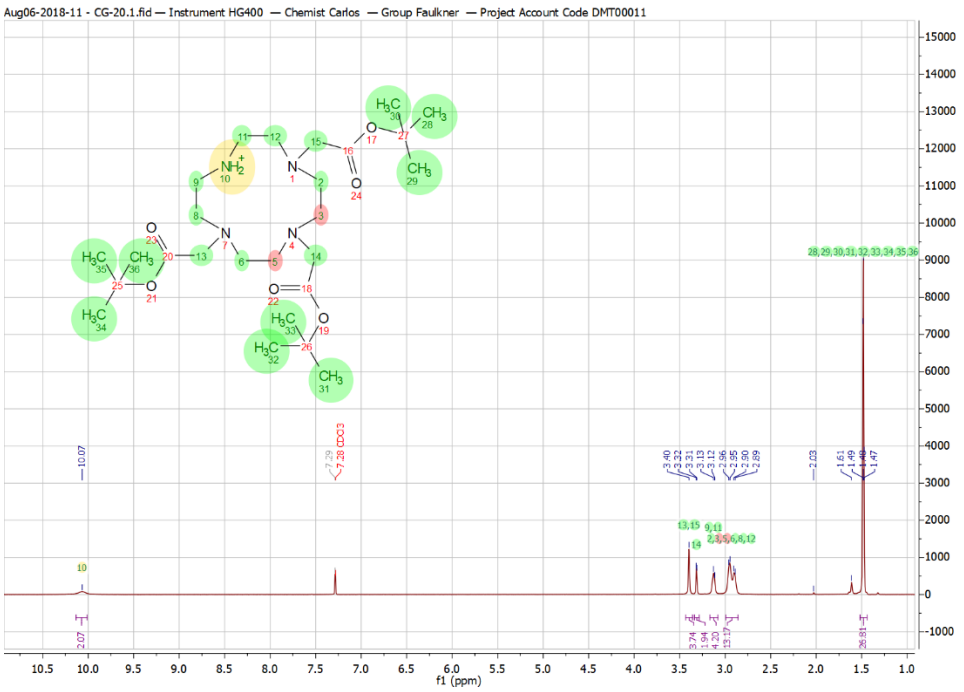
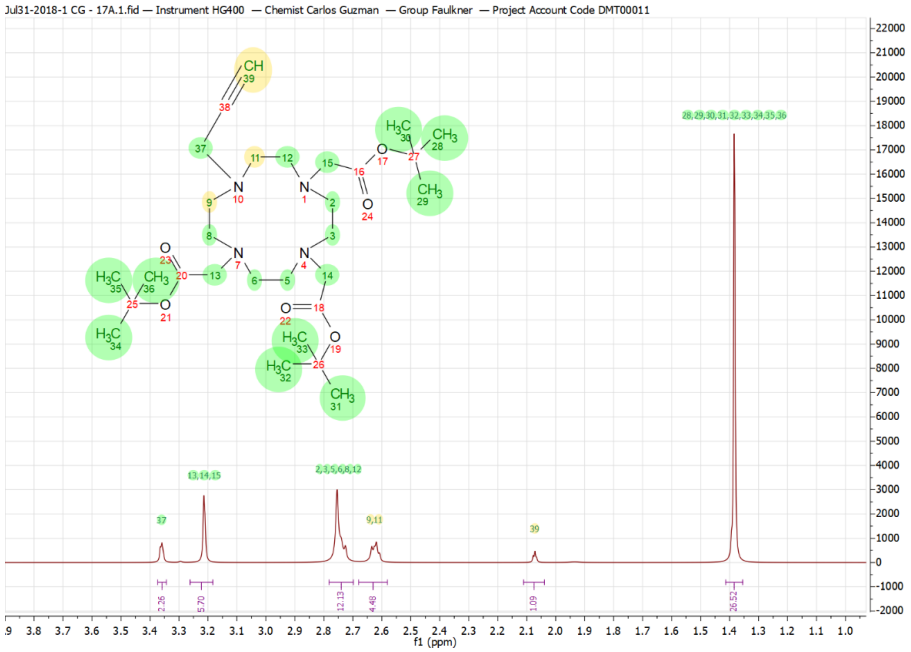


Scheme *S1.* *Triester, Compound 1.*

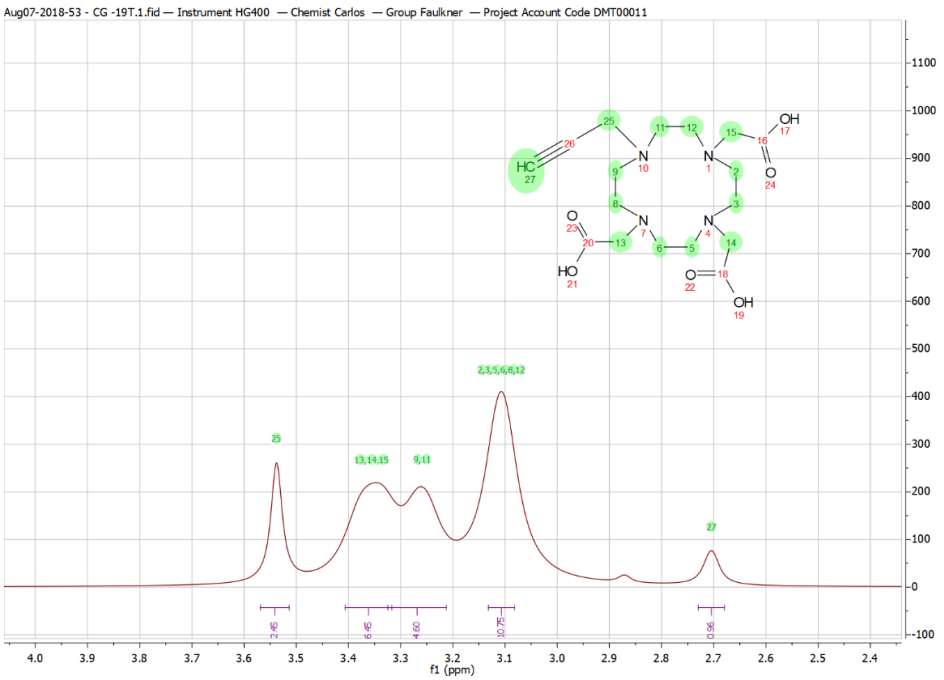
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 27 H), 2.89 – 2.95 (m, 12 H), 3.12 (d, 4 H), 3.31 (s, 2 H) and 3.40 (d, 4 H). Analysis calculated for $C_{26}H_{50}N_4O_6$: C, 60.67; H, 9.79; N, 10.89; O, 18.65%. Found: C, 60.62; H, 9.64; N, 10.19%. Purification: Hot toluene recrystallization.



Scheme *S2*. *Propargyl Triester, Compound 2.*

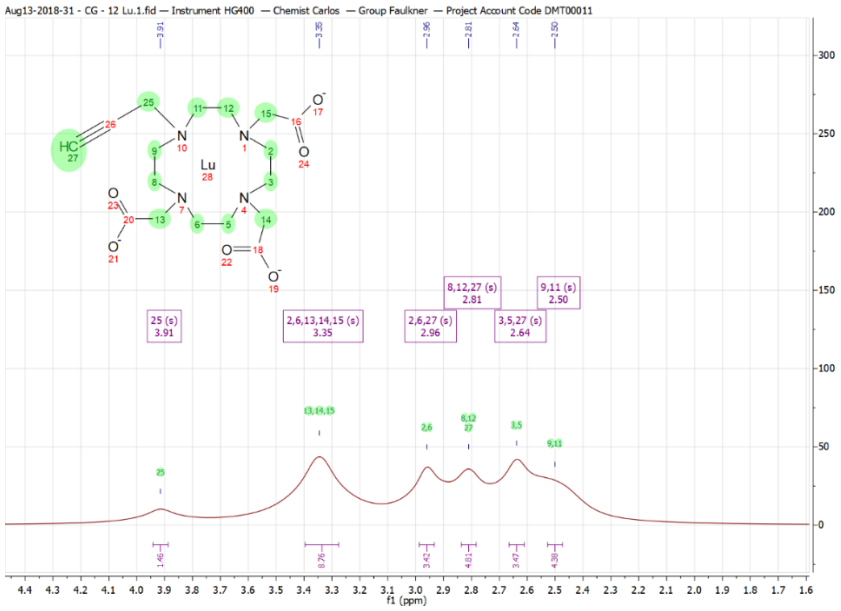
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 27 H), 2.08 (d, 1 H), 2.64 (m, 4 H), 2.75 (m, 12 H), 3.22 (d, 6 H) and 3.35 (d, 2 H). Analysis calculated for $C_{29}H_{52}N_4O_6$: C, 63.01; H, 9.48; N, 10.14%. Found: C, 62.87; H, 9.37; N, 10.26%. Purification: The inorganic solid was filtered, the solvent removed under reduced pressure to give an orange oil and it dissolved in 25 mL of Toluene. It was washed

with distilled water to remove the traces of inorganic salts, the organic layer was isolated and dried with Magnesium Sulphate, filtered and the solvent removed under reduced pressure.



