The Generalized Anomeric Effect in *gem*-Diamines: Stereoselective Synthesis of α-*N*-Linked Disaccharide Mimics

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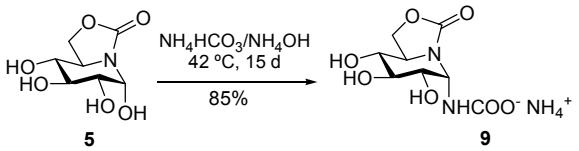
General Methods. Reagents and solvents were purchased from commercial sources and used without further purification. Optical rotations were measured at 22 ºC in 1-cm or 1-dm tubes. ^{1}H (and ^{13}C) NMR spectra were recorded at 500 (125.7) and 400 (100.6) MHz. 2D COSY and HMQC experiments were carried out to assist in signal assignment. TLC was performed with precoated TLC plates, silica gel 30F-245, with visualization by UV light and by charring with 10% H_2SO_4 or 0.2% w/v cerium (IV) sulphate-5% ammonium molybdate in 2 M H_2SO_4 or 0.1% ninhydrine in EtOH. Column chromatography was carried out with Silica Gel 60 (230-400 mesh). For ESI mass spectra, 0.1 pM sample concentration were used, the mobile phase consisting of 50% aq acetonitrile at 0.1 mL min^{-1}.

The glycosidases α-glucosidase (from yeast), β-glucosidase (from almonds), β-glucosidase/β-galactosidase (from bovine liver, cytosolic), α-galactosidase (from green coffee beans), isomaltase (from yeast), trehalase (from pig kidney), amyloglucosidase (from *Aspergillus niger*), α-mannosidase (from jack bean), β-mannosidase (from *Helix pomatia*), β-galactosidase (from *E. coli*) and naringinase (from *Penicillium decumbes*) used in the inhibition studies, as well as the corresponding *o*- and *p*-nitrophenyl glycoside substrates were purchased from Sigma Chemical Co. The cyclic carbamate nojirimycin and mannojirimycin analogues **5**[1] and **6**[2] were prepared from the 5-deoxy-5-aminosugar derivatives **8**[3] and **11**[2] following, essentially, the procedures previously reported. The last step, which involved treatment with a basic ion-exchange resin, was replaced here by successive coevaporations with water to eliminate traces of TFA, which promoted spontaneous furanose→piperidine rearrangement in quantitative yield.

Ammonium *N*-(5,6-oxomethylidenenojirimycinyl)carbamate (9).

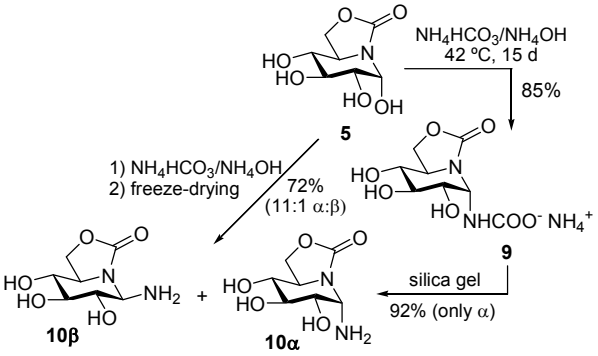


To an aqueous solution of 5,6-oxomethylenenojirimycin (**5**, 44 mg, 0.21 mmol) containing NH_4HCO_3 (68 mg, 0.86 mmol, 4.0 equiv), commercial 30% aq NH_3 (4.5

[1] (a) Jiménez Blanco, J. L.; Díaz Pérez, V. M.; Ortiz Mellet, C.; Fuentes, J.; García Fernández, J. M. *Chem. Commun.* **1997**, 1969-1970. (b) Díaz Pérez, V. M.; García Moreno, M. I.; Ortiz Mellet, C.; Fuentes, J.; Díaz Arribas, J. C.; Cañada, F. J.; García Fernández, J. M. *J. Org. Chem.*, **2000**, 65, 136-143.
[2] Díaz-Pérez, P.; García-Moreno, M. I.; Ortiz Mellet, C.; García Fernández, J. M. *Eur. J. Org. Chem.* **2005**, 2903-2913.
[3] Dax, K. ; Gaigg, B.; Grassberger, V.; Kölblinger, B. ; Stütz, A. E. *J. Carbohydr. Chem.* **1990**, *9*, 479-499.

mL) was added. This solution was heated at 42 ºC for 15 days (TLC monitoring). The solvent was removed and the residue was filtrated through a pad of silica gel (10:1 MeCN-H_2O) to afford the corresponding carbamate **9** (47 mg, 85%) as an amorphous solid; R_f 0.35 (2:1:1 BuOH-AcOH-H_2O); ^{1}H NMR (500 MHz, D_2O) δ 5.08 (d, 1 H, $J_{1,2}$ = 5.5 Hz, H-1), 4.57 (t, 1 H, $J_{6a,6b} = J_{5,6a}$ = 9.0 Hz, H-6a), 4.31 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 3.89 (td, 1 H, H-5), 3.74 (dd, 1 H, $J_{2,3}$ = 9.5 Hz, H-2), 3.62 (t, 1 H, $J_{3,4}$ = 9.5 Hz, H-3), 3.49 (t, 1 H, H-4); ^{13}C NMR (125.7 MHz, D_2O) δ 171.0 (CO), 157.7 (CO), 72.9 (C-4), 72.0 (C-3), 69.1 (C-2), 67.3 (C-1), 60.7 (C-6), 53.1 (C-5); ESIMS: *m/z* 288.3 [M + Na]$^+$.

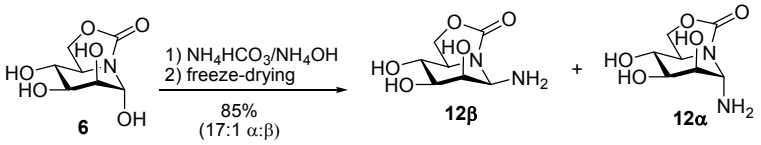
1-Amino-1-deoxy-5,6-oxomethylidenenojirimycin (10α and 10β).



The reaction mixture arising from the treatment of **5** with NH_4HCO_3 and commercial 30% aq NH_3 under the conditions above indicated for the preparation of **9** was freeze-dried twice from water (2 x 20 mL). The residue was subjected to column chromatography using 40:10:1 CH_2Cl_2-MeOH-H_2O as eluent to give **10** (31 mg, 72%) as a mixture of the α and β anomers in 11:1 ratio (H-1 integration). Column chromatography of carbamate **9** (40 mg) with the same eluent afforded the α-anomer as the only product (33 mg, 92%). R_f 0.35 (2:1:1 BuOH-AcOH-H_2O; $[\alpha]_D$ +53.3 (c 1.0 in H_2O); α anomer: ^{1}H NMR (500 MHz, D_2O): δ 4.85 (d, 1 H, $J_{1,2}$ = 4.5 Hz, H-1), 4.54 (t, 1 H, $J_{6a,6b} = J_{5,6a}$ = 9.0 Hz, H-6a), 4.29 (dd, 1 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 3.90 (td, 1 H, $J_{4,5}$ = 9.0 Hz, H-5), 3.62 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, H-3), 3.59 (dd, 1 H, H-2), 3.45 (t, 1 H, H-4); ^{13}C NMR (125.7 MHz, D_2O): δ 158.3 (CO), 73.5 (C-4), 72.0 (C-3), 70.4 (C-2), 67.1 (C-6), 61.2 (C-1), 53.0 (C-5). β anomer: ^{1}H NMR (500 MHz, D_2O) δ 4.43 (t, 1 H, $J_{6a,6b} = J_{5,6a}$ = 8.5 Hz, H-6a), 4.20 (dd, 1 H, $J_{5,6b}$ = 6.5 Hz, H-6b), 4.06 (d, 1 H, $J_{1,2}$ = 9.0 Hz, H-1), 3.65 (m, 1 H, H-5), 3.45 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.0 Hz, H-4), 3.38 (t, 1 H, $J_{2,3}$ = 9.0 Hz, H-3), 3.25 (t, 1 H, H-2); ^{13}C NMR (125.7 MHz, D_2O) δ 158.4 (CO), 75.8 (C-3), 74.4 (C-2), 71.9 (C-4), 67.4 (C-1), 66.1 (C-6), 57.8 (C-5). ESIMS: *m/z* 227.0 [M + Na]$^+$.

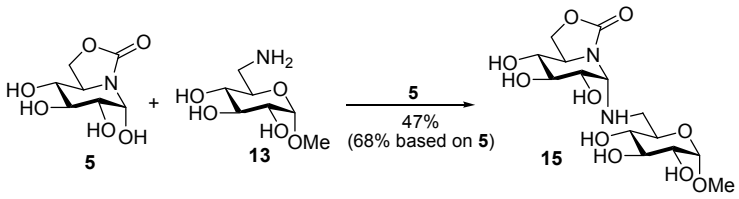
Anal. Calcd for $C_7H_{12}N_2O_5$: C, 41.18; H, 5.92; N, 13.72. Found: C, 40.79; H, 5.61, N, 13.41.

1-Amino-1-deoxy-5,6-oxomethylidenemannojirimycin (12α and 12β).



