Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Photoinduced Regioselective Difluorination of Secondary Inert C(sp^3)-H Bonds in Sulfonamides *via* 1,5-Hydrogen-Atom Transfer

Zhi Chen,[a] Wenkai Zhu,[a] Chaodong Wang,[a] Ning Xu,[a] Qianxi Jin,[a] Xule Huang,[a] Shengjie Song,[a] and Jianjun Li,[*a,b]

[a.] Key Laboratory for Green Pharmaceutical Technologies and Related Equipment of Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China.

[b.] Taizhou Research Institute, Zhejiang University of Technology, Taizhou 318000, P. R. of China.

[*] Corresponding author. E-mail: lijianjun@zjut.edu.cn.

Table of content

1. General Information

The reagents and solvents were purchased from commercial suppliers and used without further purification unless noted. All reactions were monitored by TLC with silica gel-coated plates. ^{1}H (400 MHz) NMR, ^{13}C (101 MHz) NMR, and ^{19}F (376 MHz) NMR spectra were recorded on a Varian spectrometer in $CDCl_3$ or DMSO-d_6 using tetramethylsilane (TMS) as internal standards. Data are reported as follows: Chemical shift (number of protons, multiplicity, coupling constants). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets, brs = broad singlet. Mass spectra were measured with a HRMS-APCI instrument using ESI ionization. UV/vis absorption spectra and fluorescence quenching experiments were conducted on a Hitachi F-7000 FL Spectrophotometer and F97Pro Spectrophotometer. The LED lights was purchased from Xuzhou Ai Jia Electronic Technology Co., Ltd. in Taobao.com.

2. Detailed Description of the Blue LED Light Source and Photoreactor

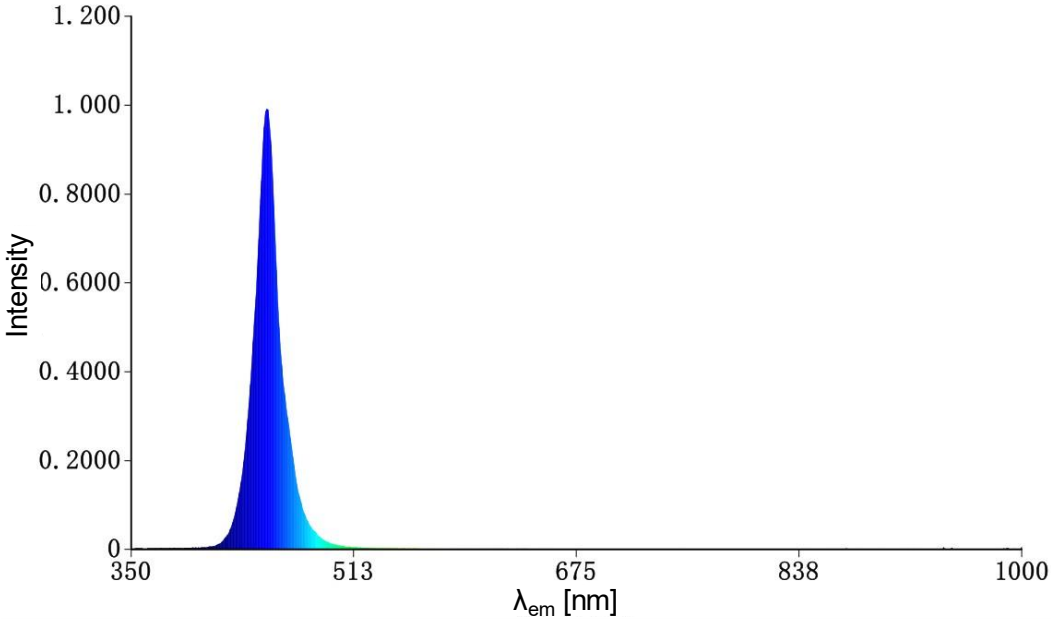


Figure S1. The emission spectrum of the 450-460 nm blue LED light.

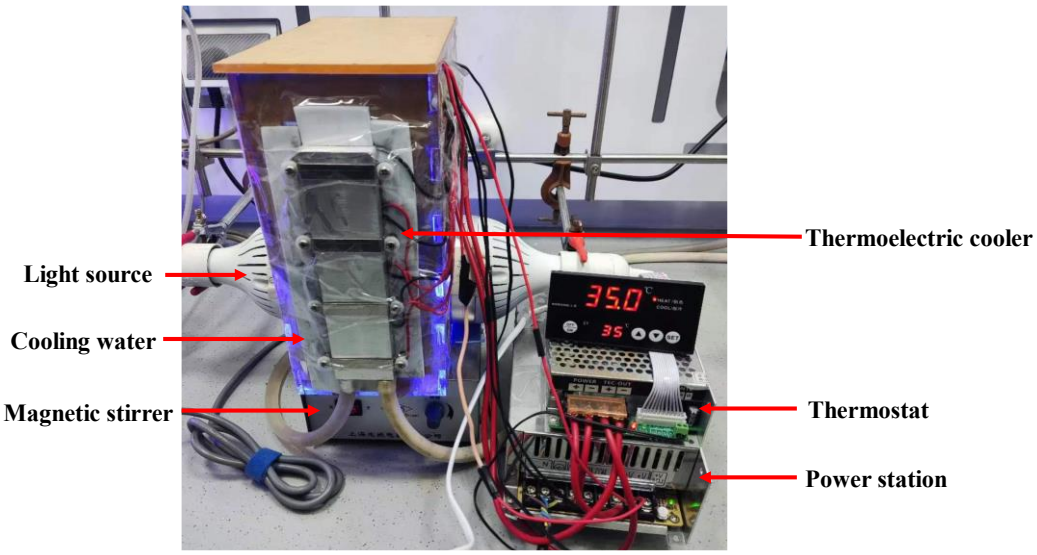


Figure S2. The detailed picture of the photoreactor with temperature control

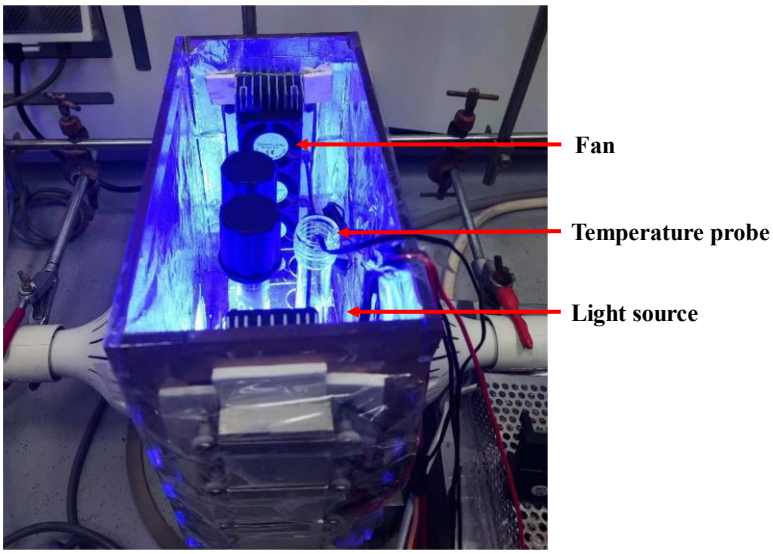
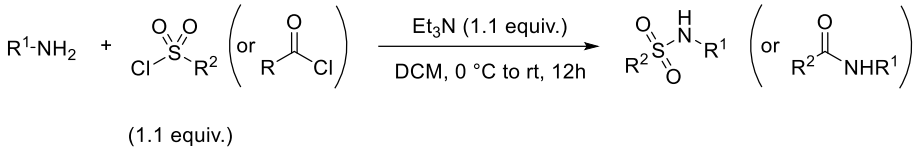


Figure S3. The internal structure of the photoreactor

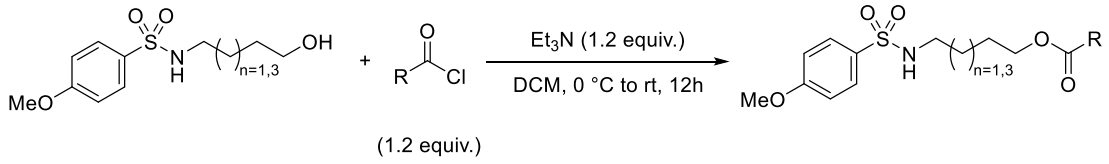
3. General Procedure

3.1 General procedure A: Preparation of N-protected amine substrates from free amines and sulfonyl chloride (or acyl chloride)



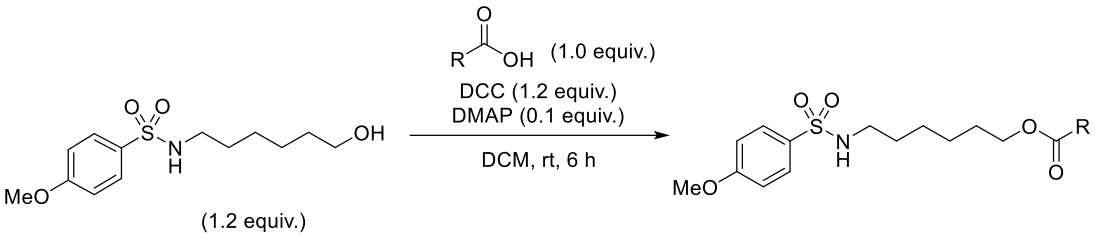
N-protected amine substrates are prepared from carboxylic amines and sulfuryl chloride (or acyl chloride) according to the literature[1] with minor modifications. Free amine (5.0 mmol, 1.0 equiv.) and Et_3N (5.5 mmol, 1.1 equiv.) were dissolved in DCM (25 mL) at 0 ºC. A DCM solution (5 mL) of corresponding sulfuryl chloride (5.5 mmol, 1.1 equiv.) (or acyl chloride) was added slowly over 5 minutes. After the addition was completed, the mixture was allowed to warm to room temperature and the solution was allowed to stir for 24 hours. The reaction mixture was quenched with water (5 mL) and 1.0 M HCl (11 mL). The aqueous phase was extracted with 10 mL×3 DCM. Combined organic phases were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc).

3.2 General procedure B: Preparation of N-protected amine substrates from free alcohols intermediates and sulfonyl chloride



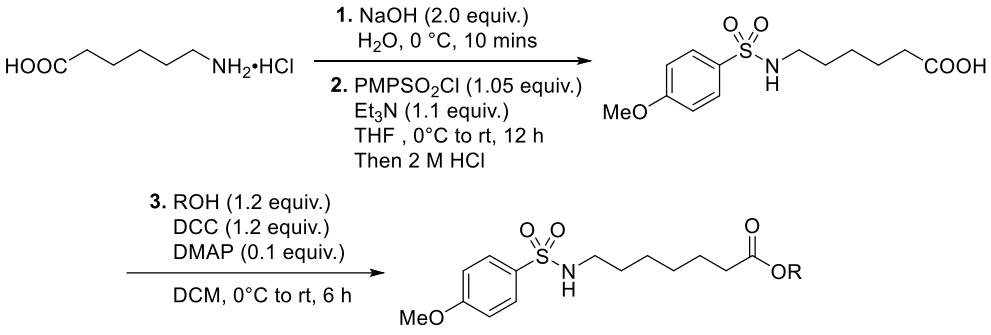
Alcohol (2.0 mmol, 1.0 equiv.) and Et_3N (2.2 mmol, 1.2 equiv.) were dissolved in DCM (25 mL) at 0 ºC. A DCM solution (5 mL) of corresponding acyl chloride (2.2 mmol, 1.2 equiv.) was added slowly over 5 minutes. After the addition was completed, the mixture was allowed to warm to room temperature and the solution was allowed to stir for 12 hours. The reaction mixture was quenched with water (5 mL) and a saturated $NaHCO_3$ solution (5 mL). The aqueous phase was extracted with 10 mL×3 DCM. Combined organic phases were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc).

3.3 General procedure C: Preparation of N-protected amine substrates from free alcohol intermediates and acid



To a solution of acid (1 mmol, 1.0 equiv.), *N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide (1.2 mmol, 1.2 equiv.), and DMAP (0.1 mmol, 0.1 equiv.) in dry DCM (5 mL) were added DCC (1.2 mmol, 1.0 equiv.). The reaction mixture was allowed to stir at room temperature for 6 hours and then concentrated under reduced pressure. Cold 10 mL EtOAc was added to the residue and dicyclohexyl urea was filtered off. The solution was concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (PE/EtOAc).

3.4 General procedure D: Preparation of N-protected amine substrates from 7-aminoheptanoic acid hydrochloride and acid



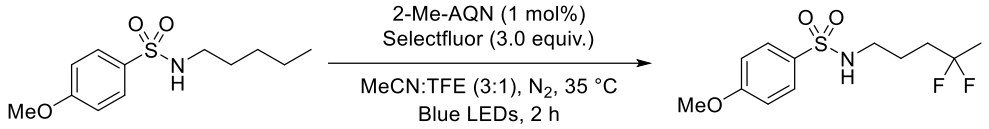
STEP 1: 7-aminoheptanoic acid hydrochloride (5 mmol, 1.0 equiv.) was dissolved in 15 mL water and stirred at 0 °C. To this solution, 10 mL 1M NaOH was added slowly over 5 minutes and the mixture was stirred for 10 minutes.

STEP 2: Et_3N (5.5 mmol, 1.1 equiv.) was added to the reaction mixture was obtained from STEP 1, and a solution of sulfuryl chloride (5.25 mmol, 1.05 equiv.) in THF (5 mL) was added slowly over 5 minutes at 0 °C. After the addition was completed, the mixture was allowed to warm to room temperature and stirred for 12 hours. After the reaction mixture (aqueous solution) was extracted

with ether (20 mL) to remove impurities, the aqueous phase was set aside. The ether phase (upper layer) was washed with 20 mL 2M NaOH aqueous solution to recover some lost product. The aqueous phase from the first extraction was combined with the NaOH solution from the second extraction. The combined solution was adjusted to pH 2 with 1M HCl aqueous solution at 0 ºC. It was extracted with 30 mL×3 EtOAc and the organic phase was dried with saturated salt water and anhydrous Na_2SO_4 sequentially, concentrated under reduced pressure. A crude product was obtained as a white solid without further purification..

STEP 3: To a solution of acid (1.2 mmol, 1.2 equiv.) from STEP 2, alcohol (1.0 mmol, 1.0 equiv.) and DMAP (0.1 mmol, 0.1 equiv.) in dry DCM (5 mL) at 0 ºC, DCC (1.2 mmol, 1.0 equiv.) was then added. The reaction mixture was allowed to stir at room temperature for 6 hours and then concentrated under reduced pressure. Cold 10 mL EtOAc was added to the residue and dicyclohexyl urea was filtered off. The solution was concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (PE/EtOAc) to give the desired product.

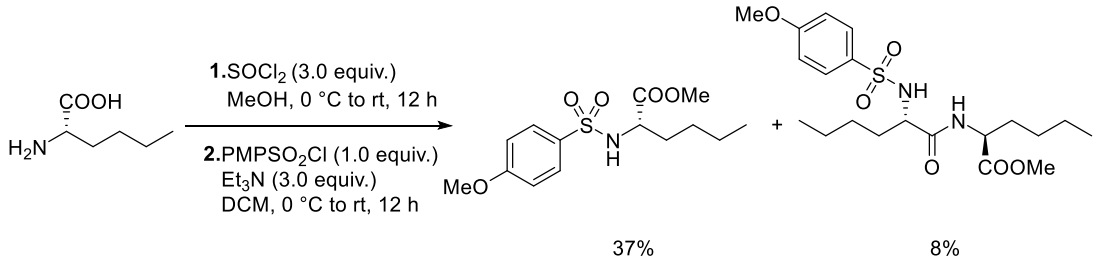
3.5 General procedure E: Remote C(sp^3)-H difluorination reaction



A mixture of N-protected amines **1a** (0.2 mmol, 1.0 equiv.), 2-methylanthraquinone (2 mL, 1.0 μmol/ml in MeCN, 2.0 μmol, 0.01 equiv.) and Selectfluor (0.6 mmol, 3.0 equiv.) were added to a 10 mL Schlenk tube containing CH_3CN/TFE (2.0 mL/1.33 mL). The tube was degassed by ultrasonication for 5 minutes and then evacuated and backfilled with nitrogen for three times. The mixture was stirred under blue LED lights (λ = 450-460 nm, 2×25 W) at 35 ºC for 2 hours and then was concentrated under reduced pressure. The residue was dissolved in EtOAc and then filtered to remove insoluble material. The solution was concentrated under reduced pressure and an internal standard of trifluorotoluene (1 drop, about 15 mg) was added. The yield was determined by comparing the integration of the crude product's ^{19}F NMR with that of the internal standard. Alternatively, the product was purified by column chromatography on silica (PE/EtOAc = 3/1).

3.6 Procedures for preparation of specific substrates

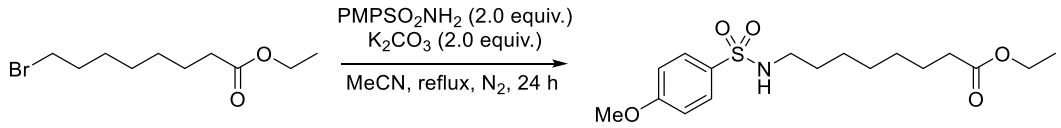
methyl (*S*)-2-((4-methoxyphenyl)sulfonamido)hexanoate and methyl (*S*)-2-((*S*)-2-((4-methoxyphenyl)sulfonamido)hexanamido)hexanoate



STEP 1: L-Norleucine (10 mmol, 1.0 equiv.) was suspended in methanol (100 mL) and cooled at 0 °C. Thionyl chloride (30 mmol, 3.0 equiv.) was added, the mixture was allowed to warm to room temperature and the solution was allowed to stir for 12 hours. The solution was concentrated under reduced pressure to obtain crude amine hydrochloride.

SETP 2: The crude amine hydrochloride and Et_3N (30 mmol, 3.0 equiv.) were dissolved in DCM (50 mL) at 0 °C. A DCM solution (20 mL) of sulfuryl chloride (10 mmol, 1.0 equiv.) was added slowly over 5 minutes. After the addition was completed, the mixture was allowed to warm to room temperature and the solution was allowed to stir for 12 hours. The reaction mixture was quenched with water (10 mL) and 1.0 M HCl (10 mL). The aqueous phase was extracted with 20 mL×3 DCM. Combined organic phases were dried with anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 2.5/1).

ethyl 8-((4-methoxyphenyl)sulfonamido)octanoate

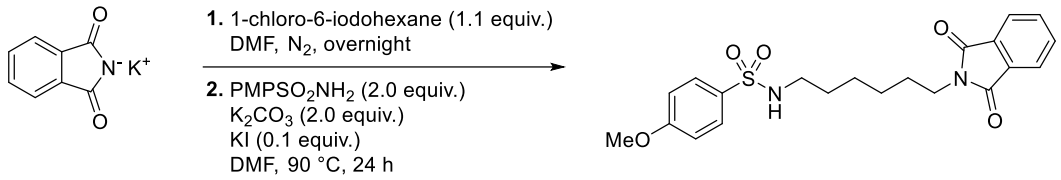


Prepared from ethyl 8-bromooctanoate according to the literature[2] with minor modifications.

Alkyl bromide (2.0 mmol, 1.0 equiv.), *p*-methoxyphenylsulfonamide (4.0 mmol, 2.0 equiv.), and K_2CO_3 (4.0 mmol, 2.0 equiv.) were added into a round-bottom flask with 10 mL MeCN. Then the reaction mixture was heated to reflux for 12 hours. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure, 5 mL EtOAc was added to the residue

and the insoluble material was filtered off. The solution was concentrated under reduced pressure. The product was purified by flash chromatography on silica gel (PE/EtOAc = 5/1) to give the desired product (63% yield).

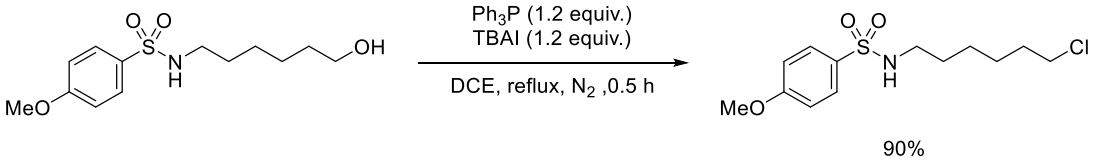
***N*-(6-(1,3-dioxoisoindolin-2-yl)hexyl)-4-methoxybenzenesulfonamide**



STEP 1: In a 25 mL Schlenk flask, potassium phthalimide (5 mmol, 1.0 equiv.) and 1-chloro-6-iodohexane (5.5 mmol, 1.1 equiv.) were dissolved in 10 mL dry DMF under a nitrogen atmosphere. The reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with 100 mL water and extracted with 10 mL×3 EtOAc. Combined organic phases were washed with saturated salt water and dried with anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc=15/1) to give the desired product as a colorless oil (66% yield).

SETP 2: Alkyl chloride (2.0 mmol, 1.0 equiv.), *p*-methoxyphenylsulfonamide (4.0 mmol, 2.0 equiv.), K_2CO_3 (4.0 mmol, 2.0 equiv.), and potassium iodide (4.0 mmol, 2.0 equiv.) were added into a round-bottom flask with 8 mL DMF. Then the reaction mixture was heated to 90 °C for 24 hours. After being cooled to room temperature, the reaction mixture was diluted with 100 mL of water and extracted with 10 mL×3 DCM. Combined organic phases were washed with saturated salt water and dried with anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 3/1) to give the desired product (77% yield).

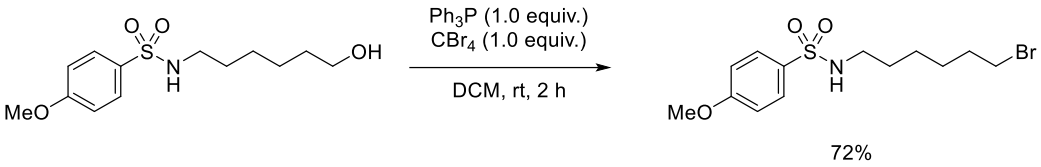
***N*-(6-chlorohexyl)-4-methoxybenzenesulfonamide**



Prepared from *N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide according to the literature[3] with minor modifications.

In a 25 mL Schlenk flask, *N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide (2.0 mmol, 1.0 equiv.), triphenylphosphine (2.4 mmol, 1.2 equiv.), tetrabutylammonium iodide (2.4 mmol, 1.2 equiv.), and dry 1,2-dichloroethane (20 mL) were added under a N_2 atmosphere. The mixture was heated to reflux for 0.5 hours. After the mixture was cooled to room temperature, the solvent was removed by concentration under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 3/1) to give the desired product (90% yield).

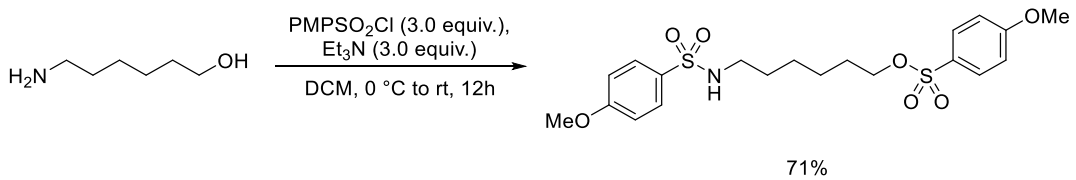
<u>*N*-(6-bromohexyl)-4-methoxybenzenesulfonamide</u>



Prepared from *N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide according to the literature[3].

To a solution of *N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide (2.0 mmol, 1.0 equiv.) in dry dichloromethane (10 mL) was added CBr_4 (2.0 mmol, 1.0 equiv.), and triphenylphosphine (2.0 mmol, 1.0 equiv.) at 0 °C. The mixture was stirred at room temperature for 2 hours and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 3/1) to give the desired product (72% yield).

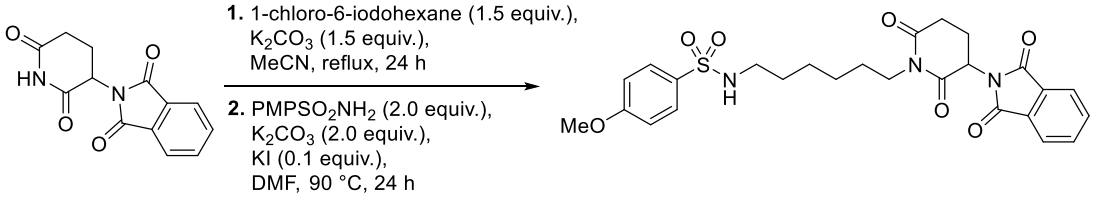
<u>6-((4-methoxyphenyl)sulfonamido)hexyl 4-methoxybenzenesulfonate</u>



6-aminohexan-1-ol (2.0 mmol, 1.0 equiv.) and Et_3N (6 mmol, 3.0 equiv.) were dissolved in DCM (10 mL) at 0 ºC. A DCM solution (10 mL) of sulfuryl chloride (6 mmol, 6 equiv.) was added slowly over 5 minutes. After the addition was completed, the mixture was allowed to warm to room

temperature and stirred for 12 hours. The reaction mixture was quenched with water (3 mL) and 1.0 M HCl (6 mL). The aqueous phase was extracted with DCM. Combined organic phases were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 2/1) to give the desired product (71% yield).

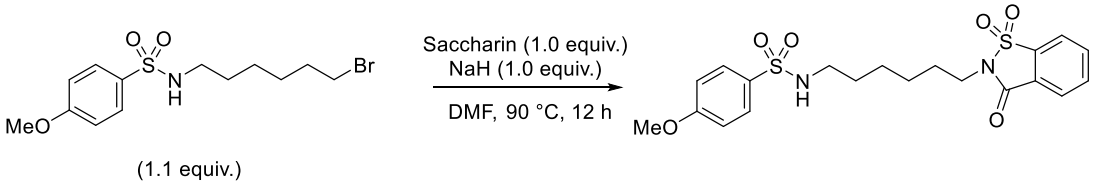
<u>*N*-(6-(3-(1,3-dioxoisoindolin-2-yl)-2,6-dioxopiperidin-1-yl)-4,4-difluorohexyl)-4-methoxybenzenesulfonamide</u>



STEP 1: Into a 25 mL Schlenk flask were added Thalidomide (3 mmol, 1.0 equiv.), 1-chloro-6-iodohexane (4.5 mmol, 1.5 equiv.), K_2CO_3 (4.5 mmol, 2.0 equiv.), and 15 mL MeCN. The reaction mixture was heated to reflux for 24 hours. The reaction mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 5/1) to give the desired product as a colorless oil (88% yield).

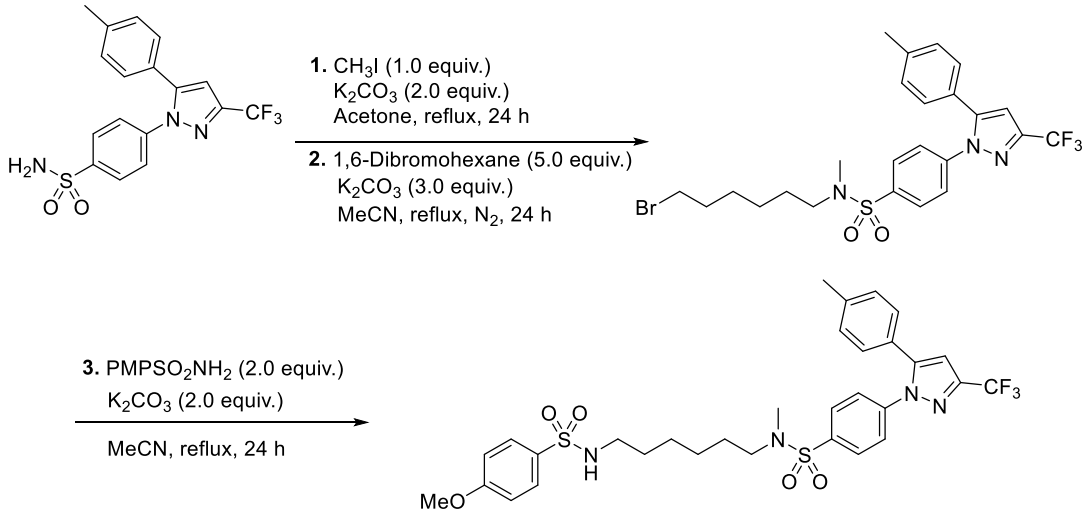
SETP 2: Alkyl chloride (2.0 mmol, 1.0 equiv.), *p*-methoxyphenylsulfonamide (4.0 mmol, 2.0 equiv.), K_2CO_3 (4.0 mmol, 2.0 equiv.), and potassium iodide (4.0 mmol, 2.0 equiv.) were added into a round-bottom flask with 8 mL DMF. Then the reaction mixture was heated to 90 ^oC for 24 hours. After being cooled to room temperature, the reaction mixture was diluted with 100 mL of water and extracted with 10 mL×3 DCM. Combined organic phases were washed with saturated salt water and dried with anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 1.5/1) to give the desired product (43% yield).

<u>*N*-(6-(1,1-dioxido-3-oxobenzo[*d*]isothiazol-2(*3H*)-yl)hexyl)-4-methoxybenzenesulfonamide</u>



To a solution of Saccharin (1.0 equiv., 5 mmol) in dry DMF at 0 °C was added sodium hydride (1.0 equiv., 60% mineral oil dispersion). The mixture was allowed to warm to room temperature and stirred for 30 minutes. Then, *N*-(6-bromohexyl)-4-methoxybenzenesulfonamide (2.2 mmol, 1.1 equiv.) was added. After that, the mixture was heated at 90 °C for 12 hours. Finally, it was cooled to room temperature, poured into a saturated aqueous ammonium chloride solution and extracted with EtOAc three times. Combined organic phases were washed with saturated salt water and dried with anhydrous Na_2SO_4. The organic phase was concentrated and purified by flash chromatography on silica gel (PE/EtOAc = 3/1) to give the desired product (52%).

<u>*N*-(6-((4-methoxyphenyl)sulfonamido)hexyl)-*N*-methyl-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide</u>



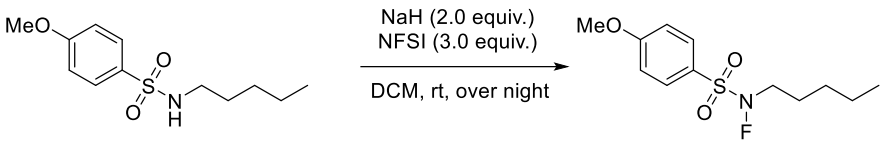
STEP1: Under N_2 atmosphere, to a solution of Celecoxib (5.0 mmol, 1.0 equiv.) and CH_3I (7.5 mmol, 1.5 equiv.) in acetone (25.0 mL) at room temperature was added K_2CO_3 (10 mmol, 2.0 equiv.). Then it was heated to reflux for 24 hours. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 5/1) to afford N-methyl-Celecoxib as a white solid (90% yield).

STEP2: Under N_2 atmosphere, to a solution of N-methyl-Celecoxib (4.5 mmol, 1.0 equiv.) and 1,6-dibromohexane (22.5 mmol, 5.0 equiv.) in anhydrous CH_3CN (20 mL) was added K_2CO_3 (13.5 mmol, 3.0 equiv.) at room temperature. Then the reaction mixture was heated for 24 hours. After

cooling to room temperature, the reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 10/1) to afford the alkyl bromide as a white solid (76 % yield).

STEP3: Alkyl bromide (2.0 mmol, 1.0 equiv.), *p*-methoxyphenylsulfonamide (4.0 mmol, 2.0 equiv.), and K_2CO_3 (4.0 mmol, 2.0 equiv.) were added into a round-bottom flask with 10 mL MeCN. Then the reaction mixture was heated to reflux for 24 hours. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure, 5 mL EtOAc was added to the residue and the insoluble material was filtered off. The solution was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 3/1) to give the desired product (46% yield).

***N*-fluoro-4-methoxy-*N*-pentylbenzenesulfonamide**



Prepared from 4-methoxy-*N*-pentylbenzenesulfonamide according to the literature[3].

In an oven dried round bottom flask with stir bar, sodium hydride (10 mmol, 2.0 equiv.) was taken. The sodium hydride was washed with pentane (2 times) and dried under vacuum and filled with nitrogen. Then dry DCM (40 mL) was added to it. A solution of sulfonamide (1 equiv.) in dry DCM (0.5 M) was added dropwise to the NaH suspension in DCM. The total reaction was stirred at room temperature for 30 min. A solution of NFSI (3.0 equiv.) in dry DCM (0.5 M). was added to dropwise to the reaction mixture at room temperature. The total reaction mixture was stirred for overnight at room temperature. The reaction was quenched with ice with constant stirring. Then 50 mL of water was added to the reaction mixture. The organic part was washed with 30 mL $NaHCO_3$, and 30 mL brine solution respectively. The organic part was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (PE/EtOAc = 10/1) to give the desired product (71% yield).

4. UV/Vis Absorption Spectra

The samples were measured in UV quartz cuvettes (chamber volume = 3.5mL, H × W × D=12.4 × 12.4 × 45 mm) fitted with a PTFE stopper in the presence of air.

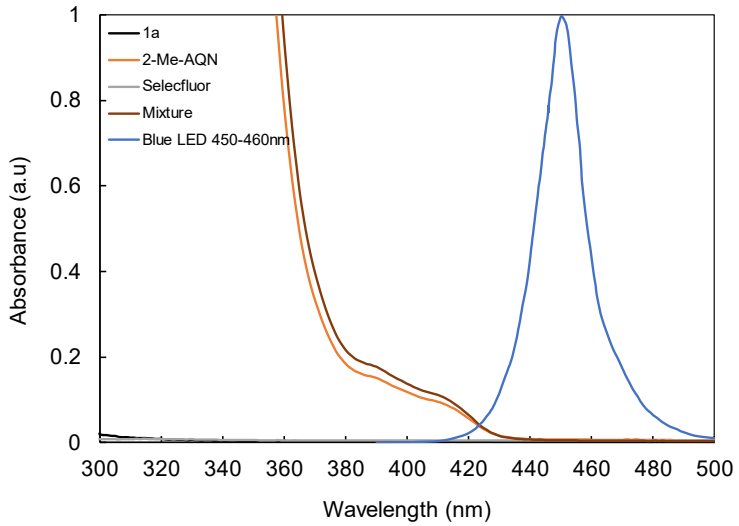


Figure S4. The absorption spectra of 1a (1mM in MeCN), 2-Me-AQN (1mM in MeCN), Selectfluor (10 mM in MeCN), the mixture (**1a**,10mM in MeCN; Selectfluor, 10mM in MeCN; 2-Me-AQN, 1mM in MeCN) and the emission spectra of 450-460 nm blue LED.

5. Stern-Volmer Quenching Experiments

A solution of 2-methylanthraquinone in MeCN was excited at 250 nm and the intensity of emission spectrum was measured at 310 nm. For each quenching experiment, the emission intensity of photosensitizer (10 uM) with different concentration of quencher (Selectfluor: 0, 1, 2, 3, 4 mM) was collected. (I_0: without quencher, I: with quencher)

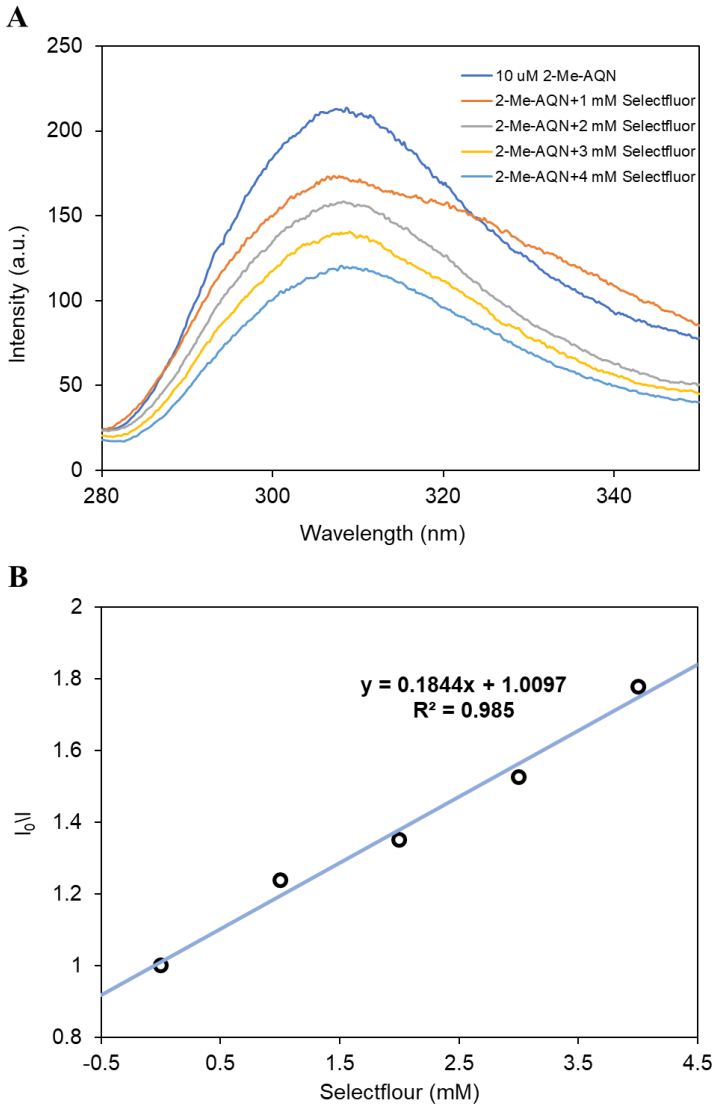


Figure S5. A) Emission intensity of 2-methylanthraquinone, with varied amount of Selectfluor. B) Stern-Volmer plot of 2-methylanthraquinone and Selectfluor.

Based on the above fluorescence quenching experiments, a notable decrease of fluorescence intensity of 2-methylanthraquinone was recorded with increasing the concentration of oxidants (Selectfluor), suggesting that the oxidants should participate in energy transfer with the excited state photocatalyst 2-methylanthraquinone* under the standard reaction conditions.

6. Quantum Yield Measurements

According to the procedure of Yoon[4], the photon flux of the LED (λ_{max} = 458 nm) was determined by standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (0.737 g) in H_2SO_4 (10 mL of 0.05 M solution). A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (5.0 mg) and sodium acetate (1.13 g) in H_2SO_4 (5.0 mL of 0.5 M solution). Both solutions were stored in the dark. To determine the photon flux of the LED, the ferrioxalate solution (3.0 mL) was placed in a cuvette and irradiated for 90 seconds at λ_{max} = 458 nm. After irradiation, the phenanthroline solution (0.525 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 hour to allow the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was measured at 510 nm. A nonirradiated sample was also prepared and the absorbance at 510 nm was measured. Conversion was calculated using eq 1.

	No-irrad	Irrad
A_{510nm}	2.479	3.806

$$\textbf{mol } Fe^{2+} = (V \times \Delta A) / (l \times \varepsilon) \quad (1)$$

$$\textbf{mol } Fe^{2+} = [3.525\times10^{-3}\ L \times (3.806-2.479)] / (1\ cm \times 11100\ L\ mol^{-1}cm^{-1}) = 4.214 \times 10^{-7}$$

V is the total volume (3.525×10^{-3} L) of the solution after addition of phenanthroline; **ΔA** is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions; **l** is the path length (1.00 cm), and **ε** is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11100 L $mol^{-1}cm^{-1}$)[5]. The photon flux can be calculated using eq 2.

$$\textbf{photo flux} = \textbf{mol } Fe^{2+} / (\Phi \times t \times f) \quad (2)$$

$$\textbf{photo flux} = 4.214 \times 10^{-7} / (0.845 \times 90 \times 0.9999) = 5.542 \times 10^{-9}\ \textbf{einstein}\ s^{-1}$$

Where **Φ** is the quantum yield for the ferrioxalate actinometer (0.845 for a 0.15 M solution at λ = 458 nm), **t** is the time (90 s), and **f** (0.9999) is the fraction of light absorbed at 458 nm by the ferrioxalate actinometer. This value is calculated using eq 3 where A_{458nm} (3.9024) is the absorbance of the ferrioxalate solution at 458 nm. The photon flux was calculated to be 5.542×10^{-9} einstein s^{-1}.

$$f = 1 - 10^{-A458\ nm} \quad (3)$$

$$f = 1 - 10^{-3.9024} = 0.9999$$

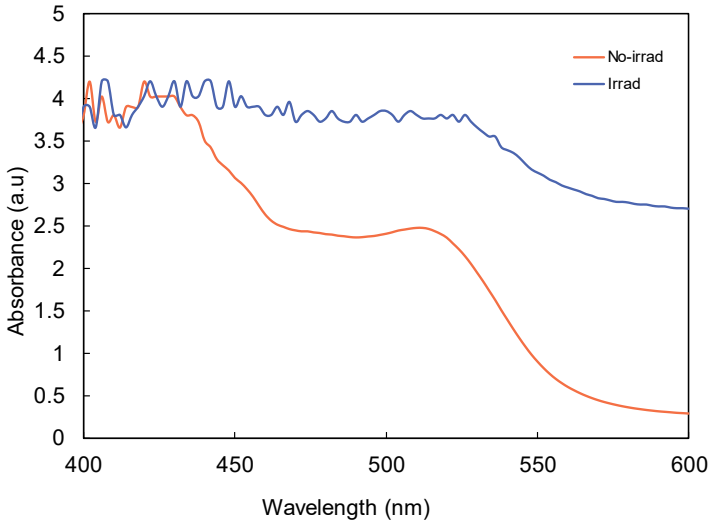
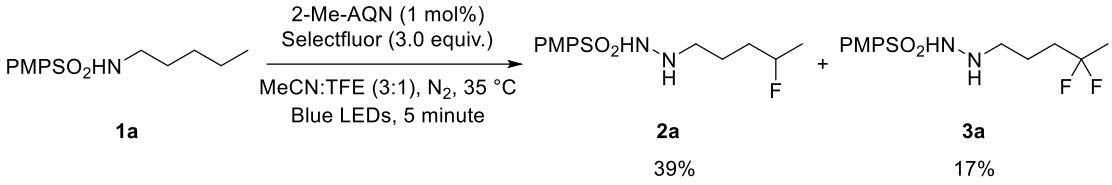


Figure S6. Absorption spectra of irradiation experiment and non-irradiation experiment

Determination of the reaction quantum yield



1a **2a** 39% **3a** 17%

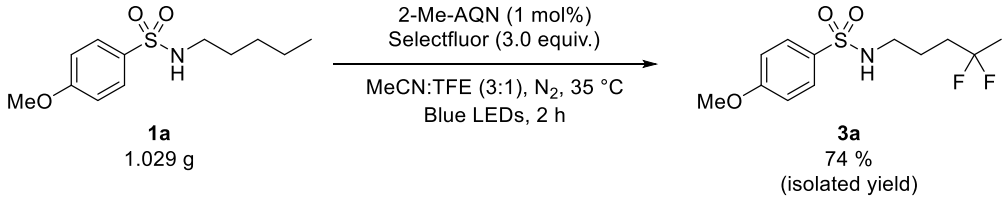
The reaction mixture was stirred and irradiated by blue LED (λ^{max} = 458 nm) for 300 s. The yield of product was determined by ^{19}F NMR analysis using trifluorotoluene as an internal standard. The yield of **2a** and **3a** was determined to be 56% (1.12×10^{-4} mol of **2a** and **3a**). The reaction quantum yield (Φ) was determined using eq 4 where the photon flux is 5.542×10^{-9} einsteins s^{-1} (determined by actinometry as described above), **t** is the reaction time (300 s) and **f** is the fraction of incident light absorbed by the catalyst, determined using eq 3.

$$\textbf{Quantum Yield } (\Phi) = \textbf{moles of product formed / (flux} \times \textbf{f} \times \textbf{t}) \qquad (4)$$

$$= 1.12 \times 10^{-4} / (5.542 \times 10^{-9} \times 0.9999 \times 300)$$

$$=67.4$$

7. Gram-scale Experiment



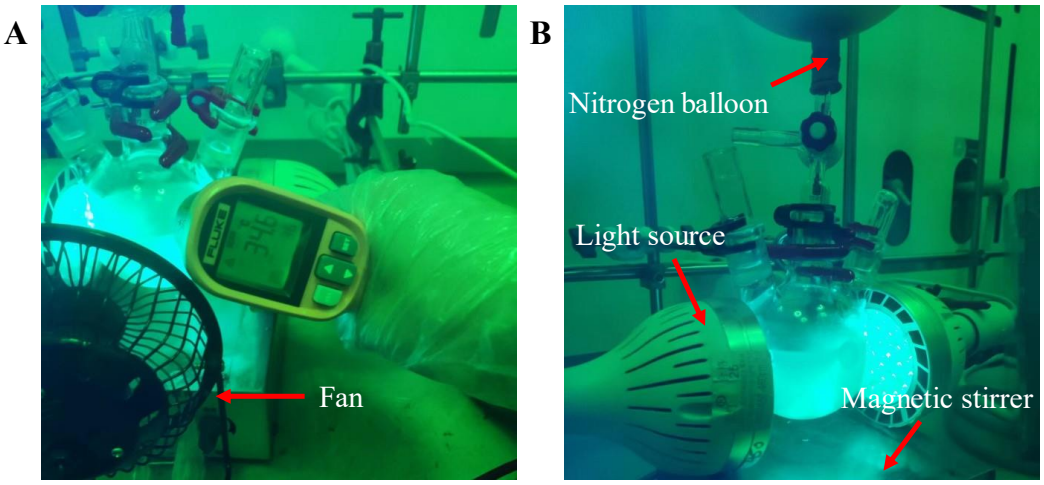
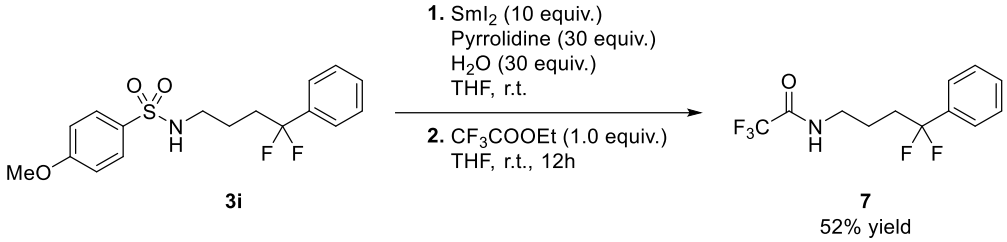


Figure S7. A) Fan cooled to 35°C. B) Schematic diagram of the reaction.

(Capture photographs with filters.)

Into a 250 mL three-neck round bottom flask equipped with a nitrogen balloon were added sulfonamide **1a** (1.029 g, 4.0 mmol, 1.0 equiv.), 2-methylanthraquinone (9 mg, 0.04 mmol, 0.01 equiv.), Selectfluor (4.251 g, 12.0 mmol, 3.0 equiv.), 80 mL MeCN, and 27 mL TFE. The flask mixture was degassed by ultrasonication for 5 minutes and then evacuated and backfilled with nitrogen three times. The mixture was stirred under blue LED light (λ = 450-460 nm, 2×25 W) for 2 hours and then concentrated under reduced pressure. The product was purified by column chromatography (PE/EtOAc = 3/1) on silica to give the product **3a**. Obtained as a white solid (74% yield) as a 1.4:98.6 mixture of mono-/difluorinated product.

8. Deprotection and Late-stage Functionalization Experiment

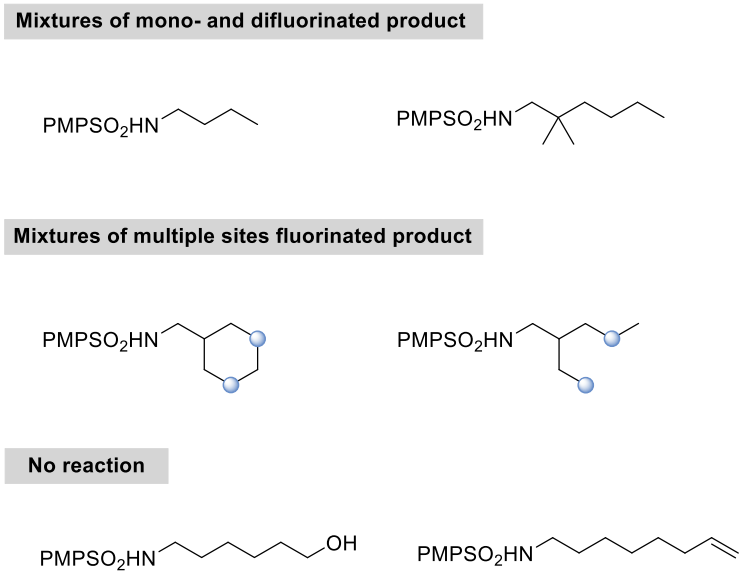


Deprotection experiment according to the literature[6] with minor modifications.

STEP 1: To a solution of samarium(II) iodide (2.0 mmol, 10 equiv.) in THF (20 mL, 0.1 M), sulfonamide (0.2 mmol in 1 mL THF, 1.0 equiv.) was added, followed by water (6.0 mmol, 30 equiv.) and pyrrolidine (4.0 mmol, 20 equiv.) under a nitrogen atmosphere. The reaction mixture turned white immediately upon the addition of amine. The resulting mixture was diluted with Et_2O (20 mL) and washed with 15 mL K_2CO_3/tartrate (10% w/v each). The aqueous phase was extracted with 10 mL×3 EtOAc. Combined organic phases were washed with saturated salt water and dried with anhydrous Na_2SO_4, concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (DCM/MeOH = 40/1 + 2% Et_3N) and visualized by 254 nm UV light and Ninhydrin stain to give the crude amine.

STEP 2: The crude amine from step 1 (1.0 equiv.) was dissolved in THF (0.2 M) at 0 ^oC, and ethyl trifluoroacetate (1.0 equiv.) was added slowly. After the addition was completed, the mixture was allowed to warm to room temperature and stirred for 12 hours. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (PE/EtOAc = 9/1) to give a white solid product (55% yield, two steps).

9. Unsuccessful Substrate



Scheme 1. Unsuccessful substrate.

10. Mechanistic Investigation

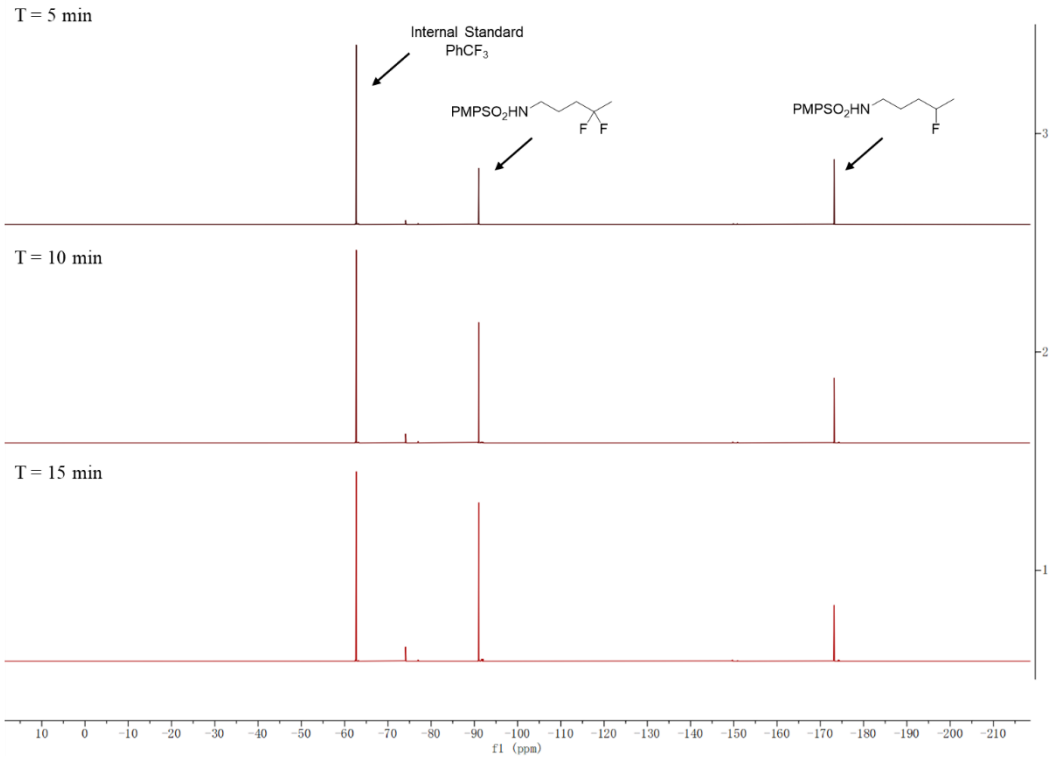
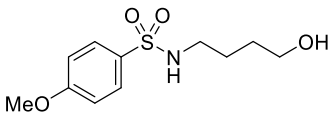


Figure S8. ^{19}F NMR chart of the reaction solution with reaction time of 5, 10, and 15 min.

We followed the reaction by ^{19}F NMR that showed that the reaction process did not involve the formation of N-F species **6** (-49.78 ppm) under standard condition.

11. Characterization Data

11.1 Intermediates



M-1

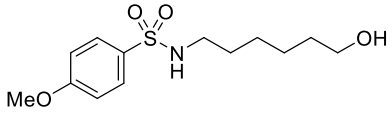
***N*-(4-hydroxybutyl)-4-methoxybenzenesulfonamide**

Prepared by **General Procedure A** on a 5 mmol scale, use 5 mmol sulfuryl chloride instead. Obtain a white solid (85% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 6.4 Hz, 2H), 7.39 (t, J = 5.9 Hz, 1H), 7.10 (d, J = 8.4 Hz, 2H), 4.37 (td, J = 5.1, 2.7 Hz, 1H), 3.82 (s, 3H), 3.38 – 3.30 (m, 2H), 2.77 – 2.61 (m, 2H), 1.48 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.48, 132.71, 129.07, 114.76, 60.66, 56.07, 42.98, 30.04, 26.20.

Data are consistent with reported in the literature[7].



M-2

***N*-(6-hydroxyhexyl)-4-methoxybenzenesulfonamide**

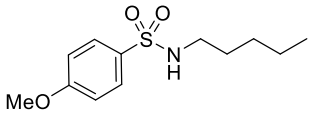
Prepared by **General Procedure A** on a 10 mmol scale, use 5 mmol sulfuryl chloride instead. Obtain a white solid (92% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.6 Hz, 2H), 7.38 (t, J = 5.9 Hz, 1H), 7.10 (d, J = 8.4 Hz, 2H), 4.35 – 4.27 (m, 1H), 3.83 (s, 3H), 3.35 – 3.30 (m, 2H), 2.67 (q, J = 6.7 Hz, 2H), 1.39 – 1.26 (m, 4H), 1.23 – 1.14 (m, 4H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.49, 132.77, 129.08, 114.76, 61.07, 56.08, 42.96, 32.85, 29.45, 26.45, 25.52.

Data are consistent with reported in the literature[3].

11.2 Sulfonamides



1a

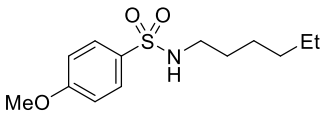
4-methoxy-*N*-pentylbenzenesulfonamide

Prepared by **General procedure A** on a 10 mmol scale. Obtain a colorless oil (95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.54 (brs, 1H), 3.86 (s, 3H), 2.90 (t, *J* = 7.1 Hz, 2H), 1.44 (p, *J* = 6.8 Hz, 2H), 1.30 – 1.16 (m, 4H), 0.83 (t, *J* = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.82, 131.61, 129.21, 114.21, 55.61, 43.18, 29.21, 28.67, 22.14, 13.87.

Data are consistent with reported in the literature[8].



1b

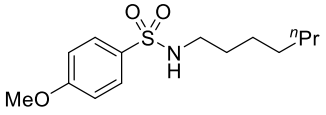
***N*-hexyl-4-methoxybenzenesulfonamide**

Prepared by **General Procedure A** on a 10 mmol scale. Obtain a white solid (96% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.43 (brs, 1H), 3.86 (s, 3H), 2.90 (t, *J* = 7.1 Hz, 2H), 1.49 – 1.38 (m, 2H), 1.31 – 1.13 (m, 6H), 0.83 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.81, 131.66, 129.20, 114.20, 55.59, 43.19, 31.23, 29.49, 26.19, 22.44, 13.91.

HRMS: Calcd for $C_{13}H_{22}NO_3S^+[M+H]^+$: 272.1315, found: 272.1323



1c

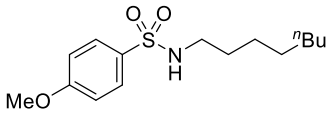
***N*-heptyl-4-methoxybenzenesulfonamide**

Prepared by **General Procedure A** on a 10 mmol scale. Obtain a white solid (93% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 4.65 – 4.44 (brs, 1H), 3.86 (s, 3H), 2.91 (q, *J* = 7.0, 6.5 Hz, 2H), 1.50 – 1.36 (m, 2H), 1.32 – 1.12 (m, 8H), 0.85 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.82, 131.58, 129.23, 114.21, 55.61, 43.19, 31.63, 29.51, 28.74, 26.49, 22.52, 14.04.

Data are consistent with reported in the literature[9].



1d

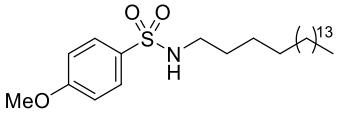
4-methoxy-*N*-octylbenzenesulfonamide(1c)

Prepared by **General Procedure A** on a 10 mmol scale. Obtain a white solid (95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 7.5 Hz, 2H), 4.67 (brs, 1H), 3.86 (s, 3H), 2.90 (t, *J* = 7.2 Hz, 2H), 1.49 – 1.35 (m, 2H), 1.30 – 1.13 (m, 10H), 0.85 (t, *J* = 6.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.81, 131.67, 129.20, 114.20, 55.58, 43.18, 31.70, 29.51, 29.07, 29.01, 26.52, 22.58, 14.03.

Data are consistent with reported in the literature[2].



1e

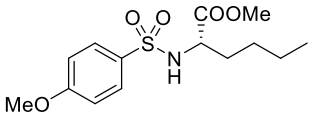
4-methoxy-*N*-octadecylbenzenesulfonamide

Prepared by **General Procedure A** on a 5 mmol scale. After preliminary purification by column chromatography, the product was recrystallized in PE/EtOAc to obtain pure product as a white solid (79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.48 (brs, 1H), 3.86 (s, 3H), 2.91 (t, *J* = 7.1 Hz, 2H), 1.43 (p, *J* = 7.1 Hz, 2H), 1.30 – 1.14 (m, 30H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.81, 131.69, 129.20, 114.20, 55.58, 43.19, 31.92, 29.69, 29.65, 29.61, 29.54, 29.53, 29.44, 29.35, 29.08, 26.54, 22.68, 14.09.

HRMS: Calcd for $C_{25}H_{46}NO_3S^+[M+H]^+$: 440.3193, found: 440.3174



1f

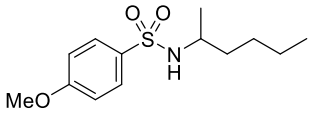
methyl (*S*)-2-((4-methoxyphenyl)sulfonamido)hexanoate

Prepared on page S9. Obtain a white solid (37% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 5.10 (d, *J* = 9.0 Hz, 1H), 3.92 – 3.86 (m, 1H), 3.85 (s, 3H), 3.50 (s, 3H), 1.77 – 1.51 (m, 2H), 1.36 – 1.18 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.41, 163.00, 131.36, 129.42, 114.12, 55.65, 55.62, 52.38, 33.07, 26.99, 22.03, 13.74.

HRMS: Calcd for $C_{14}H_{22}NO_5S^+[M+H]^+$: 316.1213, found: 316.1208



1g

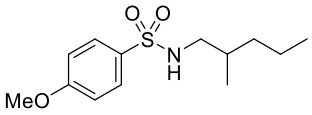
***N*-(hexan-2-yl)-4-methoxybenzenesulfonamide**

Prepared by **General Procedure A** on a 5 mmol scale. Obtain a white solid (37% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 4.42 (brs, 1H), 3.86 (s, 3H), 3.26 (h, *J* = 6.5 Hz, 1H), 1.39 – 1.29 (m, 2H), 1.25 – 1.10 (m, 4H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.80 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.73, 133.05, 129.12, 114.12, 55.57, 49.93, 37.17, 27.64, 22.31, 21.71, 13.84.

Data are consistent with reported in the literature[2].



1h

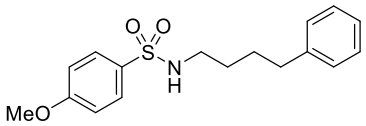
4-methoxy-*N*-(2-methylpentyl)benzenesulfonamide

Prepared by **General Procedure A** on a 1 mmol scale. Obtain a light yellow oil (96% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.61 (brs, 1H), 3.86 (s, 3H), 2.90 – 2.61 (m, 2H), 1.64 – 1.47 (m, 1H), 1.31 – 0.99 (m, 4H), 0.83 (t, *J* = 7.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.79, 131.73, 129.18, 114.19, 55.59, 49.05, 36.22, 32.87, 19.79, 17.42, 14.12.

