Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Iodine-Catalyzed Expeditious Synthesis of Sulfonamides from Sulfonyl Hydrazides and Amines

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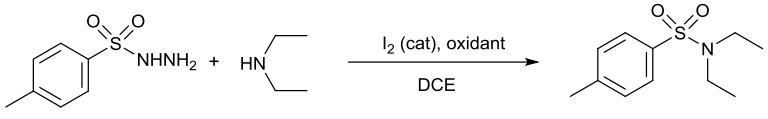
I. Reaction Optimization

Table S1. Effect of Oxidants and Temperature [a]

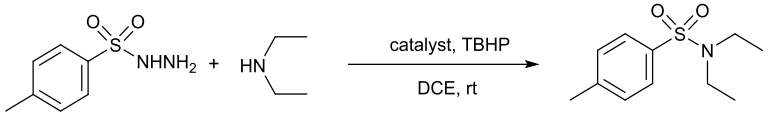


1a 2a 3a

entry	oxidant	equiv.	temperature (°C)	%yield[b]
1	-	-	rt	0
2	H_2O_2	3	rt	0
3	DTBP	3	rt	0
4	**TBHP**	**3**	**rt**	**85**
5	TBHP	1	rt	44
6	TBHP	2	rt	74
7	TBHP	4	rt	85
8	TBHP	3	40	80
9	TBHP	3	50	80
10	TBHP	3	60	80
11	TBHP	3	70	79
12	TBHP	3	80	76

[a] Conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), I_2 (0.1 mmol), DCE (4 mL), 1 h. [b] GC yield.

Table S2. Effect of Catalysts and Additives [a]

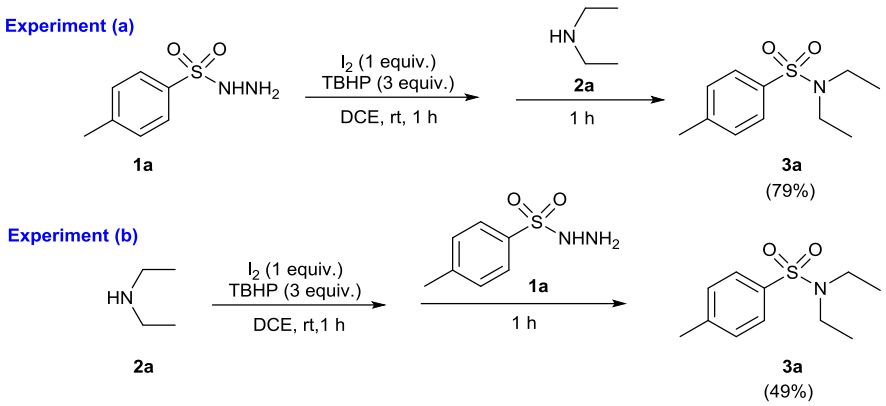


1a 2a 3a

entry	Catalyst (equiv.)	Additive (equiv.)	%yield[b]
1	CuI (0.2)	-	27
2	CuCl (0.2)	-	22
3	$Cu(OAc)_2$ (0.2)	-	11
4	$FeCl_3$ (0.2)	-	trace
5	NCS (0.2)	-	11
6	NBS (0.2)	-	11
7	NIS (0.2)	-	67
8	LiI (0.2)	-	58
9	NaI (0.2)	-	39
10	KI (0.2)	-	36
11	NH_4I (0.2)	-	64
12	TBAI (0.2)	-	45
13	HI (0.2)	-	69
14	**I_2 (0.2)**	**-**	**85**
15	I_2 (0.2)	KI (1)	80
16	I_2 (0.2)	Na_2CO_3 (1)	79
17	I_2 (0.2)	CH_3COOH (1)	61

[a] Conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), TBHP in decane (1.5 mmol), DCE (4 mL), rt, 1 h. [b] GC yield.

II. Miscellaneous Experiments

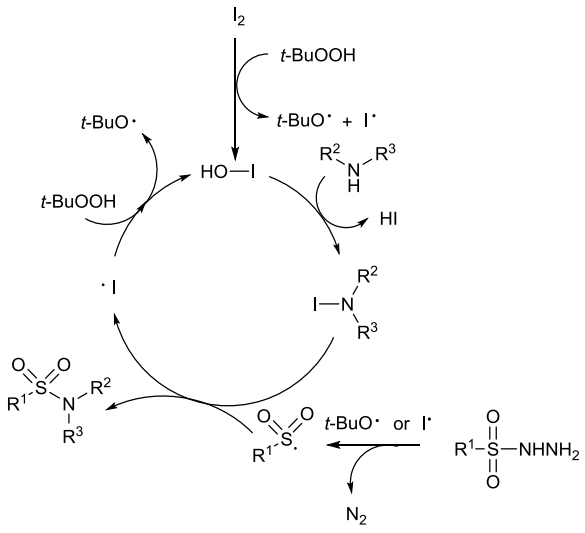


Note: when applying I_2 (20%), experiment (a) provided product **3a** in 78% and experiment (b) provided product **3a** in 45%

According to the above results, sulfonamide **3a** was obtained from experiments **(a)** and **(b)** in 79% and 49% yields, respectively. These outcomes suggested that sulfonyl hydrazide and amine might be able to react with I_2/TBHP and result in a sulfonamide formation. Although sulfonyl hydrazide has a greater tendency to react with I_2/TBHP under the given conditions, other possibilities cannot be ruled out.

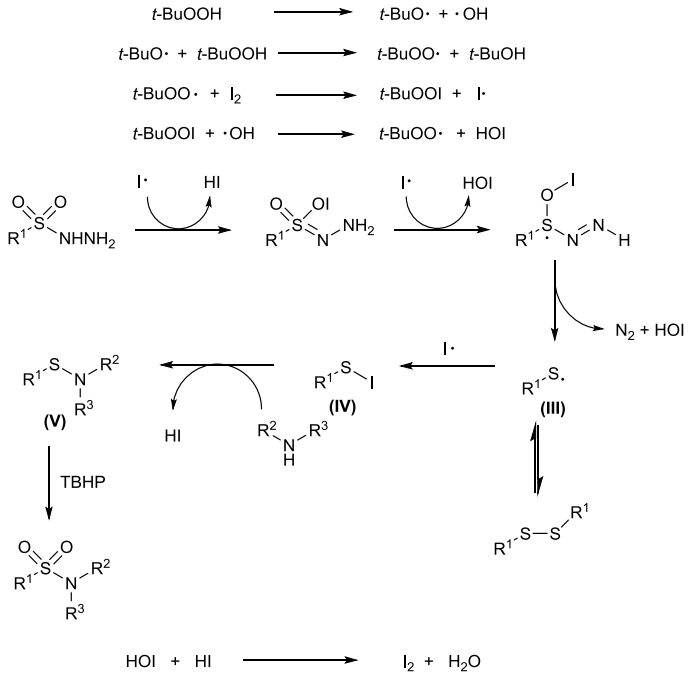
Thus, based on the relevant literature, other possible reaction mechanisms are also proposed as shown below (Pathways B and C).

