STEROIDS

XLVII. THE QUESTION OF THE STERIC HINDRANCE OF THE HYDROXY GROUPS OF 3α,11α-DIHYDROXY-16α-METHYL-5β-PREGNAN-20-ONE

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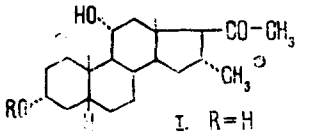
A difference in the steric hindrance of the hydroxy groups (3α and 11α) in the molecule of 3α, 11α-dihydroxy-16α-methyl-5β-pregnan-20-one (I) was shown on the basis of the hydrolysis of its diacetate. However, this difference does not appear in the acetylation of the diol (I) [1].

We assume that the greater accessibility of the 3α-hydroxy group could be observed in the reaction of the diol (I) with a reagent more voluminous than an acetyl derivative – pivaloyl chloride. In this reaction, the 3α-monopivalate (II) is formed unambiguously even with a considerable excess of the acid chloride.

To a solution of 0.1 g of 3α, 11α-dihydroxy-16α-methyl-5β-pregnan-20-one (I) in 3 ml of pyridine at ~20°C was added 0.085 g (8-fold excess) of pivaloyl chloride [2], and after a day the reaction mixture was poured into a mixture of 4 ml of concentrated HCl and ice. Then it was extracted with methylene chloride and the extract was washed with water, with saturated $NaHCO_3$ solution, and again with water, and was dried and the solvent was evaporated in vacuum. The residue was recrystallized from benzene with hexane, giving 11α-hydroxy-3-pivaloyloxy-16α-methyl-5β-pregnan-20-one (II) with mp 169-172°C; ν_{max} 1700 (CO) and 3480 cm^{-1} (OH).



I. R=H

II. R=(CH3)3C-C(=O)-

The C and H values found corresponded to the calculated figures.

The PMR spectrum of the 3α-monoester (II), as compared with the spectrum of the diacetate [1], shows an upfield shift of the less multiplet signal from the C_{11} proton (δ 3.88 ppm), since the hydroxyl at C_{11} is not esterified; at the same time, the signal from the proton at C_3 does not change its position (δ 4.74 ppm). The features of the PMR spectrum show that the less blocked hydroxyl in position 3 underwent esterification.

Thus, by using the different steric hindrances of the hydroxy groups of 3α, 11α-dihydroxy-16α-methyl-5β-pregnan-20-one it is possible selectively to obtain its esters in position 3 or position 11.

LITERATURE CITED

1. L. C. Garcia-Rodrigues, V. F. Shner, L. M. Alekseeva, and N. N. Suvorov, Khim. Prirodn. Soedin., 610 (1971).
2. H. C. Brown, J. Amer. Chem. Soc., 60, 1325 (1938).

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