Supporting Information for

Oxidative *N*-functionalization of primary sulfonamides with aliphatic aldehydes: a green synthesis of *α*-sulfonamido acetals

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Table of contents

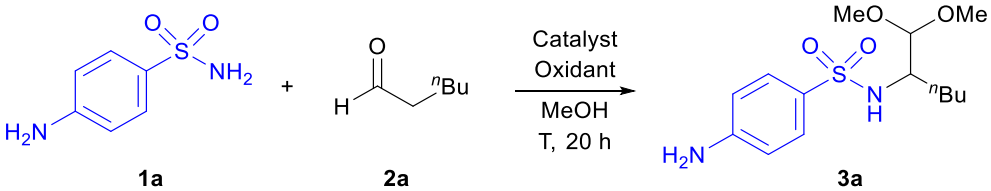
1. General information

All reactions were performed without exclusion of air. Aldehydes **2d**, **2f** and **2k** were prepared according to previous reports with minor modification. Other reagents and solvents were commercially available and directly used without further purification. Reactions were monitored by thin layer chromatography [Merck 60 F254 precoated silica gel plate (0.2 mm thickness)] and visualized using UV radiation (254 nm) on Spectroline Model ENf-24061/F 254 nm. The products were purified by column chromatography using 200-300 mesh silica gel. Melting points were measured on HUAZHI HMZ-2A automatic melting point instrument. All NMR spectra were recorded on Bruker 400 MHz or Bruker 500 MHz and Me_4Si (^1H: 0 ppm) or $CDCl_3$ (^1H: 7.26 ppm, ^{13}C: 77.00 ppm) was used as internal standard. High-resolution mass spectra (HRMS) were recorded by using a Waters Q-Tof Permier Spectrometer.

2. Optimization of reaction conditions

Our investigation began with the oxidative *N*-functionalization of sulfanilamide **1a** (free amino group) and hexanal **2a** under various conditions (Table S1). Initial trials using sodium percarbonate ($Na_2CO_3 \cdot 1.5H_2O_2$) alone in methanol (MeOH) at 70°C (entry 1) yielded no product **3a**, indicating insufficient reactivity. The introduction of an iodine/$Na_2CO_3 \cdot 1.5H_2O_2$ catalytic system dramatically improved outcomes, achieving 70% yield of *α*-sulfonamido acetal **3a** (entry 2). Catalyst screening revealed sodium iodide (NaI) to be equally effective as molecular iodine (entries 3-5 *vs*. 2), prompting its selection as the cost-effective and handleable pre-catalyst. Further optimization of oxidants demonstrated that H_2O_2 (30% w/v in water) and *tert*-butyl hydroperoxide (TBHP) produced lower yields (entries 6-7 *vs*. 4). A dose-dependent study of NaI loading showed that 0.3 equivalents significantly enhanced the yield to 78% (entry 8). Parametric analysis of reaction conditions identified 60°C as the optimal temperature (entry 9 *vs*. 8, 10) and MeOH as the superior solvent (entry 9 *vs*. 11-12), outperforming mixed systems (MeOH/DCE, MeOH/MeCN). The final optimized protocol emerged as: 0.3 equiv NaI, 1.2 equiv $Na_2CO_3 \cdot 1.5H_2O_2$, 20 h, MeOH, 60°C.

Table S1 Optimization of the reaction conditions[a]



1a **2a** **3a**

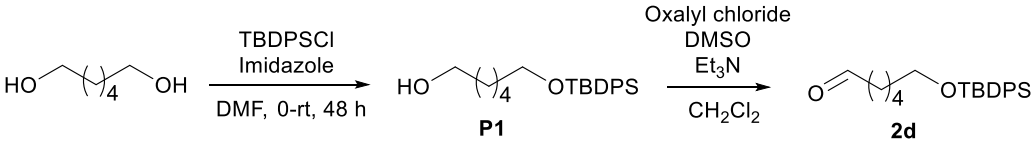
Entry	Pre-catalyst (equiv)	Oxidant	Solvent	T/°C	Yield/%[b]
1	—	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	0
2	I_2 (0.1)	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	70
3	NH_4I (0.2)	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	68
4	NaI (0.2)	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	71
5	KI (0.2)	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	62
6	NaI (0.2)	~30% H_2O_2	MeOH	70	12
7	NaI (0.2)	TBHP	MeOH	70	42
8	NaI (0.3)	$Na_2CO_3 \cdot 1.5H_2O_2$	MeOH	70	78

9	**NaI (0.3)**	**$Na_2CO_3·1.5H_2O_2$**	**MeOH**	**60**	**79**
10	NaI (0.3)	$Na_2CO_3·1.5H_2O_2$	MeOH	50	67
11[c]	NaI (0.3)	$Na_2CO_3·1.5H_2O_2$	MeOH/DCE	60	44
12[d]	NaI (0.3)	$Na_2CO_3·1.5H_2O_2$	MeOH/MeCN	60	33

[a]Reaction conditions: sulfanilamide **1a** (34.4 mg, 0.2 mmol), hexanal **2a** (40.6 mg, 0.4 mmol), pre-catalyst, oxidant (1.2 equiv), solvent (1.0 mL) at a specified temperature for 20 h. [b]Isolated yields based on **1a**. [c]MeOH (0.5 mL), DCE (0.5 mL). [d]MeOH (0.5 mL), MeCN (0.5 mL).

3. Preparation for aliphatic aldehydes

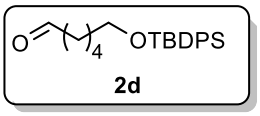
(1) Preparation of 6-((*tert*-butyldiphenylsilyl)oxy)hexanal (**2d**)[1]



Step 1: TBDPSCl (2.75 g, 10.0 mmol) in DMF (10 mL) was slowly added to a solution of 1,6-hexanediol (2.36 g, 20.0 mmol) and imidazole (1.02 g, 15.0 mmol) in DMF (50 mL) at 0 °C and the mixture was stirred at room temperature. After 48 h, the resulting solution was quenched with brine, followed by extracted with ethyl acetate. The combined organic phase was dried with anhydrous Na_2SO_4, and then concentrated using a rotary evaporator. The residue was further purified on silica gel (200-300 mesh) to give the desired **P1** as a colorless oil.

Step 2: To a solution of oxalyl chloride (0.85 mL, 9.6 mmol) in CH_2Cl_2 (30 mL), DMSO (0.86 mL, 12.0 mmol) was added at -78 °C. After stirring the mixture for 20 min, **P1** (1.43 g, 4.0 mmol) in CH_2Cl_2 (5 mL) was added under an argon atmosphere and the resulting mixture was stirred at -78 °C for 20 min. Then, Et_3N (3.95 mL, 28.1 mmol) was added, and the reaction mixture was stirred at room temperature for 1.5 h. When finished, the saturated $NaHCO_3$ aqueous solution was added and the mixture was extracted using CH_2Cl_2. Then, the combined organic phase was further washed with brine and then dried over anhydrous Na_2SO_4. After filtration and evaporation under vacuum, the crude mixture was purified by column chromatography on silica gel (200-300 mesh) to give **2d** as a colorless oil.

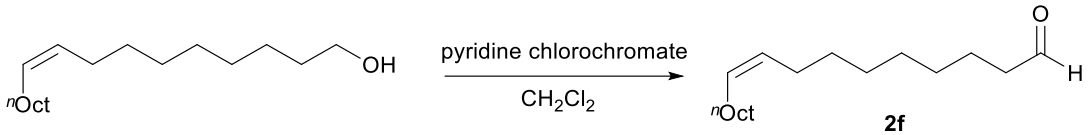
6-((*Tert*-butyldiphenylsilyl)oxy)hexanal (2d)[1]



2d

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.67 (d, J = 6.6 Hz, 4H), 7.46 – 7.35 (m, 6H), 3.67 (t, J = 6.3 Hz, 2H), 2.42 – 2.39 (m, 2H), 1.66 – 1.54 (m, 4H), 1.46 – 1.37 (m, 2H), 1.06 (s, 9H) ppm.

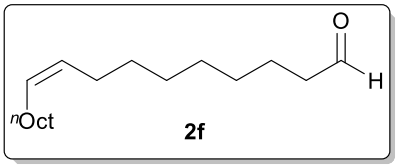
(2) Preparation of oleic aldehyde (**2f**)[2]



2f

To a solution of pyridinium chlorochromate (2.16 g, 10.0 mmol) in CH_2Cl_2 (30 mL), (*Z*)-octadec-9-en-1-ol (0.69 mL, 6.7 mmol) was added and the resulting mixture was stirred for 3 h. When finished, the mixture was filtered and the filtrate was concentrated in vacuo to give **2f** as a colourless oil.

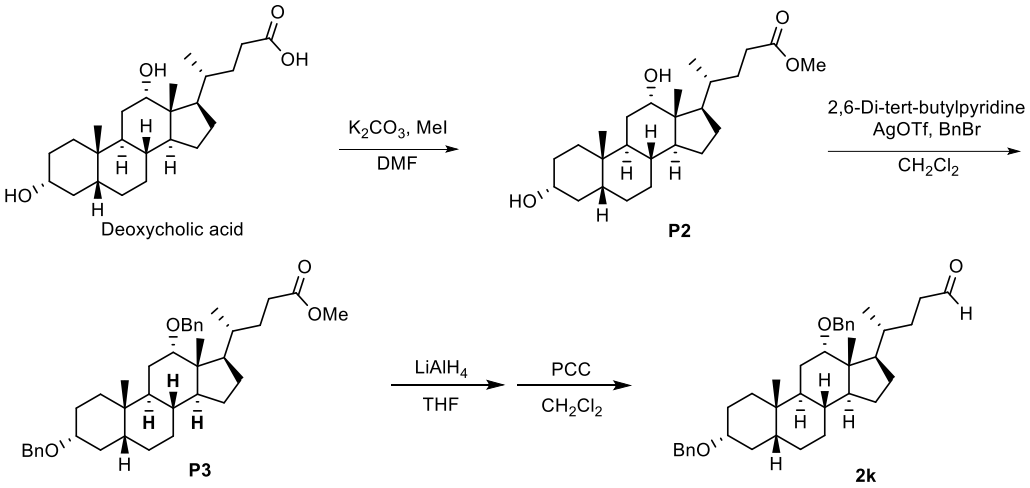
Oleic aldehyde (2f)[2]



2f

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, 1H), 5.41 – 5.26 (m, 2H), 2.43 – 2.40 (m, 2H), 2.19 – 1.93 (m, 4H), 1.67 – 1.57 (m, 2H), 1.29 (d, J = 20.8 Hz, 20H), 0.92 – 0.83 (m, 3H) ppm.

(3) Preparation of (*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-bis(benzyloxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)pentanal (**2k**)[3]



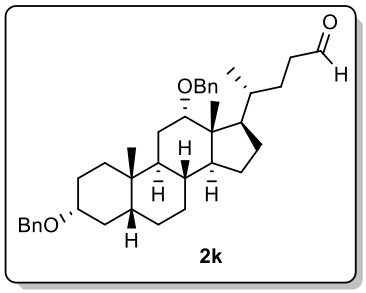
Step 1: To a solution of deoxycholic acid (7.85 g, 20.0 mmol) in DMF (80 mL), K_2CO_3 (5.53 g, 40.0 mmol) was added and the mixture was stirred at room temperature. After 30 min, MeI (1.87 mL, 30.0 mmol) was added and the resulting solution was stirred overnight. The mixture was diluted with ethyl acetate (3 × 50 mL) and washed with water (150 mL). The combined organic phase was further washed with brine (3 × 30 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography to give methyl deoxycholate **P2** as a yellow oil.

Step 2: Then, a solution of benzyl bromide (4.46 mL, 37.5 mmol) in CH_2Cl_2 (35 mL) was slowly added to a suspension of **P2** (5.89 g, 15.0 mmol), 2,6-dimethyl pyridine (6.89 mL, 36.0 mmol) and AgOTf (8.87 g, 34.5 mmol) in CH_2Cl_2 (100 mL), and the mixture was refluxed for 3 h. When finished, the resultant solution was filtered, and the organic phase was further washed with HCl (5 M, 3 × 50 mL) and H_2O (3 × 50 mL). After dried over anhydrous Na_2SO_4, organic solvent was removed under vacuum. The crude product was purified by column chromatography to afford **P3** as a yellow oil.

Step 3: Lithium aluminum hydride (1.14 g，30.0 mmol) was slowly added to the solution of **P3** (3.45 g, 6.0 mmol) in dry THF(60 mL) at 0 °C. After stirring for 10 h, diethyl ether (10 mL), water (1 mL) and 15% aqueous sodium hydroxide solution (1 mL) was sequentially added. Then, water (3 mL) was added and the mixture was stirred for 15 min at room temperature. After completion, anhydrous magnesium sulfate was added and stirred for another 15 min, followed by filtration and concentration in vacuo. The resultant mixture was further dissolved in CH_2Cl_2 (60 mL), and then pyridinium chlorochromate (PCC, 2.59 g) was added. After stirring for 5 h, the mixture was filtered and concentrated under vacuum.

The crude product was purified by silica gel column chromatography to give **2k** as a colourless oil.

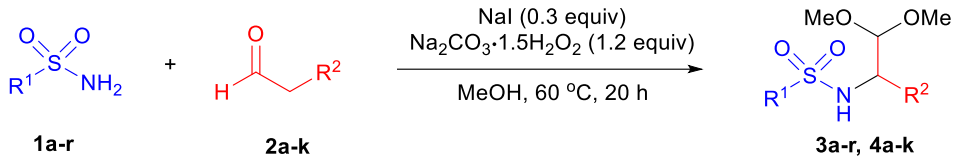
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-Bis(benzyloxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[a]phenanthren-17-yl)pentanal (2k)[3]



2k

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.39 – 7.29 (m, 8H), 7.26 (dd, *J* = 9.2, 4.8 Hz, 2H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.53 (s, 2H), 4.27 (d, *J* = 11.5 Hz, 1H), 3.67 (s, 1H), 3.38 – 3.33 (m, 1H), 2.49 – 2.39 (m, 1H), 2.35 – 2.25 (m, 1H), 2.04 (q, *J* = 9.6 Hz, 1H), 1.82 (m, 9H), 1.59 (dd, *J* = 17.2, 7.9 Hz, 2H), 1.46 – 1.20 (m, 11H), 1.07 – 1.03 (m, 1H), 0.92 (s, 3H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.70 (s, 3H) ppm.

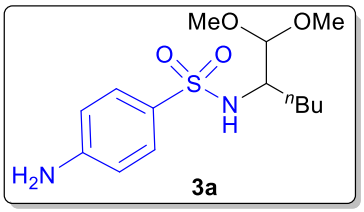
4. General procedure for oxidative *N*-functionalization of primary sulfonamides with aliphatic aldehydes



To a 10 mL screw-cap tube with a stirring bar, NaI (0.06 mmol, 9.0 mg), $Na_2CO_3{\cdot}1.5H_2O_2$ (0.24 mmol, 37.7 mg), primary sulfonamides **1a-r** (0.2 mmol), MeOH (1 mL) and aldehydes **2a-k** (0.4 mmol) were subsequently added. Then, the tube was sealed and allowed to stir at 60 °C for 20 h. When finished, the mixture was concentrated to dryness and the desired products (**3a-r**, **4a-k**) was further purified on column chromatography over silica gel (200-300 mesh).

5. Characterization data of *α*-sulfonamido acetals

4-Amino-*N*-(1,1-dimethoxyhexan-2-yl)benzenesulfonamide (3a)



3a

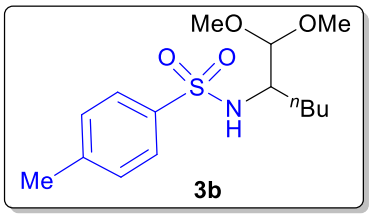
Colorless oil (50.0 mg, 79% yield);

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.64 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.6 Hz, 2H), 4.52 (d, *J* = 8.6 Hz, 1H), 4.11 (d, *J* = 3.1 Hz, 2H), 3.33 (d, *J* = 1.3 Hz, 6H), 3.26 – 3.20 (m, 1H), 1.61 – 1.52 (m, 2H), 1.33 – 1.28 (m, 1H), 1.21 – 1.14 (m, 3H), 0.79 (t, *J* = 7.1 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 150.34, 129.41, 129.24, 113.88, 106.38, 56.88, 56.16, 55.16, 28.06, 27.57, 22.44, 13.87 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{14}H_{24}N_2O_4SNa^+$ $[M+Na]^+$ 339.1349, found: 339.1345.

N-(1,1-Dimethoxyhexan-2-yl)-4-methylbenzenesulfonamide (3b)



3b

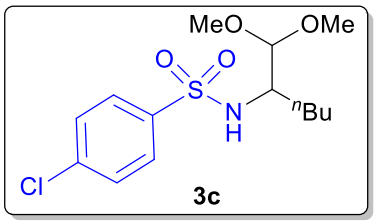
Colorless oil (47.3 mg, 75% yield);

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.76 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.69 (d, *J* = 8.4 Hz, 1H), 4.08 (d, *J* = 3.1 Hz, 1H), 3.27 (dd, *J* = 17.7, 7.9 Hz, 7H), 2.41 (s, 3H), 1.60 – 1.51 (m, 1H), 1.35 – 1.27 (m, 1H), 1.21 – 1.09 (m, 3H), 1.08 – 0.97 (m, 1H), 0.76 (t, *J* = 7.0 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 143.11, 138.23, 129.01, 127.08, 106.29, 56.64, 56.14, 55.37, 28.29, 27.51, 22.35, 21.43, 13.79 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{15}H_{25}NO_4SNa^+$ $[M+Na]^+$ 338.1397, found: 338.1391.

4-Chloro-*N*-(1,1-dimethoxyhexan-2-yl)benzenesulfonamide (3c)



3c

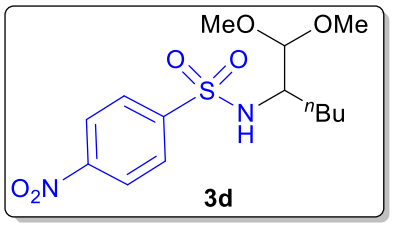
Yellow oil (42.9 mg, 64% yield);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 4.76 (d, J = 8.7 Hz, 1H), 4.03 (d, J = 3.1 Hz, 1H), 3.26 (s, 3H), 3.25 – 3.22 (m, 1H), 3.19 (s, 3H), 1.54 – 1.44 (m, 1H), 1.34 – 1.24 (m, 1H), 1.19 – 1.07 (m, 3H), 1.05 – 0.98 (m, 1H), 0.73 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.89, 138.68, 128.96, 128.56, 106.20, 56.39, 56.33, 55.76, 29.01, 27.61, 22.36, 13.81 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{14}H_{22}ClNO_4SNa^+$ $[M+Na]^+$ 358.0850, found: 358.0845.

_N_-(1,1-Dimethoxyhexan-2-yl)-4-nitrobenzenesulfonamide (3d)



3d

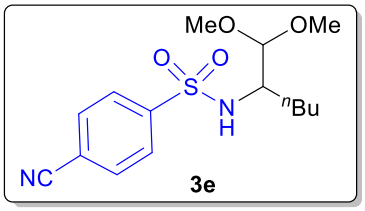
Yellow oil (36.0 mg, 52% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 2H), 4.95 (d, J = 8.9 Hz, 1H), 4.08 (d, J = 2.9 Hz, 1H), 3.42 – 3.36 (m, 1H), 3.33 (s, 3H), 3.17 (s, 3H), 1.59 – 1.52 (m, 1H), 1.42 – 1.36 (m, 1H), 1.25 – 1.19 (m, 3H), 1.17 – 1.10 (m, 1H), 0.82 (t, J = 6.9 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.71, 147.40, 128.33, 123.84, 106.11, 56.75, 56.40, 55.95, 29.96, 27.68, 22.34, 13.81 ppm;

HRMS (ESI, m/z): calcd for $C_{14}H_{22}N_2O_6SNa^+$ $[M+Na]^+$ 369.1091, found: 369.1085.

4-Cyano-_N_-(1,1-dimethoxyhexan-2-yl)benzenesulfonamide (3e)



3e

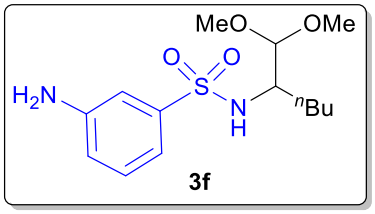
Yellow oil (29.5 mg, 45% yield);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 4.89 (d, J = 8.9 Hz, 1H), 4.07 (d, J = 3.0 Hz, 1H), 3.36 (dd, J = 10.5, 6.1 Hz, 1H), 3.33 (s, 3H), 3.18 (s, 3H), 1.59 – 1.51 (m, 1H), 1.40 – 1.36 (m, 1H), 1.25 – 1.19 (m, 3H), 1.14 – 1.11 (m, 1H), 0.82 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.79, 132.46, 127.74, 117.45, 115.78, 106.13, 56.73, 56.28, 56.02, 29.80, 27.68, 22.34, 13.83 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{15}H_{22}N_2O_4SNa^+$ $[M+Na]^+$ 349.1193, found: 349.1189.

3-Amino-*N*-(1,1-dimethoxyhexan-2-yl)benzenesulfonamide (3f)



3f

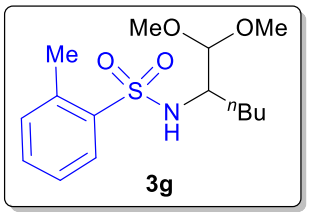
Yellow oil (28.5 mg, 45%);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 2H), 7.22 (s, 1H), 7.17 (s, 1H), 6.84 – 6.79 (m, 1H), 4.65 (d, J = 8.7 Hz, 1H), 4.04 (d, J = 3.2 Hz, 1H), 3.30 (s, 3H), 3.29 (s, 4H), 1.60 – 1.52 (m, 1H), 1.35 – 1.28 (m, 1H), 1.23 – 1.13 (m, 3H), 1.10 – 1.03 (m, 1H), 0.78 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.86, 141.94, 129.82, 118.68, 116.79, 112.94, 106.26, 56.75, 56.19, 55.44, 28.21, 27.56, 22.41, 13.85 ppm;

HRMS (ESI, m/z): calcd for $C_{14}H_{24}N_2O_4SNa^+$ $[M+Na]^+$ 339.1349, found: 339.1338.

***N*-(1,1-Dimethoxyhexan-2-yl)-2-methylbenzenesulfonamide (3g)**



3g

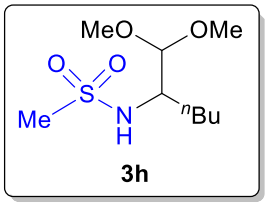
Colorless oil (27.0 mg, 43% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.3 Hz, 1H), 7.43 (t, J = 6.8 Hz, 1H), 7.29 (d, J = 7.4 Hz, 2H), 4.79 (d, J = 9.0 Hz, 1H), 4.01 (d, J = 3.0 Hz, 1H), 3.29 (s, 3H), 3.26 – 3.20 (m, 1H), 3.17 (s, 3H), 2.65 (s, 3H), 1.57 – 1.49 (m, 1H), 1.39 – 1.30 (m, 1H), 1.27 – 1.20 (m, 1H), 1.17 – 1.12 (m, 2H), 1.08 – 0.98 (m, 1H), 0.76 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.97, 137.11, 132.49, 132.23, 129.13, 125.90, 106.12, 56.26, 56.07, 55.17, 28.69, 27.50, 22.32, 20.19, 13.83 ppm;

HRMS (ESI, m/z): calcd for $C_{15}H_{25}NO_4SNa^+$ $[M+Na]^+$ 338.1397, found: 339.1391.

***N*-(1,1-Dimethoxyhexan-2-yl)methanesulfonamide (3h)**



3h

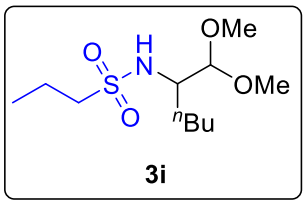
Colorless oil (28.7 mg, 60%);

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 (d, J = 9.1 Hz, 1H), 4.19 (d, J = 3.0 Hz, 1H), 3.47 (s, 3H), 3.44 (s, 4H), 3.00 (s, 3H), 1.60 – 1.53 (m, 1H), 1.51 – 1.44 (m, 1H), 1.40 – 1.27 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 106.74, 56.89, 56.22, 55.98, 41.97, 30.52, 27.82, 22.45, 13.90 ppm;

HRMS (ESI, m/z): calcd for $C_9H_{21}NO_4SNa^+$ $[M+Na]^+$ 262.1084, found: 262.1079.

***N*-(1,1-dimethoxyhexan-2-yl)propane-1-sulfonamide (3i)**



3i

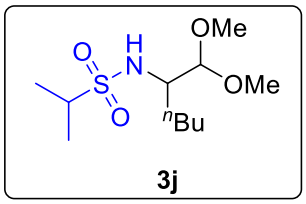
Colorless oil (37.9 mg, 71%);

^{1}H NMR (400 MHz, CDCl3) δ 4.33 (d, J = 9.1 Hz, 1H), 4.21 (s, 1H), 3.46 (d, J = 9.8 Hz, 7H), 3.04 (d, J = 5.8 Hz, 1H), 1.85 (dd, J = 15.0, 8.0 Hz, 2H), 1.56 (dd, J = 27.5, 18.6 Hz, 1H), 1.34 (d, J = 6.9 Hz, 2H), 1.25 (s, 2H), 1.04 (t, J = 7.4 Hz, 3H), 0.92 – 0.87 (m, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 106.83, 56.86, 56.06, 55.62, 30.46, 27.89, 22.51, 17.45, 13.92, 12.92 ppm.

_N_-(1,1-dimethoxyhexan-2-yl)propane-2-sulfonamide (3j)

Colorless oil (41.8 mg, 78%);

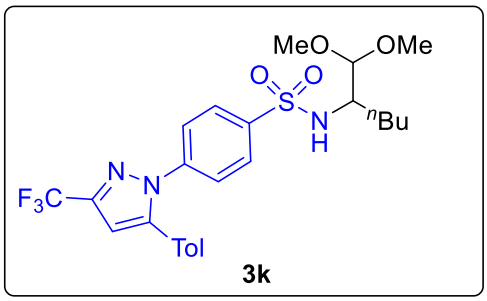


3j

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 – 4.20 (m, 2H), 3.45 (d, *J* = 6.6 Hz, 4H), 3.42 – 3.38 (m, 1H), 3.20 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.59 (dd, *J* = 18.5, 8.8 Hz, 1H), 1.38 – 1.35 (m, 6H), 1.33 – 1.30 (m, 2H), 1.25 (dd, *J* = 9.8, 6.0 Hz, 2H), 0.89 (d, *J* = 7.0 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 106.90, 56.74, 56.19, 56.08, 53.93, 30.25, 27.97, 22.52, 16.66, 16.47, 13.90 ppm.

_N_-(1,1-Dimethoxyhexan-2-yl)-4-(5-(p-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (3k)



3k

Colorless oil (92.4 mg, 88% yield);

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.85 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.73 (s, 1H), 4.76 (d, *J* = 8.7 Hz, 1H), 4.10 (d, *J* = 3.0 Hz, 1H), 3.33 (s, 4H), 3.25 (s, 3H), 2.37 (s, 3H), 1.61 – 1.53 (m, 1H), 1.38 – 1.34 (m,

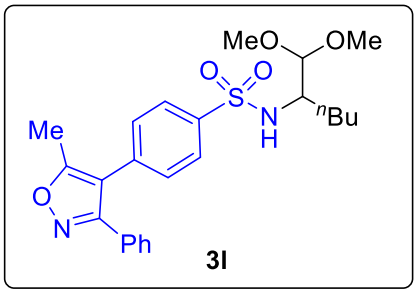
1H), 1.24 – 1.19 (m, 3H), 1.15 – 1.09 (m, 1H), 0.83 (t, *J* = 6.9 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 145.12, 144.10, 143.80, 142.17, 140.85, 139.68, 129.66, 128.69, 127.99, 125.81, 125.11, 122.12, 119.98, 106.31, 106.11, 56.38, 56.34, 55.83, 29.05, 27.60, 22.38, 21.27, 13.82 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -62.42 ppm;

HRMS (ESI, m/z): calcd for $C_{25}H_{30}F_3N_3O_4SNa^+$ $[M+Na]^+$ 548.1801, found: 548.1792.

_N_-(1,1-Dimethoxyhexan-2-yl)-4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide (3l)



3l

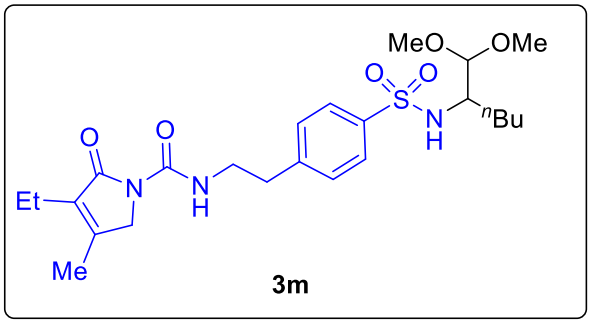
White solid (78.9 mg, 86%); m.p.: 109-110 °C;

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.88 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.37 (m, 3H), 7.34 – 7.26 (m, 4H), 4.72 (d, *J* = 8.8 Hz, 1H), 4.15 (d, *J* = 3.1 Hz, 1H), 3.39 – 3.32 (m, 4H), 3.30 (s, 3H), 2.47 (s, 3H), 1.58– 1.54 (m, 1H), 1.41 – 1.31 (m, 1H), 1.25 – 1.15 (m, 3H), 1.10 – 1.05 (m, 1H), 0.79 (t, *J* = 7.1 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 167.16, 161.04, 140.49, 134.88, 130.00, 129.69, 128.65, 128.51, 128.42, 127.50, 114.57, 106.32, 56.53, 56.38, 55.68, 28.71, 27.61, 22.37, 13.88, 11.67 ppm;

HRMS (ESI, m/z): calcd for $C_{24}H_{30}N_2O_5SNa^+$ $[M+Na]^+$ 481.1768, found: 481.1759.

_N_-(4-(_N_-(1,1-Dimethoxyhexan-2-yl)sulfamoyl)phenethyl)-3-ethyl-4-methyl-2-oxo-2,5-dihydro-1_H_-pyrrole-1-carboxamide (3m)



3m

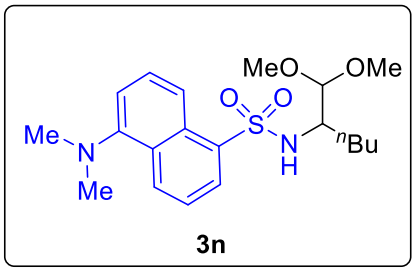
White solid (72.2 mg, 73% yield); m.p.: 95-96 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (t, J = 5.5 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 4.72 (d, J = 8.7 Hz, 1H), 4.17 (s, 2H), 4.05 (d, J = 3.2 Hz, 1H), 3.64 – 3.53 (m, 2H), 3.33 – 3.26 (m, 4H), 3.25 (d, J = 4.3 Hz, 3H), 2.95 (t, J = 7.3 Hz, 2H), 2.25 (q, J = 7.5 Hz, 2H), 2.03 (s, 3H), 1.61 – 1.49 (m, 1H), 1.36 – 1.27 (m, 1H), 1.22 – 1.10 (m, 3H), 1.04 (t, J = 7.6 Hz, 4H), 0.75 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.48, 152.50, 150.37, 144.03, 139.29, 133.76, 129.18, 127.36, 106.23, 56.60, 56.20, 55.39, 52.12, 40.63, 35.94, 28.30, 27.53, 22.34, 16.56, 13.83, 13.13, 12.77 ppm;

HRMS (ESI, m/z): calcd for $C_{24}H_{36}N_3O_6S^-$ $[M-H]^-$ 494.2330, found: 494.2327.

_N_-(1,1-Dimethoxyhexan-2-yl)-5-(dimethylamino)naphthalene-1-sulfonamide (3n)



3n

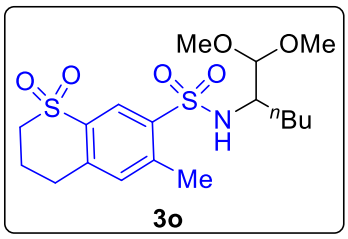
Yellow oil (75.7 mg, 96% yield);

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 8.4 Hz, 1H), 8.29 (t, J = 7.9 Hz, 2H), 7.58 – 7.49 (m, 2H), 7.18 (d, J = 7.5 Hz, 1H), 4.85 (d, J = 8.9 Hz, 1H), 3.80 (d, J = 2.9 Hz, 1H), 3.24 – 3.19 (m, 1H), 3.16 (s, 3H), 3.07 (s, 3H), 2.87 (s, 6H), 1.50 – 1.39 (m, 1H), 1.28 – 1.17 (m, 1H), 1.02 – 0.95 (m, 3H), 0.85 – 0.78 (m, 3H), 0.57 (t, J = 6.9 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.94, 135.85, 130.27, 129.79, 129.70, 129.29, 128.28, 123.10, 119.03, 115.11, 106.20, 56.64, 56.14, 55.53, 45.40, 27.54, 27.35, 22.19, 13.71 ppm;

HRMS (ESI, m/z): calcd for $C_{20}H_{30}N_2O_4SNa^+$ [M+Na]$^+$ 417.1819, found: 417.1806.

_N_-(1,1-Dimethoxyhexan-2-yl)-6-methylthio-chromane-7-sulfonamide 1,1-dioxide (3o)



3o

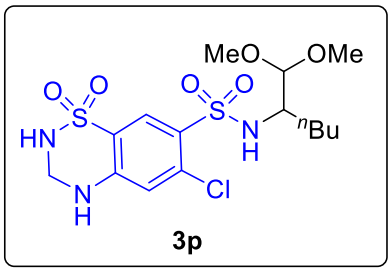
Yellow solid (79.6 mg, 95% yield); m.p.: 31-32 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.16 (s, 1H), 4.91 (d, J = 9.0 Hz, 1H), 4.05 (d, J = 2.5 Hz, 1H), 3.37 – 3.27 (m, 6H), 3.11 (s, 3H), 3.01 (t, J = 6.2 Hz, 2H), 2.62 (s, 3H), 2.51 – 2.45 (m, 2H), 1.55 – 1.47 (m, 1H), 1.42 – 1.34 (m, 1H), 1.26 – 1.12 (m, 4H), 0.80 (t, J = 7.0 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.42, 140.42, 139.47, 136.68, 133.13, 124.72, 105.99, 56.47, 55.75, 55.55, 50.62, 29.74, 28.09, 27.60, 22.33, 20.69, 20.12, 13.84 ppm;

HRMS (ESI, m/z): calcd for $C_{18}H_{29}NO_6S_2Na^+$ [M+Na]$^+$ 442.1329, found: 442.1321.

6-Chloro-_N_-(1,1-dimethoxyhexan-2-yl)-3,4-dihydro-2_H_-benzo[_e_][1,2,4]thiadiazine-7-sulfonamide 1,1-dioxide (3p)



3p

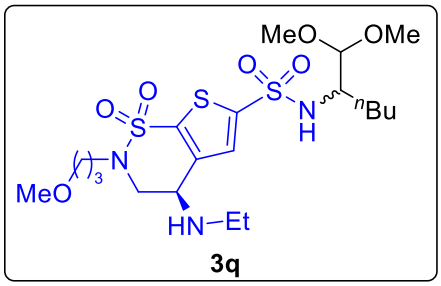
Yellow oil (45.0 mg, 51% yield);

^{1}H NMR (500 MHz,$CDCl_3$) δ 8.17 (s, 1H), 6.74 (s, 1H), 5.74 (s, 1H), 5.46 (t, J = 8.6 Hz, 1H), 5.24 (d, J = 9.6 Hz, 1H), 4.82 (d, J = 8.7 Hz, 2H), 4.01 (s, 1H), 3.32 (s, 4H), 3.16 (s, 3H), 1.57 – 1.50 (m, 1H), 1.42 – 1.34 (m, 2H), 1.30 – 1.22 (m, 3H), 0.85 (t, J = 6.3 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.86, 136.03, 127.26, 127.09, 119.32, 117.75, 105.89, 56.52, 56.18, 55.81, 55.14, 29.86, 27.63, 22.39, 13.89 ppm;

HRMS (ESI, m/z): calcd for $C_{15}H_{24}ClN_3O_6S_2Na^+$ [M+Na]$^+$ 464.0687, found: 464.0685.

(4*R*)-*N*-(1,1-Dimethoxyhexan-2-yl)-4-(ethylamino)-2-(3-methoxypropyl)-3,4-dihydro-2*H*-thieno[3,2-*e*][1,2]thiazine-6-sulfonamide 1,1-dioxide (3q)



3q

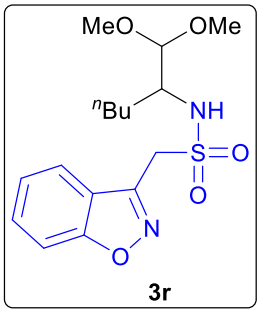
Yellow oil (43.3 mg, 41% yield, d.r. = 68:32);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 3.1 Hz, 1H), 4.99 (s, 1H), 4.14 (dd, J = 8.2, 2.8 Hz, 0.32H), 3.98 (dd, J = 7.3, 5.0 Hz, 0.68H), 3.90 (dd, J = 14.9, 7.5 Hz, 1H), 3.82 (dd, J = 14.9, 4.9 Hz, 1H), 3.57 – 3.49 (m, 2H), 3.49 – 3.40 (m, 3H), 3.39 (d, J = 4.1 Hz, 3H), 3.33 (s, 4H), 3.31 (d, J = 7.0 Hz, 2H), 3.29 – 3.20 (m, 2H), 2.78 – 2.71 (m, 2H), 1.94 – 1.87 (m, 2H), 1.63 – 1.56 (m, 1H), 1.46 – 1.38 (m, 1H), 1.34 – 1.25 (m, 4H), 1.15 – 1.10 (m, 3H), 0.88 – 0.85 (m, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.30, 144.21, 138.69, 130.36, 106.05, 69.19, 58.68, 56.73, 56.61, 56.44, 50.11, 46.39, 41.05, 29.71, 29.49, 27.70, 22.44, 15.62, 13.93 ppm;

HRMS (ESI, m/z): calcd for $C_{20}H_{36}N_3O_7S_3^-$ $[M-H]^-$ 526.1721, found: 526.1715.

1-(Benzo[*d*]isoxazol-3-yl)-*N*-(1,1-dimethoxyhexan-2-yl)methanesulfonamide (3r)



3r

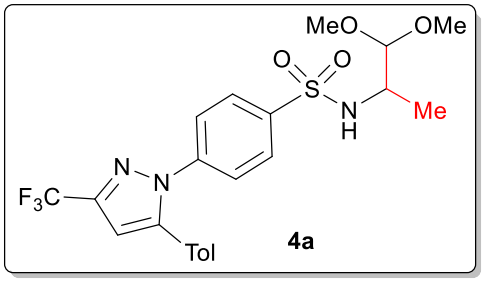
Yellow oil (49.9 mg, 70% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 1H), 7.58 (s, 2H), 7.38 – 7.34 (m, 1H), 4.82 (s, 2H), 4.71 (d, J = 9.2 Hz, 1H), 4.23 (d, J = 3.3 Hz, 1H), 3.58 – 3.52 (m, 1H), 3.45 (d, J = 4.9 Hz, 6H), 1.63 – 1.55 (m, 1H), 1.49 –1.36 (m, 2H), 1.35 – 1.25 (m, 3H), 0.88 (t, J = 6.9 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.60, 150.01, 130.27, 124.03, 122.69, 120.93, 109.78, 106.47, 56.65, 56.60, 55.87, 50.80, 30.04, 27.70, 22.41, 13.86 ppm;

HRMS (ESI, m/z): calcd for $C_{16}H_{24}N_2O_5SNa^+$ [M+Na]$^+$ 379.1304, found: 379.1301.

