323. *The* Euphorbia *Resins. Part IV. A Comparative Study of Euphol and Tirucallol.*

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It is shown that in tirucallol the hydroxy-group is secondary and the *iso*propylidene group is not attached directly to a ring.

Euphenyl and tirucallenyl acetates are oxidised by chromic acid to diketoeuphenyl acetate and *diketotirucallenyl acetate* which contain the grouping —CO—C=C—CO— and are reduced to *diketoeuphanyl* and *diketotirucallanyl acetates*, respectively.

Euphol and tirucallol are thus isomeric tetracyclic triterpenes, $C_{30}H_{50}O$, containing the groupings >CH·OH, —CH=CMe$_2$ and —CH$_2$—C=C—CH$_2$—. Tirucallenol is converted into *diketotirucallane* which is different from *diketoeuphane*.

Both euphol (euphadienol) (cf. Newbold and Spring, *J.*, 1944, 249; Jeger and Krusi, *Helv. Chim. Acta*, 1947, **30**, 2045; McDonald, Warren, and Williams, *J.*, 1949, 155) and tirucallol (tirucalladienol) (cf. Haines and Warren, *J.*, 1949, 2554) have been shown to be tetracyclic triterpene alcohols, $C_{30}H_{50}O$, containing an *iso*propylidene group and an inert double bond. We have now shown that tirucallol, like euphol, contains a secondary hydroxyl group since dehydrogenation of tirucallol and tirucallenol gives tirucalladienone (*oxime*, $C_{30}H_{49}ON$, m. p. 218—220°) and *tirucallenone*, $C_{30}H_{50}O$, m. p. 62—64° (*oxime*, m. p. 236·5—237·5°; *semicarbazone*, m. p. 214—215°) respectively. These two ketones from tirucallol are different from the corresponding ketones prepared previously by Bennett and Warren (*J.*, 1950, 697) from euphol.

To obtain further information on the mode of linkage of the *iso*propylidene group, *tirucallyl acetate dibromide*, $C_{32}H_{52}O_2Br_2$, was boiled with alcoholic potash: *monobromotirucallol*, $C_{30}H_{49}OBr$, further characterised as its *acetate*, $C_{32}H_{51}O_2Br$, was obtained. This behaviour is similar to that found for euphyl acetate dibromide by McDonald *et al.* (*loc. cit.*) so that the *iso*propylidene group is similarly joined in euphol and tirucallol and is probably not attached directly to a ring.

In a previous communication it was shown that euphenyl acetate was readily oxidised to mono- and di-ketoeuphenyl acetate, in which respect it paralleled the behaviour of cryptosterol, lanosterol, and elemolic acid. This oxidation has been repeated with larger quantities to study further the nature of the inert ethylenic linkage. Diketoeuphenyl acetate has now been obtained melting at 106—107° [previously reported by McDonald *et al.* (*loc. cit.*) as melting at 97°] and is hydrolysed to *diketoeuphenol*, $C_{30}H_{48}O_3$. *Diketoeuphenone*, $C_{30}H_{46}O_3$, was obtained by direct oxidation of euphenol with chromic acid.

The light-extinction curve for monoketoeuphenyl acetate in hexane showed a pronounced maximum at λ 246 mμ. (log $\varepsilon_{max.}$ 4·05) which, corrected for alcohol as solvent, gives $\lambda_{max.}^{alc.}$ 253 mμ. (Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123) and is indicative of an αββ-trisubstituted αβ-unsaturated ketone, as was found by Dorée, McGhie, and Kurzer (*J.*, 1948, 988) for

ketolanostenyl acetate. Furthermore, diketoeuphenyl acetate showed a pronounced shift in the absorption maximum towards the red similar to that found previously for diketolanostenyl acetate for which the chromophoric grouping —CO—C=C—CO—, formed from —CH_2—C=C—CH_2, has been suggested by Dorée *et al.* (*loc. cit.*).

The 1 : 4-arrangement of the keto-groups in diketoeuphenyl acetate is probably such that the two polar groups act in opposite directions, for then the polarity would be pronouncedly less than that of the monoketoeuphenyl acetate which is more strongly adsorbed on a column of alumina than is the diketo-compound. Furthermore, diketoeuphenyl acetate failed in our hands to give a pyridazine when heated with hydrazine.

The chromic acid oxidation of tirucallenyl acetate gave a difficultly separable mixture of mono- and di-keto-compounds, but prolonged oxidation gave pure *diketotirucallenyl acetate*, $C_{32}H_{50}O_4$, readily hydrolysed to *diketotirucallenol*, $C_{30}H_{48}O_3$. The extinction curve of diketotirucallenyl acetate shows a maximum similar to those found for the corresponding compounds from euphol and lanosterol, and the chromophoric grouping is certainly similar.

