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Influence of the dipeptide linker configuration on the activity of PSMA ligands

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Synthesis

General procedure of synthesis of Boc-amino acids (*N*-Boc-L-Phe; *N*-Boc-D-Phe; *N*-Boc-Gly). Reagent Boc_2O (1.5 eq.) and NaOH (1 eq.) were added to an amino acid suspension (1 eq.) in dioxane/water mixture (1:1, 50 ml). The mixture was stirred for 24 hours and then concentrated at low pressure. Hydrochloric acid (1 *M*) was added to the water residue to adjust pH = 6 and then it was extracted with ethyl acetate (3×50 ml). The combined organic phase was washed with saturated solutions of $NaHCO_3$ and NaCl, was dried over Na_2SO_4 and concentrated in at low pressure.

(*S*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanoic acid (*N*-Boc-L-Phe). Colorless amorphous substance; yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.31 (2H, t, *J* = 7.3 Hz), 7.28 – 7.24 (2H, m), 7.20 (1H, d, *J* = 7.1 Hz), 4.93 (1H, s), 4.61 (1H, s), 3.20 (2H, d, *J* = 13.4 Hz), 1.43 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.39, 135.85, 132.11, 130.65, 129.40, 128.60, 127.11, 80.31, 54.27, 37.79, 35.4, 32.43, 28.29. HRMS (ESI) for $C_{14}H_{19}NO_4$: m/z 266.1385 (calcd 264.1372 for $[M+H]^+$).

(*R*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanoic acid (*N*-Boc-D-Phe). Colorless amorphous substance; yield 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.88 (1 H, br. s.), 7.27 - 7.34 (4 H, m), 7.13 - 7.25 (4 H, m), 4.91 - 5.01 (1 H, m), 4.57 - 4.68 (1 H, m), 4.35 - 4.47 (1 H, m), 3.15 - 3.25 (2 H, m), 3.04 - 3.15 (1 H, m), 2.84 - 2.98 (1 H, m), 1.36 - 1.46 (10 H, m).
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 212.13, 176.44, 129.37, 129.35, 128.57, 127.07, 77.31, 54.23, 37.75, 28.26, 27.96, 27.95. HRMS (ESI) for $C_{14}H_{19}NO_4$: m/z 266.1259 (calcd 266.1392 for $[M+H]^+$).

2-(*tert*-Butoxycarbonylamino)acetic acid (*N*-Boc-Gly). Colorless amorphous substance; yield 100%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.44 (9 H, s), 3.86 - 3.92 (1 H, m), 3.95 (1 H, d, *J*=4.64 Hz), 5.19 (1 H, br. s.), 10.54 (1 H, br. s.). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 174.37, 155.60, 80.01, 42.94, 41.78, 27.86.

General procedure of synthesis of Boc-dipeptides (1a-i). Reagents EDC×HCl (1.12 eq.) and C_6F_5OH (1.12 eq.) were added to a solution of Boc-amino acid (1 eq.) in dichloromethane (50 ml), and this was stirred at room temperature for 12 hours. Then silica gel (10-fold excess of Boc-amino acid) was added, and the resulting suspension was chromatographed on a column with silica gel (eluent: dichloromethane). Then product was isolated by precipitation with petroleum ether/chloroform (1:1) in the mixture at low temperature. The obtained substance was dissolved in THF-water mixture (5:1, 60 ml), and amino acid (2 eq.) was added. DIPEA (2 eq.) was added, and this was stirred at room temperature for 12 hours. At the end of the reaction, mixture was concentrated under reduced pressure. The aqueous residue was acidified with 1 M HCl solution to pH = 2 and extracted with ethyl acetate (3×50 ml). The combined organic phase was washed with saturated solutions of $NaHCO_3$ and NaCl, dried over Na_2SO_4 and concentrated under reduced pressure. The obtained substance was dissolved in minimum diethyl ether and precipitated with equal volume of petroleum ether.

(*S*)-2-(2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)acetic acid (1a). Transparent colorless oil; yield 53%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.58 (1 H, br. s.), 8.21 - 8.32 (1 H, m), 7.21 - 7.32 (5 H, m), 7.13 - 7.21 (1 H, m), 6.89 - 6.95 (1 H, m), 4.12 - 4.23 (1 H, m), 3.67 - 3.87 (2 H, m), 2.91 - 3.03 (1 H, m), 2.63 - 2.76 (1 H, m), 1.27 (9 H, s). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.15, 171.24, 155.27, 146.32, 138.43, 138.32, 129.23, 128.01, 126.15, 77.99, 72.44, 68.99, 28.16, 27.41, 16.35.

(*S*)-2-[2-(*tert*-Butoxycarbonylamino)acetamido]-3-phenylpropanoic acid (1b). White amorphous powder; yield 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.28 (1 H, br. s.), 7.19 - 7.26 (2 H, m), 7.15 (2 H, d, *J*=7.03 Hz), 6.81 (1 H, br. s.), 4.86 (1 H, br. s.), 3.89 (1 H, d, *J*=16.87 Hz), 3.69 (1 H, d, *J*=17.00 Hz), 3.13 - 3.26 (1 H, m), 3.09 (2 H, br. s.), 1.43 (9 H, s). MS (ESI) for $C_{16}H_{22}N_2O_5$: m/z 323.20 (calcd 323.16 for $[M+H]^+$), 667.20 (calcd 667.29 $[2M+Na]^+$)

(*R*)-2-[(*S*)-2-(*tert*-Butoxycarbonylamino)-3-phenylpropanamido]-3-phenylpropanoic acid (1c). Transparent colorless oil; yield 96%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.25 - 8.34 (1 H, m), 7.09 - 7.27 (11 H, m), 6.70 - 6.75 (1 H, m), 4.42 - 4.52 (1 H, m), 3.98 - 4.21 (1 H, m), 3.01 - 3.13 (1 H, m), 2.79 - 2.90 (1 H, m), 2.62 - 2.70 (1 H, m), 1.30 - 1.36 (1 H, m), 1.20 - 1.29 (9 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.89, 171.50, 155.10, 138.14, 138.14, 137.43, 137.20, 129.29, 129.21, 128.17, 127.92, 126.51, 126.10, 77.93, 55.37, 53.31, 28.15.
MS (ESI) for $C_{23}H_{28}N_2O_5$: m/z 413.15 (calcd 413.49 for $[M+H]^+$).

(*R*)-2-((*S*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)-3-(4-hydroxyphenyl)-propanoic acid (1d). Transparent colorless oil; yield 95%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.19 (1 H, br. s.), 7.09 - 7.29 (7 H, m), 6.95 - 7.05 (2 H, m), 6.74 (1 H, d, *J*=8.74 Hz), 6.58 - 6.65 (2 H, m), 4.32 - 4.44 (1 H, m), 4.04 - 4.22 (1 H, m), 2.89 - 2.99 (1 H, m), 2.69 - 2.78 (2 H, m), 1.30

(2 H, s), 1.22 - 1.29 (9 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.45, 170.86, 155.43, 154.54, 137.61, 129.65, 128.67, 128.55, 127.60, 127.37, 126.79, 125.54, 114.39, 77.38, 54.84, 53.05, 27.58. MS (ESI) for $C_{23}H_{28}N_2O_6$: m/z 429.10 (calcd 428.48 for $[M+H]^+$).

(*S*)-2-((*R*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)-3-phenylpropanoic acid (1e). White amorphous powder; yield 100%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.29 (2 H, d, *J*=6.85 Hz), 7.19 - 7.25 (5 H, m), 7.17 (3 H, d, *J*=6.72 Hz), 6.93 (2 H, br. s.), 6.78 (1 H, d, *J*=6.11 Hz), 5.32 (1 H, d, *J*=8.38 Hz), 4.85 (1 H, br. s.), 4.64 (1 H, d, *J*=7.03 Hz), 2.93 - 3.07 (3 H, m), 2.87 (1 H, dd, *J*=13.05, 6.88 Hz), 1.40 - 1.48 (1 H, m), 1.35 (9 H, br. s.). ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 135.83, 129.00, 128.20, 128.03, 126.62, 54.87, 52.50, 38.82, 37.25, 28.88, 27.76. MS (ESI) for $C_{23}H_{28}N_2O_5$: m/z 413.15 (calcd 413.21 for $[M+H]^+$), m/z 847.25 (calcd 847.39 for $[2M+Na]^+$).

(*S*)-2-((*R*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)-3-(4-hydroxyphenyl)-propanoic acid (1f). Transparent colorless oil; yield 83%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.19 (1 H, d, *J*=8.38 Hz), 7.08 - 7.30 (6 H, m), 6.97 - 7.04 (2 H, m), 6.73 (1 H, d, *J*=8.86 Hz), 6.60 - 6.64 (2 H, m), 4.33 - 4.44 (1 H, m), 4.05 - 4.22 (1 H, m), 3.30 - 3.44 (5 H, m), 2.90 - 2.98 (1 H, m), 2.70 - 2.77 (2 H, m), 1.29 - 1.33 (1 H, m), 1.20 - 1.29 (9 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 173.01, 171.43, 168.42, 155.99, 155.10, 138.18, 130.22, 129.23, 127.93, 127.35, 126.10, 114.95, 114.94, 77.93, 55.40, 53.61, 36.34, 28.14. MS (ESI) for $C_{23}H_{28}N_2O_6$: m/z 429.15 (calcd 428.48 for $[M+H]^+$).

(*S*)-2-((*S*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)-3-(4-nitrophenyl)propanoic acid (1g). Transparent colorless oil; yield 63%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.11 (11 H, d, *J*=7.70 Hz), 7.51 (7 H, br. s.), 7.22 (18 H, br. s.), 6.84 (3 H, br. s.), 4.53 (4 H, br. s.), 4.12 (3 H, br. s.), 3.24 (5 H, br. s.), 3.06 (5 H, br. s.), 2.86 (4 H, br. s.), 2.65 (4 H, br. s.), 1.24 (31 H, br. s.), 1.08 (5 H, br. s.).

(*S*)-3-(3-Bromo-4-hydroxyphenyl)-2-((*S*)-2-*tert*-butoxycarbonylamino-3-phenylpropanamido)propanoic acid (1h). Transparent colorless oil; yield 97%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.54 (1H, br. s.), 9.99 (1 H, br. s.), 7.96 - 8.01 (1 H, m), 7.28 - 7.35 (1 H, m), 7.13 - 7.27 (5 H, m), 6.97 - 7.05 (1 H, m), 6.91 (1 H, d, *J*=8.93 Hz), 6.78 - 6.88 (1 H, m), 4.29 - 4.41 (1 H, m), 4.06 - 4.17 (1 H, m), 2.92 - 3.00 (1 H, m), 2.75 - 2.92 (2 H, m), 2.58 - 2.71 (1 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 153.08, 133.78, 129.92, 129.55, 128.41, 126.56, 116.49, 78.50, 53.88, 37.94, 35.94, 28.53. MS (ESI) for $C_{23}H_{27}BrN_2O_6$: m/z 507.10 (calcd 507.38 for $[M+H]^+$).

(*S*)-2-((*S*)-2-*tert*-Butoxycarbonylamino-3-phenylpropanamido)-3-(3,4-dihydroxy-phenyl)propanoic acid (1i). White amorphous powder; yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 12.69 (1 H, br. s.), 8.74 (2 H, br. s.), 8.00 (1 H, d, *J*=7.76 Hz), 7.25 (1 H, br. s.), 7.23 (1 H,

s), 7.21 (2 H, d, *J*=4.16 Hz), 7.18 (1 H, d, *J*=5.99 Hz), 7.13 - 7.17 (1 H, m), 6.87 (1 H, d, *J*=8.86 Hz), 6.56 - 6.64 (2 H, m), 6.47 (1 H, dd, *J*=8.07, 1.90 Hz), 4.30 - 4.38 (1 H, m), 4.10 - 4.17 (1 H, m), 2.84 (1 H, d, *J*=5.62 Hz), 1.26 (9 H, s). MS (ESI) for $C_{23}H_{28}N_2O_7$: m/z 445.20 (calcd 445.20 for $[M+H]^+$), m/z 911.35 (calcd 911.37 for $[2M+Na]^+$).

General procedure of synthesis of dipeptide trifluoroacetate with 3-azido-1-propanamine (2a-i). Stage (i): Boc-dipeptide (1 eq.) was dissolved in DMF (20 ml). Reagents HBTU (1.2 eq.), HOBT (1.2 eq.), DIPEA (2 eq.) and 3-azido-1-propanamine (1.5 eq.) were added to the solution. The mixture was stirred for 16 hours. Then the solvent was removed under reduced pressure. The product was isolated by column chromatography (Puriflash 15 μ, 25 g F0025, EtOAc/petroleum ether system, EtOAc 5→40% in 6 minutes, 40→60% in 15 minutes, 60→100% in 6 minutes, 100% in 3 minutes).

Stage (ii): A 10% solution of trifluoroacetic acid in dichloromethane (10 ml) was added to Boc-dipeptide and 3-azido-1-propanamine solution, and the reaction solution was stirred at room temperature for 3 hours (TLC control). The solvent was removed at reduced pressure and the product was re-evaporated several times from DCM. The product was isolated by resuspension into diethyl ether (50 ml).

***tert*-Butyl *N*-{(*S*)-1-[2-(3-azidopropylamino)-2-oxoethylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 73%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.14 - 8.27 (1 H, m), 7.73 (1 H, t, *J*=6.60 Hz), 7.21 - 7.29 (4 H, m), 7.13 - 7.21 (1 H, m), 7.02 - 7.10 (1 H, m), 4.05 - 4.19 (1 H, m), 3.56 - 3.76 (2 H, m), 3.04 - 3.20 (2 H, m), 2.93 - 3.04 (1 H, m), 2.69 - 2.79 (1 H, m), 1.58 - 1.69 (2 H, m), 1.23 - 1.33 (8 H, m), 1.17 (1 H, br. s.). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.05, 168.73, 155.55, 138.21, 129.25, 129.23, 129.23, 128.08, 128.07, 128.05, 126.20, 78.24, 55.96, 48.29, 42.20, 40.16, 40.15, 38.28, 35.85, 28.42, 28.15. MS (ESI) for $C_{19}H_{28}N_6O_4$: m/z 589.10 (calcd 589.49 for $[M+H]^+$)

(*S*)-1-[2-(3-Azidopropylamino)-2-oxoethylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2a). White amorphous powder; yield 93%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.68 - 8.78 (1 H, m), 8.05 - 8.18 (3 H, m), 7.95 - 8.03 (1 H, m), 7.21 - 7.38 (5 H, m), 3.63 - 3.82 (2 H, m), 3.02 - 3.19 (3 H, m), 2.85 - 2.97 (1 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 167.80, 167.47, 151.12, 134.37, 128.99, 128.04, 126.67, 108.94, 93.62, 85.85, 62.52, 52.86, 47.74, 27.84, 17.28, 4.53. MS (ESI) for $C_{16}H_{21}F_3N_6O_4$: m/z 305.36 (calcd 305.15 for $[M+H]^+$).

***tert*-Butyl *N*-{(*S*)-2-[1-(3-azidopropylamino)-1-oxo-3-phenylpropan-2-yl]amino-2-oxoethyl}-carbamate.** Transparent colorless oil; yield 49%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.99 (2 H, d, *J*=7.39 Hz), 7.13 - 7.29 (5 H, m), 6.94 (1 H, t, *J*=5.90 Hz), 4.41 (1 H, d, *J*=6.32 Hz), 3.52 (1 H, d, *J*=6.02 Hz), 3.45 (1 H, d, *J*=5.94 Hz), 3.18 (2 H, t, *J*=6.81 Hz), 3.05 - 3.15 (1 H, m), 2.96 -

3.05 (1 H, m), 2.90 (1 H, d, *J*=5.86 Hz), 2.81 (1 H, d, *J*=8.38 Hz), 1.48 - 1.59 (2 H, m), 1.36 (9 H, s). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 170.70, 169.06, 137.65, 129.18, 128.11, 126.34 , 78.13, 54.01, 48.19, 35.78, 28.20. MS (ESI) for $C_{19}H_{28}N_6O_4$: m/z 405.15 (calcd 405.22 for $[M+H]^+$), m/z 831.25 (calcd 831.42 for $[2M+Na]^+$).

(*S*)-2-[1-(3-Azidopropylamino)-1-oxo-3-phenylpropan-2-ylamino]-2-oxoethan-1-ammonium 2,2,2-trifluoroacetate (2b). White amorphous powder; yield 89%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.73 (1 H, d, *J*=8.25 Hz), 8.20 (1 H, t, *J*=5.59 Hz), 7.98 (3 H, br. s.), 7.16 - 7.31 (5 H, m), 4.45 - 4.53 (1 H, m), 3.51 - 3.61 (1 H, m), 3.19 (2 H, t, *J*=6.82 Hz), 3.08 - 3.16 (1 H, m), 2.99 - 3.05 (1 H, m), 2.95 (1 H, dd, *J*=13.75, 5.93 Hz), 2.77 (1 H, dd, *J*=13.54, 8.77 Hz), 1.48 - 1.61 (2 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 170.39, 165.66, 137.40, 129.19, 128.20, 126.50, 54.38, 48.20, 38.12, 35.80, 28.21. MS (ESI) for $C_{16}H_{21}F_3N_6O_4$: m/z 305.15 (calcd 305.35 for $[M+H]^+$), 609.25 (calcd 609.34 for $[2M+H]^+$)

***tert*-Butyl *N*-{(*S*)-1-[(*R*)-1-((3-Azidopropylamino)-1-oxo-3-phenylpropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 46%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.26 - 8.38 (1 H, m), 7.91 - 8.04 (1 H, m), 7.08 - 7.28 (12 H, m), 4.39 - 4.51 (1 H, m), 4.08 - 4.17 (1 H, m), 3.05 - 3.28 (5 H, m), 2.80 - 3.02 (3 H, m), 2.71 - 2.79 (1 H, m), 2.60 - 2.69 (1 H, m), 1.46 - 1.63 (3 H, m), 1.23 - 1.32 (9 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 171.48, 170.80, 155.36, 148.58, 129.25, 129.23, 129.18, 128.10, 128.08, 128.02, 127.94, 126.36, 126.14, 117.92, 112.48, 78.18, 78.09, 55.73, 53.96, 53.31, 48.21, 48.14, 42.89, 40.42, 40.15, 28.27, 28.22, 28.14, 28.14. MS (ESI) for $C_{26}H_{34}N_6O_4$: m/z 495.20 (calcd 494.59 for $[M+H]^+$).

(*S*)-1-[(*R*)-1-(3-Azidopropylamino)-1-oxo-3-phenylpropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2c). White amorphous powder; yield 68%.
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.77 - 8.99 (1 H, m), 8.01 - 8.19 (2 H, m), 7.05 - 7.34 (6 H, m), 6.78 - 7.00 (1 H, m), 4.38 - 4.57 (1 H, m), 3.90 - 4.07 (1 H, m), 2.97 - 3.16 (2 H, m), 2.86 - 2.95 (1 H, m), 2.78 - 2.84 (1 H, m), 2.56 - 2.71 (1 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 207.35, 170.79, 170.46, 168.06, 137.83, 137.68, 135.14, 135.08, 130.01, 129.93, 129.71, 129.61, 128.86, 128.83, 128.61, 128.56, 127.47, 126.95, 126.89, 54.91, 54.66, 53.68, 53.54, 48.62, 48.53, 38.62, 37.26, 36.22, 36.12, 28.6. MS (ESI) for $C_{23}H_{27}F_3N_6O_4$: m/z 395.15 (calcd 395.22 for $[M+H]^+$)

***tert*-Butyl *N*-{(*S*)-1-[(*R*)-1-(3-azidopropylamino)-3-(4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 58%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.04 - 9.20 (1 H, m), 8.19 - 8.29 (1 H, m), 7.87 - 8.04 (1 H, m), 7.09 - 7.26 (6 H, m), 6.87 - 7.05 (2 H, m), 6.75 - 6.87 (1 H, m), 6.55 - 6.67 (2 H, m), 4.29 - 4.40 (1 H, m), 4.06 - 4.18 (1 H, m), 3.03 - 3.17 (2 H, m), 2.75 - 2.94 (1 H, m), 2.58 - 2.75 (2 H,

m), 1.53 - 1.64 (2 H, m), 1.23 - 1.32 (10 H, m). MS (ESI) for $C_{26}H_{34}N_6O_5$: m/z 511.20 (calcd 510.59 for $[M+H]^+$)

(*S*)-1-[(*R*)-1-((3-Azidopropylamino)-3-(4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2d). White amorphous powder; yield 98%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.22 (1 H, br. s.), 8.74 - 8.86 (1 H, m), 8.15 - 8.29 (1 H, m), 8.07 - 8.15 (1 H, m), 7.94 - 8.07 (2 H, m), 7.19 - 7.35 (4 H, m), 6.94 - 7.10 (4 H, m), 6.56 - 6.71 (2 H, m), 4.35 - 4.48 (1 H, m), 3.96 - 4.08 (1 H, m), 2.98 - 3.23 (3 H, m), 2.74 - 2.95 (2 H, m), 2.51 - 2.73 (2 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 170.63, 167.56, 156.10, 134.70, 130.23, 130.11, 129.58, 128.47, 127.35, 127.11, 114.94, 54.54, 54.53, 53.28, 48.23, 37.58, 36.96, 35.80, 28.26. MS (ESI) for $C_{23}H_{27}F_3N_6O_5$: m/z 411.20 (calcd 411.21 for $[M+H]^+$).

***tert*-Butyl *N*-{(*R*)-1-[(*S*)-1-(3-azidopropylamino)-1-oxo-3-phenylpropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 46%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.33 (1 H, d, *J*=8.45 Hz), 7.95 - 8.03 (1 H, m), 7.10 - 7.28 (10 H, m), 4.45 (1 H, d, *J*=6.93 Hz), 4.12 (1 H, d, *J*=5.79 Hz), 3.24 (1 H, t, *J*=6.81 Hz), 3.17 (1 H, t, *J*=6.85 Hz), 2.87 - 3.02 (1 H, m), 2.79 - 2.87 (1 H, m), 2.64 (1 H, dd, *J*=12.98, 3.01 Hz), 1.48 - 1.65 (2 H, m), 1.28 (9 H, s). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 138.07, 137.49, 129.26, 128.08, 128.01, 127.95, 126.36, 126.15, 78.11, 48.21, 35.86, 28.27, 28.14, 27.75, 3.89. MS (ESI) for $C_{26}H_{34}N_6O_4$: m/z 495.20 (calcd 495.27 for $[M+H]^+$), m/z 517.20 (calcd 517.25 for $[M+Na]^+$), 1011.40 (calcd 1011.52 for $[2M+H]^+$).

(*R*)-1-[(*S*)-1-(3-Azidopropylamino)-1-oxo-3-phenylpropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2e). White amorphous powder; yield 65%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.85 (1 H, dd, *J*=18.58, 8.31 Hz), 8.24 (1 H, t, *J*=5.59 Hz), 8.10 - 8.17 (1 H, m), 8.06 (3 H, br. s.), 7.14 - 7.34 (12 H, m), 6.97 - 7.01 (1 H, m), 4.45 - 4.58 (1 H, m), 4.03 (1 H, br. s.), 3.23 (2 H, t, *J*=6.79 Hz), 3.12 - 3.19 (2 H, m), 3.01 - 3.12 (2 H, m), 2.87 - 3.01 (3 H, m), 2.83 (1 H, dd, *J*=14.98, 5.62 Hz), 2.59 - 2.72 (2 H, m), 1.49 - 1.62 (3 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 170.49, 170.12, 167.63, 137.33, 134.57, 129.59, 129.51, 129.31, 129.21, 128.52, 128.49, 128.26, 128.21, 127.16, 126.62, 54.48, 54.23, 53.27, 48.18, 48.09, 38.25, 36.89, 35.82, 28.19, 14.96. MS (ESI) for $C_{23}H_{27}F_3N_6O_4$: m/z 395.15 (calcd 395.22 for $[M+H]^+$), 789.30 (calcd 789.43 for $[2M+H]^+$).

***tert*-Butyl *N*-{(*R*)-1-[(*S*)-1-(3-azidopropylamino)-3-(4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 55%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.08 - 9.19 (1 H, m), 8.19 - 8.30 (1 H, m), 7.87 - 7.99 (1 H, m), 7.10 - 7.27 (6 H, m), 6.91 - 7.05 (2 H, m), 6.77 - 6.85 (1 H, m), 6.55 - 6.71 (2 H, m), 4.28 - 4.41 (1 H, m), 4.06 - 4.19 (1 H, m), 3.22 - 3.30 (2 H, m), 3.01 - 3.14 (2 H, m), 2.77 - 2.89 (1 H,

m), 2.59 - 2.73 (2 H, m), 1.54 - 1.67 (2 H, m), 1.25 - 1.31 (9 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 155.86 , 130.16 , 129.25 , 127.96 , 114.85 , 78.10 , 78.10 , 55.74 , 48.23, 28.30 , 28.14. MS (ESI) for $C_{26}H_{34}N_6O_5$: m/z 511.20 (calcd 510.59 for $[M+H]^+$).

(*R*)-1-[(*S*)-1-(3-Azidopropylamino)-3-(4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2f). White amorphous powder; yield 81%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.74 - 8.96 (1 H, m), 7.99 - 8.17 (3 H, m), 7.12 - 7.39 (3 H, m), 6.86 - 7.06 (4 H, m), 4.30 - 4.51 (1 H, m), 2.96 - 3.22 (2 H, m), 2.72 - 2.94 (2 H, m), 2.49 - 2.72 (2 H, m). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 171.02, 167.92, 156.46, 135.05, 130.60, 129.95, 128.87, 115.32, 48.61, 36.20, 28.64. MS (ESI) for $C_{23}H_{27}F_3N_6O_5$: m/z 411.20 (calcd 411.48 for $[M+H]^+$).

(*S*)-1-[(*S*)-1-(3-Azidopropylamino)-3-(4-nitrophenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2g) White amorphous powder; yield 67%. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.97 (2 H, d, *J*=8.44 Hz), 8.90 (2 H, d, *J*=8.19 Hz), 8.31 (2 H, t, *J*=5.56 Hz), 8.22 (2 H, t, *J*=5.56 Hz), 8.15 (7 H, dd, *J*=8.74, 2.63 Hz), 8.09 (11 H, br. s.), 7.48 (6 H, dd, *J*=11.43, 8.74 Hz), 7.19 - 7.32 (15 H, m), 6.95 - 7.07 (4 H, m), 4.50 - 4.67 (7 H, m), 4.03 (4 H, br. s.), 3.16 - 3.29 (9 H, m), 2.99 - 3.16 (14 H, m), 2.82 - 2.99 (8 H, m), 1.58 (8 H, m).

***tert*-Butyl *N*-{(*S*)-1-[(*S*)-1-(3-azidopropylamino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 55%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.91 - 9.99 (1 H, m) 8.23 - 8.33 (1 H, m) 7.81 - 8.05 (2 H, m) 7.26 - 7.40 (2 H, m) 7.06 - 7.24 (6 H, m) 6.97 (1 H, dt, *J*=8.22, 2.35 Hz) 6.89 (1 H, d, *J*=8.80 Hz) 6.73 - 6.82 (2 H, m) 4.26 - 4.50 (2 H, m) 4.04 - 4.18 (1 H, m) 3.18 - 3.27 (2 H, m) 2.94 - 3.15 (3 H, m) 2.74 - 2.87 (2 H, m) 2.49 - 2.74 (3 H, m) 1.47 - 1.65 (3 H, m) 1.21 - 1.33 (9 H, m)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 207.34, 152.99, 138.60, 138.43, 133.77, 129.99, 129.90, 129.65, 129.52, 128.41, 128.30, 126.57, 126.51, 116.37, 113.29, 109.26, 78.63, 78.48, 60.18, 59.79, 57.60, 48.66, 48.60, 40.58, 40.37, 40.16, 30.15, 28.71, 28.53, 19.91, 15.79, 11.02, 3.90.

MS (ESI) for $C_{26}H_{33}BrN_6O_5$: m/z 589.10 (calcd 589.49 for $[M+H]^+$)

(*S*)-1-[(*S*)-1-(3-Azidopropylamino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2h). White amorphous powder; yield 93%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.73 - 8.84 (1 H, m), 8.12 - 8.22 (1 H, m), 8.05 - 8.12 (2 H, m), 7.95 - 8.05 (1 H, m), 7.15 - 7.39 (5 H, m), 6.92 - 7.07 (2 H, m), 6.75 - 6.90 (1 H, m), 4.35 - 4.54 (1 H, m), 3.00 - 3.30 (5 H, m), 2.76 - 2.96 (2 H, m), 2.52 - 2.76 (2 H, m).

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 169.91, 169.54, 167.21, 167.09, 152.20, 134.12, 134.09, 132.83, 132.70, 129.06, 128.99, 128.94, 128.76, 127.95, 127.90, 126.61, 115.51, 115.41, 108.42, 54.07, 52.73, 52.55, 47.67, 47.60, 27.74.

MS (ESI) for $C_{23}H_{26}BrF_3N_6O_5$: m/z 489.10 (calcd 490.38 for $[M+H]^+$)

***tert*-Butyl *N*-{(*S*)-1-[(*S*)-1-(3-azidopropylamino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-yl}carbamate.** Transparent colorless oil; yield 67%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.67 (2 H, d, *J*=8.93 Hz), 7.90 - 7.97 (1 H, m), 7.87 (1 H, d, *J*=8.07 Hz), 7.19 - 7.27 (2 H, m), 7.16 (2 H, d, *J*=6.91 Hz), 6.91 (1 H, d, *J*=8.50 Hz), 6.54 - 6.62 (2 H, m), 6.40 - 6.48 (1 H, m), 4.31 (1 H, d, *J*=7.27 Hz), 4.09 (1 H, d, *J*=3.48 Hz), 3.18 - 3.25 (2 H, m), 2.96 - 3.13 (2 H, m), 2.82 - 2.91 (1 H, m), 2.70 - 2.78 (1 H, m), 2.65 (1 H, d, *J*=6.60 Hz), 1.50 - 1.60 (2 H, m), 1.28 (9 H, s)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 171.15, 170.84, 155.19, 144.89, 143.80, 138.08, 129.19, 128.14, 128.01, 126.16, 119.98, 116.69, 115.19, 78.22, 56.00, 54.37, 38.28, 37.51 , 35.73, 28.27, 28.12, 14.13

MS (ESI) for $C_{26}H_{34}N_6O_6$: m/z 527.25 (calcd 527.26 for $[M+H]^+$), 1053.55 (calcd 1053.51 for $[2M+H]^+$)

(*S*)-1-[(*S*)-1-(3-Azidopropylamino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-ylamino]-1-oxo-3-phenylpropan-2-ammonium 2,2,2-trifluoroacetate (2i). White amorphous powder; yield 100%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.77 (2 H, d, *J*=8.07 Hz), 8.10 - 8.16 (1 H, m), 8.08 (3 H, br. s.), 7.19 - 7.32 (5 H, m), 6.61 (2 H, dd, *J*=4.92, 2.96 Hz), 6.45 (1 H, dd, *J*=8.04, 1.86 Hz), 4.33 - 4.41 (1 H, m), 4.00 (1 H, br. s.), 3.18 - 3.25 (2 H, m), 3.06 - 3.14 (2 H, m), 2.99 - 3.06 (1 H, m), 2.92 (1 H, dd, *J*=14.00, 7.83 Hz), 2.71 - 2.79 (1 H, m), 2.60 - 2.69 (1 H, m), 1.56 (2 H, dq, *J*=9.64, 6.61 Hz)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 170.62, 167.59, 144.76, 143.74, 134.28, 129.51, 128.59, 127.90, 127.32, 120.07, 116.54, 54.96, 53.21, 48.09, 35.84, 28.05

MS (ESI) for $C_{23}H_{27}F_3N_6O_6$: m/z 427.20 (calcd 427.21 for $[M+H]^+$), 853.40 (calcd 853.41 for $[2M+H]^+$)

General procedure of synthesis of ligands 3a-i

Stage 1. (7*S*,11*S*)-7,11-Bis(*tert*-butoxycarbonyl)-16-(3-chlorobenzyl)-2,2-dimethyl-4,9,17-trioxo-3-oxa-8,10,16-triazadocosan-22-oic acid (1 equiv.) was dissolved in DMF (10 ml), and HOBt (1.5 equiv.), HBTU (1.5 equiv.) and DIPEA (2 eq.) were added. The mixture was stirred in argon atmosphere for 2 hours for pre-activation. After that, a dipeptide containing a 3-azidopropanamine

fragment (1.3 equiv.) was added. The mixture was stirred for 24 hours. Then the solvent was removed under reduced pressure. The product was isolated by column chromatography (Puriflash 50µ, 4 g, eluent: petroleum ether/ethyl acetate => ethyl acetate/methanol system, 5→100% EtOAc for 15 minutes, 100% EtOAc for 1 minute, from 0→100% MeOH for 5 minutes, 100% MeOH for 5 minutes).

Stage 2. A Boc-containing ligand (1 eq.) was dissolved in a solution of trifluoroacetic acid, DCM, distilled water and triisopropylsilane (46.25:46.25:5:2.5), and this was stirred for 3 hours at room temperature. The solvent was removed under reduced pressure. The resulting substance was re-evaporated three times from DCM. To the resulting oily residue diethyl ether (5 ml) was added to precipitate a white solid. The ether was decanted, and the operation was repeated two times. The product was isolated using the column chromatography with the reverse phase (Puriflash C18 15µ, 20 g, eluent: acetonitrile-water system: 10→100% MeCN in 20 minutes).

Tri-*tert*-butyl (3*S*,7*S*,25*S*)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexa-oxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 57%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.97 - 8.08 (1 H, m), 7.37 - 7.47 (1 H, m), 7.27 - 7.32 (2 H, m), 7.19 - 7.26 (4 H, m), 7.14 - 7.18 (1 H, m), 7.00 - 7.09 (1 H, m), 4.59 - 4.69 (1 H, m), 4.47 - 4.56 (2 H, m), 4.24 - 4.37 (2 H, m), 3.87 - 4.00 (2 H, m), 3.24 - 3.38 (8 H, m), 2.36 - 2.45 (1 H, m), 2.23 - 2.36 (3 H, m), 1.72 - 1.90 (4 H, m), 1.49 - 1.72 (7 H, m), 1.38 - 1.48 (30 H, m), 1.28 - 1.37 (4 H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 218.78, 218.18, 191.54, 174.47, 170.65, 164.23, 141.07, 140.11, 128.68, 121.29, 116.98, 112.07, 108.34, 89.59, 83.64, 74.32, 60.08, 38.51, 27.65, 27.62, 27.58, 16.84

HRMS (ESI) for $C_{55}H_{82}ClN_{10}O_{12}$: m/z 1111.6053 (calcd 1111.5953 for $[M+H]^+$)

(3*S*,7*S*,25*S*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3a). White amorphous powder; yield 22%.

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 174.50, 174.20, 173.81, 172.49, 172.29, 171.68, 171.38, 168.78, 158.42, 157.32, 138.10, 133.05, 130.64, 130.28, 129.09, 128.16, 127.16, 126.86, 126.33, 126.07, 124.98, 56.08, 54.84, 51.65, 48.26, 36.79, 35.86, 31.74, 30.66, 30.53, 29.89, 29.03, 28.27, 27.50, 26.20, 24.72, 22.32.

HRMS (ESI) for $C_{43}H_{59}ClN_{10}O_{12}$: m/z 943.4062 (calcd 943.4075 for $[M+H]^+$), m/z 941.3963 (calcd 941.3930 for $[M-H]^-$)

HPLC-MS purity: 100% (+), 100% (-)

Tri-*tert*-butyl (3*S*,7*S*,28*S*)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 56%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.57 (1 H, br. s.), 8.45 (1 H, br. s.), 7.28 - 7.32 (1 H, m), 7.20 - 7.26 (5 H, m), 7.15 - 7.20 (1 H, m), 6.99 - 7.15 (1 H, m), 4.70 (1 H, br. s.), 4.48 - 4.55 (2 H, m), 4.30 - 4.38 (2 H, m), 4.28 (1 H, br. s.), 3.77 - 3.90 (1 H, m), 3.26 - 3.43 (3 H, m), 3.13 - 3.26 (4 H, m), 3.06 (1 H, dd, *J*=13.59, 8.79 Hz), 2.37 - 2.46 (1 H, m), 2.33 (2 H, m), 1.81 - 1.91 (1 H, m), 1.65 - 1.78 (3 H, m), 1.50 - 1.65 (5 H, m), 1.44 (24 H, d, *J*=6.40 Hz), 1.30 - 1.40 (3 H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 173.21, 172.37,171.42, 168.91, 157.34, 157.21, 137.34, 134.97, 134.41, 130.25, 129.83, 129.19, 128.40, 127.86, 127.70, 127.42, 126.67, 126.34, 125.89, 124.32, 81.85, 80.54, 55.09, 53.47, 53.24, 53.05, 52.96, 50.57, 48.86, 45.80, 43.67, 39.62, 38.63, 36.78, 32.82, 32.48, 31.69, 31.65, 31.17, 30.77, 28.45, 28.14, 28.05, 28.02, 27.99, 26.87, 26.24, 24.47, 22.44.

HRMS (ESI) for $C_{55}H_{83}ClN_{10}O_{12}$: m/z 1111.5973 (calcd 1111.5953 for $[M+H]^+$).

(3*S*,7*S*,28*S*)-33-Azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3b). White amorphous powder; yield 43%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.37 (3 H, br. s.), 8.29 (1 H, br. s.), 8.05 - 8.11 (1 H, m), 7.85 - 7.93 (1 H, m), 7.71 (1 H, d, *J*=6.36 Hz), 7.34 - 7.39 (1 H, m), 7.29 - 7.34 (1 H, m), 7.08 - 7.29 (8 H, m), 6.23 - 6.34 (2 H, m), 4.34 - 4.41 (1 H, m), 3.99 - 4.12 (2 H, m), 3.55 - 3.61 (2 H, m), 3.19 - 3.25 (3 H, m), 3.13 - 3.19 (2 H, m), 2.94 - 3.13 (6 H, m), 2.82 - 2.89 (1 H, m), 2.26 - 2.42 (5 H, m), 2.15 - 2.26 (3 H, m), 1.85 - 1.94 (1 H, m), 1.66 - 1.75 (1 H, m), 1.59 (3 H, td, *J*=6.60, 3.42 Hz), 1.50 (3 H, dd, *J*=13.94, 6.60 Hz), 1.41 (3 H, td, *J*=15.41, 7.34 Hz), 1.12 - 1.34 (5 H, m)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 174.06, 172.58, 171.93, 171.22, 169.37, 157.69, 138.51, 129.41, 128.54, 127.64, 127.22, 126.67, 126.50, 54.83, 52.20, 48.72, 42.99, 37.66, 36.37, 32.28, 31.20, 31.03, 30.43, 29.46, 28.61, 28.11, 26.69, 25.14, 22.78

HRMS (ESI) for $C_{43}H_{59}ClN_{10}O_{12}$: m/z 943.4071 (calcd 943.4075 for $[M+H]^+$), m/z 941.3936 (calcd 941.3930 for $[M-H]^-$)

HPLC-MS purity: 98% (+), 100% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*S*,28*R*)-33-Azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 54%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.35 - 7.51 (1 H, m), 7.22 - 7.29 (1 H, m), 7.11 - 7.19 (6 H, m), 6.89 - 7.11 (6 H, m), 5.74 - 6.04 (2 H, m), 4.71 - 4.80 (1 H, m), 4.43 - 4.64 (3 H, m), 4.23 -

4.39 (2 H, m), 3.02 - 3.32 (9 H, m), 2.82 - 3.02 (3 H, m), 2.42 - 2.56 (3 H, m), 2.21 - 2.40 (5 H, m), 1.77 - 1.90 (1 H, m), 1.47 - 1.76 (9 H, m), 1.36 - 1.45 (29 H, m), 1.25 - 1.35 (3 H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 173.43, 173.05, 172.98, 172.76, 172.44, 172.40, 172.37, 172.34, 171.34, 171.19, 170.95, 170.92, 157.25, 157.17, 157.09, 139.89, 139.00, 136.89, 136.74, 134.87, 134.33, 134.31, 130.22, 129.81, 129.32, 129.14, 129.11, 128.97, 128.94, 128.65, 128.60, 128.45, 128.43, 128.39, 128.31, 127.76, 127.65, 127.59, 127.38, 126.86, 126.75, 126.25, 125.87, 124.26, 81.98, 81.90, 81.86, 81.81, 81.78, 81.50, 80.53, 80.45, 77.38, 77.06, 76.75, 60.37, 53.01, 52.84, 52.72, 48.72, 48.70, 38.59, 36.63, 32.51, 31.65, 31.61, 26.26, 24.60, 22.35, 21.02, 14.15.

HRMS (ESI) for $C_{62}H_{89}ClN_{10}O_{12}$: m/z 1201.6459 (calcd 1201.6423 for $[M+H]^+$)

(3*S*,7*S*,25*S*,28*R*)-33-Azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3c). White amorphous powder; yield 18%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.28 - 8.41 (1 H, m), 8.07 - 8.14 (1 H, m), 7.91 - 7.99 (1 H, m), 7.24 - 7.42 (3 H, m), 7.11 - 7.24 (9 H, m), 7.04 - 7.11 (1 H, m), 6.25 - 6.35 (2 H, m), 4.44 - 4.49 (1 H, m), 4.30 - 4.43 (2 H, m), 3.95 - 4.12 (2 H, m), 3.10 - 3.27 (8 H, m), 2.86 - 3.10 (6 H, m), 2.69 - 2.81 (1 H, m), 2.52 - 2.63 (1 H, m), 2.28 - 2.37 (2 H, m), 2.13 - 2.26 (5 H, m), 1.82 - 1.93 (1 H, m), 1.66 - 1.76 (1 H, m), 1.53 - 1.64 (3 H, m), 1.41 - 1.53 (4 H, m), 1.34 (2 H, br. s.), 1.12 - 1.30 (4 H, m)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 174.54, 174.24, 173.85, 172.89, 172.20, 172.18, 171.90, 171.62, 171.23, 171.15, 171.09, 170.92, 170.74, 157.28, 141.22, 140.82, 138.06, 137.99, 133.40, 133.05, 130.62, 130.26, 129.20, 129.14, 129.03, 128.20, 128.10, 128.00, 127.18, 126.85, 126.33, 126.28, 126.19, 126.08, 124.97, 54.34, 52.17, 51.74, 48.21, 48.14, 47.15, 46.88, 35.87, 32.28, 31.86, 31.80, 30.69, 30.60, 30.07, 29.09, 28.19, 28.14, 27.80, 27.68, 26.27, 26.23, 26.15, 24.72, 24.58, 22.33.

HRMS (ESI) for $C_{50}H_{65}ClN_{10}O_{12}$: m/z 1033.4583 (calcd 1033.4545 for $[M+H]^+$), m/z 1031.4400 (calcd 1031.4399 for $[M-H]^-$)

HPLC-MS purity: 100% (+), 100% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*S*,28*R*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 82%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.59 - 7.75 (1 H, m), 7.34 - 7.59 (2 H, m), 7.09 - 7.26 (7 H, m), 6.98 - 7.09 (1 H, m), 6.84 - 6.96 (2 H, m), 6.68 - 6.84 (2 H, m), 4.26 - 4.38 (2 H, m), 3.28 - 3.39 (2 H, m), 3.09 - 3.28 (7 H, m), 2.83 - 3.05 (3 H, m), 2.43 - 2.68 (3 H, m), 2.21 - 2.43 (5 H, m), 1.78 - 1.95 (1 H, m), 1.48 - 1.78 (10 H, m), 1.39 - 1.48 (30 H, m), 1.29 - 1.37 (4 H, m).

HRMS (ESI) for $C_{62}H_{89}ClN_{10}O_{13}$: m/z 1217.6475 (calcd 1217.6372 for $[M+H]^+$)

(3*S*,7*S*,25*S*,28*R*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3d). White amorphous powder; yield 28%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.30 (1 H, d, *J*=14.79 Hz), 7.91 (1 H, br. s.), 7.25 - 7.49 (2 H, m), 7.06 - 7.25 (6 H, m), 6.98 (1 H, d, *J*=8.68 Hz), 6.61 (2 H, d, *J*=8.31 Hz), 6.31 (1 H, br. s.), 4.53 (1 H, br. s.), 4.43 - 4.48 (1 H, m), 4.29 (2 H, br. s.), 4.05 (3 H, br. s.), 2.86 (2 H, d, *J*=5.32 Hz), 2.63 (2 H, d, *J*=11.74 Hz), 2.10 - 2.27 (5 H, m), 1.85 (1 H, br. s.), 1.71 (1 H, br. s.), 1.55 - 1.67 (2 H, m), 1.48 (5 H, br. s.), 1.12 - 1.29 (4 H, m)

HRMS (ESI) for $C_{50}H_{65}ClN_{10}O_{13}$: m/z 1049.4459 (calcd 1049.4494 for $[M+H]^+$), m/z 1047.4394 (calcd 1047.4348 for $[M-H]^-$)

HPLC-MS purity: 98% (+), 100% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*R*,28*S*)-33-Azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 65%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.25 (1 H, br. s.), 7.14 - 7.24 (5 H, m), 7.08 - 7.14 (2 H, m), 7.08 (1 H, br. s.), 6.98 - 7.05 (1 H, m), 4.62 - 4.75 (1 H, m), 4.51 (2 H, d, *J*=13.21 Hz), 4.31 (1 H, br. s.), 3.25 - 3.42 (3 H, m), 3.09 - 3.25 (4 H, m), 2.91 - 3.09 (3 H, m), 2.62 - 2.78 (2 H, m), 2.40 (1 H, br. s.), 2.32 (2 H, br. s.), 1.86 (1 H, d, *J*=8.80 Hz), 1.63 - 1.71 (3 H, m), 1.49 - 1.61 (3 H, m), 1.42 - 1.48 (9 H, m), 1.37 - 1.42 (6 H, m), 1.28 (2 H, br. s.)

^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 129.35, 128.57, 127.05, 92.93, 31.60, 30.81, 28.43, 28.09, 28.05, 28.03

HRMS (ESI) for $C_{62}H_{89}ClN_{10}O_{12}$: m/z 1201.6483 (calcd 1201.6423 for $[M+H]^+$)

(3*S*,7*S*,25*R*,28*S*)-33-Azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3e). White amorphous powder; yield 21%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.97 (1 H, d, *J*=7.34 Hz), 7.81 - 7.87 (1 H, m), 7.56 - 7.66 (1 H, m), 7.24 - 7.35 (2 H, m), 7.05 - 7.24 (8 H, m), 6.32 (1 H, br. s.), 4.36 (1 H, br. s.), 4.04 (1 H, d, *J*=5.75 Hz), 3.18 - 3.28 (3 H, m), 3.16 (2 H, d, *J*=6.72 Hz), 3.06 (1 H, br. s.), 2.99 (2 H, br. s.), 2.89 (1 H, d, *J*=11.68 Hz), 2.75 (1 H, d, *J*=13.63 Hz), 2.32 (2 H, br. s.), 2.20 (4 H, d, *J*=6.60 Hz), 1.81 (1 H, br. s.), 1.72 (1 H, br. s.), 1.59 (2 H, d, *J*=6.54 Hz), 1.48 (2 H, br. s.), 1.32 - 1.45 (2 H, m)

HRMS (ESI) for $C_{50}H_{65}ClN_{10}O_{12}$: m/z 1033.4538 (calcd 1033.4545 for $[M+H]^+$), m/z 1031.4410 (calcd 1031.4399 for $[M-H]^-$)

HPLC-MS purity: 92% (+), 95% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*R*,28*S*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 55%.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.50 - 7.62 (1 H, m), 7.19 - 7.26 (4 H, m), 7.10 - 7.19 (3 H, m), 7.00 - 7.09 (1 H, m), 6.88 - 6.97 (2 H, m), 6.69 - 6.79 (1 H, m), 4.50 (2 H, d, *J*=9.23 Hz), 4.28 - 4.40 (2 H, m), 3.26 - 3.39 (2 H, m), 3.10 - 3.25 (6 H, m), 2.26 - 2.40 (4 H, m), 1.77 - 1.90 (1 H, m), 1.49 - 1.75 (9 H, m), 1.38 - 1.46 (28 H, m), 1.26 - 1.38 (5 H, m).

^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 189.64, 156.24, 150.71, 129.50, 127.30, 115.04, 95.80, 81.71, 81.60, 80.30, 58.92, 48.43, 39.73, 38.31, 32.52, 31.21, 28.03, 27.65, 27.62, 27.61, 27.58, 15.67.

HRMS (ESI) for $C_{62}H_{89}ClN_{10}O_{13}$: m/z 1217.6475 (calcd 1217.6396 for $[M+H]^+$).

(3*S*,7*S*,25*R*,28*S*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3f).White amorphous powder; yield 19%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.25 - 8.33 (1 H, m), 8.06 - 8.12 (1 H, m), 7.87 - 7.94 (1 H, m), 7.73 - 7.83 (1 H, m), 7.25 - 7.41 (2 H, m), 7.17 - 7.24 (3 H, m), 7.11 - 7.17 (2 H, m), 7.06 - 7.11 (2 H, m), 6.98 (2 H, dd, *J*=8.44, 1.65 Hz), 6.58 - 6.64 (2 H, m), 6.25 - 6.34 (2 H, m), 4.50 - 4.57 (1 H, m), 4.42 - 4.49 (1 H, m), 4.26 - 4.41 (2 H, m), 3.96 - 4.13 (2 H, m), 3.02 - 3.23 (7 H, m), 2.90 - 3.02 (3 H, m), 2.72 - 2.89 (2 H, m), 2.55 - 2.69 (2 H, m), 2.29 - 2.36 (1 H, m), 2.16 - 2.28 (6 H, m), 1.83 - 1.95 (1 H, m), 1.66 - 1.76 (1 H, m), 1.55 - 1.66 (3 H, m), 1.31 - 1.54 (6 H, m), 1.11 - 1.30 (5 H, m).

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 174.53, 174.24, 173.84, 172.23, 171.87, 171.23, 171.11, 171.02, 157.30, 155.81, 141.20, 140.81, 138.01, 133.40, 133.05, 130.27, 130.12, 129.16, 128.01, 127.18, 126.85, 126.19, 126.07, 124.97, 114.86, 54.69, 54.33, 52.16, 51.72, 48.23, 35.86, 31.86, 31.78, 30.71, 30.61, 30.03, 29.08, 28.96, 28.21, 27.79, 27.64, 26.23, 24.73.

HRMS (ESI) for $C_{50}H_{65}ClN_{10}O_{13}$: m/z 1049.4468 (calcd 1049.4494 for $[M+H]^+$), m/z 1047.4385 (calcd 1047.4348 for $[M-H]^-$)

HPLC-MS purity: 100% (+), 100% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*S*,28*S*)-33-azido-25-benzyl-12-(4-chlorobenzyl)-28-(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 65%.

HRMS (ESI) for $C_{62}H_{88}ClN_{11}O_{14}$: m/z 1246.6274 (calcd 1246.6229 for $[M+H]^+$)

(3*S*,7*S*,25*S*,28*S*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3g). White amorphous powder; yield 26%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.10 (3 H, d, *J*=8.62 Hz), 7.44 (2 H, d, *J*=8.56 Hz), 7.16 (8 H, d, *J*=7.46 Hz), 7.07 (2 H, s), 6.26 (2 H, br. s.), 4.32 (1 H, br. s.), 4.06 (2 H, br. s.), 2.16 - 2.37 (8 H, m), 1.35 (9 H, br. s.).
HRMS (ESI) for $C_{50}H_{64}ClN_{11}O_{14}$: m/z 1078.4382 (calcd 1078.4395 for $[M+H]^+$), m/z 1076.4279 (calcd 1076.4250 for $[M-H]^-$)
HPLC-MS purity: 96% (+), 93% (-)

Tri-*tert*-butyl (3*S*,7*S*,25*S*,28*S*)-33-azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 50%.
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.72 – 7.47 (2 H, m), 7.02 - 7.24 (7 H, m), 6.87 - 7.02 (2 H, m), 4.45 - 4.54 (2 H, m), 4.25 - 4.40 (2 H, m), 3.10 - 3.38 (8 H, m), 2.97 (3 H, s), 2.22 - 2.43 (4 H, m), 1.99 - 2.12 (2 H, m), 1.67 - 1.80 (3 H, m), 1.50 - 1.67 (6 H, m), 1.38 - 1.47 (29 H, m), 1.18 - 1.38 (6 H, m), 1.18 - 1.38 (5 H, m), 1.18 - 1.38 (5 H, m).
(3*S*,7*S*,25*S*,28*S*)-33-Azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3h). White amorphous powder; yield 20%.
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.26 - 8.44 (1 H, m), 8.04 - 8.13 (1 H, m), 7.86 - 8.00 (1 H, m), 7.77 (1 H, d, *J*=15.96 Hz), 7.25 - 7.44 (3 H, m), 7.04 - 7.25 (6 H, m), 6.95 - 7.04 (1 H, m), 6.74 - 6.88 (1 H, m), 6.20 - 6.39 (2 H, m), 4.54 (1 H, s), 4.41 - 4.49 (1 H, m), 4.29 (2 H, d, *J*=5.14 Hz), 4.01 (2 H, br. s.), 3.08 (5 H, d, *J*=5.56 Hz), 2.80 - 2.90 (1 H, m), 2.77 (1 H, br. s.), 2.66 (1 H, d, *J*=2.08 Hz), 2.59 (1 H, br. s.), 2.28 - 2.38 (2 H, m), 2.12 - 2.28 (5 H, m), 1.76 - 1.94 (1 H, m), 1.54 - 1.76 (3 H, m), 1.36 (5 H, br. s.), 1.22 (4 H, br. s.), 1.12 (1 H, br. s.)
HRMS (ESI) for $C_{50}H_{64}BrClN_{10}O_{13}$: m/z 1127.3569 (calcd 1127.3599 for $[M+H]^+$), m/z 1125.3501 (calcd 1125.3453 for $[M-H]^-$)
HPLC-MS purity: 91% (+), 100% (-).

Tri-*tert*-butyl (3*S*,7*S*,25*S*,28*S*)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. Yellowish oil; yield 67%.
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.72 (1 H, s), 8.68 (1 H, s), 8.31 (1 H, d, *J*=6.97 Hz), 8.07 (1 H, d, *J*=8.13 Hz), 7.94 (1 H, s), 7.55 (1 H, d, *J*=5.50 Hz), 7.28 - 7.41 (2 H, m), 7.09 - 7.24 (7 H, m), 6.58 - 6.63 (2 H, m), 6.46 (1 H, d, *J*=8.25 Hz), 6.27 - 6.32 (1 H, m), 6.25 (1 H, d, *J*=8.74 Hz), 4.54 (1 H, s), 4.46 (1 H, br. s.), 4.27 (2 H, br. s.), 3.95 (1 H, br. s.), 3.21 - 3.27 (2 H, m), 3.17 (2 H, d, *J*=6.85 Hz), 3.05 (2 H, dd, *J*=11.43, 5.99 Hz), 3.00 (2 H, d, *J*=5.87 Hz), 2.93 (1 H, br. s.), 2.89 (1 H, br. s.), 2.85 (1 H, br. s.), 2.33 (3 H, d, *J*=7.09 Hz), 2.12 - 2.28 (5 H, m), 1.35 - 1.38 (27 H, m)

HRMS (ESI) for $C_{62}H_{89}ClN_{10}O_{14}$: m/z 1233.6378 (calcd 1233.6321 for $[M+H]^+$)

(3*S*,7*S*,25*S*,28*S*)-33-Azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3i). White amorphous powder; yield 21%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.31 - 8.38 (1 H, m), 8.05 - 8.12 (1 H, m), 7.89 - 7.98 (1 H, m), 7.54 (1 H, d, *J*=5.75 Hz), 7.25 - 7.41 (2 H, m), 7.20 (3 H, d, *J*=6.85 Hz), 7.12 - 7.17 (3 H, m), 6.60 (2 H, d, *J*=7.15 Hz), 6.46 (1 H, d, *J*=7.95 Hz), 6.24 - 6.36 (2 H, m), 4.53 (1 H, br. s.), 4.45 (1 H, s), 4.25 (2 H, d, *J*=4.22 Hz), 3.99 - 4.09 (2 H, m), 3.05 (2 H, dd, *J*=11.03, 5.90 Hz), 2.99 (2 H, dd, *J*=12.65, 6.66 Hz), 2.91 - 2.96 (1 H, m), 2.87 (2 H, d, *J*=17.97 Hz), 2.59 - 2.76 (2 H, m), 2.28 - 2.39 (3 H, m), 2.13 - 2.28 (5 H, m), 1.83 - 1.94 (1 H, m), 1.69 (1 H, dd, *J*=13.36, 7.61 Hz), 1.55 - 1.63 (3 H, m), 1.44 - 1.55 (4 H, m), 1.39 (3 H, dt, *J*=14.03, 7.11 Hz), 1.19 - 1.31 (3 H, m), 1.17 (1 H, br. s.)

MS (ESI) for $C_{50}H_{65}ClN_{10}O_{14}$: m/z 1065.45 (calcd 1065.44 for $[M+H]^+$)

HPLC-MS-MS purity: 100% (+), 100% (-)

General procedure of SPPS of Boc-containing ligands without APA part (4)

1) Resin activation

2-Chlorotrityl chloride resin (100-200 mesh, capacity 1 -1.5 mmol g^{-1}, 300 mg) was stirred in DCM (3 ml) for 10 minutes. Thionyl chloride (77 μl) was added to the solution. After 3-4 min, catalytic amount of DMF was added. The solution was stirred for 4 hours at 40 °C. After activation, the resin was washed three times with DMF (3 ml) for 1 minute, then three times with DCM (3 ml) for 1 minute. Excess solvent was removed, but the resin was not dried fully to prevent reaction with moisture from air.

2) Addition of the first amino acid residue

DMF (3 ml) was added to activated resin, and this was stirred for 5 min. Then Fmoc-protected amino acid was added. The amino acid was taken in double excess of the upper limit of the resin capacity. Then DIPEA was added in 5-fold excess. The reaction mixture was stirred for 2 hours. At the end of the reaction, the solvent was removed from the reactor and the resin was washed with MeOH (3×3 ml) for 1 minute, DCM (3×3 ml) 1 minute, DMF (3×3 ml) for 1 min and with DCM (2×3 ml) for 1 min. The resin was then dried.

