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Applications of Chromium(II) Chloride. Part V.¹ The Reduction of Some Nitro-steroids

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Chromium(II) chloride has been shown to reduce 6-nitro-, 17-nitro-, and 3,3-dinitro-steroids to the corresponding oximes. On the other hand the By-unsaturated 6-nitrocholest-4-enes afford the corresponding ketones or products of further reduction.

A NUMBER of reagents have been reported to reduce nitrocompounds, particularly in their *aci*-forms, to oximes. Amongst these are alkaline solutions of sodium amalgam or zinc dust,² sodium thiosulphate,³ and acidic hydrogen sulphide.⁴ We have recently reported ⁵ the reduction of a steroidal nitro-olefin with chromium(II) chloride; similar reduction ⁶ of methanolic 6β -nitro- 5α -chlorocholestan-3^β-yl acetate is reported to afford the corresponding 5α -methoxy-6-hydroxyimino-steroid. We have now examined the reduction of some saturated and βy-unsaturated nitro-steroids.

 6α -Nitro- 5α -cholestan- 3β -yl acetate, prepared by reduction of 6-nitrocholesteryl acetate with sodium borohydride,⁶ was reduced under nitrogen with acidic chromium(II) chloride to give 6-hydroxyimino-5a-cholestan-3\beta-yl acetate, and 3\beta-acetoxy-17\beta-nitroandrost-5-ene⁷ gave the corresponding 17-oxime. 3,3-Dinitro- 5α -cholestane, prepared ⁸ by nitration of the 3-oxime with fuming nitric acid, was similarly reduced to give the 3-oxime. The α -nitro-ketone, 3β-hydroxy-16-nitroand rost-5-en-17-one 9 afforded the corresponding α -hydroxyimino-ketone. If the reductions were carried out under reflux the oximes were hydrolysed and the corresponding ketones were isolated. The reduction may be envisaged as proceeding through the dihydroxy-amine, which readily eliminates water to form the oxime.

¹ Part IV, J. R. Hanson and S. Mehta, J. Chem. Soc. (C), 1969, 2349.

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³ A. A. Artem'ev, E. V. Genkina, A. B. Malimonova, V. P.

Trofil'kina, and M. A. Isaenkova, Zhur. Vsesoyuz. Khim. obshch. im. D. I. Mendeleeva, 1965, 10, 588. (Chem. Abs., 1966, 64, 1975).

⁴ B.P. 684,369 (Chem. Abs., 1954, 48, 2095).

⁵ J. R. Hanson and E. Premuzic, Tetrahedron Letters, 1966, 5441.

In contrast the By-unsaturated nitro-steroid, 68-nitrocholest-4-en-3\beta-yl acetate, 10, 11 afforded the 6-ketone rather than the oxime, presumably by hydrolysis under the acidic conditions of the reduction. There were no signs of the hydroxy-oximes as formed by reduction of nitro-olefins. Reduction of the corresponding 3-alcohol gave cholest-4-en-6-one in relatively low yield, hydrogenolysis of the allylic hydroxy-group occurring as a side reaction. Both 6a- and 6B-nitrocholest-4-en-3-one 10 gave 5a-cholestan-3,6-dione on reduction with chromium-(II) chloride. 5β -Cholestane-3,6-dione was the product of reduction of cholest-4-ene-3,6-dione.

The reduction of these nitro-steroids proceeded in good yield and the products were readily isolated. The method may therefore be of general utility.

EXPERIMENTAL

General Reduction Procedure.--Chromium(II) chloride was prepared from chromium(III) chloride (12 g.) in water (15 ml.) and 6n-hydrochloric acid (25 ml.) by reduction with excess of granulated zinc. The blue chromium(II) solution was filtered under nitrogen into a solution of the nitrosteroid (ca. 0.5 g.) in acetone (100 ml.). The mixture was poured into water and extracted with ether. The extract was dried and evaporated, and the product (when necessary) was chromatographed on alumina.

3,3-Dinitro-5a-cholestane. The steroid (400 mg.) gave 3-hydroxyimino-5a-cholestane (350 mg.) as needles, m.p.

⁶ A. Hassner and C. Heathcock, J. Org. Chem., 1964, 29, 1350. ⁷ A. A. Patchet, F. Hoffmann, F. F. Giarrusso, H. Schwan, and G. E. Arth, J. Org. Chem., 1962, 27, 3822. ⁸ J. R. Bull, E. R. H. Jones, and G. D. Meakins, J. Chem. Soc. 1965, 2601

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¹⁰ W. A. Harrison, E. R. H. Jones, G. D. Meakins, and P. A. Wilkinson, *J. Chem. Soc.*, 1964, 3210.

¹¹ J. T. Pinhey and E. Rizzardo, Chem. Comm., 1965, 362.

