

A NEW METHOD FOR THE PREPARATION OF METHYL-3 KETO-7 α , 12 α DIHYDROXY-5 β -CHOLANATE

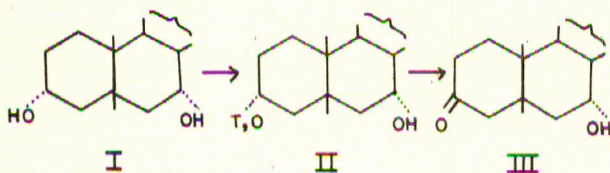
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INTRODUCTION

The authors have selectively oxidised methyl-3 β , 7 α , 12 α , -trihydroxy-5 β -cholanate (I) to methyl 3-keto-7 α , 12 α , -dihydroxy -5 β -cholanate (III) with dimethyl sulphoxide in the presence of collidine through its tosylate (II).



Methyl 3-keto-7 α , 12 α -dihydroxy-5 β -cholanate has previously been prepared from methyl 3 α , 7 α , 12 α -trihydroxy-5 α -cholanate by partial Oppenauer oxidation [1,2] and by catalytic oxidation with platinum and oxygen [3].

The authors have followed the selective oxidation of steroidal alcohols with dimethyl sulphoxide through their sulphonic esters [4,5]. The selective oxidation is possible because the hydroxyl group in different positions of the steroid skeleton can be selectively tosylated [7]. The tosylate can then be converted into the corresponding ketone by the action of dimethyl sulphoxide in the presence of collidine.

Preparation of methyl 3 α -tosyloxy-7 α , 12 α -dihydroxy-5 β -cholanate: Methyl cholate (7.8 g, m.p. 155°C) was dissolved in dry Pyridine (11 ml) and the solution was chilled to 10°C. A solution of *p*-toluene sulphonyl chloride (3.9 g) in dry pyridine (7.5 ml) was added dropwise into the solution mixture between 8°C and 12°C. The reaction mixture was allowed to stand at room temperature overnight under anhydrous

condition.

A small quantity of ice was added to decompose the unchanged acid chloride and the mixture was then diluted with glacial acetic acid (35 ml). The resulting mixture was poured into a well-stirred mixture of ice cold water (300 ml) and concentrated hydrochloric acid (22 ml). An amorphous white precipitates of methyl 3 α -tosyloxy-7 α , 12 α -dihydroxy-5 β -cholanate (10.5 g) was obtained. It was filtered, thoroughly washed with water and dried under reduced pressure over phosphorous pentoxide. It has m.p. 74-76°, TLC one spot, $\nu_{\text{max}}^{\text{KBr}}$ 1180 cm^{-1} and 1350 cm^{-1} (OTs).

Preparation of methyl 3keto-7 α , 12 α -dihydroxy-5 β -cholanate: A mixture of methyl 3 α -tosyloxy-7 α , 12 α -dihydroxy-5 β -cholanate (1.8 g), dimethyl sulphoxide (32 ml) and collidine (1.5 ml) was heated on a water bath at 90-100°C, for 6 hours. It was extracted with ether and washed with water, dilute hydrochloric acid and 10% sodium carbonate solution. The ether extract was evaporated and the residue weighed (1.27 g). The residue furnished methyl 3-keto-7 α , 12 α -dihydroxy -5 β -cholanate (0.96 g i.e. 73%), after crystallisation from benzene/hexane, m.p. 167°C, (lit. m.p. 166°C) $\nu_{\text{max}}^{\text{KBr}}$ 3575 cm^{-1} (O-H) 1710 cm^{-1} (C=O). It gave no depression of melting point when mixed with a standard sample of methyl 3-keto-7 α , 12 α -dihydroxy-5 β -cholanate.

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