# Lichens and Fungi. Part X.[1] 14α-Taraxerane

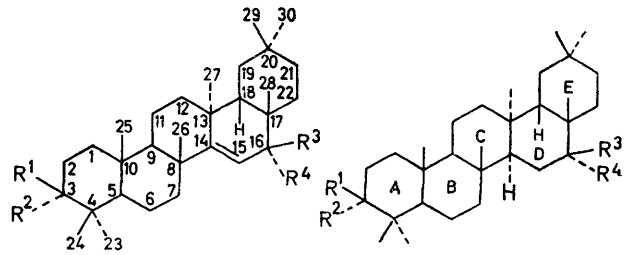
By R. E. Corbett * and Susan D. Cumming, Department of Chemistry, University of Otago, New Zealand
E. V. Whitehead, The British Petroleum Company Ltd, Chertsey Road, Sunbury-on-Thames, Middlesex

14α-Taraxerane has been synthesized and the methyl resonances in the $^1$H n.m.r. spectra of this compound and some of its derivatives have been assigned.

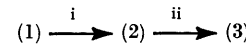
DESPITE the abundant natural occurrence of taraxerane [2] derivatives, little study has been made of the parent hydrocarbon. 14α-Taraxerane was in fact prepared by Takeda [3] in 1943 (but called dihydroskimmiene by him). Confusion arose when in the same year Winterstein,[4] assuming that the strongly acidic conditions of the transformations carried out by Takeda had caused methyl group migration, supposed that Takeda's dihydroskimmiene was oleanane (β-amyrane) and it is so described in Elsevier's Encyclopedia.[5] Two further references to taraxerane appear in the literature. Rao and Seshadri [6] isolated a triterpene diol from *Lobaria* lichens which they tentatively identified as taraxerane-3β,19β-diol. This assignment was based on the conversion of the diol into a hydrocarbon of m.p. 222—224°, close to that reported by Takeda [3] for dihydroskimmiene (224—226°). The mass spectrum of taraxerane has been referred to by Hills *et al.*[7] As an authentic specimen of taraxerane was required in order to compare its physical and spectral characteristics with hydrocarbons obtained as degradation products from certain lichen triterpenes it was necessary, because of the confusion in the literature, to synthesize a specimen by an unequivocal method.

Taraxer-14-en-3α-ol (1) was available, having been isolated in a previous study from the bark of *Suttonia australis*.[8] At the time it had not been reported to occur naturally, but has since been isolated [9] from specimens of the *Euphorbiaceae* of Hong Kong. Takeda *et al.*[3] first reported the preparation of compound (1), m.p. 267—269°, $[\alpha]_D^{20}$ +11·6° from the reduction of taraxer-14-en-3-one (6) with sodium in isopentanol. Hui and Sung reported m.p. 256—257°, $[\alpha]_D^{20}$ −0·5°, for their specimen which was pure by t.l.c. In their hands reduction of the ketone (6) with sodium in isopentanol gave a product which tailed on t.l.c., which they considered to be a mixture of taraxer-14-en-3β-ol (5) and the 3α-ol (1). The sample used in this investigation had m.p. 267—269°, $[\alpha]_D^{20}$ −11·6°, physical constants identical with those reported by Takeda [3] except that the optical rotation is negative. The sample was pure by t.l.c. and had $R_F$ 0·84 [*cf.* 0·70 for an authentic specimen of (5)]. Its identity was confirmed by oxidation to taraxer-14-en-3-one (6), identical with a sample prepared from (5). The n.m.r. spectra of the alcohols (1) and (5) showed the expected differences in the carbinol proton region. The C-3 proton in (1) appeared as a well-defined triplet centred at δ 3·38 p.p.m. (*J* 3 Hz), typical of an equatorial proton associated with a 3α-hydroxy-group in ring A of a triterpenoid, whereas the C-3 proton in (5) appeared as an ill-defined quartet (δ 3·22 p.p.m., $W_{\frac{1}{2}}$ 11 Hz), typical of the axial proton associated with a 3β-hydroxy-group.[10] These data leave no doubt that the specimens of (1) and (5) used in this study were pure and the physical constants recorded here for taraxer-14-en-3α-ol (1) can be regarded as definitive.