To an aqueous solution of 5,6-oxomethylidenemannojirimycin **6** (165 mg, 0.8 mmol) containing NH_4HCO_3 (254 mg, 3.21 mmol, 4.0 equiv), commercial aq NH_3 (17 mL) was added. This solution was heated at 42 ºC for 15 days (TLC monitoring). The solvent was removed and the residue was filtrated through a pad of silica gel (10:1 MeCN-H_2O) to give a crude mixture of **12α** and **12β** in 17:1 relative proportion (H-1 integration). Further column chromatography (40:10:1 CH_2Cl_2-MeOH-H_2O) afforded pure **12α**, which was characterized as the corresponding hydrochloride (164 mg, 85%) R_f 0.33 (2:1:1 BuOH-AcOH-H_2O); $[\alpha]_D$ = –45.9 (c 0.9 in H_2O); ^{1}H NMR (500 MHz, D_2O) δ 5.17 (d, 1 H, $J_{1,2}$ = 2.3 Hz, H-1), 4.62 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.1 Hz, H-6a), 4.40 (dd, 1 H, $J_{5,6b}$ = 4.9 Hz, H-6b), 4.23 (dd, 1 H, $J_{2,3}$ = 2.9 Hz, H-2), 3.92 (dd, 1 H, $J_{4,5}$ = 9.4 Hz, H-5), 3.84 (dd, 1 H, $J_{3,4}$ = 9.4 Hz, H-3), 3.78 (t, 1 H, H-4); ^{13}C NMR (125.7 MHz, D_2O) δ 158.2 (CO), 69.5 (C-3), 69.1 (C-4), 68.6 (C-2), 67.5 (C-6), 62.3 (C-1), 54.3 (C-5); ESIMS: *m/z* 227.1 $[M + Na - HCl]^+$. Anal. Calcd for $C_7H_{13}ClN_2O_5$: C, 34.94; H, 5.45; N, 11.64. Found: C, 34.65; H, 5.37; N, 11.14.

1-Amino-1-deoxy-*N*-(methyl 6-amino-6-deoxy-α-D-glucopyranosid-6-yl)-5,6-oxomethylidenenojirimycin (15).

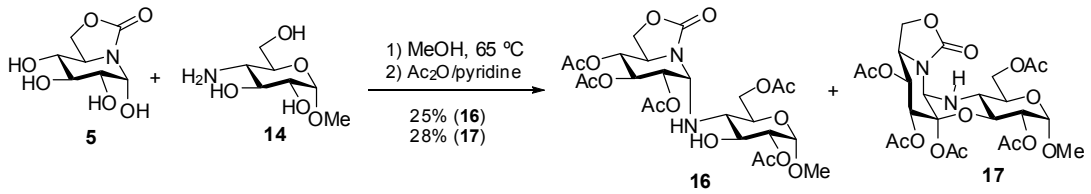


A solution of **5** (151 mg, 0.74 mmol) and methyl 6-amino-6-deoxy-α-D-glucopyranoside[4] (**13**, 1.0 equiv) in MeOH (1 mL) was stirred at 65 ºC for 4 h (TLC monitoring). The solvent was eliminated under reduced pressure, and the resulting residue was purified by column chromatography (7:1 MeCN-H_2O). Yield: 70 mg (47%); R_f 0.31 (5:1 MeCN-H_2O); $[\alpha]_D$ +112.5 (c 1.0 in H_2O); ^{1}H NMR (500 MHz,

[4] García Fernández, J. M.; Ortiz Mellet, C.; Fuentes, J.; *J. Org. Chem*. **1993**, *58*, 5192-5199.

D_2O) δ 4.74 (d, 1 H, $J_{1',2'}$ = 4.0 Hz, H-1′), 4.67 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.54 (t, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 9.0 Hz, H-6a), 4.32 (dd, 1 H, $J_{5,6b}$ = 5.0 Hz, H-6b), 3.88 (ddd, 1 H, $J_{4,5}$ = 9.7 Hz, H-5), 3.71 (ddd, 1 H, $J_{4',5'}$ = 9.5 Hz, $J_{5',6'b}$ = 8.0 Hz, $J_{5',6'a}$ = 3.0 Hz, H-5′), 3.66-3.62 (m, 2 H, H-2, H-3), 3.59 (t, 1 H, $J_{2',3'}$ = $J_{3',4'}$ = 9.5 Hz, H-3′), 3.51 (dd, 1 H, H-2′), 3.45 (m, 1 H, H-4), 3.39 (s, 3 H, OMe), 3.27 (t, 1 H, H-4′), 2.93 (dd, 1 H, $J_{6'a,6'b}$ = 13.5 Hz, H-6′a), 2.70 (dd, 1 H, H-6′b); ^{13}C NMR (125.7 MHz, D_2O) δ 158.8 (CO), 99.4 (C-1′), 73.6 (C-4), 73.0 (C-3′), 72.5 (C-3), 71.7 (C-4′), 71.3 (C-2′), 70.2 (C-2), 68.9 (C-5′), 67.1 (C-6), 67.0 (C-1), 55.3 (OMe), 52.9 (C-5), 45.8 (C-6′); ESIMS: *m/z* 403.1 [M + Na]$^+$. Anal. Calcd for $C_{14}H_{24}N_2O_{10}$: C, 44.21; H, 6.36; N, 7.37. Found: C, 44.01; H, 6.30; N, 7.12.

2,3,4-Tri-*O*-acetyl-1-amino-1-deoxy-*N*-(methyl 2,3,6-tri-*O*-acetyl-4-amino-4-deoxy-α-D-glucopyranosid-4-yl)-5,6-oxomethylidenenojirimycin (16) and per-*O*-Acetylated Tetracyclic *gem*-Diamine (17).



A solution of **5** (70 mg, 0.34 mmol) and methyl 4-amino-4-deoxy-α-D-glucopyranoside[5] (**14**, 132 mg, 0.68 mmol, 2.0 equiv) in MeOH (1 mL) was stirred at 65 ºC for 24 h (TLC monitoring). The solvent was eliminated under reduced pressure, and the resulting residue was purified by column chromatography (8:1 MeCN-H_2O) to give an inseparable mixture of compounds **18** and **19** (see hereinafter) together with unreacted **5** (37%). The crude product was subsequently acetylated by treatment with Ac_2O-pyridine (1:1, 2 mL) at RT for 3 h and the mixtures of the corresponding per-*O*-acetates was purified by column chromatography (3:1 EtOAc-petroleum ether) to give pure **16** and **17**.

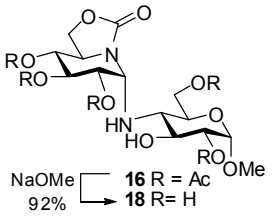
Compound **16**. Yield: 18 mg (25%). R_f 0.41 (4:1 EtOAc-petroleum ether). $[\alpha]_D$ +96.6 (*c* 1.0 in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 5.44 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3), 5.09 (dd, 1 H, H-2), 4.99 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 4.91 (d, 1 H, $J_{1',2'}$ = 3.5 Hz, H-1′), 4.78 (dd, 1 H, $J_{2',3'}$ = 10.0 Hz, H-2′), 4.48-4.38 (m, 2 H, H-6a, H-6′a), 4.30-4.23 (m, 2 H, H-6b, H-6′b), 4.08 (bq, 1 H, H-5), 3.84 (bt, 1 H, $J_{3',4'}$ = 10.0 Hz, H-3′), 3.70-3.63 (m, 1 H, H-5′), 3.42 (s, 3 H, OMe), 2.89 (t, 1 H,

[5] Reist, E. J.; Spencer, R. R.; Calkins, D. F.; Baker, B. R.; Goodman, L. *J. Org. Chem.* **1965**, *30*, 2312-2317.

$J_{4',5'}$ = 10.0 Hz, H-4′), 2.17-2.05 (5 s, 15 H, MeCO); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.6-169.2 (CO ester), 156.1 (CO carbamate), 97.3 (C-1′), 74.0 (C-3′), 73.9 (C-2′), 72.7 (C-4), 69.7 (C-5′), 69.3 (C-2), 69.0 (C-3), 66.4 (C-6), 65.5 (C-1), 62.8 (C-6′), 57.9 (C-4′), 55.3 (OMe), 51.5 (C-5), 21.0-20.6 (Me). ESIMS: *m/z* 613.2 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{34}N_2O_{15}$: C 48.81, H 5.80, N 4.74. Found: C 48.63, H 5.73, N 4.53.

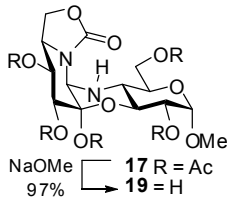
Compound **17**. Yield: 20 mg (28%). R_f 0.46 (4:1 EtOAc-petroleum ether). $[\alpha]_D$ +43.3 (c 0.95 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (d, 1 H, $J_{3,4}$ = 9.5 Hz, H-3), 5.51 (s, 1 H, H-1), 5.04 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 5.05-5.01 (m, 1 H, H-2′), 4.99 (d, 1 H, $J_{1',2'}$ = 3.5 Hz, H-1′), 4.44 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 10.0 Hz, H-3′), 4.36-4.24 (m, 3 H, H-6a, H-1′b, H-6′a), 4.18 (dd, 1 H, $J_{6'a,6'b}$ = 12.5 Hz, $J_{5,6b'}$ = 4.0 Hz, H-6′b), 3.92-3.80 (m, 2 H, H-5′, H-5), 3.43 (s, 3 H, OMe), 3.16 (t, 1 H, $J_{4',5'}$ = 10.0 Hz, H-4′), 2.16-2.06 (3 s, 15 H, MeCO); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.0-169.9 (CO ester), 157.0 (CO carbamate), 98.2 (C-2), 97.4 (C-1′), 70.2 (C-3), 69.9 (C-2′, C-8), 69.4 (C-3′), 67.9 (C-5′), 66.3 (C-6), 64.8 (C-1), 62.6 (C-6′), 56.5 (C-5), 55.4 (OMe), 50.6 (C-4′), 22.2-20.4 (*Me*CO). ESIMS: *m/z* 611.1 [M + Na]$^+$. Anal. Calcd for $C_{24}H_{32}N_2O_{15}$: C 48.98, H 5.48, N 4.76. Found: C 48.71, H 5.20, N 4.54.

