389. *The Triterpene Group. Part IV. The Triterpene Alcohols of* Taraxacum *Root.*

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Application of the alumina adsorption method to the non-saponifiable matter of *Taraxacum* root, previously examined by Power and Browning (J., 1912, **101**, 2411), has disclosed the extreme complexity of the mixture. Seven compounds have so far been isolated, namely, three new alcohols (*taraxol*, $C_{30}H_{46}O_3$; *taraxerol*, $C_{30}H_{50}O$; and *ψ-taraxasterol*, $C_{30}H_{50}O$), taraxasterol, β-amyrin, stigmasterol, and β-sitosterol. The "homotaraxasterol" of Power and Browning is shown to be a mixture, but the chemical individuality of taraxasterol is confirmed. The physical constants of the latter, the three new alcohols, and their derivatives indicate their probable triterpenoid nature.

THE common dandelion (*Taraxacum officinale*) has been the subject of several chemical investigations of somewhat inconclusive character. The isolation of apparently pure crystalline substances was first reported by Power and Browning (J., 1912, **101**, 2411), who obtained from the non-saponifiable matter of the root two alcohols, taraxasterol and homotaraxasterol, which they described as phytosterols and formulated as $C_{29}H_{48}O$ and $C_{25}H_{40}O$ respectively. More recently, Zellner and Huppert (*Monatsh.*, 1926, **47**, 681) isolated taraxasterol (evidently slightly impure) from the latex, together with a product which they considered to be identical with Power and Browning's homotaraxasterol, despite considerable discrepancies in the physical constants of the respective alcohols and their acetates.

We have recently undertaken a detailed re-examination of the non-saponifiable matter of *Taraxacum* root, because it appeared from the work of Power and Browning that this material consisted of an unusually complex mixture, of which taraxasterol and homotaraxasterol formed but a small proportion. After preliminary (and unsatisfactory) attempts to resolve the mixture by fractional crystallisation, we employed the method of adsorption on activated alumina and fractional elution, a procedure which has disclosed the complexity of the material to a degree not evidenced by ordinary crystallisation methods. Although we have as yet been unable to make a complete examination of its components, we have succeeded in isolating from the non-saponifiable material stigmasterol and β-sitosterol, together with β-amyrin, taraxasterol, and three new alcohols which we have designated *taraxol*, *taraxerol*, and *ψ-taraxasterol*; the physical constants of these new alcohols and their esters are in Table I. A careful search has failed to reveal the presence of " homotaraxasterol " as a single substance, and in our opinion this material is a difficultly separable mixture containing taraxasterol, *ψ*-taraxasterol, and possibly other unidentified substances (see Experimental).

TABLE I.

		Alcohol.		Acetate.		Benzoate.	
Name.	Formula.	M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.
Taraxol	$C_{30}H_{46}O_3$	>360°	+79°	300°	+94°	—	—
Taraxerol	$C_{30}H_{50}O$	270	—	297	8	284°	35°
ψ-Taraxasterol	$C_{30}H_{50}O$	200	47	235	53	276	72

TABLE II.

Constants of Taraxasterol and Derivatives.

Alcohol.		Acetate.		Benzoate.		*p*-Nitrobenzoate.	
M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.
221—222°	96·3°	251—252°	102·5°	232° (*a*)	—	—	—
217—219	95·6	248—250	98·7 (*b*)	—	—	—	—
221—222	95·9	251—252	100·5	240—241	106·8°	277—278°	98·3° (*c*)

(*a*) Power and Browning, J., 1912, **101**, 2411. (*b*) *Idem*, J., 1914, **105**, 1829. (*c*) This paper.

The existence of taraxasterol as a chemical entity, on the other hand, must be deemed beyond reasonable doubt, for the physical constants of our preparation are almost identical with those recorded by Power and Browning. Moreover, taraxasterol of approximately the same degree of purity was later obtained by these workers (J., 1914, **105**, 1829) from a different source (*Anthemis nobilis*, which, like *Taraxacum*, belongs to the natural order *Compositae*) (see Table II). We have ourselves repeated the isolation of taraxasterol from *Anthemis nobilis* and confirmed its identity with the *Taraxacum* preparation.

