Electronic Supplementary Material (ESI) for Chemical Communications.
This journal is © The Royal Society of Chemistry 2019

Supporting Information

A Multimeric MRI Contrast Agent based on a *closo*-borane scaffold bearing modified AAZTA chelates on the periphery

Shatadru Chakravarty,[a, b, c] Saurav J. Sarma,[a, d, e] Lalit N. Goswami,[a] Quan-Yu Cai, [a, f] Erik M. Shapiro,[b, c] M. Frederick Hawthorne[a] and Lixin Ma[*a, f]

[a]International Institute of Nano and Molecular Medicine and Department of Radiology, University of Missouri, Columbia, MO, 65212, USA

[b]Molecular and Cellular Imaging Laboratory, Department of Radiology, Michigan State University, East Lansing, MI, 48823, USA

[c]Institute for Quantitative Health Science and Engineering, Michigan State University, East Lansing, MI, 48823, USA.

[d]Bond Life Sciences Center, University of Missouri, Columbia, MO 65201, USA

[e]MU Metabolomics Centre, University of Missouri, Columbia, MO 65201, USA

[f]Harry S. Truman Memorial Veterans' Hospital, Columbia, MO 65201 USA.

Table of Contents

1. General Methods

All reactions were carried out in oven-dry glassware under an atmosphere of argon. Thin-layer chromatography (TLC) was carried out on precoated silica gel XHL TLC glass plates w/UV254 and aluminum oxide TLC glass plates w/UV254 (Sorbent Technologies). Column chromatography was performed over Silica Gel (40-63 μm particles size) obtained from Sorbent Technologies or on neutral Alumina (Brockmann grade III, 200 μm), obtained from Acros Organics. Size exclusion chromatography was performed using Lipophilic Sephadex LH-20 obtained from GE Healthcare. THF was distilled over sodium benzophenone ketyl and DCM was distilled over P_2O_5. Anhydrous DMF, anhydrous triethylamine, anhydrous pyridine and other solvents were obtained from commercial suppliers (J. T. Baker, EMD and Aldrich) and used without any further purification. NMR spectra were recorded on Bruker DRX 300, 400 and 500MHz spectrometers All chemical shifts are reported in parts per million (δ). All

NMR spectra were recorded at room temperature in CD_3CN, $CDCl_3$ or CD_3OD solutions. ^1H NMR spectra was referenced to residual $CHCl_3$ (7.26 ppm) and the ^{13}C spectra was referenced to $CDCl_3$ (77.2 ppm). The high-resolution mass spectrometry analyses were performed using Applied Biosystems Mariner ESI-TOF. IR spectra were recorded either neat on Thermo Nicolet-AEM spectrophotometer or by using Chloroform as solvent and the IR spectra consequently obtained was corrected using blank runs with chloroform solvent for background error correction to counter for the presence of chloroform as the solvent. For solids, transparent pellets made by mixing KBr and solids were used to record the IR spectra. Gd concentrations of the samples used in MRI experiments were measured by inductively coupled plasma optical emission spectroscopy (ICP-OES) using a PekinElmer OptimaTM 7000 DV instrument. Relaxivity measurements in serum and in PBS buffer were performed using a 7 Tesla Varian Unity Inova MRI system (Varian Inc./Agilent Technologies) and Bruker Avance 400 and 500 MHz spectrometers at room temperature. For Dialysis, Spectra/Por Dialysis membranes (MWCO: 1,000, wet in 0.1% NaN_3) were used. The dynamic light scattering analysis was performed on Microtrac's Zetatrac particle size analyzer.

In vivo MRI studies of closomer **CCA-I** were performed in SCID (severely compromised immunodeficient) mice bearing human PC-3 prostate cancer xenografts. Four to five week old ICR SCID outbred mice were obtained from Taconic (Germantown, NY). Mice were housed four animals per cage in sterile micro isolator cages in a temperature- and humidity-controlled room with a 12-hour light/12-hour dark schedule. The animals were fed autoclaved rodent chow (Ralston Purina Company, St. Louis, MO) and water *ad libitum.* All animal studies were conducted in accordance with the highest standards of care as outlined in the NIH guide for 'Care and Use of Laboratory Animals and the Policy and Procedures for Animal Research', and were approved by The Institutional Animal Care and Use Committee (IACUC) at the Harry S. Truman Memorial Veterans' Hospital and the University of Missouri-Columbia (IACUC # 7408). Mice were inoculated with human prostate cancer PC-3 tumor cells on the right flank; average body weight was between 25-30 grams at the time of MRI.

All MRI experiments were performed on a 7T Varian Unity Inova MRI equipped with a Millipede quadrature RF coil (40 mm ID). A T_1 weighted multi-slice spin echo sequence was performed to record sequential images pre and post injection of CAs. The animals were injected with 120 µL (10 mM Gd) of CA (in 2% Tween-80 in PBS) via the tail vein and imaged immediately. The mice were again imaged at 10 & 30 minutes as well as at 1, 4 and 24 h post injection time points. Vitals were continually monitored and mice were released to their cage after each imaging session in order to fully recover. Mice were then euthanized for tissue collection. Organs (including tumor, blood, heart, lungs, liver, spleen, stomach, large intestine, small intestine, kidney, brain, muscle) were collected for ICP-OES analysis of gadolinium and boron concentrations. No detectable gadolinium and boron contents were found in the organs collected after 24 h post injection, indicating a complete clearance of all contrast agents from body in 24 h.

Image Analysis: Image analysis and processing were performed with VnmrJ2.1D software (Varian/Agilent Technologies). Regions of interest (ROIs) were manually drawn on the tumor tissue, kidney cortex, liver, and the muscle tissue near the tumor for each time point. Signal intensities (SI) was measured as the mean of the intensity over the segmented ROI. SI were normalized according to the signal intensity of the muscle assuming the enhancement of signal of the muscle tissue is zero 4 h and 24 h post injection of CAs. The contrast enhancement ratio (CER) for a tissue was calculated according to the equation

$$CER = (SI_{post} - SI_{pre})/SI_{pre} \times 100\%$$

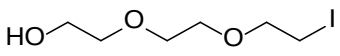
Statistical Analysis: Quantitative data were expressed as the mean ± standard deviation (SD). Means were compared by analysis of a student's t-test using t test function in Microsoft Excel (2016). P values of less than 0.05 were considered to be statistically significant.

Abbreviations: N,N'-dimethylformamide (DMF); triethylamine (Et_3N); sodium sulfate (Na_2SO_4); sodium hydride (NaH); potassium carbonate (K_2CO_3); tetrahydrofuran (THF); dichloromethane (DCM); ethyl acetate (EtOAc); acetonitrile (ACN); ammonium chloride (NH_4Cl); methanol (MeOH); pyridine (py);

hydrochloric acid (HCl); Triflouroacetic acid (TFA); Diisopropylethyl amine (DIPEA); 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDCI); room temperature (RT); hours (h); minutes (min.); calculated (*calcd*).

2. Synthetic and Spectral Details for Various AAZTA Ligands and Gd-AAZTA Chelates

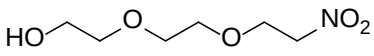
2.1 Synthesis of AAZTA-OH and AAZTA-NH_2



5

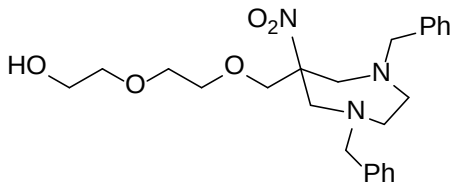
2-(2-(2-iodoethoxy)ethoxy)ethanol (5): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, commercially available **2-(2-(2-chloroethoxy)ethoxy)ethanol** (**4**, 96%, 9.0 mL, 59.3 mmol, 1.0 eqv.) and dry acetonitrile (100 mL) were taken and the contents were purged with alternate cycles of vacuum and argon. To the colorless solution so obtained, was added NaI (22.2 g, 148 mmol, 2.5 eqv.) in small portions and the contents were heated at reflux. Reaction progress was monitored using TLC analysis. After 24 h, all starting material was consumed. The reaction mixture was allowed to cool down to RT and the solvent acetonitrile was removed on a rotovap. The bright yellow residue so obtained was dissolved in a mixture of ethyl acetate and water (3:2). The product was extracted in the organic layer and washed with brine. The organic phase was separated, dried over Na_2SO_4 and concentrated to obtain yellow brown oil that was purified using flash chromatography over silica gel employing gradient elution with 1:4-4:1 EtOAc/Hexane to afford the product as a light yellow oil (14.8 g, 96%). IR (neat) $\tilde{\nu}$ 3431, 2870, 1456, 1415, 1350, 1263, 1123, 889, 754 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$) δ 3.75 (t, *J* = 6.7 Hz, 2H), 3.75-3.69 (m, 2H), 3.66 (s, 4H), 3.60 (t, *J* = 4.3 Hz, 2H), 3.25 (t, *J* = 6.9 Hz, 2H), 2.37 (t, *J* = 6.1 Hz, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 72.69, 72.11,

70.56, 70.41, 61.98, 2.87. HRMS (TIS) m/z 282.9863 ([M + Na]$^+$) calcd for $C_6H_{13}IO_3$ + Na (259.9909 + 22.9898) = 282.9807.



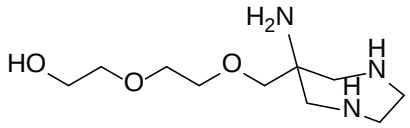
6

2-(2-(2-nitroethoxy)ethoxy)ethanol (6): In a one neck oven dried 500 mL round bottom flask containing a magnetic stir bar and a rubber septa, $AgNO_2$ (33.1 g, 215 mmol, 4.0 eqv.), DCM (70 mL) and DI water (10 mL) were taken and the flask was covered with an aluminium foil to protect from external light. To the grey slurry so obtained, **5** (14.0 g, 53.8 mmol, 1.0 eqv.) was added and the contents were stirred for 14 h. Reaction progress was monitored periodically using TLC analysis. After 14 h, no further reaction progress was noticed. The reaction mixture was filtered over a thick pad of celite and the pad was washed thoroughly with MeOH. The filtrate so obtained was concentrated to obtain yellow oily residue. It was dissolved in a mixture of EtOAc and brine (3:2). The product was extracted in the organic layer, dried over Na_2SO_4 and concentrated to obtain bright yellow oil that was purified using flash chromatography over silica gel employing gradient elution with 1-3% MeOH/DCM to afford the product as a deep yellow oil (6.8 g, 72%). IR (neat) $\tilde{\nu}$ 3440, 3016, 2875, 1632, 1556, 1468, 1421, 1367, 1217, 1121, 1067, 874, 758 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54 (t, *J* = 4.8 Hz, 2H), 4.05 (t, *J* = 5.2 Hz, 2H), 3.73 (t, *J* = 4.4 Hz, 2H), 3.70-3.64 (m, 4H), 3.58 (t, *J* = 4.8 Hz, 2H), 2.13 (br s, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 75.10, 72.50, 70.83, 70.24, 66.70, 61.71. HRMS (TIS) m/z 202.0976 ([M + Na]$^+$) calcd for $C_6H_{13}NO_5$ + Na (179.0794 + 22.9898) = 202.0691.



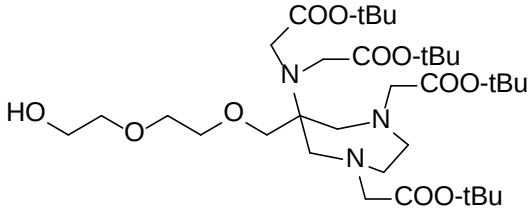
7

2-(2-((1,4-dibenzyl-6-nitro-1,4-diazepan-6-yl)methoxy)ethoxy)ethanol (7): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, commercially available **N,N'-dibenzylethane-1,2-diamine** (99%, 7.9 mL, 33.5 mmol, 1.0 eqv.) and **6** (6.0 g, 33.5 mmol, 1.0 eqv.) were dissolved in 1:1 mixture of Toluene and EtOH (50 mL each) and the contents were purged with alternate cycles of vacuum and argon. To the light yellow solution so obtained, was added **paraformaldehyde** (4.0 g, 134 mmol, 4.0 eqv.) in small portions and the contents were heated at reflux. Reaction progress was monitored using TLC analysis. After 12 h, all starting material was consumed. The reaction mixture was allowed to cool down to RT and the solvent was removed on a rotovap. The orange yellow viscous oil so obtained was dissolved in a mixture of DCM and water (3:2). The product was extracted in the organic layer and washed with brine. The organic phase was separated, dried over Na_2SO_4 and concentrated to obtain yellow oil that was purified using flash chromatography over grade IV alumina employing gradient elution with 1:9-1:1 EtOAc/Hexane to afford the product as a colorless viscous oil (12.6 g, 85%). IR (neat) $\tilde{\nu}$ 3455, 3058, 3026, 2919, 2872, 1636, 1541, 1453, 1350, 1216, 1122, 1064, 951, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.22 (m, 10H), 3.73 (d, *J* = 13.2 Hz, 2H), 3.67 (t, *J* = 3.6 Hz, 2H), 3.62 (d, *J* = 13.2 Hz, 2H), 3.60 (s, 2H), 3.52 (d, *J* = 13.9 Hz, 4H), 3.50-3.30 (m, 4H), 3.04 (d, *J* = 14.3 Hz, 2H), 2.82-2.51 (m, 4H), 2.09 (br s, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.09, 128.97, 128.29, 127.24, 94.33, 73.42, 72.36, 70.80, 70.02, 63.87, 61.80, 59.44, 58.62. HRMS (TIS) m/z 466.2627 ($[M + Na]^+$); 444.2759 ($[M + H]^+$); calcd for $C_{24}H_{33}N_3O_5$+ Na (443.2420 + 22.9898) = 466.2318; calcd for $C_{24}H_{33}N_3O_5$ + H (443.2420 + 1.0078) = 444.2498.



8

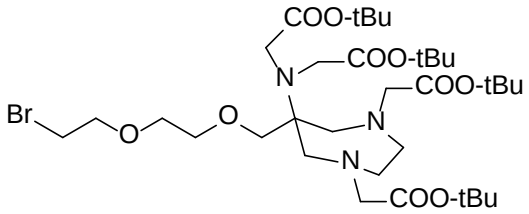
2-(2-((6-amino-1,4-diazepan-6-yl)methoxy)ethoxy)ethanol (8): In a two neck oven dried, 500 mL round bottom flask, containing a magnetic stir bar and fitted with a condenser and a rubber septa, **7** (12.0 g, 27.1 mmoL, 1.0 eqv.), Pd on C (10%, 4.0 g) and $HCOONH_4$ (34.1 g, 541 mmol, 10.0 eqv.) were taken and dry MeOH (30 mL) was added to it. The suspension so obtained was heated at reflux. The reaction progress was monitored using TLC analysis, which after 4 h indicated completed consumption of the starting material. The reaction mixture was allowed to cool down to RT and filtered over a pad of celite. The filtrate so obtained was concentrated into a pale yellow viscous oil that was used without any purification in the next step (6.2 g, crude weight). IR (neat) $\tilde{\nu}$ 3345, 2921, 2869, 1456, 1351, 1105, 1068, 889 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.67 (t, *J* = 4.0 Hz, 2H), 3.62 (s, 4H), 3.56 (t, *J* = 4.6 Hz, 2H), 3.35 (s, 2H), 2.90-2.83 (m, 4H), 2.87 (d, *J* = 13.8 Hz, 2H), 2.76 (br s, N*H*$_2$, N*H*, N*H*, O*H*, 5H), 2.68 (d, *J* = 13.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 77.08, 73.02, 70.69, 70.37, 61.60, 58.50, 58.02, 52.93. HRMS (TIS) m/z 234.1292 ($[M + H]^+$) calcd for $C_{10}H_{23}N_3O_3$ (233.1739 + 1.0078) = 234.1818.



9

Di-*tert*-butyl-2,2'-((1,4-*bis*(2-(*tert*-butoxy)-2-oxoethyl)-6-((2-(2-hydroxyethoxy) ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate (9): In a one neck oven dried 250 mL round bottom flask, containing a magnetic stir bar and a rubber septa, **8** (6.0 g, 25.7 mmoL, 1.0 eqv.) and K_2CO_3 (24.9 g, 180 mmoL, 7.0

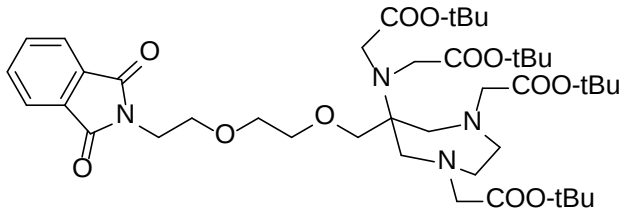
eqv.) and dry DMF (50 mL) were taken and the contents were purged with alternate cycles of vacuum and argon. The flask was placed in an ice bath. To this suspension so obtained, ***tert*-butylbromoacetate** (19.0 mL, 129 mmoL, 5.0 eqv.) was added over 1 h with the temperature maintained at 0-5 ºC. The contents were allowed to warm up to RT and stirred under an ensuing blanket of argon. Reaction progress was monitored using TLC analysis, which after 36 h indicated no further change in the relative amounts of various reaction constituents. The white suspension was dissolved in a mixture of 3:2 ethyl acetate and water. The product was extracted in an organic layer and washed with brine (80 mL). The organic layer was separated, dried over Na_2SO_4 and concentrated to obtain colorless viscous oil. It was subjected to flash column chromatography over grade IV alumina, following a gradient elution with 1:9-1:1 EtOAc/Hexane to obtain the product as a colorless, very viscous oil (12.1 g, 68%). IR (neat) $\tilde{\nu}$ 3505, 3017, 2980, 2932, 1733, 1456, 1393, 1368, 1216, 1151, 848, 746 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 4H), 3.69 (t, *J* = 4.2 Hz, 2H), 3.62-3.59 (m, 2H), 3.58-3.54 (m, 4H), 3.52 (s, 2H), 3.26 (s, 4H), 3.01 (d, *J* = 14.3 Hz, 2H), 2.90 (br s, O*H*), 2.80-2.75 (m, 2H), 2.74 (d, J = 14.4 Hz, 2H), 2.66-2.60 (m, 2H), 1.43 (s, 18H), 1.42 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.27, 171.24, 80.90, 80.44, 75.01, 72.79, 70.51, 70.44, 63.95, 62.57, 62.37, 62.05, 59.17, 51.71, 28.41, 28.37; HRMS (TIS) m/z 712.5735 ($[M + Na]^+$); 690.6052 ($[M + H]^+$); calcd for $C_{34}H_{63}N_3O_{11}$ + Na (689.4463 + 22.9898) = 712.4360; calcd for $C_{34}H_{63}N_3O_{11}$ + H (689.4463 + 1.0078) = 690.4541.



10

Di-*tert*-butyl-2,2'-(6-(*bis*(2-(*tert*-butoxy)-2-oxoethyl)amino)-6-((2-(2-bromoethoxy) ethoxy)methyl)-1,4-diazepane-1,4-diyl)diacetate (10): In a one neck oven dried 250 mL round bottom flask, containing a

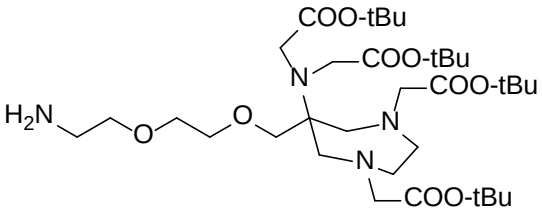
magnetic stir bar and a rubber septa, **9** (8.0 g, 11.6 mmoL, 1.0 eqv.) and **triphenylphosphine** (9.1 g, 34.8 mmoL, 3.0 eqv.) were dissolved in dry DCM (80 mL) with the flask placed in an ice bath. **N-Bromosuccinimide** (4.1 g, 23.2 mmoL, 2.0 eqv.) was added to it in small portions over a period of 30 min. The contents were allowed to warm up to RT and kept stirring under an ensuing argon blanket. Reaction progress was monitored using TLC analysis, which after 3 h indicated complete consumption of the starting alcohol. The solvent was removed on a rotovap to obtain dark yellow oil that was purified using flash chromatography over grade IV alumina employing gradient elution with 1:19-1:5 EtOAc/Hexane. The product was obtained as a colorless viscous oil (8.0 g, 92%). IR (neat) $\tilde{\nu}$ 3019, 2980, 2932, 1734, 1456, 1393, 1368, 1216, 1151, 847, 756 $cm^{-1.}$ ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (t, *J* = 6.3 Hz, 2H), 3.75 (s, 4H), 3.70-3.63 (m, 2H), 3.61-3.56 (m, 2H), 3.53 (s, 2H), 3.47 (t, *J* = 6.3 Hz, 2H), 3.30 (s, 4H), 3.05 (d, *J* = 14.3 Hz, 2H), 2.87-2.73 (m, 2H), 2.76 (d, J = 14.5 Hz, 2H), 2.72-2.61 (m, 2H), 1.47 (s, 18H), 1.46 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.71, 171.78, 81.41, 80.87, 75.84, 71.91, 71.17, 71.02, 64.59, 63.08, 62.95, 59.69, 52.44, 31.22, 29.02, 28.98; HRMS (TIS) m/z 776.2818 ($[M + Na]^+$) 752.3656 ($[M + H]^+$); calcd for $C_{34}H_{62}BrN_3O_{10}$ + Na (751.3619 + 22.9898) 774.3516; calcd for $C_{34}H_{62}BrN_3O_{10}$ + H (751.3619 + 1.0078) = 752.3697.



11

Di-*tert*-butyl-2,2'-((1,4-*bis*(2-(*tert*-butoxy)-2-oxoethyl)-6-((2-(2-(1,3-dioxoisoindolin-2-yl)ethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate (11): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **potassium phthalimide** (4.0 g, 21.3 mmol, 1.0 eqv.) and dry DMF (80 mL) were taken and the contents were purged

with alternate cycles of vacuum and argon. To the suspension so obtained, **10** (8.0 g, 10.6 mmol, 2.0 eqv.) was added in one portion and the contents were heated at 60 ˚C under an ensuing argon envelope. Reaction progress was monitored using TLC analysis. After 18 h, all starting material was consumed. The reaction mixture was allowed to cool down to RT and a mixture of ethyl acetate and water (3:2) was added to it. The product was extracted in the organic layer and washed with brine. The organic phase was separated, dried over Na_2SO_4 and concentrated to obtain a yellow residue that was purified using flash chromatography over grade IV alumina employing gradient elution with 1:19-1:4 EtOAc/Hexane. The product was obtained as a colorless very viscous oil (7.2 g, 83%). IR (neat) $\tilde{\nu}$ 3018, 2979, 2931, 1737, 1713, 1453, 1393, 1368, 1216, 1150, 756, 720 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (double d, *J* = 6.8 Hz, 3.8 Hz, 2H), 7.74 (dd, *J* = 7.2 Hz, 2H), δ 3.91 (t, 2H, *J* = 5.6 Hz), 3.74 (t, 6H, *J* = 6.4 Hz), 3.67-3.52 (m, 4H), 3.51 (s, 2H), 3.30 (s, 4H), 3.04 (d, 2H, *J* = 14.4 Hz), 2.91-2.77 (m, 2H), 2.74 (d, *J* = 14.4 Hz, 2H), 2.69-2.57 (m, 2H), 1.47 (s, 18H), 1.46 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.70, 171.83, 168.97, 134.64, 133.02, 124.04, 81.38, 80.80, 75.95, 71.09, 70.58, 68.68, 64.62, 63.12, 62.98, 59.69, 52.49, 38.17, 29.03, 28.98. HRMS (TIS) m/z 857.3535 ($[M + K]^+$) calcd for $C_{42}H_{66}N_4O_{12}$ + K (818.4677 + 38.9637) = 857.4314.

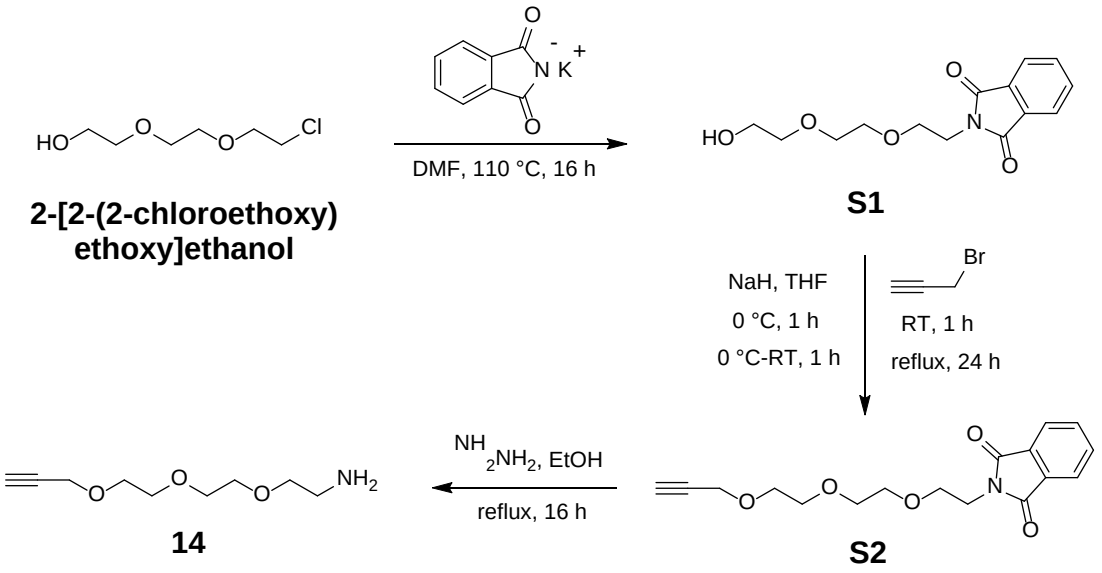


12

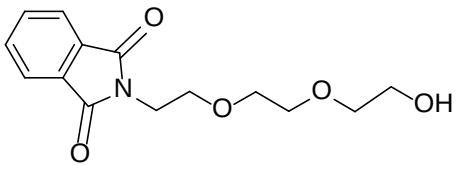
Di-*tert*-butyl-2,2'-((6-((2-(2-aminoethoxy)ethoxy)methyl)-1,4-bis(2-(*tert*-butoxy)-2-oxoethyl)-1,4-diazepan-6-yl)azanediyl)diacetate (12): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **11** (7.0 g, 8.55 mmoL, 1.0 eqv.) was dissolved in ethanol (80 mL) and the contents were purged with alternate cycles of vacuum and argon. To the light yellow solution so obtained, hydrazine (2.7 mL, 85.5 mmoL, 10 eqv.) was added and the contents

were put to heating at 60 ºC. Reaction progress was monitored using TLC analysis. After 16 h, essentially all of **11** was consumed. The contents were allowed to cool down to RT and dissolved in a 3:2 mixture of ethyl acetate and water. The product was extracted in the organic layer, dried over Na_2SO_4 and concentrated to obtain yellow green oil. It was subjected to flash chromatography over grade IV alumina employing gradient elution with 1-5% MeOH/DCM as the eluent. The product was isolated as a colorless viscous oil (5.3 g, 90%). IR (neat) $\tilde{\nu}$ 3379, 3295, 2978, 2932, 1736, 1475, 1456, 1392, 1368, 1253, 1218, 1150, 953, 849, 756 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 4H), 3.65-3.59 (m, 2H), 3.59-3.54 (m, 2H), 3.52 (t, *J* = 4.8 Hz, 4H), 3.28 (s, 4H), 3.02 (d, *J* = 14.3 Hz, 2H), 2.86 (t, *J* = 5.12 Hz, 2H), 2.82-2.70 (m, 2H), 2.74 (d, *J* = 14.4 Hz, 2H), 2.69-2.59 (m, 2H), 2.18 (br s, N*H*$_2$), 1.45 (s, 18H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 171.8, 81.45, 81.03, 75.52, 73.82, 71.19, 70.91, 64.57, 63.03, 62.96, 59.73, 52.36, 42.76, 29.01; HRMS (TIS) m/z 689.3939 ([M + H]$^+$) calcd for $C_{34}H_{64}N_4O_{10}$ + H (688.4622 + 1.0078) = 689.4701.

2.2 Synthesis of PEG-linker 14

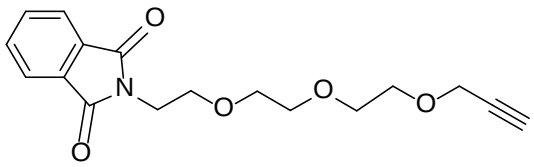


Scheme S1. Synthesis of PEG-linker, 14 for the design of alkyne-terminated AAZTA analogue.



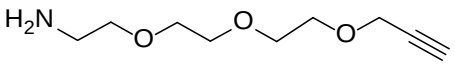
S1

2-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)isoindoline-1,3-dione (S1): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, potassium phthalimide (6.0 g, 32.6 mmol, 1.1 eqv.) and dry DMF (50 mL) were taken and the contents were purged with alternate cycles of vacuum and argon. To the suspension so obtained, commercially available **2-(2-(2-chloroethoxy)ethoxy)ethanol** (96%, 4.6 mL, 29.6 mmol, 1.0 eqv.) was added in one portion and the contents were heated at 110 ˚C for 16 h. Reaction progress was monitored using TLC analysis. After 16 h, all starting material was consumed. The reaction mixture was allowed to cool down to RT and a mixture of ethyl acetate and water (3:2) was added to it. The product was extracted in the organic layer and washed with brine. The organic phase was separated, dried over Na_2SO_4 and concentrated to obtain a yellow white solid (9.0 g, crude yield 91%). This was used in the next step without any further purification. IR (neat) $\tilde{\nu}$ 3467, 3055, 2872, 1773, 1709, 1467, 1395, 1120, 1069, 1027, 874, 720 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (double d, *J* = 6.8 Hz, 3.8 Hz, 2H), 7.69 (dd, *J* = 7.2 Hz, 2H), 3.89 (t, *J* = 7.2 Hz, 2H), 3.74 (t, *J* = 7.1 Hz, 2H), 3.64 (t, *J* = 5.1 Hz, 2H), 3.64-3.61 (m, 2H), 3.60-3.57 (m, 2H), 3.51 (t, *J* = 5.3 Hz, 2H), 2.53 (br s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 134.1, 132.3, 123.4, 72.63, 70.55, 70.19, 68.09, 61.92, 37.4. HRMS (TIS) m/z 302.1649 ($[M + Na]^+$) calcd for $C_{14}H_{17}NO_5$ + Na (279.1107 + 22.9898) = 302.1004.



S2

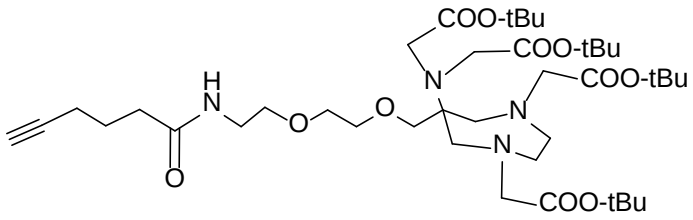
2-(2-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethoxy)ethyl)isoindoline-1,3-dione (S2): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, THF (35 mL) was taken and the flask was placed in an ice bath. NaH (60% dispersion in oil, 930 mg, 23.2 mmol, 1.2 eqv.) was added to it and the contents were stirred under an ensuing argon atmosphere. **26** (5.4g, 19.3 mmol, 1.0 eqv.) dissolved in 10 mL THF was added to the reaction mixture over a period of 5 min. The contents were allowed to warm up to RT, stirred for 1 h and propargyl bromide (80% solution in toluene, 3.2 mL, 29 mmoL, 1.5 eqv.) was added to it over a period of 1 h. The contents were put to reflux for 24 hours. After 24 h, the reaction mixture was allowed to cool down to RT and methanol (5 mL) was added to it to quench any unreacted base. The resulting deep brown solution was poured into a 500 mL separatory funnel. Ethyl acetate (120 mL) and an ice cold aqueous solution of 5% HCl (100 mL) were added to it. The product was extracted in the organic layer and washed with brine (100 mL). The organic layer was separated, dried over Na_2SO_4 and concentrated to obtain brown red very viscous oil. This crude reaction mixture was purified using gradient flash chromatography over grade IV alumina with 7:3 EtOAc/hexane as the eluent. The product was isolated as a yellow coarse solid (3.5 g, 60%). IR (neat) $\tilde{\nu}$ 3305, 3019, 2865, 1775, 1712, 1429, 1395, 1215, 1100, 928, 768 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.4 Hz, 2.4 Hz, 2H), 7.80 (double d, *J* = 5.4 Hz, 2H), 4.24 (d, *J* = 2.35 Hz, 2H), 3.98 (t, *J* = 5.9 Hz, 2H), 3.82 (t, *J* = 5.7 Hz, 2H), 3.74-3.72 (m, 2H), 3.72-3.70 (m, 4H), 3.69-3.67 (m, 2H), 2.50 (t, *J* = 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 133.9, 132.1, 123.2, 79.69, 74.49, 70.58, 70.42, 70.10, 69.06, 67.92, 58.36, 37.26. HRMS (TIS) m/z 340.0779 ($[M + Na]^+$) calcd for $C_{17}H_{19}NO_5$ + Na (317.1263 + 22.9898) = 340.1161.



14

2-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethoxy)ethanamine (14): In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **S2** (3.3 g, 10 mmoL, 1.0 eqv.) was dissolved in ethanol (120 mL) and the contents were purged with alternate cycles of vacuum and argon. To the light yellow solution so obtained, hydrazine (3.3 mL, 104 mmoL, 10 eqv.) was added and the contents were put to reflux for 16 h. Reaction progress was monitored using TLC analysis. After 8 hours, essentially all of **S2** was consumed. The contents were allowed to cool down to RT and dissolved in a 3:2 mixture of ethyl acetate and water. The product was extracted in the organic layer, dried over Na_2SO_4 and concentrated to obtain yellow green oil. It was subjected to flash chromatography over grade IV alumina with 3% methanol/DCM as the eluent. The product was isolated as a light green yellow viscous oil (1.4 g, 74%). IR (neat) $\tilde{\nu}$ 3369, 3248, 2868, 1590, 1461, 1350, 1248, 1102, 1033, 920, 745 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.26 (d, *J* = 2.4 Hz, 2H), 3.77-3.73 (m, 4H), 3.73-3.67 (m, 4H), 3.55 (t, *J* = 5.2 Hz, 2H), 2.91 (t, *J* = 5.2 Hz, 2H), 2.49 (t, *J* = 2.4 Hz, 1H), 1.46 (br s, -N*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.61, 74.53, 73.48, 70.58, 70.40, 70.24, 69.08, 58.37, 41.79. HRMS (TIS) m/z 188.1114 ([M + H]$^+$) calcd for $C_9H_{17}NO_3$ + H (187.1208 + 1.0078) = 188.1287.

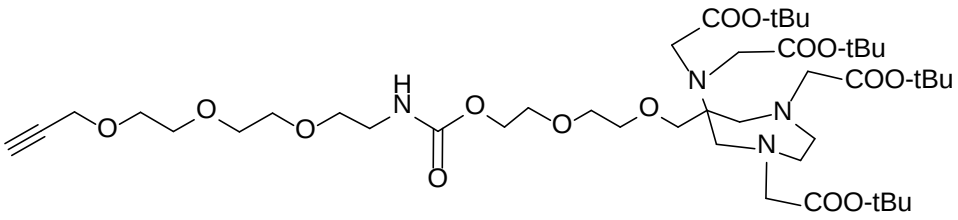
2.3 Synthesis of alkyne-terminated AAZTA analogues



13

Di-*tert*-butyl-2,2'-((1,4-*bis*(2-(*tert*-butoxy)-2-oxoethyl)-6-((2-(2-(hex-5-ynamido) ethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate (25): In a one neck oven dried 125 mL round bottom flask containing a magnetic stir bar and a rubber septa, commercially available **5-Hexynoic acid** (0.48 g, 4.36 mmol, 1.0 eqv.) and dry DCM (15 mL) were taken and the flask was placed in an ice bath. EDCI (1.25 g, 6.54 mmol, 1.5 eqv.) and DMAP (0.96 g, 7.84 mmol, 1.8 eqv.) were added to it in rapid succession. With the temperature being maintained between 0-5 ºC, **12** (3.0 g, 4.36 mmol, 1.0 eqv.) dissolved in dry DCM (20 mL) was added to the reaction mixture quickly and the contents were allowed to warm up to RT and kept stirring under an ensuing argon atmosphere. After 12 h, the TLC analysis showed complete consumption of the starting material. DCM (50 mL) was added to the reaction mixture and it was washed with 5% HCl solution (v/v, 80 mL). The organic layer was separated and washed with saturated $NaHCO_3$ solution (80 mL). Combined aqueous layers were washed with additional DCM (2 * 100 mL). The combined organic phase so obtained was dried over Na_2SO_4 and concentrated to obtain a deep yellow mixture. It was subjected to flash chromatography over silica gel employing gradient elution with 1-5% MeOH/DCM as the eluent. The product was isolated as a light yellow viscous oil (3.1 g, 91%). IR (neat) $\tilde{\nu}$ 3385, 3310, 2978, 2932, 1736, 1664, 1535, 1455, 1368, 1250, 1150, 848, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (br s, -CON*H*-), 3.74 (s, 4H), 3.54 (s, 4H), 3.52-3.47 (m, 4H), 3.45-3.39 (m, 2H), 3.27 (s, 4H), 3.00 (d, *J* = 14.3 Hz, 2H), 2.81-2.70 (m, 2H), 2.72 (d, *J* = 14.4 Hz, 2H), 2.69-2.59 (m, 2H), 2.32 (t, *J*

= 7.6 Hz, 2H), 2.26-2.19 (m, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.87-1.79 (m, 2H), 1.43 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.92, 173.27, 171.84, 84.57, 81.54, 81.16, 75.40, 71.20, 70.76, 69.72, 64.55, 63.16, 62.96, 59.80, 52.27, 40.21, 35.75, 29.02, 28.98, 25.17, 18.79. HRMS (TIS) m/z 783.2819 (100%, $[M + H]^+$) calcd for $C_{40}H_{70}N_4O_{11}$ + H (782.5041 + 1.0078) = 783.5119.

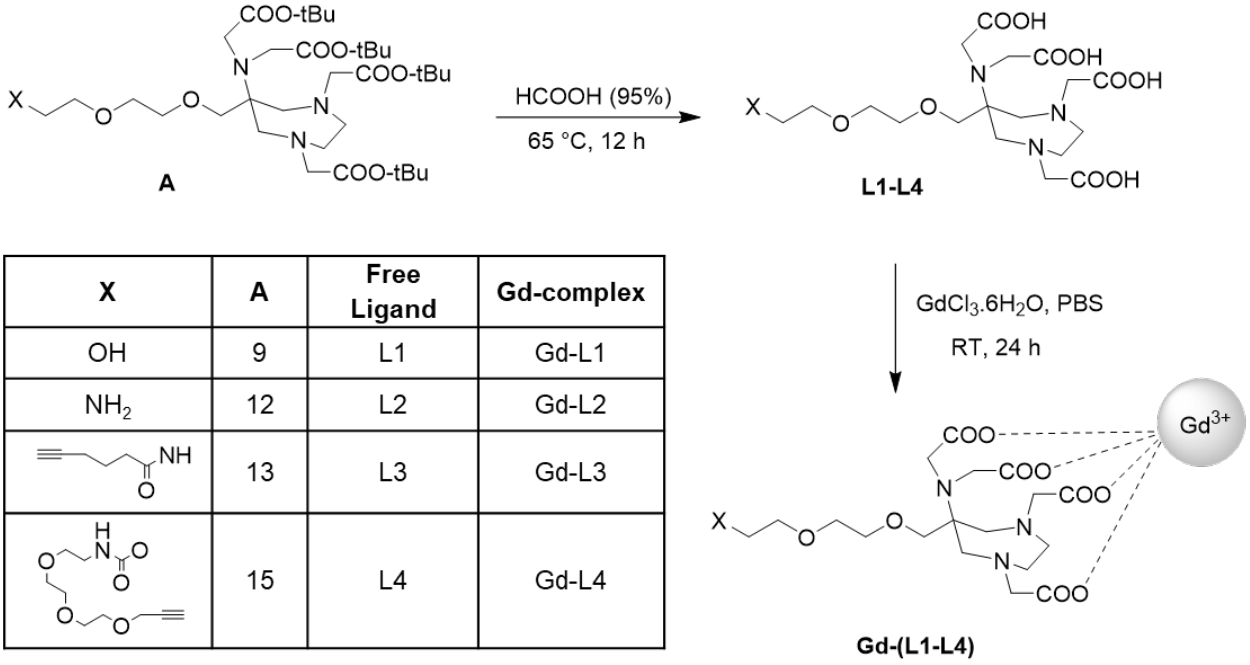


15

Di-*tert*-butyl-2,2'-((1,4-*bis*(2-(*tert*-butoxy)-2-oxoethyl)-6-(9-oxo-2,5,8,13,16,19-hexa oxa-10-azadocos-21-yn-1-yl)-1,4-diazepan-6-yl)azanediyl)diacetate (15): A two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa was charged with dry DMF (15 mL) and CDI (0.97 g, 5.80 mmol, 1.1 eqv.). The contents were purged with alternate cycles of vacuum and argon and **9** (4.0 g, 5.80 mmoL, 1.1 eqv.) dissolved in dry DMF (15 mL) over a period of 10 min. The resulting colorless solution was heated at 60ºC for 12 hours. Next, **14** (0.99 g, 5.27 mmoL, 1.0 eqv.) dissolved in dry DMF (10 mL) was added to the stirring reaction mixture and heating was continued for a further 36 h. On reaction completion, the contents were allowed to cool down to RT and solvent DMF was removed *in vacuo* to obtain orange yellow viscous oil. It was subjected to flash chromatography over grade IV alumina employing gradient elution with 1:9-3:1 EtOAc/Hexane. The product was isolated as light yellow viscous oil (3.3 g, 70%). IR (neat) $\tilde{\nu}$ 3447, 3367, 3307, 3013, 2979, 2932, 1735, 1734, 1514, 1478, 1392, 1368, 1217, 1150, 847, 759 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (br s, -OCON*H*-), 4.22 (d, J = 2.4Hz, 2H), 4.21-4.17 (m, 2H), 3.75 (s, 4H), 3.72-3.66 (m, 6H), 3.65-3.59 (m, 6H), 3.58-3.51 (m, 6H), 3.40-3.34 (m, 2H), 3.29 (s, 4H), 3.03 (d, *J* = 14.3 Hz, 2H), 2.83-2.74 (m, 2H), 2.74 (d, *J* = 14.3 Hz, 2H), 2.69-2.60 (m, 2H), 2.46 (t, *J* = 2.4Hz, 1H), 1.46 (s, 18H), 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$)

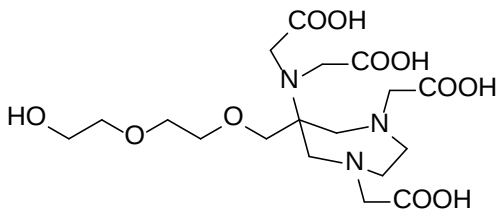
δ 173.79, 171.82, 157.36, 81.42, 80.86, 80.46, 75.97, 75.40, 71.34, 71.22, 71.05, 71.00, 70.86, 70.32, 69.87, 64.83, 64.57, 63.14, 62.96, 59.71, 59.18, 54.22, 52.37, 41.53, 37.24, 29.02, 28.98. HRMS (TIS) m/z 903.4162 ($[M + H]^+$); 925.4076 ($[M + Na]^+$); calcd for $C_{44}H_{78}N_4O_{15}$ + H (902.5464 + 1.0078) = 903.5542; calcd for $C_{44}H_{78}N_4O_{15}$ + Na (902.5464 + 22.9898) = 925.5361 .

2.4 Synthesis of Gd-AAZTA chelates



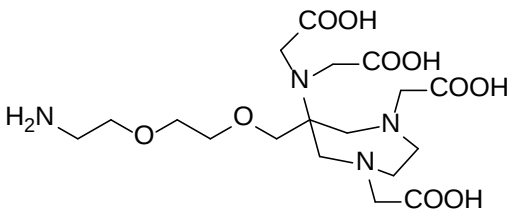
X	A	Free Ligand	Gd-complex
OH	9	L1	Gd-L1
NH_2	12	L2	Gd-L2
	13	L3	Gd-L3
	15	L4	Gd-L4

Scheme S2. Synthesis of various Gd-AAZTA chelates. The central Gd^{3+} ion is also coordinated with the three N (two ring and one exocyclic) atoms that is not shown for clarity.



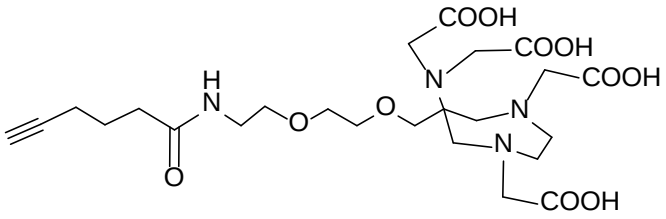
L1

2,2'-((1,4-*bis*(carboxymethyl)-6-((2-(2-hydroxyethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetic acid (L1): In a two neck oven dried 100 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **9** (1.16 g, 1.68 mmol) and formic acid (30 mL, 95%) were taken and the contents were stirred for 15 h at 65 °C. Reaction progress was monitored using NMR spectral analysis of the crude reaction mixture and the removal of all *tert*-butyl ester groups was confirmed by the absence of a sharp singlet at ~ 1.4 ppm in the ^{1}H NMR spectrum and mass spectral analysis. On reaction completion, the mixture was concentrated under reduced pressure. The residue so obtained was dissolved in a minimal amount of MeOH, and the crude product was precipitated by adding excess diethyl ether. The product so obtained was filtered and washed thoroughly with copious amounts of diethyl ether. The desired tetra-acid was obtained as a white coarse solid (740 mg, 95%). IR (KBr) $\tilde{\nu}$ 3505, 3347, 2980, 2932, 1728, 1456, 1393, 1298, 1216, 1151, 848, 746 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): δ 3.75 (s, 4H), 3.70 (s, 4H), 3.66-3.55 (m, 4H), 3.55-3.52 (m, 2H), 3.52-3.45 (m, 6H), 3.44 (s, 2H), 3.42-3.32 (m, 4H); ^{13}C NMR (100 MHz, D_2O) δ 177.10, 171.68, 72.80, 72.48, 70.92, 70.26, 63.15, 61.17, 59.67, 58.90, 53.74, 53.21. HRMS (TIS) m/z 466.2434 ($[M + H]^+$) calcd for $C_{18}H_{31}N_3O_{11}$ + H (465.1959 + 1.0078) = 466.2037.



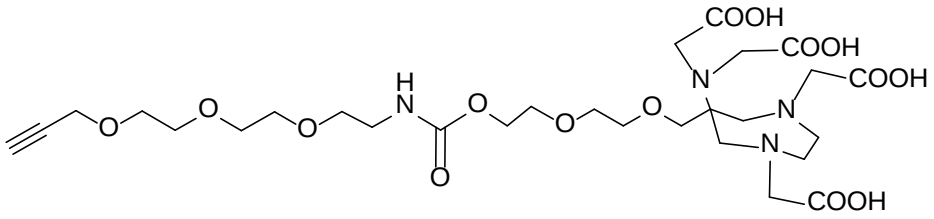
L2

2,2'-((6-((2-(2-aminoethoxy)ethoxy)methyl)-1,4-*bis*(carboxymethyl)-1,4-diazepan-6-yl)azanediyl)diacetic acid (L2): In a two neck oven dried 100 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **12** (400 mg, 0.58 mmol) and formic acid (15 mL, 95%) were taken and the contents were stirred for 15 h at 65 °C. Reaction progress was monitored using NMR spectral analysis of the crude reaction mixture and the removal of all *tert*-butyl ester groups was confirmed by the absence of a sharp singlet at ~ 1.4 ppm in the ^{1}H NMR spectrum and mass spectral analysis. On reaction completion, the mixture was concentrated under reduced pressure. The residue so obtained was dissolved in a minimal amount of MeOH, and the crude product was precipitated by adding excess diethyl ether. The product so obtained was filtered and washed thoroughly with copious amounts of diethyl ether. The desired tetra-acid **L2** was obtained as a pale yellow solid (250 mg, 93%). IR (KBr) $\tilde{\nu}$ 3502, 3379, 3295, 2978, 2932, 1475, 1456, 1392, 1253, 1218, 1150, 953, 849, 756 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): 3.73 (s, 4H), 3.71 (s, 4H), 3.62 (t, J = 4.4 Hz, 2H), 3.61-3.48 (m, 6H), 3.46 (s, 4H), 3.45-3.28 (m, 6H), 3.12-3.05 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 176.98, 171.90, 72.69, 71.00, 70.47, 67.20, 63.34, 59.86, 58.82, 53.93, 53.39, 39.87; HRMS (TIS) m/z 465.2961 (100%, $[M + H]^+$) calcd for $C_{18}H_{32}N_4O_{10}$ + H (464.2118 + 1.0078) = 465.2197.



