281. *The Chemistry of Extractives from Hardwoods. Part XXVI.* Experiments on* cyclo*Eucalenol, a New Triterpene from* Eucalyptus microcorys.

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A new triterpene has been obtained by saponification of the oily light-petroleum extract of tallow wood (*Eucalyptus microcorys*, fam. *Myrtaceae*), which, bearing a general similarity to the *cyclo*artenol sub-group, has been named *cyclo*eucalenol.

*cyclo*Eucalenol is a monohydric secondary alcohol, apparently $C_{31}H_{52}O$. It contains one ethylenic bond, present in a side chain terminated by the grouping $-CH_2\cdot C(:CH_2)\cdot CHMe_2$. The occurrence of a *cyclo*propane ring was revealed by the action of hydrogen chloride and by the infrared absorption at 3050 cm.$^{-1}$. Oxidation of the unsaturated acid-isomerisation products from demethyl*cyclo*eucalanyl acetate, a dihydro-derivative having the modified terminal group $-CH_2\cdot CH_2\cdot CHMe_2$, gave a diketone containing the transoid system $-CO\cdot\overset{|}{C}=\overset{|}{C}\cdot CO-$ but not identical with 7 : 11-dioxolanost-8-enyl acetate.

Of the various Australian timbers available commercially in the United Kingdom, several noted for their very high durability, *e.g.*, jarrah, spotted gum, are derived from *Eucalyptus* species. From several published reports [1] it may be inferred that ellagic acid is a common constituent of *Eucalyptus* woods, and we have isolated this acid from two or three varieties by extraction with alcohol, but no examination of the extractive constituents of these woods appears to have been recorded. *Eucalyptus microcorys* has been the subject of our first investigation in this group, in part because of the oily nature of this timber which is indicated by its common description as tallow wood.

Treatment with boiling light petroleum sufficed to remove the oily components and, when the resulting amber syrup was saponified, an alkali-insoluble material remained which when purified by chromatography gave a highly crystalline solid, m. p. 140°, amounting to 0·7% of the original wood. More detailed examination of this product has shown that it belongs to the *cyclo*artenol sub-group of triterpenes, whence it has been named *cyclo*eucalenol. It is remarkable that shortly afterwards *cyclo*eucalenol was again isolated in

* Part XXV, *J.*, 1955, 2948.

[1] Wade, *Pharm. J.*, 1925, **115**, 131; Anderson and Steedor, *J. Soc. Leather Trades' Chemists*, 1950, **34**, 478; Hillis, *Austral. J. Sci. Res.*, 1952, *A*, **5**, 379; M. M. Chattaway, *Austral. J. Bot.*, 1953, **1**, 27.

our laboratory, by Mr. J. M. Uprichard, from the heartwood of *Erythrophloeum guineense* (fam. *Leguminoseae*), a circumstance which may imply a wide distribution of this hitherto unknown natural product.

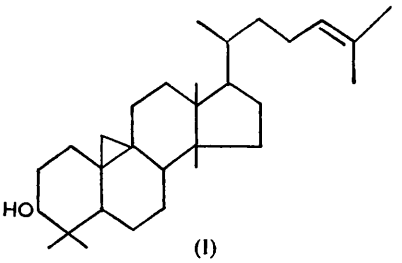
Analyses of *cyclo*eucalenol were in agreement with the formula $C_{30}H_{50-52}O$, but did not exclude $C_{31}H_{50-52}O$, and similarly for the various derivatives, *i.e.*, acetate, benzoate, 3 : 5-dinitrobenzoate, and α-naphthylurethane, by which the oxygen function was demonstrated. The alcoholic group was oxidised either with chromic oxide–acetic acid or chromic oxide–pyridine,[2] the product, *cyclo*eucalenone, being a ketone, as was shown by the light absorption maximum (368 mμ) of the derived 2 : 4-dinitrophenylhydrazone.[3] The ketone reacted to the Zimmermann test, which for triterpene nuclei is believed to be typical of the 3-oxo-group,[4] and was reduced again by sodium borohydride to the parent alcohol. In view of the unhindered nature of the 3-keto-group, this result appeared to denote an equatorial conformation for the hydroxyl and this was confirmed by the existence of a peak at 1040 cm.$^{-1}$ in the infrared spectrum. Molecular-rotation changes following acylation (Δ_1, acetylation, +106°; Δ_2, benzoylation, +167°) are also in agreement with those of a 3β(equatorial)-hydroxyl group in a triterpene or sterol nucleus with an A : B *trans* ring system.

The presence of a double bond in *cyclo*eucalenol, apparent colorimetrically (tetranitromethane), was confirmed by catalytic hydrogenation of the acetate to a dihydro-derivative, *cyclo*eucalanyl acetate, which was shown to be saturated by its stability to peracetic acid and by the absence of appreciable absorption at 200—220 mμ. *cyclo*Eucalanol was prepared by hydrolysis of the acetate and oxidised by chromic oxide–pyridine to *cyclo*eucalanone. The ketone was characterised by the usual derivatives, and when reduced by the Wolff–Kishner method afforded the saturated hydrocarbon *cyclo*eucalane.

