Deacetylation of the above Carbitol Glucoside Acetate.—A portion of the oil obtained above was deacetylated with a trace of sodium methoxide, yielding an uncrystallizable oil. Upon distillation in a molecular still at 180° and 0.004 mm. pressure a slight decrease in vacuum (to 0.01 mm.) was observed. The substance distilled, however, to give a glassy film similar to the one obtained above which reverted to an oil on warming to room temperature.

We are indebted to Dr. H. A. Campbell, Research Assistant in Biochemistry, for the micro carbon and hydrogen determinations. Our thanks are also due to Dr. P. N. Leech, Director of the Chemical Laboratory of the American Medical Association, Chicago, Illinois, and Dr. E. W. Schoeffel, chemist for the A. M. A. Chemical Laboratory, for the chemicals used in this study. Dr. Schoeffel also has checked some of the C–H determinations.

Summary

1. The properties of the monoglucosides, the monoglucoside tetraacetates, the diglucosides and the diglucoside octaacetates of ethylene and trimethylene glycol were checked with those appearing in the literature. Improvements in the methods of preparation of these glucosides are described.
2. The *β-d*-monoglucosides and the *β-d*-monoglucoside tetraacetates of diethylene glycol, propylene glycol and ethylene glycol monoethyl ether, and the *β*-diglucoside octaacetate of diethylene glycol have been prepared and the constants reported.
3. Triethylene glycol *β-d*-monoglucoside tetraacetate, the *β*-monoglucoside tetraacetate of diethylene glycol monoethyl ether and the free glucoside from the latter have been obtained as sirups.
4. A procedure is described for the large-scale preparation of diethylene glycol *β-d*-monoglucoside tetraacetate and diethylene glycol *β-d*-monoglucoside.

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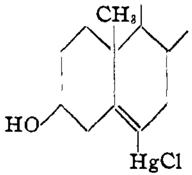
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Mercuration of Cholesterol

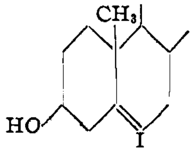
BY R. H. LEVIN AND M. A. SPIELMAN

Merz[1] mercurated cholesterol with mercuric acetate in hot glacial acetic acid, and after treating the product with sodium chloride he was able to isolate in poor yield a chloromercuricholesterol of unknown constitution. The chloromercuri derivative reacted smoothly with iodine to give an iodocholesterol which, because of the inertness of the halogen atom, resisted all efforts at structure proof. This paper presents a reinvestigation of the problem.

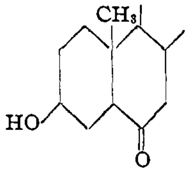
We have prepared chloromercuricholesterol and iodocholesterol with minor modifications of the Merz method. In agreement with him we have found iodocholesterol to be an exceedingly inert compound. Hydrolysis was, however, achieved with the aid of copper catalysis in a steel bomb at 225°. The product was a saturated hydroxy ketone identified as 6-ketocholestanol (III) by comparison with a synthetic specimen made by the usual methods.[2] It follows, therefore, that the compounds in question are 6-chloromercuricholesterol (I) and 6-iodocholesterol (II). The dibasic acid $C_{27}H_{43}O_4I$ from the sodium hypobromite oxidation of 6-iodocholesterol is without doubt 6-iodo-Diels' acid (IV).



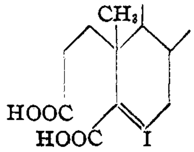
I



II



III



IV

No other products of mercuration could be isolated from the sirupy mercury-containing residues after isolation of the 6-chloromercuricholesterol. The large amounts of mercurous acetate formed indicate dehydrogenation, but no

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[1] Merz, *Z. physiol. Chem.*, **154**, 225 (1926). Compare also Montignie, *Bull. soc. chim.*, [4] **43**, 1403 (1928); [5] **2**, 1367 (1935).