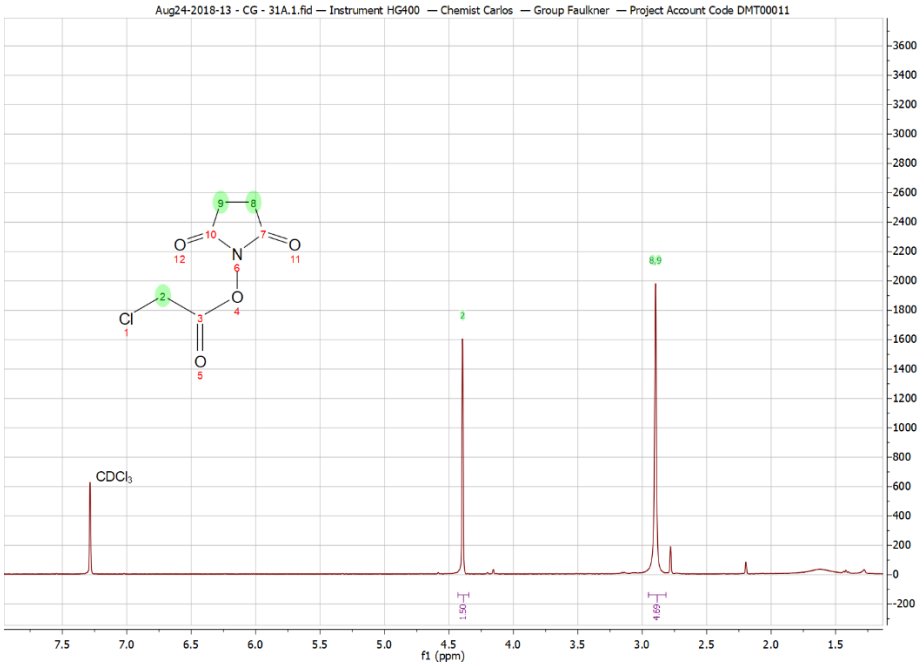
Scheme *S3.* *Propargyl DO3A, Compound 3.*

^{1}H NMR (400 MHz, D_2O): δ = 2.70 (s, 1 H), 3.12 (s, 11 H), 3.27 (s, 5 H), 3.35 (s, 6 H) and 3.55 (s, 2 H). Analysis calculated for $C_{17}H_{28}N_4O_6$: C, 53.11; H, 7.34; N, 14.57%. Found: C, 53.58; H, 7.81; N, 14.73%. Purification: The precipitate was filtered, and the solvent removed under reduced pressure.



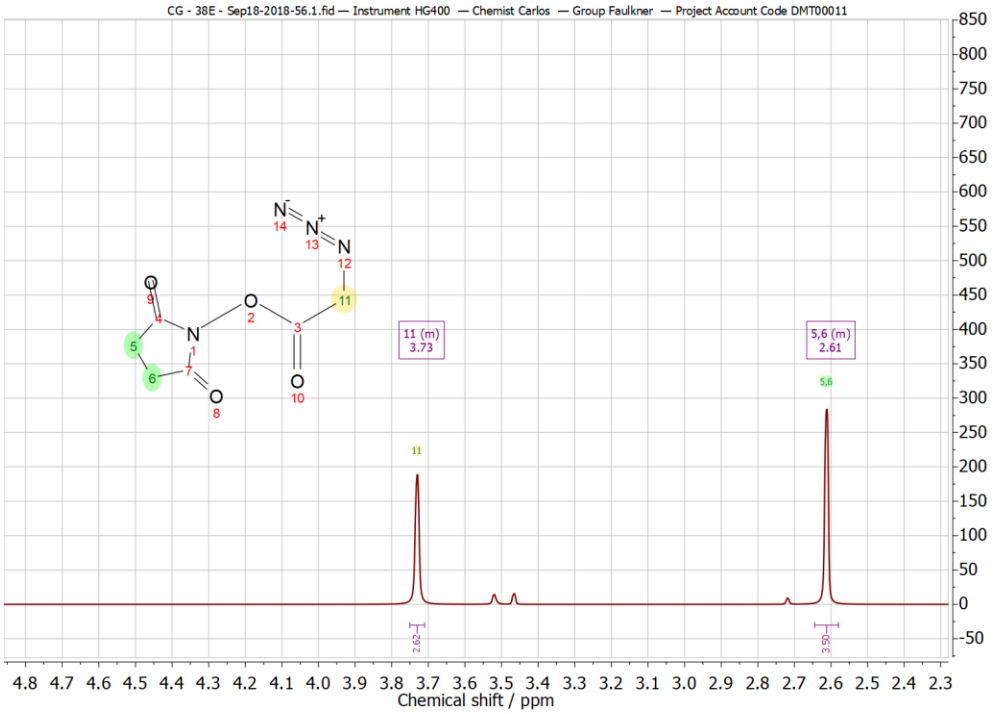
Scheme *S4*. *Lutetium-Propargyl DO3A, Compound 4.*

^{1}H NMR (400 MHz, D_2O): 2.50 (s, 4 H), 2.64 (s, 4 H), 2.81 (s, 5 H), 2.96 (s, 4 H), 3.35 (s, 6 H) and 3.91 (s, 2 H). Analysis calculated for $C_{18}H_{31}LuN_4O_6$: C, 37.64; H, 5.44; Lu, 30.46; N, 9.75%. Found: C, 37.40; H, 5.49; Lu, 30.08; N, 9.84%. Purification: Lyophilization.



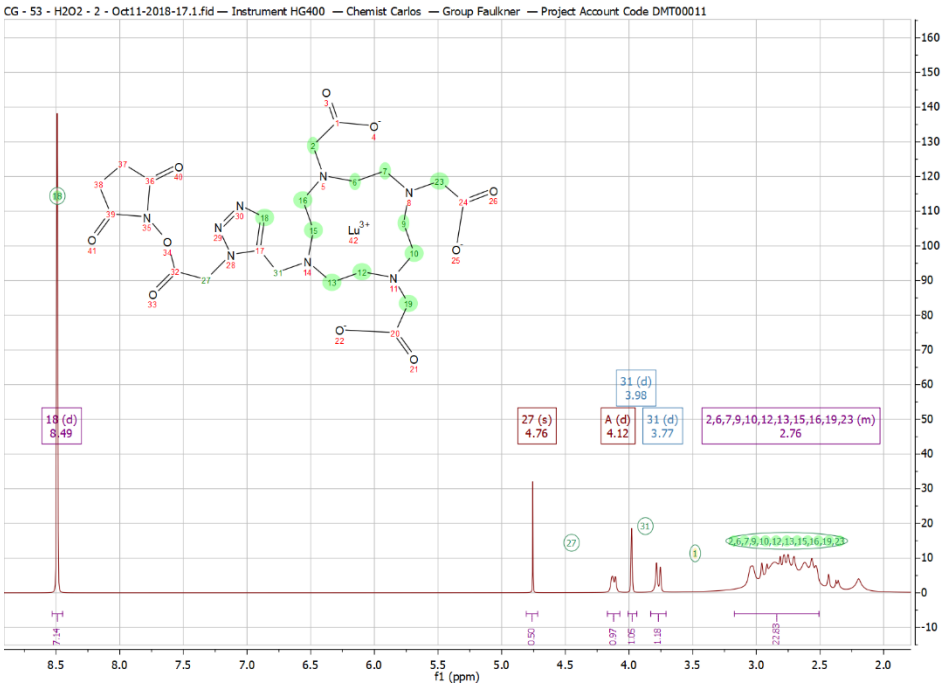
Scheme *S5.* *Compound 5.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.98 (s, 4 H) and 4.48 (s, 2 H). Analysis calculated for $C_6H_6ClNO_4$: C, 37.62; H, 3.16; Cl, 18.51; N, 7.31%. Found: C, 37.48; H, 3.09; Cl, 18.60; N, 7.28%. Purification: To the resulting solution was added 1.32 mL of Ethyl Acetate (EtOAc) and 9.6 mL of Hexane (Hex), the mixture was cooled down to 0 °C and stirred for 2 h. The white solid precipitated was filtered and washed with 80 mL ice cold portions of Hex:EtOAc (4:1), 9:1 and finally Hex twice. The solid was dried under reduce pressure.



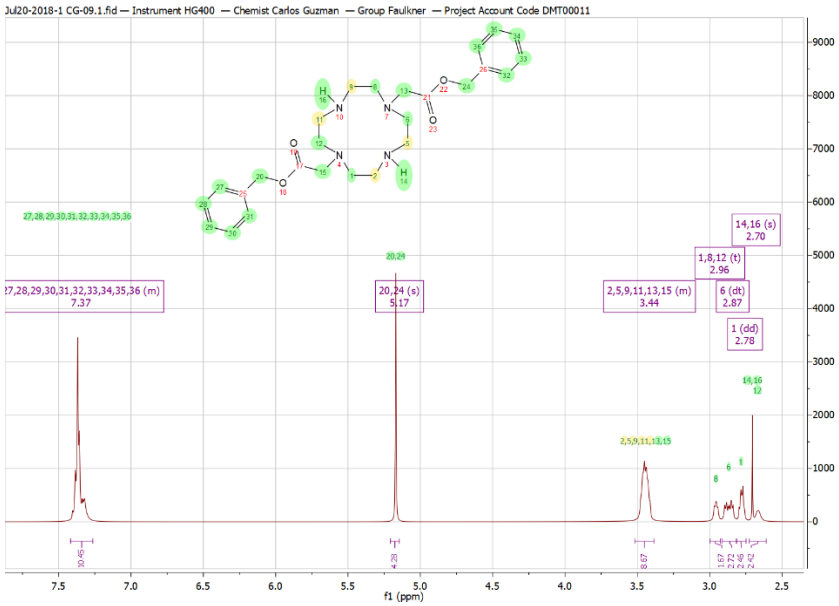
Scheme *S6.* *Compound 6.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.61 (m, 4 H) and 3.73 (m, 3 H). Analysis calculated for $C_6H_6N_4O_4$: C, 36.37; H, 3.05; N, 28.28%. Found: C, 36.31; H, 3.09; N, 28.68%. Purification: The product was extracted with Diethyl Ether and dried with Magnesium Sulphate.