HRMS: Calcd for $C_{13}H_{22}NO_3S^+[M+H]^+$: 272.1315, found: 272.1304



1i

4-methoxy-*N*-(4-phenylbutyl)benzenesulfonamide

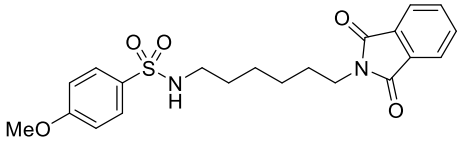
Prepared by **General Procedure A** on a 5 mmol scale. Obtain a white solid (86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 7.30 – 7.06 (m, 5H), 6.95 (d, *J* = 8.9 Hz, 2H), 4.60 (t, *J* = 6.3 Hz, 1H), 3.85 (s, 3H), 2.93 (q, *J* = 6.5 Hz, 2H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.64 – 1.53 (m, 2H), 1.53 – 1.41 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.84, 141.78, 131.63, 129.19, 128.33, 125.84, 114.24, 55.60,

43.02, 35.24, 29.09, 28.21.

Data are consistent with reported in the literature[10].



1j

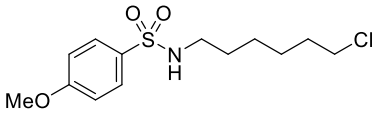
***N*-(6-(1,3-dioxoisoindolin-2-yl)hexyl)-4-methoxybenzenesulfonamide**

Prepared on page S10. Obtain a white solid (77% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.57 (brs, 1H), 3.85 (s, 3H), 3.63 (t, *J* = 7.2 Hz, 2H), 2.90 (t, *J* = 6.9 Hz, 2H), 1.61 (p, *J* = 7.3 Hz, 2H), 1.44 (p, *J* = 7.0 Hz, 2H), 1.33 – 1.22 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.45, 162.82, 133.91, 132.12, 131.72, 129.20, 123.19, 114.23, 55.59, 42.96, 37.67, 29.36, 28.33, 26.14, 25.92.

HRMS: Calcd for $C_{21}H_{25}N_2O_5S^+[M+H]^+$: 417.1479, found: 417.1474



1k

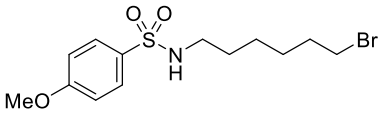
***N*-(6-chlorohexyl)-4-methoxybenzenesulfonamide**

Prepared on page S10. Obtain a light yellow solid (90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 4.55 (brs, 1H), 3.87 (s, 3H), 3.48 (t, *J* = 6.6 Hz, 2H), 2.92 (t, *J* = 6.7 Hz, 2H), 1.70 (p, *J* = 6.7 Hz, 2H), 1.47 (p, *J* = 7.2 Hz, 2H), 1.42 – 1.23 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.88, 131.63, 129.20, 114.26, 55.61, 44.83, 42.99, 32.32, 29.38, 26.29, 25.77.

Data are consistent with reported in the literature[3].



1l

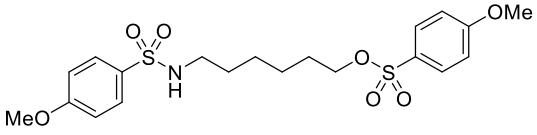
***N*-(6-bromohexyl)-4-methoxybenzenesulfonamide**

Prepared on page S11. Obtain a light yellow solid (72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.0 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 4.54 (s, 1H), 3.87 (s, 3H), 3.36 (t, *J* = 6.8 Hz, 2H), 2.92 (q, *J* = 7.5 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.47 (p, *J* = 7.2 Hz, 2H), 1.41 – 1.23 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.88, 131.63, 129.20, 114.26, 55.62, 42.98, 33.59, 32.48, 29.35, 27.56, 25.64.

Data are consistent with reported in the literature[3].



1m

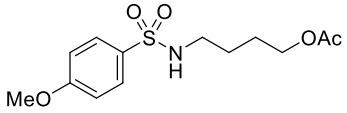
6-((4-methoxyphenyl)sulfonamido)hexyl 4-methoxybenzenesulfonate

Prepared on page S11. Obtain a white solid (71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 9.0 Hz, 2H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.54 (brs, 1H), 3.96 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 2.87 (t, *J* = 7.0 Hz, 2H), 1.58 (p, *J* = 6.5 Hz, 2H), 1.41 (p, *J* = 7.1 Hz, 2H), 1.31 – 1.16 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.75, 162.89, 131.63, 130.03, 129.18, 127.62, 114.45, 114.27, 70.12, 55.71, 55.62, 42.92, 29.33, 28.60, 25.78, 24.85.

HRMS: Calcd for $C_{20}H_{28}NO_7S_2^+[M+H]^+$: 458.1302, found: 458.1311



1n

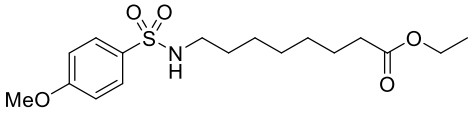
4-((4-methoxyphenyl)sulfonamido)butyl acetate

Prepared by **General Procedure B** on a 1 mmol scale. Obtain a colorless oil (92% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.74 (brs, 1H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.86 (s, 3H), 2.94 (t, *J* = 6.8 Hz, 2H), 2.01 (s, 3H), 1.69 – 1.45 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.03, 162.89, 131.55, 129.18, 114.27, 63.72, 55.61, 42.73, 26.23, 25.70, 20.88.

HRMS: Calcd for $C_{13}H_{20}NO_5S^+[M+H]^+$: 302.1057, found: 302.1064



1o

ethyl 8-((4-methoxyphenyl)sulfonamido)octanoate

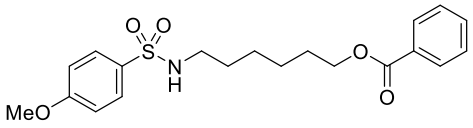
Prepared on page S9. Obtain a colorless oil (63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 4.58 (brs, 1H), 4.13 (q, *J* = 6.6 Hz, 2H), 3.89 (s, 3H), 2.92 (t, *J* = 6.1 Hz, 2H), 2.27 (t, *J* = 7.1 Hz, 2H), 1.66 – 1.52

(m, 2H), 1.52 – 1.37 (m, 2H), 1.35 – 1.16 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.82, 162.82, 131.55, 129.21, 114.22, 60.23, 55.62, 43.12, 34.25, 29.44, 28.88, 28.68, 26.31, 24.77, 14.26.

HRMS: Calcd for $C_{17}H_{28}NO_5S^+[M+H]^+$: 358.1683, found: 358.1690



1p

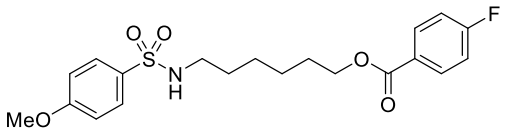
6-((4-methoxyphenyl)sulfonamido)hexyl benzoate

Prepared by **General Procedure B** on a 1 mmol scale. Obtain a colorless oil (86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.0 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.58 – 7.51 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.67 (brs, 1H), 4.27 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 3H), 2.92 (t, *J* = 7.0 Hz, 2H), 1.77 – 1.64 (m, 2H), 1.48 (p, *J* = 7.1 Hz, 2H), 1.41 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.65, 162.84, 132.86, 131.65, 130.41, 129.52, 129.19, 128.34, 114.23, 64.77, 55.59, 43.04, 29.45, 28.55, 26.17, 25.52.

HRMS: Calcd for $C_{20}H_{26}NO_5S^+[M+H]^+$: 392.1526, found: 392.1549



1q

6-((4-methoxyphenyl)sulfonamido)hexyl 4-fluorobenzoate

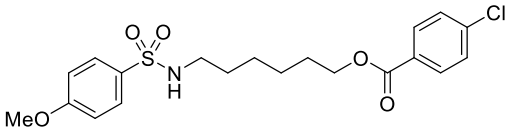
Prepared by **General Procedure B** on a 2 mmol scale. Obtain a colorless oil (97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.9, 5.5 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.10 (t, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.59 (brs, 1H), 4.26 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 3H), 2.93 (t, *J* = 7.0 Hz, 2H), 1.70 (p, *J* = 6.6 Hz, 2H), 1.49 (p, *J* = 7.1 Hz, 2H), 1.42 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.74 (d, *J* = 253.8 Hz), 165.68, 162.87, 132.06 (d, *J* = 9.3 Hz), 131.66, 129.19, 126.66 (d, *J* = 3.0 Hz), 115.48 (d, *J* = 22.0 Hz), 114.24, 64.90, 55.59, 43.02, 29.47, 28.54, 26.15, 25.50.

^{19}F NMR (376 MHz, $CDCl_3$) δ -105.89.

HRMS: Calcd for $C_{20}H_{25}FNO_5S^+[M+H]^+$: 410.1432, found: 410.1414



1r

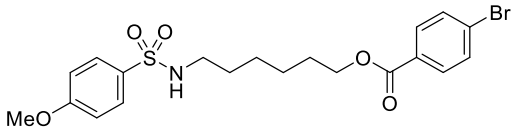
6-((4-methoxyphenyl)sulfonamido)hexyl 4-chlorobenzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a white solid (87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.43 (brs, 1H), 4.27 (t, *J* = 6.6 Hz, 2H), 3.86 (s, 3H), 2.94 (q, *J* = 6.5 Hz, 2H), 1.71 (p, *J* = 6.6 Hz, 2H), 1.49 (p, *J* = 7.0 Hz, 2H), 1.42 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.76, 162.87, 139.32, 131.70, 130.93, 129.19, 128.88, 128.70, 114.24, 65.01, 55.59, 43.01, 29.47, 28.52, 26.14, 25.49.

HRMS: Calcd for $C_{20}H_{25}ClNO_5S^+[M+H]^+$: 426.1136, found: 426.1131



1s

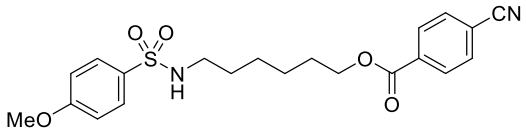
6-((4-methoxyphenyl)sulfonamido)hexyl 4-bromobenzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a white solid (87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.62 (brs, 1H), 4.26 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 3H), 2.92 (t, *J* = 6.8 Hz, 2H), 1.70 (p, *J* = 6.4 Hz, 2H), 1.49 (p, *J* = 6.9 Hz, 2H), 1.43 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.91, 162.86, 131.70, 131.66, 131.08, 129.32, 129.19, 127.96, 114.24, 65.06, 55.60, 43.00, 29.43, 28.50, 26.14, 25.48.

HRMS: Calcd for $C_{20}H_{25}BrNO_5S^+[M+H]^+$: 470.0631, found: 470.0644



1t

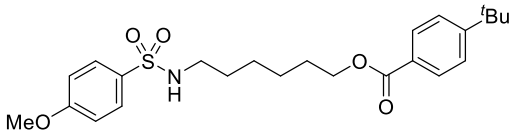
6-((4-methoxyphenyl)sulfonamido)hexyl 4-cyanobenzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a white solid (87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.58 (s, 1H), 4.31 (t, *J* = 6.6 Hz, 2H), 3.86 (s, 3H), 2.93 (t, *J* = 6.9 Hz, 2H), 1.72 (p, *J* = 6.7 Hz, 2H), 1.49 (p, *J* = 7.0 Hz, 2H), 1.42 – 1.30 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.98, 162.88, 134.22, 132.22, 131.64, 130.07, 129.18, 117.98, 116.35, 114.25, 65.60, 55.61, 42.98, 29.46, 28.45, 26.12, 25.46.

HRMS: Calcd for $C_{21}H_{25}N_2O_5S^+[M+H]^+$: 417.1479, found: 417.1459



1u

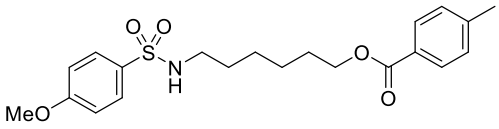
6-((4-methoxyphenyl)sulfonamido)hexyl 4-(tert-butyl)benzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a colorless oil (86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.56 (brs, 1H), 4.26 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 3H), 2.93 (t, *J* = 7.0 Hz, 2H), 1.70 (p, *J* = 6.6 Hz, 2H), 1.48 (p, *J* = 7.1 Hz, 2H), 1.41 – 1.28 (m, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.69, 162.86, 156.54, 131.71, 129.40, 129.20, 127.65, 125.32, 114.24, 64.51, 55.58, 43.04, 35.06, 31.12, 29.49, 28.60, 26.16, 25.52.

HRMS: Calcd for $C_{24}H_{34}NO_5S^+[M+H]^+$: 448.2152, found: 448.2150



1v

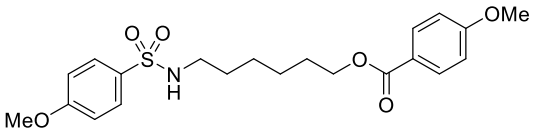
6-((4-methoxyphenyl)sulfonamido)hexyl 4-methylbenzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a white solid (82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 5.8 Hz, 2H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 6.6 Hz, 2H), 6.97 (d, *J* = 7.7 Hz, 2H), 4.63 (brs, 1H), 4.30 – 4.17 (m, 2H), 3.86 (s, 3H), 2.99 – 2.85 (m, 2H), 2.41 (s, 3H), 1.77 – 1.60 (m, 2H), 1.55 – 1.43 (m, 2H), 1.41 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.74, 162.85, 143.51, 131.69, 129.56, 129.20, 129.06, 127.70, 114.24, 64.57, 55.58, 43.04, 29.46, 28.57, 26.17, 25.52, 21.61.

HRMS: Calcd for $C_{21}H_{28}NO_5S^+[M+H]^+$: 406.1683, found: 406.1691



1w

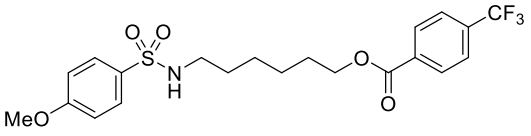
6-((4-methoxyphenyl)sulfonamido)hexyl 4-methoxybenzoate

Prepared by **General Procedure B** on a 2 mmol scale. Obtain a colorless oil (78% yield).

^{1}H NMR (400 MHz, $CDCl_3$)δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.1 Hz, 2H), 4.58 (s, 1H), 4.23 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 6H), 2.92 (t, *J* = 7.2 Hz, 2H), 1.73 – 1.64 (m, 2H), 1.52 – 1.43 (m, 2H), 1.42 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.42, 163.35, 162.85, 131.70, 131.53, 129.19, 122.86, 114.23, 113.62, 64.45, 55.58, 55.42, 43.04, 29.46, 28.60, 26.17, 25.53.

HRMS: Calcd for $C_{21}H_{28}NO_6S^+[M+H]^+$: 422.1632, found: 422.1645



1x

6-((4-methoxyphenyl)sulfonamido)hexyl 4-(trifluoromethyl)benzoate

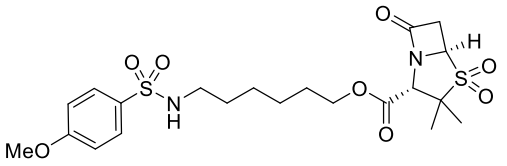
Prepared by **General Procedure B** on a 2 mmol scale. Obtain a white solid (91% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.54 (brs, 1H), 4.31 (t, *J* = 6.6 Hz, 2H), 3.85 (d, *J* = 1.7 Hz, 3H), 2.93 (t, *J* = 6.8 Hz, 2H), 1.73 (p, *J* = 6.7 Hz, 2H), 1.50 (p, *J* = 7.0 Hz, 2H), 1.45 – 1.30 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.41, 162.88, 134.40 (q, *J* = 32.6 Hz), 133.63, 131.66, 129.94, 129.19, 125.39 (q, *J* = 3.7 Hz), 123.65 (q, *J* = 272.7 Hz), 114.24, 65.34, 55.58, 42.99, 29.46, 28.48, 26.13, 25.47.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.11.

HRMS: Calcd for $C_{21}H_{25}F_3NO_5S^+[M+H]^+$: 460.1400, found: 460.1418



1y

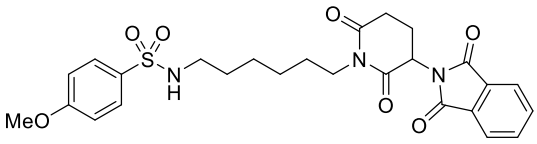
6-((4-methoxyphenyl)sulfonamido)hexyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide

Prepared by **General Procedure C** on a 1 mmol scale. Obtain a white solid (85% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.63 (brs, 1H), 4.63 – 4.60 (m, 1H), 4.36 (s, 1H), 4.19 – 4.14 (m, 2H), 3.86 (s, 3H), 3.53 – 3.38 (m, 2H), 2.90 (t, *J* = 6.5 Hz, 2H), 1.67 – 1.60 (m, 2H), 1.59 (s, 3H), 1.51 – 1.43 (m, 2H), 1.40 (s, 3H), 1.35 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.92, 167.05, 162.90, 131.51, 129.20, 114.28, 66.35, 63.29, 62.74, 61.16, 55.65, 42.91, 38.35, 29.37, 28.27, 26.00, 25.36, 20.34, 18.65.

HRMS: Calcd for $C_{21}H_{31}N_2O_8S_2^+[M+H]^+$: 503.1516, found: 503.1525



1z

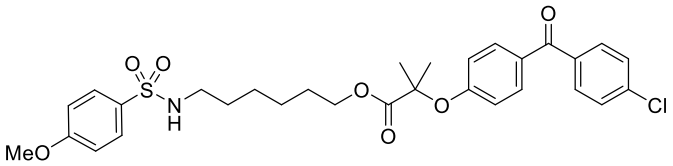
***N*-(6-(3-(1,3-dioxoisoindolin-2-yl)-2,6-dioxopiperidin-1-yl)hexyl)-4-methoxybenzenesulfonamide**

Prepared on page S12. Obtain a white solid (43% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 2H), 7.82 – 7.70 (m, 4H), 6.95 (d, *J* = 7.8 Hz, 2H), 5.04 – 4.91 (m, 1H), 4.59 (brs, 1H), 3.85 (s, 3H), 3.81 – 3.69 (m, 2H), 3.00 – 2.85 (m, 3H), 2.82 – 2.66 (m, 2H), 2.16 – 2.05 (m, 1H), 1.57 – 1.35 (m, 4H), 1.30 – 1.19 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.95, 168.56, 167.49, 162.77, 134.48, 131.75, 131.71, 129.20, 123.79, 114.21, 55.60, 50.15, 42.92, 40.35, 31.99, 29.20, 27.46, 25.99, 25.94, 22.02.

HRMS: Calcd for $C_{26}H_{30}N_3O_7S^+[M+H]^+$: 528.1799, found: 528.1792



1aa

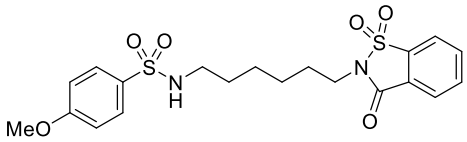
6-((4-methoxyphenyl)sulfonamido)hexyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate

Prepared by **General Procedure C** on a 1 mmol scale. Obtain a colorless oil (82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.0 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 4H), 7.44 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 4.71 (t, *J* = 5.0 Hz, 1H), 4.11 (t, *J* = 6.4 Hz, 2H), 3.86 (s, 3H), 2.83 (q, *J* = 6.7 Hz, 2H), 1.67 (s, 6H), 1.57 – 1.44 (m, 2H), 1.34 – 1.27 (m, 2H), 1.19 – 1.13 (m, 2H), 1.11 – 1.02 (m, 2z

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.53, 173.74, 162.79, 159.80, 138.60, 136.19, 132.02, 131.69, 131.29, 130.27, 129.21, 128.61, 116.96, 114.20, 79.43, 65.52, 55.61, 43.07, 29.48, 28.22, 26.05, 25.46, 25.34.

HRMS: Calcd for $C_{30}H_{35}ClNO_7S^+[M+H]^+$: 588.1817, found: 528.1839



1ab

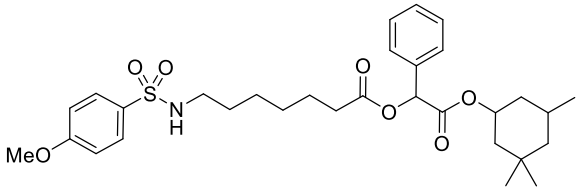
***N*-(6-(1,1-dioxido-3-oxobenzo[*d*]isothiazol-2(*3H*)-yl)hexyl)-4-methoxybenzenesulfonamide**

Prepared on page S12. Obtain a white solid (52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 1H), 7.93 – 7.81 (m, 3H), 7.78 (d, *J* = 8.9 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.62 (t, *J* = 6.2 Hz, 1H), 3.85 (s, 3H), 3.72 (t, *J* = 7.4 Hz, 2H), 2.91 (q, *J* = 6.7 Hz, 2H), 1.83 – 1.73 (m, 2H), 1.51 – 1.41 (m, 2H), 1.36 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.82, 159.03, 137.62, 134.78, 134.39, 131.57, 129.22, 127.36,

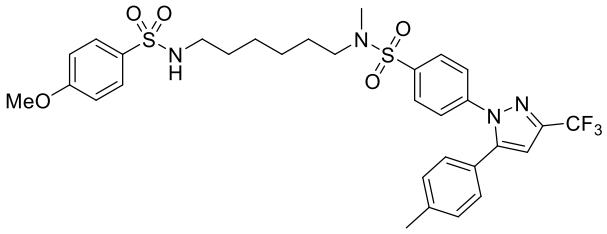
125.18, 120.93, 114.25, 55.62, 42.96, 39.13, 29.29, 28.15, 26.08, 25.85.
HRMS: Calcd for $C_{20}H_{25}N_2O_6S_2^+[M+H]^+$: 453.1149, found: 453.1132



1ac

2-oxo-1-phenyl-2-((3,3,5-trimethylcyclohexyl)oxy)ethyl 7-((4-methoxyphenyl)sulfonamido)heptanoate

Prepared by **General Procedure D** on a 2 mmol scale. Obtain a white solid (89% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.9 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.44 – 7.36 (m, 3H), 6.99 (d, *J* = 8.9 Hz, 2H), 5.87 (d, 1H), 4.93 (tt, *J* = 11.6, 4.4 Hz, 1H), 4.57 (s, 1H), 3.88 (s, 3H), 2.93 (q, *J* = 6.5 Hz, 2H), 2.52 – 2.33 (m, 2H), 1.92 (dd, *J* = 84.0, 12.1 Hz, 1H), 1.76 – 1.42 (m, 6H), 1.36 – 1.27 (m, 5H), 1.07 (dt, *J* = 61.7, 12.1 Hz, 1H), 0.95 – 0.66 (m, 11H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.01, 168.48, 168.46, 162.81, 134.05, 134.04, 131.61, 129.21, 129.09, 128.73, 127.53, 127.51, 114.23, 74.64, 74.62, 72.81, 55.61, 47.42, 43.63, 43.34, 43.03, 40.09, 39.76, 33.77, 32.96, 32.93, 32.29, 32.24, 29.30, 28.40, 27.04, 26.97, 26.10, 25.45, 25.42, 24.55, 22.23, 22.20.
HRMS: Calcd for $C_{31}H_{44}NO_7S^+[M+H]^+$: 574.2833, found: 574.2838

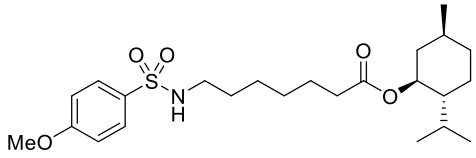


1ad

***N*-(6-((4-methoxyphenyl)sulfonamido)hexyl)-*N*-methyl-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide**

Prepared on page S13. Obtain a colorless oil (45% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 14.5, 8.8 Hz, 4H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.74 (s, 1H), 4.75 – 4.67 (m, 1H), 3.85 (s, 3H), 2.98 – 2.85 (m, 4H), 2.68 (s, 3H), 2.36 (s, 3H), 1.52 – 1.39 (m, 4H), 1.33 – 1.21 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.82, 145.32, 144.08 (q, *J* = 38.5 Hz), 142.44, 139.83, 137.16, 131.63, 129.75, 129.19, 128.71, 128.30, 125.62, 121.08 (q, *J* = 269.4 Hz), 114.25, 106.21 (d, *J* = 1.7 Hz), 106.21, 55.62, 49.79, 42.88, 34.51, 29.36, 27.20, 25.80, 25.61, 21.31.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.39.

HRMS: Calcd for $C_{31}H_{36}F_3N_4O_5S_2^+[M+H]^+$: 665.2074, found: 665.2077



1ae

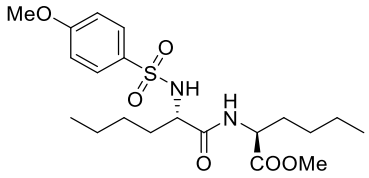
(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 7-((4-methoxyphenyl)sulfonamido)heptanoate

Prepared by **General Procedure D** on a 1 mmol scale. Obtain a white solid (67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.65 (td, *J* = 10.9, 4.2 Hz, 1H), 4.51 (s, 1H), 3.86 (s, 3H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.99 – 1.90 (m, 1H), 1.89 – 1.77 (m, 1H), 1.72 – 1.61 (m, 2H), 1.61 – 1.50 (m, 2H), 1.50 – 1.39 (m, 3H), 1.39 – 1.29 (m, 1H), 1.29 – 1.21 (m, 4H), 1.10 – 0.80 (m, 9H), 0.73 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.26, 162.83, 131.54, 129.21, 114.23, 73.99, 55.62, 47.00, 43.08, 40.95, 34.51, 34.26, 31.38, 29.38, 28.54, 26.25, 26.19, 24.86, 23.40, 22.04, 20.77, 16.29.

HRMS: Calcd for $C_{24}H_{40}NO_5S^+[M+H]^+$: 454.2622, found: 454.2638



1af

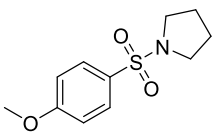
methyl (*S*)-2-((*S*)-2-((4-methoxyphenyl)sulfonamido)hexanamido)hexanoate

Prepared on page S9. Obtain a white solid (8% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 2H), 6.38 (s, 1H), 5.32 (s, 1H), 4.39 (td, *J* = 7.5, 5.5 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 3H), 3.70 – 3.64 (m, 1H), 1.76 – 1.61 (m, 2H), 1.61 – 1.45 (m, 2H), 1.29 – 1.17 (m, 6H), 1.17 – 1.07 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H), 0.81 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.50, 170.73, 163.07, 131.31, 129.46, 114.21, 56.63, 55.59, 52.39, 52.33, 33.28, 31.95, 27.21, 27.07, 22.20, 22.18, 13.81, 13.79.

HRMS: Calcd for $C_{20}H_{33}N_2O_6S^+[M+H]^+$: 429.2054, found: 429.2050



4

1-((4-methoxyphenyl)sulfonyl)pyrrolidine

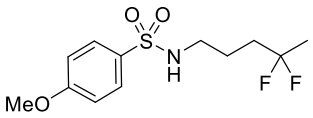
Prepared by **General Procedure B** on a 5 mmol scale. Obtain a white solid (92% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 3.26 – 3.14 (m, 4H), 1.77 – 1.70 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.85, 129.62, 128.59, 114.15, 55.60, 47.92, 25.18.

Data are consistent with reported in the literature[11].

11.3 Fluorinated Products



3a

***N*-(4,4-difluoropentyl)-4-methoxybenzenesulfonamide**

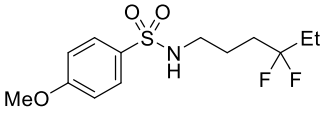
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3/1). Obtained as a white solid (80% yield) as a 0.3:99.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.89 (s, 1H), 3.86 (s, 3H), 2.95 (q, *J* = 6.7 Hz, 2H), 1.84 (tt, *J* = 16.0, 7.9 Hz, 2H), 1.65 (p, *J* = 7.0 Hz, 2H), 1.53 (t, *J* = 18.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.94, 131.41, 129.16, 123.88 (t, *J* = 238.0 Hz), 114.32, 55.62, 42.63, 34.87 (t, *J* = 25.8 Hz), 23.39 (t, *J* = 27.9 Hz), 22.94 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.10.

HRMS: Calcd for $C_{12}H_{17}F_2NNaO_3S^+[M+Na]^+$: 316.0789, found: 316.0782



3b

***N*-(4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

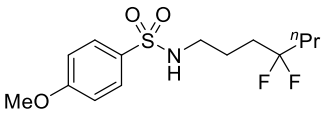
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a colorless oil (80% yield) as a 7.7:92.3 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.86 (s, 1H), 3.86 (s, 3H), 2.96 (q, *J* = 6.7 Hz, 2H), 1.90 – 1.54 (m, 6H), 0.95 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.93, 131.45, 129.17, 125.07 (t, *J* = 240.5 Hz), 114.31, 55.61, 42.73, 32.85 (t, *J* = 25.9 Hz), 29.73 (t, *J* = 26.2 Hz), 22.56, 6.53.

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.56.

HRMS: Calcd for $C_{13}H_{20}F_2NO_3S^+[M+H]^+$: 308.1126, found: 308.1016



3c

***N*-(4,4-difluoroheptyl)-4-methoxybenzenesulfonamide**

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on

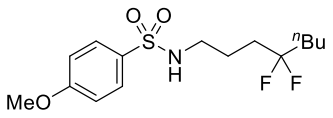
silica gel (PE/EtOAc = 4/1). Obtained as a colorless oil (71% yield) as a 3.3:96.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H), 4.87 (s, 1H), 3.86 (s, 3H), 3.04 – 2.88 (m, 2H), 1.95 – 1.55 (m, 6H), 1.50 – 1.36 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.94, 131.39, 129.19, 124.85 (t, *J* = 240.5 Hz), 114.32, 55.63, 42.73, 38.62 (t, *J* = 25.0 Hz), 33.24 (t, *J* = 25.9 Hz), 22.57 (t, *J* = 4.4 Hz), 15.75 (t, *J* = 5.0 Hz), 13.89.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.33.

HRMS: Calcd for $C_{14}H_{22}F_2NO_3S^+[M+H]^+$: 322.1283, found: 322.1291



3d

***N*-(4,4-difluorooctyl)-4-methoxybenzenesulfonamide**

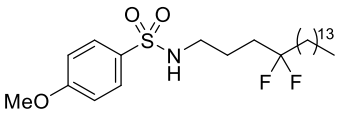
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1). Obtained as a colorless oil (68% yield) as a 5.2:94.8 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.84 (t, *J* = 6.5 Hz, 1H), 3.86 (s, 3H), 2.96 (q, *J* = 6.7 Hz, 2H), 1.89 – 1.57 (m, 6H), 1.47 – 1.20 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.93, 131.47, 129.17, 124.92 (t, *J* = 240.5 Hz), 114.30, 55.60, 42.73, 36.29 (t, *J* = 25.2 Hz), 33.26 (t, *J* = 25.9 Hz), 24.34, 22.60, 22.42, 13.78.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.34.

HRMS: Calcd for $C_{15}H_{24}F_2NO_3S^+[M+H]^+$: 336.1439, found: 336.1430



3e

***N*-(4,4-difluorooctadecyl)-4-methoxybenzenesulfonamide**

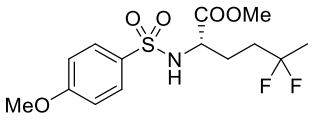
Prepared by **General procedure E** on a 0.2 mmol scale, the reaction time was extended to 4 hours and purified by flash chromatography on silica gel (PE/EtOAc = 20/1 + 2% AcOH). Obtained as a white solid (41% yield) as a 11.9:88.1 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 4.65 (s, 1H), 3.87 (s, 3H), 2.97 (q, *J* = 6.7 Hz, 2H), 1.91 – 1.56 (m, 6H), 1.45 – 1.35 (m, 2H), 1.34 – 1.16 (m, 23H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.96, 131.56, 129.18, 124.89 (t, *J* = 240.7 Hz), 114.31, 55.60, 42.74, 36.64 (t, *J* = 25.2 Hz), 33.27 (t, *J* = 25.9 Hz), 29.67, 29.66, 29.63, 29.59, 29.55, 29.47, 29.36, 29.35, 29.33, 22.63 (t, *J* = 4.0 Hz), 22.27 (t, *J* = 4.6 Hz), 14.07.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.41.

HRMS: Calcd for $C_{25}H_{44}F_2NO_3S^+[M+H]^+$: 476.3004, found: 476.3009



3f

methyl (*S*)-5,5-difluoro-2-((4-methoxyphenyl)sulfonamido)hexanoate

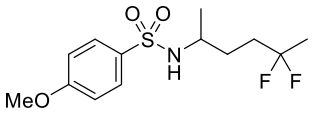
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a white solid (90% yield) as a 4.9:95.1 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.9 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 5.22 (s, 1H), 3.93 – 3.87 (m, 1H), 3.86 (s, 3H), 3.53 (s, 3H), 2.06 – 1.72 (m, 4H), 1.57 (t, *J* = 18.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.70, 163.16, 130.98, 129.43, 123.46 (t, *J* = 238.3 Hz), 114.24, 55.64, 55.18, 52.72, 33.64 (t, *J* = 25.9 Hz), 26.39 (t, *J* = 4.6 Hz), 23.56 (t, *J* = 27.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.96.

HRMS: Calcd for $C_{14}H_{20}F_2NO_5S^+[M+H]^+$: 352.1025, found: 352.1033



3g

***N*-(5,5-difluorohexan-2-yl)-4-methoxybenzenesulfonamide**

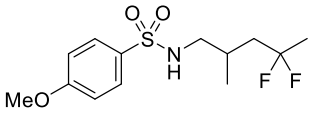
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1). Obtained as a white solid (86% yield), monofluorinated byproduct not detected.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.56 (brs, 1H), 3.87 (s, 3H), 3.38 – 3.22 (m, 1H), 1.95 – 1.47 (m, 7H), 1.07 – 0.93 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.89, 132.68, 129.11, 123.90 (t, *J* = 238.0 Hz), 114.27, 55.61, 49.62, 34.19 (t, *J* = 25.7 Hz), 30.33 (t, *J* = 4.3 Hz), 23.45 (t, *J* = 27.9 Hz), 21.63.

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.35.

HRMS: Calcd for $C_{13}H_{20}F_2NO_3S^+[M+H]^+$: 308.1126, found: 308.1136



3h

***N*-(4-fluoro-2-methylpentyl)-4-methoxybenzenesulfonamide**

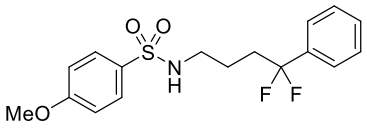
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3/1). Obtained as a colorless oil (89% yield) as a 1.3:98.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.96 (s, 1H), 3.85 (d, *J* = 0.9 Hz, 3H), 2.93 – 2.69 (m, 2H), 2.02 – 1.84 (m, 2H), 1.74 – 1.60 (m, 1H), 1.54 (t, *J* = 18.6 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.89, 131.53, 129.13, 124.23 (t, *J* = 238.4 Hz), 114.29, 55.61, 48.88, 41.46 (t, *J* = 24.6 Hz), 28.62 (t, *J* = 3.1 Hz), 24.04 (t, *J* = 27.9 Hz), 18.53.

^{19}F NMR (376 MHz, $CDCl_3$) δ -88.79 (dd, *J* = 353.1, 239.9 Hz).

HRMS: Calcd for $C_{13}H_{20}FNO_3S^+[M+H]^+$: 308.1126, found: 308.1123



3i

***N*-(4,4-difluoro-4-phenylbutyl)-4-methoxybenzenesulfonamide**

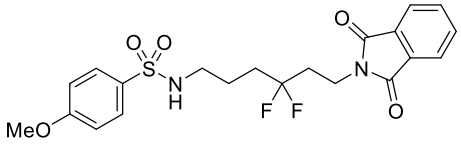
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1). Obtained as a colorless oil (51% yield) as a 7.1:92.9 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.9 Hz, 2H), 7.45 – 7.36 (m, 5H), 6.95 (d, *J* = 8.9 Hz, 2H), 4.80 (t, *J* = 6.4 Hz, 1H), 3.85 (s, 3H), 2.95 (q, *J* = 6.7 Hz, 2H), 2.22 – 2.02 (m, 2H), 1.69 – 1.56 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.94, 136.94 (t, *J* = 26.5 Hz), 131.45, 129.78, 129.15, 128.46, 124.80 (t, *J* = 6.3 Hz), 122.63 (t, *J* = 242.5 Hz), 114.31, 55.61, 42.57, 36.07 (t, *J* = 28.1 Hz), 22.94.

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.73.

HRMS: Calcd for $C_{17}H_{20}F_2NO_3S^+[M+H]^+$: 356.1126, found: 356.1116



3j

***N*-(6-(1,3-dioxoisoindolin-2-yl)-4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2/1). Obtained as a white solid (62% yield) as a 0.7:99.3 mixture of mono-/difluorinated product.

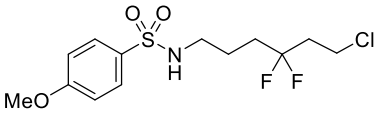
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 4.68 (s, 1H), 3.91 – 3.86 (m, 2H), 3.85 (s, 3H), 2.98 (t, *J* = 6.6 Hz, 2H), 2.20 (tt, *J* = 16.2, 7.3 Hz, 2H), 2.03 – 1.82 (m, 2H), 1.75 – 1.60 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.98, 162.95, 134.07, 132.02, 131.58, 129.19, 123.64 (t, *J* = 241.5

Hz), 123.35, 114.32, 55.60, 42.54, 34.78 (t, *J* = 25.3 Hz), 33.27 (t, *J* = 25.1 Hz), 31.82 (t, *J* = 5.8 Hz), 22.46 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.95.

HRMS: Calcd for $C_{21}H_{23}F_2N_2O_5S^+[M+H]^+$: 453.1290, found: 453.1282



3k

***N*-(6-chloro-4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

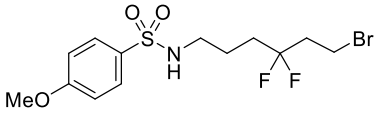
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1). Obtained as a white solid (55% yield) as a 2.3:97.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 4.88 (s, 1H), 3.86 (s, 3H), 3.65 – 3.54 (m, 2H), 2.97 (q, *J* = 6.4 Hz, 2H), 2.27 (tt, *J* = 15.8, 7.6 Hz, 2H), 1.96 – 1.80 (m, 2H), 1.72 – 1.62 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.01, 131.43, 129.18, 123.22 (t, *J* = 241.8 Hz), 114.36, 55.63, 42.52, 39.83 (t, *J* = 25.6 Hz), 36.85 (t, *J* = 6.3 Hz), 33.67 (t, *J* = 25.1 Hz), 22.43 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.72.

HRMS: Calcd for $C_{13}H_{19}ClF_2NO_3S^+[M+H]^+$: 342.0737, found: 342.0731



3l

***N*-(6-bromo-4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

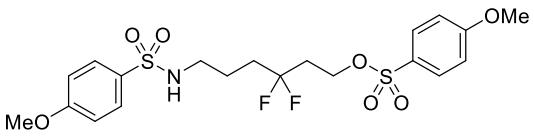
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1). Obtained as a white solid (35% yield) as a 1.8:98.2 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 9.0 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 4.66 (t, *J* = 5.8 Hz, 1H), 3.87 (s, 3H), 3.45 – 3.38 (m, 2H), 2.98 (q, *J* = 6.5 Hz, 2H), 2.46 – 2.29 (m, 2H), 1.95 – 1.79 (m, 2H), 1.72 – 1.59 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.02, 131.47, 129.18, 123.40 (t, *J* = 243.2 Hz), 114.36, 55.63, 42.53, 40.33 (t, *J* = 25.7 Hz), 33.55 (t, *J* = 25.1 Hz), 23.20 (t, *J* = 6.0 Hz), 22.45 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.24.

HRMS: Calcd for $C_{13}H_{19}BrF_2NO_3S^+[M+H]^+$: 386.0232, found: 386.0226



3m

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-methoxybenzenesulfonate

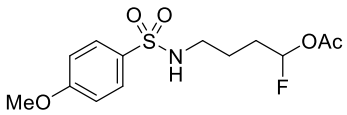
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2/1). Obtained as a colorless oil (75% yield), monofluorinated byproduct not detected.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.0 Hz, 2H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 4.68 (brs, 1H), 4.15 (t, *J* = 6.5 Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 2.95 (t, *J* = 6.7 Hz, 2H), 2.20 (tt, *J* = 15.6, 6.5 Hz, 2H), 1.94 – 1.78 (m, 2H), 1.69 – 1.59 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.05, 162.97, 131.31, 130.22, 129.21, 126.72, 123.20 (t, *J* = 241.5 Hz), 114.67, 114.36, 63.97 (t, *J* = 6.1 Hz), 55.80, 55.67, 42.48, 35.92 (t, *J* = 26.0 Hz), 33.63 (t, *J* = 25.3 Hz), 22.40 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.26.

HRMS: Calcd for $C_{20}H_{25}F_2NNaO_7S^+[M+Na]^+$: 494.1113, found: 494.1124



3n

1-fluoro-4-((4-methoxyphenyl)sulfonamido)butyl acetate

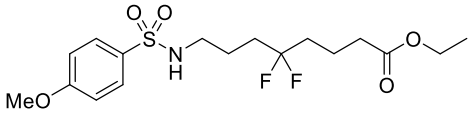
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2/1). Obtained as a colorless oil (64% yield) as a 98.7:1.3 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.25 (dt, *J* = 55.7, 4.9 Hz, 1H), 4.93 (s, 1H), 3.86 (s, 3H), 2.96 (q, *J* = 6.6 Hz, 2H), 2.09 (s, 3H), 1.89 – 1.71 (m, 2H), 1.68 – 1.54 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.98, 162.94, 131.40, 129.16, 114.32, 102.51 (d, *J* = 221.4 Hz), 55.62, 42.49, 30.20 (d, *J* = 22.7 Hz), 23.17 (d, *J* = 4.5 Hz), 20.76.

^{19}F NMR (376 MHz, $CDCl_3$) δ -129.20.

HRMS: Calcd for $C_{13}H_{19}FNO_5S^+[M+H]^+$: 320.0962, found: 320.0984



3o

ethyl 5,5-difluoro-8-((4-methoxyphenyl)sulfonamido)octanoate

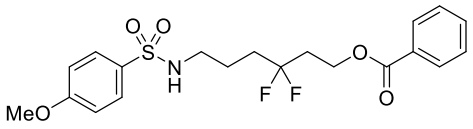
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2.5/1). Obtained as a colorless oil (76% yield) as a 14.8:85.2 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 4.73 (s, 1H), 4.12 (q, *J* = 6.8 Hz, 2H), 3.86 (s, 3H), 2.96 (t, *J* = 7.0 Hz, 2H), 2.33 (t, *J* = 6.8 Hz, 2H), 1.93 – 1.50 (m, 8H), 1.25 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.02, 162.93, 131.39, 129.19, 124.53 (t, *J* = 240.8 Hz), 114.31, 60.49, 55.64, 42.65, 35.73 (t, *J* = 25.5 Hz), 33.52, 33.27 (t, *J* = 25.8 Hz), 22.53 (t, *J* = 4.3 Hz), 17.77 (t, *J* = 4.9 Hz), 14.23.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.71.

HRMS: Calcd for $C_{17}H_{26}F_2NO_5S^+[M+H]^+$: 394.1494, found: 394.1506



3p

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl benzoate

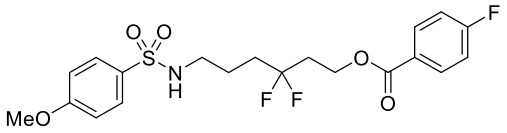
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a white solid (66% yield) as a 3.5:96.5 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 6.9 Hz, 2H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.72 (s, 1H), 4.47 (t, *J* = 6.6 Hz, 2H), 3.85 (s, 3H), 2.98 (t, *J* = 5.8 Hz, 2H), 2.29 (tt, *J* = 16.0, 6.5 Hz, 2H), 2.04 – 1.86 (m, 2H), 1.78 – 1.64 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.33, 162.95, 133.16, 131.44, 129.85, 129.58, 129.16, 128.48, 123.57 (t, *J* = 241.5 Hz), 114.32, 58.84 (t, *J* = 6.0 Hz), 55.61, 42.61, 35.85 (t, *J* = 25.6 Hz), 33.77 (t, *J* = 25.3 Hz), 22.51 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.82.

HRMS: Calcd for $C_{20}H_{24}F_2NO_5S^+[M+H]^+$: 428.1338, found: 428.1333



3q

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-fluorobenzoate

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a white solid (72% yield) as a 2.7:97.3 mixture of mono-/difluorinated product.

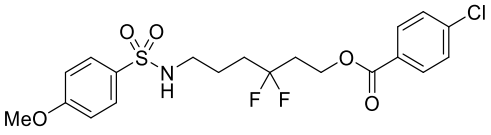
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.77 (d, *J* = 8.9 Hz, 2H), 7.14 – 7.06 (m, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 5.02 (s, 1H), 4.45 (t, *J* = 6.5 Hz, 2H), 3.84 (s, 3H), 2.96 (q, *J* = 6.3 Hz,

2H), 2.27 (tt, *J* = 16.1, 6.5 Hz, 2H), 2.02 – 1.85 (m, 2H), 1.76 – 1.63 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.88 (d, *J* = 254.2 Hz), 165.38, 162.97, 132.17 (d, *J* = 9.4 Hz), 131.47, 129.14, 126.14 (d, *J* = 3.0 Hz), 123.58 (t, *J* = 241.6 Hz), 115.62 (d, *J* = 22.0 Hz), 114.33, 58.95 (t, *J* = 5.8 Hz), 55.59, 42.59, 35.80 (t, *J* = 25.6 Hz), 33.81 (t, *J* = 25.2 Hz), 22.47 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.90, -105.29.

HRMS: Calcd for $C_{20}H_{23}F_3NO_5S^+[M+H]^+$: 446.1244, found: 446.1230



3r

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-chlorobenzoate

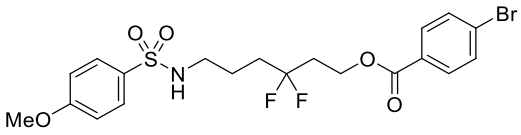
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a colorless oil (73% yield) as a 1.5:98.5 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 9.0 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 4.49 (t, *J* = 6.5 Hz, 2H), 4.38 (s, 1H), 3.87 (s, 3H), 3.02 – 2.97 (m, 2H), 2.30 (tt, *J* = 16.1, 6.5 Hz, 2H), 2.06 – 1.88 (m, 2H), 1.78 – 1.66 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.49, 162.99, 139.67, 131.45, 131.00, 129.16, 128.85, 128.32, 123.52 (t, *J* = 241.6 Hz), 114.34, 59.04 (t, *J* = 5.8 Hz), 55.61, 42.59, 35.84 (t, *J* = 25.7 Hz), 33.79 (t, *J* = 25.2 Hz), 22.50 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.03.

HRMS: Calcd for $C_{20}H_{23}ClF_2NO_5S^+[M+H]^+$: 462.0948, found: 462.0954



3s

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-bromobenzoate

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2/1). Obtained as a light yellow oil (71% yield) as a 4.4:95.6 mixture of mono-/difluorinated product.

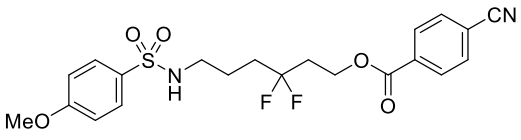
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 9.0 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.65 (s, 1H), 4.47 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 2.98 (q, *J* = 6.3 Hz, 2H), 2.29 (tt, *J* = 16.1, 6.5 Hz, 2H), 2.07 – 1.85 (m, 2H), 1.76 – 1.67 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.63, 162.99, 131.85, 131.45, 131.13, 129.16, 128.77, 128.33, 123.51 (t, *J* = 241.5 Hz), 114.34, 59.06 (t, *J* = 5.9 Hz), 55.62, 42.58, 35.83 (t, *J* = 25.7 Hz), 33.79

(t, *J* = 25.2 Hz), 22.50 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.98.

HRMS: Calcd for $C_{20}H_{23}BrF_2NO_5S^+[M+H]^+$: 506.0443, found: 506.0437



3t

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-cyanobenzoate

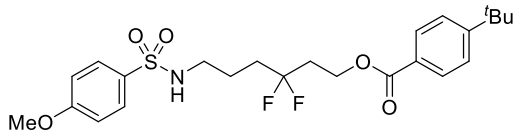
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 2.5/1 to 2/1). Obtained as a light yellow oil (65% yield) as a 3.5:96.5 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.96 (s, 1H), 4.51 (t, *J* = 6.4 Hz, 2H), 3.85 (s, 3H), 2.97 (q, *J* = 6.5 Hz, 2H), 2.30 (tt, *J* = 16.1, 6.4 Hz, 2H), 2.04 – 1.87 (m, 2H), 1.78 – 1.65 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.74, 162.99, 133.68, 132.33, 131.40, 130.14, 129.13, 123.48 (t, *J* = 241.6 Hz), 117.94, 116.56, 114.35, 59.57 (t, *J* = 5.7 Hz), 5 5.64, 42.56, 35.75 (t, *J* = 25.7 Hz), 33.86 (t, *J* = 25.1 Hz), 22.44 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.22.

HRMS: Calcd for $C_{21}H_{23}F_2N_2O_5S^+[M+H]^+$: 453.1290, found: 453.1285



3u

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-(tert-butyl)benzoate

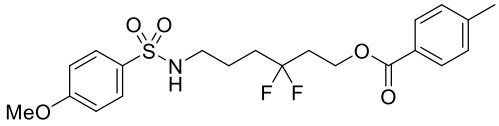
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3.5/1 to 3/1). Obtained as a colorless oil (75% yield) as a 1.0:99.0 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 4.62 (s, 1H), 4.46 (t, *J* = 6.5 Hz, 2H), 3.85 (s, 3H), 2.99 (q, *J* = 6.8 Hz, 2H), 2.29 (tt, *J* = 15.8, 6.5 Hz, 2H), 1.94 (tt, *J* = 16.7, 7.9 Hz, 2H), 1.75 – 1.66 (m, 2H), 1.34 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$)δ 166.38, 162.97, 156.93, 131.51, 129.48, 129.17, 127.05, 125.47, 123.61 (t, *J* = 241.5 Hz), 114.32, 58.65 (t, *J* = 6.0 Hz), 55.60, 42.61, 35.90 (t, *J* = 25.7 Hz), 35.11, 33.74 (t, *J* = 25.2 Hz), 31.10, 22.53 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.61.

HRMS: Calcd for $C_{24}H_{32}F_2NO_5S^+[M+H]^+$: 484.1964, found: 484.1966



3v

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-methylbenzoate

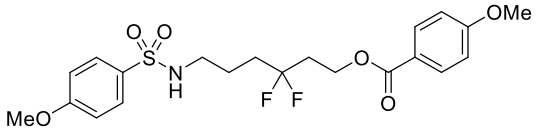
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1 + 2% AcOH). Obtained as a white solid (60% yield) as a 4.3:95.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 4.70 (brs, 1H), 4.45 (td, *J* = 6.6, 1.3 Hz, 2H), 3.85 (s, 3H), 2.97 (t, *J* = 6.8 Hz, 2H), 2.40 (s, 3H), 2.28 (tt, *J* = 15.8, 6.8 Hz, 2H), 2.05 – 1.85 (m, 2H), 1.77 – 1.63 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.42, 162.96, 143.90, 131.53, 129.62, 129.19, 129.16, 127.14, 123.62 (t, *J* = 241.5 Hz), 114.32, 58.67 (t, *J* = 6.0 Hz), 55.59, 42.61, 35.86 (t, *J* = 25.6 Hz), 33.75 (t, *J* = 25.2 Hz), 22.52 (t, *J* = 4.3 Hz), 21.62.

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.64.

HRMS: Calcd for $C_{21}H_{26}F_2NO_5S^+[M+H]^+$: 442.1494, found: 442.1503



3w

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-methoxybenzoate

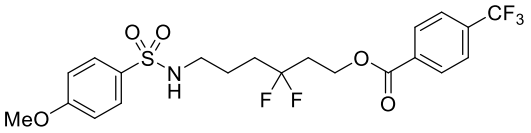
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3.5/1). Obtained as a white solid (70% yield) as a 0.3:99.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H), 7.77 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 4.96 (s, 1H), 4.42 (t, *J* = 6.5 Hz, 2H), 3.84 (s, 3H), 3.83 (s, 3H), 2.95 (t, *J* = 8.1 Hz, 2H), 2.26 (tt, *J* = 16.0, 6.6 Hz, 2H), 2.00 – 1.85 (m, 2H), 1.75 – 1.62 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.08, 163.59, 162.95, 131.63, 131.51, 129.15, 123.66 (t, *J* = 241.4 Hz), 122.25, 114.32, 113.78, 58.56 (t, *J* = 6.0 Hz), 55.59, 55.44, 42.62, 35.87 (t, *J* = 25.7 Hz), 33.77 (t, *J* = 25.3 Hz), 22.51 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.53.

HRMS: Calcd for $C_{21}H_{26}F_2NO_6S^+[M+H]^+$: 458.1443, found: 458.1444



3x

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 4-(trifluoromethyl)benzoate

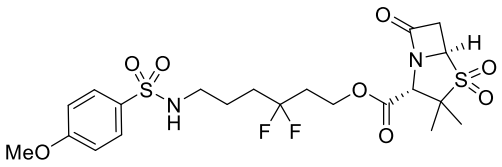
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a colorless oil (69% yield) as a 1.9:98.1 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 4.66 (s, 1H), 4.52 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 2.99 (q, *J* = 7.6, 6.5 Hz, 2H), 2.39 – 2.23 (m, 2H), 1.97 (tt, *J* = 16.7, 7.9 Hz, 2H), 1.77 – 1.67 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.15, 162.99, 134.63 (q, *J* = 32.8 Hz), 133.09, 131.41, 130.03, 129.15, 125.52 (q, *J* = 3.7 Hz), 123.61 (q, *J* = 272.8 Hz), 123.49 (t, *J* = 241.7 Hz), 114.34, 59.34 (t, *J* = 5.7 Hz), 55.60, 42.57, 35.78 (t, *J* = 25.7 Hz), 33.83 (t, *J* = 25.2 Hz), 22.48 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.16, -98.20.

HRMS: Calcd for $C_{21}H_{23}F_5NO_5S^+[M+H]^+$: 496.1212, found: 496.1226



3y

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide

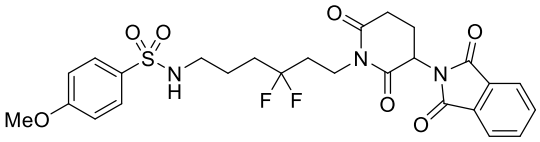
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 1.2/1). Obtained as a yellow oil (48% yield), as a 4.6:95.4 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 4.98 (t, *J* = 6.4 Hz, 1H), 4.66 (dd, *J* = 4.4, 2.0 Hz, 1H), 4.47 – 4.32 (m, 3H), 3.88 (s, 3H), 3.58 – 3.40 (m, 2H), 2.97 (q, *J* = 6.6 Hz, 2H), 2.33 – 2.15 (m, 2H), 2.03 – 1.86 (m, 2H), 1.77 – 1.65 (m, 2H), 1.61 (s, 3H), 1.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.07, 166.88, 162.98, 131.39, 129.14, 123.32 (t, *J* = 241.8 Hz), 114.36, 63.22, 62.83, 61.08, 60.18 (t, *J* = 5.6 Hz), 55.64, 42.48, 38.25, 35.48 (t, *J* = 25.7 Hz), 33.87 (t, *J* = 25.1 Hz), 22.39 (t, *J* = 4.3 Hz), 20.16, 18.36.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.37 (dd, *J* = 271.9, 244.0 Hz).

HRMS: Calcd for $C_{21}H_{29}F_2N_2O_8S_2^+[M+H]^+$: 539.1328, found: 539.1355



3z

***N*-(6-(3-(1,3-dioxoisoindolin-2-yl)-2,6-dioxopiperidin-1-yl)-4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

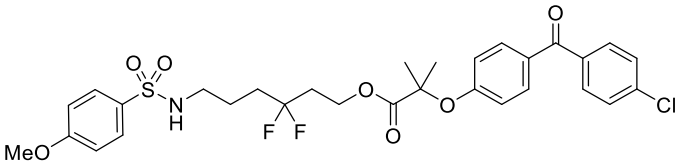
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 1/1). Obtained as a colorless oil (66% yield), monofluorinated byproduct not detected.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.83 – 7.71 (m, 4H), 6.95 (d, *J* = 8.4 Hz, 2H), 5.06 – 4.95 (m, 1H), 4.81 (s, 1H), 4.06 – 3.89 (m, 2H), 3.84 (s, 3H), 3.05 – 2.89 (m, 3H), 2.86 – 2.67 (m, 2H), 2.16 – 1.98 (m, 3H), 1.91 – 1.77 (m, 2H), 1.70 – 1.57 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.78, 168.51, 167.46, 162.87, 134.55, 131.69, 131.48, 129.18, 123.85 (t, *J* = 242.5 Hz), 123.83, 114.29, 55.63, 50.07, 42.53, 34.59 (t, *J* = 6.1 Hz), 34.09 (t, *J* = 25.3 Hz), 33.17 (t, *J* = 25.2 Hz), 31.88, 22.43 (t, *J* = 4.1 Hz), 21.94.

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.13.

HRMS: Calcd for $C_{26}H_{28}F_2N_3O_7S^+[M+H]^+$: 564.1611, found: 564.1599



3aa

3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate

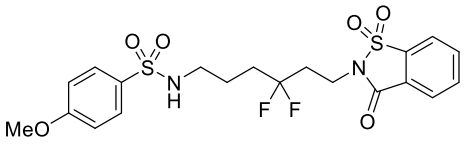
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3/1). Obtained as a yellow oil (74% yield), as a 6.1:93.9 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.74 – 7.66 (m, 4H), 7.44 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 4.85 (s, 1H), 4.32 (t, *J* = 6.6 Hz, 2H), 3.86 (s, 3H), 2.91 (q, *J* = 5.9 Hz, 2H), 2.09 (tt, *J* = 15.0, 6.3 Hz, 2H), 1.86 – 1.73 (m, 2H), 1.67 (s, 6H), 1.63 – 1.52 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.48, 173.45, 162.92, 159.56, 138.59, 136.18, 132.05, 131.43, 131.28, 130.53, 129.18, 128.61, 123.32 (t, *J* = 241.6 Hz), 117.24, 114.30, 79.38 (t, *J* = 5.8 Hz), 59.53 (t, *J* = 5.8 Hz), 55.64, 42.54, 35.42 (t, *J* = 25.8 Hz), 33.68 (t, *J* = 25.1 Hz), 25.37, 22.41 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.02.

HRMS: Calcd for $C_{30}H_{33}ClF_2NO_7S^+[M+H]^+$: 624.1629, found: 624.1604



3ab

***N*-(6-(1,1-dioxido-3-oxobenzo[*d*]isothiazol-2(3*H*)-yl)-4,4-difluorohexyl)-4-methoxybenzenesulfonamide**

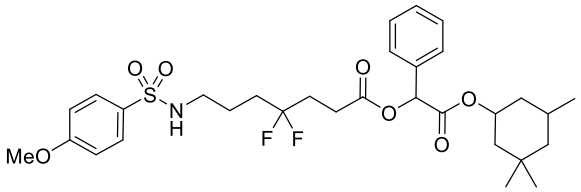
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3/1 to 1.5/1). Obtained as a white soild (71% yield), as a 0.7:99.3 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (d, J = 7.5 Hz, 1H), 8.11 (d, J = 7.5 Hz, 1H), 8.10 – 7.96 (m, 2H), 7.72 (d, J = 8.9 Hz, 2H), 7.50 (t, J = 5.9 Hz, 1H), 7.10 (d, J = 8.9 Hz, 2H), 3.86 (t, J = 7.6 Hz, 2H), 3.81 (s, 3H), 2.76 (q, J = 6.7 Hz, 2H), 2.33 (tt, J = 16.3, 7.8 Hz, 2H), 1.94 (tt, J = 17.2, 9.2 Hz, 2H), 1.58 – 1.47 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 167.32, 163.43, 141.89, 141.05, 140.53, 137.38, 133.83, 131.52, 130.33, 129.48 (t, J = 240.6 Hz), 126.79, 119.54, 60.79, 47.19, 39.41 (t, J = 25.0 Hz), 37.98 (t, J = 24.3 Hz), 37.50 (t, J = 6.0 Hz), 27.25 (t, J = 4.0 Hz).

^{19}F NMR (376 MHz, DMSO-d_6) δ -97.69.

