CORRECTION TO MODIFIED STEROID HORMONES XXX

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In Part XXX[1] of this series the preparation of 16α,17α-cyclomethylene-19-norpregn-4-ene-3,20-dione, m.p. 169.5°, $[\alpha]_D$ +165°, was described by a route involving lithium/liquid ammonia reduction of 16α,17α-cyclomethylene-3-methoxy-19-norpregna-1,3,5(10)-trien-20-ol, followed by acid treatment of the product and regeneration of the 20-oxo function by oxidation with the Jones' reagent. Similar treatment of 16α,17α-cyclomethylene-3-methoxy-19-norpregna-1,3,5(10)-trien-20-one gave a different product, m.p. 124-126°, $[\alpha]_D$ +117°. This was assigned the structure 17α-methyl-19-norpregn-4-ene-3,20-dione as 16α,17α-cyclomethylene-3β-tetrahydropyranyloxypregn-5-en-20-one was converted by the same procedure into what appeared to be 3β-hydroxy-17α-methylpregn-5-en-20-one (acetate) on the basis of its physical properties (m.p. 182-184°, $[\alpha]_D$ -30°, lit.[2] m.p. 185-187°, $[\alpha]_D$ -31.6°).

Authentic 17α-methyl-19-norpregn-4-ene-3,20-dione (m.p.142-146°, $[\alpha]_D$ +58°) has now been prepared by Dr. M. J. Weiss *et al.*[3], and as it undoubtedly differs from our material we have now re-examined the structures of our products, with particular attention to N.M.R. data, which was not available to us in 1961.

Repetition of the above two "17α-methyl" preparations has given products unequivocally identified as 16α-methylpregnan-20-ones. In

addition, the total product resulting from lithium/liquid ammonia reduction of 16α,17α-cyclomethylene-3-methoxy-19-norpregna-1,3,5(10)-trien-20-one was oxidised with the chromium trioxide-pyridine complex when 3-methoxy-16α-methyl-19-norpregna-1,3,5(10)-trien-20-one was obtained,[4] unequivocally identified with an authentic specimen.[6]

It follows that lithium/liquid ammonia reduction (and re-oxidation) of 16α,17α-cyclomethylenepregnan-20-ones effects fission of the cyclopropane ring with formation of 16α-methylpregnan-20-ones, whilst the cyclopregnane ring of the corresponding 20-ols is stable under these conditions.

EXPERIMENTAL

N.M.R. spectra were determined on a Perkin-Elmer 40 M^{c}/s permanent magnet spectrometer in deuterochloroform with tetramethylsilane as internal standard. Optical rotations were determined on ca. 1% solutions in chloroform at room temperature.

16α-Methyl-19-norpregn-4-ene-3,20-dione.

The lithium/liquid ammonia reduction, acid treatment and chromium trioxide oxidation of 16α,17α-cyclomethylene-3-methoxy-19-norpregna-1,3,5(10)-trien-20-one (10g) was carried out as described in Part XXX[1] of this series. The product was twice chromatographed on alumina and crystallised from methanol to give 16α-methyl-19-norpregn-4-ene-3,20-dione, m.p. 131-134°, $[\alpha]_D$ +138° [the previous sample of this product[1] was impure, as evidenced by its constants and by thin layer chromatography] (lit.[6] m.p. 135-137°, $[\alpha]_D$ +143°).

The N.M.R. spectrum had 3-proton singlets at 9.29τ (C18 methyl), 7.87τ (C21 methyl) and a 3-proton doublet at 9.05τ (J=6.2 c/s) (C16α methyl).

3-Methoxy-16α-methyl-19-norpregna-1,3,5(10)-trien-20-one.

16α,17α-Cyclomethylene-3-methoxy-19-norpregna-1,3,5(10)-trien-20-one (5g) was reduced with lithium/liquid ammonia as described before. The total product, in pyridine (50 ml.), was added, at room temperature, to a suspension of the complex prepared from chromium trioxide (5g) in pyridine (50 ml.) and kept overnight at room temperature. The product, isolated in the usual way, was crystallised from ether-hexane and methanol to give 3-methoxy-16α-methyl-19-norpregna-1,3,5(10)-trien-20-one as laths, m.p. 113-115°, $[\alpha]_D$ +136.2° (lit.[6] m.p. 116-118°, $[\alpha]_D$ +143°). The N.M.R. spectrum shows singlet, 3-proton peaks at 9.33τ (C18 methyl), 7.86τ (C21 methyl) and 6.24τ (methoxyl). The C16 methyl group appears as a 3-proton doublet centred at 9.03τ (J=6.2 c/s).

3β-Acetoxy-16α-methylpregn-5-en-20-one.

The lithium/liquid ammonia reduction, chromium trioxide oxidation, acid treatment and acetylation of 16α,17α-cyclomethylene-3β-tetrahydropyranyloxypregn-5-en-20-one was carried out as described in Part XXX[1] of this series and the product was purified from acetone. It had m.p. 180-182°, $[\alpha]_D$ -16°,[7] and clearly differs (mixed m.p., I.R. and N.M.R. spectra) from 3β-acetoxy-17α-methylpregn-5-en-20-one. Its identity with 3β-acetoxy-16α-methylpregn-5-en-20-one (m.p. 182-184°, $[\alpha]_D$ -8°) was confirmed by mixed m.p. and I.R. spectrum. Its N.M.R. spectrum had 3-proton singlets at 9.34τ

(C18 methyl), 8.98τ (C19 methyl), 7.97τ (acetate) and 7.87τ (C21 methyl). The 16α-methyl group was revealed as a 3-proton doublet at 9.05τ (J=6.2 c/s), the low field component being coincident with the C19 methyl signal.

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4 Aromatisation of 3-methoxy-2,5(10)-dienes on treatment with chromium trioxide/pyridine has been reported.[5]

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7 The rotation reported[1] earlier (-30°) is in error.