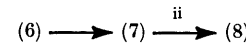
Taraxer-14-en-3α-ol (1) was smoothly converted by the series of standard steps outlined in Scheme 1 into 14α-



(1) $R^2$ = OH, $R^1$ = $R^3$ = $R^4$ = H
(2) $R^2$ = OH, $R^1$ = $R^3$ = $R^4$ = H
(3) $R^1R^2$ = O, $R^3$ = $R^4$ = H
(4) $R^1$ = $R^2$ = $R^3$ = $R^4$ = H
(5) $R^1$ = OH, $R^2$ = $R^3$ = $R^4$ = H
(6) $R^1R^2$ = O, $R^3$ = $R^4$ = H
(7) $R^1R^2$ = $R^3R^4$ = O
(8) $R^1R^2$ = $R^3R^4$ = O



SCHEME 1 Reagents: i, $H_2$, Pd–C; EtOAc–AcOH; ii, $CrO_3$; iii, Wolff-Kishner



SCHEME 2 Reagents: i, $Na_2Cr_2O_7$; ii, Li–$NH_3$ (liq.); iii, Wolff-Kishner

taraxerane (4), m.p. 226°, $[\alpha]_D^{20}$ +27·6°, 99% pure by g.l.c. Since only one product was formed in the hydrogenation of taraxer-14-en-3α-ol [(1) ⟶ (2)] it is assumed that the hydrogen atom at C-14 has the α-configuration. The α-face of (1) is considerably less hindered than the β-face. Drieding models show that steric interactions are minimized if ring C is in a boat conformation, convex on the β-face.

In an attempt to prepare 14β-taraxerane, the alternative route (Scheme 2) from taraxer-14-en-3-one (6) was

[1] Part IX, R. E. Corbett and C. K. Heng, *J. Chem. Soc.* (*C*), 1971, 1885.
[2] F. Tsunematsu, *J. Pharm. Soc. Japan*, 1954, **74**, 1271.
[3] K. Takeda, *J. Pharm. Soc. Japan*, 1943, **63**, 193.
[4] A. Winterstein, *J. Pharm. Soc. Japan*, 1943, **63**, 197.
[5] 'Elsevier's Encyclopaedia of Organic Chemistry,' vol. 14S, Elsevier, Amsterdam, 1952, p. 945S.
[6] P. S. Rao and T. R. Seshadri, *Indian J. Chem.*, 1968, **6**, 398.
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[8] I. L. Weatherall, M.Sc. Thesis, University of Otago, 1962.
[9] W. H. Hui and M. L. Sung, *Austral. J. Chem.*, 1968, **21**, 2137.
[10] L. B. Kier, L. M. Lehn, and G. Ourisson, *Bull. Soc. chim. France*, 1963, 911; N. S. Bhacca and D. H. Williams, 'Application of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 144.

investigated. It was thought that reduction of the αβ-unsaturated ketone, taraxer-14-ene-3,16-dione with lithium in liquid ammonia might give a mixture of products epimeric at C-14. The reduction gave the 14α-epimer exclusively.

The methyl resonances in the $^1$H n.m.r. spectrum of 14α-taraxerane have been assigned in the following way. Since the configuration of rings A and B is the same as that of ursane, lupane, oleanane, and 18α-oleanane the chemical shifts of the 4β-, 4α-, and 10β-methyl groups in the five classes of triterpenes should be almost identical and should be subject to similar substituent effects.[1,11] The chemical shifts of the ring A methyl groups in the examples quoted are at progressively lower field in the order 4β > 4α > 10β, and this is the order in which they have been assigned for 14α-taraxerane (4) (Table).

Chemical shifts of methyl groups (δ in p.p.m. from tetramethylsilane)

| | 4α | 4β | 10β | 8β | 13α | 17β | 20α | 20β |
|---|---|---|---|---|---|---|---|---|
| 14α-Taraxerane (4) | 0·84 | 0·82 | 0·88 | 1·10 | 0·88 | 0·84 | 0·92 | 0·95 |
| 14α-Taraxeran-3α-ol (2) | 0·95 | 0·84 | 0·95 | 1·10 | 0·90 | 0·84 | 0·92 | 0·95 |
| 14α-Taraxeran-3-one (3) | 1·08 | 1·04 | 0·95 | 1·08 | 0·89 | 0·84 | 0·92 | 0·95 |
| Taraxer-14-en-3β-ol (5) | 0·98 | 0·81 | 0·93 | 1·10 | 1·10 | 0·83 | 0·91 | 0·95 |
| Taraxer-14-en-3α-ol (1) | 0·95 | 0·82 | 0·92 | 1·10 | 1·10 | 0·85 | 0·92 | 0·95 |
| Taraxer-14-en-3-one (6) | 1·15 | 0·93 | 1·08 | 1·10 | 1·10 | 0·84 | 0·93 | 0·96 |
| Taraxer-14-ene-3,16-dione (7) | 1·20 | 0·98 | 1·08 | 1·10 | 1·10 | 1·01 | 0·93 | 0·95 |