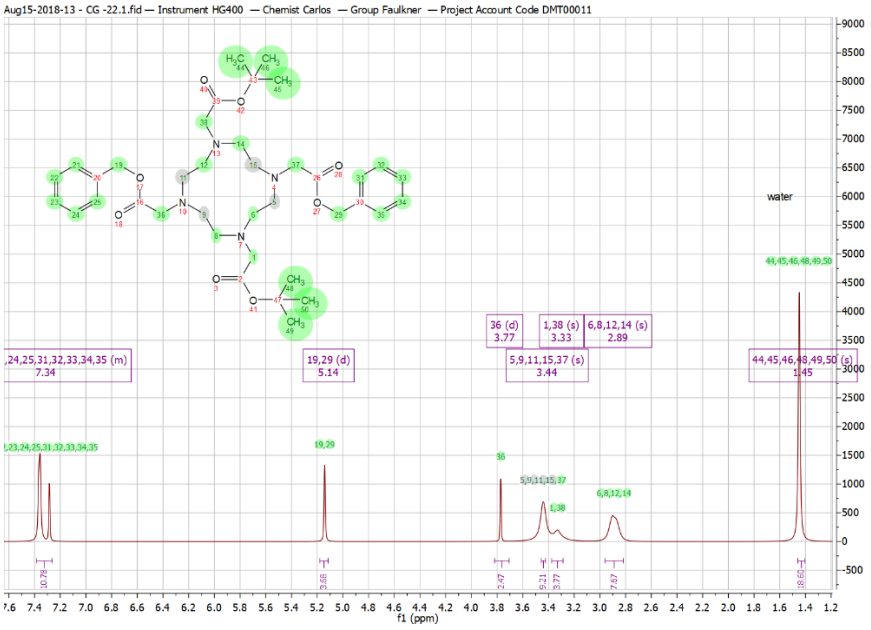
Scheme *S7.* *TMo1, Compound 7.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 – 3.10 (m, 23 H), 3.77 (d, 1 H), 3.98 (d, 1 H), 4.12 (d, 1 H), 4.76 (s, 1 H) and 8.49 (d, 1 H). Analysis calculated for $C_{20}H_{34}LuN_7O_8$: C, 35.56; H, 5.07; Lu, 25.90; N, 14.51%. Found: C, 35.65; H, 5.02; Lu, 25.83; N, 14.48%. Purification: Lyophilization and dialysis.



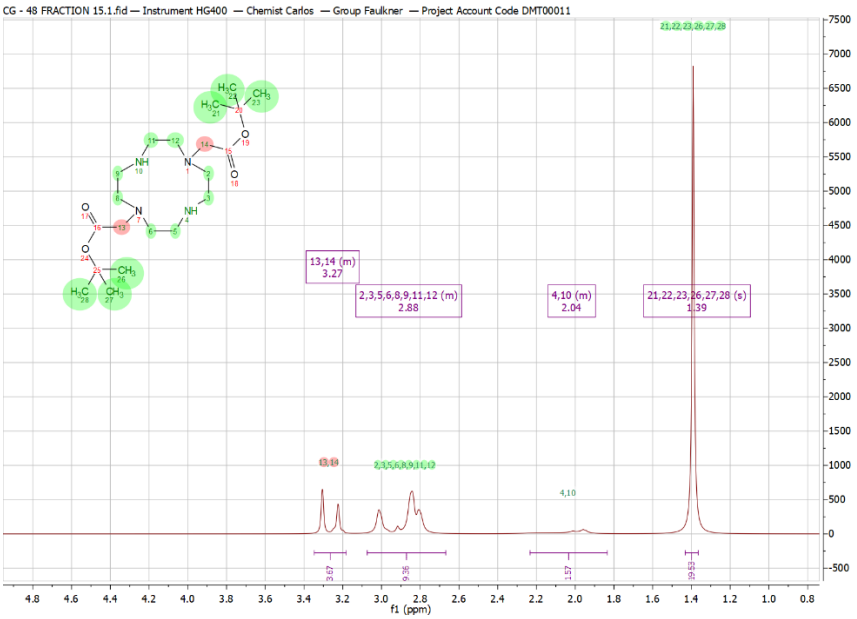
Scheme *S8.* *Compound 8.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.70 (s, 2H), 2.78 (dd, 2 H), 2.87 (dt, 2H), 2.96 (t, 2 H), 3.44 (m, 9 H), 5.17 (s, 4 H) and 7.37 (m, 10 H). Analysis calculated for $C_{24}H_{32}N_4O_4$: C, 65.43; H, 7.32; N, 12.72%. Found: C, 65.53; H, 7.21; N, 12.48%. Purification: The solvent was removed under reduced pressure to obtain a transparent oil.



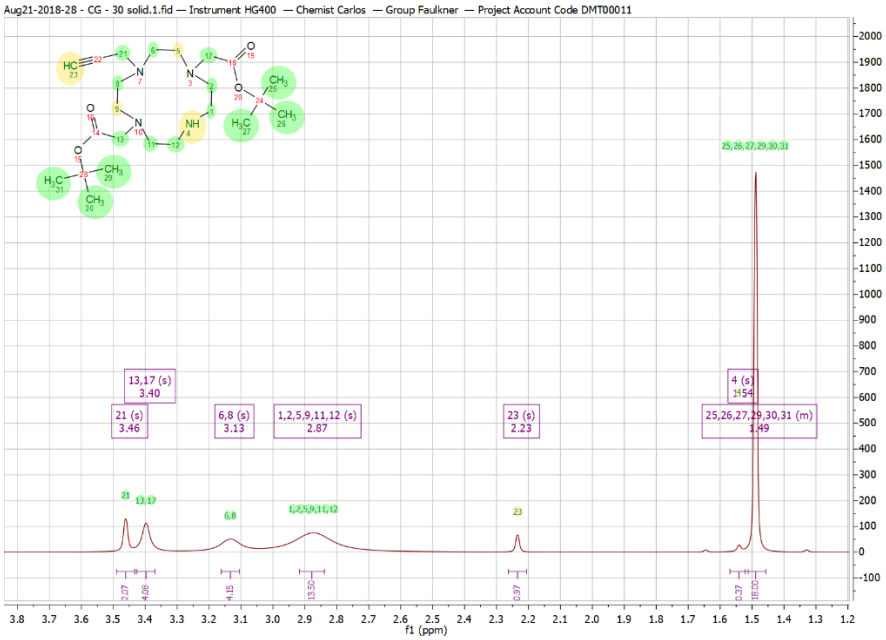
Scheme *S9*. *Compound 9.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 18 H), 2.89 (s, 8 H), 3.33 (s, 4 H), 3.44 (s, 10 H), 3.77 (d, 2 H), 5.14 (d, 4 H) and 7.23 – 7.34 (m, 10 H). Analysis calculated for $C_{36}H_{52}N_4O_8$: C, 64.65; H, 7.84; N, 8.38%. Found: C, 64.62; H, 7.97; N, 8.15%. Purification: The excess of the inorganic solid was filtered using a Celite pad and washed with Acetonitrile (3 x 20 mL), the filtered was recovered and the solvent removed under reduced pressure to give a pale oil, which was washed with distilled water to removed completely the inorganic salts, partitioned with Chloroform (3 x 20 mL) and 30 mL of water. The organic layer was recovered and dried with Magnesium Sulphate and dried under reduced pressure.



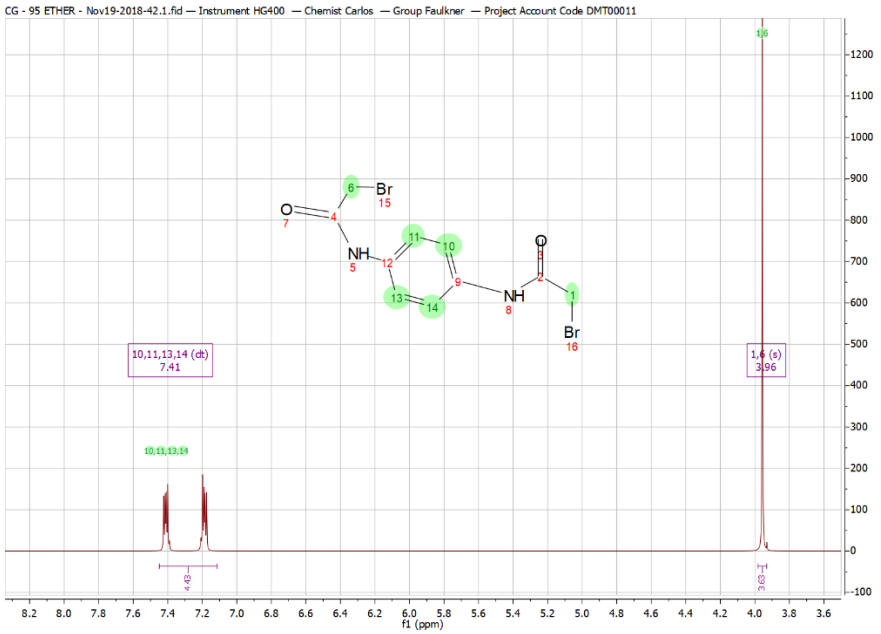
Scheme *S10.* *Compound 10.*

^{1}H NMR (400 MHz, D_2O): δ = 1.39 (s, 20 H), 2.04 (m, 2 H), 2.88 (m, 10 H) and 3.57 (m, 10 H). Analysis calculated for $C_{20}H_{40}N_4O_4$: C, 59.97; H, 10.07; N, 13.99%. Found: C, 60.08; H, 10.02; N, 14.06%. Purification: The Pd/C was filtered twice using a Celite pad and the solvent remove under reduce pressure to give a transparent oil.



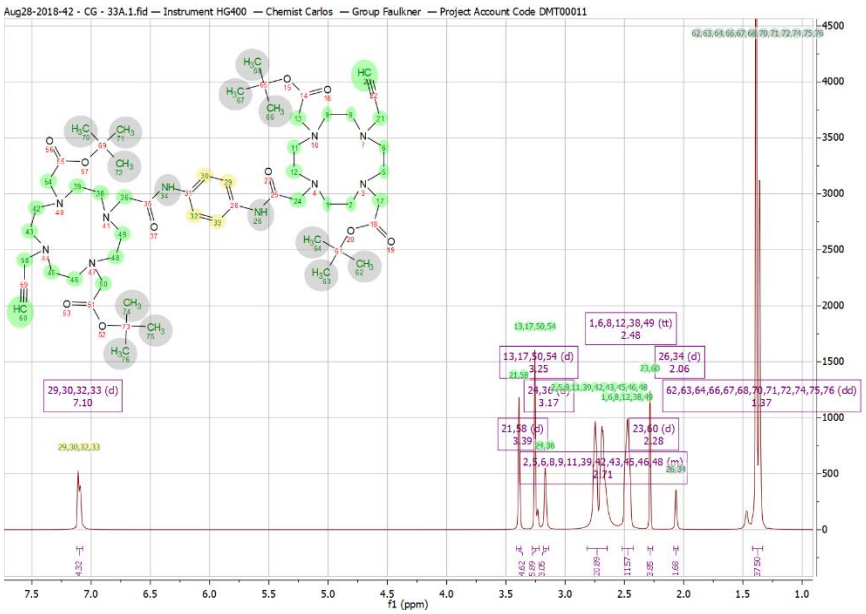
Scheme *S11.* *Compound 11.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 (s, 18 H), 1.54 (s, 1 H), 2.23 (s, 1 H), 2.87 (s, 14 H), 3.13 (s, 4 H), 3.40 (s, 4 H) and 3.46 (s, 2 H). Analysis calculated for $C_{23}H_{42}N_4O_4$: C, 62.98; H, 9.65; N, 12.77%. Found: C, 62.95; H, 9.57; N, 12.49%. Purification: The excess of Potassium Carbonate was filtered; the solvent removed under reduced pressure to get an orange oil and was partitioned in 20 mL of water and extracted with toluene (3 x 20 mL). The extractions were combined, dried with Magnesium Sulphate and solvent reduced under reduced pressure.



