SUPPORTING INFORMATION

Protecting Group-based Colorimetric Monitoring of Fluorous-phase and Solid-phase Synthesis of Oligoglucosamines

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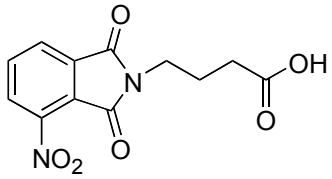
General Materials and Methods.

Reaction solvents were distilled from calcium hydride for dichloromethane. Aminomethylated SynPhase Lanterns were purchased from Mimotopes (www.mimotopes.com). Prior to use, the lanterns were converted from the TFA salt to the free amine form. The lanterns were washed with 5% triethylamine in 50% DMF/DCM (2 x 10 min), then 50% DMF/DCM (5 min), DCM (5 min), 50% DMF/DCM (5 min) and DCM (5 min). Amberlyst 15 ion-exchange resin was washed repeatedly with methanol before use. All other commercial reagents and solvents were used as received without further purification. The reactions were monitored and the R_f values determined using analytical thin layer chromatography (TLC) with 0.25 mm EM Science silica gel

plates (60F-254). The developed TLC plates were visualized by immersion in *p*-anisaldehyde solution followed by heating on a hot plate. Flash chromatography was performed with Selecto Scientific silica gel, 32-63 μm particle size. Fluorous phase chromatography was performed using fluorous solid-phase extraction cartridges containing silica gel bonded with perfluorooctylethylsilyl chains (Fluorous Technologies Inc.; Pittsburgh, PA). All moisture-sensitive reactions were performed in flame- or oven-dried glassware under a nitrogen atmosphere. All reactions were stirred magnetically at ambient temperature unless otherwise indicated. Bath temperatures were used to record the reaction temperature in all cases run without microwave irradiation. Microwave heating was carried out with a CEM-Discover continuous wave microwave. ^{1}H NMR and ^{13}C NMR were obtained with a Bruker DRX400 at 400 MHz and 100 MHz, respectively. ^{1}H NMR spectra were reported in parts per million (δ) relative to $CDCl_3$ (7.27 ppm), $(CD_3)_2SO$ (2.50 ppm) as an internal reference. ^{13}C NMR spectra were reported in parts per million (δ) relative to $CDCl_3$ (77.23 ppm) or CD_3OD (49.15 ppm), $(CD_3)_2SO$ (39.52 ppm).

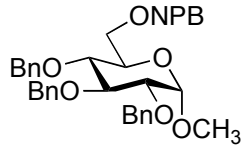
Synthesis and installation of colorimetric protecting group.



4-(*O*-Nitrophthalimido)butyric acid (NPB, 2).

3-Nitrophthalic anhydride **3** (0.65 g, 3.4 mmol) and 4-aminobutyric acid (0.35 g, 3.4 mmol) were placed in the microwave in a 10-mL reaction tube. The microwave was programmed to reach 185 °C over the course of 10 min; the reaction tube was then subjected to microwave irradiation for an additional 1 min at 185 °C. After cooling, hot methanol (10 mL) was added to dissolve the product and the solution was filtered. The filtrate was concentrated under reduced pressure. The product **2** (0.87 g, 3.1 mmol, 92%) was obtained as a white solid by crystallization with methanol. R_f 0.34 (methanol/ethyl acetate/hexane, 1/1/1 v/v/v); ^{1}H NMR (400 MHz, DMSO) δ (ppm) 8.22 (d, 1H, J = 8.0 Hz), 8.11 (d, 1H, J = 7.6 Hz), 8.00 (t, 1H, J = 8.0 Hz), 3.57 (t, 2H, J = 6.4 Hz), 2.25 (t,

2H, *J* = 7.6 Hz), 1.78 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ (ppm) 174.0, 166.2 163.5, 144.3, 136.0, 133.7, 128.1, 126.7, 123.2, 38.9, 30.9, 23.1; MS (ESI) *m/z* = found: 279.99 $[M+H]^+$.

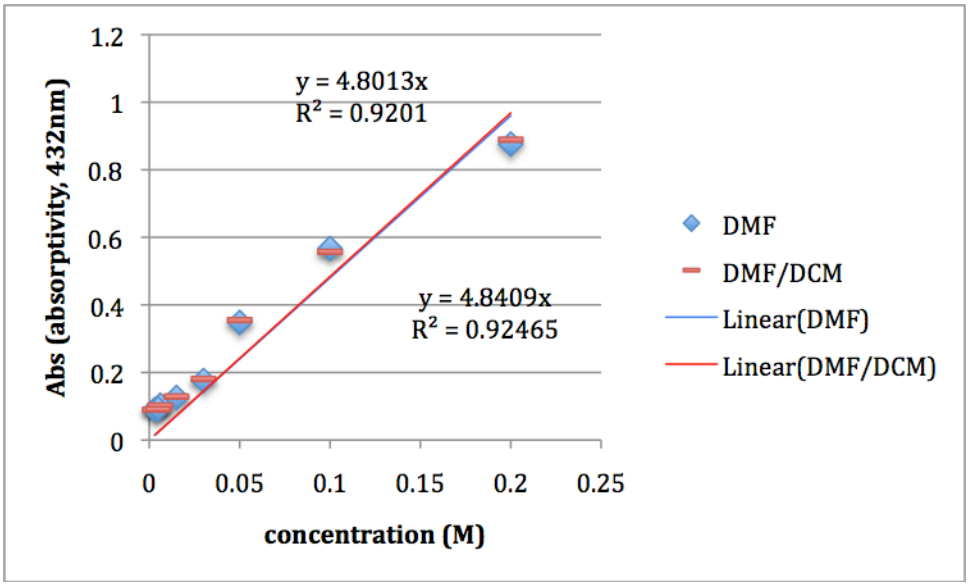


Methyl 2, 3, 4-tri-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric)-α-D-glucopyranoside (4).

Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[3] (0.38 g, 0.8 mmol), 4'-(*O*-nitrophthalimido)butyric acid **2** (0.27 g, 1.0 mmol) and DCC (0.20g, 1.0 mmol) were dissolved in CH_2Cl_2 (5 mL) in a round bottom flask and cooled to 0 °C; 4-dimethylaminopyridine (DMAP, 0.12 g, 1.0 mmol)/pyridine (0.2 mL) was then added and the reaction mixture was stirred at 0 °C. After 1 h, TLC indicated completion of the reaction. The reaction mixture was diluted with ethyl acetate (40 mL) and was quenched with saturated aqueous $NaHCO_3$, (10 mL), extracted with ethyl acetate (3 x 40 mL), and dried over magnesium sulfate. The organic layer was concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography with 15% EtOAc/hexanes elutions to provide compound **4** (0.58 g, 0.8 mmol, 98% yield) as a white solid. R_f 0.46 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.05 (d, 1H, *J* = 3.6 Hz), 8.02 (d, 1H, *J* = 2.4 Hz), 7.82 (t, 1 H, *J* = 7.6 Hz), 7.37-7.24 (m, 15H), 5.01 (d, 1H, *J* = 10.8 Hz), 4.87 (d, *J* = 11.2 Hz, 1H), 4.80 (m, 2H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 3.6 Hz, 1H), 4.56 (d, *J* = 10.8 Hz, 1H), 4.25 (d, *J* = 3.2 Hz, 1H), 4.00 (t, *J* = 9.2 Hz, 1H), 3.73 (m, 3H), 3.52 (dd, *J* = 9.6, 3.2Hz, 1H), 3.45 (t, *J* = 10.0 Hz, 1H), 3.36 (s, 3H), 2.35 (m, 2H), 2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm); 172.2, 165.8, 162.9, 138.2, 138.1, 138.0, 135.4, 134.1, 128.5, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.0, 123.8, 98.0, 82.1, 82.0, 80.4, 79.9, 77.5, 75.8, 75.8, 75.1, 75.0, 73.4, 70.7, 63.2, 61.8, 55.3, 55.3, 38.0, 31.4, 23.6: MS (ESI) *m/z* = 747.2530 $[M+Na]^+$.

Procedure for determining the extinction coefficient for nitrophthalhydrazide.

Eight different concentrations of nitrophthalhydrazide/DMF, nitrophthalhydrazide/ DMF:DCM (5:3) were prepared (3.017 x 10^{-3} M ~ 0.2 M). The molar absorptivity of each sample was obtained at 432 nm and plotted to give an extinction coefficient of 4.8013 $M^{-1}cm^{-1}$ and 4.8409 $M^{-1}cm^{-1}$ each.

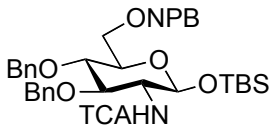


Procedure for cleavage and monitoring of protecting group

Hydrazine acetate (22.6 mg, 0.24 mmol) was added to a solution of the protected NPB compound **4** (0.15 g, 0.20 mmol) in DMF (2.0 mL). The reaction mixture was stirred at 50 °C. After 5 min, TLC indicated completion of the reaction. A solution of the crude product in DMF was checked by UV-Vis monitoring to show a quantitative yield of the deprotected NPB based on an extinction coefficient (ε = 4.8 $M^{-1}cm^{-1}$) at λ = 432 nm. The crude product was combined and diluted with CH_2Cl_2 (30 mL). The mixture was washed with saturated aqueous $NaHCO_3$, (10 mL), extracted with CH_2Cl_2 (3 x 40 mL), and dried over $MgSO_4$. The organic layer was concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 15% EtOAc/hexanes to provide by-product butyrolactam (**6**) followed by desired product methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**5**). The product was obtained as a white

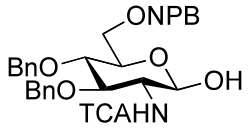
solid (95.2 mg, 0.20 mmol, 99% isolated yield). R_f 0.48 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR and ^{13}C NMR spectra matched reported data.[3]

Synthesis of NPB-protected glucosamine building block.



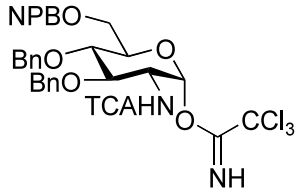
***tert*-Butyldimethylsilyl 3,4-di-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric)-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside.**

Alcohol **7**[1] (0.96 g, 1.6 mmol), 4'-(*O*-nitrophthalimido)butyric acid **2** (0.52 g, 1.9 mmol) and DCC (0.39g, 1.9 mmol) were dissolved in CH_2Cl_2 (5 mL) in a round bottom flask and cooled to 0 °C; 4-dimethylaminopyridine (DMAP, 0.23 g, 1.9 mmol)/pyridine (0.5 mL) was then added and the reaction mixture was stirred at 0 °C. After 1 h, TLC indicated completion of the reaction. The reaction mixture was diluted with ethyl acetate (50 mL) and was quenched with saturated aqueous $NaHCO_3$, (5 mL), extracted with ethyl acetate (3 x 20 mL), and dried over magnesium sulfate. The organic layer was concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 15% EtOAc/hexanes to provide *tert*-butyldimethylsilyl 3,4-di-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric)-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (1.35 g, 1.54 mmol, 99% yield) as a white solid. R_f 0.78 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.60 (s, 1H), 8.51 (d, 1H, J = 8.0 Hz), 8.11 (d, 1H, J = 5.2 Hz), 7.93 (d, 1H, J = 8.4 Hz), 7.77 (d, 1H, J = 8.4 Hz), 7.28-7.20 (m, 10H), 5.02 (d, 1H, J = 6.8Hz), 4.76 (d, 1H, J = 10.8 Hz), 4.73 (s, 2H), 4.52 (d, 1H, J = 11.2 Hz), 4.35 (d, 1H, J = 11.6 Hz), 4.08 (m, 2H), 3.75 (t, 2H, J = 6.4 Hz), 3.59 (m, 2H), 3.49 (t, 1H, J = 8.4 Hz), 3.13 (m, 1H), 2.34 (m, 2H), 1.98 (m, 2H), 0.81 (s, 9H), 0.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.1, 166.2, 165.9, 161.9, 151.7, 149.1, 137.9, 137.6, 136.4, 133.4, 129.3, 128.6, 128.5 (2), 128.2, 128.0 (2), 127.9, 124.6, 118.7,106.6, 94.6, 92.8, 80.2, 78.4, 77.4, 75.0, 74.7, 73.0, 63.3, 60.27, 55.8, 37.9, 31.4, 25.7, 23.6, -4.2, -5.1; MS (ESI) m/z = 900 $[M+Na]^+$.



3,4-Di-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric)-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (8).