3) Removal of the Fmoc protection group

The resin was washed twice with DMF (3 ml) for 1 min. A solution of 4-methylpiperidine in DMF (20%, 5 ml) was added to the resin, and this was stirred for 15 min. The resin was filtered and washed with DMF (2×3 ml) for 1 minute and then with DCM (3×3 ml) for 1 minute. The resin was dried.

4) Addition of the second amino acid residue

Dried resin was washed with DMF (2×3 ml) for 1 min. Then DMF (3 ml), the second amino acid (2 equiv.), HOBt (0.5 equiv.), HBTU (2 equiv.) and DIPEA (3 equiv.) were added. The mixture

was stirred for 2 hours. The solvent was removed, and the resin was washed with DMF (3×3 ml) for 1 min and with DCM (3×3 ml) for 1 min. The Fmoc protective group was removed in the same way as described in paragraph 3 of this procedure.

5) Urea-based vector-molecule attachment

Dried resin was washed twice with DMF (3 ml) for 1 min. Then DMF (3 ml), (7*S*,11*S*)-7,11-bis(*tert*-butoxycarbonyl)-16-(3-chlorobenzyl)-2,2-dimethyl-4,9,17-trioxo-3-oxa-8,10,16-triazadocosan-22-oic acid (2 equiv.), HOBt (0.5 equiv.), HBTU (2 equiv.) and DIPEA (3 equiv.) were added. The mixture was stirred for 2 h. The solvent was removed, and the resin was washed with DMF (3×3 ml) for 1 min and with DCM (3×3 ml) for 1 min. The resin was dried.

6) Removing the ligand from the resin.

The resin was washed with DCM (2×3 ml) for 1 min. The resin was placed in trifluoroacetic acid solution (0.5%, 5 ml) for 15 min. Then solvent from resulting filtrate was removed under reduced pressure and several times re-evaporated from DCM. The product was isolated by column chromatography with the reverse phase.

(2*S*,5*R*,23*S*,27*S*)-2-Benzyl-5-(4-*tert*-butoxybenzyl)-23,27-bis(*tert*-butoxycarbonyl)-18-(3-chlorobenzyl)-32,32-dimethyl-4,7,10,17,25,30-hexaoxo-31-oxa-3,6,11,18,24,26-hexaazatritriacontan-1-oic acid (4). White amorphous powder; yield 47%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.36 (1 H, d, *J*=7.95 Hz), 8.00 (1 H, d, *J*=8.86 Hz), 7.71 - 7.79 (1 H, m), 7.27 - 7.43 (2 H, m), 7.17 - 7.26 (5 H, m), 7.09 - 7.17 (2 H, m), 6.98 (2 H, d, *J*=8.38 Hz), 6.78 (2 H, d, *J*=8.38 Hz), 6.22 - 6.32 (2 H, m), 4.54 (1 H, s), 4.39 - 4.49 (3 H, m), 3.88 - 4.06 (2 H, m), 3.11 - 3.24 (2 H, m), 2.88 - 3.08 (3 H, m), 2.83 (1 H, dd, *J*=13.24, 9.14 Hz), 2.68 (1 H, d, *J*=10.64 Hz), 2.37 - 2.46 (1 H, m), 2.26 - 2.35 (1 H, m), 2.07 - 2.26 (7 H, m), 1.79 - 1.91 (1 H, m), 1.64 (1 H, dd, *J*=15.04, 5.87 Hz), 1.56 (1 H, dd, *J*=14.49, 7.58 Hz), 1.40 - 1.53 (5 H, m), 1.34 - 1.39 (27 H, m), 1.20 - 1.24 (11 H, m)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.89, 171.93, 171.11, 161.93, 153.29, 137.56, 129.64, 129.28, 128.16, 123.24, 80.59, 79.78, 53.74, 53.41, 28.56, 27.75, 27.66

MS (ESI) for $C_{63}H_{91}ClN_6O_{14}$: m/z 1191.65 (calcd 1191.64 for $[M+H]^+$)

General procedure of synthesis of ligand (SPPS) (5)

Stage 1. Ligand without APA-fragment was dissolved in DMF (30 ml) and cooled to 0°C. The order of reagent addition in this reaction is crucial, thus eliminating the side reaction of terminal amino acid residue racemization. Reagents were added in the following sequence: 3-azido-1-propanamine (1.5 equiv.), HOBt (1.2 equiv.), HBTU (1.2 equiv.) and DIPEA (1.5 eq.). The mixture was stirred for 24 h. The solvent was then removed under reduced pressure, and the residue was extracted with DCM/water system. The solvent was removed under reduced pressure and the product was isolated by column chromatography with the reverse phase.

Stage 2. Boc-containing ligand (1 equiv.) was dissolved in a solution of trifluoroacetic acid, DCM, distilled water and triisopropylsilane (46.25:46.25:5: .5), and this was stirred at room temperature for 3 h. The solvent was removed under reduced pressure. The residue was re-evaporated three times from DCM. To the resulting oily residue diethyl ether (5 ml) was added to precipitate white solid. Ether was decanted, and the procedure was repeated two times. The product was isolated by column chromatography with reverse phase (Puriflash C18 15μ, 20 g, eluent: acetonitrile-water system: 10→100% MeCN in 20 min).

Tri-*tert*-butyl (3*S*,7*S*,25*R*,28*S*)-33-azido-28-benzyl-25-(4-*tert*-butoxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate. White amorphous powder; yield 59%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.30 (1 H, s), 7.17 - 7.28 (5 H, m), 7.15 (2 H, br. s.), 6.99 (2 H, m, *J*=8.44 Hz), 6.78 (2 H, m, *J*=8.31 Hz), 6.22 - 6.33 (2 H, m), 4.46 (1 H, s), 3.23 (2 H, t, *J*=6.82 Hz), 3.16 (2 H, br. s.), 2.98 (2 H, d, *J*=5.32 Hz), 2.67 (1 H, s), 1.54 - 1.63 (3 H, m), 1.45 - 1.53 (3 H, m), 1.33 - 1.39 (27 H, m), 1.23 (9 H, s)

^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 172.29, 172.20, 171.21, 153.72, 143.19, 138.35, 130.02, 129.58, 128.45, 123.64, 80.17, 77.95, 48.62, 28.96, 28.59, 28.14, 28.05, 28.03

HRMS (ESI) for $C_{66}H_{97}ClN_{10}O_{13}$: m/z 1273.7029 (calcd 1273.6998 for $[M+H]^+$)

(3*S*,7*S*,25*R*,28*S*)-33-Azido-28-benzyl-12-(3-chlorobenzyl)-25-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (5). White amorphous powder; yield 26%.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.27 (1 H, dd, *J*=8.47, 3.85 Hz), 7.97 - 8.02 (1 H, m), 7.88 (1 H, d, *J*=3.25 Hz), 7.77 (1 H, s), 7.34 (1 H, d, *J*=7.70 Hz), 7.25 - 7.31 (2 H, m), 7.21 - 7.25 (1 H, m), 7.19 (3 H, d, *J*=7.01 Hz), 7.14 - 7.17 (3 H, m), 7.07 - 7.14 (2 H, m), 6.83 (2 H, m, *J*=8.38 Hz), 6.55 (2 H, m, *J*=8.38 Hz), 6.26 - 6.31 (1 H, m), 6.24 (1 H, d, *J*=2.91 Hz), 4.51 (1 H, s), 4.44 (1 H, s), 4.35 (1 H, d, *J*=5.13 Hz), 4.19 - 4.27 (1 H, m), 4.01 - 4.10 (2 H, m), 3.22 (3 H, t, *J*=6.93 Hz), 3.15 (3 H, dd, *J*=14.37, 6.67 Hz), 3.09 (1 H, d, *J*=6.33 Hz), 3.00 - 3.05 (1 H, m), 2.94 - 3.00 (2 H, m), 2.88 - 2.94 (2 H, m), 2.69 - 2.77 (2 H, m), 2.31 (2 H, t, *J*=7.27 Hz), 2.15 - 2.24 (7 H, m), 1.87 (2 H, d, *J*=7.36 Hz), 1.68 (2 H, br. s.), 1.47 (4 H, br. s.), 1.37 - 1.43 (2 H, m), 1.31 - 1.37 (2 H, m), 1.21 - 1.29 (3 H, m), 1.13 (2 H, d, *J*=7.70 Hz)

HRMS (ESI) for $C_{50}H_{65}ClN_{10}O_{13}$: m/z 1049.4471 (calcd 1049.4494 for $[M+H]^+$), m/z 1047.4390 (calcd 1047.4348 for $[M-H]^-$)

HPLC-MS purity: 100% (+), 100% (-)

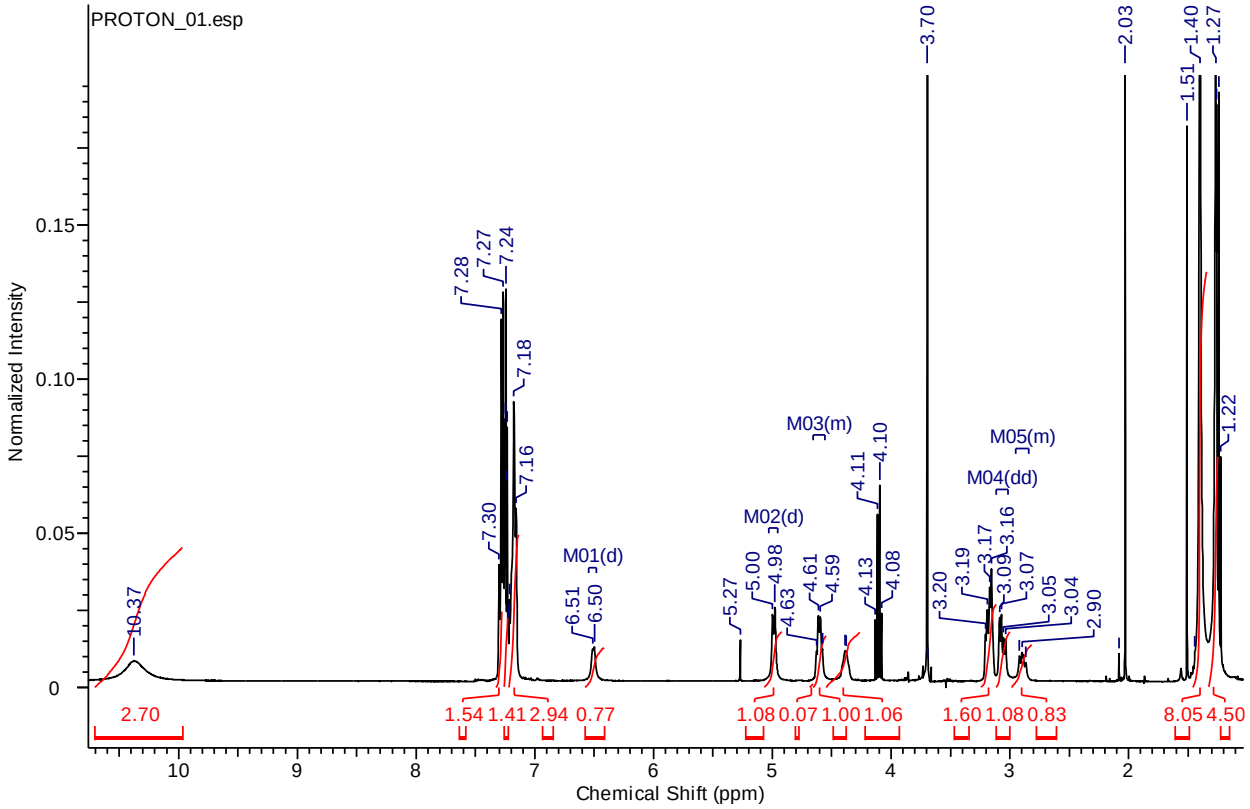

Figure S1. ^{1}H NMR (*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-L-Phe).

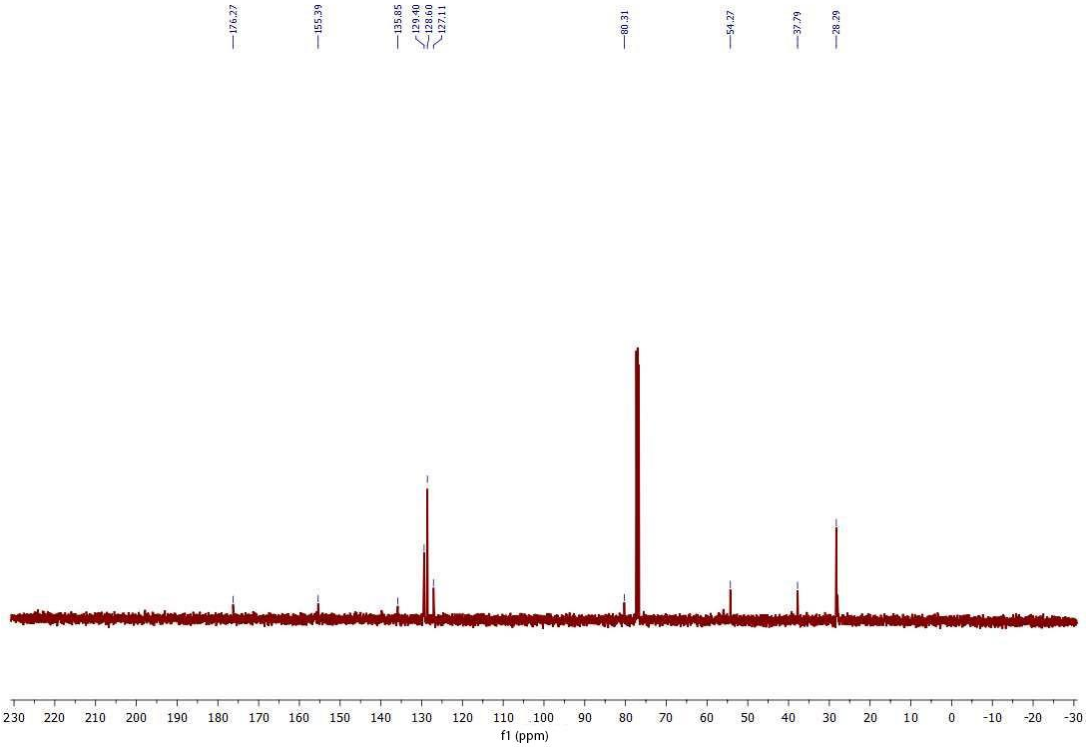

Figure S2. ^{13}C NMR (*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-L-Phe).

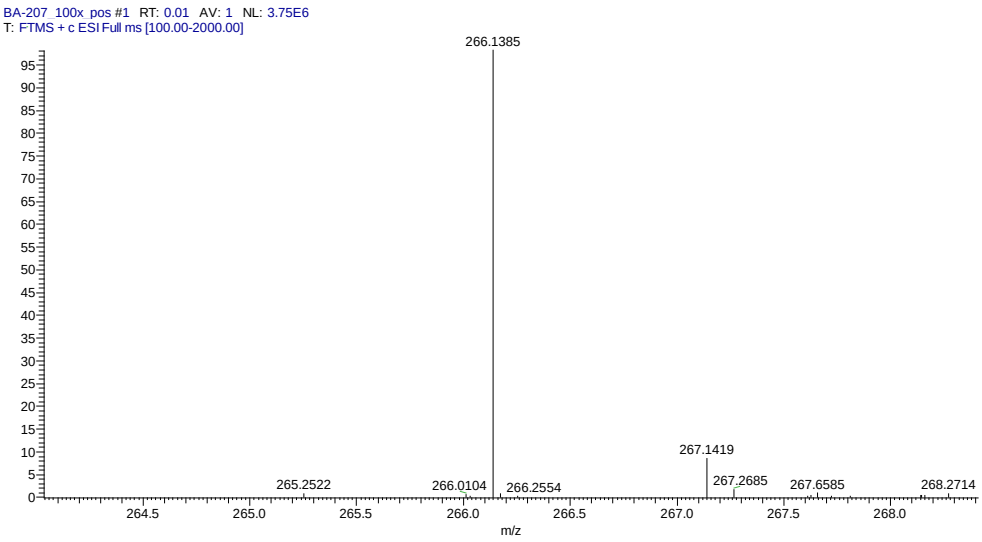

Figure S3. HRMS (*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-L-Phe).

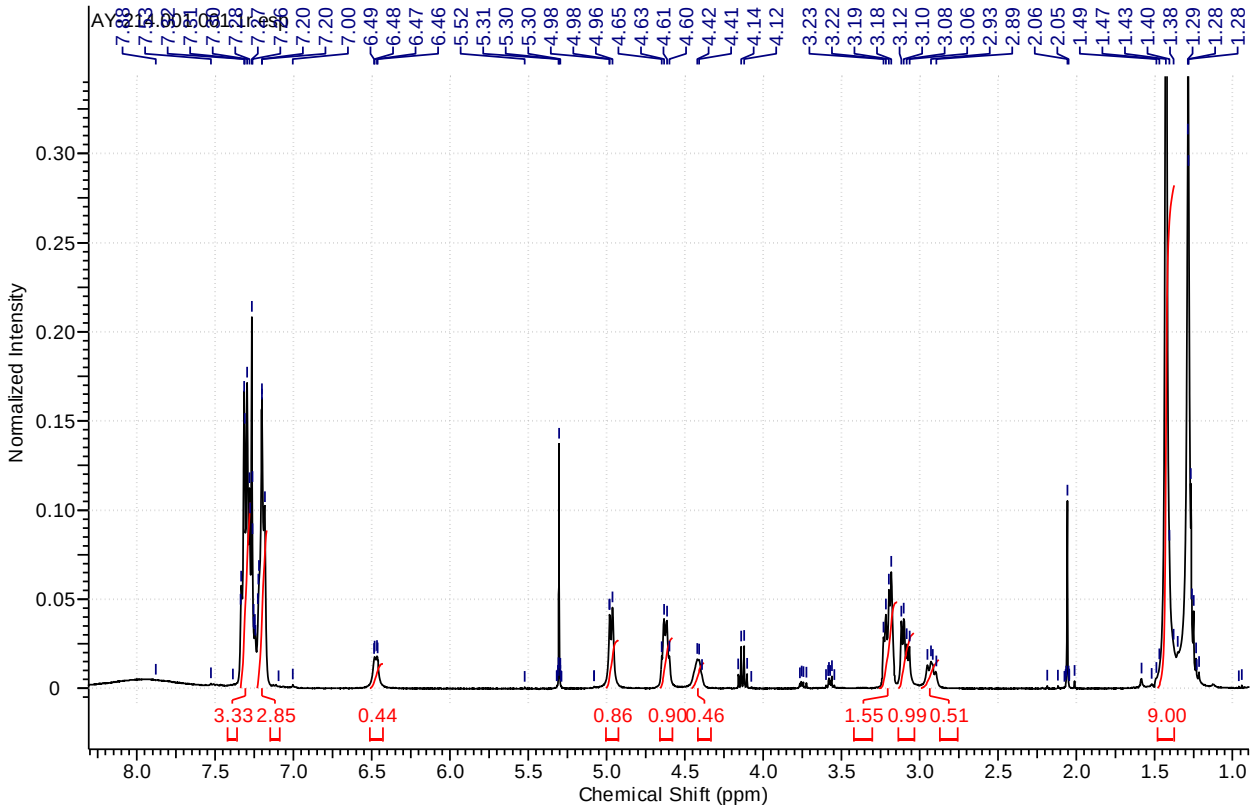

Figure S4. ^{1}H NMR (*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-D-Phe).

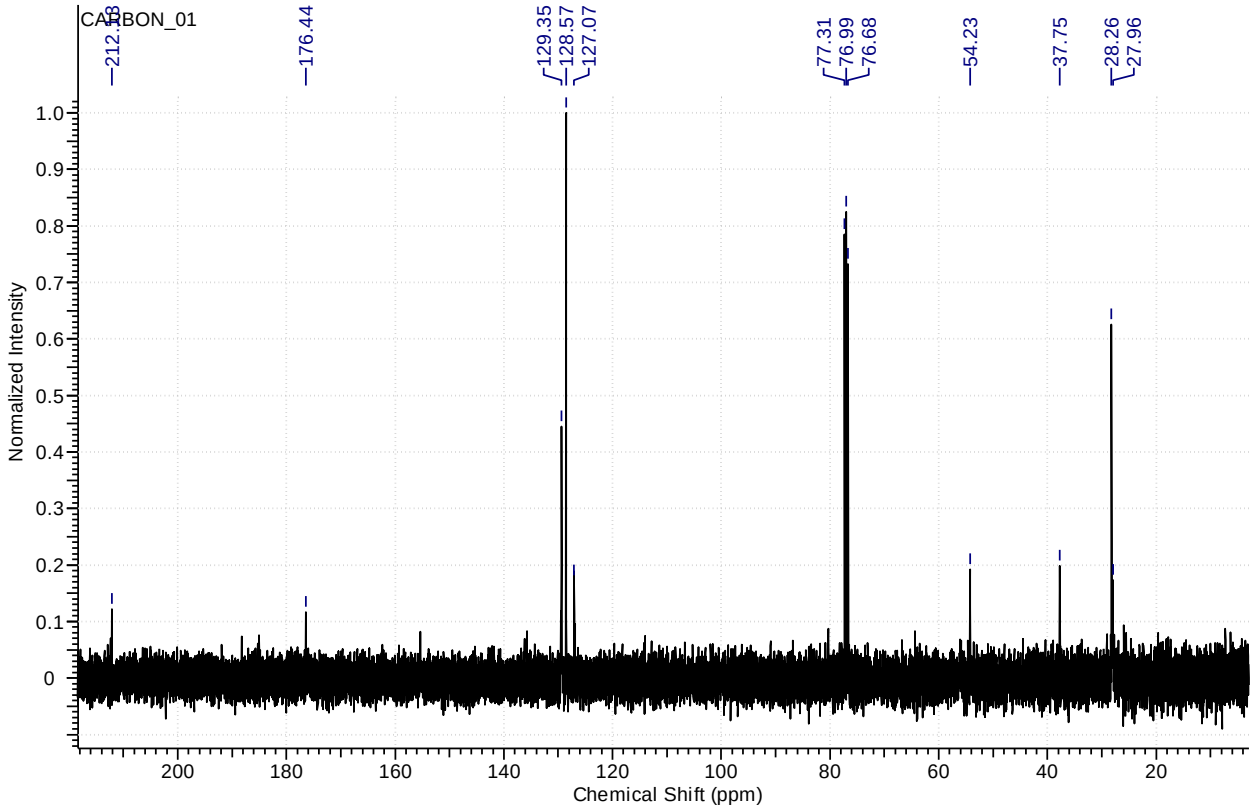

Figure S5. ^{13}C NMR (*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-D-Phe).

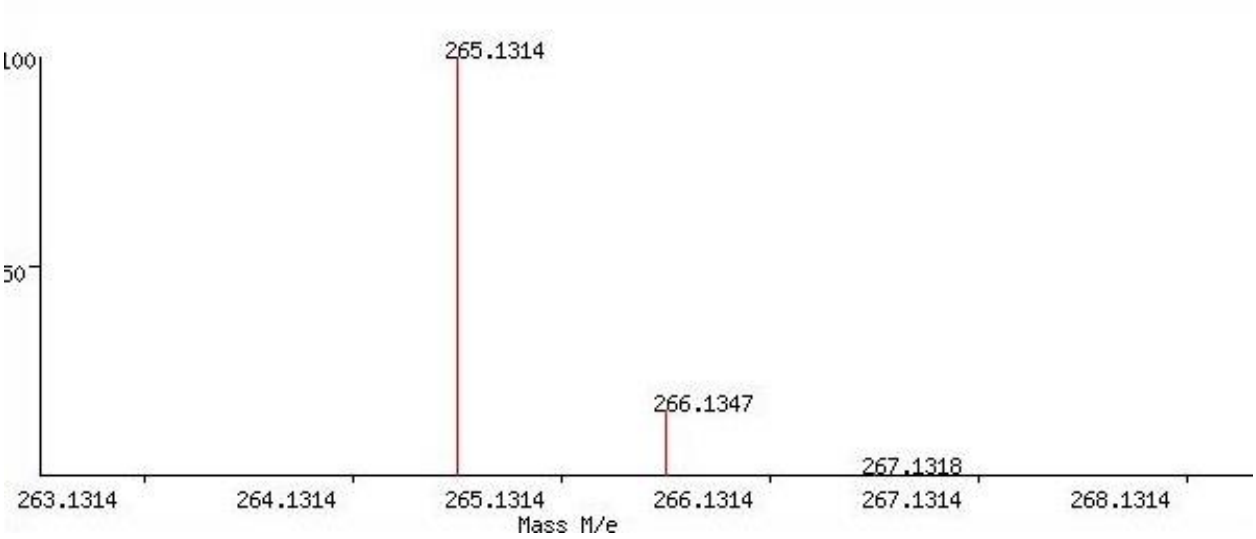

Figure S6. HRMS (*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid (*N*-Boc-D-Phe).

(ESI) for $C_{14}H_{19}NO_4$: m/z 266.1259 (calcd 266.1392 for $[M+H]^+$)

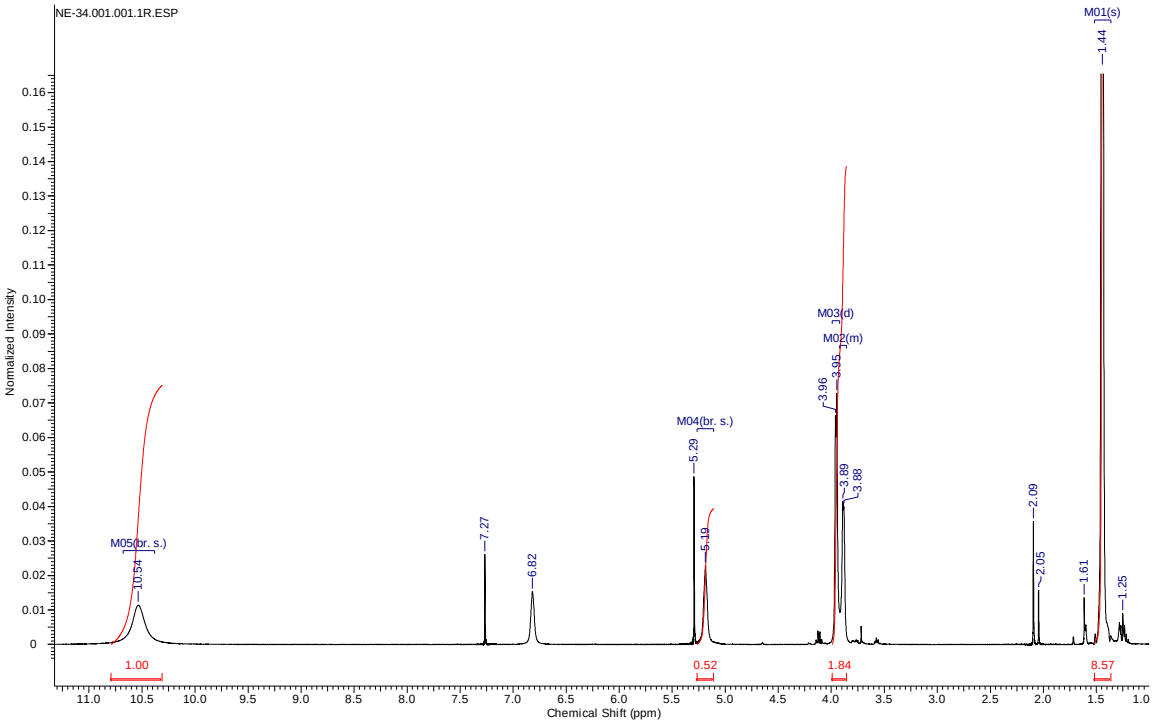

Figure S7. ^{1}H NMR 2-(*tert*-butoxycarbonylamino)acetic acid (*N*-Boc-Gly).

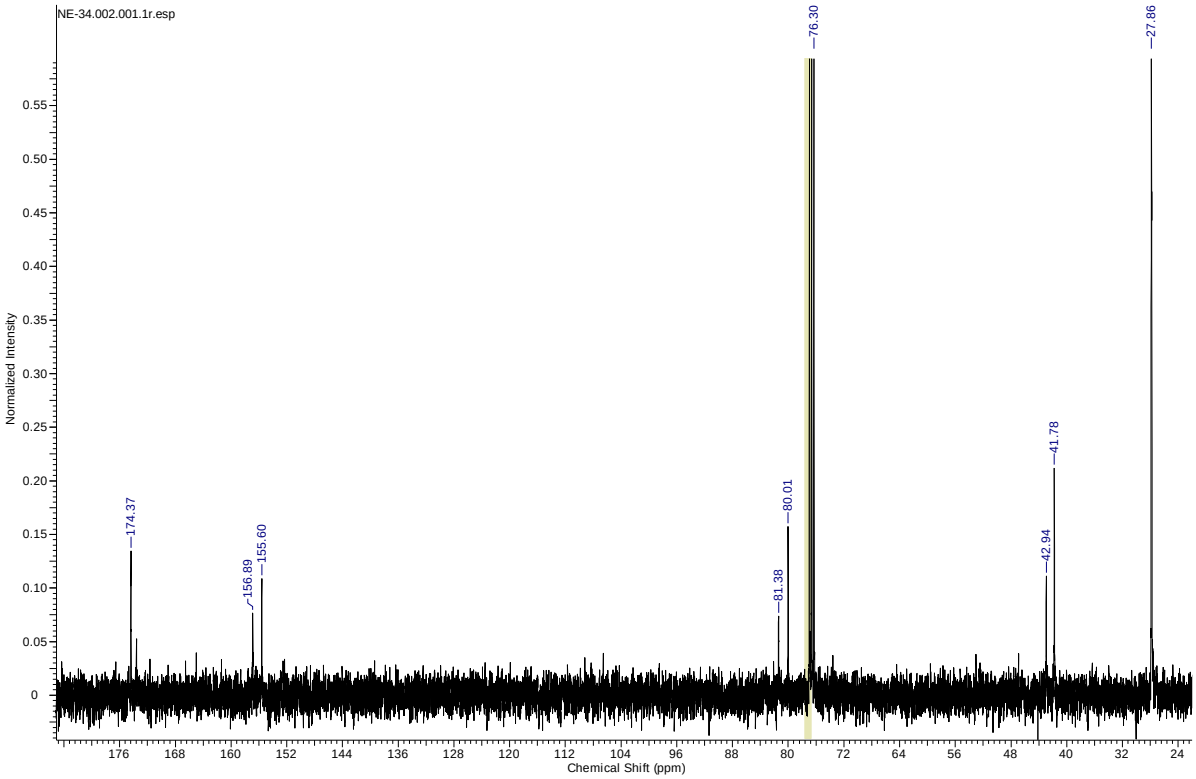

Figure S8. ^{13}C NMR 2-(*tert*-butoxycarbonylamino)acetic acid (*N*-Boc-Gly).

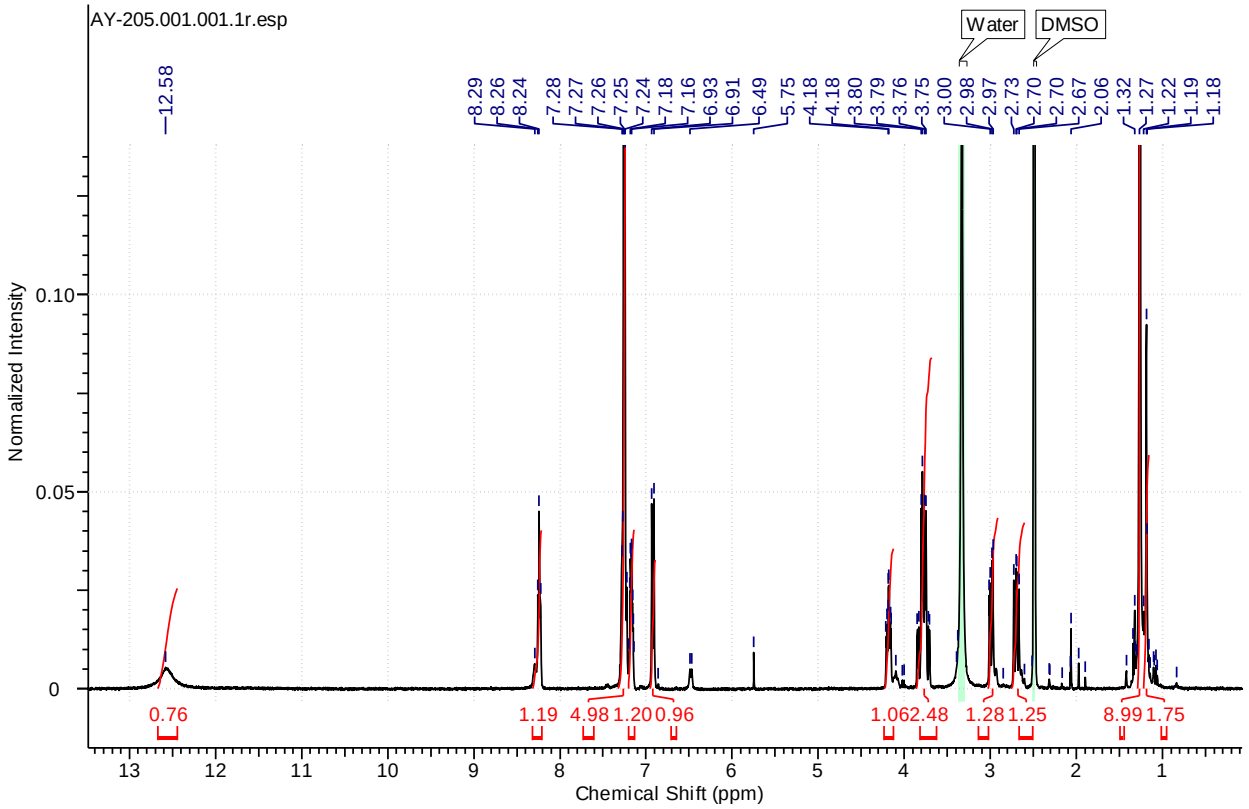

Figure S9. ^{1}H NMR (*S*)-2-(2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)acetic acid (1a).

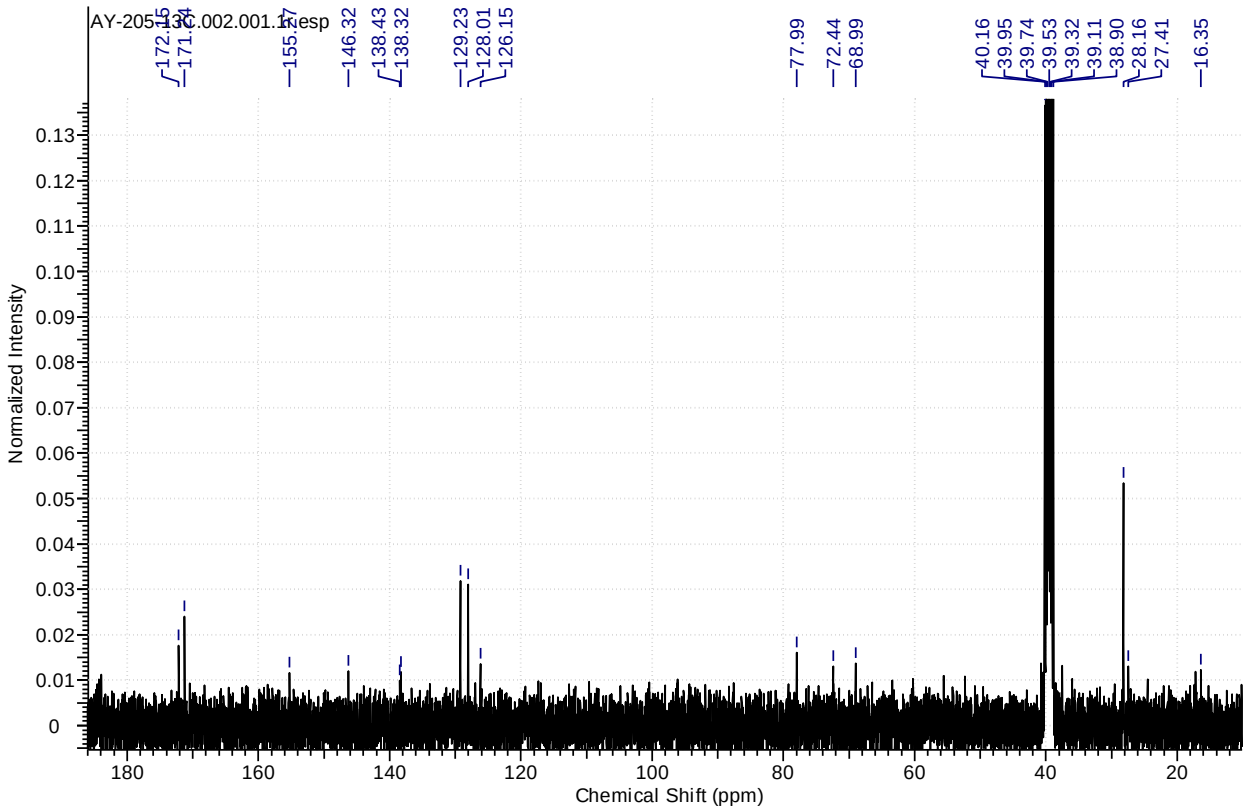

Figure S10. ^{13}C NMR (*S*)-2-(2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)acetic acid (1a).

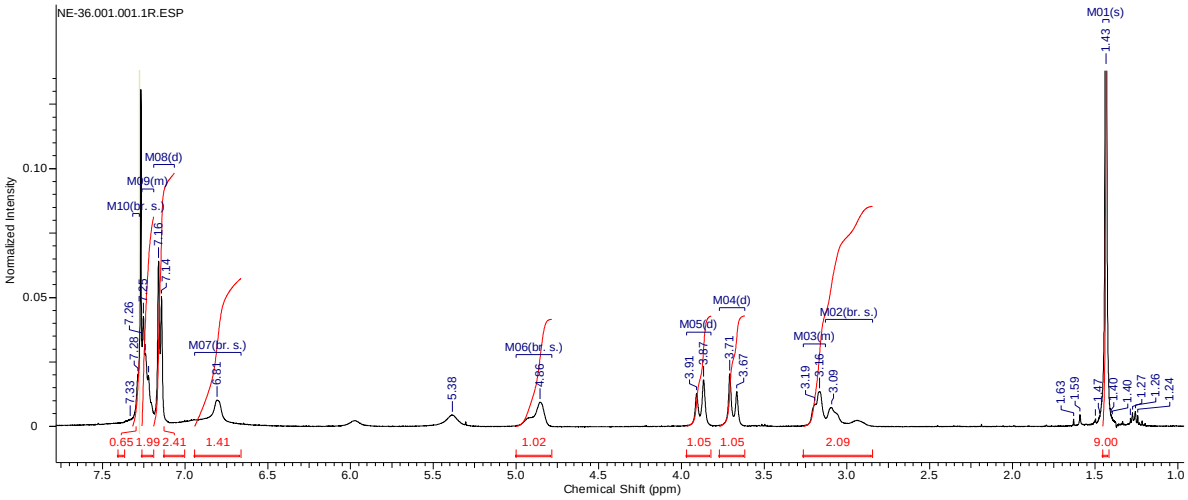

Figure S11. ^{1}H NMR (*S*)-2-(2-(*tert*-butoxycarbonylamino)acetamido)-3-phenylpropanoic acid (1b).

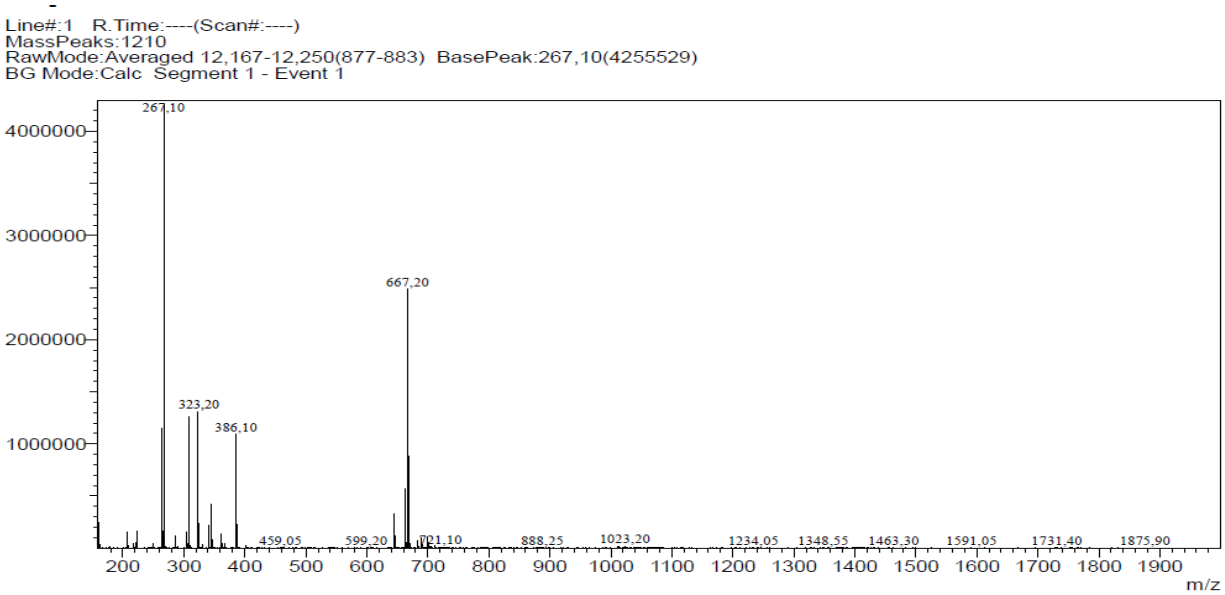

Figure S12. MS (*S*)-2-(2-(*tert*-butoxycarbonylamino)acetamido)-3-phenylpropanoic acid (1b).

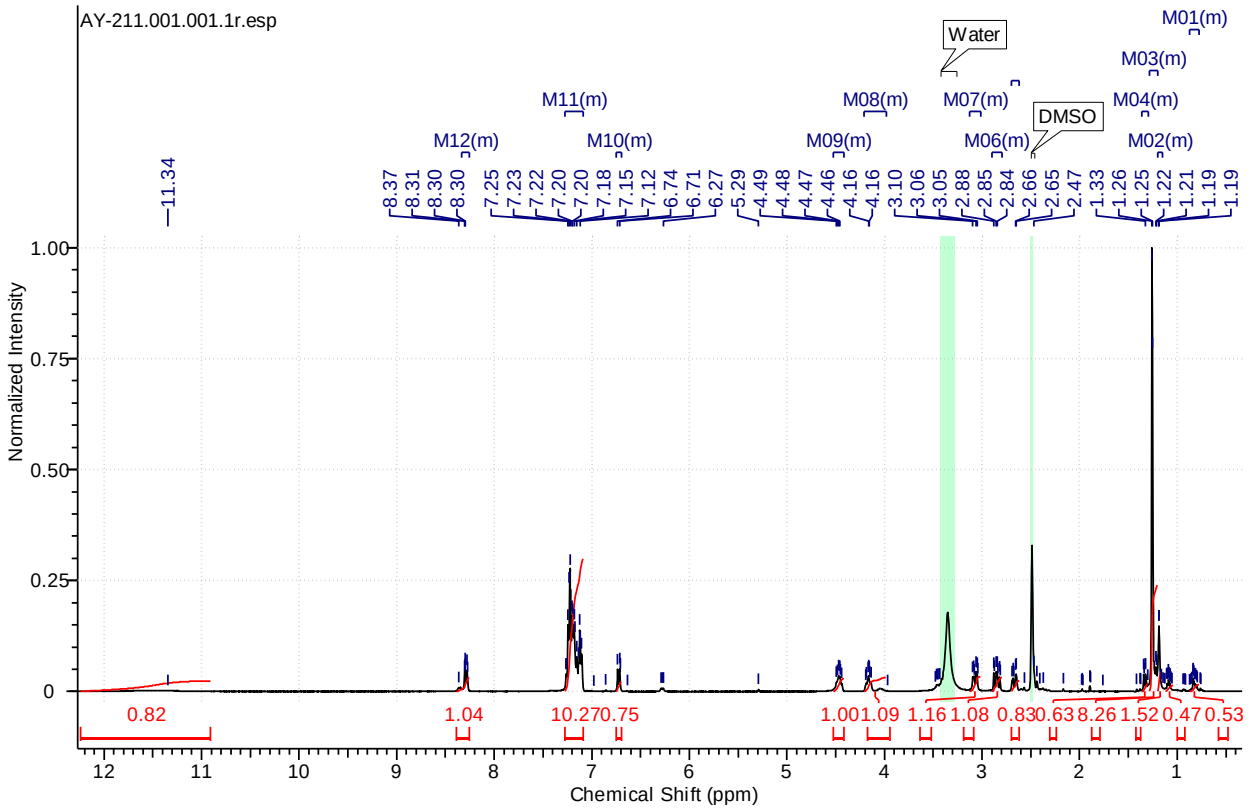

Figure S13. ^{1}H NMR (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic acid (1c).

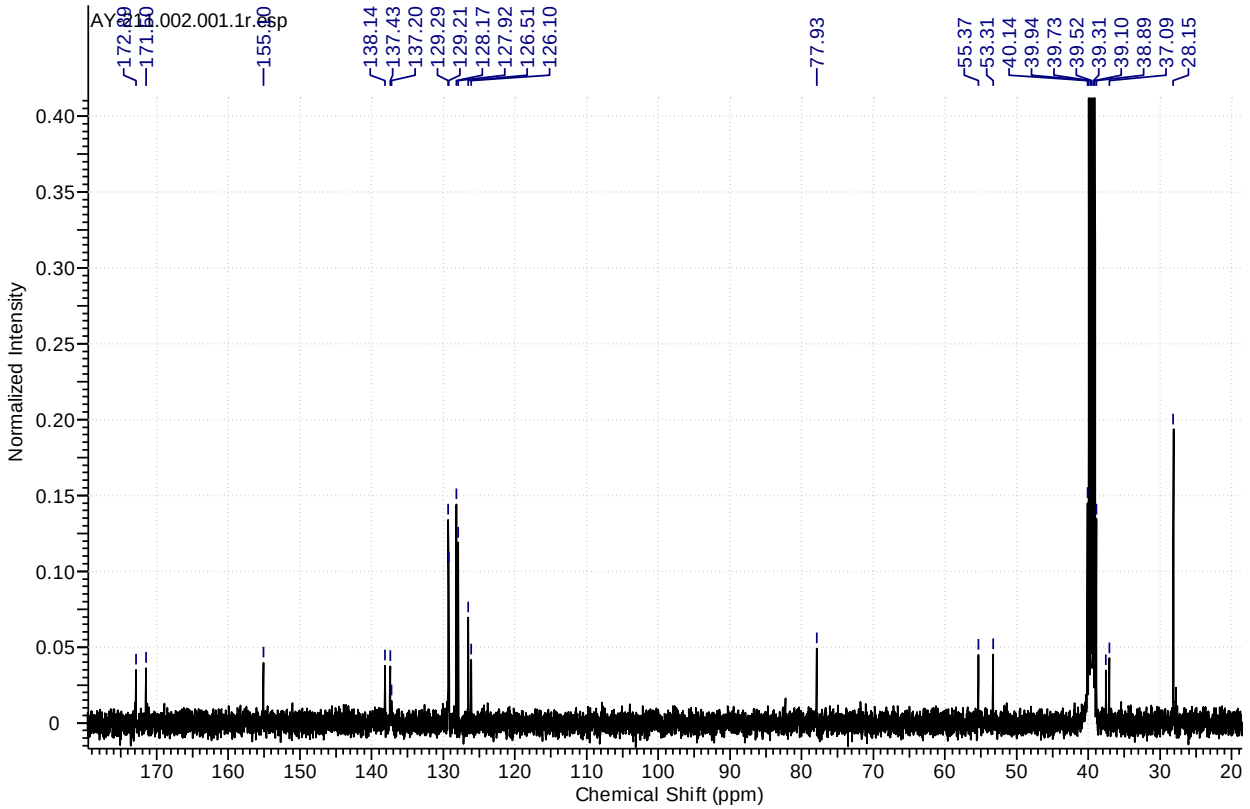

Figure S14. ^{13}C NMR (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic acid (1c).

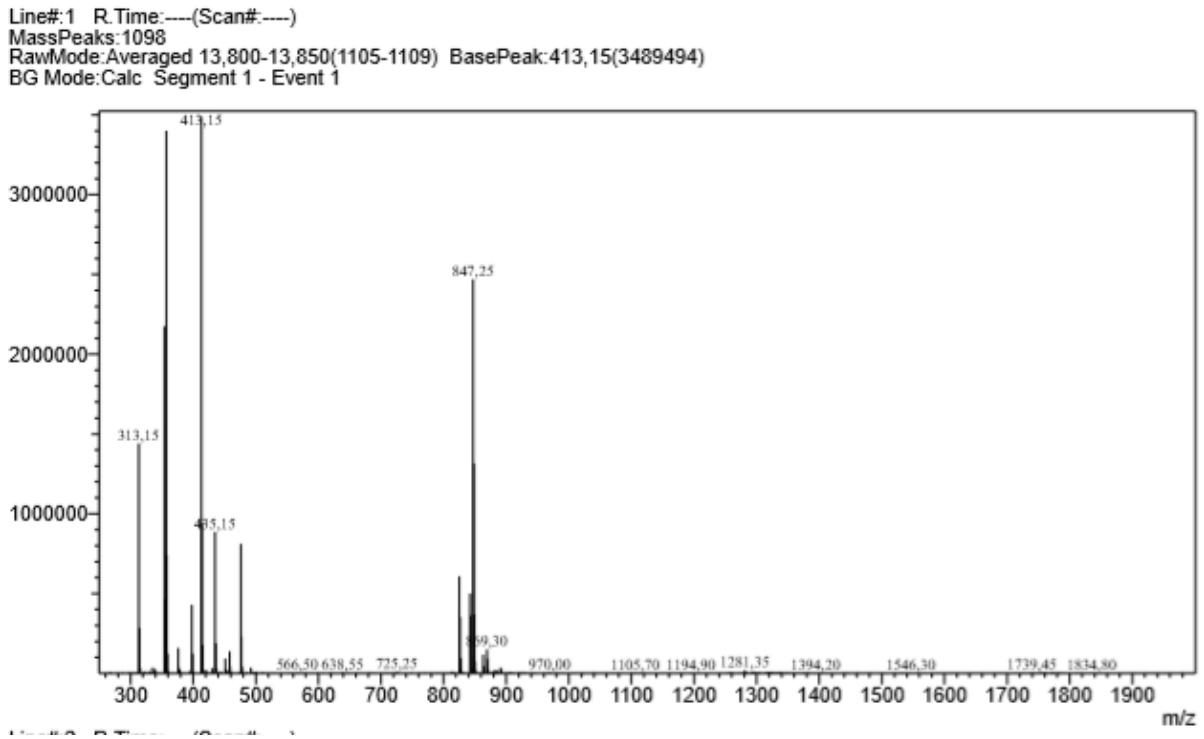

Figure S15. MS (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic acid (1c).

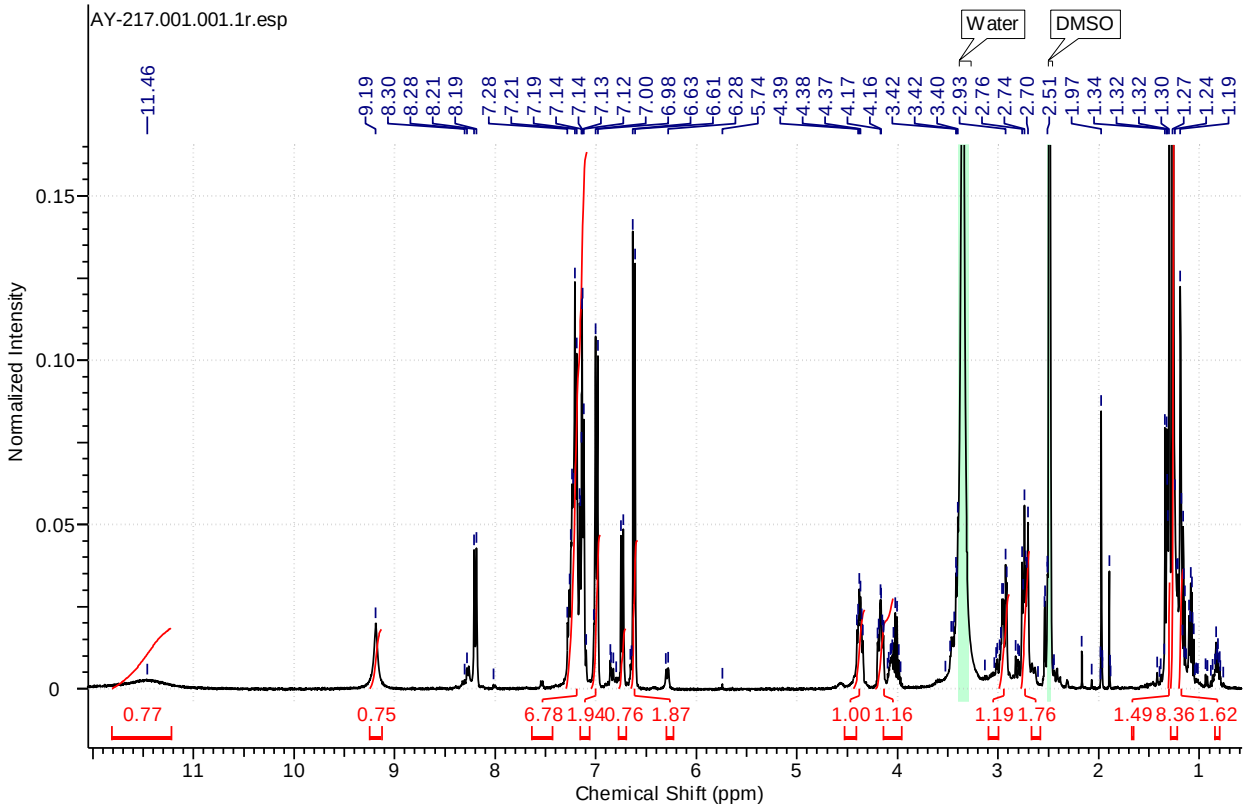

Figure S16. ^{1}H NMR (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-(4-hydroxyphenyl)propanoic acid (1d).

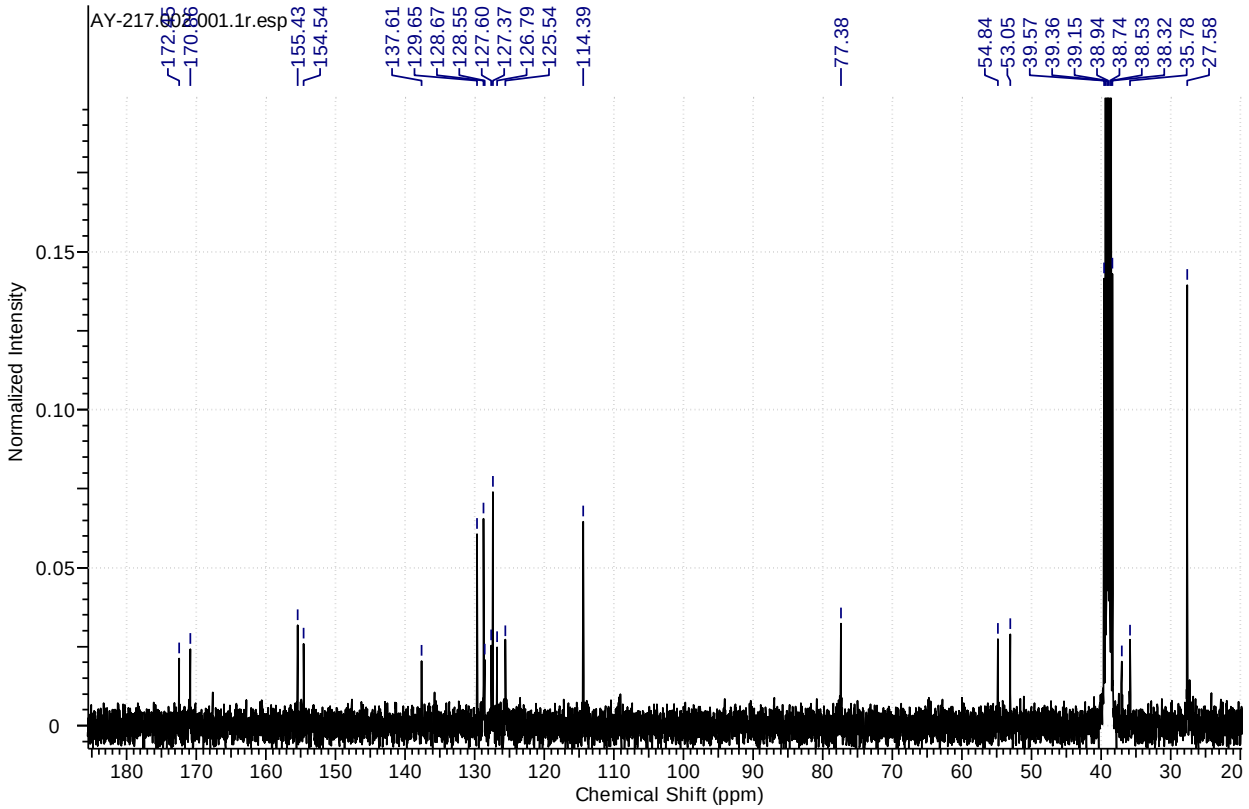

Figure S17. ^{13}C NMR (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-(4-hydroxyphenyl)propanoic acid (1d).

