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UNUSUAL HIGH REACTIVITIES OF 5α- AND 5β-CHOLESTAN-3-ONES IN THE HYDROGENATION CATALYZED BY PALLADIUM. EVIDENCE FOR AN ATTRACTIVE INTERACTION OF THE STEROID α-FACE WITH PALLADIUM

Shigeo NISHIMURA,* Mikio MURAI,* and Michio SHIOTA**
*Department of Industrial Chemistry, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184
**Department of Chemistry, Ochanomizu University, Bunkyo-ku, Tokyo 112

5α- And 5β-cholestan-3-ones are 30 and 17 times as reactive as 4-t-butylcyclohexanone in Pd catalyzed competitive hydrogenation in t-BuOH. The high reactivity of the steroid ketones and unusual hydrogenation stereochemistry on Pd have been explained on the basis of an attractive interaction of the steroid α-face with Pd.

In a previous paper,[1] we have shown that catalytic hydrogenation of 5α-cholestan-3-one with palladium in isopropyl or t-butyl alcohol gives an equatorial 3β-ol in high yield while with 5β-cholestan-3-one under the same conditions an axial 3β-ol is produced with high stereoselectivity. This unusual aspect in the stereochemistry of hydrogenation was also observed, although to a much lesser extent, with platinum, but not with the other platinum metals where the ratios of the equatorial to axial alcohol produced were not much different with both the ketones.

In order to know the reason for the unusual results obtained with palladium, we have investigated the relative reactivity of the steroid ketones to 4-t-butylcyclohexanone by employing the method of competitive hydrogenation,[2] and found that 5α- and 5β-cholestan-3-ones are, respectively, 30 and 17 times as reactive as 4-t-butylcyclohexanone in t-butyl alcohol at 26°C and atmospheric pressure.[3] Such high reactivity was not observed with the other platinum metals and the steroid ketones were less reactive than 4-t-butylcyclohexanone (Table 1).

The high reactivity of the steroid ketones might be due to their strong adsorption to the catalyst. This has been strongly supported by the fact that the rate of hydrogenation of 5α-cholestan-3-one is independent of its concentration to a concentration as low as 0.016 $mol \cdot l^{-1}$ (Fig. 1). By contrast, the rate of hydrogenation of 4-t-butylcyclohexanone is greatly dependent on concentration and almost first order in the concentration of 0.016 $mol \cdot l^{-1}$ (Fig. 2).

The relative strength of adsorption has been obtained from the values of the rates of hydrogenation of individual ketones, employing the relationship of Eq.(1),[2]

$$R/R_{Bu} = (k/k_{Bu})(b/b_{Bu}) \qquad (1)$$

where R/R_{Bu}, k/k_{Bu}, and b/b_{Bu} represent the ratios of the rate in competitive hydrogenation, the rate in individual hydrogenation and the adsorption coefficient for a

Table 1. Reactivities of 5α- and 5β-Cholestan-3-ones ($R_{5\alpha}$ and $R_{5\beta}$) vs 4-t-Butylcyclohexanone (R_{Bu}) in Competitive Hydrogenation[a)]

Catalyst	$R_{5\alpha}/R_{Bu}$	$R_{5\beta}/R_{Bu}$
Pd	30, 33,[b)] 35[c)]	17, 21[c)]
Pt	0.86	-
Rh	0.70	-
Ru	0.45	-
Os	0.40	0.27
Ir	0.39	-

a) Unless otherwise indicated, an equimolar mixture of 5α- or 5β-cholestan-3-one and 4-t-butylcyclohexanone was hydrogenated in t-BuOH at 26°C and 1 atmH_2 with the initial concentration of 0.0278 mol·l^{-1} for each ketone. b) Initial concentration: 0.0134 mol·l^{-1}. c) Obtained with a 1:10 mixture of the steroid ketone and 4-t-butylcyclohexanone in concentrations of 0.0278 and 0.278 mol·l^{-1}.

steroid ketone to those for 4-t-butylcyclohexanone. It is clearly seen from the results in Table 2 that the high reactivity of the steroid ketones on palladium is largely due to their unusually strong adsorption to the catalyst and not to their kinetic rates of hydrogenation. Such strong adsorption as observed on palladium was not seen with iridium where the strength of adsorption is not much different between 5α-cholestan-3-one and 4-t-butylcyclohexanone. In connection with these findings, it is noted that Chihara and Tanaka have recently observed an attractive interaction of alkyl substituents with palladium in the hydrogenation of 4-alkyl-substituted cyclohexanones in cyclohexane.[2b)]