_N_-(1,1-dimethoxypropan-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4a)



Yellow oil (93.7 mg, 97% yield);

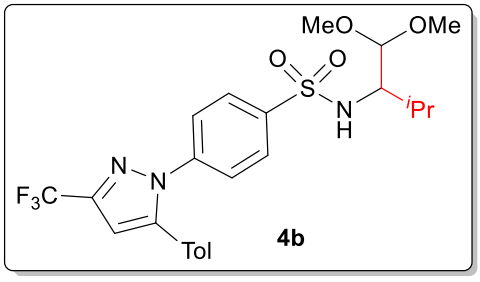
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.48 – 7.43 (m, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 6.74 (s, 1H), 4.83 (d, J = 7.9 Hz, 1H), 4.10 (d, J = 3.7 Hz, 1H), 3.50 – 3.39 (m, 1H), 3.33 (d, J = 11.6 Hz, 6H), 2.37 (s, 3H), 1.04 (d, J = 6.7 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.21, 144.17, 143.87, 142.31, 140.61, 139.74, 129.68, 128.69, 128.00, 125.73, 125.41, 122.11, 119.97, 106.27, 56.23, 55.92, 51.19, 21.28, 15.37 ppm;

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.43 ppm;

HRMS (ESI, m/z): calcd for $C_{22}H_{24}F_3N_3O_4SNa^+$ [M+Na]$^+$ 506.1332, found: 506.1326.

_N_-(1,1-Dimethoxy-3-methylbutan-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4b)



White solid (87.9 mg, 86%); m.p.: 74-75 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.7 Hz, 2H), 7.17 – 7.06

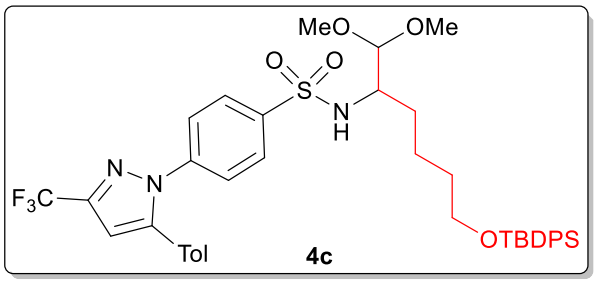
(m, 4H), 6.72 (s, 1H), 4.93 (d, *J* = 9.0 Hz, 1H), 4.12 (d, *J* = 3.3 Hz, 1H), 3.28 (s, 3H), 3.24 – 3.20 (m, 1H), 3.15 (s, 3H), 2.36 (s, 3H), 1.94 – 1.85 (m, 1H), 0.87 (dd, *J* = 6.9, 3.1 Hz, 6H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 145.11, 144.01, 143.70, 141.95, 141.29, 139.61, 129.62, 128.69, 128.06, 125.82, 124.99, 106.19, 106.18, 105.02, 60.51, 56.10, 55.36, 28.92, 21.24, 19.82, 18.25 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -62.36 ppm;

HRMS (ESI, m/z): calcd for $C_{24}H_{27}F_3N_3O_4S^-$ $[M-H]^-$ 510.1680, found: 510.1677.

_N_-(6-((_Tert_-butyldiphenylsilyl)oxy)-1,1-dimethoxyhexan-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4c)



Colorless oil (112.3 mg, 72% yield);

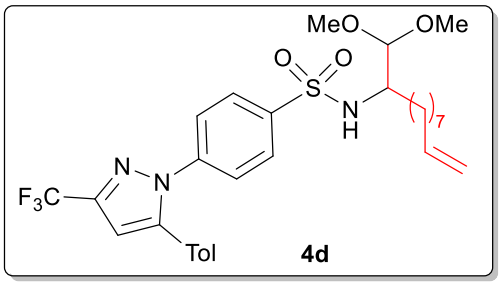
^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.84 (d, *J* = 8.7 Hz, 2H), 7.65 (d, *J* = 7.9 Hz, 4H), 7.43 – 7.35 (m, 8H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.74 (s, 1H), 4.75 (d, *J* = 8.7 Hz, 1H), 4.07 (d, *J* = 3.0 Hz, 1H), 3.65 – 3.59 (m, 2H), 3.32 (s, 4H), 3.23 (s, 3H), 2.37 (s, 3H), 1.60 – 1.55 (m, 1H), 1.54 – 1.47 (m, 2H), 1.44 – 1.39 (m, 1H), 1.31 – 1.19 (m, 2H), 1.04 (s, 9H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) *δ* 145.12, 144.09, 143.78, 142.13, 140.82, 139.66, 135.51, 133.94, 129.66, 129.50, 128.68, 127.99, 127.57, 125.80, 125.08, 120.00, 106.30, 105.95, 63.48, 56.35, 56.25, 55.80, 32.18, 29.35, 26.81, 21.80, 21.26, 19.16 ppm;

^{19}F NMR (471 MHz, $CDCl_3$) *δ* -62.36 ppm;

HRMS (ESI, m/z): calcd for $C_{41}H_{48}F_3N_3O_5SSiNa^+$ $[M+Na]^+$ 802.2923, found: 802.2930.

_N_-(1,1-Dimethoxyundec-10-en-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4d)



Colorless oil (112.7 mg, 95% yield);

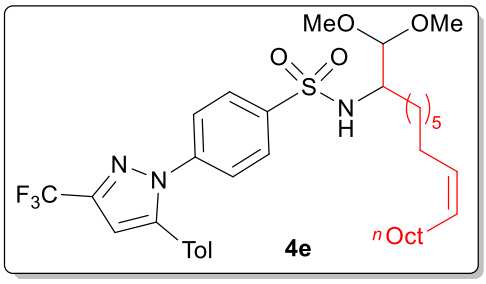
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 6.3 Hz, 2H), 7.45 (d, J = 6.5 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 7.0 Hz, 2H), 6.73 (s, 1H), 5.82 – 5.74 (m, 1H), 4.94 (dd, J = 27.6, 13.7 Hz, 2H), 4.74 (d, J = 7.6 Hz, 1H), 4.10 (s, 1H), 3.33 (s, 4H), 3.25 (s, 3H), 2.37 (s, 3H), 2.00 (d, J = 7.7 Hz, 2H), 1.26 (m, 12H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.13, 144.14, 143.84, 142.21, 140.85, 139.70, 139.12, 129.69, 128.71, 128.01, 125.84, 125.11, 124.76, 122.14, 119.99, 114.10, 106.32, 106.13, 56.40, 56.36, 55.86, 33.71, 29.37, 29.28, 29.19, 28.99, 28.80, 25.48, 21.29 ppm;

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.40 ppm;

HRMS (ESI, m/z): calcd for $C_{30}H_{37}F_3N_3O_4S^-$ $[M-H]^-$ 592.2462, found: 592.2469.

(*Z*)-*N*-(1,1-Dimethoxyoctadec-9-en-2-yl)-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (4e)



Colorless oil (98.4 mg, 85% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 6.73 (s, 1H), 5.31 (d, J = 5.0 Hz, 2H), 4.72 (d, J = 8.7 Hz, 1H), 4.09 (d, J = 3.1 Hz, 1H), 3.33 (s, 4H), 3.25 (s, 3H), 2.38 (s, 3H), 2.00 – 1.94 (m, 4H), 1.61 – 1.52 (m, 2H), 1.26 (s, 20H), 0.87 (t, J = 6.7 Hz, 3H) ppm;

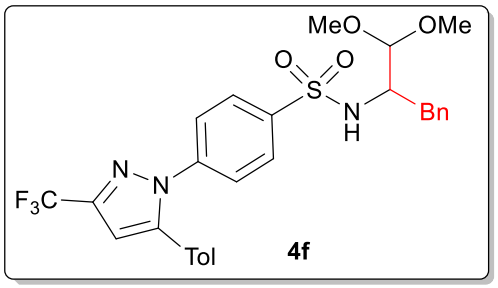
^{13}C NMR (101 MHz, $CDCl_3$) δ 145.11, 144.17, 143.79, 142.19, 140.81, 139.70, 129.97, 129.69, 128.70, 128.01, 125.12, 106.33, 106.09, 56.43, 56.36, 55.86, 31.88, 29.74, 29.66,

29.50, 29.40, 29.36, 29.30, 29.03, 27.19, 27.10, 25.48, 22.66, 21.30, 14.10 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.40 ppm;

HRMS (ESI, m/z): calcd for $C_{37}H_{51}F_3N_3O_4S^-$ $[M-H]^-$ 690.3558, found: 690.3562.

_N_-(1,1-Dimethoxy-3-phenylpropan-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4f)



Yellow solid (93.9 mg, 84% yield); m.p.: 42-43 °C;

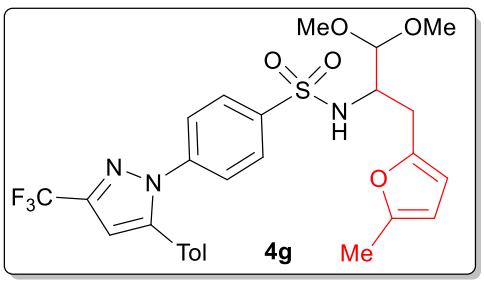
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 8.6 Hz, 2H), 7.29 (s, 1H), 7.27 (s, 1H), 7.14 (d, J = 6.1 Hz, 5H), 7.07 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 5.5 Hz, 2H), 6.73 (s, 1H), 4.79 (d, J = 7.9 Hz, 1H), 4.21 (d, J = 2.9 Hz, 1H), 3.59 – 3.54 (m, 1H), 3.40 (s, 3H), 3.31 (s, 3H), 2.93 (dd, J = 14.0, 6.0 Hz, 1H), 2.71 (dd, J = 14.0, 8.2 Hz, 1H), 2.36 (s, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.07, 144.10, 143.79, 142.04, 139.96, 139.65, 137.11, 129.66, 129.23, 128.68, 128.59, 127.83, 126.73, 125.81, 125.14, 122.17, 120.04, 106.21, 105.21, 57.13, 56.62, 56.25, 35.60, 21.27 ppm;

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.42 ppm;

HRMS (ESI, m/z): calcd for $C_{28}H_{27}F_3N_3O_4S^-$ $[M-H]^-$ 558.1680, found: 558.1680.

_N_-(1,1-Dimethoxy-3-(5-methylfuran-2-yl)propan-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4g)



Colorless oil (102.4 mg, 91%);

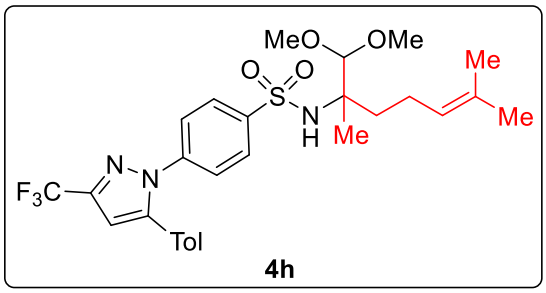
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 7.9 Hz, 2H), 6.72 (s, 1H), 5.82 (d, J = 2.7 Hz, 1H), 5.75 (s, 1H), 4.91 (d, J = 8.1 Hz, 1H), 4.25 (d, J = 3.3 Hz, 1H), 3.65 – 3.59 (m, 1H), 3.38 (s, 3H), 3.34 (s, 3H), 2.84 (dd, J = 15.3, 5.7 Hz, 1H), 2.72 (dd, J = 15.3, 7.8 Hz, 1H), 2.37 (s, 3H), 2.14 (s, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.27, 149.10, 145.09, 144.13, 143.74, 142.15, 140.23, 139.66, 129.67, 128.68, 127.93, 125.81, 125.09, 122.42, 119.75, 108.45, 106.20, 105.25, 56.59, 56.12, 54.87, 28.28, 21.25, 13.44 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.45 ppm;

HRMS (ESI, m/z): calcd for $C_{27}H_{28}F_3N_3O_5SNa^+$ $[M+Na]^+$ 586.1594, found: 586.1588.

_N_-(1,1-dimethoxy-2,6-dimethylhept-5-en-2-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4h)



4h

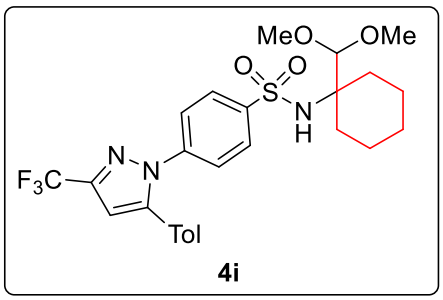
Yellow oil (101.7 mg, 90% yield).

^{1}H NMR(500 MHz, $CDCl_3$) δ 7.88 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 6.73 (s, 1H), 4.98 (t, J = 7.1 Hz, 1H), 4.91 (s, 1H), 4.19 (s, 1H), 3.55 (d, J = 7.5 Hz, 1H), 3.48 (d, J = 19.6 Hz, 6H), 2.37 (s, 3H), 1.92 – 1.87 (m, 2H), 1.64 (s, 3H), 1.55 (s, 3H), 1.11 (s, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.11, 144.06, 143.76, 142.01, 141.28, 139.64, 131.67, 129.66, 128.71, 128.07, 125.87, 124.97, 124.09, 122.16, 120.02, 106.25, 105.36, 58.58, 56.00, 55.14, 33.88, 32.98, 25.64, 25.40, 21.28, 17.69, 15.16 ppm;

HRMS (ESI, m/z): calcd for for $C_{28}H_{34}F_3N_3NaO_4S^+$ $[M+Na]^+$ 588.2114, found: 588.2095.

_N_-(1-(dimethoxymethyl)cyclohexyl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (4i)



4i

White solid (106.0 mg, 99% yield)

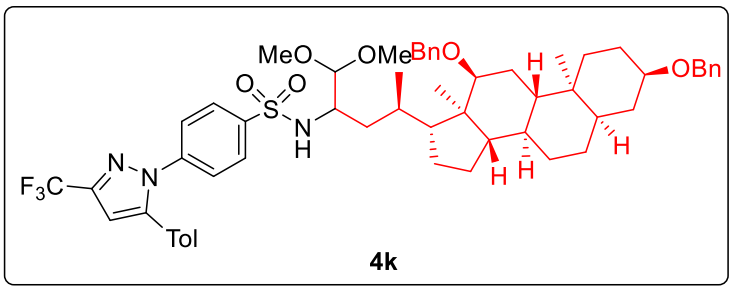
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.18 – 7.05 (m, 4H), 6.73 (s, 1H), 4.69 (s, 1H), 4.41 (s, 1H), 3.47 (s, 6H), 2.37 (s, 3H), 1.78 (d, J = 14.2 Hz, 2H), 1.62 – 1.51 (m, 2H), 1.43 (d, J = 9.9 Hz, 1H), 1.34 (d, J = 5.2 Hz, 2H), 1.20 – 1.10 (m, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.16, 144.11, 143.73, 142.52, 141.92, 139.66, 129.64, 128.71, 128.04, 125.80, 125.16, 122.40, 119.72, 108.82, 106.27, 106.25, 63.53, 58.57, 29.20, 25.32, 21.28, 21.13 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) *δ* -62.37 ppm;

HRMS (ESI, m/z): calcd for $C_{26}H_{29}F_3N_3O_4S^+$ $[M-H]^-$ 536.1836, found: 536.1838.

***N*-((4*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-Bis(benzyloxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-1,1-dimethoxypentan-2-yl)-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (4k)**



4k

Colorless oil (153.2 mg, 78%, d.r. = 52:48);

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.87 – 7.80 (m, 2H), 7.45 – 7.38 (m, 2H), 7.35 – 7.29 (m, 8H), 7.25 – 7.21 (m, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 15.3, 8.2 Hz, 2H), 6.73 (d, *J* = 5.9 Hz, 1H), 4.58 (dd, *J* = 11.6, 1.8 Hz, 1H), 4.55 – 4.50 (m, 2H), 4.25 (d, *J* = 11.4 Hz, 1H), 4.10 (d, *J* = 2.1 Hz, 1H), 3.62 (d, *J* = 13.7 Hz, 1H), 3.44 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.40 – 3.29 (m, 6H), 3.20 (s, 2H), 2.37 (s, 3H), 1.96 – 1.90 (m, 1H), 1.88 – 1.73 (m, 9H), 1.56 –

1.47 (m, 2H), 1.45 – 1.23 (m, 9H), 1.17 – 1.08 (m, 3H), 0.92 (d, *J* = 2.2 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 2H), 0.70 (d, *J* = 5.9 Hz, 1H), 0.63 (s, 2H), 0.54 (s, 1H) ppm;

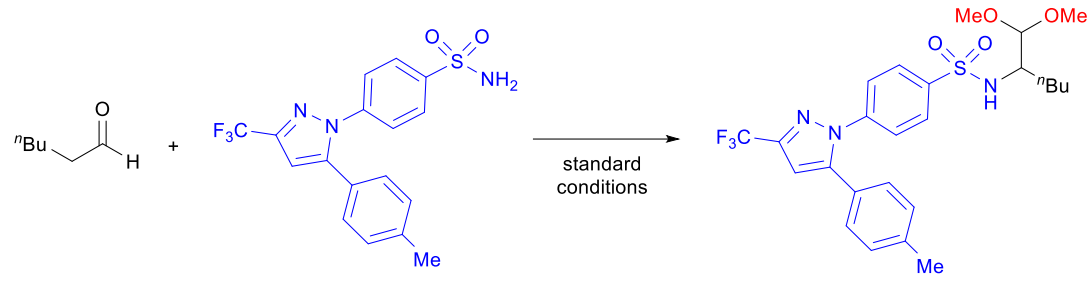
^{13}C NMR (126 MHz, $CDCl_3$) *δ* 145.09, 145.05, 144.08, 144.03, 143.77, 143.73, 142.24, 142.09, 141.04, 140.92, 139.67, 139.60, 139.34, 139.27, 139.26, 139.09, 129.68, 129.65, 128.69, 128.67, 128.25, 128.23, 128.19, 128.02, 127.93, 127.51, 127.46, 127.44, 127.35, 127.23, 127.20, 127.08, 125.79, 125.19, 125.10, 122.16, 120.02, 107.07, 106.22, 105.51, 80.86, 80.72, 78.55, 70.20, 70.08, 69.58, 69.53, 56.78, 56.64, 56.55, 55.96, 54.34, 53.63, 48.73, 48.54, 47.39, 46.76, 46.61, 46.58, 42.17, 37.62, 36.03, 35.29, 34.90, 34.50, 34.49, 33.74, 33.72, 33.33, 33.27, 33.23, 31.96, 28.06, 27.54, 27.35, 27.32, 27.24, 25.99, 23.66, 23.32, 23.25, 22.93, 21.29, 18.96, 17.43, 12.84, 12.69 ppm;

^{19}F NMR (471 MHz, $CDCl_3$) *δ* -62.31, -62.34 ppm;

HRMS (ESI, m/z): calcd for $C_{57}H_{70}F_3N_3O_6SNa^+$ $[M+Na]^+$ 1004.4836, found: 1004.4860.

6. Procedure for diversification of celecoxib

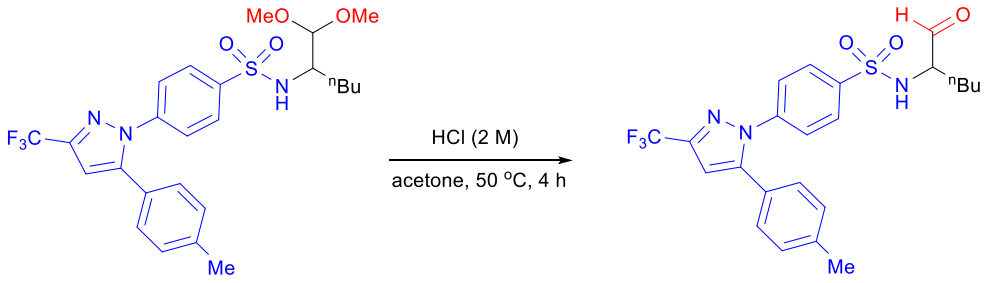
(1) Gram-scale experiment



20 mmol, 2.00 g　　10 mmol, 3.81 g　　**3k**, 71%, 3.73 g

To a 100 mL round-bottom flask with a stirring bar, NaI (3.0 mmol, 0.44 g), $Na_2CO_3{\cdot}1.5H_2O_2$ (12 mmol, 1.88 g), Celecoxib **1k** (10 mmol, 3.81 g), MeOH (40 mL) and hexanal **2a** (20 mmol, 2.00 g) were subsequently added. Then, the mixture heated at 60 °C for 20 h. When finished, the reaction mixture was concentrated to dryness and the desired product **3k** (3.73 g, 71% yield) was further purified by column chromatography as a colorless oil.

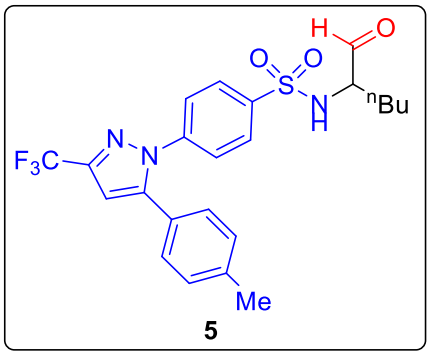
(2) Derivatization of **3k**[4]



3k　　**5**, 90%

To a 10 mL Schlenk tube with a stirring bar, HCl (2 M, 1 mL) was added to the solution of **3k** (0.5 mmol, 262.8 mg) in acetone (5 mL). Then, the resulting mixture was heated at 50 °C for 4 h. When finished, the reaction mixture was diluted with diethyl ether (20 mL) and then washed with H_2O (10 mL), saturated aqueous sodium bicarbonate solution (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. The desired product **5** (215.8 mg, 90% yield) was obtained after purification by column chromatography.

***N*-(1-Oxohexan-2-yl)-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (5)**



5

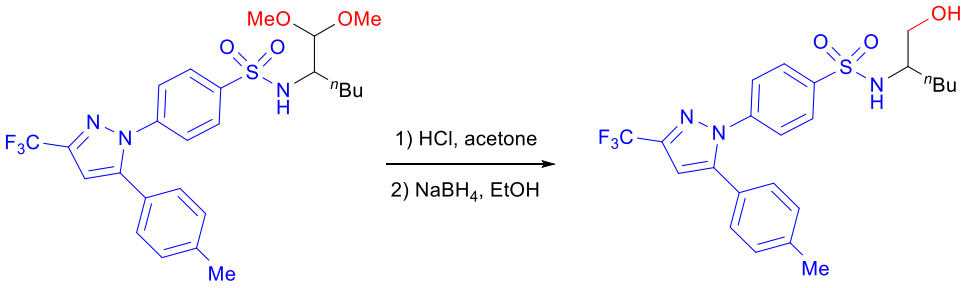
Colorless oil (218.5 mg, 90% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.7 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 6.74 (s, 1H), 5.44 (t, J = 4.5 Hz, 1H), 3.83 (d, J = 4.5 Hz, 2H), 2.38 (s, 3H), 2.34 (d, J = 7.5 Hz, 2H), 1.55 – 1.48 (m, 2H), 1.31 – 1.20 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.39, 145.24, 144.29, 143.91, 142.69, 139.82, 138.50, 129.75, 128.66, 128.15, 125.55, 122.33, 119.65, 106.28, 77.32, 51.18, 39.80, 25.55, 22.12, 21.30, 13.64 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{23}H_{23}F_3N_3O_3S^-$ $[M-H]^-$ 478.1418, found: 478.1411.

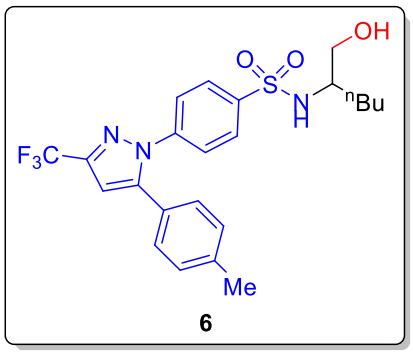


3k **6**, 91%

To a 10 mL Schlenk tube with a stirring bar, HCl (2 M, 1 mL) was added to the solution of **3k** (0.5 mmol, 262.8 mg) in acetone (5 mL). Then, the resulting mixture was heated at 50 ^{o}C for 4 h. When finished, the reaction mixture was diluted with diethyl ether (20 mL) and then washed with H_2O (10 mL), saturated aqueous sodium bicarbonate solution (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. After that, EtOH (5 mL) was added and the mixture was treated with sodium borohydride (1 mmol, 37.8 mg) and stirred at room temperature for 2 h. Finally, the solvent

was removed under vacuum and the desired product **6** (219.1 mg, 91% yield) was obtained after purification by column chromatography.

***N*-(1-Hydroxyhexan-2-yl)-4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (6)**



6

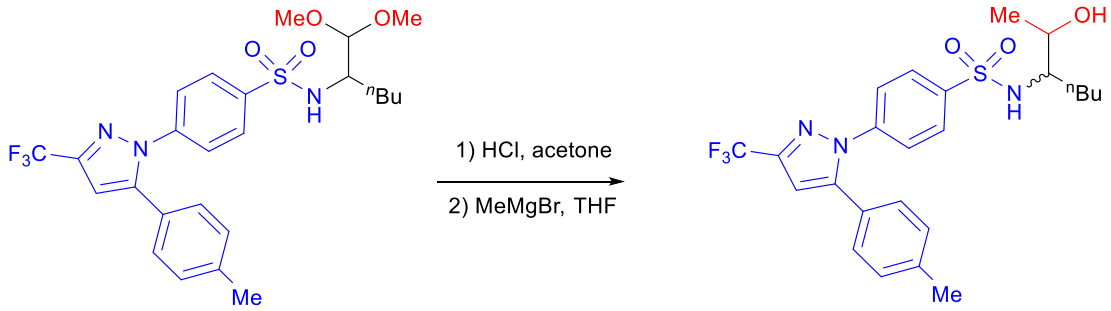
White solid (219.1 mg, 91% yield); m.p.: 124-125 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 6.74 (s, 1H), 4.91 (d, J = 8.1 Hz, 1H), 3.52 (ddd, J = 16.0, 11.1, 4.3 Hz, 2H), 3.27 (dd, J = 7.2, 3.5 Hz, 1H), 2.38 (s, 3H), 1.49 – 1.36 (m, 2H), 1.26 – 1.14 (m, 4H), 0.81 (t, J = 7.0 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.26, 144.29, 143.90, 142.46, 140.26, 139.81, 129.73, 128.70, 128.05, 125.70, 125.50, 122.38, 119.70, 106.32, 64.47, 55.76, 31.52, 27.72, 22.31, 21.31, 13.80 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.44 ppm;

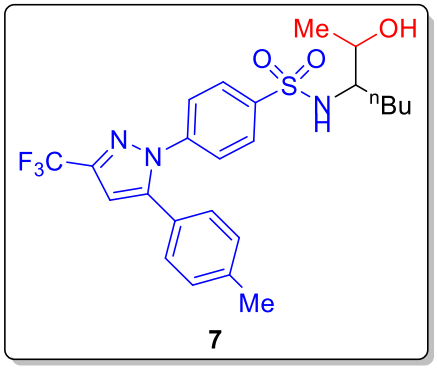
HRMS (ESI, m/z)**:** calcd for $C_{23}H_{25}F_3N_3O_3S^-$ $[M-H]^-$ 480.1574, found: 480.1569.



3k **7**, 83%

To a 10 mL Schlenk tube with a stirring bar, HCl (2 M, 1 mL) was added to the solution of **3k** (0.5 mmol, 262.8 mg) in acetone (5 mL). Then, the resulting mixture was heated at 50 °C for 4 h. When finished, the reaction mixture was diluted with diethyl ether (20 mL) and then washed with H_2O (10 mL), saturated aqueous sodium bicarbonate solution (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. After that, the obtained aldehyde was dissolved in THF (5 mL) and MeMgBr in THF (4 equiv, 2.0 mmol) was added slowly at 0 °C. Then, the solution was allowed to stir at 50 °C for 12 h. The reaction mixture was quenched with cold saturated aqueous ammonium chloride solution, and extracted with diethyl ether (3 × 10 mL). Finally, the solvent was removed under vacuum and the desired product **7** (205.7 mg, 83% yield) was obtained after purification by column chromatography.

_N_-(2-hydroxyheptan-3-yl)-4-(5-(_p_-tolyl)-3-(trifluoromethyl)-1_H_-pyrazol-1-yl)benzenesulfonamide (7)



7

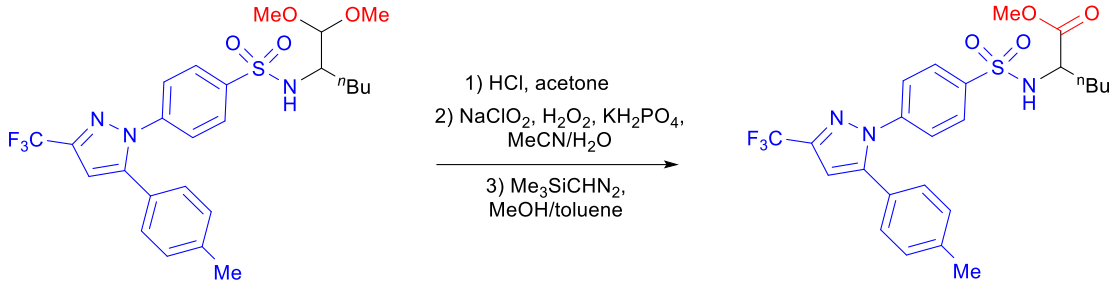
Colorless oil (205.7 mg, 83% yield, d.r. = 78:22);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.4, 4.6 Hz, 2H), 7.46 (dd, J = 8.3, 4.4 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.73 (s, 1H), 4.96 (d, J = 8.7 Hz, 1H), 3.80 (dd, J = 6.2, 3.4 Hz, 1H), 3.12 (d, J = 5.9 Hz, 1H), 2.37 (s, 3H), 1.27 (d, J = 10.9 Hz, 2H), 1.21 – 1.13 (m, 4H), 1.09 (d, J = 6.1 Hz, 3H), 0.80 (t, J = 6.9 Hz, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.17, 144.21, 143.83, 142.26, 140.86, 139.72, 129.68, 128.68, 127.88, 125.76, 125.37, 122.38, 119.71, 106.29, 68.28, 59.37, 32.21, 27.72, 22.40, 21.29, 20.44, 13.82 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.43 ppm;

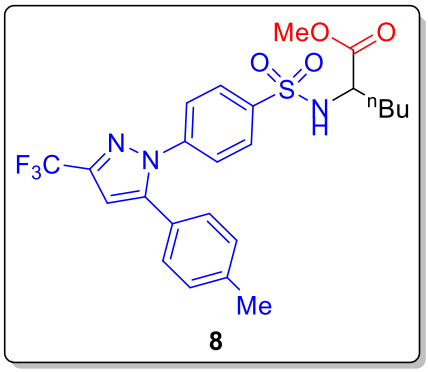
HRMS (ESI, m/z)**:** calcd for $C_{24}H_{27}F_3N_3O_3S^-$ $[M-H]^-$ 494.1731, found: 494.1728.



3k **8**, 81%

To a 10 mL Schlenk tube with a stirring bar, HCl (2 M, 1 mL) was added to the solution of **3k** (0.5 mmol, 262.8 mg) in acetone (5 mL). Then, the resulting mixture was heated at 50 ^oC for 4 h. When finished, the reaction mixture was diluted with diethyl ether (20 mL) and then washed with H_2O (10 mL), saturated aqueous sodium bicarbonate solution (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. Then, the obtained aldehyde was dissolved in CH_3CN (5 mL) and mixed with sodium chlorite and KH_2PO_4 (0.5 mmol, 60.0 mg) in water (2 mL) and H_2O_2 (35%, 1.5 mmol). After stirring the reaction mixture at 10 ^oC for 12 h, Na_2SO_3 (0.12 mmol, 15.1 mg) was added and the mixture was acidified (pH = 2) with 10% aqueous hydrochloric acid. The resulting mixture was extracted with dichloromethane and brine, and the organic phase was concentrated under vacuum. The residue was dissolved in methanol/toluene (2:1, 5 mL) and mixed with trimethylsilyldiazomethane (in Et_2O, 1 mmol) at 0 ^oC for 5 min. Excess trimethylsilyldiazomethane was treated with acetic acid and the solution was extracted with dichloromethane and brine. After removing the solvent under vacuum, the residue was further purified by column chromatography to give the desired product **8** (206.4 mg, 81% yield).

Methyl 2-((4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)phenyl)sulfonamido)hexanoate (8)



8

Yellow solid (206.4 mg, 81% yield), m.p.: 119-120 ºC;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 6.73 (s, 1H), 5.28 (d, J = 9.2 Hz, 1H), 3.94 – 3.89 (m, 1H), 3.55 (s, 3H), 2.37 (s, 3H), 1.77 – 1.70 (m, 1H), 1.66 – 1.57 (m, 1H), 1.35 – 1.23 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H) ppm;

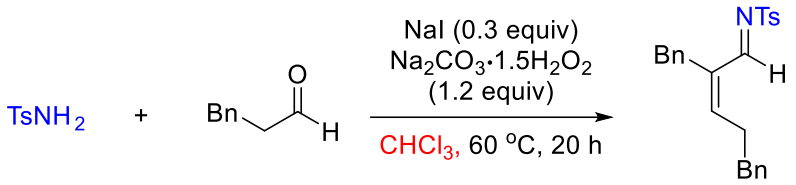
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.06, 145.20, 144.27, 143.88, 143.50, 142.58, 139.77, 139.17, 129.72, 128.67, 128.15, 125.65, 125.36, 122.35, 119.67, 106.33, 55.70, 52.54, 33.03, 26.89, 22.00, 21.28, 13.72 ppm;

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49 ppm;

HRMS (ESI, m/z)**:** calcd for $C_{24}H_{26}F_3N_3O_4SNa^+$ $[M+Na]^+$ 532.1488, found: 532.1487.

7. Mechanistic study

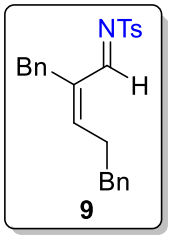
(1) Control experiment with $CHCl_3$ as the solvent



1b **2g** **9**, 55%

Experimental procedure: To a 10 mL screw-cap tube with a stirring bar, NaI (0.06 mmol, 9.0 mg), $Na_2CO_3{\cdot}1.5H_2O_2$ (0.24 mmol, 37.7 mg), *p*-toluenesulfonamide **1b** (0.2 mmol, 34.4 mg), $CHCl_3$ (1 mL) and phenylpropyl aldehyde **2g** (0.4 mmol, 20.0 mg) were subsequently added. Then, the tube was sealed and allowed to stir at 60 °C for 20 h. When finished, the mixture was concentrated to dryness and the residue was further purified by column chromatography to give imine **9** in 55% yield.

***N*-((1*E*,2*Z*)-2-Benzyl-5-phenylpent-2-en-1-ylidene)-4-methylbenzenesulfonamide (9)**



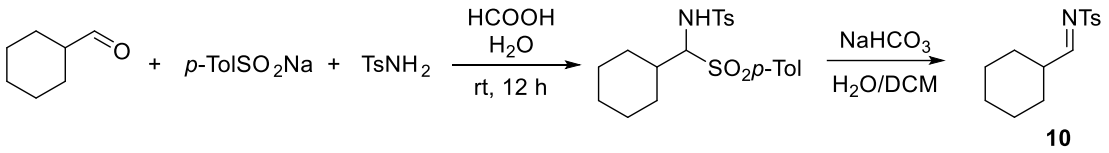
Colorless oil (44.4 mg, 55% yield);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.72 (d, J = 8.3 Hz, 2H), 7.30 – 7.26 (m, 5H), 7.21 (dd, J = 10.1, 4.5 Hz, 3H), 7.11 (dd, J = 5.7, 2.1 Hz, 5H), 7.01 (dd, J = 6.5, 2.8 Hz, 2H), 6.63 (t, J = 7.2 Hz, 1H), 3.69 (s, 2H), 2.74 (t, J = 4.2 Hz, 5H), 2.42 (s, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.30, 156.60, 144.06, 140.13, 138.70, 138.62, 135.73, 129.55, 128.62, 128.42, 128.30, 127.58, 126.42, 126.28, 126.04, 34.27, 31.71, 31.01, 21.59 ppm;

HRMS (ESI, m/z): calcd for $C_{24}H_{24}NO_4S^+$ $[M+H]^+$ 390.1528, found: 390.1520.

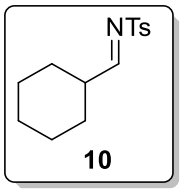
(2) Procedure for the preparation of imine (**10**)[4], enamine (**11**)[5] and *α*-iodo aldehyde (**2g'**)[6]



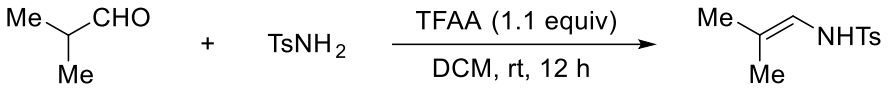
10

A mixture of cyclohexanecarbaldehyde (1.12 g, 10 mmol), sodium *p*-toluenesulfinate (1.78 g, 10 mmol) and 4-methylbenzenesulfonamide (1.71 g, 10 mmol) in HCOOH (15 mL) and H_2O (15 mL) was stirred at room temperature. After 12 h, the resulting solution was filtered and washed with H_2O and *n*-hexane. Then, DCM (100 mL) was added to dissolve the residue, followed by the addition of saturated aqueous $NaHCO_3$. After stirring for 2 h at room temperature, the mixture was extracted with DCM, and the organic phase was dried with anhydrous sodium sulfate and evaporated under vacuum. The residue was further purified by flash column chromatography to give **10** as a white solid.

***N*-(Cyclohexylmethylene)-4-methylbenzenesulfonamide (10)[4]**



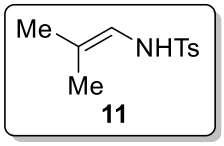
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 5 Hz, 1H), 7.74 – 7.70 (m, 2H), 7.26 – 7.24 (m, 2H), 2.35 (s, 3H), 2.33 (d, J = 2.9 Hz, 1H), 1.83 – 1.64 (m, 5H), 1.28 – 1.17 (m, 5H) ppm.



11

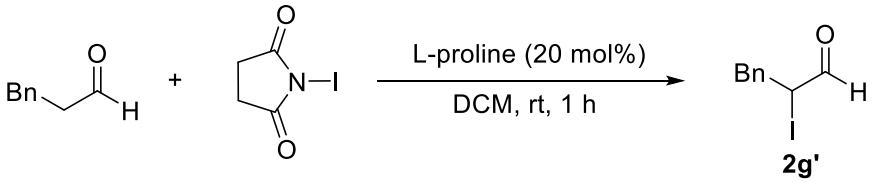
To a solution of isobutyraldehyde (0.72 g, 10 mmol) and 4-methylbenzenesulfonamide (1.88 g, 11 mmol) in DCM (50 mL), trifluoroacetic anhydride (2.31 g, 11 mmol) was added and the mixture was stirred at room temperature for 12 h. When finished, cold water was added and the mixture was extracted with DCM. The organic phase was dried with anhydrous sodium sulfate and evaporated under vacuum. The residue was further purified by flash column chromatography to give **7** as a white solid.

***N*-(2,2-Dimethylvinyl)-4-toluenesulfonamide (11)[5]**



11

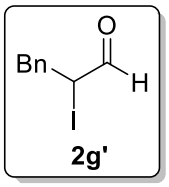
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 5.08 (d, J = 11.0 Hz, 1H), 4.81 (d, J = 5.5 Hz, 1H), 2.41 (s, 3H), 1.36 (s, 3H), 1.17 (s, 3H) ppm.



2g'

To a solution of L-proline (0.23 g, 2 mmol) and *N*-iodosuccinimide (2.70 g, 12 mmol) in DCM (20 mL), 3-phenylpropanal (1.34 g, 10 mmol) was added and the mixture was stirred at room temperature for 1 h. When finished, the mixture was filtered and then evaporated under vacuum to give **2g'** as a brown oil.

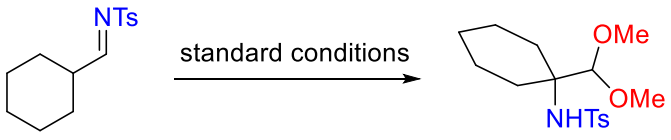
2-Iodo-3-phenylpropanal (2g')[6]



2g'

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (d, J = 2.3 Hz, 1H), 7.32 – 7.29 (m, 2H), 7.27 – 7.22 (m, 1H), 7.18 (d, J = 7.5 Hz, 2H), 4.69 (td, J = 7.3, 2.2 Hz, 1H), 3.48 (dd, J = 14.6, 7.5 Hz, 1H), 3.19 (dd, J = 14.7, 7.3 Hz, 1H) ppm.

