332. *Hydrogenation under the Action of Selenium. Part I. The Action of Selenium on Cholesterol at 230°.*

By CHARLES DORÉE and VLADIMIR A. PETROW.

WE have recently shown (J., 1934, 1129) that cholesterilene, when heated with selenium at 230°, gives the saturated hydrocarbon cholestane. At this relatively low temperature dehydrogenation to aromatic ring systems does not take place and the main effect is a transfer of hydrogen to the unsaturated linkage. Ruzicka and Peyer (*Helv. Chim. Acta*, 1935, **18**, 676; compare *ibid.*, 1934, **17**, 442) have found that indene derivatives also, in the presence of selenium at about 350°, pass smoothly into almost homogeneous hydrindene derivatives, and Yokoyama and Kotake (*Bull. Chem. Soc. Japan*, 1935, **10**, 138) mention that when oleic acid is heated with selenium at 300° partial reduction occurs, so even at these high temperatures where dehydrogenation is normal, specific types of hydrogenation may take place.

We have now investigated the action of selenium at 230° on cholesterol, the chief product being the saturated ketone cholestanone (I) in a yield of 30—40%. By diminishing the time of heating to 10 hours, cholestanone was obtained together with smaller quantities of cholestanol and cholestenone.

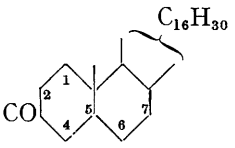
The production of ketonic derivatives from cholesterol under various conditions of heating has frequently been observed. For instance, cholesterol, when heated alone at 310°, yields β-cholesterol and cholestenone, hydrogen being evolved (Diels and Linn, *Ber.*, 1908, **41**, 260). Heilbron and Sexton (J., 1928, 347), by dry distillation of cholesterol at atmospheric pressure, obtained coprostene and coprostenone, and Windaus (*Annalen*, 1927, **453**, 101), by heating cholesterol with nickel at 180° in the absence of hydrogen, obtained the saturated ketones cholestanone and coprostanone, *allo*cholesterol (coprostenol) probably being formed as an intermediate product. The action of selenium at moderate temperatures of heating is of the same type. The hydrogen required for the reaction is probably formed by the breakdown of a portion of the cholesterol, the selenium facilitating its transfer to the unsaturated linkage. The cholestanol thus formed is then dehydrogenated to cholestanone.

Derivatives of the coprostane series have not been isolated by the action of selenium. Cholesterol gave cholestanone and no coprostanone; cholesterilene yielded only cholestane. Windaus and Seng (*Z. physiol. Chem.*, 1921, **117**, 158) have shown that by hydrogenation of cholesterilene with palladium and hydrogen both cholestane and coprostane are produced. We have noticed that *cis*-unsaturated acids such as oleic acid are readily converted into the *trans*-isomerides by heating for a few hours with selenium at 230°. By analogy, selenium may favour the production of cholestane (*trans*-form) in preference to coprostane (*cis*-form).

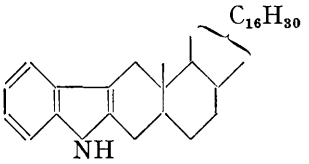
Cholestanone was characterised by the formation of a semicarbazone, m. p. 234—238°, and a tetrahydrocarbazole *derivative*, m.p. 180—181°, which gave a picrate, m. p. 209—210° (derivatives not previously described). It was originally observed that coprostanone (Dorée and Gardner, J., 1908, **93**, 1625), when heated with phenylhydrazine in glacial acetic acid solution, passed at once into the tetrahydrocarbazole derivative without formation of the hydrazone (Dorée, J., 1909, **95**, 653). The formation or non-formation of an angular tetrahydrocarbazole derivative (*e.g.*, III) in this simple way may afford useful evidence as to the relative positions of the unsaturated linking and the ketonic group in the sterol ketones. If the former is in the αβ-position as in cholestenone, the reaction does not take place. With coprostanone, cholestanone, and, as we have recently found, with lanostenone the reaction goes smoothly, thus showing that position C_4 is occupied by a methylene group. The reaction is being further examined from this point of view.

The tetrahydrocarbazole derivative of cholestanone may have structure (II) or (III); the angular formula (III) is the more probable on the grounds of chemical analogy, compounds of type (II) being very difficult to prepare (Borsche, Witte, and Bothe, *Annalen*, 1908, **359**, 64; Japp and Maitland, J., 1903, **83**, 267). Further evidence has been obtained by surface-film measurements kindly made for us by Mr. J. A. Askew. The "surface

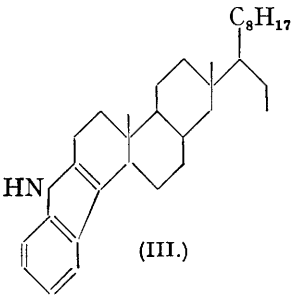
area " of the tetrahydrocarbazole derivative was found to be 43 sq. Å.; structure (II) would require 50 sq. Å. and structure (III) 45 sq. Å., values which tend to support the



(I.)