1-Amino-1-deoxy-*N*-(methyl 4-amino-4-deoxy-α-D-glucopyranosid-4-yl)-5,6-oxomethylidenenojirimycin (18).



The α-*N*-linked pseudodissacharide **18** was obtained by conventional de-*O*-acetylation of **16** (12 mg, 0.02 mmol)**.** Yield: 7 mg (92%). R_f 0.27 (6:1 MeCN/H_2O). $[\alpha]_D$ -21.3 (c 0.5 in H_2O). ^{1}H NMR (500 MHz, D_2O) δ 5.08 (d, 1 H, $J_{1,2}$ = 5.0 Hz, H-1), 4.51 (t, 1 H, $J_{6a,6b} = J_{5,6a}$ = 9.0 Hz, H-6a), 4.30 (dd, 1 H, $J_{5,6b}$ = 5.0 Hz, H-6b), 3.87-3.81 (m, 1 H, H-5), 3.80-3.71 (m, 2 H, H-6′a, H-6′b), 3.68 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 10.0 Hz, H-3′), 3.64-3.54 (m, 3 H, H-2, H-3, H-5′), 3.48 (dd, 1 H, $J_{1',2'}$ = 4.0 Hz, H-2′), 3.41 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 3.32 (s, 3 H, OMe), 2.57 (t, 1 H, $J_{4',5'}$ = 10.0 Hz, H-4′); ^{13}C NMR (125.7 MHz, D_2O) δ 158.5 (CO), 99.3 (C-1′), 74.7 (C-3′), 73.4 (C-4), 72.0 (C-2′), 72.2-70.5 (C-5′, C-2, C-3), 67.3 (C-1), 66.9 (C-6), 61.0 (C-6′), 55.9 (C-4′), 54.9 (OMe), 53.2 (C-5). ESIMS: *m/z* 403.1 [M + Na]$^+$. Anal. Calcd for $C_{14}H_{24}N_2O_{10}$: C 44.21, H 6.36, N 7.37. Found: C 43.94, H 6.09, N 7.18.

Tetracyclic *gem*-Diamine (19).

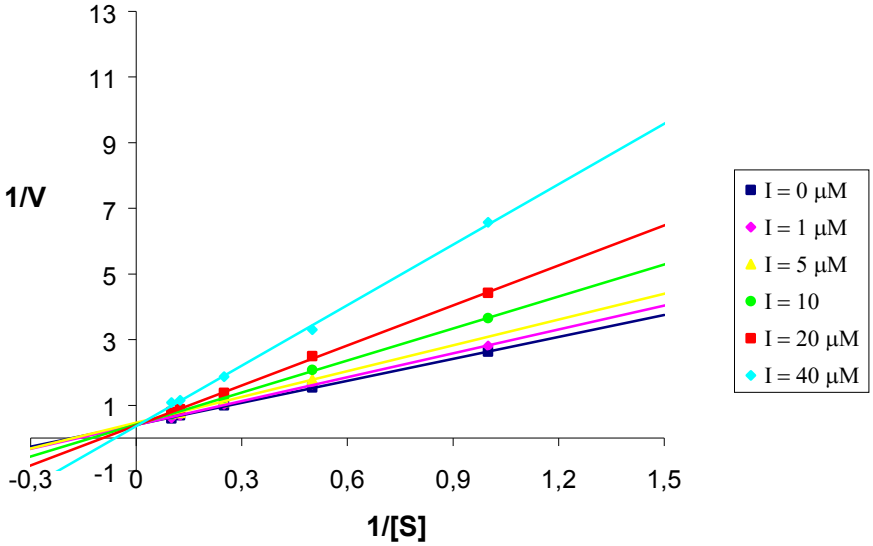


Compound **19** was obtained by conventional de-*O*-acetylation of **17** (12 mg, 0.02 mmol). Yield: 7 mg (97%). R_f 0.27 (6:1 CH_3CN/H_2O). $[\alpha]_D$ +81.0 (*c* 0.52 in H_2O). ^{1}H NMR (500 MHz, D_2O) δ 4.80 (d, 1 H, $J_{1',2'}$ = 4.0 Hz, H-1′), 4.54 (bt, 1 H, $J_{6a,6b}$ = $J_{5,6a}$ = 8.0 Hz, H-6a), 4.32 (s, 1 H, H-1), 4.18-4.08 (m, 2 H, H-3′, H-6b), 3.79-3.64 (m, 5 H, H-2′, H-5′, H-6′a, H-4, H-6a), 3.63-3.55 (m, 1 H, H-6′b), 3.41 (d, 1 H, $J_{3,4}$ = 9.2 Hz, H-3), 3.37 (s, 3 H, OMe), 2.80 (t, 1 H, $J_{3',4'}$ = $J_{4',5'}$ = 9.6 Hz, H-4′); ^{13}C NMR (125.7 MHz, D_2O) δ 158.6 (CO), 99.3 (C-1′), 92.9 (C-2), 77.2 (C-3), 70.5, 70.4, 69.0 (C-2′, C-5′, C-4), 69.9 (C-3′), 67.5 (C-1), 67.0 (C-6), 60.6 (C-6′), 57.3 (C-5), 55.1 (OMe), 50.0 (C-4′). ESIMS: *m/z* 401.1 $[M + Na]^+$. Anal. Calcd for $C_{14}H_{22}N_2O_{10}$: C 44.45, H 5.86, N 7.40. Found: C 44.14, H 5.51, N 7.18.

General Procedure for the Glycosidase Inhibition Assay. Inhibitory potencies were determined by spectrophotometrically measuring the residual hydrolytic activities of the glycosidases against the respective *o*- (for β-glucosidase/β-galactosidase from bovine liver and β-galactosidase from *E. coli*) or *p*-nitrophenyl α- or β-D-glycopyranoside or α,α′-trehalose (for trehalase), in the presence of the corresponding gem-diamine derivative. Each assay was performed in phosphate buffer at the optimal pH for each enzyme. The K_m values for the different glycosidases used in the tests and the corresponding working pHs are listed herein: α-glucosidase (yeast), K_m = 0.35 mM (pH 6.8); isomaltase (yeast) K_m = 1.0 mM (pH 6.8), β-glucosidase (almonds), K_m = 3.5 mM (pH 7.3); β-glucosidase/β-galactosidase (bovine liver), K_m = 2.0 mM (pH 7.3); β-galactosidase (*E. coli*), K_m = 0.12 mM (pH 7.3); α-galactosidase (coffee beans), K_m = 2.0 mM (pH 6.8); trehalase (pig kidney), K_m = 4.0 mM (pH 6.2); amyloglucosidase (*Aspergillus niger*), K_m = 3.0 mM (pH 5.5); β-mannosidase (*Helix pomatia*), K_m = 0.6 mM (pH 5.5); α-mannosidase (jack bean), K_m = 2.0 mM (pH 5.5); naringinase (*Penicillium decumbens*, β-glucosidase/β-rhamnosidase activity). The reactions were initiated by addition of enzyme to a solution of the substrate in the absence or presence of various concentrations of inhibitor. After the mixture was incubated for 10-30 min at 37 ºC or 55 ºC the reaction was quenched by addition of 1 M Na_2CO_3 or a solution of

Glc-Trinder (Sigma, for trehalase). The absorbance of the resulting mixture was determined at 405 nm or 505 nm. In a first screening, K_i values were determined using the equation

$$K_i = \frac{[I]}{\frac{K_{app}}{K_m} - 1}, \text{ where } K_{app} = \frac{v_0}{v_i}([S + Km]) - [S],$$ [I] is the concentration of inhibitor and [S] is the concentration of substrate. Each experiment was performed in duplicate using [I] = 2, 0.4, 0.08, 0.04 y 0.02 μM and [S] nearly K_m value. In those cases were K_i values lower that 10 μM were obtained by this procedure (**10α** against bovine liver β-glucosidase/β-galactosidase and yeast isomaltase, and **12α** against jack bean α-mannosidase), refined K_i values and the enzyme inhibition mode were determined from the slope of Lineweaver-Burk plots and double reciprocal analysis (Figures 1S-3S).



