Synthesis of a Δ^5-19-Methyl-19-oxo-steroid

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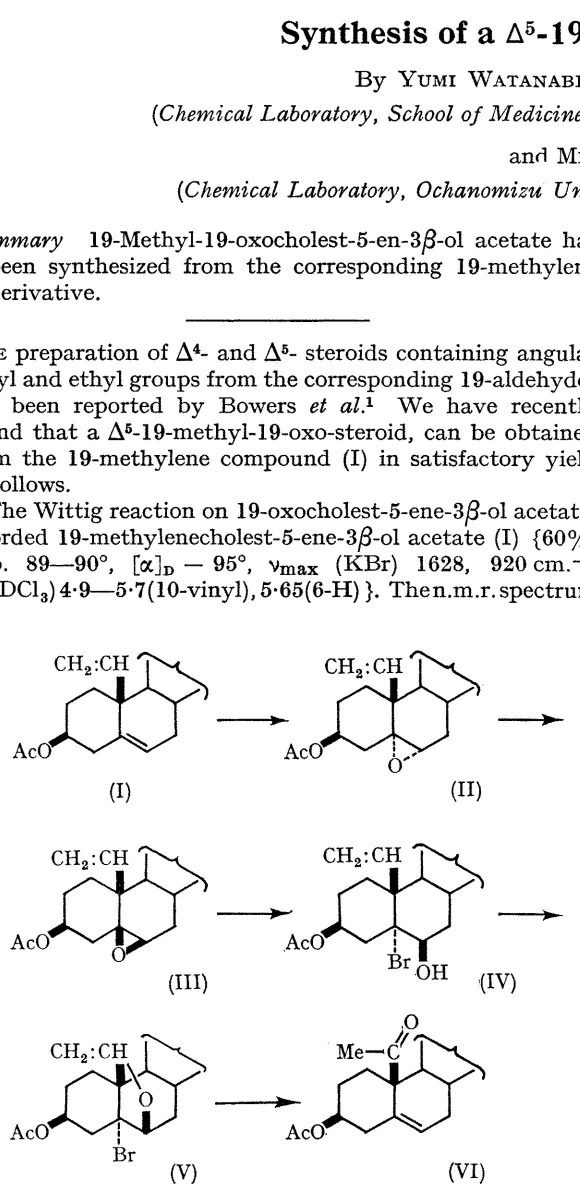
Summary 19-Methyl-19-oxocholest-5-en-3β-ol acetate has been synthesized from the corresponding 19-methylene derivative.

THE preparation of Δ^4- and Δ^5- steroids containing angular vinyl and ethyl groups from the corresponding 19-aldehydes has been reported by Bowers *et al.*[1] We have recently found that a Δ^5-19-methyl-19-oxo-steroid, can be obtained from the 19-methylene compound (I) in satisfactory yield as follows.

The Wittig reaction on 19-oxocholest-5-ene-3β-ol acetate[2] afforded 19-methylenecholest-5-ene-3β-ol acetate (I) {60%, m.p. 89—90°, $[\alpha]_D$ − 95°, ν_{max} (KBr) 1628, 920 cm.$^{-1}$, δ($CDCl_3$) 4·9—5·7(10-vinyl), 5·65(6-H)}. The n.m.r. spectrum of (I) showed a signal due to the three C-18 protons at 0·57 p.p.m., *ca.* 0·1 p.p.m. up-field from those of the 19-unsubstituted derivatives; this was observed for all derivatives having the 19-methylene group.



Treatment of (I) with an excess of monoperphthalic acid in ether at room temperature led to the selective oxidation of the 5,6-double bond giving the 5α,6α-epoxide (II) {90%, m.p. 77°, $[\alpha]_D$ − 53°, ν_{max} (KBr) 1630, 920 cm.$^{-1}$, δ(CDCl)$_3$ 3·02(6-H), 4·8—6·0(10-vinyl)} as a major product. The epoxide (II) was converted into an isomeric 5β,6β-epoxide (III) {m.p. 89·5—90·5°, $[\alpha]_D$ − 5°, ν_{max} (KBr) 1635, 927 cm.$^{-1}$, δ($CDCl_3$) 3·13(6-H), 5·0—6·2(10-vinyl)] by the method of Petrow *et al.*[3] The 5α-bromo-6β-hydroxy-19-methylene derivative (IV) {80%, m.p. 149·5°(decomp.), $[\alpha]_D$ −12°, ν_{max} (KBr) 3440, 1628, 935, and 755 cm.$^{-1}$, δ($CDCl_3$) 4.4(6-H), 4·9—5·6(vinyl 2H), 6·8(vinyl 1H)} was obtained by addition of an equimolar amount of 47% hydrogen bromide solution to (III) in acetic acid. A solution of (IV) in cyclohexane was heated under reflux with lead tetra-acetate for 5 hr. to give the 5α-bromo-6β,19-epoxy compound (V) {60%, m.p. 156—157°, $[\alpha]_D$ − 15°, ν_{max} (KBr) 1642, 922 cm.$^{-1}$, δ($CDCl_3$) 4·4 and 4·9 (19-methylene) 4·4(6-H)}. Reduction of (V) with zinc in acetic acid gave (quantitatively) the 19-methyl-19-oxo-compound (VI) {m.p. 127—128°, $[\alpha]_D$ − 115°, ν_{max} (KBr) 1707 cm.$^{-1}$, δ($CDCl_3$) 2·18(10-acetyl), 5·8(6-H)}, probably *via* an enol form. The appearance of an unsplit methyl signal in the n.m.r. spectrum of (VI) at 2·18 p.p.m. supported the 19-methyl-19-oxo-structure. The structure of (VI) was also confirmed by the Wolff–Kishner reduction of the compound, followed by acetylation, to give 19-methylcholest-5-ene-3β-ol acetate (yield *ca.* 10%, the starting material being recovered almost unchanged probably because of steric hindrance), which was identical with an authentic sample.

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