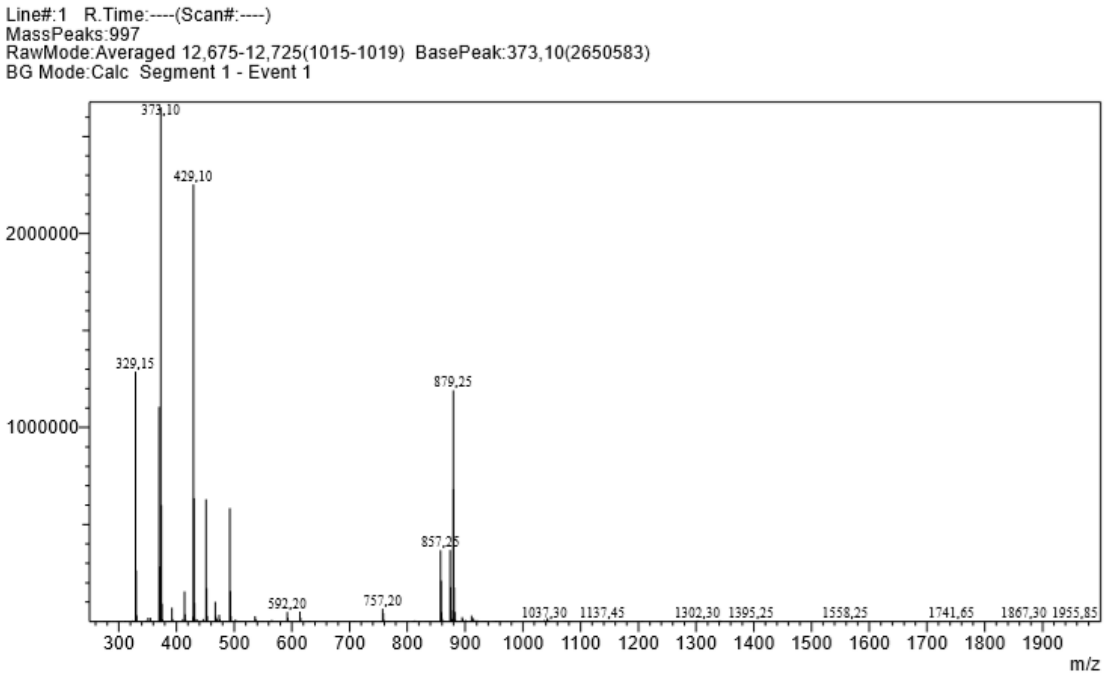

Figure S18. MS (*R*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-(4-hydroxyphenyl)propanoic acid (1d).

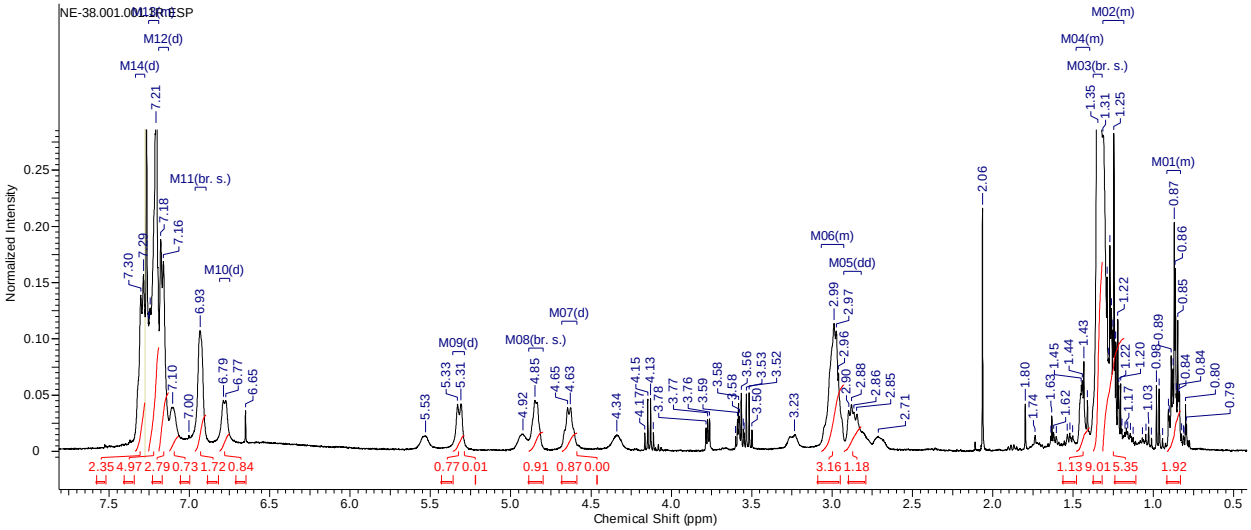

Figure S19. ^{1}H NMR (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic acid (1e).

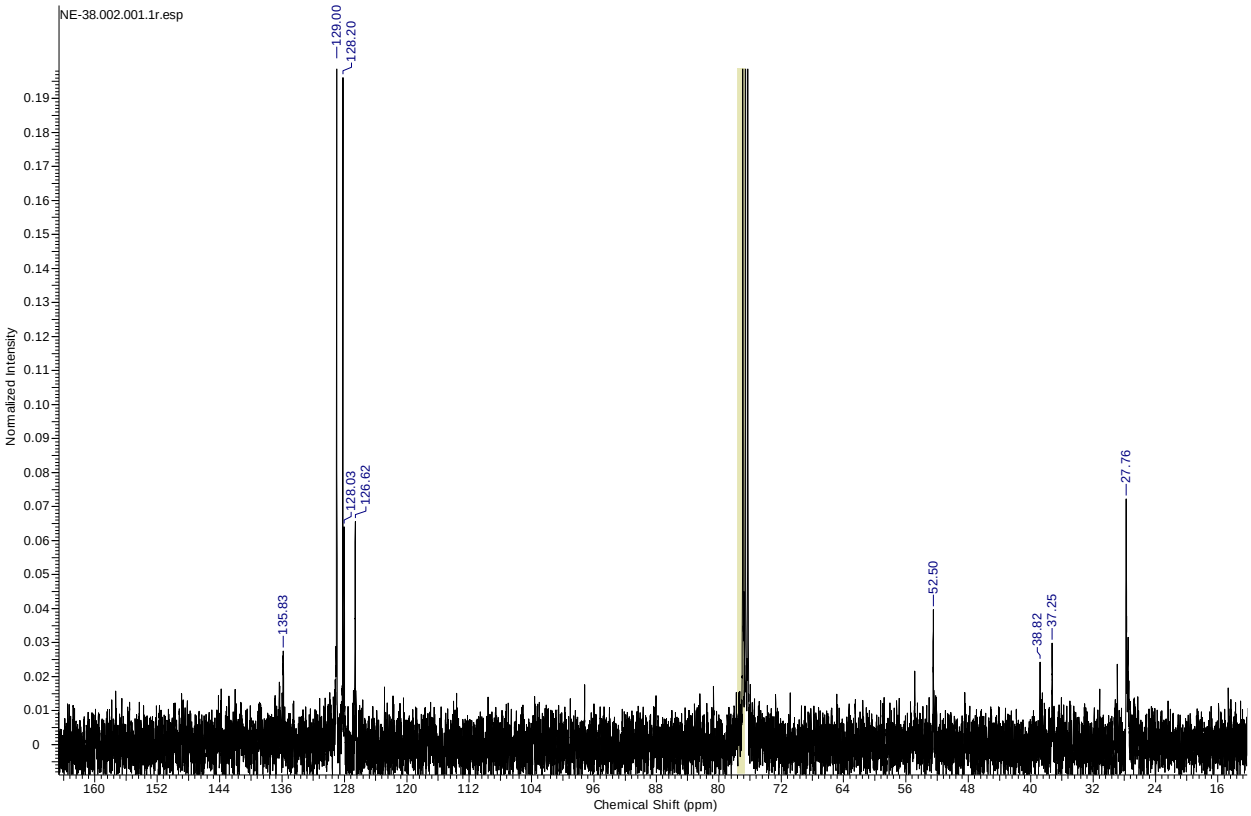

Figure S20. ^{13}C NMR (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic acid (1e).

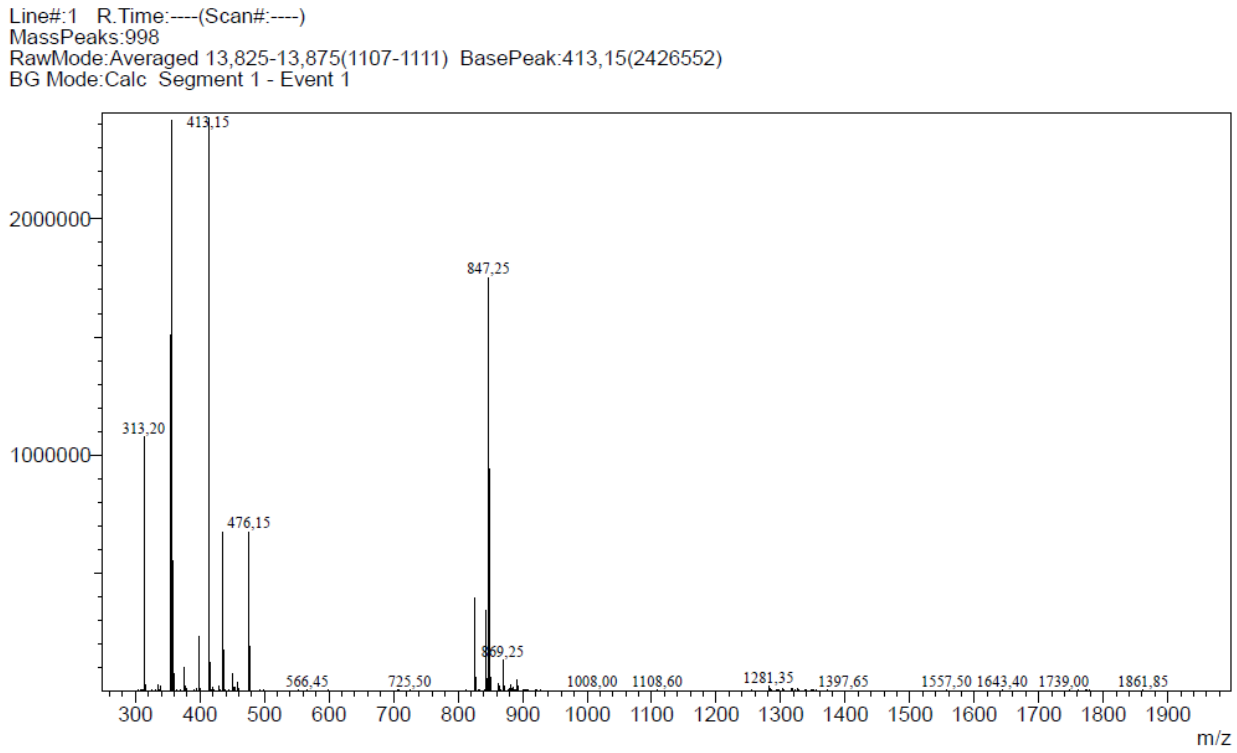

Figure S21. MS (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)-3-phenylpropanoic (1e).

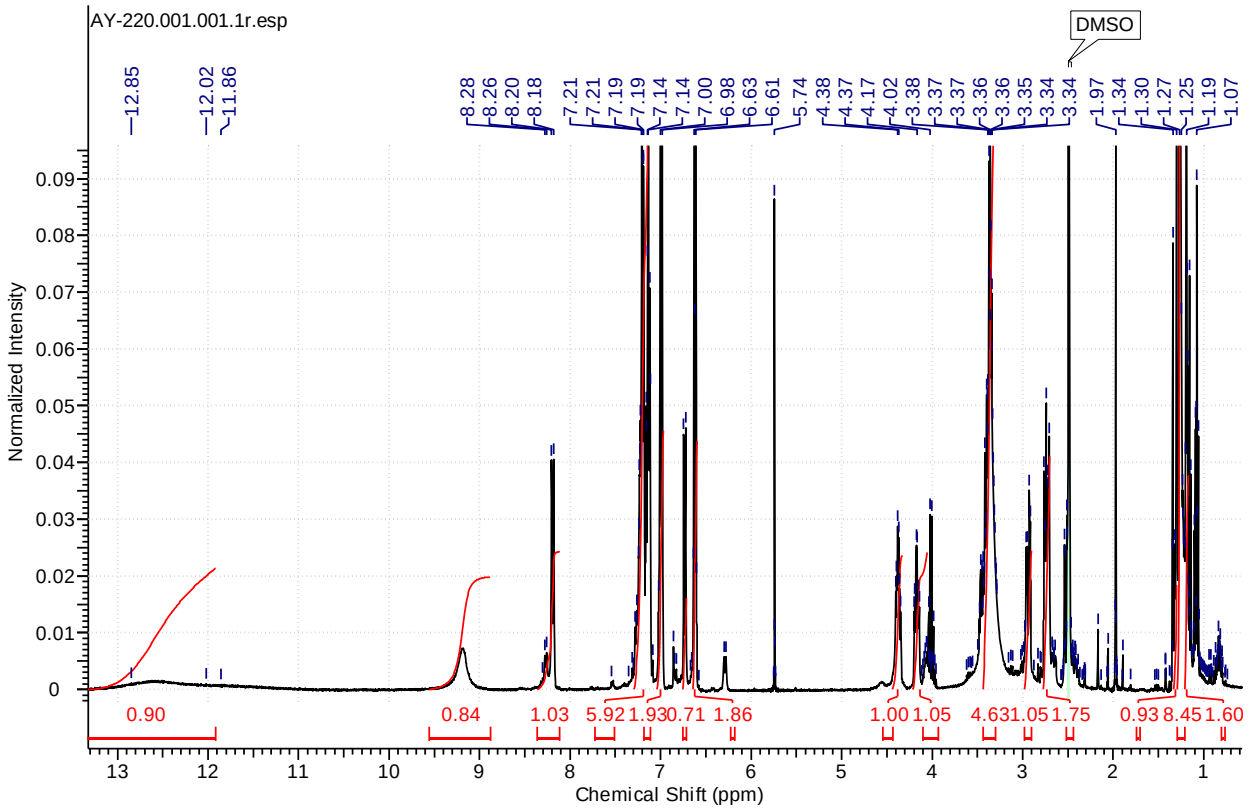

Figure S22. ^{1}H NMR (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--3-(4-hydroxyphenyl)propanoic acid (1f).

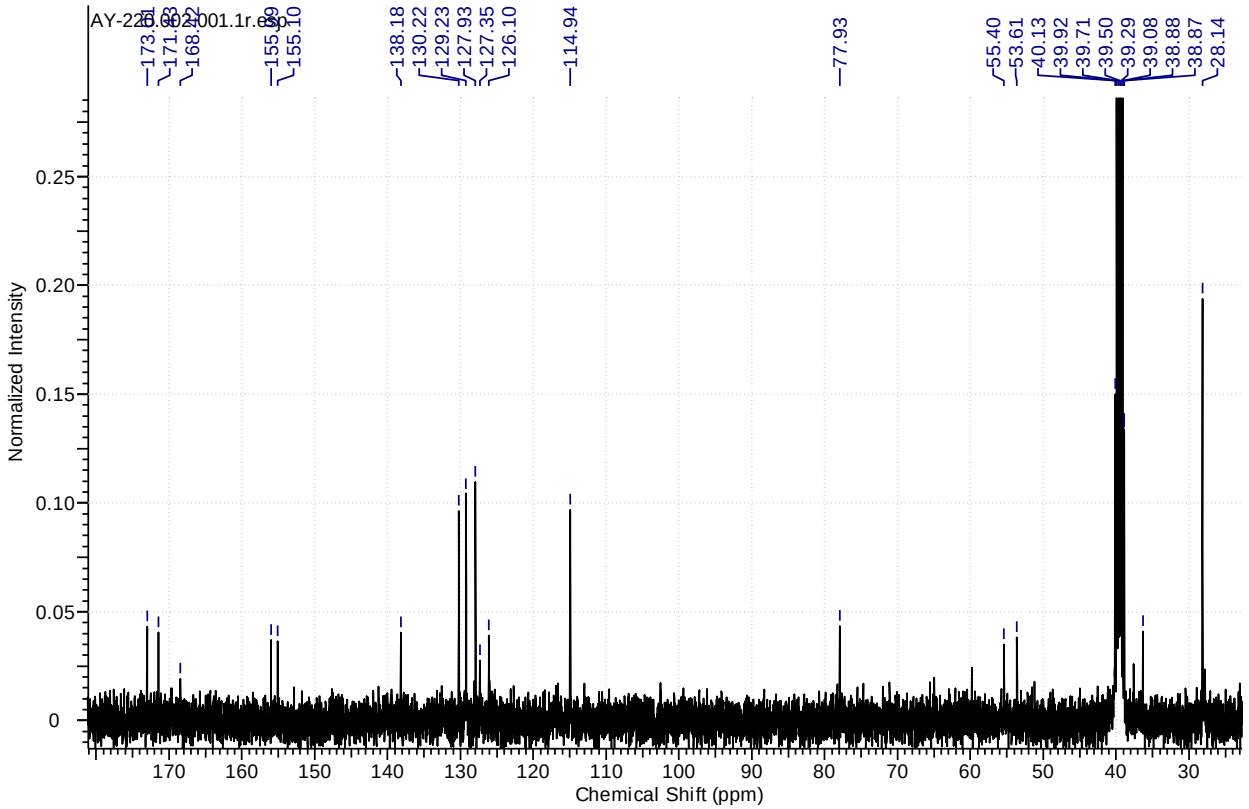

Figure S23. ^{13}C NMR (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--(4-hydroxyphenyl)propanoic acid (1f).

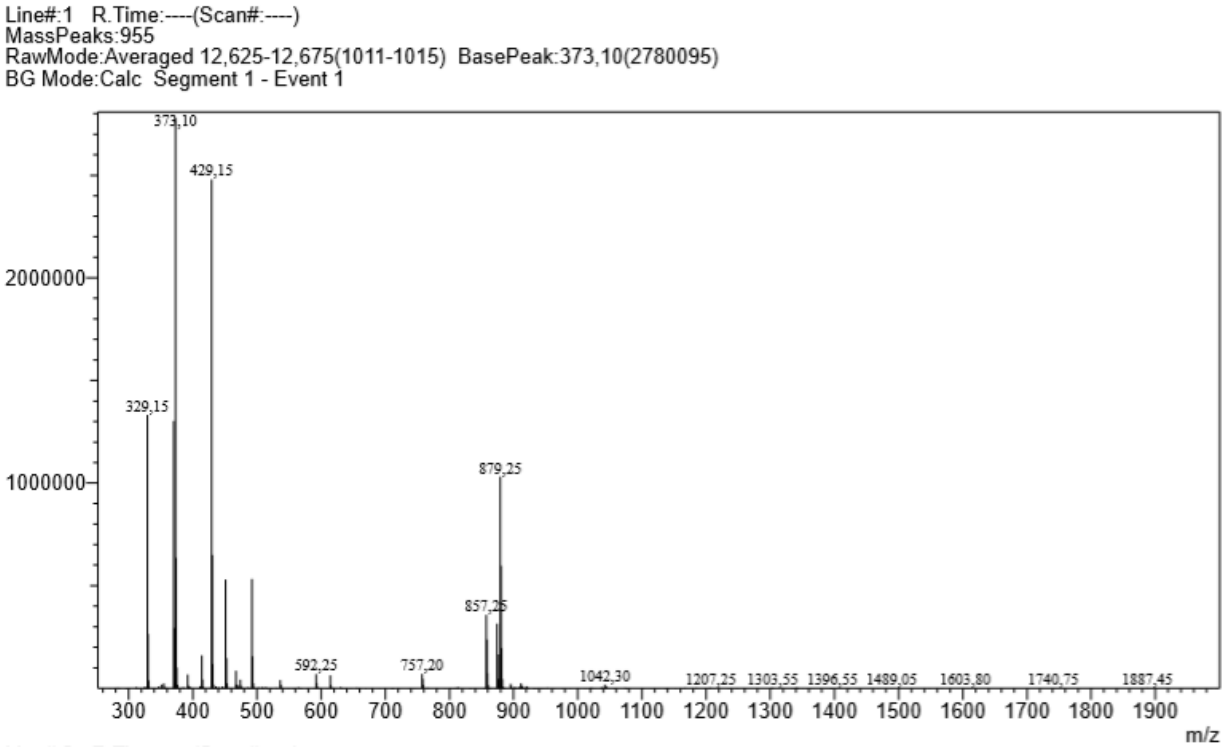

Figure S24. MS (*S*)-2-((*R*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--(4-hydroxyphenyl)propanoic acid (1f).

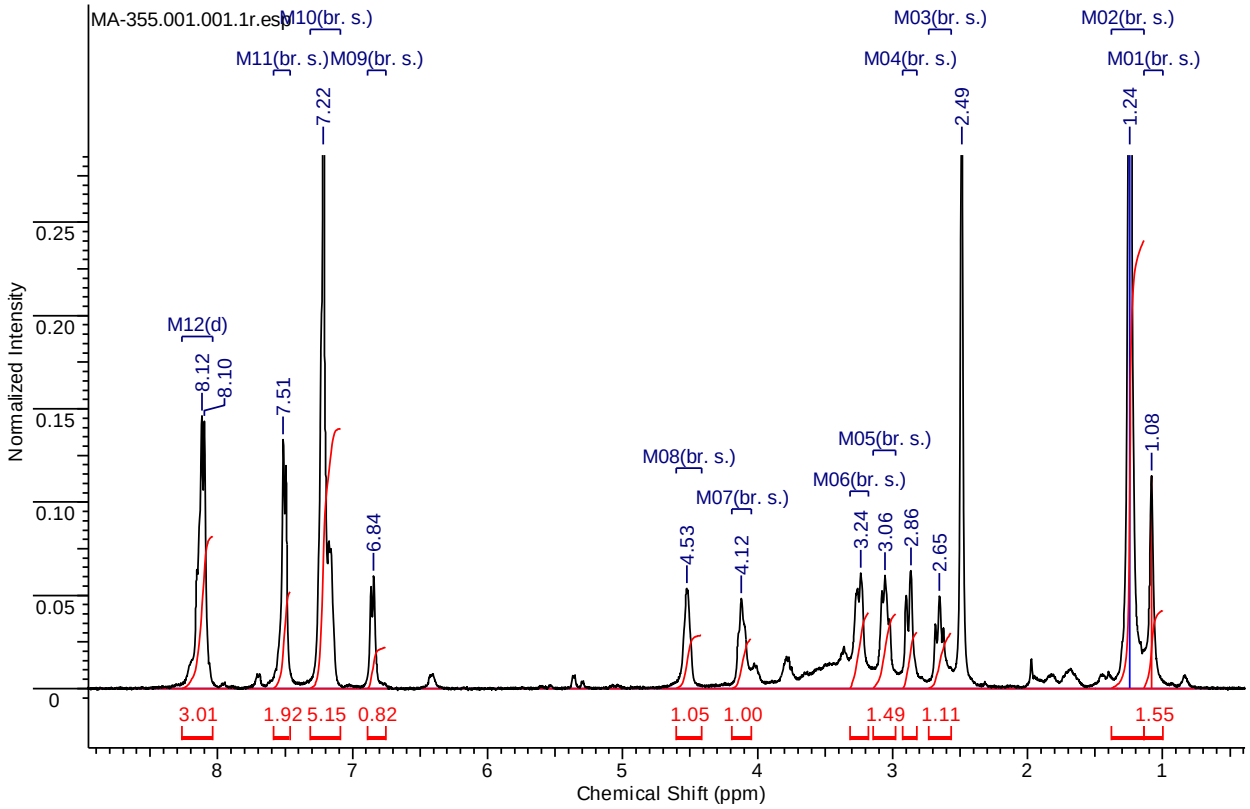

Figure S25. ^{1}H NMR (*S*)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--3-(4-nitrophenyl)propanoic acid (1g).

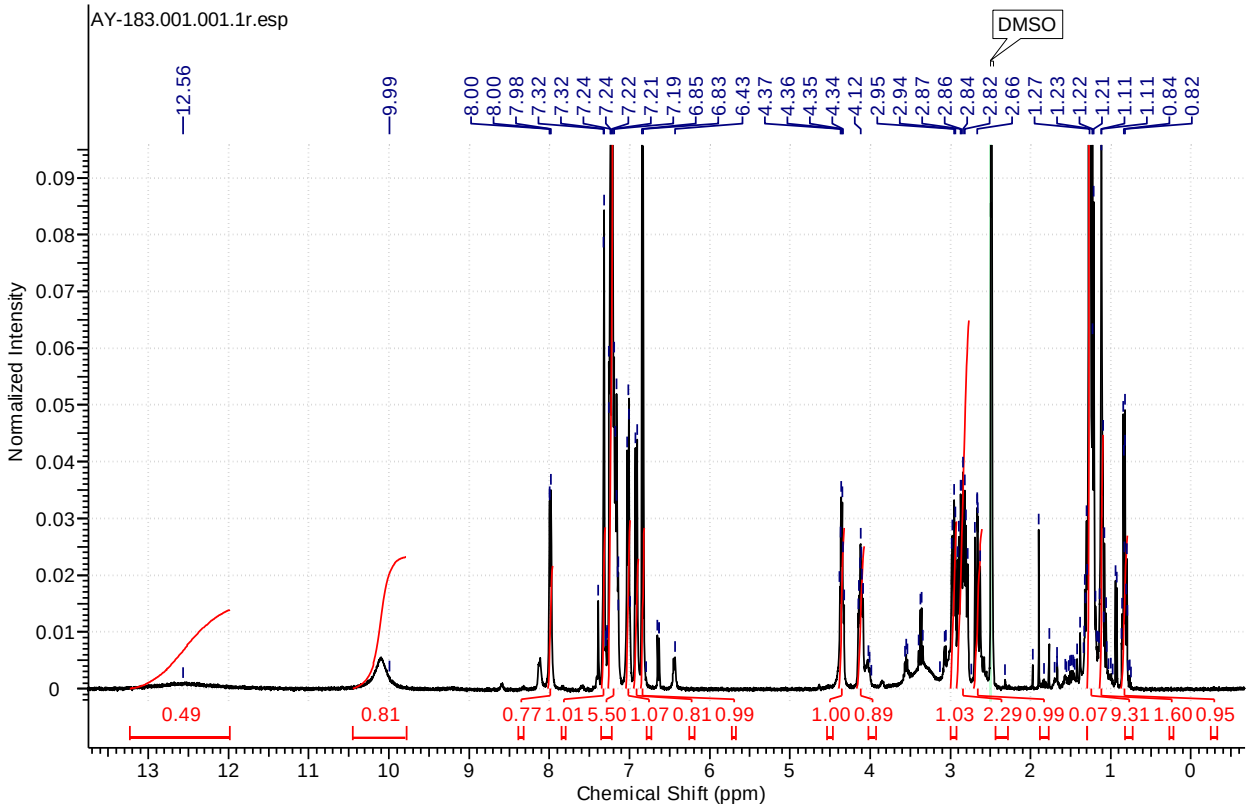

Figure S26. ^{1}H NMR (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)propanoic acid (1h).

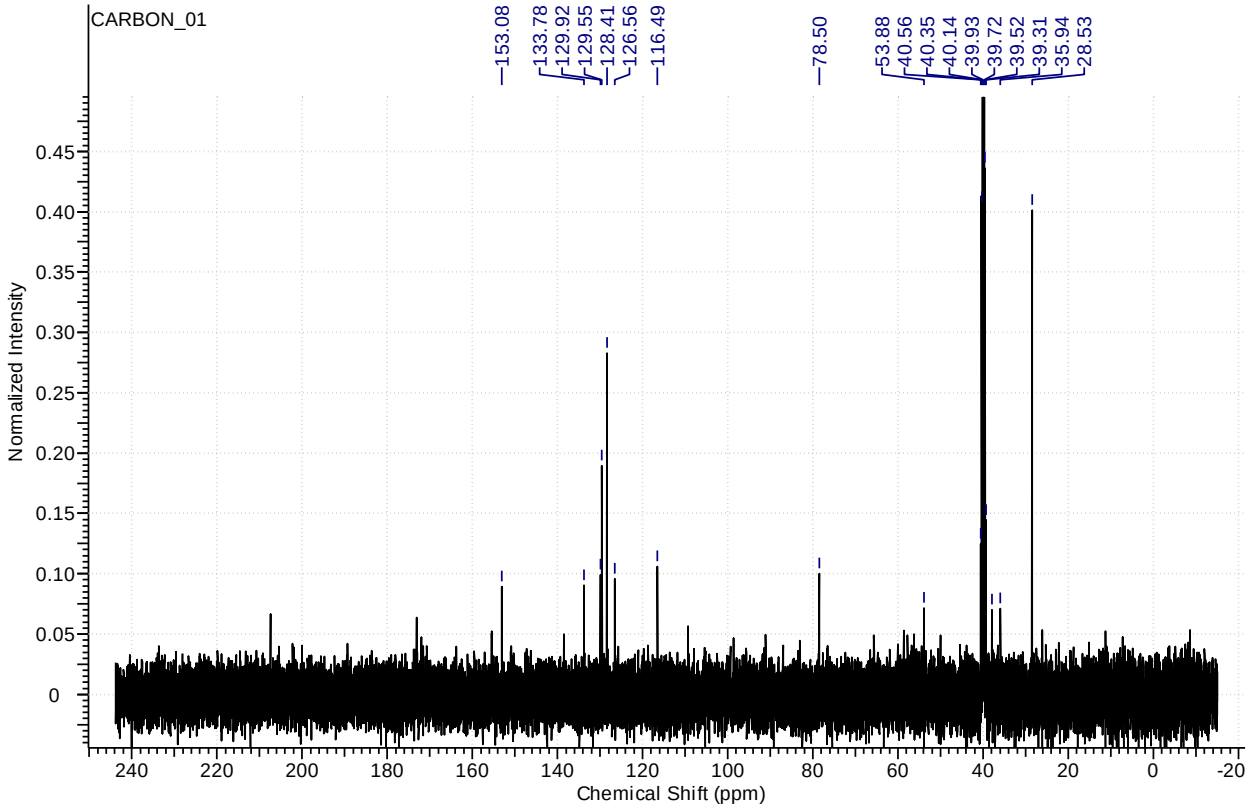

Figure S27. ^{13}C NMR (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)propanoic acid (1h).

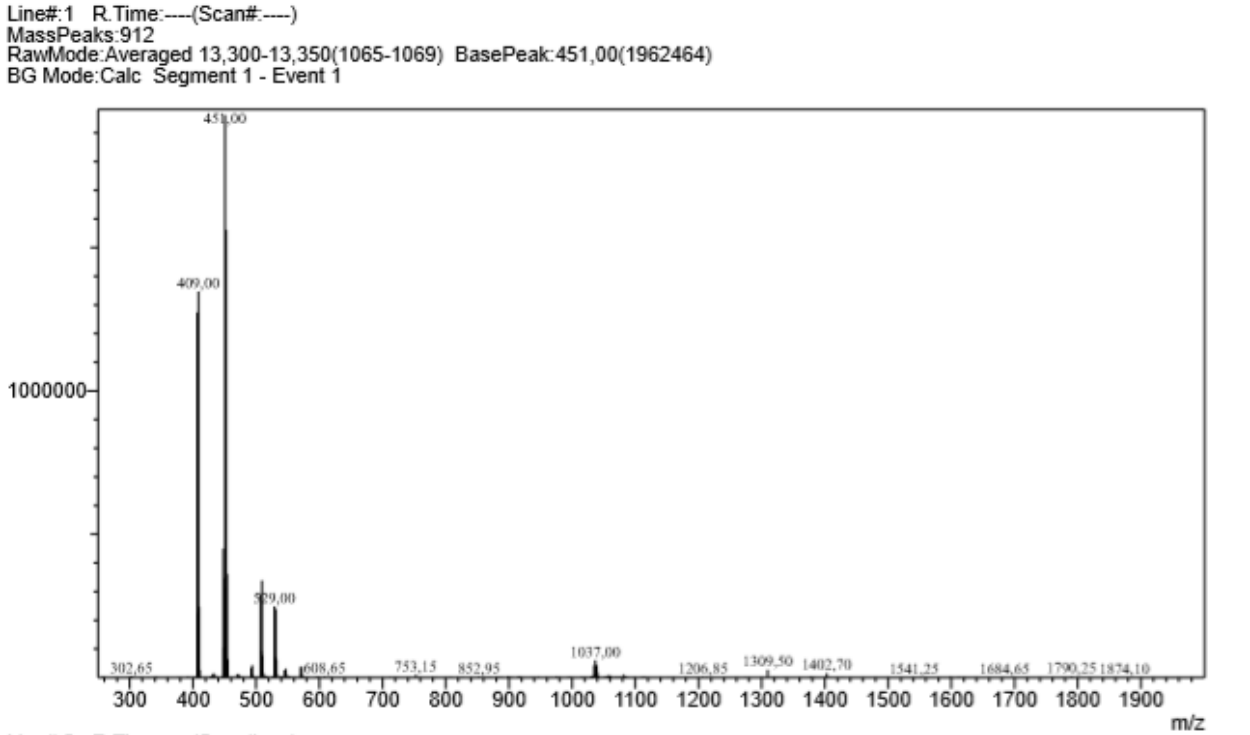

Figure S28. MS (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)propanoic acid (1h).

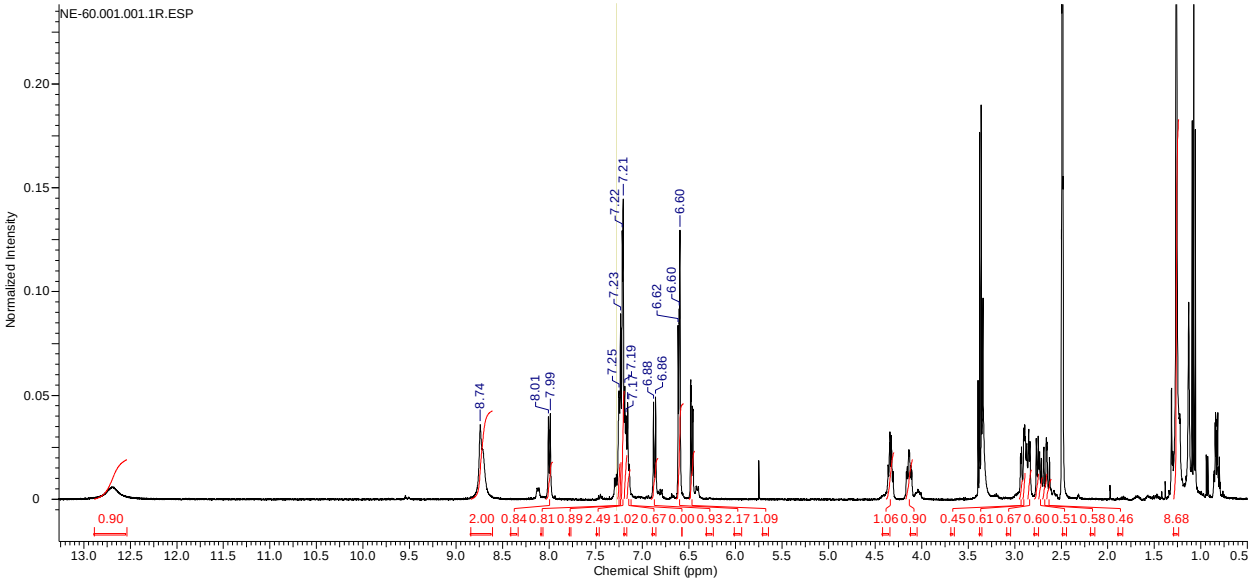

Figure S29. ^{1}H NMR (*S*)-2-((S)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--3-(3,4-dihydroxyphenyl)propanoic acid (1i).

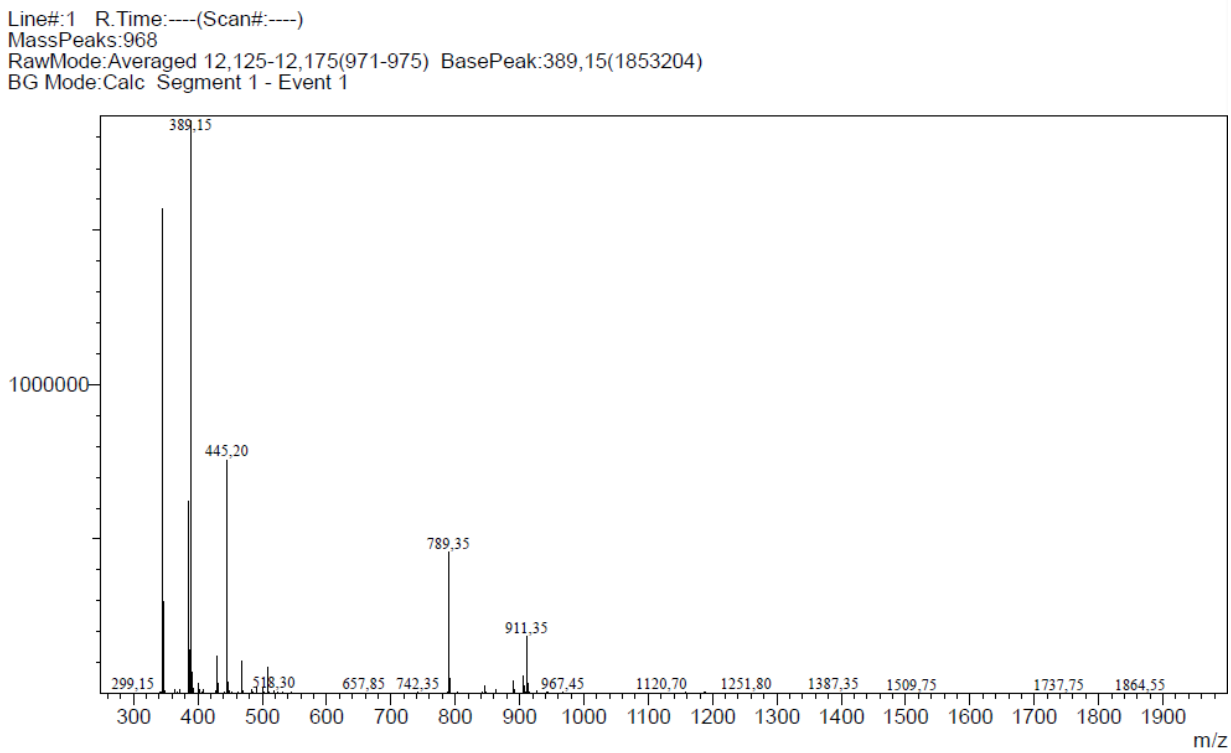

Figure S30. MS (*S*)-2-((S)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanamido)--3-(3,4-dihydroxyphenyl)propanoic acid (1i).

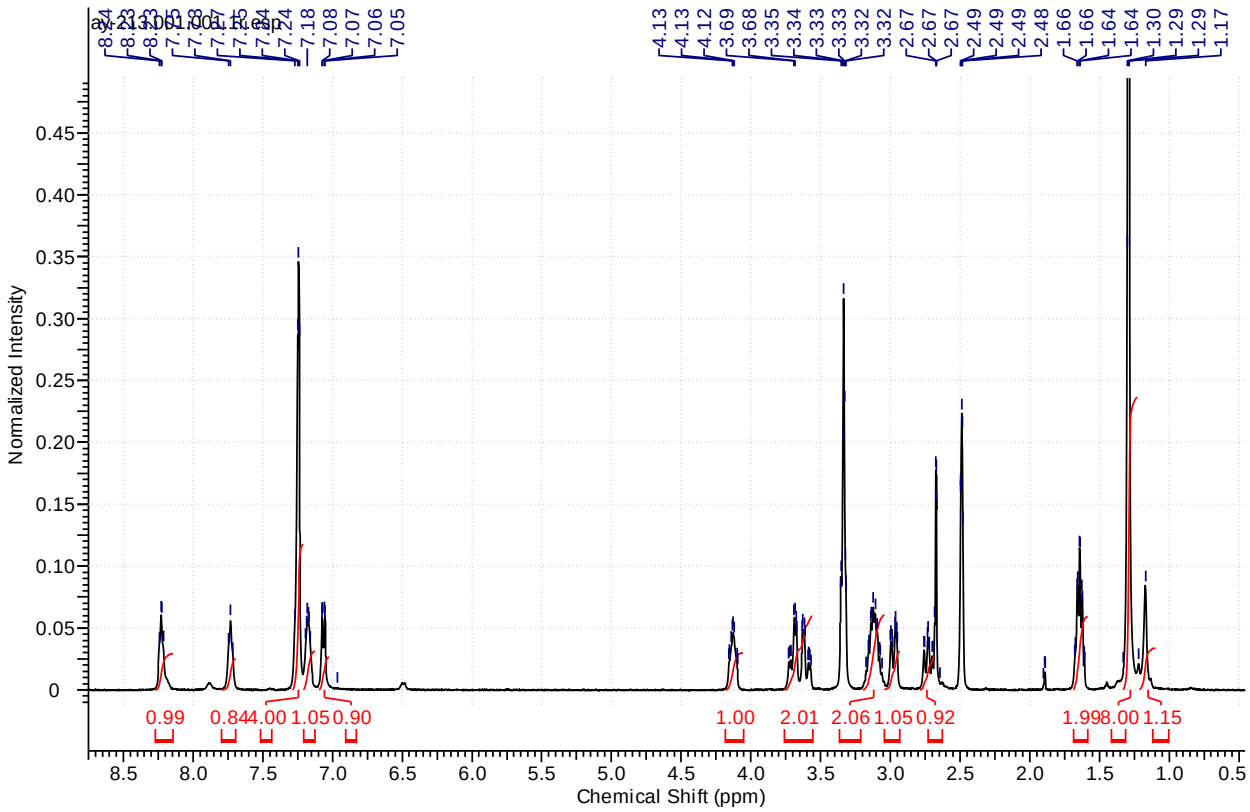

Figure S31. ^{1}H NMR tert-butyl (S)-(1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

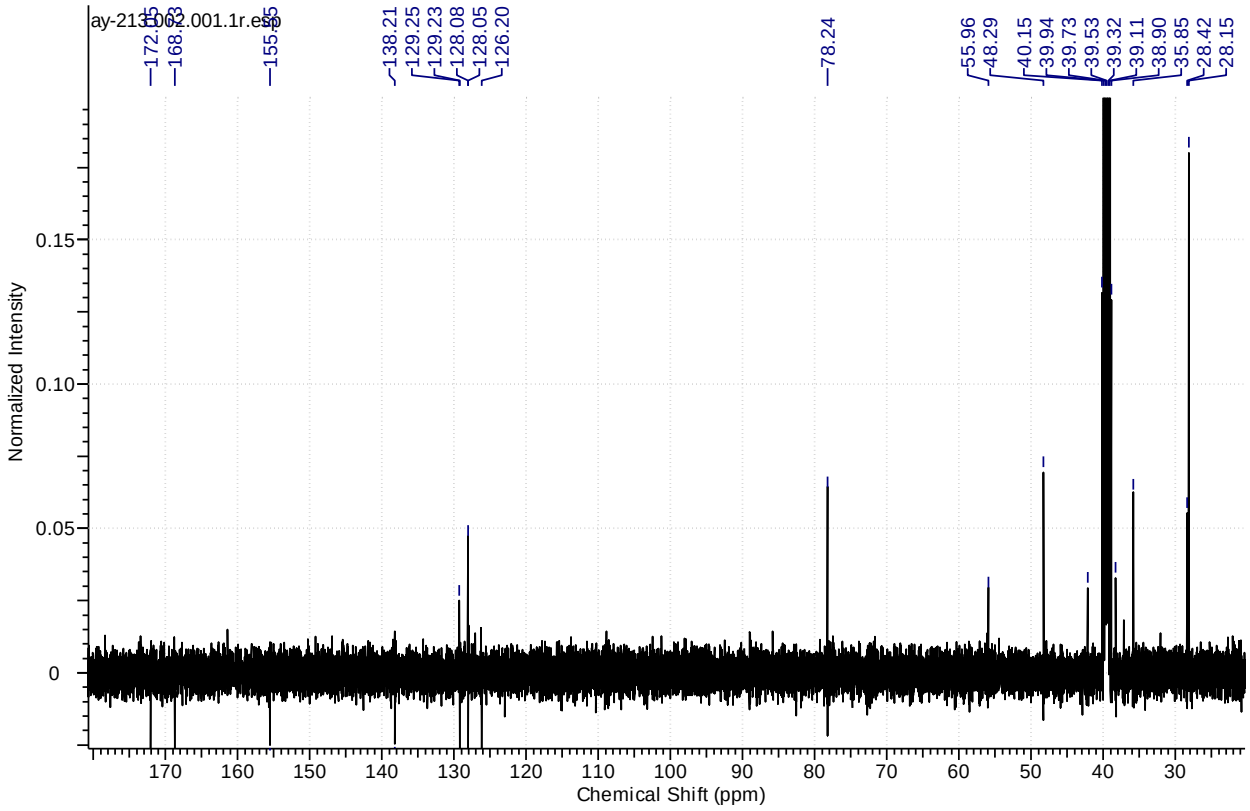

Figure S32. ^{13}C NMR tert-butyl (S)-(1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

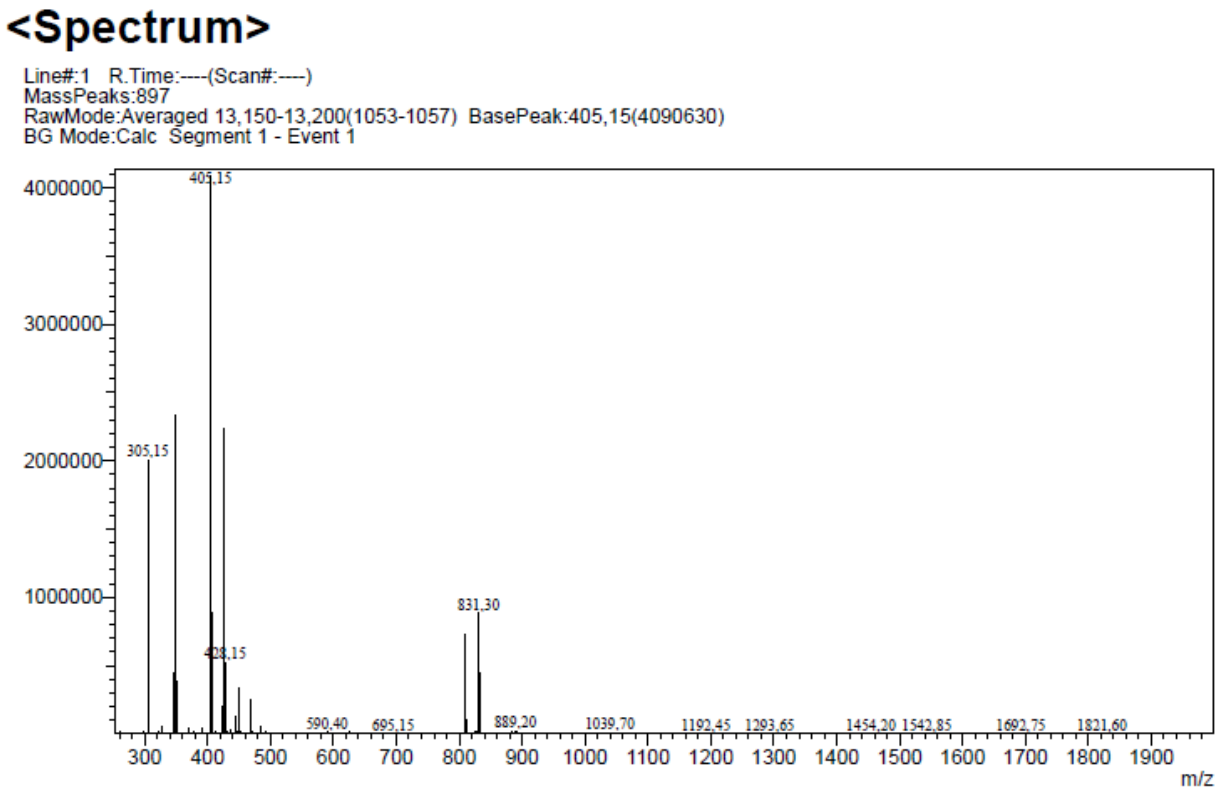

Figure S33. MS tert-butyl (S)-(1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

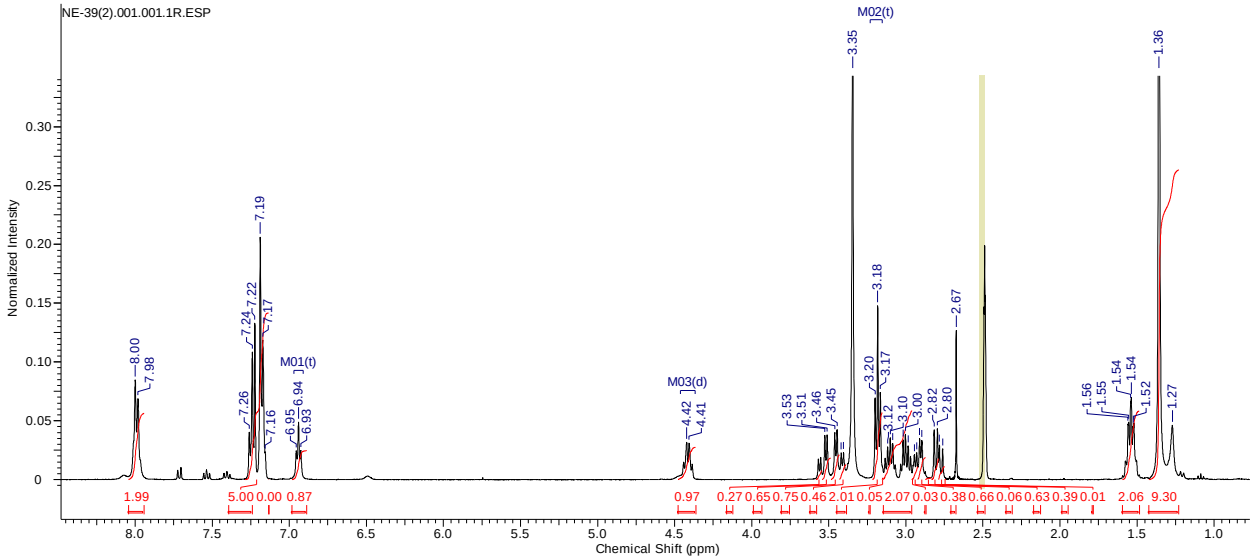

Figure S34. ^{1}H NMR tert-butyl (S)-(2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate.

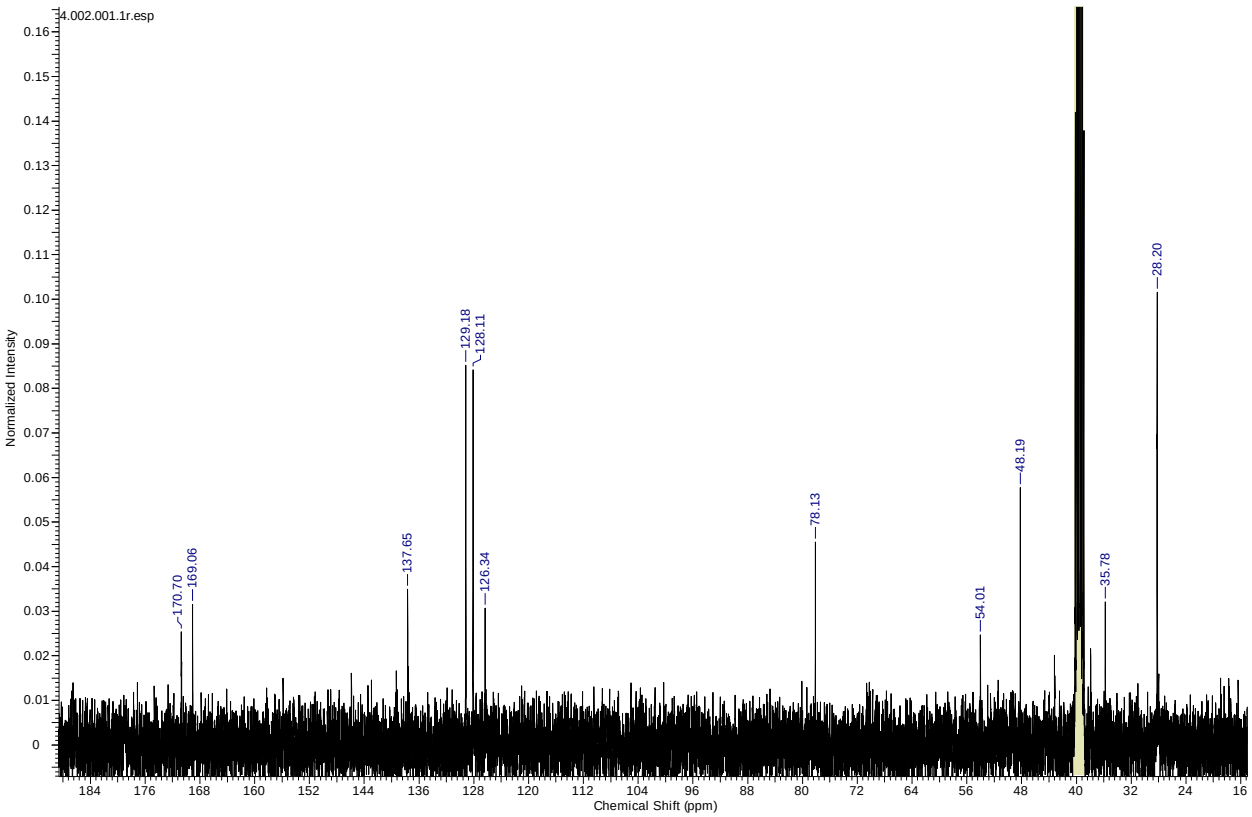

Figure S35. ^{13}C NMR tert-butyl (S)-(2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate.

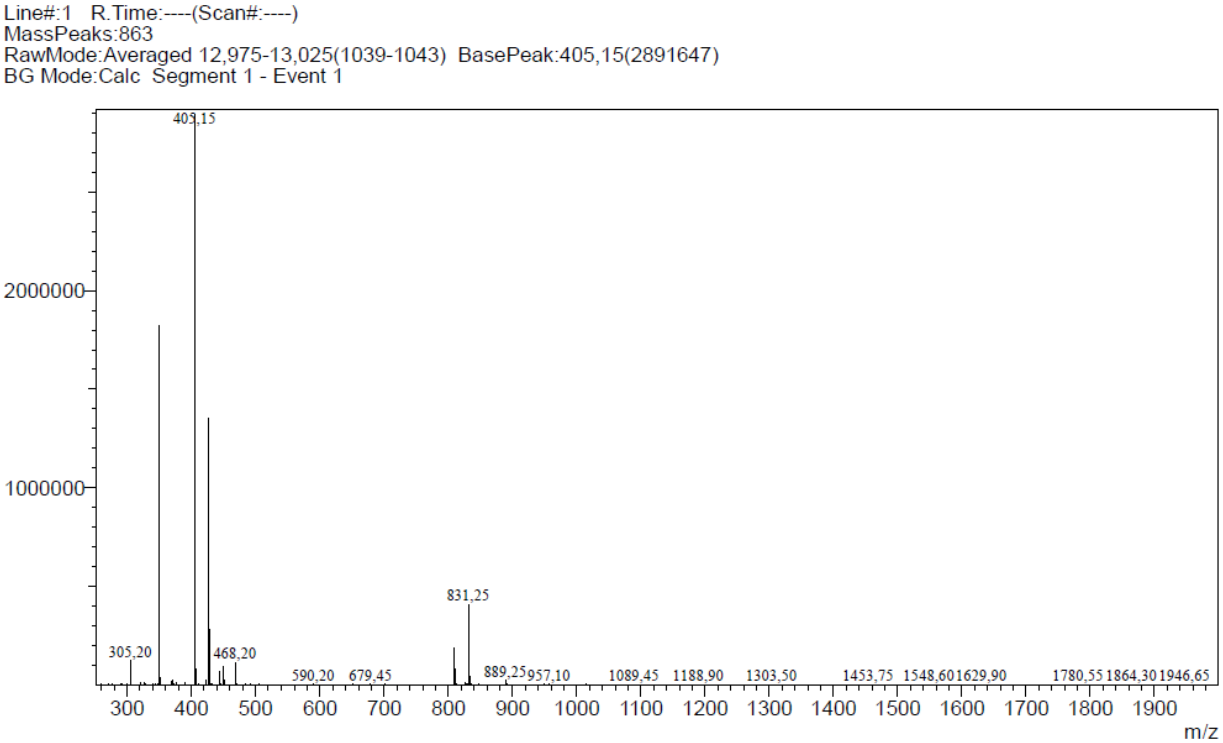

Figure S36. MS tert-butyl (S)-(2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)carbamate.

