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LETTERS TO THE EDITOR

Reduction of Steviolbioside

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Alkaline hydrolysis of stevioside (**I**), the major component of sweet glycosides (rebaudiosides) isolated from *Stevia rebaudiana* Bertoni [1], yields steviolbioside (**II**) [2]. Unlike stevioside (**I**), steviolbioside (**II**) is a weaker sweetener [3], but it also exhibits biological activity (hypoglycemic effect [4]), so that it can be used as a basis for the design of new biologically active compounds. In fact, esters [5] and amides [6] derived from steviolbioside were found to possess antitumor and antibacterial activity.

In continuation of our studies on the reactivity of steviolbioside in the present work we examined its behavior under the reduction conditions. Treatment of steviolbioside (**II**) with excess $LiAlH_4$ in boiling tetrahydrofuran gave 73% of a product which was assigned the structure of alcohol **III** on the basis of its IR and ^{1}H NMR spectra (Scheme 1).

The ^{1}H NMR spectrum of **III** resembles that of initial steviolbioside (**II**) [6], except for the presence of doublets at δ 3.53 and 3.93 ppm, which were assigned to methylene protons on C^{19}. These findings indicated that the carboxy group in **II** was reduced to hydroxymethyl. The same also followed from the absence in the IR spectrum of the product of carbonyl absorption band at 1690 cm^{-1} typical of carboxy group. On the other hand, the IR spectrum of **III** contained an absorption band at 1665 cm^{-1} typical of stretching vibrations of double C=C bond. This means that the C^{16}=C^{17} double bond was not reduced in the above reaction. In the ^{1}H NMR spectrum of **III** we observed singlets at δ 5.07 and 5.74 ppm, which clearly belong to protons in the exocyclic methylene group ($C^{17}H_2$=) [6]. The structure of the isolated product was unambiguously proved by the X-ray diffraction data (see figure).

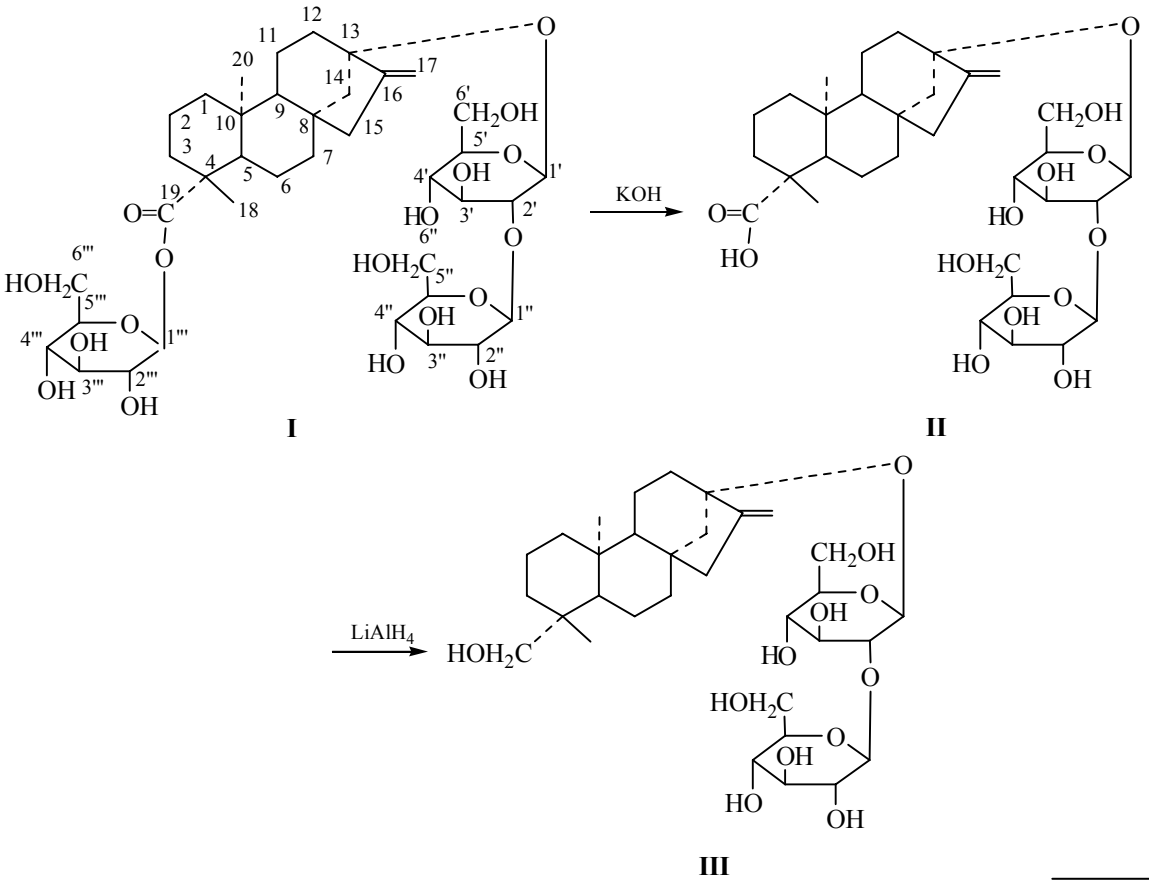
Thus we were the first to reduce glycoside (rebaudioside) of the *ent*-kaurene series, namely steviolbioside (**II**), and obtain alcohol **III**.

