Observations on Taraxerol (Skimmiol).

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The structure assigned to taraxerol by Spring and his collaborators is confirmed in some details, and identity of taraxerol and skimmiol is finally proved. Ready isomerisation of taraxerol epoxide by acid involves a molecular rearrangement.

Taraxerol, $C_{30}H_{50}O$, first isolated from roots of *Taraxacum officinale* (Burrows and Simpson, *J.*, 1938, 2042), was shown to be *iso*olean-14-en-3β-ol by Beaton, Spring, Stevenson, and Stewart (*Chem. and Ind.*, 1954, 1454; 1955, 35) who also achieved its partial synthesis from β-amyrin. Its probable identity with skimmiol, obtained from *Skimmia* species, and much of its chemistry were reported by Takeda and his collaborators (*J. Pharm. Soc. Japan*, 1941, **61**, 117, 506; 1942, **62**, 390; 1943, **63**, 193, 197). On the other hand, Koller, Hiestand, Dietrich, and Jeger (*Helv. Chim. Acta*, 1950, **33**, 1050), working with material (from *Alnus glutinosa*) which appeared (see Table) but was not proved to be identical with the other alcohols mentioned, considered that it was not a 3-hydroxy-derivative, since they could not reduce the derived ketone by the Wolff–Kishner procedure—Takeda (*loc. cit.*, p. 117) found no steric hindrance when he prepared skimmione oxime.

Our work was carried out with skimmiol generously provided by Dr. Takeda. It confirms the structure proposed by Beaton *et al.* Our earlier conclusion (Brooks, *Chem. and Ind.*, 1953, 1178) that the double bond was at position 18 was based specifically on the assumption that no rearrangement occurs in the reaction of taraxerol acetate with selenium dioxide: this was invalidated by the later discovery (Allan, Johnston, and Spring, *J.*, 1954, 1546) of the ready conversion of *iso*oleanane into oleanane derivatives.

	Skimmiol [a]		Taraxerol [b]		Taraxerol [c]	
	M. p.	$[\alpha]_D$	M. p.	$[\alpha]_D$	M. p.	$[\alpha]_D$
Alcohol	279—281°	+ 3°	270°	—	282—283°	+ 3°
Acetate	298—299	+14	297	+ 8°	304—305	+ 9
Benzoate	287—289	+36	284	+35	292—293	+37
Ketone	241—243	+12	—	—	240—241	+12
"Oxide" *	283—286	+79	—	—	287	+73
Hydrocarbon †	187—190	−21	—	—	184	−24

[a] Takeda, *locc. cit.* [b] Burrows and Simpson, *loc. cit.* [c] Koller *et al.*, *loc. cit.*
* See text. † Identified as olean-13-ene in each case.

We have confirmed, by direct comparison, the identity of skimmiol and its benzoate with taraxerol and its benzoate, kindly supplied by Professor E. R. H. Jones, F.R.S.

Takeda had regarded skimmiol as a double-bond isomer of β-amyrin. We noted (Thesis, London, 1952) that this was consistent with the molecular-rotation differences on epimerisation of the hydroxyl group and Takeda's conversion of dihydroskimmiol into the A-nor-ketone (Δ +293°; cf. Klyne, *J.*, 1952, 2916); the same applies to skimmiol and its A-nor-ketone (Δ +402°). Further, in disagreement with Koller *et al.* (*loc. cit.*) we found taraxerone to be readily reduced by the Wolff–Kishner method to taraxerene, $C_{30}H_{50}$, corresponding to Takeda's "skimmiene II*a*" and recently isolated by Bruun (*Acta Chem. Scand.*, 1954, **8**, 1291) from the lichen, *Cladonia deformis*.

Taraxeryl acetate with selenium dioxide gives oleana-11 : 13-dienyl acetate (27%) and 12 : 19-dioxo-oleana-9 : 13-dienyl acetate (5%).

The trisubstituted nature of the ethylenic linkage in taraxerol is consistent with an infrared absorption band at 814 cm.$^{-1}$ (cf. Koller *et al.*, *loc. cit.*) and the ultraviolet absorption at 210—223 mμ (cf. p. 1676).

Taraxerol and its esters smoothly consume one mol. of per-acid, affording well-defined epoxides. These are easily isomerised by acid to unsaturated alcohols: the compound described by Koller *et al.* (*loc. cit.*) as "taraxeryl acetate oxide" and eluted from alumina by benzene–ether (9 : 1) was evidently the isomeric alcohol, the acetate of Takeda's "β-hydroxyskimmiol" (see Table). This is not an allylic alcohol, since the corresponding

diketone, prepared by chromic acid oxidation, and reducible back to the alcohol (Takeda, *loc. cit.*, p. 390), shows no high-intensity absorption in the ultraviolet ($\lambda_{max.}$ 295 mμ, ε 67); similarly the monoketone "β-ketoskimmiol acetate" exhibits only the band at 300 mμ (ε 40) expected for a saturated ketone. It is thus clear that the isomerisation of the epoxides under the influence of acids is accompanied by a molecular rearrangement, doubtless of carbonium-ion type.

