SECTION C
Organic Chemistry

Applications of Chromium(II) Chloride. Part III.[1] Chromium(II) Chloride Reduction of Some Enediones

By **J. R. Hanson** * and **E. Premuzic**, The Chemical Laboratory, University of Sussex, Brighton, BN1 9QJ

Chromium(II) chloride has been shown to reduce some enediones to the corresponding dihydro-compounds under conditions which do not reduce the simple αβ-unsaturated ketones. Reduction of cholest-4-ene-3,6-dione afforded 5β-cholestane-3,6-dione whilst reduction of cholest-1,4-diene-3,6-dione afforded 5β-cholest-1-ene-3,6-dione and reduction of cholest-3,5-diene-2,7-dione gave cholest-4-ene-2,7-dione.

CHROMIUM(II) chloride is a powerful reducing agent capable of bringing about hydrogenolysis, hydrogenation, and deoxygenation depending on the substrate.[2] In their initial survey of chromium(II) chloride as a reducing agent, Traube and Passarge noted[3] that it would reduce both maleic and fumaric acids to succinic acid. Since then there has been a discussion[4] of these and related acids as bridging groups in reduction by low-valent transition-metal ions. However there has been no description of its ability to reduce enediones or of the stereochemistry of the product. It is therefore the purpose of this paper to examine the application of chromium(II) chloride to the reduction of enediones in an alicyclic environment.

Cholest-4-ene-3,6-dione was reduced by chromium(II) chloride in both tetrahydrofuran and acetone. The product, unlike the product of zinc and acetic acid reduction,[5] was 5β-cholestane-3,6-dione. The formation of the 5β-cholestane rather than the more normal 5α-cholestane was demonstrated by the strongly negative o.r.d. curve[6] and by isomerization with alkali of the 5β-cholestane-3,6-dione to the more stable 5α-cholestane-3,6-dione. Molecular models suggest that a chelate complex between the chromium(II) ion and the carbonyl groups in the transition state would favour the formation of the *cis*-A/B ring junction. Such a complex has been proposed in the reduction of maleic acid. Cholest-4-en-3-one and 3β-acetoxycholest-5-en-7-one were not reduced by chromium(II) chloride under these conditions. However cholest-1,4-diene-3,6-dione[7] was readily reduced with chromium(II) chloride. The product was identified as 5β-cholest-1-ene-3,6-dione. The u.v. spectrum indicated the presence of the ring A αβ-unsaturated ketone whilst the n.m.r. spectrum confirmed the double-bond substitution pattern. The 5β-stereochemistry was confirmed by catalytic hydrogenation which gave 5β-cholestane-3,6-dione. Cholest-1,4-dien-3-one and cholest-4,6-diene-3-one were both recovered unchanged from these conditions.

In view of the possible requirement for chelate complexing between the carbonyl groups and the chromium(II) ion, reduction of the transoid enedione, 3β-acetoxylanost-8-ene-7,11-dione, was examined. The system was readily reduced to give the known[8] 3β-acetoxylanostane-7,11-dione. This has been assigned the B/C *trans*-stereochemistry. Hence an intermediate involving a single chromium(II) ion complexing to both carbonyl groups is not a mandatory requirement. As an extension of this a diene-dione was studied. Chromium(II) chloride reduction of cholest-3,5-diene-2,7-dione gave a dihydro-compound. The n.m.r. spectrum showed a broad 1H resonance at τ 4·18. Since the compound lacked strong u.v. absorption, it was assigned the cholest-4-ene-2,7-dione structure.

Chromium(II) chloride is known to deoxygenate αβ-epoxy-ketones to the corresponding αβ-unsaturated ketones, whilst chromium(II) acetate reduces them to β-hydroxy-ketones. Reduction of the γδ-epoxy-αβ-unsaturated ketone, 3α,4α-epoxycholest-5-en-7-one with chromium(II) chloride gave cholest-3,5-dien-7-one following the normal pattern rather than generating the alternative 3α-hydroxycholest-4-en-7-one. Another system in which a chromium complex is possible involves a γ-bromo-αβ-unsaturated ketone. However hydrogenolysis of 6β-bromocholest-4-en-3-one occurred with the formation of cholest-4-en-3-one.

