

Supplementary Material

Mechanistic Investigation of β -galactosidase- activated MR Contrast Agents

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Part 1. Experimental details and characterization of S-diastereomers and racemic mixtures.

S-(-)-2-bromopropan-1-ol (7b). The same procedure was used as described for **7a** beginning with 3.0 mL (5.09 g, 0.033 mol) of S-(-)-2-bromopropionic acid. Yield: 72% ¹H NMR (400 MHz, CDCl₃) δ 1.62 (d, 3H, CH₃CHBrCH₂OH, J = 8), 2.14-2.24 (s, 1H, CH₃CHBrCH₂OH), 3.60-3.82 (m, 2H, CH₃CHBrCH₂OH), 4.20-4.36 (m, 1H, CH₃CHBrCH₂OH). ¹³C NMR (100 MHz, CDCl₃) δ 22.1, 53.74, 68.90.

2-bromopropan-1-ol (7c). The same procedure was used as described for **7a** beginning with 10.0 ml (16.96 g, 0.111 mol) of 2-bromopropionic acid. Yield: 66%. ¹H NMR (400 MHz, CDCl₃) δ 1.52-1.62 (d, 3H, CH₃CHBrCH₂OH, J = 8), 3.1 (s, 1H, CH₃CHBrCH₂OH), 3.54-3.70 (m, 2H, CH₃CHBrCH₂OH), 4.02-4.15 (m, 1H, CH₃CHBrCH₂OH). ¹³C NMR (100 MHz, CDCl₃) δ 21.23, 52.73, 67.42.

S-(-)-2-bromopropan-1-β-D-galactose tetraacetate (8b). The S-diastereomer was synthesized by the same procedure described for **8a** beginning with 0.2820 g (0.0020 mol) **7b** in a 74.4% yield. ¹H NMR (500 MHz, CDCl₃) δ 1.66-1.67 (d, 3H, methyl, J = 6.5), 1.99-2.16 (m, 12H, OAc), 3.65-3.69 (m, 2H, CH₃CHBrCH₂O-sugar), 3.90-3.93 (m, 1H, CH₃CHBrCH₂O-sugar), 4.00-4.03 (m, 2H, H-6), 4.11-4.20 (m, 1H, H-4), 4.53-4.55 (m, 1H, H-5), 5.02-5.05 (m, 1H, H-3), 5.22-5.26 (m, 2H, H-2), 5.40-5.40 (m, 1H, H-1). ¹³C NMR (125 MHz) δ 20.87, 20.95, 21.14, 22.69, 46.15, 61.44, 67.14, 68.80, 70.91, 70.97, 75.14, 101.91, 170.28, 170.36, 170.54. ESI-MS *m/z* = 492.8 (M + Na⁺).

2-bromopropan-1-β-D-galactose tetraacetate (8c). The racemic mixture of **8** was synthesized by the same procedure as for **8a** beginning with 6.46 g (0.046 mol) **7c** in a yield of 70%. ¹H NMR (400 MHz) δ 1.62-1.76 (d, 3H, methyl, J = 6.5), 1.88-2.18 (m, 12H, OAc), 3.60-3.68 (m, 2H, CH₃CHBrCH₂O-sugar), 3.86-3.92 (m, 1H, CH₃CHBrCH₂O-sugar), 4.16-4.22 (m, 3H, H-5 and H-6), 4.52-4.58 (m, 1H, H-4), 5.0-5.18 (m, 1H, H-2), 5.20-5.28 (m, 1H, H-3), 5.39 (m, 1H, H-1). ¹³C NMR (100 MHz) δ 20.49, 20.57, 20.78, 20.94, 22.19, 22.37, 45.95, 46.34, 60.27, 61.19, 66.96, 68.53, 68.60, 70.67, 74.84, 75.07, 101.31, 101.60, 169.36, 169.99, 170.14, 170.26. ESI-MS *m/z* = 492.8 (M+Na⁺).

S-(-)-(2-(1,4,7,10-tetraazacyclododecyl)propan)-1-β-D-galactose tetraacetate (9b). Synthesized **9b** according to the procedure for **9a** beginning with 1.8441 g (0.00393 mol) of **8a**. ¹H NMR (400 MHz, CD₃CN) δ 0.78-0.84 (d, 3H, methyl, J = 6.0), 1.85-2.22 (m, 12H, OAc), 2.74-3.35(br, 16H, cyclen), 3.92-4.08 (m, 2H, methylene on linker), 4.16-4.2

(m, 1H, methine on linker), 4.38-4.42 (m, 3H, H-5 and H-6), 4.72 (m, d, 1H, H-4), 4.98-5.08 (m, 1H, H-2), 5.10-5.18 (m, 1H, H-3), 5.40 (m 1H, H-1). ^{13}C NMR (125 MHz, CD_3CN) δ 7.92, 20.15, 20.30, 20.37, 20.40, 53.41, 61.52, 67.47, 68.76, 70.56, 72.04, 73.49, 104.5, 170.02, 170.75, 170.79, 171.28. ESI-MS m/z = 561.3 ($\text{M} + \text{H}^+$).

(2-(1,4,7,10-tetraazacyclododecyl)propan)-1- β -D-galactose tetraacetate (9c):

Compound **9c** was synthesized using the procedure described for **9a**. ^1H NMR (400 MHz, CDCl_3) δ 0.82-0.98 (d, 3H, methyl, J = 6.0), 1.95-2.18(m, 12H, OAc), 2.8-3.42 (br, 16H, cyclen), 3.80-4.1 (m, 3H, methylene and methine on linker), 4.18-4.22 (m, 2H, H-6), 4.48 (d, 1H, H-4), 4.96-4.98 (m, 1H, H-5), 5.0-5.06 (m, 1H, H-3), 5.40 (m, 2H, H-2 and H-1). ^{13}C NMR (125 MHz, CD_3CN) δ 7.85, 8.20, 20.09, 20.21, 20.34, 53.11, 53.43, 61.29, 61.52, 67.47, 67.66, 68.77, 69.09, 70.31, 70.56, 70.89, 71.55, 72.07, 101.5, 104.5, 170.02, 170.26, 170.55, 171.27, 171.49. ESI-MS m/z = 561.2 ($\text{M} + \text{H}^+$).

(S)-(-)-(2-(4,7,10-trimethylcarboxymethyl-(1,4,7,10-tetraazacyclododecyl))propan)-1- β -D-galactose tetraacetate (10b). The S-diastereomer **10b**, was synthesized

according to the procedure for **10a** beginning with 1.1828 g of **9b**. The yield was calculated over last two reactions beginning with **8a**: 25%. ^1H NMR (500 MHz, CD_3CN) δ 1.3 (d, 3H, methyl, J = 6), 1.98-2.2 (m, 12H, OAc), 2.3-3.6 (m, 16H, cyclen), 3.8-3.98 (m, 9H, $-\text{OCH}_3$), 4.0-4.15 (m, 5H, methylene and methine on linker and H-6), 4.55-4.80 (br, 3H, H-5, H-4, and H-3), 5.1 (s, 1H, H-2), 5.4 (s, 1H, H-1). ^{13}C NMR (CD_3CN , 125 MHz) δ 20.72, 20.76, 20.90, 54.40, 60.33, 67.32, 68.72, 70.25, 71.43, 71.54, 101.24, 169.46, 169.93, 170.75, 171.48. ESI-MS: m/z = 777.6 ($\text{M} + \text{H}^+$), 799.5 ($\text{M} + \text{Na}^+$).

(2-(4,7,10-trimethylcarboxymethyl-(1,4,7,10-tetraazacyclododecyl))propan)-1- β -D-galactose tetraacetate (10c). The racemic mixture was synthesized according to

procedure described for **10a** beginning with 1.0148 g of **9c**. Yield was calculated over the last two reactions beginning with **8c**: 37%. ^1H NMR (500 MHz, CD_3CN) δ 1.2-1.3 (d, 3H, methyl, J = 6.0), 1.9-2.2 (m, 12H, OAc), 2.4-3.6 (br, 16H, cyclen), 3.65-3.8 (m, 9H, $-\text{OCH}_3$), 3.9-4.2 (br, methylene and methine on linker and H-6), 4.6 (m, 1H, H-4), 4.7 (m, 1H, H-5), 5.0-5.2 (m, 1H, H-3), 5.4 (m, 1H, H-2), 5.5 (s, 1H, H-1). ^{13}C NMR (125 MHz, CD_3CN) δ 20.05, 20.10, 20.20, 20.35, 20.38, 51.17, 51.41, 51.46, 52.18, 52.28, 52.38, 52.52, 55.12, 55.57, 55.67, 61.49, 61.55, 67.55, 67.62, 68.95, 69.06, 69.14, 70.68, 70.80, 70.96, 71.13, 100.48, 101.24, 170.05, 170.48, 171.30, 171.51, 171.57, 174.33, 174.76, 175.15. ESI-MS: m/z = 777.2 ($\text{M} + \text{H}^+$), 799.2 ($\text{M} + \text{Na}^+$).

Kinetic resolution of S-(-)-propylene oxide (11b). Propylene oxide was kinetically resolved as described above beginning with 5 mL (4.15 g, 0.071 mol) of propylene oxide and 0.008 eq. of (S,S)-(+)-N,N'-bis (3,5-di-tertbutylsalicylidene)-1,2-cyclohexane diaminocobalt(II). (S)-propylene oxide was obtained after distillation in 23% yield (vapor temperature = 33 °C). ^1H NMR (500 MHz, CDCl_3) δ 1.26-1.34 (d, 3H, methyl, J = 5), 2.42-2.46 (m, 1H, methylene), 2.74-2.78 (m, 1H, methylene), 2.96-3.00 (m, 1H, methine). ^{13}C NMR (125 MHz, CDCl_3) δ 18.12, 48.16, 48.39.

S-(-)-1-bromopropan-2-ol (12b). The S-diastereomer was synthesized using the procedure described for **12a** beginning with 8 mL (6.63 g, 0.11 mol) of **11b**. Yield: 57%.

^1H NMR (500 MHz, CDCl_3) δ 1.28-1.36 (d, 3H, methyl, $J = 6.0$), 1.88 (br, 1H, -OH), 3.34-3.40 (m, 1H, methylene), 3.48-3.04 (m, 1H, methylene), 3.96-4.02 (m, 1H, methine). ^{13}C NMR (125 MHz, CDCl_3) δ 21.22, 41.50, 68.11.

1-bromopropan-2-ol (12c). The racemic mixture of **12** was synthesized according to the procedure described for **12a** beginning with 10 mL (8.29 g, 0.14 mol) of **11c**. Yield: 76%. ^1H NMR (500 MHz, CDCl_3) δ 1.25-1.32 (d, 3H, methyl, $J = 6.0$), 1.85 (br, 1H, -OH), 3.32-3.38 (m, 1H, methylene), 3.45-3.51 (m, 1H, methylene), 3.94-4.02 (m, 1H, methine). ^{13}C NMR (125 MHz, CDCl_3) δ 21.23, 41.51, 68.11.

S-(-)-1-bromopropan-2- β -D-galactose tetraacetate (13b). The S-diastereomer was synthesized using the procedure described for **13a** beginning with 4.3867 g (0.0315 mol) of **12b** and 10.1832 g (0.026 mol) of β -D-galactosepentaacetate. Single crystals of compound **13b** were obtained from a solution of ether/pet. ether, methanol, and ethyl acetate. Yield: 70%. ^1H NMR (500 MHz, CDCl_3) δ 1.30-1.38 (d, 3H, methyl, $J = 6.5$), 1.98-2.40 (m, 12H, OAc), 3.28-3.36 (m, 2H, $-\text{CH}_2\text{Br}$), 3.86-3.98 (m, 2H, methine on linker and H-5), 4.05-4.20 (m, 2H, H-6), 4.55-4.64 (m, 1H, H-4), 4.96-5.02 (m, 1H, H-3), 5.18-5.24 (m, 1H, H-2), 5.38 (m, 1H, H-1). ^{13}C NMR (125 MHz, CDCl_3) δ 20.85, 20.94, 21.01, 21.28, 36.23, 61.18, 67.13, 68.86, 70.79, 70.98, 76.98, 101.67, 168.57, 176.13, 170.27, 170.37. ESI-MS: $m/z = 493.0$ ($\text{M} + \text{Na}^+$), 509.2 ($\text{M} + \text{K}^+$).

1-bromo-propan-2- β -D-galactose tetraacetate (13c). The racemic mixture was synthesized using the procedure described for **13a** beginning with 5.2619 g (0.038 mol) of **12c** and 12.2332 g (0.031 mol) of β -D-galactosepentaacetate. Yield: 45%. ^1H NMR (500 MHz, CDCl_3) δ 1.33-1.38 (d, 3H, methyl, $J = 6.5$), 1.92-2.20 (m, 12H, OAc), 3.32-3.40 (m, 1H, $-\text{CH}_2\text{Br}$), 3.42-3.48 (m, 1H, $-\text{CH}_2\text{Br}$), 3.88-3.98 (m, 2H, methine on linker and H-5), 4.12-4.20 (m, 2H, H-6), 4.50-4.58 (m, 1H, H-4), 4.98-5.10 (m, 1H, H-3), 5.28-5.40 (m, 2H, H-1 and H-2). ^{13}C NMR (125 MHz, CDCl_3) δ 18.92, 20.55, 20.89, 20.92, 20.98, 36.18, 36.52, 61.54, 62.09, 62.14, 66.77, 67.17, 67.66, 67.71, 68.22, 68.30, 68.39, 68.47, 70.87, 71.03, 75.00, 75.37, 95.25, 96.70, 170.46, 170.67, 170.69, 170.88. ESI-MS: $m/z = 493.1$ ($\text{M} + \text{Na}^+$), 509.1 ($\text{M} + \text{K}^+$).

S-(-)-1-(1,4,7,10-tetraazacyclododecyl)propan-2- β -D-galactose tetraacetate (14b). The S-diastereomer was synthesized using the method described for **14a** beginning with 3.1863 g (0.0068 mol) of **13b**. ^1H NMR (500 MHz, CDCl_3) δ 1.08-1.18 (d, 3H, methyl, $J = 6.5$), 1.95-2.28 (m, 12H, OAc), 2.70 (s, 2H, methylene on linker), 2.90-3.50 (br, 16H, cyclen), 3.90-4.02 (m, 1H, methine on linker), 4.16-4.24 (m, 1H, H-5), 4.25-4.36 (m, 2H, H-6), 4.62-4.68 (m, 1H, H-4), 4.90-4.98 (m, 1H, H-3), 5.02-5.12 (m, 1H, H-2), 5.42 (m, 1H, H-1). ESI-MS: $m/z = 561.2$ ($\text{M} + \text{H}^+$).

1-(1,4,7,10-tetraazacyclododecyl)propan-2- β -D-galactose tetraacetate (14c). The racemic mixture was synthesized according to the method described for **14a** beginning with 3.5534 g (0.0076 mol) of **13c**. ^1H NMR (500 MHz, CDCl_3) δ 1.08-1.16 (d, 3H, methyl, $J = 6.5$), 1.95-2.30 (m, 12H, OAc), 2.70 (s, 2H, methylene on linker), 2.92-3.52 (br, 16H, cyclen), 3.90-4.02 (m, 1H, methine on linker), 4.18-4.28 (m, 1H, H-5), 4.25-

4.36 (m, 2H, H-6), 4.62-4.68 (m, 1H, H-4), 4.90-4.98 (m, 1H, H-3), 5.02-5.12 (m, 1H, H-2), 5.42 (m, 1H, H-1). ESI-MS: $m/z = 561.2$ (M + H⁺).

S-(-)-1-(4,7,10-trimethylcarboxymethyl-(1,4,7,10-tetraazacyclododecyl))propan-2-β-D-galactose tetraacetate (15b). The S-diastereomer was synthesized using the procedure described for **15a** beginning with 1.6147 g (0.0029 mol) of **14b**. The yield over last two reactions starting from **13b**: 39%. ¹H NMR (500 MHz, CDCl₃) δ 1.18-1.19 (d, 3H, methyl, J = 6.5), 1.89-2.09 (m, 12H, acetates), 2.73-3.42 (m, 16H, cyclen), 3.64-3.74 (m, 9H, -OCH₃), 3.90-4.15 (br, methylene and methine on linker and H-6), 4.55-4.62 (m, 1H, H-4), 4.91-5.00 (m, 2H, H-3 and H-5), 5.07-5.15 (m, 1H, H-2), 5.32 (s, 1H, H-1). ¹³C NMR (125 MHz, CDCl₃) δ 20.39, 20.74, 20.89, 21.41, 48.31, 50.69, 51.96, 52.09, 52.89, 52.96, 55.69, 55.99, 55.87, 61.56, 67.26, 67.38, 69.31, 69.42, 70.87, 70.94, 71.41, 73.25, 95.01, 100.98, 169.66, 169.96, 170.08, 170.17, 170.42, 170.62, 171.40, 171.82, 174.20. ESI-MS: $m/z = 777.2$ (M + H⁺), 799.3 (M + Na⁺).

