Zinc Reductions of Keto-steroids

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Summary Zinc reductions of keto-groups to methylene groups in such typical organic solvents as diethyl ether and benzene saturated with dry hydrogen chloride have been carried out successfully at 0° (1hr.).

WE reported[1] a useful method for conversion of keto-groups into methylene groups by using active zinc powder in acetic anhydride saturated with hydrogen chloride. In such reactions, easy reduction of keto-groups is attributable to the formation of acylium cation from acetic anhydride and dry hydrogen chloride. However, treatment of cholestan-3-one with active zinc powder in acetic anhydride–toluene-*p*-sulphonic acid (or BF_3 etherate) did not afford any reduction products. We further examined zinc reductions of keto-groups by using common organic solvents saturated with dry hydrogen chloride, without using acetic anhydride. Cholestan-3-one (100 mg.) was dissolved, with stirring, in diethyl ether (15 ml.) saturated with dry hydrogen chloride at 0°. To the resulting solution active zinc powder (1 g.) was added slowly, with ice cooling.† After having been stirred at 0° for 1 hr., the reaction mixture was treated according to the usual procedure to give a 89%

† Zinc powder was used immediately after activation with 0·5% hydrochloric acid.

yield of cholestane.[1] Zinc reductions of other keto-steroids were carried out under similar conditions. The results are summarized in the Table. In particular, diethyl ether seems to be much better for the reaction than other solvents (see the Table). Furthermore, 2α-bromo- or -acetoxy-cholestan-3-one can be reduced to cholestane, in contrast to the usual reduction of an α-halogeno- or -acetoxy-ketone with zinc powder in acetic acid (or hydrochloric acid) leading to the corresponding ketone.[3]

Zinc reductions of keto-steroids (0°, 1 *hr.*)

Ketone	Solvent[a]	Product	Yield (%)
Cholestan-3-one	Diethyl ether	Cholestane	89
	Tetrahydrofuran	Cholestane	44
	Benzene	Cholestane	64
		3-Chlorocholestane	21
	n-Hexane[b]	Cholestane	57
		3-Chlorocholestane	8
2α-Bromocholestan-3-one	Diethyl ether	Cholestane	85
α-Acetoxycholestan-3-one[c]	Diethyl ether	Cholestane	79
Androstane-3,17-dione	Diethyl ether	Androstane	75

[a] Methanol and ethyl acetate are not good as solvents.
[b] Starting material was recovered (30%).
[c] A mixture of 2α- and 4α-acetoxycholestan-3-one (1 : 1)[2].

The mechanism of the above reduction, which must be carried out under anhydrous conditions, may be essentially similar to that of a Clemmensen reduction.

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[3] H. O. House, "Modern Synthetic Reactions," Benjamin, New York, 1965, p. 56.