> A. Yoshikoshi, M. Kitadani, and Y. Kitahara, *Tetrahedron*, 1967, 23, 1175.

<sup>5</sup> K. H. Kapadi and S. Dev, *Tetrahedron Letters*, 1965, 1255.

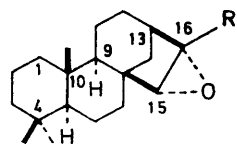
<sup>6</sup> J. G. St. C. Buchanan and B. R. Davis, *Chem. Comm.*, 1967, 1142.

<sup>7</sup> L. H. Briggs, R. C. Cambie, and P. S. Rutledge, *J. Chem. Soc.*, 1963, 5374; R. Henderson and R. Hodges, *Tetrahedron*, 1960, 11, 226.

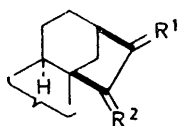
<sup>8</sup> P. A. Gunn, R. McCrindle, and R. G. Roy, *J. Chem. Soc. (C)*, 1971, 1018.

<sup>9</sup> L. H. Zalkow and A. C. Oehlschlagel, *J. Org. Chem.*, 1967, 32, 808.

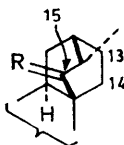
ester to form a carbonium ion, which then undergoes a rearrangement and elimination. A model shows that alkyl-oxygen cleavage would be assisted by relief of the non-bonded interaction of the ester group with the C-10 methyl group.



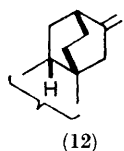
- (1) R = Me  
(2) R = CH<sub>2</sub>-OH



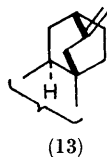
- (3) R<sup>1</sup> =  $\alpha$ -Me,  $\beta$ -H, R<sup>2</sup> = O  
(4) R<sup>1</sup> = CH<sub>2</sub>, R<sup>2</sup> =  $\alpha$ -OH,  $\beta$ -H  
(5) R<sup>1</sup> =  $\beta$ -CHO,  $\alpha$ -H; R<sup>2</sup> = H<sub>2</sub>  
(6) R<sup>1</sup> = CH<sub>2</sub>, R<sup>2</sup> = H<sub>2</sub>  
(7) R<sup>1</sup> = CH<sub>2</sub>, R<sup>2</sup> = O<sub>2</sub>H, H  
(8) R<sup>1</sup> =  $\alpha$ -Me,  $\beta$ -H, R<sup>2</sup> =  $\beta$ -OH,  $\alpha$ -H  
(9) R<sup>1</sup> = CH<sub>2</sub>, R<sup>2</sup> = O



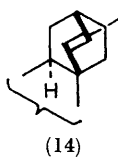
- (10) R = O  
(11) R =  $\beta$ -OH,  $\alpha$ -H



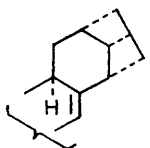
(12)



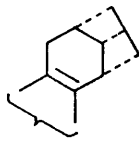
(13)



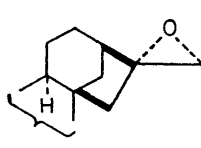
(14)



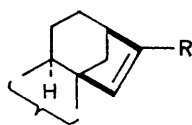
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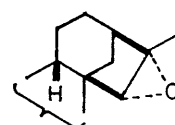
(16)



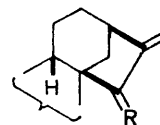
(17)



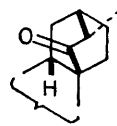
- (18) R = CH<sub>2</sub>-OH  
(19) R = Me  
(20) R = CHO



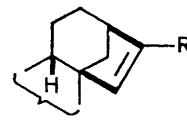
(21)



- (22) R =  $\alpha$ -OH,  $\beta$ -H  
(23) R = H<sub>2</sub>  
(24) R = O



(25)



- (26) R = Me  
(27) R = CH<sub>2</sub>-OH  
(28) R = CHO

In these and succeeding diagrams the bracket denotes a derivative of phyllocladane where H-9 has an  $\alpha$ -configuration and of kaurane where it has a  $\beta$ -configuration. (-)-Kaurane has a 10 $\alpha$ -methyl group and a 5 $\beta$ -hydrogen atom.

