

Zinc Reductions of Keto-steroids

By S. YAMAMURA,* S. UEDA, and Y. HIRATA

(Chemical Institute, Nagoya University, Chikusa, Nagoya, Japan)

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 |
| 3 β -Acetoxycholestan-6-one | 3 β -Acetoxycholestane | 54 ^a |
| 3 β -Acetoxycholestan-6-one | 3 β -Acetoxycholestane | 35 ^{†b} |
| 17 β -Acetoxyandrostane-3-one | 17 β -Acetoxyandrostane | 79 ^a |
| 3 β -Acetoxy-5 α -pregnan-20-one | 3 β -Acetoxy-5 α -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.

We thank Dr. K. Okabe, Shionogi Pharmaceutical Co., Ltd., for providing us with keto-steroids.

(Received, August 24th, 1967; Com. 911.)

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 17 β -acetoxyandrostane was obtained.