(3) Procedure for identifying possible intermediates

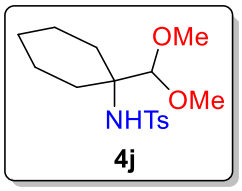


10 **4j**, 80%

To a 10 mL screw-cap tube with a stirring bar, NaI (0.06 mmol, 9.0 mg), $Na_2CO_3{\cdot}1.5H_2O_2$ (0.24 mmol, 37.7 mg), *N*-(cyclohexylmethylene)-4-methylbenzenesulfonamide (0.2 mmol, 53.1 mg) and MeOH (1 mL) were subsequently added. Then, the tube was sealed and

allowed to stir at 60 °C for 20 h. When finished, the mixture was concentrated to dryness and the residue was further purified by column chromatography to give *α*-sulfonamide acetal **4j** in 80% yield.

***N*-(1-(Dimethoxymethyl)cyclohexyl)-4-methylbenzenesulfonamide (4j)**



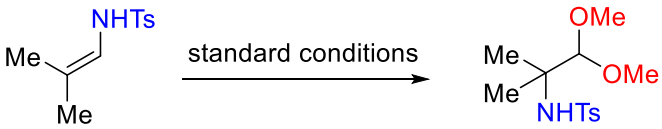
4j

White solid (52.4 mg, 80% yield); m.p.: 110-111 °C;

^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.78 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.25 (m, 2H), 4.57 (s, 1H), 4.37 (s, 1H), 3.45 (s, 6H), 2.41 (s, 3H), 1.77 (d, *J* = 13.5 Hz, 2H), 1.56 – 1.49 (m, 2H), 1.43 (s, 1H), 1.31 (s, 2H), 1.12 (t, *J* = 10.8 Hz, 3H) ppm;

^{13}C NMR (126 MHz, $CDCl_3$) *δ* 142.80, 140.14, 129.30, 127.09, 109.04, 63.19, 58.53, 28.87, 25.42, 21.46, 20.89 ppm;

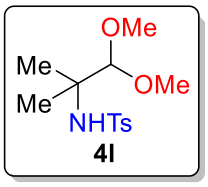
HRMS (ESI, m/z): calcd for $C_{16}H_{25}NO_4SNa^+$ $[M+Na]^+$ 350.1391, found: 350.1398.



11 **4l**, 70%

To a 10 mL screw-cap tube with a stirring bar, NaI (0.06 mmol, 9.0 mg), $Na_2CO_3{\cdot}1.5H_2O_2$ (0.24 mmol, 37.7 mg), 4-methyl-*N*-(2-methylprop-1-en-1-yl)benzenesulfonamide (0.2 mmol, 45.1 mg) and MeOH (1 mL) were subsequently added. Then, the tube was sealed and allowed to stir at 60 °C for 20 h. When finished, the mixture was concentrated to dryness and the residue was further purified by column chromatography to give *α*-sulfonamide acetal **4l** in 70% yield.

***N*-(1,1-Dimethoxy-2-methylpropan-2-yl)-4-methylbenzenesulfonamide (4l)**



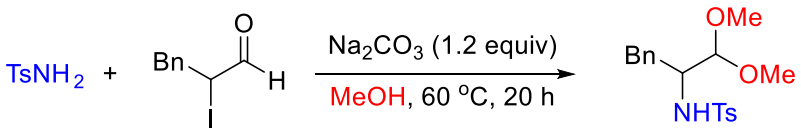
4l

White solid (40.2 mg, 70% yield); m.p.: 122-123 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.1 Hz, 2H), 7.31 – 7.25 (m, 2H), 4.95 (s, 1H), 4.10 (s, 1H), 3.51 (s, 6H), 2.42 (s, 3H), 1.13 (s, 6H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.88, 140.25, 129.39, 126.98, 110.21, 59.56, 58.46, 21.68, 21.42 ppm;

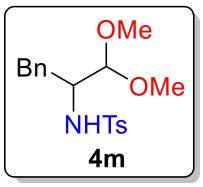
HRMS (ESI, m/z): calcd for $C_{13}H_{21}NO_4SNa^+$ $[M+Na]^+$ 310.1084, found: 310.1077.



1b **2g'** **4m**, 24%

To a 10 mL screw-cap tube with a stirring bar, Na_2CO_3 (0.24 mmol, 25.4 mg), *p*-toluenesulfonamide **1b** (0.2 mmol, 34.4 mg), MeOH (1 mL) and 2-iodo-3-phenylpropanal **2g'** (0.4 mmol, 103.6 mg) were subsequently added. Then, the tube was sealed and allowed to stir at 60 °C for 20 h. When finished, the mixture was concentrated to dryness and the residue was further purified by column chromatography to give *α*-sulfonamide acetal **4m** in 24% yield.

_N_-(1,1-Dimethoxy-3-phenylpropan-2-yl)-4-methylbenzenesulfonamide (4m)



4m

Yellow oil (16.7 mg, 24% yield);

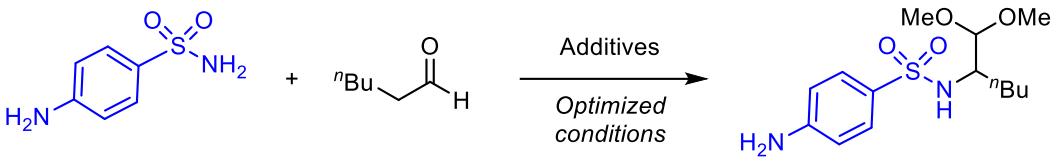
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 6.4 Hz, 2H), 7.13 (t, J = 6.9 Hz, 5H), 7.01 (d, J = 2.5 Hz, 2H), 4.68 (d, J = 7.4 Hz, 1H), 4.23 (s, 1H), 3.51 (d, J = 2.8 Hz, 1H), 3.37 (d, J = 2.0 Hz, 3H), 3.32 (d, J = 2.0 Hz, 3H), 2.93 (dd, J = 14.0, 3.6 Hz, 1H), 2.68 (dd, J = 12.1, 8.5 Hz, 1H), 2.38 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.87, 137.37, 137.26, 129.35, 129.31, 128.40, 126.96, 126.29, 105.35, 56.75, 56.69, 56.02, 35.18, 21.44.

HRMS (ESI, m/z): calcd for $C_{18}H_{23}NO_4SNa^+$ $[M+Na]^+$ 372.1235, found: 372.1227.

(4) Control experiments for exploring active iodine species

Table S2. Investigation on the valence state of active iodine species[a]



1a **2a** **3a**

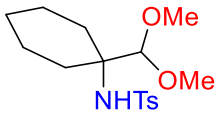
Entry	Additives (equiv)	**3a** Yield (%)[b]
1	NaI (1.0)	0
2	I_2 (1.0)	trace
3	I_2 (1.0) + NaOH (2.0)	33
4	$NaIO_3$ (1.0)	0
5	$NaIO_4$ (1.0)	0

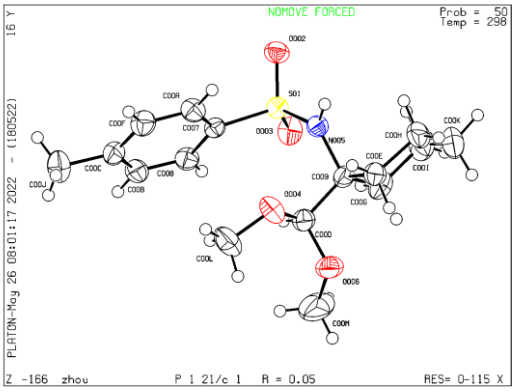
[a] Reaction conditions: **1a** (0.2 mmol, 34.4 mg), **2a** (0.4 mmol, 40.6 mg), additives, MeOH (1 mL) reacting at 60 °C for 20 h. [b] Isolated yield based on **1a**.

8. X-Ray crystallographic data

A single crystal of **4j** was grown from hexane/ethyl acetate at room temperature. Single-crystal X-ray diffraction data were collected by the Bruker AXS apexII diffractometer, using graphite-monochromatized Mo-Kα radiation (*l* = 0.71073 Å). In the Olex2 package[7], the structures were solved by using SHELXT[8] (direct methods), and all non-hydrogen atoms were refined by using SHELXL[9] (full-matrix least-squares techniques) on *F*2 with anisotropic thermal parameters). All hydrogen atoms were introduced in calculated positions and refined with fixed geometry relative to their carrier atoms. Crystallographic data for compounds **4j** were deposited with the Cambridge Crystallographic Data Centre with deposition numbers CCDC 2224138.

Table S3. Crystal data and structure refinement for **4j**





Empirical formula	$C_{16}H_{25}NO_4S$
Formula weight	327.43
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 11.7519(8) Å alpha = 90° b = 17.4233(10) Å beta = 106.248(7)° c= 8.7618(6) Å gamma = 90°
Volume	1722.4(2) $Å^3$
Z	4

Density (calculated)	1.263 Mg/m^3
Absorption coefficient	0.205 mm^{-1}
F(000)	704.0
Crystal size	0.20 x 0.19 x 0.18 mm^3
Radiation	MoKα (λ = 0.71073)
Theta range for data collection	3.367 to 29.202°
Index ranges	-16<=h<=15,-22<=k<=23,-11<=l<=11
Reflections collected	12092
Independent reflections	4095 [R_{int} = 0.0314, R_{sigma} = 0.0416]
Data / restraints / parameters	4095/12/202
Goodness-of-fit on F^2	1.050
Final R indices [I>2sigma(I)]	R_1 = 0.0524 wR_2 = 0.1194
Final R indices (all data)	R_1 = 0.0703 wR_2 = 0.1294
Largest diff. peak and hole	0.32 and -0.35 e.$Å^{-3}$

9. References

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7. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339-341.
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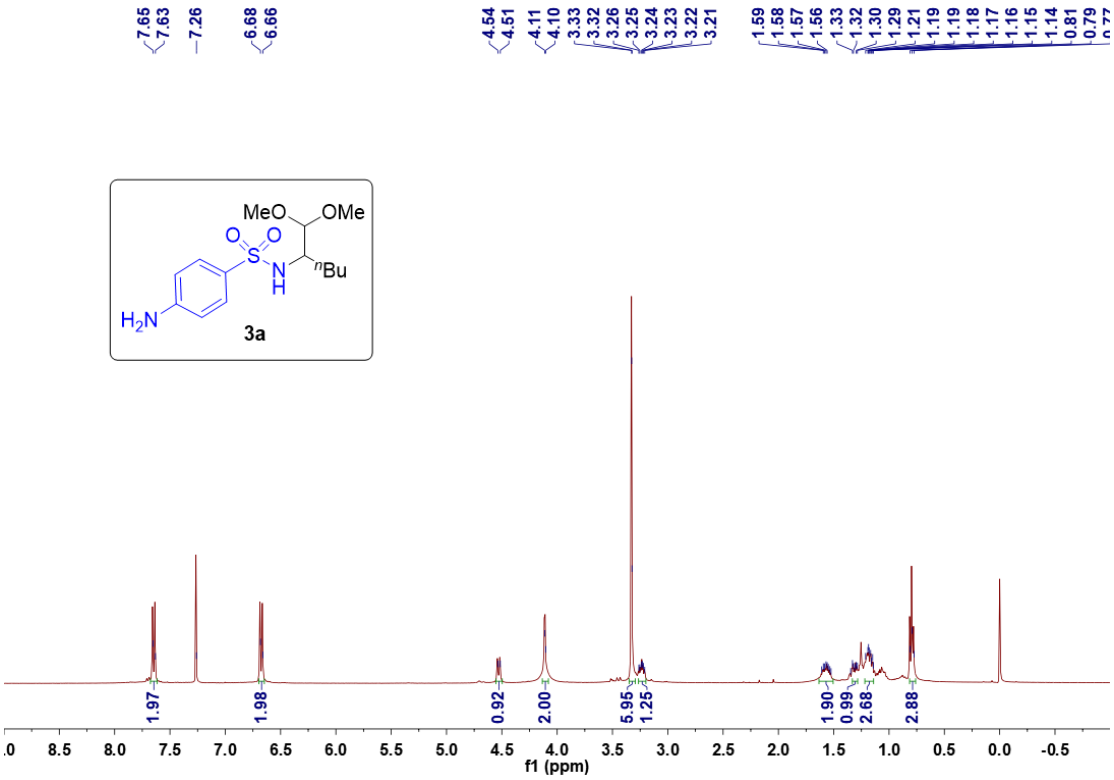
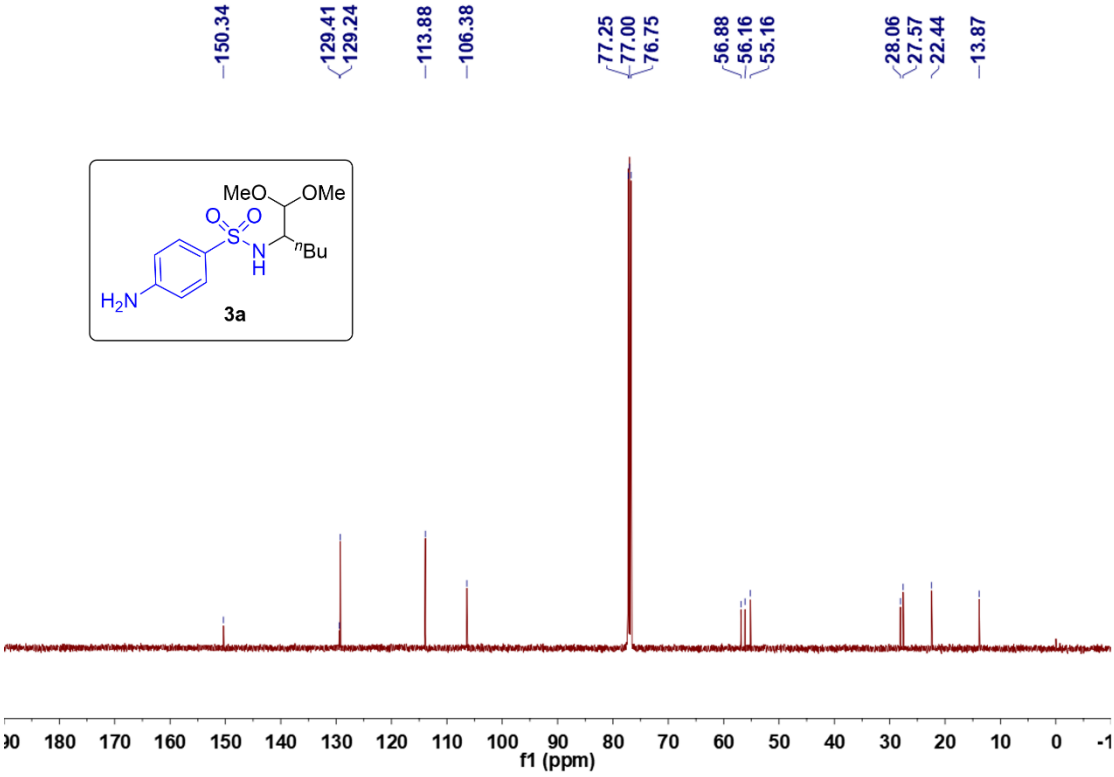
9. G. Sheldrick, *Acta Crystallographica Section C* **2015**, *71*, 3-8.

10. NMR spectra

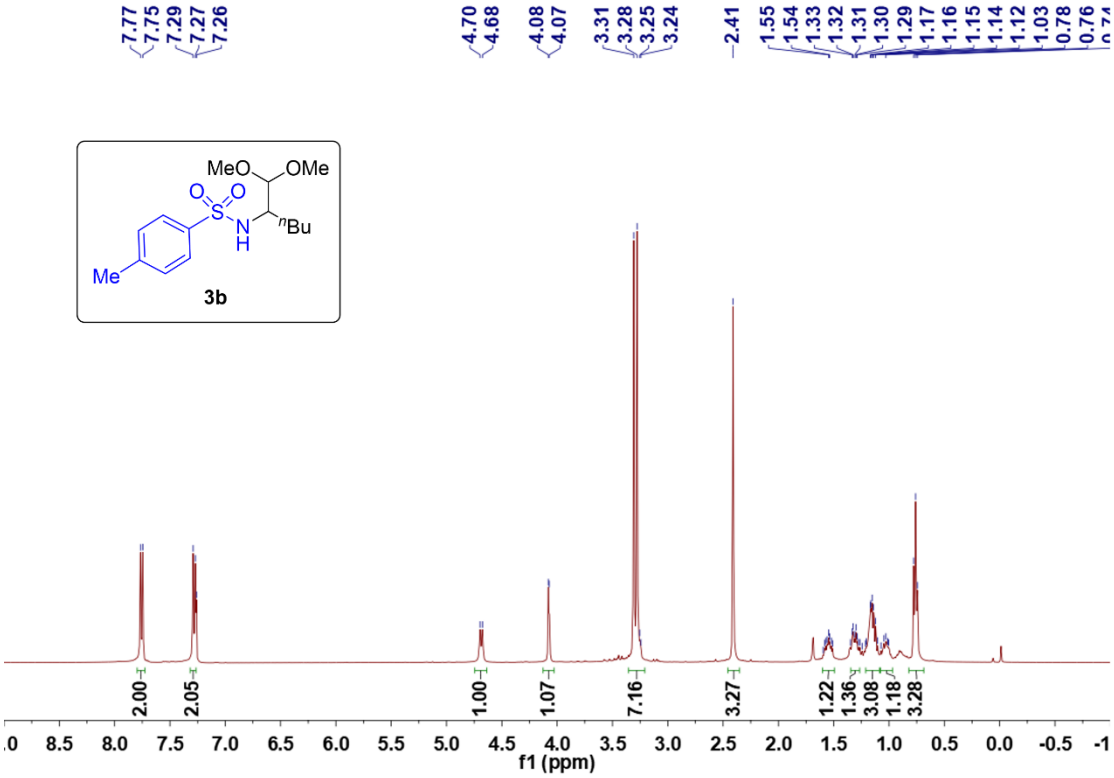
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**



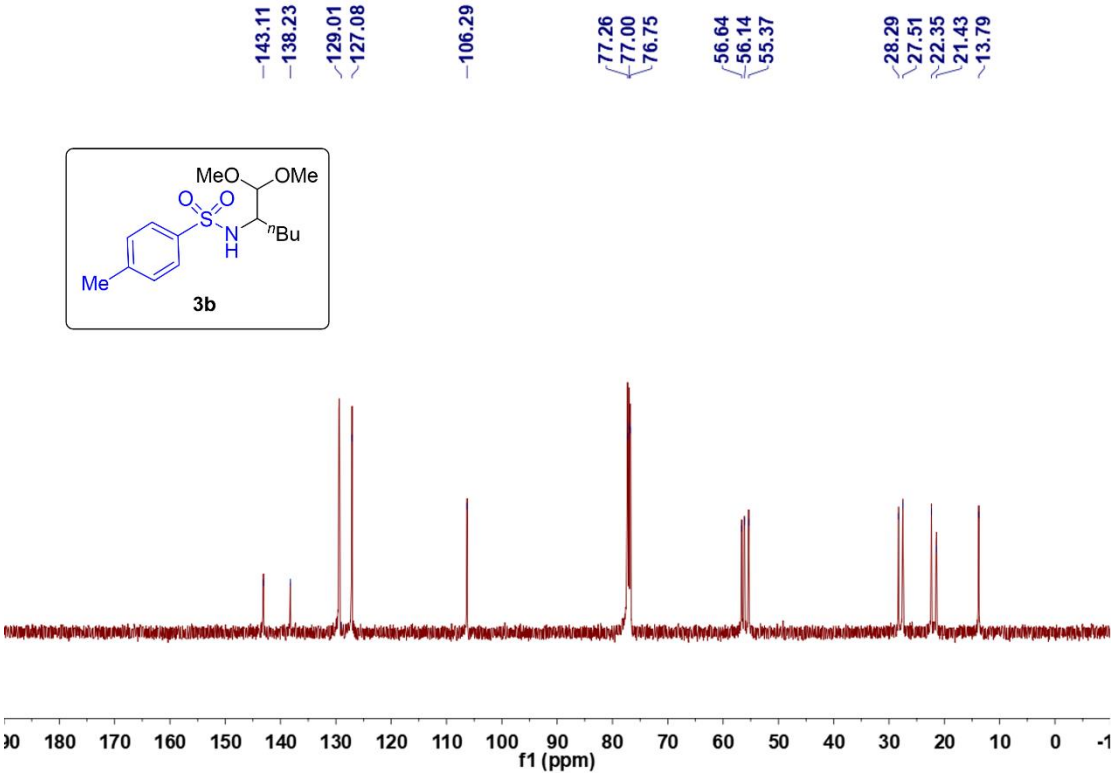
^{13}C NMR (101 MHz, $CDCl_3$) of **3a**



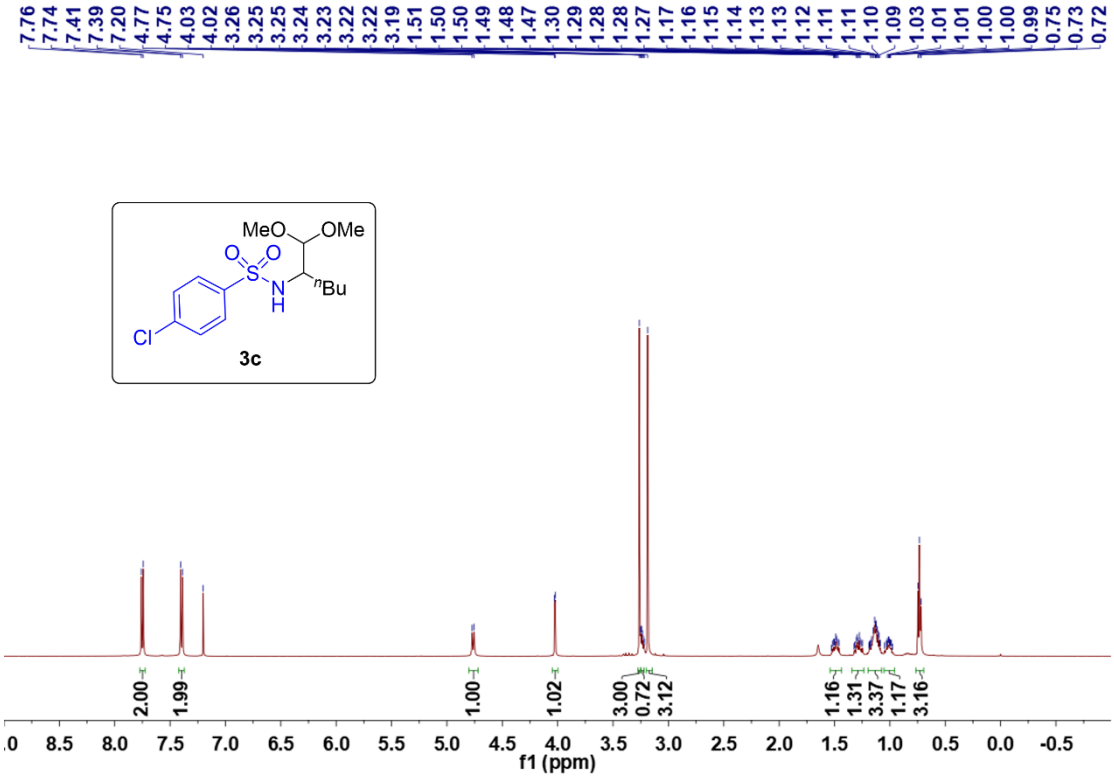
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**



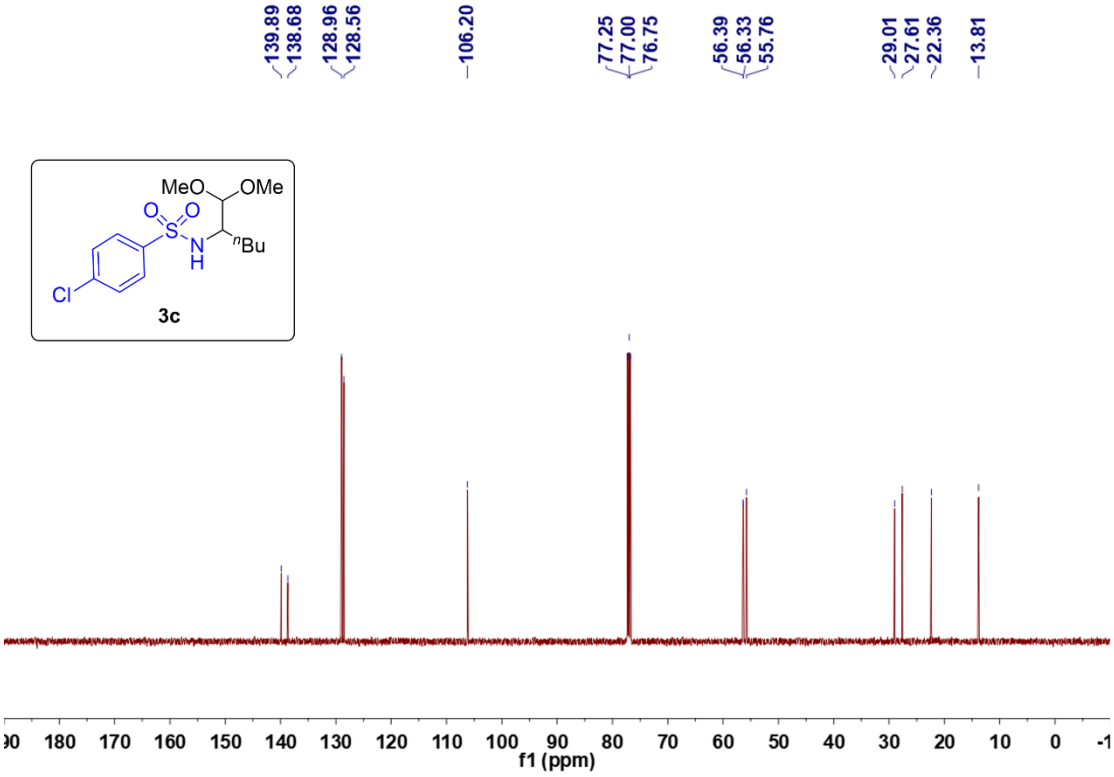
^{13}C NMR (101 MHz, $CDCl_3$) of **3b**



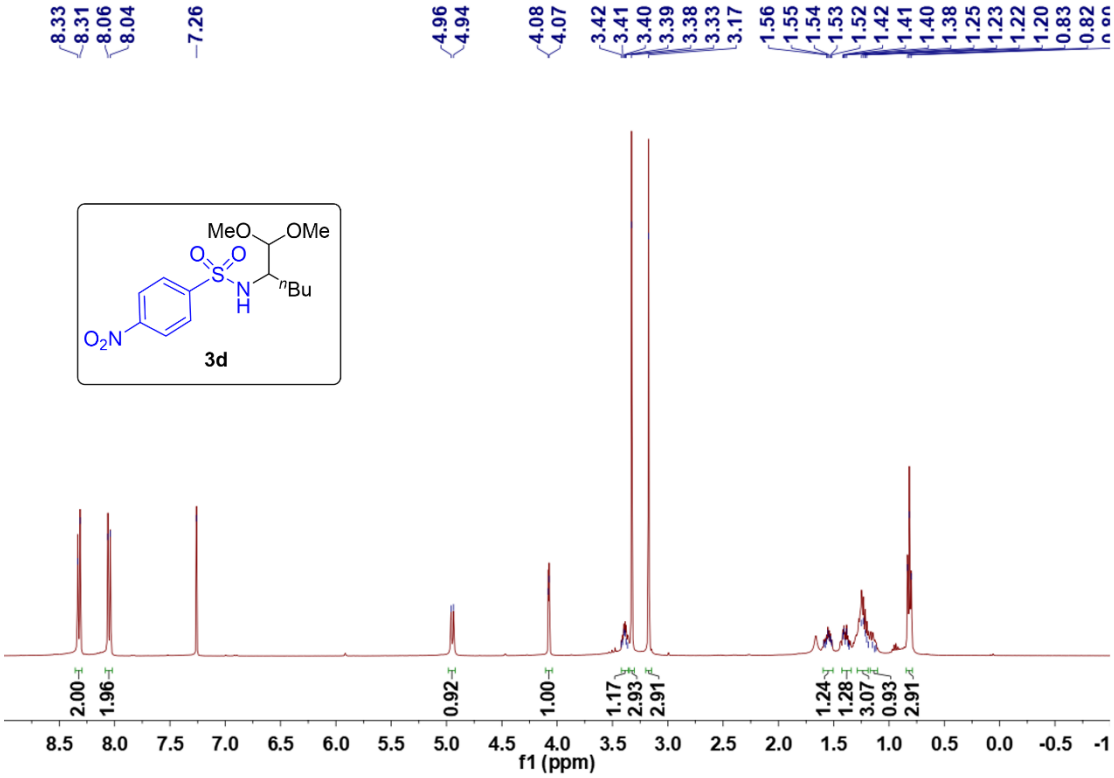
^{1}H NMR (500 MHz, $CDCl_3$) of **3c**



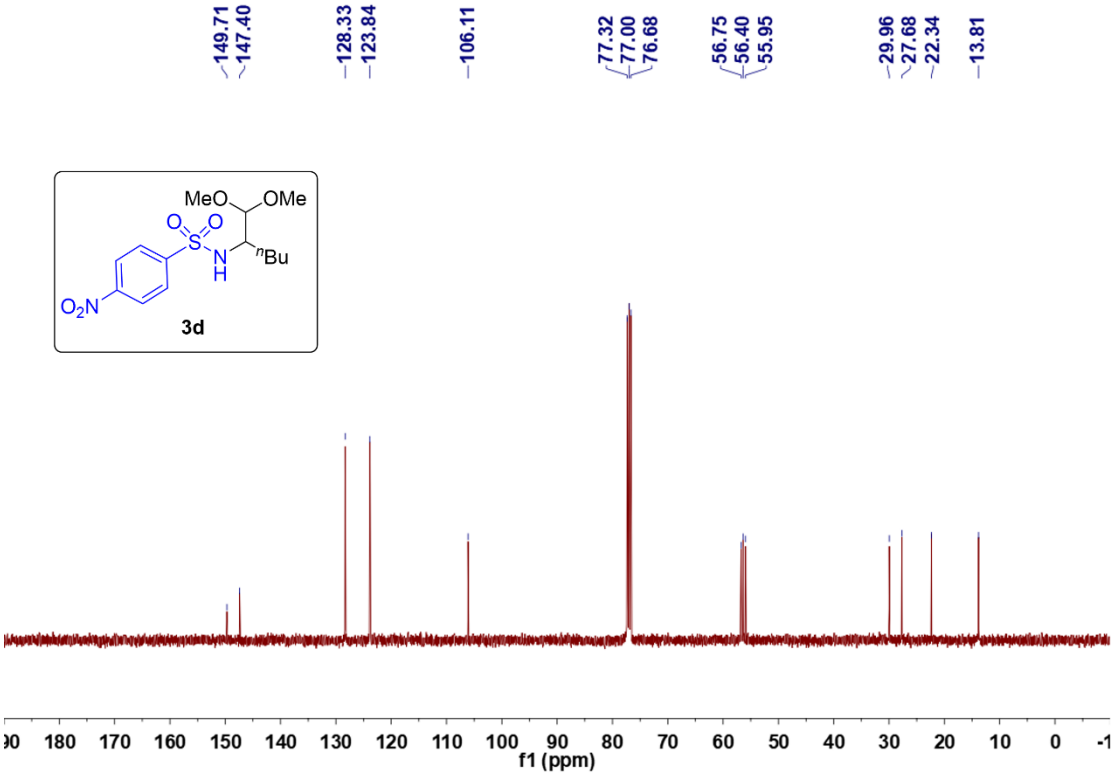
^{13}C NMR (126 MHz, $CDCl_3$) of **3c**



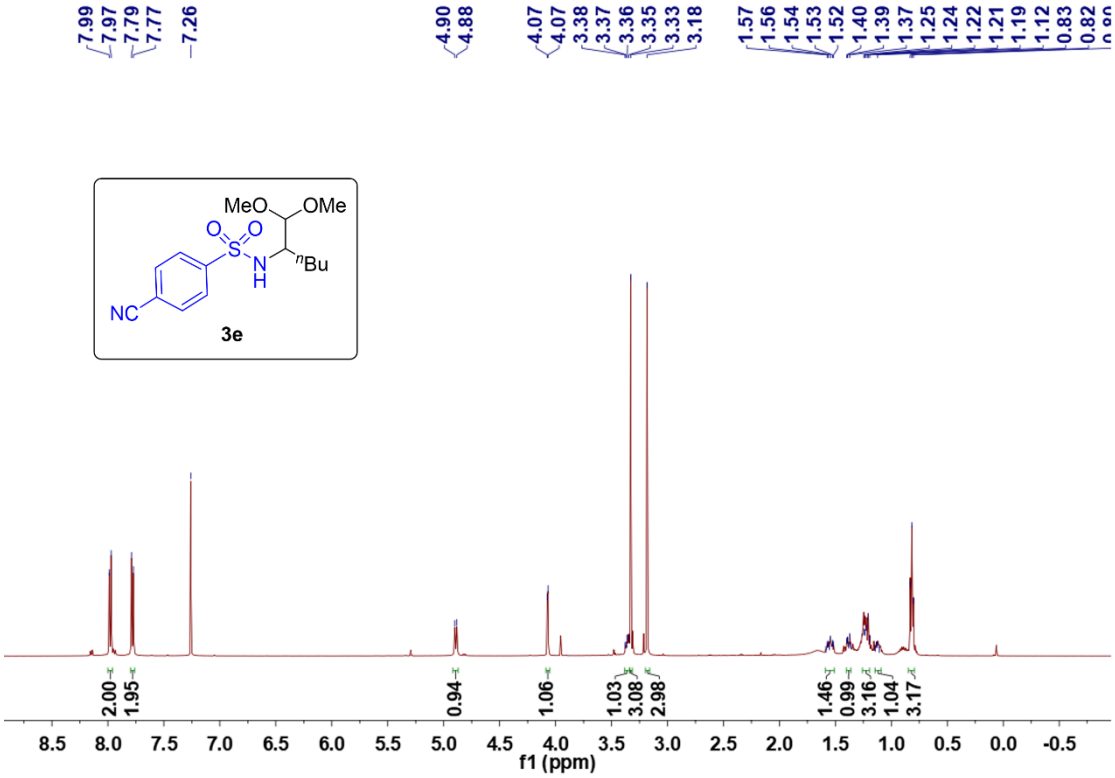
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**



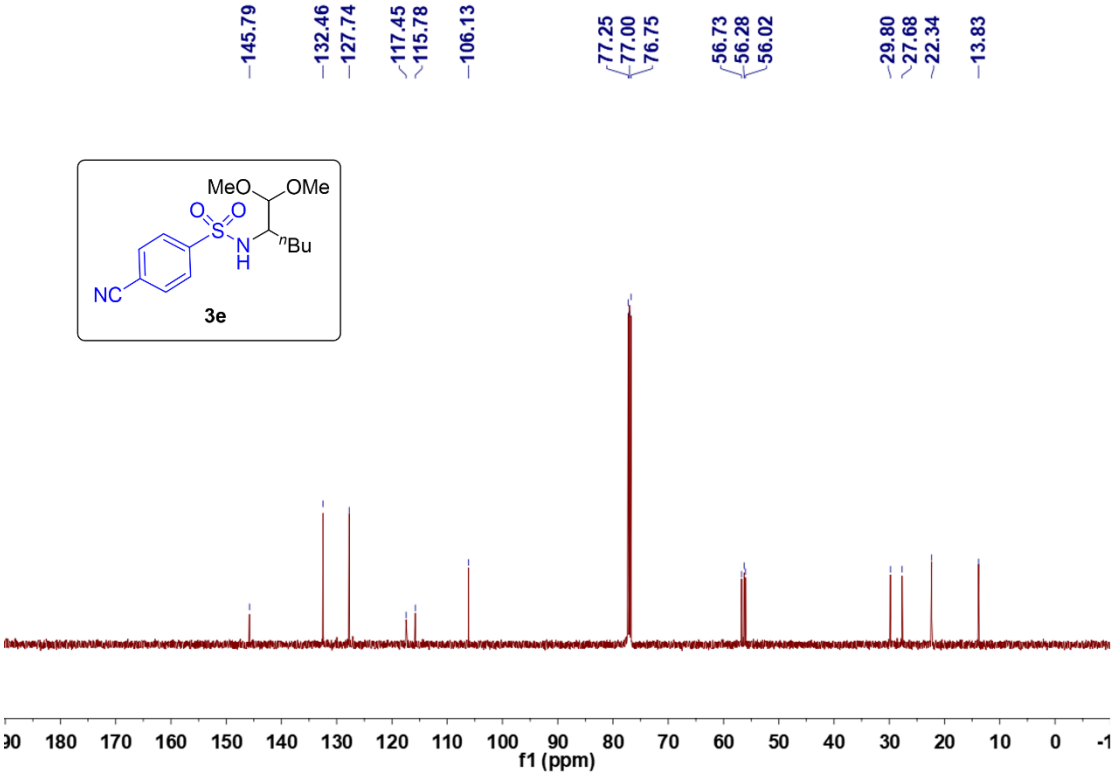
^{13}C NMR (101 MHz, $CDCl_3$) of **3d**