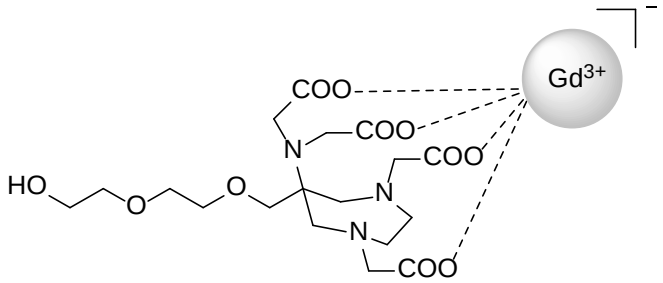
L3

2,2'-((1,4-*bis*(carboxymethyl)-6-((2-(2-(hex-5-ynamido)ethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetic acid (L3): In a two neck oven dried 100 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **13** (230 mg, 0.29 mmol) and formic acid (15 mL, 95%) were taken and the contents were stirred for 15 h at 65 ˚C. Reaction progress was monitored using NMR spectral analysis of the crude reaction mixture and the removal of all *tert*-butyl ester groups was confirmed by the absence of a sharp singlet at ~ 1.4 ppm in the ^{1}H NMR spectrum and mass spectral analysis. On reaction completion, the mixture was concentrated under reduced pressure. The residue so obtained was dissolved in a minimal MeOH and the crude product was precipitated by adding excess diethyl ether. The product so obtained was filtered and washed thoroughly with copious amounts of diethyl ether. The desired tetra-acid, **L3** was obtained as white coarse solid (150 mg, 91%). IR (neat) $\tilde{\nu}$ 3375, 3290, 2968, 2932, 1724, 1663, 1535, 1435, 1373, 1264, 1148, 862, 748 cm^{-1} ^{1}H NMR (500 MHz, D_2O): δ 3.76 (s, 8H), 3.63-3.56 (m, 4H), 3.56-3.53 (m, 4H), 3.53-3.47 (m, 4H), 3.47-3.48 (m, 4H), 3.31 (t, 2H, *J* = 5 Hz), 2.31 (t, 1H, *J* = 2.5 Hz), 2.31-2.26 (m, 2H), 2.23-2.10 (m, 2H), 1.81-1.64 (m, 2H), 1.10 (t, 1H, *J* = 10 Hz); ^{13}C NMR (125 MHz, D_2O) δ 176.79, 176.74, 171.82, 85.40, 72.57, 70.91, 70.63, 70.06, 69.48, 66.61, 63.27, 59.90, 58.52, 53.65, 53.56, 35.28, 24.79, 17.72, 14.75; HRMS (TIS) m/z 557.2631 ([M - H]$^{-}$) calcd for $C_{24}H_{38}N_4O_{11}$ - H (558.2537 – 1.0078) = 557.2459.



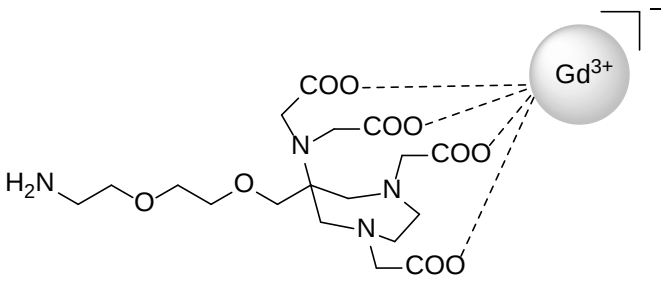
L4

2,2'-((1,4-*bis*(carboxymethyl)-6-(9-oxo-2,5,8,13,16,19-hexaoxa-10-azadocos-21-yn-1-yl)-1,4-diazepan-6-yl)azanediyl)diacetic acid (L4): In a two neck oven dried 100 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, **15** (260 mg, 0.29 mmol) and formic acid (15 mL, 95%) were taken and the contents were stirred for 15 h at 65 ˚C. Reaction progress was monitored using NMR spectral analysis of the crude reaction mixture and the removal of all *tert*-butyl ester groups was confirmed by the absence of a sharp singlet at ~ 1.4 ppm in the ^{1}H NMR spectrum and mass spectral analysis. On reaction completion, the mixture was concentrated under reduced pressure. The residue so obtained was dissolved in a minimal amount of MeOH, and the crude product was precipitated by adding excess diethyl ether. The product so obtained was filtered and washed thoroughly with copious amounts of diethyl ether. The desired tetra-acid, **L4** was obtained as white coarse solid (180 mg, 92%). IR (neat) $\tilde{\nu}$ 3380, 3307, 3013, 2979, 1723, 1524, 1482, 1387, 1368, 1220, 1148, 850, 746 cm^{-1}. ^{1}H NMR (500 MHz, D_2O): δ 4.14 (d, 2H, *J* = 2.0 Hz), 4.12 (m, 2H), 3.73 (s, 8H), 3.69-3.60 (m, 8H), 3.59 (s, 4H), 3.56-3.50 (m, 6H), 3.50-3.30 (m, 8H), 3.23 (t, 2H, *J* = 4.5 Hz), 2.83 (t, 1H, *J* = 2.5 Hz); ^{13}C NMR (125 MHz, D_2O) δ 176.00, 171.10, 158.18, 79.42, 76.05, 71.85, 70.05, 69.52, 69.38, 69.33, 69.20, 68.91, 68.60, 65.91, 64.19, 62.62, 59.18, 57.82, 53.05, 52.86, 39.98, 14.11; HRMS (TIS) m/z 679.2468 (100%, $[M + H]^+$) calcd for $C_{28}H_{46}N_4O_{15}$ + H (678.2960 + 1.0078) = 679.3038.



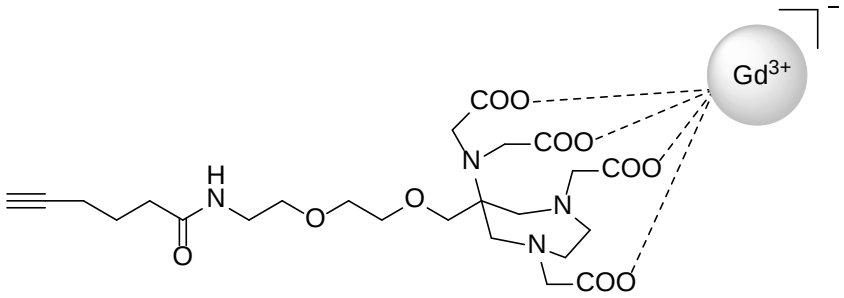
Gd-L1

2,2'-((1,4-*bis*(carboxylatomethyl)-6-((2-(2-hydroxyethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate-Gd(III) chelate (Gd-L1): In a one neck oven dried 50 mL round bottom flask containing a magnetic stir bar and a rubber septa, a mixture of **L1** (90 mg, 0.19 mmol, 1.0 eqv.) and $GdCl_3.6H_2O$ (72 mg, 0.19 mmol, 1.0 eqv.) in PBS buffer (pH 7) was stirred for 24 h at RT. Reaction progress was monitored using mass spectral analysis of small aliquots of reaction mixture drawn out at periodic intervals that after 24 h indicated product formation. On reaction completion, a concentrated solution of NaOH was added dropwise to the reaction mixture so as to precipitate any unreacted Gd^{3+} salt as the insoluble hydroxide. On addition of NaOH, the reaction solution became cloudy and a white amorphous solid separated out on standing. The reaction mixture was filtered and the filtrate was concentrated and dried under vacuum to obtain a sticky solid. This residue was dissolved in a minimum amount of methanol and the product was precipitated by adding excess diethyl ether. The residue was filtered and washed with diethyl ether to isolate the product as a dirty white solid (110 mg, 90%). HRMS (ESI) *m/z* 618.0989 ($[M]^-$) calcd for $[C_{18}H_{27}GdN_3O_{11}]^-$ = 619.0892.



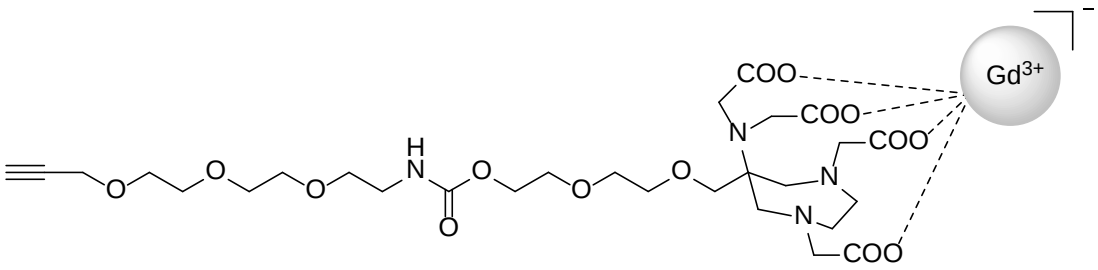
Gd-L2

2,2'-((6-((2-(2-aminoethoxy)ethoxy)methyl)-1,4-*bis*(carboxylatomethyl)-1,4-diazepan-6-yl)azanediyl)diacetate-Gd(III) chelate (Gd-L2): In a one neck oven dried 50 mL round bottom flask containing a magnetic stir bar and a rubber septa, a mixture of **L2** (230 mg, 0.49 mmol, 1.0 eqv.) and $GdCl_3.6H_2O$ (184 mg, 0.49 mmol, 1.0 eqv.) in PBS buffer (pH 7) was stirred for 24 h at RT. Reaction progress was monitored using mass spectral analysis of small aliquots of reaction mixture drawn out at periodic intervals that after 24 h indicated product formation. On reaction completion, a concentrated solution of NaOH was added dropwise to the reaction mixture so as to precipitate any unreacted Gd^{3+} salt as the insoluble hydroxide. On addition of NaOH, the reaction solution became cloudy and a white amorphous solid separated out on standing. The reaction mixture was filtered and the filtrate was concentrated and dried under vacuum to obtain a sticky solid. This residue was dissolved in a minimum amount of MeOH and the product was precipitated by adding excess diethyl ether. The residue was filtered and washed with diethyl ether to isolate the product as an off white colored coarse solid (270 mg, 88%). HRMS (ESI) *m/z* 618.9951 ($[M]^-$) calcd for $[C_{18}H_{28}GdN_4O_{10}]^-$ = 618.1052.



Gd-L3

2,2'-((1,4-*bis*(carboxylatomethyl)-6-((2-(2-(hex-5-ynamido)ethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate-Gd(III) chelate (Gd-L3): In a one neck oven dried 50 mL round bottom flask containing a magnetic stir bar and a rubber septa, a mixture of **L3** (150 mg, 0.27 mmol, 1.0 eqv.) and Gd_2O_3 (58 mg, 0.16 mmol, 0.6 eqv.) in deionized water was heated to reflux with vigorous stirring. Reaction progress was monitored using mass spectral analysis of small aliquots of reaction mixture drawn out at periodic intervals that after 15 h indicated product formation. On reaction completion, the reaction mixture was allowed to cool down to RT and filtered. The filtrate so obtained was concentrated and dried under vacuum to obtain a sticky solid. This residue was dissolved in a minimum amount of methanol and the product was precipitated by adding excess diethyl ether. The residue was filtered and washed with diethyl ether to isolate the product as an off white colored fluffy solid (90 mg, 78%). HRMS (TIS) *m/z* 712.1656 ($[M]^-$) calcd for $[C_{24}H_{34}GdN_4O_{11}]^-$ = 712.1471.



Gd-L4

2,2'-((1,4-*bis*(carboxylatomethyl)-6-(9-oxo-2,5,8,13,16,19-hexaoxa-10-azadocos-21-yn-1-yl)-1,4-diazepan-6-yl)azanediyl)diacetate-Gd(III) chelate (Gd-L4): In a one neck oven dried 50 mL round bottom flask containing a magnetic stir bar and a rubber septa, a mixture of **L4** (180 mg, 0.26 mmol, 1.0 eqv.) and Gd_2O_3 (58 mg, 0.16 mmol, 0.6 eqv.) in deionized water was heated to reflux with vigorous stirring. Reaction progress was monitored using mass spectral analysis of small aliquots of reaction mixture drawn out at periodic intervals that after 15 h indicated product formation. On reaction completion, the reaction mixture was allowed to cool down to RT and filtered. The filtrate so obtained was concentrated and dried under vacuum to obtain a sticky solid. This residue was dissolved in a minimum amount of methanol and the product was precipitated by adding excess diethyl ether. The residue was filtered and washed with diethyl ether to isolate the product as an off white colored solid (110 mg, 80%). HRMS (TIS) *m/z* 832.1674 (100%, $[M]^-$) calcd for $[C_{28}H_{42}GdN_4O_{15}]^-$ = 832.1893.

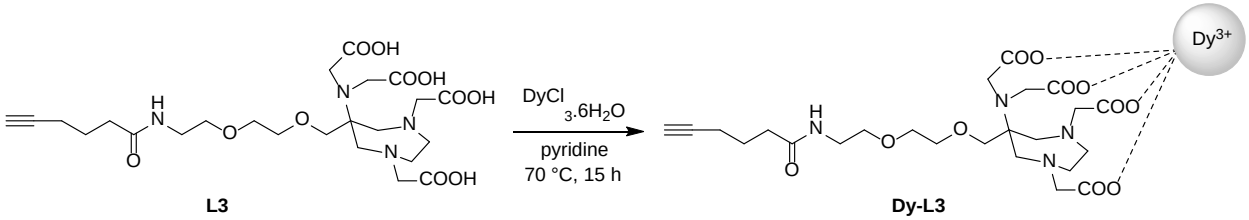
3. Relaxivity of various Gd-AAZTA chelates

Table S1 Relaxivity of modified Gd-AAZTA chelates

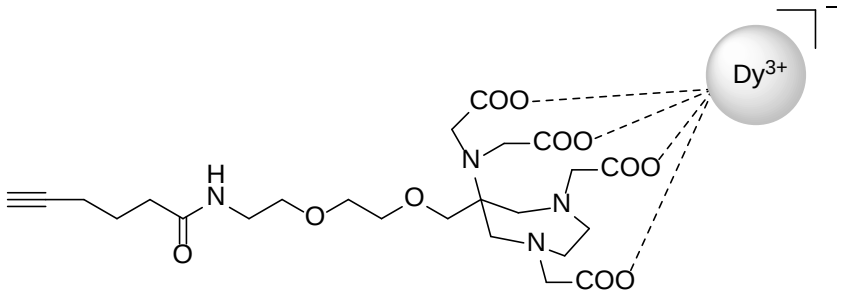
Entry	Relaxivity, r_1[a] ($s^{-1}mM^{-1}$)	
	PBS	**Serum**
Gd-L1	7.5	7.3
Gd-L2	7.7	7.6
Gd-L3	7.3	7.2
Gd-L4	7.2	7.1
Omniscan	4.1	4.0

[a] Measured at 7T and 25 °C.

4. Synthesis of Dy-AAZTA chelate



Scheme S3 Synthesis of the Dy-alkyne-AAZTA chelate, Dy-L3. The central Dy^{3+} ion is also coordinated with the three N (two ring and one exocyclic) atoms that is not shown for clarity.



Dy-L3

2,2'-((1,4-*bis*(carboxylatomethyl)-6-((2-(2-(hex-5-ynamido)ethoxy)ethoxy)methyl)-1,4-diazepan-6-yl)azanediyl)diacetate-Dy(III) chelate (Dy-L3): In a one neck oven dried 50 mL round bottom flask containing a magnetic stir bar and a rubber septa, a mixture of **L3** (300 mg, 0.54 mmol, 1.0 eqv.) and $DyCl_3.6H_2O$ (202 mg, 0.54 mmol, 1.0 eqv.) in pyridine (50 mL) was heated at 70 °C with vigorous stirring. Reaction progress was monitored using mass spectral analysis of small aliquots of reaction mixture drawn out at periodic intervals that after 15 h indicated product formation. On reaction completion, a concentrated solution of NaOH was added dropwise to the reaction mixture so as to precipitate any unreacted Dy^{3+} salt as the insoluble hydroxide. On addition of NaOH, the reaction became cloudy and a white amorphous solid separated out on standing. The reaction mixture was filtered and the filtrate was concentrated and dried under vacuum to obtain a sticky solid. This residue was dissolved in a minimum amount of methanol and

the product was precipitated by adding excess diethyl ether. The residue was filtered and washed with diethyl ether to isolate the product as a pale yellow colored fluffy solid (310 mg, 80%). HRMS (TIS) *m/z* 717.1301 ([M - H]$^-$) calcd for $C_{24}H_{34}DyN_4O_{11}$ – H (718.1521 – 1.0078) = 717.1438.

5. Determination of Hydration Number (*q*)

In general, the hydration number of the Gd^{3+} complex of AAZTA is predicted to be two (q = 2); however, the PEG oxygen donors in the family of modified AAZTA ligands **L1-L4** can partially displace the water molecules coordinated to central Gd^{3+} ion, consequently reducing the overall relaxivity of the CA. To ascertain the hydration number for the newly synthesized AAZTA ligand L3, the corresponding q value was determined using the Dy^{3+}-induced water ^{17}O NMR shifts (d.i.s.).[1,2] The basis of this method derives from the fact that for a paramagnetic lanthanide ion (Ln^{3+})-bound ^{17}O nucleus, the contribution of a *contact coordination* of the Ln^{3+} ion towards the value of Ln^{3+}-induced ^{17}O shift is virtually independent of the nature of the ligands coordinated to the lanthanide ion. As a result, this Ln^{3+}-induced ^{17}O shift can be used to determine the ligand coordination module as well as the stoichiometry of the Ln^{3+}-ligand complex. Of a number of Ln^{3+} ions available, Dy^{3+} was selected as the corresponding Dy^{3+} induced shift (d.i.s.) is influenced mostly by the contact contribution and the pseudo-contact contribution is very small. Accordingly, the arduous dissection of the observed ^{17}O shifts into a contact and pseudo-contact contribution is not required and the d.i.s. values obtained can be directly used to calculate the ligand coordination. This method proposed by Geraldes and co-workers in 1992 takes into account the d.i.s. of ^{17}O of water as a function of the concentration of a Dy^{3+}-ligand complex for the determination of the number of inner sphere water molecules (q value) for the concerned ligand.[1,3,4] On addition of a Dy^{3+}-ligand to water, the ^{17}O NMR signals were found to shift to lower frequencies and this experimentally induced shift, d.i.s. for the complex, $Dy(ligand)_n(H_2O)_q$ would be given by the **equation S1**;

$$\text{d.i.s.} = \frac{q\text{D}[\text{Dy(ligand)}_n(\text{H}_2\text{O})_q]}{[\text{H}_2\text{O}]} \qquad \text{(S1)}$$

In **equation S1**, q refers to the number of inner sphere water molecules for the Dy^{3+}-ligand complex and Δ refers to the shift of a water ^{17}O nucleus bound to the complex. The concentration of the complex, $[Dy(ligand)_n(H_2O)_q]$ was very small (~ 100 mmol dm^{-3}) and thus the concentration of water, $[H_2O]$ would be a virtual constant. Accordingly, a plot between the d.i.s. and $[Dy(ligand)_n(H_2O)_q]$ would generate a straight line, with a slope given by $q\Delta/[H_2O]$. At low concentrations, a Dy^{3+} ion is hydrated with nine water molecules (q = 9)[5] and using this assumption, an experimental run with different concentrations of an aqueous solution of $DyCl_3.6H_2O$ provides a numerical value for $\Delta/[H_2O]$ that can be used to determine the q value for a Dy^{3+}-ligand complex. The results obtained using this method for the ligand **L3** would be applicable for the all the other AAZTA based ligands reported in the present work.

In order to find out the d.i.s. for the AAZTA analogues, an initial control experiment to determine the d.i.s. ($\Delta\delta$) in the ^{17}O NMR for solutions containing different concentrations of $DyCl_3.6H_2O$ in 80% D_2O/H_2O were performed. Solutions with five different concentrations (0, 20, 40, 60 and 80 mmol dm^{-3}) were made and the corresponding shifts obtained in the ^{17}O NMR were recorded. A plot between the shifts and the different concentrations is shown in **Figure S1** (top line). Using **equation S1** the slope of this line was calculated and used to determine the value of $\Delta/[H_2O]$, with the q value fixed at 9 for a Dy^{3+}-aqua complex. In an identical fashion, solutions of varying concentrations (0-80 mmol dm^{-3}) for the **Dy-L3**, were prepared and the d.i.s. ($\Delta\delta$) was measured (**Figure S1**, bottom line). Fitting the value of $\Delta/[H_2O]$ obtained previously, the q value of the complex **Dy-L3** was determined to be 2.

The chemical shifts obtained for both the complexes and the various concentrations being used have been detailed in **Table S2**. Detailed accounts of the calculations being performed are hereby presented;

From **equation S1**, the slope of the top line in **Figure S1** is given by

slope = $q\Delta/[H_2O]$

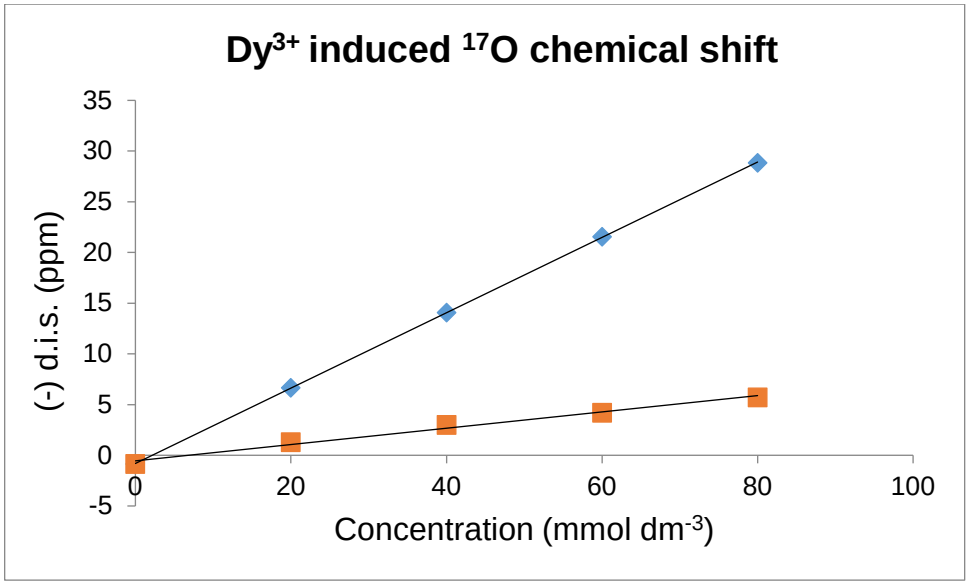


Figure S1. Plot of the Dy^{3+}-induced water ^{17}O NMR shift as a function of the concentration of the complex $[Dy(ligand)_n(H_2O)_q]$. For the top line, n = 0 (no ligand, ♦) and q = 9. For the bottom line, ligand = L3 (■) and the corresponding complex is Dy-L3. The q value was calculated to be 2.

From the graph, the slope was calculated as,

slope = -371.3 ppm dm^3 mol^{-1}

$q\Delta/[H_2O]$ = -371.3 ppm dm^3 mol^{-1}

For the complex $DyCl_3.6H_2O$, the value of q was taken as nine and henceforth, the value of $\Delta/[H_2O]$ was obtained as

$\Delta/[H_2O]$ = -371.3 ppm dm^3 mol^{-1} /9

$\Delta/[H_2O]$ = -41.25 ppm dm^3 mol^{-1} (S2)

Now, for the graph (bottom line) obtained for the complex **Dy-L3**, the slope was calculated to be

slope = -81.25 ppm dm^3 mol^{-1}

or, $q\Delta/[H_2O] = -81.25$ ppm dm^3 mol^{-1} (S3)

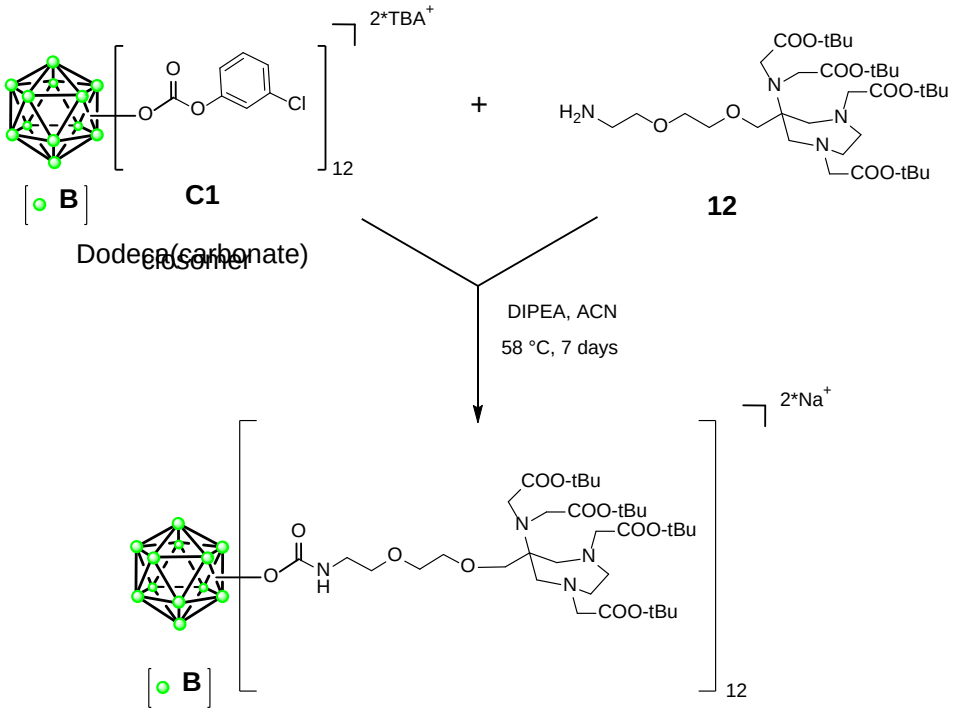
Combining **equations S2** and **S3**, the value of *q* for **Dy-L3** was obtained as;

$q = 1.97 \sim 2.$

Table S2. The list of ^{17}O NMR chemical shifts obtained for the two complexes $DyCl_3.6H_2O$ and the Dy-AAZTA complex, **32** at varying concentrations in 80% D_2O in deionized water.

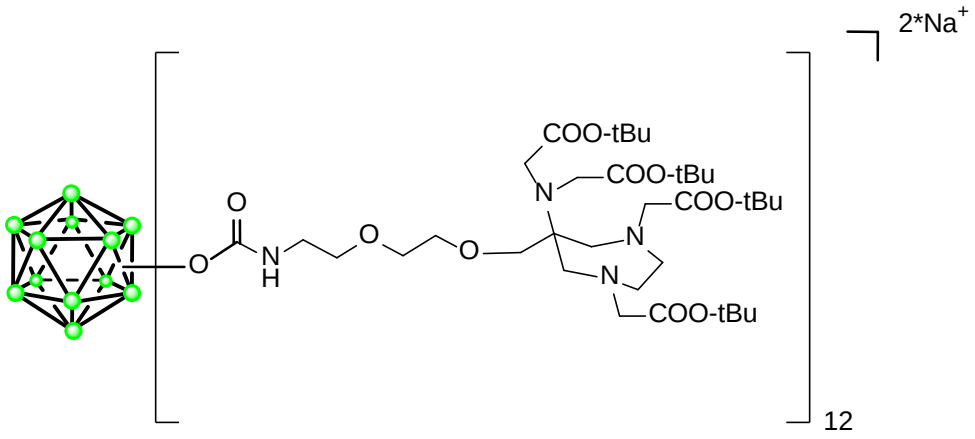
Concentration (*mmol dm*$^{-3}$)	**Dy^{3+} induced shift; d.i.s.** (*ppm*)	
	$DyCl_3.6H_2O$	Dy-L3
0	0.86	0.86
20	-6.66	-1.24
40	-14.07	-2.96
60	-21.57	-4.17
80	-28.84	-5.64

6. Conjugation of AAZTA-NH_2 to Closomer core



Closomer C2

Scheme S4. Synthesis of Closomer **C2** via the conjugation of amine-terminated AAZTA linker, **12** with the twelve-fold functionalized carbonate closomer, **C1**.

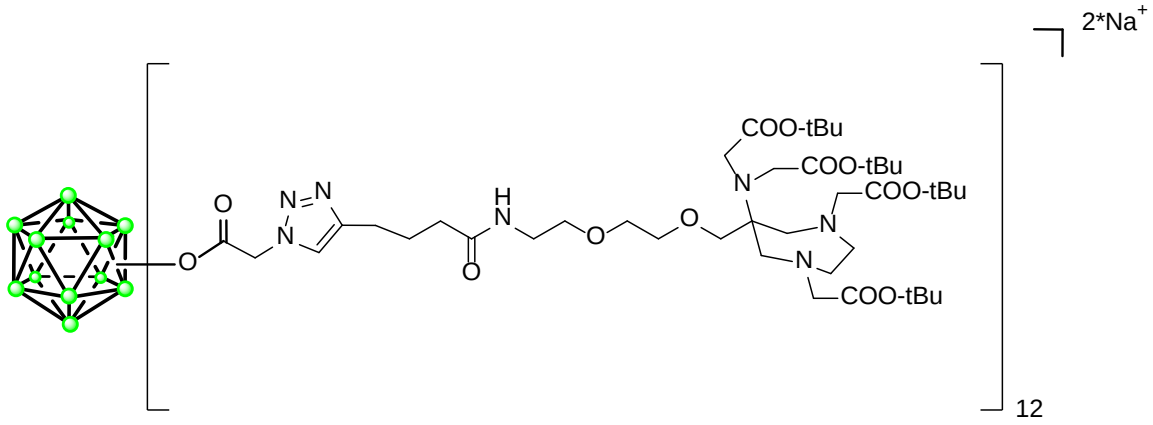


Closomer C2

Closomer C2: In a two neck oven dried 250 mL round bottom flask containing a magnetic stir bar and fitted with a condenser and a rubber septa, *bis*(*tetra*butylammonium)-*hypercloso*-dodeca(3-chlorophenyl)dodecaboranylcarbonate, **C1** *(synthesized using a previously reported procedure)*[6] (100 mg, 0.0374 mmol, 1.0 eqv.), N,N-diisopropylethyl amine (0.8 mL, 4.48 mmol, 120 eqv, 10 fold per boron vertex of the carbonate closomer) and dry acetonitrile (15 mL) were taken and the contents were purged with alternate cycles of vacuum and argon. The reaction flask was placed in an ice bath and after 10 min., **12** (1.54 g, 2.24 mmol, 60 eqv., 5 folds per boron vertex of the carbonate closomer) dissolved in dry acetonitrile (30 mL) was added to the reaction mixture over a period of 3 h. Once addition was complete, the contents were allowed to warm up to ambient temperature and finally heated at 58 °C for 7 days under an ensuing blanket of argon. Reaction completion was indicated by the appearance of a sharp singlet in the ^{11}B NMR spectra of the crude reaction mixture. After 7 days, the reaction mixture was concentrated and then directly purified on a size exclusion column (SEC) over Sephadex LH-20 using acetonitrile as the eluent. After multiple attempts, the pure closomer **C2** was isolated as a brown colored very viscous oil (0.29 mg, 86%). IR (neat) $\tilde{\nu}$ 3350, 3019, 2981, 2931, 1731, 1524, 1455, 1393, 1369, 1215, 1152, 929 cm^{-1}. ^{1}H NMR (400 MHz, CD_3CN): δ 6.54 (very br s, 12H, -NH-), 3.70 (s, 48H), 3.65-3.58 (m, 24H), 3.58-3.47 (m, 48H), 3.47-3.38 (m, 24H), 3.28 (s, 48H), 3.24-3.09 (m, 24H), 3.09-2.95 (m, 24H), 2.91-2.76 (m, 24H),

2.75-2.53 (m, 48H), 2.53-2.32 (m, 12H), 1.46 (s, 216H), 1.45 (s, 216); ^{13}C NMR (100 MHz, CD_3CN): δ 173.35, 171.43, 156.85, 81.07, 80.62, 75.26, 71.02, 70.59, 70.33, 64.52, 63.11, 62.69, 59.65, 51.99, 41.88, 28.48, 28.36. ^{11}B NMR (160 MHz, CD_3CN): δ -18.526.

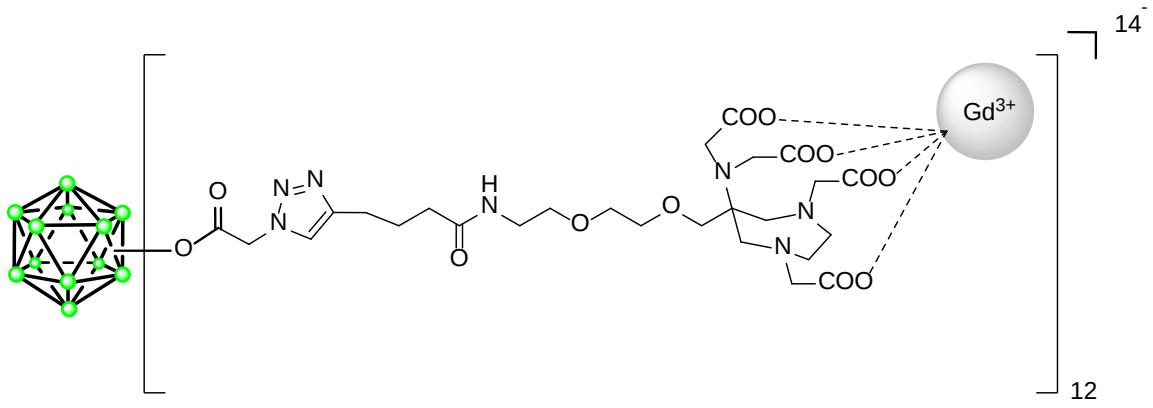
7. Synthesis of Closomer Contrast Agent, CCA-I



Closomer C4

Closomer C4: In a one neck oven dried 100 mL round bottom flask, containing a magnetic stir bar and a rubber septa, a mixture of twelve-fold azidoacetate closomer **Closomer C3** *(synthesized using a previously reported procedure)*[7] **(**85 mg, 0.047 mmol, 1.0 eqv.) and the AAZTA ligand **13** (2.20 g, 2.81 mmol, 60.0 eqv., 5 folds per boron vertex of the azidoacetate closomer) was dried thoroughly. To this mixture of reactants were added DIPEA (1.0 mL, 5.62 mmol, 120 eqv., 10 fold per boron vertex of the carbonate closomer) and copper (I) iodide (107 mg, 0.56 mmol, 12.0 eqv., 1 fold per boron vertex of the azidoacetate closomer) in rapid succession, followed by a 1:1 mixture of solvents ACN and THF (30 mL each). The contents so obtained were purged with alternate cycles of vacuum and argon and stirred for 4 days at RT under an ensuing argon atmosphere. Reaction completion was indicated by the appearance of a sharp singlet in the ^{11}B NMR spectra of the crude reaction mixture. The reaction mixture was then concentrated to dryness and the residue was redissolved in DCM and filtered. The filtrate was washed with a saturated

aqueous solution of ethylenediaminetetraacetic acid disodium salt (EDTA.2Na^{+}) solution till the green color (indicates presence of copper) persisted in the organic layer. After repeated washings, the crude product was extracted in the organic layer, dried over Na_2SO_4 and concentrated to obtain a dirty yellow colored viscous oil. The oil was purified via size-exclusion chromatography over Lipophilic Sephadex (LH-20) using ACN as eluent to isolate the product as a light yellow brown colored crystalline solid (0.46 g, 91%). IR (neat) $\tilde{\nu}$ 3306, 2977, 2930, 2863, 1735, 1658, 1548, 1457, 1392, 1368, 1255, 1233, 1151, 754 cm^{-1}. ^{1}H NMR (500 MHz, CD_3CN): δ 7.37 (s, 12H), 7.07 (br s, 12H), 4.85 (s, 24H), 3.67 (s, 48H), 3.52-3.40 (m, 96H), 3.32-3.28 (m, 24H), 3.23 (s, 48H), 2.99-2.92 (m, 24H), 2.78-2.73 (m, 24H), 2.67-2.60 (m, 48H), 2.59-2.54 (m, 24H), 2.22-2.13 (m, 48H), 1.89-1.81 (m, 24H), 1.42 (s, 216H), 1.41 (s, 216H); ^{13}C NMR (125 MHz, CD_3CN): δ 172.80, 172.63, 166.00, 147.15, 122.86, 80.33, 80.04, 74.10, 70.10, 69.55, 63.66, 62.18, 61.87, 58.88, 51.25, 38.95, 35.29, 27.55, 25.55, 24.86; ^{11}B NMR (128 MHz, CD_3CN): δ -18.141.



CCA-I

CCA-I: In a one neck oven dried 50 mL round bottom flask, containing a magnetic stir bar and a rubber septa, closomer **C4** (200 mg, 0.018 mmol) was taken and DCM (2 mL) was added to it. The reaction mixture was purged with alternate cycles of vacuum and argon and TFA (8 mL) was added to it slowly over a period of 5 minutes. The reaction mixture was stirred for 6 h under an ensuing atmosphere of argon. Reaction progress was monitored using NMR spectral analysis of the crude reaction mixture and the removal of all

tert-butyl ester groups was confirmed by the absence of a sharp singlet at ~ 1.4 ppm in the ^{1}H NMR spectrum. On reaction completion, the mixture was concentrated under reduced pressure and dried thoroughly under high vacuum. The residue so obtained was dissolved in a minimal amount of MeOH, and the crude product was precipitated by adding excess diethylether. The product so obtained was filtered and washed thoroughly with copious amounts of diethyl ether. The light grey solid so obtained was filtered, washed thoroughly using copious amounts of diethyl ether and dried thoroughly to obtain the product B_{12}-AAZTA-Closomer acid as a grey white solid (145 mg, 97%). The B_{12}-AAZTA Closomer acid so obtained was next dissolved in 1M citrate buffer (15 mL, pH 7) and added to a solution of **$GdCl_3.6H_2O$** (0.8 g, 2.15 mmol, 120 eqv.) in 15 mL of 1M citrate buffer over 5 h at RT with vigorous stirring. The pH of the reaction mixture was maintained at approximately pH 7 using 0.3 N NaOH. The reaction mixture was stirred for an additional 12 h at RT and was sonicated a few times during the course of the reaction. The reaction mixture was then dialyzed in deionized water for 2 days using 1,000 MWCO membrane tubes (Spectra/Por). The product **CCA-I** was obtained as a grey white solid after lyophilization (0.14 g, 79%). IR (KBr) $\tilde{\nu}$ 3391, 2929, 2869, 1740, 1607, 1408, 1256, 1131, 1095, 1055, 915, 843, 812, 715, 673, 623 cm^{-1}. ICP-OES for Gd calcd 12, found 10.8 ~ 11.

NMR and Mass spectroscopy data of all newly synthesized compounds are appended in the Spectra section.

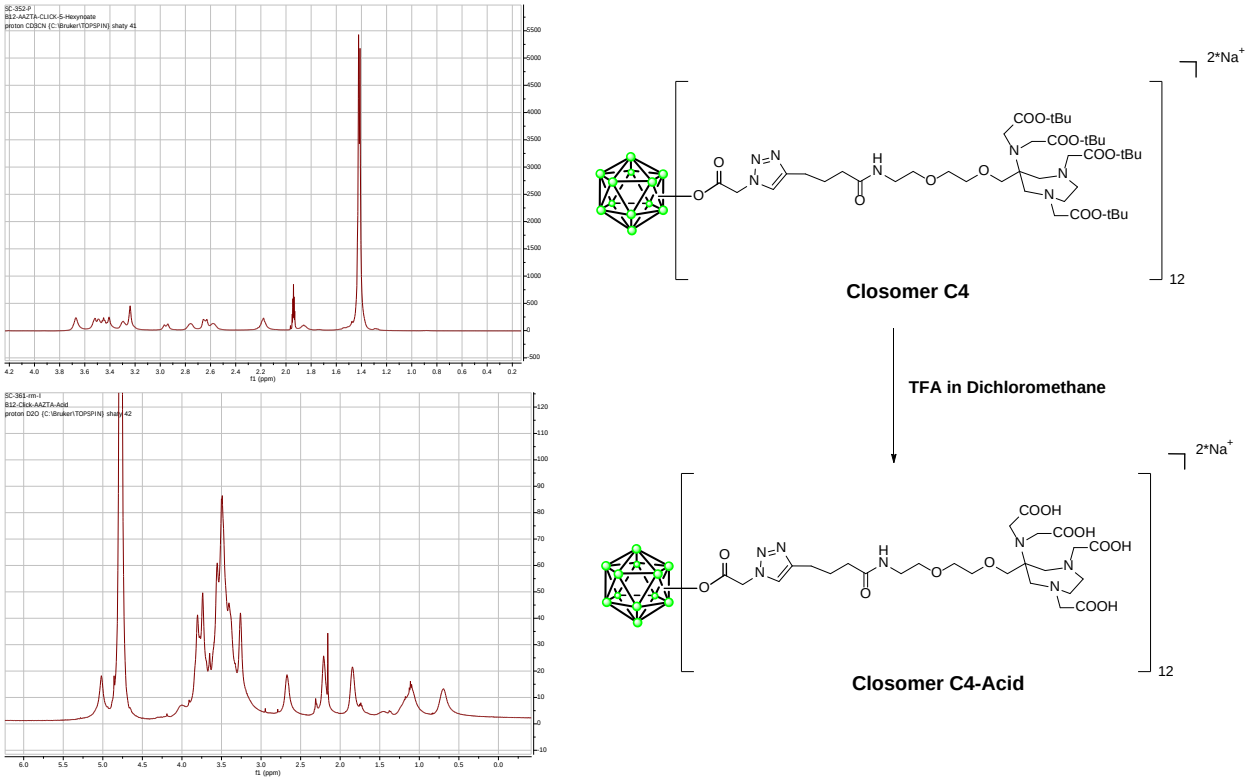


Fig. S2. ^{1}H NMR showing the complete removal of *tert*-butyl ester groups in Closomer 4 using 80% Trifluoroacetic acid in Dichloromethane yield the corresponding Closomer C4-Acid.

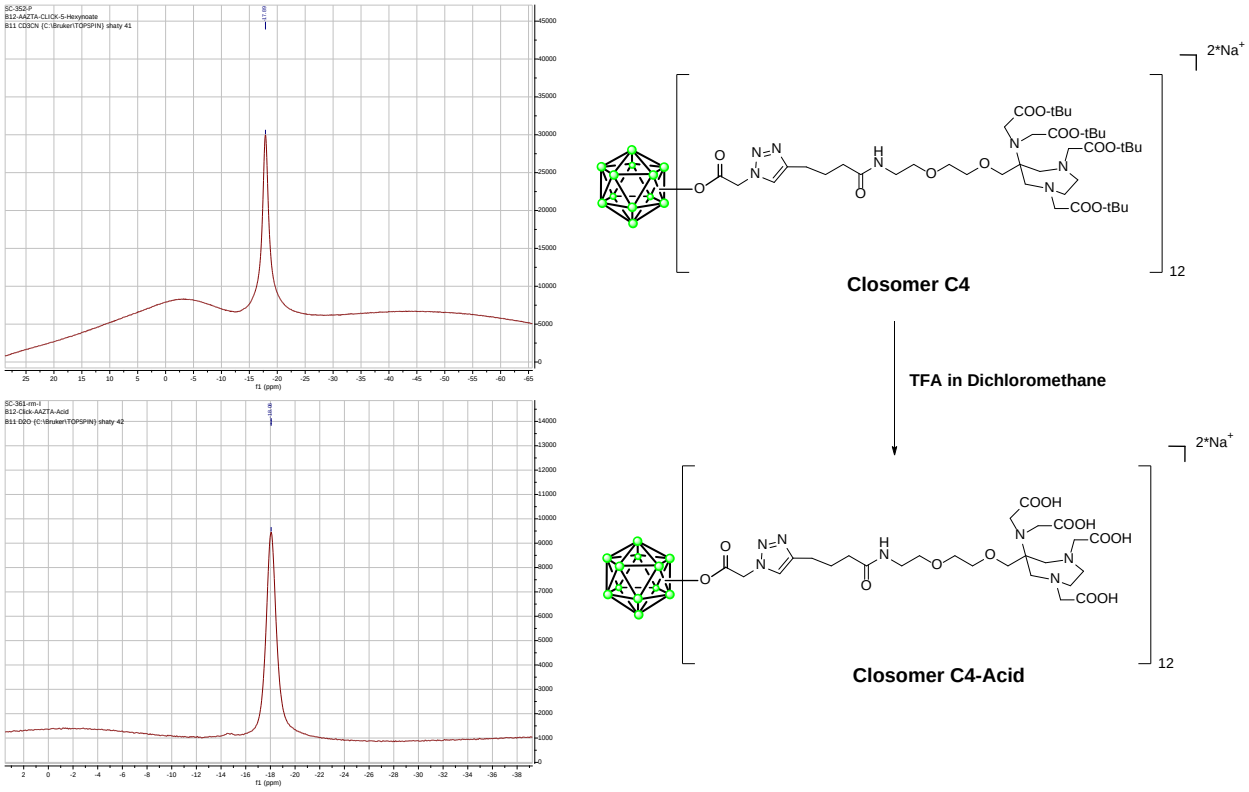


Fig. S3. Retention of a singlet peak in the ^{11}B NMR confirms the integrity of the 12-fold Closomer 4-Acid when subjected to treatment with 80% Trifluoroacetic acid in Dichloromethane for the complete removal of *tert*-butyl ester groups, thus facilitating the Gd-complexation carried out in the next step.