	Monoketone.		Diketone.	
	$\lambda_{max.}^{alc.}$, mμ.	log $\varepsilon_{max.}$.	$\lambda_{max.}^{alc.}$, mμ.	log $\varepsilon_{max.}$.
Euphenyl acetate	253	4·05	275	3·94
Tirucallenyl acetate	—	—	274	3·98
Lanostenyl acetate	255	4·08	275	3·94

Thus both euphol and tirucallol possess a secondary hydroxyl and the groupings —CH=CMe_2 and —CH_2—C=C—CH_2—. In order to find whether the hydrocarbon skeletons were the same, attempts were made to dehydrate euphol with phosphorus oxychloride and pentachloride, but only oily products were obtained. Attempts to prepare the hydrocarbon by the Wolff–Kishner reduction of tirucallenone semicarbazone, as well as by the modified Clemmensen reduction of the ketone (cf. Dorée, McGhie, and Kurzer, *J.*, 1947, 1468), gave only oily products. The appreciable increase in melting point recorded by Dorée, McGhie, and Kurzer (1948, *loc. cit.*) on reducing diketolanostenyl acetate to diketolanostanyl acetate led us to attempt to reduce the inert double bond in euphol and tirucallol in a similar way, with a view to obtaining later crystalline derivatives of the fully saturated deoxy-compounds. The yellow diketoeuphenyl acetate was hydrogenated smoothly with Adams's catalyst and hydrogen to give colourless *diketoeuphanyl acetate*, $C_{32}H_{52}O_4$; but, when reduction was attempted with zinc in either hot or cold acetic acid, colourless compounds were obtained which appeared from analyses to be impure. Furthermore, diketoeuphanyl acetate on hydrolysis failed to give a crystalline alcohol. The hydrolysis product, however, on oxidation with chromic acid gave *diketoeuphanone*, $C_{30}H_{48}O_3$, also obtained by the catalytic reduction of diketoeuphenone.

Diketotirucallenyl acetate was readily hydrogenated either catalytically or with zinc and acetic acid, to give colourless *diketotirucallanyl acetate*, $C_{32}H_{52}O_4$, which was hydrolysed to *diketotirucallanol*, $C_{30}H_{50}O_3$, which in turn gave *diketotirucallanone*, $C_{30}H_{48}O_3$. The physical constants for these compounds, compared with those for lanosterol, are shown in the table.

	Diketodihydro-compound,		Diketotetrahydro-compound,	
	m. p.	$[\alpha]_D$.	m. p.	$[\alpha]_D$.
Euphyl acetate	106—107°	+25·7°	190—191·5°	−15·2°
Euphol	115—116	+32·1	—	—
Euphone	63—64	+31·1	186—187	−144·7
Tirucallyl acetate	135—136	−17·1	222—224	−131
Tirucallol	136—137	−24·5	199—200	−144·3
Tirucallone	—	—	230—231	−168·2
Lanosteryl acetate	156·5—158·8 [a]	+90·5 [a]	222—224 [b]	+54·6 [b]
Lanosterol	113—115 [a] 145 [c]	+78·3 [a]	183—184 [b]	+25·7 [b]
Lanosterone	105—107	+172·6 [a]	165—167 [b]	+121·1 [b]

[a] Ruzicka, Rey, and Muhr, *Helv. Chim. Acta*, 1944, **27**, 472. [b] Dorée, McGhie, and Kurzer, *J.*, 1948, 988. [c] McGhie, private communication.

The success attending the formation of euphatriene from euphyl toluene-*p*-sulphonate by Bennett and Warren (*loc. cit.*) was not met with on heating *tirucallyl toluene*-p-*sulphonate* which was recovered unchanged after being boiled with pyridine. The action of phosphorus oxychloride on tirucallenol gave an oily product which was hydrogenated to an oily compound, probably

tirucallene, which with chromic acid gave a yellow oil. Attempts to obtain crystalline compounds at the different stages failed. The yellow oil on catalytic hydrogenation gave colourless *diketotirucallane*, m. p. 139—141°, which was different from *diketoeuphane*, m. p. 112—113°, prepared by reduction of diketoeuphene.

Experimental.