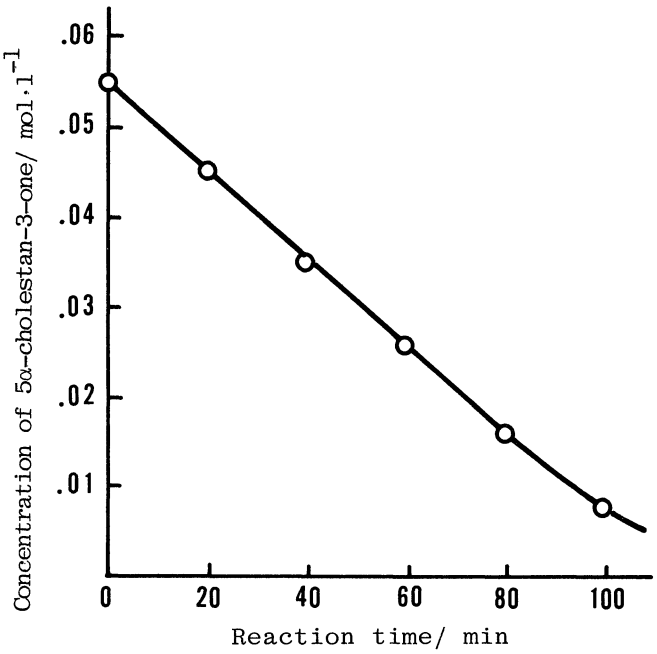

Fig. 1. Decrease in the concentration of 5α-cholestan-3-one with reaction time during hydrogenation on Pd (5 mg) in t-BuOH (1.4 ml) at 26°C and 1 atmH_2.

If we assume that the strong adsorption of the steroid ketones to palladium results from an attractive interaction of the steroid α-face with the surface of palladium catalyst, the unusual stereochemistry of hydrogenation observed over this metal (see Table 2)[1)] can easily be explained. Thus, both 5α- and 5β-cholestan-3-ones would be adsorbed to the catalyst with their α-faces and under

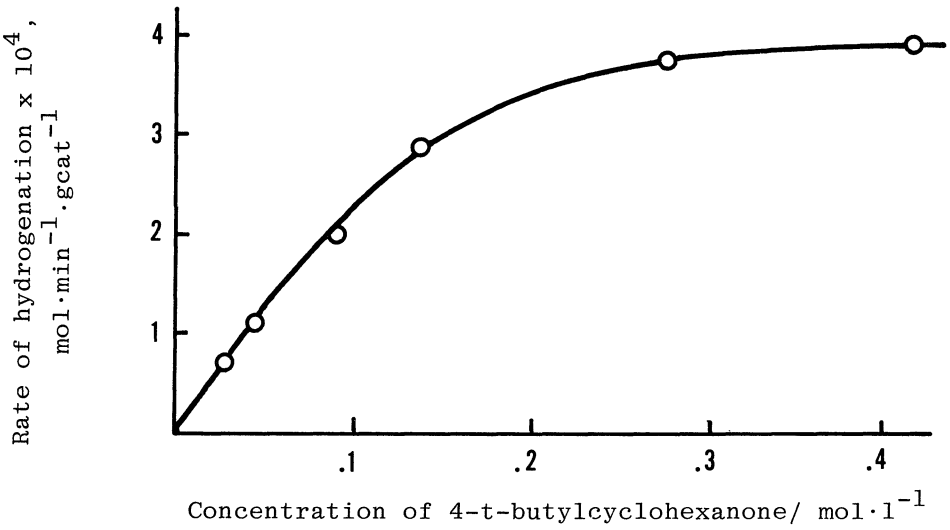

Fig. 2. Dependence of the rate of hydrogenation of 4-t-butylcyclohexanone upon concentration (Pd catalyst; t-BuOH solvent; 26°C; 1 atmH_2). Each circle in the figure was obtained with individual experiments employing the initial rate method.

Table 2. Rates of Hydrogenation of Individual Ketones and Related Data[a)]

Catalyst	Ketone	10^4k mol·min^{-1}·gcat^{-1}	k/k_{Bu}	R/R_{Bu}	b/b_{Bu}	Selectivity to 3β-ol, %
Pd	5α-Cholestan-3-one	1.43	0.37	30	81	98
	5β-Cholestan-3-one	1.03	0.27	17	63	95
	4-t-Butylcyclohexanone	3.89	-	-	-	-
Ir	5α-Cholestan-3-one	3.25	0.27	0.39	1.4	74
	4-t-Butylcyclohexanone	12.0	-	-	-	-

a) The rates were obtained in zero or almost zero order region in concentration in t-BuOH at 26°C and 1 atmH_2. k, R, and b indicate the rate in individual hydrogenation, the rate in competitive hydrogenation, and the adsorption coefficient, respectively.