To a solution of *tert*-butyldimethylsilyl 3,4-di-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (0.92 g, 1.0 mmol) in THF (10 mL) was added dropwise a 1 M solution of tetrabutylammonium fluoride (3.0 mL, 3.0 mmol)/AcOH (0.6 mL) in THF at 0 °C. The cooling bath was removed and the reaction mixture stirred for 1 h at room temperature and then diluted with ethyl acetate (40 mL). The mixture was washed with saturated aqueous $NaHCO_3$ (2 x 20 mL), water (3 x 20 mL), and brine (30 mL) and then the organic layer was dried over magnesium sulfate. The organic layer was concentrated under reduced pressure to give a crude product that was purified by silica gel column chromatography to obtain compound **8** (0.74 g, 1.0 mmol, 93%) as an oil. R_f 0.46 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.58 (d, 1H, J = 2.0 Hz), 8.50 (dd, 1H, J = 8.0, 1.6 Hz), 7.96 (d, 1 H, J = 8.0 Hz), 7.32-7.24 (m, 10H), 7.0 (d, 1H, J = 9.2 Hz), 5.24 (d, 1H, J = 3.6 Hz), 4.77 (m, 3H), 4.57 (d, 1H, J = 10.8 Hz), 4.37 (dd, 1H, J = 11.6, 1.6 Hz), 4.18 (m, 2H), 4.11 (m, 1H), 3.91 (t, 1H, J = 9.2), 3.77 (t, 2H, J = 6.8 Hz), 3.58 (t, 1H, J = 9.2 Hz), 2.38 (m, 2H), 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 166.5, 166.2, 161.9, 151.8, 137.7, 137.6, 136.4, 133.3, 129.5, 128.6, 128.1, 128.0, 127.9, 124.7, 118.8, 92.6, 91.3, 80.1, 78.0, 75.6, 75.1, 69.2, 63.0, 55.1, 37.9, 31.3, 23.5; MS (ESI) m/z = 786 $[M+Na]^+$.

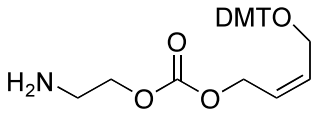


3,4-Di-*O*-benzyl-6-(4'-(*O*-nitrophthalimido)butyric)-2-deoxy-2-trichloroacylamino-α-D-glucopyranoside trichloroacetimidate (9).

To a solution of alcohol **8** (0.68 g, 0.9 mmol) in dichloromethane (10 mL) were added powdered 4 Å molecular sieves (100 mg) and trichloroacetonitrile (0.1 mL, 1.2 mmol).

The reaction was stirred for 30 min and Cs_2CO_3 (0.29 g, 0.9 mmol) was added. The reaction mixture was further stirred for 45 min and filtered over Celite. The eluent was concentrated and the crude product was purified by flash column chromatography on silica gel using 28% EtOAc/hexane as eluent to provide trichloroacetimidate **9** as a white solid (0.74 g, 0.8 mmol, 92%). R_f 0.67 (ethyl acetate/hexane, 1/1 v/v). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.78 (s, 1H), 8.63 (d, 1H, *J* = 2.0 Hz), 8.55 (dd, 1H, J = 8.0, *J* = 2.0 Hz), 8.01 (d, 1H, *J* = 8.0 Hz), 7.32-7.29 (m, 10H), 6.57 (d, 1H, *J* = 8.8 Hz), 6.37 (d, 1H, *J* = 3.6 Hz), 4.91 (dd, 2H, *J* = 10.8, 2.0 Hz), 4.83 (d, 1H, *J* = 11.4 Hz), 4.66 (d, 1H, *J* = 10.4 Hz), 4.45 (m, 1H), 4.38 (dd, 1H, *J* = 12.4, 2.0 Hz), 4.30 (dd, 1H, *J* = 12.0, 3.6 Hz), 4.04 (m, 1H), 3.98 (m, 1H), 3.80 (m, 3H), 2.39 (m, 2H), 2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.0, 166.3, 166.0, 161.9, 160.0, 151.8, 137.2, 136.5, 129.4, 128.9, 128.7, 128.5, 128.4, 128.3, 124.8, 118.8, 94.7, 92.1, 90.7, 78.5, 77.2, 75.4, 75.3, 72.1, 62.1, 54.2, 37.9, 31.3, 23.6; MS (ESI) *m/z* = 929 $[M+Na]^+$.

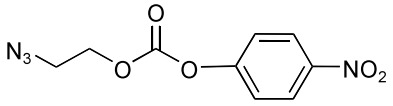
Synthesis and Installation of Linker for Solid Phase Chemistry.



Carbonic acid 2-amino-ethyl ester 4-[bis-(4-methoxy-pheyl)-phenylmethoxy]-but-2-enyl ester (12).

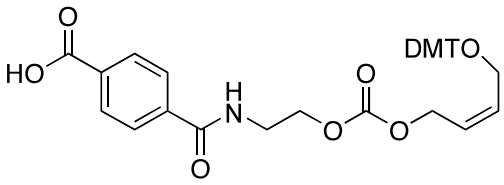
To a solution of the dimethoxytrityl-2-butenol **11**[2] (0.3 g, 0.8 mmol) in CH_2Cl_2 (6 mL), DMAP (0.1 g, 0.9 mmol), pyridine (1 mL), and 2-azidoethyl-4-nitrophenyl carbonate **13** (0.23 g, 0.9 mmol) were added at ambient temperature. The mixture was stirred at ambient temperature for 8 h. The mixture was diluted with ethyl acetate (30 mL), washed with saturated aqueous $NaHCO_3$ (3 x 10 mL), and washed with water (2 x 10 mL). The organic layer was concentrated under reduced pressure. To the residue, a solution of 2-azidoethyl-dimethoxytrityl-2-butene carbonate (0.35 g, 0.7 mmol) in MeOH (5 mL) was stirred with Et_3N (0.5 mL) and 1,3-propanedithiol (0.35 mL) at ambient temperature. The mixture was stirred at room temperature for 8 h. The mixture was diluted with ethyl acetate (30 mL), washed with saturated aqueous $NaHCO_3$ (3 x 10 mL), and washed with water (2 x 10 mL). The organic layer was concentrated under reduced pressure. The product was isolated by silica gel column chromatography (ethyl

acetate/hexane, 2/3, v/v) to afford 2-amino-ethyl-(4-oxydimethoxytrityl)-2-butenyl carbonate **12** as a solid (0.34 g, 0.66 mmol, 96 %). R_f 0.69 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.46 (d, 2H, *J* = 8.0 Hz), 7.35 (d, 4H, *J* = 8.8 Hz), 7.29 (t, 2H, *J* = 7.6 Hz), 7.22 (dd, 1H, *J* = 14.4, 7.2 Hz), 6.83 (d, 4H, *J* = 8.8 Hz), 5.83 (m, 1H), 5.62 (m, 1H), 5.38 (t, 1H, *J* = 6.4 Hz), 4.49 (d, 2H, *J* = 8.4 Hz), 3.77 (s, 6H), 3.72 (d, 2H, *J* = 8.0 Hz), 3.62 (t, 2H, *J* = 6.0 Hz), 3.25 (dd, 2H, *J* = 13.6, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.5, 145.2, 136.2, 131.2, 130.1, 128.9, 128.2, 127.0, 126.1, 113.2, 86.7, 62.2, 61.4, 60.7, 55.4, 43.6; MS (ESI) *m/z* = 500 $[M+Na]^+$.



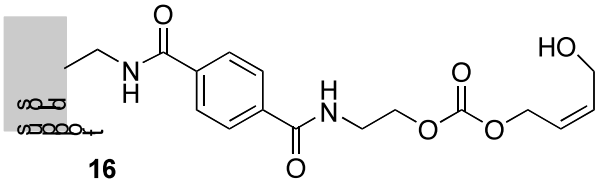
2-azidoethyl-4-nitrophenyl carbonate (13).

To a solution of the 2-azidoethanol (2.3 g, 26 mmol) in pyridine (40 mL), 4-nitrophenyl chloroformate (6.3 g, 32 mmol) was added at room temperature. The mixture was stirred at room temperature for 8h. The mixture was diluted with ethyl acetate (60 mL), washed with saturated aqueous $NaHCO_3$ (3 x 30 mL), and washed with water (2 x 30 mL). The organic layer was concentrated under reduced pressure. The product was filterated by silica gel column chromatography (ethyl acetate/hexane, 1/1, v/v) to afford 2-azidoethyl-4-nitrophenyl carbonate **13** as a solid (6.7 g, 26.4 mmol, 100%). R_f 0.76 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.31 (d, 1H, *J* = 9.2 Hz), 8.25 (d, 2H, *J* = 6.8 Hz), 7.47 (d, 1H, *J* = 9.2 Hz), 7.36 (d, 2H, *J* = 6.8 Hz), 4.42 (t, 2H, *J* = 5.2 Hz), 3.61 (t, 2H, *J* = 5.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.3, 152.3, 145.6, 125.6, 125.4, 121.8, 121.7, 67.4, 49.5; MS (ESI) *m/z* = 275 $[M+Na]^+$.



***N*-(2-{4-[Bis-(4-methoxy-phenyl)-phenyl-methoxy]-but-2-enyloxycarbonyloxy}-ethyl)-terephthalamic acid (14).**

To a solution of the 2-aminoethyl-(4-oxydimethoxytrityl)-2-butenyl carbonate **12** (98.0 mg, 0.21 mmol) and terephthalic acid (320.3 mg, 19.3 mmol) in DMF (6 mL), DMAP (37.6 mg, 0.31 mmol) and pyridine (0.5 mL) were added at ambient temperature. The mixture was stirred at ambient temperature for 1 h. The mixture was diluted with ethyl acetate (30 mL), washed with saturated aqueous $NaHCO_3$ (3 x 10 mL), and washed with water (2 x 10 mL). The organic layer was concentrated under reduced pressure. The product was filterated by silica gel column chromatography (ethyl acetate/hexane, 1/1, v/v) to afford **14** as a solid (85.7 mg, 0.14 mmol, 64%). R_f 0.23 (ethyl acetate/hexane, 1/1 v/v). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.79 (br. s, 1H), 8.14-8.06 (m, 4H), 7.40 (d, 2H, J = 6.8 Hz), 7.23 (m, 6H), 7.17 (d, 1H, J = 12.0 Hz), 6.83 (d, 4H, J = 8.8 Hz), 5.80 (m, 1H), 5.62 (m, 1H), 5.58 (m, 1H), 5.11 (m, 0.5 H), 4.58 (m, 0.5H), 4.46 (d, 1H, J = 8.4 Hz), 4.37 (m, 2H), 3.75 (s, 6H), 3.67 (d, 2H, J = 6.0 Hz), 3.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.5, 156.4, 148.3, 144.9, 137.4, 136.2, 131.1, 130.2, 130.0, 129.9, 129.6, 128.1, 127.9, 126.8, 126.6, 125.7, 113.2, 86.5, 61.3, 60.5, 60.2, 55.4, 43.6; MS (ESI) m/z = 648 $[M+Na]^+$.



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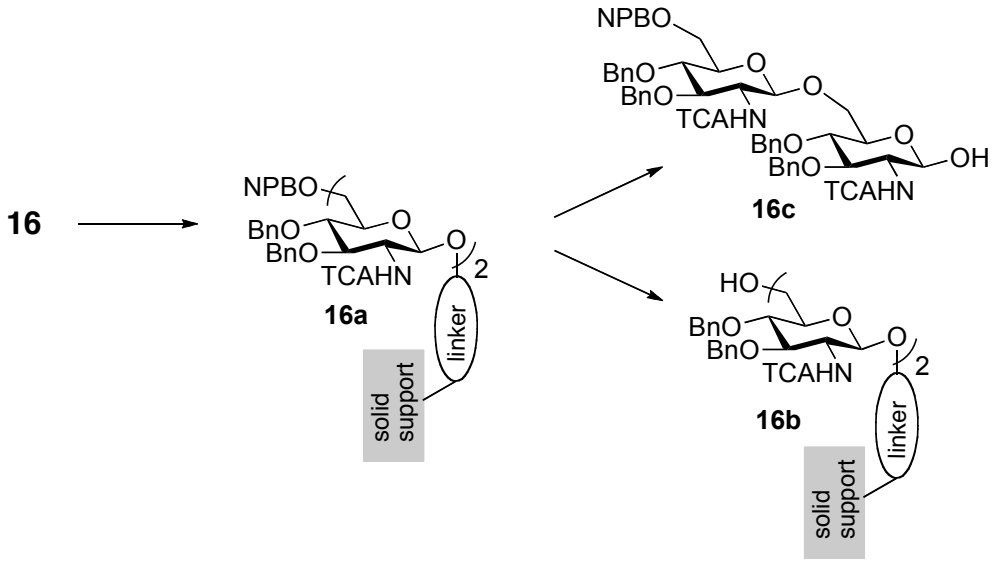
The SynPhase aminomethylated lanterns **15** (45 μmol, 15 μmol/lantern) were loaded into a reaction vial. The lanterns in 3 mL of DCM/DMF (1/1 v/v) were reacted with compound **14** (0.14 g, 225 μmol) using DCC (0.056 g, 0.27 mmol). The mixture was shaken for 30 min at room temperature. The lanterns were washed with DMF (3 x 5 mL) and DCM (3 x 5 mL). Then 5% TFA (0.2 mL) was added to a solution of lanterns in DMF (3 mL). The mixture was shaken for 5 min to cleave the DMT. The rinse solution was collected in a vial. The lanterns were washed with DMF (5 x 3 mL) and the rinse

solution was collected in the same vial. The collected rinse solutions were then analyzed by UV to determine the concentration of DMT present to show a 92% overall yield. The procedure for the solid-phase reaction was repeated and the compound **16** was obtained in 90%-95% overall yield.

Procedure for the Glycosylation Cycles/the cleavage of linker on Solid Phase.



The monosaccharide cycles were carried out with the following procedure. The glycosyl donor **9** (220 μmol) was added to lantern **16** (44 μmol) in CH_2Cl_2 (3 mL) and TMSOTf (0.5 equiv, 0.5 mL, 0.1 M TMSOTf in CH_2Cl_2) at room temperature. The lanterns were shaken for 15 min at room temperature. Triethylamine (0.3 mL) was added to the mixture of lanterns to quench the reaction. The lanterns were washed as listed above and held under high vacuum for 5 h to completely remove solvents for a mass reading; the cycle was then repeated.

