Supporting Information for

Water-soluble fluorinated metal–organic cage based on paramagnetic copper as an efficient ^{1}H and ^{19}F MRI nanoprobe

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Section S1. General Materials and Methods

1.1 Materials

All reagents were commercially available and used as received without further purification. 3,6,9,12,15,18,21,24,27,30,33-Undecaoxapentatriacontane-1,35-diol (97%), 5-hydroxyisophthalic acid (98%), di(1H-imidazol-1-yl)methanone (CDI, 98%), 2,3,4,6,7,8,9,10-octahydropyrimido[1,2-a]azepine (DBU, 98%), N,N-dicyclohexylcarbodiimide (DCC, 98%), 4-dimethylaminopyridine (DMAP, 98%), 3,3,3-trifluoropropanoic acid (97%), copper(II) acetate hydrate ($Cu(OAc)_2 \cdot H_2O$, 97%) were purchased from Bide Pharmatech Co., Ltd. (China). *p*-Toluenesulfonyl chloride (≥99%), *tert*-butanol (99.5%), trifluoroacetic acid (TFA, 99%), sodium hydroxide (NaOH, ≥96%), sodium chloride (NaCl, 99.99%), magnesium sulfate ($MgSO_4$, ≥98%), potassium carbonate (K_2CO_3, 99.99%) were purchased from Shanghai Titan Scientific Co., Ltd. (China). Tetrahydrofuran (THF), N,N-dimethylformamide (DMF), dichloromethane (DCM), ethanol (EtOH), methanol (MeOH), petroleum ether (PE), ethyl acetate (EA) hydrochloric acid (HCl, 37%) were purchased from Sinopharm Chemical Reagent Co., Ltd. (China).

1.2 Characterization

Nuclear Magnetic Resonance (NMR): NMR spectra were measured using a Bruker Avance 500 (500 MHz) instrument at room temperature. The chemical structures of the synthesized compounds were recorded in $CDCl_3$ or D_2O with an internal deuterium lock to ensure the stability of the residual protons.

Mass Spectrometry (MS): The precise molecular weights of the synthesized compounds were recorded through mass spectra. Quadrupole Time of Flight LC/MS mass spectra were performed on Bruker impact II (Bruker, Germany). Matrix-assisted laser desorption ionization time of flight (MALDI-TOF) mass spectra were performed on a Bruker Speed MALDI-TOF 7090 (Bruker, Germany).

Fourier Transform Infrared (FT-IR) Spectroscopy: Fourier transform infrared spectra were recorded on a Bruker Tensor 27 FT-IR using ATR measurements for solids as neat samples.

Size Exclusion Chromatography (SEC): The molecular weights and polydispersity indexes (PDI) of ligands and MOCs were accessed by size exclusion chromatography on a Malvern GPC using polymethylmethacrylate as standard. Tetrahydrofuran (THF) was used as the eluent at a flow rate of 1.0 mL/min at 35 °C.

Dynamic Light Scattering (DLS) and Zeta Potential: The Particle Size and Zeta

Potential Analyzer in a ZS90 instrument is mainly used to test particle size and size distribution and particle charges.

Transmission electron microscopy (TEM): The morphologies and sizes of MOC-F were also estimated by transmission electron microscopy (TEM) performed on Talos F200X G2 (Thermo Scientific).

Atomic Force Microscopy (AFM): The morphologies and sizes of MOC-F were further estimated by atomic force microscopy (AFM) performed on MFP-3D (Oxford).

Relaxation Time Measurements: ^{1}H longitudinal relaxation time (T_1) and transverse relaxation time (T_2) of each sample were measured on a Low Filed NMR Analyzer (MesoMR23-060H-I, Niumai Corporation). ^{19}F relaxation times were measured using a magnetic resonance spectrometer (Bruker Advance III, 500 MHz). Longitudinal relaxation times (T_1) were measured using inversion recovery (IR) sequence. Transverse relaxation times (T_2) were measured using CPMG sequence. Vdlist (T_1 fitting) and vclist (T_2 fitting) were set according to the following equations:

$$f(t) = I_0 * [1 - 2 * e^{-t/T_1}]$$

$$f(t) = 2 * e^{-t/T_2}$$

T_1 and T_2 values were given directly by the fitting report.

***In vitro* ^{1}H MRI:** Samples MOC-OH, MOC-F, and L-F were prepared in specific concentration gradients and placed in centrifuge tubes. The samples were prepared in 1 × PBS at indicated concentrations. For acquiring ^{1}H MR images, a RARE sequence was used with the following parameters: RARE factor = 4, repetition time (TR) / echo time (TE) = 1000 ms/8.5 ms, flip angle = 90°, FOV = 4 × 4 cm^2, slice thickness (ST) = 1 mm (20 slices in total), matrix (MTX) = 256 × 256, NEX = 4. The total time for each acquisition was about 1.2 min.

***In vitro* ^{19}F MRI:** Samples MOC-F and L-F were prepared into specific concentration gradients in microtiter plates based on fluorine concentration. The RARE sequence was employed to scan the model during acquisition of ^{19}F MRI images: TR/TE= 600/3.36 ms, FA = 135.88°, NEX = 60, FOV = 40 mm × 40 mm, the collection time is approximately 15 minutes.

Section S2. Details of the biological experiment

Cytotoxicity Assessment: Using a commercially available assay kit, the survival rate of HK-2 cells was evaluated via the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) method to assess the cytotoxic effects of MOC and MOC-F. The procedure was as follows: HK-2 cells were seeded at a density of 7,000 cells per well in a 96-well plate containing DMEM medium supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin dual antibiotics. After 12 hours of incubation at 37°C with 5% CO_2, MOC or MOC-F was prepared at various concentrations and added to fresh medium for cell incubation. Following 24 hours of incubation, the probe was removed and cells were washed. Next, add 100 μL fresh medium and 10 μL MTT solution to each well. Incubate for 4 hours at 37 °C, 5% CO_2, and 90% humidity. After aspirating the supernatant, add 100 μL dimethyl sulfoxide (DMSO) to each well and allow the purple phenylthiazine crystals to dissolve completely. Wells containing only PBS served as blank controls, while wells containing cells and medium alone served as positive controls. Measure the absorbance (OD570) of each sample at 570 nm using a microplate reader. Calculate the survival rate of HK-2 cells by comparing results to the blank and control groups. Repeat this procedure at 36 and 48 hours to assess long-term toxicity.

Cell Uptake: In the in vitro cell uptake assay, HK-2 cells were seeded at a density of 10,000 cells/mL in 10 mm tissue culture dishes and cultured for 24 hours. Subsequently, MOC or MOC-F (2 mg/mL, 100 μL) was added to each well and incubated for 2, 4, 8, or 12 hours. In vitro cell retention assay: HK-2 cells were seeded at a density of 10,000 cells/mL in 10 mm tissue culture dishes and cultured for 24 hours. Subsequently, MOC or MOC-F (2 mg/mL, 100 μL) was added to each well and incubation continued for 12 hours. The medium was then removed and replaced with fresh medium. Cells were harvested at two time points: “12+4” hours and “12+8” hours. Cell uptake of MOC or MOC-F was quantified using ICP-MS analysis. Following trypsin digestion and centrifugation, cell pellets were washed three times with PBS buffer. For routine ICP-MS analysis, samples were treated with a digestion solution containing 68% nitric acid (0.25 mL) and 38% hydrochloric acid (0.75 mL), digested at 110 °C for 4 hours. After cooling, samples were diluted to a final volume of 10 mL with 2% hydrochloric acid, followed by copper content determination via ICP-MS.

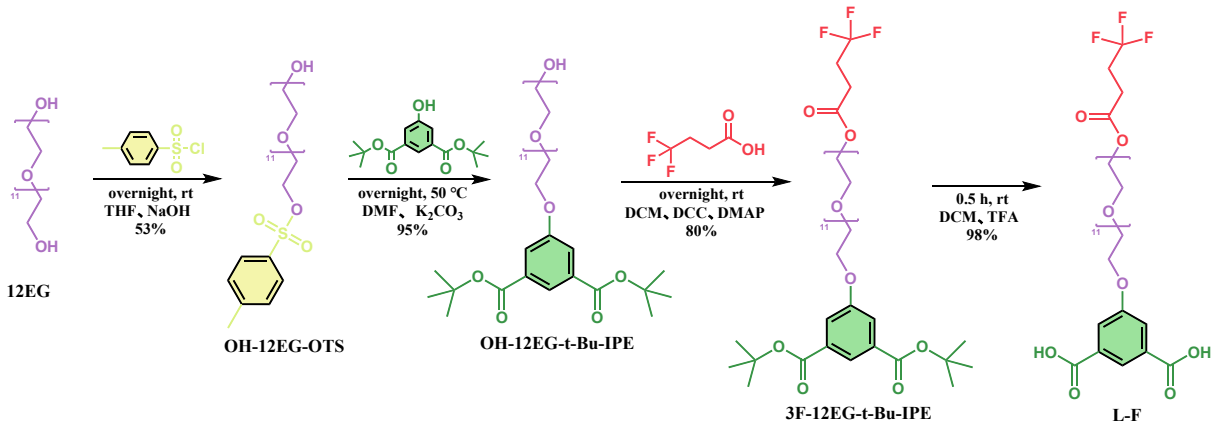
Animal Experimentation: C57BL/6 mice (7–8 weeks old) were obtained from Shanghai Laboratory Animal Center, China. All animal experiments were performed in accordance with the guidelines of the National Institute of Health for the Care and Use of Laboratory Animals and approved by the Scientific Investigation Committee of

Shanghai Jiao Tong University (No. 202501014).

Histopathological evaluation: C57BL/6 mice were intravenously injected with 200 μL of probe MOC, MOC-F (the concentration of MOC is 1.2 mM, corresponding to 22.2 mg/mL and the concentration of MOC-F is also 1.2 mM, corresponding to 25.8 mg/mL), or 200 μL PBS. Major organs (heart, liver, spleen, lung, and kidney) were collected on day 2 post-injection (n=3 per group). Organs were fixed in 4% formaldehyde solution, paraffin-embedded, and sectioned into 5μm thick slices. Sections were processed with hematoxylin and eosin (H&E) staining.

***In vivo* ^{1}H/^{19}F MRI:** C57BL/6 mice were anesthetized via inhalation of isoflurane, followed by subcutaneous injection of 200 μL MOC or MOC-F aqueous solution (the concentration of MOC is 1.2 mM, corresponding to 22.2 mg/mL and the concentration of MOC-F is also 1.2 mM, corresponding to 25.8 mg/mL) into the left and right hind thighs. Mice were maintained under anesthesia throughout the scanning process. ^{1}H MR images were acquired using a RARE sequence with the following parameters: MTX = 32×32, FOV = 40 mm×40 mm, ST = 1 mm, FA = 135.88°, TR/TE = 1000/3.36 ms, NEX = 2, acquisition time = 2 min. ^{19}F MR images were also acquired using a RARE sequence with the following parameters: MTX = 32×32, FOV = 40 mm×40 mm, ST = 40 mm, FA = 135.88°, TR/TE = 600/3.36 ms, NEX = 60, acquisition time = 15 min.

