ChemistrySELECT

Supporting Information

Monoamide Derivatives of EDTA Incorporating Pendent Carboxylates or Pyridyls: Synthesis, Metal Binding, and Crystal Structure of a Dinuclear Ca^{2+} Complex Featuring Bridging Na^{+} Ions

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Supporting Information Contents

Experimental Procedures

Synthesis: General remarks

Materials. Reagents were obtained from commercial sources and used without further purification unless otherwise stated. Solvent extractions were performed in a 100 cm^3 separating funnel with ca. 50 cm^3 for each phase, unless otherwise stated. For procedures involving dry solvent, glassware was oven-dried for at least eight hours prior to use. Dedicated oxygen-free nitrogen or argon cylinders (BOC, UK) were used to provide an inert atmosphere.

Instrumentation. NMR: Routine ^1H (400MHz) and ^{13}C NMR (101MHz) spectra were acquired on Bruker Avance 400, or Varian Mercury 400 NMR spectrometers. Two-dimensional NMR (COSY, HSQC and HMBC), and certain ^1H / ^{13}C NMR spectra were acquired by the solution state NMR service at Durham University on Varian VNMRS-600 (600 MHz) or VNMRS-700 (700 MHz) instruments. Where visible, signals corresponding to $CDCl_3$ were referenced to δ =7.26 ppm in ^1H NMR spectra and δ =77.2 ppm for ^{13}C spectra. For ^{13}C NMR spectra in D_2O, an appropriate compound was added to the sample to facilitate referencing.

Mass spectrometry: ES-MS data (positive and negative ionisation modes) were obtained on a Waters TQD mass spectrometer interfaced with an Acquity UPLC system. GC-MS (EI ionisation) was performed on an Agilent instrument equipped with a 5973 model quadrupole mass spectrometer.

FT-IR*:* All infra-red spectra were recorded on a Perkin-Elmer Spectrum 90 spectrometer equipped with an ATR stage. Substances for analysis were used neat unless otherwise indicated.

Chromatography: TLC was performed on either alumina or silica using Merck foil-backed TLC plates. Column chromatography was using a standard glass column and silica (Fluorochem) or alumina (Merck). Elution was performed according to the method of Clark Still.[1] Analytical HPLC was performed by the chromatography service at Durham University.

Titrimetric studies:

Quantitative ^1H NMR for molecular weight correction: A sample of **$AmGly_1$** or **$AmPy_1$** at a known mass was dissolved in K_2HPO_4 (0.5 cm^3, 0.2 mol dm^{-3}) and was then diluted into a solution of t-butanol in D_2O (0.5cm^3, 1 wt. % t-butanol) to prepare an NMR sample with a final volume of 1cm^3. A ^1H NMR spectrum was then acquired on a Bruker Avance 400 NMR spectrometer using the ROBUST5[2] pulse sequence with a relaxation delay of 15 seconds, and the spectrum was integrated using the t-butanol signal as a reference (integral set to 9H). The ratio of the N-CH_2-COO^- signals of **$AmGly_1$** or **$AmPy_1$** to t-butanol could then be used to calculate the concentration of the prepared sample, which in turn was used to calculate an apparent molecular weight, accounting for hydration, for the samples of **$AmGly_1$** or **$AmPy_1$** under study.

Potentiometric titration. Titrations were carried out at 298.1±0.1 K using KCl 0.15 M as the supporting electrolyte. The experimental procedure (burette, potentiometer, cell, stirrer, microcomputer, etc.) has been fully described elsewhere.[3] The acquisition of titration data was performed using the computer program PASAT.[4] An Ag/AgCl electrode in saturated KCl solution was used as the reference electrode and the glass electrode was calibrated as an hydrogen-ion concentration probe via titrating previously standardized amounts of hydrochloric acid with carbonate-free sodium hydroxide solutions, and determining the equivalence point by Gran's method,[5,6] to give the standard potential, E°', and the ionic product of water (pK_w = 13.73(1)).

The computer program HYPERQUAD[7] was used to fit the protonation and stability constants. Solutions containing the ligand, and the ligand and metal ions, with concentrations 1 x 10^{-3} M were then titrated with sodium hydroxide. Initially, the titration curves for each ligand were treated as separated curves without significant variations in the values of the stability constants. Then, the datasets were merged, and treated simultaneously to give the final stability constants.

Distribution diagrams for $AmGly_1$, $AmPy_1$ and their associated complexes

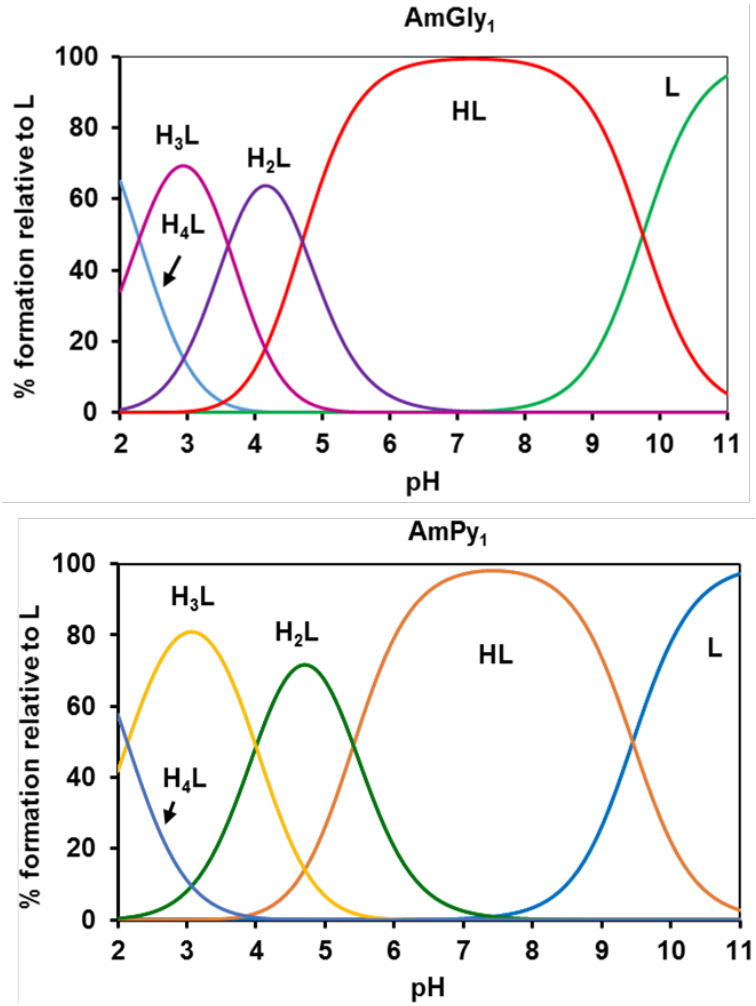


Figure S1. *Plot of the distribution diagrams of the protonation of* ***$AmGly_1$*** *and* ***$AmPy_1$****, [L] = 1 x* 10^{-3} *M*

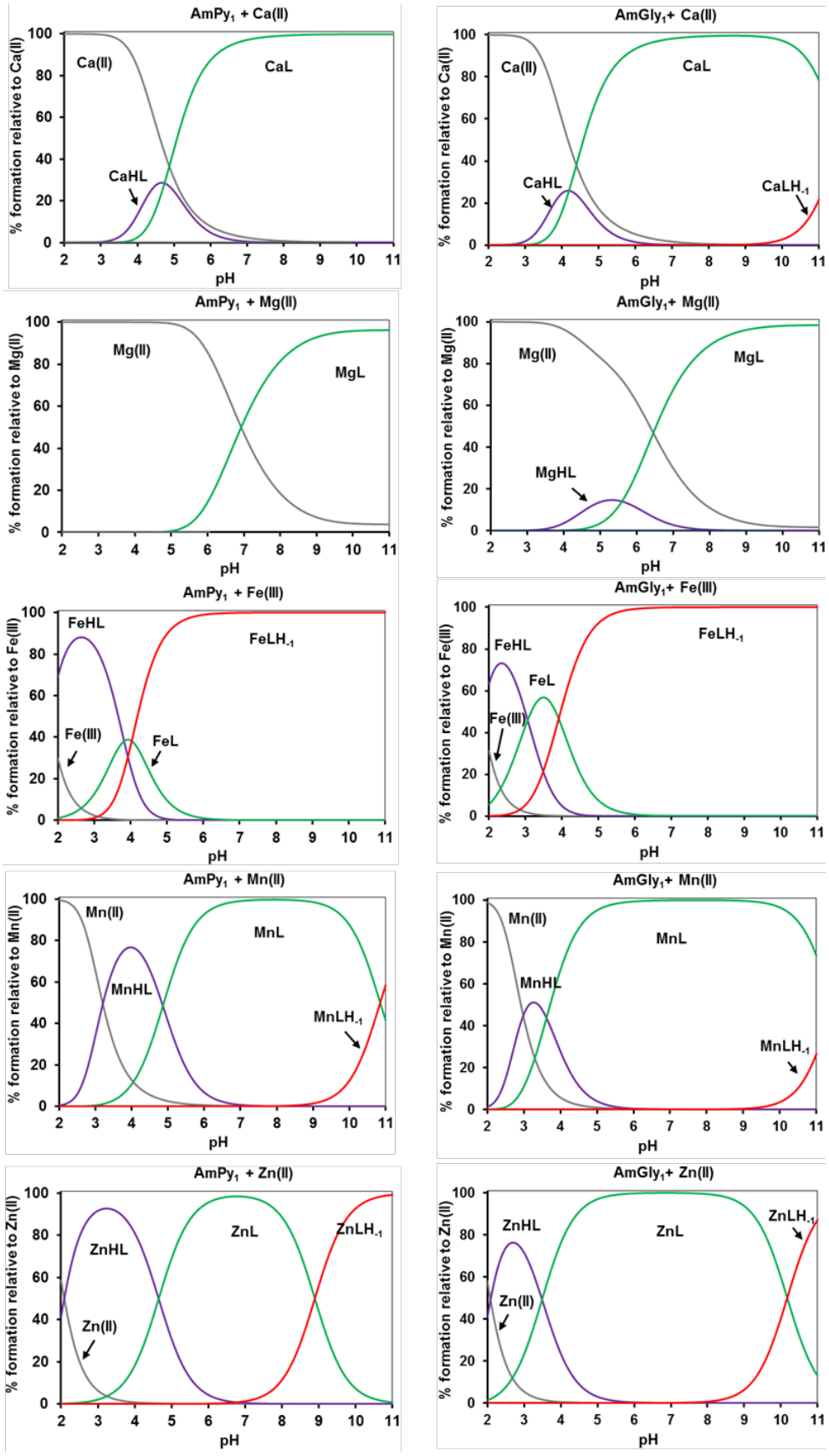


Figure S2: *Plot of the distribution diagrams of the systems* ***L:M*** *(M = Ca(II), Mg(II), Fe(III), Mn(II) and Zn(II)) in 1:1 molar ratio [**L**]=[**M**]=1x10^{-3} M (charges omitted)*

