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LETTERS TO THE EDITOR

Stereospecific Reduction of Keto Group in 3β-Triphenylmethoxy-5α-cholest-8(14)-en-15-one

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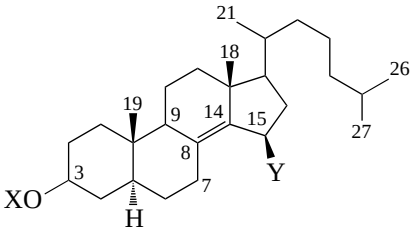
Abstract—The reduction of 3β-triphenylmethoxy-5α-cholest-8(14)-en-15-one with lithium aluminum hydride resulted in a quantitative yield of 3β-triphenylmethoxy-5α-cholest-8(14)-en-15β-ol.

Key words: *oxysterols, synthesis*

The development of synthetic methods for sterols containing a hydroxyl or carbonyl group in position 15 is an important issue, since 15-oxygenated cholesterol and lanosterol derivatives possess hypocholesterolemic and antiatherogenic properties in mammals and exhibit a wide spectrum of biological activities in cell cultures [1].[2]

The reduction of 15-ketosterol (**I**) and its 3-*O*-acetyl or 3-*O*-benzoyl derivative with $LiAlH_4$ results in a mixture of isomeric diols (**V**), 3β15α- and 3β15β-dihydroxy-5α-cholest-8(14)-ene, in a 2 : 3 ratio [2]. Although these diols can be chromatographically separated, it is obvious that the development of a reduction method resulting in only one of the isomers is of interest for the preparative synthesis of 15-hydroxysterols. We found that the reduction of tritylated 15-ketosterol (**II**) with $LiAlH_4$ in diethyl ether leads exclusively to one product, 3β-triphenylmethoxy-5α-cholest-8(14)-en-15β-ol (**III**).



(**I**) X = H; Y = O
(**II**) X = Ph_3C; Y = O
(**III**) X = Ph_3C; Y = OH
(**IV**) X = Ph_3C; Y = OAc
(**V**) X = H; Y = βOH

Trityl-containing ketosterol (**II**) was obtained in a 70% yield by refluxing 15-ketosterol (**I**) with a fourfold excess of trityl chloride in pyridine for 8 h and the subsequent twofold recrystallization of the product from 1 : 2 acetone–EtOH; ^{1}H NMR (hereinafter: δ, ppm; *J*, Hz; $CDCl_3$; Bruker WM 500): 0.633 (3 H, s, 19-CH_3), 0.834 (6 H, d, *J* 6.6, 26-CH_3 and 27-CH_3), 0.911 (3 H, s, 18-CH_3), 0.949 (3 H, d, *J* 6.6, 21-CH_3), 3.410 (1 H, m, H3), 4.018 (1 H, m, H7), and 7.18–7.50 (15 H, m, trityl).

The reduction of (**II**) with excess $LiAlH_4$ in diethyl ether resulted in the quantitative yield of (**III**); ^{1}H NMR: 0.663 (3 H, s, 19-CH_3), 0.834 and 0.839 (total 6 H, two d, *J* 6.6, 26-CH_3 and 27-CH_3), 0.895 (3 H, d, *J* 6.6, 21-CH_3), 0.992 (3 H, s, 18-CH_3), 2.625 (1 H, m, H7), 3.412 (1 H, m, H3), 4.572 (1 H, m, H15), and 7.180–7.550 (15 H, m, trityl).

The removal of the trityl protection from (**III**) was achieved at 20°C by treatment with aqueous HCOOH in ether for 20 min or with 0.1 N HCl in aqueous dioxane for 4 h. It was accompanied by the elimination of the 15-hydroxy group and resulted in 3β-hydroxy-5α-cholesta-8,14-diene; ^{1}H NMR: 0.816 (3 H, s, 19-CH_3), 0.868 and 0.870 (total 6 H, two d, *J* 6.6, 26-CH_3 and 27-CH_3), 0.938 (3 H, d, *J* 6.6, 21-CH_3), 0.992 (3 H, s, 18-CH_3), 2.356 (1 H, m, H7), 3.631 (1 H, m, H3), and 5.360 (1 H, br. s, H15) (cf. [3]).

To obtain 3β,15β-dihydroxy-5α-cholest-8(14)-ene (**V**), (**III**) was preliminarily acetylated (Ac_2O/Py, 20°C, 14 h) to give acetate (**IV**); ^{1}H NMR: 1.992 (3 H, s, CH_3CO), 2.320 (1 H, m, H7), and 5.485 (1 H, m, H15). Then the protective groups (first trityl and then acetyl) were removed from (**IV**) by successive treatment with 90% aqueous HCOOH in ether (20 min, 20°C) and then with 0.4 N NaOH in aqueous methanol (20 min, 20°C). Diol (**V**) resulted; yield 78% from (**III**); ^{1}H NMR: 0.709 (3 H, s, 19-CH_3), 0.855 and 0.857 (total 6 H, two

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[2] Abbreviations: 15-ketosterol, 3β-hydroxy-5α-cholest-8(14)-en-15-one.

d, *J* 6.6, 26-CH_3 and 27-CH_3), 0.915 (3 H, d, *J* 6.6, 21-CH_3), 1.014 (3 H, s, 18-CH_3), 2.327 (1 H, m, H7β), 3.627 (1 H, m, H3), and 4.615 (1 H, m, H15). It was identical to 3β,15β-dihydroxy-5α-cholest-8(14)-ene described previously in [2].

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2. The article by **A. V. Komarova, L. S. Tchufistova, E. V. Supina, and I. V. Boni** Extensive Complementarity of the Shine–Dalgarno Region and 3'-End of 16S rRNA Is Inefficient for Translation *in vivo* (*Russian J. Bioorg. Chem.*, vol. 27, no. 4, pp. 248–255).

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