

139. The Euphorbia Resins. Part III. The Epimerisation and Dehydration of Euphol.

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Euphone is reduced with difficulty by aluminium *isopropoxide* to give *epieuphol* (hydrogenated to *dihydroepieuphol*), which is not identical with any of the known tetracyclic triterpene alcohols. Similar reduction of dihydroeuphone gave dihydroeuphol. *Euphyl toluene-p-sulphonate* in boiling acetic acid or pyridine gave *euphatriene* which was hydrogenated to euphene.

IN view of the isolation from the *Euphorbia* species of several isomeric tetracyclic triterpene alcohols, $C_{30}H_{50}O$, containing an *isopropylidene* group and an inactive double bond, it became of interest to prepare the hydrocarbon, ketone, and epimeric form of the principal constituent euphol for comparison purposes. Whilst this work was in progress, Roth and Jeger (*Helv. Chim. Acta*, 1949, **32**, 1625) reported the dehydrogenation of euphol and dihydroeuphol to euphone and dihydroeuphone, respectively, which have properties in agreement with our findings. We have observed, however, that these dehydrogenations are effected in higher yields with copper oxide (cf. Diels and Abderhalden, *Ber.*, 1904, **37**, 3099) than with precipitated copper. Euphone is not an $\alpha\beta$ -unsaturated ketone since the light-extinction curve which shows λ_{\max} . 210 $m\mu$. ($\log \epsilon_{\max}$. 3.7) and λ_{\max} . 295 $m\mu$. ($\log \epsilon_{\max}$. 1.4) is identical in the ultra-violet with that of euphyl acetate. Dutta and Karimulla (*J. Sci. Ind. Res. India*, 1944, **3**, 212) report that the dried latex from *E. tirucalli* yielded a ketone, $C_{27}H_{42}O$. We have failed to

isolate a ketone from the fresh latex (cf. Haines and Warren, *J.*, 1949, 2554), and this ketone is probably formed during the drying, for the *Euphorbia* latices readily give positive tests for indirect oxidases. This ketone is certainly identical with euphone (see table below), the formula for which follows from the rigid establishment of euphol as $C_{30}H_{50}O$ by McDonald, Warren, and Williams (*J.*, 1949, S 155).

	This paper.		Dutta and Karimulla.	
	M. p.		M. p.	
Euphone	$C_{30}H_{50}O$	117—118°	$C_{27}H_{42}O$	119°
Euphoxime	$C_{30}H_{49}ON$	192—193	Oxime	194—195
Dihydroeuphoxime ...	$C_{30}H_{51}ON$	205—206	Tetrahydro(?) -oxime	207—208

Catalytic reduction of euphone in the presence of Adams's catalyst at atmospheric pressure gave dihydroeuphone as reported by Roth and Jeger (*loc. cit.*), but under pressure dihydroeuphol was obtained. Attempts to reduce euphone by the Meerwein-Ponndorf-Verley reaction, using the standard procedure of refluxing with *isopropyl* alcohol as solvent, gave, even after prolonged treatment, pure euphone in quantitative yield. By carrying out the reaction in toluene (cf. Bachmann and Struve, *J. Org. Chem.*, 1939, 4, 461) or in *isobutanol* (cf. Malcom and Read, *J.*, 1939, 1037) it was possible to obtain small quantities of *epieuphol*, $C_{30}H_{50}O$, m. p. 125°, $[\alpha]_D^{20} + 22.6^\circ$, yielding an *acetate*, m. p. 112—113°, $[\alpha]_D^{20} - 66^\circ$. The small quantity of *epieuphol* was readily eluted from a column of alumina and the residual product, which was more strongly adsorbed, gave no pure substance. The difficulty of reducing euphone by the Meerwein-Ponndorf-Verley reaction may be attributed to the keto-group's being sterically hindered, and is interesting in the light of the statement made by Newbold and Spring (*J.*, 1944, 250) that "the ease with which euphol is washed from alumina with light petroleum is remarkable and . . . this property is probably of constitutional significance."

Catalytic reduction of *epieuphyl acetate* at atmospheric pressure in the presence of Adams's catalyst gave an *acetate*, m. p. 108—110°, which showed no depression when mixed with starting material (it was at first thought that the dihydro-compound had not been formed). Reduction of *epieuphol* under pressure gave *dihydroepieuphol*, $C_{30}H_{52}O$, m. p. 128—129°, $[\alpha]_D^{20} + 33.9^\circ$, which showed a decided depression when mixed with *epieuphol*. It yielded an *acetate*, $C_{32}H_{54}O_2$, m. p. 111°, $[\alpha]_D^{20} - 61.2^\circ$, which, when mixed with *epieuphyl acetate*, m. p. 112—113°, was depressed only to 108—110°. Attempts to obtain *dihydroepieuphol* by the reduction of dihydroeuphone with aluminium *isopropoxide* or with sodium and *isopropyl* alcohol gave only dihydroeuphol as the isolable product.

