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Preparation of the diastereomerically pure 2*S*-hydroxy derivative of dihydrolevoglucosenone (cyrene)

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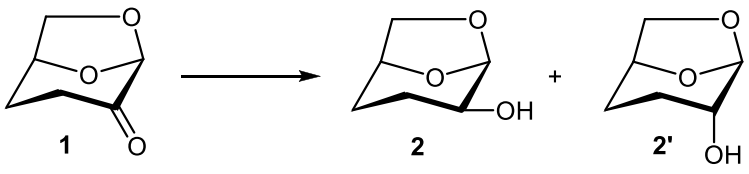
Experimental section

The spectral and analytical data were obtained using the equipment of the Khimiya Joint Center at Ufa Institute of Chemistry, Ufa Research Center of the Russian Academy of Sciences. ^{1}H and ^{13}C NMR spectra were registered on a Bruker AM-300 spectrometer (300 MHz for ^{1}H and 75.47 MHz for ^{13}C) and on a Bruker Avance III spectrometer (500.13 MHz for ^{1}H and 125.47 MHz for ^{13}C). IR spectra were recorded on a Shimadzu IRPrestige-21 or a Bruker Tensor 27 spectrophotometer (neat or mulls in mineral oil). Mass spectra were recorded on a Shimadzu LCMS-2010 EV single quadrupole system in positive and negative ion modes at capillary voltages of 4.5 and –3.5 kV, respectively, with electrospray ionization, Phenomenex C18 column (150 x 4.6 mm i.d., 5 μm) and MeCN–H_2O as eluent. The elemental composition was determined on a Euro-2000 CHNS(O) analyzer. Optical rotation was determined on a Perkin Elmer-341 polarimeter. Analytical TLC was carried out on PTSKh-AF-A Sorbfil plates (Sorbpolymer Company, Krasnodar) with R_f values calculation. The melting points were measured on a Boëtius 05 heating block. Macherey–Nagel silica gel 60 (0.063–0.2 mm particle size) was used for column chromatography. Commercially available reagents, catalysts, baker's yeast and solvents were used as received. We used baker's yeast from Pakmaya Company (Turkey). Cyrene **1**[1], levoglucosenone **3**[2] and ketones **5a–b**[3], **5d**[4] were prepared according to known procedures.

Reduction of cyrene 1



Reduction of cyrene **1** *with* $NaBH_4$

A magnetically stirred solution of cyrene **1** (200 mg, 1.56 mmol) in methanol (10 ml) maintained at 0 °C was treated with $NaBH_4$ (30 mg, 0.78 mmol). After 15 min, acetic acid (0.5 ml) was added to decompose the excess of the reagent. The solvent was evaporated *in vacuo*. The residue thus obtained was subjected to column

chromatography to give an inseparable mixture of alcohols **2** and **2'** (201 mg, 99%) as a clear, colorless oil, $[\alpha]_D^{20}$ -117.1° (*c* 1.0 in $CHCl_3$).

Reduction of cyrene **1** *with* $NaBH_4$, $CeCl_3 \cdot 7H_2O$.

A magnetically stirred solution of cyrene **1** (200 mg, 1.56 mmol) in methanol (10 ml) maintained at 0 °C was treated with $CeCl_3 \cdot 7H_2O$ (698 mg, 1.87 mmol) then, in portions, with $NaBH_4$ (30 mg, 0.78 mmol). The ensuing mixture was stirred at 0 °C for 3 h before being concentrated *in vacuo*. The residue thus obtained was subjected to column chromatography to give an inseparable mixture of alcohols **2** and **2'** (175 mg, 86%) as a clear, colorless oil, $[\alpha]_D^{20}$ -122.9° (*c* 1.0 in $CHCl_3$).

Reduction of cyrene **1** *with* $LiAlH_4$.

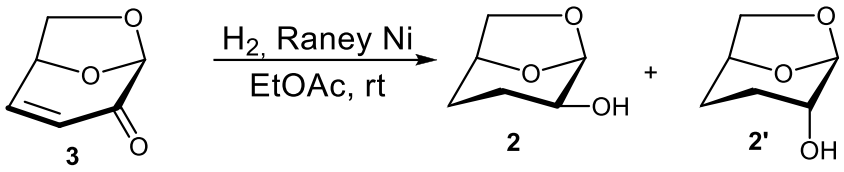
A solution of cyrene **1** (200 mg, 1.56 mmol) in dry ether (10 mL) at 0 °C was added dropwise to $LiAlH_4$ (59 mg, 1.56 mmol) in ether (10 ml) and stirred for 1 h. The mixture was neutralized with 3% aqueous HCl and extracted with ethyl acetate. The extract was dried over $MgSO_4$ and evaporated, and the residue was subjected to silica gel chromatography to isolate alcohols **2** and **2'** (152 mg, 75%) as a clear, colorless oil, $[\alpha]_D^{20}$ -110.6° (*c* 1.0 in $CHCl_3$).

Reduction of cyrene **1** *with* $(i\text{-}Bu)_2AlH$.

A solution of cyrene **1** (200 mg, 1.56 mmol) in dry dichloromethane (10 ml) was cooled to 0°C, $(i\text{-}Bu)_2AlH$ (1.87 ml, 1.87 mmol, 1 M solution in toluene) was added dropwise, and the mixture was stirred for 30 min at this temperature. The mixture was treated with 3% aqueous HCl to destroy gel. The organic phase was separated, the aqueous phase was extracted with dichloromethane, the extracts were combined with the organic phase, washed with water, and dried over $MgSO_4$. The solvent was distilled off and the residue was subjected to silica gel chromatography to isolate alcohols **2** and **2'** (138 mg, 68%) as a clear, colorless oil, $[\alpha]_D^{20}$ -99.2° (*c* 1.0 in $CHCl_3$).

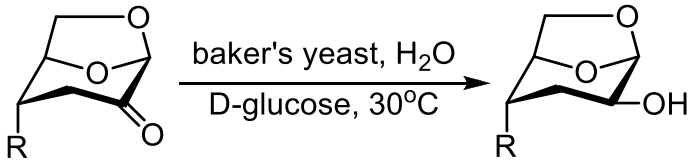
Alcohols **2** and **2'** (174 mg, 86%) as a clear, colorless oil, $[\alpha]_D^{20}$ -96.4° (*c* 1.0 in $CHCl_3$), were prepared from cyrene **1** (200 mg, 1.56 mmol) at –78°C.

*Hydrogenation of levoglucosenone **3** with Raney Ni.*



A solution of levoglucosenone **3** (200 mg. 1.59 mmol) in ethyl acetate (10 ml) was hydrogenated for 48 h at 1 atm in the presence of 100 mg of Raney Ni. The resulting suspension was celite-filtered and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford alcohols **2** and **2'** (185 mg, 90%) as a clear, colorless oil, $[\alpha]_D^{20}$ -87.6° (*c* 1.0 in $CHCl_3$).

Microbial reduction of ketones with baker's yeast. General Procedure.



A suspension of baker's yeast (1.3 g) and D-glucose (1 g) in water (10 ml) was stirred for 1 h at about 30°C, then a solution of ketone (1 mmol) in water (3 ml) was added to the suspension. The reaction mixture was stirred at about 30°C. The reaction was monitored by silica gel TLC analysis until the disappearance of the starting ketone. After the ketone faded (about 24 h) ethanol (10 ml) was added and the precipitate was collected by filtration and washed with ethanol. The filtrate was evaporated *in vacuo*, the residue was separated by column chromatography.

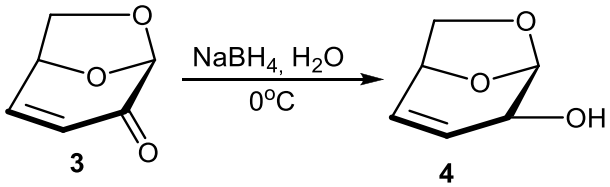
1,6-Anhydro-3,4-dideoxy-β-D-threo-*hexopyranose* **(2)**.

Alcohol **2** (201 mg, 99%) was prepared from cyrene **1** (200 mg, 1.56 mmol) according to the general procedure for microbial reduction. **2** is a clear oil that partially crystallizes, $[\alpha]_D^{20}$ -134.2° (*c* 1.0 in $CHCl_3$); $[\alpha]_D^{20}$ -132.8° (*c* 1.0 in H_2O), {ref[5]. m.p. about 28° (unsharp), $[\alpha]_D$ -133° (*c* 0.6 in H_2O)}. R_f 0.3 (hexane–EtOAc, 1:1). IR ν_{max} 3418 (OH), 2954 (C–H), 1131 and 1070 (C–O–C), 985 and 900 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.49 (dtd, 1H, H-3, *J* 12.9, 10.0, 6.1 Hz), 1.57 (dd, 1H, H-4, *J* 13.9, 6.1 Hz), 1.82–1.91 (m, 1H, H-4), 1.98–2.04 (m, 1H, H-3), 2.18 (br.s, 1H, OH),

3.58 (dd, 1H, H-2, *J* 10.0, 6.2 Hz), 3.79 (dd, 1H, H-6, *J* 7.1, 5.4 Hz), 3.83 (d, 1H, H-6, *J* 7.1 Hz), 4.46–4.49 (m, 1H, H-5), 5.30 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 26.02 (C^3), 27.82 (C^4), 68.17 (C^6), 69.98 (C^2), 72.80 (C^5), 102.92 (C^1). Found: C, 55.45; H, 7.79. MS (APCI) *m/z*: 130.1 $[M]^+$. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74.

1,6-Anhydro-3,4-dideoxy-β-D-erythro-*hexopyranose* **(2')** (from mixture with compound **2**). R_f 0.3 (hexane–EtOAc, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.40 (dd, 1H, H-3, *J* 13.5, 5.6 Hz), 1.55–1.60 (m, 1H, H-4), 1.93 (dddd,1H, H-3, *J* 13.5, 10.5, 6.3, 4.3 Hz), 2.01–2.10 (m, 1H, H-4), 2.65 (br.s, 1H, OH), 3.59 (dd, 1H, H-2, *J* 6.3, 1.7 Hz), 3.77–3.81 (m, 1H, H-6), 3.88 (d, 1H, H-6, *J* 7.2 Hz), 4.46–4.49 (m, 1H, H-5), 5.30 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.17 (C^3), 24.72 (C^4), 66.74 (C^2), 66.79 (C^6), 73.29 (C^5), 102.05 (C^1).

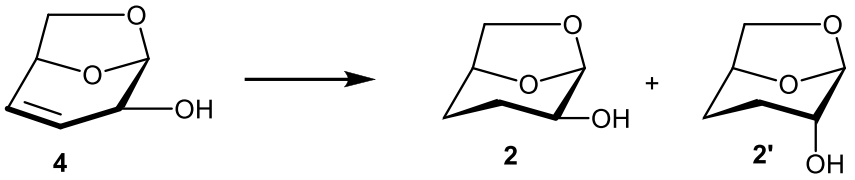
Reduction of levoglucosenone (**3**). *1,6-Anhydro-3,4-dideoxy- β-D*-threo-*hex-3-enopyranose* **(4)**



Levoglucosenone **3** (1.00 g, 7.93 mmol) was dissolved in water (20 m) and cooled at 0 °C. $NaBH_4$ 98% (0.31 mg, 7.93 mmol, 1 equiv.) was added. After 15 min, acetone (2 ml) was added to decompose the excess of the reagent. The solution was extracted with chloroform, the organic phase was dried with $MgSO_4$ and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford allylic alcohol **4** (0.82 g, 81%). **4** is a white solid. m.p. 67–68 °C, $[\alpha]_D^{20}$ -33.7° (*c* 1.0 in $CHCl_3$); Recrystallization from light petroleum ether–CH_2Cl_2 gave needles, m.p. 70–71°, $[\alpha]_D^{20}$ -29.4 (*c* 1.0 in $CHCl_3$). {ref[3]. m.p. 70–70.5°, $[\alpha]_D$ -30°($CHCl_3$)}. R_f 0.35 (hexane–EtOAc, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.55 (br.s, 1H, OH), 3.67 (dd, 1H, H-6, *J* 6.6, 4.2 Hz), 3.78 (d, 1H, H-6, *J* 6.6 Hz), 4.25 (br.s, 1H, H-2), 4.58 (t, 1H, H-5, *J* 4.2 Hz), 5.43 (d, 1H, H-1, *J* 2.0 Hz), 5.63 (dt, 1H, H-3, *J* 9.9, 2.1 Hz), 6.04 (dd, 1H, H-

4, *J* 9.9, 4.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 68.73, 70.68, 71.13, 101.29, 129.08, 130.61 Found: C, 56.31; H, 6.36. MS (APCI) *m/z*: 129.0 $[M+H]^+$. Calcd for $C_6H_8O_3$: C, 56.24; H, 6.29.

Hydrogenation of 4



*Hydrogenation of **4** with Raney Ni.*

A solution of **4** (200 mg. 1.56 mmol) in ethyl acetate (10 ml) was hydrogenated for 24 h at 1 atm in the presence of 100 mg of Raney Ni. The resulting suspension was celite-filtered and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford alcohols **2** and **2'** (200 mg, 99%) as a clear, colorless oil, $[\alpha]_D^{20}$ -123.7° (*c* 1.0 in $CHCl_3$).