HRMS: Calcd for $C_{20}H_{23}F_2N_2O_6S_2^+$[M+H]$^+$: 489.0960, found: 489.0978



3ac

2-oxo-1-phenyl-2-((3,3,5-trimethylcyclohexyl)oxy)ethyl 4,4-difluoro-7-((4-methoxyphenyl)sulfonamido)heptanoate

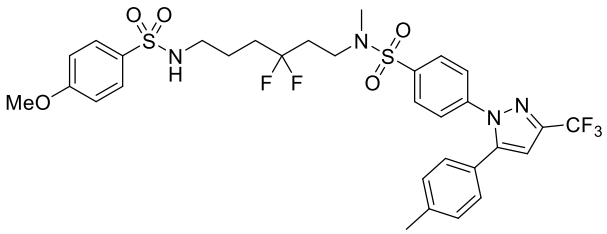
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 5/1 to 4/1). Obtained as a colorless oil (87% yield) as a 1.3:98.7 mixture of mono-/difluorinated product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.9 Hz, 2H), 7.47 – 7.41 (m, 2H), 7.41 – 7.35 (m, 3H), 6.96 (d, J = 8.9 Hz, 2H), 5.85 (s, 1H), 4.99 (t, J = 6.3 Hz, 1H), 4.91 (tt, J = 11.6, 4.4 Hz, 1H), 3.84 (s, 3H), 2.95 (q, J = 6.6 Hz, 2H), 2.74 – 2.54 (m, 2H), 2.18 (tt, J = 15.2, 7.1 Hz, 2H), 2.02 – 1.75 (m, 3H), 1.73 – 1.44 (m, 4H), 1.33 – 1.23 (m, 1H), 1.04 (dt, J = 63.2, 12.2 Hz, 1H), 0.93 – 0.64 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.79, 168.33, 168.31, 162.91, 133.73, 133.71, 131.47, 129.22, 129.18, 128.79, 127.56, 127.54, 123.79 (t, J = 241.2 Hz), 114.32, 75.03, 75.01, 73.01, 55.63, 47.38, 43.62, 43.30, 42.57, 40.07, 39.72, 33.52 (t, J = 25.4 Hz), 32.95, 32.91, 32.30, 32.24, 31.62 (t, J = 25.9 Hz), 27.04, 27.00, 26.97, 25.43, 25.41, 22.39 (t, J = 4.2 Hz), 22.23, 22.19.

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.21.

HRMS: Calcd for $C_{31}H_{42}F_2NO_7S^+[M+H]^+$: 610.2645, found: 610.2649



3ad

<u>*N*-(3,3-difluoro-6-((4-methoxyphenyl)sulfonamido)hexyl)-*N*-methyl-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide</u>

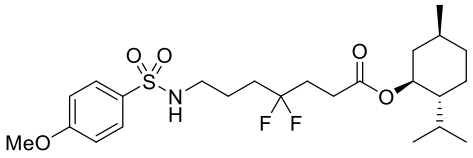
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3/1 to 2/1). Obtained as a colorless oil (33% yield), monofluorinated byproduct not detected.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 4H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.75 (s, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 3.87 (s, 3H), 3.19 (t, *J* = 7.6 Hz, 2H), 2.97 (q, *J* = 6.5 Hz, 2H), 2.75 (s, 3H), 2.38 (s, 3H), 2.15 – 2.05 (m, 2H), 1.94 – 1.83 (m, 2H), 1.69 – 1.64 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.96, 145.33, 144.17 (q, *J* = 38.3 Hz), 142.69, 139.89, 136.72, 131.35, 129.78, 129.19, 128.73, 128.37, 125.72, 123.61 (t, *J* = 242.6 Hz), 121.04 (q, *J* = 270.5 Hz), 114.34, 106.31 (d, *J* = 1.6 Hz), 106.31, 55.66, 44.31 (t, *J* = 5.3 Hz), 42.50, 35.32, 35.20 (t, *J* = 24.9 Hz), 33.50 (t, *J* = 25.1 Hz), 22.54 (t, *J* = 4.2 Hz), 21.34.

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.46, -98.25.

HRMS: Calcd for $C_{31}H_{34}F_5N_4O_5S_2^+[M+H]^+$: 701.1885, found: 701.1891



3ae

<u>(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl 4,4-difluoro-7-((4-methoxyphenyl)sulfonamido)heptanoate</u>

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 4/1). Obtained as a colorless oil (72% yield), as a 5.8:94.2 mixture of mono-/difluorinated product.

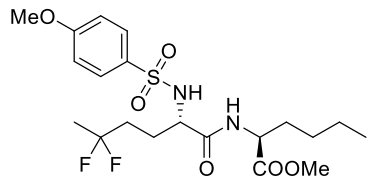
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 7.9 Hz, 2H), 4.75 – 4.55 (m, 2H), 3.87 (s, 3H), 2.97 (s, 2H), 2.46 (t, *J* = 7.5 Hz, 2H), 2.12 (tt, *J* = 15.8, 7.5 Hz, 2H), 2.00 – 1.92 (m, 1H), 1.92 – 1.76 (m, 3H), 1.73 – 1.61 (m, 4H), 1.54 – 1.41 (m, 1H), 1.36 (t, *J* = 11.2 Hz, 1H), 1.08 – 0.82 (m, 9H), 0.74 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.93, 162.96, 131.36, 129.19, 123.92 (t, *J* = 241.2 Hz), 114.33,

74.68, 55.64, 46.95, 42.61, 40.82, 34.20, 33.60 (t, *J* = 25.4 Hz), 31.85 (t, *J* = 25.7 Hz), 31.37, 27.43 (t, *J* = 4.5 Hz), 26.26, 23.40, 22.51 (t, *J* = 4.1 Hz), 22.02, 20.76, 16.30.

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.32.

HRMS: Calcd for $C_{24}H_{38}F_2NO_5S^+[M+H]^+$: 490.2433, found: 490.2410



3af

methyl (*S*)-2-((*S*)-5,5-difluoro-2-((4-methoxyphenyl)sulfonamido)hexanamido)hexanoate

Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 3.5/1 + 2% AcOH). Obtained as a white solid (60% yield) as a 3.8:96.2 mixture of mono-/difluorinated product.

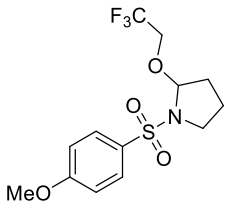
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 6.35 (d, *J* = 6.1 Hz, 1H), 5.56 (d, *J* = 8.7 Hz, 1H), 4.35 (q, *J* = 7.0 Hz, 1H), 3.84 (s, 3H), 3.82 – 3.74 (m, 1H), 3.71 (s, 3H), 2.01 – 1.61 (m, 6H), 1.55 (t, *J* = 18.5 Hz, 3H), 1.28 – 1.20 (m, 2H), 1.16 – 1.01 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.39, 170.10, 163.13, 131.14, 129.40, 123.83 (t, *J* = 238.3 Hz), 114.28, 55.76, 55.59, 52.46, 52.45, 33.42 (t, *J* = 25.6 Hz), 31.76, 27.21, 26.88 (t, *J* = 4.2 Hz), 23.55 (t, *J* = 27.8 Hz), 22.13, 13.75.

^{19}F NMR (376 MHz, $CDCl_3$) δ -91.34 (dd, *J* = 257.2, 238.4 Hz).

HRMS: Calcd for $C_{20}H_{31}F_2N_2O_6S^+[M+H]^+$: 465.1865, found: 465.1855

11.4 Other



5

1-((4-methoxyphenyl)sulfonyl)-2-(2,2,2-trifluoroethoxy)pyrrolidine

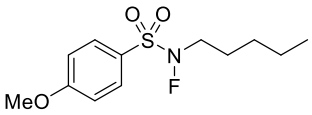
Prepared by **General procedure E** on a 0.2 mmol scale and purified by flash chromatography on silica gel (PE/EtOAc = 8/1). Obtained as a colorless oil (27% yield)

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (d, J = 8.9 Hz, 2H), 7.13 (d, J = 8.9 Hz, 2H), 5.34 (d, J = 5.1 Hz, 1H), 4.25 – 4.11 (m, 2H), 3.85 (s, 3H), 3.41 – 3.33 (m, 1H), 3.05 – 2.92 (m, 1H), 1.94 – 1.78 (m, 2H), 1.78 – 1.67 (m, 1H), 1.41 – 1.27 (m, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.30, 129.95, 129.40, 124.83 (q, J = 278.2 Hz), 115.09, 91.36, 64.07 (q, J = 33.4 Hz), 56.19, 48.07, 32.81, 22.99.

^{19}F NMR (376 MHz, DMSO-d_6) δ -72.75.

Data are consistent with reported in the literature[12].



6

***N*-fluoro-4-methoxy-*N*-pentylbenzenesulfonamide**

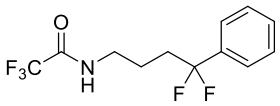
Prepared on page S14. Obtained as a yellow oil (71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.9 Hz, 2H), 7.06 (d, J = 9.0 Hz, 2H), 3.90 (s, 3H), 3.19 (dt, J = 41.0, 7.0 Hz, 2H), 1.71 (p, J = 7.3 Hz, 2H), 1.43 – 1.25 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.75, 132.22, 123.06, 114.56, 55.82, 53.76 (d, J = 12.4 Hz), 28.73, 25.98, 22.20, 13.89.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.78.

Data are consistent with reported in the literature[13].



7

***N*-(4,4-difluoro-4-phenylbutyl)-2,2,2-trifluoroacetamide**

Prepared on page S20. Obtained as a white solid (52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.36 (m, 5H), 6.54 – 6.25 (m, 1H), 3.41 (q, J = 7.2 Hz, 2H), 2.18 (tt, J = 15.7, 7.6 Hz, 2H), 1.87 – 1.70 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.36 (q, J = 37.3 Hz), 136.75 (t, J = 26.3 Hz), 129.99 (t, J = 1.3

Hz), 128.61, 124.79 (t, J = 6.3 Hz), 122.53 (t, J = 242.5 Hz), 115.78 (q, J = 288.4 Hz), 39.31, 36.23 (t, J = 28.3 Hz), 22.40 (t, J = 3.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.93, -95.84.

HRMS: Calcd for $C_{12}H_{13}F_5NO^+[M+H]^+$: 282.0912, found: 282.0914

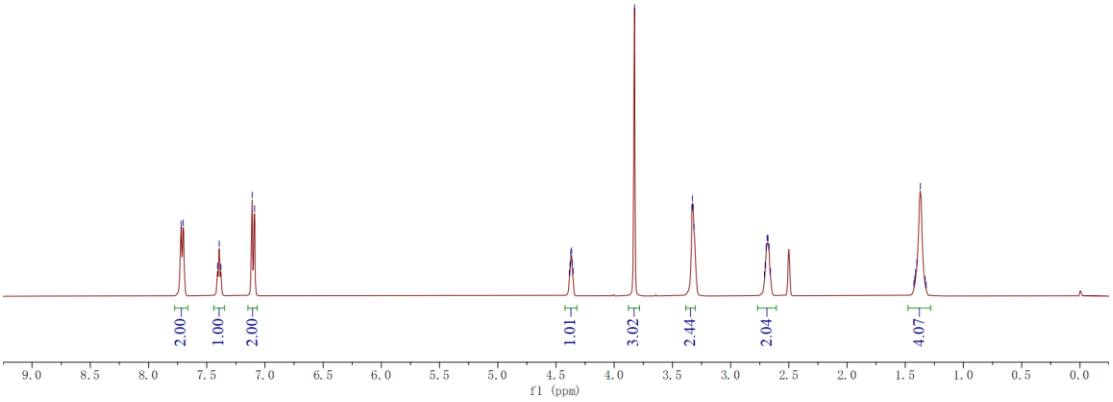
12. References

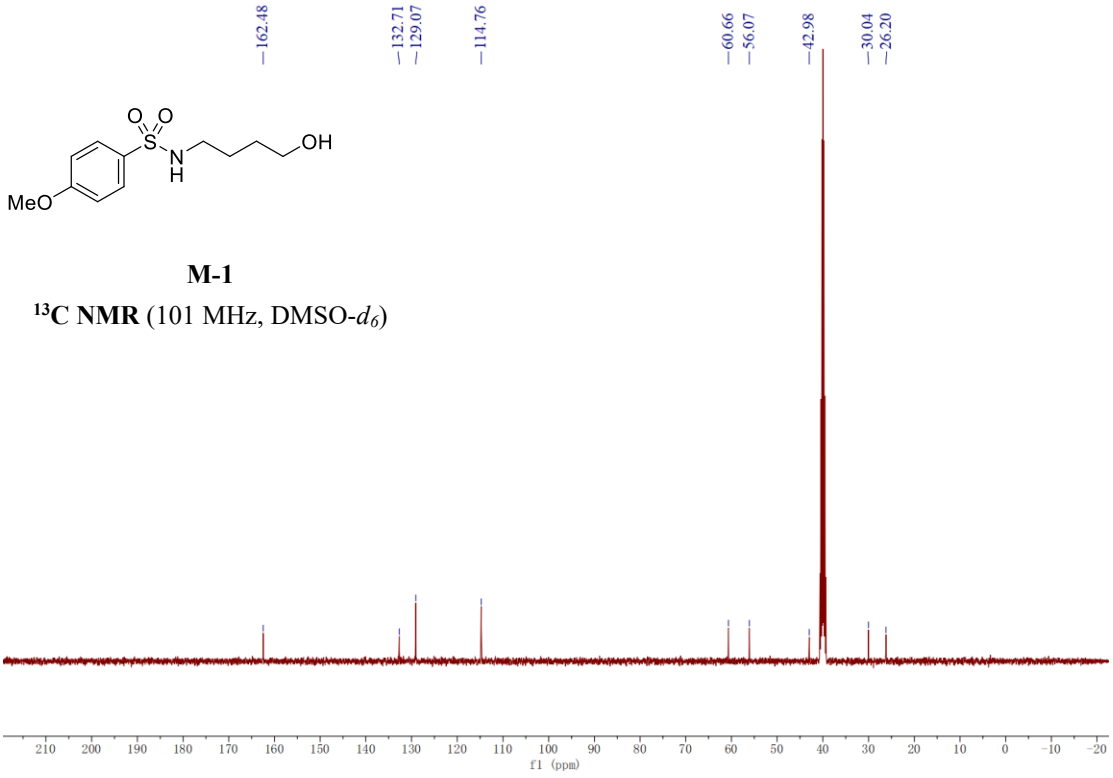
1. Y. Zhu, J. Shi and W. Yu, Photoinduced Site-Selective C(sp^3)–H Chlorination of Aliphatic Amides, *Org. Lett.*, 2020, **22**, 8899-8903.
2. Z. Deng, Z. Zhao, G. He and G. Chen, Photoredox-Mediated Mono- and Difluorination of Remote Unactivated Methylene C(sp^3)–H Bonds of N-Alkyl Sulfonamides, *Org. Lett.*, 2021, **23**, 3631-3635.
3. A. Modak, E. N. Pinter and S. P. Cook, Copper-Catalyzed, N-Directed Csp^3–H Trifluoromethylthiolation ($-SCF_3$) and Trifluoromethylselenation ($-SeCF_3$), *J. Am. Chem. Soc.*, 2019, **141**, 18405-18410.
4. M. A. Cismesia and T. P. Yoon, Characterizing chain processes in visible light photoredox catalysis, *Chem. Sci.*, 2015, **6**, 5426-5434.
5. J. N. Demas, W. D. Bowman, E. F. Zalewski and R. A. Velapoldi, Determination of the quantum yield of the ferrioxalate actinometer with electrically calibrated radiometers, *J. Phys. Chem.*, 1981, **85**, 2766-2771.
6. T. Ankner and G. Hilmersson, Instantaneous Deprotection of Tosylamides and Esters with SmI_2/Amine/Water, *Org. Lett.*, 2009, **11**, 503-506.
7. B. P. Babu, Y. Endo and J.-E. Bäckvall, Biomimetic Aerobic Oxidation of Amino Alcohols to Lactams, *Chem. Eur. J.*, 2012, **18**, 11524-11527.
8. E. F. Flegeau, J. M. Harrison and M. C. Willis, One-Pot Sulfonamide Synthesis Exploiting the Palladium-Catalyzed Sulfination of Aryl Iodides, *Synlett*, 2016, **27**, 101-105.
9. Q. Zhu, D. E. Graff and R. R. Knowles, Intermolecular Anti-Markovnikov Hydroamination of Unactivated Alkenes with Sulfonamides Enabled by Proton-Coupled Electron Transfer, *J. Am. Chem. Soc.*, 2018, **140**, 741-747.
10. C.-Y. Wang, Z.-Y. Qin, Y.-L. Huang, Y.-M. Hou, R.-X. Jin, C. Li and X.-S. Wang, Enantioselective Copper-Catalyzed Remote C(sp^3)–H Alkynylation of Linear Primary Sulfonamides, *Org. Lett.*, 2020, **22**, 4006-4009.
11. H. Jiang, X. Tang, Z. Xu, H. Wang, K. Han, X. Yang, Y. Zhou, Y.-L. Feng, X.-Y. Yu and Q. Gui, TBAI-catalyzed selective synthesis of sulfonamides and β-aryl sulfonyl enamines: coupling of arenesulfonyl chlorides and sodium sulfinates with tert-amines, *Org. Biomol. Chem.*, 2019, **17**, 2715-2720.
12. L. F. T. Novaes, J. S. K. Ho, K. Mao, K. Liu, M. Tanwar, M. Neurock, E. Villemure, J. A. Terrett and S. Lin, Exploring Electrochemical C(sp^3)–H Oxidation for the Late-Stage Methylation of Complex Molecules, *J. Am. Chem. Soc.*, 2022, **144**, 1187-1197.
13. Z. Liu, H. Xiao, B. Zhang, H. Shen, L. Zhu and C. Li, Copper-Catalyzed Remote C(sp^3)−H Trifluoromethylation of Carboxamides and Sulfonamides, *Angew. Chem. Int. Ed.*, 2019, **58**, 2510-2513.

13. NMR Spectra

M-1

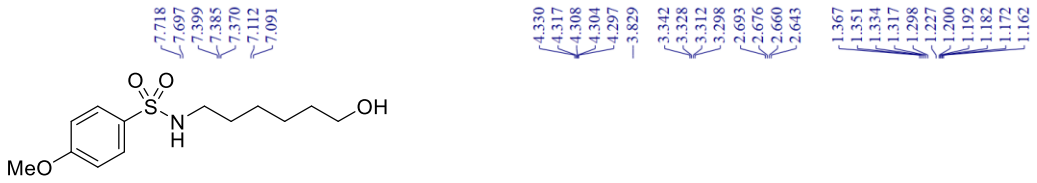
^{1}H NMR (400 MHz, DMSO-d_6)





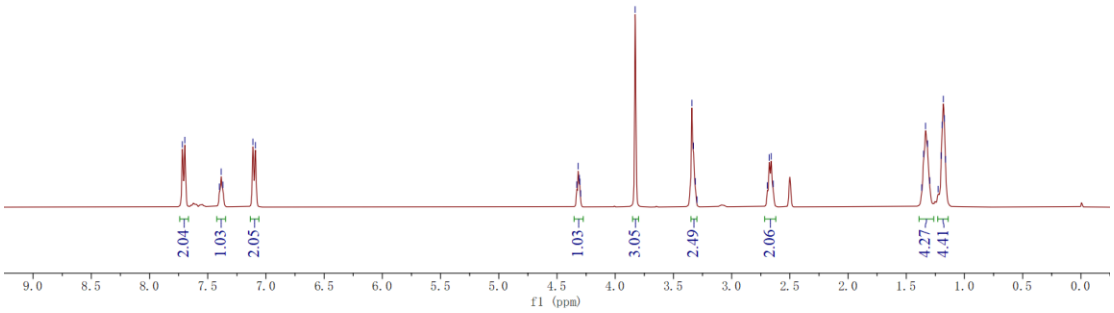
M-1

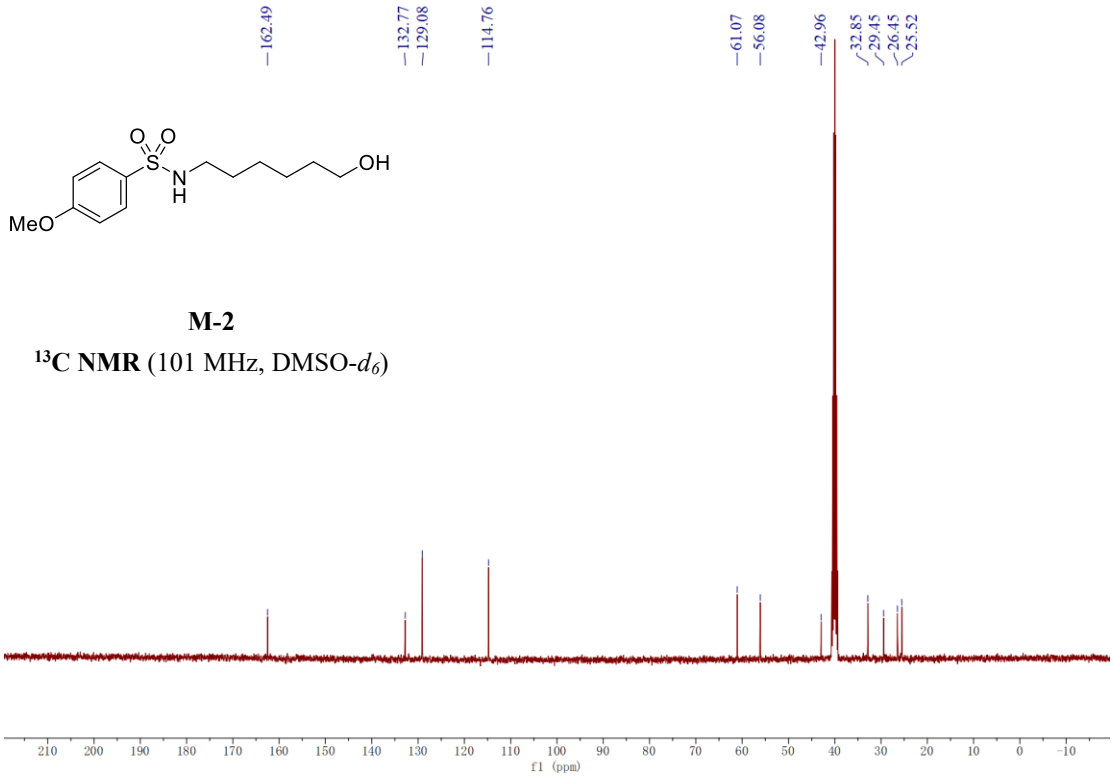
^{13}C NMR (101 MHz, DMSO-d_6)



M-2

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



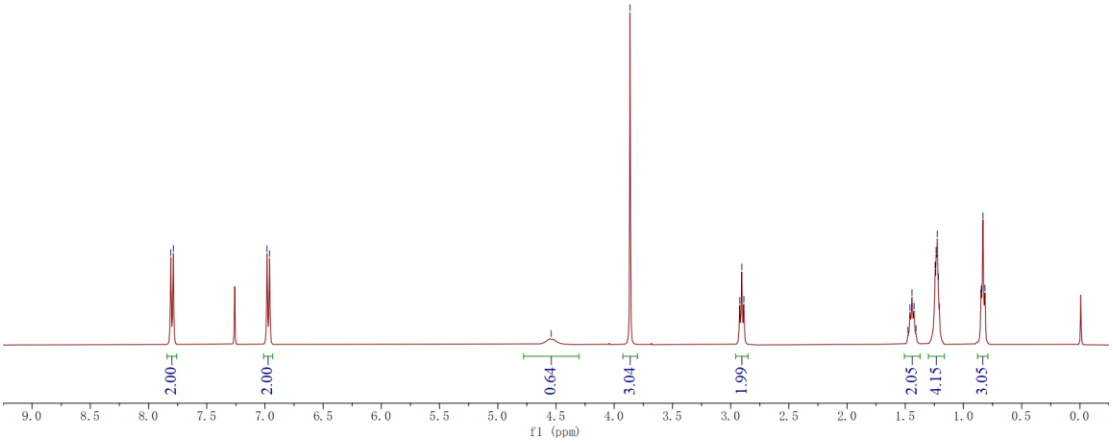


M-2

^{13}C NMR (101 MHz, DMSO-d_6)

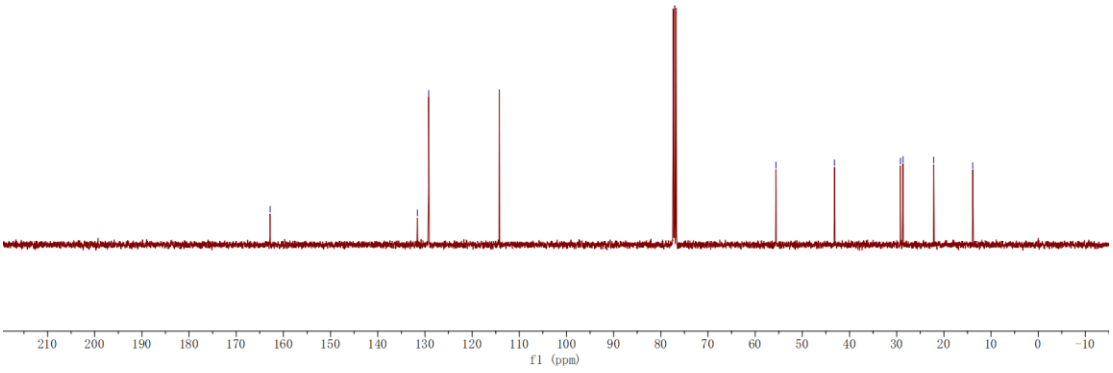
1a

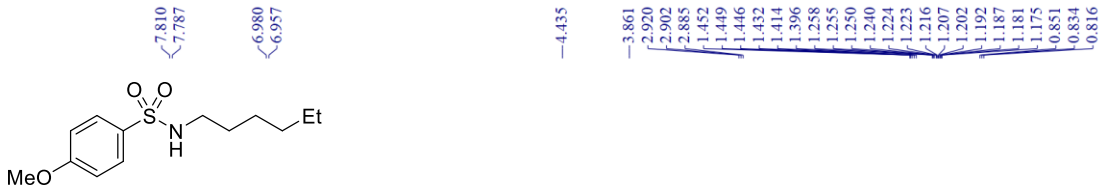
^{1}H NMR (400 MHz, $CDCl_3$)



1a

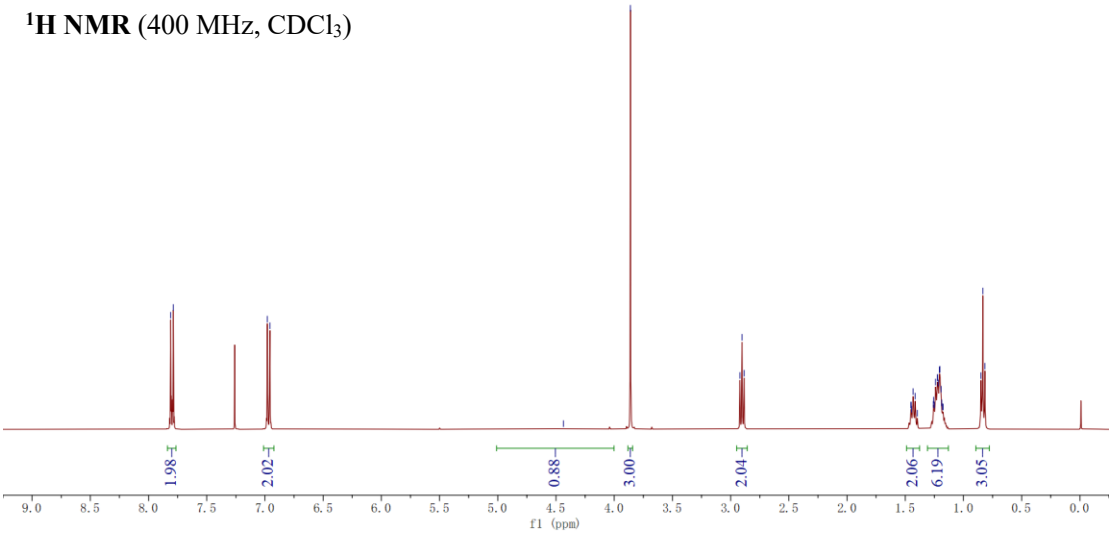
^{13}C NMR (101 MHz, $CDCl_3$)





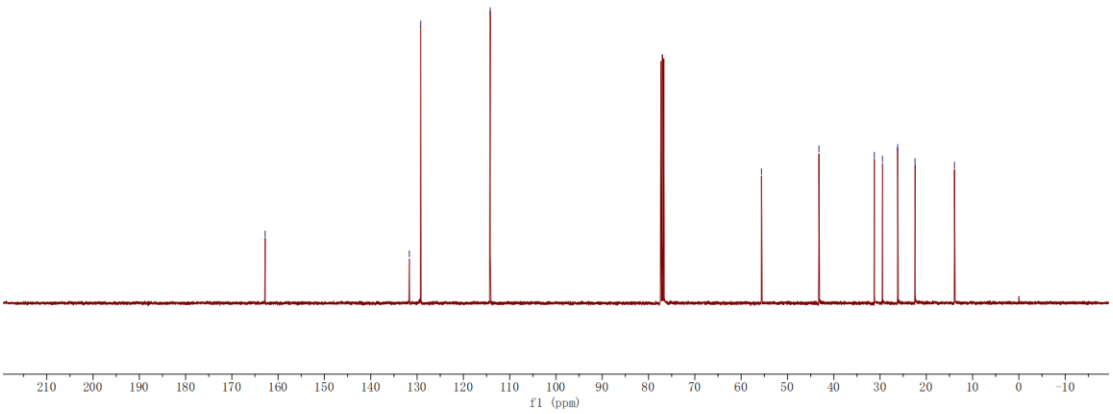
1b

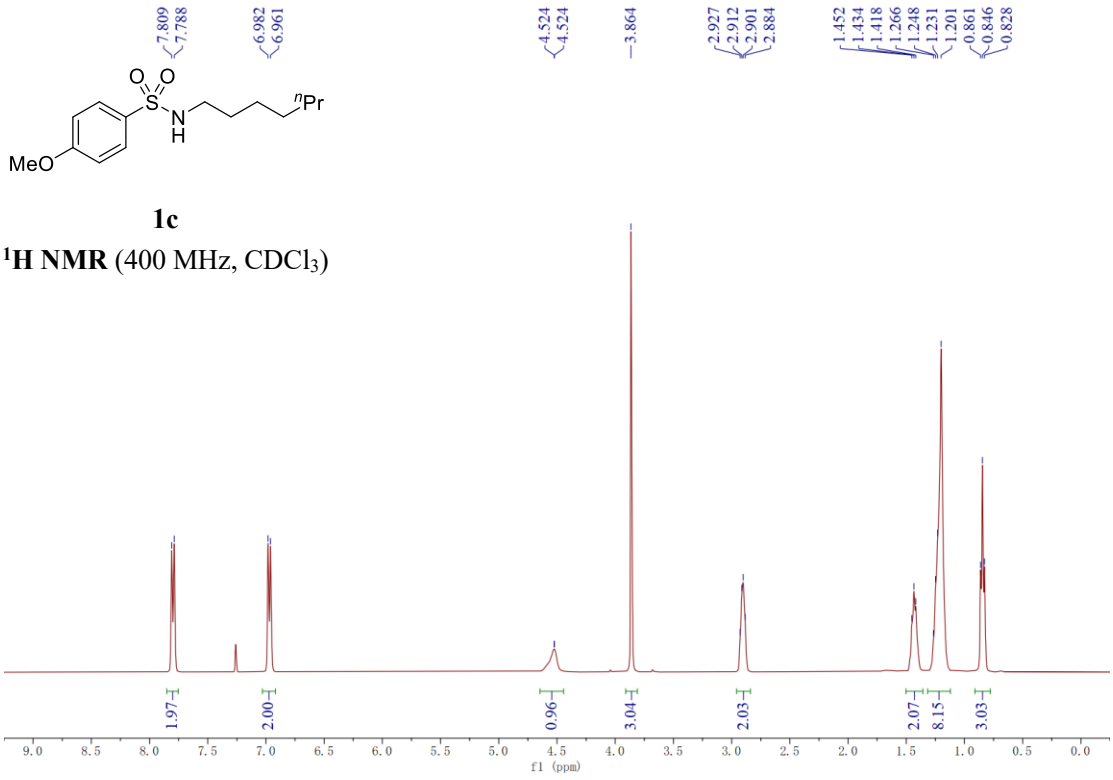
^{1}H NMR (400 MHz, $CDCl_3$)



1b

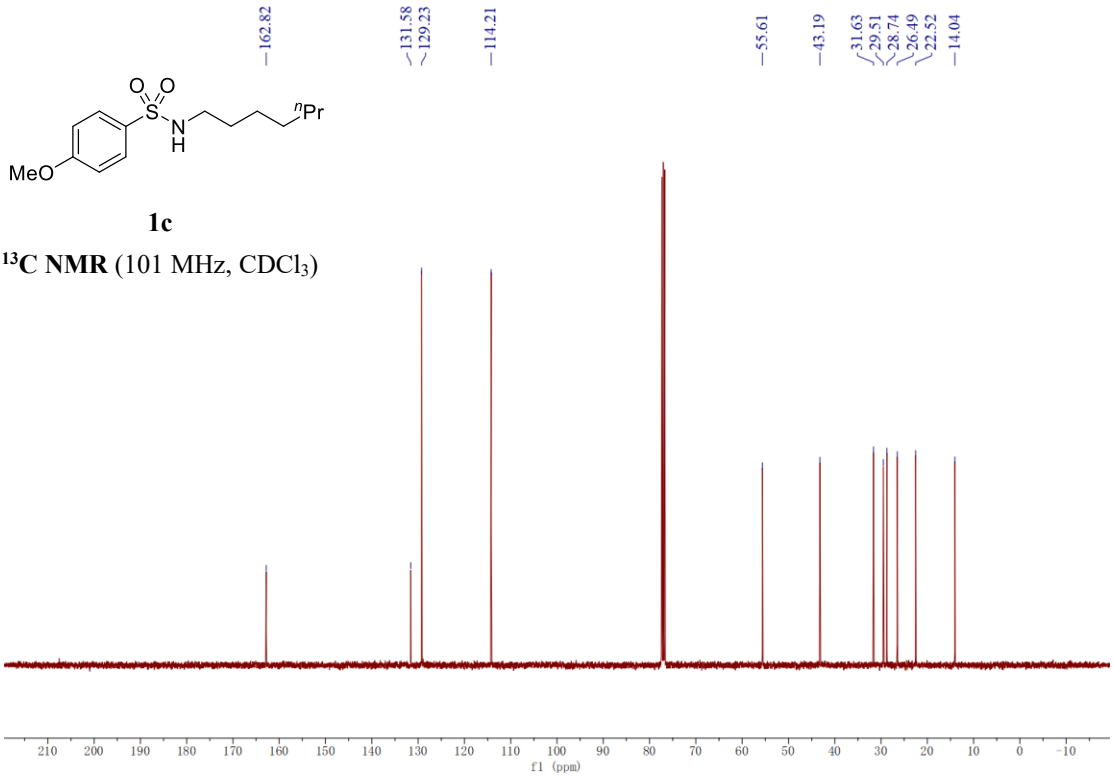
^{13}C NMR (101 MHz, $CDCl_3$)





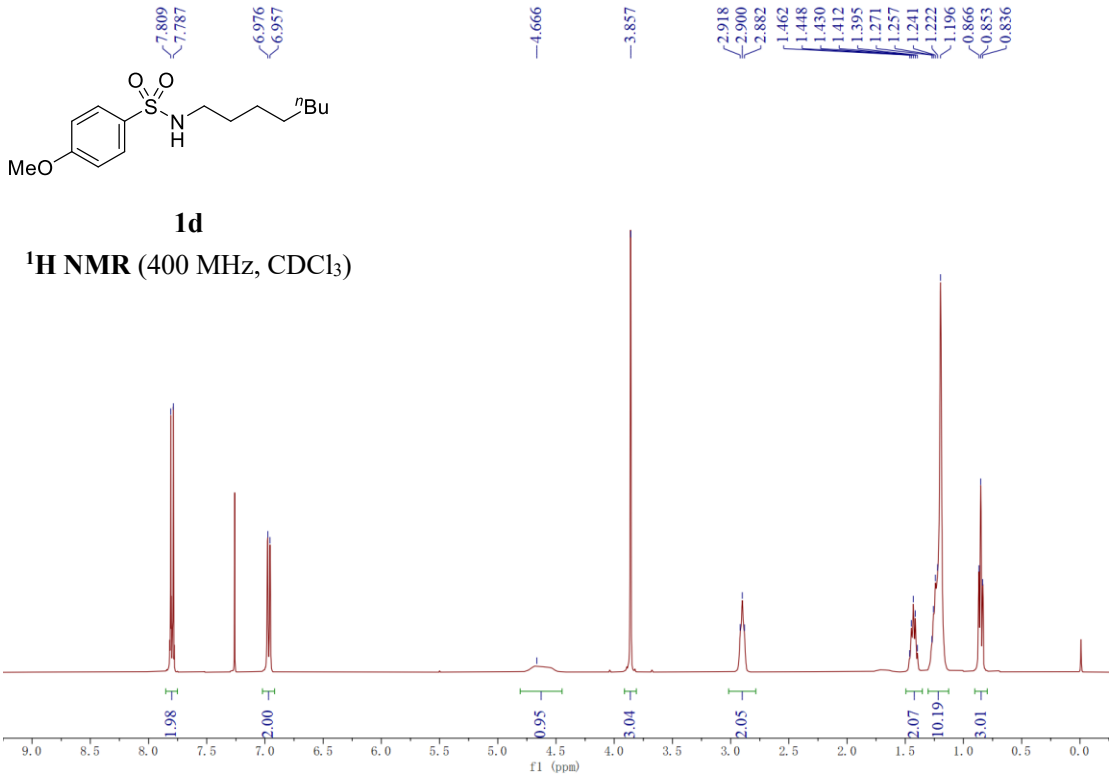
1c

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



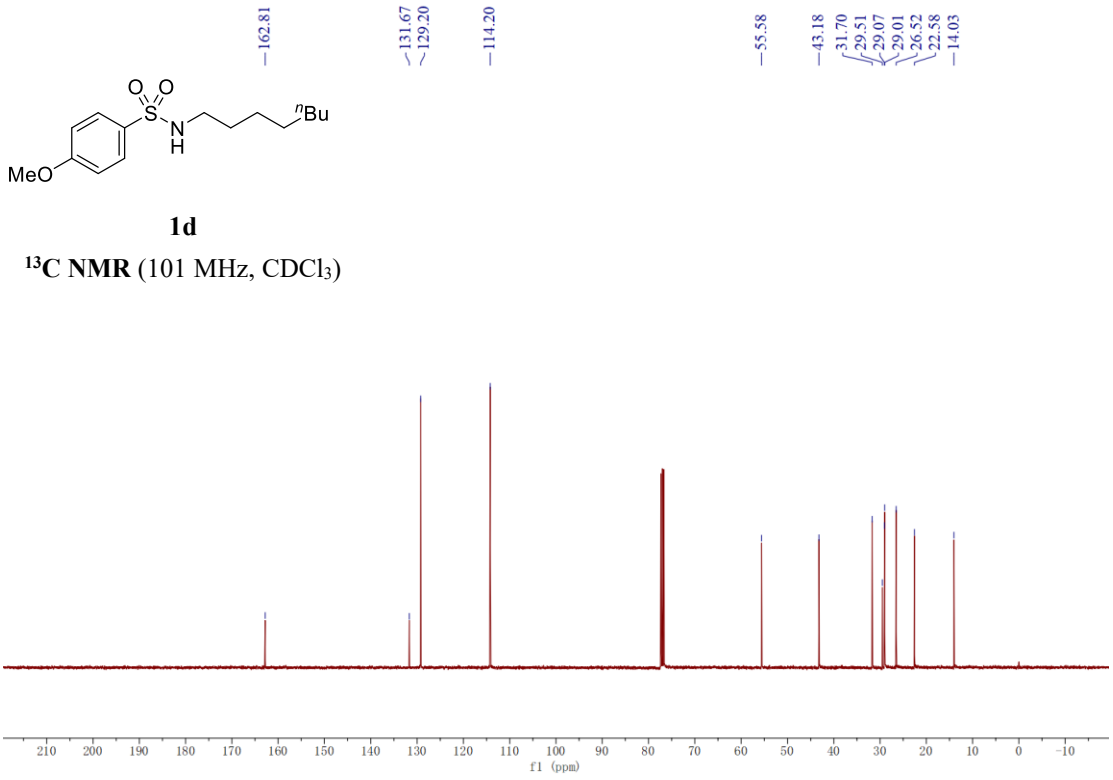
1c

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



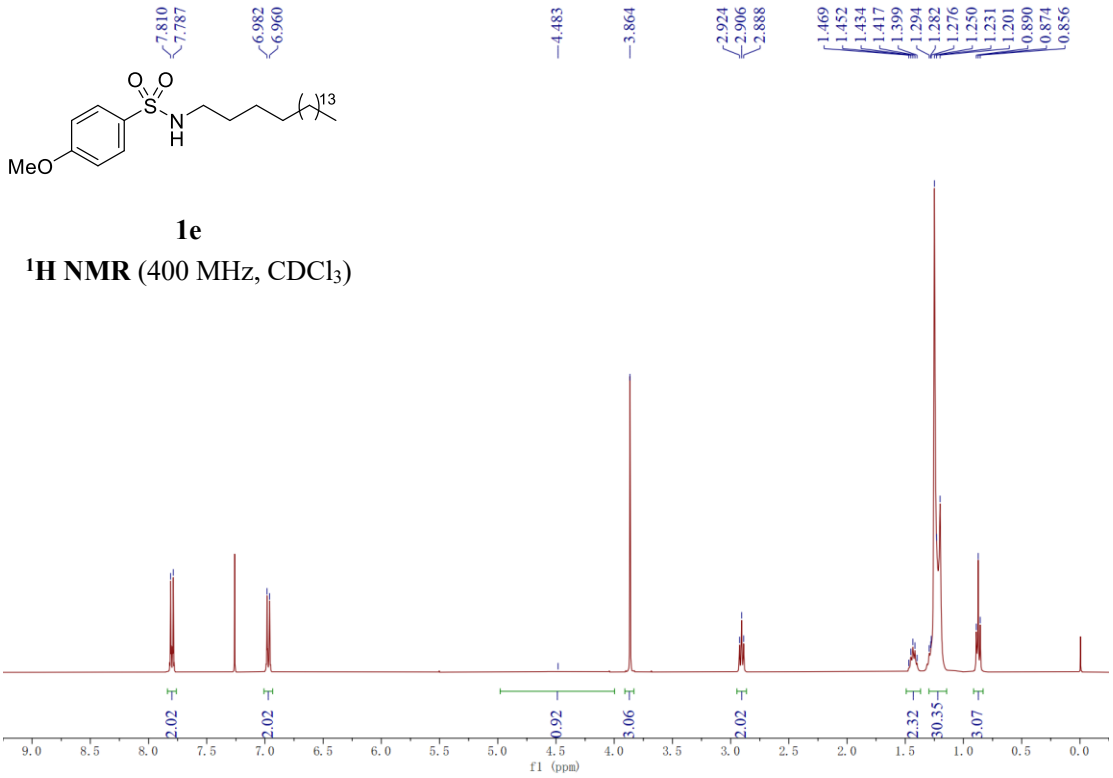
1d

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



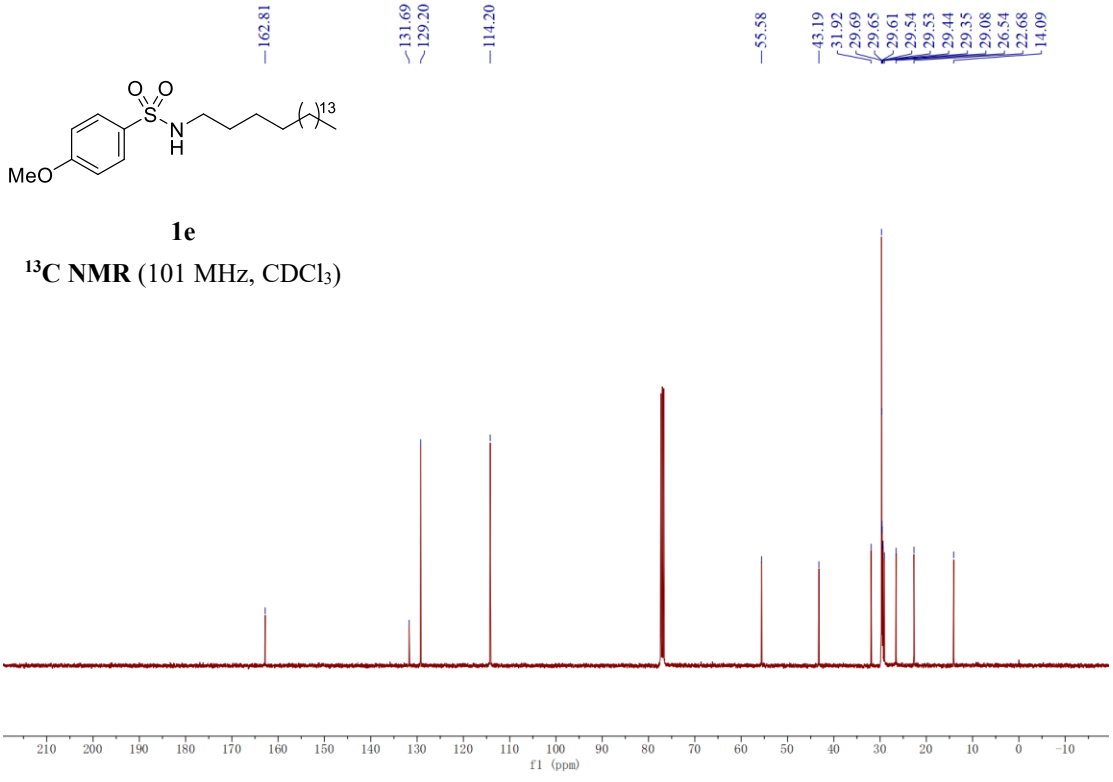
1d

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



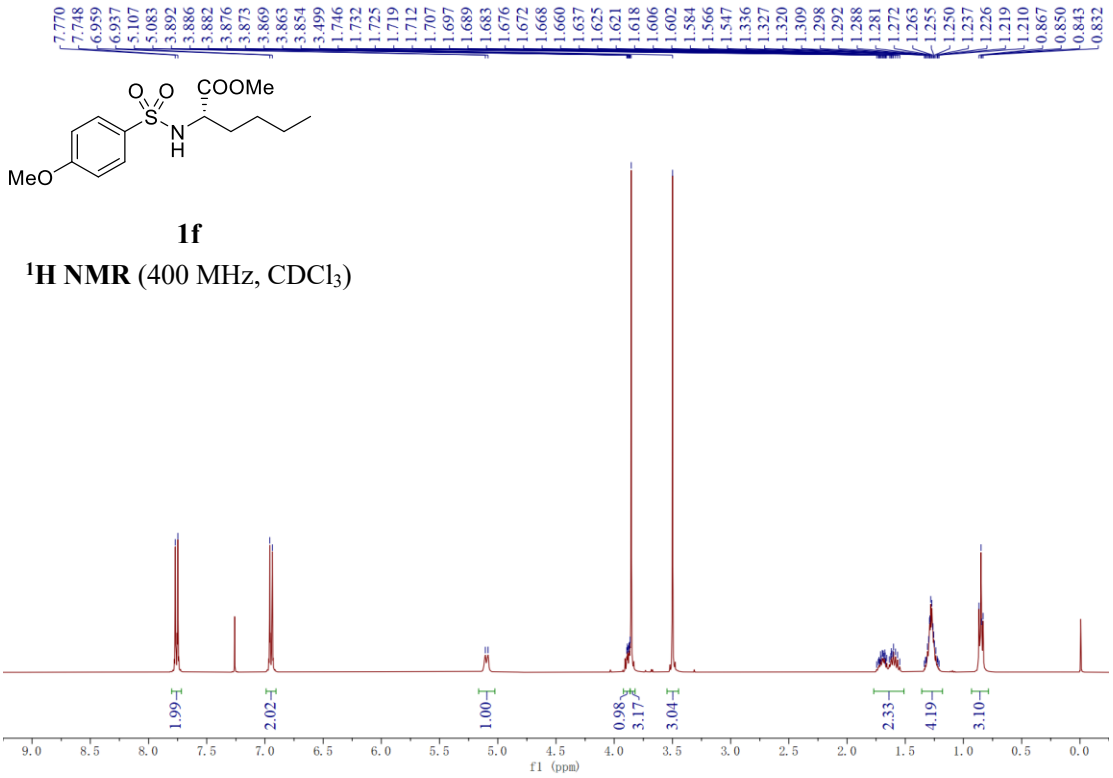
1e

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



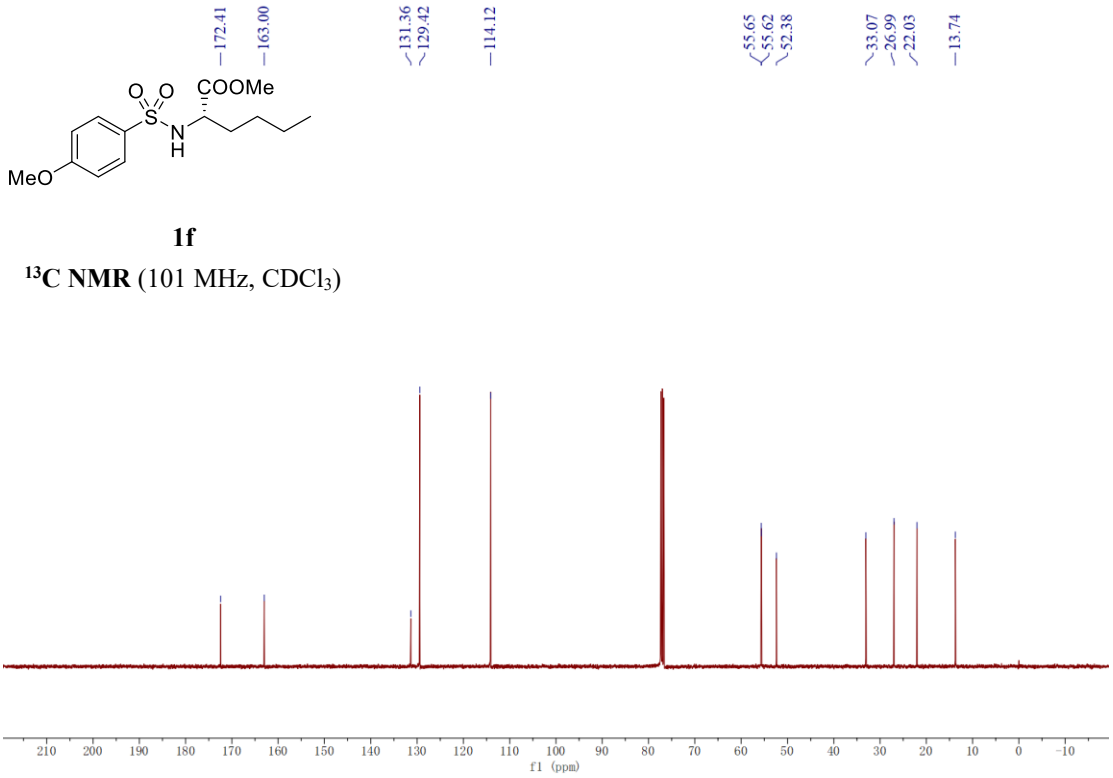
1e

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



1f

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

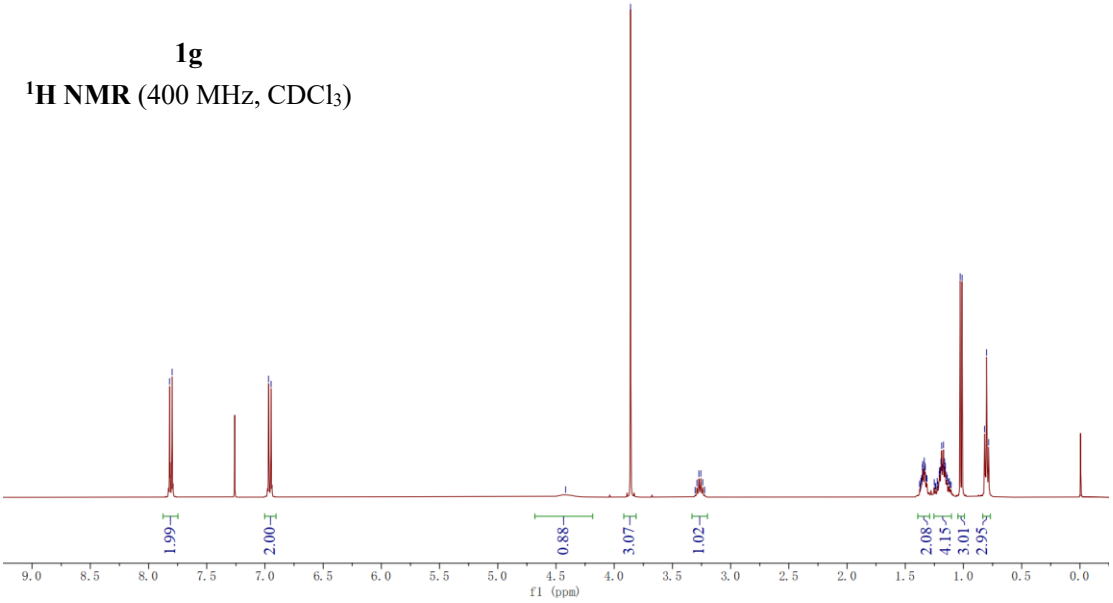


1f

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

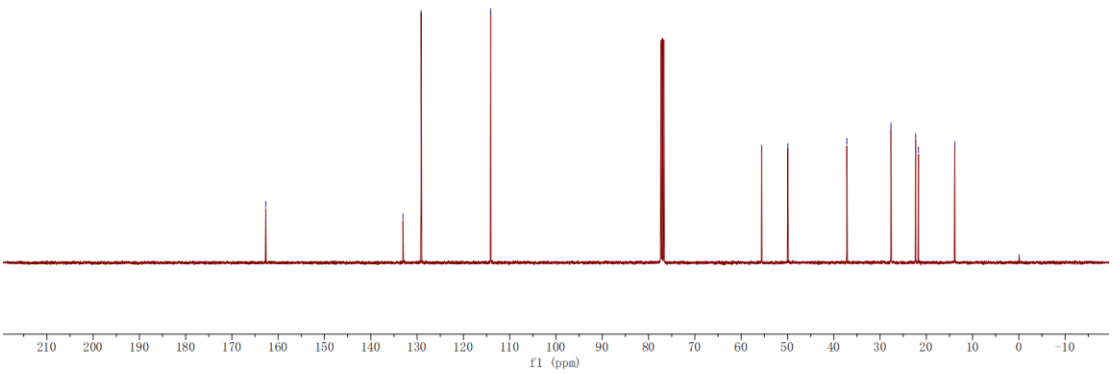
1g

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



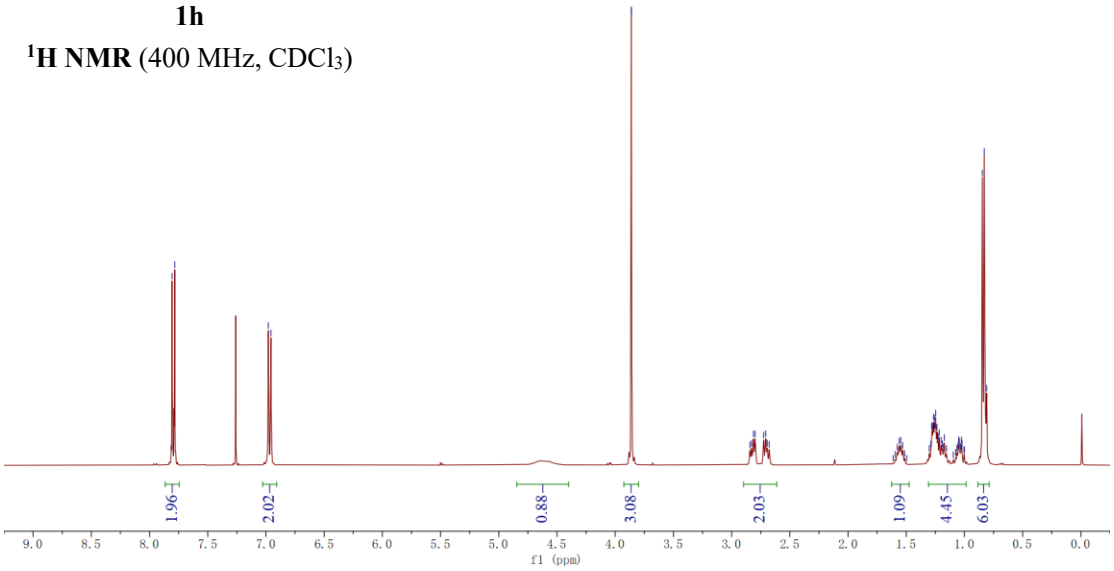
1g

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



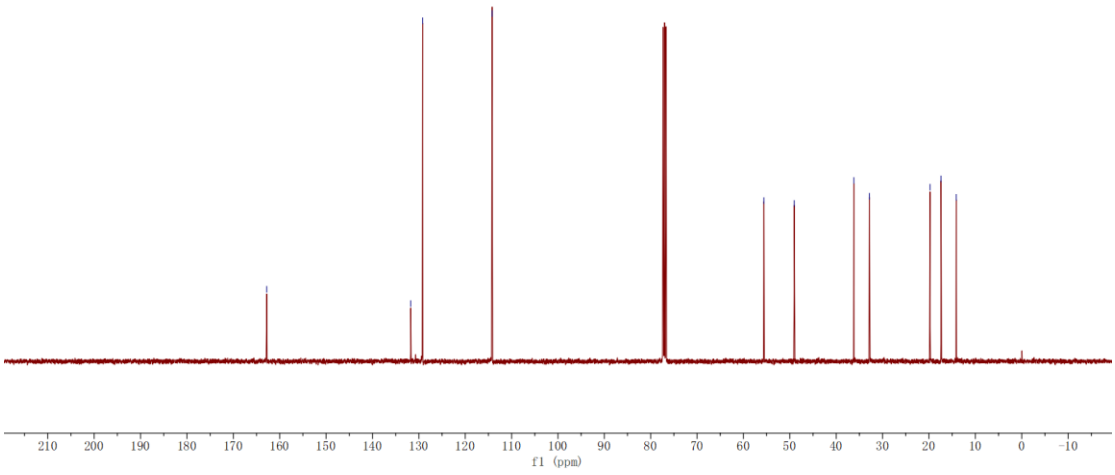
1h

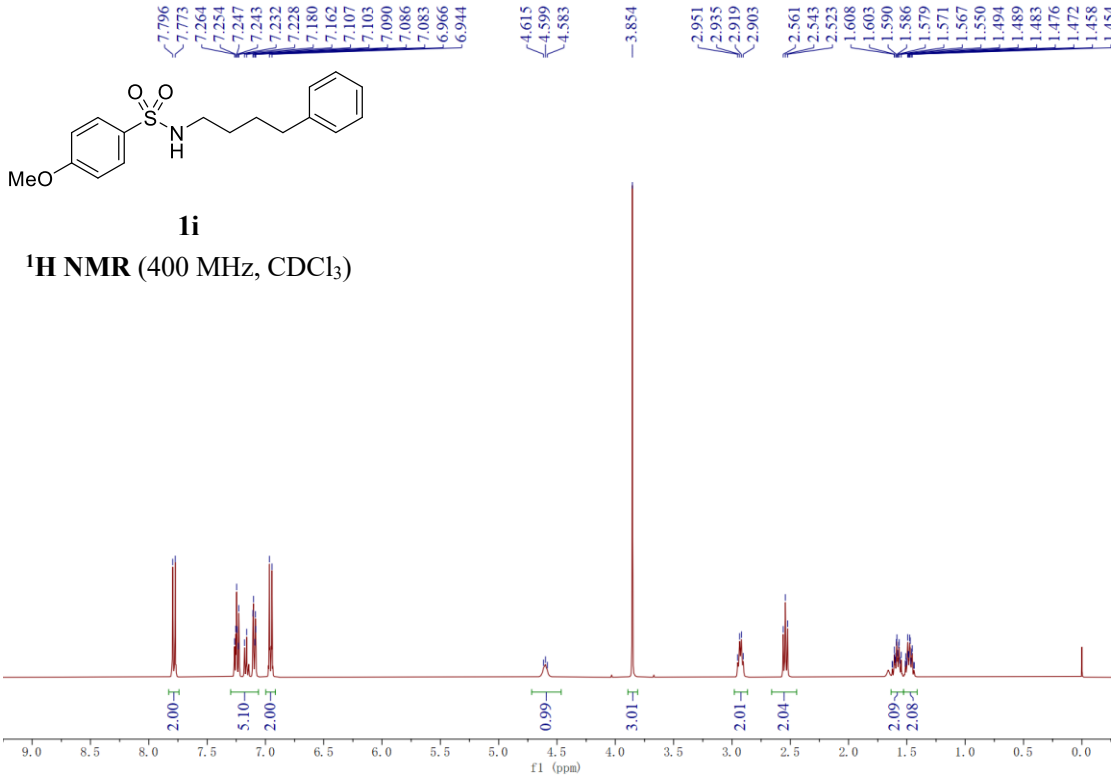
^{1}H NMR (400 MHz, $CDCl_3$)