1-(4,7,10-trimethylcarboxymethyl-(1,4,7,10-tetraazacyclododecyl))propan-2-β-D-galactose tetraacetate (15c). The racemic mixture was synthesized using the method described for **15a** beginning with 1.6173 g (0.0029 mol) of **14c**. Yield over last two reactions starting with **13c**: 51%. ¹H NMR (500 MHz, CDCl₃) δ 1.17-1.18 (d, 3H, methyl, J = 6.5), 1.89-2.09 (m, 12H, acetates), 2.65-3.60 (m, 16H, cyclen), 3.64-3.75 (m, 9H, -OCH₃), 3.92-3.98 (br, methylene and methine on linker and H-6), 4.99-5.36 (m, 4H, H-3, H-5, H-2, H-1). ¹³C NMR (125 MHz, CDCl₃) δ 20.93, 48.24, 50.99, 52.13, 52.73, 52.98, 55.87, 56.16, 61.59, 66.86, 67.51, 67.94, 70.63, 94.51, 95.01, 170.39, 170.54, 170.72, 171.24, 171.41, 171.59, 174.27, 174.92. ESI-MS: $m/z = 777.2$ (M + H⁺), 799.3 (M + Na⁺).

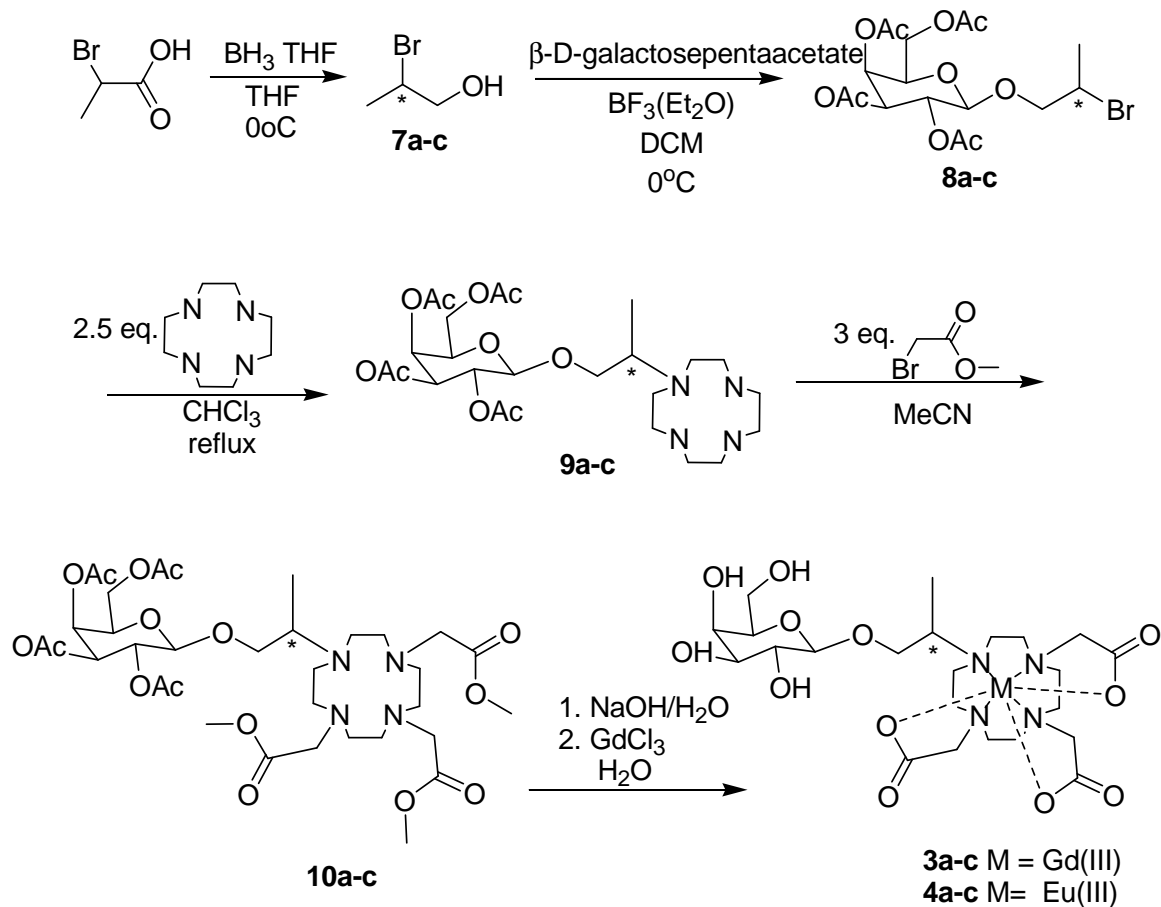


Figure S1. Synthetic Scheme for preparation of α -series.

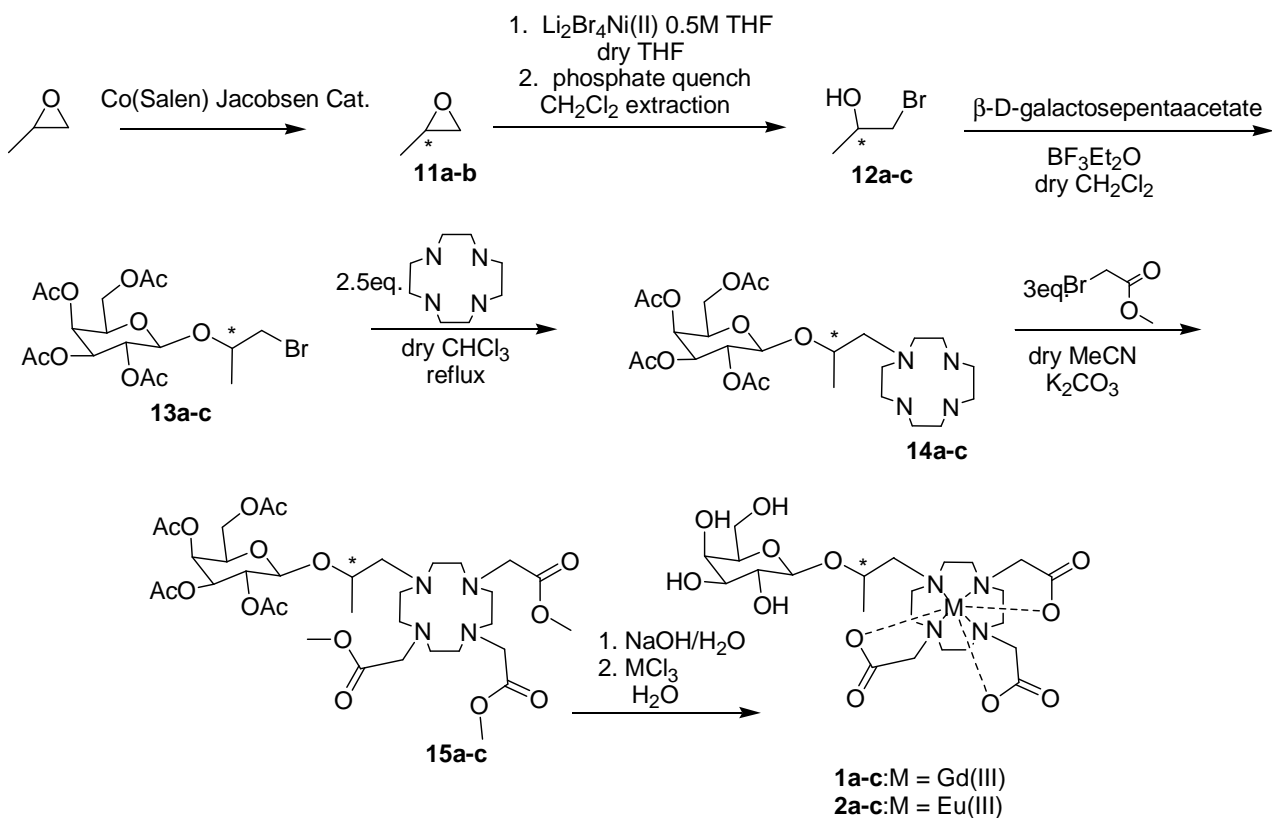


Figure S2. Synthetic Scheme for the preparation of the β -series.

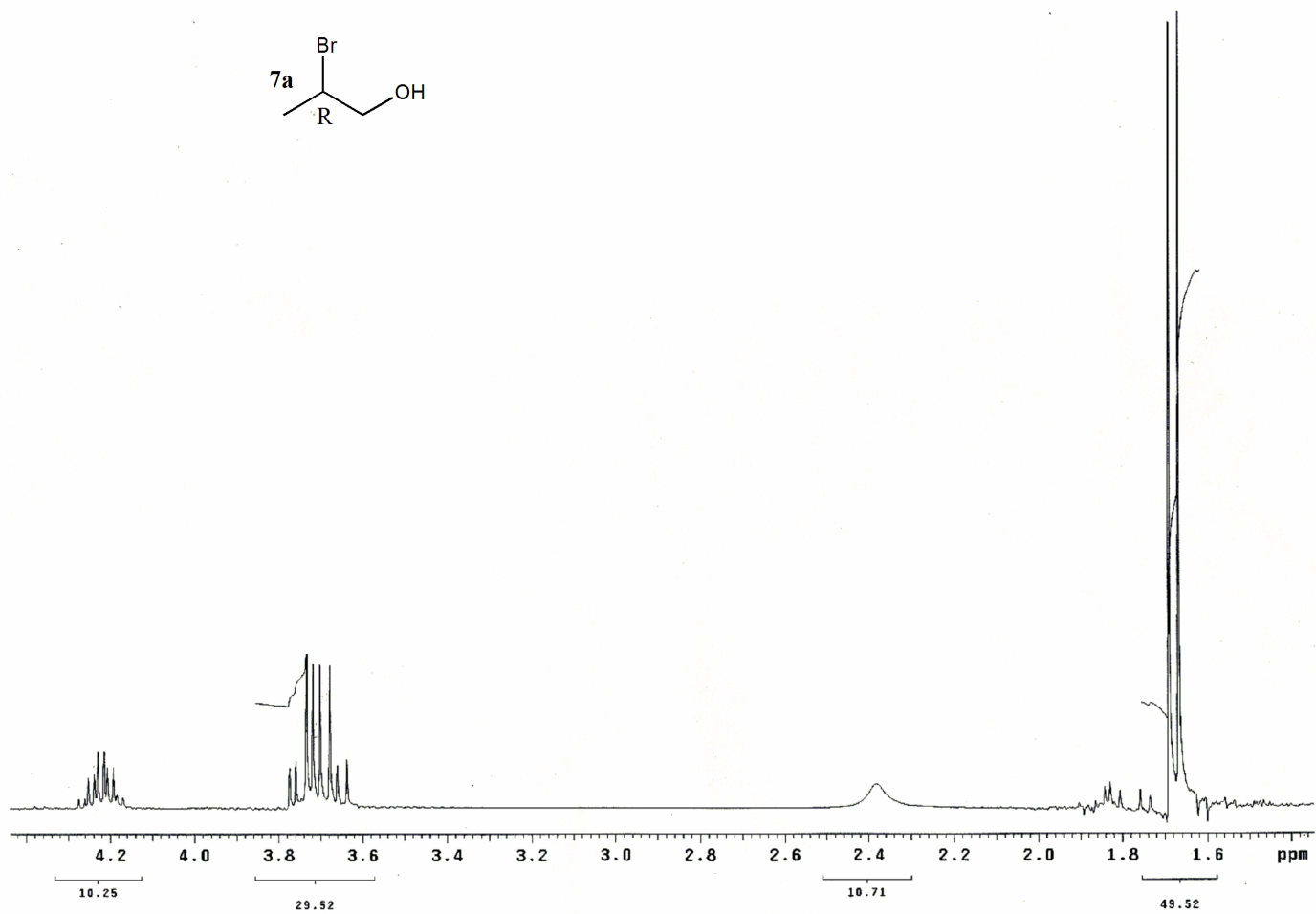
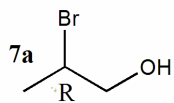


Figure S3. ^1H NMR (400 MHz, CDCl_3) 1.62 (d, 3H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$, $J = 8$), 2.05 (s, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 3.59-3.75 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 4.14-4.23 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$)

Analysis temperature
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PULSE SEQU-01
Relax. delay 1.000 sec
Pulse 12.0 degrees
Acq. time 1.100 sec
Width 20480.0 Hz
150 read lines
CROSSPO 0.8, 100.6217637 MHz
DECOUPLE H1, 400.1679541 MHz
Power 37 dB
or during acquisition
off during delay
not 2.0 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 10000
Total time 38 hr. 53 min. 0 sec

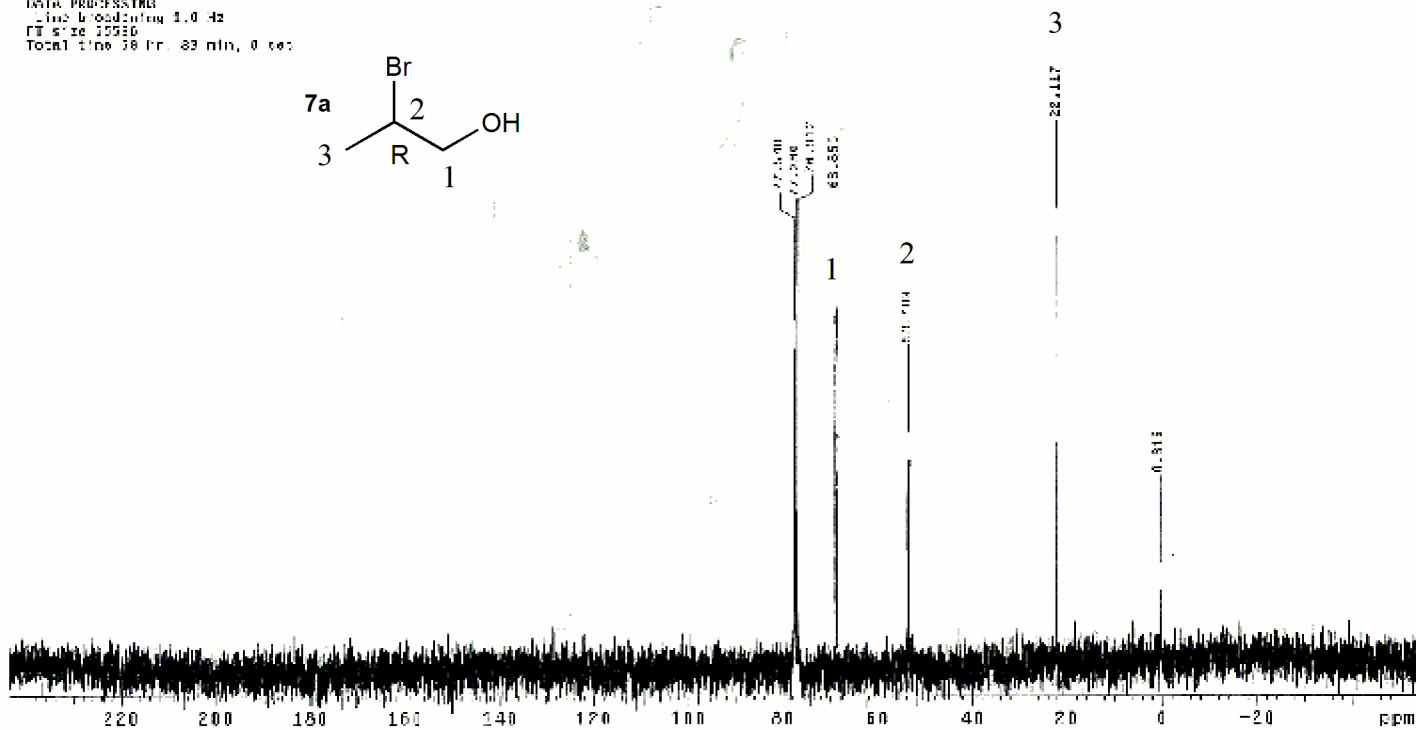
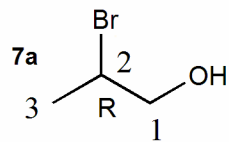


