## Steroids. Part XXXII.<sup>1</sup> Epoxidation of $3\beta$ -Acetoxy- $5\alpha$ -lanosta-7,9(11)diene

By C. W. Shoppee \* and J. C. Coll, Department of Organic Chemistry, The University of Sydney, Sydney 2006, New South Wales, Australia

Epoxidation of 3β-acetoxy-5α-lanosta-7,9(11)-diene with m-chloroperbenzoic acid or monoperphthalic acid gives the  $\Delta^{\mathfrak{g}(11)}$ -7 $\alpha$ ,8 $\alpha$ -epoxide, the  $\Delta^{\mathfrak{g}(11)}$ -7 $\beta$ ,8 $\beta$ -epoxide, and the  $\Delta^7$ -9 $\alpha$ ,11 $\alpha$ -epoxide. The compound, described in the literature as a  $\Delta^{-(9)11}7\xi,8\xi$ -epoxide, is shown to be the  $\Delta^7$ -9 $\alpha$ ,11 $\alpha$ -epoxide.

IN Part XXXI,<sup>1</sup> we described the conversion of 3β-acetoxy- $5\alpha$ -lanosta-7,9(11)-diene by treatment with mchloroperbenzoic acid (1 mol.) into the  $\Delta^{9(11)}$ -7 $\beta$ ,8 $\beta$ epoxide (m.p. 177°) (I) and the  $\Delta^7$ -9 $\alpha$ ,11 $\alpha$ -epoxide (m.p. 187°) (II), which were then isomerised by boron trifluoride to, respectively, the  $\Delta^{8}$ -7-ketone (III) and to a mixture of the  $\Delta^7$ -11-ketone (IV) and the  $\Delta^8$ -11-ketone (V). Jeger *et al.*<sup>2</sup> by treatment of  $3\beta$ -acetoxy- $5\alpha$ lanosta-7,9(11)-diene with an excess of monoperphthalic acid isolated an epoxide (m.p. 184°), which they regarded as a  $\Delta^{9(11)}$ -7,8-epoxide since treatment of the reaction product with boron trifluoride yielded the  $\Delta^{8}$ -7-ketone (III). We have reinvestigated the reaction of the 7,9(11)-diene with *m*-chloroperbenzoic acid and with monoperphthalic acid, and show that the compound, m.p. 184°, is the  $\Delta^{7}$ -9 $\alpha$ , 11 $\alpha$ -epoxide (II) (cf. ref. 3).



 $3\beta$ -Acetoxy- $5\alpha$ -lanosta-7,9(11)-diene with *m*-chloroperbenzoic acid (1 mol.) yielded three products by t.l.c. on silica. Column chromatography on neutral alumina<sup>4</sup> gave unchanged diene and the epoxides (I) and (II) in approximately equal amounts. The third, most polar, product was unstable under these chromatographic conditions, but was isolated by crystallisation of the

crude epoxide mixture from ether, which removed most of the epoxide (II), followed by preparative t.l.c. on silica. This furnished the  $\Delta^{9,11}$ -7 $\alpha$ ,8 $\alpha$ -epoxide (m.p.  $158-160^{\circ}$  (VI), converted by treatment with boron trifluoride in benzene at 20° for 72 hr. into the  $\Delta^{8}$ -7ketone (III).

Treatment of  $3\beta$ -acetoxy- $5\alpha$ -lanosta-7,9(11)-diene with monoperphthalic acid and t.l.c. on silica of the product gave the same three epoxides (I), (II), and (VI). A study was made to determine what effect the peracid concentration had on the product ratio; small quantities of the diene were treated under the same conditions<sup>2</sup> with 0.6M-, 0.9M-, 1.2M-, 1.5M-, and 2.0M-mono-perphthalic acid, and the crude reaction products were examined by g.l.c. The results and the retention times of the diene and the three epoxides (I), (II), and (VI) are given in the Table.

				Katio
	Peracid	Diene	Epoxides	(II)
Expt.	(mol.)	(%)	<b>^</b> (%)	(I) + (VI)
(1)	0.6	60	40	1:2
(2)	0.9	40	60	1:3
(3)	$1 \cdot 2$	25	75	1:5
(4)	1.2	5	95	1:5
(5)	$2 \cdot 0$	0	100	1:5
Retention	1			
times on		Epoxide	Epoxide	Epoxide
XE60	} Diene	(I)	-(II)	(VI)
column at	4.0	11.5	8.5	$11 - 11 \cdot 5$
260° (min.)				

