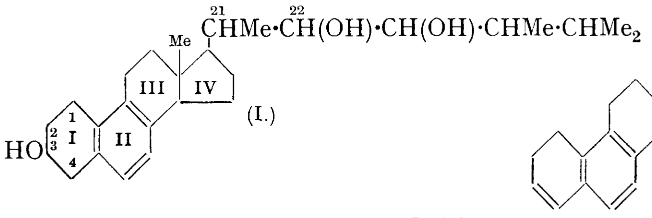
101. *Hydrocarbons from Neoergosterol.*

By G. A. D. Haslewood and (Miss) E. Roe.

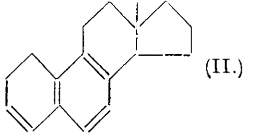
The only crystalline product obtained in a long series of experiments aiming at the degradation of neoergosterol to a compound offering a reasonable hope of synthetic preparation was *neoergostatriol* (I). This was obtained in poor yield by oxidation of neoergosterol with perbenzoic acid, followed by hydrolysis of the crude resinous oxide.

Neoergostatetraene (II) was prepared by dehydration of the 22-dihydroneoergosterol of Windaus and Langer (*Annalen*, 1934, **508**, 105). Attempts to dehydrogenate (II) to the corresponding naphthalene derivative by a variety of methods gave indications that the required compound was probably formed, but it could not be isolated in the crystalline state.

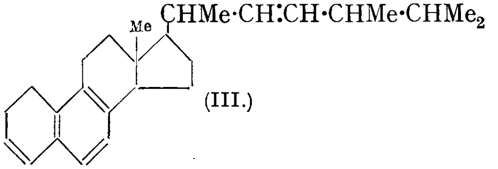
Comparison of the absorption spectrum of the new neoergostatetraene and of neoergostapentaene (III) (Cook and Haslewood, *Chem. and Ind.*, 1934, **53**, 507) with that of the previously known neoergostatriene (IV) (Bonstedt, *Z. physiol. Chem.*, 1929, **185**, 165) has given strong evidence of the conjugation in (II) and (III) of the double bond in ring I with those comprising the neoergosterol benzene nucleus.



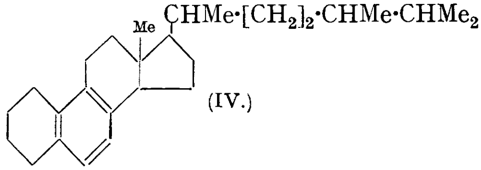
(I.)



(II.)



(III.)

