Trimethylsilylnitrate-Trimethylsilylazide: A Novel Reagent System for the Synthesis of 2-Deoxy Glycosyl Azides from Glycals: Application in the Synthesis of 2-Deoxy-β-N-glycopeptides

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Supporting Information

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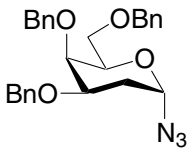
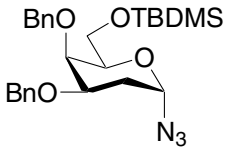
Spectral and analytical data for compounds **4a-8** are given on pages S2 to S10 whereas ^{13}C NMR spectra of these compounds are reproduced on pages S11 to S24 as indicated below:

3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*lyxo*-hexopyranosyl azide (4a).



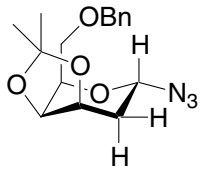
$[\alpha]_D^{25}$ = + 126 (c 1, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2113 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.82-1.90 (dd, *J* = 12.84, 4.28 Hz, 1H), 2.22-2.30 (dt, *J* = 12.68, 4.40 Hz, 1H), 3.57-3.64 (m, 2H), 3.77-3.81 (ddd, *J* = 11.72, 4.40, 2.20 Hz), 3.93 (br s, 1H), 4.00-4.03 (t, *J* = 6.32 Hz, 1H), 4.41-4.61(m, 6H), 5.54-5.55 (d, *J* = 3.64 Hz, 1H), 7.22-7.36 (m, 15 H); ^{13}C NMR (100MHz, $CDCl_3$): δ 30.3, 68.9, 70.4, 72.0, 72.5, 73.4, 74.0, 87.9, 127.3-138.5 (m, aromatic); MSES$^+$: 482 $[M + Na]^+$; Anal. calc. for $C_{27}H_{29}N_3O_4$ (459.53) C 70.57, H 6.37, N 9.15; found: C 70.54, H 6.35, N 9.17.

3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-α-D-*lyxo*-hexopyranosyl azide (4b).



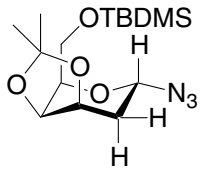
$[\alpha]_D^{25}$ = + 107.3 (c 1.5, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2116 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.83 (s, 9H), 1.76-1.80 (dd, *J* = 13.06, 4.02 Hz, 1H), 2.15-2.21 (dt, *J* = 12.44, 4.40 Hz, 1H), 3.63-3.65 (br d, *J* = 6.60 Hz, 2H), 3.71-3.77 (m, 2H), 3.87 (br s, 1H), 4.52-4.89 (m, 4H), 5.47-5.50 (d, *J* = 3.68 Hz, 1H), 7.20-7.30 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.2, 25.8, 30.4, 62.9, 70.5, 72.5, 73.9, 74.2, 74.4, 87.9, 127.3-138.7 (m, aromatic); MSES$^+$: 506 $[M + Na]^+$; Anal. calc. for $C_{26}H_{37}SiN_3O_4$ (483.67) C 64.56, H 7.70, N 8.68; found: C 64.57, H 7.68, N 8.67.

6-*O*-Benzyl-3,4-*O*-isopropylidene-2-deoxy-β-D-*lyxo*-hexopyranosyl azide (4c).



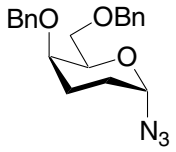
$[\alpha]_D^{25}$ = + 125.5 (c 0.90, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2109 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.46 (s, 3H), 1.58-1.65 (m, 1H), 2.17-2.23 (m, 1H), 3.65-3.69 (dd, *J* = 10.24, 5.36 Hz, 2H), 3.97-4.01 (dt, *J* = 5.36, 2.0 Hz, 1H), 4.18-4.21 (dd, *J* = 7.44, 2.00 Hz, 1H), 4.45-4.49 (dd, *J* = 10.72, 3.40 Hz, 1H), 4.55-4.58 (br d, *J* = 12.00 Hz, 1H), 4.62-4.65 (br d, *J* = 12.20 Hz, 1H), 5.43-5.47 (dd, *J* = 8.04, 5.60 Hz, 1H), 7.25-7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 26.4, 29.8, 69.1, 69.9, 70.0, 72.5, 73.4, 85.1, 109.2, 127.5, 127.6, 128.3, 138.1.; MSES$^+$: 337 $[M + NH_4]^+$; Anal. calc. for $C_{16}H_{21}N_3O_4$ (319.35) C 60.17, H 6.62, N 13.15; found: C 60.20, H 6.68, N 13.18.

6-*O*-(*tert*-Butyldimethylsilyl)-3,4-*O*-isopropylidene-2-deoxy-β-D-*lyxo*-hexopyranosyl azide (4d).



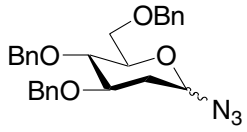
$[\alpha]_D^{25}$ = + 129.5 (c 2.1, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2109 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.82 (s, 9H), 1.23 (s, 3H),1.40 (s, 3H), 1.50-1.56 (m, 1H), 2.05-2.11 (m, 1H), 3.70-3.75 (m, 3H), 4.10-4.12 (dd, *J* = 7.46, 1.34 Hz, 1H), 4.36-4.40 (m, 1H), 5.32-5.35 (dd, *J* = 8.10, 5.60 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3, 25.0, 25.8, 26.5, 30.1, 62.0, 69.9, 71.5, 72.0, 85.1, 109.0; MSES$^+$: 366 $[M + Na]^+$; Anal. calc. for $C_{15}H_{29}SiN_3O_4$ (343.48) C 52.45, H, 8.50, N 12.23; found: C 52.43, H 8.60, N, 12.19.

4,6-Di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl azide (4e).



$[\alpha]_D^{25}$ = + 62.0 (c 2.5, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2112 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42-1.45(br d, *J* = 13.64 Hz, 1H), 1.70-1.79 (ddt, *J* = 14.16, 4.16, 2.44 Hz, 1H), 1.90-1.95(qd, *J* = 14.16, 3.10 Hz, 1H), 2.04-2.13 (tt, *J* = 13.64, 4.16Hz, 1H), 3.57 (br s, 1H), 3.59-3.63 (dd, *J* = 9.76, 6.36 Hz, 1H) 3.64-3.68 (dd, *J* = 9.76, 6.36 Hz, 1H), 4.09-4.12 (dt, *J* = 6.22, 1.24 Hz, 1H), 4.38-4.62 (m, 2H), 4.45-4.58 (br d, *J* = 11.72 Hz, 1H), 4.59-4.62 (br d, *J* = 11.96 Hz, 1H), 5.46 (d, *J* = 3.68 Hz, 1H),7.23-7.34 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5, 23.6, 69.6, 70.2, 70.9, 71.6, 73.6, 87.5, 127.5-138.1(m, aromatic); MSES$^+$: 376 $[M + Na]^+$; Anal. calc. for $C_{20}H_{23}N_3O_3$ (353.41) C 67.98, H 6.56, N 11.89 ; found: C 67.93, H 6.49, N 11.18.

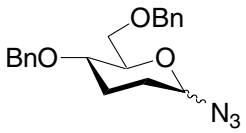
3,4,6-Tri-*O*-benzyl-2-deoxy-α/β-D-*arabino*-hexopyranosyl azide (4f).



$[\alpha]_D^{25}$ = + 84 (c 0.5, CH_2Cl_2); IR: (CH_2Cl_2) ν_{max}: 2111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): (mixture of anomers α:β, 2:1) δ 1.58-1.66(q, *J* = 11.48 Hz, 1H, α- anomer), 1.70-1.77 (dt, *J* = 13.40, 3.76 Hz, 1H, β-anomer), 2.11-2.15 (dd, *J* = 13.06, 4.02 Hz, 1H, α-anomer), 2.26-2.30 (dd, *J* = 12.68, 2.68 Hz, 1H, β-anomer), 3.46-3.88 (m, 5H, both anomers), 4.49-4.68 (m, 7H, both anomers), 5.52-5.53 (d, *J* = 3.16 Hz, 1H, α-anomer), 7.16-7.51 (m, 15H, both anomers); ^{13}C NMR (100 MHz, $CDCl_3$): (mixture of anomers) δ 34.6, 36.1, 68.3, 68.6, 71.6, 71.9, 73.0, 73.4, 74.9, 75.0, 76.8, 77.5, 79.1, 86.3, 87.3, 127.6-138.2 (m,

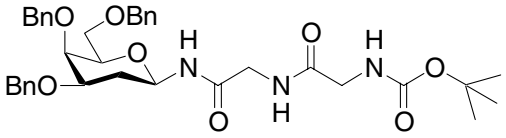
aromatic); MSES$^+$: 482 [M + Na]$^+$; Anal. calc. for $C_{27}H_{29}N_3O_4$ (459.53) C 70.57, H 6.37, N 9.15; found: C 70.59, H 6.33, N 9.12.

4,6-Di-*O*-benzyl-2,3-dideoxy-α/β-D-*threo*-hexopyranosyl azide (4g).



$[\alpha]_D^{25}$ = + 138.9 (c 2.9, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 2111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): (mixture anomers α:β 1.6:1) δ 1.44-1.59 (m, 2H, β-anomer), 1.63-1.79 (m, 3H, H-2, α- anomer), 1.85-1.89 (m, 1H, β-anomer), 2.0-2.05 (m, 1H, α-anomer), 2.20-2.25 (m, 1H, β-anomer), 4.37-4.68 (m, 5H, both anomers), 5.40-5.41 (d, *J* = 2.68 Hz, 1H, α-anomer), 7.20-7.35 (m, 10H, both anomer); ^{13}C NMR (100 MHz, $CDCl_3$): (mixture anomers): δ 23.7, 27.4, 28.3, 29.6, 68.6, 69.0, 70.7, 71.1, 71.8, 71.9, 73.3, 73.4, 79.7, 86.8, 88.1, 127.4-138.1 (m, aromatic); MSES$^+$: 376 [M + Na]$^+$; Anal. calc. for $C_{20}H_{23}N_3O_3$ (353.41) C 67.98, H 6.56, N 11.89 ; found: C 67.99, H 6.53, N 11.86.