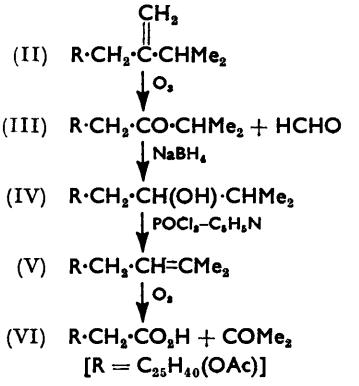
From ultraviolet end absorption measurements the *cyclo*eucalenol ethylene bond appeared to be disubstituted.[5] Ozonolysis, which resulted in the liberation of formaldehyde—isolated as 2 : 4-dinitrophenylhydrazone and dimedone derivatives—proved the centre of unsaturation to be a vinylidene group, and the existence of infrared absorption bands at 889 and 1640 cm.$^{-1}$ gave independent support to this. Absorption due to unsaturation was absent also from the infrared spectrum of the dihydro-compound, *cyclo*eucalanyl acetate, but a shoulder was observed at *ca* 3050 cm.$^{-1}$, thus affording the first indication of the *cyclo*propane ring[6] afterwards found by chemical methods to be a characteristic feature of the molecule. The hydrocarbon *cyclo*eucalane which was prepared in the course of these experiments also exhibits absorption at 1010 cm.$^{-1}$ sometimes associated with a *cyclo*propane ring.[6] The features disclosed by this preliminary survey of *cyclo*eucalenol enabled it to be formulated as a pentacyclic, monohydroxy-, monoethylenic triterpene, and its many points of resemblance to *cyclo*artenol[7] (I) seemed at first to imply a close structural relationship between the two compounds. Further experiments, however, disclosed important differences. For example, an examination of the volatile fraction from the ozonolysis of *cyclo*eucalenyl acetate (II), by chromatography of the crude 2 : 4-dinitrophenylhydrazone,[8] revealed no trace of acetone such as is formed from the terminal group of the *cyclo*artenol side chain. An explanation of this divergency was found in the further degradation of the principal ozonolysis product of *cyclo*eucalenyl acetate, which at low temperatures consisted of a crystalline ketone, demethyloxo*cyclo*eucalanyl acetate (III). The ketone, which from the Zimmermann reaction appeared to contain a $-CO\cdot CH_2-$ group, was first reduced by sodium borohydride to the corresponding alcohol (IV), and the latter was then dehydrated with phosphoryl chloride in pyridine. The product (V), though it did not give satisfactory analyses, had a strong tetranitromethane reaction, and its ultraviolet absorption was indicative of a trisubstituted double bond. Ozonolysis of this olefin gave acetone and an acid (VI), characterised by its methyl ester, to which the

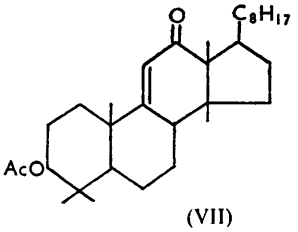
[2] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.
[3] Braude and Jones, *J.*, 1945, 498.
[4] Barton and de Mayo, *J.*, 1954, 887.
[5] Bladon, Henbest, and Wood, *J.*, 1952, 2737.
[6] Cole, *Chem. and Ind.*, 1953, 946; *J.*, 1954, 3807.
[7] Barton, Page, and Warnhoff, *J.*, 1954, 2715; Irvine, Henry, and Spring, *J.*, 1955, 1316.
[8] Meigh, *Nature*, 1952, **170**, 579.

formula $C_{26}H_{42}(OAc)\cdot CO_2H$ is assigned. These reactions, illustrated in the accompanying diagram, not only enable the terminal unit of the side chain to be identified as $-CH_2\cdot C(:CH_2)\cdot CHMe_2$ but, by analogy with eburicoic acid,[9] euphorbol,[10] and *cyclo*laudenol,[11] imply that the complete substituent is $-CHMe\cdot CH_2\cdot CH_2\cdot C(:CH_2)\cdot CHMe_2$ thereby adding further support to the C_{31} formula.

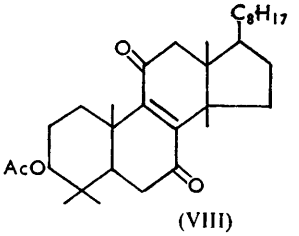


(I)





(VII)



(VIII)

Confirmation for the *cyclo*propane ring was obtained as with *cyclo*artenol by the action of hydrogen chloride on *cyclo*eucalanyl acetate, whereupon isomerisation occurred with the formation of a mixed product showing marked short-wave ultraviolet absorption and olefinic bands in the infrared spectrum. Repeated crystallisation of a sample afforded a small yield of a seemingly pure compound (eucalenyl acetate) $C_{31}H_{53}OAc$, having ultraviolet absorption indicative of a trisubstituted double bond. Following the procedure developed by Bentley, Henry, Irvine, and Spring for the investigation of *cyclo*artenol,[12] the crude mixture was oxidised with chromic oxide in acetic acid and the resulting material fractionated by chromatography. In addition to unchanged eucalenyl acetate, two further products were isolated, one an unsaturated ketone (acetate) $C_{31}H_{51}O\cdot OAc$ with αβ-ethylenic absorption, and the other a pale yellow compound $C_{31}H_{49}O_2\cdot OAc$. For convenience the unsaturated ketone is at present designated oxoeucalenyl acetate although it does not follow that the position of the double bond is identical with that on eucalenyl acetate or that the enone system is necessarily situated as in the corresponding *cyclo*artenol derivative (VII). On the other hand, there is little doubt that the compound $C_{31}H_{49}O_2\cdot OAc$, which has the characteristic ultraviolet light absorption of a transoid enedione, is closely related to 7 : 11-dioxolanost-8-enyl acetate (VIII) obtained by the oxidation of certain triterpenes unsaturated at the 7 : 8- or 8 : 9-position,[13] including the isomerised *cyclo*artenyl acetate. The dioxoeucalenyl acetate was hydrolysed to the parent alcohol, and

[9] Gascoigne, Holker, Ralph, and Robertson, *J.*, 1951, 2346; Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2414, 2422.

[10] Arigoni, Wyler, and Jeger, *Helv. Chim. Acta*, 1954, **37**, 1553; Arigoni, Jeger, and Ruzicka, *ibid.*, 1955, **38**, 222; Barbour, Warren, and Wood, *J.*, 1951, 2537; Christian, Vogel, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 510; Barbour, Lourens, Warren, and Watling, *J.*, 1955, 2194.

[11] Bentley, Henry, Irvine, Mukerji, and Spring, *J.*, 1955, 596; Henry, Irvine, and Spring, *ibid.*, p. 1607.

[12] Bentley, Henry, Irvine, and Spring, *J.*, 1953, 3673.