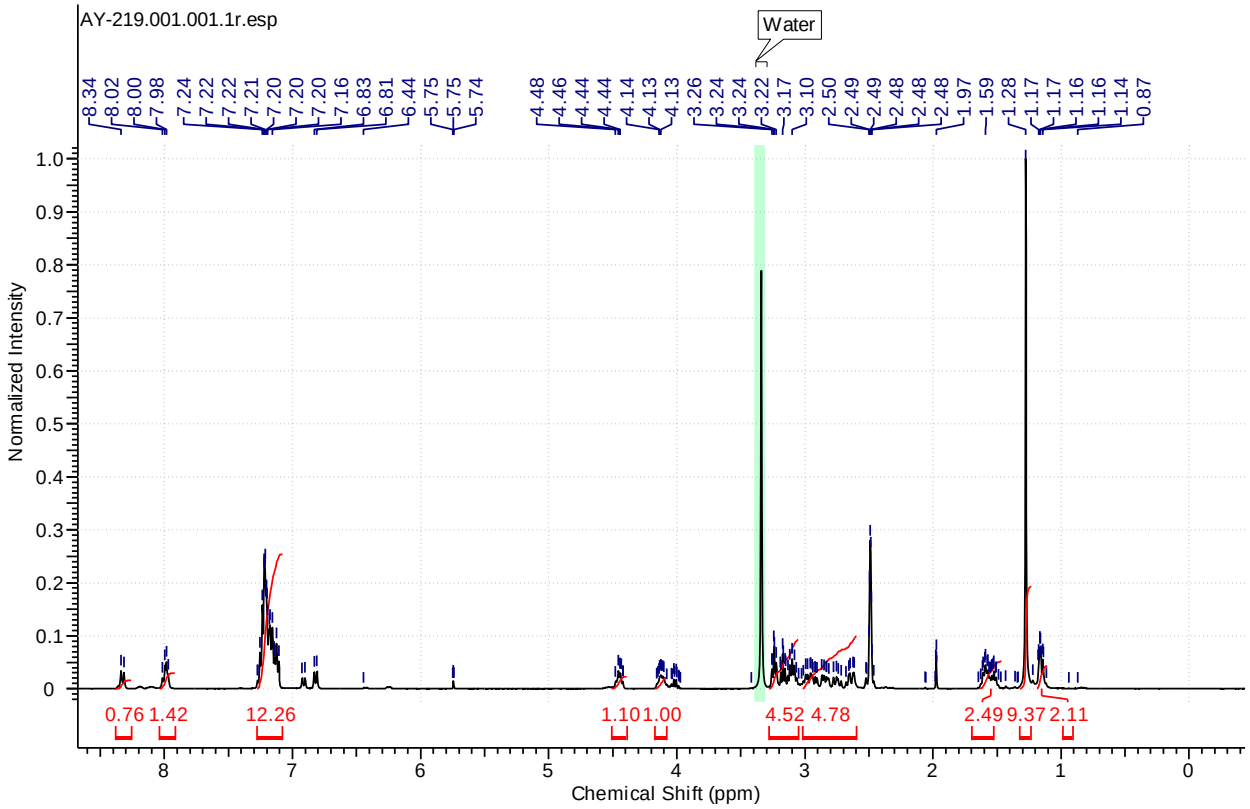

Figure S37. ^{1}H NMR tert-butyl ((S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

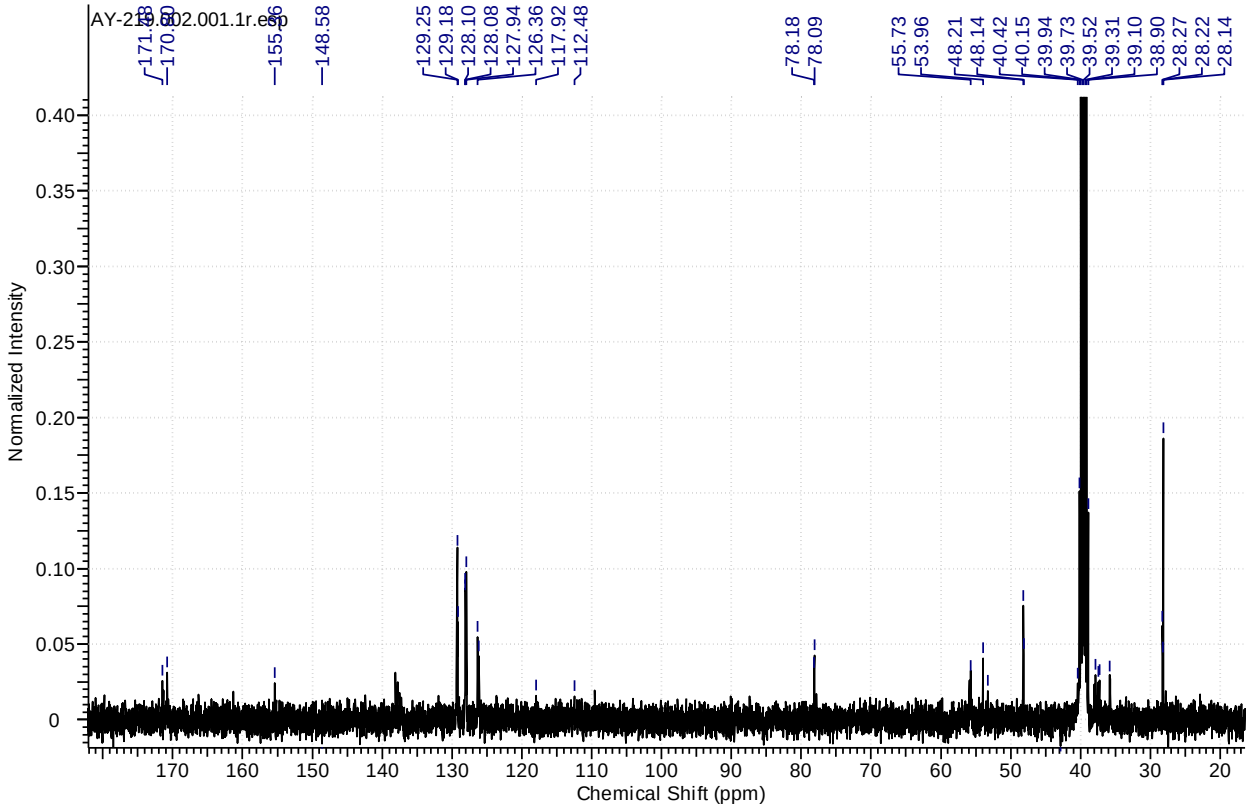

Figure S38. ^{13}C NMR tert-butyl ((S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

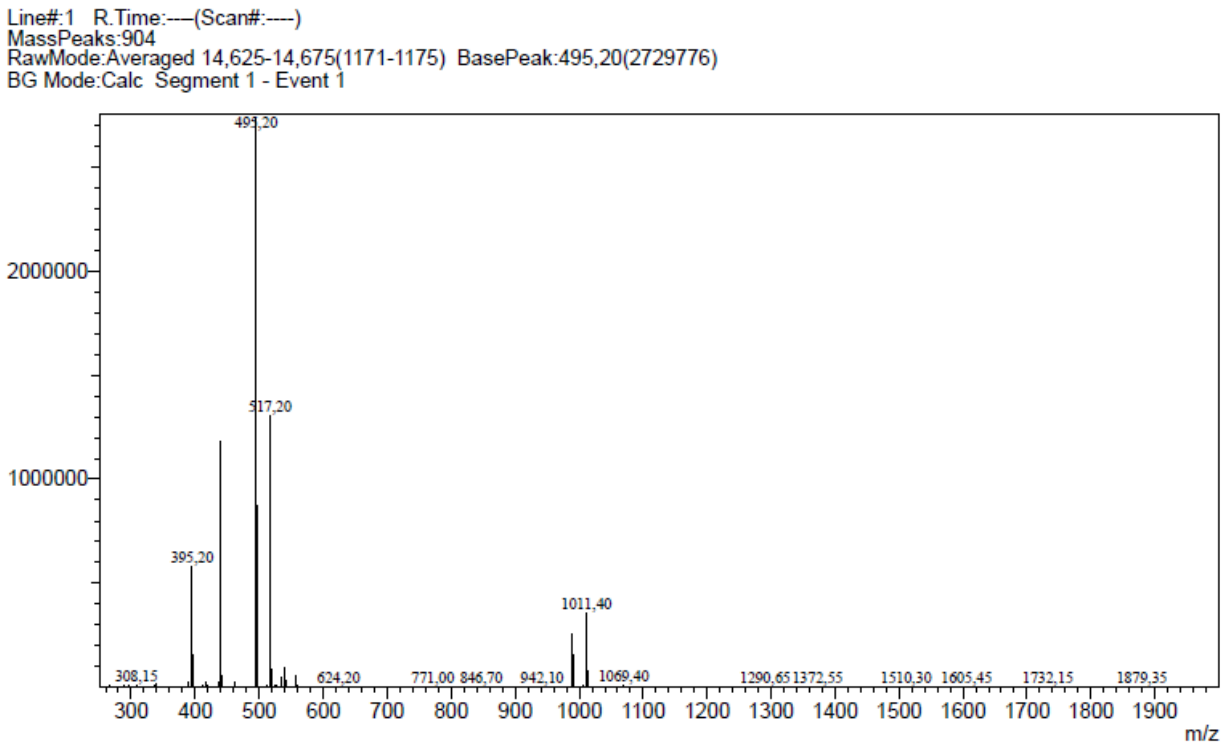

Figure S39. MS tert-butyl ((S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

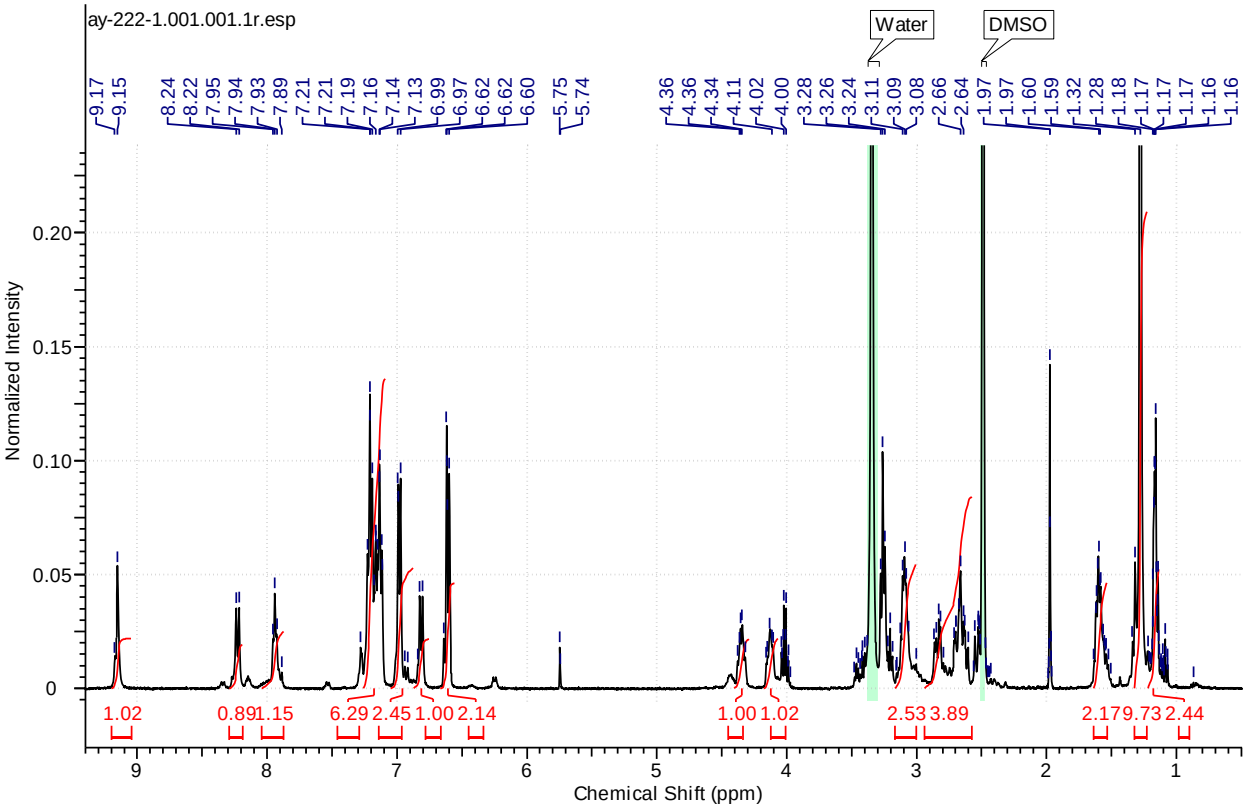

Figure S40. ^{1}H NMR tert-butyl ((S)-1-(((R)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

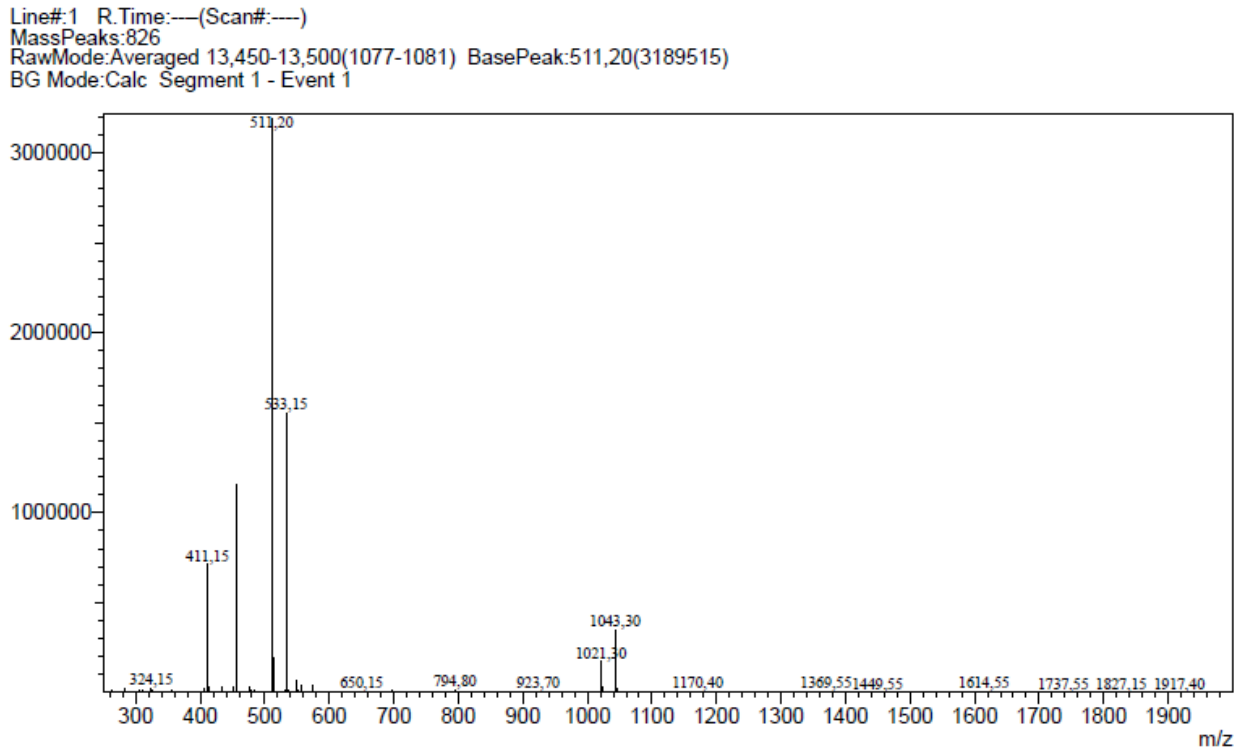

Figure S41. MS tert-butyl ((S)-1-(((R)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

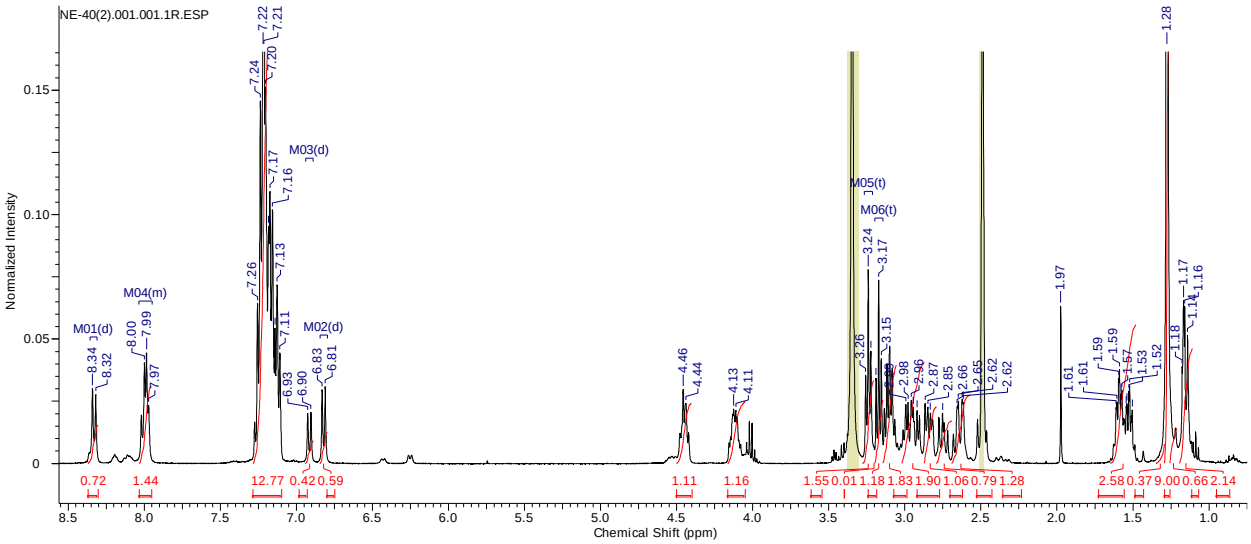

Figure S42. ^{1}H NMR tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

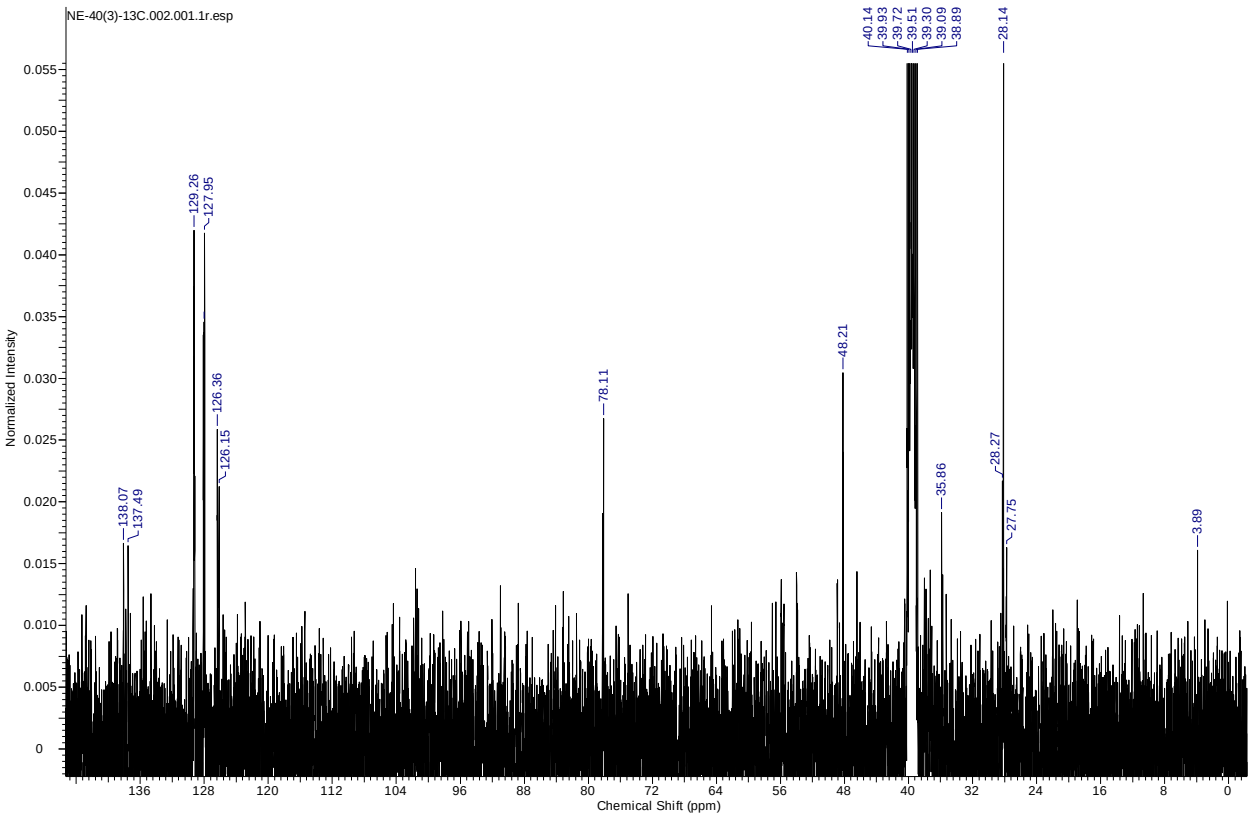

Figure S43. ^{13}C NMR tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

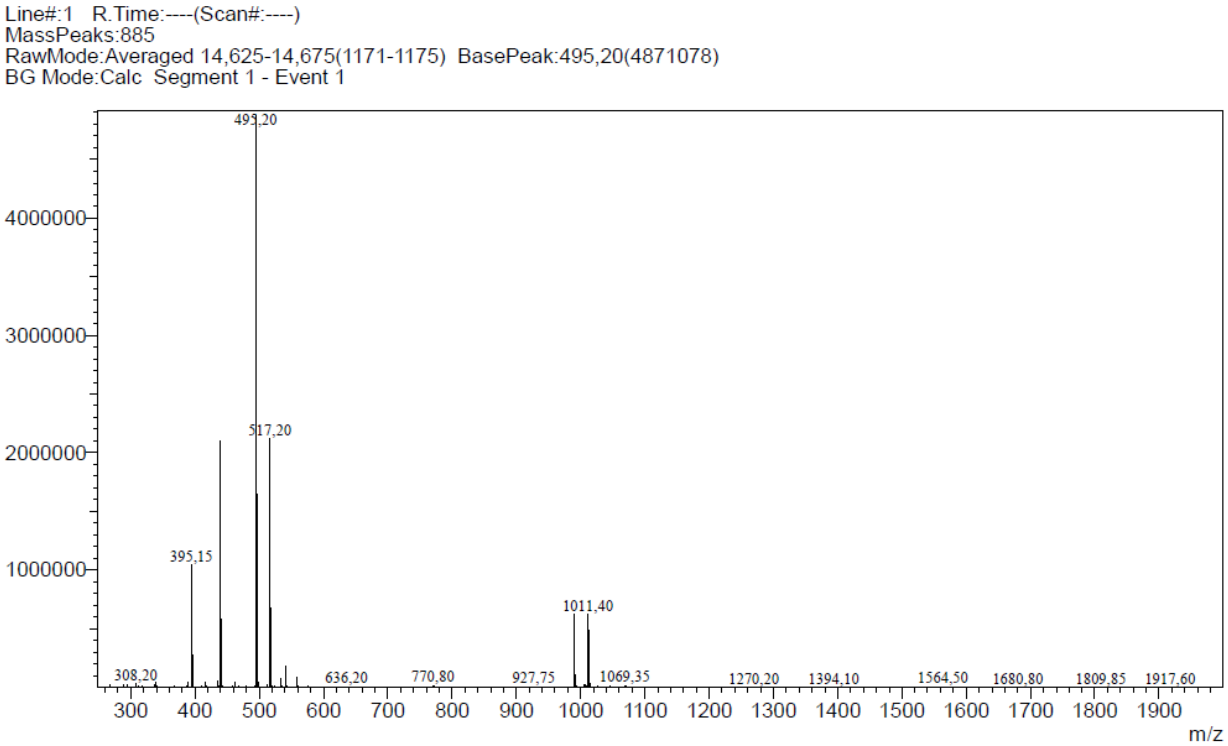

Figure S44. MS tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

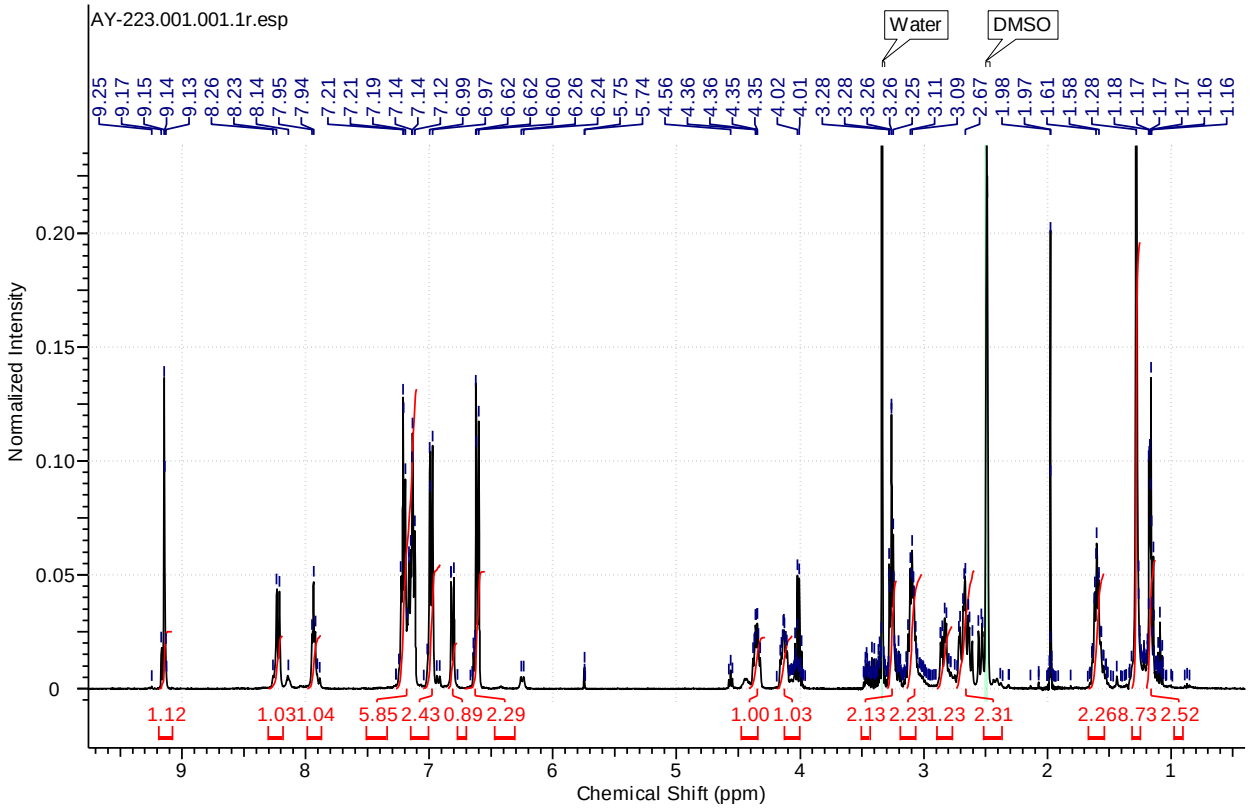

Figure S45. ^{1}H NMR tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

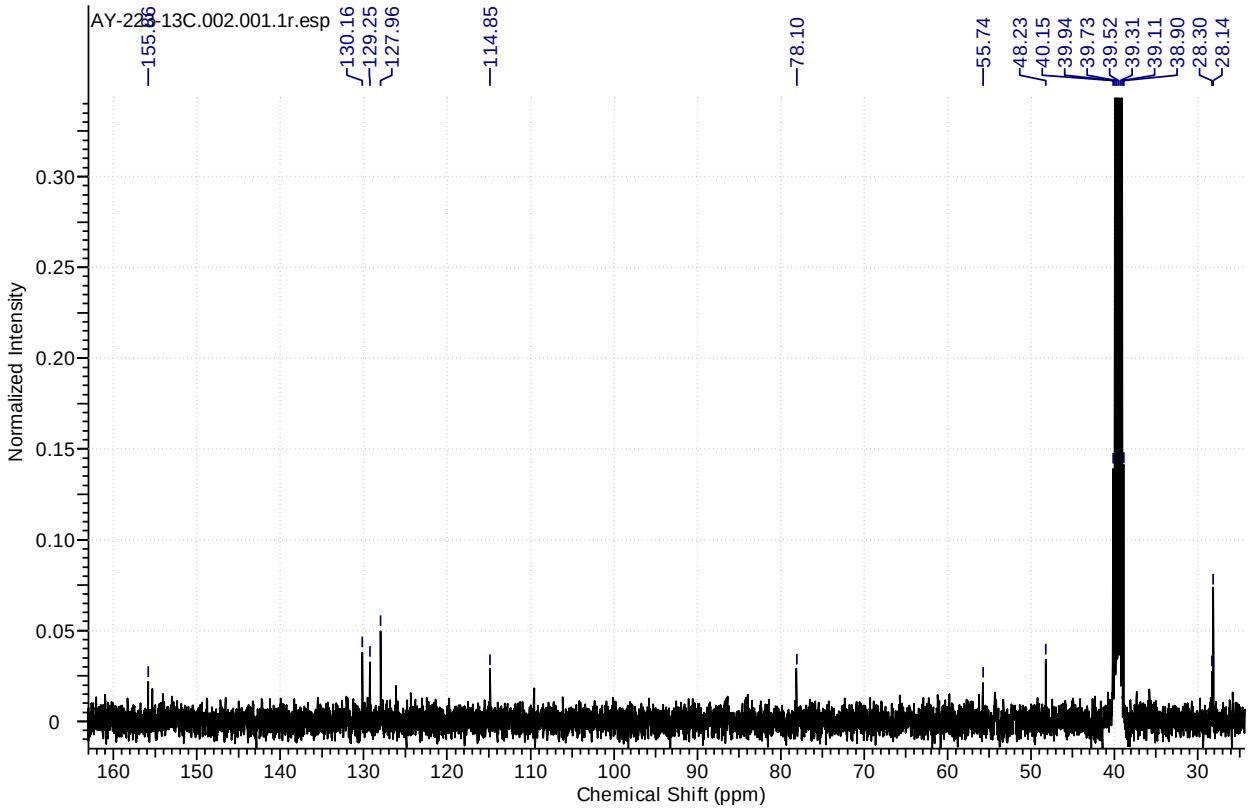

Figure S46. ^{13}C NMR tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

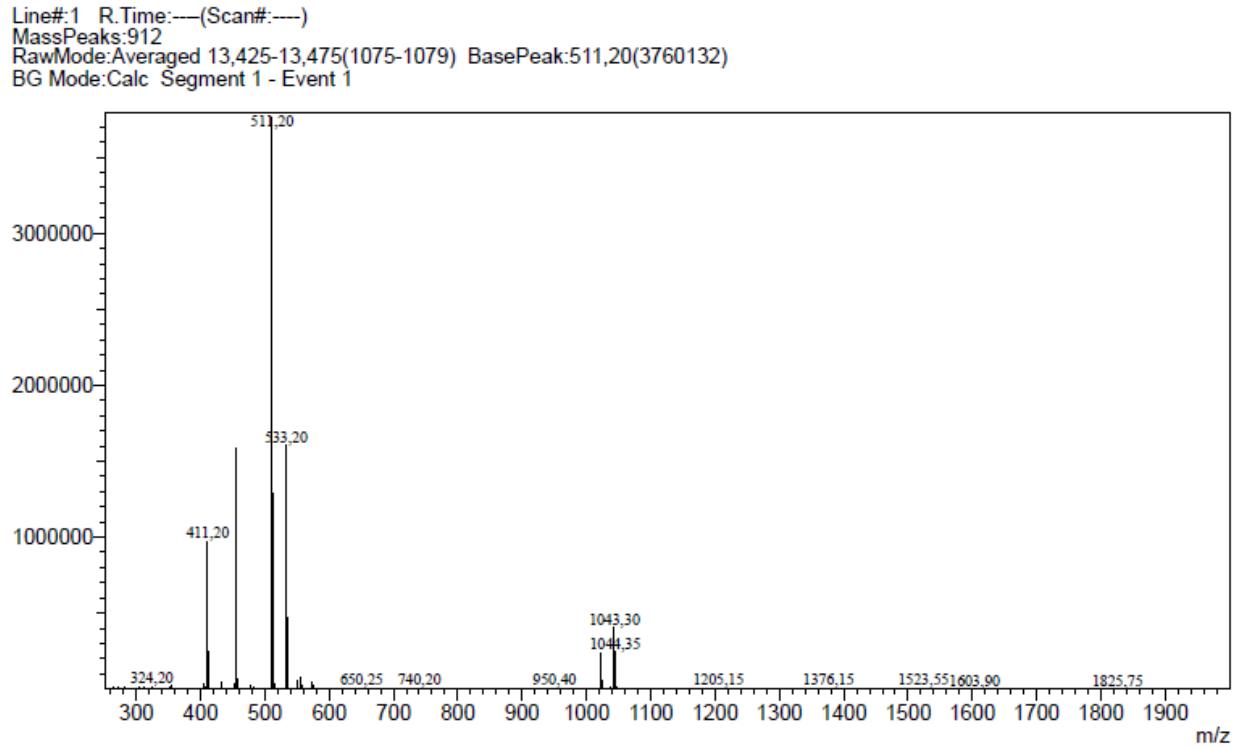

Figure S47. MS tert-butyl ((R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

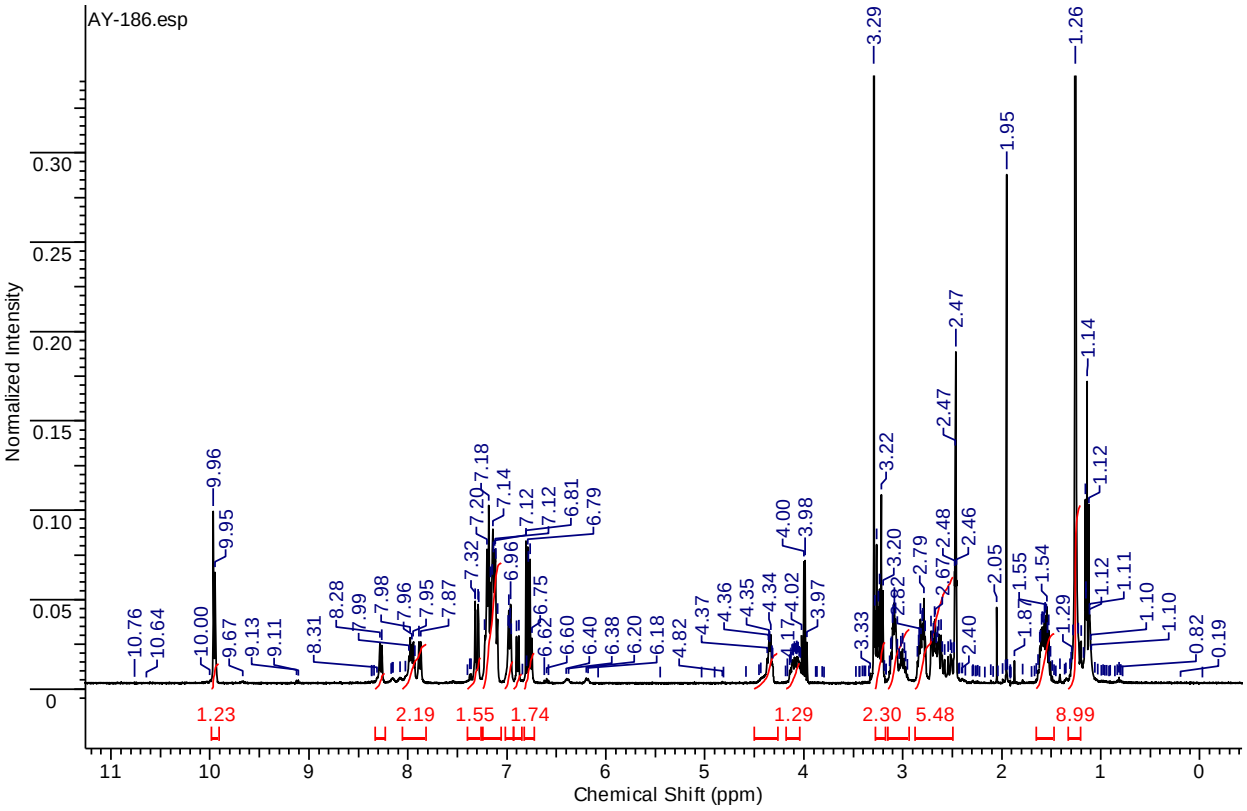

Figure S48. ^{1}H NMR tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

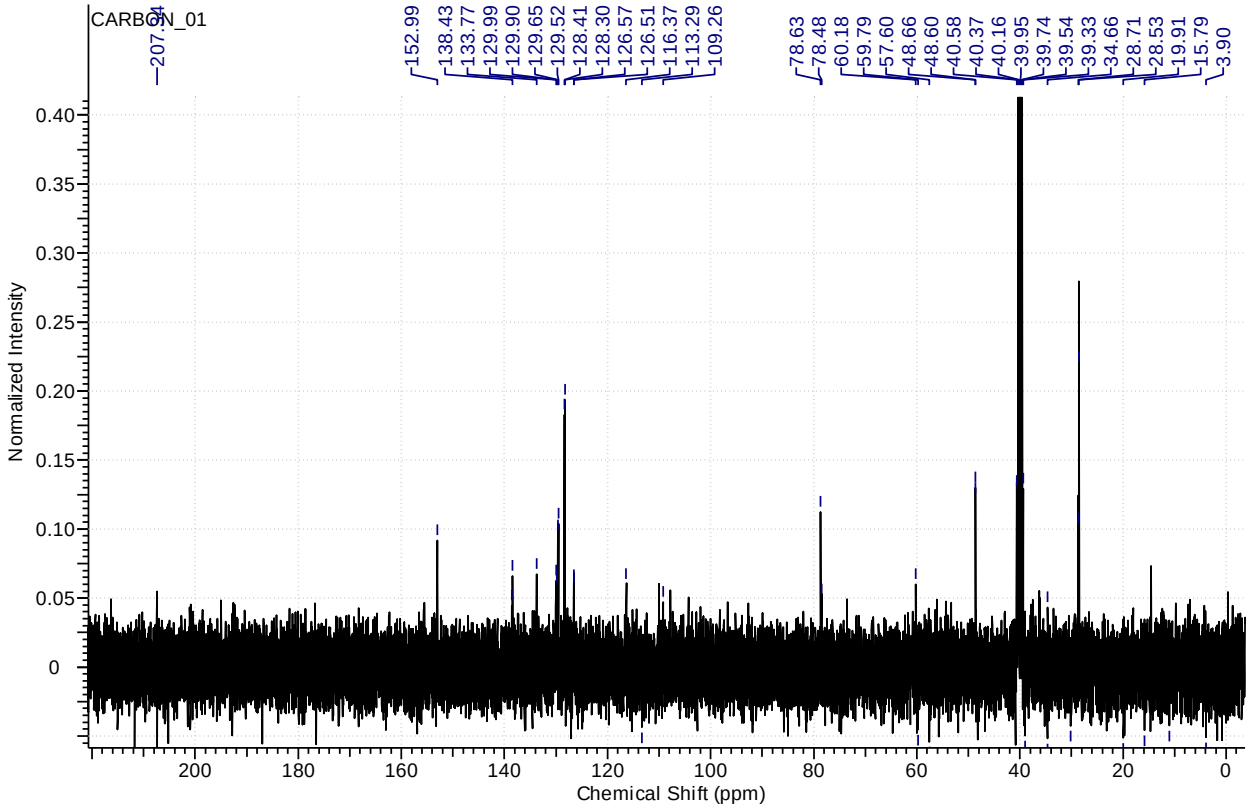

Figure S49. ^{13}C NMR tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

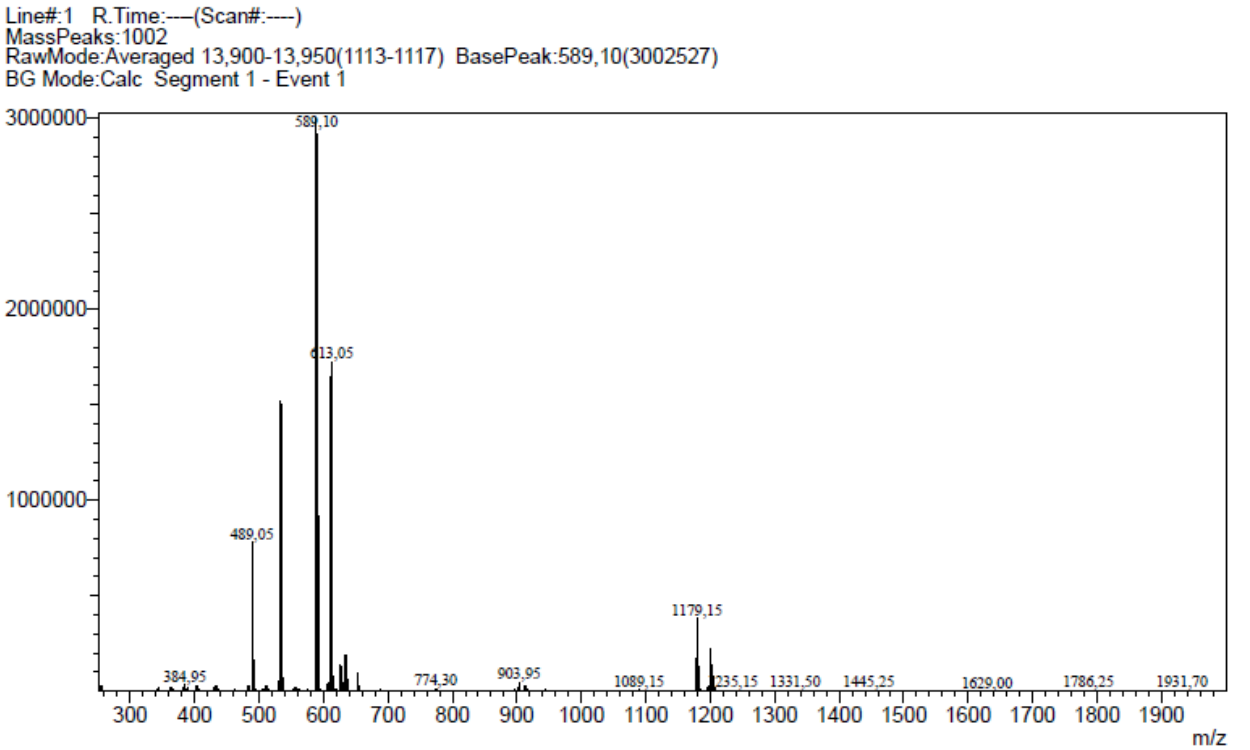

Figure S50. MS tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

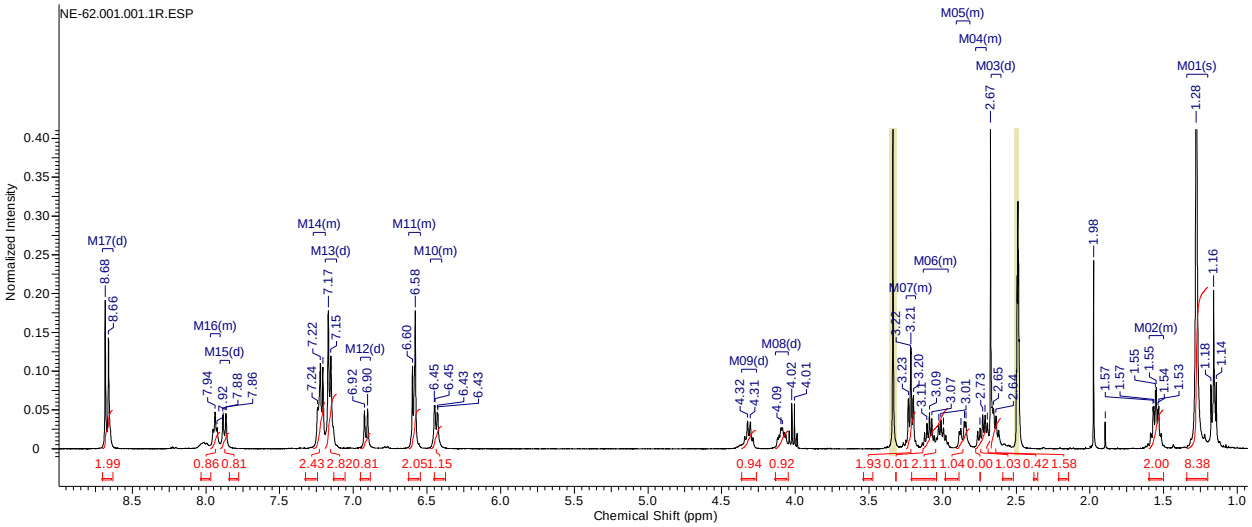

Figure S51. ^{1}H NMR tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

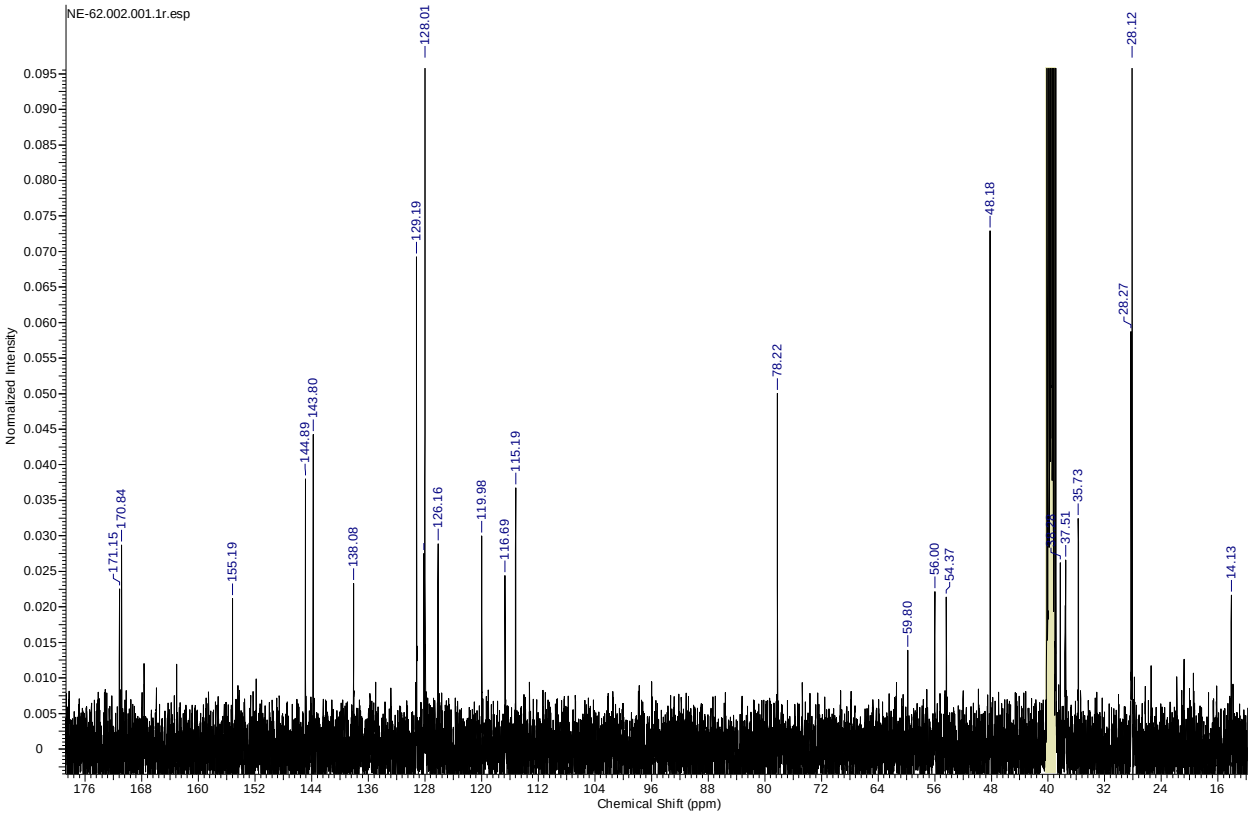

Figure S52. ^{13}C NMR tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

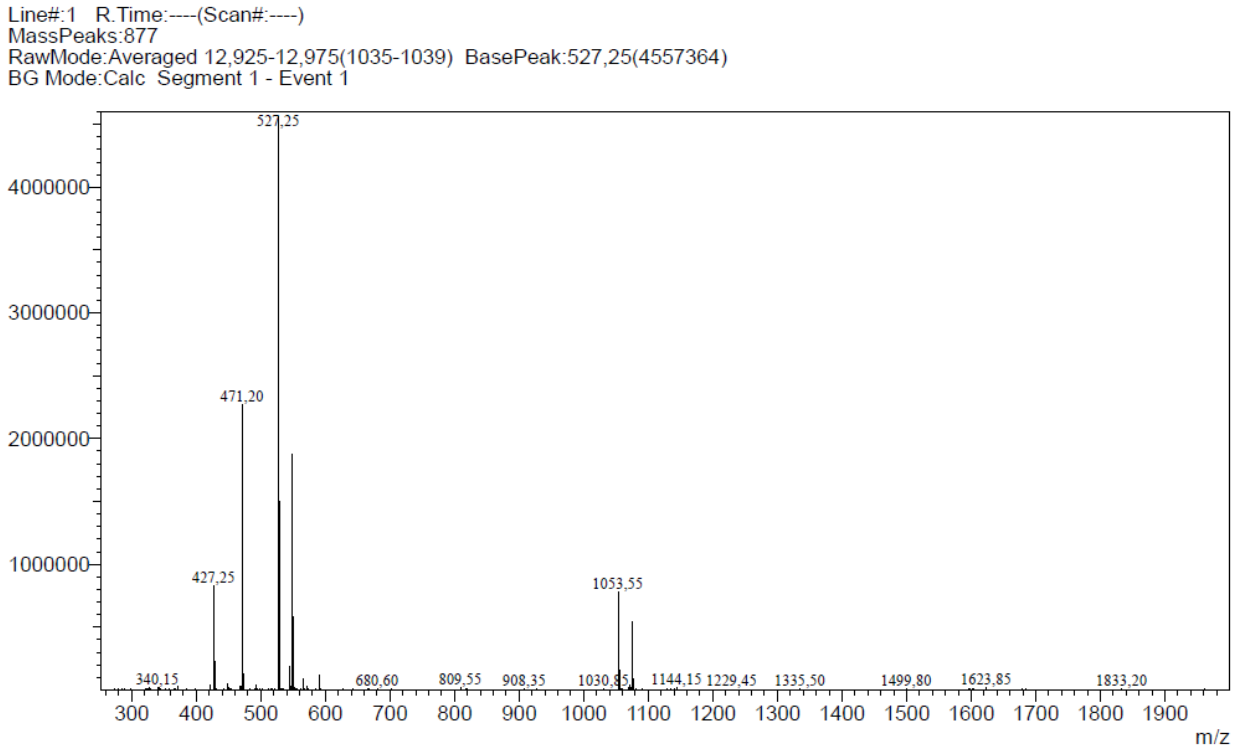

Figure S53. MS tert-butyl ((S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate.

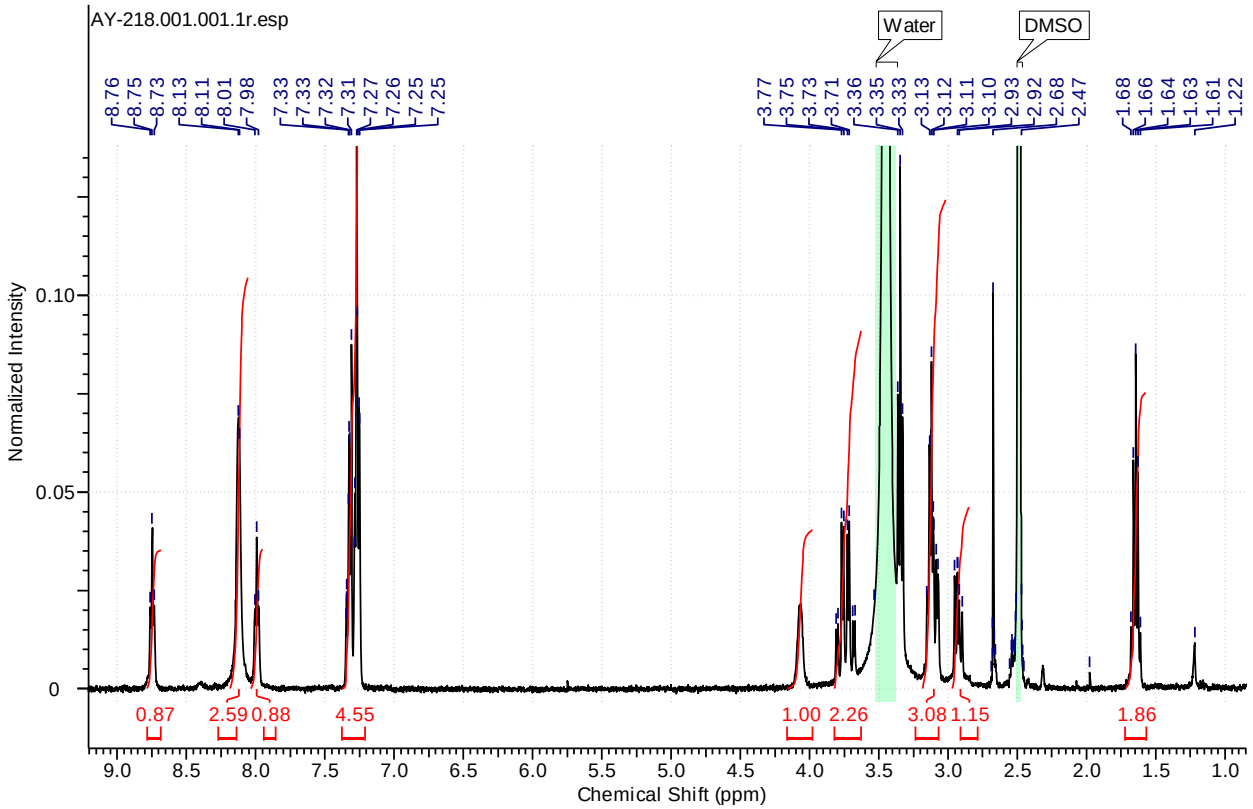

Figure S54. ^{1}H NMR (S)-1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2a).

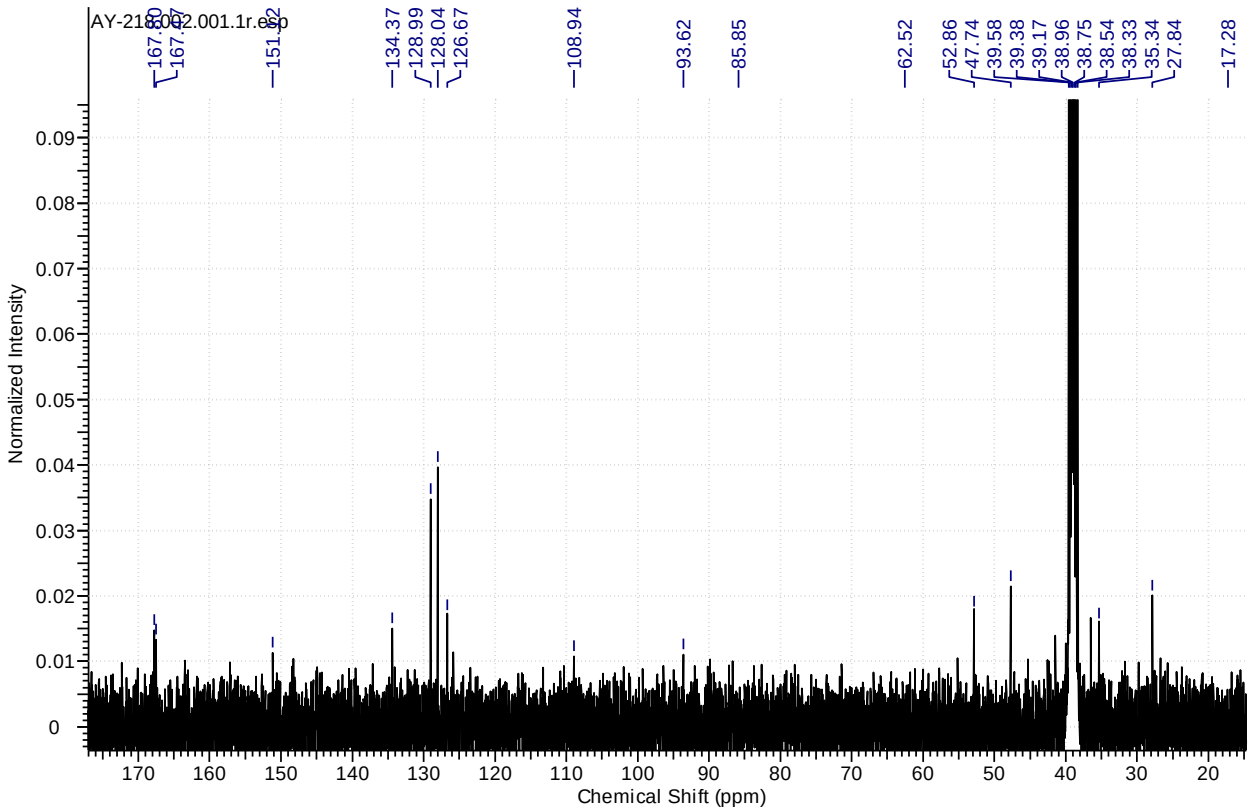

Figure S55. ^{13}C NMR (S)-1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2a).

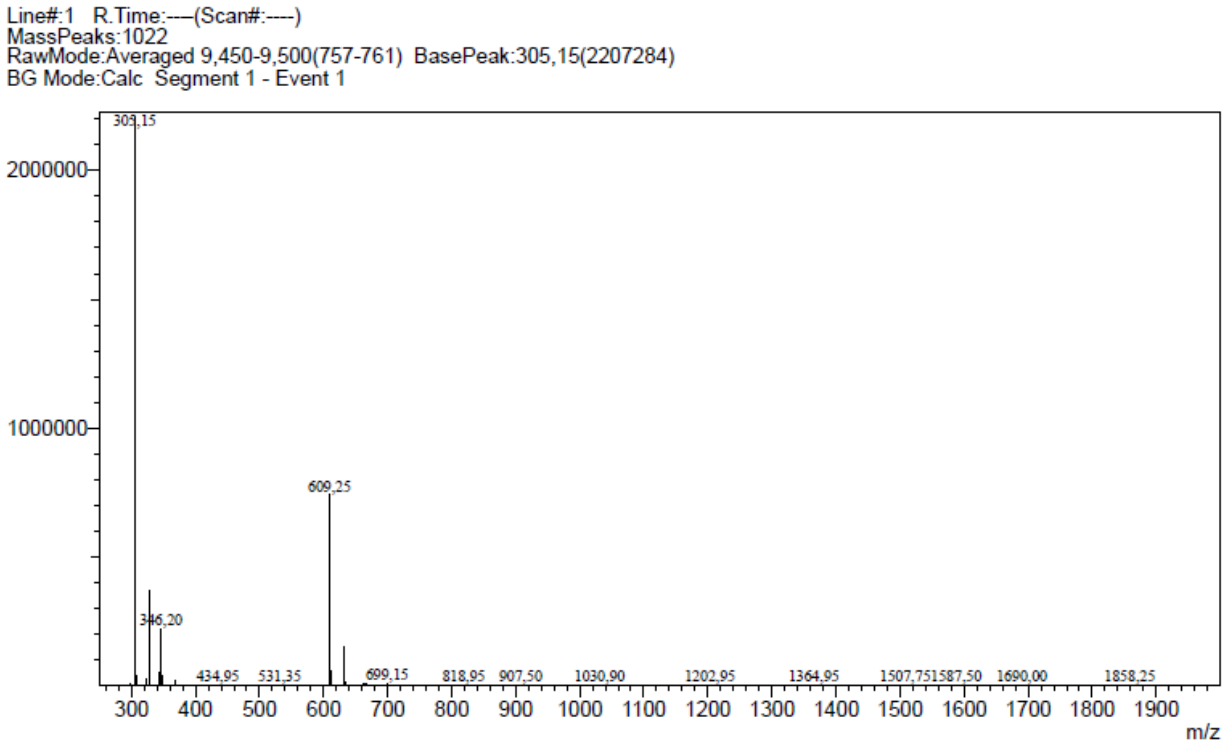

Figure S56. MS (S)-1-((2-((3-azidopropyl)amino)-2-oxoethyl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2a).

