SYNTHESIS OF 2α-METHYLDIHYDROTESTOSTERONE FROM TIGOGENIN

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2α-Methyldihydrotestosterone propionate is used in medicine to cure breast cancer.

We describe the synthesis of 2α-methyldihydrotestosterone using C-alkylation of 2α-bromoketones [1]. Tigogenin, which was proposed by the Institute of Pharmacochemistry of the Academy of Sciences of Georgia as starting material, was used to synthesize 5α-steroidal hormonal preparations [2].

Tigogenin was converted to pregnenolone acetate [3]. The oxime of pregnenolone acetate underwent a Beckmann rearrangement according to Schmidt—Thom. Alkaline hydrolysis of epiandrosterone acetate gives epiandrosterone. Oxidation of the free hydroxy by Jones reagent gives 5α-androstan-3,17-dione.

Selective methoxylation of the last gives 3,3′-dimethoxy-5α-androstan-17-one. Reduction of the 17-ketosteroid by $NaBH_4$ gives dihydrotestosterone [4].

Dihydrotestosterone was brominated according to the literature method [5]; C-alkylation of 2α-bromodihydrotestosterone, by methyl iodide in C_6H_6:DMSO (10:1) under N_2 in the presence of activated zinc for 18 h.

Further work up of the reaction mixture and chromatography over a silica-gel (100/250) column gave 2α-methyldihydrotestosterone (62.5%) (from dihydrotestosterone) with mp 149-152°C (according to the literature, 51% yield, mp 147-154°C) [6].

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