564. *The* Euphorbia *Resins. Part VII.* The Characterisation of the Groups in Euphorbol.*

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The latices from *E. triangularis* and *E. ingens* contain euphol and euphorbol, and from *E. triangularis* also tirucallol.

Euphorbadienyl (euphorbyl) acetate was oxidised to yield the following substances: (i) Ozonolysis gave formaldehyde. (ii) Osmic acid and hydrolysis yielded euphorbenetriol which was oxidised further to ketonoreuphorbenol. (iii) Perbenzoic acid formed α- and β-epoxyeuphorbenyl acetate.

Euphorbenyl acetate with chromic acid gave diketoeuphorbenyl acetate containing the group $\cdot\mathrm{CO}\cdot\underset{|}{\mathrm{C}}{:}\underset{|}{\mathrm{C}}\cdot\mathrm{CO}\cdot$.

Thus euphorbadienol contains a secondary hydroxyl group, an active ethylenic linkage as a methylene group, and an inactive ditertiary double bond between two methylene groups.

CONTINUING our studies of the resins from the *Euphorbia* species we have reinvestigated the latices from *E. triangularis* and *E. ingens* from which euphol was previously reported by McDonald, Warren, and Williams (*loc. cit.*). The latex from *E. ingens* is a powerful vesicant when left on the skin, and the dust from the crude resin causes painful swelling of the face and reddening of the eyes. The splashing of small drops into the eye during the tapping of the trees causes acute pain from which relief is only given by washing with borax.

Chromatographic separation of the resins and acetylation of the several fractions gave from the petroleum fraction euphyl acetate, and from the benzene fraction a mixture, m. p. 89—92°, which yielded euphorbyl acetate only after numerous crystallisations. The resin from *E. triangularis* gave also a small quantity of tirucallyl acetate, m. p. 159—160°, which had previously only been obtained from *E. tirucalli* (cf. Haines and Warren, *J.*, 1949, 2554; 1950, 1562).

Euphorbol, first isolated by Bauer and Schenkel (*Arch. Pharm.*, 1928, **266**, 633), was characterised by Newbold and Spring (*J.*, 1944, 249) as a tetracyclic triterpene alcohol having one reducible and one non-reducible ethylenic bond. Our euphorbol was identified by the preparation of its acetate as well as of dihydroeuphorbol and dihydroeuphorbyl acetate the properties of which corresponded with those reported by Newbold and Spring (*loc. cit.*). Euphorbyl acetate was obtained in about 5—7% yield according to the season of collection of both species; but purification from *E. triangularis* proved more difficult owing to the presence of tirucallyl acetate, and the two corresponding alcohols were not readily separable by chromatographic methods. The mixture of the two acetates appeared as plates, m. p. 118—120°, and the isolation of euphorbyl acetate as needles, m. p. 124—125°, was a tedious process. These difficulties were not encountered when using the resin from *E. ingens*.

The oxidation of euphorbadienol (euphorbol) and euphorbenol gave respectively euphorbadienone and euphorbenone, which showed no strong absorption in the near ultraviolet and were characterised further as their oximes. These ketones differ from the corresponding ketones from euphol (cf. Bennett and Warren, *J.*, 1950, 697) and from tirucallol (Haines and Warren, 1950, *loc. cit.*).

Ozonolysis of euphorbadienyl acetate was reported by Bauer and Schenkel (*loc. cit.*) as giving formic acid. In view of the isolation of formaldehyde from the ozonolysis of the *iso*propylidene group in euphadienyl acetate (cf. McDonald, Warren, and Williams, *J.*, 1949, S 155), this experiment was repeated. Formaldehyde, identified as its dimedone compound, m. p. 189°, was found and no trace of acetone was detected, so that the active ethylenic linkage is present as a methylene group. No other product could be isolated pure from the ozonolysis; but the crude product showed no reactions for methyl ketones.

The treatment of euphorbadienyl acetate with osmic acid and hydrolysis of the product gave in small yield euphorbenetriol, m. p. 191—192°, but falling to m. p. 173—174° after sublimation. This triol was oxidised with lead tetra-acetate to ketonoreuphorbenol. With a view to obtaining larger quantities of the glycol, euphorbadienyl acetate was oxidised with one

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* Part VI, preceding paper.

molecular proportion of perbenzoic acid whereupon two products, α- and β-epoxyeuphorbenyl acetates, m. p. 157° and 143° respectively, were readily obtained.