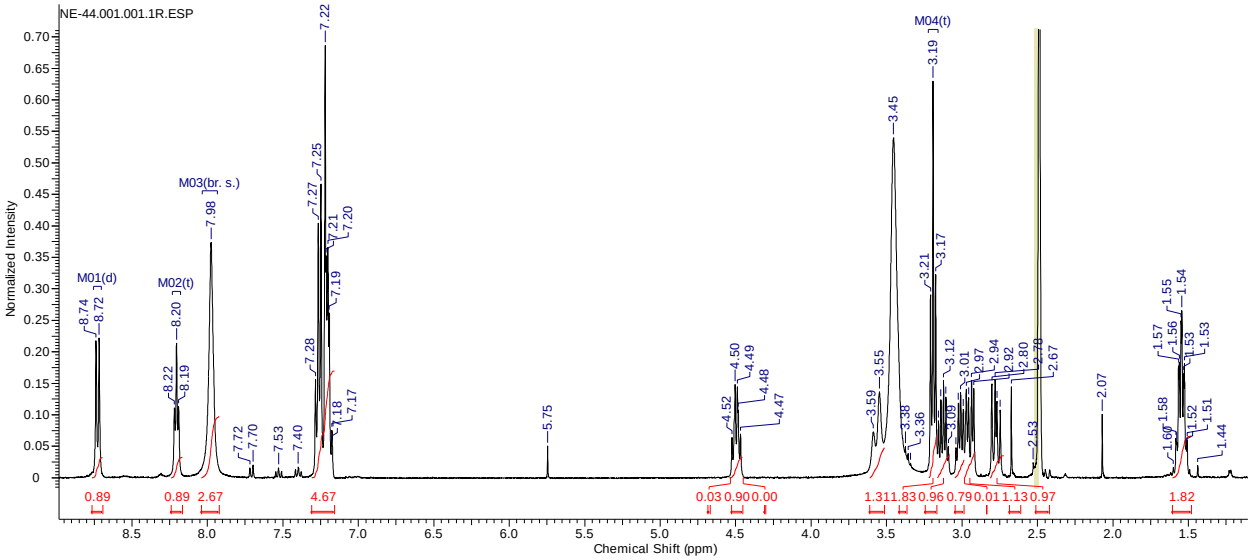

Figure S57. ^{1}H NMR (S)-2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethan-1-aminium 2,2,2-trifluoroacetate (2b).

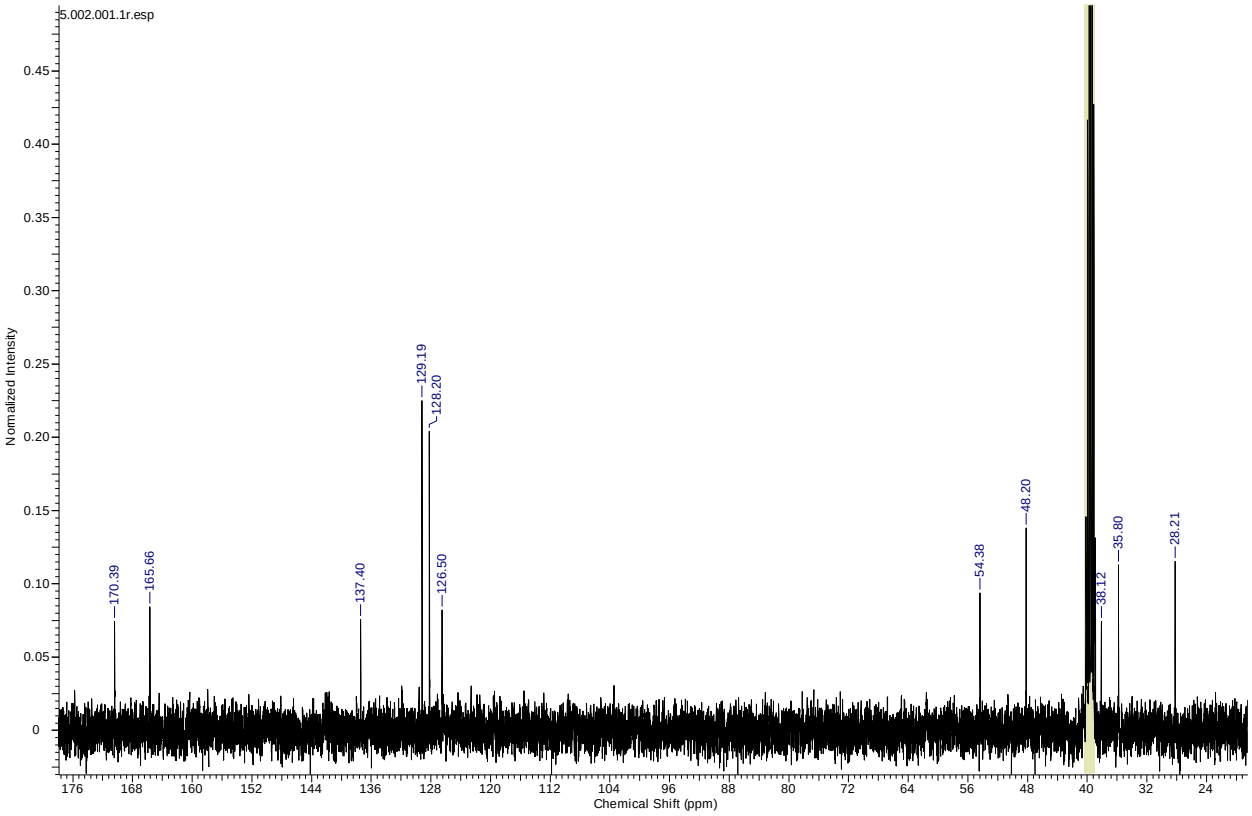

Figure S58. ^{13}C NMR (S)-2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethan-1-aminium 2,2,2-trifluoroacetate (2b).

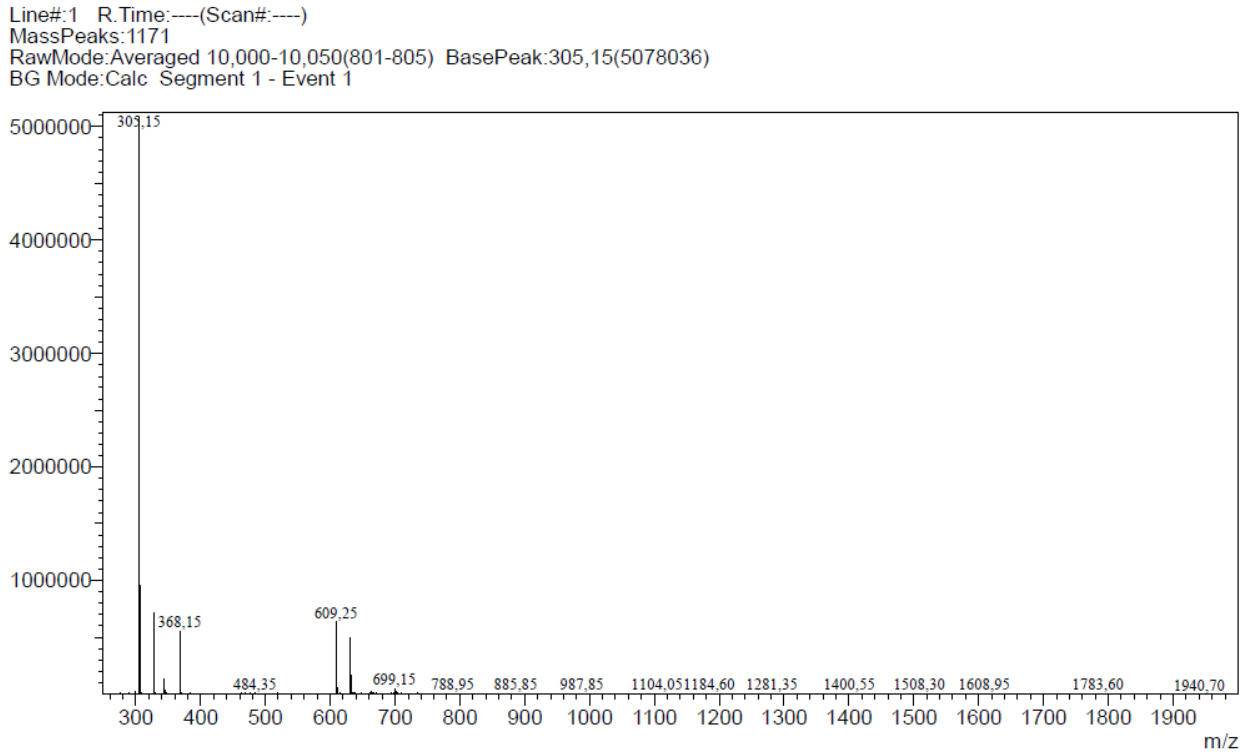

Figure S59. MS (S)-2-((1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethan-1-aminium 2,2,2-trifluoroacetate (2b).

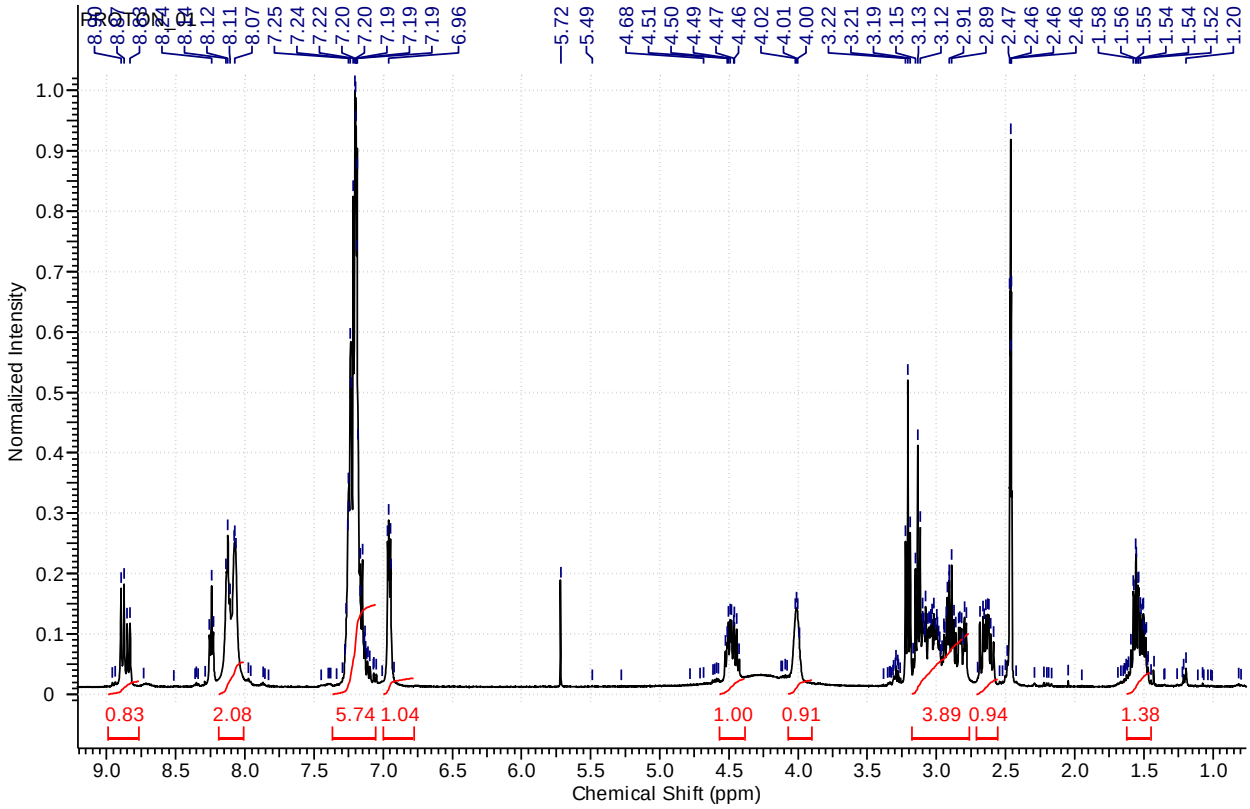

Figure S60. ^{1}H NMR (S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2c).

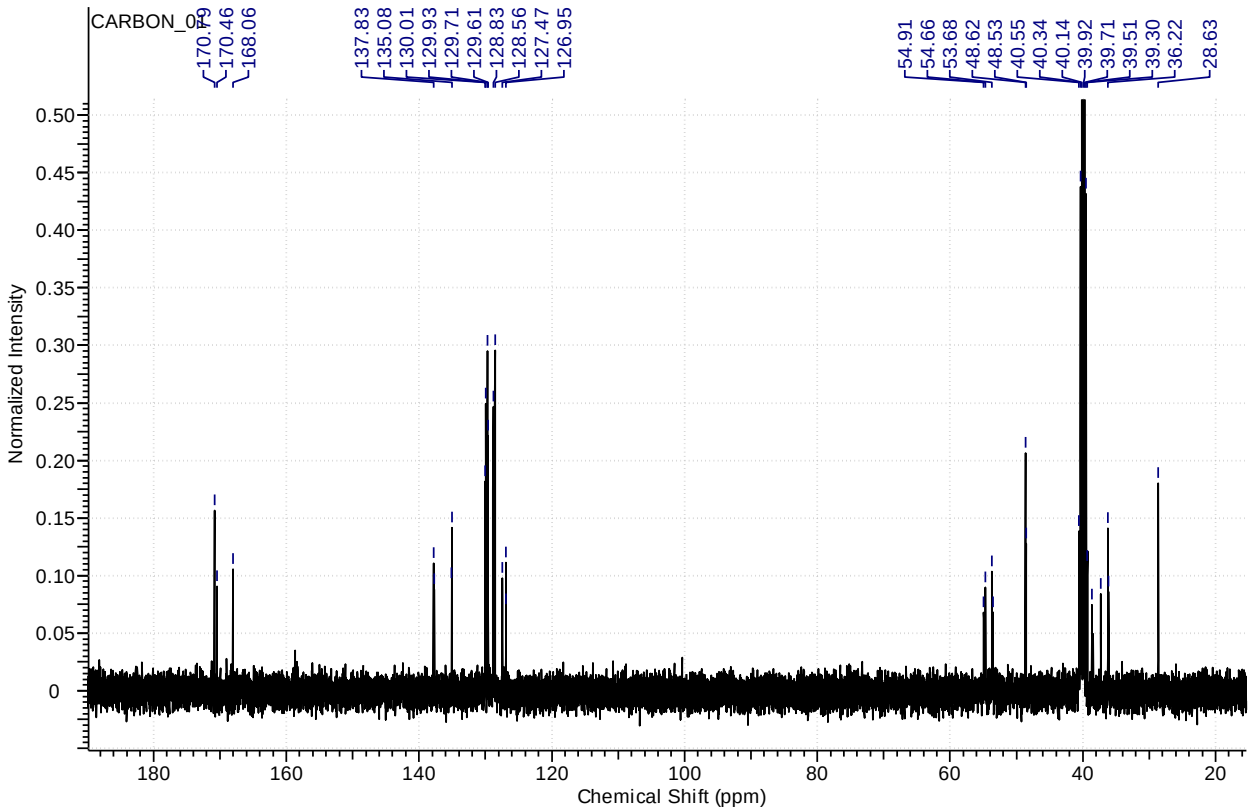

Figure S61. ^{13}C NMR (S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2c).

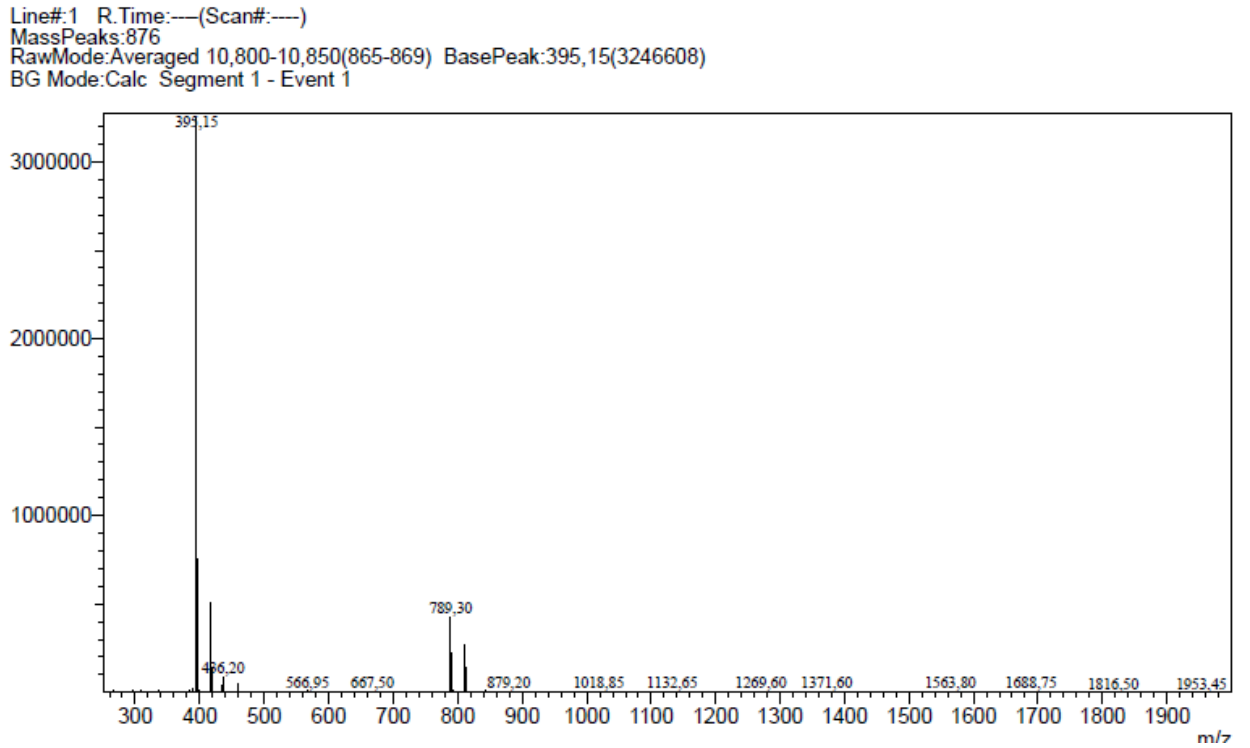

Figure S61. MS (S)-1-(((R)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2c).

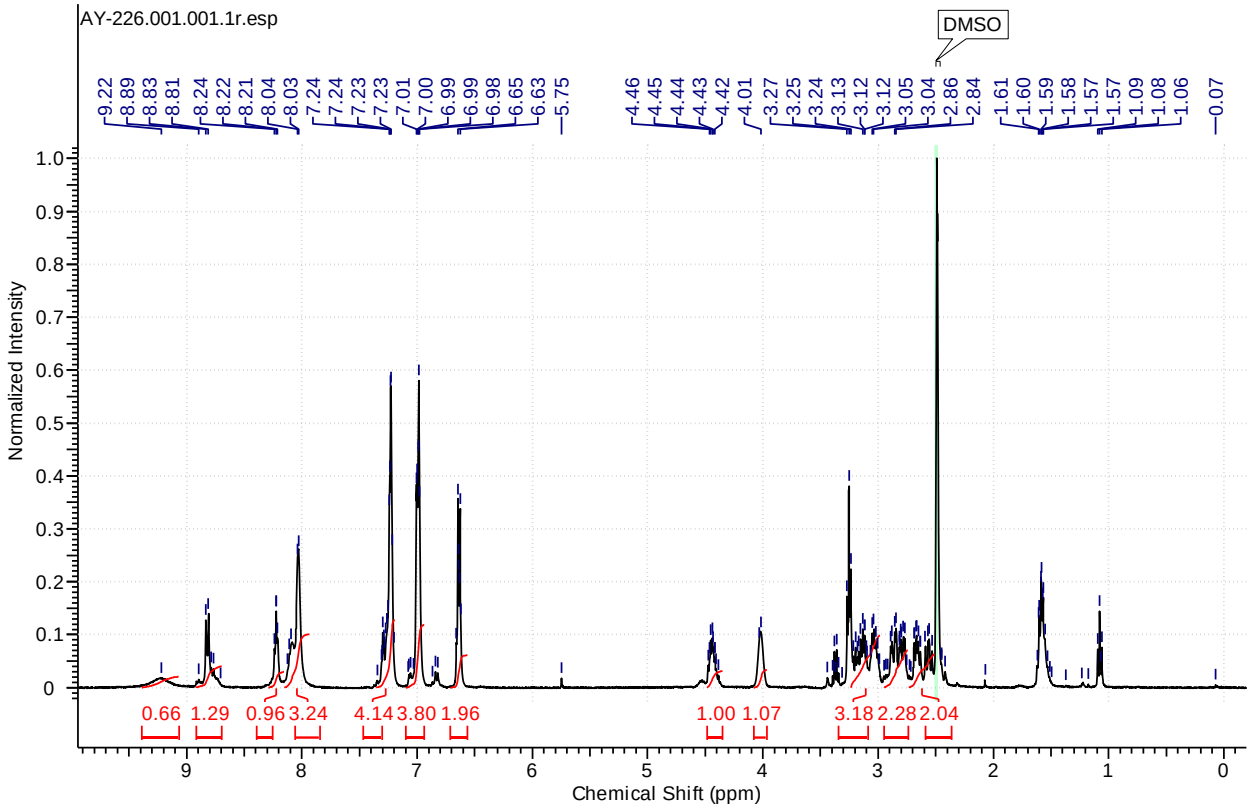

Figure S62. ^{1}H NMR (S)-1-(((R)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2d).

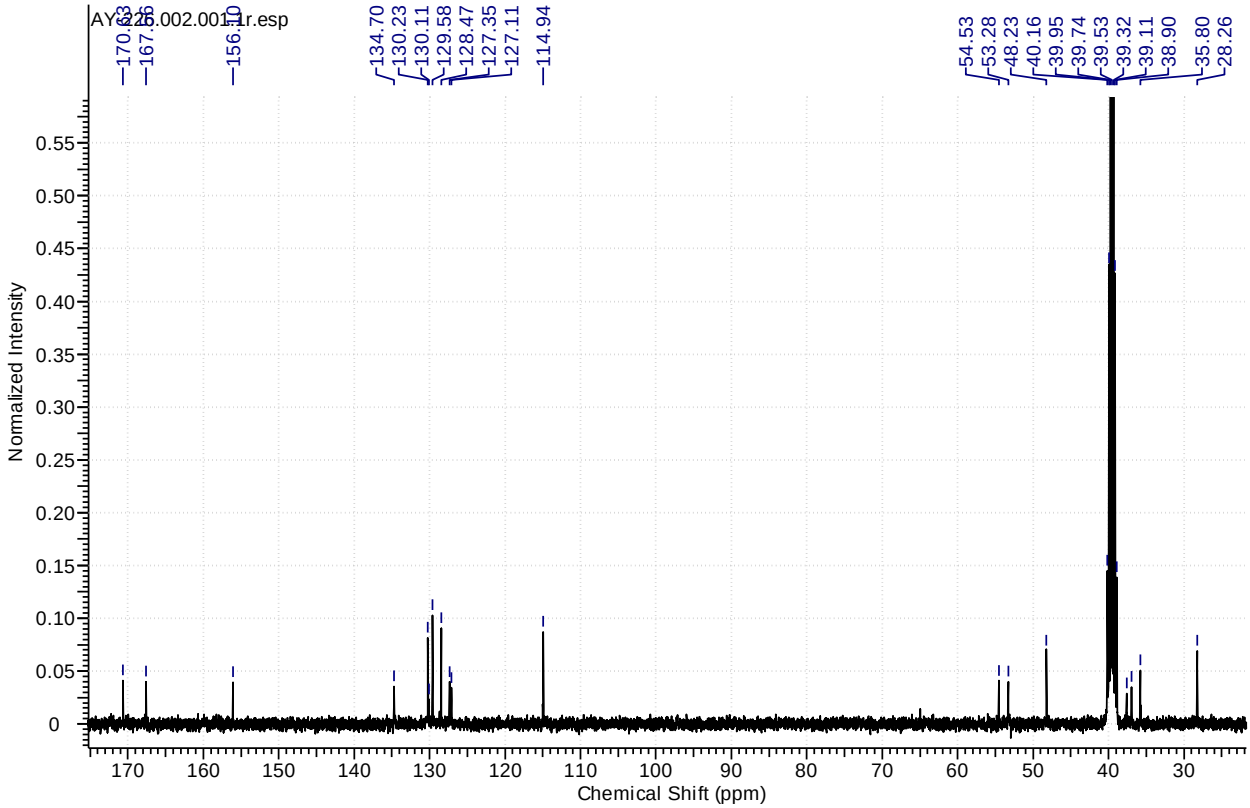

Figure S63. ^{13}C NMR (S)-1-(((R)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2d).

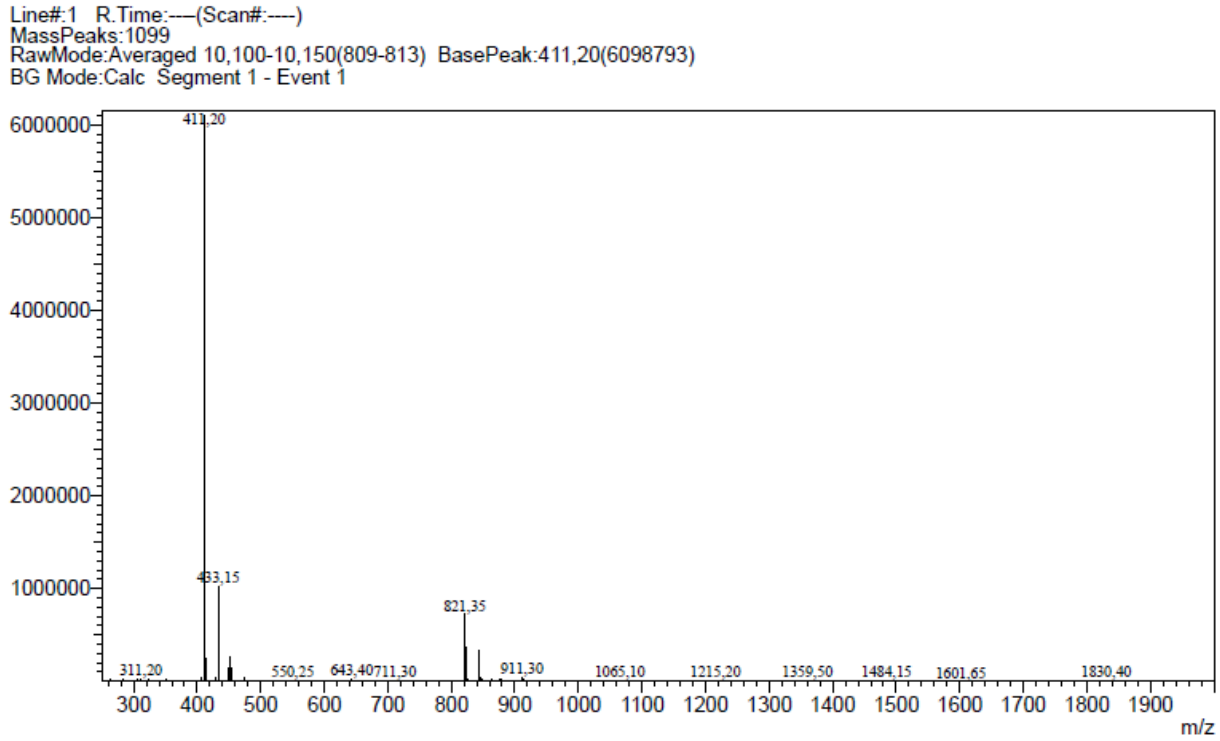

Figure S64. MS (S)-1-(((R)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2d).

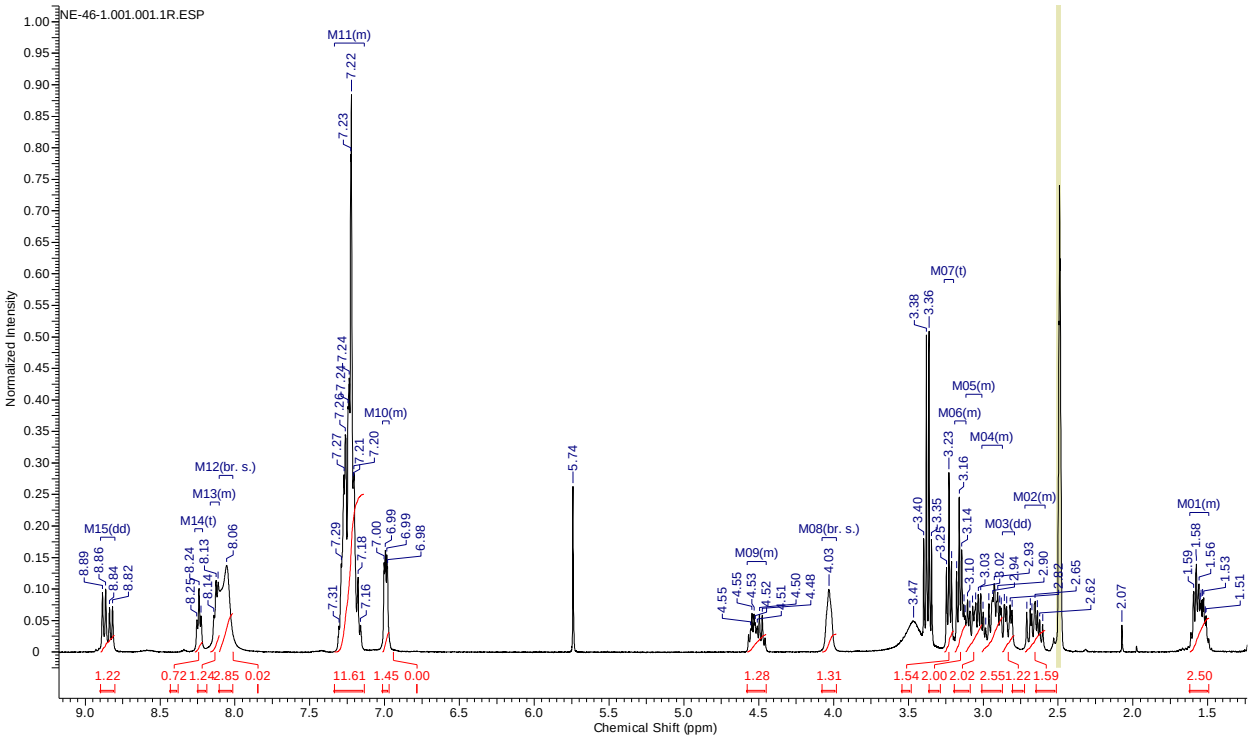

Figure S65. ^{1}H NMR (R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2e).

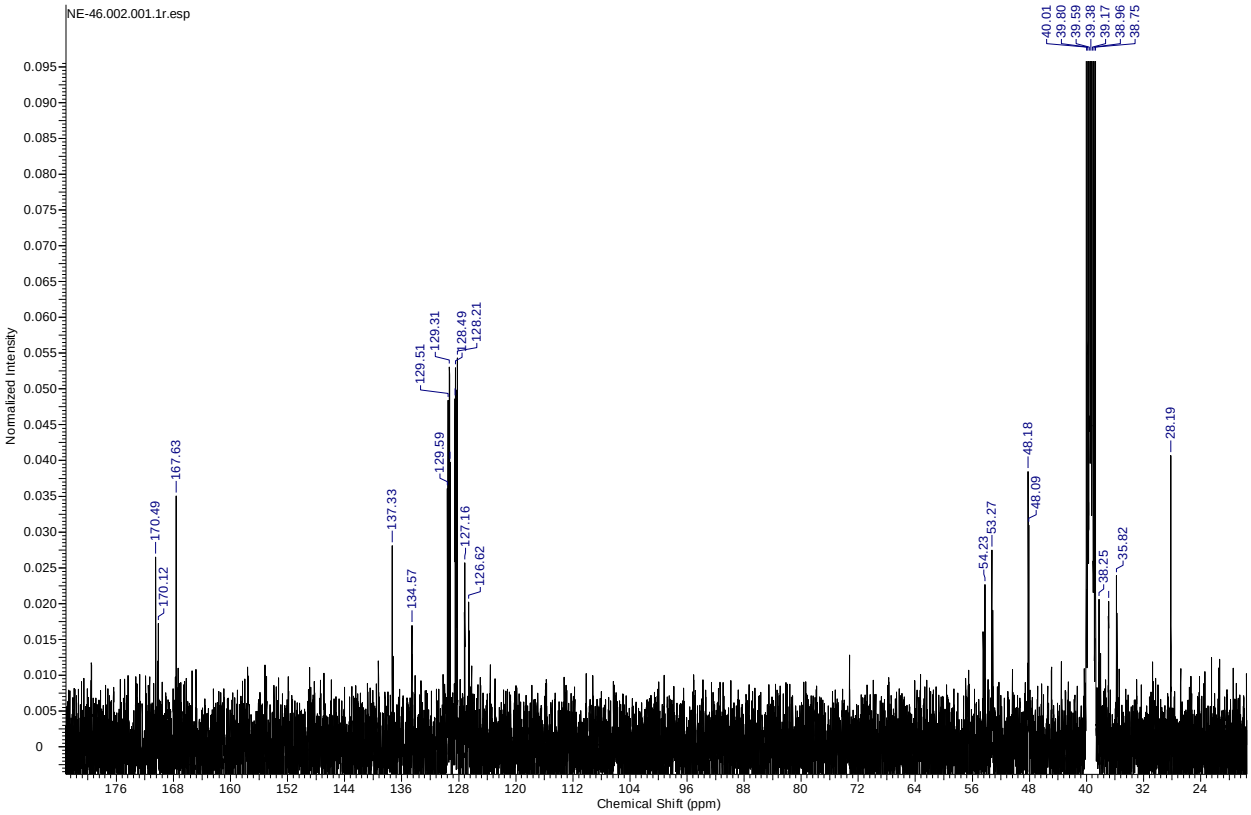

Figure S66. ^{13}C NMR (R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2e).

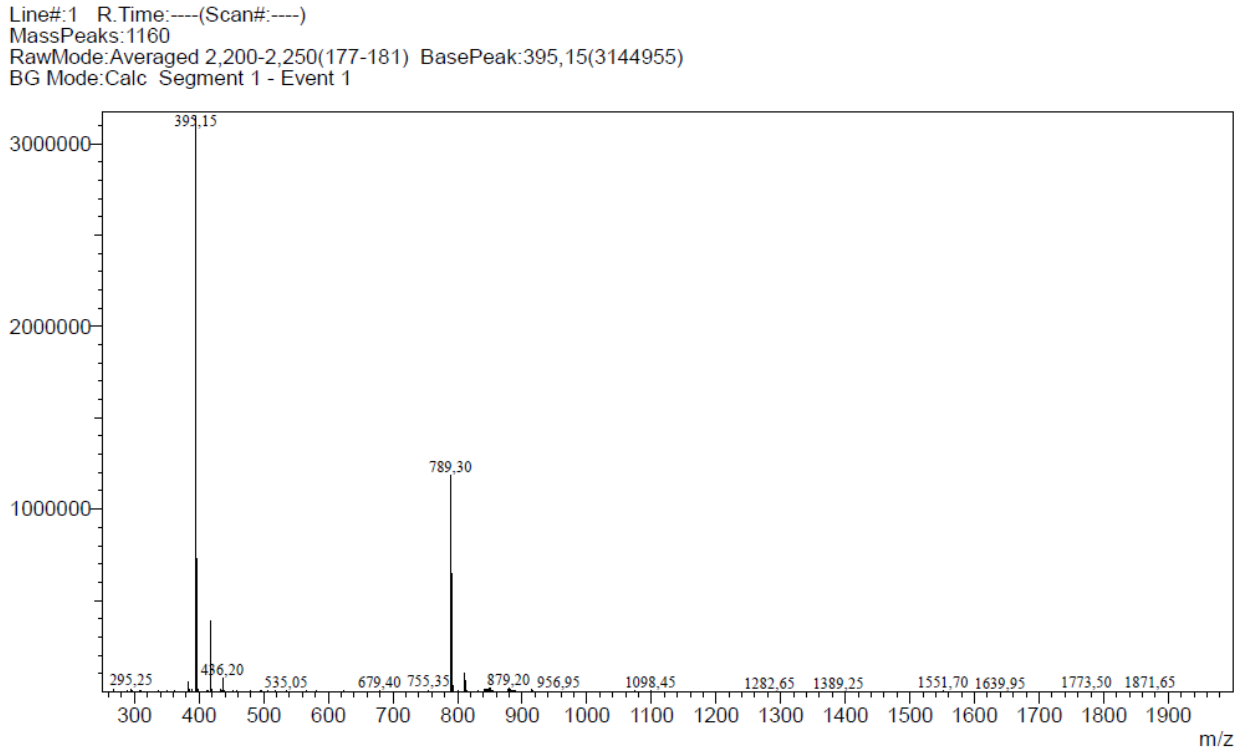

Figure S67. MS (R)-1-(((S)-1-((3-azidopropyl)amino)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2e).

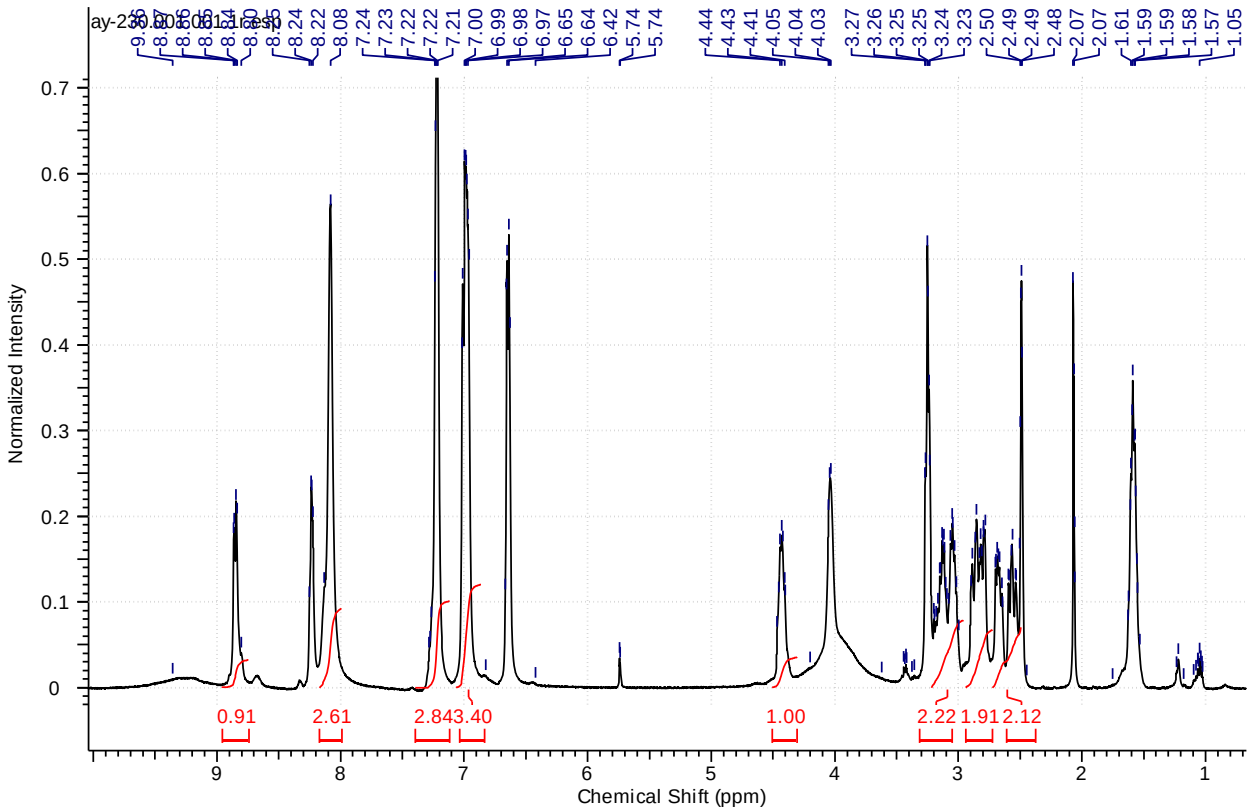

Figure S68. ^{1}H NMR (R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2f).

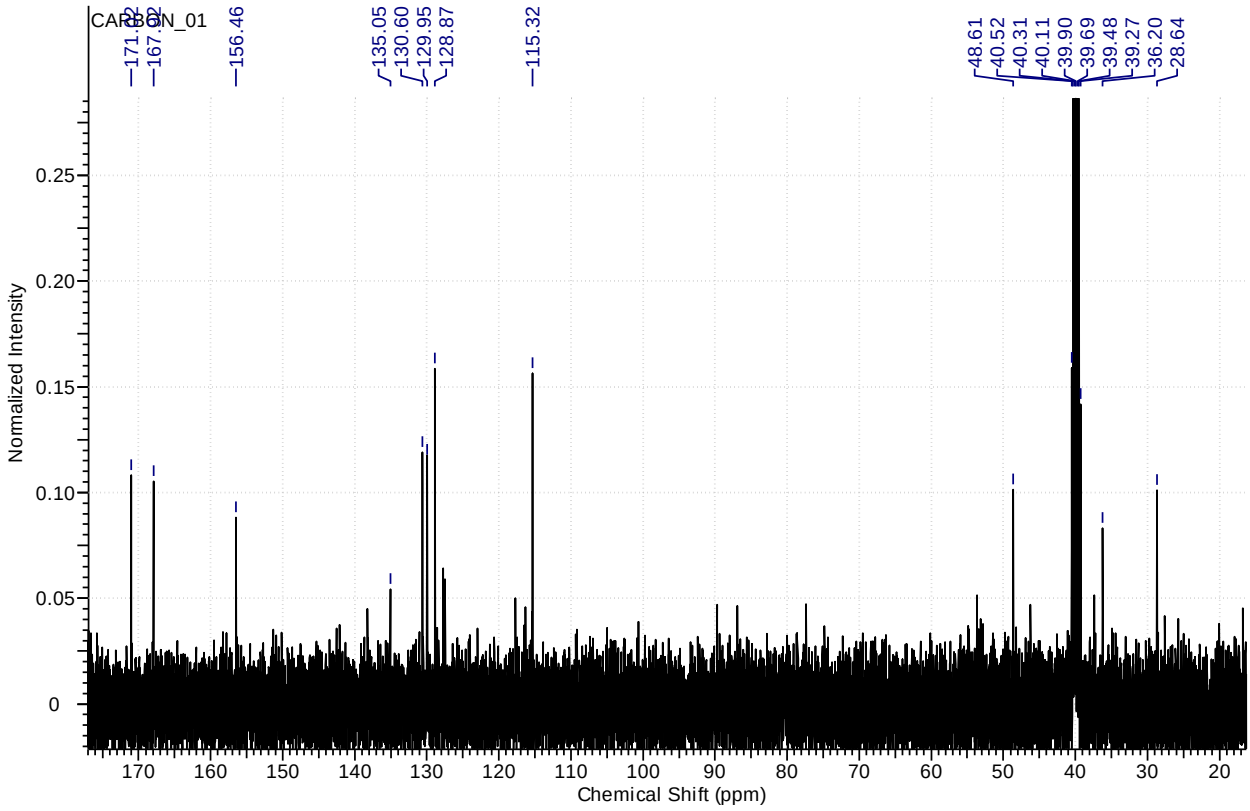

Figure S68. ^{13}C NMR (R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2f).

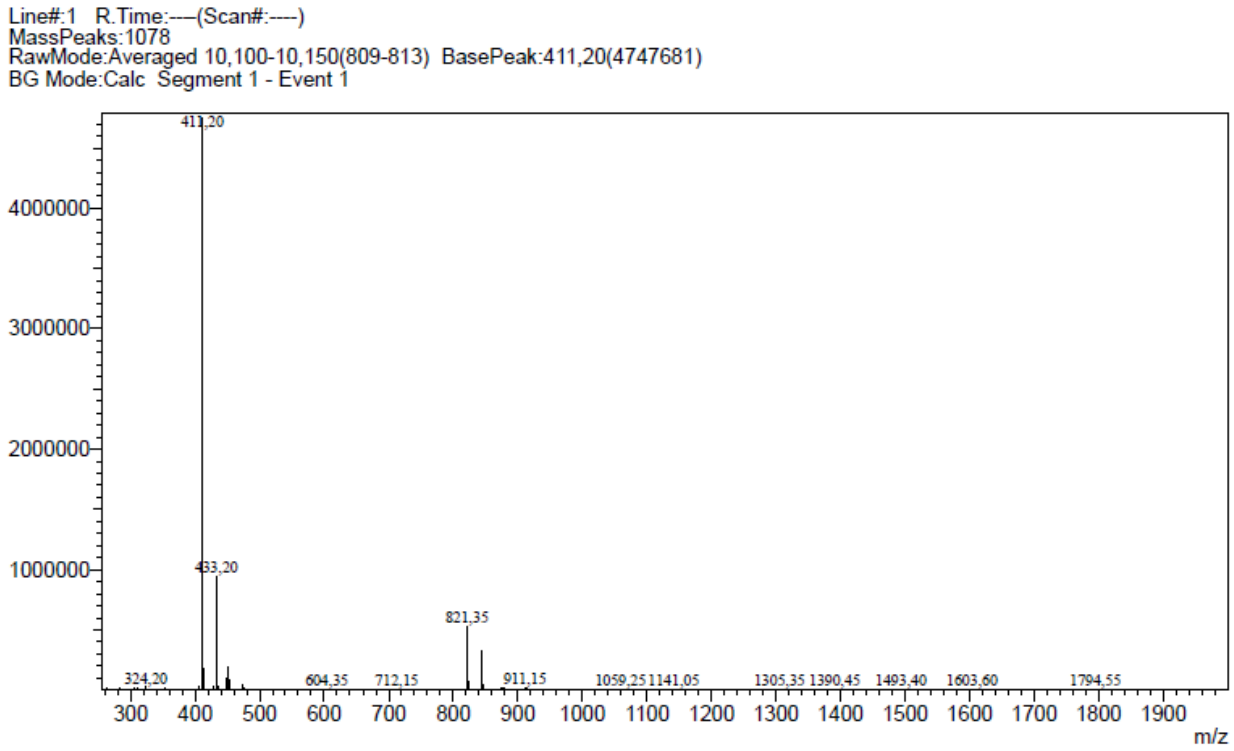

Figure S69. MS (R)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2f).

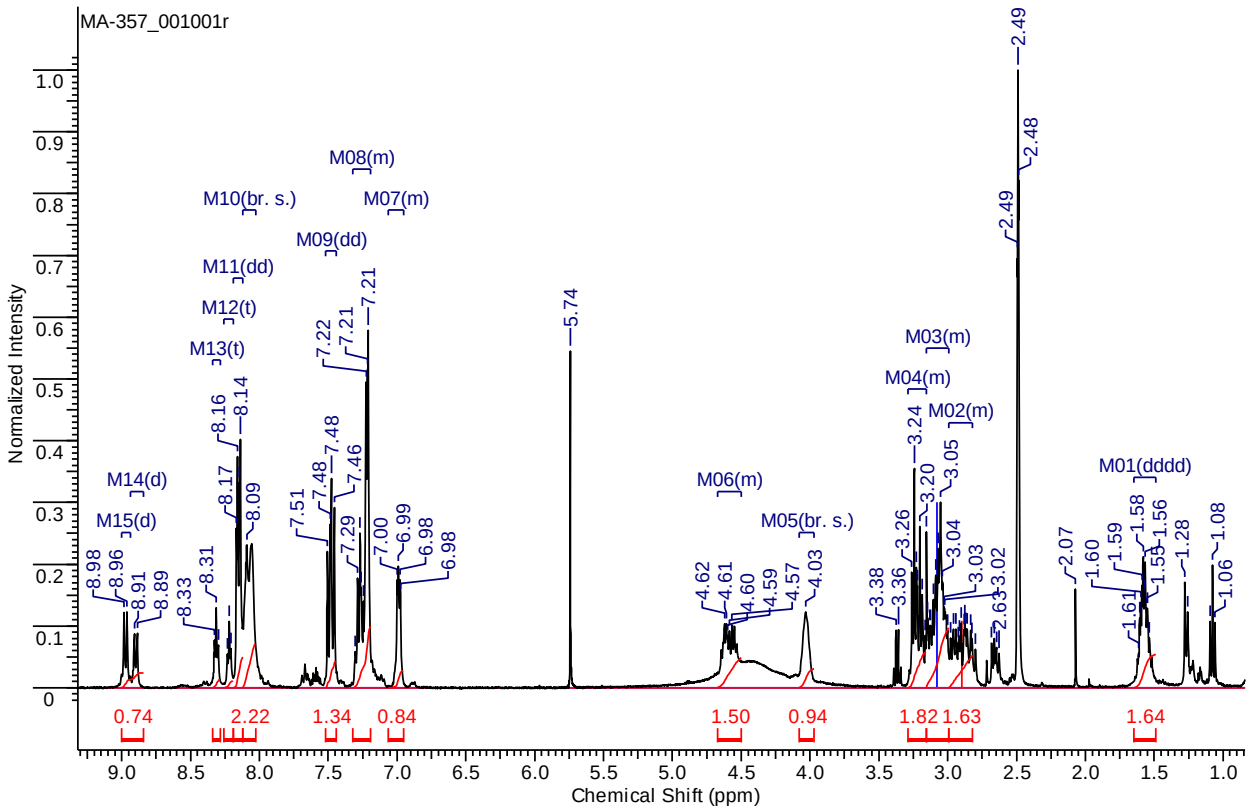

Figure S70. ^{1}H NMR (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2g)

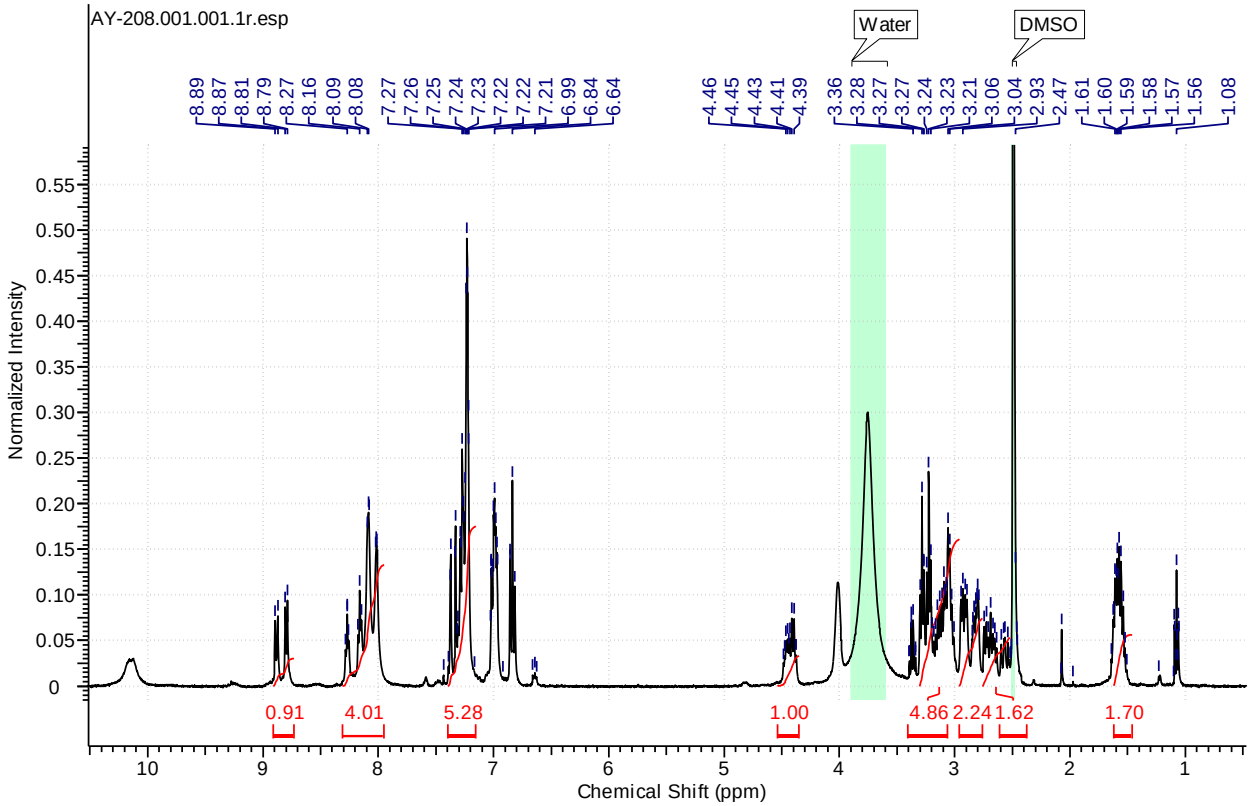

Figure S71. ^{1}H NMR (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2h).

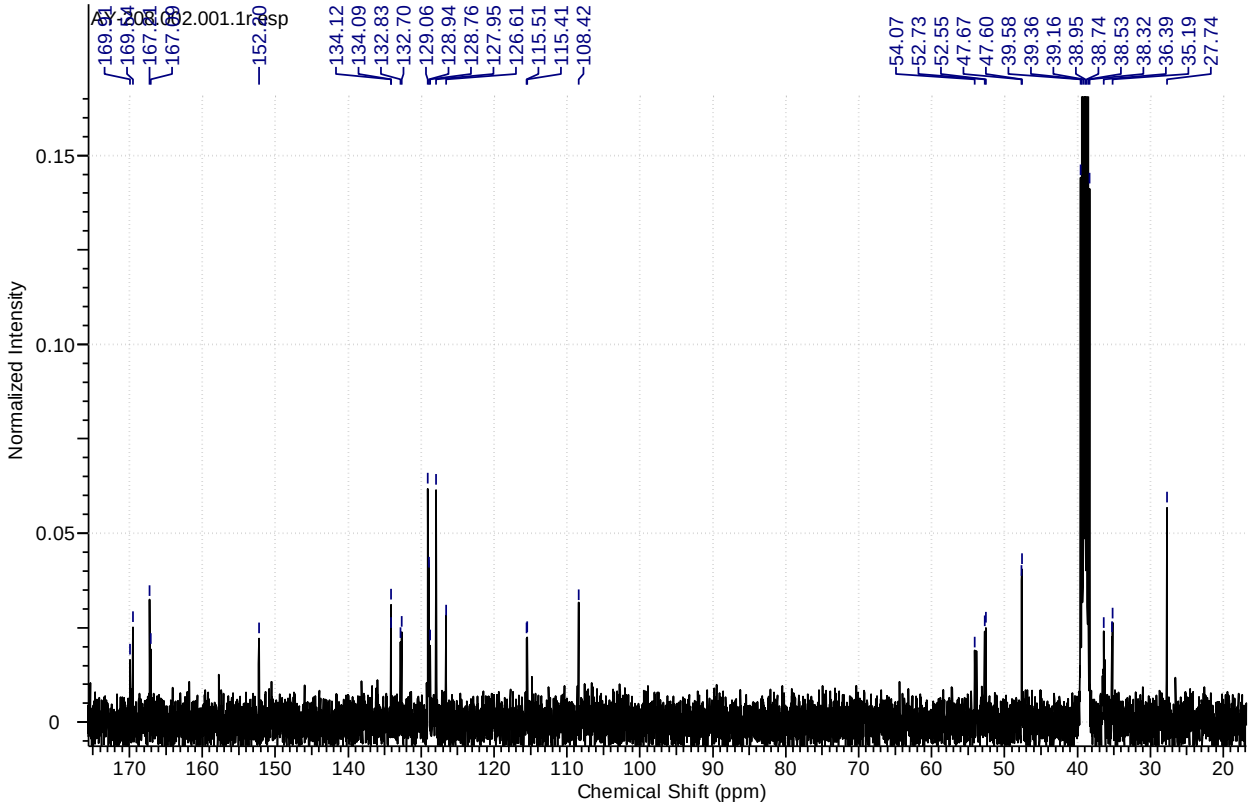

Figure S72. ^{13}C NMR (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2h).

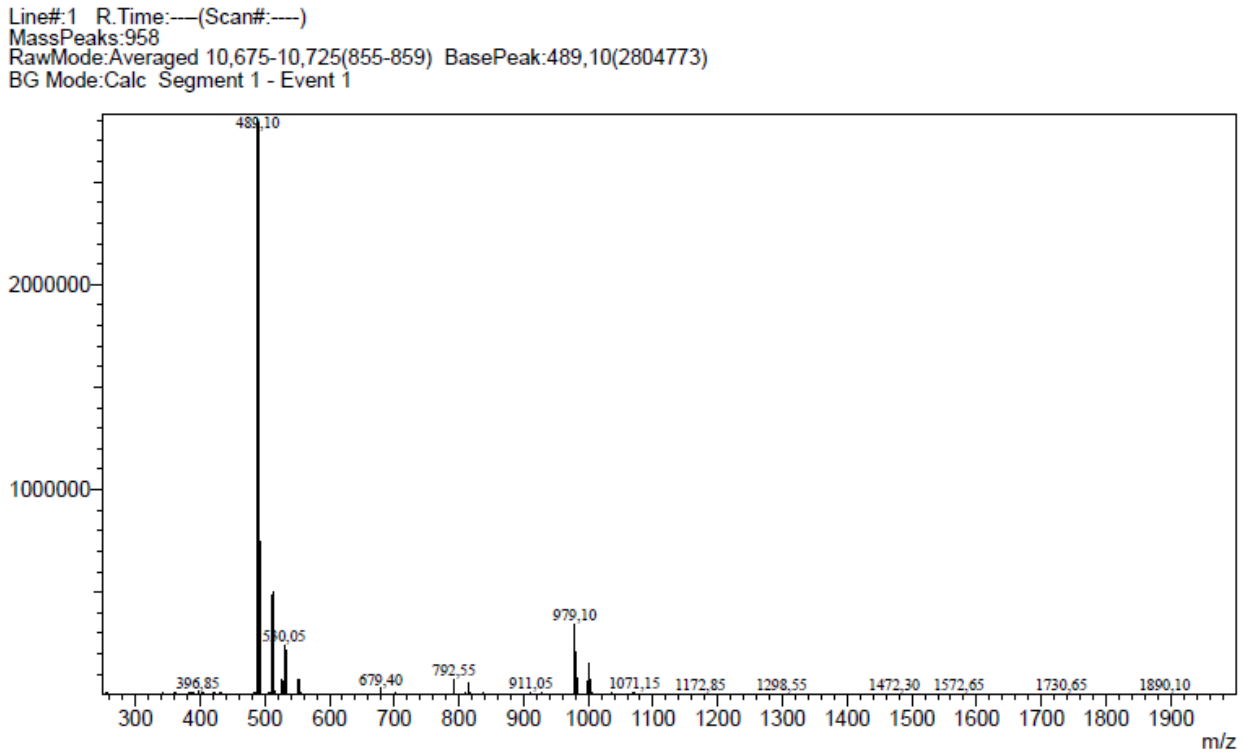

Figure S73. MS (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3-bromo-4-hydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2h).