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

Diketoeuphenol.—Euphenyl acetate (15 g.) was oxidised as described previously by McDonald, Warren, and Williams (*loc. cit.*), and the diketoeuphenyl acetate crystallised from chloroform–methanol in brittle yellow needles, m. p. 106—107°, $[\alpha]_D^{20}$ +25·7° (Found: C, 76·9; H, 10·2. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%). The light-extinction curve in hexane showed $\lambda_{max.}$ 268 mμ., log $\varepsilon_{max.}$ 3·94. The acetate (1·5 g.) was boiled under reflux for 3 hours with 8% alcoholic potassium hydroxide (100 ml.). The product, crystallised several times from acetone and finally from methanol, gave *diketoeuphenol* as yellow felted needles, m. p. 115—116°, $[\alpha]_D^{21}$ +32·1° in chloroform (*c*, 1·06) (Found: C, 78·6; H, 10·45. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Diketoeuphenone.—Euphenol (10 g.) in glacial acetic acid (650 ml.) was treated with chromic acid (12 g.) in 90% acetic acid (160 ml.). The solution was stirred for 6 hours at room temperature, poured into water, and extracted with ether. The ethereal solution, washed with sodium carbonate solution, gave an oil. The oil in light petroleum was filtered through activated alumina (250 g.), and the column washed with light petroleum (2·5 l.) and developed with light petroleum–benzene (8 l.). The different fractions all gave yellow oils (total weight, 6 g.) which, dissolved in acetone–methanol (1 : 1) and set aside, gave a waxy solid, which, crystallised several times from methanol at 0°, gave *diketoeuphenone* as light yellow felted needles, m. p. 63—64°, $[\alpha]_D^{21}$ +31·1° in chloroform (*c*, 0·868) (Found: C, 79·4; H, 10·4%. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%).

Diketoeuphanyl Acetate.—Diketoeuphenyl acetate (700 mg.) in glacial acetic acid (45 ml.) and platinic oxide (200 mg.) absorbed hydrogen during 30 minutes (observed, less blank: 36·9 ml. at N.T.P. Calc. for $C_{32}H_{50}O_4$: 1 mol. = 37·4 ml.). The product crystallised from chloroform–methanol to give *diketoeuphanyl acetate* in lustrous needles, m. p. 190—191·5°, $[\alpha]_D^{20}$ −15·2° in chloroform (*c*, 1). After sublimation at 140—150° in a high vacuum, the product had m. p. 198—199° (Found: C, 76·7; H, 10·4. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·4%). It gave no colour with tetranitromethane.

Diketoeuphanone.—(*a*) Diketoeuphanyl acetate (2·5 g.) was hydrolysed as described for diketoeuphenyl acetate. The product in benzene (75 ml.) and glacial acetic acid (15 ml.) was treated with stirring below 5° with 10% aqueous chromic acid (25 ml.) during 10 minutes, and stirring continued for 1 hour. Benzene was added to dissolve the separated tarry mass, and the solution was treated with excess of sulphur dioxide. The benzene layer, washed with aqueous sodium hydroxide and water, gave an oil which was dissolved in light petroleum and filtered through alumina (15 g.). The filtrate gave a colourless oil which, dissolved in chloroform–methanol and set aside, deposited an amorphous solid. The mother-liquors gave crystals which, crystallised 3 times from methanol, gave a small yield of *diketoeuphanone* as colourless plates, m. p. 186—187°, $[\alpha]_D^{20}$ −144·7° in chloroform (*c*, 0·553) (Found: C, 78·8; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·95; H, 10·5%).

(*b*) Diketoeuphenone (600 mg.) in glacial acetic acid (25 ml.) was hydrogenated in the presence of Adams's catalyst (50 mg.). In 30 minutes 0·9 mol. of hydrogen had been absorbed. After 12 hours the product was crystallised from methanol to give diketoeuphanone, m. p. 185—186° undepressed when mixed with a specimen from (*a*).

Diketoeuphane.—Euphene, obtained from euphatriene (cf. Bennett and Warren, *loc. cit.*), was oxidised to diketoeuphene as described by Roth and Jeger (*Helv. Chim. Acta*, 1949, **32**, 1625).

(*a*) Diketoeuphene (100 mg.) in glacial acetic acid (30 ml.) and zinc dust (400 mg.) were boiled for 2 hours. The ethereal extract, washed with aqueous sodium hydroxide and water, gave an oil. This oil in light petroleum was filtered through alumina (5 g.), and the colourless oil, crystallised 3 times from methanol, gave *diketoeuphane* as colourless felted needles, m. p. 112—113° (Found: C, 81·9; H, 11·3. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

(*b*) Diketoeuphene was hydrogenated at 60 atmospheres for 6 hours in the presence of Adams's catalyst; the product, crystallised as above, gave diketoeuphane, m. p. 106—110°, undepressed when mixed with a specimen from (*a*).