During an examination of the effect of changing the solvent on the course of the reaction, 15 $\alpha$ ,16-epoxyphyllocladane (1) was treated with boron trifluoride-dimethyl sulphoxide, a reagent which is reported to effect smooth oxidation of epoxides to hydroxy-ketones.<sup>10</sup> The reaction afforded no hydroxy-ketone but, in addition to traces of the ketones (3) and (10), gave the allylic alcohol (4) <sup>7</sup> by preferential loss of a C-17 proton from a partially or fully developed C-16 carbonium ion. Since the products from the boron trifluoride rearrangement of

epoxides are dependent on the solvent,<sup>11</sup> the reaction was also examined in a solvent of polarity intermediate between that of benzene and dimethyl sulphoxide, *viz.* diethyl ether. In this case the reaction was much slower than when benzene was used as solvent, and it gave the allylic alcohol (4) as the major product with only traces of the ketones (3) and (10). A similar solvent dependence was found for the boron trifluoride-ether ring-opening of 16,17-epoxyphyllocladane (17). In benzene this reaction was fast, giving the aldehyde (5) as the sole product, but in both dimethyl sulphoxide and diethyl ether the reaction was slower, affording the allylic alcohol (18).<sup>12</sup> With diethyl ether as solvent some of the aldehyde (5) was also produced. Results similar to the above have been reported by Hartshorn and his co-workers<sup>11</sup> for the boron trifluoride-induced rearrangement of 5 $\beta$ ,6 $\beta$ -epoxycholestanes.

When 15 $\alpha$ ,16-epoxyphyllocladane (1) is treated with a Lewis acid weaker than boron trifluoride-ether, *viz.* magnesium bromide-ether, the product is 16-epiphyllolcladan-15-one (3).<sup>7</sup> Reinvestigation of this reaction showed that although the 15-ketone (3) is the major product, the allylic alcohol (4) is also formed, albeit in low yield. In this case, it is probable that cleavage of the epoxide ring involves a synchronous process resembling an S<sub>N</sub>2 reaction, while with boron trifluoride-ether a carbonium ion will be almost fully developed in the transition state.<sup>13</sup> Other examples of the influence of the Lewis acid on the course of epoxide reactions have been

reported,<sup>14</sup> including that of tin(IV) chloride, which would also be expected to react by a synchronous process since it is a weaker Lewis acid than boron trifluoride.<sup>15</sup> However, with 15 $\alpha$ ,16-epoxyphyllocladane it gave products identical with those formed by use of boron trifluoride. The allylic alcohol (4) is also formed when 15 $\alpha$ ,16-epoxyphyllocladane (1) is treated with lithium aluminium hydride.<sup>7</sup> This reaction probably occurs by a rearrangement involving attack by a hydride ion.

<sup>10</sup> W. W. Epstein and F. W. Sweat, *Chem. Rev.*, 1967, **67**, 247.

<sup>11</sup> B. N. Blackett, J. M. Coxon, M. P. Hartshorn, and K. E. Richards, *Tetrahedron*, 1969, **25**, 4999.

<sup>12</sup> L. H. Briggs, B. F. Cain, R. C. Cambie, B. R. Davis, and P. S. Rutledge, *J. Chem. Soc.*, 1962, 1850.

<sup>13</sup> J. M. Diggle, M. P. Halliday, A. Kasal, G. D. Meakins, and M. S. Saltmarsh, *J. Chem. Soc. (C)*, 1970, 2325.

<sup>14</sup> V. N. Yandovskii, V. S. Karavan, and T. I. Temnikova, *Russ. Chem. Rev.*, 1970, **39**, 265.

<sup>15</sup> G. A. Olah, 'Friedel-Crafts and Related Reactions,' Interscience, Wiley, New York, 1963, p. 856.

Treatment of the epoxide with the stronger base lithium diethylamide<sup>16</sup> also gave the allylic alcohol (4).

The positive charge which would form at C-16 from a boron trifluoride-ether epoxide-opening of 15 $\alpha$ ,16-epoxykaurene (21) is also suitably placed for non-classical carbonium ion formation and thus for skeletal rearrangement. Treatment of this epoxide with boron trifluoride-ether gave a trace of the allylic alcohol (22)<sup>12</sup> and, as the major product, a compound C<sub>20</sub>H<sub>32</sub>O, m.p. 111–112.5°, which is tentatively formulated as atisiran-15-one (25) by analogy with the corresponding product from the reaction with 15 $\alpha$ ,16-epoxyphyllocladane. Like its isomer (10), this compound showed a cyclohexanone peak at 1715 cm<sup>-1</sup> in its i.r. spectrum and its carbonyl group was markedly unreactive, the compound failing to form a 2,4-dinitrophenylhydrazone, an oxime, or a hemiacetal with methanol. In addition to three tertiary methyl signals at  $\delta$  0.84, 0.86, and 1.04 p.p.m., its n.m.r. spectrum showed a doublet at  $\delta$  1.09 due to the C-16 methyl group, and, in accord with the octant rule, its o.r.d. curve showed a positive Cotton effect.

