Electronic Supplementary Information

Synthesis of *N*-Substituted *ε*-Hexonolactams as Pharmacological Chaperones for the Treatment of N370S Mutant Gaucher Disease

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Table of contents

Chemistry Section:

General. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon using flame-dried glassware and standard syringe/septa techniques. All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Dichloromethane (CH_2Cl_2) and pyridine were distilled over calcium hydride (CaH_2). Methanol was distilled from magnesium. DMF was stirred with CaH_2 and distilled under reduced pressure. Tetrahydrofuran (THF) was distilled over sodium/benzophenone. Reactions were monitored by analytical thin-layer chromatography on silica gel 60 F_{254} precoated on aluminium plates (E. Merck). Spots were detected under UV (254 nm) and/or by staining with acidic ceric ammonium molybdate. Column chromatography was performed on silica gel (200-300 mesh). ^{1}H-NMR spectra were recorded on a JEOL AL-300, or Varian INOVA-500 spectrometers at 25 ^{o}C. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in deuterated chloroform. ^{13}C-NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm) or CD_3OD (δ = 49.00 ppm). Mass spectra were recorded using a PE SCLEX QSTAR spectrometer. Elemental analysis data were recorded on a Vario EL-III elemental analyzer. All the tested compounds possess a purity of at least 95% as determined by HPLC. Analytical HPLC was run on the Shimadzu LC-20AD HPLC instrument coupled with SPD-M20A detector, using SHIMADZU C18 VP-ODS column 150L×4.6 or Agilent 1100 Series instrument equipped with VWD-detector, using C-18 reversed column (DIKMA, Diamonsil C18 250mm*4.6mm, 5μm) and UV detection at 210 nm. Flow rate = 1 mL/min. The eluent system is: for method A, linear gradient from 95% H_2O (with phosphoric acid, pH = 3) to 100% MeOH at 40 min; for method B, isocratic 80% methanol in water. Retention times (t_R) are given in minutes.

General procedure for the synthesis of *N*-substituted *ε*-gluconolactams: IBX (3.5 g, 12.4 mmol) was added to a solution of compound **4**[1] (1.4 g, 3.1 mmol) in ethyl acetate (30 mL). The mixture was heated under reflux overnight and then cooled to room temperature. The mixture was filtered through Celite and the filtrate was concentrated to afford product **5** (1.39 g) as a light yellow oil which was able to be stored at -20 ^{o}C under Argon for three months. To a solution of compound **5** (190 mg, 0.43 mmol) in MeOH (30 mL), amine (0.85 mmol), $NaCNBH_3$ (56 mg, 0.85 mmol), and $ZnCl_2$ (12 mg, 0.085 mmol) were added, and the mixture was heated under reflux for 2 h, followed by quenching with saturated $NaHCO_3$. After removal of the solvent, the residue was dissolved in ethyl acetate (80 mL) and washed by saturated sodium chloride aqueous solution (20 mL ×2). The organic phase was dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel to provide the products.

(3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-(2-hydroxyethyl)azepan-2-one (6a). Yield: 72%, colorless oil after column chromatography (petroleum ether-ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 1H), 3.07-3.14 (m, 1H), 3.45-3.50 (m, 1H), 3.56-3.60 (m, 1H), 3.69-3.72 (m, 2H), 3.83 (t, *J* = 10.5 Hz, 1H), 3.91-3.99 (m, 4H), 4.26, (d, *J* = 6.6 Hz, 1H), 4.41-4.46 (m, 2H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.70-4.77 (m, 2H), 4.88 (d, *J* = 11.7 Hz, 1H), 7.29-7.42 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.6, 53.4, 61.1, 67.6, 72.6, 73.8, 74.0, 78.0, 80.3, 80.6, 127.65, 127.74, 127.98, 128.05, 128.2, 128.3, 128.4, 137.2, 137.6, 137.7, 169.7; HRMS: Calcd for $C_{29}H_{34}NO_6[M+H]^+$, 492.2381; Found, 492.2380.

(3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-(6-hydroxyhexyl)azepan-2-one (6b). Yield: 82%, colorless oil after column chromatography (petroleum ether-ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26-1.43 (m, 4H), 1.48-1.58 (m, 4H), 1.78 (s, 1H), 2.88 (d, *J* = 6.9 Hz, 1H), 3.18-3.34 (m, 2H), 3.59 (t, *J* = 6.3 Hz, 2H), 3.62-3.69 (m, 1H), 3.74 (t, *J* = 5.1 Hz, 1H), 3.78-3.87 (m, 1H), 3.93 (m, 1H), 4.00 (t, *J* = 5.7 Hz, 1H), 4.34-4.38 (m, 2H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 4.73-4.82 (m, 3H), 7.22-7.40 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 26.2, 27.7,

32.5, 48.8, 48.9, 62.5, 67.5, 72.3, 73.2, 73.5, 75.9, 80.1, 82.0, 127.7, 127.9, 127.95, 128.03, 128.3, 128.4, 128.5, 137.3, 137.6, 137.7, 168.9; Anal. Calcd for $C_{33}H_{41}NO_6$: C, 72.37; H, 7.55; N, 2.56; Found: C, 72.52; H, 7.36; N, 2.70; ESI-MS: 548 $[M+H]^+$.

(3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-butylazepan-2-one (6c). Yield: 89% as a mixture of diastereomers (ratio 9:1, **6c** as the major isomer). The two diastereomers were isolated after benzoylation by the procedure as described in the following: benzoyl chloride (330 μL, 2.88 mmol) was added dropwise to a solution of **6c** with its 6-hydroxy epimer (180 mg, 0.36 mmol) and DMAP (10 mg, 0.072 mmol) in pyridine (20 mL) under Argon. The reaction was stirred at room temperature for 2 h, then pyridine was removed under reduced pressure and co-evaporated with toluene (20 mL × 2). The residue was dissolved in ethyl acetate (50 mL), to which saturated potassium carbonate solution (10 mL) was added and stirred for 30 min. The organic phase was separated from aqueous phase, washed by brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether-ethyl acetate, 11:1 to 10:1) to afford compound **14c** (191 mg, 88% yield).

(3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-benzoyloxy-1-butylazepan-2-one (14c). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.5 Hz, 3H), 1.24-1.34 (m, 2H), 1.49-1.53 (m, 2H), 3.26 (m, 1H), 3.44-3.53 (m, 1H), 3.65 (m, 1H), 3.96-4.00 (m, 3H), 4.40-4.41 (m, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.54-4.60 (m, 2H), 4.64 (d, *J* = 11.5 Hz, 1H), 4.75 (d, *J* = 11.5 Hz, 1H), 4.81-4.83 (m, 1H), 5.38 (s, 1H), 7.21-7.45 (m, 17H), 7.57-7.60 (m, 1H), 7.98-8.00 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 20.1, 29.9, 46.6, 48.9, 70.5, 72.4, 73.5, 73.6, 77.2, 79.1, 127.6, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 129.7, 133.3, 137.7, 137.8, 165.7, 168.9. Anal. Calcd for $C_{38}H_{41}NO_6$: C, 75.10; H, 6.80; N, 2.30; Found: C, 74.89; H, 6.62; N, 2.31; ESI-MS: 608 $[M+H]^+$.

Compound **14c** (191 mg, 0.31 mmol) was dissolved in methanol (10 mL), to which NaOMe (1 M solution in methanol, 1 mL, 1 mmol) was added and the mixture was stirred for 1 h at room temperature. The solution was neutralize to pH = 7 with Dowex 50w H^+ resin. The resin was then removed by filtration and washed with ethyl acetate.

The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel (petroleum ether-ethyl acetate, 3:1) to afford compound **6c** (155 mg, 98% yield) as colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.0 Hz, 3H), 1.25-1.33 (m, 2H), 1.46-1.52 (m, 2H), 2.85 (d, *J* = 7.5 Hz, 1H), 3.20-3.25 (m, 1H), 3.31-3.34 (m, 1H), 3.60-3.66 (m, 1H), 3.73 (dd, *J* = 4.5, 5.5 Hz, 1H), 3.78-3.82 (m, 1H), 3.92-3.96 (m, 1H), 4.00 (t, *J* = 5.5 Hz, 1H), 4.35 (d, *J* = 5.5 Hz, 1H), 4.37 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.73-4.76 (m, 2H), 4.80 (d, *J* = 11.5 Hz, 1H), 7.23-7.39 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.0, 30.0, 48.8, 49.0, 67.5, 72.3, 73.2, 73.5, 76.0, 80.1, 82.1, 127.7, 127.8, 127.97, 128.01, 128.04, 128.3, 128.36, 128.45, 137.3, 137.66, 137.73, 168.7; Anal. Calcd for $C_{36}H_{47}NO_5$: C, 73.93; H, 7.41; N, 2.78; Found: C, 73.80; H, 7.25; N, 2.75; ESI-MS: 504 $[M+H]^+$.

(3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-nonylazepan-2-one (6d). Yield: 91% as a mixture of diastereomers (ratio 9:1, **6d** as the major isomer). The two diastereomers were isolated by benzoylation as the procedure described in the preparation of compound **6c**. After debenzolation, compound **6d** (78% yield from **4** after three steps) was provided as colorless oil after column chromatography (petroleum ether-ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 3H), 1.25 (s, 12H), 1.50 (m, 2H), 2.87 (d, *J* = 7.5 Hz, 1H), 3.17-3.27 (m, 1H), 3.30-3.34 (m, 1H), 3.57-3.67 (m, 1H), 3.71-3.74 (m, 2H), 3.94 (m, 1H), 4.00 (t, *J* = 5.7 Hz, 1H), 4.34-4.38 (m, 2H), 4.47 (d, *J* = 11.4 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 4.73-4.83 (m, 3H), 7.22-7.39 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 26.8, 27.9, 29.2, 29.4, 29.5, 31.8, 48.9, 49.1, 67.5, 72.3, 73.2, 73.4, 80.1, 82.0, 127.7, 127.8, 127.96, 128.00, 128.29, 128.34, 128.4, 137.3, 137.6, 137.7, 168.6; Anal. Calcd for $C_{36}H_{47}NO_5$: C, 75.36; H, 8.26; N, 2.44; Found: C, 75.41; H, 8.08; N, 2.48; ESI-MS: 596 $[M+Na]^+$.

(3*R*,4*S*,5*R*,*6R*)-3,4,5,6-Tetrahydroxy-1-(2-hydroxyethyl)azepan-2-one (7a). A mixture of **6a** (30.0 mg, 0.061 mmol) and 10% Pd-C (10.0 mg) in THF (4.0 mL), H_2O (2.0 mL), and HOAc (1.0 mL) was stirred under hydrogen atmosphere (4 atm) for 48

h. The catalyst was then removed by filtration through Celite, and the filtrate was concentrated. The residue was subjected to a C-18 reversed-phase column chromatography (eluent, H_2O) to give **7a** (13.0 mg, 92%) as a colorless oil. ^{1}H NMR (300 MHz, D_2O) δ 3.07-3.16 (m, 1H), 3.30-3.62 (m, 6H), 3.68-3.80 (m, 1H), 3.97 (dd, *J* = 3.3, 6.0 Hz, 1H), 4.13 (d, *J* = 9.9 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 49.7, 53.6, 60.0 69.4, 70.6, 70.9, 77.0, 174.0; HRMS: Calcd for $C_8H_{15}NO_6Na$ [M+Na$^+$], 244.0792; Found, 244.0797. HPLC: 100% (method A, t_R = 2.29 min).

(3*R*,4*S*,5*R*,6*R*)-3,4,5,6-Tetrahydroxy-1-(6-hydroxyhexyl)azepan-2-one (7b). Compound **7b** was prepared from compound **6b** as described in the preparation of compound **7a**, yielding **7b** (94% yield) as a colorless oil. ^{1}H NMR (300 MHz, D_2O) δ 1.10-1.24 (m, 4H), 1.32-1.44 (m, 4H), 2.75-2.85 (m, 1H), 3.28-3.55 (m, 6H), 3.70-3.80 (m, 1H), 3.95-3.98 (m, 1H), 4.09 (d, *J* = 9.6 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 25.8, 26.7, 27.6, 32.2, 48.8, 51.9, 62.7, 69.3, 70.6, 70.7, 77.0, 173.1; HRMS: Calcd for $C_{12}H_{23}NO_6Na$ [M+Na]$^+$, 300.1418; Found, 300.1419. HPLC: 98.1% (method A, t_R = 10.17 min).

(3*R*,4*S*,5*R*,6*R*)-1-Butyl-3,4,5,6-tetrahydroxyazepan-2-one (7c). Compound **7c** was prepared from compound **6c** as described in the preparation of compound **7a**, yielding **7c** (96% yield) as a colorless oil. ^{1}H NMR (300 MHz, D_2O): δ 0.73 (t, *J* = 7.2 Hz, 3H), 1.05-1.17 (m, 2H), 1.28-1.41 (m, 2H), 2.75-2.84 (m, 1H), 3.28-3.55 (m, 4H), 3.70-3.80 (m, 1H), 3.97 (dd, *J* = 3.3, 6.0 Hz, 1H), 4.09 (d, *J* = 9.9 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 14.1, 20.4, 29.9, 48.8, 51.8, 69.3, 70.6, 70.7, 77.0, 173.1; HRMS: Calcd for $C_{10}H_{20}NO_5$ [M+H]$^+$, 234.1336; Found, 234.1331. HPLC: 98.7% (method A, t_R = 11.38 min).

(3*R*,4*S*,5*R*,6*R*)-1-Nonyl-3,4,5,6-tetrahydroxyazepan-2-one (7d). Compound **7d** was prepared from compound **6d** as described in the preparation of compound **7a**, yielding **7d** (95% yield) as an amorphous solid after lyophilization. ^{1}H NMR (300 MHz, CD_3OD) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.29 (s, 12H), 1.52-1.57 (m, 2H), 2.97-3.07 (m, 1H), 3.40-3.63 (m, 4H), 3.84-3.94 (m, 1H), 3.99 (dd, *J* = 3.3, 6.3 Hz, 1H), 4.08 (d, *J* = 9.3 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.5, 23.7, 28.0, 28.6, 30.4, 30.5, 30.7,

33.0, 49.1, 52.0, 69.8, 71.3, 71.6, 78.1, 173.2; HRMS: Calcd for $C_{15}H_{29}NO_5Na$ $[M+Na]^+$, 326.1938; Found, 326.1938. HPLC: 100.0% (method A, t_R = 27.55 min).

(3*R*,4*S*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-(2-hydroxyethyl)azepan-2-one (9a). Compound **9a** was prepared from compound **8**[1] as described in the preparation of **6a**. Yield: 77% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85 (brs, 1H), 2.91 (brs, 1H), 3.27-3.73 (m, 6H), 4.03-4.11 (m, 3H), 4.38-4.72 (m, 7H), 7.27-7.34 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.5, 53.0, 61.3, 68.9, 72.1, 72.8, 73.0, 82.1, 82.6, 127.9, 128.0, 128.3, 128.5, 128.6, 136.9, 137.5, 170.3; HRMS: Calcd for C_{29} $H_{34}NO_6$ $[M+H]^+$, 492.2381; Found, 492.2377.

(3*R*,4*S*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-(6-hydroxyhexyl)azepan-2-one (9b). Compound **9b** was prepared from compound **8** as described in the preparation of **6a**. Yield: 71% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22-1.36 (m, 4H), 1.40-1.56 (m, 4H), 2.12 (brs, 1H), 2.80 (brs, 1H), 3.16-3.20 (m, 1H), 3.25-3.34 (m, 1H), 3.54 (t, *J* = 6.0 Hz, 2H), 3.58-3.63 (m, 1H), 3.70 (m, 1H), 3.95-4.00 (m, 2H), 4.07 (dd, *J* = 2.4, 6.6 Hz, 1H), 4.36-4.74 (m, 7H), 7.27-7.37 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.0, 25.9, 27.5, 32.3, 49.0, 62.2, 68.6, 71.9, 72.6, 81.9, 82.8, 127.7, 127.8, 128.0, 128.2, 128.4, 128.5, 136.9, 137.5, 137.6, 169.0; Anal. Calcd for $C_{33}H_{41}NO_6$: C, 72.37; H, 7.55; N, 2.56; Found: C, 72.26; H, 7.53; N, 2.70; ESI-MS: 548 $[M+H]^+$.

(3*R*,4*S*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-butylazepan-2-one (9c). Compound **9c** was prepared from compound **8** as described in the preparation of **6a**. Yield: 82% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.2 Hz, 3H), 1.25-1.37 (m, 2H), 1.47-1.57 (m, 2H), 2.56 (s, 1H), 3.18 (m, 1H), 3.31-3.40 (m, H), 3.49-3.59 (m, 1H), 3.71-3.75 (m, 1H), 3.96-4.01 (m, 2H), 4.09 (dd, *J* = 2.7, 6.6 Hz, 1H), 4.34-4.75 (m, 7H), 7.26-7.38 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 20.0, 29.9, 49.0, 49.2, 68.7, 71.9, 72.6, 82.0, 82.8, 127.7, 127.9, 128.0, 128.3, 128.5, 128.6, 137.0, 137.5, 137.6, 168.8; HRMS: Calcd for $C_{31}H_{38}NO_5$ $[M+H]^+$, 504.2744; Found,

504.2747.

(3*R*,4*S*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-nonylazepan-2-one (9d). Compound **9d** was prepared from compound **8** as described in the preparation of **6a**. Yield: 78% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 6:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.23 (s, 12H), 1.52 (m, 2H), 2.53 (s, 1H), 3.21 (m, 1H), 3.32-3.41 (m, 1H), 3.47-3.54 (m, 1H), 3.71 (m, 1H), 3.96-3.99 (m, 2H), 4.09 (dd, *J* = 2.4, 6.6 Hz, 1H), 4.34-4.76 (m, 7H), 7.26-7.38 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 26.8, 27.8, 29.2, 29.4, 29.5, 31.8, 49.0, 49.5, 68.7, 71.9, 72.6, 82.0, 82.8, 127.7, 127.9, 128.0, 128.3, 128.4, 128.6, 137.0, 137.5, 137.7, 168.8; Anal. Calcd for $C_{36}H_{47}NO_5$: C, 75.36; H, 8.26; N, 2.44; Found: C, 75.42; H, 8.19; N, 2.52; ESI-MS: 574 $[M+H]^+$.

(3*R*,4*S*,5*S*,6*R*)-3,4,5,6-Tetrahydroxy-1-(2-hydroxyethyl)azepan-2-one (10a). Compound **10a** was prepared from compound **9a** as described in the preparation of compound **7a**, yielding **10a** (94% yield) as a colorless oil: ^{1}H NMR (300 MHz, D_2O) δ 3.08-3.32 (m, 2H), 3.57 (t, *J* = 5.4 Hz, 3H), 3.74-3.81 (m, 4H), 4.44 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 48.7, 52.7, 59.6, 68.8, 69.4, 70.0, 73.3, 174.2; HRMS: Calcd for $C_8H_{15}NO_6Na$ $[M+Na]^+$, 244.0792; Found, 244.0797. HPLC: 100.0% (method A, t_R = 2.04 min).

(3*R*,4*S*,5*S*,6*R*)-3,4,5,6-Tetrahydroxy-1-(2-hydroxyhexyl)azepan-2-one (10b). Compound **10b** was prepared from compound **9b** as described in the preparation of compound **7a**, yielding **10b** (95% yield) as a colorless oil: ^{1}H NMR (300 MHz, D_2O) δ 1.11-1.25 (m, 4H), 1.34-1.43 (m, 4H), 2.94 (m, 1H), 3.08-3.25 (m, 1H), 3.43 (t, *J* = 6.6 Hz, 2H), 3.50-3.74 (m, 5H), 4.41 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 25.4, 26.3, 27.2, 31.7, 48.1, 50.9, 62.3, 68.7, 69.3, 70.2, 73.4, 173.4; HRMS: Calcd for $C_{12}H_{23}NO_6Na$ $[M+Na]^+$, 300.1418; Found, 300.1415. HPLC: 96.9% (method A, t_R = 10.93 min).

(3*R*,4*S*,5*S*,6*R*)-1-Butyl-3,4,5,6-tetrahydroxyazepan-2-one (10c). Compound **10c** was prepared from compound **9c** as described in the preparation of compound **7a**, yielding **10c** (98% yield) as a colorless oil: ^{1}H NMR (300 MHz, D_2O) δ 0.73 (t, *J* =

7.2 Hz, 3H), 1.05-1.15 (m, 2H), 1.31-1.41 (m, 2H), 2.88 (m, 1H), 3.24 (m, 1H), 3.39-3.73 (m, 5H), 4.40 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 13.7, 20.0, 29.5, 48.0, 50.7, 63.0, 69.3, 70.2, 73.4, 173.4; HRMS: Calcd for $C_{10}H_{20}NO_5$ $[M+H]^+$, 234.1336; Found, 234.1330. HPLC: 97.1% (method A, t_R = 12.53 min).

(3*R*,4*S*,5*S*,6*R*)-1-Nonyl-3,4,5,6-tetrahydroxyazepan-2-one (10d). Compound **10d** was prepared from compound **9d** as described in the preparation of compound **7a**, yielding **10d** (95% yield) as an amorphous solid after lyophilization; ^{1}H NMR (300 MHz, CD_3OD) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.29 (s, 12H), 1.50-1.59 (m, 2H), 3.07 (brs, 1H), 3.61 (brs, 1H), 3.76-3.85 (m, 5H), 4.46 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.4, 23.7, 27.9, 28.6, 30.4, 30.5, 30.7, 33.0, 48.1, 51.5, 68.7, 70.4, 70.8, 74.6, 174.0; HRMS: Calcd for $C_{15}H_{29}NO_5Na$ $[M+Na]^+$, 326.1938; Found, 326.1936. HPLC: 98.0% (method A, t_R = 28.02 min).

(3*S*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-(2-hydroxyethyl)azepan-2-one (12a). Compound **12a** was prepared from compound **11**[1] as described in the preparation of **6a**. Yield: 83% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (brs, 2H), 3.47-3.81 (m, 6H), 4.10 (m, 3H), 4.42-4.98 (m, 7H), 7.18 (m, 2H), 7.30-7.37 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.5, 52.8, 61.1, 72.6, 73.4, 127.7, 127.8, 127.9, 128.1, 128.3, 128.3, 128.5, 137.4, 137.7, 170.4; HRMS: Calcd for $C_{29}H_{34}NO_6$ $[M+H]^+$, 492.2381; Found, 492.2391.

(3*S*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-butylazepan-2-one (12c). Compound **12c** was prepared from compound **11** as described in the preparation of **6a**. Yield: 90% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.25-1.37 (m, 2H), 1.46-1.55 (m, 2H), 2.38 (d, *J* = 9.0 Hz 1H), 2.98 (m, 1H), 3.27-3.33 (m, 1H), 3.60-3.67 (m, 2H), 3.77-3.84 (m, 2H), 4.06 (d, *J* = 4.5 Hz, 1H), 4.36-4.46 (m, 2H), 4.56-4.67 (m, 3H), 4.88-4.99 (m, 2H), 7.15-7.41 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 20.0, 30.1, 48.3, 48.5, 67.3, 72.4, 72.8, 73.4, 77.3, 78.6, 127.55, 127.64, 127.9, 128.0, 128.2, 128.3, 128.6, 137.2, 138.0, 138.2, 168.8; Anal. Calcd for

$C_{31}H_{37}NO_5$: C, 73.93; H, 7.41; N, 2.78; Found: C, 73.74; H, 7. 51; N, 2.66; ESI-MS: 504 $[M+H]^+$.

(3*S*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-hydroxy-1-nonylazepan-2-one (12d). Compound **12d** was prepared from compound **11** as described in the preparation of **6a**. Yield: 89% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 6:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.6 Hz, 3H), 1.24 (s, 12H), 1.49-1.54 (m, 2H), 2.41 (s, 1H), 2.96 (m, 1H), 3.26-3.31 (m, 1H), 3.58-3.71 (m, 2H), 3.76-3.84 (m, 2H), 4.05 (d, *J* = 4.8 Hz, 1H), 4.38 (d, *J* = 12.0 Hz, 2H), 4.55-4.69 (m, 3H), 4.88-4.99 (m, 2H), 7.13-7.20 (m, 2H), 7.26-7.41 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.03, 22.2, 26.7, 28.0, 29.2, 29.3, 29.4, 31.8, 48.2, 48.7, 67.2, 72.2, 72.7, 73.3, 77.2, 127.5, 127.6, 127.8, 127.9, 128.1, 128.2, 128.5, 137.1, 137.9, 138.1, 168.7; HRMS: Calcd for $C_{36}H_{48}NO_5$ $[M+H]^+$, 574.3528; Found, 574.3532.

(3*S*,4*S*,5*R*,6*R*)-1-(4-Methoxybenzyl)-3,4,5-tris(benzyloxy)-6-hydroxyazepan-2-one (12e). Compound **12e** was prepared from compound **11** as described in the preparation of **6a**. Yield: 89% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (brs, 1H), 2.92 (brs, 1H), 3.50-3.79 (m, 3H), 3.75 (s, 3H), 4.08 (d, *J* = 4.8 Hz, 1H), 4.20-4.25 (m, 1H), 4.36-4.46 (m, 2H), 4.55-4.64 (m, 2H), 4.73 (s, 1H), 4.94-5.07 (m, 3H), 6.67 (d, *J* = 8.1 Hz, 2H), 7.15-7.18 (m, 4H), 7.30-7.43 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.6, 51.02 55.1, 66.8, 72.4, 72.8, 73.6, 77.8, 113.7, 127.6, 127.7, 127.9, 128.2, 128.3, 128.6, 129.2, 129.7, 137.1, 137.9, 138.1, 158.9, 169.2; Anal. Calcd for $C_{35}H_{37}NO_6$: C, 74.05; H, 6.57; N, 2.47; Found: C, 73.82; H, 6.56; N, 2.45; ESI-MS: 568 $[M+H]^+$.

(3*S*,4*S*,5*R*,6*R*)-3,4,5,6-Tetrahydroxy-1-(2-hydroxyethyl)azepan-2-one (13a). Compound **13a** was prepared from compound **12a** as described in the preparation of compound **7a**, yielding **13a** (95% yield) as a colorless oil: ^{1}H NMR (300 MHz, D_2O) δ 2.89-2.93 (m, 1H), 3.27-3.35 (m, 1H), 3.39-3.62 (m, 4H), 3.74-3.89 (m, 3H), 4.73 (s, 1H); ^{13}C NMR (75 MHz, D_2O) δ 48.1, 51.5, 59.6, 66.5, 69.2, 72.3, 75.5, 173.8; HRMS: Calcd for $C_8H_{16}NO_6$ $[M+H]^+$, 244.0792; Found, 244.0791. HPLC: 99.9% (method A, t_R = 2.54 min).

(3*S*,4*S*,5*R*,6*R*)-1-Butyl-3,4,5,6-tetrahydroxyazepan-2-one (13c). Compound **13c** was prepared from compound **12c** as described in the preparation of compound **7a**, yielding **13c** (97% yield) as a colorless oil: ^{1}H NMR (300MHz, CD_3OD) δ 0.94 (t, *J* = 7.2 Hz, 3H), 1.29-1.40 (m, 2H), 1.50-1.60 (m, 2H), 2.85-2.90 (m, 1H), 3.45 (t, *J* = 7.2 Hz, 2H), 3.75-3.79 (m, 1H), 3.91-3.99 (m, 3H), 4.71 (s, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.2, 21.0, 31.0, 48.30, 49.8, 68.1, 70.1, 73.7, 76.8, 173.7; HRMS: Calcd for $C_{10}H_{20}NO_5$ $[M+H]^+$, 234.1336; Found, 234.1332. HPLC: 99.0% (method A, t_R = 12.45 min).

(3*S*,4*S*,5*R*,6*R*)-1-Nonyl-3,4,5,6-tetrahydroxyazepan-2-one (13d). Compound **13d** was prepared from compound **12d** as described in the preparation of compound **7a**, yielding **13d** (98% yield) as a colorless oil: ^{1}H NMR (300 MHz, CD_3OD) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.29 (s, 12H), 1.53-1.59 (m, 2H), 2.85-2.90 (m, 1H), 3.42-3.47 (m, 2H), 3.76-3.79 (m, 1H), 3.91-3.99 (m, 3H), 4.71 (s, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.5, 23.7, 27.8, 28.8, 30.4, 30.6, 30.7, 33.1, 48.3, 50.2, 68.1, 70.1, 73.7, 76.8, 173.7; HRMS: Calcd for $C_{15}H_{30}NO_5$ $[M+H]^+$, 304.2118; Found, 304.2123. HPLC: 100.0% (method A, t_R = 27.64 min).

(3*S*,4*S*,5*R*,6*R*)-1-(4-Methoxybenzyl)-3,4,5,6-tetrahydroxyazepan-2-one (13e). Compound **13e** was prepared from compound **12e** as described in the preparation of compound **7a**, yielding **13e** (98% yield) as an amorphous solid after lyophilization. ^{1}H NMR (300MHz, CD_3OD) δ 2.85-2.90 (m, 1H), 3.28-3.34 (m, 2H), 3.60-3.63 (m, 1H), 3.76 (s, 3H), 3.77-3.98 (m, 3H), 4.60 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR(75 MHz, CD_3OD) δ 48.1, 52.8, 56.2, 68.2, 70.9, 74.2, 77.6, 115.6, 130.5, 131.2, 161.3, 174.9; HRMS: Calcd for $C_{14}H_{19}NO_6Na$ $[M+Na]^+$, 320.1105; Found, 320.1101. HPLC: 98.0% (method A, t_R = 13.65 min).

(3*R*,4*R*,5*R*,6*S*)-4,5,6-Tris(benzyloxy)-1-butylazepan-3-yl benzoate (15c). BH_3-THF (1 M, 0.4 mL, 0.40 mmol) was added dropwise to the solution of lactam **14c** (61 mg, 0. 10 mmol) in anhydrous THF (10 mL) at 0 °C under nitrogen, and after stirring for 20 min at room temperature, the solution was heated under reflux for 4 h. Then the mixture was cooled to 0 °C, 6N HCl (1 mL) was added dropwise until no further

evolution of gas occurred. After heating under reflux for 30 min, the mixture was concentrated under reduced pressure. This acidic residue was diluted with water, basified with solid NaOH and then extracted with CH_2Cl_2 (50 mL). The combined organic phase was washed by water (15 mL ×2), dried, concentrated and the residue was purified by column chromatography (petroleum ether-ethyl acetate, 3:1) on silica gel to provide compound **15c** (56 mg, 94%) as colorless and amorphous solids. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.26-1.33 (m, 2H), 1.35-1.43 (m, 2H), 2.49-2.58 (m, 2H), 2.79 (dd, *J* = 1.5, 14.0 Hz, 1H), 2.86 (dd, *J* = 4.0, 12.5 Hz, 1H), 2.95 (dd, *J* = 10.0, 14.0 Hz, 1H), 3.09 (dd, *J* = 8.0, 12.0 Hz, 1H), 3.73-3.77 (m, 1H), 3.90 (dd, *J* = 5.0, 6.5 Hz, 1H), 3.96 (d, *J* = 5.0 Hz, 1H), 4.62-4.71 (m, 6H), 5.47-5.50 (m, 1H), 7.23-7.36 (m, 15H), 7.42-7.45 (m, 2H), 7.54-7.58 (m, 1H), 8.00-8.02 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 20.4, 29.7, 53.7, 54.5, 56.9, 72.4, 72.5, 72.6, 73.4, 79.8, 82.8, 82.9, 127.5, 127.6, 127.8, 127.9, 128.0, 128.3, 128.4, 129.7, 130.4, 133.0, 138.2, 138.5, 138.6, 165.5; HRMS: Calcd for $C_{38}H_{44}NO_5$ $[M+H]^+$, 594.3214; Found, 594.3216.

(**3*R*,4*R*,5*R*,6*S*)-1-Butyl-tetrahydroxyazepane (7c')**. Compound **15c** (52 mg, 0.088 mmol) was dissolved in methanol (10 mL), to which NaOMe (1 M solution in methanol, 1 mL, 1 mmol) was added and the resulting solution was stirred for 30 min at room temperature. Dowex 50w H^+ resin was added to neutralize the solution (pH = 7), after which the resin was removed by filtration and washed with ethyl acetate. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel (petroleum ether-ethyl acetate, 3:1) to afford a colorless oil. The oil was dissolved in THF-H_2O-HOAc (4:2:1, 7 mL), and 10% Pd-C (10.0 mg) was added. The mixture was stirred under hydrogen atmosphere (4 atm) for 48 h. The catalyst was then removed by filtration through Celite, and the filtrate was concentrated. The residue was subjected to a C-18 reversed-phase column chromatography (eluent, H_2O) to give **7c'** (22 mg, 92%) as an amorphous solid after lyophilization in the form of acetic acid salt. ^{1}H NMR (300 MHz, D_2O): δ 0.76 (t, *J* = 7.2 Hz, 3H), 1.14-1.26 (m, 2H), 1.50-1.60 (m, 2H), 1.74 (s, 3H), 3.07 (t, *J* = 8.1 Hz,

2H), 3.19 (t, *J* = 14.4 Hz, 2H), 3.31-3.40 (m, 2H), 3.57-3.64 (m, 2H), 3.78 (t, *J* = 6.6 Hz, 1H), 4.10 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 13.3, 19.7, 26.1, 54.8, 55.0, 59.2, 67.3, 68.2, 74.8, 75.5; HRMS: Calcd for $C_{10}H_{21}NO_4Na$ $[M+Na]^+$, 242.1363; Found, 242.1364. HPLC: 97.9% (method B, t_R = 3.03 min).