*Hydrogenation of **4** with Raney Ni, CH_3COOH.*

To a stirred solution of freshly prepared Raney Ni (250 mg) in ethyl acetate (10 ml) at 25 °C, acetic acid (0.1 ml) was added and the mixture stirred for 1 h. Then a solution of **4** (0.5 g. 3.91 mmol) in ethyl acetate (10 ml) was added, and the mixture was stirred under a hydrogen atmosphere (1 atm) for 24 h at room temperature. The resulting suspension was celite-filtered and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford alcohols **2** and **2'** (198 mg, 98%) as a clear, colorless oil, $[\alpha]_D^{20}$ -127.0° (*c* 1.0 in $CHCl_3$).

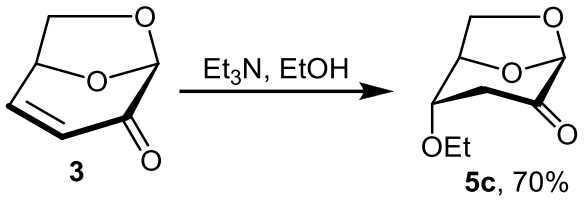
*Hydrogenation of **4** with $Pd/BaSO_4$.*

A solution of **4** (200 mg. 1.56 mmol) in ethyl acetate (10 ml) was hydrogenated for 24 h at 1 atm in the presence of 20 mg of 10% $Pd/BaSO_4$. The resulting suspension was celite-filtered and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford alcohol **2** (177 mg, 87%) and cyrene **1** (24 mg, 12%). **2** is a clear, colorless oil, $[\alpha]_D^{20}$ -131.7° (*c* 1.0 in $CHCl_3$).

*Hydrogenation of **4** with Pd/C.*

A solution of **4** (200 mg. 1.56 mmol) in ethyl acetate (10 ml) was hydrogenated for 2 h at 1 atm in the presence of 20 mg of 10% Pd/C. The resulting suspension was celite-filtered and the solvent was evaporated *in vacuo*. Reaction products were separated by column chromatography to afford alcohol **2** (144 mg, 71%) and cyrene **1** (56 mg, 28%). **2** is a clear, colorless oil, $[\alpha]_D^{20}$ -133.7° (*c* 1.0 in $CHCl_3$).

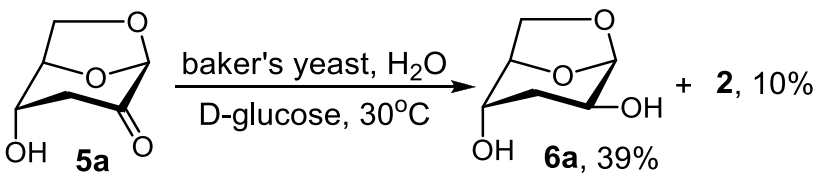
*1,6-Anhydro-3-deoxy-4-O-ethyl-β-D-*erythro-*hexopyranos-2-ulose* **(5c)**



3 **5c**, 70%

A solution of levoglucosenone **3** (0.34 g, 2.70 mmol) and triethylamine (0.10 ml, 1.35 mmol) in ethanol (35 ml) was stirred at room temperature for 36 h. Concentration and chromatography on silica afforded ether **5c** (0.33 g, 70%). **5c** is a yellow oil, $[\alpha]_D^{20}$ -214.1° (*c* 1.0 in $CHCl_3$), R_f 0.3 (hexane–EtOAc, 3:1). IR ν_{max} 2977 (C–H), 1739 (C=O), 1117 and 1095 (C–O–C), 909 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.11 (t, 3H, CH_2CH_3, *J* 7.0 Hz), 2.41 (d, 1H, H-3, *J* 17.0 Hz), 2.63 (dd, 1H, H-3, *J* 17.0, 5.9 Hz), 3.45 (qd, 2H, CH_2CH_3, *J* 7.0, 2.5 Hz), 3.73 (d, 1H, H-4, *J* 5.9 Hz), 3.79 (d, 1H, H-6, *J* 7.9 Hz), 3.84 (dd, 1H, H-6, *J* 7.9, 5.6 Hz), 4.65–4.68 (m, 1H, H-5), 5.01 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 15.25, 37.49, 64.56, 65.16, 74.93, 76.98, 101.23, 198.65. Found: C, 55.76; H, 7.11. MS (APCI) *m/z*: 207.0 $[M+^{35}Cl]^-$. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02.

Microbial reduction of ketone **5a**. *l,6-Anhydro-3-deoxy-β-D-*arabino-*hexopyranose* **(6a)**

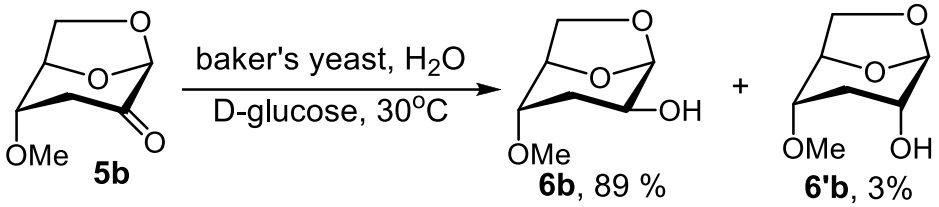


5a **6a**, 39%

Alcohols **6a** (79 mg, 39%) and **2** (17 mg, 10%) were prepared from ketone **5a** (200 mg. 1.39 mmol) according to the general procedure for microbial reduction.

6a is a white amorphous substance $[\alpha]_D^{20}$ -156º (*c* 1.0 in H_2O). {ref[6]. $[\alpha]_D^{20}$ -156º (*c* 0.73 in H_2O)}. R_f 0.2 (EtOAc). IR ν_{max} 3374 (OH), 2959 (C–H), 1181 (C–O), 1091 (CH–OH), 971 and 902 (O–C–O). ^{1}H NMR (500 MHz, CD_3OD) δ: 1.70 (ddd, 1H, H-3, *J* 14.3, 10.7, 4.5 Hz), 1.91 (dddd, 1H, H-3, *J* 14.3, 6.0, 3.1, 1.7 Hz), 3.71 (dd, 1H, H-6, *J* 7.6, 5.5 Hz), 3.76 (d, 1H, H-6, *J* 7.6 Hz), 3.74–3.80 (m, 1H, H-4), 3.79 (ddd, 1H, H-2, *J* 10.7, 6.0, 1.1 Hz), 4.36–4.40 (m, 1H, H-5), 5.22 (s, 1H, H-1). ^{13}C NMR (125 MHz, CD_3OD) δ: 32.55 (C^3), 65.97 (C^6), 66.05 (C^2), 67.42 (C^4), 76.64 (C^5), 102.83 (C^1). Found: C, 49.43; H, 6.83. MS (APCI) *m/z*: 188.0 $[M+MeCN+H]^+$. Calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.90.

Microbial reduction of ketone **5b**. *1,6-Anhydro-3-deoxy-4-O-methyl-β-D*-arabino-*hexopyranose* **(6b)** and *1,6-anhydro-3-deoxy-4-O-methyl-β-D*-ribo-*hexopyranose* **(6'b)**

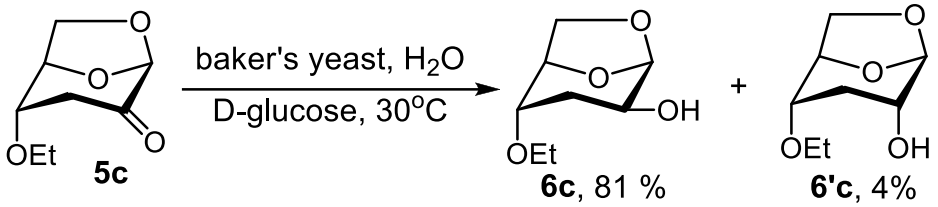


Alcohols **6b** (180 mg, 89%) and **6'b** (6 mg, 3%) were prepared from ketone **5b** (200 mg. 1.27 mmol) according to the general procedure for microbial reduction.

6b is a clear, colorless oil, $[\alpha]_D^{22}$ -142.0º (*c* 1.0 in $CHCl_3$) R_f 0.25 (EtOAc). IR ν_{max} 3388 (OH), 2957 (C–H), 1142 (C–O), 1075 and 1035 (C–O–C), 972 and 905 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.49 (ddd, 1H, H-3, *J* 14.2, 10.5, 4.5 Hz), 2.08 (br.s, 1H, OH), 2.23 (ddd, 1H, H-3, *J* 14.2, 6.0, 1.4 Hz), 3.27–3.32 (m, 1H, H-4), 3.39 (s, 3H, CH_3), 3.72 (d, 1H, H-6, *J* 7.6 Hz), 3.79 (ddd, 1H, H-2, *J* 10.5, 6.0, 1.4 Hz), 3.81 (dd, 1H, H-6, *J* 7.6, 5.6 Hz), 4.56–4.60 (m, 1H, H-5), 5.33 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 29.84 (C^3), 56.45 (CH_3), 66.49 (C^6), 66.49 (C^2), 73.57 (C^4), 76.72 (C^5), 102.75 (C^1). Found: C, 52.41; H, 7.60. MS (APCI) *m/z*: 143.0 $[M-H_2O+H]^+$. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55.

6'b is a clear, colorless oil, $[\alpha]_D^{25}$ -68.5º (*c* 0.4 in $CHCl_3$). R_f 0.15 (hexane–EtOAc, 1:1). IR ν_{max} 3380 (OH), 2963 (C–H), 1140 (C–O), 1074 and 1034 (C–O–C), 972 and 903 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.90–1.97 (m, 2H, H-3), 3.25–3.30 (m, 1H, H-4), 3.44 (s, 3H, CH_3), 3.51–3.55 (m, 1H, H-2), 3.78 (d, 1H, H-6, *J* 7.7 Hz), 3.85 (dd, 1H, H-6, *J* 7.6, 5.5 Hz), 4.63–4.67 (m, 1H, H-5), 5.29 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 29.51 (C^3), 56.47 (CH_3), 66.28 (C^6), 68.02 (C^2), 74.43 (C^4), 76.82 (C^5), 103.35 (C^1). Found: C, 52.55; H, 7.63. MS (APCI) *m/z*: 202.1 $[M+MeCN+H]^+$. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55.

Microbial reduction of ketone **5c**. *1,6-Anhydro-3-deoxy-4-O-ethyl-β-D*-arabino-*hexopyranose* (**6c**) and *1,6-anhydro-3-deoxy-4-O-ethyl-β-D*-ribo-*hexopyranose* (**6'c**)



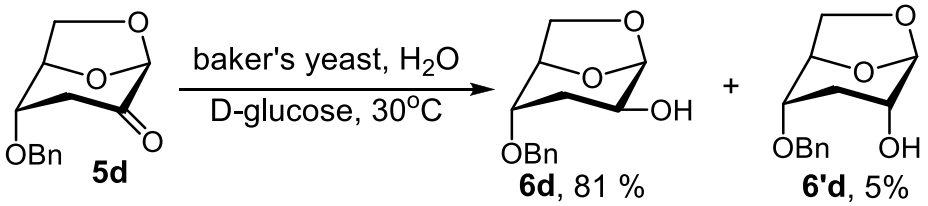
Alcohols **6c** (164 mg, 81%) and **6'c** (8 mg, 4%) were prepared from ketone **5c** (200 mg. 1.16 mmol) according to the general procedure for microbial reduction.

6c is a clear, colorless oil, $[\alpha]_D^{20}$ -132.2º (*c* 1.0 in $CHCl_3$) R_f 0.35 (EtOAc). IR ν_{max} 3420 (OH), 2974 (C–H), 1096 and 1074 (C–O–C), 976 and 908 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.09 (t, 3H, CH_2CH_3, *J* 6.9 Hz), 1.40 (ddd, 1H, H-3, *J* 14.5, 10.5, 4.6 Hz), 2.01 (ddd, 1H, H-3, *J* 14.5, 4.7, 1.2 Hz), 3.25–3.29 (m, 1H, H-2), 3.41 (q, 2H, CH_2CH_3, *J* 6.9 Hz), 3.58 (d, 1H, H-6, *J* 7.7 Hz), 3.65 (dd, 1H, H-6, *J* 7.7, 5.5 Hz), 3.65–3.70 (m, 1H, H-4), 4.39–4.42 (m, 1H, H-5), 5.20 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 15.32, 30.61, 64.29, 66.26, 66.61, 74.18, 74.97, 102.73. Found: C, 55.23; H, 8.11. MS (APCI) *m/z*: 216.0 $[M+MeCN+H]^+$. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10.

6'c is a clear, colorless oil, $[\alpha]_D^{26}$ -91.9º (*c* 0.4 in $CHCl_3$). R_f 0.2 (hexane–EtOAc, 1:1). IR ν_{max} 3440 (OH), 2970 (C–H), 1074 (C–O–C), 903 (O–C–O). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.25 (t, 3H, CH_2CH_3, *J* 7.0 Hz), 1.89 (dt, 1H, H-3, *J* 15.3, 1.7 Hz), 1.96 (dt, 1H, H-3, *J* 15.3, 4.0 Hz), 3.03 (br.s, 1H, OH), 3.34–3.39 (m, 1H, H-2), 3.49–3.54 (m, 1H, H-4), 3.54 (ddd, 1H, CH_2CH_3, *J* 14.0, 9.0, *J* 7.0 Hz), 3.64 (ddd, 1H, CH_2CH_3, *J*

14.0, 9.0, *J* 7.0 Hz), 3.77 (d, 1H, H-6, *J* 7.7 Hz), 3.83 (dd, 1H, H-6, *J* 7.7, 5.4 Hz), 4.58–4.62 (m, 1H, H-5), 5.37 (s, 1H, H-1). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 15.43, 27.98, 64.30, 65.43, 67.22, 74.15, 74.18, 102.44. Found: C, 55.30; H, 8.16. MS (APCI) *m/z*: 175.0 $[M+H]^+$. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10.