19-Hydroxy-*ent*-kaur-16-en-13-yl β-D-sophoroside (III). A solution of 1 g of steviolbioside (**II**) in 30 ml of anhydrous tetrahydrofuran was added dropwise to a suspension of 1.5 g of $LiAlH_4$ in 40 ml of anhydrous THF. The mixture was heated for 12 h under reflux with stirring, excess $LiAlH_4$ was decomposed by treatment with water, the precipitate was filtered off and ground with 5% hydrochloric acid, and the product was extracted into butanol. The extracts were combined and evaporated, and the residue (0.90 g) was recrystallized from methanol. Yield 0.71 g (73%), mp 146°C (from MeOH), $[\alpha]_D^{20}$ = –24° (*c* = 0.1, H_2O). IR spectrum (mineral oil), ν, cm^{-1}: 3373 (OH), 1660 (C=C). ^{1}H NMR spectrum (pyridine-d_5), δ, ppm (*J*, Hz): 1.04 s (3H, $C^{20}H_3$), 1.14 s (3H, $C^{18}H_3$), 1.5–2.3 m (14H, aglycone), 3.53 d (1H, 19-H_A, *J* = 10.79), 3.93 d (1H, 19-H_B, *J* = 10.79), 3.8–4.5 m (12H, sophorose), 5.07 s (1H, 17-H_A), 5.17 d (1H, 22-H, *J* = 7.6,), 5.28 d (1H, 36-H, *J* = 7.6), 5.74 s (1H, 17-H_B). Found, %: C 61.75; H 8.47. $C_{32}H_{52}O_{12}$. Calculated, %: C 61.11; H 8.35.

Steviolbioside was synthesized according to the procedure described in [2], mp 190°C (from MeOH), $[\alpha]_D^{20}$ = –32.5° (*c* = 0.2, MeOH); published data [2]: mp 188–192°C, $[\alpha]_D^{20}$ = –37.4° (*c* = 1,4-dioxane).

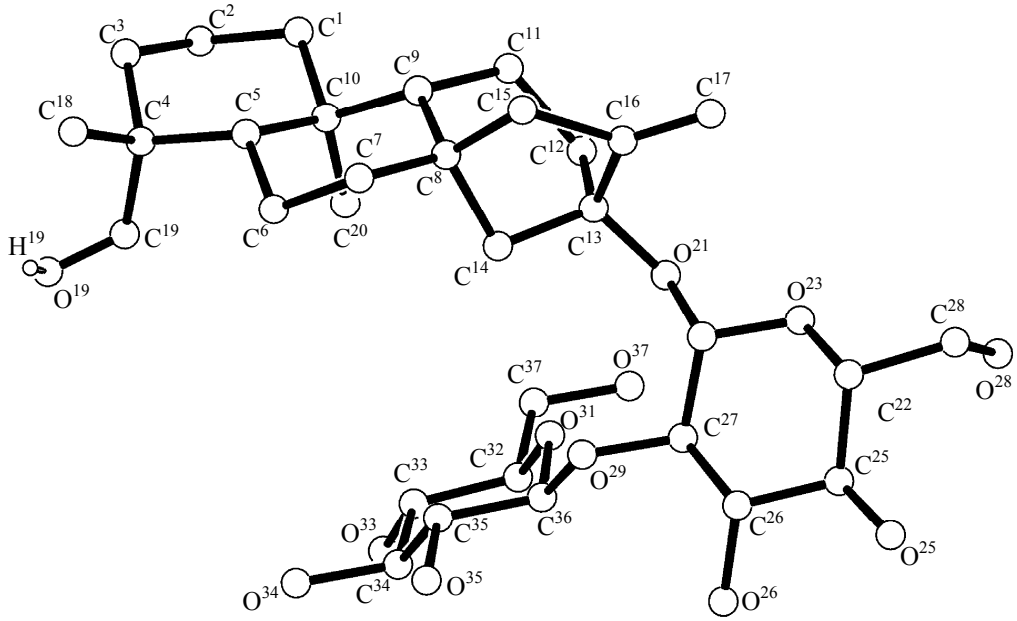
The ^{1}H NMR spectrum was recorded on a Bruker Avance-600 spectrometer (600 MHz) from a solution in pyridine-d_5. The IR spectrum was obtained in mineral oil on a UR-20 spectrometer (spectral range 400–3600 cm^{-1}). The optical rotation was determined

Scheme 1.



on a Perkin–Elmer M341 polarimeter (cell path length 55 mm). The melting point was measured on a Boetius melting point apparatus.

The X-ray diffraction data for a single crystal of compound **III** were acquired at 293 K on a SMART Apex II diffractometer (MoK_α irradiation) at the X-Ray



Geometry of alcohol molecule **III** in the crystal by X-ray anlysis data. Hydrogen atoms are shown selectivitely.

Analysis Department, Collective Use Spectral and Analytical Center of the Russian Foundation for Basic Research (Diffraction Laboratory, Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center, Russian Academy of Sciences). Crystals of **III** suitable for X-ray analysis were obtained from a solution in methanol. Monoclinic crystal system, $C_{32}H_{52}O_{12}\cdot 3H_2O$, space group $P2_1$ (no. 4); unit cell parameters: a = 11.9996(5), b = 7.7603(3), c = 18.9624(8) Å; V = 1764.1(1) Å^3; M 682.74; Z = 2. The structure was solved by the direct method using SIR program [7] and was refined first in isotropic and then in anisotropic approximation using SHELXL97 [8] and WinGX [9]. Hydrogen atoms that are not involved in hydrogen bonding were placed into calculated positions. Hydrogen atoms in hydroxy groups were visualized by difference syntheses of electron density, and their positions were refined in isotropic approximation in the final refinement step. The molecular structure was plotted using PLATON software [10].

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