Spectrophotometric titration of AmPy$_1$. UV-Visible spectra were recorded in an Agilent 8453 spectrophotometer at 298.15 K. Spectra were measured after adding a concentrated solution of sodium hydroxide to a 0.001 M aqueous solution of **AmPy$_1$** in 0.15M KCl that was acidified with hydrochloric acid until a pH of 2.05 was reached. The data were then fitted with the program HYPSPEC.[7]

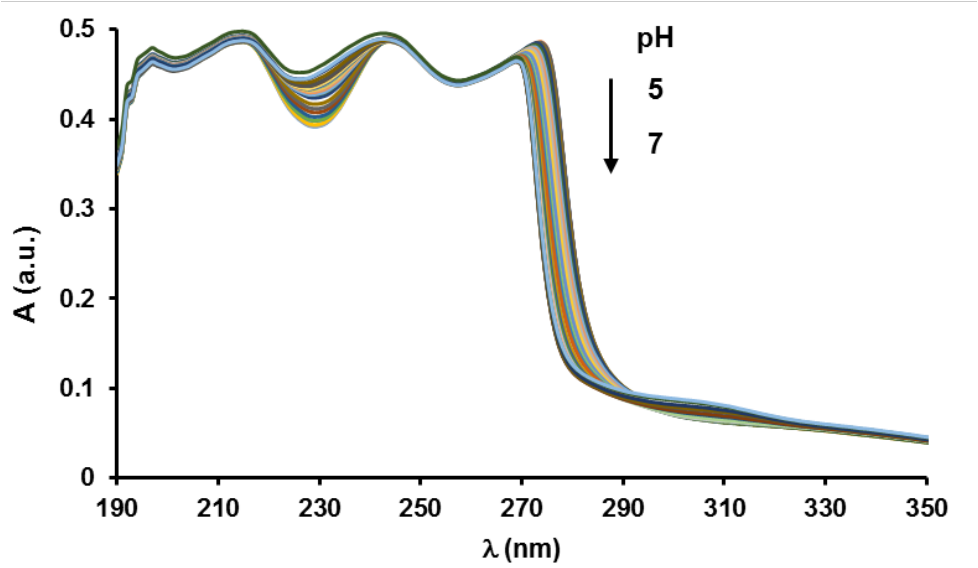


Figure S3. *UV-Vis spectra of a 0.001 M aqueous solution of **AmPy$_1$** recorded at variable pH in KCl 0.15 M*

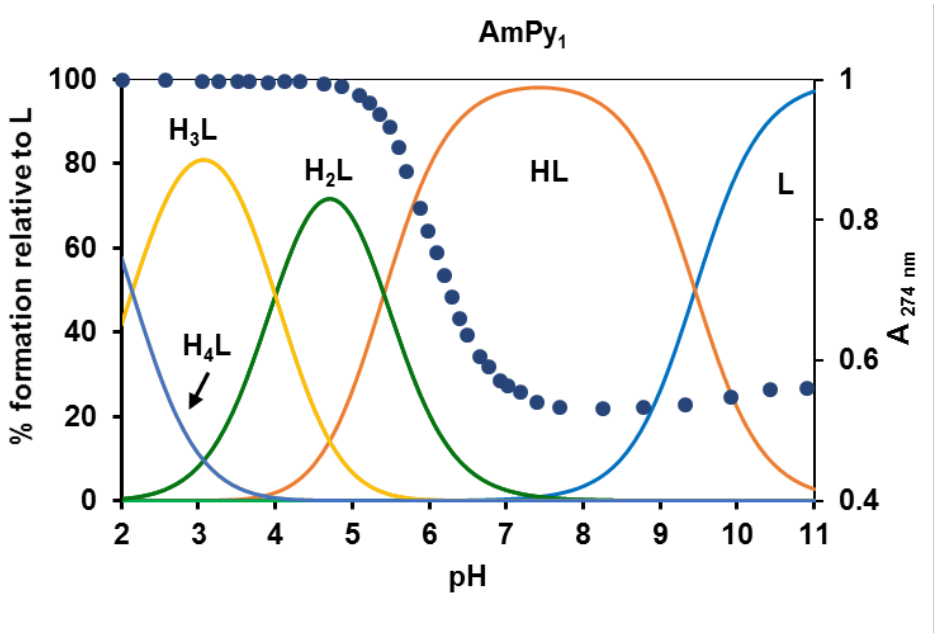


Figure S4. *Plot of the distribution diagram of protonation of **AmPy$_1$** with the variation of the normalized absorption at 274 nm (charges omitted)*

***X-Ray Crystallography*:** Single crystals of **$AmGly_1$**, and **$Ca_2(AmGly_1)_2$** were diffracted in an Oxford diffraction Supernova diffractometer using MoKα radiation (λ = 0.71073 Å) at 123 K. Structures were solved via direct methods using SHELXT[8] and refined by full-matrix least-squares on all F^2 using SHELXL [9] with the Olex2 suite.[10] Molecular drawings were produced with Mercury.[11]

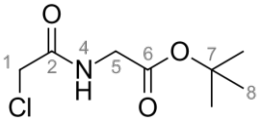
CCDC-1508044 and CCDC-1508045 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S1. *Crystallographic data for* ***$AmGly_1$*** *and* ***$Ca_2(AmGly_1)_2$***

	$AmGly_1$	**$Ca_2(AmGly_1)_2$**
Empirical formula	$C_{12}H_{19}N_3O_9$	$C_{48}H_{114}Ca_4Cl_4N_{12}Na_{12}O_{63}$
Formula weight	349.30	2445.51
Temperature/K	120.00(10)	120.00(10)
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	P2/n
a	5.4251(3)	13.8850(9)
b	9.5386(4)	8.8663(5)
c	28.5858(18)	21.6439(16)
α	90	90
β	91.682(5)	105.003(7)
γ	90	90
Volume ($Å^3$)	1478.62(13)	2573.7(3)
Z	4	1
$\rho_{calc}g/cm^3$	1.569	1.578
μ/mm^{-1}	0.136	0.473
F(000)	736.0	1270.0
Crystal size(mm^3)	0.3 × 0.2 × 0.1	0.2 × 0.1 × 0.1
Radiation(Å)	0.71073	0.71073
2Θ range (°)	7.12 to 49.98	7.18 to 49.99
Reflections collected	7340	9684
Independent reflections	2602	4524
R_{int}	0.0630	0.0353
Data/restraints/parameters	2602/0/219	4524/20/360
Goodness-of-fit on F^2	1.010	1.069
Final R indexes [I>=2σ (I)]	R_1 = 0.0558 wR_2 = 0.1054	R_1 = 0.0604 wR_2 = 0.163
Final R indexes [all data]	R_1 = 0.0877 wR_2 = 0.1181	R_1 = 0.0778 wR_2 = 0.1756

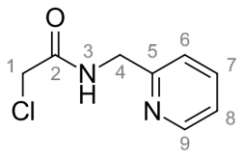
Synthetic procedures

tert-Butyl (2-chloroacetylamino)acetate, 1



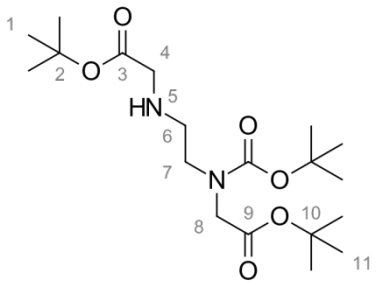
A solution of triethylamine (3 cm^3, 21.2 mmol) in anhydrous dichloromethane (30 cm^3) was used to suspend glycine t-butyl ester hydrochloride (1.00 g, 5.99 mmol). The resulting mixture was then cooled using a dry ice/acetone bath and allowed to stir under nitrogen for 10 minutes prior to the dropwise addition of a solution of chloroacetyl chloride (0.54 cm^3, 7.41 mmol) in dichloromethane (20 cm^3) over a period of 40 minutes, following which the reaction mixture was allowed to warm to room temperature overnight and filtered. The filtrate was washed with saturated aqueous sodium carbonate (2x), aqueous hydrochloric acid (1 mol dm^{-3}, 2x) and then with brine. Drying of the organic layer over magnesium sulphate followed by solvent removal in vacuo gave the title compound (0.84 g, 4.03 mmol, 67%) as an oil that rapidly solidified. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.06 (t, 1H, ***H4***), 4.08 (s, 2H, ***H1***), 3.98 (d, 2H, ***H5***), 1.49 (s, 9H, ***H8***) ppm. GC-MS (EI^+) 238.9 ($M^{\bullet+}$), 209.9 (M-2Me$^+$), 180.9 (M-2Me-$O_2^{\bullet+}$).