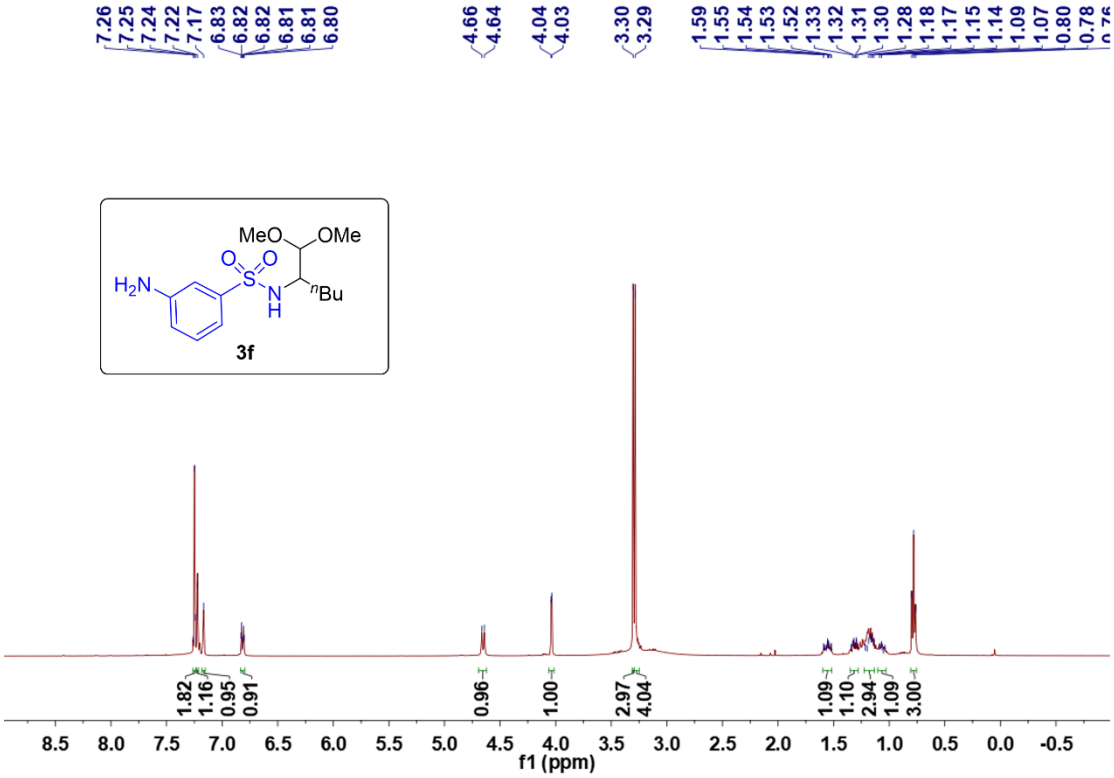
^{1}H NMR (500 MHz, $CDCl_3$) of **3e**



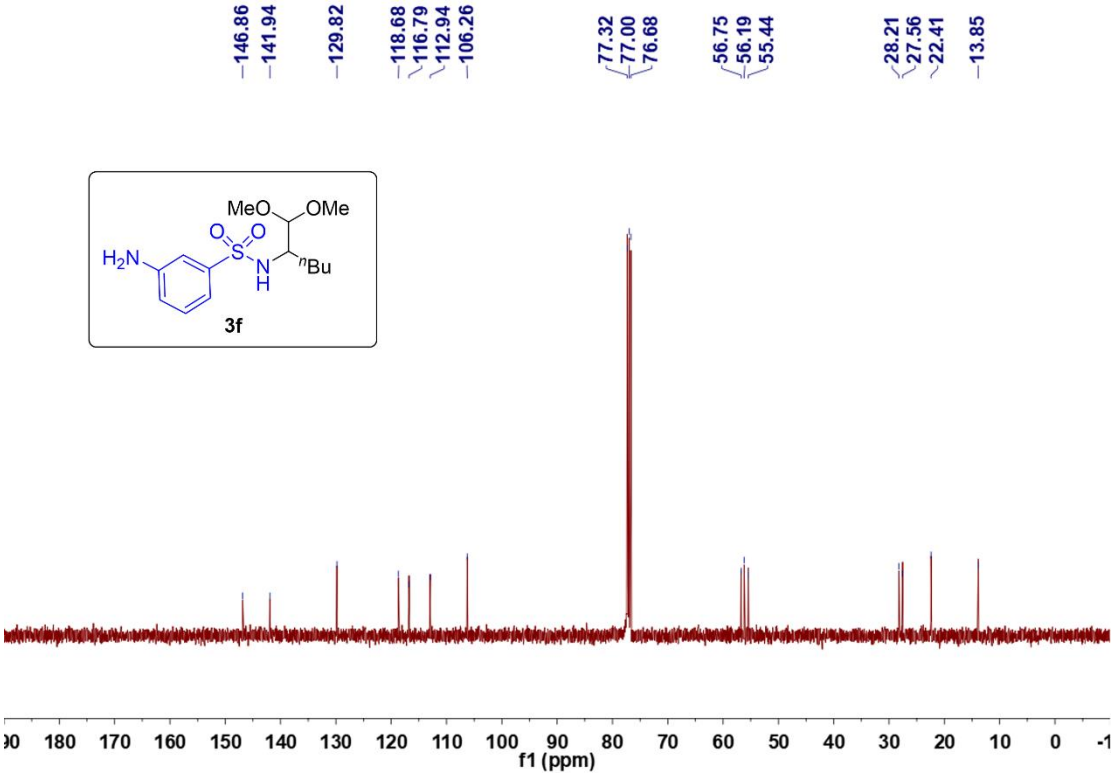
^{13}C NMR (126 MHz, $CDCl_3$) of **3e**



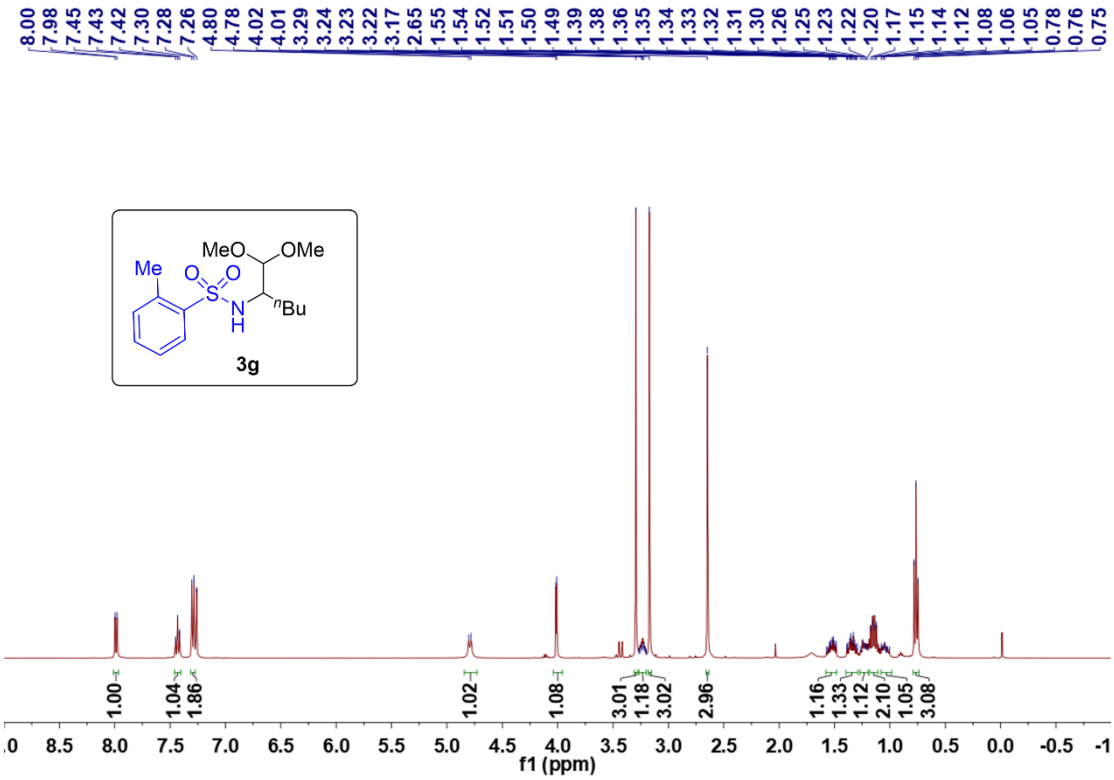
^{1}H NMR (400 MHz, $CDCl_3$) of **3f**



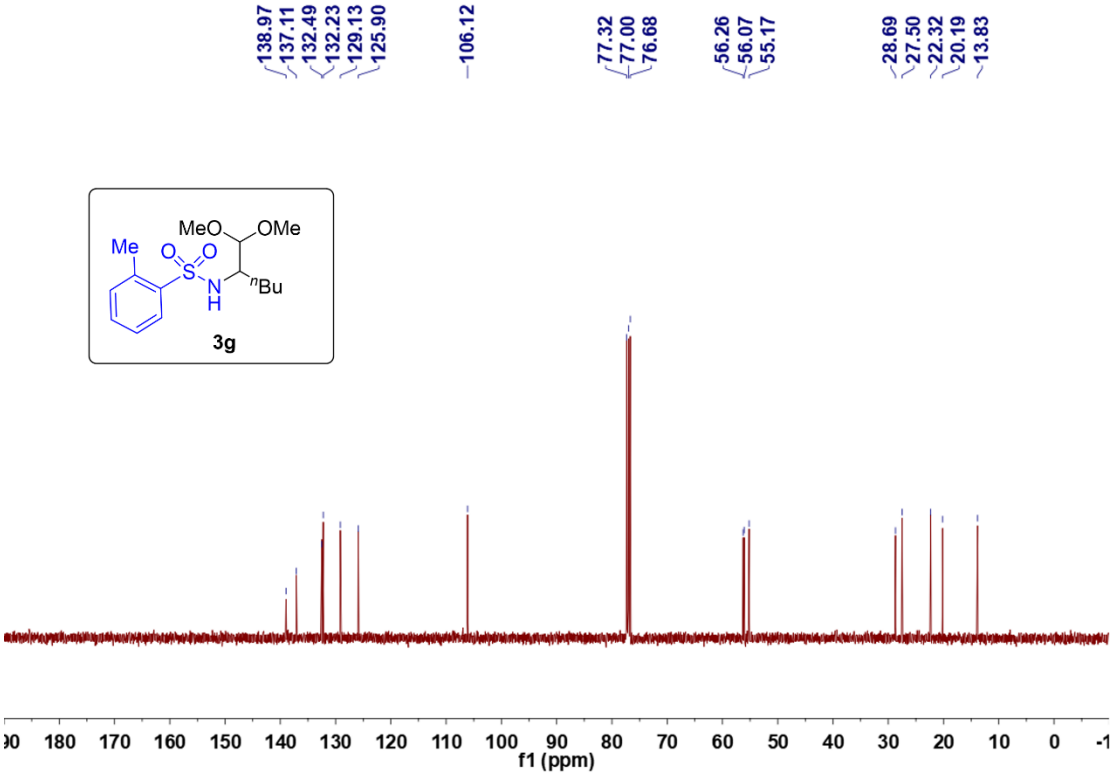
^{13}C NMR (101 MHz, $CDCl_3$) of **3f**



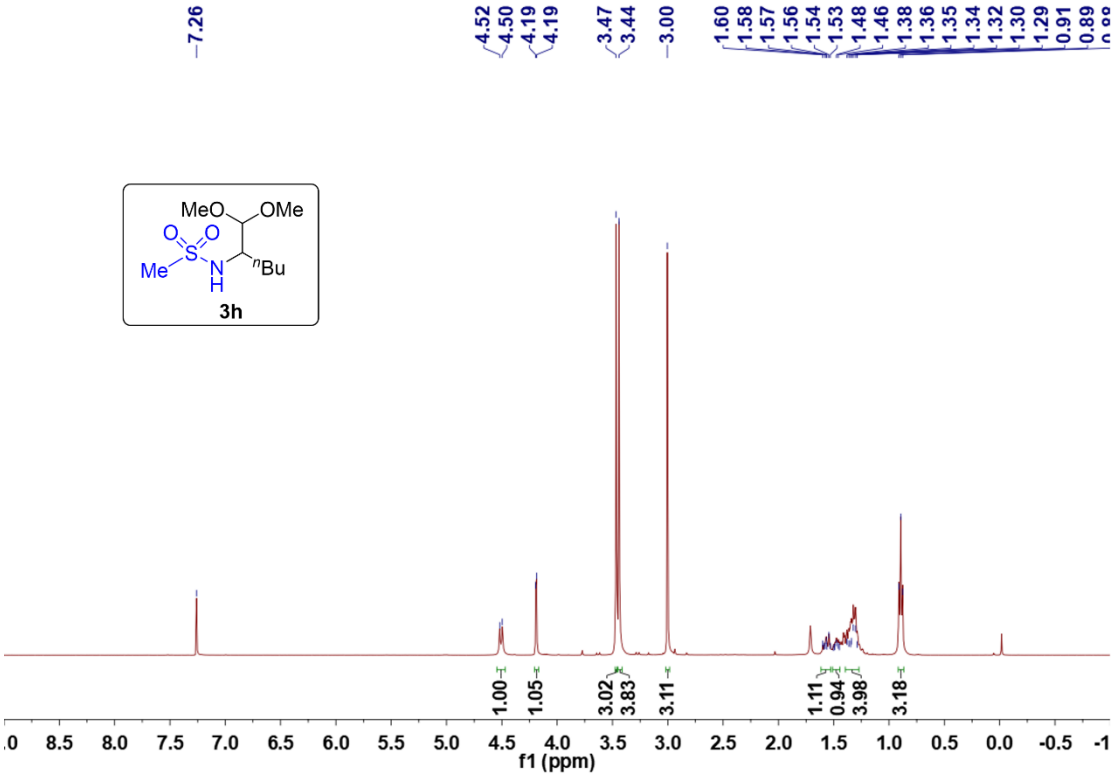
^{1}H NMR (400 MHz, $CDCl_3$) of **3g**



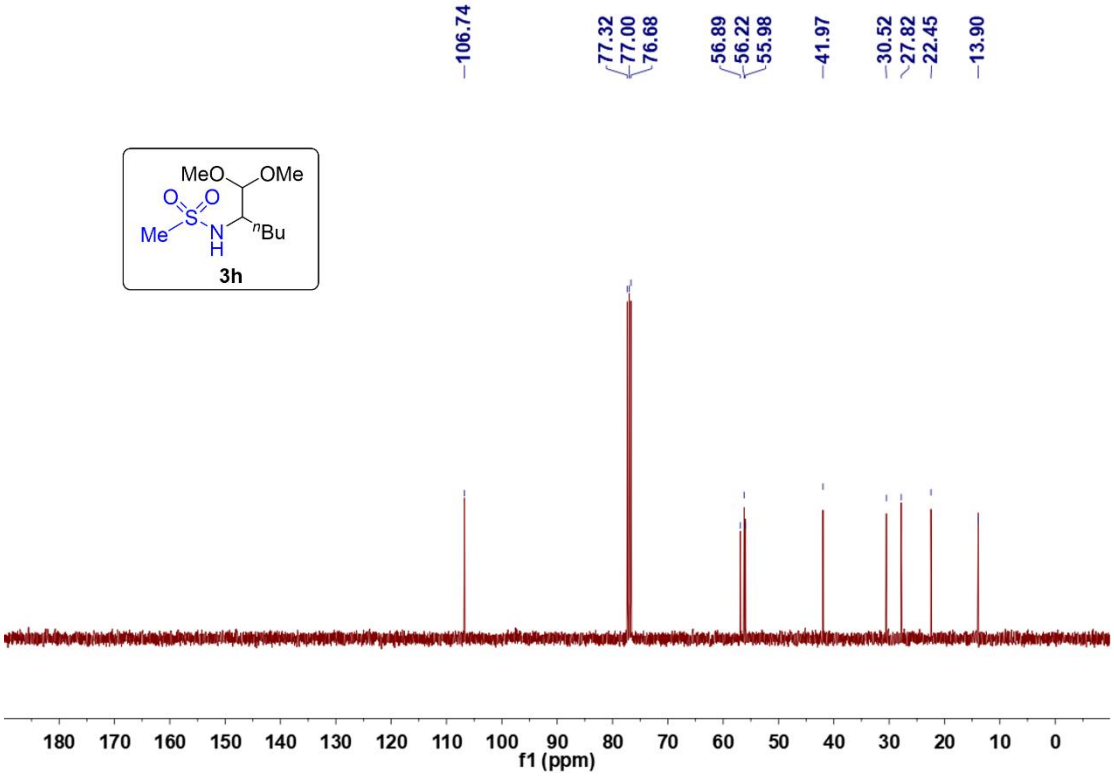
^{13}C NMR (101 MHz, $CDCl_3$) of **3g**



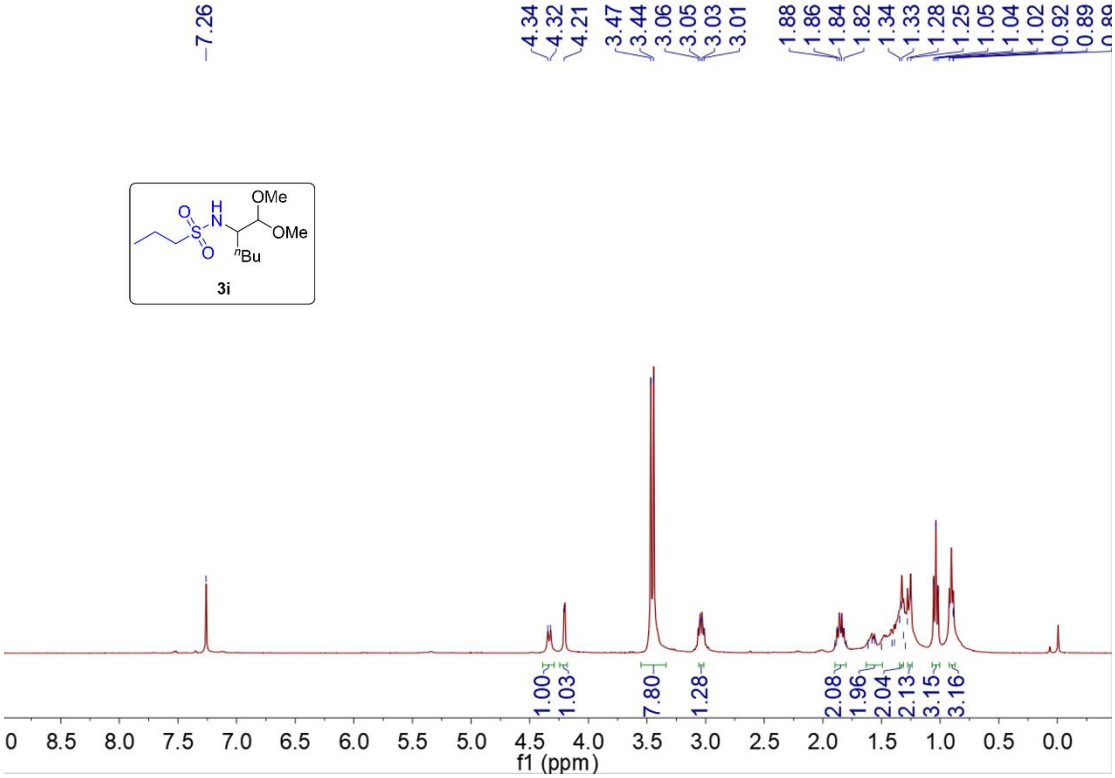
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**



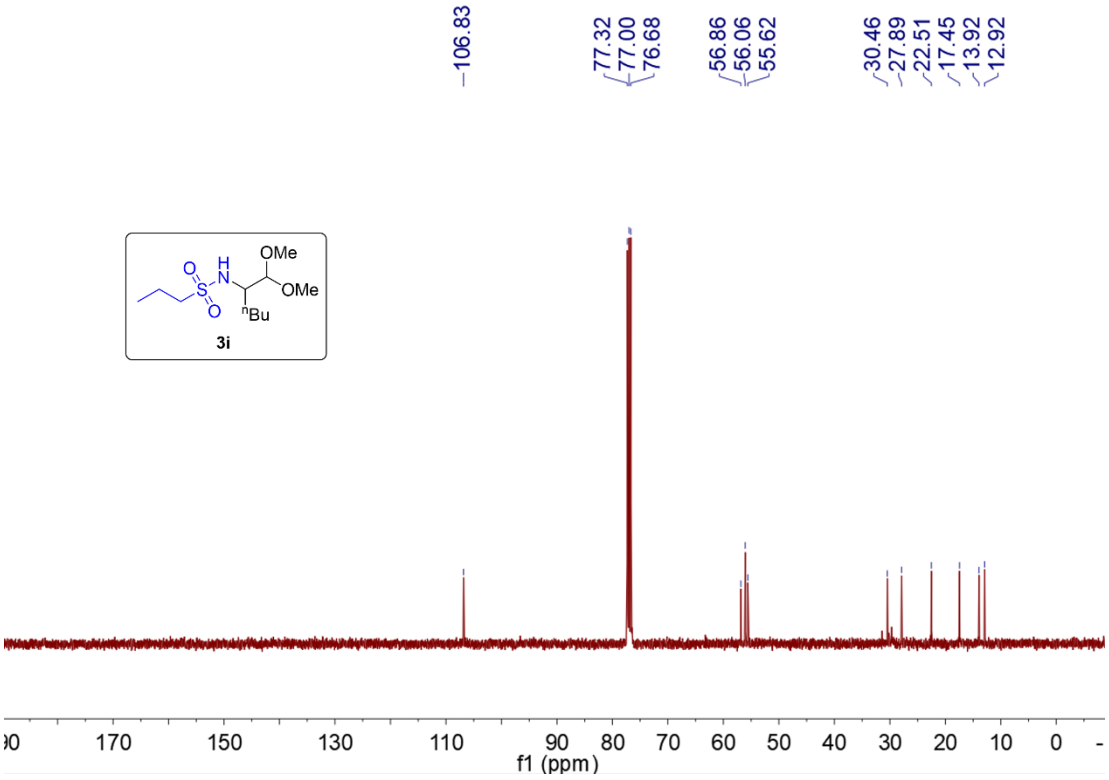
^{13}C NMR (101 MHz, $CDCl_3$) of **3h**



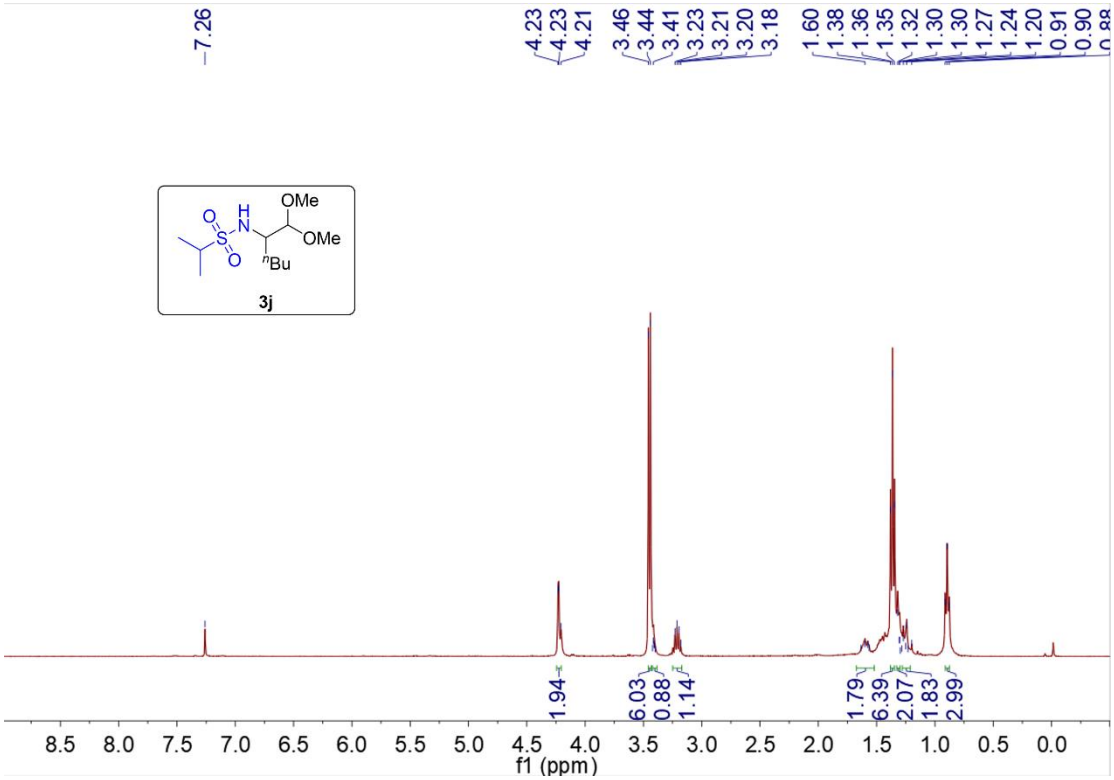
^{1}H NMR (400 MHz, $CDCl_3$) of **3i**



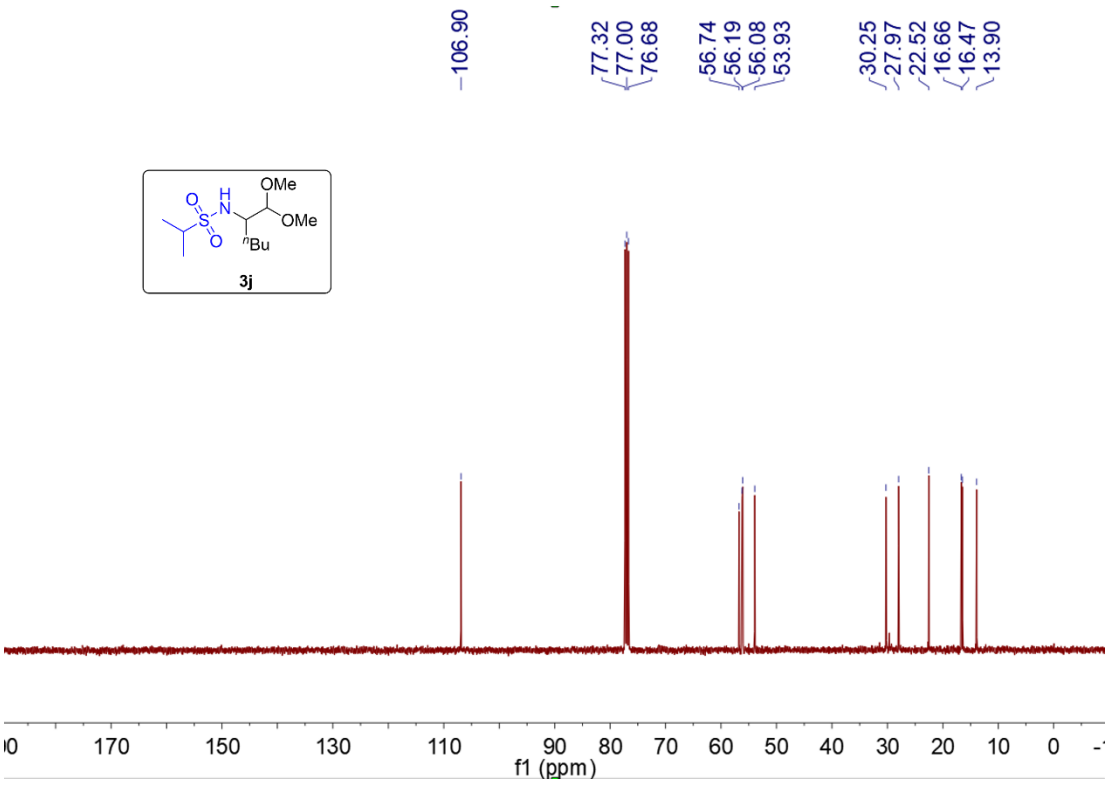
^{13}C NMR (101 MHz, $CDCl_3$) of **3i**



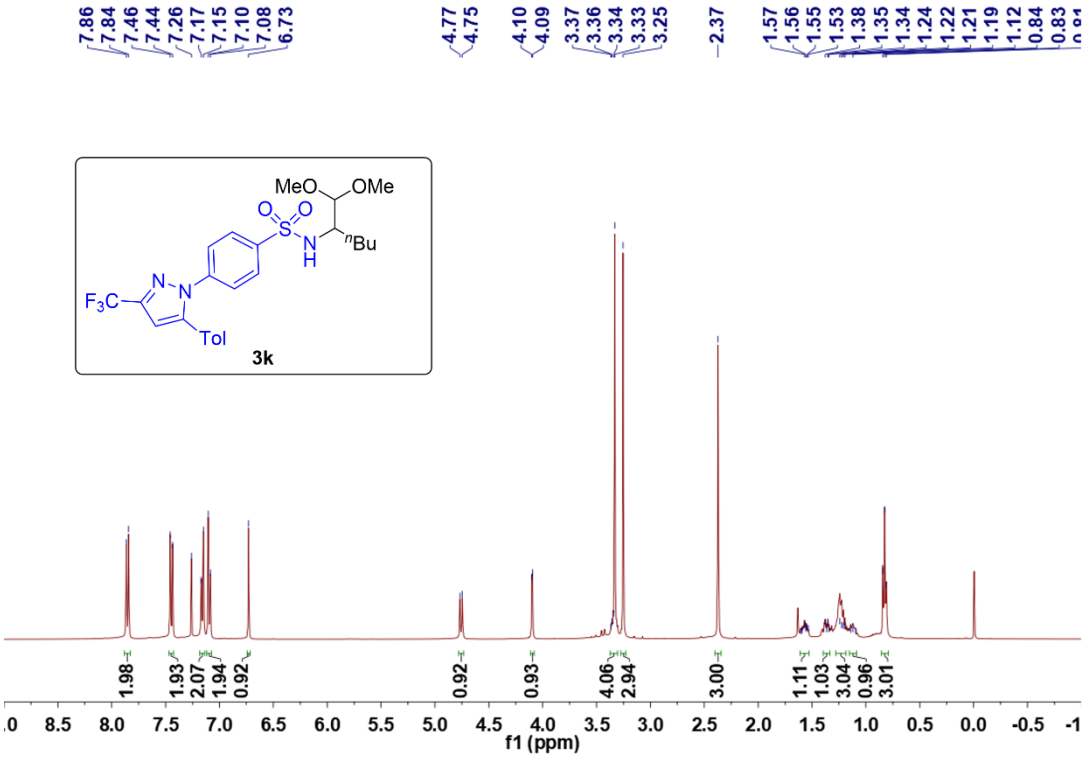
^{1}H NMR (400 MHz, $CDCl_3$) of **3j**



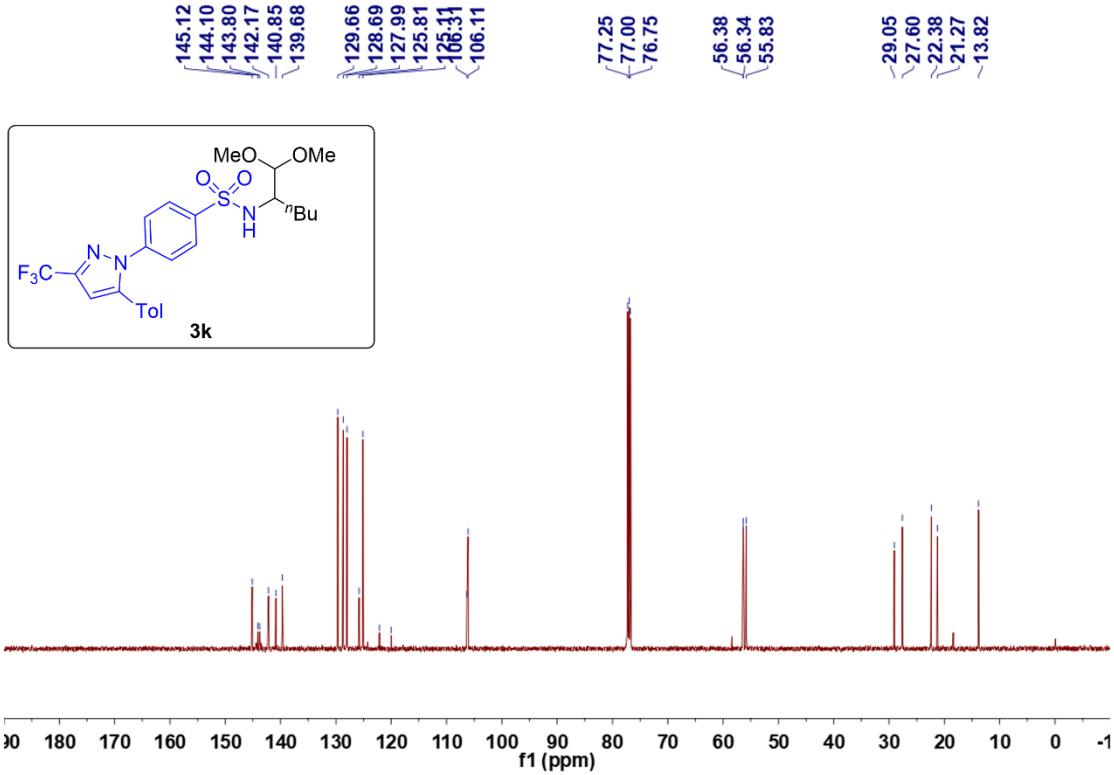
^{13}C NMR (101 MHz, $CDCl_3$) of **3j**



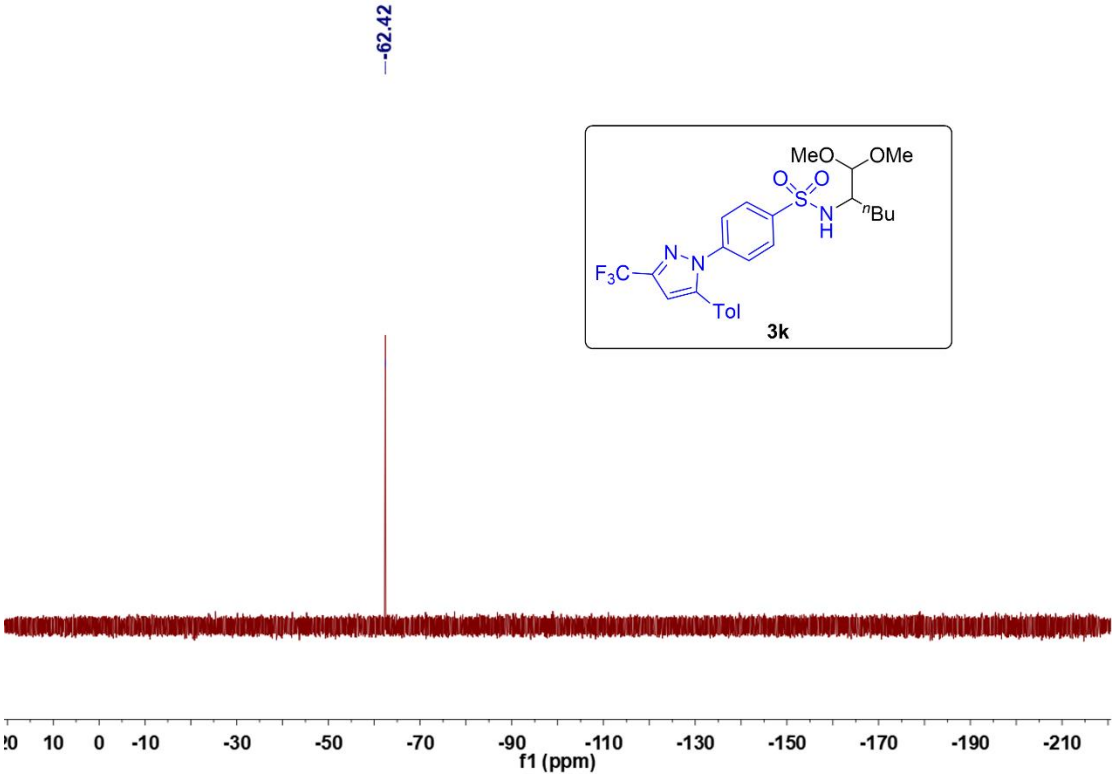
^{1}H NMR (400 MHz, $CDCl_3$) of **3k**



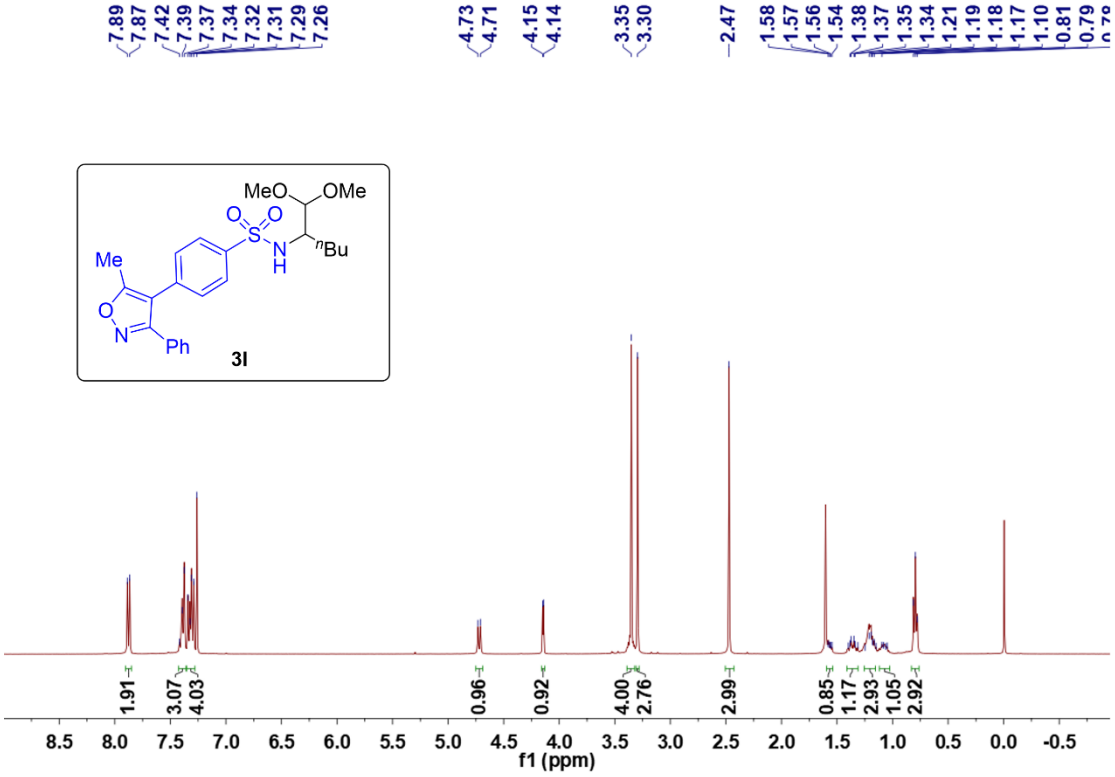
^{13}C NMR (101 MHz, $CDCl_3$) of **3k**



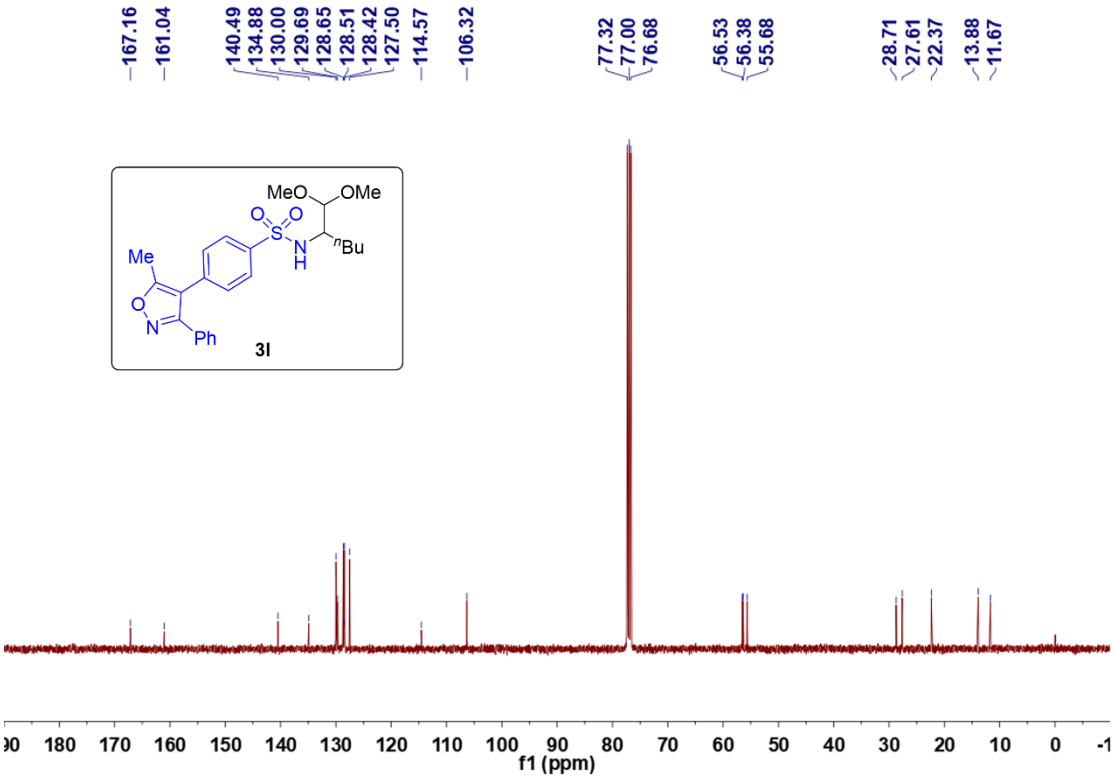
^{19}F NMR (376 MHz, $CDCl_3$) of **3k**