Figure S4. ^{13}C NMR (100 MHz, CDCl_3) 22.1, 53.4, 68.9

HN_510 P-TetraSEIP H2O 0008 RT
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SOLVENT: CDCl3
Spectrometer: Nova500
NUC1: 13C

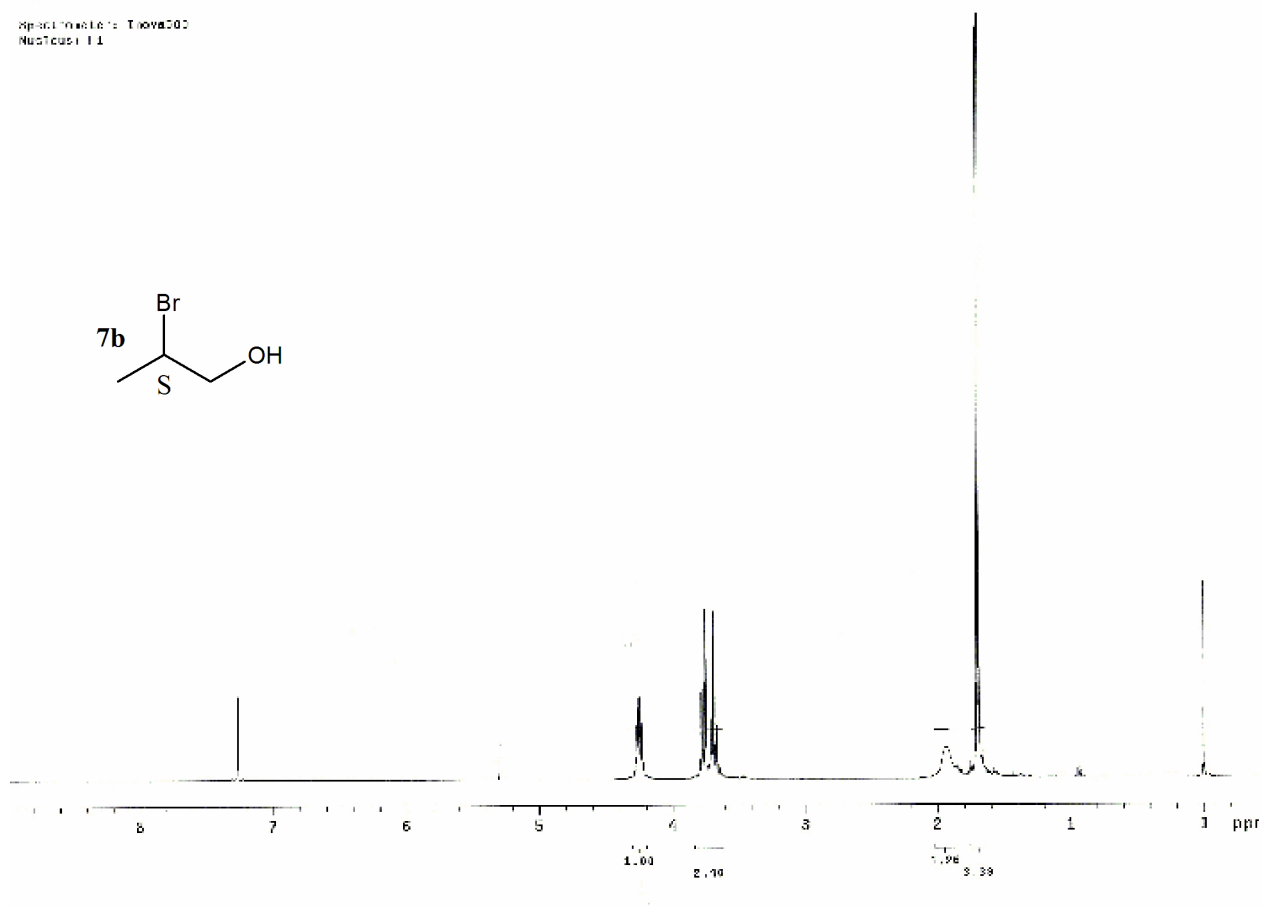
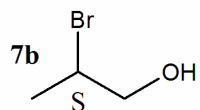


Figure S5. ^1H NMR (400 MHz, CDCl_3) 1.62 (d, 3H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$, $J = 8$), 2.14-2.24 (s, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 3.60-3.82 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 4.20-4.36 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$)

014 300 MHz Bruker Avance III
Date_081006 08:54:00
Solvent: CDCl3
Spectrometer: Avance III
Nucleus: 13C

INDEX	FREQUENCY	PPM	HEI611
1	1740.383	77.518	149.4
2	1708.355	77.265	175.0
3	1675.157	74.000	158.1
4	3657.012	60.688	68.7
5	3777.178	52.101	68.8

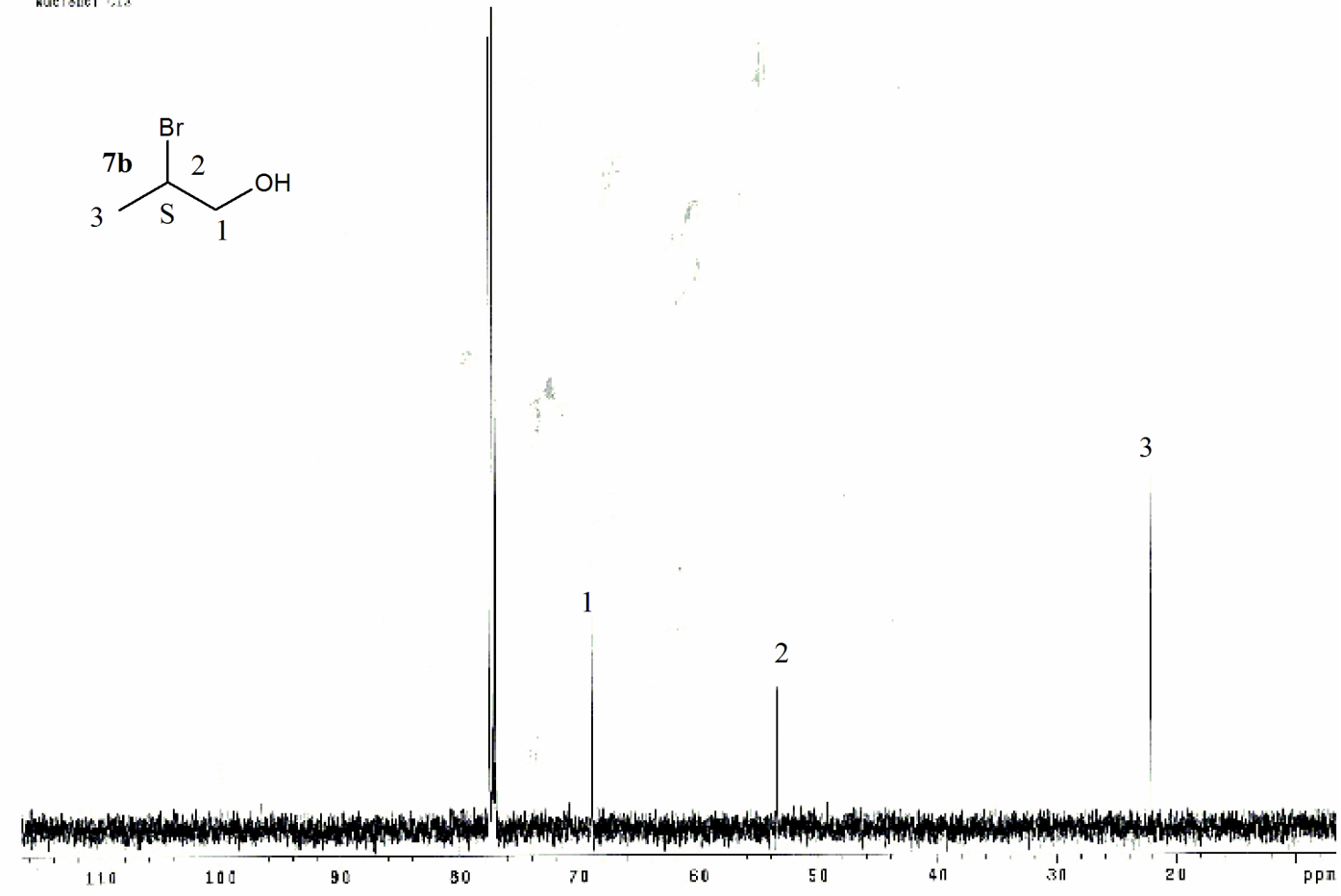
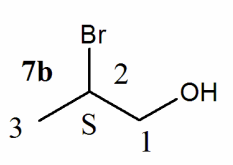


Figure S6. ¹³C NMR (100 MHz, CDCl₃) 22.1, 53.74, 68.90

STANDARD 1H NMR

Pulse Sequence: zgpg30
Solvent: CDCl3
Acquired: 10/14/10
Mercury-401DB "Mercury401"
PULSE SEQUENCE
Relax: delay 1.000 sec
Pulse: zgpg30
Acq: Time 0.168 sec
Width 1001.0 Hz
S: 2000000
CARRIER: H2, 400.146000 MHz
F2: 400.146000 MHz
F1: 100.626100 MHz
FT size 16384
Total time 1 min, 17 sec

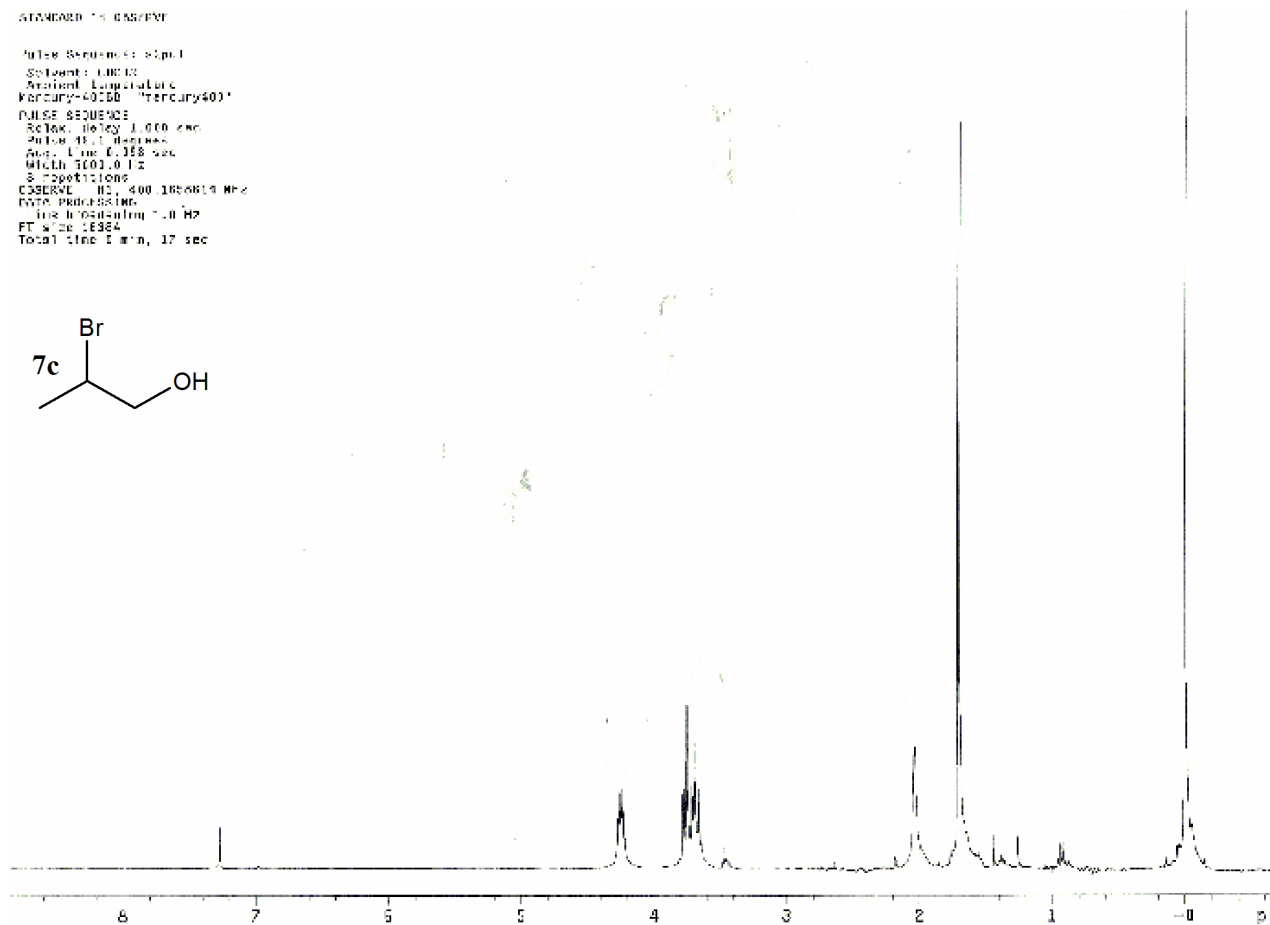
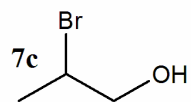


Figure S7. ^1H NMR (400 MHz, CDCl_3) 1.52-1.62 (d, 3H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$, $J = 8$), 3.1 (s, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 3.54-3.70 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$), 4.02-4.15 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{OH}$)

1sC OBSERVE

Pulse Sequence: s2pu1
Solvent: CDC13
Ambient temperature
Mercury-400BB "mercury400"

PULSE SEQUENCE
Relax. delay 1.000 sec
Pulse 72.0 degrees
Acq. time 1.001 sec
Width 30000.0 Hz
24 repetitions

OBSERVE C13, 100.6217804 MHz
DECOUPLE H1, 400.1678541 MHz
Power 37 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 695 hr, 31 min, 21 sec

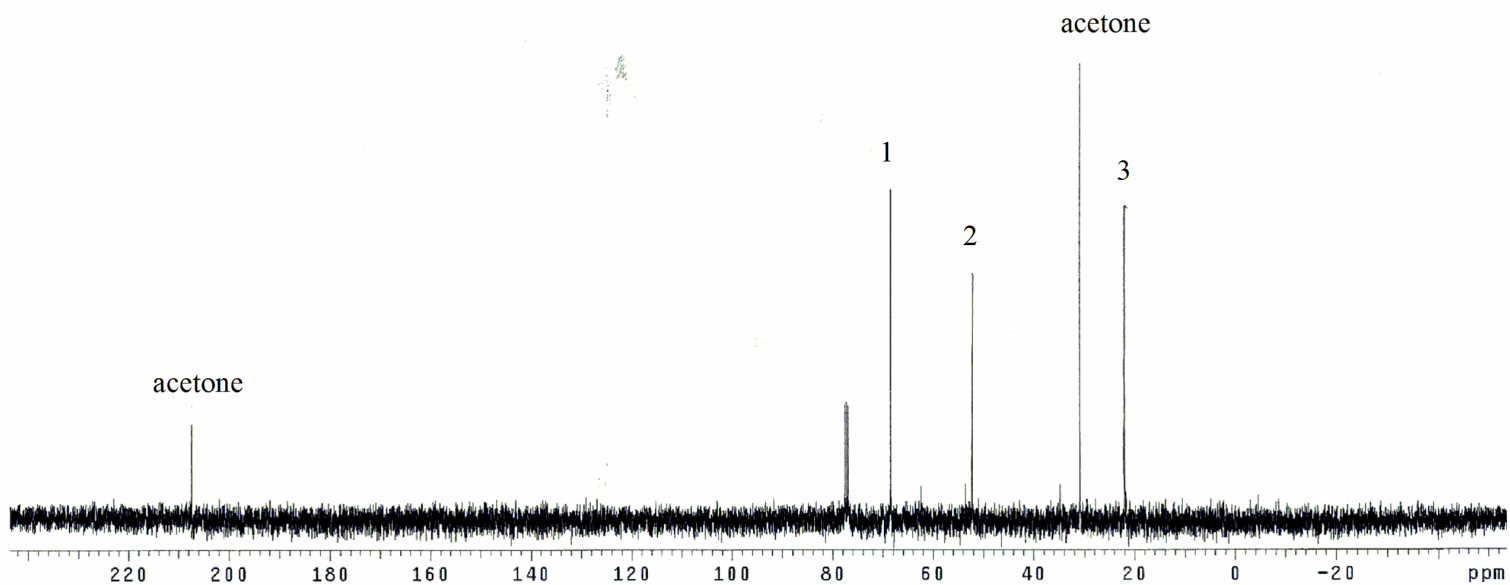
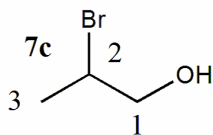