[13] *Inter alia* Ruzicka, Ray, and Muhr, *Helv. Chim. Acta*, 1944, **27**, 472; Dorée and McGhie, *Nature*, 1954, **173**, 148; Dorée and Kurzer, *J.*, 1948, 988; 1949, 570; Lahey and Strasser, *J.*, 1951, 873.

as in the case of the diketone (VIII) was reduced with zinc–acetic acid to the saturated dione. Oxidation of eucalenyl acetate with chromic oxide in acetic acid also gave oxo-eucalenyl acetate, identical (mixed m. p.) with that obtained from the acid-isomerisation product of *cyclo*eucalanyl acetate. Eucalanyl acetate, and thence eucalanol, was obtained by vigorous catalytic reduction of eucalenyl acetate, from which an epoxide was also prepared.

From the general structural similarity of *cyclo*eucalenol and *cyclo*artenol apparent in the foregoing reactions it seemed possible that after elimination of the obvious difference due to the additional carbon atom at position 24, a derivative common to the two compounds might be obtained, which would thus establish the remaining structural features of the new alcohol. In the first attempt to relate the two triterpenes in this way, demethyloxo-*cyclo*eucalanol was reduced by the Wolff–Kishner method to demethyl*cyclo*eucalanol, characterised by its acetate, when it became obvious that the reduction product was not identical with *cyclo*artanol. Accordingly, the effect of eliminating the *cyclo*propane ring was next investigated, using for this purpose the newly prepared demethyl*cyclo*eucalanol. Isomerisation of the acetate with hydrogen chloride, as outlined for the higher homologue, gave a mixture which, when oxidised, yielded the expected products, *viz.*, demethyl-eucalenyl acetate and demethyloxo- and -dioxo-eucalenyl acetate. However, a comparison of the dioxo-compound with 7 : 11-dioxolanost-8-enyl acetate, which caused a large melting-point depression, indicated their dissimilarity.

The failure of these experiments to relate *cyclo*eucalenol to known triterpene compounds may be due to one or more causes. In the first place, although the transformations recorded are compatible with the occurrence of the methylene bridge (*cyclo*propane ring) at the 9 : 10-position, as in *cyclo*artenol, a significant difference is observed between the alteration of optical rotatory power which follows the oxidation of *cyclo*eucalenol to *cyclo*eucalenone (positive shift) and that which occurs in passing from *cyclo*artenol to *cyclo*artenone (negative shift). It has been suggested[14] that in the case of *cyclo*artenol the (exceptional) negative change is occasioned by the β-conformation of the substituent (CH_2) at $C_{(9)}$. If this inference is valid and the 9-position in *cyclo*eucalenol is involved in a *cyclo*propane ring, it would accordingly imply that the methylene bridge is linked with $C_{(11)}$, as was formerly proposed for *cyclo*artenol. The possible union of other carbon atoms, giving an alternative site for the *cyclo*propane ring cannot be excluded at this stage. However, the non-identity of dioxodemethyleucalenyl acetate and the dioxolanostenyl acetate (VIII) shows that, apart from any lack of correspondence with respect to the *cyclo*propane unit, at least one further point of dissimilarity exists with respect to *cyclo*artenol. It is probable that the difference is one of configuration, possibly at position 17 and/or 20, as already postulated, for example, or euphol. It is unlikely that the angular methyl groups attached to $C_{(13)}$ and $C_{(14)}$ have the euphol configuration[15] since no derivative corresponding to the hypothetical *iso*eucalenol series has been detected among the acid-isomerisation products of *cyclo*eucalenol and its compounds. Further experiments designed to elucidate the undetermined structural or stereochemical features of *cyclo*eucalenol are in progress.

Experimental

Specific rotations were measured with $CHCl_3$ solutions at room temperature, and ultra-violet absorption spectra with EtOH and a Unicam S.P.500 Spectrophotometer. Light petroleum refers to the fraction of b. p 60—80° unless otherwise specified.

Extraction of Eucalyptus microcorys *with Light Petroleum.*—The finely shredded heartwood (3·95 kg.) was extracted with boiling light petroleum for 24 hr., evaporation of the solution leaving a clear amber syrup (90 g., 2·33%). This was redissolved in light petroleum (300 c.c.), and after filtration from gelatinous solid (5·2 g., 0·13%), the solution was evaporated and the residual oil (85 g.) heated under reflux for 4 hr., with a 25% solution of potassium hydroxide in aqueous ethanol (800 c.c., 85% ethanol). The non-saponifiable fraction (47 g.) was isolated with ether in the usual manner as a semicrystalline solid (47 g.) which was dissolved in benzene (250 c.c.) and percolated through a column (43 × 4·5 cm.) of alumina (600 g.), the chromatogram

[14] Dawson, Halsall, Jones, Meakins, and Phillips, *Chem. and Ind.*, 1955, 918.
[15] Barton, McGhie, Pradhan, and Knight, *J.*, 1955, 876.

being eluted with (*a*) benzene (2 l.), (*b*) benzene–ether (9 : 1; 3 l.), (*c*) benzene–ether (4 : 1; 2 l.), (*d*) benzene–ether (1 : 1; 3 l.), and (*e*) ether (3 l.). Evaporation of the combined fractions (*b*) and (*c*) left a pale yellow solid (28·5 g.) which when crystallised from light petroleum or ethyl acetate gave cyclo*eucalenol* as colourless feathery needles, $[\alpha]_D$ +45° (*c*, 2·9), m. p. 138—139°, raised to 140° after drying for 3 hr. *in vacuo* at 100° (Found in a specimen dried above the m.p.: C, 84·2, 84·0; H, 11·4, 11·8. $C_{31}H_{52}O$ requires C, 84·5; H, 11·9%).

