ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 5, pp. 768–770. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © L.Kh. Faizullina, M.G. Safarov, L.V. Spirikhin, F.A. Valeev, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 5, pp. 772–774.

SHORT COMMUNICATIONS

Synthesis of Levoglucosenone Oxazoline Derivative

L. Kh. Faizullina[b], M. G. Safarov[b], L. V. Spirikhin[a], and F. A. Valeev[a]

[a]*Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences*
[b]*GOU VPO "Bashkir State University," Ufa, 450074 Russia*
e-mail: *lfajzullina@yandex.ru*

Received June 25, 2008

DOI: 10.1134/S1070428010050313

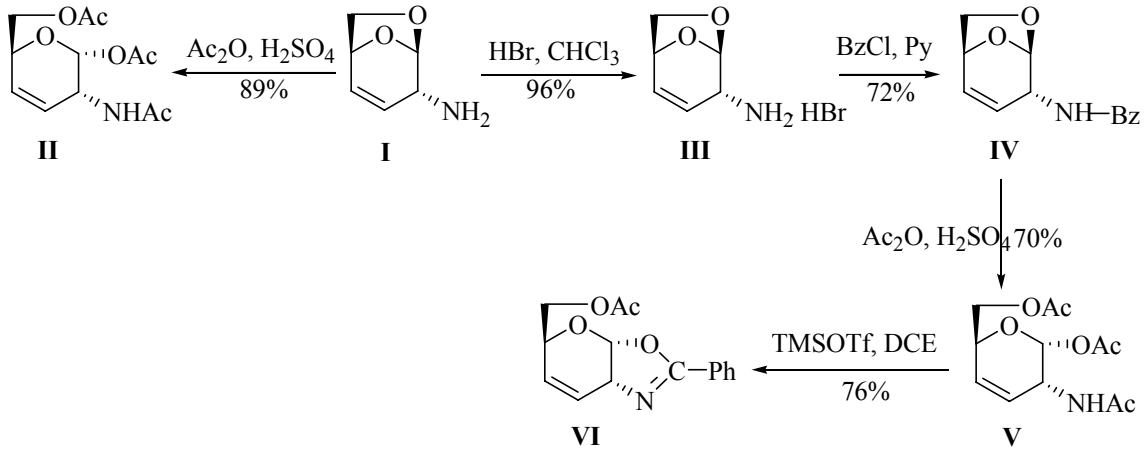
Aminosugars are extensively used in the chemistry of natural compounds for preparation of modified glycosides. The amino derivative of levoglucosenone **I** [1] is a promosing compound for the synthesis of unsaturated glycopyranoside fused with an oxazoline ring for its further application as a glycosylation agent [2–5].

Amine **I** necessary for the oxazoline synthesis we prepared by the procedure previously developed [1]. One of the most difficult stages in the planned synthesis was the cleavage of the 1,6-anhydro bridge. Therefore this stage was tested on a model of initial amine **I**. It turned out that unlike the other levoglucosenone derivatives [6] the 1,6-anhydro bridge in amine **I** cleanly opened under the action of H_2SO_4–Ac_2O within 3 days giving exclusively *a*-anomer **II**. The structure of obtained compound **II** is confirmed by the coupling constant $J_{6,5}$ 4.0 Hz characteristic of the α-anomer. The data obtained are in agreement with the published data on the preparation of oxazolines from sugars [7].

Benzoyl derivative **IV** was obtained by converting aminosugar **I** into hydrobromide **III** which was treated with benzoyl chloride. The subsequent stages of the opening of the 1,6-anhydro bridge in the N-benzoyl derivative and ring closure under the action of TMSOTf resulted in stable crystalline oxazoline **VI** [8].

In the ^{13}C NMR spectrum of precursor **V** the signal of "amide" carbon atom appeared at 165.1 ppm, and the closure into the oxazoline ring led to the upfield shift of this signal to 163.9 ppm.

In the proton spectrum the change in the coupling constant of the signal of proton H^1 at 6.34 ppm should be mentioned that on cyclization into oxazoline grows from 4.0 to 7.1 Hz, and also the difference in the chemical



II **I** **III** **IV** **V** **VI**

shifts of the protons at the double bond registered as a doublet of doublets at 6.0 ppm and a multiplet at 6.22 ppm. The coupling was observed between the protons of acetoxymethyl group, of proton H^2 with J 11.8 and proton H^5 with $J_{5,6}$ 6.1 and 3.8 Hz.

Therefore oxazoline of high stability was obtained necessary for the study as a glycosylating reagent.