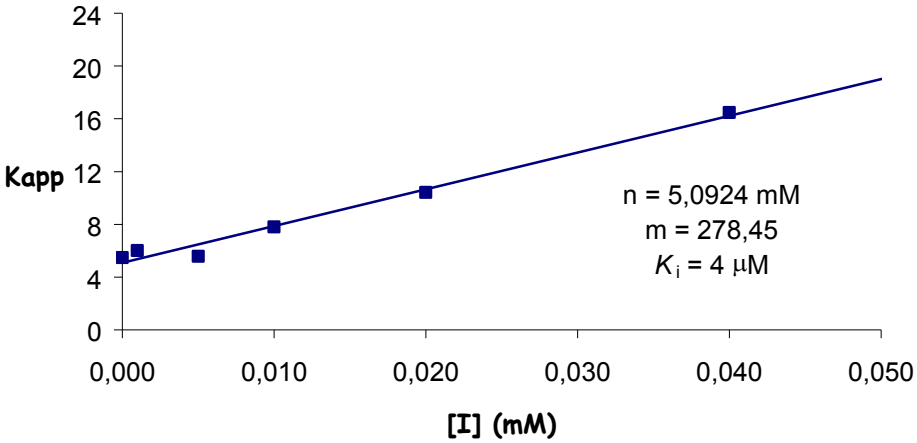


Figure 1S. Lineweaver-Burk plots and double reciprocal analysis of **10α** against β-glucosidase/β-galactosidase from bovine liver (pH 7.3).

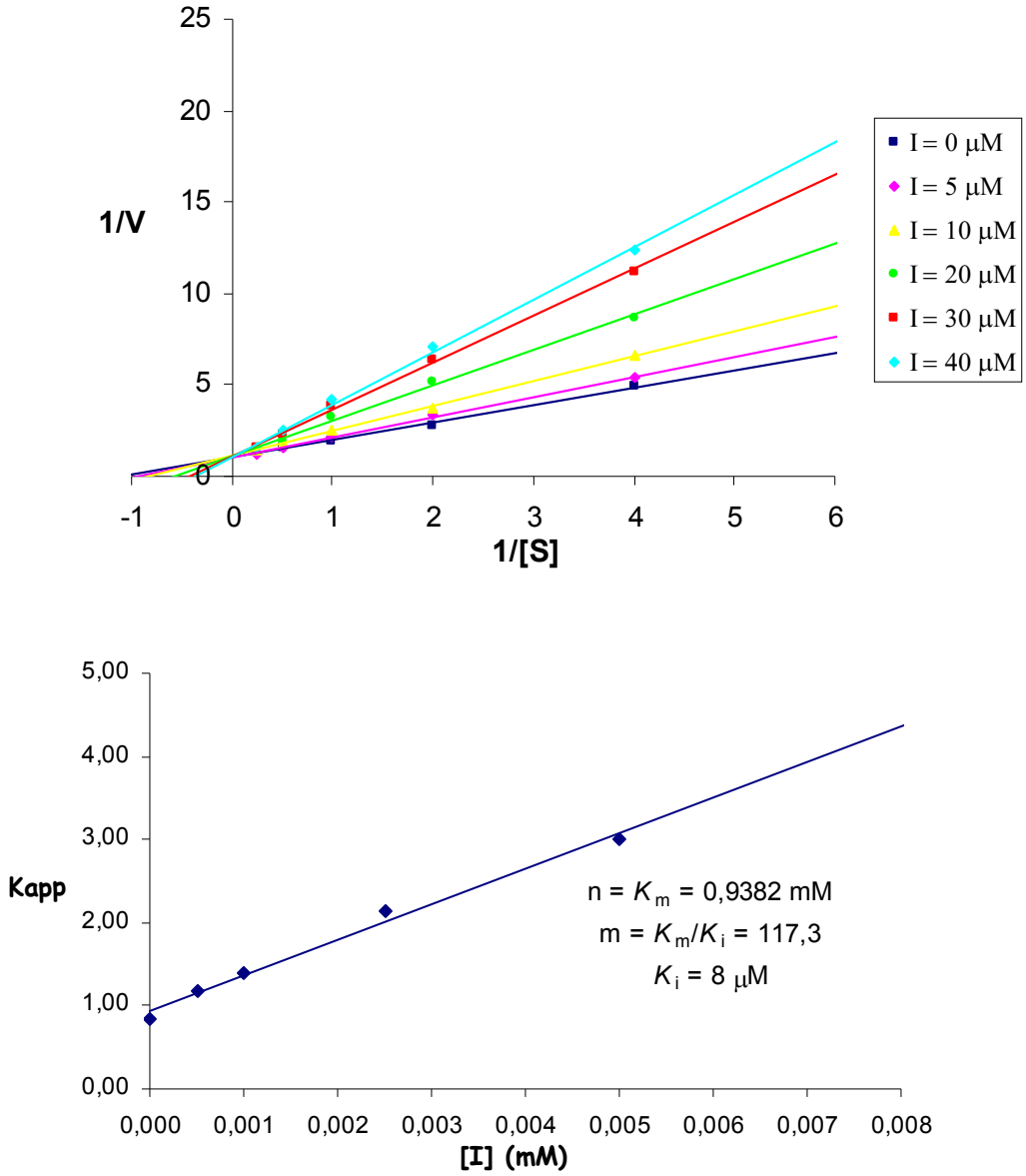


Figure 2S. Lineweaver-Burk plots and double reciprocal analysis of **10α** against isomaltase from yeast (pH 6.8).

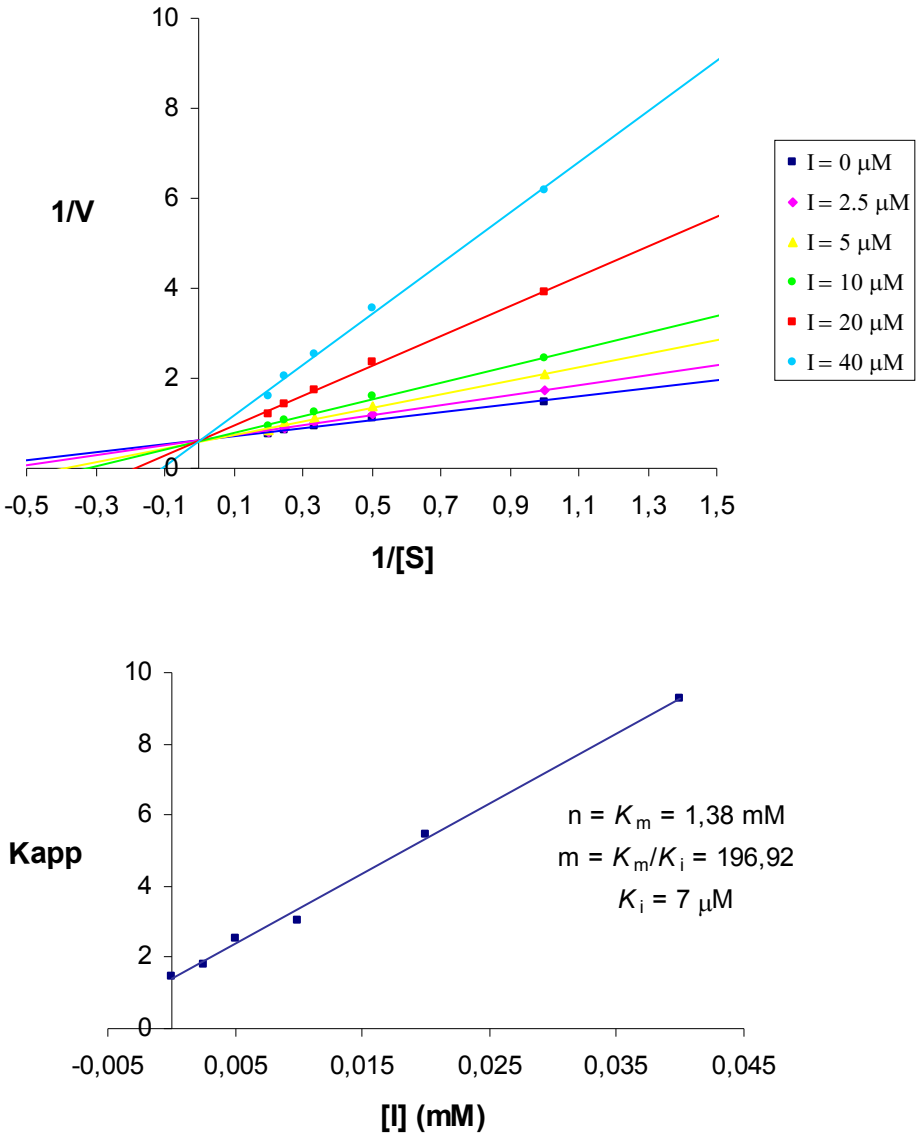


Figure 3S. Lineweaver-Burk plots and double reciprocal analysis of **12α** against α-mannosidase from jack beans (pH 5.5).