It is of interest that attempts to epimerise euphol by boiling *euphyl toluene-p-sulphonate* with acetic acid (cf. Plattner and Fürst, *Helv. Chim. Acta*, 1943, 26, 2266) gave *euphatriene*, which was also obtained by boiling the toluenesulphonate with pyridine. This *euphatriene* was hydrogenated catalytically to euphene having physical properties identical with those reported by Roth and Jeger (*loc. cit.*) for euphene obtained by Wolff-Kishner reduction of euphone.

EXPERIMENTAL.

(Microanalyses were by Drs. Weiler and Strauss, Oxford. All m. p.s are uncorrected.)

Euphone.—(a) Euphol (2 g.) and dry, freshly precipitated copper (4 g.) were heated at 330—340° for 12 minutes, and the product distilled at 180—240°/5 mm. to give a glassy solid. Crystallisation from methanol-acetone and finally from ethanol gave euphone as stout needles, m. p. 117—118°, $[\alpha]_D^{20} + 78.2^\circ$ (c, 1 in chloroform) (Found: C, 84.65; H, 11.0. Calc. for $C_{30}H_{48}O$: C, 84.8; H, 11.4%). Roth and Jeger (*loc. cit.*) give m. p. 119—120°, $[\alpha]_D^{20} + 69^\circ$. *Euphone oxime* crystallised from ethanol in colourless plates, m. p. 192—193°, $[\alpha]_D^{20} + 7.5^\circ$ (c, 1 in chloroform) (Found: C, 82.0; H, 11.0. $C_{30}H_{49}ON$ requires C, 81.9; H, 11.2%).

(b) Euphol (2 g.) was heated to 300° for 15 minutes in an atmosphere of carbon dioxide, and copper oxide (0.4 g.) added slowly. The product in light petroleum (b. p. 50—70°) was chromatographed through alumina (25 g.). Light petroleum (250 ml.) eluted a solid which was crystallised as above to give 1.6 g. of pure euphone. This method was preferred to method (a).

Dihydroeuphone.—(a) Dihydroeuphol, oxidised with copper oxide as above and crystallised from ethanol, gave dihydroeuphone, m. p. 64°. Roth and Jeger (*loc. cit.*) give m. p. 68°. *Dihydroeuphone oxime* crystallised from ethanol in colourless pearly plates, m. p. 205—206°, $[\alpha]_D^{20} + 3^\circ$ (c, 1 in chloroform) (Found: C, 82.2; H, 11.65; N, 3.2. $C_{30}H_{51}ON$ requires C, 81.7; H, 11.6; N, 3.2%). (b) Catalytic hydrogenation of euphone gave dihydroeuphone identical with the above.

Dihydroeuphol.—(a) Euphone (1 g.), hydrogenated with Adams's catalyst at 50 atm. pressure, gave quantitatively dihydroeuphol, m. p. 117—118°, undepressed with authentic specimen. (b) Dihydroeuphone (1 g.) was treated with aluminium *isopropoxide* in toluene as described below for the preparation of *epieuphol*. Chromatographic analysis of the product in ether and two crystallisations from methanol gave only dihydroeuphol, as felted needles, m. p. 120—121°, undepressed on admixture with an authentic specimen. (c) Dihydroeuphone (250 mg.) and *isopropyl* alcohol (38 ml.) were refluxed with sodium (1.25 g.)

for 1 hour. The solution was poured into water and extracted with ether, and the ethereal extract washed with water and dried. The ethereal solution gave a gum which was treated with acetic anhydride (3 ml.) and pyridine (1.8 ml.) and worked up in the usual way. The product, twice crystallised from methanol, gave dihydroeuphyl acetate, m. p. 122—124°, undepressed on admixture with an authentic specimen.

epiEuphol.—(a) Euphone (1 g.), freshly distilled aluminium isopropoxide (2 g.), and isobutyl alcohol (20 ml.) were refluxed in an oil-bath at 160°. After each hour isobutyl alcohol (10 ml.) was added, and 10 ml. were allowed to distil off. After 6 such operations a further quantity of aluminium isopropoxide (4 g.) was added to replace loss and hasten the reaction. The product was steam-distilled and then acidified with dilute sulphuric acid, and the dried ethereal extract was chromatographed through alumina (20 × 2 cm.). The first 180 ml. eluted a solid (200 mg.), m. p. 117—119°, which, crystallised twice from acetone and twice from methanol, gave *epieuphol* as fine felted needles, m. p. 125°, $[\alpha]_D^{20} + 22.6^\circ$ (*c*, 0.9 in chloroform) (Found : C, 84.4; H, 12.0. $C_{30}H_{50}O$ requires C, 84.45; H, 11.8%). Mixed m. p.s with euphol, m. p. 116°, and dihydroeuphol, m. p. 120—121.5°, gave depressions to 88—94° and 90—95°, respectively. Further elution of the column gave a solid, m. p. ca. 50—70°, from which a pure component could not be isolated.