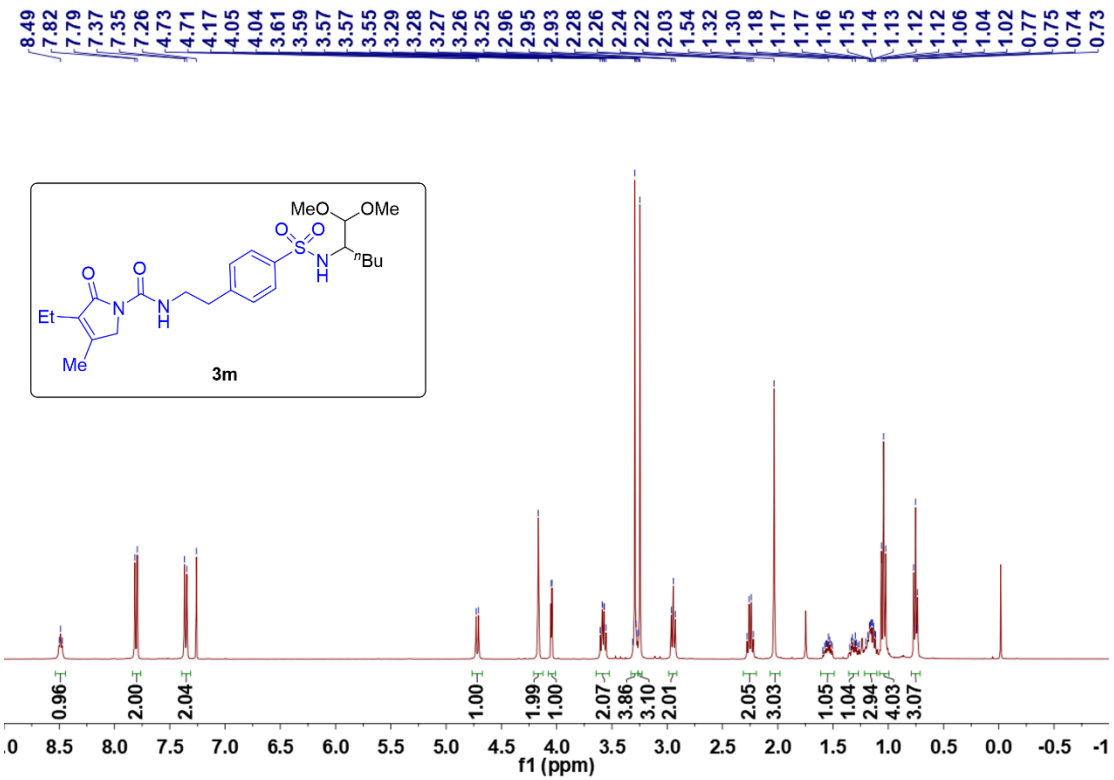
^{1}H NMR (400 MHz, $CDCl_3$) of **3l**



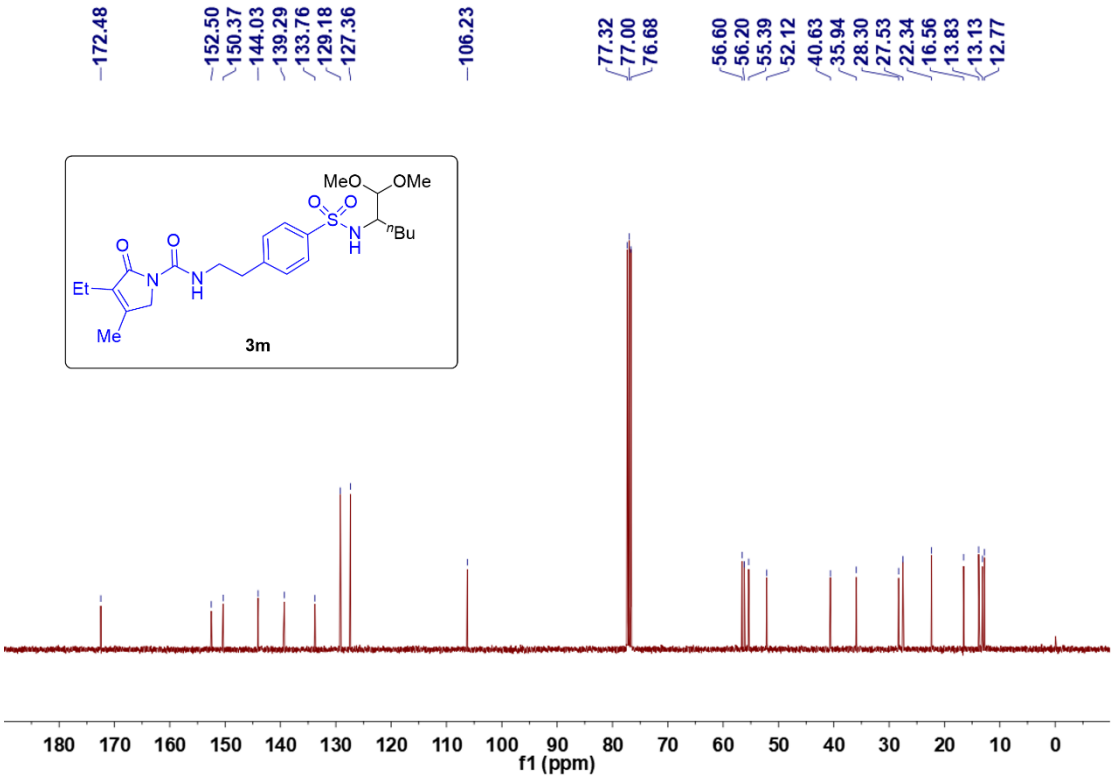
^{13}C NMR (101 MHz, $CDCl_3$) of **3l**



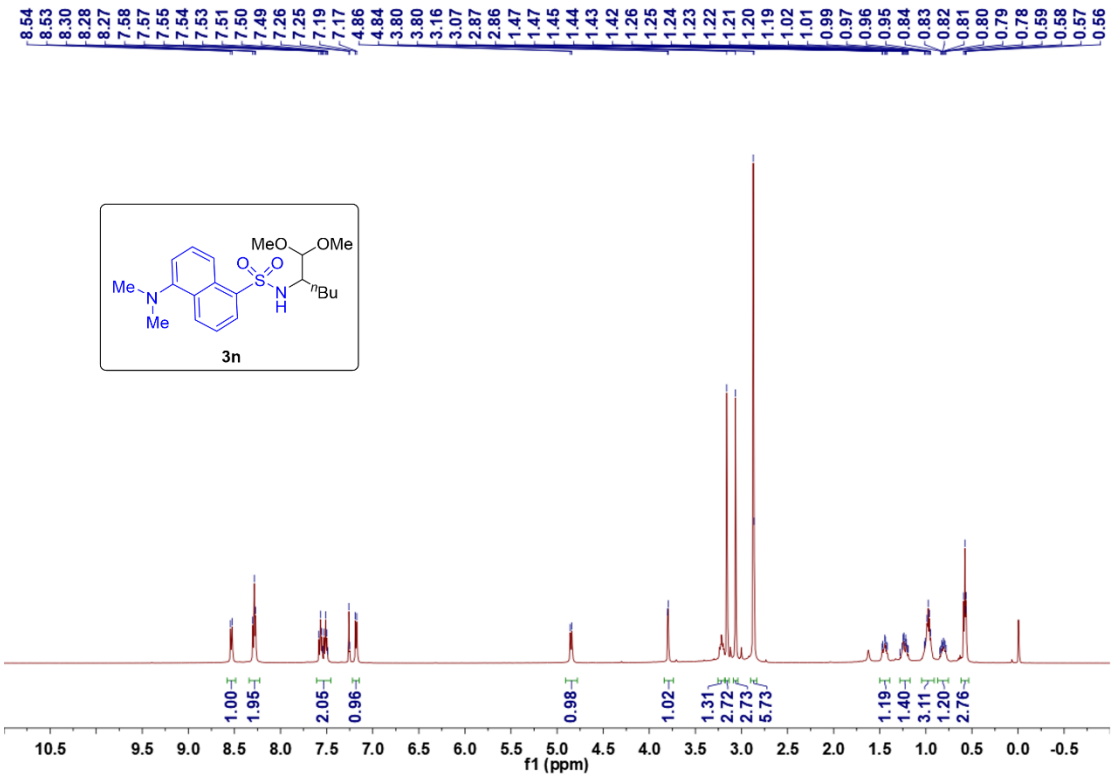
^{1}H NMR (400 MHz, $CDCl_3$) of **3m**



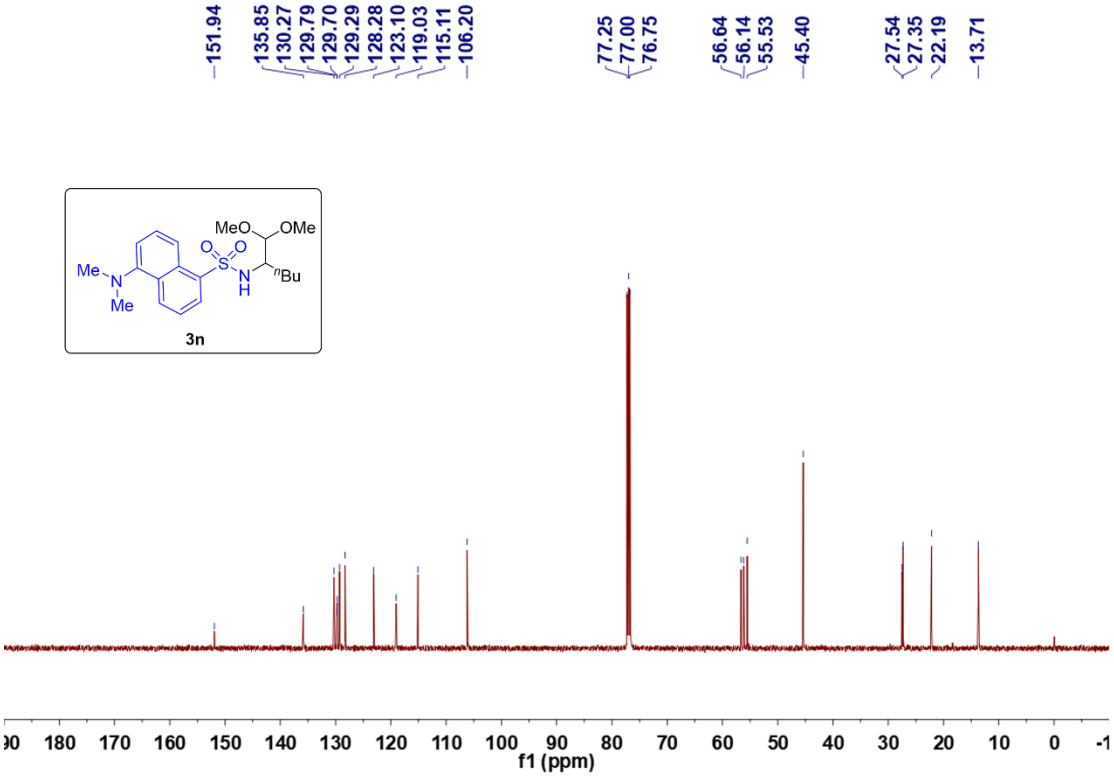
^{13}C NMR (101 MHz, $CDCl_3$) of **3m**



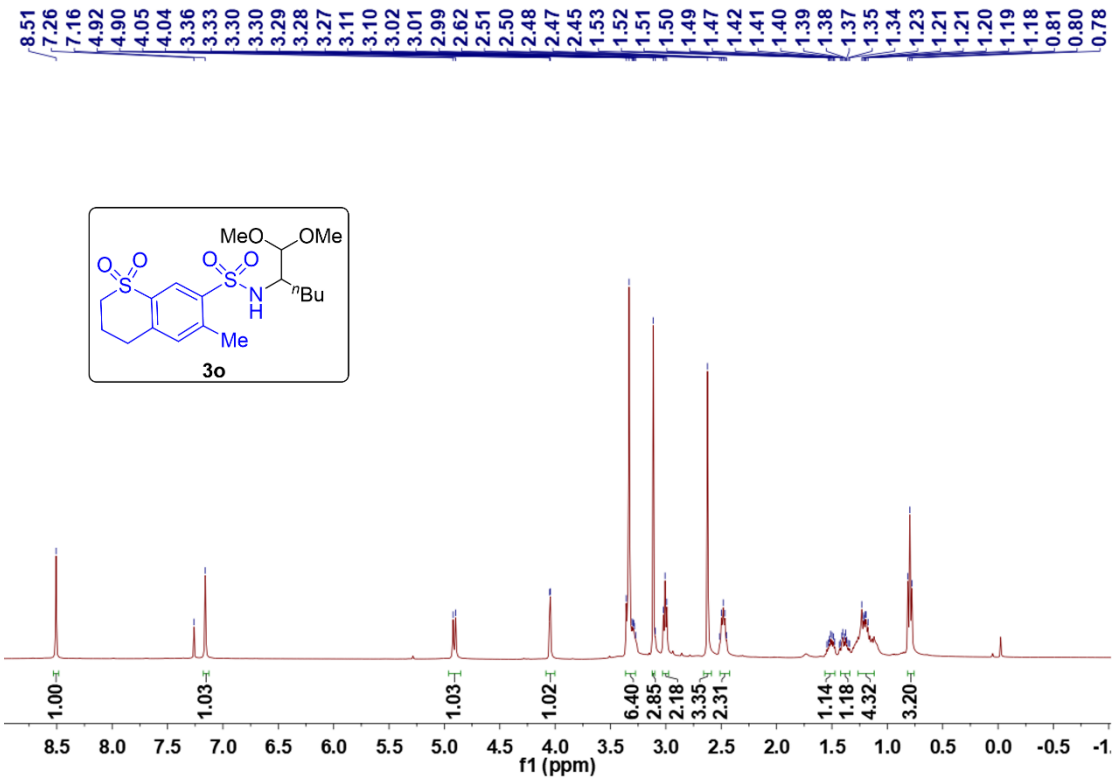
^{1}H NMR (500 MHz, $CDCl_3$) of **3n**



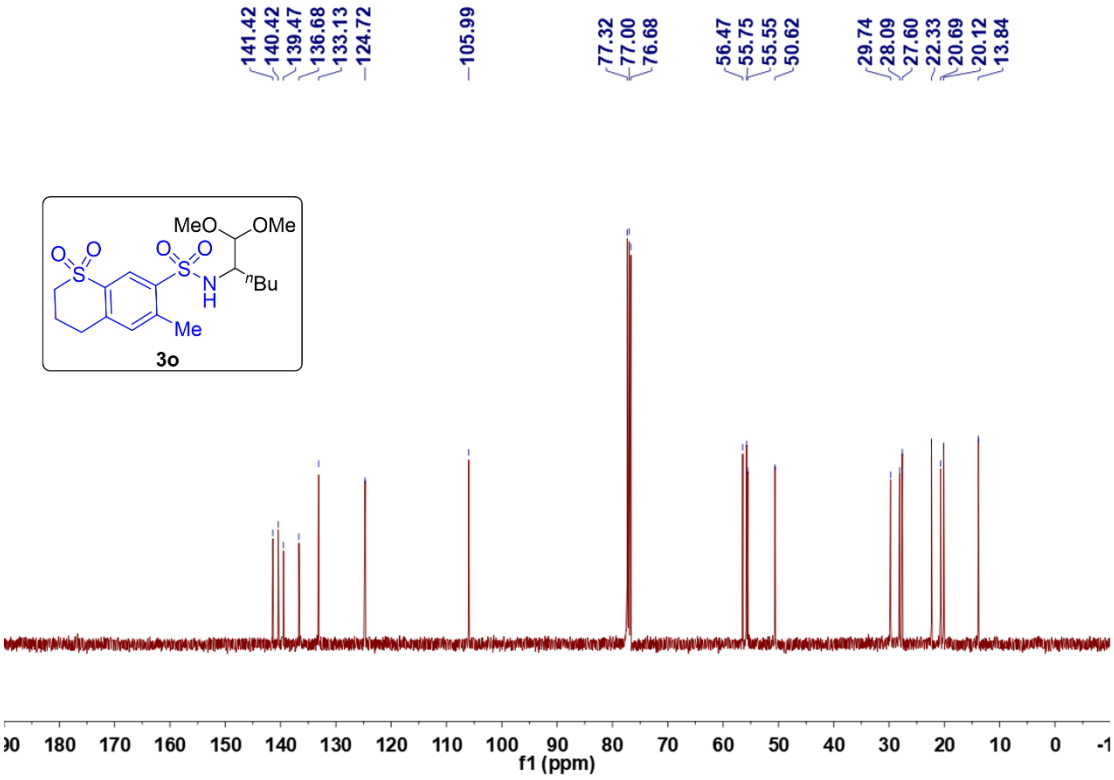
^{13}C NMR (126 MHz, $CDCl_3$) of **3n**



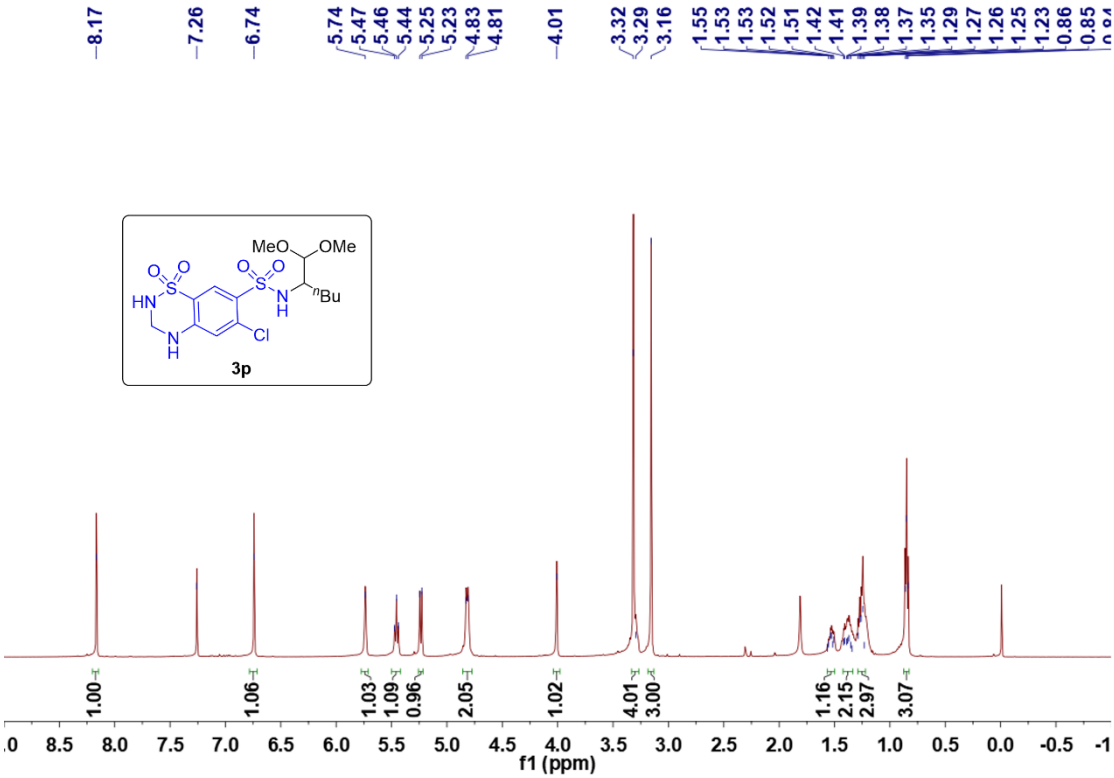
^{1}H NMR (400 MHz, $CDCl_3$) of **3o**



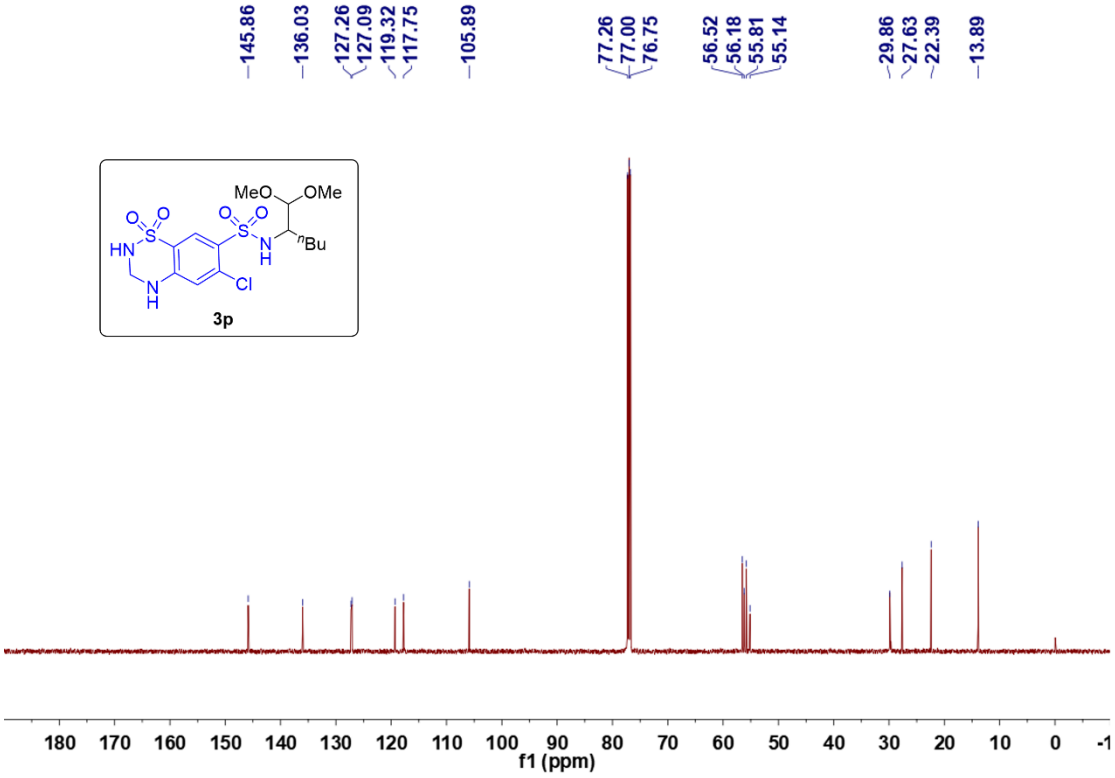
^{13}C NMR (101 MHz, $CDCl_3$) of **3o**



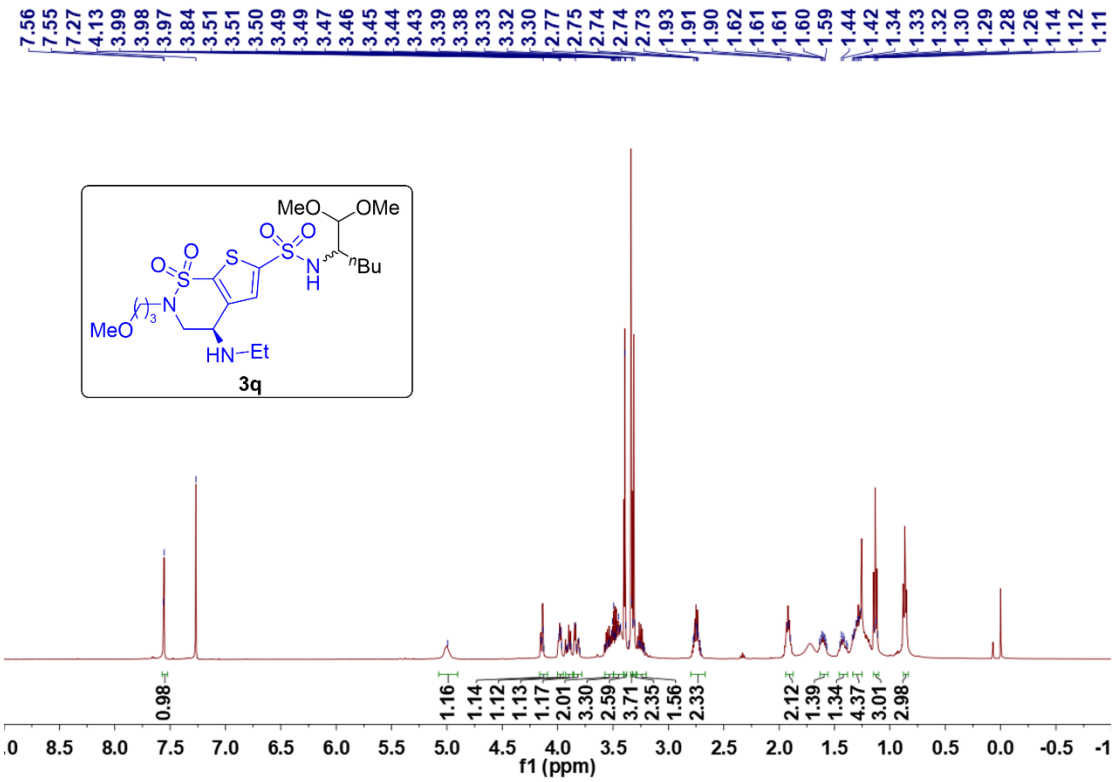
^{1}H NMR (500 MHz, $CDCl_3$) of **3p**



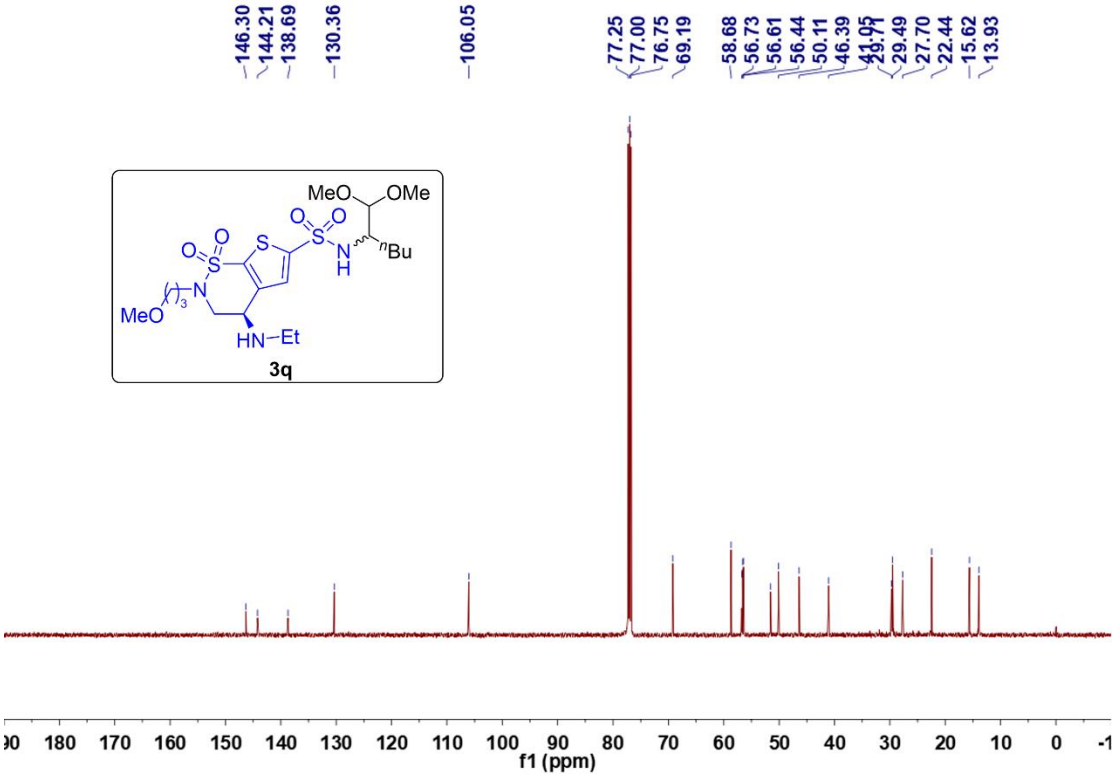
^{13}C NMR (126 MHz, $CDCl_3$) of **3p**



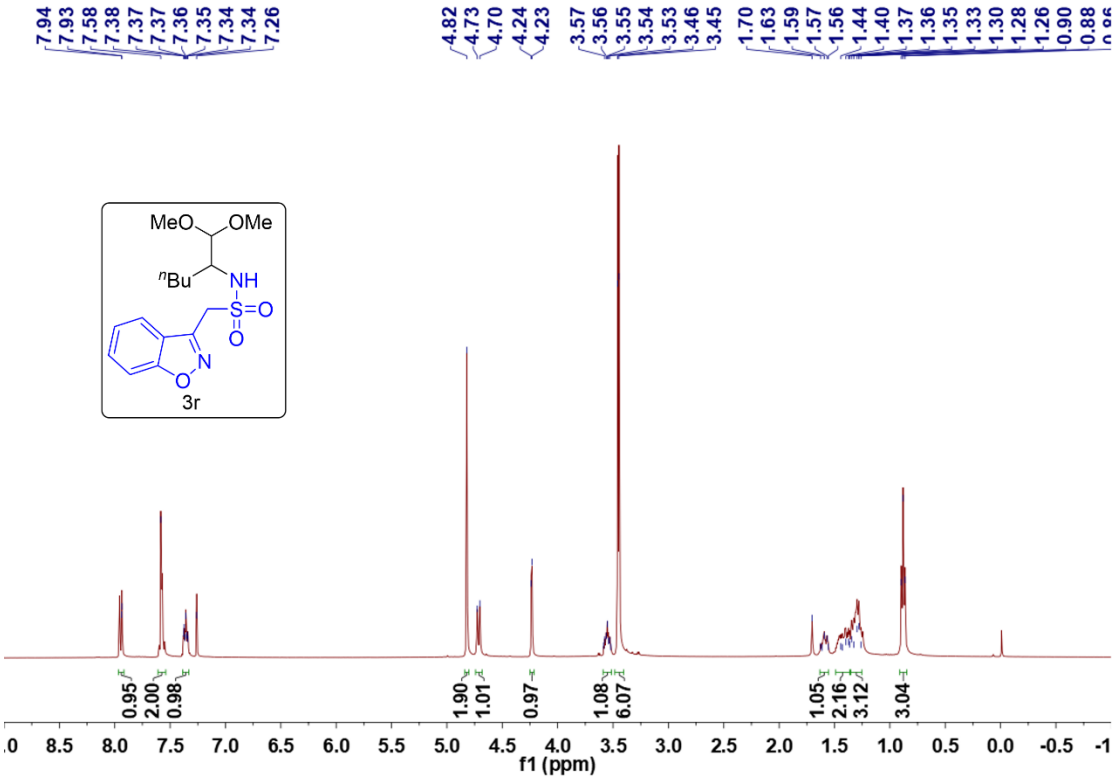
^{1}H NMR (500 MHz, $CDCl_3$) of **3q**



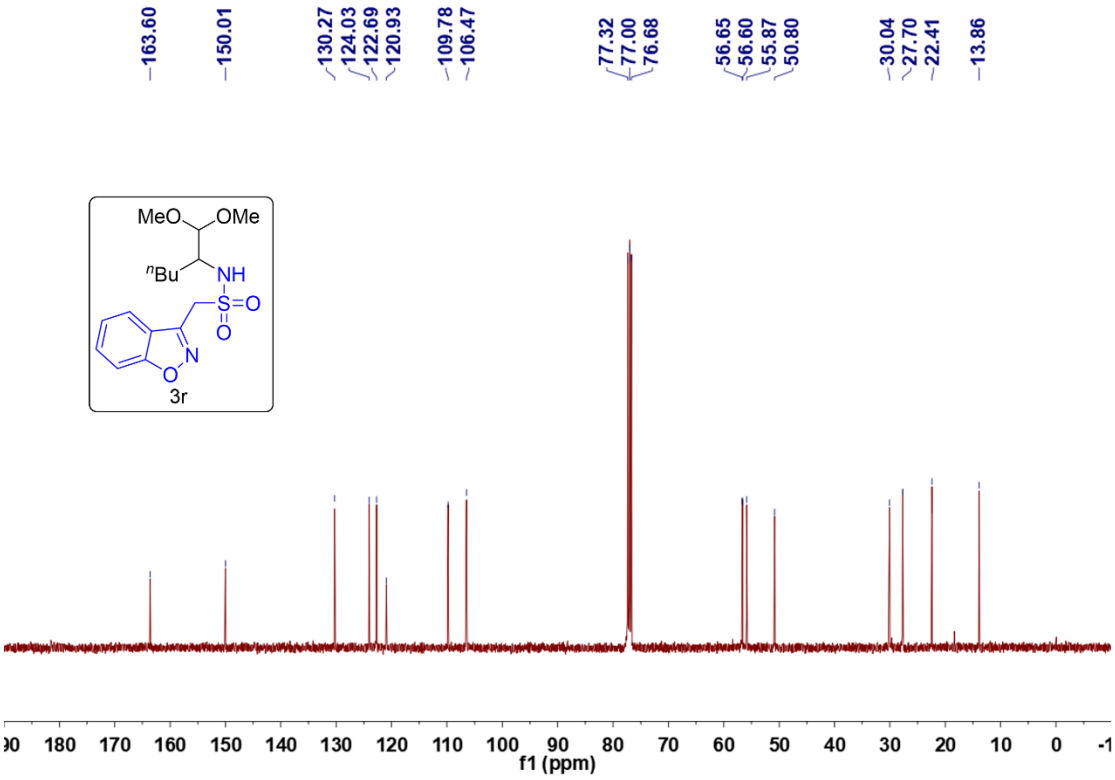
^{13}C NMR (126 MHz, $CDCl_3$) of **3q**



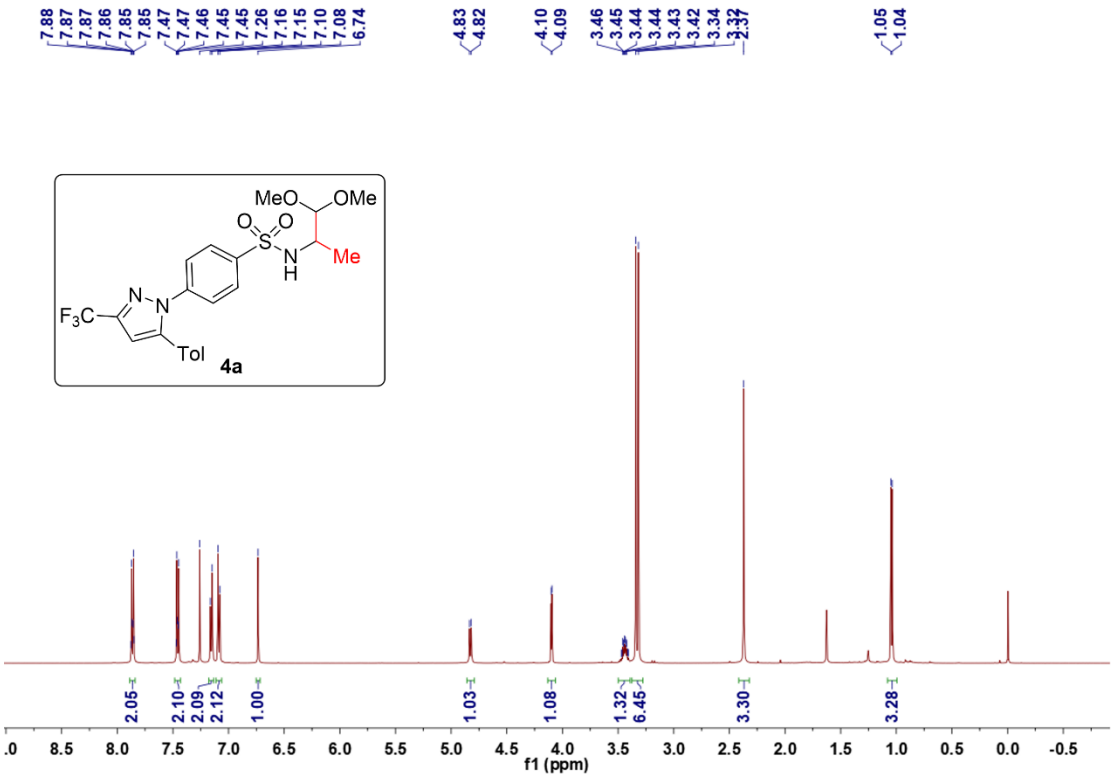
^{1}H NMR (400 MHz, $CDCl_3$) of **3r**



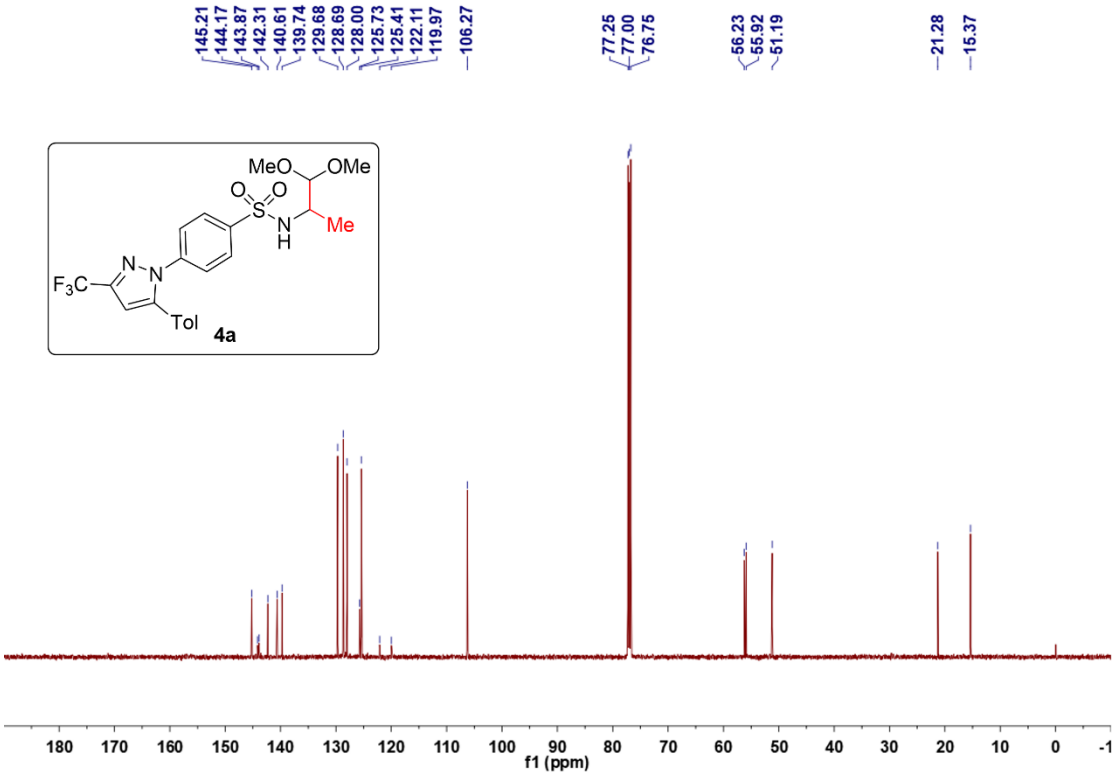
^{13}C NMR (101 MHz, $CDCl_3$) of **3r**