EXPERIMENTAL

For general experimental details see previous part.[1]

Reduction of Cholest-4-ene-3,6-dione.—The steroid (503 mg.) in tetrahydrofuran (70 ml.) was heated under reflux with 0·1N-chromium(II) chloride (120 ml.) in an atmosphere of nitrogen. The solution was diluted with water and the product was recovered in ether. 5β-Cholestane-3,6-dione (250 mg.) crystallized from acetone as needles, m.p. 170—

[1] Part II, J. R. Hanson and E. Premuzic, *Tetrahedron*, 1967, **23**, 4105.
[2] For a review see J. R. Hanson and E. Premuzic, *Angew. Chem.*, 1968, **7**, 247.
[3] W. Traube and W. Passarge, *Ber.*, 1916, **49**, 1692.
[4] D. W. Sebera and H. Taube, *J. Amer. Chem. Soc.*, 1961, **83**, 1785.
[5] A. Windaus, *Ber.*, 1906, **39**, 2249.
[6] S. Julia and J. P. Lavaux, *Bull. Soc. chim. France*, 1963, 1223.
[7] D. Burn, V. Petrow, and G. Weston, *J. Chem. Soc.*, 1962, 29.
[8] C. Doree, J. F. McGhie, and F. Kurzer, *J. Chem. Soc.*, 1949, 570.

172°, $[\alpha]_D^{20}$ −62·5° (*c* 0·64 CH_2Cl_2), $\nu_{max.}$ 1700 cm.$^{-1}$ (lit.,[9] m.p. 170—174°, $[\alpha]_D^{18}$ −57°); $[\Phi]_{600} = -250°$, $[\Phi]_{400}$ −1502°; $[\Phi]_{350}$ −4006°, $[\Phi]_{320}$ −15,024°, $[\Phi]_{310}$ −9768°, $[\Phi]_{302}$ 0, and $[\Phi]_{280}$ +14,272. Treatment with methanolic 2N-sodium hydroxide gave 5α-cholestane-3,6-dione, m.p. 170—173°, $[\alpha]_D^{20}$ +4·4° (*c* 0·226 CH_2Cl_2); $[\Phi]_{400}$ −36°, $[\Phi]_{350}$ 0, $[\Phi]_{320}$ −300°; $[\Phi]_{312}$ −1244°, $[\Phi]_{302}$ 0, and $[\phi]_{288}$ +2216°.

Reduction of Cholest-1,4-diene-3,6-dione.—The steroid [7] (400 mg.) in acetone (10 ml.) was treated with 0·1N-chromium(II) chloride (130 ml.) containing hypophosphorus acid (1 ml.) under nitrogen and then heated under reflux for 1 hr. The product was filtered off and crystallized from acetone to give 5β-*cholestan-1-ene-3,6-dione* as needles, m.p. 168—169° (Found: C, 80·7; H, 10·8. $C_{27}H_{42}O_2$ requires C, 81·35; H, 10·6%), $\nu_{max.}$ 1710 and 1685 cm.$^{-1}$; $\lambda_{max.}$ 227 nm; τ 9·25, 9·16, 9·04, 8·97, 4·08 (d), and 2·87 (d, *J* 10 Hz). Hydrogenation over 10% palladized charcoal in ethyl acetate afforded 5β-cholestane-3,6-dione as needles, m.p. 169—170° identical with a sample prepared above.

Cholest-4-en-3-one, 3β-acetoxycholest-5-en-7-one, cholest-1,4-dien-3-one and cholest-4,6-dien-3-one were recovered unchanged from the above conditions.

Reduction of 3β-Acetoxylanost-8-ene-7,11-dione.—The diketone (400 mg.) in acetone (10 ml.) was treated with 0·1N-chromium(II) chloride (120 ml.) containing hypophosphorus acid (1 ml.) under nitrogen and then heated under reflux for 3 hr. The product was filtered off and crystallized from acetone to give 3β-acetoxylanostane-7,11-dione as plates, m.p. 220—222° (lit.,[8] 222—224°), $\nu_{max.}$ 1700 cm.$^{-1}$.

Reduction of Cholest-3,5-diene-2,7-dione.—The steroid (350 mg.) in acetone (15 ml.) was treated with 0·1N-chromium(II) chloride (130 ml.) containing hypophosphorus acid (1 ml.) under nitrogen and then heated under reflux for 3 hr. The product was filtered off and crystallized from acetone to give *cholest-4-ene-2,7-dione* as needles, m.p. 158—160° (Found: C, 81·1; H, 10·7. $C_{27}H_{42}O_2$ requires C, 81·35; H, 10·6%), $\nu_{max.}$ 1710 cm.$^{-1}$; τ 9·32, 9·20, 9·08, 8·82, and 4·18.

Reduction of 3α,4α-Epoxycholest-5-en-7-one.—The steroid (300 mg.) was treated as above. Recovery gave cholest-3,5-diene-7-one (180 mg.), m.p. 110—112° identified by its i.r. spectrum.

Reduction of 6β-Bromocholest-4-en-3-one.—The steroid (512 mg.) was treated as above. Recovery gave cholest-4-en-3-one (270 mg.), m.p. 81—82°, $[\alpha]_D^{20}$ +86° identified by its i.r. spectrum.

[9/062 *Received, January 13th,* 1969]

[9] V. Prelog and E. Tagmann, *Helv. Chim. Acta,* 1944, **27**, 1880.