2-Chloro-1-{[(2-pyridyl)methyl]amino}-1-ethanone, 2[12]



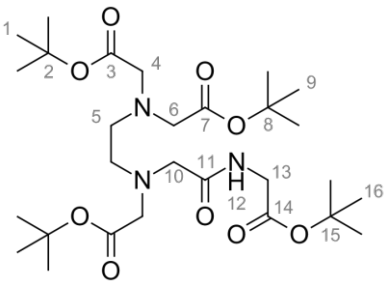
Anhydrous dichloromethane (50 cm^3), was used to dissolve chloroacetyl chloride (1.93 cm^3, 24.2 mmol) and the solution cooled using a dry ice/acetone bath under nitrogen. 2-Aminomethylpyridine (2.5 cm^3, 24.5 mmol) was then added dropwise via syringe. As addition proceeded, the reaction mixture became purple and a solid precipitated. At this point, the reaction was bought to room temperature and more dichloromethane (as much as was necessary to enable free stirring) was added. The reaction mixture was then allowed to stir at room temperature for a further 20 hours and the mixture bought to basic pH via the addition of aqueous sodium carbonate (pH ≥ 10) before washing the crude mixture in the same. The organic layer was then dried over magnesium sulphate and the solvent removed in vacuo. The residue was purified via column chromatography (dichloromethane:tetrahydrofuran 70:30 v/v) to afford the title compound (3.31 g, 17.9 mmol, 75%) as a yellow oil that solidified to a brown solid upon refrigeration. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (ddd, 1H, ***H9***), 7.86 (s, 1H, ***H3***), 7.66 (ddd, 1H, ***H7***), 7.24 (dd, 1H, ***H6***), 7.20 (ddd, 1H, ***H8***), 4.58 (d, 2H, ***H4***), 4.10 (s, 2H, ***H1***) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1 (***C2***), 155.5 (***C9***), 149.2 (***C5***), 136.9 , 122.6 (***C7***), 122.2, 44.6, 42.6 ppm.

Tert-Butyl {2-[(tert-butoxycarbonylmethyl) -N-tert-butoxycarbonylamino] ethylamino} acetate, 3



Ethylene diamine (0.5 cm^3, 7.5 mmol) and triethylamine (4.2 cm^3, 30 mmol) were dissolved in acetonitrile (37 cm^3 , dried over molecular sieves), and a solution of t-butyl bromoacetate (3.32 cm^3 , 22.6 mmol in 15 cm^3 in acetonitrile) was added dropwise to the mixture, which was then stirred at room temperature under argon for 17 hours under argon. After this, the reaction vessel was placed in the freezer (ca. 30 min) during which time a solid precipitated. This precipitate was filtered off, and the filtrate concentrated in vacuo, redissolved in dichloromethane, and then washed with water and then brine. The dichloromethane layer was then dried over magnesium sulphate, concentrated in vacuo and the residue purified by column chromatography (silica, diethyl ether:hexanes 0:100 → 100:0 compound eluted in diethyl ether) to afford the title compound (0.60 g, 1.5 mmol, 20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (s, 4H, ***H8***), 3.29 (s, 2H, ***H4***), 2.85 (t, 2H, ***H6***), 2.65 (t, 2H, ***H7***), 2.12 (s, 1H, ***H5***), 1.44 (s, 9H, ***H1***), 1.43 (s, 18H, ***H11***) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.4 (***C9***), 171 (***C3***), 81 (***C10***), 80.6 (***C2***) , 56 (***C8***), 54 (***C4***), 52 (***C7***), 47 (***C6***), 28 (***C1***, ***C11***) ppm. GC-MS (EI^+) 402.3 ($M^{+\bullet}$).

Tert-Butyl [(tert-butoxycarbonylmethyl){2-[(tert-butoxycarbonylmethyl){2-oxo-2-[(tertbutoxycarbonylmethyl)amino]ethyl}amino]ethyl}amino]acetate, 4

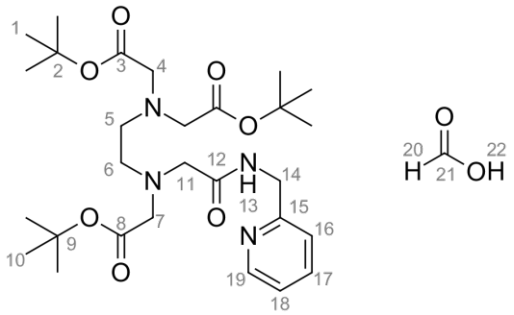


Aminoester **3** (0.20 g, 0.50 mmol) and haloamide **1** (0.12 g, 0.58 mmol) were dissolved in acetonitrile (1.5 cm^3, dried over molecular sieves). Potassium carbonate (0.14 g, 1.01 mmol), potassium iodide and sodium sulphate (ca. 25 mg each) were then added and the mixture was heated at 60^{o}C under nitrogen. Reaction progress was monitored by TLC (alumina, ethyl acetate:hexanes 50:50) and ^{1}H NMR techniques.

Once a steady state was observed with respect to the depletion of **3** from the ^{1}H NMR spectrum, the reaction mixture was cooled to room temperature, filtered concentrated in vacuo and purified by column chromatography (alumina, ethyl acetate:hexanes 50:50, isocratic) to afford the title compound (0.19 g, 0.33 mmol, 66%) as a yellow oil.

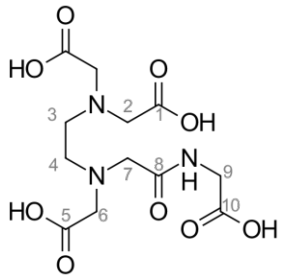
ν_{max} /cm^{-1} (ATR) 2977 (sp^3 C-H st), 1730 (ester C=O st), 1675 (amide C=O st), 1147 (C-O st). ^{1}H NMR (700 MHz, $CDCl_3$): δ = 8.52 (t, J = 6.0 Hz, 1H, ***H12***), 3.93 (d, J = 6.0 Hz, 2H, ***H13***), 3.42 (s, 4H, ***H4***), 3.35 (m, 4H, ***H6, H10***), 2.81 (s, 4H, ***H5***), 1.52 – 1.36 (m, 36H, ***H1, H9, H16***) ppm. ^{13}C NMR (176 MHz, $CDCl_3$): δ = 172.2 (***C7***), 170.5 (***C3***), 169.1 (***C14***), 81.4 - 81.0 (***C2, C8, C15***), 58.3 (***C10***), 56.5 (***C10***), 55.4 (***C4***), 52.8-52.2 (***C5, C6***), 41.7 (***C13***), 28.1 - 28.0 (***C1, C9, C16***) ppm. (ES-MS$^+$) 574.7 (100%, $[M+H]^+$). HR-MS Found 574.3705, $C_{28}H_{52}N_3O_9$ $[M+H]^+$ requires 574.3704.

Tert-Butyl [(tert-butoxycarbonylmethyl){2-[(tert-butoxycarbonylmethyl)(2-oxo-2-{[(2-pyridyl)methyl]amino}ethyl)amino]ethyl}amino]acetate, 1:1 formate adduct, 5



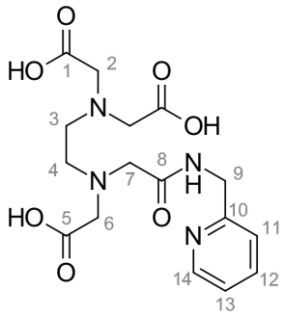
Aminoester **3** (0.53 g, 1.3 mmol) and haloamide **2** (0.26, 1.4 mmol) were dissolved in acetonitrile (4.3 cm^3, dried over molecular sieves) and potassium carbonate (0.36 g, 2.6 mmol) and potassium iodide (0.04 g, 0.24 mmol) were suspended in the solution. The reaction mixture was then heated at 60^{o}C under argon until ^{1}H NMR analysis indicated the consumption of starting aminoester **3** (within 24 hours). Acetonitrile was then removed in vacuo and the residue partitioned between dichloromethane and saturated sodium carbonate. The organic layer was extracted (3x) and dried over magnesium sulphate. The residue was purified via preparative reverse-phase column chromatography (water:acetonitrile, 0.5% v/v formic acid as additive 0:100 → 100:0 compound eluted in ca. 50:50 v/v water:acetonitrile) to afford the title compound (0.57 g, 0.96 mmol, 74%). ν_{max} /cm^{-1} (ATR) 3250 (acid O-H st), 2980 (sp^3 C-H st), 1730 (acid/ester C=O st), 1670 (amide C=O st), 1150 (acid/ester C-O st). ^{1}H NMR (700 MHz, $CDCl_3$): δ = 9.39 (t, J = 6.0 Hz, 1H, ***H13***), 9.06 (s, 1H, ***H22***), 8.94 (d, J = 5.5 Hz, 1H, ***H19***), 8.13 (dd, 1H, ***H17***), 8.11 (s, 1H, ***H20***) 7.75 (d, 1H, ***H16***), 7.61 (dd, 1H, ***H18***), 4.84 (d, J = 5.5 Hz, 2H, ***H14***), 3.87 (s, 2H, ***H11***), 3.76 (s, 4H, ***H4***), 3.71 (s, 2H, ***H7***), 3.24 (t, J = 5.0 Hz, 2H, ***H5***), 3.19 (t, J = 5.0 Hz, 2H, ***H6***), 1.47 (s, 1H, ***H10***), 1.44 (s, 1H, ***H1***) ppm. ^{13}C NMR (176 MHz, $CDCl_3$): δ = 170.3 (***C12***), 168.4 (***C3***), 168.2 (***C8***), 162.9 (***C21***), 155.2 (***C15***), 143.7 (***C19***), 143.0 (***C17***), 124.7 (***C16***), 124.2 (***C18***), 117.1 (***C12***), 83.1 (***C2***), 83.0 (***C9***), 57.3 (***C11***), 55.1 (***C7***), 54.8 (***C4***), 51.8 (***C6***), 50.7 (***C5***), 41.5 (***C14***), 28.0 (***C10***), 27.9 (***C1***) ppm.