*Tirucallyl Toluene-*p*-sulphonate.*—Tirucallol (1·9 g.) was treated with toluene-*p*-sulphonyl chloride (2 g.) in pyridine (10 ml.) on a water-bath. The product in dry ether was chromatographed through alumina (40 g.). Fraction (1), 50 ml., eluted a solid (0·6 g.) which crystallised from aqueous acetone to give colourless needles of *tirucallyl toluene-*p*-sulphonate*, m. p. 147·5—148° (Found: C, 76·4; H, 10·2; S, 5·4. $C_{37}H_{56}O_3S$ requires C, 76·5; H, 9·7; S, 5·5%). Fraction (2), 450 ml., eluted tirucallol (1·25 g.).

Tirucalladienone Oxime.—Tirucallol, treated with copper in a vacuum or with copper oxide at 300° for 10 minutes in an atmosphere of carbon dioxide, failed to give a crystalline ketone. *Tirucalladienone oxime* crystallised from methanol in large, thin laminæ, m. p. 218—220°, $[\alpha]_D^{20}$ −71·8° in chloroform (*c*, 1) (Found: C, 81·9; H, 11·3; N, 3·16. $C_{30}H_{49}ON$ requires C, 81·9; H, 11·2; N, 3·19%).

Tirucallenone. Tirucallenol (2·5 g.) was heated with copper oxide (600 mg.) at 300° for 10 minutes in an atmosphere of carbon dioxide. The reaction product in light petroleum (b. p. 50—70°; 50 ml.) was filtered through freshly activated alumina (20 g.); the material obtained from the filtrate, crystallised once from acetone and 3 times from methanol, gave *tirucallenone* as fine, colourless needles, m. p. 62—64°, $[\alpha]_D^{20}$ +40·2° in chloroform (*c*, 1·02). A depression of 15° was observed on admixture with euphenone (Found: C, 83·9; H, 11·6. $C_{30}H_{50}O$ requires C, 84·45; H, 11·8%). *Tirucallenone oxime* crystallised from ethanol in pearly plates, m. p. 236·5—237·5°, $[\alpha]_D^{20}$ −66° in chloroform (*c*, 1) (Found: C, 81·2; H, 11·5; N, 2·66. $C_{30}H_{51}ON$ requires C, 81·6; H, 11·6; N, 3·16%). *Tirucallenone semicarbazone* crystallised once from ethanol and 3 times from acetone–methanol as pearly plates, m. p. 214—215°

$[\alpha]_D^{20}$ −10·5° in chloroform (*c*, 1·05) (Found: C, 76·9; H, 10·9; N, 9·2. $C_{31}H_{53}ON_3$ requires C, 77·0; H, 11·05; N, 8·7%).

Diketotirucallenol.—Tirucallenyl acetate (4·5 g.) was oxidised with chromic acid (4·5 g.) as above. The product in light petroleum (b. p. 50—70°) was filtered through alumina (150 g.) and developed successively with the same solvent (5 l.), light petroleum–benzene (5 : 1; 3 l.) and finally light petroleum–benzene (1 : 1; 2 l.) to give yellow crystals (2·6 g.) with m. p. varying between 126° and 132°. Crystallisation from chloroform–methanol and finally from methanol gave *diketotirucallenyl acetate* as yellow brittle needles, m. p. 135—136°, $[\alpha]_D^{18}$ −17·1° in chloroform (*c*, 1·17) (Found: C, 77·2; H, 10·1. $C_{32}H_{50}O_4$ requires C, 77·05; H, 10·1%). Light-extinction curve in hexane showed $\lambda_{max.}$ 267 mμ., log $\varepsilon_{max.}$ 3·98. The acetate (1 g.) was refluxed with 8% alcoholic potassium hydroxide (150 ml.) for 3 hours and gave, on crystallisation from methanol, *diketotirucallenol* as yellow felted needles, m. p. 136—137°, $[\alpha]_D^{18}$ −24·5° in chloroform (*c*, 1) (Found: C, 78·9; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Reacetylation with pyridine and acetic anhydride gave diketotirucallenyl acetate, m. p. 135—136°, undepressed on admixture with original specimen.