Section S3. Synthesis Procedures of Ligand and MOCs



Scheme S1. Synthesis Routes of Fluorinated Ligand, L-F.

3.1 Synthesis of Ligands

Synthesis of OH-12EG-OTS: (53% yield). 3,6,9,12,15,18,21,24,27,30,33-Undecaoxapentatriacontane-1,35-diol (12EG) (5 g, 9.15 mmol, 1 eq) was dissolved in 35 mL of THF, aqueous NaOH (5 mol/L, 8 mL) was added and cooled to 0 °C. Tosyl chloride (1.74 g, 9.15 mmol, 1 eq) was dissolved in 17 mL of THF and added dropwise to the above mixture. After the addition was completed, the reaction was stirred at room temperature for 24 h. The reaction solution was then extracted three times with DCM (100 mL) and saturated saline. The organic phase was collected, dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporator. Finally, it was purified by column chromatography on silica gel using DCM/MeOH (20:1, v/v) as eluent to obtain 3.50 g of **OH-12EG-OTS** in oil form. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 4.22 – 4.11 (m, 2H), 3.75 – 3.58 (m, 46H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.90, 133.11, 129.94, 128.10, 72.78, 70.85, 70.66, 70.36, 69.36, 68.79, 61.80, 21.77. MS (ESI): Calculated for $C_{31}H_{56}O_{15}S$, $[M+Na]^+$ 723.3232, found 723.3241.

Synthesis of *t*-Bu-IPE: (80% yield). 5-Hydroxyisophthalic acid (2 g, 10.98 mmol, 1 eq) and CDI (4.45 g, 27.45 mmol, 2.5 eq) were dissolved in 13 mL of DMF in a round-bottomed flask, and stirred under nitrogen at 40 °C for 1 h. Subsequently, DBU (4.1790 g, 27.45 mmol, 2.5 eq) was added, and the reaction was carried out with *tert*-butanol (5.25 mL, 54.7 mmol, 5 eq) at 40 °C for 24 h. At the end of the reaction, the product was poured into 13 mL of ether, filtered and precipitated, and the filtrate was collected and adjusted to pH 3 with dilute hydrochloric acid, concentrated by rotary evaporator, and purified by column chromatography on silica gel using PE/DCM (2:1 v/v) as eluent. The final product was a white solid with a total yield of 2.58 g. ^{1}H NMR (500 MHz,

Chloroform-*d*) δ 8.17 (s, 1H), 8.09 (s, 1H), 7.70 (s, 2H), 1.57 (s, 18H).

Synthesis of OH-12EG-*t*-Bu-IPE: (95% yield). ***t*-Bu-IPE** (2 g, 6.91 mmol, 1 eq) was completely dissolved in 50 mL DMF and anhydrous potassium carbonate (1.91 g, 13.83 mmol, 2 eq) was added, and the reaction was heated to 50 °C under nitrogen and stirred for 10 min. OH-12EG-OTS (5 g, 6.91 mmol, 1 eq) was dissolved in 50 mL of DMF and slowly dripped into the above solution. After addition, the reaction was carried out for 18 h. At the end of the reaction, the organic phase was extracted with DCM (100 mL) and saturated saline three times, and the organic phase was collected, which was dried with $MgSO_4$, then filtered and concentrated by rotary evaporator, and vacuum-dried to obtain 5.31 g of **OH-12EG-*t*-Bu-IPE** in oil form. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (t, *J* = 1.4 Hz, 1H), 7.68 (d, *J* = 1.4 Hz, 2H), 4.23 – 4.16 (m, 2H), 3.90 – 3.84 (m, 2H), 3.72 – 3.60 (m, 44H), 1.59 (s, 18H).

Synthesis of 3F-12EG-*t*-Bu-IPE: (80% yield). **OH-12EG-t-Bu-IPE** (1.35 g, 1.64 mmol, 1 eq), DCC (0.68 g, 3.28 mmol, 2 eq), and DMAP (0.04 g, 0.33 mmol, 0.2 eq) were completely dissolved in 10 mL DCM, and trifluorobutyric acid (0.23 g, 1.64 mmol, 1 eq) was dissolved in 10 mL DCM and the above solution was slowly added dropwise. The reaction was carried out overnight at room temperature. After the reaction, it was filtered and concentrated by rotary evaporator, and purified by column chromatography on a silica gel column using DCM/MeOH (50:1) as eluent. The final product was a light yellow oil with a total yield of 1.24 g. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17 (s, 1H), 7.68 (s, 2H), 4.31 – 4.23 (m, 2H), 4.19 (t, *J* = 4.5 Hz, 2H), 3.90 – 3.85 (m, 2H), 3.74 – 3.60 (m, 42H), 2.67 – 2.56 (m, 2H), 2.46 (dd, *J* = 17.9, 8.9 Hz, 2H), 1.59 (s, 18H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 165.06, 158.75, 133.55, 123.09, 119.46, 81.74, 70.71, 69.71, 69.09, 67.99, 64.32, 28.30. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -66.99. MS (ESI): Calculated for $C_{44}H_{73}F_3O_{18}$, $[M+Na]^+$ 969.4641, found 969.4649.

Synthesis of L-F: (98% yield). **3F-12EG-*t*-Bu-IPE** (0.1 g, 0.1 mmol, 1 eq) was dissolved in 2 mL of DCM, and trifluoroacetic acid (1 mL) was added and stirred for 0.5 h. At the end of the reaction, the solvent was removed by spin distillation, and the solvent was extracted with a solution of DCM (100 mL) and dilute hydrochloric acid for three times, and the organic phase was collected, and the organic phase was dried with anhydrous $MgSO_4$, then filtered and concentrated by rotary evaporator. After vacuum drying, 0.086 g of **L-F** in oil form was obtained. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.20 (s, 1H), 7.73 (s, 2H), 4.30 – 4.24 (m, 2H), 4.23 – 4.19 (m, 2H), 3.90 – 3.88 (m, 2H), 3.77 – 3.74 (m, 2H), 3.66 (s, 40H), 2.64 – 2.58 (m, 2H), 2.51 – 2.40 (m, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 171.15, 167.98, 158.94, 131.71, 123.98, 120.56, 70.61, 69.84, 69.08, 68.11, 64.29, 29.31, 27.18. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -66.97. MS (ESI): Calculated for $C_{36}H_{57}F_3O_{18}$, $[M+Na]^+$ 857.3389, found 857.3389.

Synthesis of L: (98% yield). **OH-12EG-t-Bu-IPE** (0.1 g, 0.1 mmol, 1 eq) was dissolved in 2 mL of DCM, and trifluoroacetic acid (1 mL) was added and stirred for 0.5 h. At the end of the reaction, the solvent was removed by spin distillation, and the solvent was extracted with a solution of DCM (100 mL) and dilute hydrochloric acid for three times, and the organic phase was collected, and the organic phase was dried with anhydrous $MgSO_4$ and then filtered and concentrated by rotary evaporator. After vacuum drying, 0.085 g of **L** in oil form was obtained. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 4.7 Hz, 1H), 7.71 (d, *J* = 3.8 Hz, 2H), 4.56 – 4.40 (m, 2H), 4.20 (s, 2H), 3.89 (s, 2H), 3.79 – 3.63 (m, 42H).

3.2 Synthesis of MOCs

Synthesis of MOC-F: (85% yield). **L-F** (0.1 g, 0.12 mmol, 1 eq) and $Cu(OAc)_2 \cdot H_2O$ (0.024 g, 0.12 mmol, 1 eq) were completely dissolved in dispersed THF (5 mL), and the two solutions were mixed together and stirred at room temperature for 3 h. At the end of the reaction, the reaction solution was concentrated, and the cages were precipitated by dropwise addition to ether. The precipitate was centrifuged, washed and dried to obtain **MOC-F**.

Synthesis of MOC: (82% yield). **L** (0.10 g, 0.14 mmol, 1 eq) and $Cu(OAc)_2 \cdot H_2O$ (0.028 g, 0.14 mmol, 1 eq) were completely dissolved in dispersed THF (5 mL), and the two solutions were mixed together and stirred at room temperature for 3 h. At the end of the reaction, the reaction solution was concentrated, and the cages were precipitated by adding it dropwise to ether. The precipitate was centrifuged, washed and dried to obtain **MOC**.

Section S4. Supplemental Data

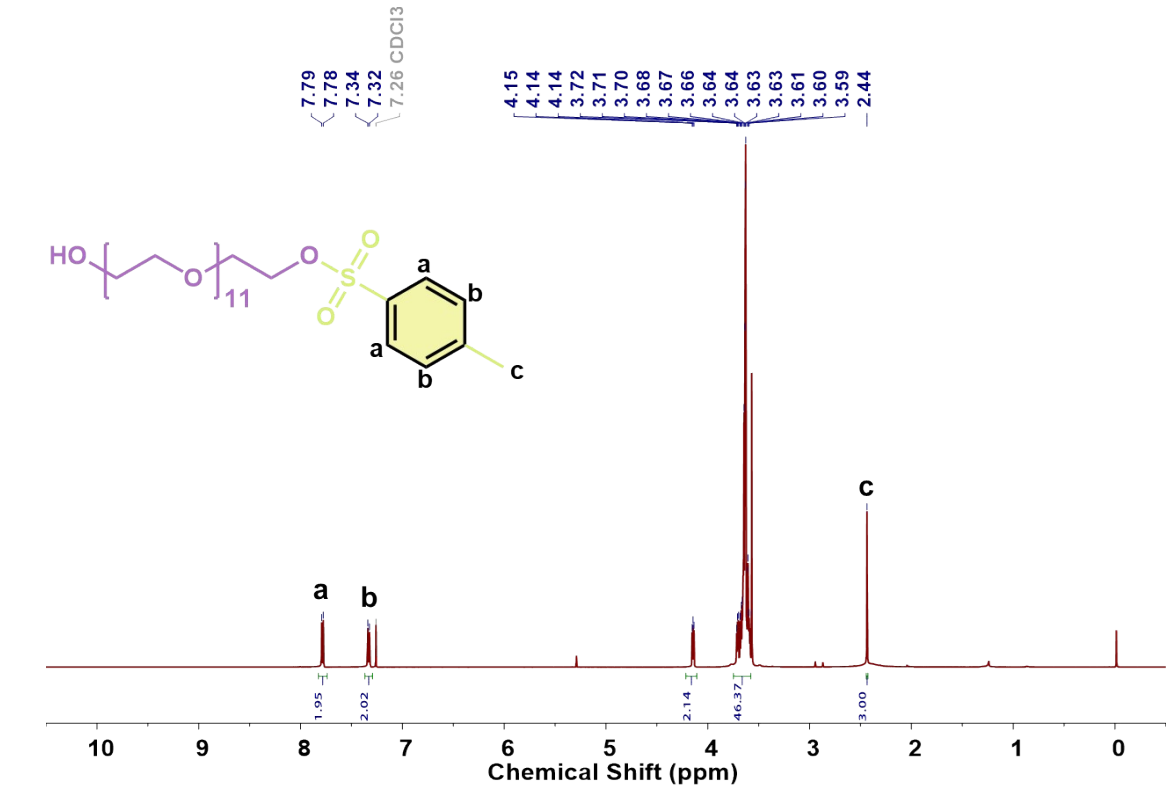


Figure S1. The ^{1}H-NMR of **OH-12EG-OTS** in $CDCl_3$.

