

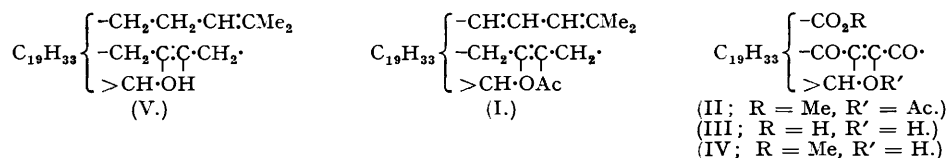
### 555. *The Euphorbia Resins. Part V. Oxidative Degradation in the Side Chain of Euphol.*

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Euphyl acetate was dehydrogenated with *N*-bromosuccinimide and the resulting acetate mixture, containing a new euphatrienyl acetate (I), was oxidised with chromium trioxide. From the reaction mixture was isolated a degradation acid (III),  $C_{25}H_{36}O_5$ , which was purified by way of the methyl ester (II),  $C_{28}H_{40}O_6$ , of its acetyl derivative, and on esterification gave a methyl ester (IV),  $C_{26}H_{38}O_5$ .

EUPHOL,  $C_{30}H_{50}O$ , was characterised by Newbold and Spring (*J.*, 1944, 2497) as a tetracyclic triterpene alcohol containing one active and one inactive ethylenic linkage. The active double bond was shown by Jeger and Krüsi (*Helv. Chim. Acta*, 1947, 30, 2045) to exist as an *isopropylidene* group which, according to McDonald, Warren, and Williams (*J.*, 1949, 155) was not attached directly to a ring but formed part of a longer chain. The present communication is concerned with the degradation of this carbon chain.

Euphyl acetate,  $C_{32}H_{52}O_2$ , was heated under reflux with 1 mole of *N*-bromosuccinimide in carbon tetrachloride with light as catalyst (Wohl-Ziegler). Purification of the product led to a mixture of acetates, m. p. 105–106°, which gave a brown colour in tetranitromethane and depressed the m. p. of euphyl acetate by 2°. The ultra-violet extinction curve of the acetate mixture showed the presence of three maxima: at  $\lambda = 232$  m $\mu$ . ( $\log \epsilon = 3.50$ ), 238.5 m $\mu$ . ( $\log \epsilon = 3.52$ ), and 247 m $\mu$ . ( $\log \epsilon = 3.33$ ). The extinction curve is different from that of the starting material, but the values of  $\lambda$  at the three maxima are similar to those of dihydroagosterol (and  $\gamma$ -lanosterol), which also contains a system of double bonds. Bellamy and Dorée (*J.*, 1941, 178) report maxima at  $\lambda = 236$ , 244, and 250 m $\mu$ ., and Ruzicka, Denss, and Jeger (*Helv. Chim. Acta*, 1946, 29, 206) report a maximum at 240 m $\mu$ .. The low extinction values of the mixture indicated the presence of impurities in what was essentially the compound (I), containing a system of conjugated double bonds.



Oxidative degradation of the acetate mixture with chromium trioxide gave neutral and acidic reaction products in the ratio 1 : 2; both fractions were oily. Chromatographic separation of the neutral part gave no crystalline organic eluates. The acidic oils were esterified with diazomethane, giving in good yield the methyl ester  $C_{28}H_{40}O_6$  (II) of a diketo-acetoxy-acid, readily hydrolysed to the corresponding diketo-hydroxy-acid (III),  $C_{25}H_{36}O_5$ . The ease of hydrolysis indicated the presence of a primary or secondary carboxyl group. The action of diazomethane on the acid (III) gave its methyl ester (IV),  $C_{26}H_{38}O_5$ .

The ultra-violet extinction curves of the acid (III) ( $\lambda_{max.} = 272$  m $\mu$ .,  $\log \epsilon_{max.} = 3.99$ ) and of the ester (II) ( $\lambda_{max.} = 271.5$  m $\mu$ .,  $\log \epsilon_{max.} = 3.94$ ) were similar to those found by Haines and Warren (*J.*, 1950, 1562) for diketodihydroeuphyl acetate ( $\lambda_{max.} = 275$  m $\mu$ .,  $\log \epsilon_{max.} = 3.94$ ), which was believed to contain the chromophoric system  $-CO-C=C-CO-$ .

The results of the molecular-weight determination of the diketo-hydroxy-acid (III) and of the methyl ester (II) exclude molecular formulæ containing either more or less oxygen.

The new  $C_{25}$ -diketo-hydroxy-acid (III) is therefore a tetracyclic degradation product of euphol (V) containing the original hydroxy-group of the starting material, the grouping  $\cdot CO \cdot C \cdot CO \cdot$  as chromophoric system, and a primary or secondary carboxyl group. It was probably formed by introduction of a new double bond in conjugation with the isopropylidene group by dehydrogenation to give (I), followed by oxidative fission of five carbon atoms with simultaneous formation of the chromophoric system.

Further work on the separation of the dehydrogenation mixture, the structure of the degradation products, and application of the same methods to related triterpenes is in progress.

#### EXPERIMENTAL.

(Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorr.)