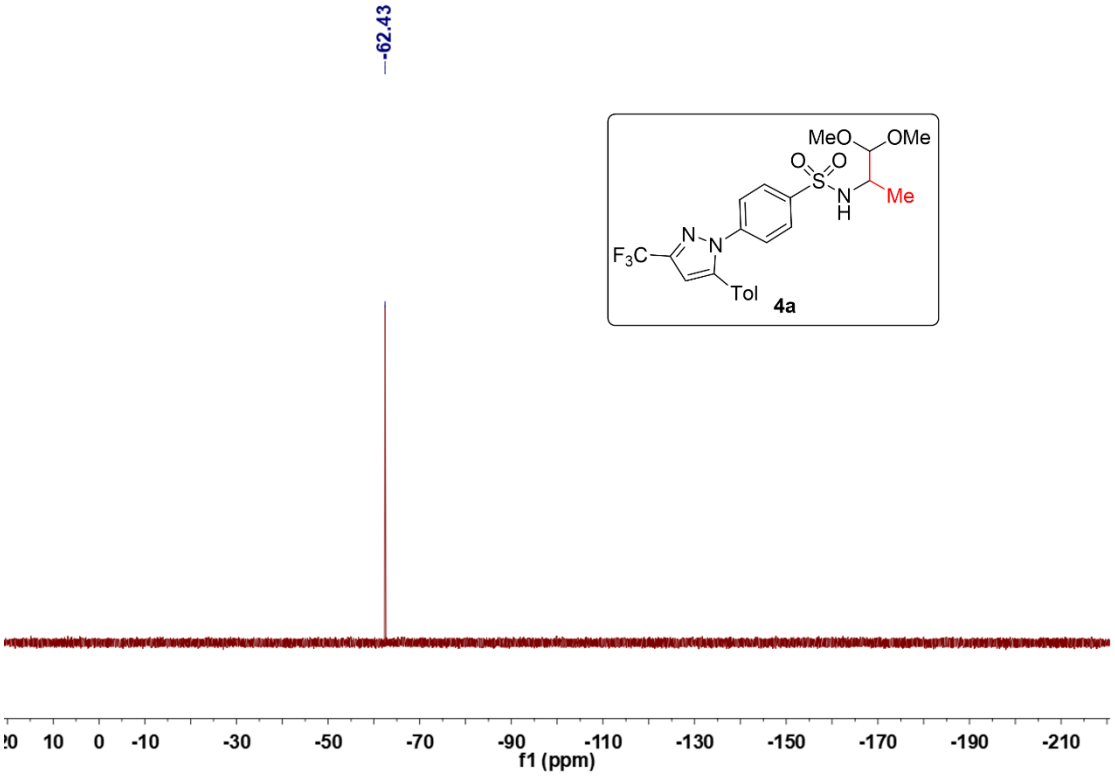
^{1}H NMR (500 MHz, $CDCl_3$) of **4a**



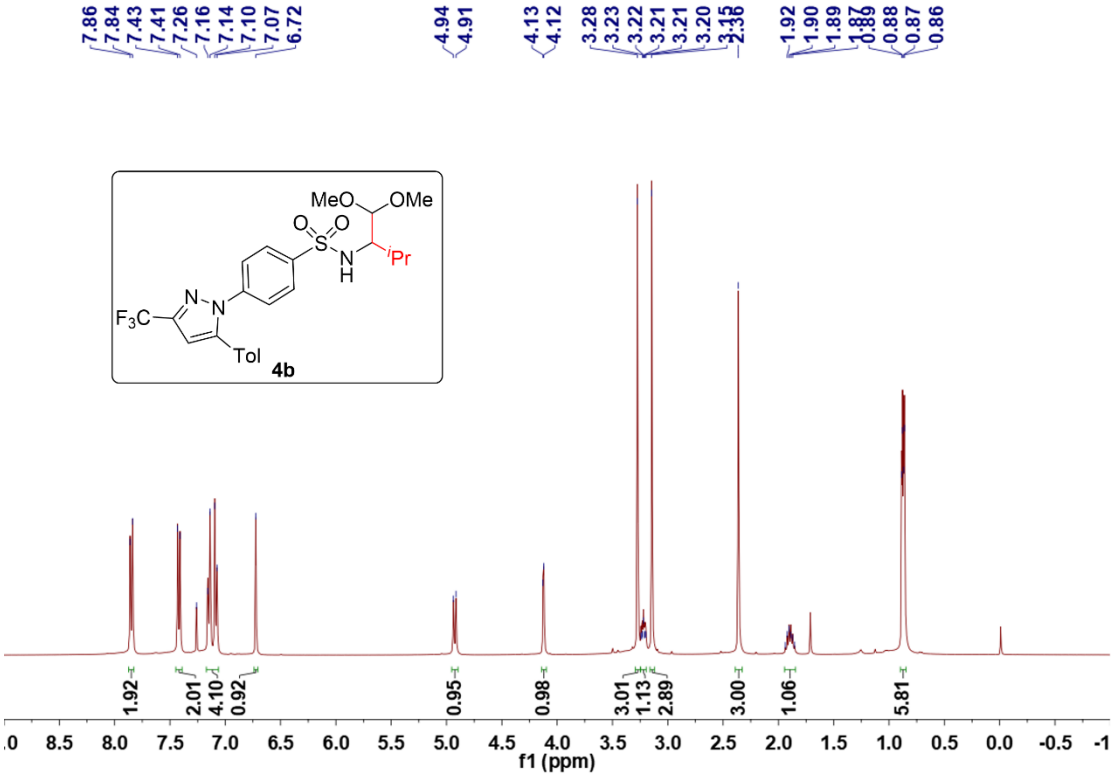
^{13}C NMR (126 MHz, $CDCl_3$) of **4a**



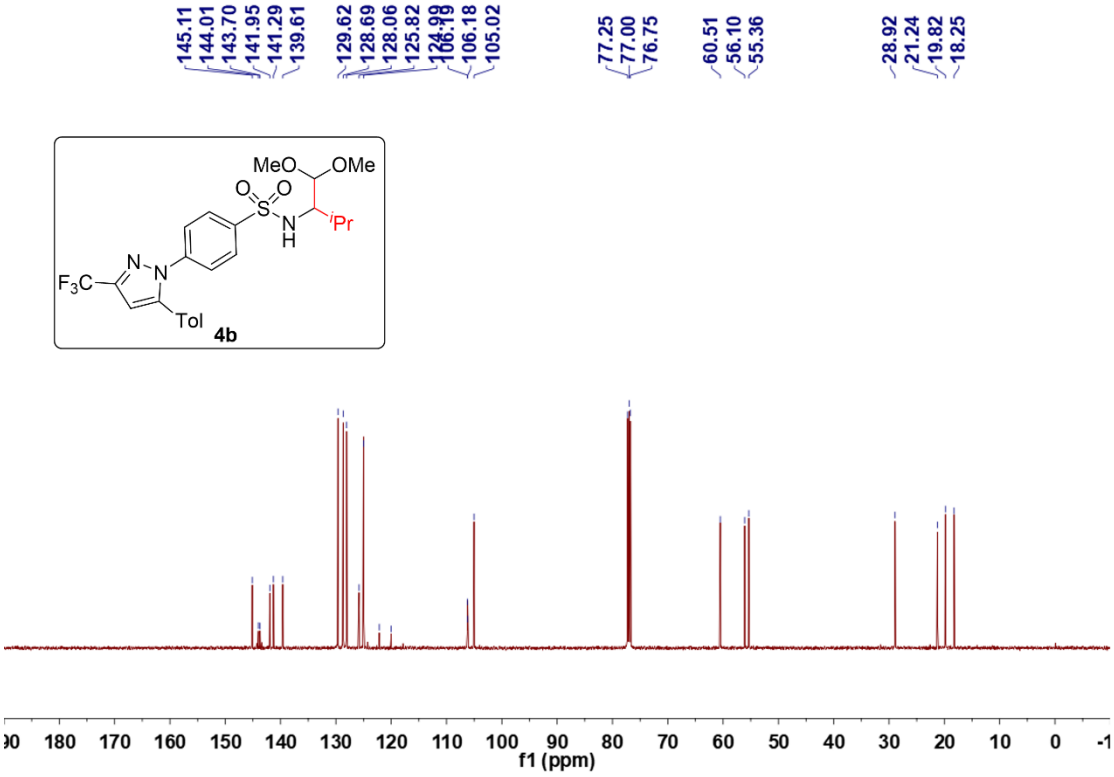
^{19}F NMR (471 MHz, $CDCl_3$) of **4a**



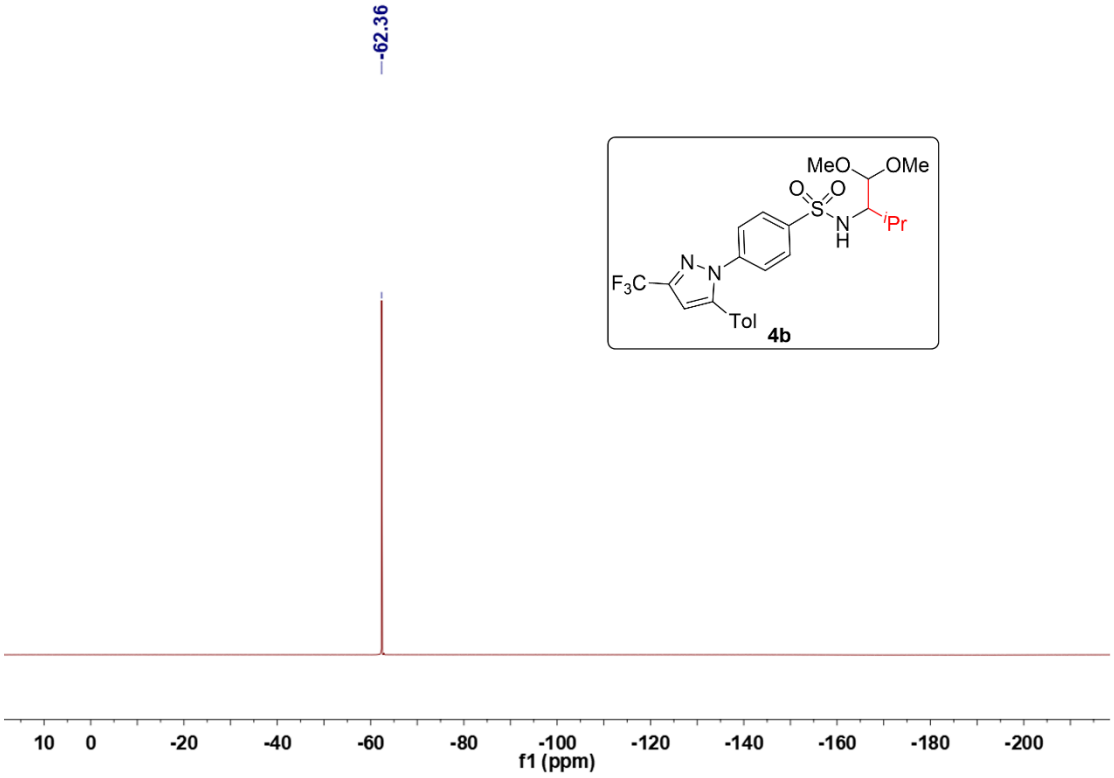
^{1}H NMR (400 MHz, $CDCl_3$) of **4b**



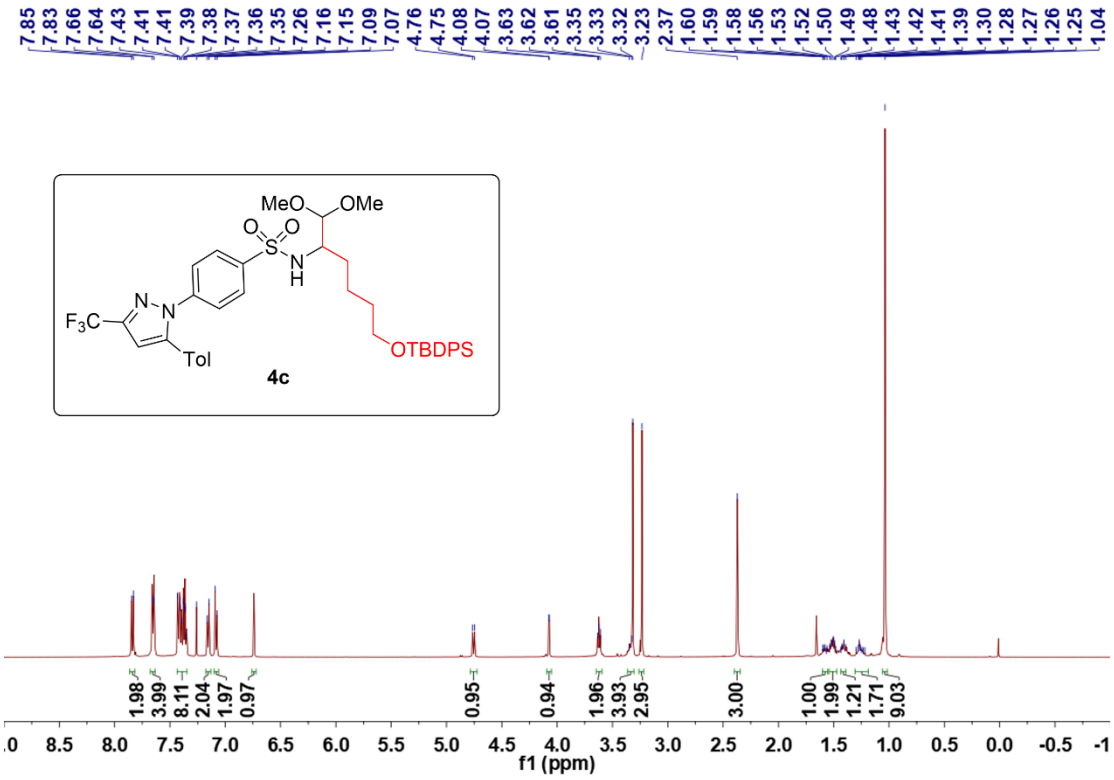
^{13}C NMR (101 MHz, $CDCl_3$) of **4b**



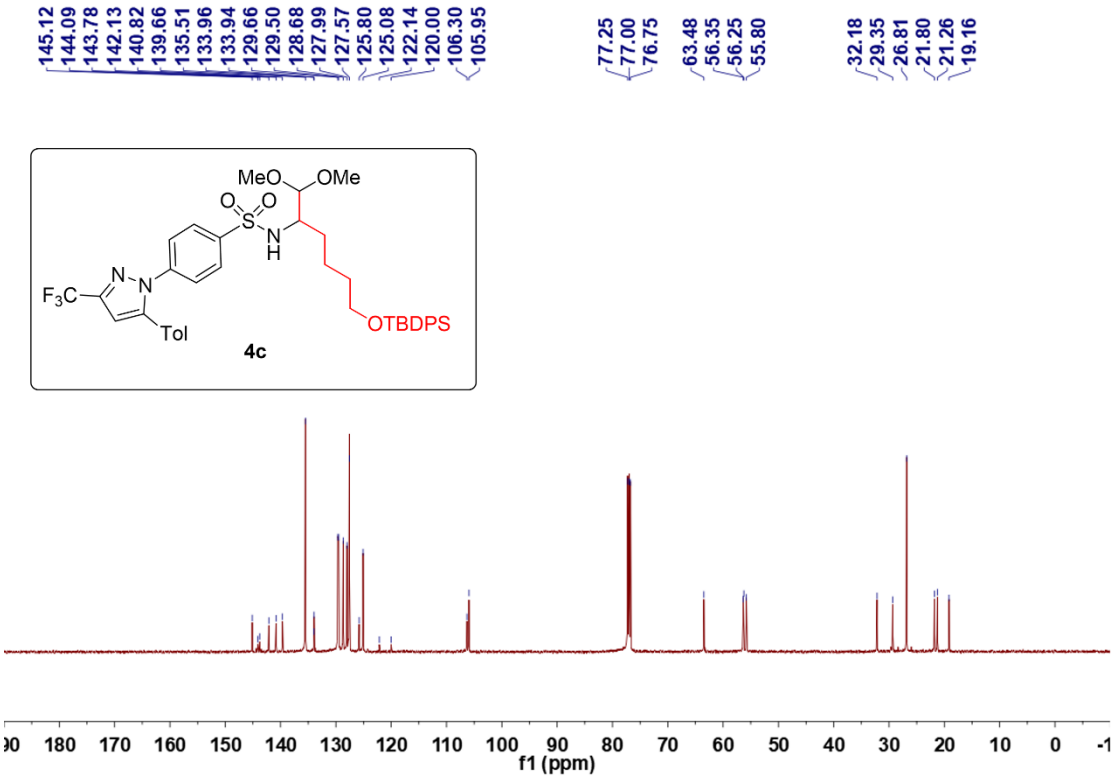
^{19}F NMR (376 MHz, $CDCl_3$) of **4b**



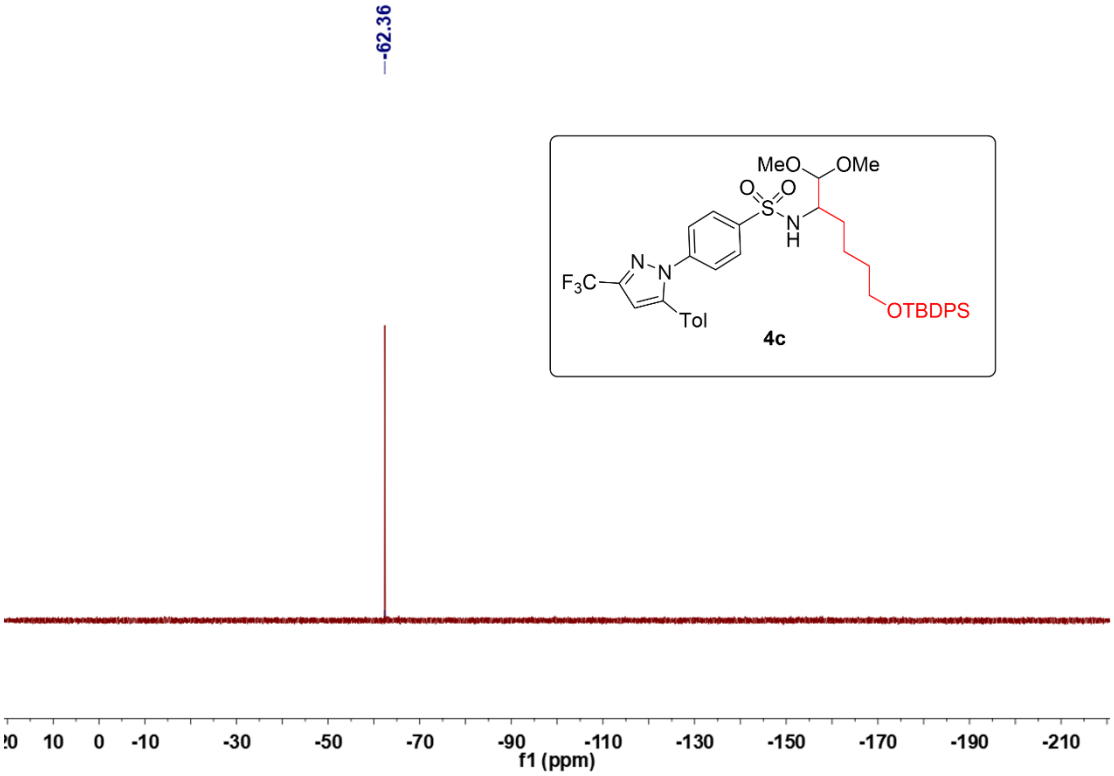
^{1}H NMR (500 MHz, $CDCl_3$) of **4c**



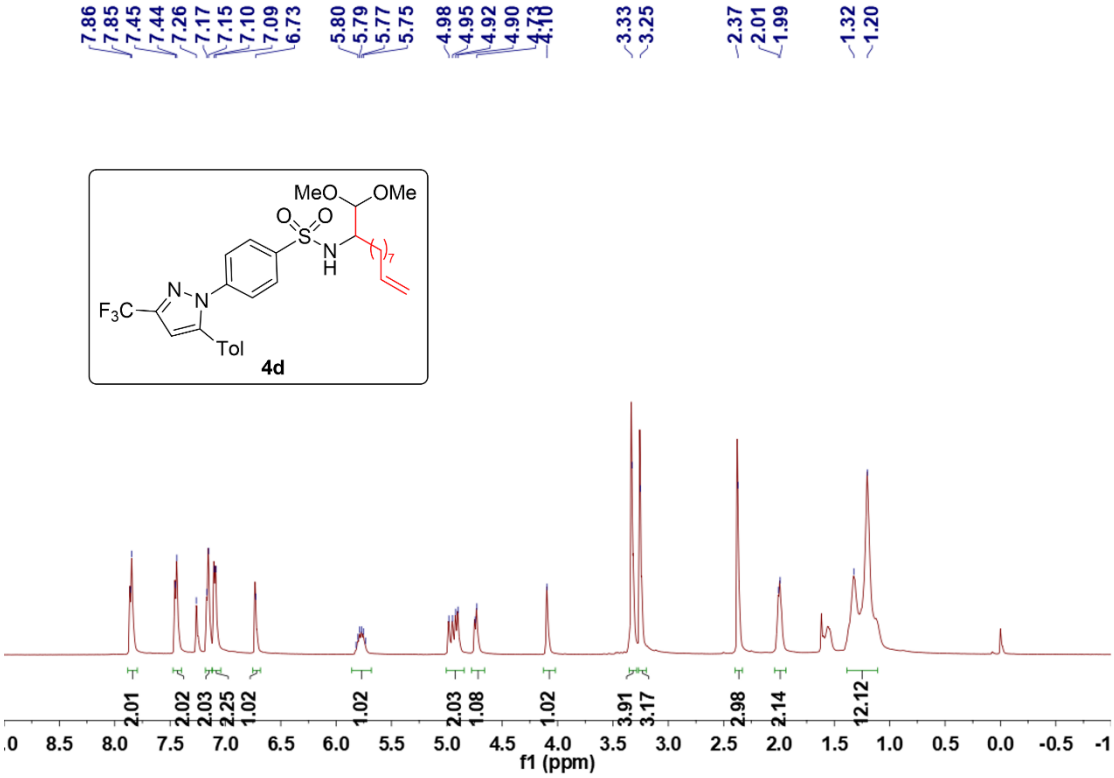
^{13}C NMR (126 MHz, $CDCl_3$) of **4c**



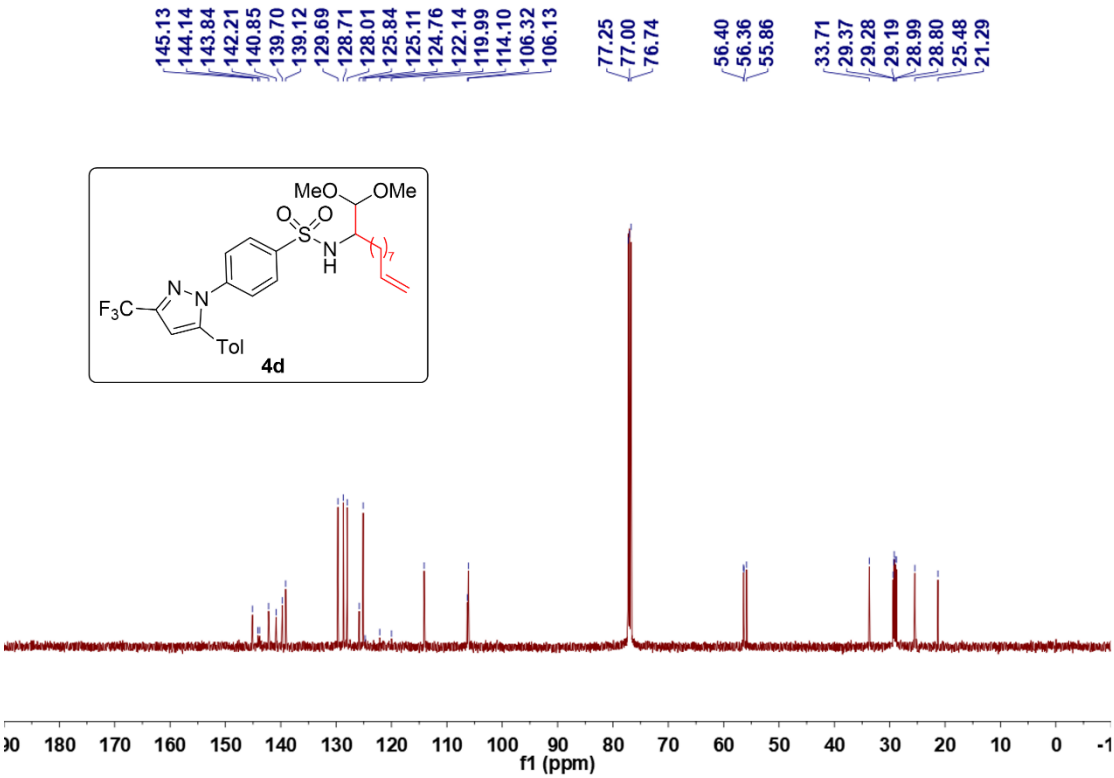
^{19}F NMR (471 MHz, $CDCl_3$) of **4c**



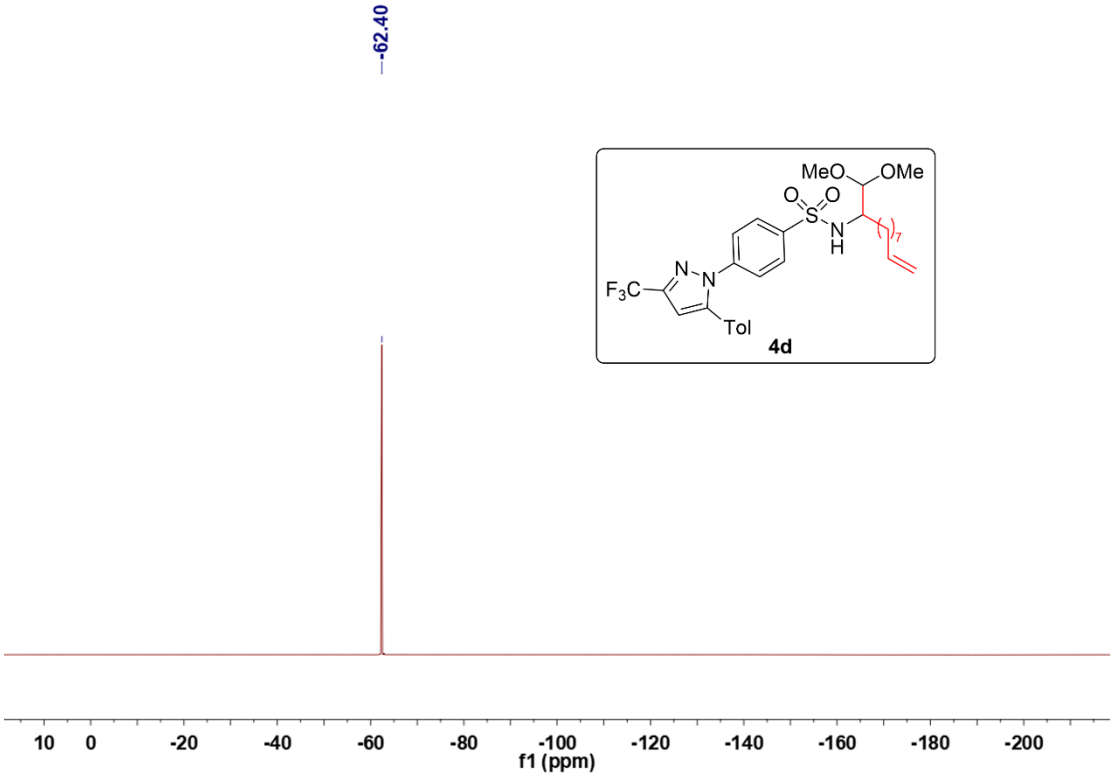
^{1}H NMR (500 MHz, $CDCl_3$) of **4d**



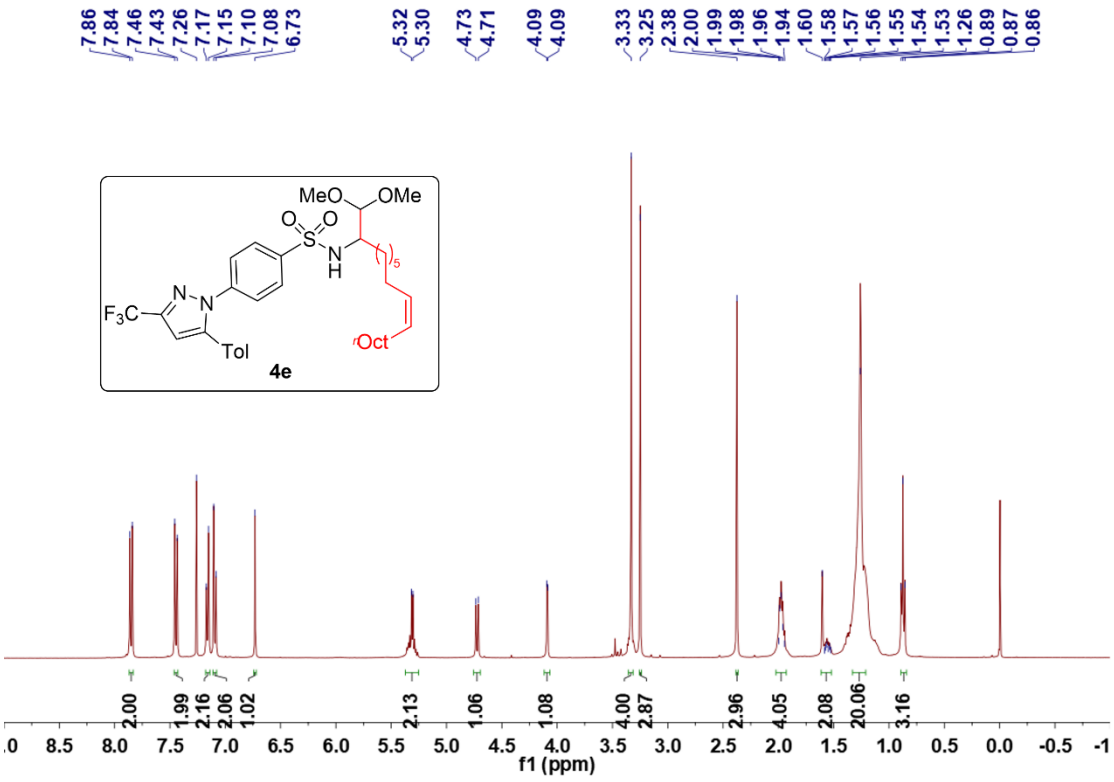
^{13}C NMR (126 MHz, $CDCl_3$) of **4d**



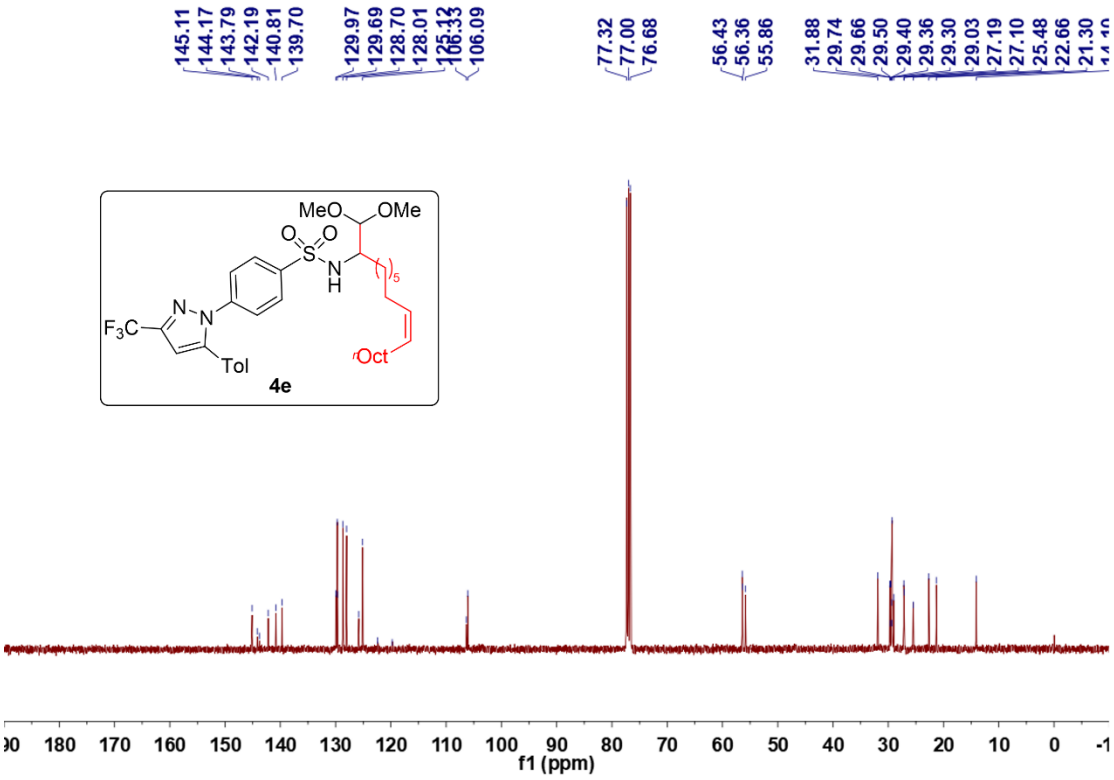
^{19}F NMR (471 MHz, $CDCl_3$) of **4d**



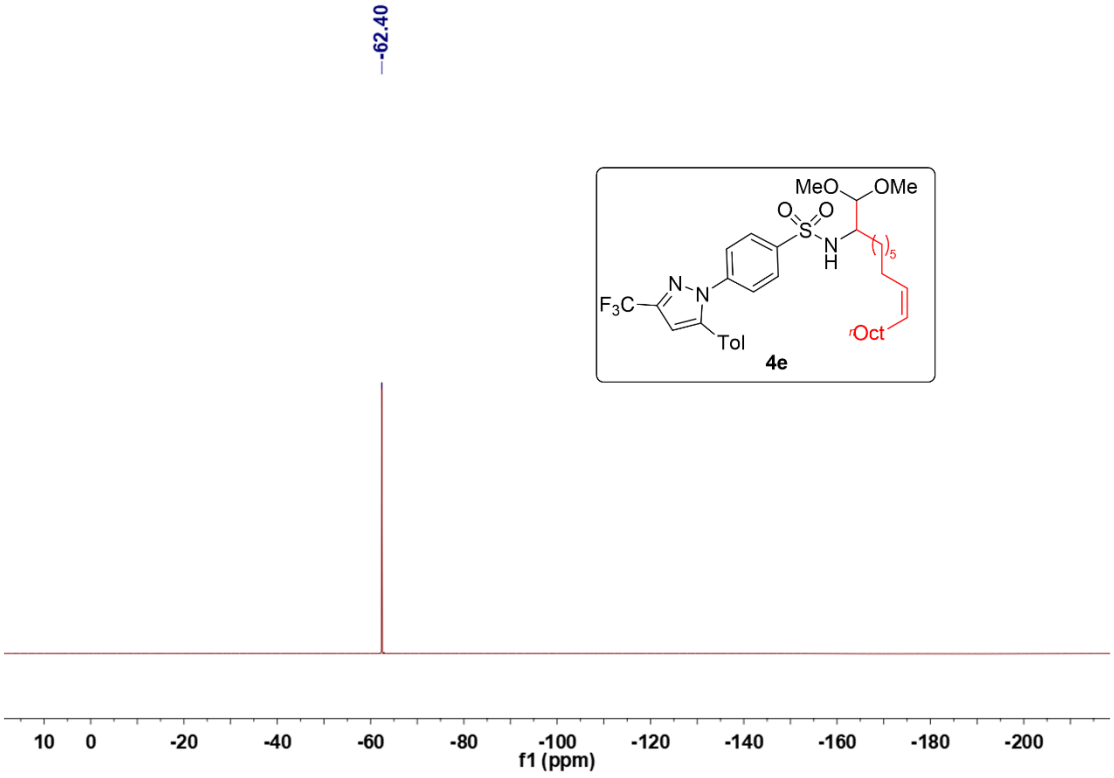
^{1}H NMR (400 MHz, $CDCl_3$) of **4e**



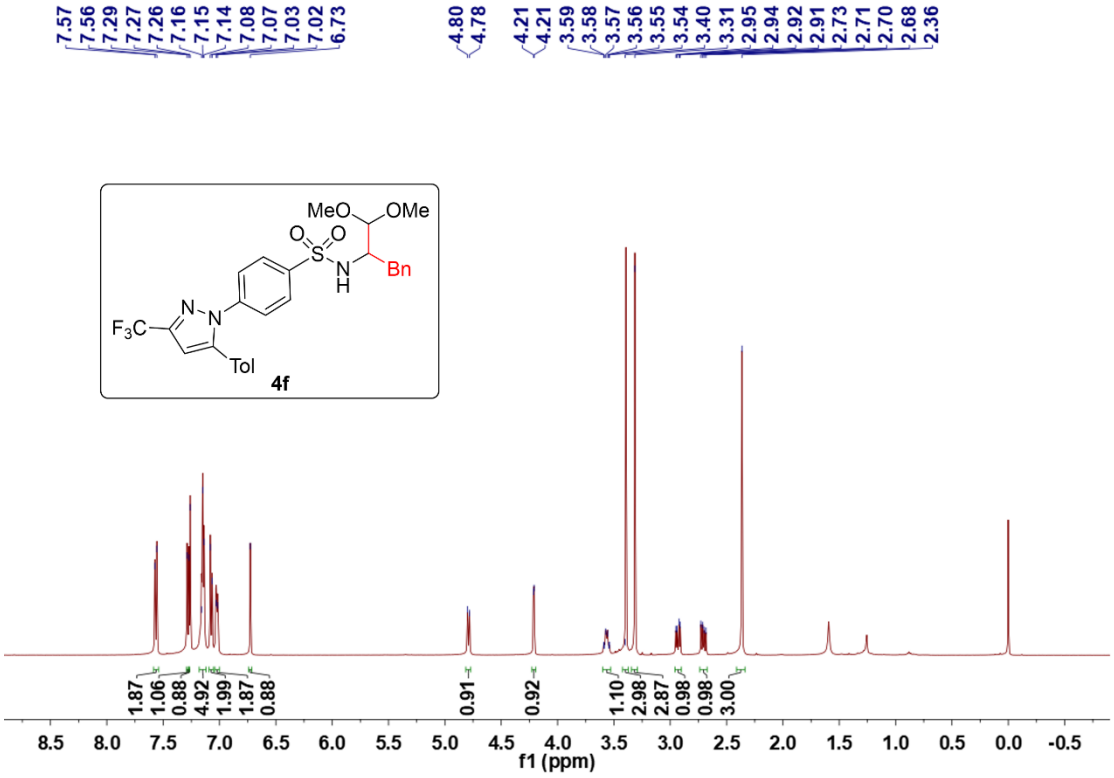
^{13}C NMR (101 MHz, $CDCl_3$) of **4e**



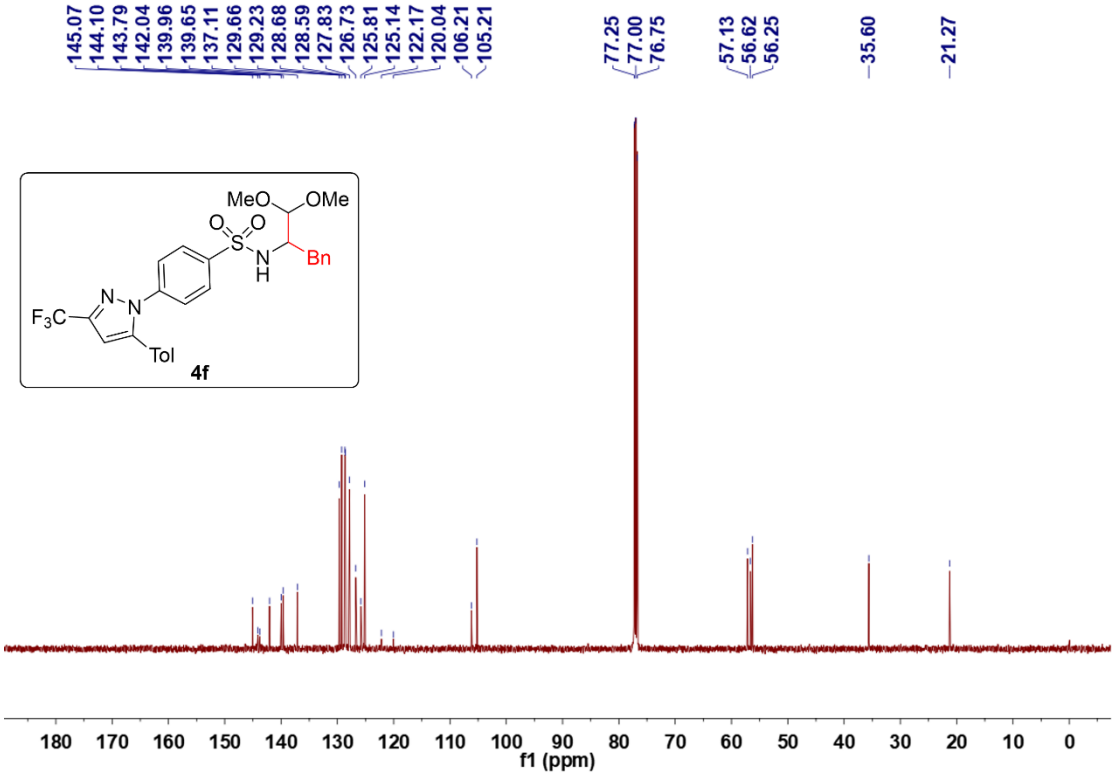
^{19}F NMR (376 MHz, $CDCl_3$) of **4e**



