

Some Cholesterol Derivatives.

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3-Phenyl-cholestadiene and 3- α -Naphthyl-cholestadiene. The reaction mixture of cholestenone (I) (1 mol) and phenyl magnesium bromide (3 mols) as Grignard's reagent was treated with dilute sulphuric acid. The product was freed from diphenyl and unchanged bromobenzene by steam distillation, and recrystallized from a mixture of acetone and methyl alcohol, colourless plates, m.p. 174-5° (corr.), $[\alpha]_D^{29} = -133^\circ$ (12.0 mg. in 1 c.c. CHCl_3 solution, $l = 1$ dm., $\alpha_D^{29} = -1.60^\circ$), absorption maxima in hexane, 235, 285 $m\mu$. The substance was found to be a 3-phenyl-cholestadiene (III, $R = \text{C}_6\text{H}_5$) (Found: C, 89.60, 89.32; H, 11.76, 12.12; molecular weight by Rast's method, 449. Calculated for $\text{C}_{33}\text{H}_{48}$: C, 89.12; H, 10.88%; molecular weight, 445).⁽¹⁾

Similarly, from cholestenone and α -naphthyl magnesium bromide a 3- α -naphthyl-cholestadiene (III, $R = \alpha\text{-C}_{10}\text{H}_7$) was obtained in colourless prisms, m.p. 131-3° (corr.), $[\alpha]_D^{29} = -49.7^\circ$ (14.3 mg. in 1 c.c. CHCl_3 solution, $l = 1$ dm., $\alpha_D^{29} = -0.71^\circ$), absorption maximum in hexane, 283 $m\mu$ (Found: C, 90.57, 90.95; H, 10.51, 10.51; molecular weight by Rast's method, 501. Calculated for $\text{C}_{37}\text{H}_{50}$: C, 89.80; H, 10.20%; molecular weight, 495).⁽¹⁾

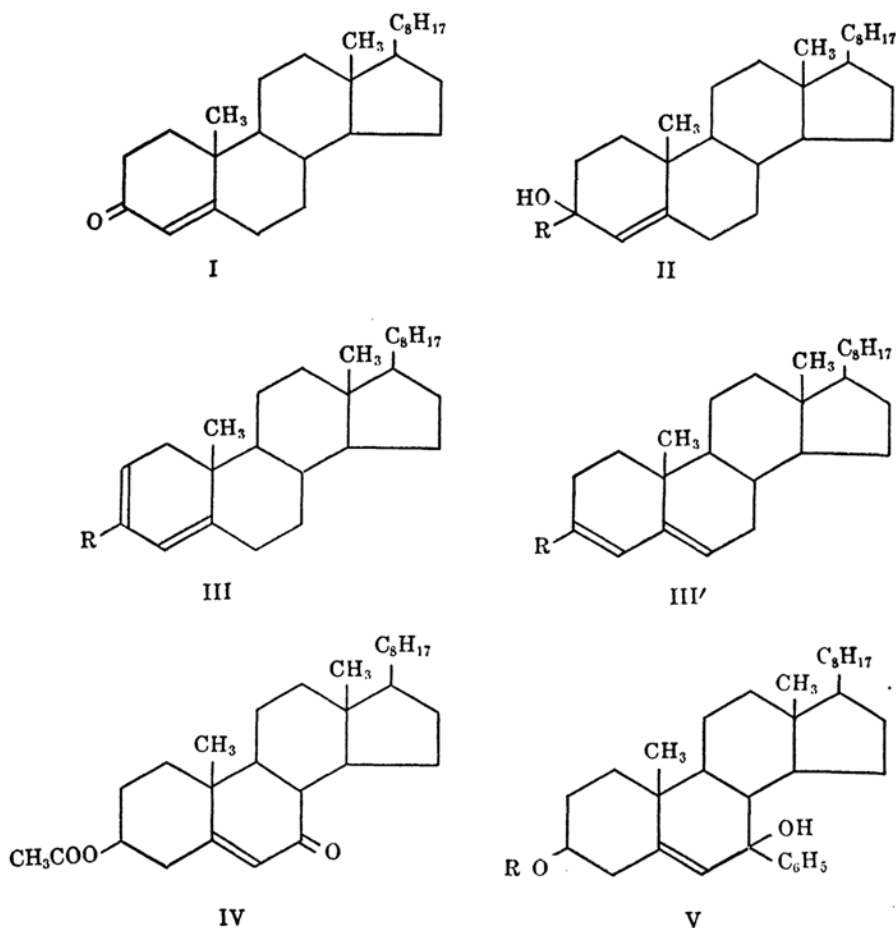
These cholestadiene derivatives distil unchanged in high vacuum. In Rosenheim test the phenyl compound gives a violetish blue colouration, while the α -naphthyl compound a greenish blue colouration. No exact evidence is yet available for the positions (as accepted in formula III) of the two double bonds in the cholestadiene part of these compounds, and the alternative formula III' can not totally be excluded.