The inactive double bond is seemingly situated as in euphadienol and tirucalladienol (Haines and Warren, *loc. cit.*). Chromic acid oxidation of euphorbenyl acetate readily gave diketoeuphorbenyl acetate, which was hydrolysed to diketoeuphorbenol, which in turn was oxidised to diketoeuphorbenone. These compounds showed a maximum absorption at 272·5 mμ. (log $\varepsilon_{max.}$ 3·94) in alcohol, which is indicative of the grouping $\cdot CO\cdot \underset{|}{C}\colon\underset{|}{C}\cdot CO\cdot$.

Euphorbadienol is thus a tetracyclic triterpene secondary alcohol containing one methylene group joined directly to a ring and one ethylenic linkage situated between two methylene groups, $\cdot CH_2\cdot \underset{|}{C}\colon\underset{|}{C}\cdot CH_2\cdot$. It thus differs from the two isomeric compounds euphadienol and tirucalladienol, which occur associated with it in the plant, in that the active ethylenic linkage is present as a methylene and not an *iso*propylidene group.

EXPERIMENTAL.

Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

Extraction.—The trees located in the Umgeni Valley, Natal, were tapped in the early morning when the flow of sap is fastest. The fresh latex was poured in a thin stream into boiling alcohol, and the solid material extracted with successive lots of hot alcohol. The alcoholic solution, concentrated under reduced pressure, deposited on cooling an amorphous solid.

(*a*) The solid (300 g.) from *E. triangularis* Desf. was dissolved in benzene, and the solvent removed completely under reduced pressure. The residual brown solid was dissolved in light petroleum (b. p. 50—70°) and chromatographed through alumina (1250 g.; activity I—II). Light petroleum (25 l.) eluted a colourless solid (200 g.), m. p. *ca.* 106—112°; benzene (19 l.) eluted a yellow waxy solid (52·5 g.); and ether removed brown gums (12 g.).

The petroleum fraction gave on acetylation euphadienyl acetate (2·5 g.), m. p. 108—109°, leaving a colourless crystalline solid (180 g.), m. p. 90—95°, unchanged on further crystallisation. The benzene fraction was acetylated and the product crystallised from ethanol and finally from acetone, to give euphorbyl (euphorbadienyl) acetate (7 g.), m. p. 124—125°, hydrolysed to euphorbadienol, m. p. 126—127°, and hydrogenated to euphorbenyl acetate, m. p. 133—134°, which gave euphorbenol, m. p. 132—133°. Newbold and Spring (*J.*, 1944, 255) give m. p.s 124—125°, 126—127°, 133—135°, and 132·5—134·5° respectively for these compounds. The mother-liquors from the crystallisation of euphorbyl acetate slowly deposited a white amorphous solid, m. p. 89—92°, and hard white nodules, m. p. 130—134°. On warming of the solution the amorphous solid dissolved, and the white nodules, which were filtered off, crystallised from acetone to yield tirucallyl acetate (1·2 g.), m. p. 159—160°, undepressed on admixture with an authentic specimen.

(*b*) The resin (50 g.; m. p. 110—112°) from *E. ingens* in light petroleum (600 ml.; b. p. 50—70°) was filtered through deactivated alumina and then chromatographed on a column of alumina (500 g.; 6·5 × 36 cm.) activated at 300°. Elution with six 5-l. portions of light petroleum (b. p. 50—70°) yielded 11·1, 4·8, 3·5, 2·4, 2·1, and 1·3 g. respectively, and subsequent elution with four 5-l. portions of light petroleum (b. p. 60—90°) yielded 1·9, 1·6, 1·4, 1·8 g. respectively. The above fractions were acetylated and the acetates recrystallised several times from ethanol, to give euphadienyl acetate, m. p. 108° (Found: C, 81·6; H, 11·1. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). The mother-liquors gave euphorbadienyl acetate, m. p. 124—125° (Found: C, 82·0; H, 11·3. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%), further characterised as euphorbenyl acetate, m. p. 134° (Found: C, 81·5; H, 11·6. Calc. for $C_{32}H_{54}O_2$: C, 81·6; H, 11·6%). Further elution of the column with benzene (5 l.) gave a solid (9·4 g.) which on acetylation and recrystallisation of the product from ethanol gave euphorbadienyl acetate, m. p. 124—125°. Continued elution with benzene (10 l.) and then with ether (5 l.) gave intractable oils.