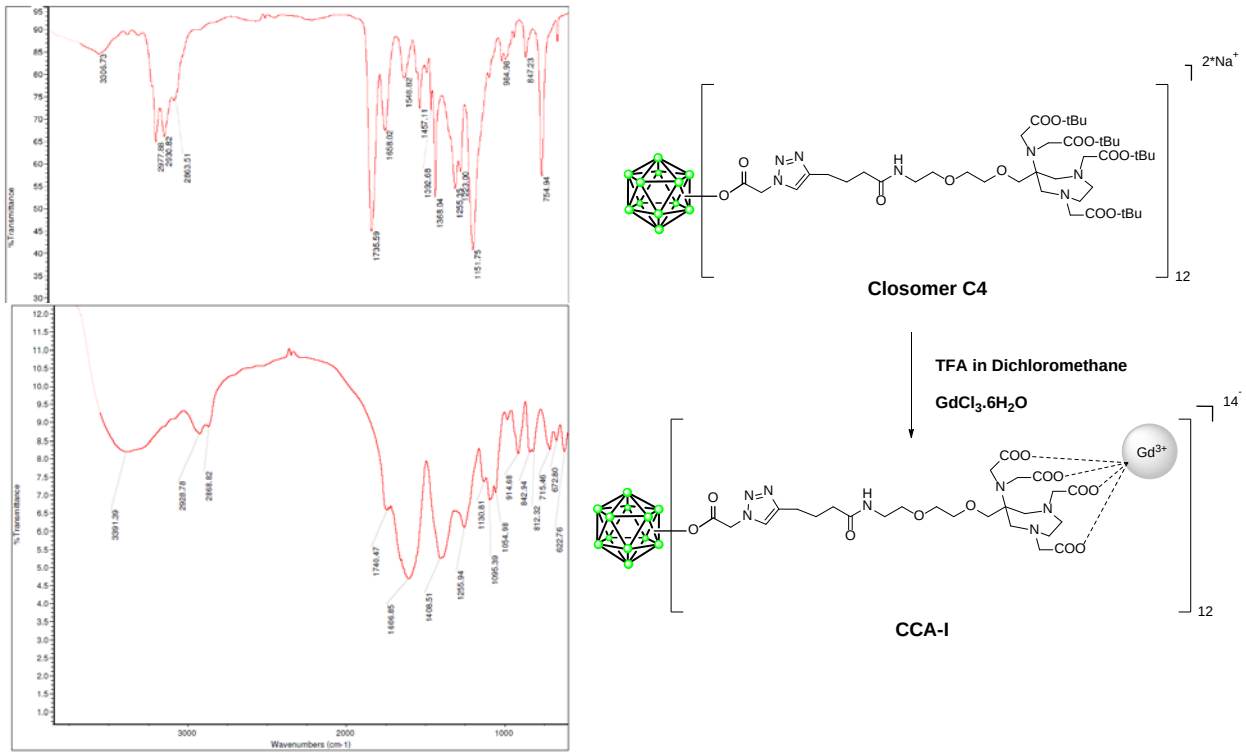


Fig. S4. The shift in the IR spectrum (1736 cm^{-1} to 1607 cm^{-1})observed due to Gd-complexation of the Closomer C4-Acid to form CCA-I.

8. Characterization of CCA-I

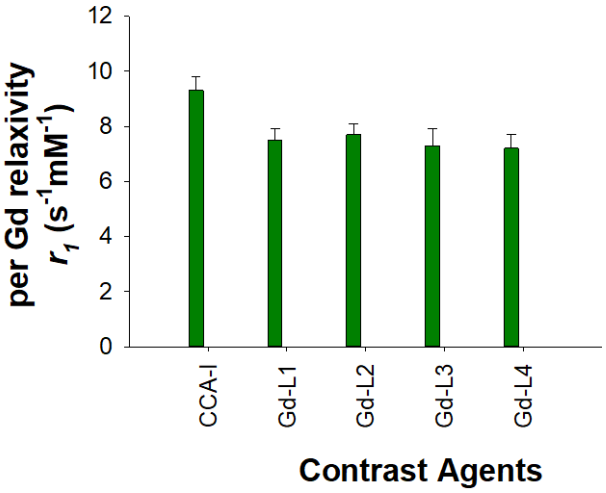


Fig. S5. Per Gd relaxivity comparison of **CCA-I** with the modified AAZTA chelates, Gd-**L1**, Gd-**L2**, Gd-**L3** and Gd-**L4**. Clearly, the close packing of individual chelates in CCA-I further restricts their internal rotation and consequently there is an resultant increase of two units in the per-Gd relaxivity of CCA-I as compared to the individual chelates. r_1 values are measured at 7 T and 25°C.

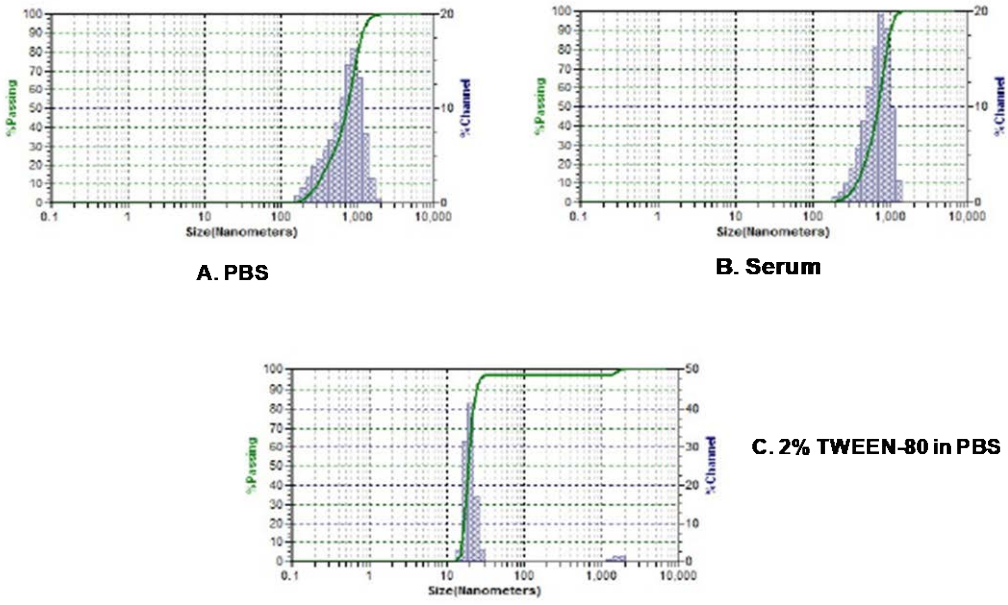


Fig. S6. Particle-size distribution data for 1 mM solution of the contrast agent CCA-I in A.) PBS; B.) Serum and C.) 2% TWEEN-80 in PBS.

Table S3. Comparison of the r_1 of CCA-I and various poly- and mono-functional MRI CAs reported in the literature.

Contrast Agents	**Magnetic Field Strength** (*Tesla, T*)	**Relaxivity per Gd**, $\mathbf{r}_1$/Gd ($s^{-1}mM^{-1}$)	**No. of Gd^{3+} ions per molecule** (*n*)	**Molar relaxivity** [$\mathbf{r}_1$/Gd] × *n*
CCA-I;[a]	7	9.3 (±0.18)	11	100.4
B_{12}-$(DTTA)_{12}$;[8]	7	13.8 (±0.49)	11	155.9
Cyclodextrin-$(DTTA)_7$;[9]	9.4	6.2	7	43.4
Cyclodextrin-$(DOTA)_7$;[10]	1.4	12.2 (±0.54)	7	85.4
$[Fe[Gd_2$-*bpy*$(DTTA)_2(H_2O)_4]_3]^{4-}$;[11]	9.4	9.32	6	55.9
$[Gd_3$-*Bn*$DTTA(H_2O)_6]^{3-}$;[12]	9.4	10.7	3	32.1
$[Gd_2$-(*p*$X(DTTA)_2)(H_2O)_4]^{2-}$;[13]	9.4	10.7	2	21.4
$[Gd_2$-(*m*$X(DTTA)_2)(H_2O)_4]^{2-}$;[13]	9.4	9.18	2	18.4
$[Gd(DTPA)(H_2O)]^{2-}$;[14]	9.4	4.06	1	4.06
[Gd(DTPA)(BMA)(H_2O)];[a]	7	4.05	1	4.28
$[Gd(DOTA)(H_2O)]^{-}$;[14]	9.4	3.86	1	3.86

[a] current work

9. *In vivo* MRI for CCA-I

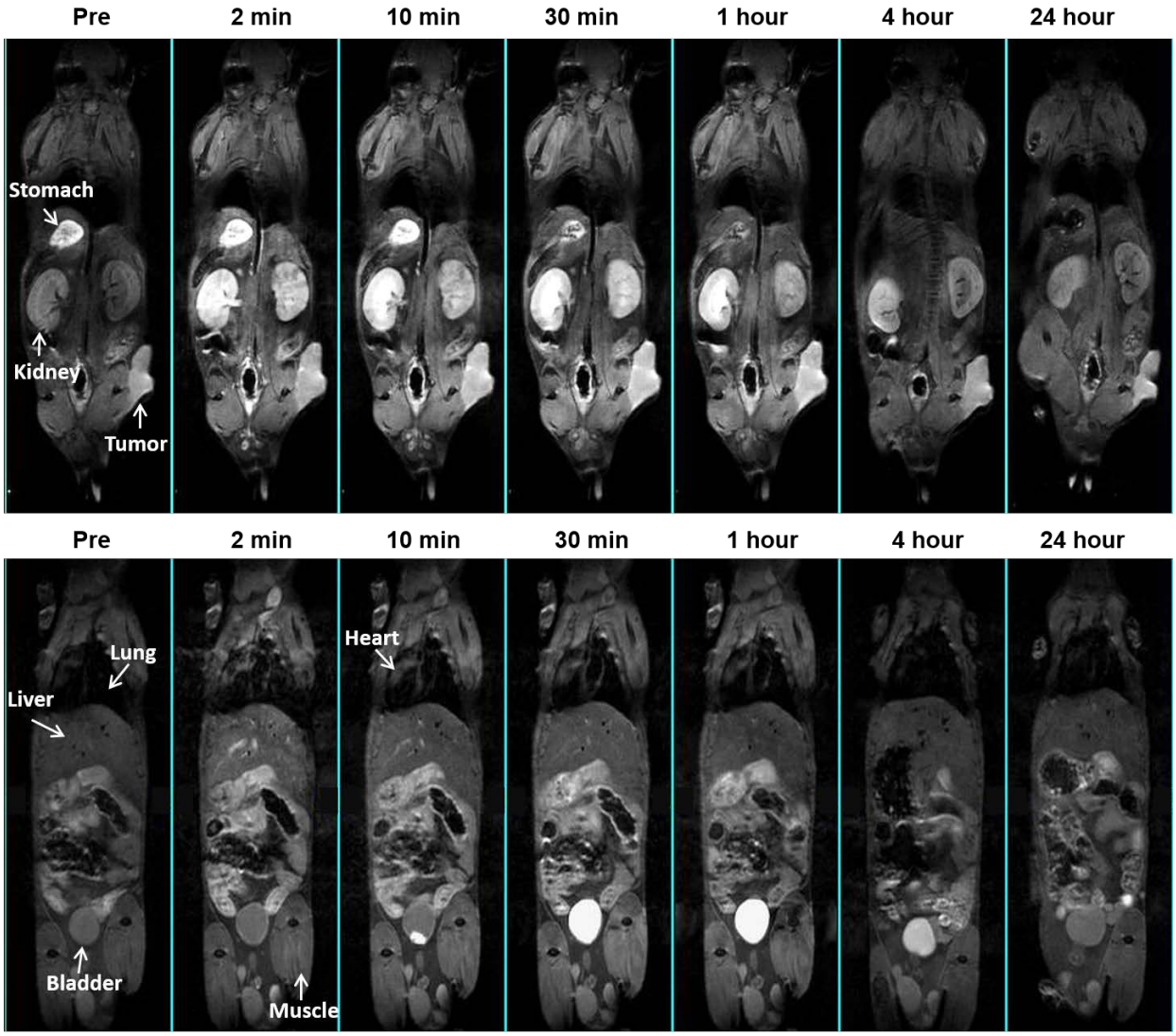


Fig. S7. *In vivo* T_1-weighted MRI scans (coronal views) of mice over a period of 24 h injected with 10 mM Gd, 120 μL of CCA-I, or with a net gadolinium dose of 0.04 mmol/kg.

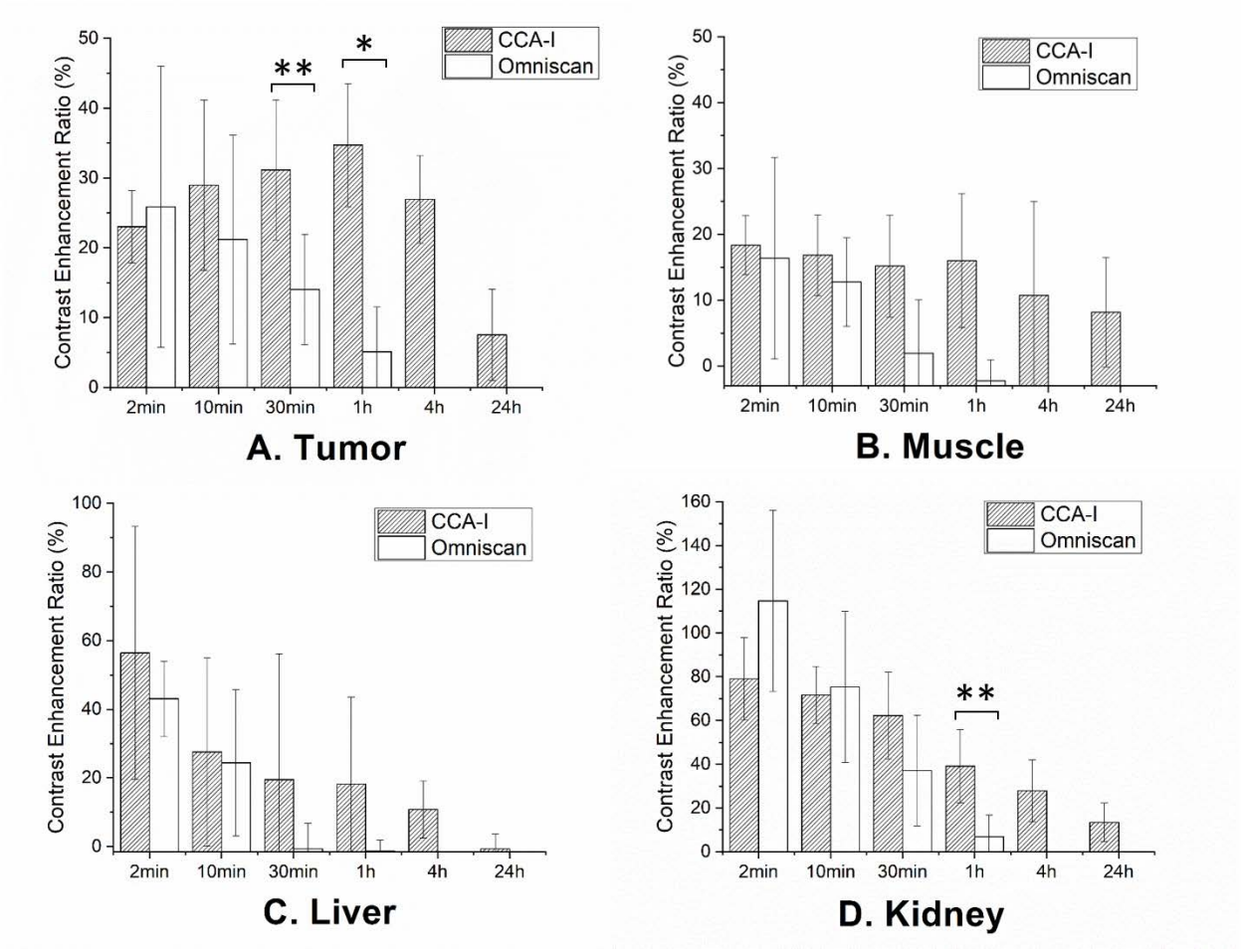
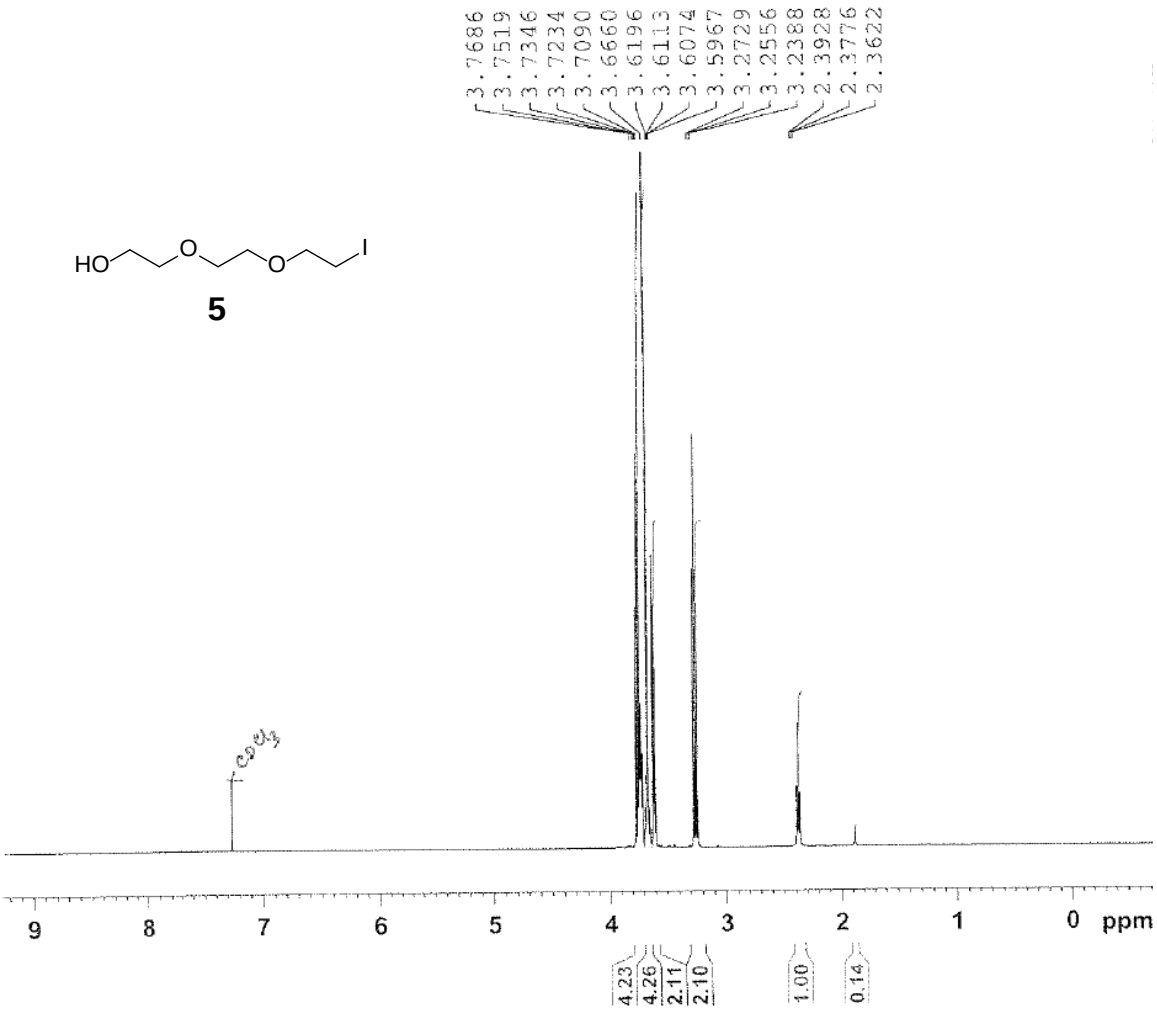


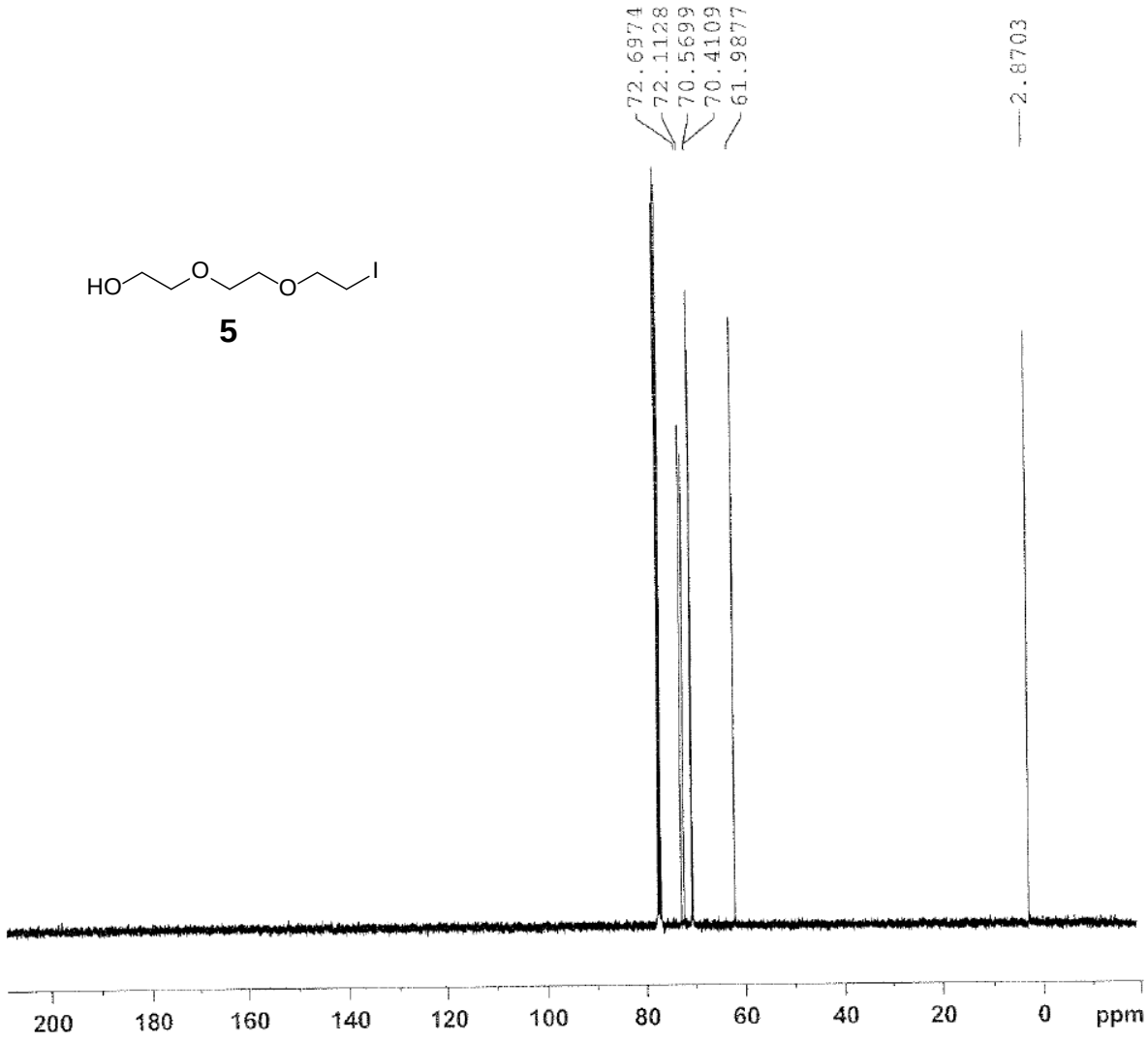
Fig. S8. Comparison of the relative increase in contrast measured by the contrast enhancement ratio (CER) for various organs A.) Tumor; B.) Muscle; C.) Liver and D.) Kidney of mice at different points of time post injection of **CCA-I** and Omniscan with a gadolinium dose of 0.04 mmol/kg. **P* < 0.0002, ***P* < 0.02, n = 6 per group.

10. Spectra

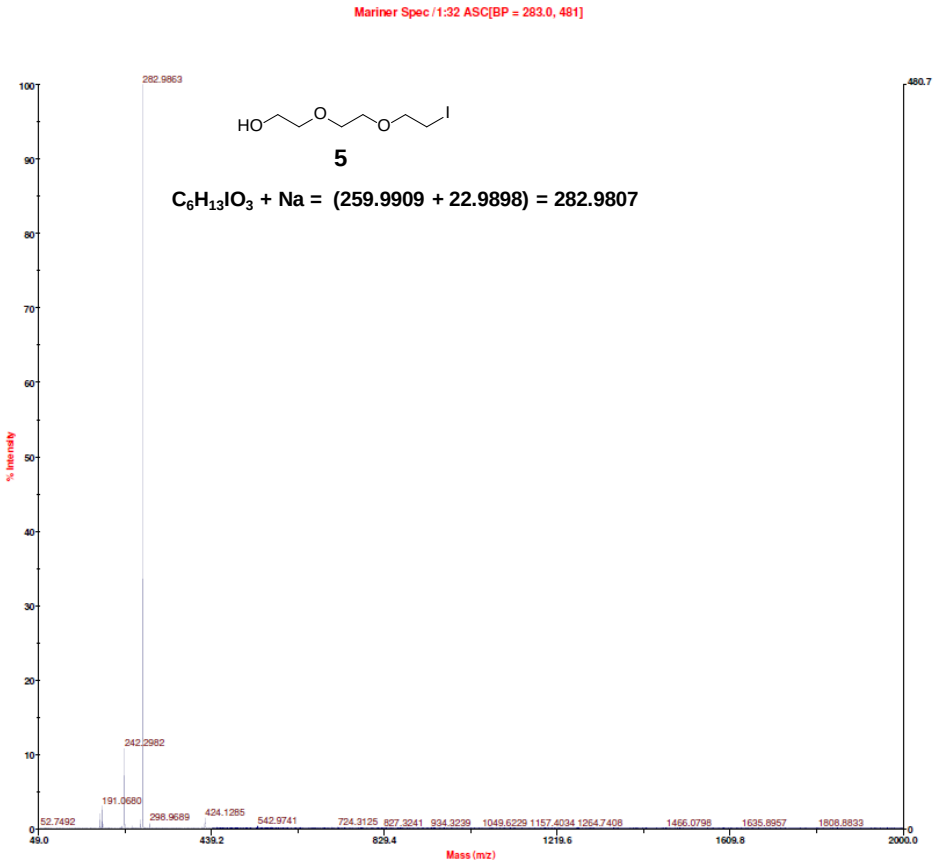
PEG-3-I-OH
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 2



PEG-3-I-OH
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 2



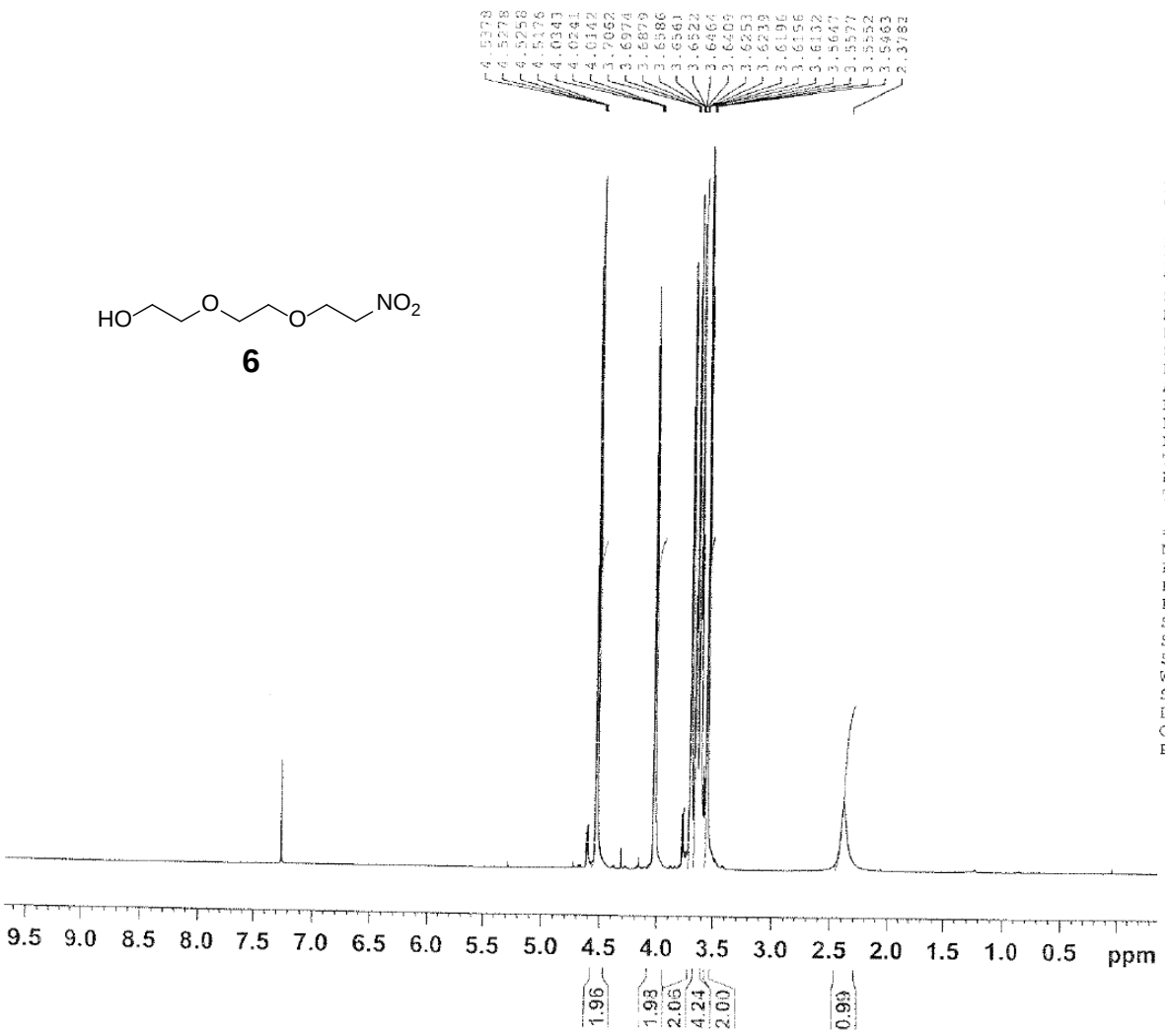
Applied Biosystems Mariner System 5268



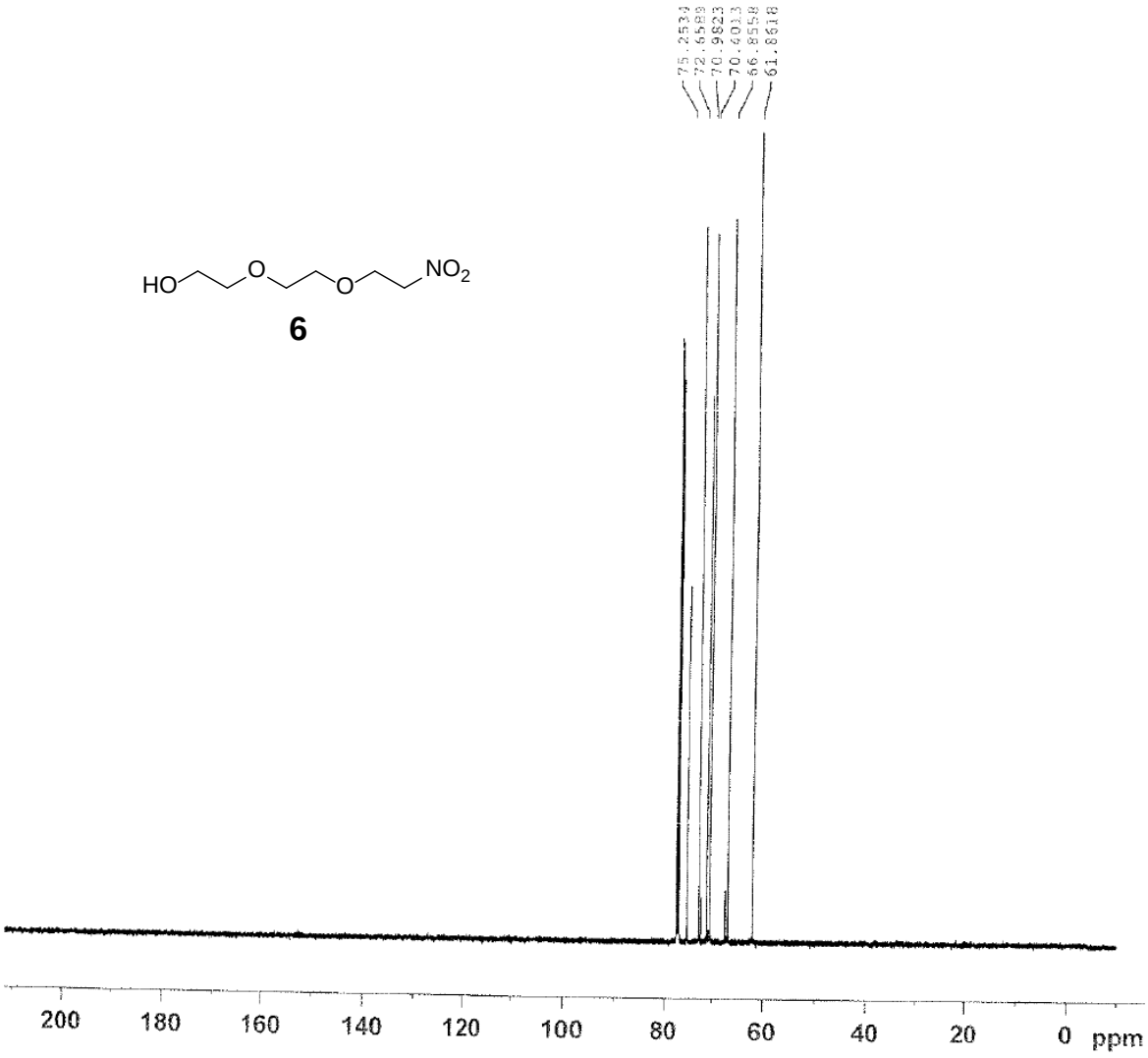
5

$C_6H_{13}IO_3$ + Na = (259.9909 + 22.9898) = 282.9807

--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0142059E-007
Calibration Constant B	75.342573
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	149.90
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.89
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

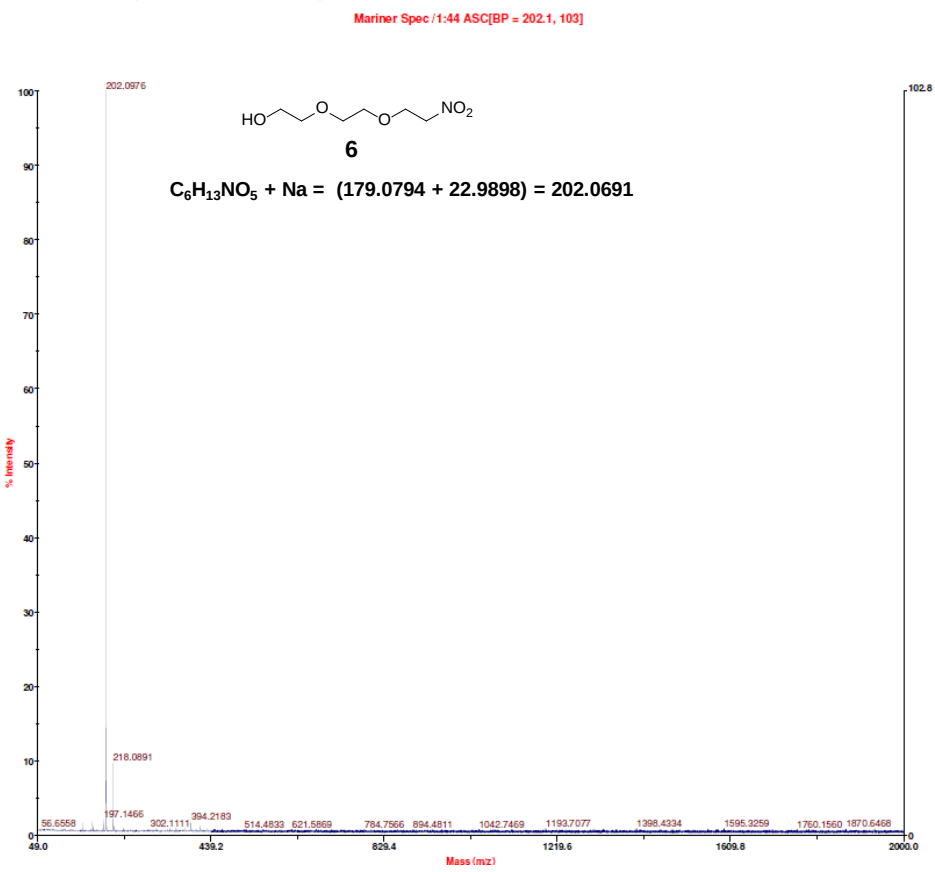

DEG-3-NO2-OH
proton CDCl3 (C:\Bruker\TOPSPIN) shaty 41
4.5378
4.5278
4.5258
4.5176
4.0343
4.0241
4.0142
3.7052
3.6974
3.6879
3.6686
3.6561
3.6522
3.6466
3.6409
3.6253
3.6239
3.6196
3.6156
3.6132
3.5647
3.5577
3.5552
3.5463
2.3782
HO
O
O
NO2
6
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.96
1.93
2.06
4.24
2.00
0.99

PEG-3-NO2-OH
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 41



6

Applied Biosystems Mariner System 5268

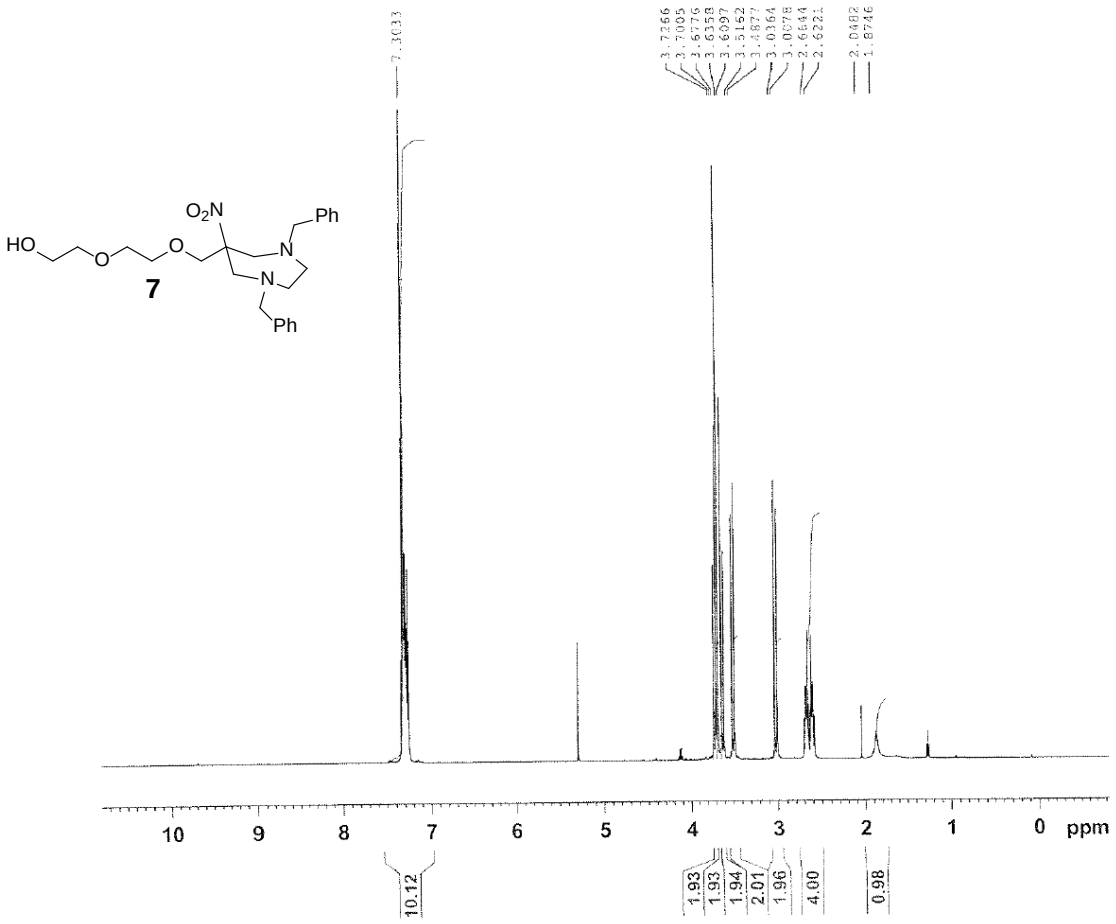


6

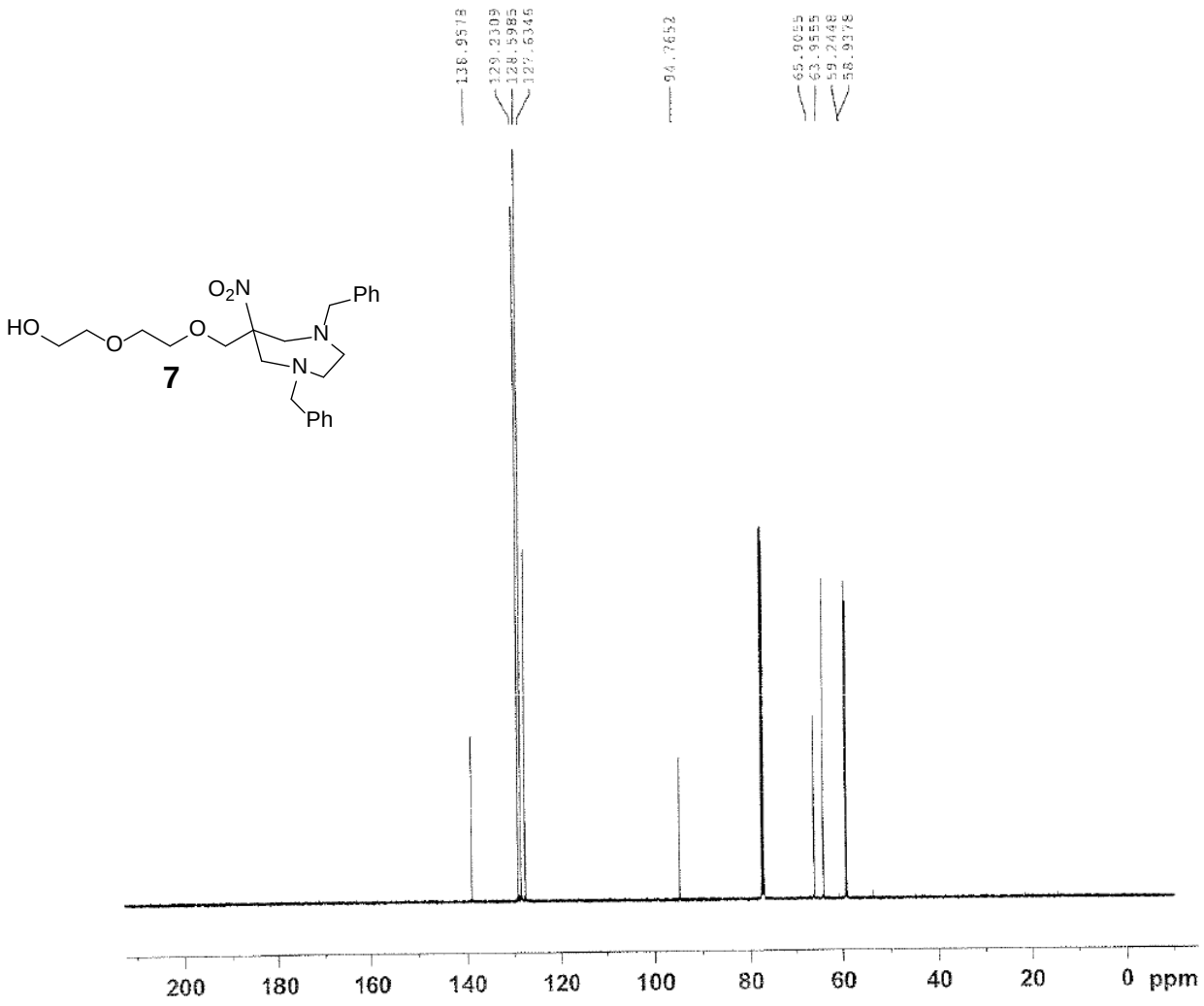
$C_6H_{13}NO_5$ + Na = (179.0794 + 22.9898) = 202.0691

--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0153553E-007
Calibration Constant B	76.658842
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

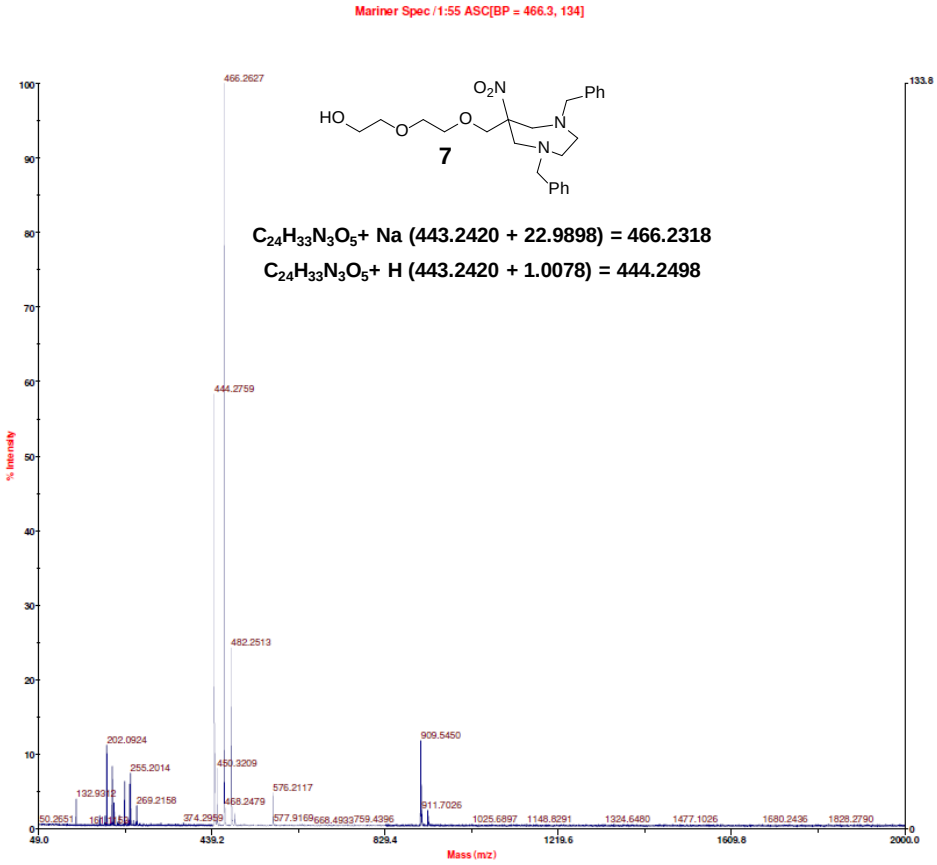
Diazepine-NO2-OH
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 42