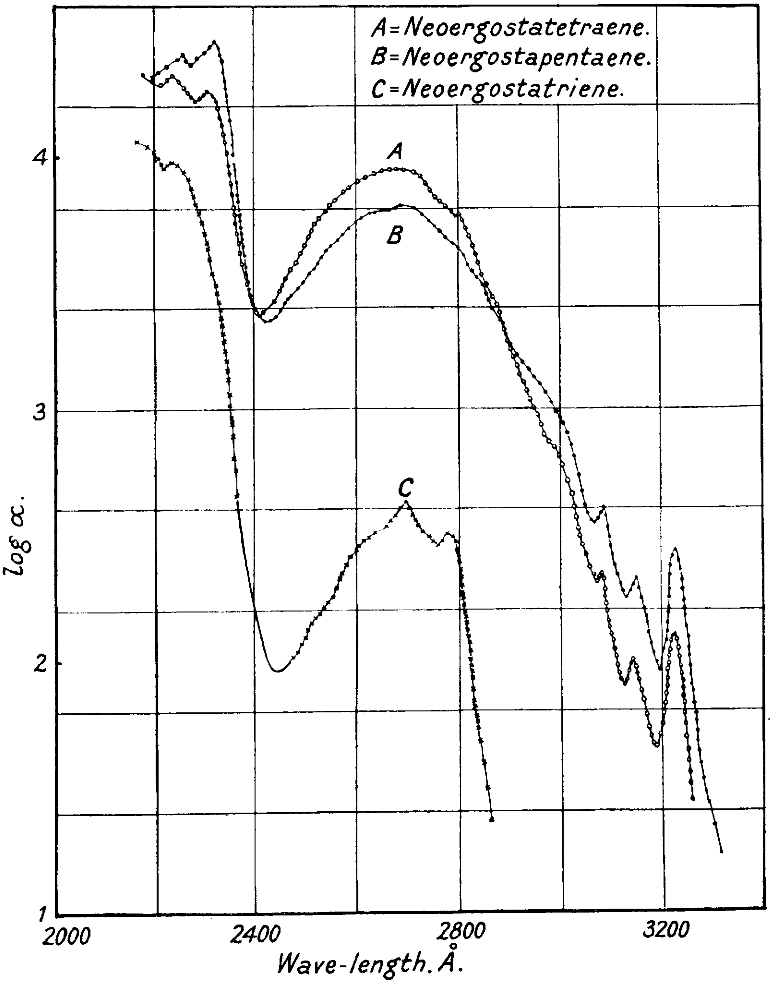


(IV.)

It is well known that when a chromophoric group, such as C:O or C:C, is directly linked to a benzene nucleus, the absorption spectrum differs considerably from that given by a compound in which such a group is separated from the nucleus (see, for example, Arnold and Kistiakovsky, *J. Amer. Chem. Soc.*, 1932, **54**, 1713; Ramart-Lucas, *Bull. Soc. chim.*, 1932, **51**, 289). The curves of the tetraene and the pentaene closely resemble each other, but differ widely from that of the triene. Hence it may be concluded that the double bond in the side chain of the pentaene has little influence on the absorption, and that the new double bonds arising in the preparation of both the tetraene and the pentaene are conjugated with the benzene nucleus. Differences of the same order are shown in the absorption spectra of styrene, allylbenzene, and δ-phenyl-Δ^{α}-butene (Ramart-Lucas, *loc. cit.*). The spectroscopic technique used in our experiments was that described in a previous paper (J., 1934, 1727).

In view of the recent proof of the position of the hydroxyl group (at C_3) in ergosterol (Fernholz and Chakrovorty, *Ber.*, 1934, **67**, 2021), the spectroscopic evidence clearly shows that the tetraene and the pentaene are correctly represented by formulæ (II) and (III), from which it follows that the aromatic ring of neoergosterol must be ring II, a result in harmony with the conclusions of Honigmann (*Annalen*, 1934, **511**, 292) and of Dunn, Heilbron, Phipers, Samant, and Spring (J., 1934, 1576) with regard to the location in ring II of the nuclear double bonds of ergosterol.

The mode of dehydration of neoergosterol and dihydroneoergosterol is analogous to that of β-tetralol, which gives Δ^1-dihydronaphthalene (Strauss and Lemmel, *Ber.*, 1921, **54**, 25). The tetraene (II) and the pentaene (III) are resistant to reduction by sodium and alcohol, in which respect they differ from Δ^1-dihydronaphthalene (compare Strauss and Lemmel, *Ber.*, 1913, **46**, 232).



EXPERIMENTAL.

All analyses are microanalyses by Dr. A. Schoeller.

Dihydroneoergosterol was prepared by hydrogenation of (*a*) neoergosterol in moist ether or (*b*) neoergosteryl acetate in acetone (Windaus and Langer, *loc. cit.*), with palladium-black, during 5—7 hours at atmospheric temperature and pressure. Hydrogenation for a much longer period resulted, in both methods, in complete conversion into neoergostatriene (IV), m. p. 67—69°.

Dihydroneoergosterol, m. p. 141—143° (*lit.* 150°), showed no depression in m. p. with neoergosterol, and its 3 : 5-dinitrobenzoate (m. p. 216—218°) did not depress the m. p. (217—219°) of neoergosteryl 3 : 5-dinitrobenzoate. The dihydro-compound was readily distinguished from neoergosterol by its extremely slow absorption of bromine (in chloroform solution), and by its saturation towards perbenzoic acid, which showed a value for one double bond with neoergosterol.