1h

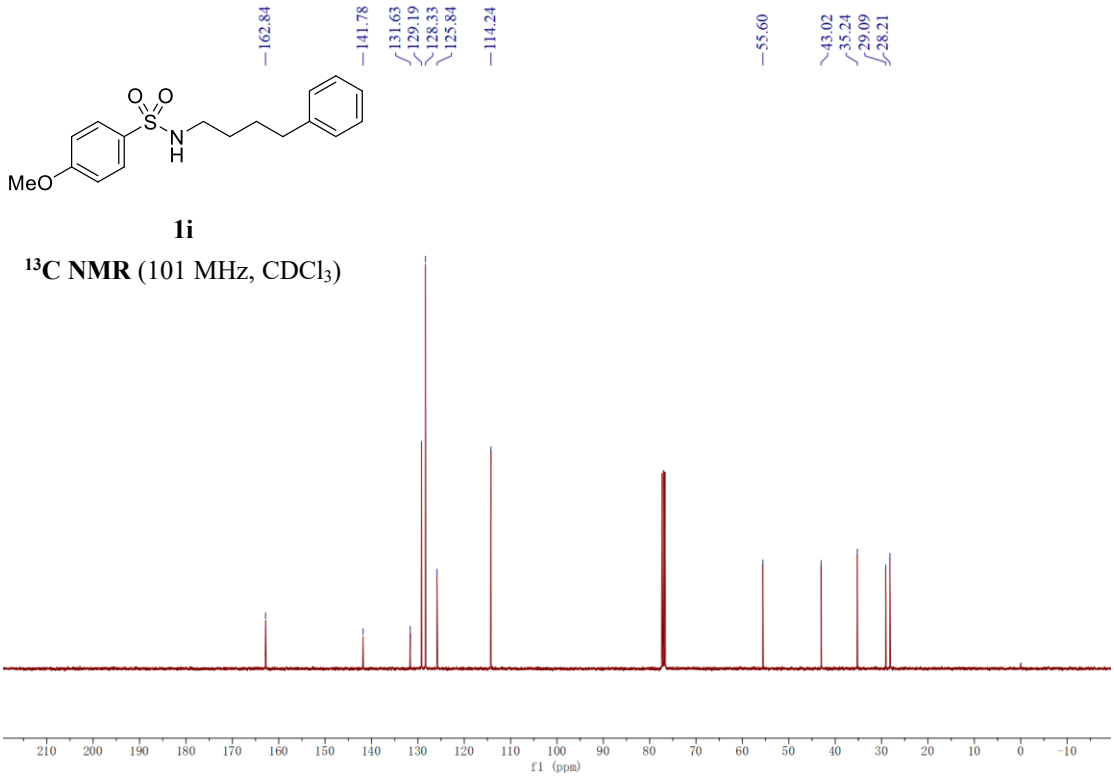
^{13}C NMR (101 MHz, $CDCl_3$)





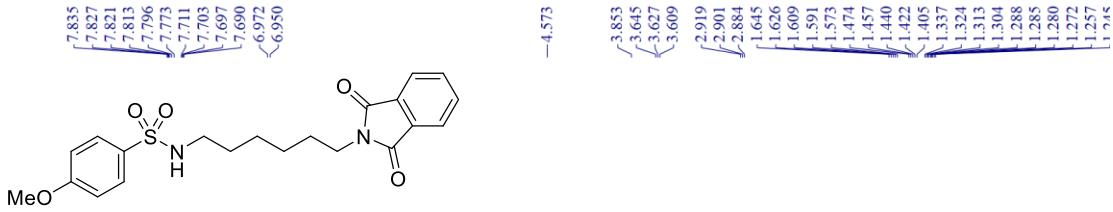
1i

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



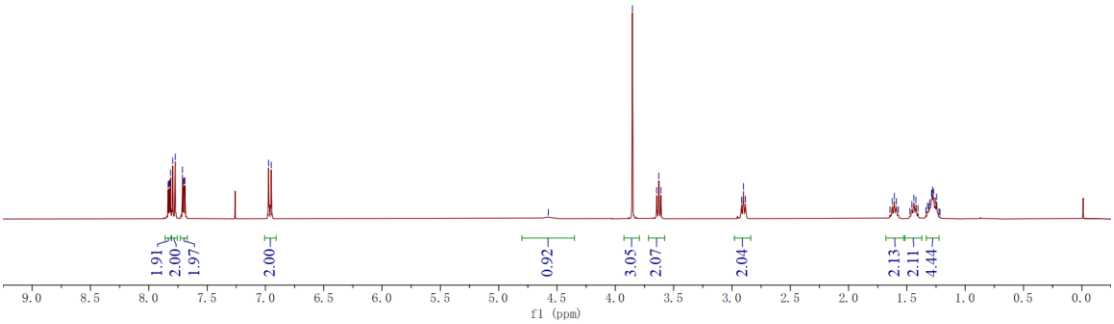
1i

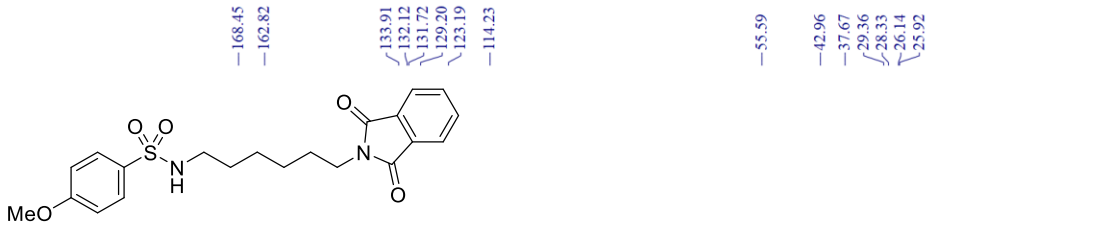
^{13}C NMR (101 MHz, $CDCl_3$)



1j

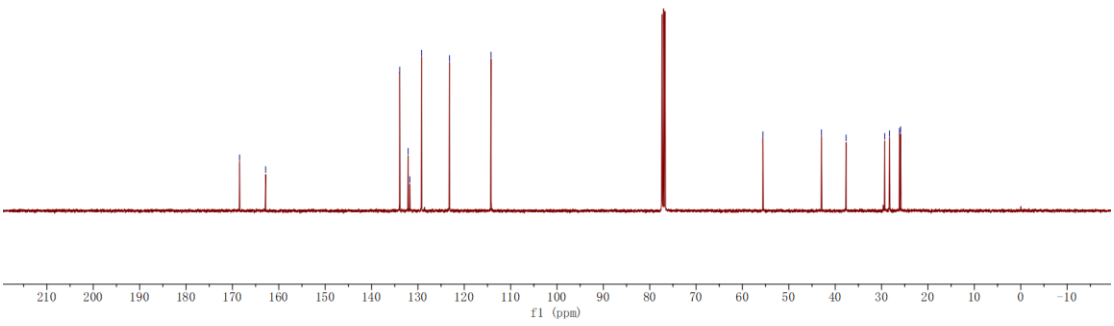
^{1}H NMR (400 MHz, $CDCl_3$)

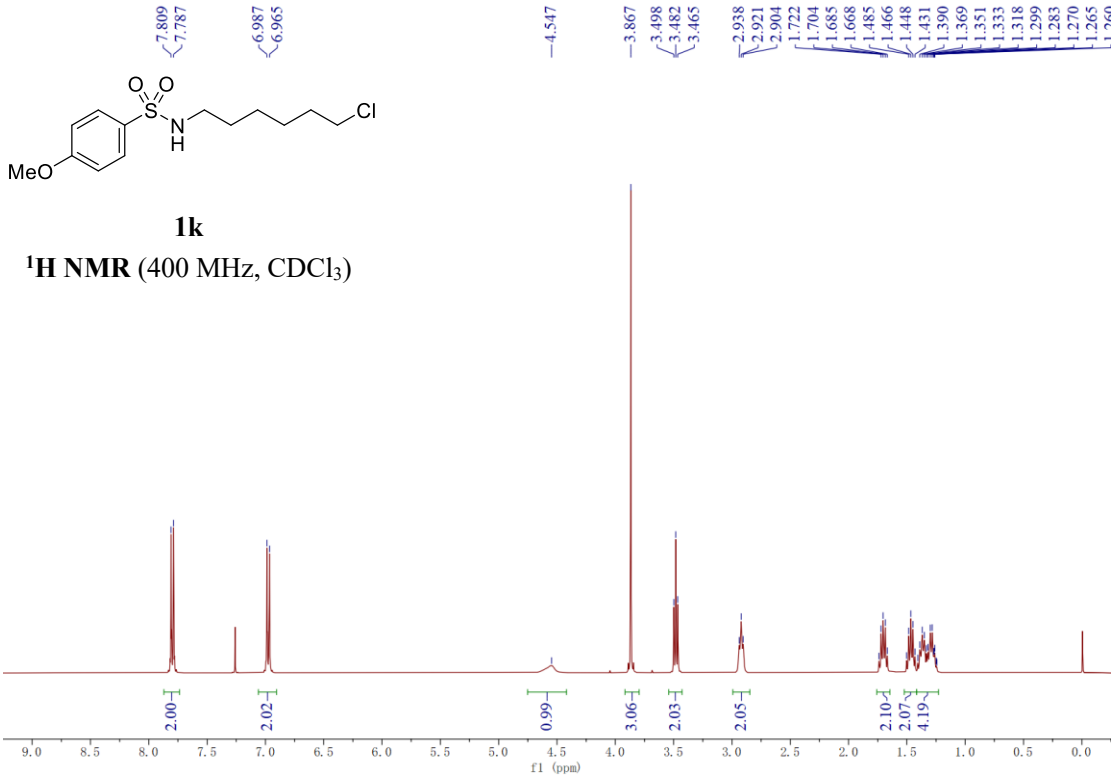




1j

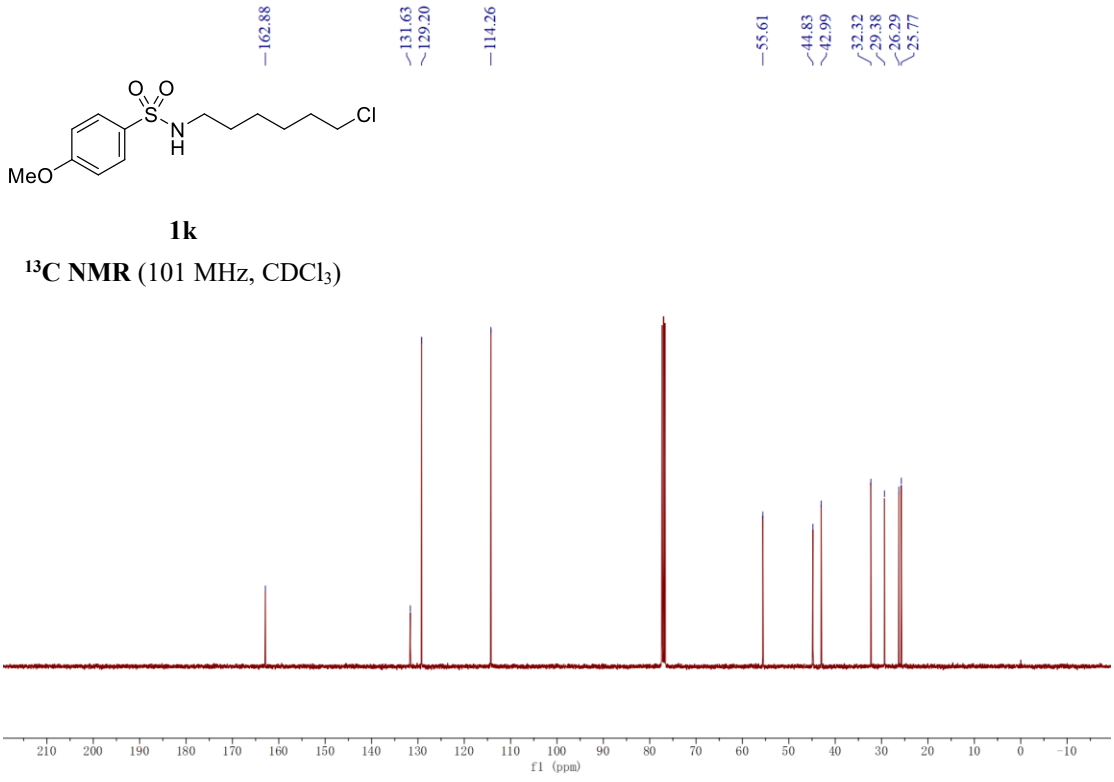
^{13}C NMR (101 MHz, $CDCl_3$)





1k

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

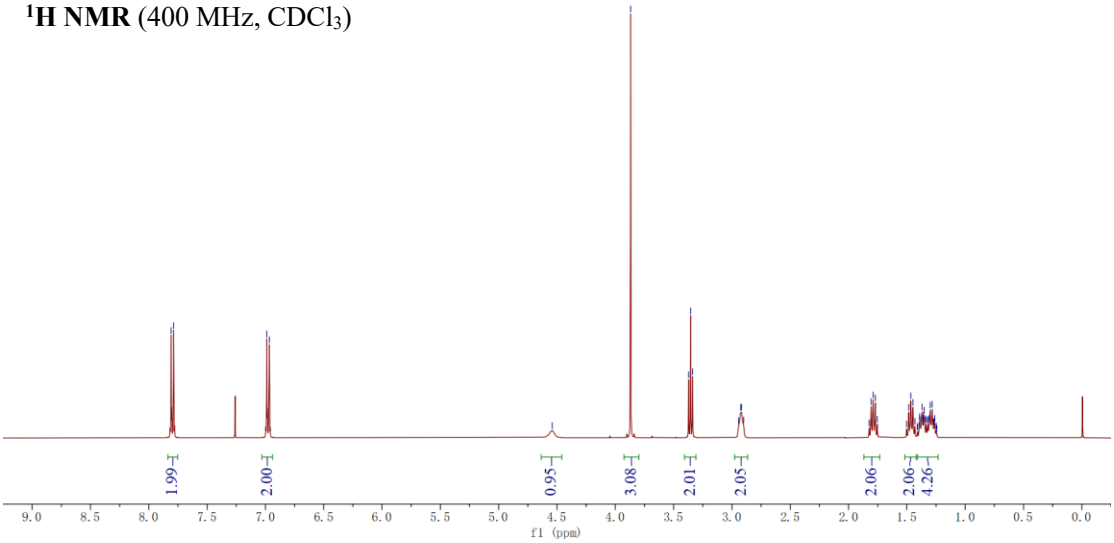


1k

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

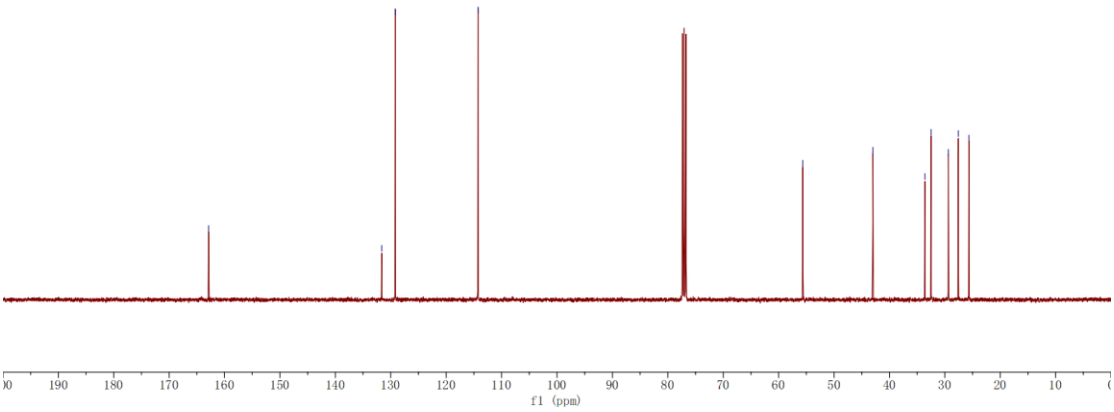
1l

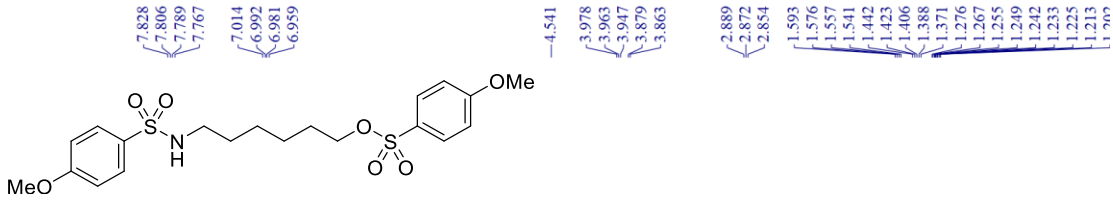
^{1}H NMR (400 MHz, $CDCl_3$)



1l

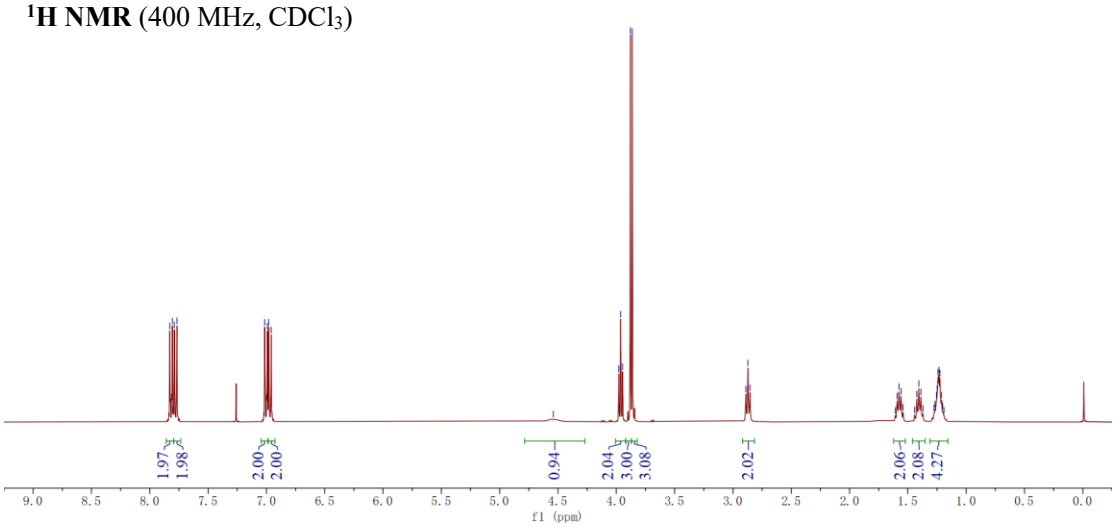
^{13}C NMR (101 MHz, $CDCl_3$)

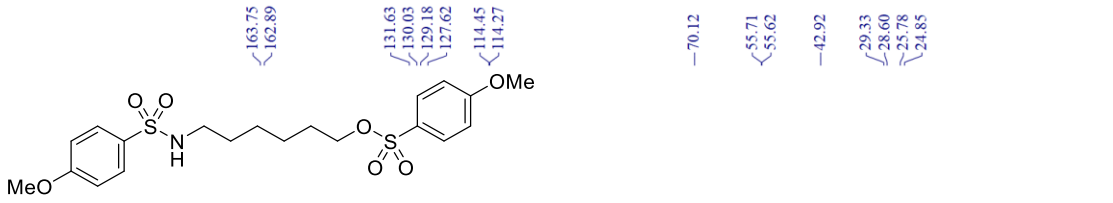




1m

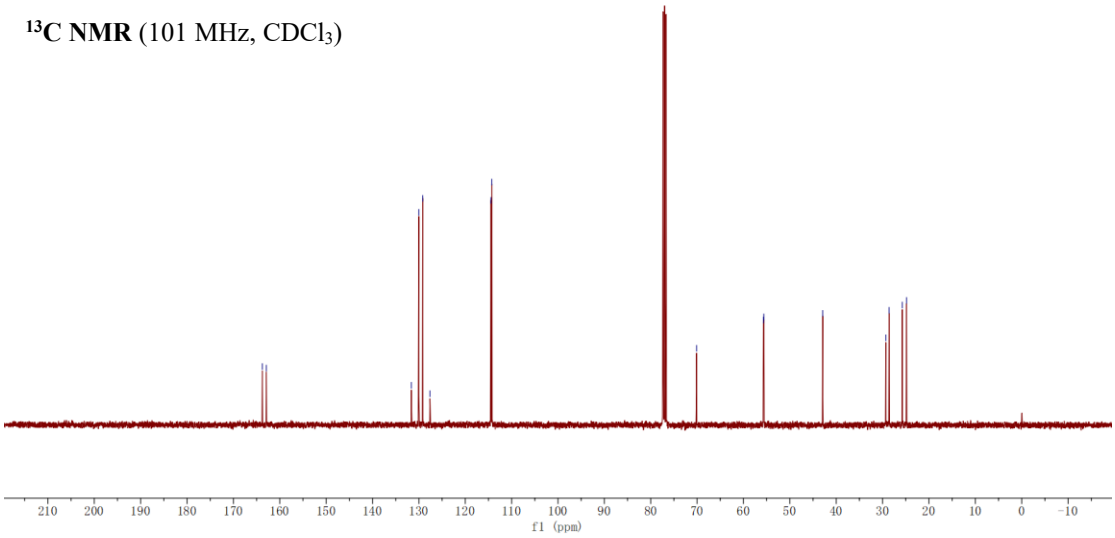
^{1}H NMR (400 MHz, $CDCl_3$)

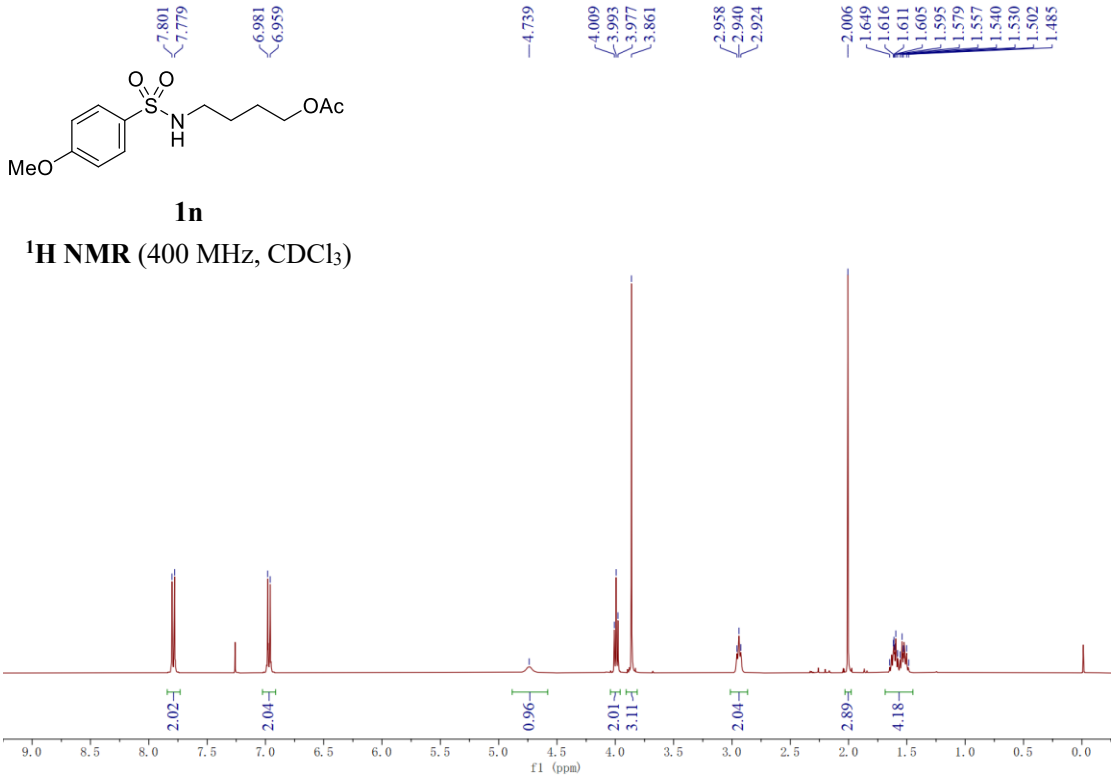




1m

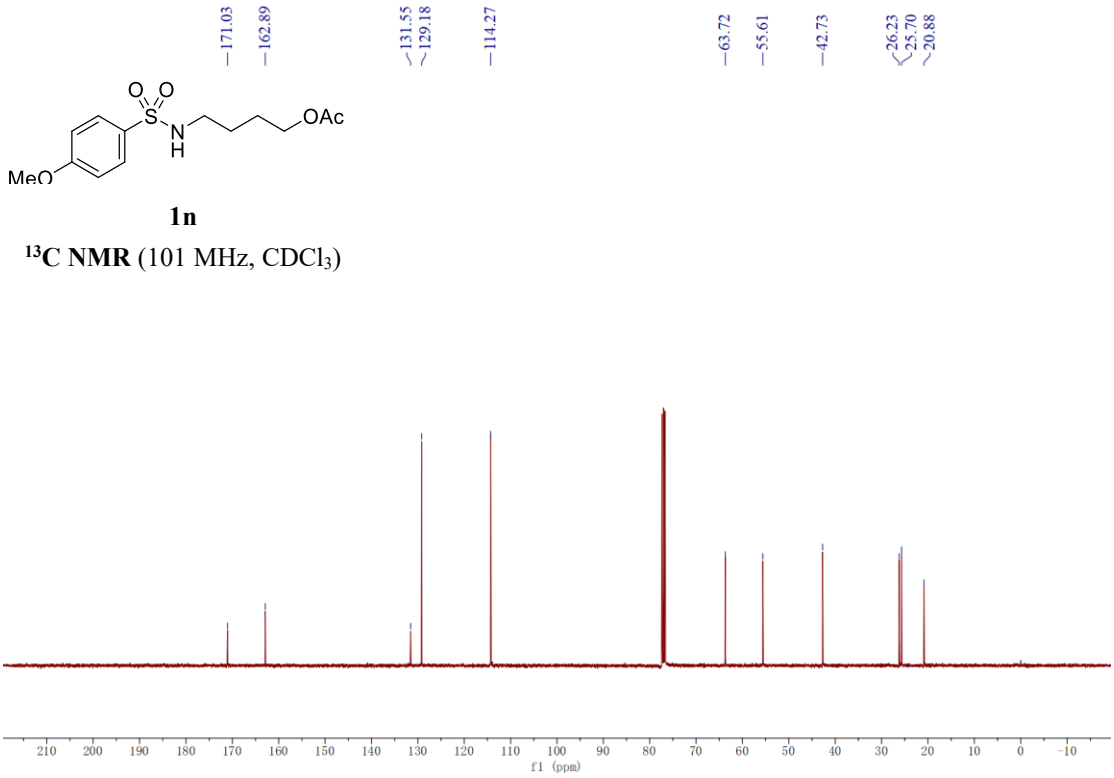
^{13}C NMR (101 MHz, $CDCl_3$)





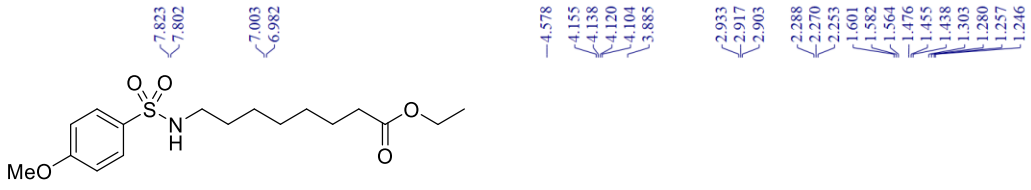
1n

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



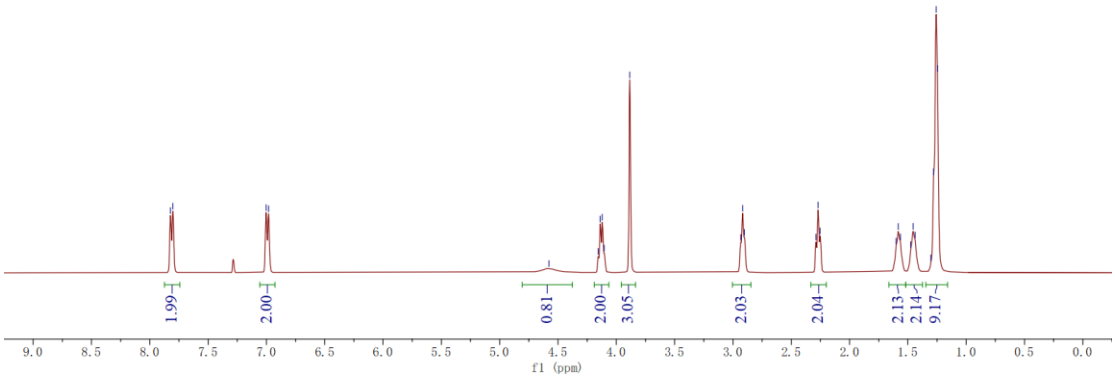
1n

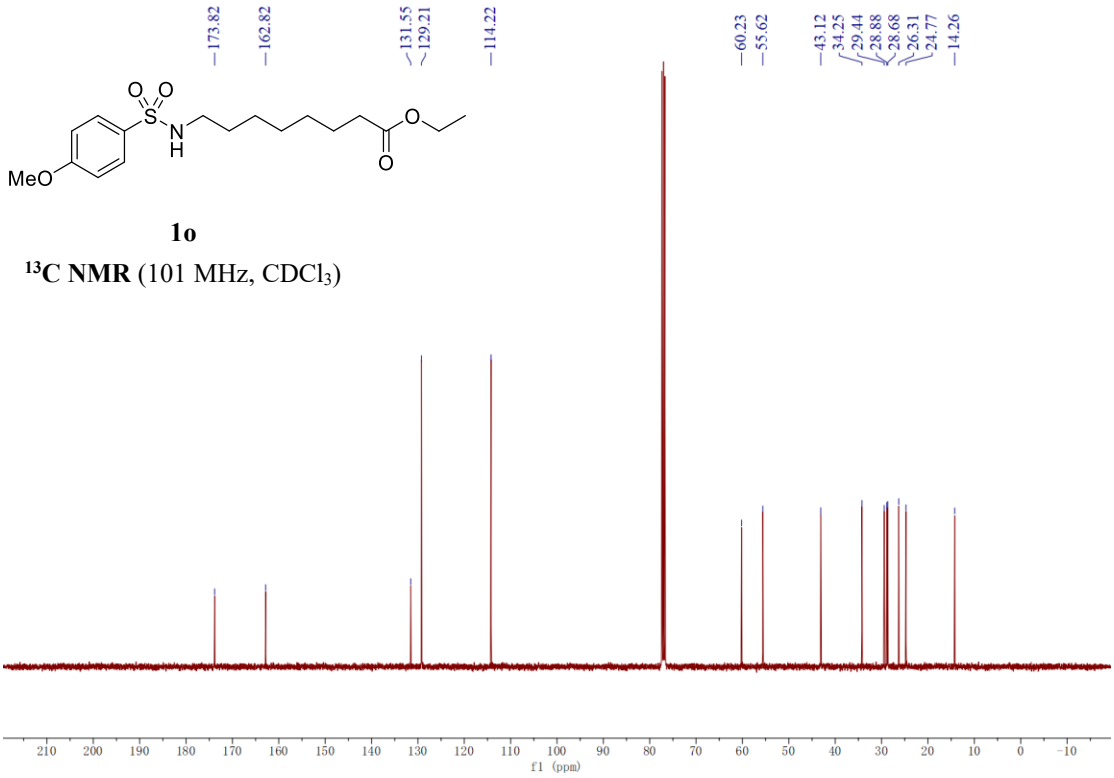
^{13}C NMR (101 MHz, $CDCl_3$)



1o

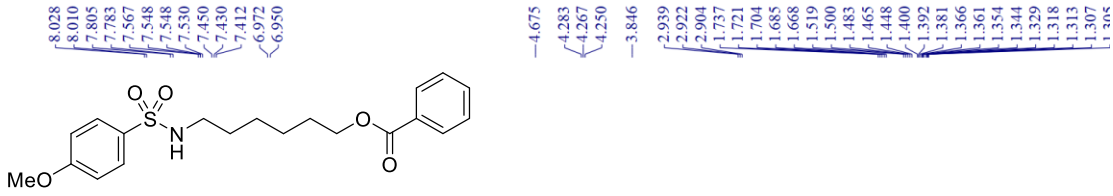
^{1}H NMR (400 MHz, $CDCl_3$)





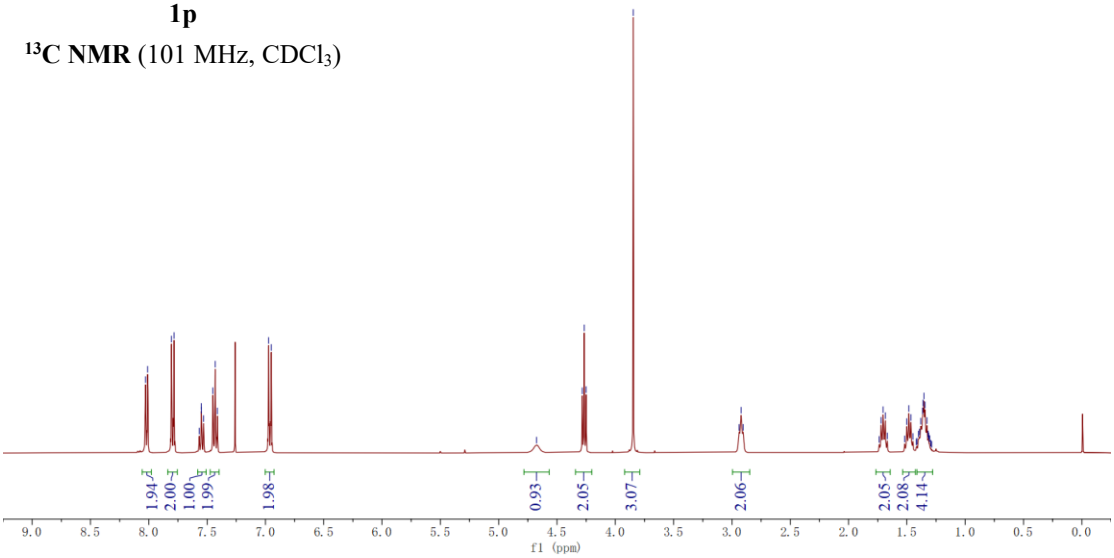
1o

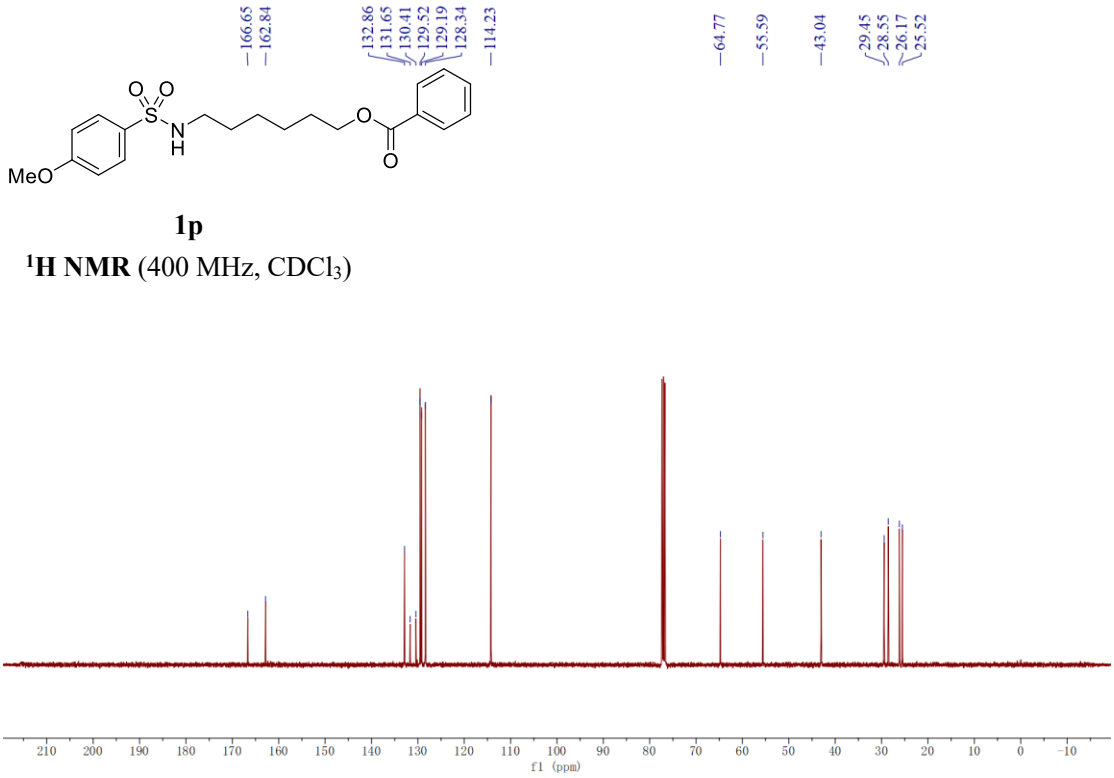
^{13}C NMR (101 MHz, $CDCl_3$)



1p

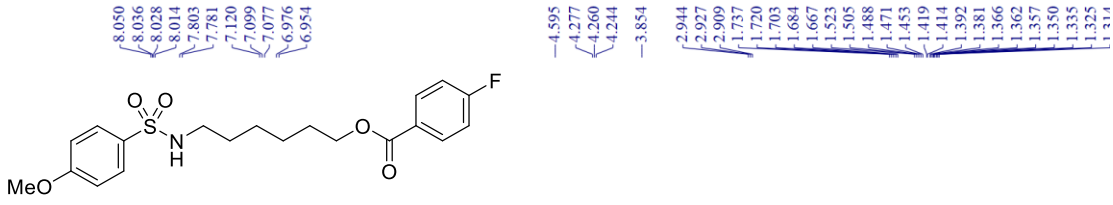
^{13}C NMR (101 MHz, $CDCl_3$)





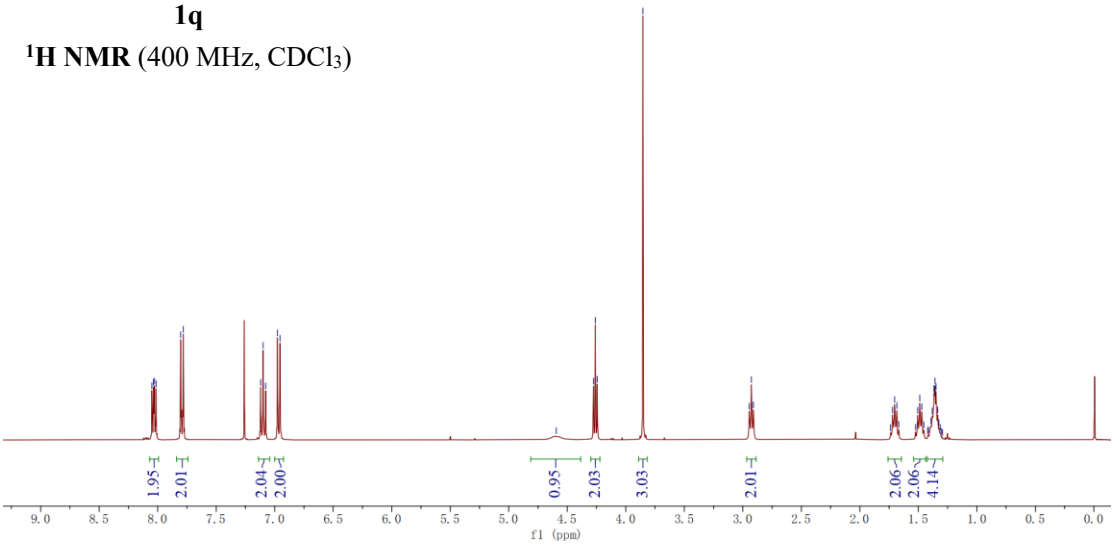
1p

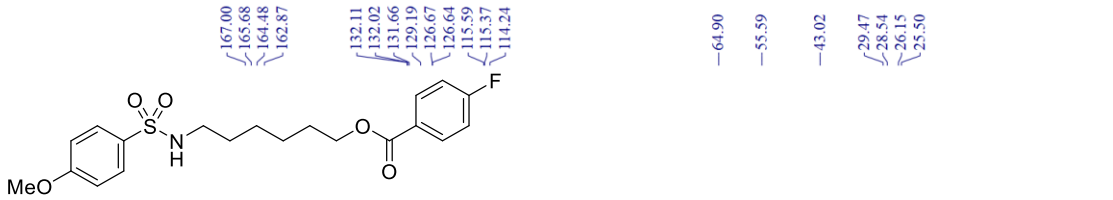
^{1}H NMR (400 MHz, $CDCl_3$)



1q

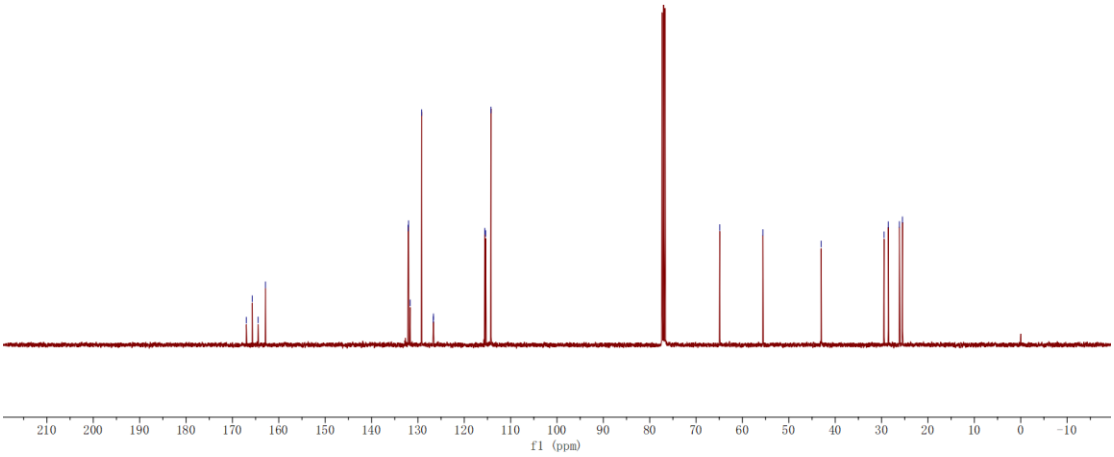
^{1}H NMR (400 MHz, $CDCl_3$)

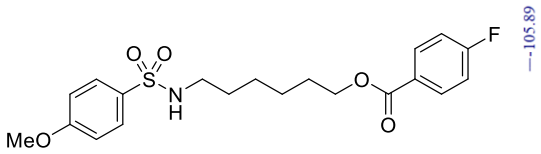




1q

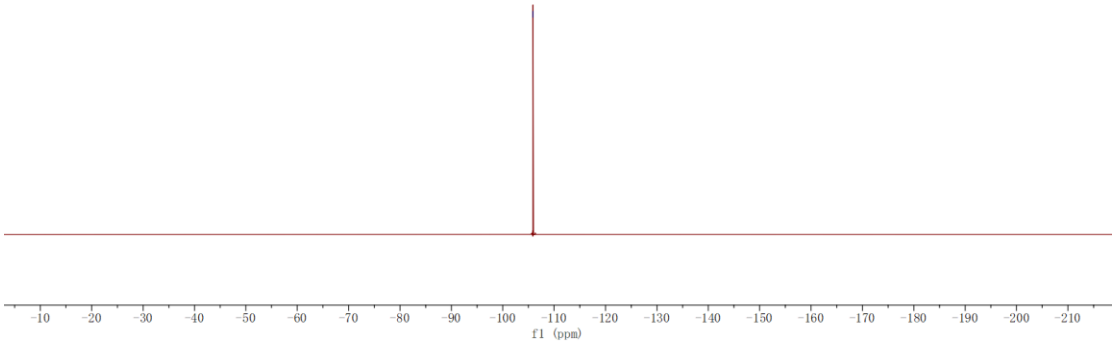
^{13}C NMR (101 MHz, $CDCl_3$)

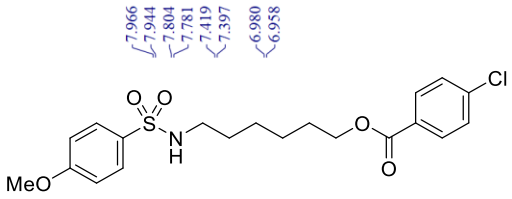




1q

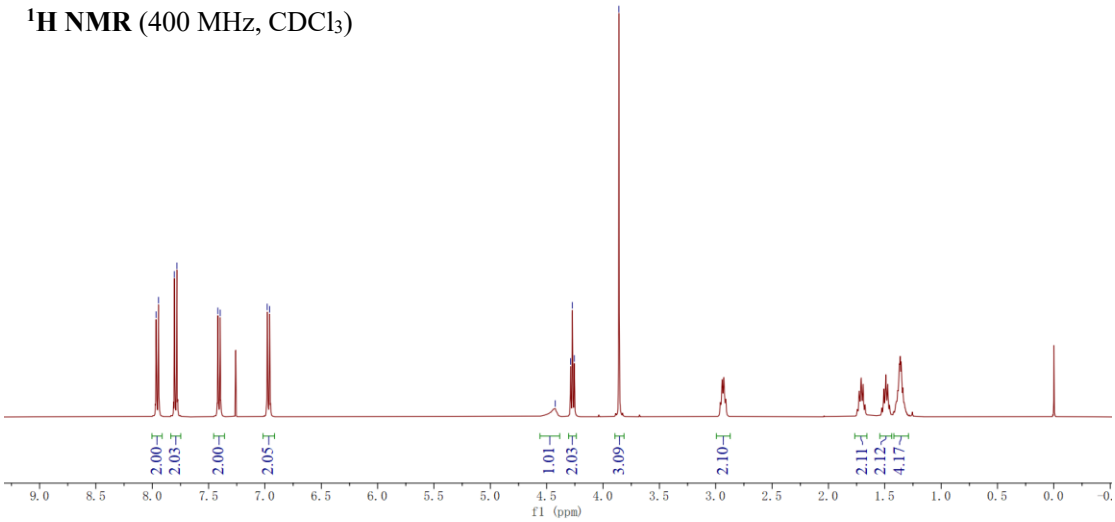
^{19}F NMR (376 MHz, $CDCl_3$)

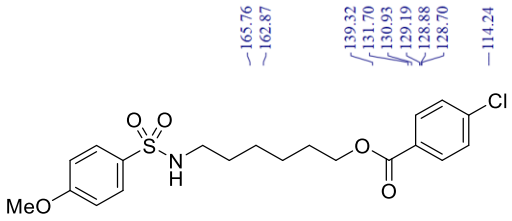




1r

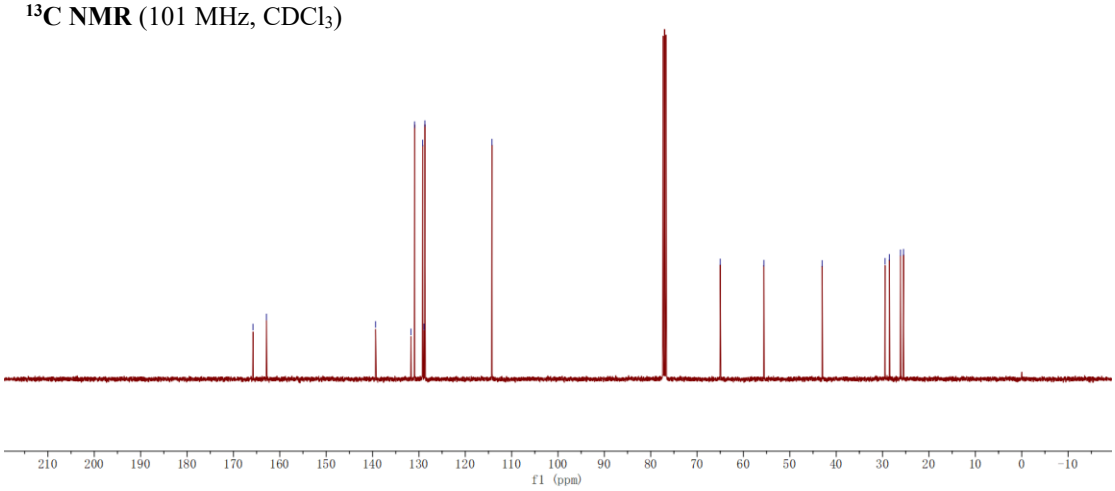
^{1}H NMR (400 MHz, $CDCl_3$)

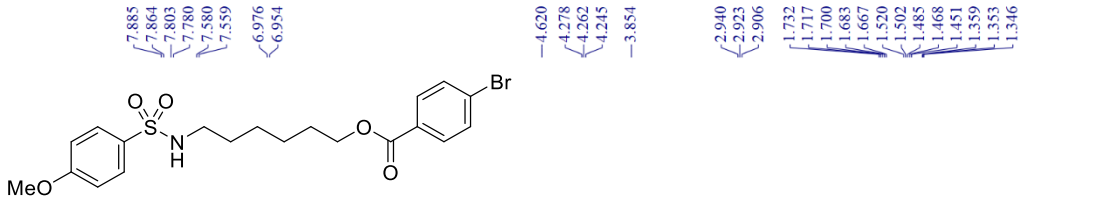




1r

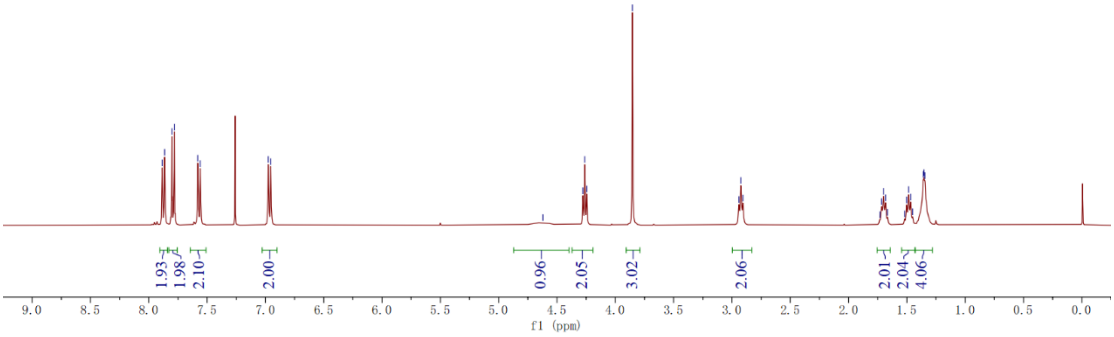
^{13}C NMR (101 MHz, $CDCl_3$)

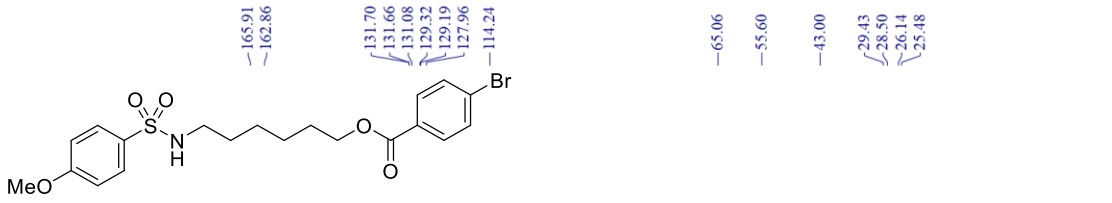




1s

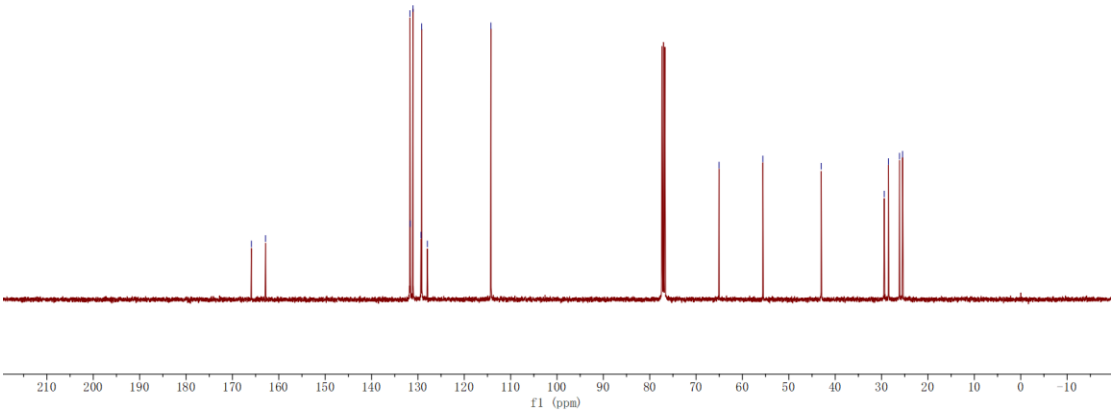
^{1}H NMR (400 MHz, $CDCl_3$)

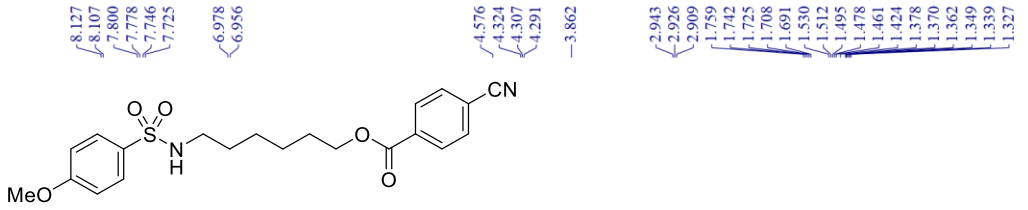




1s

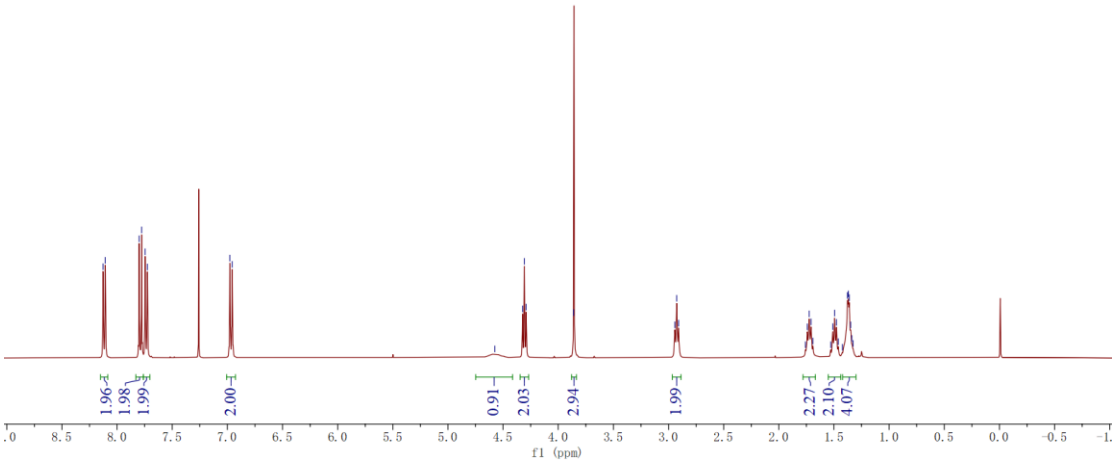
^{13}C NMR (101 MHz, $CDCl_3$)

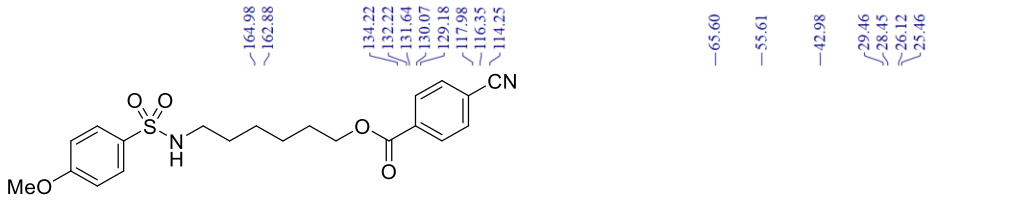




1t

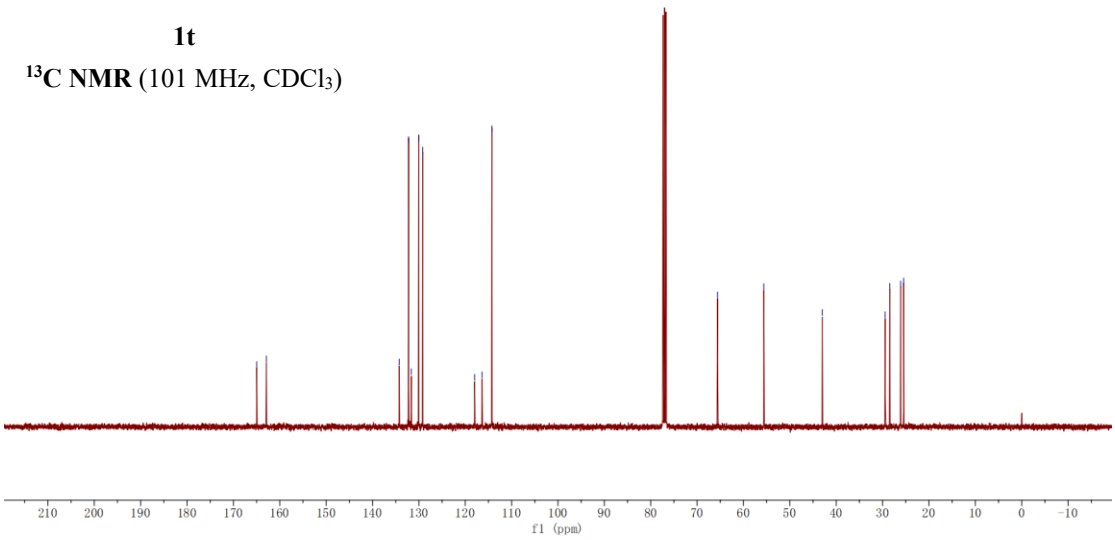
^{1}H NMR (400 MHz, $CDCl_3$)

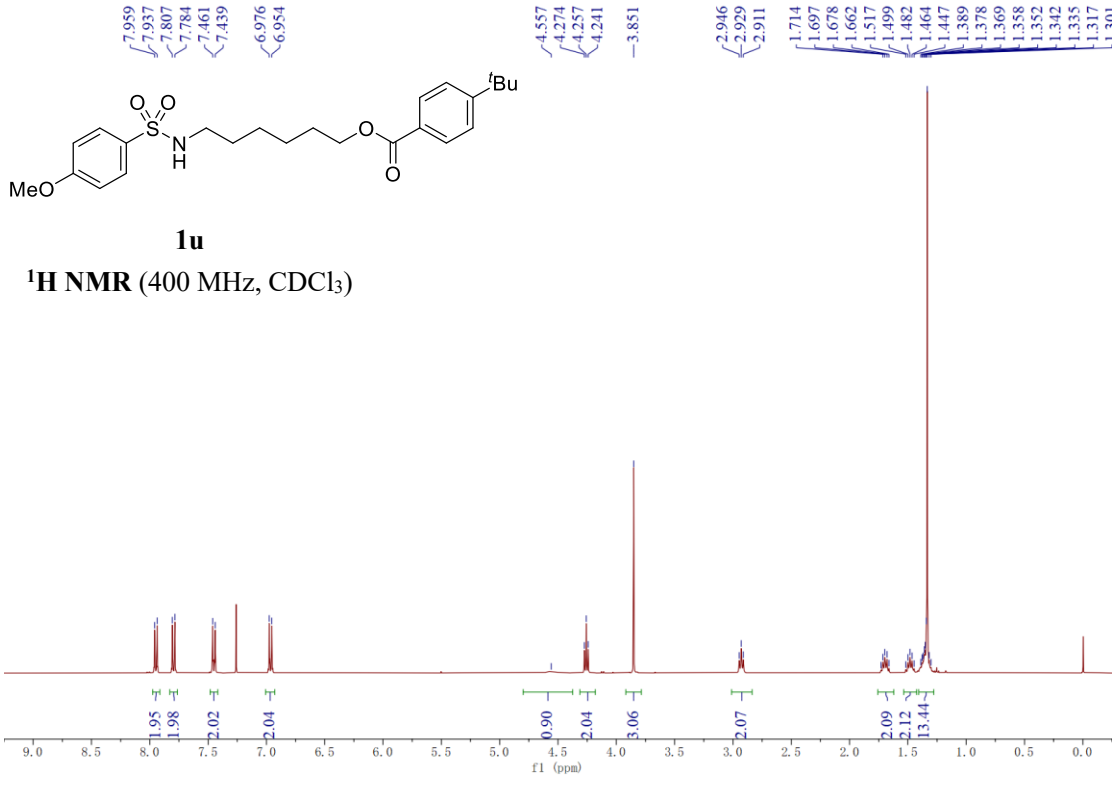




1t

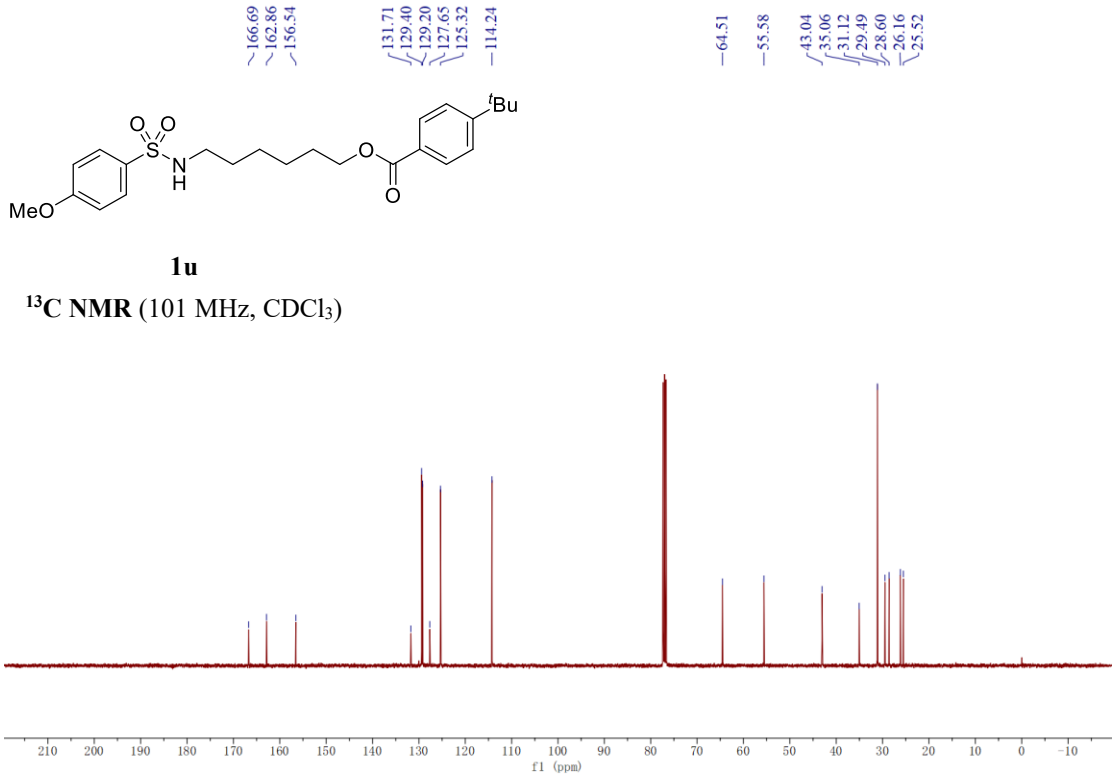
^{13}C NMR (101 MHz, $CDCl_3$)