Euphorbadienone.—Euphorbadienyl acetate (1·1 g.) was hydrolysed with alcoholic potassium hydroxide, the dried euphorbadienol (0·9 g.) heated to 250° in an atmosphere of carbon dioxide, copper oxide powder added, the temperature raised to 300°, and the whole heated for a further 10 minutes. The product in light petroleum (b. p. 50—70°) was filtered through alumina (10 g.) to give a white solid which, crystallised from ethanol, gave *euphorbadienone* as rectangular plates, m. p. 95°, $[\alpha]_D^{17}$ +22° (*c* = 1 in chloroform) (Found: C, 84·7; H, 11·8. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). The *oxime* crystallised from ethanol as plates, m. p. 238—239° (Found: C, 81·8; H, 11·3; N, 3·2. $C_{30}H_{49}ON$ requires C, 81·9; H, 11·2; N, 3·2%).

Euphorbenone.—Euphorbenol (800 mg.) in benzene (36 ml.) was stirred for 36 hours at room temperature with chromium trioxide (1·2 g.) in water (12 ml.) and acetic acid (36 ml.). Methanol (2 ml.) was added, and the lower layer was separated from the benzene solution and extracted three times with benzene. The combined benzene solutions were washed with water and aqueous sodium hydrogen carbonate. Evaporation of the solvent gave a yellow oil (600 mg.) which was dissolved in light petroleum (b. p. 50—70°) and chromatographed through alumina (15 g.; grade I—II). The first petroleum eluate (120 ml.) gave a light yellow oil (530 mg.) which solidified readily in an evacuated desiccator to an amorphous solid, m. p. 88°. Three crystallisations from ethanol gave *euphorbenone* (130 mg.) as colourless flat needles, m. p. 96—97°, $[\alpha]_D^{20}$ +3·9° in chloroform (*c*, 0·7), $\lambda_{max.}$ 295 mμ., log ε 1·36 in hexane (Found: C, 84·05; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The *oxime* crystallised from ethanol in plates, m. p. 244—245° (Found: C, 82·1; H, 11·7; N, 3·0. $C_{30}H_{51}ON$ requires C, 81·7; H, 11·6; N, 3·2%).

Ozonolysis of Euphorbadienyl Acetate.—Euphorbadienyl acetate (600 mg.) in pure chloroform was ozonised for 4 hours and the chloroform removed under reduced pressure. The yellow solid was heated gently under reflux with water (70 ml.) for 30 minutes, and 10 ml. were distilled off. The distillate gave with dimedone colourless needles, m. p. 189°, undepressed when mixed with the formaldehyde compound. The remainder (9 ml.) of the distillate was treated with potassium permanganate and redistilled. This second distillate showed no tests for acetone.

Euphorbenetriol.—Euphorbadienyl acetate (1·82 g.) and osmic acid (0·98 g.) in dry ether (75 ml.) gave immediately a black solution which was set aside for 6 days. The ether was removed under reduced pressure, and the product refluxed with benzene (70 ml.), ethanol (70 ml.), potassium hydroxide (3·5 g.), and mannitol (5·5 g.) for 5 hours. After removal of the solvent, the ethereal solution of the residue was chromatographed on alumina, but yielded the undecomposed complex (2·0 g.). This was refluxed with potassium hydroxide (4·0 g.) in ethanol (100 ml.) for a further 5 hours. The ethanol was removed under reduced pressure and the residue extracted with ether, washed with water, dried, and chomatographed on alumina. Elution with ether yielded 1·3 g. of a yellow solid, m. p. 184—189°. Repeated crystallisation from ether–light petroleum gave *euphorbenetriol* as colourless needles, m. p. 191—192° (Found : C, 77·6; H, 11·4. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%). After crystallisation a yellow oil remained which deposited a few nodules on storage for several weeks but could not be readily crystallised. The oil gave a positive Criegee's test for 1 : 2-glycols (*Ber.*, 1931, **64**, 260). Sublimation of euphorbenetriol at 160° in a high vacuum yielded a small amount of white substance, m. p. 173—174° (Found : C, 77·9; H, 11·7. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%).