The procedure for the removal of NPB group was as follows. After the lanterns were washed 2 times with CH_2Cl_2 and DMF, the lanterns were stirred in DMF (5 mL) with hydrazine acetate (0.011 g) for 5 min at 50 °C before rinsing with CH_2Cl_2 (3 mL) for yield evaluation using UV-Vis. The procedure for the disaccharide cycles was repeated the same as for the monosaccharide cycle (Table 1). The procedure for the glycosylation reaction was repeated and compound **16b** was obtained in ~95% overall yield.

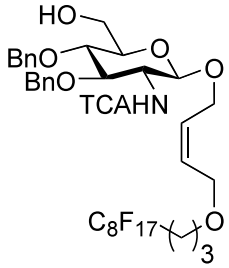
The procedure for the cleavage of linker on solid-phase was as follows. $PdCl_2$ (9.4 mg, 53 μmol) was added to the lantern **16a** in MeOH (3 mL). The mixture was stirred at room temperature for 8 h. The mixture was filtered with MeOH (3 x 5 mL) and CH_2Cl_2 (3 x 5 mL). The solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel to obtain compound **16c** (45.6 mg, 36.5 μmol, 83%) from the lantern **16** (44 μmol). R_f 0.28 (ethyl acetate/hexane, 1/1 v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.62 (d, 1H, *J* = 2.4 Hz), 8.55 (dd, 1H, *J* = 8.8, 2.8 Hz), 7.99 (d, 1 H, *J* = 10.8 Hz), 7.35-7.25 (m, 21H), 6.85 (d, 1H, *J* = 12.4 Hz), 4.93 (d, 1H, *J* = 4.8 Hz), 4.77 (m, 6H), 4.55 (m, 3H), 4.27 (m, 4H), 3.89 (m, 7H), 3.65 (m, 2H), 2.42 (m, 2H), 2.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm); 172.3, 166.4, 166.1, 161.8, 152.0, 137.8, 137.7, 136.6, 133.5, 129.5, 128.9, 128.8, 128.8, 128.7, 128.7, 128.3, 128.1, 128.1, 124.8, 119.0, 96.3, 92.7, 80.7, 77.8, 77.5, 76.9, 75.8, 75.4, 70.1, 69.9, 62.9, 62.8, 54.9, 54.9, 38.1, 31.5, 23.8; MS (ESI) *m/z* = found: 1271.1564 $[M+H]^+$.

Table 1. Summary of the glycosylation/deprotection cycles

	Function	Reagent	Time(min)	Yield based on extinction coefficient**
Monosaccharide cycles				
1	Couple (5 equiv. **9**)	TMSOTf	15	
2	Wash	20% MeOH/CH_2Cl_2	~15	
3	Wash	MeOH	~15	
4	Wash	20% MeOH/THF	~15	
5	Wash	THF	~15	
6	Wash	CH_2Cl_2 (2 times)		
7	Repeated from step 1 to step 6			
8	Deprotection	Hydrazine acetate/DMF	5	98%
Disaccharide cycles				
9	Repeated from step 1 to step 8			96%

** Extinction coefficient (ε = 4.8 $M^{-1}cm^{-1}$ at λ = 432 nm)

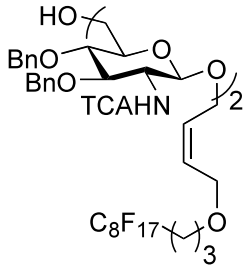
Procedures for Fluorous-phase Synthesis.



1H,1H,2H,2H,3H,3H-(Perfluorooctyl)propanyloxybutenyl-3,4-di-*O*-benzyl-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (18).

To a solution of **9** (0.53 g, 0.6 mmol) and 4-[3-(perfluorooctyl)propyloxy]-*cis*-2-butenyl alcohol **17**[4] (0.26 g, 0.5 mmol) in dichloromethane (5 mL) was added powdered 4 Å molecular sieves (10 mg); the mixture was cooled down to -15 ^{o}C. TMSOTf (38 μL, 0.18 mmol) was added and the reaction mixture was stirred at –15 °C for 30 min. The reaction was quenched with triethylamine (0.1 mL) and concentrated under reduced pressure. The crude product was purified by solid-phase extraction by using a fluorous solid-phase extraction (FSPE) cartridge. Non-fluorous compounds were eluted with 80% MeOH/water and the desired compound (R_f: 0.49 (ethyl acetate/hexane/2/3) was eluted by 100% MeOH. The solvent was removed under reduced pressure and the residue was immediately carried on to remove the NPB group. Hydrazine acetate (1.2 equiv.) was added to a solution of the protected NPB compound in DMF (5.0 mL). The reaction mixture was stirred at 50 °C. After 5 min, TLC indicated completion of the reaction and the solution was orange. The crude product was purified by solid-phase extraction by using a fluorous solid-phase extraction (FSPE) cartridge. Non-fluorous compounds were eluted with 80% MeOH/water and the desired product was eluted by 100% MeOH to provide the free alcohol **18** as a colorless oil (0.47 g, 0.46 mmol, 97%). The washes could also be collected to measure the yield using UV-Vis. R_f: 0.48 (ethyl acetate/hexane/2/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.32-7.28 (m, 10H), 7.12 (d, 1H, *J* = 6.8 Hz), 5.68 (m, 2H), 4.92 (d, 1H, *J* = 8.0 Hz), 4.82 (d, 1H, *J* = 10.8 Hz), 4.71 (d, 1H, *J* = 11.2 Hz), 4.67 (d, 1H, *J* = 10.8 Hz), 4.35 (dd, 1H, *J* = 12.8, 5.2 Hz), 4.18 (m, 2H), 3.99 (d, 2H, *J* = 4.8 Hz), 3.88 (dd, 1H, *J* = 10.4, 2.8 Hz), 3.75 (dd, 1H, *J* = 12.0, 3.6), 3.65 (t, 1H, *J* = 9.2 Hz), 3.56 (m, 1H), 3.45 (m, 3H), 2.15 (m, 2H), 1.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.1, 137.8, 137.7, 130.3, 128.6, 128.1, 128.0, 127.9, 98.6, 92.5, 79.7,

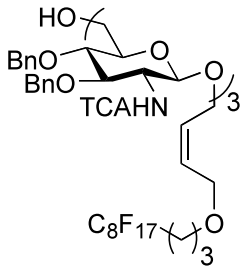
78.2, 75.5, 75.2, 74.9, 68.9, 66.5, 65.1, 61.7, 58.4, 28.2, 28.0, 27.8, 20.8; MS (ESI) *m/z* = calcd for $C_{37}H_{35}Cl_3F_{17}NO_7Na$: 1056.1105; found: 1056.43 $[M+Na]^+$.



1H,1H,2H,2H,3H,3H-(Perfluorooctyl)propanyloxybutenyl(3,4-di-*O*-benzyl-deoxy-2-trichloroacetylamino-β-D-glucopyranosyl)-(1→6)-3,4-di-*O*-benzyl-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (19).

To a solution of **9** (0.43 g, 0.49 mmol) and a solution of alcohol **18** (0.33 g, 0.32 mmol) in dichloromethane (5 mL) was added powdered 4 Å molecular sieves (10 mg); the mixture was cooled down to -15 ^oC. TMSOTf (18 μL) was added and the reaction mixture was stirred at –15 °C for 30 min. The reaction was quenched with triethylamine (0.1 mL) and concentrated under reduced pressure. The crude product was purified by solid-phase extraction by using a fluorous solid-phase extraction (FSPE) cartridge. Non-fluorous compounds were eluted with 80% MeOH/water and the desired compound (R_f: 0.46 (ethyl acetate/hexane/2/3) was eluted by 100% MeOH. The solvent was removed under reduced pressure and the residue was carried on directly to remove the NPB group. Hydrazine acetate (1.2 equiv.) was added to a solution of the disaccharide in DMF (5.0 mL). The reaction mixture was stirred at 50 °C. After 5 min, TLC indicated completion of the reaction. The crude product was purified by solid-phase extraction by using a fluorous solid-phase extraction (FSPE) cartridge. Non-fluorous compounds were eluted with 80% MeOH/water and the desired product was eluted by 100% MeOH to provide free alcohol **19** as a colorless oil (0.46 g, 0.30 mmol, 95%). The washes could also be collected to measure the yield using UV-Vis. R_f: 0.42 (ethyl acetate/hexane/2/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34-7.26 (m, 20H), 7.13 (d, 1H, *J* = 8.0 Hz), 7.02 (d, 1H, *J* = 7.6 Hz), 5.66 (m, 2H), 4.88 (t, 2H, *J* = 7.6 Hz), 4.77 (m, 4H), 4.68 (t, 1H, *J* = 8.0 Hz), 4.66 (d, 1H, *J* = 8.0 Hz), 4.61 (t, 2H, *J* = 9.2 Hz), 4.33 (dd, 1H, *J* = 12.8, 5.6 Hz), 4.17 (dd, 1H, *J* = 12.8, 6.8 Hz), 4.12 (m, 2H), 4.05 (m, 3H), 3.83 (dd, 1H, *J* = 11.6, 4.0 Hz), 3.76 (m, 2H), 3.60 (m, 4H0, 3.50 (m, 2H), 3.44 (m, 2H), 2.14 (m, 2H), 1.82 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.9, 161.8, 137.7 (3), 137.5, 130.5, 128.6 (3), 128.5, 128.2, 128.1, 128.0 (5), 99.4, 98.1, 92.5, 92.4, 79.2, 79.0, 78.0, 78.9, 77.3, 75.5, 75.0, 74.9, 74.6 (2), 68.8, 68.0, 66.5, 65.0, 62.0, 57.9, 57.6, 28.3, 28.0, 27.9, 20.9 (2); MS (ESI) *m/z* = calcd for $C_{39}H_{37}Cl_6F_{17}N_2O_{12}Na$: 1541.1669; found: 1541.99 $[M+Na]^+$.



1H,1H,2H,2H,3H,3H-(Perfluorooctyl)propanyloxybutenyl(3,4-di-*O*-benzyl-deoxy-2-trichloroacetylamino-β-D-glucopyranosyl)-(1→6)-3,4-di-*O*-benzyl-deoxy-2-trichloroacetylamino-β-D-glucopyranosyl)-(1→6)-3,4-di-*O*-benzyl-2-deoxy-2-trichloroacetylamino-β-D-glucopyranoside (20).

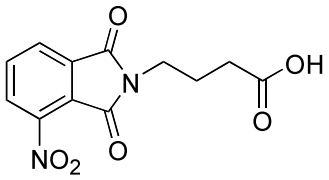
The reaction was repeated as for the monomeric- and dimeric glucosamines reported above to provide free alcohol **20** (0.46 g, 0.21 mmol, 91%). R_f: 0.36 (ethyl acetate/hexane/2/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34-7.26 (m, 30H), 7.10 (m, 1H), 7.10 (d, 1H, *J* = 8.0 Hz), 6.90 (d, 1H, *J* = 9.2 Hz), 4.93 (d, 1H, *J* = 8.0 Hz), 4.84-4.68 (m, 10H), 4.56 (m, 3H), 4.38 (m, 2H), 4.21 (m, 5H), 4.09 (m, 3H), 4.00 (d, 2H, *J* = 7.6 Hz), 3.89 (m, 3H), 3.76 (m, 3H), 3.62 (m, 3H), 3.47 (m, 4H), 2.16 (m, 2H), 1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.0,161.9, 161.8, 137.7 (3), 137.6 (2), 137.5, 130.5, 128.6 (3), 128.5, 128.2, 128.1, 128.0 (5), 98.5, 92.5 (2), 92.4, 79.8, 79.2, 79.0, 78.2, 78.9, 77.3, 75.6, 75.2, 75.1, 74.9, 74.6, 69.4, 69.0 (2), 66.5 (2), 65.1, 62.7, 61.8, 58.8, 58.5, 28.3, 28.0, 27.9, 20.9 (2); MS (ESI) *m/z* = calcd for $C_{81}H_{79}Cl_9F_{17}N_3O_{17}Na$: 2026.2232; found: 2026.08 $[M+Na]^+$.

References

(1) Melean, L. G.; Love, K. R.; Seeberger, P. H. *Carbohydr. Res.* **2002**, *337*, 1893.
(2) Ruhela, D.: Vishwakarma, R. A. *J. Org. Chem*. **2003**, *68*, 4446-4456.
(3) Shie, C.–R.; Tzeng, Z.–H.; Kulkarni, S. S.; Uang, B.–J.; Hsu, C.–Y.; Hung, S.–C. *Angew. Chem Int. Ed*. **2005**, *44*, 1665-1668.

(4) Mamidyala, S. K.; Ko, K.–S.; Jaipuri, F. A.; Park, G.; Pohl, N. L. *J. Fluorine Chem*. **2006**, *127*, 571.

Copies of ^{1}H NMR/^{13}C NMR spectra of compounds.