***N-tert*-Butoxycarbonyl-*N*-(3,4,6 tri-*O*-benzyl- 2-deoxy-β-D-*lyxo*-hexopyranosyl)-glycylglycine (5a).**

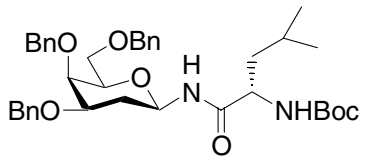


Procedure: To a stirred solution of glycosyl azide **4a** (60 mg, 0.130 mmol) in dry THF (2 mL) at room temperature were added triphenyl phosphine (41 mg, 0.156 mmol) and water (10μL). The mixture was stirred for 1 h followed by evaporation of THF and extraction of the reaction mixture with diethyl ether (2 x 30 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and then concentrated to give the crude amine. To the crude amine dissolved in dry THF (2 mL) was added *1-succinimidyl-N-tert-butyloxycarbonylglycylglycinate* (Boc-Gly-Gly-NHSE) (42 mg, 0.127 mmol) at room temperature. The reaction mixture was stirred for 1 h and after completion of reaction (TLC

monitoring) it was extracted with ethyl acetate (2 x 20 mL). The organic layer was washed with 1N HCl (2 x 5 mL) followed by saturated aqueous $NaHCO_3$ solution (2 x 5 mL) and then with brine. Evaporation of the solvent gave a residue which was purified by column chromatography to give (46 mg, 55%, over two steps) as a semi-solid.

$[\alpha]_D^{25}$ = - 10.0 (c 3.45, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.39 (s, 9H), 1.88-1.91 (br d, *J* = 11.96 Hz, 1H), 2.02-2.11 (q, *J* = 11.48 Hz, 1H), 3.53-3.63 (m, 4H), 3.72-3.73 (br d, *J* = 4.40 Hz, 2H), 3.85 (br s, 3H), 4.38-4.90 (m, 6H), 5.15-5.20 (br t, *J* = 9.00 Hz, 1H), 5.33-5.36 (t, *J* = 5.60 Hz, 1H), 6.84 (br s, 1H), 7.08-7.10 (br d, *J* = 9.00 Hz, 1H), 7.22-7.35 (m, 15H);^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 32.0, 42.9, 44.4, 68.9, 70.5, 72.2, 73.7, 74.8, 75.5, 76.6, 80.4, 127.5-128.8 (m, aromatic),137.9, 138.3, 138.8, 156.4, 169.2, 170.6; $MSES^+$: 670 $[M + Na]^+$; Anal. calc. for $C_{36}H_{45}N_3O_8$ (647.75); C 66.75, H 7.00, N 6.49. found; C 66.78, H 7.02, N 6.47.

***N-tert*-Butoxycarbonyl-*N*-(3,4,6 tri-*O*-benzyl- 2-deoxy-β-D-*lyxo*-hexopyranosyl)-L-leucine (5b).**

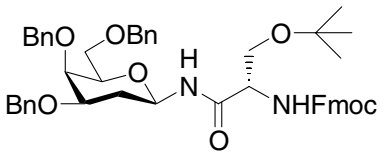


Procedure: The same experimental procedure was followed as for compound **5a** but Boc-L-Leu-NHSE was used instead of Boc-Gly-Gly-NHSE.

Yield: 57% (47 mg, over two steps). $[\alpha]_D^{25}$ = - 17.3 (c 0.75, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.90-0.92 (2 d, J = 7.5 Hz, 6H), 1.42 (s, 9H), 1.58-1.70 (m, 3H), 1.98-2.02 (m, 2H), 3.54-3.60 (m, 4H), 3.88-3.89 (d, *J* = 2.20 Hz, 1H), 4.05 (br s, 1H), 4.39-4.93 (m, 6H), 4.79 (br s, 1H), 5.14-5.19 (q, *J* = 8.55 Hz, 1H), 6.59-6.62 (d, *J* = 9.0 Hz, 1H), 7.25-7.36 (m, 15H); ^{13}C NMR (100 MHz $CDCl_3$): δ 21.7, 23.1, 24.6, 28.2, 32.5, 41.0, 68.5, 70.3, 71.5, 73.4, 74.5, 75.5, 76.5, 77.4, 127.3-

138.6 (m, Aromatic), 169.0, 172.0; MSES$^+$: 664.3 [M + NH_4]$^+$; Anal. calc. for $C_{38}H_{50}N_2O_7$ (646.36); C 70.56, H 7.79, N 4.33. found: C 70.58, H 7.81, N 4.30.

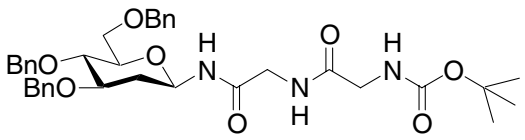
Fluorenylmethyloxycarbonyl-*N*-(3,4,6 tri-*O*-benzyl-2-deoxy-β-D-*lyxo*-hexopyranosyl)-*O*-(*tert*-butyl)-L-serine (5c).



Procedure: The same experimental procedure was followed as for compound **5a** but Fmoc-(O-t-butyl)-L-Ser-NHSE was used instead of Boc-Gly-Gly-NHSE.

Yield: 57% (59 mg, over two steps); $[\alpha]_D^{25}$ = - 6.6 (c 0.6, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1726, 1696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (s, 9H), 1.92-2.03 (m, 2H), 3.36-3.40 (t, *J* = 8.06 Hz, 2H), 3.55-3.65 (m, 4H), 3.78-3.79 (br. d, *J* = 4.64 Hz, 1H), 3.90-3.91 (d, *J* = 2.20 Hz, 1H), 4.20-4.23 (t, *J* = 7.08 Hz), 4.38-4.95 (m, 8H), 5.15-5.21 (q, *J* = 9.04 Hz, 1H), 5.66-5.68 (d, *J* = 6.56 Hz, 1H), 7.23-7.76 (m, 24H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 24.8, 25.5, 27.2, 27.3, 32.6, 33.7, 47.1, 67.1, 68.5, 70.3, 71.6, 73,4, 74.3, 75.3, 119.9, 125.1-138.8 (m, aromatic), 141.2, 170.0; MSES$^+$: 821 [M + Na]$^+$; Anal. calc. for $C_{49}H_{54}N_2O_8$ (798.96); C 73.66, H 6.81, N 3.51. found: C 73.64, H 6.78, N 3.49.

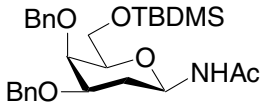
***N-tert*-Butoxycarbonyl-*N*-(3,4,6 tri-*O*-benzyl- 2-deoxy-β-D-*arabino*-hexopyranosyl)-glycylglycine (5d).**



Procedure: The same experimental procedure was followed as for compound **5a** but 2-deoxy-glucopyranosyl azide was used instead of 2-deoxy-galactopyranosyl azide.

Yield: 50% (42 mg, over two steps); $[\alpha]_D^{25}$ = + 2.4 (c 1.25, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1711, 1694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H), 1.53-1.62 (q, *J* = 11.72 Hz, 1H), 2.04-2.06 (m, 1H) 3.50-3.83 (m, 9H), 4.36-4.90 (m, 7H), 5.15-5.20 (br t, *J* = 9.76 Hz, 1H), 7.16-7.18 (d, *J* = 7.56 Hz, 2H), 7.26-7.34 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 35.8, 42.5, 44.2, 68.7, 71.48, 72.2, 73.5, 74.9, 75.9, 76.1, 79.6, 127.6-129.7 (m, aromatic), 137.3, 138.1, 138.2, 169.0, 170.5; $MSES^+$: 670 $[M + Na]^+$; Anal. calcd for $C_{36}H_{45}N_3O_8$ (647.75); C 66.75, H 7.00, N 6.49. Found: C, 66.72; H, 7.68; N, 6.43.

***N*-Acetyl [3,4-di-*O*- benzyl- 6-*O*-(*tert*- butyldimethylsilyl)-2 -deoxy-β-D-*lyxo*-hexopyranosyl] amine (6).**

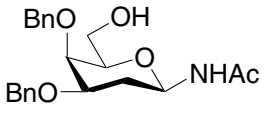


Procedure: To a stirred solution of the glycosyl azide **4b** (300 mg, 0.621 mmol) in THF (5 mL) at room temperature were added triphenyl phosphine (195 mg, 0.744 mmol) and water (50 µL). The reaction mixture was stirred for 1 h followed by evaporation of THF and extraction with diethyl ether (2 x 30 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and then concentrated to give crude amine which was acetylated using pyridine and acetic anhydride (2:0.5, 2.5 mL) at room temperature (4 h). The reaction mixture was extracted with ethyl acetate (2 x 15 mL) and the organic layer was washed twice with 1N HCl (2 x 10 mL) and finally with brine. Evaporation of the solvent gave a crude product whose purification by column chromatography yielded compound **6** (217 mg, 70% over two steps) as a viscous liquid.