The photo-oxygenation of kaurene (23) and isokaurene (26) has been examined by Barnes and MacMillan,<sup>17</sup> who obtained kaur-15-en-17-ol (27) and the minor products kaur-15-en-17-al (28) and kaur-16-en-15 $\alpha$ -ol (22) from the former compound. From isokaurene they obtained kaur-16-en-15 $\alpha$ -ol (22) and, as minor products, kaurene and kaur-15-en-17-ol (27), which were formed either by allylic oxidation of isokaurene or by photo-oxygenation of kaurene formed during the reaction. Other products were the  $\alpha\beta$ -unsaturated ketone (24) and the aldehyde (28), which were probably formed by dehydration of the respective hydroperoxides. In the present study, photo-oxygenation of phyllocladene (6) with haematoporphorin as the sensitiser, followed by reductive work-up with sodium iodide,<sup>18</sup> gave phylloclad-15-en-17-ol (18) as the major product and phylloclad-15-en-17-al (20), while isophyllocladene (19) gave the expected product, phylloclad-16-en-15 $\alpha$ -ol (4), and traces of phylloclad-15-en-17-ol (18), phylloclad-15-en-17-al (20), and phylloclad-16-en-15-one (9). Phylloclad-16-en-15 $\alpha$ -ol and phylloclad-15-en-17-ol were unaffected by further photo-oxygenation. In one experiment, 15 $\alpha$ ,16-epoxyphyllocladan-17-ol (2) was obtained as a minor product from phyllocladene. It was identified by comparison with the product from epoxidation of phylloclad-15-en-17-ol (18); it was different from that from phylloclad-16-en-15 $\alpha$ -ol (4). It seems unlikely that the compound (2) is formed as a direct photo-oxygenation product of phyllocladene; more probably it arises from an allylic hydroperoxide (7) which is formed either by an allylic oxidation of phyllocladene or, less likely, from photo-oxygenation of isophyllocladene.

During the present work an attempt was made to functionalise the C-10 methyl group of a phyllocladene

<sup>16</sup> B. Richborn and R. P. Thummel, *J. Org. Chem.*, 1969, **34**, 3583; *J. Amer. Chem. Soc.*, 1970, **92**, 2064; A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.*, 1966, **20**, 119.

<sup>17</sup> M. F. Barnes and J. MacMillan, *J. Chem. Soc. (C)*, 1967, 361.

derivative by photolysis of the nitrite ester of 16-epiphyllocladan-15 $\beta$ -ol (8), since in this compound the C-10 angular methyl group is  $\gamma$  to the nitrite ester.<sup>19</sup> However, although no starting material remained after photolysis for 1 h, the product was a complex mixture in which 16-epiphyllocladan-15-one (3) was the major component, this compound presumably arising by disproportionation of an alkoxyl radical.

#### EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 237 spectrophotometer and u.v. spectra were recorded with a Unicam SP 800 spectrophotometer. N.m.r. spectra were measured by use of Varian A60 or T60 spectrometers, with tetramethylsilane as internal reference. O.r.d. data were obtained with a Jasco ORD/UV-5 instrument. Alumina for chromatography was Spence type H material, deactivated with 5% v/v of aqueous 10% acetic acid, and silica gel for chromatography was Kieselgel S (Riedel de Haen) deactivated with 15% v/v of water.

Photo-oxygenations were carried out in a column in which the liquid was supported by oxygen diffusing through a sintered glass disc at the bottom of the column, which was illuminated externally along its length by means of a fluorescent tube (20 W) mounted 2 cm from its side.