The crude reaction products from experiments (4) and (5) were combined and recrystallised twice from ether to give the nearly pure epoxide (II).

These results strongly suggest that Jeger *et al.*<sup>2</sup> isolated the  $\Delta^7$ -9 $\alpha$ , 11 $\alpha$ -epoxide (II) by crystallisation from ether. On the assumption that only one epoxide was formed, Jeger et al.<sup>2</sup> incorrectly identified their product as a  $\Delta^{9(11)}$ -75,85-epoxide, (I) or (VI), on the basis of the boron trifluoride-isomerisation of their crude reaction product to the  $\Delta^{8}$ -7-ketone (III). The crude reaction product, obtained with monoperphthalic acid, by isomerisation with boron trifluoride at 20° for 72 hr., column chromatography on alumina, and recrystallisation from methylene chloride-methanol<sup>2</sup>, in fact readily gave the  $\Delta^{8}$ -7-ketone (m.p. 146°) (III) as reported,<sup>2</sup> whilst the  $\Delta^{8}$ -11-ketone (V) failed to crystallise from methylene chloride-methanol; as shown by Table 1,

<sup>8</sup> M. J. Birchenough and J. F. McGhie, J. Chem. Soc., 1950,

1249. <sup>4</sup> T. Reichstein and C. W. Shoppee, Discuss. Faraday Soc., 1949, 305.

<sup>&</sup>lt;sup>1</sup> C. W. Shoppee, J. C. Coll, and R. E. Lack, J. Chem. Soc. (C), 1968, 1581.
<sup>2</sup> M. V. Mijovic, W. Voser, H. Heusser, and O. Jeger, *Helv.*

Chim. Acta, 1952, 35, 964.

the crude product contained >80% of the epoxides, (I) and (VI), giving, by rearrangement, the  $\Delta^{8}$ -7-ketone (III).

## EXPERIMENTAL

For general experimental directions see J. Chem. Soc., 1959, 345. M.p.s were determined on a Kofler hot-stage apparatus and are corrected. N.m.r. spectra were measured with Varian A60 and HA100 instruments with deuteriopyridine as solvent and tetramethylsilane as internal reference. Column chromatography was performed with silica gel (Davison), neutralised aluminium oxide,4 or aluminium oxide (Spence, type H, activity II). T.l.c. was carried out on silica, plates being sprayed with concentrated sulphuric acid and developed at 110°. For preparative t.l.c., plates were sprayed with berberine hydrochloride and examined under u.v. light. G.l.c. was performed on an F and M 400 instrument fitted with a disc integrator with a column 1.75 m.  $\times$  3 mm. (diam.) packed with 1% silicone rubber (nitrile) XE60 on an acid-washed 100-140 mesh silanised Gas Chrom P at 260°; the injection port and detector temperatures were ca. 60° higher than the column temperature, and helium was used as the carrier gas at a flow rate of 75 ml./min.

Epoxidation of  $3\beta$ -Acetoxy-5 $\alpha$ -lanosta-7,9(11)-diene.-(a) The diene (400 mg.) was treated with m-chloroperbenzoic acid (200 mg., 1 mol.) in chloroform (40 ml.) at 0° for 24 hr. The product, isolated in the usual way, was shown by t.l.c. on silica in ether-hexane (1:19) to consist of three components in addition to unchanged diene. Column chromatography on neutralized alumina<sup>4</sup> in hexane afforded by elution with hexane unaltered diene (100 mg.), m.p. and mixed m.p. 169° from methanol. Further elution with hexane gave 3β-acetoxy-7β,8β-epoxy-5α-lanost-9(11)-ene<sup>1</sup> (I) (105 mg.), m.p. 177-178° (from ether), whilst elution with ether-hexane (1:49) yielded 3 $\beta$ -acetoxy-9 $\alpha$ , 11 $\alpha$ -epoxy-5α-lanost-7-ene<sup>1</sup> (90 mg.) m.p. 187-188° (from ether). Further elution with more polar solvents furnished none of the third product, and unidentified residues from such eluates totalled 100 mg.; compounds of similar polarity arose when ether solutions of any of the epoxides were allowed slowly to evaporate in air, or on prolonged chromatography on alumina.

