2. The presence of a third sterol (m. p. 120–125°, $[\alpha]_D$ −2°, acetate, m. p. 121–124°) is established.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY, THE UPJOHN COMPANY]

SOME NEW ESTERS OF ERGOSTEROL

BY HAROLD EMERSON AND FREDERICK W. HEYL

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In continuation of our study of the sterols of ergot, we have prepared several new esters of ergosterol with acid derivatives which have frequently been used to characterize alcohols, namely, phthalic anhydride, phenyl isocyanate, and chloro-acetyl *o*- and *p*-nitrobenzoyl chlorides. Since it was found that the action of the acid chlorides in the absence of an agent to absorb the hydrogen chloride evolved yielded derivatives of isoergosterol, it was necessary to work in pyridine solution.

Experimental

Ergosteryl Acid Phthalate.—Ergosterol (2 g.) was refluxed with phthalic anhydride (3 g.) in 5 cc. of pyridine. The resulting product appeared in the form of prisms melting at 169° after several recrystallizations from alcohol; $[\alpha]_D$ was −51°.

Anal. Calcd. for $C_{35}H_{46}O_4$: C, 79.2; H, 8.7; mol. wt., 530. Found: C, 79.1; H, 8.9; mol. wt., 532 (by titration).

Upon hydrolysis with alcoholic potassium hydroxide, this gave ergosterol identical with the starting material.

The silver salt was made by adding a slight excess of an alcoholic solution of silver nitrate to the portion neutralized in titrating for the molecular weight. It separated as white crystals melting with decomposition at 170–180°, and blackening upon standing.

Anal. Calcd. for $C_{35}H_{45}O_4Ag$: Ag, 16.9. Found: Ag, 17.1.

The copper salt was prepared from cupric acetate in an analogous manner and separated as a green amorphous precipitate.

Anal. Calcd. for $(C_{35}H_{45}O_4)_2Cu$: Cu, 7.06. Found: Cu, 7.17.

Ergosteryl Phenylurethan.—Ergosterol (1.6 g.) was refluxed with 5 cc. of phenylisocyanate and 25 cc. of benzene for three hours. The solvent and excess reagent were removed by distillation at 15 mm. and the residue was recrystallized by dissolving in hot benzene and adding alcohol to incipient precipitation. It crystallizes in short hard needles melting at 236.5–238° (corr.).

Ergosteryl *m*-Nitrobenzoate was prepared by refluxing 1 g. of ergosterol with 0.6 g. of *m*-nitrobenzoyl chloride in 5 cc. of pyridine for one hour. The reaction mixture was poured into hot alcohol and allowed to crystallize. It was purified by recrystallization from alcohol, forming tiny plates melting at 151°; $[\alpha]_D$ was −71°.

Ergosteryl *p*-Nitrobenzoate was made in a similar manner. It formed clusters of plates melting at 182°; $[\alpha]_D$ was −49.5°. Both this and the meta compound yielded ergosterol upon hydrolysis.

The *m*- and *p*-nitrobenzoates of isoergosterol were formed by melting together ergosterol and the corresponding acid chloride either in toluene or without a solvent. Upon crystallization from alcohol they melted at 172° (*m*-) and 189° (*p*-), respectively, and were both optically inactive.

Anal. Calcd. for $C_{34}H_{46}O_4N$: C, 76.8; H, 8.5. Found: (meta) C, 76.6; H, 8.9; (para) C, 76.5; H, 8.9.

When hydrolyzed, both yielded isoergosterol, as plates melting at 137° with $[\alpha]_D$ of $-32.6°$. Bills and Cox[1] give m. p. 140°, $[\alpha]_D$ (= $[\alpha]_{5461} \div 1.27$) = $-31.2°$ for isoergosterol made by treatment with cinnamoyl chloride.

Chloro-acetyl Derivatives.—An attempt was made to prepare ergosteryl chloroacetate by warming ergosterol with the acid chloride in pyridine, but this resulted in a halogen-free compound, due to a further condensing effect of the pyridine. The nature of this reaction will be reported in a later paper.

Isoergosteryl chloro-acetate was readily obtained by warming 1.7 g. of ergosterol with 2 cc. of chloro-acetyl chloride on a steam-bath for three minutes. Crystallized from acetic acid and from ether it gave 1.2 g. of plates melting at 190°; $[\alpha]_D$ was $-45°$.

Anal. Calcd. for $C_{29}H_{43}O_2Cl$: Cl, 7.7. Found: Cl, 8.0.

Hydrolysis gave the same isoergosterol described above.

Summary

Ergosteryl acid phthalate and its silver and copper salts, ergosteryl phenylurethan and *m*- and *p*-nitrobenzoates have been prepared from the ergosterol of ergot, as well as the *m*- and *p*-nitrobenzoates and chloroacetate of isoergosterol.

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ALPHA-ERGOSTENOL AND ITS ISOMERIZATION TO BETA-ERGOSTENOL

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Since ergosterol itself and its esters, containing as they do three double bonds, are decidedly unstable and acquire a distinct yellow color on standing even in a black vacuum desiccator, we decided to continue our investigation of the ergosterol from ergot by studying its very stable tetrahydro derivatives, α- and β-ergostenol. α-Ergostenol was first prepared by Reindel and co-workers[1] from yeast ergosterol by catalytically reducing the acetate and hydrolyzing the product obtained thereby. The same compound has later been prepared by other authors with variations of the catalyst and solvents used. α-Ergostenol as we have prepared it from ergot ergosterol differs slightly in physical constants from Reindel's values, and did not react at all to his method of isomerization to the β-form (passing dry hydrogen chloride gas into a chloroform solution of α-ergostenol acetate). The statement of Reindel, Walter and Rauch that "the chloroacetyl derivative of α-ergostenol cannot be made by chloro-acetyl chloride, since thereby isomerization to β-ergostenol chloro-acetate takes place"

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[1] Bills and Cox, *J. Biol. Chem.*, **84**, 455 (1929).

[1] Reindel, Walter and Rauch, *Ann.*, **452**, 34 (1927); Reindel and Walter, *ibid.*, **460**, 212 (1928).