Figure S8. ¹³C NMR (100 MHz, CDCl₃) 21.23, 52.73, 67.42

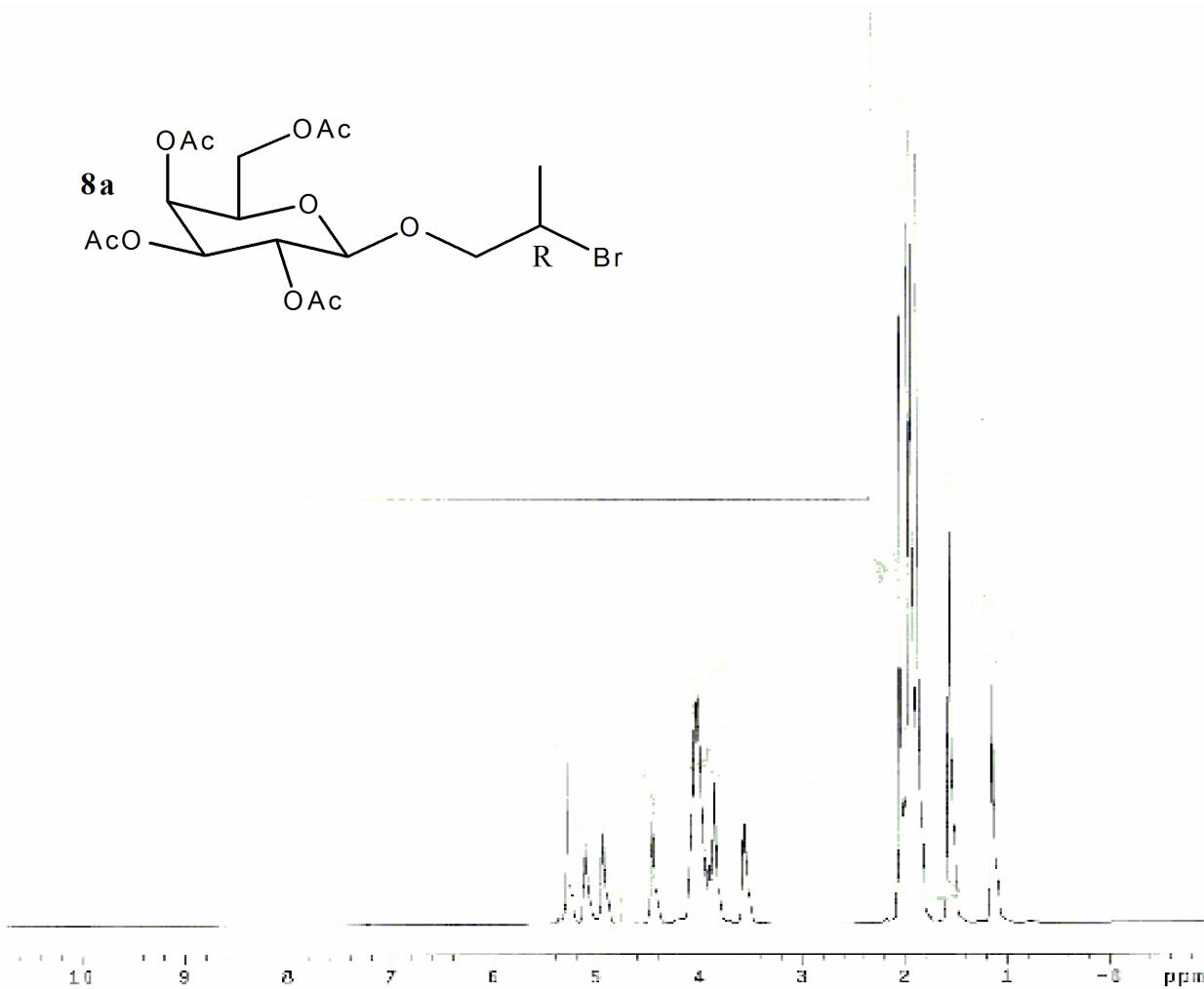


Figure S9. ^1H NMR (500 MHz, CDCl_3) 1.51 (d, 3H, methyl, $J = 6.5$), 1.80-2.05 (m, 12H, OAc), 3.54-3.59 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{O-sugar}$), 3.84-3.91 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{O-sugar}$), 3.97-4.11 (m, 3H, H-5 and H-6) 4.45-4.49 (m, 1H, H-4), 4.93-4.95 (m, 1H, H-2), 5.09-5.13 (m, 1H, H-3), 5.23-5.29 (m, 1H, sugar anomeric H)

13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-400BB "mercury400"

PULSE SEQUENCE
 Relax. delay 1.000 sec
 Pulse 67.5 degree
 Acq. time 1.001 sec
 Width 30000.0 Hz
 #64reps#1100as

OBSERVE C13, 100.621722 MHz
 DECOUPLE H1, 400.1678541 MHz
 Power 37 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated

DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 69 hr, 33 min, 7 sec

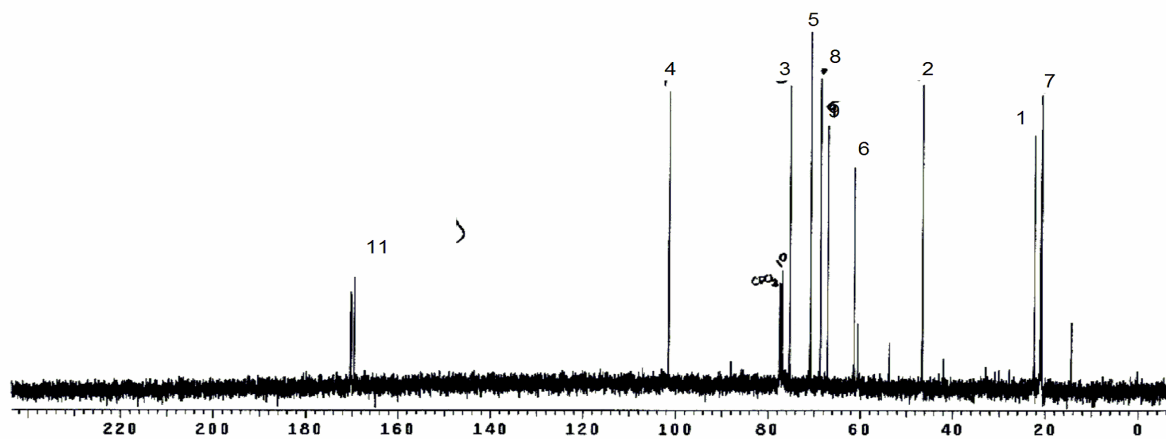
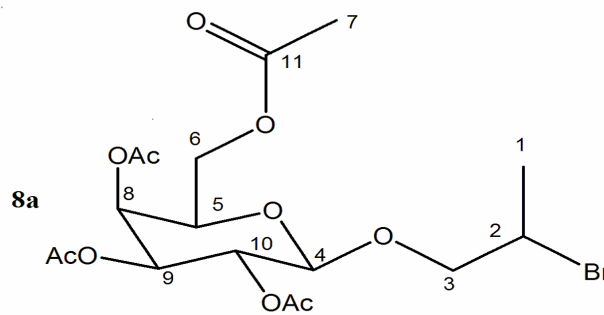


Figure S10. ¹³C NMR (100 MHz, CDCl₃) 20.80, 20.88, 21.08, 22.45, 46.58, 61.41, 67.11, 68.70, 70.12, 70.68, 70.91, 75.08, 101.48, 170.21, 170.30

NAME: 8b

File: 8b_001
Date: 10/10/10
Time: 10:10:10
Pulse: zgpg30
F2: 500.136000
SFO: 500.136000
AQ: 1.000000
RG: 655.36
WDW: EM
SSB: 0
GB: 0
PC: 2.00
DC: 0.00
HF: 0.00
WD: 1.00
TE: 300.2
D1: 1.00
d11: 0.05
d12: 0.05
d13: 0.05
d14: 0.05
d15: 0.05
d16: 0.05
d17: 0.05
d18: 0.05
d19: 0.05
d20: 0.05
d21: 0.05
d22: 0.05
d23: 0.05
d24: 0.05
d25: 0.05
d26: 0.05
d27: 0.05
d28: 0.05
d29: 0.05
d30: 0.05
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d43: 0.05
d44: 0.05
d45: 0.05
d46: 0.05
d47: 0.05
d48: 0.05
d49: 0.05
d50: 0.05
d51: 0.05
d52: 0.05
d53: 0.05
d54: 0.05
d55: 0.05
d56: 0.05
d57: 0.05
d58: 0.05
d59: 0.05
d60: 0.05
d61: 0.05
d62: 0.05
d63: 0.05
d64: 0.05
d65: 0.05
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d79: 0.05
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d83: 0.05
d84: 0.05
d85: 0.05
d86: 0.05
d87: 0.05
d88: 0.05
d89: 0.05
d90: 0.05
d91: 0.05
d92: 0.05
d93: 0.05
d94: 0.05
d95: 0.05
d96: 0.05
d97: 0.05
d98: 0.05
d99: 0.05
d100: 0.05

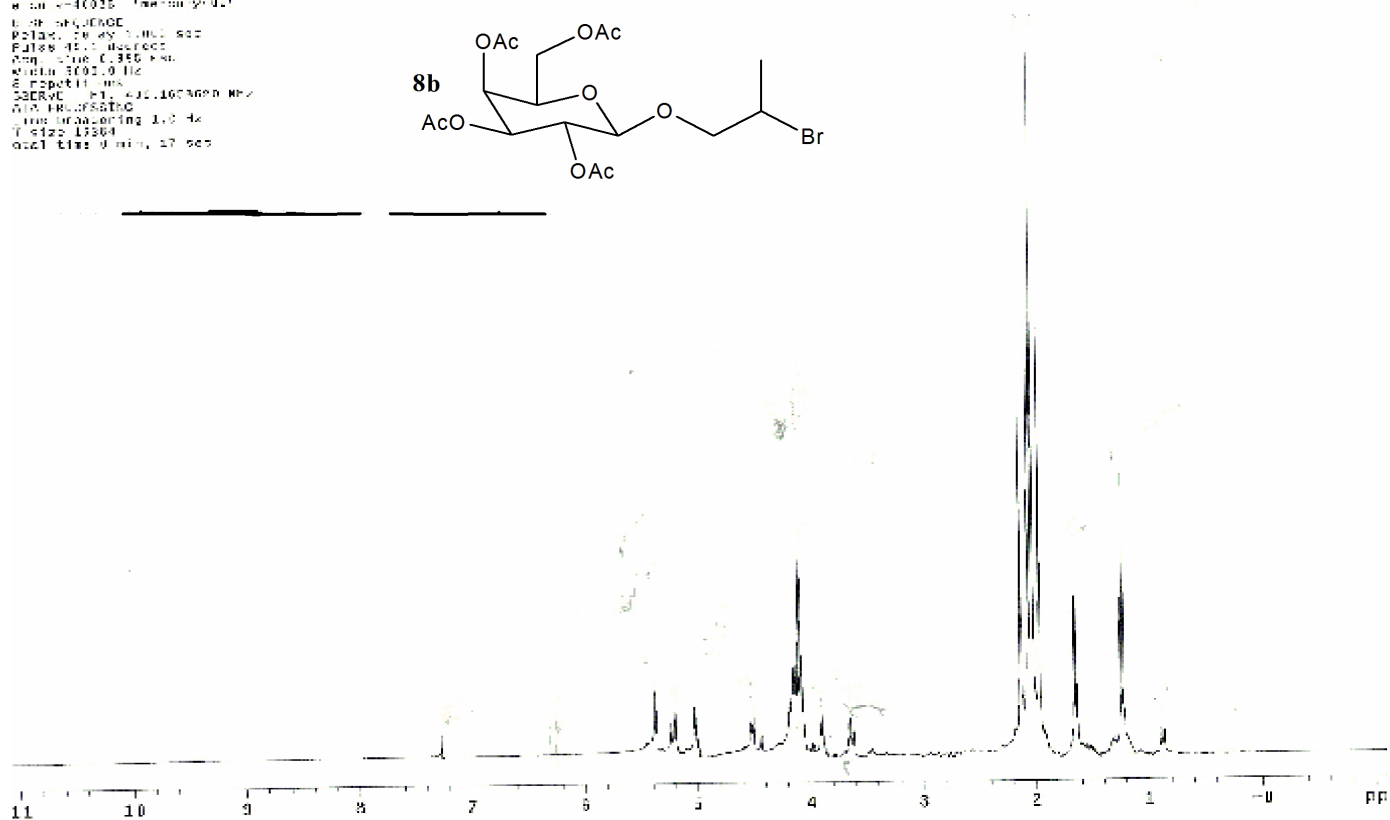
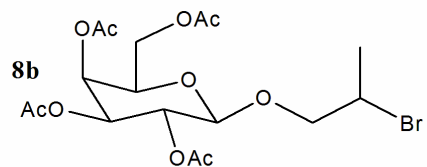


Figure S11. ^1H NMR (500 MHz, CDCl_3) 1.66-1.67 (d, 3H, methyl, $J = 6.5$), 1.99-2.16 (m, 12H, OAc), 3.65-3.69 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{O-sugar}$), 3.90-3.93 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{O-sugar}$), 4.00-4.03 (m, 2H, H-6), 4.11-4.20 (m, 1H, H-4), 4.53-4.55 (m, 1H, H-5), 5.02-5.05 (m, 1H, H-3), 5.22-5.26 (m, 2H, H-2), 5.40-5.40 (m, 1H, H-1)

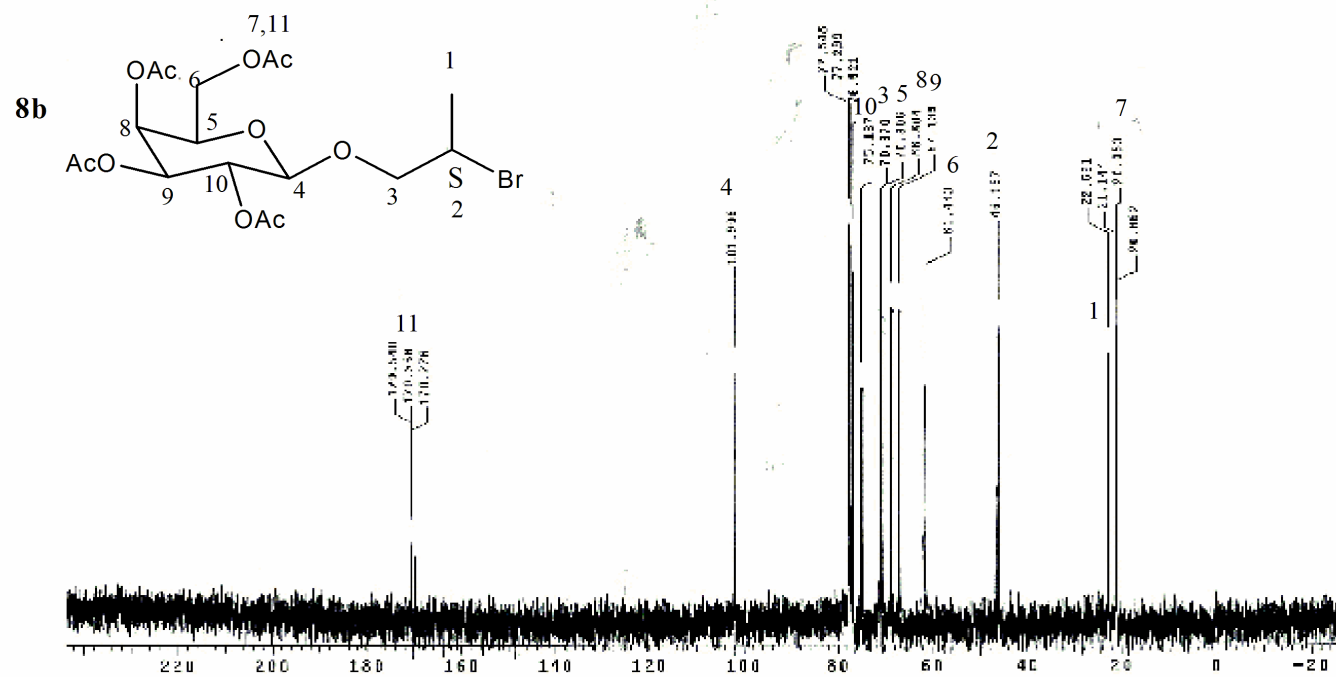


Figure S12. ¹³C NMR (125 MHz) 20.87, 20.95, 21.14, 22.69, 46.15, 61.44, 67.14, 68.80, 70.91, 70.97, 75.14, 101.91, 170.28, 170.36, 170.54