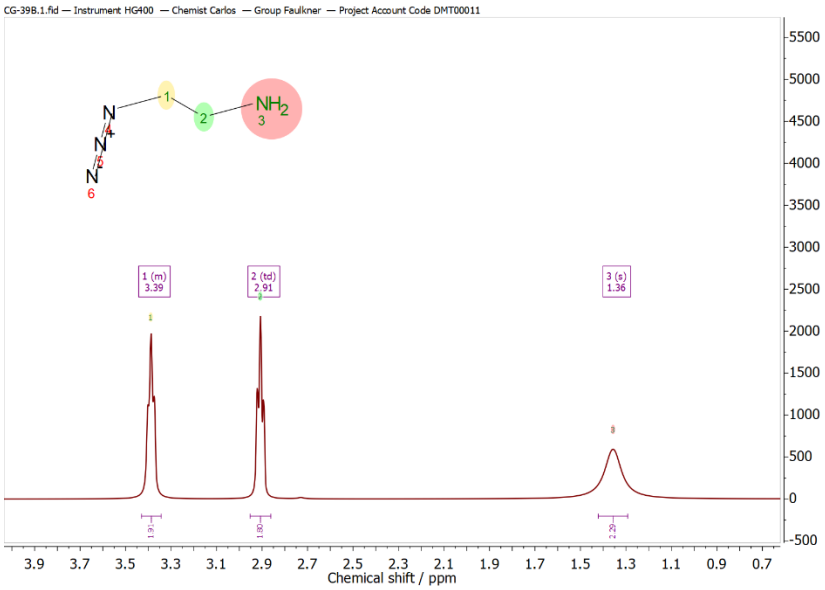
Scheme *S12.* *Compound 12.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96 (s, 4 H) and 7.20 – 7.41 (dt, 4 H). Analysis calculated for $C_{11}H_{14}Br_2N_2O_2$: C, 36.09; H, 3.85; Br, 43.66; N, 7.65%. Found: C, 35.98; H, 3.83; Br, 43.79; N, 7.57 %. Purification: The pink solid was filtered and washed with a saturate solution of Sodium Bicarbonate and water, and dried under vacuum to obtain a pink volatile powder.



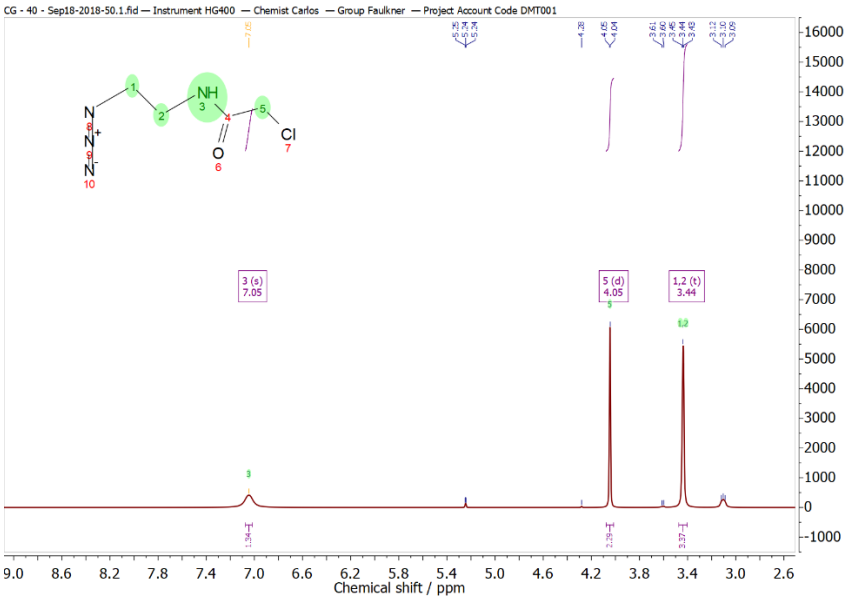
Scheme *S13.* *Compound 13.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (dd, 38 H), 2.06 (d, 2 H), 2.28 (d, 4 H), 2.48 (tt, 12 H), 2.71 (m, 20 H), 3.17 (d, 3 H), 3.25 (d, 6 H), 3.39 (d, 5 H) and 7.10 (d, 4 H). Analysis calculated for $C_{56}H_{92}N_{10}O_{10}$: C, 63.13; H, 8.70; N, 13.15%. Found: C, 63.08; H, 8.72; N, 13.19%. Purification: The inorganic solids were filtered, the solvent removed under reduced pressure to obtain a red oil, purified by FCC DCM:MeOH:Toluene (5:1:0.5), R_f = 0.34.



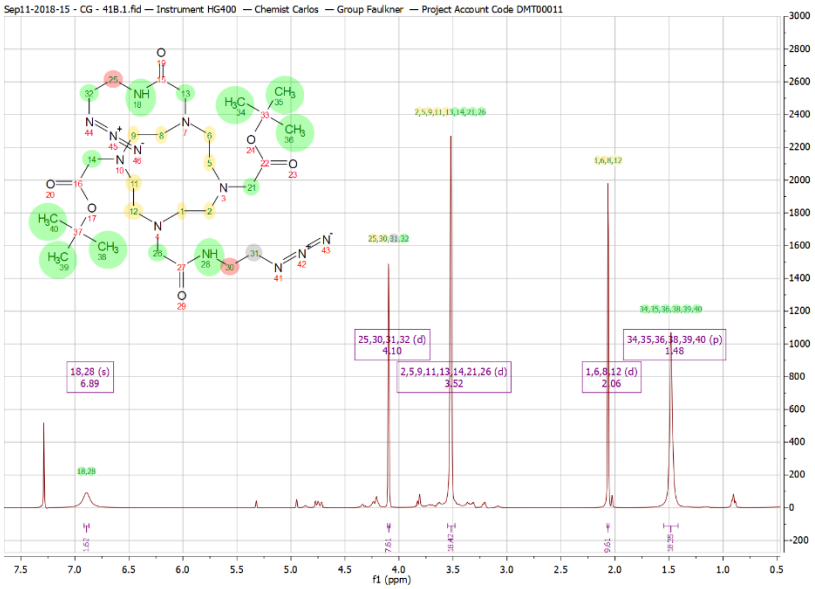
Scheme *S14*. *Compound 14.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 2 H), 2.91 (td, 2 H) and 3.39 (m, 2 H). Analysis calculated for $C_2H_6N_4$: C, 27.90; H, 7.02; N, 65.07%. Found: C, 27.57; H, 7.12; N, 65.30%. Purification: The solution was concentrated until get a colorless and highly volatile oil.



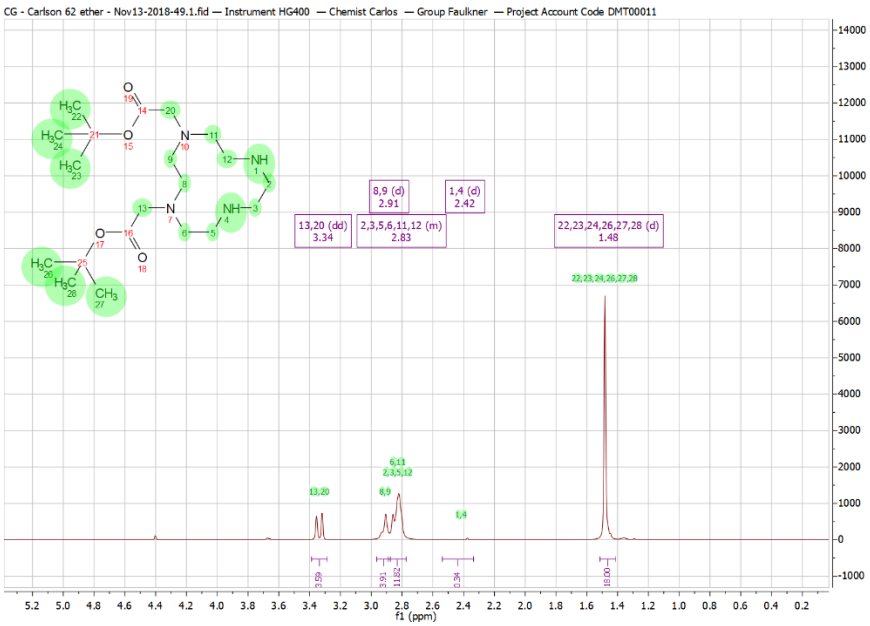
Scheme *S15.* *Compound 15.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.44 (t, 4 H), 4.05 (d, 2 H) and 7.05 (s, 1 H). Analysis calculated for $C_4H_7ClN_4O$: C, 29.55; H, 4.34; Cl, 21.81; N, 34.46%. Found: C, 30.03; H, 4.17; Cl, 21.71; N, 34.54%. Purification: The solution was washed with Hydrochloric Acid 1M (2 x 25 mL) and extracted with Dichloromethane (2 x 25 mL) and dried with Magnesium Sulphate. FCC Cyclohexene:Ethyl Acetate (3:2), R_f = 0.28



