PREPARATION OF 19-NOR-17α-ETHINYLTESTOSTERONE PIVALATE ESTER

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19-Nor-17α-ethinyltestosterone (19-NET) esters of hindered acids are potentially useful as long acting anticonceptive agents. However, they cannot be prepared by the usual methods of esterification, such as the reaction between an alcohol and an acid chloride. Kaiser and Woodruff[1] describe a method for the formation of the pivalate esters of 1-ethinyl-1-hydroxycyclohexane which consists in the formation of the lithium salt of the alcohol by reaction with an alkyl lithium compound which is then treated with the acyl chloride. We were able to use a modification of this method to prepare the pivalate ester of 19-NET. In order to avoid the formation of side products it was necessary to protect the 3-keto group of 19-NET as the ethylene dioxy derivative[2]. An earlier publication[3] describes the esterification of certain steroidal alcohols by means of their bromomagnesium salts. When we tried to apply this method to the synthesis of the title compound very low yields of the product were obtained.

EXPERIMENTAL PART

Pivalate Ester of 19-NET:

To 1.026 g (3 m moles) of the 3-ethylene ketal of 19-NET[2],

dissolved in 25 ml anh. THF are added dropwise with stirring, under N_2, 3 ml of 1.58 M n-butyl lithium in hexane (Aldrich). Stirring is continued at room temperature for 30 minutes. A solution of 750 mg (6.25 m moles) pivaloyl chloride in 15 ml dry THF is then added dropwise with stirring. After the addition of the acyl chloride the mixture is refluxed under N_2 for 5 hours, during which time the solution turns slightly turbid. The solvent is then removed under vacuum in a rotary evaporator and the residue taken up in ether, the ether solution washed several times with water, dried and evaporated. The residue is taken up in 25 ml dry acetone and 25 mg p-toluenesulfonic acid monohydride and refluxed under exclusion of moisture for 8 hours. The acetone solution is concentrated until the ester crystallises out.

19-NET pivalate: mp. 214-15°C $[\alpha]_D$ -38°(Chf) $\lambda_{max}^{CH_3OH}$ 238 mμ (log ε = 3.82)

NMR (δ) 0.98, 1.2, 2.55, 5.8 ppm

IR, 1625, 1675, 1740, 3330 cm^{-1}

Anal. $C_{25}H_{34}O_3$ Calc. C: 78.49 H: 8.96

found C: 78.44 H: 9.03

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