Experimental

M. p.s taken on a Kofler stage are indicated by (K). Optical rotations were determined in $CHCl_3$ at room temperature (15—25°). Ultraviolet absorption spectra were measured in ethanol solution with a Unicam S.P. 500 Spectrophotometer. "Neutralised alumina" was prepared by treatment with ethyl acetate overnight, followed by exhaustive washing with water and reactivation at 200°. Light petroleum refers to the fraction of b. p. 40—60°.

Taraxerol crystallised from benzene–hexane as needles, m. p. 278—280° (K), $[\alpha]_D$ +2° (*c*, 1·32). Light absorption: 210 (ε 3900), 215 (ε 2400), 220 (ε 700), and 223 mμ (ε 250).

Taraxeryl acetate crystallised from benzene as large prisms, m. p. 303—307° (K), giving a very pale yellow colour with tetranitromethane. The infrared spectrum in Nujol mull revealed a band at 814 $cm.^{-1}$: this determination was kindly made by Dr. J. E. Page.

Taraxeryl Benzoate.—Taraxerol (132 mg.), chloroform (5 ml.), pyridine (1 ml.), and benzoyl chloride (0·5 ml.) were mixed and left at room temperature overnight. The usual working up afforded a crude product which was dissolved in benzene and filtered through alumina, yielding on evaporation the benzoate (167 mg.) which formed glittering prisms (121 mg.), m. p. 282—288°, $[\alpha]_D$ +34° (*c*, 0·98), from chloroform–methanol. One further recrystallisation raised the m. p. to 288—289°. To test the homogeneity of the taraxerol, a sample (1·05 g.) was benzoylated affording 727 mg. of pure benzoate. The mother-liquor was evaporated and the residue (550 mg.) chromatographed on alumina (Savory and Moore; 30 g.). Practically all the material (486 mg.) was eluted in one band by light petroleum–benzene (1 : 1) and had $[\alpha]_D$ +34° (*c*, 1·00).

Taraxerone.—When prepared according to Koller *et al.* (*loc. cit.*) and recrystallised from chloroform–methanol, this had m. p. 245—249° (K), $[\alpha]_D$ +12° (*c*, 1·38), and gave a strong purple colour in the Zimmermann test (Barton and de Mayo, *J.*, 1954, 887).

Taraxerene.—A mixture of taraxerone (50 mg.) suspended in ethanol (0·5 ml.), hydrazine (0·6 ml.), and sodium (125 mg.) dissolved in ethanol (1·3 ml.) was heated for 18 hr. at 200°. Working up as usual gave a crude product (47 mg.) which was chromatographed in light petroleum on alumina (Savory and Moore; 2 g.). The first 25 ml. of eluate afforded taraxerene (34 mg.), m. p. 238—243°, $[\alpha]_D$ +3° (*c*, 0·68), sparingly soluble (about 1% at 25°) in chloroform, from which it crystallised as large hexagonal plates, m. p. 238—240°. A sample sublimed in a high vacuum had the same m. p. (Found: C, 87·8; H, 12·2. Calc. for $C_{30}H_{50}$: C, 87·7; H, 12·3%).

Taraxerol Oxide.—A solution of taraxerol (364 mg.) in "AnalaR" chloroform (20 ml.) was treated with a solution (50 ml.; 0·025M) of monoperphthalic acid in ether and left in the dark at room temperature for 3½ days. Titration indicated that approx. 80% of the required amount of oxidant had been consumed. Working up in the usual way afforded a crude product which, after removal of a substance sparingly soluble in acetone, crystallised from aqueous acetone to give taraxerol oxide as long prisms (178 mg.), m. p. 204—208° (K), $[\alpha]_D$ +33° (*c*, 1·00).

Taraxeryl acetate oxide, prepared similarly (92% of the required uptake of peracid), was purified by chromatography on neutralised alumina. Light petroleum–benzene (1 : 1) eluted the oxide, which formed plates, m. p. 245—247° (K), from chloroform–methanol, $[\alpha]_D$ +51° (*c*, 0·93), and gave no colour with tetranitromethane (Found: C, 79·2; H, 10·65. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%).