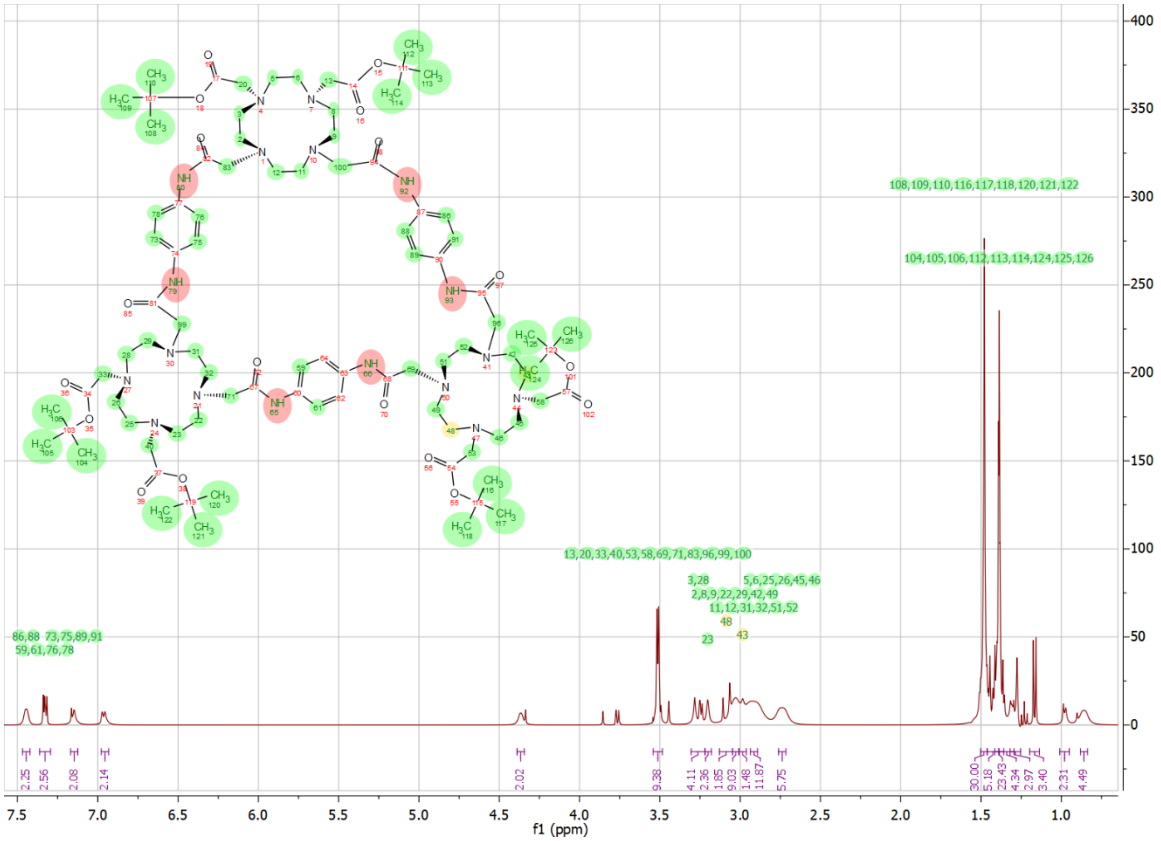
Scheme *S16.* *Compound 15.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (p, 18 H), 2.06 (8 H), 3.52 (d, 18 H), 4.10 (d, 8 H) and 6.89 (s, 2 H). Analysis calculated for $C_{28}H_{52}N_{12}O_6$: C, 51.52; H, 8.03; N, 25.75%. Found: C, 51.46; H, 7.98; N, 25.53%. Purification: The inorganic solids were filtered using a Celite pad, solvent was removed under reduced pressure and partitioned in 20 mL of water, extracted with Ethyl Acetate (2 x 20 mL) and dried with Magnesium Sulphate, concentrate under reduced pressure and triturate with hexane. The solid was isolated and purified by preparative TLC of DCM:MeOH:TEA (7:1:0.01) R_f = 0.57 to give a yellow oil.



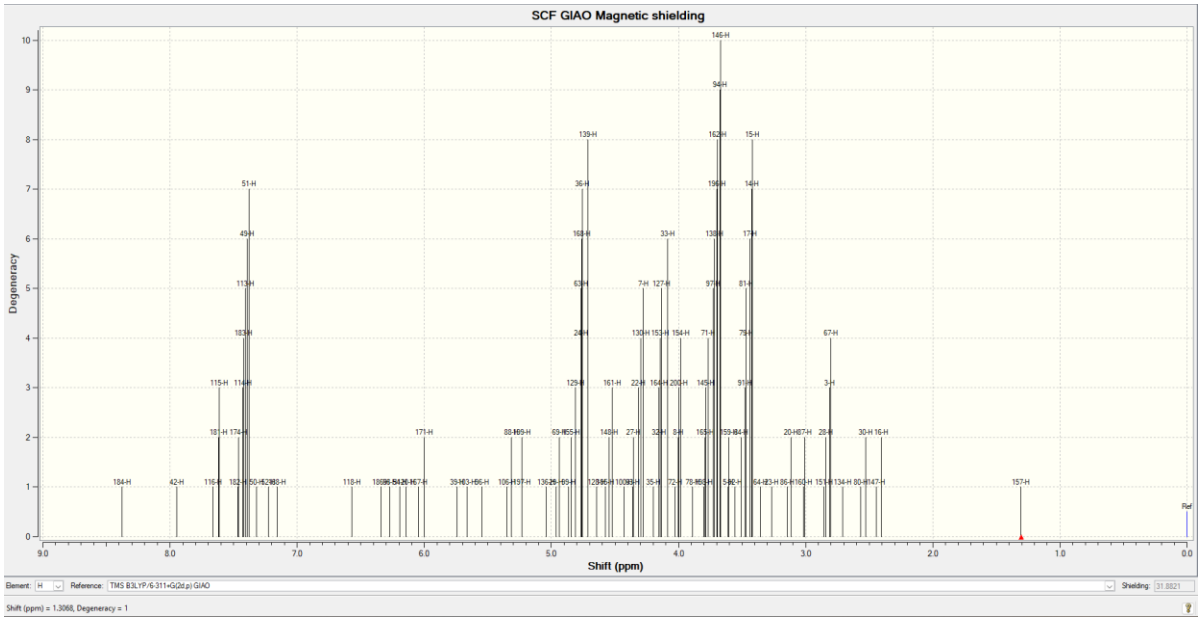
Scheme *S17.* *Compound 16.*

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (s, 18 H), 2.42 (d, 0.34 H), 2.83 (m, 12 H), 2.91 (d, 4 H) and 3.34 (dd, 4 H). Analysis calculated for $C_{20}H_{40}N_4O_4$: C, 59.97; H, 10.07; N, 13.76%. Found: C, 59.94; H, 10.01; N, 14.06%. Purification: The solvent was removed under reduced pressure, re-dissolved in 10 mL of water, adjusted the pH between 11 – 12 by addition of Sodium Hydroxide and extracted with Chloroform (4 x 15 mL), dried with Sodium Sulphate and the solvent removed under reduced pressure, re-dissolved in the minimal amount of DCM and triturate with Hexane and recrystallized with Methanol.