[(Carboxymethyl) {2-[(carboxymethyl) {2-[(carboxymethyl) amino]- 2-oxoethyl} amino] ethyl}amino] acetic acid, $AmGly_1$



Amide **4** (0.54 g, 0.94 mmol) and anisole (0.44 cm^3 4.07 mmol), were dissolved in dichloromethane (2 cm^3), and trifluoroacetic acid (4 cm^3) was added to the yellow solution which was allowed to stir at room temperature under nitrogen for 18 hours. Volatiles were then removed in vacuo and the residue redissolved in dichloromethane which was once again removed in vacuo. Diethyl ether was then added to the residual oil and the mixture agitated ultrasonically to afford a white precipitate that was collected via centrifugation. This solid was dissolved in aqueous hydrochloric acid (1 mol dm^{-3}) and passed through a short column of DOWEX 1X8 (chloride form) that had been pre-washed with aqueous hydrochloric acid (1 mol dm^{-3}) and water. Once loaded onto the resin, elution of the compound was achieved with more hydrochloric acid (1 mol dm^{-3}, ca. 100 cm^3). Removal of the solvent in vacuo followed by further drying under high vacuum gave the title compound (0.2 g, 0.57 mmol, 61%) as an off-white solid. t_R (H_2O:MeOH, MS detection): 1.63 min. ^{1}H NMR (700 MHz, D_2O, pD ≈ 8): δ = 3.64 (s, 2H, ***H9***), 3.13 (s, 2H, ***H7***), 3.02 (s, 2H, ***H6***), 2.95 (s, 4H, ***H2***), 2.47 (t, J = 6.0 Hz, 2H, ***H4***), 2.43 (t, J = 6.0 Hz, 2H, ***H3***) ppm. ^{13}C NMR (176 MHz, D_2O, pD ≈ 8, t-Butanol added as reference): δ = 179.6 (***C1***), 179.3 (***C5***), 176.7 (***C10***), 173.8 (***C8***), 58.9 (***C6***), 58.7 (***C2***), 57.9 (***C7***), 52.2 (***C4***), 51.9 (***C3***), 43.1 (***C9***) ppm. (ES-MS^+) 350.6 (100 %, $[M+H]^+$). HR-MS Found 350.1201 , $C_{12}H_{20}N_3O_9$ $[M+H]^+$ requires 350.1200.

[(Carboxymethyl) {2-[(carboxymethyl) (2-oxo-2- {[(2-pyridyl) methyl] amino}ethyl) amino]ethyl} amino] acetic acid, $AmPy_1$



Amide **5** (0.57g, 0.96 mmol) was dissolved in dichloromethane (2 cm^3) and anisole (0.35 cm^3, 3.2 mmol) dissolved into the solution immediately after. Trifluoroacetic acid (2 cm^3) was then added and the mixture was stirred under argon for 17 hours, after which time volatiles were removed in vacuo. A semi-solid material was then isolated after trituration in diethyl ether (50 cm^3) of the resulting residue using ultrasonic agitation, and the material collected via centrifugation. Aqueous hydrochloric acid (1 mol dm^{-3}, ca. 50 cm^3) was the used to dissolve the solid, and then removed in vacuo to afford a buff material. This solid was then redissolved in hydrochloric acid (1 mol dm^{-3}, minimum volume) and the residue loaded onto DOWEX 1X8 (chloride form) that had been pre-washed with 1 mol dm^{-3} hydrochloric acid and water. Once loaded onto the resin, elution of the compound was achieved with water (ca. 100 cm^3) and then hydrochloric acid (1 mol dm^{-3}, ca. 100 cm^3). Removal of the solvent in vacuo followed by further drying under high vacuum gave the title compound (0.22 g, 0.58 mmol, 60%) as an orange-brown solid. t_R (H_2O:MeOH, UV detection): 1.24 min. ^1H NMR (600 MHz, D_2O, pD ≈ 11 via addition of Na_2CO_3, CO_3^{2-} referenced to 166 ppm in ^{13}C spectrum.): δ = 8.32 (d, 1H, ***H14***), 7.72 (dd, 1H , ***H12***), 7.22 (m, 2H, ***H11, H13***), 4.40 (s, 2H, ***H9***), 3.23 (s, 2H, ***H7***), 3.11 (m, 6H, ***H3, H4, H6***), 2.65 (s, 4H, ***H2***) ppm. ^{13}C NMR (151 MHz, D_2O, pD ≈ 11): δ = 179.3, 178.1 (***C1, C5***) , 175.1 (***C8***), 156.6 (***C10***), 148.4 (***C14***), 138.4 (***C12***), 122.9 , 121.6 (***C12, C13***), 58.9 (***C4***), 58.4 (***C7***), 58.2 (***C3***), 52.4, 51.9 (***C1, C6***), 44.0 (***C9***) ppm. (ES-MS^+) 383.2 (100 %, $[M+H]^+$). HR-MS Found 383.1570 , $C_{16}H_{23}N_4O_7$ $[M+H]^+$ requires 383.1567.

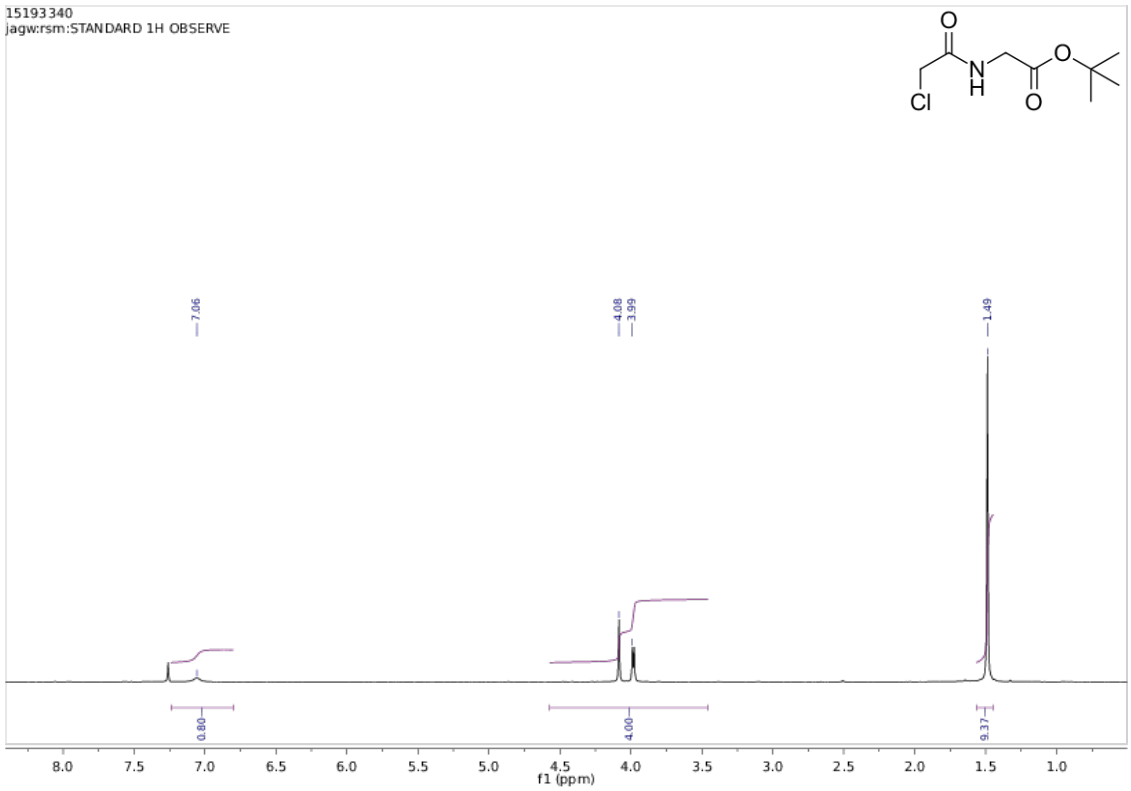
Crystallisation studies on $AmGly_1$:

The crystal structure of the **$AmGly_1$** ligand was obtained by dissolving 10 mg of **$AmGly_1$** in 2 cm^3 of de-ionised water at pH 2. Slow evaporation of this solution gave crystals suitable for analysis via X-ray crystallography.