Diazepine-NO2-OH
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 42



Applied Biosystems Mariner System 5268

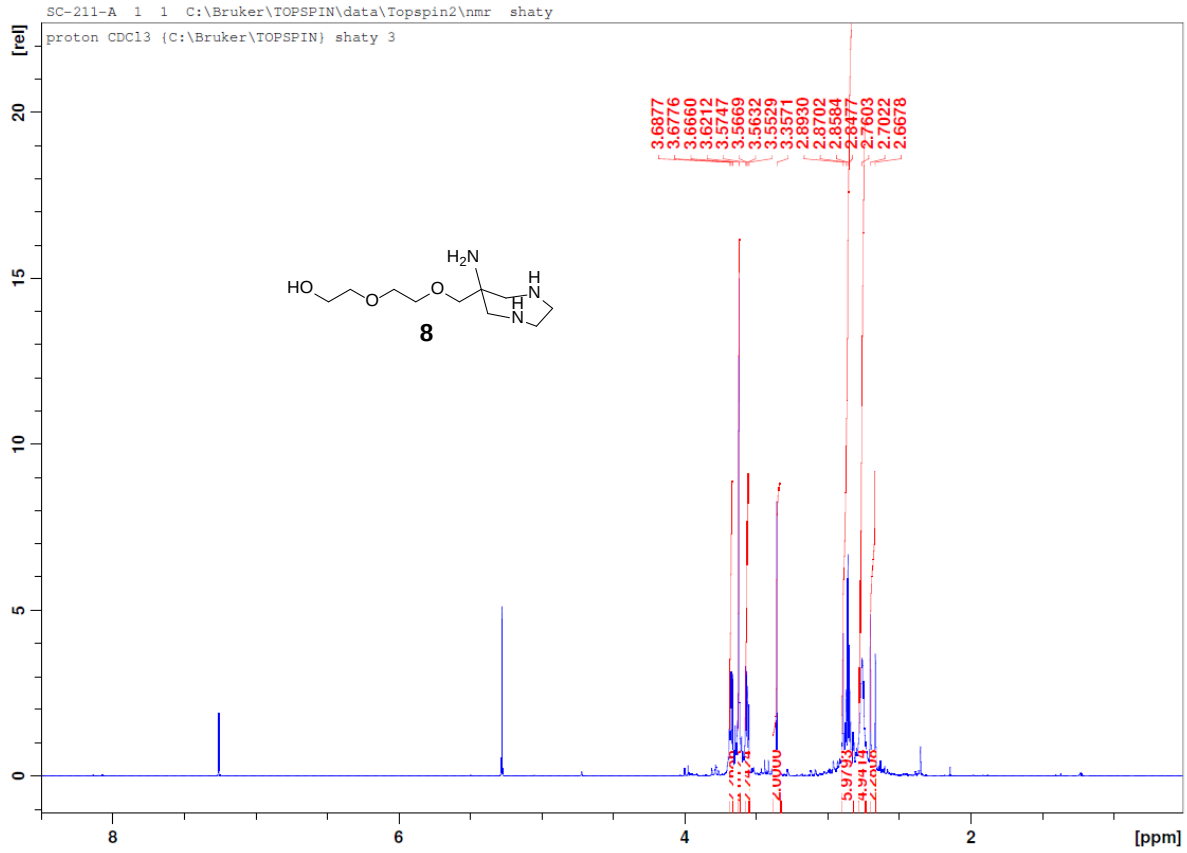


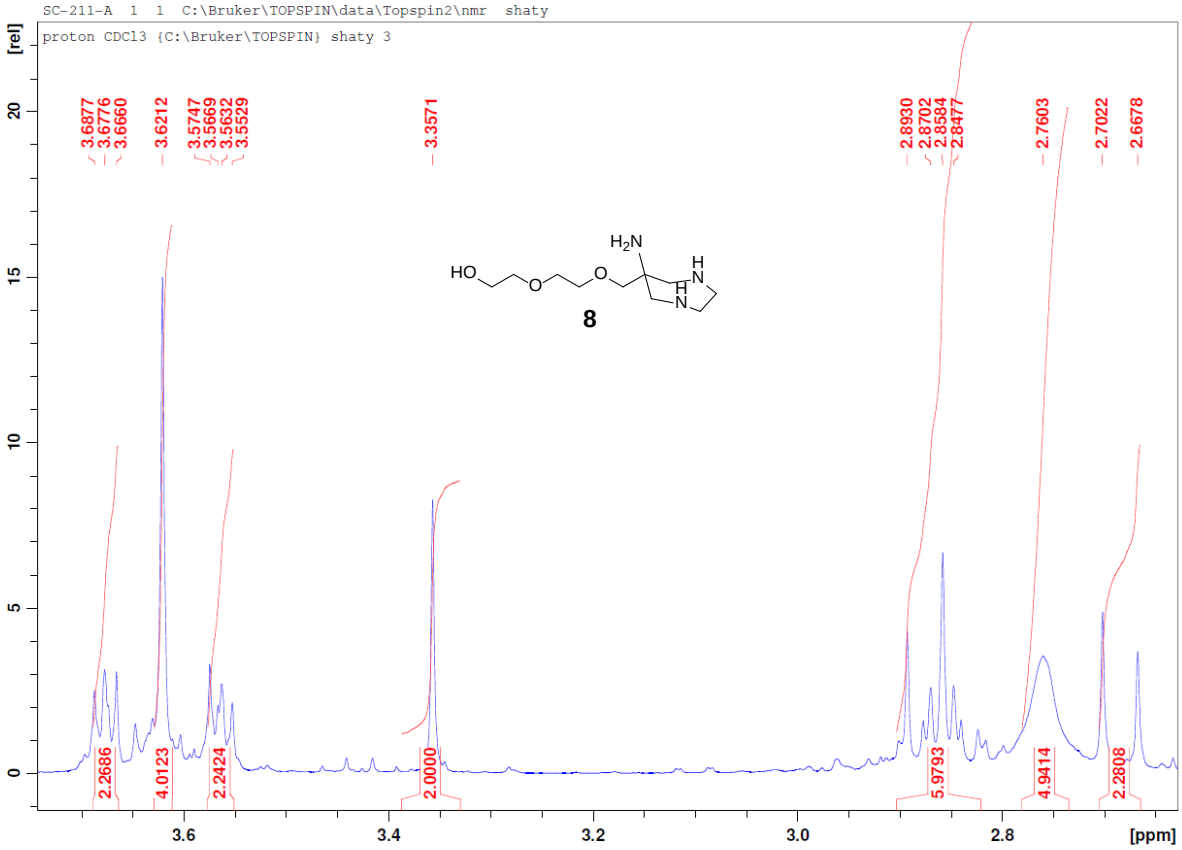
7

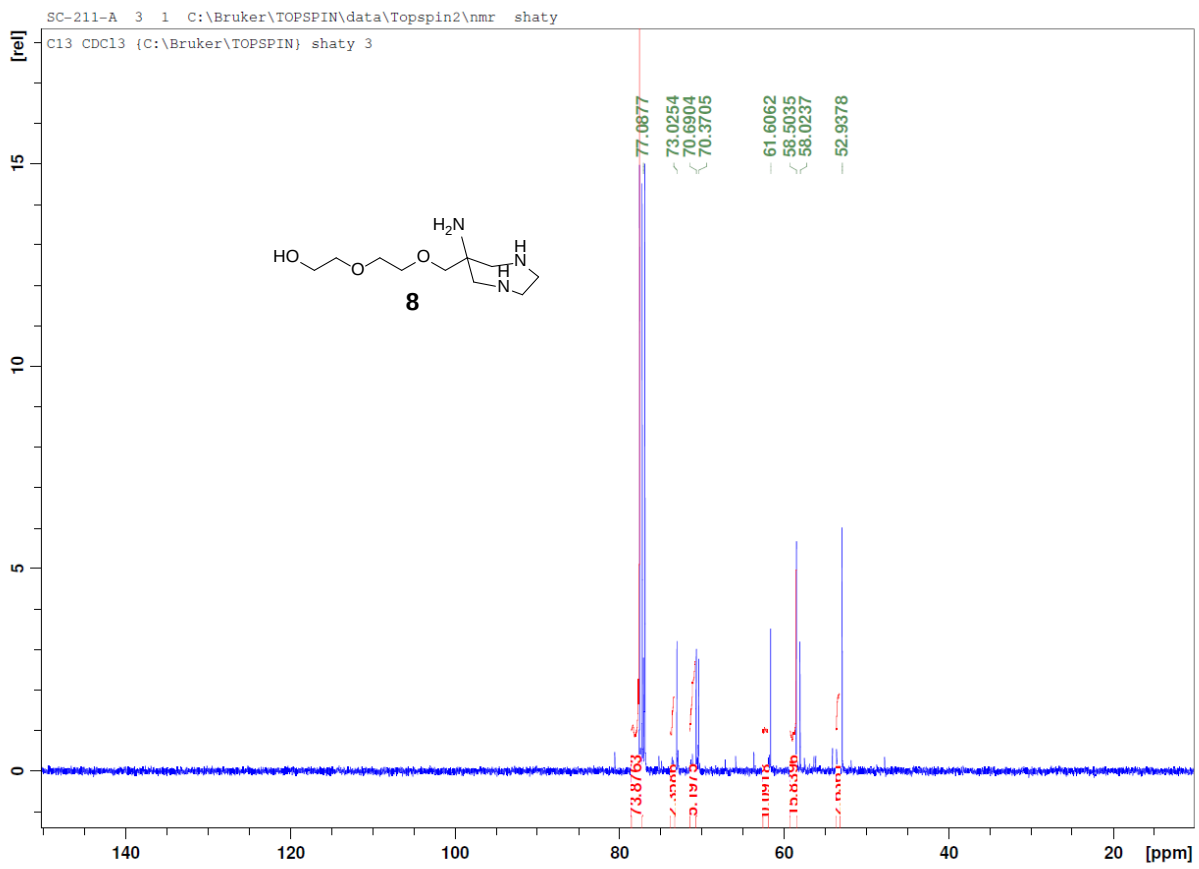
$C_{24}H_{33}N_3O_5$+ Na (443.2420 + 22.9898) = 466.2318

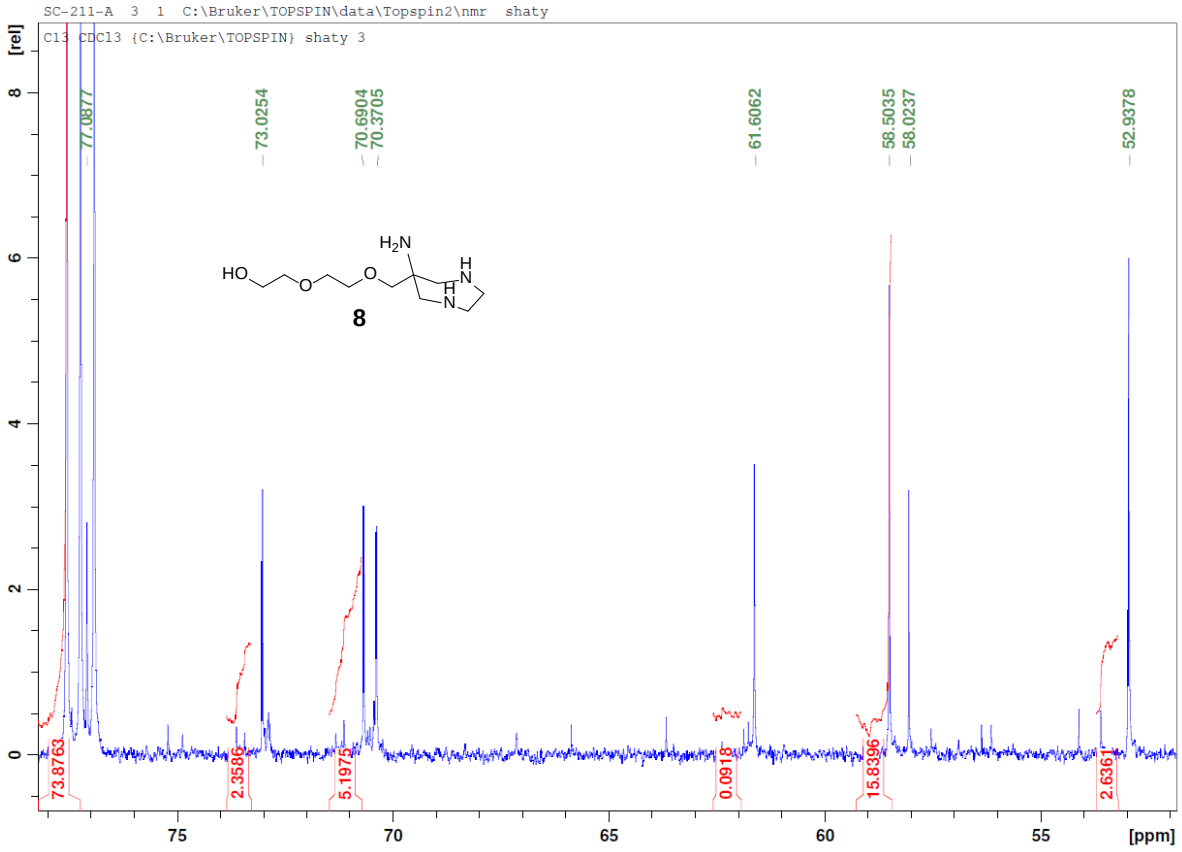
$C_{24}H_{33}N_3O_5$+ H (443.2420 + 1.0078) = 444.2498

--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0147896E-007
Calibration Constant B	77.719613
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

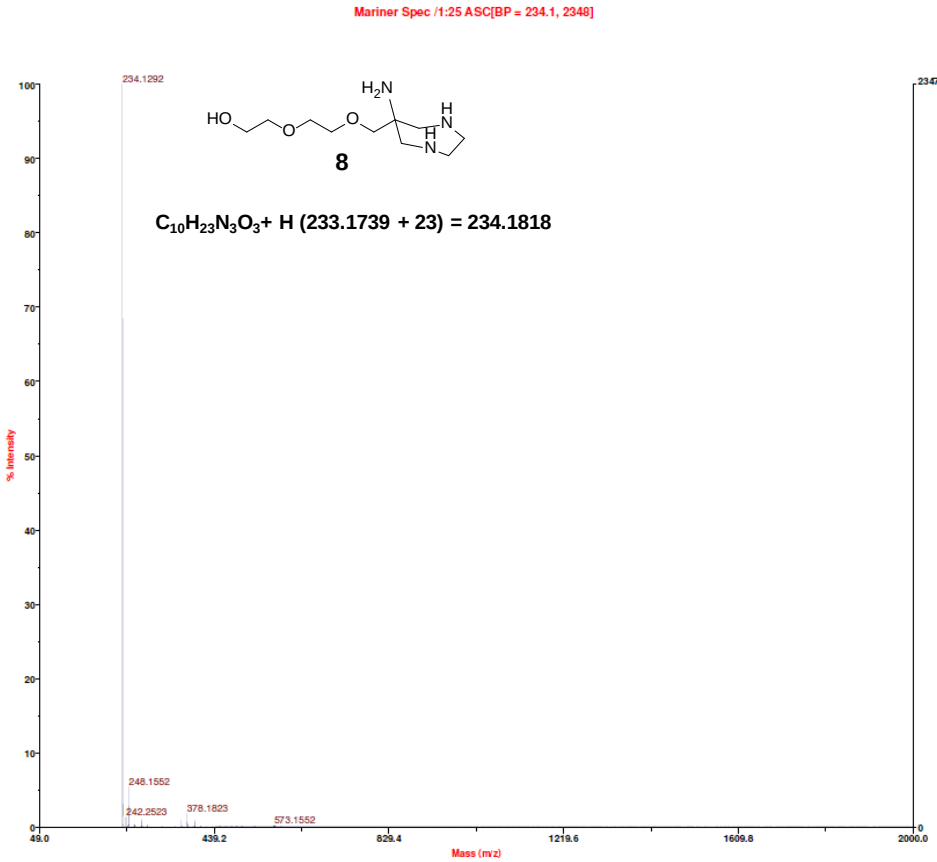

SC-211-A 1 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr shaty
proton CDCl3 (C:\Bruker\TOPSPIN) shaty 3
[rel]
20
15
10
5
0
8
6
4
2
[ppm]
3.6877
3.6776
3.6660
3.6212
3.5747
3.5669
3.5632
3.5529
3.3571
2.8930
2.8702
2.8584
2.8477
2.7603
2.7022
2.6678
HO
O
O
H2N
H
N
H
N
8


SC-211-A 1 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr shaty
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 3
[rel]
20
15
10
5
0
3.6877
3.6776
3.6660
3.6212
3.5747
3.5669
3.5632
3.5529
3.3571
2.8930
2.8702
2.8584
2.8477
2.7603
2.7022
2.6678
2.2686
4.0123
2.2424
2.0000
5.9793
4.9414
2.2808
3.6
3.4
3.2
3.0
2.8
[ppm]
HO
O
O
H2N
H
N
H
N
8


SC-211-A 3 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr shaty
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 3
[rel]
77.0877
73.0254
70.6904
70.3705
61.6062
58.5035
58.0237
52.9378
HO
O
O
H2N
H
N
H
N
8
[ppm]


SC-211-A 3 1 C:\Bruker\TOPSPIN\data\Topspin2\nmr shaty
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 3
[rel]
77.0877
73.0254
70.6904
70.3705
61.6062
58.5035
58.0237
52.9378
73.8763
2.3586
5.1975
0.0918
15.8396
2.6361
[ppm]
8

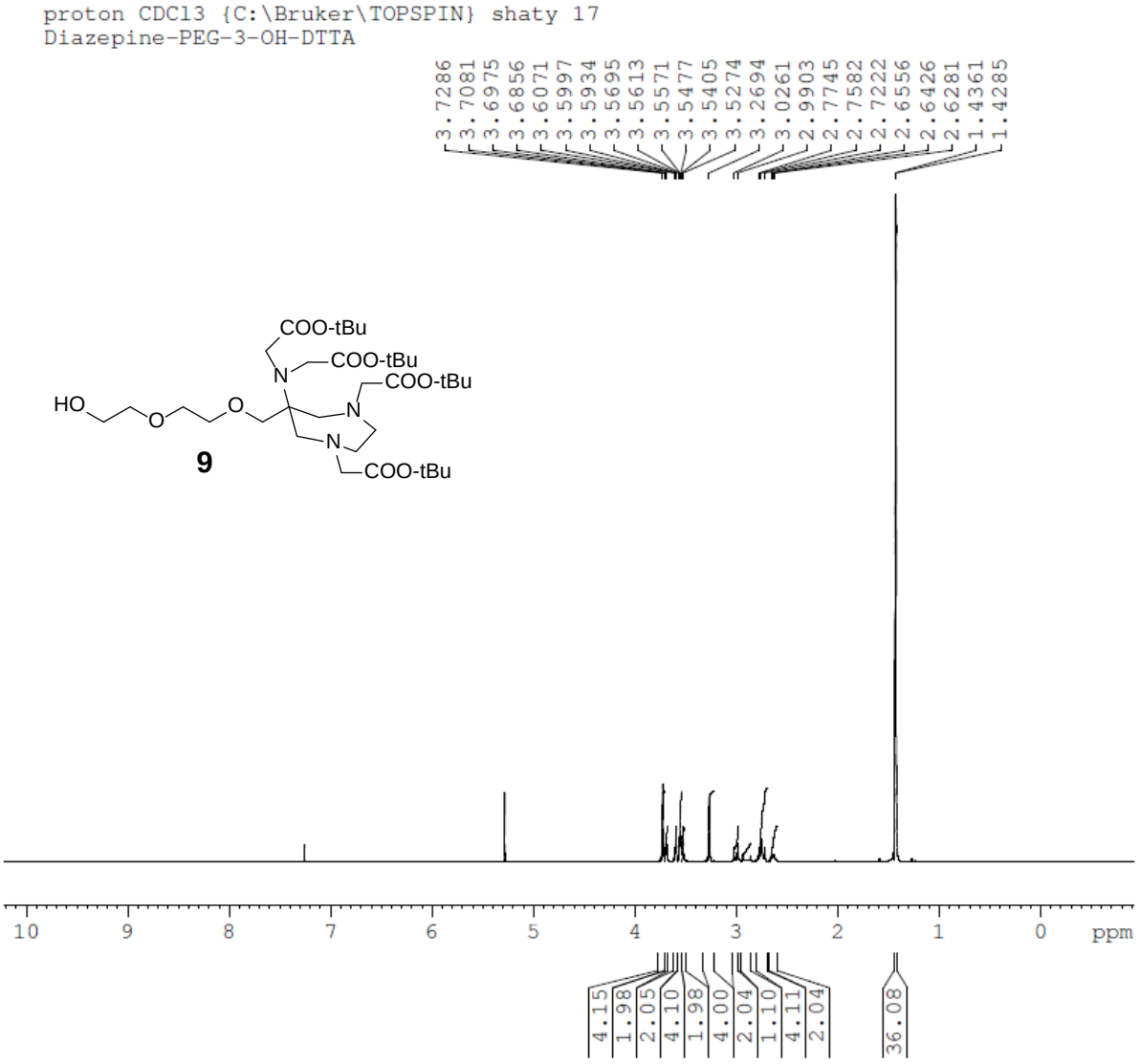
Applied Biosystems Mariner System 5268

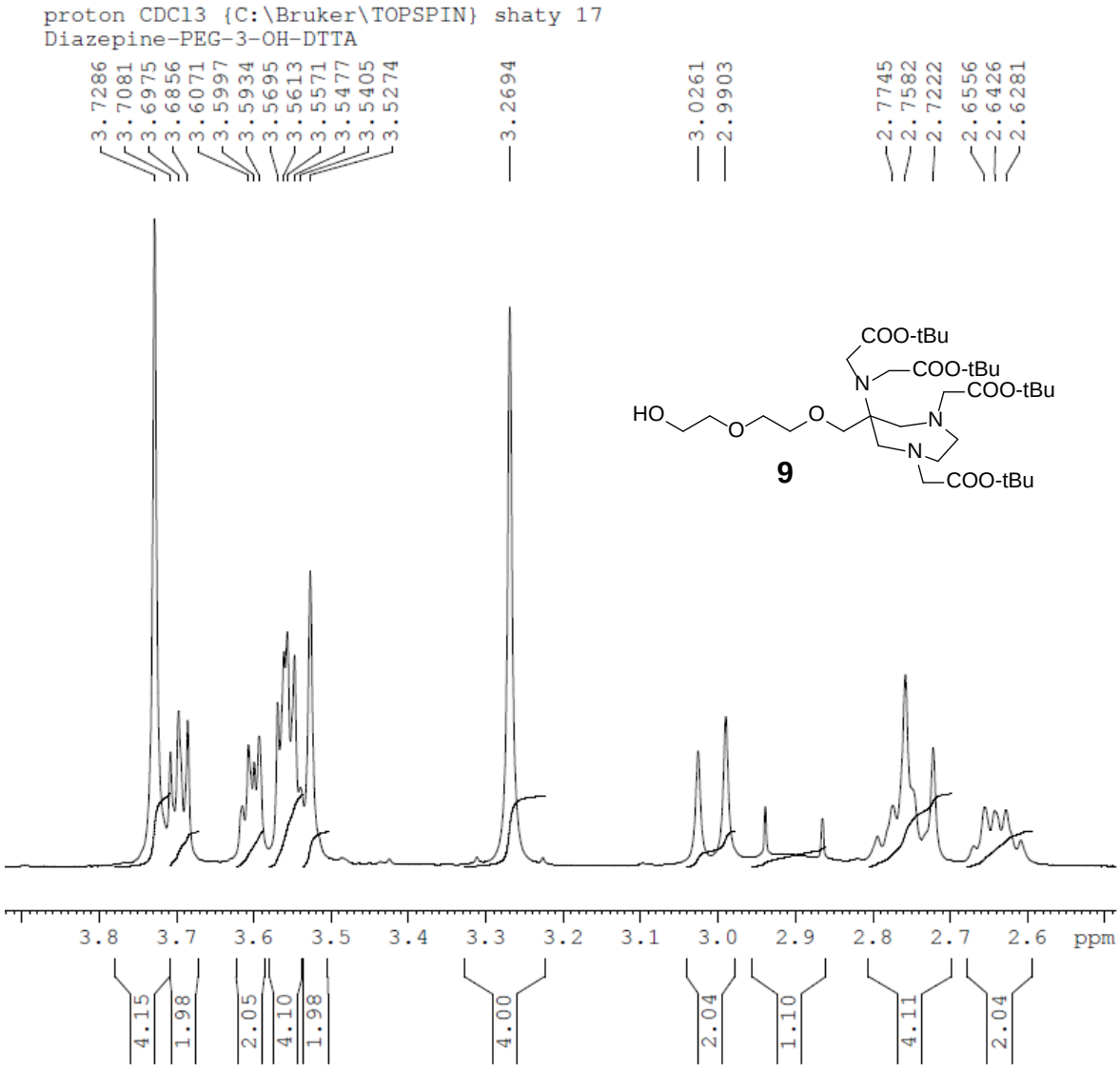


8

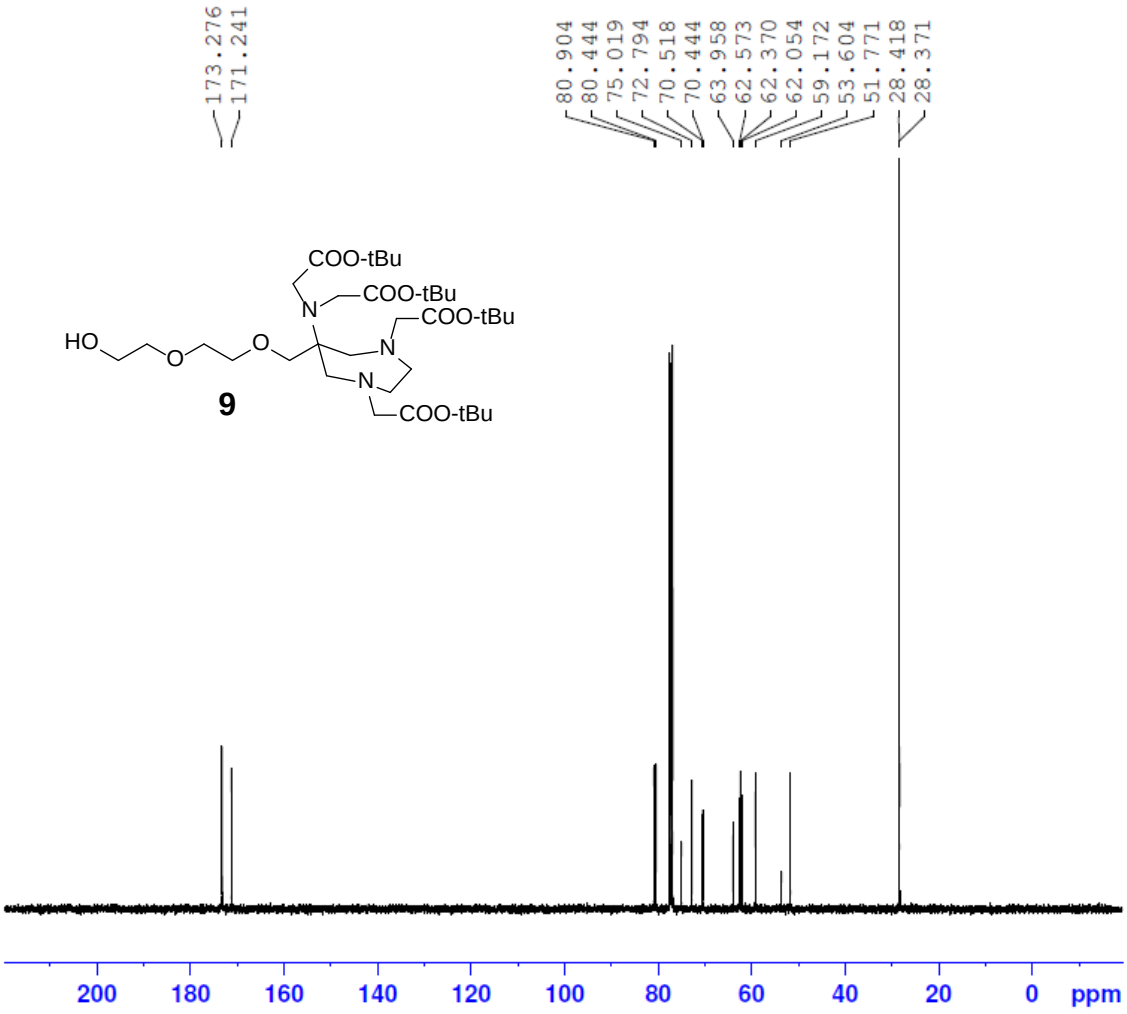
$C_{10}H_{23}N_3O_3$+ H (233.1739 + 23) = 234.1818

--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.01472E-007
Calibration Constant B	78.097724
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

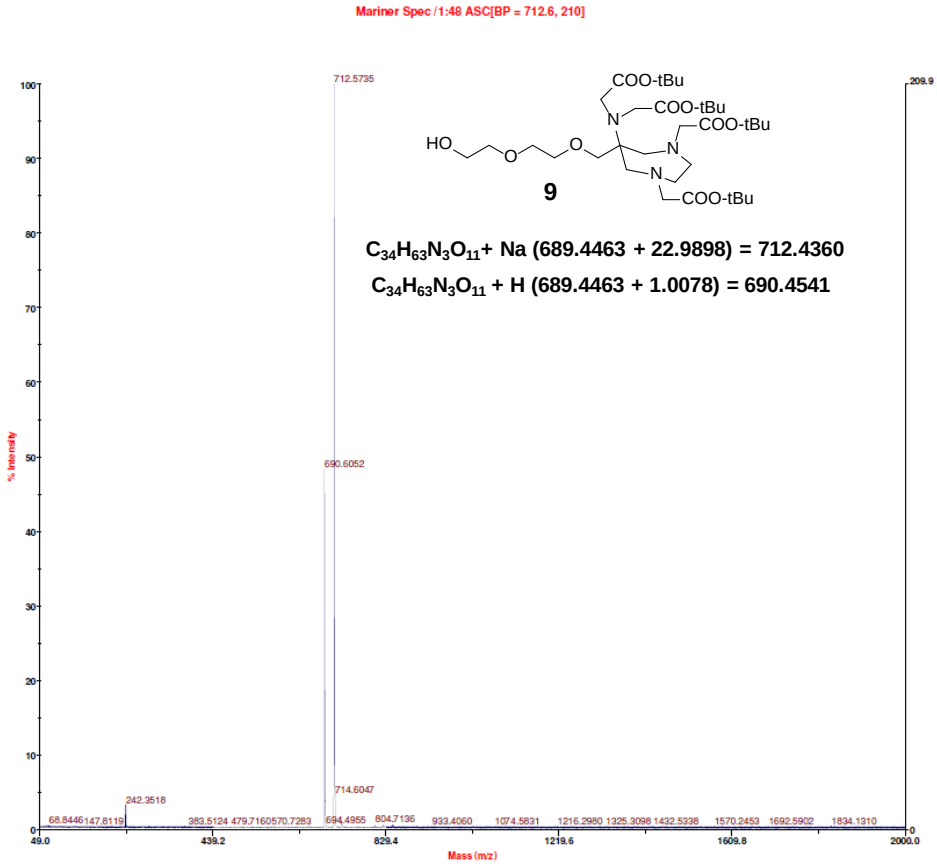

proton CDCl3 {C:\Bruker\TOPSPIN} shaty 17
Diazepine-PEG-3-OH-DTTA
3.7286
3.7081
3.6975
3.6856
3.6071
3.5997
3.5934
3.5695
3.5613
3.5571
3.5477
3.5405
3.5274
3.2694
3.0261
2.9903
2.7745
2.7582
2.7222
2.6556
2.6426
2.6281
1.4361
1.4285
COO-tBu
COO-tBu
COO-tBu
COO-tBu
HO
O
O
N
N
N
9
10
9
8
7
6
5
4
3
2
1
0
ppm
4.15
1.98
2.05
4.10
1.98
4.00
2.04
1.10
4.11
2.04
36.08


proton CDCl3 {C:\Bruker\TOPSPIN} shaty 17
Diazepine-PEG-3-OH-DTTA
3.7286
3.7081
3.6975
3.6856
3.6071
3.5997
3.5934
3.5695
3.5613
3.5571
3.5477
3.5405
3.5274
3.2694
3.0261
2.9903
2.7745
2.7582
2.7222
2.6556
2.6426
2.6281
HO
O
O
N
N
N
COO-tBu
COO-tBu
COO-tBu
COO-tBu
9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
ppm
4.15
1.98
2.05
4.10
1.98
4.00
2.04
1.10
4.11
2.04

C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 17
Diazepine-PEG-3-OH-DTTA



Applied Biosystems Mariner System 5268

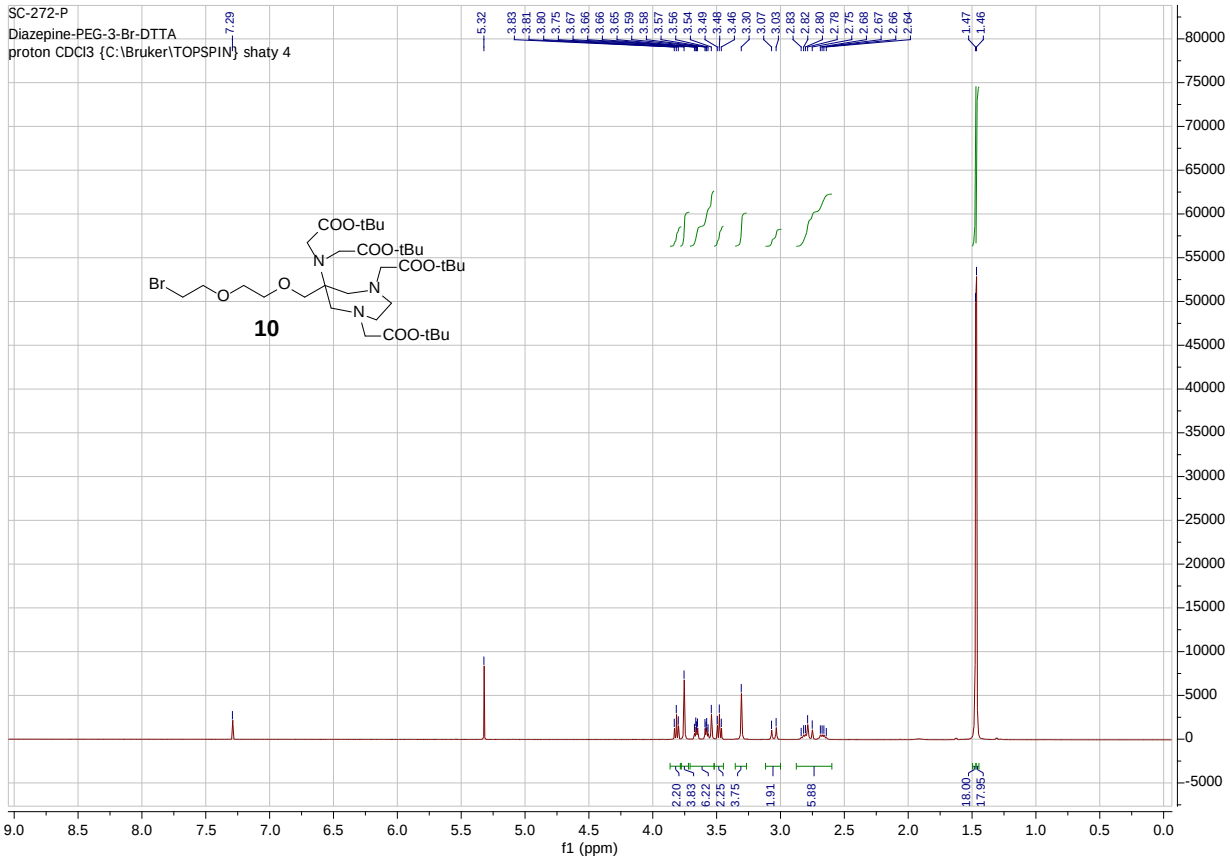


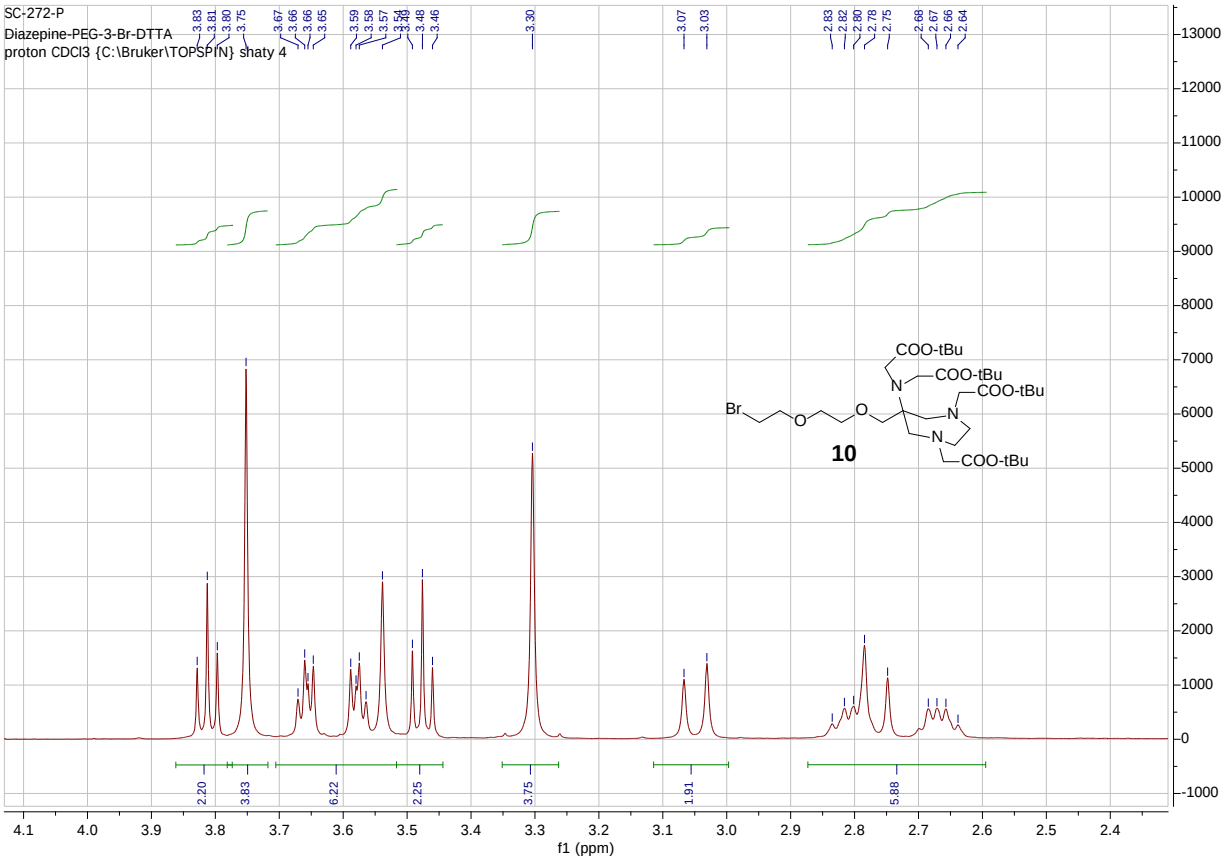
9

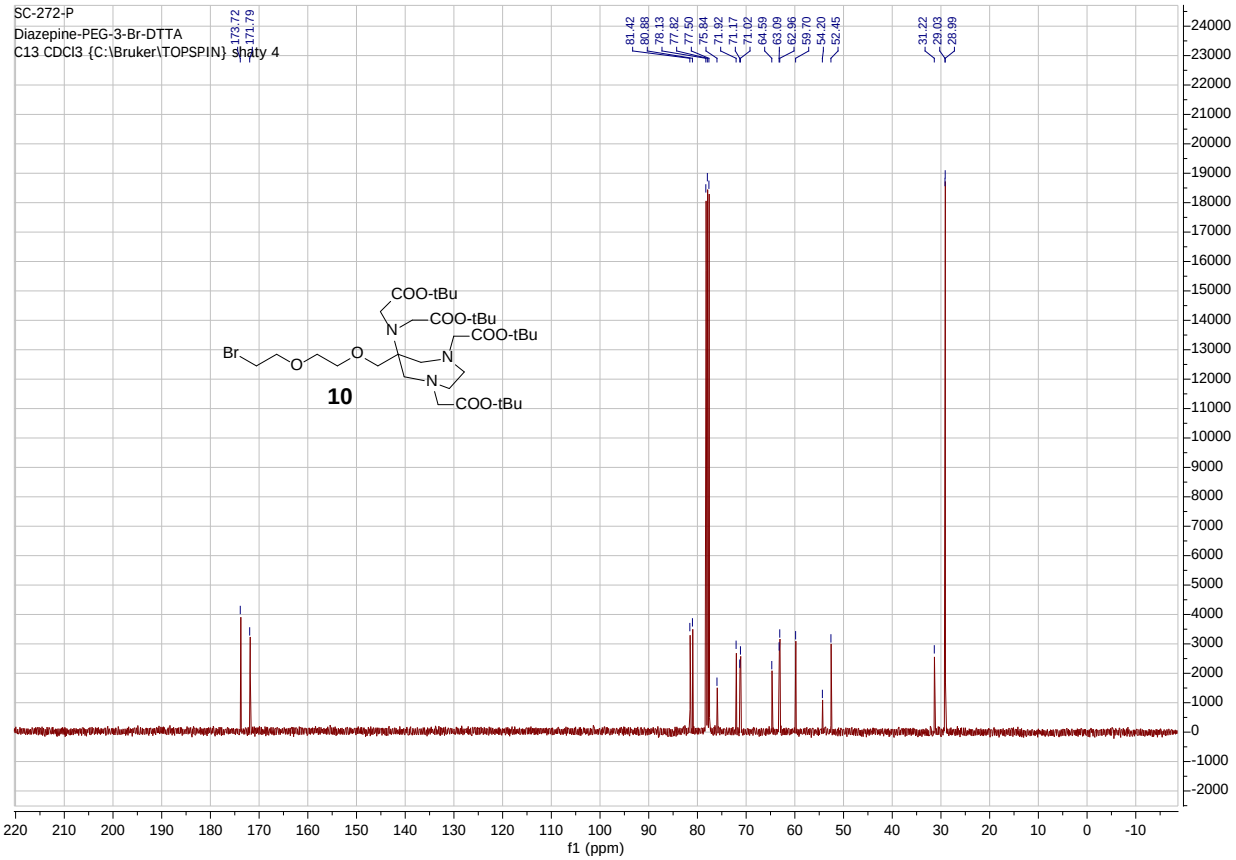
$C_{34}H_{63}N_3O_{11}$+ Na (689.4463 + 22.9898) = 712.4360

$C_{34}H_{63}N_3O_{11}$ + H (689.4463 + 1.0078) = 690.4541

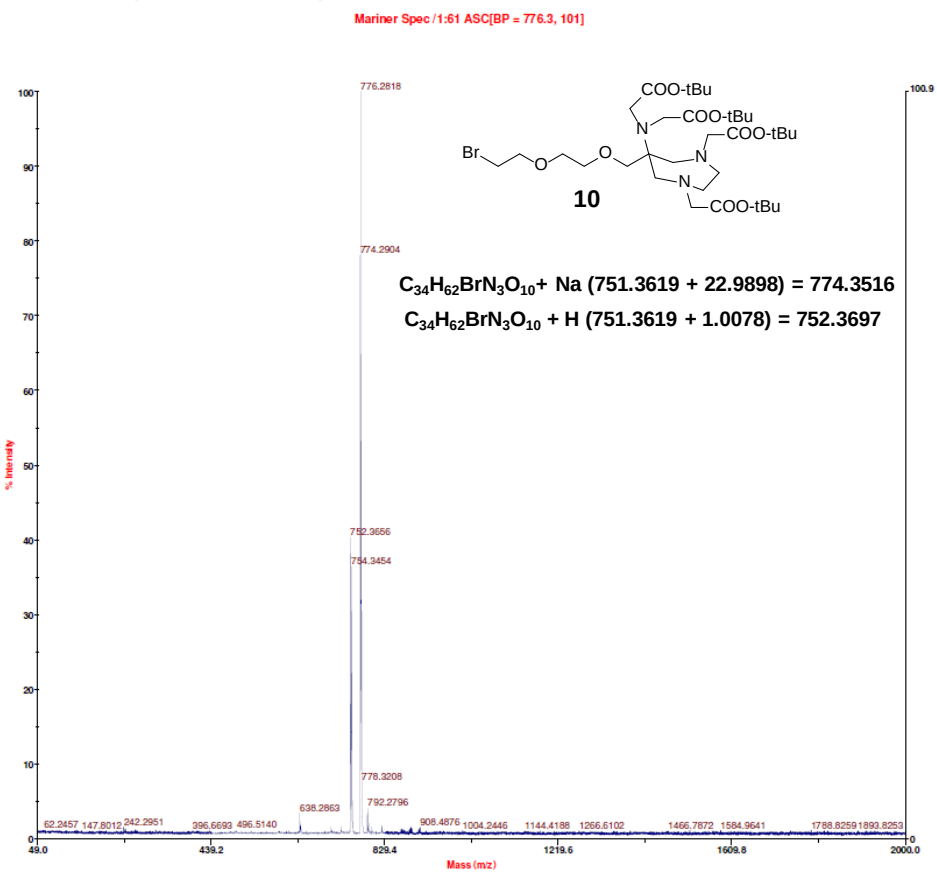
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0154242E-007
Calibration Constant B	77.058851
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-272-P
Diazepine-PEG-3-Br-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 4
COO-tBu
COO-tBu
COO-tBu
COO-tBu
Br
O
O
N
N
N
10
f1 (ppm)


SC-272-P
Diazepine-PEG-3-Br-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 4
3.83
3.81
3.80
3.75
3.67
3.66
3.66
3.65
3.59
3.58
3.57
3.54
3.49
3.48
3.46
3.30
3.07
3.03
2.83
2.82
2.80
2.78
2.75
2.68
2.67
2.66
2.64
COO-tBu
COO-tBu
COO-tBu
Br
O
O
N
N
N
COO-tBu
10
2.20
3.83
6.22
2.25
3.75
1.91
5.88
f1 (ppm)


SC-272-P
Diazepine-PEG-3-Br-DTTA
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 4
173.72
171.79
81.42
80.88
78.13
77.82
77.50
75.84
71.92
71.17
71.02
64.59
63.09
62.96
59.70
54.20
52.45
31.22
29.03
28.99
COO-tBu
COO-tBu
COO-tBu
COO-tBu
Br
O
O
N
N
N
10
f1 (ppm)