Two signals appear at or close to δ 0·92 and 0·95 p.p.m. in all the spectra listed, and these are assigned to the 20α- and 20β-methyl groups, respectively. These groups will not be affected by ring A substituents or by a C-14 double bond. The axial methyl group of the 4,4-dimethyl pair in a triterpene normally resonates at higher field, and in this case the anisotropic effects of the C-18(19) and C-21(22) bonds should lead to a similar result; thus the resonance at higher field is attributed to the axial 20α-methyl group. The only significant difference between the spectra of compounds (6) and (7) is the downfield shift of a signal from 0·84 to 1·01 p.p.m. An oxo-function at C-16 would deshield the 17β-methyl group. The signal at 0·84 p.p.m. in (6) and at 0·84 ± 0·01 p.p.m. in compounds (1)—(5) is thus assigned to the 17β-methyl group.

There remain two signals at 1·10 p.p.m. in the spectra of all taraxer-14-ene derivatives which can only arise from the 8β- and 13α-methyl groups, deshielded by the C-14 double bond. Hydrogenation of the C-14 double bond gives 14α-taraxerane and its derivatives in which one of the signals at 1·10 p.p.m. has moved upfield to 0·89 ± 0·01 p.p.m. Drieding models show that in 14α-taraxerane and its derivatives the 8β-methyl group suffers severe steric interaction with the methylene group at C-15, while the 13α-methyl group is relatively free from steric strain. Thus while hydrogenation of the C-14 double bond eliminates the deshielding of the 8β-methyl group from this source, it is replaced by steric deshielding from the C-15 methylene group. The signals at 1·10 p.p.m. for compounds (4) and (2) are for this reason assigned to the 8β-methyl group and those at 0·88 and 0·90 p.p.m. to the 13α-methyl group. Thus on the internal evidence from the compounds studied and from existing data it has proved possible to make a complete assignment of all the methyl signals.

Mass spectroscopy has been applied widely to the study of pentacyclic triterpenes, and much structural information can be deduced by recognition of the principal mass spectral peaks. The mass spectrum of 14α-taraxerane is very similar to that of 18α-oleanane and to those of lupane, gammacerane, and moretane reported by Hills *et al.*[7] A mass spectrum appears to be of relatively little value for distinguishing these particular triterpenes, all of which show a fragment at *m/e* 191 as the most intense peak.[12,13]

## EXPERIMENTAL

Experimental procedures were as described in Part VI.[14]

*Taraxer-14-en-3α-ol* (*Isotaraxerol*) (1).—An authentic sample had m.p. 267—269° (from benzene), $[\alpha]_D^{20}$ −11·6° (*c* 0·875 in $CHCl_3$); $\nu_{max.}$ 3615 (OH) cm$^{-1}$; δ 0·82(3H), 0·85(3H), 0·92(6H), 0·95(6H), 1·10(6H), 3·38 (1H, t), and 5·52 (1H, t) p.p.m.; *m/e* 426 ($M^+$) and 204 (base peak) (Found: C, 84·0; H, 11·6. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%).

*Taraxer-14-en-3β-ol* (*Taraxerol*) (5).—An authentic sample had m.p. 282—283° (from benzene); $[\alpha]_D^{20}$ +0·72° (*c* 0·974 in $CHCl_3$) (lit.,[15] m.p. 278—280°, $[\alpha]_D^{20}$ +2°); δ 0·81(3H), 0·83(3H), 0·91(3H), 0·93(3H), 0·95(3H), 0·98(3H), 1·10(6H), 3·22(1H, q, $W_{\frac{1}{2}}$ 11 Hz), and 5·54(1H, m) p.p.m.