[2] Mauthner and Suida, *Monatsh.*, **24**, 652 (1903); Heilbron Jackson, Jones and Spring, *J. Chem. Soc.*, 102 (1938).

ketones were present and spectroscopic examination revealed no absorption in the region characteristic of 7-dehydrocholesterol.[3]

Experimental Part[4]

6-Chloromercuricholesterol.—The method of Merz was used with essentially the same results. A product melting at 185–205° and giving no antimony trichloride color reaction was found satisfactory for the subsequent experiment. The yield was 27% of theoretical, or corrected for recovered cholesterol, 35%. The numerous crystallizations from acetone necessary to produce a white preparation melting at 200–205° reduced the yield to 17–20% of theoretical. The mother liquors were freed of mercury by hydrolysis with hydrochloric acid. The thick brown residue gave a purple color with antimony trichloride in chloroform. No pure product could be isolated from it other than cholesterol.

6-Iodocholesterol.—The Merz method was modified as follows. Twenty-five grams of crude chloromercuricholesterol was dissolved in 300 cc. of chloroform; the solution was filtered and 10 g. of iodine was added in portions with shaking. The mixture was allowed to stand six hours and was then filtered to remove the vermilion precipitate of mercuric iodochloride. Excess iodine was eliminated by adding 30 cc. of water and bubbling in sulfur dioxide for fifteen minutes. The solution was again filtered, 50 cc. of water was added and the chloroform was removed by distillation. The water was decanted and the residue was taken up in 500 cc. of hot absolute alcohol. The mixture was treated twice with norite and allowed to cool; 9.5 g. of 6-iodocholesterol separated, and concentration of the mother liquor yielded 4.5 g. more. Crystallization from glacial acetic acid gave colorless needles melting at 156–158°; yield 50%. When pure chloromercuricholesterol was used the yield was 75% of the theoretical.

Anal. Calcd. for $C_{27}H_{45}OI$: C, 63.2; H, 8.85. Found: C, 63.4; H, 9.06.

6-Iodocholesterol benzoate is a new compound prepared by benzoylation in pyridine at room temperature for thirty minutes. Crystallization from chloroform–ether, and from dioxane, gave colorless prisms; m. p. 214–215°.

Anal. Calcd. for $C_{34}H_{49}O_2I$: C, 66.2; H, 8.02. Found: C, 66.2; H, 8.30.

6-Ketocholestanol Benzoate.—Ten grams of 6-iodocholesterol was placed in a small steel bomb (80 cc. void) together with 6 g. of sodium bicarbonate, 20 cc. of water and 50 mg. of cupric chloride. The mixture was heated to 225° for nine hours with continuous shaking. The water was decanted after cooling and the residue was taken up in chloroform. The residue after evaporation of the chloroform was benzoylated in pyridine at room temperature with 4 cc. of benzoyl chloride. The product was crystallized from methanol–chloroform and from ethanol–ether. It melted at 171–172° in agreement with the figure given by Windaus[5]; yield 89%; $[\alpha]^{20}$D +4.0 in chloroform.

Anal. Calcd. for $C_{34}H_{50}O_3$: C, 80.6; H, 10.0. Found: C, 80.9; H, 10.1.

6-Ketocholestanol was obtained by saponification of the benzoate. It formed needles, m. p. and mixed m. p. 143–144°.[5]

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.6; H, 11.8.

The 6-ketocholestanol was also characterized as the acetate, m. p. and mixed m. p. 129–130°; the formate, m. p. 104–105°; and the *p*-nitrophenylhydrazone, m. p. 194°. Melting points all agreed with literature values.[5]

6-Ketocholestanol 3,5-dinitrobenzoate is a new derivative made by benzoylation in cold pyridine during twenty-four hours. Repeated crystallizations from chloroform–methanol yielded colorless crystals melting at 226–228°.

Anal. Calcd. for $C_{37}H_{48}O_7N_2$: C, 68.4; H, 8.1. Found: C, 68.2; H, 8.2.

Summary

1. Mercuric acetate in acetic acid mercurates cholesterol at position 6.

2. The mercurated product has been converted by a series of reactions to 6-ketocholestanol.

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[3] Milas and Heggie, THIS JOURNAL, **60**, 984 (1938).

[4] Preliminary experiments by John Legler, M.S. Thesis, University of Wisconsin, 1937.

[5] Windaus, *Ber.*, **36**, 3754 (1903).