Applied Biosystems Mariner System 5268

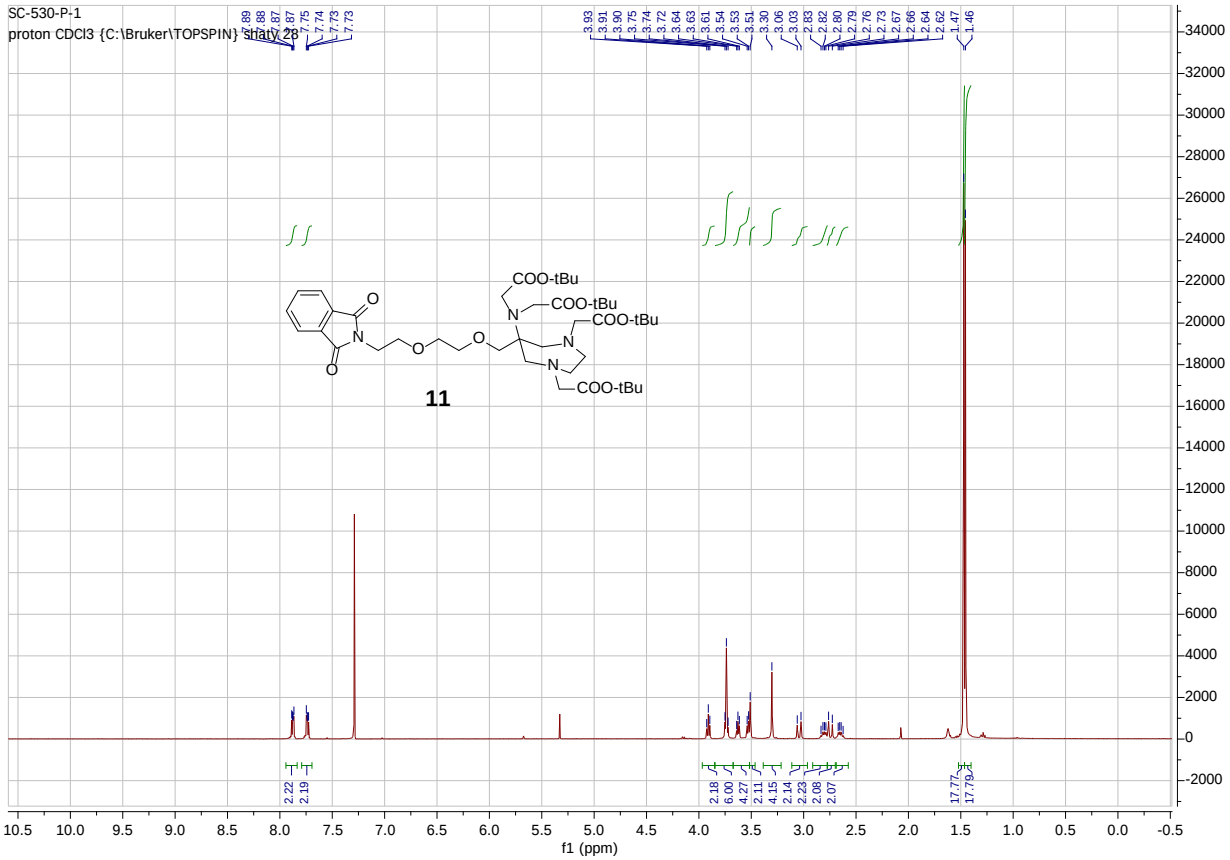


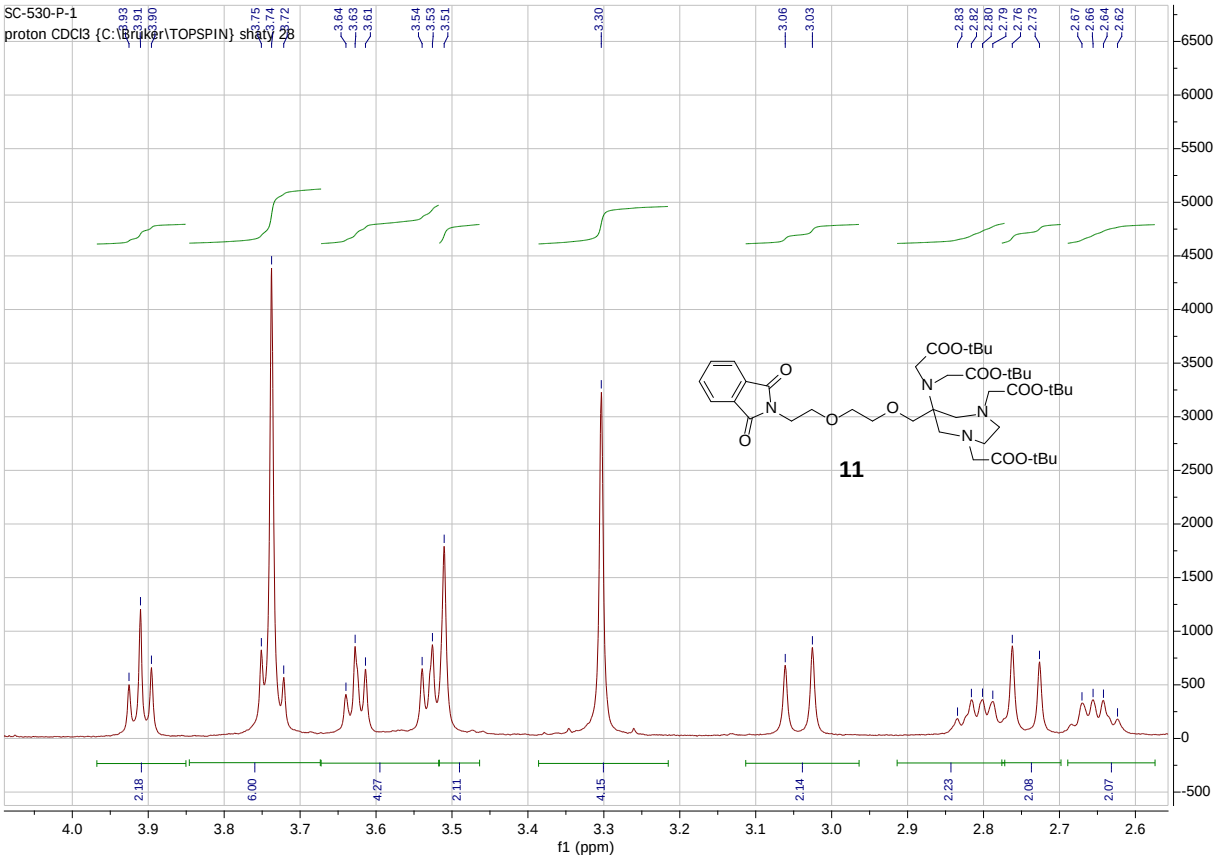
10

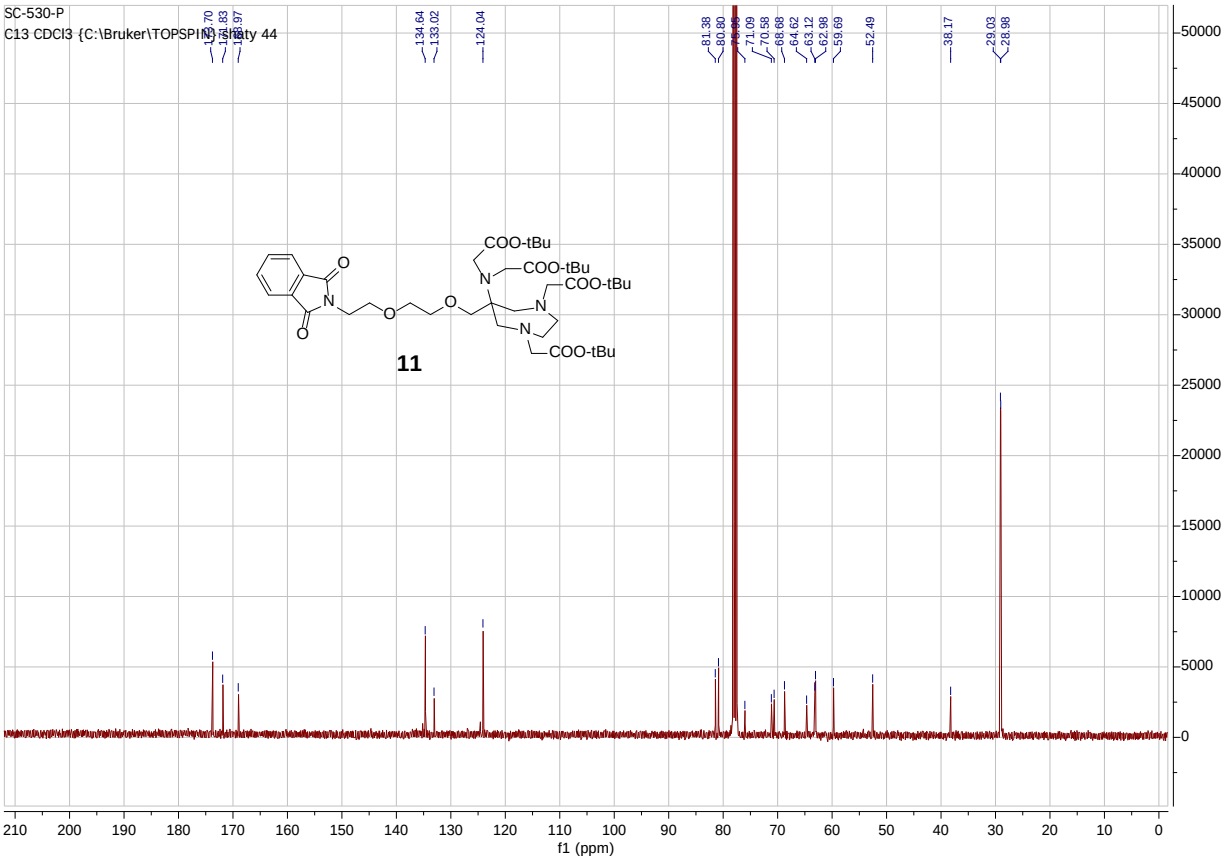
$C_{34}H_{62}BrN_3O_{10}$+ Na (751.3619 + 22.9898) = 774.3516

$C_{34}H_{62}BrN_3O_{10}$ + H (751.3619 + 1.0078) = 752.3697

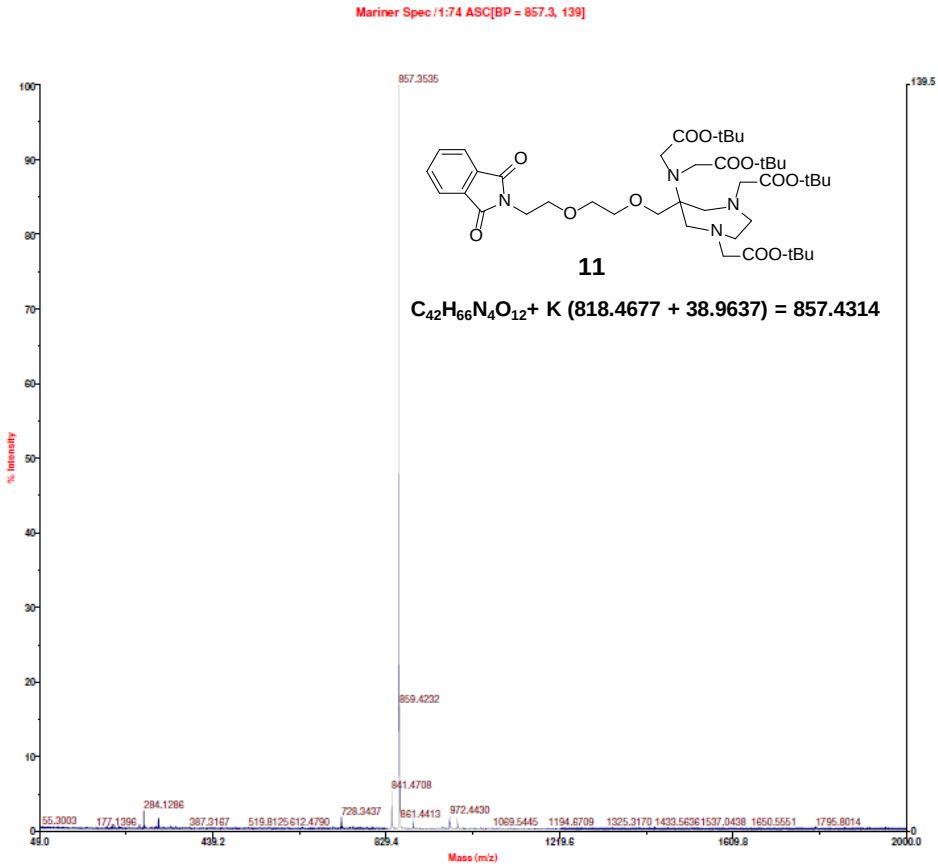
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0142059E-007
Calibration Constant B	75.342573
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-530-P-1
proton CDCl3 {C:\Bruker\TOPSPIN} study 28
COO-tBu
COO-tBu
COO-tBu
COO-tBu
11
f1 (ppm)

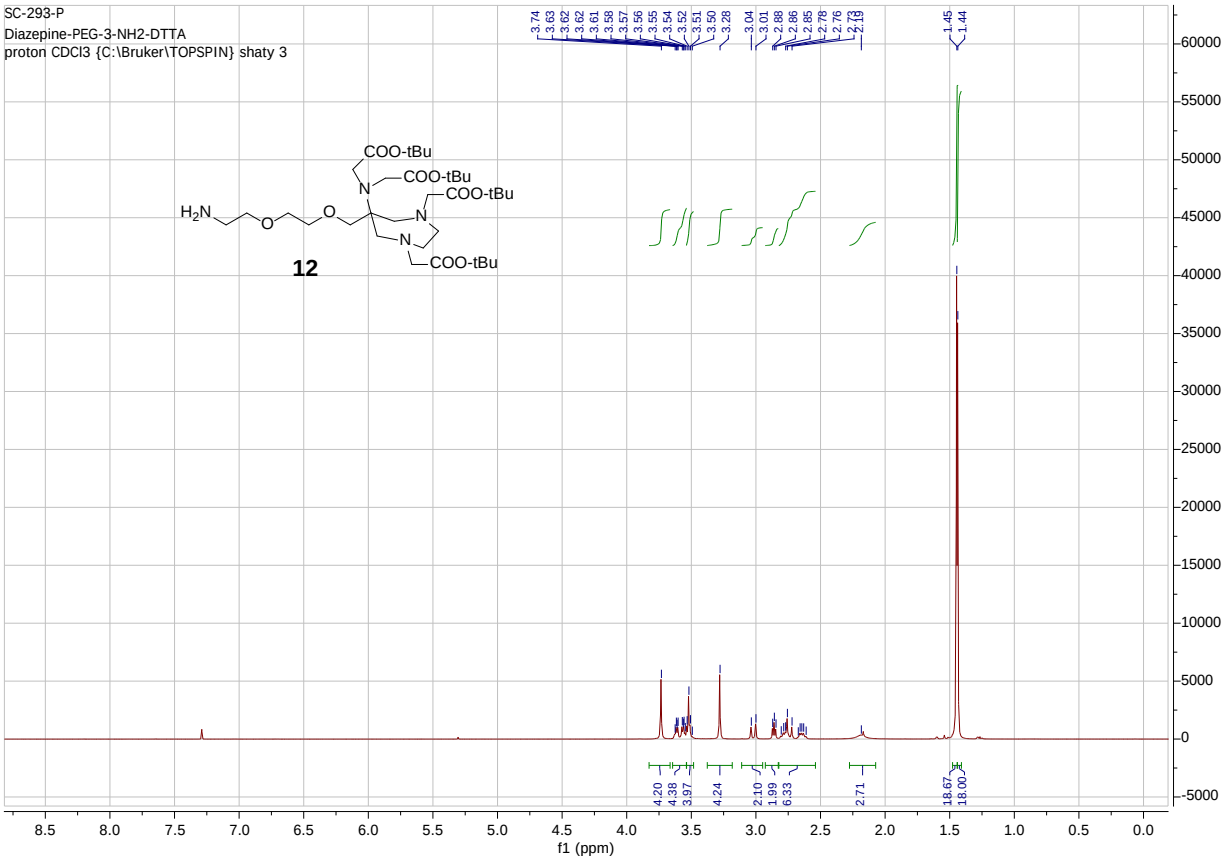

SC-530-P-1
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 28
3.93
3.91
3.90
3.75
3.74
3.72
3.64
3.63
3.61
3.54
3.53
3.51
3.30
3.06
3.03
2.83
2.82
2.80
2.79
2.76
2.73
2.67
2.66
2.64
2.62
COO-tBu
COO-tBu
COO-tBu
COO-tBu
11
2.18
6.00
4.27
2.11
4.15
2.14
2.23
2.08
2.07
f1 (ppm)

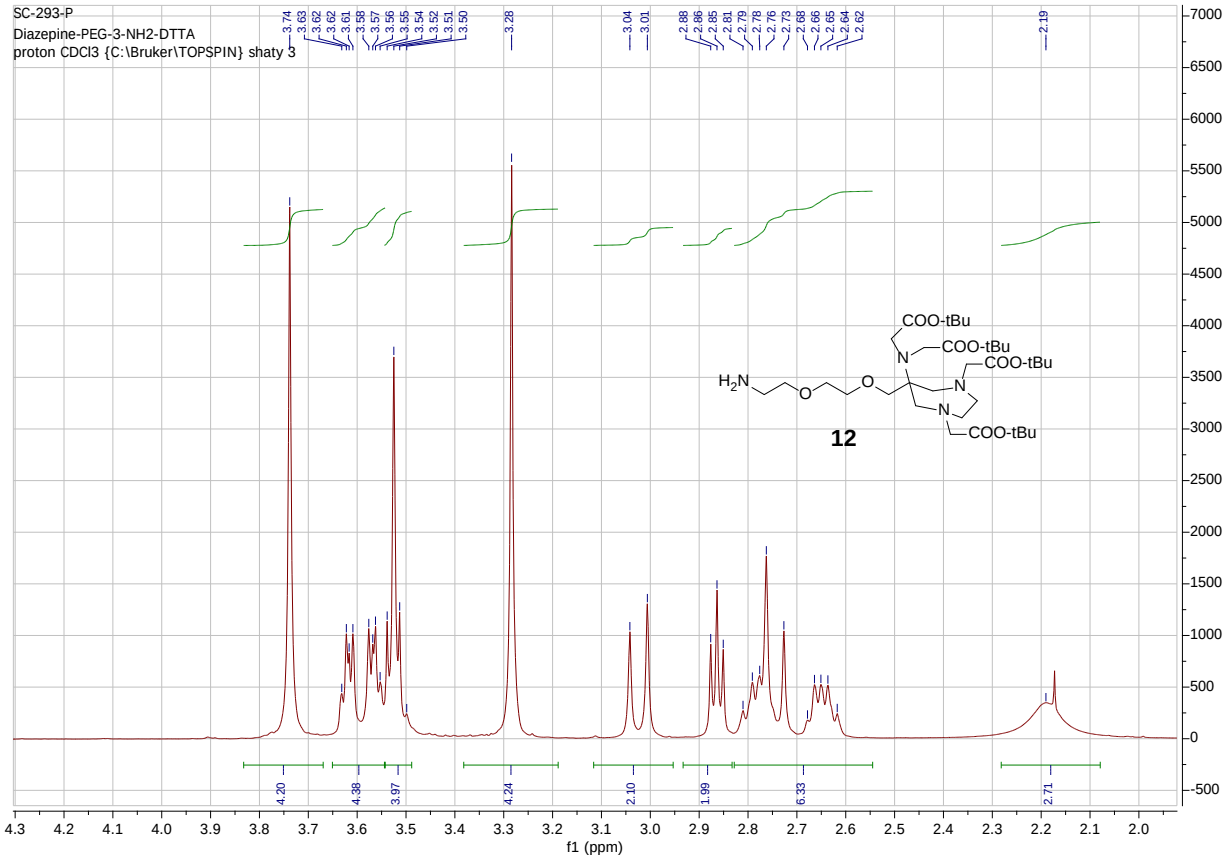

SC-530-P
C13 CDCl3 {C:\Bruker\TOPSPIN3} Shaty 44
170.70
169.83
169.97
134.64
133.02
124.04
81.38
80.80
71.09
70.58
68.68
64.62
63.12
62.98
59.69
52.49
38.17
29.03
28.98
COO-tBu
COO-tBu
COO-tBu
COO-tBu
11
f1 (ppm)

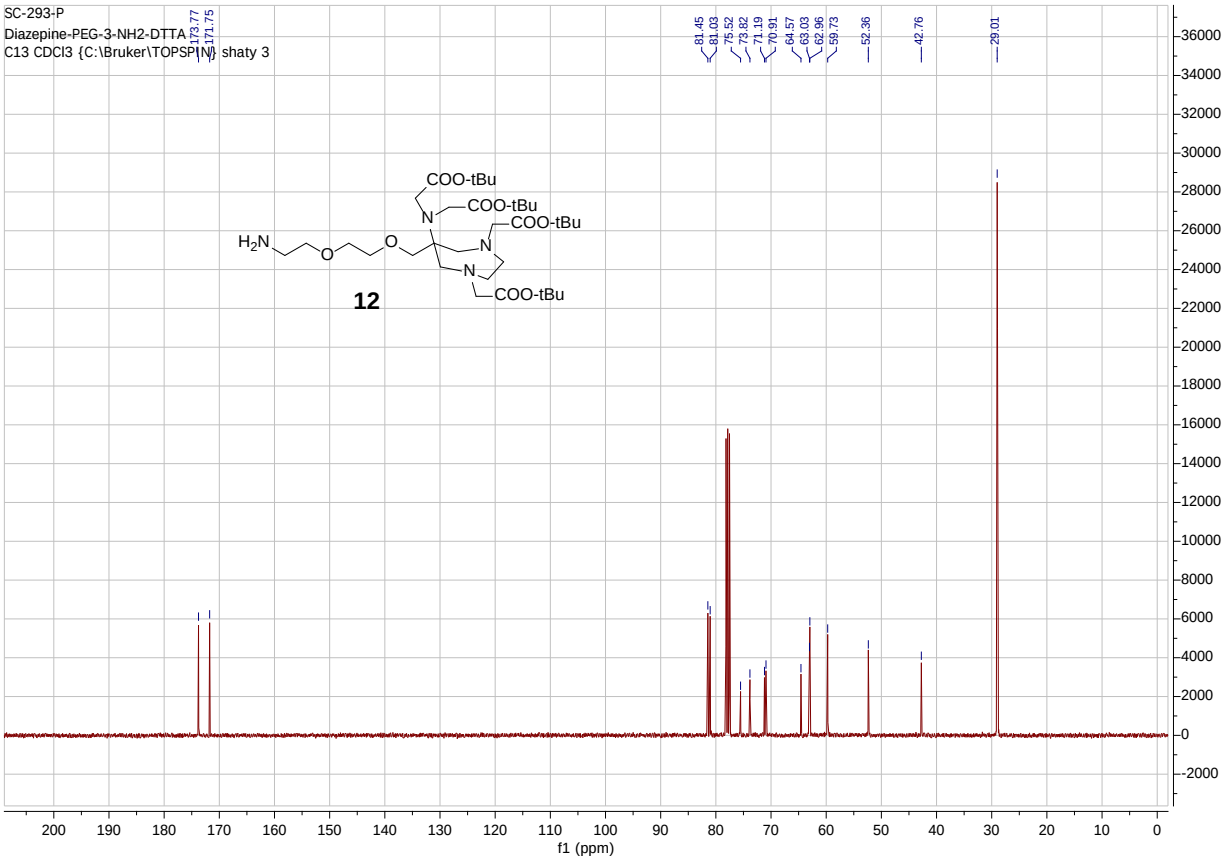
Applied Biosystems Mariner System 5268



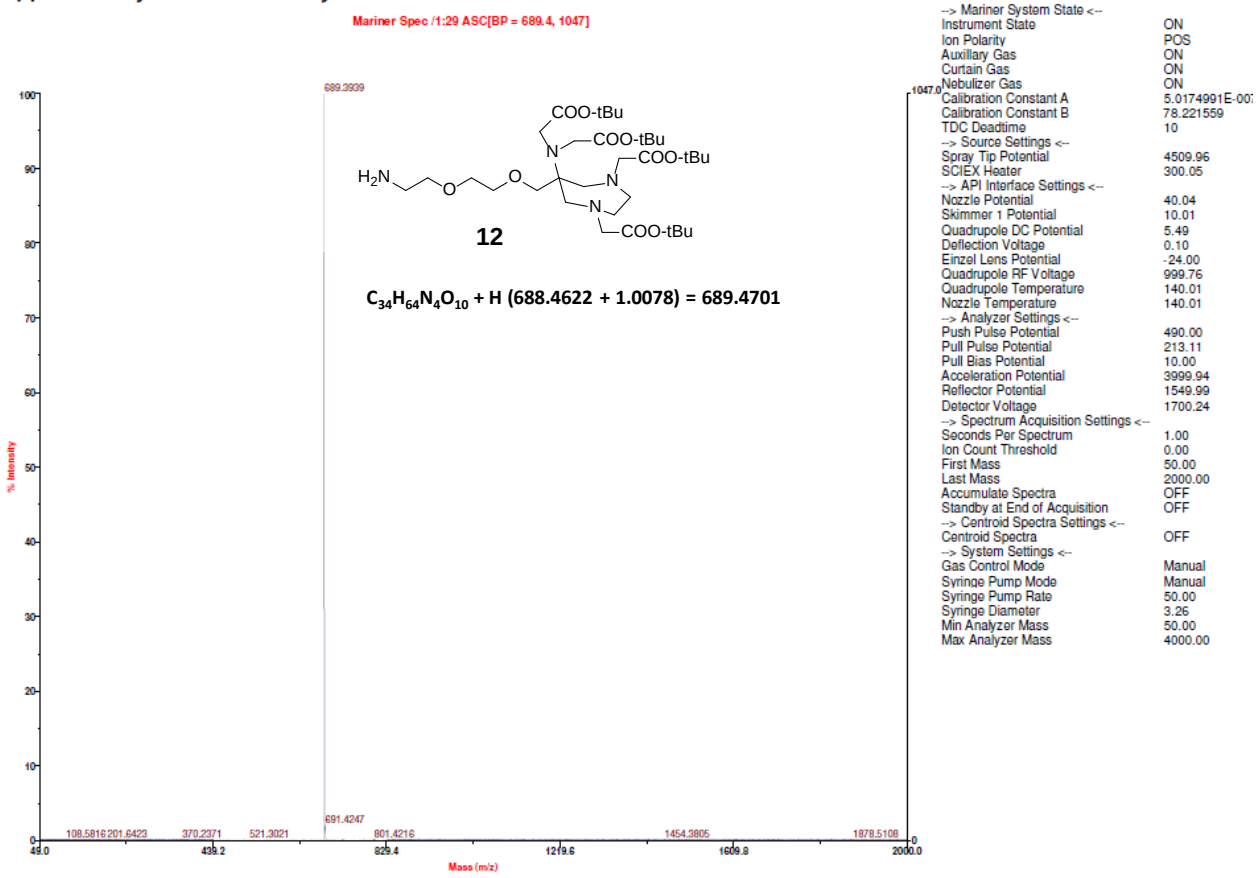
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0142059E-007
Calibration Constant B	75.342573
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.89
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-293-P
Diazepine-PEG-3-NH2-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 3
COO-tBu
COO-tBu
COO-tBu
COO-tBu
H2N
O
O
N
N
N
12
f1 (ppm)


SC-293-P
Diazepine-PEG-3-NH2-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 3
3.74
3.63
3.62
3.62
3.61
3.58
3.57
3.56
3.55
3.54
3.52
3.51
3.50
3.28
3.04
3.01
2.88
2.86
2.85
2.81
2.79
2.78
2.76
2.73
2.68
2.66
2.65
2.64
2.62
2.19
4.20
4.38
3.97
4.24
2.10
1.99
6.33
2.71
f1 (ppm)
COO-tBu
COO-tBu
COO-tBu
COO-tBu
H2N
O
O
N
N
N
12


SC-293-P
Diazepine-PEG-3-NH2-DTTA
C13 CDCl3 {C:\Bruker\TOPSPIN\...} shaty 3
173.77
171.75
81.45
81.03
75.52
73.82
71.19
70.91
64.57
63.03
62.96
59.73
52.36
42.76
29.01
COO-tBu
COO-tBu
COO-tBu
COO-tBu
H_2N
O
O
N
N
12
f1 (ppm)

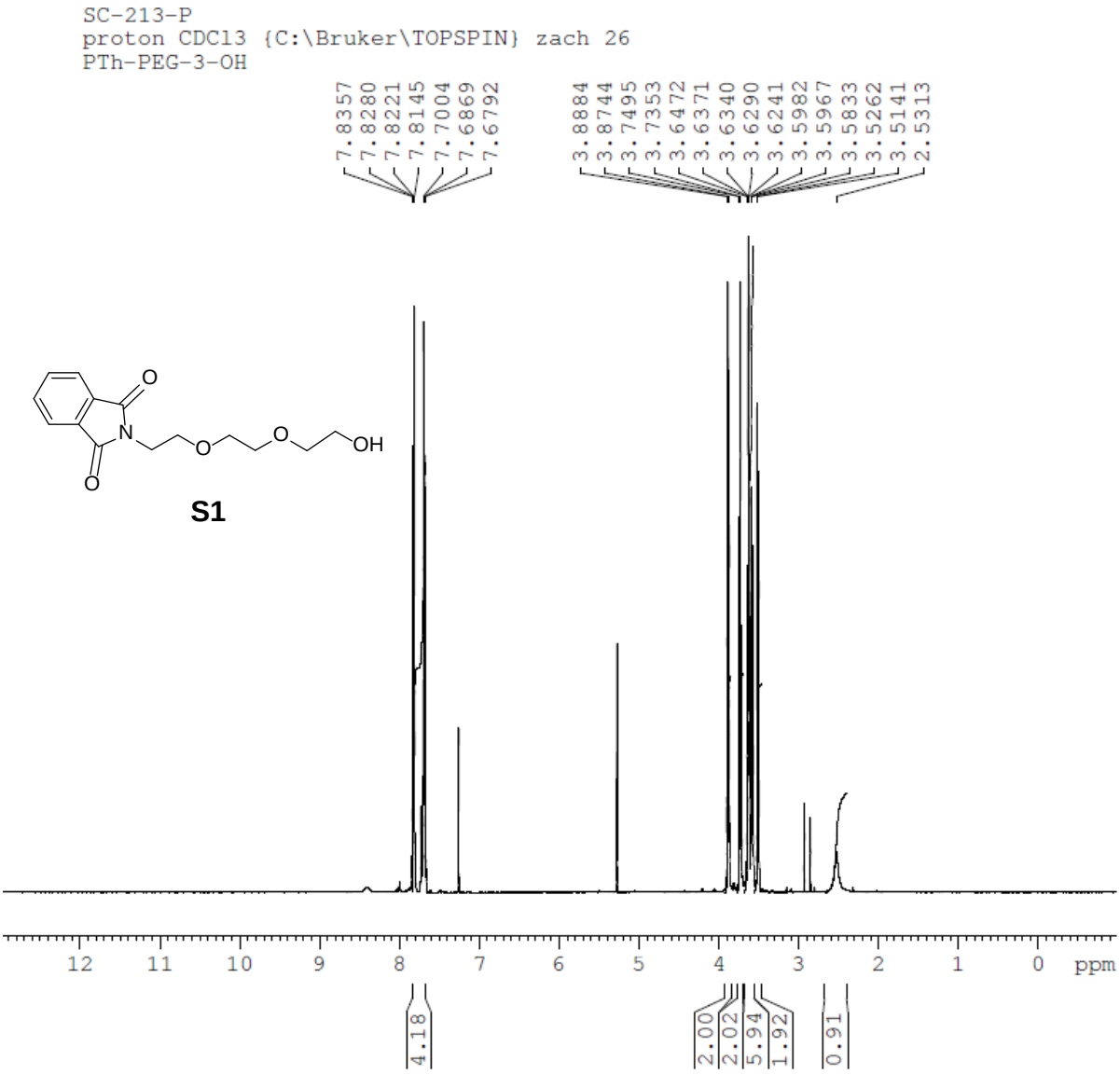
Applied Biosystems Mariner System 5268

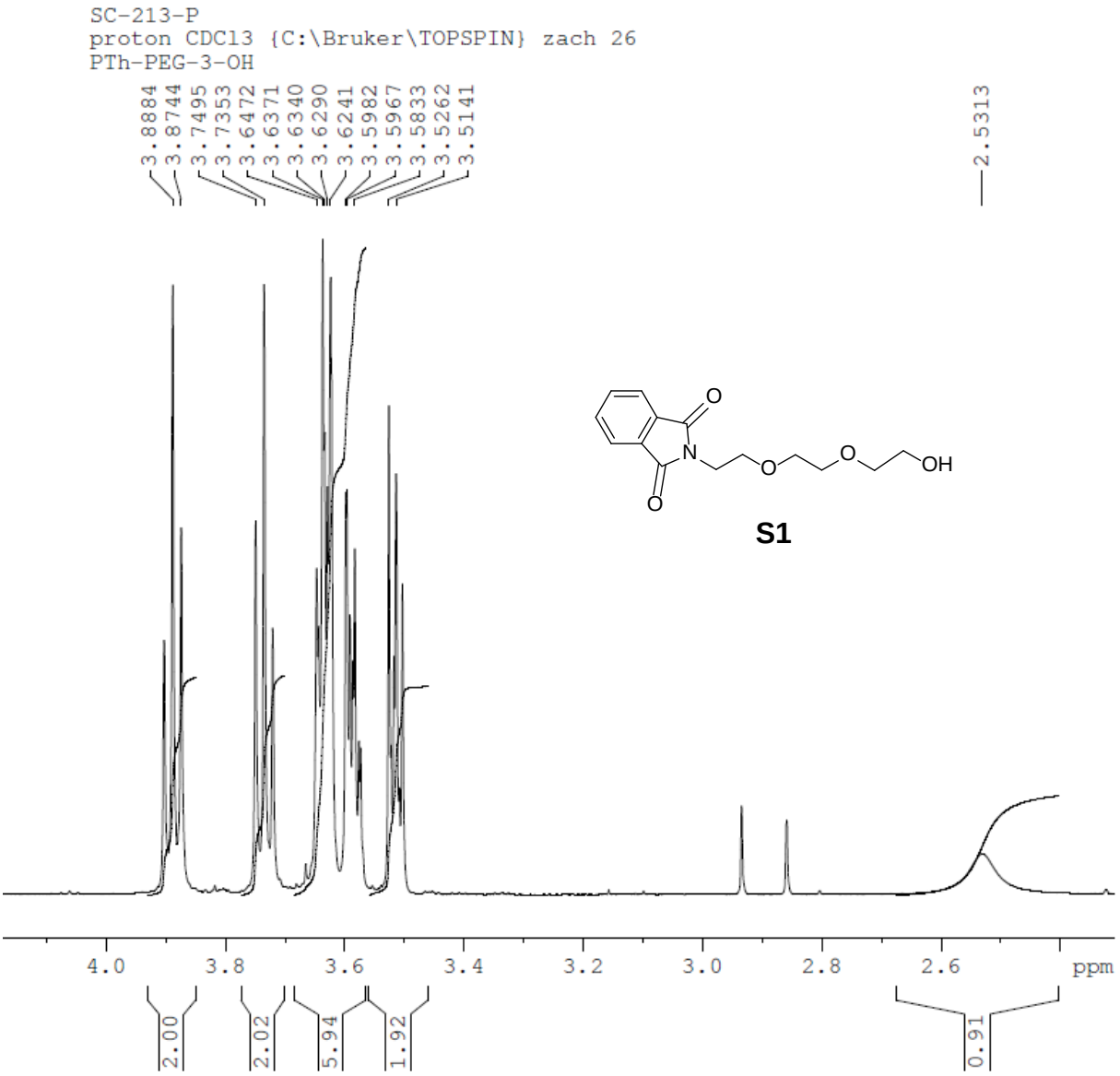


12

$C_{34}H_{64}N_4O_{10}$ + H (688.4622 + 1.0078) = 689.4701

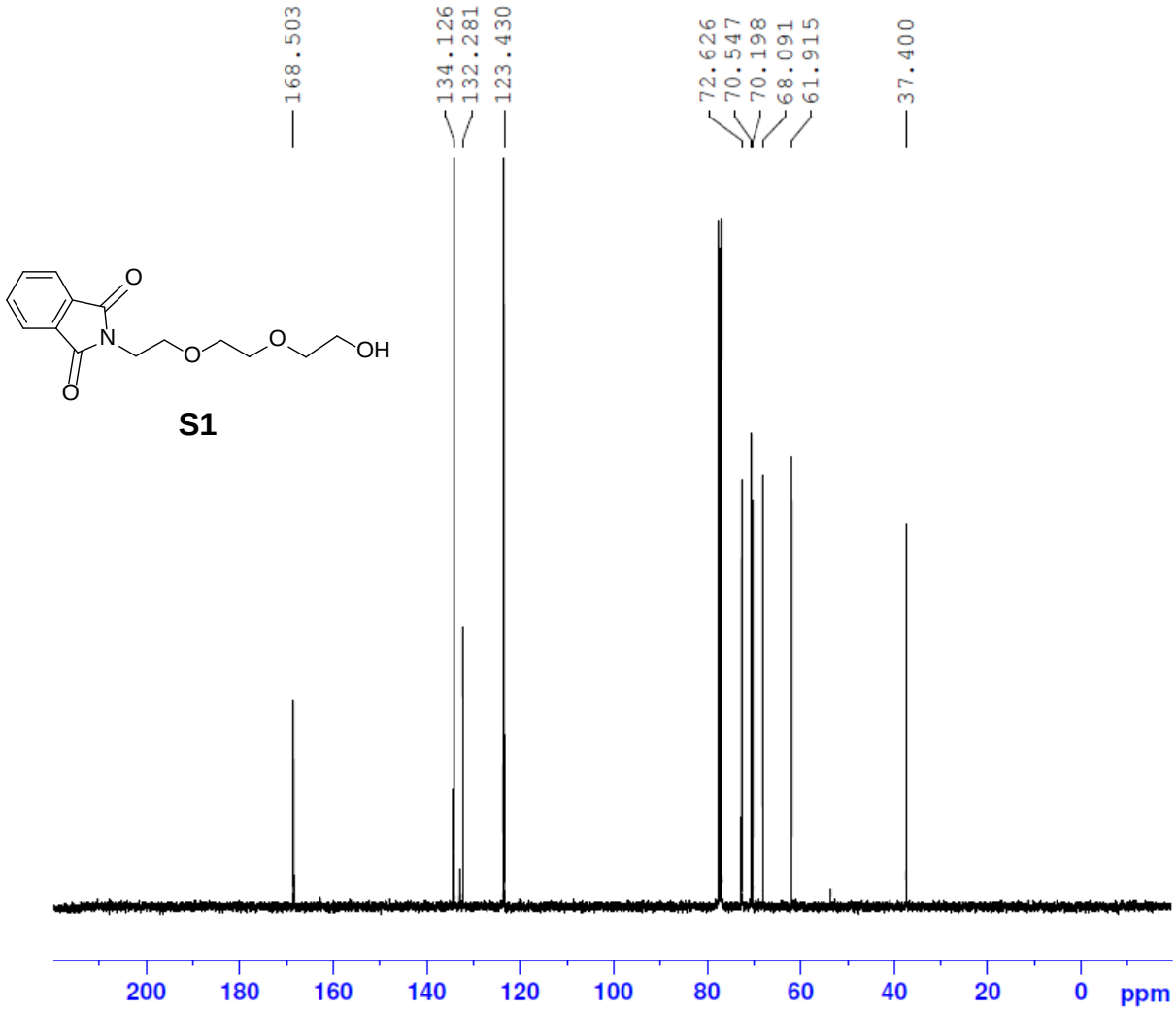
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0174991E-00
Calibration Constant B	78.221559
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-213-P
proton CDCl3 {C:\Bruker\TOPSPIN} zach 26
PTh-PEG-3-OH
7.8357
7.8280
7.8221
7.8145
7.7004
7.6869
7.6792
3.8884
3.8744
3.7495
3.7353
3.6472
3.6371
3.6340
3.6290
3.6241
3.5982
3.5967
3.5833
3.5262
3.5141
2.5313
O
N
O
O
O
OH
S1
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
4.18
2.00
2.02
5.94
1.92
0.91


SC-213-P
proton CDCl3 {C:\Bruker\TOPSPIN} zach 26
PTh-PEG-3-OH
3.8884
3.8744
3.7495
3.7353
3.6472
3.6371
3.6340
3.6290
3.6241
3.5982
3.5967
3.5833
3.5262
3.5141
2.5313
O
N
O
O
OH
O
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
ppm
2.00
2.02
5.94
1.92
0.91

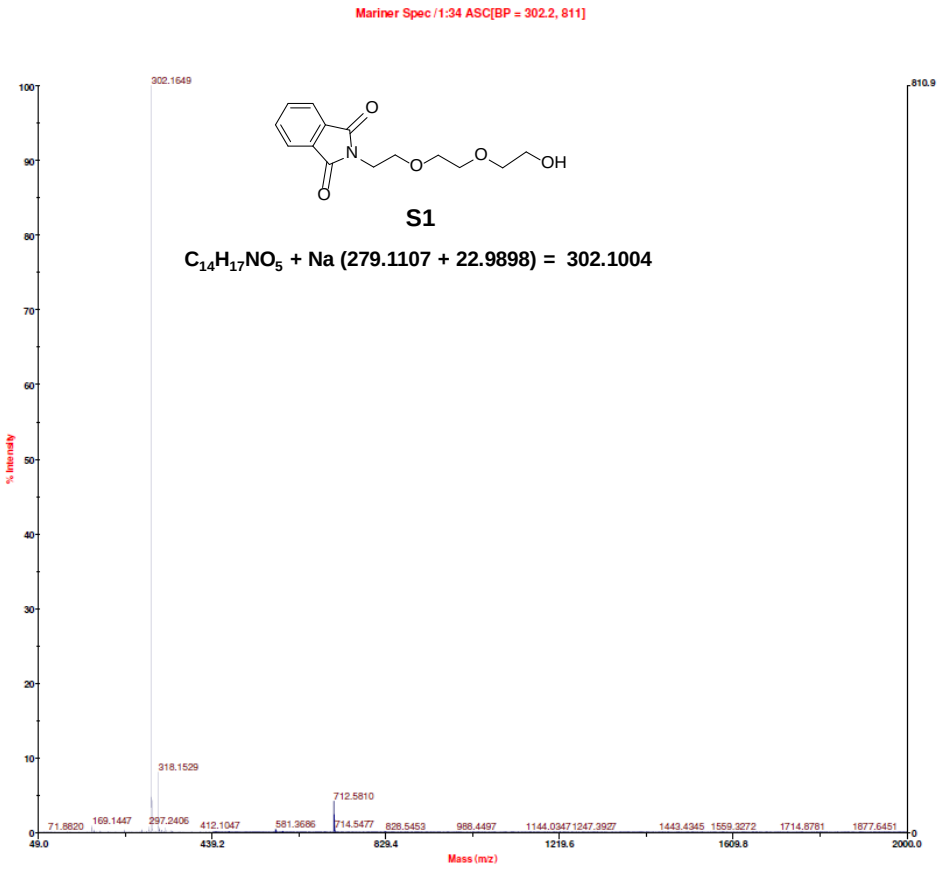
S1

SC-213-P
C13 CDCl3 {C:\Bruker\TOPSPIN} zach 26
PTH-PEG-3-OH



S1

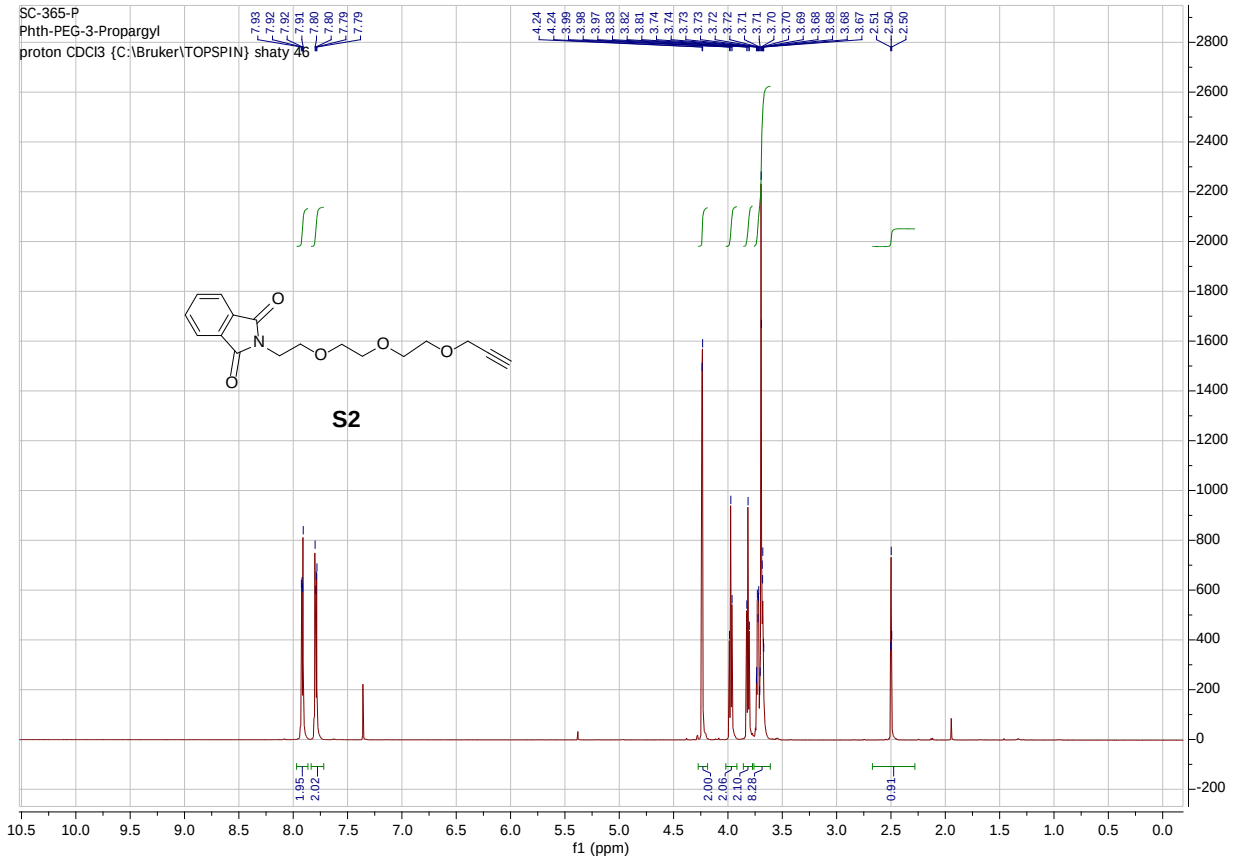
Applied Biosystems Mariner System 5268

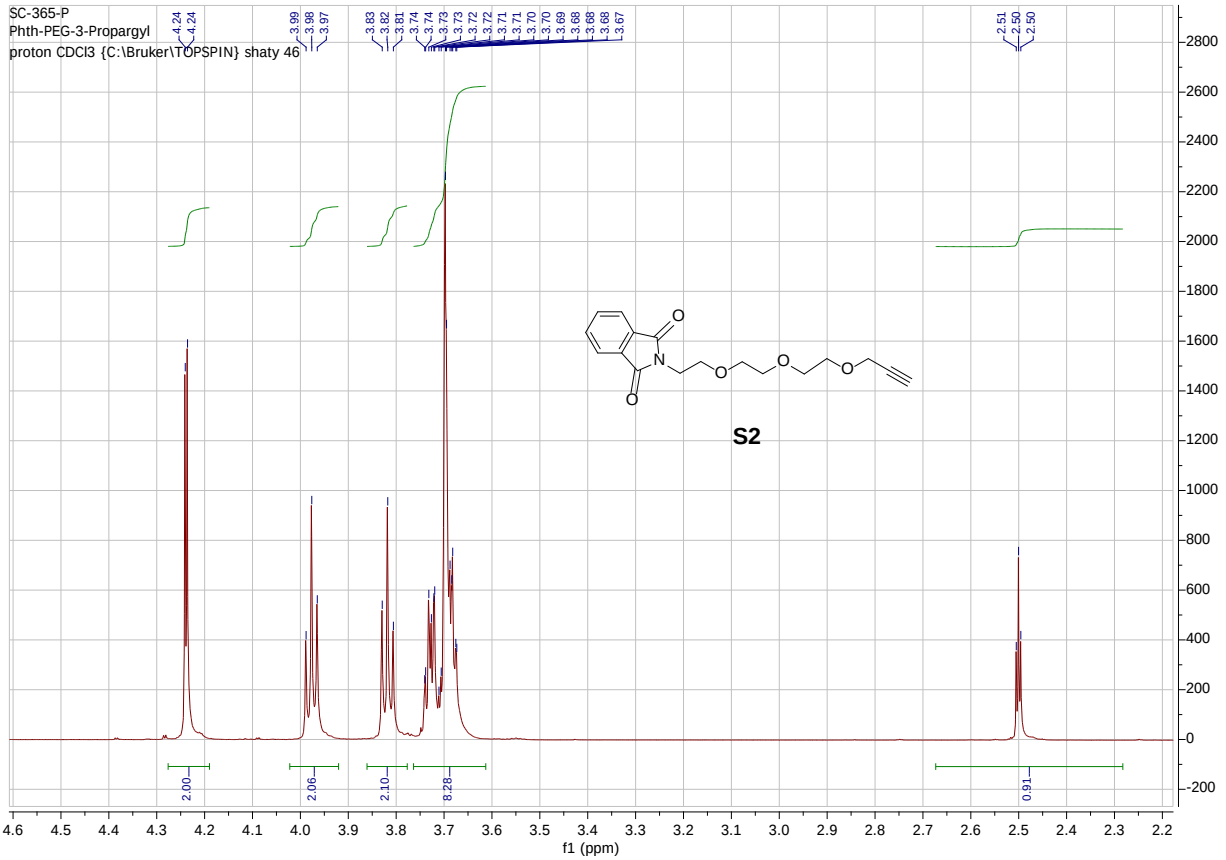


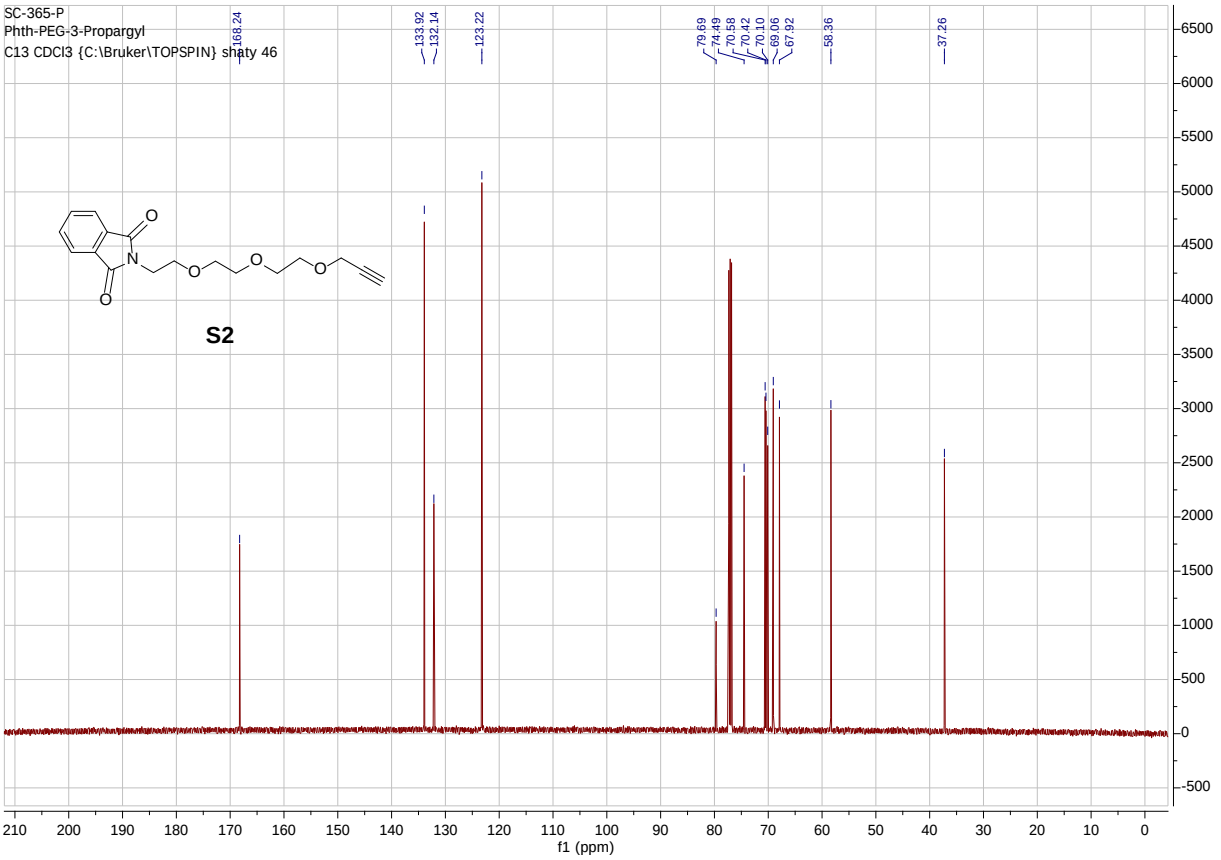
S1

$C_{14}H_{17}NO_5$ + Na (279.1107 + 22.9898) = 302.1004

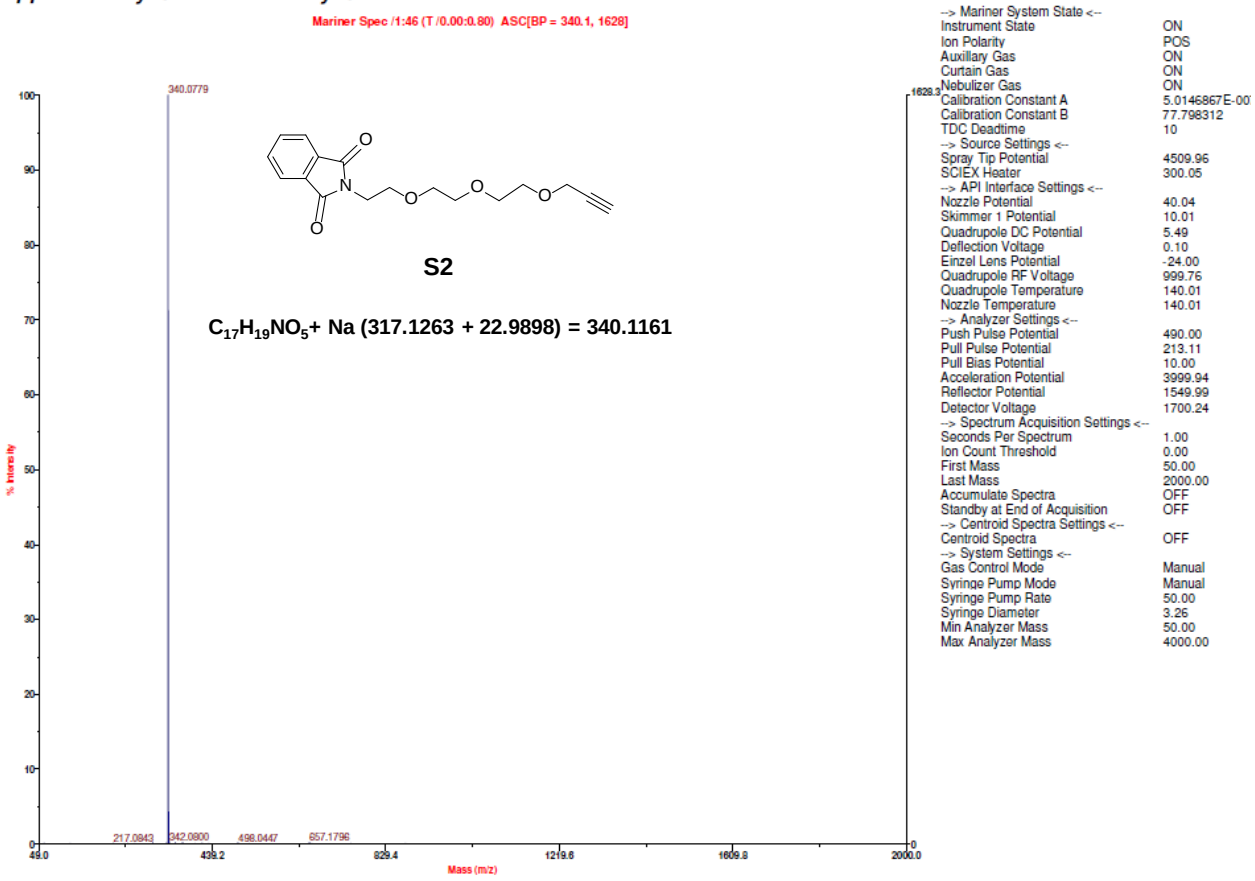
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0154242E-00
Calibration Constant B	77.058851
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-365-P
Phth-PEG-3-Propargyl
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 46
S2
f1 (ppm)