Alternative Mechanism: Pathway B



Pathway B: An initial oxidation of iodine (I_2) with TBHP could lead to an *in situ* generation of the active specie (HO–I). Subsequent reaction of HO-I and amine would provide iodoamine. Then, the iodoamine reacts with sulfone radical, which is generated by the reaction of sulfonyl hydrazide with I_2/TBHP and gives sulfonamide product as well as iodine radical, which undergoes further oxidation furnishing HO–I specie to resume the catalytic cycle.

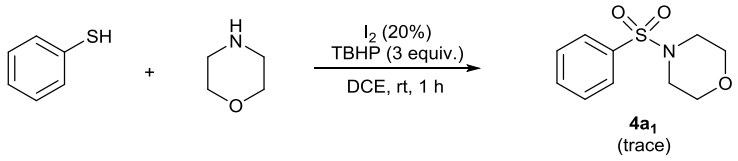
Alternative mechanism: Pathway C



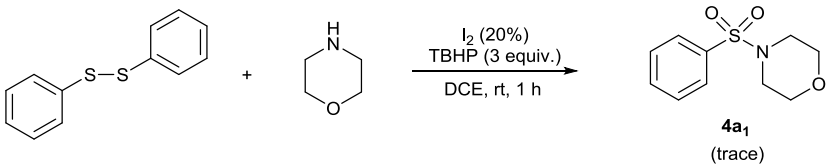
Pathway C: A reaction of iodine radical with sulfonyl hydrazide might generate a sulfenyl radical (**III**). This radical intermediate **III** would possibly react with iodine radical and give sulfenyl iodide (**IV**), which could subsequently combine with amine and result in a formation of S−N bond (intermediate **V**). Then, an oxidation reaction of intermediate **V** ($R^1S{-}NR^2R^3$) by TBHP would produce the desired sulfonamide product.

Note to mechanism C:

Experiment (c)

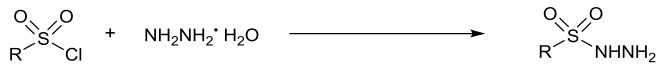


Experiment (d)



Even though only trace amount of product was detected upon subjecting PhSH or PhSSPh to standard conditions (replacing sulfonyl hydrazide substrate), mechanism C could not be completely ruled out because intermediate **V** ($R^1S{-}NR^2R^3$) might be generated *in situ* from a reaction of amine and sulfonyl hydrazide under the optimal conditions. In this regard, additional studies to identify the mechanism of this transformation are currently under investigation in our laboratory.

General Procedure for the Preparation of Sulfonyl Hydrazide

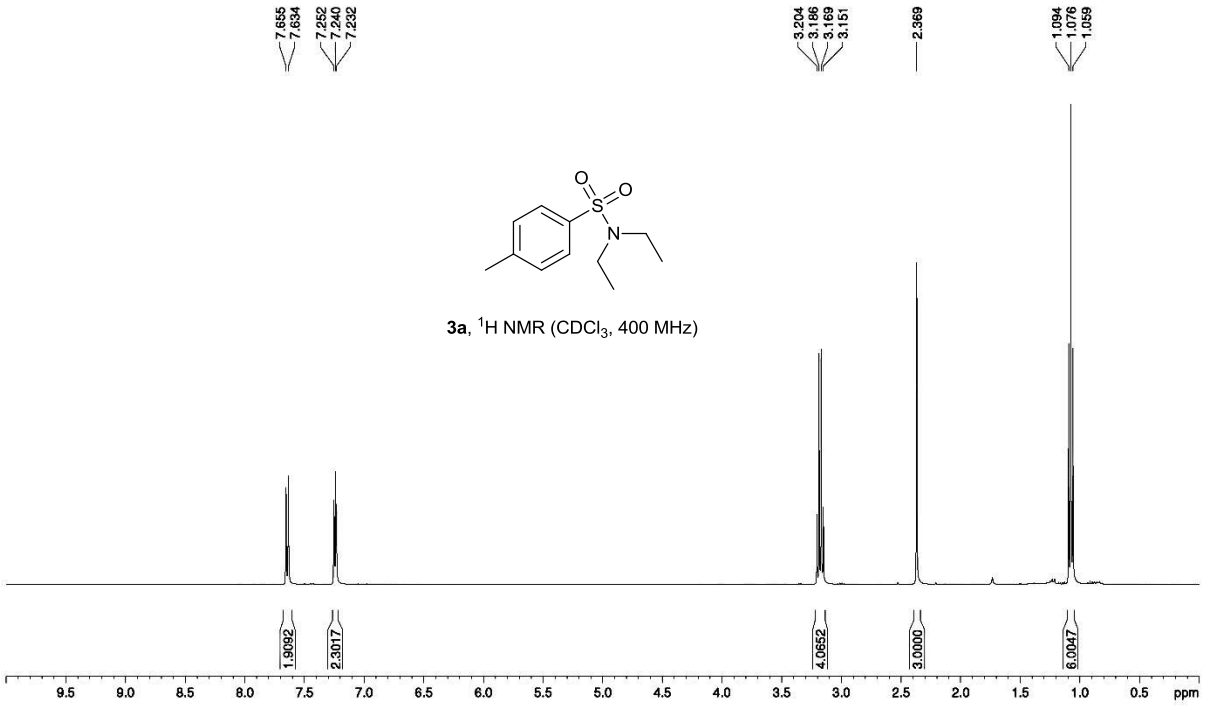


Sulfonyl hydrazide was prepared according to literature procedure. To a stirred of solution of sulfonyl chloride (5 mmol) in 25 mL THF was added hydrazine monohydrate (10 mmol) dropwise at 0 °C. The mixture was stirred at room temperature for 30 min. Upon completion, the solvent was removed by evaporation, and the residue was extracted with dichloromethane. The organic layer was washed with water and brine, dried over Na_2SO_4. The organic solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to give the corresponding sulfonyl hydrazine.

