760. *The Chemistry of Triterpenes and Related Compounds. Part XL.* Final Clarification of the Stereochemistry of Hydroxyhopanone.*

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The only remaining stereochemical problem in the structure of hydroxyhopanone has now been resolved with the proof that the 21-hydroxyisopropyl side-chain of hydroxyhopanone has the α-configuration (cf. II).

Hydroxyhopanone has structure (I),[1] only the configuration at $C_{(21)}$ being in doubt. If it is biosynthesised from squalene by a completely concerted cyclisation then either the α- or the β-configuration [2] at $C_{(21)}$ may result depending on the conformation of the squalene molecule during cyclisation. Evidence has now been obtained in favour of the α-configuration, hydroxyhopanone being therefore (II).

Dehydration of hydroxyhopane (III) gave a mixture (hopene) of hopene-a (IV) and hopene-b (V).[3] Treatment of the mixture with osmium tetroxide led to the isolation of hopene-b glycol (VII). Cleavage of this glycol with lead tetra-acetate under the mild conditions devised [1] for the isolation of the unstable *trans*-trisnor-ketone (VIII) from hopene-a glycol (VI) gave a nor-ketone (IX), $[\alpha]_D$ +83°, which was isomerised by ethanolic sulphuric acid to the more stable nor-ketone (X), $[\alpha]_D$ −4°. Treatment of the less stable ketone with methylmagnesium iodide gave hydroxyhopane (III) whereas the isomerisation product gave an isomeric alcohol.

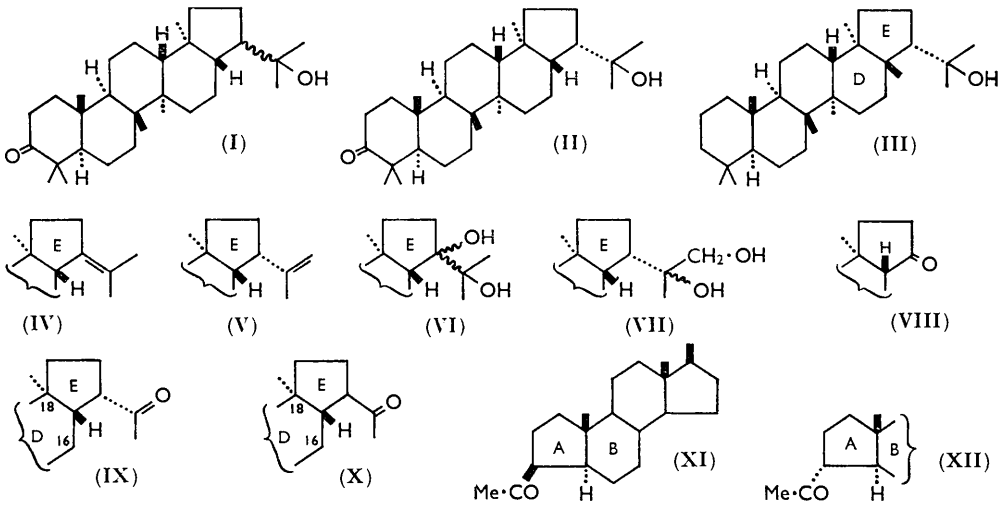
Of the two structures (IX) and (X), the latter must be the more stable as it lacks the 1,3-interactions of the 21α-side-chain with both the 18-methyl group and the 16-axial hydrogen atom of structure (IX). Formula (IX) must then represent the nor-ketone first formed from hopene-b glycol (VII), and hence hydroxyhopane (III) and hydroxyhopanone (II) must have the 21-side-chain in the α-configuration. The carbon skeleton of

* Part XXXIX, *J.*, 1961, 2725.

[1] Baddeley, Halsall, and Jones, *J.*, 1960, 1715.
[2] Cf. Schaffner, Caglioti, Arigoni, and Jeger, *Helv. Chim. Acta*, 1958, **41**, 152.
[3] Dunstan, Fazakerley, Halsall, and Jones, *Croat. Chim. Acta*, 1957, **29**, 173.

structure (II) can be biosynthesised by cyclisation of the all-chair conformation of squalene.

The isomerisation behaviour of the nor-ketone (IX) is closely paralleled by that of 3β-acetyl-A-norcholestane [4] (XI) which can be converted by acid or by base into the more



stable ketone (XII) in which the 1,3-steric interactions of the acetyl group no longer occur. The molecular-rotation differences between the two pairs of methyl ketones are very similar: $\Delta[M_D]$ [(IX)—(X)] −359°; $\Delta[M_{6000Å}]$ [(XI)—(XII)] −361°. The $\Delta[M]$ values refer to slightly different wavelengths, but it is uncommon for molecular rotations to vary appreciably between the sodium-D line (5890 Å) and 6000 Å. Both the less stable ketones have lower carbonyl stretching frequencies than the corresponding isomers: (IX) 1700, (X) 1710, (XI) 1710, and (XII) 1720 cm.$^{-1}$.

Experimental

M. p.s were determined on a Kofler block and are corrected. Rotations were determined for chloroform solutions, unless otherwise stated, at room temperature. The alumina used for chromatography was Peter Spence's grade " H " which had been deactivated with 5% of 10% aqueous acetic acid.