*cyclo*Eucalenol gives a pale yellow colour with tetranitromethane. In the Liebermann–Burchard test it forms a brown solution with a strong green fluorescence. Treatment of the terpene (500 mg.) with acetic anhydride (10 c.c.) and pyridine (20 c.c.) for 24 hr. at room temperature gave cyclo*eucalenyl acetate*, which separated from chloroform–methanol as blades, $[\alpha]_D$ +63° (*c*, 1·54), m. p. 110° (Found: C, 81·9; H, 11·5. $C_{33}H_{54}O_2$ requires C, 82·1; H, 11·3%); light absorption: $\varepsilon_{210} = 1048$, $\varepsilon_{220} = 261$, $\varepsilon_{210}/\varepsilon_{220} = 4·01$. Infrared bands in CS_2: 3050 (sh.), 1640, and 889 cm.$^{-1}$. The *benzoate*, prepared from *cyclo*eucalenol (500 mg.) in pyridine (5 c.c.) under reflux with benzoyl chloride (2 c.c.) for 2 hr., crystallised from ethyl acetate as needles, $[\alpha]_D$ +67° (*c*, 0·9), m. p. 130° (Found: C, 83·7; H, 10·5. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%). The 3 : 5-*dinitrobenzoate*, prepared similarly, crystallised from light petroleum as needles, m. p. 205° (Found: C, 71·9; H, 8·31; N, 4·5. $C_{38}H_{54}O_6N_2$ requires C, 71·9; H, 8·6; N, 4·5%). The α-*naphthylurethane* formed plates (from ethanol), m. p. 176° [Found: C, 82·6; H, 9·5%; *M*(Rast), 548. $C_{42}H_{59}O_2N$ requires C, 82·7; H, 9·75%; *M*, 609].

In later experiments the isolation of *cyclo*eucalenol was carried out *via* the acetate prepared from the crude unsaponifiable material (47 g.), with acetic anhydride (200 c.c.) and pyridine (300 c.c.) at room temperature for 48 hr. The crude product (50 g.), isolated by means of ether, was chromatographed in light petroleum (200 c.c.) on alumina (1200 g.; 82·0 × 4·5 cm.), the column being eluted with (*a*) light petroleum (5 l.), (*b*) light petroleum–benzene (4 : 1; 4 l.), (*c*) light petroleum–benzene (1 : 1; 3 l.), and (*d*) benzene (2 l.). Evaporation of fraction (*a*) gave a colourless solid (33 g.) which crystallised from chloroform–methanol as needles, m. p. 109—110°, consisting of *cyclo*eucalenyl acetate identical with that obtained from pure *cyclo*eucalenol. A further quantity (5 g.) was obtained by evaporation of the combined fractions (*b*) and (*c*).

Isolation of a Sterol Fraction.—Evaporation of chromatogram fraction (*e*) from the crude unsaponifiable matter gave a colourless solid (1·8 g.) which crystallised from methanol as needles, m. p. 138—139°, raised to 140° after repeated recrystallisation from light petroleum (Found: C, 84·0; H, 12·1. $C_{29}H_{50}O$ requires C, 84·0; H, 12·2%), $[\alpha]_D$ −5° (*c*, 1·1); light absorption: $\varepsilon_{210} = 2490$, $\varepsilon_{220} = 556$; $\varepsilon_{210}/\varepsilon_{220} = 4·48$. In the Liebermann–Burchard test this sterol underwent the colour changes, pink ⟶ purple ⟶ blue ⟶ green. No fluorescence was observed. It gave a yellow colour with tetranitromethane and a positive Tortelli–Jaffe reaction indicative of the presence of a double bond at $C_{(8)}$. The *sterol acetate* separated from chloroform–methanol as needles, $[\alpha]_D$ −10° (*c*, 1·0), m. p. 118—119° (Found: C, 81·3; H, 11·2. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·4%). The *benzoate* crystallised from chloroform–methanol in plates, $[\alpha]_D$ +15° (*c*, 0·8), m. p. 135—136° (Found: C, 83·5; H, 10·2. $C_{36}H_{54}O_2$ requires C, 83·3; H, 10·5%). The 3 : 5-*dinitrobenzoate*, very pale yellow needles (from light petroleum), had m. p. 195—196° (Found: C, 71·0; H, 8·4. $C_{36}H_{52}O_6N_2$ requires C, 71·0; H, 8·6%).

cyclo*Eucalenone*.—(i) A solution of *cyclo*eucalenol (1 g.) in pyridine (10 c.c.) was added at room temperature, during 30 min., to a slurry of chromic oxide (1 g.) in pyridine (10 c.c.) prepared as by Poos, Arth, Beyler, and Sarett.[2] After 24 hr. the neutral product was isolated with ether and crystallised from ethanol, to yield cyclo*eucalenone* as needles (780 mg.), $[\alpha]_D$ +54° (*c*, 0·8), m. p. 84° (Found: C, 84·6; H, 11·4. $C_{31}H_{50}O$ requires C, 84·9; H, 11·3%).

(ii) A solution of *cyclo*eucalenol (1 g.) in acetic acid (200 c.c.) was treated at room temperature with chromic oxide (200 mg.) in acetic acid (50 c.c.) during 30 min. After 12 hr., the neutral product was isolated in the usual manner, and yielded *cyclo*eucalenone as needles (820 mg.) (from ethanol), m. p. and mixed m. p. 84°.

cyclo*Eucalenone oxime* separated as needles (from light petroleum), m. p. 176—177° (Found: C, 82·1; H, 11·3. $C_{31}H_{51}ON$ requires C, 82·1; H, 11·3%). The 2 : 4-*dinitrophenylhydrazone* crystallised from xylene–ethanol in needles, m. p. 246° (Found: C, 71·9; H, 8·7; N, 9·35. $C_{37}H_{54}O_4N_4$ requires C, 71·8; H, 8·8; N, 9·1%); light absorption in $CHCl_3$: $\lambda_{max.}$ 368 mμ (ε 24,000).