*Rearrangement of 15 $\alpha$ ,16-Epoxyphyllocladane with Boron Trifluoride-Ether Complex.*—(a) *In benzene.* Treatment of the epoxide (1) in benzene as described,<sup>7</sup> followed by chromatography of the product from light petroleum on deactivated alumina or by dry-column chromatography from benzene on silica gel gave 16-epiphyllocladan-15-one (3) (70%), m.p. and mixed m.p. 129–129.5°, identical (i.r. and n.m.r. spectra) with authentic material, and then *neoatisiran-15-one* (10) (29%), plates (from methanol), m.p. 137°, [ $\alpha$ ]<sub>D</sub> –33° (Found: C, 83.6; H, 10.9; O, 5.8. C<sub>20</sub>H<sub>32</sub>O requires C, 83.3; H, 11.2; O, 5.6%),  $\nu_{\max}$  (CHCl<sub>3</sub>) 1714 cm<sup>-1</sup> (CO),  $\delta$  0.66 (s, 10-Me), 0.80 and 0.86 (2 s, *gem*-Me<sub>2</sub>), and 1.08 p.p.m. (d, J 7 Hz, 16-Me), o.r.d. (c 2.0 in MeOH) [ $\phi$ ]<sub>589</sub> –30°, [ $\phi$ ]<sub>500</sub> –40°, [ $\phi$ ]<sub>400</sub> –190°, [ $\phi$ ]<sub>350</sub> –460°, [ $\phi$ ]<sub>304</sub> –2100°, [ $\phi$ ]<sub>283</sub> 0°, and [ $\phi$ ]<sub>238</sub> +1170°.

(b) *In diethyl ether.* A solution of the epoxide (1) (50 mg) in dry ether was treated with freshly distilled boron trifluoride-ether complex (1 drop). The reaction was followed by t.l.c.; after 20 h the epoxide had disappeared. The products were identified as 16-epiphyllocladan-15-one and phylloclad-16-en-15 $\alpha$ -ol (4) by comparative t.l.c.

(c) *In dimethyl sulphoxide.* A mixture of the epoxide (1) (0.50 g), dry dimethyl sulphoxide (40 ml), and boron trifluoride-ether complex (2 drops) was heated at 100° under anhydrous conditions for 20 h. Work-up gave phylloclad-16-en-15 $\alpha$ -ol (0.26 g, 52%), needles (from methanol-ether), m.p. and mixed m.p. 109–110°, identical (i.r. spectrum) with authentic material,  $\delta$  0.87 and 0.90 (2 s, *gem*-Me<sub>2</sub>), 0.98 (s, 10-Me), 2.61 (m, 13-H), 4.43 (s, 15-H), and 5.21 and 5.03 p.p.m. (d, J 0.5 Hz, 17-H<sub>2</sub>). Little reaction occurred at 20° during 24 h.

[16-<sup>2</sup>H<sub>1</sub>]Neoatisiran-15-one.—Neoatisiran-15-one (0.10 g), sodium methoxide (0.10 g), methan[<sup>2</sup>H]ol (14 ml), and deuterium oxide (0.5 ml) were heated under reflux for 70 h.

<sup>18</sup> A. Nickon and J. F. Bagli, *J. Amer. Chem. Soc.*, 1961, **83**, 1498.

<sup>19</sup> D. H. R. Barton, J. N. Bearton, L. E. Geller, and M. N. Pechet, *J. Amer. Chem. Soc.*, 1961, **83**, 4076; K. Akhtar, *Adv. Photochem.*, 1964, **2**, 263.

Addition of deuterium oxide gave a product which was sublimed (120° and 0.9 mmHg) to give [16-<sup>2</sup>H<sub>1</sub>]neoatisiran-15-one as plates, m.p. 123—133°,  $M^+$  289,  $\nu_{\max}$  (CCl<sub>4</sub>) 1714 cm<sup>-1</sup> (CO),  $\delta$  0.64 (s, 10-Me), 0.80, 0.85 (2 s, *gem*-Me<sub>2</sub>), and 1.05br p.p.m. (s, 16-Me).

**16-Chloroneoatisiran-15-one.**—Neoatisiran-15-one (0.38 g), sulphuryl chloride (2 ml), and dry carbon tetrachloride (10 ml) were stirred at 25° for 36 h. The solution was then poured into water to yield a solid (0.31 g) containing two compounds (t.l.c.). The major one was isolated by chromatography on deactivated alumina and crystallised from methanol-ether to give 16-chloroneoatisiran-15-one as plates, m.p. 127—129° (decomp.),  $\nu_{\max}$  (CCl<sub>4</sub>) 1728 cm<sup>-1</sup> (CO),  $\delta$  0.65 (s, 10-Me), 0.82 and 0.85 (2 s, *gem*-Me<sub>2</sub>), and 1.72 p.p.m. (s, 16-Me).