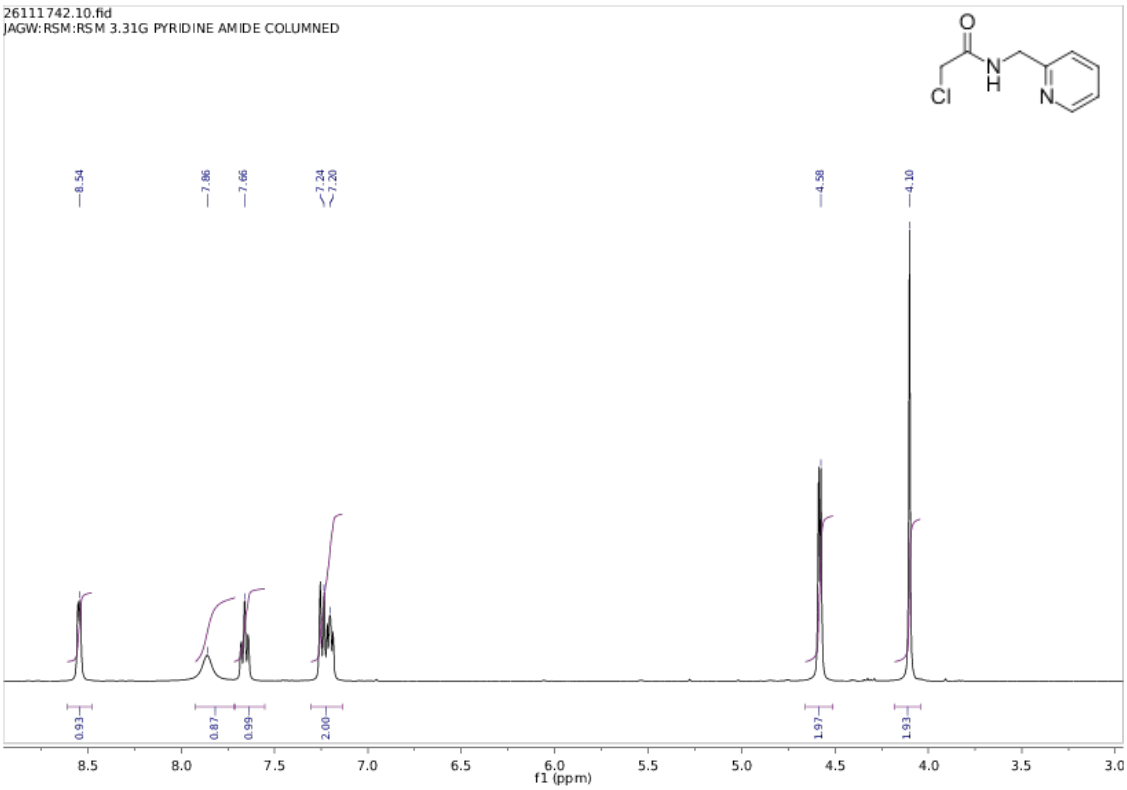
Crystals of **$Ca_2(AmGly_1)_2$** ($4[Na_3Ca(\mathbf{H_{-4}AmGly_1})(H_2O)_6]$ $4Cl•3H_2O$) were obtained via slow evaporation of a basic solution (pH 11, basified using NaOH) of a 1:1 mixture of **$AmGly_1$** and $CaCl_2$ (10 mg of **$AmGly_1$** in 2 cm^3 of de-ionised water).

Supporting characteristic data:

