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## Deoxygenation of Some 3-Oxo-steroids by Chlorotrimethylsilane and Zinc

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 $5\alpha$ -Cholestan-3-one reacted with chlorotrimethylsilane and zinc dust in ether or tetrahydrofuran to give  $5\alpha$ -cholest-2-ene.  $17\beta$ -Acetoxy- $5\alpha$ -androstan-3-one and methyl 3-oxo- $5\beta$ -cholanate behaved similarly, but examples of 6-, 7-, 12-, 17-, and 20-oxo-steroids did not react. Diones containing a 3-oxo-group reacted selectively at the 3-position.

MOTHERWELL recently reported <sup>1</sup> that ketones can be deoxygenated to olefins by treatment with an excess of chlorotrimethylsilane and zinc in ether. Cyclohexanone, for example, gave cyclohexene in 72% yield when treated with the reagent for 18 h in ether at 25°. We report here the action of this reagent on some steroid ketones.

yields. Deoxygenation also occurred when tetrahydro-furan was the solvent and use of this solvent at reflux temperature (65°) allowed a good yield to be obtained in 20 h. Under the latter conditions other 3-ketones and examples of 6-, 7-, 12-, 17-, and 20-ketones were treated with the reagent. 17 $\beta$ -Acetoxy-5 $\alpha$ -androstan-3-one gave 17 $\beta$ -acetoxy-5 $\alpha$ -androst-2-ene in 53% yield and

Table
Reactions of oxo-steroids with chlorotrimethylsilane-zinc dust

Conditions				
Solvent	Temp.	Time (h)	Major product(s)	Yield (%) a
Et <sub>o</sub> O		72	1	69
		48		56
THF			5α-Cholest-2-ene	ca. 70 b
THF	65	6		ca. 50 b
THF	65	20		69
THF	65	20	17β-Acetoxy-5α-androst-2-ene	53
THF	65	20	Methyl 5β-chol-2- and -3-enate	37
THF	65	20	) , ,	
THF	65	20		
THF	65	20	No reaction c	
THF	65	20		
THF	65	20	}	
THF	40	120	$5\alpha$ -Cholest-2-en-6-one	61
THF	21	168	$5\alpha$ -Cholest-2-ene-7-one	72
THF	65	20	No reaction <sup>c</sup>	
THF	21	216	5α-Androst-2-en-17-one	60
THF	65	20	$5\alpha$ -Pregnan-2-en-20-one	67
	Solvent Et.2O Et.2O THF			Solvent         (°C)         (h)         Major product(s)           Et <sub>2</sub> O         21         72           Et <sub>2</sub> O         35         48           THF         21         96           THF         65         6           THF         65         20           THF         5α-Cholest-2-en-6-one           5α-Cholest-2-ene-7-one         No reaction $^c$ THF         21         168         5α-Cholest-2-ene-7-one           THF         21         216         5α-Androst-2-en-17-one

<sup>6</sup> Of crystalline material unless indicated otherwise. <sup>b</sup> Estimated from <sup>1</sup>H n.m.r. spectrum of crude product. <sup>c</sup> In each case where no reaction occurred, <sup>1</sup>H n.m.r. and t.l.c. analysis of the crude product indicated that it was starting material. This was recrystallised (at least 70% recovered) and its identification confirmed by m.p., mixed m.p., and spectral data. <sup>d</sup> 12-ketone. <sup>e</sup> 17-ketone.

Our results are summarised in the Table. Treatment of  $5\alpha$ -cholestan-3-one with the reagent in ether, the solvent used by Motherwell, gave  $5\alpha$ -cholest-2-ene (together with a small amount of  $5\alpha$ -cholest-3-ene), but long reaction periods were required to obtain good

methyl 3-oxo-5 $\beta$ -cholanate gave a mixture of methyl 5 $\beta$ -chol-2- and -3-enates in 37% yield. None of the other substrates reacted. This suggested that diones containing a 3-oxo-group react selectively at this position,

<sup>&</sup>lt;sup>1</sup> W. B. Motherwell, J.C.S. Chem. Comm., 1973, 935.

and to test this we treated several diones with the reagent. 5α-Cholestane-3,6-dione, 5α-cholestane-3,7-dione,  $5\alpha$ -androstane-3,17-dione, and  $5\alpha$ -pregnane-3,20dione all reacted selectively to give the corresponding  $\Delta^2$ -steroids in good yield. Some of these reactions were carried out below 65° to increase the chance of selectivity. Surprisingly, methyl 3,12-dioxo-5β-cholanate did not react. The olefinic products were identified by spectroscopic methods and by hydrogenation.

In summary, chlorotrichloromethylsilane-zinc provides a one-step method for deoxygenating 3-ketones to olefins under mild neutral conditions and for doing so selectively in the presence of other oxo-groups. Also, the deoxygenation reaction followed by hydrogenation provides a mild neutral alternative to the Clemmensen reduction <sup>2</sup> which is selective for 3-ketones. In the present work  $5\alpha$ -cholestan-6-one,  $5\alpha$ -cholestan-7-one,  $5\alpha$ -androstan-17-one, and  $5\alpha$ -pregnan-20-one have been obtained in this way.