*cyclo*Eucalenone (300 mg.) in methanol (35 c.c.) with sodium borohydride (100 mg.) in methanol (20 c.c.) at room temperature for 24 hr. gave *cyclo*eucalenol (250 mg.); the product, isolated in the usual way, crystallised from light petroleum as needles, m. p. and mixed m. p. 138—139°.

cyclo*Eucalanyl Acetate.*—*cyclo*Eucalenyl acetate (2 g.) in acetic acid (100 c.c.) was shaken with hydrogen and platinum (from 150 mg. of platinum oxide) for 45 min.; the uptake of hydrogen being 97 c.c. at N.T.P. (theor. for 1 double bond, 95·7 c.c.). Crystallised from chloroform–methanol, the resultant cyclo*eucalanyl acetate* formed needles (1·85 g.), $[\alpha]_D$ +62° (*c* 0·6), m. p. 112—113° (Found: C, 82·0; H, 11·9. $C_{33}H_{56}O_2$ requires C, 81·8; H, 11·6%). It gave a pale yellow colour with tetranitromethane and showed very weak light absorption between 200 and 225 mμ, $\varepsilon_{210} = 284$, $\varepsilon_{220} = 108$, $\varepsilon_{210}/\varepsilon_{220} = 2·62$. It was almost quantitatively recovered on treatment with a 10-fold excess of monoperphthalic acid at 0° for 14 days and with perhydrol–acetic acid on the steam-bath for 2 hr.

cyclo*Eucalanol.*—Hydrolysis of *cyclo*eucalanyl acetate with 5% ethanolic potassium hydroxide solution gave cyclo*eucalanol*, which separated from methanol as plates, $[\alpha]_D$ +52° (*c* 0·7), m. p. 149—150° (Found: C, 84·2; H, 12·1. $C_{31}H_{54}O$ requires C, 84·1; H, 12·3%); light absorption: $\varepsilon_{210} = 235$, $\varepsilon_{220} = 31$, $\varepsilon_{210}/\varepsilon_{220} = 7·52$.

cyclo*Eucalanyl benzoate* separated from ethyl acetate as needles, $[\alpha]_D$ +64° (*c* 0·64), m. p. 130° (Found: C, 83·3; H, 10·4. $C_{38}H_{58}O_2$ requires C, 83·5; H, 10·7%).

cyclo*Eucalanone.*—Oxidation of *cyclo*eucalanol (500 mg.) with chromic acid (500 mg.) in pyridine (10 c.c.) for 24 hr. at room temperature and isolation of the product with ether gave cyclo*eucalanone* (400 mg.) as plates (from ethanol), $[\alpha]_D$ +49° (*c* 0·9), m. p. 107—108° (Found: C, 84·2; H, 11·7. $C_{31}H_{52}O$ requires C, 84·5; H, 11·9%); light absorption: $\lambda_{max.}$ 280 mμ (ε 35). The *oxime*, needles from ethanol, had m. p. 191—192° (Found: C, 81·6; H, 12·1; N, 3·4. $C_{31}H_{53}ON$ requires C, 81·5; H, 11·7; N, 3·1%). The *semicarbazone* crystallised from ethanol in needles, m. p. 210° (Found: C, 77·4; H, 11·4; N, 8·8. $C_{32}H_{55}ON_3$ requires C, 77·2; H, 11·4; N, 8·4%); light absorption: $\lambda_{max.}$ 229 mμ (ε 16,200). The 2 : 4-*dinitrophenylhydrazone* separated from ethanol–xylene in plates, m. p. 247° (Found: C, 71·4; H, 9·0; N, 9·3. $C_{37}H_{56}O_4N_4$ requires C, 71·6; H, 9·1; N, 9·0%); light absorption: $\lambda_{max.}$ 368 mμ (ε 24,000).

cyclo*Eucalanane.*—*cyclo*Eucalanone (500 mg.) in anhydrous hydrazine (5 c.c.) and ethanol (20 c.c.) containing dissolved sodium (630 mg.) was heated at 180° for 18 hr. The product, worked up in the normal way, was purified by chromatography in light petroleum on alumina, thus giving cyclo*eucalanane* (420 mg.) which separated from chloroform–methanol as needles, $[\alpha]_D$ +25° (*c* 0·5), m. p. 58—59° (Found: C, 87·3; H, 12·4. $C_{31}H_{54}$ requires C, 87·3; H, 12·7%).

Oxidation of cyclo*Eucalenyl Acetate.*—(i) *By ozonolysis.* *cyclo*Eucalenyl acetate (2 g.) in methylene dichloride (60 c.c.) was treated at −45° with ozonised oxygen (5—7%) for 1 hr. After attaining room temperature, the solution was treated with acetic acid (15 c.c.) and portionwise with zinc dust (4 g.) during 30 min. After 1 hour's stirring, the filtered solution was washed, and the aqueous washings were adjusted to pH 7·0 and treated with saturated aqueous dimedone (150 c.c.). Formaldehyde–dimedone (0·37 g., 30%) was obtained as needles (from ethanol), m. p. and mixed m. p. 189—190°. Evaporation of the dried methylene dichloride solution gave *demethyloxo*cyclo*eucalanyl acetate* (1·8 g.), which crystallised from methanol in needles, $[\alpha]_D$ +35° (*c* 0·6), m. p. 97—98° (Found: C, 79·4; H, 10·5. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%); light absorption: $\lambda_{max.}$ 282 mμ (ε 43).

*cyclo*Eucalenyl acetate (3 g.) was also ozonised at 0° in dry carbon tetrachloride (60 c.c) for 2 hr., and the residue left by evaporation was decomposed with boiling water (250 c.c.). The mixture was distilled and the distillate (150 c.c.) treated with saturated aqueous 2 : 4-dinitrophenylhydrazine hydrochloride. The precipitate formaldehyde 2 : 4-dinitrophenylhydrazone (400 mg., 30%) formed orange needles (from methanol), m. p. and mixed m. p. 168° (Found: C, 40·0; H, 2·9. Calc. for $C_7H_6O_4N_4$: C, 40·0; H, 2·9%). The residual solid, dissolved in ether, was washed with water (100 c.c.) and aqueous potassium hydroxide (3%; 3400 c.c.), a potassium salt separating at the solvent interface. The salt was collected and suspended in water (100 c.c.), the mixture acidified with 2N-sulphuric acid, and the precipitate removed in ether. The product, an *acid acetate* (520 mg.), separated from aqueous acetone as prisms, $[\alpha]_D$ +54° (*c* 0·4), m. p. 204—206° (Found: C, 75·5, 75·7; H, 10·1, 10·3. $C_{28}H_{44}O_4$ requires C, 75·6; H, 10·0. $C_{29}H_{46}O_4$ requires C. 75·9; H, 10·1%). With ethereal diazomethane it gave a *methyl ester*, needles (from methanol), m. p. 122° (Found: C, 76·3; H, 9·9; OMe, 5·8. $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1; OMe, 6·7. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2; OMe, 6·5%). The neutral, non-volatile, ozonolysis product was fractionated by Girard-T reagent. Attempted chromatographic purification of the non-ketonic material was unsuccessful; the ketonic product (1·1 g.), by crystallisation from methanol, gave demethyloxo-*cyclo*eucalanyl acetate of m. p. 96—97° identical with that described above. In the Zimmermann reaction the ketone gave a violet colour, fading after dilution with alcohol.