STANDARD 1F 00000000
Vial# 88454000 82p01
Solvent: CDCl3
Acq. temperature
January-09-08 10:00:00
PULSE PROGRAM
Pulse delay 1.000 sec
Pulse 45.1 degrees
Acq. time 0.339 sec
Width 5000.0 Hz
S 200011000
F3SERV# F1, 400.100000 MHz
DATA PROCESSING
Time processing 1.0 Hz
File size 18564
Total time 0 min, 17 sec

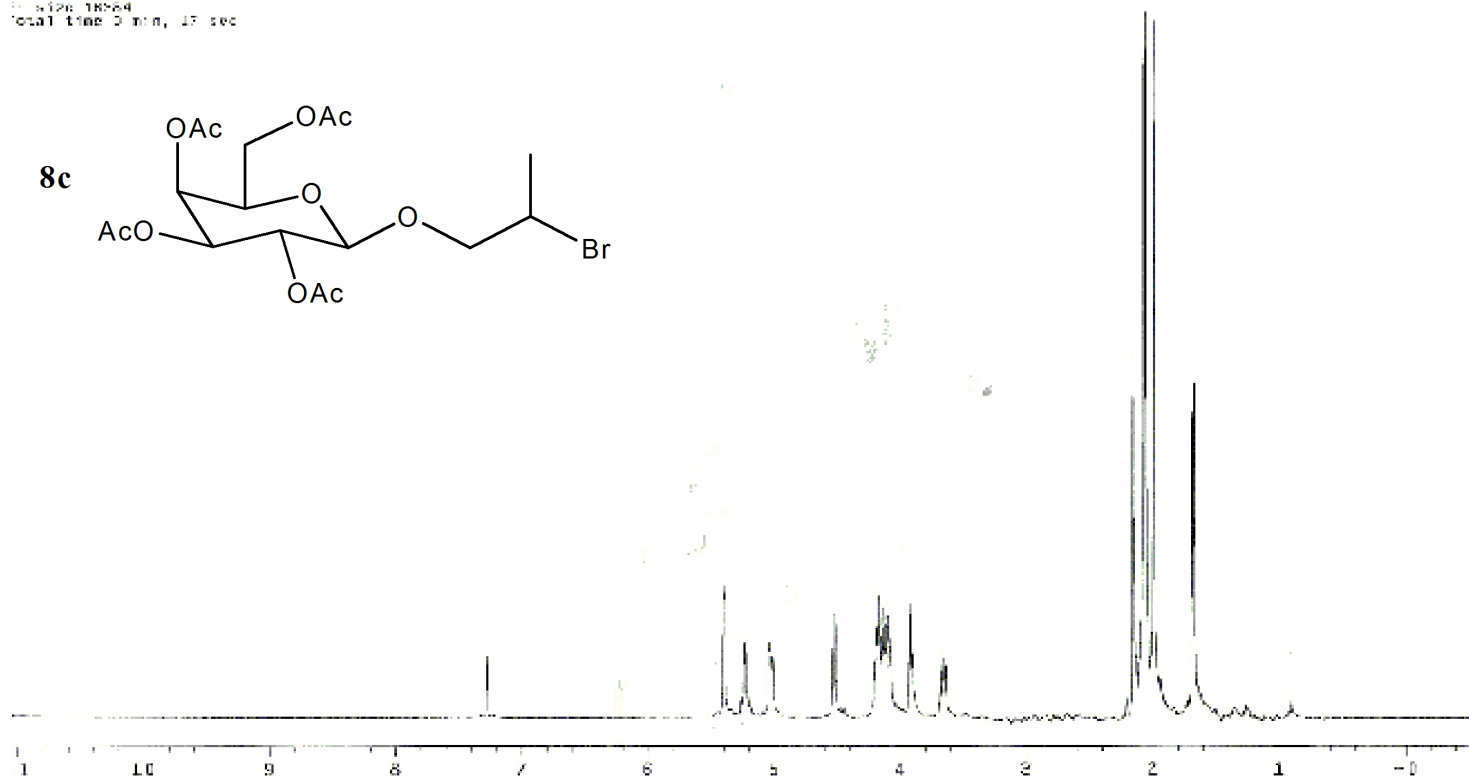


Figure S13. ^1H NMR (400 MHz) 1.62-1.76 (d, 3H, methyl, $J = 6.5$), 1.88-2.18 (m, 12H, OAc), 3.60-3.68 (m, 2H, $\text{CH}_3\text{CHBrCH}_2\text{O}$ -sugar), 3.86-3.92 (m, 1H, $\text{CH}_3\text{CHBrCH}_2\text{O}$ -sugar), 4.16-4.22 (m, 3H, H-5 and H-6), 4.52-4.58 (m, 1H, H-4), 5.0-5.18 (m, 1H, H-2), 5.20-5.28 (m, 1H, H-3), 5.39 (m, 1H, H-1)

HN_31a1 p=500 tL_500 RT Mordato
Pulse Sequence: zgpg30
Solvent: CDCl3
Acquisition Temperature
INSTRUMENT: spect
1500MHz

Relax. delay: 1.000 sec
Pulse: 19.7 degrees
Pulse time: 2.000 sec
Width: 10000.0 Hz
of acquisitions: 1
OBSERVE: H1, 499.7526978 MHz
DATA PROCESSING
Line broadening: 0.0 Hz
SI size: 65536
Total time: 2 min, 24 sec

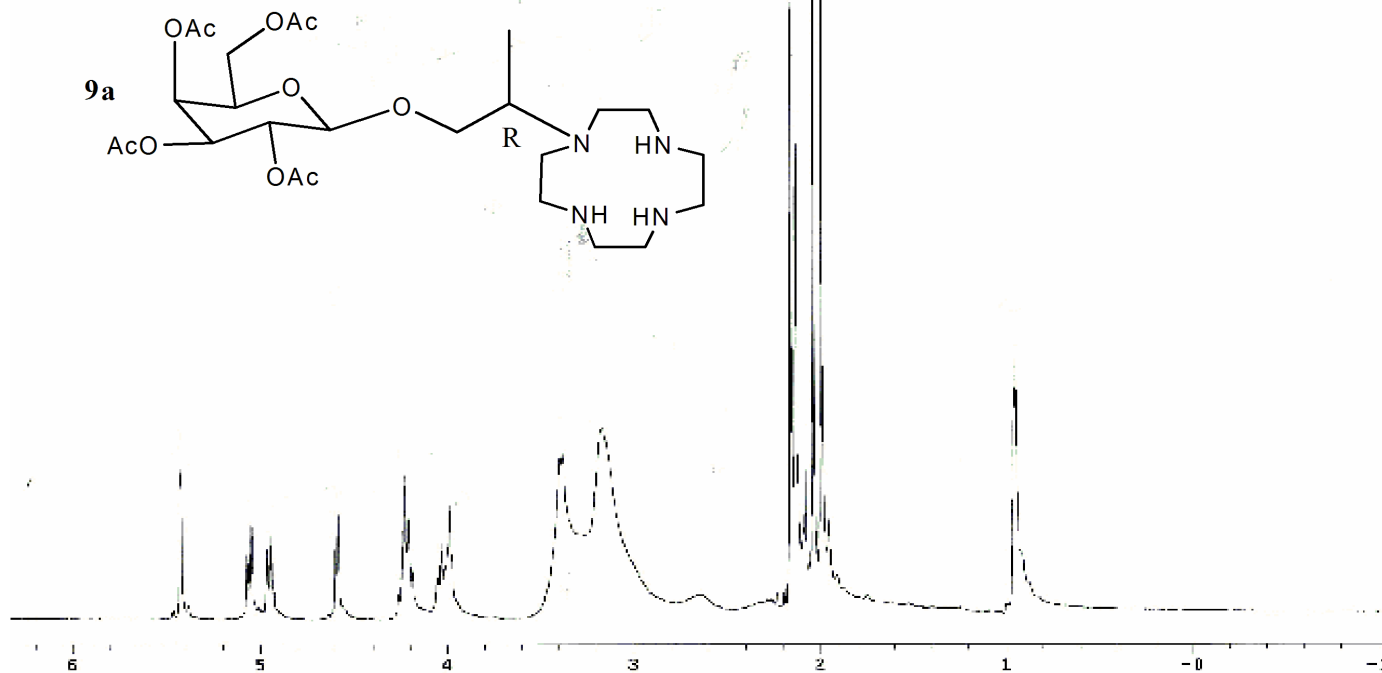


Figure S15. ^1H NMR (500 MHz, CDCl_3) 0.82-0.98 (d, 3H, methyl, $J = 6.0$), 1.85-2.18 (m, 12H, sugar acetate CH_3), 3.0-3.5 (br, 16H, cyclen), 3.95-4.04 (m, 3H, methylene and methine on linker), 4.18-4.28 (m, 3H, H-6 and H-5), 4.50 (d, 1H H-4), 4.92-4.99 (m, 1H, H-2), 5.02-5.15 (m, 1H, H-3), 5.42 (m, 1H, H-1)

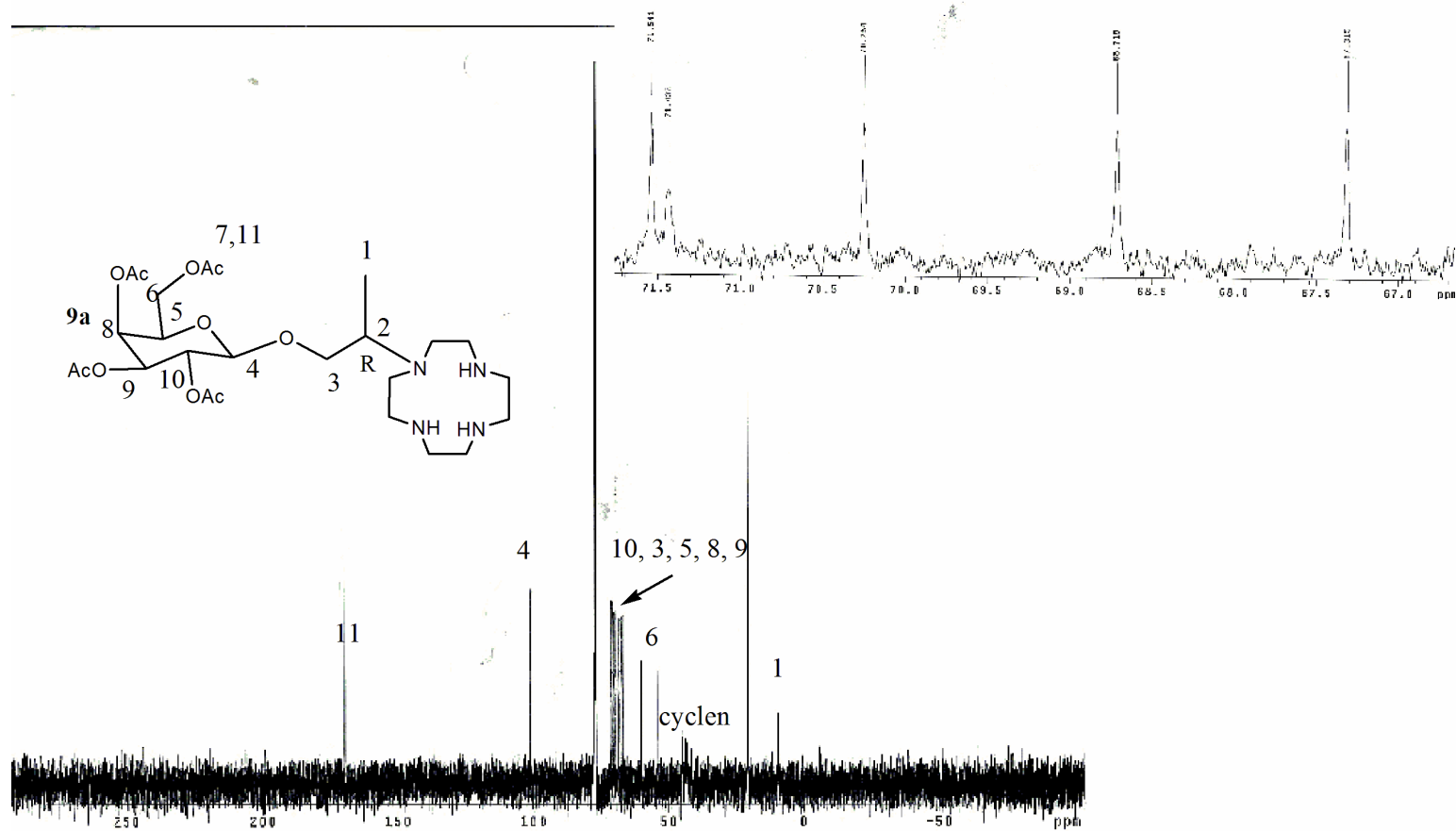


Figure S16. (125 MHz, CDCl₃) 9.54, 20.72, 20.76, 20.90, 54.40, 60.33, 67.32, 68.72, 70.25, 71.43, 71.54, 110.2, 169.46, 169.93, 170.75, 171.48. Enlargement of peaks found between 76-71.6 ppm. Only one peak is seen for each of the sugar carbons.

STANDARD IN OBSERVE

Pulse Sequence: zgpg30
Solvent: CD3CN
Acquire Temperature: 300.2 K
Sweep Rate: 10000 Hz
Pulse Program: zgpg30
Relax: delay 1.000 sec
Pulse: 40.1 degrees
Acq. Time: 0.330 sec
Date_ Time: 08.08.12
5 repetitions
F2: 401.1478827 MHz
VIA PROCESSING
11.00 hours
17.12.12
Total time 0 min, 17 sec

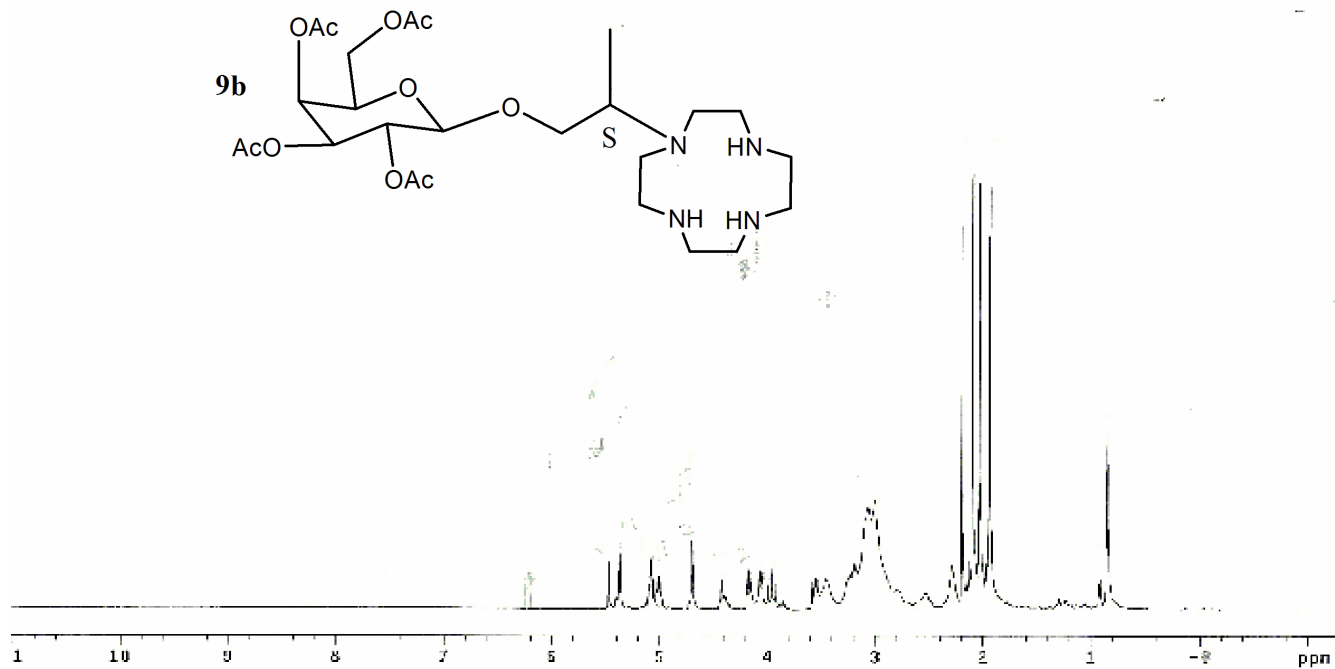


Figure S17. ^1H NMR (400 MHz, CD_3CN) 0.78-0.84 (d, 3H, methyl, $J = 6.0$), 1.85-2.22 (m, 12H, OAc), 2.74-3.35(br, 16H, cyclen), 3.92-4.08 (m, 2H, methylene on linker), 4.16-4.2 (m, 1H, methine on linker), 4.38-4.42 (m, 3H, H-5 and H-6), 4.72 (m, d, 1H, H-4), 4.98-5.08 (m, 1H, H-2), 5.10-5.18 (m, 1H, H-3), 5.40 (m 1H, H-1)

