The Configurations of Δ^5-Cholestenone Oxides.[1]

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L. Ruzicka and W. Bosshard[2] were unable to prepare an oxide of Δ^5-cholestenone by oxidation of α-cholesterol oxide with chromic acid, but obtained two stereoisomeric oxides from the action of perbenzoic acid on Δ^5-cholestenone (I). In analogy with cholesterol oxides, they called the compound with higher melting point (m. p. 202°) "α-oxide" and the isomeride with lower melting point (m. p. 122°) "β-oxide". The 5,6-position of the oxido group was demonstrated by transforming the "β-oxide" into the known cholestanedione-(3,6). For the "α-oxide" such an evidence was lacking but the 4,5-position of the oxido group which might result from displacement of the double bond was considered improbable from the fact that Δ^4-cholestenone did not give an oxide with perbenzoic acid.

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(1) Abstract from the doctor theses by M. Chuman. Read before the monthly meeting of the Chemical Society of Japan on March 8, 1947.

(2) *Helv. Chim. Acta*, **20** (1937), 244.

The configurations of cholesterol oxides had already been deduced by one of the present authors,⁽³⁾ while those of Δ^5-cholestenone oxides remained undetermined. The authors attempted to correlate Δ^5-cholestenone oxides with cholesterol oxides, but, in spite of every effort, the aimed transformation of the former into the latter, or *vice versa*, was not attained. The undesired changes experienced during the unsuccessful attempts will not be recorded in this paper.

In the previous paper⁽⁴⁾ one of the authors presented a stereochemical representation of the structures of cholesterol oxides and the courses of the scission reactions of the oxido ring in them. As the structures of Δ^5-cholestenone oxides can be represented quite similarly, it may reasonably be assumed that the rules for the oxido ring rupture of cholesterol oxides hold good as well in the case of Δ^5-cholestenone oxides. Namely, the α-oxido ring is opened between carbon atom 6 and the oxido oxygen atom, while the β-oxido ring between carbon atom 5 and the oxido oxygen atom; the oxygen atom with the hydrogen atom derived from the addenda forms a hydroxyl group with the original configuration; and the residues from the addenda enter the carbon atom cut off from the oxido oxygen atom, all attached to carbon atom 5 taking the α-configuration, thus the β-oxido ring as well as the α-oxido ring producing cholestane derivatives on scission, and certain groups including the hydroxyl group from water and the acetoxy group from acetic acid being determined to assume the β-configuration at carbon atom 6. Now, hydrogen chloride has afforded the key to the determination of the configurations of Δ^5-cholestenone oxides. The configurations of the scission products described below have been inferred from the above-mentioned rules, and the accompanying formulas assume that the chlorine atom entering carbon atom 6 takes the β-configuration like the hydroxyl and the acetoxy groups.

The "β-oxide" of Δ^5-cholestenone gave a scission reaction analogous to that of α-cholesterol oxide: The action of hydrogen chloride on α-cholesterol oxide (V) gave 6-chloro-cholestanediol-(3β,5α) (VI), m.p. 168–169°, which was then oxidized to 5-hydroxy-6-chloro-cholestanone-(3) (III), m. p. 200°, and dehydration of the latter with hydrogen chloride yielded 6-chloro-Δ^4-cholestenone-(3) (IV), m. p. 125–126°. The same 6-chloro-Δ^4-cholestenone-(3) was obtained by the action of hydrogen chloride on the "β-oxide" of Δ^5-cholestenone. In the latter case the intermediate 5-hydroxy-6-chloro-cholestanone-(3) lost water at once in conformity with its structure of a 3-ketone with a tertiary hydroxyl group at carbon atom 5.

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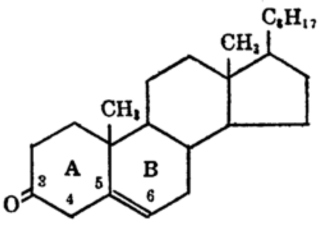
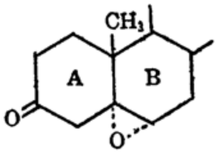
(3) Y. Urushibara, This Bulletin, **16** (1941), 182.