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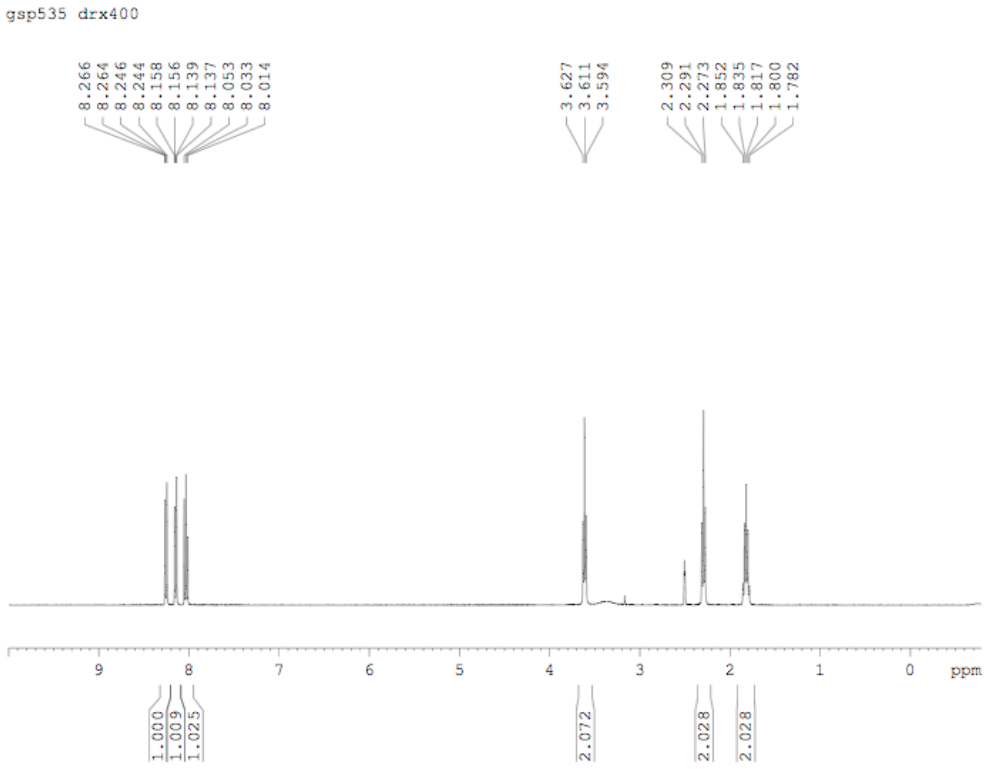

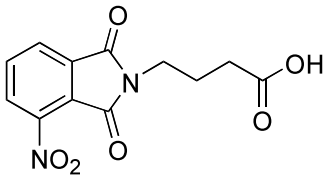

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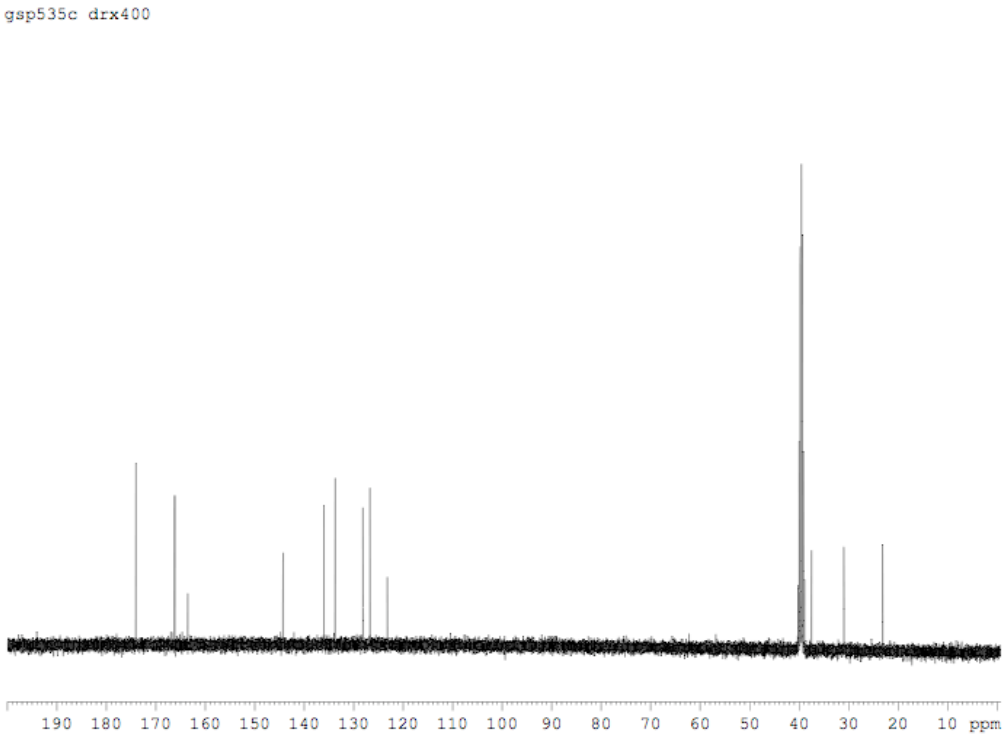