Microbial reduction of ketone **5d**. *1,6-Anhydro-4-O-benzyl-3-deoxy-β-D*-arabino-*hexopyranose* (**6d**) and *1,6-anhydro-4-O-benzyl-3-deoxy-β-D*-ribo-*hexopyranose* (**6'd**)



Alcohols **6d** (164 mg, 81%) and **6'd** (10 mg, 5%) were prepared from ketone **5d** (200 mg. 0.85 mmol) according to the general procedure for microbial reduction. A suspension of baker's yeast was added to ketone **5d**, because the ketone **5d** is poorly soluble in water.

6d is a white needles, m.p. 121–123º, $[\alpha]_D^{25}$ -92.4º (*c* 1.0 in $CHCl_3$). {ref[7]. m.p. 117.5–119, $[\alpha]_D^{20}$ -91º ($CHCl_3$)}. R_f 0.25 (hexane–EtOAc, 1:1). IR ν_{max} 3421 (OH), 2901 (C–H), 1117 and 1100 (C–O), 966 (O–C–O), 897, 865, 737 and 695 (C–H ar) ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.51 (ddd, 1H, H-3, *J* 14.5, 10.3, 4.5 Hz), 2.13 (br.s, 1H, OH), 2.23 (ddd, 1H, H-3, *J* 14.5, 6.0, *J* 1.5 Hz), 3.45–3.47 (m, 1H, H-4), 3.67 (d, 1H, H-6, *J* 7.6 Hz), 3.78 (dd, 1H, H-6, *J* 7.6, 5.5 Hz), 3.87 (ddd, 1H, H-2, *J* 10.3, 6.0, *J* 1.2 Hz), 4.53–4.59 (m, 1H, H-5), 4.58 (d, 1H, CH_2O, *J* 12.3 Hz), 4.62 (d, 1H, CH_2O, *J* 12.3 Hz), 5.36 (s, 1H, H-1), 7.25–7.37 (m, 5H, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 30.88, 66.40, 66.88, 70.64, 74.10, 74.30, 102.83, 127.69, 127.85, 128.85, 137.91. Found: C, 66.02; H, 6.80. MS (APCI) *m/z*: 277.9 $[M+MeCN+H]^+$. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83.

6'd is a clear oil that partially crystallizes, $[\alpha]_D^{25}$ -56.7º (*c* 1.0 in $CHCl_3$). {ref[7]. m.p. 56–57, $[\alpha]_D^{20}$ -60º ($CHCl_3$)}. R_f 0.35 (hexane–EtOAc, 1:1). IR ν_{max} 3420 (OH), 2929 (C–H), 1142 and 1097 (C–O), 966 (O–C–O), 896, 860, 730 and 695 (C–H ar). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.95–2.05 (m, 2H, H-3), 3.00 (br.s, 1H, OH), 3.43–3.47 (m, 1H, H-4), 3.54–3.58 (m, 1H, H-2), 3.76 (d, 1H, H-6, *J* 7.7 Hz), 3.83 (dd, 1H, H-6, *J* 7.6,

5.5 Hz), 4.62–4.66 (m, 1H, H-5), 4.63 (d, 1H, CH_2O, *J* 11.9 Hz), 4.66 (d, 1H, CH_2O, *J* 11.9 Hz), 5.40 (d, 1H, H-1, *J* 2.2 Hz), 7.27–7.39 (m, 5H, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 27.93, 65.47, 67.16, 70.64, 73.38, 74.15, 102.49, 127.69, 127.95, 128.56, 137.56. Found: C, 65.98; H, 6.86. MS (APCI) *m/z*: 254.2 $[M+H_2O]^+$. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83.

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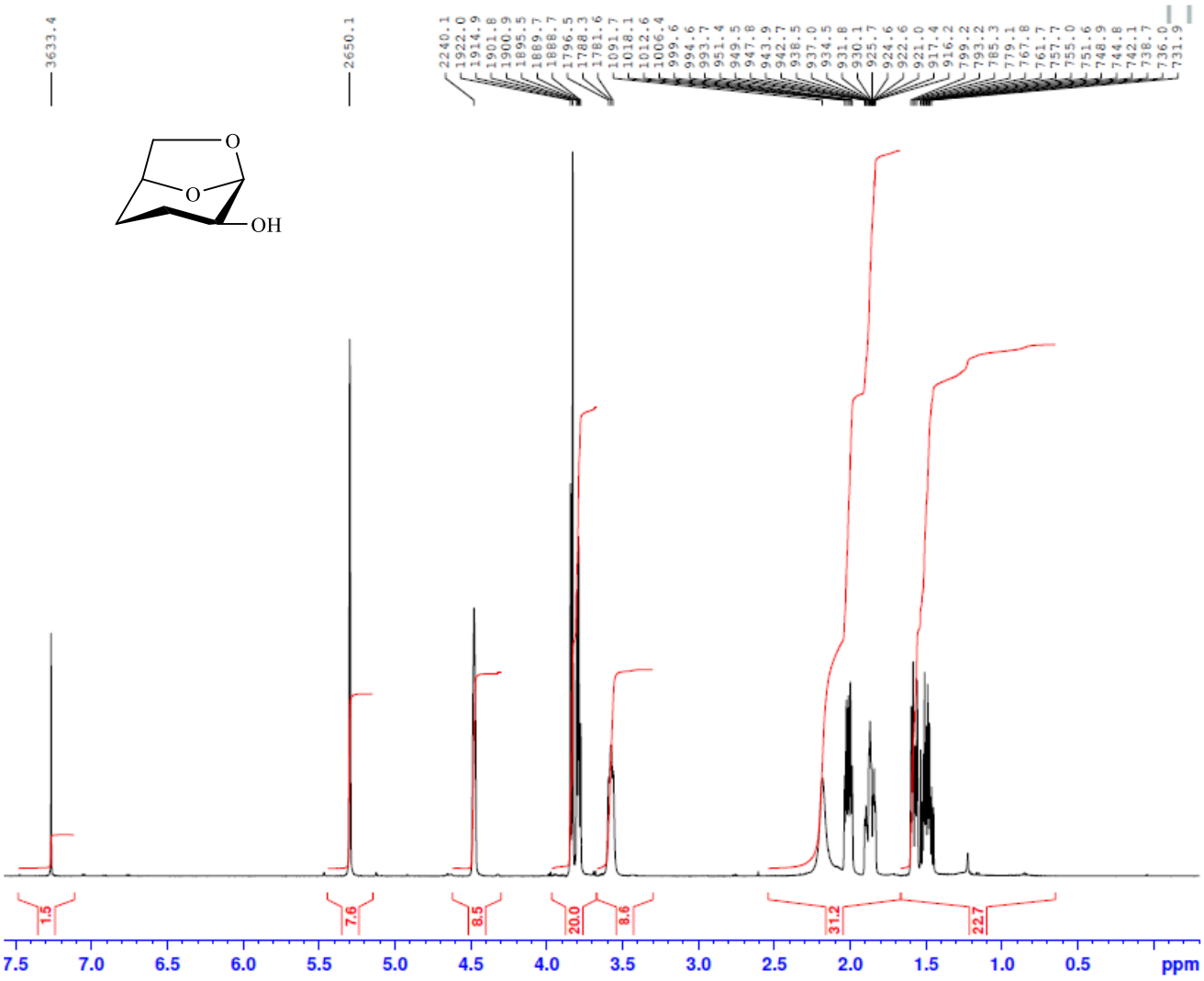
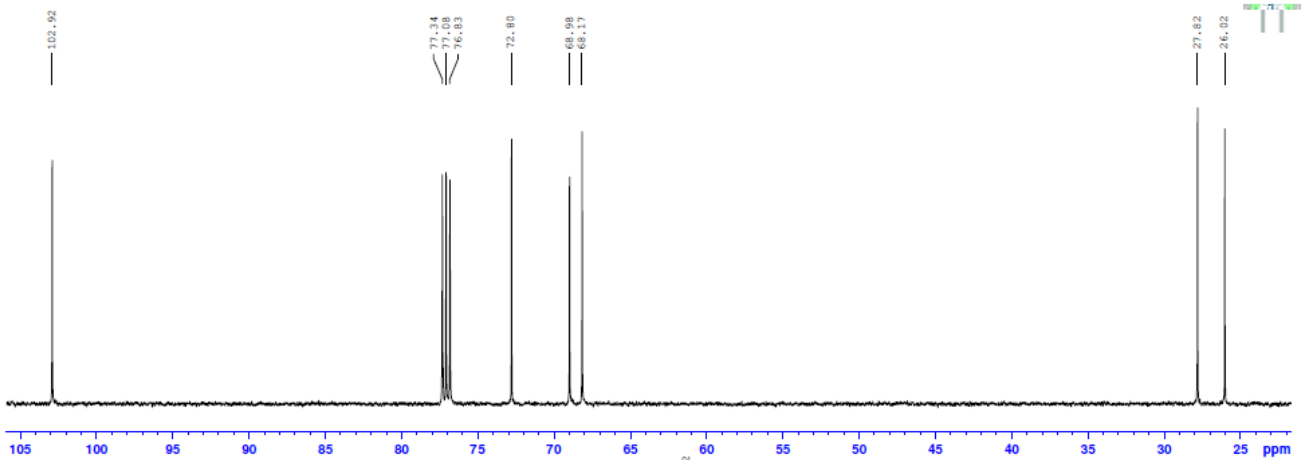
NMR Spectra:

1,6-Anhydro-3,4-dideoxy-β-D-*threo*-hexopyranose (2)

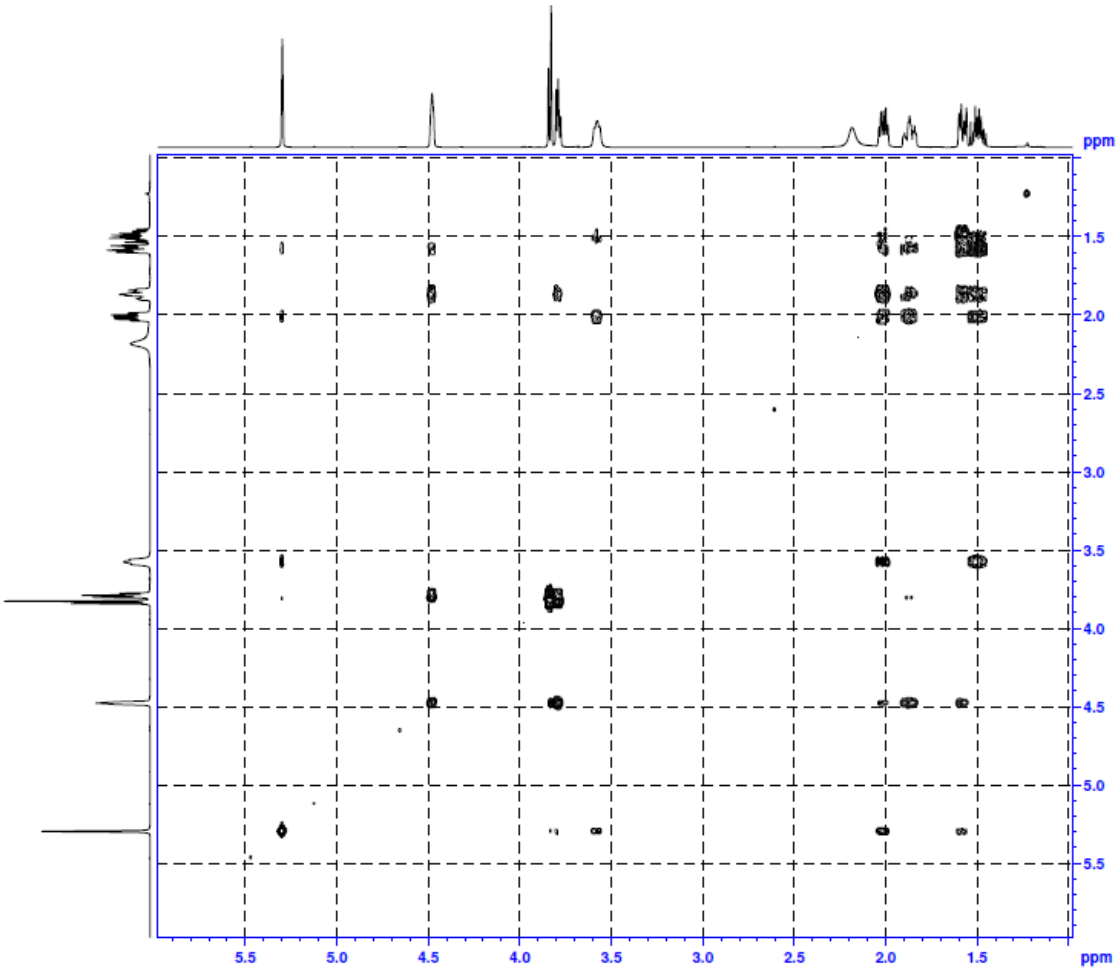
^{1}H NMR (500 MHz, $CDCl_3$)



