39. *The Triterpene Group. Part VIII. The Minor Triterpenoid Constituents of* Manila elemi *Resin (continued).*

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Previous work (Morice and Simpson, J., 1940, 795) pointed to the existence in *Manila elemi* resin of a precursor of ψ-taraxasterol. The precursor, *ψ-taraxastanediol*, has now been isolated. It is a saturated dihydric alcohol containing a tertiary hydroxyl group, and it is converted by means of hot formic acid into ψ-taraxasteryl formate, the reaction being one of dehydration. The biogenetic relationship thus disclosed is novel to the triterpene series.

Very small quantities of two further new alcohols have been isolated from the resin; these are a *diol*, m. p. 236°, and an *alcohol*, m. p. 254°, containing an uncharacterised oxygen atom, and their probable formulæ are $C_{30}H_{48}O_2$ and $C_{30}H_{54}O_2$ respectively.

In Part VII (Morice and Simpson, *loc. cit.*) we described the isolation of ψ-taraxasterol from *Manila elemi* resin. On the basis of the evidence then available, it seemed unlikely that this alcohol existed as such in the resin, particularly since the employment of formic acid, which is well known as an isomerising agent in the triterpene series (Beynon, Heilbron, and Spring, J., 1937, 989; Zimmermann, *Helv. Chim. Acta*, 1938, **21**, 853), appeared to be a *sine qua non* for the successful isolation of the compound; we accordingly postulated the existence in *Manila elemi* resin of an isomeric precursor of ψ-taraxasterol. We have now

achieved the isolation of this precursor under conditions which do not involve the use of formic acid, and have demonstrated its facile conversion into ψ-taraxasterol by subsequent treatment of it with this acid.

Contrary to expectation, however, ultimate analysis showed that the new compound has the molecular formula $C_{30}H_{52}O_2$; its conversion into ψ-taraxasterol is therefore not an isomerisation, but a dehydration. We have named the precursor *ψ-taraxastanediol* in order to indicate its relationship to ψ-taraxasterol and also to show that it has the character of a saturated dihydric alcohol. The saturated nature of the substance follows from the facts (*a*) that its acetate does not react with perbenzoic acid, in contrast to the conversion of ψ-taraxasteryl acetate into an *oxide* under similar conditions; and (*b*) that it is inert towards tetranitromethane and is also transparent to ultra-violet light. Both oxygen atoms in the molecule of ψ-taraxastanediol are present as hydroxyl groups (Zerewitinoff), but only one (*i.e.*, that contained in ψ-taraxasterol) is esterifiable under ordinary conditions; the other is therefore presumably tertiary, a supposition which explains both its inertness towards acetic anhydride (in pyridine) and also its ready elimination as water under the influence of hot formic acid.

ψ-Taraxastanediol and ψ-taraxasterol represent a new biogenetic relationship in the triterpene series, which is comparable with the classical α-terpineol–terpinolene relationship in the simple terpenes. The diol is isomeric with zeorin, which has been shown by Asahina and Akagi (*Ber.*, 1938, **71**, 980) to belong to the triterpene group. Like ψ-taraxastanediol, zeorin readily undergoes dehydration (the authors employed boiling acetic anhydride, but did not report on the behaviour of the diol towards formic acid), but the product, anhydrozeorin, is not known to occur in Nature.

It is somewhat remarkable that ψ-taraxastanediol is more strongly adsorbed on alumina (see Experimental) than the unsaturated diols breïn and maniladiol; it would appear that spatial factors may over-ride purely structural considerations in the formation of complexes between molecules of alumina and these substances.

In the course of the search for ψ-taraxastanediol, small amounts of two new, lævorotatory alcohols were isolated. The first of these, which we have provisionally named *diol A*, was obtained from the fractions immediately preceding those containing ψ-taraxastanediol. The presence of two esterifiable hydroxyl groups in diol A was shown by the preparation of the *diacetate*, and analyses of this ester and of the parent diol suggest the formula $C_{30}H_{48}O_2$ for the latter. The second compound, *alcohol B*, formed only a *monoacetate*; it appears from analysis to have the formula $C_{30}H_{54}O_2$, but behaves as an unsaturated compound despite its high hydrogen content. The small quantities of diol A and alcohol B which were available, however, precluded further investigation, and consequently their molecular formulæ cannot be deemed to be established with certainty.

Experimental.

(Melting points are uncorrected. Specific rotations are in chloroform solution. The ligroin used had b. p. 80—100° except where otherwise stated.)