On evaporating a benzene solution (orange red) containing equi-molecular amounts of the α -naphthyl-cholestadiene and picric acid a picrate melting at 161-3° (corr.) was obtained in orange red crystals. The fusion curve of the two compounds also shows the existence of a molecular compound (1:1), giving a maximum (161°) at the molecular ratio 1:1⁽²⁾.

Tertiary alcohols as represented by formula II are considered to be the primary products of the Grignard reactions described above. But they

(1) Owing to the sultry weather of the rainy season when the experiments were carried out, the data of micro-analyses are not quite satisfactory.

(2) The fusion curve was obtained by Dr. C. Shinomiya, to whom the authors' thanks are due.



could not be isolated and dehydration took place readily under the conditions of the experiments, giving rise to the cholestadiene derivatives (III). Such easy dehydration of tertiary alcohols is sometimes the case in Grignard reactions. To give an example in the sterol series, 7-methylene-cholesterol is formed in the reaction of methyl magnesium iodide with 7-keto-cholesteryl acetate⁽³⁾⁽⁴⁾. The ready formation of the cholestadiene derivatives (III) may be quite natural in view of the fact that the tertiary alcohols (II) are 3-aryl derivatives of either allocholesterol or *epi*-allocholesterol, because both

(3) B. Bann, I. M. Heilbron, and F. S. Spring, *J. Chem. Soc.*, **1936**, 1274.

(4) S. Weinhouse and M. S. Kharasch, *J. Org. Chem.*, **1** (1936-7), 490.

allocholesterol and *epi*-allocholesterol lose easily water⁽⁵⁾, and the tertiary nature of the hydroxyl group would facilitate dehydration.

7-Hydroxy-7-phenyl-cholesterol and Its Benzoate. Action of phenyl magnesium bromide (4 mols) on 7-keto-cholesteryl acetate (IV) (1 mol), followed by decomposition by aqueous ammonium chloride and recrystallization from benzene, yielded 7-hydroxy-7-phenyl-cholesterol (V, R = H) in colourless needles, m.p. 150.5–151.5° (corr.), $[\alpha]_D^{25} = -137^\circ$ (18.1 mg. in 1 c.c. CHCl₃ solution, $l = 1$ dm., $\alpha_D^{25} = -2.48^\circ$). Its monobenzoate (V, R = C₆H₅CO), prepared by the action of benzoyl chloride and pyridine, was recrystallized from acetone in colourless needles, m.p. 205.5–206° (corr.), $[\alpha]_D^{25} = -79.1^\circ$ (21.5 mg. in 1 c.c. CHCl₃ solution, $l = 1$ dm., $\alpha_D^{25} = -1.70^\circ$) (Found: C, 82.31; H, 10.12. Calculated for C₄₀H₅₄O₃: C, 82.41; H, 9.35%).

When the benzoate was heated in high vacuum (0.0005 mm.), a small amount of benzoic acid sublimed (about 200°), but the most part (90%) of the material distilled unchanged (up to 280°). On heating the benzoate under a higher pressure (200–250°, 0.18 mm.), a greater amount of benzoic acid sublimed, but from the residue the unchanged material only was isolated. Thus it seems that 7-hydroxy-7-phenyl-cholesteryl benzoate loses practically neither water nor benzoic acid on heating in vacuum. S. Weinhouse and M.S. Kharasch⁽⁴⁾ also have described 7-hydroxy-7-phenyl-cholesterol, which they could not dehydrate. Informations so far obtained show that elimination of water from the tertiary hydroxyl group at carbon atom 7 in cholesterol derivatives is either effected with the formation of an exocyclic double linkage or not effected at all⁽³⁾⁽⁴⁾⁽⁶⁾. 7-Hydroxy-7-phenyl-cholesterol can not afford the formation of an exocyclic double linkage, and must necessarily resist dehydration.

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(5) R. Schoenheimer and E. A. Evans, Jr., *J. Biol. Chem.*, **114** (1936), 567.

(6) E. R. H. Jones and F. S. Spring, *J. Chem. Soc.*, **1937**, 302.