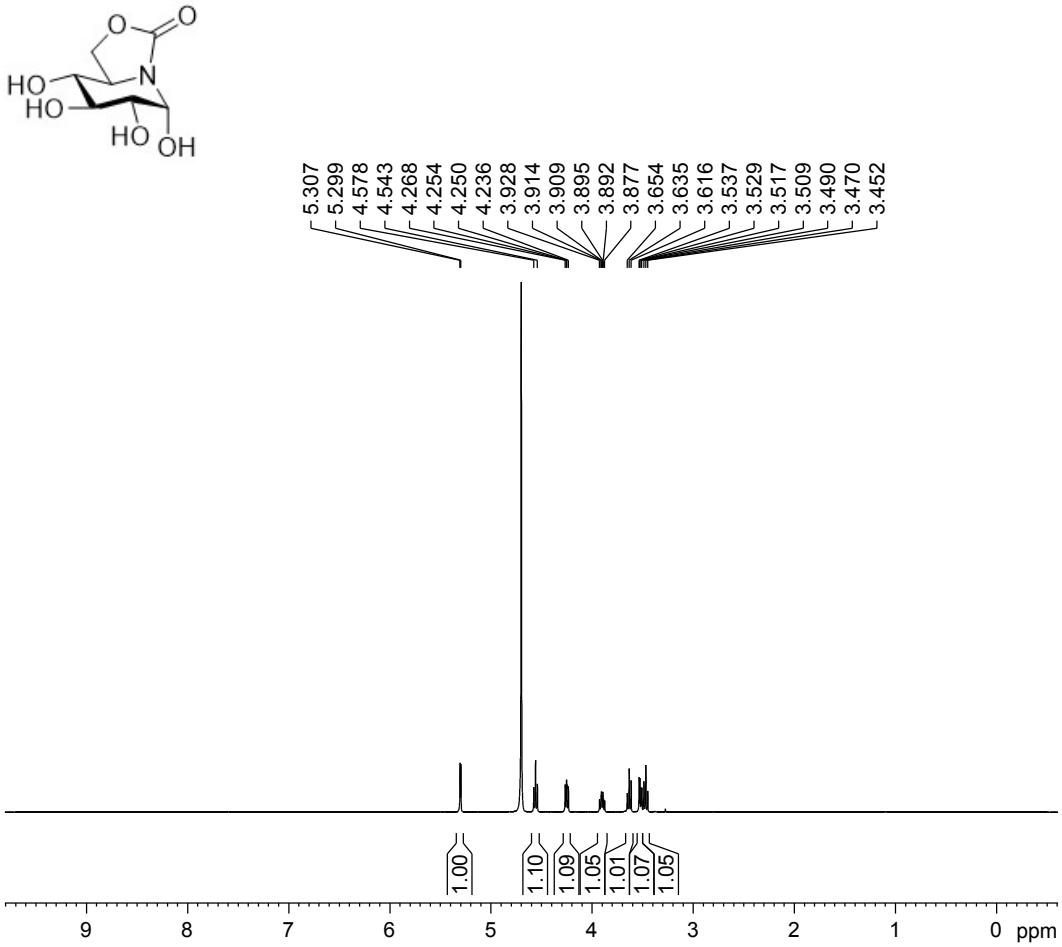


Figure 4S. ^{1}H NMR spectrum (500 MHz, D_2O) of **5**.

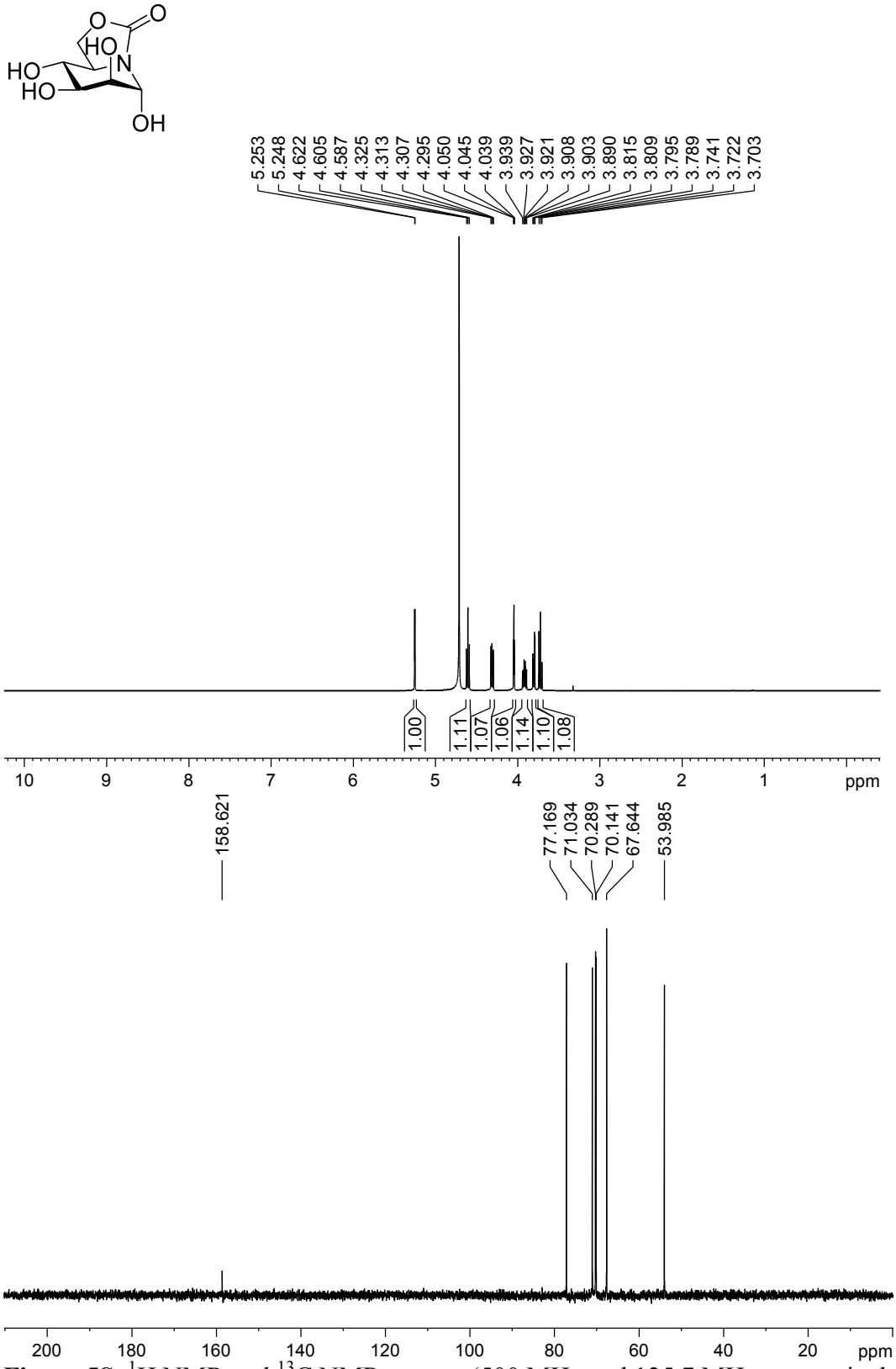


Figure 5S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **6**.

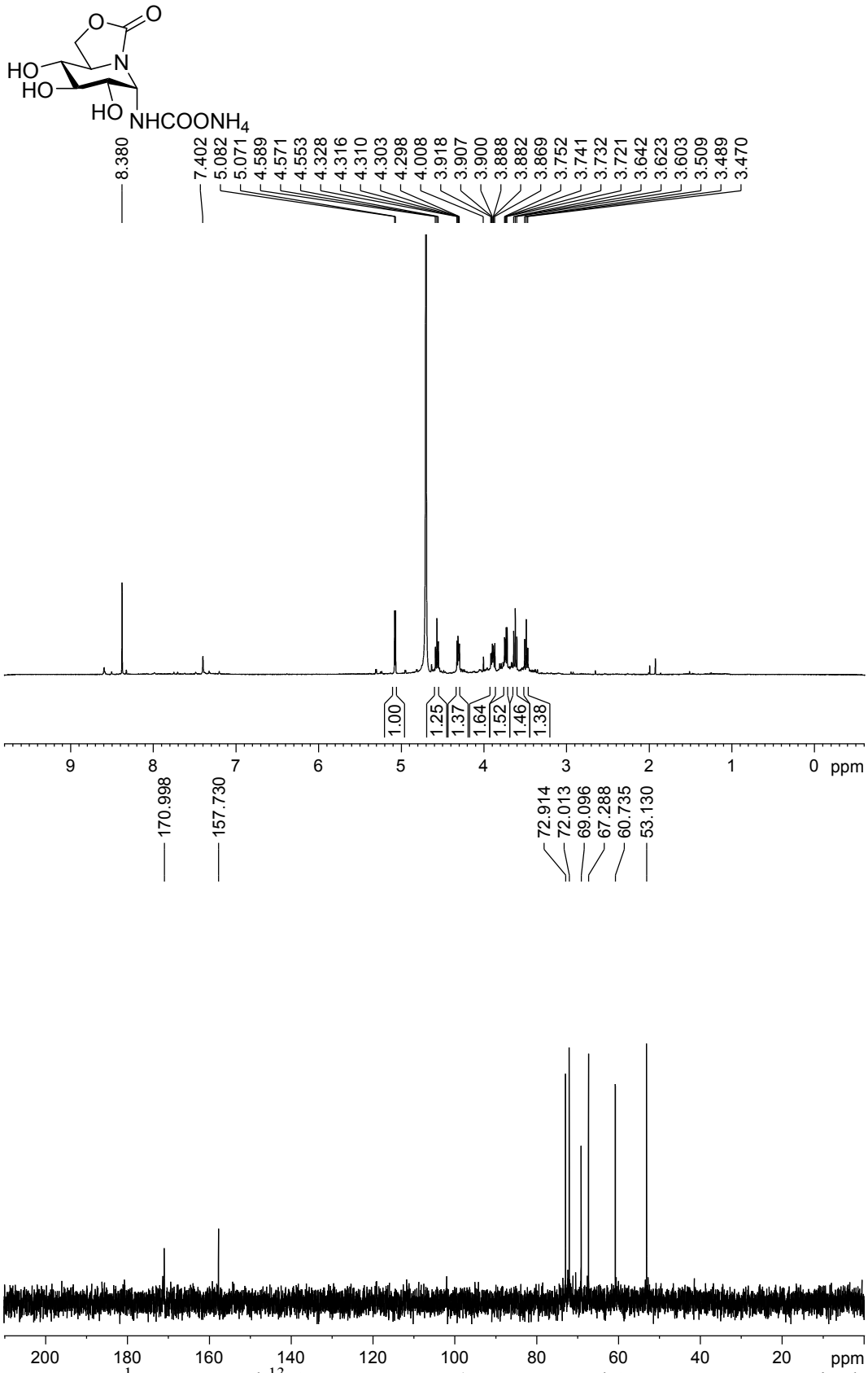


Figure 6S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **9**.