The *ketoxime* separated from aqueous ethanol as needles, m. p. 170° (Found: C, 76·5;

H, 10·4; N, 2·95. $C_{32}H_{53}O_3N$ requires C, 76·9; H, 10·7; N, 2·8%), and the 2 : 4-*dinitrophenylhydrazone* from xylene–ethanol in needles, m. p. 202—203° (Found: N, 8·4. $C_{38}H_{56}O_6N_6$ requires N, 8·4%); light absorption: $\lambda_{max.}$ 368 mμ (ε 22,400).

The crude 2 : 4-dinitrophenylhydrazone from the volatile ozonolysis product of *cyclo*eucalenyl acetate was subjected to paper partition chromatography in a heptane–methanol atmosphere with heptane as the mobile phase. It was thus shown to be homogeneous, the R_F value corresponding exactly with that of formaldehyde 2 : 4-dinitrophenylhydrazone, and no trace of acetone could be detected.

(ii) *With potassium permanganate.* A mixture of *cyclo*eucalenyl acetate (5 g.) in acetone (500 c.c.), and aluminium sulphate (6 g.), was stirred while potassium permanganate (8 g.) in acetone (150 c.c.) was added during 30 min. The resulting mixture was heated under reflux for 4 hr., cooled, and filtered, and the acetone was evaporated. The residual yellow oil (4·1 g.) was fractionated by Girard-T reagent. The non-ketonic portion consisting of *cyclo*eucalenyl acetate (1·6 g.) formed needles (from chloroform–methanol), m. p. and mixed m. p. 110°. Crystallisation of the ketonic fraction from methanol gave demethyloxo*cyclo*eucalanyl acetate (1·5 g.), m. p. and mixed m. p. 96—97°. The ketone was recovered (95%) after treatment for 15 min. at 60°, in dioxan solution, with aqueous potassium iodide–iodine.

*Demethyloxo*cyclo*eucalanol.*—Hydrolysis of demethyloxo*cyclo*eucalanyl acetate (500 mg.) with 10% methanolic potassium hydroxide (25 c.c.), and repeated recrystallisation of the product from aqueous acetone gave *demethyloxo*cyclo*eucalanol* as needles, m. p. 110—111° (Found: C, 81·3; H, 11·2. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The *oxime* crystallised from aqueous ethanol in needles, m. p. 150° (Found: C, 78·4; H, 11·3; N, 3·3. $C_{30}H_{51}O_2N$ requires C, 78·7; H, 11·2; N, 3·1%), and the 2 : 4-*dinitrophenylhydrazone* as needles (from xylene–ethanol), m. p. 222—224° (Found: C, 68·9; H, 8·9; N, 9·2. $C_{36}H_{54}O_5N_4$ requires C, 69·4; H, 8·7; N, 9·0%).

*Demethylhydroxy*cyclo*eucalanyl Acetate.*—Demethyloxo*cyclo*eucalanyl acetate (1 g.) in methanol (60 c.c.) was treated with sodium borohydride (300 mg.) in methanol (5 c.c.) at room temperature for 24 hr. Crystallisation of the product from aqueous methanol afforded *demethylhydroxy*cyclo*eucalanyl acetate* as needles, $[\alpha]_D$ +60° (*c* 1·2), m. p. 123—126° (Found: C, 78·9; H, 10·9. $C_{32}H_{54}O_3$ requires C, 79·0; H, 11·2%). Acetylation with pyridine–acetic anhydride at room temperature for 24 hr. gave *demethylhydroxy*cyclo*eucalanyl diacetate,* needles (from chloroform–methanol), m. p. 138—140° (Found: C, 77·3; H, 10·2; OAc, 16·3. $C_{34}H_{56}O_4$ requires C, 77·2; H, 10·6; OAc, 16·3%).

*Dehydration of Demethylhydroxy*cyclo*eucalanyl Acetate and Ozonolysis of the Product.*—The alcohol monoacetate (500 mg.) in dry pyridine (5 c.c.) was heated with phosphorus oxychloride (1·3 c.c.) on a steam-bath for 1·5 hr. The mixture was then poured on ice (200 g.) and hydrochloric acid (6·5 c.c.), and the dehydration product (340 mg.) extracted with ether and crystallised from methanol–chloroform. It consisted of needles, $[\alpha]_D$ +54° (*c* 0·6), m. p. 96—100° (Found: C, 79·6; H, 10·5%), which gave a strong yellow colour with tetranitromethane; light absorption: ε_{210} = 1400, ε_{220} = 224, $\varepsilon_{210}/\varepsilon_{220}$ = 6·27.

Ozonolysis of the dehydration product (700 mg.) in acetic acid (50 c.c.) for 40 min., followed by treatment with water (200 c.c.) and distillation into saturated aqueous 2 : 4-dinitrophenylhydrazine hydrochloride, gave acetone 2 : 4-dinitrophenylhydrazone (110 mg. 25%) as orange needles (from methanol), m. p. and mixed m. p. 125—126° (Found: C, 45·3; H, 3·8; N, 23·9. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·2; N, 23·5%). The involatile product was dissolved in ether and washed with water (100 c.c.) and aqueous potassium hydroxide (3%; 3 × 100 c.c.), solid separating at the interface. This potassium salt was collected and shaken with aqueous sulphuric acid, and the product, which consisted of an *acid acetate,* collected with ether. It separated from aqueous acetone as elongated prisms (260 mg.), $[\alpha]_D$ +59° (*c* 1·1), m. p. 193—195° (Found: C, 75·6; H, 9·8%; equiv., 468. $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%; equiv., 458). With ethereal diazomethane the acid formed a *methyl ester acetate,* needles (from aqueous methanol), m. p. 99—100° (Found: C, 75·7; H, 10·1; OMe, 5·9. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2; OMe, 6·5%).