The mechanism of the deoxygenation reaction is probably closely related to that of the Clemmensen reduction.3 The 3-ketones are the least hindered of those studied in the present work and the selectivity of the reaction suggests that it proceeds through a very bulky intermediate such as (I). This may be formed via the radical anion of the ketone and may react further to give a carbenoid 1,4 which inserts into a neighbouring C-H bond to yield an olefin.5

## EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Optical rotations were measured for solutions in chloroform. <sup>1</sup>H N.m.r. spectra were recorded at 60 MHz for ca. 10% solutions in deuteriochloroform containing tetramethylsilane as internal reference. Tetrahydrofuran was distilled from calcium hydride and stored over molecular sieves. The zinc dust used was obtained from Hopkin and Williams.

Deoxygenation of 5α-Cholestan-3-one.—5α-Cholestan-3one (2.50 g, 6.4 mmol) in tetrahydrofuran (THF) (20 ml) was added to a stirred suspension of zinc dust (4.80 g, 73 mmol) in tetrahydrofuran (10 ml) containing chlorotrimethylsilane (4.00 g, 37 mmol). The mixture was stirred and heated under reflux for 20 h, cooled, and filtered. The filtrate was evaporated to dryness and the residue in ether was washed with sodium hydrogen carbonate solution and water, dried (MgSO<sub>4</sub>), and evaporated to give the crude product (2.3 g), a clear oil. T.l.c. indicated

- <sup>2</sup> W. Reusch in 'Reduction,' ed. R. L. Augustine, Dekker, New
- York, 1968, p. 186.

  3 H. O. House, 'Modern Synthetic Reactions,' 2nd edn.,
- Benjamin, California, 1972, p. 166.

  4 I. Elphimoff-Felkin and P. Sarda, Chem. Comm., 1969, 1065. <sup>5</sup> W. Kirmse in 'Carbene Chemistry,' Academic Press, 1971,
- ch. 7.

  <sup>8</sup> G. M. L. Cragg, C. W. Davey, D. N. Hall, G. D. Meakins, E. E. Richards, and T. L. Whateley, J. Chem. Soc. (C), 1966, 1266.

  <sup>7</sup> H. Bockova and K. Syhora, Coll. Czech. Chem. Comm., 1966,

that this was largely a mixture of olefin and starting material. 1H N.m.r. analysis confirmed this and showed that the reaction yield was ca. 70%. The crude product in ether was chromatographed over alumina to give an olefinic fraction (1.80 g). Comparison of the olefinic region of the <sup>1</sup>H n.m.r. spectrum of this fraction with the spectra of authentic 5α-cholest-2- and 3-enes indicated that the fraction contained the 2-ene (ca. 95%) and the 3-ene (ca. 5%). Recrystallisation from ethanol gave  $5\alpha$ -cholest-2-ene (1.60 g, 69%), m.p.  $70-72^{\circ}$  (lit.,  $^{6}$   $75^{\circ}$ ),  $[\alpha]_n^{21} + 65^\circ$  (c 1.0) (lit.,  $^6 + 64^\circ$ ), identical with an authentic sample.

Other Reactions in the Table.—The substrates, obtained commercially or prepared by standard methods, were treated with the reagent under conditions given, the scale and the procedure being similar to those described above. The following olefinic products were obtained from reactions in which deoxygenation occurred: (a) 17β-acetoxy-5αandrost-2-ene, m.p. 95-95.5° (from ethanol) (lit.,7 94°), [ $\alpha$ ]<sub>D</sub><sup>21</sup> +48° (c 1·7) (lit., 7 +49°),  $\nu$ <sub>max.</sub> (Nujol) 1740 and 1660 cm<sup>-1</sup>,  $\delta$  0·76 and 0·78 (18- and 19-H), and 5·65br (2H, d, olefinic): (b) a mixture of methyl  $5\beta$ -chol-2- and 3-enates, m.p. 45—50°,  $v_{\text{max}}$  (CS<sub>2</sub>) 1740, 678, and 660 cm<sup>-1</sup>; analysis of the i.r. spectrum 8 indicated that the sample contained both the  $\Delta^2$ - and the  $\Delta^3$ -isomer and comparison of the <sup>1</sup>H n.m.r. spectrum of the mixture with that of authentic methyl 5 $\beta$ -chol-3-enate 8 suggested that the ratio of  $\Delta^2$ - to  $\Delta^3$ -isomer was 20:80; (c)  $5\alpha$ -cholest-2-en-6-one, m.p. 98—100° (from ethanol-chloroform) (lit.,  $^9$  105°),  $[\alpha]_{D}^{21}$  $+31^{\circ}$  (c 1.8) (lit., 9 +30°),  $\nu_{\rm max}$  (CCl<sub>4</sub>) 1705 cm<sup>-1</sup>,  $\delta$  0.73 and 0.76 (18- and 19-H), and 5.68br (2H, d, olefinic); (d)  $5\alpha$ -cholest-2-en-7-one, m.p.  $98-100^{\circ}$  (from methanol) (lit.,  $^{10}$   $156-158^{\circ}$ ),  $[\alpha]_{D}^{21}$   $-12\cdot5^{\circ}$  (c  $1\cdot2$ ) (lit.,  $^{10}$   $-16\cdot7^{\circ}$ ),  $\nu_{\rm max.}$  (CCl<sub>4</sub>) 1700 and 1660 cm<sup>-1</sup>,  $\delta$  0.64 (18-H), 0.80 (19-H), and 5.58br (2H, d, olefinic) (a sample of this enone prepared by us, using essentially the literature method, 10 had m.p.  $99-100^{\circ}$ ); (e)  $5\alpha$ -androst-2-en-17-one, m.p.  $103-105.5^{\circ}$  (from methanol) (lit.,  $^{7}$   $106-107^{\circ}$ ),  $[\alpha]_{D}^{20}$  $+140^{\circ}$  (c 1·2) (lit.,  $^{7}+140^{\circ}$ ),  $\nu_{\rm max.}$  (Nujol) 1750 and 1660 cm<sup>-1</sup>, 8 0.80 (18-H), 0.88 (19-H), and 5.64br (2H, d, olefinic); and (f) 5α-pregn-2-en-20-one, m.p. 118-121° (from methanol) (lit.,  $^7$  120—125°),  $[\alpha]_D^{20}$  + 143° (c 1·3) (lit.,  $^7$  + 147°),  $\nu_{\rm max.}$  (Nujol) 1710 and 1660 cm<sup>-1</sup>,  $\delta$  0.64 (18-H), 0.79 (19-H), 2·12 (21-H), and 5·67br (2H, d, olefinic).