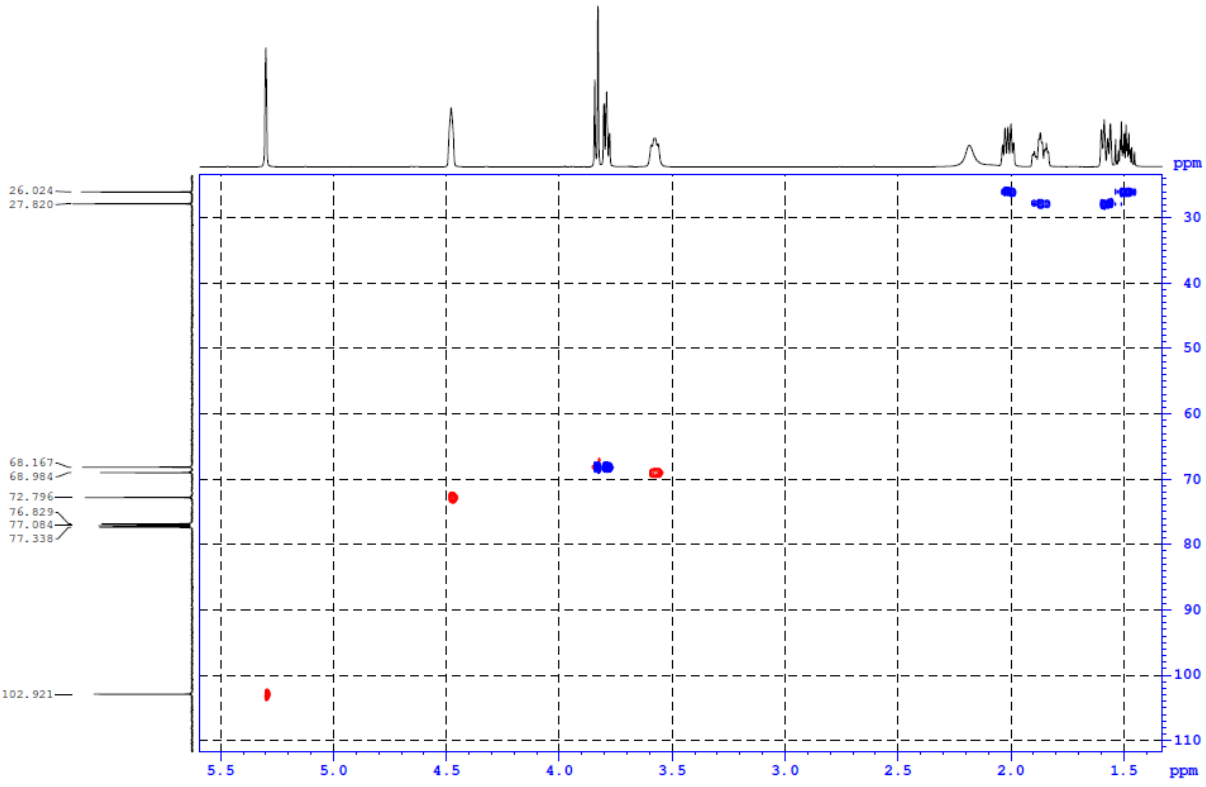
^{13}C NMR (125 MHz, $CDCl_3$)



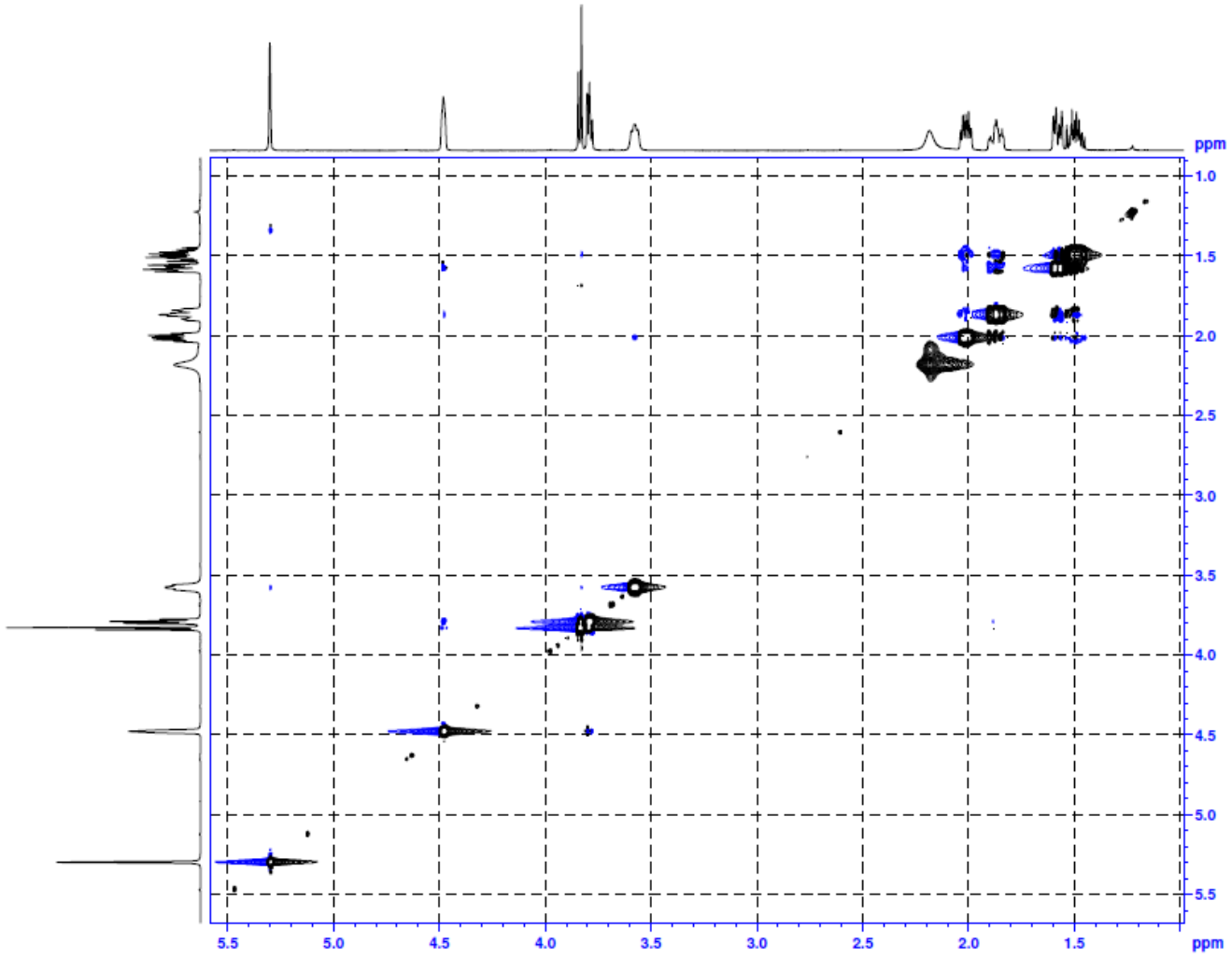
COSY $^{1}H–^{1}H$ ($CDCl_3$)



HSQC $^{1}H–^{13}C$ ($CDCl_3$)

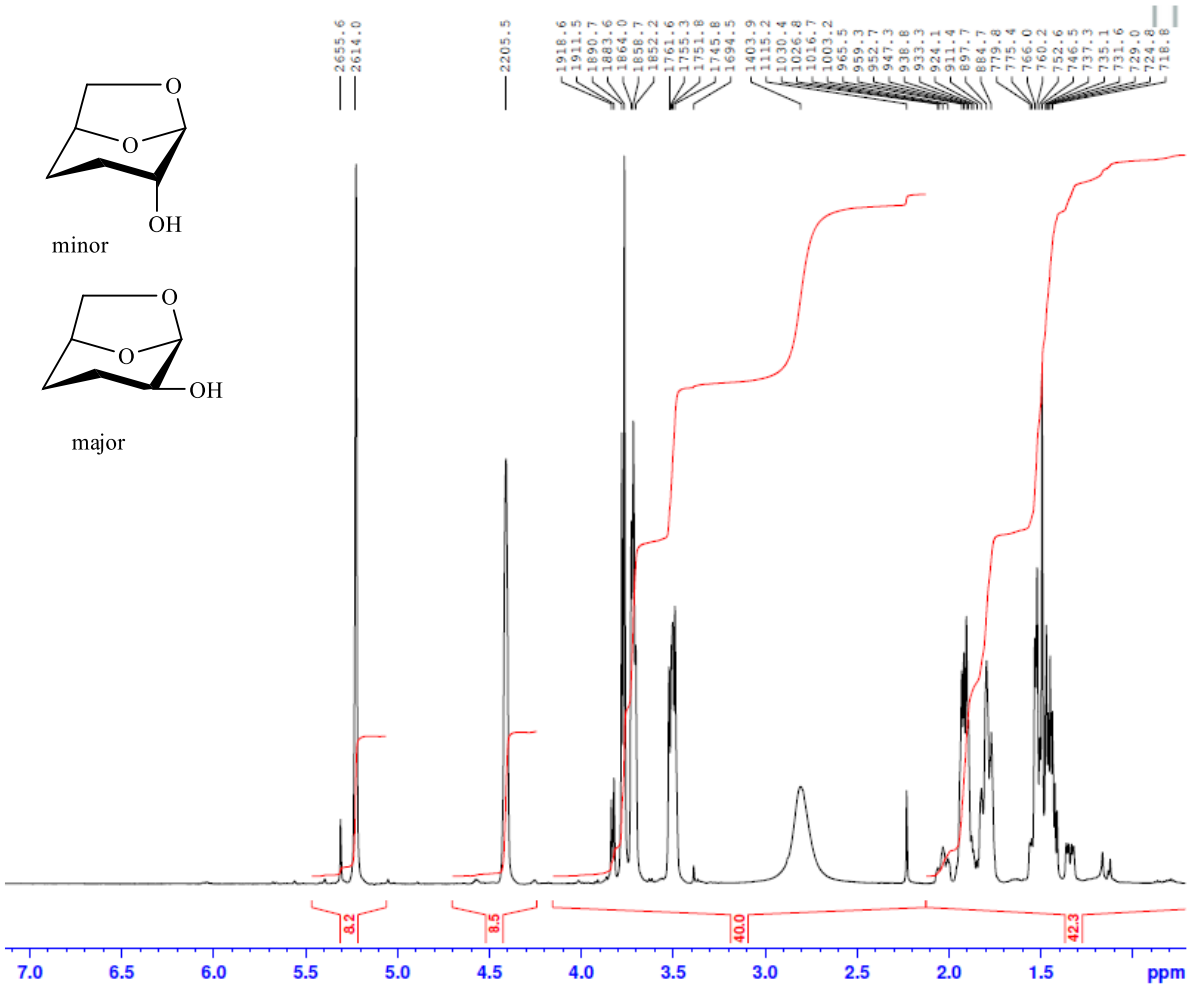


NOE $^{1}H–^{1}H$ ($CDCl_3$)

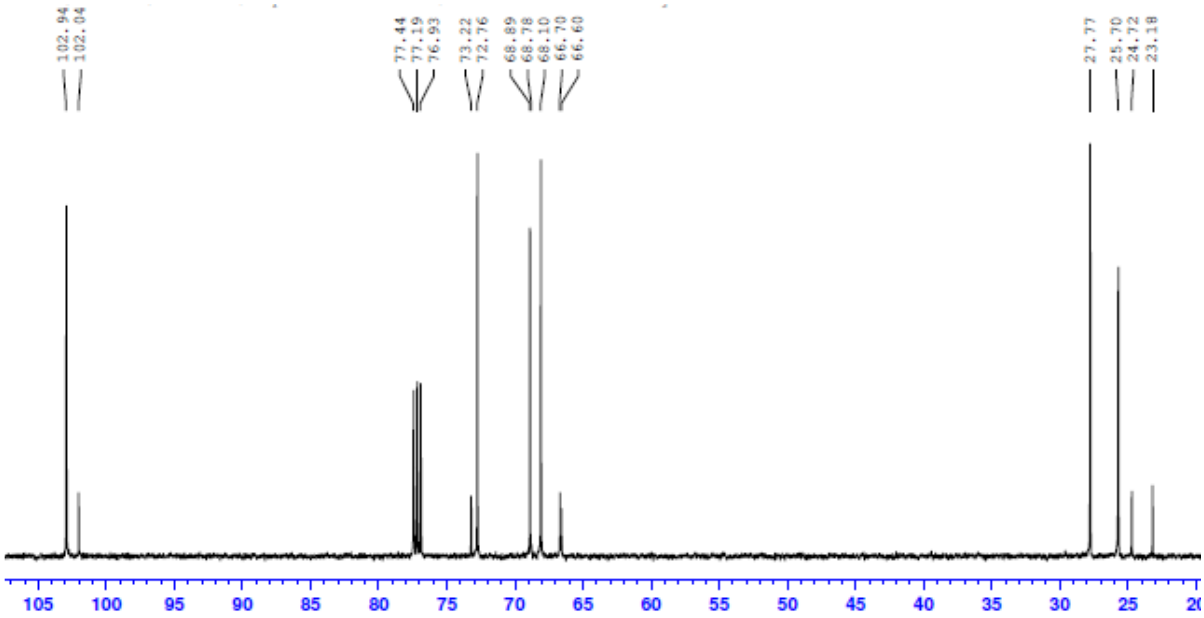


1,6-Anhydro-3,4-dideoxy-β-D-*erythro*-hexopyranose (2') (from mixture with compound **2**).