$[\alpha]_D^{25}$ = - 3.52 (c 3.45, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.84, 0.86 (2s, 9H), 1.90 (br s, 3H), 1.91-2.0 (m, 2H),3.41-3.44 (dd, *J* = 8.56, 5.40 Hz, 1H), 3.55-3.60 (ddd, *J* =

14.16, 4.16, 2.20 Hz, 1H), 3.62-3.73 (m, 2H), 3.88 (br s, 1H), 4.50-4.94 (m, 4H), 5.13-5.20 (dt, *J* = 11.00, 2.20 Hz, 1H), 6.29-6.31 (d, *J* = 9.28 Hz), 6.33-6.35 (d, *J* = 9.20 Hz, 1H), 7.20-7.60 (m, 10H); ^{13}C NMR (100MHz, $CDCl_3$): (mixture of anomers): δ 23.2, 25.7, 25.8, 26.0, 29.6, 32.3, 35.5, 60.9, 68.5, 70.2, 71.4, 71.6, 73.3, 74.5, 74.6, 74.8, 75.0, 75.9, 76.1, 76.7, 77.4, 127.2-128.4 (m, aromatic), 137.7, 138.0, 138.8, 169.7; MSES$^+$: 522 $[M + Na]^+$; Anal. calc. for $C_{28}H_{41}SiNO_5$ (499.71); C 67.30, H 8.27, N 2.80., found: C 67.31, H 8.24, N 2.79.

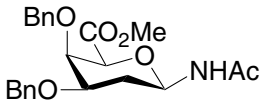
_N_-Acetyl [3,4-di-_O_- benzyl-6-(hydroxy)-2 -deoxy-β-D-_lyxo_-hexopyranosyl] amine (7).



Procedure: To a stirred solution of compound **6** (200 mg, 0.40 mmol) in dry THF (4 mL) was added dropwise 1M solution of TBAF (0.48 mL, 0.48 mmol) at 0 °C. The cooling bath was removed and the reaction mixture stirred for 1 h at room temperature and then extracted with ethyl acetate (2 x 30 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude product which was purified by column chromatography to obtain compound **7** (141 mg, 92%) as a semi-solid.

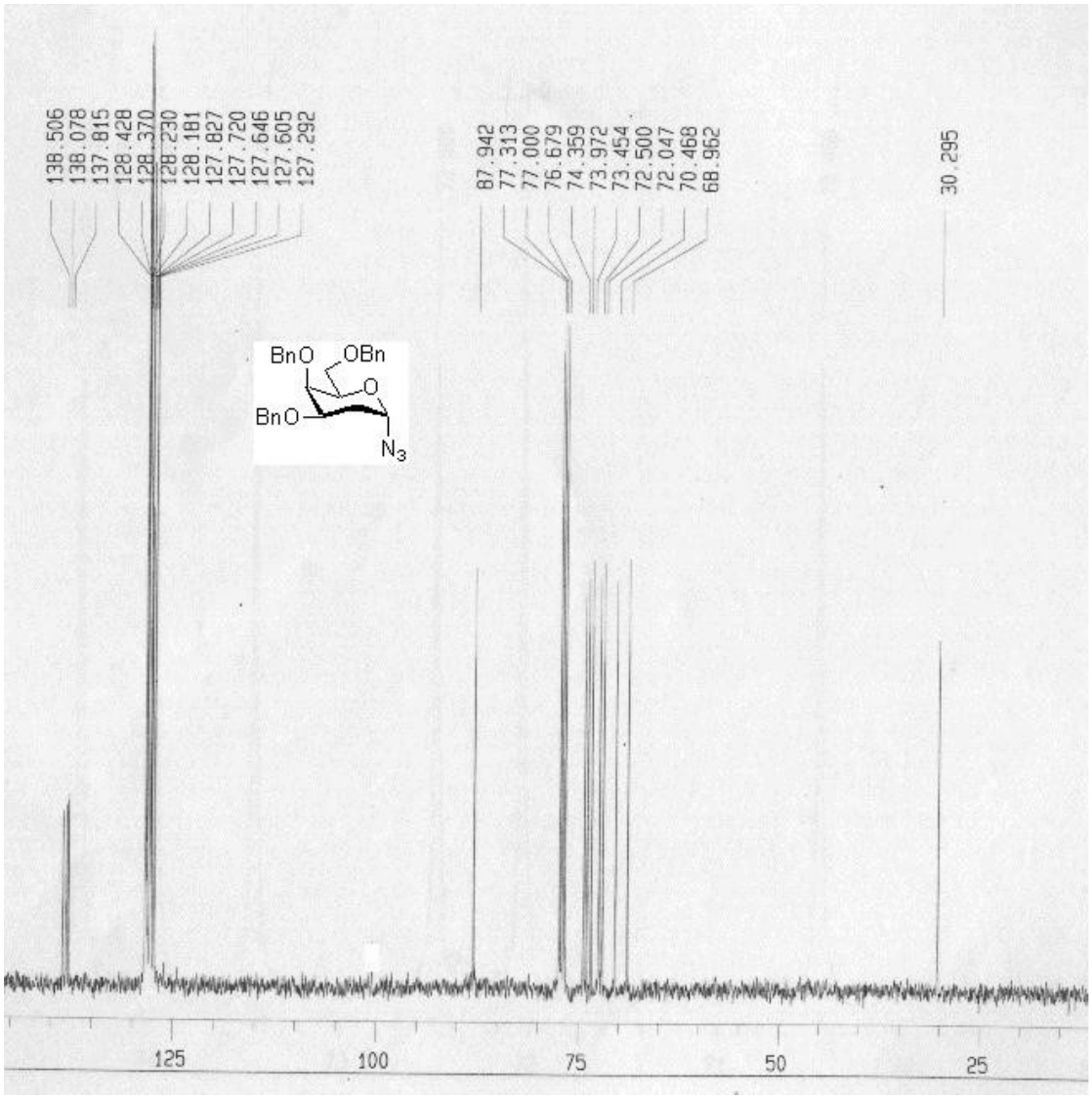
$[\alpha]_D^{25}$ = - 4.7 (c 1.75, CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 3305, 1669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of anomers, α:β, 1:6.7): δ 1.93, 1.94 (2 s, 3H), 1.95-2.10 (m, 2H), 2.79 (br s, 1H), 3.44-3.47(t, *J* = 5.62 Hz, 1H), 3.49-3.53 (dd, *J* = 11.24, 4.88 Hz, 1H), 3.58-3.61 (m, 1H), 3.71-3.75 (dd, *J* = 11.20, 6.46 Hz, 1H), 3.77 (br s 1H), 4.58-4.94 (m, 4H), 5.11-5.17 (dt, *J* = 9.28, 2.44 Hz, 1H), 6.60-6.62 (d, *J* = 9.16 Hz,1H), 6.67-6.69 (d, *J* = 9.00 Hz 1H), 7.26-7.37 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): (mixture of anomer): δ 23.2, 29.6, 31.8, 35.2, 62.4, 68.1, 69.1, 70.4, 71.9, 73.3, 74.1, 74.6, 74.7, 75.2, 75.9, 76.2, 77.5, 127.3-138.1 (m, aromatic), 170.1, 170.5; MSES$^+$: 408 $[M + Na]^+$; Anal. calc. for $C_{22}H_{27}NO_5$ (385.45); C 68.55, H 7.05, N 3.63, found: C 68.58, H 7.08, N 3.61.

Methyl [*N*-(1-acetamido)]-3,4-di-*O*- benzyl-2-deoxy-β-D-*lyxo*-hexopyranosyl derivative (8).



Procedure: Compound **7** (80 mg, 0.207 mmol) was dissolved in acetone (3 mL) and aqueous 5% $NaHCO_3$ solution (0.6 mL) was added to it. The reaction mixture was cooled to 0 °C and treated with KBr (3 mg, 0.025 mmol) and TEMPO (32 mg, 0.205 mmol). NaOCl (0.5 mL, 0.255 mmol) was then added dropwise to this reaction mixture which was stirred for 1 h at same temperature. Additional NaOCl (0.2 mL, 0.107 mmol) was added to it and stirring continued for further 1 h at 0 °C followed by addition of 5% $NaHCO_3$ solution (0.8 mL). Evaporation of acetone under reduced pressure was followed by washing of the aqueous layer with ether (2 x 10 mL). The reaction mixture was then acidified to pH 6 with 10% aqueous citric acid and extracted with ethyl acetate (2 x 10 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and solvent evaporated to obtain the crude acid which was dissolved in dry THF, cooled to 0 °C and reacted with excess of CH_2N_2. The mixture was stirred for 30 min. at the same temperature followed by evaporation of the solvent to give the crude product which was purified by column chromatography to yield compound **8** (61 mg, 72%, over two steps) as a colorless solid. m.p. 184-186 °C (dec).