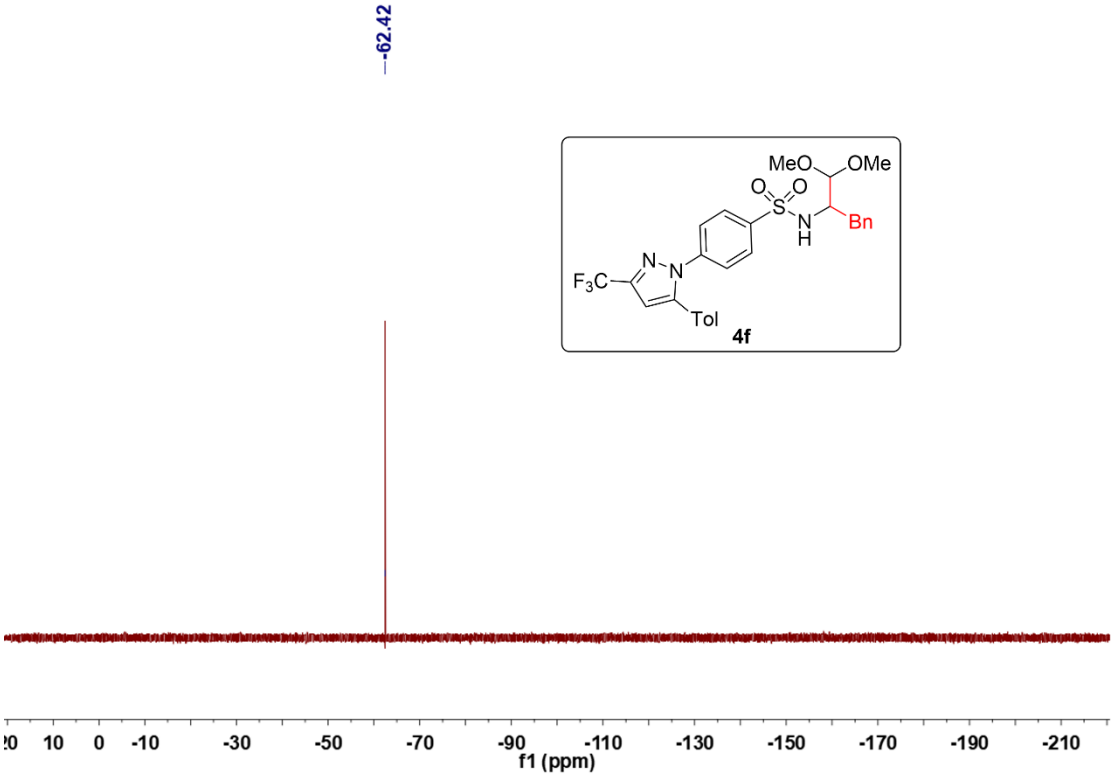
^{1}H NMR (500 MHz, $CDCl_3$) of **4f**



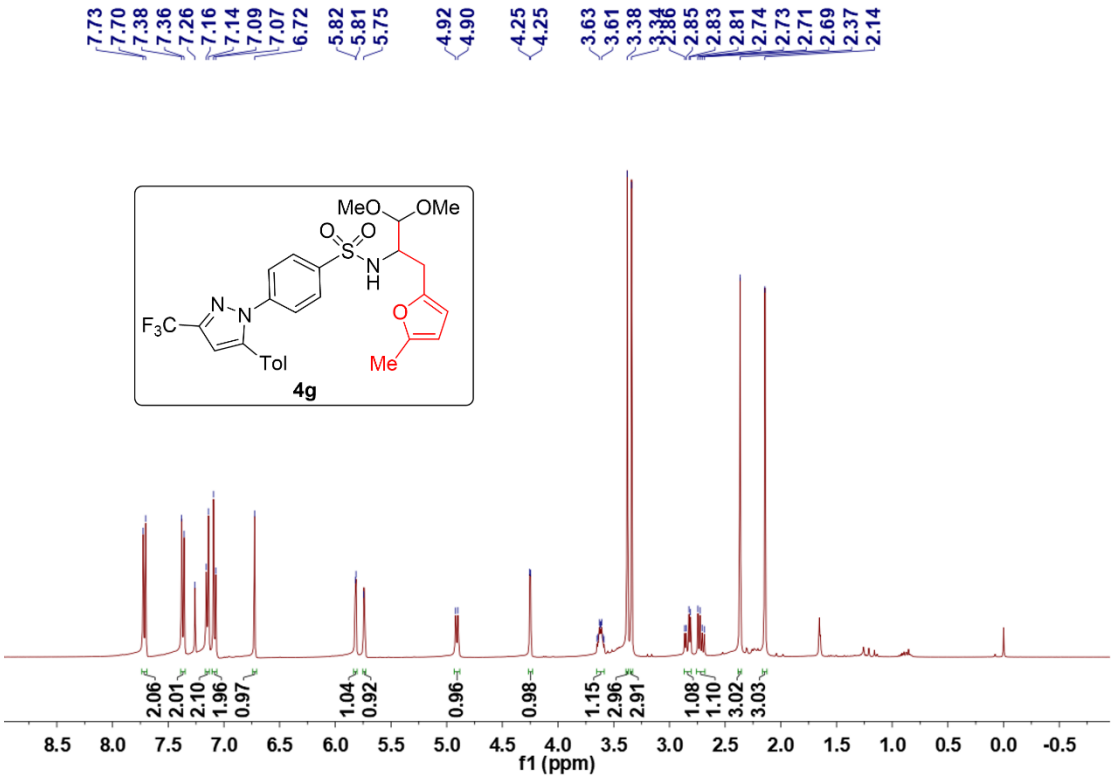
^{13}C NMR (126 MHz, $CDCl_3$) of **4f**



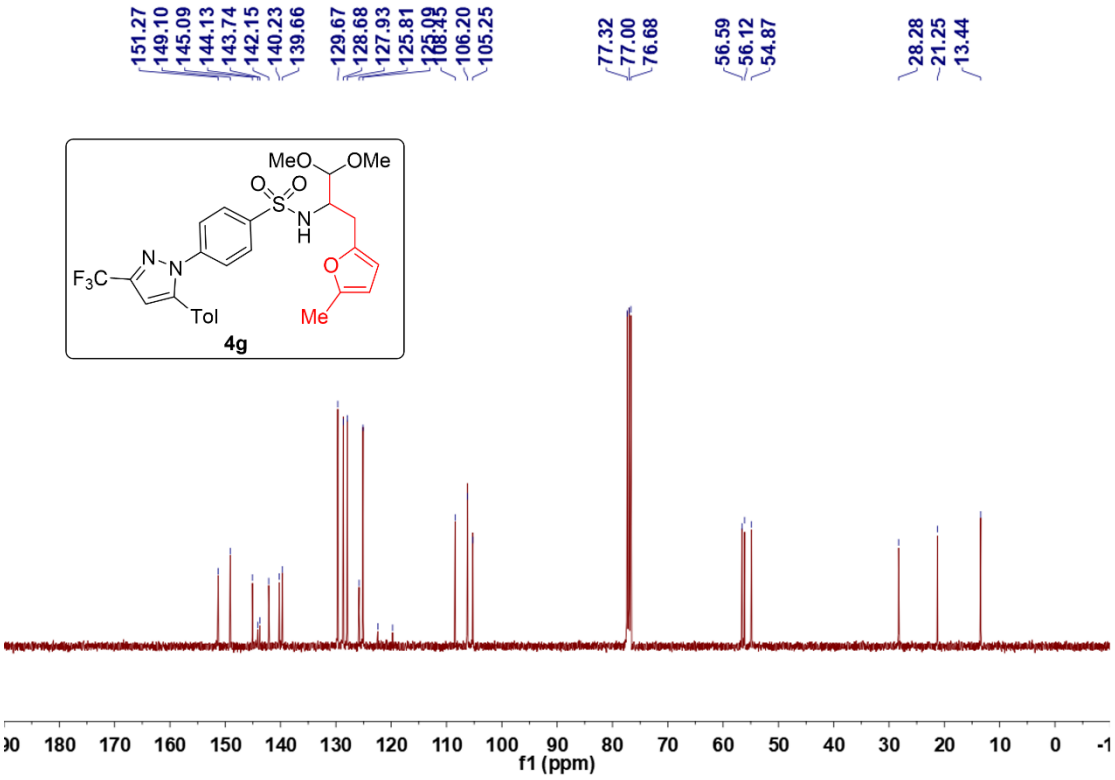
^{19}F NMR (471 MHz, $CDCl_3$) of **4f**



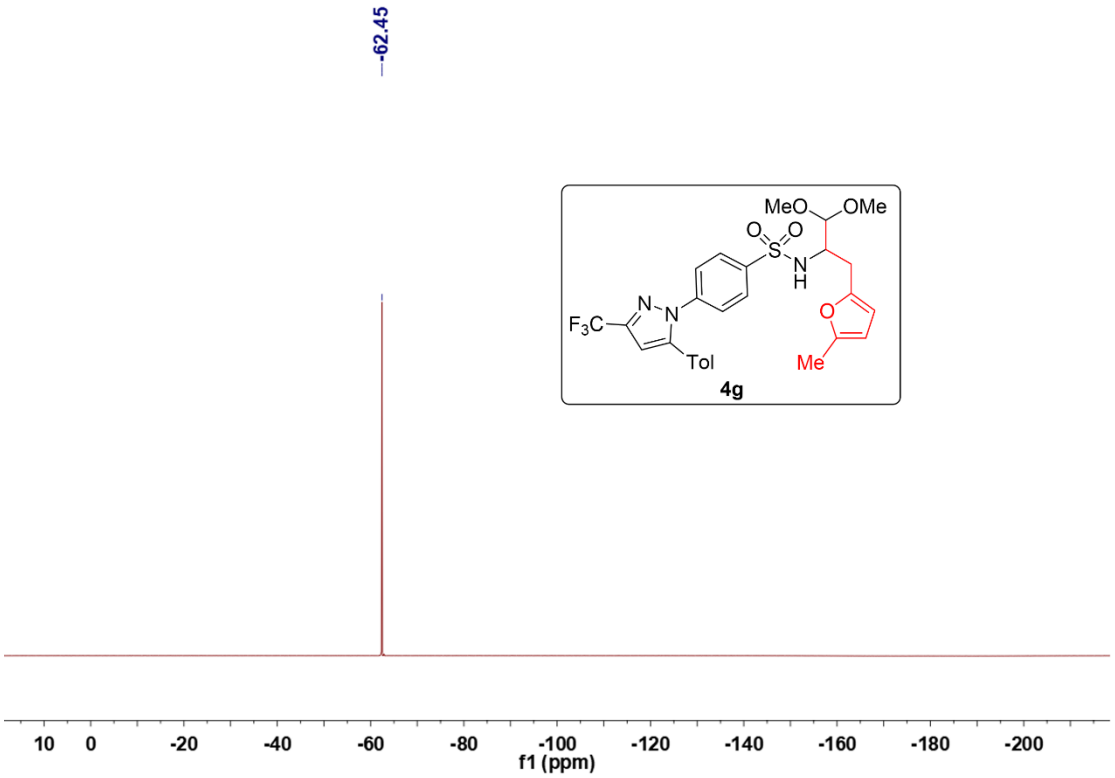
^{1}H NMR (400 MHz, $CDCl_3$) of **4g**



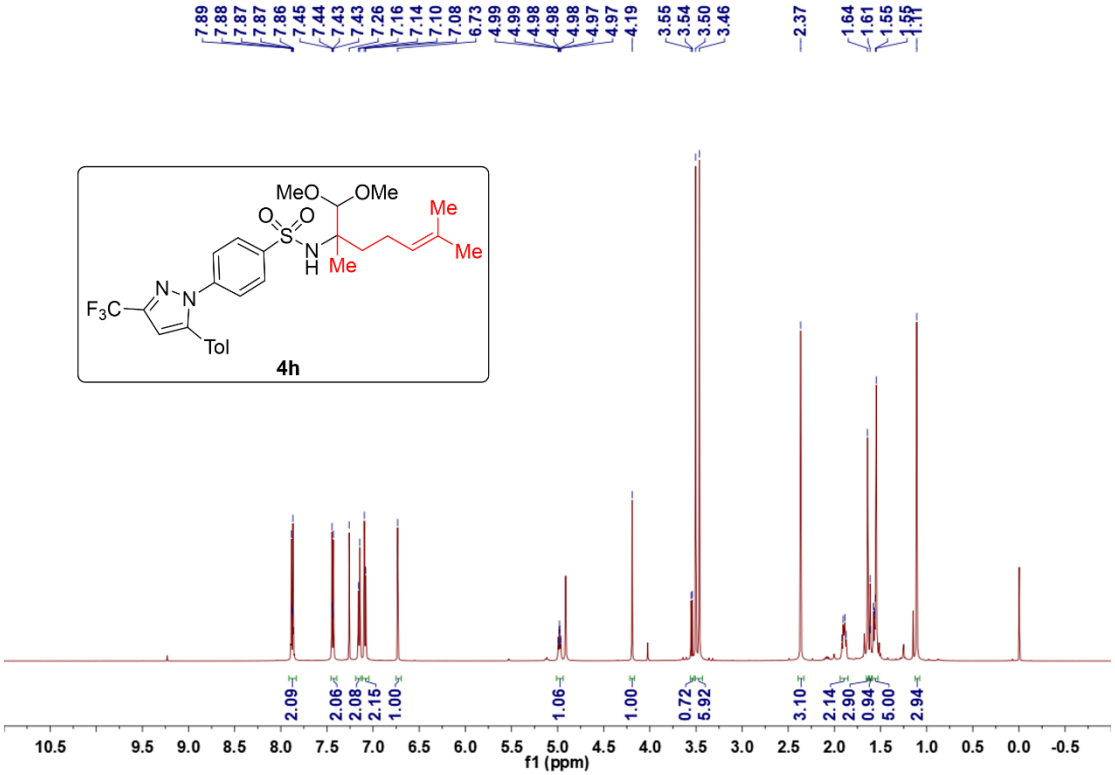
^{13}C NMR (101 MHz, $CDCl_3$) of **4g**



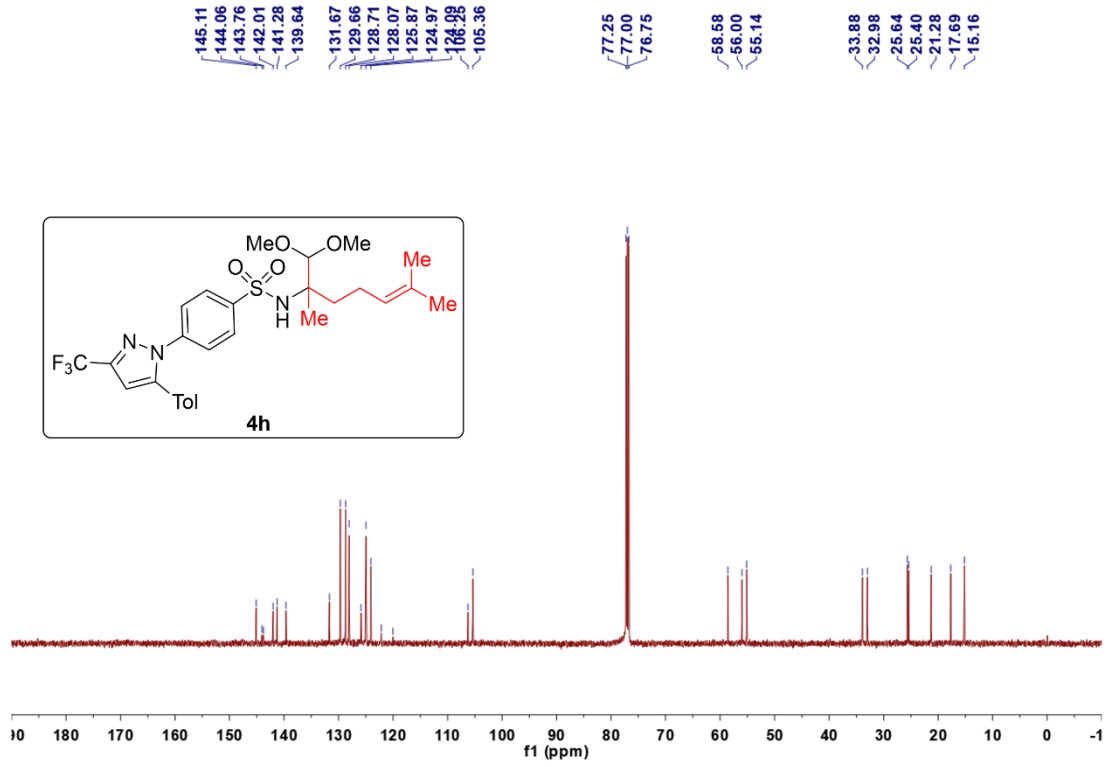
^{19}F NMR (376 MHz, $CDCl_3$) of **4g**



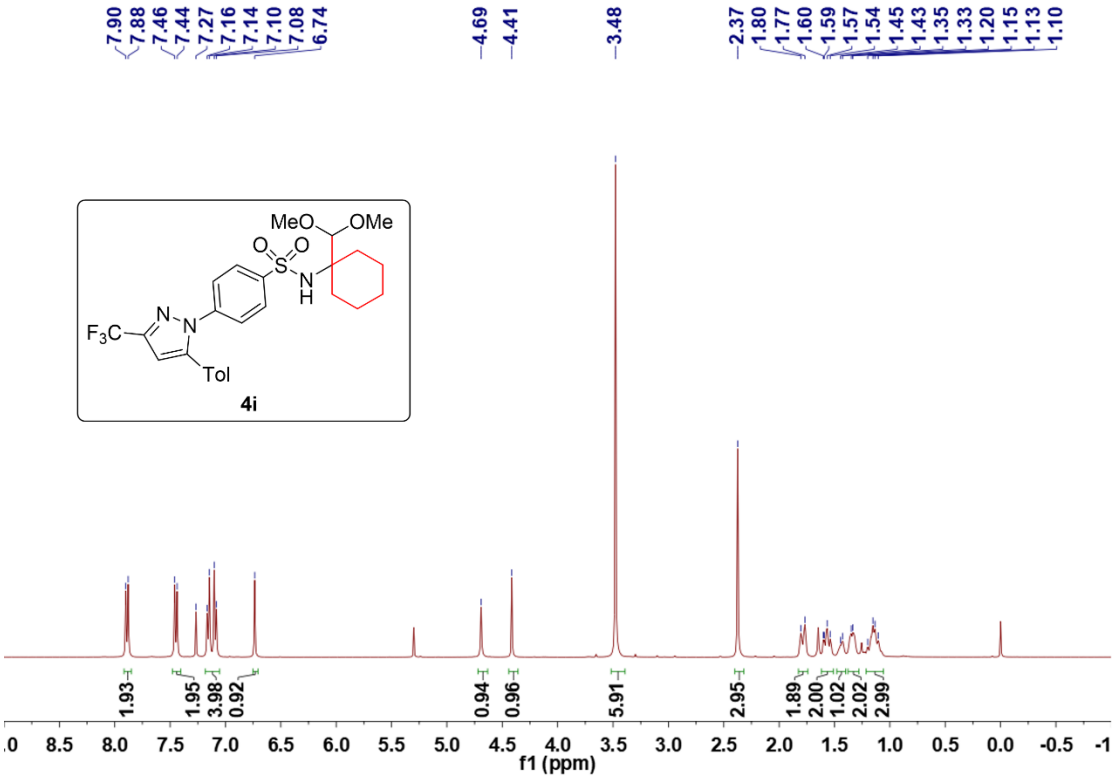
^{1}H NMR (400 MHz, $CDCl_3$) of **4h**



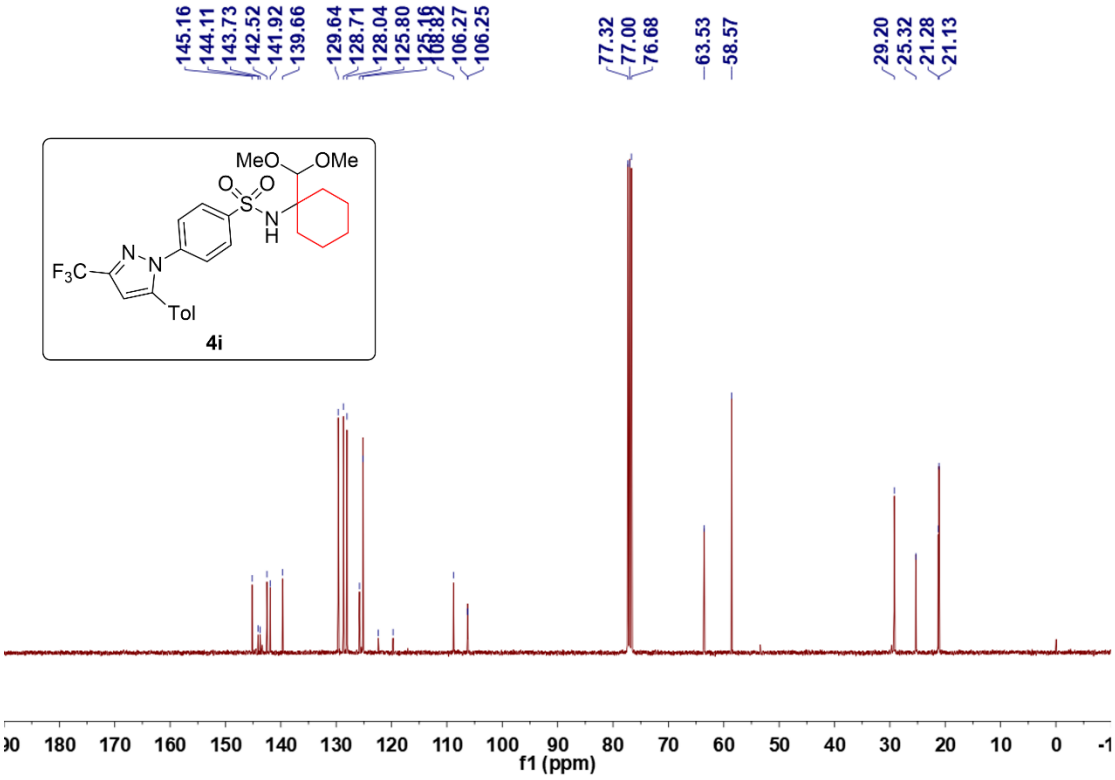
^{13}C NMR (101 MHz, $CDCl_3$) of **4h**



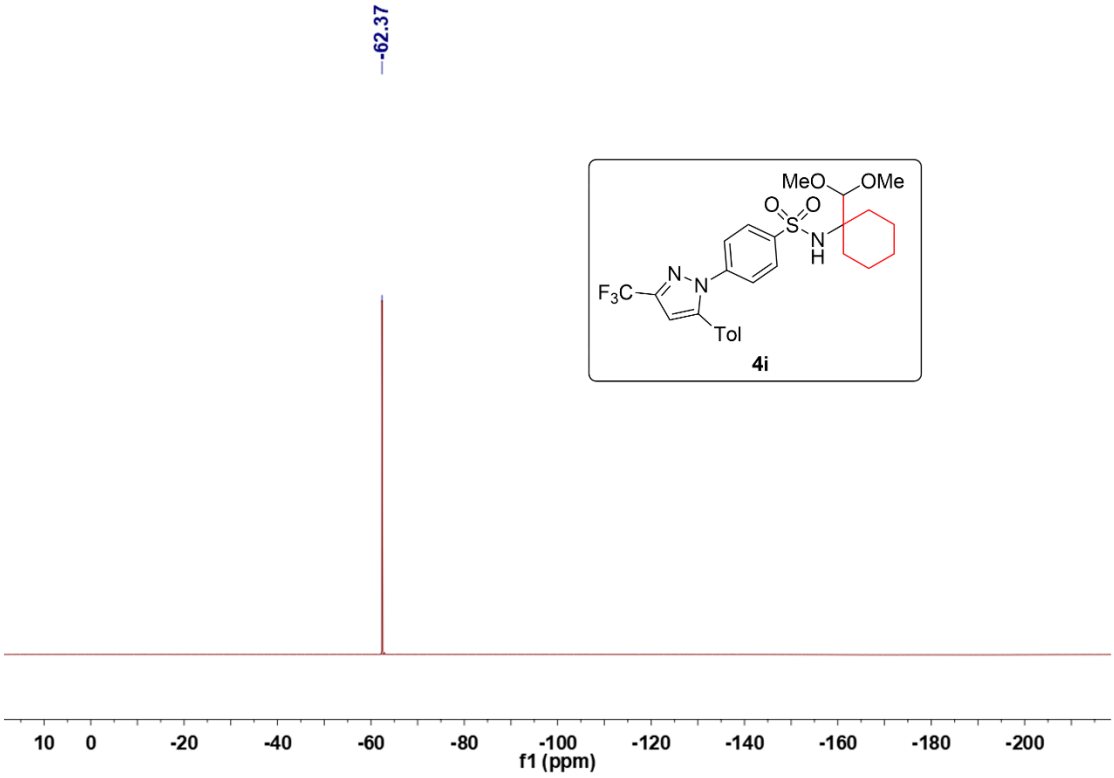
^{1}H NMR (400 MHz, $CDCl_3$) of **4i**



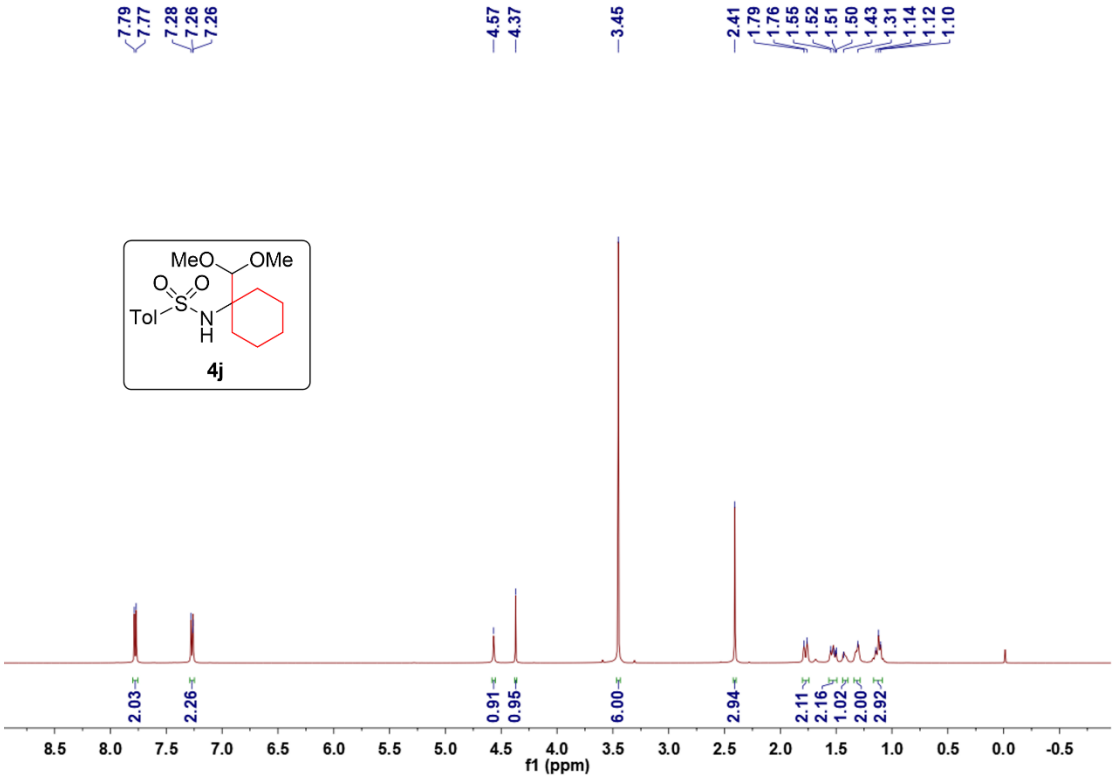
^{13}C NMR (101 MHz, $CDCl_3$) of **4i**



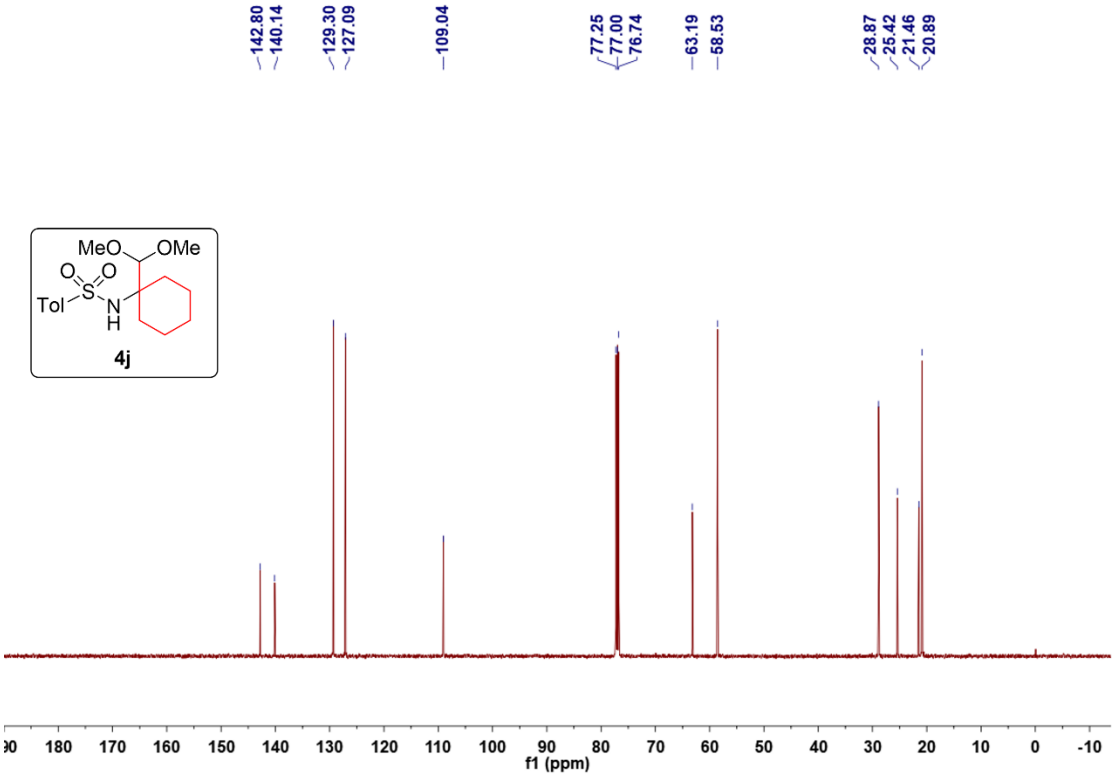
^{19}F NMR (376 MHz, $CDCl_3$) of **4i**



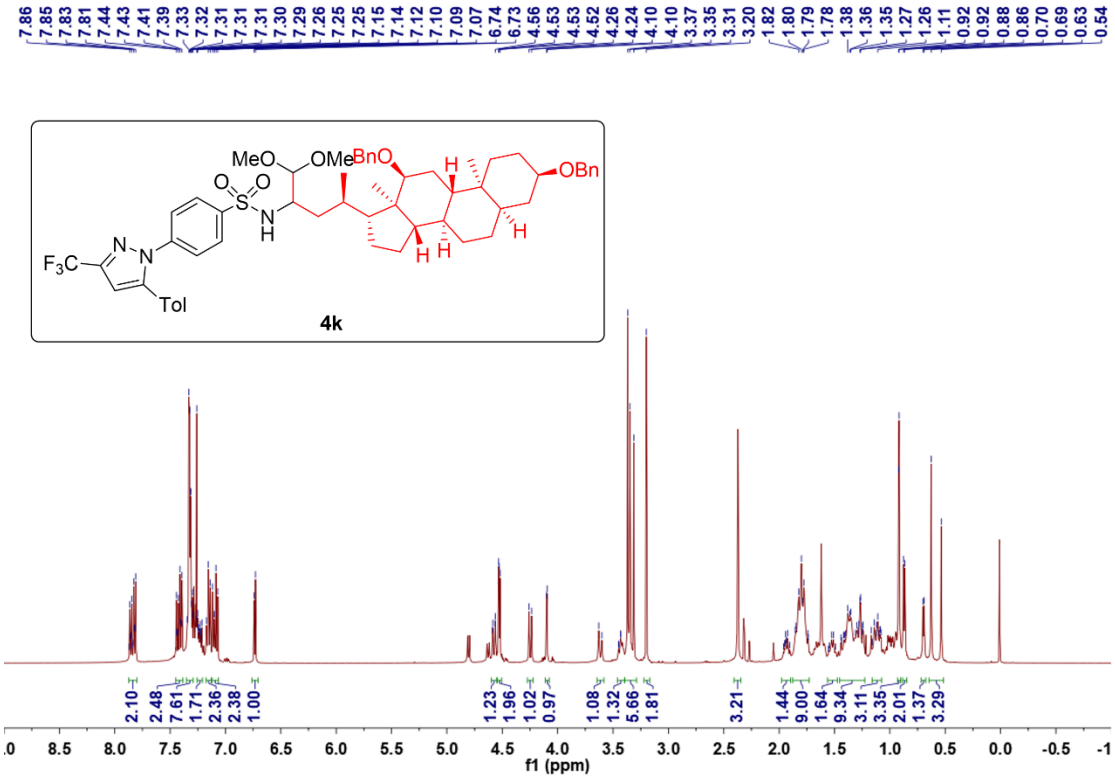
^{1}H NMR (500 MHz, $CDCl_3$) of **4j**



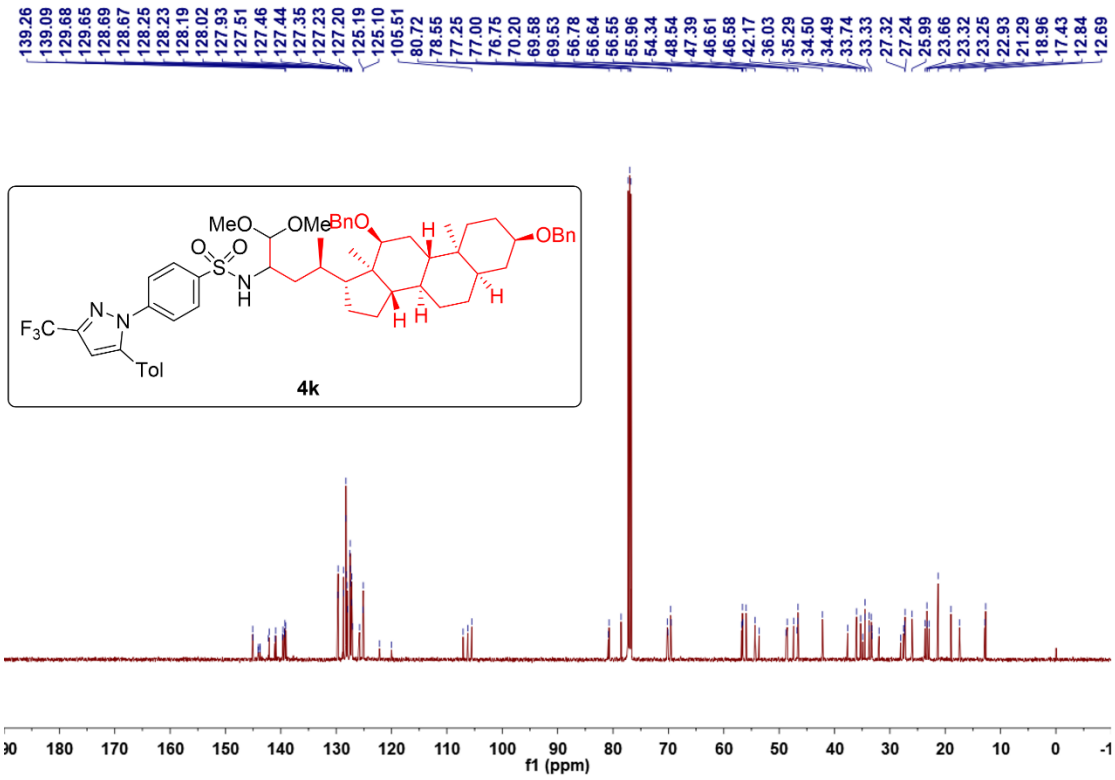
^{13}C NMR (126 MHz, $CDCl_3$) of **4j**



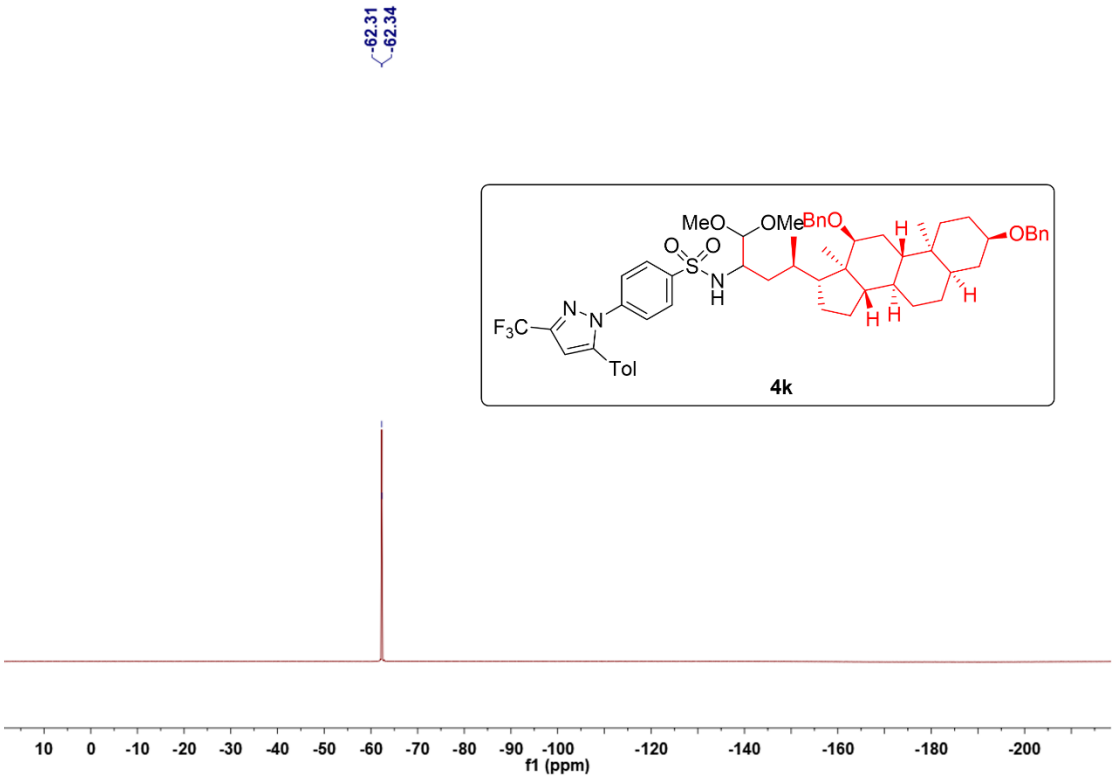
^{1}H NMR (500 MHz, $CDCl_3$) of **4k**



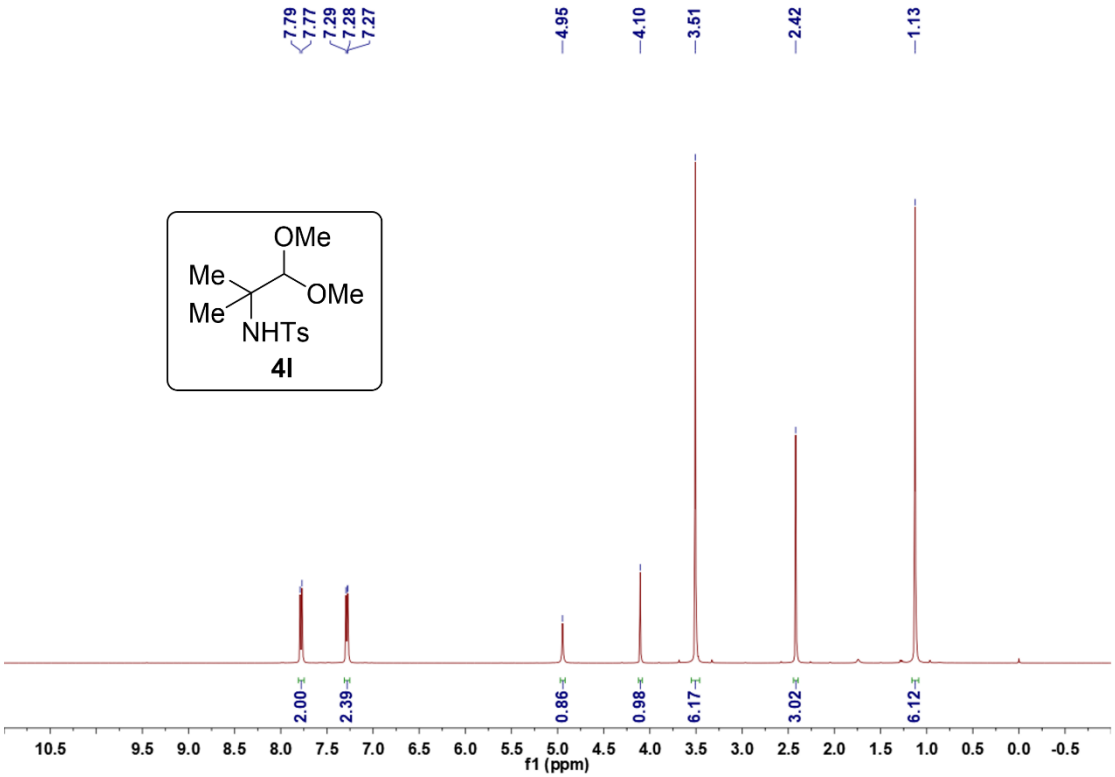
^{13}C NMR (126 MHz, $CDCl_3$) of **4k**