213 stupeur ST 00_Sun 11024500
 Pulse Sequence: zgpg30
 Solvent: CD3CN
 Ambient Temperature
 Date_1: 1-14-07
 INOVA-500 "11024500"
 Relax. delay: 1.000 sec
 Pulse: 92.0 degrees
 Acq. time: 1.001 sec
 Date_2: 01-14-07
 RSO: zgpg30
 RSO repetitions:
 DPMFREQ: 015, 125.6147705 MHz
 NUC1: 13C, 101.6261194 MHz
 Power: 99.43
 On during acquisition
 Off during delay
 WALTZ16: acdubalca
 DATA PROCESSING:
 F2: 125.6147705 MHz
 FT size: 131072
 Total time: 00 hr, 21 min, 37 sec

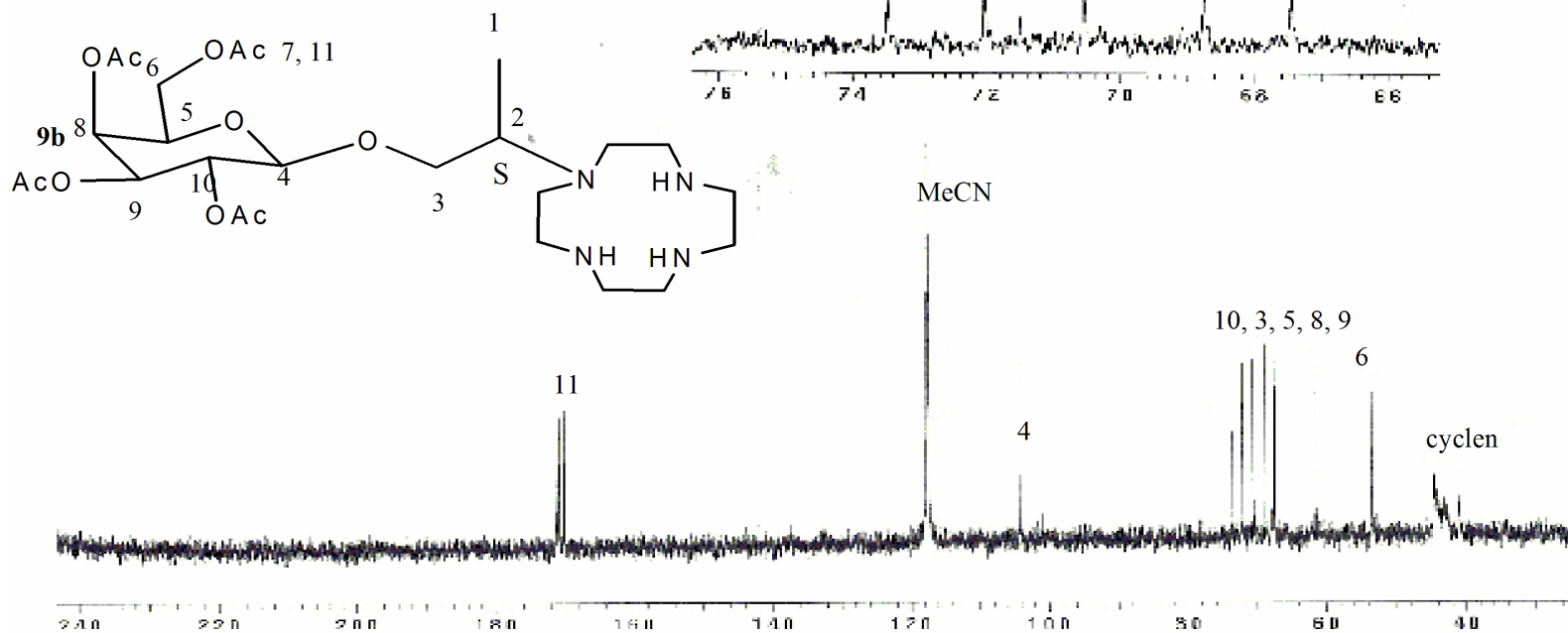


Figure S18. ¹³C NMR (125 MHz, CD₃CN) 7.92, 20.15, 20.30, 20.37, 20.40, 53.41, 61.52, 67.47, 68.76, 70.56, 72.04, 73.49, 104.5, 170.02, 170.75, 170.79, 171.28. Enlargement of peaks between 66 ppm and 76 ppm. Only one peak is seen for each of the sugar carbons.

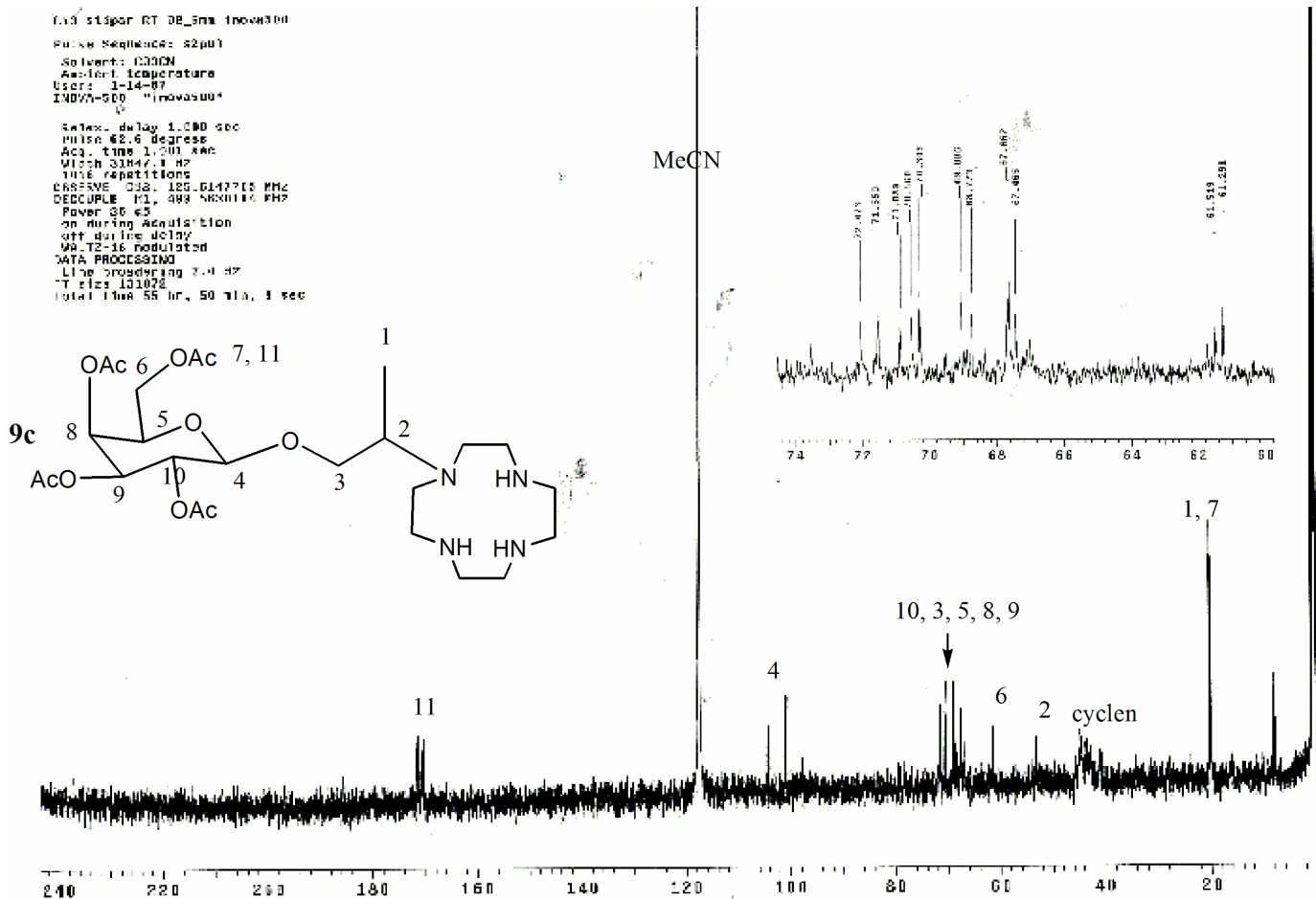
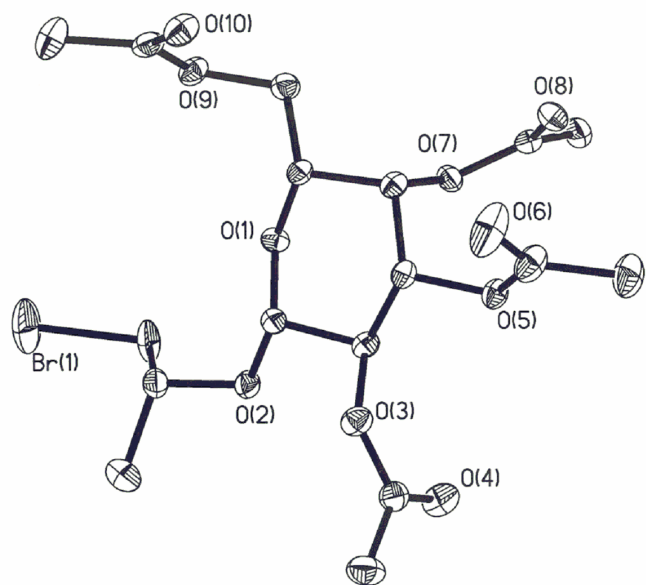


Figure S19. ^{13}C NMR (125 MHz, CD_3CN) 7.85, 8.20, 20.09, 20.21, 20.34, 53.11, 53.43, 61.29, 61.52, 67.47, 67.66, 68.77, 69.09, 70.31, 70.56, 70.89, 71.55, 72.07, 101.5, 104.5, 170.02, 170.26, 170.55, 171.27, 171.49. Enlargement of peaks found between 60-74 ppm. Two peaks are seen for each of the sugar carbons.

X-ray Crystal Structure: *R*-Bromo-Galactose Pentaacetate



Monoclinic
 $P2_1$

$a = 9.6159(8)$
 $b = 10.7202(9)$
 $c = 10.6943(8)$

$\alpha = \gamma = 90^\circ$ $\beta = 103.868(1)^\circ$

Chirality: Clockwise (*R*)

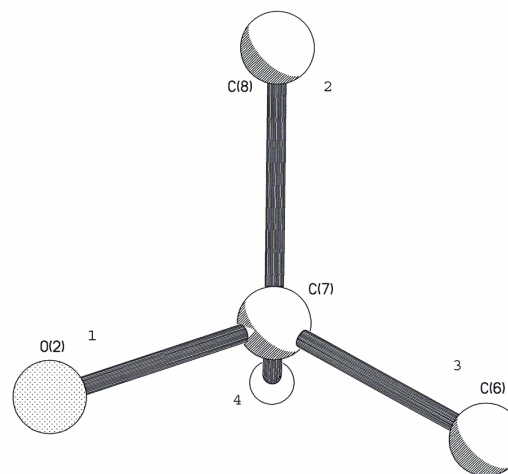
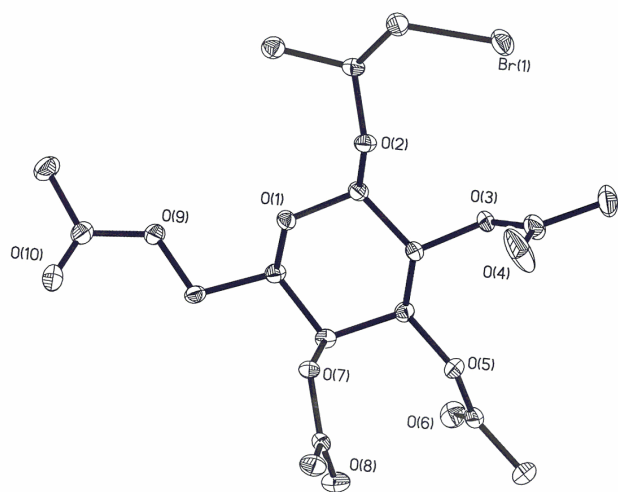
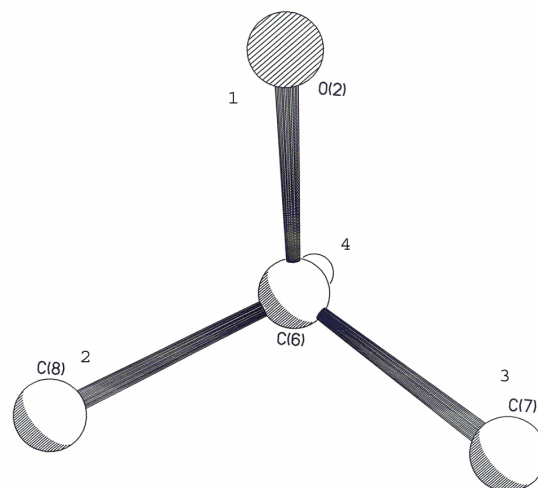


Figure S22. Crystal structure of *R*-(+)-1-bromopropan-2-yl β -D-galactopyranoside tetraacetate (13a). CIF file is attached as supplementary material.

X-ray Crystal Structure: S-Bromo-Galactose Pentaacetate



Chirality: CounterClockwise (S)



Orthorhombic
 $P2_12_12_1$

$a = 8.9183(7)$
 $b = 10.5142(8)$
 $c = 22.198(2)$

$\alpha = \beta = \gamma = 90^\circ$

Figure S23. Crystal structure of structure S-(-)-1-bromopropan-2- -D-galactose tetraacetate (13b). CIF file attached as supplementary material.