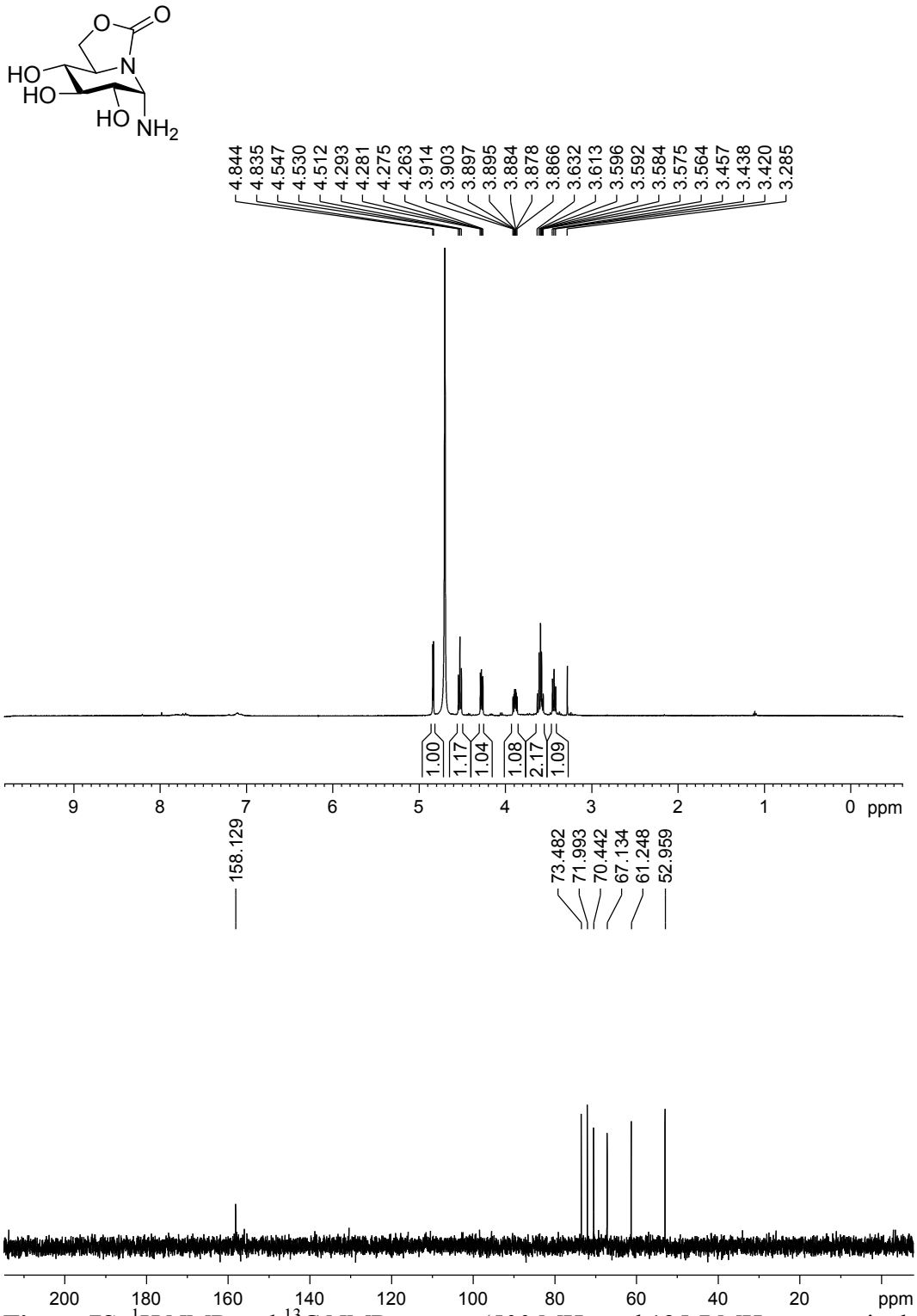


Figure 7S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **10α**.

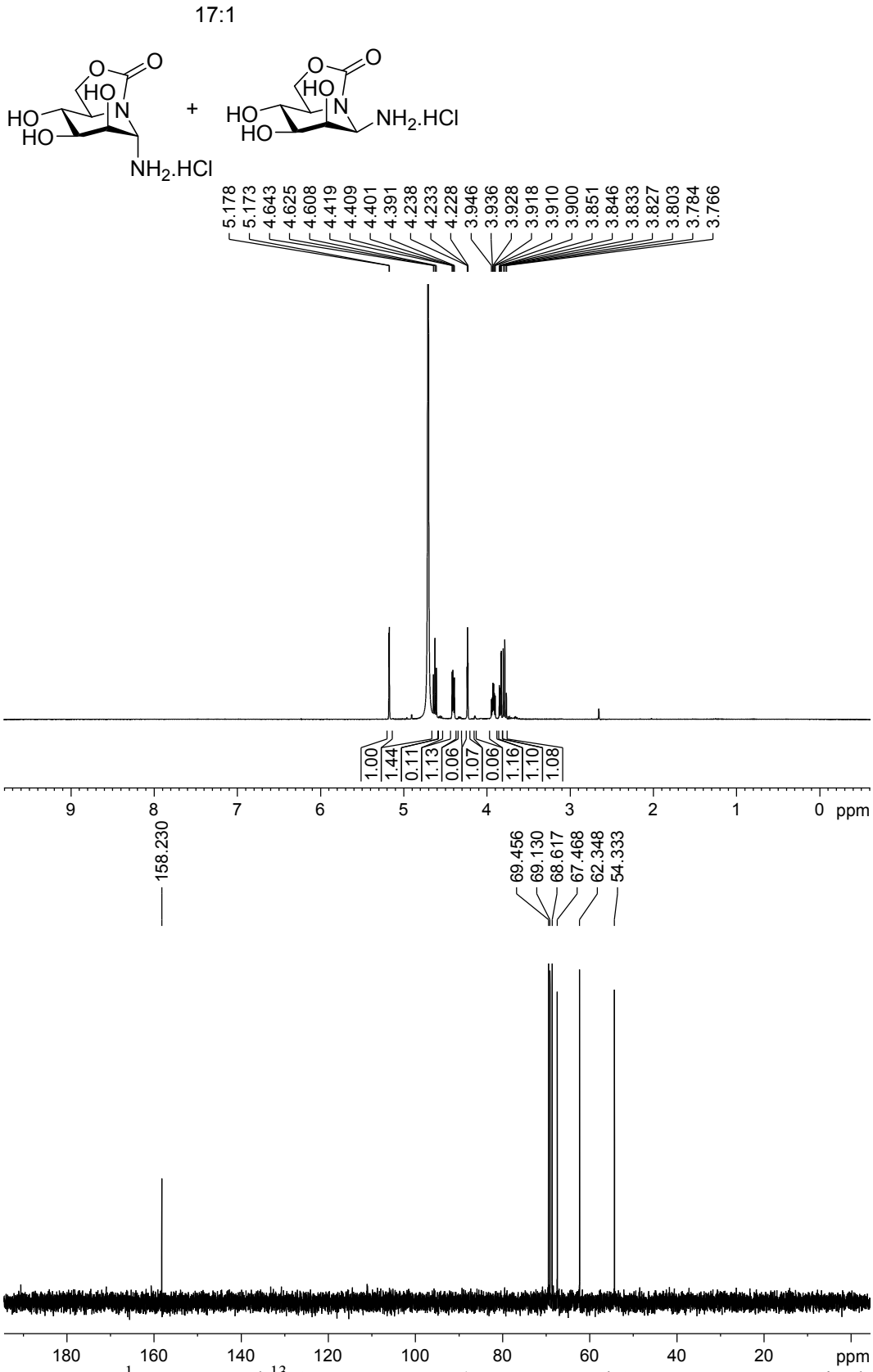


Figure 8S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **12**.