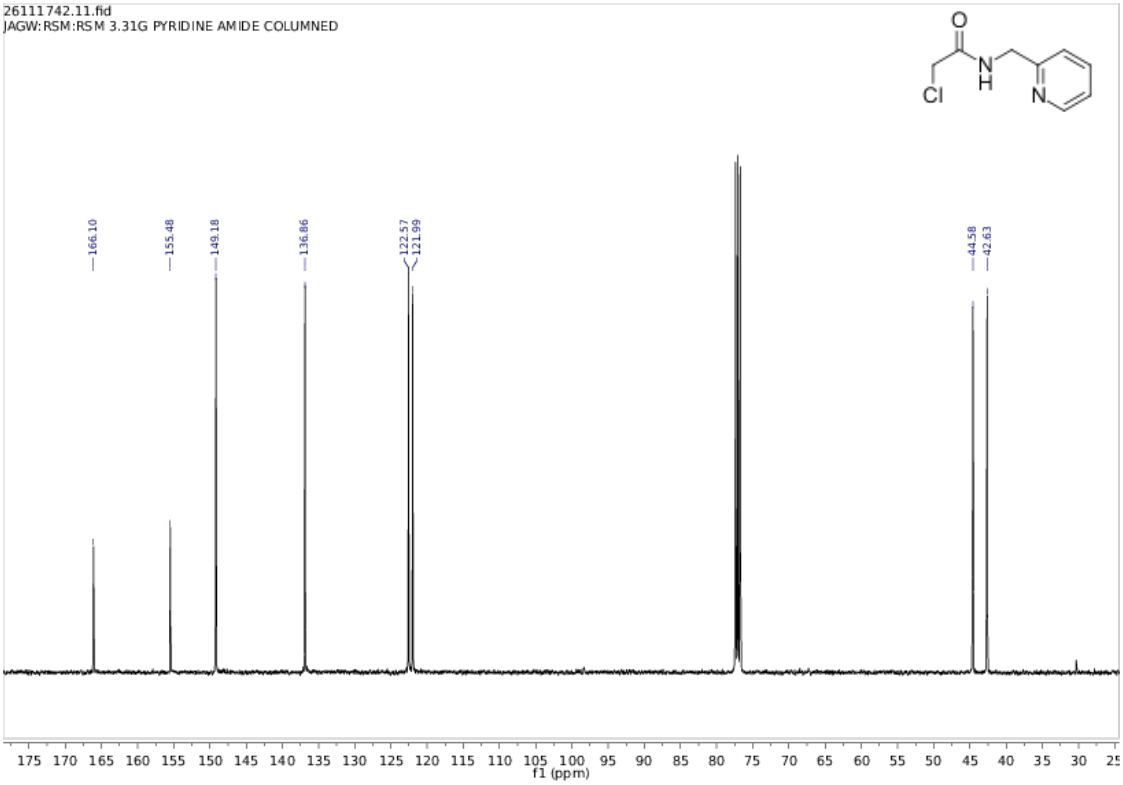
^{1}H NMR of **1**



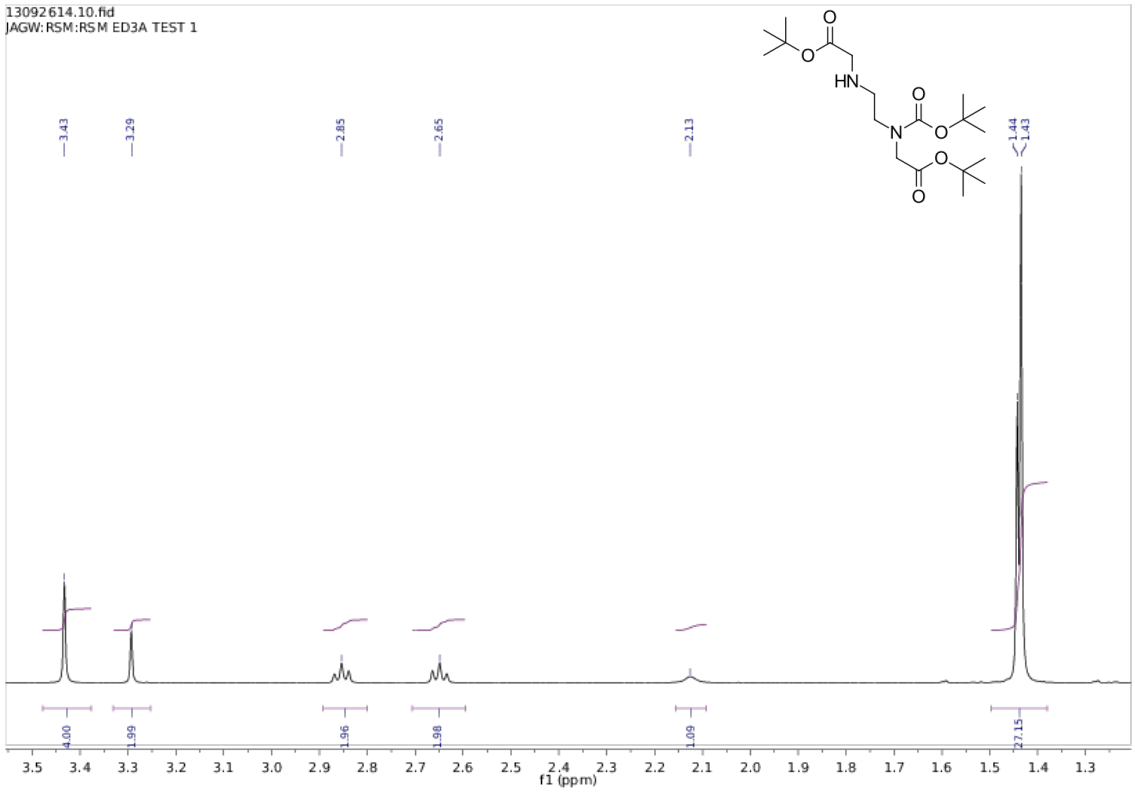
^{1}H NMR of **2**



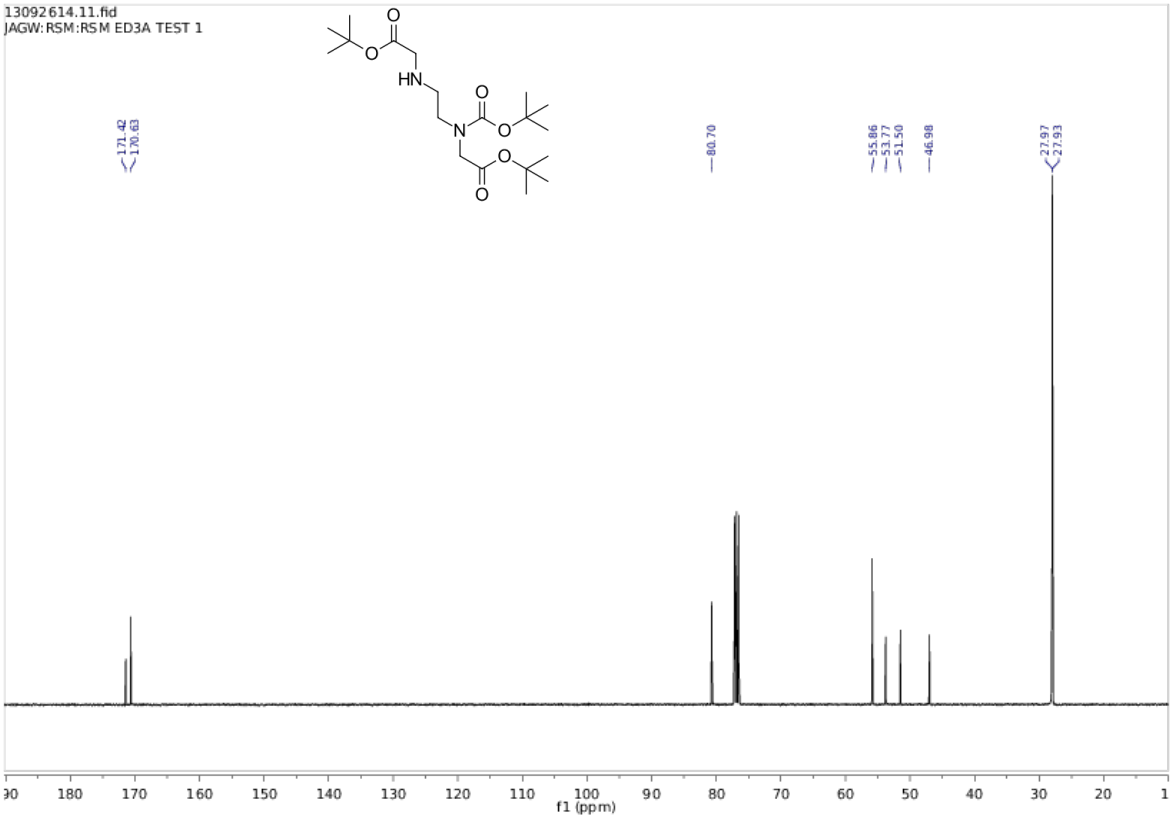
^{13}C NMR of **2**



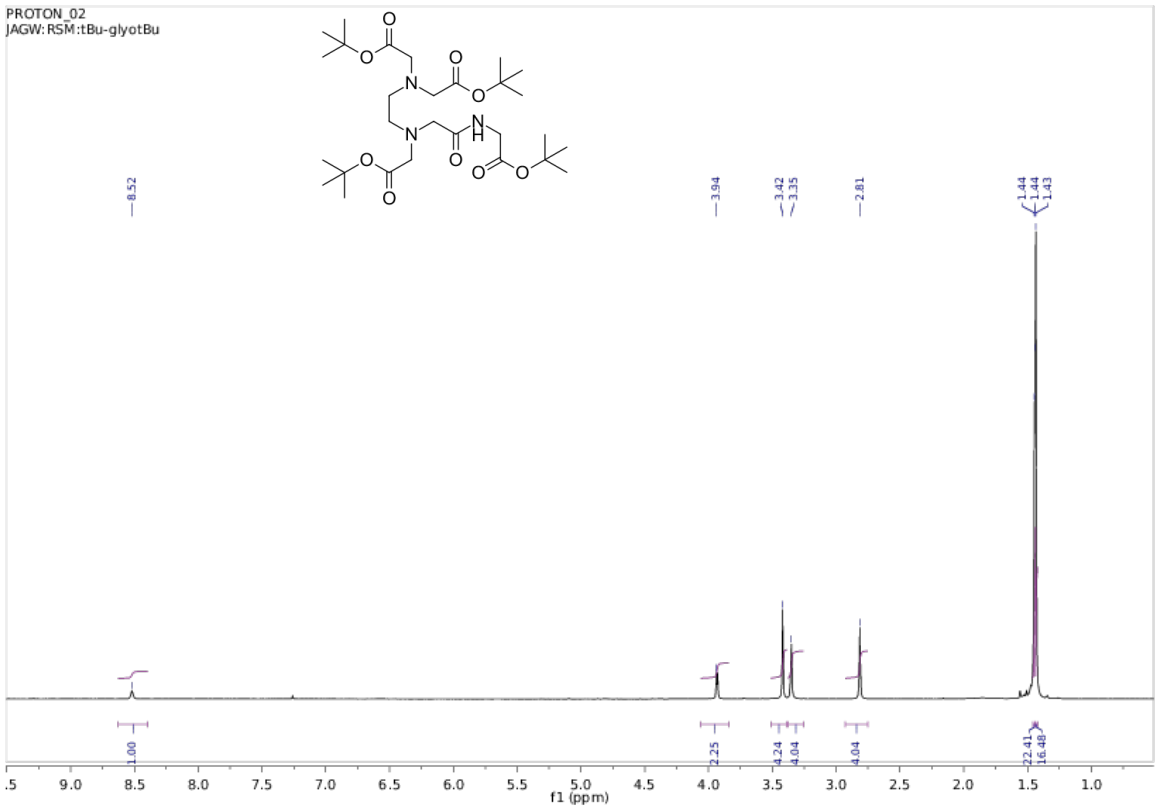
^{1}H NMR of **3**