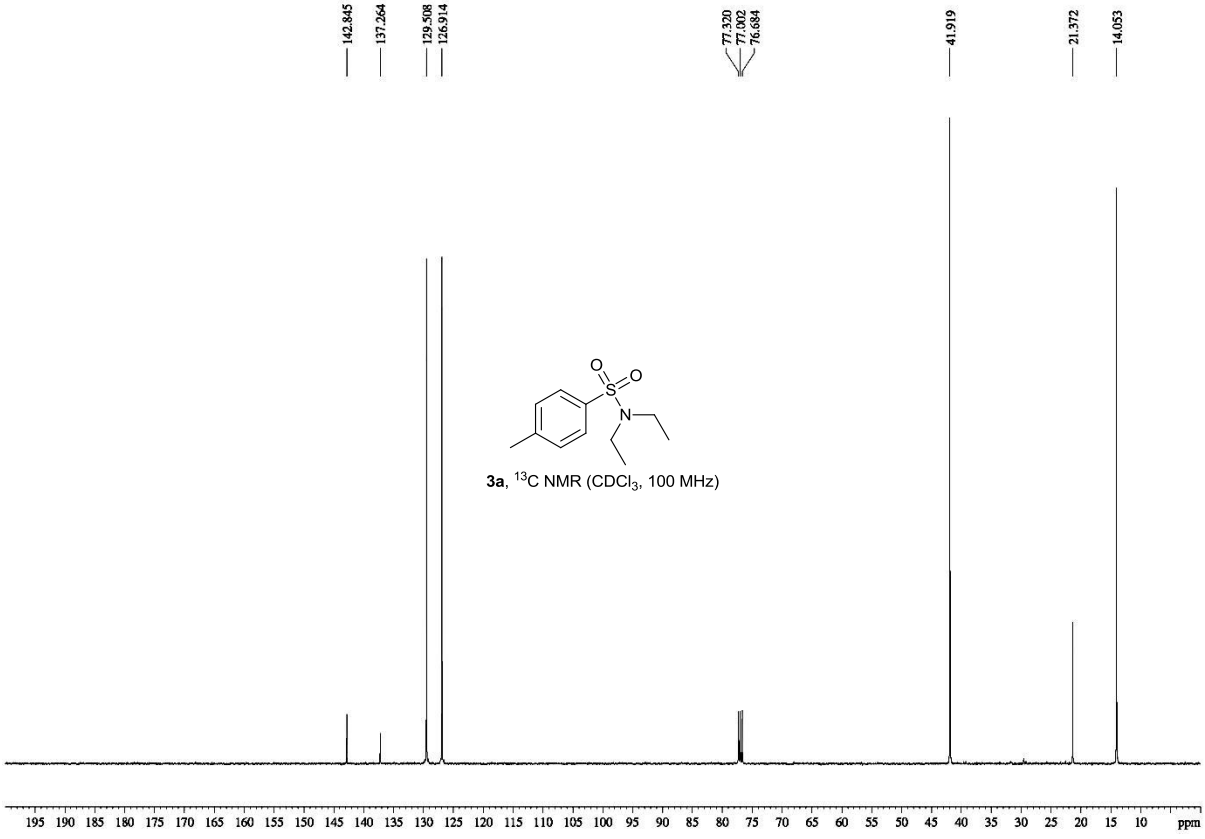
(Reference: X. Zhao, L. Zhang, T. Li, G. Liu, H. Wanga and K. Lu; *Chem. Commun.*, 2014, **50**, 13121.)

III. Spectral Data of Compounds 3a−3i, 3k and 4a$_1$–4e

N,N-diethyl-4-methylbenzenesulfonamide (3a).

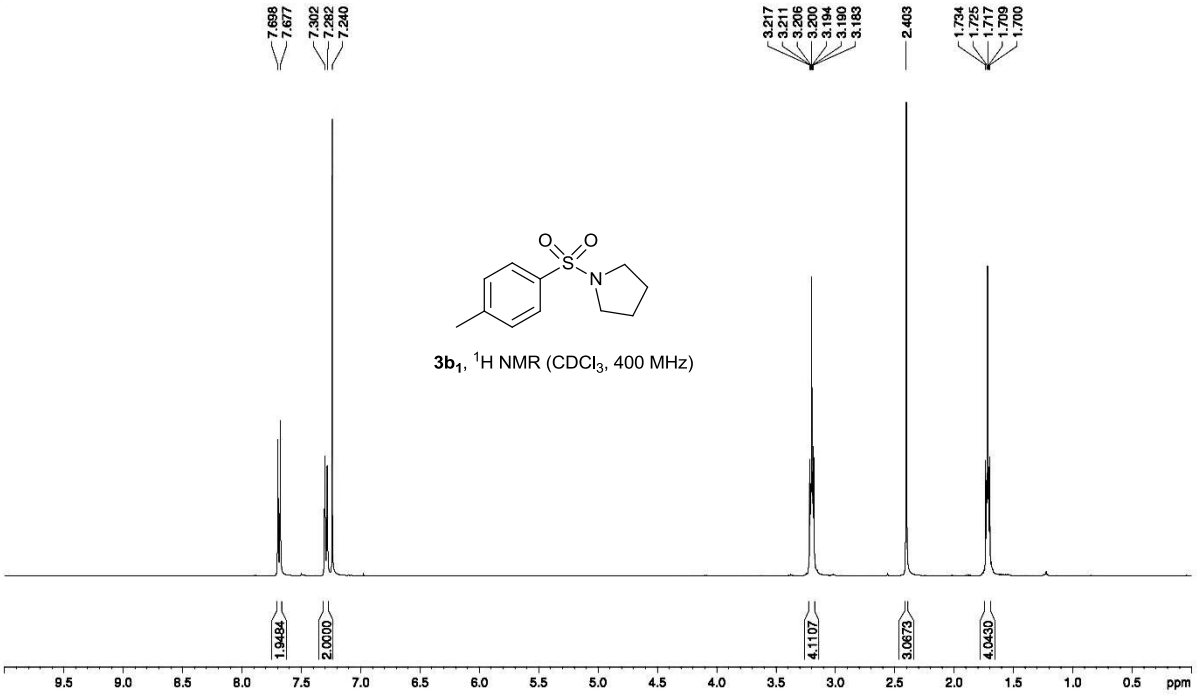


3a, ^{1}H NMR ($CDCl_3$, 400 MHz)

