Supporting Information

Fluorinated macromolecular amphiphiles as prototypic molecular drones

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1. Materials

Human breast adenocarcinoma cell line MCF-7, normal human breast epithelial cell line MCF-10A, and lung cancer A549 cells were procured from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China). The MCF-7 cells, MCF-10A cells, and A549 cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin. The cells were maintained at a temperature of 37 ^{o}C in a humidified atmosphere containing 5% CO_2.

Female BALB/c nude mice at the age of 5 weeks were sourced from Beijing Vital River Laboratory Animal Technology Co., Ltd. (Beijing, China). All experimental procedures involving animals strictly adhered to the Guideline for Animal Care and Use, Innovation Academy for Precision Measurement Science and Technology, Chinese Academy of Sciences (APM23042A). The mouse experimental protocols were conducted in accordance with the Regulations for the Administration of Affairs Concerning Experimental Animals, which were approved by the State Council of the People's Republic of China.

2. General Information

Unless otherwise indicated, all reagents were obtained from commercial suppliers and used without prior purification. Column flash chromatography was performed on silica gel (200-300 mesh) with the eluent as indicated in the procedures. ^{1}H, ^{13}C, ^{19}F NMR spectra and ^{1}H-^{1}H ROESY spectrum were recorded on a Bruker 400 MHz, 500 MHz or 600 MHz spectrometer. Chemical shifts are in ppm and coupling constants (*J*) are in Hertz (Hz). ^{1}H NMR spectra were referenced to tetramethylsilane (d, 0.00 ppm) using $CDCl_3$ (s, 7.26 ppm) or DMSO-d_6 (s, 2.50 ppm) as solvent, ^{13}C NMR spectra were referenced to solvent carbons (77.2 ppm for $CDCl_3$). ^{19}F NMR spectra were referenced to 2% perfluorobenzene (s, -164.90 ppm) in $CDCl_3$ or 2% sodium triflate (s, -79.61 ppm) in D_2O. The splitting patterns for ^{1}H NMR spectra are denoted as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and combinations thereof. High-resolution mass spectra (HRMS) were recorded on a Thermo Fisher Scientific Q Exactive Focus. MALDI-TOF mass spectra were recorded on a Bruker Ultraflex III TOF/TOF spectrometer.

The UV-vis and PL spectra were carried out by a Shimadzu UV-2600 spectrophotometer (UV-vis spectrometer) and Horiba Fluoromax-4 spectrofluorometer (PL), respectively. High performance liquid chromatography (HPLC, Shimadzu LC-20A) was used with an Amethyst C18-H reversed-phase column (particle size 5.0 μm, column dimension 4.6 × 250 mm). The size distribution, polymer dispersion index (PDI) and zeta potential of nanoparticles were determined by a dynamic light scattering (DLS) instrument (Malvern, Nano ZS 90, UK). The morphology of the nanoparticles was studied using transmission electron microscopy (TEM, JEM-2100, JEOL). Small animal fluorescence imaging was carried out by IVIS imaging system (PerkinElmer).

TPE **5**[1] was synthesized in our previous work and the corresponding reference was cited.

3. Supplementary Figures and Tables

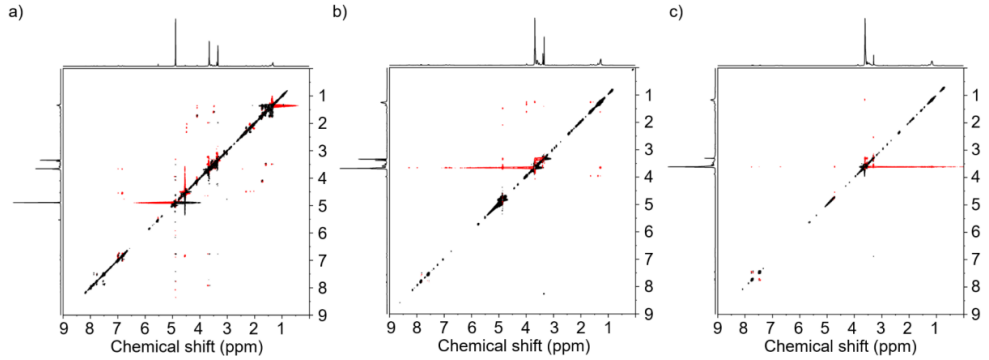


Figure S1. 2D ^{1}H-^{1}H ROESY spectra of FMA **2** at 1000 μM in MeOD (a), in MeOD and D_2O (50/50, v/v) (b), and in D_2O (c).

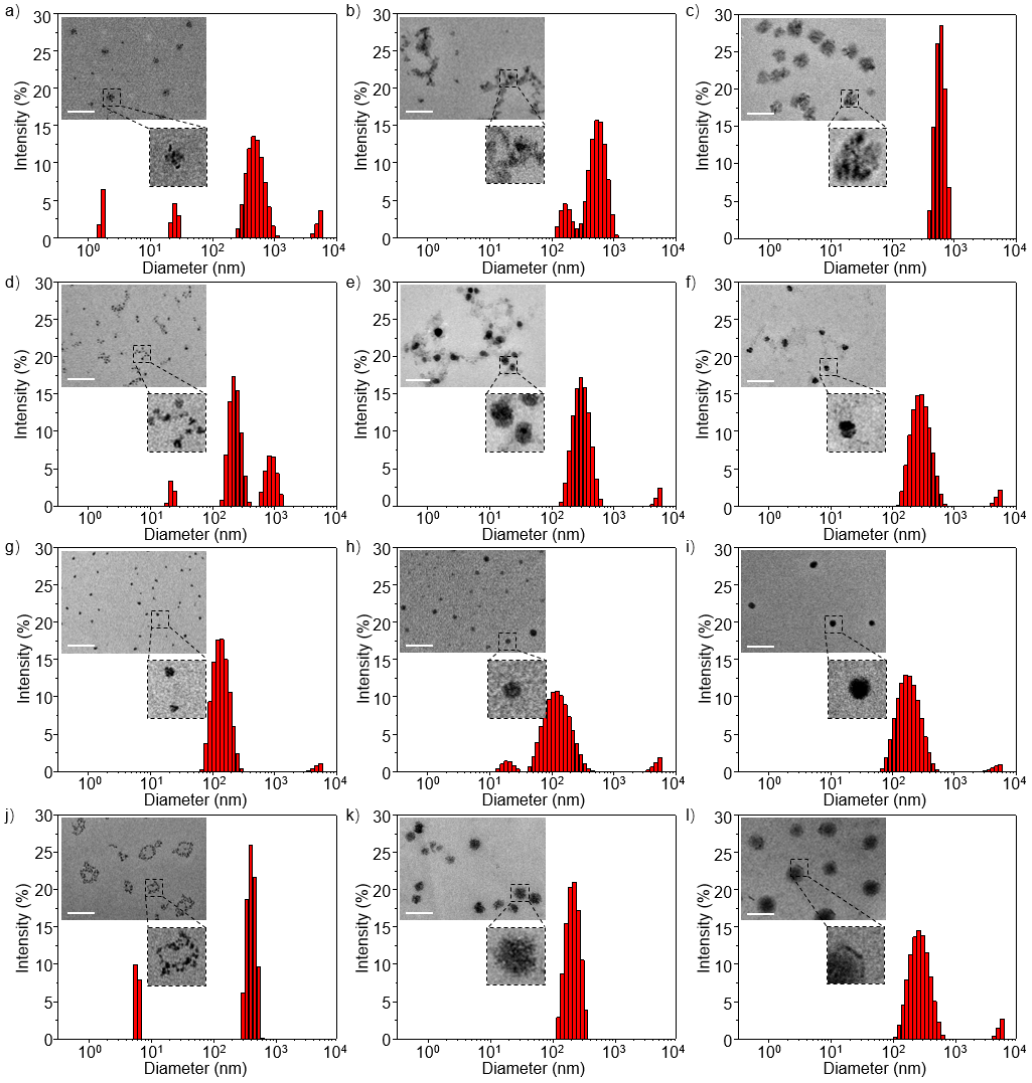


Figure S2. DLS with inset TEM images of FMA **1** (a-c), **3** (d-f), **4** (g-i) and TPE **5** (j-l) (a, d, g, j: 5 μM, b, e, h, k: 100 μM, c, f, i, l: 1000 μM), scale bar: 200 nm.

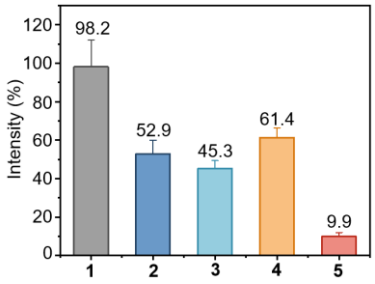


Figure S3. Semiquantitative analysis of the mean fluorescence intensity signal of MCF-7 cells uptake of FMA **1**-**4** and TPE **5**.

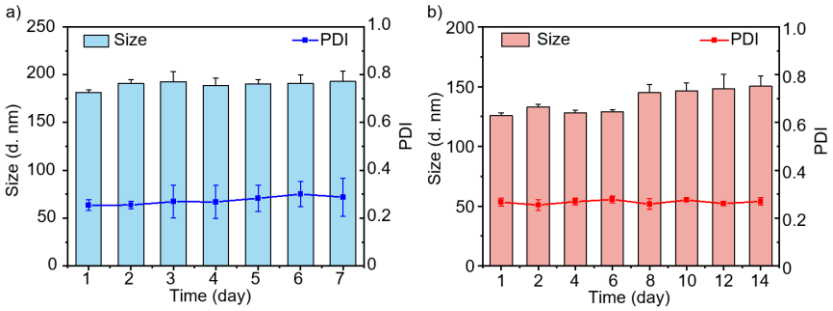


Figure S4. Size and PDI stability of **FMA@IR780** (a) and **FMA@DOX** (b).

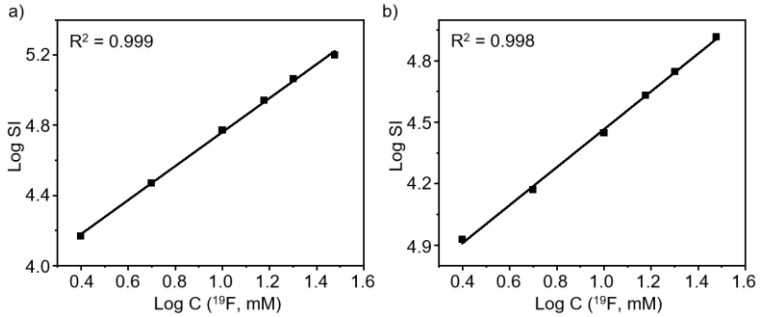


Figure S5. The logarithm plot of signal intensity (SI) versus ^{19}F concentration (g) of **FMA@IR780** (a) and **FMA@DOX** (b).

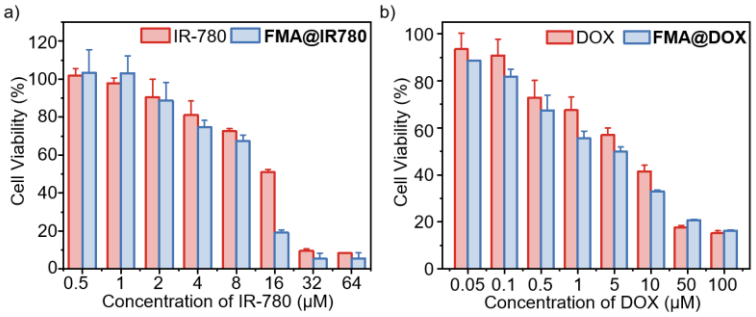


Figure S6. Cytotoxicity assay of IR-780 and **FMA@IR780** towards A549 cells (a), cytotoxicity assay of DOX and **FMA@DOX** towards MCF-7 cells (b).

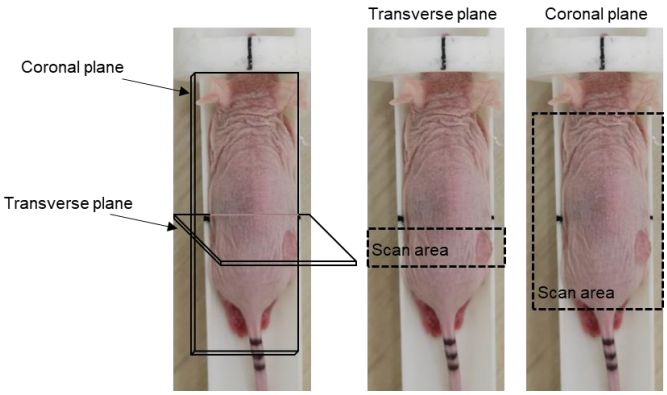


Figure S7. ^{19}F MRI section diagram of a BALB/c nude mouse carrying xenograft A549 tumor.

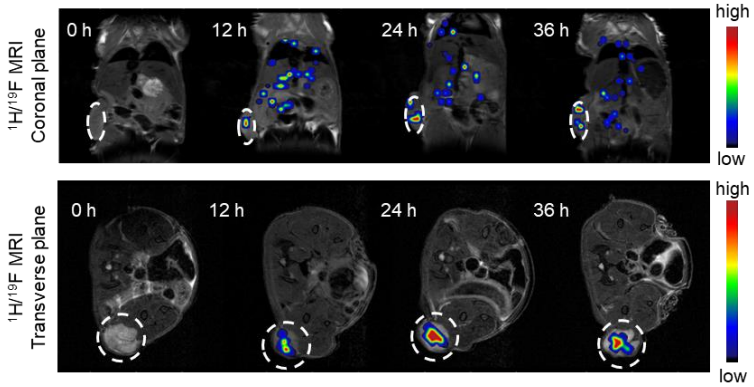


Figure S8. ^{19}F MRI coronal plane and ^{19}F MRI transverse plane of BALB/c nude mouse carrying xenograft A549 tumor at the indicated times after intravenous injection of **FMA@IR780**.

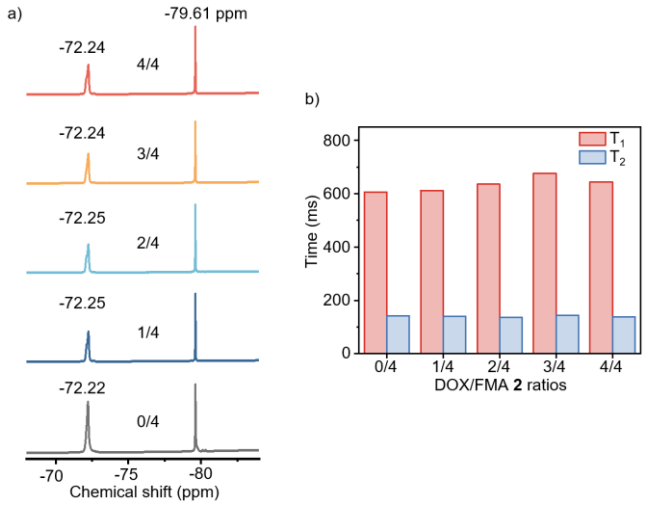


Figure S9. ^{19}F NMR spectra (a) and ^{19}F relaxation times (b) of DOX-loaded nanoparticles with indicated DOX/FMA **2** ratios.

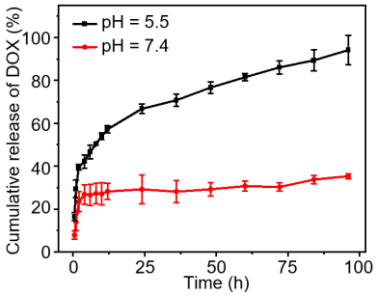
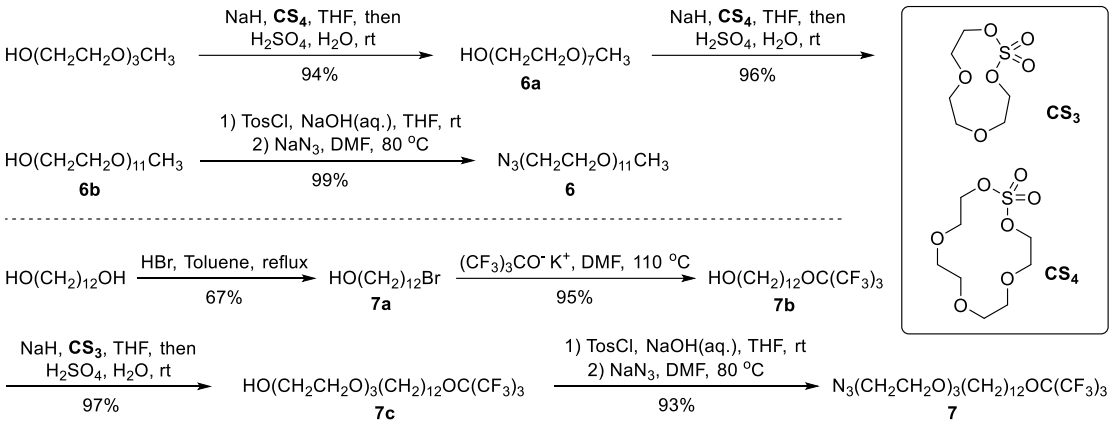


Figure S10. DOX release curve of **FMA@DOX** at pH 7.4 and pH 5.5.

4. Synthesis of Compounds



Scheme S1. Synthesis of azides **6** and **7**

$$HO(CH_2CH_2O)_7CH_3$$

Compound 6a. Under a nitrogen atmosphere, anhydrous tetrahydrofuran (THF, 100 mL) was added to a reaction flask containing NaH (7.3 g, 60% in mineral oil, 182.9 mmol), and the resulting suspension was cooled to 0 °C. The solution of triethylene glycol dimethyl ether (20.0 g, 121.9 mmol) in anhydrous THF (150 mL) was added slowly. Then, the mixture were stired at 0 °C for 0.5 h, by the addition of a THF solution (150 mL) of tetraethylene glycol macrocyclic sulfate (**CS4**, 37.5 g, 146.3 mmol), and the reaction mixture was stirred overnight at room temperature. TLC analysis indicated complete consumption of the starting materials. Water (5.5 mL, 304.8 mmol) was added, and the pH was adjusted to 3.0 with concentrated sulfuric acid. Then, the mixture was stirred for 12 h. Upon completion of hydrolysis, the reaction mixture was neutralized

with saturated sodium bicarbonate solution and extracted with dichloromethane (DCM). The organic phase was combined, dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (MeOH/DCM = 1/20) to give compound **6a** as pale yellow oily liquid (38.9 g, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 - 3.65 (m, 2H), 3.65 - 3.57 (m, 22H), 3.57 - 3.54 (m, 2H), 3.52 - 3.47 (m, 2H), 3.33 (s, 3H).

$$HO(CH_2CH_2O)_{11}CH_3$$

Compound 6b. Compound **6b** was prepared as light yellow oily liquid (29.1 g, 96% yield) using a procedure identical to the preparation of compound **6a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (q, *J* = 3.7 Hz, 2H), 3.68 - 3.59 (m, 38H), 3.59 - 3.56 (m, 2H), 3.54 - 3.49 (m, 2H), 3.35 (s, 3H).

$$N_3(CH_2CH_2O)_{11}CH_3$$

Compound 6. In a reaction flask, an aqueous solution (25 mL) of NaOH (5.5 g, 136.5 mmol) and compound **6b** (20.1 g, 39.0 mmol) in THF (100 mL) was prepared. The reaction mixture was stirred at 0 °C for 0.5 h, followed by the addition of a THF solution (100 mL) of *p*-toluenesulfonyl chloride (8.9 g, 46.8 mmol). The reaction mixture was stirred overnight at room temperature. After complete consumption of the starting materials as indicated by TLC analysis, THF was removed under reduced pressure. The residue was washed with water, extracted with DCM, and the organic phase was combined. After drying, the intermediate product was obtained by rotary evaporation. Then, NaN_3 (3.7 g, 50.3 mmol) was added to the solution of the intermediate product in *N*,*N*-dimethylformamide (DMF, 100 mL), and the reaction was stirred overnight at 80 °C. After complete consumption of the starting materials as indicated by TLC analysis, DMF was removed under reduced pressure. The residue was washed with water, extracted with DCM, and the organic phase was combined. After drying over anhydrous sodium sulfate, the crude product was concentrated and purified by column chromatography on silica gel (MeOH/DCM = 1/20) to give compound **6** as light yellow oily liquid (20.9 g, 99% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 - 3.59 (m, 42H),

3.54 - 3.50 (m, 2H), 3.35 (s, 3H).

$HO(CH_2)_{12}Br$

Compound 7a. In a reaction flask, 1,12-dodecanediol (30 g, 148.3 mmol) was added with toluene (300 mL) as the solvent. Hydrobromic acid (48%, 33.6 mL, 296.5 mmol) was slowly added dropwise with stirring, and the reaction mixture was refluxed at 110 ^oC for 24 h. After completion of the reaction, the solvent was removed under reduced pressure, and the resulting residue was subjected to silica gel column chromatography purification (PE/EA = 10/1) to give compound **7a** as a white solid (17.6 g, 67% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.7 Hz, 2H), 3.38 (t, *J* = 6.9 Hz, 2H), 1.83 (dt, *J* = 14.5, 6.9 Hz, 2H), 1.74 (s, 1H), 1.53 (dt, *J* = 13.2, 6.8 Hz, 2H), 1.39 (p, *J* = 7.1 Hz, 2H), 1.25 (s, 14H).

$HO(CH_2)_{12}OC(CF_3)_3$

Compound 7b. Compound **7a** (22.1 g, 83.2 mmol) and potassium *tert*-butoxide (20.0 g, 73.0 mmol) were added to a reaction flask with DMF (200 mL) as the solvent. The reaction mixture was refluxed at 110 ^oC for 12 hours. After completion of the reaction, the solvent was removed under reduced pressure, and ice water was added. The organic phase was extracted with DCM. The combined organic extracts were dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (PE/EA = 10/1) to give compound **7b** as white solid (29.1 g, 95% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 3.98 (t, *J* = 6.4 Hz, 2H), 3.63 (t, *J* = 6.7 Hz, 2H), 1.66 (p, *J* = 6.5 Hz, 2H), 1.55 (d, *J* = 7.4 Hz, 2H), 1.37 - 1.24 (m, 16H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.61 (s).

$HO(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

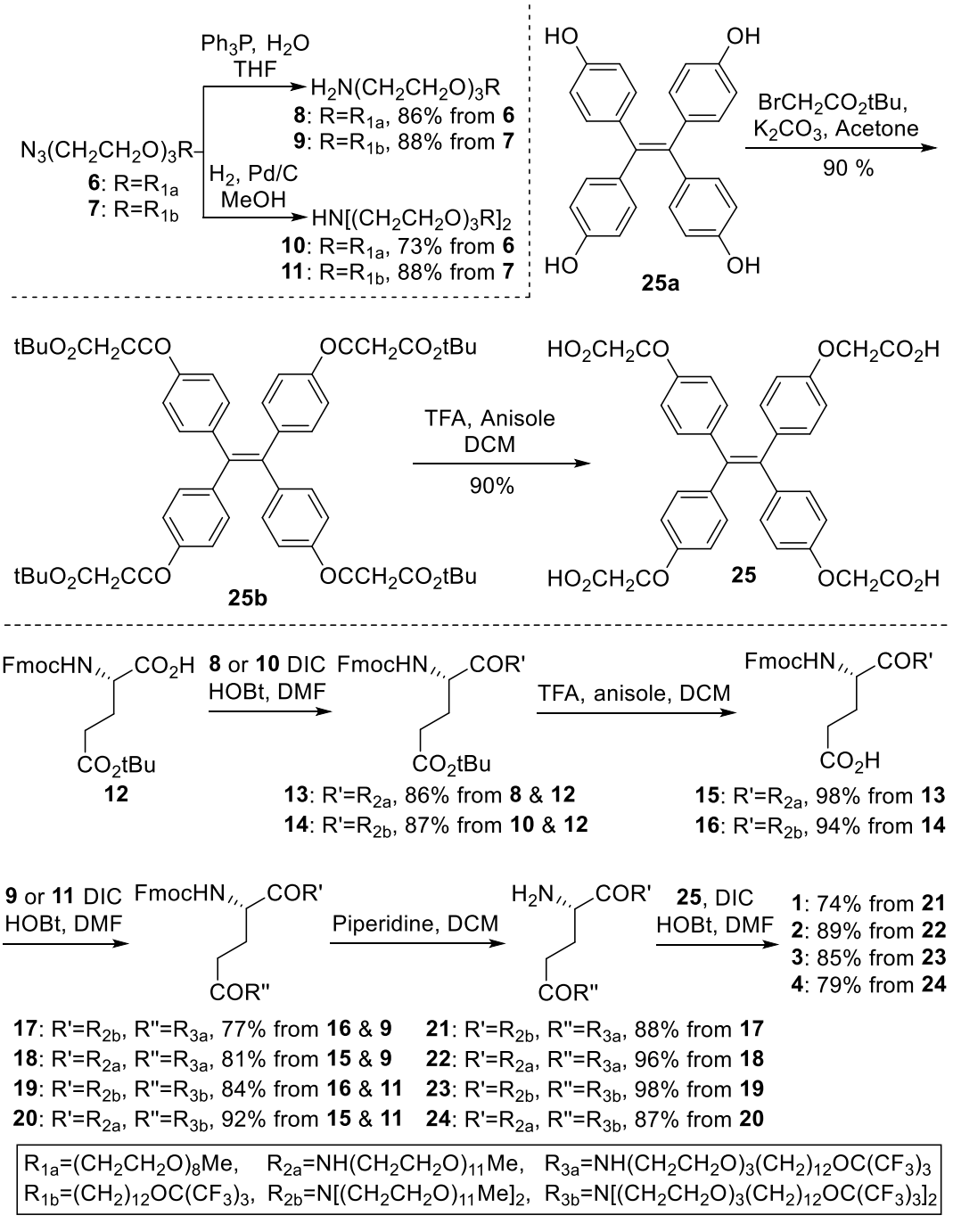
Compound 7c. Under a nitrogen atmosphere, the suspension of NaH (3.2 g, 60% in mineral oil, 78.5 mmol) in anhydrous THF (100 mL) was cooled to 0 ^oC. Then, the solution of **7b** (22.0 g, 52.3 mmol) in anhydrous THF (50 mL) was added slowly. After stirring the reaction mixture at 0 ^oC for 0.5 h, a solution of triethylene glycol macrocyclic sulfate (**CS_3**, 13.3 g, 62.8 mmol) in THF (50 mL) was added, and the

reaction mixture was stirred overnight at room temperature. Upon completion of the reaction, as indicated by TLC, H_2O (2.4 mL, 130.8 mmol) was added, and the pH was adjusted to 3.0 with concentrated sulfuric acid, followed by continued stirring. After completion of hydrolysis, the reaction mixture was neutralized with saturated $NaHCO_3$ aqueous solution, extracted with DCM, and the organic layer was collected. After drying over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (MeOH/DCM = 1/20) to give compound **7c** as pale yellow oily liquid (27.7 g, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (t, *J* = 6.4 Hz, 2H), 3.73 (t, *J* = 4.6 Hz, 2H), 3.71 - 3.64 (m, 6H), 3.61 (ddd, *J* = 11.6, 5.7, 3.5 Hz, 4H), 3.45 (t, *J* = 6.8 Hz, 2H), 1.71 - 1.62 (m, 2H), 1.58 (p, *J* = 7.0 Hz, 2H), 1.40 - 1.23 (m, 16H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.61 (s).

$$N_3(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$$

Compound 7. An aqueous solution (25 mL) of NaOH (5.4 g, 135.5 mmol) and compound **7c** (21.3 g, 38.7 mmol) in THF (100 mL) was added to a reaction flask. The reaction mixture was stirred at 0 °C for 0.5 h, followed by the addition of *p*-toluenesulfonyl chloride (8.9 g, 46.4 mmol) in THF (100 mL). The reaction mixture was stirred overnight at room temperature. TLC analysis indicated complete consumption of the starting materials. The THF solvent was removed under rotary evaporation, and the residue was washed with water and extracted with DCM. The organic phase was combined and dried to obtain the intermediate product. To a DMF solution (100 mL) of the intermediate product, NaN_3 (3.7 g, 50.3 mmol) was added, and the reaction mixture was stirred at 80 °C overnight. TLC analysis indicated complete consumption of the starting materials. The DMF solvent was removed under reduced pressure, and the residue was washed with water and extracted with DCM. The organic phase was combined and dried over anhydrous sodium sulfate. The crude product was purified by column chromatography on silica gel (PE/EA = 5/1) to give compound **7** as pale yellow oily liquid (22.4 g, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$)

δ 3.98 (t, *J* = 6.5 Hz, 2H), 3.68 - 3.63 (m, 8H), 3.58 (dd, *J* = 5.7, 3.4 Hz, 2H), 3.44 (t, *J* = 6.8 Hz, 2H), 3.38 (t, *J* = 5.1 Hz, 2H), 1.70 - 1.61 (m, 2H), 1.57 (p, *J* = 6.9 Hz, 2H), 1.37 - 1.24 (m, 16H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.62 (s).



Scheme S2. Convenient synthesis of FMA **1-4**.

$H_2N(CH_2CH_2O)_{11}CH_3$

Compound 8. Under a nitrogen atmosphere, compound **6** (18.7 g, 34.6 mmol) and triphenylphosphine (13.6 g, 51.9 mmol) were added to a reaction flask with anhydrous THF (150 mL) as the solvent, and the reaction mixture was stirred overnight at room temperature. After complete consumption of compound **6** as indicated by TLC analysis, water (3.1 mL, 173 mmol) was added, and the reaction was continued at room temperature for 12 h. After completion of the reaction, the reaction mixture was rotary evaporated and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was rotary evaporated. The crude product was purified by silica gel column chromatography (MeOH/DCM = 1/20) to give compound 8 as pale yellow oily liquid (15.3 g, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 - 3.51 (m, 40H), 3.51 - 3.47 (m, 2H), 3.44 (t, *J* = 5.2 Hz, 2H), 3.31 (s, 3H), 2.80 (t, *J* = 5.2 Hz, 2H).

$H_2N(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

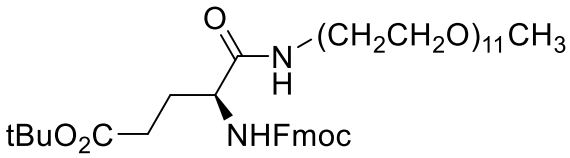
Compound 9. Compound **9** was prepared as a pale yellow oily liquid (16.8 g, 88% yield) using a procedure identical to the preparation of compound **8**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (t, *J* = 6.5 Hz, 2H), 3.68 - 3.59 (m, 6H), 3.57 (dd, *J* = 5.8, 3.4 Hz, 2H), 3.49 (t, *J* = 5.2 Hz, 2H), 3.43 (t, *J* = 6.8 Hz, 2H), 2.85 (t, *J* = 5.2 Hz, 2H), 1.59 (m, 6H), 1.43 - 1.06 (m, 16H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.63 (s).

$HN[(CH_2CH_2O)_{11}CH_3]_2$

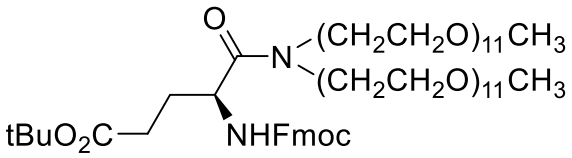
Compound 10. Under a H_2 atmosphere, palladium on carbon (0.4 g, 10%, 1.8 mmol) and compound **6** (1.0 g, 1.8 mmol) in methanol (36 mL) were added to the reaction flask. After overnight reaction, the progress of the reaction was monitored by TLC. After the reaction was completed, the mixture was filtrated through a pad of Celite, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (MeOH/DCM = 1/10) to give compound **10** as pale yellow oily liquid (0.7 g, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (d, *J* = 4.4 Hz, 84H), 3.23 (s, 6H), 2.68 (t, *J* = 5.3 Hz, 4H).

$HN[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

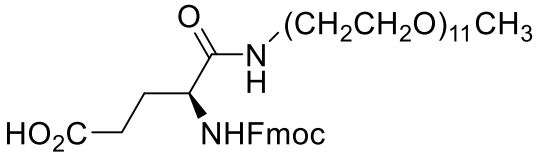
Compound 11. Compound **11** was prepared as a pale yellow oily liquid (0.9 g, 88% yield) using a procedure identical to the preparation of compound **10**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (t, J = 6.5 Hz, 4H), 3.71 - 3.54 (m, 20H), 3.45 (t, J = 6.8 Hz, 4H), 2.86 (t, J = 5.3 Hz, 4H), 1.67 (p, J = 6.6 Hz, 4H), 1.58 (p, J = 6.9 Hz, 4H), 1.39- 1.24 (m, 32H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.60 (s).



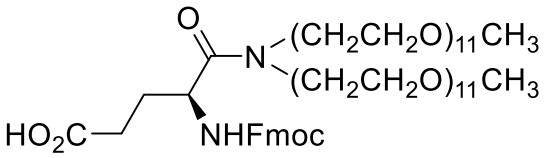
Compound 13. Under a nitrogen atmosphere, N-(9-Fmoc)-L-glutamic acid γ-tert-butyl ester monohydrate (**12**) (9.9 g, 23.3 mmol) and HOBT (3.3 g, 23.3 mmol) were added to the reaction flask. DMF (20 mL) was used as a solvent, and DIC (2.9 g, 23.3 mmol) was added at room temperature for 0.5 h. A DMF solution of compound **8** (8.0 g, 15.5 mmol) was then added to the reaction flask, and the reaction was carried out at 45 °C overnight. TLC analysis indicated complete conversion of the starting materials. The DMF solvent was removed under reduced pressure, and the resulting mixture was acid-washed and extracted with DCM. The organic phases were combined, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (MeOH/DCM = 1/20) to give compound **13** as pale yellow oily liquid (11.9 g, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.34 - 7.30 (m, 2H), 4.37 (d, *J* = 7.6 Hz, 2H), 4.22 (d, *J* = 7.1 Hz, 2H), 3.66 - 3.61 (m, 38H), 3.57 - 3.53 (m, 4H), 3.50 - 3.44 (m, 2H), 3.38 (s, 3H), 2.22 (s, 2H), 2.10 (dd, *J* = 13.7, 6.2 Hz, 1H), 1.93 (dt, *J* = 14.6, 7.3 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 171.7, 156.7, 144.3, 141.7, 128.1, 127.5, 125.6, 120.4, 72.3, 71.0, 70.7, 70.1, 59.5, 54.6, 47.6, 39.8, 32.0, 28.5. HRMS-ESI m/z: $[M+Na]^+$ calcd for $C_{47}H_{74}N_2NaO_{16}^+$ 945.4931, found 945.4968.