^{1}H NMR (500 MHz, $CDCl_3$)

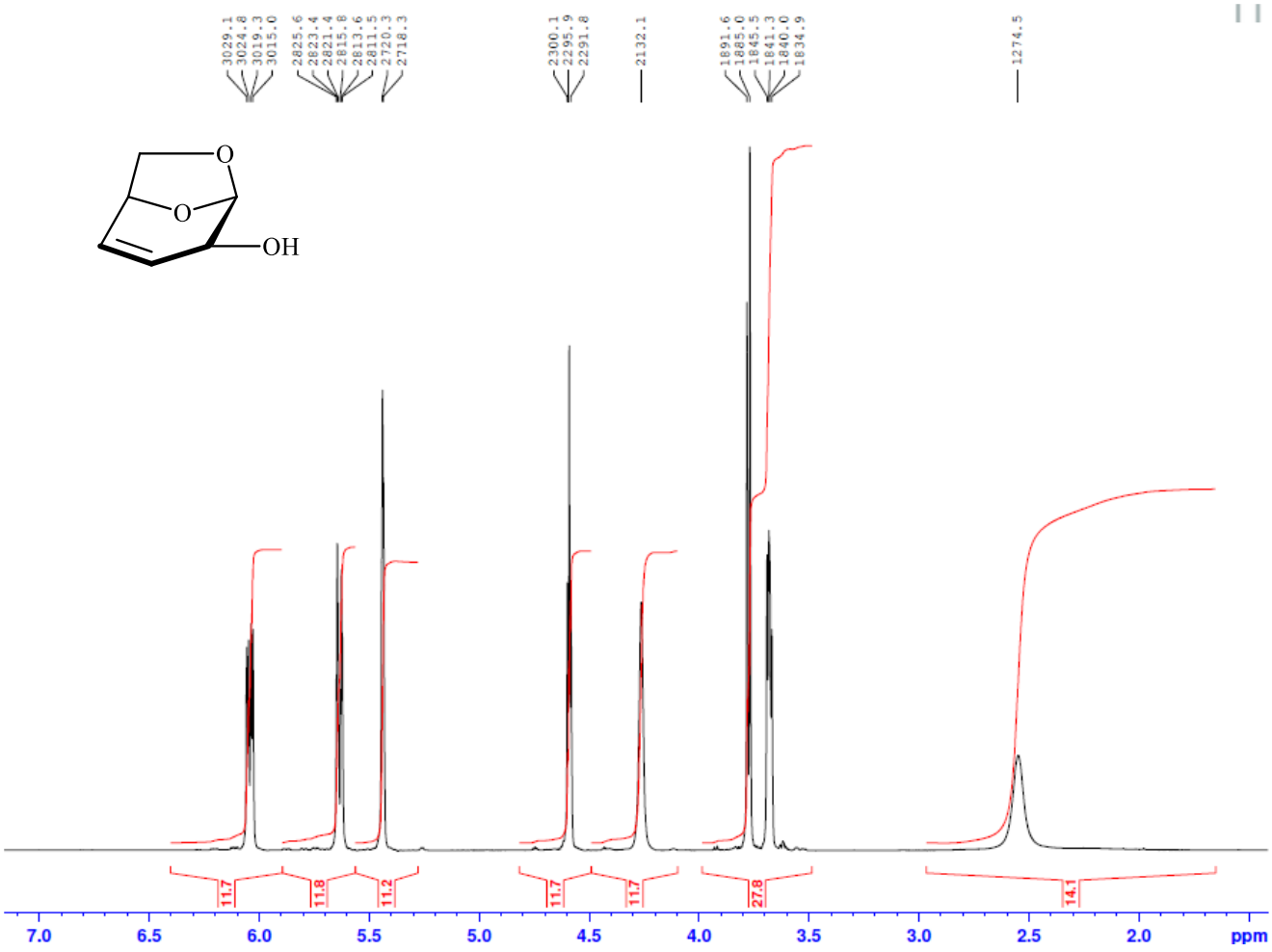


^{13}C NMR (125 MHz, $CDCl_3$)

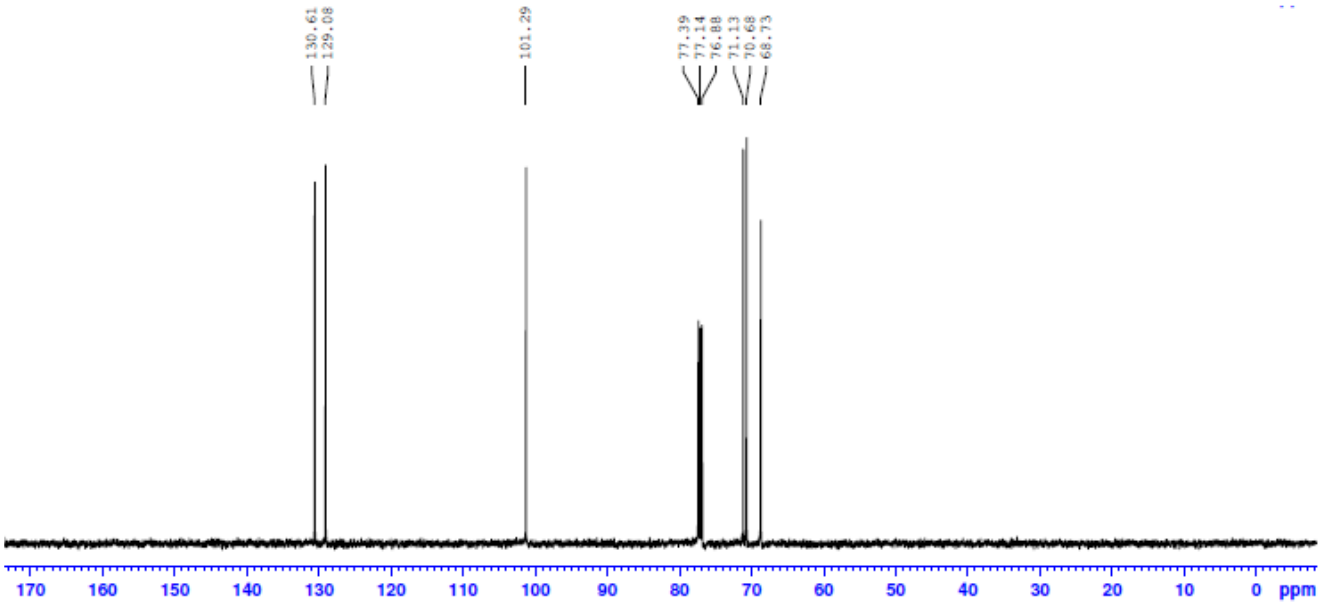


1,6-Anhydro-3,4-dideoxy- β-D-*threo*-hex-3-enopyranose (4)

^{1}H NMR (500 MHz, $CDCl_3$)

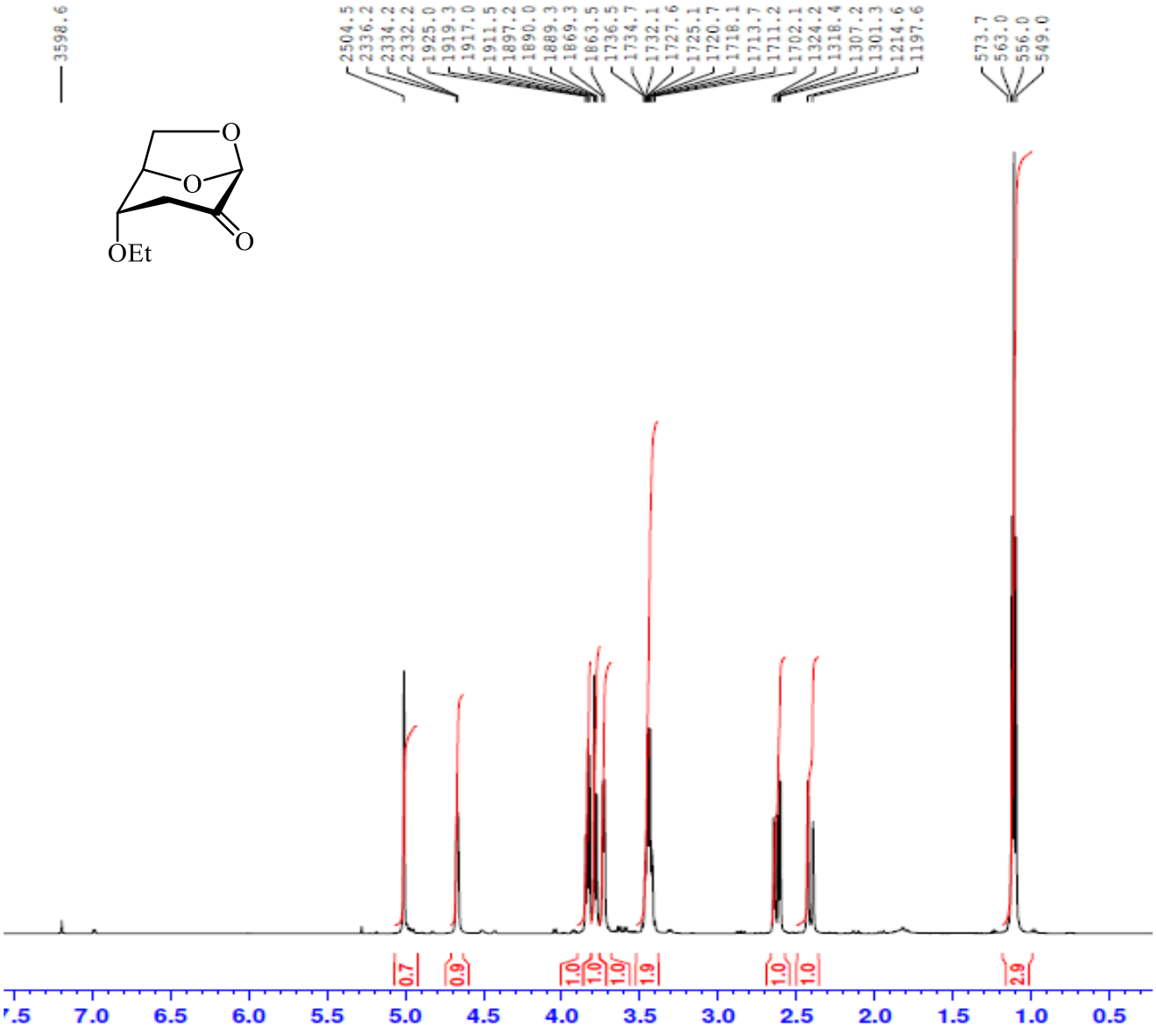


^{13}C NMR (125 MHz, $CDCl_3$)

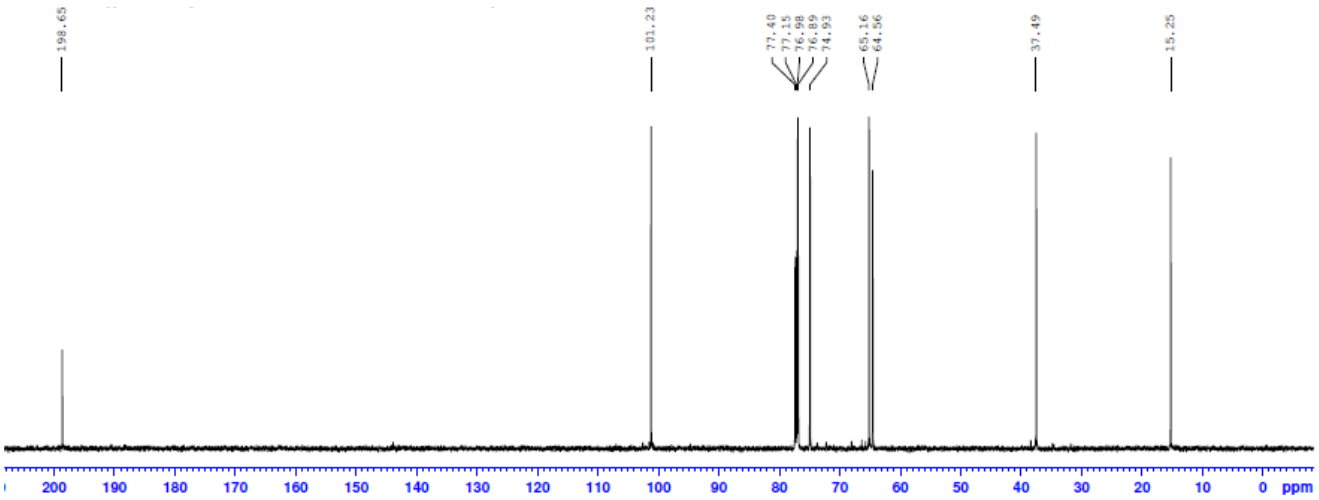


1,6-Anhydro-3-deoxy-4-O-ethyl-β-D-*erythro*-hexopyranos-2-ulose (5c)

^{1}H NMR (500 MHz, $CDCl_3$)