Hydrogenation Reactions.—The olefinic products were hydrogenated in ethanol at 21° and 1 atm over palladiumcharcoal. This gave the following products: 5α-cholestane (yield of recrystallised material from hydrogenation, 47%), m.p. 77·5—78·5° (lit.,  $^{11}$  80°),  $[α]_p^{20}$  +21° (c 1·1) (lit.,  $^{11}$  +24°); 17β-acetoxy-5α-androstane (88%), m.p.  $73-74\cdot5^{\circ}$  (lit.,  $^{12}$   $72-75^{\circ}$ ),  $[\alpha]_{D}^{21}$   $+4^{\circ}$  (c 1·4) (lit.,  $^{12}$   $+5^{\circ}$ ); methyl 5β-cholanate (63%), m.p. 85—86·5° (lit.,  $^{13}$  86—87°),  $[\alpha]_{\rm p}^{21}$  +25° (c 1·3) (lit.,  $^{13}$  +23°); 5α-cholestan-6-one (87%), m.p. 93—94° (lit.,  $^{14}$  98°),  $[\alpha]_{\rm p}^{21}$  -4° (c 1·4) (lit.,  $^{14}$ 

- 8 C. H. Issidorides, M. Fieser, and L. F. Fieser, J. Amer. Chem. Soc., 1960, 82, 2002.
  L. Blunschy, E. Hardegger, and H. L. Simon, Helv. Chim.
- Acta, 1946, 29, 199.
- 10 A. R. Davies and G. H. R. Summers, J. Chem. Soc. (C), 1967,
- <sup>11</sup> D. H. R. Barton and J. D. Cox, J. Chem. Soc., 1948, 783. <sup>12</sup> G. Rosenkranz, S. Kaufmann, and J. Romo, J. Amer. Chem.
- Soc., 1949, 71, 3689.

  13 L. F. Fieser and R. Ettorre, J. Amer. Chem. Soc., 1953, 75,
- 14 C. W. Shoppee, R. H. Jenkins, and G. H. R. Summers, J. Chem. Soc., 1958, 1657.

 $-7^{\circ});~5\alpha\text{-cholestan-7-one}~(67\%),~\text{m.p.}~111-113^{\circ}~(\text{lit.,}^{15}~113\cdot5-115^{\circ}),~[\alpha]_{\text{D}}^{~22}~-44^{\circ}~(c~1\cdot3)~(\text{lit.,}^{15}~-47^{\circ});~5\alpha\text{-androstan-17-one}~(80\%),~\text{m.p.}~117-119^{\circ}~(\text{lit.,}^{16}~120-121^{\circ}),$ 

O. Wintersteiner and M. Moore, J. Amer. Chem. Soc., 1950, 72, 1923.
 L. Ruzicka and A. C. Muhr, Helv. Chim. Acta, 1944, 27, 503.

 $\text{[$\alpha$]}_{\text{\tiny D}}^{21}$   $+87^{\circ}$  (c 1·0) (lit., ^16 +88°); and 5\$\alpha\$-pregnan-20-one (78%), m.p. 132—134° (lit., ^1 136—137°), [\$\alpha\$]\_{\text{\tiny D}}^{21}  $+96^{\circ}$  $(lit., 17 + 100^\circ)$ .

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 $^{17}$  J. Romo, M. Romero, C. Djerassi, and G. Rosenkranz,  $\emph{J.}$   $\emph{Amer. Chem. Soc.},$  1951, 73, 1528.