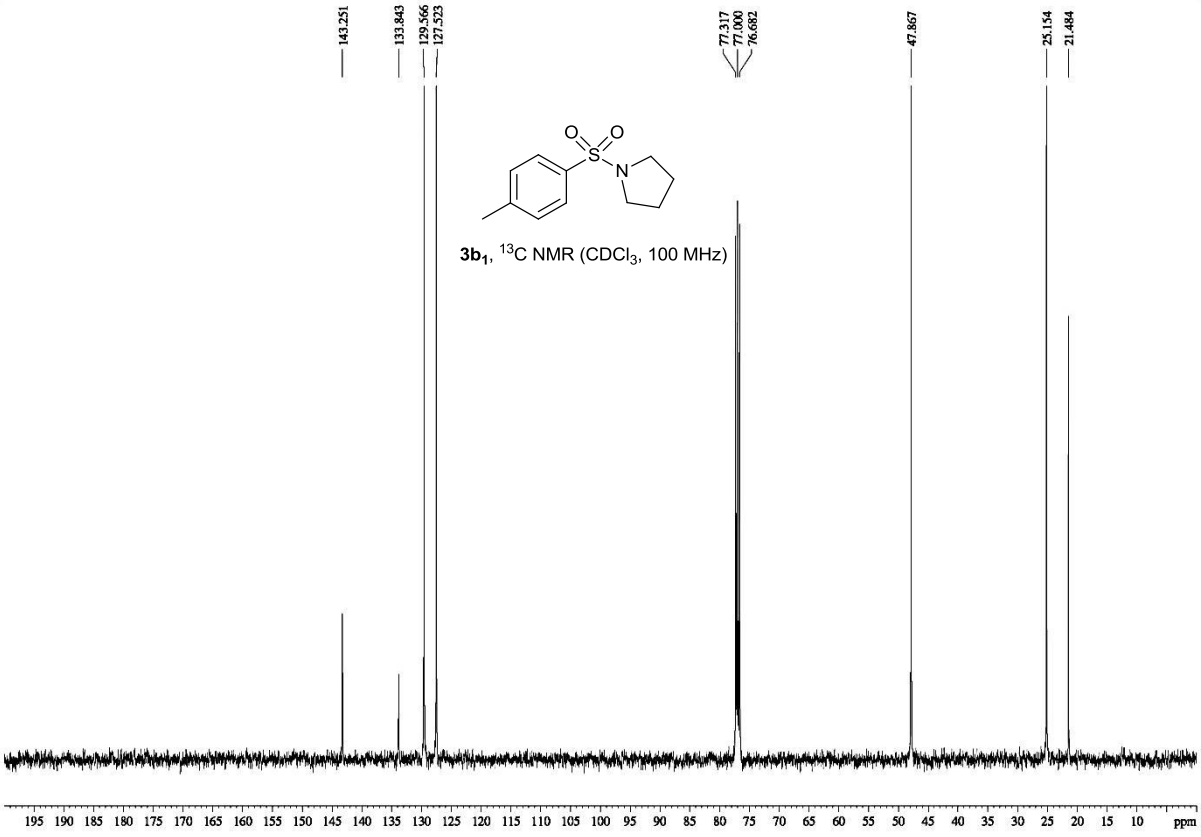


3a, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-tosylpyrrolidine ($3b_1$).

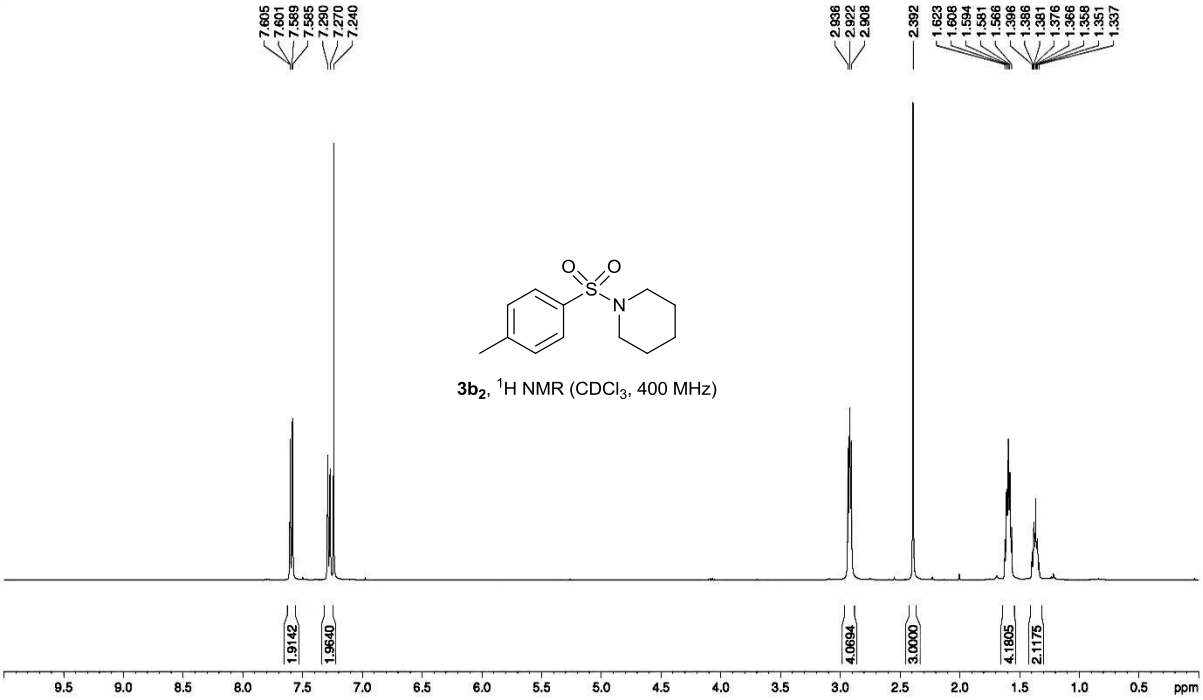


$3b_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

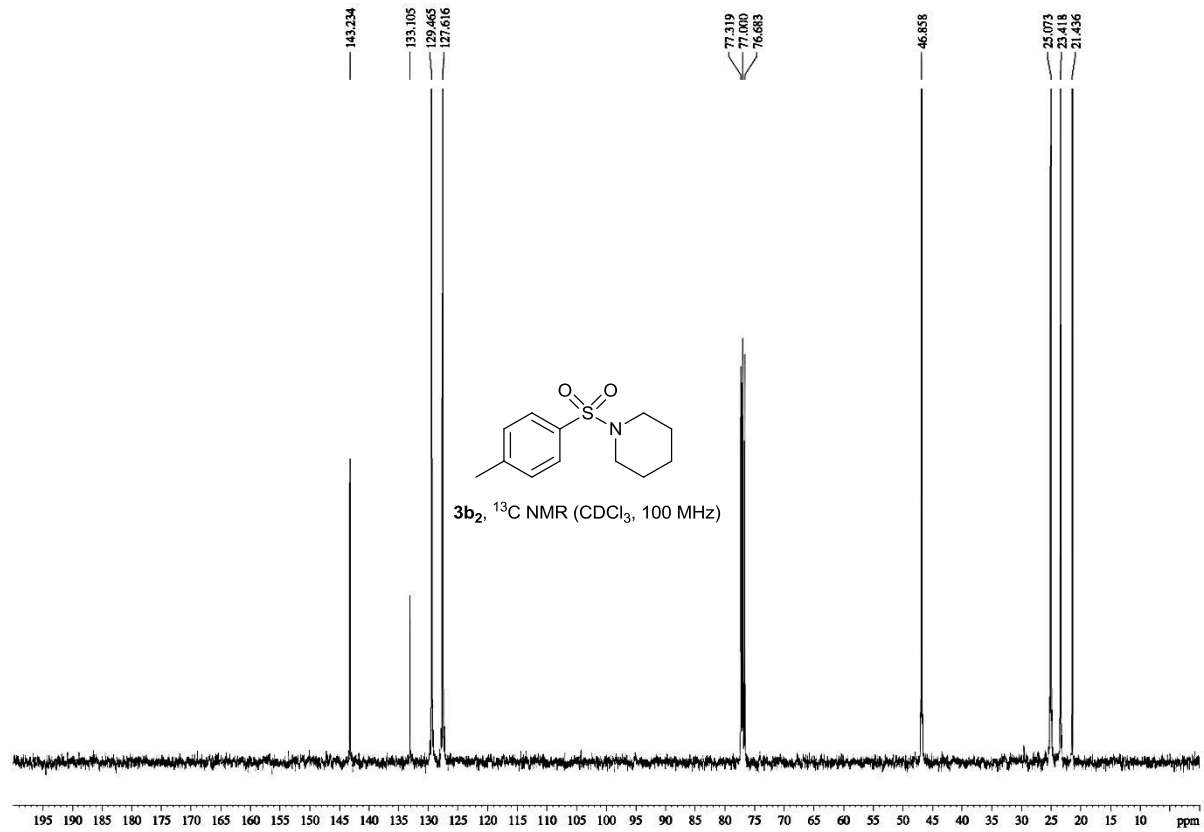


$3b_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-tosylpiperidine ($3b_2$).