(3*R*,4*S*,5*R*,6*S*)-4,5,6-Tris(benzyloxy)-1-butylazepan-3-yl benzoate (16c). Compound **16c** was prepared from compound **9c** as described in the preparation of **15c**. Yield: 92% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.2 Hz, 3H), 1.26-1.36 (m, 4H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.79 (dd, *J* = 3.0, 14.4 Hz, 1H), 2.97-3.04 (m, 3H), 3.57-3.59 (m, 1H), 4.10 (dd, *J* = 6.0, 14.4 Hz, 1H), 4.39 (d, *J* = 7.2 Hz, 1H), 4.50-4.66 (m, 5H), 4.76 (d, *J* = 12.0 Hz, 1H), 5.32-5.34 (m, 1H), 7.19-7.55 (m, 18H), 7.99-8.02 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 20.2, 29.5, 58.4, 58.6, 59.5, 71.4, 72.6, 73.1, 76.0, 77.8, 79.4, 79.7, 127.36, 127.45, 127.51, 127.6, 127.8, 128.2, 128.3, 129.7, 130.5, 132.8, 138.47, 138.51, 138.7, 166.1; HRMS: Calcd for $C_{38}H_{44}NO_5$ $[M+H]^+$, 594.3214; Found, 594.3221.

(3*R*,4*S*,5*R*,6*S*)-1-Butyl-tetrahydroxyazepane (10c'). Compound **10c'** was prepared from compound **16c** as described in the preparation of **7c'**, providing compound **10c'** as an amorphous solid after lyophilization in the form of acetic acid salt. Yield: 95% after two steps. ^{1}H NMR (300 MHz, D_2O): δ 0.75 (t, *J* = 7.2 Hz, 3H), 1.12-1.25 (m, 2H), 1.46-1.57 (m, 2H), 1.73 (s, 3H), 2.93-2.98 (m, 2H), 3.12 (dd, *J* = 4.8, 13.8 Hz, 2H), 3.28 (dd, *J* = 2.7, 14.1 Hz, 2H), 3.88-3.94 (m, 4H); ^{13}C NMR (75 MHz, D_2O) δ 13.4, 19.9, 23.8, 26.2, 57.3, 59.9, 67.7, 73.0; HRMS: Calcd for $C_{10}H_{21}NO_4Na$ $[M+Na]^+$, 242.1363; Found, 242.1363. HPLC: 98.3% (method B, t_R = 3.09 min).

(3*R*,4*S*,5*R*,6*R*)-1-Benzyl-3,4,5-tris(benzyloxy)-6-hydroxyazepan-2-one (17). Compound **17** was prepared from compound **4** as described in the preparation of **6a**. Yield: 92% as colorless oil after column chromatography (petroleum ether-ethyl acetate, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.54 (d, *J* = 8.1 Hz, 1H), 3.24 (d, *J* = 14.4 Hz, 1H), 3.61-3.64 (m, 2H), 3.74 (m, 1H), 3.96 (t, *J* = 5.7 Hz, 1H), 4.25-4.31 (m, 2H), 4.37 (d, *J* = 6.0 Hz, 1H), 4.42-4.51 (m, 2H), 4.64-4.71 (m, 2H), 4.80 (d, *J* = 11.7 Hz,

1H), 4.89 (d, *J* = 14.4 Hz, 1H), 7.17-7.33 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.3, 51.9, 67.4, 72.5, 73.2, 73.6, 79.9, 81.8, 127.5, 127.8, 127.9, 128.0, 128.1, 128.40, 128.44, 128.5, 137.3, 137.6, 137.7, 169.2; HRMS: Calcd for $C_{34}H_{36}NO_5$ $[M+H]^+$, 538.2588; Found, 538.2581.

(3*R*,4*R*,5*R*,6*S*)-1-Benzyl-4,5,6-tris(benzyloxy)azepan-3-yl benzoate (18). Compound **18** was prepared from compound **17** as described in the preparation of **15c**. Yield: 86% after two steps as colorless oil after column chromatography (petroleum ether-ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.78-2.82 (m, 1H), 2.89-2.95 (m, 2H), 3.13 (dd, *J* = 8.4, 12.3 Hz, 1H), 3.64 (d, *J* = 13.5 Hz, 1H), 3.72-3.81 (m, 2H), 3.89 (t, *J* = 4.8 Hz, 1H), 3.99 (d, *J* = 4.8 Hz, 1H), 4.36 (ABq, *J* = 11.4 Hz, 2H), 4.61-4.72 (m, 4H), 5.56 (dd, *J* = 3.9, 7.5 Hz, 1H), 7.18-7.36 (m, 20H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.99 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.5, 54.7, 61.7, 71.9, 72.5, 72.6, 73.4, 79.9, 82.6, 83.2, 127.1, 127.5, 127.6, 127.75, 127.80, 128.0, 128.3, 128.8, 129.7, 130.3, 133.0, 138.1, 138.4, 138.5, 139.0, 165.4; HRMS: Calcd for $C_{41}H_{42}NO_5$ $[M+H]^+$, 628.3057; Found, 628.3057.

(3*R*,4*R*,5*R*,6*S*)-3,4,5,6-Tetrahydroxyazepane (19). Compound **18** (50 mg, 79.6 μmol) was dissolved in methanol (10 mL), to which NaOMe (1 M solution in methanol, 1 mL, 1 mmol) was added and the resulting solution was stirred for 30 min at room temperature. Dowex 50w H^+ resin was added to neutralize the solution (pH = 7), after which the resin was removed by filtration and washed with ethyl acetate. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel (petroleum ether-ethyl acetate, 3:1) to afford a colorless oil (42 mg). This oil was dissolved in methanol (5 mL), and 10% Pd-C (10.0 mg) was added. To the solution 2N HCl was added dropwise to adjust pH = 2. The mixture was stirred under hydrogen atmosphere (4 atm) for 48 h. The catalyst was then removed by filtration through Celite, and the filtrate was concentrated. The residue was subjected to a C-18 reversed-phase column chromatography (eluent, H_2O) to give compound **19** (14 mg, 92%) as an amorphous solid after lyophilization in the form of hydrochloride salt. ^{1}H NMR (300 MHz, D_2O) δ 3.08-3.32 (m, 4H), 3.59-3.67 (m, 2H),

3.76-3.81 (m, 1H), 4.12 (d, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 46.7, 46.9, 67.7, 68.6, 75.2, 75.7. The spectroscopic data of compounds **19** coincided with those reported in the literature.[2]

(3*R*,4*R*,5*R*,6*R*)-1-(4-Methoxybenzyl)-4,5,6-tris(benzyloxy)azepan-3-yl benzoate (20). Compound **20** was prepared from compound **12e** as described in the preparation of **15c**. Yield: 70% after two steps as colorless oil after column chromatography (petroleum ether-ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.78-2.90 (m, 2H), 2.99 (dd, *J* = 7.8, 12.9 Hz, 1H), 3.13 (dd, *J* = 7.8, 12.9 Hz, 1H), 3.67 (s, 2H), 3.76 (s, 3H), 4.04-4.12 (m, 3H), 4.49-4.79 (m, 6H), 5.62-5.67 (m, 1H), 6.74 (d, *J* = 9.0 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.24-7.37 (m, 15H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.97 (d, *J* = 7.2, Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.07, 53.42, 55.18, 61.79, 71.40, 71.87, 73.27, 73.32, 76.64, 79.05, 79.60, 113.52, 127.39, 127.42, 127.50, 127.72, 128.25, 129.66, 129.76, 130.40, 131.26, 132.85, 138.41, 138.62, 138.80, 158.54, 165.67; HRMS: Calcd for $C_{42}H_{44}NO_6$ [M+H$^+$], 658.3163; Found, 658.3168.

(3*R*,4*R*,5*R*,6*R*)-3,4,5,6-Tetrahydroxyazepane (21). Compound **21** was prepared from compound **20** as described in the preparation of compound **19**, providing compound **21** as colorless oil in the form of hydrochloride salt. Yield: 91% after two steps; ^{1}H NMR (300 MHz, D_2O) δ 3.25-3.27 (m, 4H), 3.71 (s, 2H), 4.16 (m, 2H); ^{13}C NMR (75 MHz, D_2O) δ 45.7, 67.5, 73.8. The spectroscopic data of compounds **21** coincided with those reported in the literature.[3]

Biology Section

Cell culture. HL60 cells and Gaucher lymphoblasts (N370S) were cultured in RPMI1640 medium supplemented with 10% or 15% (v/v) foetal bovine serum, respectively, 2 mM L-glutamine, 100 U/mL penicillin and 100 mg/mL streptomycin at 37 ºC and 5 % CO_2.

Cytotoxicity assay. HL60 cells were seeded at densities of 500 cells / well in 96-well plates in 200 µL of supplemented media containing either 0.01 % DMSO or water as

controls, and concentrations up to 250 µM of each compound added for 3 days. Cell viability was assessed in triplicate using the Cell Titer-96 AQueous cellular proliferation assay kit according to manufacturer's (Promega, Southampton, UK) instructions.

ß-Glucocerebrosidase inhibition assay. Human placental ß-glucocerebrosidase was isolated and partially purified from modified procedure of Furbish and co-workers.[4] Enzyme activity was measured in 50 µL of 5 mM 4-methylumbelliferyl-ß-glucoside in 0.1 M citrate phosphate buffer, pH 5.2 containing 0.25% sodium taurocholate, 0.1 % TX100 at 37 °C for 15-60 min. The reaction was stopped by the addition of 200 µL of 0.5 M sodium carbonate and the fluorescence measured at ex 350 nm, em 460 nm. Inhibition constants were generated for placental *ß*-glucocerebrosidase (Km for 4-MU-ß-glucoside, 1.9 ± 0.3 mM) using 0.1 mM to 3 mM substrate concentrations for Ki determinations or 0.5 mM substrate for IC_{50} determinations.

ß-Glucocerebrosidase activation assay. HL60 cells and Gaucher lymphoblasts (N370S) were cultured in the presence of various concentrations of inhibitor (0-50 µM) for 3 days before *ß*-glucocerebrosidase activity was measured. Cells were washed twice in phosphate buffered saline, homogenized in water using a small dounce homogenizer, centrifuged at 800g for 5 min and the supernatant taken for protein and ß-glucocerebrosidase activity. Protein concentration was determined using the BCA assay (Pierce, UK) according to manufacturer's instructions. All enzyme activation measurements were made using aliquots of homogenate and 5 mM 4-methylumbelliferyl-*ß*-glucoside in 0.1 M citrate phosphate buffer, pH 5.2 containing 0.25% sodium taurocholate, 0.1 % TX100 as described above. Bromoconduritol (500 µM - 2.5 mM) was added to some enzyme activity determinations to confirm the specific hydrolysis of substrate by ß-glucocerebrosidase. Enzyme activation is defined as the fold increase in enzyme activity (U/mg protein) in treated cells compared to untreated cells. The activation of *N*-nonyl-DNJ in various concentrations is shown in the Supporting Information.

The activations of *N*-nonyl-DNJ in various concentrations for N370S GC is shown in Figure 1.

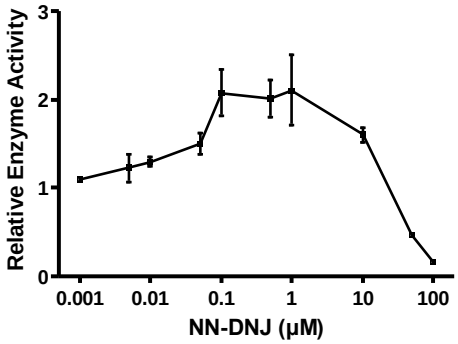

Fig. 1. The influence of *N*N-DNJ to *β*-glucocerebrosidase activities in N370S Gaucher lymphoblasts. The fold increase in enzyme activity is compared to untreated cells, ie., normalised value = 1 and shown as relative enzyme activity. The mean and SD obtained from an experiment performed in triplicate are shown.

Computer Section

Compound **7d** were flexibly docked into the binding site of GC (PDB code: 2V3E, chain B, complexed with NN-DNJ)[5] using AutoDock 3.05 program.[6] Default parameters were used as described in the AutoDock manual unless otherwise specified. The molecule was docked with 100 genetic algorithm runs of up to 250,000 energy evaluations in the docking study of compound **7d** with the binding site. Docking result with the lowest energy was then selected for further energy minimization, for the consideration of induced conformational changes in the amino acid side chains of the protein and an energy-optimum binding mode.

Energy minimization calculations were done within the Amber Molecular Dynamics Package version 8.0 with an Amber99 force field.[7] The geometries and partial atomic charges (AM1-BCC charges) for compound **7d** was computed using Divcon and Antechamber modules so as to obtain the molecular mechanical parameters of it. With the backbone atoms of the GlcCerase was fixed by a large constraint of 500 kcal mol^{-1} $Å^{-2}$, the selected docking complex of compound **7d**-GC was energetically minimized in Sander module with 500 steps of steepest descent minimization,

followed by 500 steps of conjugate gradient minimization. A cutoff of 12 Å was used for the Lennard-Jones interactions. The optimized docking complex was analyzed with in-house software and Pymol 0.99. The geometric criterion for the formation of H-bonds is common with a donor-acceptor distance less than 3.5 Å and the donor-H-acceptor angle larger than 120°.

References:

(1) R. Namme, T. Mitsugi, H. Takahashi, M. Shiro and S. Ikegami, *Tetrahedron* 2006, **62**, 9183-9192.

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(5) B. Brumshtein, H. M. Greenblatt, T. D. Butters, Y. Shaaltiel, D. Aviezer, I. Silman, A. H. Futerman and J. L. Sussman, *J. Biol. Chem.* 2007, **282**, 29052-29058.

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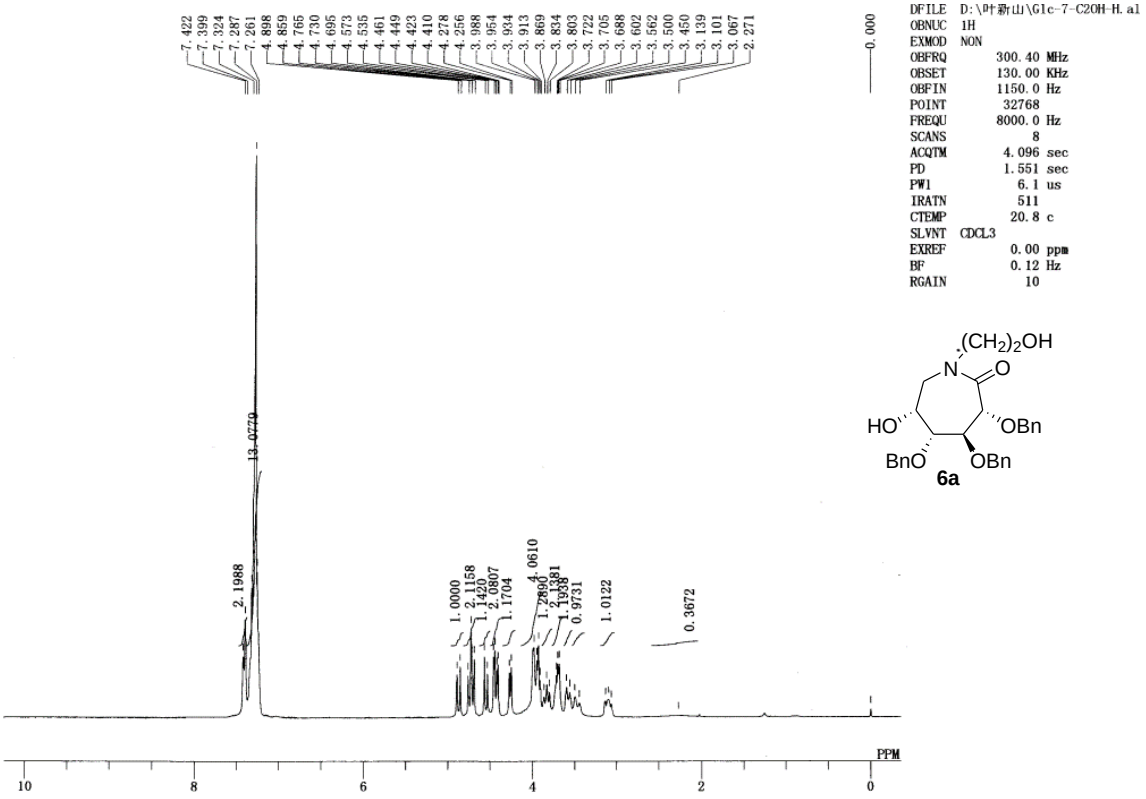
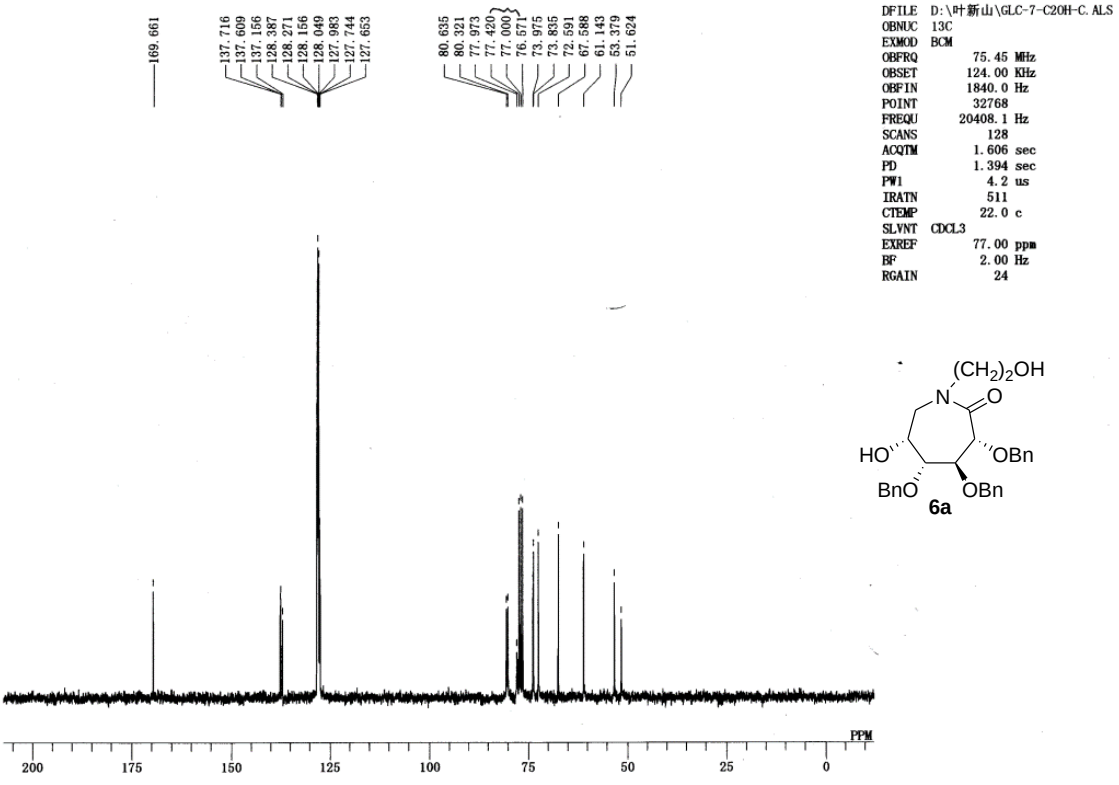
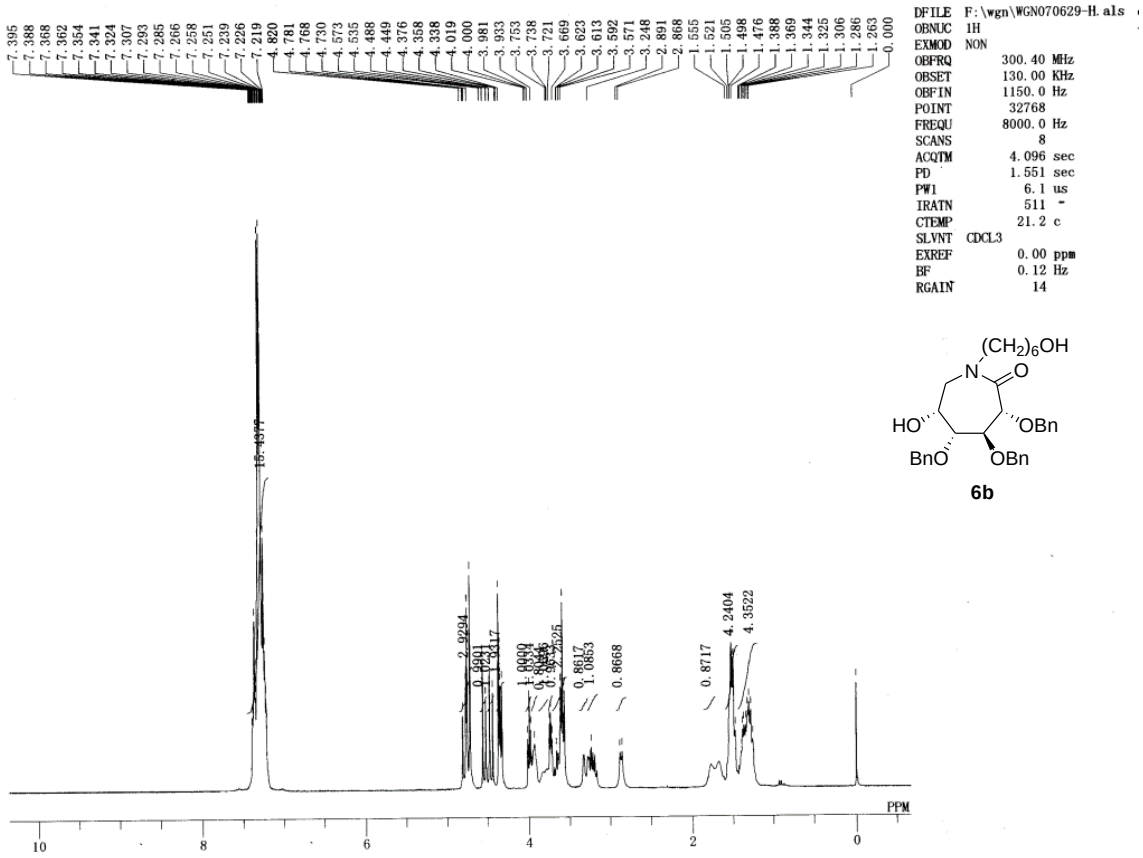
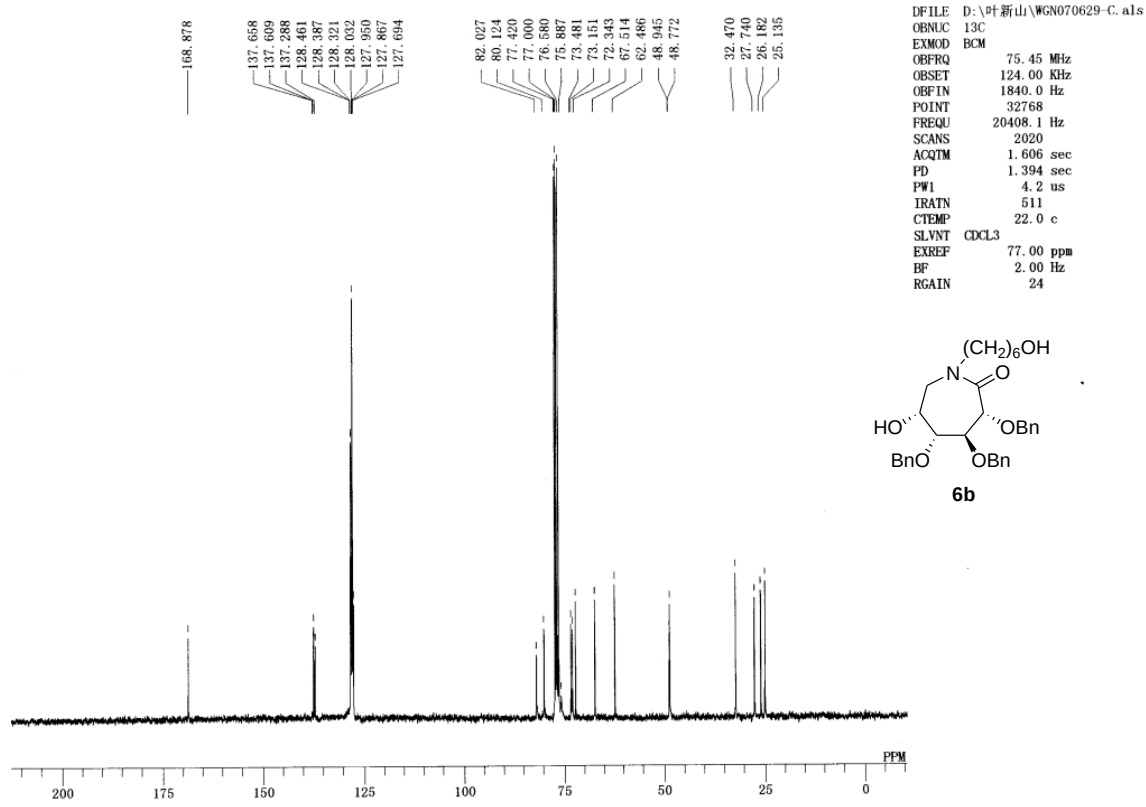
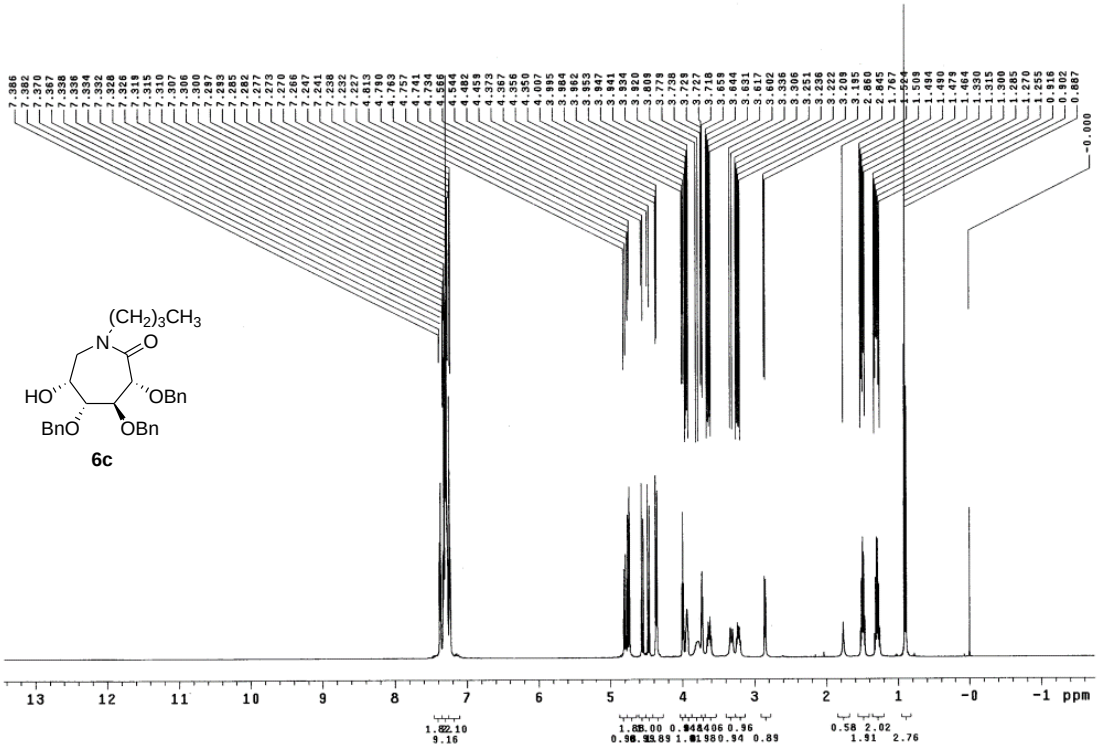
(7) D. A. Pearlman, D. A. Case, J. W. Caldwell, W. S. Ross, T. E. Cheatham, S. Debolt, D. Ferguson, G. Seibel and P. Kollman, *Comput. Phys. Commun.* 1995, **91**, 1-41.







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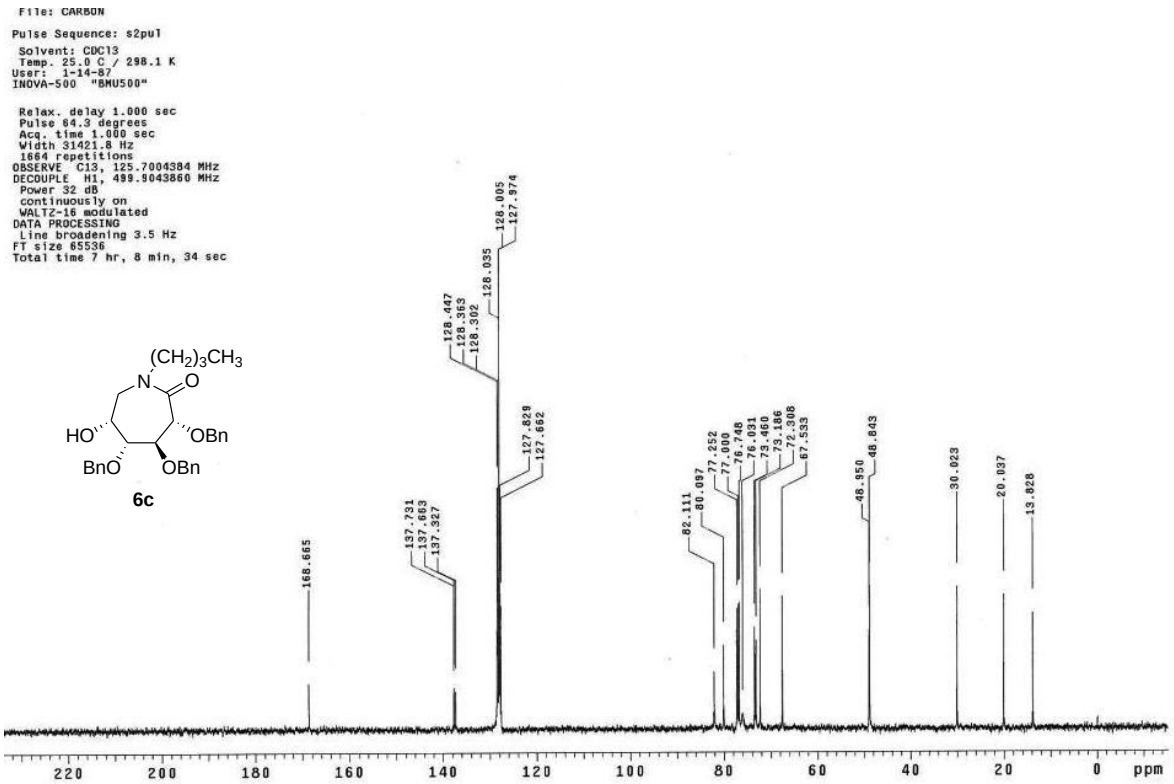
N
O
HO
OBn
BnO
OBn
6c
ppm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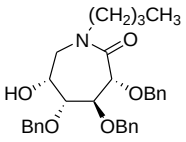
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "8MU500"
Relax. delay 1.000 sec
Pulse 84.3 degrees
Acq. time 1.000 sec
Width 31421.8 Hz
1664 repetitions
OBSERVE C13, 125.7004384 MHz
DECOUPLE H1, 499.9043860 MHz
Power 32 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.5 Hz
FT size 65536
Total time 7 hr, 8 min, 34 sec
(CH2)3CH3
N
O
HO
OBn
BnO
OBn
6c
ppm

glc-7-C4-2

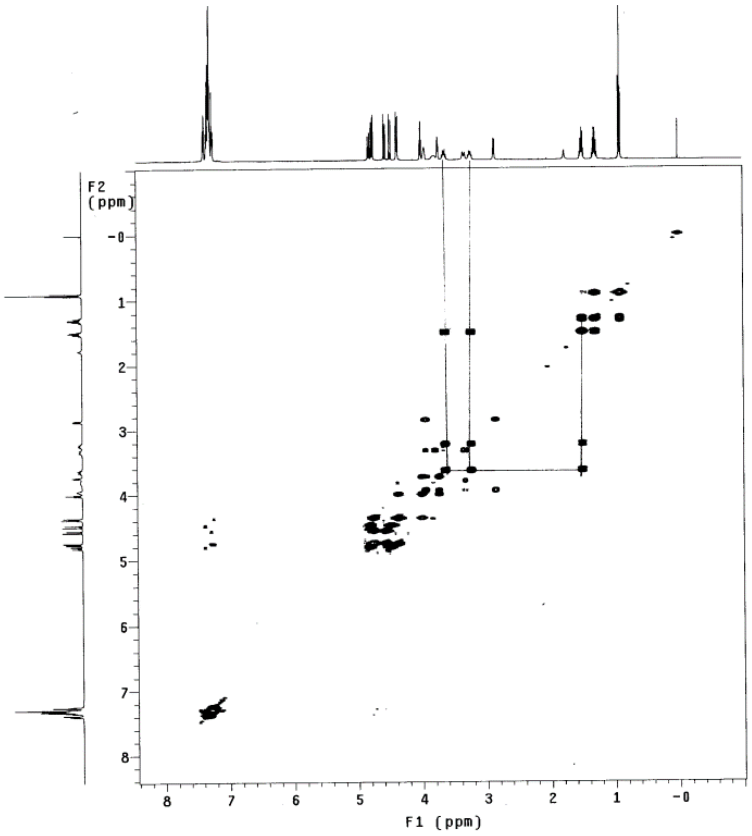
File: PROTON

Pulse Sequence: gCOSY
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
INOVA-500 "BMU500"