*Dehydrogenation of Euphyl Acetate with N-Bromosuccinimide.*—*N*-Bromosuccinimide (0.78 g., 1.03 mols.; purity 99.5%) was added to euphyl acetate (2 g.), m. p. 104–105°, in carbon tetrachloride (50 ml.), and the solution heated under reflux for 1 hour; hydrogen bromide was evolved and succinimide began to float on the surface of the solution. Pyridine (5 ml.) was then added to the reaction mixture, which was boiled for a further 15 minutes. The solution was cooled, succinimide filtered off, and the filtrate distilled under reduced pressure on a steam-bath. The brown, oily residue was reacylated with acetic anhydride–pyridine (1:1; 5 ml.) and dissolved in ether. The ethereal solution was washed with dilute sulphuric acid, saturated potassium carbonate solution, and finally water. The brown residue (1.8 g.), obtained after evaporation of the solvent, was dissolved in light petroleum (b. p. 50–70°) and percolated through a column of alumina (15 g.; activity I–II). The same solvent (50 ml.) eluted a yellow oil (1.2 g.). The more strongly adsorbed material could not be obtained in crystalline form from the fractions eluted later. The first fraction (1.2 g.) was again washed with light petroleum through a column of alumina (40 g.): (i) 10 ml. (30 mg.), (ii) 10 ml. (800 mg.), (iii) 10 ml. (200 mg.), (iv) 20 ml. (50 mg.). The later fractions were neglected.

All four fractions were obtained as oils, but fractions (ii) and (iii) crystallised after the addition of a few drops of ethanol. A solution of the crystals in ethanol gave an amorphous solid on cooling. Seeding and shaking the ethanol solution, however, gave crystals. Four such recrystallisations gave the acetate mixture as long needles, m. p. 105–106°, which, mixed with euphyl acetate, m. p. 107°, gave a depression of 2°. In tetranitromethane the surface of the crystals was coloured dark brown, giving later a brown-yellow solution. For analysis the crystals were dried over phosphoric oxide at 70° in a high vacuum for 2 days (Found: C, 81.9; H, 10.7. Calc. for  $C_{32}H_{50}O_2$ : C, 82.3; H, 10.8. Calc. for  $C_{32}H_{52}O_2$ : C, 82.0; H, 11.2%).

*Oxidation of the Acetate Mixture with Chromium Trioxide.*—Chromium trioxide (800 mg.) in acetic acid (8 ml.) was added to the acetate mixture (440 mg.) in acetic acid (50 ml.) at 40°. The mixture was kept for 7 hours at 40–45°, and then overnight at room temperature. It was poured into water (500 ml.), treated with a solution of potassium iodide (2 g.) in *n*-sulphuric acid (20 ml.), and titrated against 0.1*N*-sodium thiosulphate (Found: equivs. of oxygen used, 17.9). The water-insoluble oxidation product was filtered off and dissolved in ether, and the ethereal solution extracted with 10% potassium carbonate solution, *n*-sodium hydroxide, and water. The carbonate solution readily extracted a red, water-soluble potassium salt. The sodium hydroxide extract contained only traces of acid material. The neutral fraction (150 mg.), obtained by evaporation of the ether, was a dark yellow oil. Reacetylation as above and chromatographic separation gave no crystalline material.

The alkaline solution of the potassium salt was acidified with dilute sulphuric acid, and the yellow amorphous acid extracted with ether. The ethereal solution, washed until neutral with water, gave a yellow oil (290 mg.) which did not crystallise. This was treated with diazomethane in ether, and the ethereal solution washed with dilute sulphuric acid, potassium carbonate solution, and water. The methyl ester remained in the ether and crystallised after removal of this solvent in thick, long needles, m. p. 160–162°. The crystals were dissolved in light petroleum and adsorbed on activated alumina (20 g.). The same solvent (260 ml.) eluted yellow needles (220 mg.) which, after recrystallising 4 times from alcohol, gave the *diketo-acetoxy-acid methyl ester* (II), m. p. 170–171°. The substance was sublimed in a high vacuum at 165° (block-temp.), and then had m. p. 168–170° [Found: C, 71.5; H, 8.3%; *M* (Rast), 469.  $C_{28}H_{40}O_6$  requires C, 71.2; H, 8.5%; *M*, 472.6].

*Hydroxy-diketo-acid* (III).—The above ester (II) 160 mg.) was refluxed with 10% alcoholic potash (20 ml.) for 2 hours. The acidified reaction mixture was extracted with ether, which was re-extracted with 10% sodium carbonate solution. Neutral hydrolysis products were not isolated. The reddish alkaline solution of the water-soluble sodium salt was neutralised with dilute sulphuric acid to yield yellow needles (150 mg.). Four crystallisations from acetone–water gave the *hydroxy-diketo-acid* (III), m. p. 233–234°. A specimen sublimed at 195–200° in a high vacuum gave thick yellow prisms, m. p. 231–233°, and a brown oily residue [Found: C, 71.9; H, 8.8%; *M* (Rast), 425; equiv. (Pregl), 383.  $C_{25}H_{36}O_5$  requires C, 72.1; H, 8.7%; *M*, 416.5].

*Methyl ester* (IV). The hydroxy-diketo-acid (III) (50 mg.) was added to diazomethane in ether. The ethereal solution was washed with *n*-sulphuric acid, 10% potassium carbonate solution, and water, and gave on evaporation, a crystalline solid which was purified by percolating through a column of alumina (2 g., activity I–II). Mixtures of light petroleum and benzene (10:1–1:1) eluted yellow needles, m. p. 172–177°. Recrystallisation of the combined fractions from chloroform–methanol, and sublimation at 169° in a high vacuum gave long, thin, yellow needles of the *methyl ester* (IV), m. p. 185–186° after sintering at 181° (Found: C, 72.8; H, 9.0.  $C_{26}H_{38}O_5$  requires C, 72.5; H, 8.8%). On admixture with the methyl ester (II) the m. p. was indefinite between 135° and 145°.

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The author gratefully thanks Professor F. L. Warren, of these laboratories, for much helpful discussion and for the correction of the manuscript, and Mr. E. C. Leisegang, also of these laboratories, for the determination of the extinction curves.

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[Received, June 28th, 1950.]

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