these circumstances they would be hydrogenated preferentially by the α-attack of hydrogen to afford selectively the corresponding 3β-ols, as illustrated in Fig. 3.[4)] The result that the 5β-ketone is adsorbed less strongly than the 5α-ketone is also understandable on the basis of this model of adsorption. It is thus suggested that the stereochemistry of hydrogenation over palladium is controlled to a greater part by the attractive interaction of the α-face and palladium and only partly by a much weaker adsorption at the carbonyl group that is indicated by the results with 4-t-butylcyclohexanone (Fig. 2). With other platinum metals, the stereochemistry of hydrogenation is likely to be determined usually by the steric requirements around the 3-oxo groups, and, therefore, the results which are not contradictory to the

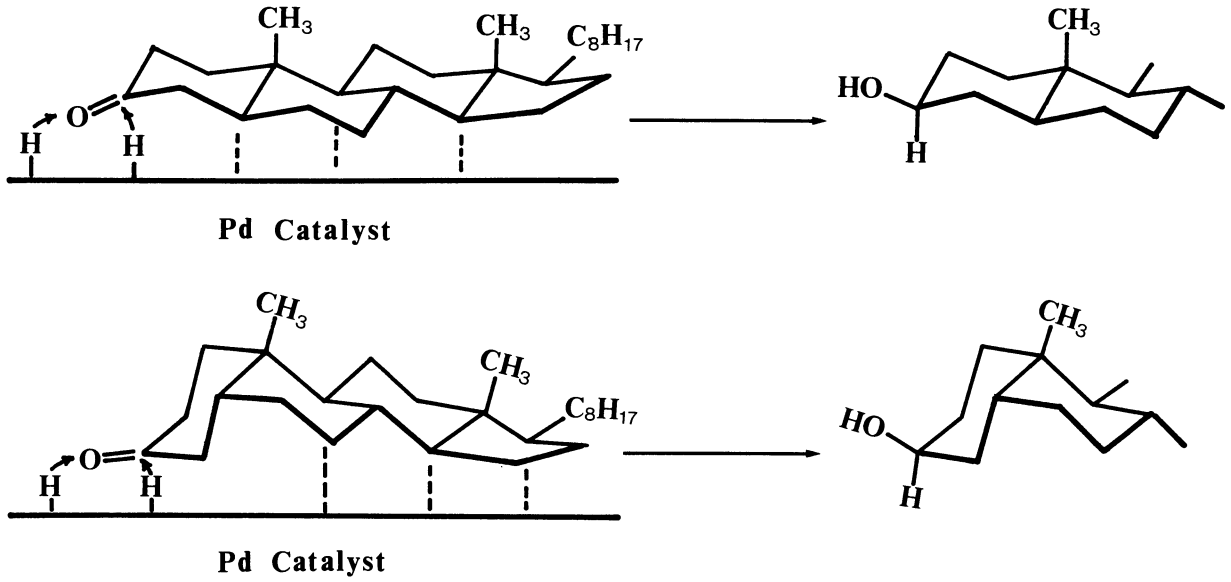

Fig. 3. Stereochemistry of the hydrogenation of 5α- and 5β-cholestan-3-ones on Pd based on the interaction of the steroid α-faces and the catalyst.

usual stereochemical outcome may be obtained.[5] The catalysts used in this study were prepared as described previously.[1] Analysis of reaction mixtures was carried out by gas chromatography.

References and Notes

1) S. Nishimura, M. Ishige, and M. Shiota, Chem. Lett., 1977, 535.
2) For the competitive hydrogenation of alicyclic ketones: a) K. Tanaka, Y. Takagi, O. Nomura, and I. Kobayashi, J. Catal., 35, 24 (1974); b) T. Chihara and K.Tanaka, Chem. Lett., 1977, 843; c) P. Geneste, M. Bonnet, and M. Rodriguez, J. Catal., 57, 147 (1979).
3) The relative reactivity of 5α-cholestan-3-one decreases in concentrations greater than 0.0278 $mol \cdot l^{-1}$ but not in higher concentrations of 4-t-butylcyclohexanone.
4) The 17β-alkyl chain of cholestan-3-ones may also contribute to the adsorption to palladium, as presumed from the results by Chihara and Tanaka,[2b] although high reactivities of 3-oxo-steroids have also been observed with 17β-hydroxy-5α- and -5β-androstan-3-ones and their acetates (unpublished observations).
5) Some unusual results in the stereochemistry of hydrogenation of 3-oxo-steroids have also been obtained with nickel and cobalt as catalysts (M. Ishige and M. Shiota, Can. J. Chem., 58, 1061 (1980)).

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