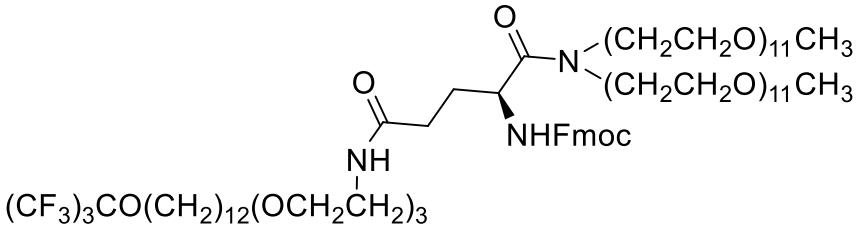
Compound 14. Compound **14** was prepared as a pale yellow oily liquid (0.8 g, 77% yield) using a procedure identical to the preparation of compound **13**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.34 - 7.30 (m, 2H), 4.75 (td, *J* = 8.9, 3.7 Hz, 1H), 4.42 - 4.19 (m, 3H), 3.85 - 3.73 (m, 2H), 3.66 - 3.59 (m, 86H), 3.38 (s, 6H), 2.38 - 2.28 (m, 2H), 2.03 (dq, *J* = 11.3, 4.2, 3.7 Hz, 1H), 1.82 - 1.74 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 171.7, 156.4, 144.2, 141.6, 128.1, 127.4, 125.5, 120.3, 81.1, 72.2, 70.7, 70.5, 70.2, 70.0, 67.3, 59.4, 54.5, 47.5, 39.7, 31.9, 28.9, 28.4. HRMS-ESI m/z: $[M+H]^+$ calcd for $C_{70}H_{120}N_2O_{27}^+$ 1421.8151, found 1421.8083.



Compound 15. Compound **13** (5.0 g, 5.4 mmol) and benzyl methyl ether (0.9 g, 5.8 mmol) were added to a reaction flask containing DCM (140 mL) as a solvent. Trifluoroacetic acid (6.2 g, 54.2 mmol) was added, and the reaction mixture was stirred at room temperature for 4 h. TLC analysis indicated complete conversion of the starting materials. The reaction mixture was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (MeOH/DCM = 1/20) to give compound **15** as pale yellow oily liquid (4.7 g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.33- 7.26 (t, 2H), 4.35 (p, *J* = 10.4 Hz, 3H), 4.20 (t, *J* = 7.1 Hz, 1H), 3.68- 3.42 (m,44H), 3.37 (s, 4H), 2.53 -2.38 (m, 2H), 2.10 (dd, J = 13.6, 6.6 Hz, 1H), 2.01 (dt, *J* = 14.2, 7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 171.5, 144.1, 144.0, 141.3, 127.8, 127.3, 125.4, 120.0, 72.0, 70.6, 70.5, 70.4, 70.3, 70.2, 70.0, 69.9, 67.2, 59.1, 47.2, 39.2, 29.3. HRMS-ESI m/z: $[M+H]^+$ calcd for $C_{43}H_{66}N_2O_{16}^+$ 889.4305, found 889.4327.

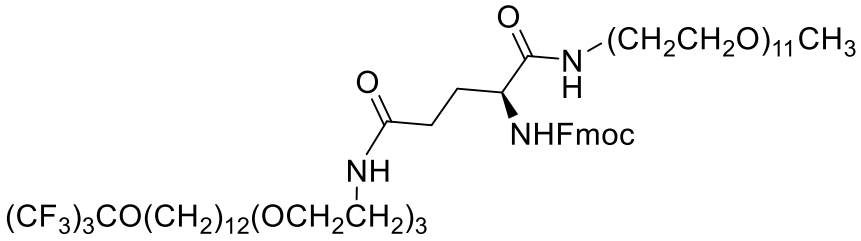


Compound 16. Compound **16** was prepared as pale yellow oily liquid (5.0 g, 94% yield) using a procedure identical to the preparation of compound **15**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.33 - 7.28 (m, 2H), 4.83 (td, *J* = 8.9, 3.5 Hz, 1H), 4.40 - 4.18 (m, 3H), 3.81 (d, *J* = 5.3 Hz, 2H), 3.67 - 3.56 (m, 86H), 3.37 (s, 6H), 2.44 (h, *J* = 10.8, 10.1 Hz, 2H), 2.08 (d, *J* = 7.5 Hz, 1H), 1.84 (dq, *J* = 13.9, 6.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 171.4, 144.0, 141.3, 127.8, 127.3, 125.4, 120.0, 71.9, 70.4, 67.2, 59.1, 47.1, 39.2, 29.5. HRMS-ESI m/z: $[M+Na]^+$ calcd for $C_{66}H_{112}N_2NaO_{27}^+$ 1387.7345, found 1387.7378.

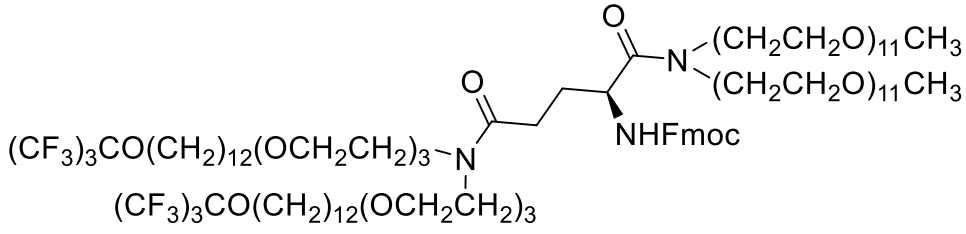


Compound 17. Under a nitrogen atmosphere, compound **16** (2.9 g, 2.1 mmol) and HOBT (0.42 g, 3.1 mmol) were added to the reaction flask with DMF (20 mL) as a solvent, followed by the addition of DIC (0.39 g, 3.1 mmol). The reaction mixture was stirred at room temperature for 0.5 h. Next, a DMF solution of compound **9** (1.7 g, 3.1 mmol) was added to the reaction flask, and the reaction was carried out overnight at 45 °C. TLC analysis indicated complete consumption of the starting materials. The DMF solvent was then removed under reduced pressure, and the resulting mixture was acid-washed and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (MeOH/DCM = 1/10) to give compound **17** as pale yellow oily liquid (3.0 g, 77% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.63 (dt, *J* = 7.3, 3.9 Hz, 2H), 7.41 (dd, *J* = 8.4, 6.7 Hz, 2H), 7.32 (ddd, *J* = 8.2, 6.3, 1.7 Hz, 2H), 4.35 (qd, *J* = 10.5, 7.2 Hz, 2H), 4.21 (t, *J*

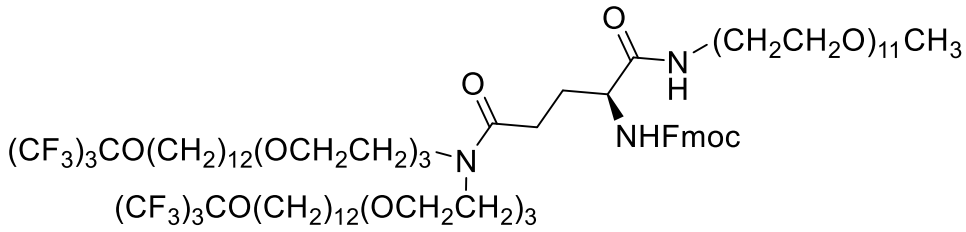
= 7.1 Hz, 2H), 3.83 - 3.75 (m, 4H), 3.69 - 3.58 (m, 92H), 3.39 (s, 6H), 1.68 (q, *J* = 7.0 Hz, 4H), 1.55 (q, *J* = 7.0 Hz, 4H), 1.27 (dt, *J* = 7.5, 3.6 Hz, 24H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 156.3, 143.9, 143.8, 141.29, 141.25, 127.7, 127.1, 125.2, 125.1, 120.4 (q, *J* = 289.8 Hz), 120.0, 119.9, 80.1-79.4 (m), 71.9, 71.5, 70.6, 70.5, 70.5, 70.5, 70.2, 70.0, 69.9, 69.0, 59.0, 47.2, 39.3, 29.7, 29.58, 29.55, 29.52, 29.48, 29.46, 29.4, 29.1, 26.1, 25.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.63 (s). HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{88}H_{148}F_9N_3NaO_{30}^+$ 1920.9896, found 1920.98.



Compound 18. Compound **18** was prepared as pale yellow oily liquid (2.8 g, 81% yield) using a procedure identical to the preparation of compound **17**. ^{1}H NMR (400 MHz, $CDCl_3$ δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.34 -7.29 (m, 2H),4.36 (dd, *J* = 7.3, 4.1 Hz, 2H), 4.21 (t, *J* = 7.1 Hz, 2H), 3.99 (t, *J* = 6.5 Hz, 2H), 3.66-3.53 (m, 52H), 3.44 (dt, *J* = 13.7, 5.8 Hz, 6H), 3.38 (s, 3H), 2.36 - 2.22 (m, 2H), 2.06 (td, *J* = 13.9, 13.0, 6.8 Hz, 2H), 1.71 -1.62 (m, 2H), 1.59- 1.52 (m, 2H), 1.38-1.33 (m, 2H), 1.30 -1.24 (m, 16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 171.4, 156.2, 143.9, 143.8, 141.3, 127.8, 127.1, 125.2, 120.5 (q, *J* = 292.9 Hz), 120.0, 80.3 - 79.4 (m), 71.6, 70.64, 70.59, 70.52, 70.48, 70.3, 70.2, 70.0, 69.8, 69.6, 67.0, 59.1, 54.5, 47.2, 39.4, 32.4, 29.8, 29.7, 29.63, 29.59, 29.56, 29.5, 29.2, 26.1, 25.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.64 (s). HRMS-ESI m/z: $[M+Na]^+$ calcd for $C_{65}H_{102}F_9N_3NaO_{19}^+$ 1422.6856, found 1422.6890.

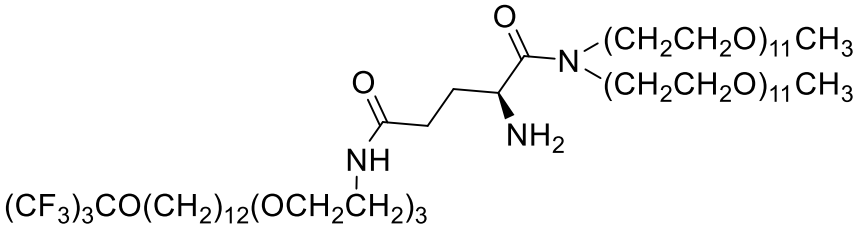


Compound 19. Compound **19** was prepared as pale yellow oily liquid (3.2 g, 84% yield) using a procedure identical to the preparation of compound **17**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.61 (dd, *J* = 9.6, 7.5 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.35 - 7.29 (m, 2H), 4.81- 4.64 (m, 1H),4.35 - 4.05(m, 3H), 3.99 (t, *J* = 6.5 Hz, 4H), 3.68 -3.49 (m, 112H), 3.42 (dt, *J* = 14.0, 7.0 Hz, 4H), 3.38 (s, 6H), 2.58 - 2.39 (m, 4H), 1.71 - 1.63 (m, 4H), 1.61 - 1.52 (m, 4H), 1.31 - 1.24 (m, 32H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 172.3, 156.2, 144.0, 143.8, 141.2, 127.7, 127.1, 125.3, 125.2, 120.8 (q, *J* = 289.8 Hz), 120.4, 120.0, 79.7 - 78.8 (m), 71.9, 71.6, 71.5, 70.6, 70.5, 70.45, 70.0, 69.8, 69.6, 69.58, 69.2, 69.0, 59.0, 48.6, 48.2, 47.1, 46.6, 46.4, 29.7, 29.6, 29.57, 29.54, 29.49, 29.4, 29.1, 28.9, 26.1, 25.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.64 (s). MS (MALDI-TOF) m/z: $[M+Na]^+$ calcd for $C_{110}H_{183}F_{18}N_3NaO_{34}^+$ 2455.229, found 2455.126.

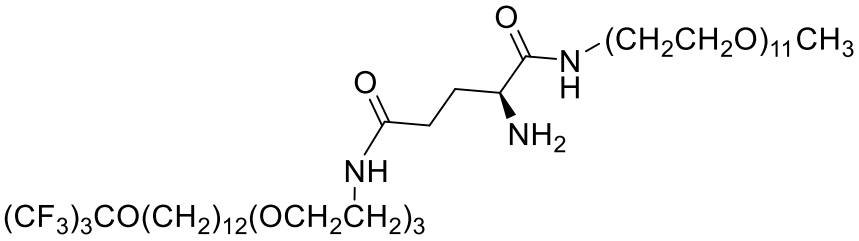


Compound 20. Compound **20** was prepared as pale yellow oily liquid (3.3 g, 92% yield) using a procedure identical to the preparation of compound **17**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.62 (dd, *J* = 7.5, 4.2 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 4.34 (t, *J* = 6.6 Hz, 2H), 4.26 - 4.10 (m, 2H), 4.00 (t, *J* = 6.5 Hz, 4H), 3.69 - 3.53 (m, 68H), 3.39 (s, 3H), 2.69 (dt, *J* = 14.5, 6.7 Hz, 2H), 2.50 (dt, *J* = 16.4, 6.4 Hz, 2H), 2.24 - 1.94 (m, 2H), 1.76 - 1.62 (m, 4H), 1.62 - 1.52 (m, 4H), 1.52 - 1.21 (m, 33H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 171.9, 156.4, 144.0, 143.9, 141.3, 127.7, 127.1, 125.24, 125.18, 121.6, 120.4 (q, *J* = 293.6 Hz), 120.0, 119.3, 80.4 - 79.2 (m), 71.9, 71.57, 71.55, 70.7, 70.59, 70.55, 70.53, 70.50, 70.4, 70.2, 70.01, 70.00, 69.9, 69.7, 69.5, 69.1, 67.0, 59.0, 54.7, 48.9, 47.2, 46.5, 39.3, 29.7, 29.62, 29.60, 29.58, 29.55, 29.51, 29.49, 29.43, 29.35, 29.1, 28.8, 26.1, 25.3, 14.1. ^{19}F NMR (376 MHz,

$CDCl_3$) δ -73.63 (s). HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{87}H_{137}F_{18}N_3NaO_{23}^+$ 1956.9248, found 1956.9246.

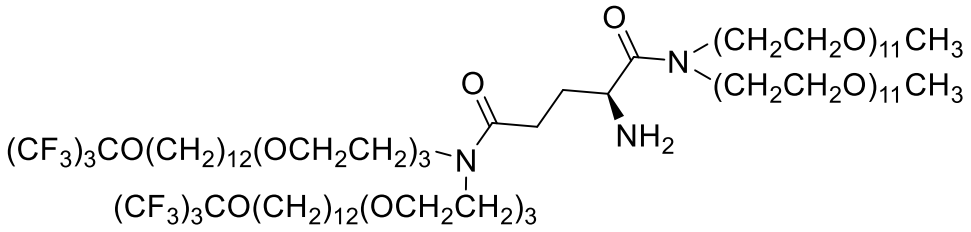


Compound 21. In a reaction flask, compound **17** (3.0 g, 1.6 mmol) was added to a solution of DMF (30 mL) containing 20% pyridine. The reaction mixture was stirred at room temperature for 3 h with continuous monitoring using TLC. Upon completion of the reaction, the DMF solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (MeOH/DCM = 1/10) to give compound **17** as colorless oily liquid product (2.3 g, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (t, J = 5.6 Hz, 1H), 4.02 - 3.83 (m, 6H), 3.70 - 3.41 (m, 84H), 3.38 (t, J = 6.8 Hz, 4H), 3.31 (s, 6H), 3.08 (t, J = 5.6 Hz, 6H), 1.85 (p, J = 5.6 Hz, 6H), 1.55 (dt, J = 37.2, 6.8 Hz, 7H), 1.34 - 1.10 (m, 17H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 120.4 (q, J = 294.8 Hz), 80.1 - 79.2 (m), 71.9, 71.5, 70.6, 70.5, 70.4, 70.0, 69.9, 59.0, 53.4, 50.0, 48.2, 46.2, 39.1, 32.2, 29.7, 29.6, 29.52, 29.47, 29.4, 29.10, 26.06, 25.3, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.63 (s). HRMS (ESI) m/z: $[M/2+H]^+$ calcd for $C_{73}H_{140}F_9N_3O_{282}^+$ 1677.9468, found 1677.9438.

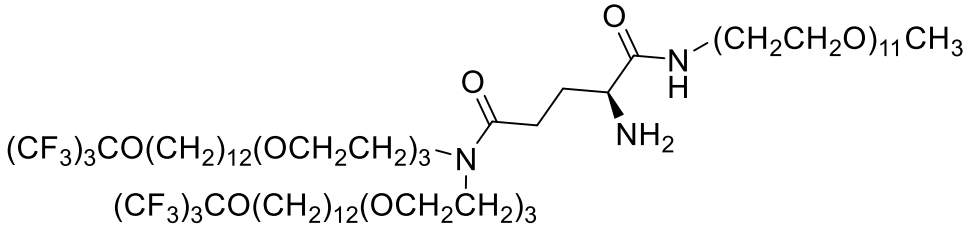


Compound 22. Compound **22** was prepared as pale yellow oily liquid (2.1 g, 96% yield) using a procedure identical to the preparation of compound **21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (t, J = 6.3 Hz, 2H), 3.62 (q, J = 3.8 Hz, 45H), 3.56 - 3.51 (m, 8H), 3.44 - 3.38 (m, 6H), 3.35 (s, 3H), 2.35 - 2.24 (m, 2H), 2.04 - 1.97 (m, 1H), 1.89 (dt, J = 14.0,

7.1 Hz, 1H), 1.68 - 1.61 (m, 2H), 1.54 (d, J = 6.7 Hz, 2H), 1.23 (s, 16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 173.1, 120.4 (q, J = 295.9 Hz), 79.9 - 79.0 (m), 71.9, 71.6, 70.5, 70.47, 70.43, 70.40, 70.2, 70.05, 69.96, 69.8, 69.7, 59.0, 54.3, 39.2, 39.0, 32.6, 30.9, 29.7, 29.6, 29.53, 29.48, 29.46, 29.4, 29.1, 26.0, 25.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.62 (s). HRMS-ESI m/z: $[M+H]^+$ calcd for $C_{50}H_{92}F_9N_3O_{17}^+$ 1178.6356, found 1178.6392.

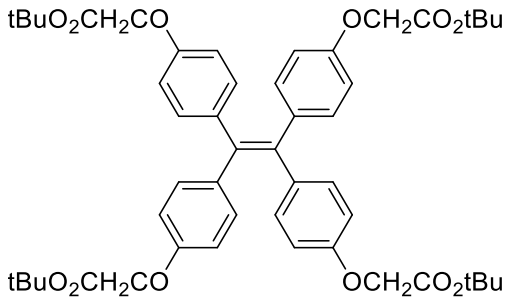


Compound 23. Compound **23** was prepared as pale yellow oily liquid (2.5 g, 98% yield) using a procedure identical to the preparation of compound **21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 4H), 3.85 - 3.38 (m, 115H), 3.36 (s, 6H), 2.58 (s, 2H), 2.18 - 1.80 (m, 4H), 1.65 (s, 4H), 1.55 (s, 4H), 1.24 (s, 32H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 172.8, 120.2 (q, J = 294.9 Hz), 80.4 - 79.5 (m), 71.6, 71.3, 70.4, 70.3, 70.1, 69.8, 69.7, 69.6, 69.2, 69.1, 68.9, 58.8, 58.7, 49.9, 48.4, 47.9, 46.0, 29.4, 29.4, 29.3, 29.2, 29.19, 29.17, 28.9, 28.5, 25.8, 25.0, 25.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.59 (s). MS (MALDI-TOF) m/z: $[M+Na]^+$ calcd for $C_{95}H_{173}F_{18}N_3NaO_{32}^+$ 2233.161, found 2233.085.

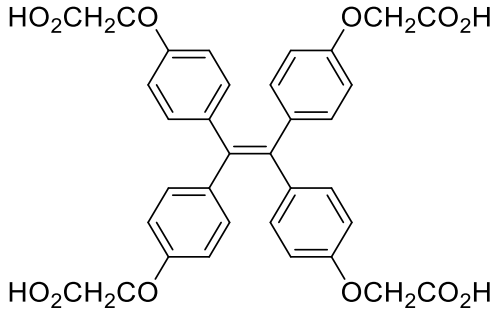


Compound 24. Compound **24** was prepared as pale yellow oily liquid (2.5 g, 98% yield) using a procedure identical to the preparation of compound **21**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (t, J = 6.4 Hz, 3H), 3.69 - 3.47 (m, 66H), 3.46 - 3.39 (m, 6H), 3.36 (s, 3H), 2.77 (s, 2H), 2.59 (td, J = 7.0, 4.1 Hz, 2H), 2.10 (ddd, J = 13.9, 12.3, 6.5 Hz, 1H),

1.91 (dt, J = 14.1, 7.1 Hz, 1H), 1.73 - 1.60 (m, 4H), 1.55 (p, J = 6.9 Hz, 4H), 1.38 - 1.18 (m, 32H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.5, 173.2, 120.4 (q, J = 294.8 Hz), 80.1 - 79.4 (m), 71.9, 71.6, 70.7, 70.64, 70.59, 70.56, 70.54, 70.52, 70.50, 70.42, 70.38, 70.2, 70.0, 69.9, 69.4, 69.3, 59.0, 54.7, 48.8, 46.3, 39.0, 31.9, 29.7, 29.63, 29.58, 29.56, 29.5, 29.4, 29.1, 26.1, 25.3, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.62 (s). HRMS (ESI) m/z: $[M/2+Na]^+$ calcd for $C_{72}H_{127}F_{18}N_3NaO_{212}^+$ 1735.8640, found 1735.8620.

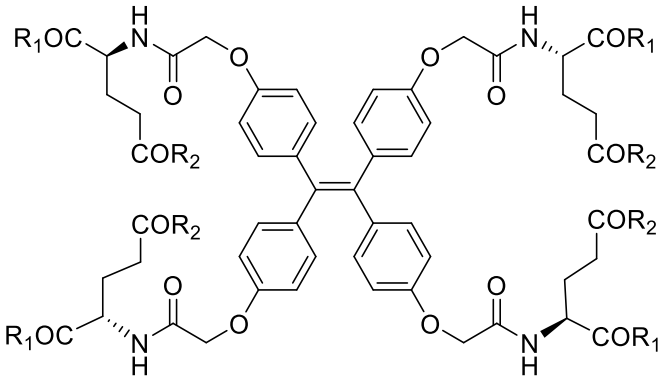


Compound 25b. In a reaction flask, 4,4′,4″,4‴-(Ethene-1,1,2,2-tetrayl)tetraphenol (**25a**) (4.0 g, 10 mmol) and potassium carbonate (8.3 g, 60 mmol) were added, followed by the addition of *tert*-butyl bromoacetate (11.7 g, 60 mmol) in acetone (100 mL). The reaction mixture was heated under reflux for 12 h with continuous monitoring using TLC. After completion of the reaction, the reaction mixture was evaporated under reduced pressure, and the crude product was purified through silica gel column chromatography (PE/EA = 5:1) to give compound **25b** as white solid product (7.7 g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 - 6.75 (m, 8H), 6.67 - 6.50 (m, 8H), 4.43 (s, 8H), 1.46 (s, 36H).



Compound 25. Compound **25b** (6.8 g, 8 mmol), benzyl ether (1.3 g, 12 mmol), and trifluoroacetic acid (36.4 g, 320 mmol) were added to a reaction flask with DCM (100

mL) as a solvent. The reaction mixture was stirred at room temperature for 6 h and monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure, and the resulting residue was recrystallized from acetone to give compound **25** as white solid (4.5 g, 90% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.83 (d, J = 8.7 Hz, 8H), 6.66 (d, J = 8.8 Hz, 8H), 4.56 (s, 8H).

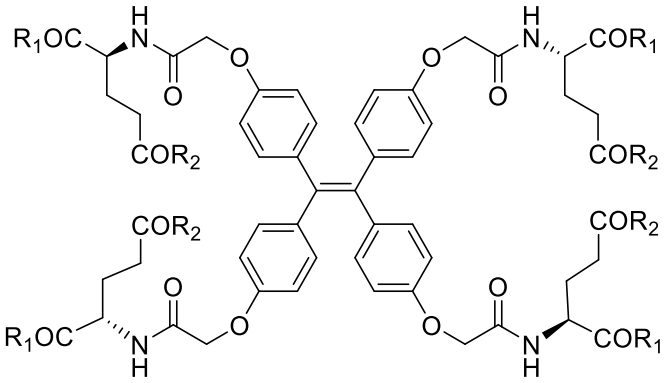


1

R_1 = $N[(CH_2CH_2O)_{11}Me]_2$, R_2 = $NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

FMA 1. Under a nitrogen atmosphere, compound **25** (0.6 g, 1 mmol) and HOBT (0.81 g, 6 mmol) were added to the reaction flask with DMF (20 mL) as a solvent, followed by the addition of DIC (0.76 g, 6 mmol). The reaction mixture was stirred at room temperature for 0.5 h. Next, a DMF solution of compound **21** (10.1 g, 6 mmol) was added to the reaction flask, and the reaction was carried out overnight at 60 ºC. TLC analysis indicated complete consumption of the starting materials. The DMF solvent was then removed under reduced pressure, and the resulting mixture was acid-washed and extracted with DCM. The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (MeOH/DCM = 1/10) to give compound FMA **1** as light yellow liquid product (5.4 g, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 7.8 Hz, 2H), 6.91 (dd, J = 19.9, 8.2 Hz, 6H), 6.82 – 6.75 (m, 2H), 6.73 - 6.64 (m, 6H), 5.06 (d, J = 8.1 Hz, 2H), 4.61 (d, J = 3.2 Hz, 2H), 4.47 - 4.33 (m, 5H), 3.99 (t, J = 6.5 Hz, 8H), 3.88 - 3.41 (m, 380H), 3.38 (s, 24H), 2.24 (s, 6H), 2.01 (d, J = 7.4 Hz, 2H), 1.88 - 1.79 (m, 2H), 1.67 (p, J = 6.6 Hz, 8H), 1.57 (t, J =

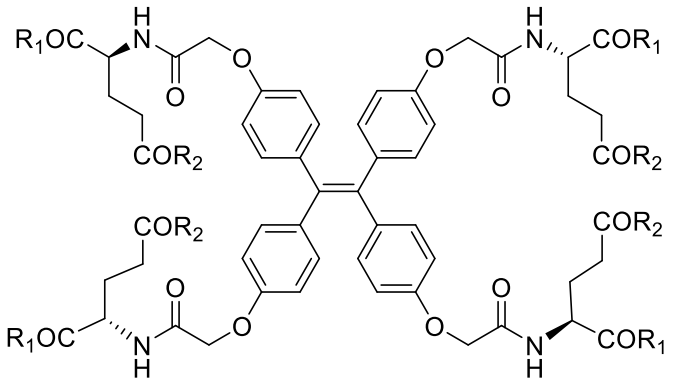
6.9 Hz, 8H), 1.44 (d, J = 6.4 Hz, 4H), 1.39 - 1.23 (m, 64H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.2, 167.9, 155.6, 132.7, 120.4 (q, J = 293.6 Hz), 114.0, 80.1 - 79.4 (m), 71.9, 71.6, 70.7, 70.60, 70.56, 70.5, 70.5, 70.4, 70.3, 70.0, 69.9, 69.7, 69.4, 69.2, 67.0, 59.0, 48.8, 46.5, 39.3, 29.7, 29.63, 29.59, 29.56, 29.5, 29.4, 29.1, 26.1, 25.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.57 (s). MS (MALDI-TOF) m/z: $[M+H_3O]^+$ calcd for $C_{326}H_{575}F_{36}N_{12}O_{121}^+$ 7279.863, found 7279.398.



2

R_1 = $NH(CH_2CH_2O)_{11}Me$, R_2 = $NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

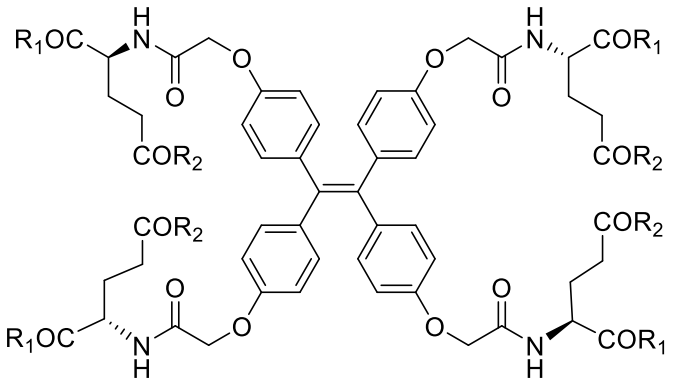
FMA 2. FMA **2** was prepared as yellow oily liquid (1.8 g, 89% yield) using a procedure identical to the preparation of FMA **1**. The reaction substrates were Compound **22** and **25.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 7.3 Hz, 2H), 7.58 - 7.55 (m, 2H), 6.92 (d, J = 8.5 Hz, 6H), 6.70 (d, J = 8.5 Hz, 6H), 4.49 (q, J = 7.0 Hz, 4H), 4.41 (s, 4H), 3.99 (t, J = 6.3 Hz, 8H), 3.73 - 3.61 (m, 190H), 3.60 - 3.52 (m, 32H), 3.43 (t, J = 6.9 Hz, 16H), 3.38 (s, 12H), 2.37 - 2.23 (m, 6H), 2.06 (ddd, J = 31.3, 14.2, 7.2 Hz, 8H), 1.71 - 1.64 (m, 8H), 1.58 - 1.54 (m, 8H), 1.26 (s, 64H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 171.0, 168.2, 166.2, 155.7, 132.8, 120.5 (q, J = 293.6 Hz), 114.1, 80.1 - 79.5 (m), 72.0, 71.7, 70.8,69.4, 67.1, 59.1, 39.4 , 33.9, 32.5, 32.0, 30.4, 28.3, 29.2, 29.1, 26.2, 25.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -73.57 (s). MS (MALDI-TOF) m/z: $[M+Na]^+$ calcd for $C_{234}H_{388}F_{36}N_{12}NaO_{76}^+$ 5289.619, found 5288.126.



3

$R_1 = N[(CH_2CH_2O)_{11}Me]_2$, $R_2 = N[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

FMA 3. FMA **3** was prepared as yellow oily liquid (1.5 g, 85% yield) using a procedure identical to the preparation of FMA **1**. The reaction substrates were Compound **23** and **25.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 2H), 7.58 (d, *J* = 6.4 Hz, 2H), 6.92 (d, *J* = 7.5 Hz, 6H), 6.70 (d, *J* = 8.1 Hz, 6H), 4.38 (q, *J* = 14.7 Hz, 8H), 3.99 (t, *J* = 6.5 Hz, 16H), 3.69 - 3.53 (m, 436H), 3.43 (d, *J* = 3.7 Hz, 24H), 3.38 (s, 24H), 2.92 (d, *J* = 31.0 Hz, 8H), 2.41 - 2.12 (m, 16H), 1.71 - 1.63 (m, 16H), 1.60 - 1.54 (m, 16H), 1.27 (s, 128H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 172.7, 170.9, 168.2, 155.7, 132.7, 120.5 (q, *J* = 293.6 Hz), 114.1, 80.7 - 79.7 (m), 72.1, 71.6, 70.5, 70.1, 69.7, 69.6, 67.0, 59.1, 52.1, 39.7,39.2, 29.9,29.7, 29.2, 26.2, 25.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.60 (s). MS (MALDI-TOF) m/z: $[M+4(Na+K+CH_3OH-H)]^{4+}$ calcd for $C_{418}H_{725}F_{72}K_4N_{12}Na_4O_{140}^{4+}$ 9769.697, found 9770.393.



4

$R_1 = NH(CH_2CH_2O)_{11}Me$, $R_2 = N[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

FMA 4. FMA **4** was prepared as yellow liquid (2.6 g, 79% yield) using a procedure identical to the preparation of FMA **1**. The reaction substrates were Compound **24** and

25. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 5.7 Hz, 2H), 7.56 (d, *J* = 5.6 Hz, 2H), 6.93 - 6.89 (m, 6H), 6.68 (d, *J* = 8.4 Hz, 6H), 4.45 – 4.37 (m, 8H), 3.98 (t, *J* = 6.5 Hz, 16H), 3.69 - 3.48 (m, 258H), 3.42 (td, *J* = 6.9, 2.3 Hz, 24H), 3.37 (s, 12H), 2.84 – 2.66 (m, 4H), 2.45 (dt, *J* = 16.6, 6.2 Hz, 4H), 2.14 (t, *J* = 9.9 Hz, 16H), 1.70 - 1.61 (m, 16H), 1.60 - 1.52 (m, 16H), 1.37 - 1.24 (m, 128H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.2, 155.6, 132.7, 120.4 (q, *J* = 293.6 Hz), 116.9, 114.0, 80.4 - 79.4 (m), 71.9, 71.6, 70.7, 70.59, 70.56, 70.53, 70.50, 70.4, 70.3, 70.03, 70.02, 69.9, 69.7, 69.4, 69.2, 66.9, 59.0, 52.2, 48.8, 46.5, 39.3, 29.7, 29.63, 29.59, 29.56, 29.5, 29.4, 29.1, 26.1, 25.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.62 (s). MS (MALDI-TOF) m/z: $[M+H_3O]^+$ calcd for $C_{322}H_{531}F_{72}N_{12}O_{93}^+$ 7422.604, found 7422.946.

5. LogP Measurement

The lipid-water partition coefficient (LogP) values of FMA **1**-**4** and TPE **5** were measured using the shake flask method.[2] Calibration curves for each compound in octanol-saturated water were plotted using the HPLC method. The compounds were weighed and dissolved in 4 mL of water and octanol (50/50, v/v), and the mixed solutions were dispensed by shaking at 120 rpm in a shaker at 37 ºC for 12 h. Finally, the aqueous phase solutions were analysed quantitatively by HPLC, and the LogP was determined using the equation: $LogP = Lg[(C_s\text{-}C_w)/C_w]$, where C_s and C_w represent the concentrations of the initial aqueous solution and the aqueous phase of the compounds, respectively.