**Neoatisiran-15 $\beta$ -ol** (11).—Neoatisiran-15-one (0.50 g) in ether (30 ml) was added during 15 min to a stirred suspension of lithium aluminium hydride (0.2 g) in ether (30 ml). The mixture was heated under reflux for 8 h and stirred at 20° for 12 h. Work-up gave *neoatisiran-15 $\beta$ -ol*, needles (from ethanol-ethyl acetate), m.p. 156—158°, sublimation at 110° and 0.2 mmHg,  $[\alpha]_D^{20} +16^\circ$  (Found: C, 82.6; H, 11.7; O, 5.7. C<sub>20</sub>H<sub>34</sub>O requires C, 82.7; H, 11.8; O, 5.5%),  $\nu_{\max}$  (CCl<sub>4</sub>) 3628s (monomeric OH), 3480w,br (H-bonded OH), and 1068 and 1037 cm<sup>-1</sup> (OH),  $\delta$  0.85 (6H, *gem*-Me<sub>2</sub>), 1.01 (d, *J* 5.5 Hz, 16-Me), 1.01 (s, 10-Me), and 3.08 p.p.m. (d, *J* 6.2 Hz, 16-H).

**Dehydration of Neoatisiran-15 $\beta$ -ol.**—(a) *With thionyl chloride-pyridine.* Thionyl chloride (2.0 ml) was added dropwise to a solution of neoatisiran-15 $\beta$ -ol (0.20 g) in pyridine (20 ml) at 0°. The mixture was kept at 20° for 1.5 h and then poured into water. Extraction with ether gave an oil (0.19 g) which was chromatographed on alumina. Elution with light petroleum gave a solid showing only one spot on t.l.c. (silver nitrate-impregnated silica gel). Crystallisation from methanol gave 13-methyl-17-nor-12(8  $\rightarrow$  14 $\beta$ H)abeo-atisiran-7-ene (15) (0.12 g), m.p. 104—105° (lit.,<sup>8</sup> 103—105°),  $\nu_{\max}$  (CCl<sub>4</sub>) 1670 and 825 cm<sup>-1</sup> (trisubst. C=C),  $\delta$  0.75 (d, *J* 7 Hz, 13-Me), 0.88 (6H *gem*-Me<sub>2</sub>), 0.90 (s, 10-Me), and 5.18 p.p.m. (m, 7-H).

(b) *With boron trifluoride-ether complex.* Boron trifluoride-ether (0.5 ml) was added to neoatisiran-15 $\beta$ -ol (0.20 g) in glacial acetic acid (5 ml) and the solution was held at 20° for 2.5 h. Light petroleum was added and the mixture was washed with water and with sodium hydrogen carbonate solution. Evaporation of the solvent left a solid (0.14 g) which was separated by preparative t.l.c. on silver nitrate-impregnated silica gel into two fractions (approximately equal amounts). One was the alkene (15), m.p. and mixed m.p. 104—105°, identical (i.r. spectrum) with authentic material, and the other was a compound [needles (from methanol-ether), m.p. 52—57°] tentatively identified as the alkene (16).

(c) *With bromoacetyl bromide.* Bromoacetyl bromide (0.2 g, 0.95 mmol) was added to a solution of neoatisiran-15 $\beta$ -ol (0.25 g, 0.78 mmol) in dry benzene (5 ml), and the mixture was stirred at 25° for 17 h, poured into ice-water, and extracted with ether. The ether layer was washed with aqueous 5% sodium hydrogen carbonate and water, and dried. Removal of solvent left an oil (100%) which contained two compounds (t.l.c. on silver nitrate-silica gel). Chromatography on alumina gave the unsaturated hydrocarbon (15), m.p. and mixed m.p. 104—105°, identical (i.r. and n.m.r. spectra) with authentic material.

**Rearrangement of 15 $\alpha$ ,16-Epoxyphyllocladane with Mag-**

**nesium Bromide-Ether Complex.**—A mixture of magnesium powder (0.30 g, 12 mmol) and mercury(II) bromide (2.16 g, 6 mmol) in dry ether (60 ml) and benzene (30 ml) was heated under reflux under nitrogen for 2 h. Solids were removed, the epoxide (1) (1.0 g, 3.4 mmol) was added, and refluxing under nitrogen was continued for 12 h. The mixture was set aside at 24° for a further 24 h and worked up to give a solid, which was chromatographed on alumina. Elution with hexane gave unchanged epoxide (0.60 g, 60%); elution with benzene gave 16-epiphyllocladan-15-one (3) (0.30 g), m.p. and mixed m.p. 129°,  $\delta$  0.78 (s, 10-Me), 0.83 (s, *gem*-Me<sub>2</sub>), and 1.01 p.p.m. (d, *J* 7 Hz, 16-Me). T.l.c. and i.r. spectroscopy showed the presence of the allylic alcohol (4) in the crude product.

