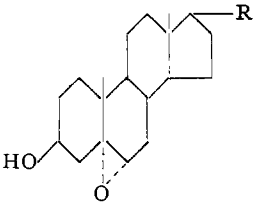
A Method for Reduction of Steroid Oxides

By L. Carroll King and J. Allan Campbell

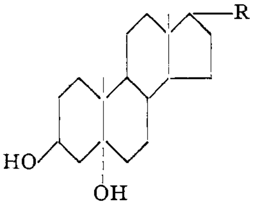
Recent interest in the reduction of steroid oxides[1] impels us to record a method for reduction of these substances which has been under investigation in this Laboratory.

(α)-Cholesteryl oxide (I) reacts with thiourea and *p*-toluenesulfonic acid in alcoholic solution to give 3(β),5(α)-dihydroxycholestanyl-6-isothiuronium tosylate (II) in 73–92% yield. An alcoholic solution of II on shaking with an equivalent amount of sodium hydroxide and an excess of standard nickel catalyst[2] was reduced to 3(β),5(α)-dihydroxycholestane (III), yield 88–95%. The identity of III was established by conversion to 3(β)-acetoxy-5(α)-hydroxycholestane.

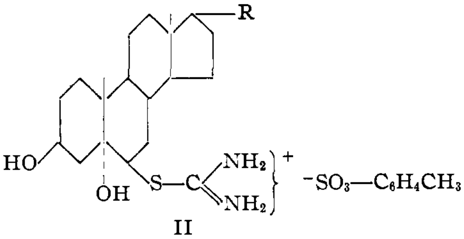
The application of this method of reduction to the preparation of 17-hydroxysteroids from the corresponding 16,17- or 17,20-oxido compounds is in progress.



I



III



II

3(β),5(α)-Dihydroxycholestane-6-isothiuronium Tosylate (II).—Prepared from (α)-cholesteryl oxide by refluxing with thiourea and *p*-toluenesulfonic acid in alcoholic solution; yield 73–92%, m. p. 228–229°. *Anal.* Calcd. for $C_{35}H_{58}N_2O_5S_2$: C, 64.57; H, 8.98. Found: C, 64.57; H, 8.39%.

3(β),5(α)-Dihydroxycholestane (III).—Prepared from II by action of standard nickel catalyst and an equivalent of sodium hydroxide in alcoholic solution; yield 88–95%, m. p. 222–224°. *Anal.* Calcd. for $C_{27}H_{48}O_2$: C, 80.13; H, 11.96. Found: C, 80.03; H, 11.93.

3(β)-Acetoxy-5(α)-hydroxycholestane.—From III by warming with acetic anhydride; m. p. 182–184°. *Anal.* Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28. Found: C, 76.94; H, 10.91.

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[1] Plattner, Heusser and Feurer, *Helv. Chim. Acta.*, **31**, 2210 (1948); *ibid.*, **32**, 587 (1949); Julian, Meyer and Ryden, This Journal, **71**, 756 (1949).

[2] Adkins, "Reactions of Hydrogen with Organic Compounds, etc.," The University of Wisconsin Press, Madison, Wis., 1937, p. 20.

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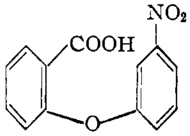
Camps Reaction with 1-Xanthonamine[1]

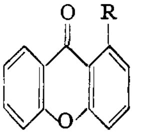
By C. F. Koelsch and F. J. Lucht

This paper describes a synthesis of [1]benzopyrano[4,2,de]quinoline (IX) and some reactions designed to yield its 6-methoxy derivative. It is planned to use these substances in experiments which it is hoped will furnish 4-*o*-hydroxyphenylquinolinic acid and ultimately morphine analogs.[2]

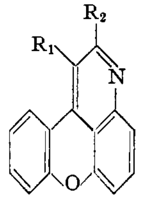
The synthesis involved intermediates I–VIII, formulated below. The route from VI to IX through X and XI instead of VII and VIII gave poorer yields. Yield of each substance is indicated by the figure in parentheses.



I (85)



II, R = NO_2 (35)
III, R = NH_2 (100)
IV, R = $NHCOCH_2$-$COOC_2H_5$ (86)



	R1	R2
V	$COOC_2H_5$	OH (90)
VI	COOH	OH (94)
VII	H	OH (98)
VIII	H	Cl (89)
IX	H	H (28 from VIII; good from XI
X	COOH	Cl (25)
XI	COOH	H (59)

Experimental

***o*-(*m*-Nitrophenoxy)-benzoic Acid, I.**—The substance has been prepared but not isolated by Dhar.[3] In the present work it was obtained by heating and stirring a mixture of 62 g. of *o*-chlorobenzoic acid, 63 g. of *m*-nitrophenol, 50 g. of sodium carbonate, 5 g. of copper filings, 0.2 g. of cuprous chloride, and 150 ml. of *n*-amyl alcohol for three hours in an oil-bath at 160–170°. The crude crystalline product (55 g.) was suitable for cyclization. Crystallization from benzene gave pale yellow prisms, m. p. 138–139°.

Anal. Calcd. for $C_{13}H_9NO_5$: C, 60.2; H, 3.5. Found: C, 60.2; H, 3.8.

Xanthone Ring Closure.—A solution of 55 g. of crude nitrophenoxybenzoic acid in 300 ml. of sulfuric acid was heated on a steam-bath for thirty minutes and then poured into water. Acidic materials were removed, and the crude neutral residue (25 g., m. p. 160–170°) was separated by crystallization from acetic acid into 18 g. of 1-nitroxanthone (II), pale yellow prisms m. p. 206–207° (reported[3] 210°), and 7 g. of brown crystalline material, m. p. 155–160°. The latter contained the still unknown 3-nitroxanthane, for by reducing it with stannous chloride and alcoholic hydrochloric acid, and fractionally crystallizing the product from alcohol, there was obtained 3.7 g. of 3-xanthonamine, m. p. 231–232° (reported[4] 232°).

Anal. Calcd. for $C_{13}H_9NO_2$: C, 73.9; H, 4.3. Found: C, 74.0; H, 4.4.

1-Xanthonamine, III.—Reduction of 11.5 g. of 1-nitroxanthone with 45 g. of stannous chloride in 115 ml. of alcohol containing 50 ml. of hydrochloric acid and crystallization of the product from alcohol gave 9.5 g. of yellow prisms, m. p. 150–151°.

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[1] From the Ph.D. Thesis of Fred J. Lucht, submitted to the Graduate Faculty of the University of Minnesota, September, 1946.

[2] Koelsch, This Journal, **67**, 569 (1945).

[3] Dhar, *J. Chem. Soc.*, **117**, 1061 (1920).

[4] Ullmann and Wagner, *Ann.*, **355**, 359 (1907).