A SIMPLE PREPARATION OF 2-METHYL-5a-CHOLEST-2-ENE

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ABSTRACT

A convenient preparation of 2-methyl-5 α -cholest-2-ene from 5 α -cholestan-3 β -ol is described.

In connection with our study on the reactions of trisubstituted olefins with iodine and silver salts, we required large amounts of 2-methyl- 5α -cholest-2-ene l.

Preparation of 1 had previously been accomplished starting from 5α -cholestan-3-one. Reaction with HCOOEt/MeONa gave¹ 2-hydroxymethylene- 5α -cholestan-3-one which was transformed into 2α -methyl- 5α -cholestan-3one 2 either by catalytic hydrogenation¹ or by methylation with MeI/K₂CO₂ and deformylation. Introduction of the double bond was achieved either by treatment of p-tosylhydrazone of $\underline{2}$ with a base or by LiAlH₄ reduction of 2 to 2α -methyl- 5α -cholestan- 3β -of and dehydration of this alcohol via its p-toluenesulfonate². The overall yields of 1 by these procedures were reported to be low (<20%). In addition, in our hands both above routes from 5α -cholestan-3-one to 2 proved to give erratic results, the former giving yields which depended upon the batch of catalyst (Pd/C) used and solvent purity, the latter affording large amounts of starting material from the deformylation step. Thus we sought an alternative route to $\underline{1}$ through 5_{α} -cholestan-2-one, as the recently reported³ acetoxyiodination of easily available 5α -cholest-2-ene provides a very convenient method to introduce an oxygenated function at C_2 .

 5α -cholest-2-ene was prepared in a 85% yield from commercial 5α cholestan-3 β -ol by tosylation and subsequent standing of an hexane solution of p-toluenesulfonate on grade 1 alumina Woelm for 24 hr⁴. 5α cholest-2-ene (1 mmole), I₂ (0.5 mmoles), KIO₃ (0.25 mmoles) and AcOH (22

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ml) were stirred at 60° for 2 hr. After cooling, water(10 ml) was added and the mixture was extracted with hexane (3x30 ml). The extracts were



washed with 5% NaHCO₃, 5N Na₂S₂O₃ and water and evaporated to give crude 3α -iodo-5 α -cholestan-2 β -yl acetate <u>3</u>. Crystallization from acetone-MeOH gave pure <u>3</u> (75 to 80% yield), m.p.95-97° (lit.⁵:96-97°). <u>3</u> was reduced with LiAlH₄ in ether (2 hr reflux) to 5 α -cholestan-2 β -ol, >95% yield,m. p. 154° (lit.⁵:151-153°), which was quantitatively oxidized with the Jones reagent to 5 α -cholestan-2-one⁶, m.p. 131.5-132°. This ketone (1 mmole) was added to a solution of MeMgI (prepared from 5 mmoles of MeI) in ether (10 ml). After 30 min reflux, usual work up and chromatography on neutral alumina (98:2 hexane-ether) gave 2α -methyl-5 α -cholestan-2 β ol <u>4</u>⁷, 95% yield, m.p. 148-149°. Dehydration of <u>4</u> (1 mmole) was achieved by treatment with HClO₄ (traces) in AcOH (10 ml) for 1 hr at 80°. Extraction with hexane and evaporation quantitatively afforded 2-methyl-5 α -cholest-2-ene <u>1</u>, m.p. 99-100° (lit. :100-101°², 97-97.5°¹). The overall yield of <u>1</u> from 5 α -cholestan-3 β -ol was ca. 55%.

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