6. Relative Fluorescence Quantum Yields Determination

The measurement of relative fluorescence quantum yields was same as our previous work.[1] Quinine sulphate in 0.1 M $HClO_4$ was used as the reference solution (QY_R = 0.60 ± 0.02).[3, 4] The quinine sulfate reference solution was prepared at concentrations of 32 μM, 24 μM, 16 μM, and 8 μM. Similarly, TPE **1**-**4** were dissolved in 0.1 M $HClO_4$ to obtain a series of sample solutions at concentrations of 48 μM, 36 μM, 24 μM, and 12 μM, respectively. The UV absorbance at a wavelength of 350 nm

of each reference and sample solution was measured using a UV-Visible spectrometer (Thermo Fisher, Evolution 220). Fluorescence emission spectra of each reference and sample solution at an excitation wavelength of 350 nm was measured using a fluorescence spectrometer (HORIBA, Fluoromax-4) with a slit width of 2.5 nm, and the integrated area of the fluorescence emission spectra in the wavelength range of 360 nm to 650 nm was analyzed. The relative quantum yield (QY) can be calculated from the following equation:

$$QY_S = QY_R \left(\frac{I_S}{I_R}\right)\left(\frac{1-10^{-A_R}}{1-10^{-A_S}}\right)\left(\frac{n_S}{n_R}\right)^2$$

where QY_S and QY_R are the photoluminescence QY of the sample and that of quinine sulphate, respectively; I is the integrated emission areas (excitation wavelength: 350 nm); A is the UV absorbance at 350 nm; n is the refractive index of the medium, and the subscripts S and R refer to the measured sample and quinine sulphate, respectively.

7. CMC Measurement

The Nile Red method was used to measure the CMC of compounds, which was same as our previous work.[1, 5] The ratio of fluorescence intensity at 635 and 660 nm from the Nile Red was plotted against the compound concentration to calculate the CMC.

8. DLS Measurement and TEM

DLS measurement was performed to determine the average hydrodynamic size and the zeta potential of nanoparticles at different concentrations using Malvern Zetasizer. Data were given as mean ± standard deviation (SD) based on three independent measurements.

TEM was used to observe the morphology of FMA **1**-**4** and TPE **5** of different concentrations (5, 100, and 1000 μM). Samples were prepared by dropping 3 μL of the solution on 230 mesh carbon support films (copper mesh), and imaged without external staining. Nanoparticles **FMA@IR780** was stained with 1% phosphotungstic acid solution for 30 s before taking images.

9. *In Vitro* ^{19}F MRI Study

FMA **1**-**4** were serially diluted with water to give a series of ^{19}F concentrations: 40, 20, 10, 5 and 2.5 mM, respectively. The ^{19}F magnetic resonance imaging (^{19}F MRI) phantom experiments were performed on a 400 MHz Bruker BioSpec MRI system at 25 °C. The ^{19}F *in vitro* phantom images were acquired using a spin-echo pulse sequence, method = RARE, matrix size = 32 × 32, FOV = 30 mm × 30 mm, TR = 3000 ms, TE = 3.00 ms, RARE factor = 4, number of average = 20, scan time = 480 s.

The imaging conditions of nanoparticles **FMA@IR780** and **FMA@DOX** were the same as those of FMA **1**-**4**.

10. Cytocompatibility and Cytotoxicity Assay

The cytotoxicity of MCF-10A cells, MCF-7 cells and A549 cells was assessed by the CCK-8 assay. These cells were cultured to a suitable state and then inoculated into 96-well plates at a density of 1×10^4 cells per well and cultured for 24 h. 100 μL of medium containing the compounds at a concentration of 2.5, 5, 10, 20, 40, and 80 μM was added to each well in the experimental group and 100 μL of blank medium was added to the blank control group and the cells were incubated for 24 h protected from light. A solution of 10% CCK-8 was prepared by mixing phenol-free red DMEM medium with 2% fetal bovine serum. The medium was removed from the 96-well plate, 100 μL of CCK-8 solution was added and the cells were incubated in the cell culture incubator for 1.5 h. The absorbance (A) was measured at 450 nm using a microplate reader (BIO-RAD 550). The relative cell viability was calculated as follows:

$$\text{Cell Viability (\%)} = [(A_{sample} - A_{blank})/ (A_{control} - A_{blank})] \times 100$$

Where A_{sample}, $A_{control}$, and A_{blank} represented the absorbance of the cells treated with samples, the cells without treatment, and the PBS solution, respectively. Data were given as mean ± SD based on three independent measurements.

The cytotoxicity assay of nanoparticles **FMA@IR780** and **FMA@DOX** was the same

and the concentration was diluted based on the IR-780 or DOX content in the nanoparticles.

11. Cellular Uptake

MCF-7 cells and A549 cells were inoculated in confocal dishes at a density of 1×10^5, and the cells were cultured for 24 hours at 37 ºC with 5% CO_2. After the cells were sufficiently attached to the wall, the medium was removed, and 1 mL of 10 μM FMA **1**-**4** and TPE **5** solution was added respectively. After 24 hours of incubation protected from light, the cells were washed three times with cold PBS (pH 7.4), stained with Dil, and then the cells were washed again, and observed with a laser scanning confocal microscope (A1R/A1, Nikon).

The steps of the cellular uptake experiments with nanoparticles were consistent with those described above, except for a different time of incubation.

12. Preparation of Nanoparticles

Nanoparticles loaded with different drugs were prepared using the solvent evaporation method with FMA **2**.[6] The preparation process of **FMA@DOX** was presented as an example. Firstly, 21.1 mg of FMA **2** and 2.2 mg of DOX were dissolved in an appropriate amount of DCM. After mixing the two substances, 4 mL of purified water was added to the mixture, and the system was fully emulsified by ultrasonication for 15 minutes to form an oil-in-water (O/W) emulsion. Then, the nanoparticle crude was obtained as a clarified and transparent liquid after continuing ultrasonication for 15 minutes. The final **FMA@DOX** nanoparticles solution was obtained by removing the residual DCM solvent.

13. Entrapment Efficiency and Drug Loading Content

Entrapment efficiency (EE%) and drug loading content (DLC%) of **FMA@IR780** nanoparticles were determined using HPLC. Briefly, 200 μL of nanoparticles was diluted with 800 μL of MeOH, the mixture was sonicated for 20 minutes, centrifuged

at 12,000 rpm for 20 minutes, and the IR-780 content in the supernatant was determined by HPLC as the total IR-780 content in nanoparticles (W_t). Another 200 μL of nanoparticles was diluted with H_2O, the sample was transferred to an ultrafiltration centrifuge tube, and centrifuged at 12,000 rpm for 20 min. MeOH was added to dissolve the trapped nanoparticles, the content of IR-780 in the MeOH solution was determined by HPLC as the encapsulated IR-780 content in nanoparticles (W_o). EE% and DLC% were calculated by equations (1) and (2), respectively. Where W_d is the weight of the nanoparticles.

$$EE\% = W_o/W_t \times 100\% \quad (1)$$

$$DLC\% = W_o/W_d \times 100\% \quad (2).$$

The content of DOX in the **FMA@DOX** nanoparticles was determined by UV.

14. Standard Curve of DOX and *In Vitro* Drug Release of FMA@DOX

DOX was accurately weighed and dissolved into a series of concentration gradient samples with water. UV absorption spectra of the solutions were obtained. The standard curve was obtained by plotting the UV absorption intensities at 500 nm versus the corresponding DOX concentrations.

2 mL of **FMA@DOX** nanoparticles were added to the uniform pore dialysis bag (MWCO = 3.5 kDa), the bag was sealed and placed in 30 mL of PBS at pH 7.4 and 5.5, respectively, and shaken on a 37 ºC constant temperature shaker at 120 rpm. Then 1 mL of dialysate was removed at 0.5, 1, 2, 4, 6, 8, 10, 12, 24, 36, 48, 60, 72, 84, and 96 h as samples to be tested and replenished with the same volume of fresh buffer, and the samples were passed through the UV to determine the DOX content.

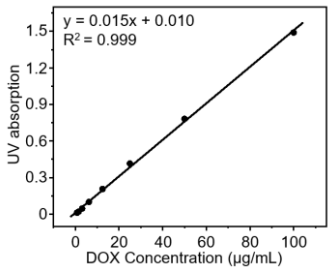


Figure S11. UV-vis absorption standard curves of DOX.

15. Animals and Tumor Model

The A549 tumor model was established by subcutaneously injecting A549 cells (1×10^7) suspended in 0.1 mL of PBS on the flank of the female BALB/c nude mouse.

16. *In Vivo* Biodistribution and Tumor Accumulation

When the tumour volume reached approximately 150 mm^3, the *in vivo* distribution and tumour accumulation of nanoparticles were investigated using an IVIS imaging system (PerkinElmer) (exciation/emission, 780/820 nm) at specific time points after the mice were injected in the tail vein with 0.1 mL of **FMA@IR780** nanoparticles (IR-780, 1.56 mg/kg). After 24 h, the mice were sacrificed and major organs and tumours were dissected for *ex vivo* NIR fluorescence imaging.

17. *In Vivo* ^{19}F MRI Study

The mice had free access to water and food until tumor size reached approximately 200 mm^3. The tumor-bearing mice were intravenously injected 0.1 mL **FMA@IR780** (C_F = 180 mmol/kg). ^{19}F MRI was performed on 9.4T Bruker BioSpec MRI system. ^{1}H MRI scan using a RARE sequence (TR = 7522 ms, TE = 11 ms, FOV = 30 mm × 30 mm, 1 mm slice thickness, RARE factor = 8, matrix size = 256 × 256). Transverse ^{19}F MRI was performed through a RARE sequence (TR = 4000 ms, TE = 3 ms, FOV = 37 mm × 37 mm, 15 mm slice thickness, matrix size = 32 × 32, 64 averages). Coronal ^{19}F MRI was performed through a RARE sequence (TR = 4000 ms, TE = 3 ms, FOV = 49 mm × 49 mm, 20 mm slice thickness, matrix size = 32 × 32, 64 averages).

18. *In Vivo* Tumor Inhibition

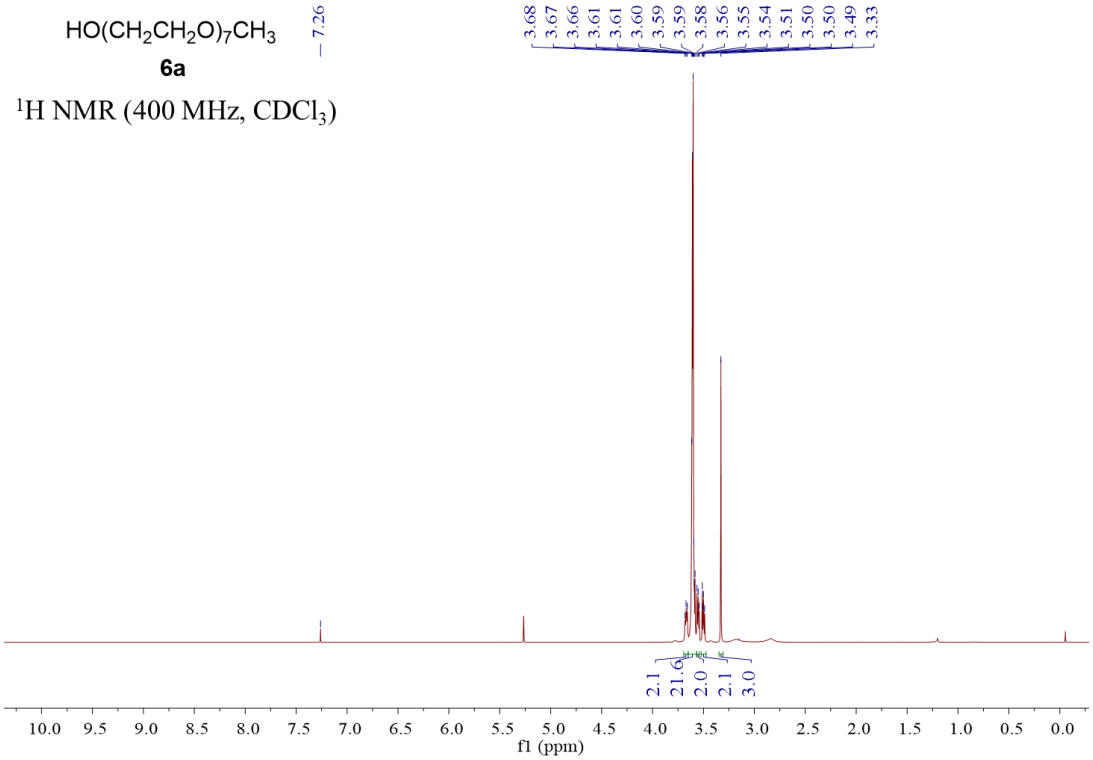
The mice bearing A549 tumors were randomly divided into three groups (G1, G2 and G3). When the tumor volume reached approximately 100 mm^3, the mice in the G1, G2 and G3 groups were intravenously injected every 4 days with 0.1 mL PBS, DOX and **FMA@DOX** (DOX, 1.38 mg/kg), respectively. The body weights and the tumor volumes were measured every 2 days. The tumor volume was calculated as $V = W^2 \times L/2$, in which W and L are the shortest and longest diameters of the tumor, respectively. After 20 days of treatment, the mice were sacrificed, and the major organs and tumors were dissected to detect histological changes and antiproliferative activity by H&E staining, Ki-67 staining, and TUNEL staining.

19. Statistical Analysis.

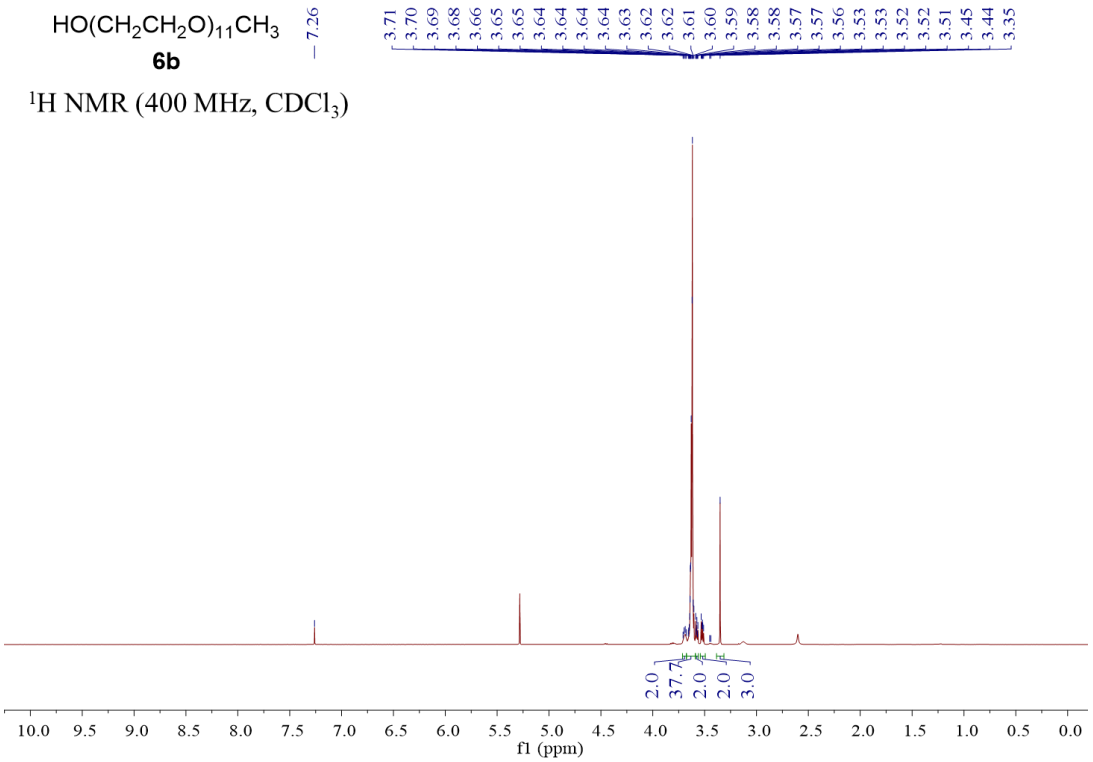
The analyzed data are presented as mean ± standard deviation of n = 3 replicates. Asterisks indicate significant differences (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$) by unpaired Student two-sided t test.

20. $^{1}H/^{13}C/^{19}F$ NMR and MS Spectra of Compounds

^{1}H NMR of compound **6a**



^{1}H NMR of compound **6b**

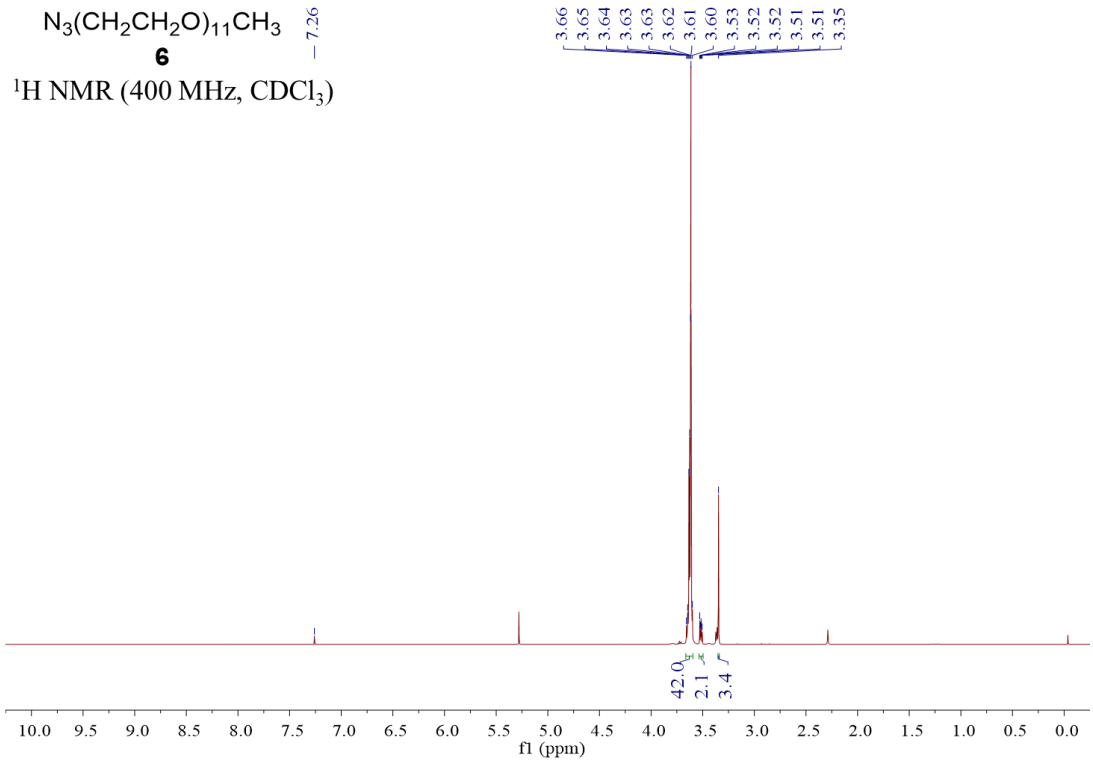


^{1}H NMR of compound **6**

$N_3(CH_2CH_2O)_{11}CH_3$

6

^{1}H NMR (400 MHz, $CDCl_3$)

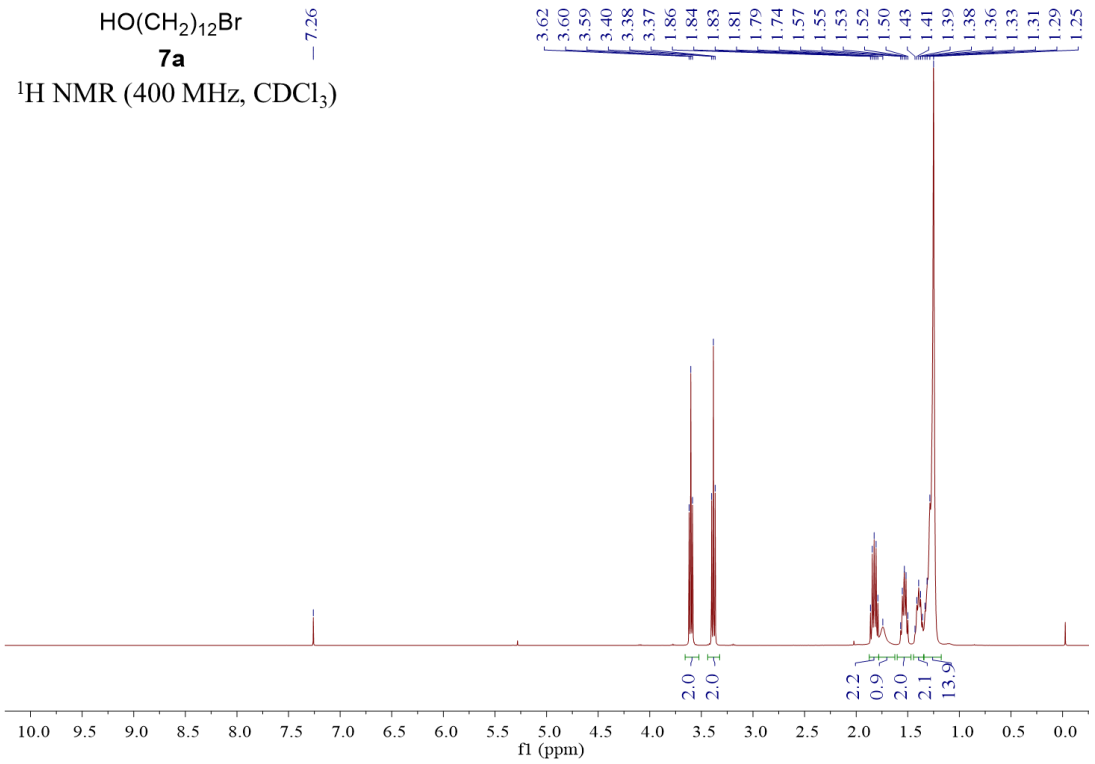


^{1}H NMR of compound **7a**

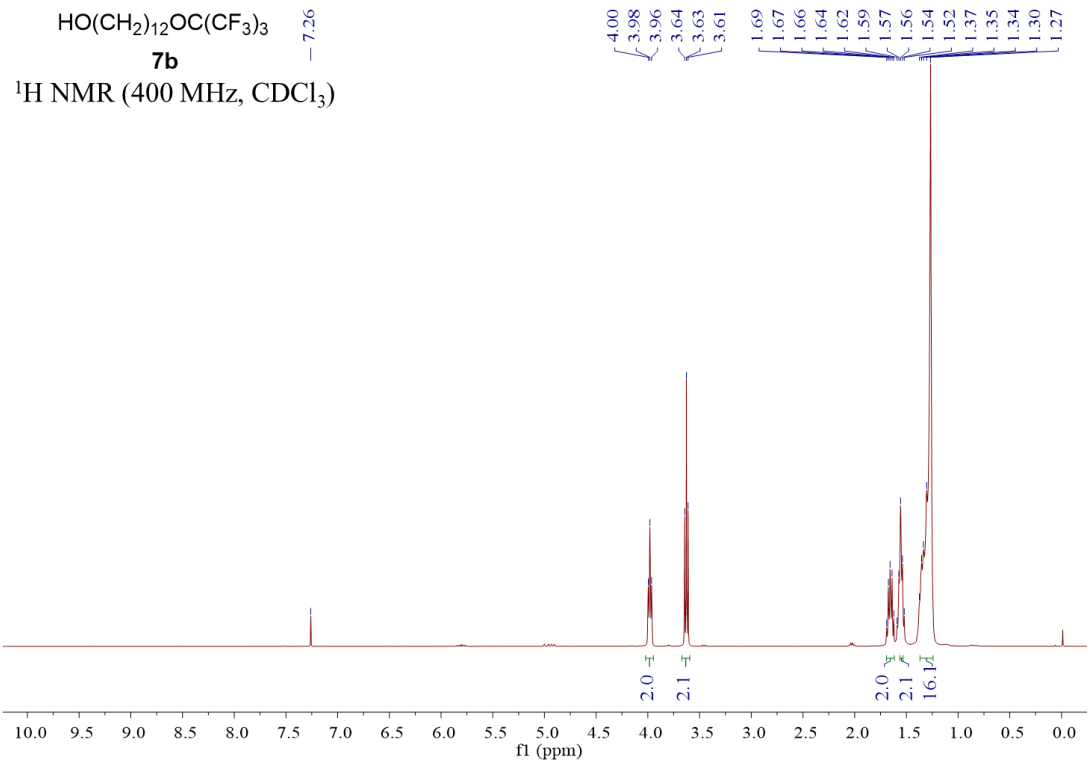
$HO(CH_2)_{12}Br$

7a

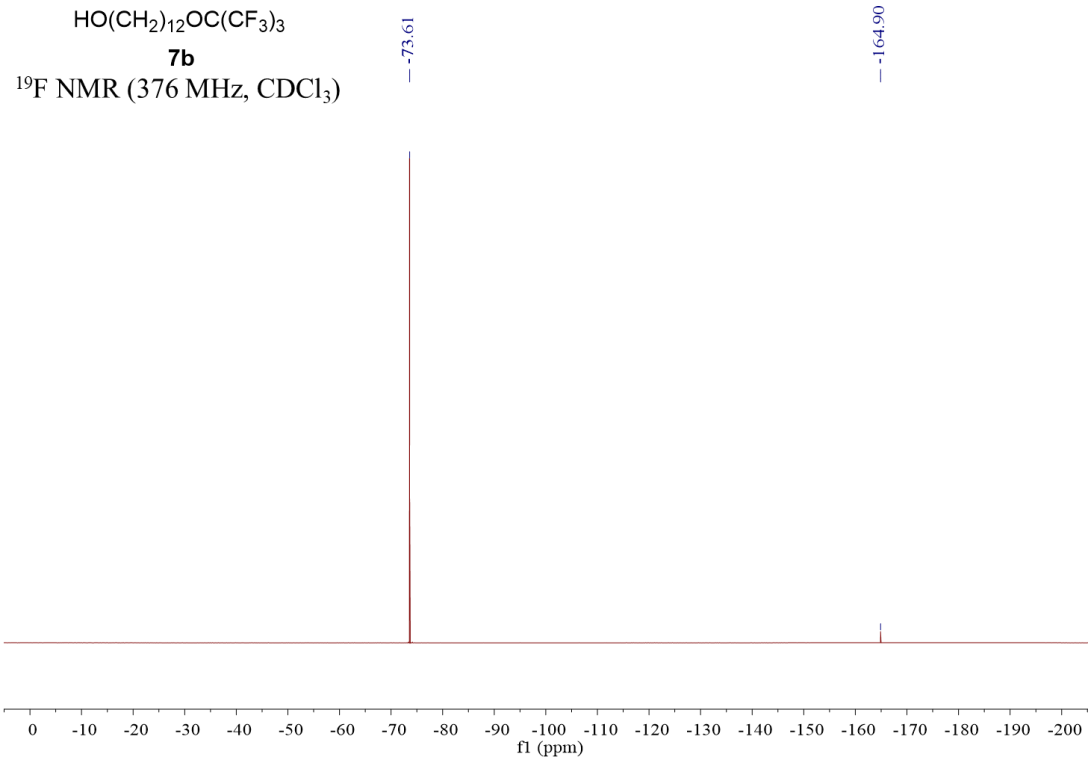
^{1}H NMR (400 MHz, $CDCl_3$)