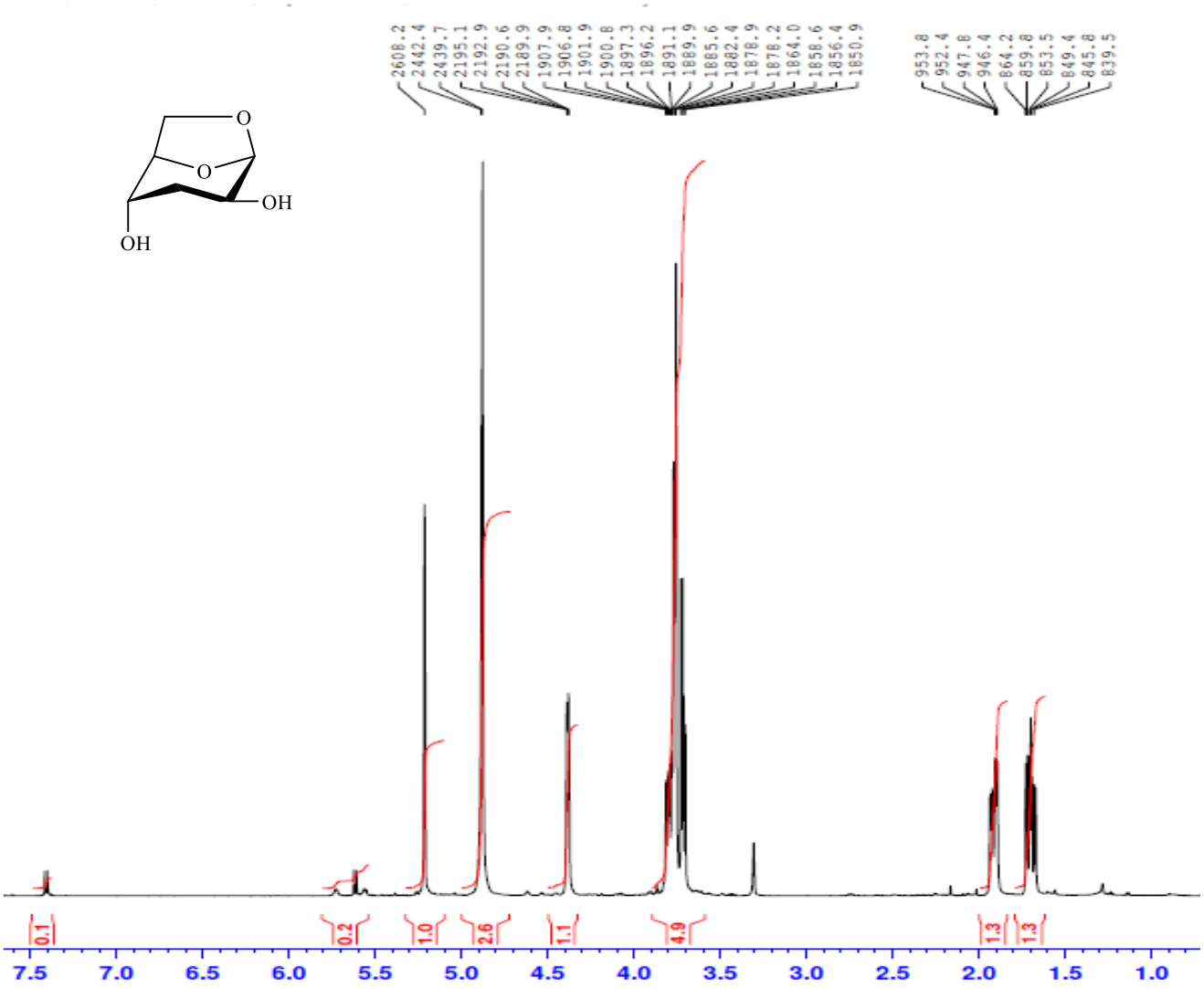


^{13}C NMR (125 MHz, $CDCl_3$)

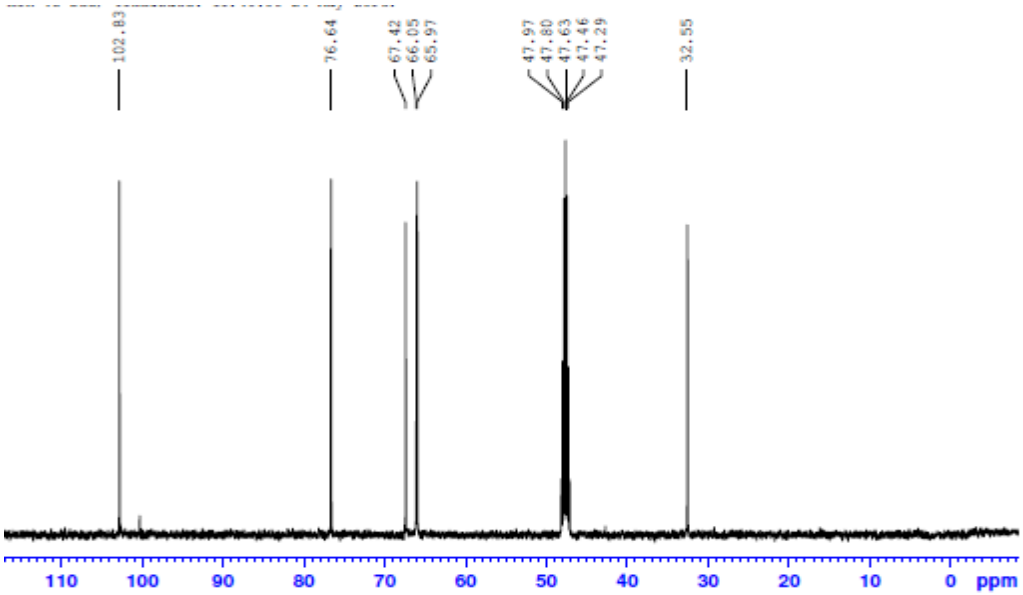


l,6-Anhydro-3-deoxy-β-D-*arabino*-hexopyranose (6a)

^{1}H NMR (500 MHz, CD_3OD)

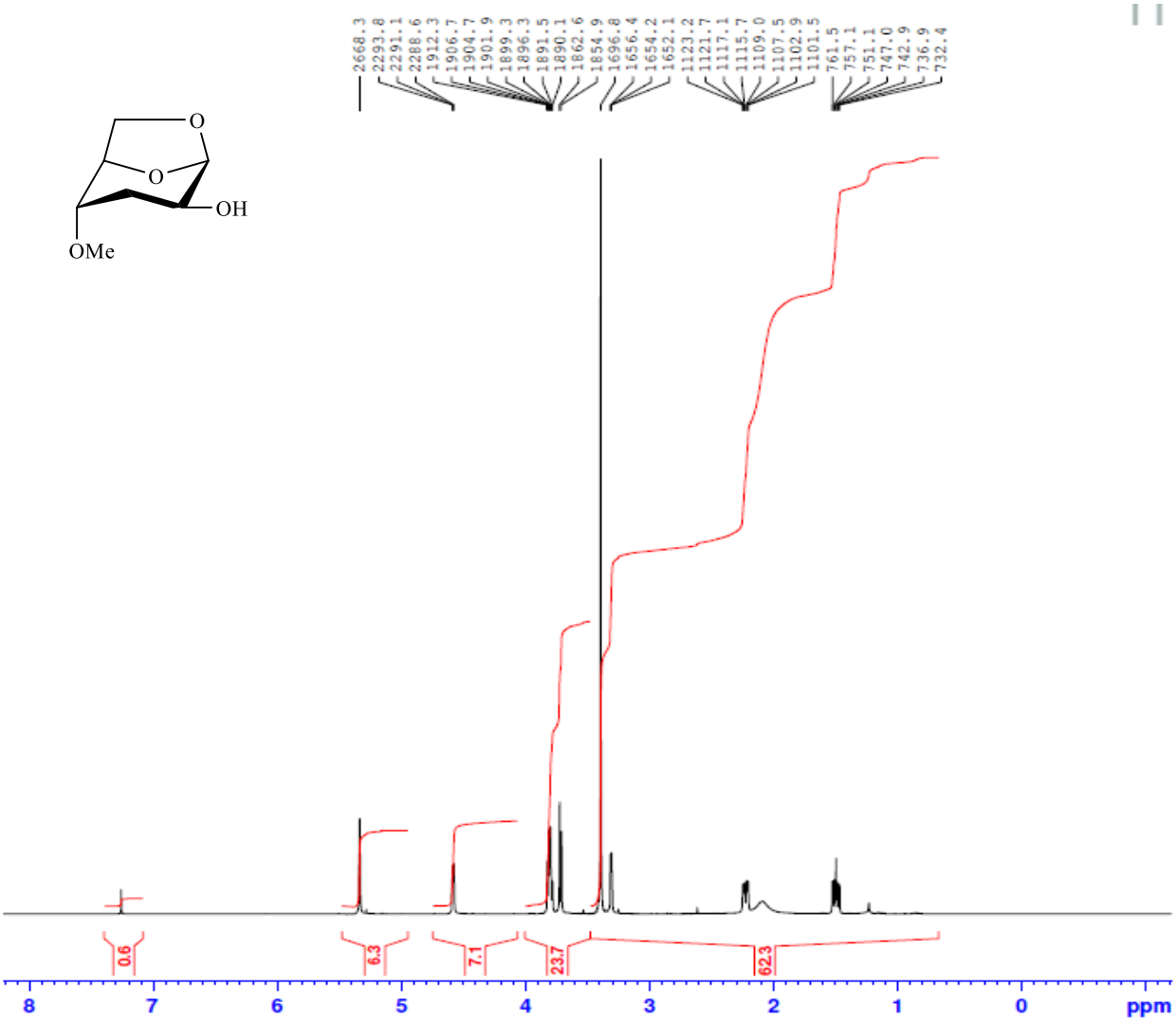


^{13}C NMR (125 MHz, CD_3OD)

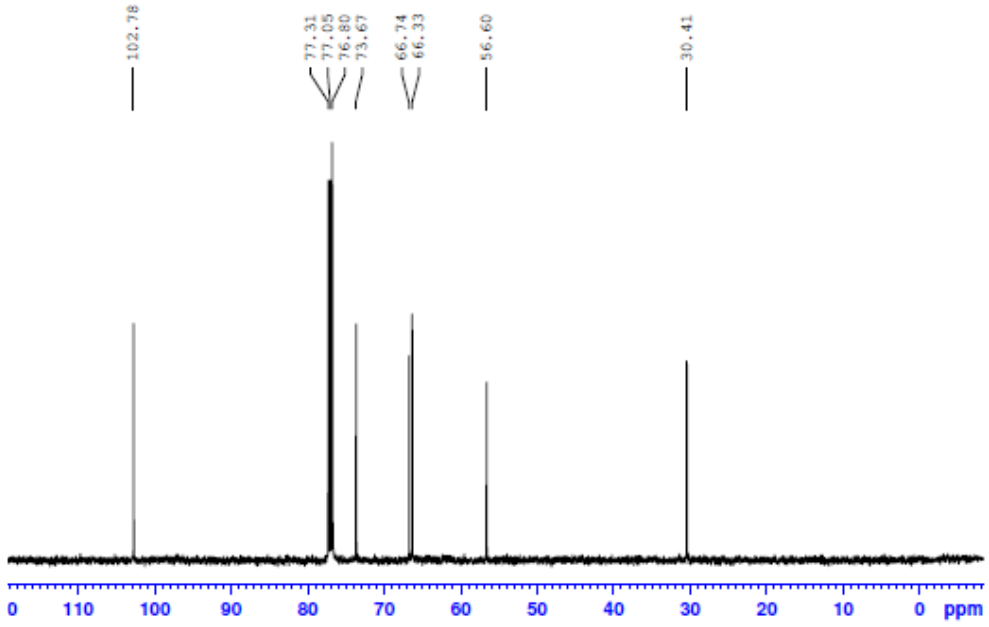


1,6-Anhydro-3-deoxy-4-O-methyl-β-D-*arabino*-hexopyranose (6b)

^{1}H NMR (500 MHz, $CDCl_3$)

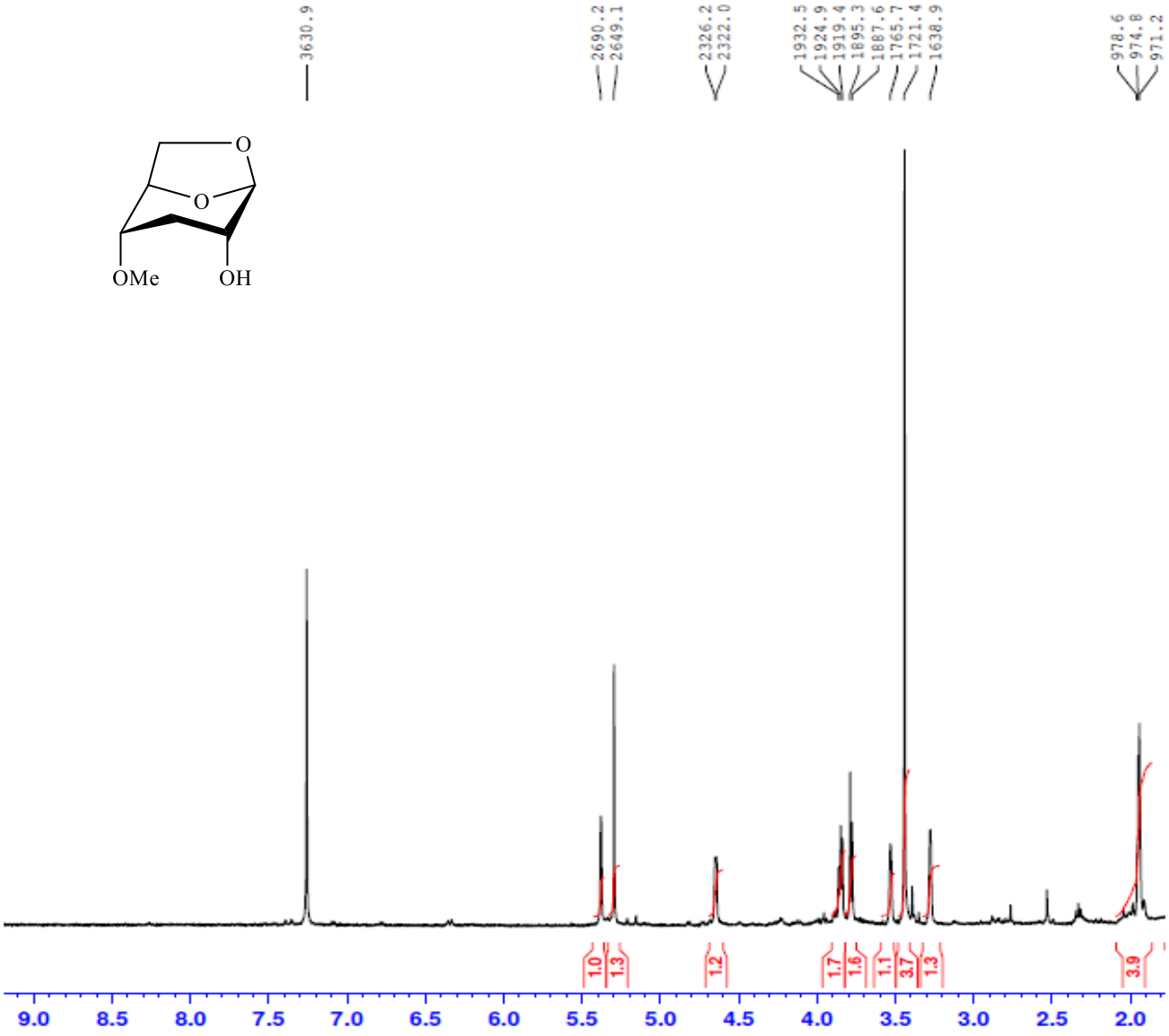


^{13}C NMR (125 MHz, $CDCl_3$)