Relax. delay 1.000 sec
Acq. time 0.217 sec
Width 4717.5 Hz
2D Width 4717.5 Hz
16 repetitions
300 increments
OBSERVE H1, 499.9019053 MHz
DATA PROCESSING
Sq. sine bell 0.109 sec
F1 DATA PROCESSING
Sq. sine bell 0.033 sec
FT size 4096 x 4096
Total time 1 hr, 41 min, 16 sec



6c



glc-7-C4-2

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INOVA-500 "BMU500"

Relax. delay 1.000 sec
Mixing 0.600 sec
Acq. time 0.213 sec
Width 4810.0 Hz
2D Width 4810.0 Hz
32 repetitions
2 x 256 increments
OBSERVE H1, 499.9019053 MHz
DATA PROCESSING
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F1 DATA PROCESSING
Gauss apodization 0.027 sec
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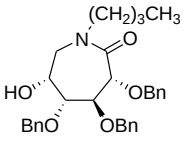

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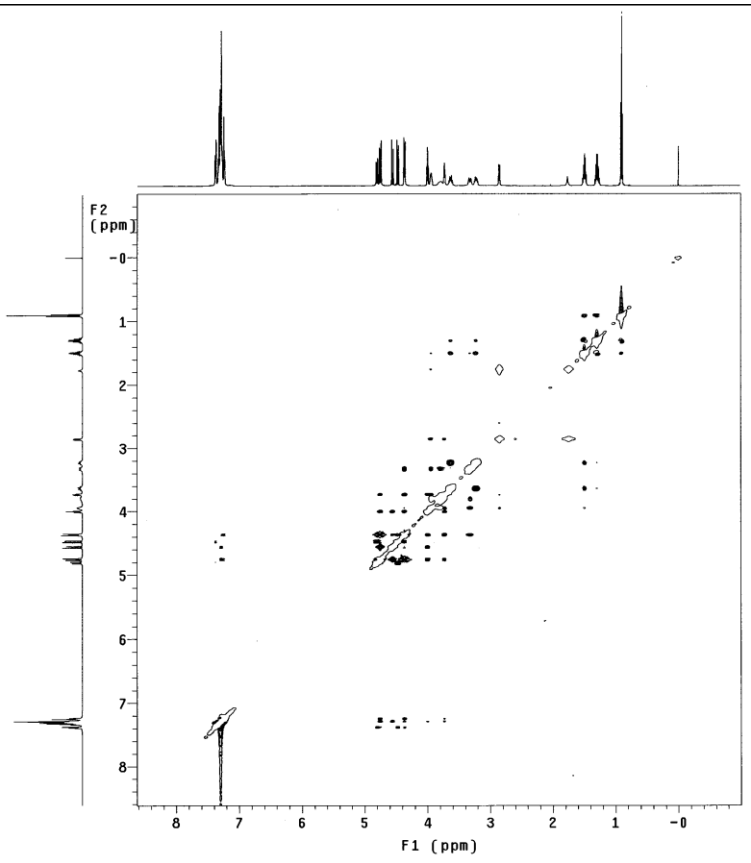

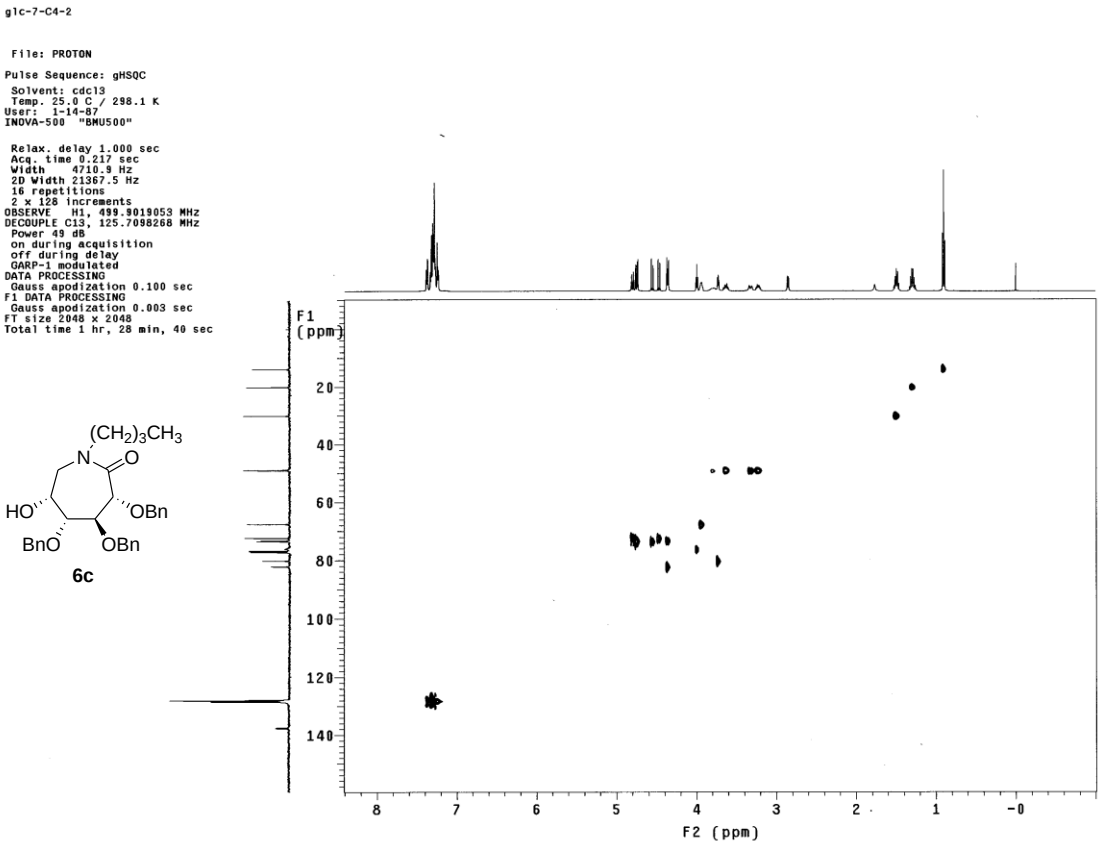
glc-7-C4-2
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Solvent: cdcl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
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Relax. delay 1.000 sec
Acq. time 0.217 sec
Width 4710.9 Hz
2D Width 21367.5 Hz
16 repetitions
2 x 128 increments
OBSERVE H1, 499.9019053 MHz
DECOUPLE C13, 125.7098268 MHz
Power 49 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Gauss apodization 0.100 sec
F1 DATA PROCESSING
Gauss apodization 0.003 sec
FT size 2048 x 2048
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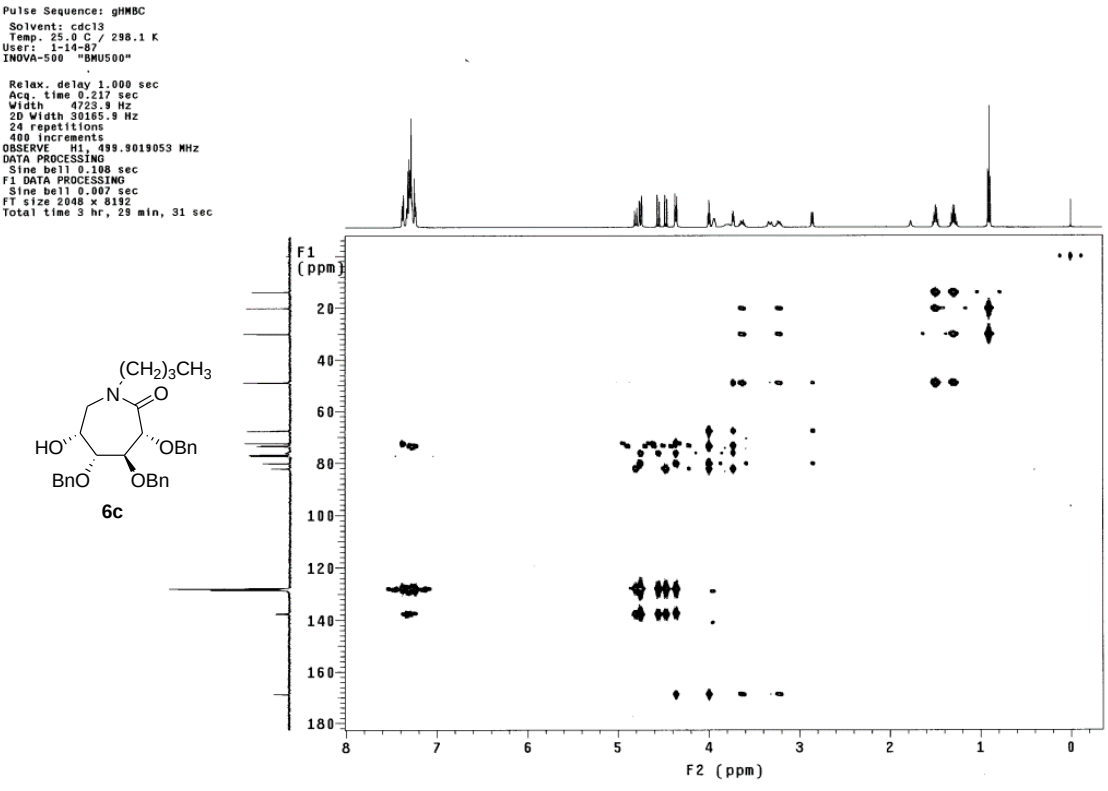
(CH2)3CH3
N
O
HO
OBn
BnO
OBn
6c
F1 (ppm)
F2 (ppm)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Solvent: cdcl3
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User: 1-14-87
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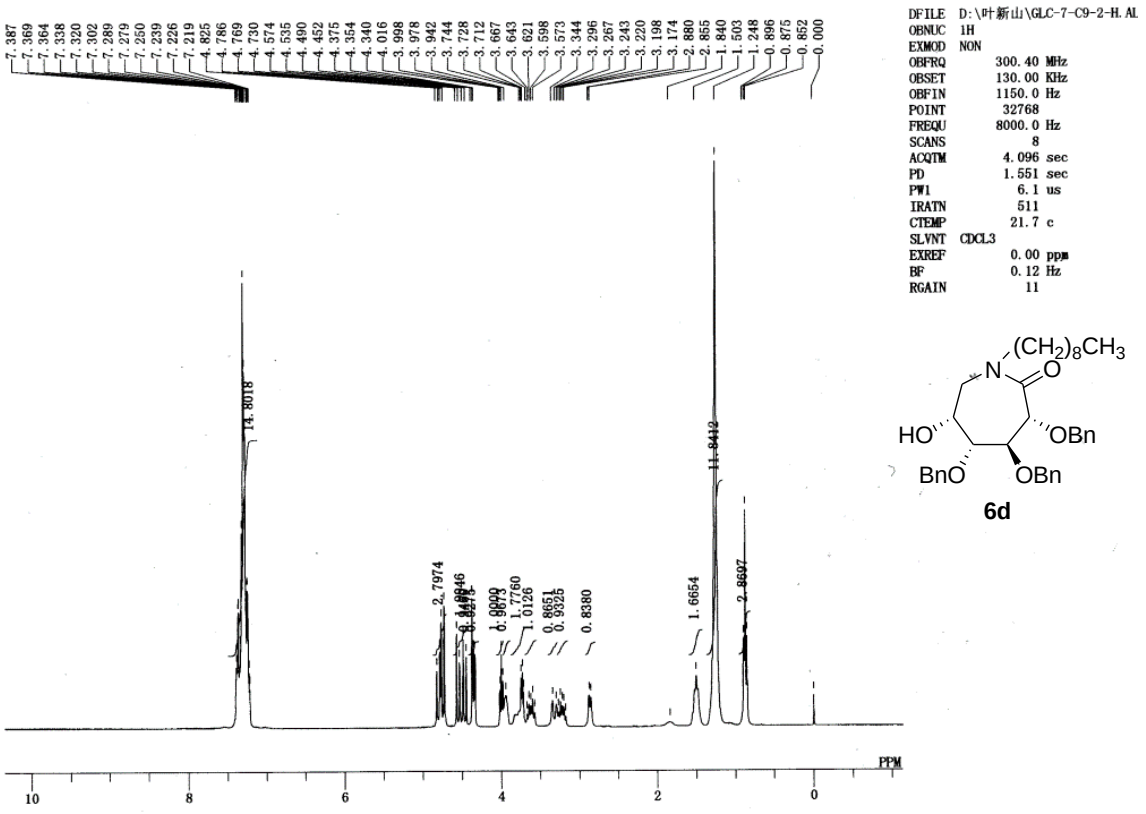
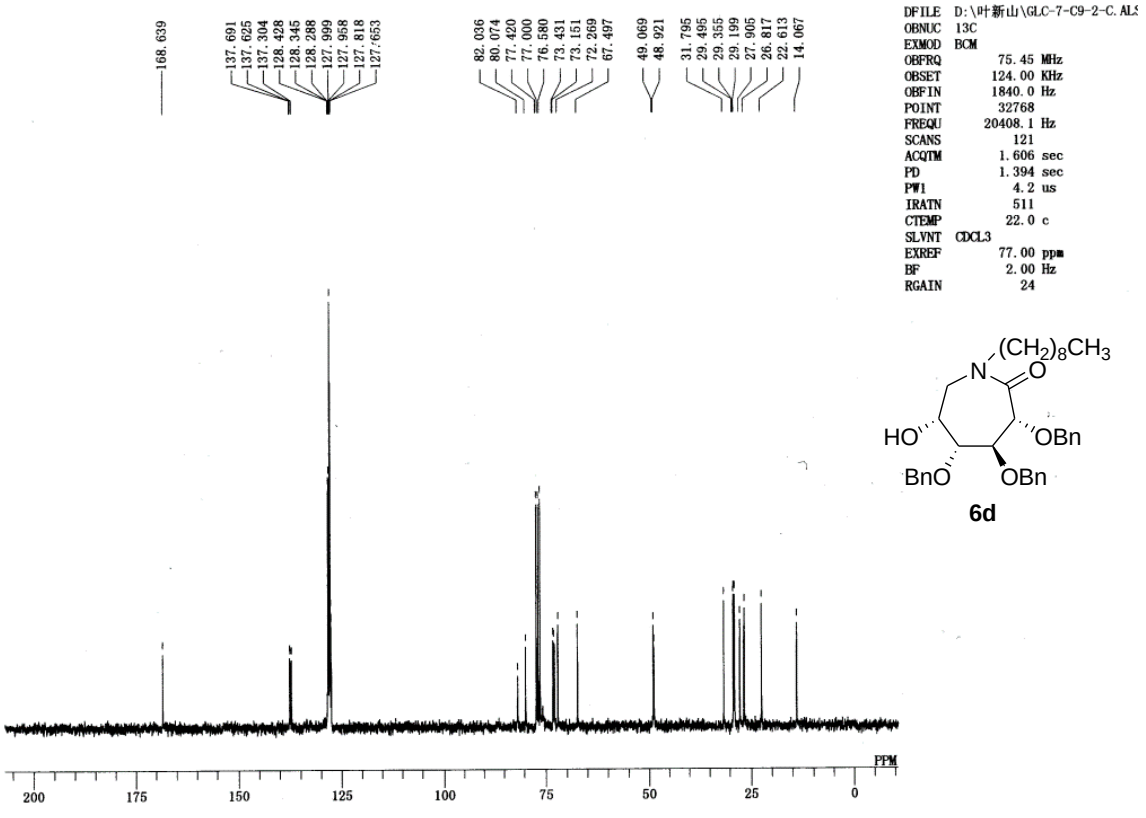
Relax. delay 1.000 sec
Acq. time 0.217 sec
Width 4723.9 Hz
2D Width 30165.9 Hz
24 repetitions
400 increments
OBSERVE H1, 499.9019053 MHz
DATA PROCESSING
Sine bell 0.108 sec
F1 DATA PROCESSING
Sine bell 0.007 sec
FT size 2048 x 8192
Total time 3 hr, 29 min, 31 sec
(CH2)3CH3
N
O
HO
OBn
BnO
OBn
6c
F1 (ppm)
F2 (ppm)



6d



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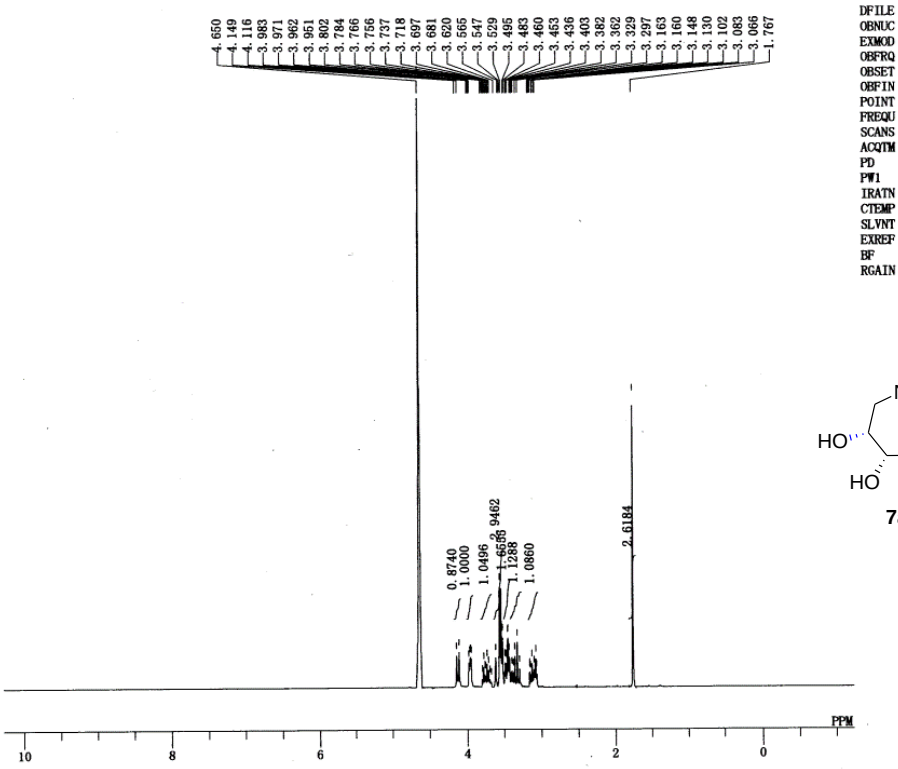

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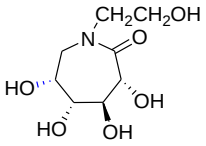
CTEMP 20.7 c
SLVNT D2O
EXREF 4.65 ppm
BF 0.12 Hz
RGAIN 13



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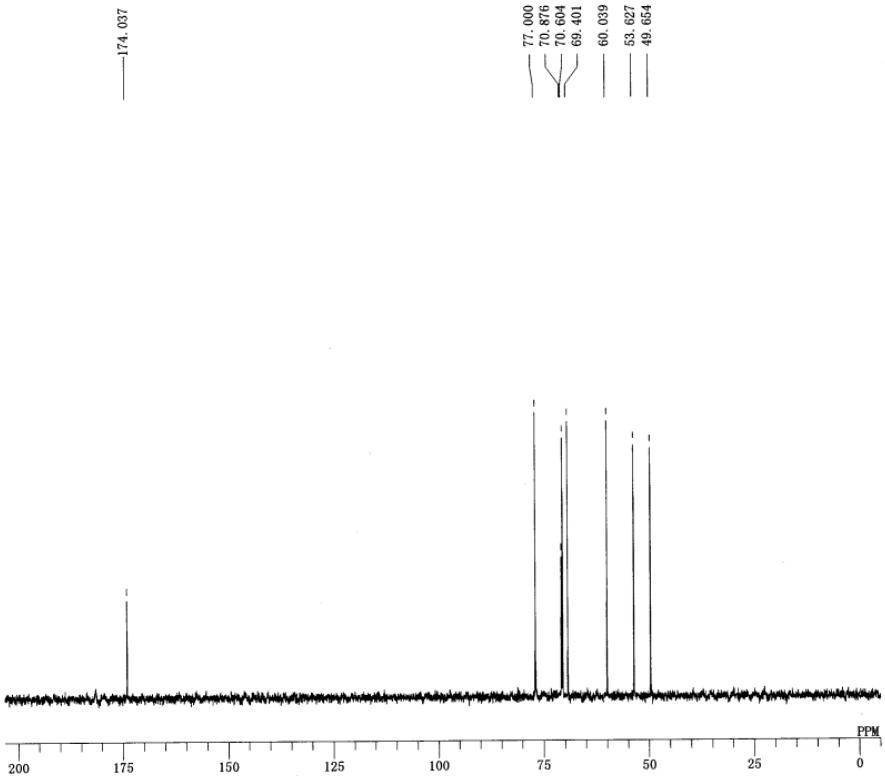

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SCANS 865
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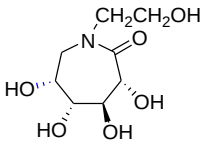

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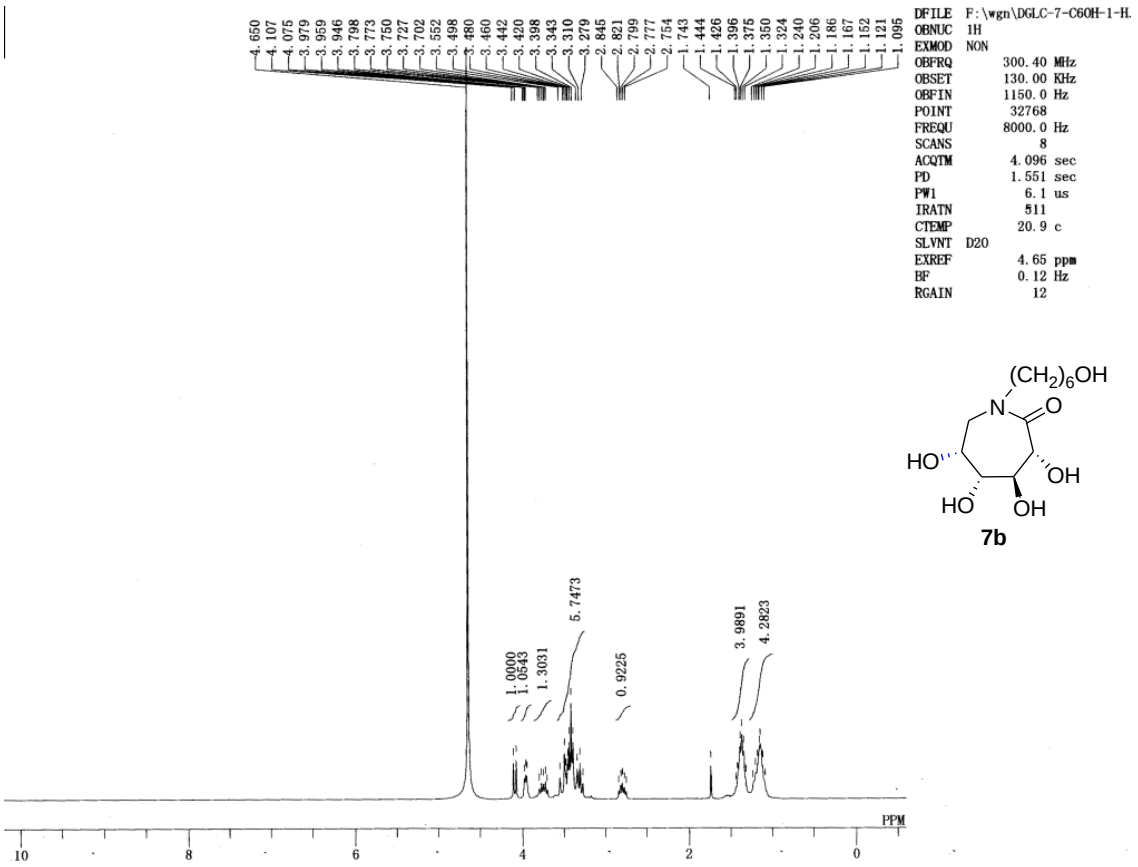

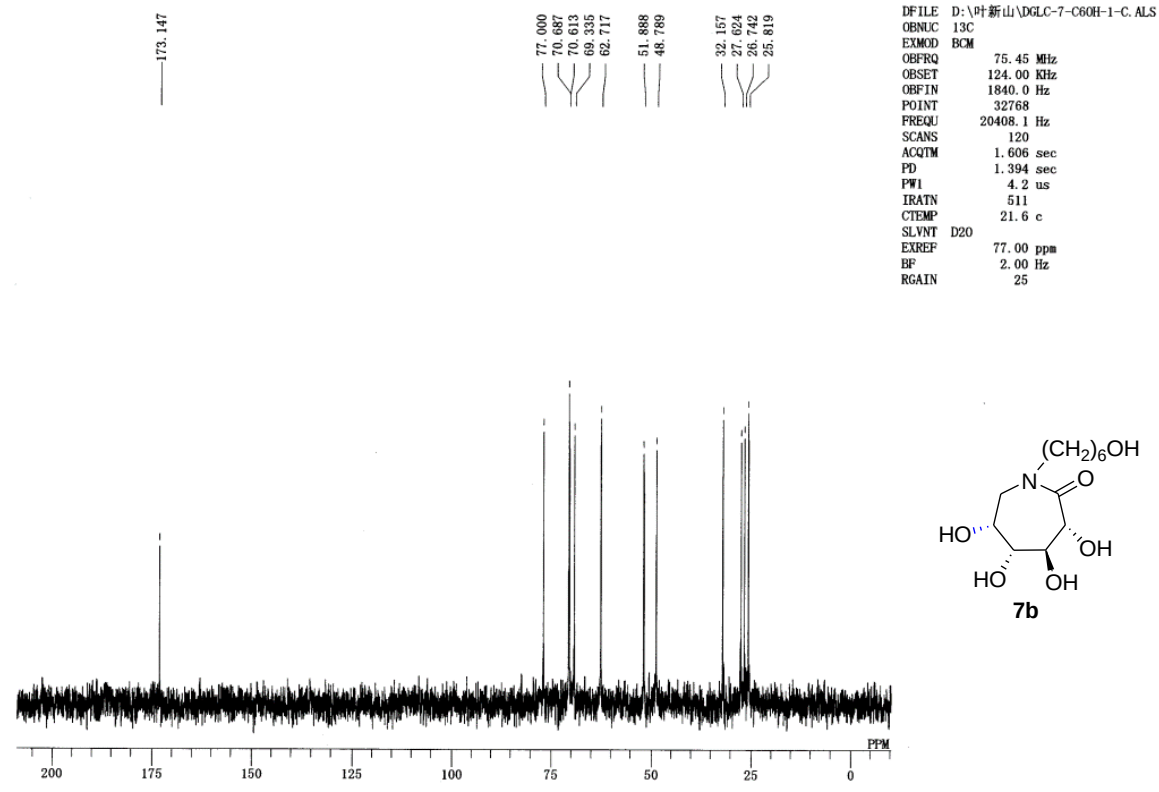

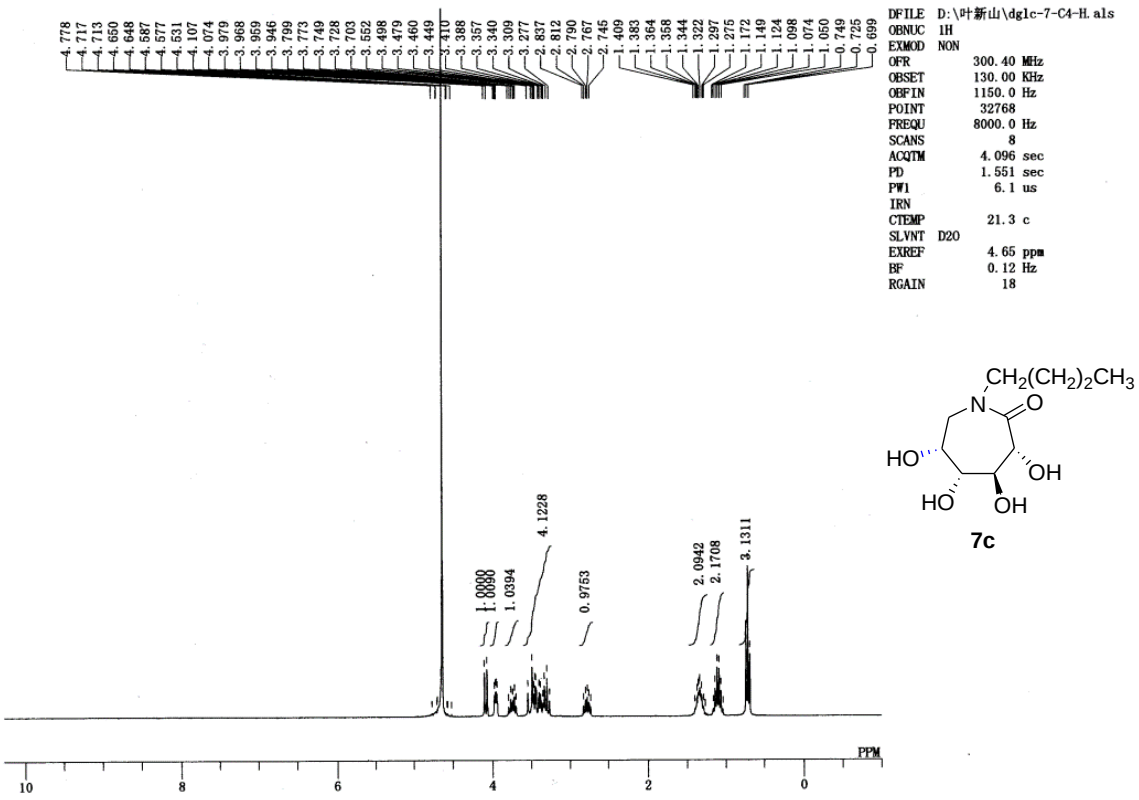
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IRN
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SLVNT D2O
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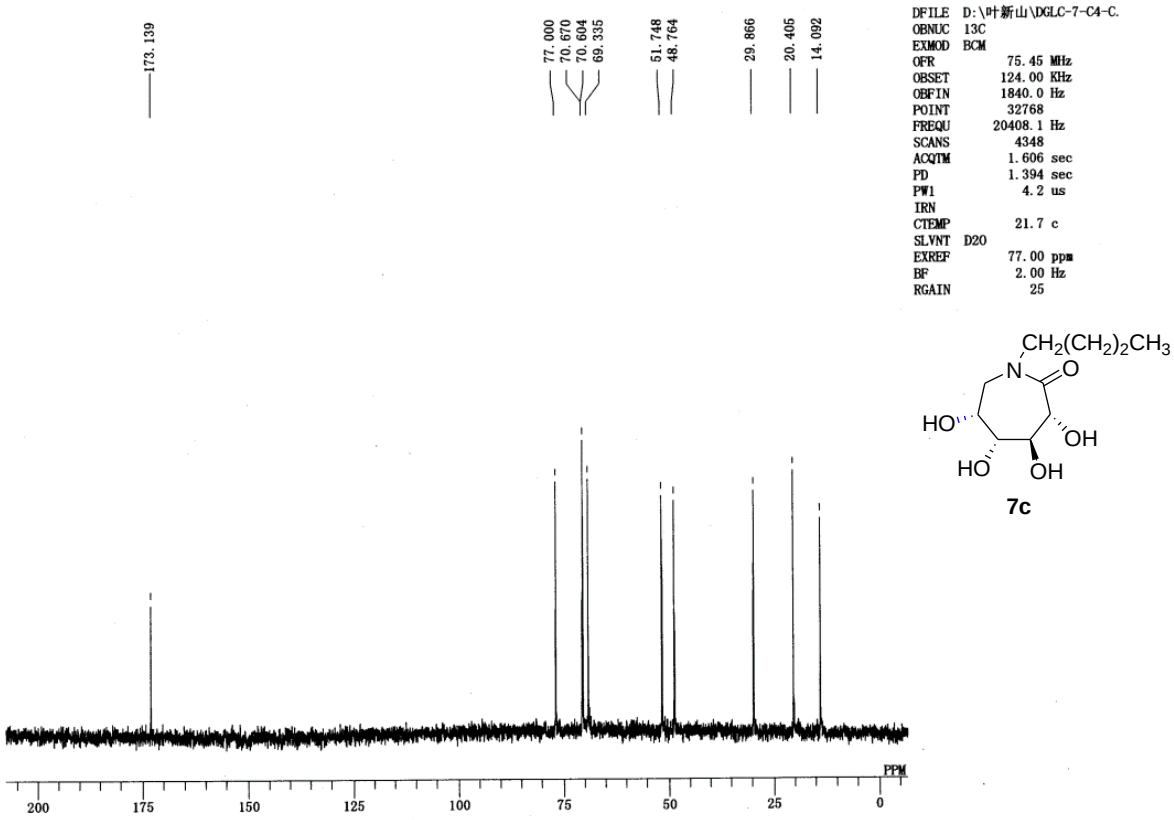
BF 0.12 Hz
RGAIN 18
1.0000
0.8880
1.0394
4.1228
0.9753
2.0942
2.1708
3.1311
PPM
10
8
6
4
2
0