*Taraxer-14-en-3-one* (*Taraxerone*) (6).—An authentic sample had m.p. 245° (from benzene), $[\alpha]_D^{20}$ +12·8° (*c* 0·047 in $CHCl_3$) (lit.,[15] m.p. 245—249°, $[\alpha]_D^{20}$ +12°); δ 0·84(3H), 0·93(6H), 0·96(3H), 1·08(3H), 1·10(6H), 1·15(3H), and 2·45(2H, m, $CH_2$·CO) p.p.m.

*18α-Oleanane.*—An authentic sample [1] had m.p. 210°; δ 0·76(3H), 0·81(3H), 0·84(3H), 0·87(3H), 0·88(3H), 0·92(3H), 0·94(3H), and 1·03(3H) p.p.m., *m/e* 412 ($M^+$), 191 (base peak), 109, 123, and 137.

*14α-Taraxeran-3α-ol* (2).—Taraxer-14-en-3α-ol (150 mg) in ethyl acetate (70 ml) and glacial acetic acid (35 ml) was hydrogenated over 5% palladium–charcoal for 6 days. Filtration and evaporation gave a crude solid (150 mg), which was purified by p.l.c. with E–H (1 : 1) to give needles of *14α-taraxeran-3α-ol* (2), m.p. 238° (from benzene), $[\alpha]_D^{20}$ +3·07° (*c* 1·3 in $CHCl_3$); $\nu_{max.}$ 3620(OH) cm$^{-1}$; δ 0·84(6H), 0·90(3H), 0·92(3H), 0·95(9H), 1·10(3H), and 3·39 (1H, t) p.p.m.; *m/e* 428 ($M^+$), 207, 191, 190, 189 (base peak), 135, 81, and 69 (Found: C, 84·4; H, 12·4. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

[11] H. T. Cheung and D. G. Williamson, *Tetrahedron*, 1969, **25**, 119.
[12] M. N. Galbraith, C. J. Miller, J. W. L. Rawson, E. Ritchie, J. S. Shannon, and W. C. Taylor, *Austral. J. Chem.*, 1965, **18**, 226
[13] R. E. Corbett and H. Young, *J. Chem. Soc.* (*C*), 1966, 1556.
[14] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (*C*), 1969, 44.
[15] C. J. W. Brooks, *J. Chem. Soc.*, 1955, 1674.

14α-*Taraxeran*-3-*one* (3).—(*a*) 14α-Taraxeran-3α-ol (130 mg) in pyridine (20 ml) was added to a suspension of chromium trioxide (96 mg) in pyridine (0·96 ml) and stirred at room temperature for 12 h. Work-up in the usual way followed by p.l.c. with E–H (1 : 3) gave (at higher $R_F$) the oxidation product (40 mg) and (at lower $R_F$) unchanged 14α-taraxeran-3α-ol (identical by m.p. and t.l.c.).

(*b*) Jones reagent was added dropwise to 14α-taraxeran-3α-ol (60 mg) in AnalaR acetone (30 ml) until a permanent orange colour resulted, and the mixture was worked up in the usual way. Crystallization from benzene gave 14α-*taraxeran*-3-*one* (3) (40 mg), identical with the oxidation product prepared by method (*a*); m.p. 229°, $[\alpha]_D^{20}$ +31·0° (*c* 0·5 in $CHCl_3$); $\nu_{max.}$ 1695 (C=O) $cm^{-1}$; c.d. $\Delta\varepsilon$ +0·61 max. (290 nm); o.r.d. $[\phi]_{308}$ +1860°pk, $[\phi]_{269}$ −530°tr, *a* +24; δ 0·84(3H), 0·89(3H), 0·92(3H), 0·95(6H), 1·04(3H), 1·08(6H), and 2·36(2H, m) p.p.m.; *m/e* 426 ($M^+$), 273 (base peak), 205, and 191 (Found: C, 84·6; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

14α-*Taraxerane* (4).—14α-Taraxeran-3-one (30 mg) in freshly distilled diethylene glycol (30 ml) was treated with 98% hydrazine hydrate (2·5 ml) and the mixture was refluxed at 120° for 12 h. Potassium hydroxide pellets (0·5 g) were added and the temperature was kept at 120° for a further 1 h. Removal of the hydrazine by distillation raised the temperature to 215°, and the mixture was kept under reflux at this temperature for 12 h. Work-up in the usual way gave a crude solid which was adsorbed from benzene on to Woelm neutral alumina (20 g; grade III). Elution with benzene gave 14α-taraxerane (4) (20 mg), which formed needles, m.p. 226° (from ethanol) (lit.,[3] m.p. 224—226°), $[\alpha]_D^{20}$ +27·6° (*c* 0·0682 in $CHCl_3$), δ 0·82(3H), 0·84(6H), 0·88(6H), 0·92(3H), 0·95(3H), and 1·10(3H) p.p.m.; *m/e* 412 ($M^+$) and 191 (base peak) (Found: C, 87·6; H, 12·3. Calc. for $C_{30}H_{52}$: C, 87·3; H, 12·7%).