Dehydration of Dihydroneoergosterol.—(a) *With phosphoric oxide.* Dihydroneoergosterol (0·1 g.) in benzene (0·5 c.c.) was refluxed for $\frac{1}{2}$ hour with phosphoric oxide (0·1 g.). The *product*, obtained by dilution with water, and benzene extraction, was crystallised from alcohol–benzene, sublimed at 260°/0·1—0·05 mm., and recrystallised from alcohol–benzene. It formed white crystals, m. p. 187—190° (Found: C, 88·4; H, 10·9; *M*, Rast method, 626, 550. $C_{54}H_{80}$ requires C, 89·0; H, 11·0%; *M*, 729). Hence the substance is probably a dimeride.

(b) *With potassium hydrogen sulphate.* Dihydroneoergosterol (0·6 g.) was heated with freshly fused, finely powdered potassium hydrogen sulphate (1·2 g.) at 145—155° for 1 hour in a slow current of dry carbon dioxide. The product, obtained by ether extraction from the diluted mixture, was re-extracted with warm alcohol (to remove polymeric products which made distillation very difficult) and the residue obtained on evaporating the filtered alcoholic extract was distilled at 200—205°/0·1 mm. *Neoergostatetraene* (II) (0·2 g.), so obtained, formed white plates from alcohol, and had m. p. 63—64°, depressed by neoergostatriene but not by neoergostapentaene (Found: C, 88·6; H, 11·4. $C_{27}H_{40}$ requires C, 89·0; H, 11·0%). Iodine value, Rosenmund–Kuhnhenn method, 57; calc. for 1 double bond, 70.

Dehydrogenation of this product was attempted (i) by treatment with aluminium chloride in ice-cold carbon disulphide; (ii) by attempted removal of hydrogen bromide from the unstable crystalline bromide (formed by bromination in chloroform solution) by (*a*) heating at 200° in a vacuum, (*b*) heating in quinoline solution at 200°, (*c*) refluxing in pyridine solution for 12 hours, (*d*) heating with acetone and sodium iodide in a sealed tube at 120—125° for 16 hours; (iii) by treatment with selenium in a sealed tube at 240—250° for 5 hours; (iv) by boiling with lead peroxide in xylene suspension for 7 hours; (v) by heating with a 10% solution of sulphuric acid in acetic acid at 100° for 2 hours; (vi) by heating with platinum-black in a current of carbon dioxide at 290—295° for 40 minutes. All the products were distilled at 0·1 mm. None formed a stable picrate in alcoholic solution. In experiments (i), (iii), and (vi) a mobile oil was obtained. In the case of (vi), an unstable *s*.-trinitrobenzene complex was formed in alcoholic solution, but decomposition of this complex, followed by redistillation, gave a still uncrystallisable product. Experiment (ii) in every case gave crystalline products which still contained appreciable amounts of bromine and were unsaturated. Experiments (iv) and (v) gave the unchanged tetraene.

The tetraene (50 mg.) was unaffected by boiling with amyl alcohol (4 c.c.) and sodium (0·3 g.) during 1 hour.

Neoergostatriol (I).—Neoergosterol (0·5 g.), dissolved in chloroform (5 c.c.), was treated in the cold with perbenzoic acid (18 c.c. of a solution containing 3·6 g. of "active oxygen" per litre). The mixture was kept in the cold for 70 hours with addition of anhydrous sodium sulphate. The product, obtained by dilution and ether extraction, followed by removal of benzoic acid with sodium carbonate, was a yellow gum, which did not crystallise after being in contact with light petroleum for several months. It was treated with glacial acetic acid (25 c.c.) and sulphuric acid (1 drop) at 60—75° during 1 hour. The product was hydrolysed with alcoholic potassium hydroxide (10 c.c. of 10% solution); the dark gum obtained, after removal of acids, crystallised from benzene (charcoal) in white plates of *neoergostatriol* (I), m. p. 202—204°. Yield, about 30 mg. (Found: C, 78·45; H, 10·1. $C_{27}H_{42}O_3$ requires C, 78·2; H, 10·2%).

We are indebted to the International Cancer Research Foundation for grants to each of us. We also thank Prof. J. W. Cook, who suggested this investigation.

THE CANCER HOSPITAL (FREE), LONDON, S.W. 3.

[*Received, January* 31*st*, 1935.]