Zellner has stated (Stern and Zellner, *Monatsh.*, 1925, **46**, 459; Zellner and co-workers, *ibid.*, 1926, **47**, 681) that the α-lactuceryl alcohol (α-lactucerol) first obtained by Hesse (*Annalen*, 1886, **234**, 243; 1888, **244**, 268) from lactucarium, the latex of *Lactuca virosa* (*Compositae*), is identical with taraxasterol and also with a number of fesin alcohols isolated by Zellner from various species of *Compositae*. Although this statement may be correct, it is undoubtedly premature, for Zellner has adduced no formal evidence of identity, and furthermore the melting points of his *Compositae* resinols and their acetates are in all cases

appreciably lower than those of taraxasterol and taraxasteryl acetate. Moreover, the properties of α-lactucerol from lactucarium have been recently investigated by Bauer and Schub (*Arch. Pharm.*, 1929, **267**, 413), and Ichiba (*Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1937, **34**, 132) has recorded the isolation of an " amyrin-like alcohol " from lettuce oil; in both these cases, also, the melting points of the alcohols are considerably lower than that of taraxasterol. Until convincing data are available, therefore, the identity of these resin alcohols with taraxasterol should, in our opinion, be regarded only as an attractive hypothesis.

The elementary analyses of taraxasterol, the new alcohols, and their derivatives do not exclude C_{29}-formulae, but the C_{30}-formulations advanced in this paper receive provisional justification from the physical constants of these compounds, which are strongly indicative of their triterpenoid character. Each of the alcohols is unsaturated, and gives positive reactions with tetranitromethane and the Liebermann–Burchard reagent. In agreement with this observation, taraxyl acetate reacts smoothly with perbenzoic acid to give *taraxyl acetate oxide*, m. p. 294—297°, which on alkaline hydrolysis yields *taraxol oxide*, m. p. 261°.

Of the three oxygen atoms in taraxol, only one is contained in a secondary (or primary) alcoholic group, because the alcohol forms only a monoacetate on treatment with acetic anhydride. The two remaining oxygen atoms are probably oxidic, because the acetate does not react with hydroxylamine; the possibility that they may be present as two inert carbonyl groups is not, however, excluded.

An investigation of the structure of taraxasterol has been commenced. The alcohol contains an easily reducible double bond, and is oxidised by chromic anhydride under mild conditions to a *product* (probably the corresponding ketone), m. p. 176°. Further work is in progress.

Experimental.

(Melting points uncorrected; specific rotations in chloroform.)

Preparation of Non-saponifiable Material.—Dry *Taraxacum* root was ground and thrice extracted, in batches of 3 kg., with boiling carbon tetrachloride (15 l. per extraction per batch). Evaporation of the solvent furnished a dark, viscous resin (1·8% of the dry weight of the root), which was refluxed, in portions of 110 g., with 10% alcoholic potassium hydroxide solution (1 l.) for 3 hours. After removal of 700 c.c. of alcohol by distillation the cold residue was poured into water (2 l.) and set aside. The resultant suspension was decanted from a quantity of heavy rubber-like material and extracted six times with ether. After drying and evaporation, the non-saponifiable material (about 30 g.) was obtained as a light brown, mainly crystalline mass.

Adsorption on, and Fractional Elution from, Alumina.—A dried solution of non-saponifiable material (60 g.) in benzene (900 c.c.) was slowly drawn through a column of alumina (500 g. of Merck's " standardisiert nach Brockmann " in a tube of 2·8 cm. diameter); the column was washed with successive 500-c.c. portions of benzene until the filtrates (collected separately) gave no appreciable residue on evaporation, whereupon it was divided into two portions, each of which was thoroughly eluted with hot chloroform–alcohol. By this means 180 g. of non-saponifiable material were divided into six fractions, which (except the two obtained by chloroform–alcohol elution) were further sub-divided by readsorption on alumina, followed by fractional elution as already described. By combining sub-fractions of similar melting point and colour reactions (Liebermann–Burchard), the following final fractions (listed in increasing order of adsorbability) were isolated:

Fraction.	Wt. (g.).	Liebermann–Burchard reaction.	Appearance.	M. p.
1	5·5	—	Waxy; mainly crystalline	<90°
2	6·5	—	Waxy	<90
3	34	Red	Brown amorphous solid	*ca.* 95
4	43	Red	White crystalline mass	145—151
5	24·5	Red	White crystalline mass	152—158
6	3·5	Red	White crystalline mass	170—190
7	7	Red	Partly crystalline	140—150
8	3·5	Brown-red	Brown, semi-crystalline	105—115
9	11	Brown-red	Dark amorphous solid	Soft at 100
10	6·5	Greenish-blue	Brown amorphous solid	Soft at 100
11	5·5	Greenish-blue	Mainly crystalline	126—131