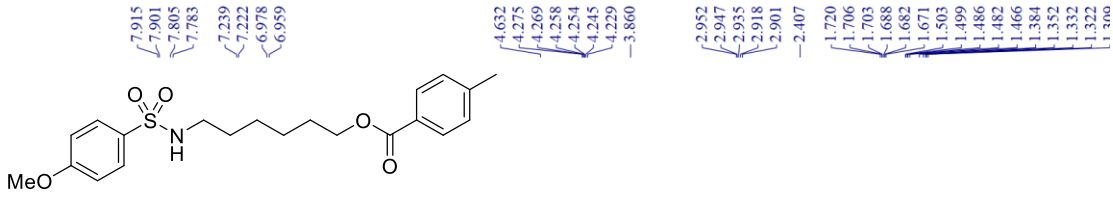
1u

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



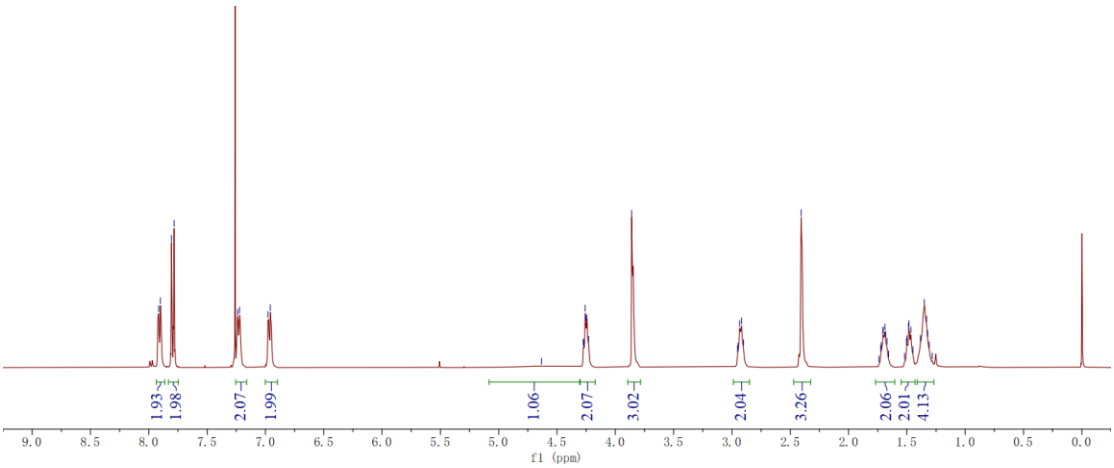
1u

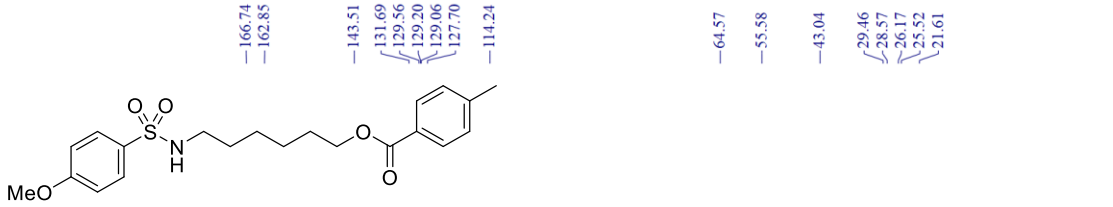
^{13}C NMR (101 MHz, $CDCl_3$)



1v

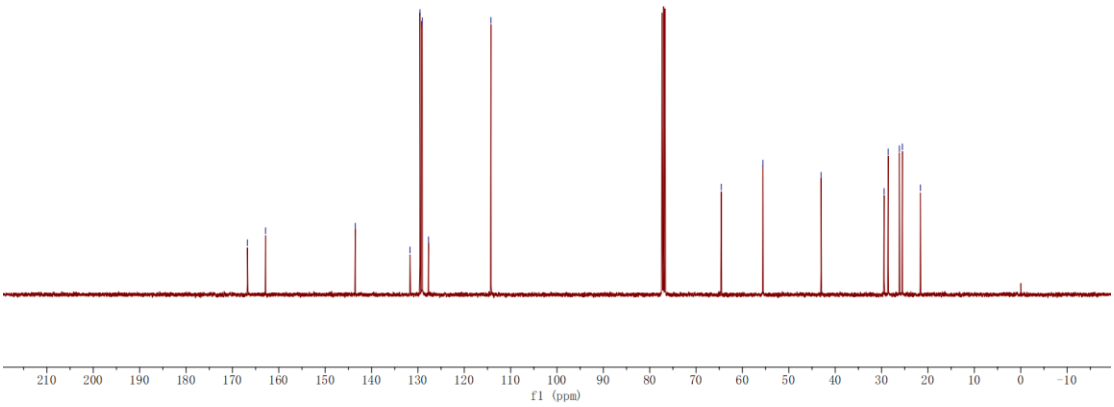
^{1}H NMR (400 MHz, $CDCl_3$)

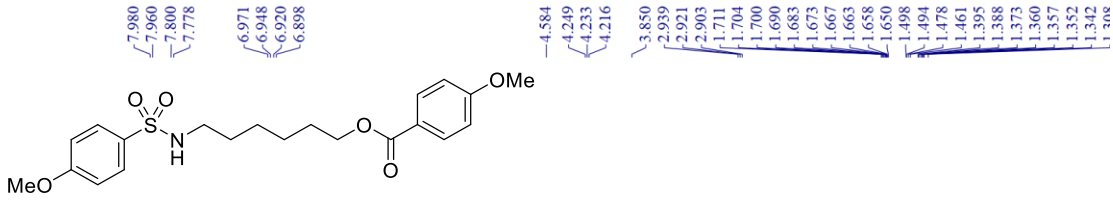




1v

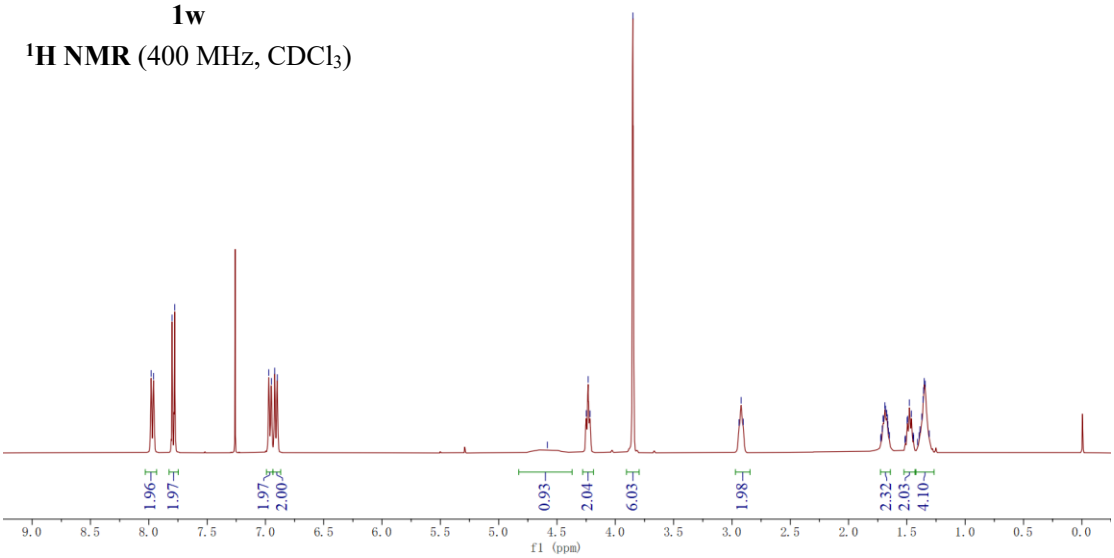
^{13}C NMR (101 MHz, $CDCl_3$)

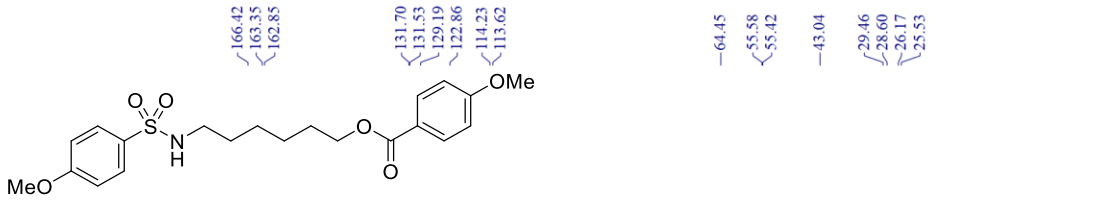




1w

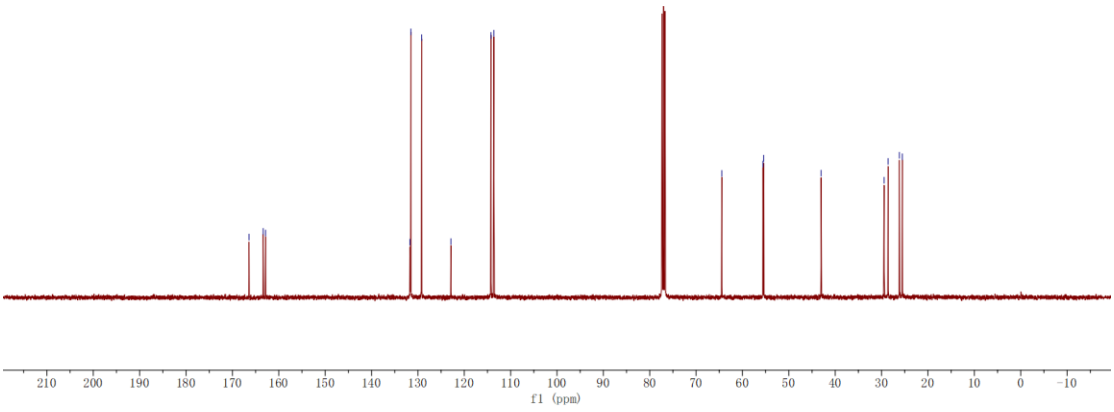
^{1}H NMR (400 MHz, $CDCl_3$)

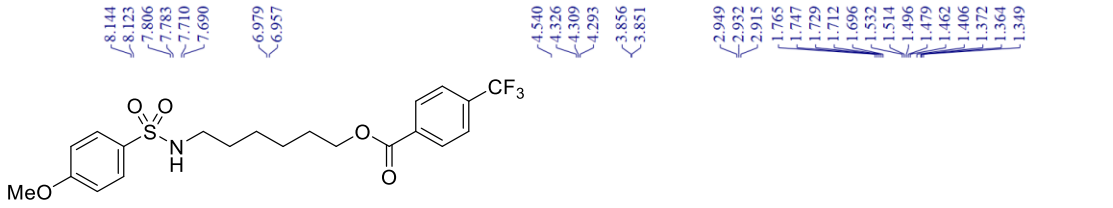




1w

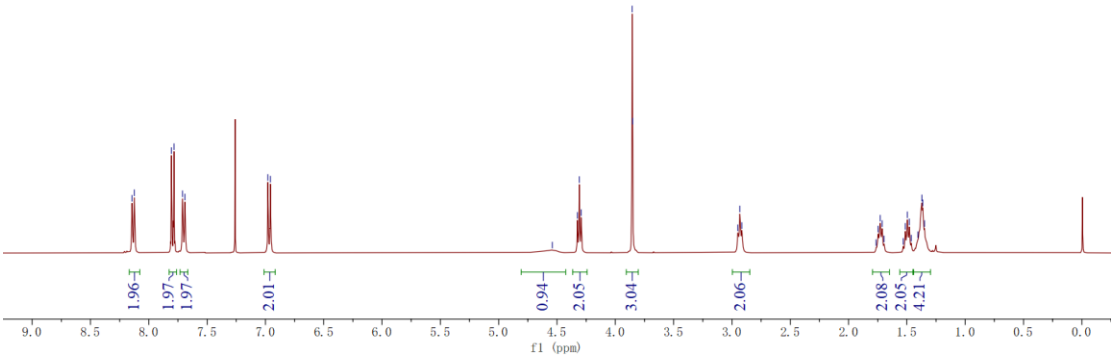
^{13}C NMR (101 MHz, $CDCl_3$)

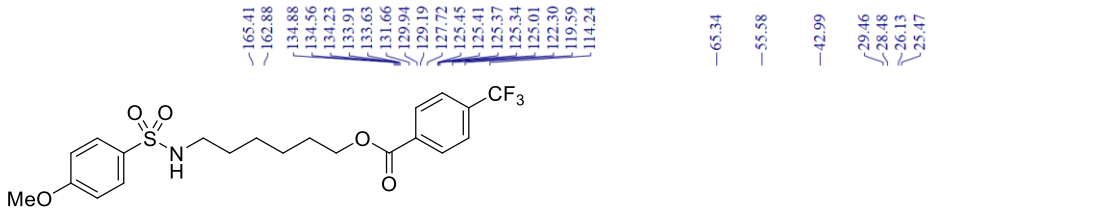




1x

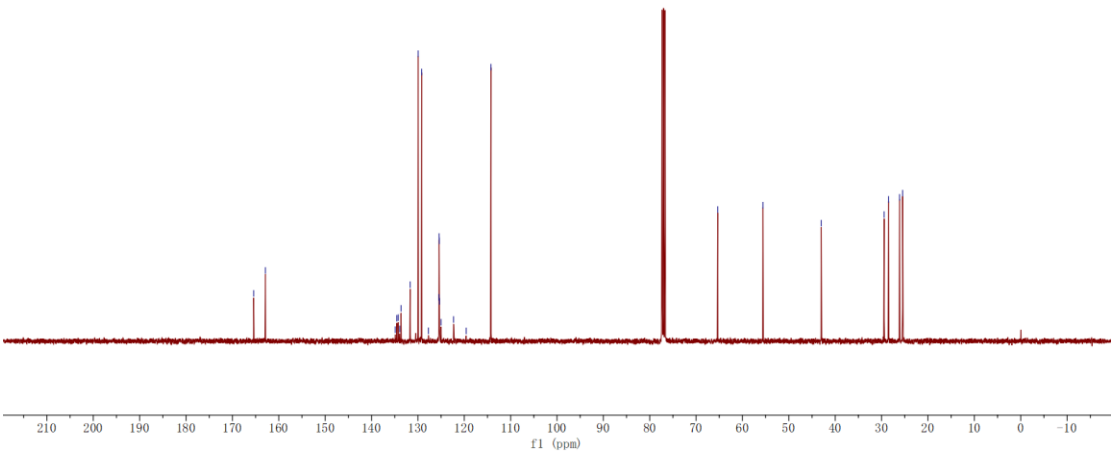
^{1}H NMR (400 MHz, $CDCl_3$)

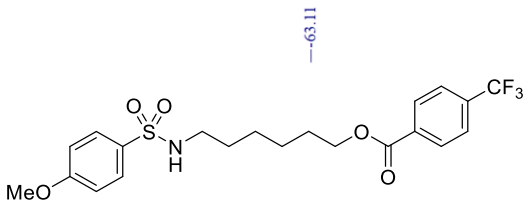




1x

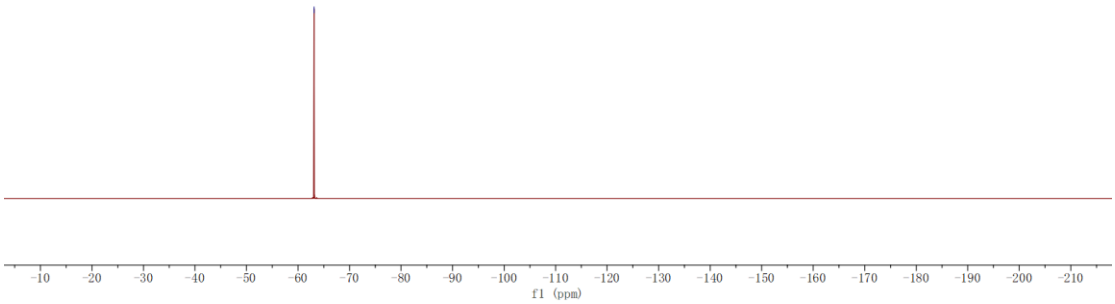
^{13}C NMR (101 MHz, $CDCl_3$)

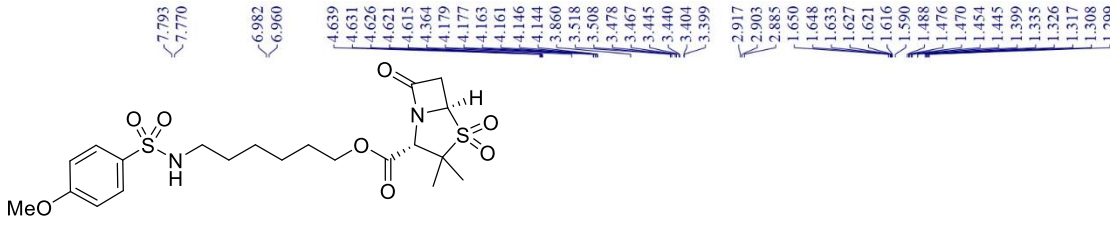




1x

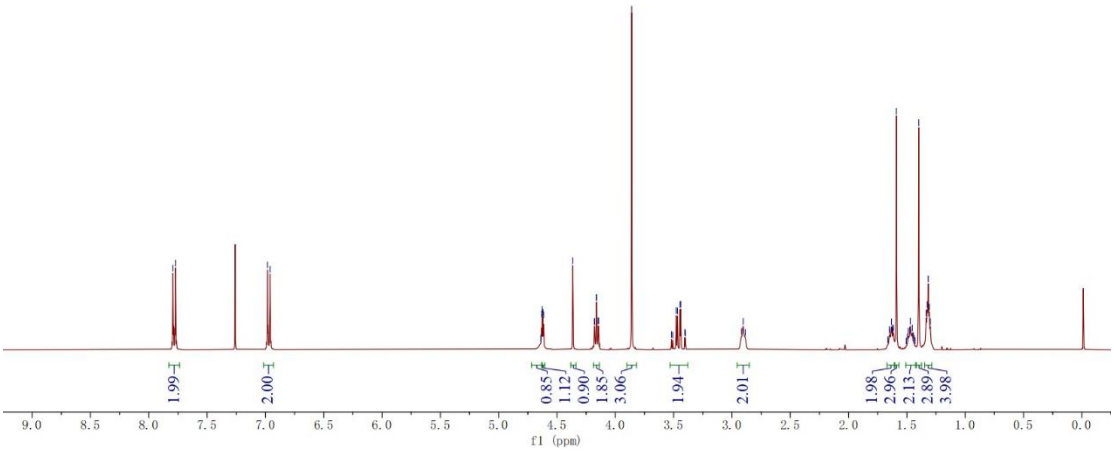
^{19}F NMR (376 MHz, $CDCl_3$)

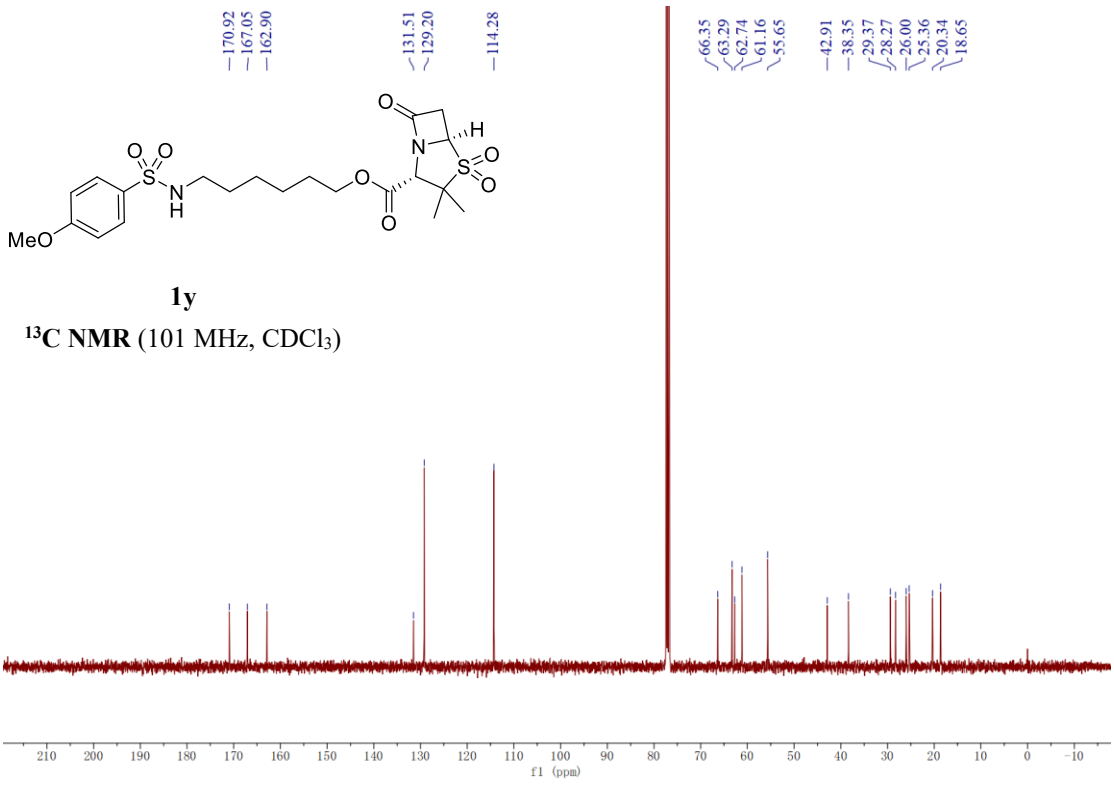




1y

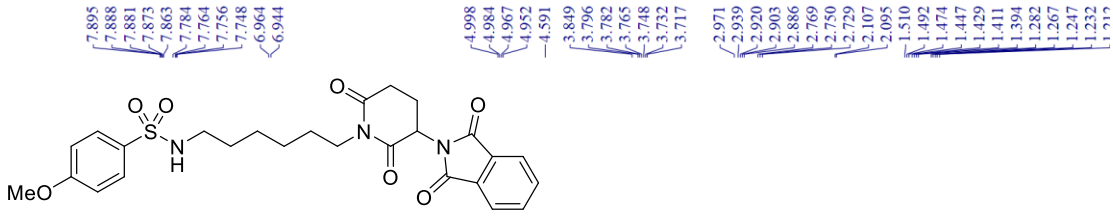
^{1}H NMR (400 MHz, $CDCl_3$)





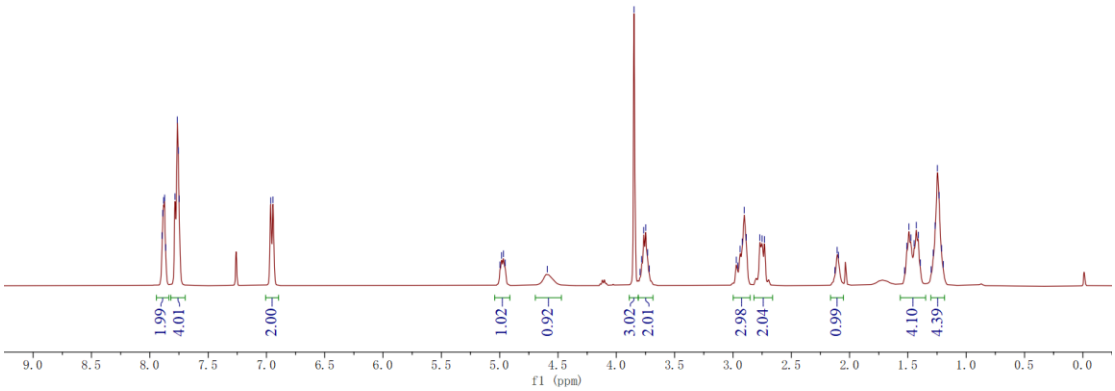
1y

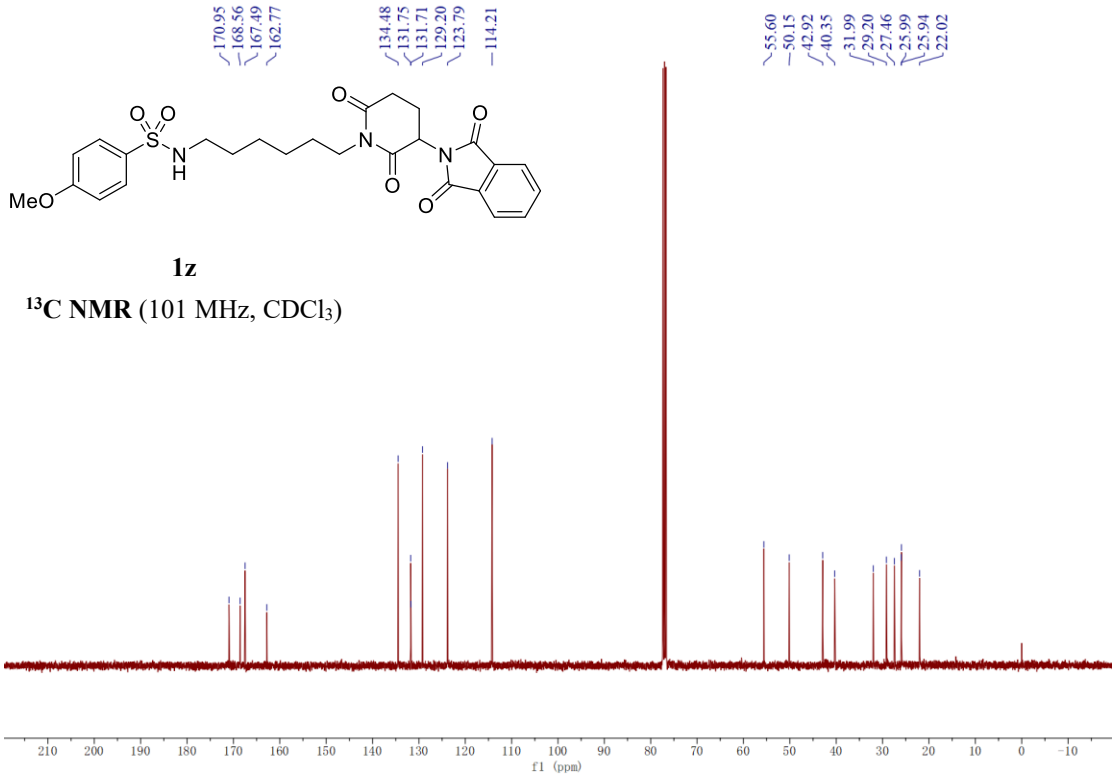
^{13}C NMR (101 MHz, $CDCl_3$)



1z

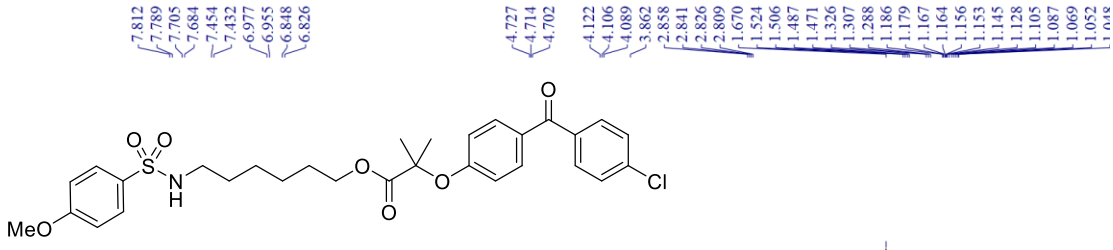
^{1}H NMR (400 MHz, $CDCl_3$)





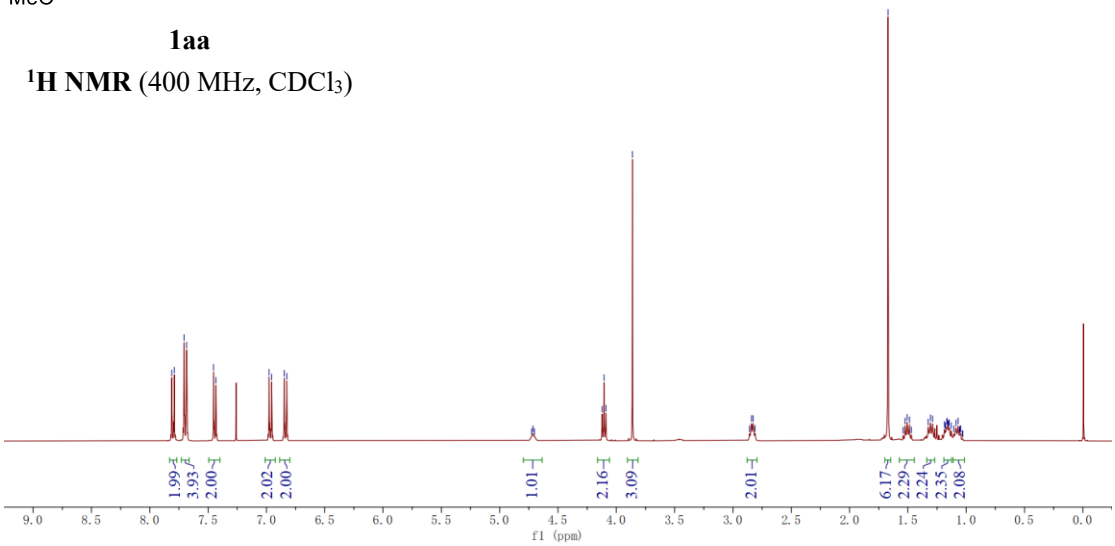
1z

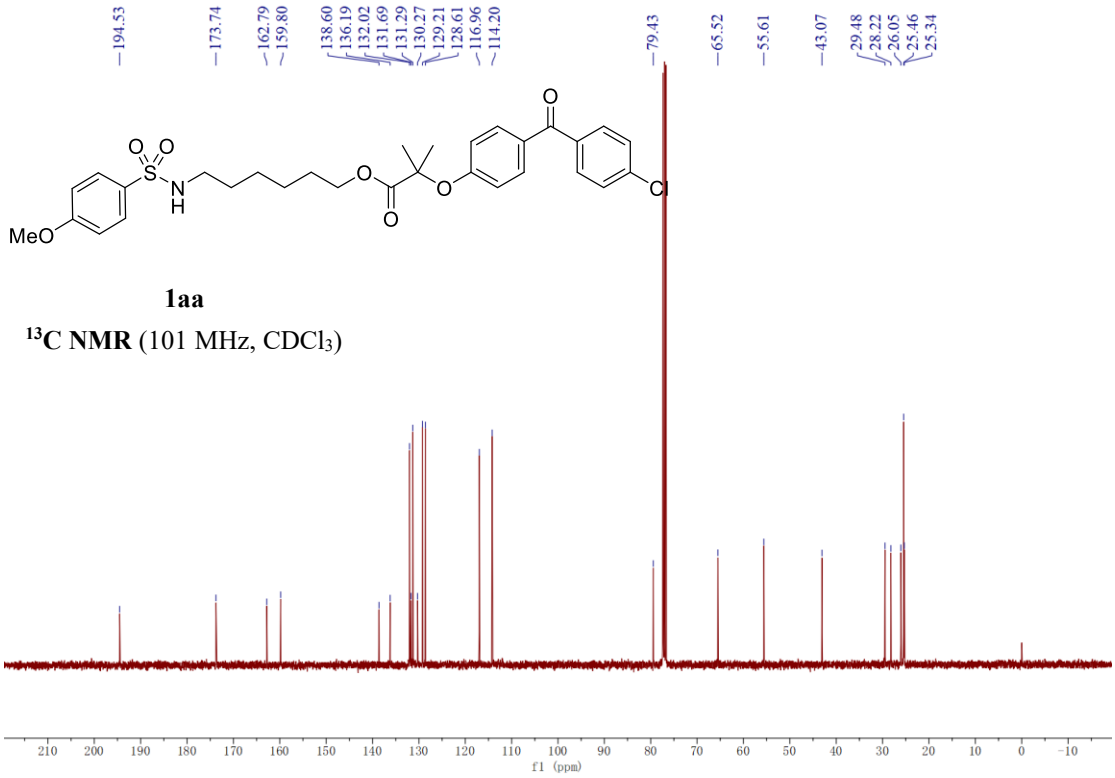
^{13}C NMR (101 MHz, $CDCl_3$)



1aa

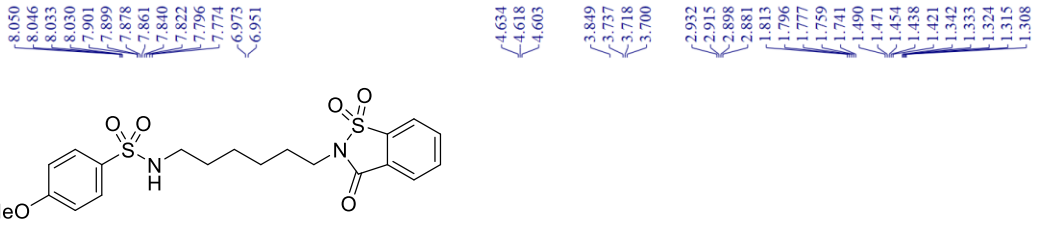
^{1}H NMR (400 MHz, $CDCl_3$)





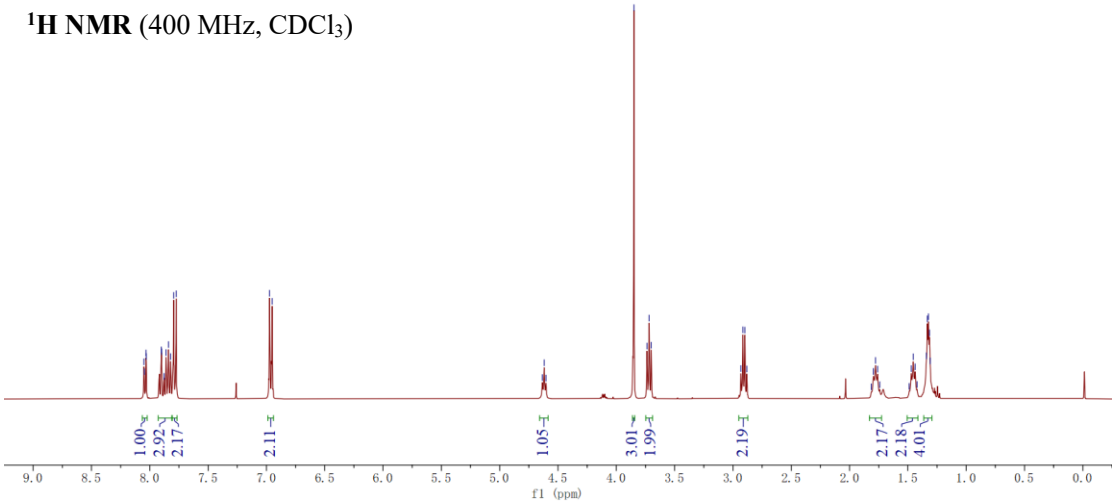
1aa

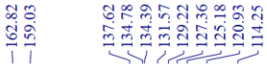
^{13}C NMR (101 MHz, $CDCl_3$)

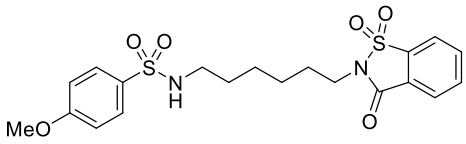


1ab

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

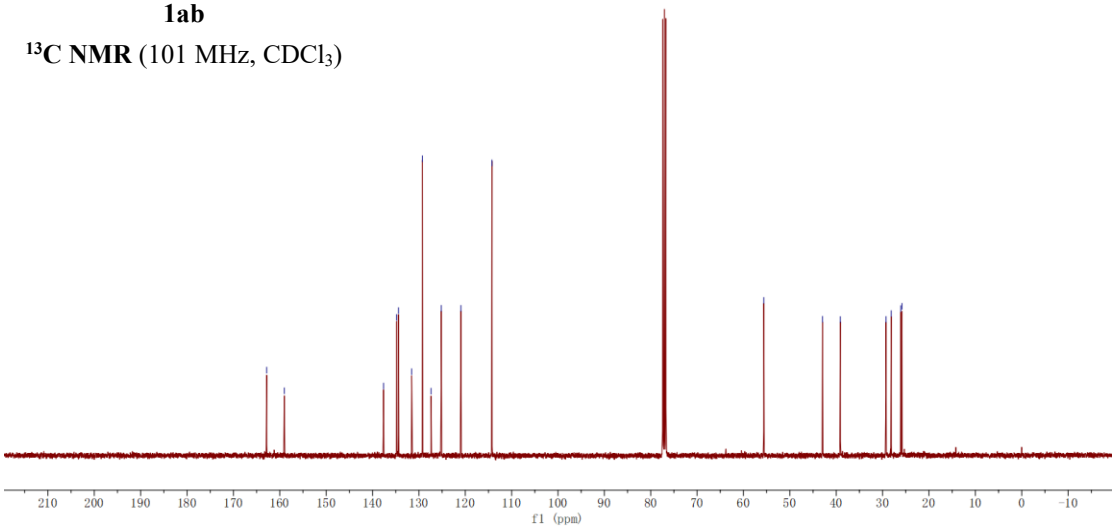


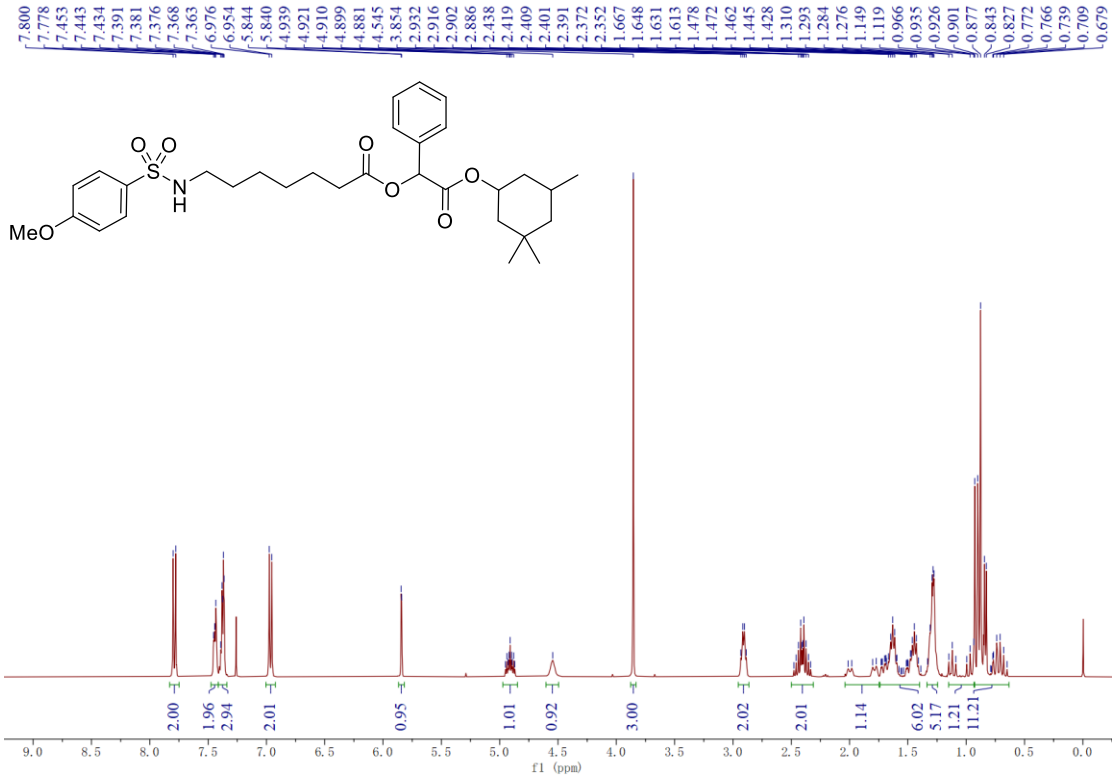


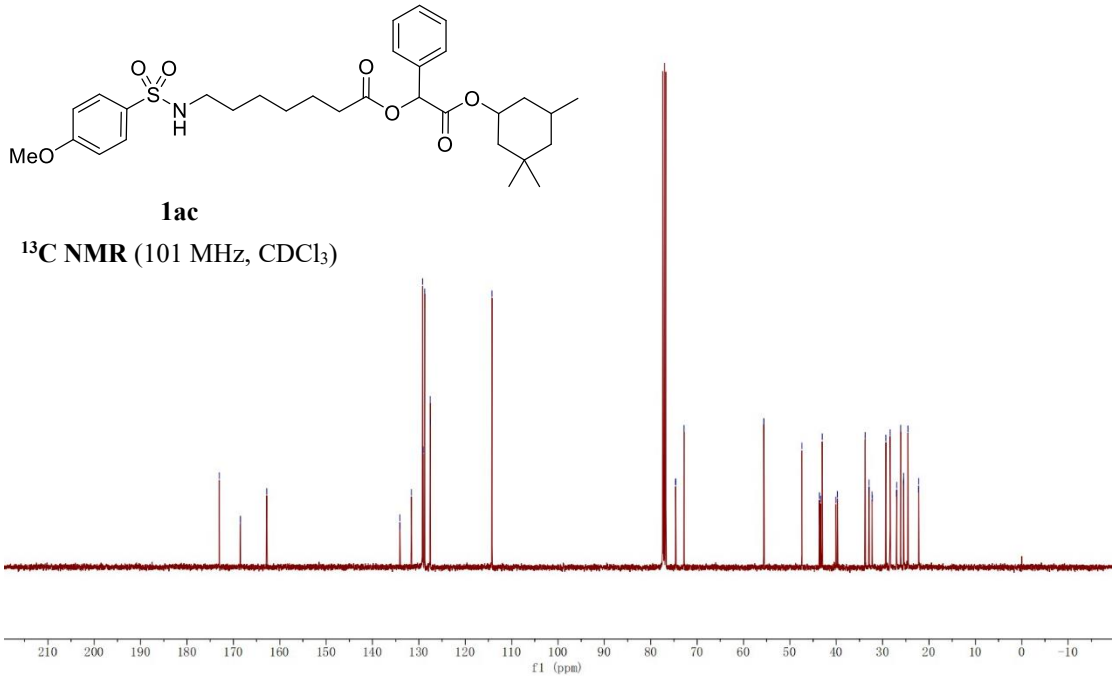


1ab

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

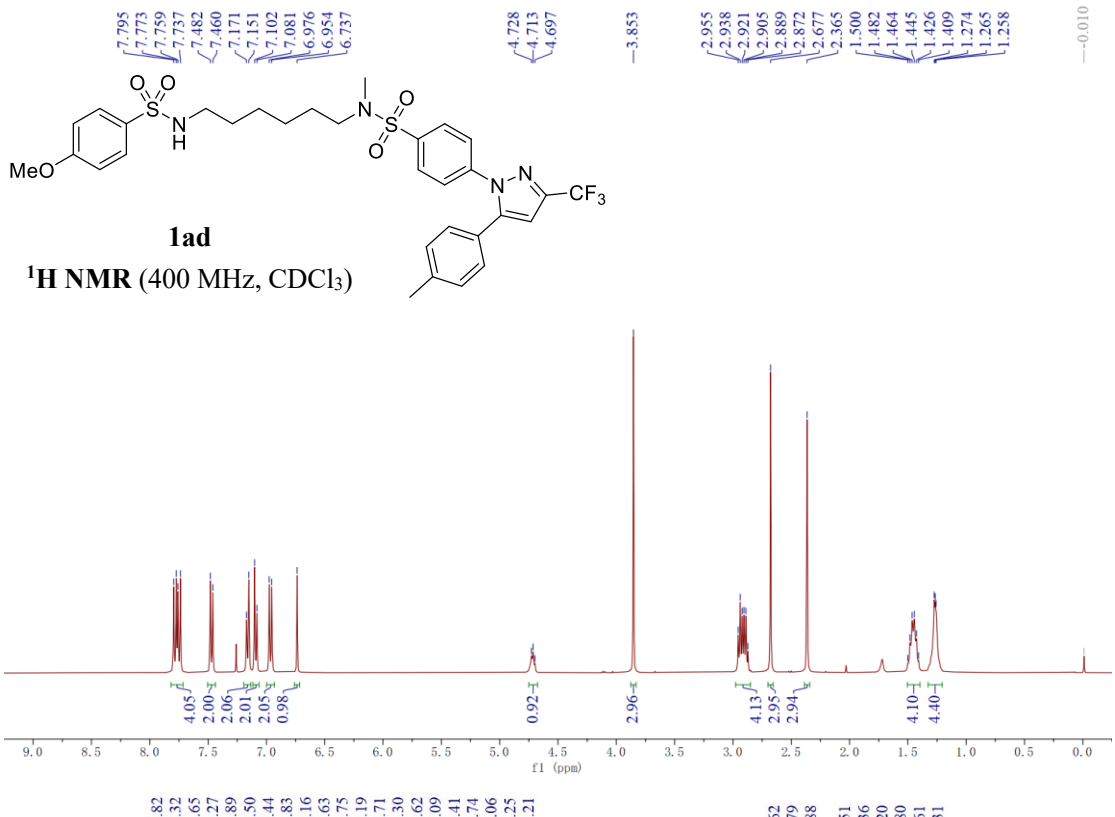






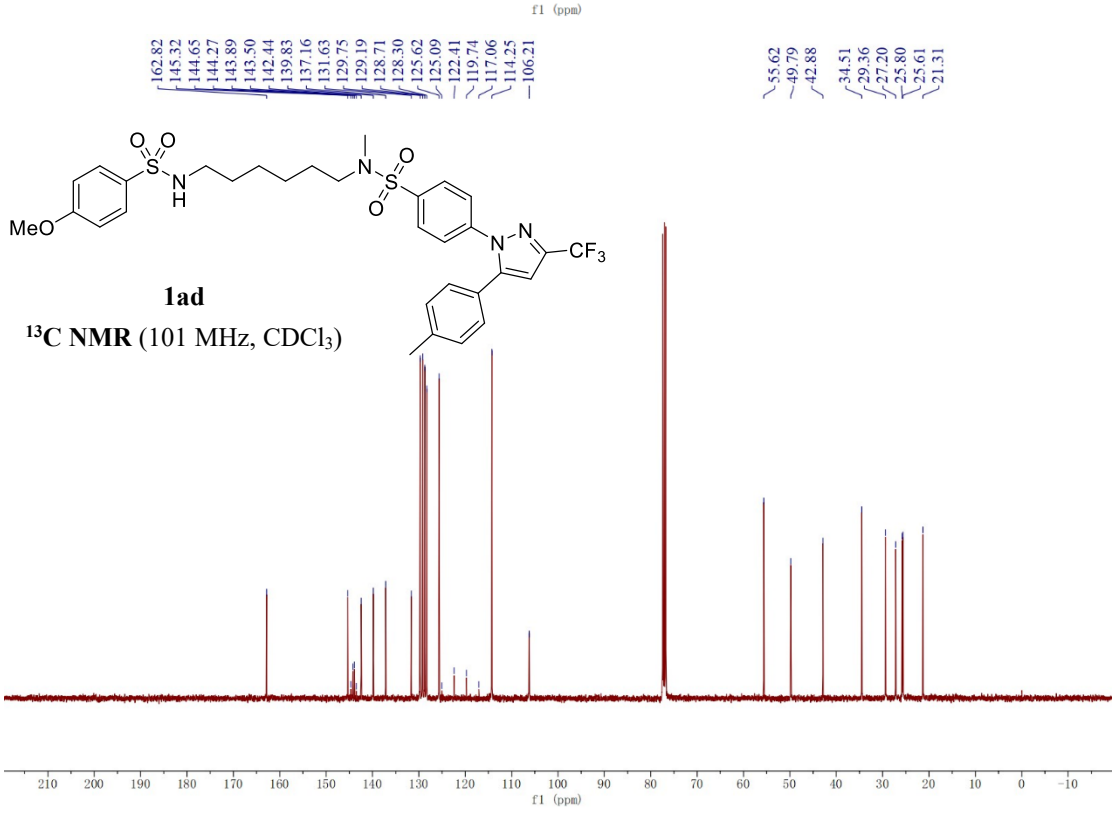
1ac

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



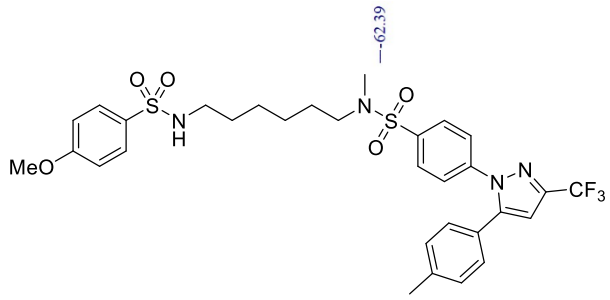
1ad

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



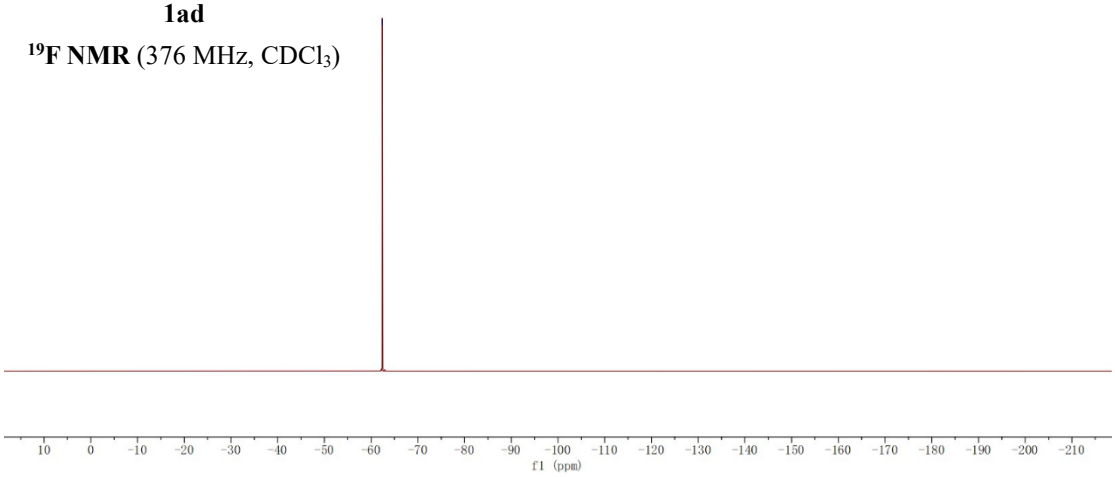
1ad

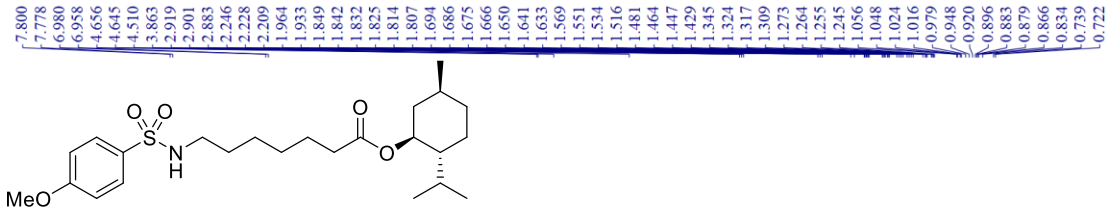
^{13}C NMR (101 MHz, $CDCl_3$)



1ad

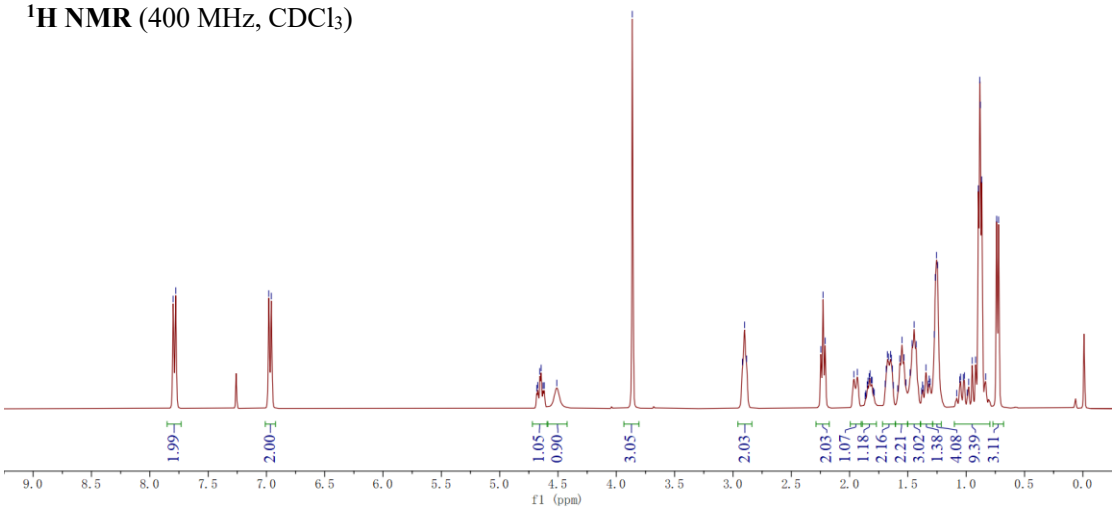
^{19}F NMR (376 MHz, $CDCl_3$)

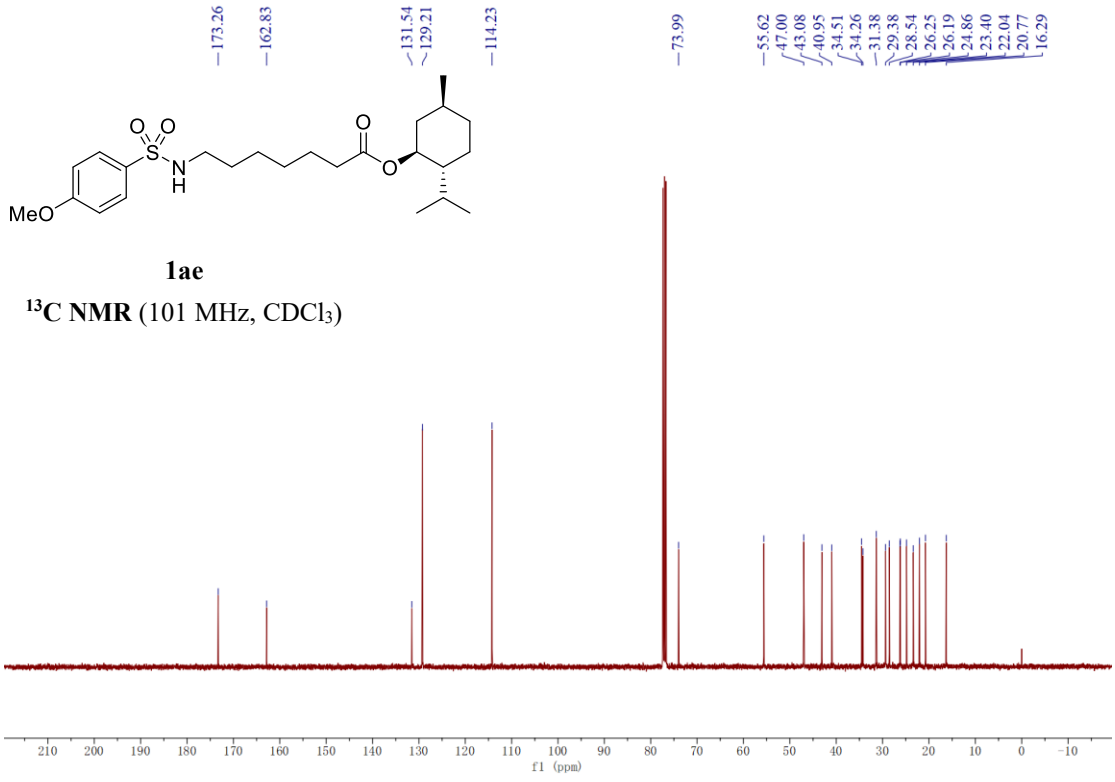




1ae

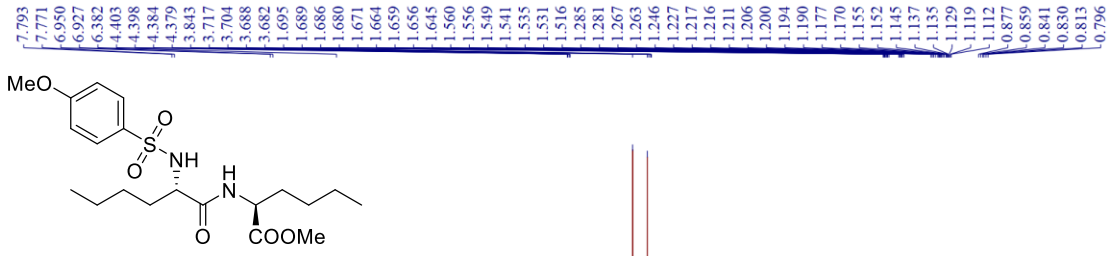
^{1}H NMR (400 MHz, $CDCl_3$)





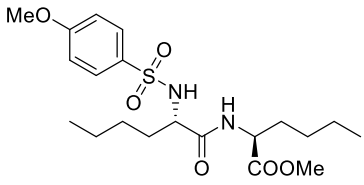
1ae

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



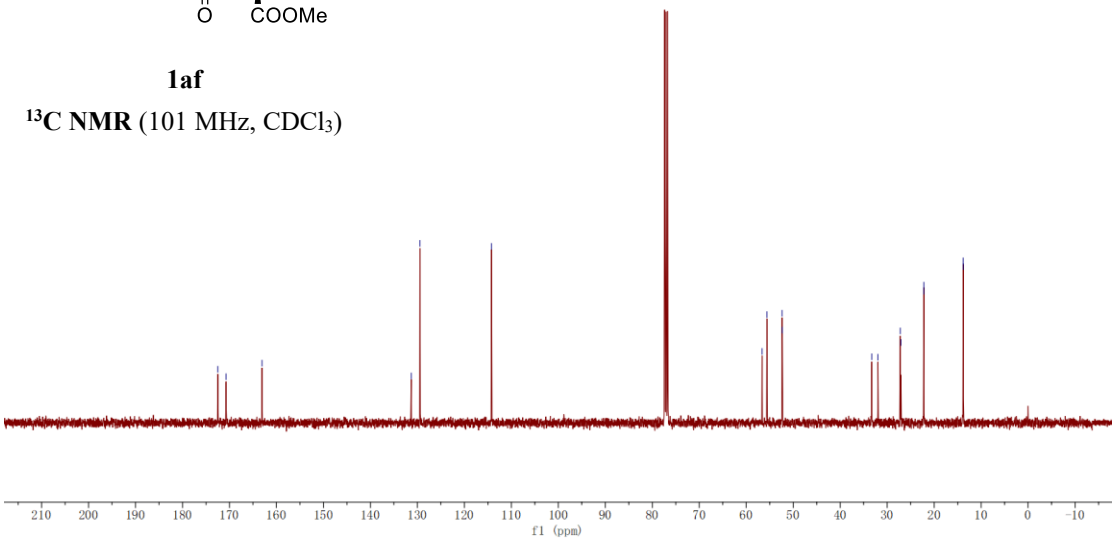
1af

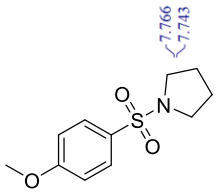
^{1}H NMR (400 MHz, $CDCl_3$)



