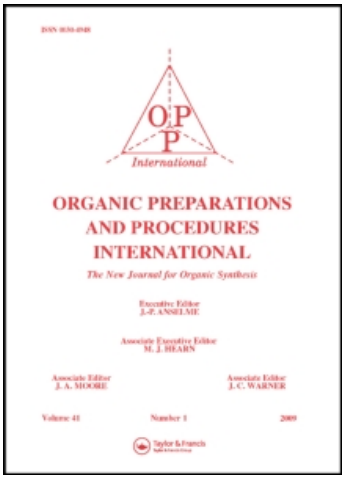

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THE PALLADIUM CATALYZED HYDROGENATION OF CHOLESTEROL

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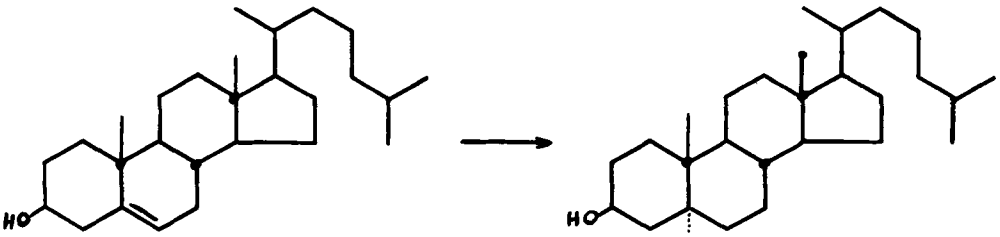

There appears to be an unwritten rule that for the hydrogenation of cholesterol and other non-conjugated Δ^5 steroids platinum is the catalyst of choice. This is rather surprising since palladium is generally a much better catalyst for the saturation of double bonds than is platinum.[2] While the hydrogenation of cholesterol over platinum leads to generally good yields of 5α-cholestanol, product isolation is sometimes rather difficult. In acetic acid acetate formation occurs, thus requiring a hydrolysis step prior to product isolation.[3] In ethyl acetate varying amounts of the 5β isomer and deoxygenated species are also formed along with the 5α product.[4]

A few examples of the use of palladium for the hydrogenation of unconjugated[5] and 19-substituted[6] Δ^5 steroids have been reported and in one instance[7] it was shown that the use of this catalyst gave better yields of product than were obtained with platinum. It has now been found that in the hydrogenation of cholesterol palladium is also superior to platinum. This hydrogenation proceeds smoothly in ethanol at room

temperature and atmospheric as well as slightly elevated pressures. The product obtained is essentially pure 5α-cholestanol. After one recrystallization over 90% of this isomer can be isolated. Examination of the C_{19}-methyl resonance peaks in the nmr spectrum of the residue left from evaporation of the mother liquors from this recrystallization shows that this residue is also the 5α product along with a small amount of cholesterol (about 1% of the total reaction product). Essentially none of the 5β isomer or deoxygenated species is present.

It thus appears that palladium is the catalyst of choice for the hydrogenation of cholesterol and, presumably, other Δ^5 steroids as well. Not only does this hydrogenation proceed readily but it also gives almost quantitatively the pure 5α product.

Experimental

5α-Cholestanol: Two grams of commercial grade cholesterol (mp 143-7°) was dissolved in 200 ml of absolute ethanol and hydrogenated over 200mg of 5% palladium on charcoal at room temperature and 30-35 psig. After 70-80% completion (about 30 min) the reaction became sluggish. The addition of fresh catalyst did not change the rate of the reaction nor the product composition. After 10 hr the catalyst was removed by filtration and the ethanol evaporated. One recrystallization of the residue from ethanol gave a 90% yield of 5α-cholestan-3β-ol, mp 140-141° (lit.[3] mp 140-141°). Examination of the nmr spectrum of the residue obtained from evaporation of the mother liquors indicated the presence of about 10% cholesterol with none of the 5β and deoxygenated species detected. The hydrogenation mixture was therefore comprised of 99% 5α-cholestanol and 1% cholesterol.

The same results were obtained with atmospheric pressure hydrogenation conditions. The use of ethyl acetate as the solvent or co-solvent with ethanol slowed the reaction considerably with at least 5% of the cholesterol remaining after 26 hr at 30-35 psig. Even in this instance, however, the saturated material formed was essentially the pure 5α isomer. Under these same conditions 5% rhodium on charcoal does not catalyze this hydrogenation.[9]

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