*Taraxer*-14-*ene*-3,16-*dione* (7).—(*a*) Potassium chromate (200 mg) was added to a solution of taraxer-14-en-3-one (150 mg) in glacial acetic acid (50 ml) and acetic anhydride (25 ml). The mixture was stirred at room temperature for 1 h, then the temperature was raised to 40° and maintained there for 24 h. Work-up in the usual way gave a crude solid (130 mg), which was purified by p.l.c. with E–H (1 : 1). The compound of highest $R_F$ value was taraxer-14-en-3-one (40 mg) (m.p., mixed m.p., and t.l.c.). The compound of lowest $R_F$ value was *taraxer*-14-*ene*-3,16-*dione* (7) (25 mg), which was purified by multiple p.l.c. (× 3) in E–H (1 : 19). Crystallization from hexane–ethanol gave needles, m.p. 262° (decomp. from 230°); $\nu_{max.}$ 1695 and 1670 (C=C–C=O) $cm^{-1}$; δ 0·93(3H), 0·95(3H), 0·98(3H), 1·01(3H), 1·08(3H), 1·10(6H), 1·20(3H), 5·86(1H), and 2·40(2H,m) p.p.m.; $\lambda_{max.}$ (EtOH) 310 and 240 nm (and end-absorption); sublimation (180° at 0·01 mmHg) gave crystals (Found: C, 82·3; H, 10·85. $C_{30}H_{46}O_2$ requires C, 82·2; H, 10·5%).

(*b*) Taraxer-14-en-3-one (40 mg), freshly recrystallized *N*-bromosuccinimide (45 mg), and finely divided calcium carbonate (25 mg) in tetrahydrofuran (40 ml) and water (4 ml) were stirred at room temperature for 1 h while being irradiated with visible light. Work-up in the usual way gave a solid (40 mg), which was separated by p.l.c. with E–H (3 : 7) into taraxer-14-en-3-one (20 mg), identical (m.p., mixed m.p., and t.l.c.) with an authentic sample, and taraxer-14-ene-3,16-dione (20 mg), identical (m.p., mixed m.p., and t.l.c.) with the sample prepared by method (*a*).

14α-*Taraxerane*-3,16-*dione* (8).—Lithium (*ca.* 0·2 g) was added in small pieces to liquid ammonia (30 ml), and taraxer-14-ene-3,16-dione (35 mg) in dry ether was added dropwise to the dark blue solution. The mixture was stirred for 0·75 h, then ammonium chloride (4 g) was added to destroy the excess of lithium. The ammonia was allowed to evaporate, and the mixture worked up in the usual way. Purification of the product (35 mg) by p.l.c. with E–H (1 : 1) gave (at higher $R_F$ value) unchanged taraxer-14-ene-3,16-dione (20 mg), identified by m.p., mixed m.p., and t.l.c., and (at lower $R_F$ value) 14α-*taraxerane*-3,16-*dione* (8) (10 mg), which formed needles, m.p. 259° (from ethanol) (Found: C, 81·4; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·7; H, 10·9%).

*Wolff–Kishner Reduction of* 14α-*Taraxerane*-3,16-*dione* (8).—14α-Taraxerane-3,16-dione (8 mg) in hexane was added to freshly redistilled diethylene glycol (15 ml) which had been treated with sodium (0·15 g). The hexane was distilled off as the temperature was increased to 180°. Hydrazine hydrate (98%) was added until the solution was refluxing freely at 180° (solution temperature). After heating under reflux for 24 h the temperature was raised to 210° by distilling off some of the hydrazine. After a further 24 h at 210° the mixture was cooled, neutralized (2M-HCl), and worked up in the usual way. The product was adsorbed from benzene on to Woelm neutral alumina (5 g; grade III). Elution with benzene gave 14α-taraxerane (5 mg), m.p. 226° (ethanol), identical (m.p., mixed m.p., and t.l.c.) with the product prepared by the previous synthesis.

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