Action of Selenium Dioxide on Taraxeryl Acetate.—The acetate (200 mg.) in "AnalaR" acetic acid (75 ml.) was refluxed for 20 hr. with selenium dioxide (100 mg.). Working up in the usual way afforded a crude product (207 mg.) which was chromatographed on neutralised alumina (7 g.). Two main crystalline fractions were obtained: (i) eluted by light petroleum–benzene (9 : 1) amounted to 136 mg., (ii) eluted by benzene–ether (95 : 5) amounted to 19 mg. Fraction (i), recrystallised from chloroform–methanol, gave prisms (26 mg.), m. p. 304—305°, identified as taraxeryl acetate (mixed m. p.). Fractional crystallisation from the mother-liquor afforded 55 mg. of a compound crystallising as plates (from ethyl acetate–methanol), m. p. 226—227° (K), $[\alpha]_D$ −58° (*c*, 1·94), $\lambda_{max.}$ 242, 250, and 259·5 mμ (log ε 4·35, 4·4, and 4·2) giving no depression in m. p. on admixture with oleana-11 : 13-dienyl acetate (Ruzicka and Jeger, *Helv.*

Chim. Acta, 1941, **24**, 1236) of the same m. p., $[\alpha]_D$ −68°. Fraction (ii), recrystallised from aqueous methanol, formed dense quadrilateral tablets (11 mg.), m. p. 237—240° (K), $[\alpha]_D$ −90° (*c*, 0·60), $\lambda_{max.}$ 276 mμ (log ε 4·07), undepressed in m. p. on admixture with 12 : 19-dioxo-oleana-9 : 13-dienyl acetate of similar crystal form and m. p., $[\alpha]_D$ −94° (*c*, 1·16).

Isomerisation of Taraxerol Oxide.—Taraxerol oxide (148 mg.) was refluxed for 3 hr. in ethanol (50 ml.) containing aqueous 2·5N-sulphuric acid (2 ml.). Working up in the usual way furnished a crude product which crystallised from aqueous acetone as fine needles (75 mg.), m. p. 240—242° (K). Sublimation in a high vacuum gave rectangular prisms, m. p. 244—245° (K), $[\alpha]_D$ +83° (*c*, 0·69), of " β-hydroxyskimmiol."

Isomerisation of Taraxeryl Acetate Oxide.—Taraxeryl acetate oxide (500 mg.) was heated for 3 hr. on the steam-bath with acetic acid (80 ml.) containing aqueous 4N-hydrochloric acid (2 ml.). Working up in the usual way gave, after crystallisation from benzene, prisms (300 mg.), m. p. 279—282° (K), $[\alpha]_D$ +75° (*c*, 1·07), of " β-hydroxyskimmiol acetate."

Chromic Acid Oxidation of " β-*Hydroxyskimmiol.*"—" β-Hydroxyskimmiol " (54 mg.) in acetic acid (30 ml.) was treated dropwise with a solution (5 ml.) of chromium trioxide (3·75 mg./ml.) in 99% acetic acid. The solution became green in a few hours. Working up in the usual way gave a crude product (52·5 mg.) which was chromatographed on neutralised alumina (2 g.). Light petroleum–benzene (9 : 1) eluted crystalline material (26 mg.), m. p. 208—212° (K), raised by recrystallisation from methanol to 210—213° (K), $[\alpha]_D$ +29° (*c*, 0·82), $\lambda_{max.}$ 295 mμ (ε 67) (Found : C, 82·0; H, 10·4. Calc. for $C_{30}H_{46}O_2$: C, 82·1; H, 10·6%). There was no high-intensity absorption in the ultra-violet above 220 mμ.

Chromic Acid Oxidation of " β-*Hydroxyskimmiol Acetate.*"—" β-Hydroxyskimmiol acetate " (51 mg.), partly dissolved in acetic acid (15 ml.), was treated with a solution (5 ml.) of chromium trioxide (0·065N) in acetic acid and shaken for 20 min. A clear solution was formed, and titration of an aliquot portion indicated that 120% of the required amount of oxidant (for one secondary hydroxyl group) had been consumed. Working up in the usual way and crystallisation of the product from benzene–light petroleum gave prisms (23 mg.), m. p. 274—276°, $[\alpha]_D$ +15° (*c*, 0·96). In a second preparation the product was entirely eluted from alumina (Savory and Moore) by light petroleum–benzene (1 : 1) and had, when recrystallised from benzene–light petroleum, m. p. 274—277°, $[\alpha]_D$ +15° (*c*, 0·91), $\lambda_{max.}$ 300 mμ (ε 40). Takeda (*loc. cit.*, p. 390) gave $[\alpha]_D$ +4°, while Beaton *et al.* (*Chem. and Ind.*. 1954, 1454) reported $[\alpha]_D$ +27°.

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