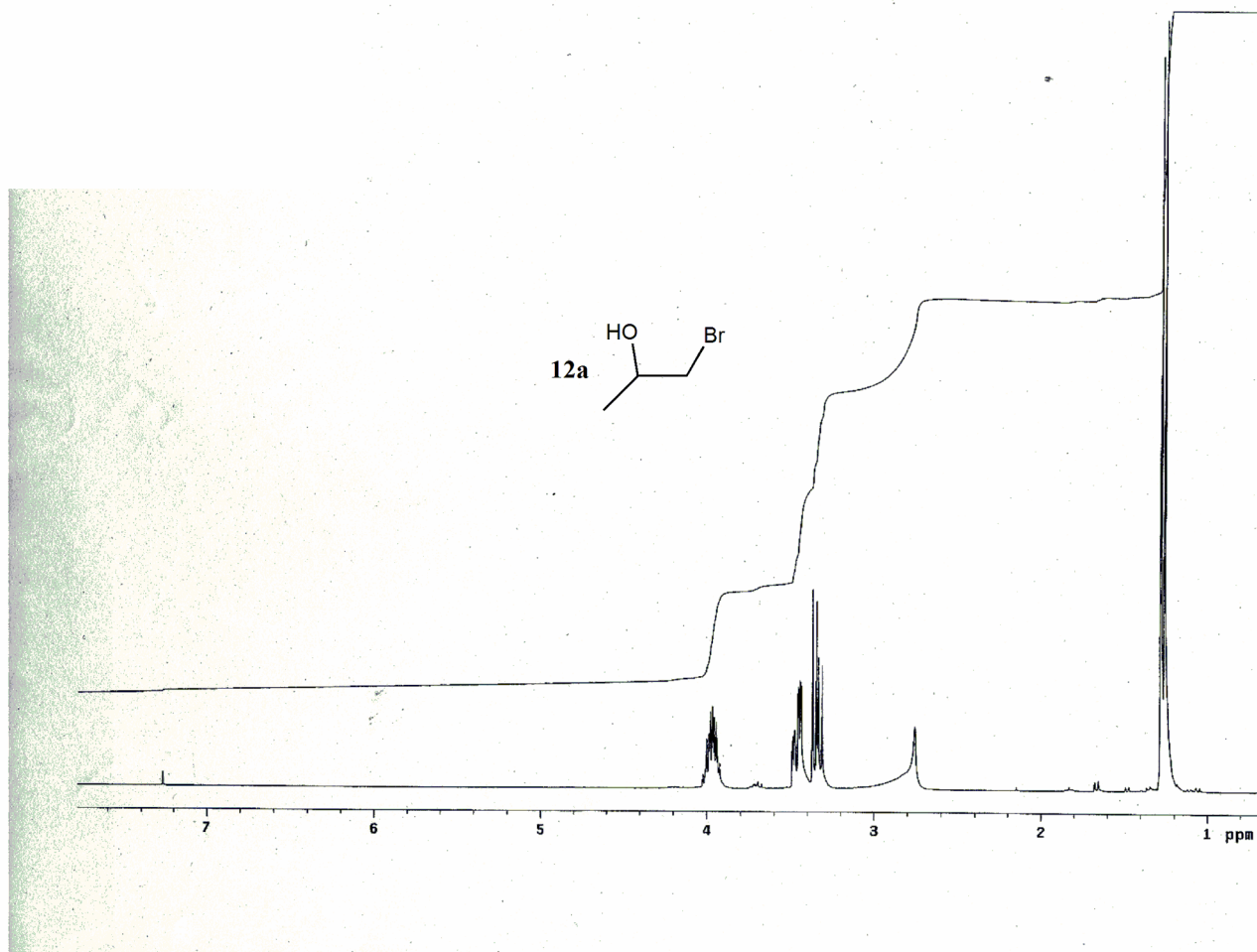


Figure S24. ¹H NMR (500 MHz, CDCl₃) 1.25-1.32 (d, 3H, methyl, J = 6.0), 1.85 (br, 1H, -OH), 3.32-3.38 (m, 1H, methylene), 3.45-3.51 (m, 1H, methylene), 3.94-4.02 (m, 1H, methine)

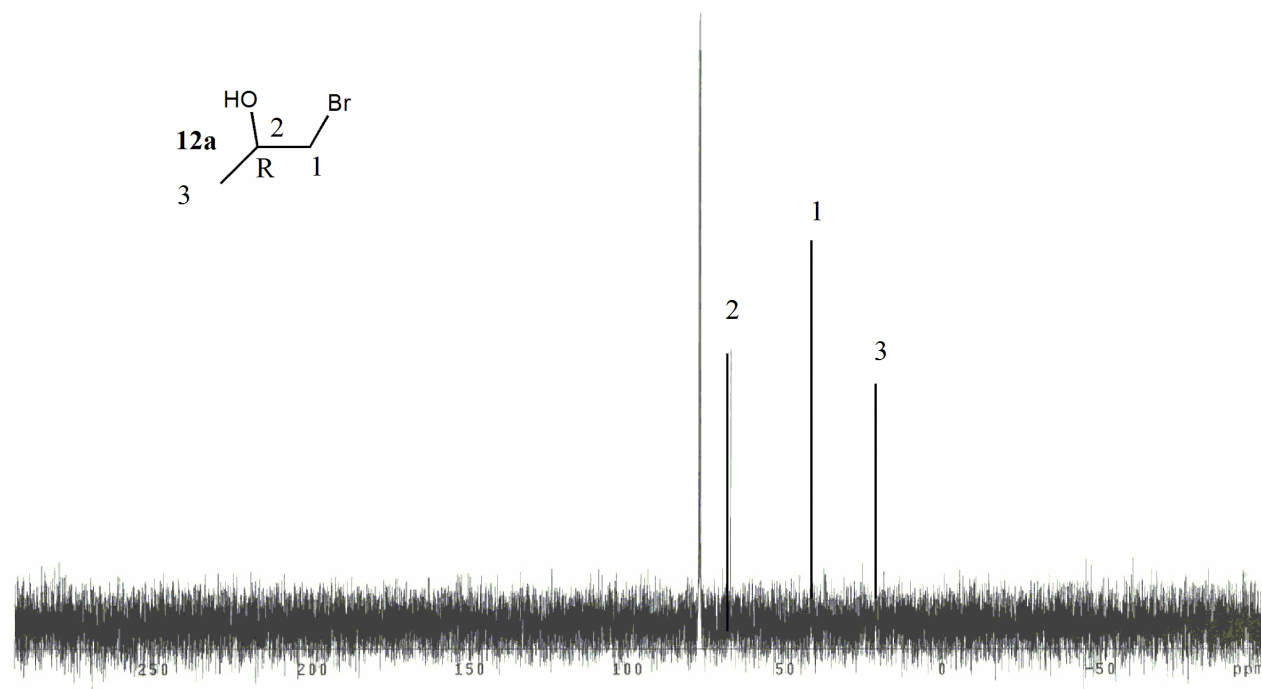


Figure S25. ^{13}C NMR (125 MHz, CDCl_3): 21.18, 40.77, 67.20

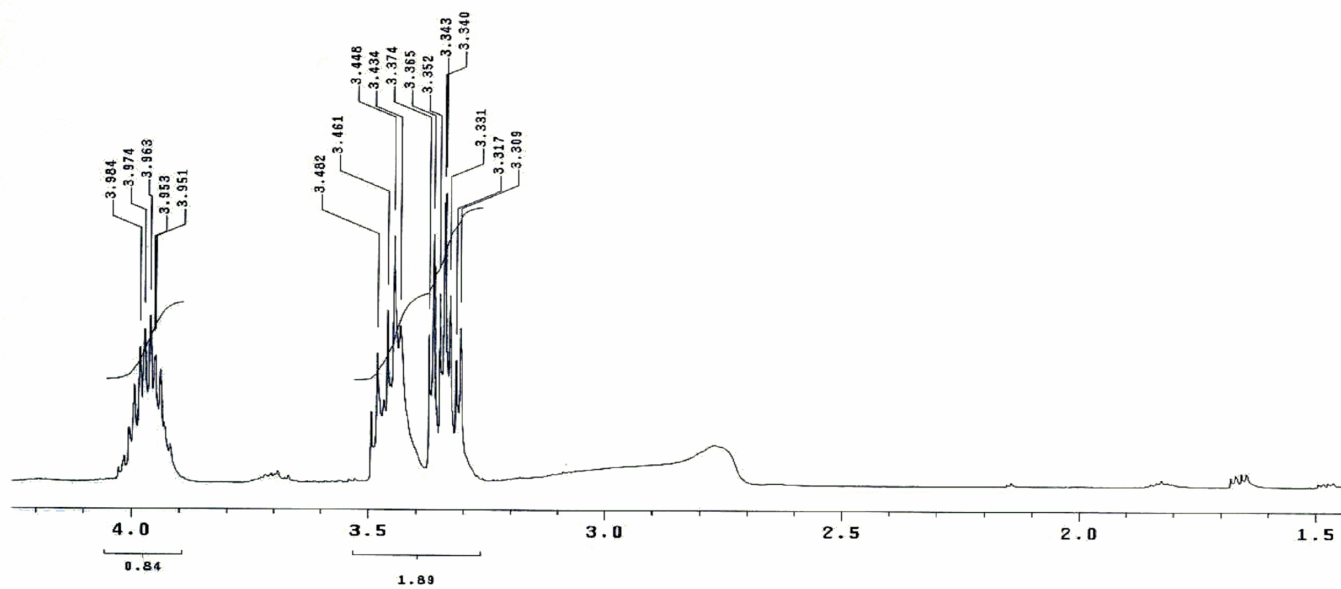
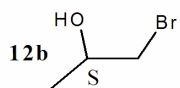


Figure S26. ^1H NMR (500 MHz, CDCl_3) 1.28-1.36 (d, 3H, methyl, $J = 6.0$), 1.88 (br, 1H, -OH), 3.34-3.40 (m, 1H, methylene), 3.48-3.04 (m, 1H, methylene), 3.96-4.02 (m, 1H, methine)

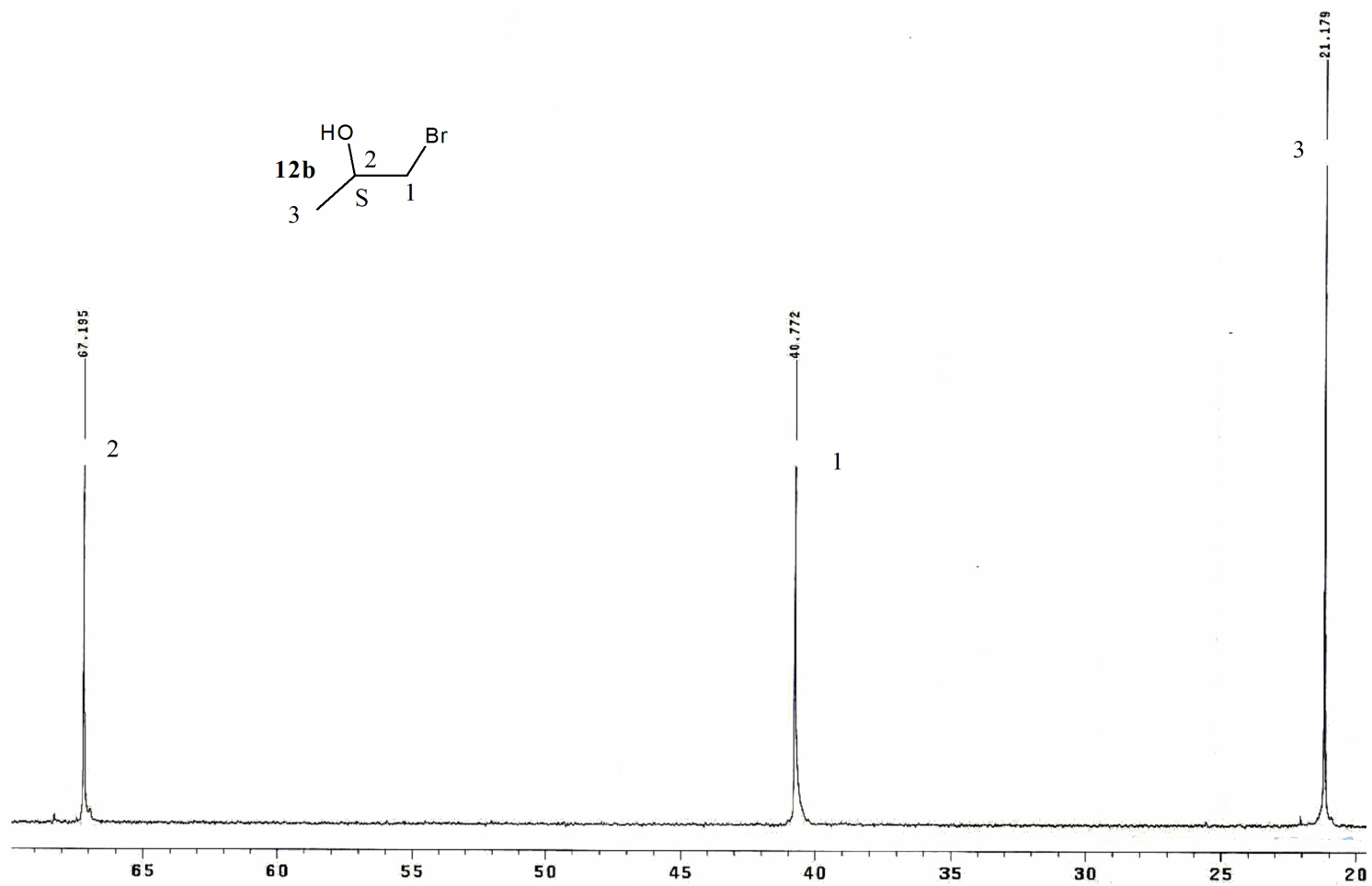


Figure S27. ^{13}C NMR. (125 MHz, CDCl_3) 21.22, 41.50, 68.11

13a

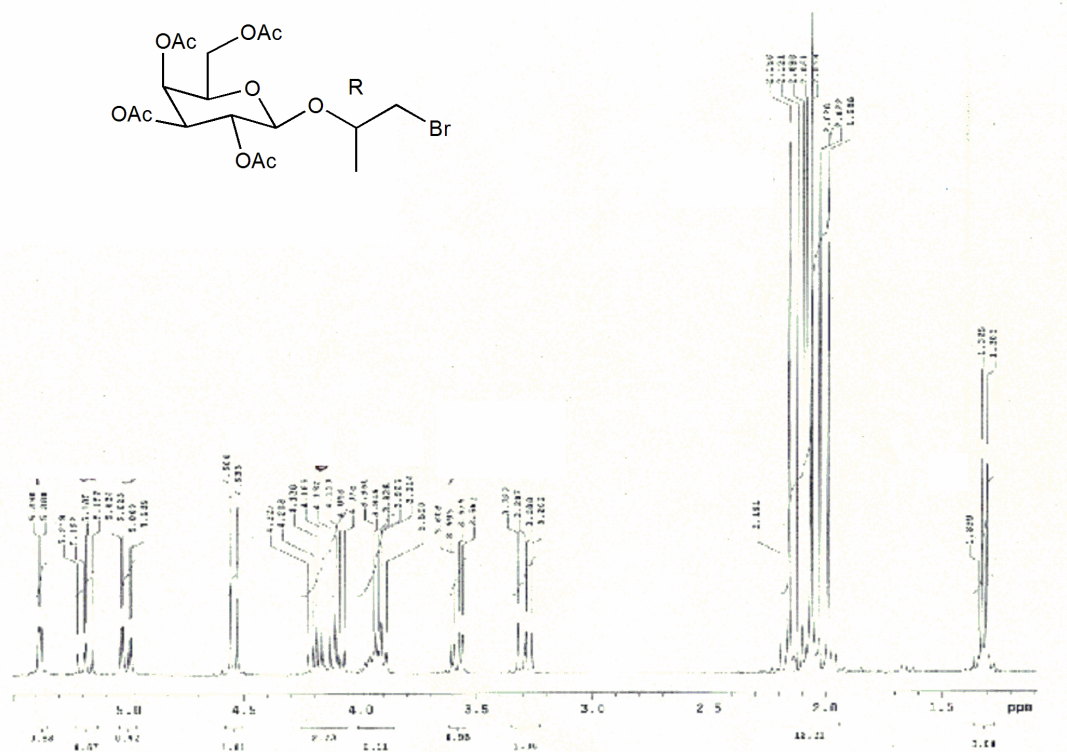
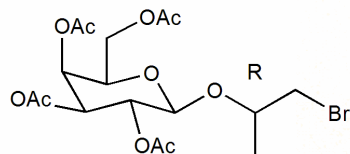


Figure S28. ¹H NMR (500 MHz, CDCl₃) 1.26-1.32 (d, 3H, methyl, J = 6.5), 1.85-2.32 (m, 12H, OAc), 3.24-3.32 (m, 1H, -CH₂Br), 3.50-3.62 (m, 1H, -CH₂Br), 3.89-4.02 (m, 2H, methine on linker, H-5), 4.05-4.22 (m, 2H, H-6), 4.52-4.64 (m, 1H, H-4), 4.98-5.08 (m, 1H, H-3), 5.24-5.34 (m, 1H, H-2), 5.40 (m, 1H, H-1)