Isolation of Taraxyl Acetate.—Fractions 3, 4, 5, 6, and 7 were separately acetylated with pyridine and acetic anhydride and the mixed acetates were precipitated with methanol. In each case small amounts of material were found to be very sparingly soluble in ether, and after several digestions with this solvent yielded pure *taraxyl acetate*, m. p. 299—301° (decomp., evacuated tube). The acetate was almost insoluble in hot alcohol, and separated from benzene or *cyclo*hexane in long, brittle, rectangular plates of unchanged m. p.; $[\alpha]_D^{14°}$ + 93·9° (l = 1, c = 1·15) (Found : C, 77·35, 77·6; H, 9·4, 9·6. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·8%).

Taraxol.—The foregoing acetate (0·8 g.) in benzene (50 c.c.) was refluxed with a solution of potassium hydroxide in 95% alcohol (50 c.c. of 4%) for 2 hours. On evaporation of the benzene, *taraxol* separated in fine soft needles, which after two crystallisations from benzene–alcohol did not melt at 360° but shrank at 280—290° (evacuated tube) (Found : C, 79·1; H, 9·9. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). The alcohol was successively crystallised from ethyl acetate, *cyclo*hexane, acetone, and benzene–alcohol without affecting the analytical data (Found : C, 78·9; H, 9·7%). $[\alpha]_D^{14°}$ + 78·6° (l = 1, c = 1·03). Taraxol gives a yellow colour in chloroform with tetranitromethane, and a reddish-purple Liebermann–Burchard reaction.

Taraxyl Acetate Oxide.—A solution of the acetate (0·2 g.) in a 0·25N-chloroform solution of perbenzoic acid (20 c.c.) was left at 0° for 12 days. The oxygen consumption was determined in the usual manner (Found : 7·25 c.c. of N/10. $C_{32}H_{48}O_4$ requires 8·07 c.c. for $\overline{\text{I}}$), and the product isolated by washing the chloroform solution with aqueous sodium carbonate, drying, and evaporation of the solvent. The residue was crystallised from chloroform–alcohol and finally from benzene, from which the *oxide acetate* separated in rectangular plates, m. p. 294—297°; the m. p. was not depressed by admixture with taraxyl acetate. The oxide gives a positive Liebermann–Burchard reaction, but no colour with tetranitromethane in chloroform (Found : C, 75·1; H, 9·3. $C_{32}H_{48}O_5$ requires C, 74·9; H, 9·5%).

Taraxol Oxide.—The oxide acetate (50 mg.) in benzene (2·5 c.c.) was refluxed for 1 hour with 2% alcoholic potassium hydroxide (3 c.c.). The solution was concentrated to half bulk, and the product precipitated with water. The *oxide* was twice crystallised from aqueous alcohol, and finally from aqueous methanol, from which it separated in soft needles, m. p. 261—261·5° (Found : C, 77·2; H, 10·0. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·9%).

Isolation of β-Amyrin Acetate.—After removal of taraxyl acetate the ether-soluble acetates from fractions 4 and 5 were separately crystallised from ethyl acetate–alcohol, whereby large amounts of crude taraxasteryl acetate were first deposited. The filtrates from these crops were concentrated, and the residues continually crystallised from alcohol. Prismatic needles were finally obtained, which melted at 237—238·5°, $[\alpha]_D^{14°}$ + 81·0° (l = 1, c = 2·16), and did not depress the m. p. of authentic β-amyrin acetate. The identity of this material was confirmed by its hydrolysis to β-amyrin, m. p. 196—197° both alone and when mixed with an authentic specimen.

No taraxasteryl acetate appeared to be present in fraction 3, and the least soluble fractions (after removal of taraxyl acetate) yielded β-amyrin acetate on crystallisation from benzene–alcohol (total yield from fractions 3—5, 2·5 g.).