$[\alpha]_D^{25}$ = + 8.0 (c 0.5 CH_2Cl_2); IR (CH_2Cl_2) ν_{max}: 1756,1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.92-1.94 (br d, *J* = 11.24 Hz, 1H), 1.99 (s, 3H) 2.42-2.51 (q, *J* = 11.90, 1H), 3.51 (s, 3H), 3.65-3.68 (ddd, *J* = 11.96, 4.12, 2.44 Hz, 1H), 4.13-414 (br d, *J* = 3.64 Hz, 2H), 4.52-4.55 (br d, *J* = 12.20 Hz, 2H), 4.63-4.66 (br d, *J* = 12.44 Hz, 1H), 4.91-4.94 (br d, *J* = 12.48 Hz, 1H), 5.21-5.26 (dt, *J* = 9.52, 2.00 Hz, 1H), 7.22-7.31 (m, 10H)7.47-7.49 (d, *J* = 9.52 Hz, 1H); ^{13}C NMR(100 MHz, $CDCl_3$): δ 23.0, 30.7, 51.9, 70.3, 72.5, 73.5, 75.9, 76.2, 127.2, 127.5, 127.7, 128.1, 128.2, 128.4, 137.7, 138.4, 169.0, 170.8; $MSES^+$: 431 $[M + NH_4]^+$, 414 $[M + H]^+$; Anal. calc. for $C_{23}H_{27}NO_6$ (413.18); C 66.81, H 6.58, N 3.39. found: C 66.83, H 6.56, N 3.40.