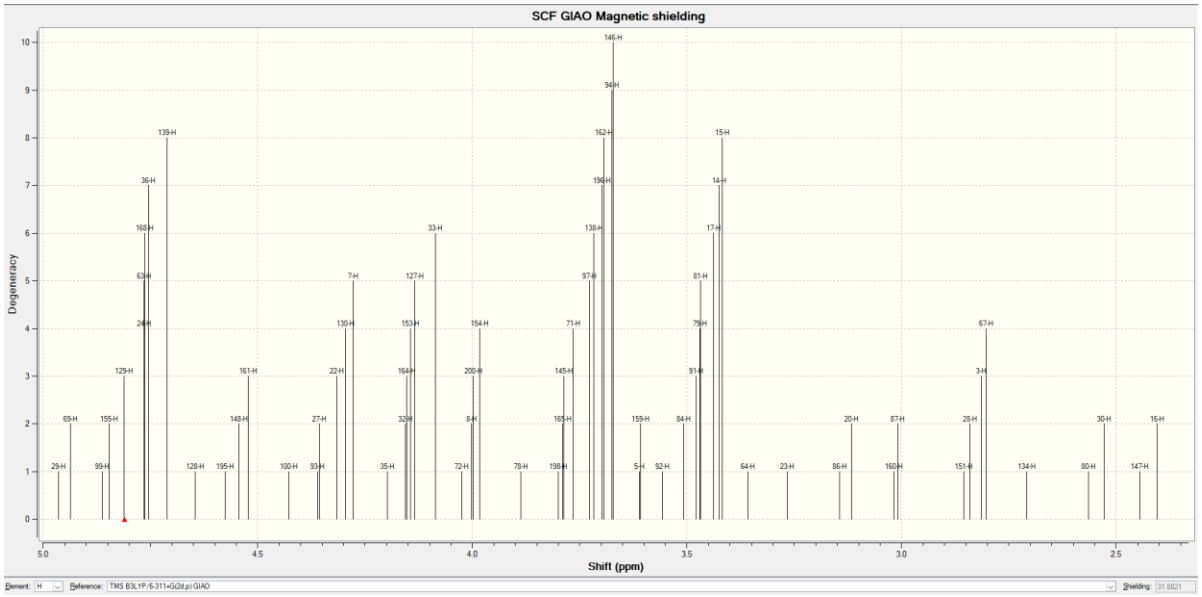


Scheme *S18.* *Possible compound obtained.*

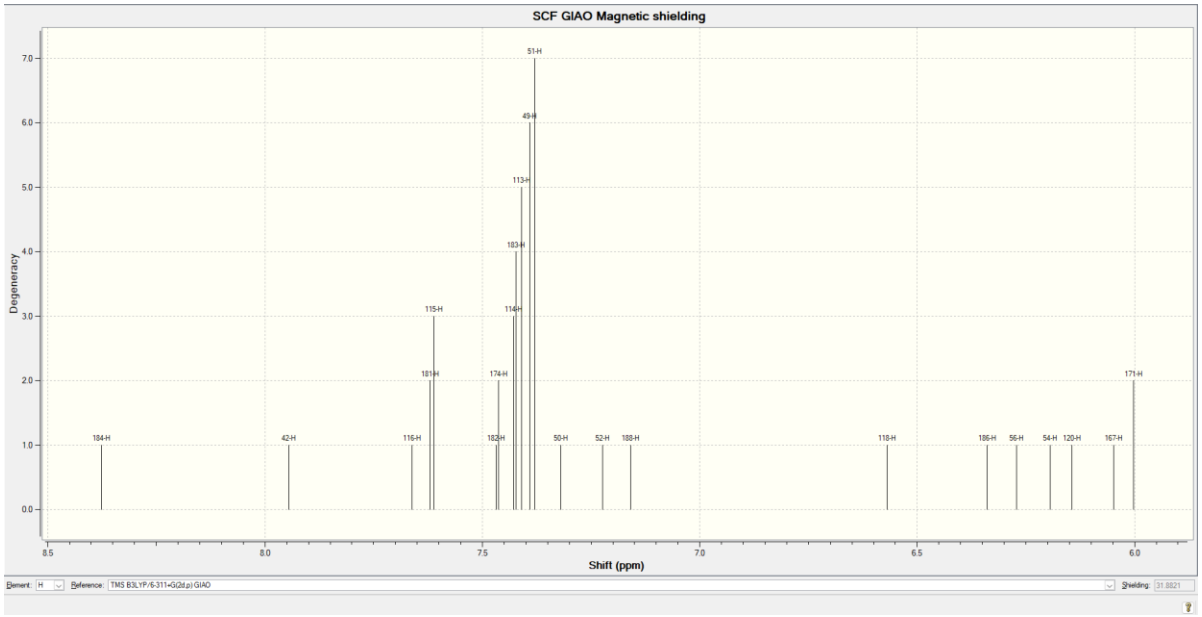
Purification: in order to purify the samples by FCC and TLC, two solutions were used as eluents. To obtain a low RF for unreacted starting materials with a high relative polarity, polar eluents (DCM(90%):MeOH (9.9%):TEA(0.1%)) were used, while nonpolar eluents (Toluene(30%):Hexane(69.9%):TEA(0.1%)) were used to separate multiple products with significantly lower polarity after each reaction.



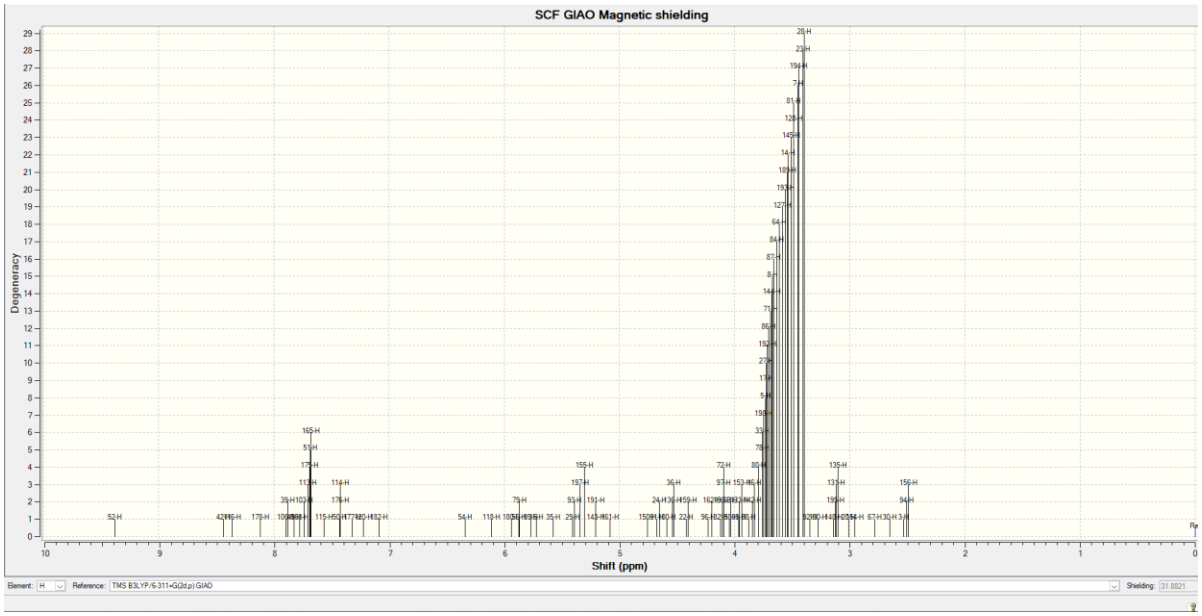
Scheme *S19*. *Predicted ^{1}H-NMR open trimer.*



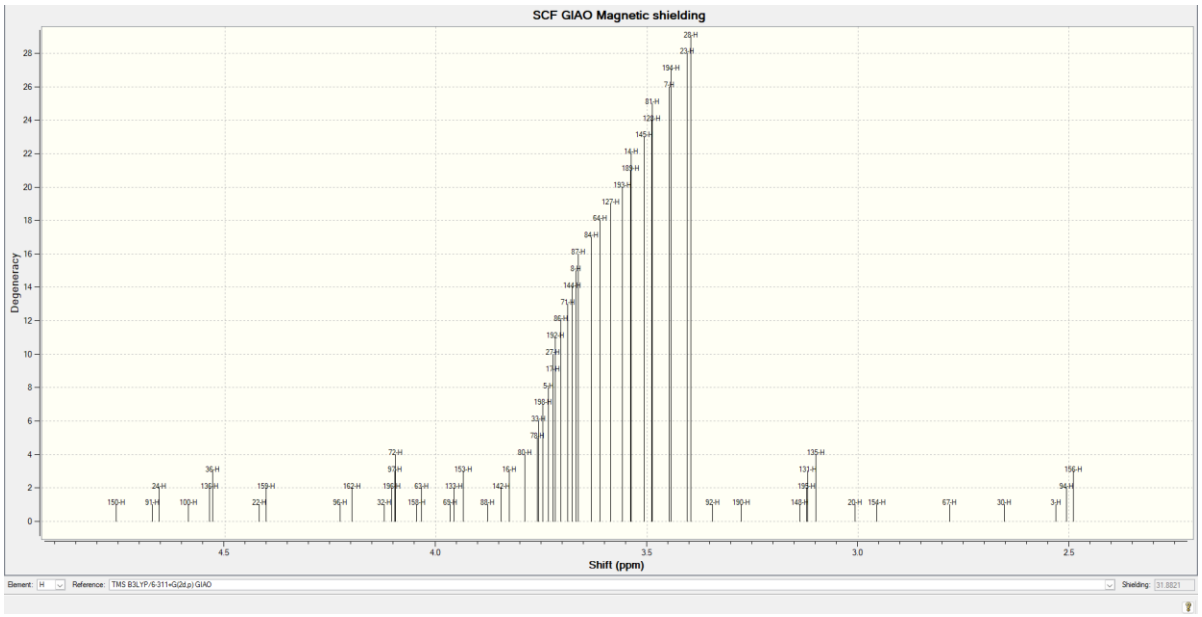
Scheme *S20*. *Predicted ^{1}H-NMR open trimer, range 2 - 5 ppm.*



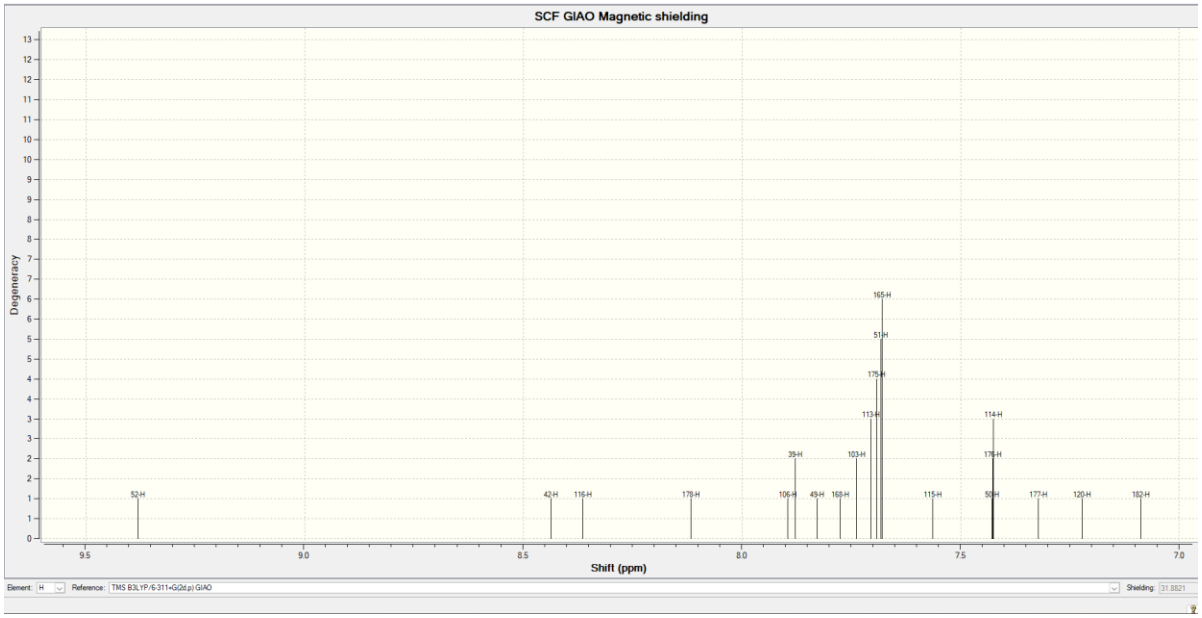
Scheme *S21.* *Predicted ^{1}H-NMR open trimer, range 6 - 9 ppm.*