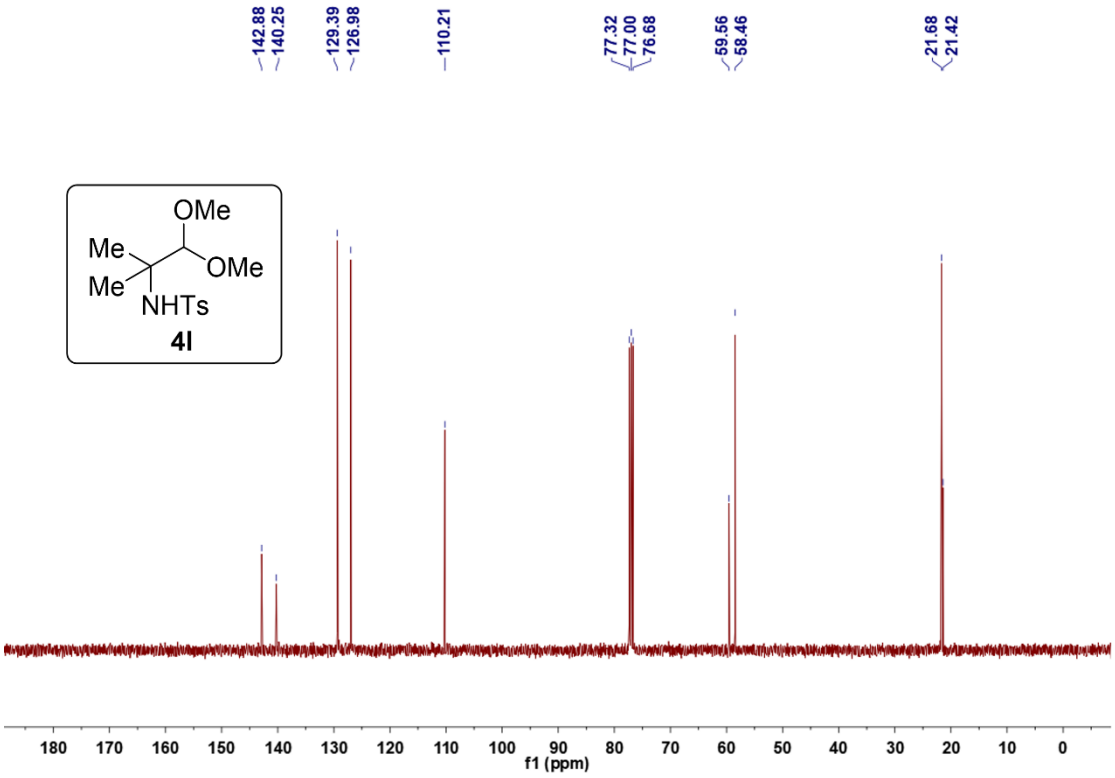
^{19}F NMR (471 MHz, $CDCl_3$) of **4k**



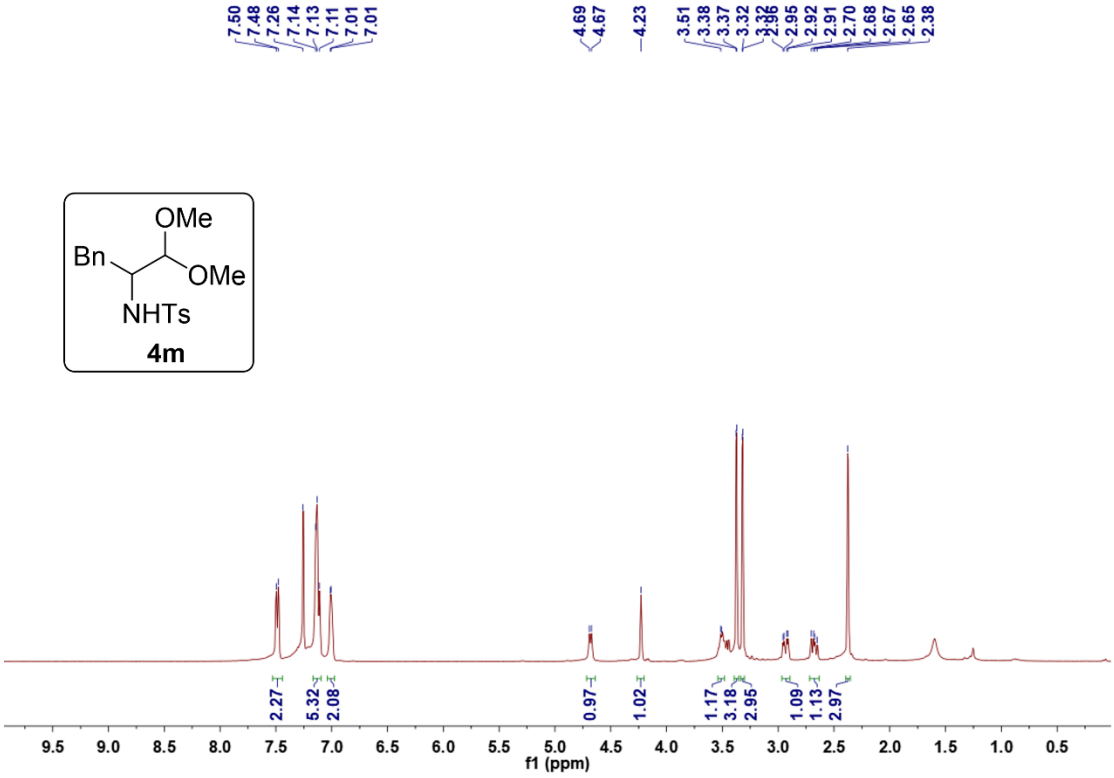
^{1}H NMR (400 MHz, $CDCl_3$) of **4l**



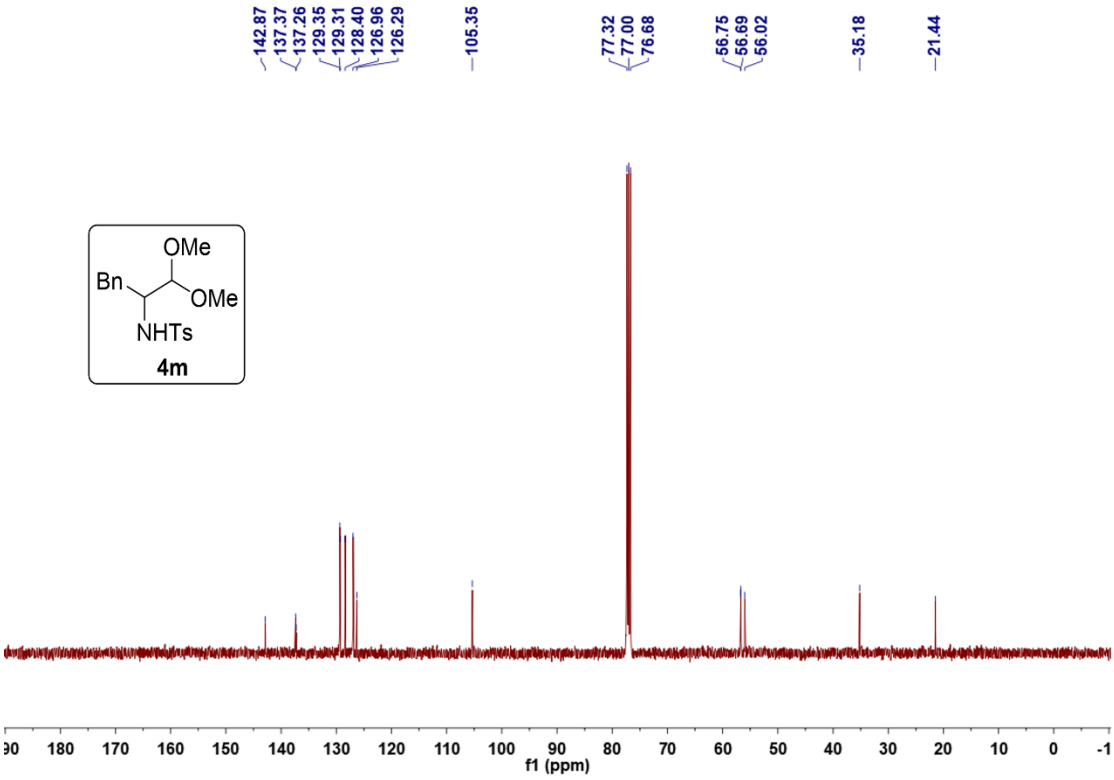
^{13}C NMR (101 MHz, $CDCl_3$) of **4l**



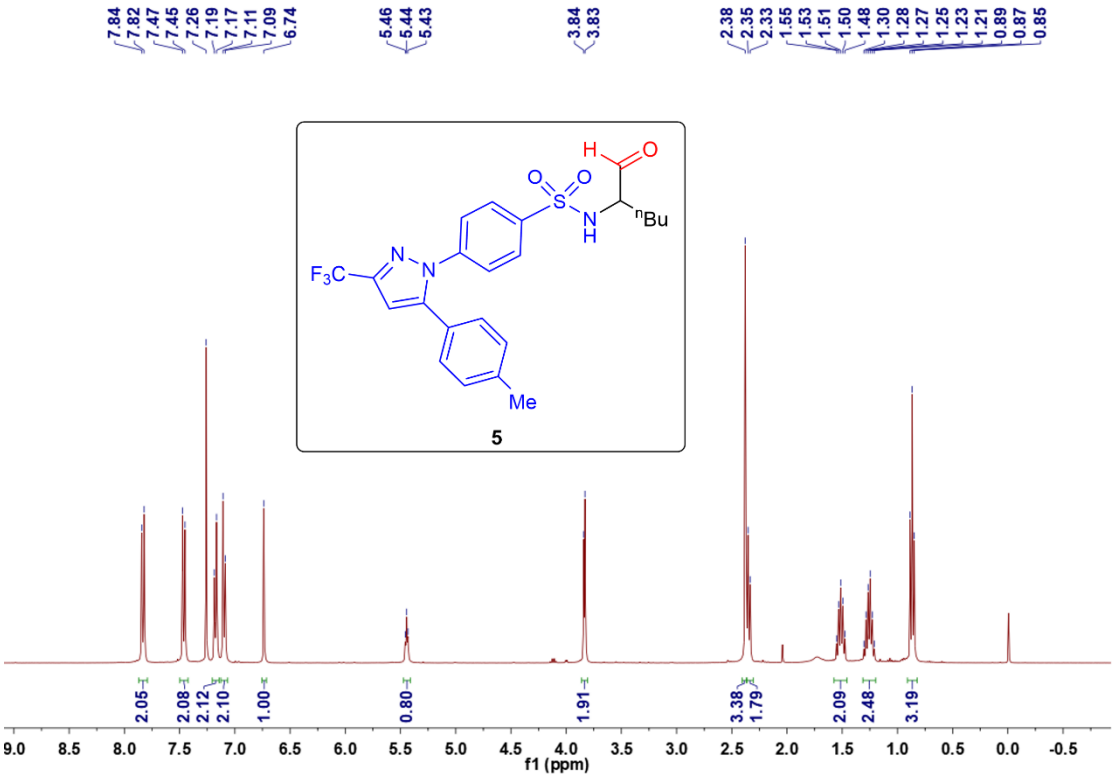
^{1}H NMR (400 MHz, $CDCl_3$) of **4m**



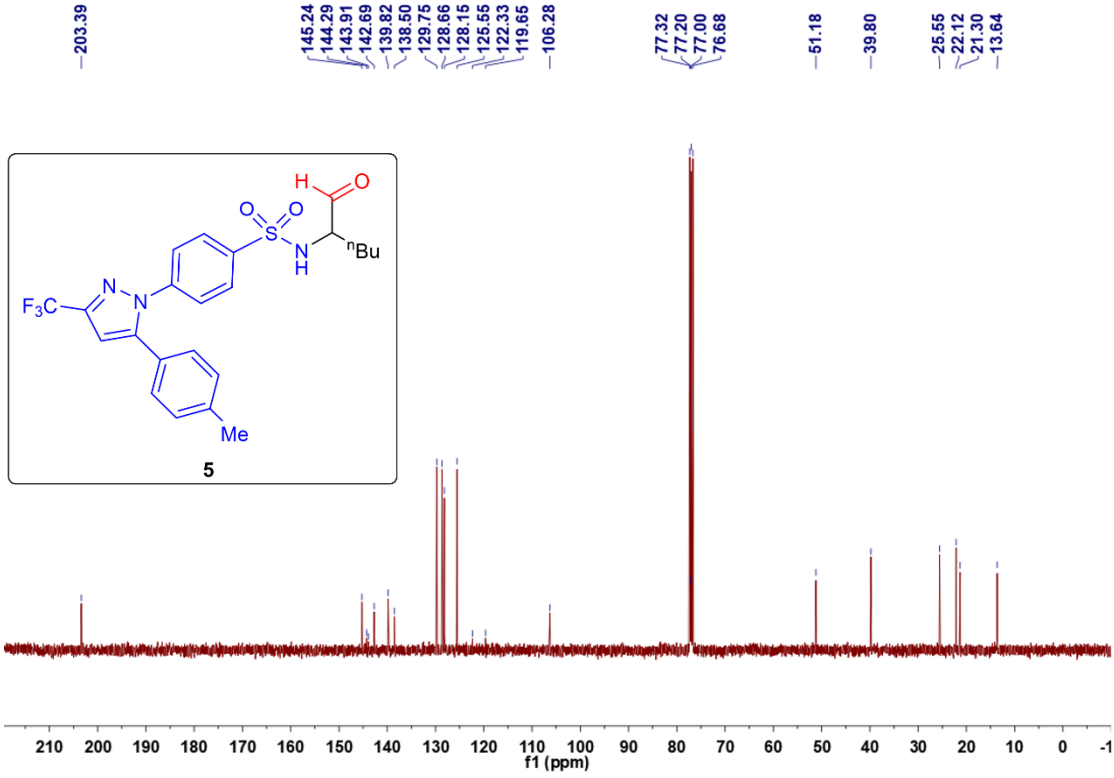
^{13}C NMR (101 MHz, $CDCl_3$) of **4m**



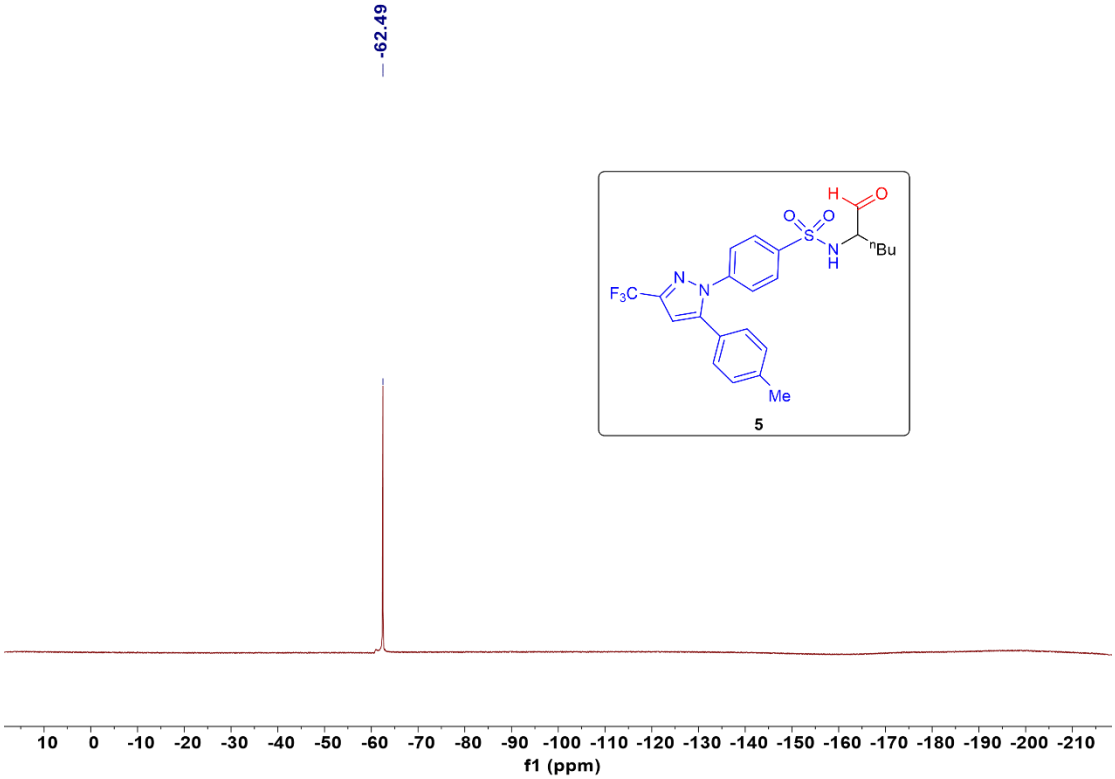
^{1}H NMR (400 MHz, $CDCl_3$) of **5**



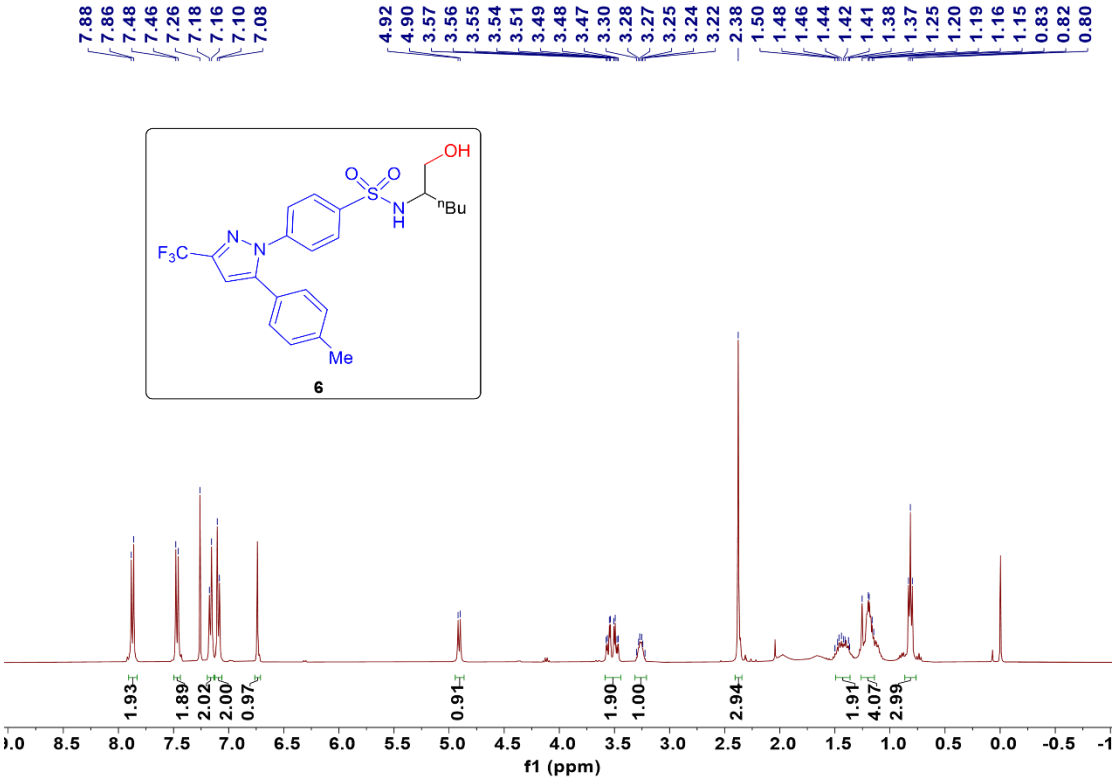
^{13}C NMR (101 MHz, $CDCl_3$) of **5**



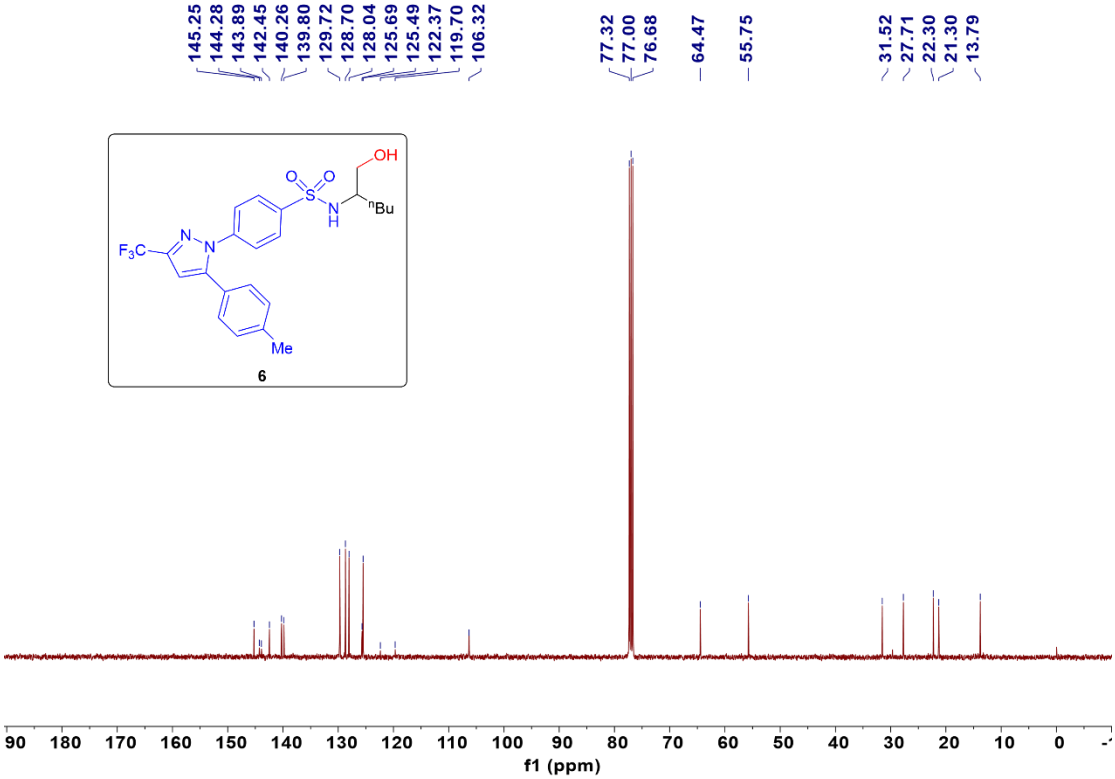
^{19}F NMR (376 MHz, $CDCl_3$) of **5**



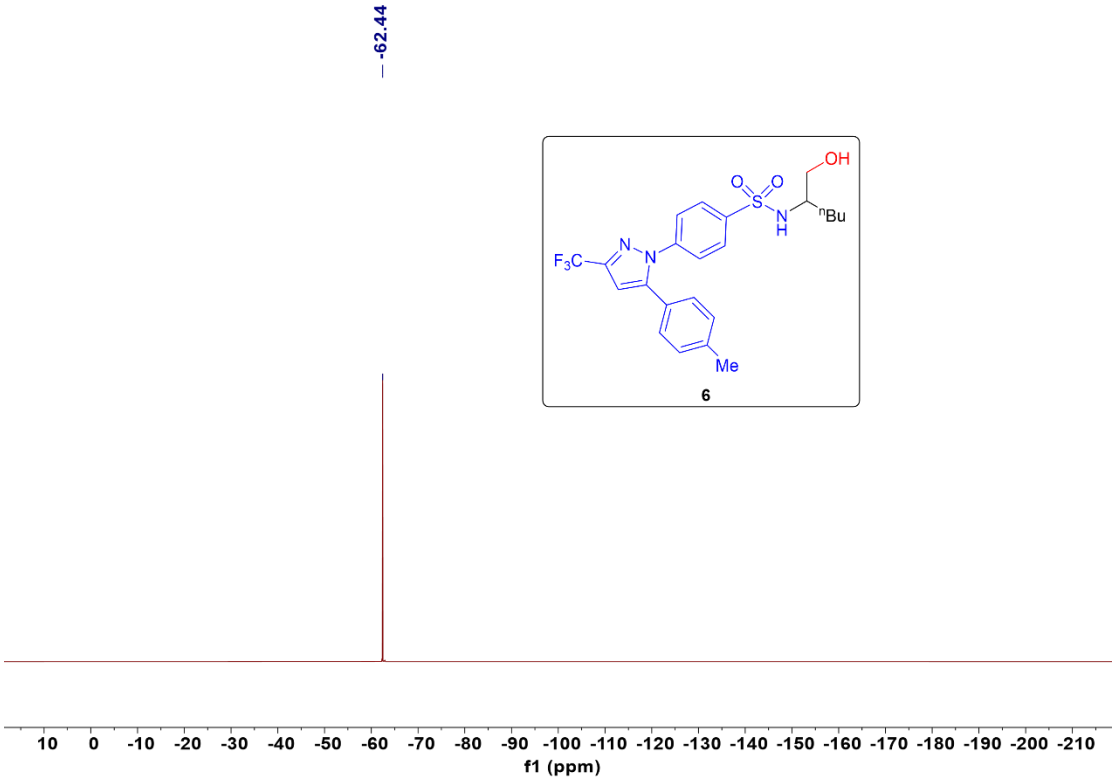
^{1}H NMR (400 MHz, $CDCl_3$) of **6**



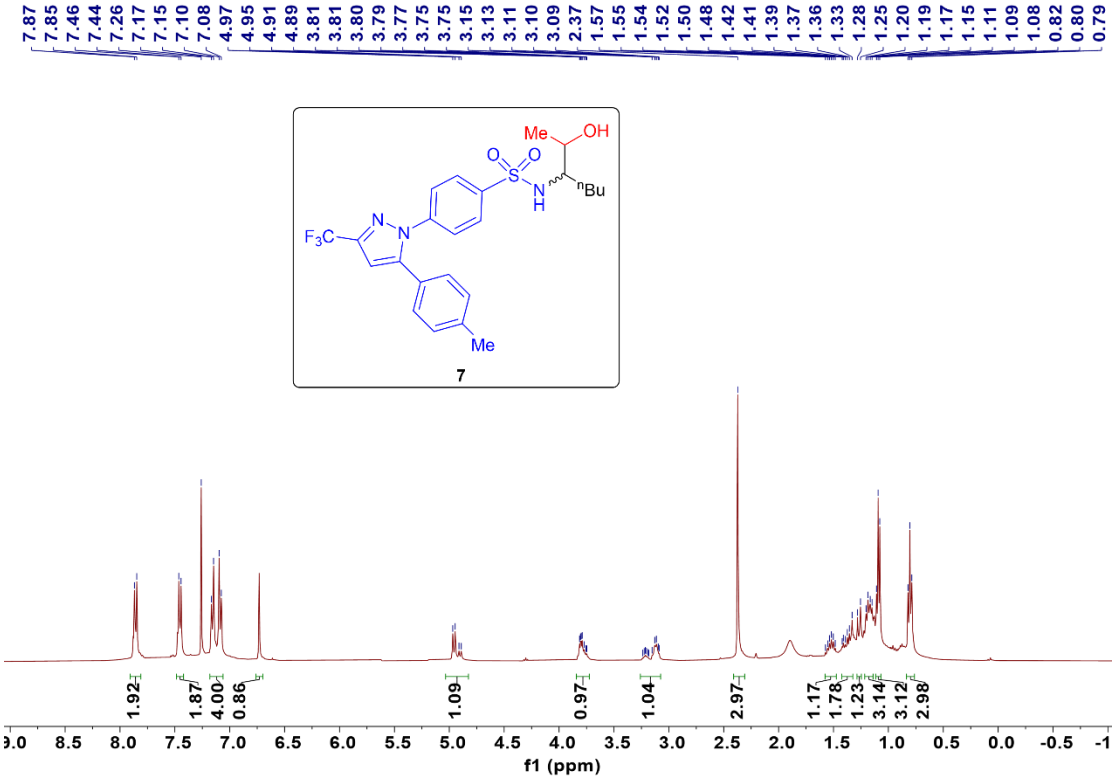
^{13}C NMR (101 MHz, $CDCl_3$) of **6**



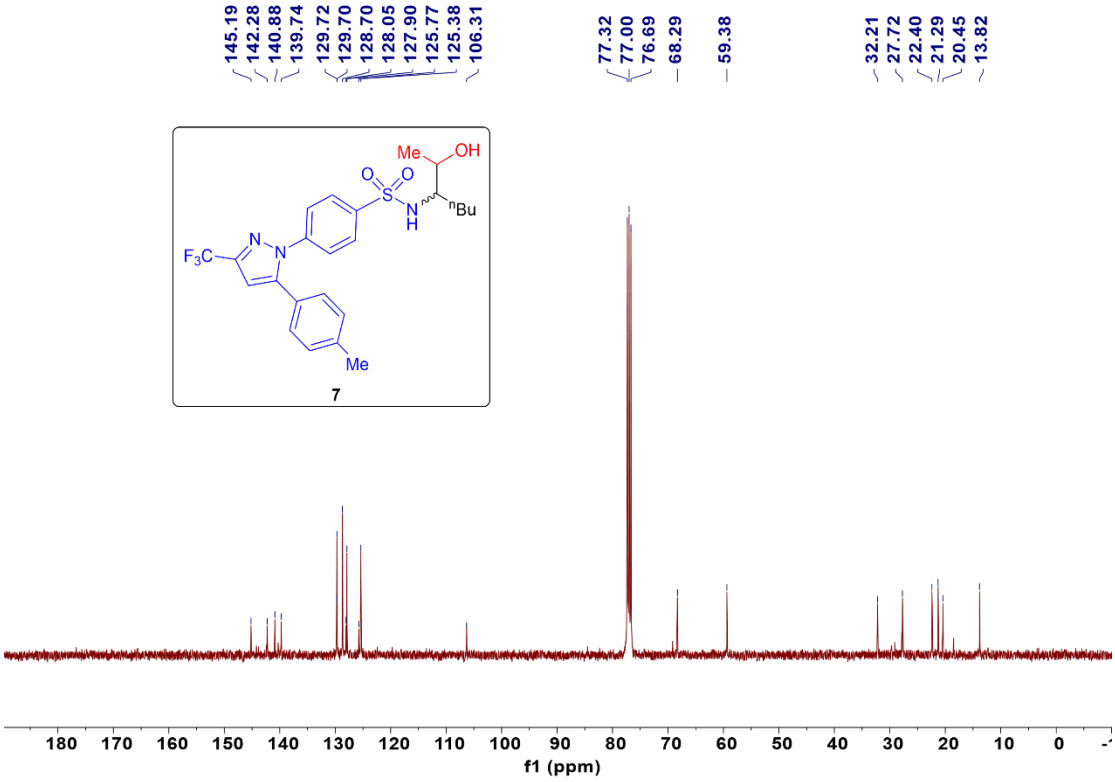
^{19}F NMR (376 MHz, $CDCl_3$) of **6**



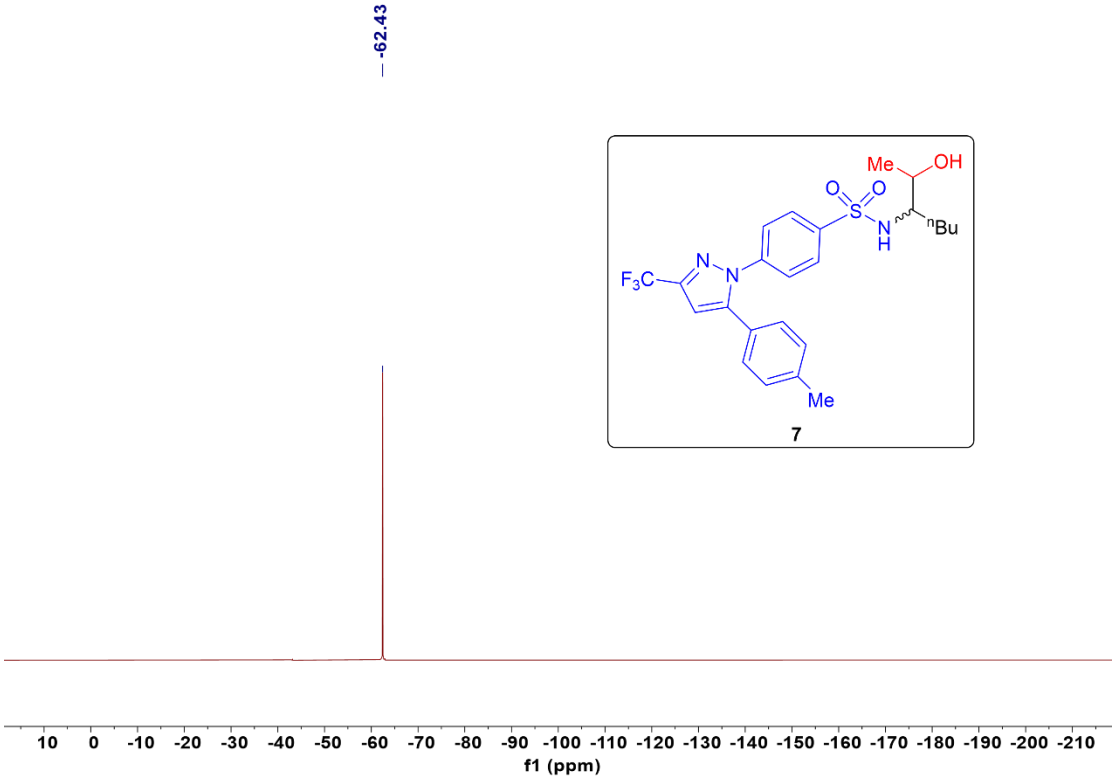
^{1}H NMR (400 MHz, $CDCl_3$) of **7**



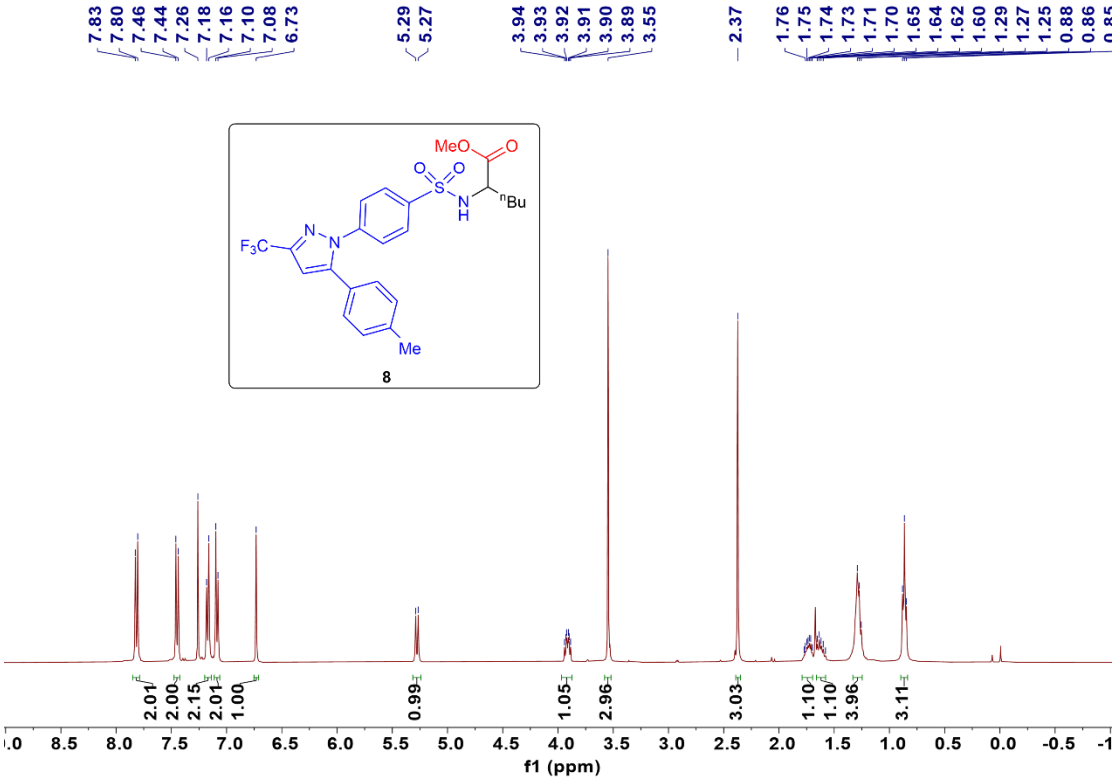
^{13}C NMR (101 MHz, $CDCl_3$) of **7**



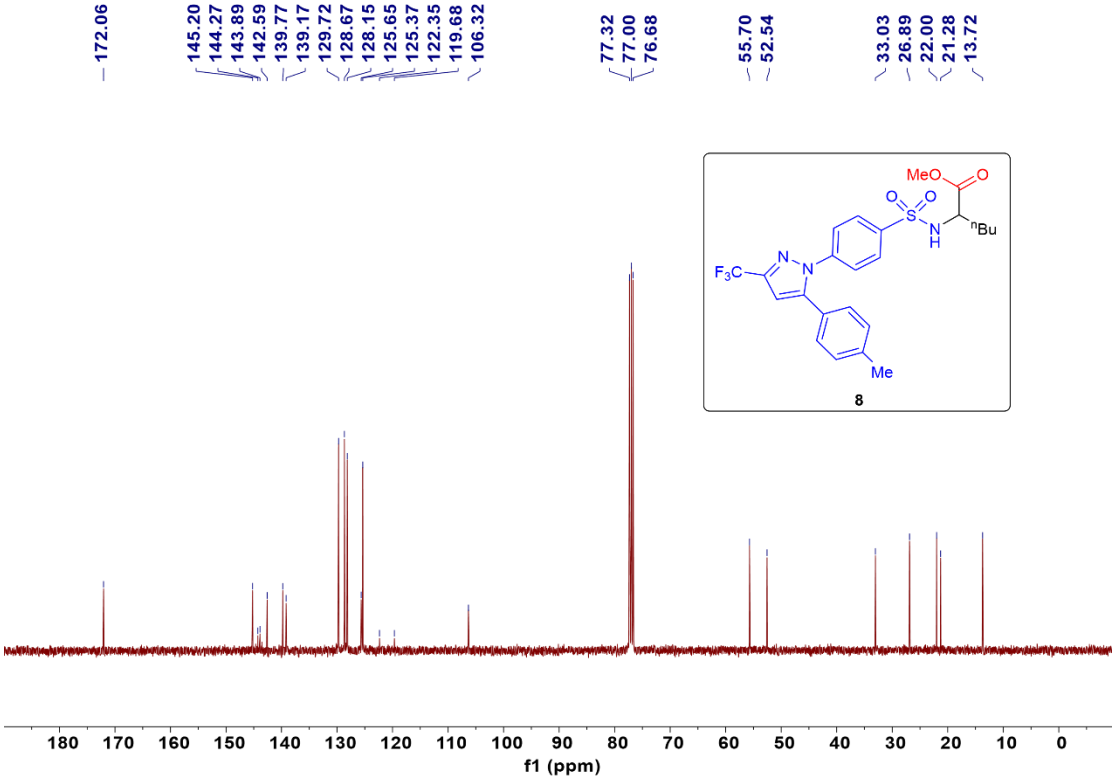
^{19}F NMR (376 MHz, $CDCl_3$) of **7**



^{1}H NMR (400 MHz, $CDCl_3$) of **8**



^{13}C NMR (101 MHz, $CDCl_3$) of **8**



^{19}F NMR (376 MHz, $CDCl_3$) of **8**