THE FORMATION OF CHOLESTANEDIONE-(3,6) FROM CHOLESTENONE DIBROMIDE AND FROM Δ^4- AND Δ^5-CHOLESTENONES.

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Received June 2nd, 1936. Published June 28th, 1936.

On April 3rd of this year, on the occasion of the 58th annual meeting of the Chemical Society of Japan at Sendai, one of the authors (Ando) read a paper entitled "some compounds obtained from cholesterol dibromide" before Section II, and reported that cholestenone dibromide isolated in crystalline state from the oxidation product of cholesterol dibromide, on heating in absolute alcohol, was transformed into cholestanedione-(3,6) first prepared by A. Windaus⁽¹⁾. Then no mention was made of the mechanism of this transformation, because there was no experimental evidence to prove the intermediate course from cholestenone dibromide to cholestanedione. Nevertheless the fact that bromine was set free in the first stage of the reaction and the final product was a saturated 3,6-diketone made it very probable that Δ^5-cholestenone was the first intermediate of the transformation, although Δ^5-cholestenone was then unknown. On the appearance of the work by A. Butenandt and J. Schmidt-Thomé⁽²⁾ furnishing a method of preparing Δ^5-cholestenone by the debromination of cholestenone dibromide with zinc and alcohol, the present authors heated Δ^5-cholestenone with an equivalent quantity of bromine in absolute alcohol, when the same cholestanedione was obtained. But the matter proved not to be so simple as expected, because the same diketone was also obtained in a good yield by a similar treatment of Δ^4-cholestenone. None of these specimens of the diketone has yet been compared with cholestanedione produced by the methods of A. Windaus, but the specimen obtained directly from cholestenone dibromide was identified with cholestanedione-(3,6) by the melting point, elementary analysis, preparation of dioxime and dibromo-substitution product, and the colour reaction of the latter.

On heating cholesterol dibromide in absolute alcohol cholesterol was regenerated in a good yield.

The authors are much interested in the recent work by H. H. Inhoffen⁽³⁾ dealing with a similar treatment of 4-bromocholestenone dibromide.

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(1) *Ber.*, **36** (1903), 3755; **39** (1906), 2253.

(2) *Ber.*, **69** (1936), 832.

(3) *Ber.*, **69** (1936), 1134.

Experimental.

Cholestenone Dibromide, $C_{27}H_{44}OBr_2$. The benzene solution of cholestenone dibromide obtained by the oxidation of cholesterol dibromide, $C_{27}H_{46}OBr_2$, according to the directions of L. Ruzicka, H. Brüngger, E. Eichenberger, and J. Meyer(4) was evaporated by blowing with an electric fan. The residue, on rubbing with a small amount of absolute alcohol, yielded colourless fine needles, which were washed with cold absolute alcohol (decomposition point 67–70°). Recrystallized carefully from acetone or aqueous acetone, the substance was obtained in fine long plates, decomposition point 65–66° (Found: Br, 29.70. Calculated for $C_{27}H_{44}OBr_2$: Br, 29.40%). Cholestenone dibromide thus isolated in crystalline state is very unstable, and becomes gradually orange-red and then greyish yellow at ordinary temperature. The decomposition is naturally quicker at higher temperature or under diminished pressure. It is transformed into Δ^4-cholestenone (m. p. 79–80°, decomposition point of semicarbazone 232°, corr.) by debromination with sodium iodide in alcohol(5). Inhoffen(3) gives decomposition point 68–69° for cholestenone dibromide, and the properties described by him coincide with those observed by the present authors.

Cholestanedione-(3,6), $C_{27}H_{44}O_2$, from Cholestenone Dibromide. When crude cholestenone dibromide was warmed with alcohol, the resulting solution became reddish brown. Alcohol was evaporated off under diminished pressure, and the remaining dark brown mass was recrystallized repeatedly from acetone or aqueous acetone, when colourless prisms melting at 172–174° (corr.) were obtained. No bromine was detected in this substance and no change was observed on boiling it with acetic anhydride. It was identified with cholestanedione-(3,6) by the examination of its properties, results of analysis (Found: C, 81.0, 80.7, 80.5; H, 10.9, 11.3, 11.2. Calculated for $C_{27}H_{44}O_2$: C, 80.91; H, 11.08%), and preparation of its derivatives. Windaus gives melting point 170–171°.