Scheme *S22.* *Predicted ^{1}H-NMR closed trimer.*

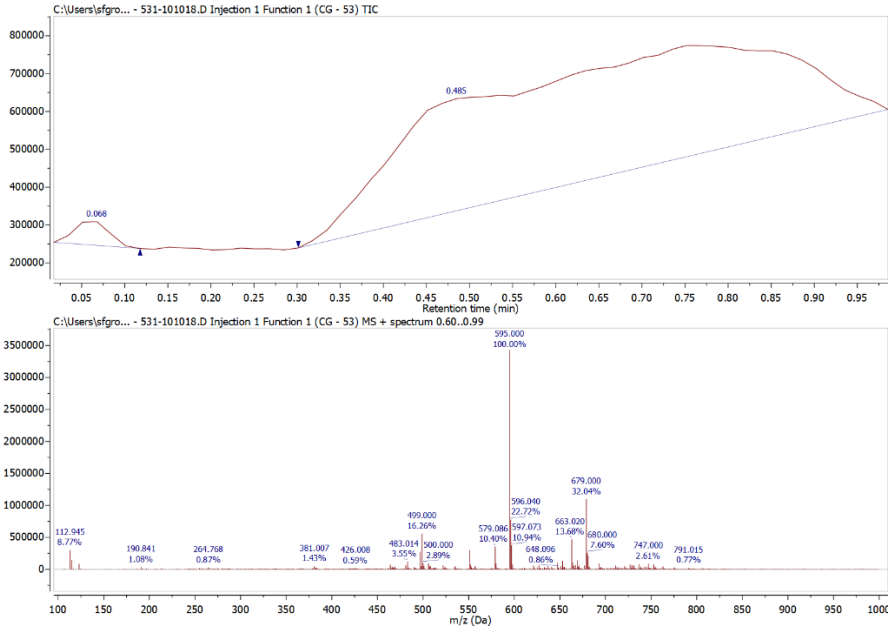


Scheme *S23.* *Predicted ^{1}H-NMR closed trimer, range 2 - 5 ppm.*



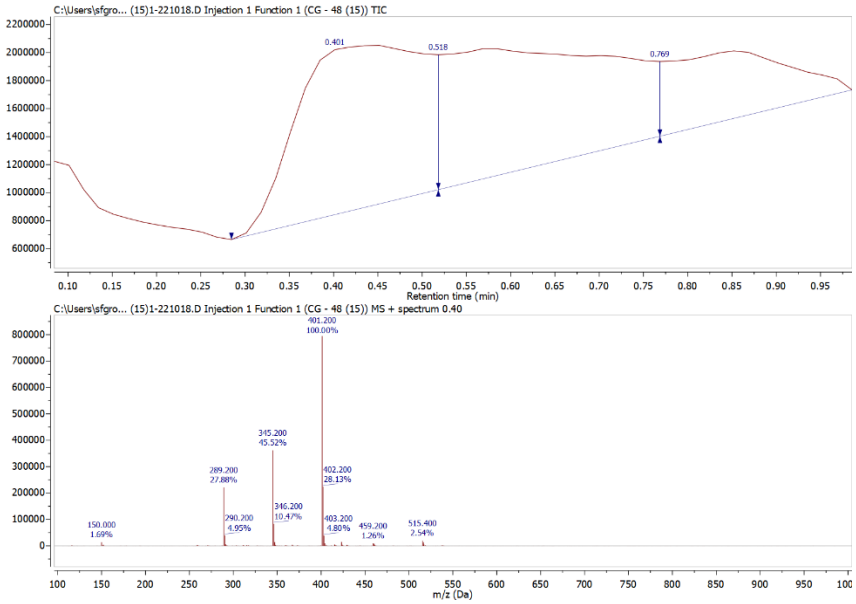
Scheme *S24*. *Predicted 1H-NMR closed trimer, range 7 - 10 ppm.*

10.2 Mass Chromatogram



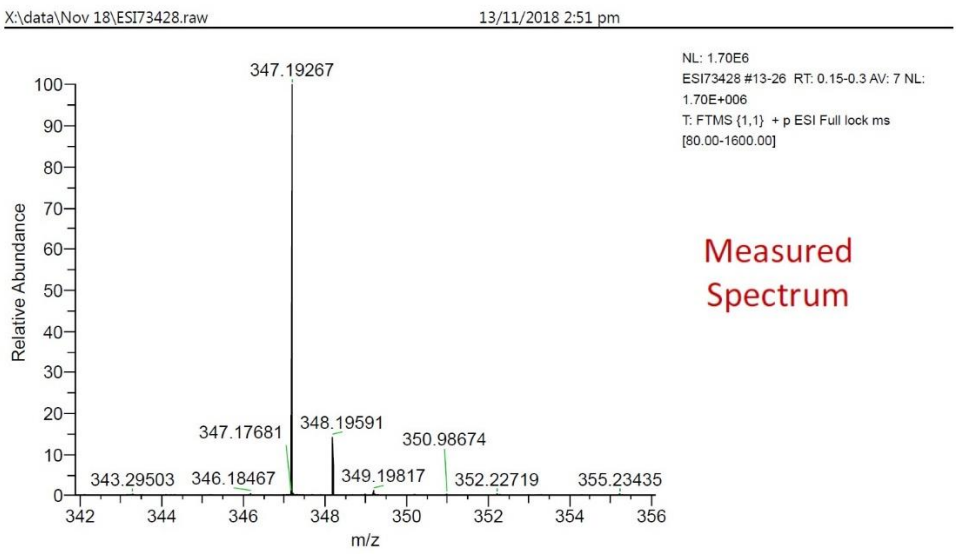
Chromatogram S1*. Compound 7.*

MS (TIC, 60 eV): *m/z* 747.000 ([M+Na]$^+$, 2.61%), 679.000 (32.04), 595.000 (100), 579.086 (10.40).



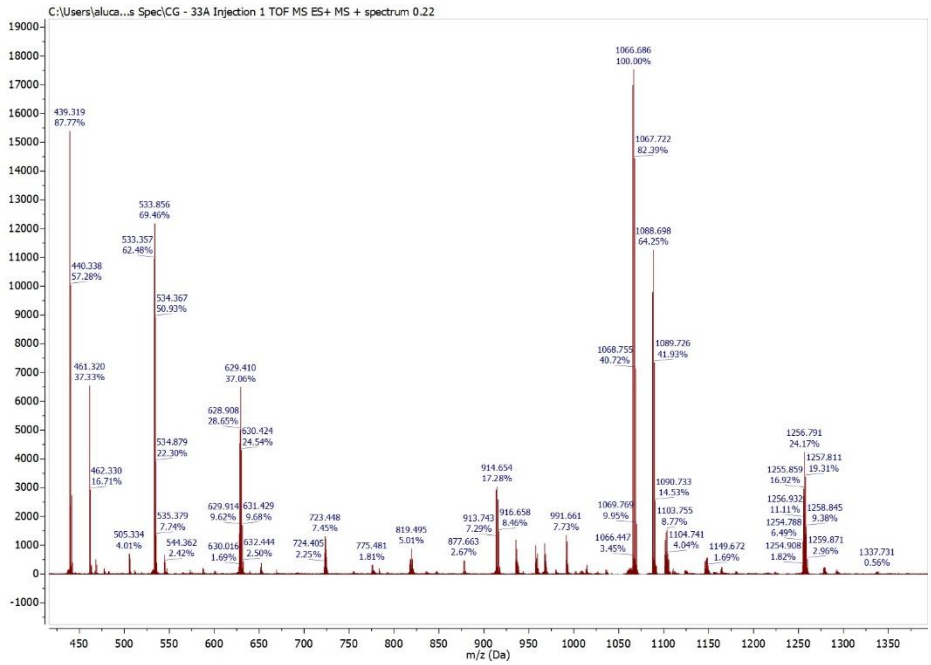
Chromatogram S2. *Compound 10.*

MS (TIC, 40 eV) : *m/z* 401.200 ([M+H]$^+$, 100%), 345.200 (45.52), 289.200 (27.88). M calculated for $C_{20}H_{40}N_4O_4$ was 400.300.



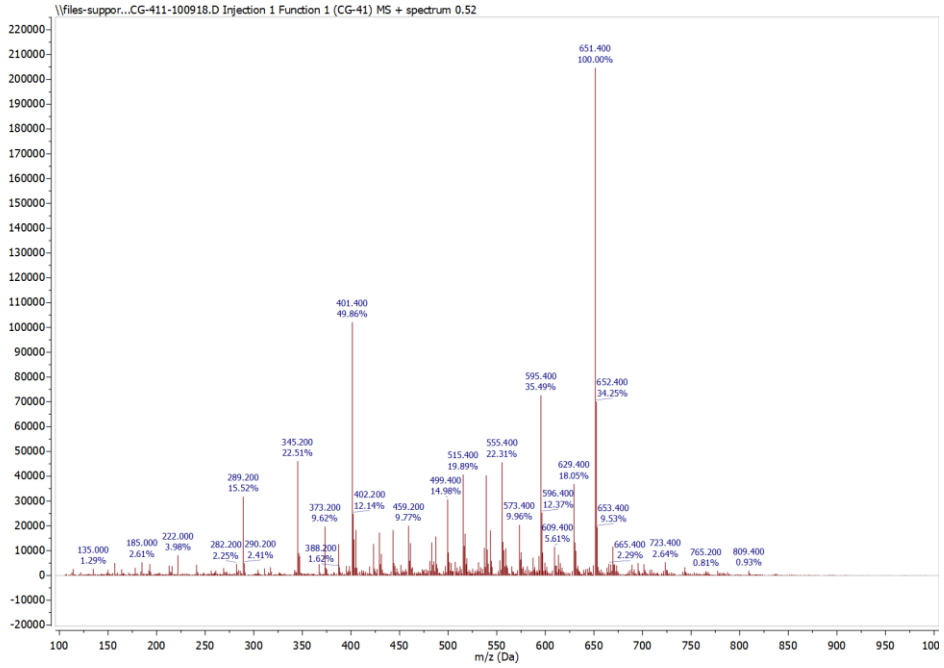
Chromatogram S3. *Compound 12.*

HRMS (ESI): *m/z* $[M]^+$ calculated for $C_{10}H_{10}Br_2N_2O_2$ was 349.9100; found 350.9867.