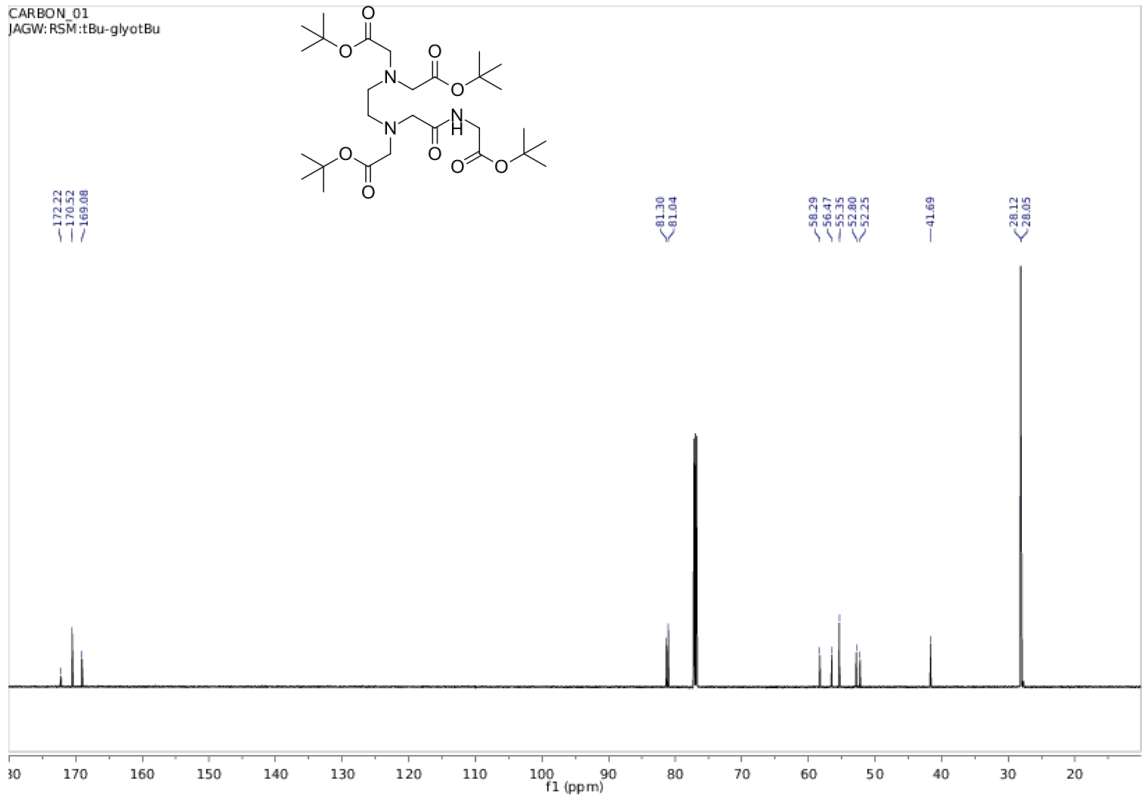
^{13}C NMR of **3**



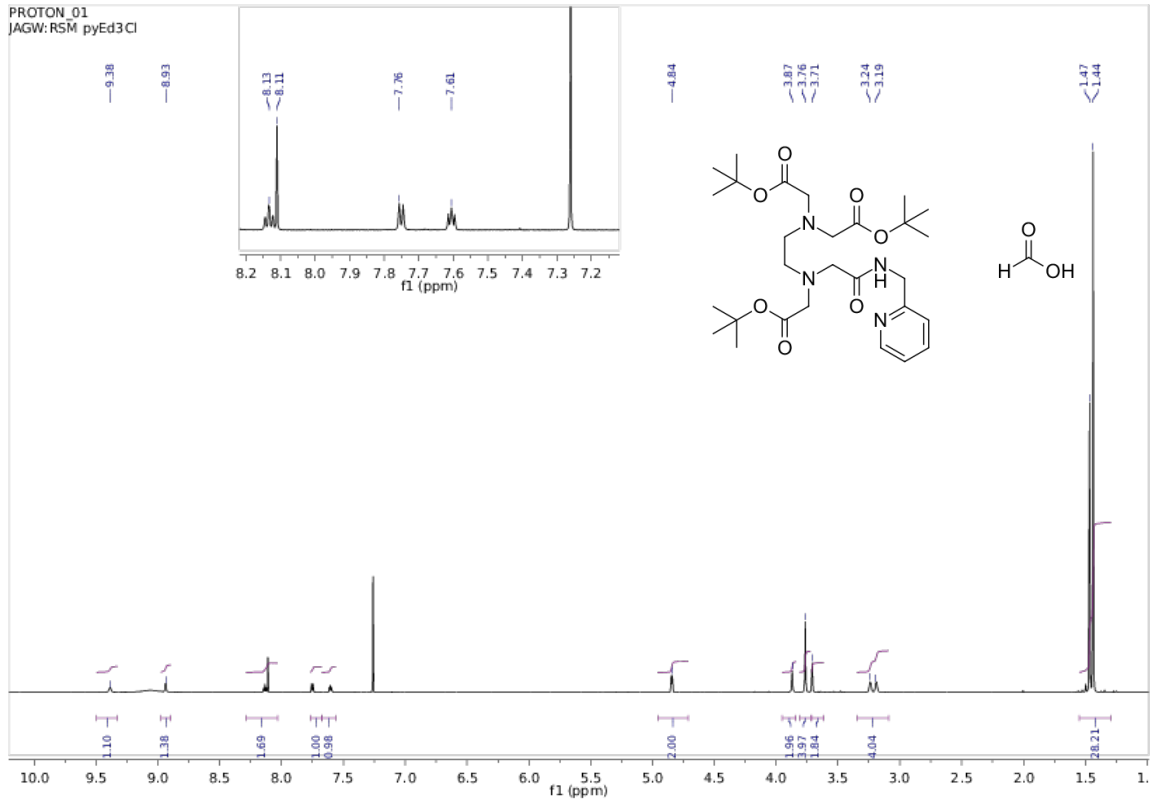
^{1}H NMR of **4**



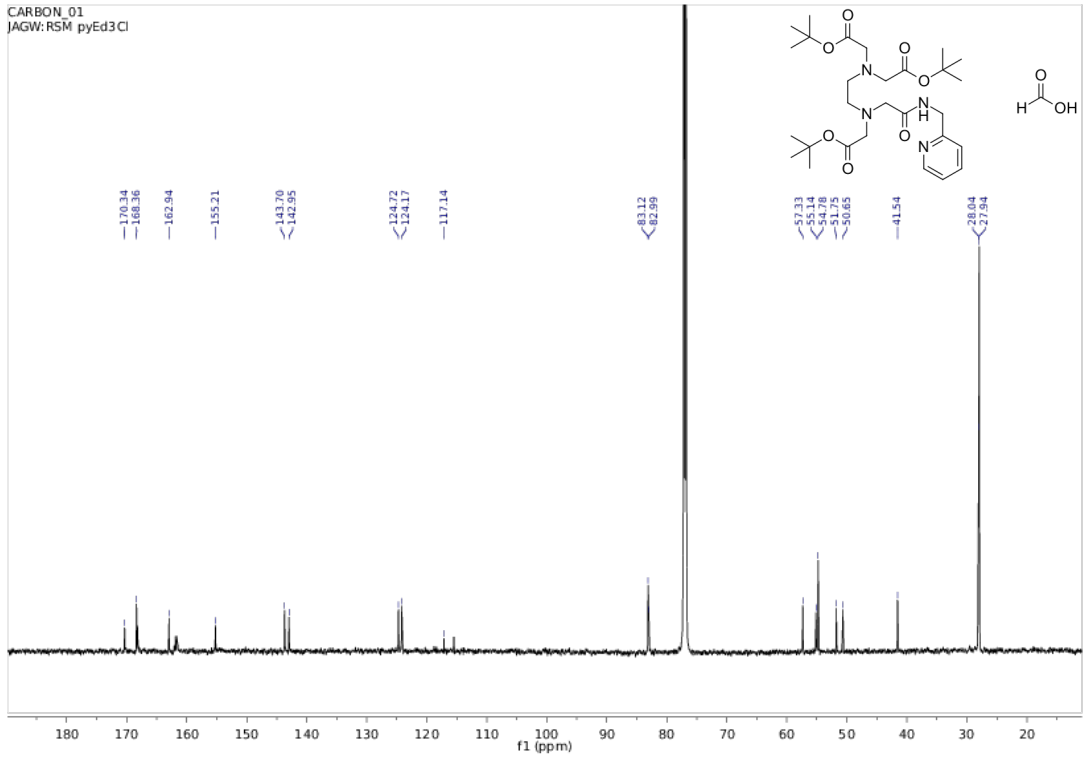
^{13}C NMR of **4**



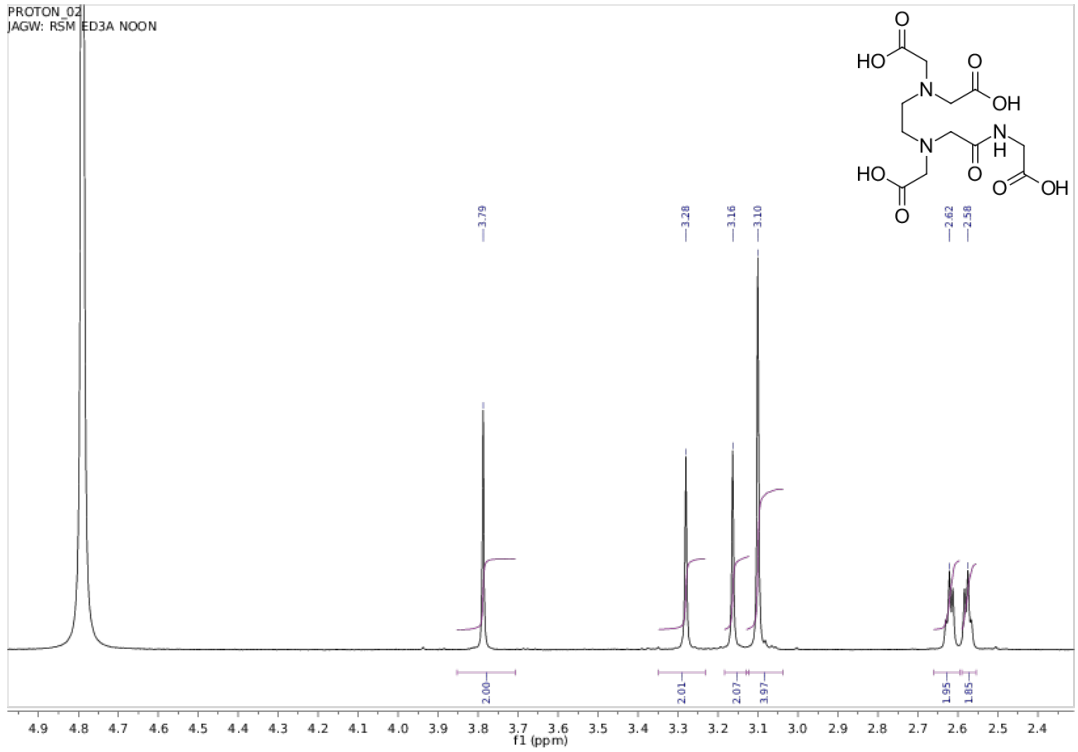
^{1}H NMR of **5**



^{13}C NMR of **5**[i]