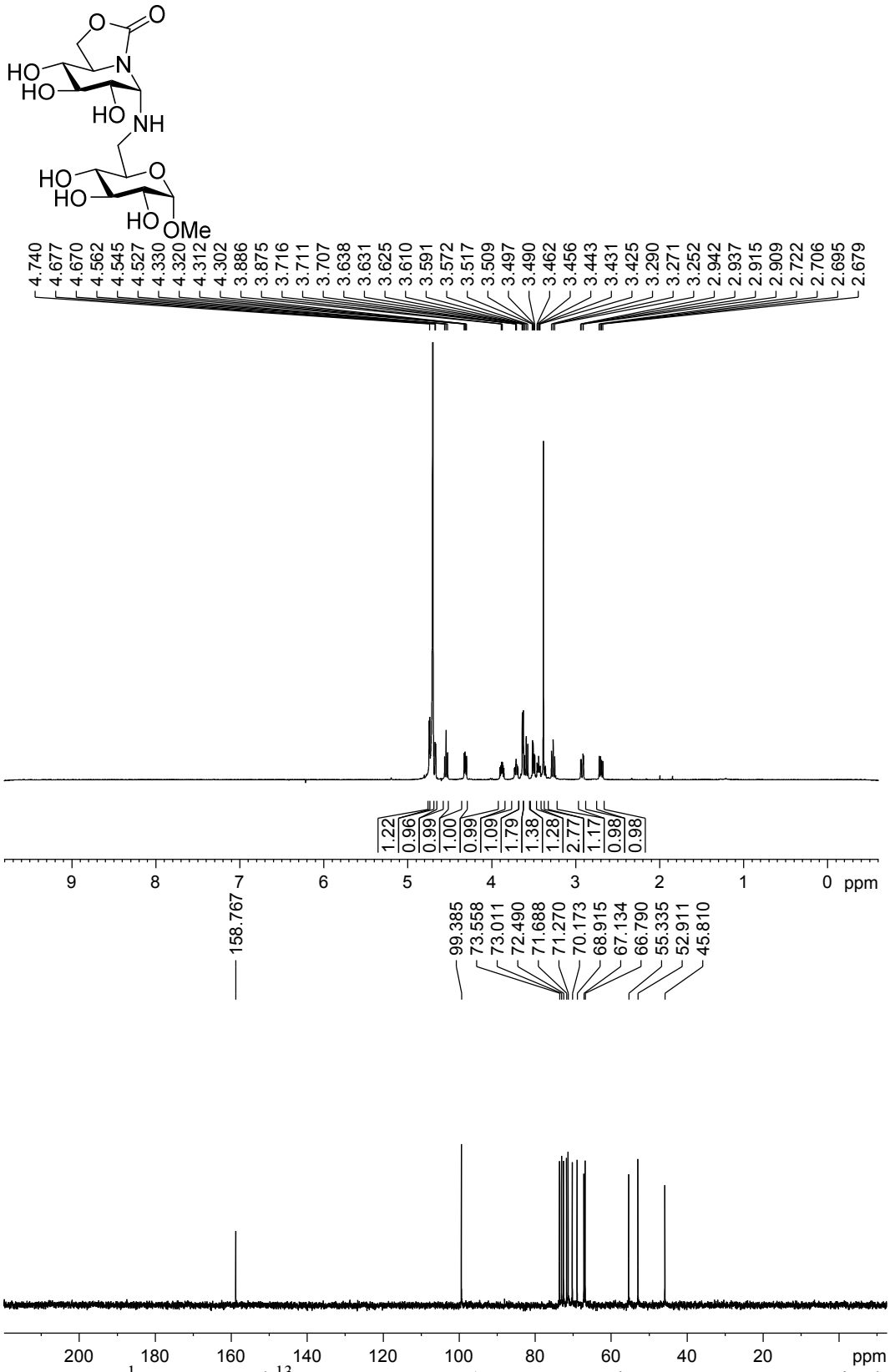


Figure 9S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **15**.

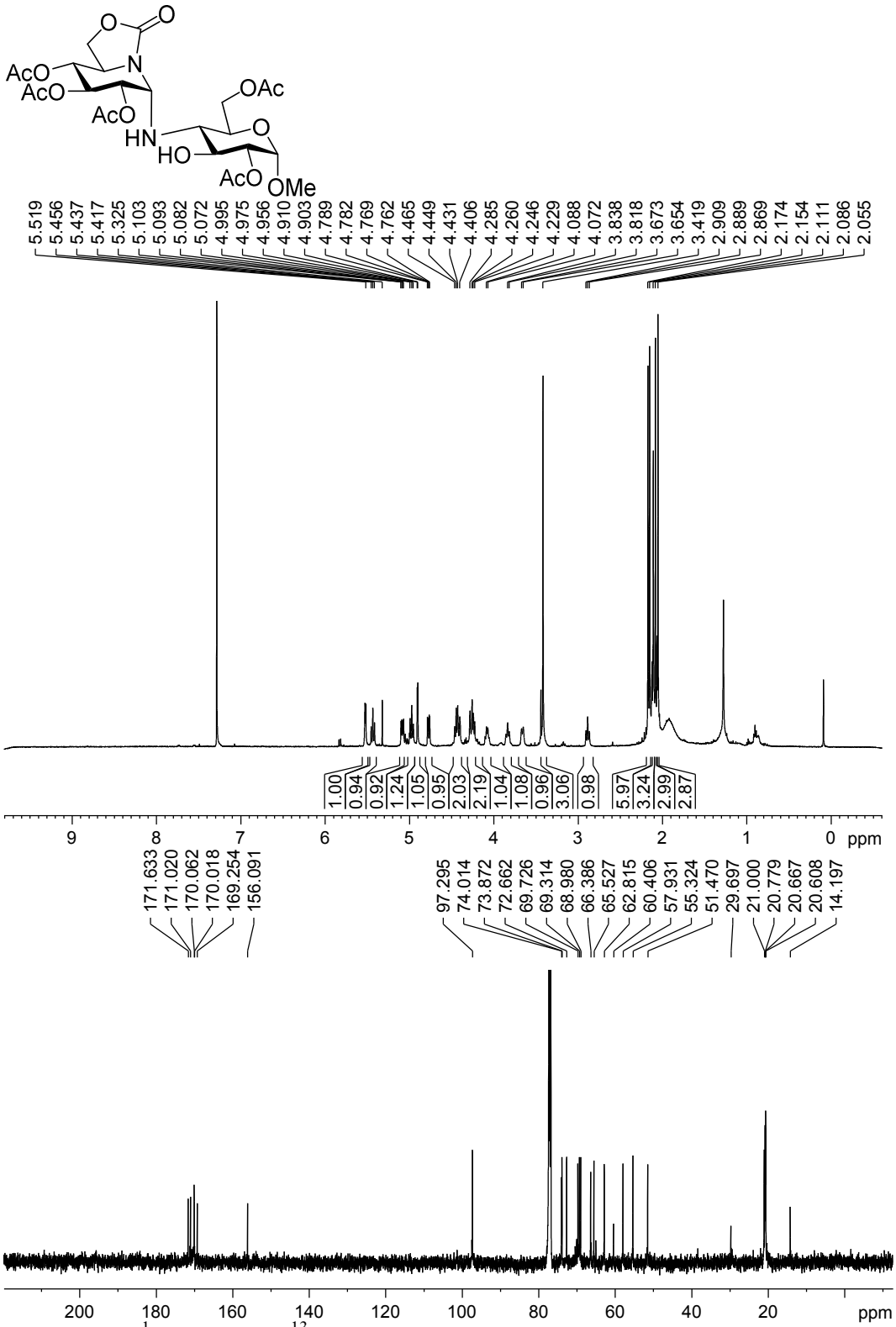


Figure 10S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, $CDCl_3$) of **16**.

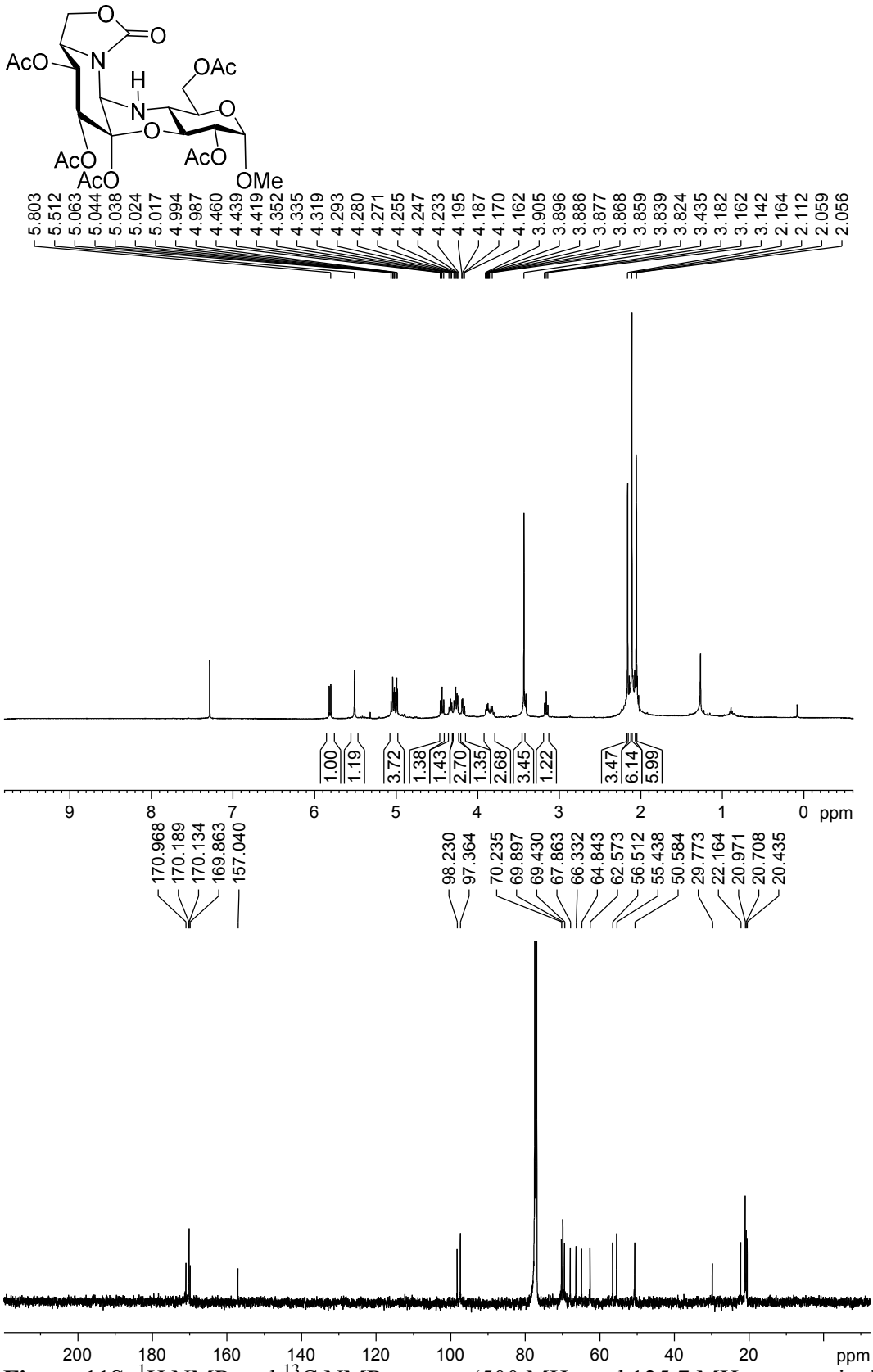


Figure 11S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, $CDCl_3$) of **17**.