Diketotirucallanol.—Diketotirucallenyl acetate (600 mg.) was hydrogenated as above (observed: 25 ml. at N.T.P. Calc. for $C_{32}H_{56}O_4$: 1 mol. = 26·9 ml.). The product crystallised from chloroform–methanol to give *diketotirucallanyl acetate* in brittle laminæ, m. p. 222—224°, $[\alpha]_D^{20}$ −131° in chloroform (*c*, 0·63) (Found: C, 77·1; H, 10·6. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·4%). It gave no colour with tetranitromethane. The acetate (200 mg.) was refluxed for 3 hours with 8% alcoholic potassium hydroxide (50 ml.). The product was crystallised 6 times from methanol to give *diketotirucallanol* as white felted needles, m. p. 199—200°, $[\alpha]_D^{19}$ −144·3° in chloroform (*c*, 0·82) (Found: C, 78·6; H, 10·4. $C_{30}H_{50}O_3$ requires C, 78·5; H, 11·0%).

Diketotirucallanone.—Diketotirucallanol (400 mg.) in benzene (15 ml.) and glacial acetic acid (2·5 ml.) was treated with 10% aqueous chromic acid (2·5 ml.) at a temperature below 5° and stirred for 1 hour. The same procedure in working up the product was adopted as that described for diketo-euphanone above. The reaction product was taken up in methanol and acetone, and crystallised 4 times from acetone, to give *diketotirucallanone* as colourless needles, m. p. 230—231°, $[\alpha]_D^{20}$ −168·2° in chloroform (*c*, 0·56) (Found: C, 77·7; H, 10·5%). After sublimation at 160° in high vacuum, the ketone had m. p. 220—224° (Found: C, 78·7; H, 10·5. $C_{30}H_{48}O_3$ requires C, 78·95; H, 10·5%).

Diketotirucallane.—Phosphorus oxychloride (5 ml.) was added slowly with shaking to a solution of tirucallenol (3·0 g.) in pyridine (30 ml.), then heated on a water-bath for 1½ hours, and boiled for 5 minutes. The cold solution was poured slowly on crushed ice and extracted with ether. The ethereal solution, washed with concentrated hydrochloric acid and then with water until neutral, gave a yellow oil which was run in light petroleum through a column of alumina (30 g.). A colourless oil resulted, which could not be crystallised. This oil (1·5 g.), in a mixture of glacial acetic acid and ethyl acetate (100 ml.), was shaken for 12 hours with Adams's catalyst (50 mg.) and hydrogen at 120°/50 atmospheres. The product was again a yellow oil which, dissolved in light petroleum (250 ml.) and chromatographed through alumina (100 g.), gave only colourless glassy oils which could not be crystallised. The hydrogenated oil (1·3 g., 1 mol.) in acetic acid (30 ml.) was treated with chromic acid (1·3 g., 4 mols.) in 90% acetic acid at 90° for 4 hours. The neutral product in light petroleum run through alumina gave a few yellow crystals, m. p. 114—116°, but the main eluate was obtained as a yellow oil. This (200 mg.) was reduced by amalgamated zinc in boiling acetic acid, the product in light petroleum filtered through alumina (5 g.) and crystallised 6 times from methanol, to give *diketotirucallane* as colourless felted needles, m. p. 139—141° (Found: C, 81·8; H, 10·8. $C_{30}H_{48}O_2$ requires C, 81·8; H, 10·9%).

Tirucallyl Acetate Dibromide.—Tirucallyl acetate (1·6 g.) in carbon tetrachloride (15 ml.) was treated with a 3% solution (20 ml.) of bromine in the same solvent; the bromine was smoothly absorbed. The solvent was removed under reduced pressure and the product crystallised 3 times from acetone, to give *tirucallyl acetate dibromide* as colourless plates, m. p. 159—160° (Found: C, 61·5; H, 8·4; Br, 25·2. $C_{32}H_{52}O_2Br_2$ requires C, 61·2; H, 8·3; Br, 25·4%).

Monobromotirucallol.—The above dibromide (1·5 g.) was refluxed with 3% alcoholic potassium hydroxide (100 ml.) for 4 hours and then poured into water. The insoluble product was crystallised from acetone–methanol (1 : 1) to give *monobromotirucallol* as colourless plates, m. p. 179—180° (Found: C, 71·1; H, 9·9; Br, 15·1. $C_{30}H_{49}OBr$ requires C, 71·3; H, 9·7; Br, 15·8%). *Monobromotirucallyl acetate*, obtained from the alcohol (400 mg.) by boiling it with acetic anhydride and pyridine, crystallised from acetone–methanol as colourless needles, m. p. 173—174° (Found: C, 70·5; H, 9·2; Br, 15·2. $C_{32}H_{51}O_2Br$ requires C, 70·2; H, 9·4; Br, 14·6%).

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