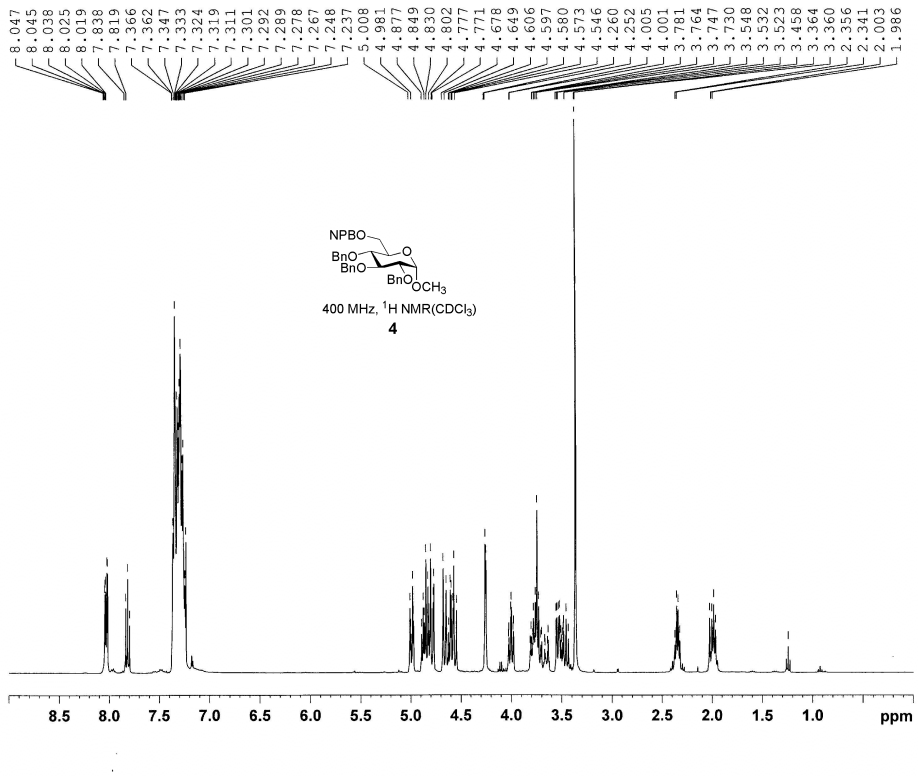
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BnO
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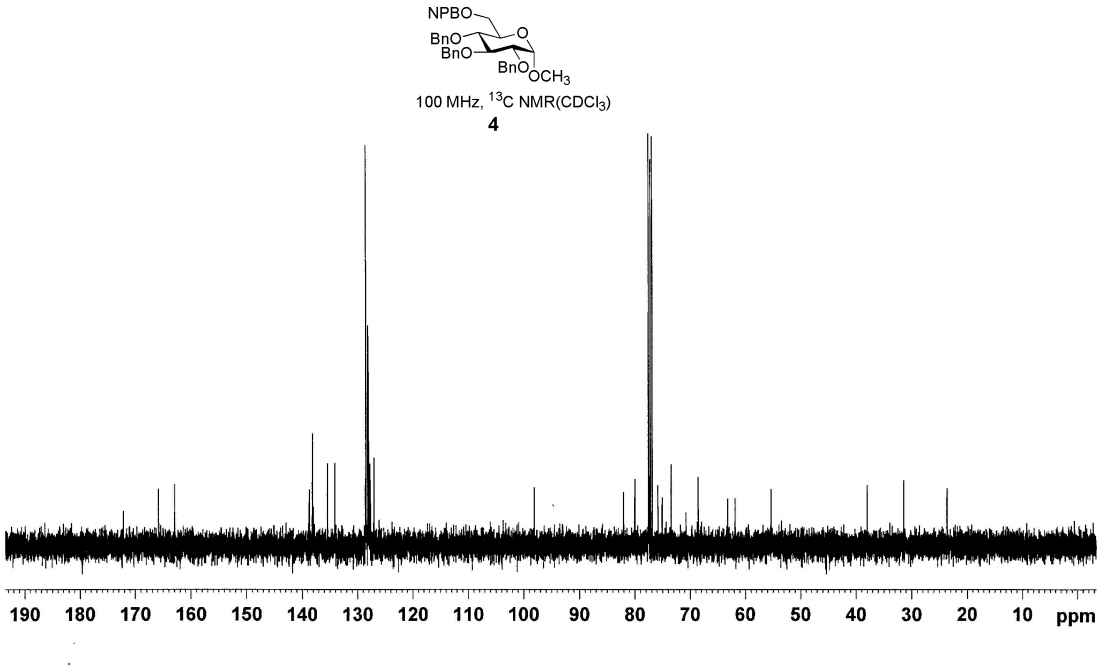
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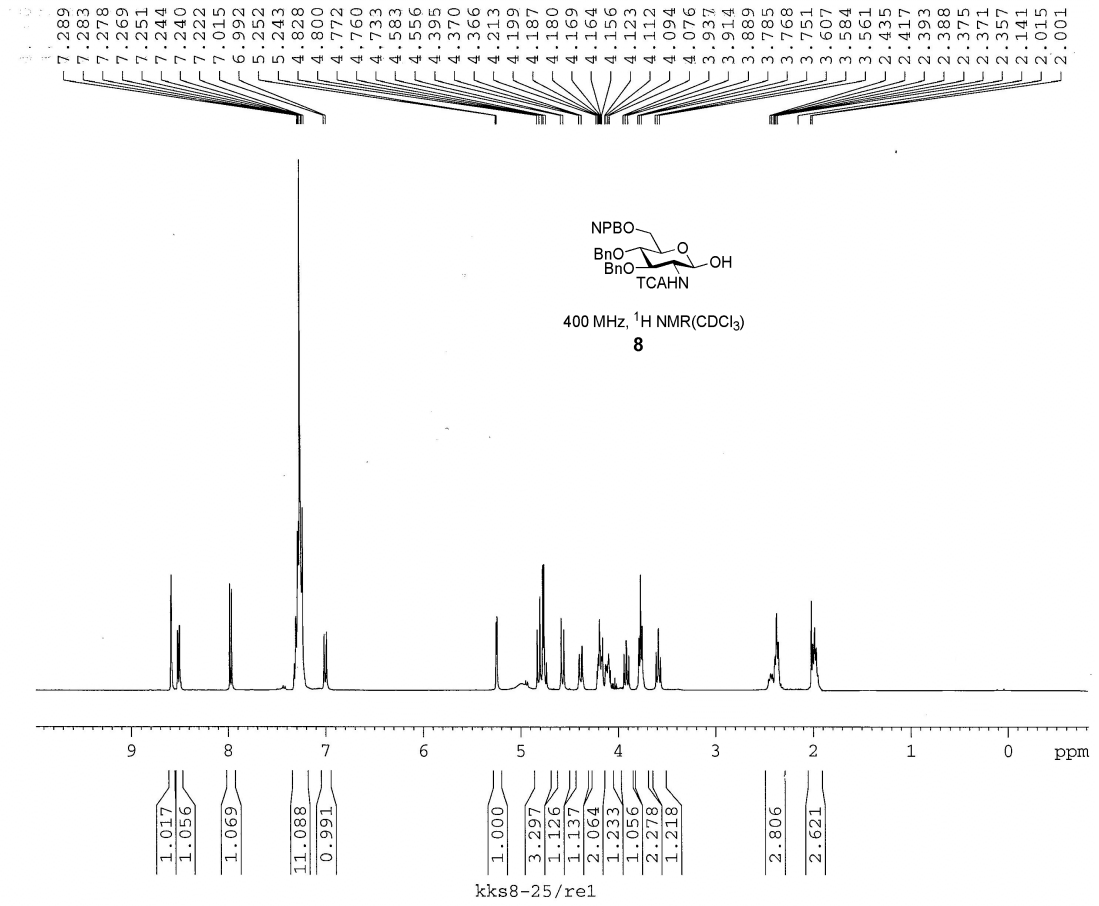
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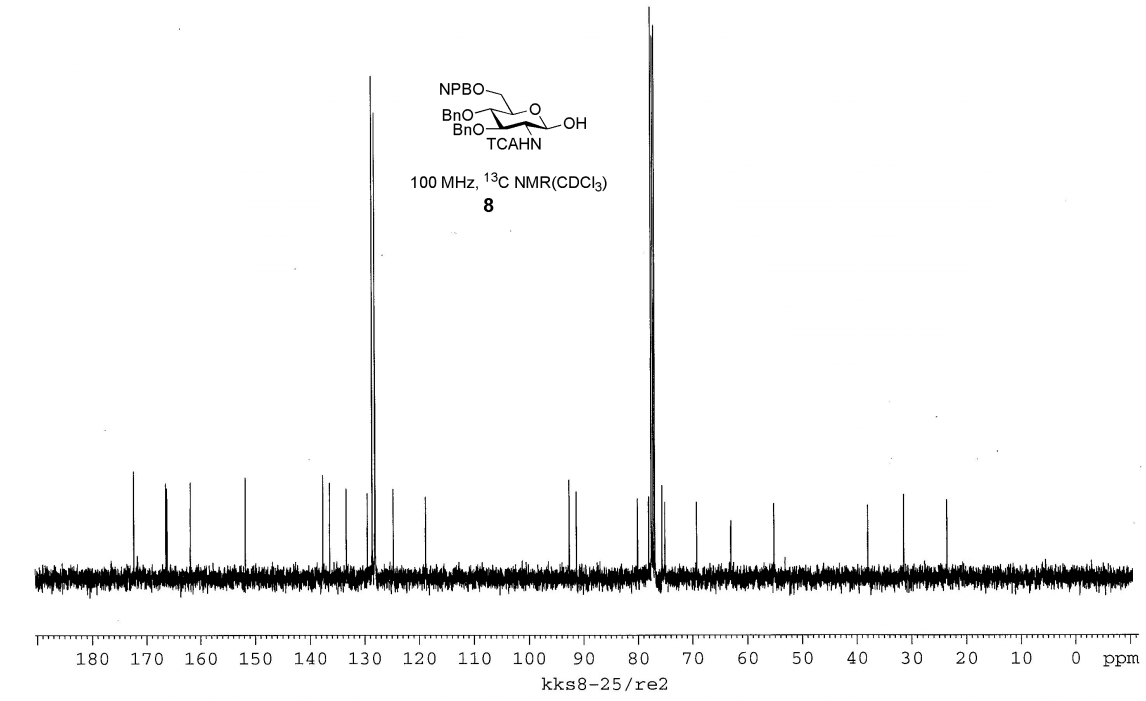
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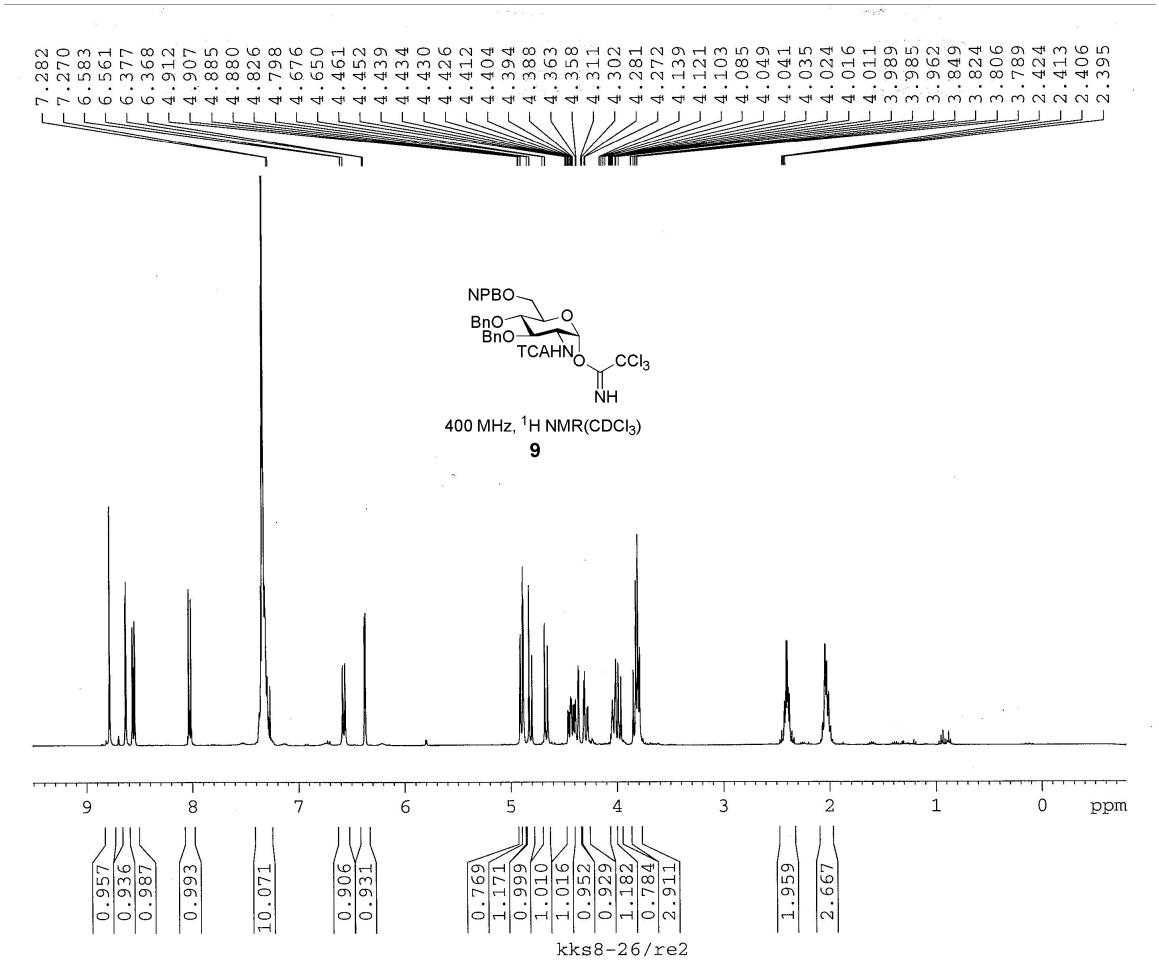
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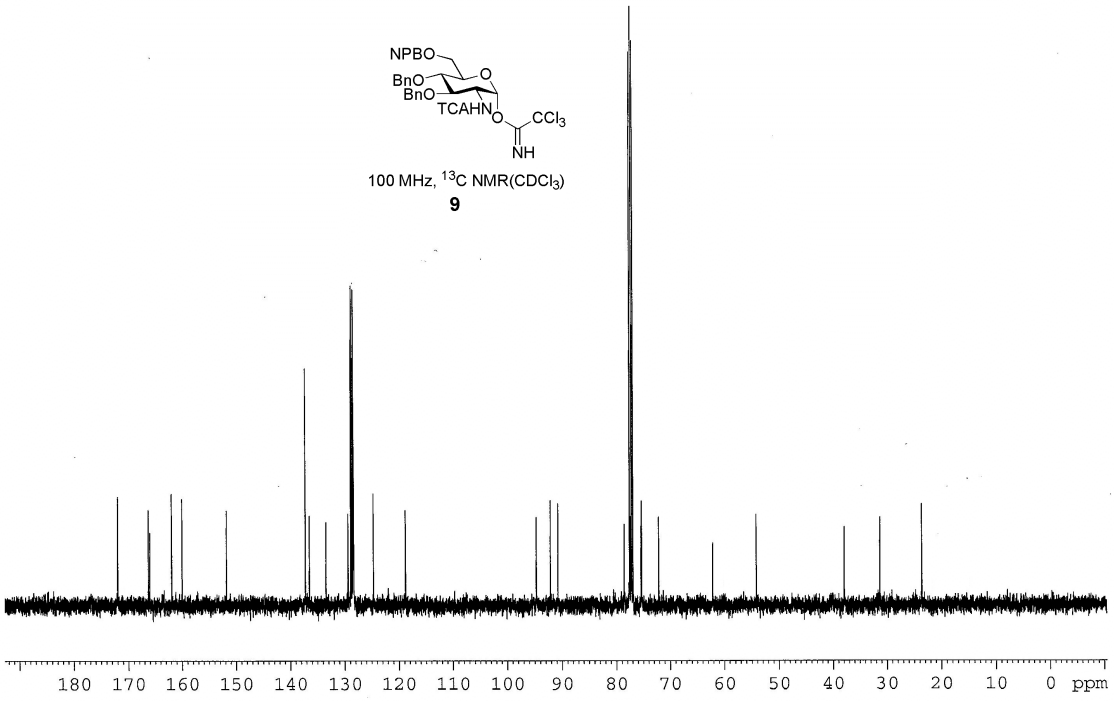