(b) Euphone (1 g.) and aluminium isopropoxide (15 g.) in dry toluene (20 ml.) were refluxed in an oil-bath for 4 hours. Absolute isopropyl alcohol was added and then distilled off. The ethereal extract gave a solid which was dissolved in ether and chromatographed through alumina (22 × 2 cm.). The first 100 ml. of ether eluted a solid (200 mg.), m. p. 117—120°, which gave as above *epieuphol*. Light petroleum proved less satisfactory for the chromatogram.

epiEuphyl Acetate.—*epiEuphol* (300 mg.), acetic anhydride (9 ml.), and pyridine (2 ml.) were heated at 100° for 4 hours. The solid product was dissolved in chloroform, and the solvent gradually replaced by methanol, from which *epieuphyl acetate* crystallised on cooling in highly refractive plates, m. p. 112—113°, $[\alpha]_D^{20} - 66^\circ$ (*c*, 0.95 in chloroform), unchanged by further crystallisation (Found : C, 82.0; H, 11.2. $C_{32}H_{52}O_2$ requires C, 82.0; H, 11.2%).

Dihydroepieuphol.—(a) *epiEuphyl acetate* (250 mg.) in ethyl acetate (12 ml.) and glacial acetic acid (3 ml.) was reduced in the presence of platinum oxide (30 mg.). Absorption of hydrogen (11.9 ml. at N.T.P. Calc. for $C_{32}H_{52}O_2$: 1 mol. = 11.2 ml.) was complete after 10 hours. The product crystallised from methanol in plates, m. p. 108—110°, showing no depression when mixed with *epieuphyl acetate*.

(b) *epiEuphol* (250 mg.) in ethanol (100 ml.) was hydrogenated in the presence of platinum oxide (300 mg.) at 80 atm. pressure for 6 hours. The product crystallised from methanol to give *dihydroepieuphol* as felted needles, m. p. 128—129°, $[\alpha]_D^{20} + 33.9^\circ$ (*c*, 0.73 in chloroform) (Found : C, 84.1; H, 12.0. $C_{30}H_{52}O$ requires C, 84.05; H, 12.2%). A mixture with *epieuphol* had m. p. 108—110°. Acetylation in the presence of pyridine and crystallisation of the product from methanol gave *dihydroepieuphyl acetate* as highly refractive plates, m. p. 111°, $[\alpha]_D^{20} - 61.2^\circ$ (*c*, 0.97 in chloroform) (Found : C, 81.8; H, 11.5. $C_{32}H_{54}O_2$ requires C, 81.6; H, 11.55%). The m. p. of a mixture with *epieuphyl acetate*, m. p. 112—113°, was 108—110°.

Oxidation of epiEuphol.—*epiEuphol* (250 mg.) was heated with copper oxide (50 mg.) at 300° for 10 minutes in an atmosphere of carbon dioxide. The product was chromatographed through alumina (10 g.) with light petroleum to yield a solid which crystallised from ethanol as needles, m. p. 115—116°, showing no depression when mixed with euphone.

Euphyl Toluene-p-sulphonate.—Euphol (5 g., 1 mol.), pyridine (50 ml.), and toluene-*p*-sulphonyl chloride (5 g., 2 mols.) were allowed to react at 20° for 18 hours, and then poured into water. The ethereal extract, washed with dilute hydrochloric acid and dried, was chromatographed through alumina (30 g.). Crystallisation from acetone-water and twice from methanol gave *euphyl toluene-p-sulphonate* as felted needles, m. p. 103.5—104.5° (Found : C, 76.3; H, 9.7. $C_{37}H_{56}O_3S$ requires C, 76.5; H, 9.65%).

Euphatriene.—Euphyl toluene-*p*-sulphonate (5 g.), dry powdered calcium carbonate (6 g.), and pyridine (50 ml.) were refluxed for 2 hours under anhydrous conditions. The product was poured into water, and the ethereal extract, washed with acid, gave an oil. One chromatographic separation through alumina gave a solid which still contained a trace of sulphur. The product was hydrolysed with alcoholic potash and rechromatographed with ether as solvent. The oily solid was crystallised four times from acetone to give *euphatriene* as stout, long, colourless needles, m. p. 116—117°, $[\alpha]_D^{20} + 115.8^\circ$ (*c*, 1 in chloroform) (Found : C, 88.2; H, 11.8; Found, after sublimation : C, 88.3; H, 11.7. $C_{30}H_{48}$ requires C, 88.2; H, 11.8%).

Euphene.—Euphatriene (300 mg.) in ethyl acetate-acetic acid (1 : 1; 250 ml.) was hydrogenated in the presence of Adams's catalyst. The product crystallised from acetone to give euphene as needles, m. p. 58—60°, $[\alpha]_D^{20} + 37.6^\circ$ (*c*, 1.03 in chloroform) (Found : C, 87.6; H, 12.4. Calc. for $C_{30}H_{52}$: C, 87.3; H, 12.7%), unchanged by hydrogenation under pressure. Roth and Jeger (*loc. cit.*) give m. p. 60.5—61°, $[\alpha]_D^{20} + 34^\circ$.

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