CH2(CH2)2CH3
N
O
HO
OH
HO
OH

7c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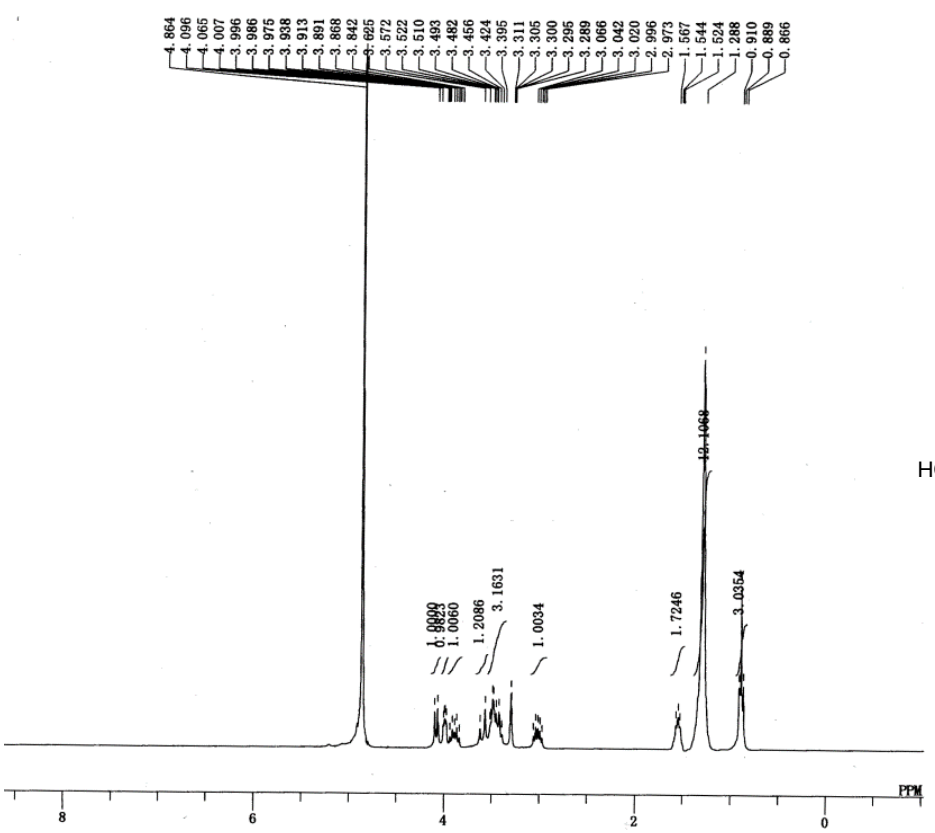
PD 1.394 sec
PW1 4.2 us
IRN
CTEMP 21.7 c
SLVNT D2O
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 25
PPM
200
175
150
125
100
75
50
25
0

CH2(CH2)2CH3
N
O
HO
OH
HO
OH

7c



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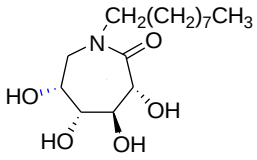
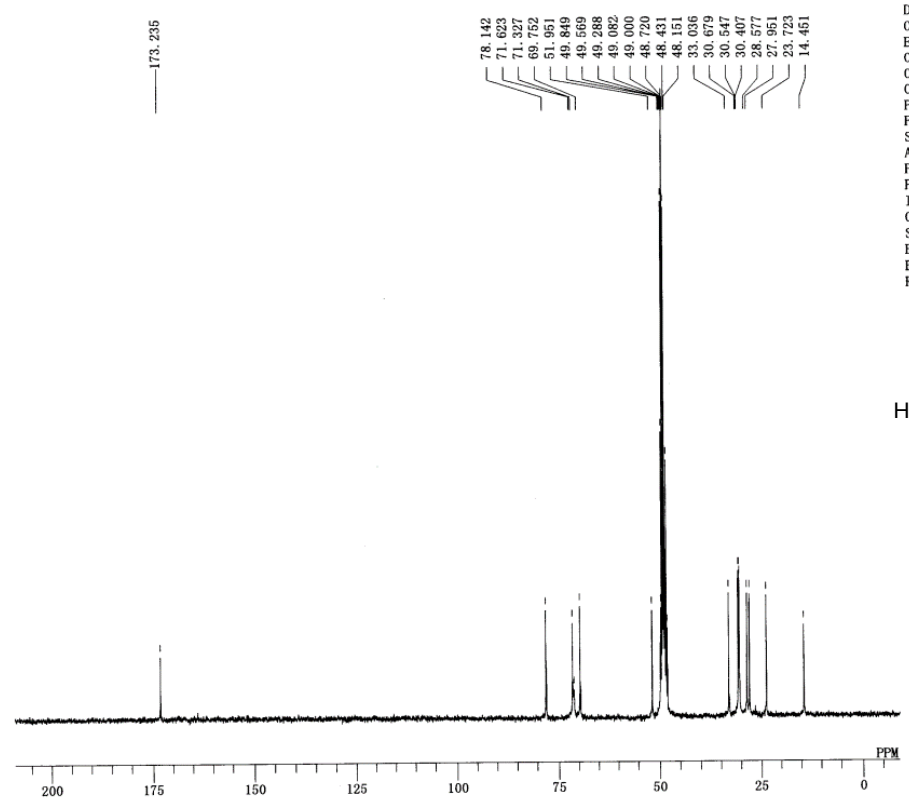


7d



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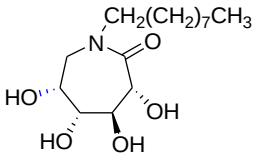

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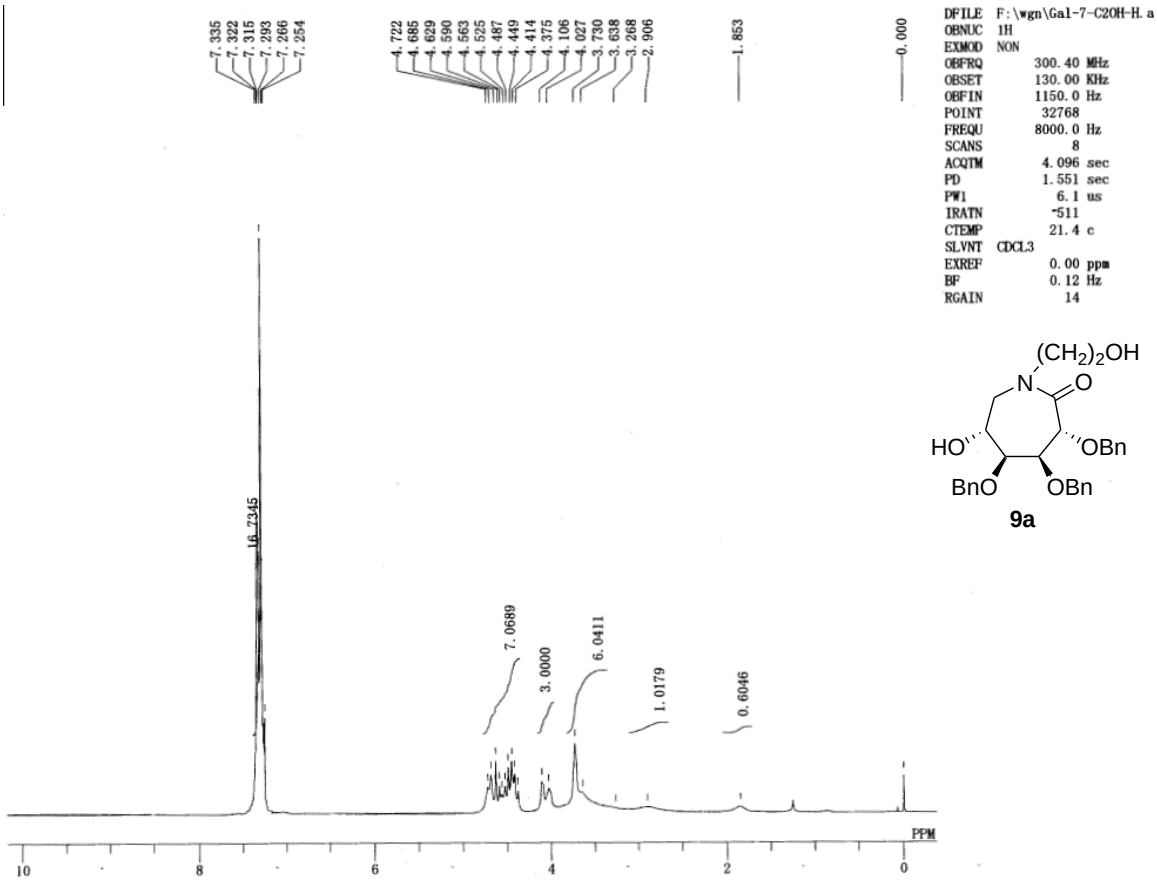

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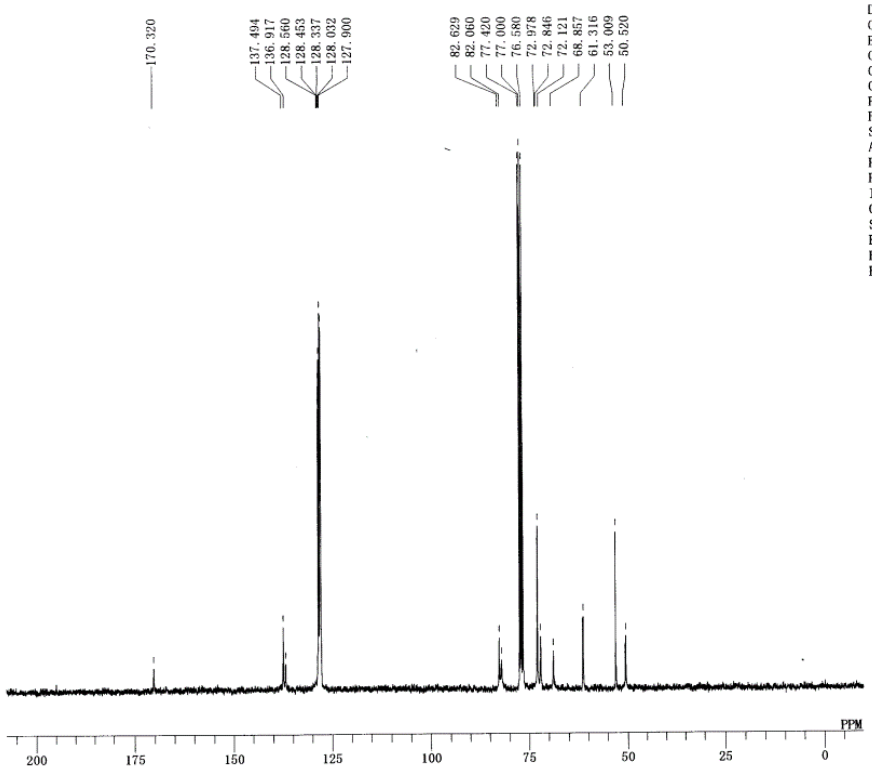
RGAIN 14

9a



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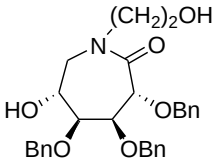
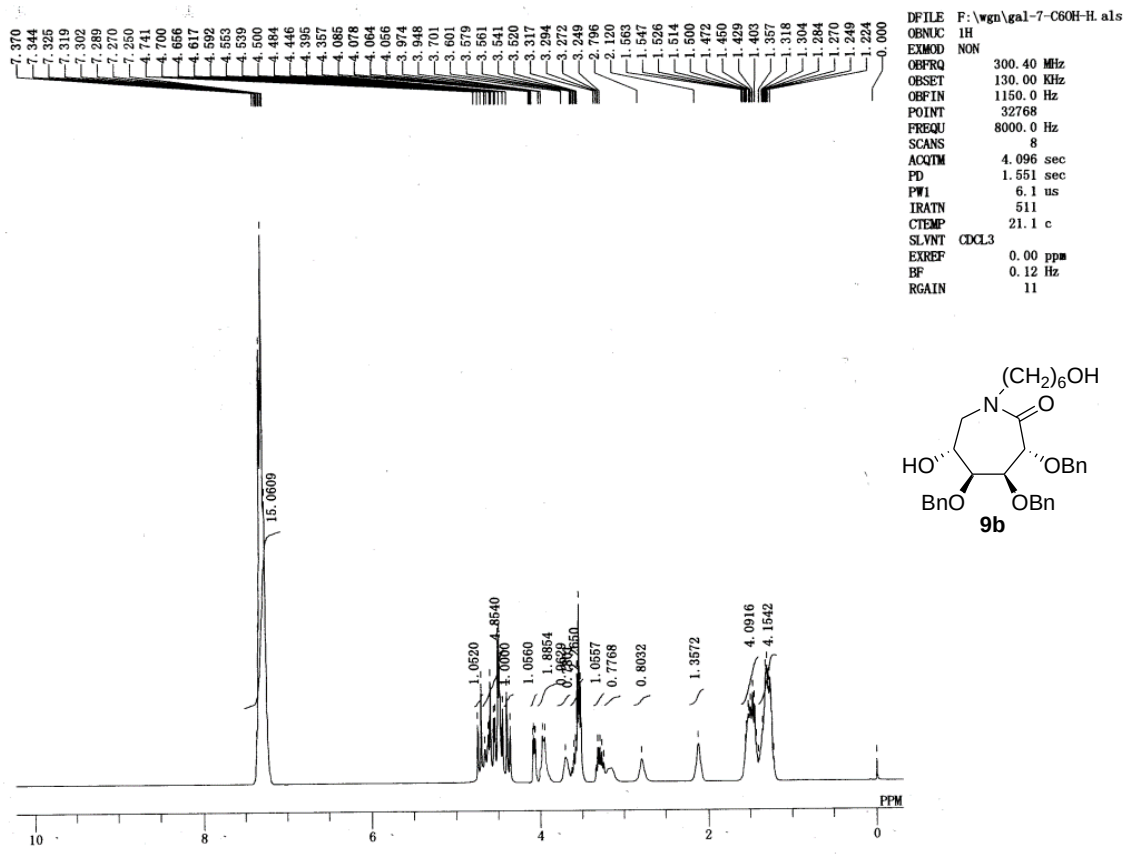
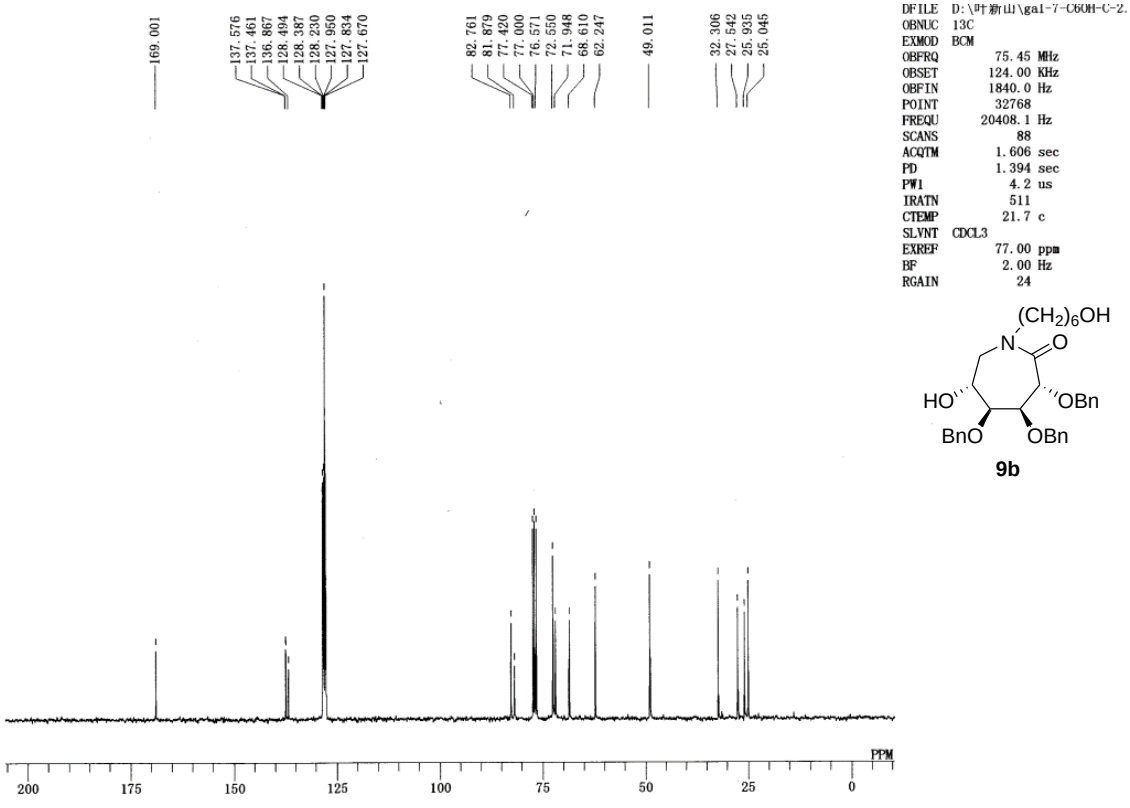
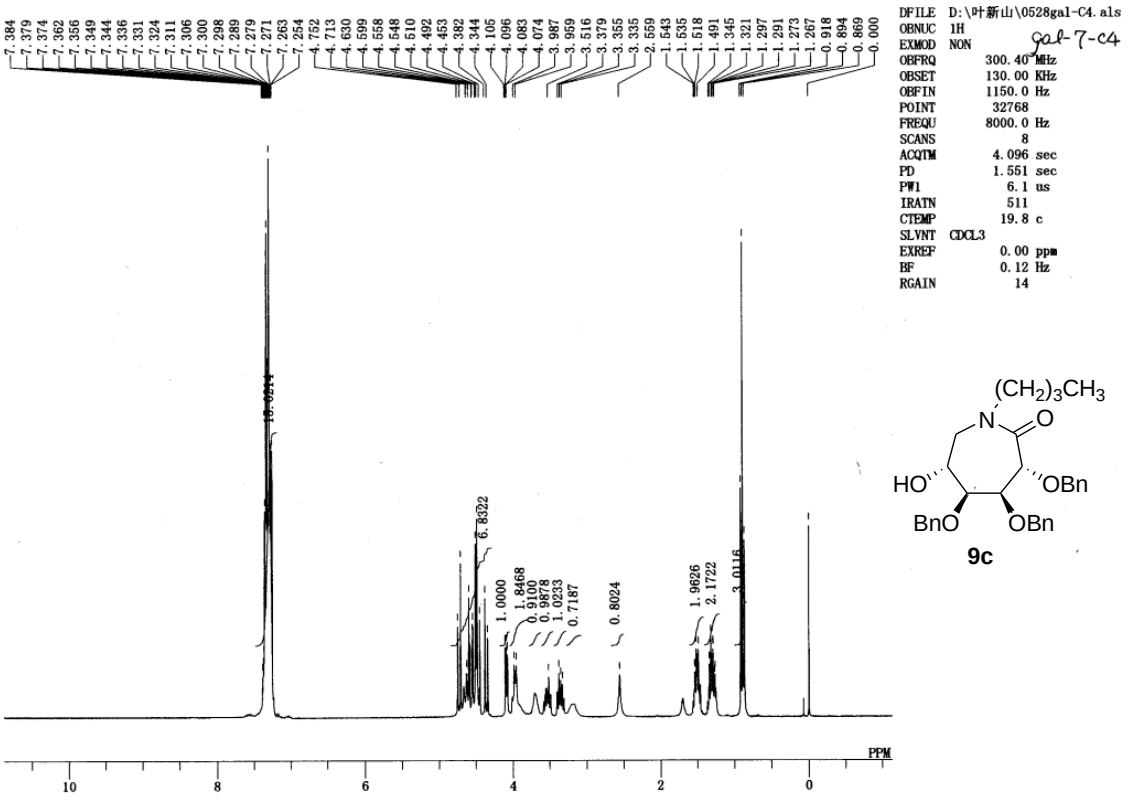
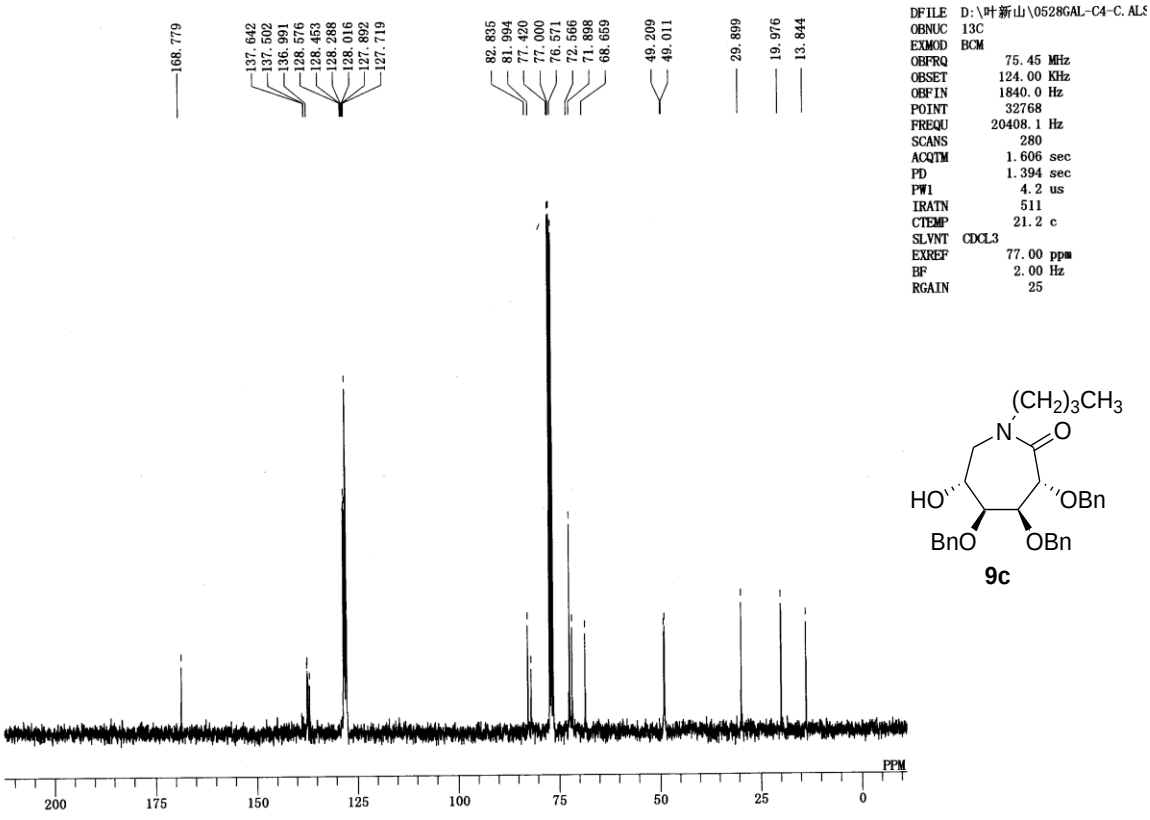


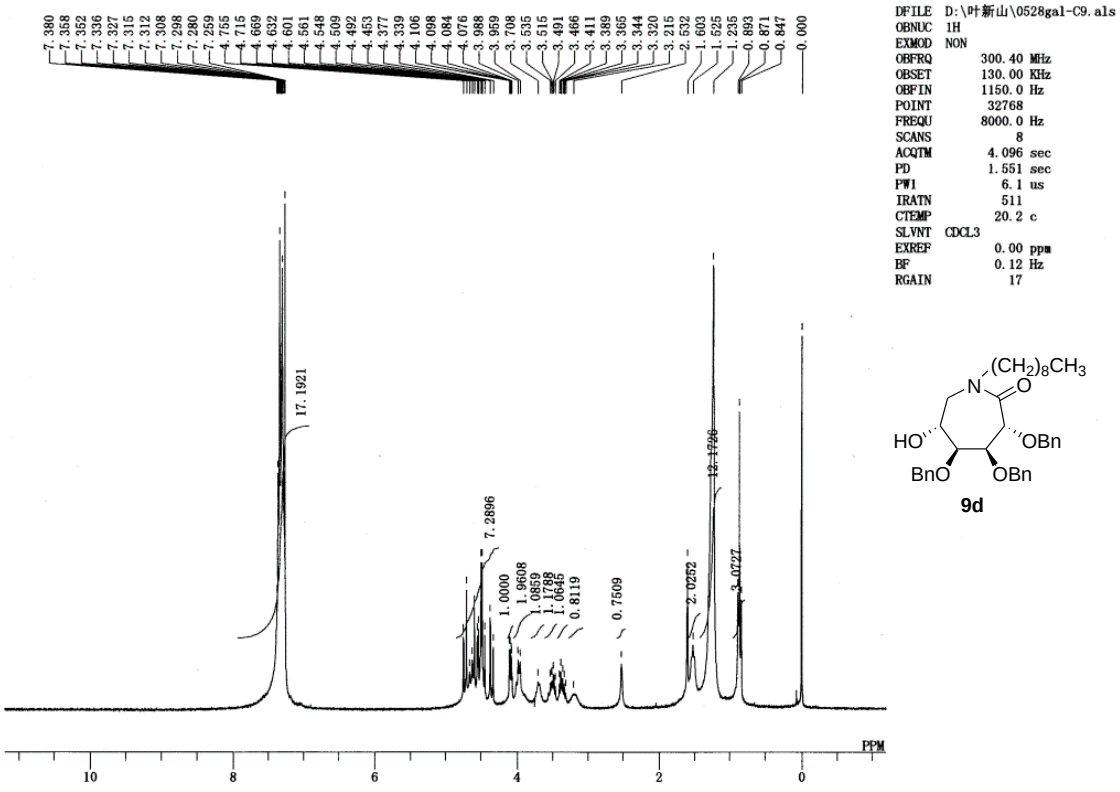
9a


DFILE F:\wgn\gal-7-C6OH-H.als
OBNUC 1H
EXMOD NON
OBFRQ 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRATN 511
CTEMP 21.1 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 11
(CH2)6OH
N
O
HO
OBn
BnO
OBn
9b
PPM

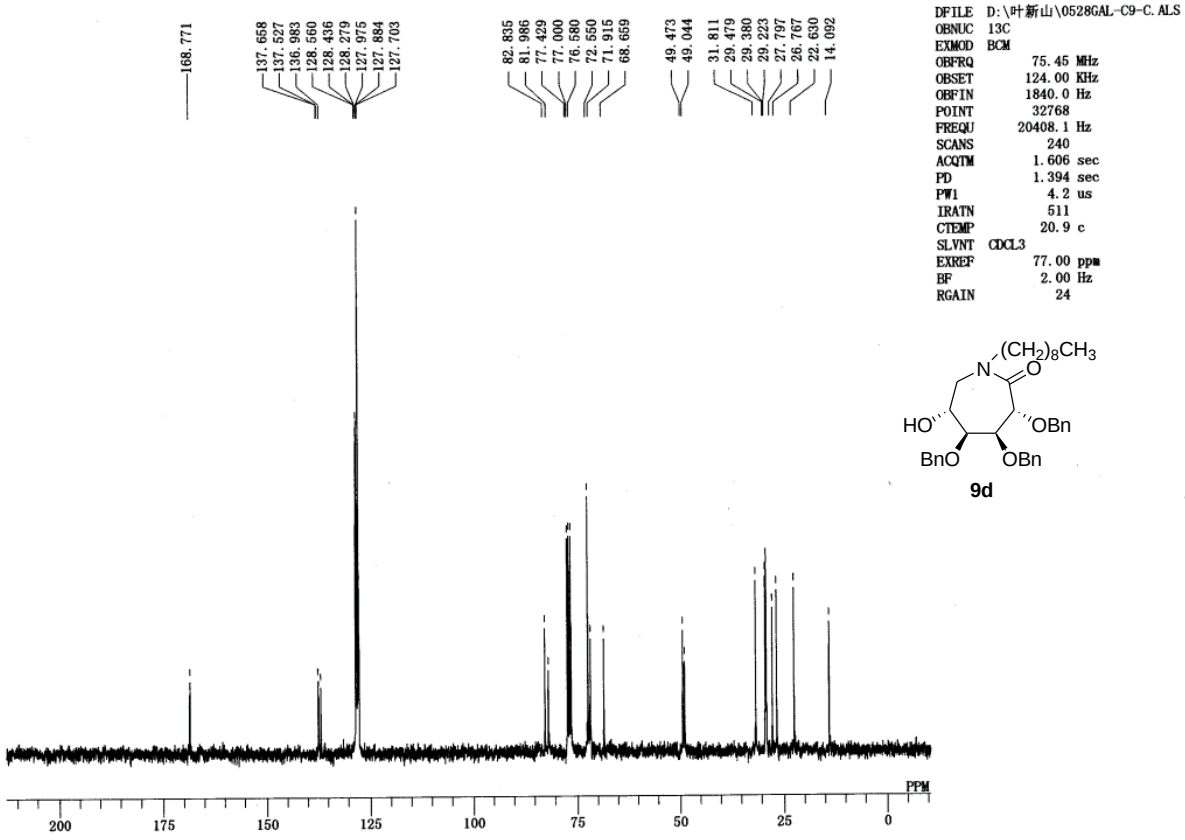

DFILE D:\叶新山\gal-7-C6OH-C-2.
OBNUC 13C
EXMOD BCM
OBFRQ 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 88
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRATN 511
CTEMP 21.7 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 24
(CH2)6OH
N
O
HO
OBn
BnO
OBn
9b
PPM



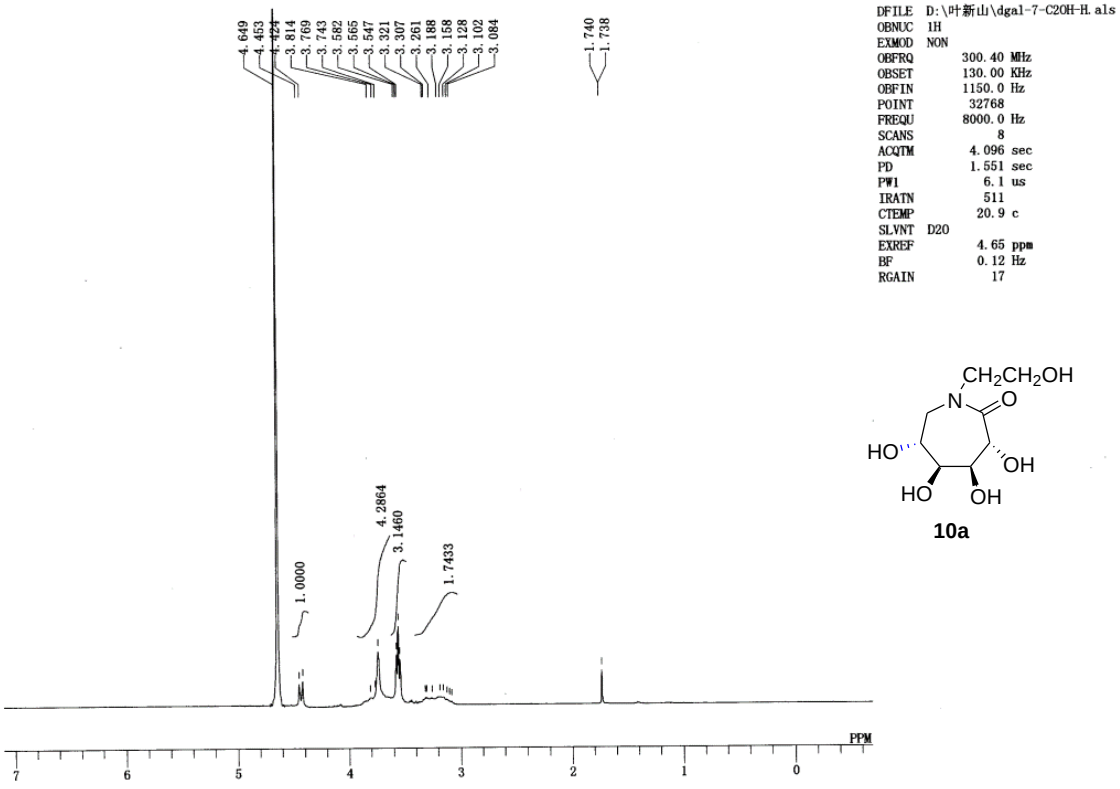




9d

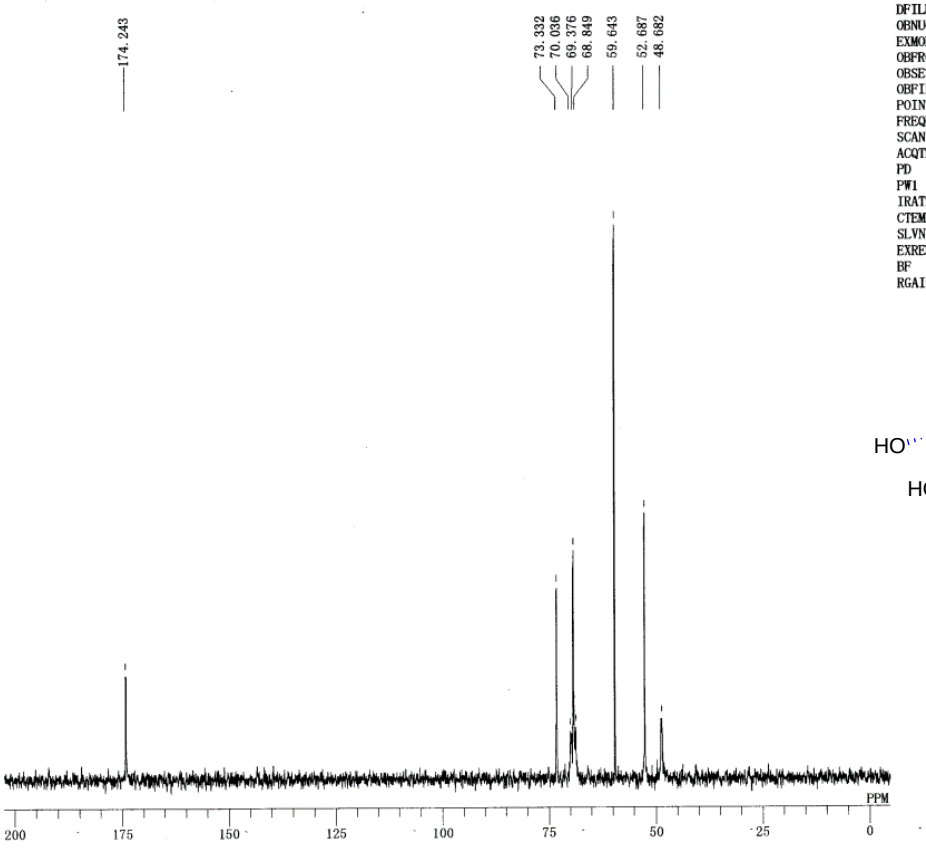


9d

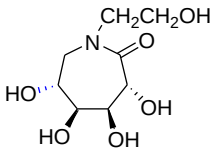


DFILE D:\叶新山\dgal-7-C2OH-H.als
OBNUC 1H
EXMOD NON
OBFRQ 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRATN 511
CTEMP 20.9 c
SLVNT D2O
EXREF 4.65 ppm
BF 0.12 Hz
RGAIN 17