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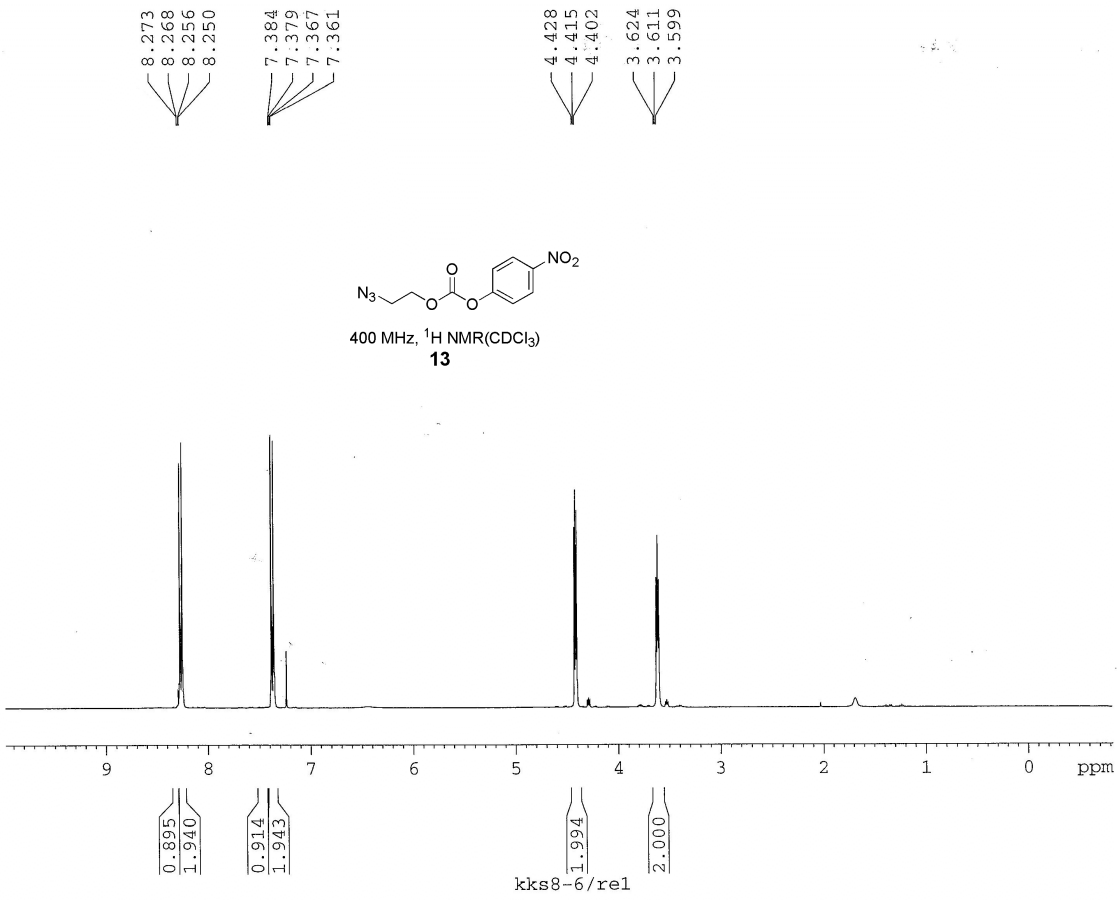
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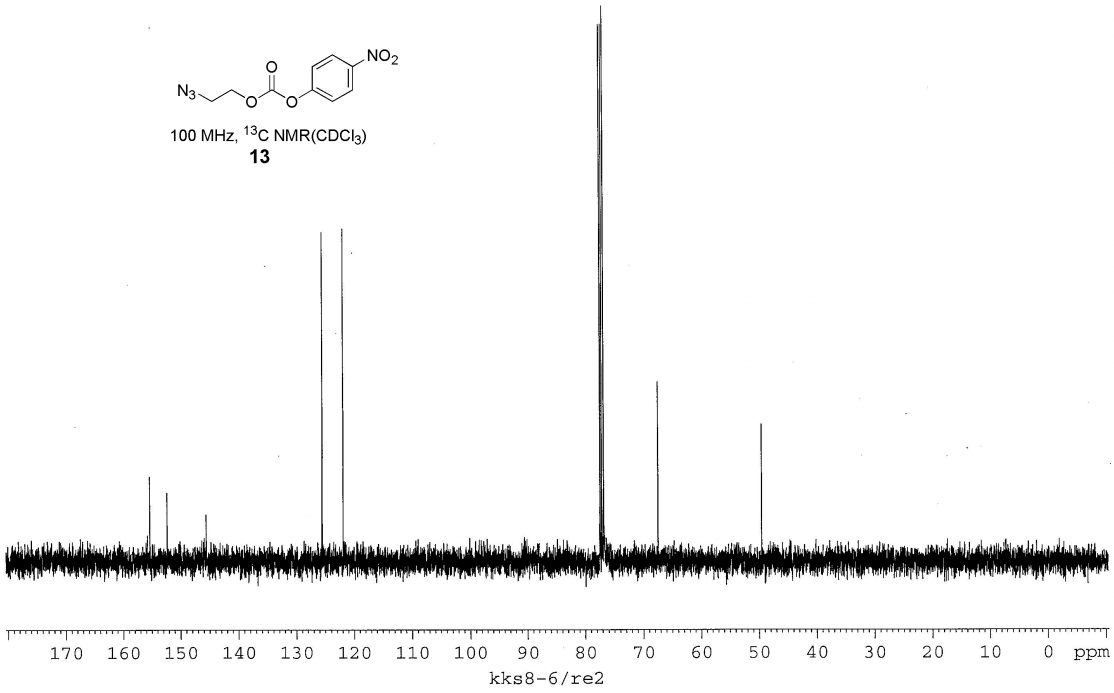
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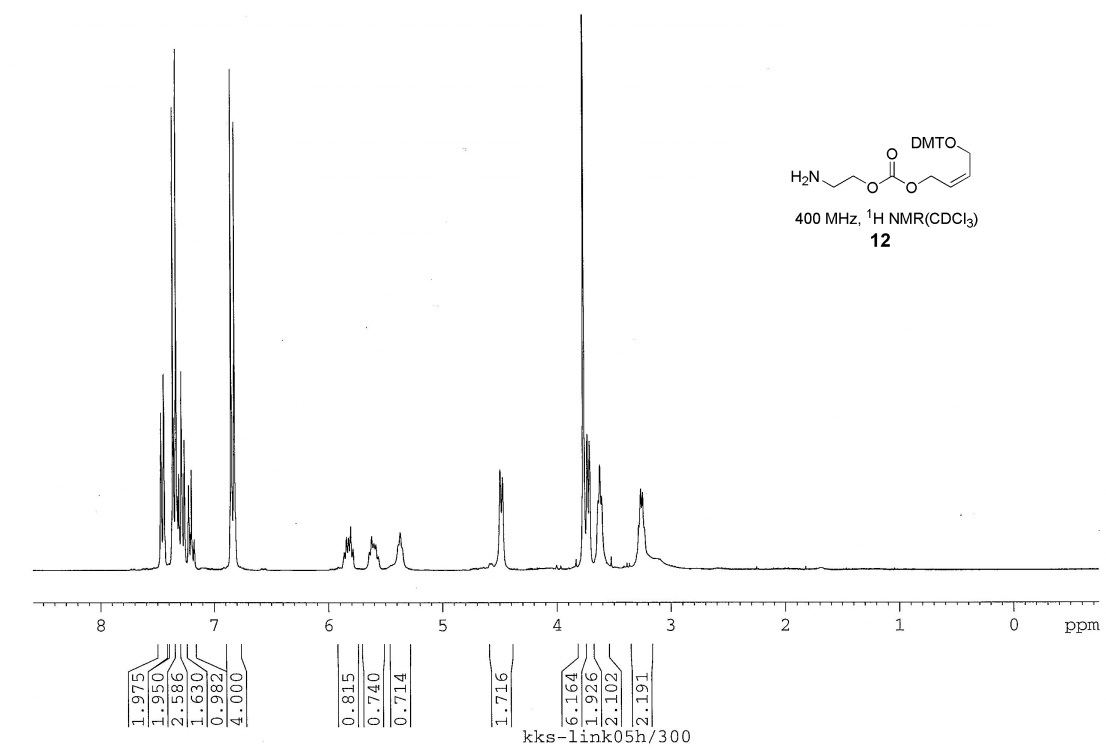
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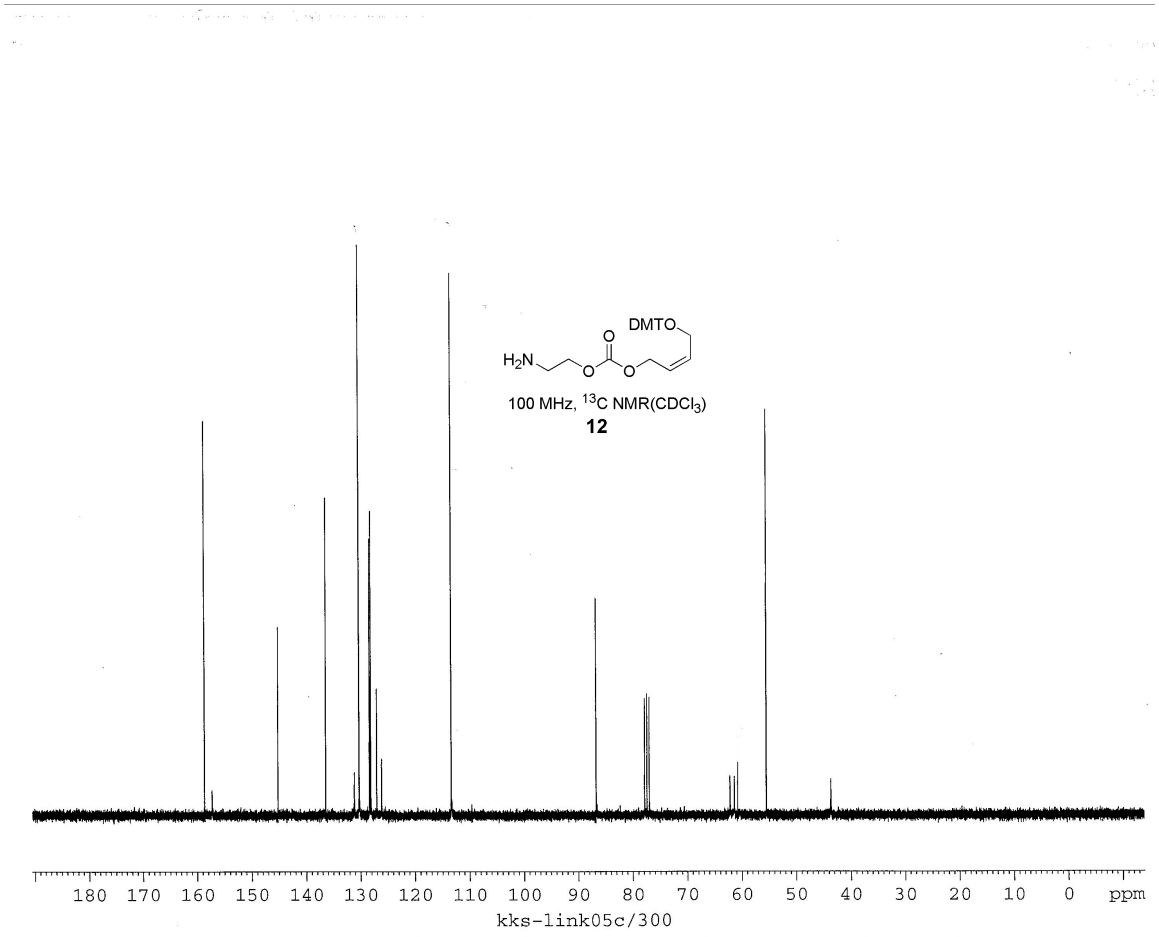
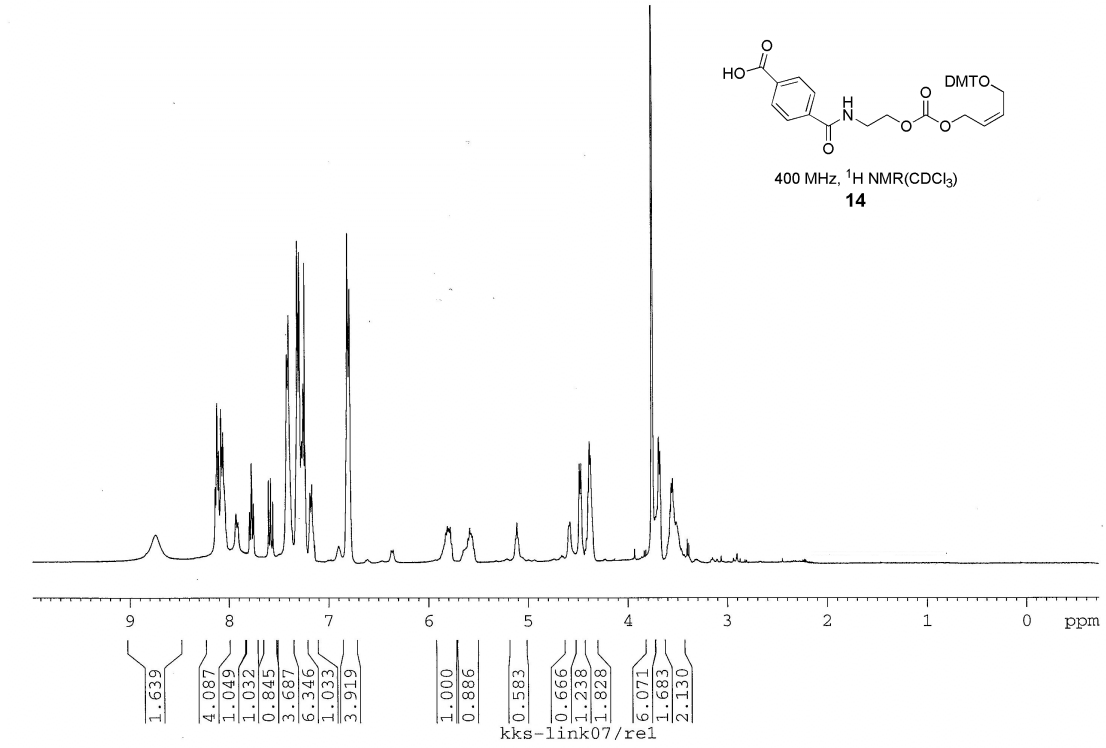
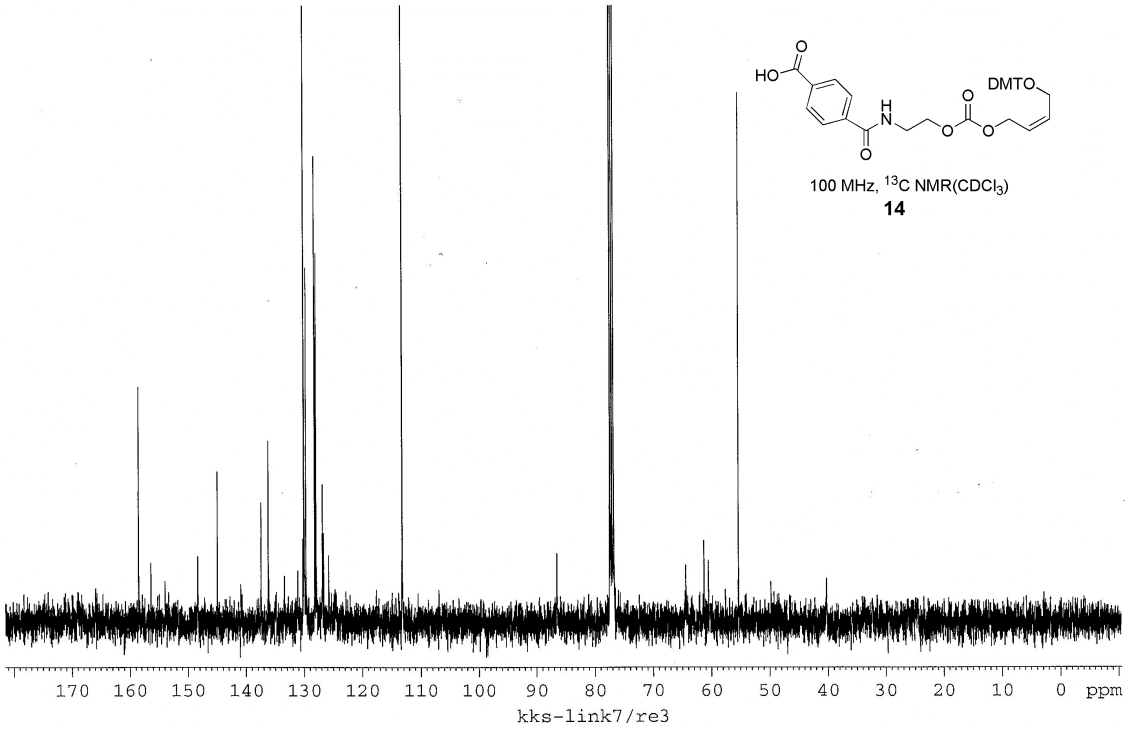
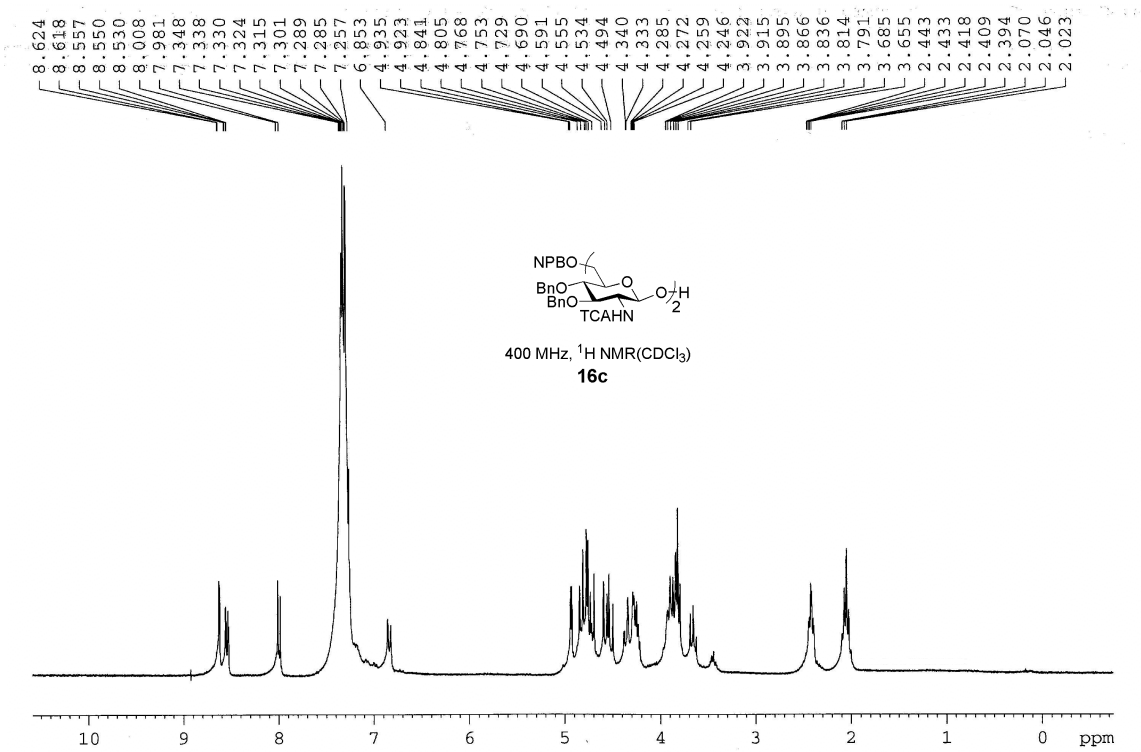
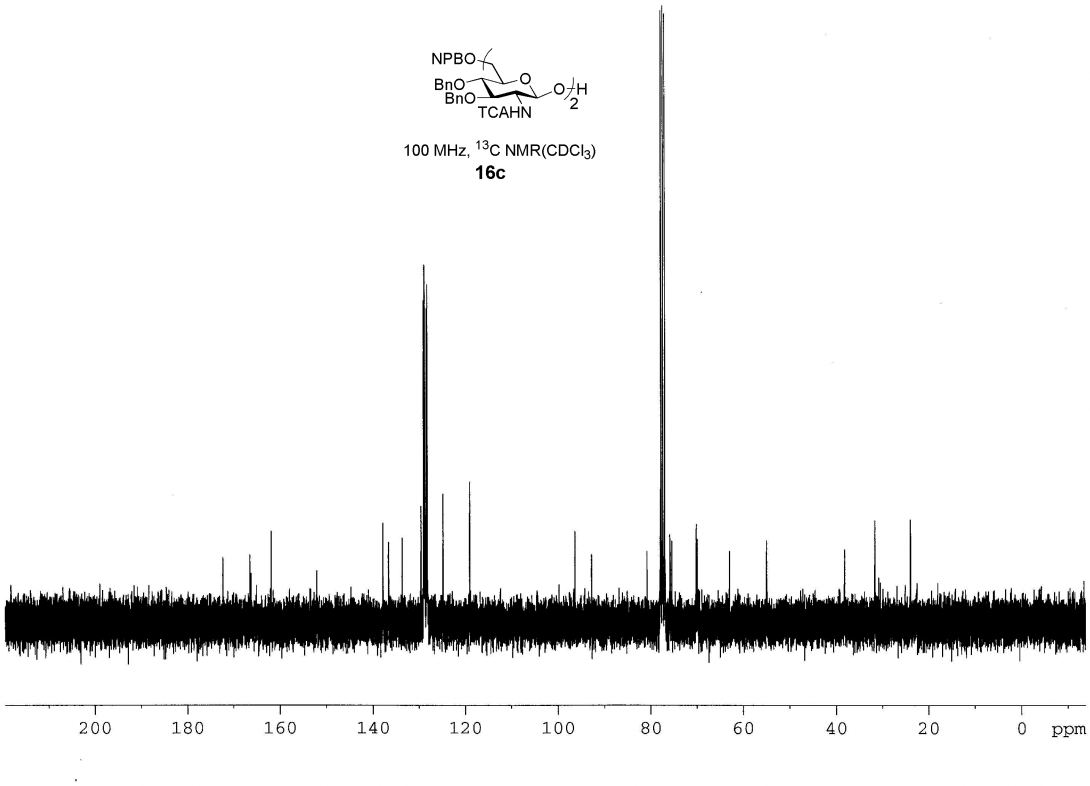
4
3
2
1
0
ppm
1.975
1.950
2.586
1.630
0.982
4.000
0.815
0.740
0.714
1.716
6.164
1.926
2.102
2.191
kks-link05h/300

