Tetrahedron Letters No.48, pp. 4343-4346, 1965. Pergamon Press Ltd.
Printed in Great Britain.

FURTHER EXPERIMENTS ON THE SYNTHESIS OF 32-OXYGENATED LANOSTANE DERIVATIVES

D.H.R. Barton

Imperial College of Science and Technology,

London, S.W.7

and A. Hameed and J. F. McGhie

Chelsea College of Science and Technology,

London, S.W.3.

(Received 27 September 1965)

Two recent communications(1, 2) described the synthesis of various 32-oxygenated derivatives of lanostane from which, in principle, certain critical intermediates in cholesterol biosynthesis may be derived. The appearance of a further communication(3) on the same subject makes it desirable to report an additional approach by us to this objective. In brief our new work covers the same area as does that of Shoppee and his colleagues(3), but in certain respects we have obtained more detailed and extensive results.

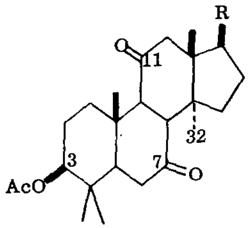
Reduction of 7:11-diketolanostanyl acetate (I, R = C_8H_{17}) with sodium borohydride in methanol gave 7β-hydroxy-11-ketolanostanyl acetate (II, R = C_8H_{17}, 7β-OH) (85-90%), m.p. (all crystallisations from $CHCl_3$-MeOH) 219-220°, $[\alpha]_D$ (all rotations in $CHCl_3$ at c = 1) + 52° and the 7-epimer (II, R = C_8H_{17}, 7α-OH) (10-15%), m.p. 270-271°, $[\alpha]_D$ + 39°. The latter compound was more readily prepared by catalytic hydrogenation of the diketone (I, R = C_8H_{17}) in 1:1-ethylacetate : glacial acetic acid over platinum oxide in the presence of perchloric acid(4). Treatment of this alcohol with pyridine and nitrosyl chloride gave the corresponding nitrite (III, X = Me, R = C_8H_{17}, R' = NO), m.p. 193-194°, $[\alpha]_D$ -35°, which on photolysis in the usual way[2,5] gave 32-oximino-7α-hydroxy-11-ketolanostanyl acetate (III, X = (CH=NOH), R = C_8H_{17}, R' = H), m.p. 190-192°, $[\alpha]_D$ +16°. Treatment of the latter with acetic anhydride containing sodium acetate under reflux gave 32-cyano--7α-hydroxy-11-ketolanostanyl acetate (III, X = CN, R = C_8H_{17}, R' = H), m.p. 246-247°, $[\alpha]_D$ +38°, and the corresponding diacetate (III, X = CN, R = C_8H_{17}, R' = Ac), m.p. 203-204°, $[\alpha]_D$ +31°. Treatment of the 7α-hydroxy-oxime (III, X = (CH = NOH), R = C_8H_{17}, R' = H) with methanesulphonyl chloride in dry pyridine at room temperature at 0 - 5° overnight gave the mesylate-nitrile (III, X = CN, R = C_8H_{17}, R' = SO_2Me), a compound well suited for further elaboration.

In a similar series of reactions 3β-acetoxy-7:11-diketotrisnorlanostanoic acid methyl ester[6] (I, R = CHMe-$(CH_2)_2$-CO_2Me) gave (with sodium borohydride) the 7β-ol (II, R = CHMe-$(CH_2)_2$-CO_2Me, 7β-OH), m.p. 208-209°, $[\alpha]_D$ +48° and (by acid catalysed hydrogenation) the 7α-ol (II, R = CHMe-$(CH_2)_2$-CO_2Me, 7α-OH), m.p. 250-251°, $[\alpha]_D$ +42°. Photolysis of the nitrite, m.p. 185-186°, $[\alpha]_D$ -38°, of the latter alcohol afforded the expected oxime (III, X = (CH = NOH), R = CHMe - (CH_2)-CO_2Me, R' = H), m.p. 249-251°, $[\alpha]_D$ +12°.

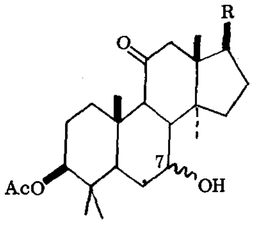
Reduction of 7:11-diketolanost-8-enyl acetate with sodium borohydride gave an alcohol, m.p. 212-214°, $[\alpha]_D$ +149°, which we formulate as (IV, R = Ac, R' = H). The compound was further characterised by hydrolysis to the diol (IV, R = R' = H), m.p. 190-192°, $[\alpha]_D$ +143° and by acetylation to the diacetate (IV, R = R' = Ac), m.p. 112-114°, $[\alpha]_D$ +123°, reduction of which with zinc dust and acetic acid afforded 11-ketolanostenyl acetate. Reduction of 7:11-diketolanost-8-

-enyl benzoate with sodium borohydride gave the monobenzoate (IV, R = Bz, R' = H), m.p. 245-247°, $[\alpha]_D$ +156°, from which the derived dibenzoate (IV, R = R' = Bz), m.p. 198-199°, $[\alpha]_D$ +151°, was prepared in the usual way.

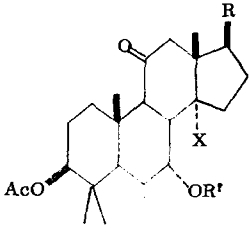
All new compounds showed the expected microanalytical, infrared, ultraviolet and, in selected cases, nuclear magnetic resonance data. We thank Dr. D.A. Lewis for assistance in preparing (1954-1957) some of the compounds not hitherto reported in the literature.



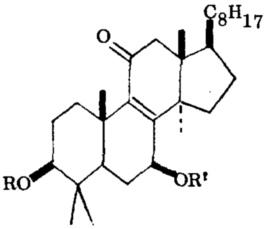
(I)



(II)



(III)



(IV)

REFERENCES

1. J. Fried, J.W. Brown and L. Borkenhagen, Tetrahedron Letters, 2499 (1965).
2. T.J. Bentley, J.F. McGhie and D.H.R. Barton, Tetrahedron Letters, 2497 (1965).
3. C.W. Shoppee, J.C. Coll, N.W. Hughes and R.E. Lack, Tetrahedron Letters, 3249 (1965).
4. D.H.R. Barton and B.R. Thomas, J.Chem.Soc., 1842 (1953).
5. D.H.R. Barton, J.M. Beaton, L.E. Geller and M.M. Pechet, J. Amer. Chem. Soc., **83**, 4076 (1961).
6. W. Voser, O. Jeger and L. Ruzicka, Helv. Chim. Acta, **35**, 497 (1952).