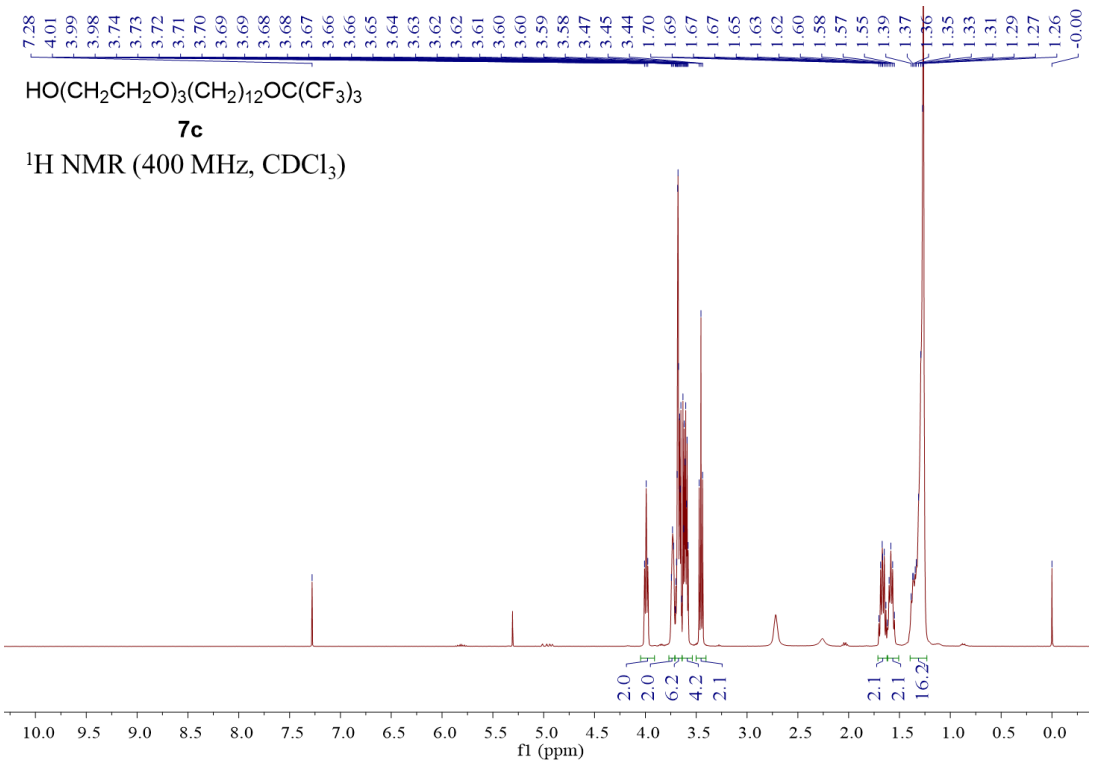
^{1}H NMR of compound **7b**



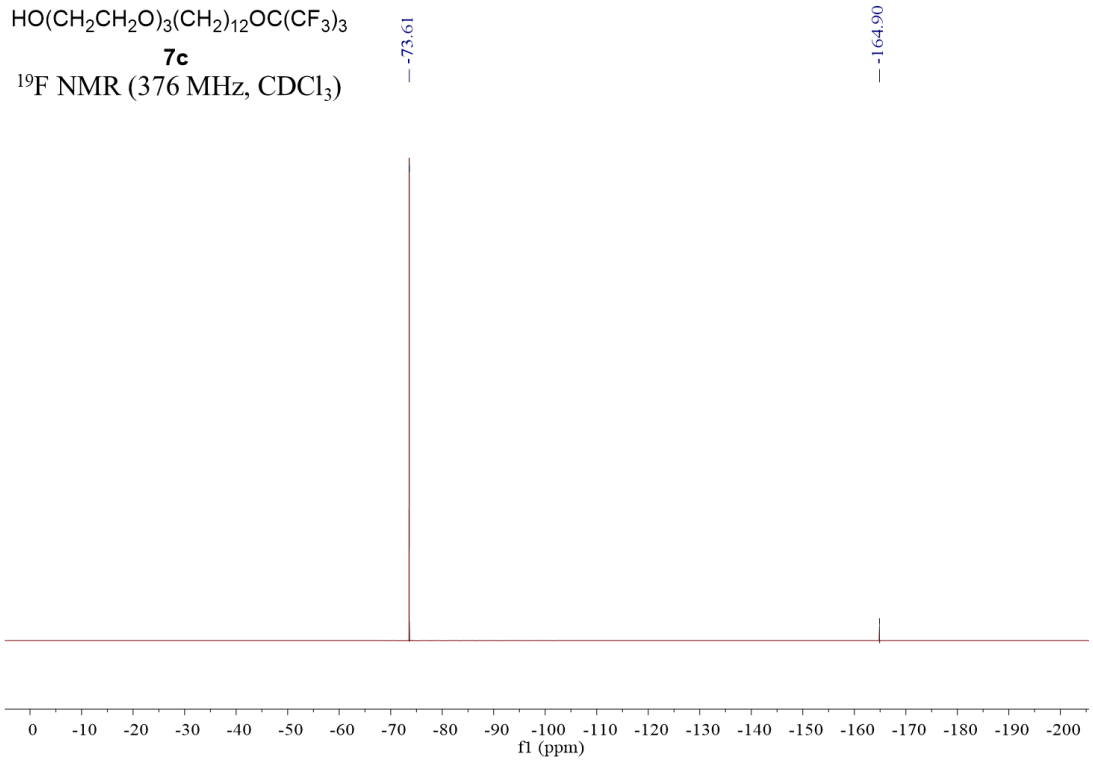
^{19}F NMR of compound **7b**



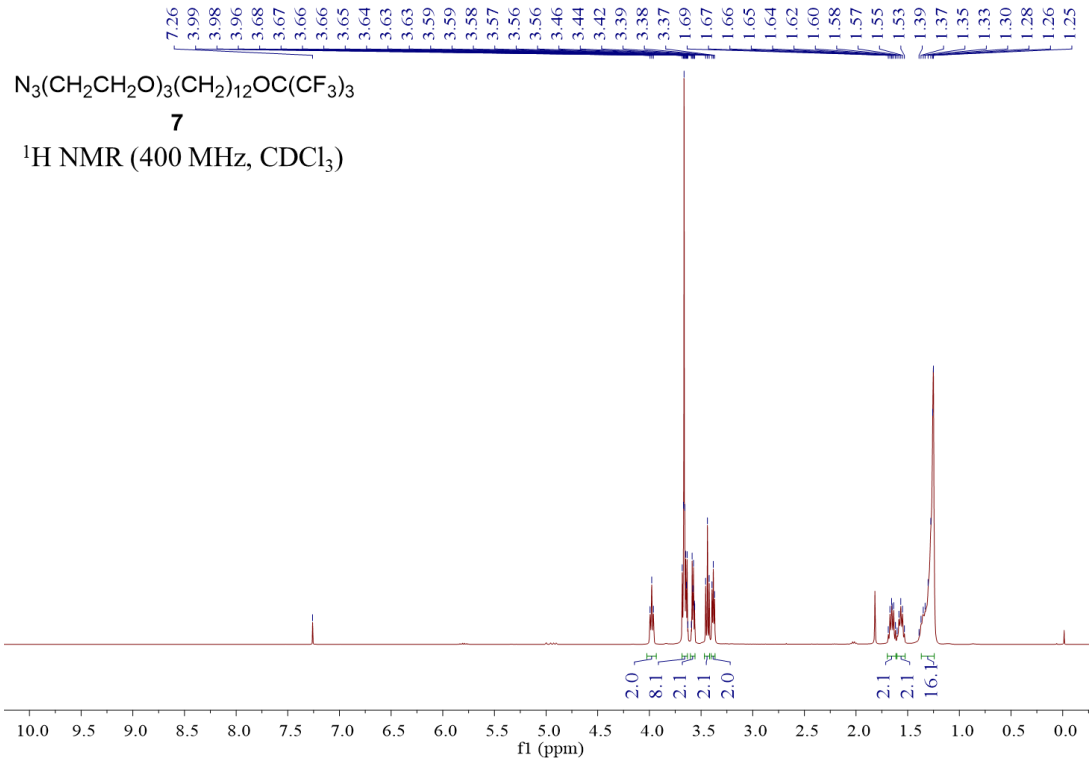
^{1}H NMR of compound **7c**



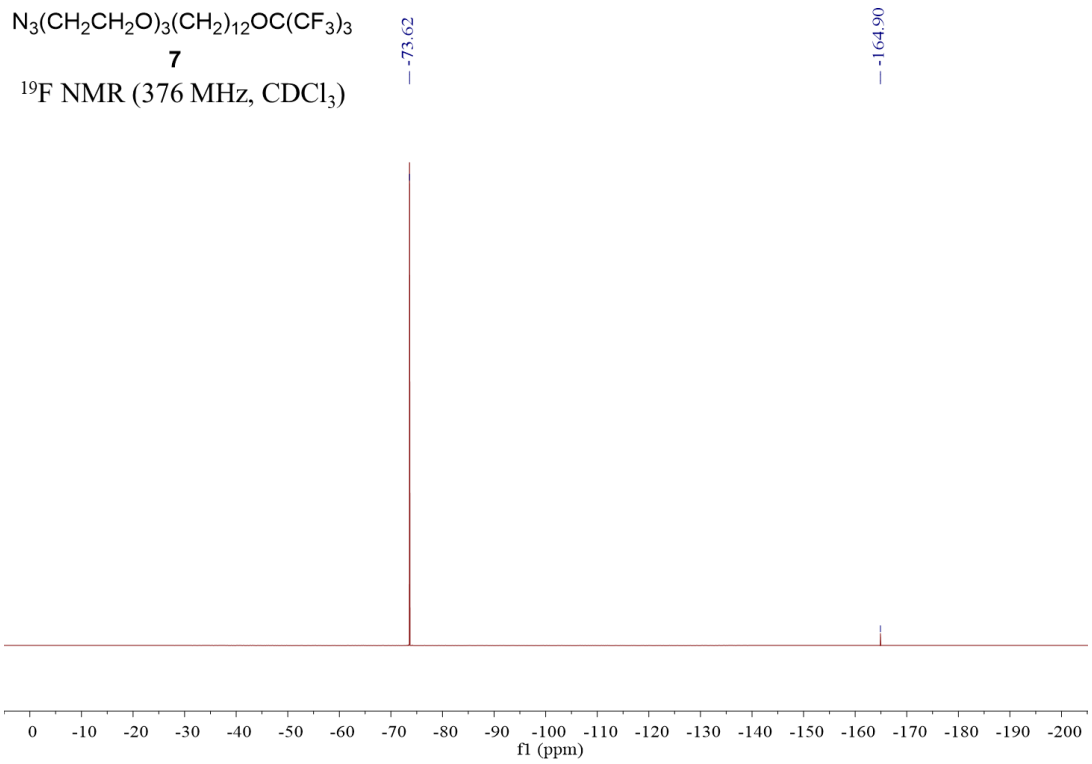
^{19}F NMR of compound **7c**



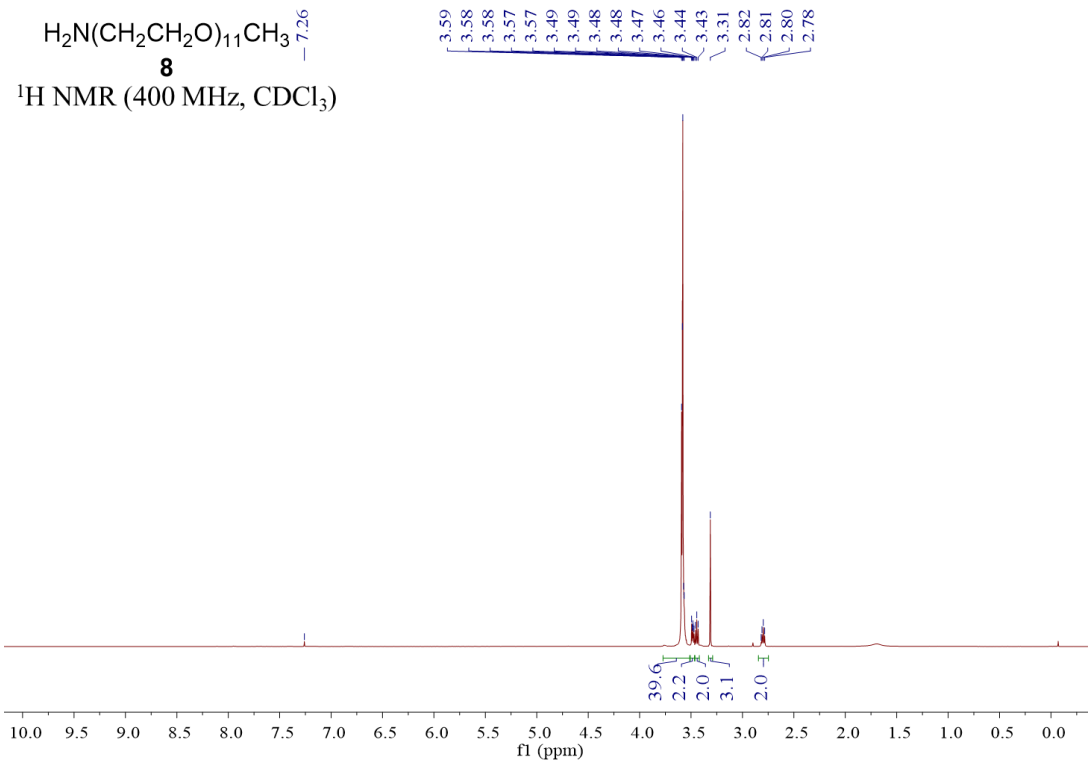
^{1}H NMR of compound **7**



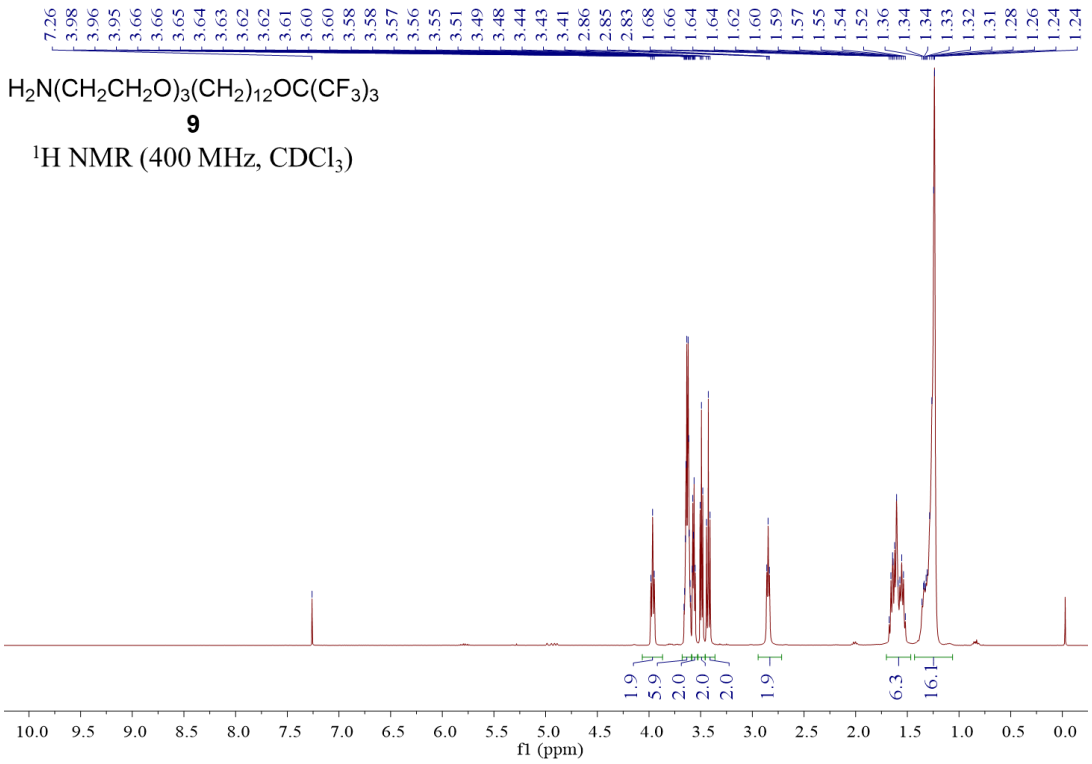
^{19}F NMR of compound **7**



^{1}H NMR of compound **8**



^{1}H NMR of compound **9**

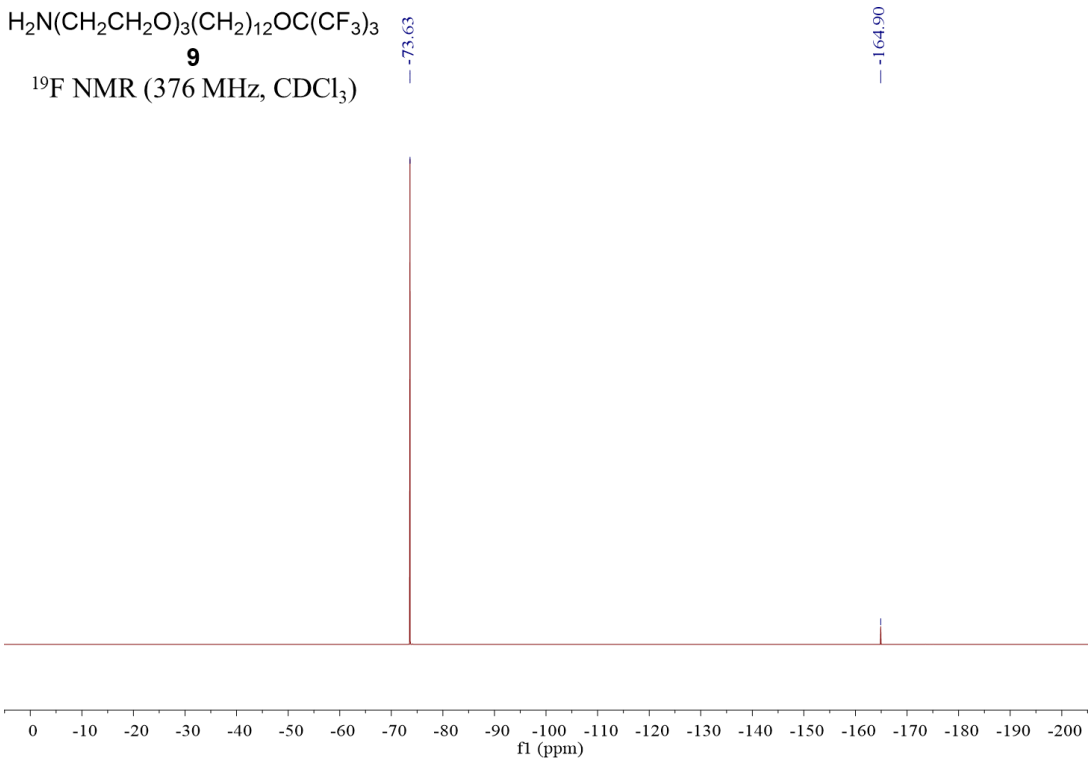


^{19}F NMR of compound **9**

$H_2N(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

9

^{19}F NMR (376 MHz, $CDCl_3$)

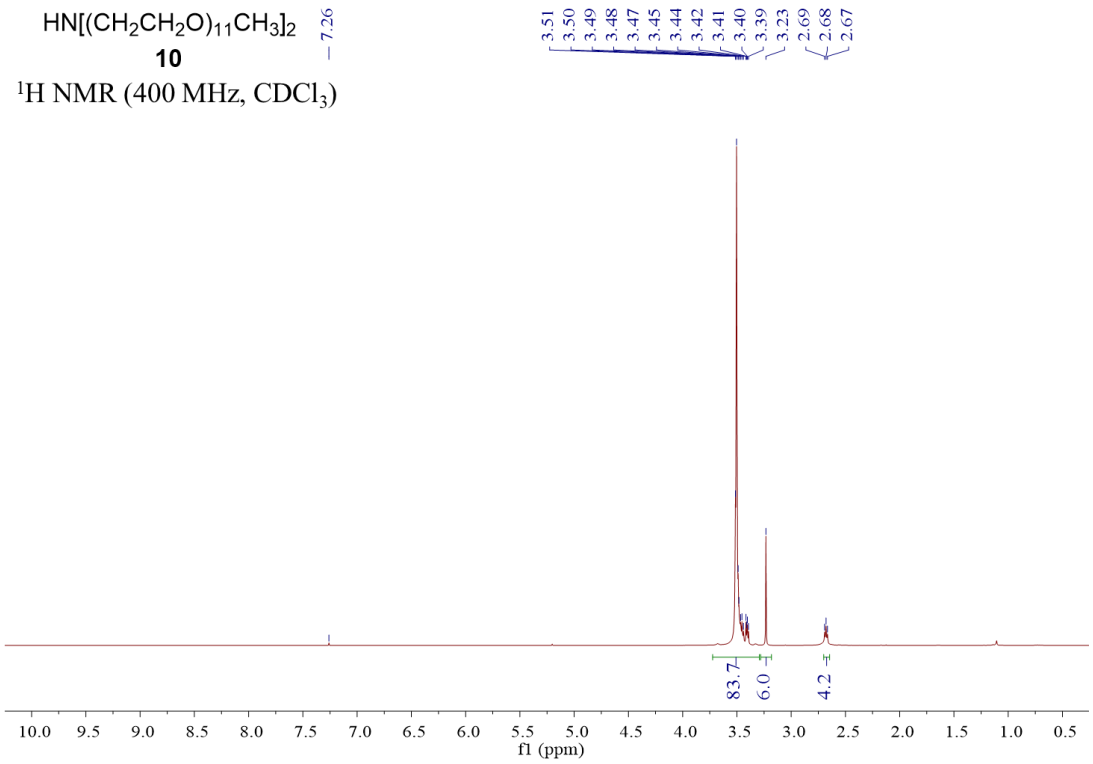


^{1}H NMR of compound **10**

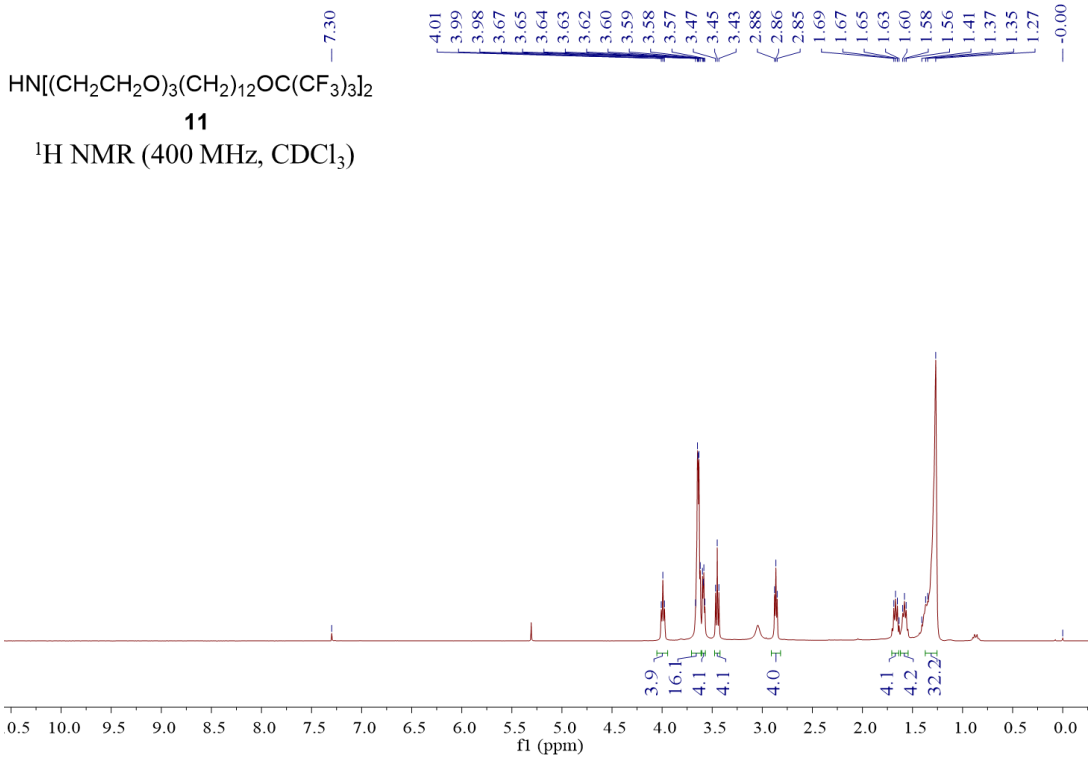
$HN[(CH_2CH_2O)_{11}CH_3]_2$

10

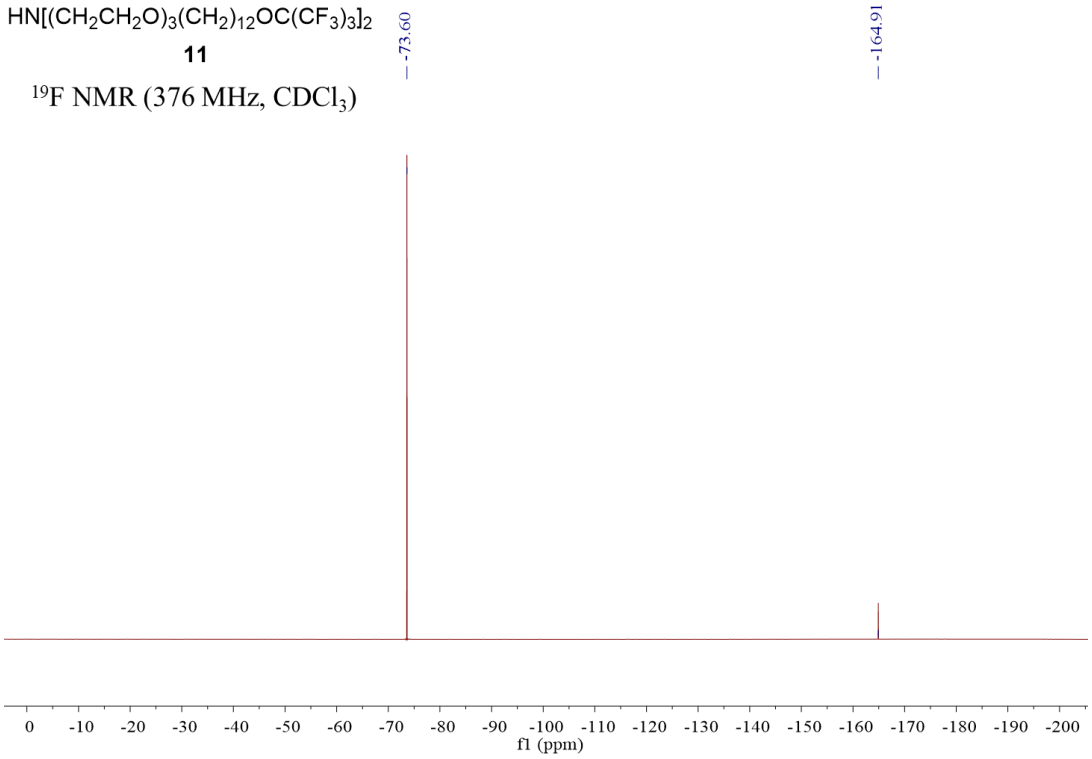
^{1}H NMR (400 MHz, $CDCl_3$)



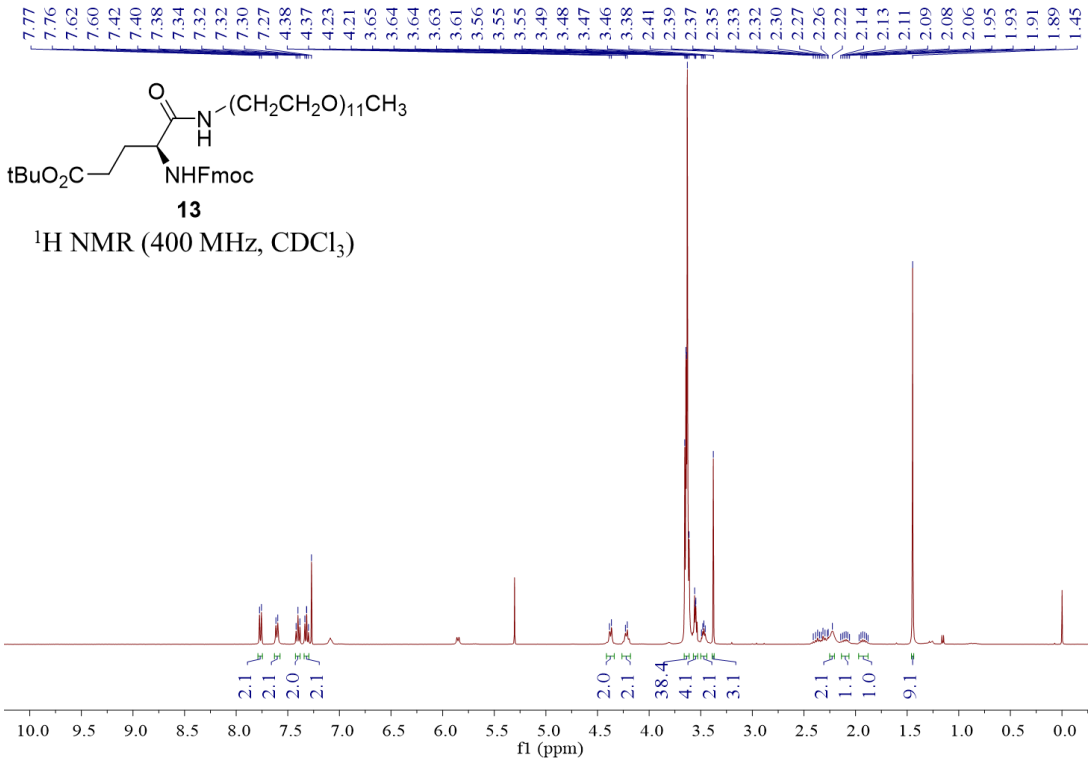
^{1}H NMR of compound **11**



^{19}F NMR of compound **11**



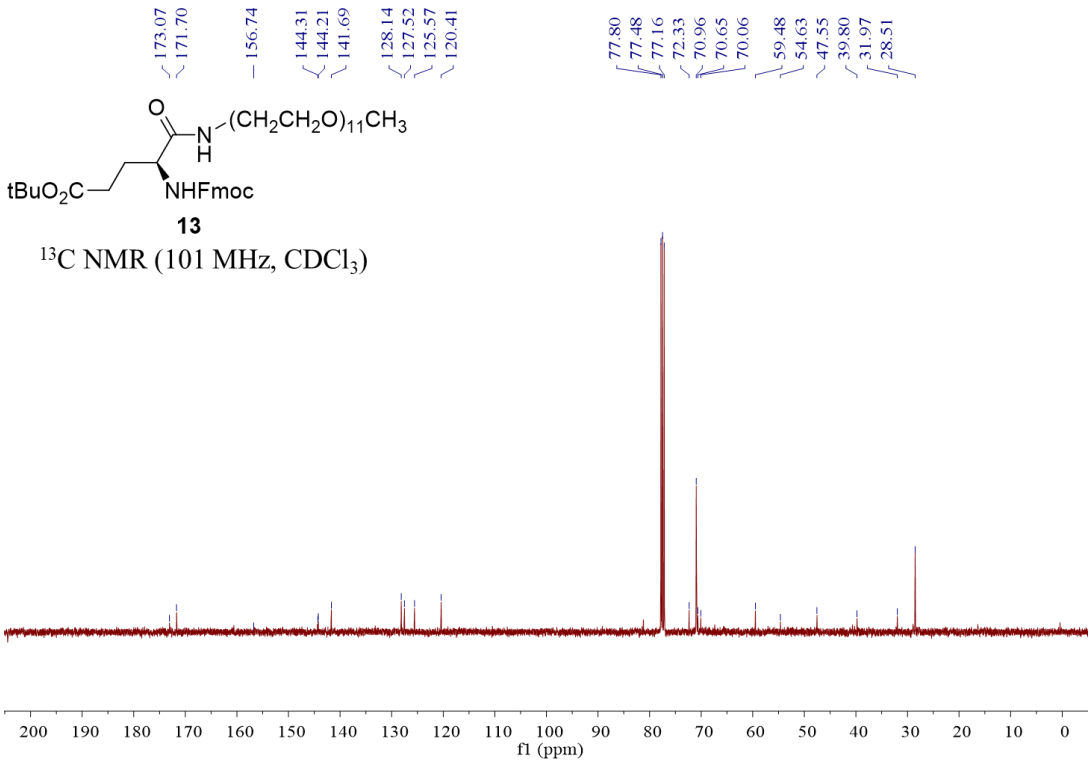
^{1}H NMR of compound **13**



13

^{1}H NMR (400 MHz, $CDCl_3$)

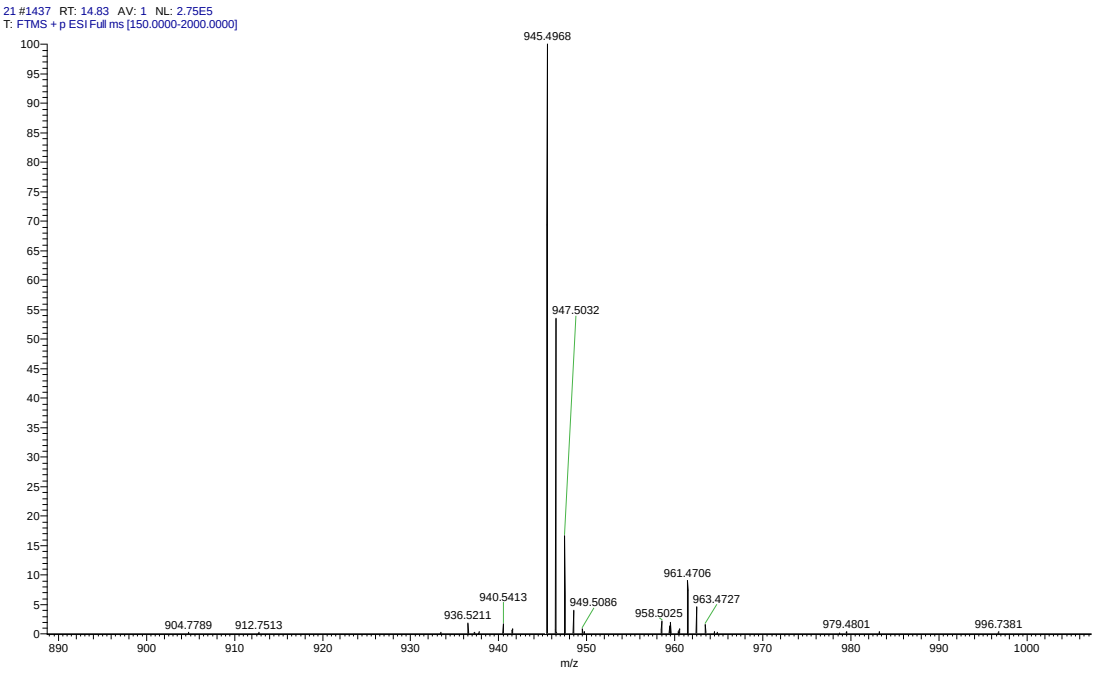
^{13}C NMR of compound **13**



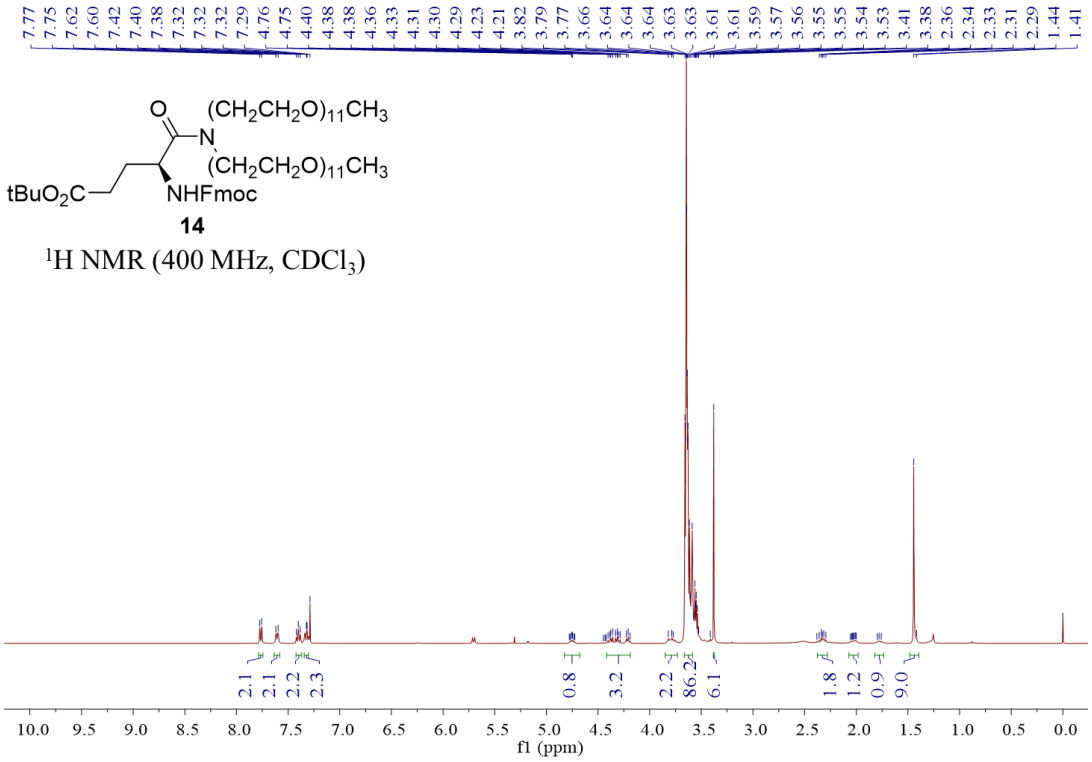
13

^{13}C NMR (101 MHz, $CDCl_3$)

HRMS(ESI) of compound **13**

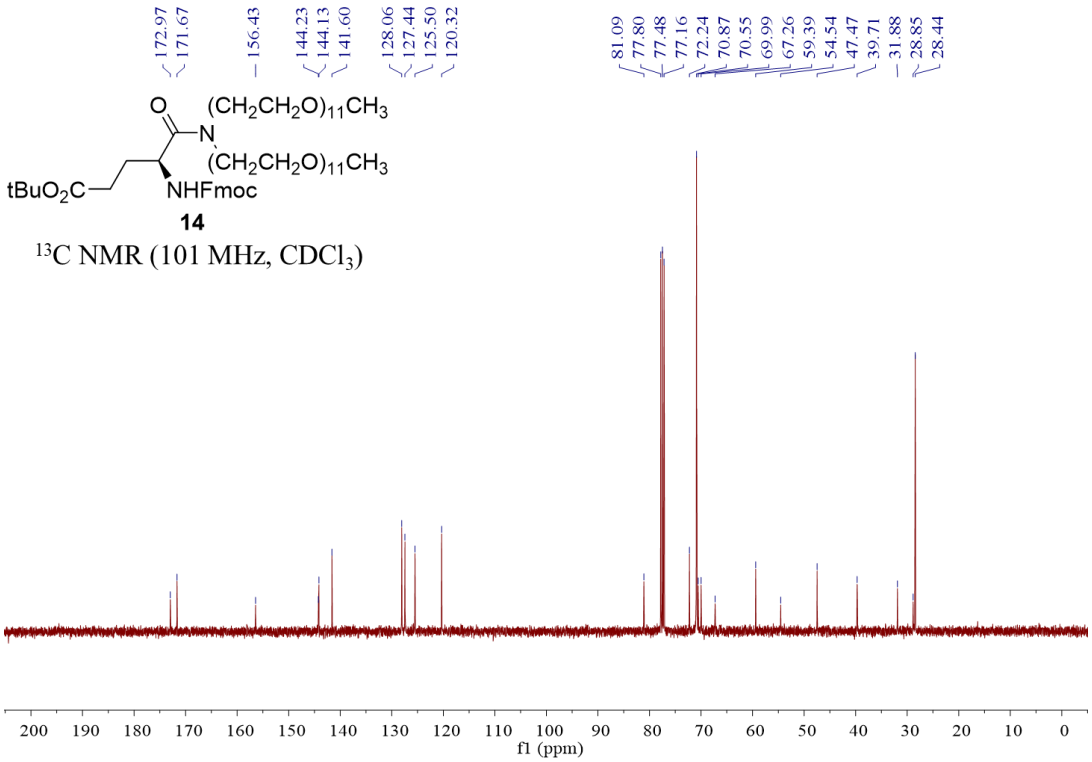


^{1}H NMR of compound **14**



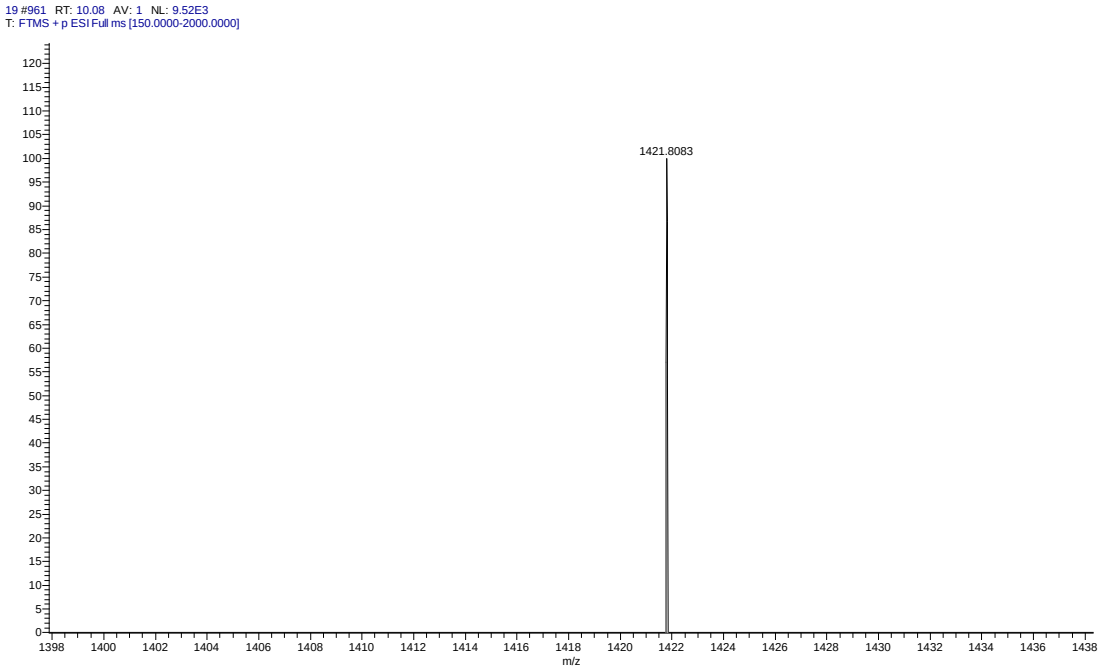
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **14**