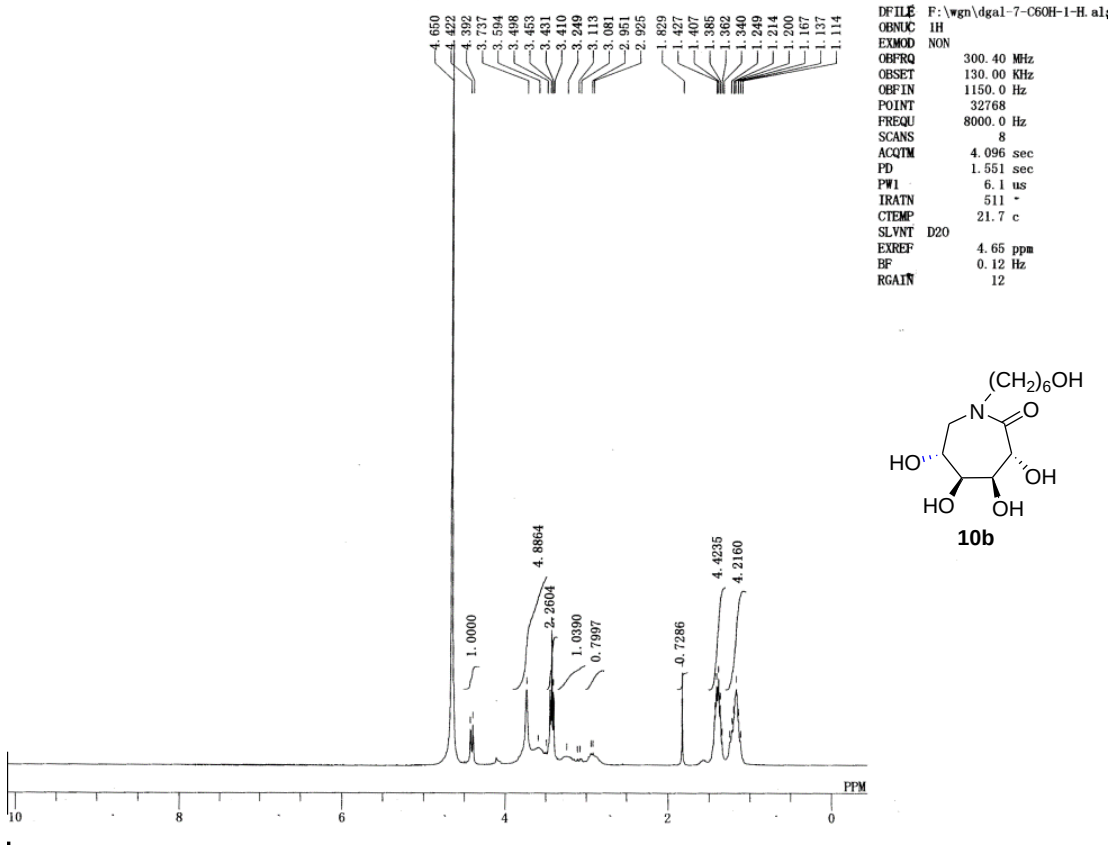
10a

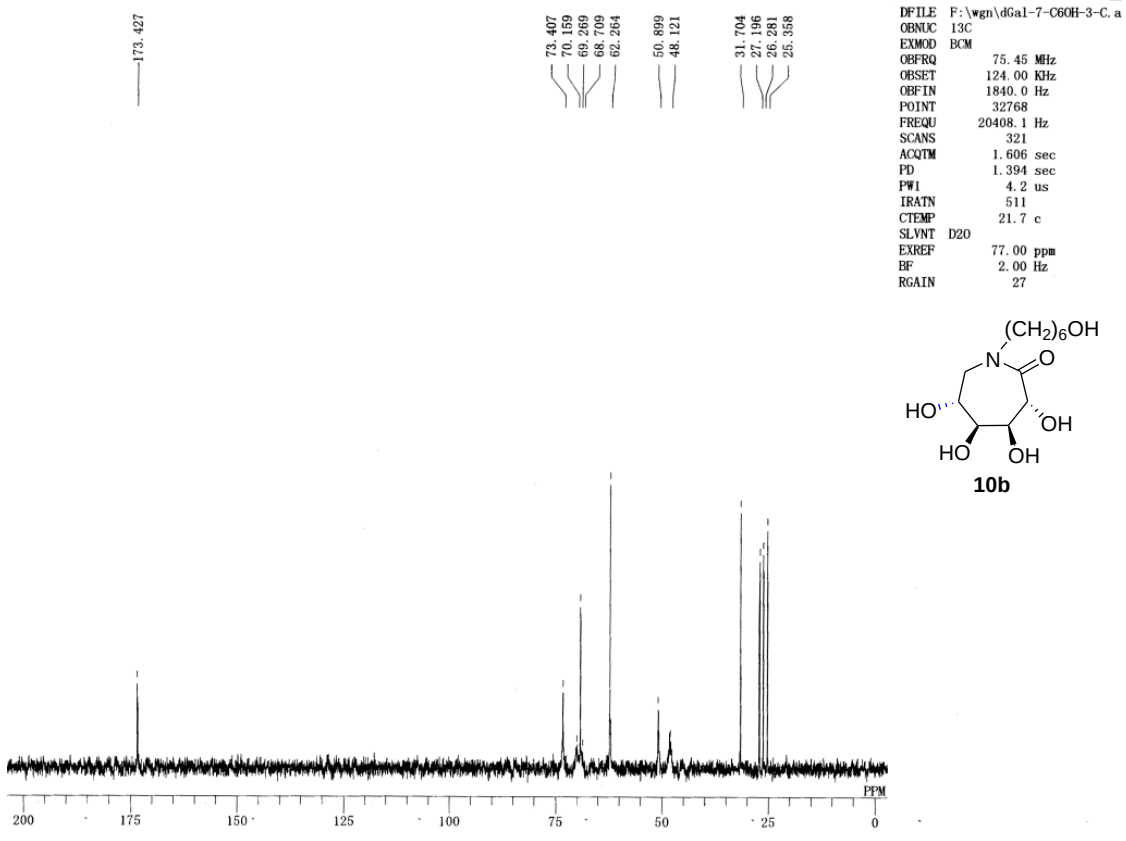


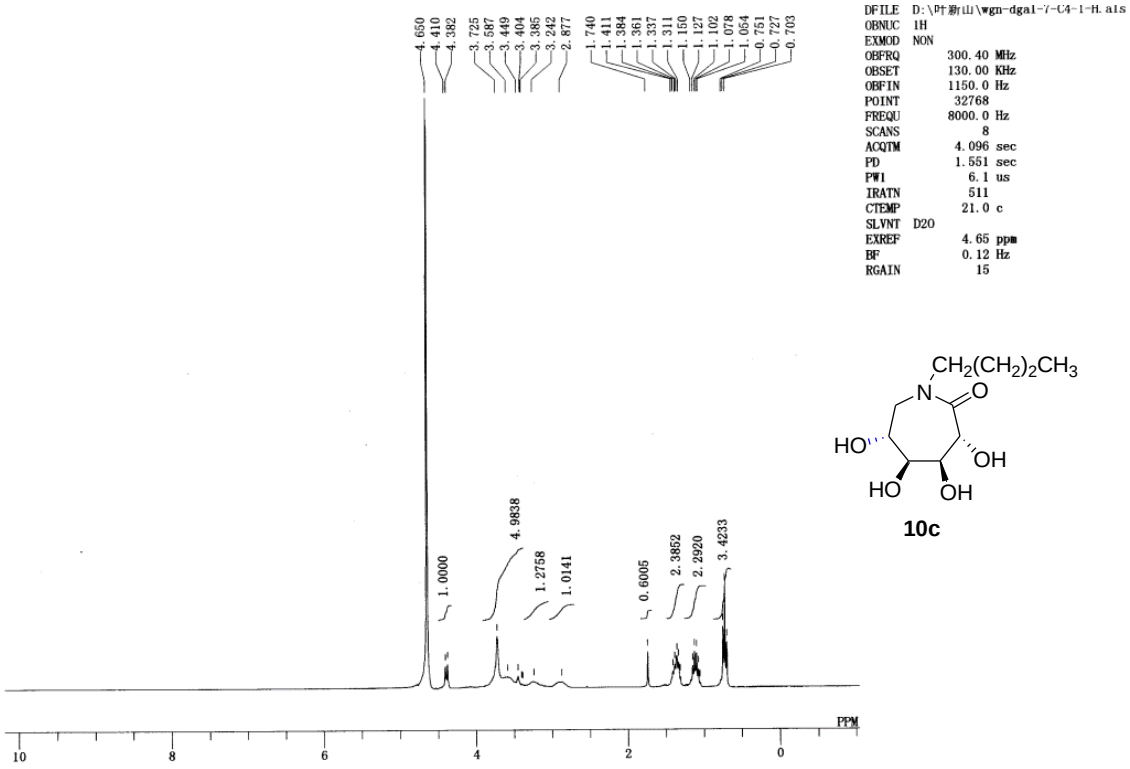
DFILE F:\wgn\DGAL-7-C2OH-C.ALS
OBNUC 13C
EXMOD BCM
OBFRQ 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 3568
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRATN 511
CTEMP 21.7 c
SLVNT D2O
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 25



10a

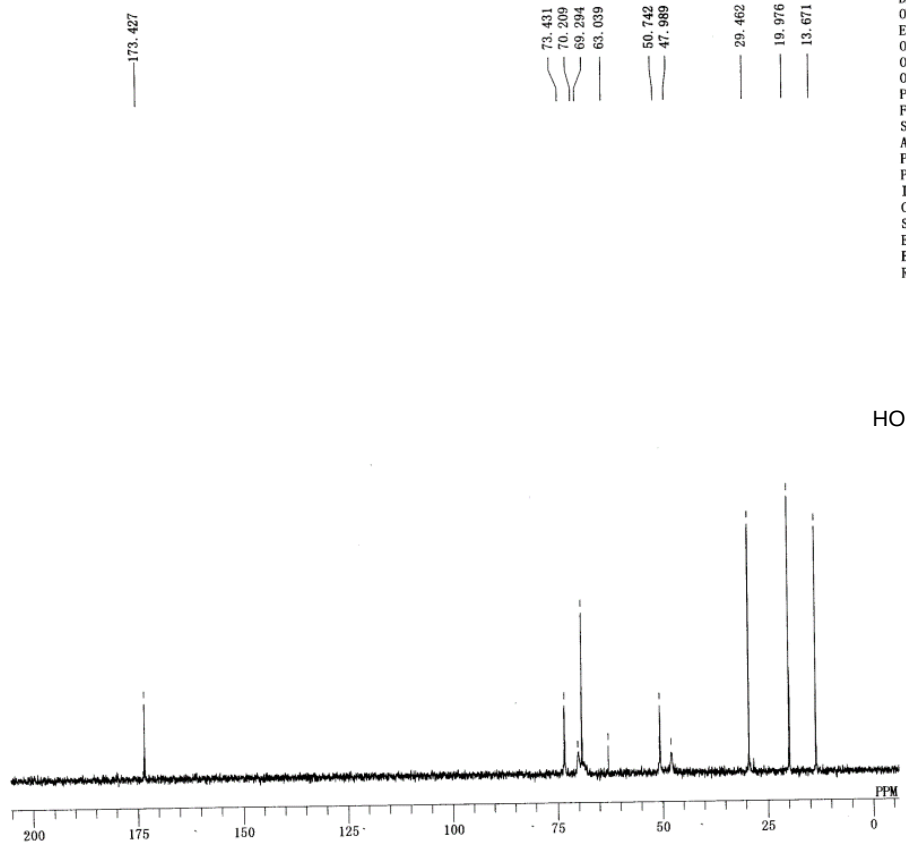




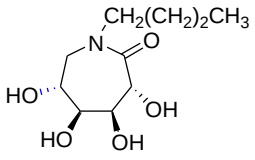


DFILE D:\叶源山\wgn-dgal-7-C4-1-H.als
OBNUC 1H
EXMOD NON
OBFRQ 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRATN 511
CTEMP 21.0 c
SLVNT D2O
EXREF 4.65 ppm
BF 0.12 Hz
RGAIN 15

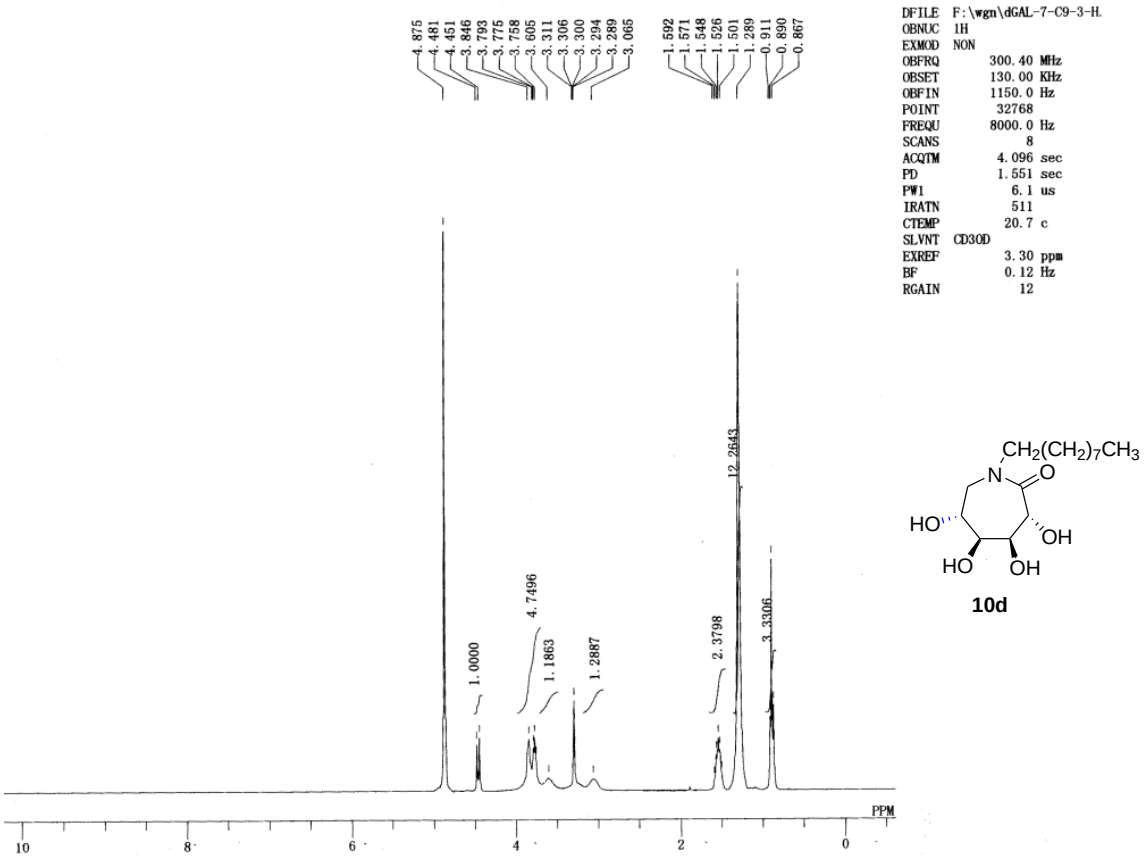
10c



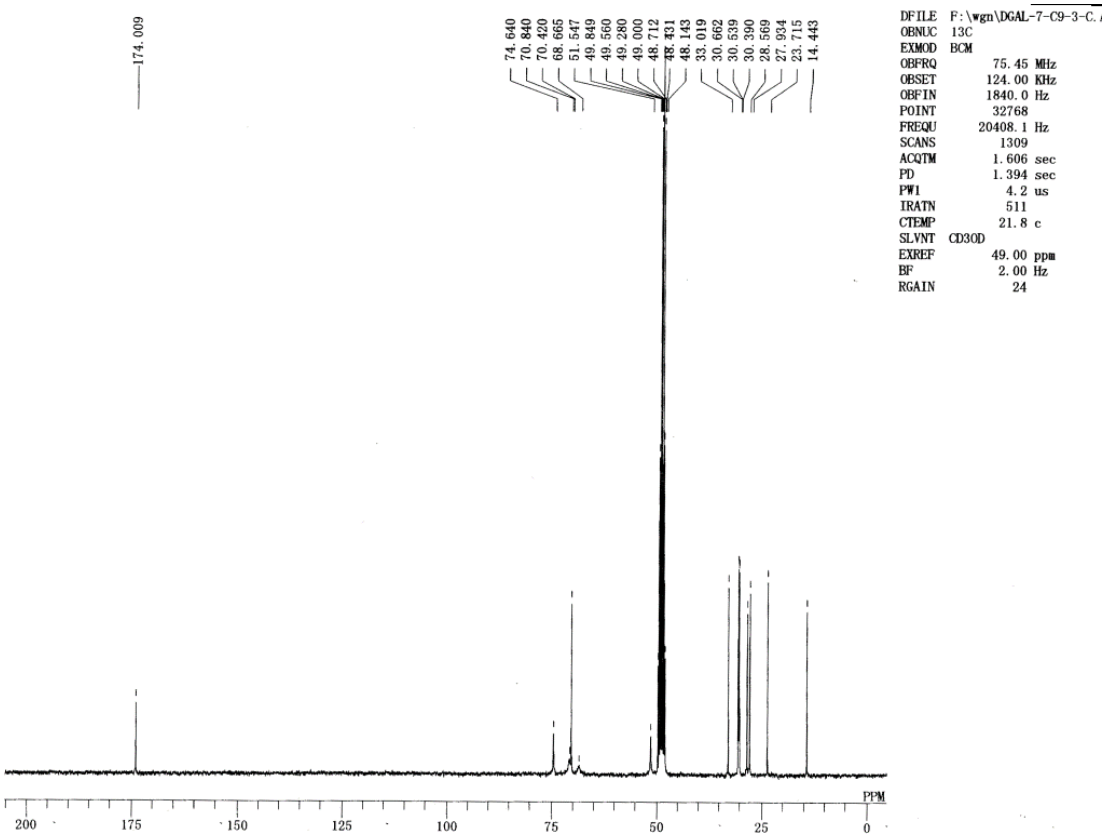
DFILE F:\wgn\DGAL-7-C4-C-3.AL
OBNUC 13C
EXMOD BCM
OBFRQ 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 1281
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRATN 511
CTEMP 22.0 c
SLVNT D2O
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 25

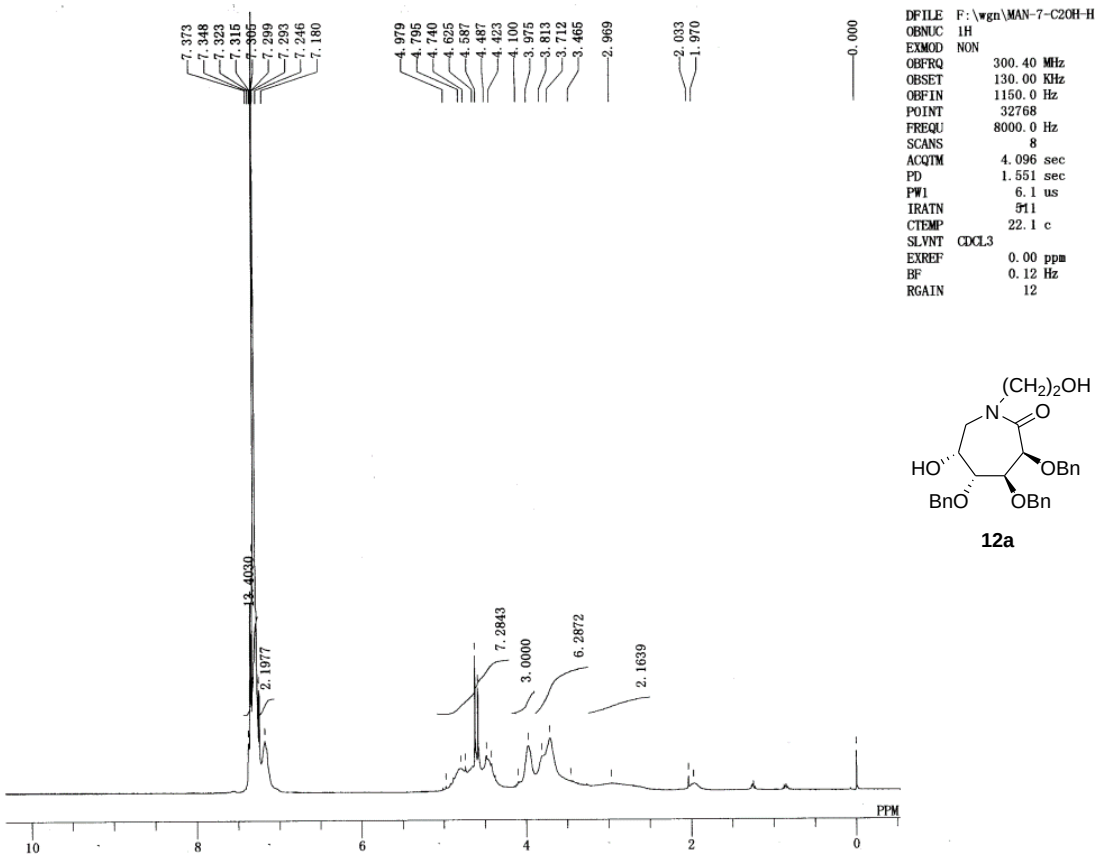


10c

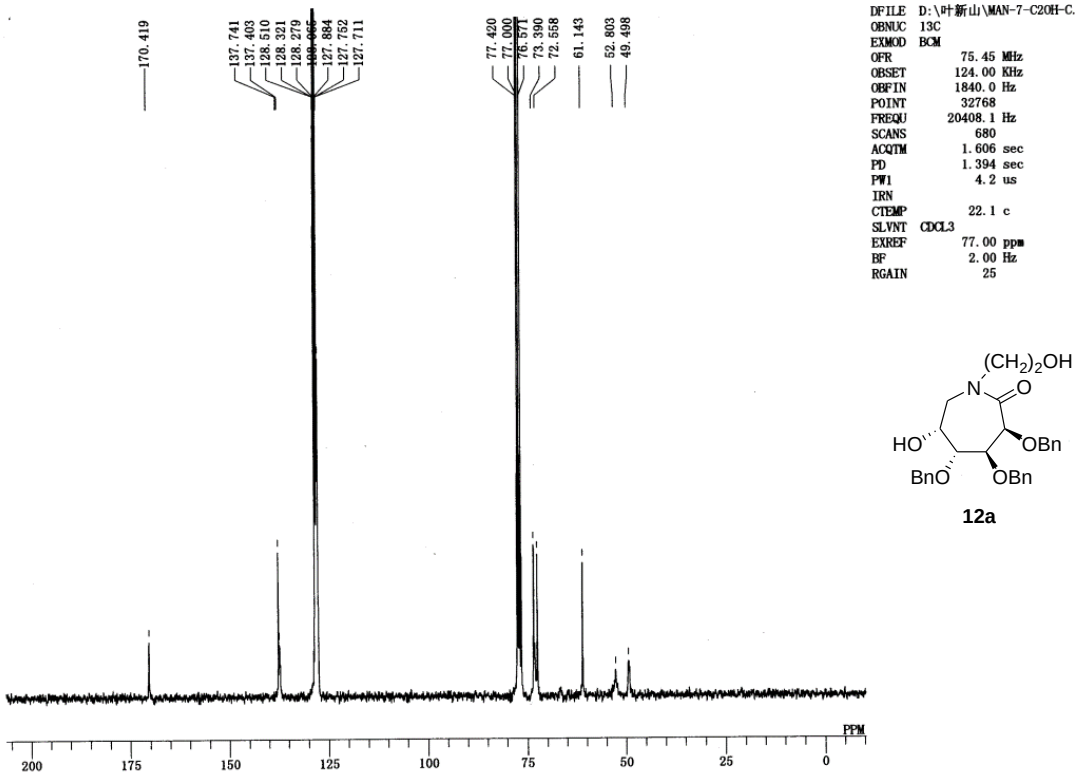


10d

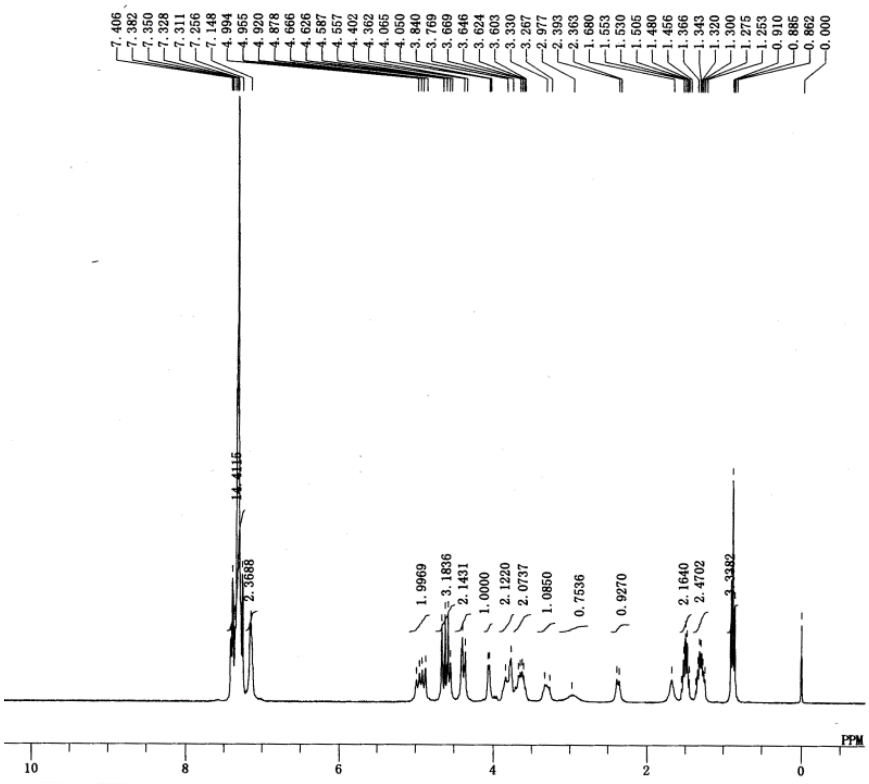




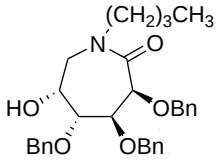
12a



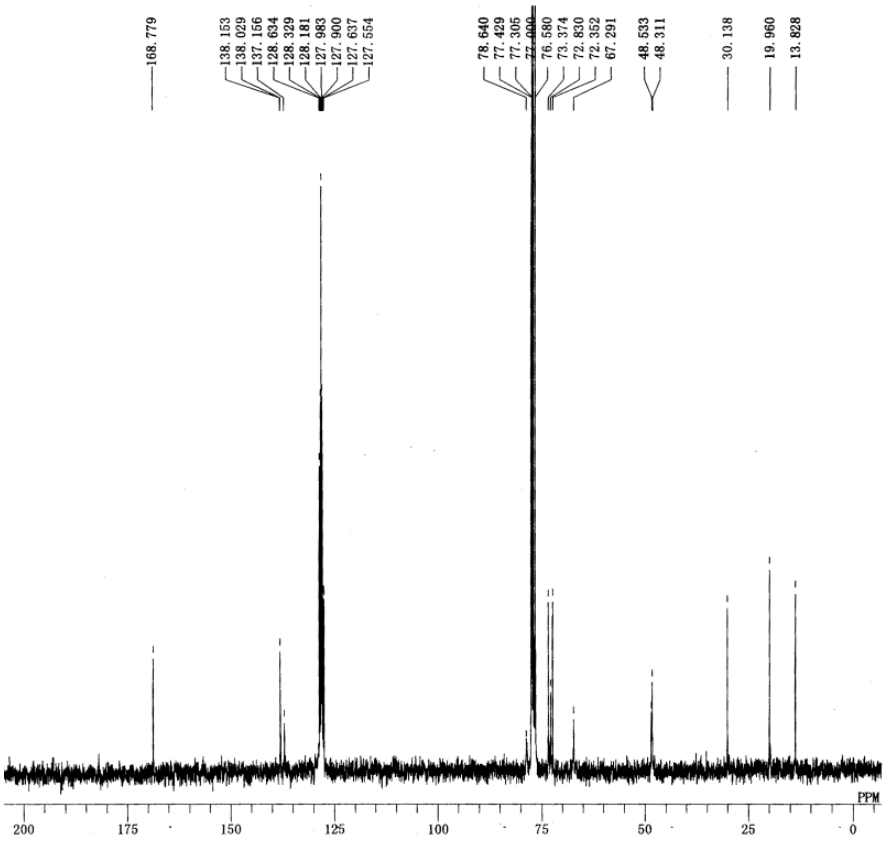
12a



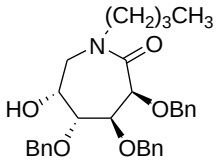

```
DFILE   D:\叶新山\MAN-7-C4-P-H.ALS
OBNUC   1H
EXMOD   NON
OFR          300.40 MHz
OBSET        130.00 KHz
OBFIN       1150.0 Hz
POINT        32768
FREQU       8000.0 Hz
SCANS            8
ACQTM        4.096 sec
PD           1.551 sec
PW1            6.1 us
IRN
CTEMP         21.8 c
SLVNT   CDCL3
EXREF        0.00 ppm
BF           0.12 Hz
RGAIN          16
```



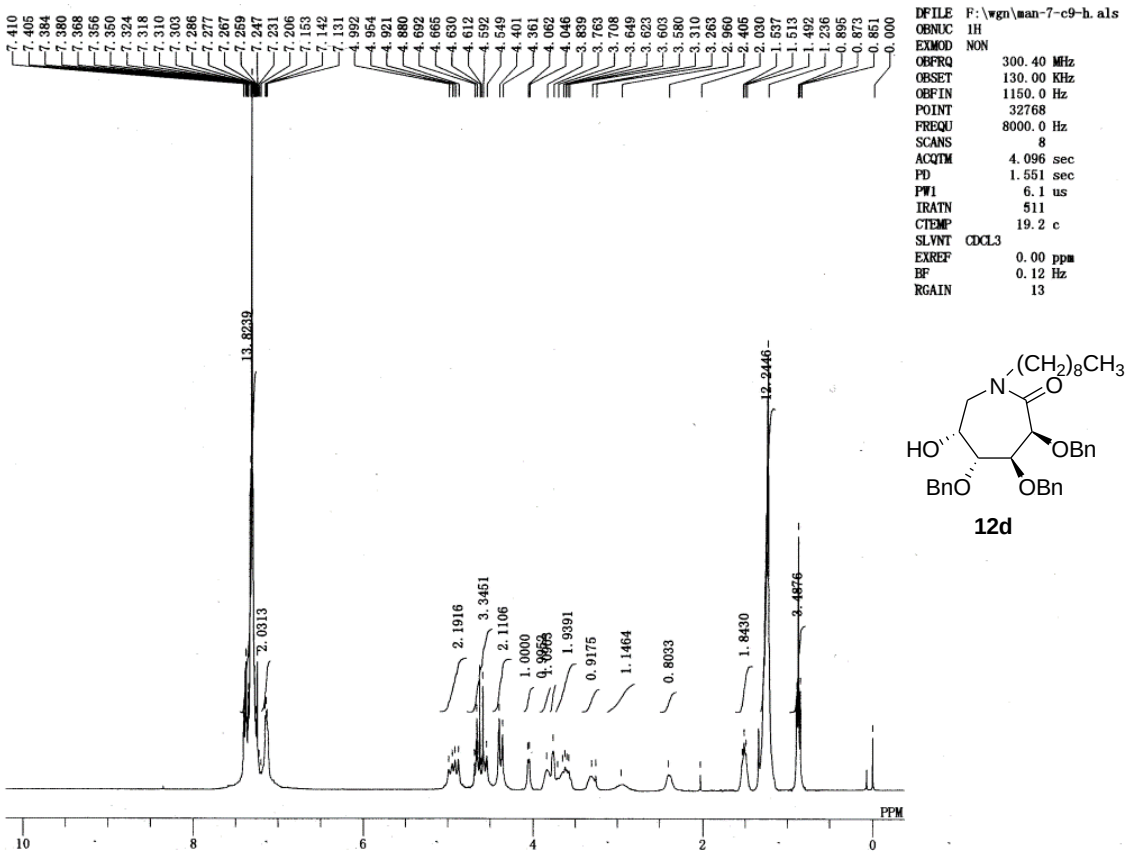
12c



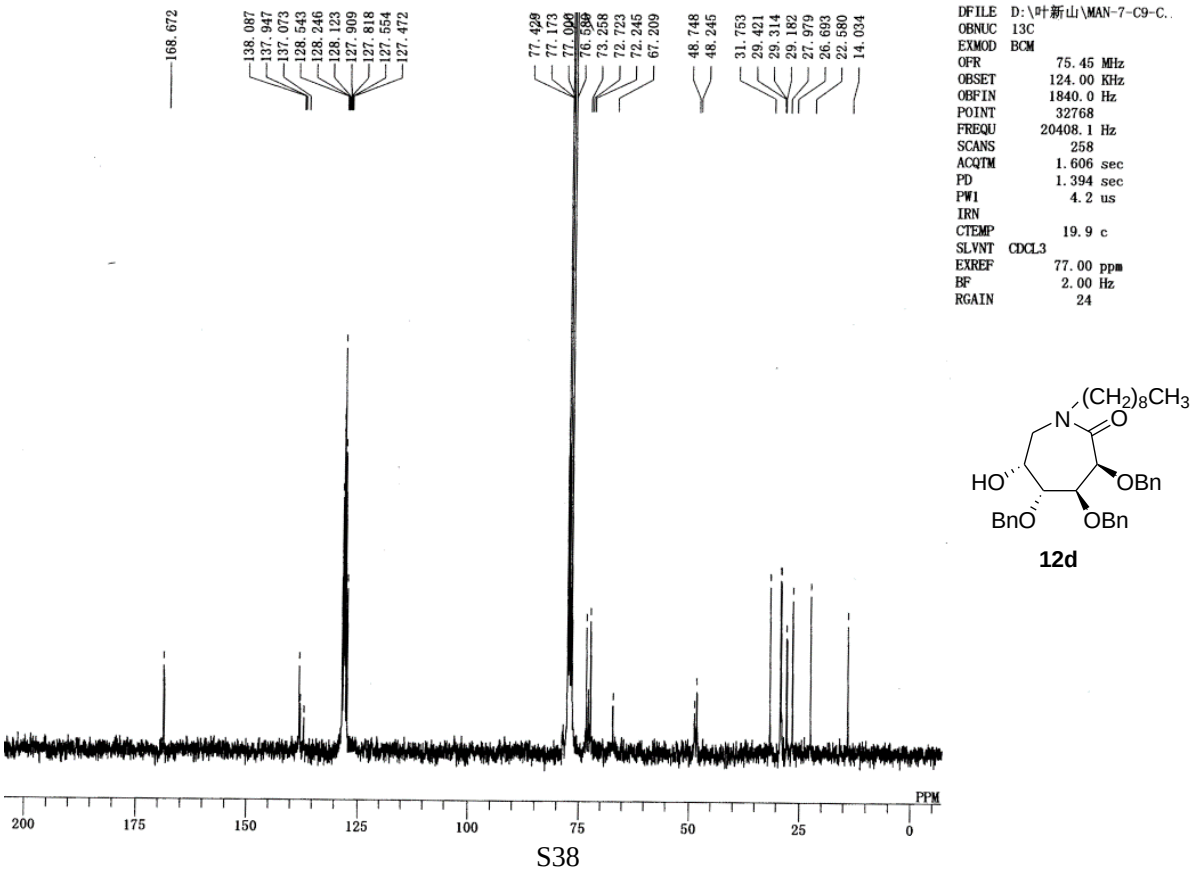

```
DFILE   F:\wgn\MAN-7-C4-P-C.ALS
OBNUC   13C
EXMOD   BCM
OBFRQ        75.45 MHz
OBSET       124.00 KHz
OBFIN       1840.0 Hz
POINT        32768
FREQU      20408.1 Hz
SCANS         1408
ACQTM        1.606 sec
PD           1.394 sec
PW1            4.2 us
IRATN          511
CTEMP         21.9 c
SLVNT   CDCL3
EXREF       77.00 ppm
BF           2.00 Hz
RGAIN          24
```