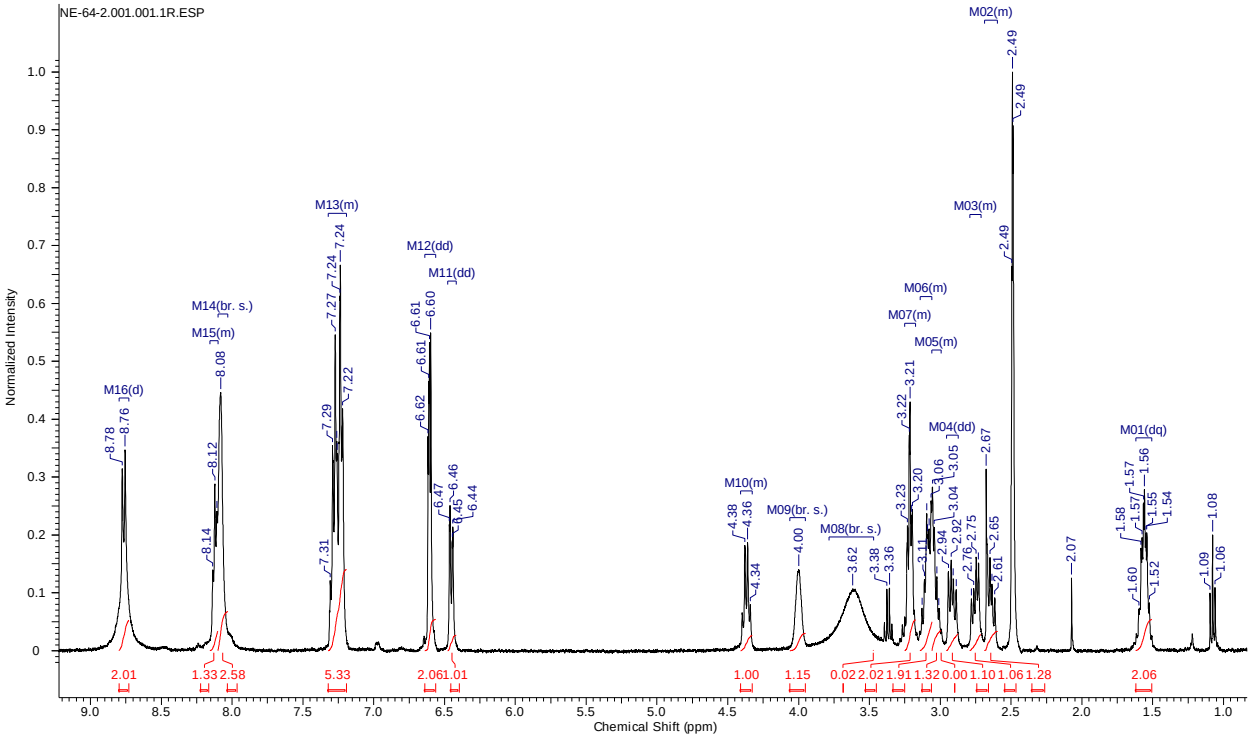

Figure S74. ^{1}H NMR (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2i).

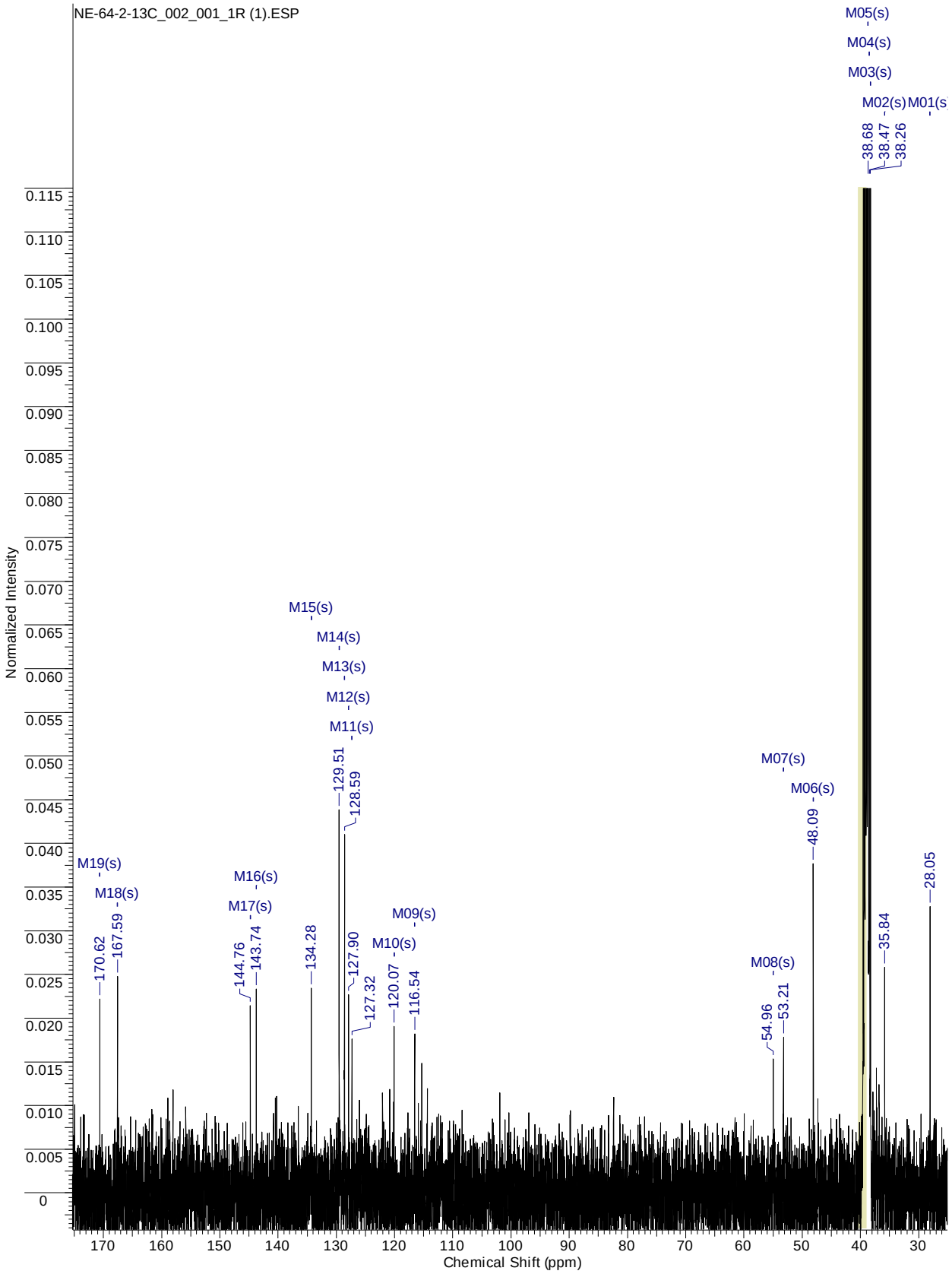

Figure S74. ^{13}C NMR (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2i).

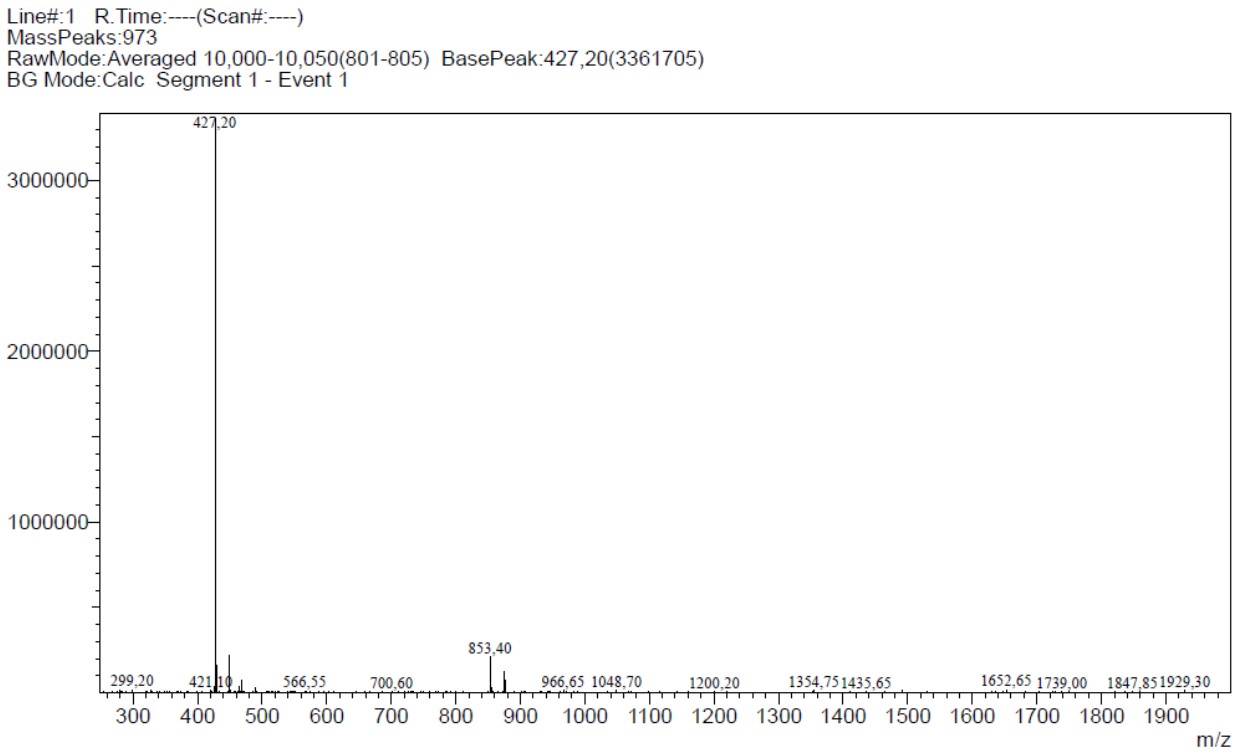

Figure S75. MS (S)-1-(((S)-1-((3-azidopropyl)amino)-3-(3,4-dihydroxyphenyl)-1-oxopropan-2-yl)amino)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (2i).

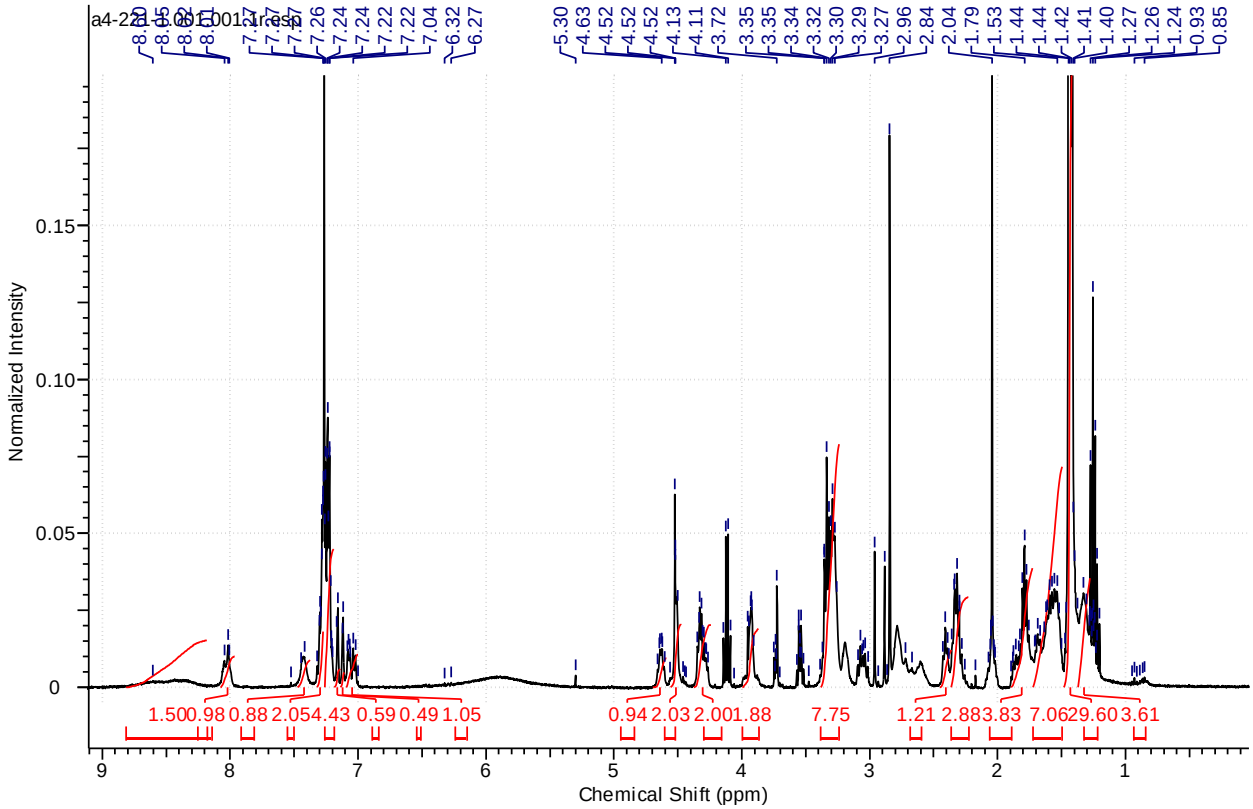

Figure S76. ^{1}H NMR tri-tert-butyl (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

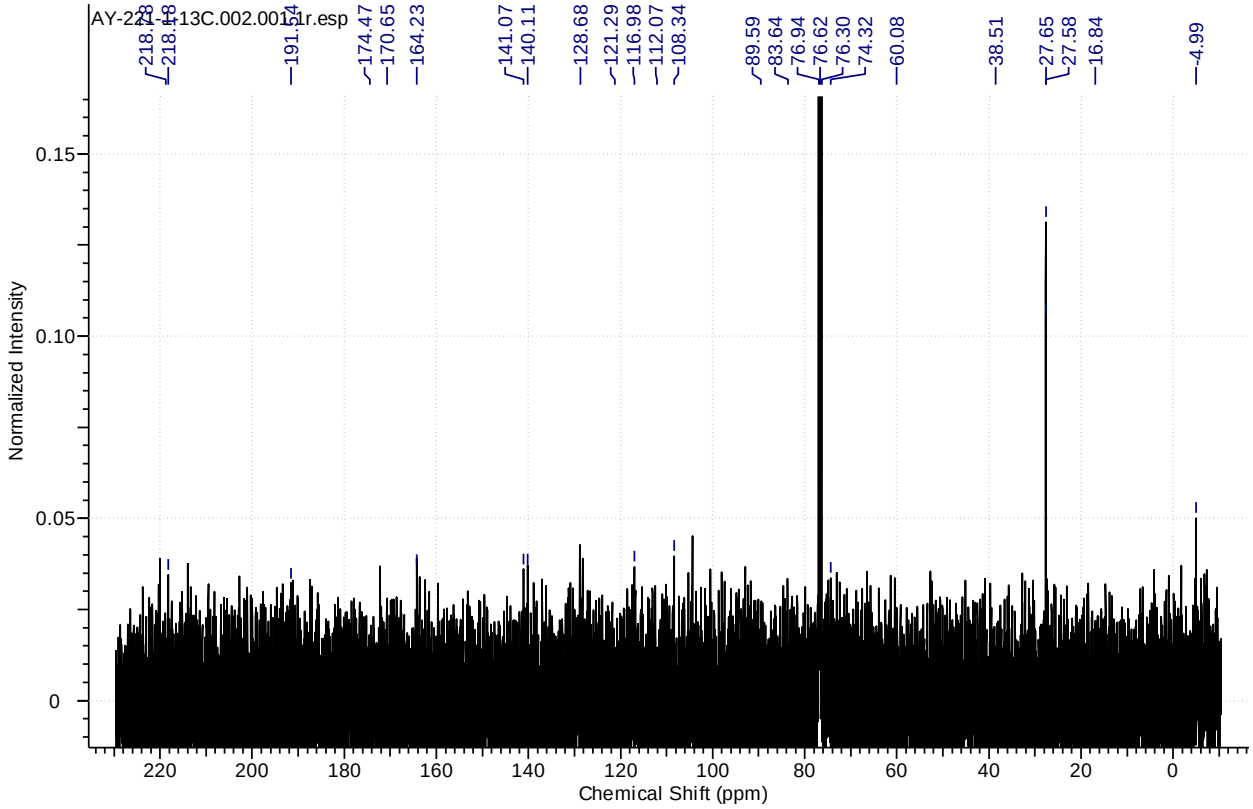

Figure S77. ^{13}C NMR tri-tert-butyl (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

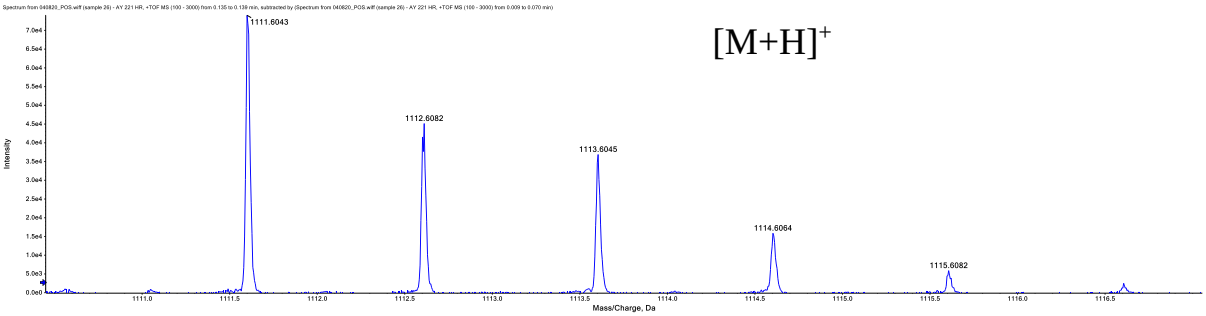

Figure S78. HRMS tri-tert-butyl (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

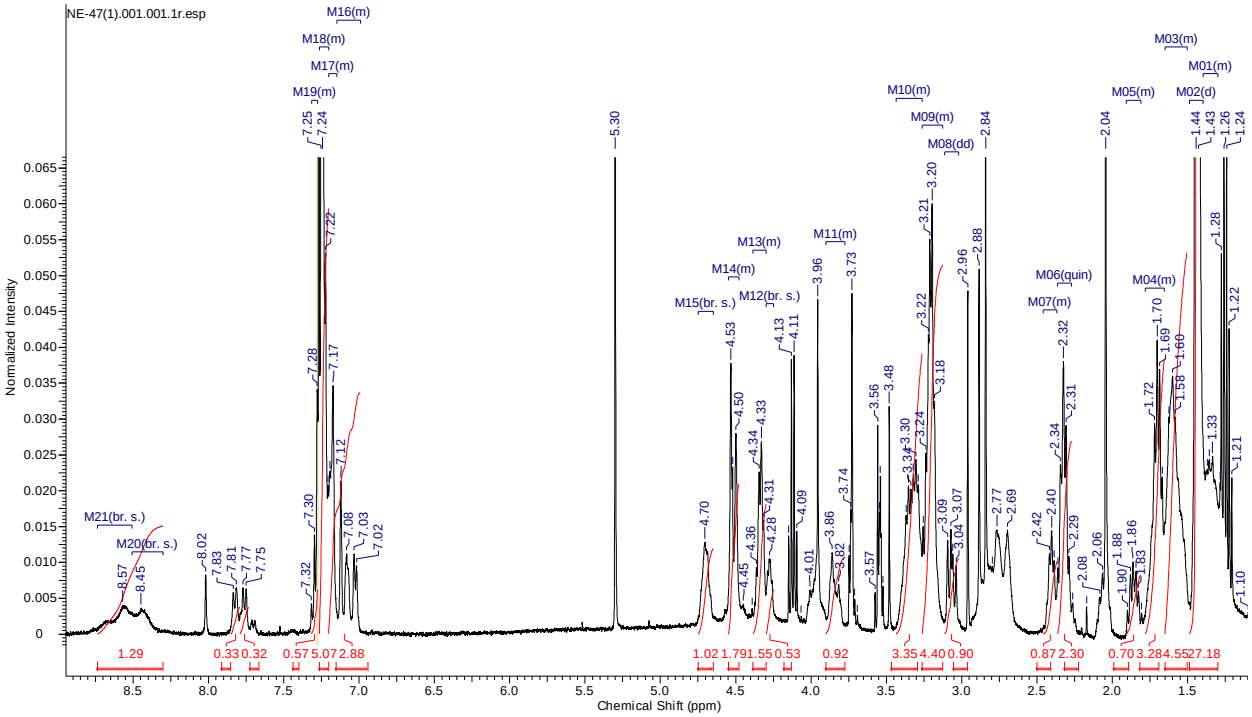

Figure S79. ^{1}H NMR tri-tert-butyl (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

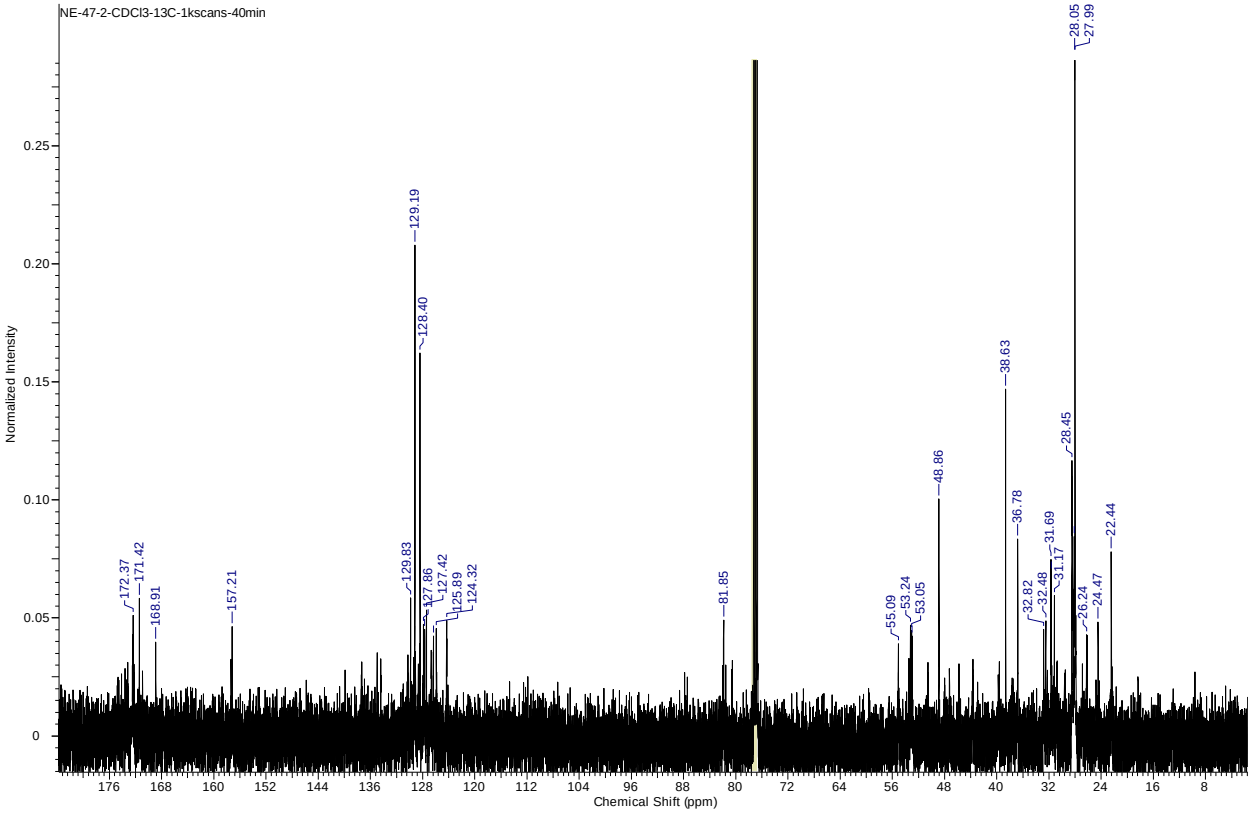

Figure S80. ^{13}C NMR tri-tert-butyl (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

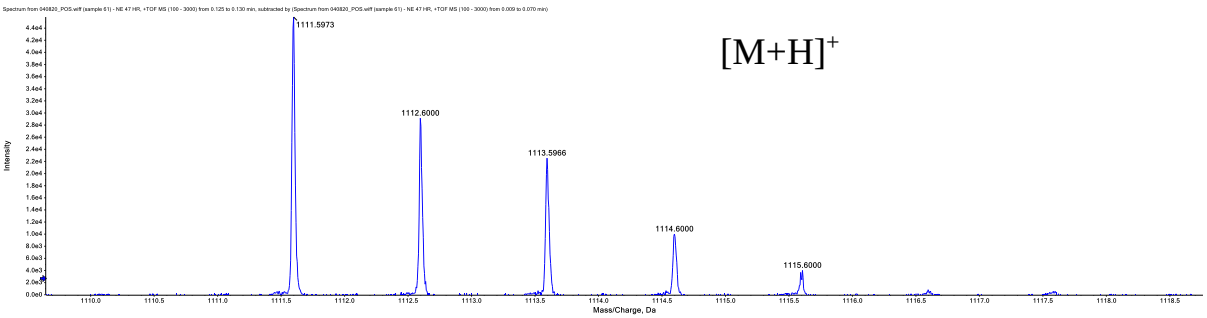

Figure S81. HRMS tri-tert-butyl (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

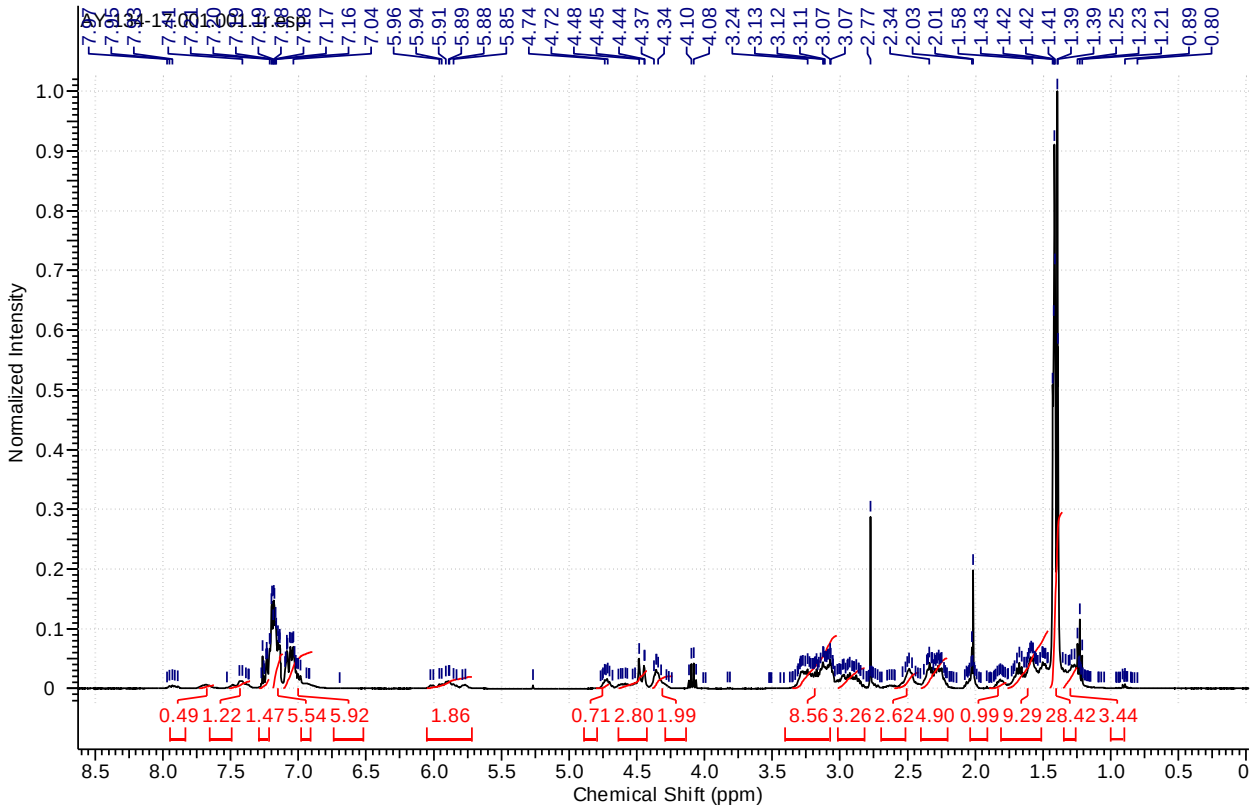

Figure S82. ^{1}H NMR tri-tert-butyl (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

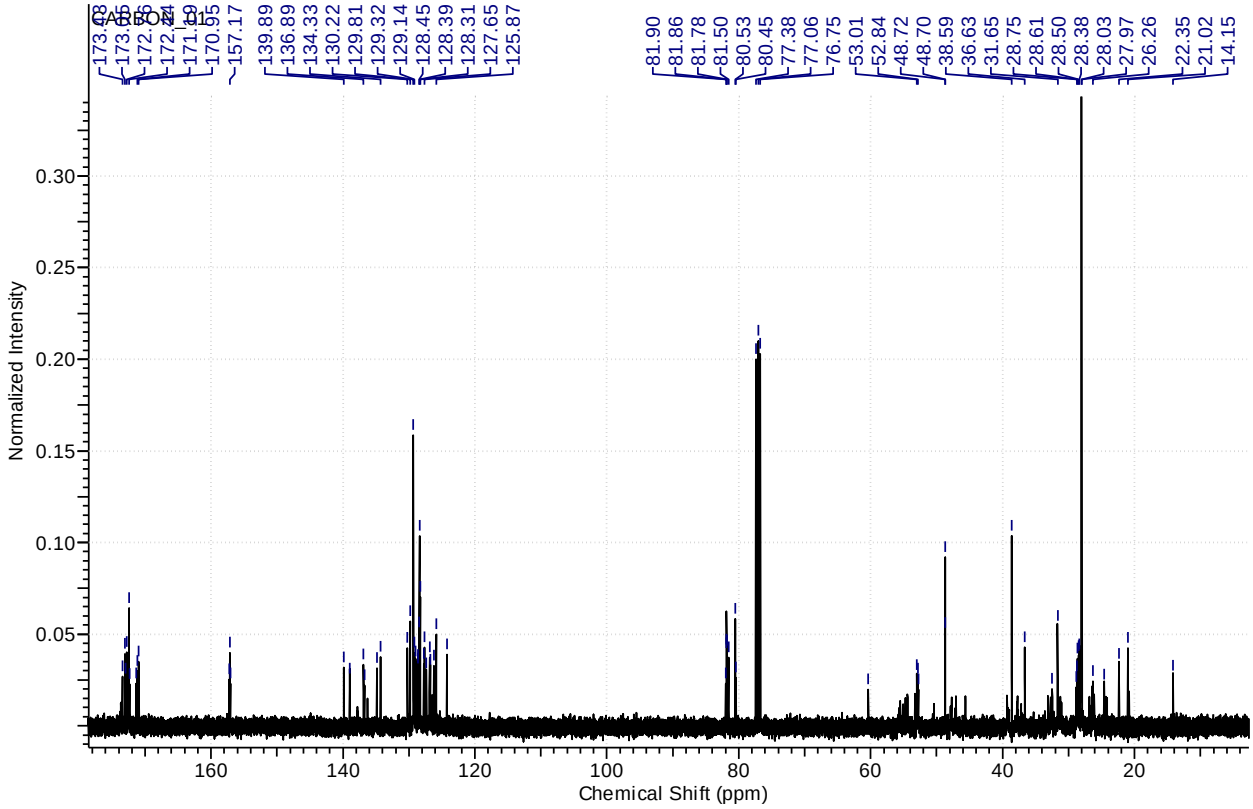

Figure S83. ^{13}C NMR tri-tert-butyl (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

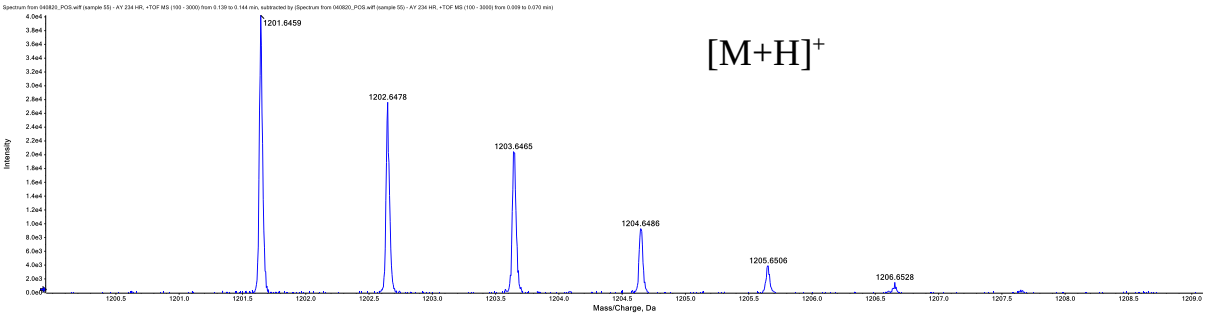

Figure S84. HRMS tri-tert-butyl (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

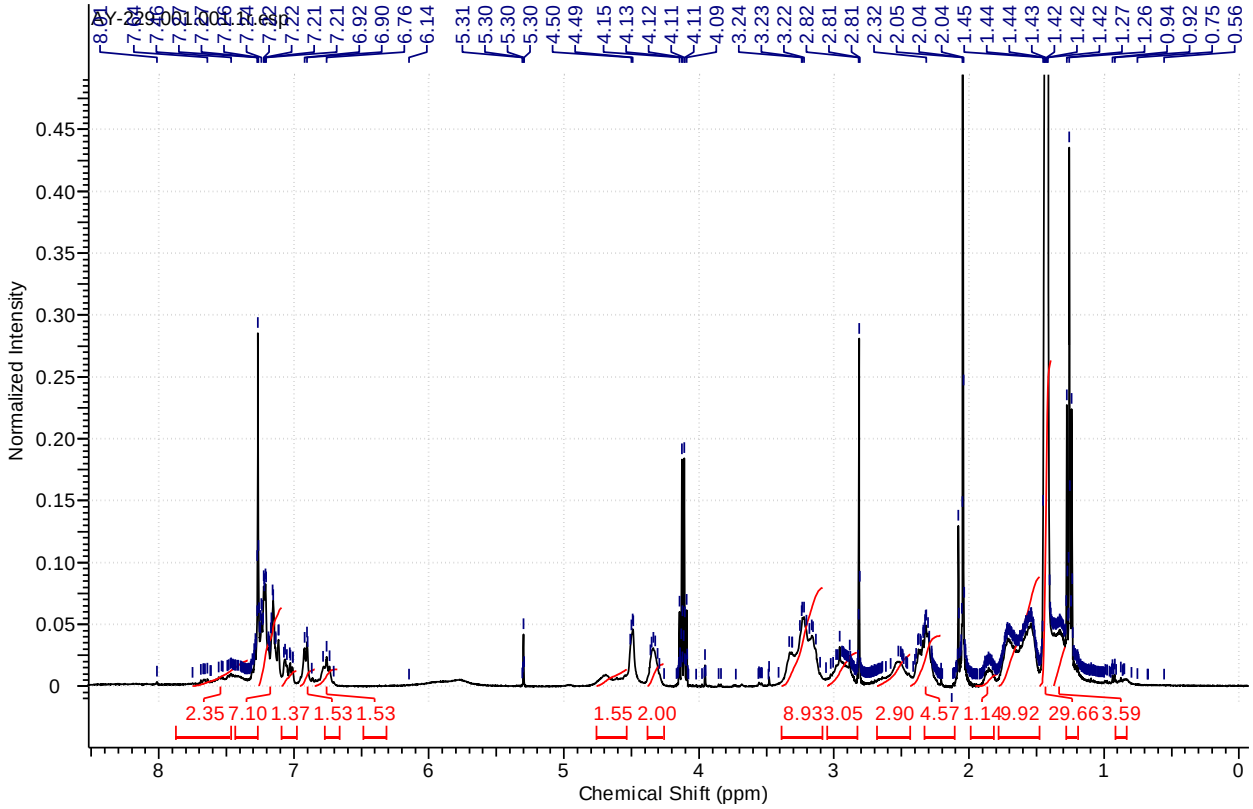

Figure S85. ^{1}H NMR tri-tert-butyl (3S,7S,25S,28R)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

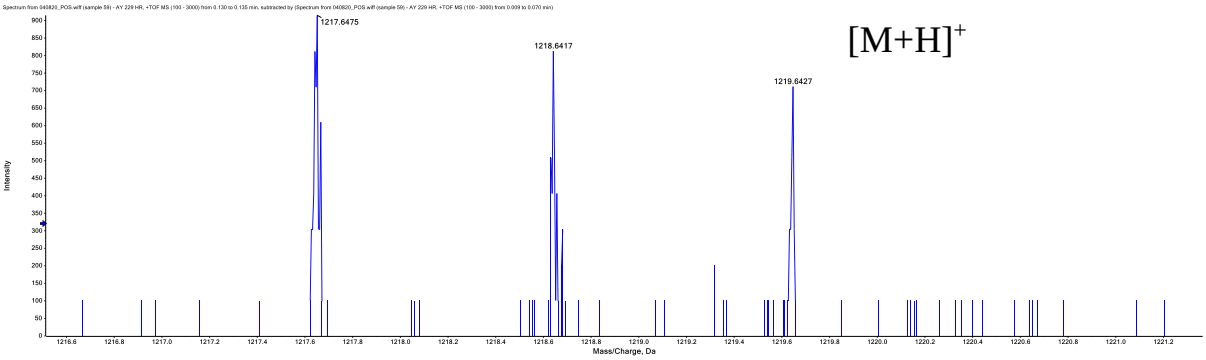

Figure S86. HRMS tri-tert-butyl (3S,7S,25S,28R)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

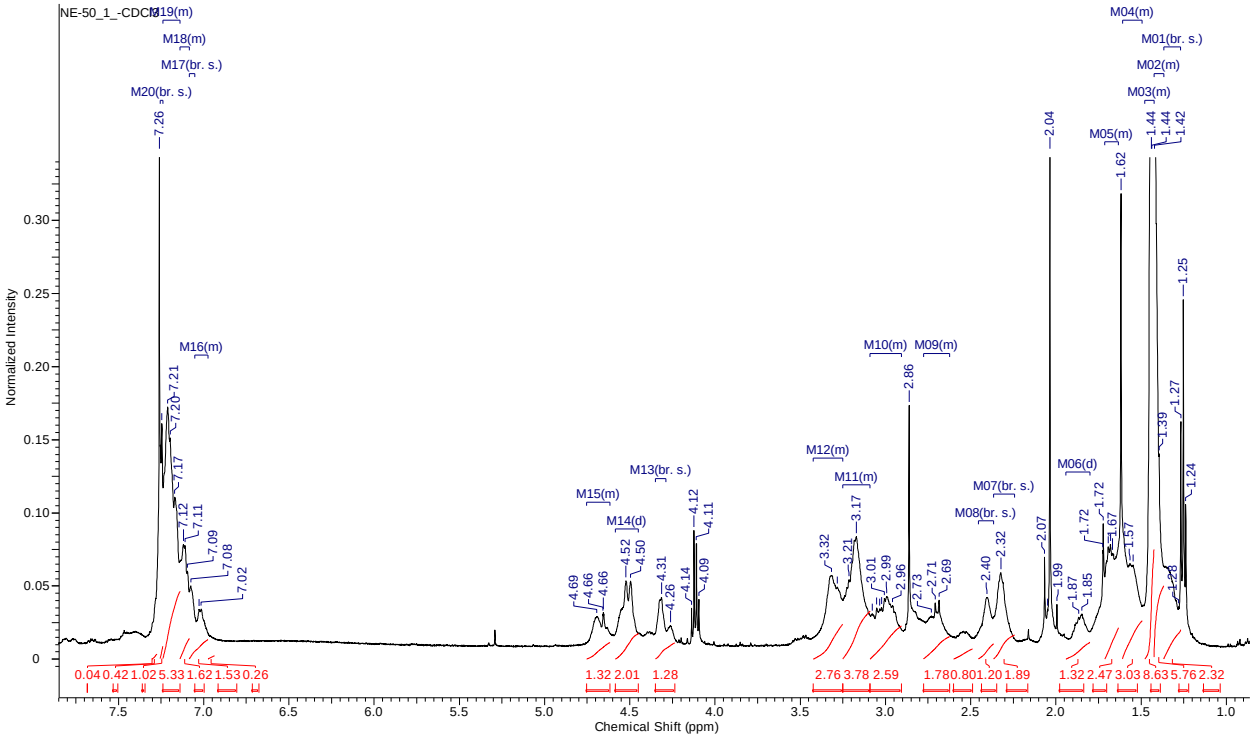

Figure S87. ^{1}H NMR tri-tert-butyl (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

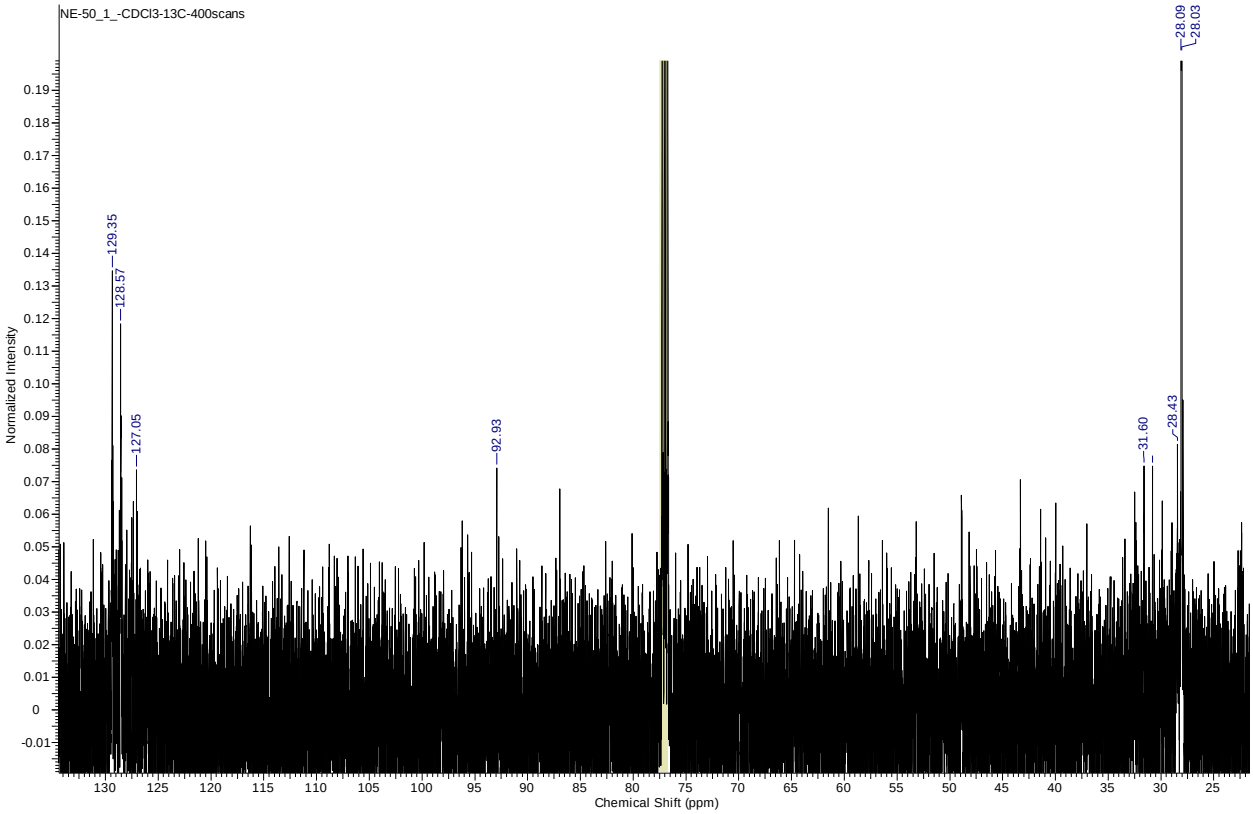

Figure S88. ^{13}C NMR tri-tert-butyl (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

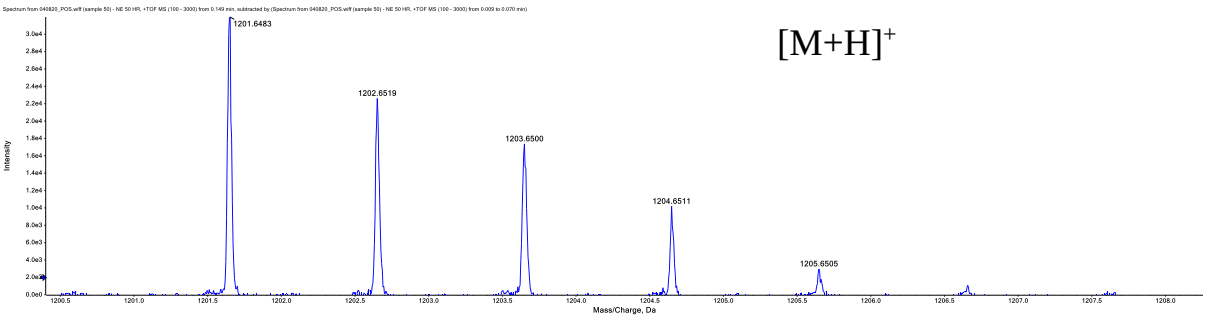

Figure S89. HRMS tri-tert-butyl (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

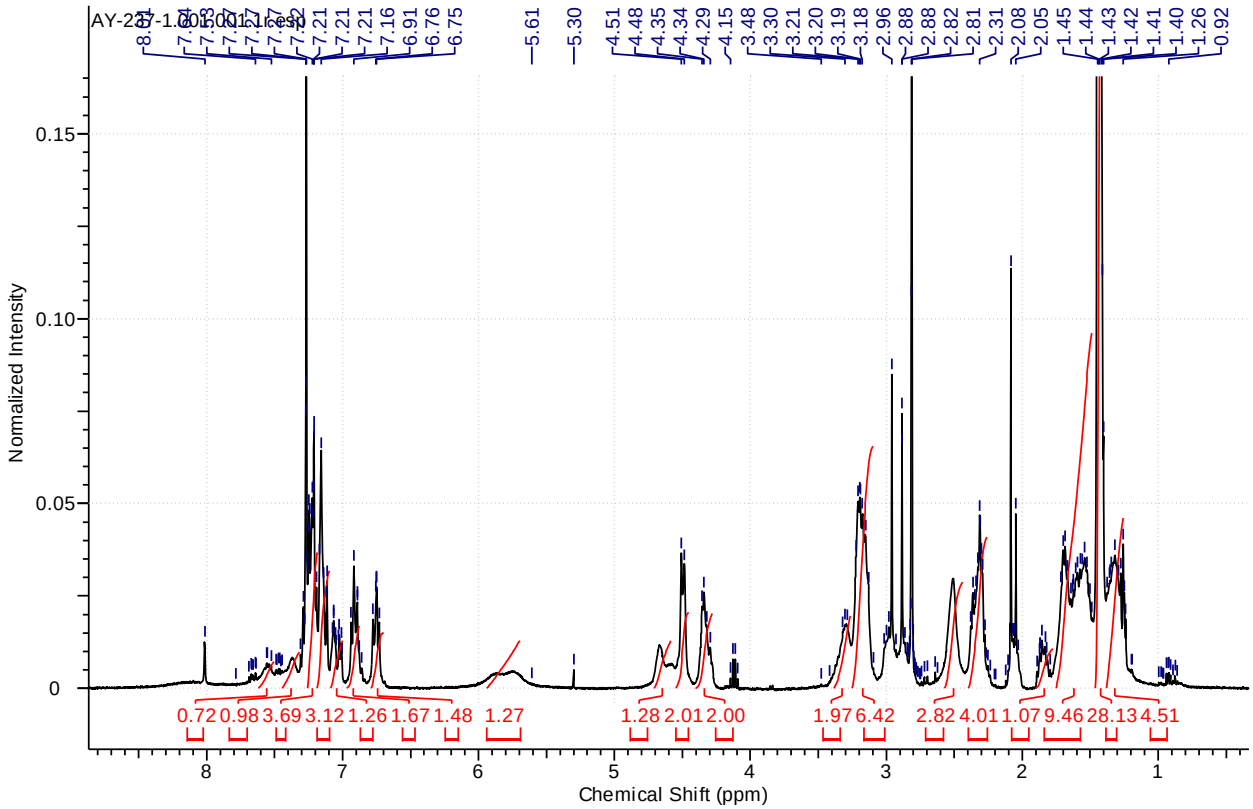

Figure S90. ^{1}H NMR tri-tert-butyl (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

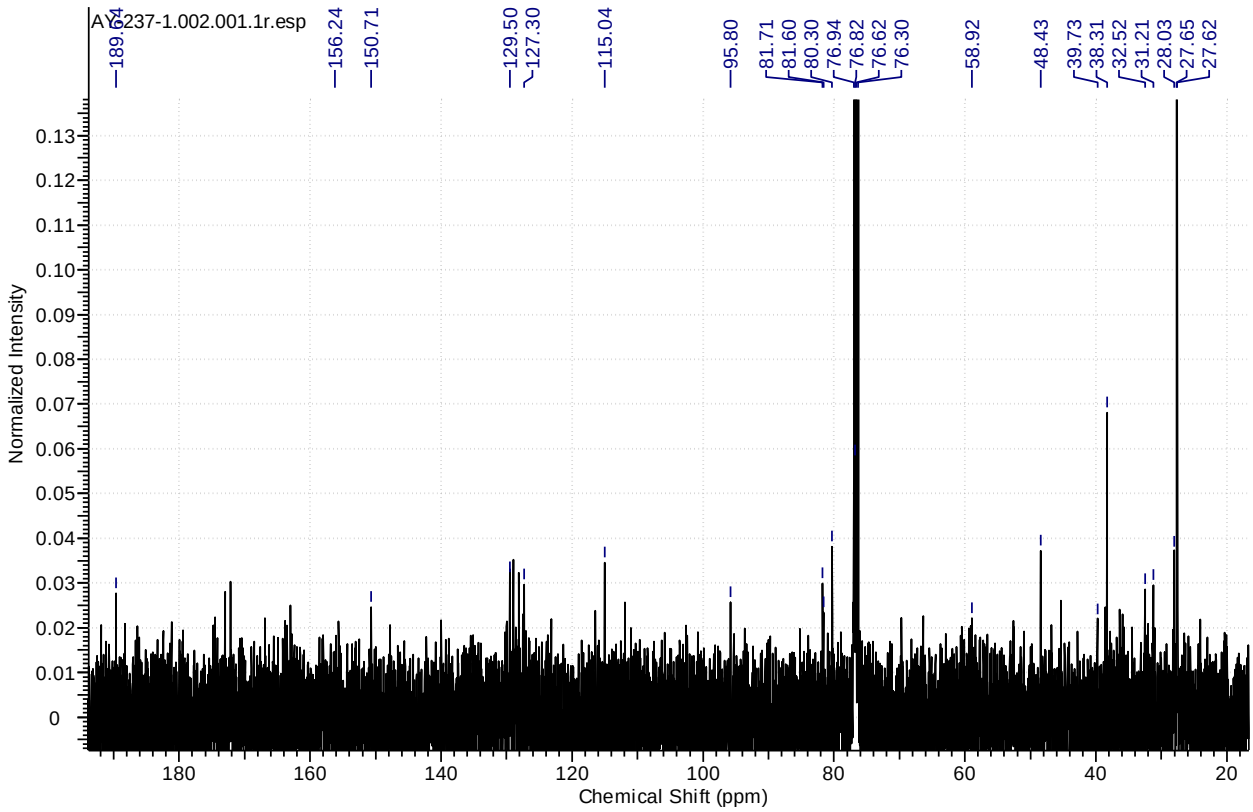

Figure S90. ^{13}C NMR tri-tert-butyl (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

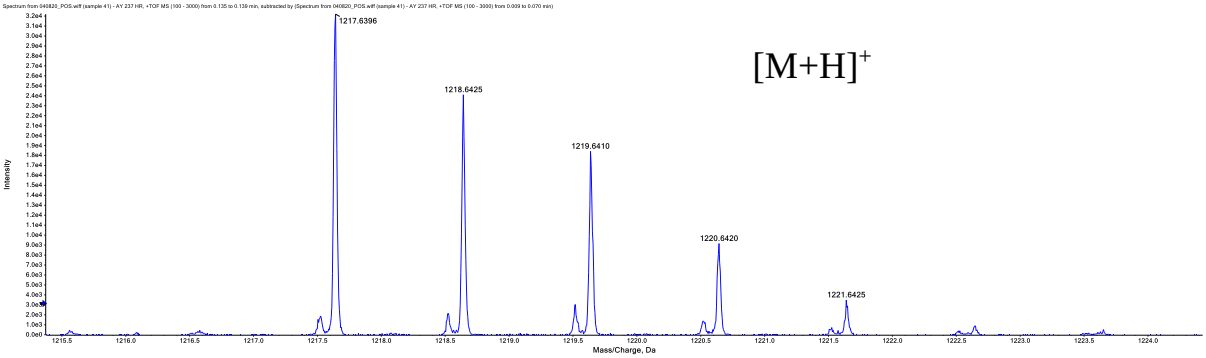

Figure S91. HRMS tri-tert-butyl (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

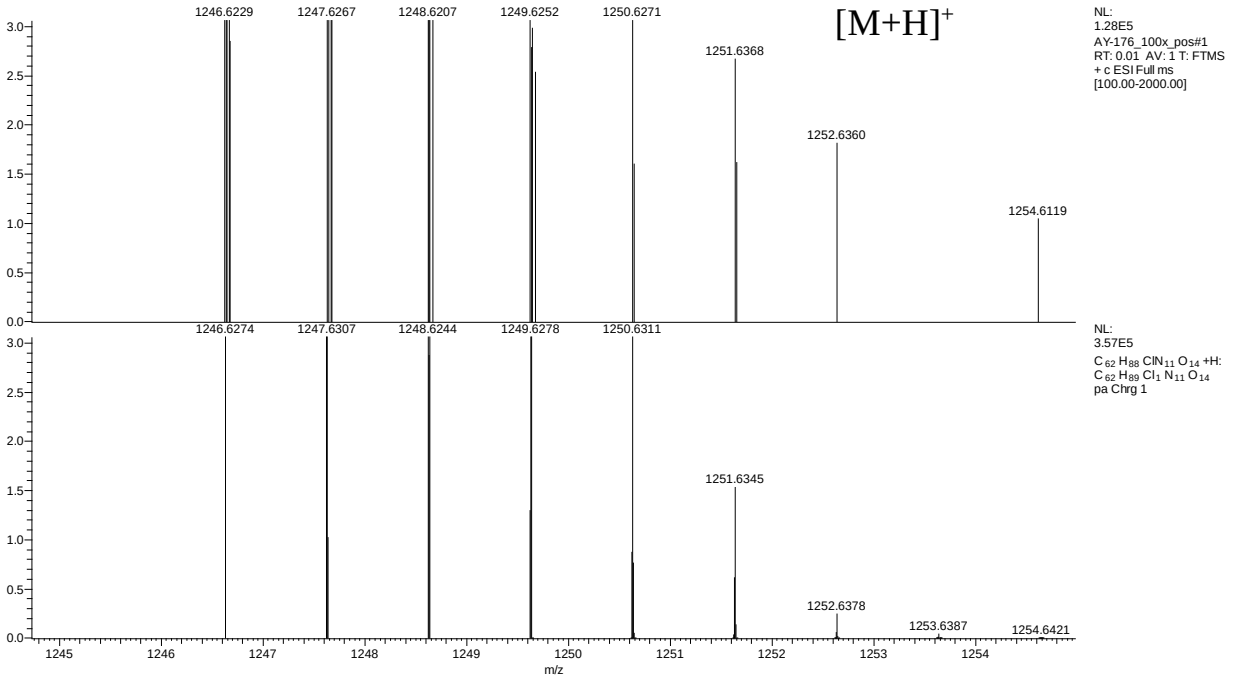

Figure S92. HRMS tri-tert-butyl (3S,7S,25S,28S)-33-azido-25-benzyl-12-(4-chlorobenzyl)-28-(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

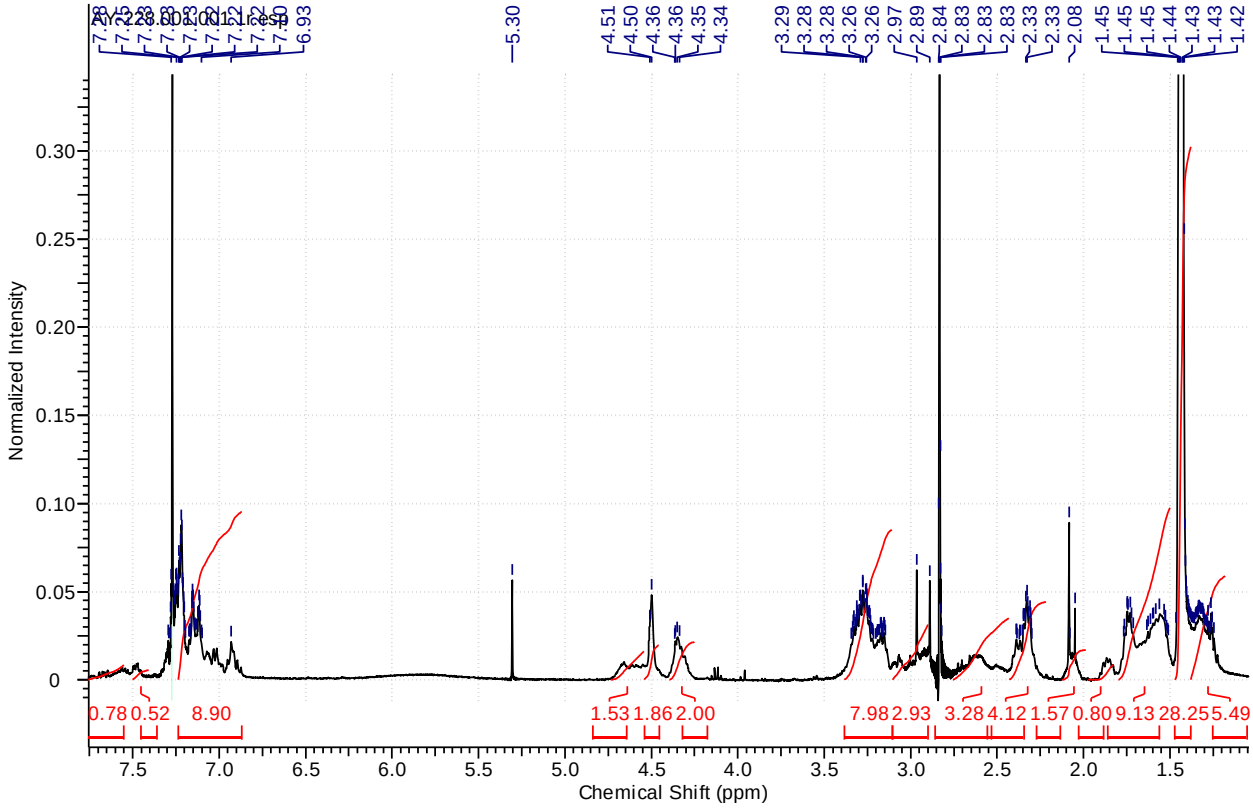

Figure S93. ^{1}H NMR tri-tert-butyl (3S,7S,25S,28S)-33-azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

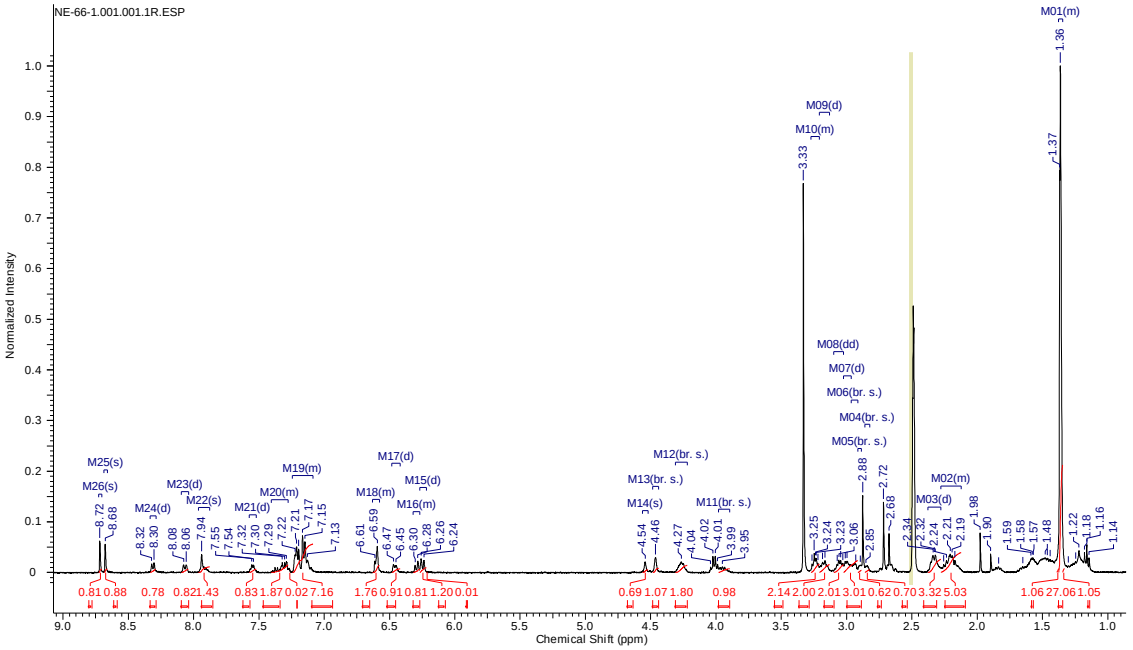

Figure S94. ^{1}H NMR tri-tert-butyl (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

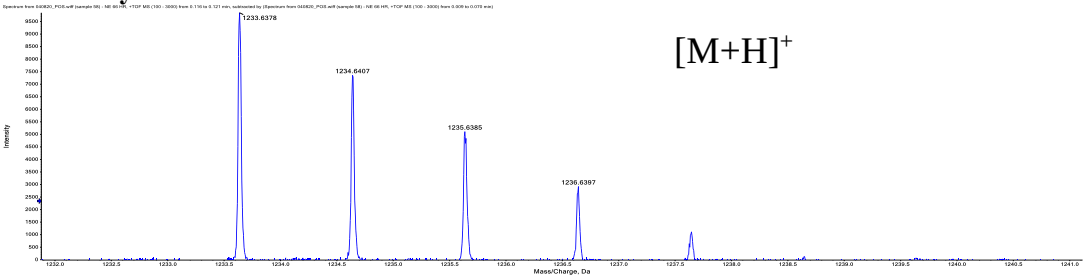

Figure S95. HRMS tri-tert-butyl (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

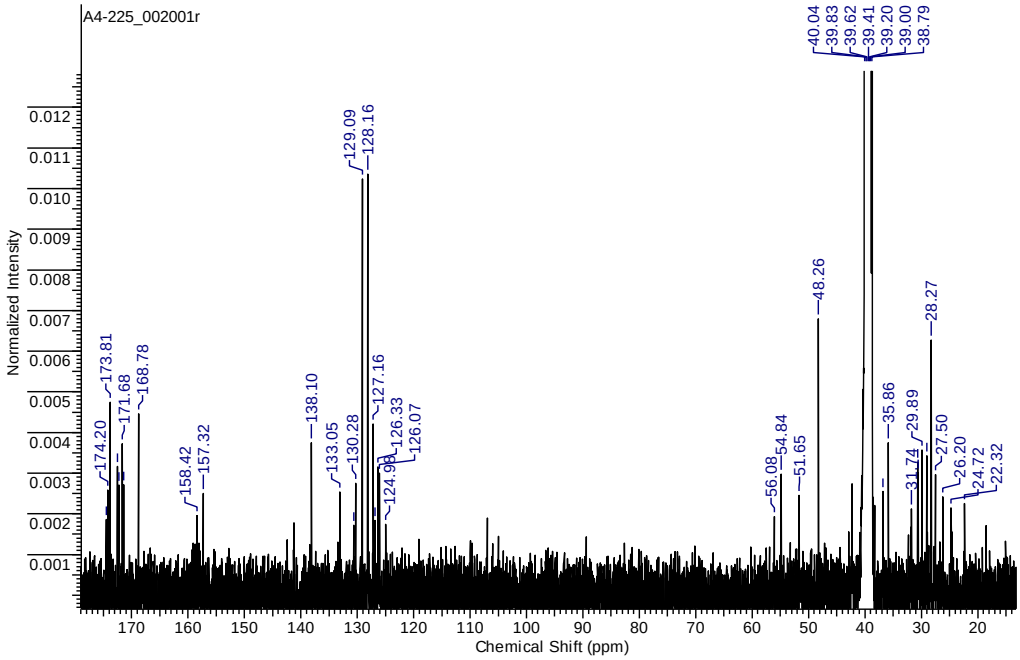

Figure S96. ^{13}C NMR (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3a).