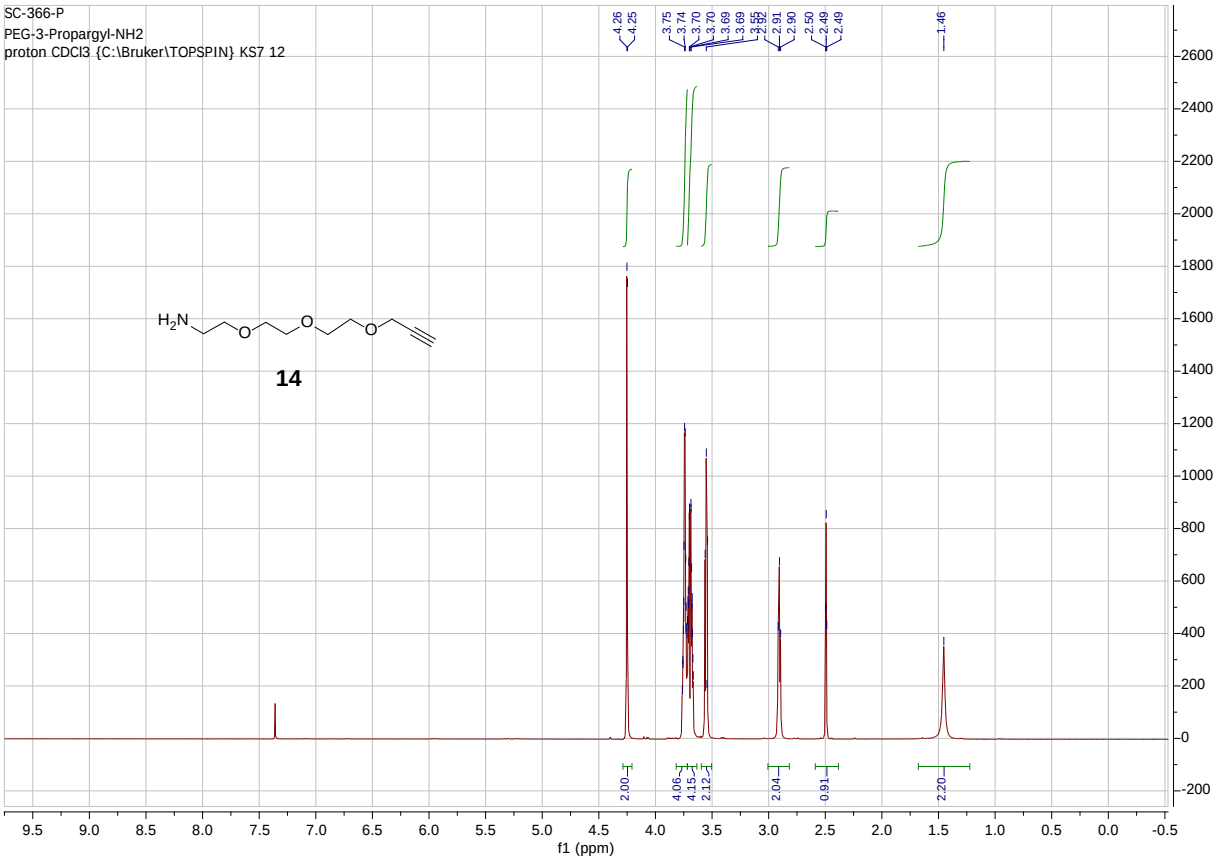

SC-365-P
Phth-PEG-3-Propargyl
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 46
4.24
4.24
3.99
3.98
3.97
3.83
3.82
3.81
3.74
3.73
3.72
3.71
3.70
3.69
3.68
3.67
2.51
2.50
2.50
2.00
2.06
2.10
8.28
0.91
S2
f1 (ppm)

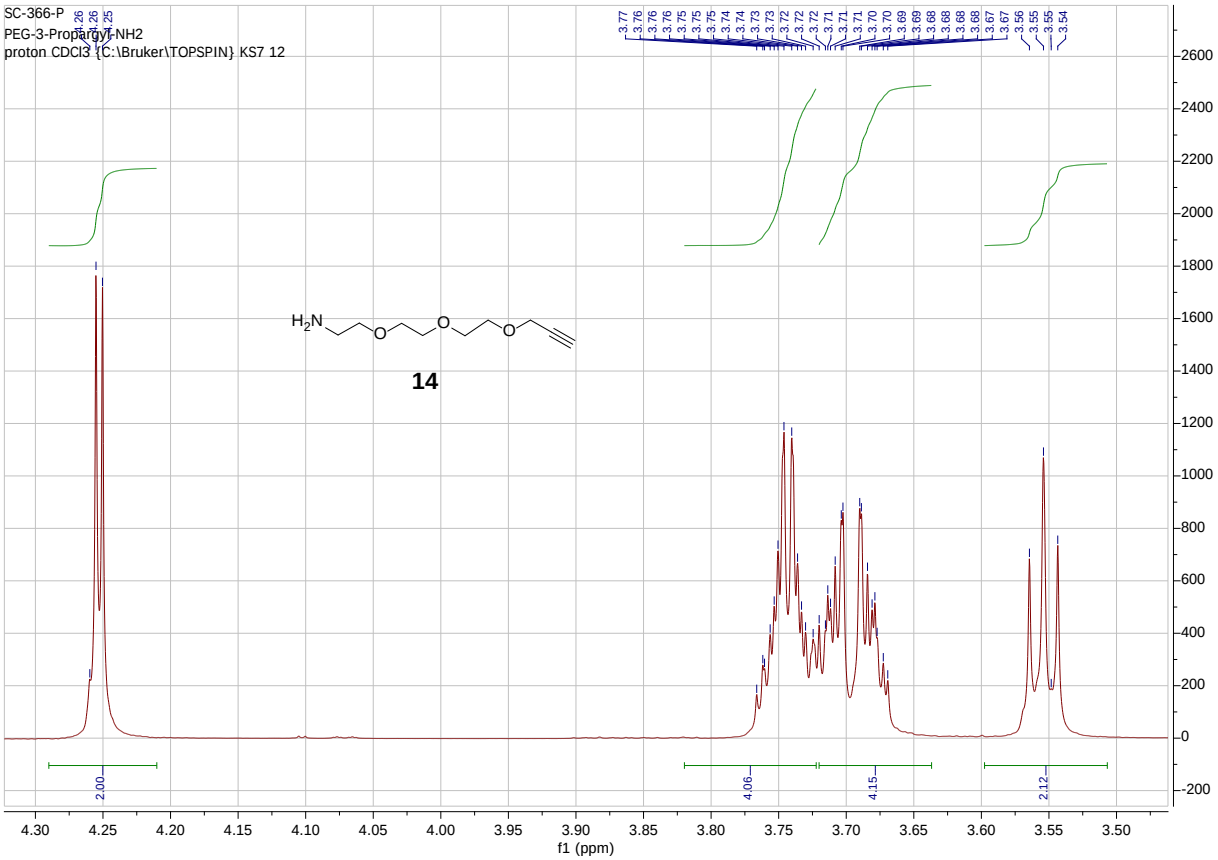

SC-365-P
Phth-PEG-3-Propargyl
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 46
168.24
133.92
132.14
123.22
79.69
74.49
70.58
70.42
70.10
69.06
67.92
58.36
37.26
S2
f1 (ppm)

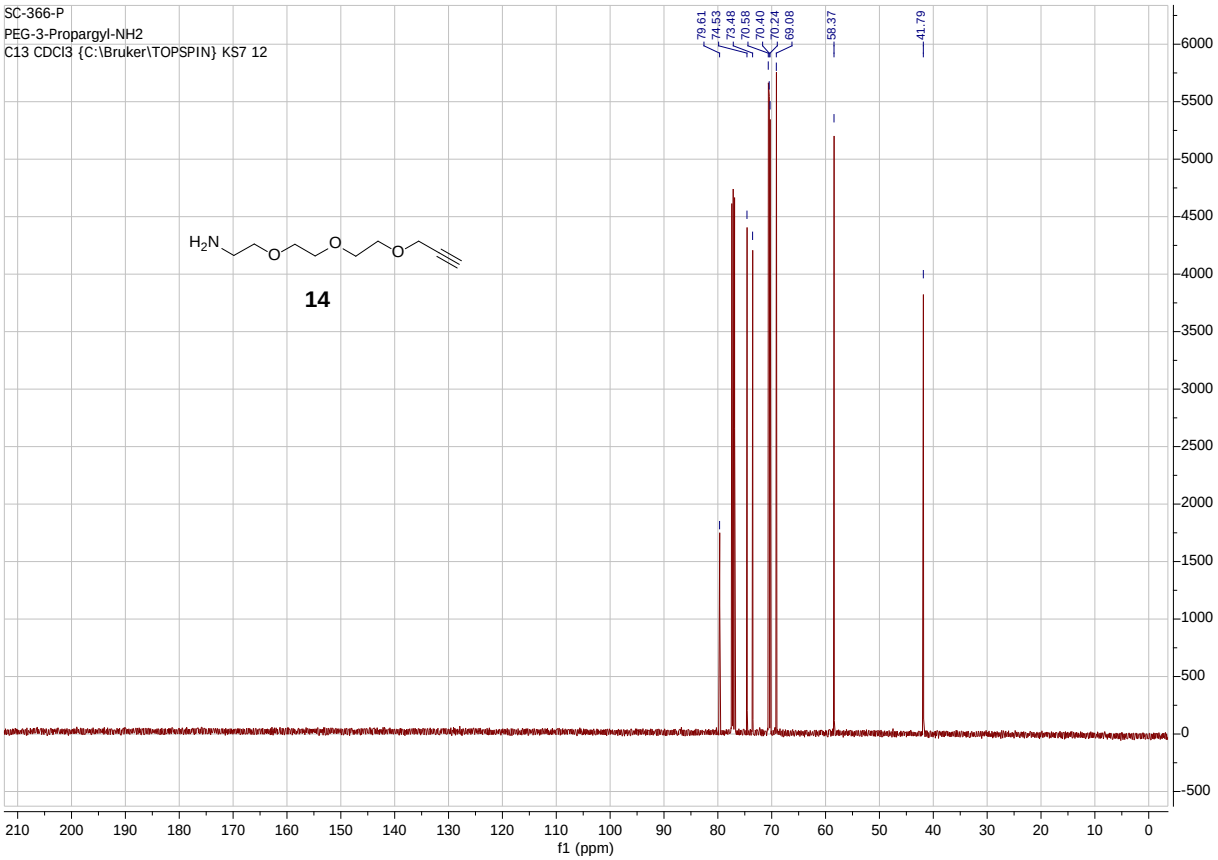
Applied Biosystems Mariner System 5268



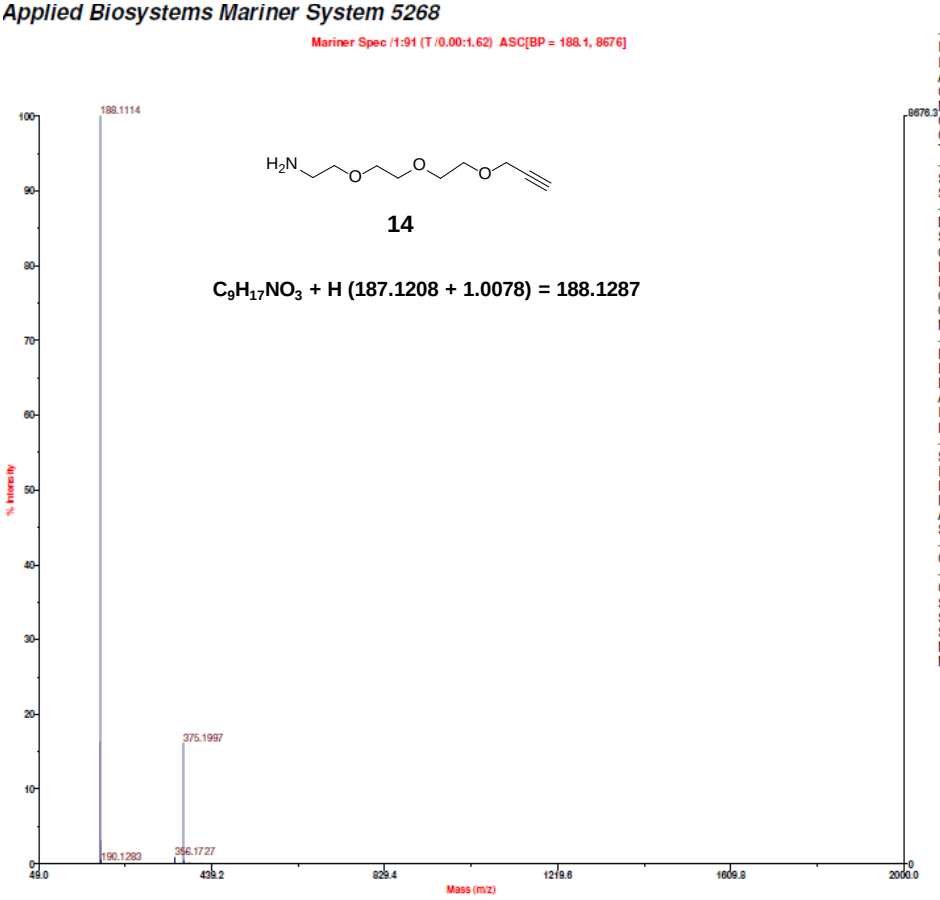
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0146867E-00
Calibration Constant B	77.798312
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-366-P
PEG-3-Propargyl-NH2
proton CDCl3 {C:\Bruker\TOPSPIN} KS7 12
4.26
4.25
3.75
3.74
3.70
3.70
3.69
3.69
2.91
2.90
2.50
2.49
2.49
1.46
2.00
4.06
4.15
2.12
2.04
0.91
2.20
H2N
O
O
O
14
f1 (ppm)


SC-366-P
PEG-3-Propargyl-NH2
proton CDCl3 {C:\Bruker\TOPSPIN} KS7 12
14
f1 (ppm)


SC-366-P
PEG-3-Propargyl-NH2
C13 CDCl3 {C:\Bruker\TOPSPIN} KS7 12
79.61
74.53
73.48
70.58
70.40
70.24
69.08
58.37
41.79
H2N
O
O
O
14
f1 (ppm)

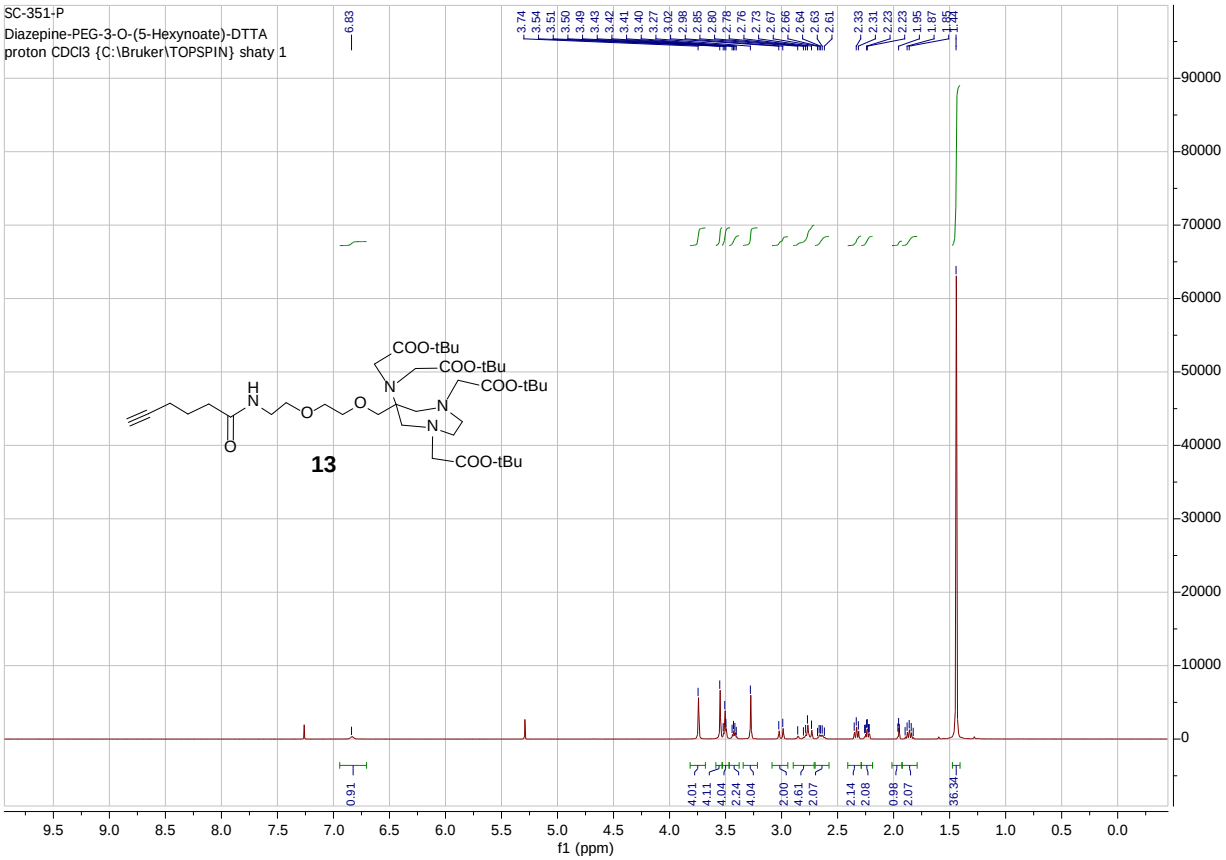
Applied Biosystems Mariner System 5268

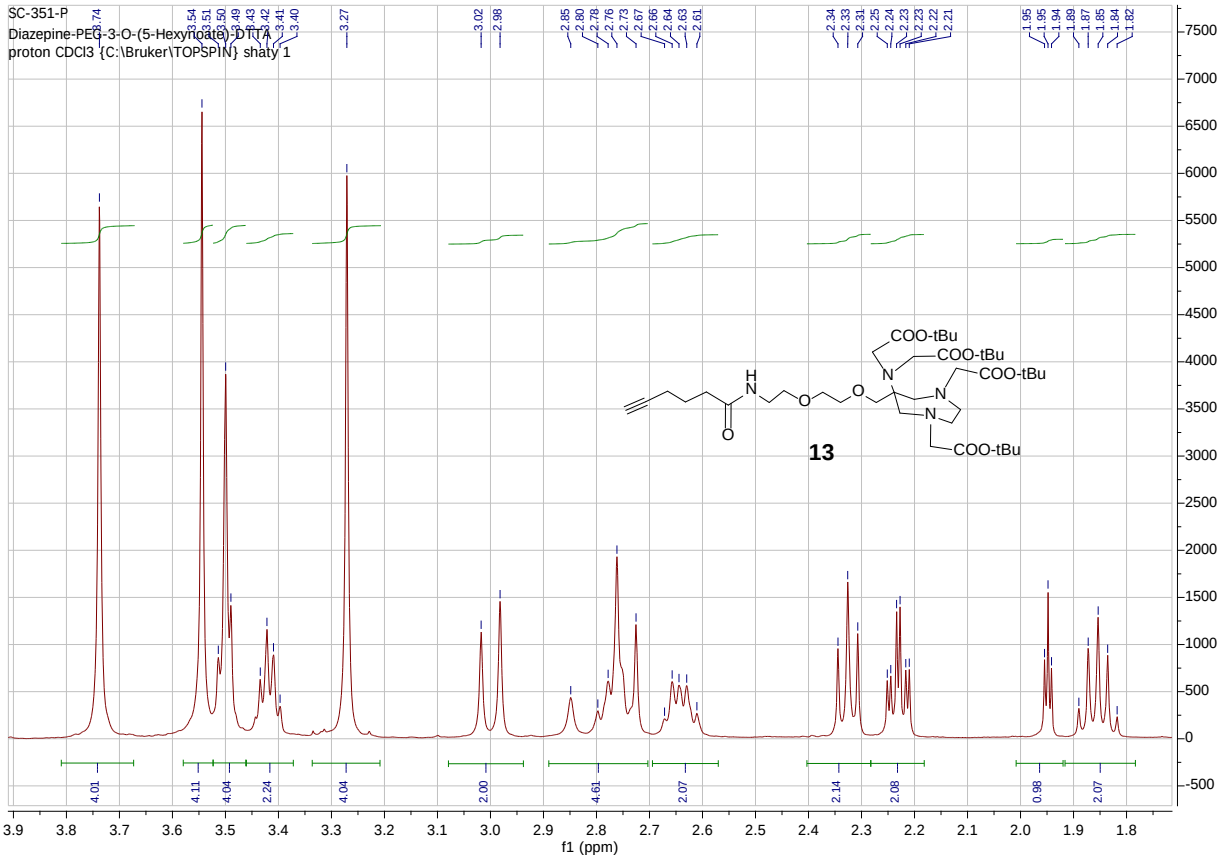


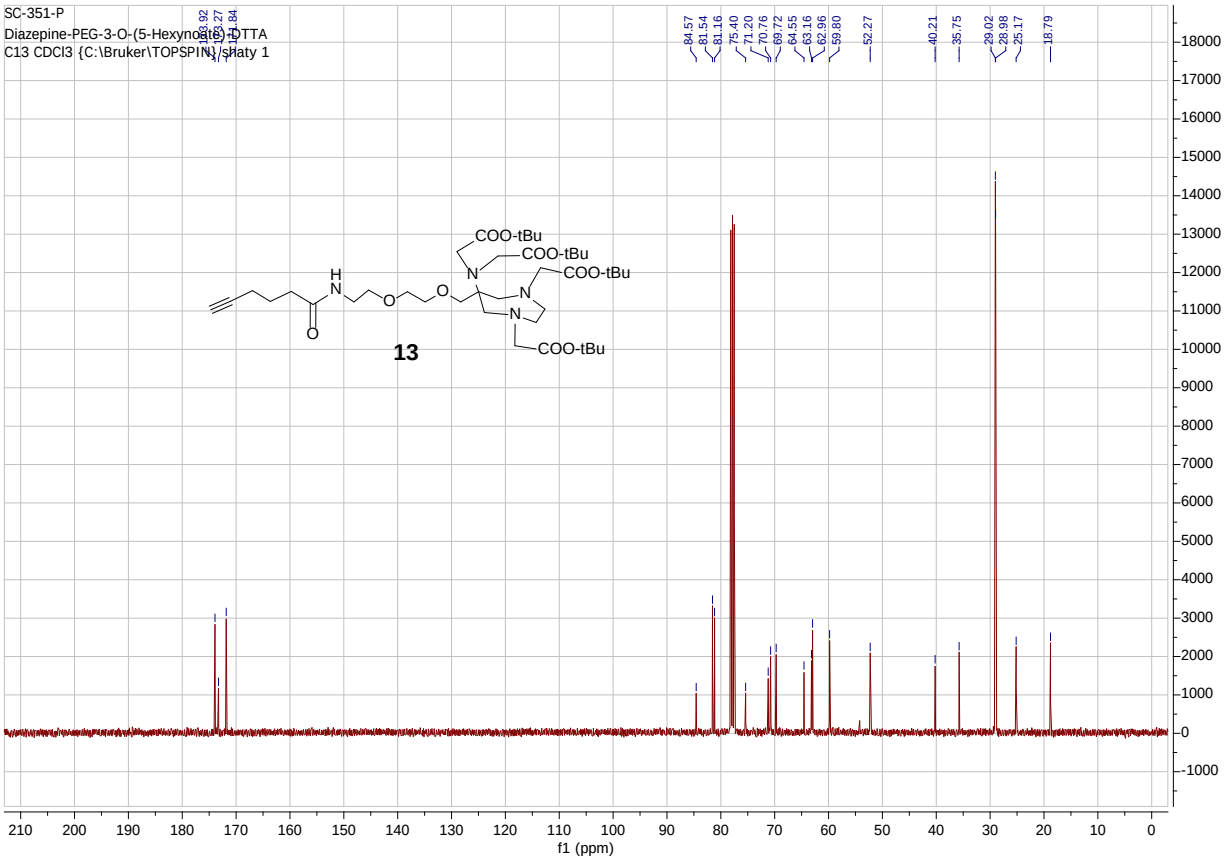
14

$C_9H_{17}NO_3$ + H (187.1208 + 1.0078) = 188.1287

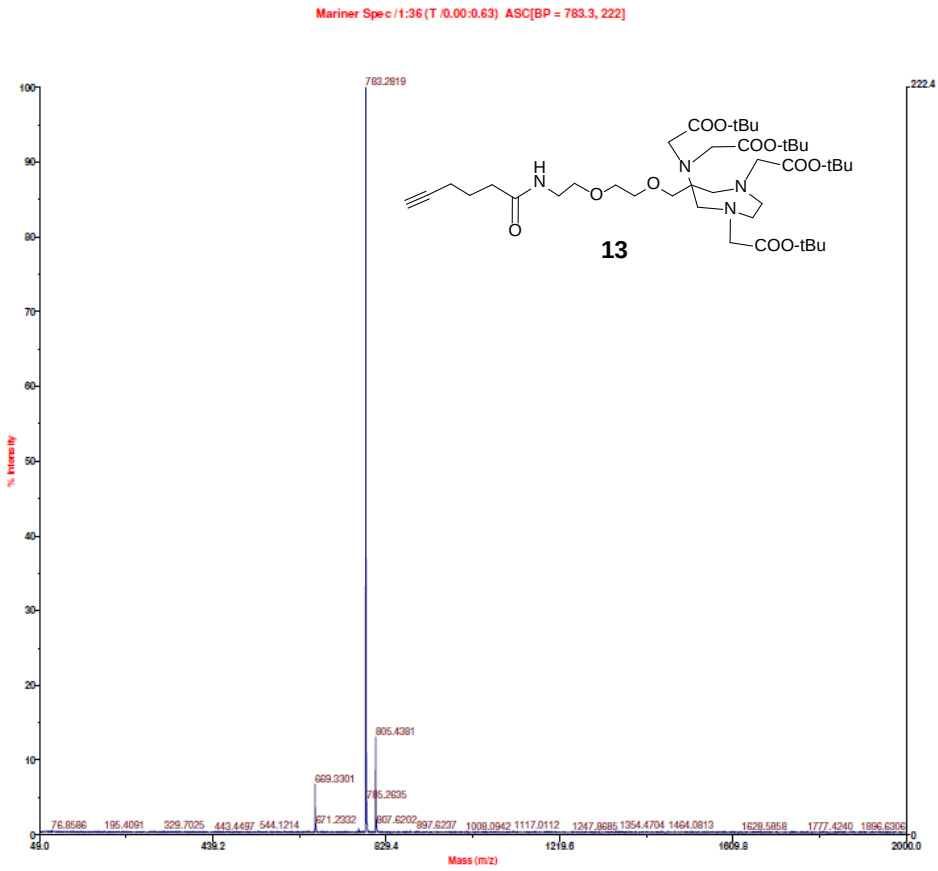
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0146867E-007
Calibration Constant B	77.798312
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-351-P
Diazepine-PEG-3-O-(5-Hexynoate)-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 1
COO-tBu
COO-tBu
COO-tBu
COO-tBu
13
f1 (ppm)

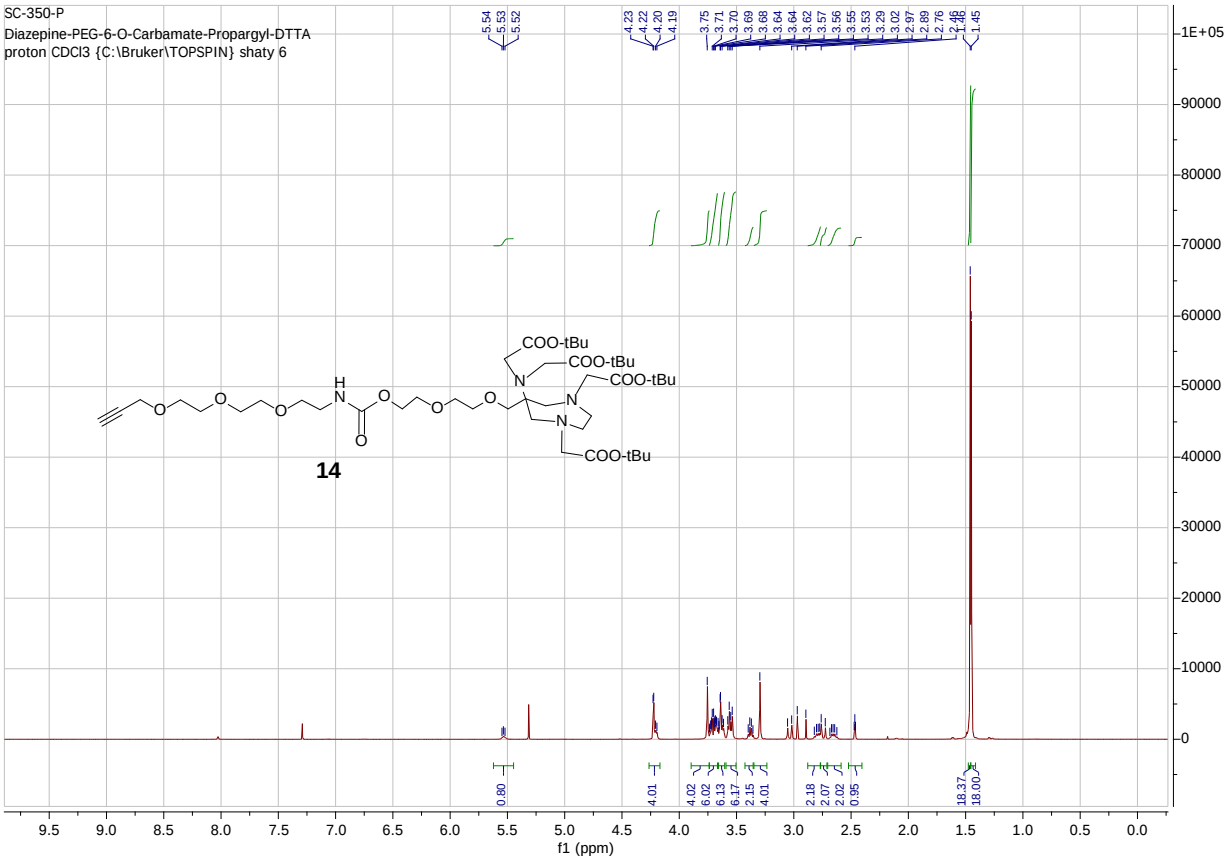

SC-351-P
Diazepine-PEG-3-O-(5-Hexynoate)-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 1
COO-tBu
COO-tBu
COO-tBu
COO-tBu
13
f1 (ppm)

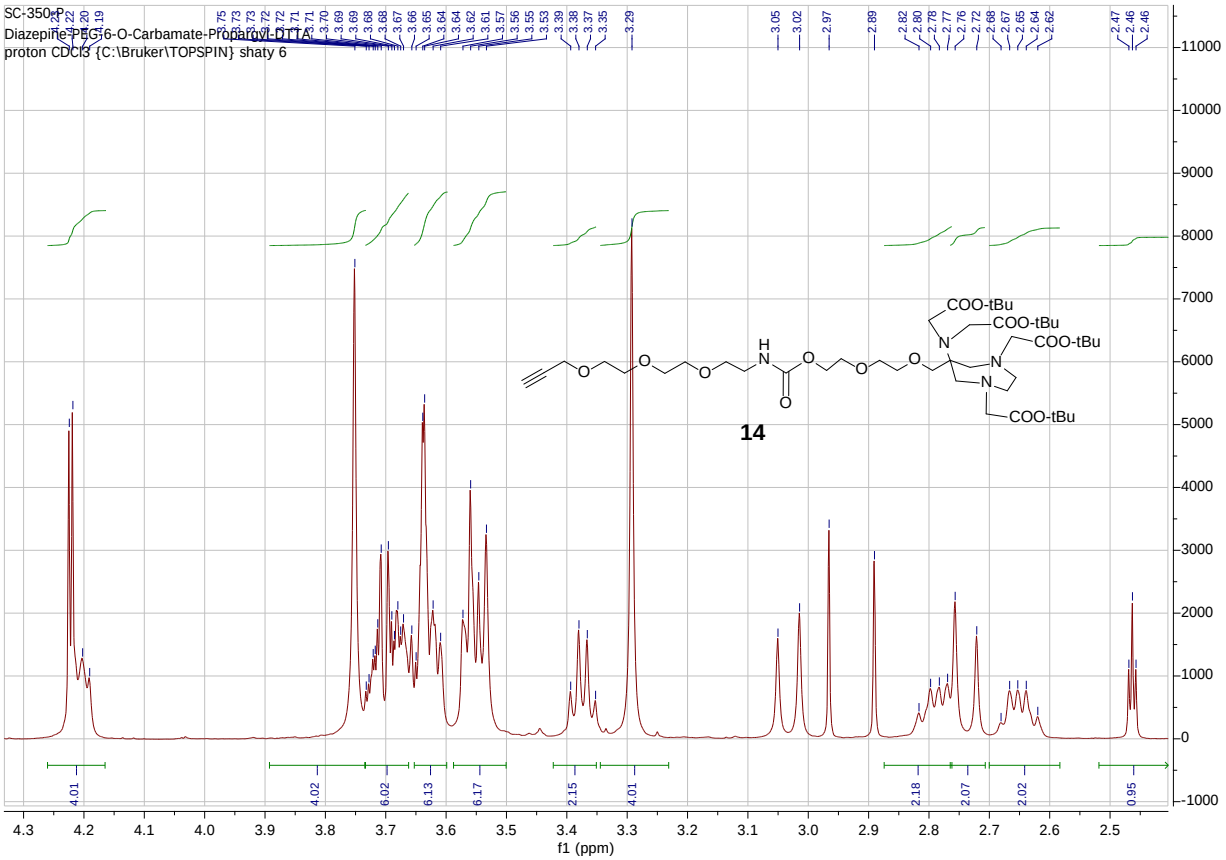

SC-351-P
Diazepine-PEG-3-O-(5-Hexynoate)-DTTA
C13 CDCl3 {C:\Bruker\TOPSPIN\}/shaty 1
173.92
171.27
171.84
84.57
81.54
81.16
75.40
71.20
70.76
69.72
64.55
63.16
62.96
59.80
52.27
40.21
35.75
29.02
28.98
25.17
18.79
COO-tBu
COO-tBu
COO-tBu
COO-tBu
H
N
O
O
N
N
O
13
f1 (ppm)

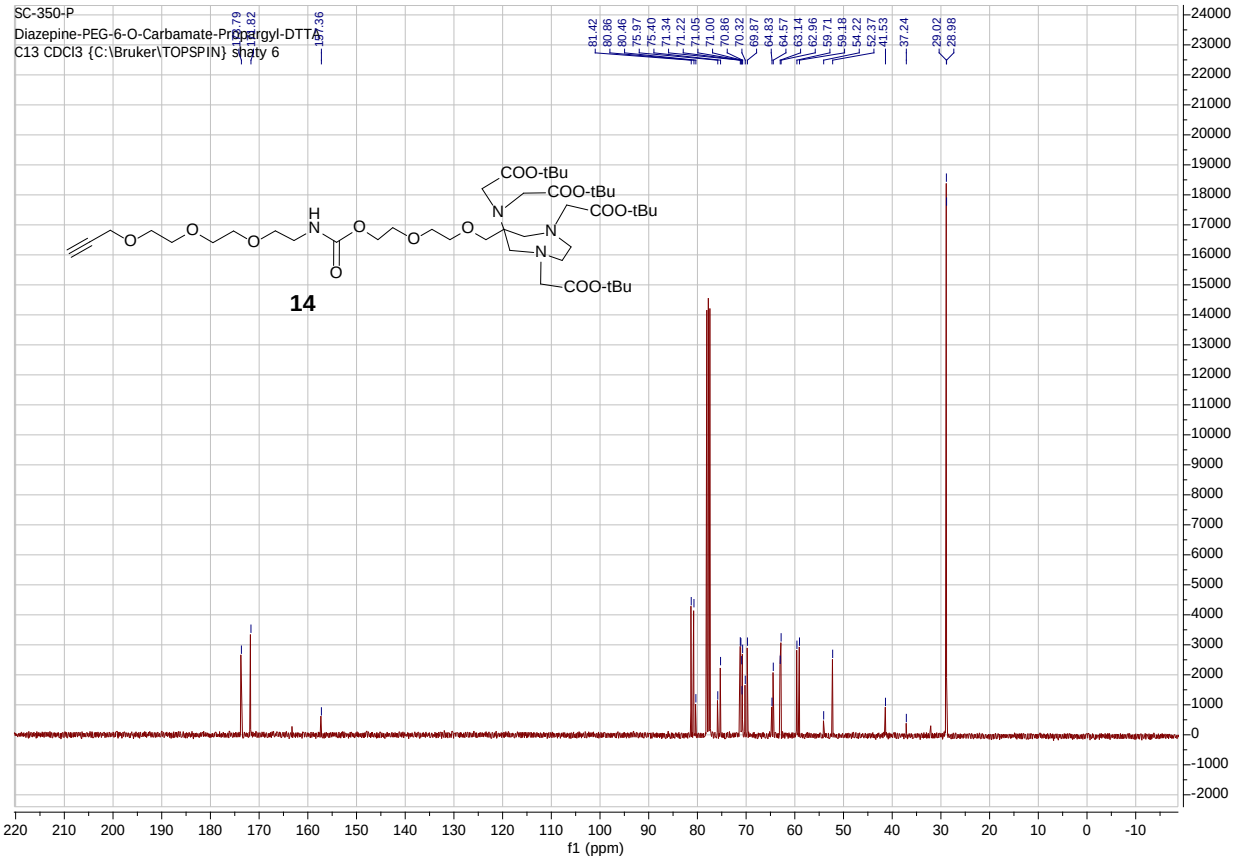
Applied Biosystems Mariner System 5268



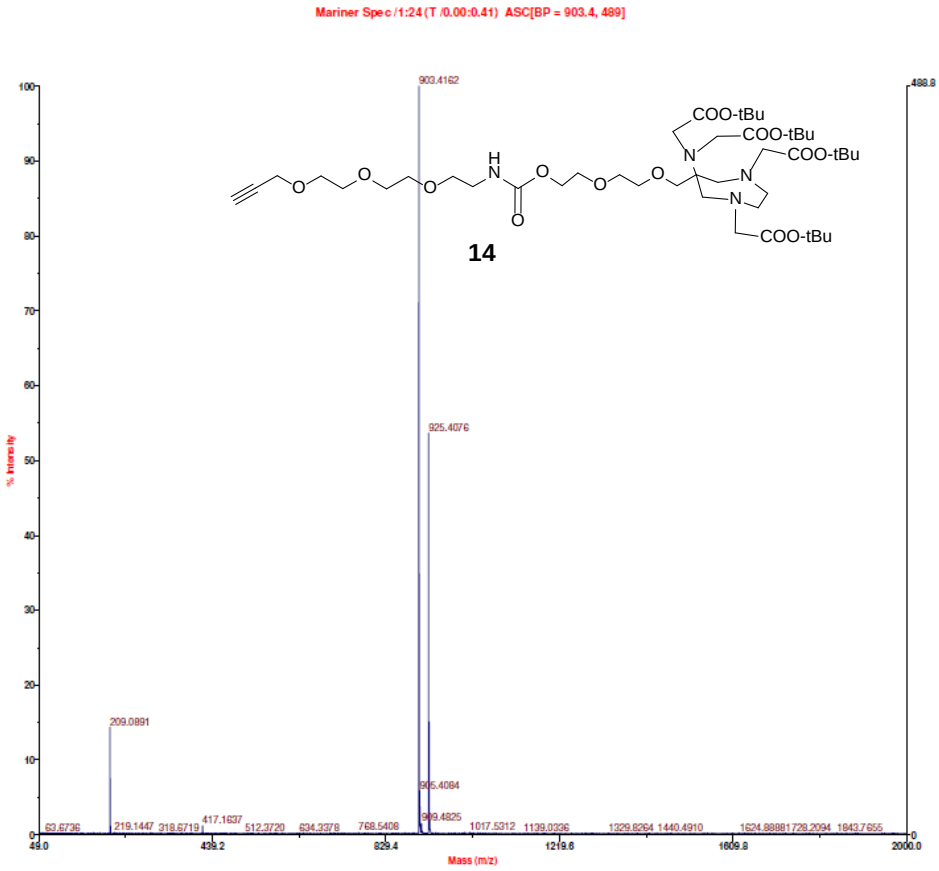
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0146867E-007
Calibration Constant B	77.798312
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-350-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DTTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 6
COO-tBu
COO-tBu
COO-tBu
COO-tBu
14
f1 (ppm)