1af

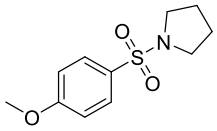
^{13}C NMR (101 MHz, $CDCl_3$)





4

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

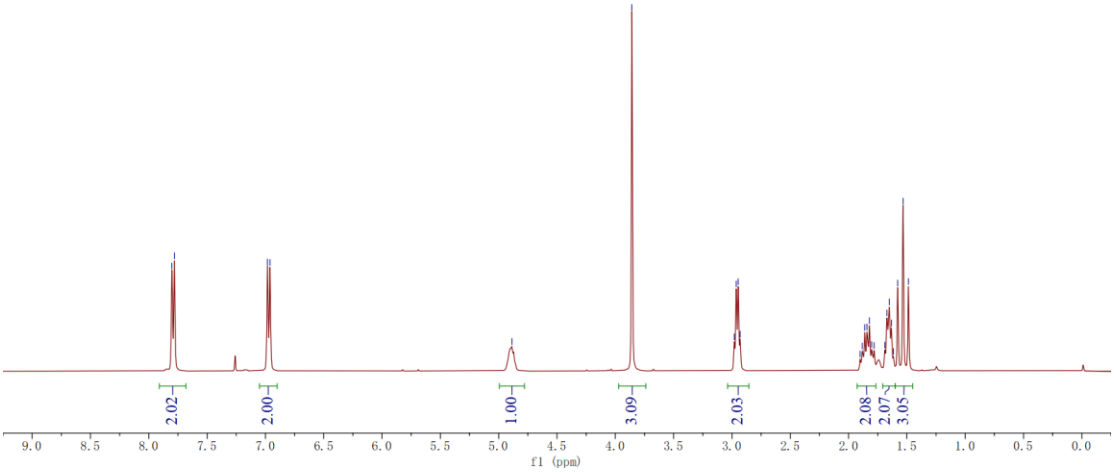


4

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

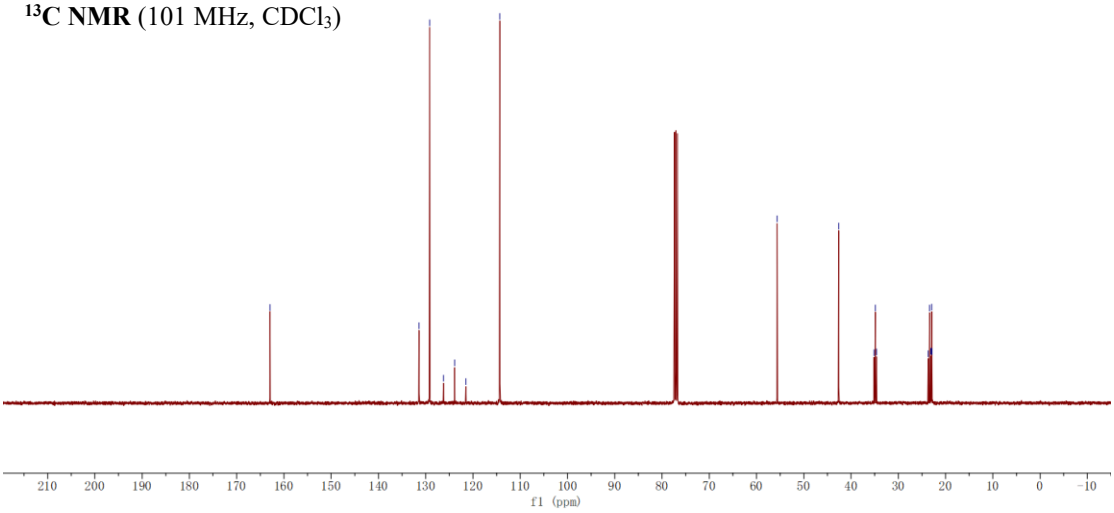
3a

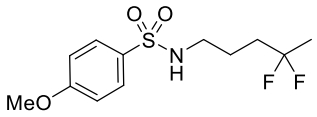
^{1}H NMR (400 MHz, $CDCl_3$)



3a

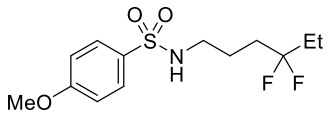
^{13}C NMR (101 MHz, $CDCl_3$)





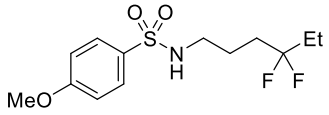
3a

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



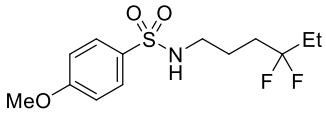
3b

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



3b

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

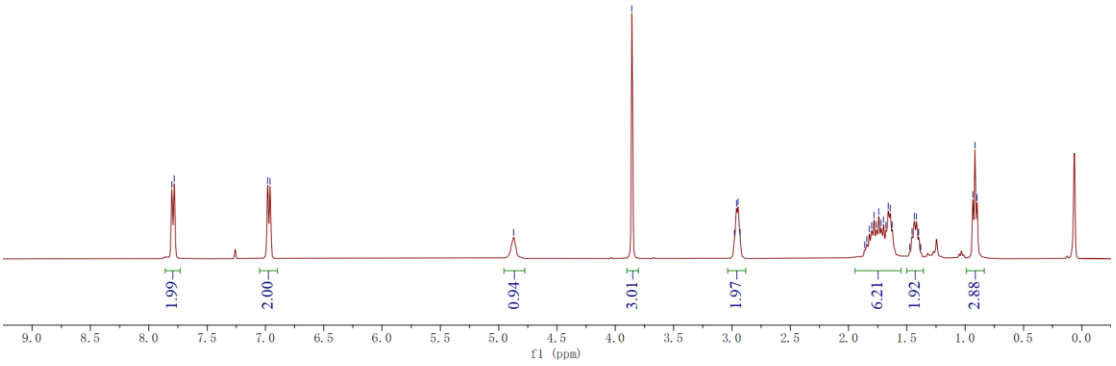


3b

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

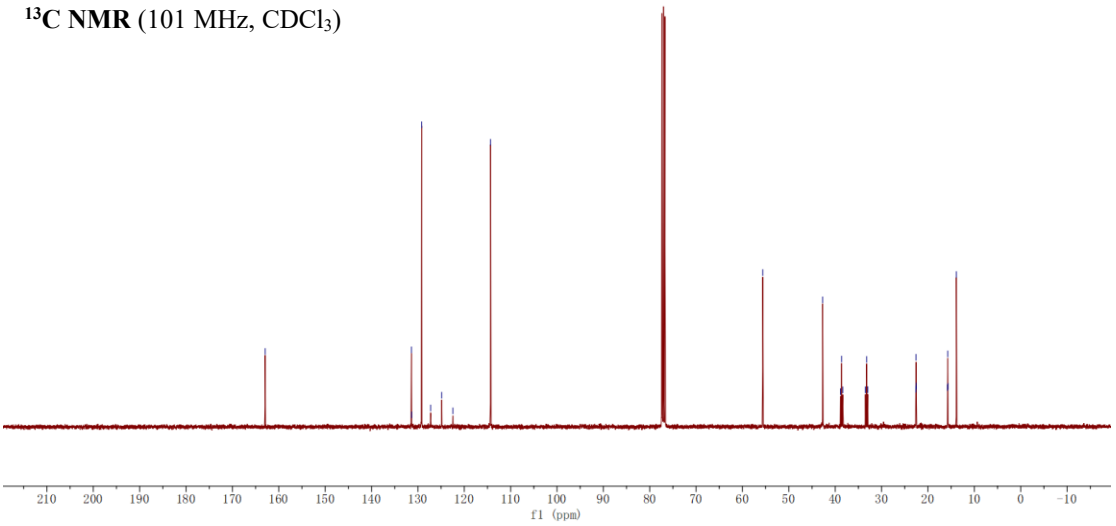
3c

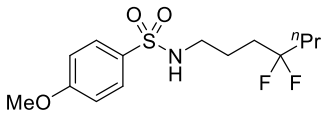
^{1}H NMR (400 MHz, $CDCl_3$)



3c

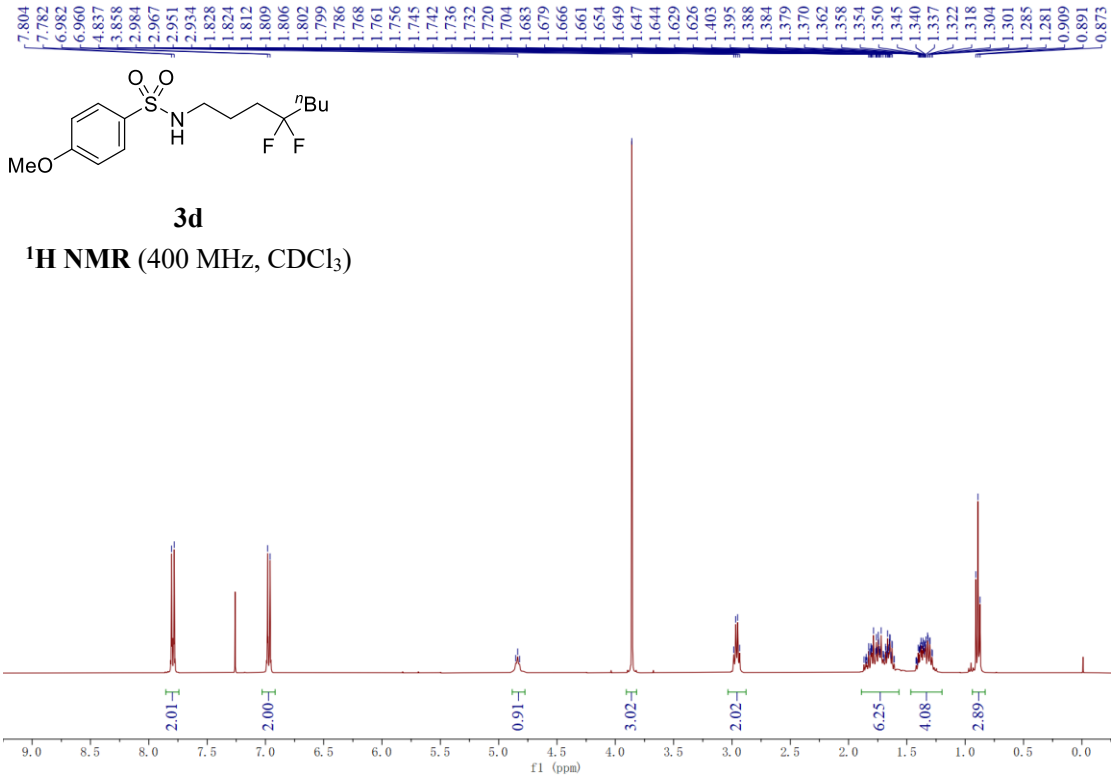
^{13}C NMR (101 MHz, $CDCl_3$)





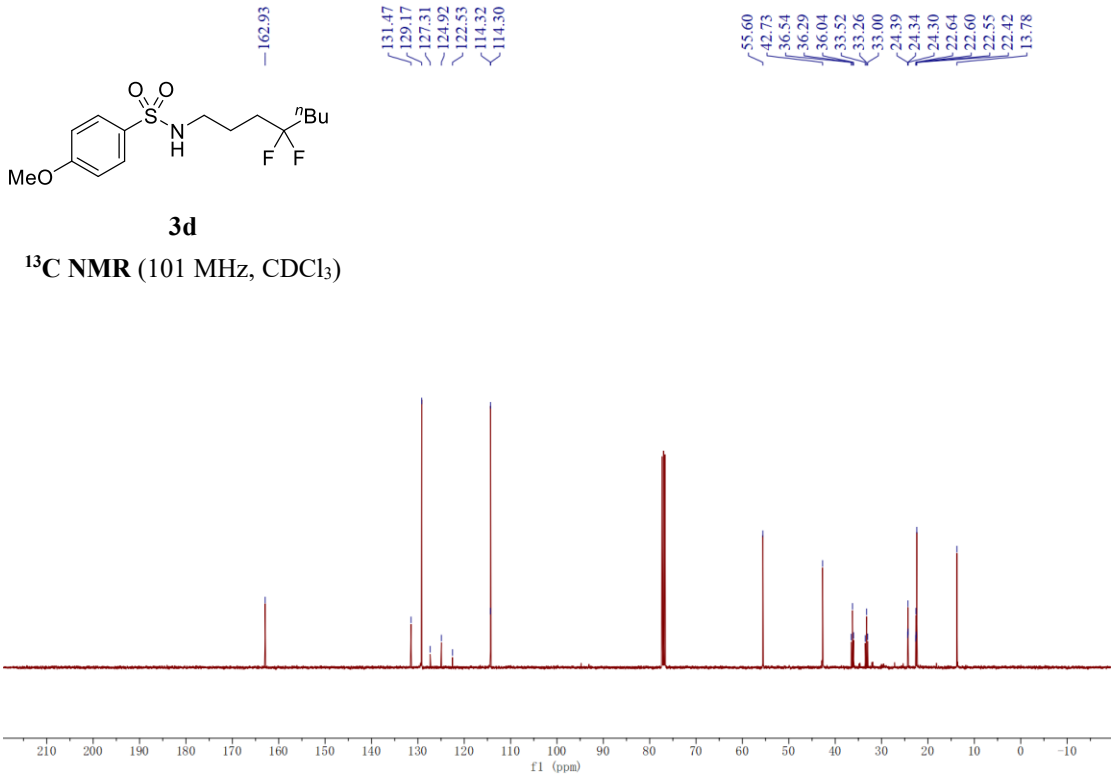
3c

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



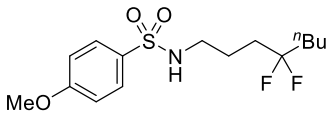
3d

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



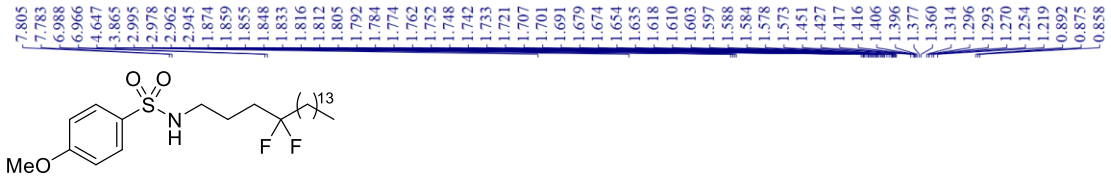
3d

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



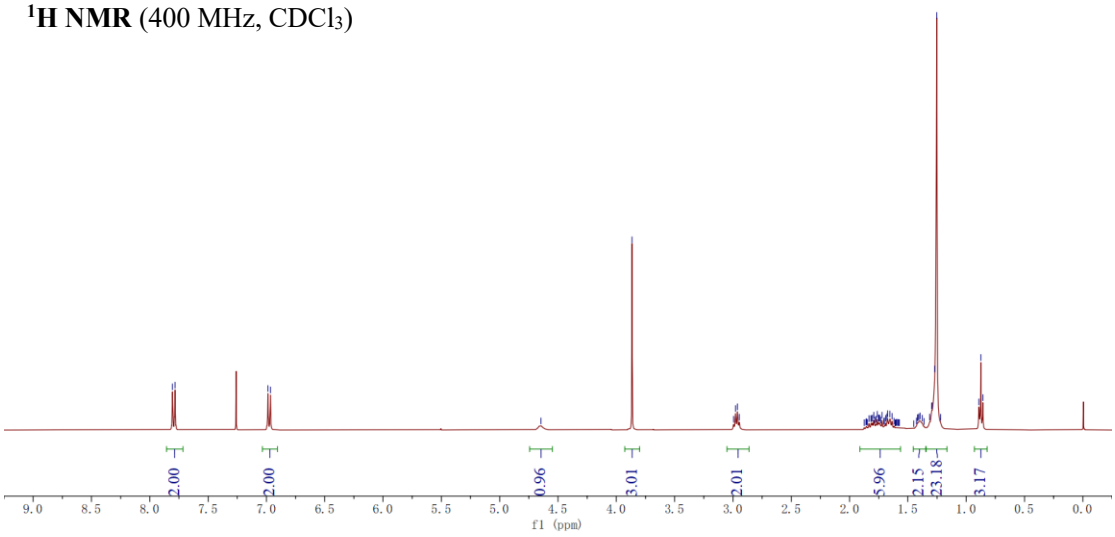
3d

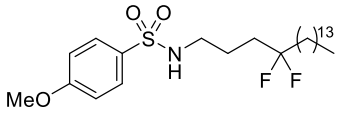
^{19}F NMR (376 MHz, $CDCl_3$)



3e

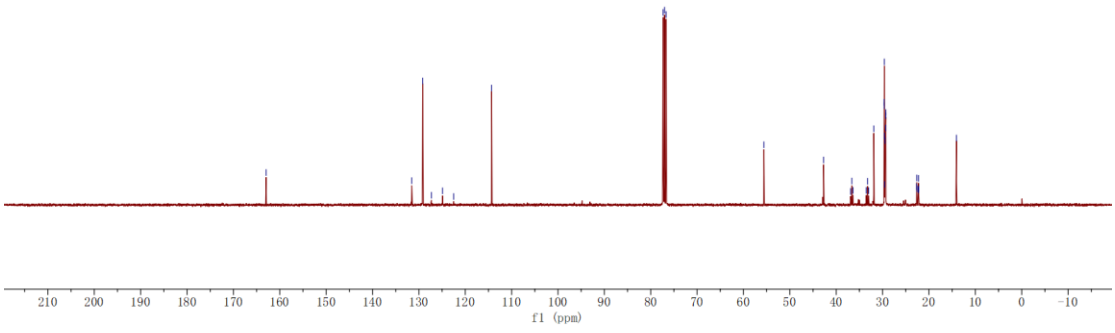
^{1}H NMR (400 MHz, $CDCl_3$)

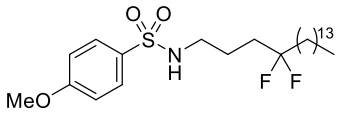




3e

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



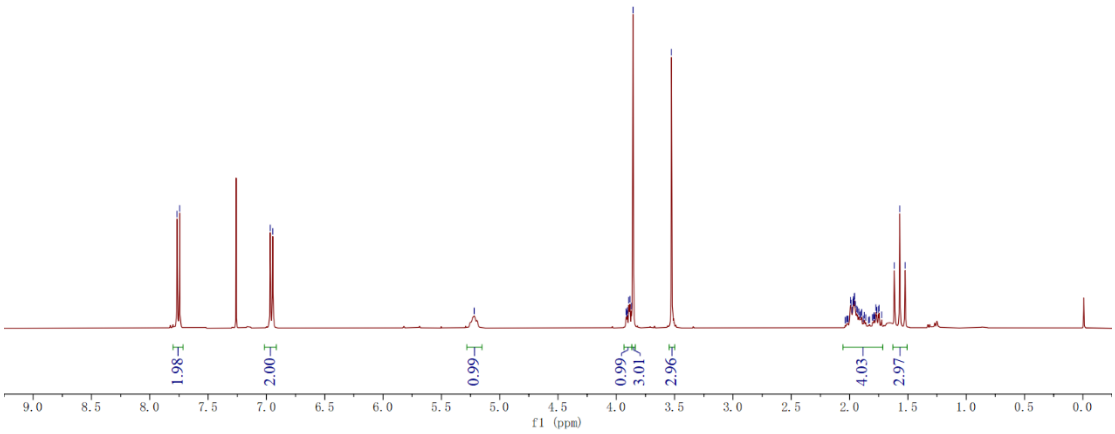


3e

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

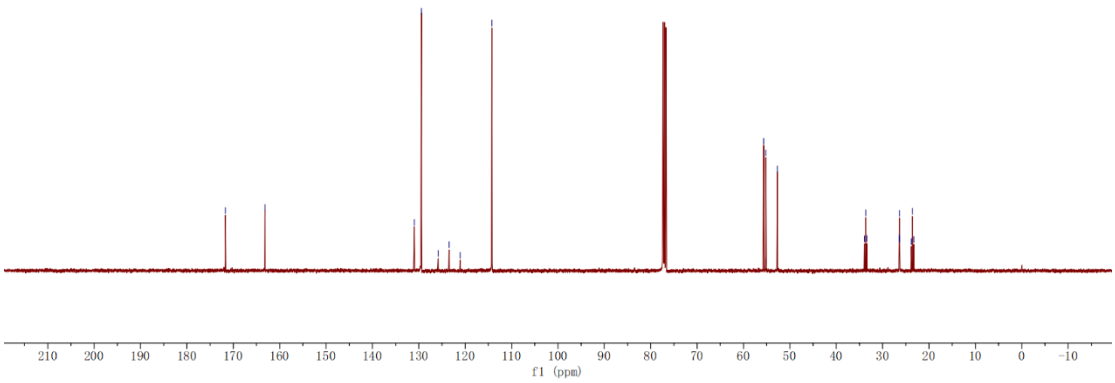
3f

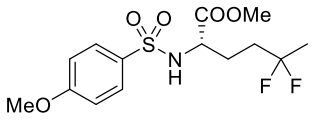
^{1}H NMR (400 MHz, $CDCl_3$)



3f

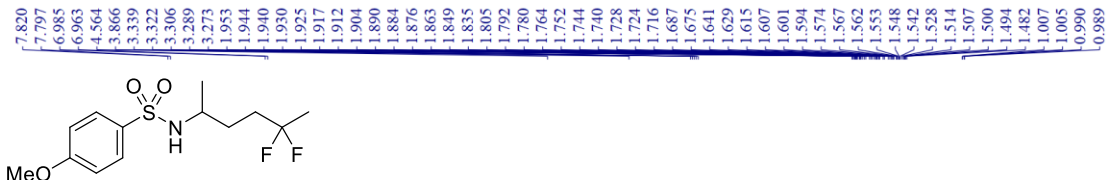
^{13}C NMR (101 MHz, $CDCl_3$)





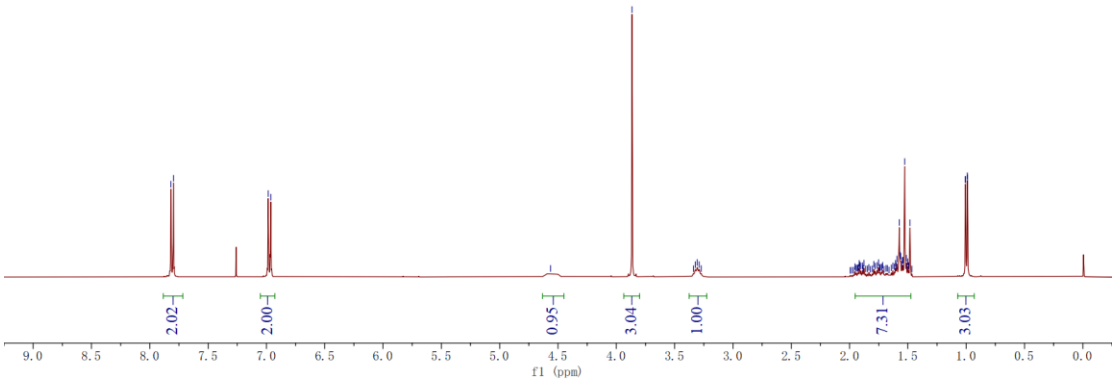
3f

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



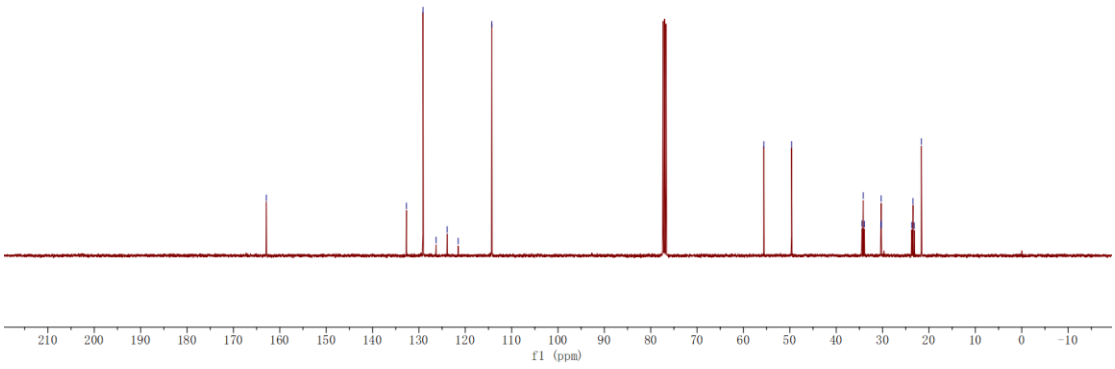
3g

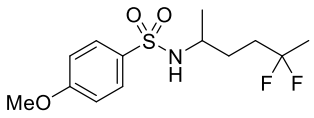
^{1}H NMR (400 MHz, $CDCl_3$)



3g

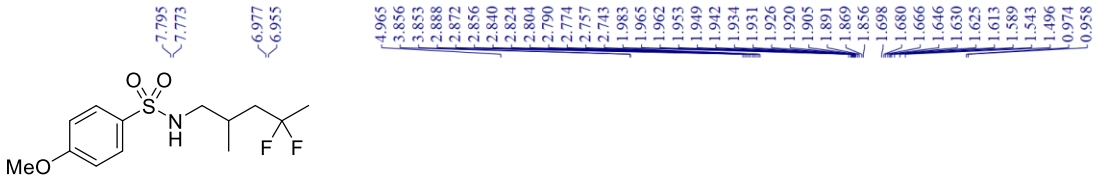
^{13}C NMR (101 MHz, $CDCl_3$)





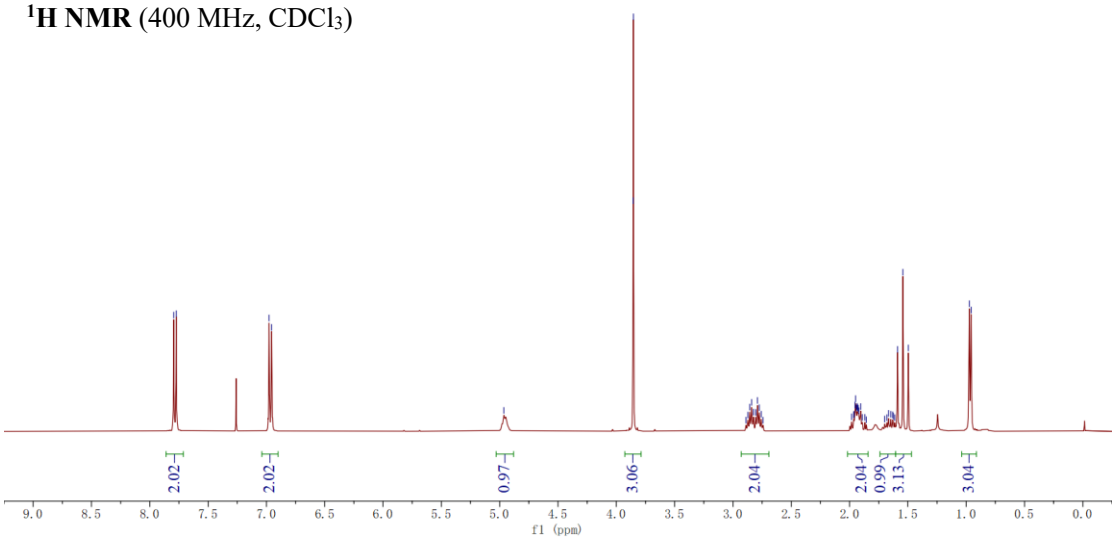
3g

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



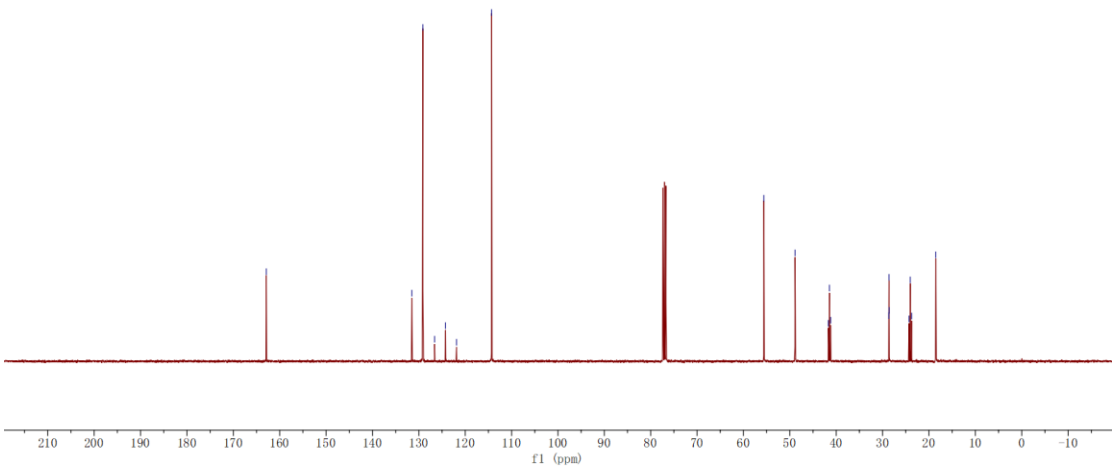
3h

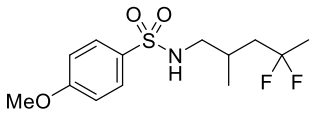
^{1}H NMR (400 MHz, $CDCl_3$)



3h

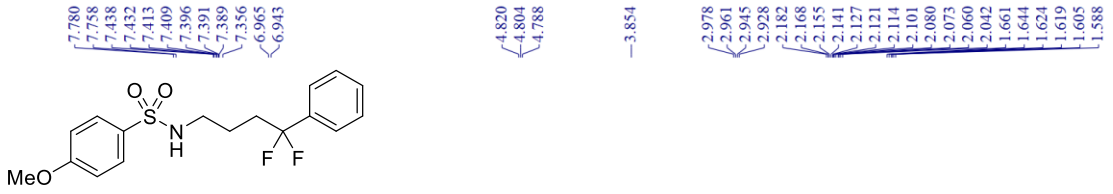
^{13}C NMR (101 MHz, $CDCl_3$)





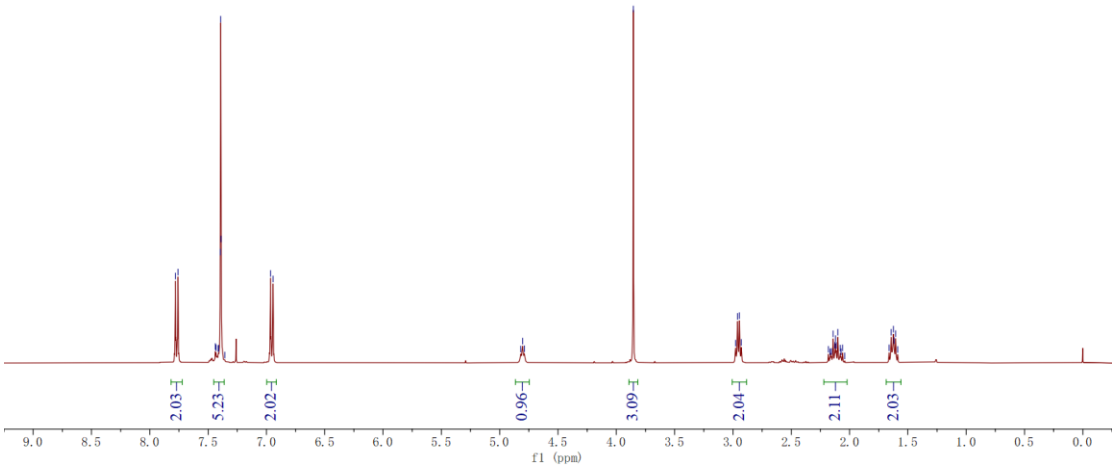
3h

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



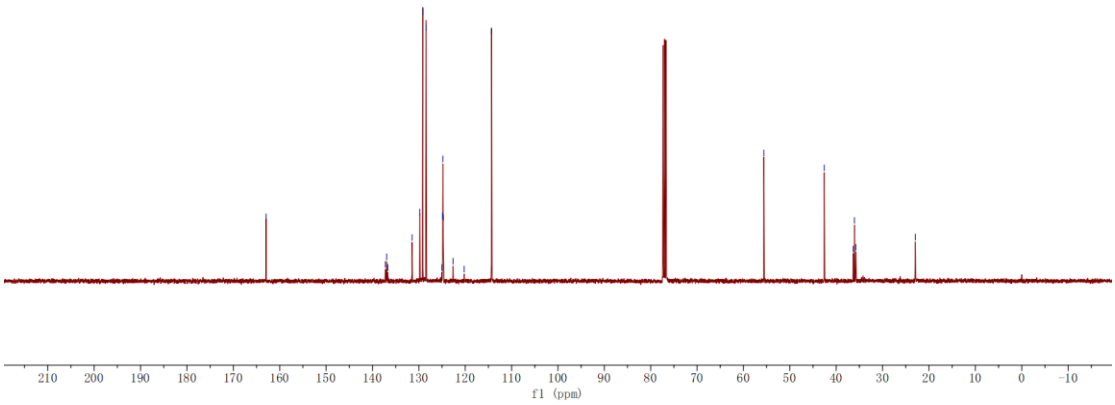
3i

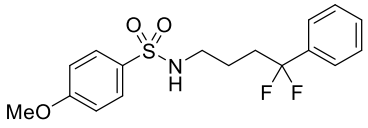
^{1}H NMR (400 MHz, $CDCl_3$)



3i

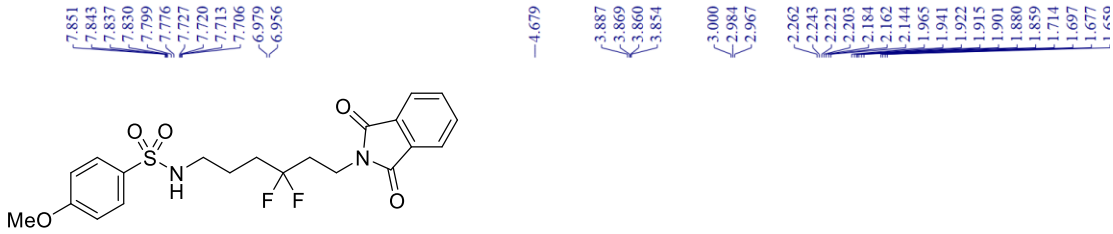
^{13}C NMR (101 MHz, $CDCl_3$)





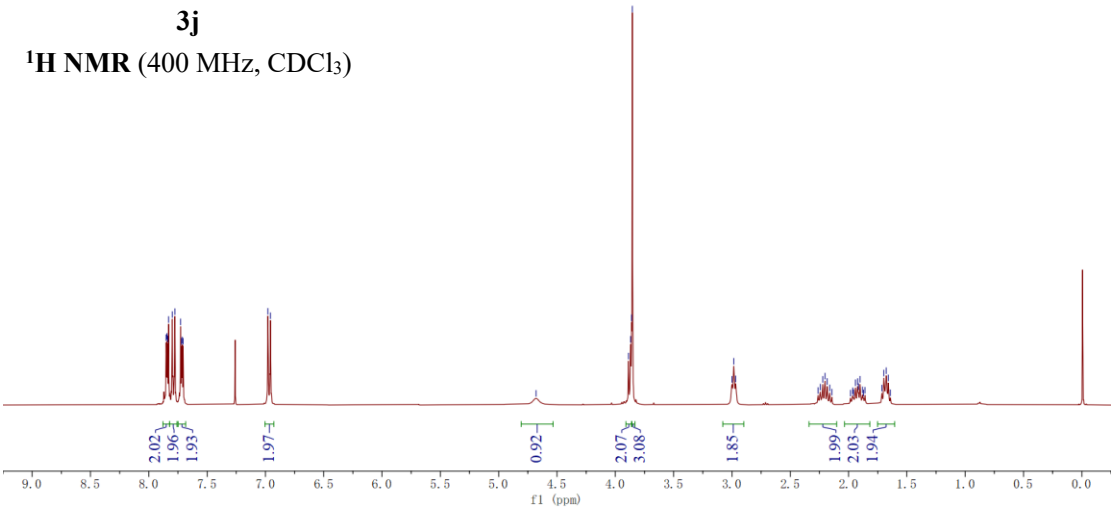
3i

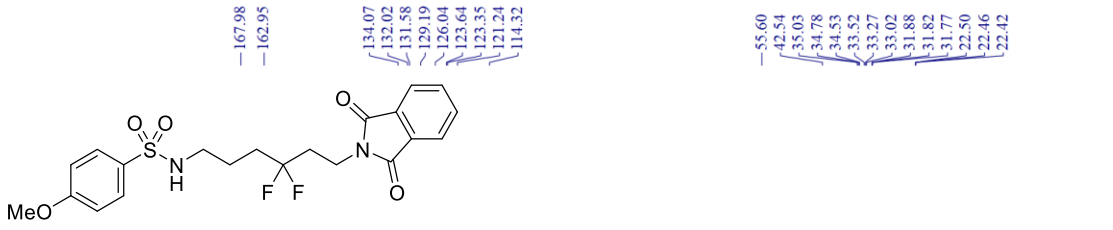
^{19}F NMR (376 MHz, $CDCl_3$)



3j

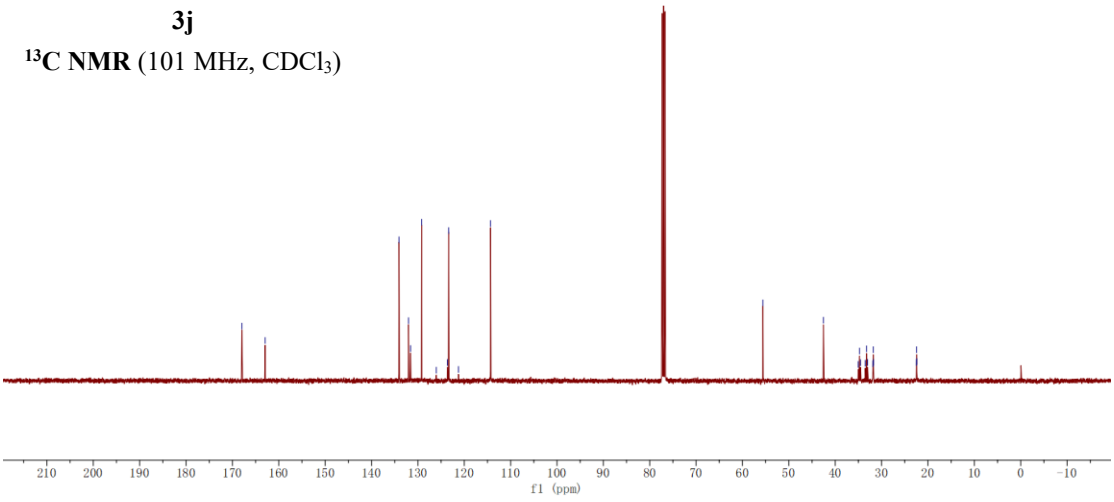
^{1}H NMR (400 MHz, $CDCl_3$)

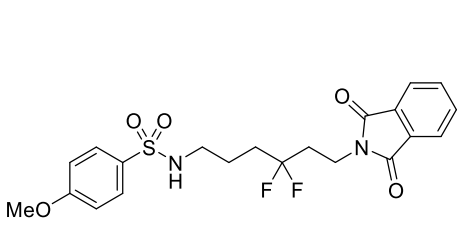




3j

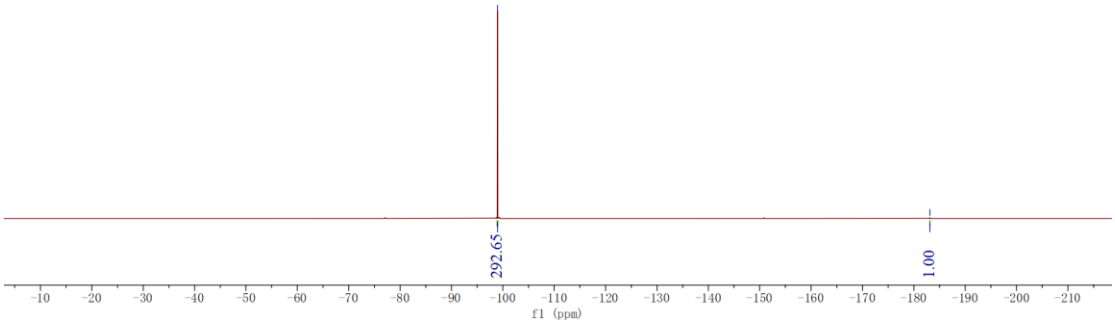
^{13}C NMR (101 MHz, $CDCl_3$)

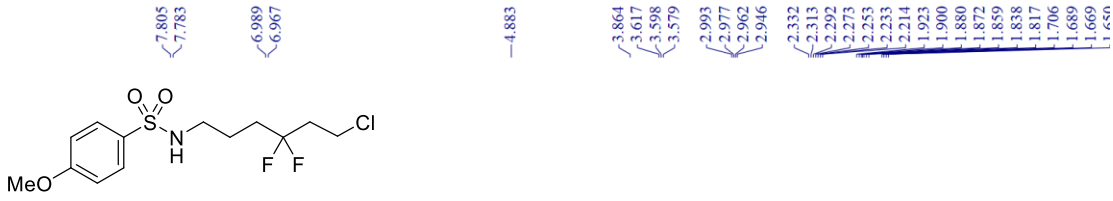




3j

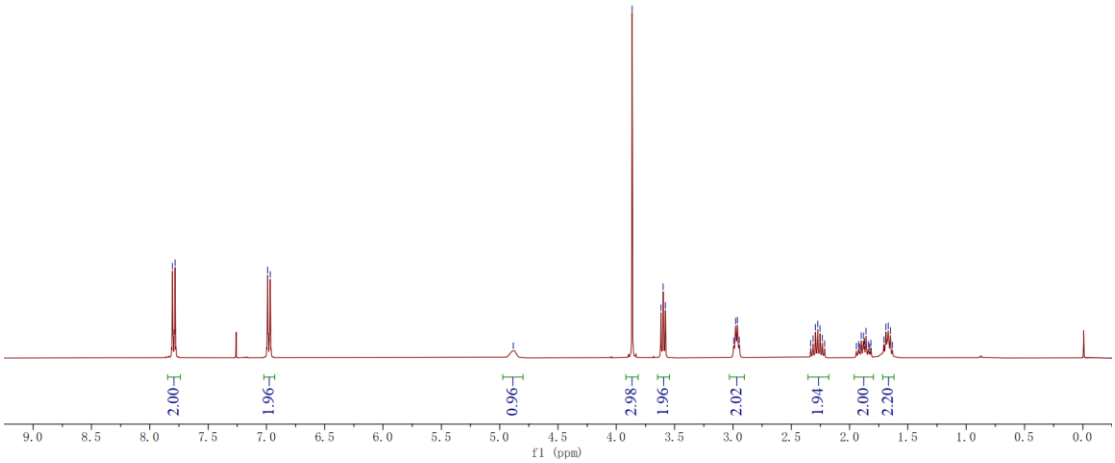
^{19}F NMR (376 MHz, $CDCl_3$)





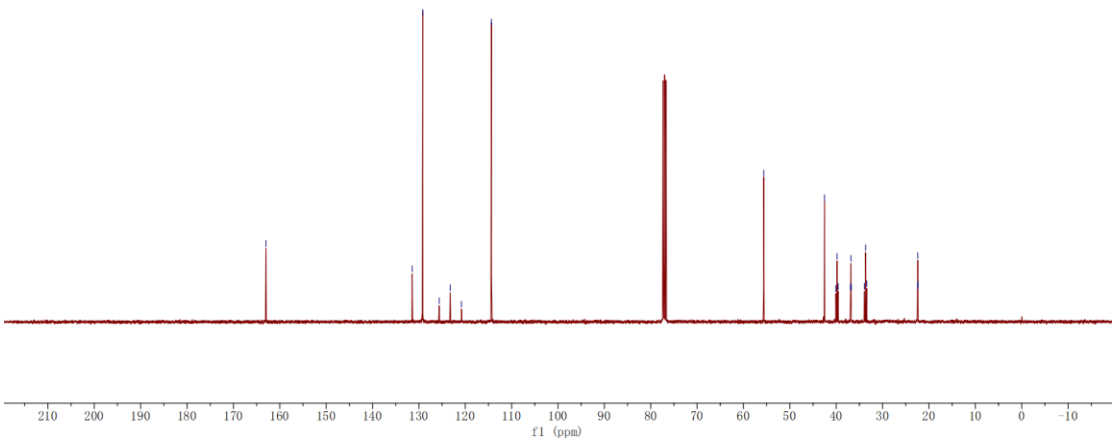
3k

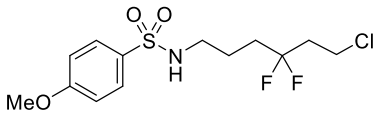
[1]H NMR (400 MHz, $CDCl_3$)



3k

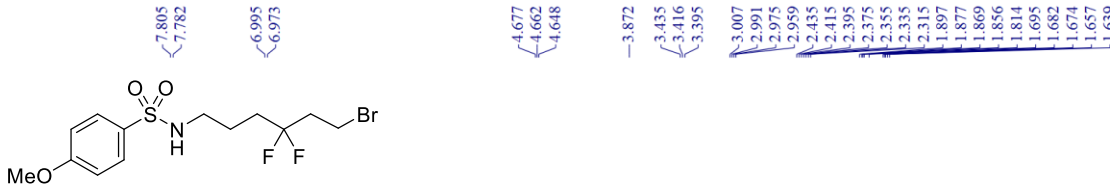
[13]C NMR (101 MHz, $CDCl_3$)





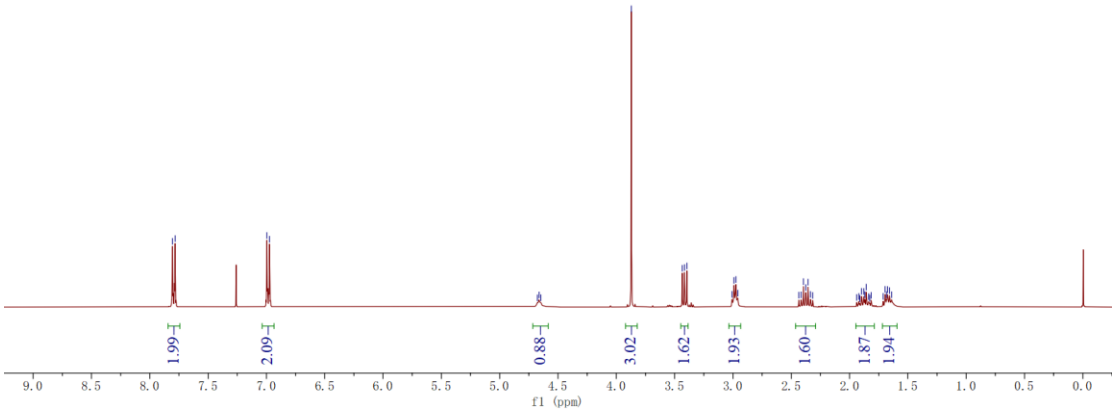
3k

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



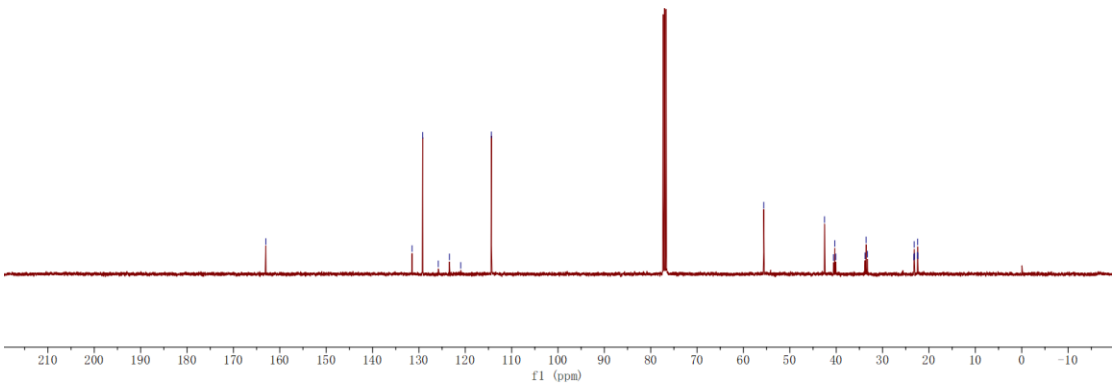
3l

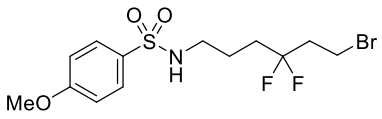
^{1}H NMR (400 MHz, $CDCl_3$)



3l

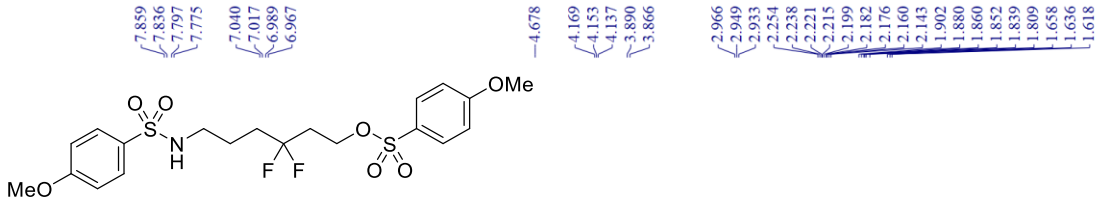
^{13}C NMR (101 MHz, $CDCl_3$)





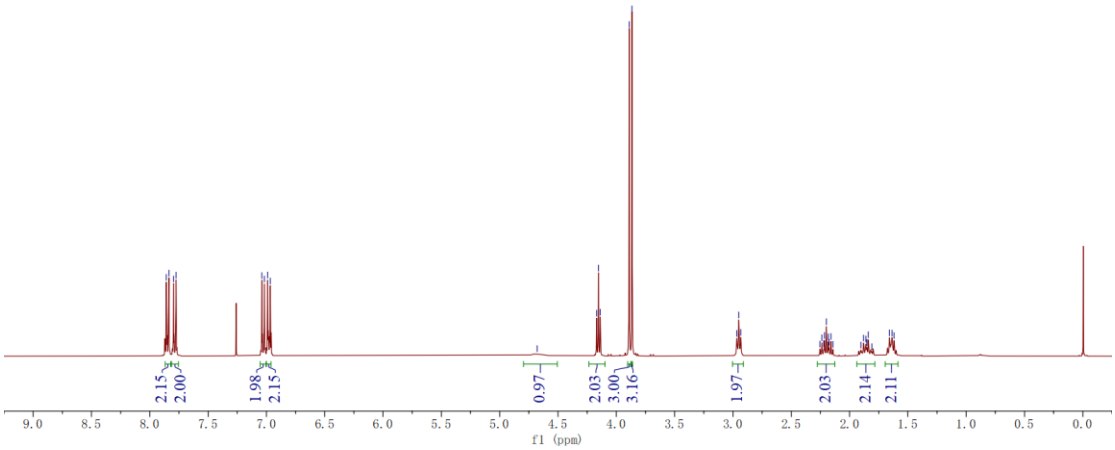
3l

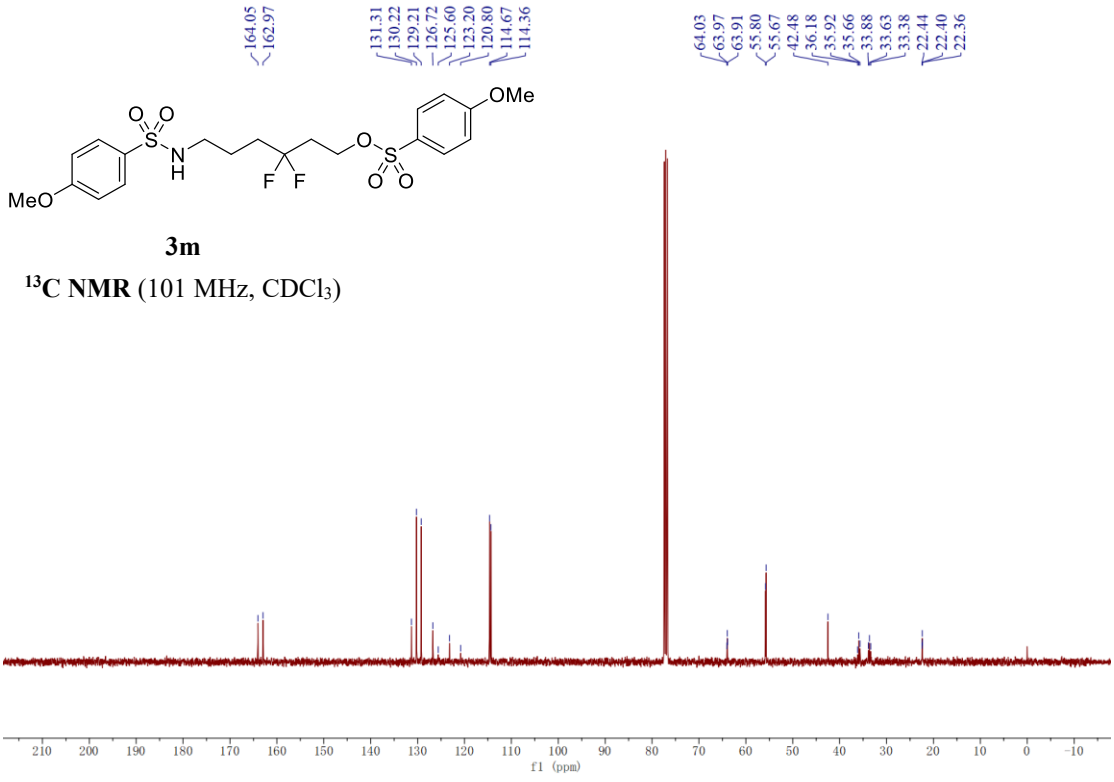
^{19}F NMR (376 MHz, $CDCl_3$)



3m

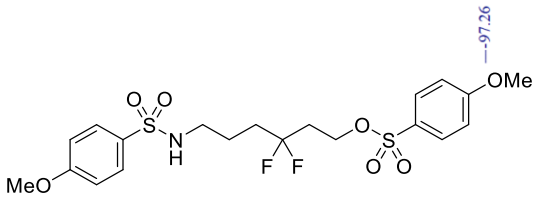
^{1}H NMR (400 MHz, $CDCl_3$)





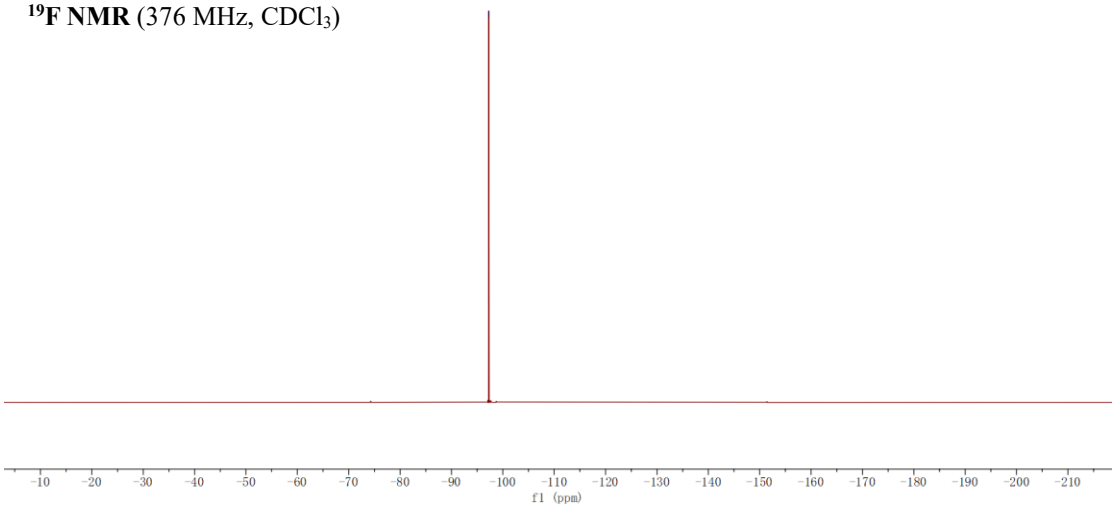
3m

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



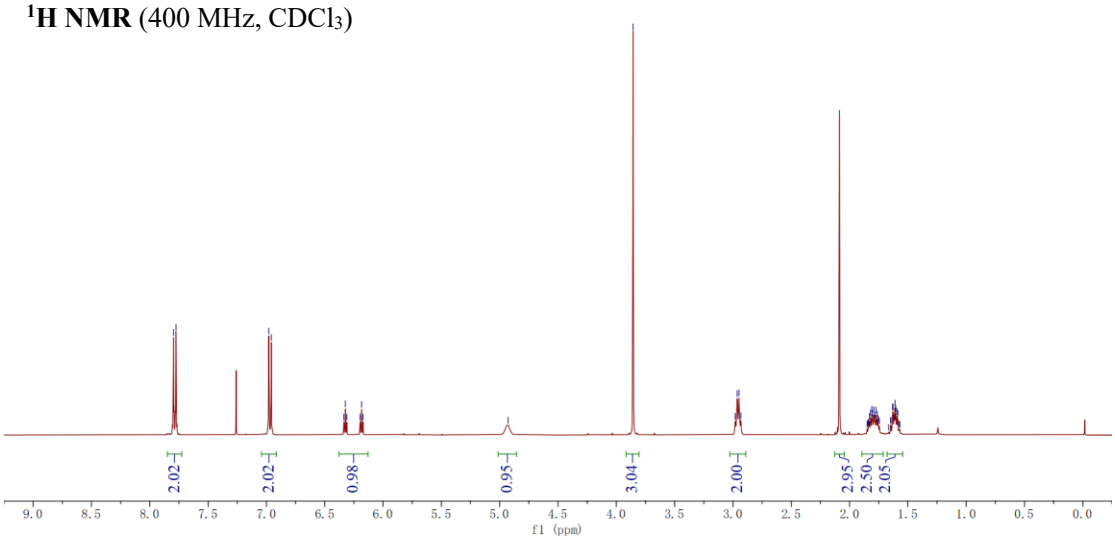
3m

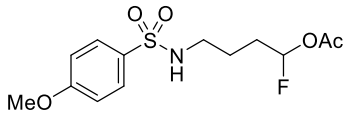
^{19}F NMR (376 MHz, $CDCl_3$)



3n

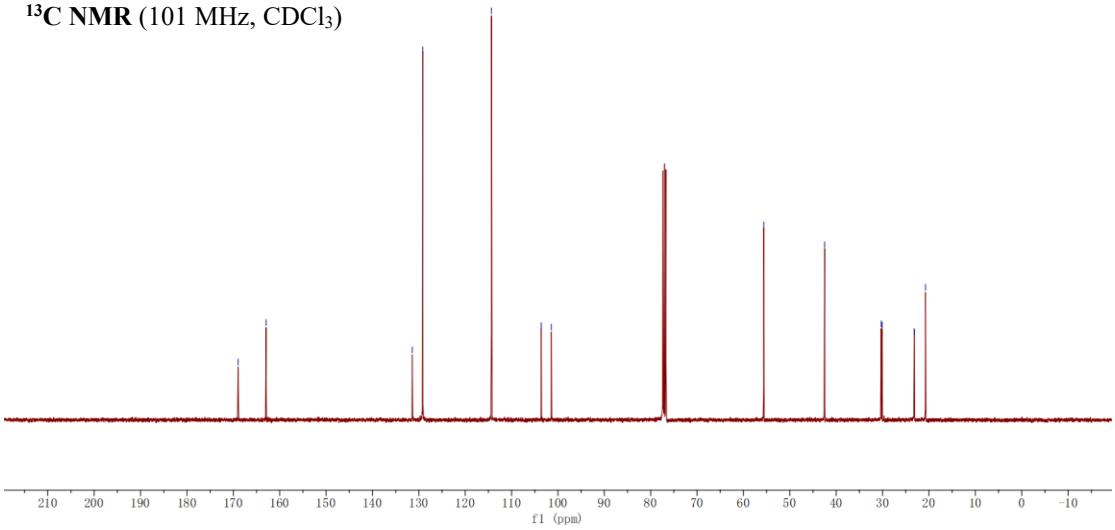
^{1}H NMR (400 MHz, $CDCl_3$)