Hydroxylation of Hopene-ab.—Hopene-ab [3] (3·81 g.) in pyridine (40 c.c.) and ether (400 c.c.) was heated under reflux with osmium tetroxide (2·90 g., 1·2 mol.) for 3 days. The solvents were then removed and the residual osmate ester was cleaved by heating it in benzene (80 c.c.), ethanol (170 c.c.), and water (100 c.c.) with potassium hydroxide (20 g.) and mannitol (25 g.) until, after 3 hr., the upper layer became colourless. Dilution with water followed by extraction with ether afforded a product (4·15 g.), which gave only a slight colour with tetranitromethane. It was adsorbed from benzene on alumina (200 g.). Elution with benzene gave gums (950 mg.) giving a positive reaction with tetranitromethane. Elution with benzene–ether (9 : 1) yielded hopene-a glycol [17(22 ⟶ 21)abeogammacerane-21ξ,22-diol] (2·51 g.) as plates (from acetone–methanol), m. p. 272—281°, $[\alpha]_D$ +30° (*c* 0·87) (lit.,[3] m. p. 260—265°, $[\alpha]_D$ +31°). Elution with benzene–ether (1 : 1) gave *hopene-b glycol* [(21βH)-17(22 ⟶ 21)*abeogammacerane-22ξ,29-diol*] (VII) (430 mg.) as platelets (from methanol–acetone), m. p. 239—245°, $[\alpha]_D$ +32° (*c* in pyridine, 0·81) (Found: C, 80·8; H, 11·75. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%), $\nu_{max.}$ (Nujol mull) 3350, 1040 cm.$^{-1}$.

Cleavage of Hopene-b Glycol (VII).—Lead tetra-acetate (600 mg., 1·5 mol.) was added with stirring to a fine suspension of hopene-b glycol (400 mg.) in benzene (200 c.c.) at 10°. The mixture was stirred for 18 hr. at 20°, then the benzene solution was filtered, washed with water, and dried. On evaporation it gave a product which was filtered in benzene through alumina (18 g.), to give a *norhopanone* [30-*nor*-(21βH)-17(22 ⟶ 21)*abeogammaceran-22-one*]

[4] Biellmann and Ourisson, *Bull. Soc. chim. France*, 1960, 348.

(IX) (300 mg.) as prisms (from acetone), m. p. 218°, $[\alpha]_D$ +83° (*c*, 1·43) (Found: C, 84·4; H, 11·75. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%), $\nu_{max.}$ (in CS_2) 1700 cm.$^{-1}$.

Reaction of Methylmagnesium Iodide with the Norhopanone (IX).—The ketone (103 mg.) in benzene (4 c.c.) and ether (15 c.c.) was added to the Grignard reagent derived from magnesium (200 mg.) and methyl iodide (0·8 c.c.) in ether (6 c.c.). The mixture was heated under reflux for 18 hr., then the excess of Grignard reagent was destroyed by methanol. Acidification followed by extraction with ether gave a product (110 mg.) which afforded hydroxyhopane [3] (III) as platelets (from acetone–methanol), m. p. and mixed m. p. 254—256°, $[\alpha]_D$ +44° (*c* 1·21).

Acid-catalysed Isomerisation of the Norhopanone (IX).—The ketone (260 mg.) was heated under reflux for 4 hr. in ethanol (12 c.c.) containing 2N-sulphuric acid (0·2 c.c.). When kept at 20° for 15 hr. the solution deposited plates which were washed with methanol and recrystallised from ethanol to give 30-*nor*-(21αH)-17(22 ⟶ 21)*abeogammaceran*-22-*one* (X) (162 mg.) as plates, m. p. 230—231·5°, $[\alpha]_D$ −40° (*c* 0·92) (Found: C, 84·1; H, 11·8. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%), $\nu_{max.}$ (in CS_2) 1710 cm.$^{-1}$.

Reaction of Methylmagnesium Iodide with the Norketone (X).—The ketone (160 mg.) was treated with the Grignard reagent from methyl iodide [as for the norhopanone (IX)]. The product (165 mg.) obtained by acidification and extraction with ether gave an isomer of hydroxyhopane [(21αH)-17(22 ⟶ 21)*abeogammaceran*-22-*ol*] as needles (from acetone–methanol), m. p. 225—227°, $[\alpha]_D$ +19° (*c* 1·63) (Found: C, 82·35; H, 12·0. $C_{30}H_{52}O,\frac{1}{2}CH_3{\cdot}OH$ requires C, 82·35; H, 12·25%), $\nu_{max.}$ (in CCl_4) 3550 cm.$^{-1}$. The mixed m. p. on admixture with hydroxyhopane, m. p. 255—256°, showed a marked depression, 218—240°.

Acetylation of (21αH)-17(22 ⟶ 21)*Abeogammaceran*-22-*ol*.—The alcohol (92 mg.) in chloroform (7 c.c.) was heated under reflux for 20 hr. with dimethylaniline (4 c.c.) and acetyl chloride (3 c.c.). The product was isolated through ether to give 22-*acetoxy*-21αH-17(22 ⟶ 21)*abeogammacerane* (100 mg.) as needles (from ethyl acetate–methanol), m. p. 202—205°, $[\alpha]_D$ +30° (*c* 1·81) (Found: C, 82·0; H, 11·45. $C_{32}H_{54}O_2$ requires C, 81·65; H, 11·55%), $\nu_{max.}$ (in CS_2) 1730, 1250, 1130, 1014 cm.$^{-1}$.

Acetylation of Hydroxyhopane.—Hydroxyhopane (147 mg.) was acetylated (as above) to give *acetoxyhopane* (150 mg.) as prisms (from ethyl acetate–methanol), m. p. 183—184°, $[\alpha]_D$ +35° (*c* 0·68) (Found: C, 82·0; H, 11·6. $C_{32}H_{54}O_2$ requires C, 81·65; H, 11·6%), $\nu_{max.}$ (in CS_2) 1730, 1253, 1225 cm.$^{-1}$.

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