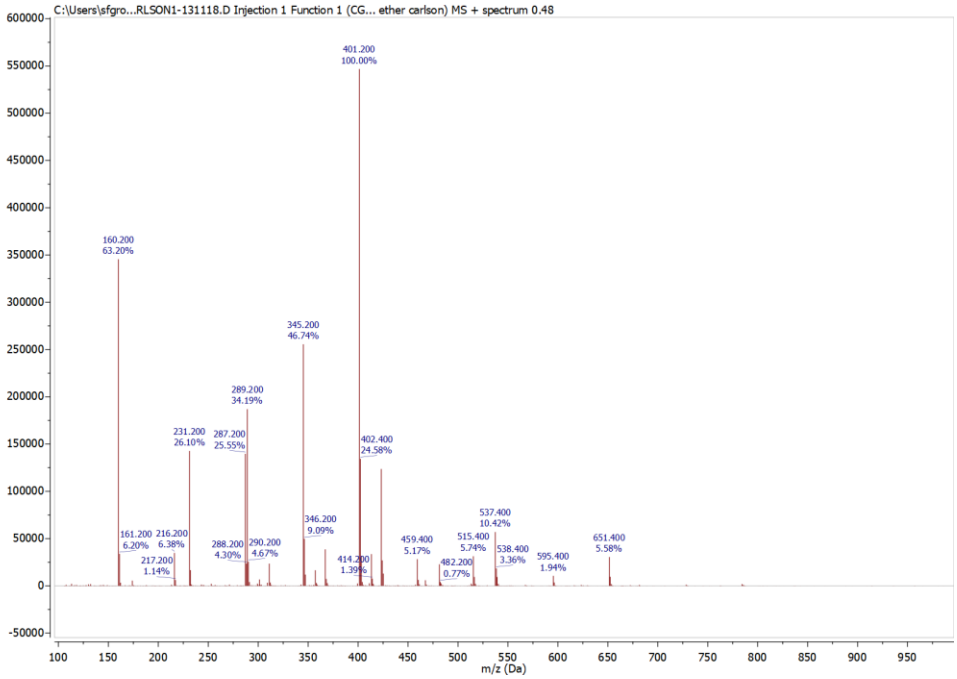
Chromatogram S4*. Compound 13.*

MS (TOF, 22 eV): *m/z* 1066.686 ($[M+2H]^+$, 100%), 629.410 (37.06), 533.856 (69.46) and 439.319 (87.77). M calculated for $C_{56}H_{92}N_{10}O_{10}$ was 1064.70.



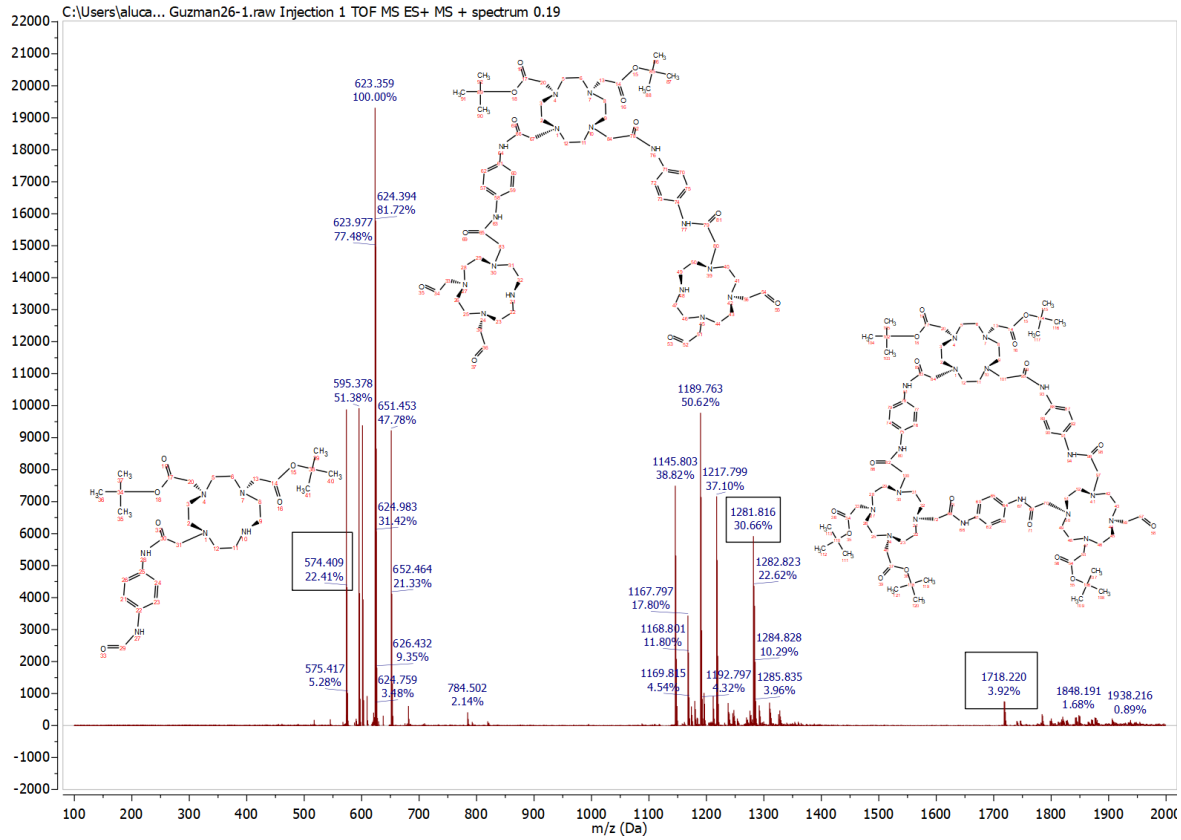
Chromatogram S5. *Compound 16.*

MS (TOF, 52 eV): m/z 680.445 (M+, 0%), 651.440 (100), 595.400 (35.49) and 401.400 (49.86).



Chromatogram S6. *Compound 17.*

MS (TIC, 48 eV): *m/z* 401.400 ($[M+H]^+$, 100%), 345.200 (34.19) and 289.200 (34.19).



***Chromatogram S7**. Possible compound obtained.*

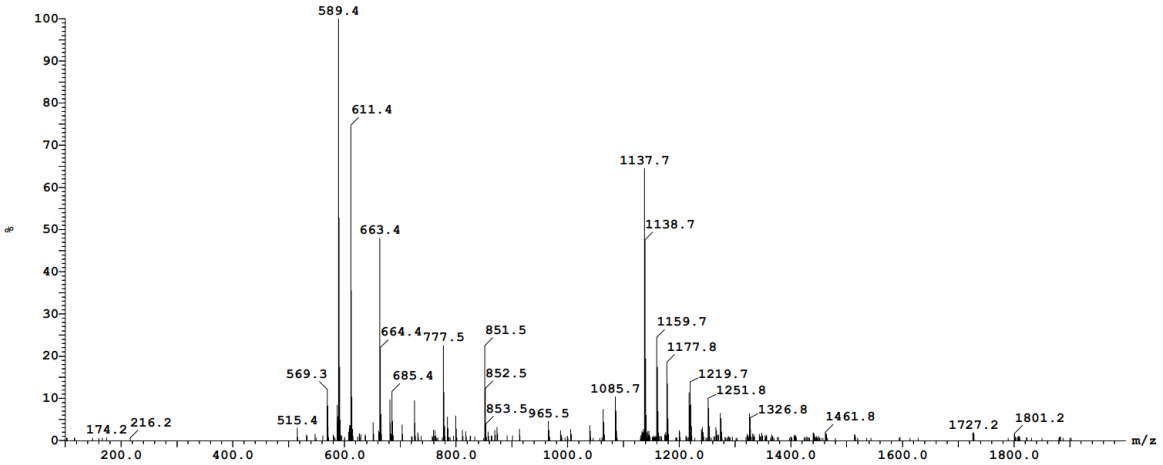
Sample Report:

Sample 1 Vial 2:34 ID CG - 98 File Carlos Guzman34-1 Date 26-Nov-2018 Description other

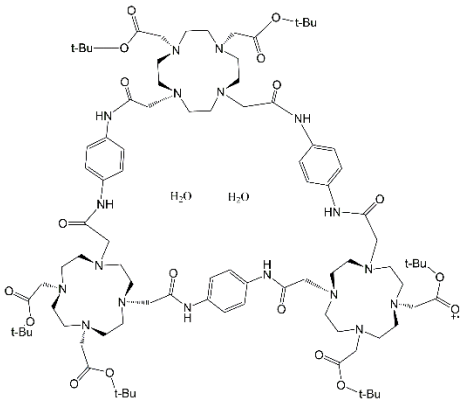
Peak ID Compound
1

1:(Time: 0.20) Center (Top,4, Ar); Smooth (Mn, 2x0.75); Subtract (1,40.00 ,0.010); Combine (10:16-(1:3+23:25))

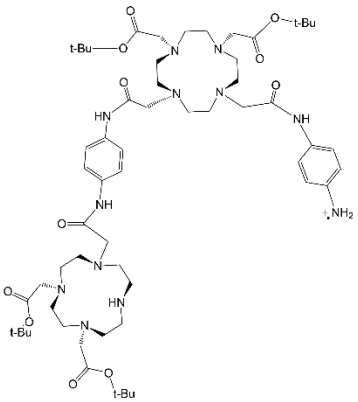
1:TOF MS ES+
9.2e+002



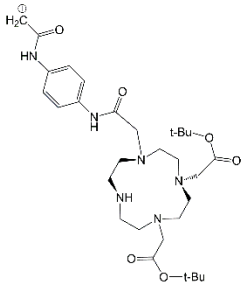
***Chromatogram S8.** Possible compound obtained.*



Chemical Formula: $C_{90}H_{144}N_{18}O_{18}^{\bullet+} \cdot 2H_2O$
Exact Mass: 1801.179



Chemical Formula: $C_{58}H_{96}N_{12}O_{11}^{\bullet+}$
Exact Mass: 1136.732



Chemical Formula: $C_{30}H_{49}N_6O_6^+$
Exact Mass: 589.371

Figure S1. *Mass fragments Chromatogram S8 Compound 18.*