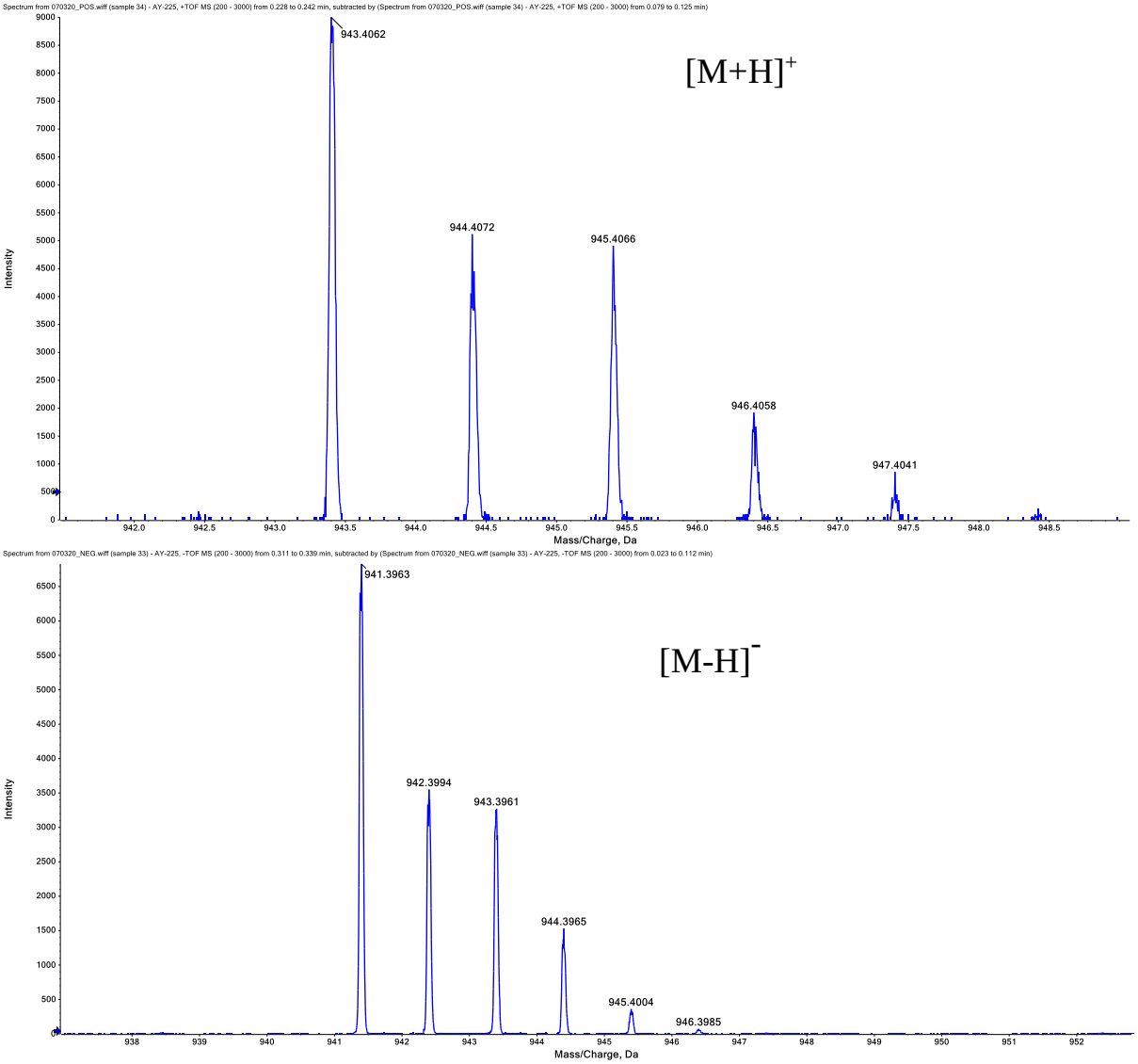

Figure S97 HRMS (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3a).

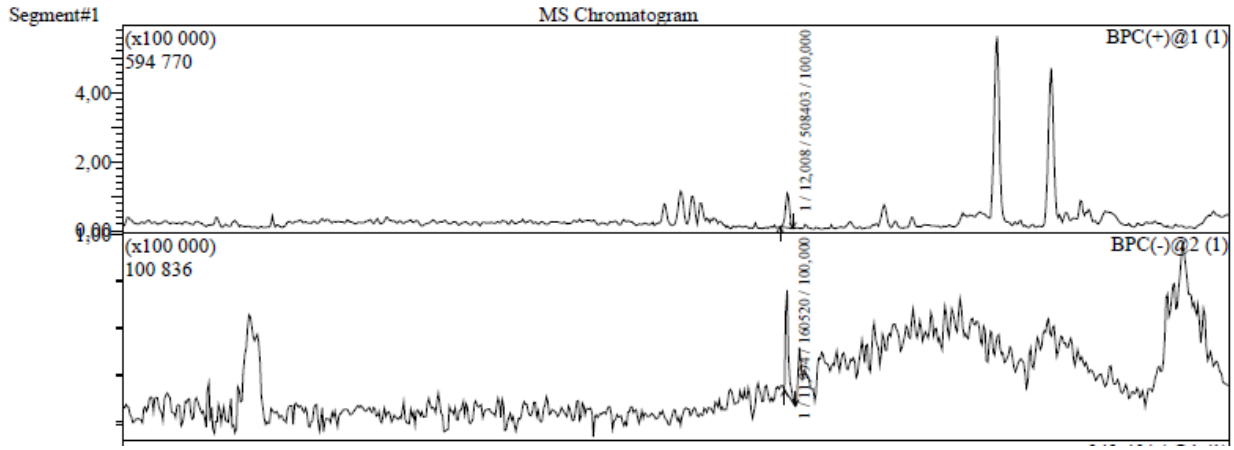

Figure S98. HPLC-MS (3S,7S,25S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3a).

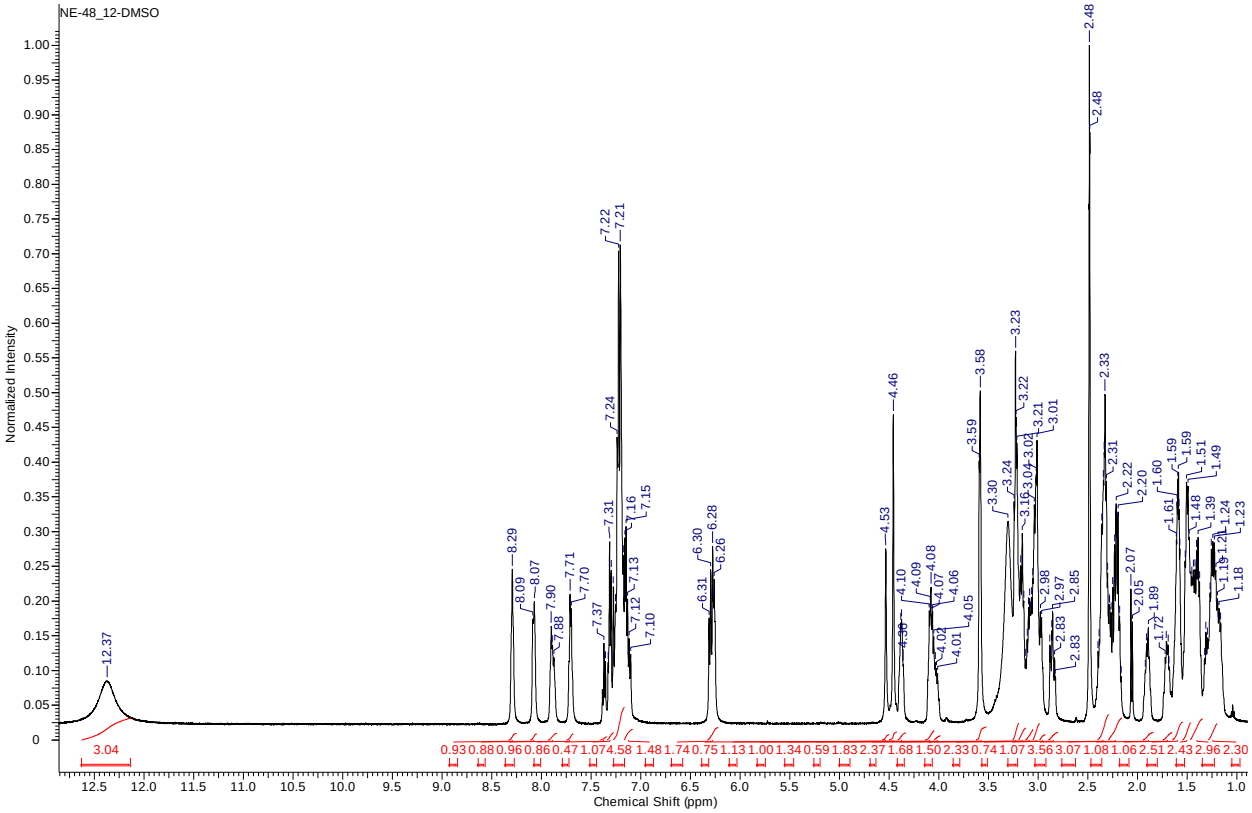

Figure S99. ^{1}H NMR (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3b).

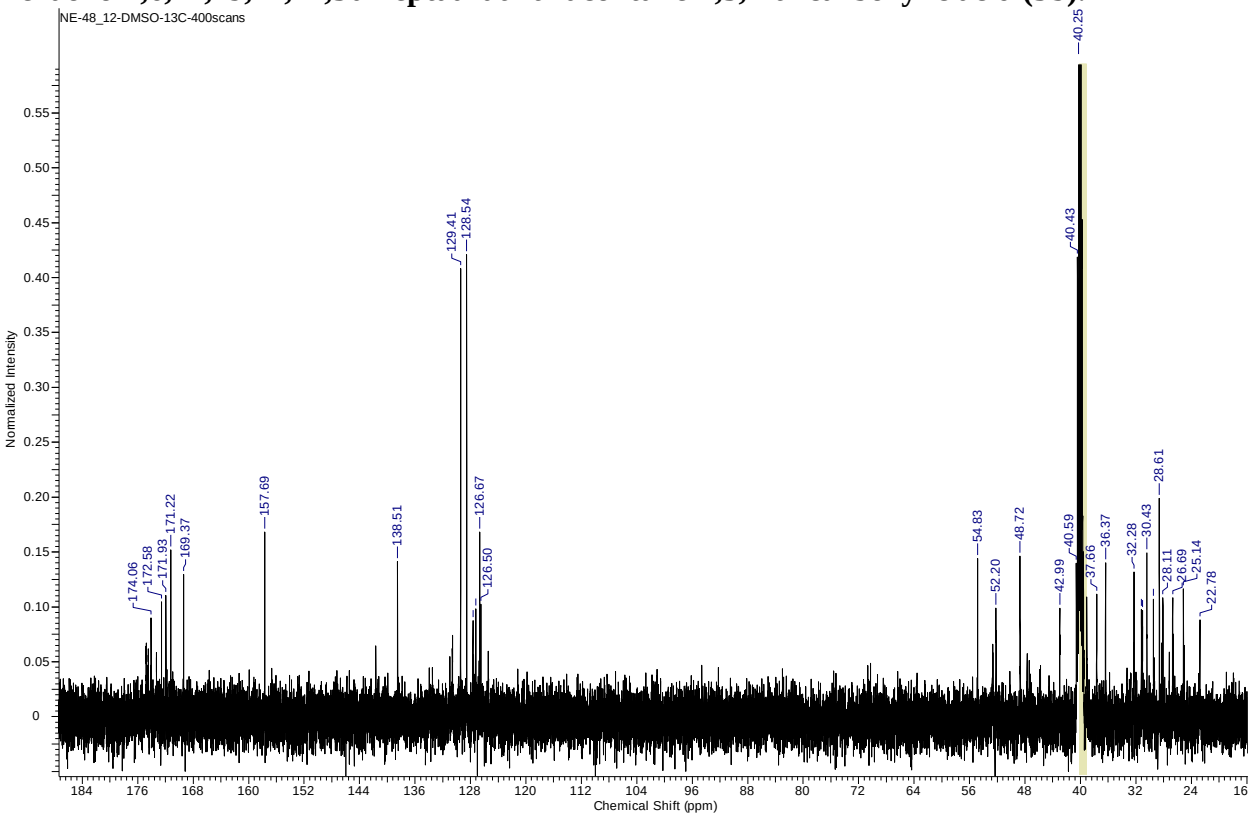

Figure S100. ^{13}C NMR (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3b).

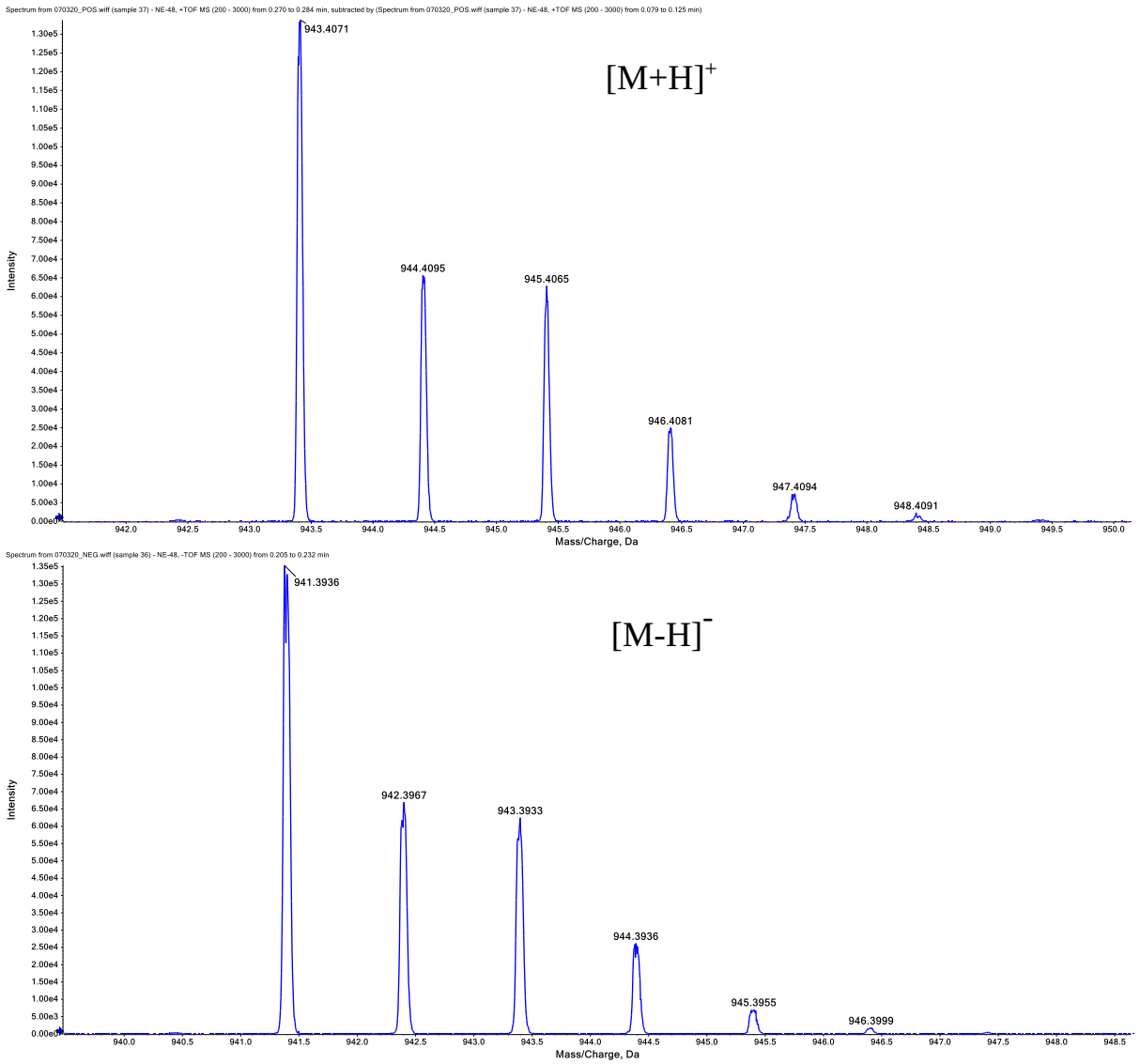

Figure S101 HRMS (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3b).

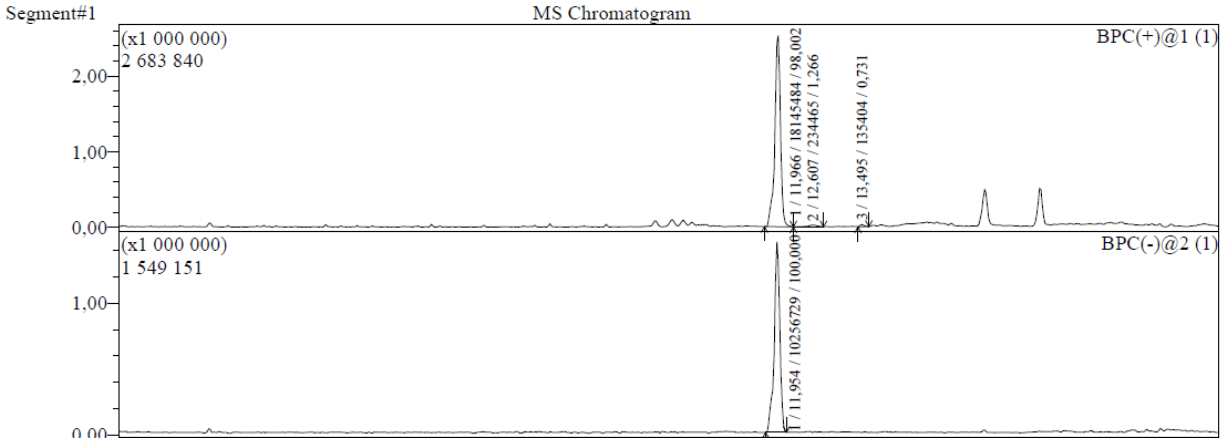

Figure S102. HPLC-MS (3S,7S,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3b).

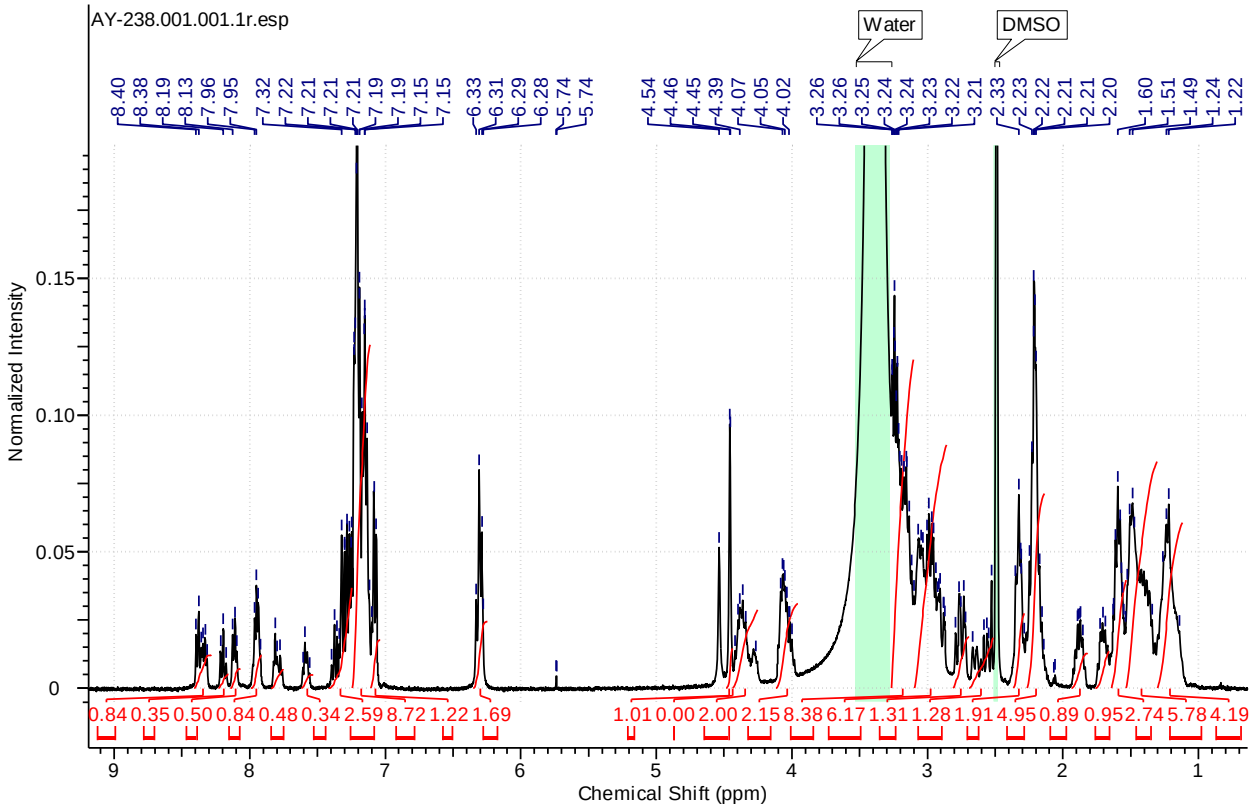

Figure S103. ^{1}H NMR (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3c).

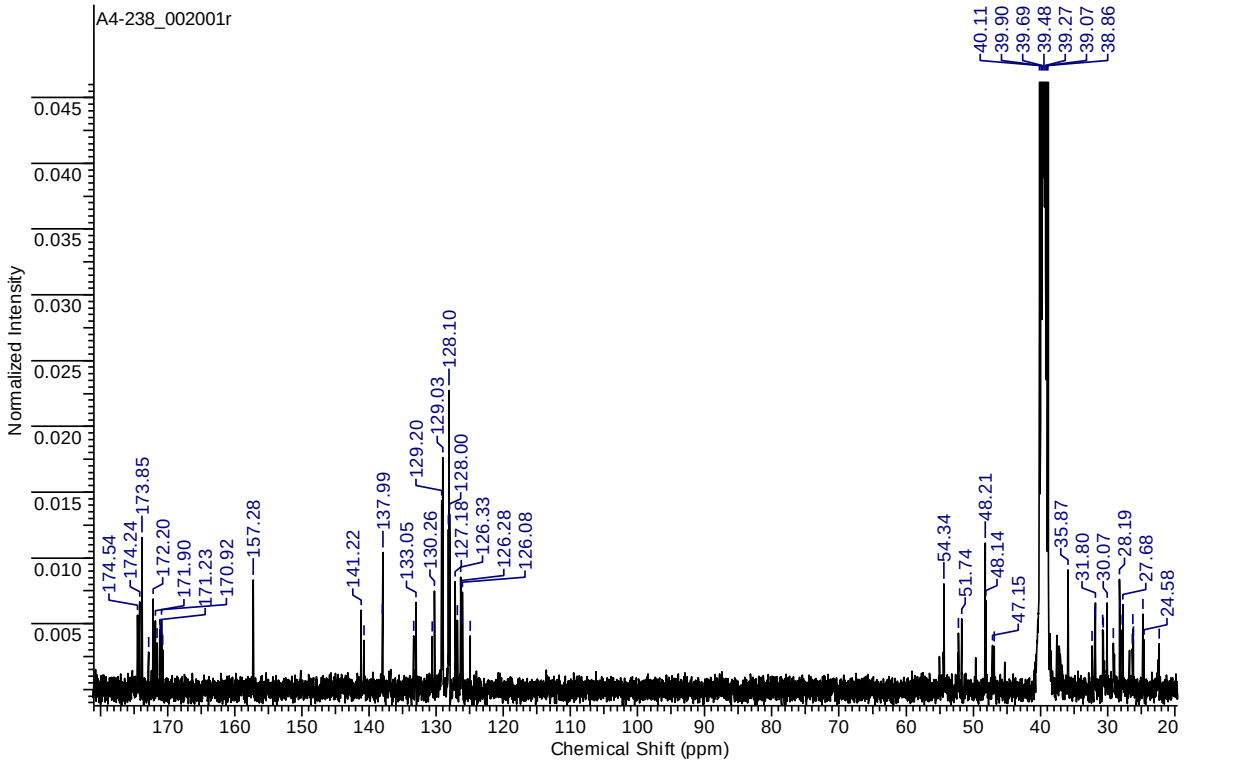

Figure S104. ^{13}C NMR (3*S*,7*S*,25*S*,28*R*)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3c).

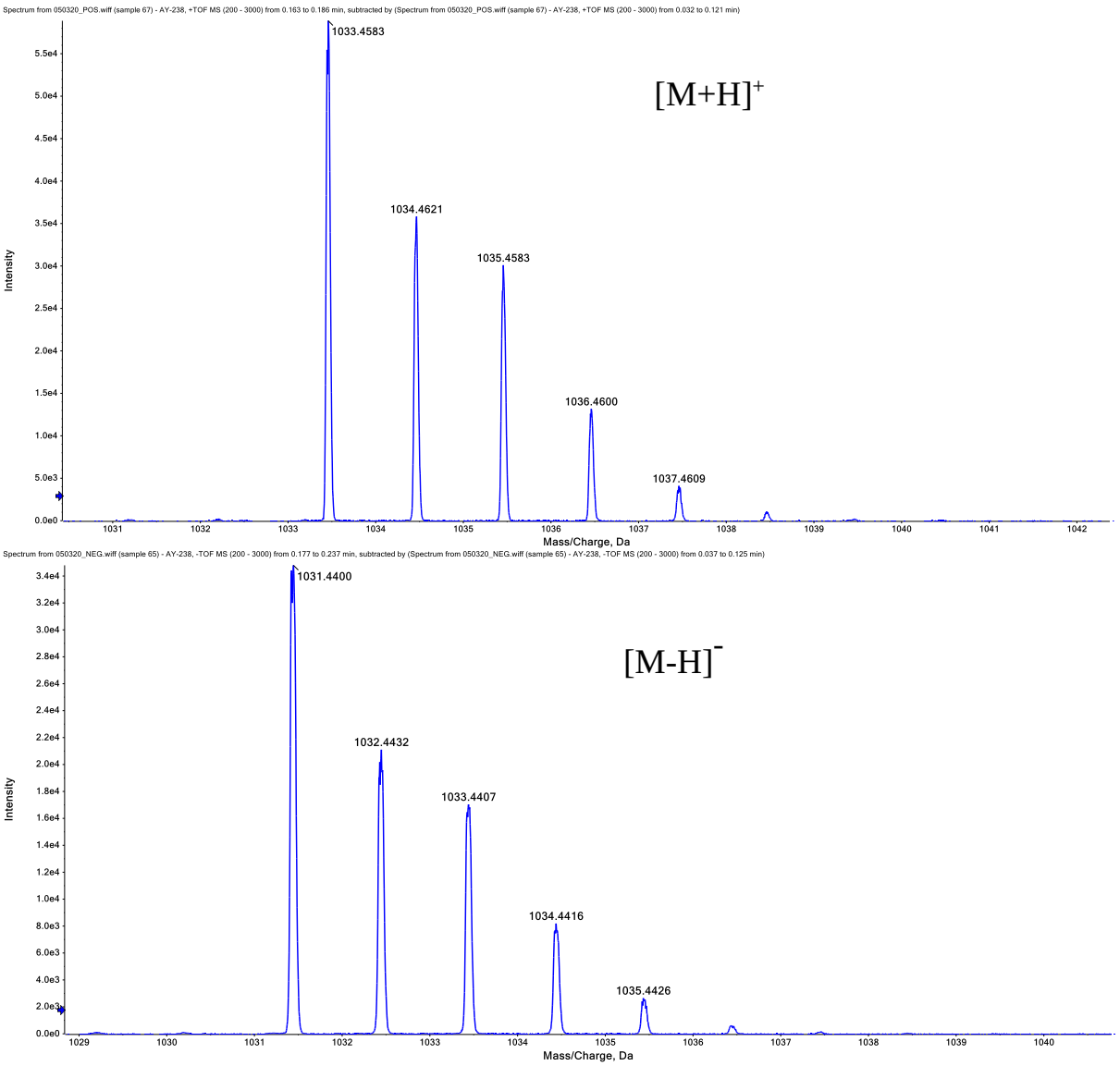

Figure S105. HRMS (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3c).

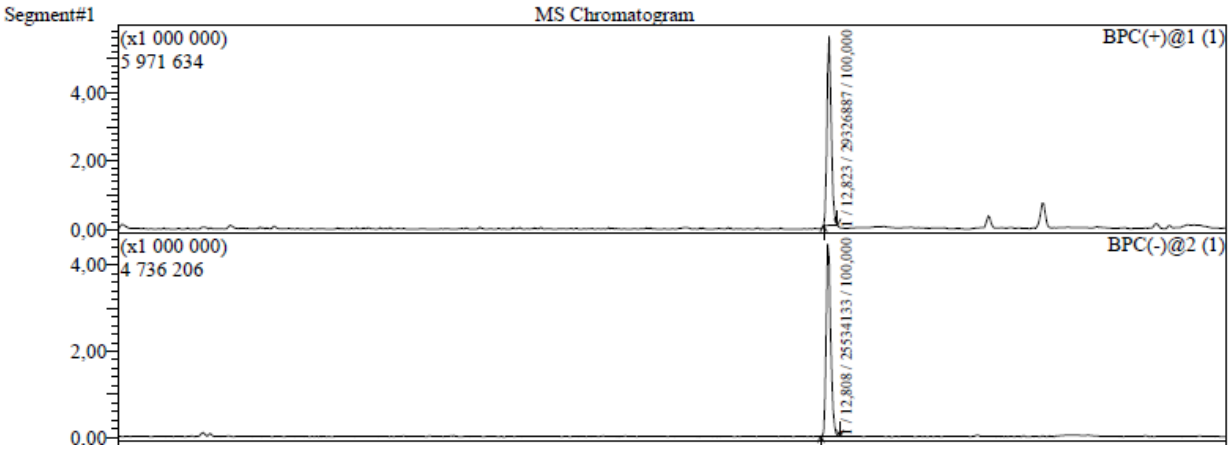

Figure S106. HPLC-MS (3S,7S,25S,28R)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3c).

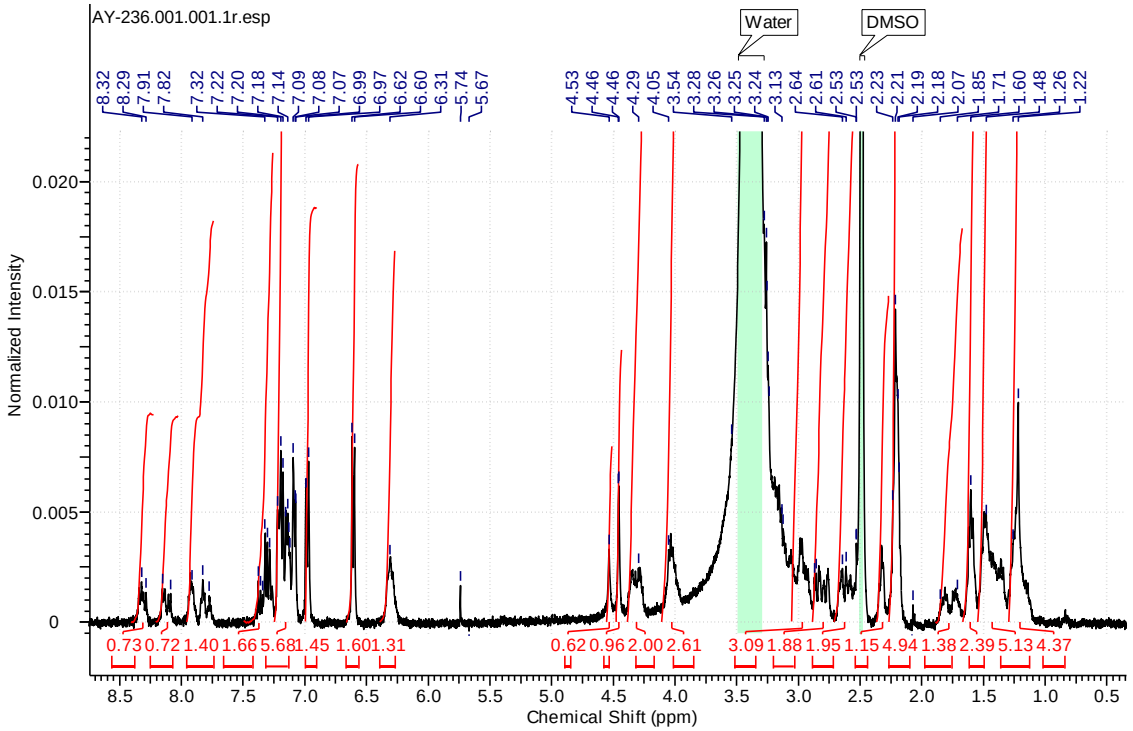

Figure S107. ^{1}H NMR (3S,7S,25S,28R)-33-azido-25-benzyl-12-(3-chlorobenzyl)--28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3d).

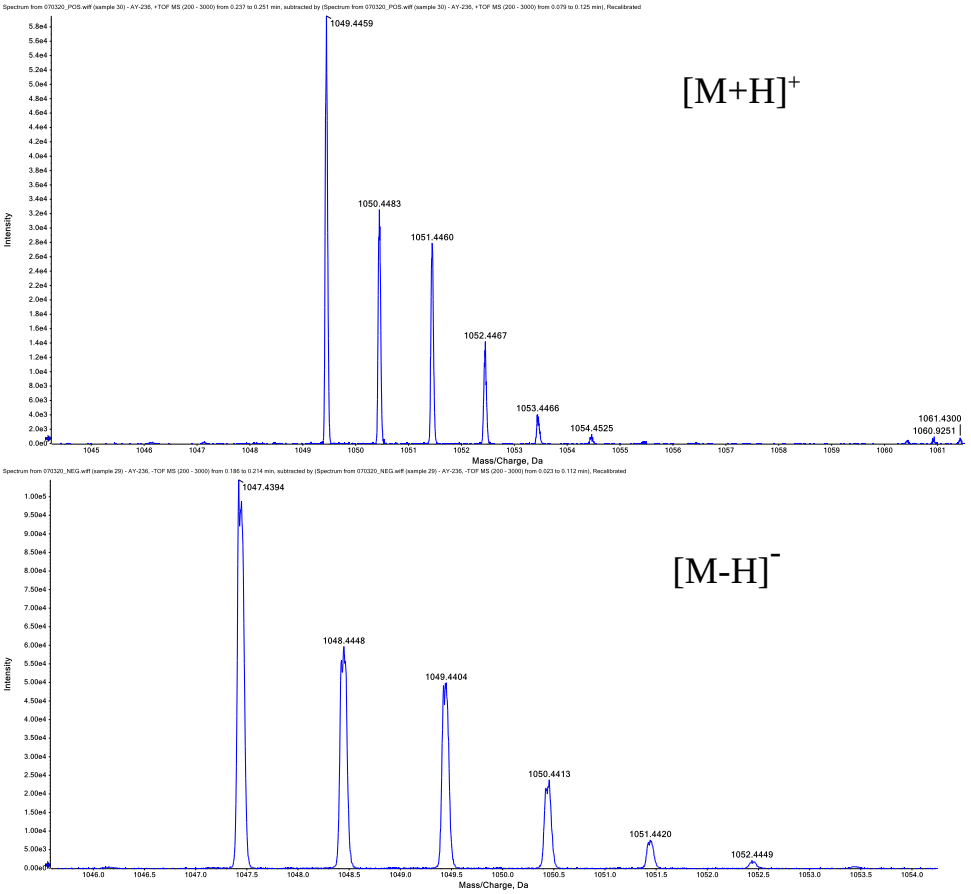

Figure S108. HRMS (3S,7S,25S,28R)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3d).

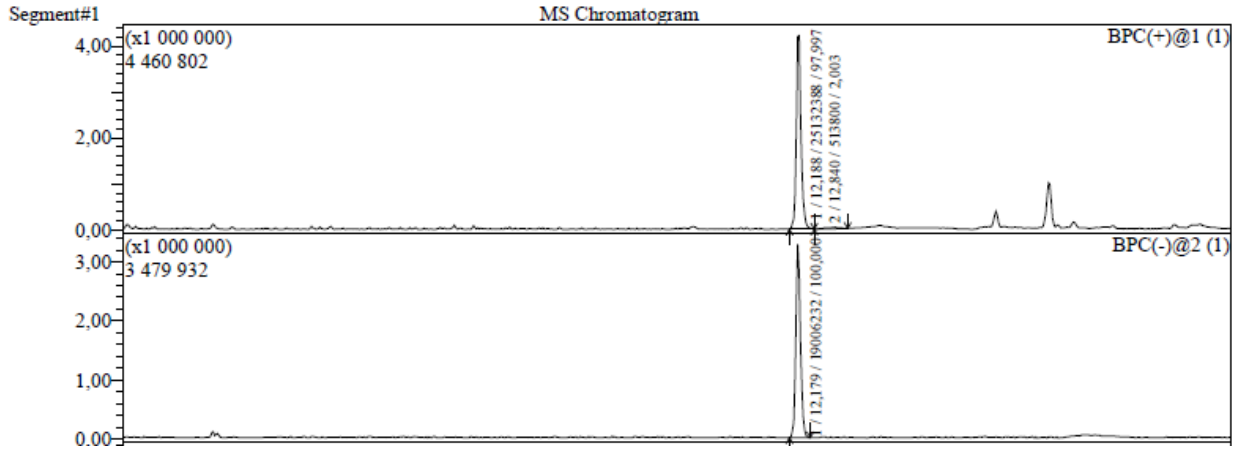

Figure S109. HPLC-MS (3S,7S,25S,28R)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3d).

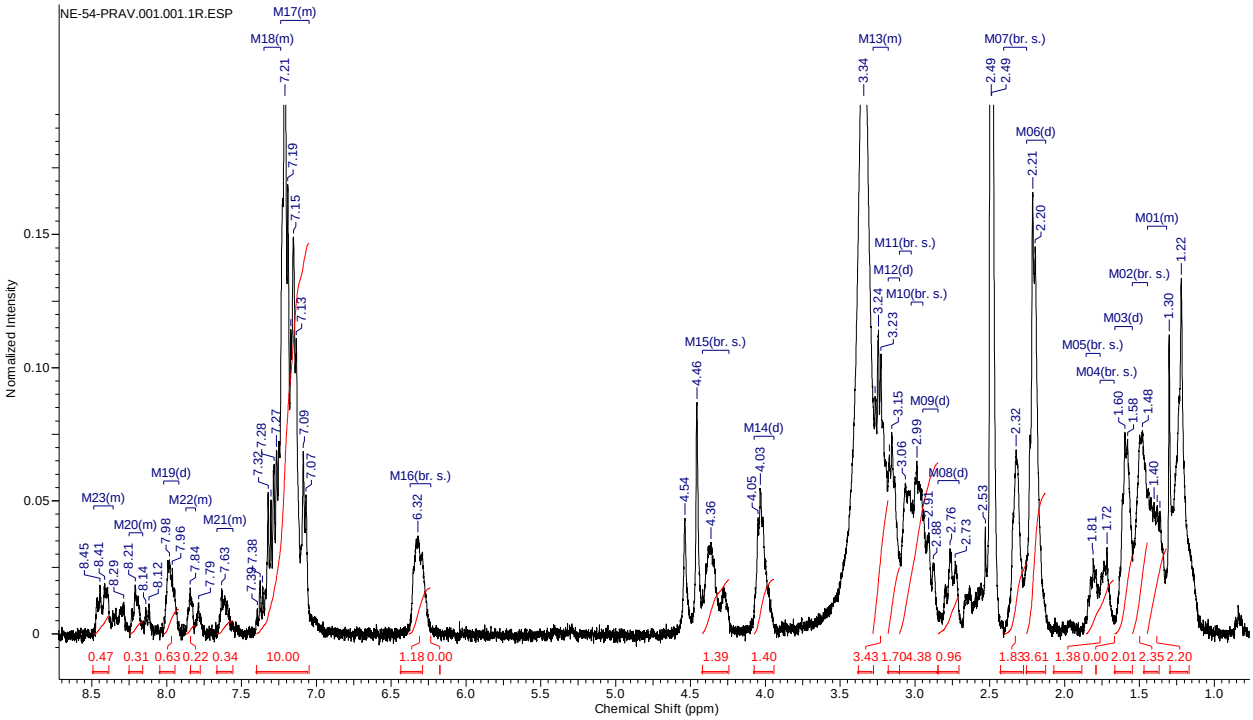

Figure S110. ^{1}H NMR (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3e).

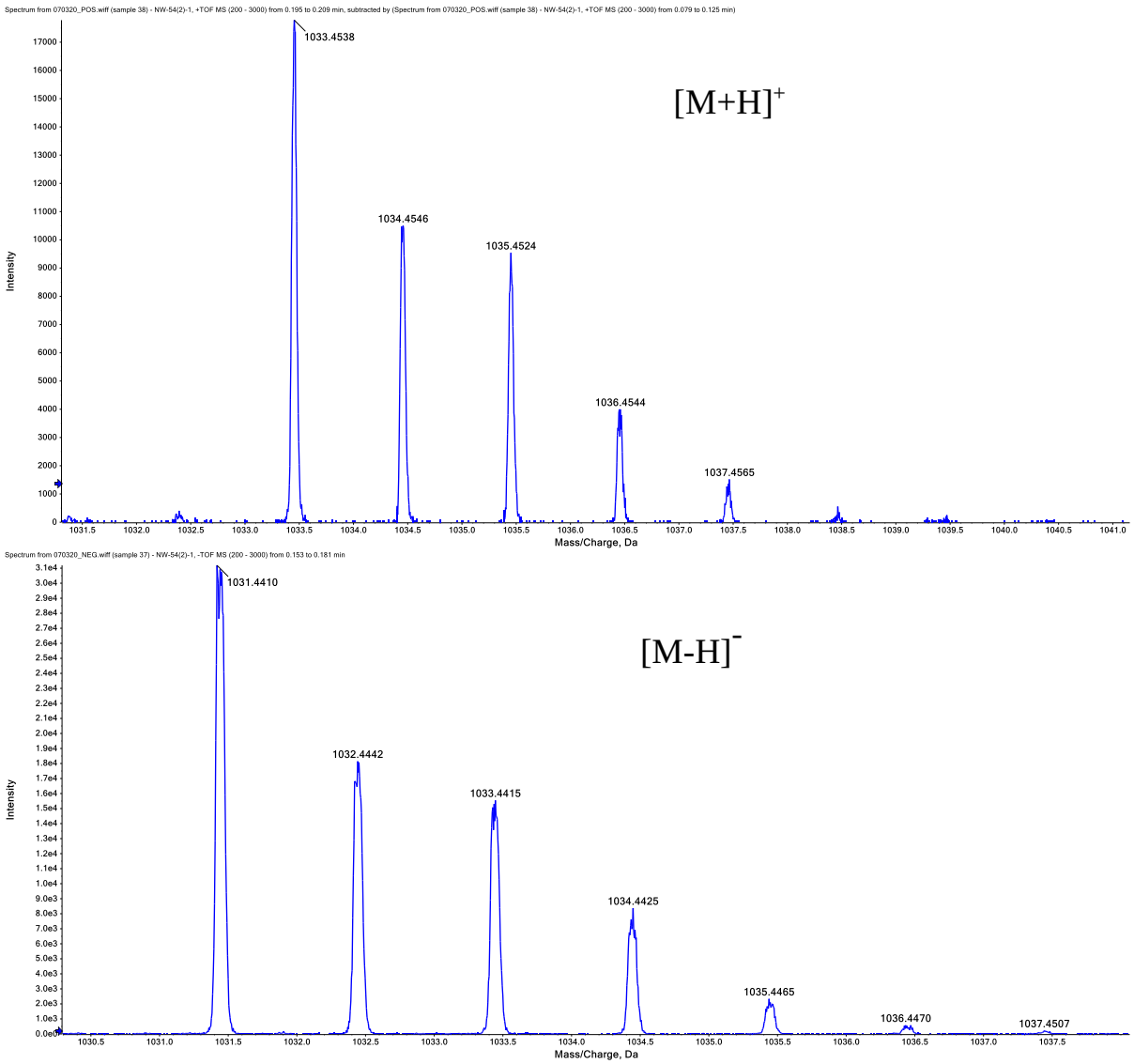

Figure S111. HRMS (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3e).

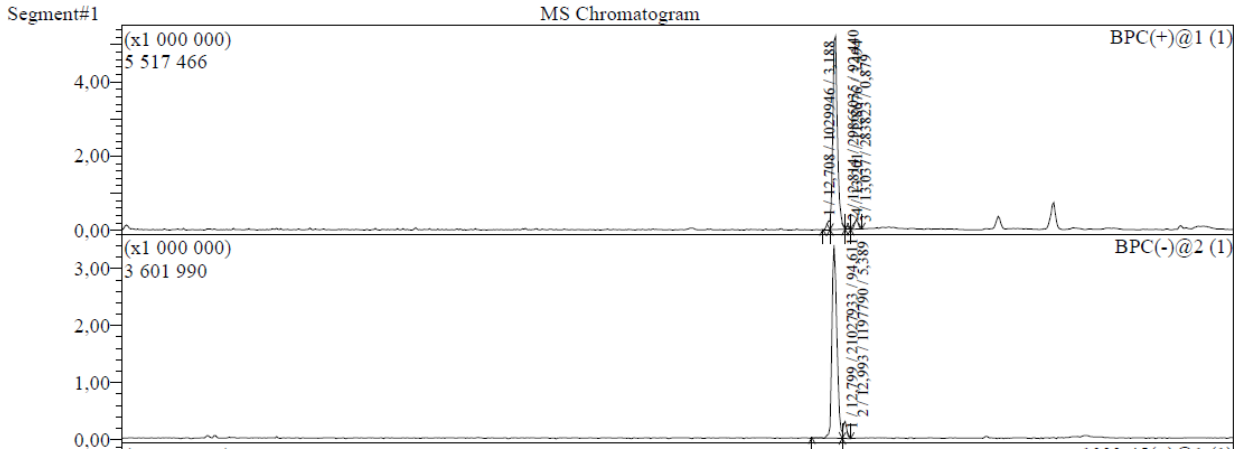

Figure S112. HPLC-MS (3S,7S,25R,28S)-33-azido-25,28-dibenzyl-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3e).

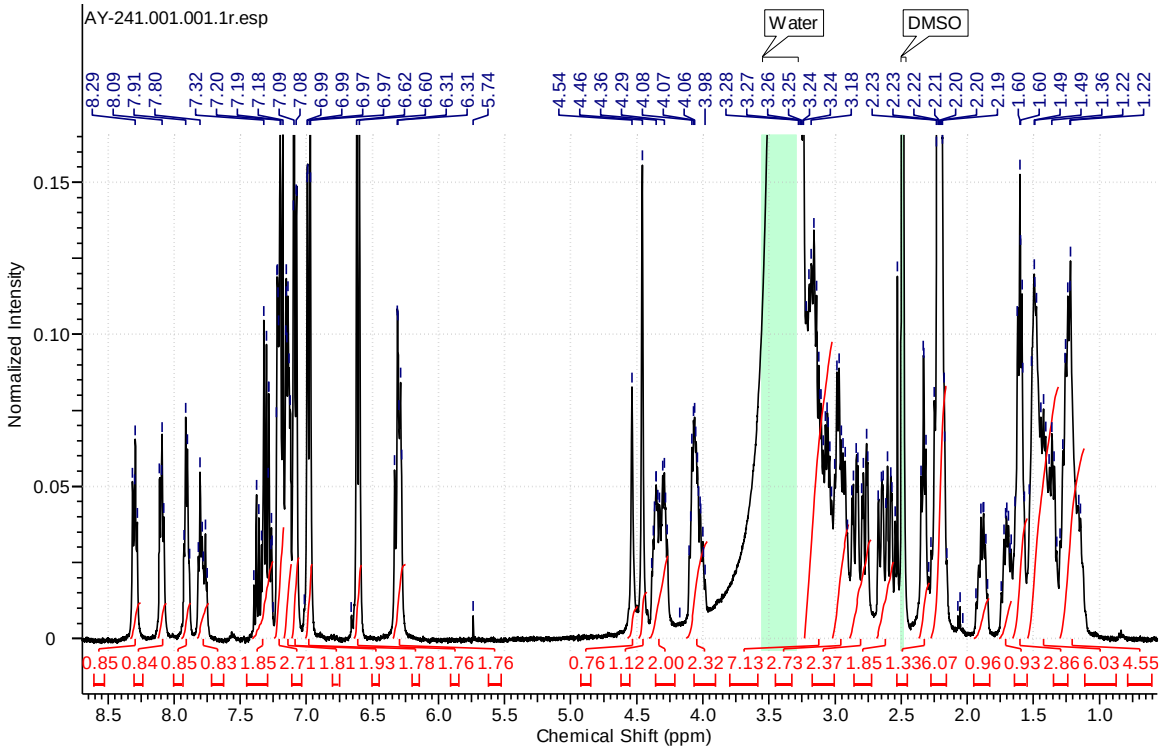

Figure S113. ^{1}H NMR (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3f).

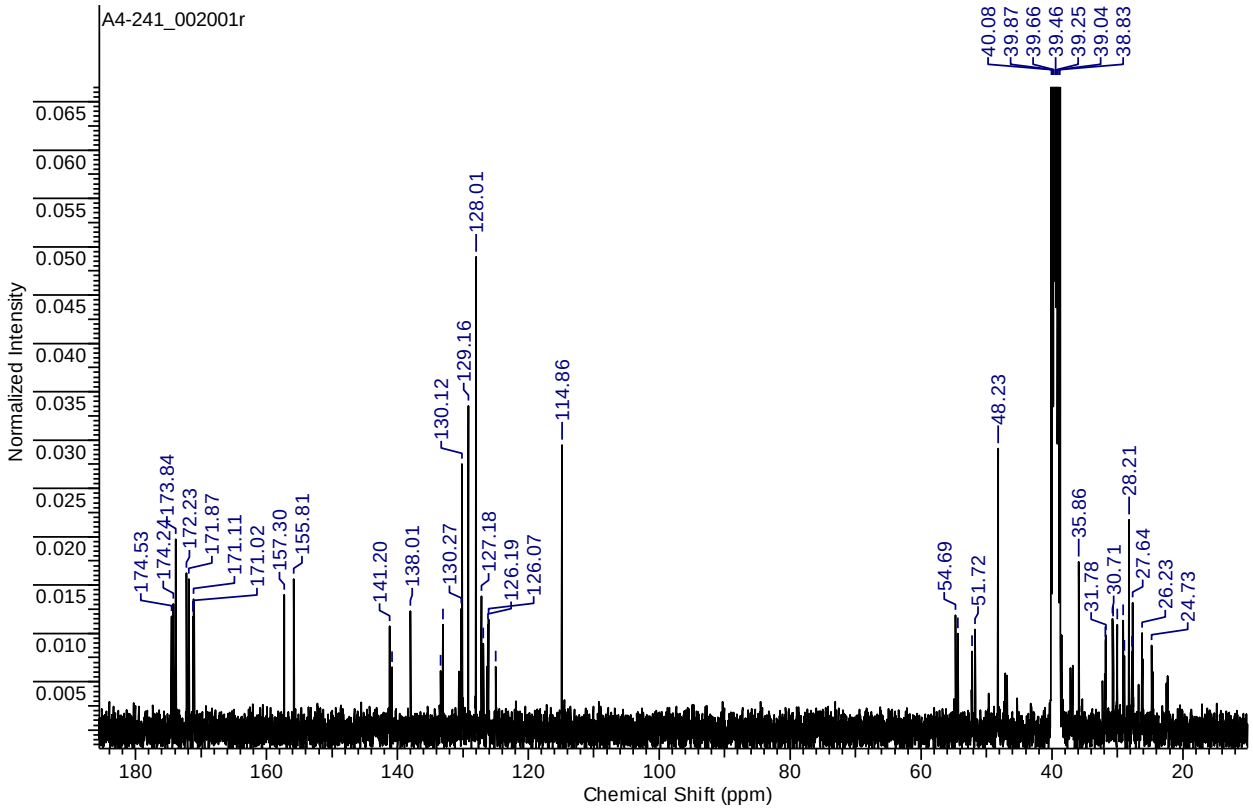

Figure S114. ^{13}C NMR (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3f).