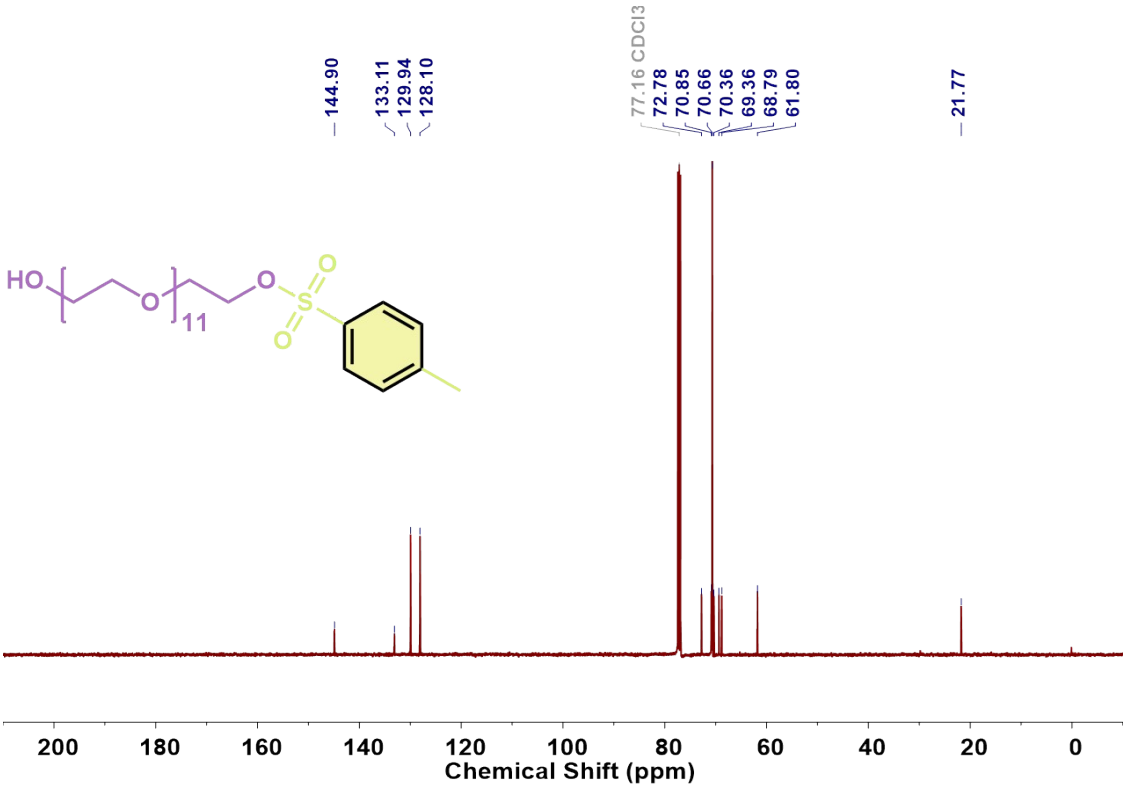


Figure S2. The ^{13}C-NMR of **OH-12EG-OTS** in $CDCl_3$.

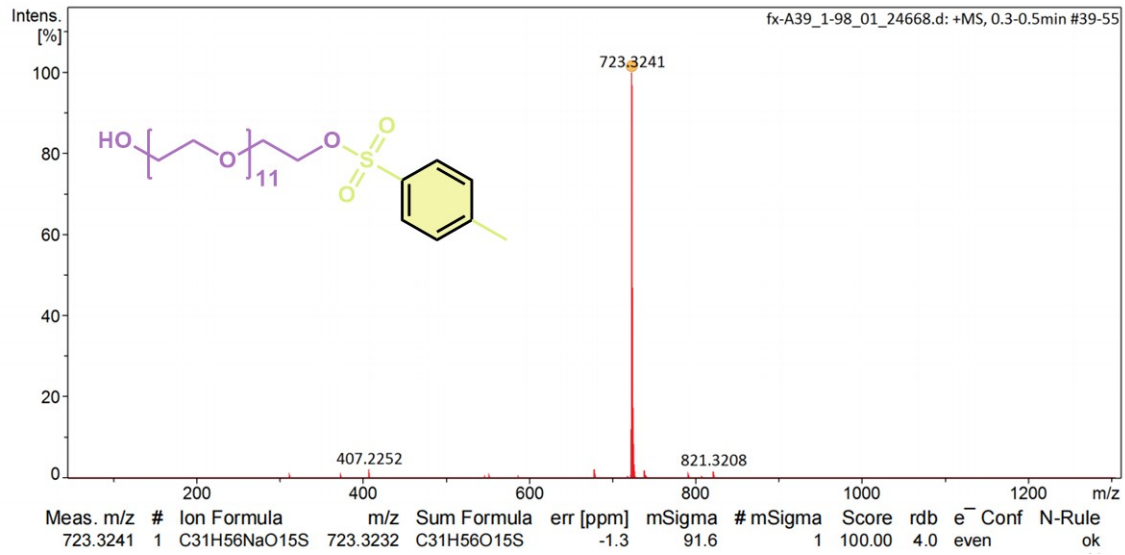


Figure S3. The ESI mass spectrum of **OH-12EG-OTS**.

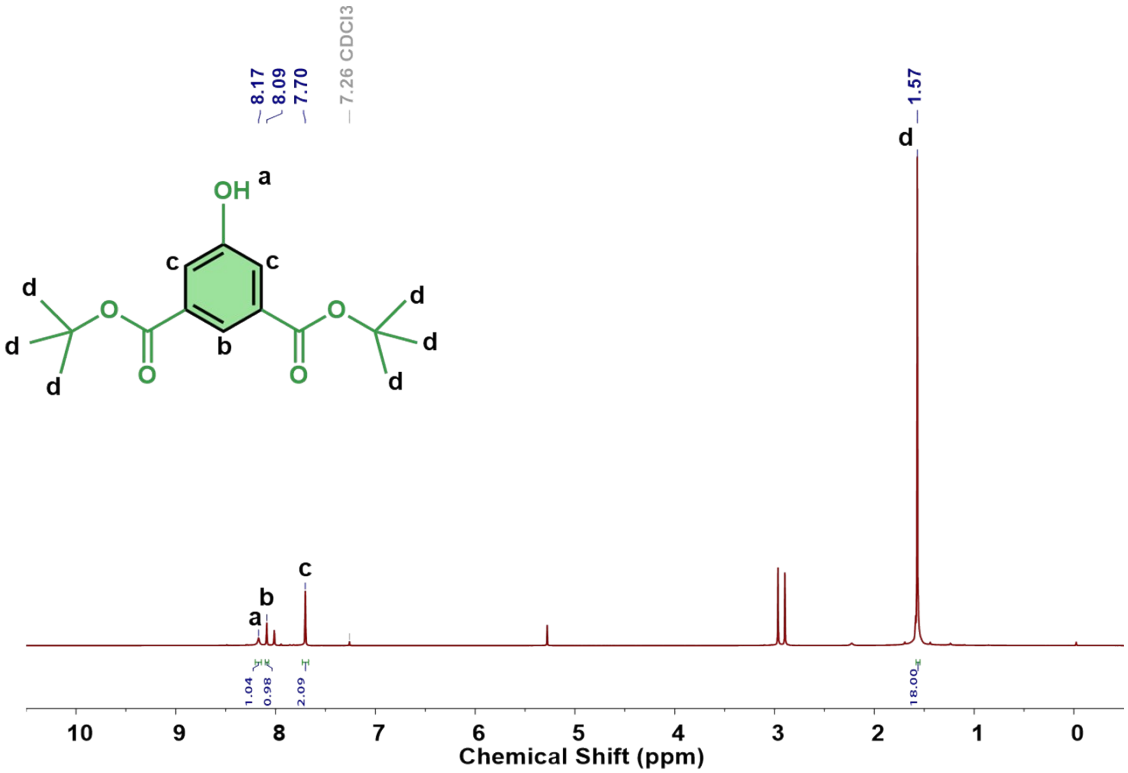


Figure S4. The ^{1}H-NMR of ***t*-Bu-IPE** in $CDCl_3$.

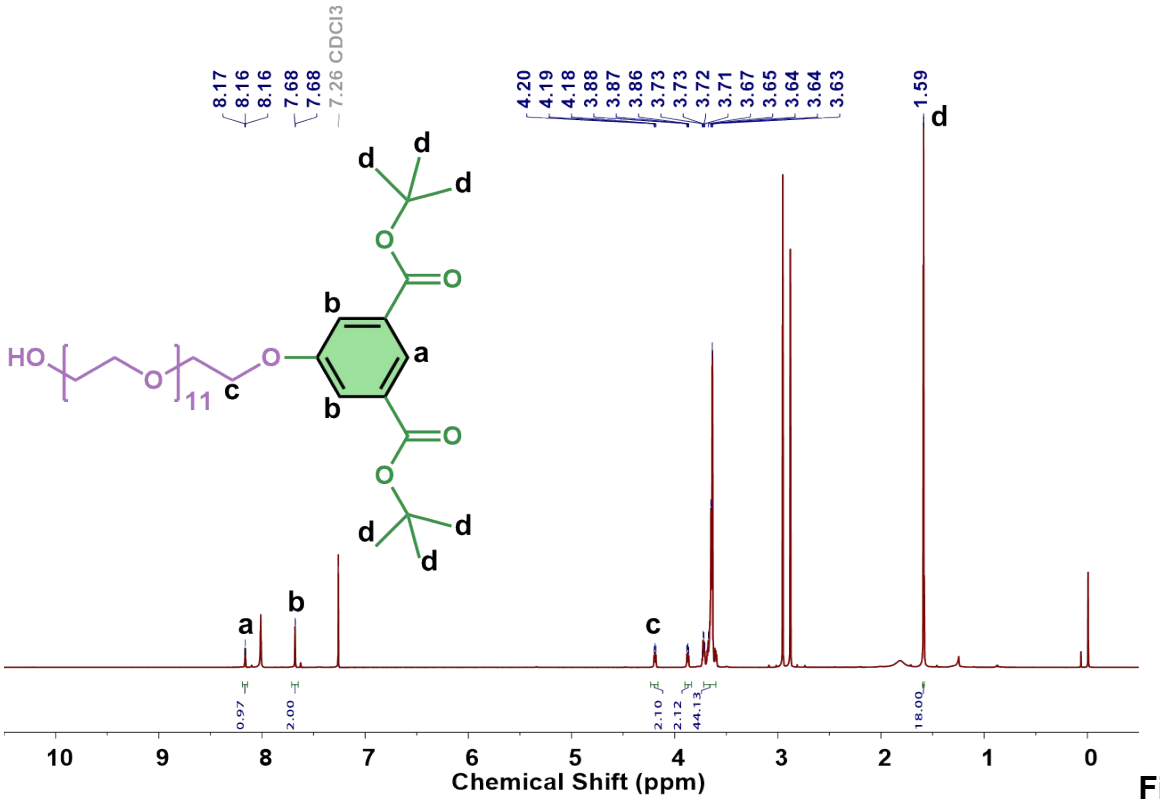


Figure S5. The ^{1}H-NMR of **OH-12EG-*t*-Bu-IPE** in $CDCl_3$.