**Rearrangement of 15 $\alpha$ ,16-Epoxyphyllocladane with Tin(IV) Chloride.**—(a) *In benzene.* A solution of the epoxide (1) (50 mg) in dry benzene was treated with tin(IV) chloride (1 drop) at 20°, and after 1 h the reaction was quenched with ice-water. T.l.c. indicated that no epoxide remained and that the products were the same as when boron trifluoride in benzene was used.

(b) *In ether.* The epoxide (1) (50 mg) in dry ether was treated with tin(IV) chloride as in (a). Most of the epoxide had reacted after 20 h, and the products were the same as when boron trifluoride was used, although more ketonic products were formed.

**Rearrangement of 16,17-Epoxyphyllocladane with Boron Trifluoride-Ether Complex.**—(a) *In benzene.* A solution of the epoxide (17)<sup>7</sup> (50 mg) in dry benzene (10 ml) was treated with boron trifluoride-ether (1 drop) and the reaction was allowed to proceed for 10 min before being quenched with ice-water. Work-up gave phyllocladan-17-al (5) (100%) as a clear oil,  $\nu_{\max}$  (film) 2920, 2840 (CH<sub>2</sub>), 2700 (CHO), 1715 (CHO), 1460 (CH<sub>2</sub>), and 1390 and 1370 cm<sup>-1</sup> (*gem*-Me<sub>2</sub>),  $\delta$  0.83 and 0.87 (2 s, *gem*-Me<sub>2</sub>), 1.03 (s, 10-Me), 2.44 (m, 13-H and 15-H), 2.70 (s, 16-H), and 9.45 p.p.m. (s, CHO). Lack of coupling between the C-16 proton and an adjacent aldehydic proton has been observed previously.<sup>20</sup>

The 2,4-dinitrophenylhydrazones crystallised from aqueous methanol as prisms, double m.p. 167 and 188—190° (Found: C, 66.6; H, 7.75; N, 11.7. C<sub>26</sub>H<sub>36</sub>N<sub>4</sub>O<sub>4</sub> requires C, 66.6; H, 7.7; N, 12.0%),  $\delta$  0.86 (s, *gem*-Me<sub>2</sub>), 1.00 and 1.04 (2 s, 10-Me, geometric isomers), 2.30 (m, 13-H and 15-H), 2.58 (s, 16-H), 7.43—8.33 (m, aromatic H), and 8.74 and 8.76 p.p.m. (2 s, 17-H, geometric isomers).

(b) *In dimethyl sulphoxide.* A mixture of the epoxide (17) (50 mg), dry dimethyl sulphoxide (10 ml), and boron trifluoride-ether (1 drop), was heated at 100° for 7 h. Comparative t.l.c. showed that in addition to traces of unchanged epoxide and aldehyde (5), the major product, which was isolated (25 mg, 50%) by dry-column chromatography on alumina, was phylloclad-15-en-17-ol (18), identical (i.r. spectrum) with authentic material,  $\delta$  0.76 (s, 10-Me), 0.81 and 0.88 (2 s, *gem*-Me<sub>2</sub>), 1.60 (s, OH), 2.40 (m, 13-H), 4.17 (d, *J* 1.5 Hz, 17-H<sub>2</sub>), and 5.60 p.p.m. (s, 15-H).

A similar reaction carried out at 20° required a time of 60 h before most of the epoxide had reacted. The products were the same as those formed at 100°.

**Rearrangement of 15 $\alpha$ ,16-Epoxyphyllocladane with Lithium Diethylamide.**—An ethereal solution of *n*-butyl-lithium (2.0 ml) was treated at 0° under nitrogen with redistilled diethylamine (1.0 ml) in dry ether (5 ml), and the mixture was

<sup>20</sup> R. M. Carman, D. E. Cowley, and R. A. Marty, *Austral. J. Chem.*, 1969, **22**, 1681.

set aside at 0° for 10 min until evolution of butane had ceased. The epoxide (1) (0.10 g) was added in portions and the mixture was refluxed gently under nitrogen for 20 h and then worked-up to give an oil (85 mg), which was chromatographed on silica gel. Elution with benzene gave phylloclad-16-en-15 $\alpha$ -ol (4) (20 mg, 20%), identical (i.r. and n.m.r. spectra) with authentic material.