2-Amino-2,3,4-trideoxy-1,6-anhydro-β-D-*eritro*-hex-3-enopyranose (I) was obtained by method [1]. R_f 0.3 (ethyl acetate), $[a]_D^{20}$ –240° (*C* 1.0, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 1.5 br.s (2H, NH_2), 2.8 d (1H, H^2, *J* 3.7 Hz), 3.64 d.d (1H, H^6_{exo}, *J* 6.4, 4.7 Hz), 3.72 d (1H, H^6_{endo}, *J* 6.4 Hz), 4.58 d.d (1H, H^5, *J* 4.6, 4.4 Hz), 5.35 s (1H, H^1), 5.68 d.d (1H, H^3, *J* 9.8, 3.9 Hz), 6.0 d.d (1H, H^4, *J* 9.8, 4.7 Hz). ^{13}C NMR spectrum, δ, ppm: 51.22 (C^2), 70.22 (C^6), 70.85 (C^5), 104.83 (C^1), 128.55 (C^3, C^4). Found, %: C 56.81; H 7.12; N 11.70. $C_6H_9NO_2$. Calculated, %: C 56.68; H 7.13; N 11.02.

(–)-(2*S*,5*R*,6*R*)-6-Acetoxy-5-acetoxyamino-2-acetoxymethyl-5,6-dihydro-2*H*-pyran (II). At stirring and cooling to 0°C to a solution of 0.478 g (3.73 mmol) of amine **I** in 20 ml of Ac_2O was added a mixture of 0.38 ml of H_2SO_4 and 18.4 ml of Ac_2O. The reaction mixture was stirred for 39 h at room temperature, then it was poured into ice water containing 132 g of $NaHCO_3$, and the mixture was stirred for 2 h at room temperature and extracted with $CHCl_3$ (5 × 10 ml). Organic solutions were combined, dried with $MgSO_4$, evaporated, and the residue was subjected to chromatography. Yield 0.712 g (89 %). Colorless crystals, mp149–150°C, R_f 0.3 (ethyl acetate–hexane, 1:1), $[a]_D^{20}$ –16.2° (*c* 1.0, CH_3OH). ^{1}H NMR spectrum, δ, ppm: 1.94 s (3H, CH_3), 2.02 s (3H, CH_3), 2.06 s (3H, CH_3), 4.08 d.d (1H, CH_2, *J* 11.6, 3.4 Hz), 4.14 d.d (1H, CH_2, *J* 5.3, 11.6 Hz), 4.38 d (1H, H^6, *J* 2.0, 3.4 Hz), 4.85 m (1H, H^3), 5.63 d.t (1H, H^4, *J* 1.3, 10.4 Hz), 5.76 d.t (1H, H^5, *J* 10.4, 2.0 Hz), 6.10 d (1H, NH, *J* 9.1, 4.0 Hz), 6.22 d (1H, H^2, *J* 4.0 Hz). ^{13}C NMR spectrum, δ, ppm: 20.06 (CH_3), 20.8 (CH_3), 22.9 (CH_3), 44.0 (C^5), 64.9 (CH_2), 68.1 (C^2), 89.2 (C^6), 125.8 (C^3) 126.4 (C^4), 169.5 ($COOCH_3$), 170.0 ($COOCH_3$), 170.8 ($CONHCH_3$). Found, %: C 50.81; H 5.12; N 4.70. $C_{12}H_{17}O_7N$. Calculated, %: C 50.17; H 5.96; N 4.88.

2-Amino-2,3,4-trideoxy-1,6-anhydro-β-D-*eritro*-hex-3-enopyranose hydrobromide (III). To a solution of 0.168 g (1.3 mmol) of amine **I** in 2 ml of $CHCl_3$ was added at stirring 0.2 ml (1.3 mmol) of a solution of 46% HBr in 2 ml $CHCl_3$. In 15 min crystals precipitated. The solution was evaporated. Yield 0.264 g (97%).

***N*-(7,8-Dioxabicyclo[3.2.1]oct-3-en-2-yl)benzamide (IV).** In 3.25 ml of pyridine was dissolved 0.264 g (1.3 mmol) of salt **III**, at 0°C 0.197 ml was added of freshly distilled benzoyl chloride. In the course of 5 h crystals precipitated, the reaction mixture was poured into ice water, and the product was extracted with ethyl acetate (3×5 ml), after evaporating the solvent the residue was recrystallized. Yield 0.281 g (96%). White crystals, mp 104–106°C, R_f 0.3 (ethyl acetate), $[a]_D^{20}$ –96.3° (*C* 1.0, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 3.76 d.d (1H, H^6, *J* 6.5, 4.1 Hz), 3.88 d (1H, H^6, *J* 6.5 Hz), 4.52 m (1H, H^2), 4.58 d.d (1H, H^5, *J* 4.1, 4.3 Hz), 5.10 s (1H, H^1), 5.26 d.d (1H, H^3, *J* 9.6, 2.4 Hz), 6.25 d.d (1H, H^4, *J* 9.6, 4.3 Hz), 7.48 m (2H, Ph), 7.60 t (1H, 7.3 Hz), 8.14 d (5H, Ph), 10.9 br.s (NH). ^{13}C NMR spectrum, δ, ppm: 48.0 (C^2), 70.4 (C^6), 70.5 (C^5), 101.8 (C^1), 124.4 (C^3), 128.6 (C^4), 127.1, 128.5, 133.7, 133.9 (Ph), 166.7 (HNC=O). Found, %: C 67.41; H 5.12; N 6.07. $C_{13}H_{13}NO_3$. Calculated, % : C 67.52; H 5.67; N 6.06.