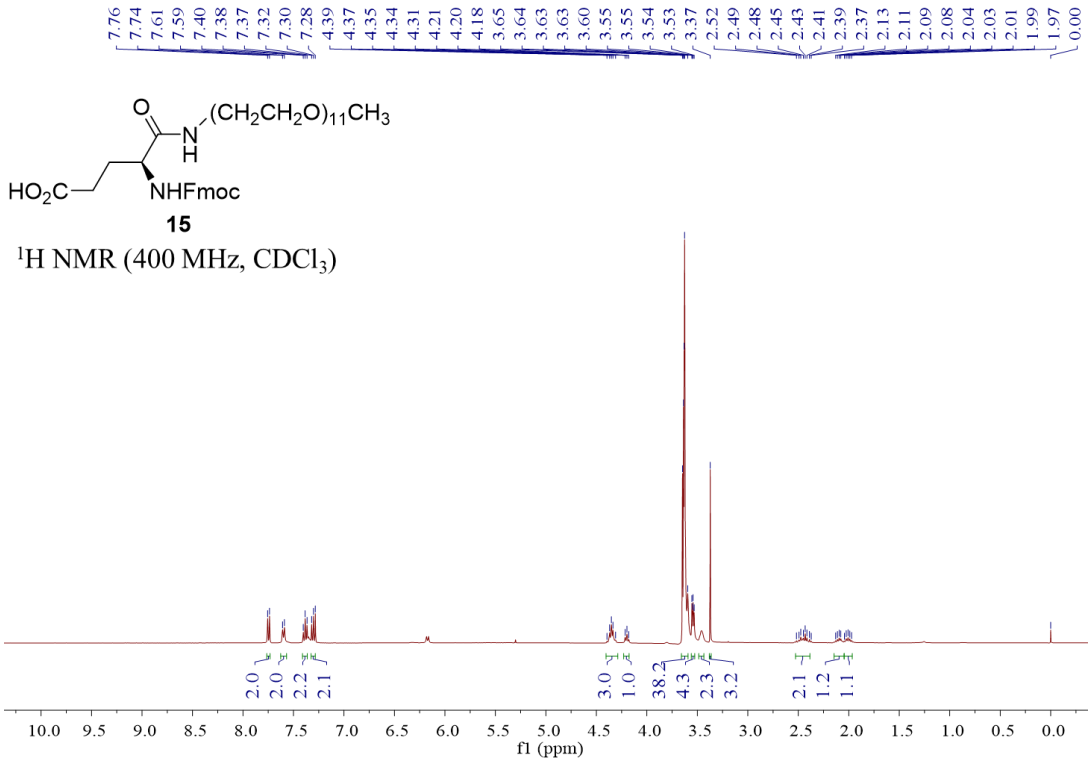


^{13}C NMR (101 MHz, $CDCl_3$)

HRMS(ESI) of compound **14**

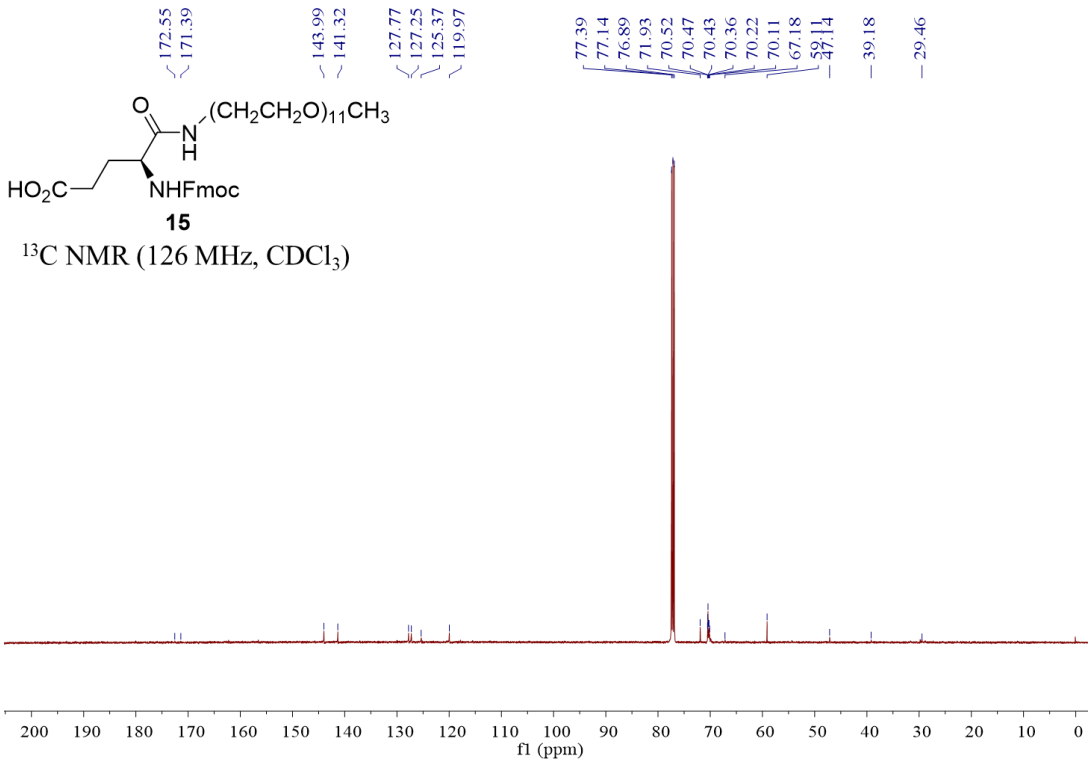


^{1}H NMR of compound **15**



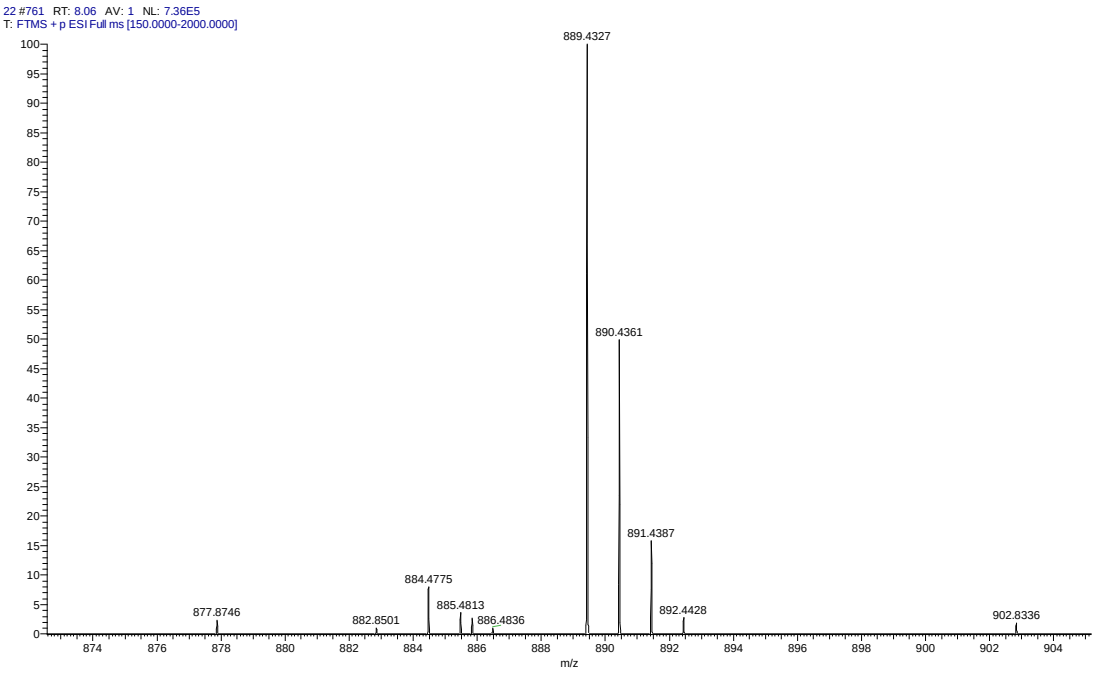
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **15**

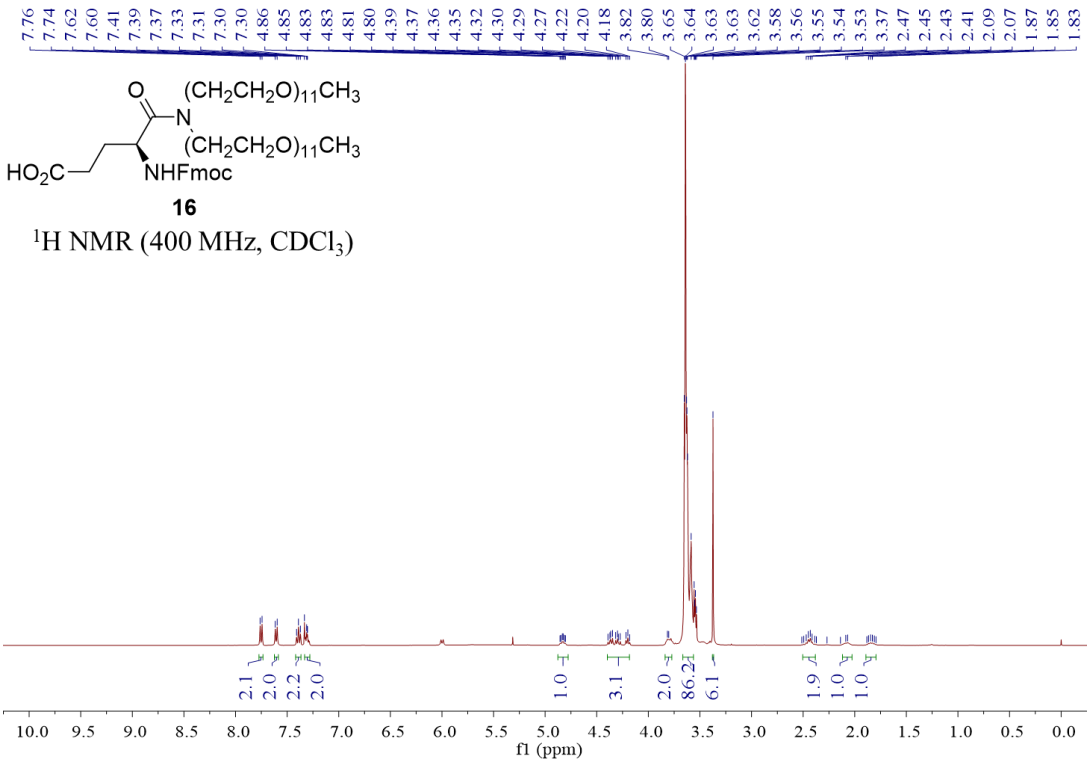


^{13}C NMR (126 MHz, $CDCl_3$)

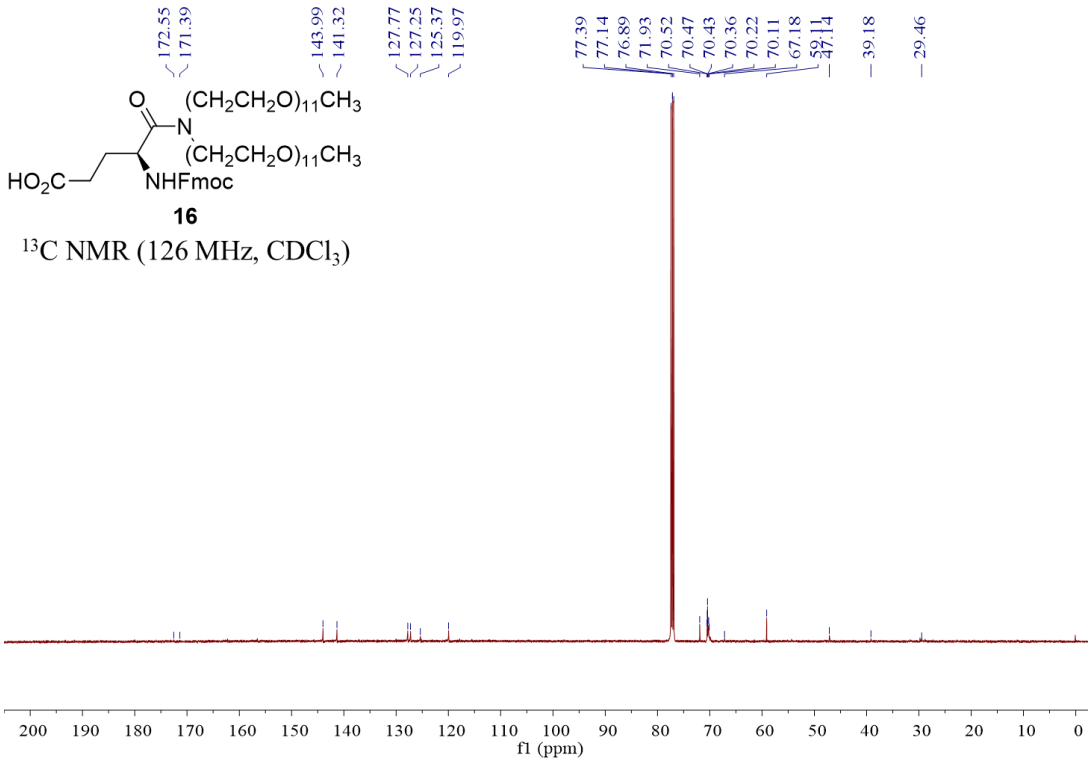
HRMS(ESI) of compound **15**



^{1}H NMR of compound **16**

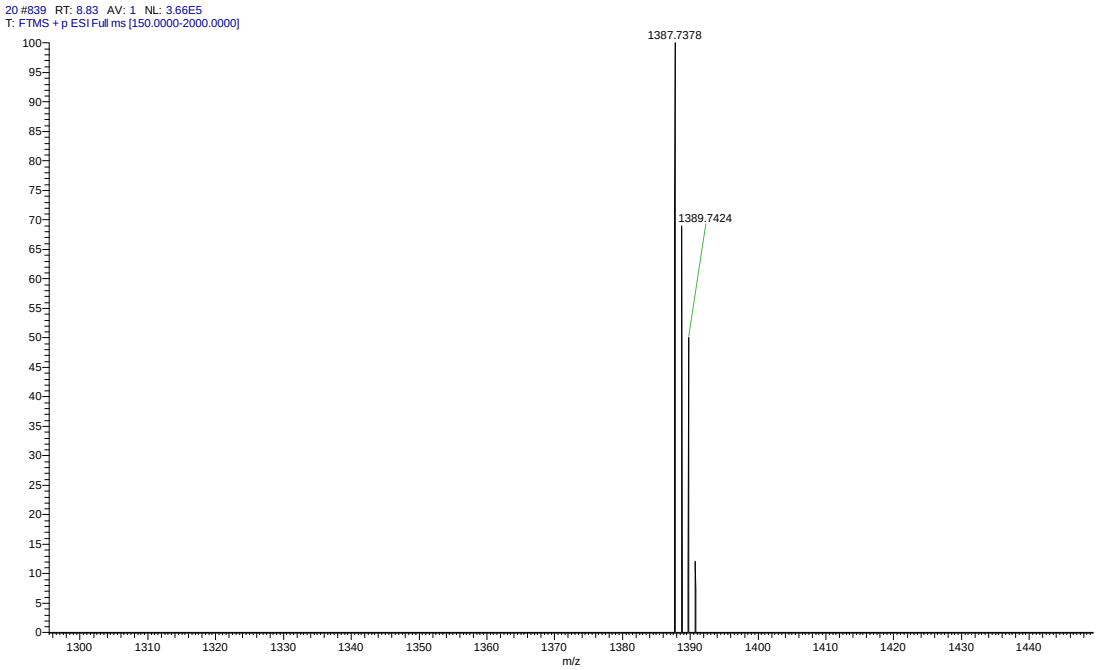


^{13}C NMR of compound **16**

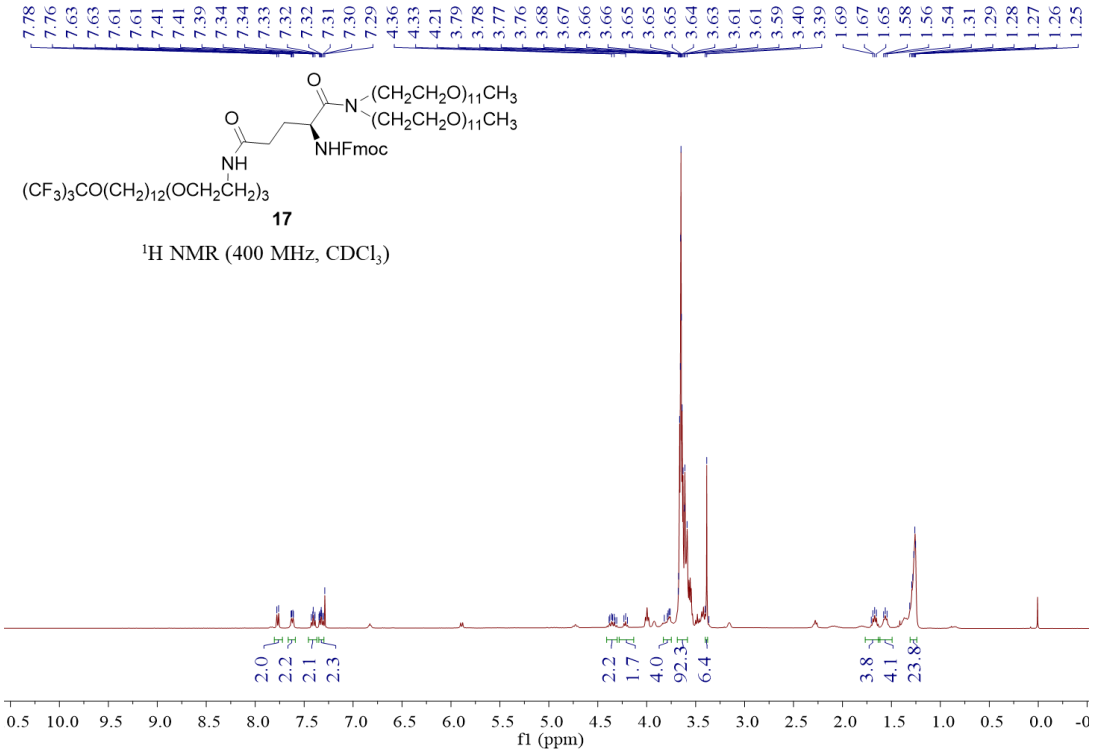


^{13}C NMR (126 MHz, $CDCl_3$)

HRMS(ESI) of compound **16**

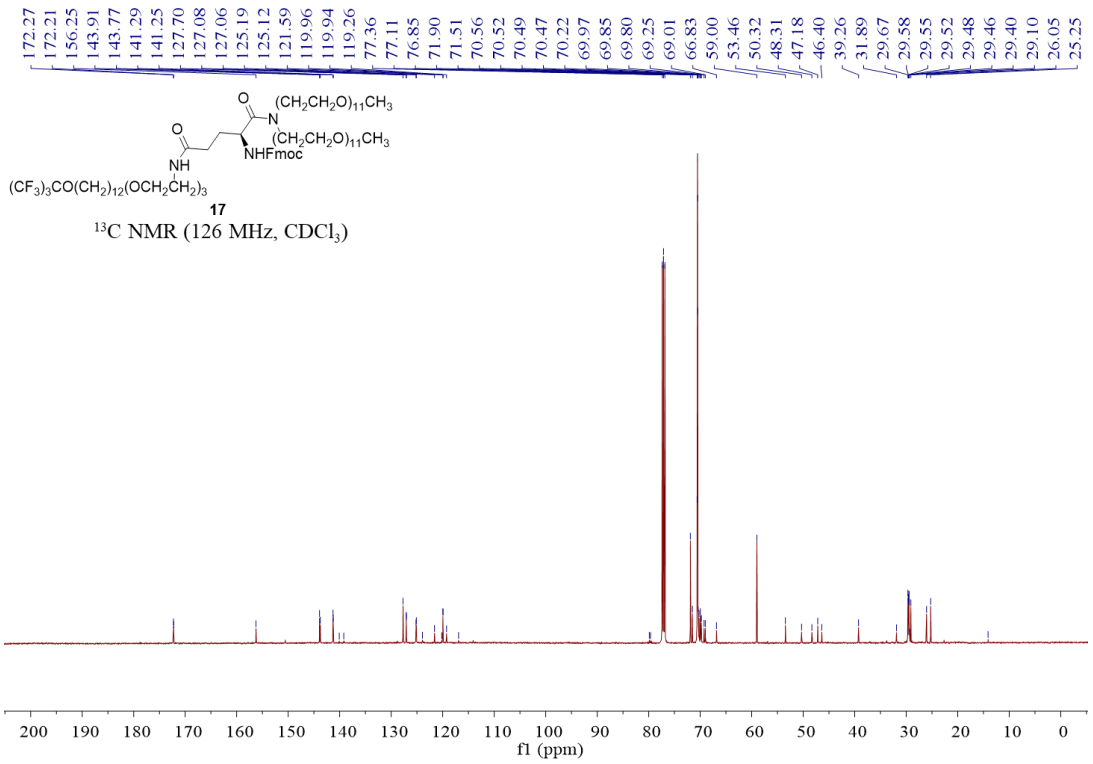


^{1}H NMR of compound **17**



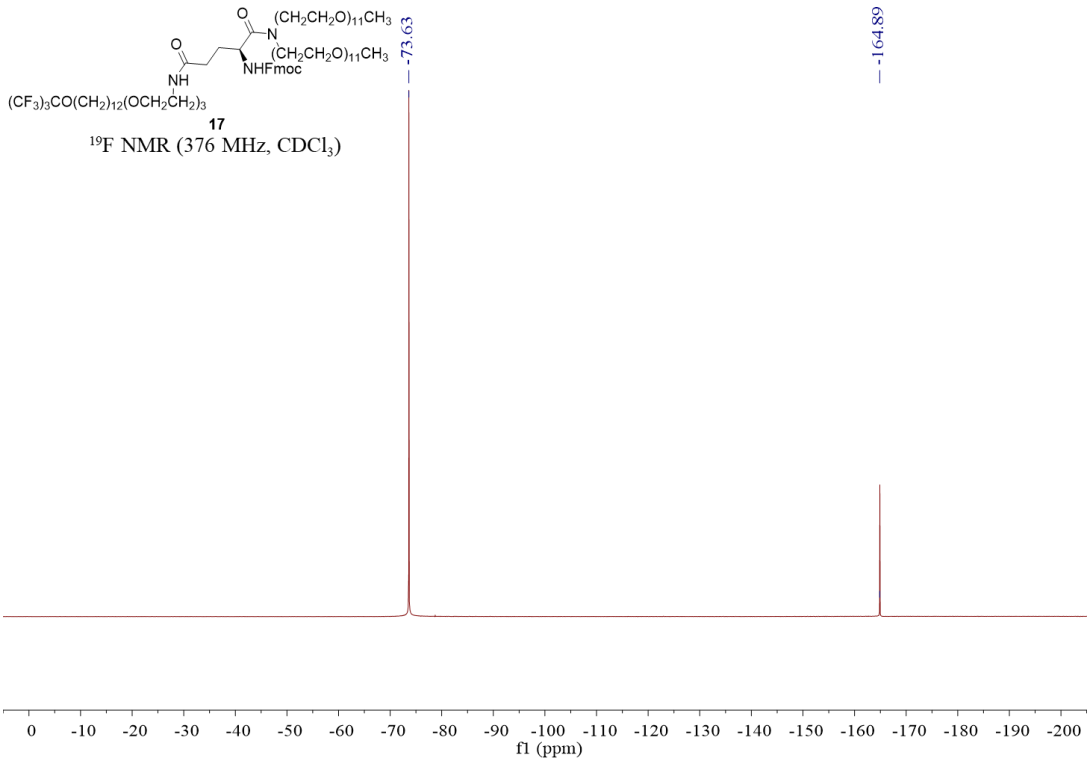
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **17**



^{13}C NMR (126 MHz, $CDCl_3$)

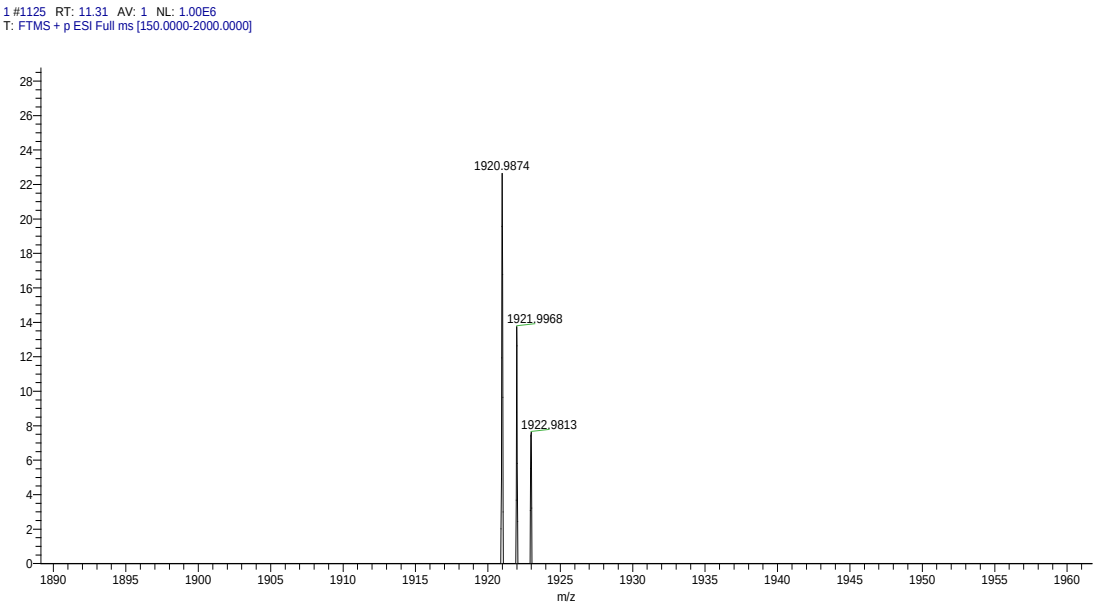
^{19}F NMR of compound **17**



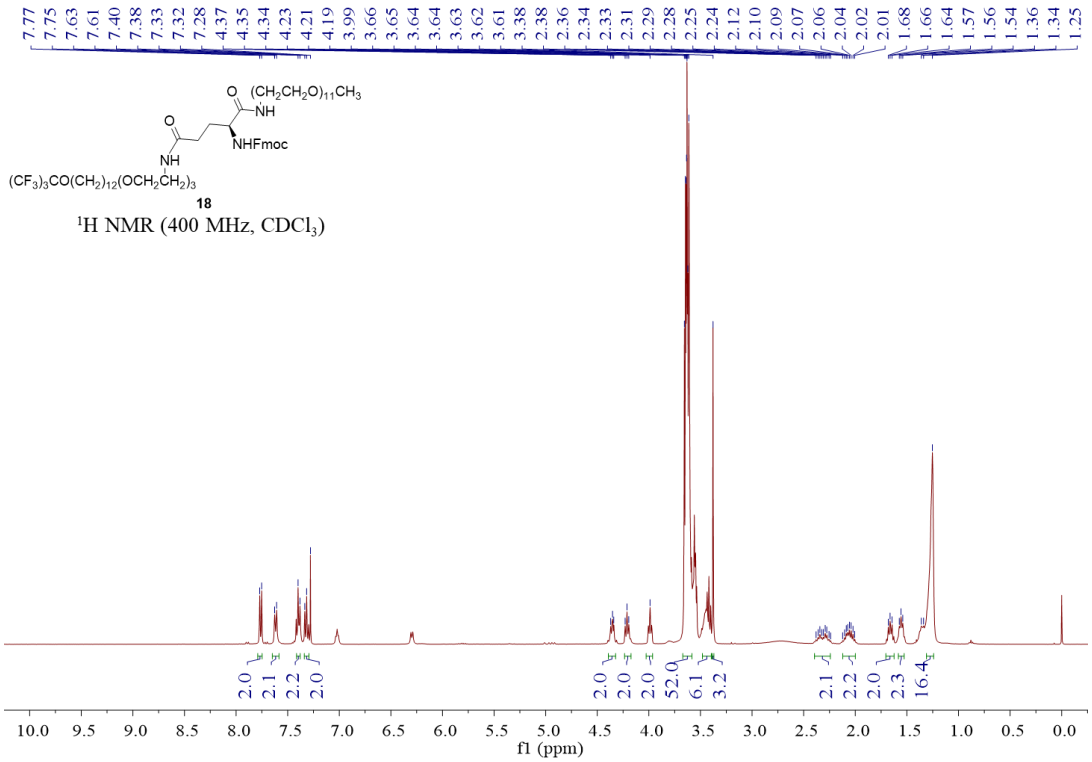
17

^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **17**

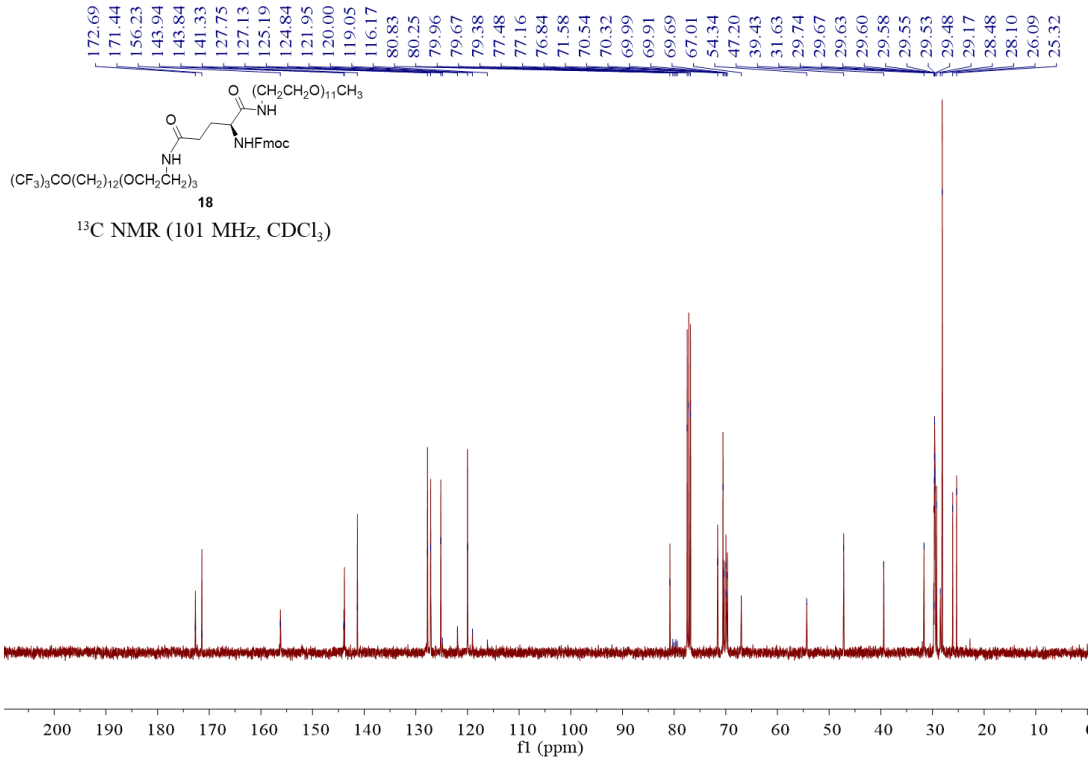


^{1}H NMR of compound **18**



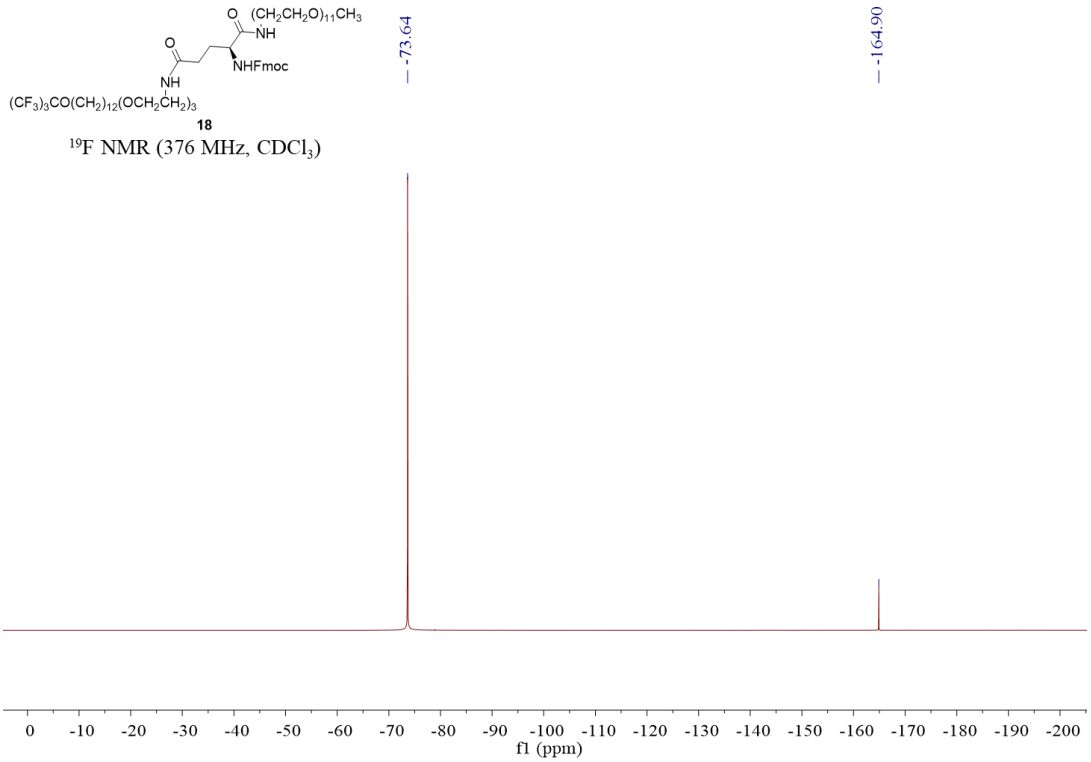
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **18**



