Zinc Reductions of Keto-steroids

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DURING our studies of the transformation of daphniphylline into the other minor alkaloids isolated from the same plant, we found a useful method to convert keto-groups into methylene groups in a Clemmensen-type reduction.[1]

In the field of keto-steroids, we have examined such reduction methods to find the scope and the optimum conditions for the conversion of keto-groups into methylene groups by active zinc powder in acetic anhydride saturated with hydrogen chloride.

To cholestan-3-one (250 mg.), a typical keto-steroid, in acetic anhydride (10 ml.) saturated with hydrogen chloride gas a large amount of active zinc powder (2·5 g.) was added slowly at 0°. The reaction solution was stirred at room temperature for 10 hr. Since self-condensation reactions of acetic anhydride take place at room temperature, the reaction was carried out also with stirring at 0° for 6 hr. Zinc reductions of several keto-steroids were carried out under these conditions. The results are summarized in the Table.

TABLE. *Zinc reductions of keto-steroids*

Ketone	Product	Yield (%)
Cholestan-3-one	Cholestane	85[a]
Cholestan-3-one	Cholestane	87[b]
3β-Acetoxycholestan-6-one	3β-Acetoxycholestane	54[a]
3β-Acetoxycholestan-6-one	3β-Acetoxycholestane	35†[b]
17β-Acetoxyandrostan-3-one	17β-Acetoxyandrostane	79[a]
3β-Acetoxy-5α-pregnan-20-one	3β-Acetoxy-5α-pregnane	70[a]
Androstane-3,17-dione	Androstane	50[a]
Androstane-3,17-dione	Androstan-17-one	67[b]
	Androstane	15[b]

[a] At room temperature for 10 hr. [b] At 0° for 6 hr.
† Starting material was recovered (60%).

As reported in the previous paper,[1] this reduction system seems to be very convenient to selective reductions of less hindered keto-groups to methylene groups. In case of androstane-3,17-dione, a carbonyl group at C-3 can be reduced easily, but the one at C-17 is less reactive.

The mechanism of this reduction is probably similar to that of a Clemmensen reduction.[2] The formation of an acyl cation from acetic anhydride and hydrogen chloride plays an important role in ease of the former reduction.

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[1] S. Yamamura, H. Irikawa and Y. Hirata, *Tetrahedron Letters*, 1967, in the press.

[2] H. O. House, "Modern Synthetic Reactions," Benjamin, New York, 1965, p. 58. In the case of zinc reduction of androstane-3,17-dione, a small amount of 17β-acetoxyandrostane was obtained.