13b

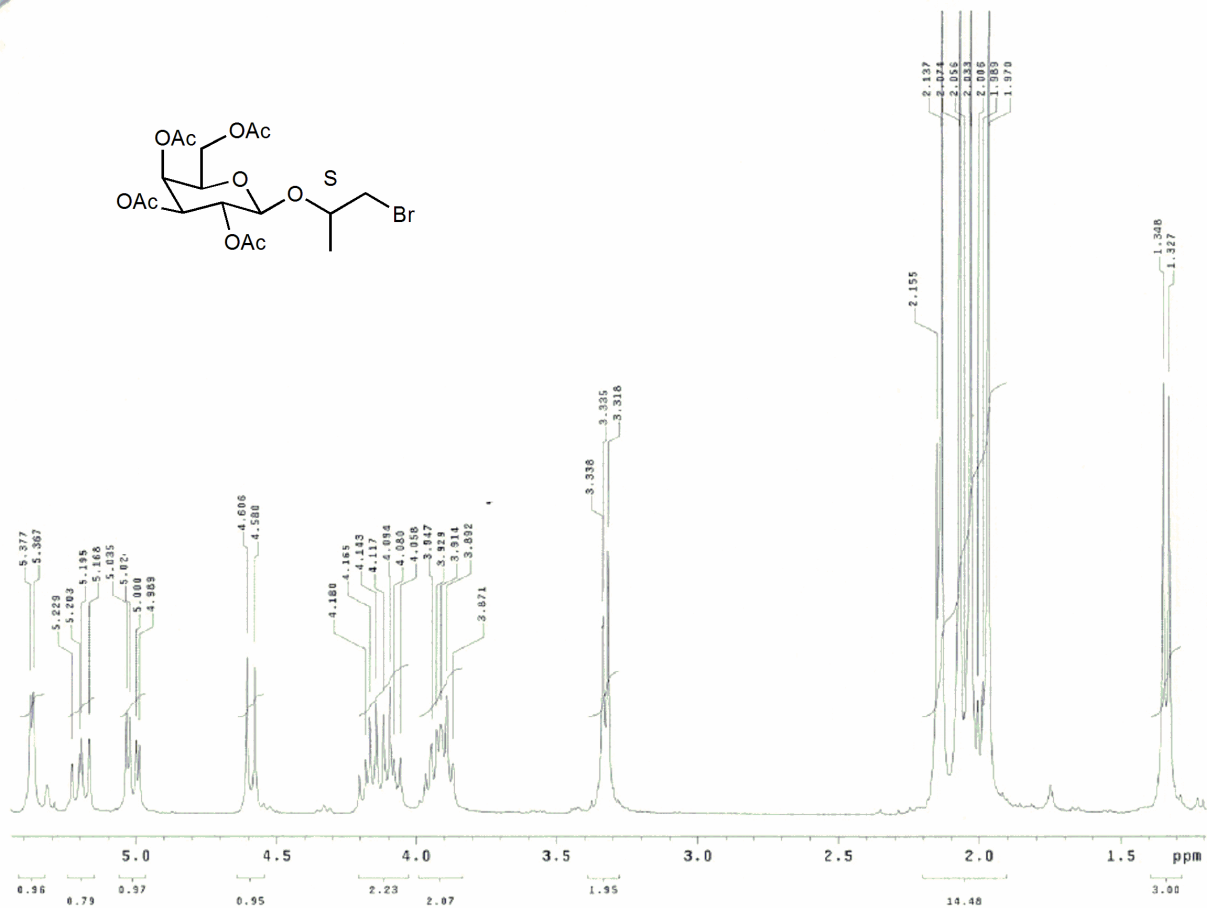
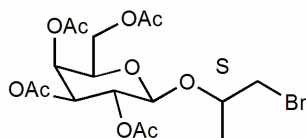


Figure S30. ^1H NMR (500 MHz, CDCl_3) 1.30-1.38 (d, 3H, methyl, $J = 6.5$), 1.98-2.40 (m, 12H, OAc), 3.28-3.36 (m, 2H, $-\text{CH}_2\text{Br}$), 3.86-3.98 (m, 2H, methine on linker and H-5), 4.05-4.20 (m, 2H, H-6), 4.55-4.64 (m, 1H, H-4), 4.96-5.02 (m, 1H, H-3), 5.18-5.24 (m, 1H, H-2), 5.38 (m, 1H, H-1)

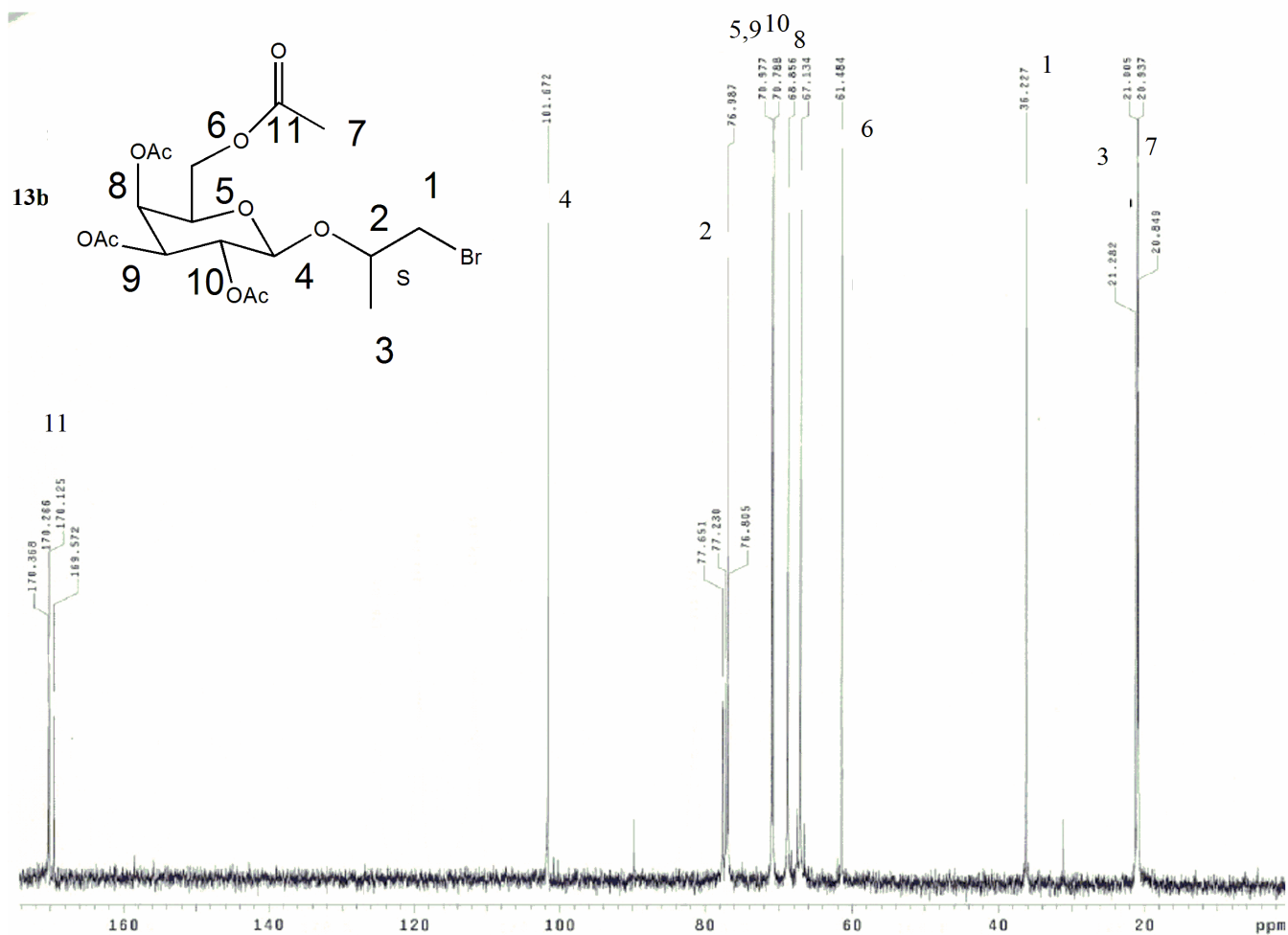


Figure S31. (125 MHz, CDCl_3) 20.85, 20.94, 21.01, 21.28, 36.23, 61.18, 67.13, 68.86, 70.79, 70.98, 76.98, 101.67, 168.57, 176.13, 170.27, 170.37

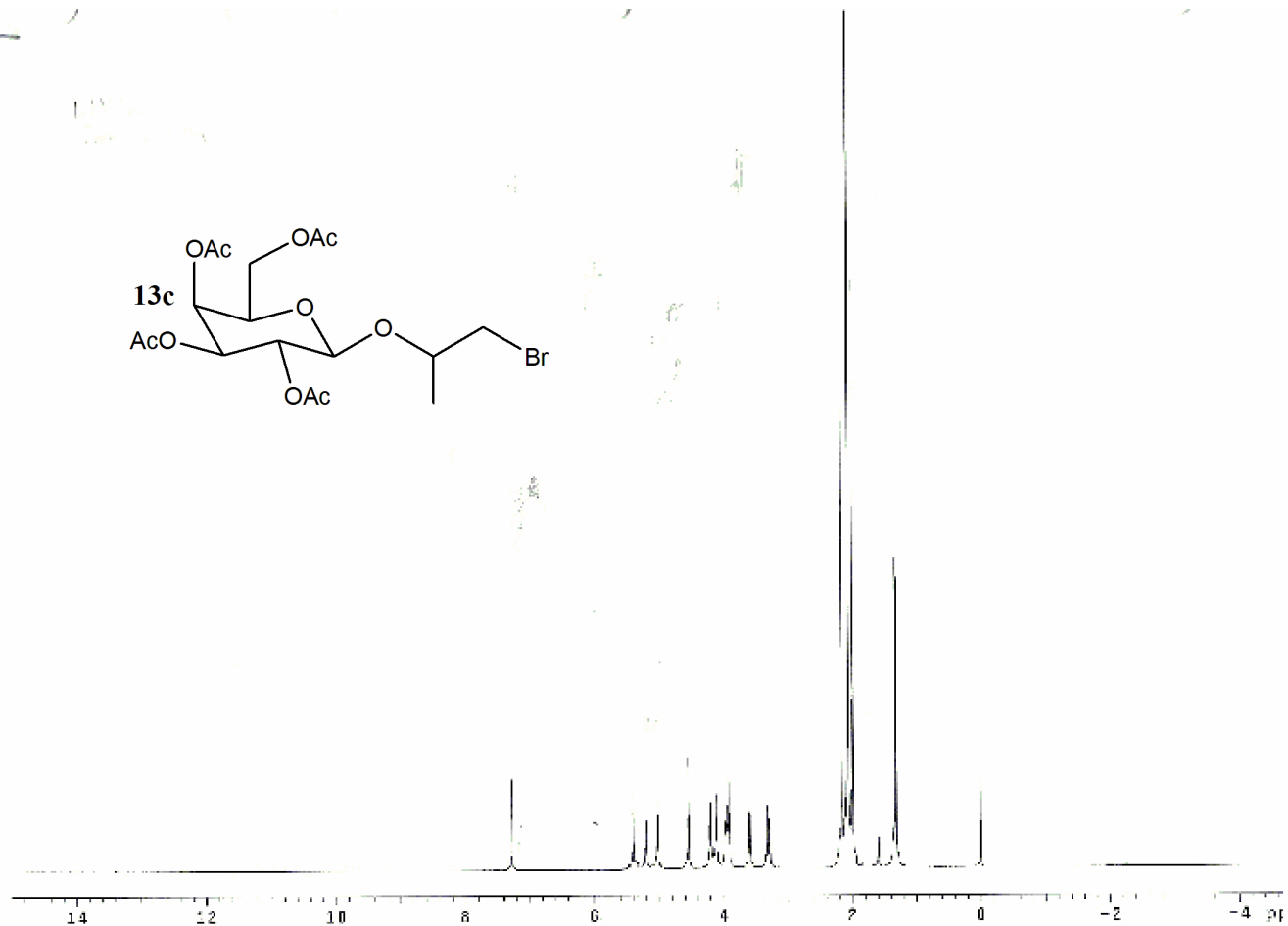


Figure S32. ^1H NMR. (500 MHz, CDCl_3) 1.33-1.38 (d, 3H, methyl, $J = 6.5$), 1.92-2.20 (m, 12H, OAc), 3.32-3.40 (m, 1H, $-\text{CH}_2\text{Br}$), 3.42-3.48 (m, 1H, $-\text{CH}_2\text{Br}$), 3.88-3.98 (m, 2H, methine on linker and H-5), 4.12-4.20 (m, 2H, H-6), 4.50-4.58 (m, 1H, H-4), 4.98-5.10 (m, 1H, H-3), 5.28-5.40 (m, 2H, H-1 and H-2).

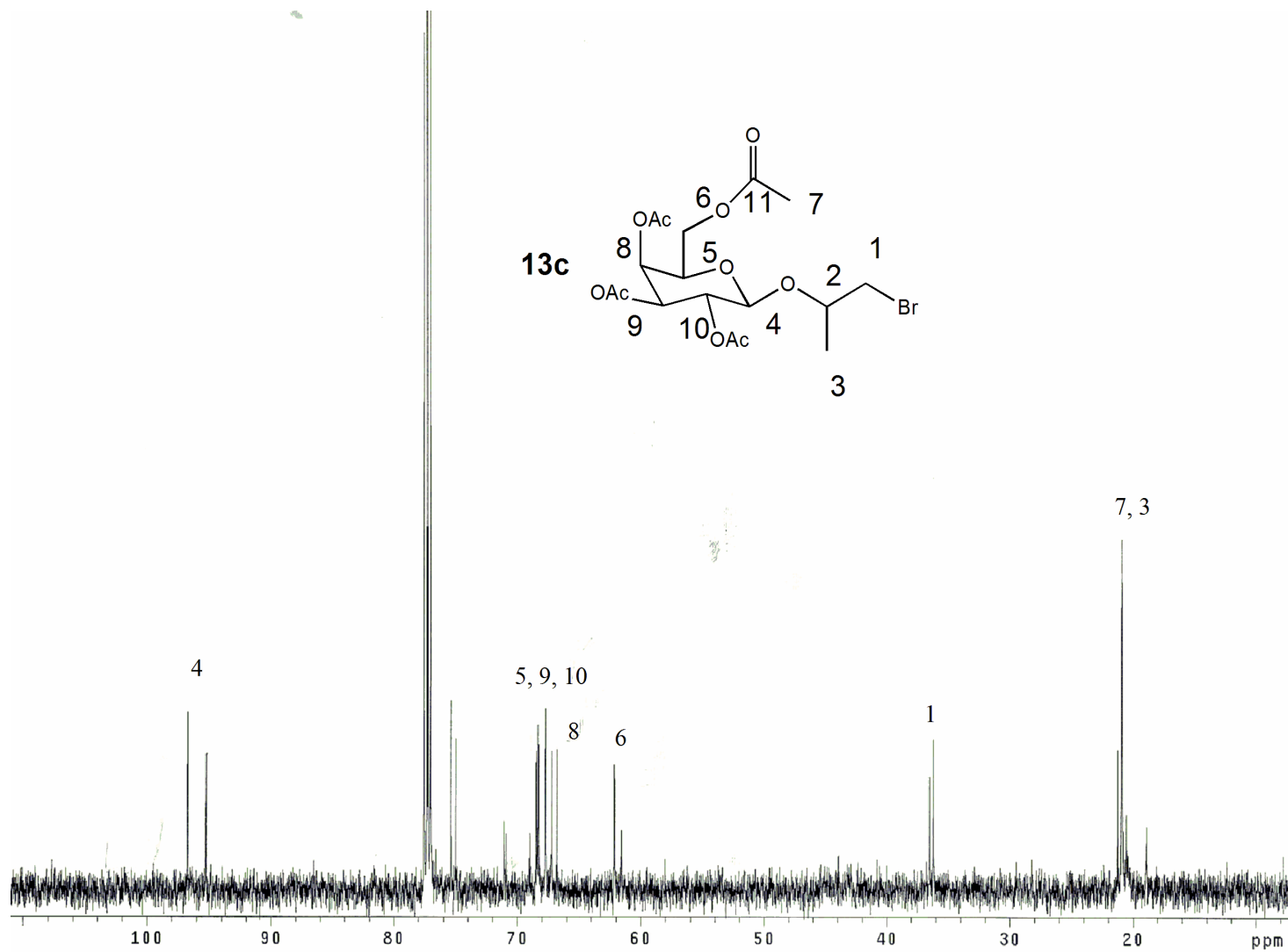


Figure S33. ^{13}C NMR (125 MHz, CDCl_3) 18.92, 20.55, 20.89, 20.92, 20.98, 36.18, 36.52, 61.54, 62.09, 62.14, 66.77, 67.17, 67.66, 67.71, 68.22, 68.30, 68.39, 68.47, 70.87, 71.03, 75.00, 75.37, 95.25, 96.70, 170.46, 170.67, 170.69, 170.88