(II.)



(III.)

angular structure (III). 1 : 2-Naphthacarbazole (Japp and Maitland, *loc. cit.*) and 2 : 3-naphthacarbazole (Graebe and Knecht, *Annalen*, 1880, **202**, 1) were prepared for comparison of their surface film areas, but did not form films on water, acids, or alkalis.

The results of experiments on the action of selenium at 230° on coprostanol, coprostene, and lanosterol will shortly be reported.

Experimental.

Cholesterol and selenium, intimately mixed by grinding, were heated in a Pyrex flask placed in a metal bath; the temperatures recorded are those of the bath.

(A) *Heating for* 10 *Hours.*—The product obtained from 25 g. of cholesterol and 50 g. of selenium deposited, from acetone solution (40 ml.) at 0°, a brown microcrystalline powder. After 2 hours the solution was filtered (filtrate A); the solid obtained, on repeated crystallisation from ether–alcohol, gave about 5 g. of white plates, m. p. 119° (acetate, m. p. 97°). 1 G. of this product in 10 ml. of dry ether at 0° was treated with a 10% solution of bromine in slight excess. The cholesterol dibromide obtained was washed with glacial acetic acid and recrystallised from ether–acetic acid; m. p. 113° (Found : Br, 28·3. Calc. for $C_{27}H_{46}OBr_2$: Br, 29·3%). The yield of cholesteryl dibromide being 0·7—0·8 g., the product of m. p. 119° contained about 80% of cholesterol. The filtrate from the dibromide was poured into water; the solid obtained, crystallised from methyl alcohol, yielded about 0·15 g. of white plates, m. p. 140—141° alone or mixed with authentic cholestanol (m. p. 142°). The acetate prepared from it had m. p. 109°, alone or mixed with authentic cholestanyl acetate.

The acetone was removed from filtrate A and the oily residue (17—18 g.) was dissolved in 700 ml. of alcohol and treated with an aqueous-alcoholic solution of 6·6 g. of semicarbazide hydrochloride and 5 g. of sodium acetate; a gelatinous semicarbazone was collected after 12 hours (evaporation of the filtrate gave 6 g. of crystals, m. p. 119°) and was obtained from alcohol as a pale yellow powder (8 g.), m. p. 234—238°. It was heated with 30% sulphuric acid for an hour in a water-bath. The regenerated ketone, on crystallisation from acetone and then from alcohol, gave cholestanone, m. p. 127—128° (Found : C, 83·4; H, 12·2. Calc. for $C_{27}H_{46}O$: C, 83·9; H, 12·0%), identified by mixed m. p. and by conversion into the tetrahydrocarbazole derivative.

The alcoholic mother-liquor deposited a brown oil and a small quantity of needle-shaped crystals. These were removed by hand and after recrystallisation from alcohol had m. p. 80°. There was insufficient material for complete purification, but from the m. p. and ketonic character these crystals were probably cholestenone.

(B) *Heating for* 25 *Hours at* 220—250°.—The product obtained from 30 g. of cholesterol and 60 g. of selenium gave no deposit from acetone at 0°. Treatment with semicarbazide hydrochloride gave 16 g. of cholestanone semicarbazone, representing a yield of about 40% of cholestanone. No other single compound could be isolated.

(C) *Heating for* 40 *Hours at* 220—250°.—30 G. of cholesterol gave 6 g. of cholestanone. No other product could be obtained.

Tetrahydrocarbazole Derivative from Cholestanone.—1 G. of cholestanone in 30 ml. of glacial acetic acid was heated with 2 g. of phenylhydrazine in 10 ml. of glacial acetic acid for 20 minutes on a water-bath; on cooling, the *tetrahydrocarbazole* crystallised. It was obtained from benzene–alcohol as white plates, m. p. 180—181° (Found : N, 3·2. $C_{33}H_{49}N$ requires N, 3·05%),

extremely soluble in benzene and ethyl acetate and sparingly soluble in ethyl alcohol, methyl alcohol and glacial acetic acid. Yield, 60—70%. The picrate was obtained from benzene–alcohol as bronze-brown needles, m. p. 209—210°, extremely soluble in benzene and sparingly soluble in alcohol.

CHELSEA POLYTECHNIC, LONDON, S.W. 3. [*Received July 31st*, 1935.]