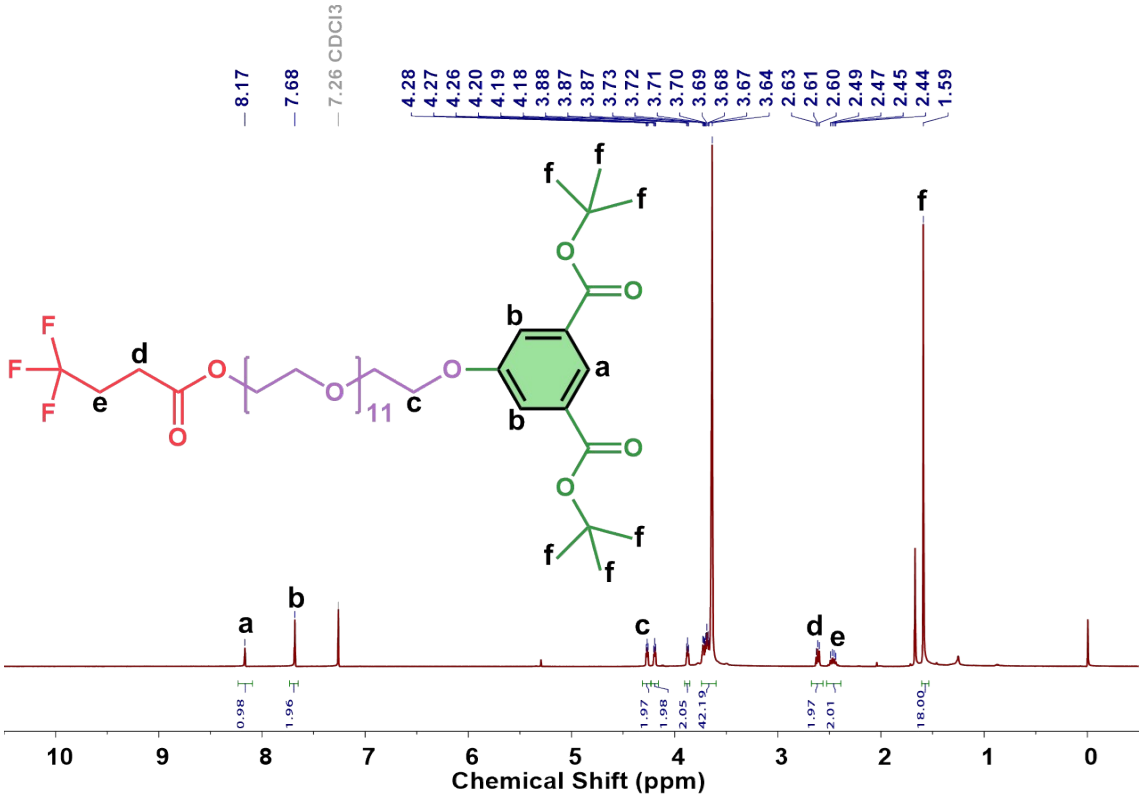


Figure S6. The ^{1}H-NMR of **3F-12EG-*t*-Bu-IPE** in $CDCl_3$.

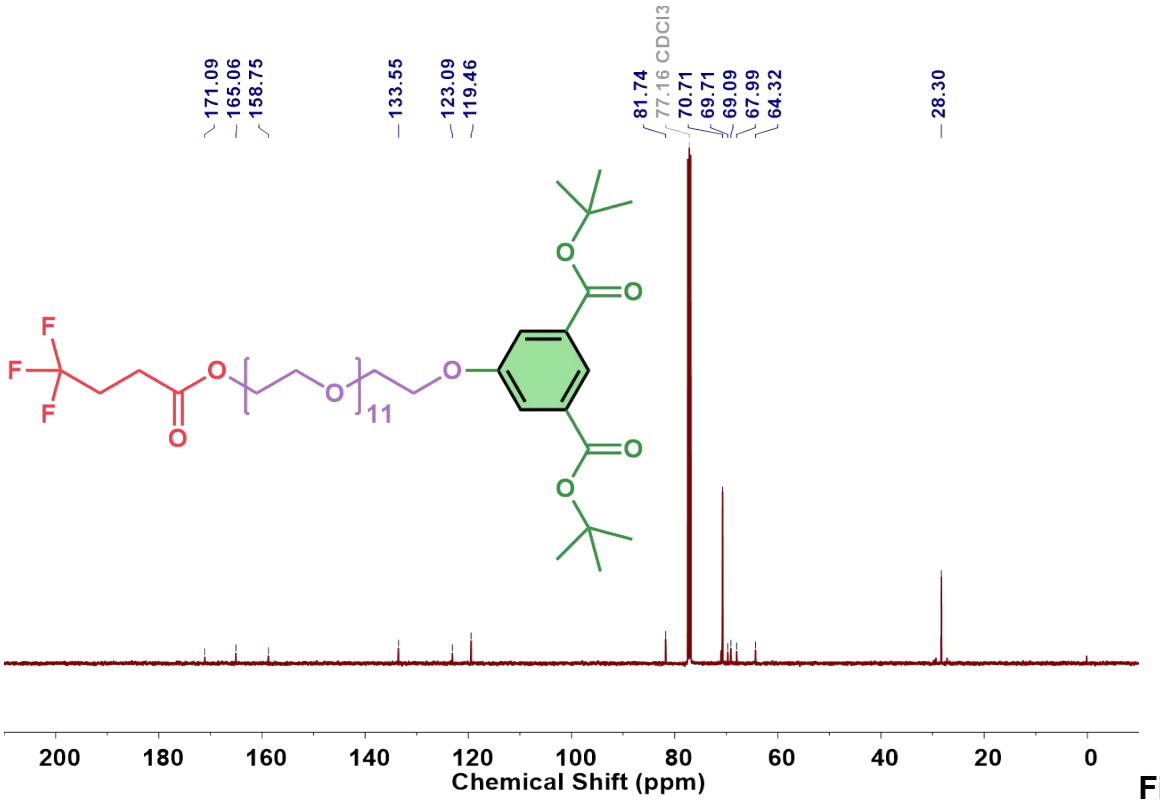


Figure S7. The ^{13}C-NMR of **3F-12EG-*t*-Bu-IPE** in $CDCl_3$.

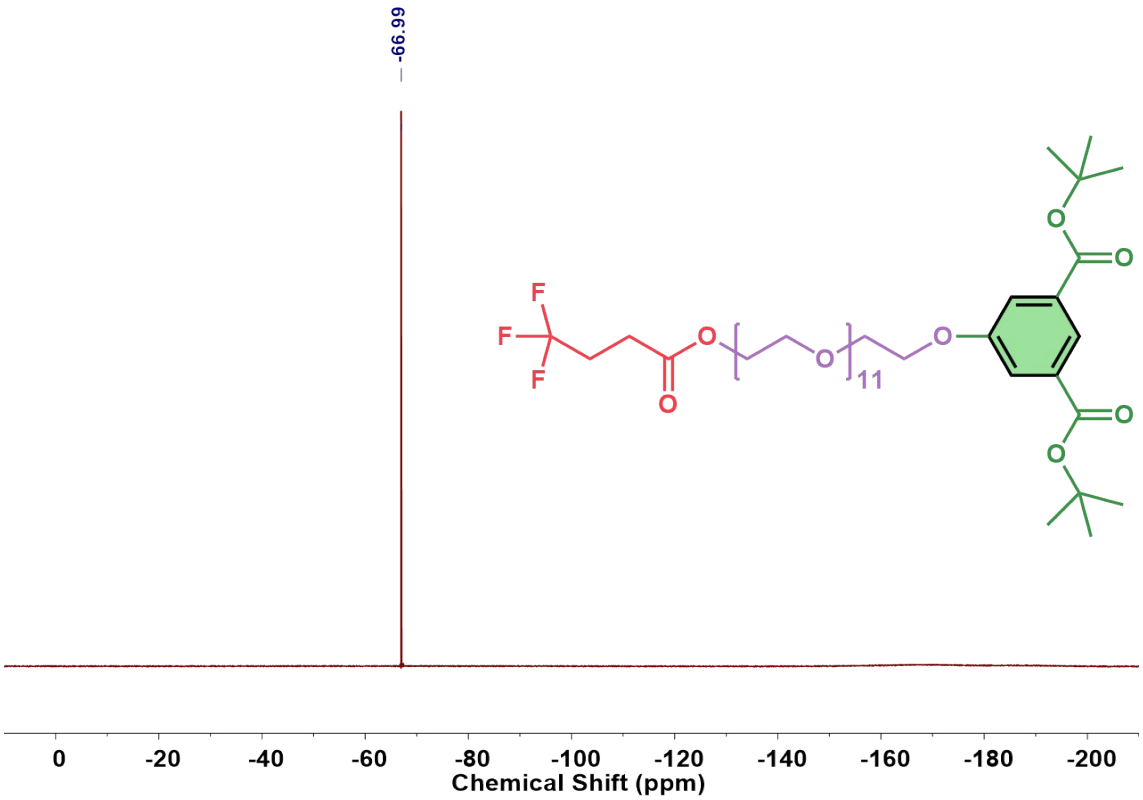


Figure S8. The ^{19}F-NMR of **3F-12EG-*t*-Bu-IPE** in $CDCl_3$.

