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UNUSUAL HIGH REACTIVITIES OF Δ^5 STEROIDS IN PALLADIUM CATALYZED HYDROGENATION

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Hydrogenation of a mixture of 3β-hydroxyandrost-5-en-17-one or cholesterol with α-pinene has revealed that the Δ^5 steroids are more reactive than α-pinene over palladium while α-pinene is much more reactive than the Δ^5 steroids with other platinum metals.

Recently it has been shown that 5α- and 5β-cholestan-3-ones are 30 and 17 times as reactive as 4-t-butylcyclohexanone in the palladium catalyzed competitive hydrogenation in t-butyl alcohol.[1] The high reactivity of the steroid ketones has been found to result from their strong adsorption on palladium. The unusual stereochemistry of hydrogenation observed with palladium[2] that the equatorial 3β-ol is formed from 5α-cholestan-3-one and the axial 3β-ol is produced from 5β-cholestan-3-one has thus been explained with the assumption that the strong adsorption of the steroid ketones is the result of a strong interaction of the steroid α-face with palladium.[1]

We present here further examples showing an unusual high activity of palladium which has been observed in the hydrogenation of Δ^5 steroids. An equimolar mixture of 3β-hydroxyandrost-5-en-17-one (dehydroepiandrosterone, DEA) or cholesterol and α-pinene has been hydrogenated in isopropyl alcohol at atmospheric pressure and 25°C with unsupported platinum metals[2] as catalysts. The relative reactivity of the steroid to α-pinene (R_s/R_p) has been obtained by applying Eq.(1)[3] to the variation in composition of reaction mixture during hydrogenation. The results are summarized

$$\log (C_s^\circ/C_s) = (R_s/R_p) \log (C_p^\circ/C_p) \qquad (1)$$

in Table 1. It is seen that with the catalysts other than palladium α-pinene is far more reactive than the Δ^5 steroids while with palladium the Δ^5 steroids are more reactive than α-pinene. Since the rate of hydrogenation for DEA (8.9×10^{-4} mol·min^{-1}·gcat^{-1}) was smaller than that for α-pinene (14.7×10^{-4} mol·min^{-1}·gcat^{-1}) when the compounds were individually hydrogenated, the high reactivity of DEA over α-pinene in competitive hydrogenation is considered to result from a stronger adsorption of DEA on palladium.

For the hydrogenation of Δ^5 steroids platinum catalysts have been widely used in acidic medium.[4] However, in a few examples palladium catalysts have been successfully employed.[5] In particular, Augustine and Reardon[5] has reported that palladium is superior to platinum in the hydrogenation of cholesterol, since the hydrogenation proceeds smoothly in ethanol at room temperature. It is now suggested that the excellent

nature of palladium in the hydrogenation of Δ^5 steroids is considered to be due to strong affinity of the steroids for palladium.

Augustine and Reardon used 5% palladium on charcoal as a catalyst in the hydrogenation of cholesterol and noted that the reaction became sluggish after 70-80% completion and 1% of cholesterol remained unchanged even after 10 hr hydrogenation.[5] In this study we used palladium black as a catalyst which had been prepared as described previously[2] and found no difficulty in completing the hydrogenation.[6] In a preparative run 1 g of cholesterol was hydrogenated with 50 mg of palladium black in 20 ml of isopropyl alcohol at room temperature and atmospheric pressure. The hydrogenation was complete within 4 hr and afforded a mixture of 95% of 5α-cholestan-3β-ol and 5% of cholestanes with no starting material (GC analysis). Chromatography on silica gel gave 876 mg of pure 5α-cholestan-3β-ol, mp 141-141.5°C (lit.[7] mp 142-143°C after thorough drying). Similarly, 1 g of DEA was completely hydrogenated in 2 hr with 50 mg of palladium black in 25 ml of isopropyl alcohol to give 95.5% of 3β-hydroxy-5α-androstan-17-one and 4.5% of hydrogenolysis products. Chromatography on silica gel gave 826 mg of a pure sample, mp 174-175°C (lit.[8] mp 175°C).

Table 1. Relative Reactivities of Δ^5 Steroids to α-Pinene (R_s/R_p) in Competitive Hydrogenation[a]

Catalyst	R_s/R_p	
	DEA	Cholesterol
Pt	0.39	0.16
Rh	0.21	0.14
Ir	0.19	0.12
Ru	b)	0.12
Os	b)	c)
Pd	1.8	1.2

a) A mixture of 3β-hydroxyandrost-5-en-17-one (DEA)(20mg) or cholesterol (27 mg) and α-pinene (9.4 mg) was hydrogenated with 2 mg of palladium in 2 ml of isopropyl alcohol at atmospheric pressure and 25°C. The composition of reaction mixture during hydrogenation was determined by GC (column: OV-210 for steroids; PEG 20M for α-pinene). b) Hydrogenation of 17-oxo group in preference to Δ^5 unsaturation occurred extensively. c) Hydrogenation of cholesterol vs α-pinene was too slow to obtain reasonably accurate data.

References and Note

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5) R. L. Augustine and E. J. Reardon, Jr., Org. Prep. Proc., 1, 107 (1969) and references cited therein.
6) Hydrogenation of Δ^5 steroids with the palladium black was always accompanied by some 4-5% of hydrogenolysis, while hydrogenolysis products were not found with the palladium charcoal used by Augustine and Reardon.[5]
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