Tetrahedron Letters No. 36, pp. 3249-3251, 1965. Pergamon Press Ltd.
Printed in Great Britain.

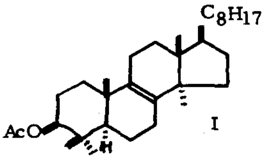
MODIFICATION OF THE 14α-METHYL GROUP IN LANOSTEROL

C. W. Shoppee, J. C. Coll, N. W. Hughes, and R. E. Lack
Department of Organic Chemistry,
University of Sydney
Sydney, Australia

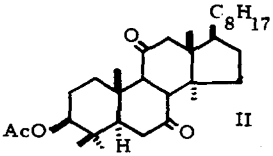
(Received 16 June 1965)

Methods for the removal of the 4-methyl groups in lanosterol have been described[1, 2, 3, 4] by its conversion to 14α-methyl-11-oxo-progesterone[2], 14α-methyltestosterone[3] and 14α-methylprogesterone[4] but functionalization of the 14α-methyl group leading to its elimination has not yet been reported.

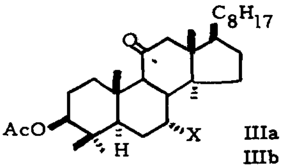
A recent publication[5] describing the attempted functionalization of the 14α-methyl group by photochemically initiated hydrogen abstraction [Barton reaction][6] with the 9α-nitrite ester of 9α-hydroxy-5α-lanostanyl acetate and similar compounds, which gave mainly 9,10-seco-steroids, has prompted us to report our successful results using the same reaction with the 7α-nitrite ester [IIIb] of 3β-acetoxy-7α-hydroxy-5α-lanostan-11-one [IIIa].



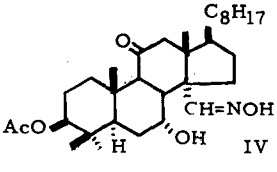
I



II



IIIa X=OH
IIIb X=ONO



IV

Lanostenyl acetate [I] was readily converted to the 7,11-diketone [II] by chromic acid oxidation[7] followed by reduction with zinc and acetic acid.[8] On catalytic hydrogenation of this diketone [II] with platinum oxide in ethyl acetate containing a few drops of perchloric acid, a 60% yield of 3β-acetoxy-7α-hydroxy-5α-lanostan-11-one [IIIa] separated from the reaction mixture, m.p. 260-261°, p.m.r.: τ 5.5 [3α-H], τ5.84 [7β-H] [W_H 6 cps.][9,10] τ 7.97 [3β-OAc], τ 8.68 [14α-Me], τ 8.94 [10β-Me], τ 9.28 [13β-Me]. Surprisingly, sodium borohydride reduction of the diketone [II] gave mainly 3β-acetoxy-7β-hydroxy-5α-lanostan-11-one, m.p. 224-226°, p.m.r.: τ 5.5 [3α-H], τ 6.4 [7α-H], [W_H 23 cps.][9,10].

Treatment of the 7α-hydroxy compound [IIIa] in pyridine with nitrosyl chloride[11] gave an almost quantitative yield of the nitrite [IIIb], m.p. 184-185°, $\nu_{max.}^{CCl_4}$ 1735 [OAc], 1700 [C=O] and 1650 cm.$^{-1}$ [ONO]; p.m.r.: τ 5.5 [3α-H], τ 4.16 [7β-H] [W_H 6 cps][9,10] τ 7.99 [3β-OAc], τ 8.87 [14α-Me], τ 8.99 [10β-Me] and τ 9.29 [13β-Me].

Photolysis of the nitrite [IIIb] in toluene[11], using a 125 watt Hanovia mercury lamp, and following the course of the reaction by thin layer chromatography, gave as the major product the oxime [IV], m.p. 196-199°, analysing correctly for $C_{32}H_{53}O_5N$, $\nu_{max.}^{CCl_4}$ 3580, 3400 [OH, NOH], 1735 [OAc] and 1710 [C=O]; p.m.r.: τ 1.92 [14α-methinealdoxime proton], τ 5.5 [3α-H], τ 5.86 [7α-H] [W_H 5 cps.][9,10] τ 7.97 [3β-OAc], τ 8.92 [10β-Me]. In addition the spectrum revealed the absence of the signal for the 14α-methyl group whilst the signal for the 13β-methyl group had moved downfield and was indistinguishable from the other methyl groups. Several minor products are still being investigated.

Further work is continuing in an attempt to remove this functional group leading to complete conversion of lanosterol to 11-oxoprogesterone, testosterone and progesterone.

We thank Dr. C.S. Barnes, Colonial Sugar Refining Co. Ltd., Sydney for a gift of commercial lanosterol.

References

1. W. Voser, O. Jeger, and L. Ruzicka, Helv. Chim. Acta, 35, 503 [1952].
2. W. Voser, H. Heusser, O. Jeger, and L. Ruzicka, Helv. Chim.Acta, 36, 299 [1953].
3. G.R. Pettit and P. Hofer, Experientia, 19, 67 [1963].
4. G.R. Pettit and P. Hofer, J. Chem. Soc., 4439 [1963].
5. J. Fried, J.W. Brown, and M. Applebaum, Tetrahedron Letters, 849 [1965].
6. D.H.R. Barton, J.M. Beaton, L.E. Geller, and M.M. Pechet, J. Amer. Chem. Soc., 82, 2640 [1960].
7. L. Ruzicka, E. Rey, and A.C. Muhr, Helv. Chim Acta, 27, 472 [1944].
8. C. Doree, J.F. McGhie, and F. Kurzer, J. Chem. Soc., 988 [1948].
9. A. Hassner and C. Heathcock, J. Org. Chem., 29, 1350 [1964].
10. C.W. Shoppee, T.E. Bellas, R.E. Lack, and S. Sternhell, J. Chem. Soc., 2483 [1965].
11. D.H.R. Barton, J.M. Beaton, L.E. Geller, and M.M. Pechet, J. Amer. Chem. Soc., 83, 4076 [1961].