Isomerisation of cyclo*Eucalanyl Acetate.*—(i) Hydrogen chloride was bubbled through a solution of the acetate (1 g.) in chloroform (50 c.c.) at 0° for 1·5 hr. and the mixed product (800 mg.), isolated in the usual manner, crystallised from chloroform–methanol. It formed needles, $[\alpha]_D$ +66° (*c* 0·5), m. p. 118—127° (Found: C, 81·9; H, 11·5. $C_{33}H_{56}O_2$ requires C, 81·8; H, 11·6%), exhibiting a strong yellow colour with tetranitromethane; light absorption: ε_{210} = 3710, ε_{220} = 938, $\varepsilon_{210}/\varepsilon_{220}$ = 3·96.

(ii) *cyclo*Eucalanyl acetate (200 mg.) was dissolved in acetic acid (10 c.c.), and concentrated

hydrochloric acid (2 c.c.) added. The solution was then heated under reflux for ½ hr. and poured into water. Extraction with ether gave needles (130 mg.) (from chloroform–methanol), $[\alpha]_D$ +64° (*c* 0·6), m. p. 119—130°, unaffected when mixed with a sample of the acetate obtained as in (i).

Eucalenyl Acetate.—(i) Numerous crystallisations of the mixture, m. p. 118—127° (800 mg.), from chloroform–methanol gave *eucalenyl acetate* (50 mg.) as needles, $[\alpha]_D$ +85° (*c* 0·6), m. p. 120—122° (Found: C, 81·7; H, 11·5. $C_{33}H_{56}O_2$ requires C, 81·8; H, 11·6%); light absorption: $\varepsilon_{210} = 3400$, $\varepsilon_{220} = 277$, $\varepsilon_{210}/\varepsilon_{220} = 12{\cdot}4$.

(ii) Chromic oxide (660 mg.) in 90% acetic acid (30 c.c.) was added during 5 min. to a solution of the mixed acetates (1·6 g.) in acetic acid (100 c.c.) at 93°. After further heating for 10 min., the liquid was diluted with water, and the precipitate (1·65 g.) isolated with ether. A solution of the product in light petroleum (100 c.c.) was filtered through a column (2·1 × 18 cm.) of alumina (60 g.) which was then eluted with (*a*) light petroleum (1 l.), (*b*) light petroleum–benzene (9 : 1; 500 c.c.), (*c*) light petroleum–benzene (4 : 1; 500 c.c.), (*d*) benzene (350 c.c.), and (*e*) benzene–ether (1 : 1; 1 l.). The combined fractions (*a*) and (*b*) were evaporated, and the product (450 mg.) twice crystallised from chloroform–methanol to give eucalenyl acetate, m. p. and mixed m. p. 120—122°.

Dioxoeucalenyl Acetate.—Fraction (*d*) from the above chromatogram yielded a yellow crystalline solid (460 mg.), which crystallised from methanol to give *dioxoeucalenyl acetate* as light yellow blades, $[\alpha]_D$ +98° (*c* 1·3), m. p. 157° (Found: C, 77·0; H, 9·9. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·2%); light absorption: $\lambda_{max.}$ 271 mμ (ε 7600). Hydrolysis of dioxoeucalenyl acetate with 5% methanolic potassium hydroxide gave *dioxoeucalenol*, as pale yellow needles (from methanol), m. p. 165° (Found: C, 78·9; H, 10·3. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%); light absorption: $\lambda_{max.}$ 271 mμ (ε 6300), 344 mμ (ε 96).

Oxoeucalenyl Acetate.—(i) Chromic oxide (250 mg.) in acetic acid (50 c.c.) was added during 1 hr. to a boiling solution of eucalenyl acetate (450 mg.) in acetic acid (50 c.c.) and the heating continued for 2 hr. The neutral product, isolated with ether, was dissolved in light petroleum (25 c.c.), and the solution filtered through a column (5·0 × 2·2 cm.) of alumina (20 g.). Elution with light petroleum (500 c.c.) and light petroleum–benzene (4 : 1; 500 c.c.) gave a fraction consisting of eucalenyl acetate (100 mg.) which separated from chloroform–methanol as needles, m. p. and mixed m. p. 120—122°. Elution of the chromatogram with benzene (500 c.c.) and benzene–ether (9 : 1; 500 c.c.) gave a solid (270 mg.) which, after several crystallisations from methanol, yielded *oxoeucalenyl acetate* as blades, $[\alpha]_D$ +76° (*c* 0·3), m. p. 136° (Found: C, 79·2; H, 10·9. $C_{33}H_{54}O_3$ requires C, 79·5; H, 10·9%); light absorption: $\lambda_{max.}$ 241 mμ (ε 3400), not giving a colour with tetranitromethane.

(ii) Fraction (*e*) from the chromatogram used in the separation of eucalenyl acetate consisted of oxoeucalenyl acetate (100 mg.) which when recrystallised from methanol gave blades, m. p. and mixed m. p. 136°.

Dioxoeucalanyl Acetate.—Zinc dust (1·2 g.) was slowly added to a boiling solution of dioxoeucalenyl acetate (300 mg.) in acetic acid (15 c.c.) and the heating continued for 1 hr. *Dioxoeucalanyl acetate*, isolated by means of ether, crystallised from methanol in plates, m. p. 198—200° (Found: C, 77·3; H, 10·6. $C_{33}H_{54}O_4$ requires C, 77·0; H, 10·6%); light absorption: $\lambda_{max.}$ 290 mμ (ε 67).