(–)-(2*S*,5*R*,6*R*)-6-Acetoxy-2-acetoxymethyl-5-benzoylamino-5,6-dihydro-2*H*-pyran (V). At stirring and cooling to 0°C to a solution of 0.1 g (0.43 mmol) of imide **IV** in 8 ml of Ac_2O was added dropwise a solution of 0.08 ml of H_2SO_4 in 3.85 ml of Ac_2O. The reaction mixture was stirred for 39 h at room temperature, then it was poured into ice water containing 22 g of $NaHCO_3$, and the mixture was stirred for 2 h at room temperature and extracted with $CHCl_3$ (5 × 10 ml). Organic solutions were combined, dried with $MgSO_4$, evaporated, and the residue was subjected to chromatography. Yield 0.086 g (60%). Yellow crystals, mp 130–132°C, R_f 0.35 (ethyl acetate), $[a]_D^{20}$ –56.15° (*C* 1.0, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 2.02 s (6H, CH_3), 4.20 d (2H, CH_2, *J* 4.6 Hz), 4.68 m (1H, H^5), 4.98 m (1H, H^2), 6.02 m (2H, H^3, H^4), 6.32 d (1H, H^6, *J* 4.0 Hz), 7.45 m (3H, Ph), 7.78 m (1H, Ph), 8.10 m (1H, Ph ^{13}C NMR spectrum, δ, ppm: 20.07 (CH_3), 45.9 (C^5), 65.7 (CH_2), 71.7 (C^2), 92.7 (C^6), 125.4 (C^4) 128.5 (C^3), 127.0, 128.5, 133.6, 133,7 (Ph), 165.1 (CONHPh), 167.1 ($COOCH_3$), 170.7 ($COOCH_3$). Found, %: C 61.81; H 5.19; N 4.01. $C_{17}H_{19}O_6N$. Calculated, %: C 61.25; H 5.75; N 4.20.

(–)-(1*S*,3*S*,6*R*)-2,9-Dioxa-7-aza-8-phenylbicyclo-3-acetoxymethyl-[4.3.0]nona-4,7-diene (VI). A solution of 0.17 ml (0.99 mmol) trimethylsilane triflate in 3.7 ml of anhydrous dichloroethane was added to 0.242 g (0.9 mmol) of compound **V** in 5 ml of dichloroethane. The mixture was stirred at 15°C till the disappearance of the initial compound (TLC monitoring).

The reaction mixture was passed through a thin bed of SiO_2, the solvent was evaporated, and the residue was subjected to chromatography. Yield 0.160 g (76%), mp 89–92°C, R_f 0.5 (hexane–ethyl acetate, 1:1), $[a]_D^{20}$ –81.8° (*C* 1.0, $CHCl_3$). ^1H NMR spectrum, δ, ppm: 2.10 s (3H, CH_3), 4.12 d.d (1H, CH_2, *J* 11.8, 6.1 Hz), 4.25 d.d (1H, CH_2, *J* 11.8, 3.8 Hz), 4.48 m (1H, H^3), 4.62 m (1H, H^6), 6.0 d.d (1H, H^5, *J* 10.4, 1.8 Hz), 6.22 m (1H, H^4), 6.34 d (1H, H^1, *J* 7.1 Hz), 7.42 m (3H, Ph), 7.98 m (2H, Ph). ^{13}C NMR spectrum, δ, ppm: 20.8 (CH_3), 45.9 (C^6), 65.2 (CH_2), 66.0 (C^3), 101.5 (C^1), 126.0 (C^5), 127.1, 128.2, 128.4, 128.6 (Ph), 131.8 (C^4), 163.9 (–HN=COPh), 170.8 ($COOCH_3$). Found, %: C 65.81; H 5.12; N 5.00. $C_{15}H_{15}O_4N$. Calculated, %: C 65.92; H 5.53; N 5.13.

^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-300 at operating frequencies 300 (^1H) and 75.47 (^{13}C) MHz in $CDCl_3$, otherwise the other solvents are indicated in each separate case. The melting points were measured on a Koeffler device of the type S 30A/G. The analytical TLC was performed on Sorbfil PTSKh-AF-A plates, anise developer. Elemental analysis was carried out on CHNS(O) – analyzer Euro-2000. The optical rotation was measured on an instrument Perkin-Elmer-141. The synthesized products were separated by column chromatography on silica gel L-40/100 using 30–100 g per 1 g of substance.

The study was carried out under a financial support of the Russian Foundation for Basic Research (grant no. 08-03-97033-p_povolzh'e a) and of the Council for grant of the President of the Russian Federation (program NSh -1725.2008.3).

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