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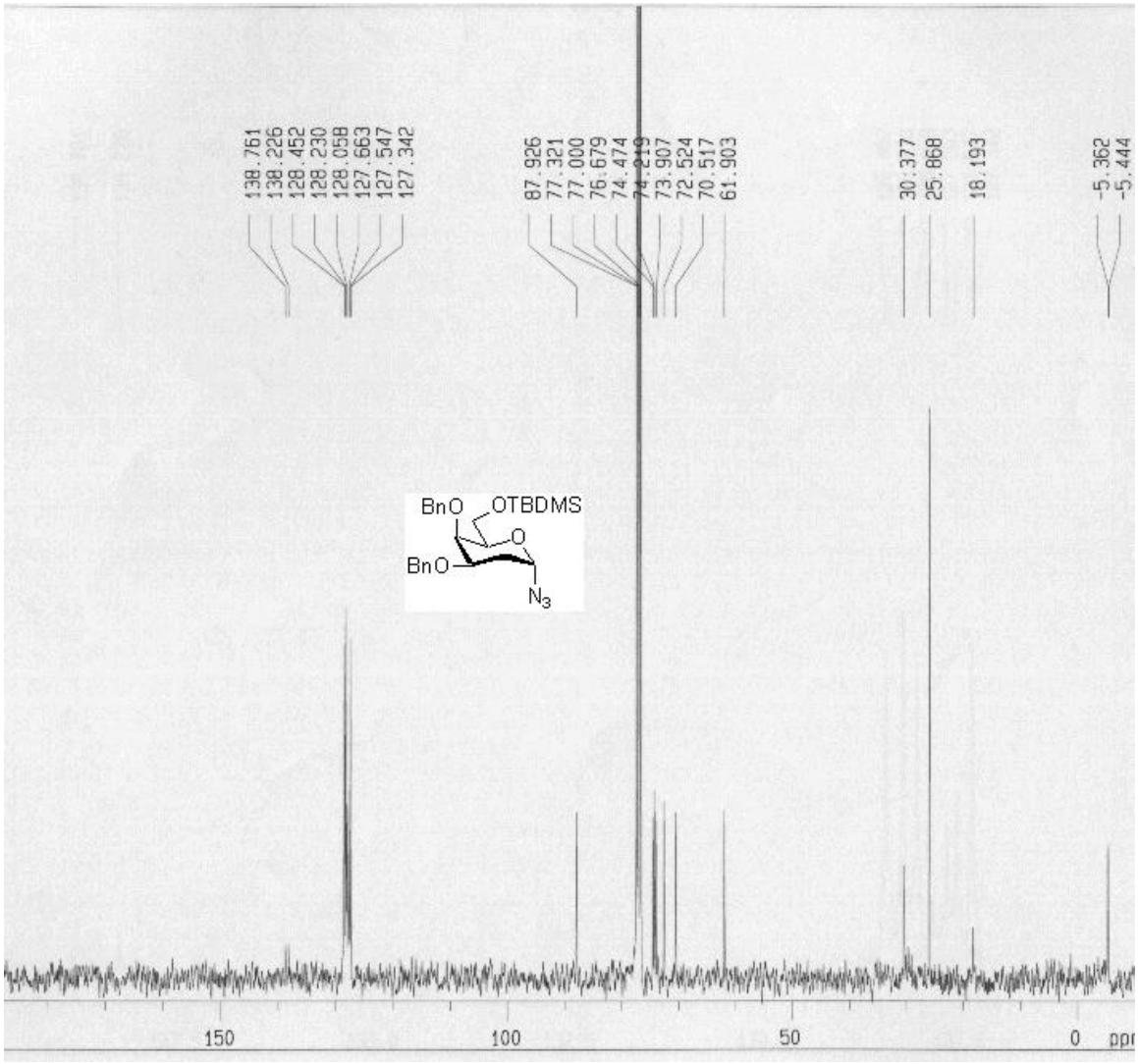
50
25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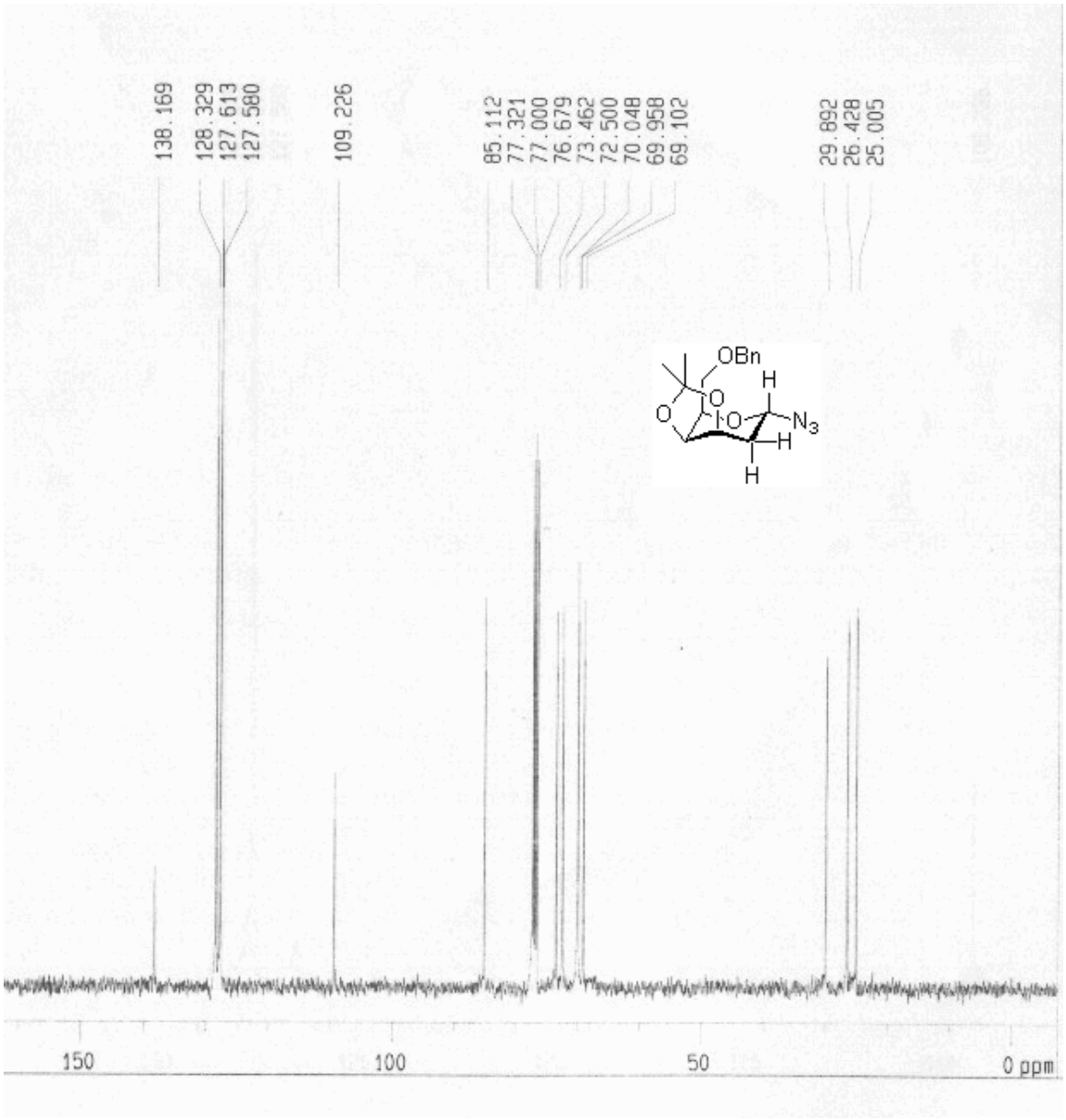
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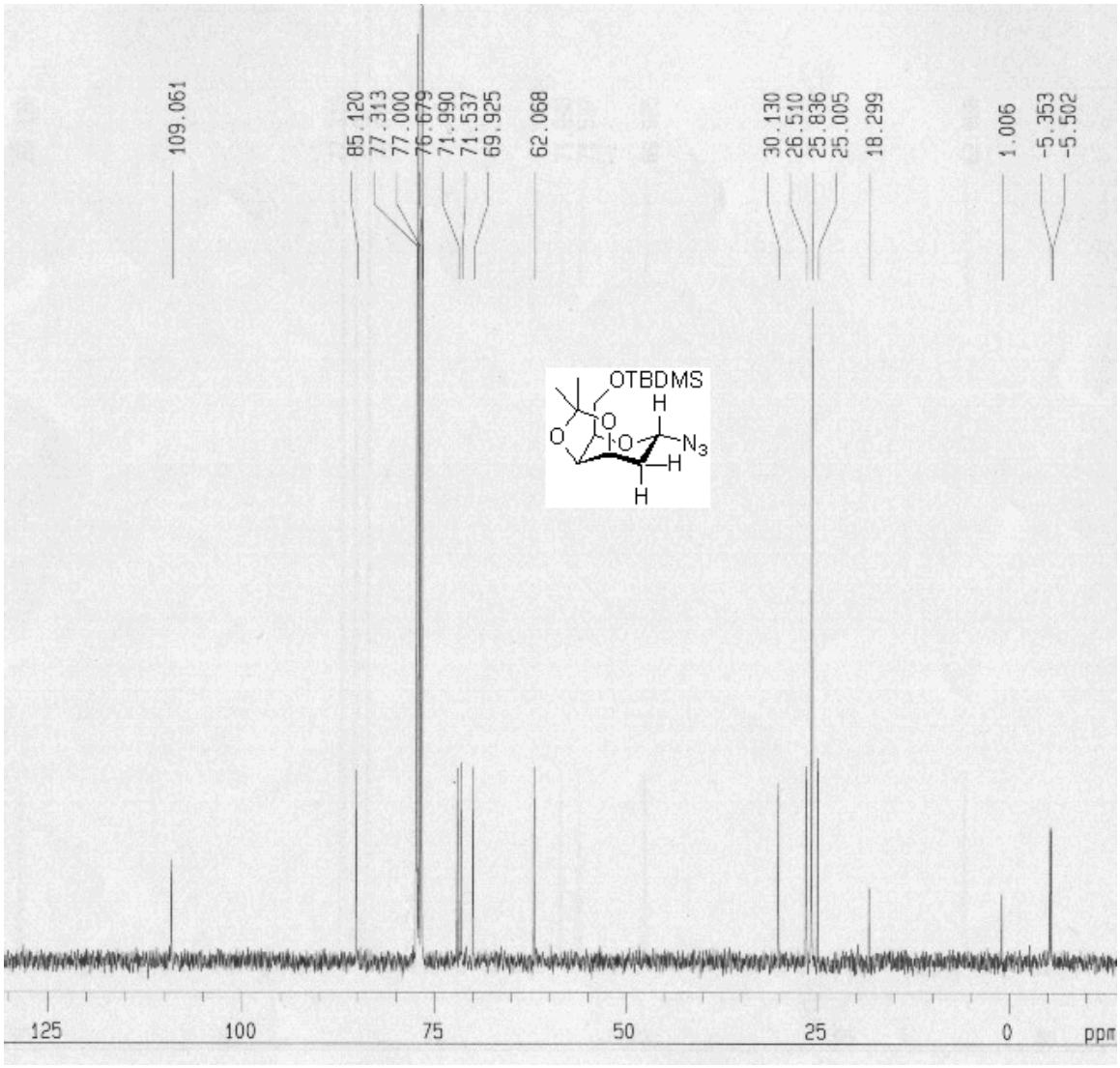
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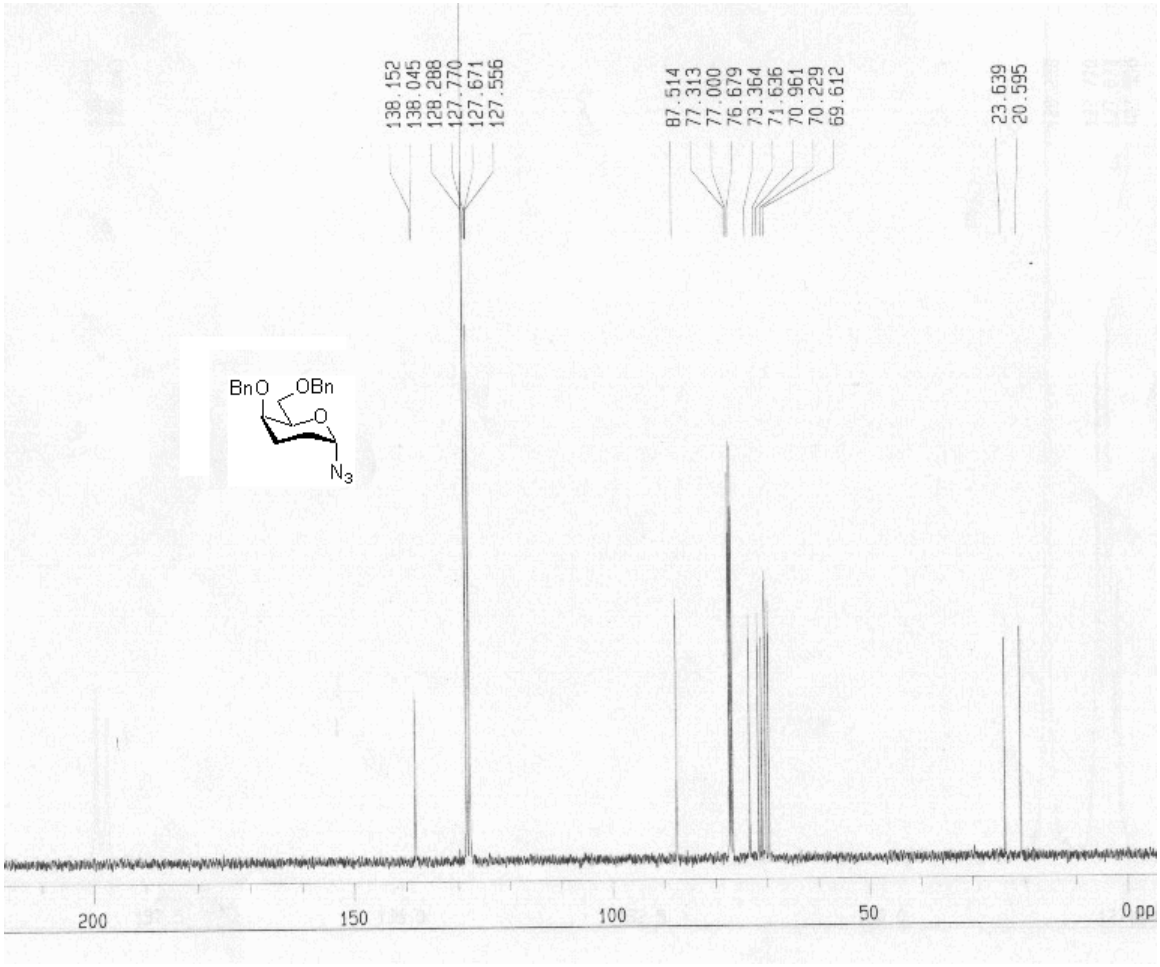
ppm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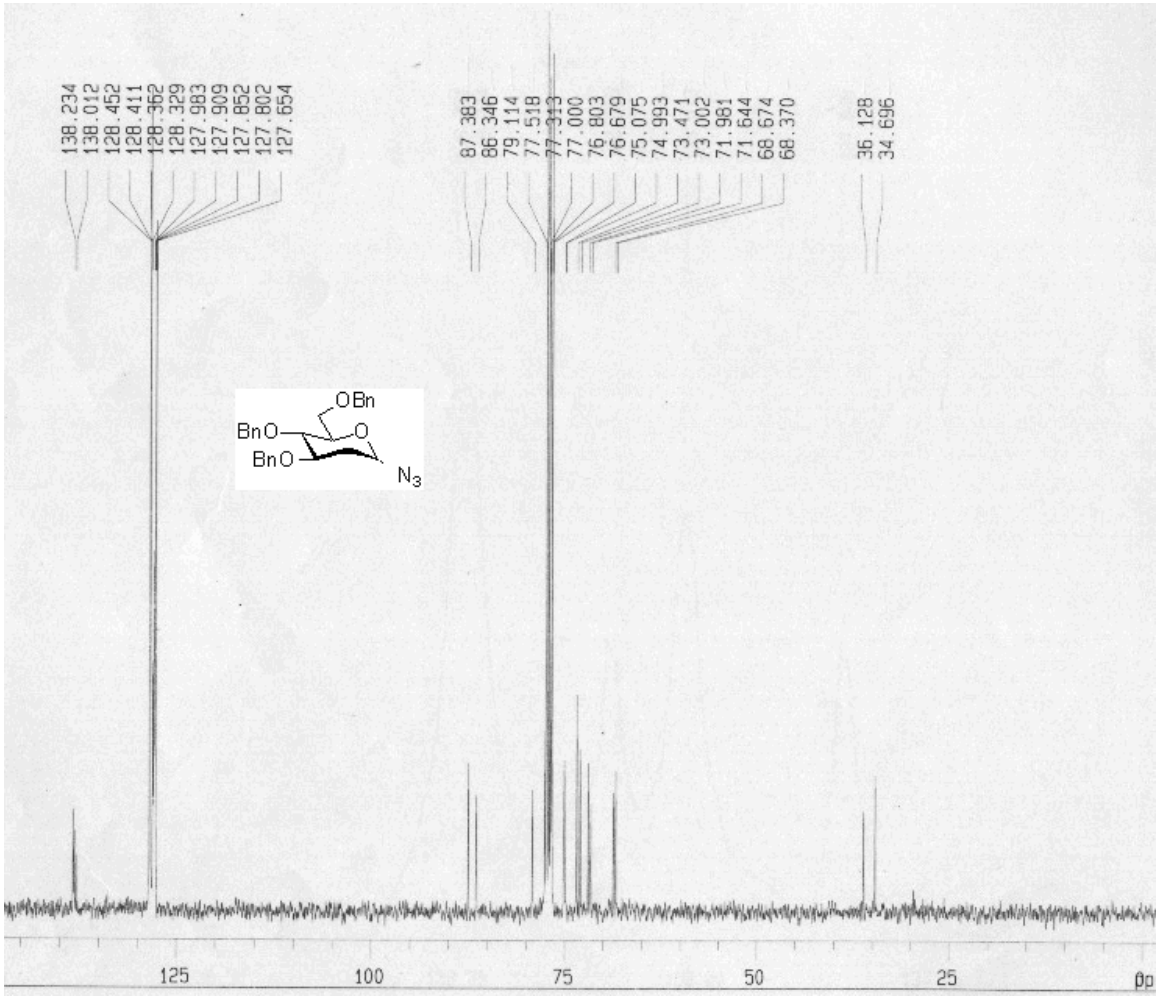