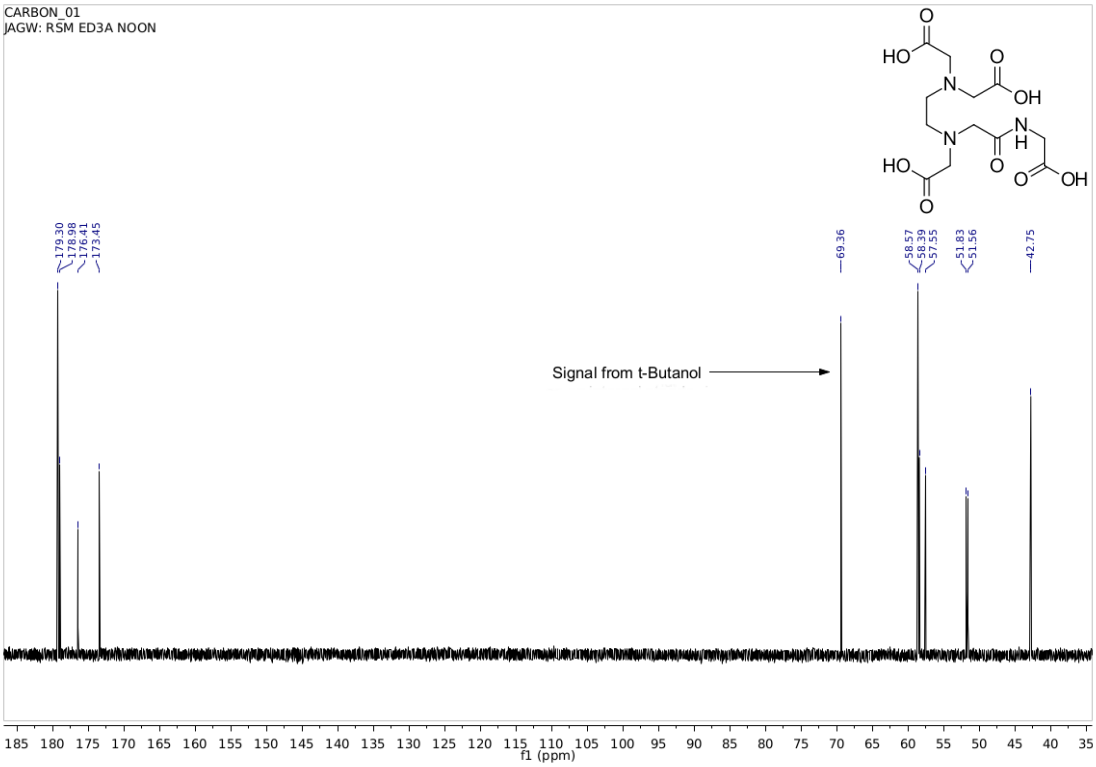


^{1}H NMR of **AmGly$_1$**

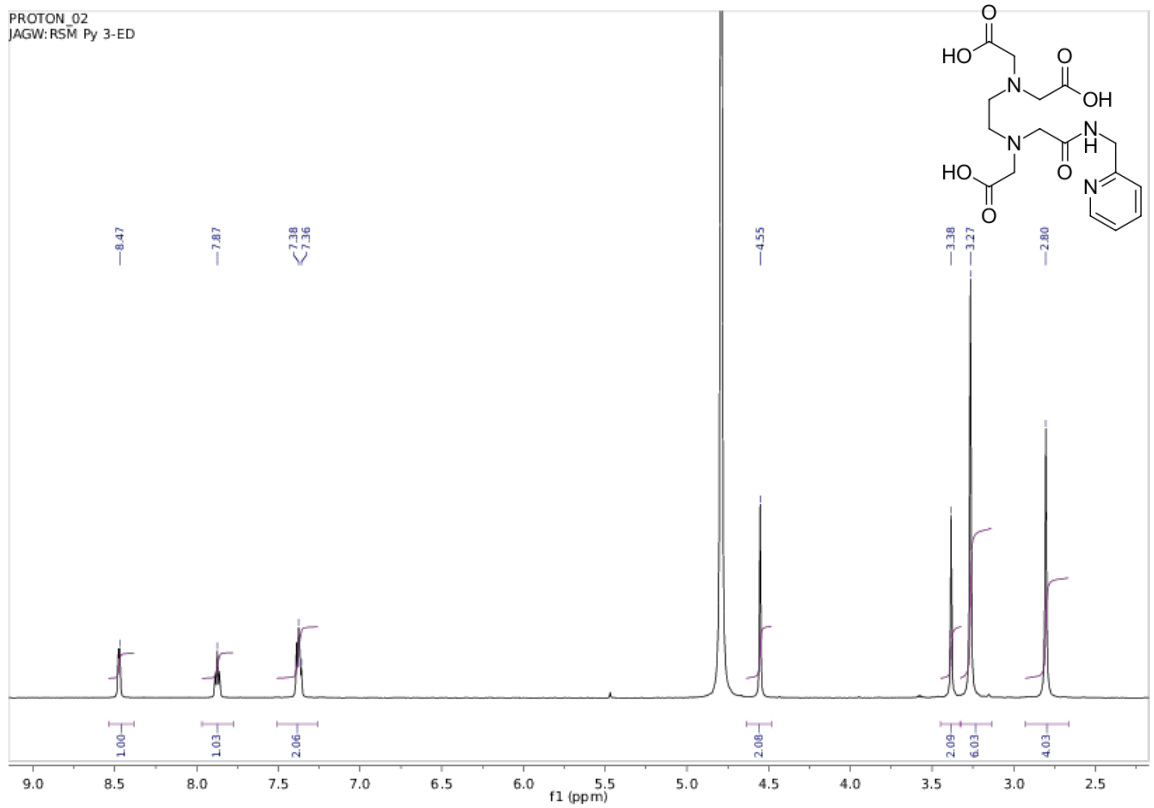


[i] It is noted that the ^{13}C NMR spectrum of this compound displays impurities, but it has been included here to demonstrate that they are removed following the deprotection of **5** and subsequent workup.

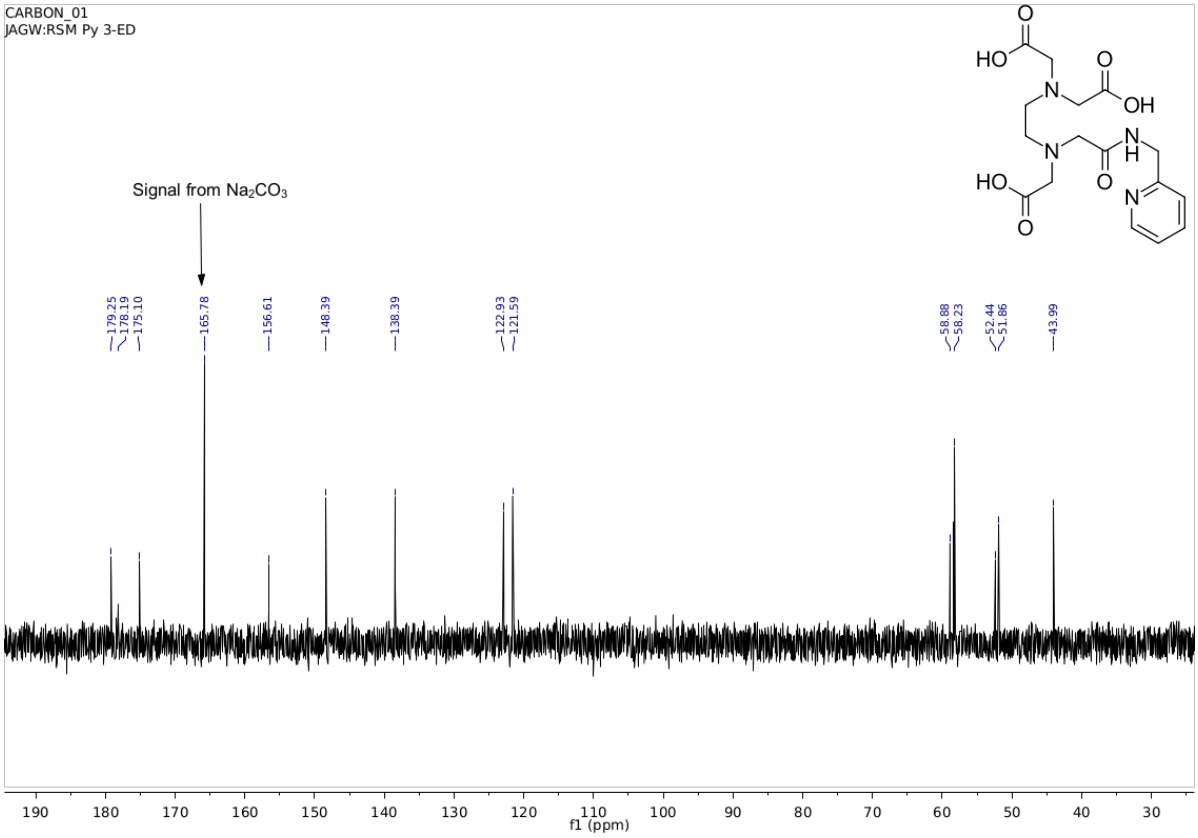
^{13}C NMR of **AmGly$_1$**



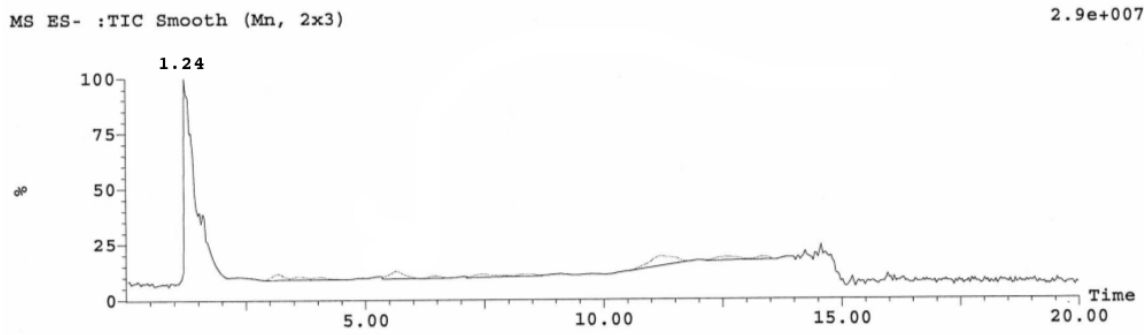
^{1}H NMR of **AmPy$_1$**



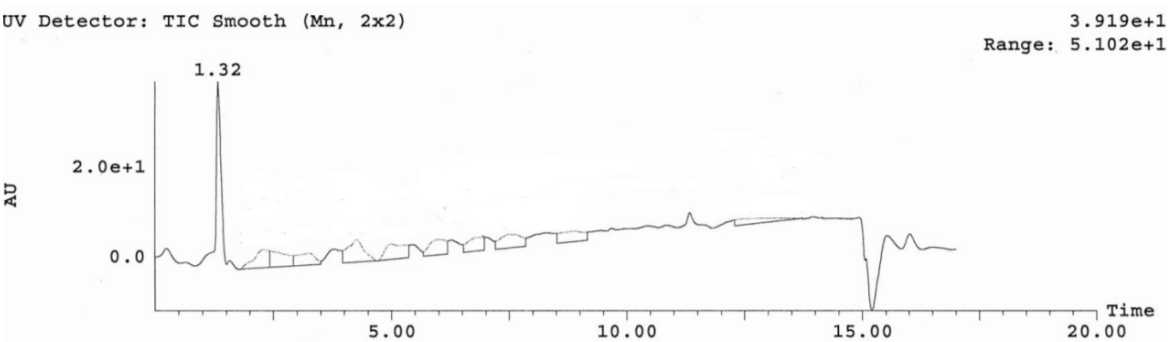
^{13}C NMR of **AmPy$_1$**



HPLC Trace for **AmGly$_1$**



HPLC Trace for **AmPy$_1$**



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