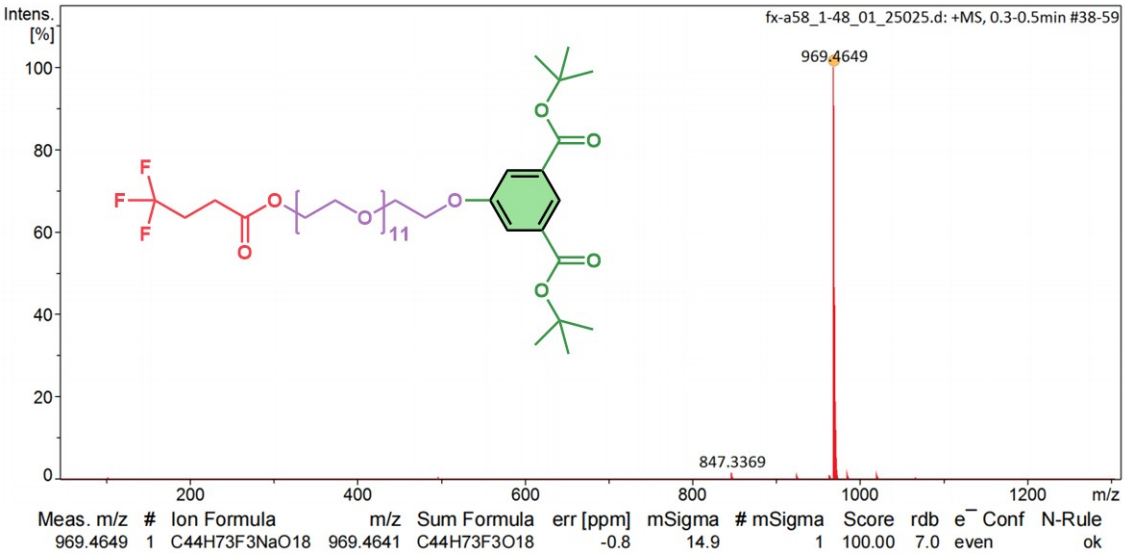


Figure S9. The ESI mass spectrum of **3F-12EG-*t*-Bu-IPE**.

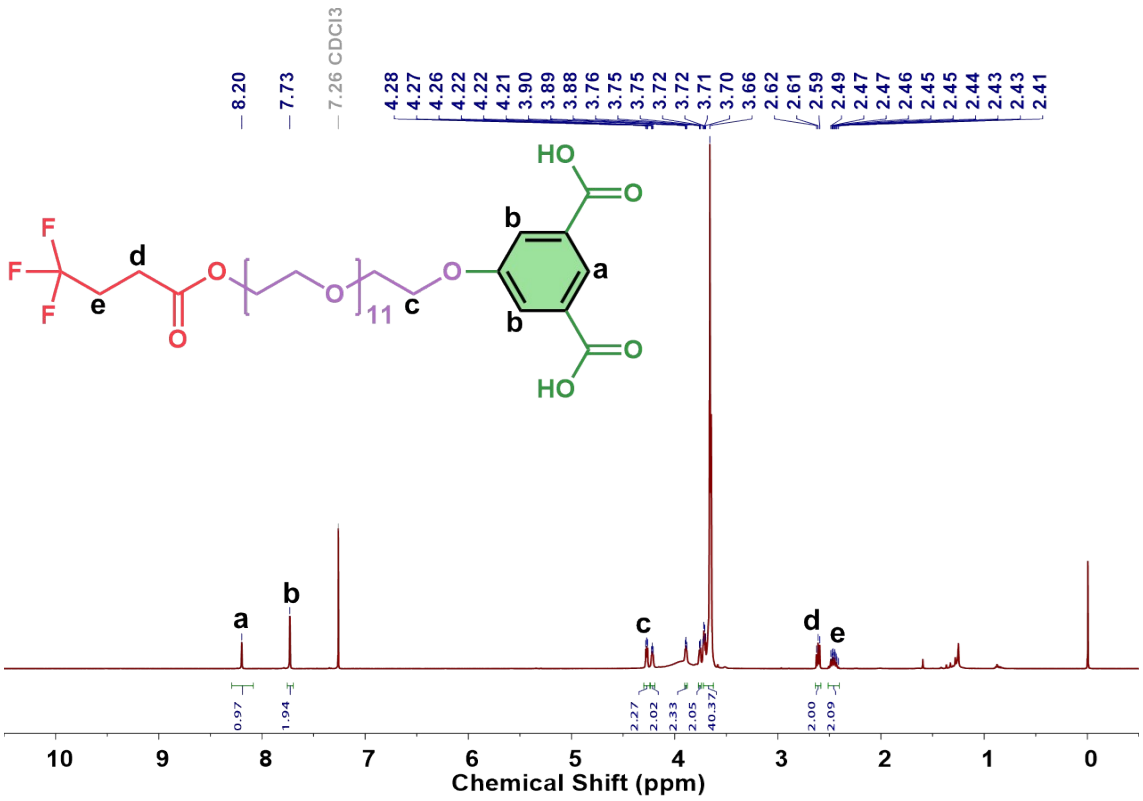


Figure S10. The ^{1}H-NMR of **L-F** in $CDCl_3$.

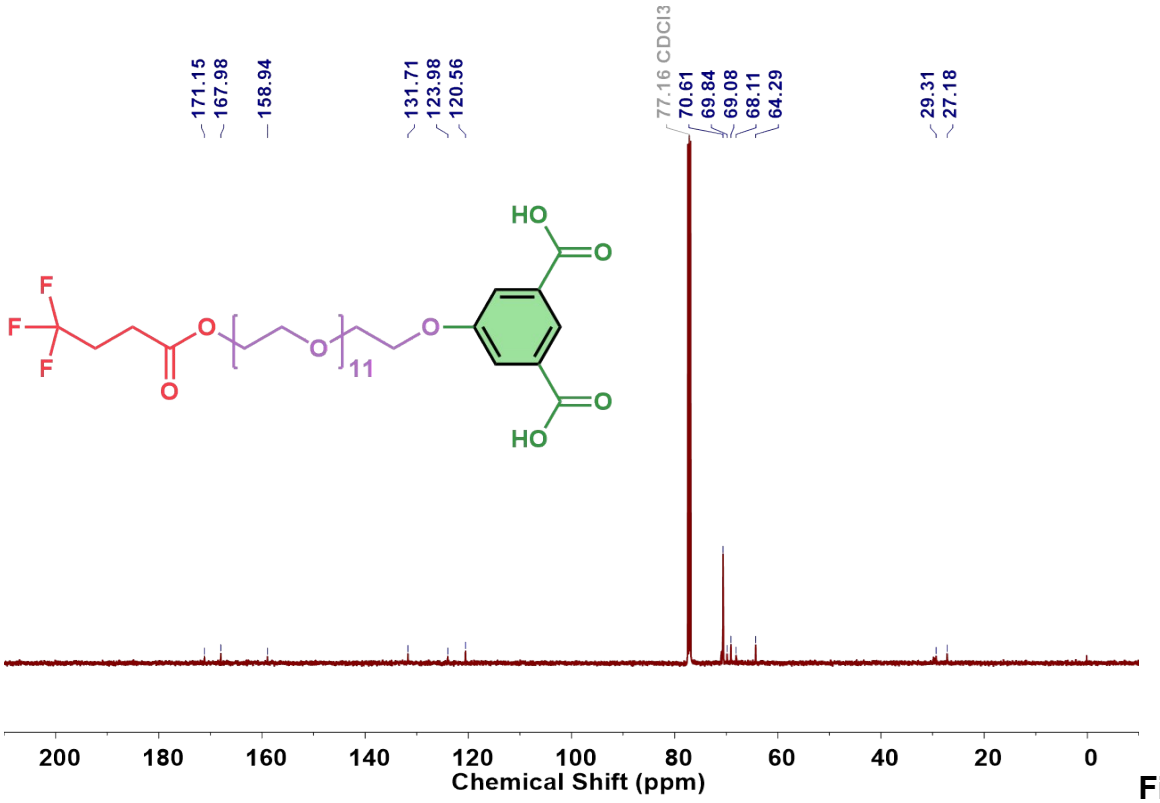


Figure S11. The ^{13}C-NMR of **L-F** in $CDCl_3$.

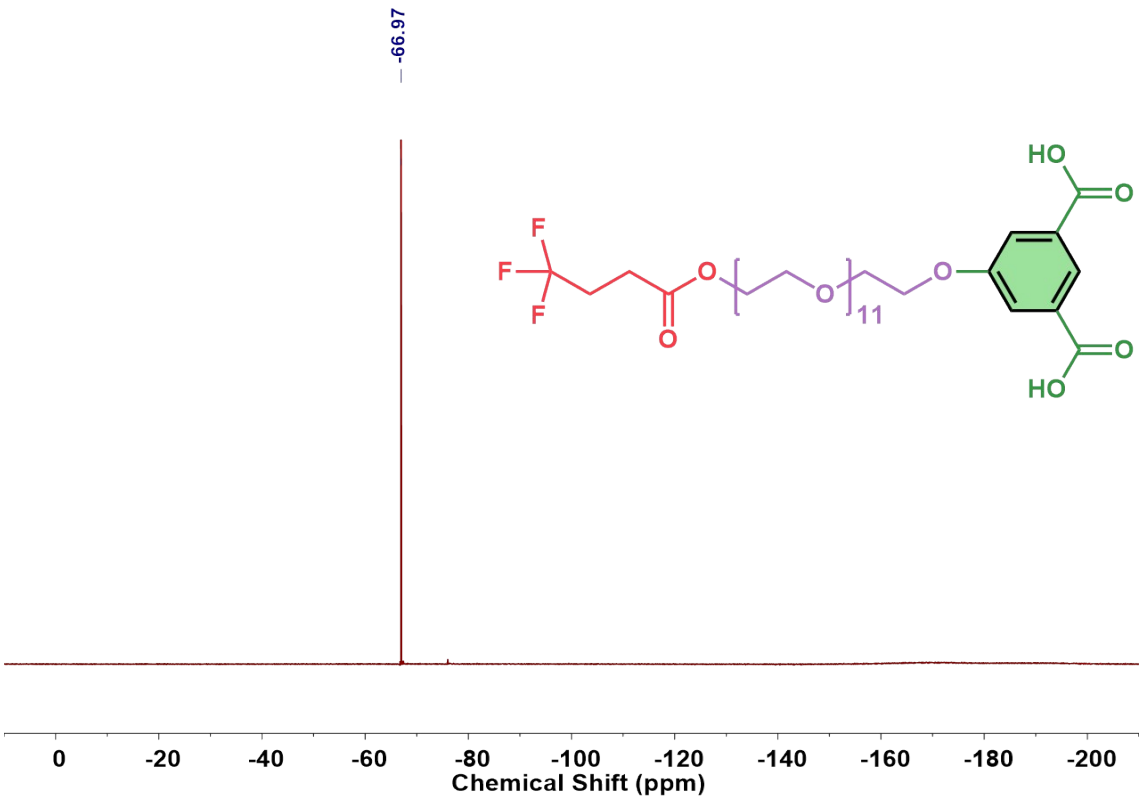


Figure S12. The ^{19}F-NMR of **L-F** in $CDCl_3$.