Isolation of Taraxerol.—(a) *As benzoate.* After removal of the foregoing products from fraction 4, the filtrates were concentrated, yielding a further amount of crystalline material (m. p. *ca.* 150°), from which no individual substance could be isolated by further crystallisation. The mixture was therefore refluxed with 3% alcoholic potassium hydroxide for 3 hours, the solution diluted with water, and the free alcohols isolated by extraction with ether. The product separated from alcohol in needles, m. p. *ca.* 140°, raised to 160—161° after three crystallisations. The m. p. of this material was unchanged after several further crystallisations, indicating its probable identity with Power and Browning's homotaraxasterol (m. p. 163—164°). On continued recrystallisation the m. p. rose slowly (184—189°), but no pure compound could be isolated. This final crop and its filtrates were accordingly combined (12 g.) and benzoylated in pyridine solution, and the mixed benzoates precipitated with methyl alcohol. Continued digestion with ether furnished, as the least soluble fraction, a " benzoate complex " (m. p. 256—263°), which was further treated as described below. The ethereal filtrates from the " benzoate complex " were evaporated, and the residue crystallised from chloroform–alcohol. A gelatinous product first separated; this was removed, and the solution concentrated; a crystalline mass was then slowly deposited. This was sparingly soluble in ether, and after threefold digestion with this solvent yielded *taraxeryl benzoate*, m. p. 282—284°. This m. p. was unchanged after further digestion of the ester with ether and also after crystallisation from acetone and chloroform–alcohol, from which the benzoate separated in small, thin, brittle

needles, $[\alpha]_D^{11°}$ + 35·0° (l = 1, c = 2·0) (Found: C, 83·3; H, 10·2. $C_{37}H_{54}O_2$ requires C, 83·8; H, 10·3%). The compound gave a deep red colour with the Liebermann–Burchard reagent.

Similar treatment of fraction 5 gave 11 g. of mixed alcohols, from which, after benzoylation, a " benzoate complex," m. p. 270—272°, and a small quantity of taraxeryl benzoate were successively isolated.

(b) *As acetate.* The crude taraxasteryl acetate crops from fractions 4, 5, and 6 were combined and crystallised from ethyl acetate–alcohol. The first filtrate, on standing, deposited small amounts of material (m. p. 220—230°), which after crystallisation from ethyl acetate and then repeatedly from benzene–alcohol melted finally at 296—297°. This compound crystallised in flat needles, $[\alpha]_D^{18°}$ + 8·4° (l = 1, c = 1·56) (Found: C, 81·9; H, 11·1. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%), and was identified as *taraxeryl acetate* by hydrolysis in benzene solution with 1% alcoholic potash to *taraxerol*, which separated from chloroform–alcohol in plates, m. p. 269—271° (Found: C, 84·4; H, 11·7. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

Taraxerol, m. p. 268—270° either alone or when mixed with the above specimen, was also obtained by hydrolysis of taraxeryl benzoate in benzene solution with 4% alcoholic potassium hydroxide.

Isolation of ψ-Taraxasteryl Acetate.—(a) Great difficulty was experienced during the final stages of purification (by crystallisation from ethyl acetate or ethyl acetate–alcohol) of the crude taraxasteryl acetate obtained from fractions 4, 5, and 6. The mother-liquors from the later crystallisations were therefore combined and concentrated, and the material so obtained worked up for ψ-taraxasteryl acetate in either of the two following ways, depending on its purity:

(i) The mixture of acetates was directly crystallised from *cyclo*hexane and finally from ethyl acetate, yielding *ψ-taraxasteryl acetate*, which separated in glistening plates, m. p. (constant) 234—235·5°.

(ii) The mixed acetates were heated under reflux with 2% benzene-alcoholic potassium hydroxide, and the resultant alcohols treated with *p*-nitrobenzoyl chloride in pyridine at 100°. The crude *p*-nitrobenzoates were isolated by decomposition of the reaction mixture with ice and dilute sulphuric acid, followed by extraction with chloroform. The extract was dried and evaporated, and the residue digested with ether. Recrystallisation of the insoluble fraction from alcohol, acetone, benzene–alcohol, and ethyl acetate yielded a product of constant m. p. 265—270°, depressed by admixture with taraxasteryl *p*-nitrobenzoate. This fraction was hydrolysed and converted into the acetate in the usual manner; the latter, after crystallisation from ethyl acetate, had m. p. 232—235°, giving no depression in m. p. when mixed with the acetate obtained by method (i), but depressed by taraxasteryl acetate and by α- and β-amyrin acetates. The pure acetate (m. p. 234—235·5°) showed $[\alpha]_D^{20°}$ + 53·2° (l = 1, c = 2·21), and gave an immediate yellow coloration with tetranitromethane in chloroform, and a red colour, with marked green fluorescence, with the Liebermann–Burchard reagent (Found: C, 81·7; H, 11·1. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

(b) The " benzoate complexes " described above were heated under reflux for 2 hours with 5% benzene-alcoholic potassium hydroxide. The product had m. p. 207—209° after several crystallisations from ligroin, and was then acetylated in the usual way. The mixture of acetates was fractionated from ethyl acetate, the less soluble crops consisting of impure taraxasteryl acetate (m. p. 239—241°, undepressed by an authentic specimen). The more soluble crops were crystallised from ethyl acetate–alcohol, from which ψ-taraxasteryl acetate separated in plates, m. p. 233—235° [223—225° when mixed with taraxasteryl acetate, but giving no depression with the acetate prepared by method (a)].