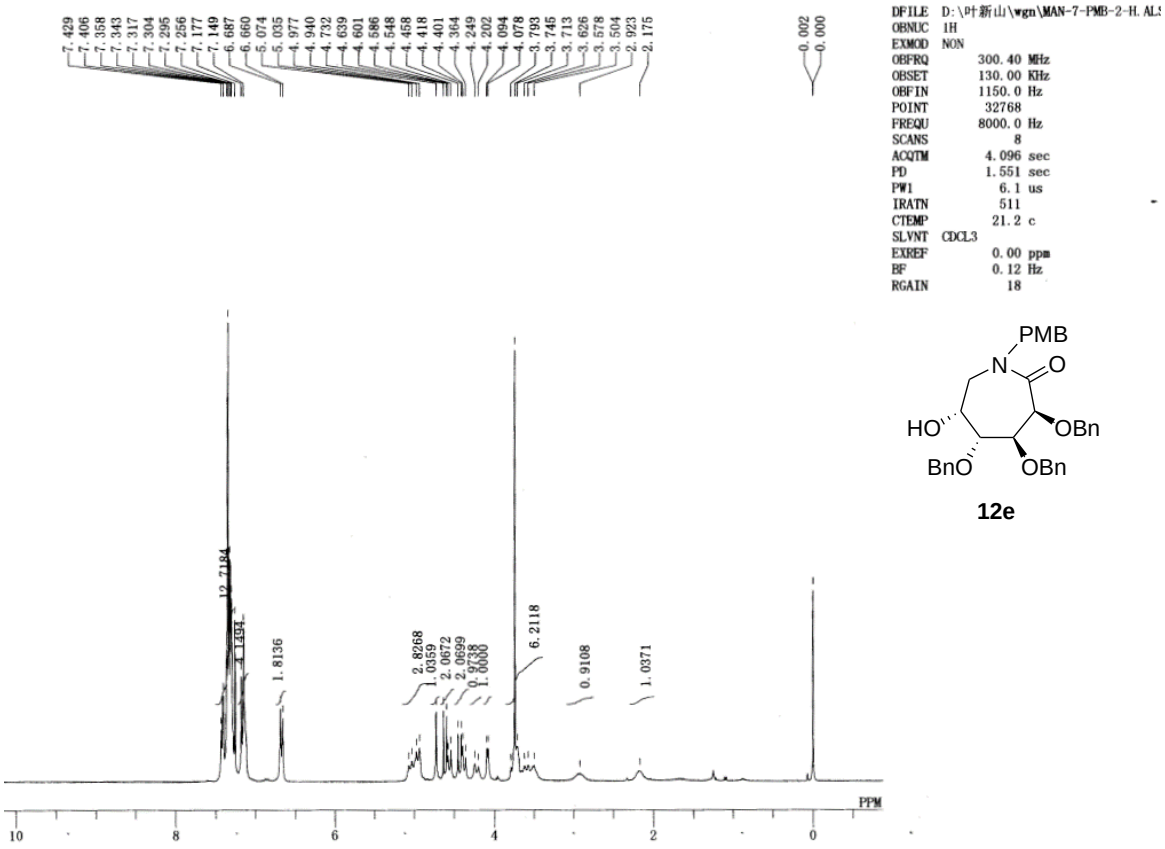
12c



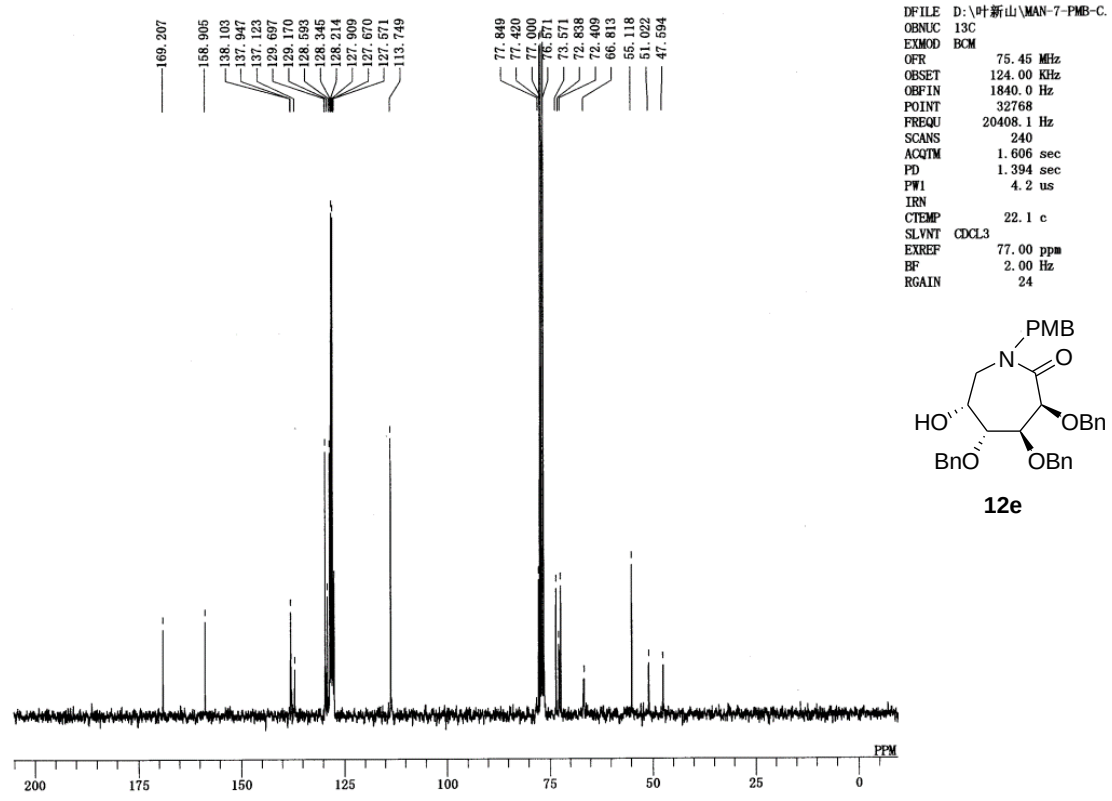
12d



12d


7.429
7.406
7.358
7.343
7.317
7.304
7.295
7.256
7.177
7.149
6.687
6.660
5.074
5.035
4.977
4.940
4.732
4.639
4.601
4.586
4.548
4.458
4.418
4.401
4.364
4.249
4.202
4.094
4.078
3.793
3.745
3.713
3.626
3.578
3.504
2.923
2.175
0.002
0.000
12.7184
3.1494
1.8136
2.8268
1.0359
2.0672
2.0699
0.9738
1.0000
6.2118
0.9108
1.0371
PPM
10
8
6
4
2
0
DFILE D:\叶新山\wgn\MAN-7-PMB-2-H.AL
OBNUC 1H
EXMOD NON
OBFRQ 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRATN 511
CTEMP 21.2 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 18
PMB
N
O
HO
OBn
BnO
OBn

12e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137.947
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127.909
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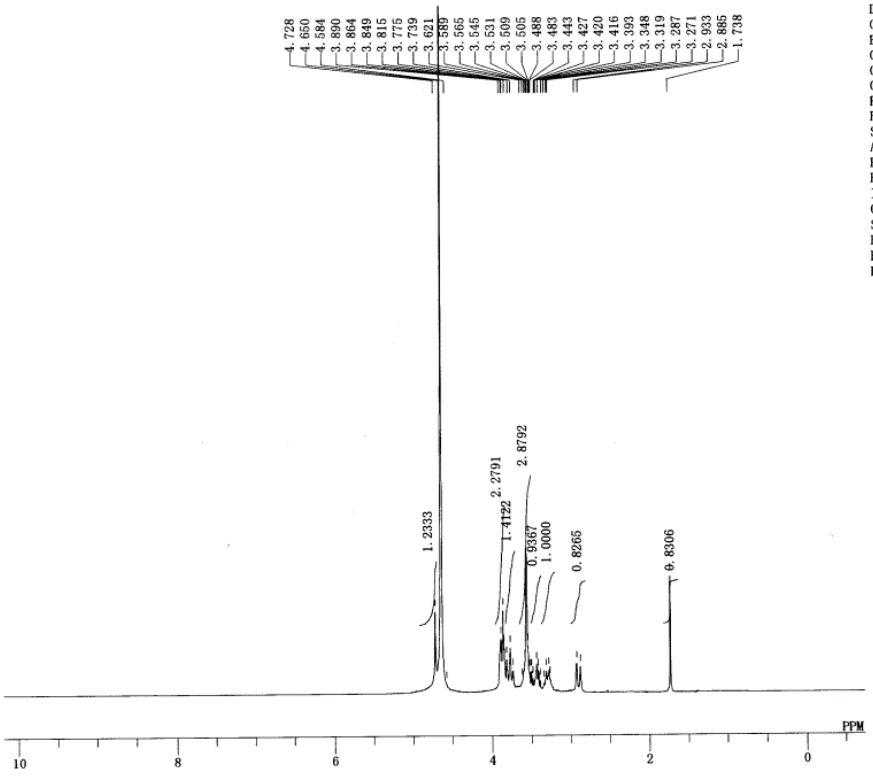
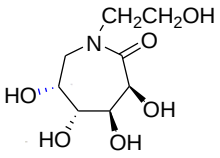
127.571
113.749
77.849
77.420
77.000
76.571
73.571
72.838
72.409
66.813
55.118
51.022
47.594
PPM
200
175
150
125
100
75
50
25
0
DFILE D:\叶新山\MAN-7-PMB-C.
OBNUC 13C
EXMOD BCM
OFR 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 240
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRN
CTEMP 22.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 24
PMB
N
O
HO
OBn
BnO
OBn

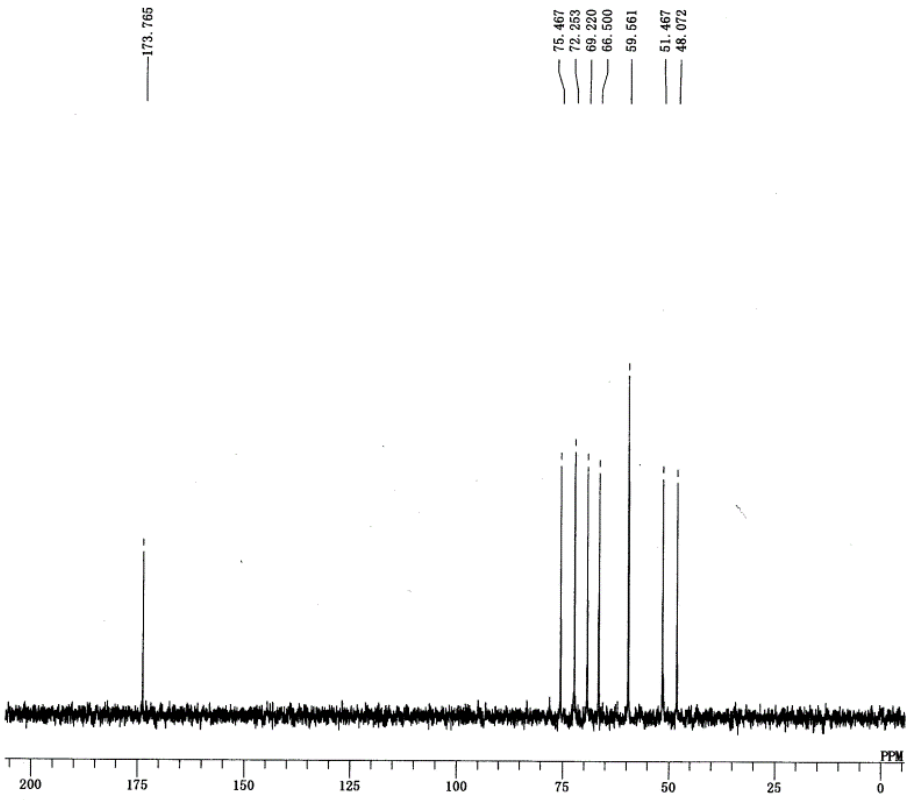
12e



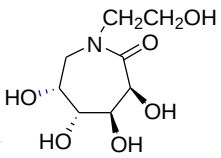

```
DFILE  D:\叶新山\DMAN-7-C2OH-H-4.ALS
OBNUC  1H
EXMOD  NON
OBFRQ        300.40 MHz
OBSET        130.00 KHz
OBFIN        1150.0 Hz
POINT         32768
FREQU        8000.0 Hz
SCANS            8
ACQTM        4.096 sec
PD           1.551 sec
PW1            6.1 us
IRATN          511
CTEMP        20.4 c
SLVNT  D2O
EXREF        4.65 ppm
BF           0.12 Hz
RGAIN            16
```



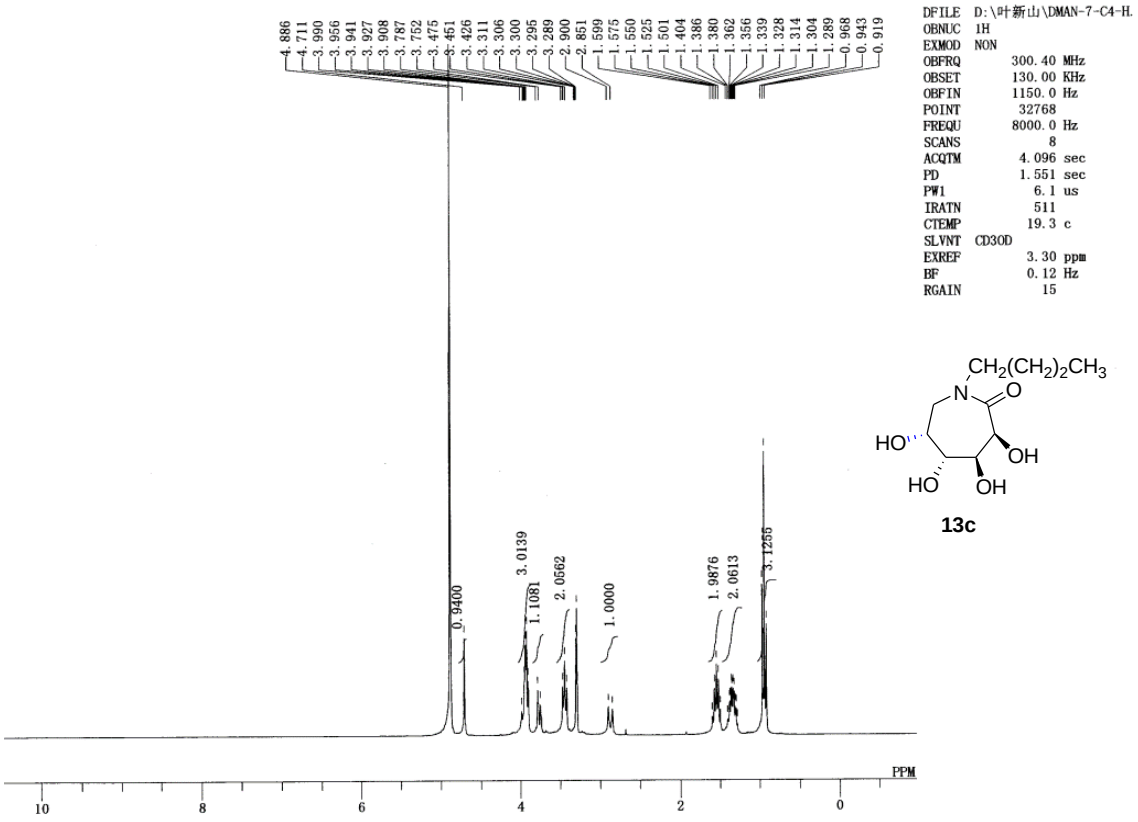
13a



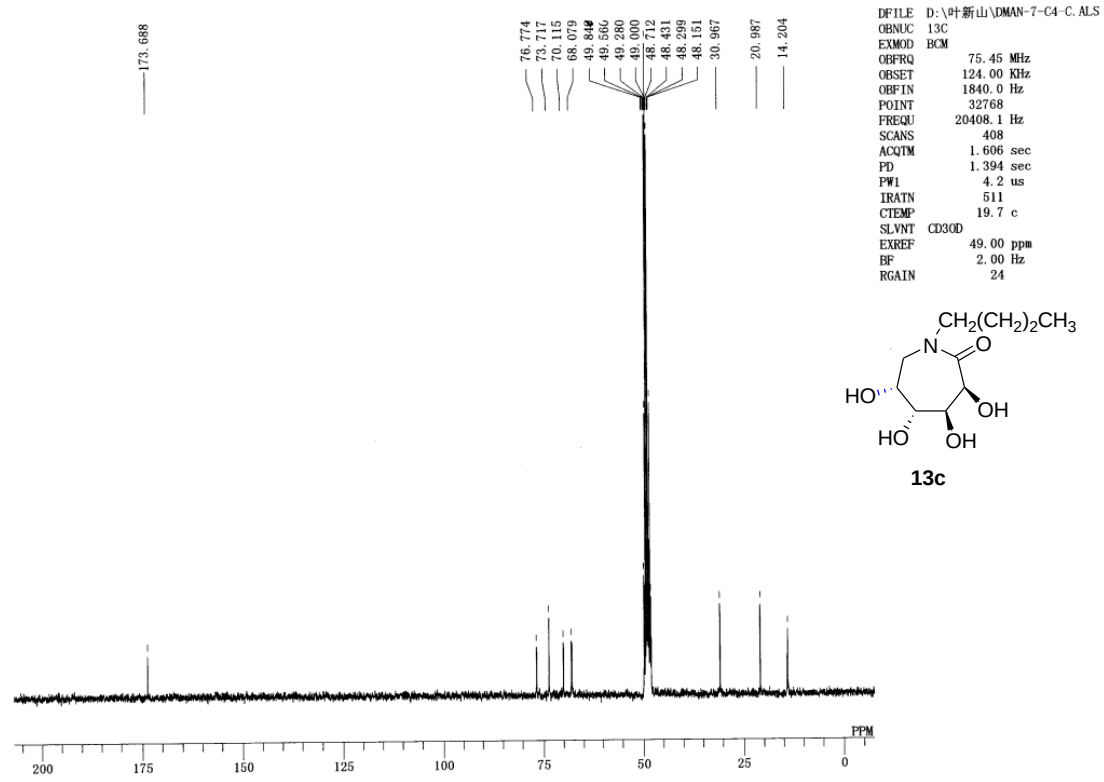

```
DFILE  D:\叶新山\DMAN-7-C2OH-C-4.ALS
OBNUC  13C
EXMOD  BCM
OBFRQ         75.45 MHz
OBSET        124.00 KHz
OBFIN        1840.0 Hz
POINT         32768
FREQU        20408.1 Hz
SCANS          3988
ACQTM        1.606 sec
PD           1.394 sec
PW1            4.2 us
IRATN          511
CTEMP        20.7 c
SLVNT  D2O
EXREF        77.00 ppm
BF           2.00 Hz
RGAIN            25
```



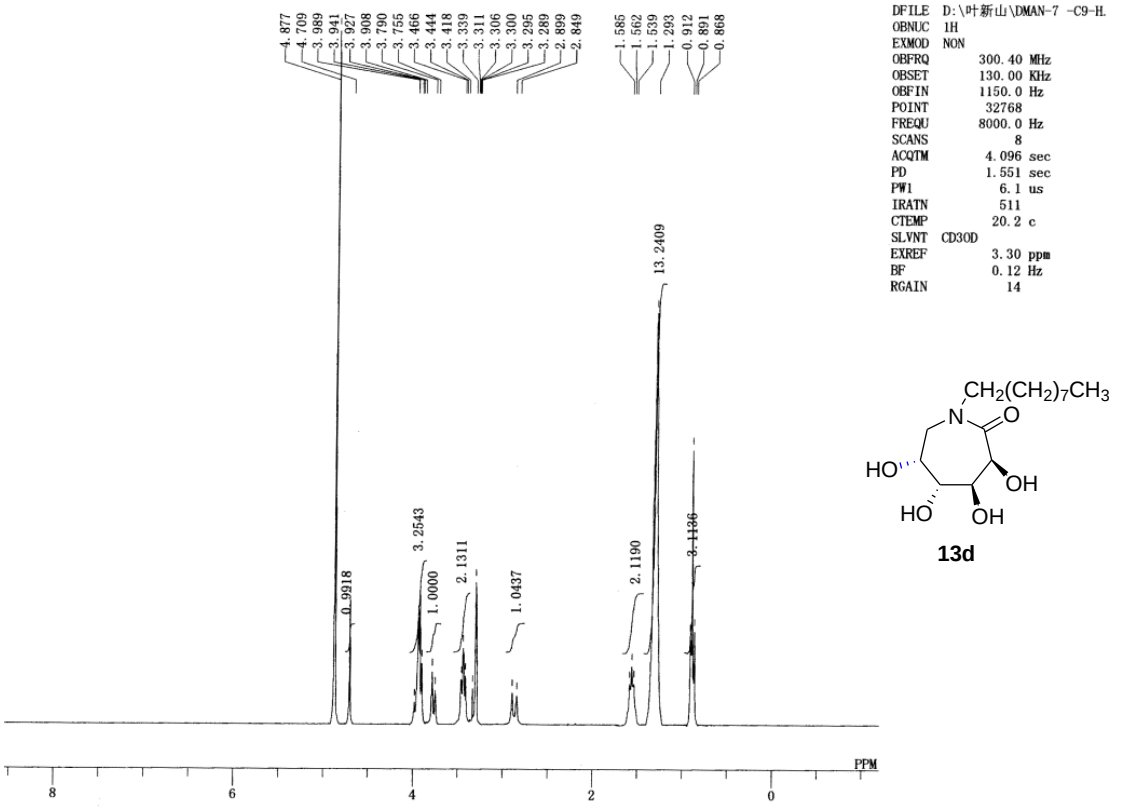
13a



13c

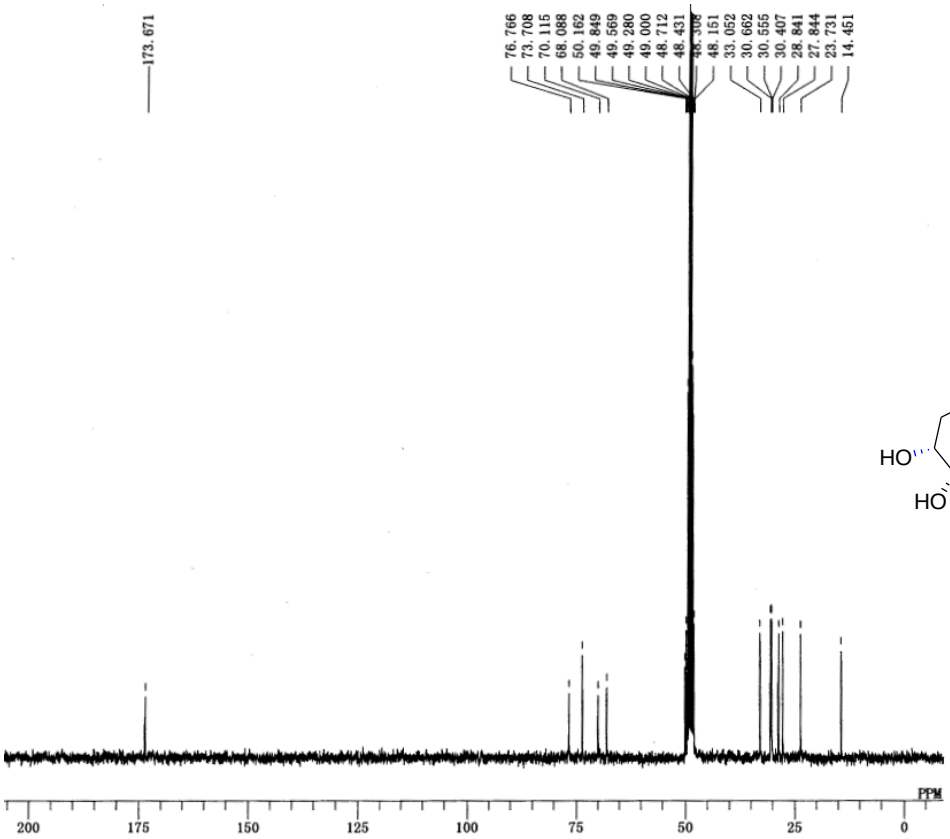


13c

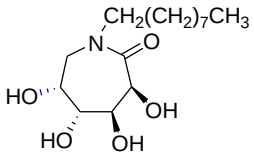


DFILE	D:\叶新山\DMAN-7 -C9-H.
OBNUC	1H
EXMOD	NON
OBFRQ	300.40 MHz
OBSET	130.00 KHz
OBFIN	1150.0 Hz
POINT	32768
FREQU	8000.0 Hz
SCANS	8
ACQTM	4.096 sec
PD	1.551 sec
PW1	6.1 us
IRATN	511
CTEMP	20.2 c
SLVNT	CD3OD
EXREF	3.30 ppm
BF	0.12 Hz
RGAIN	14

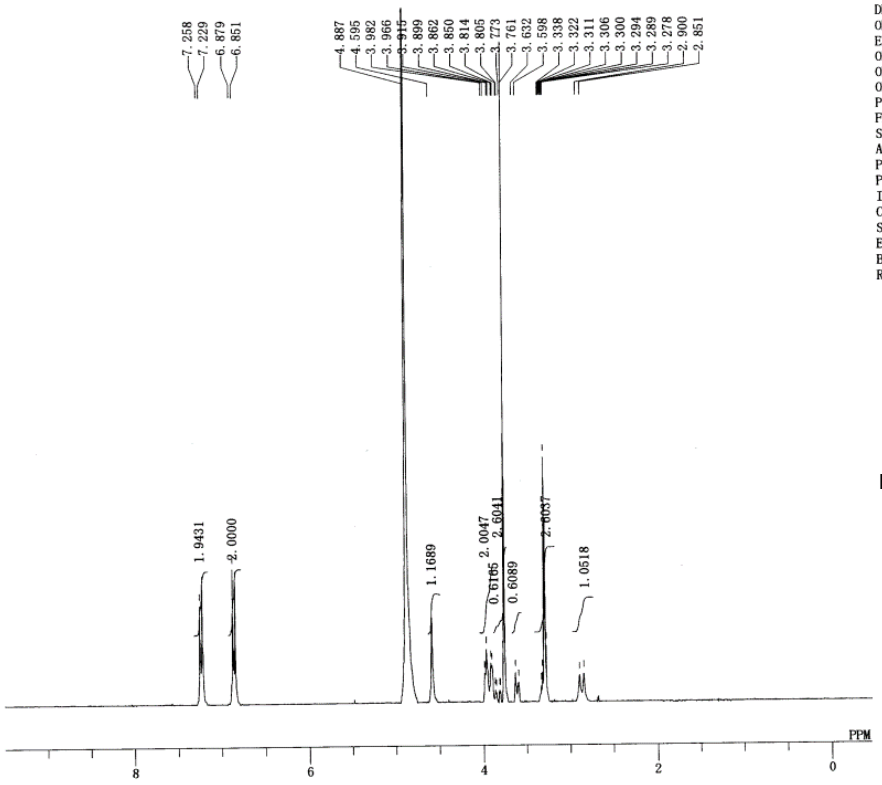
13d



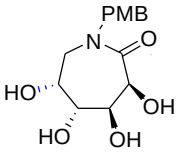
OBNUC	13C
EXMOD	BCM
OBFRQ	75.45 MHz
OBSET	124.00 KHz
OBFIN	1840.0 Hz
POINT	32768
FREQU	20408.1 Hz
SCANS	256
ACQTM	1.606 sec
PD	1.394 sec
PW1	4.2 us
IRATN	511
CTEMP	19.7 c
SLVNT	CD3OD
EXREF	49.00 ppm
BF	2.00 Hz
RGAIN	24



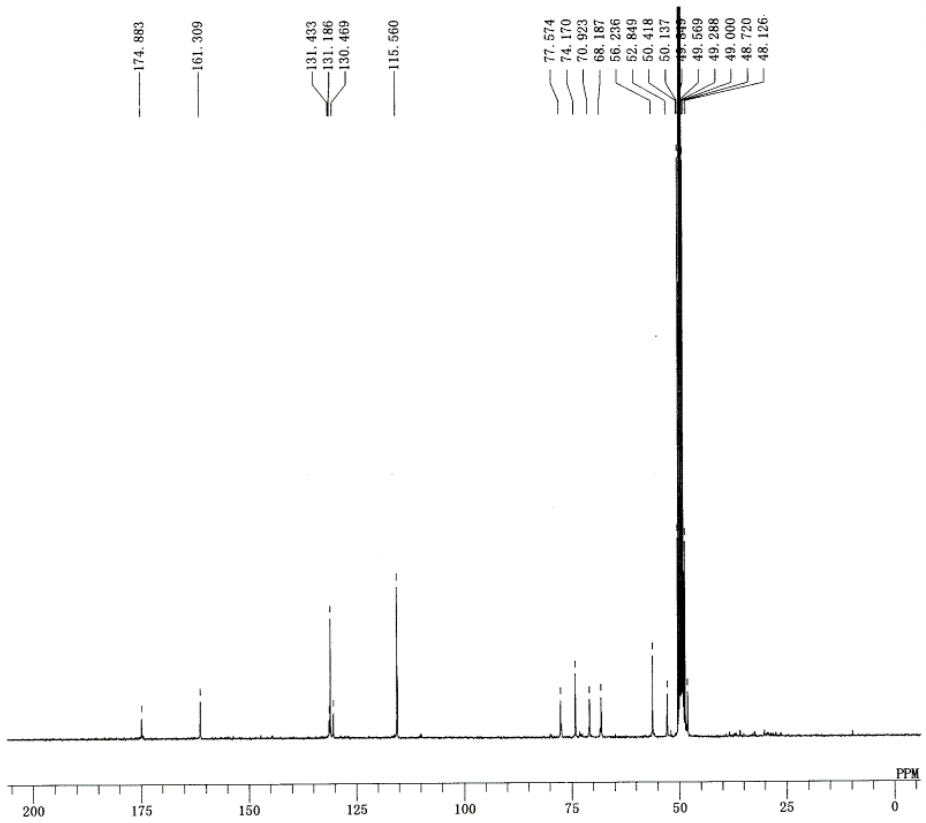
13d



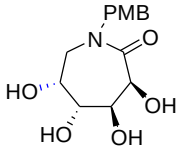

```
DFILE  D:\叶新山\DMAN-7-PMB-h-2.ALS
OBNUC  1H
EXMOD  NON
OBFRQ        300.40 MHz
OBSET        130.00 KHz
OBFIN        1150.0 Hz
POINT         32768
FREQU        8000.0 Hz
SCANS            8
ACQTM        4.096 sec
PD           1.551 sec
PW1            6.1 us
IRATN          511
CTEMP        20.2 c
SLVNT  CD3OD
EXREF        3.30 ppm
BF           0.12 Hz
RGAIN            15
```



