230. *Studies in the Sterol Group. Part XV. The Relationship between α- and β-Ergostenol and their Derived Hydrocarbons.*

By Alexander Lang Morrison and James Charles Edward Simpson.

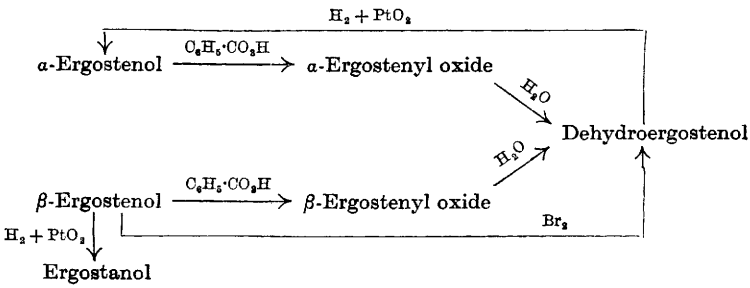
The action of various oxidising agents upon β-ergostenol (Heilbron and Wilkinson, preceding paper) has been studied with the object of determining the position of the double bond in this compound. Although nitric acid, chromic anhydride, and potassium permanganate have so far failed to give serviceable products, we have found that treatment of β-ergostenol with excess of perbenzoic acid gives a practically quantitative yield of a well-defined *oxide*, m. p. 152—153°, which with dilute alcoholic sulphuric acid easily passes into an unsaturated monohydric *alcohol*, $C_{27}H_{44}O$, m. p. 141—142°, giving an *acetate*, m. p. 138°. The physical constants of this alcohol and the fact that on catalytic hydrogenation it readily yields α-ergostenol, pointed to its identity with the dehydroergostenol obtained by Windaus and Lüttringhaus by the action of perbenzoic acid upon α-ergostenol (*Annalen*, 1930, **481**, 119). In order to confirm this we have ourselves treated α-ergostenol with perbenzoic acid and have isolated the hitherto unknown *α-ergostenyl oxide*, m. p. 114—116°. Hydration of this substance, followed by acetylation of the crude product, yielded dehydroergostenyl acetate, which did not depress the melting point of the corresponding compound obtained from β-ergostenol.

A precisely similar relationship exists between the corresponding hydrocarbons α-ergostene and β-ergostene (this vol., p. 1708). These react with perbenzoic acid, forming α- and β-*ergostene oxides*, m. p. 118—119° and 122—123° respectively, both of which with alcoholic sulphuric acid provide *dehydroergostene*, m. p. 71—72°, which on hydrogenation gives α-ergostene, m. p. 77—78°.

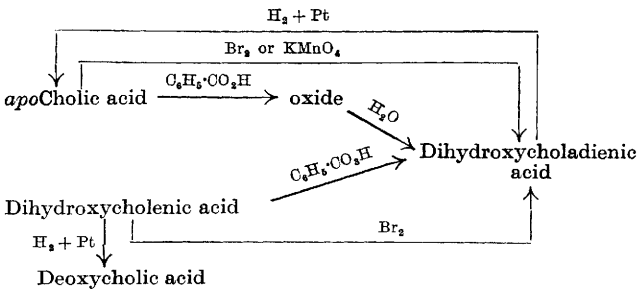
Windaus and Lüttringhaus (*loc. cit.*) observed further that dehydrogenation took place during the attempted bromination of α-ergostenol, but were unable to isolate a pure product. This we have confirmed, but have found, on the other hand, that β-ergostenol when treated with one molecule of bromine in strongly cooled chloroform solution is almost quantitatively transformed into dehydroergostenol. Attempts to prepare dehydroergostenol by the action of mercuric acetate on β-ergostenol were unsuccessful, unchanged material alone being recovered. In no case have we ever obtained dehydroergostenol or its acetate having the melting points 144—145° (acetate, m. p. 145—146°) ascribed to them by Hart and Heyl (*J. Amer. Chem. Soc.*, 1931, **53**, 1413).

The series of changes outlined above bear a marked resemblance to those reported by Borsche and Todd (*Z. physiol. Chem.*, 1931,

Ergosterol Series.



Bile Acid Series.