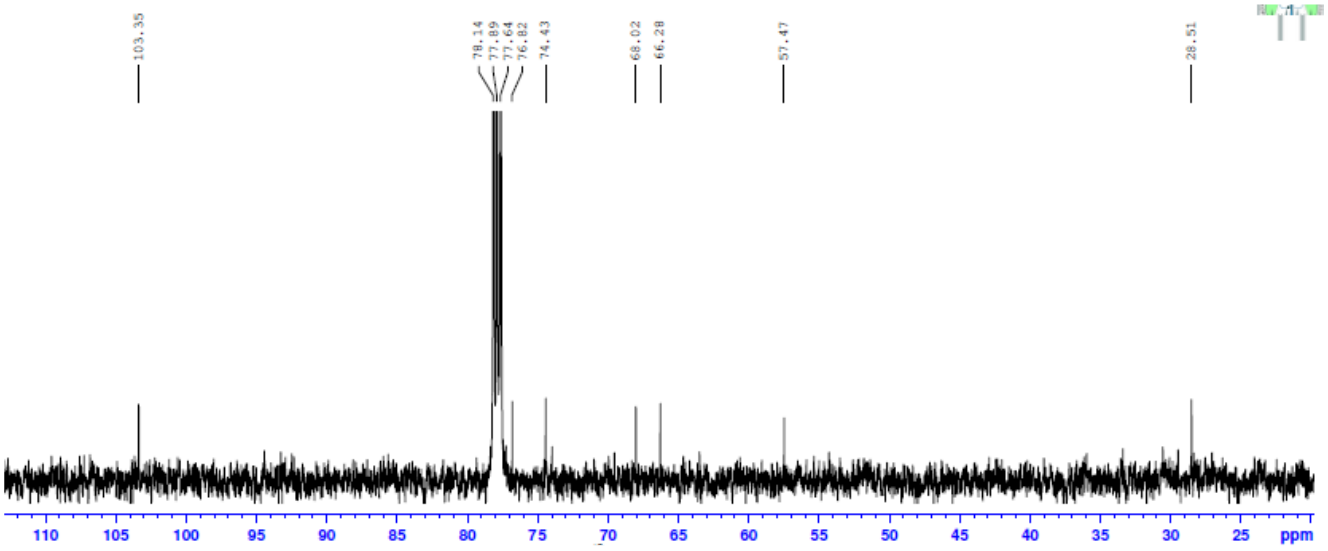


1,6-anhydro-3-deoxy-4-O-methyl-β-D-*ribo*-hexopyranose (6'b)

^{1}H NMR (500 MHz, $CDCl_3$)

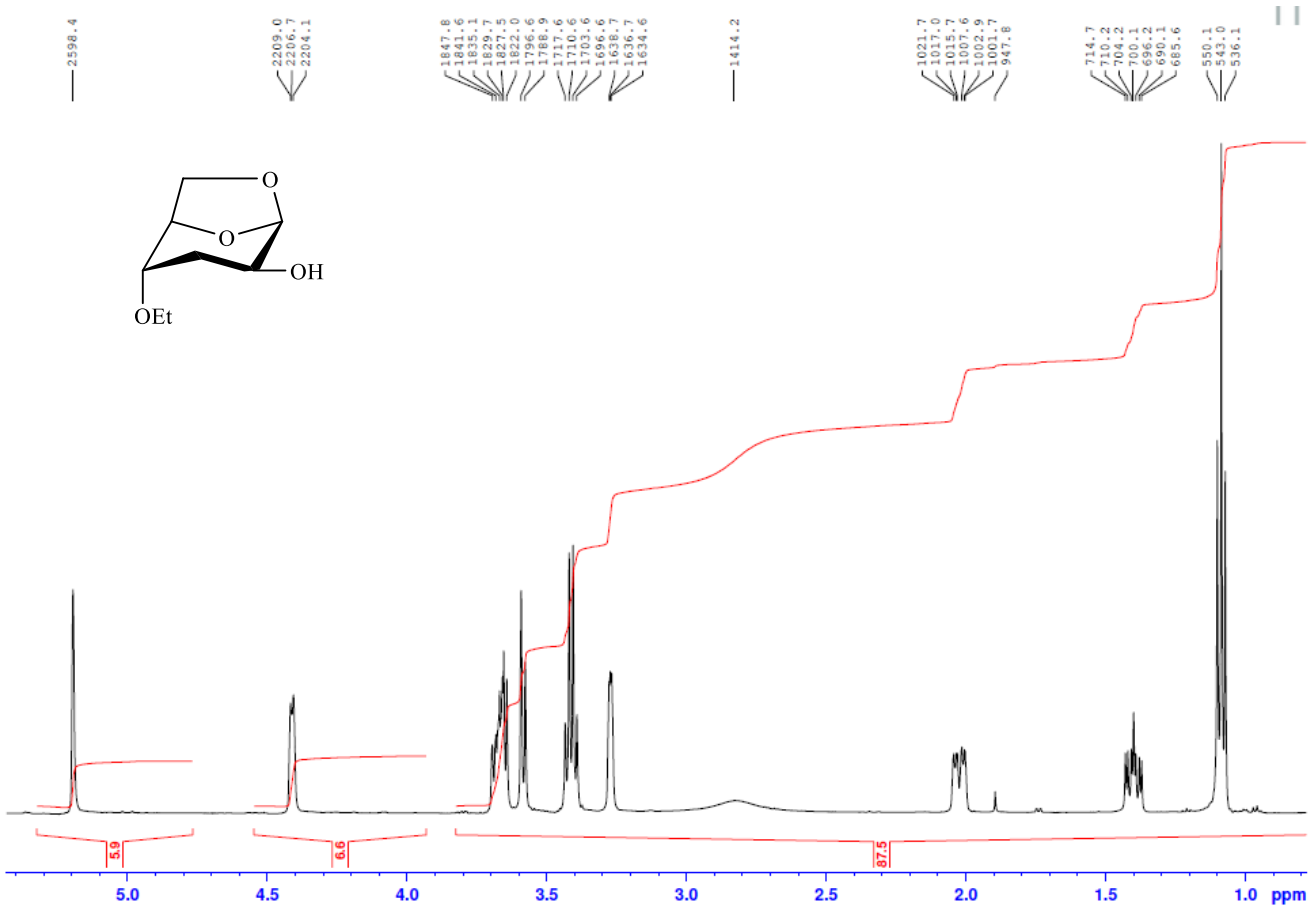


^{13}C NMR (125 MHz, $CDCl_3$)

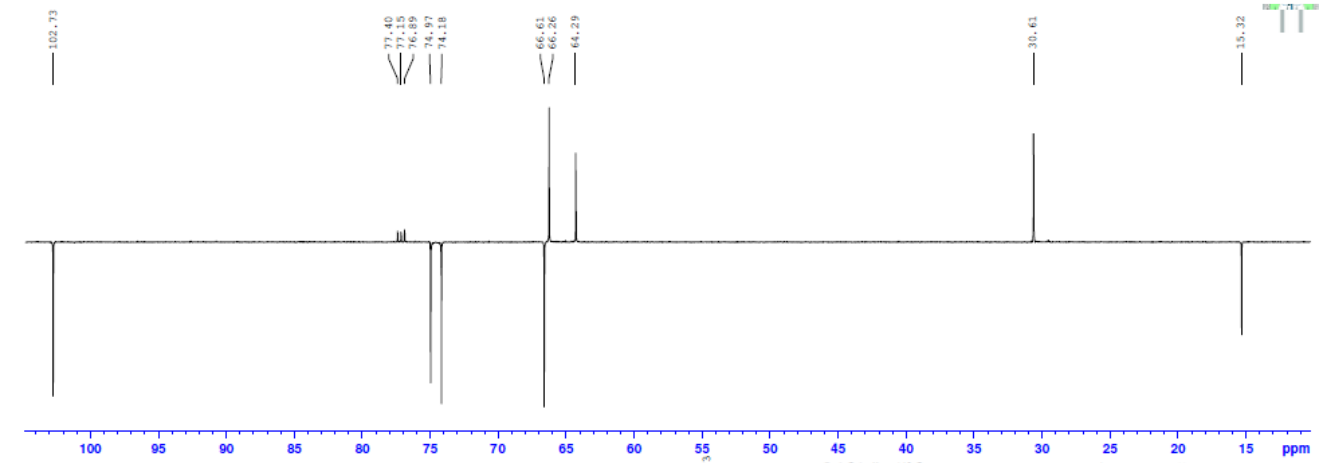


1,6-Anhydro-3-deoxy-4-O-ethyl-β-D-*arabino*-hexopyranose (6c)

^{1}H NMR (500 MHz, $CDCl_3$)

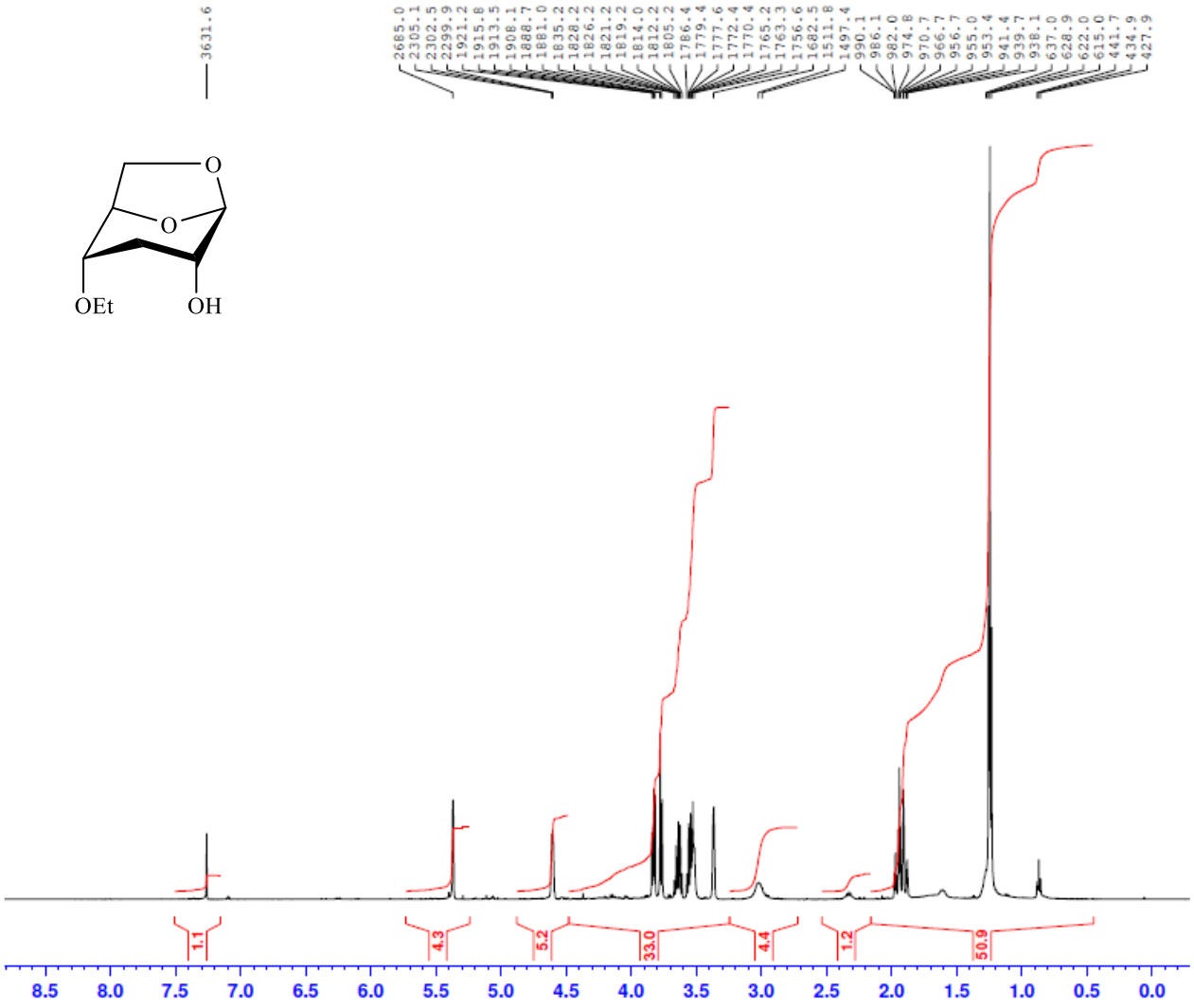


^{13}C NMR (125 MHz, $CDCl_3$)