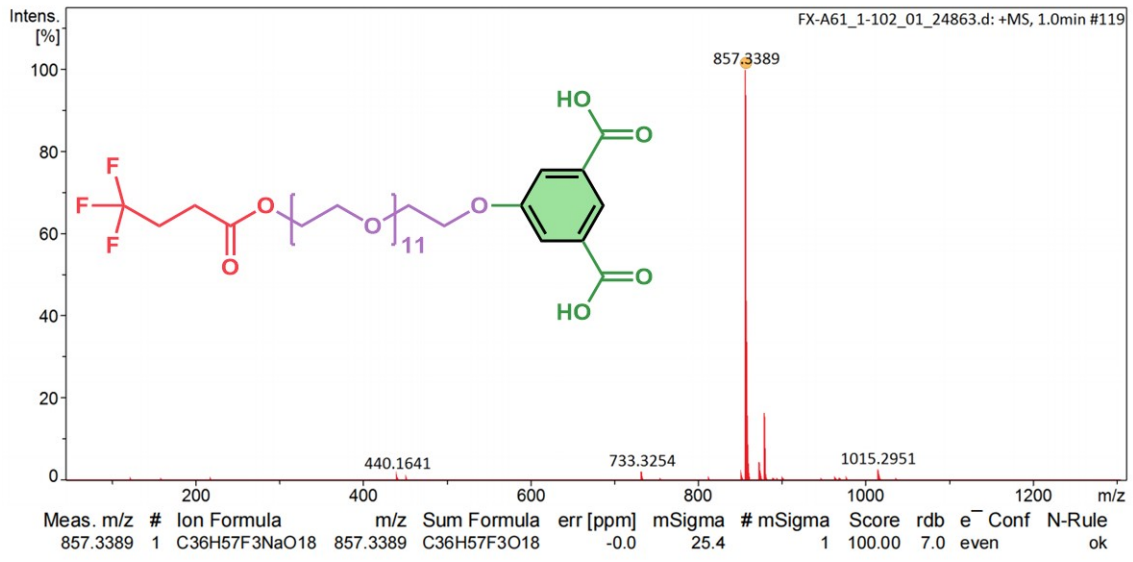


Figure S13. The ESI mass spectrum of **L-F**.

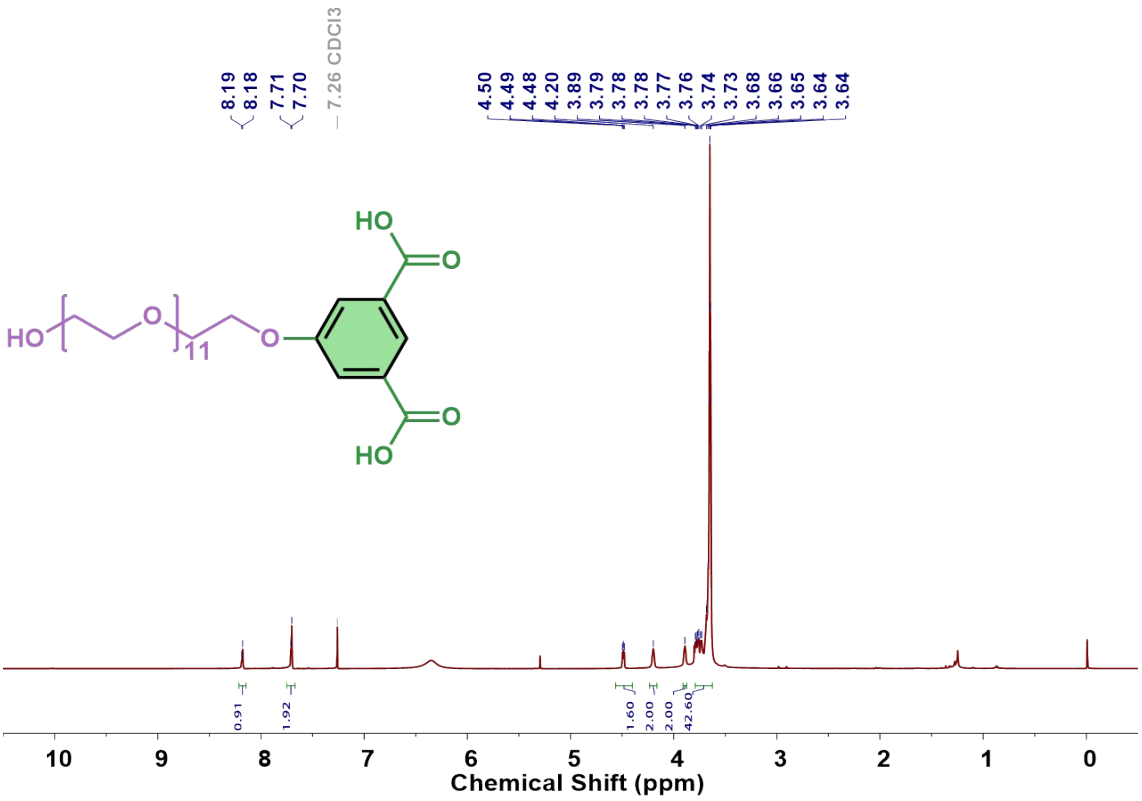


Figure S14. The ^{1}H-NMR of **L** in $CDCl_3$.

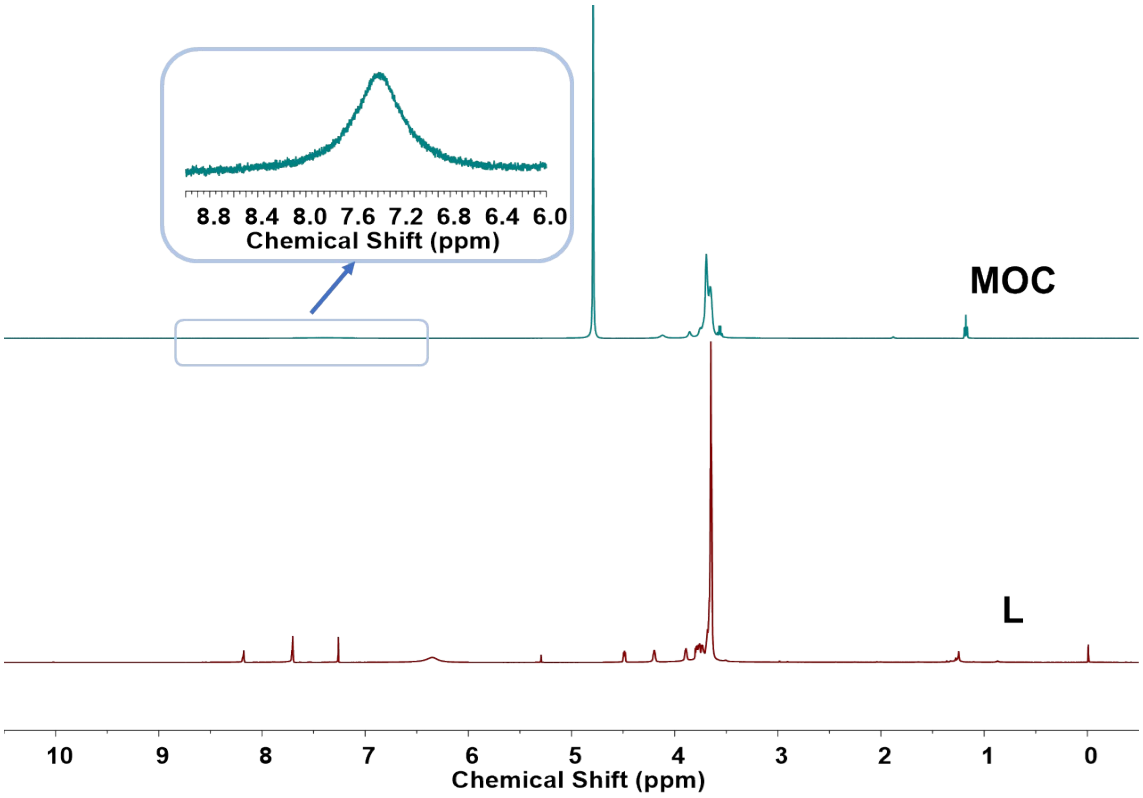


Figure S15. The ^{1}H-NMR spectra of **L** and **MOC** in $CDCl_3$ and D_2O.

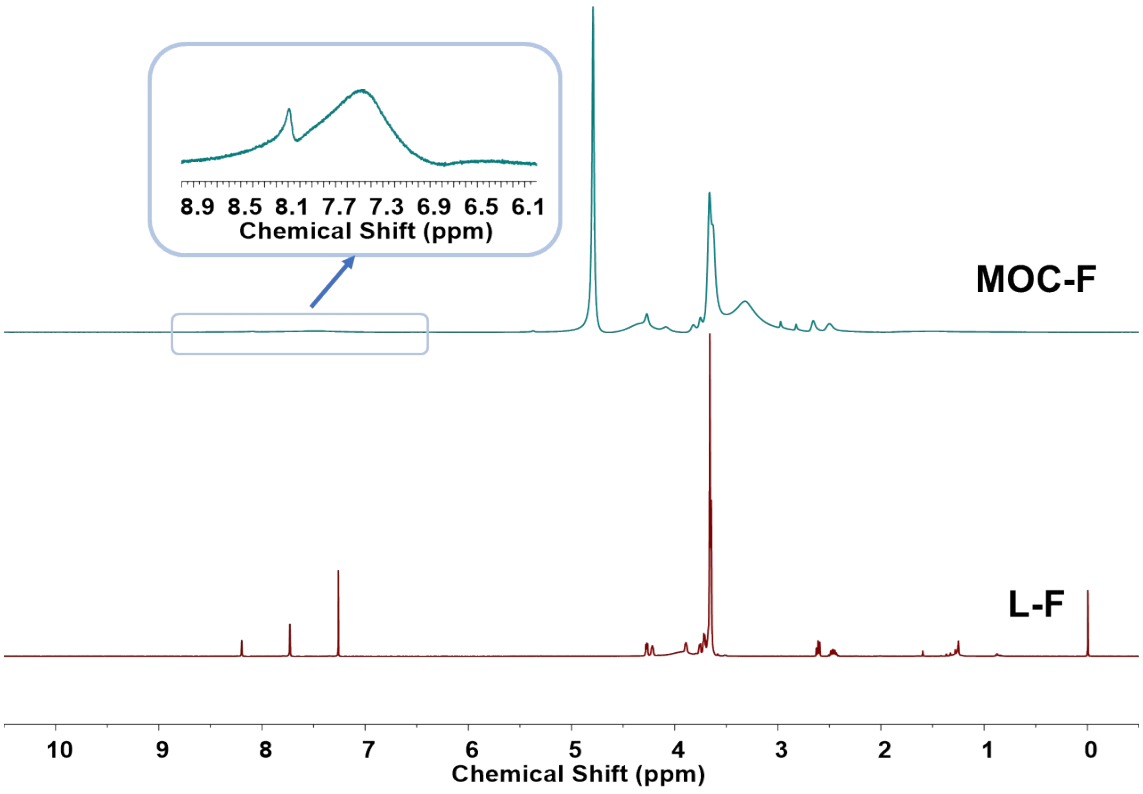


Figure S16. The ^{1}H-NMR spectra of **L-F** and **MOC-F** in $CDCl_3$ and D_2O.