197, 173) and by Wieland and Deulofeu (*ibid.*, 1931, **198**, 127) in connexion with the isomeric bile acids *apo*cholic acid and dihydroxycholenic acid, both of which on treatment with perbenzoic acid and with bromine undergo dehydrogenation to give dihydroxycholadienic acid. Further points of resemblance between cholic acid and the ergosterol groups are found in the facts (*a*) that dihydroxycholadienic acid gives rise to *apo*cholic acid, which, like α-ergostenol, is completely resistant to further hydrogenation, and (*b*) that dihydroxycholenic acid can be hydrogenated to the saturated deoxycholic acid (Boedecker and Volk, *Ber.*, 1922, **55**, 2302) analogous to the formation of ergostanol from β-ergostenol. The preceding schemes illustrate the striking similarity between the two groups.

Although the results so far obtained do not enable us to assign definite structural formulæ to either α- or β-ergostenol, the analogy between these compounds and *apo*cholic and dihydroxycholenic acids renders it probable that the same molecular configurations appertain in both cases in so far as the condensed ring systems are concerned.

Experimental.

β-Ergostenyl Oxide.—β-Ergostenol (2 g.) was treated with a solution of perbenzoic acid in chloroform (0·2 g. of active oxygen) and left for 16 hours at 0°. The solution was washed with sodium carbonate solution and dried over sodium sulphate. The residue obtained after removal of solvent was crystallised from methyl alcohol, from which *β-ergostenyl oxide* separated in plates, m. p. 152—153°, sparingly soluble in cold methyl alcohol, moderately easily soluble in acetone, and very soluble in chloroform and ether. Since the oxide contained water of crystallisation, it was prepared for analysis by drying in a vacuum at 115° for 5 hours (Found : C, 80·5, 80·4; H, 11·4, 11·6. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·4%).

Dehydroergostenol from β-Ergostenyl Oxide.—A solution of β-ergostenyl oxide (0·5 g.) in hot alcohol (50 c.c.) was treated with dilute sulphuric acid until a precipitate just appeared and was then heated for 15 minutes on the steam-bath. On cooling, dehydroergostenol separated in irregular plates which, after three recrystallisations from alcohol, had a constant m. p. 141—142° and $[\alpha]_D^{25°}$ — 16·4° ($c = 1{\cdot}16$ in chloroform). With antimony trichloride it gave a yellow colour which gradually changed to pink. An acetone solution of the compound did not decolorise potassium permanganate in the cold and only slowly when heated.

Dehydroergostenol and β-ergostenyl oxide both yielded α-ergostenol when hydrogenated in acetic acid solution in the presence of platinum oxide.

*Dehydroergostenyl Acetate.**—A solution of dehydroergostenol (0·2 g.) in acetic anhydride (2 c.c.) was heated under reflux for 30 minutes. On cooling, the acetate crystallised in plates and after recrystallisation from alcohol had m. p. 137—138°, which was not raised by further crystallisation (Found: C, 81·9, 81·7; H, 11·3, 11·2. Calc. for $C_{29}H_{46}O_2$: C, 81·7; H, 10·8%).

α-Ergostenyl Oxide.—α-Ergostenol (2 g.) was treated with a solution of perbenzoic acid in chloroform under the same conditions as in the case of β-ergostenol, and gave a product which, recrystallised from methyl alcohol, formed fine needles, m. p. 114—116° (clear at 122°). *α-Ergostenyl oxide* is very soluble in hot methyl alcohol, but sparingly soluble in the cold solvent (Found for vacuum-dried product: C, 80·4, 80·8; H, 11·6, 11·7. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·4%).

Dehydroergostenol from α-Ergostenyl Oxide.—α-Ergostenyl oxide was treated as described for β-ergostenyl oxide. The product crystallised from alcohol in plates, m. p. 114—120°, and was unchanged by further recrystallisation. The compound was therefore acetylated in the usual manner, and the acetate after two crystallisations from alcohol melted at 134—136°, the value given by Windaus and Lüttringhaus (*loc. cit.*). A mixture of the compound with the dehydroergostenyl acetate, m. p. 137—138°, obtained from β-ergostenyl oxide melted at 134—137°. On hydrolysis with alcoholic caustic potash the acetate yielded dehydroergostenol, m. p. 140—141°.