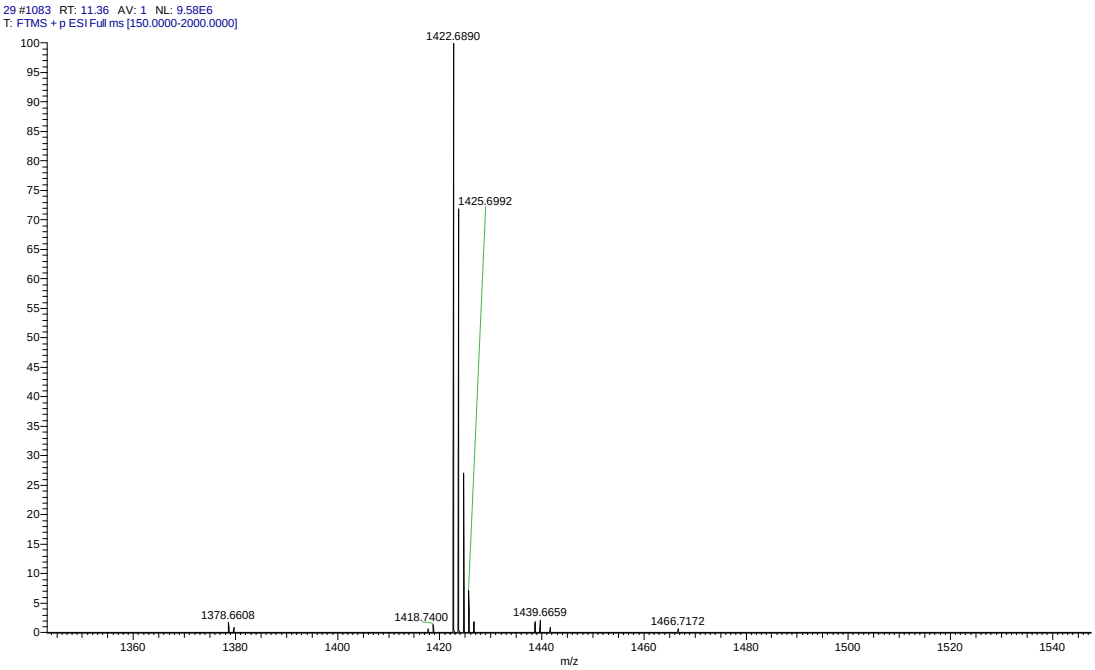
^{13}C NMR (101 MHz, $CDCl_3$)

^{19}F NMR of compound **18**

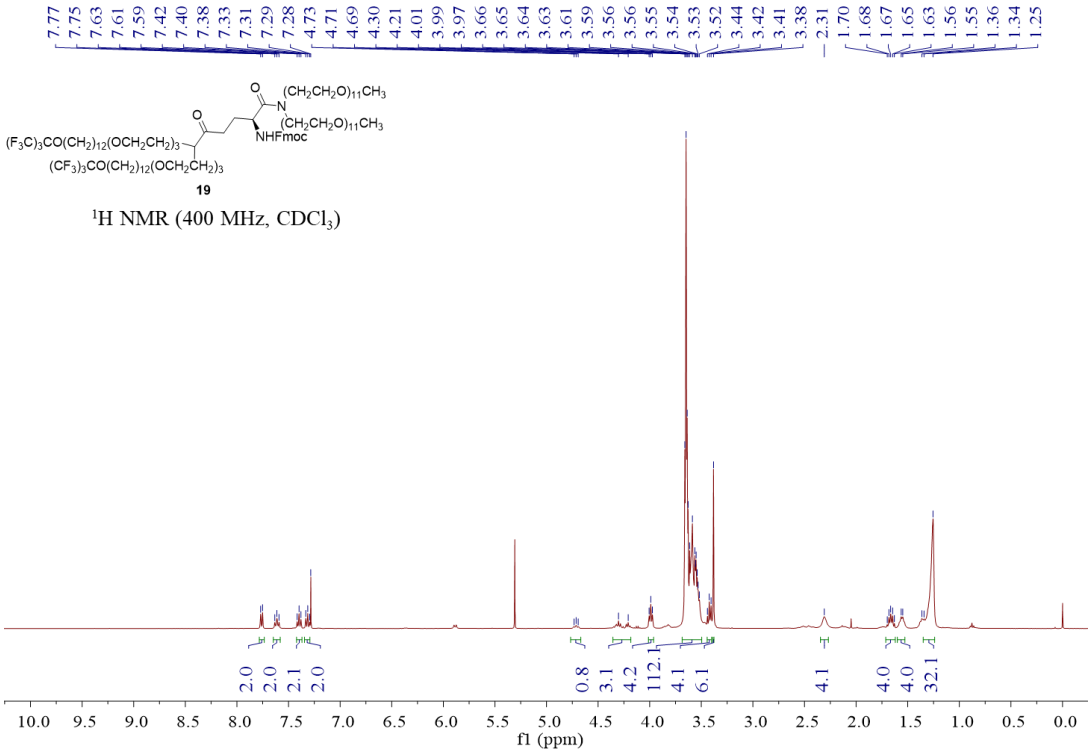


^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **18**

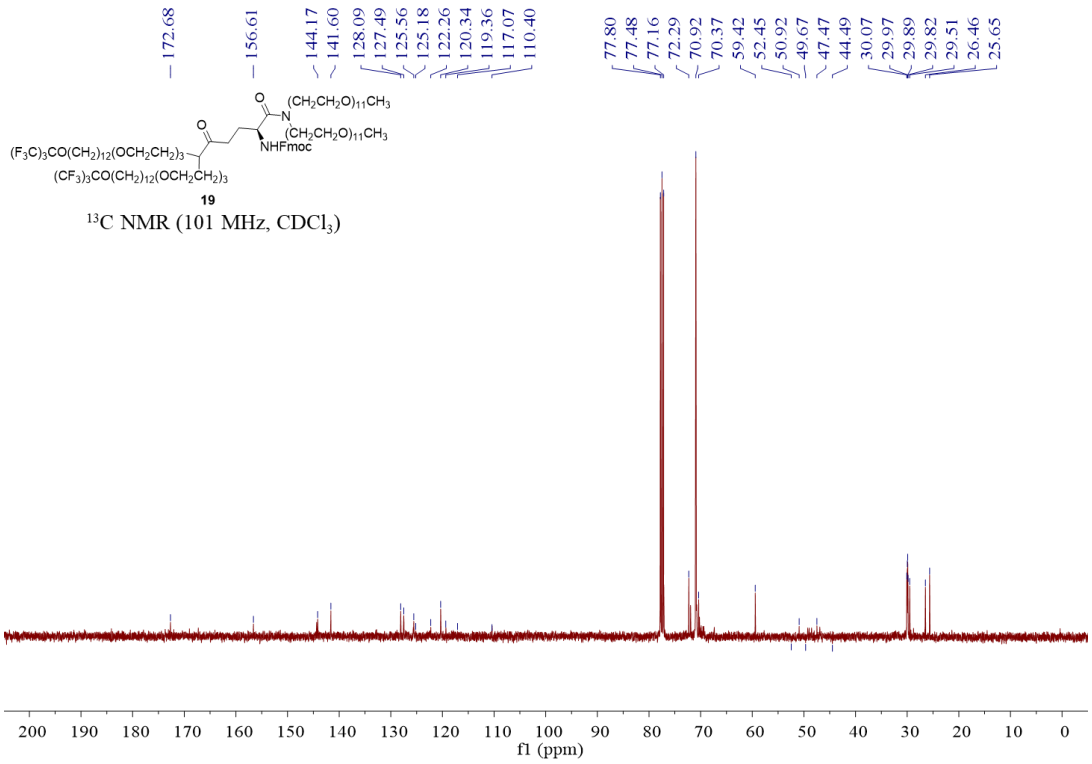


^{1}H NMR of compound **19**



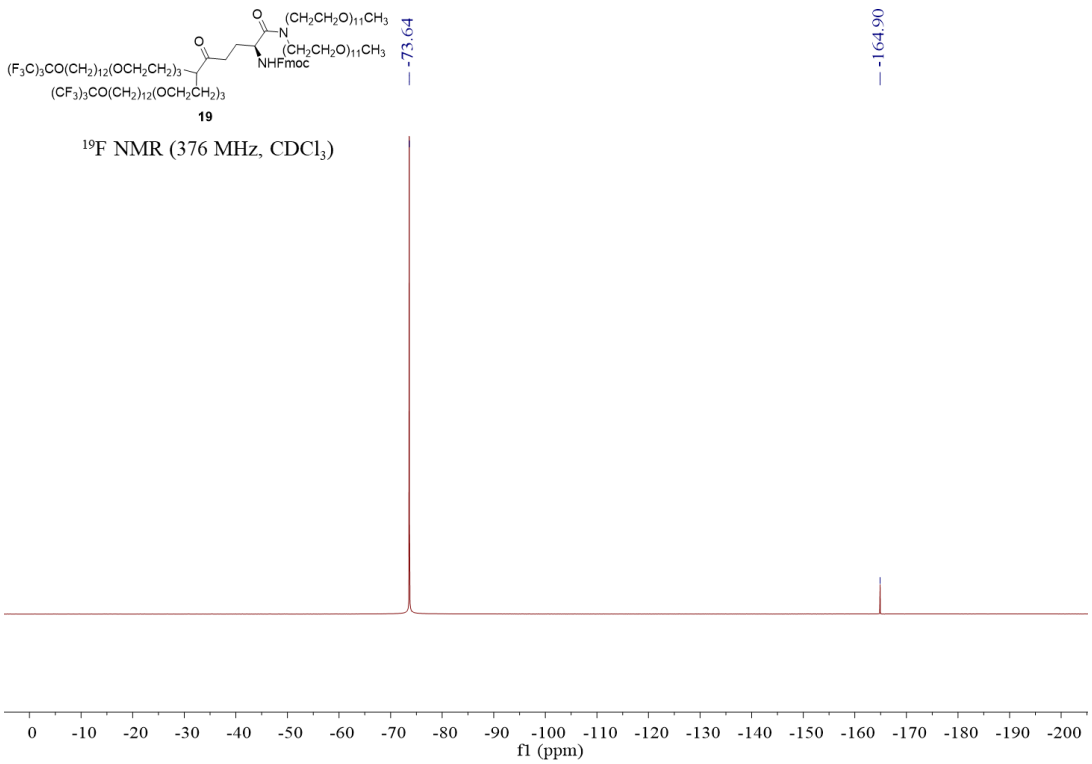
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **19**



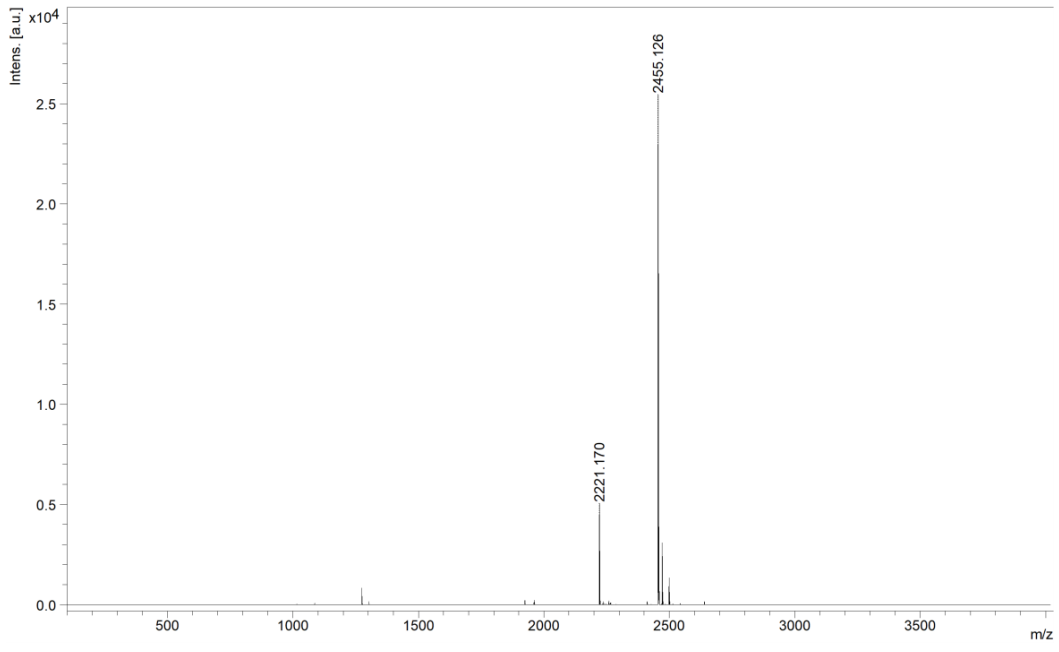
^{13}C NMR (101 MHz, $CDCl_3$)

^{19}F NMR of compound **19**

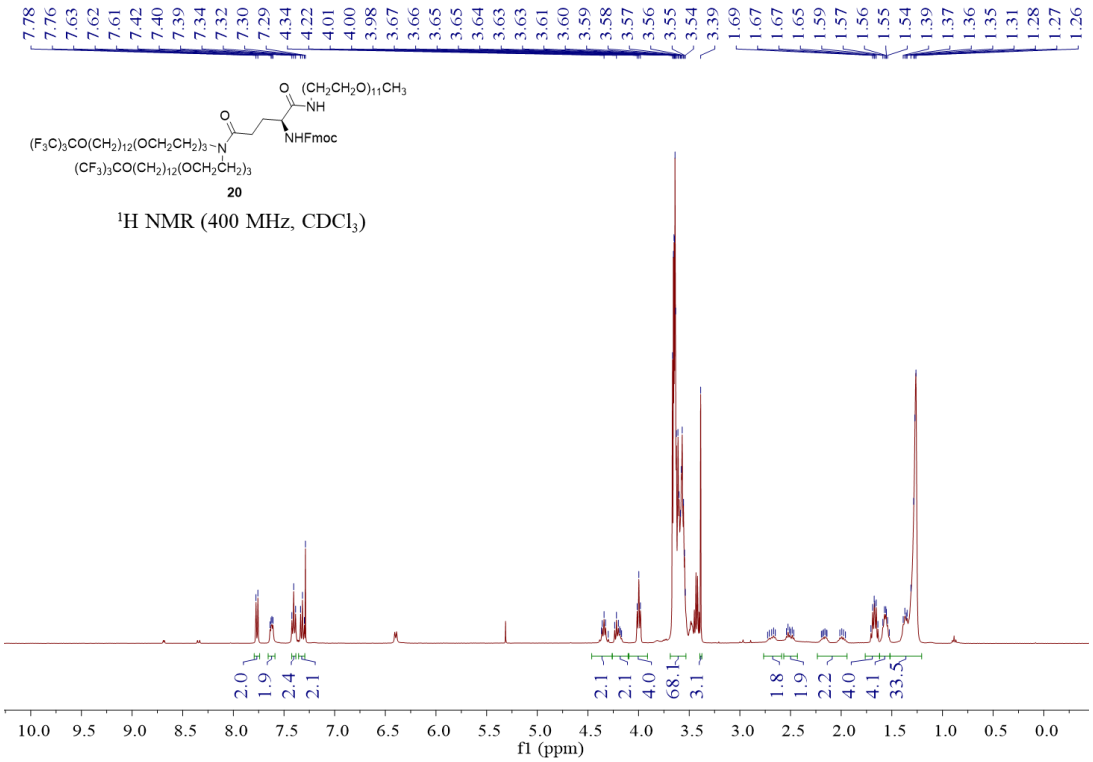


^{19}F NMR (376 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound **19**

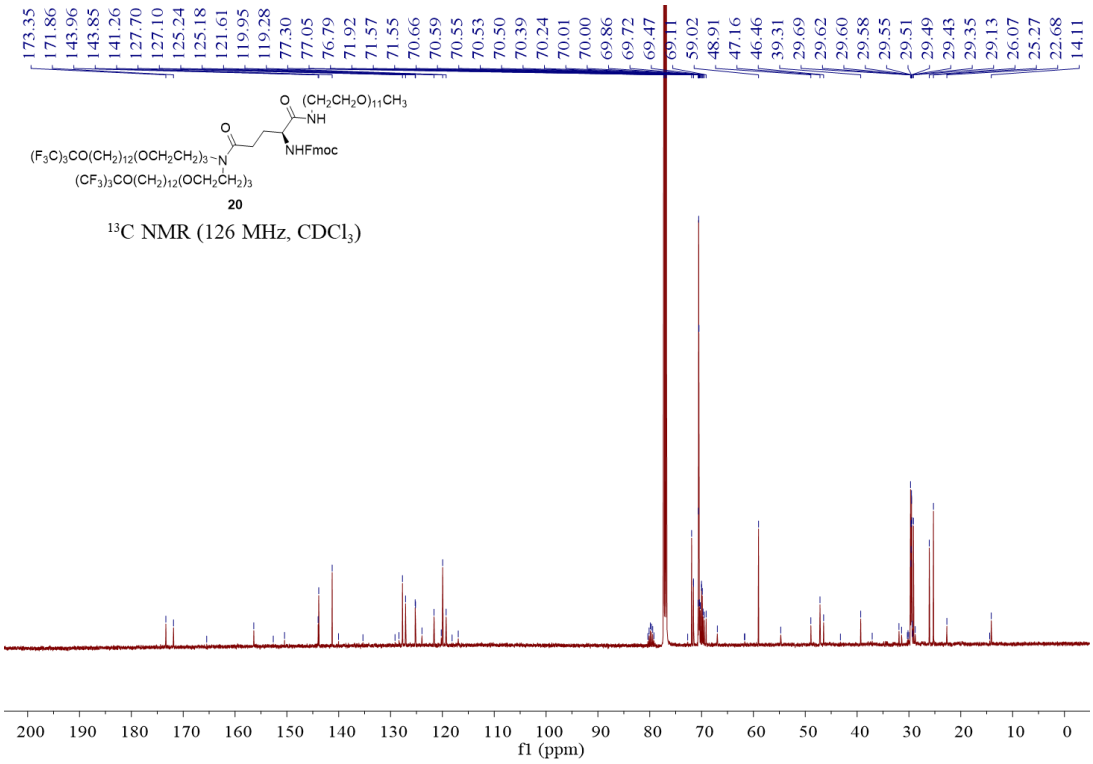


^{1}H NMR of compound **20**



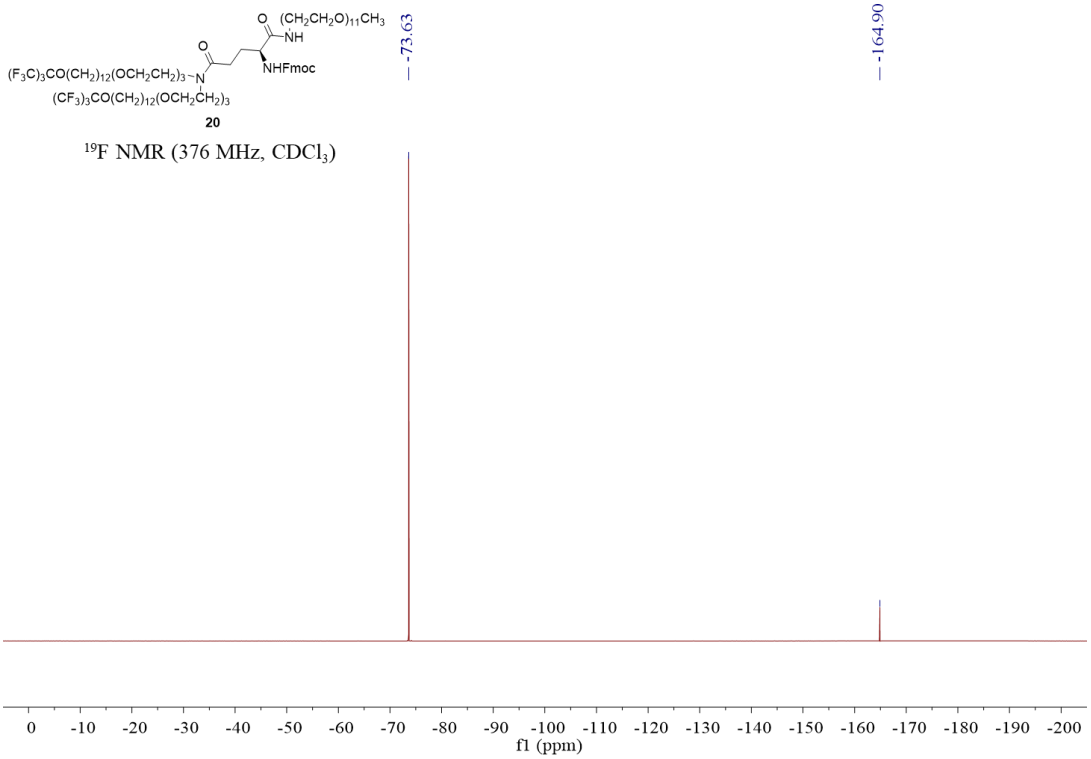
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **20**



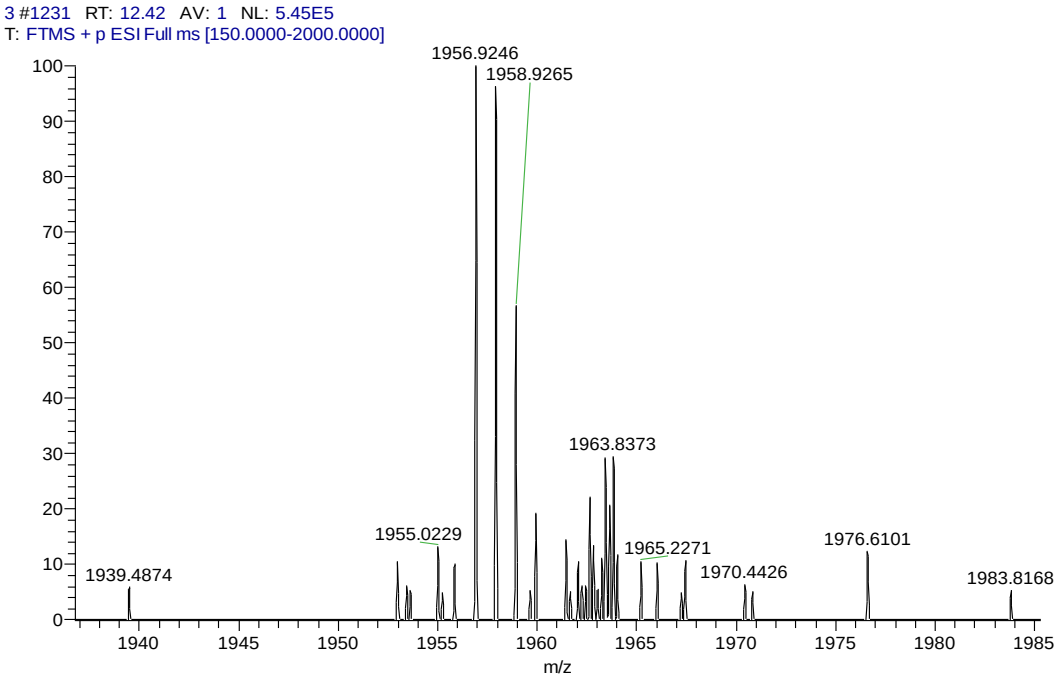
^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound **20**

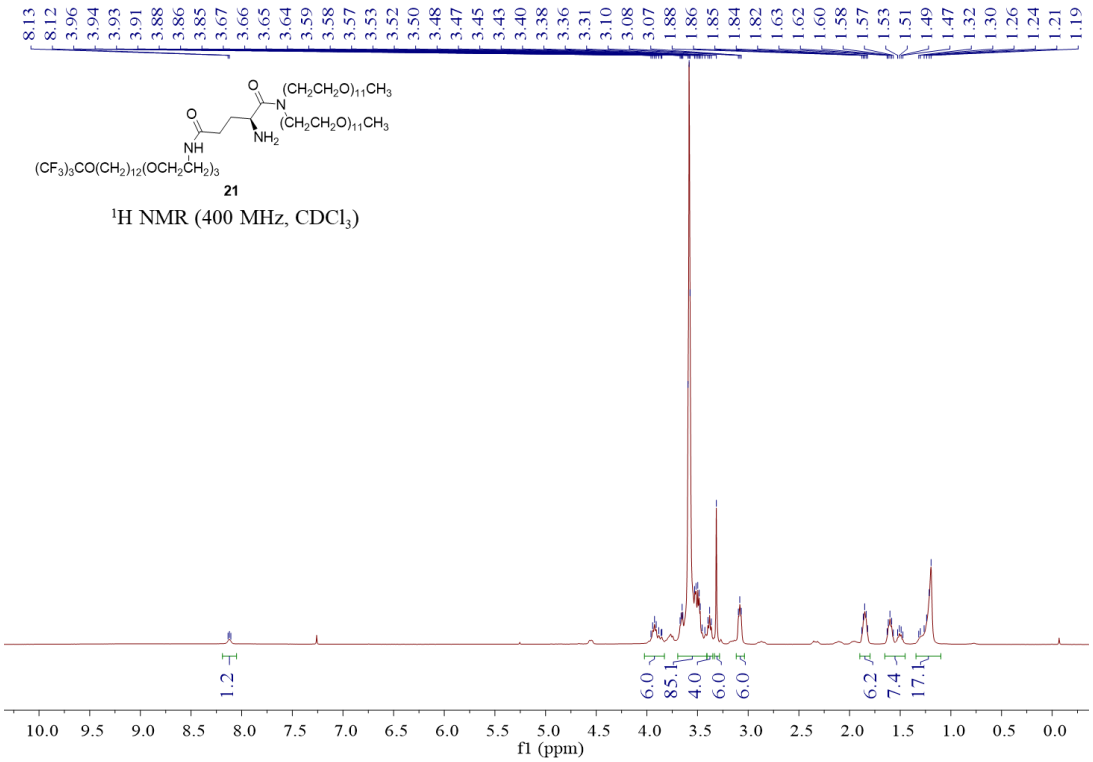


^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **20**

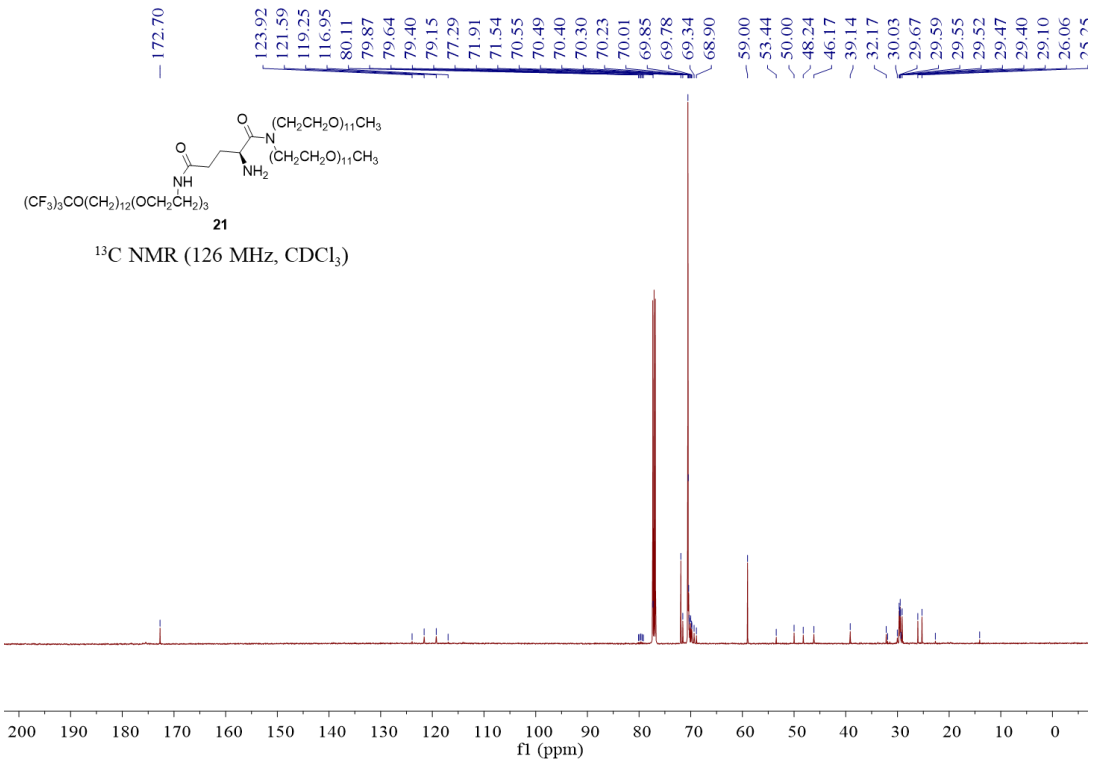


^{1}H NMR of compound **21**



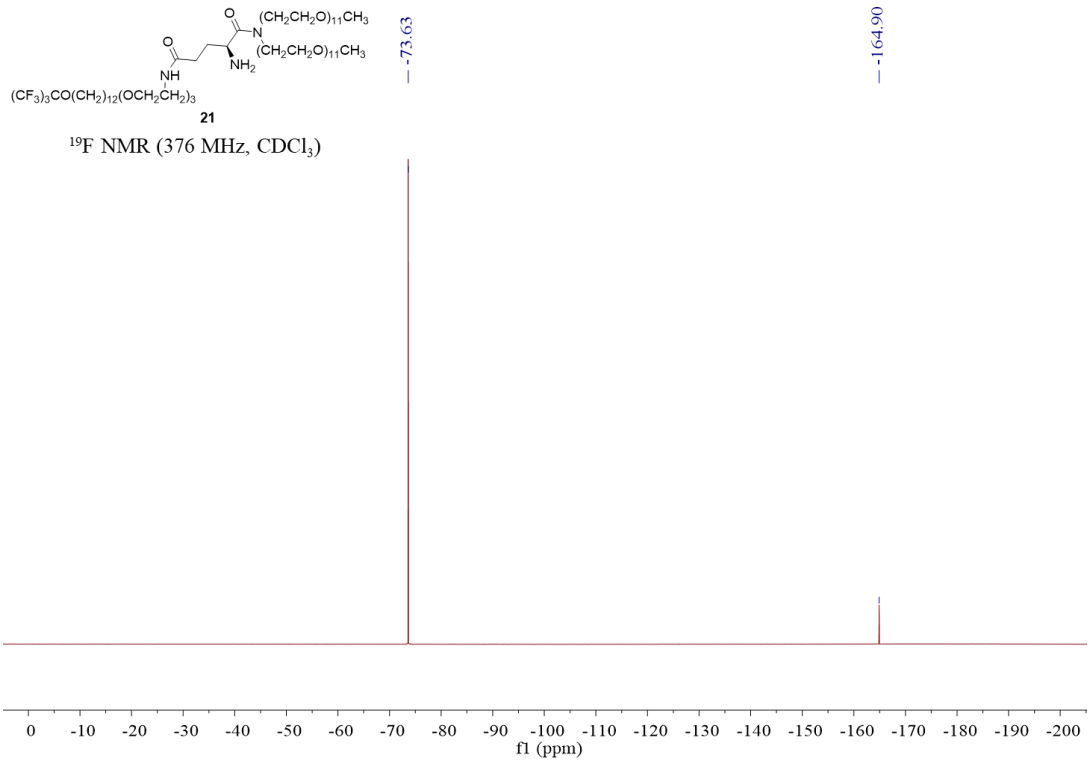
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **21**



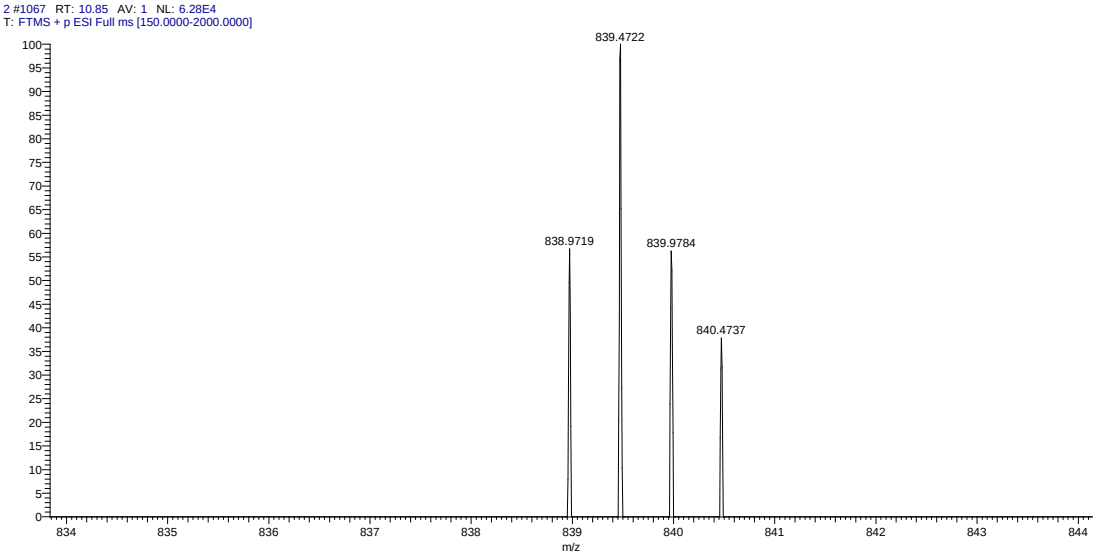
^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound **21**