ψ-Taraxasterol.—This *alcohol*, obtained by alkaline hydrolysis of the above acetate, separated from ethyl alcohol in fine needles, m. p. 198—200°, $[\alpha]_D^{21°}$ + 47·1° (l = 1, c = 2·60) (Found: C, 83·8; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The *benzoate*, prepared by the pyridine–benzoyl chloride method, separated from acetone in flat needles, m. p. 274—276°, $[\alpha]_D^{21°}$ + 72·3° (l = 1, c = 1·59) (Found: C, 83·3; H, 10·3. $C_{37}H_{54}O_2$ requires C, 83·8; H, 10·3%).

Taraxasterol and Derivatives.—No convenient method for the purification of this alcohol has yet been devised, as all recrystallisations of it and of its esters involve heavy losses of material. The acetate separated from ethyl acetate in glistening plates, m. p. 251—252°, $[\alpha]_D^{18°}$ + 100·5° (l = 1, c = 2·18) (Found: C, 82·15; H, 11·7. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). Taraxasterol formed long soft needles from alcohol and had m. p. 221—222°, $[\alpha]_D^{17°}$ + 95·9° (l = 1, c = 1·84) (Found: C, 84·5; H, 11·7. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%). It gave a pale yellow colour with tetranitromethane in chloroform, and a red colour, with green fluorescence, with the Liebermann–Burchard reagent. Taraxasteryl benzoate

separated from acetone or benzene–alcohol in flat needles, m. p. 240—241°, $[\alpha]_D^{12°}$ + 106·8° (l = 1, c = 2·06) (Found : C, 83·5; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·8; H, 10·3%). *Taraxasteryl* p-*nitrobenzoate* formed needles from chloroform–alcohol, m. p. 277—278°, $[\alpha]_D^{17°}$ + 98·3° (l = 1, c = 0·58) (Found : C, 77·5; H, 9·2. $C_{37}H_{53}O_4N$ requires C, 77·2; H, 9·3%).

With the exception of the benzoates of taraxasterol and ψ-taraxasterol, which give no depression in m. p. when mixed with each other, depressions in m. p. are given by comparable mixtures of any of the compounds described above.

Oxidation of Taraxasterol.—Chromic anhydride (30 mg.) in 90% acetic acid was added slowly at room temperature to a suspension of taraxasterol (150 mg.) in 90% acetic acid (20 c.c.). After standing overnight, the clear solution was diluted with water, and the precipitated *product* recrystallised from alcohol, from which it separated in needles, m. p. 175—176°, $[\alpha]_D^{18°}$ + 109·5° (l = 1, c = 1·31) (Found : C, 84·6; H, 11·0. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%).

Taraxasterol from Anthemis nobilis.—Dried camomile flowers (1 kg.) were extracted in two batches with boiling carbon tetrachloride. The fatty material (33 g.) obtained by evaporation of the solvent was heated under reflux with 10% alcoholic potassium hydroxide (500 c.c.), and the non-saponifiable material isolated by concentration of the solution, dilution with water, and extraction with ether. A dried solution of the latter fraction (13 g.) in petroleum (300 c.c., b. p. 80—100°) was drawn through a column of Merck's alumina (50 g. in a tube 1·5 cm. in diameter). The column was washed with a mixture of petroleum (50 c.c.) and chloroform (25 c.c.) and then eluted with petroleum–methanol. The material contained in the elutriate (4·5 g.) was acetylated, and the product crystallised till it had m. p. 239—241° (1·2 g.). Hydrolysis of this, followed by five crystallisations of the product from alcohol, gave 0·5 g. of taraxasterol, m. p. 220—221°. The acetate obtained from this sample had m. p. 250—252° and $[\alpha]_D^{20°}$ + 101·4° (l = 1, c = 1·86). The preparation of taraxasterol from this source is considerably easier than from *Taraxacum* root, and the yield of pure product is also higher.

A description of the isolation of stigmasterol and β-sitosterol from *Taraxacum* root is deferred until our examination of the non-triterpenoid fractions has been completed.

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