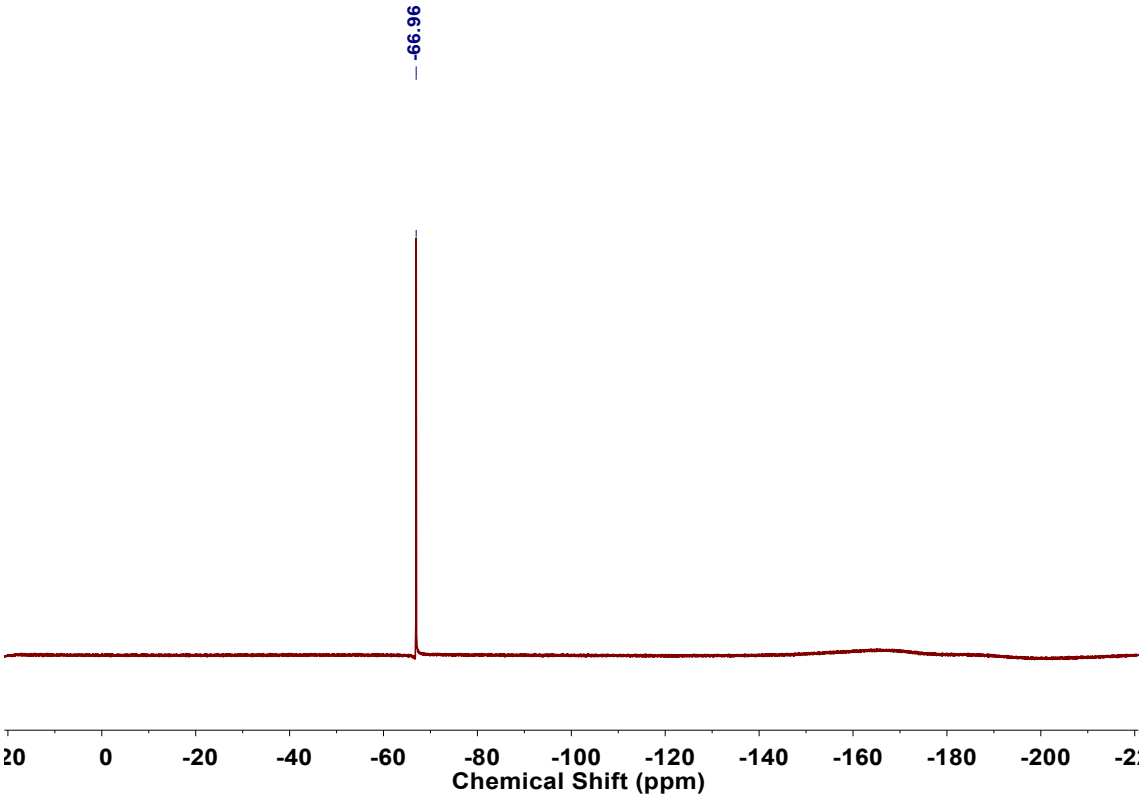


Figure S17. The ^{19}F-NMR of **MOC-F** in D_2O.

Table S1. Molecular formula, molecular weight, and fluorine mass fraction of the relevant compounds.

Compound	Molecular Formula	Molecular Weight (g/mol)	Fluorine Mass Fraction (wt%)
L-F	$C_{36}H_{57}F_3O_{18}$	834.83	6.83
MOC	$C_{768}H_{1248}O_{408}$	18535.2	0
MOC-F	$C_{864}H_{1320}F_{72}O_{432}$	21512.64	6.36

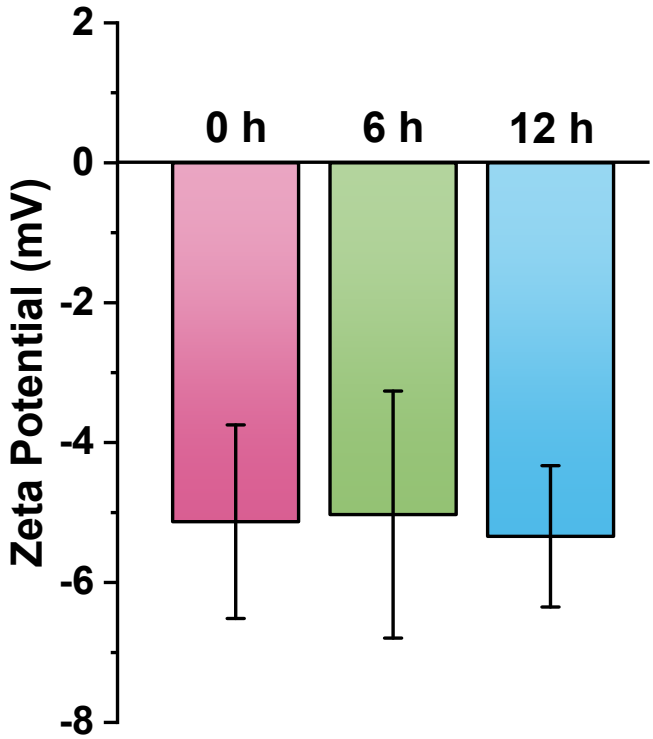


Figure S18. Zeta potential of **MOC-F** in water.

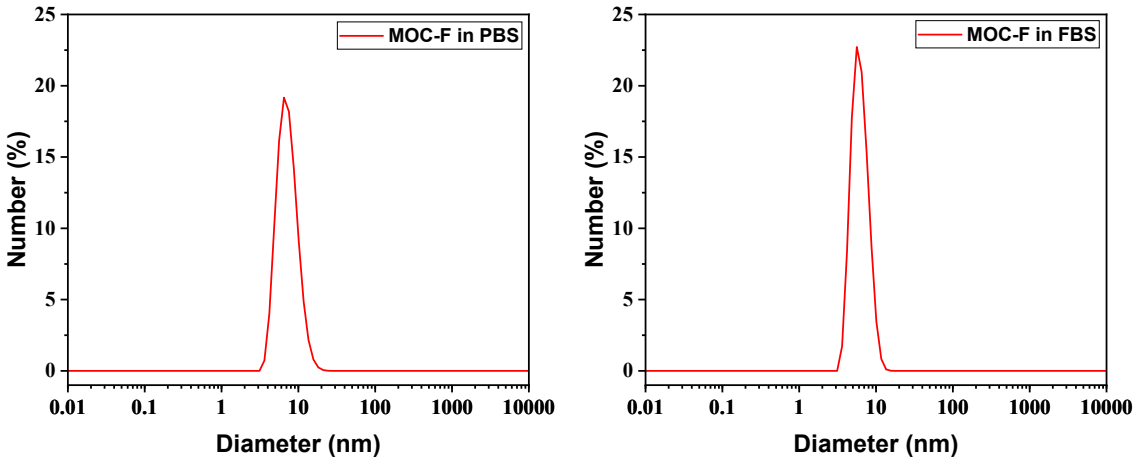


Figure S19. The DLS plots of **MOC-F** in PBS and FBS over a period of two days.

Table S2. The relaxation times of ^{1}H for the solutions of **L-F**, **MOC** and **MOC-F**.

Concentration (mM)	L-F			MOC			MOC-F		
	T_1 (s)	T_2 (s)	T_2/T_1	T_1 (s)	T_2 (s)	T_2/T_1	T_1 (s)	T_2 (s)	T_2/T_1
0.01	2.35	1.65	0.70	1.74	1.09	0.63	1.69	1.12	0.66
0.02	2.39	1.65	0.69	1.04	0.80	0.77	1.08	0.78	0.72
0.04	2.36	1.68	0.71	0.75	0.53	0.71	0.78	0.51	0.66
0.08	2.39	1.67	0.70	0.41	0.31	0.76	0.40	0.30	0.74
0.16	2.36	1.67	0.71	0.22	0.17	0.76	0.22	0.17	0.74

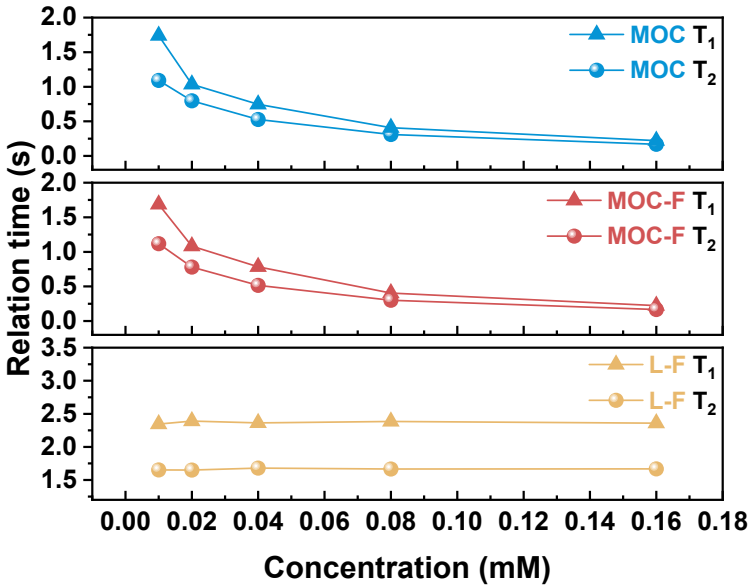


Figure S20. Plot of ^{1}H relaxation time versus concentrations for **L-F**, **MOC**, **MOC-F**.

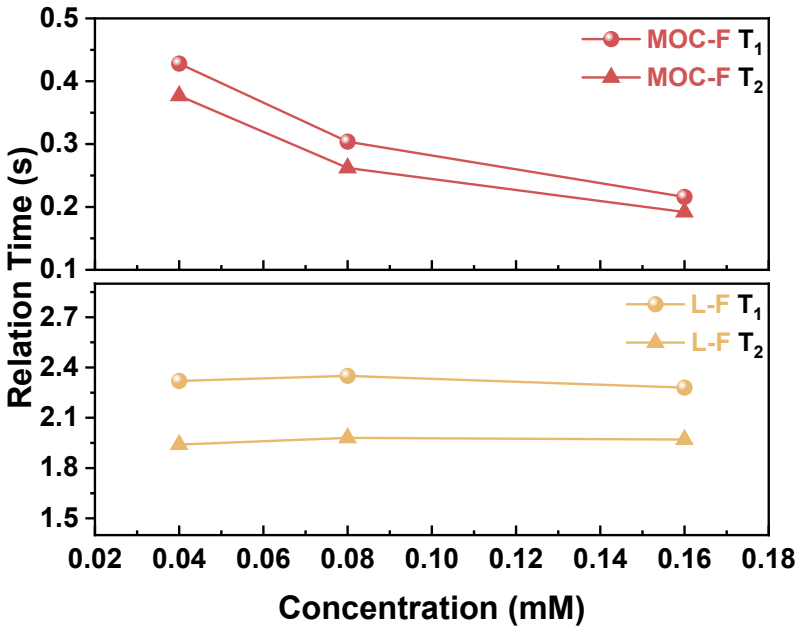


Figure S21. Plot of ^{19}F relaxation time versus concentrations for **L-F** and **MOC-F**.