Eucalanyl Acetate.—A solution of the isomerised acetates, m. p. 118—127° (1 g.), from *cyclo*eucalanyl acetate, in acetic acid (100 c.c.), was shaken with hydrogen and platinum (650 mg.) at 80° for 24 hr. The product crystallised from chloroform–methanol in needles, m. p. 115—120°. The hydrogenation caused a significant drop in the light-absorption intensity in the ethylenic region from $\lambda = 1920$ to $\lambda = 2140$. Light absorption change: $\varepsilon_{210} = 3680$, $\varepsilon_{220} = 910$, $\varepsilon_{210}/\varepsilon_{220} = 4{\cdot}05$ before hydrogenation; $\varepsilon_{210} = 1600$, $\varepsilon_{220} = 457$, $\varepsilon_{210}/\varepsilon_{220} = 3{\cdot}48$ after hydrogenation. A solution of the reduced material in acetic acid (100 c.c.) was treated on a steam-bath with chromic oxide (850 mg.) in acetic acid (45 c.c.) added during 30 min. After further heating, the mixture was set aside overnight, the neutral product (1·0 g.) being then isolated with ether. When dissolved in light petroleum (100 c.c.) it was chromatographed on alumina (30 g.), elution with light petroleum (500 c.c.) giving *eucalanyl acetate* (300 mg.) which crystallised from chloroform–methanol as needles, $[\alpha]_D$ +56° (*c* 0·8), m. p. 132° (Found: C, 81·4; H, 11·7. $C_{33}H_{58}O_2$ requires C, 81·4; H, 12·0%). Elution with light petroleum–benzene (4 : 1; 500 c.c.) and benzene (500 c.c.) yielded a fraction (90 mg.) separating from methanol as pale yellow needles, m. p. 155—157°, alone or mixed with dioxoeucalenyl acetate.

Eucalanol.—Hydrolysis of eucalanyl acetate in 5% ethanolic potassium hydroxide gave *eucalanol* which crystallised from chloroform–methanol in needles, m. p. 167—169° (Found:

C, 83·4; H, 12·8. $C_{31}H_{56}O$ requires C, 83·7; H, 12·7%), which remained colourless in tetranitromethane.

Epoxyeucalanyl Acetate.—A mixture of eucalenyl acetate (200 mg.) and perhydrol (1 c.c.) in acetic acid (100 c.c.), heated on the steam-bath for 2 hr. and then diluted with water, gave *epoxyeucalanyl acetate* (100 mg.) which crystallised from chloroform–methanol as plates, m. p. 141—143° (Found: C, 79·3; H, 10·9. $C_{33}H_{56}O_3$ requires C, 79·1; H, 11·3%). The compound gave a negative tetranitromethane reaction and had no selective ultraviolet light absorption.

*Demethyl*cyclo*eucalanol.*—The ketone acetate (430 mg.) in anhydrous hydrazine (5 c.c.) and absolute alcohol (20 c.c.) containing dissolved sodium (620 mg.) was heated at 180° for 18 hr. The cooled mixture was diluted with water and extracted with ether. The product (370 mg.) crystallised from aqueous methanol, affording *demethyl*cyclo*eucalanol* as needles, $[\alpha]_D$ +33° (*c* 0·4), m. p. 126—127° (Found: C, 84·1; H, 12·3. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%). Acetic anhydride–pyridine at room temperature (24 hr.) gave *demethyl*cyclo*eucalanyl acetate* as needles (from chloroform–methanol), $[\alpha]_D$ +57° (*c* 1·0), m. p. 98—100° (Found: C, 81·9; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%).

*Rearrangement of Demethyl*cyclo*eucalanyl Acetate with Hydrogen Chloride.*—Demethyl*cyclo*eucalanyl acetate (350 mg.) in dry chloroform (30 c.c.) was isomerised as for the higher homologue with hydrogen chloride at 0°. After 45 min., the *product* was isolated in the usual manner and crystallised from chloroform–methanol as plates (300 mg.), m. p. 108—112° (Found: C, 81·9; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%); light absorption: $\varepsilon_{210} = 3940$, $\varepsilon_{220} = 777$, $\varepsilon_{210}/\varepsilon_{220} = 5{\cdot}08$.

Demethyleucalenyl Acetate.—Chromic oxide (500 mg.) in 90% acetic acid (20 c.c.) was added during 5 min. to a solution of the mixed acetates of m. p. 108—112° (950 mg.) in acetic acid (80 c.c.) at 93°. Further heating for 10 min. and then treatment with water led to a product (960 mg.), which was isolated with ether, dissolved in light petroleum (80 c.c.), chromatographed on alumina (30 g.), and eluted with (*a*) light petroleum (300 c.c.), (*b*) light petroleum–benzene (9 : 1; 300 c.c.), (*c*) light petroleum–benzene (4 : 1; 600 c.c.), (*d*) benzene (300 c.c.), and (*e*) ether (500 c.c.). The combined contents (150 mg.) of fractions (*b*) and (*c*), twice crystallised from methanol, yielded *demethyleucalenyl acetate* as needles, m. p. 110—111° (Found: C, 81·5; H, 11·6. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%).

Demethyldioxoeucalenyl Acetate.—Evaporation of fraction (*d*) from the above chromatogram left a residue (170 mg.) which, when crystallised from methanol, gave *demethyldioxoeucalenyl acetate* as pale yellow blades, m. p. 151—153° (Found: C, 76·7; H, 10·1. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%); light absorption: $\lambda_{max.}$ 271 mμ (ε 7200).

Demethyloxoeucalenyl Acetate.—Evaporation of fraction (*e*) afforded a solid (100 mg.) consisting of *demethyloxoeucalenyl acetate* and crystallising from methanol in plates, m. p. 141° (Found: C, 78·9; H, 10·5. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%); light absorption: $\lambda_{max.}$ 241 mμ (ε 10,200).

The authors express their thanks to Dr. G. D. Meakins, University of Manchester, for the infrared absorption data recorded in this paper and for his valuable help in their interpretation.

THE UNIVERSITY, NOTTINGHAM. [*Received, November 4th,* 1955.]