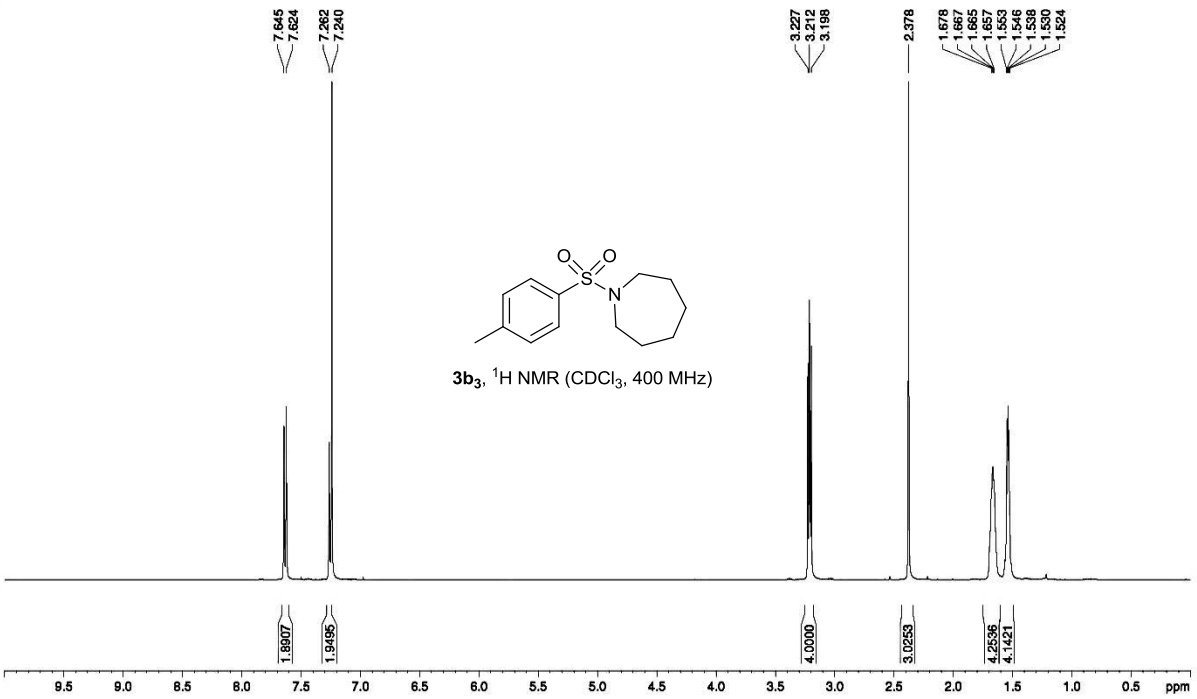


$3b_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

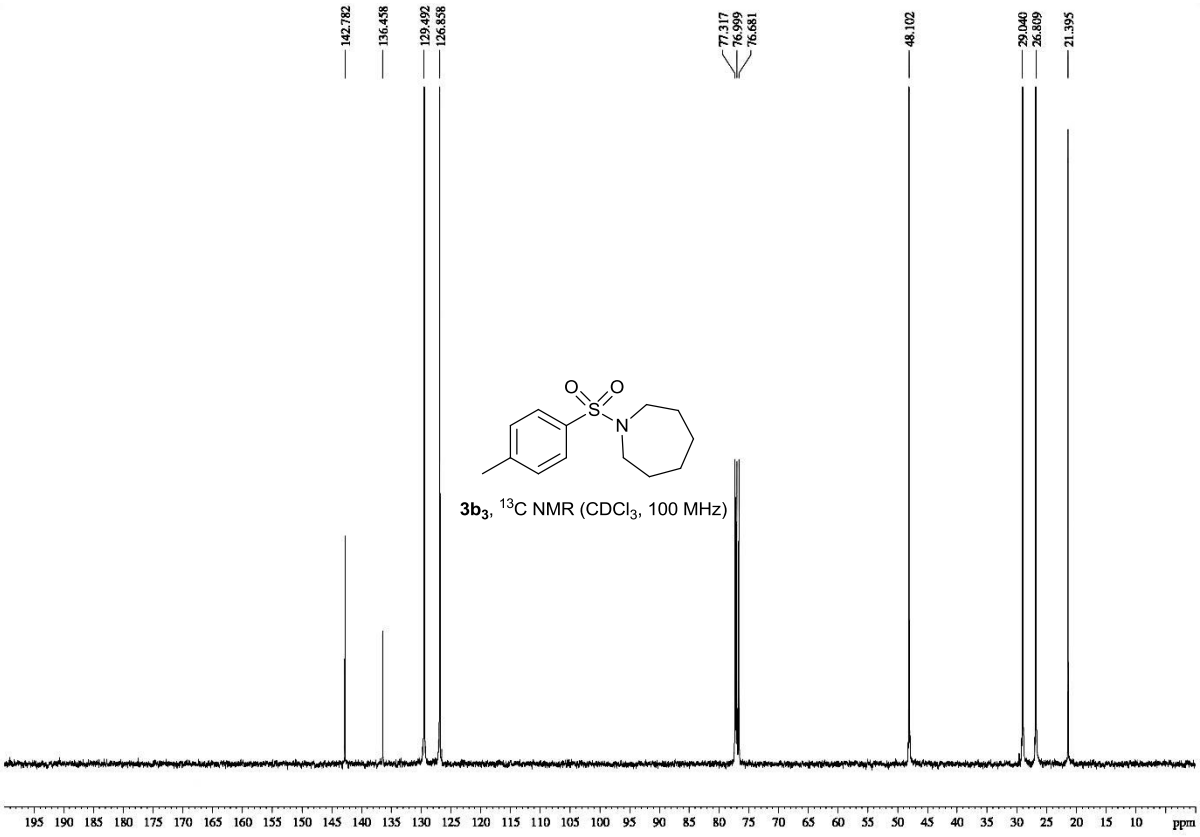


$3b_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-tosylazepane (3b$_3$).