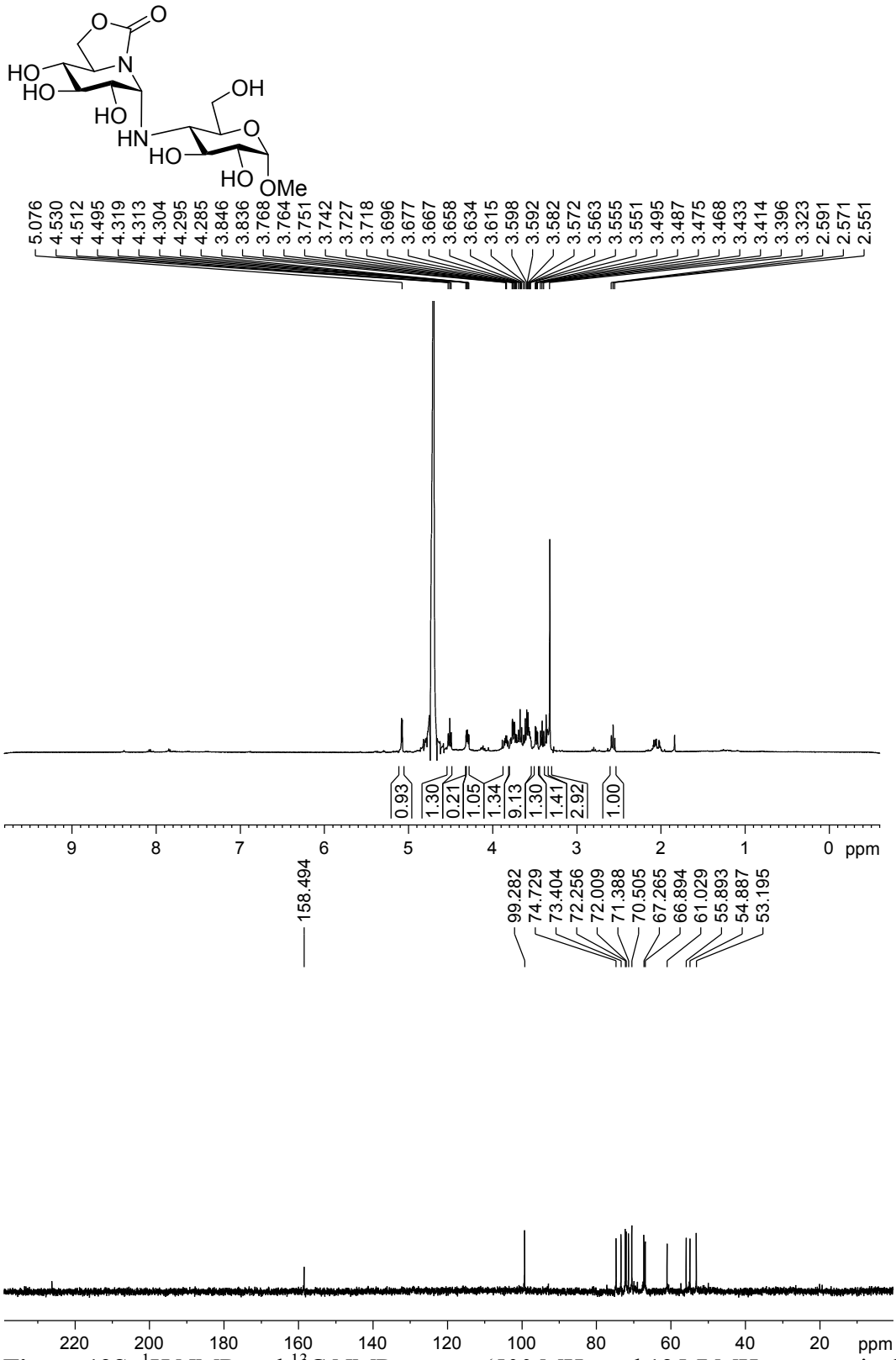


Figure 12S. ^{1}H NMR and ^{13}C NMR spectra (500 MHz and 125.7 MHz, respectively, D_2O) of **18**.

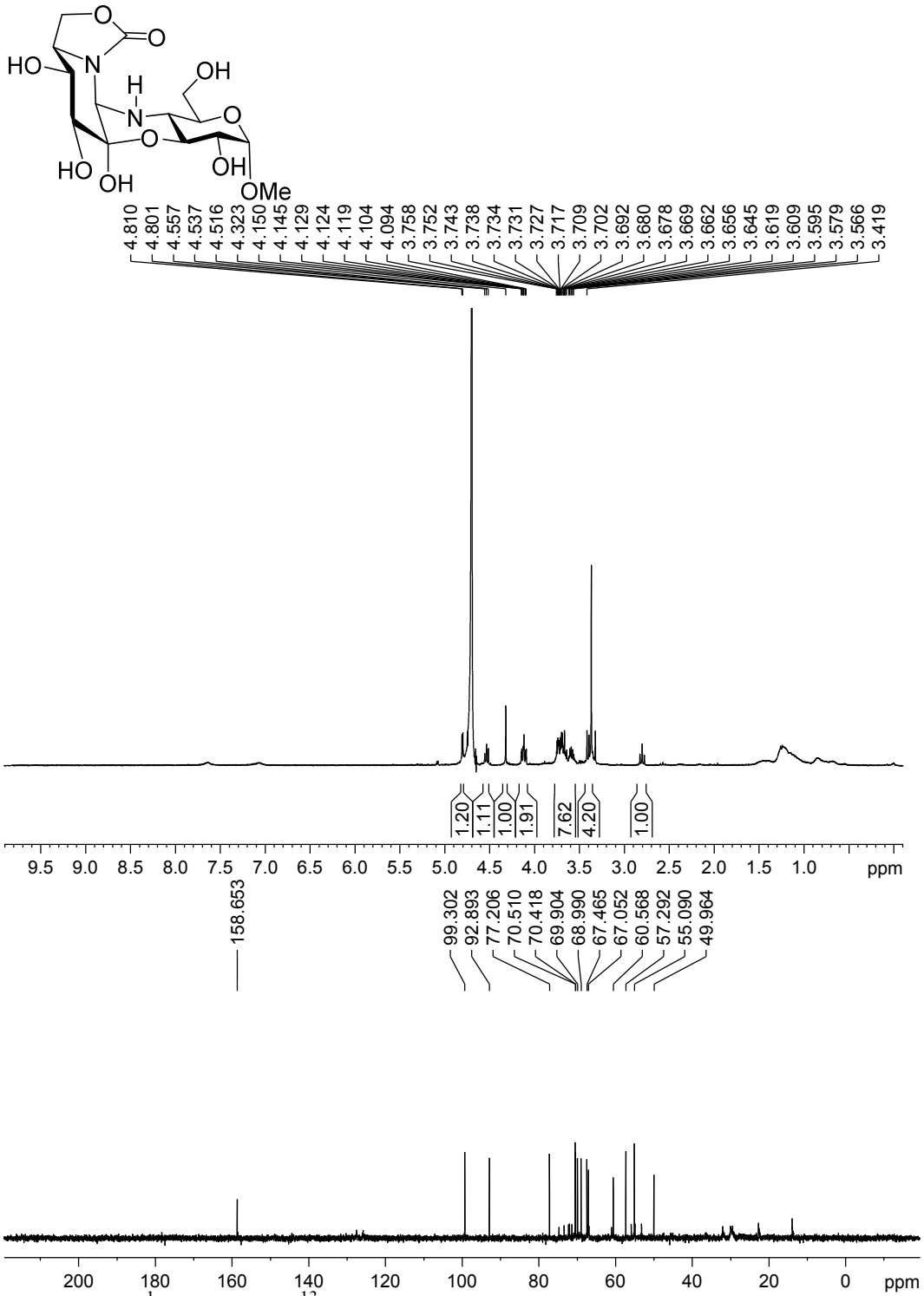


Figure 13S. ^{1}H NMR and ^{13}C NMR spectra (400 MHz and 100.6 MHz, respectively, D_2O) of **19**.