The material employed in this investigation consisted mainly of the non-crystalline residue remaining after fraction X (Morice and Simpson, *loc. cit.*) had been acetylated and the crystalline product removed, together with smaller quantities of similar residues from fractions VI—IX. The solvent-free material (65 g.) was refluxed for 2 hours with alcoholic potassium hydroxide (2%, 975 c.c.), the free alcohols (54 g.) being isolated by precipitation with water and extraction with ether. After careful drying and removal of solvent, the residue was dissolved in benzene–ligroin (2700 c.c., 7 : 3) and filtered through a column (120 × 4 cm.) of alumina (1350 g. of Merck's, " standardisiert nach Brockmann "), which had been prepared from a suspension in benzene–ligroin (7 : 3). The column was then washed with successive portions of solvent mixtures of various compositions, following on general lines the procedure of Reichstein and von Euw (*Helv. Chim. Acta*, 1939, **22**, 1222). Fractions 1—7 (see Table) showed no tendency to crystallise, and were not examined further. Fractions 8—35 were separately acetylated by heating the material (1 part) on the water-bath with pyridine (2 parts) and acetic anhydride (1 part) for 2 hours. The acetates were obtained by precipitation with water, followed by extraction with ether or by filtration. Continued recrystallisation (from aqueous alcohol, alcohol, or benzene–alcohol) of the crude products led to the isolation of the following acetates,

listed in increasing order of adsorbability : β-Amyrin (0·25 g.), ψ-taraxasterol (0·43 g.), a mixture of breïn and maniladiol (6·4 g.), diol A (0·05 g.), ψ-taraxastanediol (1·0 g.), and alcohol B (0·1 g.). The conditions employed enabled a much more complete separation to be achieved than in our earlier work (*loc. cit.*), but formylation was still necessary to effect the resolution of the breïn–maniladiol mixture.

TABLE.

Fraction.	Washing solvent (in c.c.).	Weight (g.) of recovered material.	Description.	Alcohol (isolated as acetate).
1	Original filtrate	0·35	Resinous	—
2	Benzene–ligroin (7 : 3), 1080	0·54	,,	—
3	,, (8 : 2), 1080	0·38	,,	—
4	,, (9 : 1), 1080	0·15	,,	—
5	Benzene, 1080	0·56	,,	—
6	,, , 1080	0·82	,,	—
7	,, , 2160	2·11	,,	—
8	,, ,,	3·30	Crystalline	β-Amyrin
9	,, ,,	2·76	,,	ψ-Taraxasterol
10	,, ,,	2·11	Resinous	,,
11	,, ,,	2·52	Frothy	Breïn–maniladiol
12	,, ,,	2·73	,,	,,
13	,, ,,	2·41	,,	,,
14	,, ,,	2·14	,,	,,
15	,, ,,	1·70	,,	,,
16	,, ,,	1·65	,,	,,
17	,, ,,	1·24	Crystalline	,,
18	,, ,,	1·20	,,	,,
19	,, ,,	0·77	,,	,,
20	Ether–benzene (1 : 5·6), 2870	1·93	Gelatinous	Diol A
21	,, (1 : 4), 2160	2·16	,,	,,
22	,, ,, ,,	1·72	,,	,,
23	,, ,, ,,	1·42	,,	ψ-Taraxastanediol
24	,, ,, ,,	1·05	Crystalline	,,
25	,, (2 : 5), ,,	1·26	,,	,,
26	,, ,, ,,	1·96	,,	,,
27	,, ,, ,,	1·75	,,	,,
28	,, ,, ,,	1·24	Resinous	
29	,, ,, ,,	0·48	,,	—
30	,, (1 : 1), ,,	0·29	,,	—
31	,, ,, ,,	0·15	,,	—
32	Ether ,,	0·23	,,	—
33	,, ,,	0·22	,,	—
34	Ether–acetone (3 : 1), 2160	2·31	,,	Alcohol B
35	,, ,, ,,	2·19	,,	—

Monoacetate of ψ-Taraxastanediol.—This *compound* crystallised from benzene–alcohol in prismatic needles, m. p. 281—284° (with slight discoloration), $[\alpha]_D^{23°}$ −1·5° ($l = 1$, $c = 1·01$) (Found : C, 78·8; H, 11·3. $C_{32}H_{54}O_3$ requires C, 78·9; H, 11·2%). *Active hydrogen determination (Zerewitinoff) :* 4·022 Mg. gave 0·20 c.c. of methane at 21°/778 mm., corresponding to 1·03 active hydrogen atom.

Hydrolysis of this acetate with boiling 2% alcoholic potassium hydroxide gave *ψ-taraxastanediol*, which separated from benzene in small dense prisms, and from alcohol in soft matted needles; m. p. 270—272° (discoloration), $[\alpha]_D^{23°}$ −10·9° ($l = 1$, $c = 1·105$) (Found : C, 81·1; H, 11·9. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%). Owing to its ready dehydration, the alcohol gave a Liebermann–Burchard reaction (pink, changing to purplish-red with a green fluorescence) indistinguishable from that of ψ-taraxasterol. The tetranitromethane reaction in chloroform was negative.

Dehydration of ψ-Taraxastanediol.—(*a*) The monoacetate was refluxed for 2 hours with benzene (20 parts) and formic acid (20 parts). Water was then added, and the benzene layer, after addition of ether, followed by washing with 2% aqueous sodium carbonate and water, was dried and evaporated. The residue crystallised from alcohol in shining plates, m. p. 237—239°, $[\alpha]_D^{23°}$ +52° ($l = 1$, $c = 1·30$); no lowering of melting point was observed when this material was mixed with authentic ψ-taraxasteryl acetate of the same m. p. and $[\alpha]_D$ +53°.