Ketonoreuphorbenol.—Euphorbenetriol (80 mg.) in acetic acid (8 ml.) was treated with lead tetra-acetate (110 mg.) in acetic acid (10 ml.). After 7 hours at 20° water was added, and the precipitate filtered off, dried, and dissolved in light petroleum (b. p. 50—70°). Elution with the same solvent (200 ml.) through alumina (3 g.) gave traces of resinous material, whilst light petroleum–benzene (1 : 1; 300 ml.) gave a solid which crystallised from methanol to yield *ketonoreuphorbenol* as fine colourless needles, m. p. 120—121°. Sublimation at 100° in a high vacuum gave a solid, m. p. 123—124° (Found : C, 80·3; H, 11·2. $C_{29}H_{48}O_2$ requires C, 81·3; H, 11·3%).

Epoxyeuphorbenyl Acetates.—Perbenzoic acid (0·5 g., 1·1 mols.) in chloroform and euphorbadienyl acetate (1·53 g., 1·0 mol.) were allowed to react for 18 hours at 0°, one mol. of oxygen, as determined iodometrically, being absorbed. The solution was washed with 5% sodium carbonate solution, then water, and dried. Removal of the chloroform under reduced pressure gave an oil which solidified rapidly. Fractiona crystallisation from ethanol on the triangular scheme gave *α-epoxyeuphorbenyl acetate* as colourless needles, m. p. 157°, $[\alpha]_D^{20}$ +5·6° (*c*, 1·1 in chloroform) (Found : C, 79·7; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The more soluble fraction gave *β-epoxyeuphorbenyl acetate* as colourless plates, m. p. 143°, $[\alpha]_D^{20}$ −1·5° (*c*, 1·3 in chloroform) (Found : C, 79·2; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

Diketoeuphorbenol.—Euphorbenyl acetate (3 g.) in glacial acetic acid (350 ml.) was treated during 30 minutes with chromium trioxide (3 g.) in 90% acetic acid (350 ml.), and the solution kept at 40—50° for 5 hours. Methanol was then added, the mixture poured into water (1500 ml.), and the solution extracted with ether. The ethereal solution, washed with sodium hydrogen carbonate and water, gave a dark yellow gum which slowly solidified. The yellow solid (3·2 g.) in light petroleum (b. p. 50—70°) was chromatographed through alumina (100 g.) : (i) light petroleum (2·2 l.) and light petroleum–benzene (2 : 1; 1·5 l.) eluted a yellow solid (1·9 g.), m. p. 152—156°; (ii) light petroleum–benzene (1 : 1; 750 ml.) gave a trace of yellow oil, benzene (1 l.) a minute quantity of white solid, m. p. 154—160°, and benzene (2 l.) a trace of oil; (iii) benzene (1 l.) gave an orange solid (60 mg.), m. p. 148—156° which on admixture with the solid from fraction (i) had m. p. 120—126°.

Fraction (i), crystallised twice from methanol, gave *diketoeuphorbenyl acetate* as stout, canary-yellow needles (800 mg.), m. p. 163—164°, $[\alpha]_D^{20}$ −39·8° in chloroform (*c*, 0·86), $\lambda_{max.}$ 272·5 mμ., log ε 3·91 in alcohol (Found : C, 76·9; H, 10·1. $C_{32}H_{50}O_4$ requires C, 77·05; H, 10·1%). Hydrolysis of the acetate (200 mg.) with 8% alcoholic potassium hydroxide (20 ml.) for 3 hours gave a dark red solution, and the product, crystallised once from acetone and water and finally from methanol, gave *diketoeuphorbenol*, m. p. 166—167°, $[\alpha]_D^{20}$ −59° (*c*, 0·6 in chloroform) (Found : C, 78·6; H, 10·5. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Diketoeuphorbenone.—Diketoeuphorbenol (100 mg.) in benzene (30 ml.) was shaken with a solution of chromium trioxide (150 mg.) in 80% acetic acid (25 ml.) for 30 hours. The product was worked up as for euphorbenone (see above), leaving a yellow solid which was crystallised three times from chloroform–methanol, to give *diketoeuphorbenone* (20 mg.) as canary-yellow needles, m. p. 139°, $\lambda_{max.}$ 269 mμ., log ε 3·93 in alcohol (Found : C, 79·8; H, 10·2. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). Chromic acid oxidation of euphorbenol in glacial acetic acid at 50° also gave diketoeuphorbenone, m. p. 139°, undepressed on admixture with the above ketone.

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