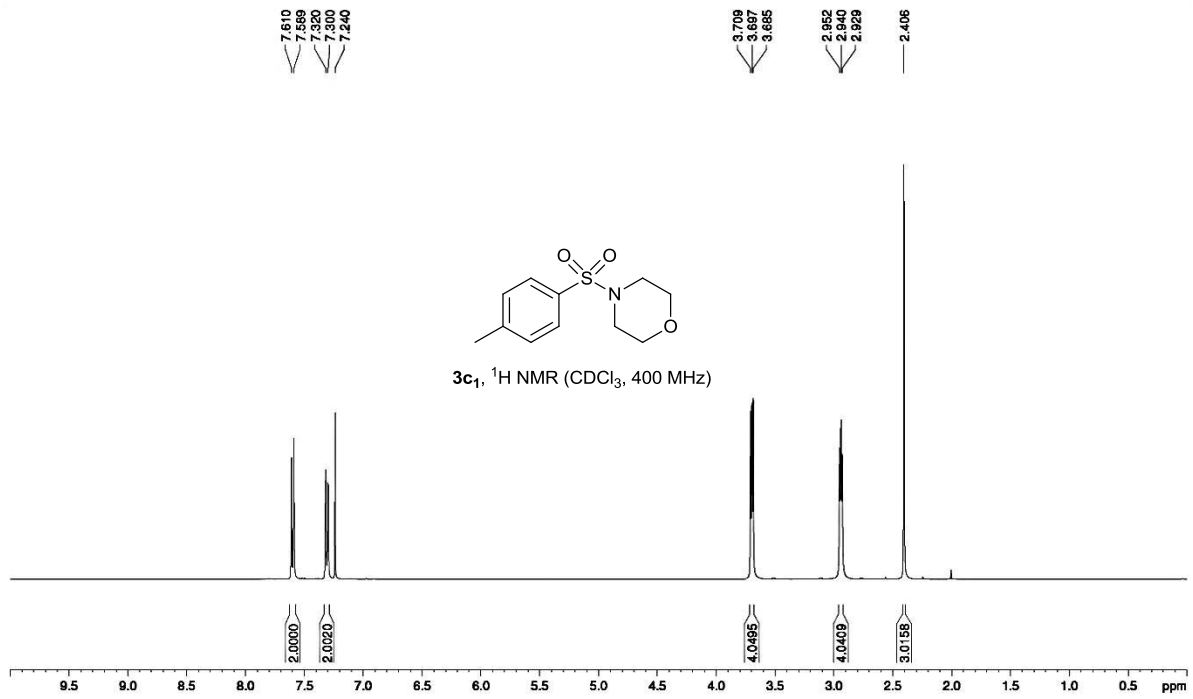


3b$_3$, ^{1}H NMR ($CDCl_3$, 400 MHz)

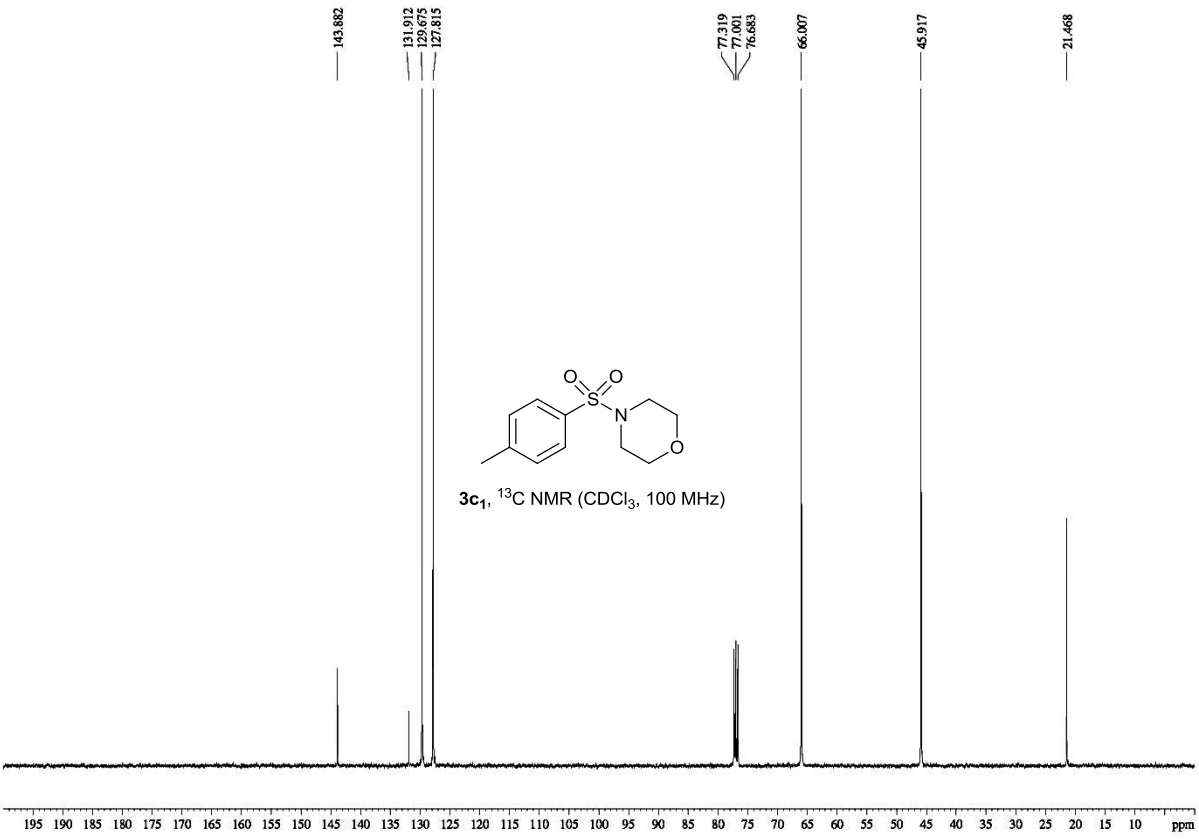


3b$_3$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-tosylmorpholine ($3c_1$).