(*b*) ψ-Taraxastanediol was refluxed for 2 hours with benzene (80 parts) and formic acid (80 parts). The resultant ψ-taraxasteryl formate, isolated as described above, separated in needles from benzene–alcohol; it had m. p. 219—220°, $[\alpha]_D^{23°}$ +48° ($l = 1$, $c = 1·89$), and did not depress the m. p. (219—221°) of an authentic specimen ($[\alpha]_D$ + 51°; Morice and Simpson, *loc. cit.*).

(*c*) The extreme ease with which ψ-taraxastanediol undergoes dehydration was illustrated by an attempt to benzoylate the diol. A solution of the compound (1 part) in pyridine (40 parts) and benzoyl chloride (10 parts) was heated at 100° for 2 hours; water was then added, and the product extracted with ether. The extract was washed successively with dilute acetic acid, dilute sodium hydroxide solution, and water. The residue obtained by evaporation of the dried solution had m. p. 259—263°, $[\alpha]_D^{19°}$ +57° ($l = 1$, $c = 1{\cdot}21$), and a mixture of it with authentic ψ-taraxasteryl benzoate (m. p. 280—282°, $[\alpha]_D$ +68°) melted at 266—275°.

Diacetate of Diol A.—Continued recrystallisation of the combined crystalline acetates from fractions 20—22 involved large losses of material without achieving the isolation of any single substance. The various fractions were therefore again combined (2·2 g.) and hydrolysed with boiling alcoholic potassium hydroxide (100 c.c. of 2%). The mixture of alcohols, isolated by means of ether, was dissolved in benzene (160 c.c.), and the solution was drawn through a column (55 × 1·4 cm.) of activated alumina (Merck, 80 g.). By fractional elution with 80 c.c. portions of benzene, benzene–ether, and acetone, the material was divided into 21 sub-fractions. These were acetylated, either separately or in pairs, but no apparent purification was accomplished in the majority of cases. However, sub-fractions 10, 11, and 12 yielded acetates, which were combined after one crystallisation (0·21 g.) and crystallised a further five times from aqueous alcohol and finally from ligroin (b. p. 40—60°). The *diacetate* of diol A was thus obtained as small prisms (50 mg.), m. p. (constant) 211—212°, $[\alpha]_D^{19°}$ + 35° ($l = 1$, $c = 1{\cdot}68$) (Found: C, 78·2; H, 10·35. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%).

Diol A.—The foregoing acetate (40 mg.) was refluxed for 2 hours with alcoholic potassium hydroxide (10 c.c. of 2%). The solution was then concentrated to half volume, diluted with water, and extracted with ether. Evaporation of the washed and dried extract furnished *diol A*, which after two crystallisations from ether–ligroin (b. p. 40—60°) formed clusters of needles, m. p. 234—236°, $[\alpha]_D^{22°}$ −70°±10° ($l = 1$, $c = 0{\cdot}145$) (Found: C, 82·15; H, 11·3. $C_{30}H_{48}O_2$ requires C, 81·75; H, 11·0%). The diol gave a yellow colour with tetranitromethane in chloroform, and the Liebermann–Burchard reagent produced an orange-red coloration, which changed to brownish-pink with a green fluorescence.

Monoacetate of Alcohol B.—Continued recrystallisation from alcohol of the crude acetate from fraction 34 finally yielded the *monoacetate* as rectangular prisms, m. p. 227—229°, $[\alpha]_D^{23°}$ −39° ($l = 1$, $c = 1{\cdot}38$) (Found: C, 78·45; H, 11·4. $C_{32}H_{56}O_3$ requires C, 78·6; H, 11·5%).

Alcohol B.—Hydrolysis of the monoacetate (60 mg.) with 2% alcoholic potash (10 c.c.), followed by precipitation with water and recrystallisation of the product from aqueous methanol, gave *alcohol B*, which separated in needles, m. p. 252—254°, $[\alpha]_D^{19°}$ −17° ($l = 1$, $c = 1{\cdot}10$) (Found: C, 80·1; H, 11·8. $C_{30}H_{54}O_2$ requires C, 80·65; H, 12·2%). Addition of tetranitromethane to a chloroform solution of the alcohol gave a very pale yellow solution, and the Liebermann–Burchard reagent produced a magenta coloration.

ψ-Taraxasteryl Acetate Oxide.—ψ-Taraxasteryl acetate was dissolved in a large excess of an approximately 0·3N-solution of perbenzoic acid in chloroform, and the solution was set aside (with accompanying blank experiment) for 10 days; titration then showed that 0·9 atom of active oxygen had been absorbed. The solution was washed with aqueous sodium carbonate and water, dried, and evaporated, and the residue crystallised from alcohol; *ψ-taraxasteryl acetate oxide* separated in lustrous plates, which melted at 265—267°, and then resolidified and again melted at 300° (Found: C, 79·3; H, 11·0. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

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