(b) The diene (400 mg.) was treated with *m*-chloroperbenzoic acid (500 mg., 2.5 mol.) as above until all diene had been consumed as indicated by t.l.c. on silica in etherhexane (1:19). The product, isolated in the usual manner, dissolved in ether, was allowed to crystallise at 0°. The crystals were filtered off; the volume of the filtrate was reduced to one half, and the concentrate was set aside at 0°. The crystals were again removed, the filtrate was evaporated, and the residue was submitted to preparative t.l.c. on silica in ether-hexane (1:19). The appropriate region of the plate was removed, extracted with ether, and the product was recrystallised from methanol containing a trace of View Article Online

pyridine <sup>5</sup> to give  $3\beta$ -acetoxy- $7\alpha$ , $8\alpha$ -epoxy- $5\alpha$ -lanost-9(11)-ene (VI) (30 mg.), m.p. 158—160° [Found: M (mass spectrometry), 484·3918,  $C_{32}H_{52}O_3$  requires M, 484·3916]; the mass spectrum showed the parent peak (100%), and a peak at M-15 (99%); n.m.r. spectrum:  $\tau$  4·4 (vinyl 11-H), 5·2 (3 $\alpha$ -H), and 6·6 ( $W_{\rm H}$  5 c./sec.) for one proton (7 $\beta$ -H) on carbon attached to oxygen.

(c) The diene (750 mg. in 5 equal portions) in ether (50 ml.) was treated with ethereal monoperphthalic acid [(i) 1 ml., 0.6 mol.; (ii) 1.5 ml., 0.9 mol.; (iii) 2.0 ml., 1.2 mol.; (iv) 2.5 ml., 1.5 mol.; and (v) 3.0 ml., 2.0 mol.] at 20° for 6 days. Each reaction product was examined by t.l.c. on silica in ether-hexane (1:19); products (i), (ii), and (iii) contained the same four components, whilst products (iv) and (v) contained three epoxides but no diene. Samples (5  $\mu$ g.) from each reaction product were subjected to g.l.c. with the result shown in the Table; retention times were  $\pm 0.5$  min., whilst the integral sensitivity under the operating conditions was ca.  $\pm 5\%$ .

Reaction products (iv) and (v) were combined and crystallised from ether; the first crop of crystals (100 mg.) by recrystallisation from ether furnished the  $\Delta^7$ -9 $\alpha$ , 11 $\alpha$  epoxide (II) (40 mg.), nearly homogeneous by t.l.c. on silica in etherhexane (1:19), giving, by recrystallisation, from ethyl acetate-methanol<sup>2</sup> 3 $\beta$ -acetoxy-9 $\alpha$ , 11 $\alpha$ -epoxy-5 $\alpha$ -lanost-7-ene (II) (16 mg.), m.p. and mixed m.p. 185°.

Reaction products (ii) and (iii) were combined and treated with ethereal monoperphthalic acid (3 ml., 1 mol.) until an aliquot by t.l.c. showed that all diene had disappeared. The crude product was then isomerised with boron trifluoride-ether in benzene at 20° for 72 hr.; the reaction product was isolated and chromatographed on a column of basic alumina (10 g.) in hexane. Elution with benzene-hexane (1:5) gave  $3\beta$ -acetoxy- $5\alpha$ -lanost-8-en-7-one <sup>1,2</sup> (III) (160 mg.), m.p. and mixed m.p. 145—146° (from methylene chloride-methanol).<sup>2</sup> Elution with benzene-hexane (1:2) and (1:1) gave a yellow oil; this failed to crystallise from methylene chloride-methanol, but from acetonitrile yielded  $3\beta$ -acetoxy- $5\alpha$ -lanost-8-en-11-one <sup>1,2</sup> (40 mg.) (V), m.p. and mixed m.p. 126°.

Rearrangement of  $3\beta$ -Acetoxy- $7\alpha$ , $8\alpha$ -epoxy- $5\alpha$ -lanost-9,(11)ene (VI).—The  $\Delta^{9,(11)}$ - $7\alpha$ , $8\alpha$ -epoxide (10 mg.) in benzene (5 ml.) was treated with boron trifluoride-ether (5 drops) at  $20^{\circ}$  for 72 hr. The product was identified as  $3\beta$ -acetoxy- $5\alpha$ -lanost-8-en-7-one <sup>1,2</sup> (III) by m.p. and mixed m.p. 145— 146° and by t.l.c. on silica in ether-hexane (1:4).

One of us (J.C.C) acknowledges the award of a C.S.I.R.O. Senior Research Studentship; we thank the Australian Research Grants Committee for a research grant.

## [9/647 Received, April 21st, 1969]

<sup>5</sup> J. Fried, J. W. Brown, and M. Applebaum, *Tetrahedron Letters*, 1965, 849.