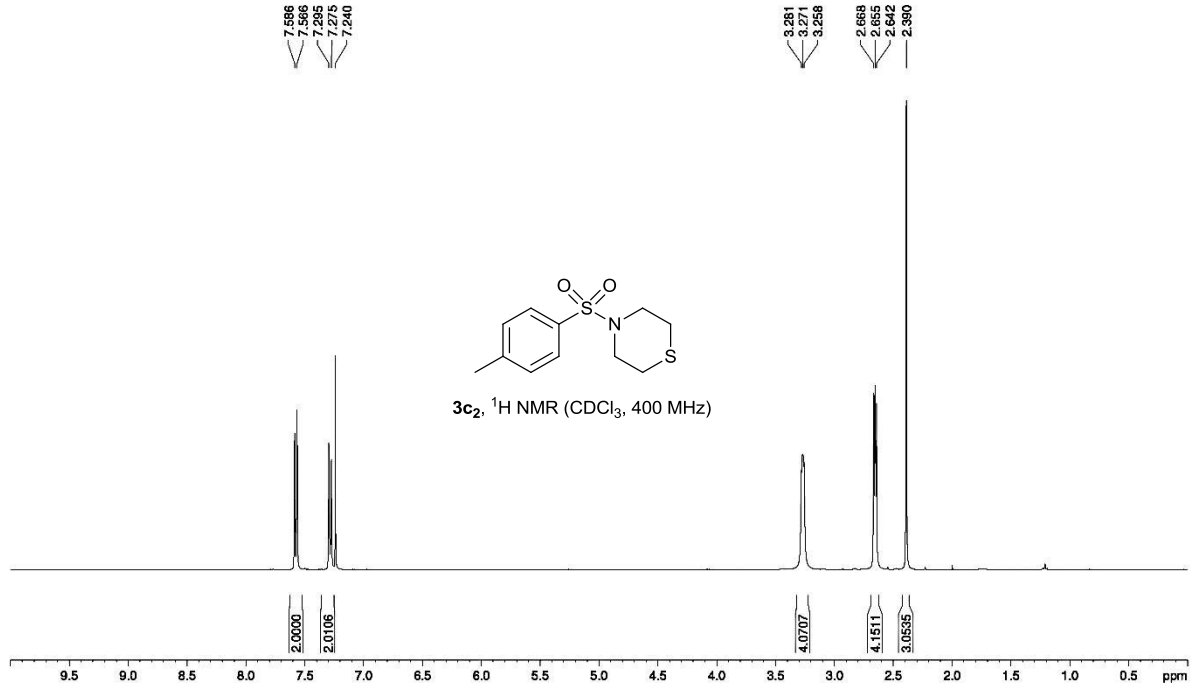


$3c_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

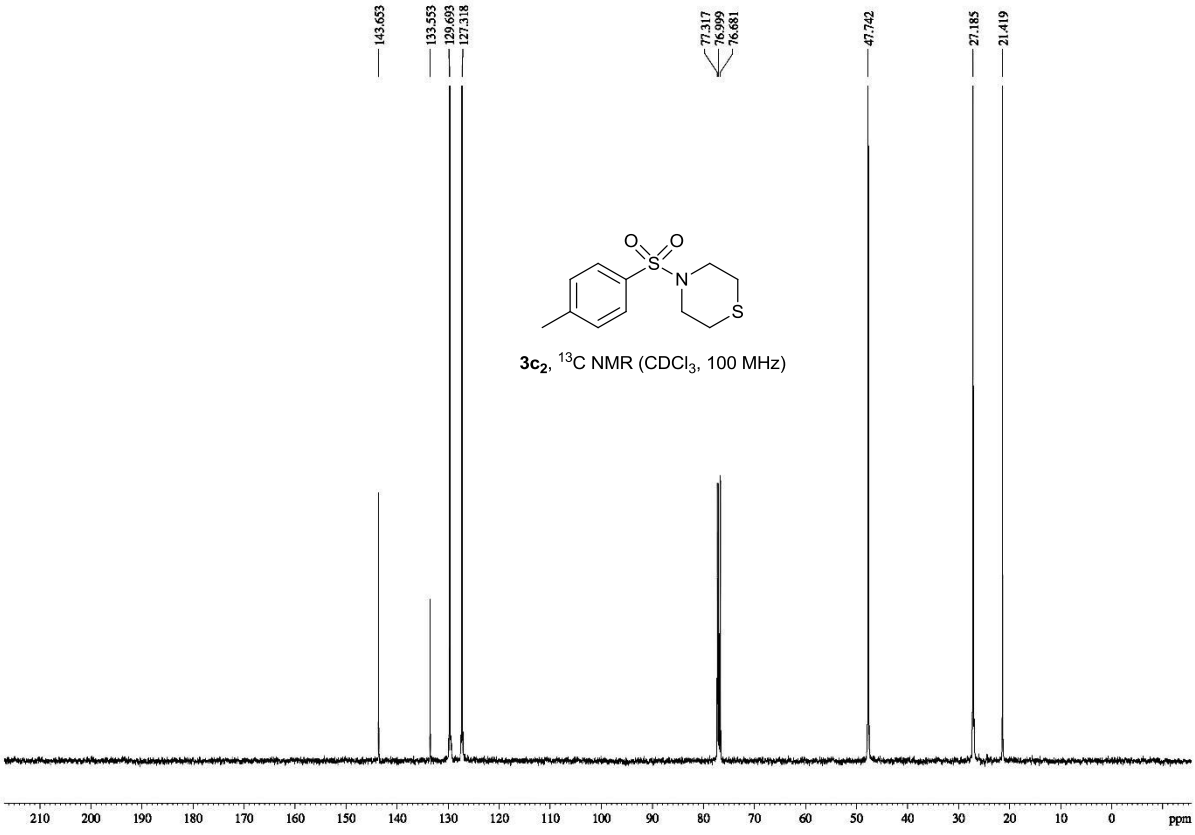


$3c_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-tosylthiomorpholine ($3c_2$).

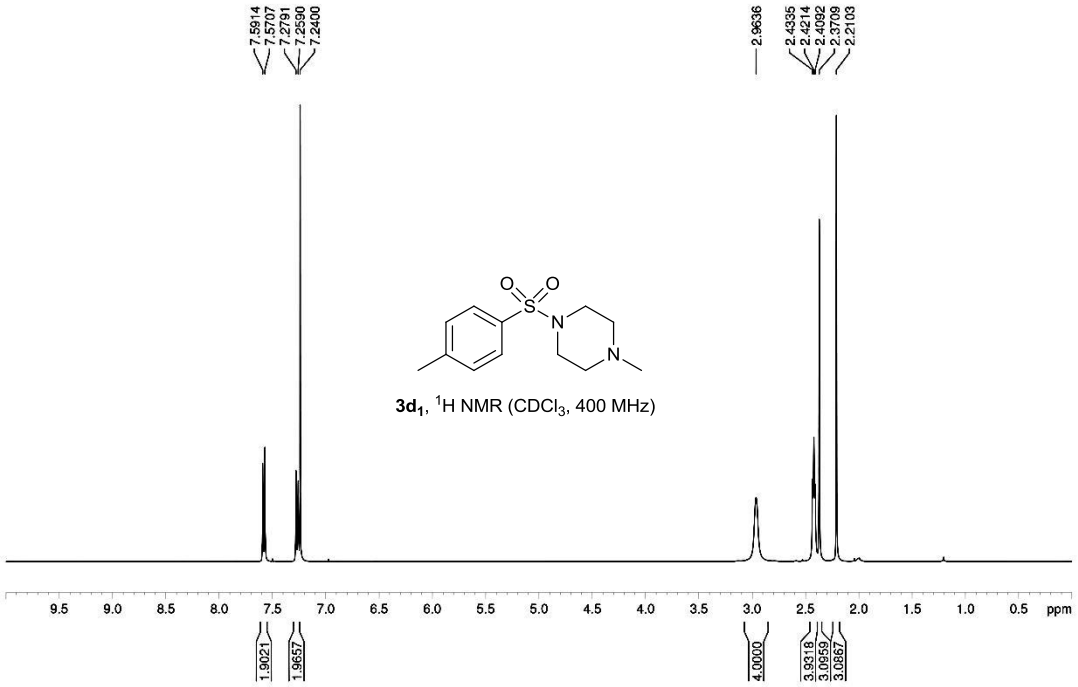


$3c_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)



$3c_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

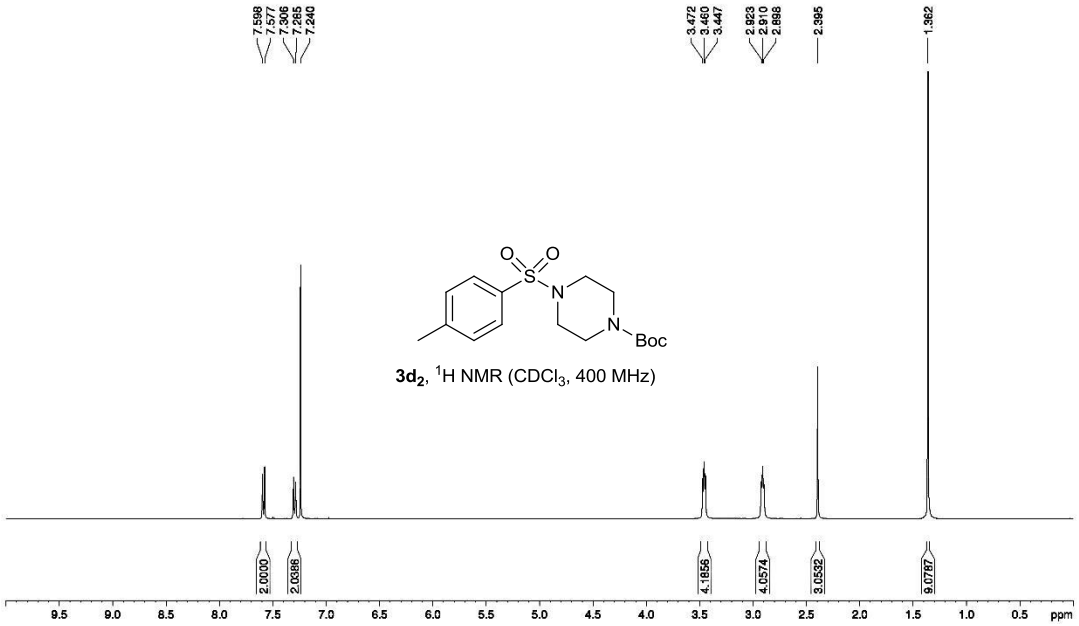
1-methyl-4-tosylpiperazine ($3d_1$).



