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THE SYNTHESIS OF A-NOR-19-NORTESTOSTERONE

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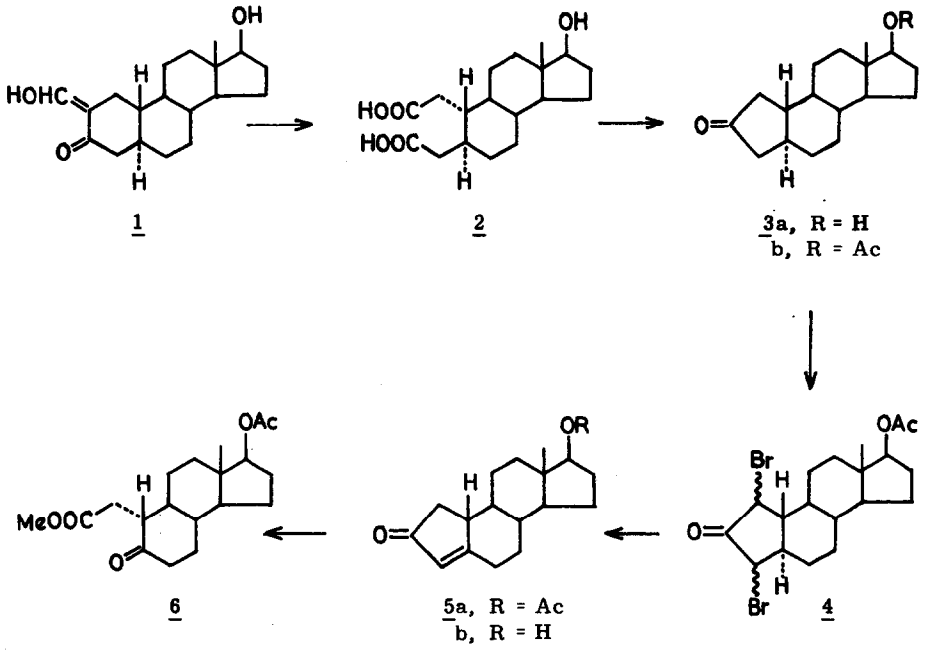
It has been shown that certain 19-norsteroids as well as A-norsteroids possess interesting biological activities.[2] It was therefore desirable to prepare steroids lacking a carbon atom both at C-19 and in ring-A. We now describe the synthesis of A-nor-19-nortestosterone (5b), an example of a hormone analogue of this type.[3]

2-Hydroxymethylene-19-norandrostan-17β-ol-3-one (1)[4] was ozonised in acetic acid and ethyl acetate at -10°, and then oxidised with hydrogen peroxide. The resulting 2,3-seco di-acid 2 (m.p. 205-207°) was subjected to the Blanc reaction (1 hr. reflux with acetic anhydride, followed by evaporation and pyrolysis at 260° for 25 min.). Saponification with ethanolic potassium hydroxide then gave 17β-hydroxy-A-nor-19-norandrostan-2-one-17β-ol (3a) (m.p. 166-167°).

The corresponding 17-acetate (3b) (m.p. 83-85°) on bromination with two molar equivalents of bromine in acetic acid yielded the 1ξ,3ξ-dibromide (4)[5] (m.p. 132-135°), which was treated with sodium iodide in boiling acetone and then reduced with chromous chloride.[6] The resulting A-nor-19-nortestosterone acetate (5a) [m.p. 121-123°, $\lambda_{max.}$ (EtOH)233mμ (ε 16,300)] was saponified to A-nor-19-nortestosterone (5b) [m.p. 163-165°, $\lambda_{max.}$ (EtOH) 234mμ (ε 16,500)].

The spectral data of 5a (UV, IR, NMR, ORD and mass spectra) were in accord with the assigned structure, but were also compatible with the alternative $\Delta^{1(10)}$-2-keto formulation. The structure 5a was established in the following way. Ozonolysis of 5a in acetic acid and ethyl acetate at -20°, followed by treatment with hydrogen



peroxide and then with diazomethane, led to the keto-ester 6 (m.p. 151-153°). This substance was identified by direct comparison with an authentic sample.[7] Treatment of 6 with ethylene glycol and p-toluenesulphonic acid in boiling benzene gave the corresponding cycloethylene ketal (m.p. 107-109°), which also proved to be identical with an authentic specimen.[7]

All new compounds gave satisfactory elemental analyses, and showed spectral data in accord with the assigned structures.

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