**Rearrangement of 15 $\alpha$ ,16-Epoxykaurane with Boron Trifluoride-Ether Complex.**—A solution of boron trifluoride-ether (0.15 ml) and 15 $\alpha$ ,16-epoxykaurane (21) (74 mg) in dry benzene (10 ml) was shaken at 20° for 15 min. The mixture was washed with water, dried, and concentrated to give *atisiran-15-one* (25), which crystallised from aqueous acetone as needles (27 mg, 57%), m.p. 111–112.5°,  $[\alpha]_D^{20}$  0° (Found: C, 83.2; H, 11.3. C<sub>26</sub>H<sub>32</sub>O requires C, 83.3; H, 11.2%),  $\nu_{\max}$  (CCl<sub>4</sub>) 1715 cm<sup>-1</sup> (CO),  $\delta$  0.84 and 0.86 (2 s, *gem*-Me<sub>2</sub>), 1.04 (s, 10-Me), and 1.09 p.p.m. (d, *J* 7 Hz, 16-Me), o.r.d. (*c* 0.02 in MeOH)  $[\phi]_{589}^{20}$  0°,  $[\phi]_{350}^{20} + 460^\circ$ ,  $[\phi]_{307}^{20} + 2570^\circ$ pk,  $[\phi]_{282}^{20}$  0°, and  $[\phi]_{249}^{20} - 3390^\circ$ tr.

In a further experiment the crude product was chromatographed on alumina. Elution with light petroleum gave *atisiran-15-one* (21%); elution with benzene gave *kaur-16-en-15 $\alpha$ -ol* (22) (5%), identical (i.r. spectrum) with authentic material, and then unidentified compounds. *Kaur-16-en-15 $\alpha$ -yl acetate* crystallised from methanol as plates, m.p. 100–101° (Found: C, 80.0; H, 10.3. C<sub>22</sub>H<sub>34</sub>O<sub>2</sub> requires C, 79.95; H, 10.4%),  $\nu_{\max}$  (CS<sub>2</sub>) 1733 and 1240 cm<sup>-1</sup> (OAc).

**Photo-oxygenation of Phyllocladene.**—A solution of phyllocladene (6) (1.8 g; purified by chromatography on silver nitrate-impregnated silical gel) and haematoporphyrin (40 mg) in dry pyridine (100 ml) was irradiated in a stream of oxygen for 5 days. Ether (20 ml) and charcoal (20 mg) were added and the mixture was swirled and filtered. The filtrate was evaporated at 20° to yield a crude hydroperoxide (1.2 g), which was suspended in dry ether (12 ml) and dry ethanol (50 ml) and reduced with sodium iodide (5.2 g) at 20° for 20 h. Work-up gave a solid which was chromatographed (dry-column) on silica gel. Elution with benzene gave the following compounds, each identified by t.l.c., i.r., and n.m.r. comparison with authentic samples: (i) phyllocladene (0.52 g, 29%), (ii) phylloclad-15-en-17-ol (0.85 g, 47%), (iii) phylloclad-15-en-17-al (0.24 g, 13%). Similar results were obtained when lithium aluminium hydride was used in the reduction.

In another experiment, elution of the column with ether gave 15 $\alpha$ ,16-epoxyphyllocladan-17-ol (2) (7%), which crystallised from light petroleum as needles, m.p. 145.5–147° (Found: C, 78.8; H, 10.2. C<sub>26</sub>H<sub>32</sub>O<sub>2</sub> requires C, 78.9; H, 10.6%),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3450 (OH), 2940, 2863, and 1465 (CH<sub>2</sub>), 1390 and 1375 (*gem*-Me<sub>2</sub>), 1063 (prim. OH), and 927 and 840 cm<sup>-1</sup> (epoxide),  $\delta$  0.76 (d, *J* 12 Hz, 14 $\beta$ -H), 0.83 and 0.89 (2 s, *gem*-Me<sub>2</sub>), 0.92 (s, 10-Me), 2.20 (m, 13-H), 3.50 (s, 15-H), and 3.8 and 4.1 p.p.m. (2 d, *J* 12.5 Hz, 17-H<sub>2</sub>).

**Photo-oxygenation of Isophyllocladene.**—A solution of isophyllocladene (19) (1.18 g; pure by chromatography on silver nitrate-impregnated silica gel) in dry pyridine (100 ml) was irradiated in a stream of oxygen for 3.5 days.