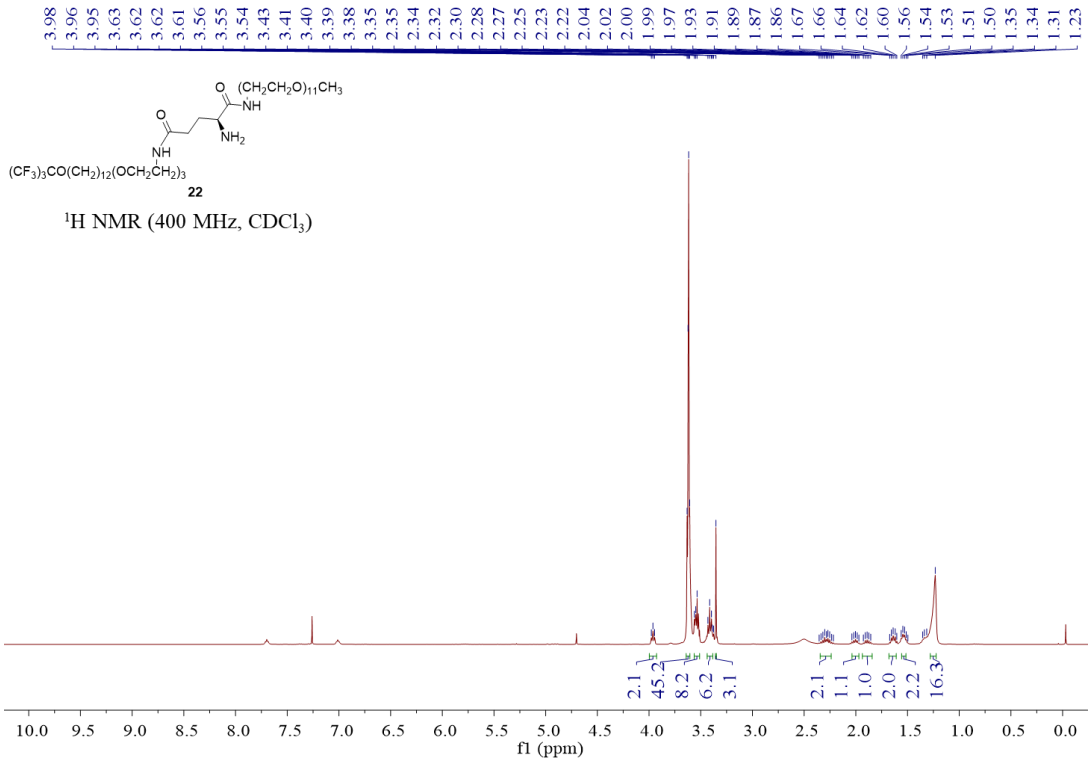


^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **21**

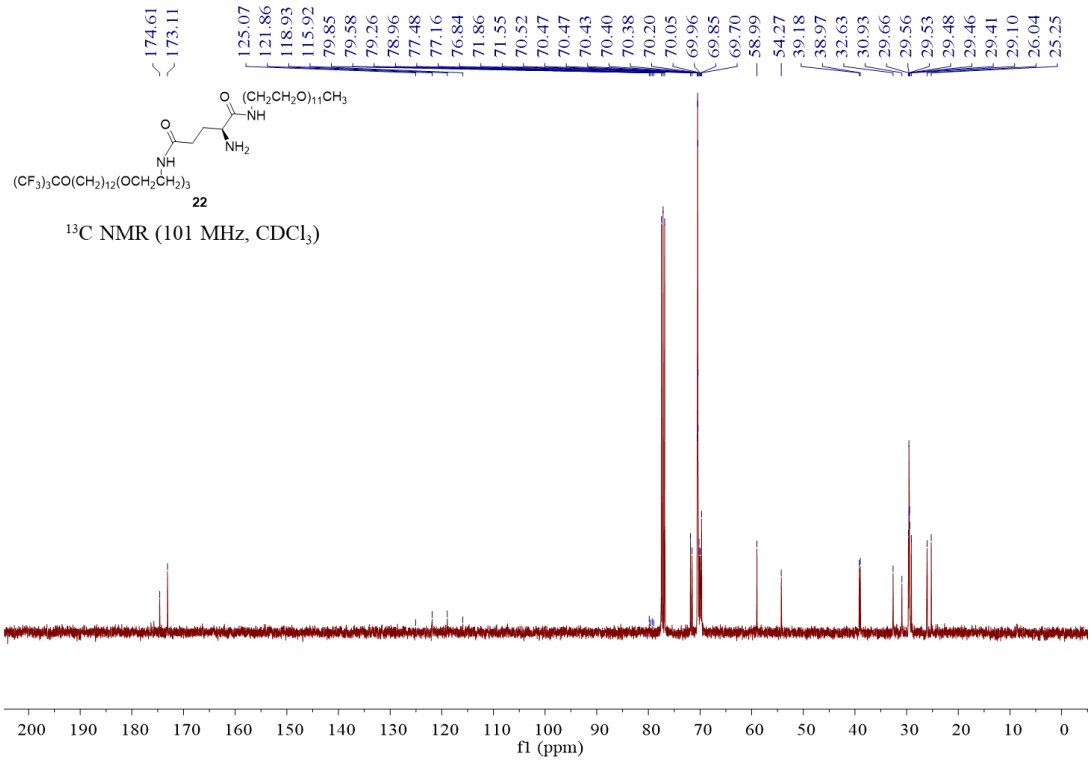


^{1}H NMR of compound **22**



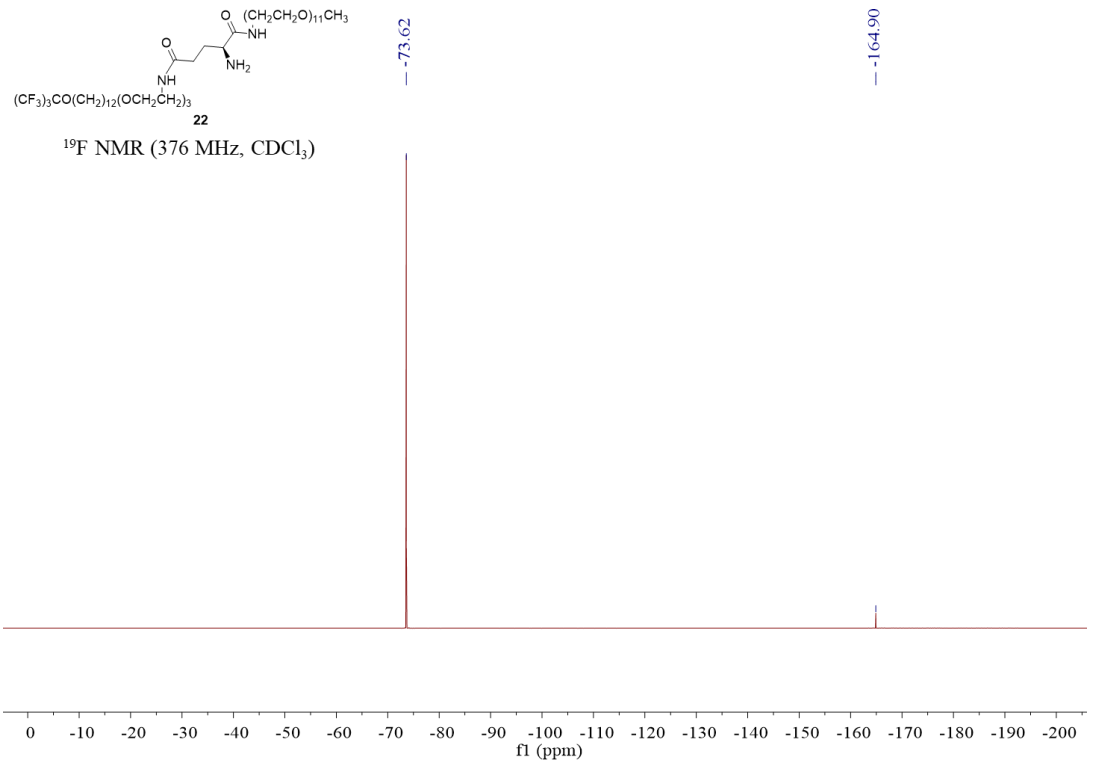
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **22**



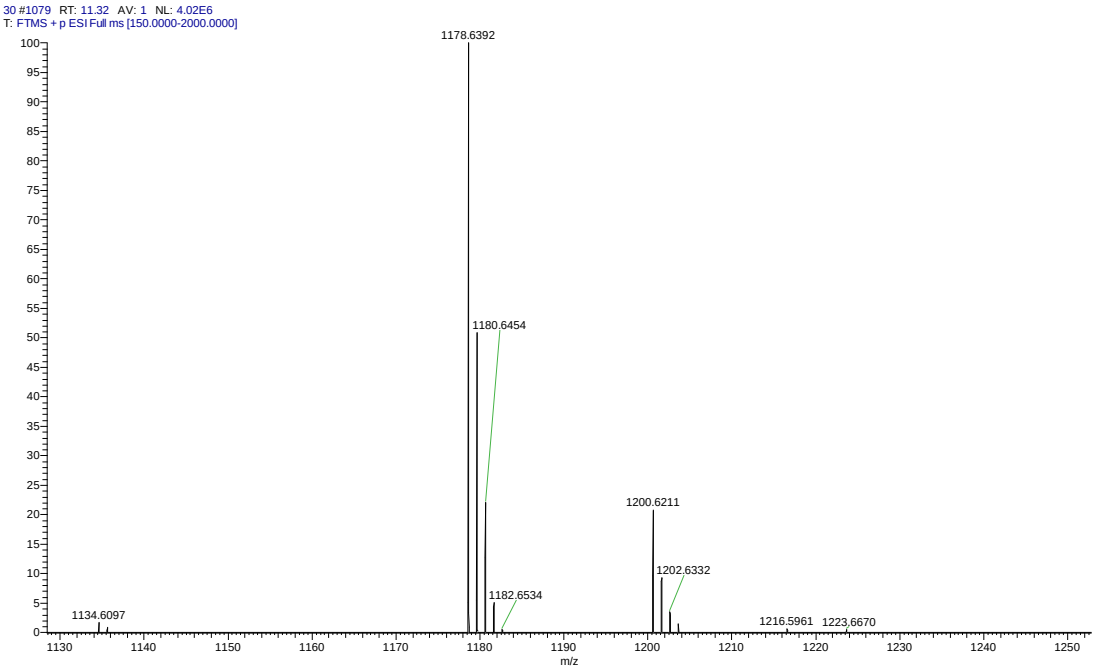
^{13}C NMR (101 MHz, $CDCl_3$)

^{19}F NMR of compound **22**

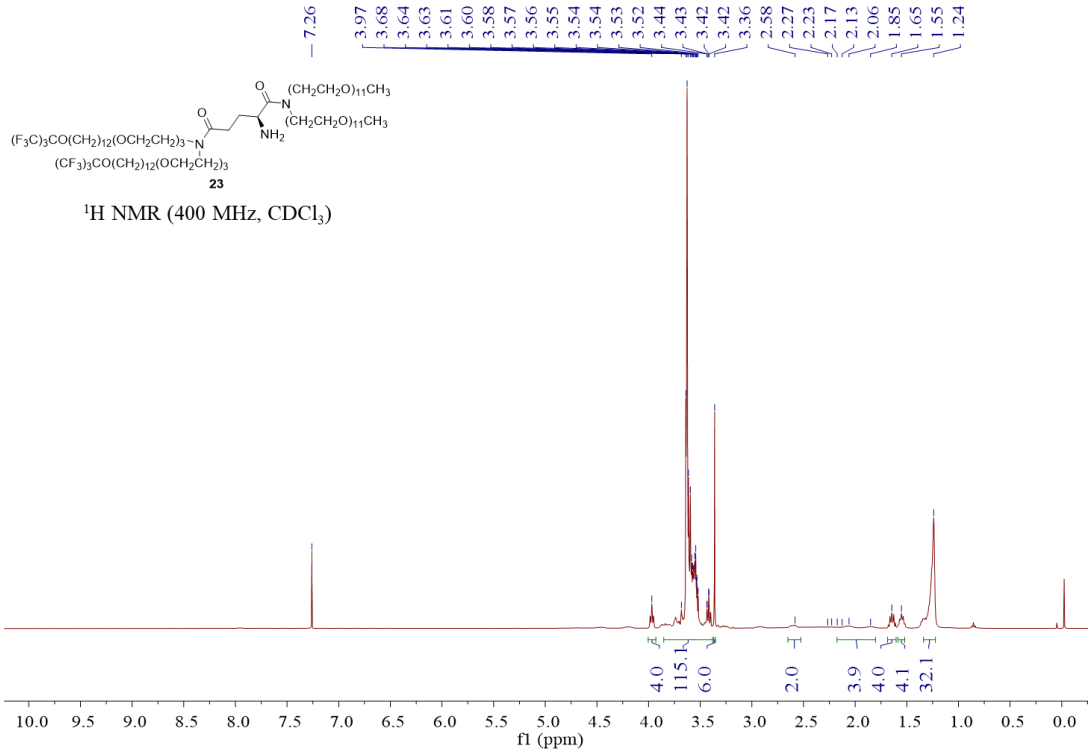


^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **22**

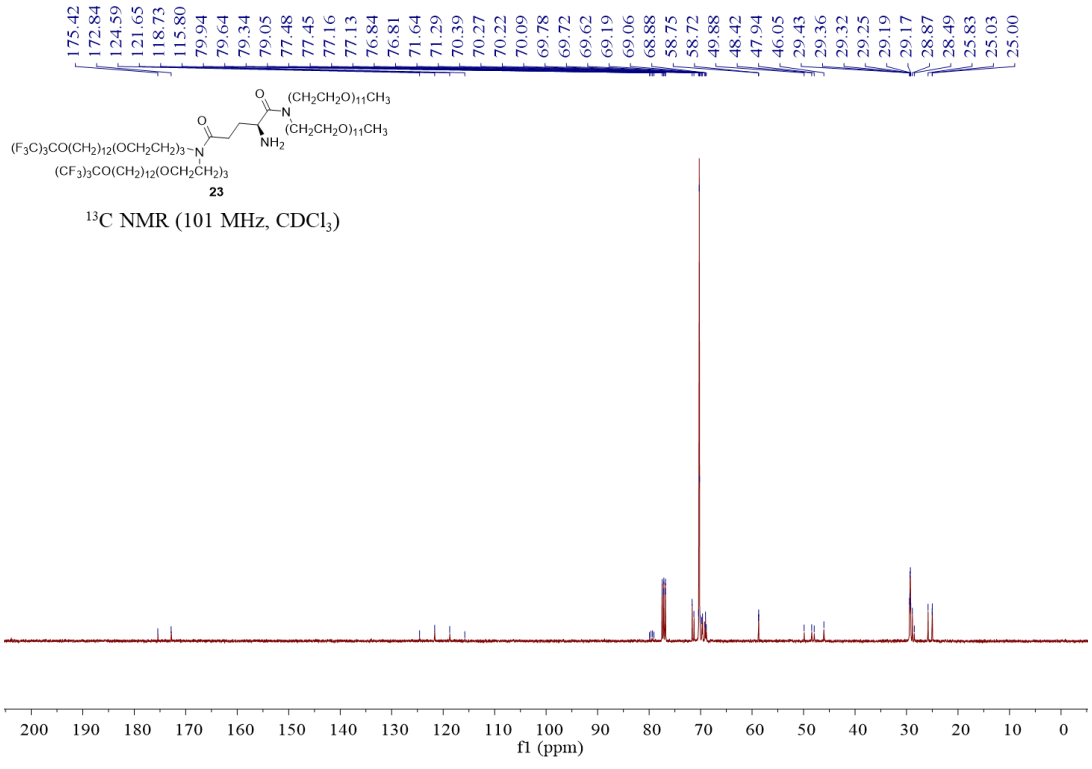


^{1}H NMR of compound **23**



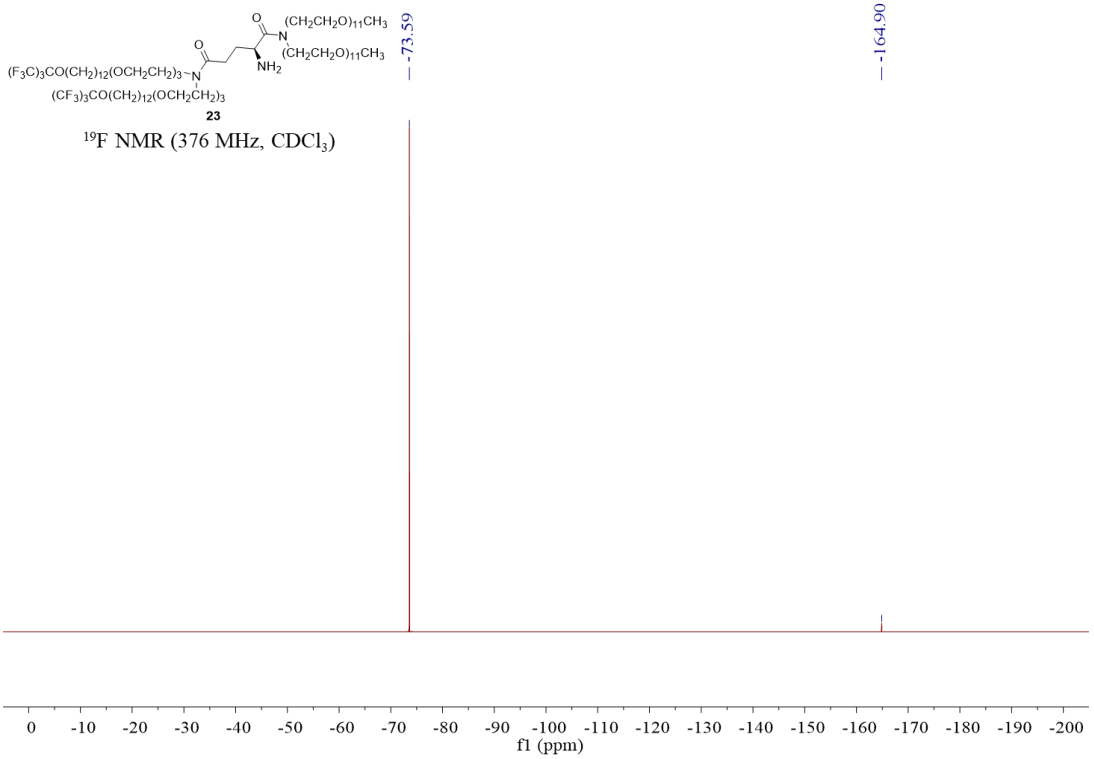
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **23**



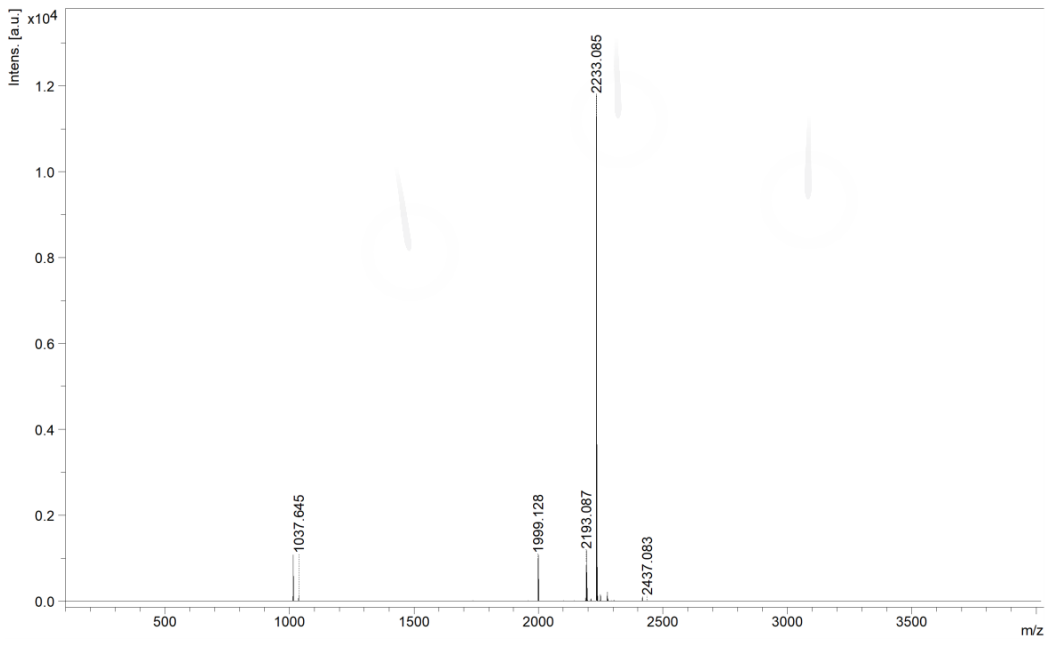
^{13}C NMR (101 MHz, $CDCl_3$)

^{19}F NMR of compound **23**

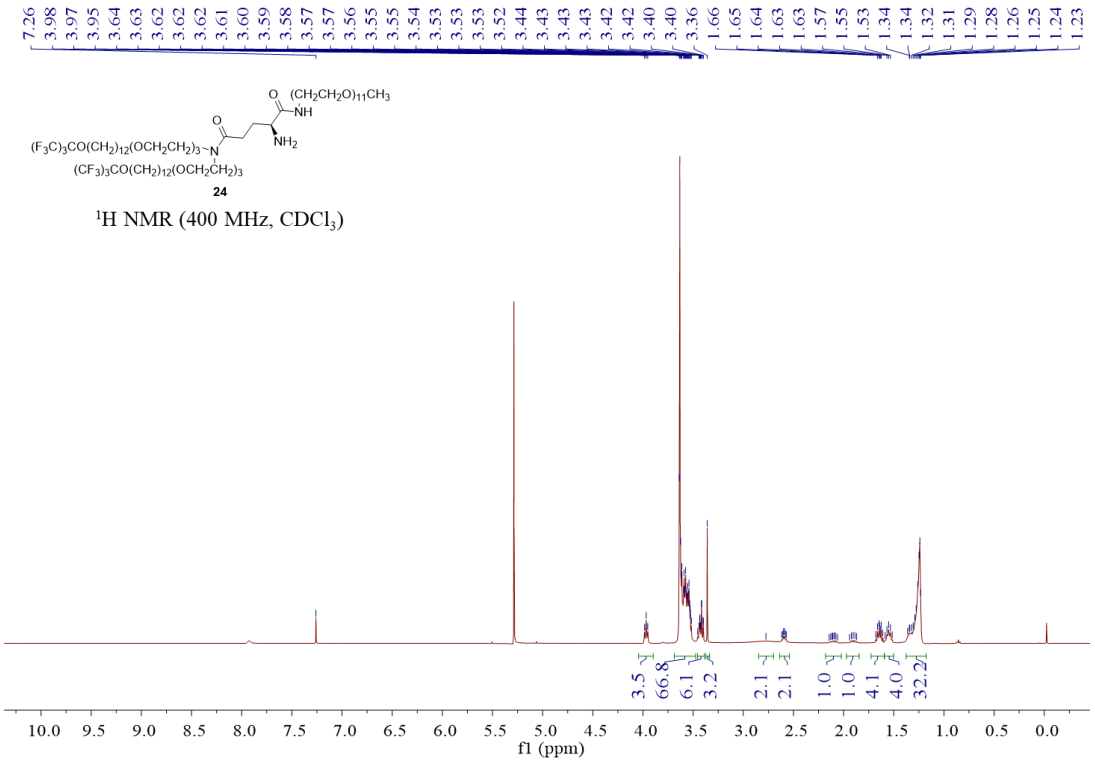


^{19}F NMR (376 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound **23**

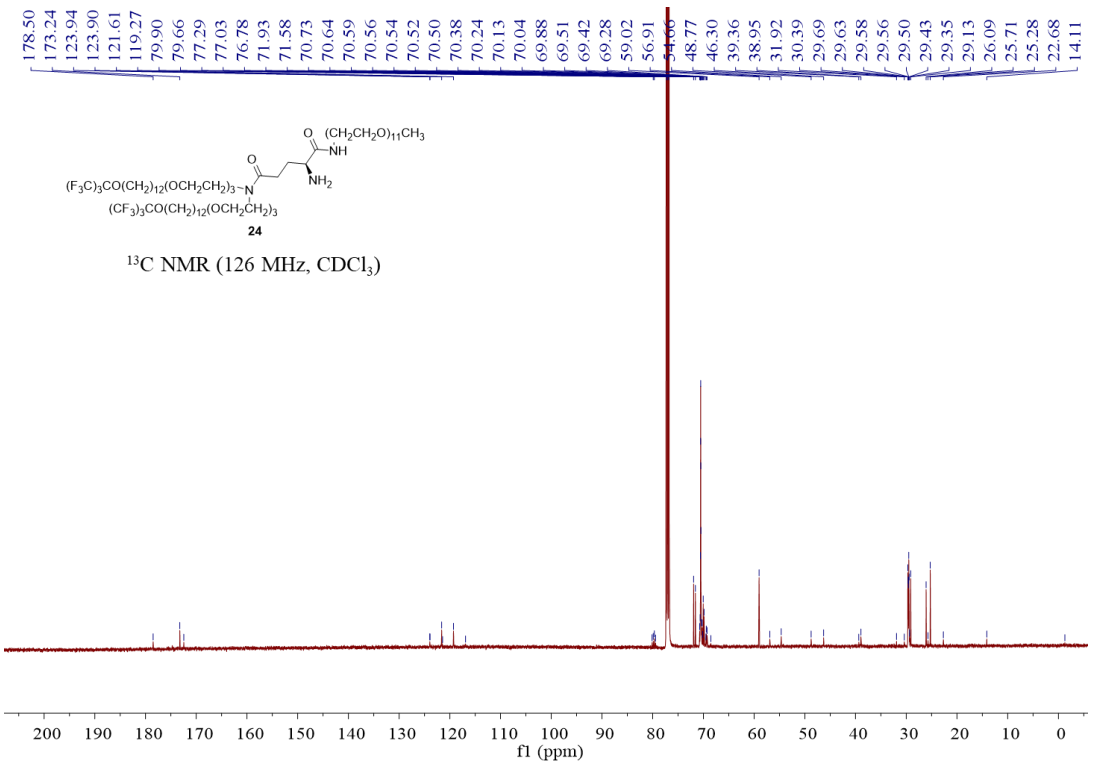


^{1}H NMR of compound **24**



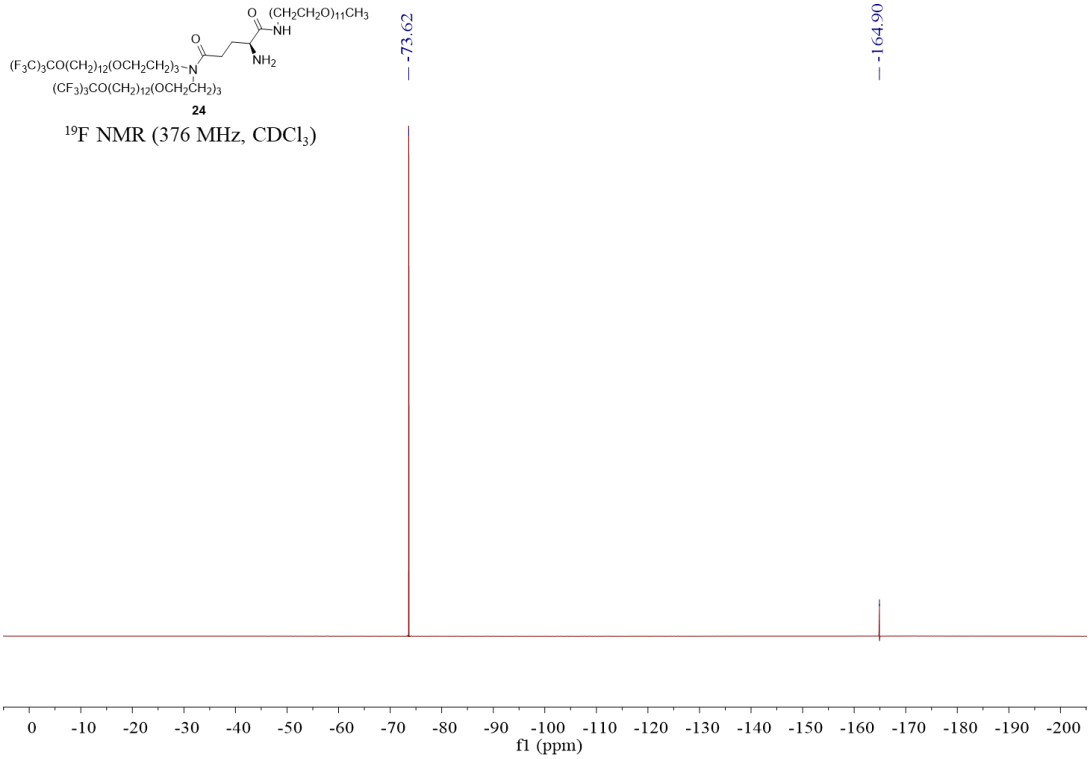
^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR of compound **24**



^{13}C NMR (126 MHz, $CDCl_3$)

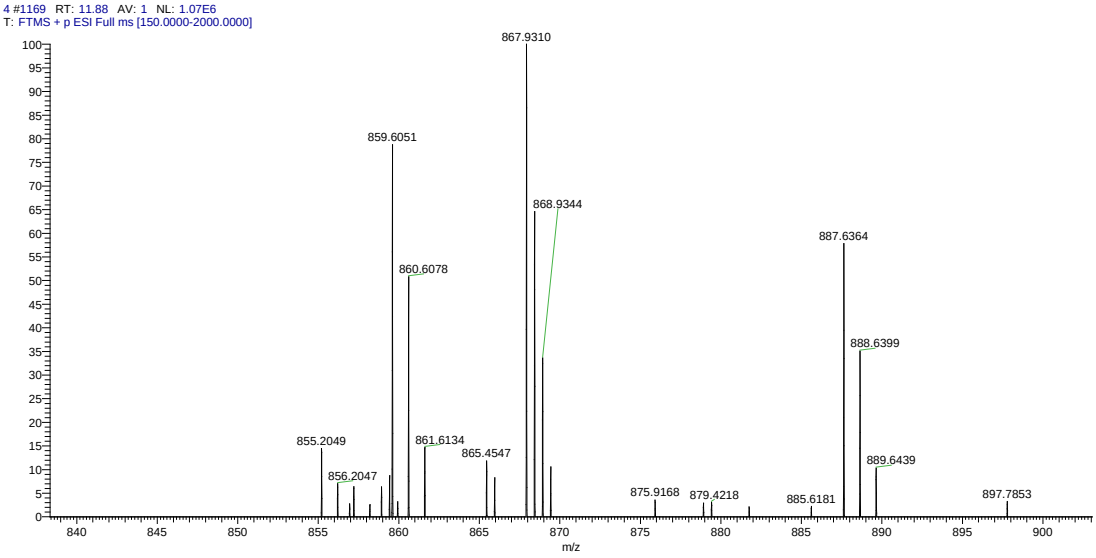
^{19}F NMR of compound **24**



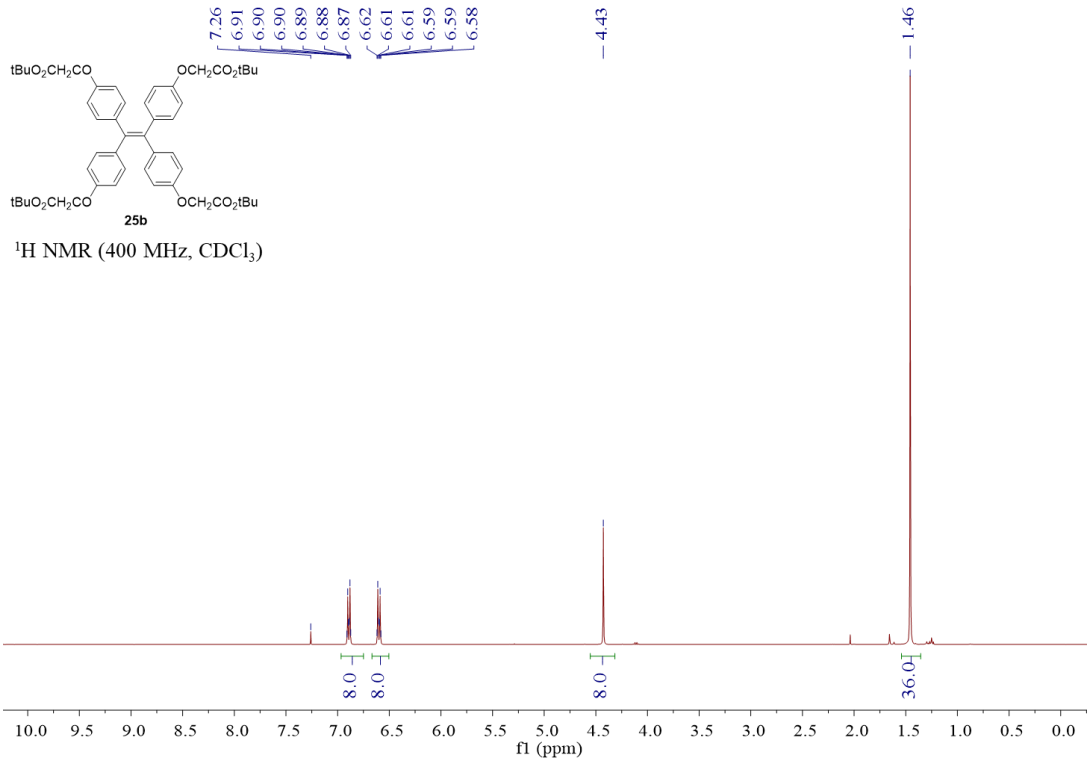
24

^{19}F NMR (376 MHz, $CDCl_3$)

HRMS(ESI) of compound **24**

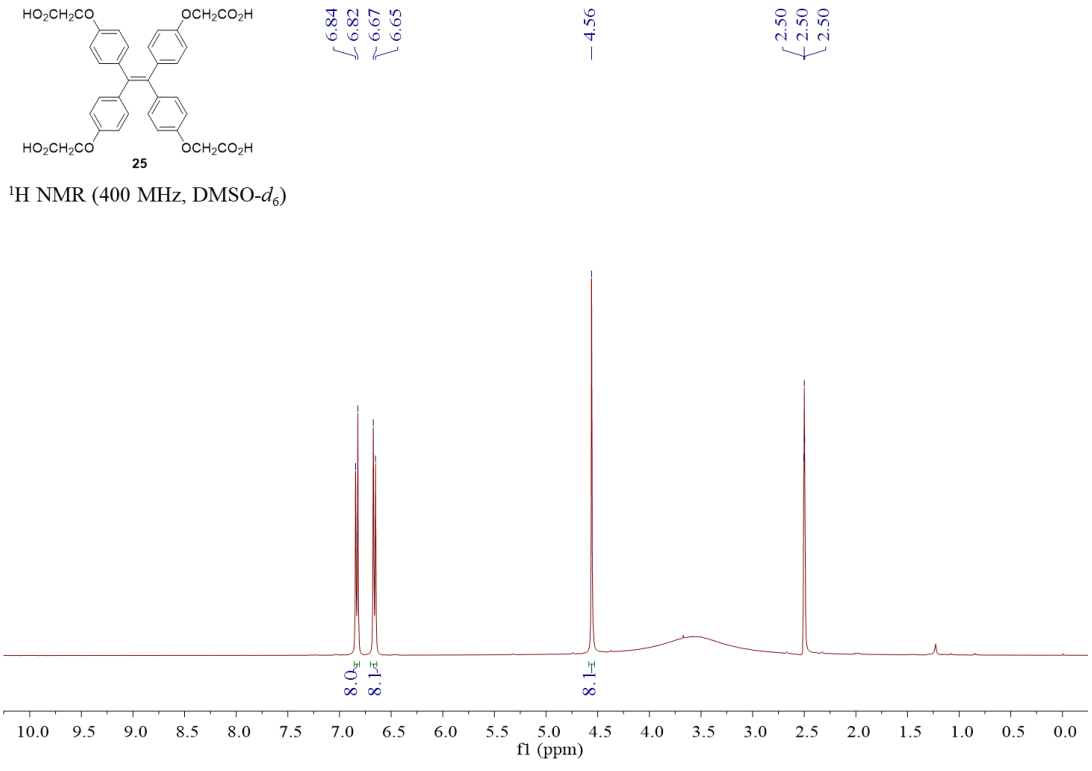


^{1}H NMR of compound **25b**



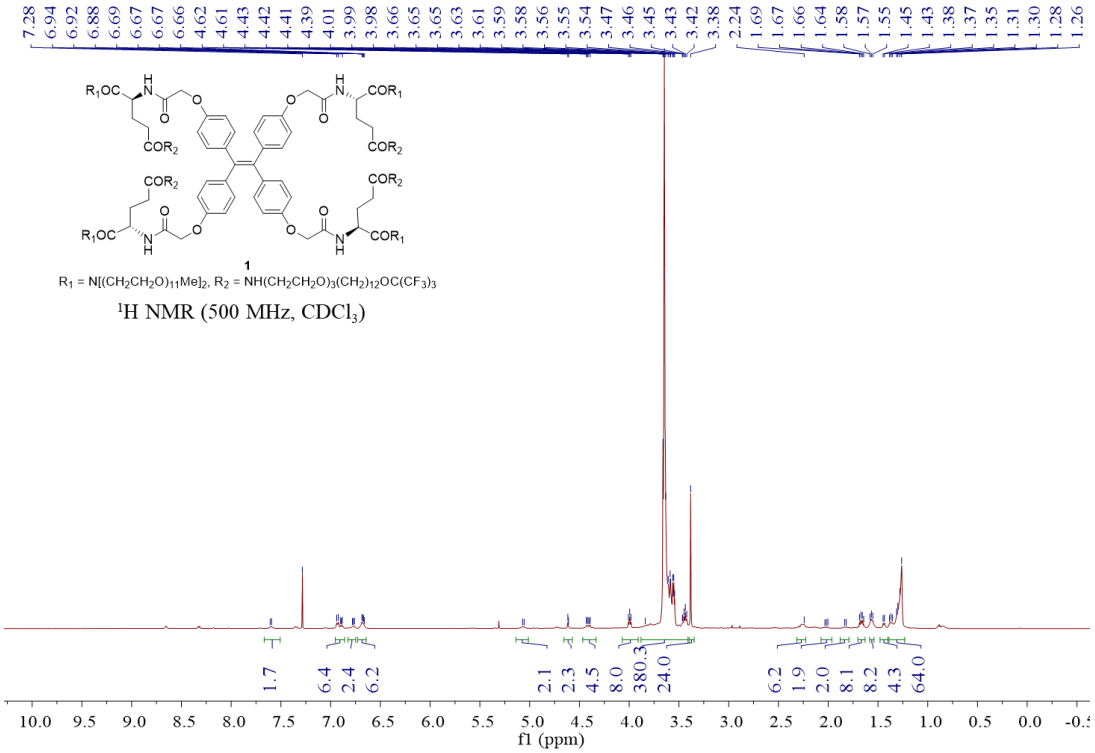
^{1}H NMR (400 MHz, $CDCl_3$)

