When mixed with Δ^{16}-*allo*-pregnenetrione-3,6,20 prepared from naturally occurring chlorogenin there was no depression in melting point.

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.8; H, 8.6. Found: C, 76.4; H, 8.9.

Clemmensen Reduction of *allo*-Pregnanetrione-3,6,20 (VIII) to *allo*-Pregnane (IX).—To a solution of 400 mg. of *allo*-pregnanetrione-3,6,20 in 200 cc. of 95% ethanol was added 25 g. of amalgamated zinc (20-mesh). The mixture was heated to boiling and 60 cc. of concentrated hydrochloric acid was added over a four-hour period. The product was diluted with water and extracted with ether. It was crystallized from methanol, m. p. 80–82°. Mixed with pregnane (m. p. 80°), it melted at 55–60°. When mixed with *allo*-pregnane (82–83°) it gave no depression in melting point.

Anal. Calcd. for $C_{21}H_{36}$: C, 87.4; H, 12.6. Found: C, 87.2; H, 12.5.

Oxidation of Δ^5-Pregnenol-3-one-20 (IV) to *allo*-Pregnanetrione-3,6,20 (VIII).—To a solution of 100 mg. of Δ^5-*allo*-pregnenol-3-one-20 (from stigmasterol, III) in 20 cc. of glacial acetic acid was added a solution of 100 mg. of chromic anhydride in 3 cc. of 90% acetic acid. It was allowed to stand at 20° for one hour. At the end of this time 3 g. of zinc dust and 3 cc. of water was added and the product was refluxed for four hours. The product was separated from the zinc and extracted well with ether. The ethereal solution was washed with water and dilute alkali. The residue after removal of the solvent was crystallized from ether–acetone, m. p. 232–235°. When mixed with *allo*-pregnanetrione-3,6,20, m. p. 232–235° prepared from naturally occurring chlorogenin, it gave no depression in melting point.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.1; H, 9.4.

We wish to thank Parke, Davis and Company for their assistance.

Summary

1. Transformations have been carried out which indicate conclusively that the hydroxyl groups of chlorogenin occupy positions 3 and 6.

2. In the course of the work a method has been developed for converting 3-hydroxy-Δ^5 sterols into the corresponding 3,6-diketones.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. CXI. Sapogenins. XL. The Conversion of Chlorogenin to Tigogenin

BY RUSSELL E. MARKER, D. L. TURNER AND PAUL R. ULSHAFER

When the semicarbazones of steroidal ketones with the carbonyl group in the 3 position are heated with sodium ethylate, the 3-hydroxyl compounds are formed. Thus Marker and Lawson[1] observed that pregnanol-20(α)-one-3 semicarbazone gave pregnanediol-3(α),20(α) in 85% yield and Marker and Rohrmann[2] obtained sarsasapogenin from the semicarbazone of sarsasapogenone. Dutcher and Wintersteiner[3] studied a number of other sterol semicarbazones and found that the semicarbazone group at the 3 position "yields mainly the corresponding C-3 epimeric carbinols," but semicarbazones at the 7 and 12 positions give the usual reduction to the methylene stage.

We have now taken advantage of the sodium ethylate reaction to convert the disemicarbazone of chlorogenone to tigogenin. As a model experiment the disemicarbazone of cholestanedione-3,6 was first heated with sodium ethylate. Cholestanol-3(β) was separated from the other reaction products by precipitation with digitonin. The disemicarbazone of chlorogenone[4] was then similarly treated. The digitonin precipitable fraction gave material which was identified in its original form and as the acetate with tigogenin and tigogenin acetate.

We wish to thank Parke, Davis and Company for their generous help.

Experimental Part

Treatment of Cholestanedione-3,6 Disemicarbazone with Sodium Ethylate.—The disemicarbazone of cholestanedione-3,6 was prepared in the usual way.

Sodium (2 g.) was dissolved in 25 cc. of absolute ethanol and 3 g. of the disemicarbazone of cholestanedione-3,6 was added. The mixture was heated in a bomb tube at 180° for seven hours. The product was poured into water and extracted with ether. The ether was removed and the residue was dissolved in 25 cc. of ethanol and treated with a solution of 5 g. of digitonin in 250 cc. of ethanol. The precipitated digitonide was decomposed with pyridine in the usual manner and gave material which when recrystallized from acetone melted at 138–139°. When mixed with an authentic sample of cholestanol-3(β) there was no depression in melting point.

(1) Marker and Lawson, THIS JOURNAL, **61**, 852 (1939).
(2) Marker and Rohrmann, *ibid.*, **61**, 1284 (1939).
(3) Dutcher and Wintersteiner, *ibid.*, **61**, 1992 (1939).
(4) Marker and Rohrmann, *ibid.*, **61**, 946 (1939).