198—203° (from acetone), $[a]_{\rm D}{}^{20}$ +20° (c 0.8) (lit.,⁸ m.p. 197—201°, $[a]_{\rm D}$ +21°) (Found: C, 80.2; H, 11.7. Calc. for C₂₇H₄₇NO: C, 80.7; H, 11.8%). 5α-Cholestan-3-one (5 mg.), m.p. 129—131° (lit.,¹² 129°) (Found: C, 83.65; H, 12.3. Calc. for C₂₇H₄₆O: C, 83.9; H, 12.0%), was isolated from the mother liquors.

6α-Nitro-5α-cholestan-3β-yl acetate. The steroid gave 6-hydroxyimino-5α-cholestan-3β-yl acetate (480 mg.) as needles, m.p. 203-206° (from acetone-light petroleum), (lit.,¹³ 202-204°), $[\alpha]_{\rm p}^{20}$ -1° (c 0.8 CHCl₃) (Found: C, 75.7; H, 10.35; N, 2.8. Calc. for C₂₉H₄₉O₃N: C, 75.8; H, 10.7; N, 3.0%).

3β-Acetoxy-17β-nitroandrost-5-ene. The steroid (500 mg.) gave 17-hydroxyiminoandrost-5-en-3β-yl acetate (350 mg.) as needles, m.p. 178—179° (from methanol), $[\alpha]_{\rm p} -73°$ (c 0.8 CHCl₃) (lit.,¹⁴ m.p. 178—180°, $[\alpha]_{\rm p} -72.4°$) (Found: C, 73.1; H, 8.7; N, 4.2. Calc. for C₂₁H₂₉NO₃: C, 73.4; H, 8.5; N, 4.1%).

6β-Nitrocholest-4-en-3β-yl acetate. The steroid (500 mg.) gave 6-oxocholest-4-en-3β-yl acetate (350 mg.), m.p. 109— 110° (from acetone-light petroleum), $[\alpha]_{\rm D} -50°$ (c 0.8 in CHCl₃) (lit.,¹⁵ m.p. 110°, $[\alpha]_{\rm D} -50.5°$) (Found: C, 78.6; H, 10.6. Calc. for C₂₉H₄₆O₃: C, 78.7; H, 10.5%), $\lambda_{\rm max.}$ 234 nm. (ε 6300), $\nu_{\rm max.}$ 1735, 1680, and 1625 cm.⁻¹.

nm. (ε 6300), $\nu_{max.}$ 1735, 1680, and 1625 cm.⁻¹. 6 β -Nitrocholest-4-en-3 β -ol. The product obtained from the steroid (500 mg.) was chromatographed on alumina. Elution with 5% ethyl acetate-light petroleum gave

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Q. R. Peterson, Proc. Indiana Acad. Sci., 1963, 73,127.

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¹⁴ S. Kaufmann, J. Amer. Chem. Soc., 1951, 73, 1779.

cholest-4-en-6-one (75 mg.) as needles, m.p. 107—108° (from light petroleum), $[\alpha]_{D}^{20} + 36\cdot5^{\circ}$ (c 0.8 CHCl₃) (lit.,¹⁶ m.p. 108—109°, $[\alpha]_{D}^{20} + 36\cdot2^{\circ}$) (Found: C, 84.5; H, 11.3. Calc. for $C_{27}H_{44}O$: C, 84.3; H, 11.5%).

3β-Hydroxy-16-nitroandrost-5-en-17-one. The steroid (500 mg.) gave 3β-hydroxy-16-hydroxyiminoandrost-5-en-17-one (200 mg.) as an unstable amorphous powder, m.p. 330–335° (from methanol) (Found: C, 71·4; H, 8·95; N, 4·6. C₁₉H₂₇NO₃ requires C, 71·9; H, 8·6; N, 4·4%), ν_{max} . 3420br and 1705 cm.⁻¹.

 6α -Nitrocholest-4-en-3-one. The steroid (500 mg.) in acetone (100 ml.) gave 5α -cholestan-3,6-dione (450 mg.) as needles, m.p. 171—172° (from acetone), $[\alpha]_{\rm p}^{20} + 9°$ (c 0.8 in CHCl₃) (lit.,¹⁷ m.p. 169—171°, $[\alpha]_{\rm p}^{20} + 10°$), identical (i.r. and n.m.r. spectra) with an authentic sample.

6β-Nitrocholest-4-en-3-one. The steroid (500 mg.) in acetone (100 ml.) gave 5α-cholestane-3,6-dione (480 mg.) as needles, m.p. 171—172° (from acetone), $[\alpha]_{\rm D}^{20} + 9\cdot4^{\circ}$ (c 0.8 CHCl₃) (lit.,¹⁷ m.p. 169—171°, $[\alpha]_{\rm D}^{20} + 10^{\circ}$) (Found: C, 81·1; H, 11·15. Calc. for C₂₇H₄₄O₂: C, 80·9; H, 11·1%), identical (mixed m.p. and i.r. and n.m.r. spectra) with an authentic sample.

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