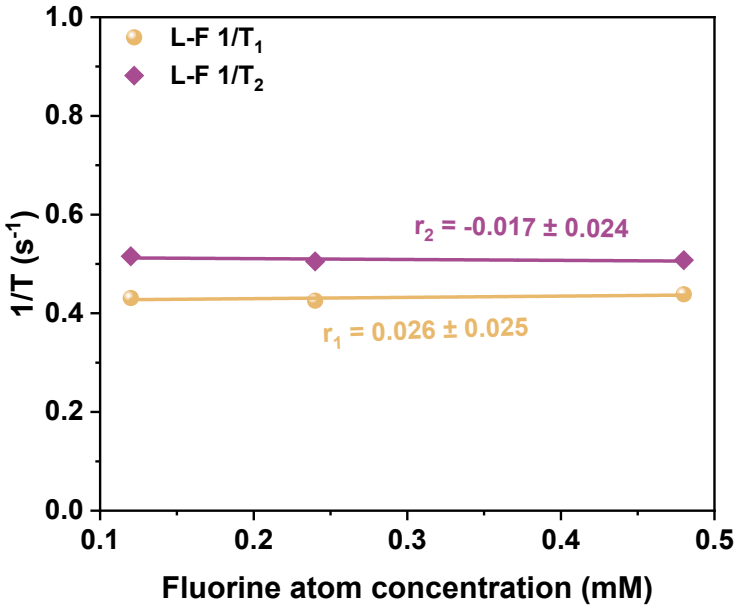


Figure S22. The relationship between relaxation rates and the concentrations of **L-F** for ^{19}F.

Table S3. The relaxation times of ^{19}F for **L-F** and **MOC-F**.

Concentration (mM)	L-F			MOC-F		
	T_1 (s)	T_2 (s)	T_2/T_1	T_1 (s)	T_2 (s)	T_2/T_1
0.04	2.32	1.94	0.84	0.43	0.38	0.88
0.08	2.35	1.98	0.84	0.30	0.26	0.86
0.16	2.28	1.97	0.86	0.22	0.19	0.89

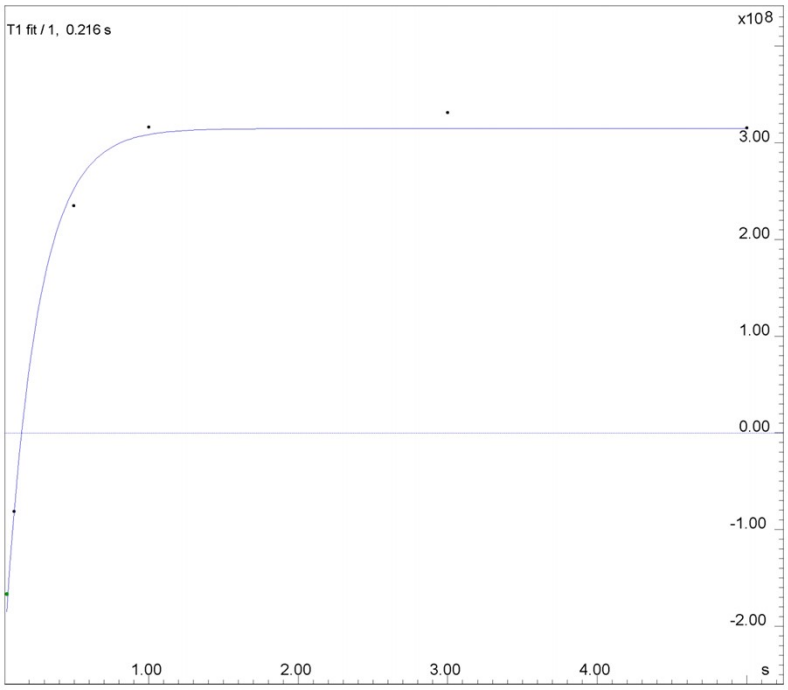


Figure S23. Fitting curve of **MOC-F** versus T_1 at a concentration of 0.16 mM.

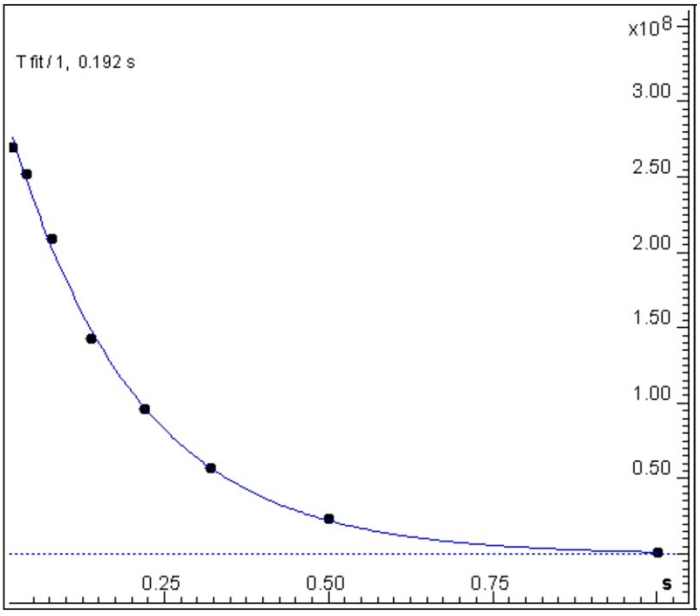


Figure S24. Fitting curve of **MOC-F** regarding T_2 at a concentration of 0.16 mM.

Table S4. Relaxation times of the mixture of free Cu^{2+} and tert-butyl protected ligand in water.

Concentration (mM)	T_1 (ms)	T_2 (ms)	T_2/T_1
0.96	37.77	22.56	0.60
1.92	27.78	16.73	0.60
3.84	20.81	13.05	0.63

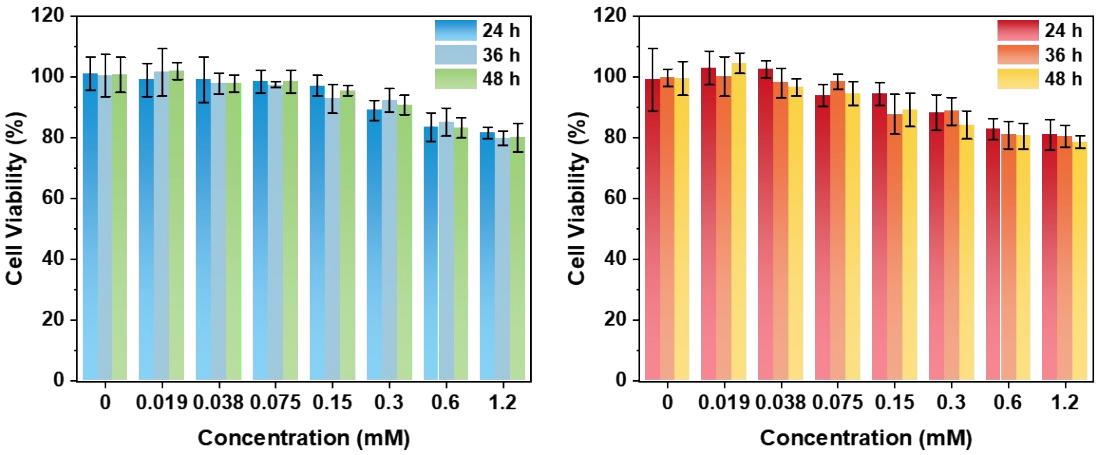


Figure S25. Using the MTT assay to evaluate the effect of **MOC** (left) and **MOC-F** (right) on the survival rate of HK-2 cells.

Table S5. Comparison of key information between this study and relevant conventional ^{19}F. MRI probes

Probe Type	Fluorine Content	^{19}F Relaxation	Key Advantages	Major Limitations
This Work: MOC-F	~ 6.35 wt%; 72 fluorine atoms.	T_1=0.43 s, T_2=0.38 s (at 0.16 mM) T_2/T_1 > 0.8.	1. Precise & tunable structure. 2. Intrinsic dual-mode: efficient ^1H (r_1=25.96) & ^{19}F relaxation. 3. Excellent water solubility. 4. Good biocompatibility.	Ligand synthesis is somewhat cumbersome, and the detection limit is slightly high.
Perfluorocarbons (PFCs) Ref. 1	Using PFCE, each molecule contains 20 ^{19}F atoms.	T_1=0.11 s, T_2=0.05 s (20 mM Fe)	1. SNR improved by 2.6 times. 2. Excellent stability. 3. Low cytotoxicity, suitable for cell labeling.	The structure is prone to damage, and its safety is uncertain.
Small fluorinated molecules (SFMs) Ref. 2	6 fluorine atoms.	T_1 ≈ 2-3 ms T_2/T_1 ≈ 0.8	1. It also serves as an efficient ^1H relaxant (r_1 ≈ 5.36 mM^{-1} s^{-1}). 2. Features a well-defined structure, excellent water solubility, and outstanding biocompatibility.	1. ^{19}F signal splitting leads to reduced peak intensity 2. Slightly lower fluorine content
Fluorinated Ionic Liquid (FILs) Ref. 3	~ 10-18 wt%	T_1=4.9 s, T_2=4.4 s	1. Excellent responsiveness. 2. High load efficiency and good water solubility.	1. Requires the use of nano-encapsulation technology. 2. T_1 is too long.
Fluorinated polymers Ref. 4	25 wt%	T_2 spanning from 0.36 to 0.50 s.	1. Efficient and eco-friendly synthesis: One-step aqueous synthesis. 2. High fluorine loading. 3. Dual potential in imaging and drug delivery.	Some ^{19}F atoms exhibit extremely short T_2 relaxation times, reducing the utilization rate of fluorine atoms.
Inorganic fluoride nanoparticles (IFNPs) Ref. 5	High fluorine density	T_1 ≈ 0.1 s， T_2 ≈ 2 ms	1. Expanded the library of ^{19}F MRI nanoprobes. 2. Sm^{3+} accelerates relaxation, effectively shortening T_1 and enhancing imaging sensitivity.	1. Insoluble in water and exhibits an extremely short T_2 relaxation time. 2. Its imaging requires specialized UTE sequences, limiting its development.

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