Tigogenin from Chlorogenone Disemicarbazone.—Sodium (1 g.) was dissolved in 25 cc. of absolute ethanol and 2.7 g. of chlorogenone disemicarbazone was added. The mixture was heated in a bomb tube at 180° for seven hours. The product was poured into water and filtered. The combined product from three bomb tubes (representing 8 g. of chlorogenone disemicarbazone) was dissolved in ethanol and this was mixed with a solution of digitonin in ethanol. The digitonide which separated after standing for one hour was collected and dried; it weighed 6.5 g. and was decomposed with pyridine. The product (1.4 g.) was recrystallized from methanol and melted at 202–205°. Recrystallized from acetone it melted at 204–206°. When mixed with tigogenin, m. p. 204–207°, it gave no depression in melting point.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 97.7; H, 10.9.

The acetate was recrystallized from acetone, m. p. 204–206°. A mixture with tigogenin acetate, m. p. 204–206°, melted at 204–206°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 76.2; H, 10.0.

Summary

Chlorogenin has been converted to tigogenin.

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The Preparation of Phenylarsenoxides. II. Derivatives of Amino- and Hydroxyphenylarsenoxides

BY GEORGE O. DOAK, HARRY EAGLE AND HARRY G. STEINMAN

Pharmacological studies[1] on the series of compounds described in the first paper of this series[2] have shown that the chemotherapeutic index of *m*- and *p*-amino- and *m*- and *p*-hydroxyphenylarsenoxides was significantly higher than that of the unsubstituted phenylarsenoxide, as judged by *in vitro* activity against *T. pallidum* and by toxicity in white mice. Accordingly, a series of arsenoxides has been prepared in which the amino or hydroxy group was either blocked, as by ether formation, or extended on a side chain.

The arsenoxides described in the present paper (Table I) were all prepared by reduction with sulfur dioxide and potassium iodide in the usual manner. Whenever possible they were recrystallized from appropriate solvents; otherwise they were dissolved in alkali and reprecipitated with acid. They usually softened on heating without giving a definite melting point.

With the exception of *p*-arsonobenzylamine, *p*-arsonobenzylacetamide and *p'*-amino-*p*-benzoylaminophenylarsonic acid, which were amorphous powders, and *p*-arsonoacetophenoneoxime, which crystallized as rhomboids, the arsonic acids all crystallized as needles.

p-Arsono-N-ethylaniline was prepared by the method of Emerson and Walters[3] applied to arsanilic acid. *p'*-Amino-*p*-benzoylaminophenylarsonic acid was prepared by reduction of the corresponding nitro compound,[4] but using Raney catalyst in a low-pressure apparatus instead of ferrous hydroxide. The precautions taken by Hamilton and Major[5] to avoid oxidation were found unnecessary with this catalytic method.

The method of Barrowcliff, Pyman and Remfry[6] for the preparation of *p*-acetoxyphenylarsonic acid, which gave a colored product, was modified in that sodium *p*-hydroxyphenylarsonate was ground with acetic anhydride, the sodium salt precipitated with ether and recrystallized from alcohol–ether mixture.

For the preparation of *p*-arsenosodimethylaniline the method of Michaelis and Rabinerson[7] in our hands failed repeatedly to give a satisfactory yield. Accordingly, the Bart reaction was applied to *p*-dimethylaminoaniline and the resulting arsonic acid reduced to the arsenoxide in the cold. At temperatures exceeding 30°, tri-(*p*-dimethylaminophenyl)-arsine was the sole product. The arsenoxide rearranged to the same product when dissolved in alkali and then acidified.

Experimental Part[8]

***p*-Cyanophenylarsonic acid**[9] was prepared in the expectation that it could be reduced to *p*-arsonobenzylamine.

(1) Eagle, Hogan, Doak and Steinman, *J. Pharmacol.*, in press.
(2) Doak, Eagle and Steinman, THIS JOURNAL, **62**, 168 (1940).
(3) Emerson and Walters, *ibid.*, **60**, 2023 (1938).
(4) King and Murch, *J. Chem. Soc.*, **125**, 2595 (1924).
(5) Hamilton and Major, THIS JOURNAL, **47**, 1128 (1925).
(6) Barrowcliff, Pyman and Remfrey, *J. Chem. Soc.*, **93**, 1893 (1908).
(7) Michaelis and Rabinerson, *Ann.*, **270**, 139 (1892).
(8) All melting points are corrected.
(9) Bertheim, *Ber.*, **41**, 1853 (1908), previously prepared this compound but failed to isolate it from solution.