Pure cholestenone dibromide gave the same compound on heating with absolute alcohol.

Cholestanedione-(3,6)-dioxime. Prepared according to Windaus(6). Colourless silky crystals, decomposition point 205–207° (uncorr.) or 209–211° (corr.) (Found: C, 75.34; H, 10.73; N, 6.95. Calculated for $C_{27}H_{44}(NOH)_2$: C, 75.26; H, 10.77; N, 6.51%).

Dibromocholestanedione-(3,6). Prepared according to Windaus(7). Colourless small prisms, decomposition point 169–170° (uncorr.) or 172–173° (corr.) with evolution of gas (Found: C, 57.92; H, 7.82; Br, 29.70. Calculated for $C_{27}H_{42}O_2Br_2$: C, 58.03; H, 7.58; Br, 28.63%). The substance gave the characteristic colour reaction of dibromocholestanedione:(8) An alcoholic solution of a minute quantity of this substance gave deep red colouration on adding one drop of aqueous potassium hydroxide, turning colourless on acidifying.

Cholestanedione-(3,6) from Δ^5-Cholestenone. Crude Δ^5-cholestenone prepared by the method of A. Butenandt and J. Schmidt-Thomé(2) from pure cholestenone dibromide was boiled with an equivalent amount of bromine in absolute alcohol. The dark brown

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(4) *Helv. Chim. Acta*, **17** (1934), 1413.

(5) R. Schoenheimer, *J. Biol. Chem.*, **110** (1935), 461.

(6) *Ber.*, **36** (1903), 3756. Windaus gives decomposition point about 205°.

(7) *Ber.*, **37** (1904) 2031. Windaus gives decomposition point about 165° with evolution of gas.

(8) *Ber.*, **37** (1904), 2032.

resinous matter remaining after the evaporation of alcohol was dissolved in warm acetone and the solution was cooled to crystallization. By repeated recrystallization from aqueous acetone cholestanedione was obtained in colourless fine needles, m.p. 170–172° (corr.) alone or in admixture with the specimen obtained directly from cholestenone dibromide.

Cholestanedione-(3,6) from Δ^4-Cholestenone. Δ^4-Cholestenone (m.p. 79–80°) prepared by the method of R. Schoenheimer(5) was treated similarly with bromine and alcohol. In this case the product seemed to be a mixture. By repeated recrystallization cholestanedione-(3,6) was separated in colourless fine needles, m.p. 171–172.5° (corr.), no depression of the melting point (171–173°, corr.) when mixed with the specimen obtained from cholestenone dibromide.

Debromination of Cholesterol Dibromide with Alcohol. Cholesterol dibromide was boiled with absolute alcohol. The dark brown resinous matter obtained on distilling off alcohol was dissolved in warm acetone, and the solution was cooled to crystallization. Repeated recrystallization from aqueous acetone and acetone (with use of charcoal) yielded cholesterol in colourless small prisms, m.p. 149° (corr.). A mixture with an authentic specimen of cholesterol (m.p. 148–149°, corr.) melted at the same point 148–149° (corr.).

In conclusion the authors express their hearty thanks to Mr. Yasohachi Yamaguchi of Teikokusha Co. for his generous support of this work.

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Added in Proof (June 18th): The three specimens of cholestanedione-(3,6) melted at 172–3° (corr.), at 171–3° (corr.), and at 172–3° (corr.), respectively in order of the above description, in admixture with the cholestanedione, m.p. 173–4° (corr.), prepared by the reduction of Δ^4-cholestenedione-(3,6), m.p. 123.5–124° (corr.), according to the directions of A. Windaus, *Ber.*, **39** (1906), 2249.