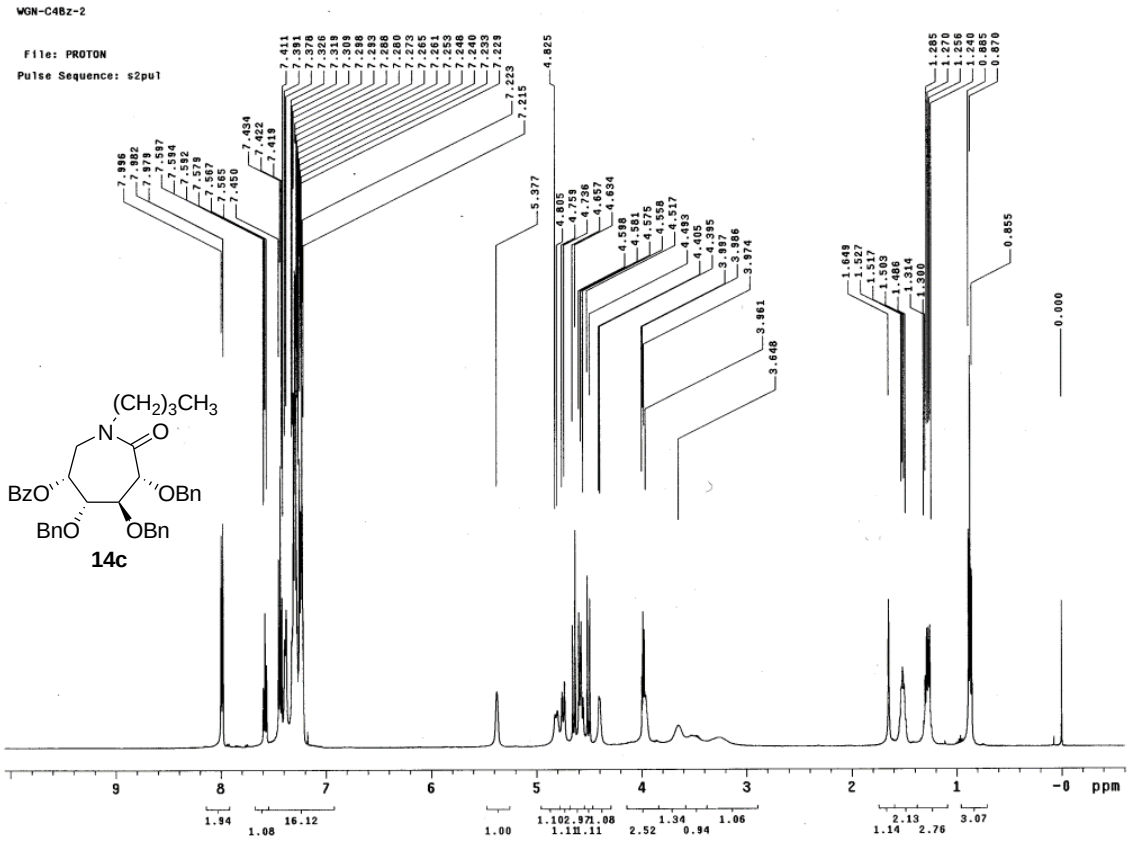
13e

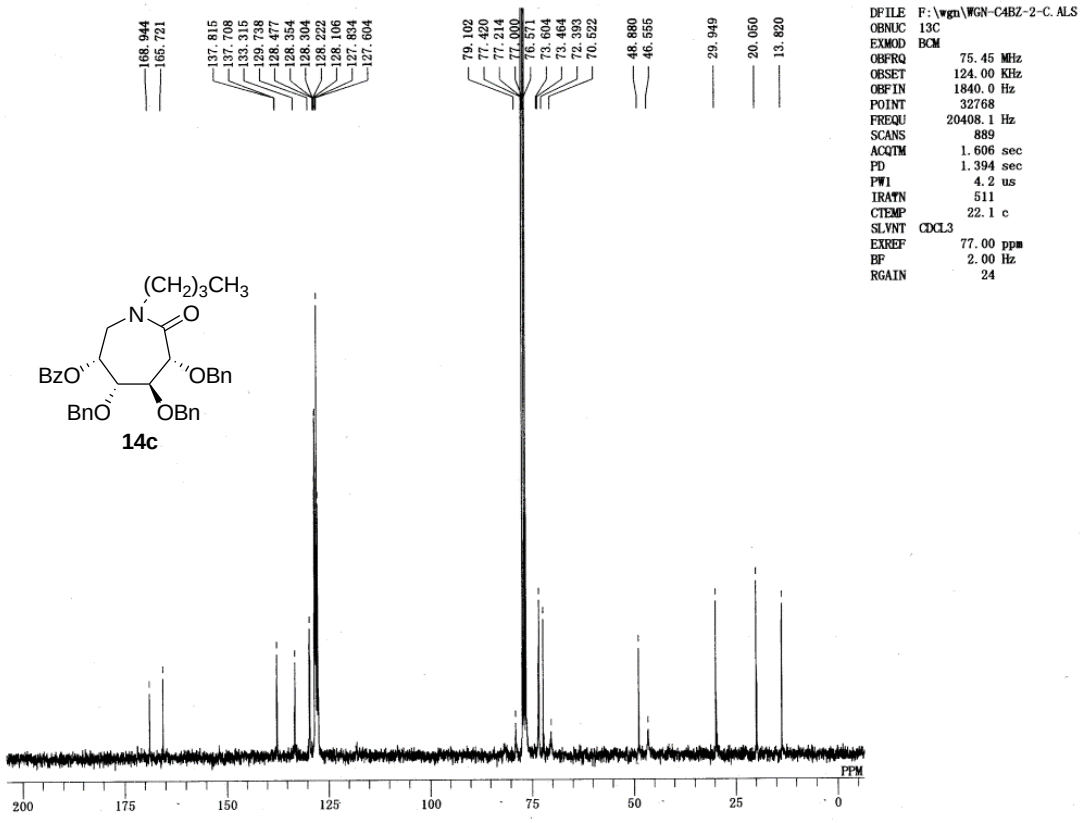


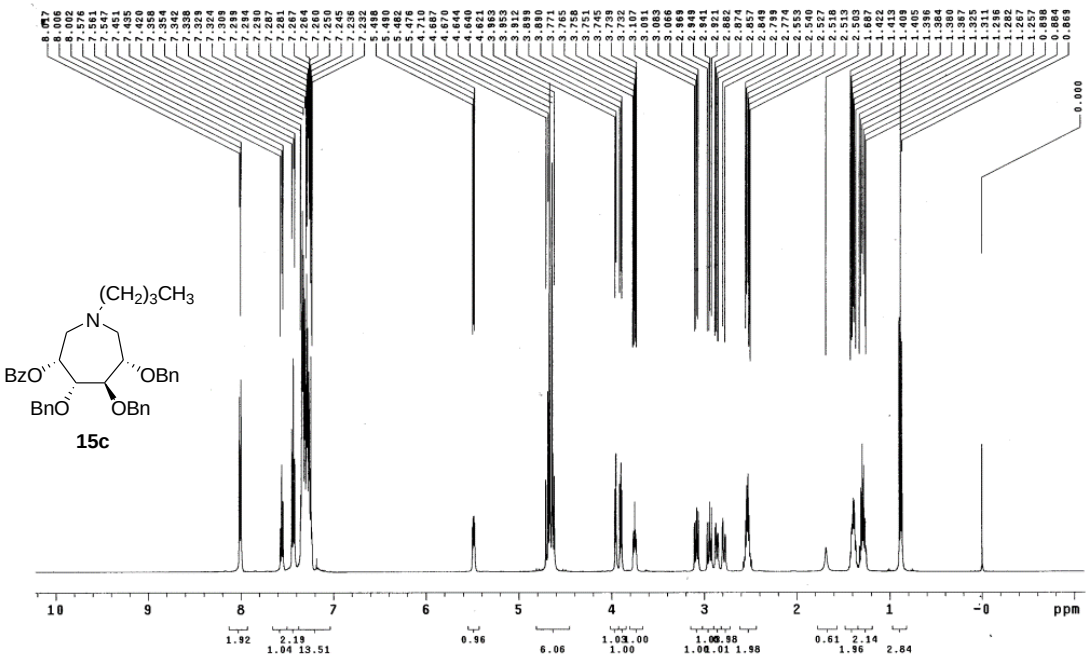

```
DFILE  D:\叶新山\DMAN-7-PMB-C.ALS
OBNUC  13C
EXMOD  BCM
OBFRQ         75.45 MHz
OBSET        124.00 KHz
OBFIN        1840.0 Hz
POINT         32768
FREQU        20408.1 Hz
SCANS           14064
ACQTM        1.606 sec
PD           1.394 sec
PW1            4.2 us
IRATN          511
CTEMP        20.5 c
SLVNT  CD3OD
EXREF        49.00 ppm
BF           2.00 Hz
RGAIN            25
```

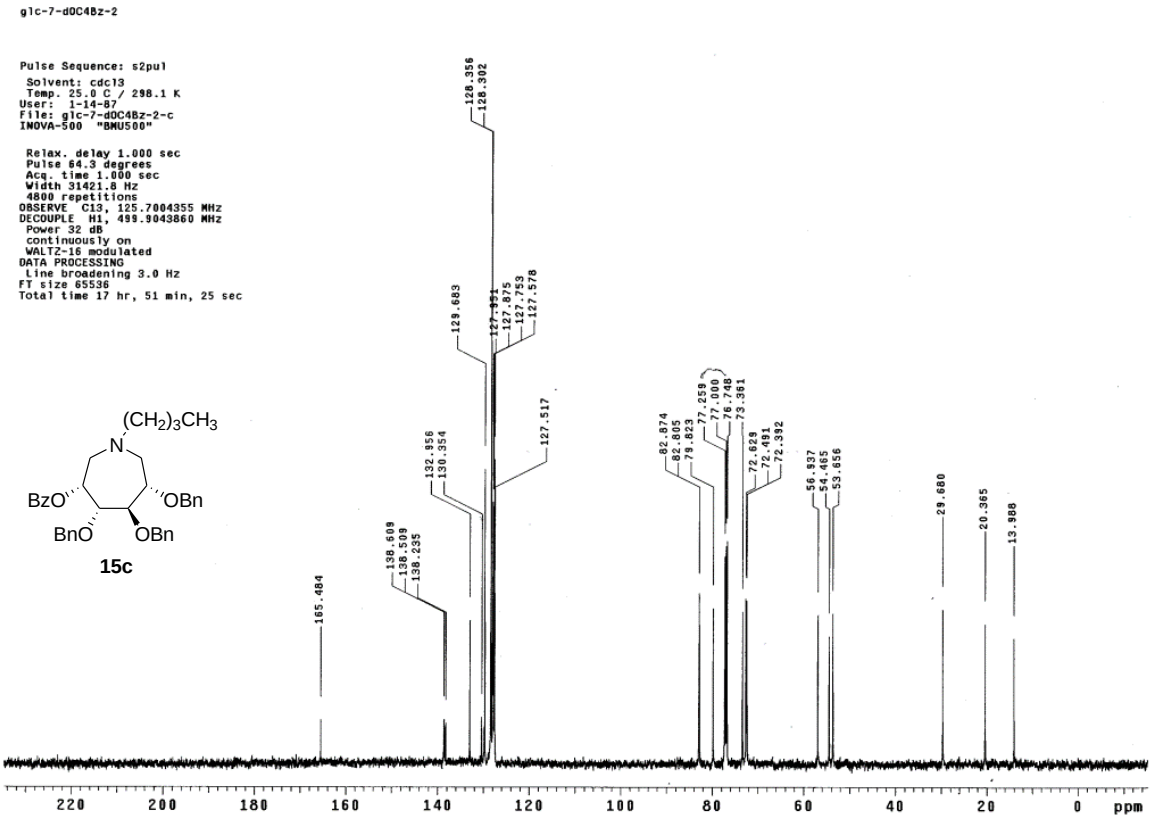


13e





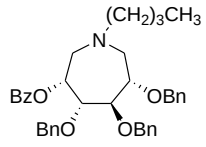




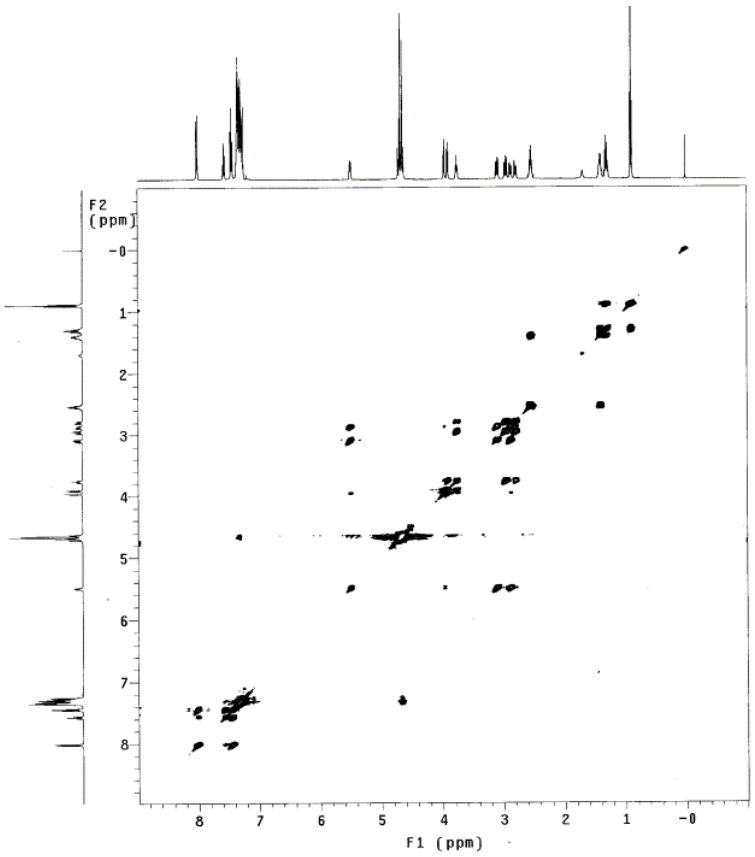
glc-7-d0C4Bz-2

Pulse Sequence: gCOSY
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
File: glc-7-d0C4Bz-2-cosy
INOVA-500 "BMU500"

Relax. delay 1.000 sec
Acq. time 0.205 sec
Width 4990.0 Hz
2D Width 4990.0 Hz
8 repetitions
512 increments
OBSERVE H1, 499.9019071 MHz
DATA PROCESSING
Sq. sine bell 0.103 sec
F1 DATA PROCESSING
Sq. sine bell 0.051 sec
FT size 8192 x 8192
Total time 1 hr, 26 min, 59 sec



15c

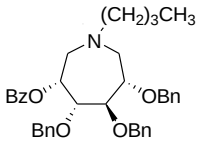


glc-7-d0C4Bz-2

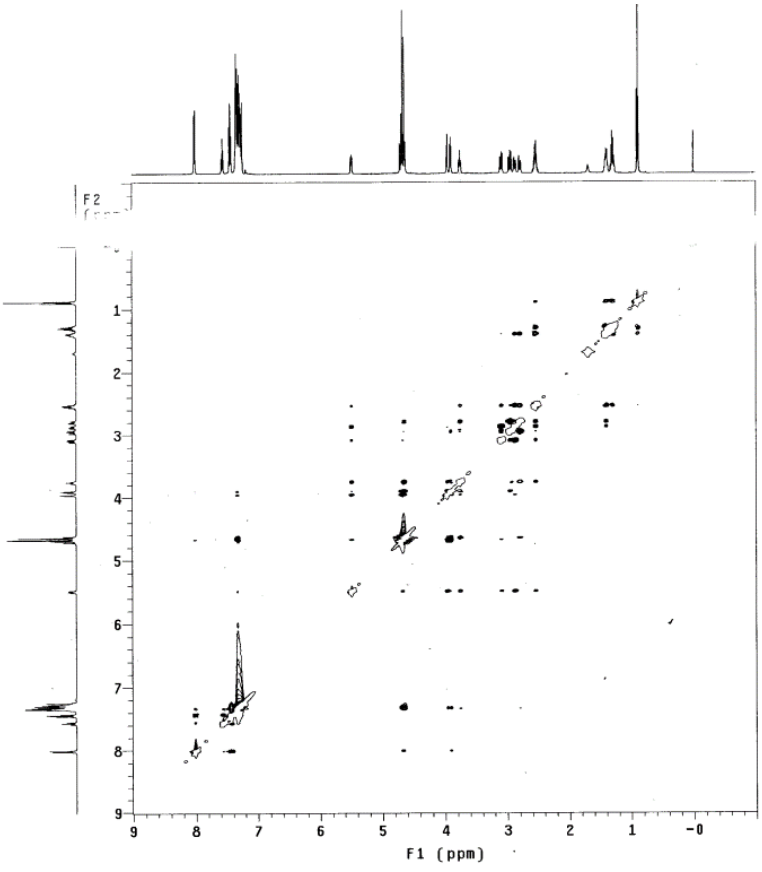
File: PROTON

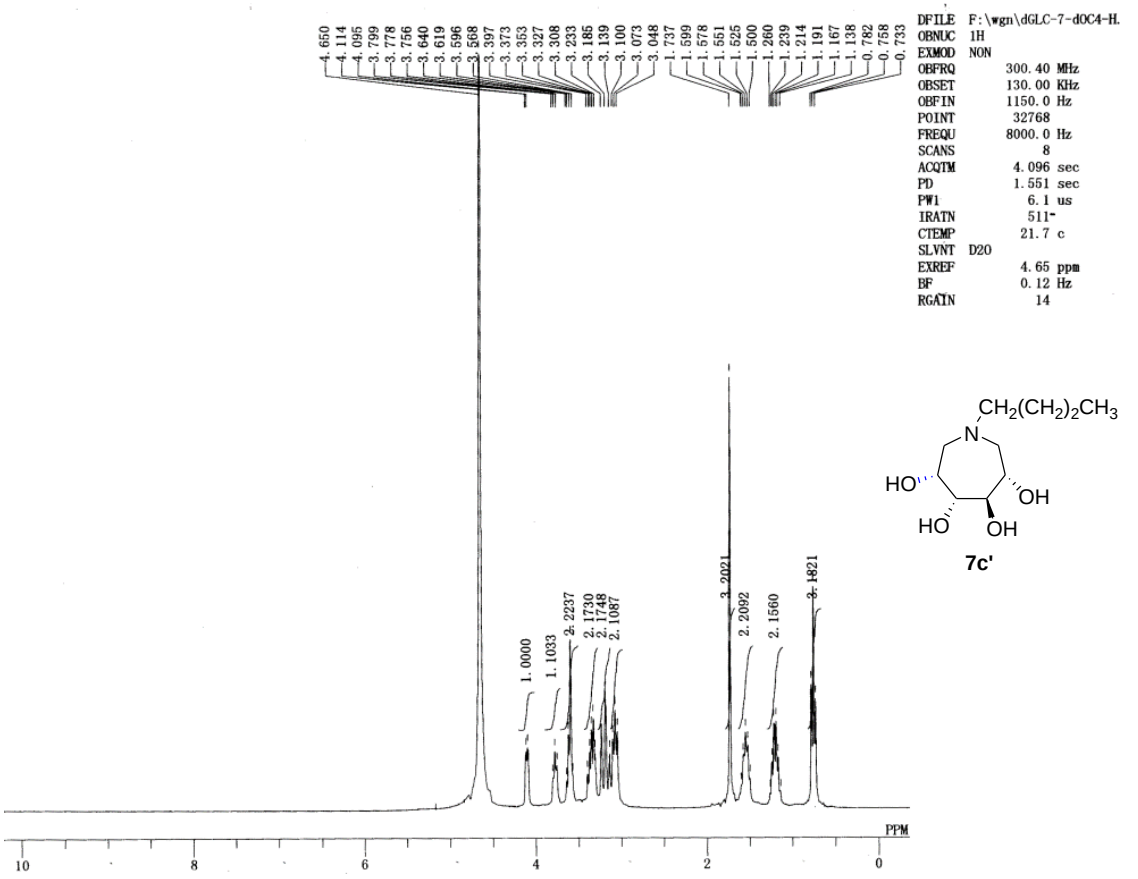
Pulse Sequence: NOESY
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
INOVA-500 "BMU500"

Relax. delay 1.000 sec
Mixing 0.600 sec
Acq. time 0.204 sec
Width 5007.5 Hz
2D Width 5007.5 Hz
32 repetitions
2 x 256 increments
Gauss apodization 0.034 sec
F1 DATA PROCESSING
Gauss apodization 0.029 sec
FT size 4096 x 4096
Total time 8 hr, 24 min, 25 sec

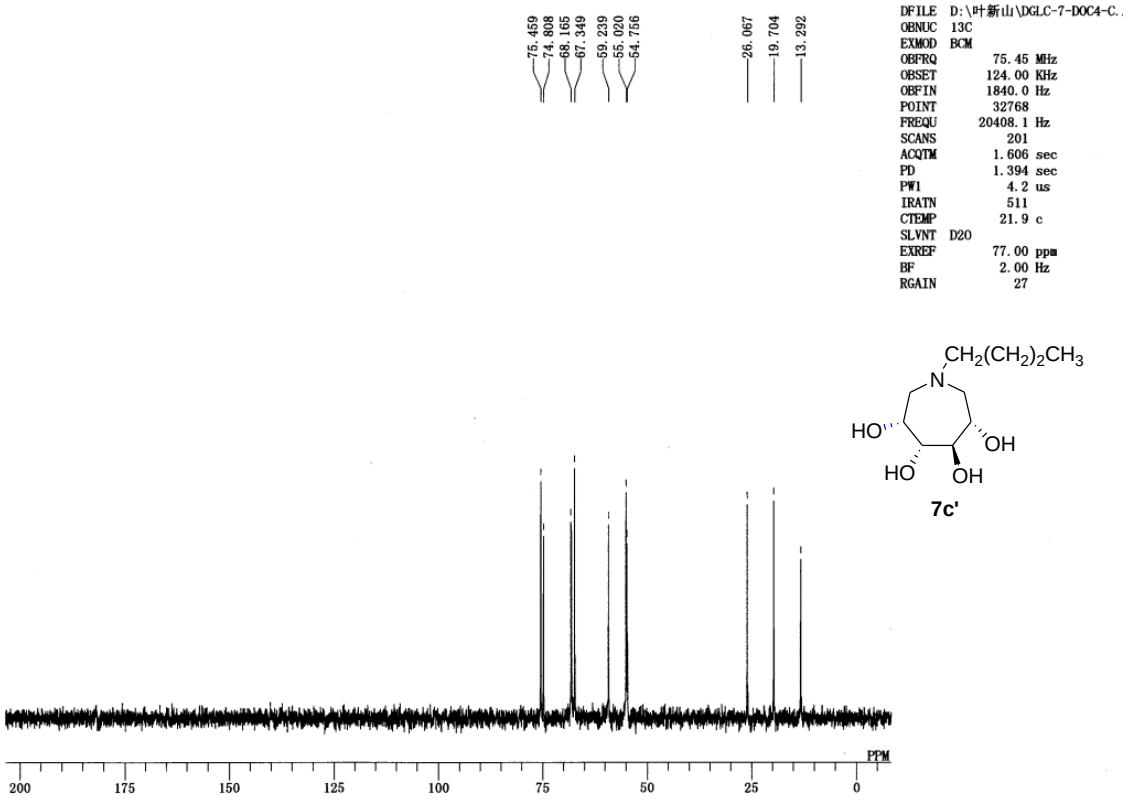


15c

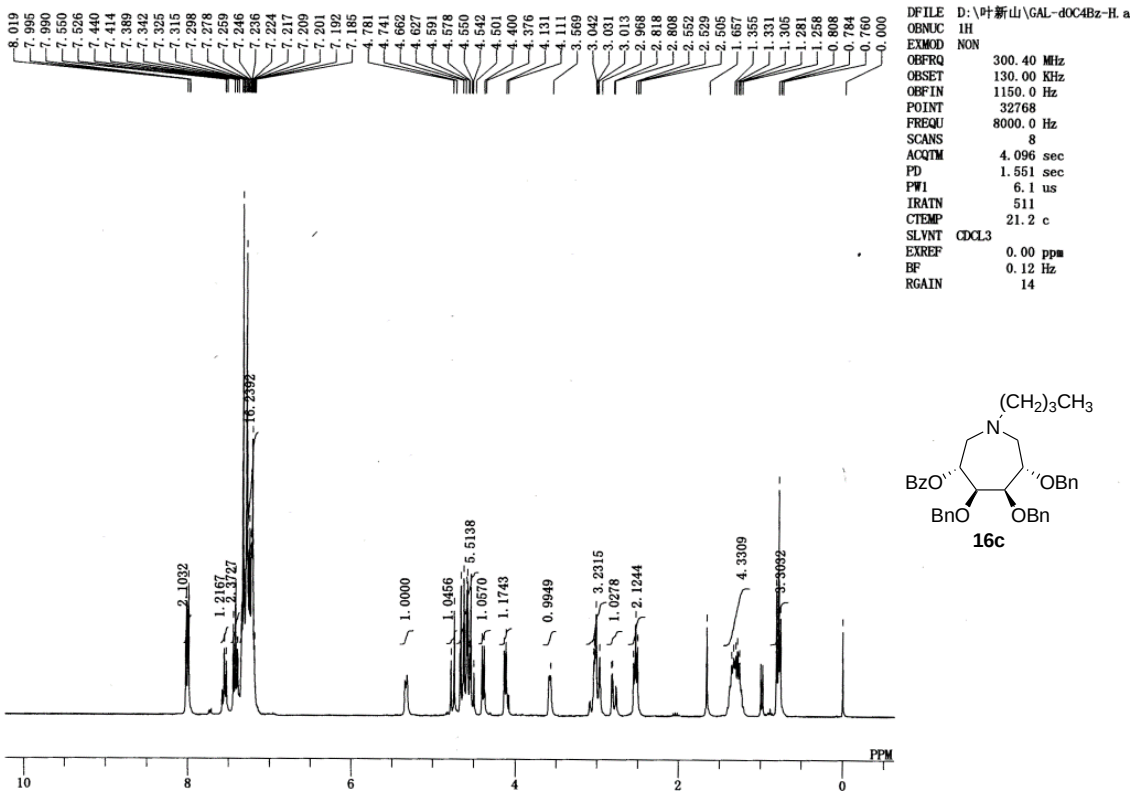




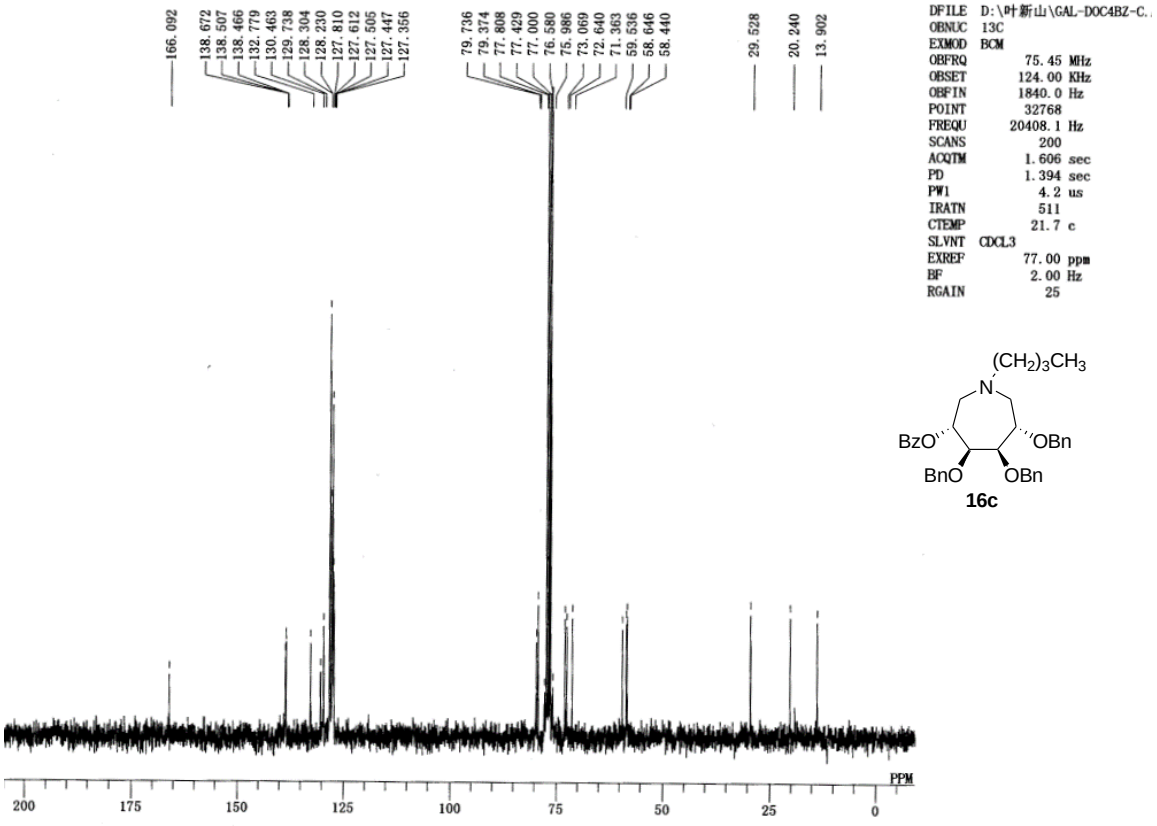
7c'



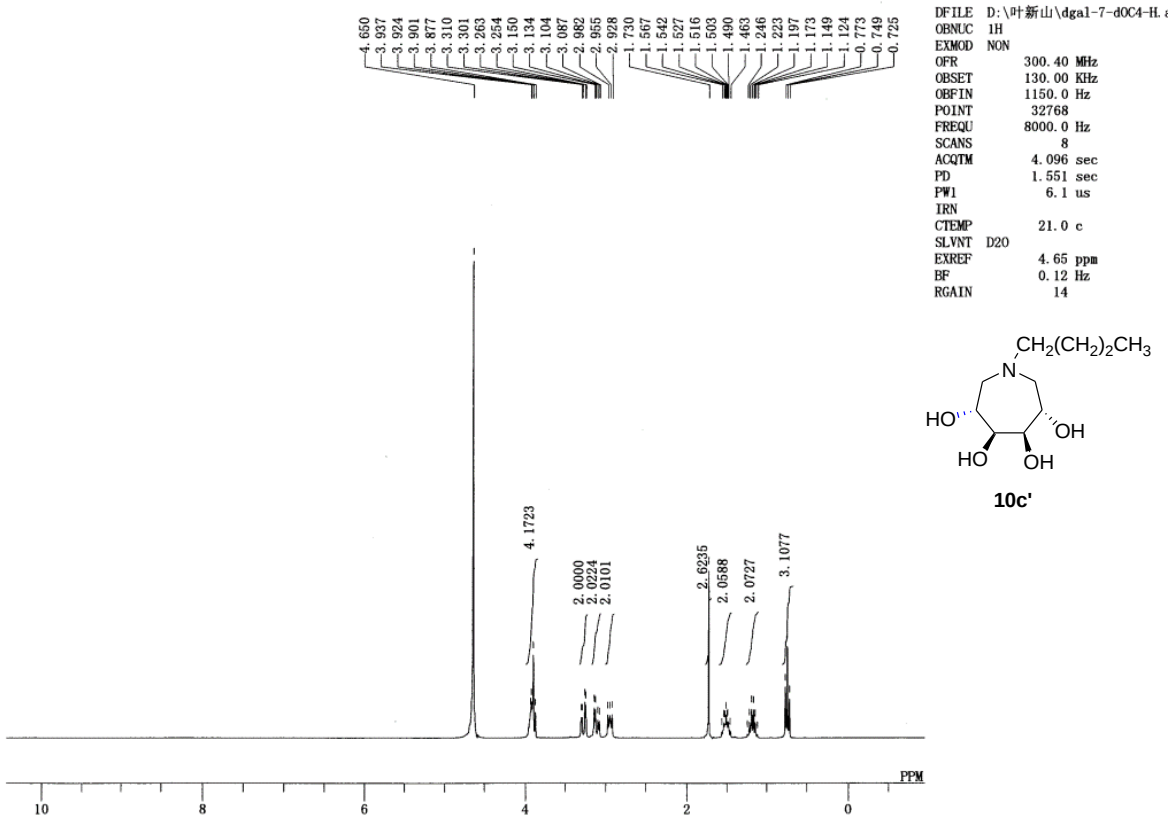
7c'