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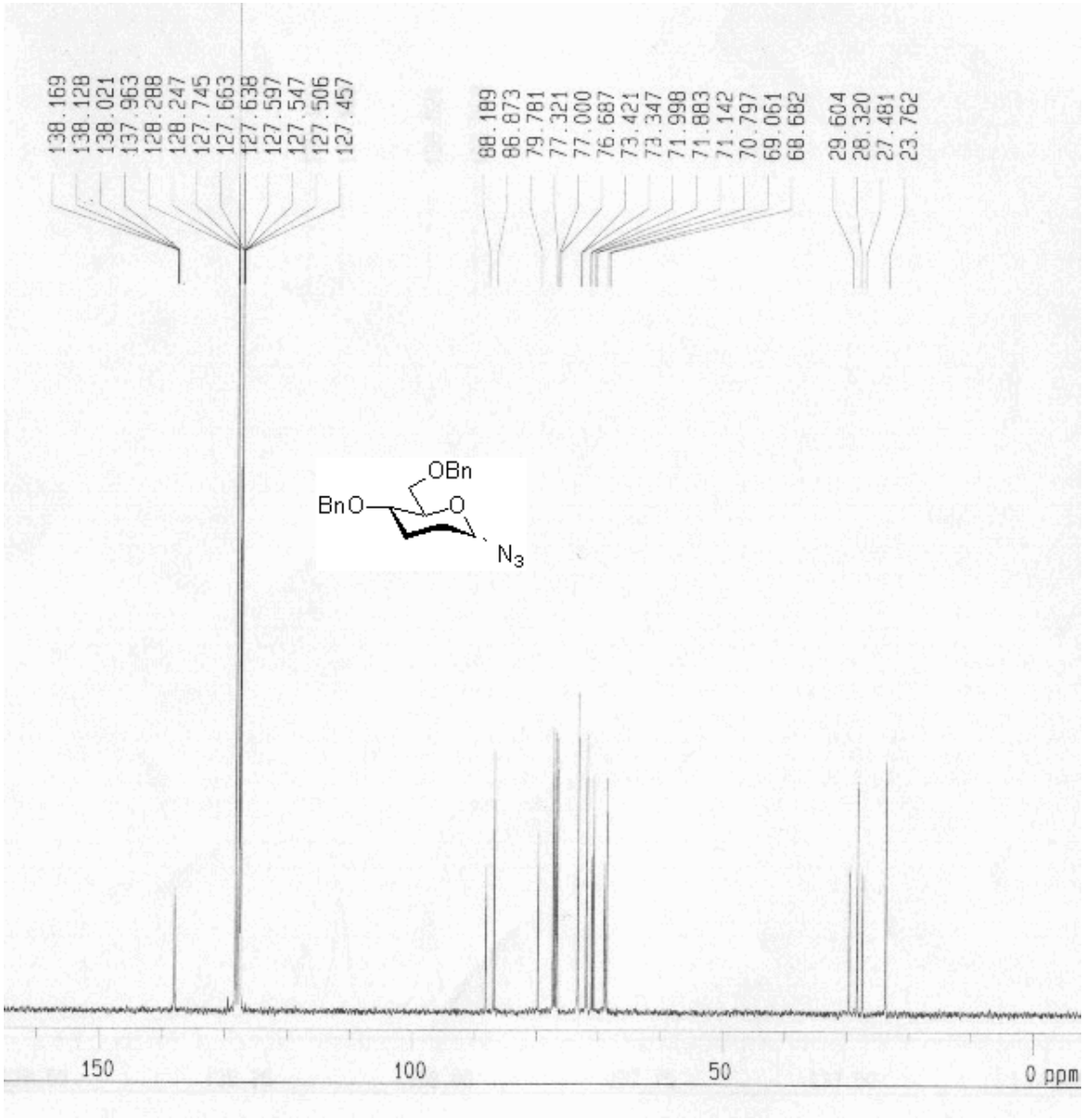
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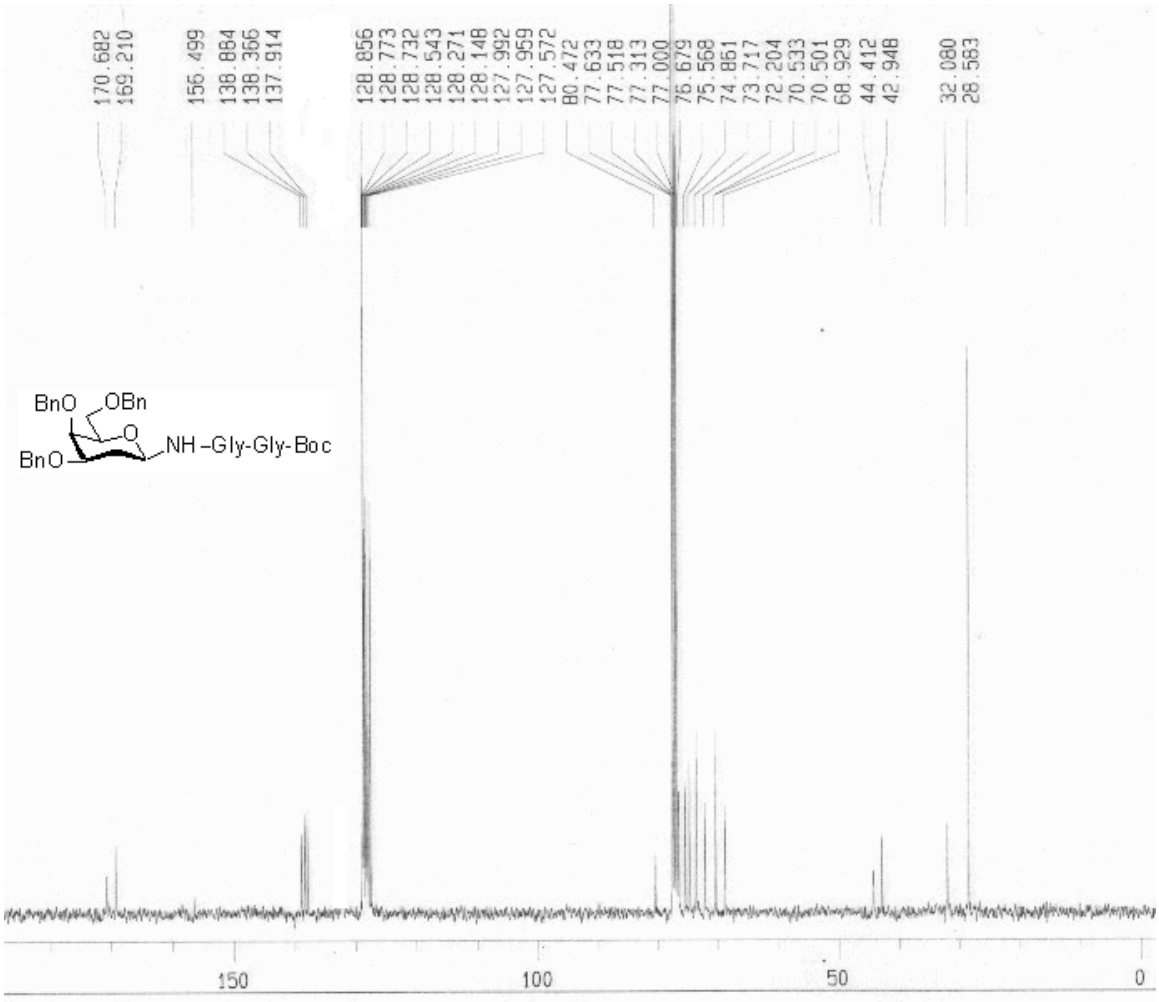
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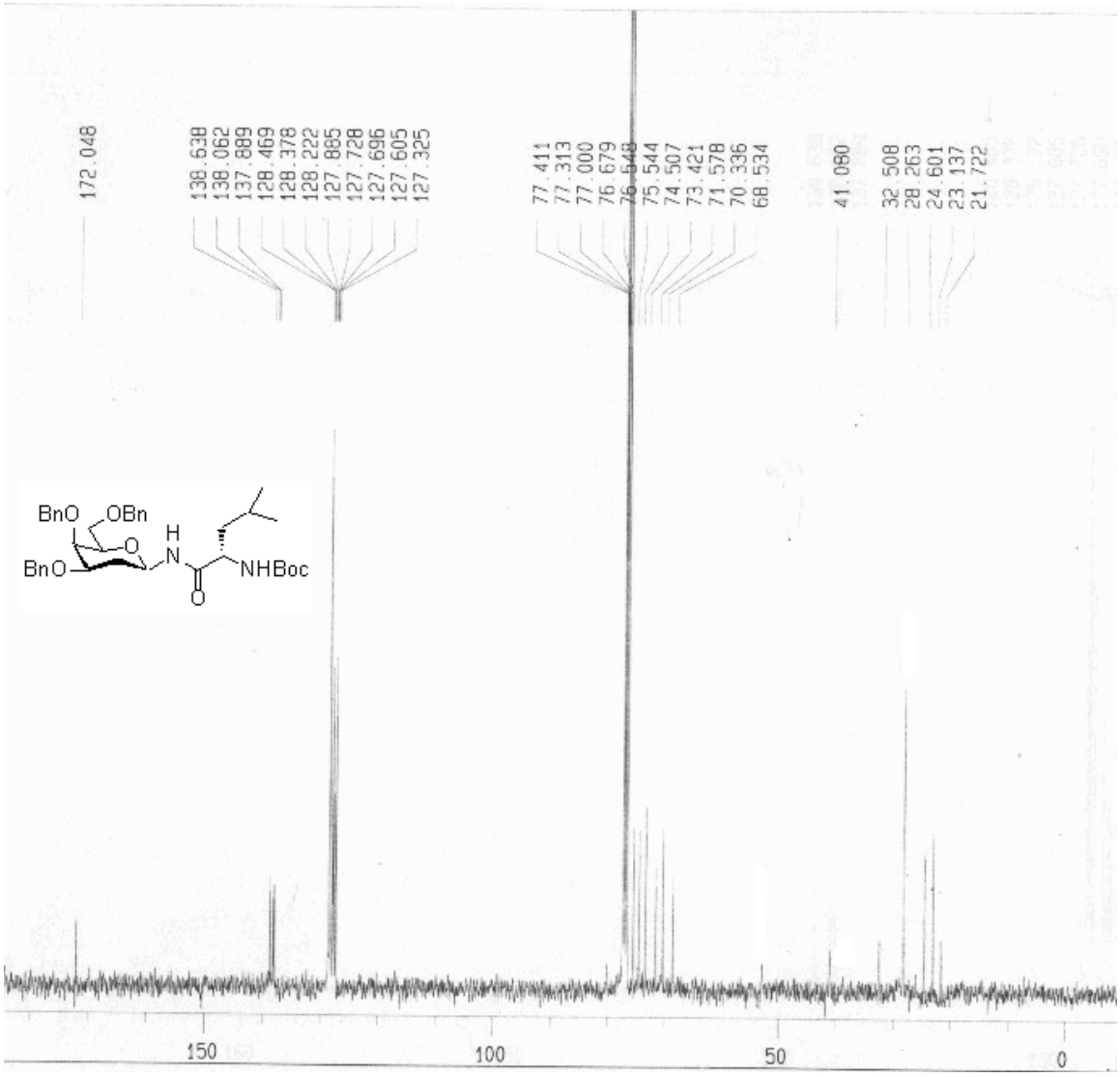
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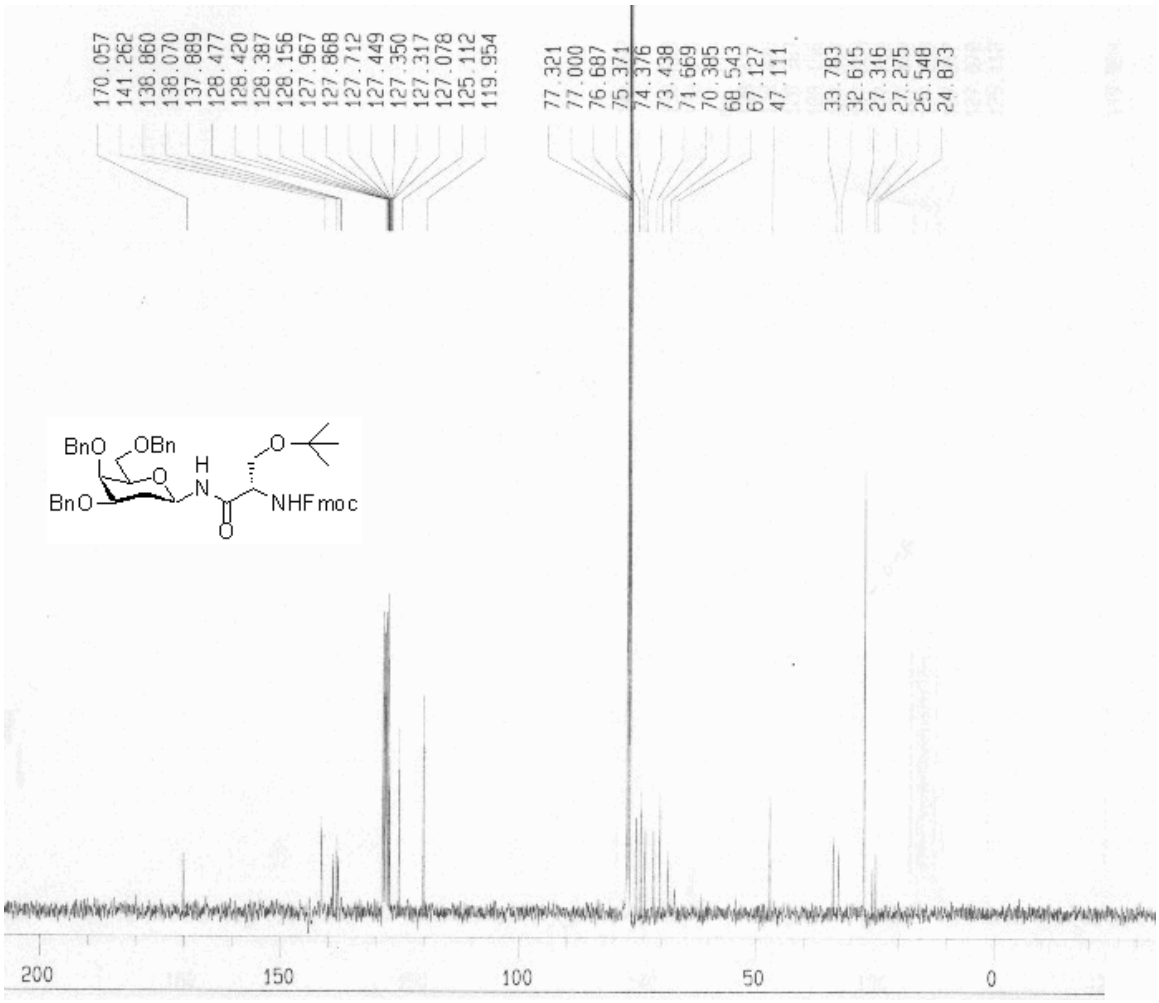