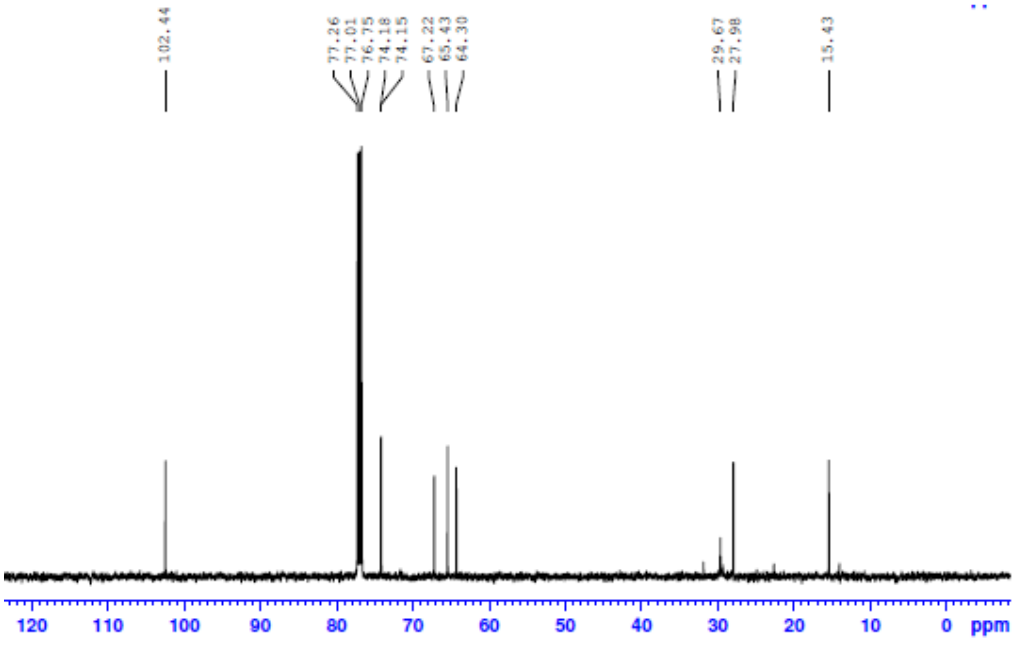


1,6-anhydro-3-deoxy-4-O-ethyl-β-D-*ribo*-hexopyranose (6'c)

^{1}H NMR (500 MHz, $CDCl_3$)

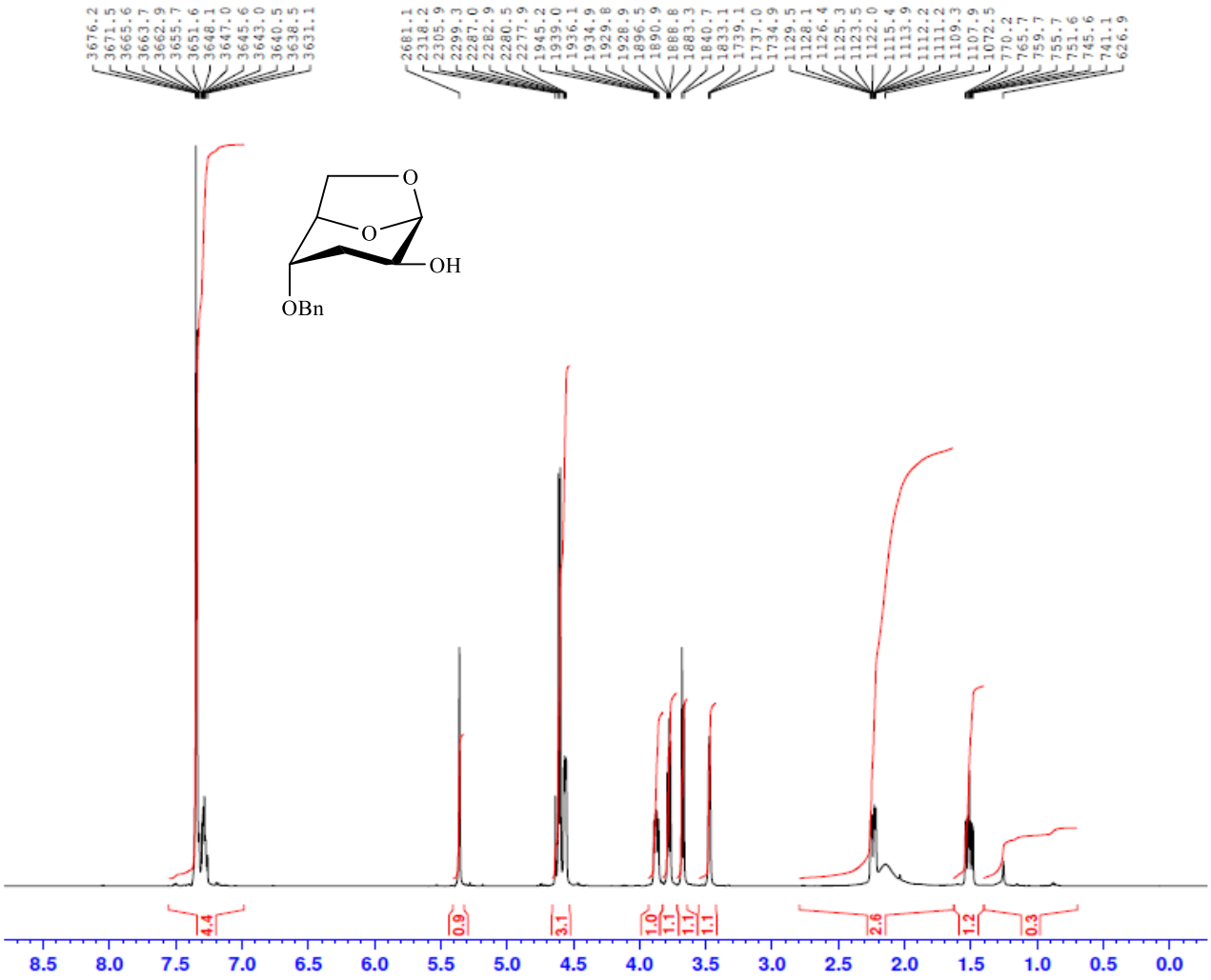


^{13}C NMR (125 MHz, $CDCl_3$)

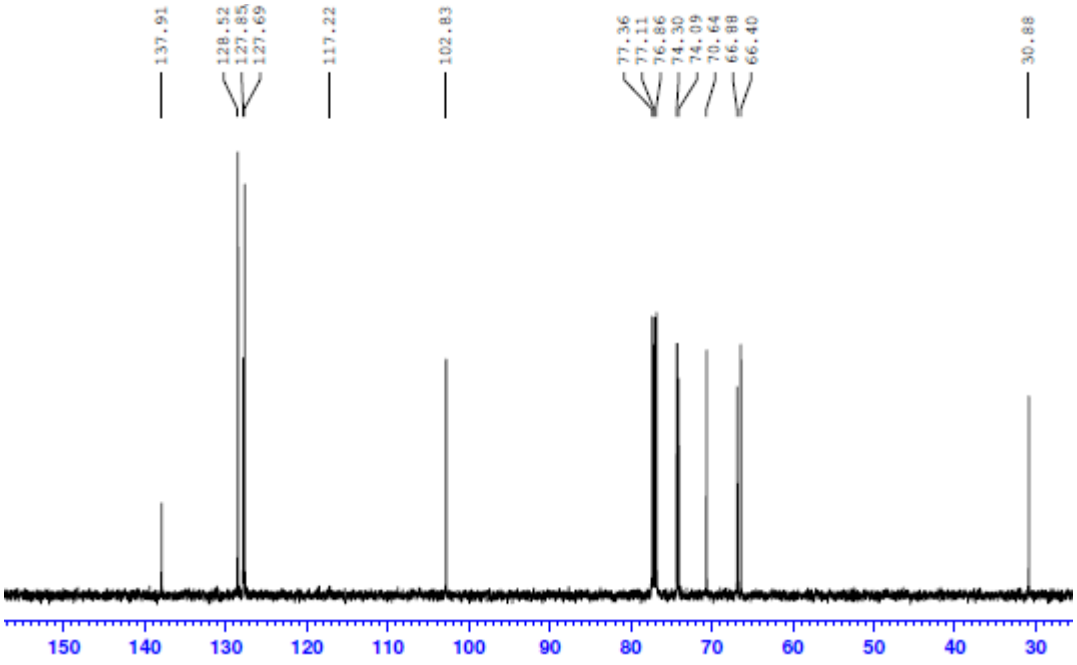


1,6-Anhydro-4-O-benzyl-3-deoxy-β-D-*arabino*-hexopyranose (6d)

^{1}H NMR (500 MHz, $CDCl_3$)

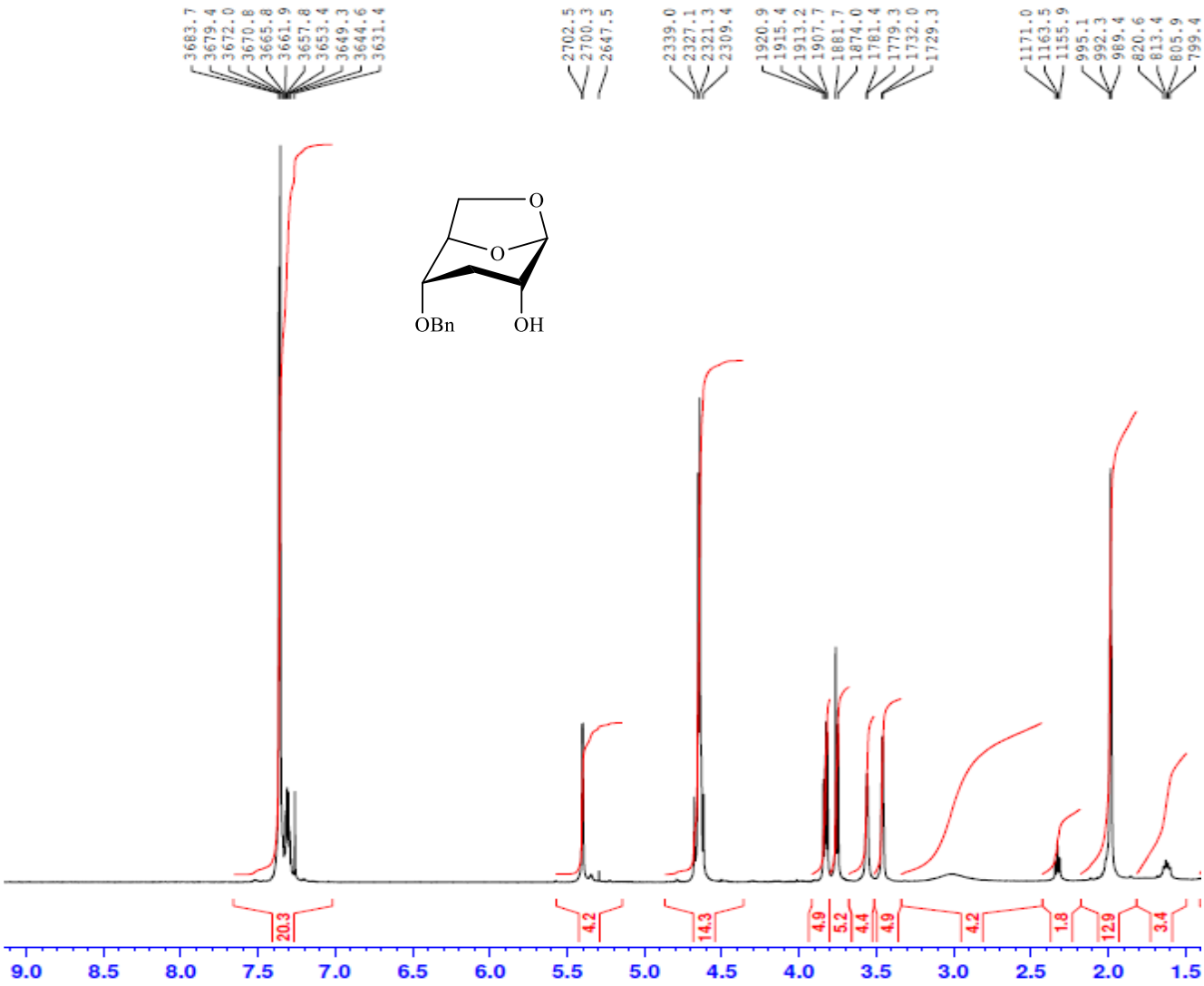


^{13}C NMR (125 MHz, $CDCl_3$)



1,6-anhydro-4-O-benzyl-3-deoxy-β-D-*ribo*-hexopyranose (6'd)

^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)