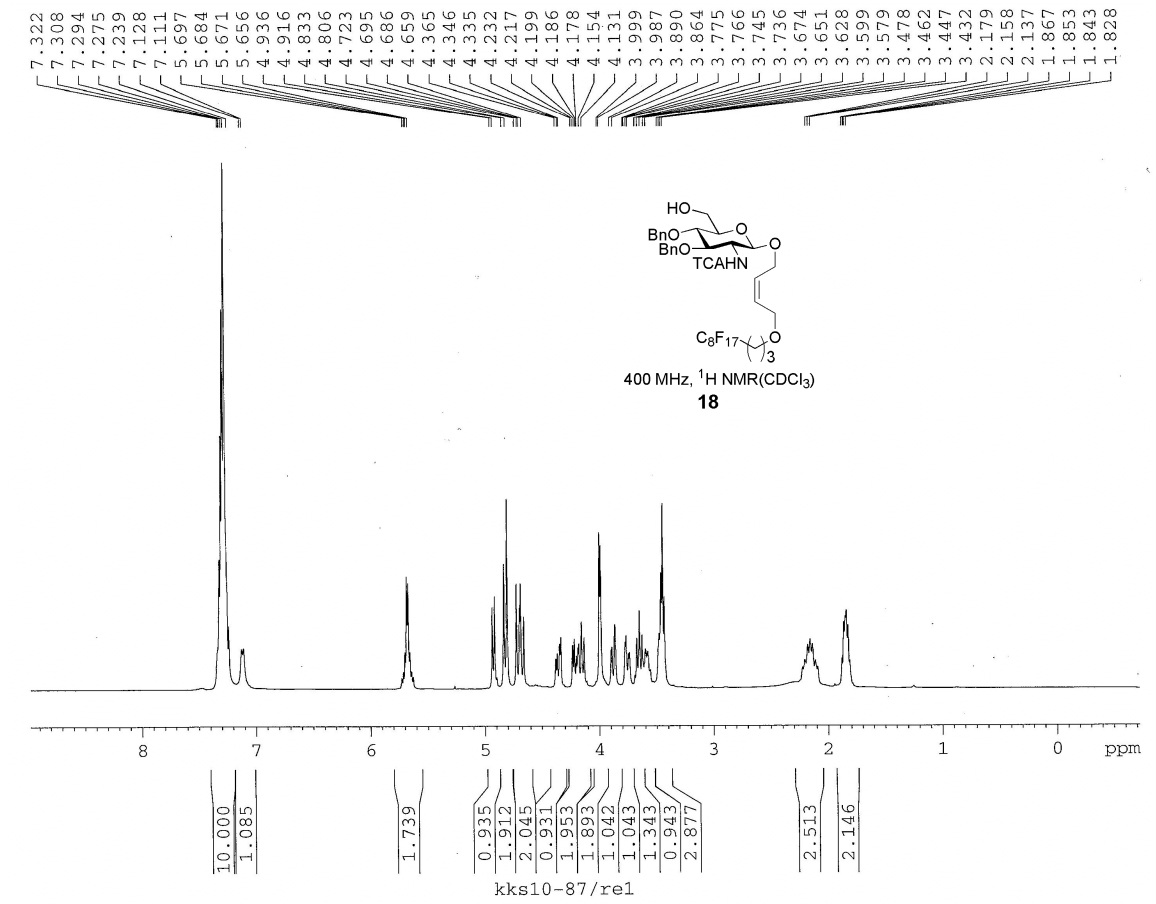

DMTO
O
H2N
O
O
100 MHz, 13C NMR(CDCl3)
12
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
kks-link05c/300

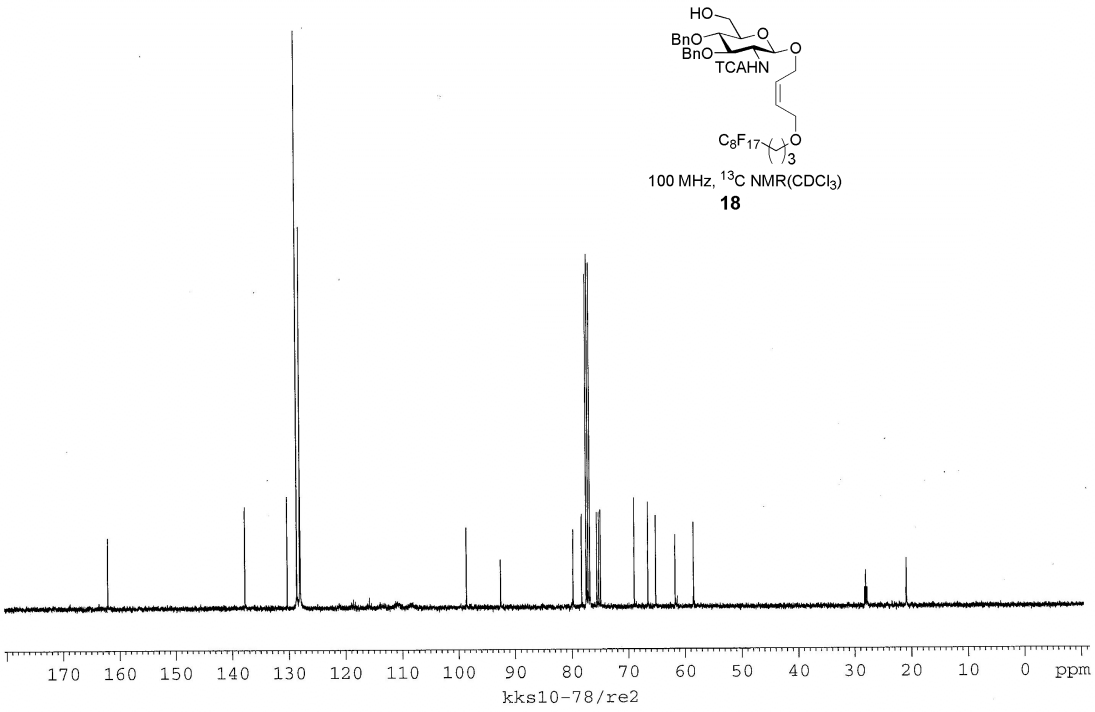

HO
O
H
N
O
O
O
O
DMTO
400 MHz, ^{1}H NMR(CDCl$_3$)
14
9
8
7
6
5
4
3
2
1
0
ppm
1.639
4.087
1.049
1.032
0.845
3.687
6.346
1.033
3.919
1.000
0.886
0.583
0.666
1.238
1.828
6.071
1.683
2.130
kks-link07/re1

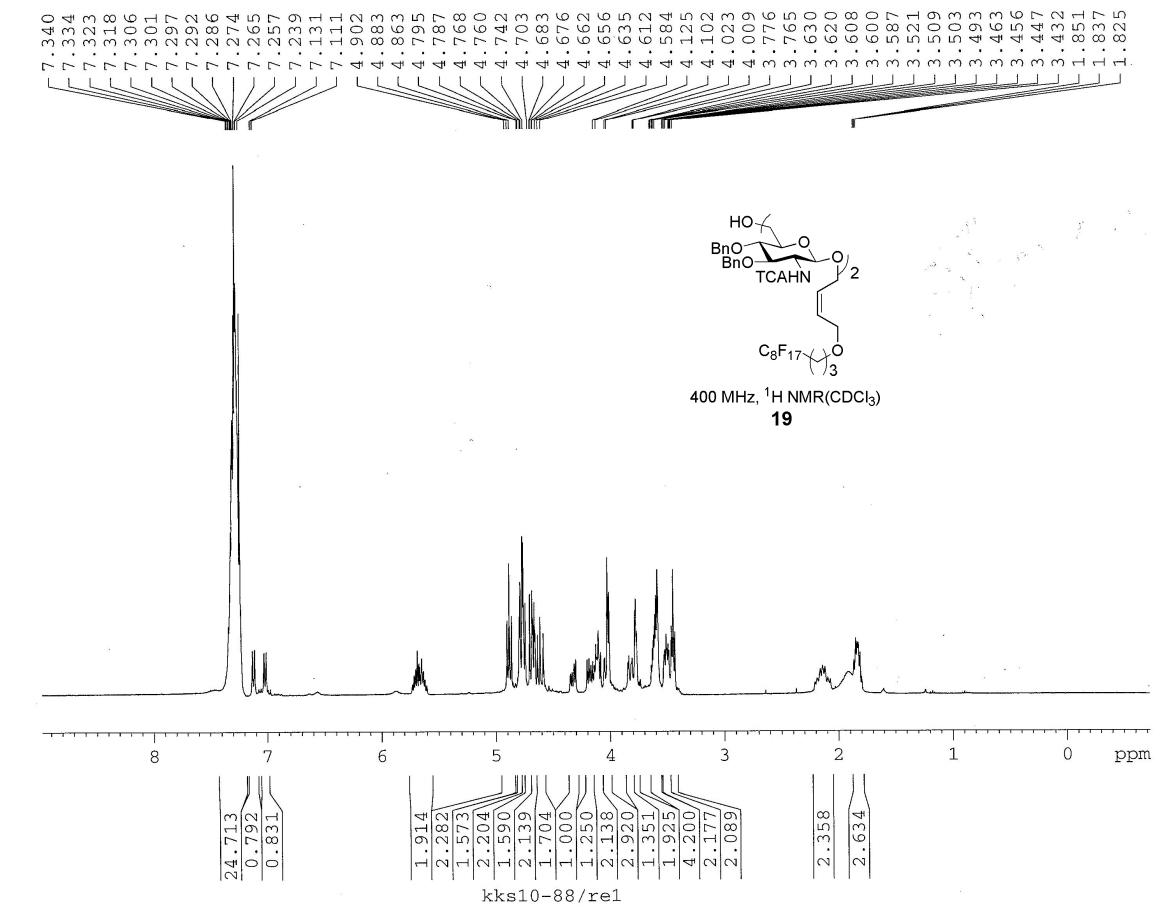

HO
O
H
N
O
O
O
O
DMTO
100 MHz, ^{13}C NMR($CDCl_3$)
14
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
kks-link7/re3