^{1}H NMR of compound **25**



^{1}H NMR (400 MHz, DMSO-d_6)

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

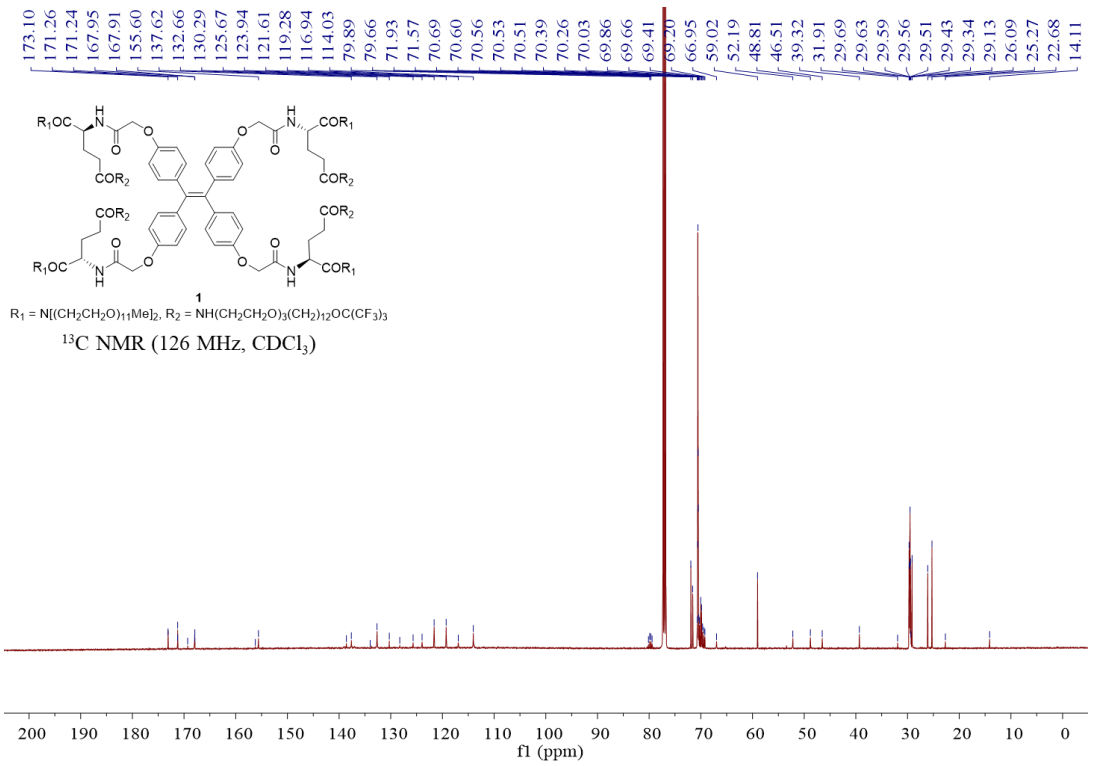


1

R_1 = N[$(CH_2CH_2O)_{11}Me]_2$, R_2 = $NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{1}H NMR (500 MHz, $CDCl_3$)

^{13}C NMR of compound FMA **1**

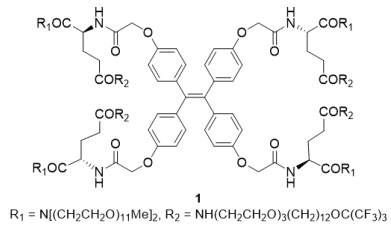


1

R_1 = N[$(CH_2CH_2O)_{11}Me]_2$, R_2 = $NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound FMA **1**

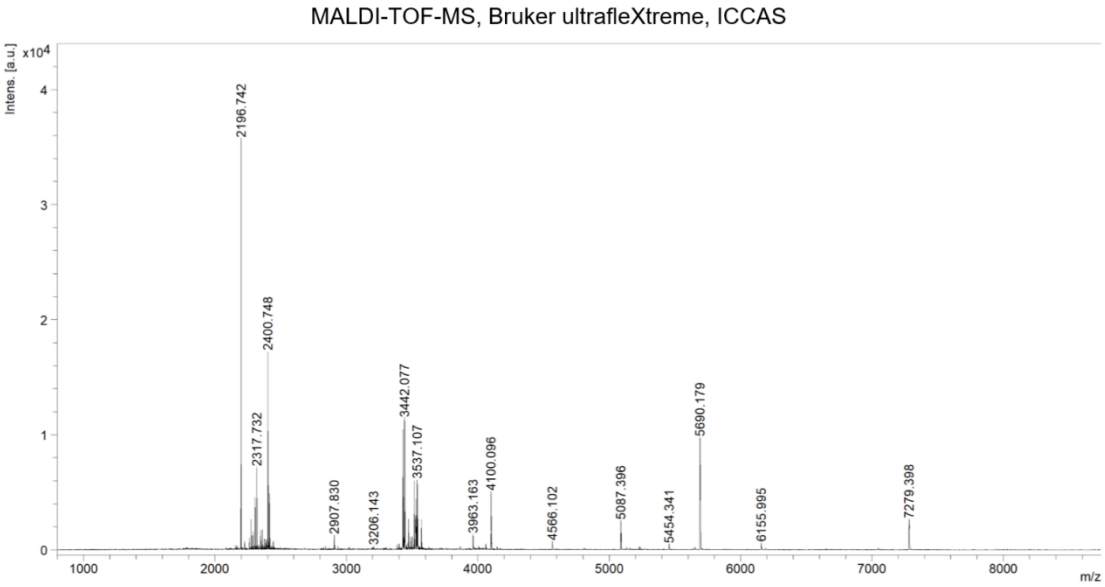


1

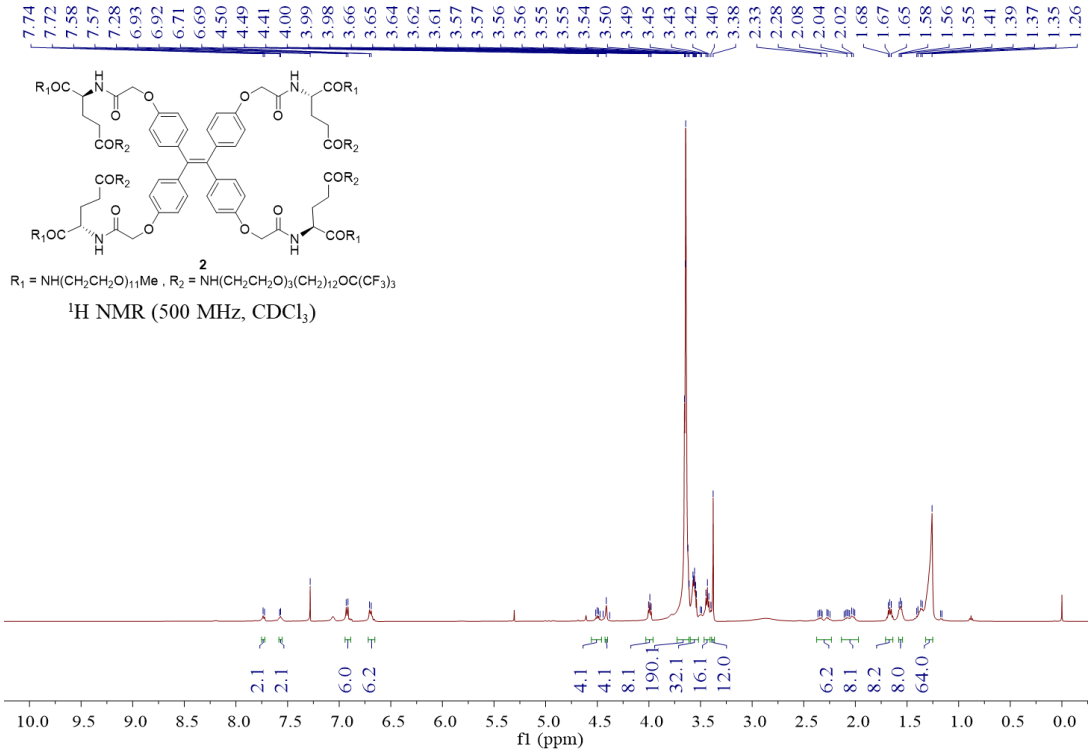
R_1 = N[$(CH_2CH_2O)_{11}Me$]$_2$, R_2 = NH$(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{19}F NMR (471 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound FMA **1**



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

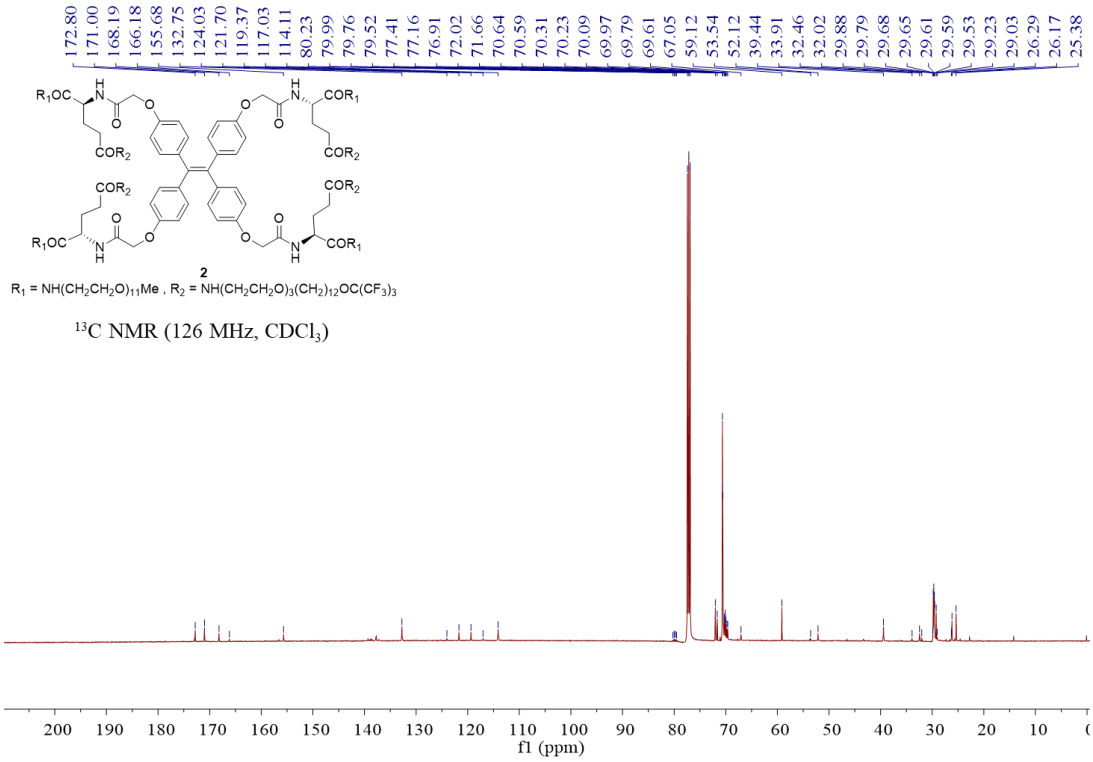


2

$R_1 = NH(CH_2CH_2O)_{11}Me$, $R_2 = NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{1}H NMR (500 MHz, $CDCl_3$)

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

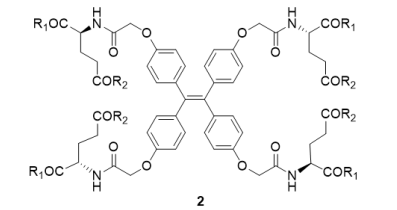


2

$R_1 = NH(CH_2CH_2O)_{11}Me$, $R_2 = NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound FMA **2**

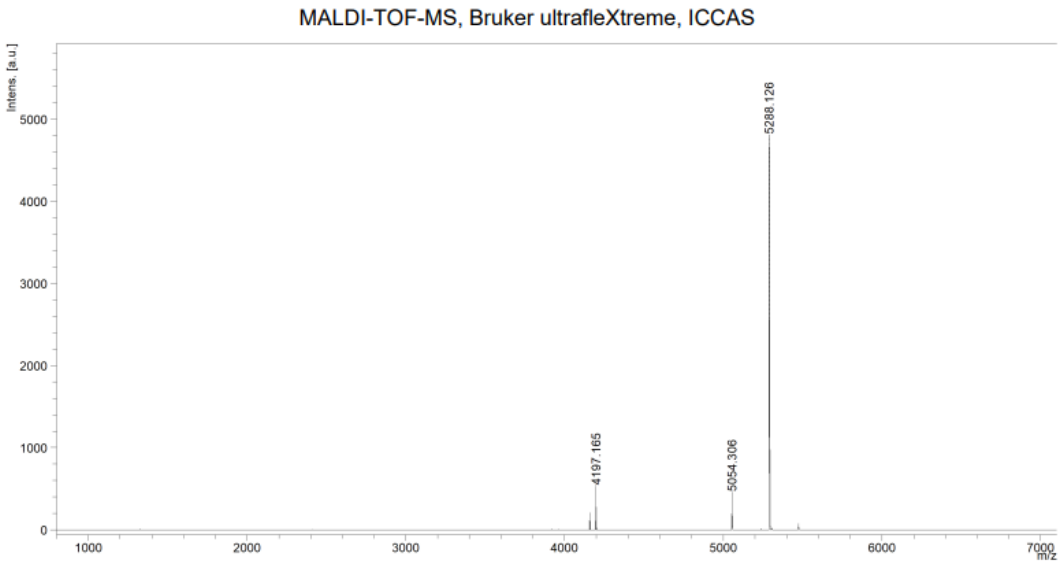


2

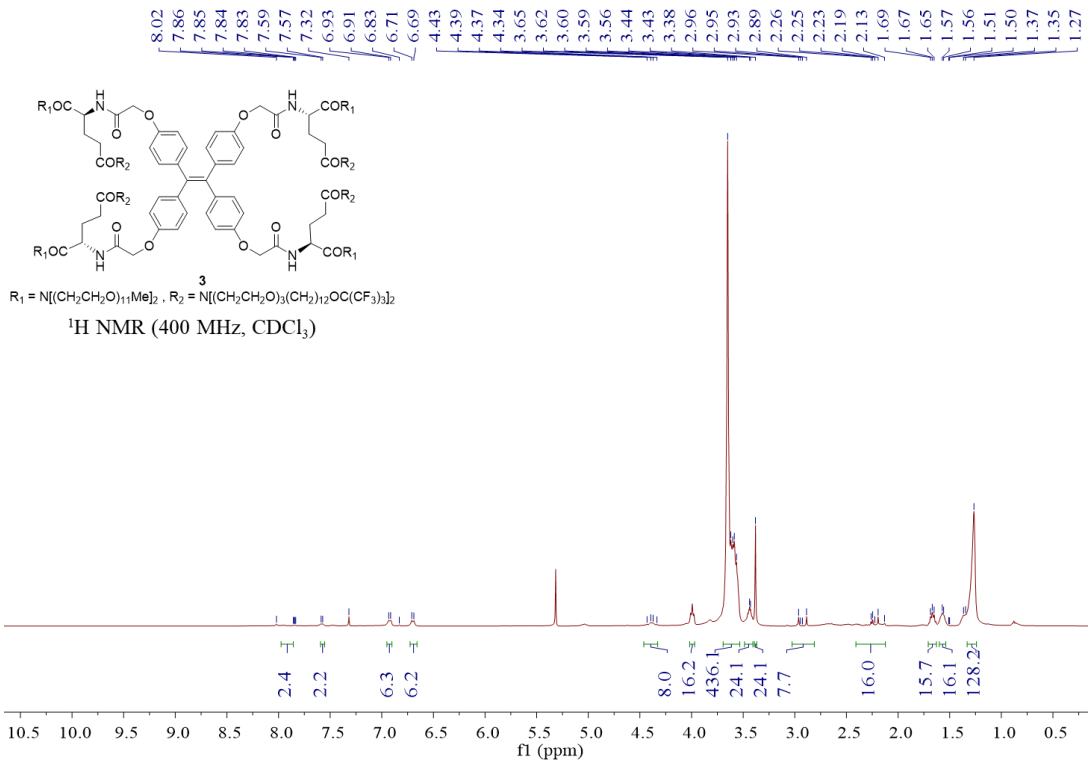
R_1 = $NH(CH_2CH_2O)_{11}Me$, R_2 = $NH(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3$

^{19}F NMR (471 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound FMA **2**

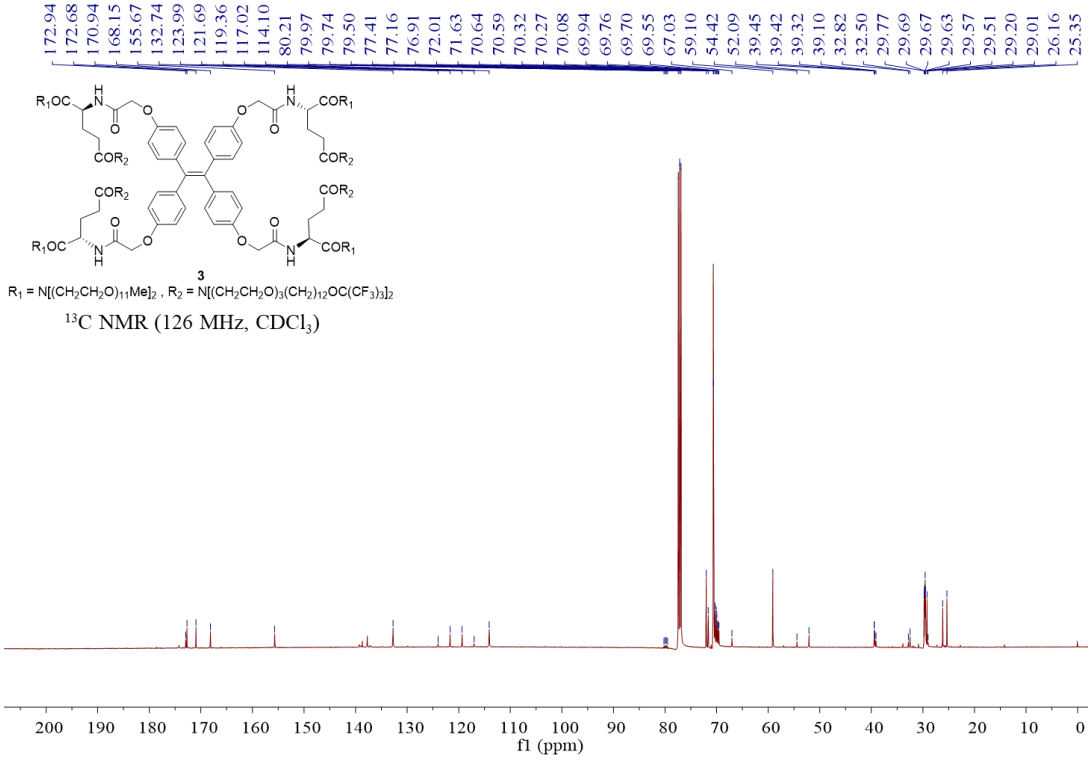


^{1}H NMR of compound FMA **3**



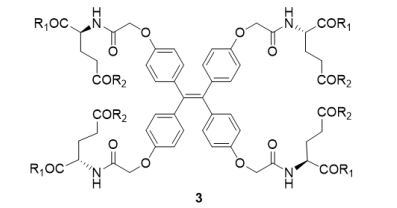
^{1}H NMR (400 MHz, $CDCl_3$)

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



^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound FMA **3**

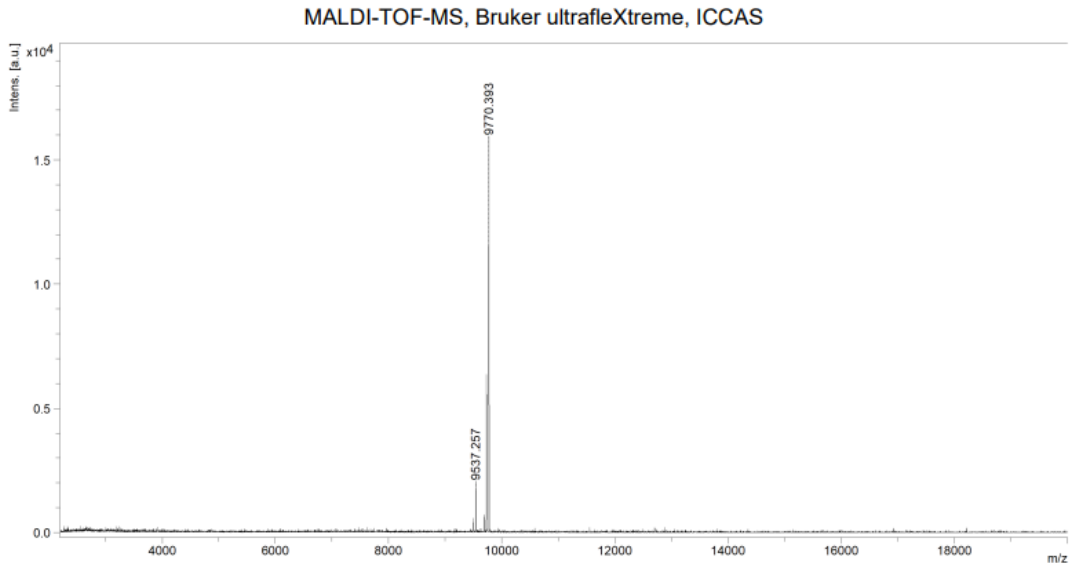


3

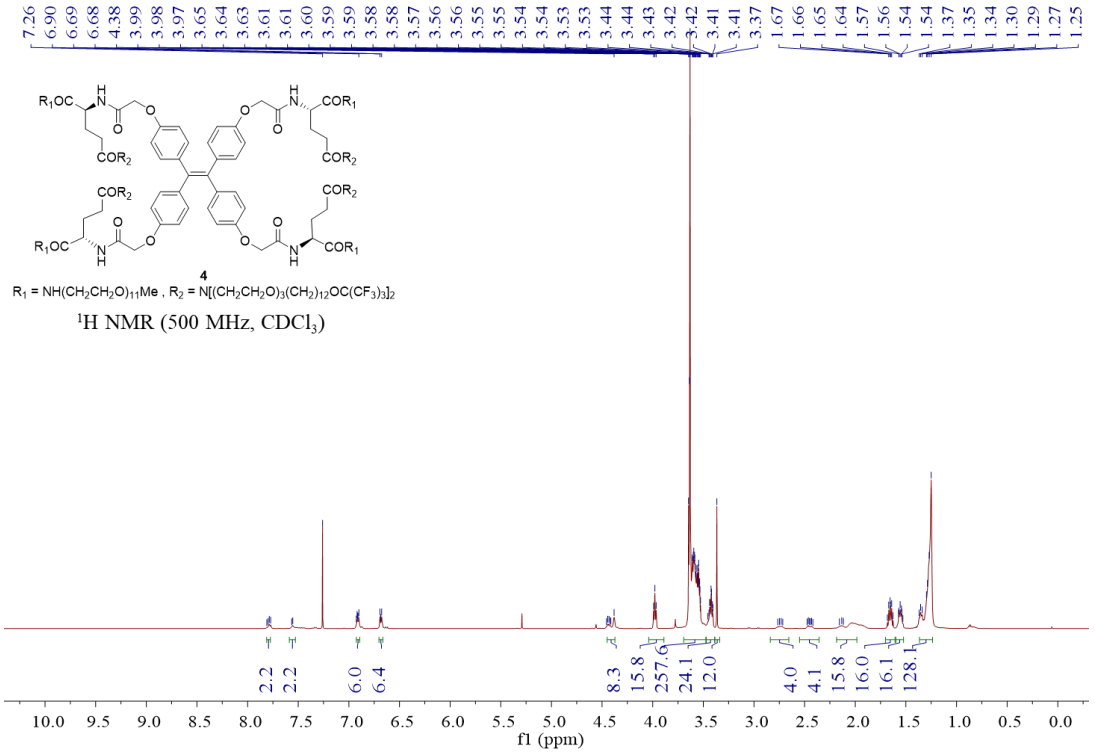
R_1 = N[(CH$_2$CH$_2$O)$_{11}$Me]$_2$, R_2 = N[(CH$_2$CH$_2$O)$_3$(CH$_2$)$_{12}$OC(CF$_3$)$_3$]$_2$

^{19}F NMR (376 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound FMA **3**



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

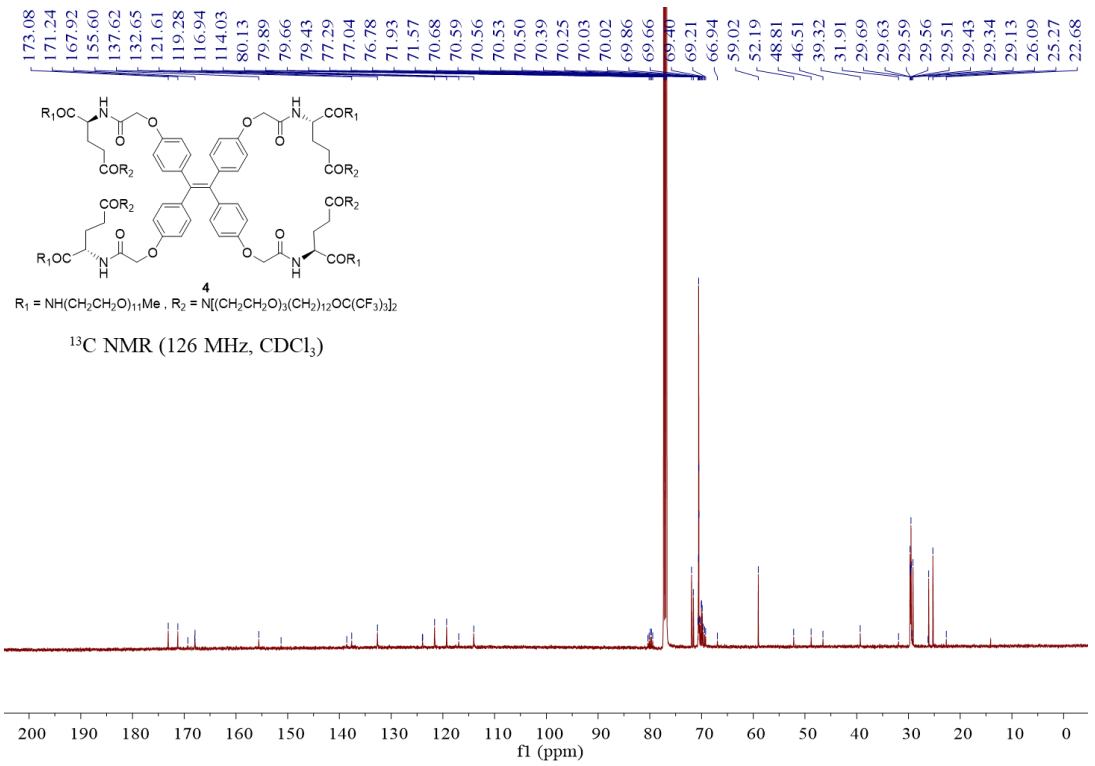


4

R_1 = $NH(CH_2CH_2O)_{11}Me$, R_2 = $N[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

^{1}H NMR (500 MHz, $CDCl_3$)

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

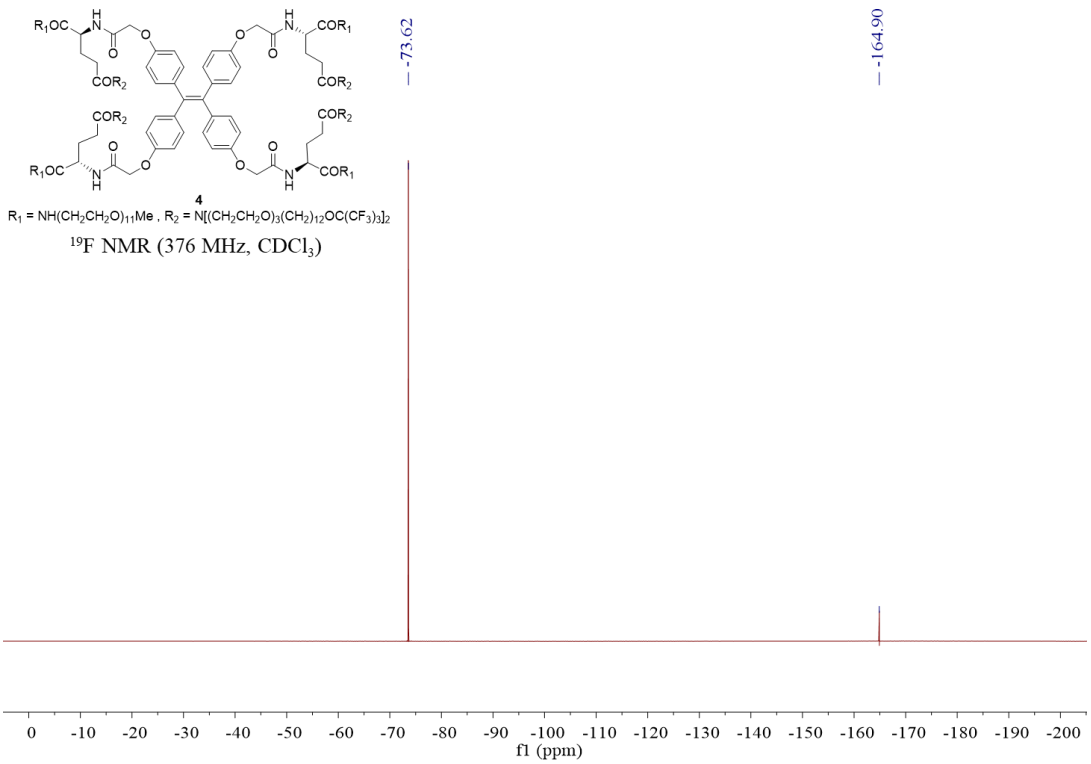


4

R_1 = $NH(CH_2CH_2O)_{11}Me$, R_2 = $N[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

^{13}C NMR (126 MHz, $CDCl_3$)

^{19}F NMR of compound FMA **4**

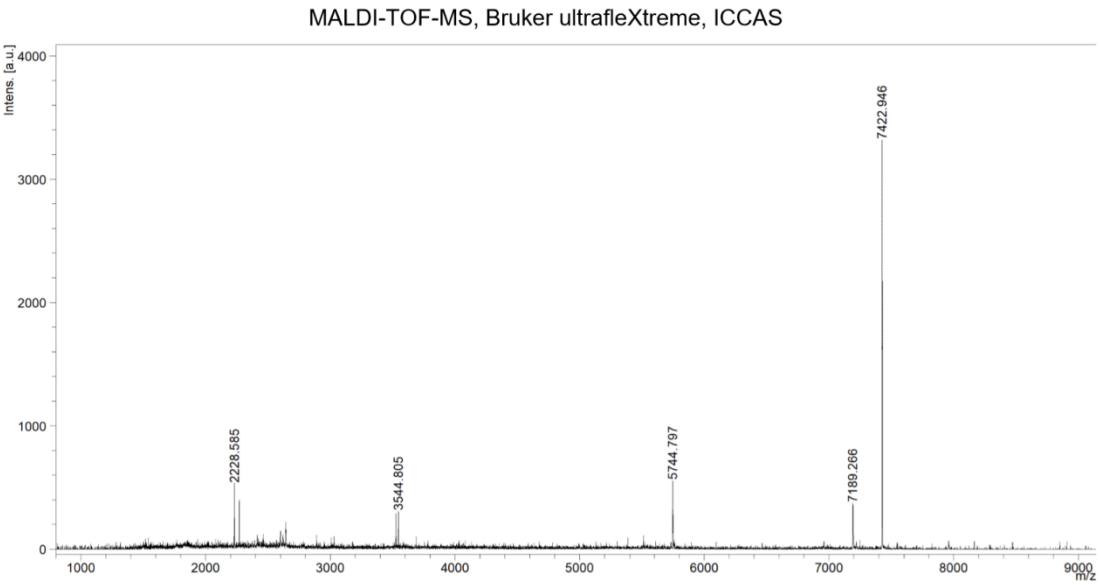


4

R_1 = $NH(CH_2CH_2O)_{11}Me$, R_2 = $N[(CH_2CH_2O)_3(CH_2)_{12}OC(CF_3)_3]_2$

^{19}F NMR (376 MHz, $CDCl_3$)

MS(MALDI-TOF) of compound FMA **4**



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