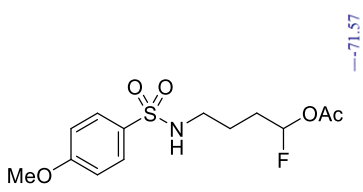




3n

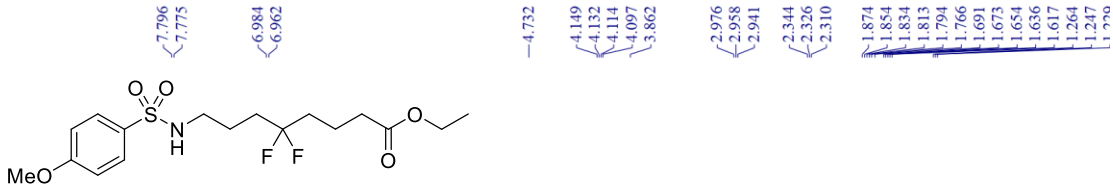
^{13}C NMR (101 MHz, $CDCl_3$)





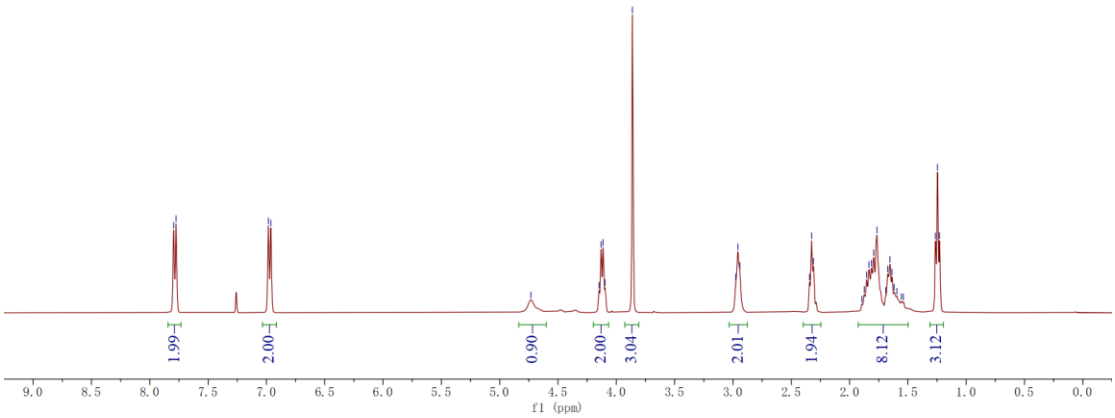
3n

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



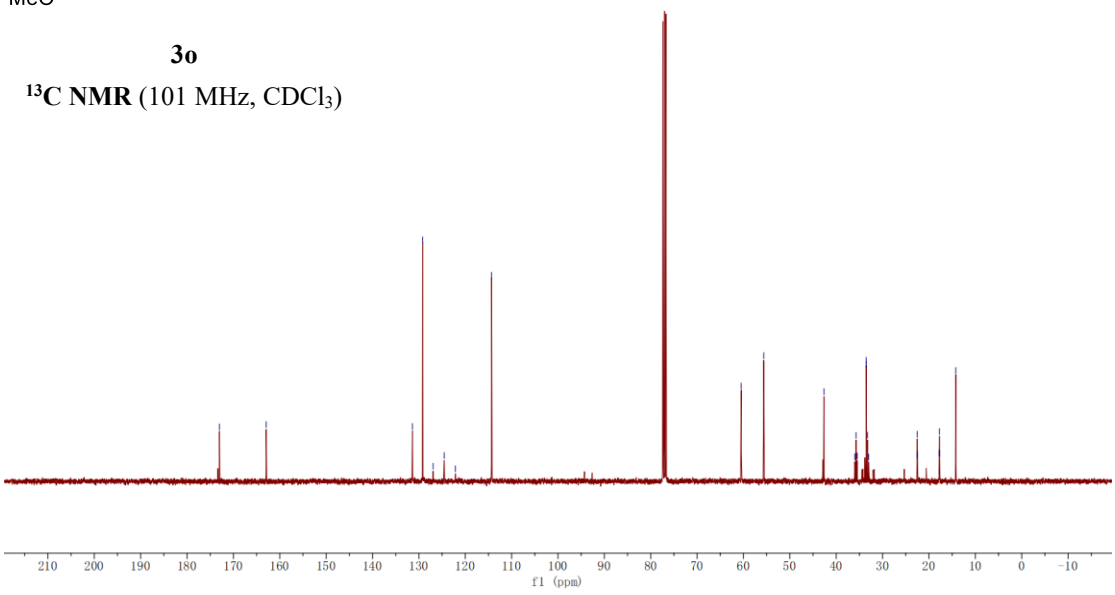
3o

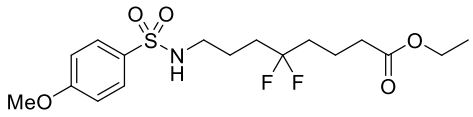
^{1}H NMR (400 MHz, $CDCl_3$)



3o

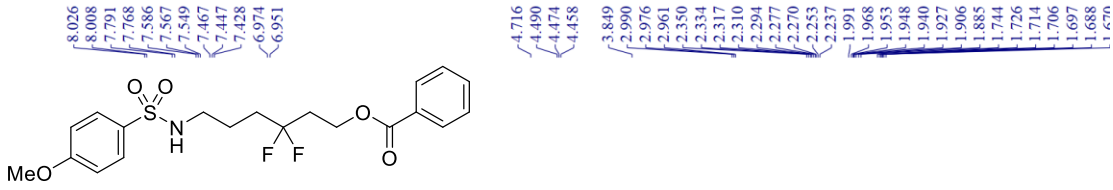
^{13}C NMR (101 MHz, $CDCl_3$)





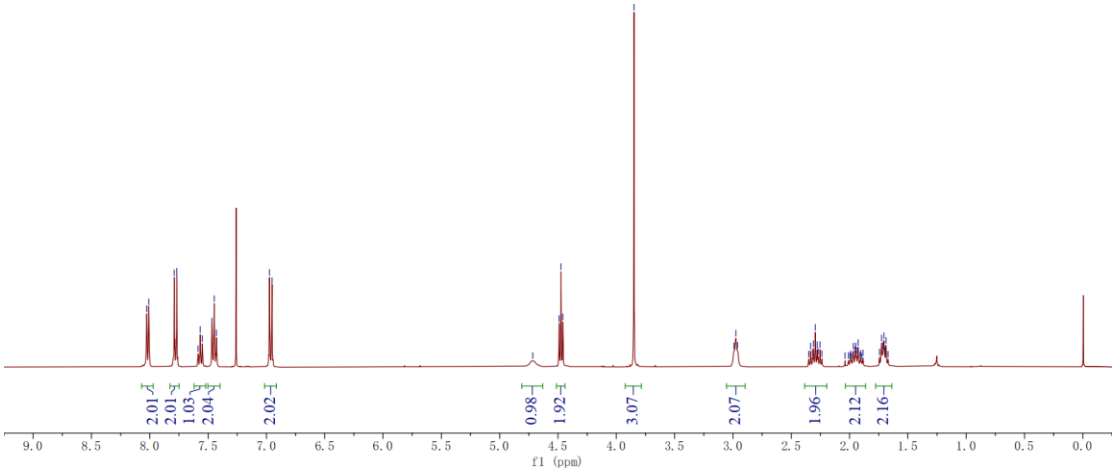
3o

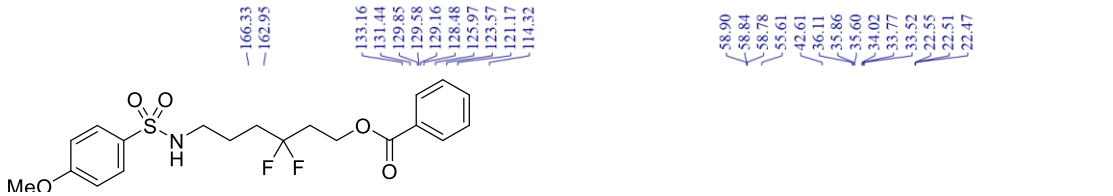
^{19}F NMR (376 MHz, $CDCl_3$)



3p

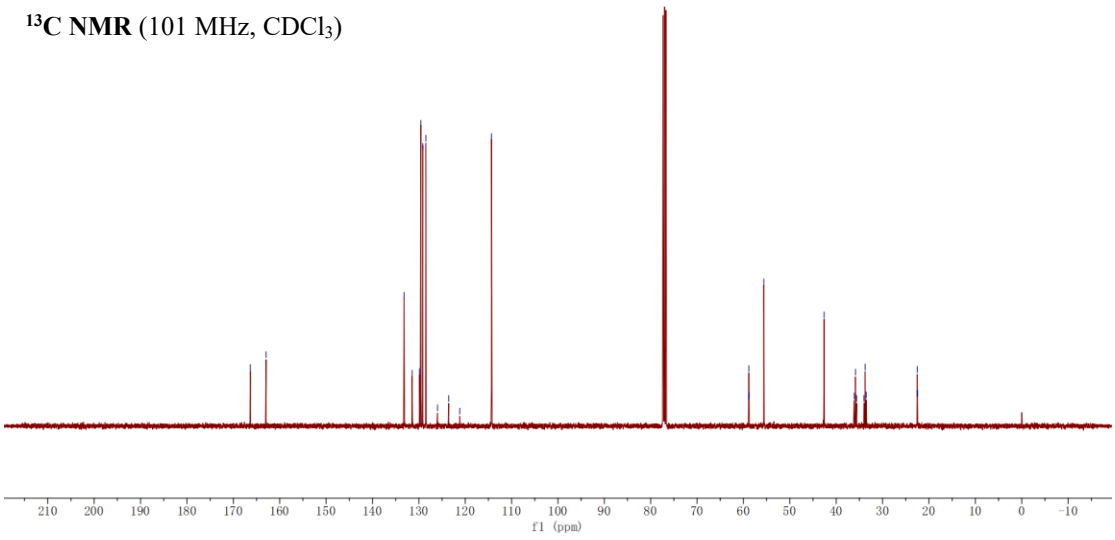
^{1}H NMR (400 MHz, $CDCl_3$)

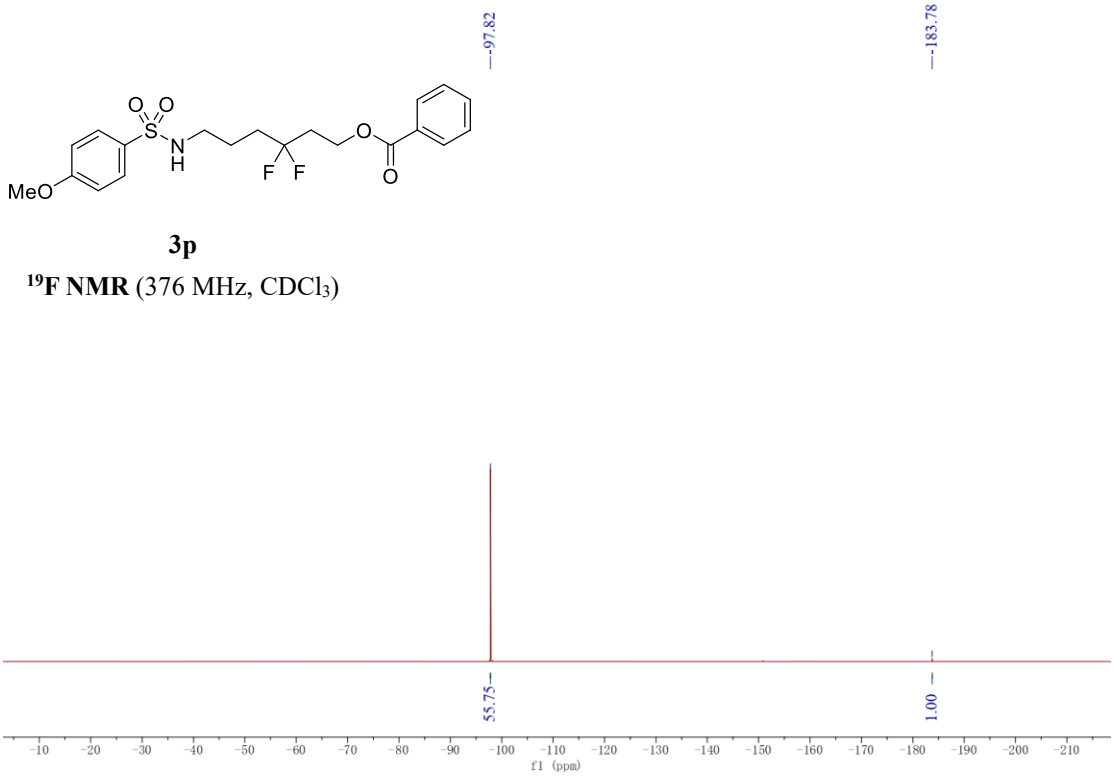




3p

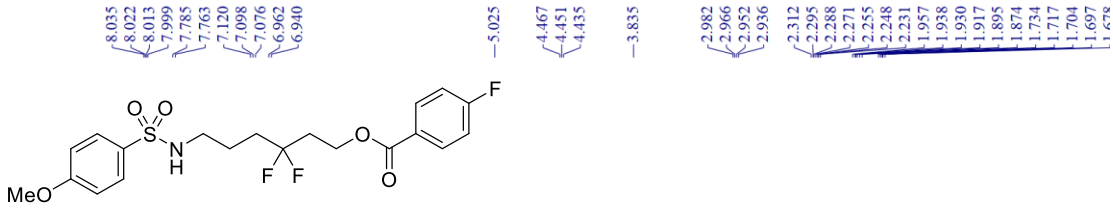
^{13}C NMR (101 MHz, $CDCl_3$)





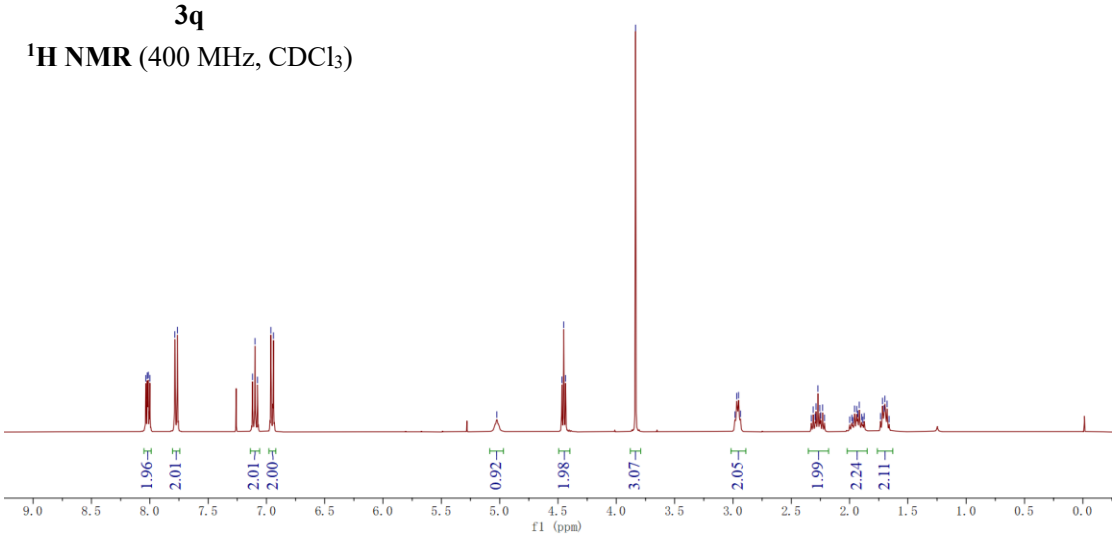
3p

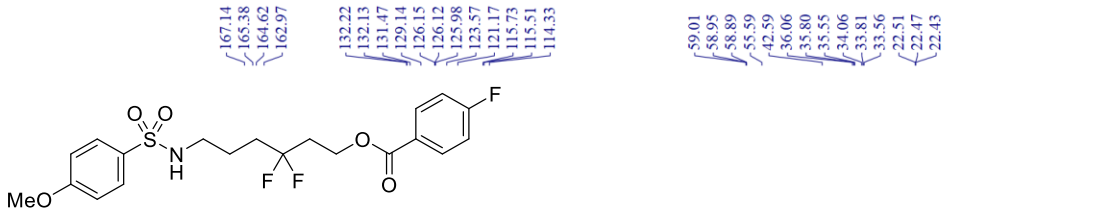
^{19}F NMR (376 MHz, $CDCl_3$)



3q

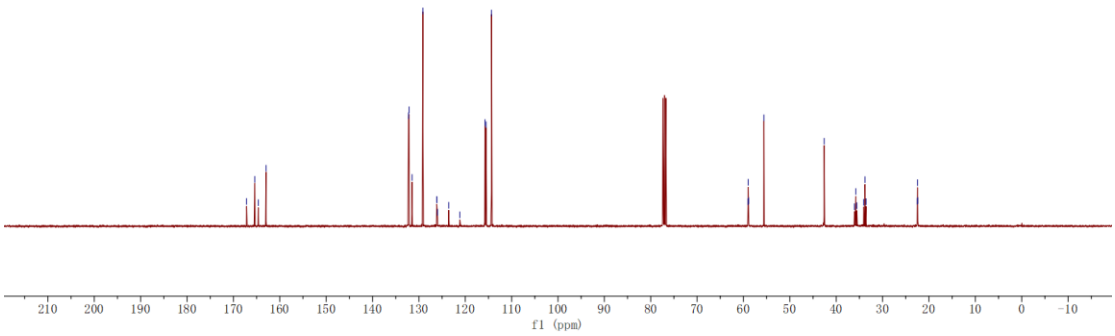
^{1}H NMR (400 MHz, $CDCl_3$)

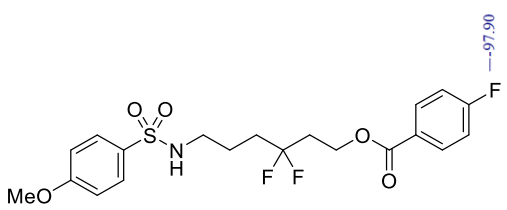




3q

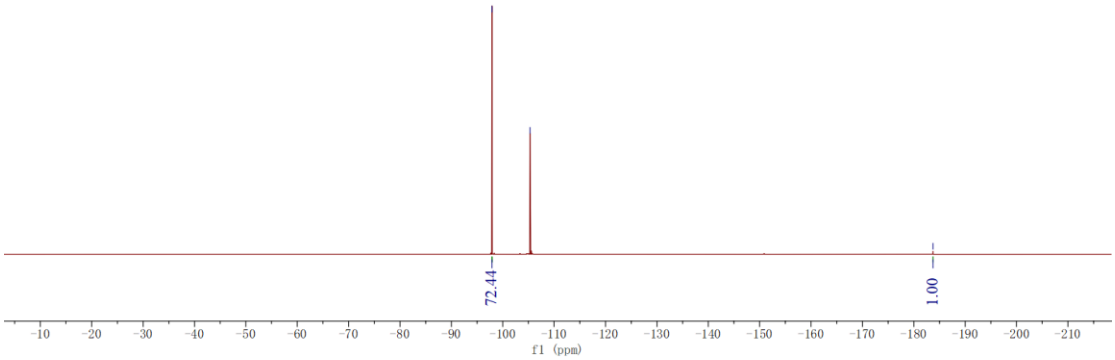
^{13}C NMR (101 MHz, $CDCl_3$)

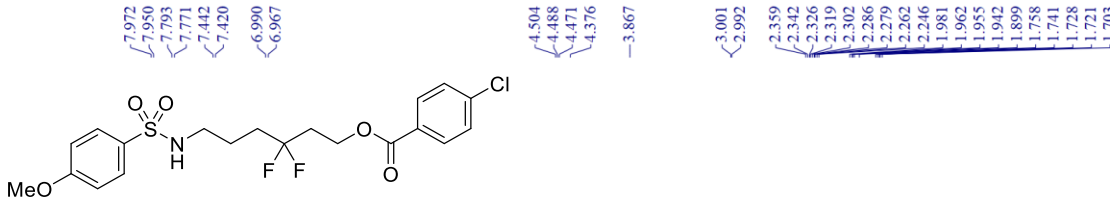




3q

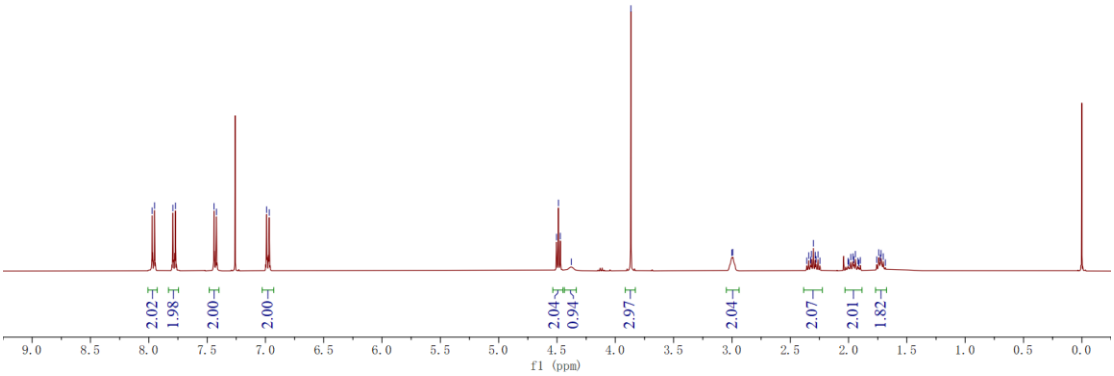
^{19}F NMR (376 MHz, $CDCl_3$)

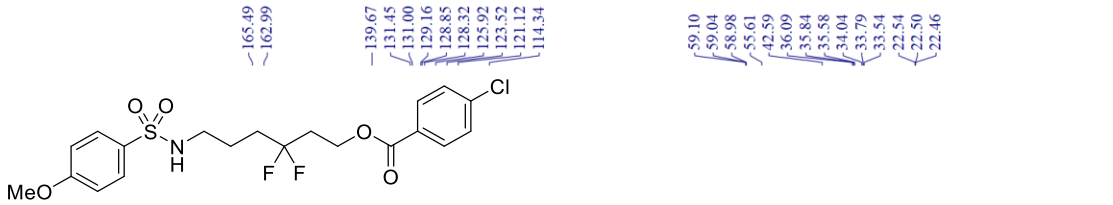




3r

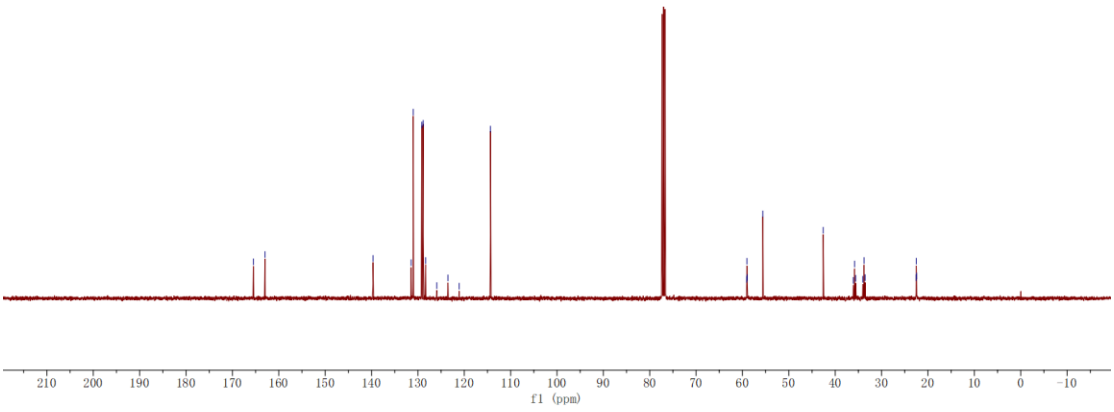
^{1}H NMR (400 MHz, $CDCl_3$)

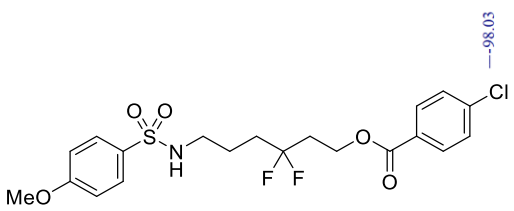




3r

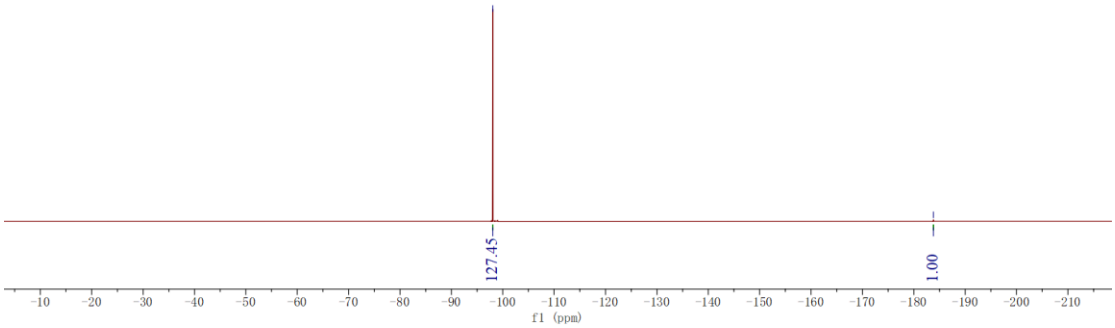
^{13}C NMR (101 MHz, $CDCl_3$)

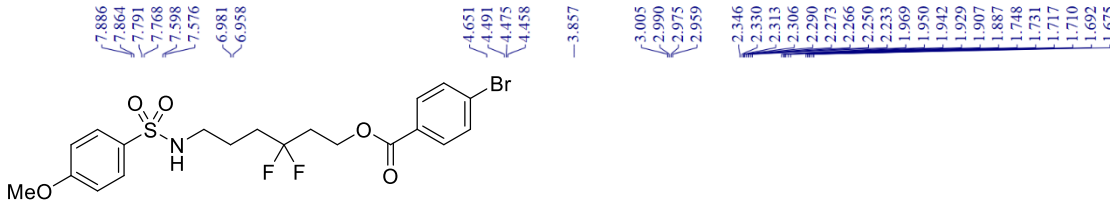




3r

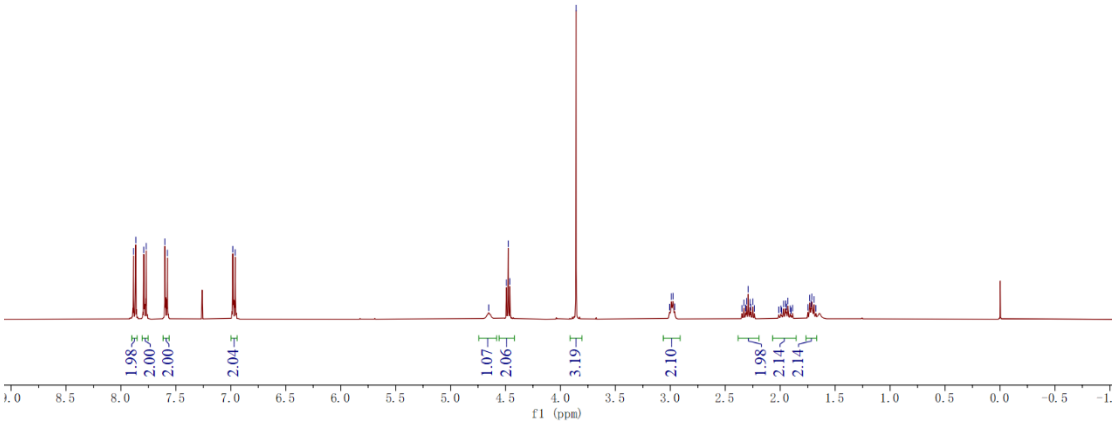
^{19}F NMR (376 MHz, $CDCl_3$)

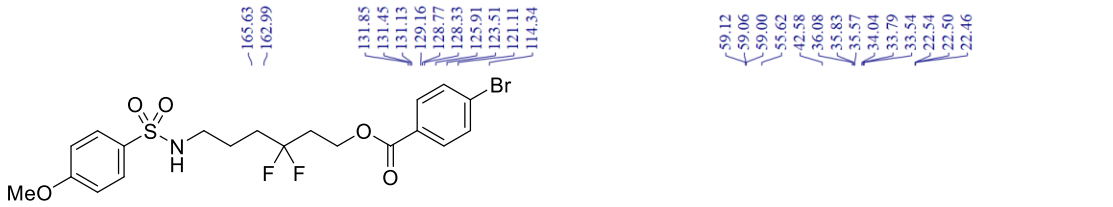




3s

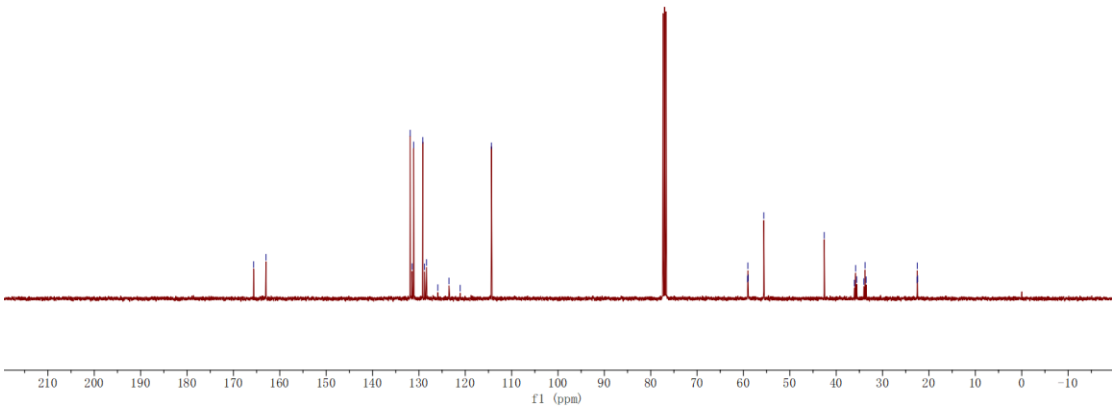
^{1}H NMR (400 MHz, $CDCl_3$)

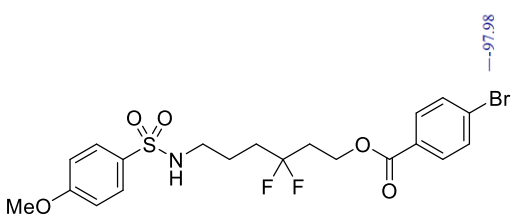




3s

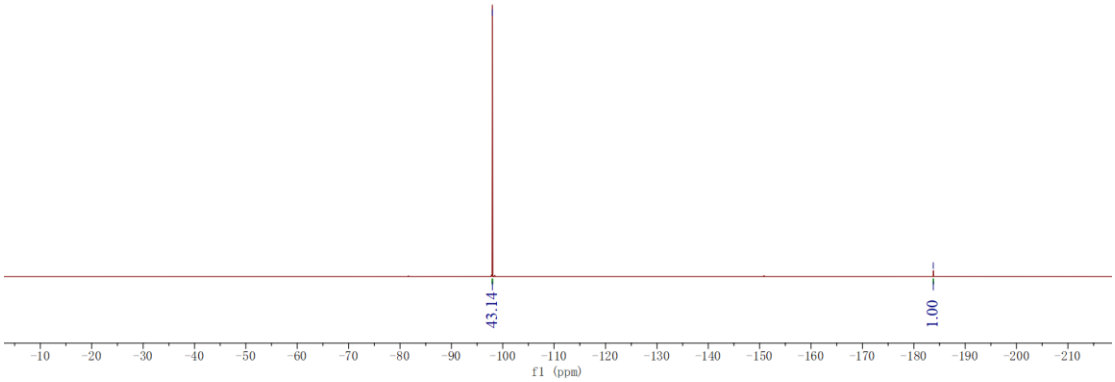
^{13}C NMR (101 MHz, $CDCl_3$)

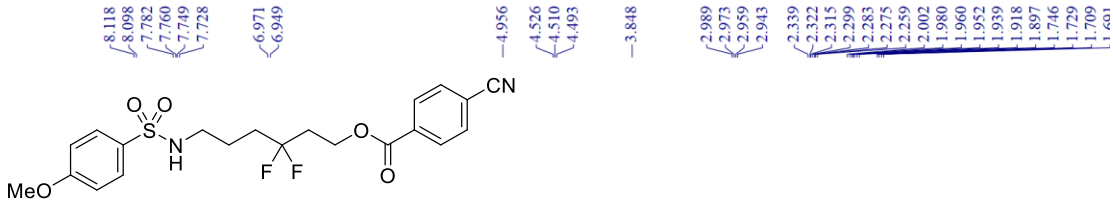




3s

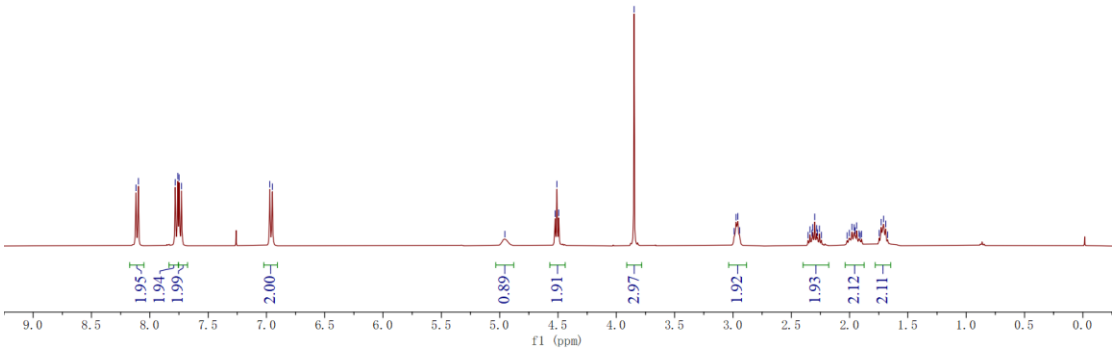
^{19}F NMR (376 MHz, $CDCl_3$)

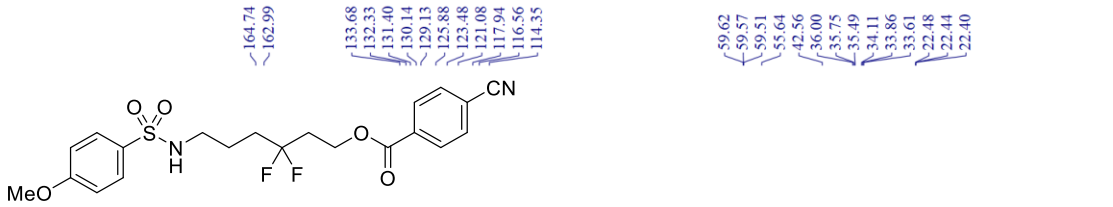




3t

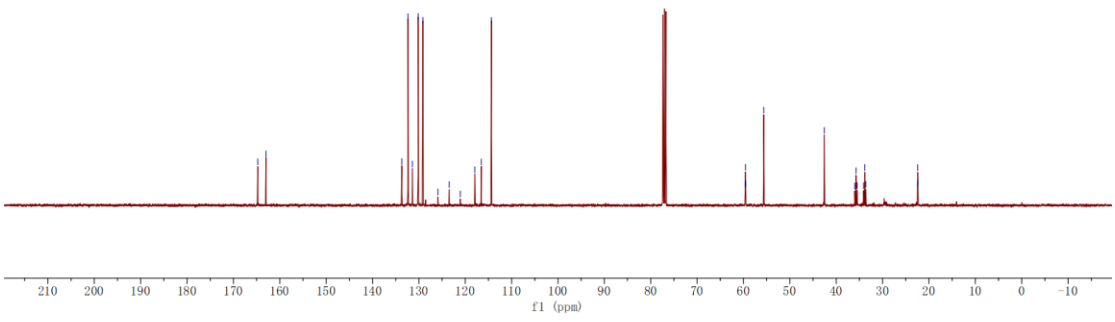
^{1}H NMR (400 MHz, $CDCl_3$)

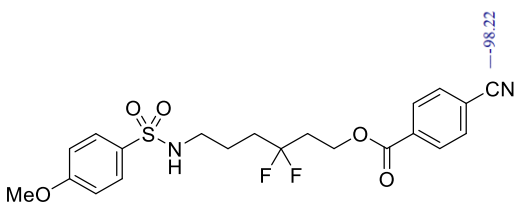




3t

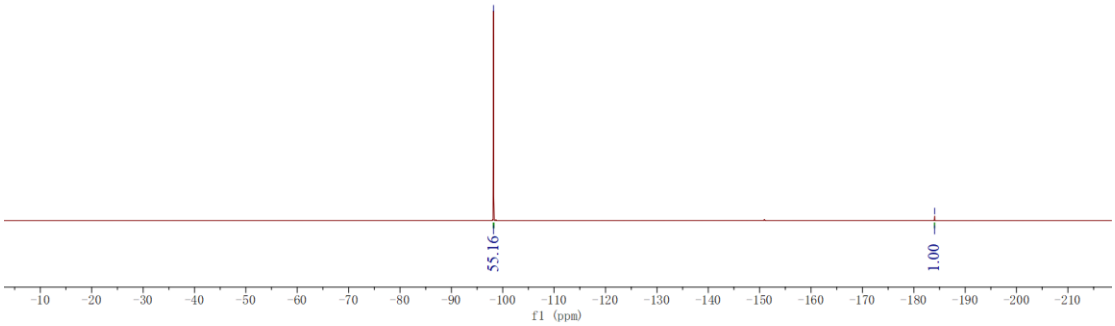
^{13}C NMR (101 MHz, $CDCl_3$)



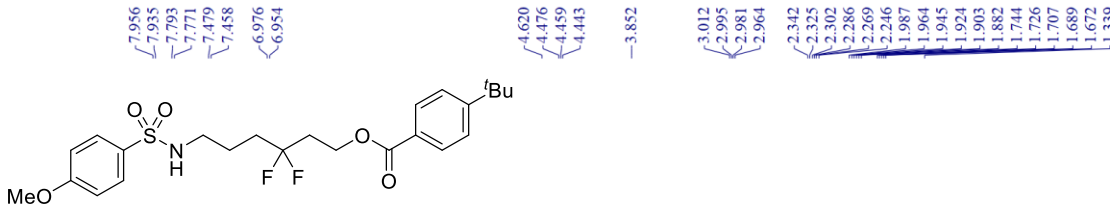


3t

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

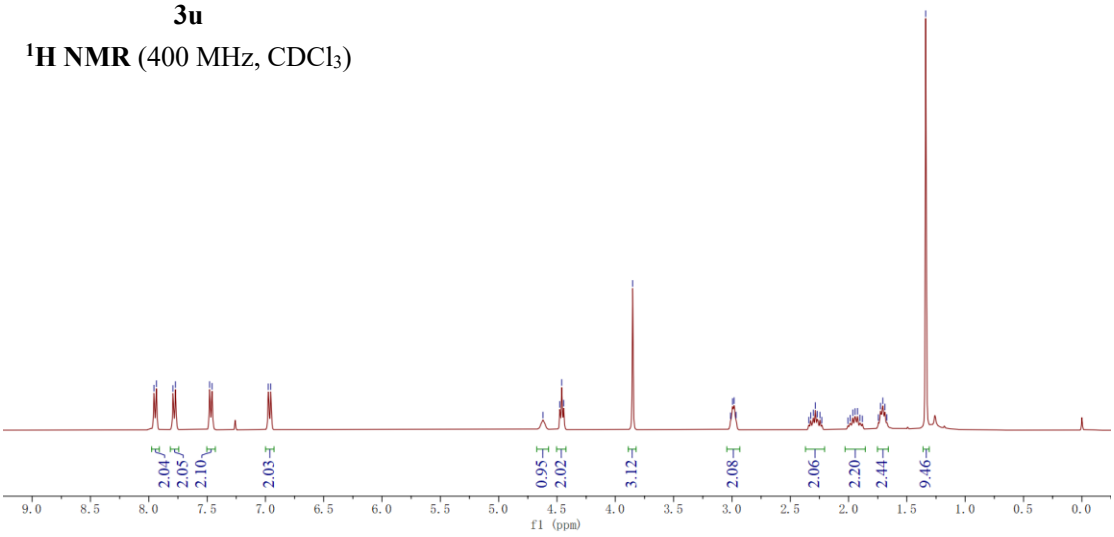


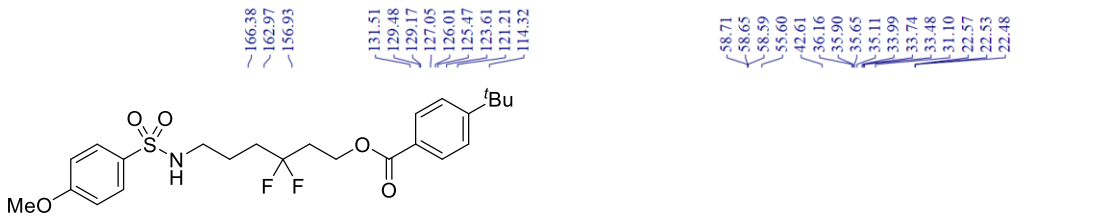
z



3u

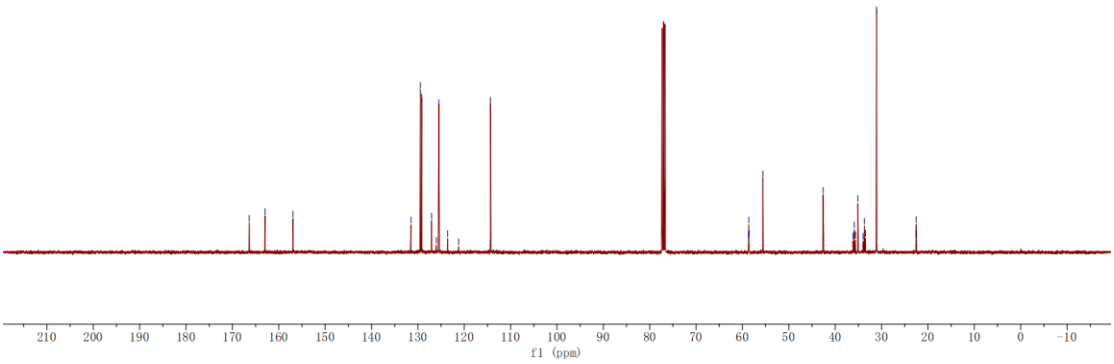
^{1}H NMR (400 MHz, $CDCl_3$)

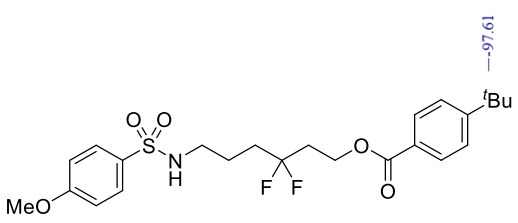




3u

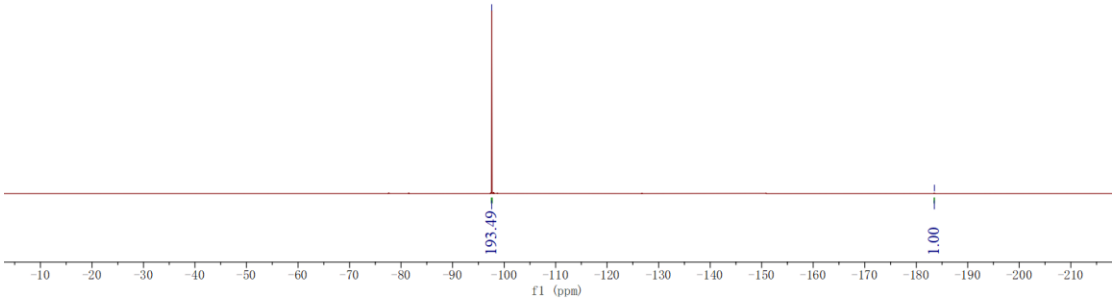
^{13}C NMR (101 MHz, $CDCl_3$)

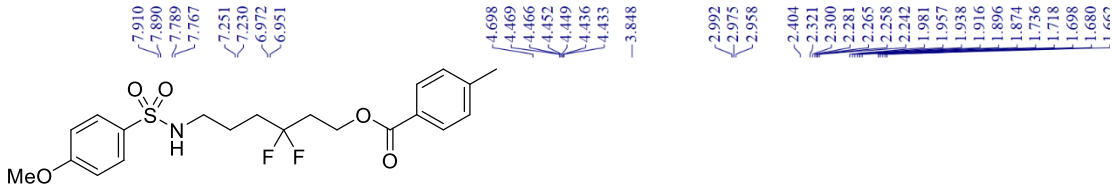




3u

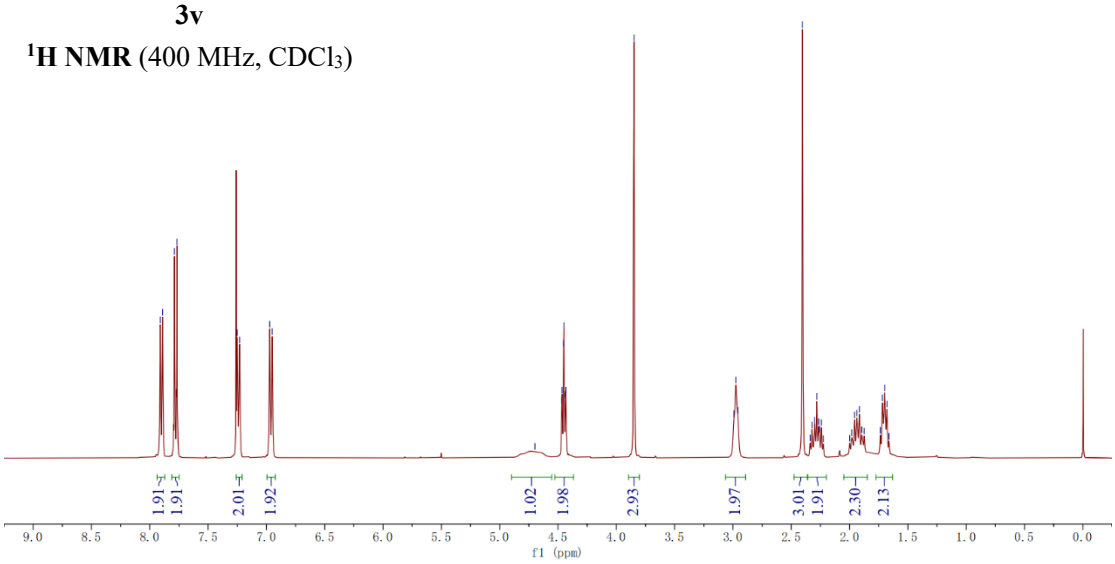
^{19}F NMR (376 MHz, $CDCl_3$)

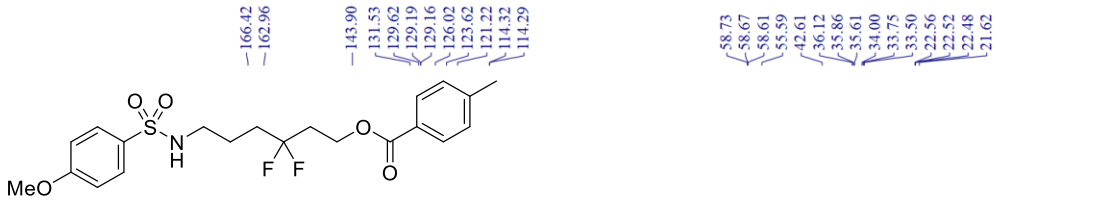




3v

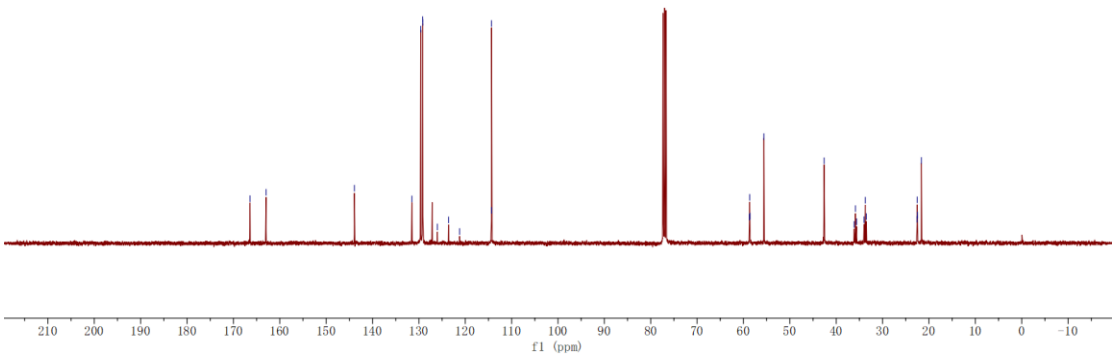
^{1}H NMR (400 MHz, $CDCl_3$)

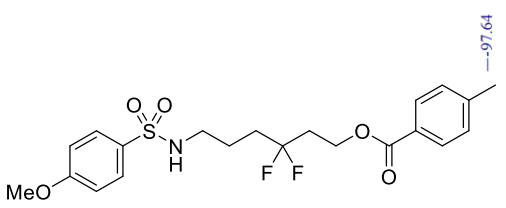




3v

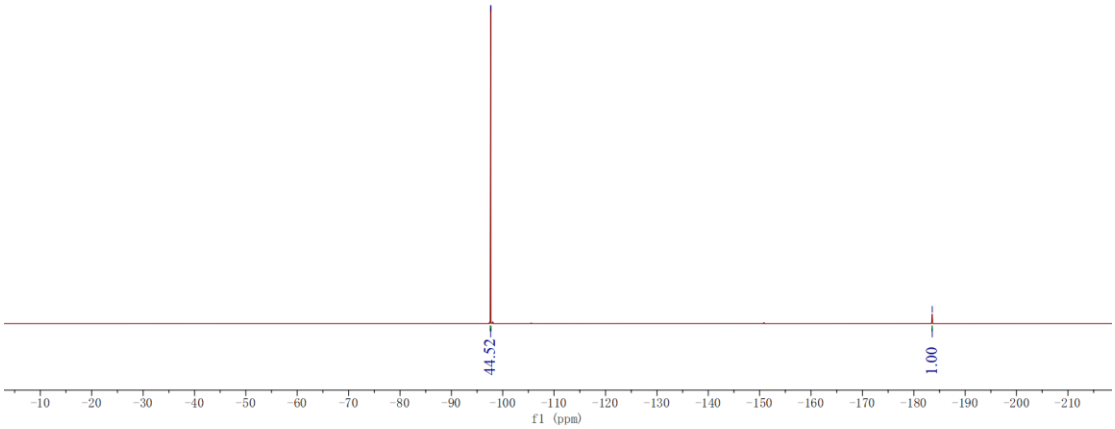
^{13}C NMR (101 MHz, $CDCl_3$)

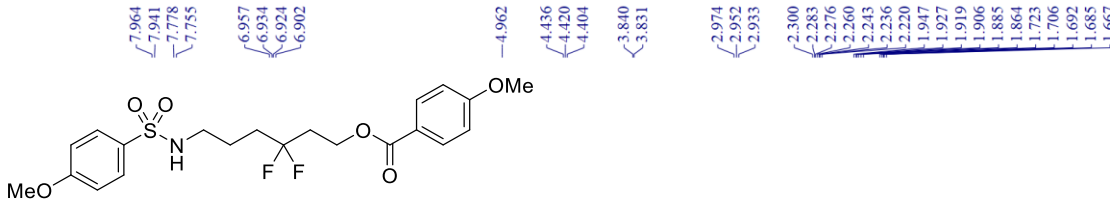




3v

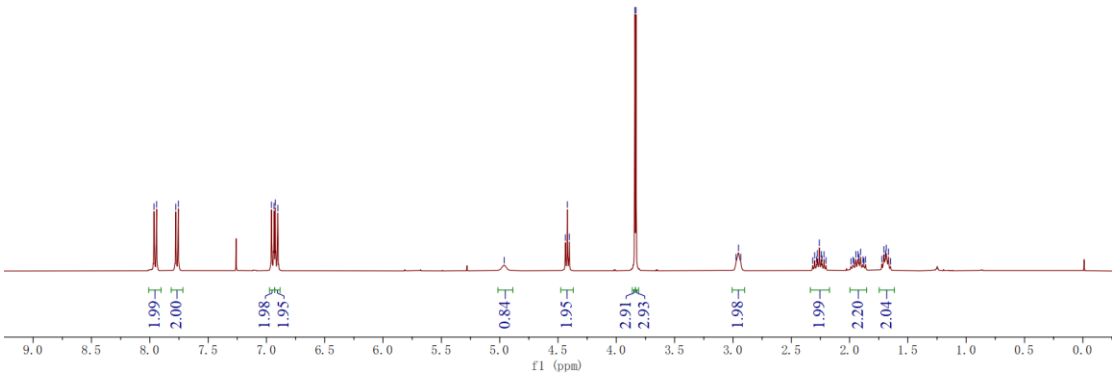
^{19}F NMR (376 MHz, $CDCl_3$)

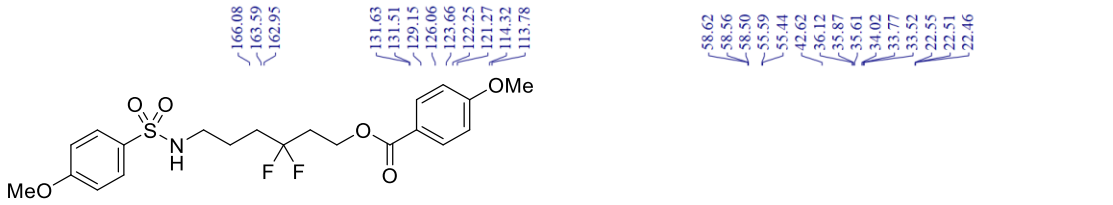




3w

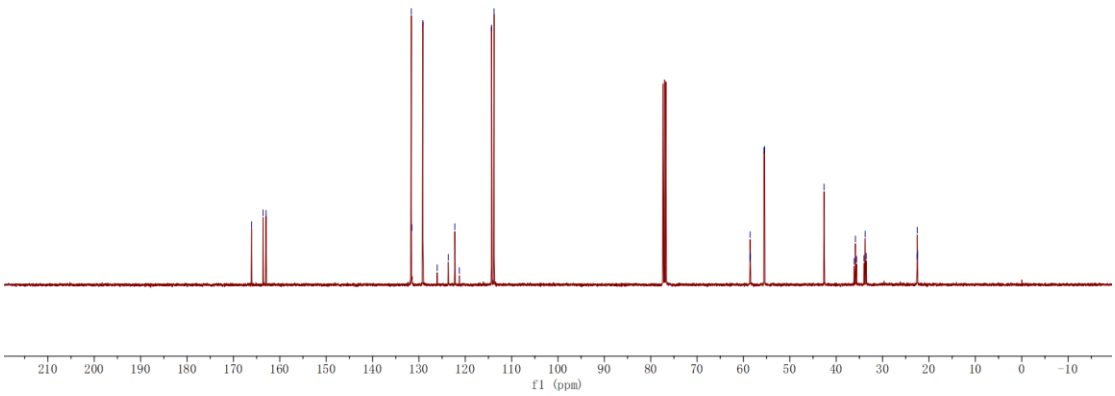
^{1}H NMR (400 MHz, $CDCl_3$)

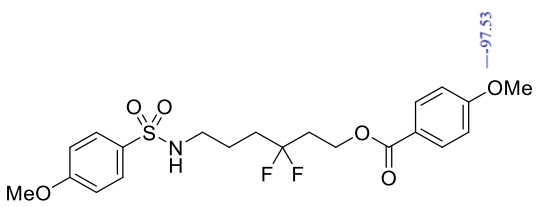




3w

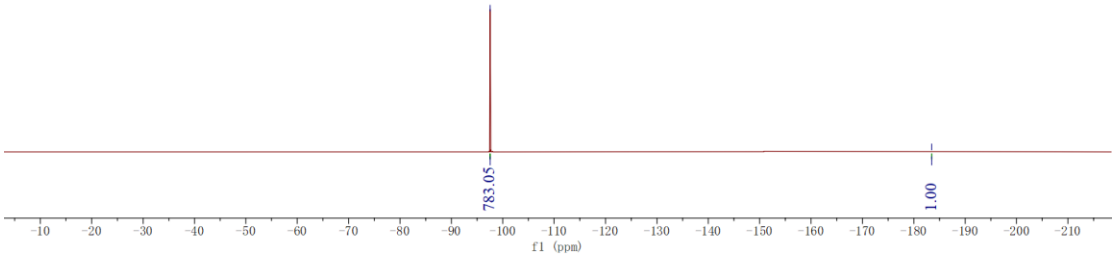
^{13}C NMR (101 MHz, $CDCl_3$)

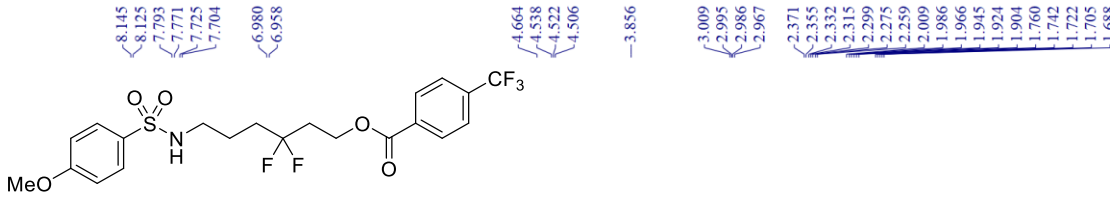




3w

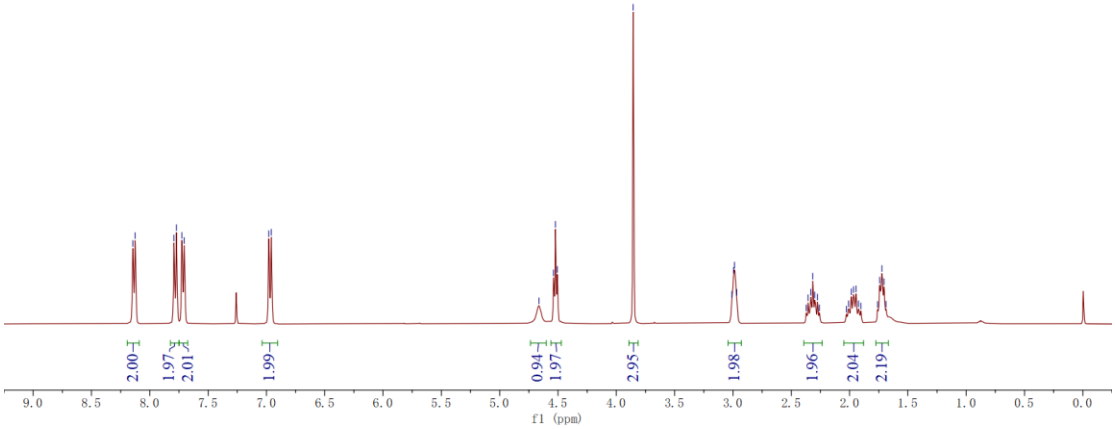
^{19}F NMR (376 MHz, $CDCl_3$)

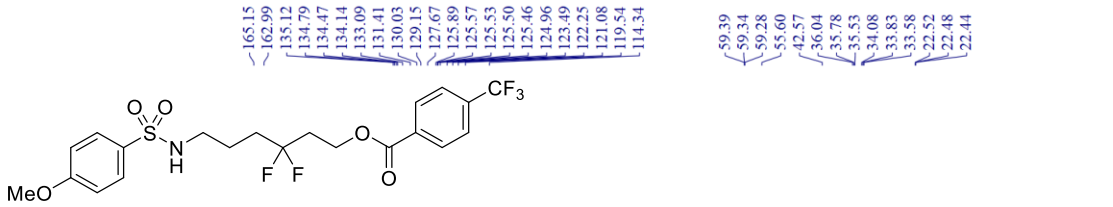




3x

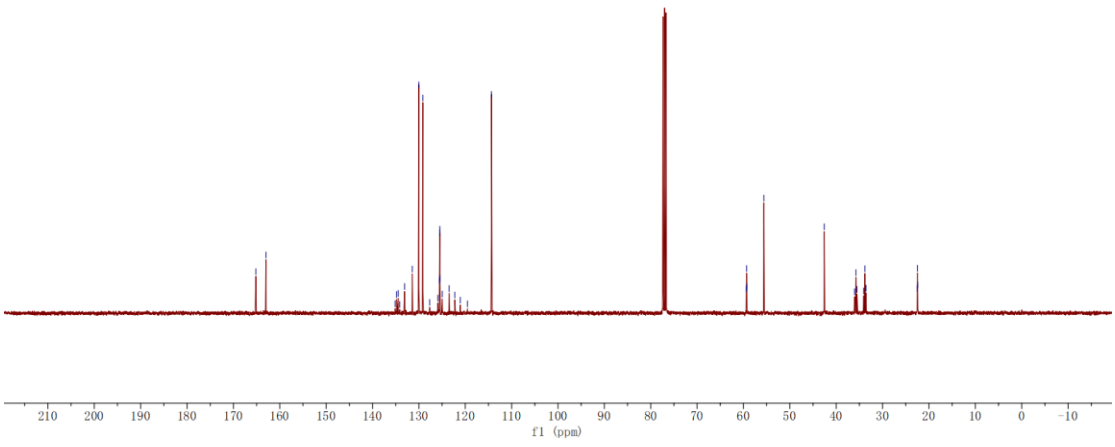
^{1}H NMR (400 MHz, $CDCl_3$)