(4) Y. Urushibara, This Bulletin, **22** (1949), 132.

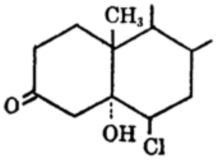


(I) Δ^5-Cholestenone



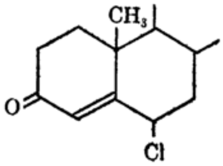
(II) "β-Oxide" of Δ^5-cholestenone

$\swarrow$



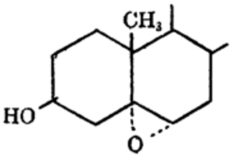
(III) 5-Hydroxy-6-chloro-cholestanone-(3)

$\longrightarrow$



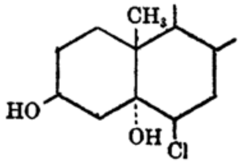
(IV) 6-Chloro-Δ^4-cholestenone-(3)

$\nwarrow$

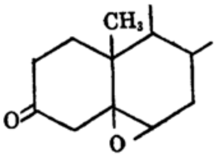


(V) α-Cholesterol oxide.

$\longrightarrow$

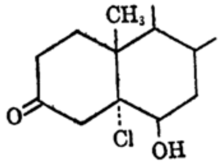


(VI) 6-Chloro-cholestane-diol-(3β,5α)

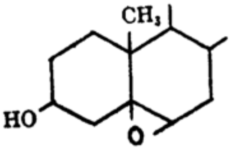


(VII) "α-Oxide" of Δ^5-cholestenone

$\underset{\text{KOH}}{\overset{\text{HCl}}{\rightleftarrows}}$

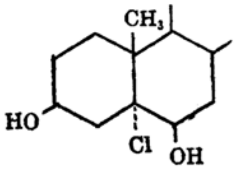


(VIII) 5-Chloro-6β-hydroxy-cholestanone-(3)



(IX) β-Cholesterol oxide

$\underset{\text{KOH}}{\overset{\text{HCl}}{\rightleftarrows}}$



(X) 5-Chloro-cholestane-diol-(3β,6β)

The "α-oxide" of Δ^5-cholestenone behaves like β-cholesterol oxide: The former gave a product on the action of hydrogen chloride. It differed from 5-hydroxy-6-chloro-cholestanone-(3) (III), m. p. 200°, and melted at 125–126°, but a deep depression of the melting point was observed in admixture with 6-chloro-Δ^4-cholestenone-(3) (IV) with the same melting point. Treatment with alcoholic potash or with many other reagents not enumerated here regenerated the "α-oxide" of Δ^5-cholestenone, while neither 5-hydroxy-6-chloro-cholestanone-(3) (III) nor 6-chloro-Δ^4-cholestenone-(3) (IV) gave either oxide of Δ^5-cholestenone on the action of alcoholic potash or on any other treatment. Hence, the product from the action of hydrogen chloride on the "α-oxide" of Δ^5-cholestenone is 5-chloro-6β-hydroxy-cholestanone-(3) (VIII), and its formation from the "α-oxide" by the action of hydrogen chloride and the regeneration of the oxide from it by the action of alcoholic potash correspond to the behaviour of β-cholesterol oxide (IX) which gives 5-chloro-cholestanediol-($3\beta,6\beta$) (X) with hydrogen chloride and is regenerated from the latter by the action of alcoholic potash.

The observations outlined in the preceding paragraphs lead to an assignment of a β-oxido (VII) and an α-oxido (II) structures, respectively, to the "α-oxide" and the "β-oxide" of Δ^5-cholestenone. As both cholesterol oxides are derivatives of cholestanol,(4) both Δ^5-cholestenone oxides are derivatives of cholestanone, and consequently the names expressing the stereochemical structures should be 5,6β-epoxy-cholestanone-(3) for the "α-oxide" and 5,6α-epoxy-cholestanone-(3) for the "β-oxide".

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