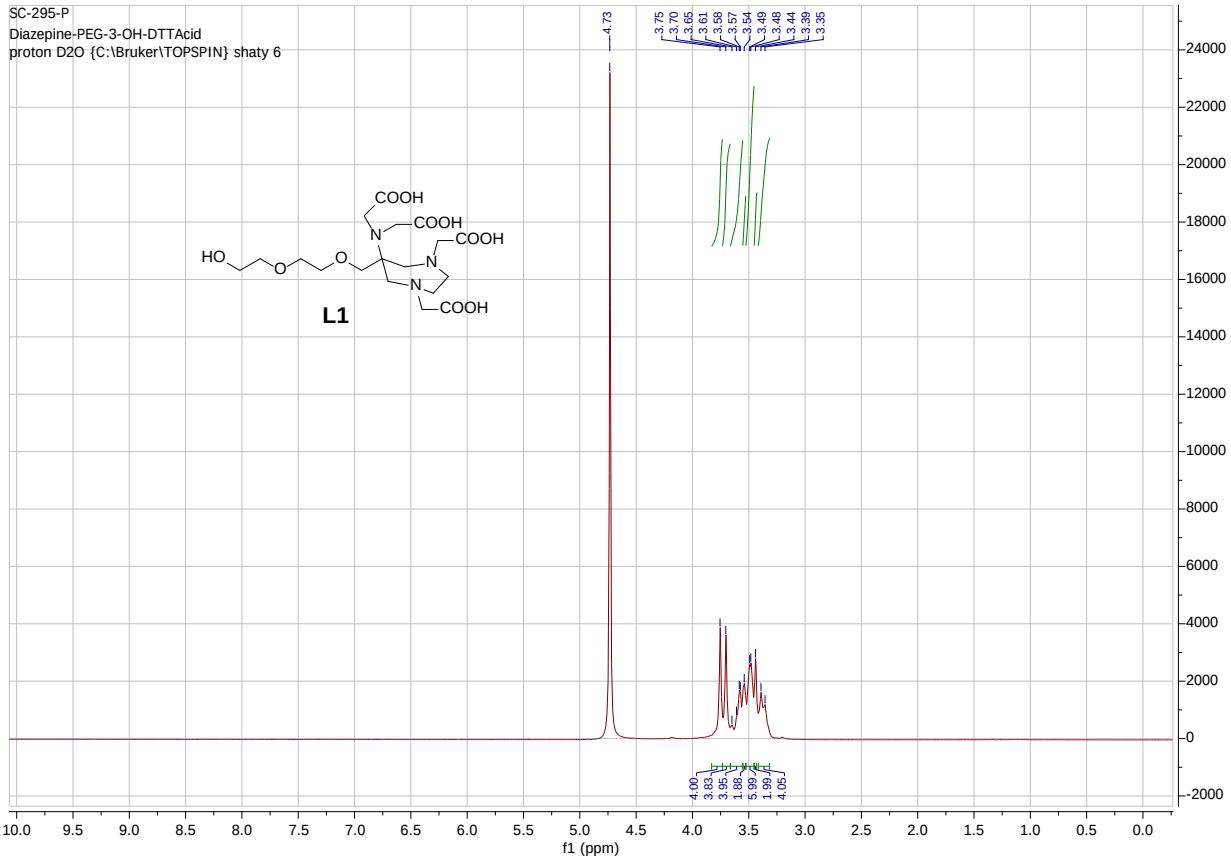

SC-350-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DOTA
proton CDCl3 {C:\Bruker\TOPSPIN} shaty 6
COO-tBu
COO-tBu
COO-tBu
COO-tBu
14
f1 (ppm)

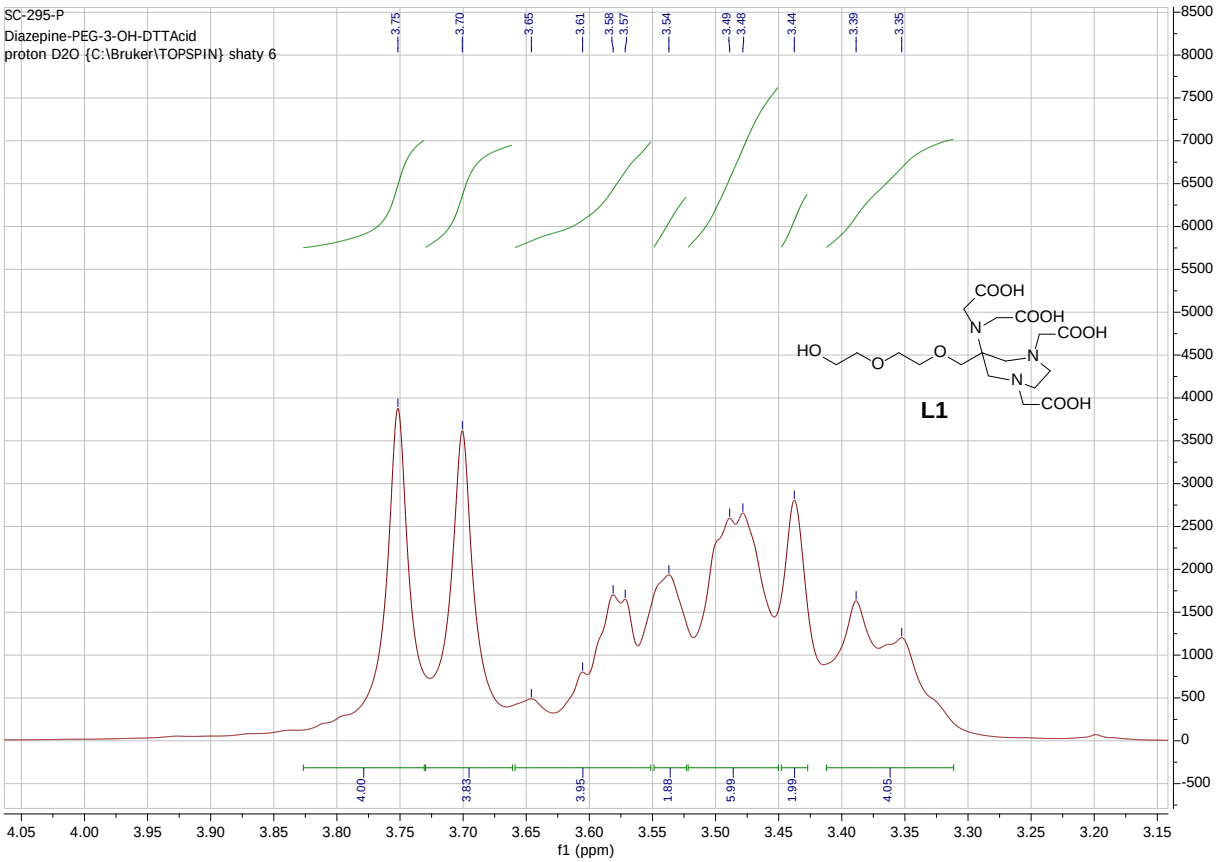

SC-350-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DTTA
C13 CDCl3 {C:\Bruker\TOPSPIN} shaty 6
167.79
161.82
137.36
81.42
80.86
80.46
75.97
75.40
71.34
71.22
71.05
71.00
70.86
70.32
69.87
64.83
64.57
63.14
62.96
59.71
59.18
54.22
52.37
41.53
37.24
29.02
28.98
COO-tBu
COO-tBu
COO-tBu
COO-tBu
14
f1 (ppm)

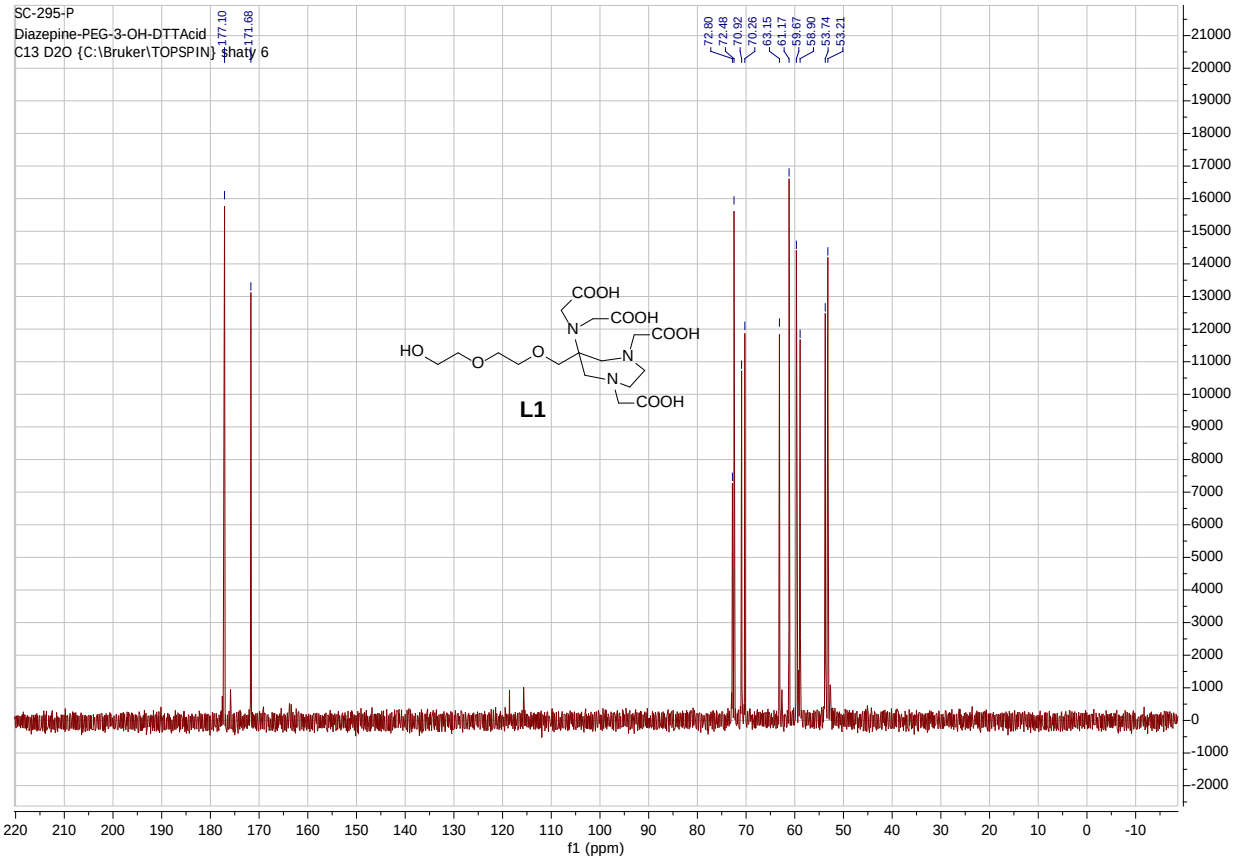
Applied Biosystems Mariner System 5268



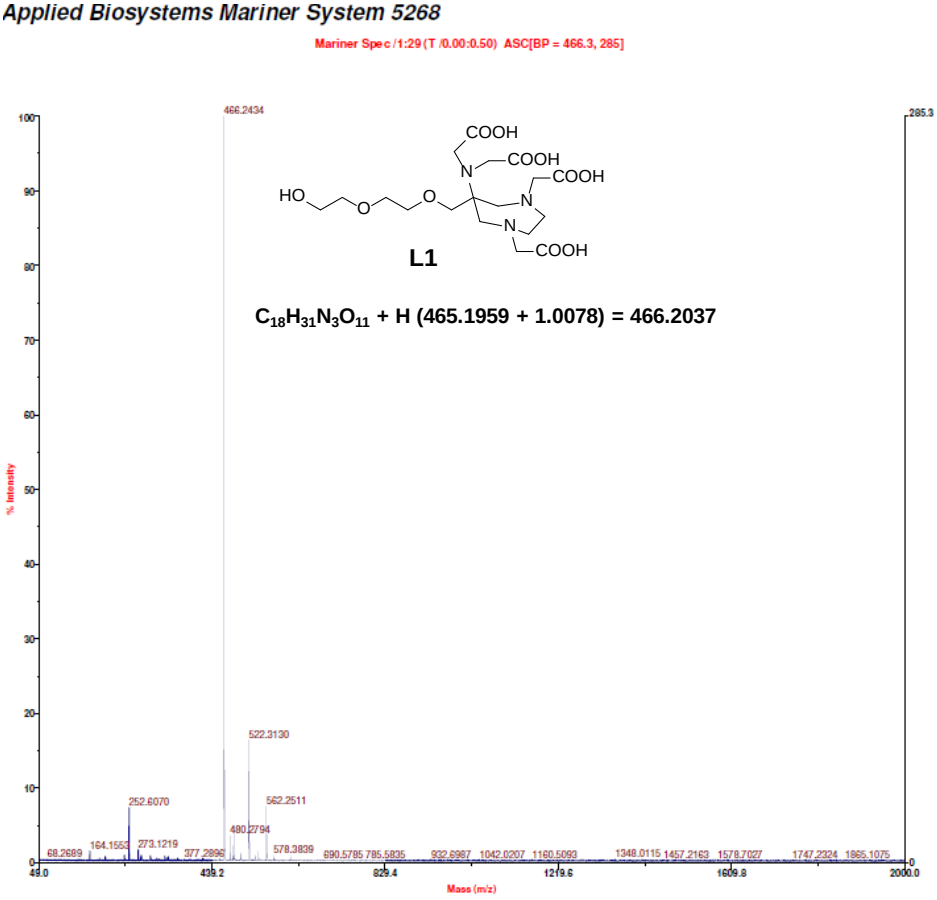
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0146867E-00
Calibration Constant B	77.798312
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-295-P
Diazepine-PEG-3-OH-DTTAcid
proton D2O {C:\Bruker\TOPSPIN} shaty 6
4.73
3.75
3.70
3.65
3.61
3.58
3.57
3.54
3.49
3.48
3.44
3.39
3.35
COOH
COOH
COOH
COOH
HO
O
O
N
N
N
L1
4.00
3.83
3.95
1.88
5.99
1.99
4.05
f1 (ppm)


SC-295-P
Diazepine-PEG-3-OH-DTTAcid
proton D2O {C:\Bruker\TOPSPIN} shaty 6
3.75
3.70
3.65
3.61
3.58
3.57
3.54
3.49
3.48
3.44
3.39
3.35
COOH
COOH
COOH
COOH
HO
O
O
N
N
N
L1
4.00
3.83
3.95
1.88
5.99
1.99
4.05
f1 (ppm)


SC-295-P
Diazepine-PEG-3-OH-DTTAcid
C13 D2O {C:\Bruker\TOPSPIN} shaty 6
177.10
171.68
72.80
72.48
70.92
70.26
63.15
61.17
59.67
58.90
53.74
53.21
HO
O
O
N
N
N
COOH
COOH
COOH
COOH
L1
f1 (ppm)

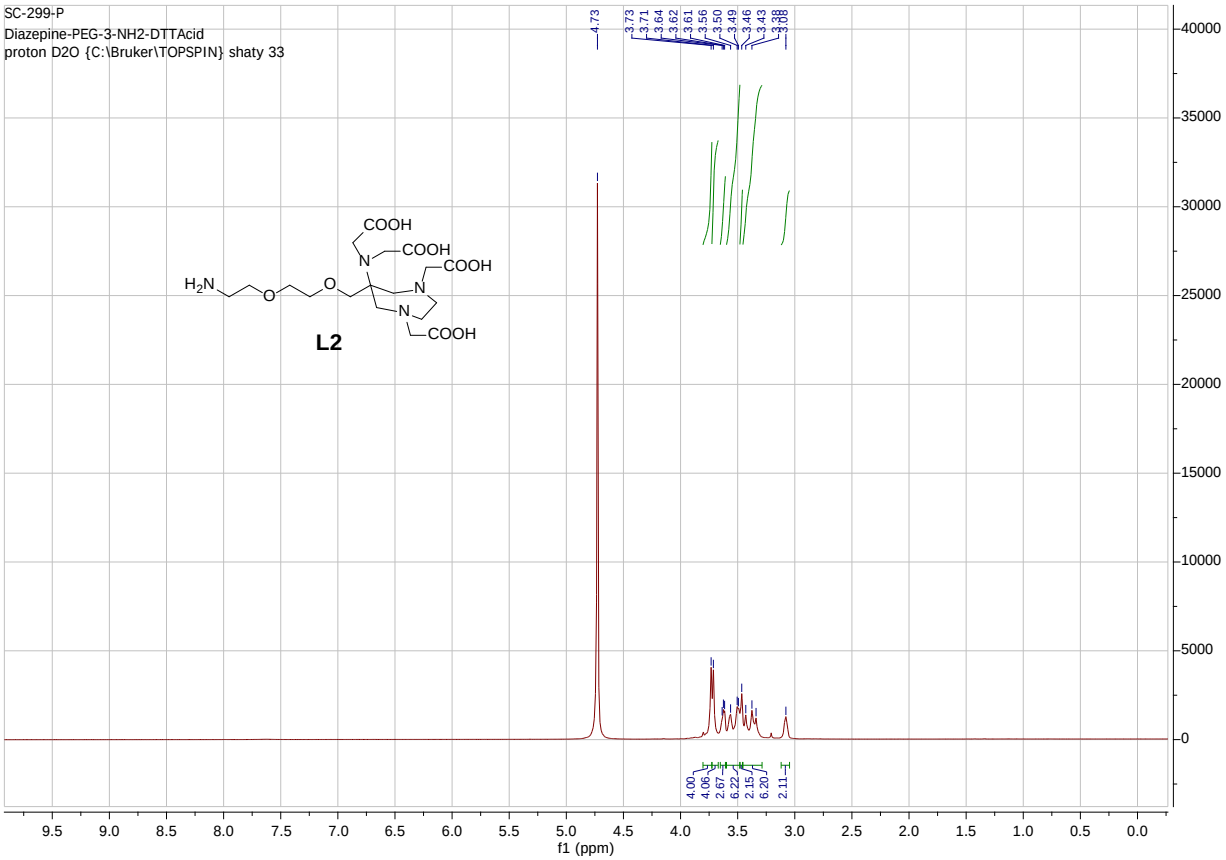
Applied Biosystems Mariner System 5268

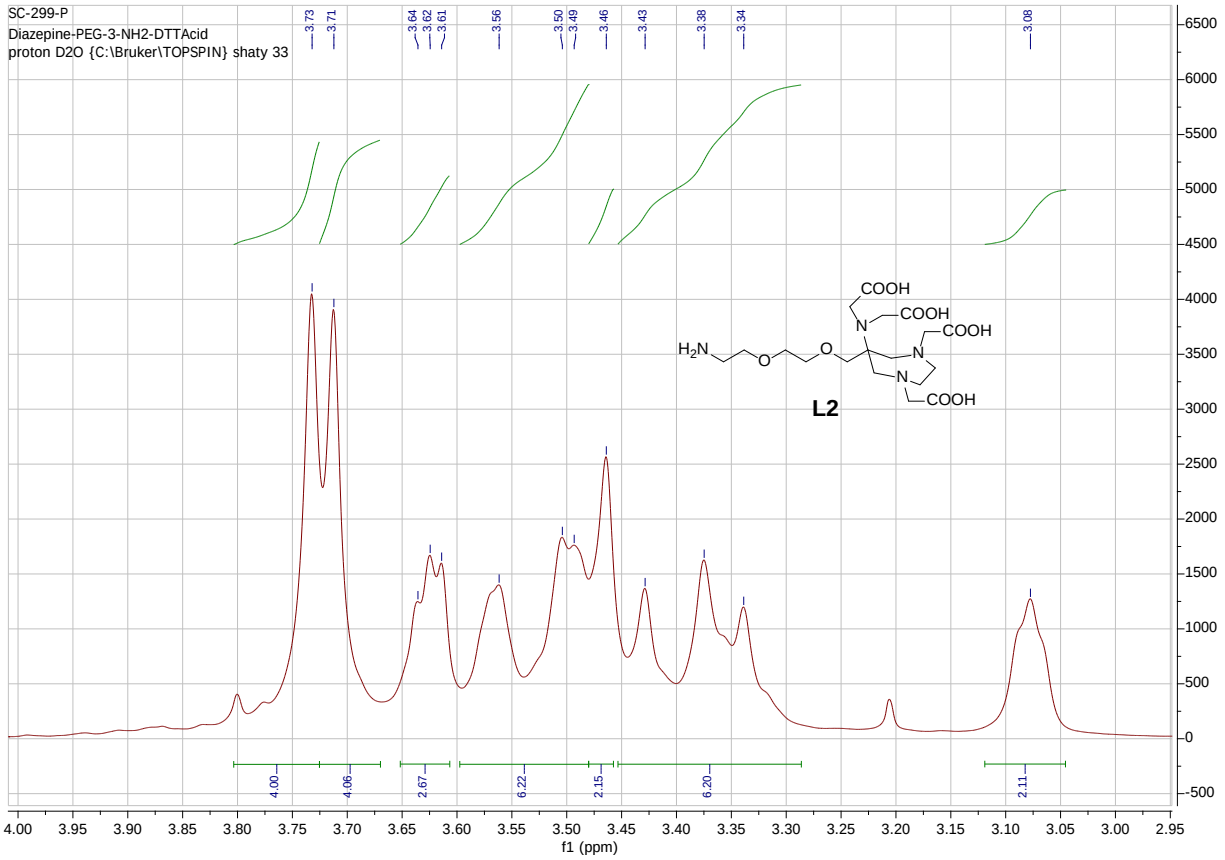


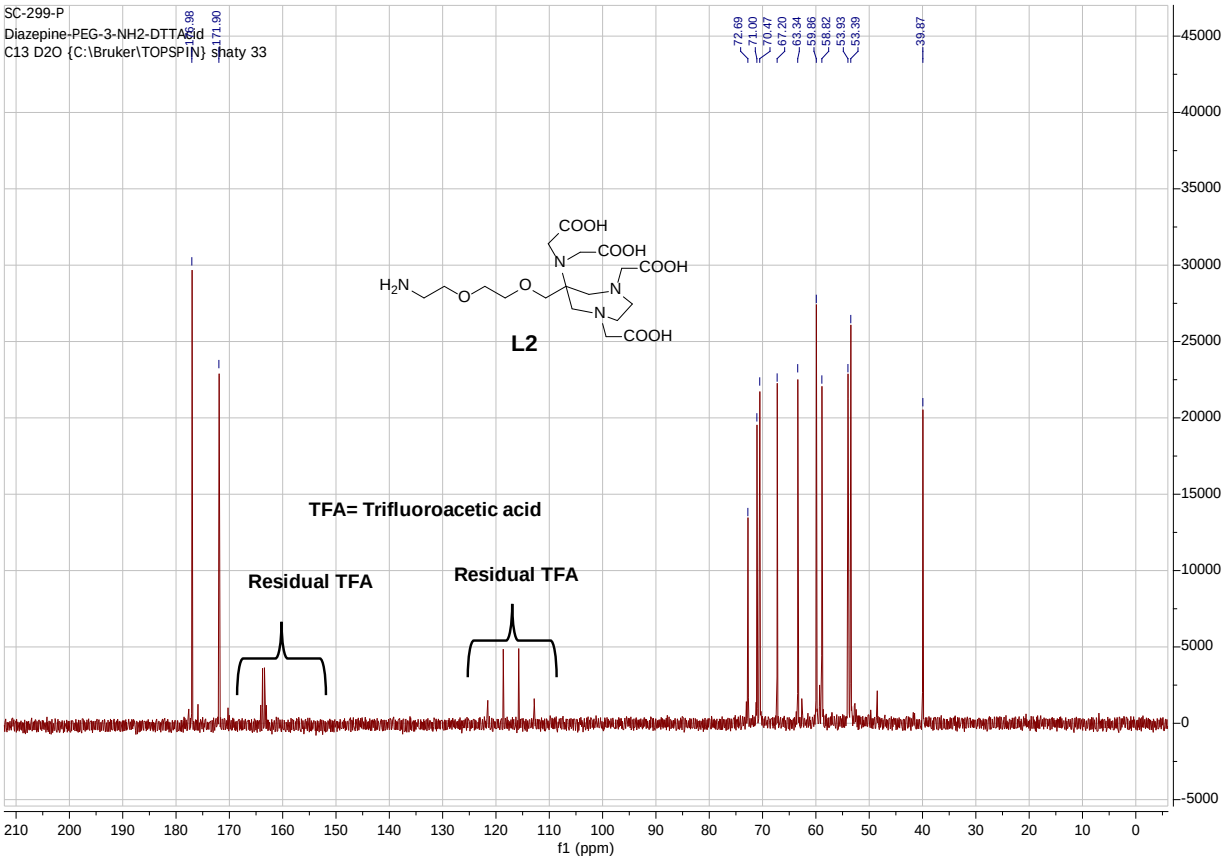
L1

$C_{18}H_{31}N_3O_{11}$ + H (465.1959 + 1.0078) = 466.2037

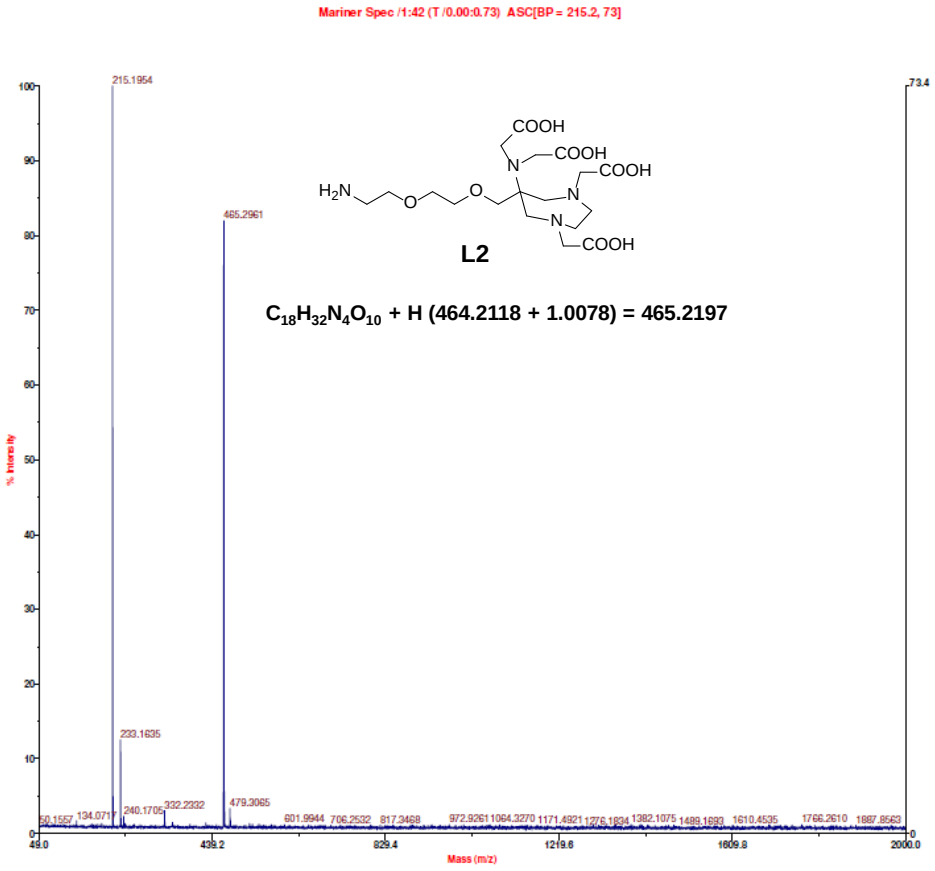
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0174991E-007
Calibration Constant B	78.221559
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	120.12
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.89
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-299-P
Diazepine-PEG-3-NH2-DTTAcid
proton D2O {C:\Bruker\TOPSPIN} shaty 33
L2
f1 (ppm)


SC-299-P
Diazepine-PEG-3-NH2-DTTAcid
proton D2O {C:\Bruker\TOPSPIN} shaty 33
3.73
3.71
3.64
3.62
3.61
3.56
3.50
3.49
3.46
3.43
3.38
3.34
3.08
COOH
COOH
COOH
COOH
N
N
N
O
O
H2N
L2
4.00
4.06
2.67
6.22
2.15
6.20
2.11
f1 (ppm)


SC-299-P
Diazepine-PEG-3-NH2-DTTAcid
C13 D2O {C:\Bruker\TOPSPIN} shaty 33
171.98
171.90
72.69
71.00
70.47
67.20
63.34
59.86
58.82
53.93
53.39
39.87
COOH
COOH
COOH
COOH
N
N
N
O
O
H_2N
L2
TFA= Trifluoroacetic acid
Residual TFA
Residual TFA
f1 (ppm)

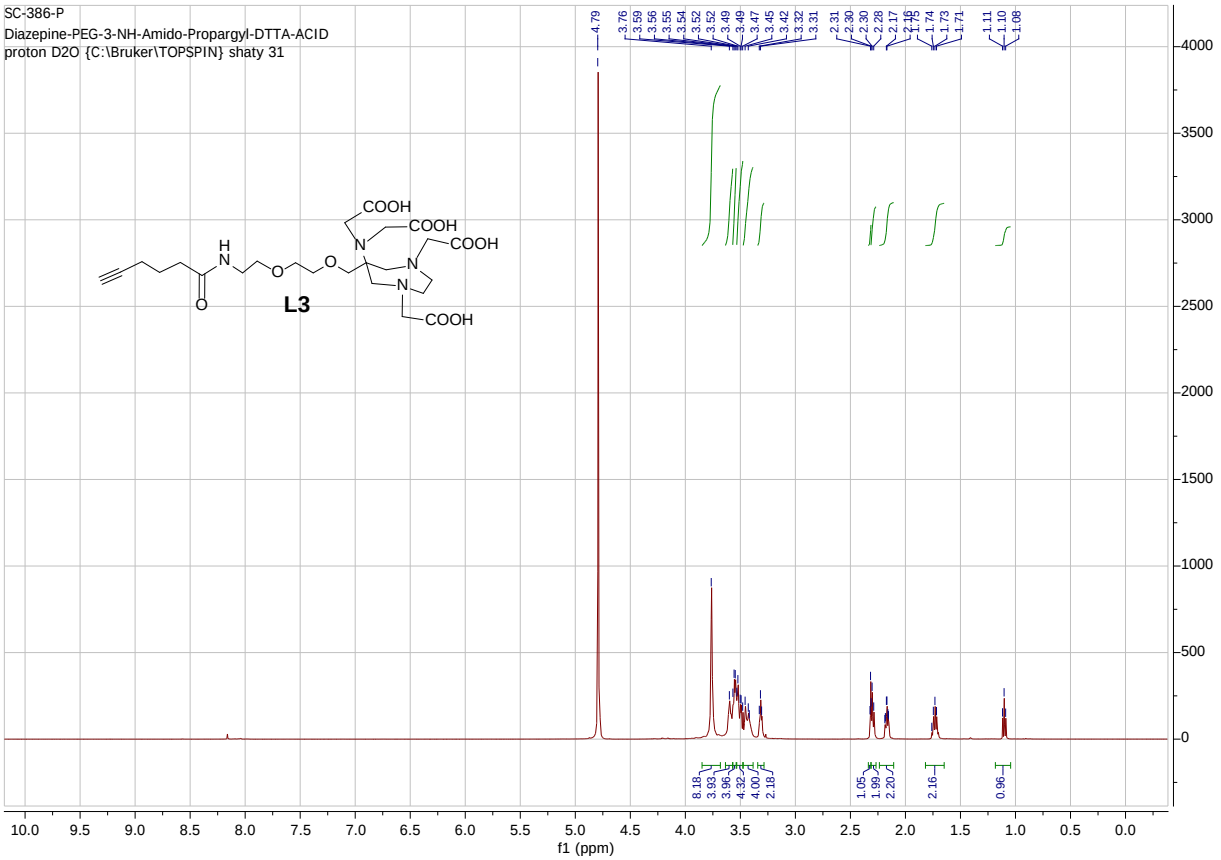
Applied Biosystems Mariner System 5268

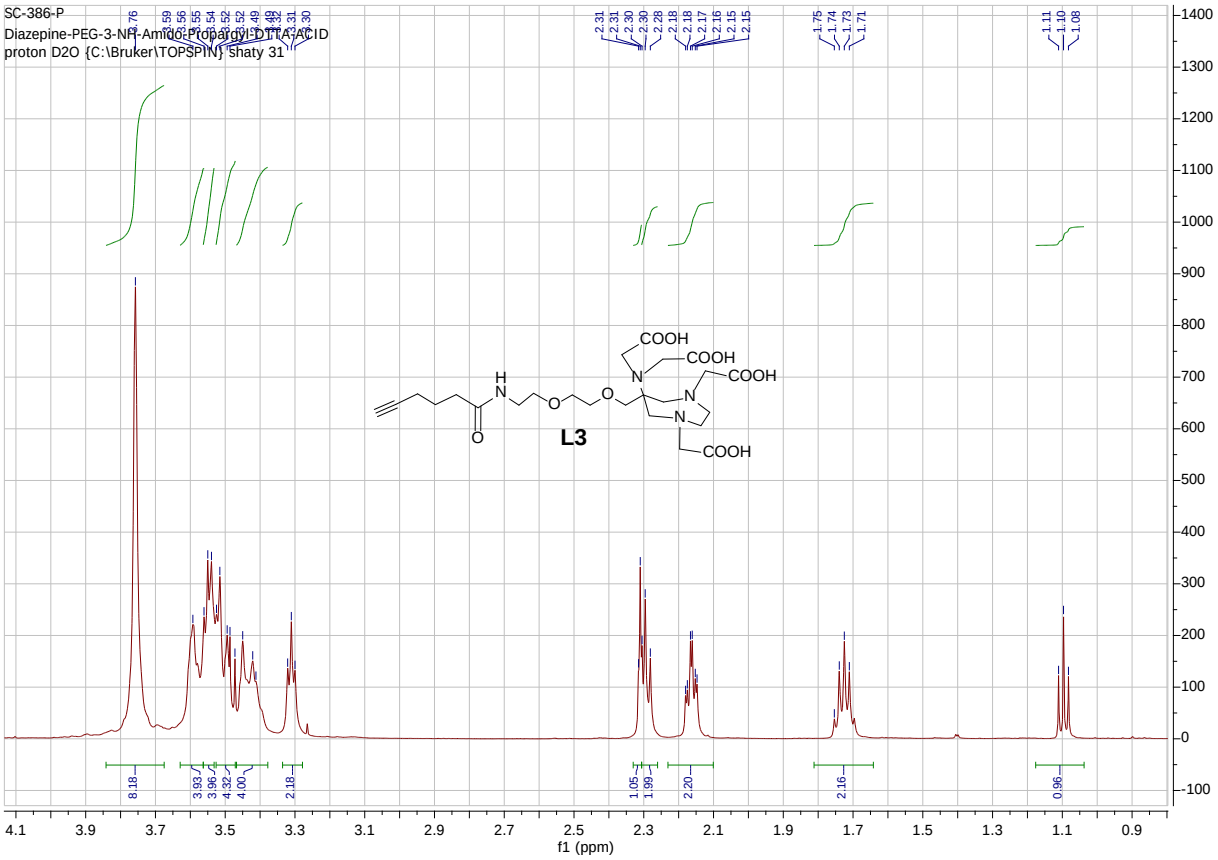


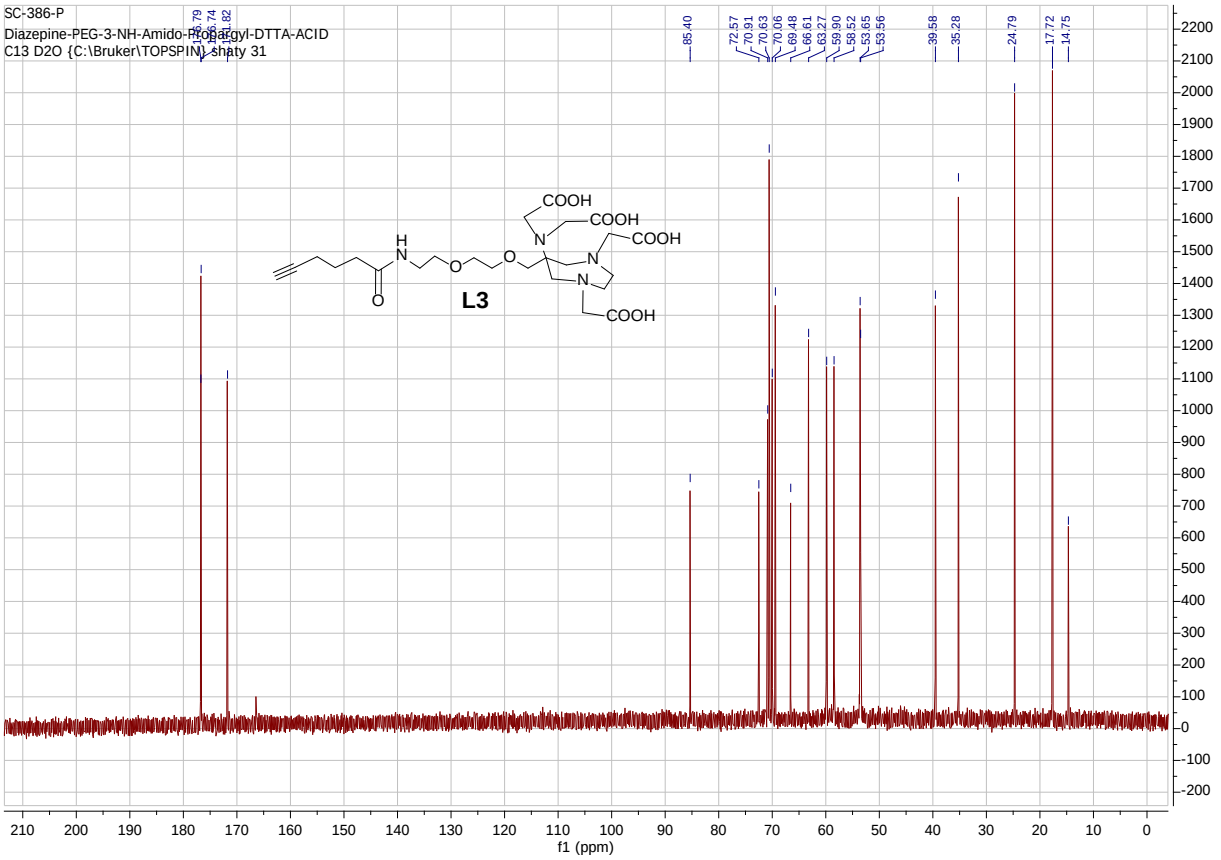
L2

$C_{18}H_{32}N_4O_{10}$ + H (464.2118 + 1.0078) = 465.2197

--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0174991E-00
Calibration Constant B	78.221559
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	120.12
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

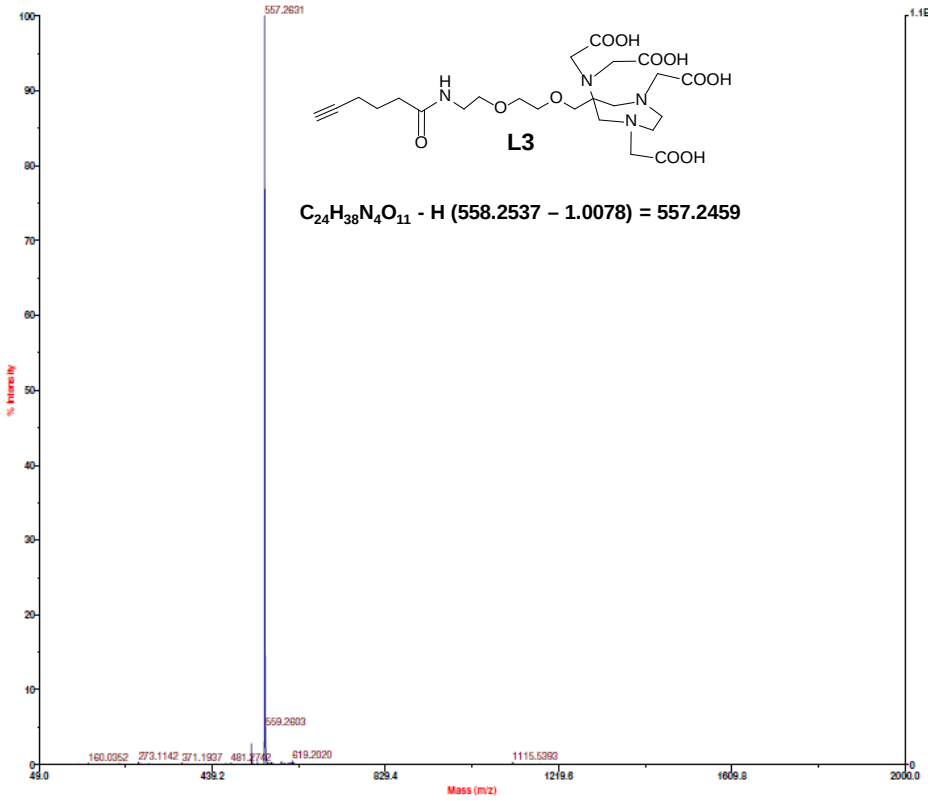

SC-386-P
Diazepine-PEG-3-NH-Amido-Propargyl-DTTA-ACID
proton D2O {C:\Bruker\TOPSPIN} shaty 31
L3
f1 (ppm)


SC-386-P
Diazepine-PEG-3-NH-Amide-Propargyl-DOTA-ACID
proton D2O {C:\Bruker\TOPSPIN} shaty 31
L3
COOH
COOH
COOH
COOH
N
H
N
O
O
N
N
O
8.18
3.93
3.96
4.32
4.00
2.18
1.05
1.99
2.20
2.16
0.96
f1 (ppm)


SC-386-P
Diazepine-PEG-3-NH-Amido-Propargyl-DTTA-ACID
C13 D2O {C:\Bruker\TOPSPIN} shaty 31
85.40
72.57
70.91
70.63
70.06
69.48
66.61
63.27
59.90
58.52
53.65
53.56
39.58
35.28
24.79
17.72
14.75
COOH
COOH
COOH
COOH
N
N
N
H
N
O
O
O
L3
f1 (ppm)

Applied Biosystems Mariner System 5268

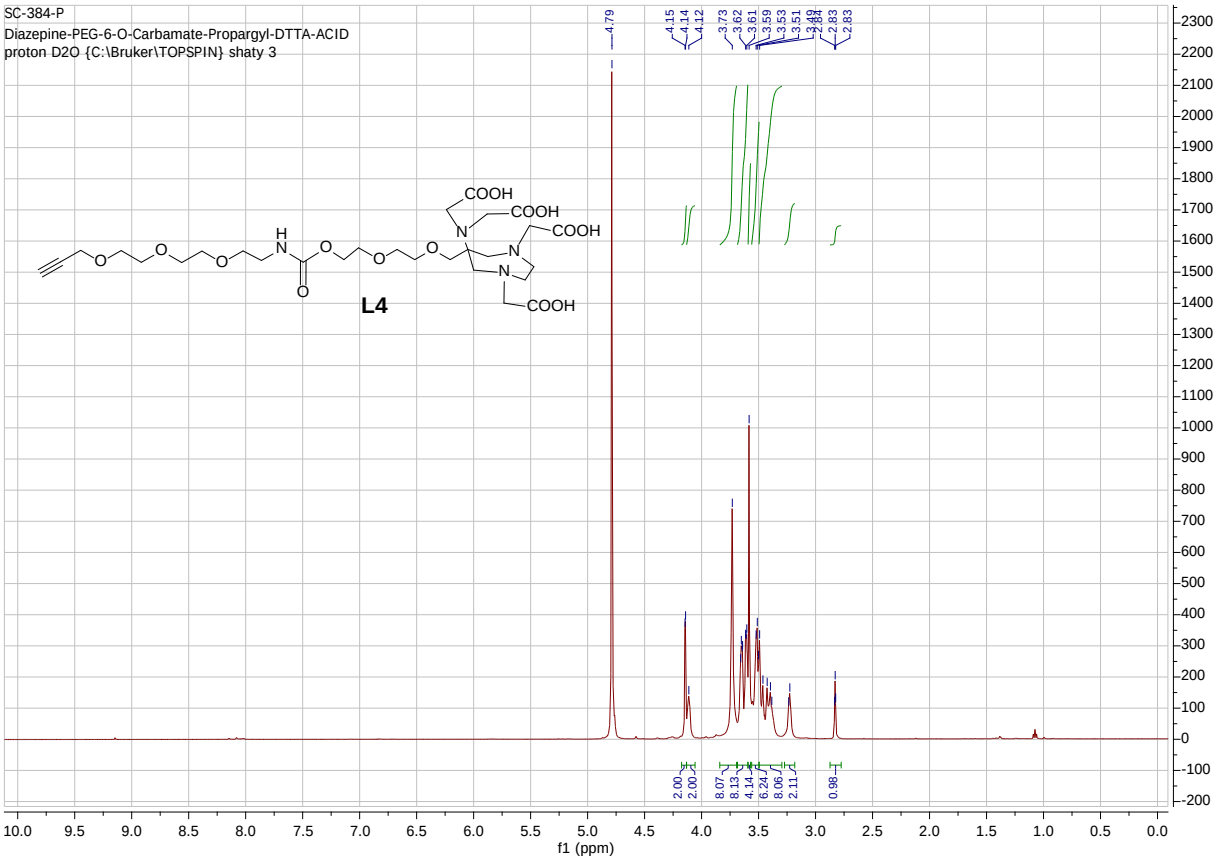
Mariner Spec /1:40 (T /0.00:0.70) ASC[BP = 557.3, 11329]

