Selective Homogeneous Hydrogenation of 3-Oxo-1,4-diene Steroids with a Ruthenium Complex as Catalyst

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Recently, an excellent example of selective homogeneous hydrogenation has been described in the reduction of 3-oxo-1,4-diene steroids to the corresponding 3-oxo-4-enes using chlorotris(triphenylphosphine)rhodium as catalyst.[1,2] Although the hydrogenation with this catalyst seems to proceed quite selectively, it usually does not stop at 3-oxo-4-enes and further hydrogenation to saturated ketones may occur with prolonged reaction period.[1-3]

We have investigated the hydrogenation of 1,4-androstadiene-3,17-dione (I) with a ruthenium complex prepared from hydrated ruthenium chloride and triphenylphosphine,[4] and found that the hydrogenation with this complex is also applicable to the selective reduction of I to 4-androstene-3,17-dione (II). The hydrogenation proceeds rather readily at below 50°C under a high pressure of hydrogen. In contrast to the hydrogenation with the rhodium complex, II was practically not hydrogenated further with this ruthenium complex. A small amount of androstane-3,17-dione (III), the most part of which was the 5α isomer, was produced along with II. The yield of II decreased with elevation of the reaction temperature, although the rate of hydrogenation increased greatly. A noteworthy feature of this hydrogenation is that the selectivity for the formation of II varies considerably with the pressure of hydrogen, as shown in Table 1. Thus, a high yield of II may be obtained by hydrogenating at a relatively low temperature and under a high hydrogen pressure. In a typical run, 750 mg of I was hydrogenated with 150 mg of the catalyst in 15 m*l* of benzene at 40°C under the hydrogen pressure of 125 kg/cm^2 for 10 hr.

Table 1. Effect of hydrogen pressure on the selectivity of hydrogenation of 1,4-androstadiene-3,17-dione (I)[a]

Hydrogen pressure (kg/cm^2)	Reaction time (hr)	% of I converted	Composition of hydrogenated product (%)[b]	
			II	III
10	1.5	12.3	66.4	33.6
30	1.5	19.4	78.9	21.1
50	1.5	26.2	85.8	14.2
100	1.5	45.1	89.5	10.5
162	1.5	64.8	92.5	7.5

a) I (300 mg) was hydrogenated with 300 mg of the ruthenium complex in 60 m*l* of benzene at 50°C.

b) II: 4-androstene-3,17-dione.
III: androstane-3,17-dione, the most part of which was the 5α isomer. The product was analyzed by gas chromatography after evaporation of the solvent followed by extraction with methylcyclohexane.

The product was 94% of II and 6% of III, and contained no starting material, as analyzed by gas chromatography. After the solution was passed through alumina and the solvent removed, recrystallization of the solid residue from acetone-hexane gave 640 mg of almost pure II, mp 165—169°C, $[\alpha]_D^{22}$ +189 (chloroform). Its infrared spectrum was identical in all respects with that of an authentic sample of II. Under similar conditions, 17β-hydroxy, 17β-acetoxy and 17β-acetyl derivatives of 1,4-androstadien-3-one were also hydrogenated to the corresponding 4-en-3-ones with high selectivity as in the case of I.

Analysis of the product during the course of hydrogenation of I showed that the ratio of the II to III formed was nearly constant throughout the reaction. This indicates that III was produced from I simultaneously with II. A further evidence for this is that a very prolonged hydrogenation of II gave a small amount of III which was a mixture of 5β and 5α isomers. A probable course of the formation of III seems to be the one *via* 5α-androst-1-ene-3,17-dione, which was found to be hydrogenated readily to III under the conditions in which II did not hydrogenate.

Further studies on this hydrogenation are in progress.

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3) P. Wieland and G. Anner, *Helv. Chim. Acta*, **51**, 1698 (1968).
4) T. A. Stephenson and G. Wilkinson, *J. Inorg. Nucl. Chem.*, **28**, 945 (1966). The catalyst used in this study was prepared by refluxing hydrated ruthenium chloride (1 g) and triphenylphosphine (6 g) in ethanol (120 m*l*), according to the procedure for the preparation of chlorotris(triphenylphosphine)rhodium [J. A. Osborn, A. H. Jardine, J. F. Young and G. Wilkinson, *J. Chem. Soc.*, (*A*), **1966**, 1711].