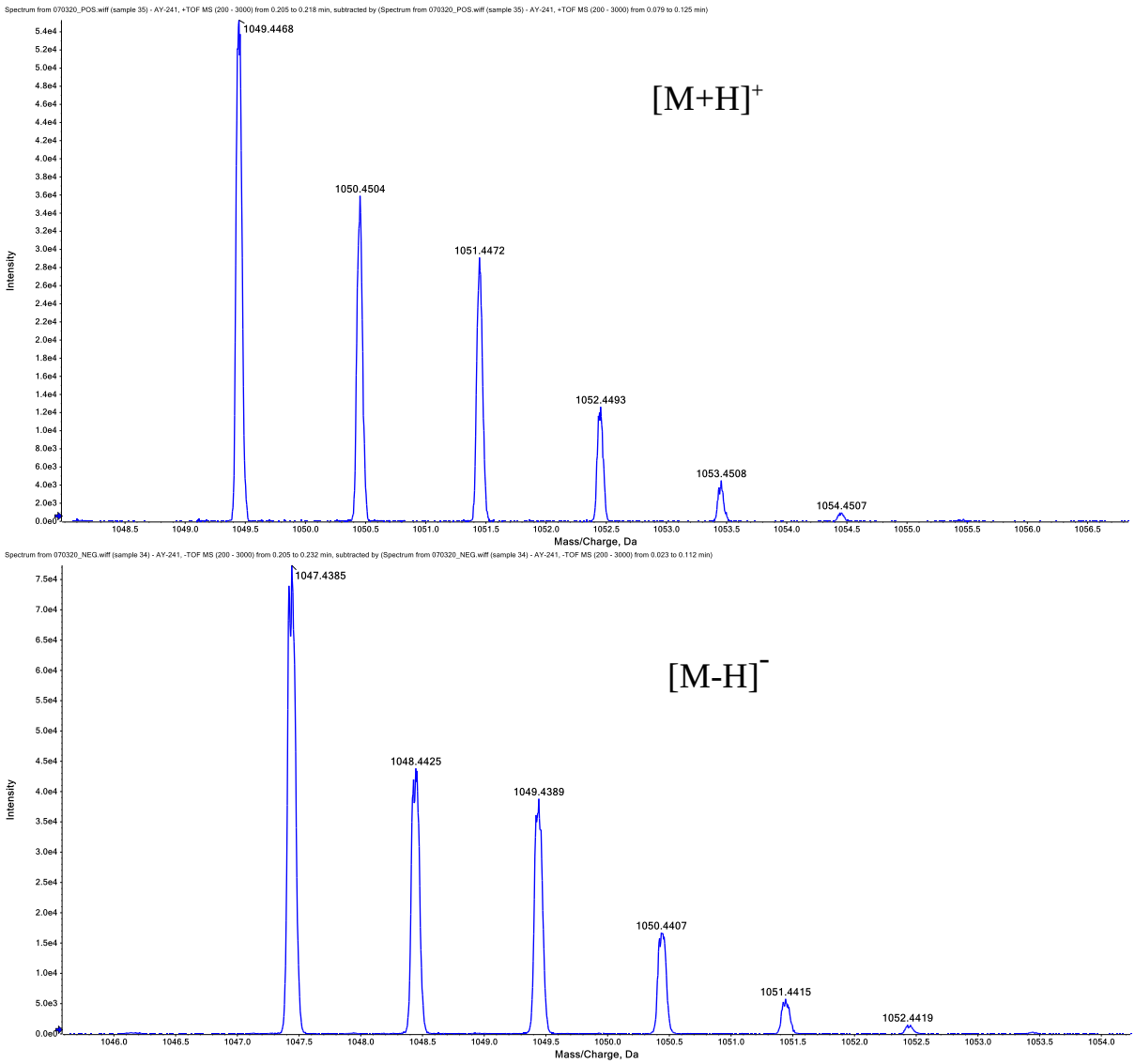

Figure S115. HRMS (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3f).

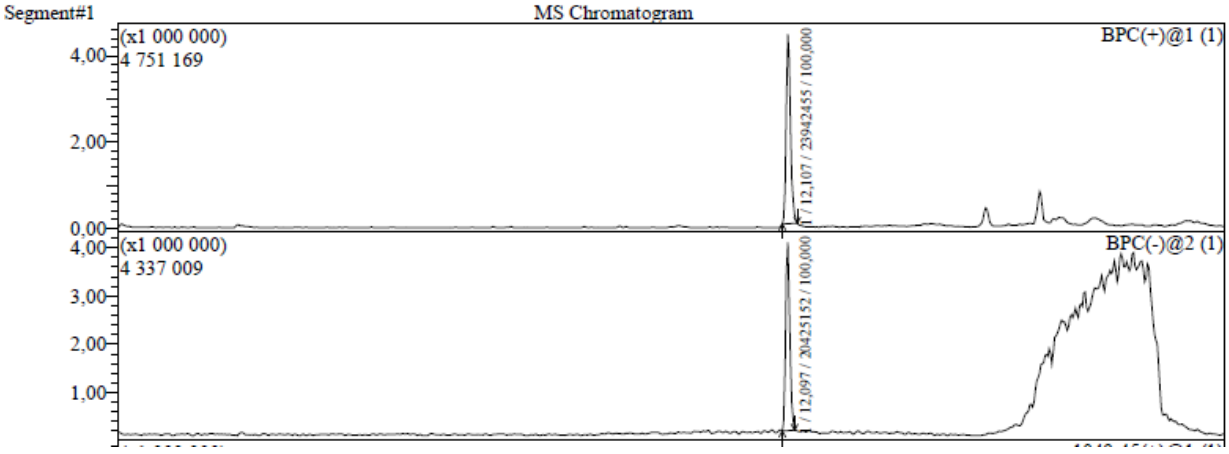

Figure S116. HPLC-MS (3S,7S,25R,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3f).

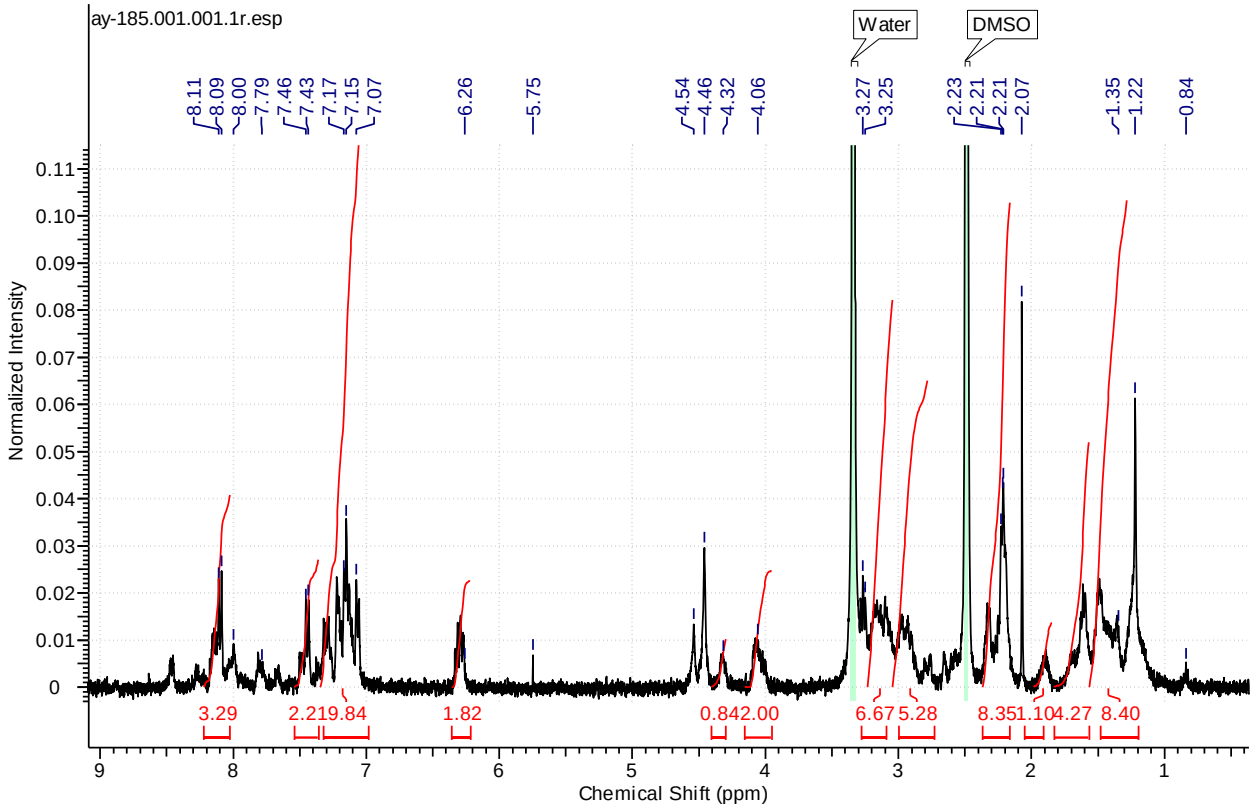

Figure S117. ^{1}H NMR (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3g).

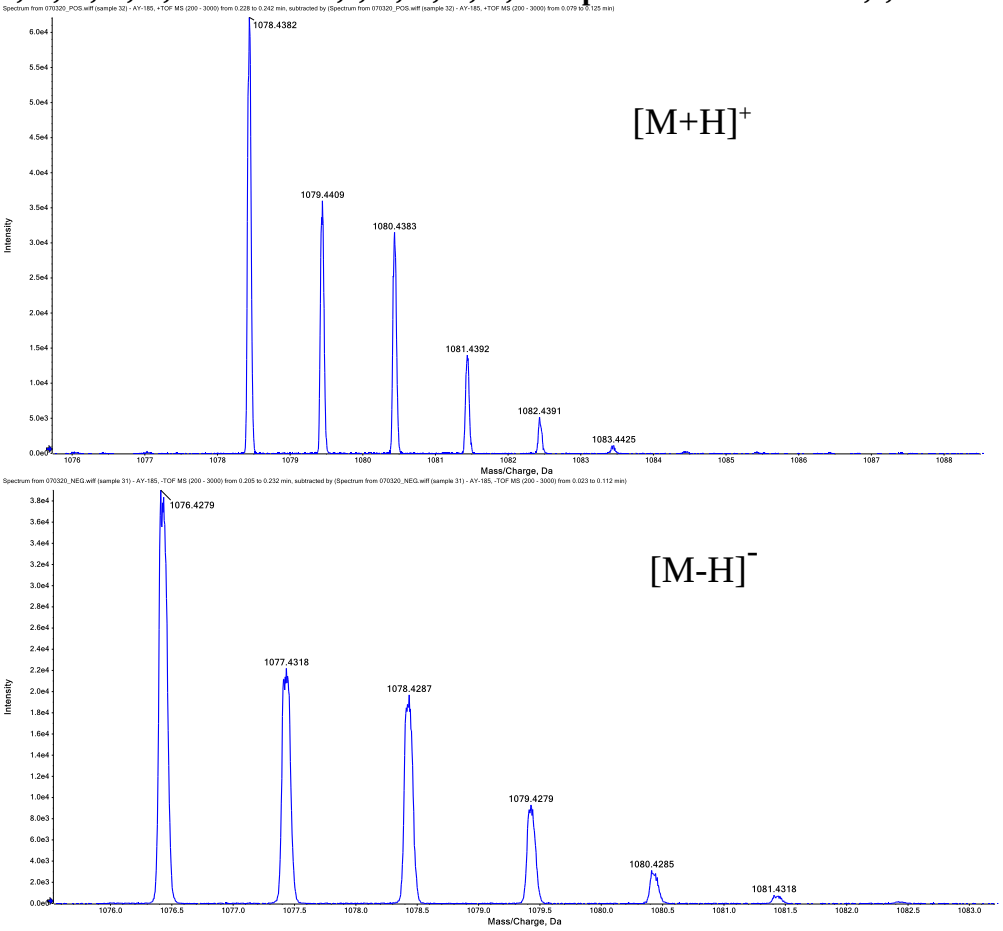

Figure S118. HRMS (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3g).

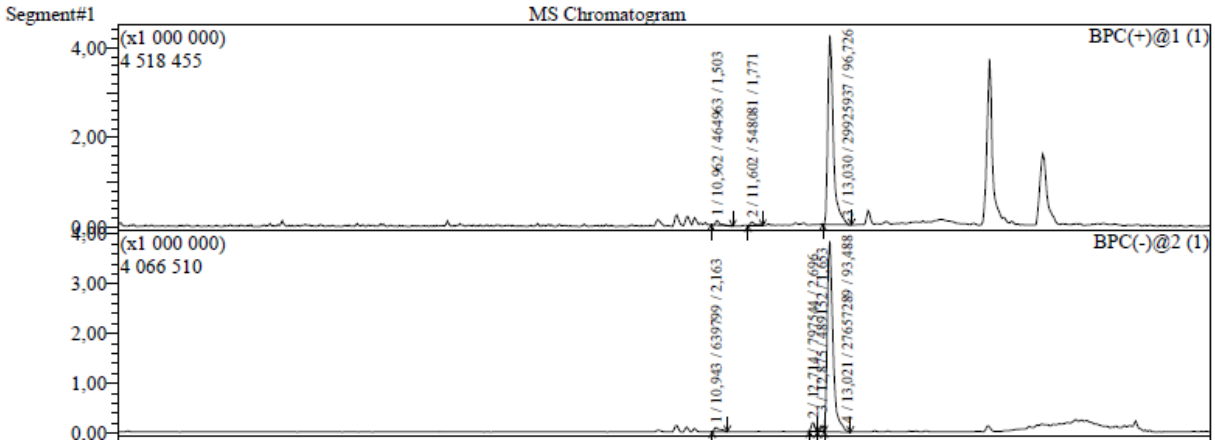

Figure S119. HRMS (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28--(4-nitrobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3g).

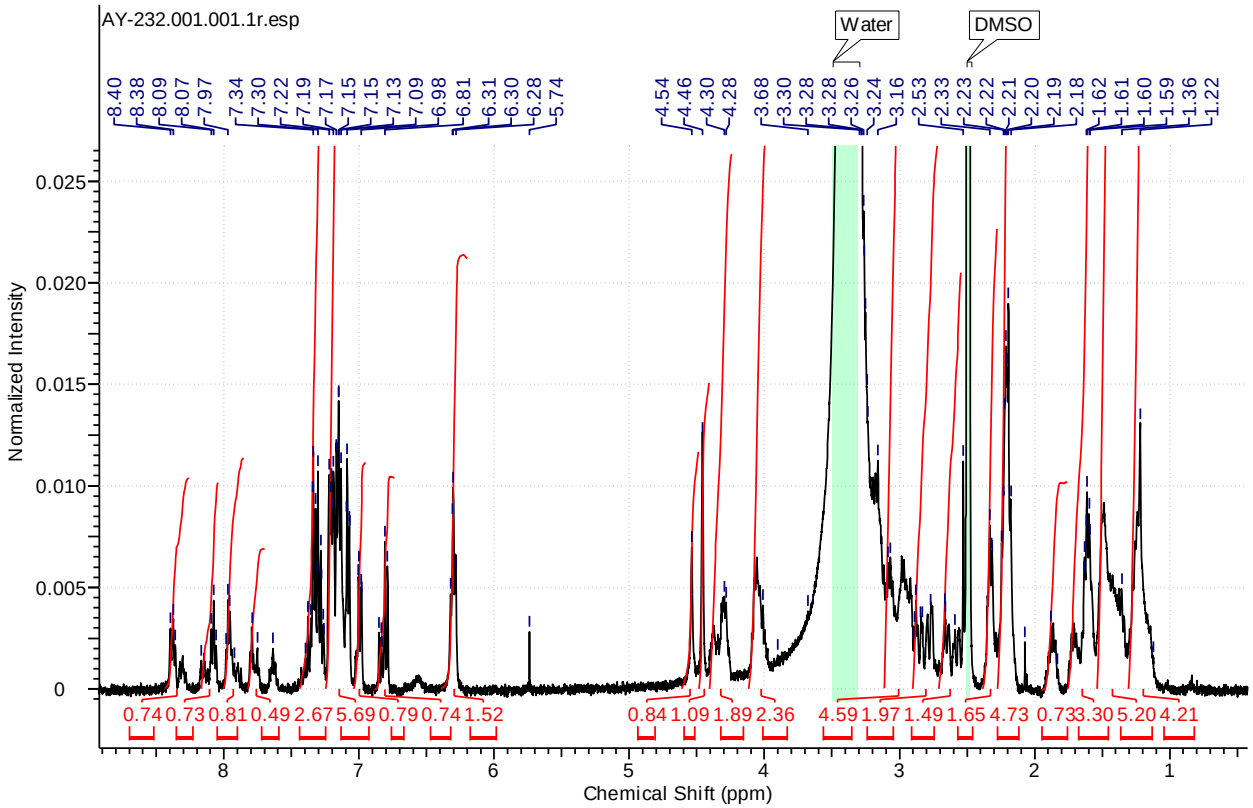

Figure S120. ^{1}H NMR (3S,7S,25S,28S)-33-azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3h).

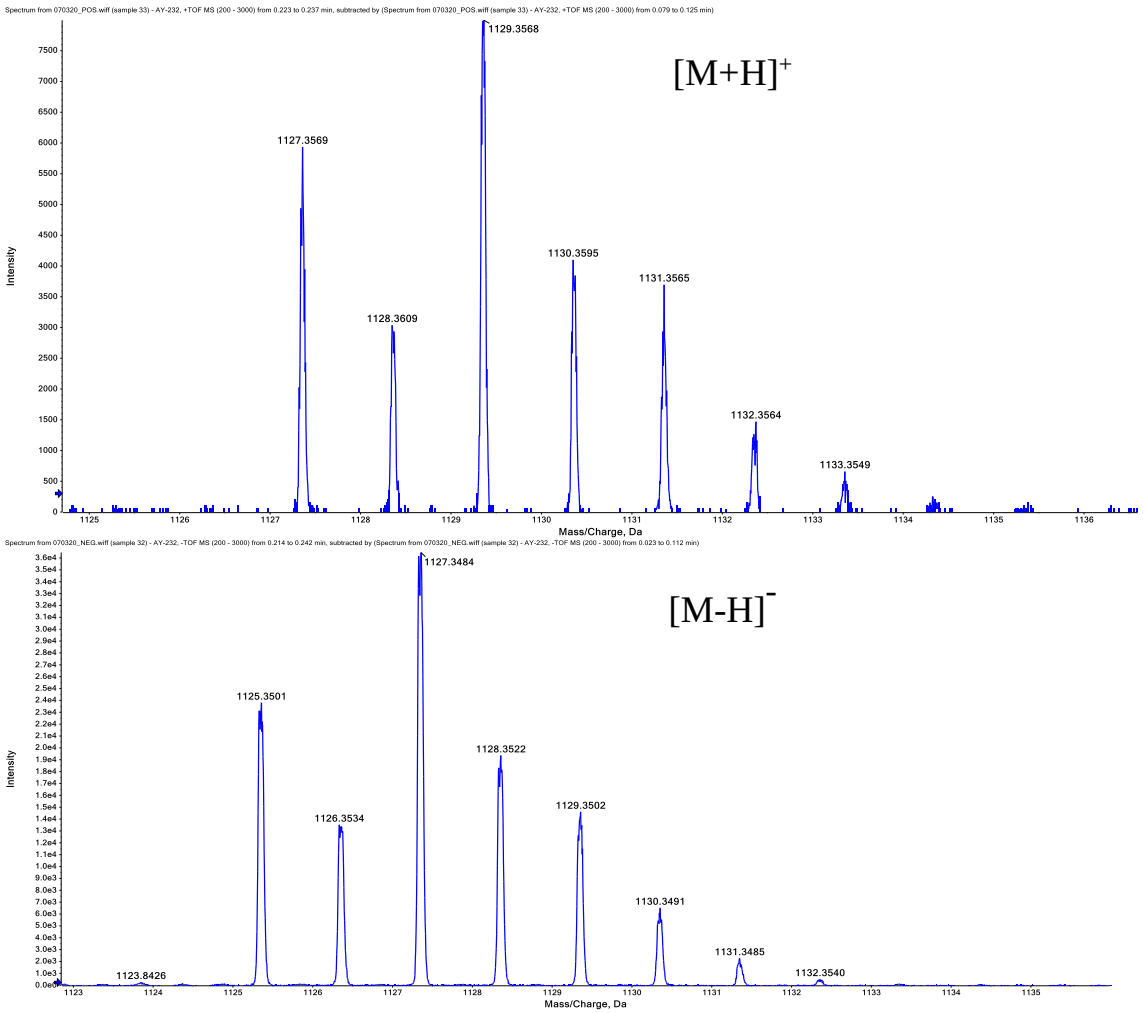

Figure S121. HRMS (3S,7S,25S,28S)-33-azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3h).

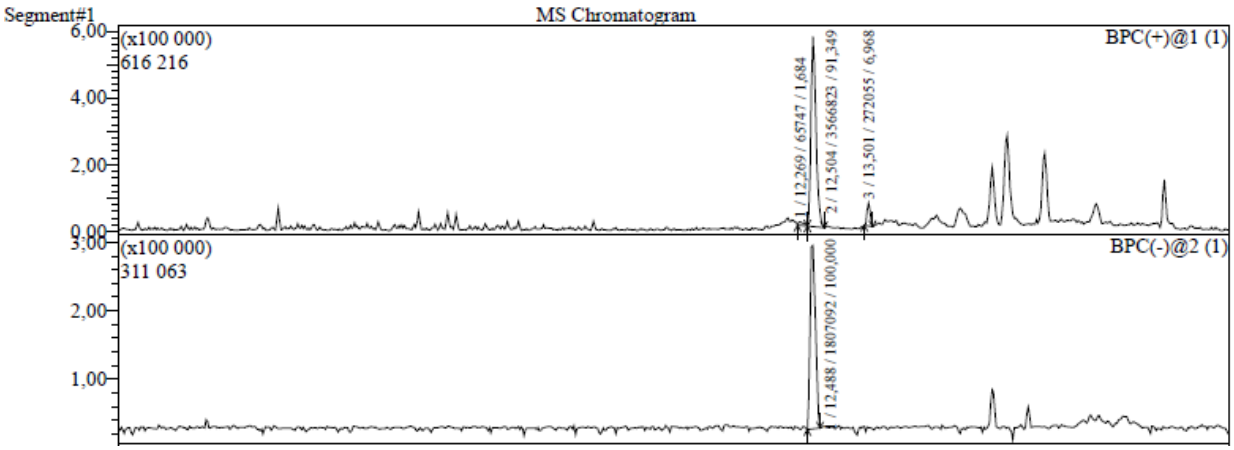

Figure S122. HPLC-MS (3S,7S,25S,28S)-33-azido-25-benzyl-28-(3-bromo-4-hydroxybenzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3h).

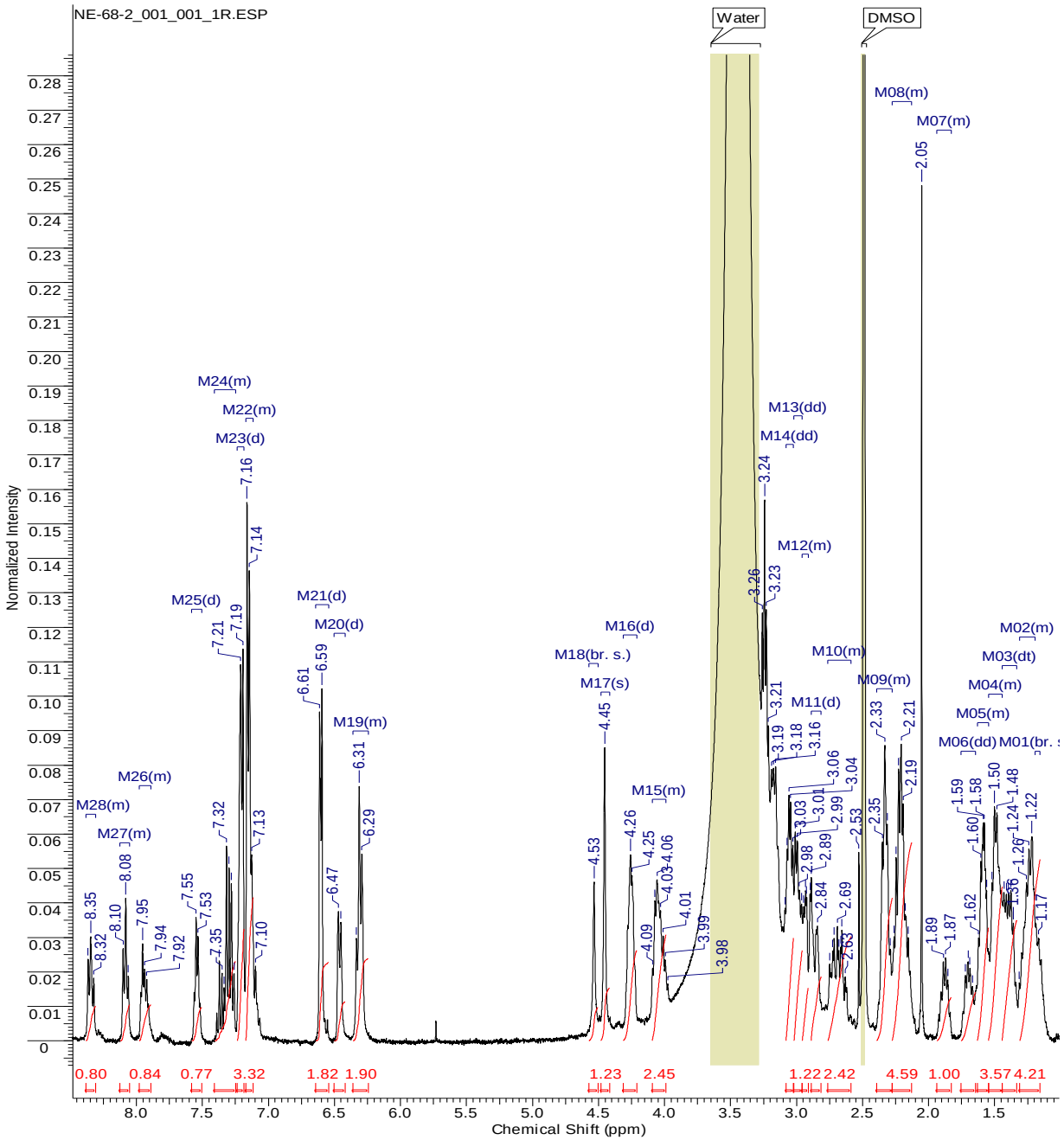

Figure S123. ^{1}H NMR (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3i).

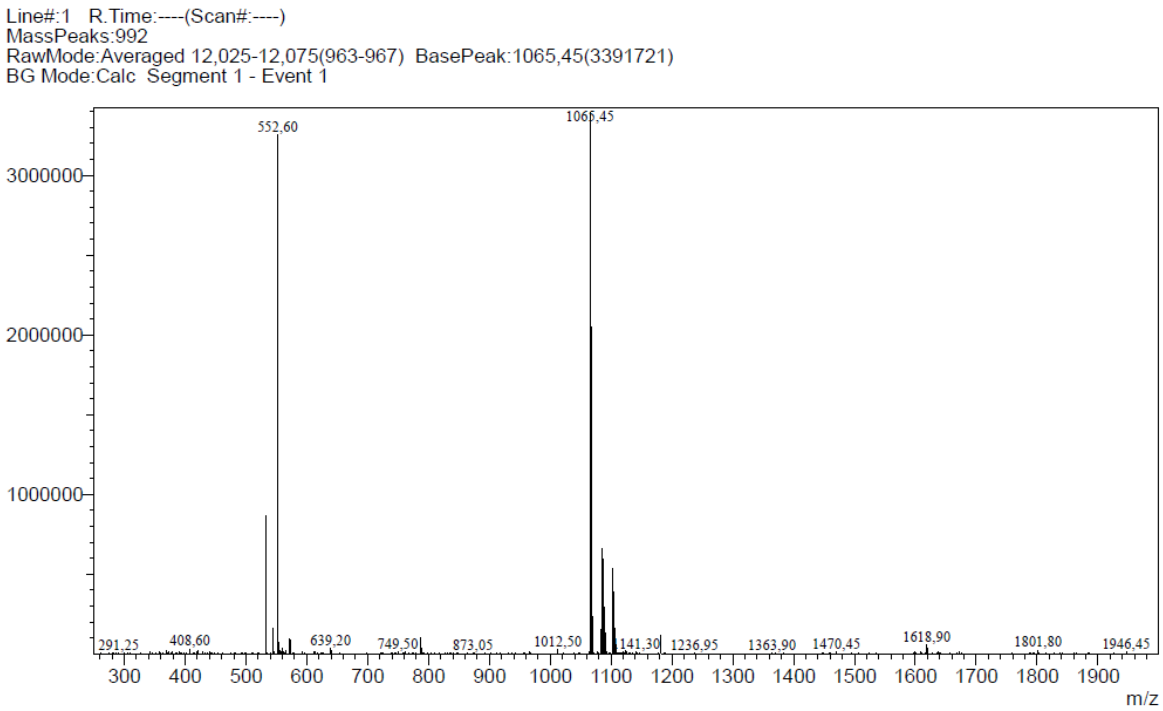

Figure S124. MS (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3i).

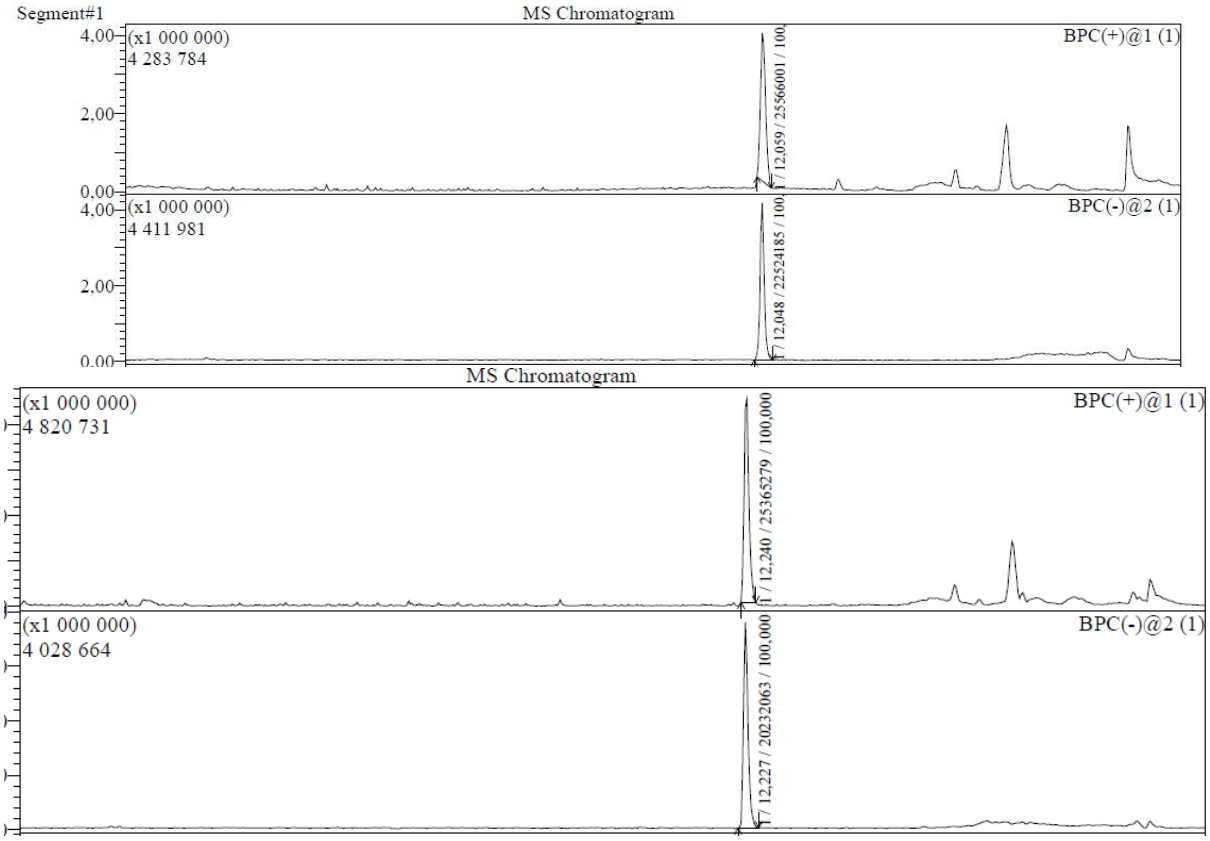

Figure S125. MS (3S,7S,25S,28S)-33-azido-25-benzyl-12-(3-chlorobenzyl)-28-(3,4-dihydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (3i).

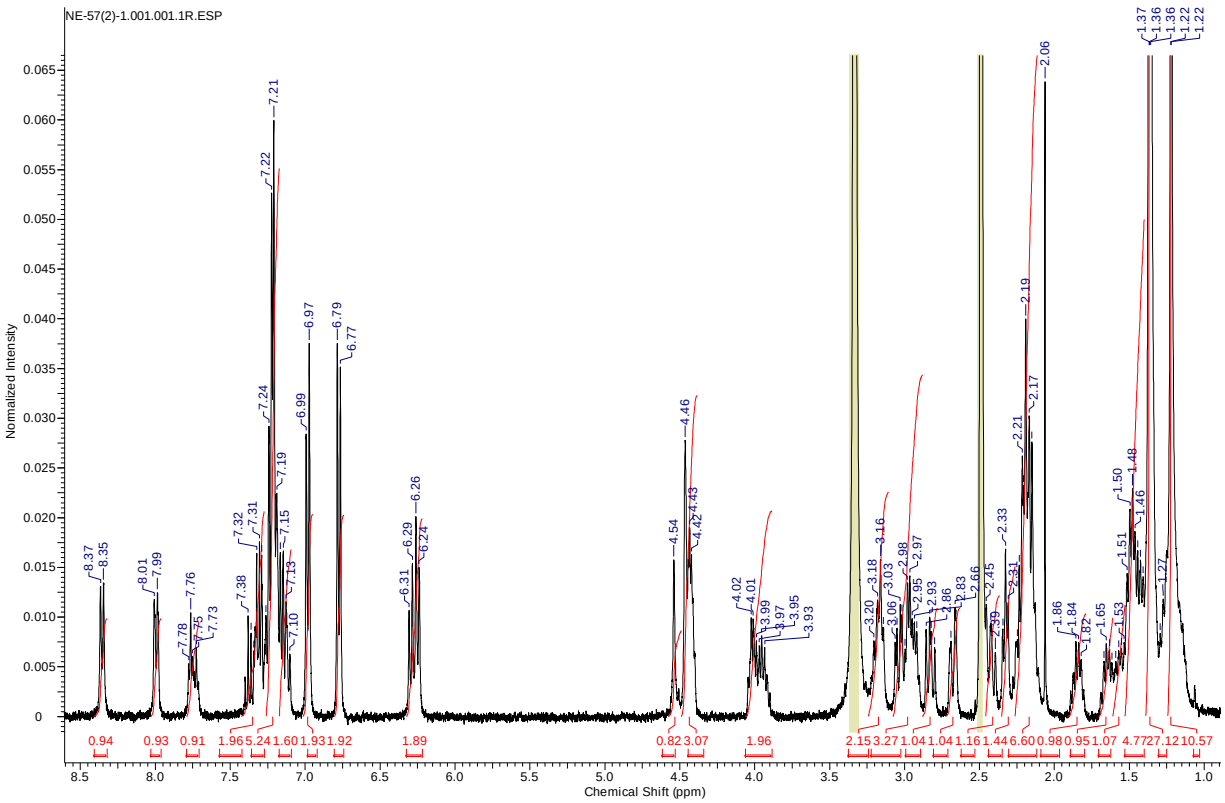

Figure S126. ^{1}H NMR (2S,5R,23S,27S)-2-benzyl-5-(4-(tert-butoxy)benzyl)-23,27-bis(tert-butoxycarbonyl)-18-(3-chlorobenzyl)-32,32-dimethyl-4,7,10,17,25,30-hexaoxo-31-oxa-3,6,11,18,24,26-hexaazatritriacontan-1-oic acid (4).

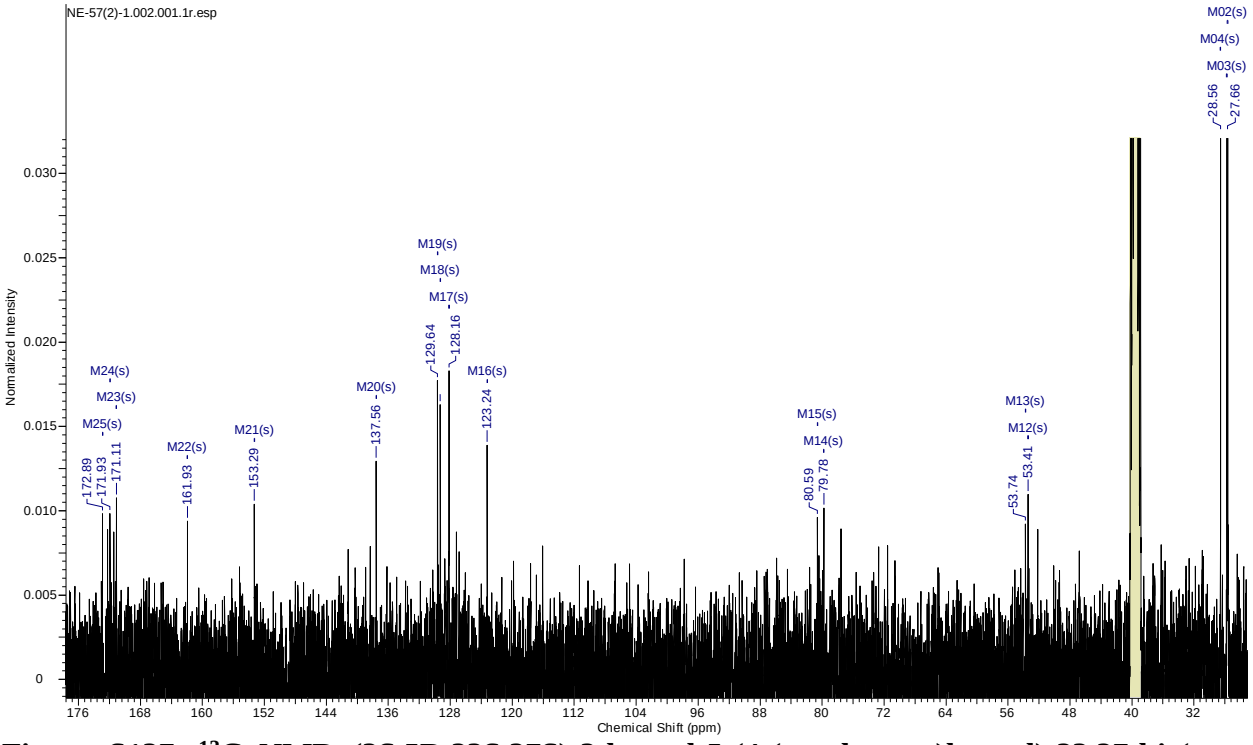

Figure S127. ^{13}C NMR (2S,5R,23S,27S)-2-benzyl-5-(4-(tert-butoxy)benzyl)-23,27-bis(tert-butoxycarbonyl)-18-(3-chlorobenzyl)-32,32-dimethyl-4,7,10,17,25,30-hexaoxo-31-oxa-3,6,11,18,24,26-hexaazatritriacontan-1-oic acid (4).

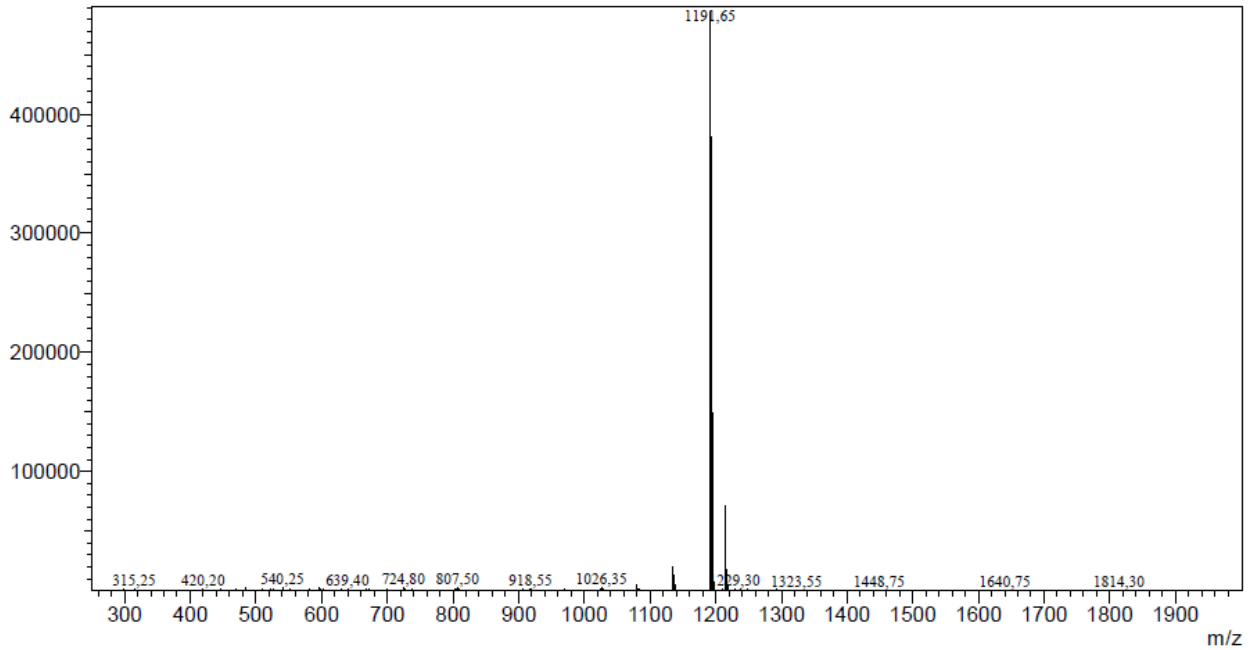

Figure S128. MS (2S,5R,23S,27S)-2-benzyl-5-(4-(tert-butoxy)benzyl)-23,27-bis(tert-butoxycarbonyl)-18-(3-chlorobenzyl)-32,32-dimethyl-4,7,10,17,25,30-hexaoxo-31-oxa-3,6,11,18,24,26-hexaazatritriacontan-1-oic acid (4).

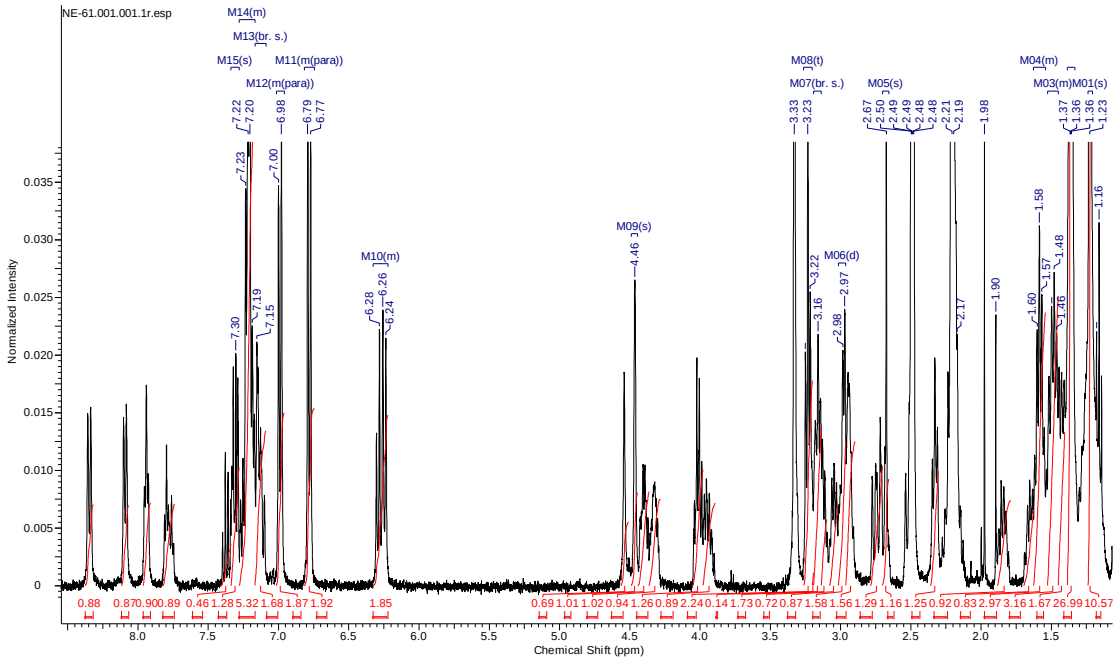

Figure S129. ^{1}H NMR (3S,7S,25R,28S)-tri-tert-butyl 33-azido-28-benzyl-25-(4-(tert-butoxy)benzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

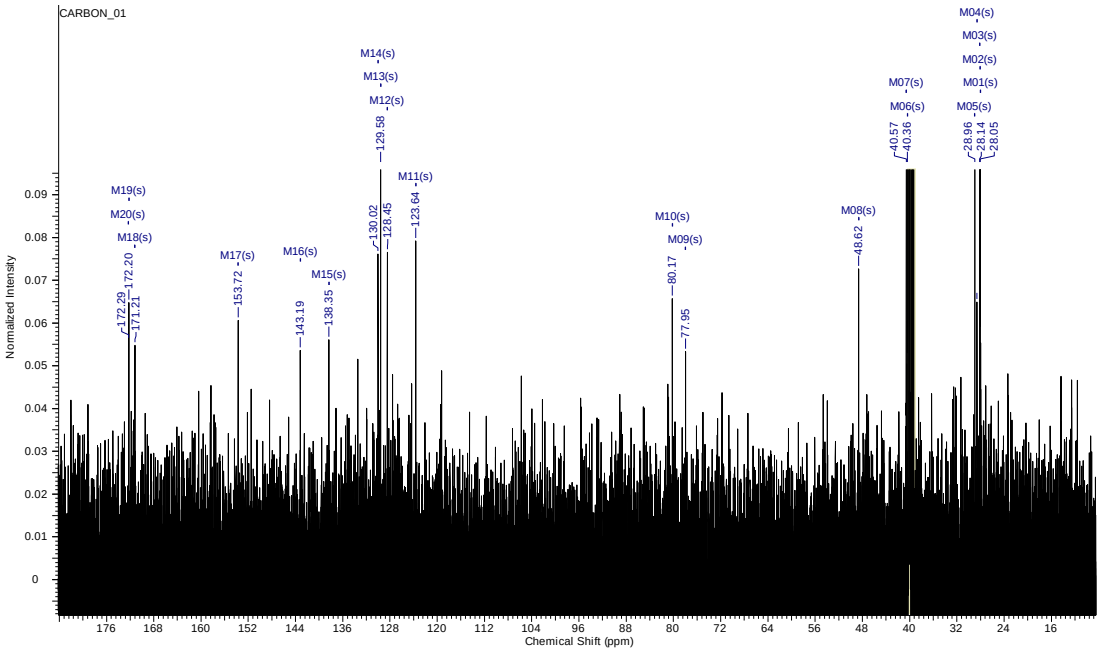

Figure S130. ^{13}C NMR (3S,7S,25R,28S)-tri-tert-butyl 33-azido-28-benzyl-25-(4-(tert-butoxy)benzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

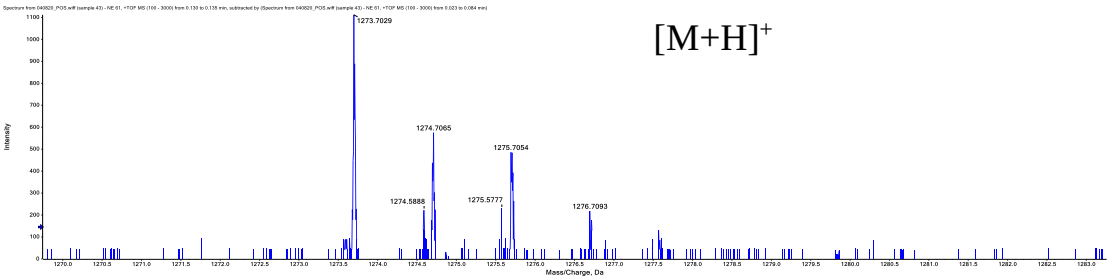

Figure S131. HRMS (3S,7S,25R,28S)-tri-tert-butyl 33-azido-28-benzyl-25-(4-(tert-butoxy)benzyl)-12-(3-chlorobenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylate.

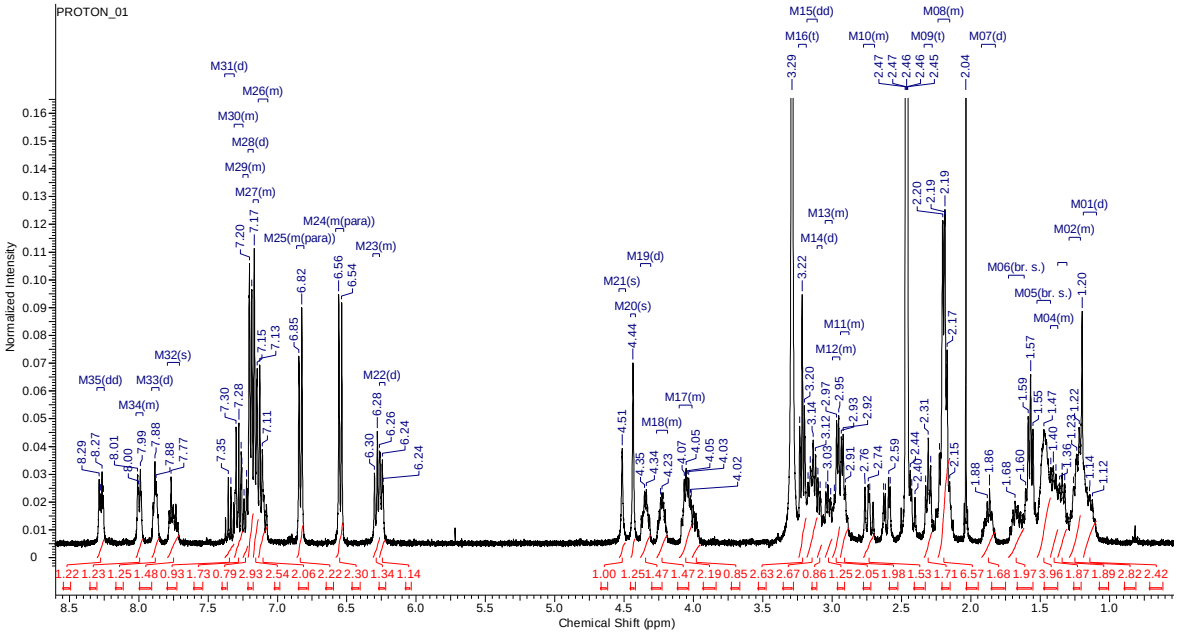

Figure S132. ^{1}H NMR (3S,7S,25R,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-25-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane--1,3,7-tricarboxylic acid (5).

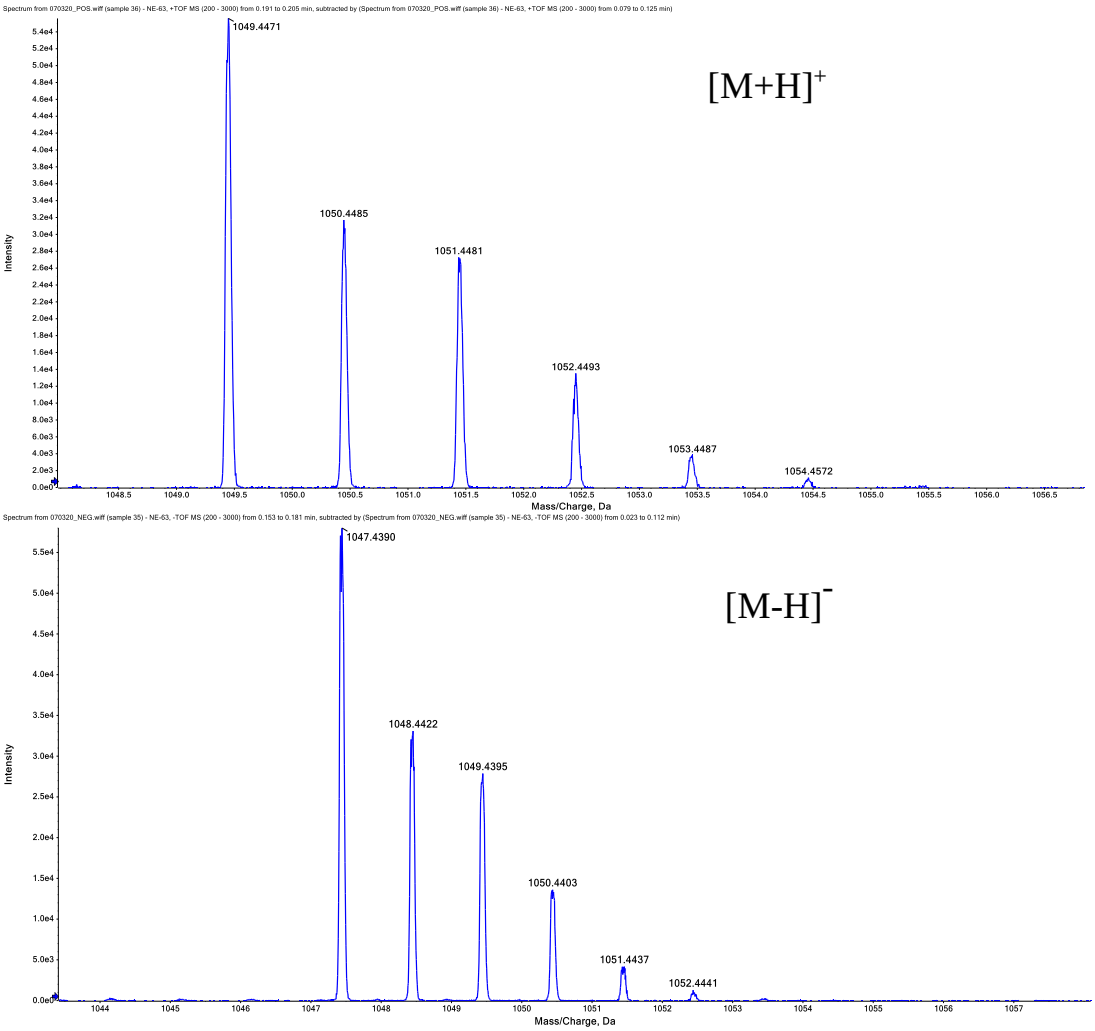

Figure S133. HRMS (3S,7S,25R,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)--25-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane--1,3,7-tricarboxylic acid (5).

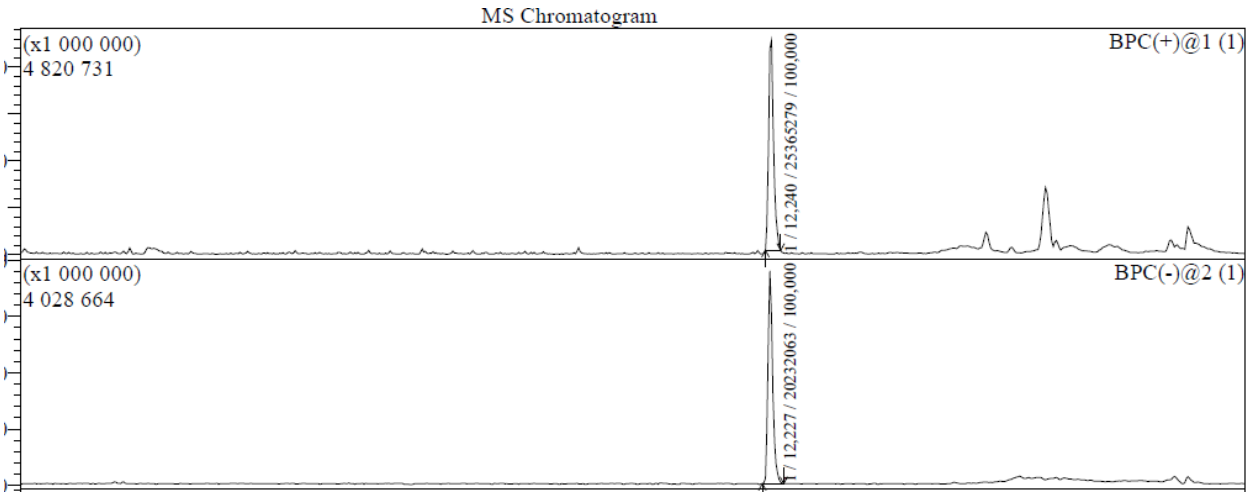

Figure S134. HPLC-MS (3S,7S,25R,28S)-33-azido-28-benzyl-12-(3-chlorobenzyl)-25-(4-hydroxybenzyl)-5,13,20,23,26,29-hexaoxo-4,6,12,19,24,27,30-heptaazatritriacontane-1,3,7-tricarboxylic acid (5).