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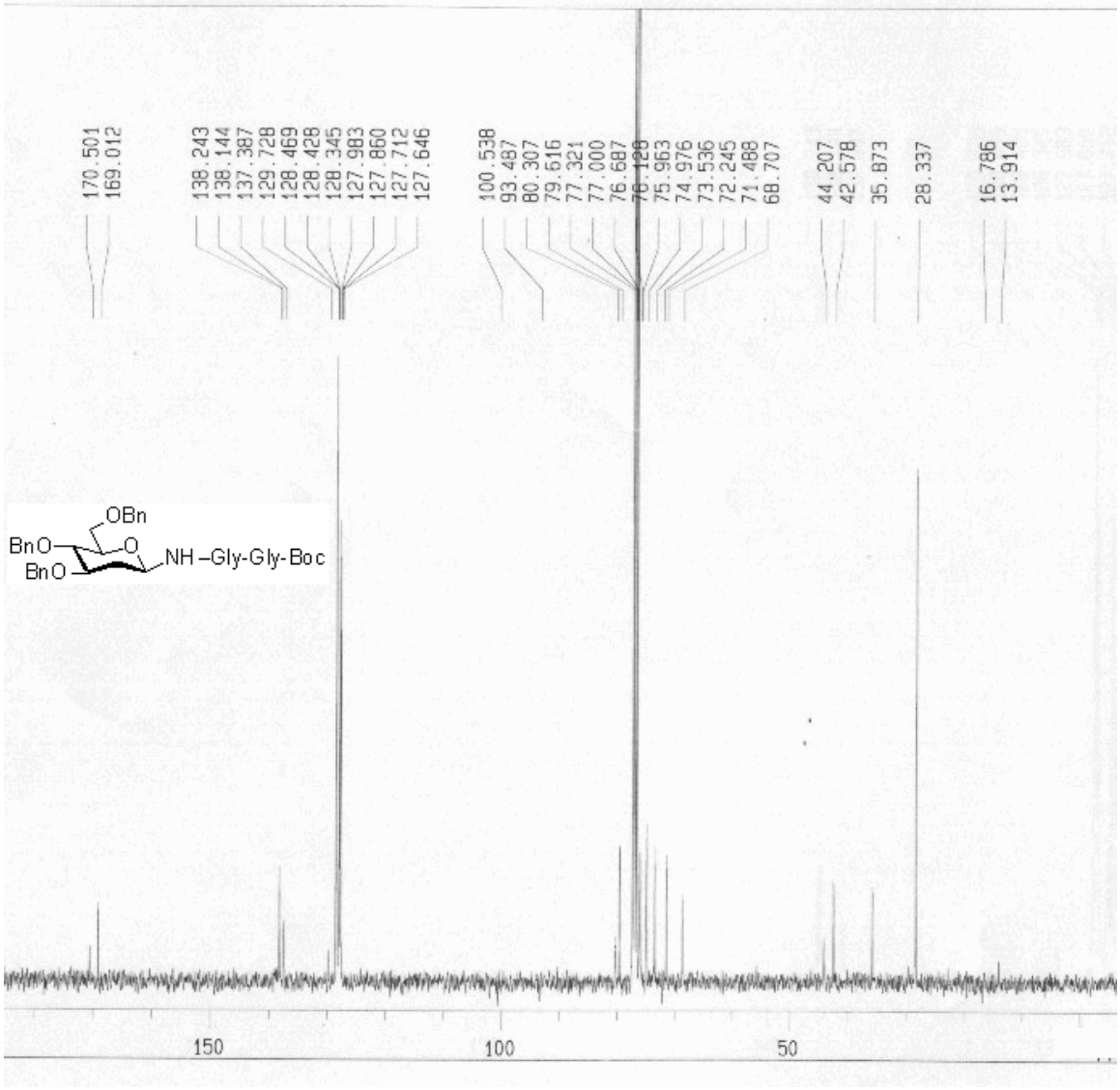
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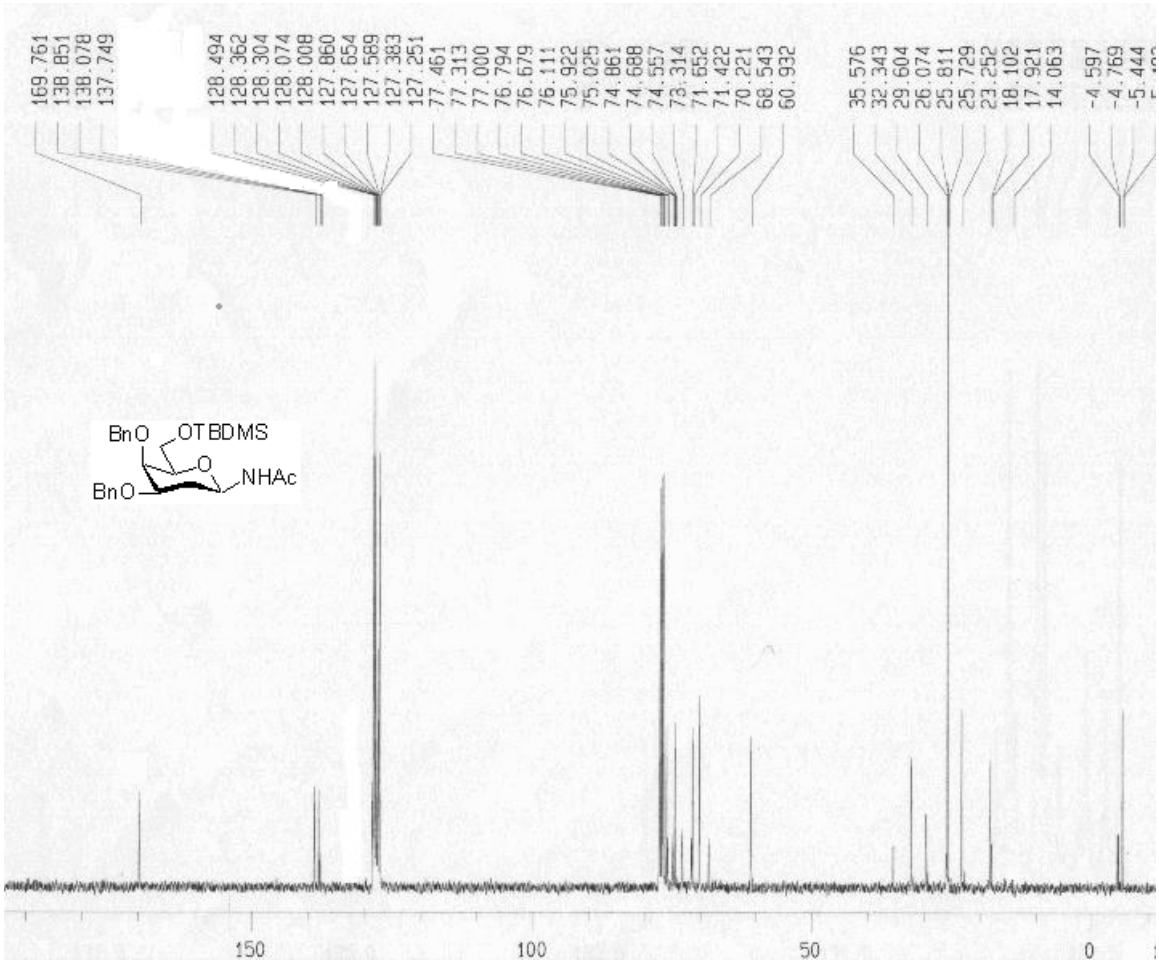
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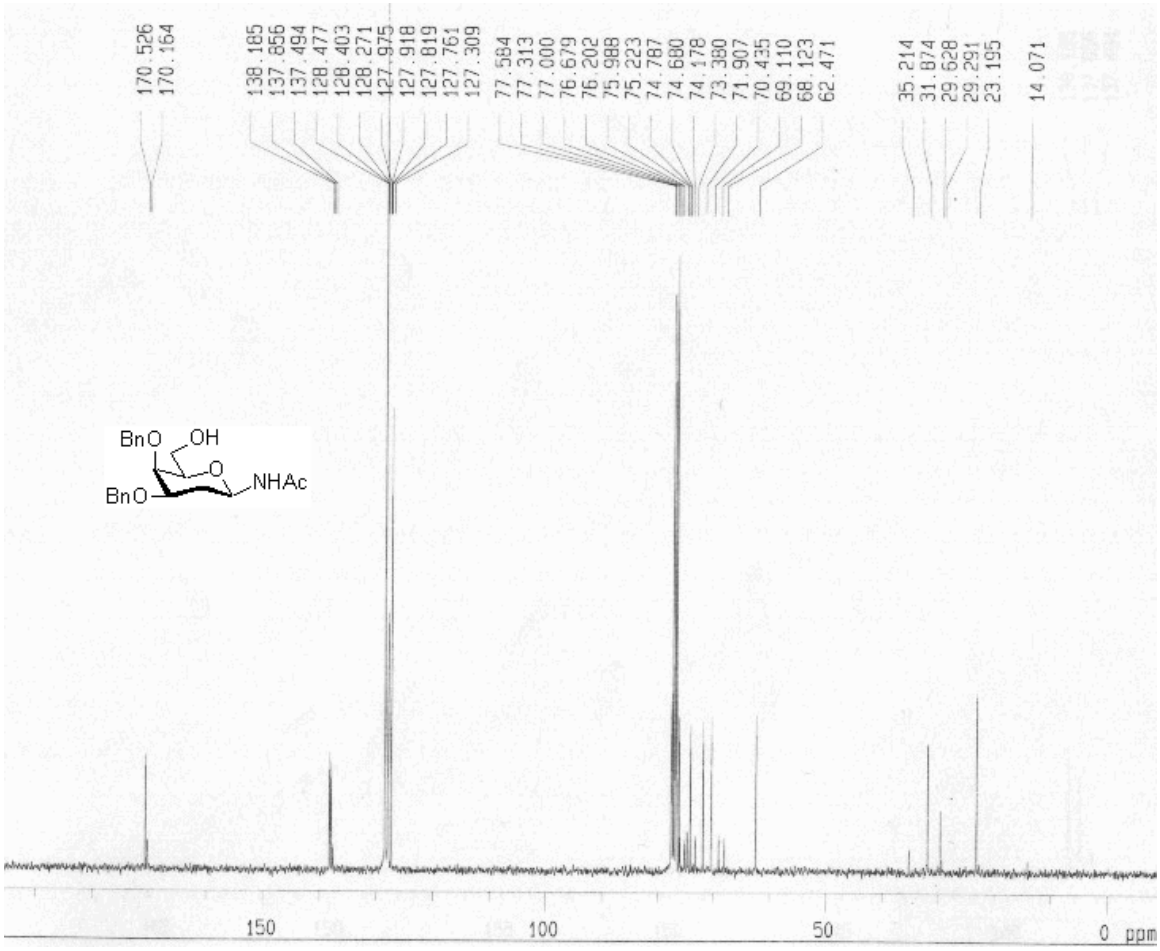
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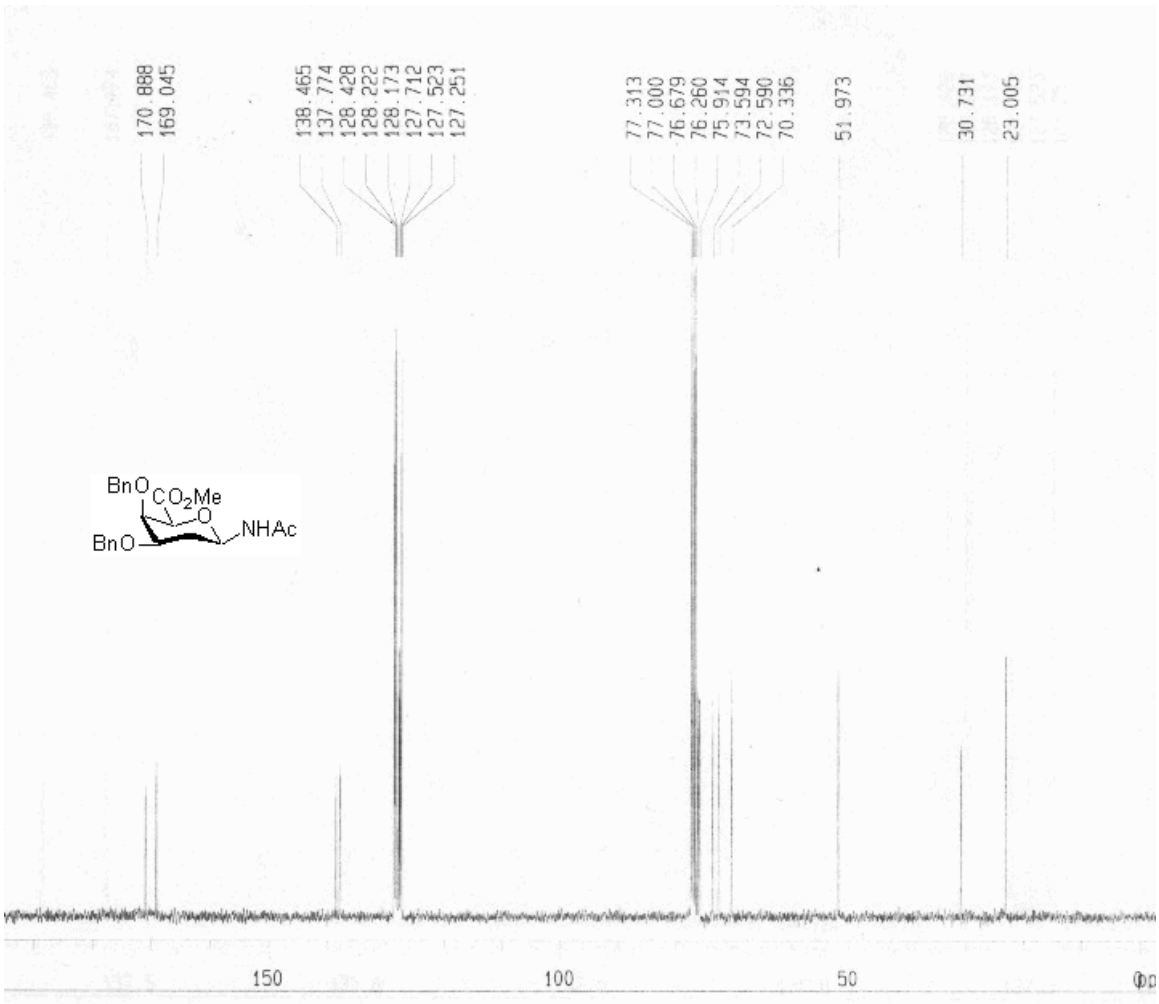
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