16c

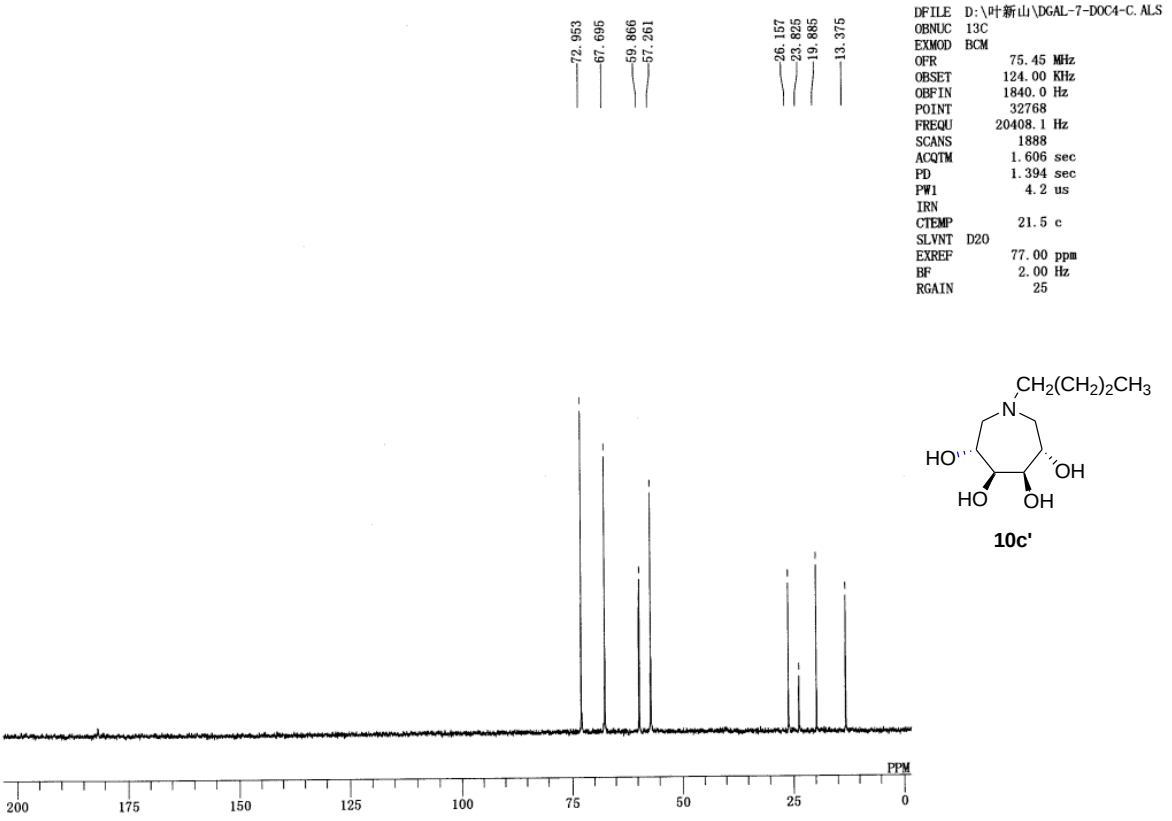


16c


4.650
3.937
3.924
3.901
3.877
3.310
3.301
3.263
3.254
3.150
3.134
3.104
3.087
2.982
2.955
2.928
1.730
1.567
1.542
1.527
1.516
1.503
1.490
1.463
1.246
1.223
1.197
1.173
1.149
1.124
0.773
0.749
0.725
DFILE D:\叶新山\dgal-7-dOC4-H.
OBNUC 1H
EXMOD NON
OFR 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRN
CTEMP 21.0 c
SLVNT D2O
EXREF 4.65 ppm
BF 0.12 Hz
RGAIN 14
4.1723
2.0000
2.0224
2.0101
2.6235
2.0588
2.0727
3.1077
PPM
10
8
6
4
2
0

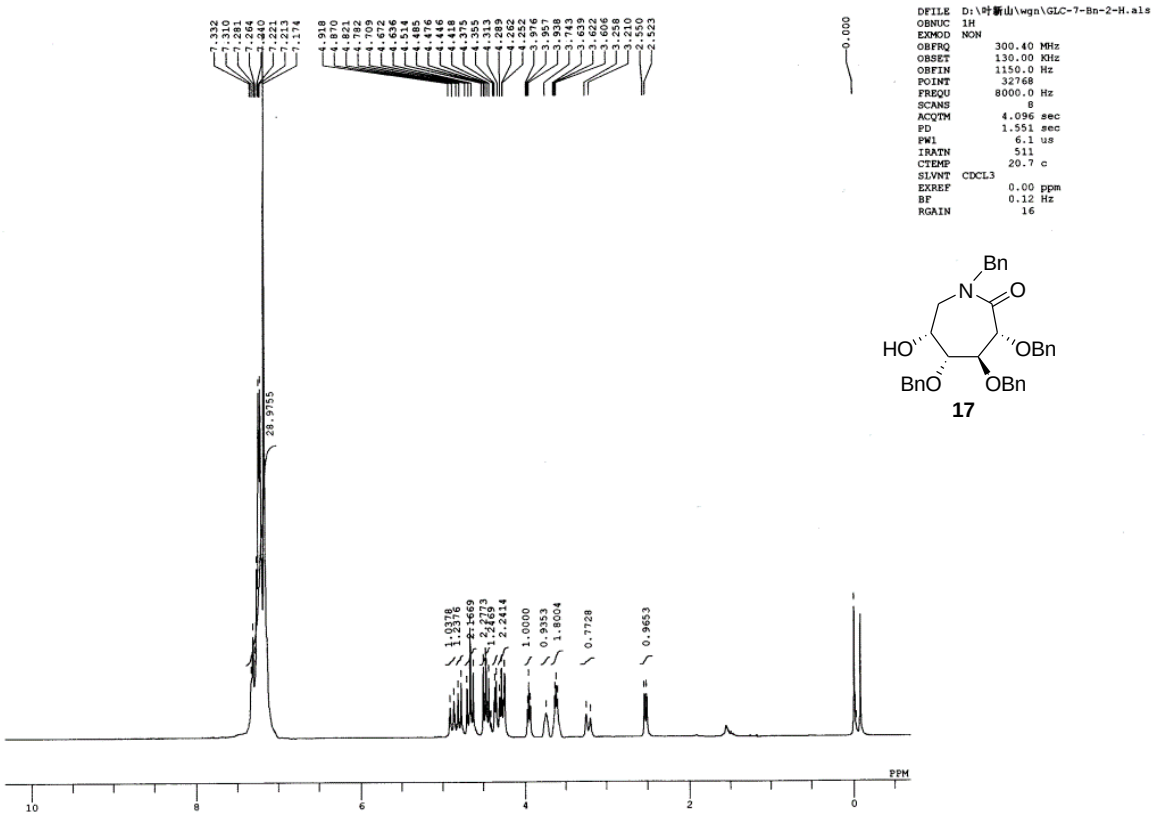
CH2(CH2)2CH3
N
HO
OH
HO
OH

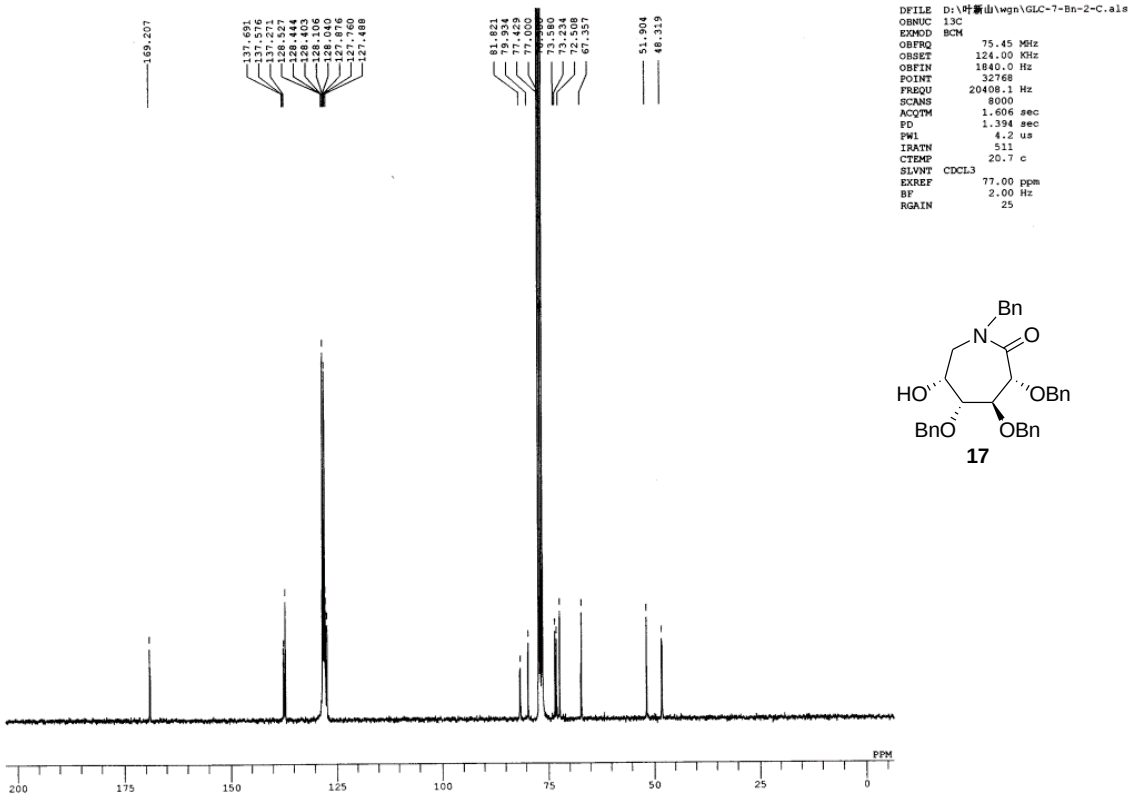
10c'

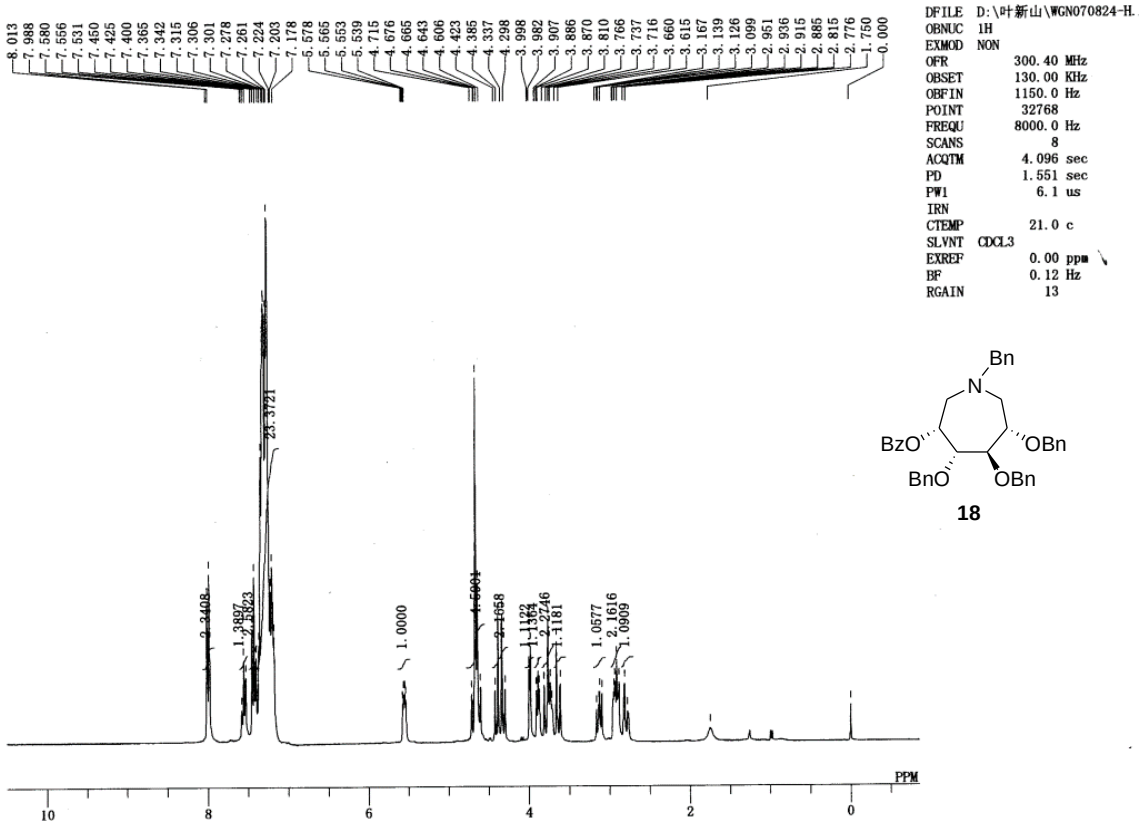

72.953
67.695
59.866
57.261
26.157
23.825
19.885
13.375
DFILE D:\叶新山\DGAL-7-DOC4-C.ALS
OBNUC 13C
EXMOD BCM
OFR 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 1888
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRN
CTEMP 21.5 c
SLVNT D2O
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 25
PPM
200
175
150
125
100
75
50
25
0

CH2(CH2)2CH3
N
HO
OH
HO
OH

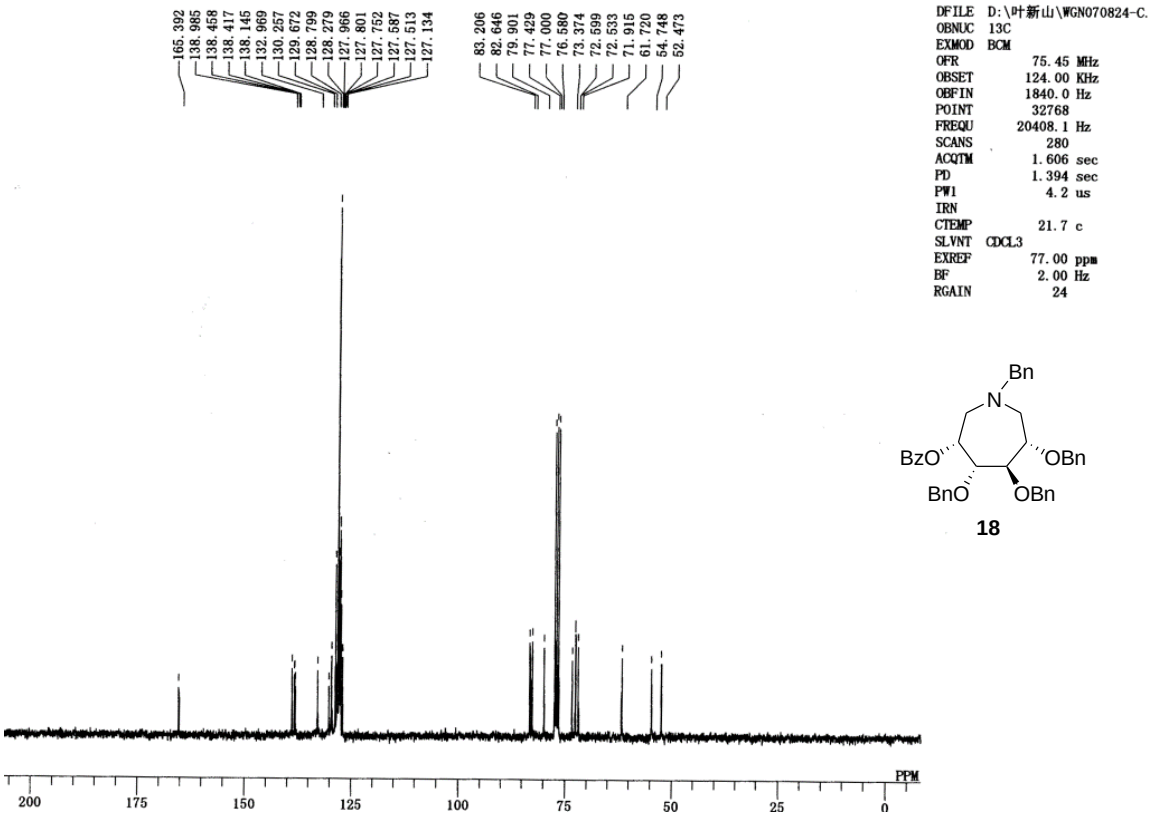
10c'



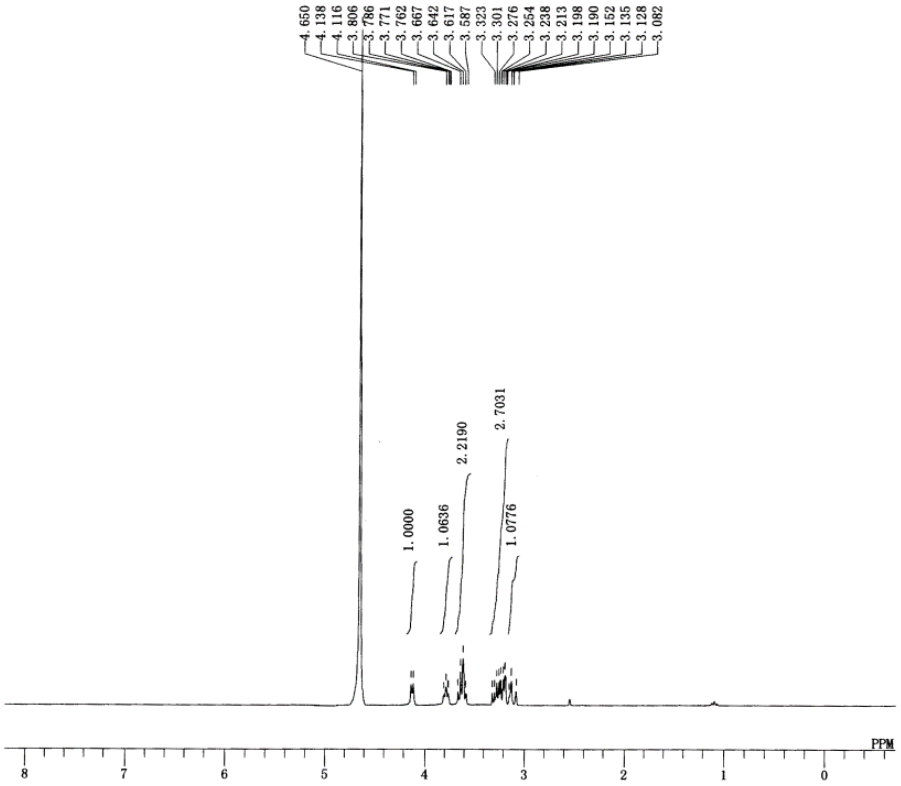




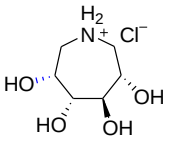
18



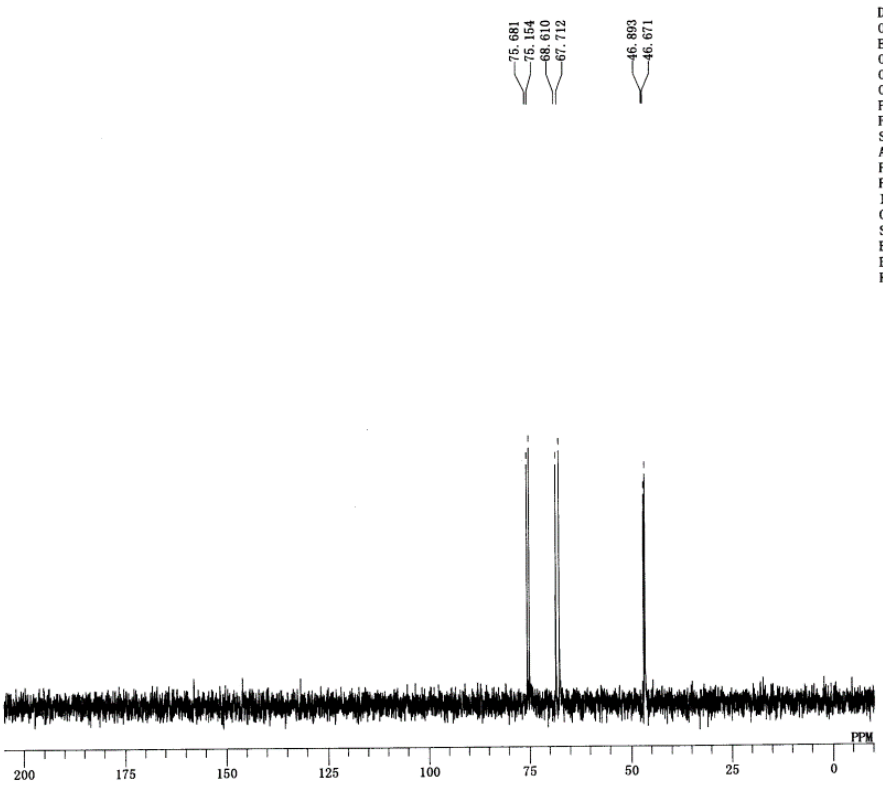
18



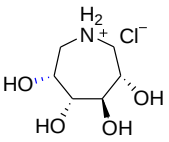

```
DFILE  D:\叶新山\dGLC-7-dONH-H.
OBNUC  1H
EXMOD  NON
OFR          300.40 MHz
OBSET        130.00 KHz
OBFIN        1150.0 Hz
POINT         32768
FREQU        8000.0 Hz
SCANS            8
ACQTM          4.096 sec
PD             1.551 sec
PW1              6.1 us
IRN
CTEMP           21.1 c
SLVNT  D2O
EXREF          4.65 ppm
BF             0.12 Hz
RGAIN            17
```



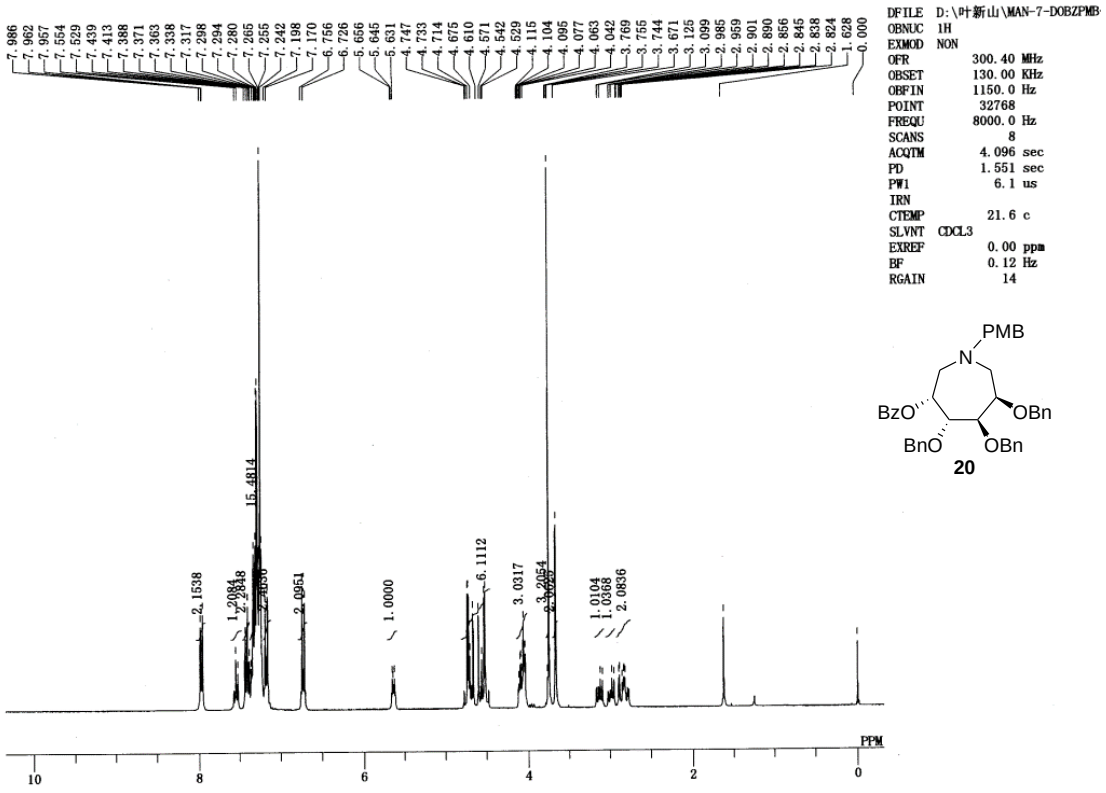
19

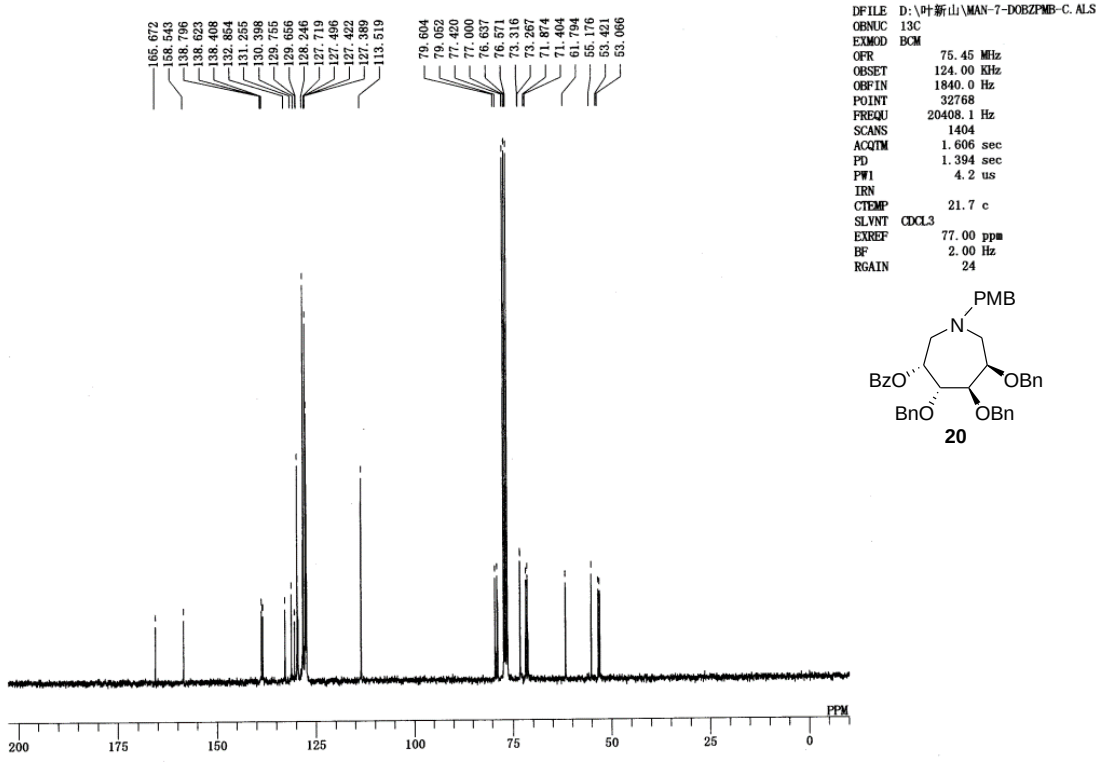


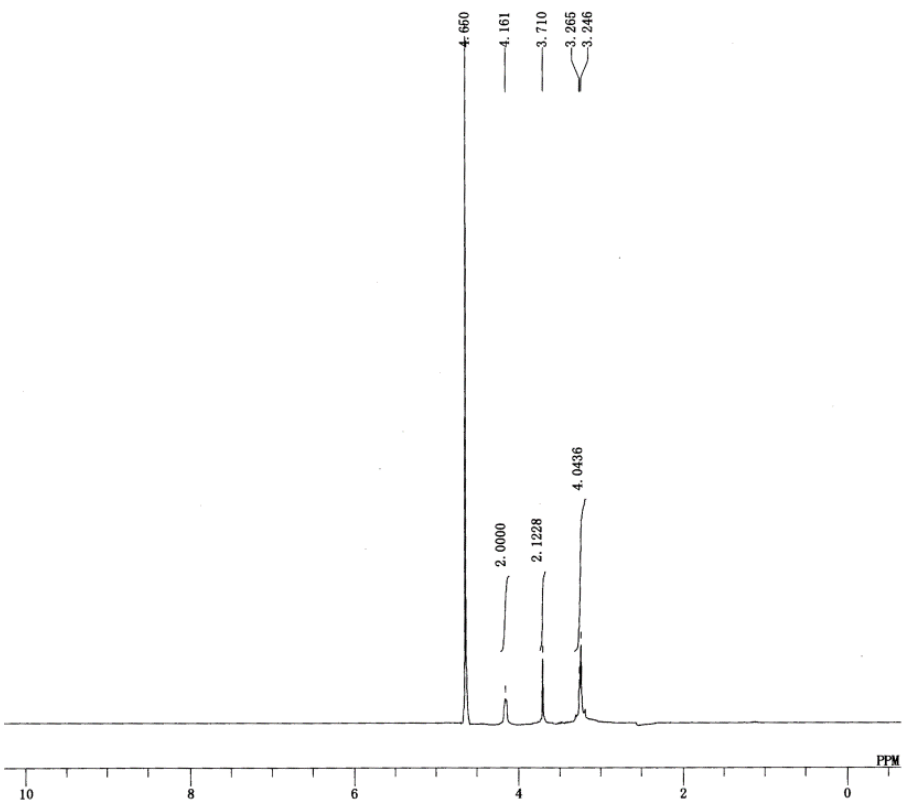

```
DFILE  D:\叶新山\DGLC-7-DONH-C.ALS
OBNUC  13C
EXMOD  BCM
OFR           75.45 MHz
OBSET        124.00 KHz
OBFIN        1840.0 Hz
POINT         32768
FREQU        20408.1 Hz
SCANS           840
ACQTM          1.606 sec
PD             1.394 sec
PW1              4.2 us
IRN
CTEMP           21.9 c
SLVNT  D2O
EXREF          77.00 ppm
BF             2.00 Hz
RGAIN            25
```



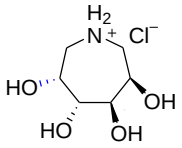
19


DFILE D:\叶新山\MAN-7-DOBZPMB
OBNUC 1H
EXMOD NON
OFR 300.40 MHz
OBSET 130.00 KHz
OBFIN 1150.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQTM 4.096 sec
PD 1.551 sec
PW1 6.1 us
IRN
CTEMP 21.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 14
PMB
N
BzO
OBn
BnO
OBn
20
PPM

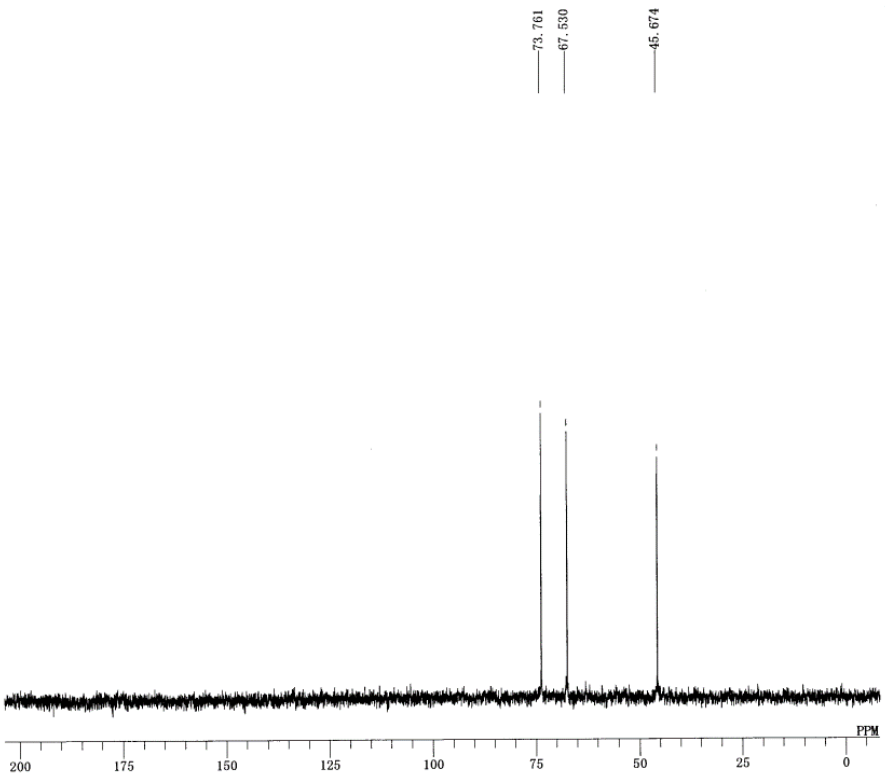

DFILE D:\叶新山\MAN-7-DOBZPMB-C.ALS
OBNUC 13C
EXMOD BCM
OFR 75.45 MHz
OBSET 124.00 KHz
OBFIN 1840.0 Hz
POINT 32768
FREQU 20408.1 Hz
SCANS 1404
ACQTM 1.606 sec
PD 1.394 sec
PW1 4.2 us
IRN
CTEMP 21.7 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 2.00 Hz
RGAIN 24
PMB
N
BzO
OBn
BnO
OBn
20
PPM



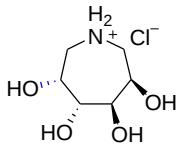

```
DFILE   D:\叶新山\dman-7-dONH-H.
OBNUC   1H
EXMOD   NON
OFR          300.40 MHz
OBSET        130.00 KHz
OBFIN        1150.0 Hz
POINT         32768
FREQU        8000.0 Hz
SCANS            8
ACQTM         4.096 sec
PD            1.551 sec
PW1             6.1 us
IRN
CTEMP          21.6 c
SLVNT   D2O
EXREF          4.65 ppm
BF             0.12 Hz
RGAIN            16
```



21




```
DFILE   D:\叶新山\DMAN-7-DONH-C.
OBNUC   13C
EXMOD   BCM
OFR          75.45 MHz
OBSET       124.00 KHz
OBFIN       1840.0 Hz
POINT         32768
FREQU       20408.1 Hz
SCANS           912
ACQTM         1.606 sec
PD            1.394 sec
PW1             4.2 us
IRN
CTEMP          21.7 c
SLVNT   D2O
EXREF          77.00 ppm
BF             2.00 Hz
RGAIN            25
```



21