Reduction and work-up of the mixture followed by chromatography as before gave (i) a trace of alkene which was not identical with either phyllocladene or isophyllocladene (25 mg, 2%), (ii) phylloclad-16-en-15 $\alpha$ -ol (1.0 g, 85%), (iii) phylloclad-15-en-17-ol (35 mg, 3%), (iv) phylloclad-16-en-15-one (13 mg, 1%), and (v) phylloclad-15-en-17-al (22 mg, 2%).

**Epoxidation of Phylloclad-15-en-17-ol.**—*m*-Chloroperbenzoic acid (80 mg, 0.46 mmol) was added with stirring to a solution of the alcohol (18) (0.10 g, 0.36 mmol) in methylene dichloride (10 ml) at 20°, and the mixture was set aside for 2 h, whereupon t.l.c. showed that no starting material remained. Work-up and recrystallisation of the crude product from hexane gave 15 $\alpha$ ,16-epoxyphyllocladan-17-ol (2) (90 mg, 90%) as needles, m.p. and mixed m.p. 148–148.5°, identical (i.r. and n.m.r. spectra) with authentic material.

**Epoxidation of Phylloclad-16-en-15 $\alpha$ -ol.**—The alcohol (4) (0.10 g, 0.36 mmol) was treated with *m*-chloroperbenzoic acid (80 mg, 0.46 mmol) as in the previous experiment, and the crude product was chromatographed (dry-column) on silica gel. Elution with benzene and recrystallisation from anhydrous methanol gave 16,17-epoxyphyllocladan-15 $\alpha$ -ol (84 mg, 84%) as needles, m.p. 127–128° (Found: C, 78.6; H, 10.6; O, 10.6. C<sub>16</sub>H<sub>22</sub>O<sub>2</sub> requires C, 78.0; H, 10.5; O, 10.35%),  $\nu_{\max}$  (CHCl<sub>3</sub>) 3500 (OH), 2940, 2860, and 1465 (CH<sub>2</sub>), 1390 and 1375 (*gem*-Me<sub>2</sub>), 1063 (sec. OH), and 930 and 830 cm<sup>-1</sup> (epoxide),  $\delta$  0.80 and 0.86 (2 s, *gem*-Me<sub>2</sub>), 0.93 (s, 10-Me), 2.05 (m, 15-OH and 13-H), 2.98 (s, 17-H<sub>2</sub>), and 3.98 p.p.m. (s, 15-H).

**16-Epiphylocladan-15 $\beta$ -yl Nitrite.**—A solution of nitrosyl chloride (3 ml) (prepared from sodium nitrite and concentrated hydrochloric acid<sup>21</sup>) in pyridine (7 ml) was added to a cold solution of 16-epiphylocladan-15 $\beta$ -ol (8)<sup>7</sup> in dry pyridine (5 ml), and the mixture was kept in anhydrous conditions at 25° for 2 h. The mixture was then poured into ice-water and the flocculent precipitate was collected. T.l.c. showed an absence of starting material, but the nitrite ester was unstable and all attempts to purify it caused decomposition to the starting alcohol. The nitrite had  $\nu_{\max}$  (CHCl<sub>3</sub>) 2996, 2950, 2912, 2850, 1650, 1465, 1390, 1370, 885, 832, and 800 cm<sup>-1</sup> (NO),  $\lambda_{\max}$  (EtOH) 246 and 325–390 nm (five bands),  $\delta$  0.72 (s, 10-Me), 0.79 and 0.81 (2 s, *gem*-Me<sub>2</sub>), 1.07 (d, *J*<sub>16,17</sub> 8 Hz, 16-Me), 2.53 (m, 13-H), and 5.11 p.p.m. (d, 15-H).

**Photolysis of 16-Epiphylocladan-15 $\beta$ -yl Nitrite.**—A solution of the nitrite ester (0.25 g) in dry benzene (200 ml) was flushed with dry, oxygen-free nitrogen for 1 h and then photolysed with a Hanovia 450 W medium-pressure mercury-vapour lamp (Pyrex filter). T.l.c. indicated the absence of starting material after 1.5 h. Removal of solvent and chromatography of the residue on alumina yielded 16-epiphylocladan-15-one (3) (50%) and a small amount of 16-epiphylocladan-15 $\beta$ -ol, each identified by comparative t.l.c.

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<sup>21</sup> J. R. Morton and H. W. Wilcox, *Inorg. Synth.*, 1953, 4, 48.