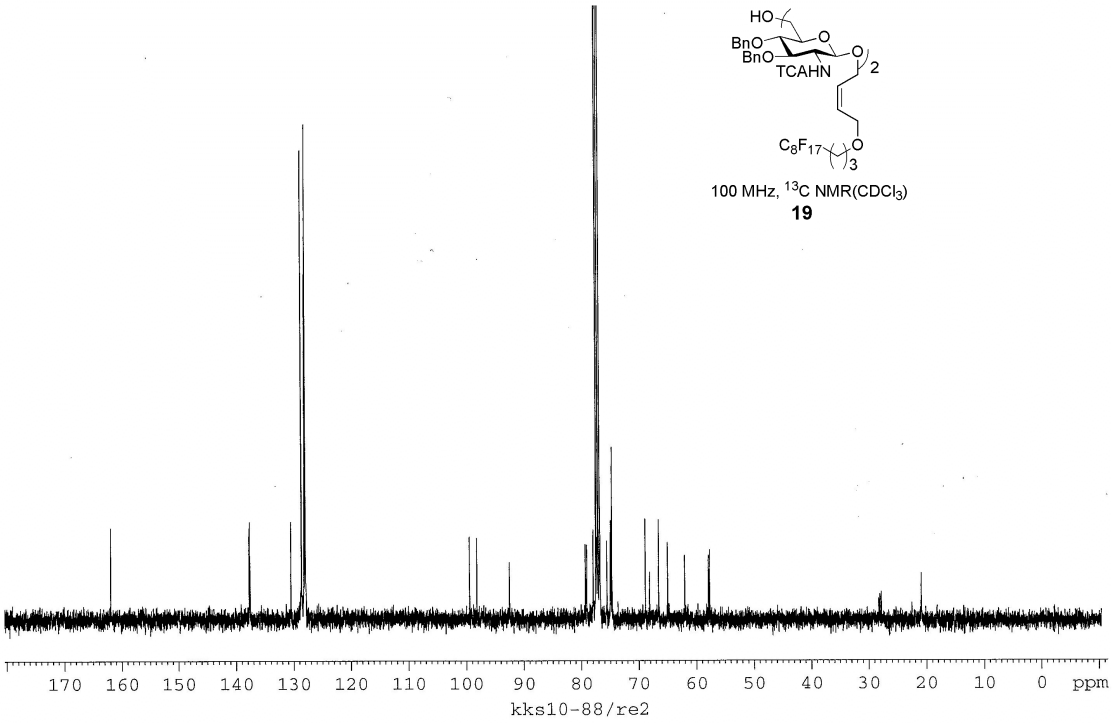

8.624
8.618
8.557
8.550
8.530
8.008
7.981
7.348
7.338
7.330
7.324
7.315
7.301
7.289
7.285
7.257
6.853
4.935
4.923
4.841
4.805
4.768
4.753
4.729
4.690
4.591
4.555
4.534
4.494
4.340
4.333
4.285
4.272
4.259
4.246
3.922
3.915
3.895
3.866
3.836
3.814
3.791
3.685
3.655
2.443
2.433
2.418
2.409
2.394
2.070
2.046
2.023
NPBO
BnO
BnO
O
O
H
2
TCAHN
400 MHz, 1H NMR(CDCl3)
16c
10
9
8
7
6
5
4
3
2
1
0
ppm

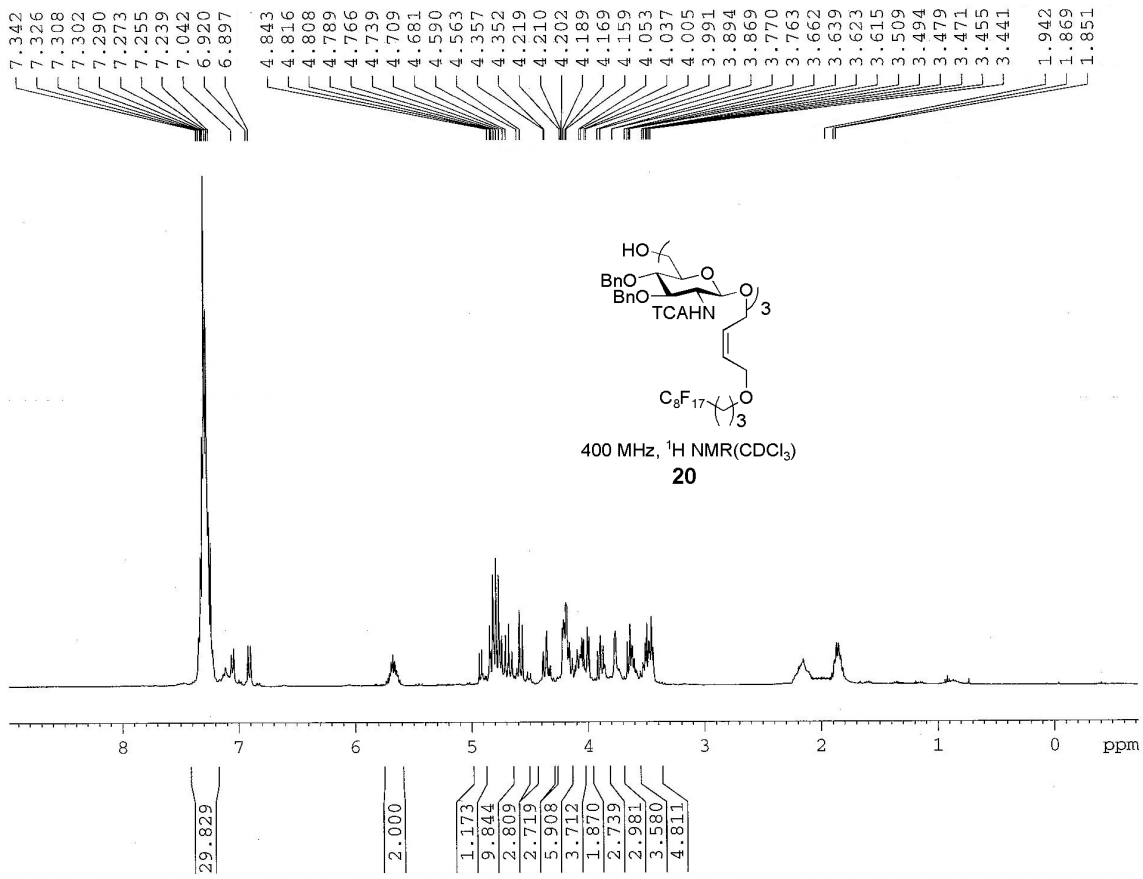

NPBO
BnO
BnO
TCAHN
O
O
H
2
100 MHz, ^{13}C NMR($CDCl_3$)
16c
200
180
160
140
120
100
80
60
40
20
0
ppm

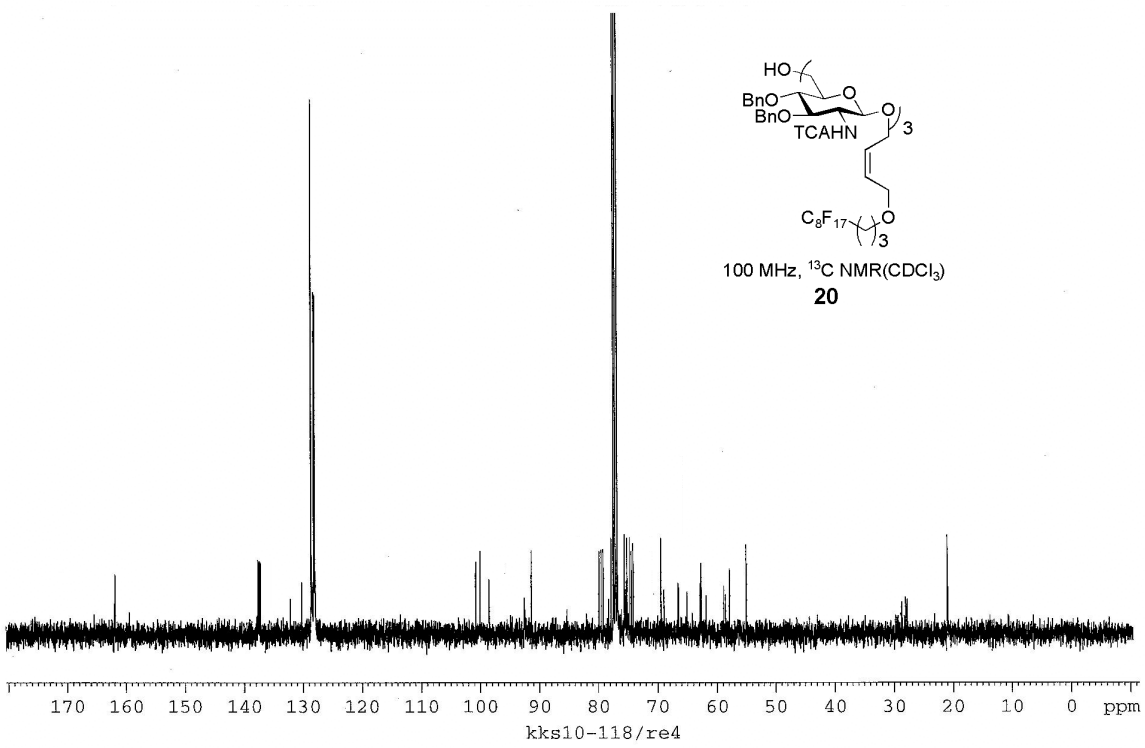

7.322
7.308
7.294
7.275
7.239
7.128
7.111
5.697
5.684
5.671
5.656
4.936
4.916
4.833
4.806
4.723
4.695
4.686
4.659
4.365
4.346
4.335
4.232
4.217
4.199
4.186
4.178
4.154
4.131
3.999
3.987
3.890
3.864
3.775
3.766
3.745
3.736
3.674
3.651
3.628
3.599
3.579
3.478
3.462
3.447
3.432
2.179
2.158
2.137
1.867
1.853
1.843
1.828
HO
BnO
BnO
TCAHN
O
O
C8F17
O
3
400 MHz, 1H NMR(CDCl3)
18
8
7
6
5
4
3
2
1
0
ppm
10.000
1.085
1.739
0.935
1.912
2.045
0.931
1.953
1.893
1.042
1.043
1.343
0.943
2.877
2.513
2.146
kks10-87/re1


HO
BnO
BnO
TCAHN
O
O
C_8F_{17}
3
100 MHz, ^{13}C NMR($CDCl_3$)
18
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
kks10-78/re2


7.340
7.334
7.323
7.318
7.306
7.301
7.297
7.292
7.286
7.274
7.265
7.257
7.239
7.131
7.111
4.902
4.883
4.863
4.795
4.787
4.768
4.760
4.742
4.703
4.683
4.676
4.662
4.656
4.635
4.612
4.584
4.125
4.102
4.023
4.009
3.776
3.765
3.630
3.620
3.608
3.600
3.587
3.521
3.509
3.503
3.493
3.463
3.456
3.447
3.432
1.851
1.837
1.825
HO
BnO
BnO
TCAHN
O
O
2
C8F17
O
3
400 MHz, 1H NMR(CDCl3)
19
8
7
6
5
4
3
2
1
0
ppm
24.713
0.792
0.831
1.914
2.282
1.573
2.204
1.590
2.139
1.704
1.000
1.250
2.138
2.920
1.351
1.925
4.200
2.177
2.089
2.358
2.634
kks10-88/re1


HO
BnO
BnO
TCAHN
O
O
2
C8F17
O
3
100 MHz, 13C NMR(CDCl3)
19
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
kks10-88/re2


7.342
7.326
7.308
7.302
7.290
7.273
7.255
7.239
7.042
6.920
6.897
4.843
4.816
4.808
4.789
4.766
4.739
4.709
4.681
4.590
4.563
4.357
4.352
4.219
4.210
4.202
4.189
4.169
4.159
4.053
4.037
4.005
3.991
3.894
3.869
3.770
3.763
3.662
3.639
3.623
3.615
3.509
3.494
3.479
3.471
3.455
3.441
1.942
1.869
1.851
HO
BnO
BnO
TCAHN
O
3
C8F17
400 MHz, 1H NMR(CDCl3)
20
8
7
6
5
4
3
2
1
0
ppm
29.829
2.000
1.173
9.844
2.809
2.719
5.908
3.712
1.870
2.739
2.981
3.580
4.811


HO
BnO
BnO
TCAHN
O
O
3
C_8F_{17}
O
3
100 MHz, ^{13}C NMR($CDCl_3$)
20
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
kks10-118/re4