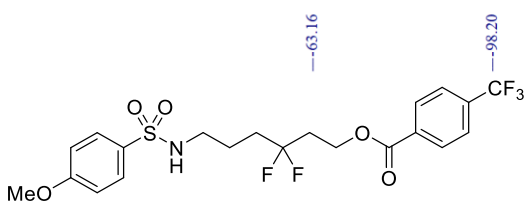




3x

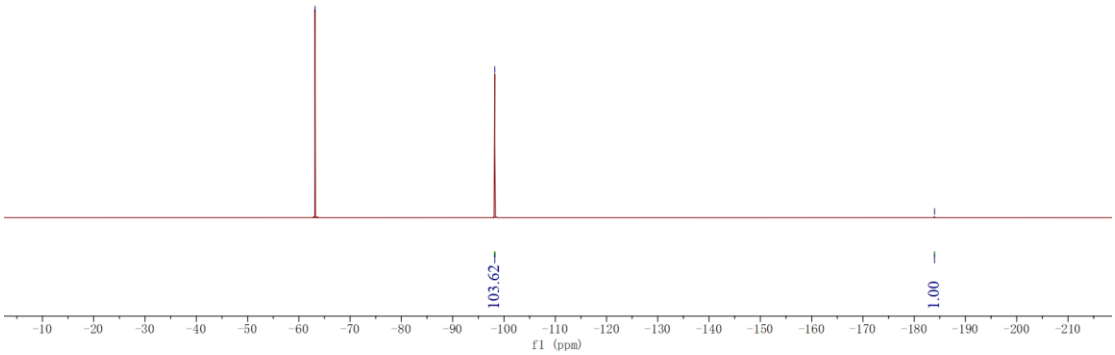
^{13}C NMR (101 MHz, $CDCl_3$)

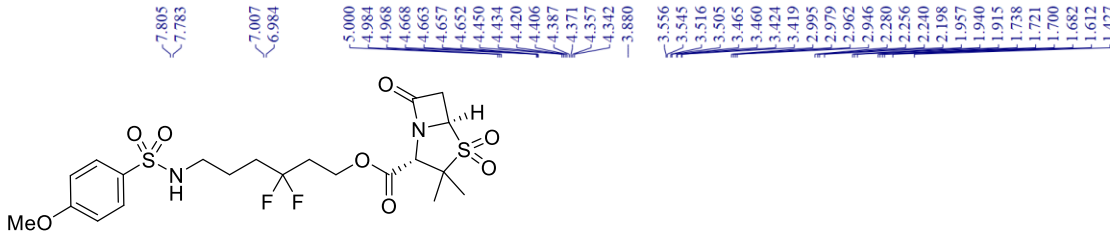




3x

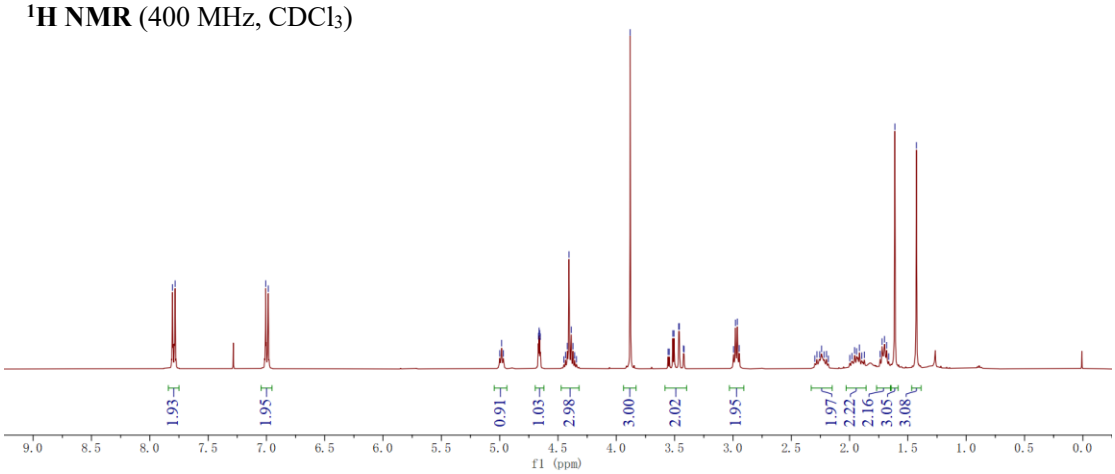
^{19}F NMR (376 MHz, $CDCl_3$)

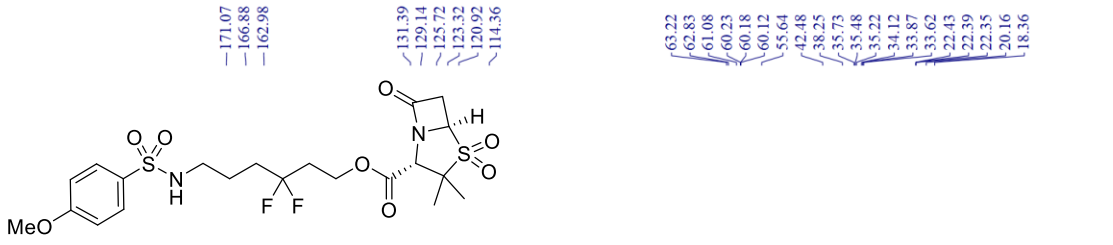




3y

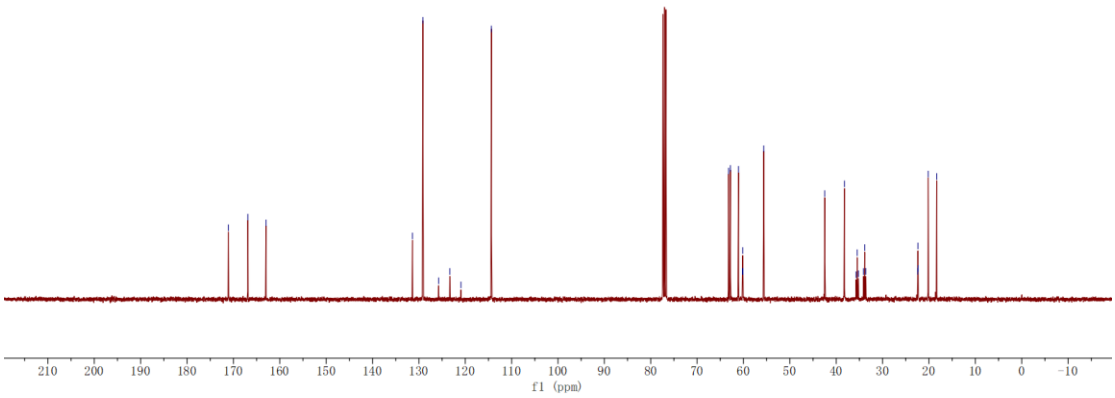
^{1}H NMR (400 MHz, $CDCl_3$)

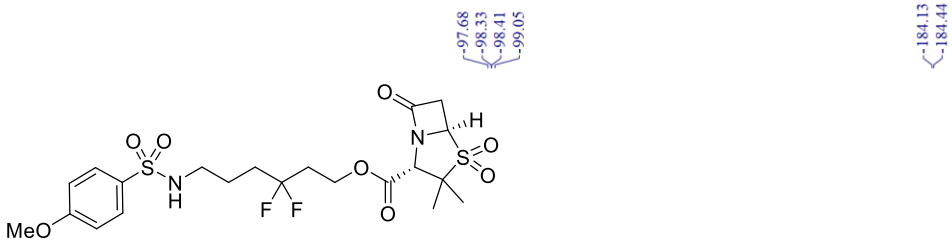




3y

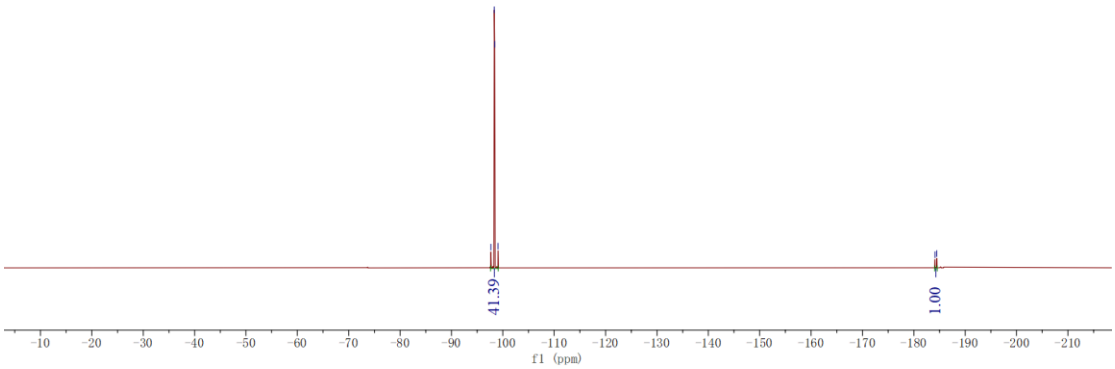
^{13}C NMR (101 MHz, $CDCl_3$)

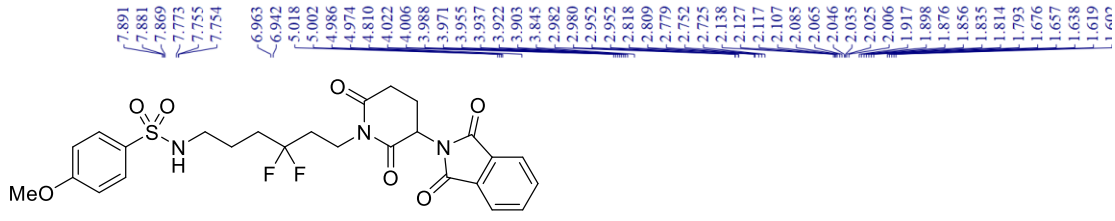




3y

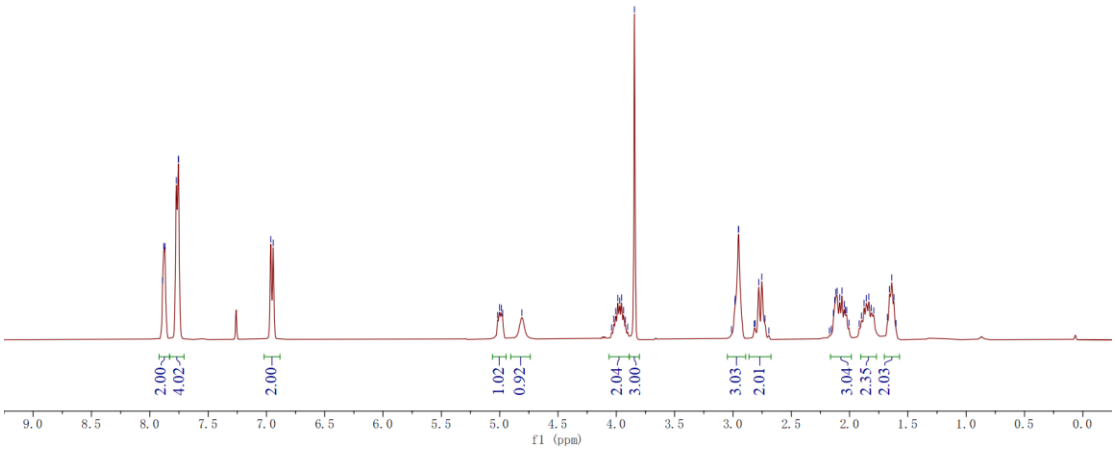
^{19}F NMR (376 MHz, $CDCl_3$)

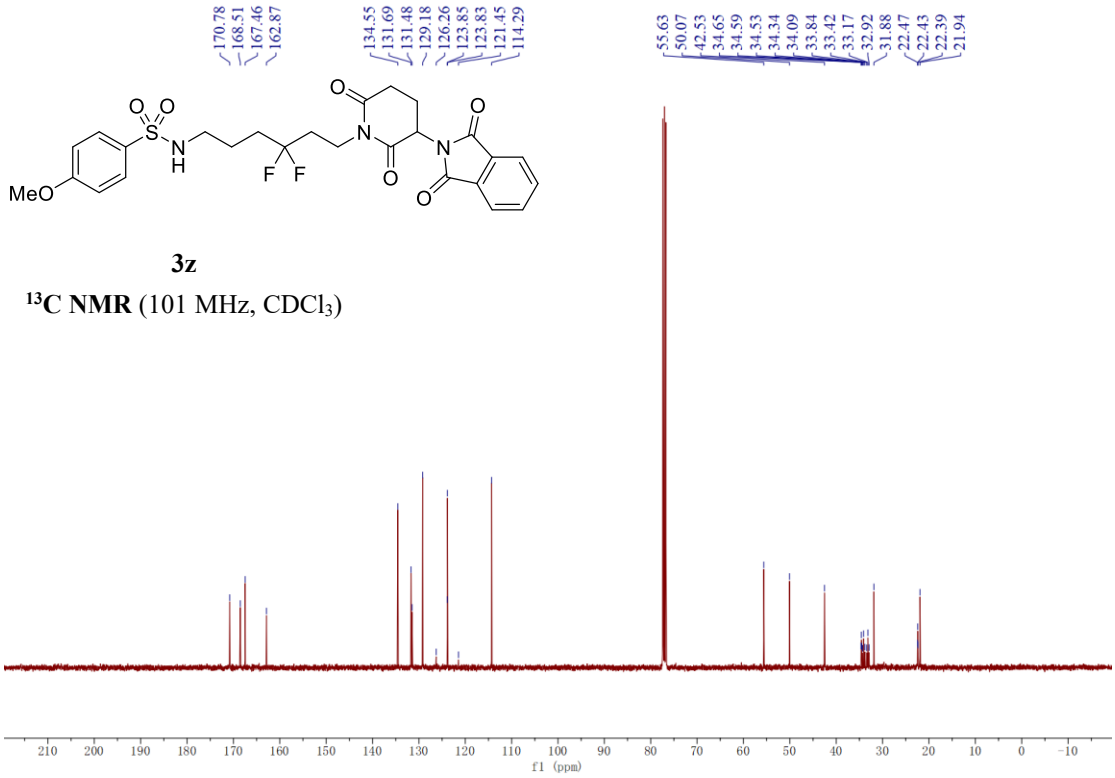




3z

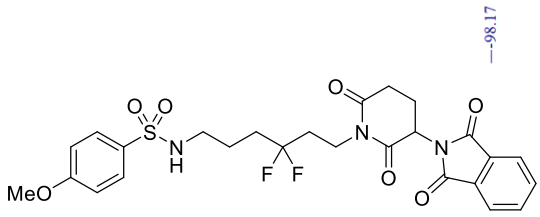
^{1}H NMR (400 MHz, $CDCl_3$)





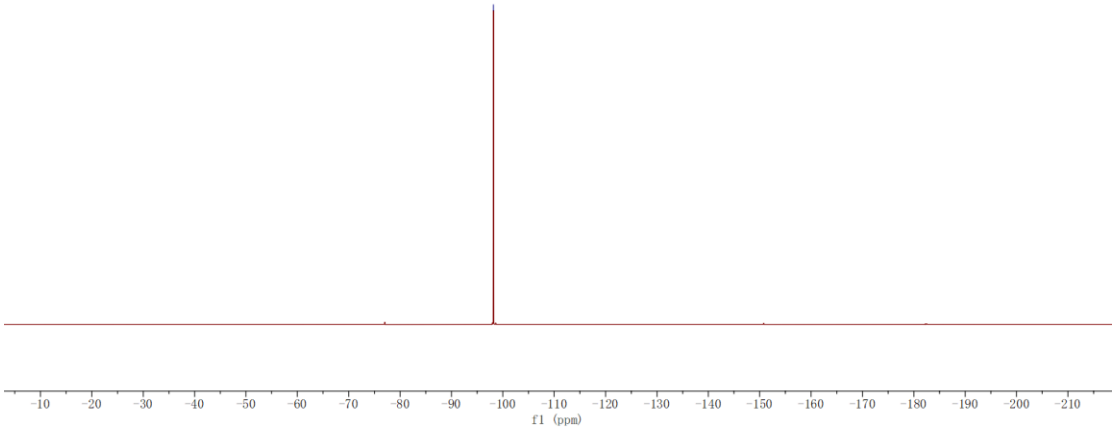
3z

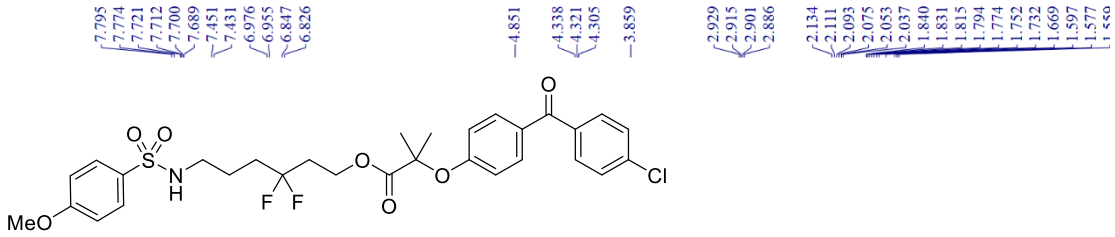
^{13}C NMR (101 MHz, $CDCl_3$)



3z

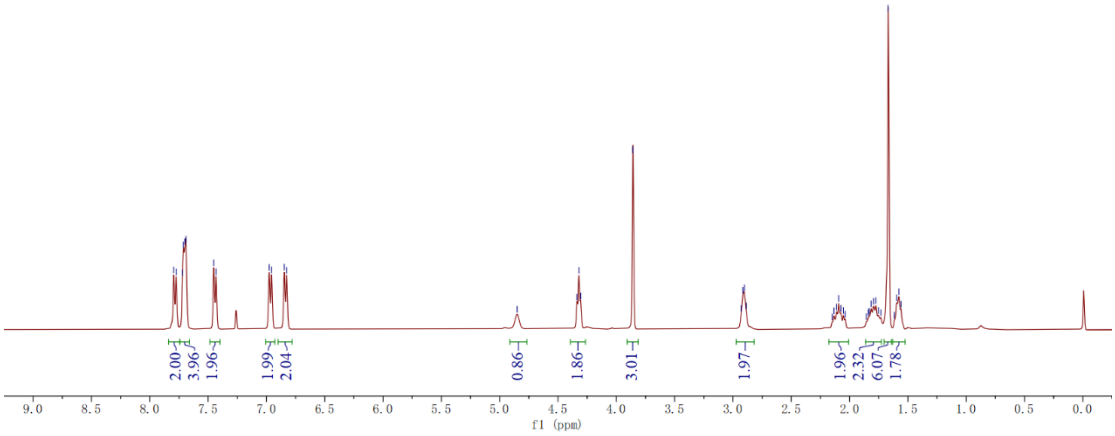
^{19}F NMR (376 MHz, $CDCl_3$)

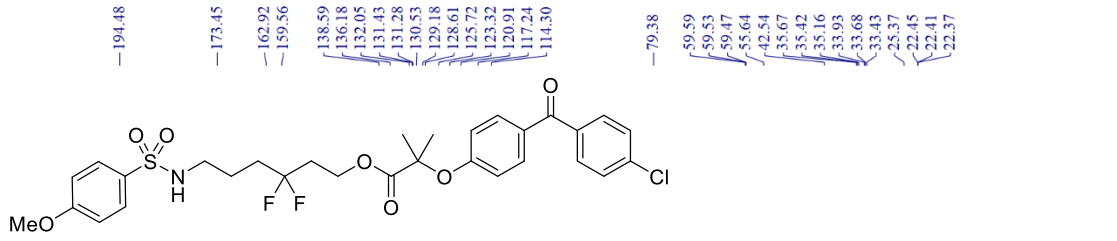




3aa

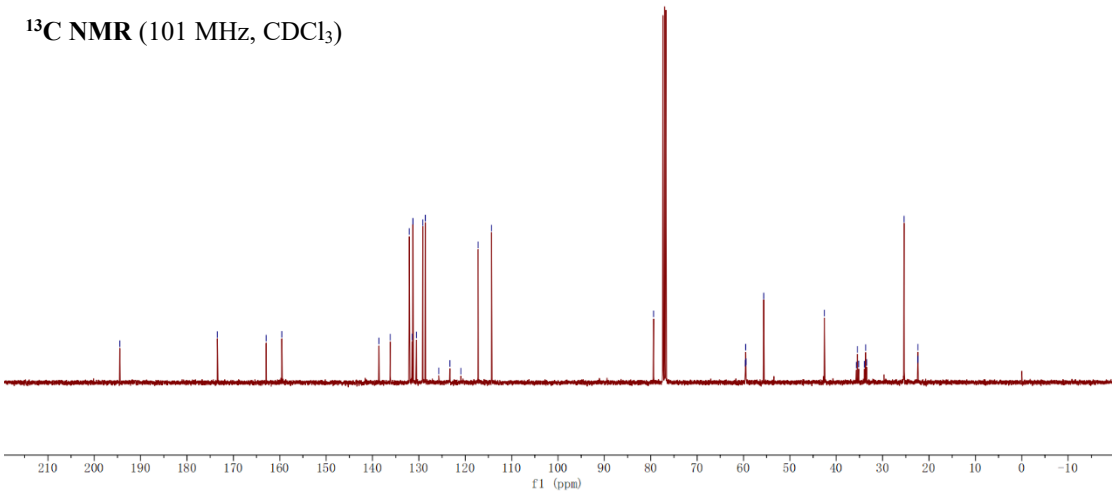
^{1}H NMR (400 MHz, $CDCl_3$)

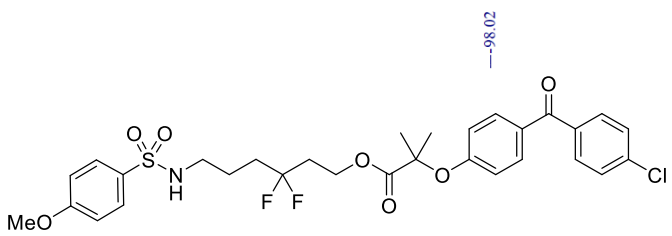




3aa

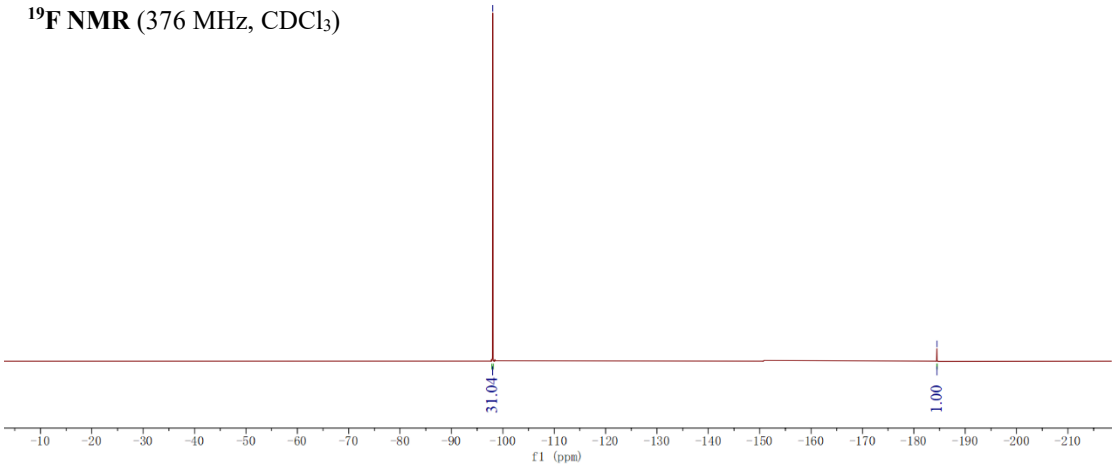
^{13}C NMR (101 MHz, $CDCl_3$)

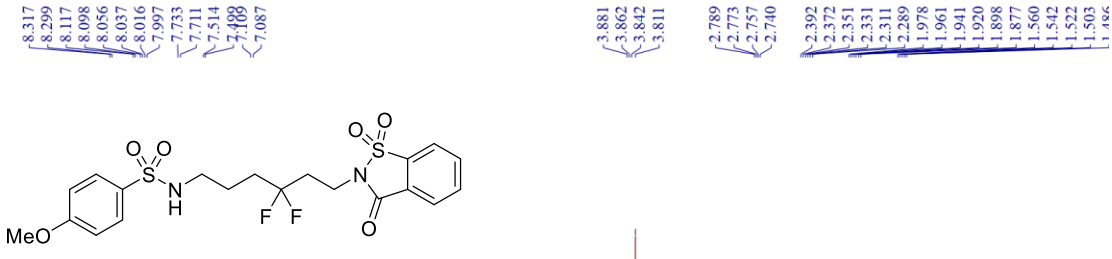




3aa

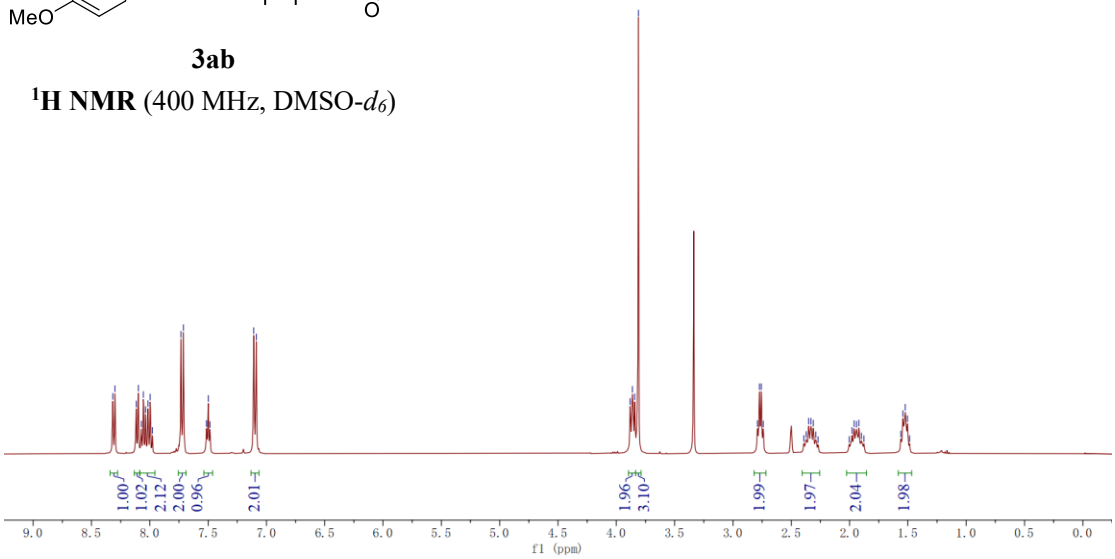
^{19}F NMR (376 MHz, $CDCl_3$)

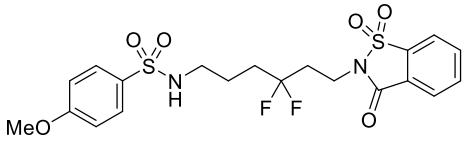




3ab

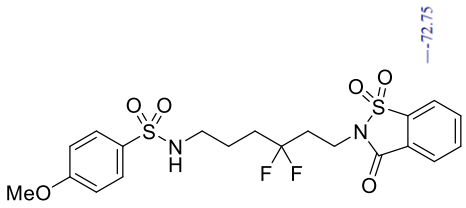
^{1}H NMR (400 MHz, DMSO-d_6)





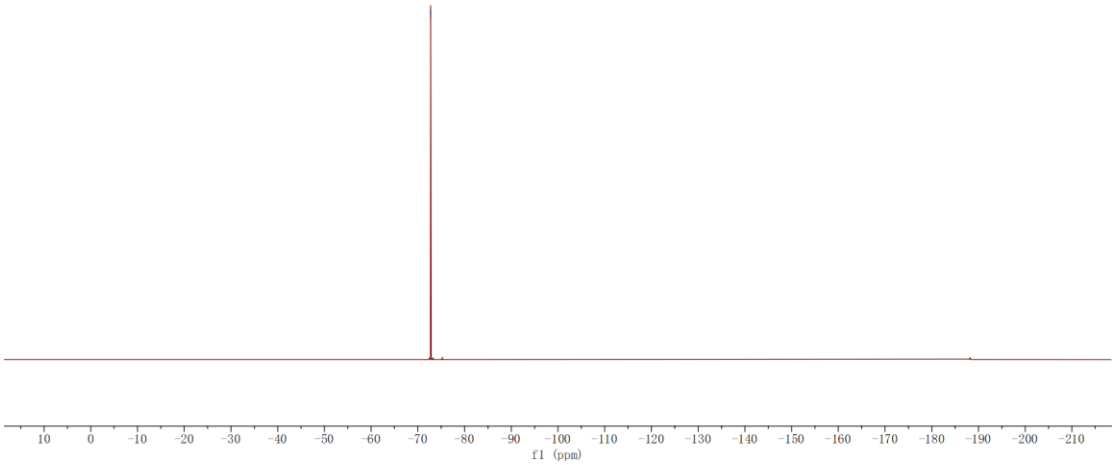
3ab

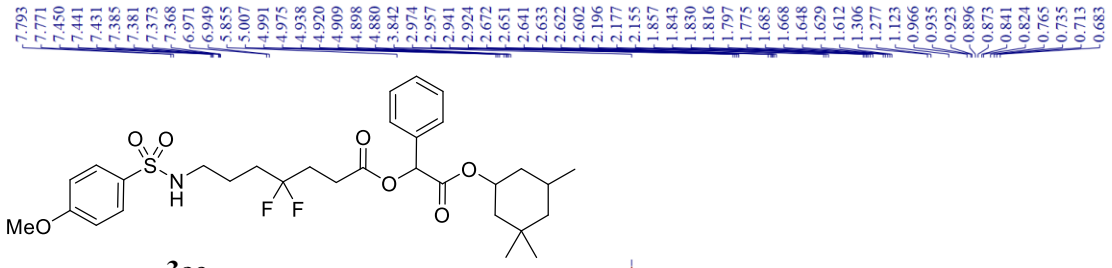
^{13}C NMR (101 MHz, DMSO-d_6)



3ab

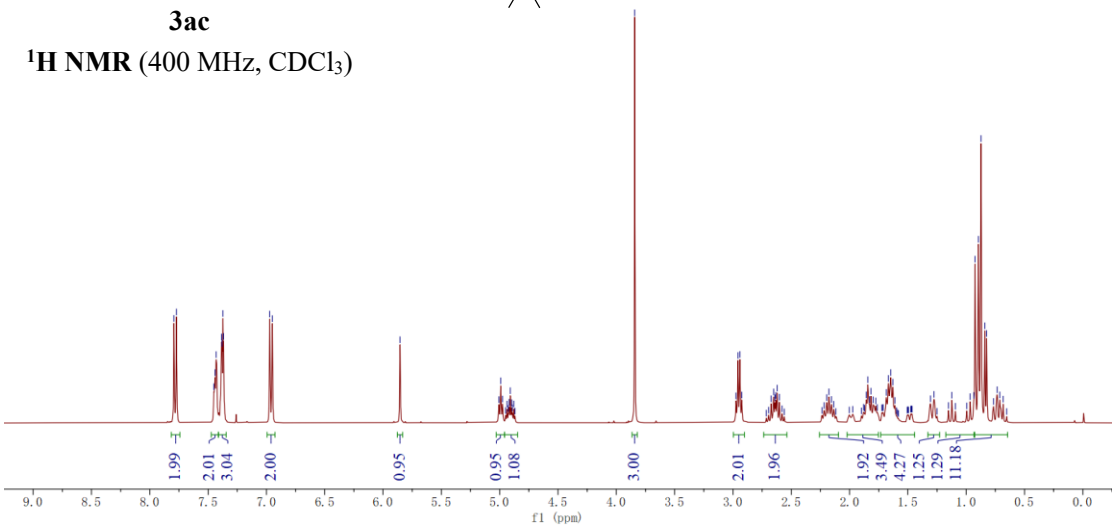
^{19}F NMR (376 MHz, DMSO-d_6)

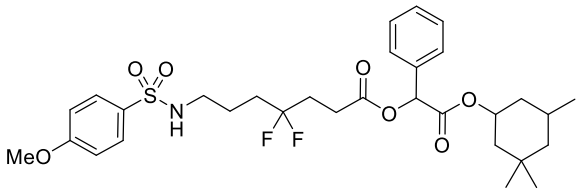




3ac

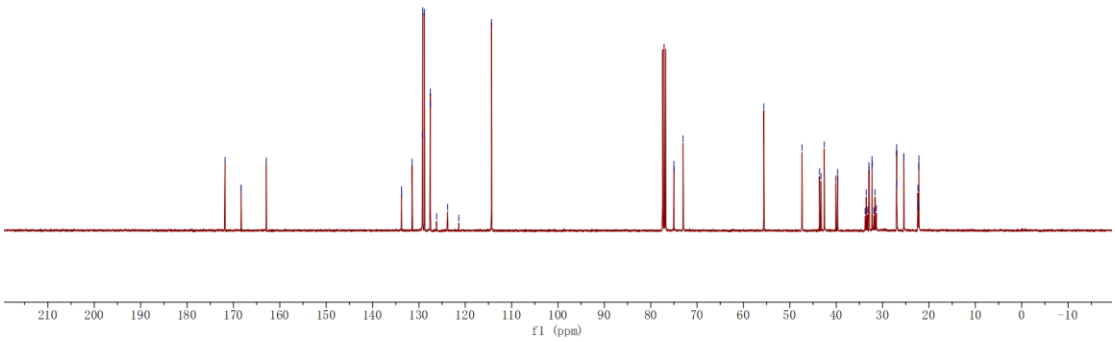
^{1}H NMR (400 MHz, $CDCl_3$)

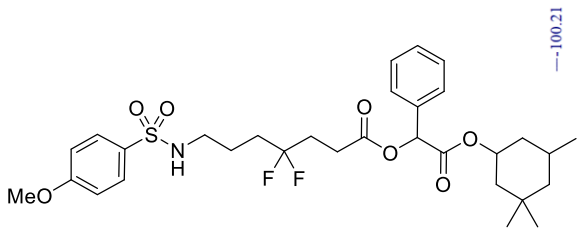




3aec

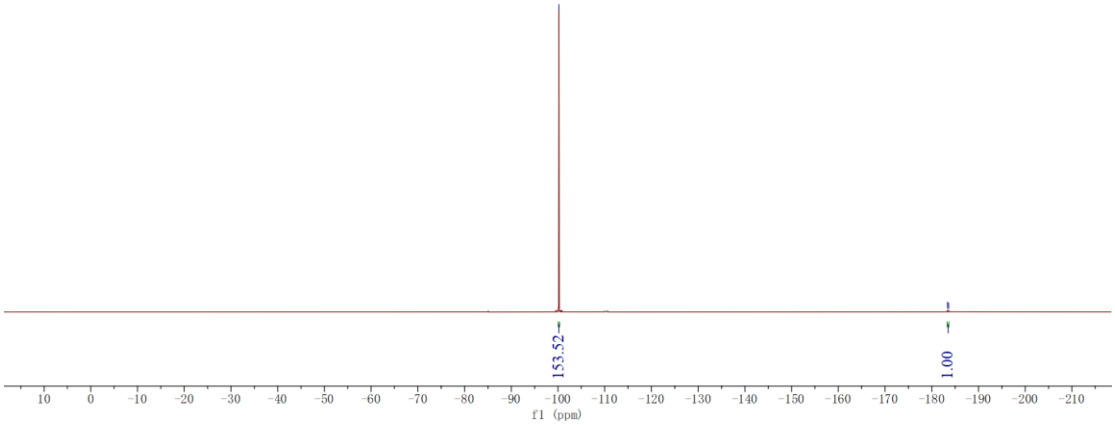
^{13}C NMR (101 MHz, $CDCl_3$)

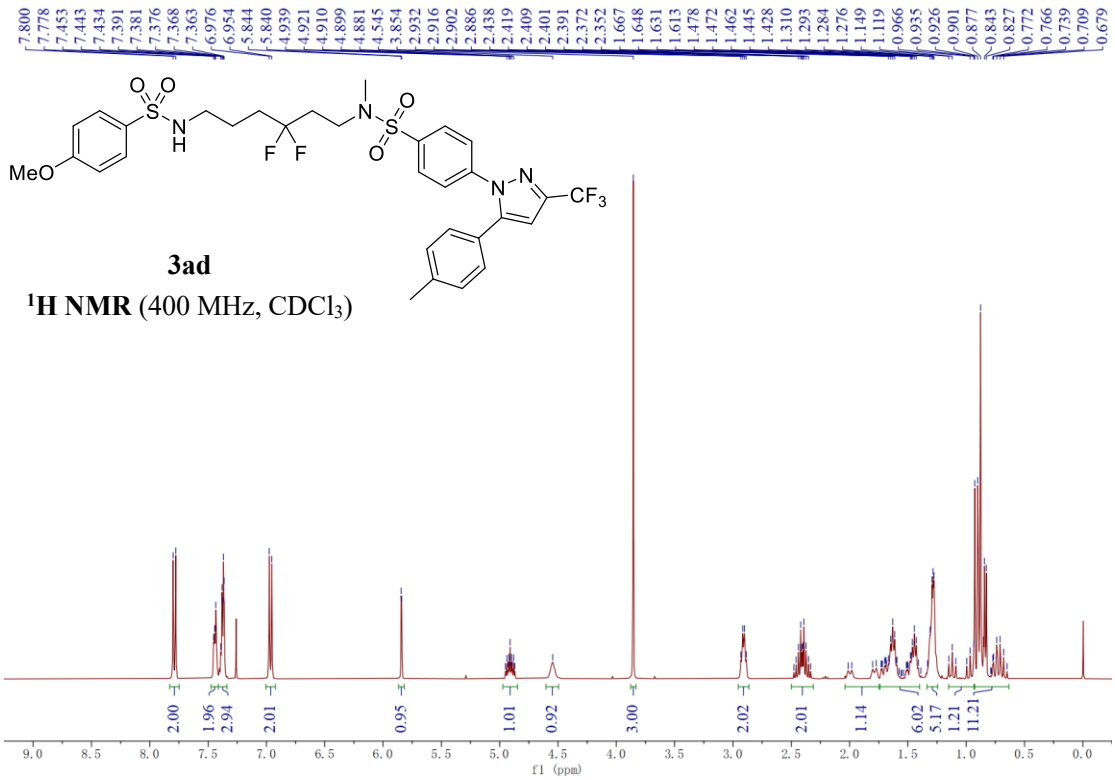




3ac

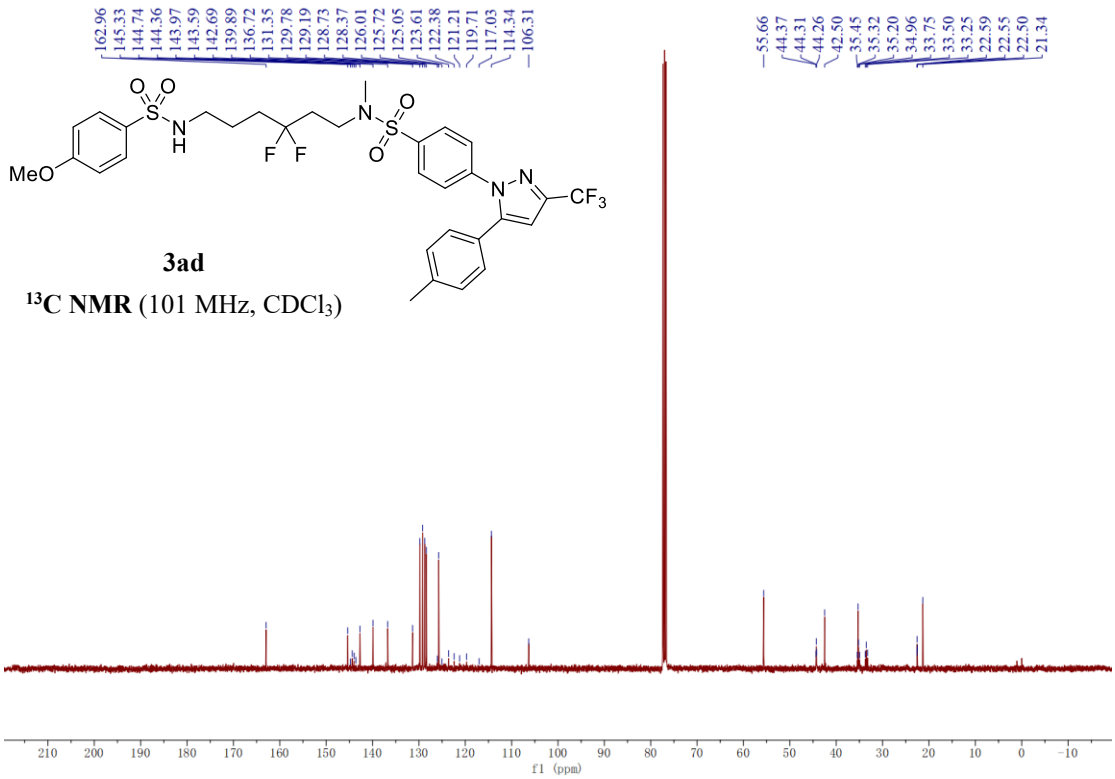
^{19}F NMR (376 MHz, $CDCl_3$)





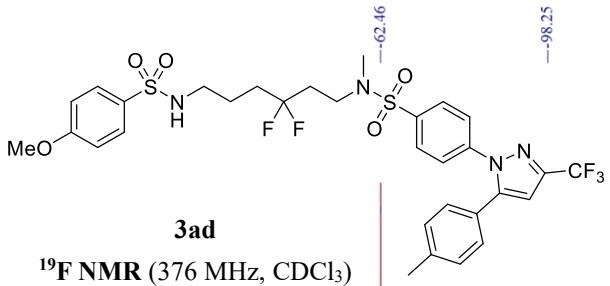
3ad

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



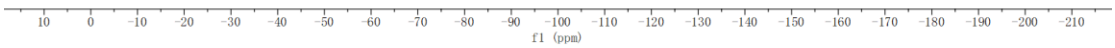
3ad

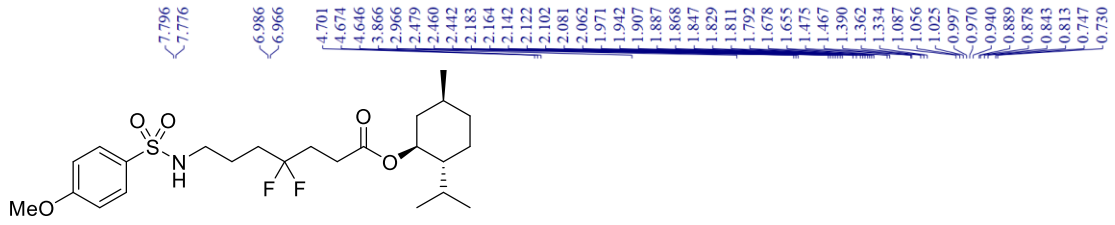
^{13}C NMR (101 MHz, $CDCl_3$)



3ad

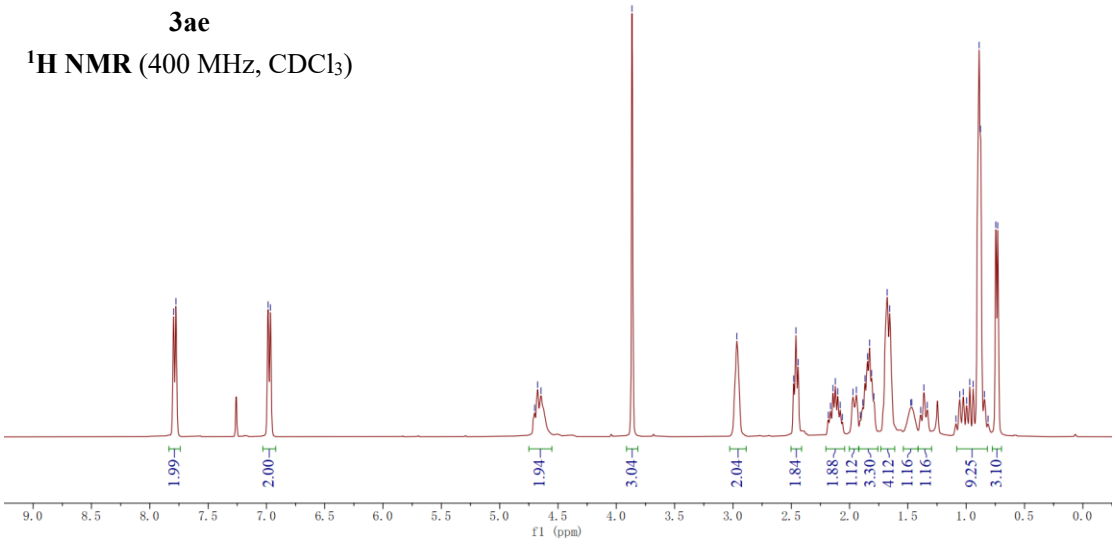
^{19}F NMR (376 MHz, $CDCl_3$)

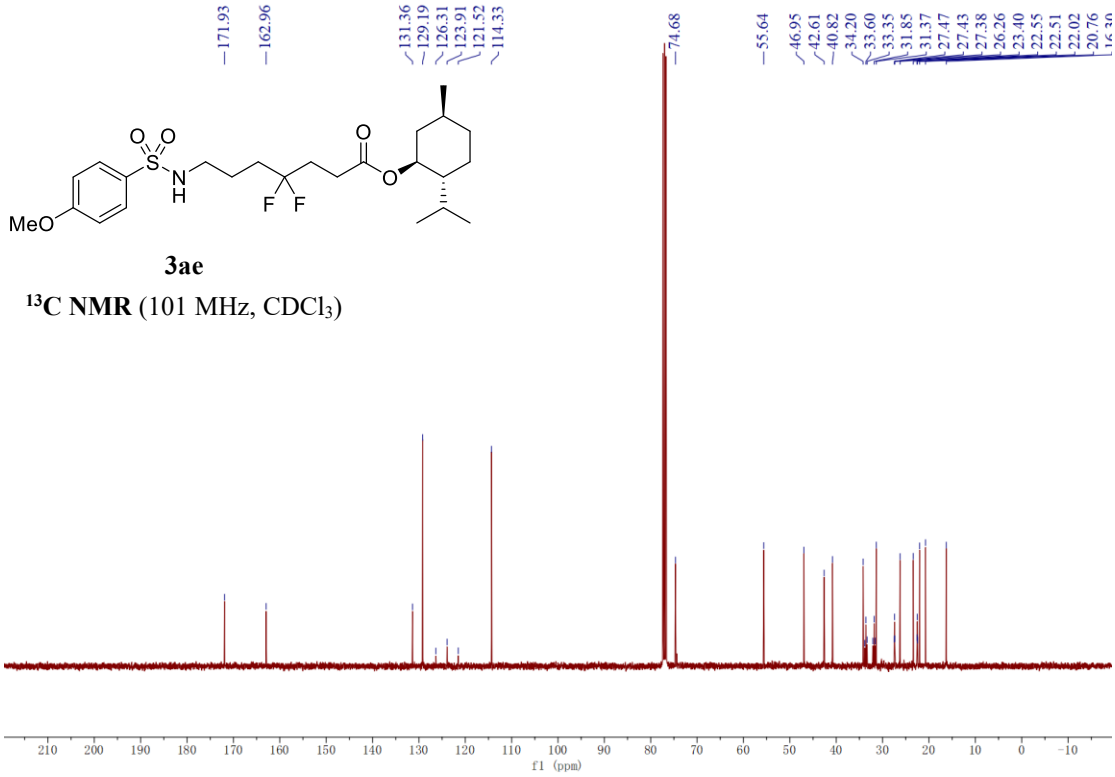




3ae

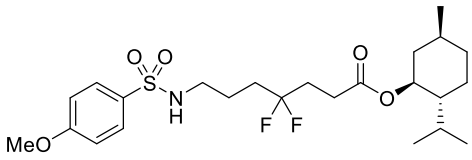
^{1}H NMR (400 MHz, $CDCl_3$)





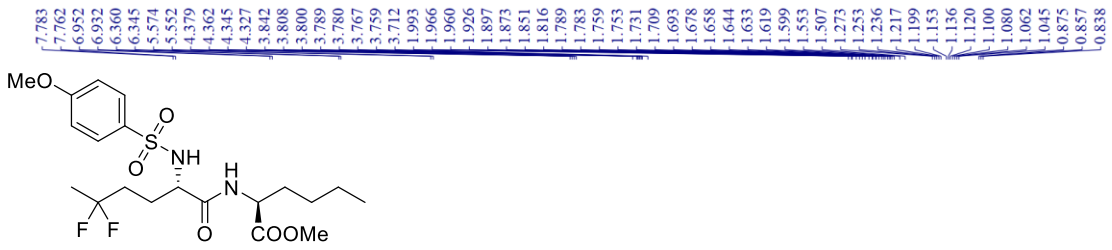
3ae

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



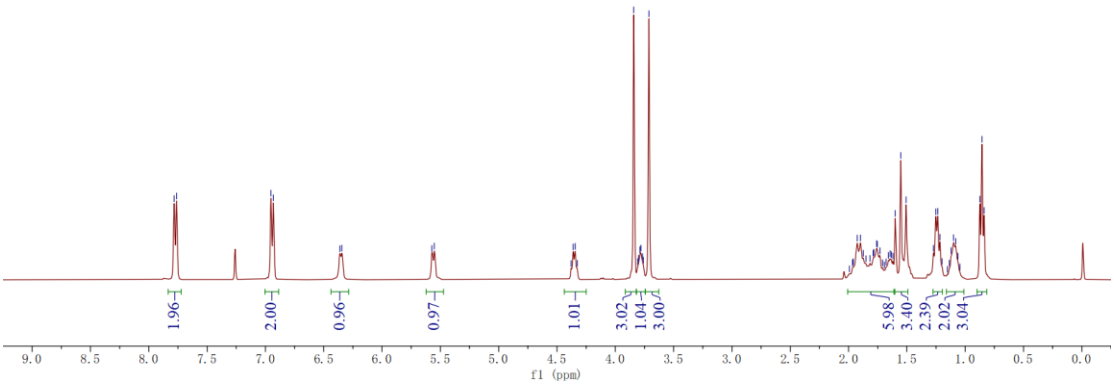
3ae

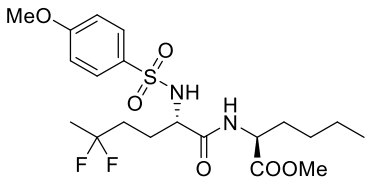
^{19}F NMR (376 MHz, $CDCl_3$)



3af

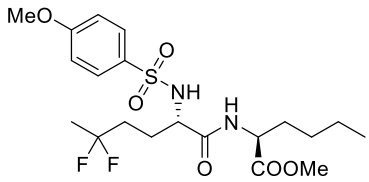
^{1}H NMR (400 MHz, $CDCl_3$)





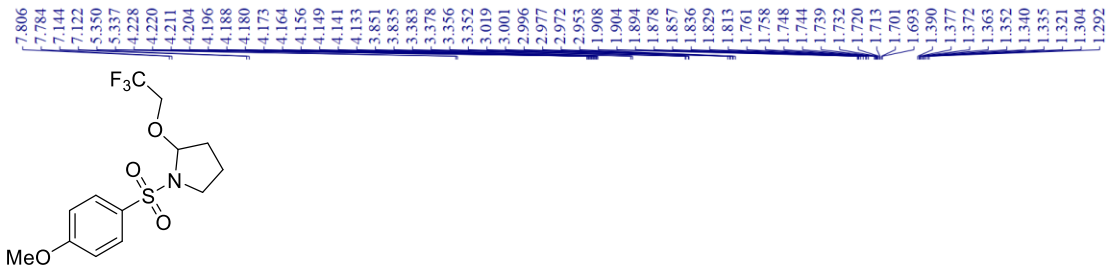
3af

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



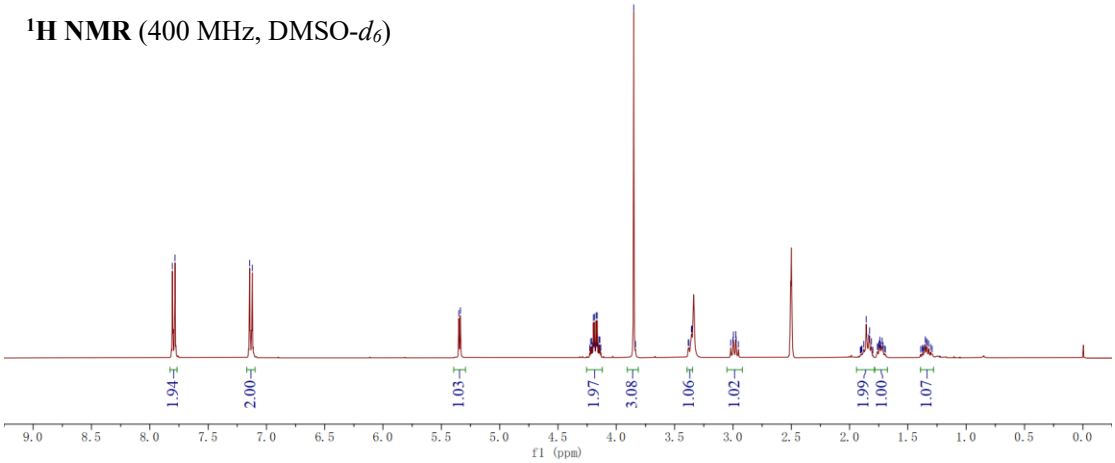
3af

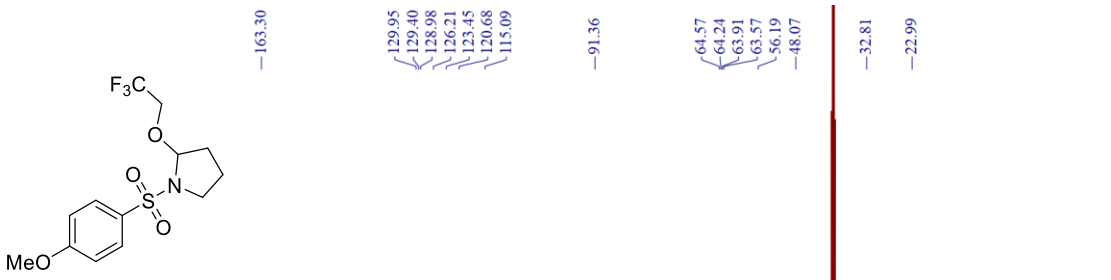
^{19}F NMR (376 MHz, $CDCl_3$)



5

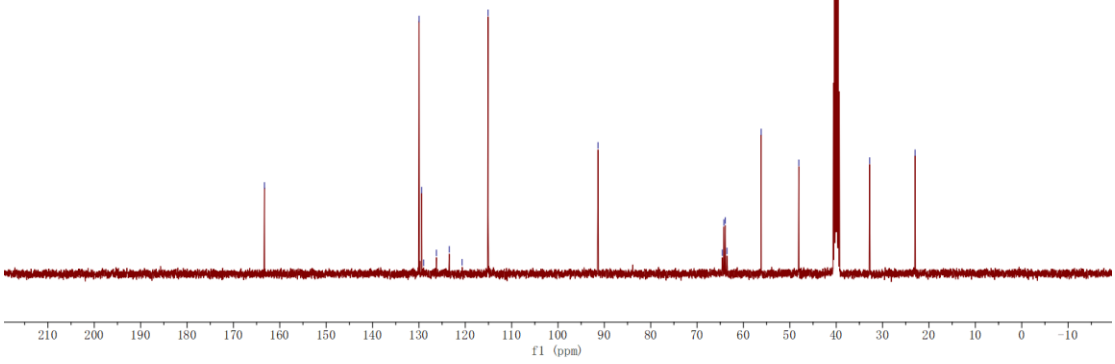
^{1}H NMR (400 MHz, DMSO-d_6)

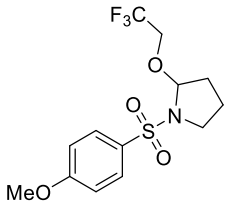




5

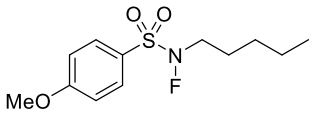
^{13}C NMR (101 MHz, DMSO-d_6)





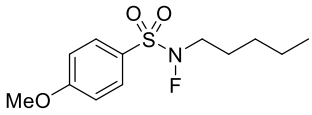
5

^{19}F NMR (376 MHz, DMSO-d_6)



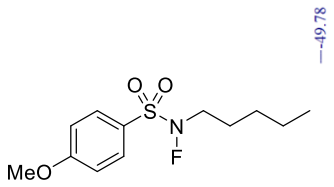
6

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



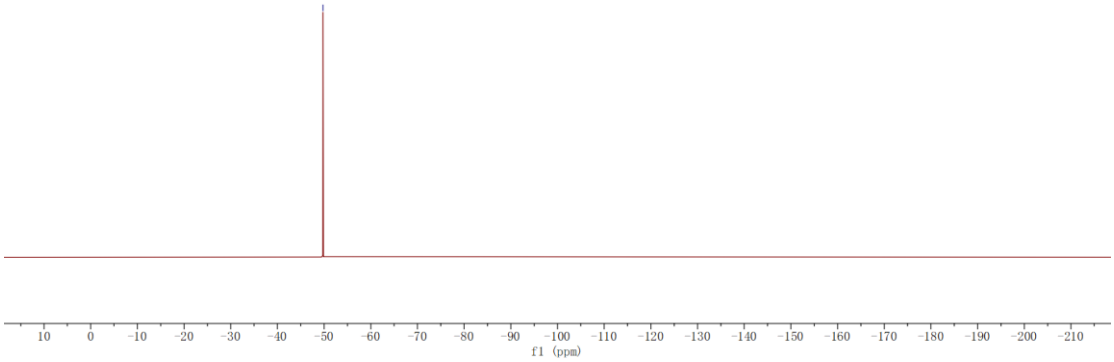
6

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



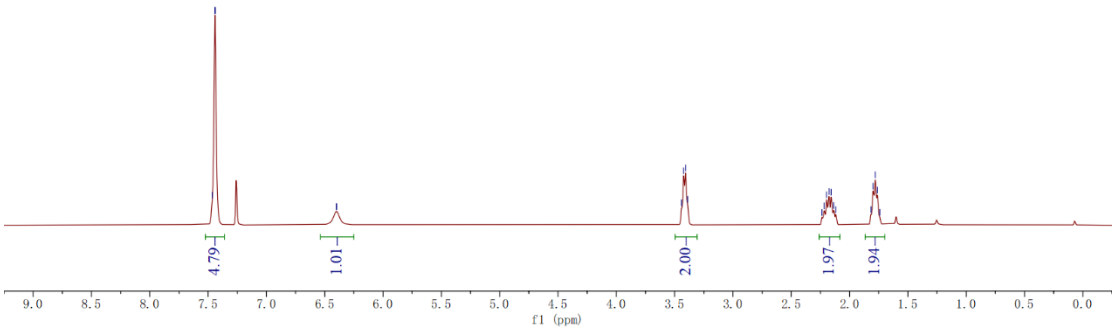
6

^{19}F NMR (376 MHz, DMSO-d_6)



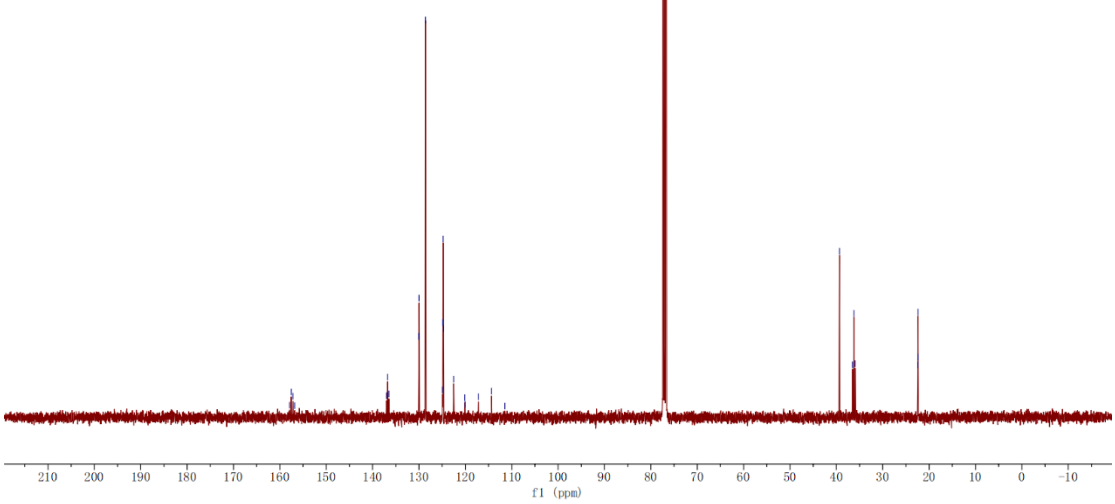
7

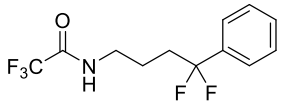
^{1}H NMR (400 MHz, $CDCl_3$)



7

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





7

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