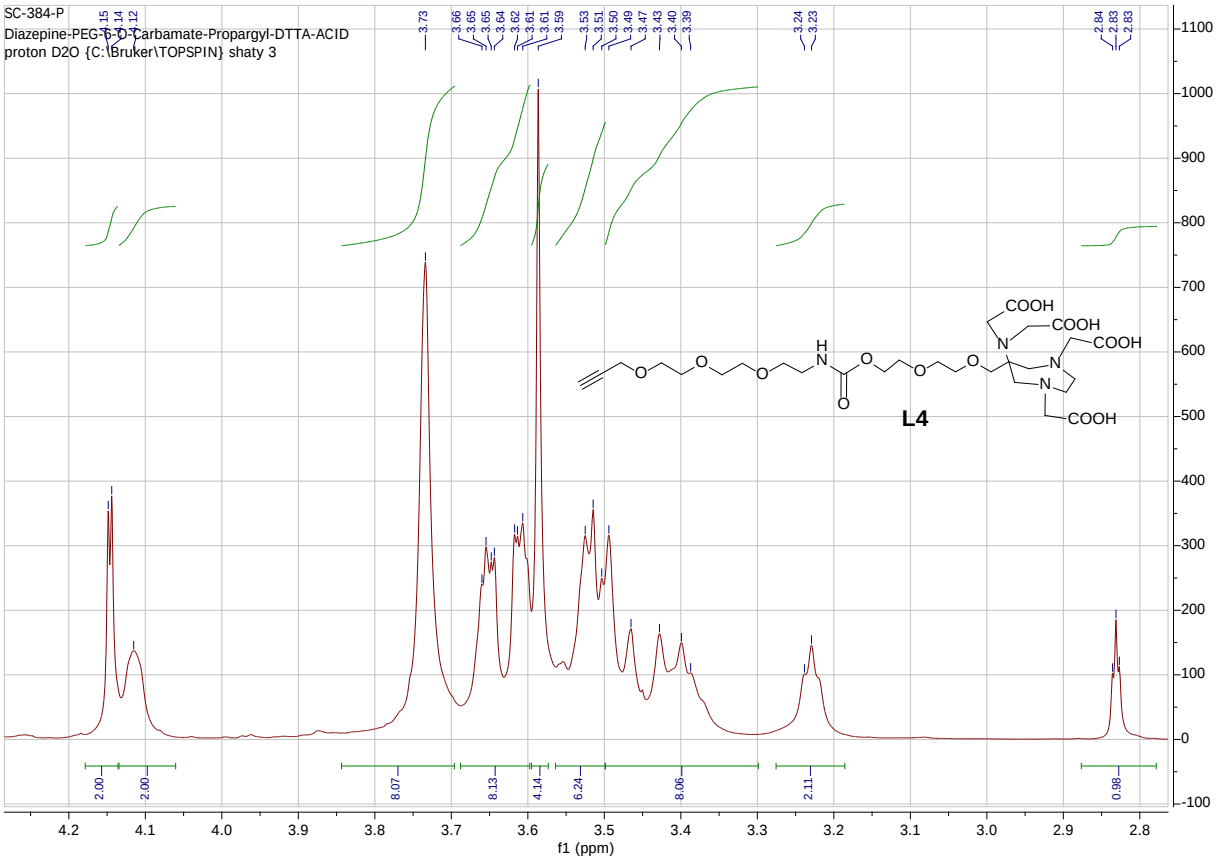


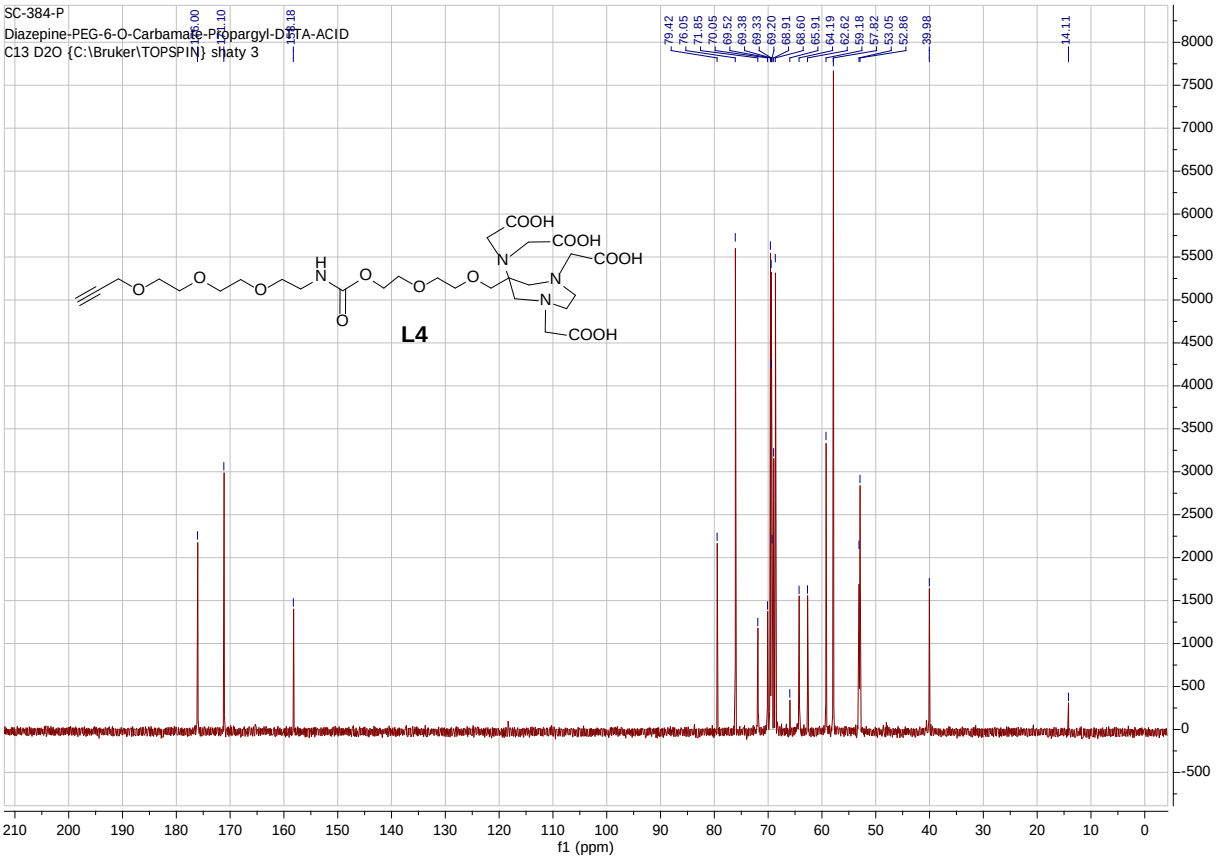
L3

$C_{24}H_{38}N_4O_{11}$ - H (558.2537 – 1.0078) = 557.2459

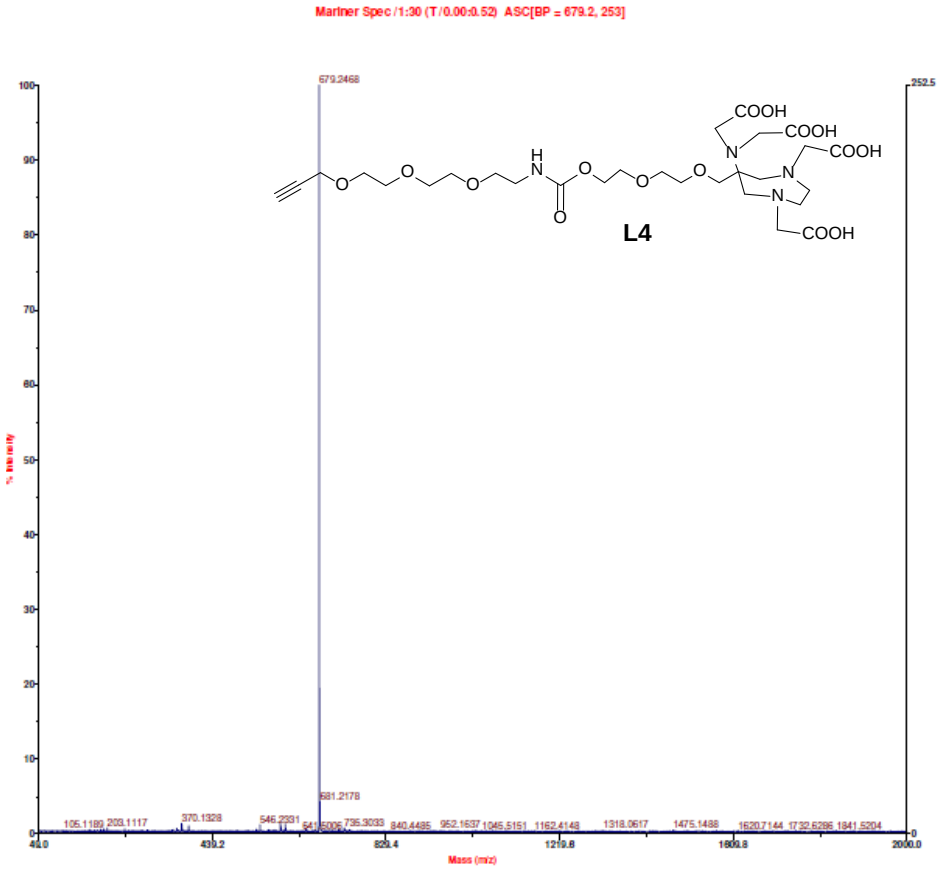
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	NEG
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0076312E-00
Calibration Constant B	75.729094
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	120.12
Skimmer 1 Potential	9.20
Quadrupole DC Potential	5.91
Deflection Voltage	-0.20
Einzel Lens Potential	-23.61
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	185.00
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.80
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1849.69
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	50.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00


SC-384-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DTTA-ACID
proton D2O {C:\Bruker\TOPSPIN} shaty 3
L4
f1 (ppm)

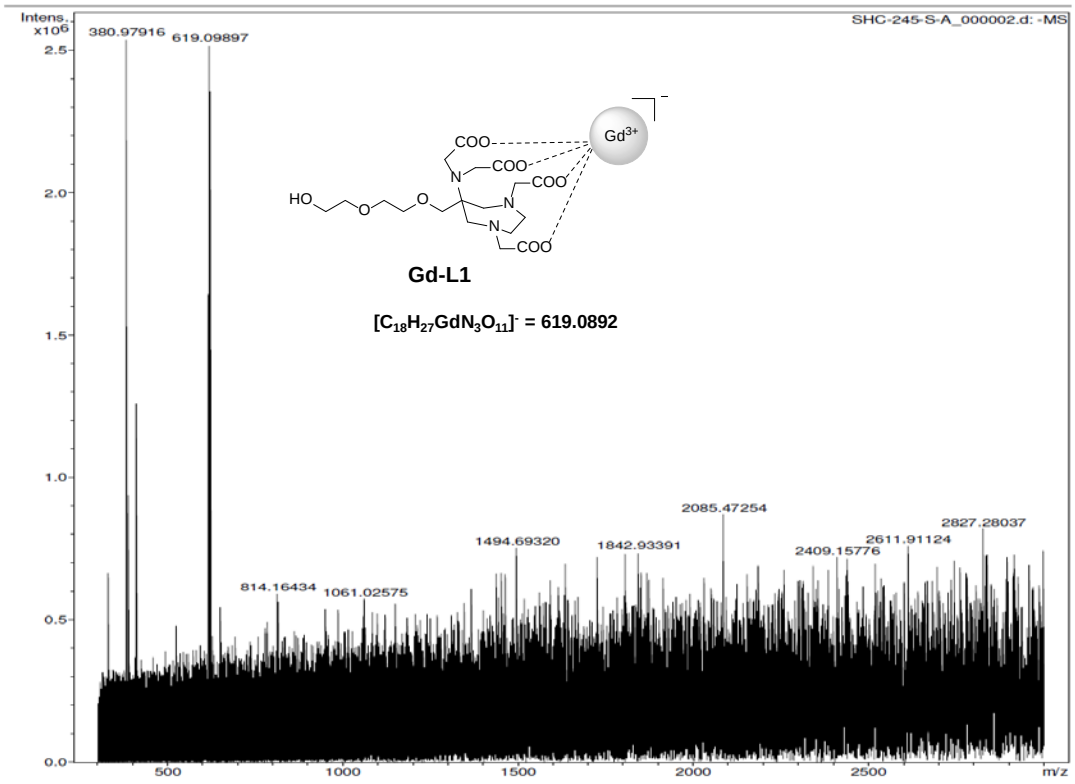

SC-384-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DTTA-ACID
proton D2O {C:\Bruker\TOPSPIN} shaty 3
L4
COOH
f1 (ppm)


SC-384-P
Diazepine-PEG-6-O-Carbamate-Propargyl-DOTA-ACID
C13 D2O {C:\Bruker\TOPSPIN} shaty 3
L4
f1 (ppm)

Applied Biosystems Mariner System 5268

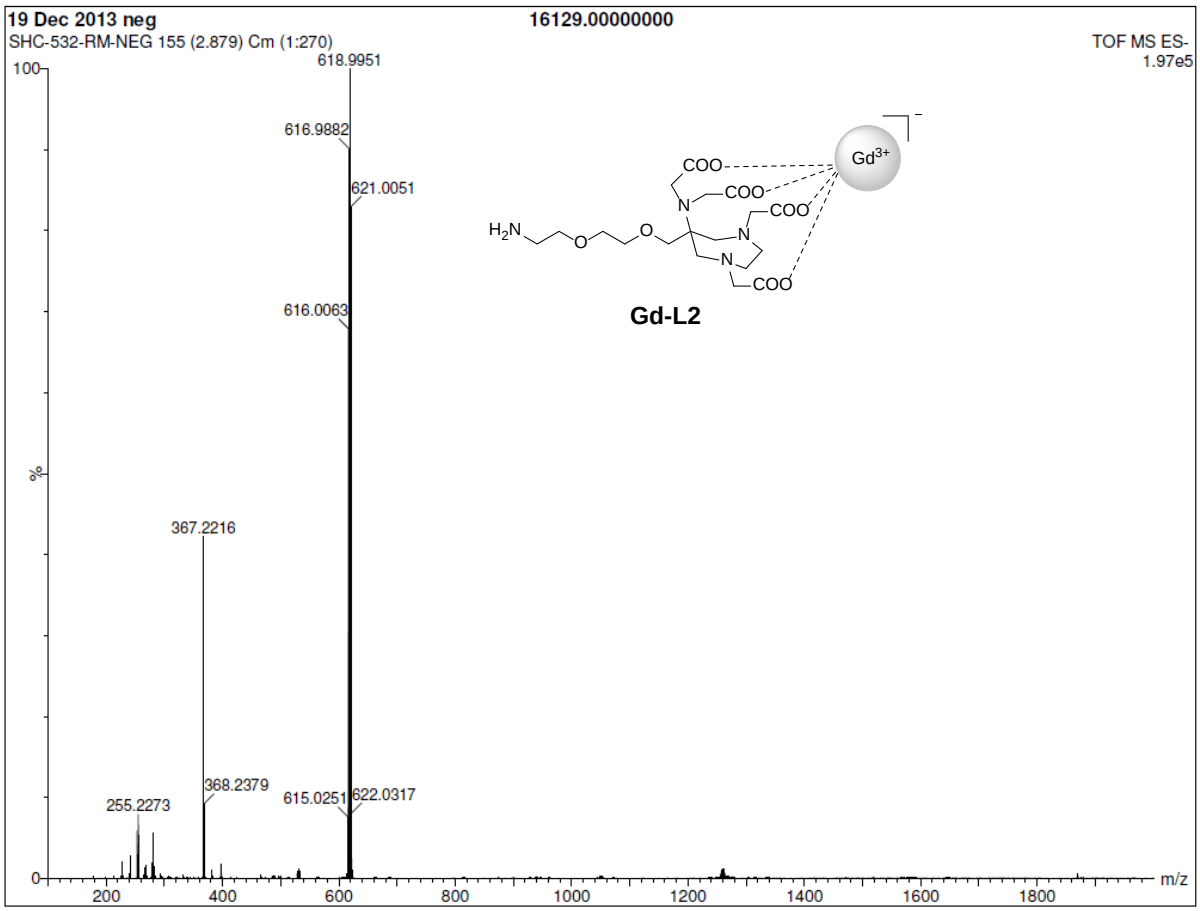


--> Mariner System State <--	
Instrument State	ON
Ion Polarity	POS
Auxiliary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0149194E-00
Calibration Constant B	78.267402
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	10.01
Quadrupole DC Potential	5.49
Deflection Voltage	0.10
Einzel Lens Potential	-24.00
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	140.01
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.00
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1700.24
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	80.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

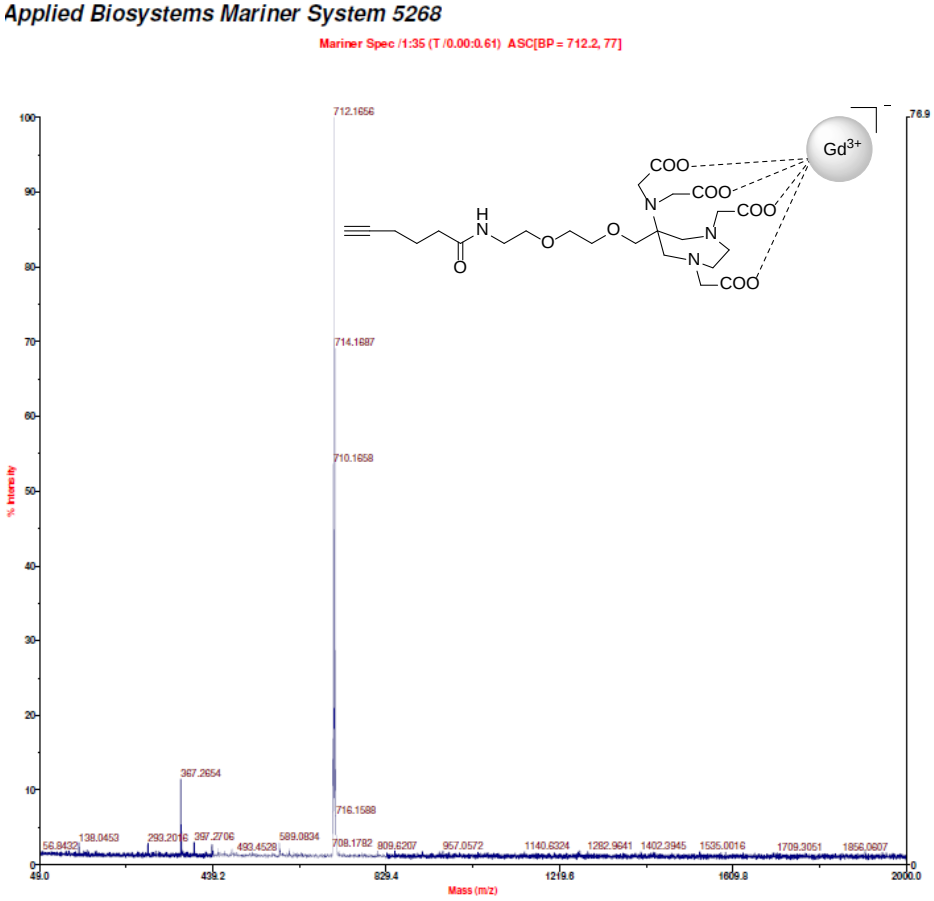


Gd-L1

$[C_{18}H_{27}GdN_3O_{11}]^-$ = 619.0892

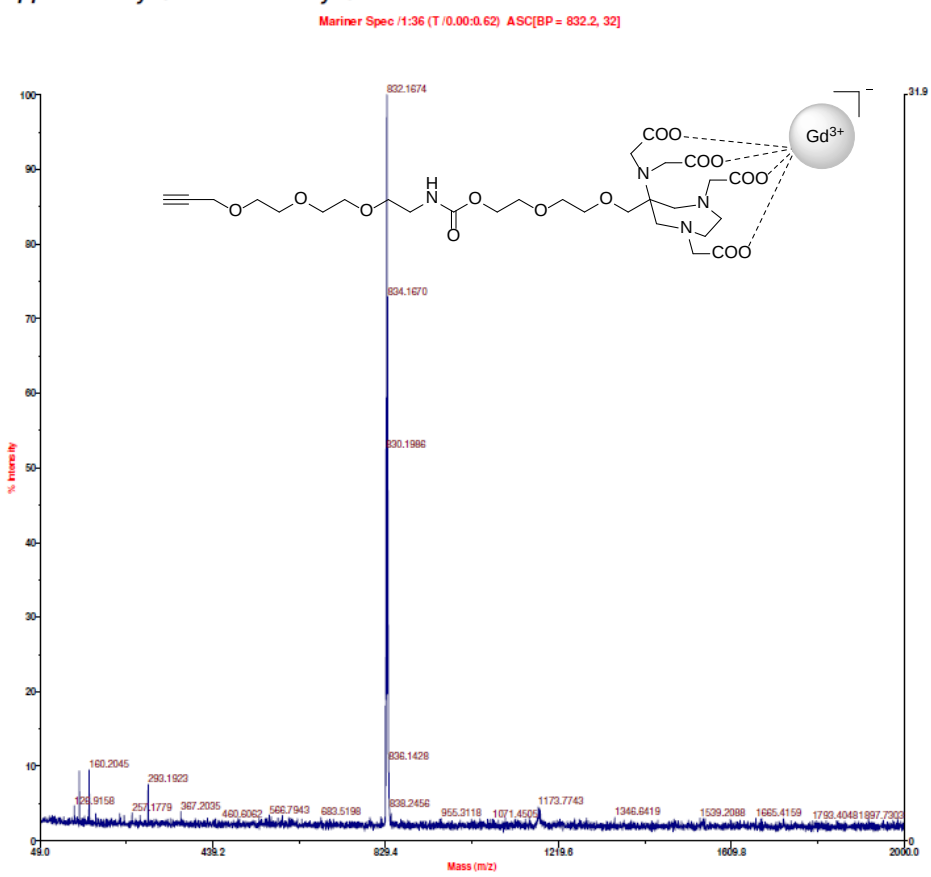

19 Dec 2013 neg
16129.00000000
SHC-532-RM-NEG 155 (2.879) Cm (1:270)
TOF MS ES-
1.97e5
100
%
0
618.9951
616.9882
621.0051
616.0063
367.2216
368.2379
255.2273
615.0251
622.0317
200
400
600
800
1000
1200
1400
1600
1800
m/z
Gd3+
COO
N
H2N
O
Gd-L2

Applied Biosystems Mariner System 5268



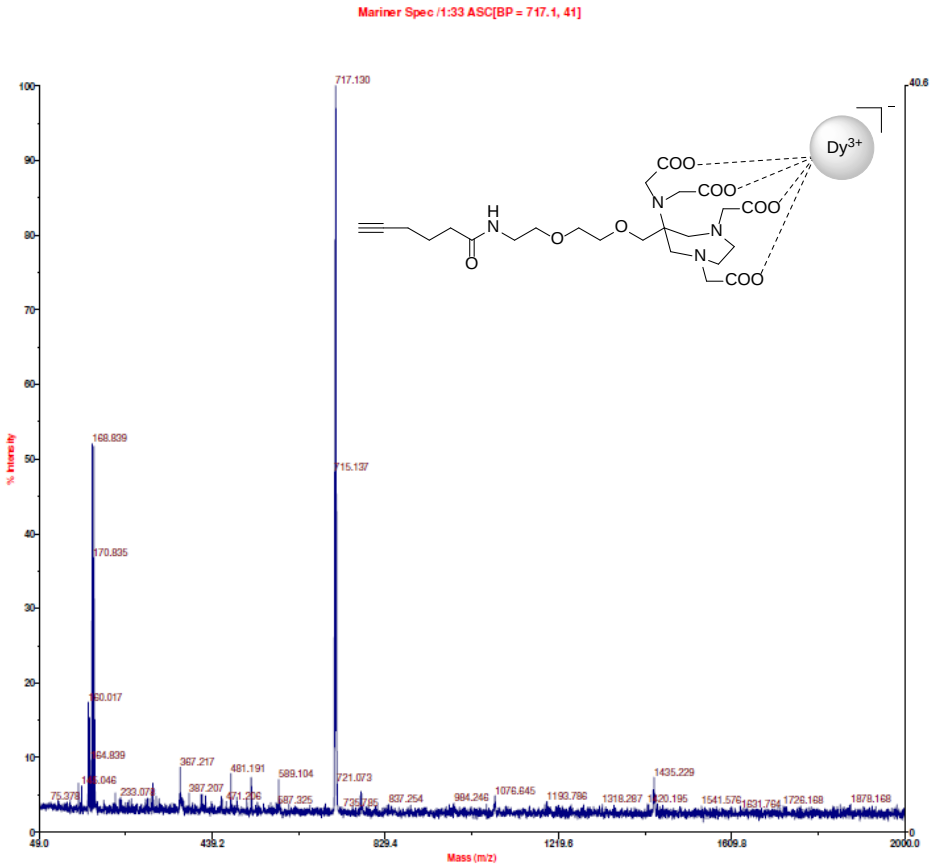
--> Mariner System State <--	
Instrument State	ON
Ion Polarity	NEG
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0076312E-007
Calibration Constant B	75.729094
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	80.08
Skimmer 1 Potential	9.20
Quadrupole DC Potential	5.91
Deflection Voltage	-0.20
Einzel Lens Potential	-23.61
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	185.00
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.80
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1849.69
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	80.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

Applied Biosystems Mariner System 5268

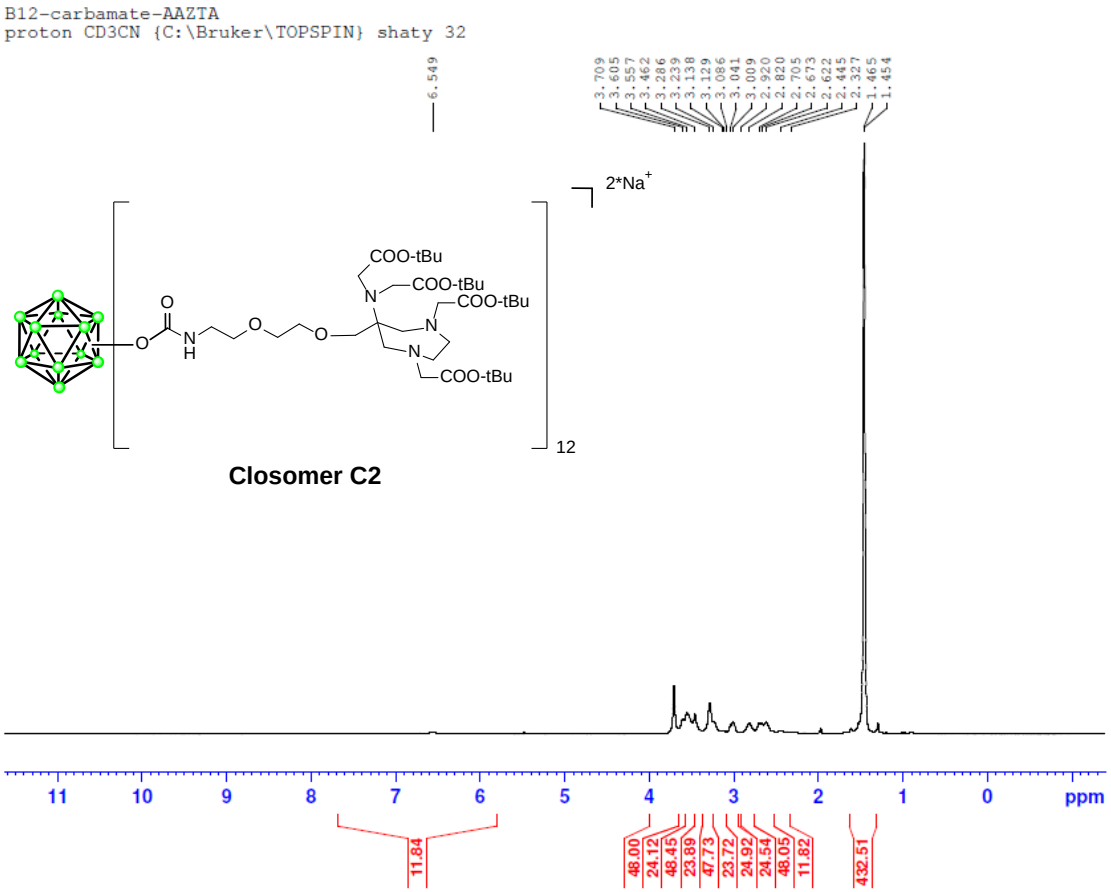


--> Mariner System State <--	
Instrument State	ON
Ion Polarity	NEG
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0076312E-007
Calibration Constant B	75.729094
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	40.04
Skimmer 1 Potential	9.20
Quadrupole DC Potential	5.91
Deflection Voltage	-0.20
Einzel Lens Potential	-23.61
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	185.00
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.80
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1849.69
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	80.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

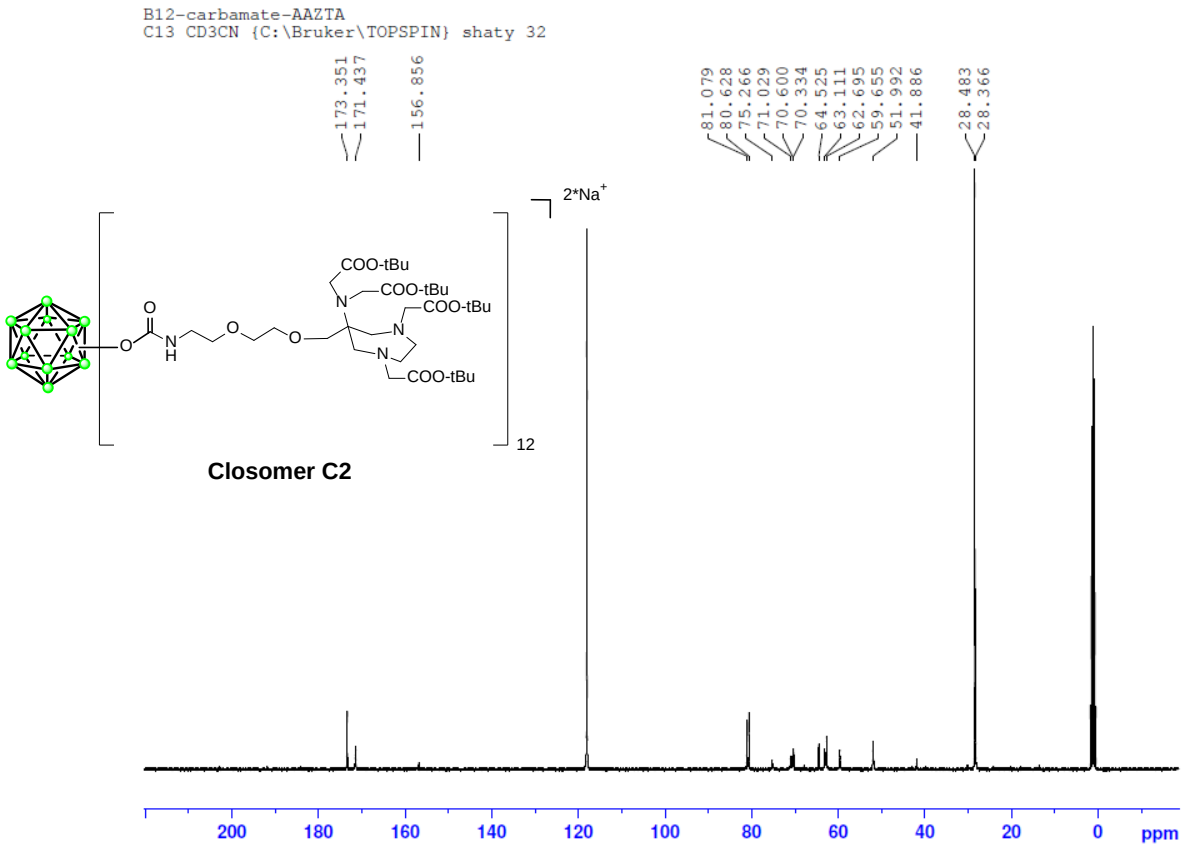
Applied Biosystems Mariner System 5219

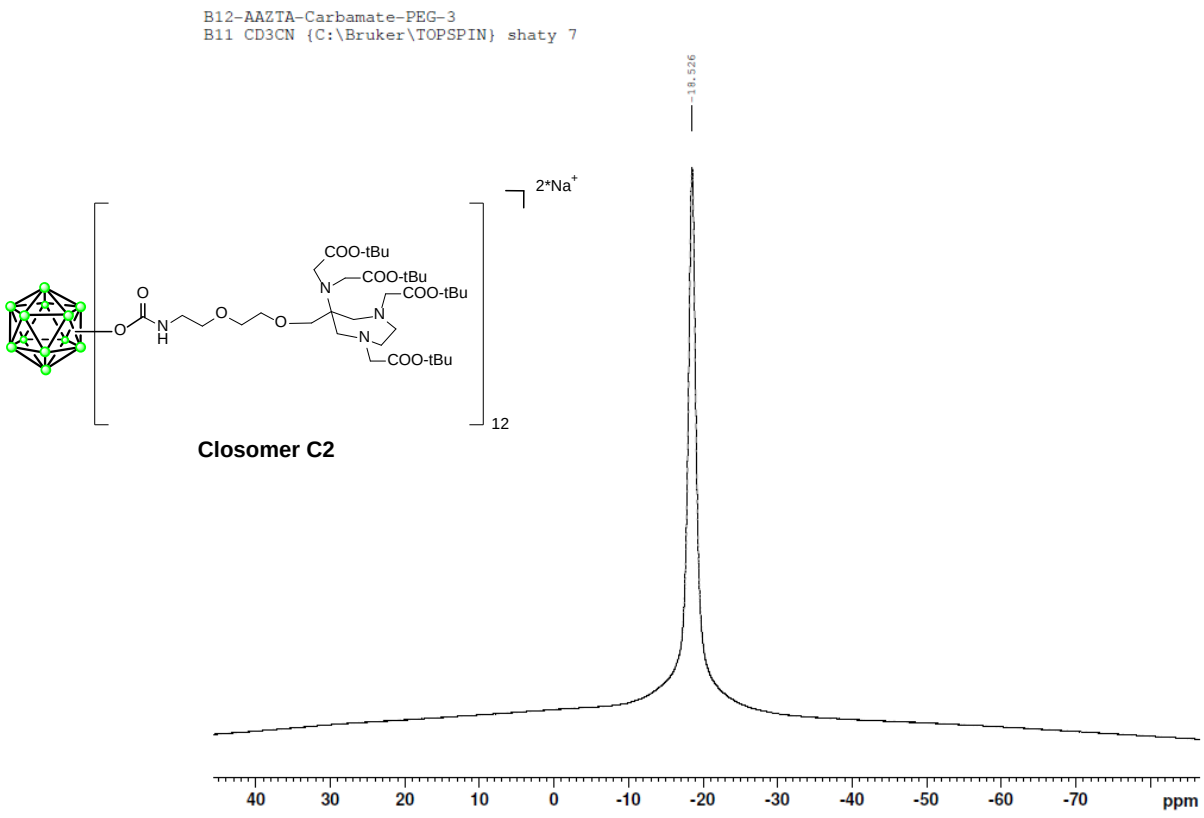


--> Mariner System State <--	
Instrument State	ON
Ion Polarity	NEG
Auxillary Gas	ON
Curtain Gas	ON
Nebulizer Gas	ON
Calibration Constant A	5.0078095E-007
Calibration Constant B	75.241693
TDC Deadtime	10
--> Source Settings <--	
Spray Tip Potential	4509.96
SCIEX Heater	300.05
--> API Interface Settings <--	
Nozzle Potential	149.90
Skimmer 1 Potential	9.20
Quadrupole DC Potential	5.91
Deflection Voltage	-0.20
Einzel Lens Potential	-23.61
Quadrupole RF Voltage	999.76
Quadrupole Temperature	140.01
Nozzle Temperature	185.00
--> Analyzer Settings <--	
Push Pulse Potential	490.00
Pull Pulse Potential	213.11
Pull Bias Potential	10.80
Acceleration Potential	3999.94
Reflector Potential	1549.99
Detector Voltage	1849.69
--> Spectrum Acquisition Settings <--	
Seconds Per Spectrum	1.00
Ion Count Threshold	0.00
First Mass	50.00
Last Mass	2000.00
Accumulate Spectra	OFF
Standby at End of Acquisition	OFF
--> Centroid Spectra Settings <--	
Centroid Spectra	OFF
--> System Settings <--	
Gas Control Mode	Manual
Syringe Pump Mode	Manual
Syringe Pump Rate	80.00
Syringe Diameter	3.26
Min Analyzer Mass	50.00
Max Analyzer Mass	4000.00

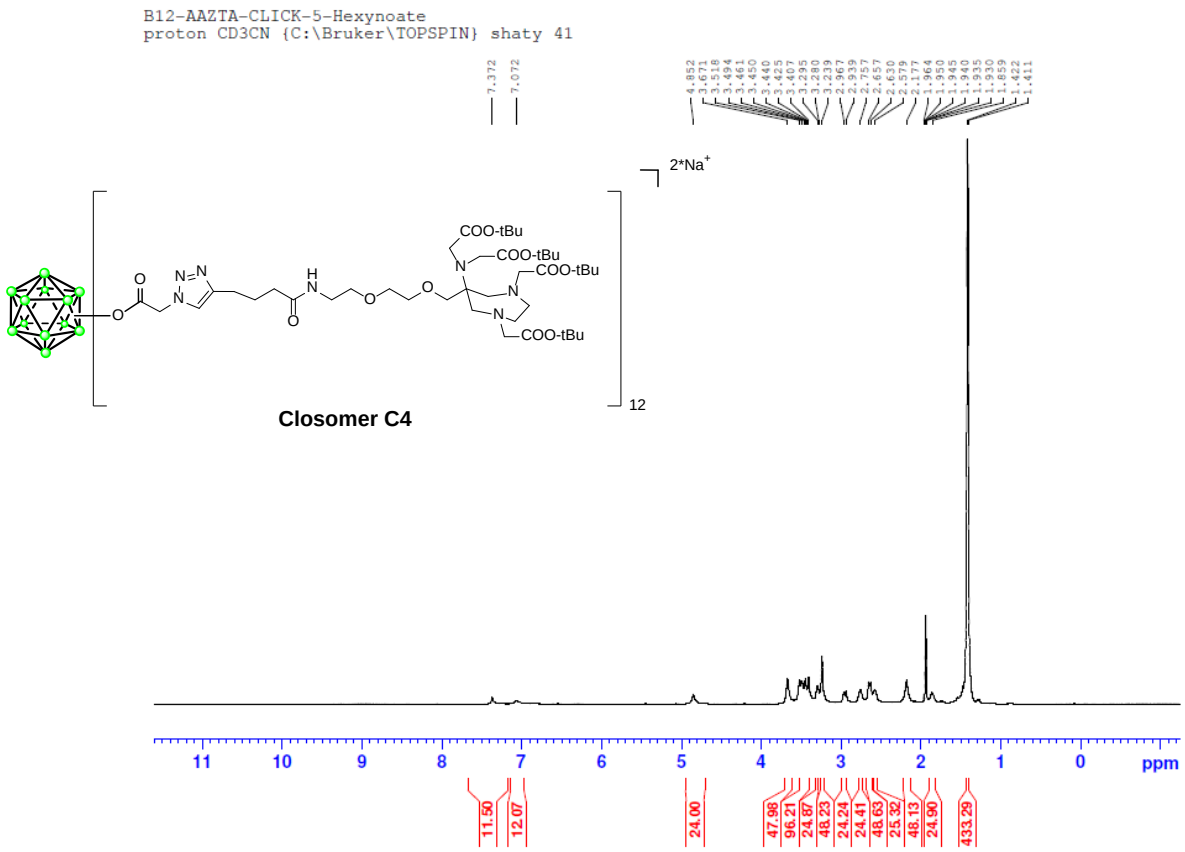

B12-carbamate-AAZTA
proton CD3CN {C:\Bruker\TOPSPIN} shaty 32
6.549
3.709
3.605
3.557
3.462
3.286
3.239
3.138
3.129
3.086
3.041
3.009
2.920
2.820
2.705
2.673
2.622
2.445
2.327
1.465
1.454
2*Na+
COO-tBu
COO-tBu
COO-tBu
COO-tBu
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
11.84
48.00
24.12
48.45
23.89
47.73
23.72
24.92
24.54
48.05
11.82
432.51

Closomer C2

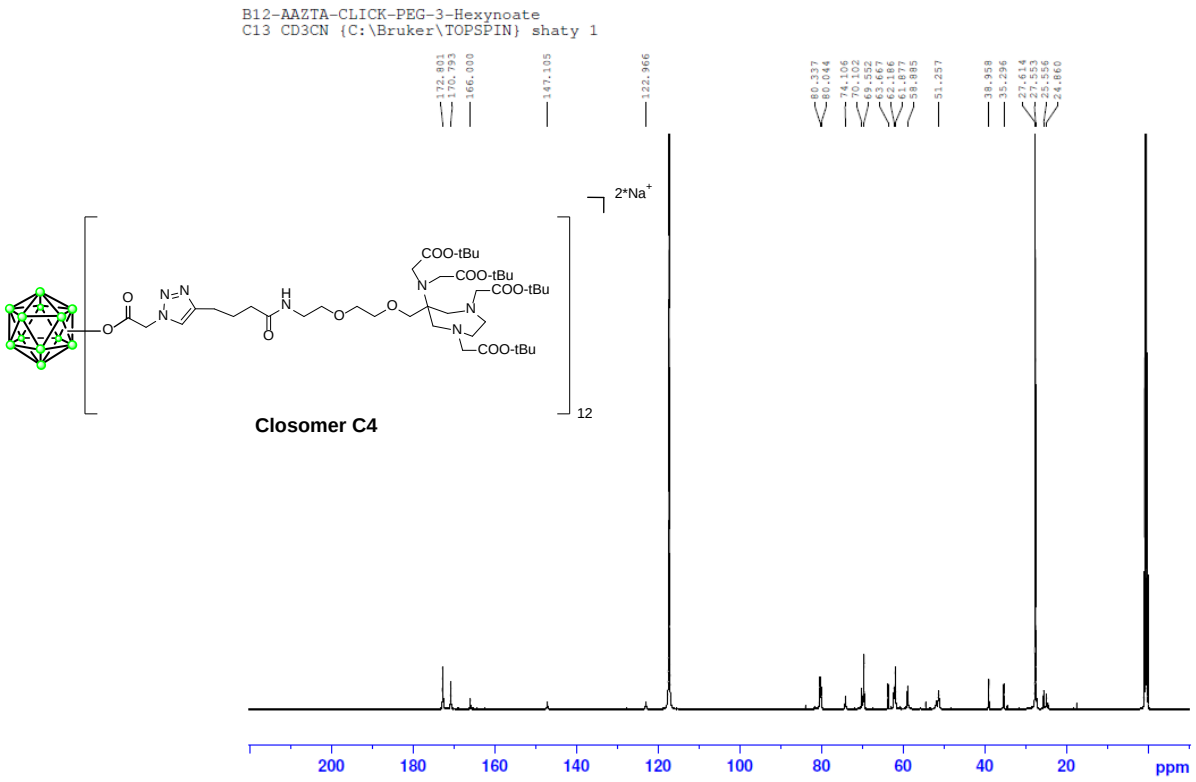

B12-carbamate-AAZTA
C13 CD3CN {C:\Bruker\TOPSPIN} shaty 32
173.351
171.437
156.856
81.079
80.628
75.266
71.029
70.600
70.334
64.525
63.111
62.695
59.655
51.992
41.886
28.483
28.366
2*Na+
COO-tBu
COO-tBu
COO-tBu
COO-tBu
12
Closomer C2
200
180
160
140
120
100
80
60
40
20
0
ppm

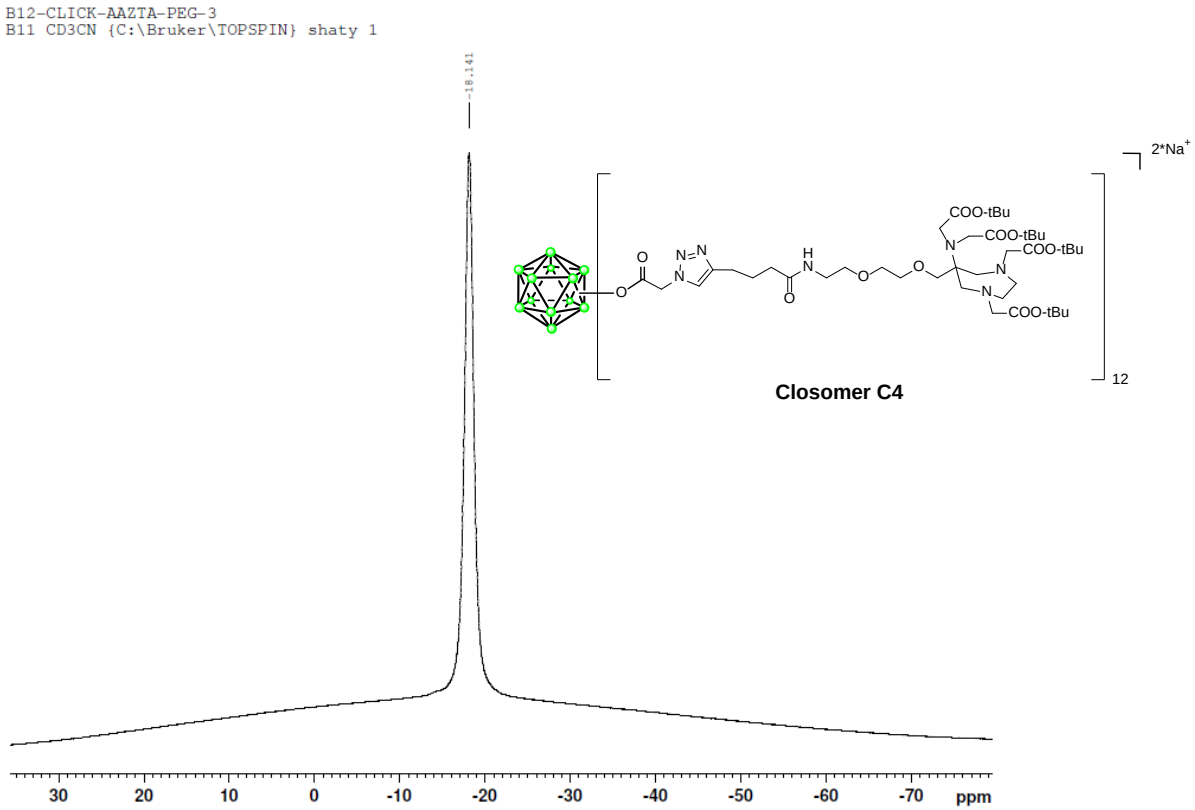

B12-AAZTA-Carbamate-PEG-3
B11 CD3CN {C:\Bruker\TOPSPIN} shaty 7
-18.526
2*Na+
COO-tBu
COO-tBu
COO-tBu
COO-tBu
O
N
H
O
O
O
N
N
N
12
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
ppm

Closomer C2


B12-AAZTA-CLICK-5-Hexynoate
proton CD3CN {C:\Bruker\TOPSPIN} shaty 41
7.372
7.072
4.852
3.671
3.518
3.494
3.461
3.450
3.440
3.425
3.407
3.295
3.280
3.239
2.967
2.939
2.757
2.657
2.630
2.579
2.177
1.964
1.950
1.945
1.940
1.935
1.930
1.659
1.422
1.411
2*Na+
COO-tBu
COO-tBu
COO-tBu
COO-tBu
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
11.50
12.07
24.00
47.96
96.21
24.67
48.23
24.24
24.41
48.63
25.32
48.13
24.90
433.29

Closomer C4


B12-AAZTA-CLICK-PEG-3-Hexynoate
C13 CD3CN {C:\Bruker\TOPSPIN} shaty 1
172.801
170.793
166.000
147.105
122.966
80.337
80.044
74.106
70.102
69.552
63.667
62.186
61.977
59.885
51.257
38.958
35.296
27.614
27.553
25.556
24.860
2*Na+
COO-tBu
12
Closomer C4
200
180
160
140
120
100
80
60
40
20
ppm


B12-CLICK-AAZTA-PEG-3
B11 CD3CN {C:\Bruker\TOPSPIN} shaty 1
-18.141
2*Na+
COO-tBu
12
Closomer C4
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
ppm

11. References

1 M. C. Alpoim, A. M. Urbano, C. F. G. C. Geraldes and J. A. Peters, *J. Chem. Soc. Dalt. Trans.*, 1992, 463–467.

2 K. Djanashvili and J. A. Peters, *Contrast Media Mol. Imaging*, 2007, **2**, 67–71.

3 E. Brücher, J. Glaser, I. Grenthe and I. Puigdomènech, *Inorganica Chim. Acta*, 1985, **109**, 111–116.

4 C. Cossy, A. C. Barnes, J. E. Enderby and A. E. Merbach, *J. Chem. Phys.*, 1989, **90**, 3254–3260.

5 C. Cossy and A. E. Merbach, *Pure Appl. Chem.*, 1988, **60**, 1785–1796.

6 S. S. Jalisatgi, V. S. Kulkarni, B. Tang, Z. H. Houston, M. W. Lee and M. F. Hawthorne, *J. Am. Chem. Soc.*, 2011, **133**, 12382–12385.

7 L. N. Goswami, S. Chakravarty, M. W. Lee, S. S. Jalisatgi and M. F. Hawthorne, *Angew. Chem. Int. Ed. Engl.*, 2011, **50**, 4689–91.

8 L. N. Goswami, L. Ma, S. Chakravarty, Q. Cai, S. S. Jalisatgi and M. F. Hawthorne, *Inorg. Chem.*, 2013, **52**, 1694–700.

9 J. M. Bryson, W.-J. Chu, J.-H. Lee and T. M. Reineke, *Bioconjug. Chem.*, 2008, **19**, 1505–1509.

10 Y. Song, E. K. Kohlmeir and T. J. Meade, *J. Am. Chem. Soc.*, 2008, **130**, 6662–6663.

11 J. B. Livramento, A. Sour, A. Borel, A. E. Merbach and É. Tóth, *Chem. – A Eur. J.*, 2006, **12**, 989–1003.

12 J. B. Livramento, L. Helm, A. Sour, C. O'Neil, A. E. Merbach and É. Tóth, *Dalt. Trans.*, 2008, 1195–1202.

13 J. Costa, É. Tóth, L. Helm and A. E. Merbach, *Inorg. Chem.*, 2005, **44**, 4747–4755.

14 J. B. Livramento, C. Weidensteiner, M. I. M. Prata, P. R. Allegrini, C. F. G. C. Geraldes, L. Helm, R. Kneuer, A. E. Merbach, A. C. Santos, P. Schmidt and É. Tóth, *Contrast Media Mol. Imaging*, 2006, **1**, 30–39.