Hydrogenation of β-Ergostene to Ergostane.—A solution of β-ergostene (2 g., m. p. 85—86°) in ethyl acetate–glacial acetic acid (150 c.c.) was shaken for 14 hours with hydrogen at room temperature together with Adams's platinum oxide (about 0·2 g.), and, after filtering, was concentrated under reduced pressure to small volume and mixed with ether. The ethereal solution was washed free from acetic acid with sodium carbonate, dried, and evaporated. The crystalline residue was dissolved in chloroform (2 c.c.) and treated with acetic anhydride (2 c.c.) and concentrated sulphuric acid (0·5 c.c.) in order to remove traces of unchanged β-ergostene. After ¼ hour, more chloroform was added and the solution was repeatedly washed with water, dried, and evaporated. The residue after recrystallising once from acetone gave pure ergostane (1·5 g.), m. p. 82—83°, $[\alpha]_D^{23°}$ + 21° (c = 1·6 in chloroform) (Found: C, 86·8; H, 13·1. Calc. for $C_{27}H_{48}$: C, 87·1; H, 12·9%).

β-Ergostene Oxide.—β-Ergostene was treated with perbenzoic acid

* Work on this compound carried out after this paper was submitted for publication shows that it contains a conjugated system of double bonds as manifested by its combination with maleic anhydride in xylene at 135° to give a *product*, m. p. 164—166° (Found: C, 75·3; H, 8·8. $C_{33}H_{48}O_5$ requires C, 75·6; H, 9·2%).

as previously described. The crude product was crystallised from acetone, from which β-*ergostene oxide* separated in small soft plates (yield, 80%), m. p. 122—123°, moderately easily soluble in alcohol and acetone and easily in chloroform (Found: C, 84·0; H, 12·4. $C_{27}H_{46}O$ requires C, 83·9; H, 11·9%).

Dehydroergostene from β-Ergostene Oxide.—A solution of β-ergostene oxide (1 g.) in hot alcohol (50 c.c.) was treated with 5 c.c. of alcohol containing a few drops of concentrated sulphuric acid. The mixture was boiled for 15 minutes and the *dehydroergostene* was then precipitated with water and extracted with ether. The residue obtained after removal of solvent was repeatedly crystallised from ether–methyl alcohol, from which dehydroergostene separated in plates, m. p. 71—72°, $[\alpha]_D^{23°}$ — 15° (c = 1·29 in chloroform), insoluble in methyl alcohol but readily soluble in acetone and ether (Found: C, 87·7; H, 12·2. $C_{27}H_{44}$ requires C, 88·0; H, 12·0%). With antimony trichloride a pink coloration was obtained on standing. Hydrogenation with a platinum oxide catalyst gave α-ergostene, m. p. 77—78°.

α-*Ergostene Oxide.*—α-Ergostene (2 g.) reacted with perbenzoic acid as described under β-ergostenol. The product on crystallisation from ether–methyl alcohol and then from chloroform–methyl alcohol yielded pure α-*ergostene oxide* in irregular plates, m. p. 118—119° (Found: C, 83·9; H, 12·1. $C_{27}H_{46}O$ requires C, 83·9; H, 11·9%). A mixture with β-ergostene oxide (m. p. 122—123°) melted at 95—100°. The compound is very sparingly soluble in alcohol, but readily soluble in acetone, ether, and chloroform. On hydration it yielded dehydroergostene, m. p. 71—72°, which gave no depression in m. p. on admixture with the product obtained from β-ergostene oxide.

Action of Bromine on β-Ergostenol.—A solution of β-ergostenol (1 g.) in chloroform (10 c.c.), cooled to — 20°, was treated with a solution of bromine (0·42 g.) in chloroform (10 c.c.), added drop by drop and with continual shaking during 10 minutes. Towards the end of the addition the chloroform solution turned green. The solution was washed with water and dried, and the solvent removed. When the residue was crystallised from alcohol, dehydroergostenol, m. p. 139—141°, separated.

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