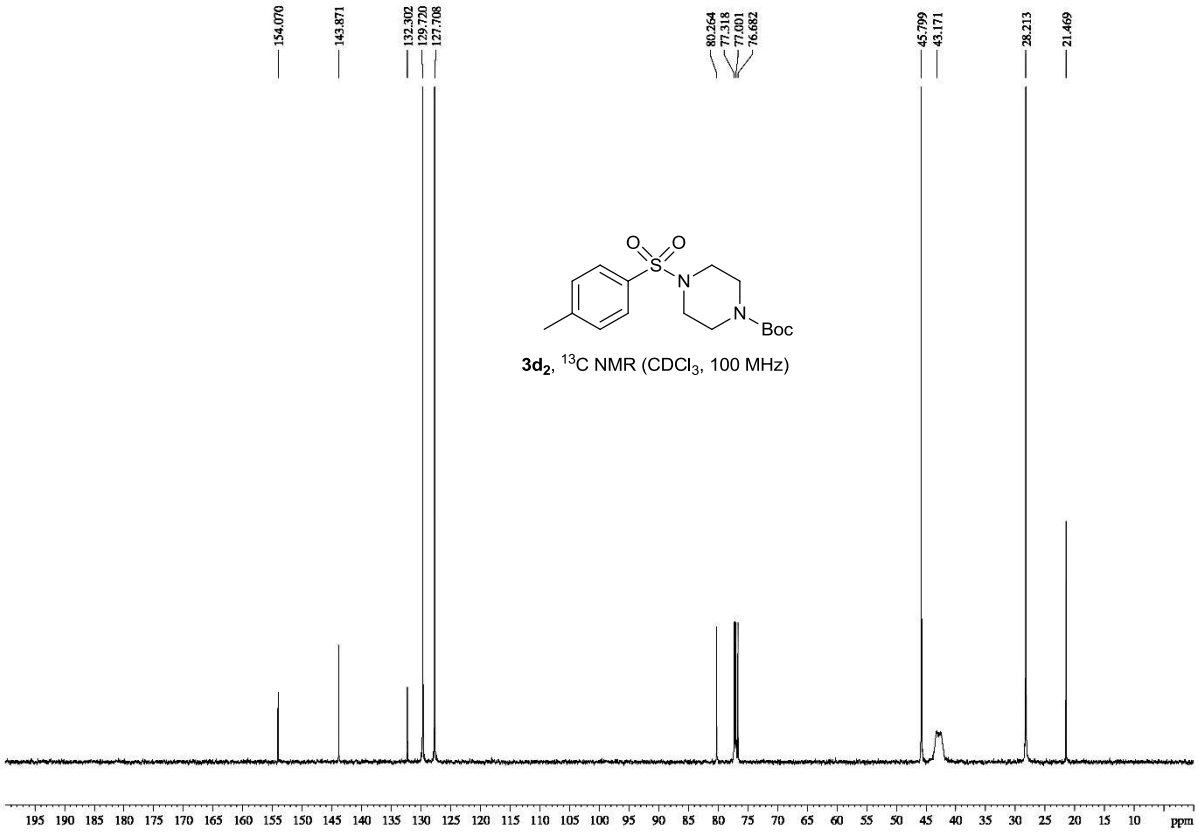
$3d_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

$3d_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***tert*-butyl 4-tosylpiperazine-1-carboxylate ($3d_2$).**

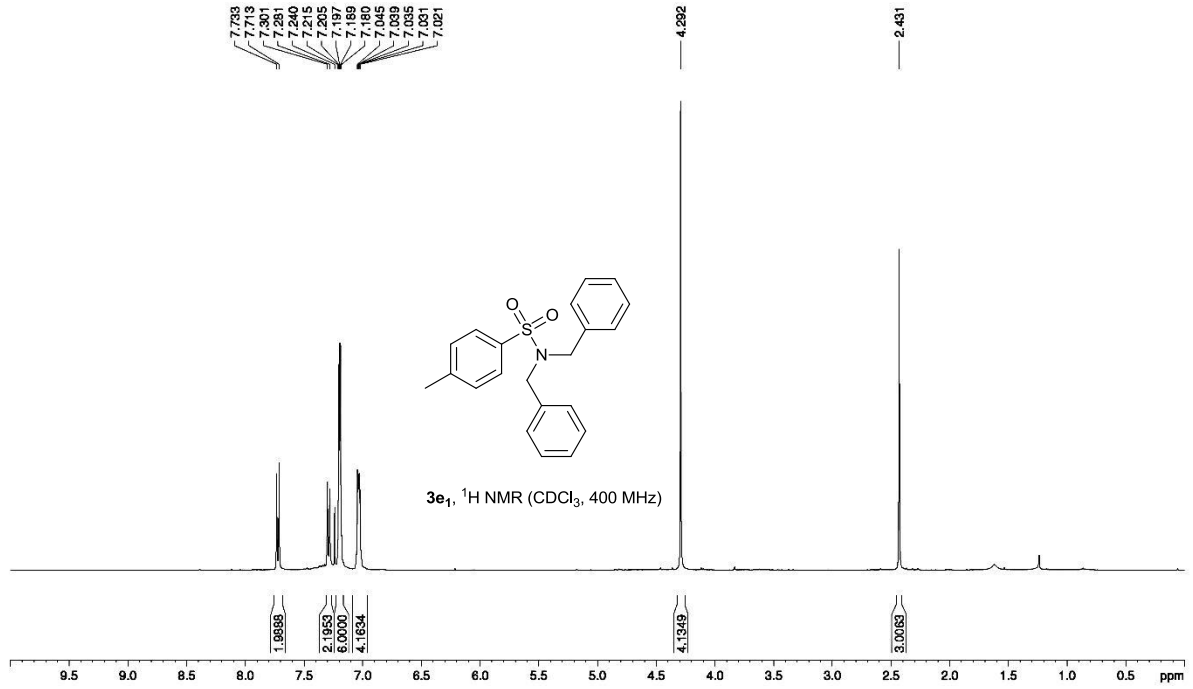


$3d_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

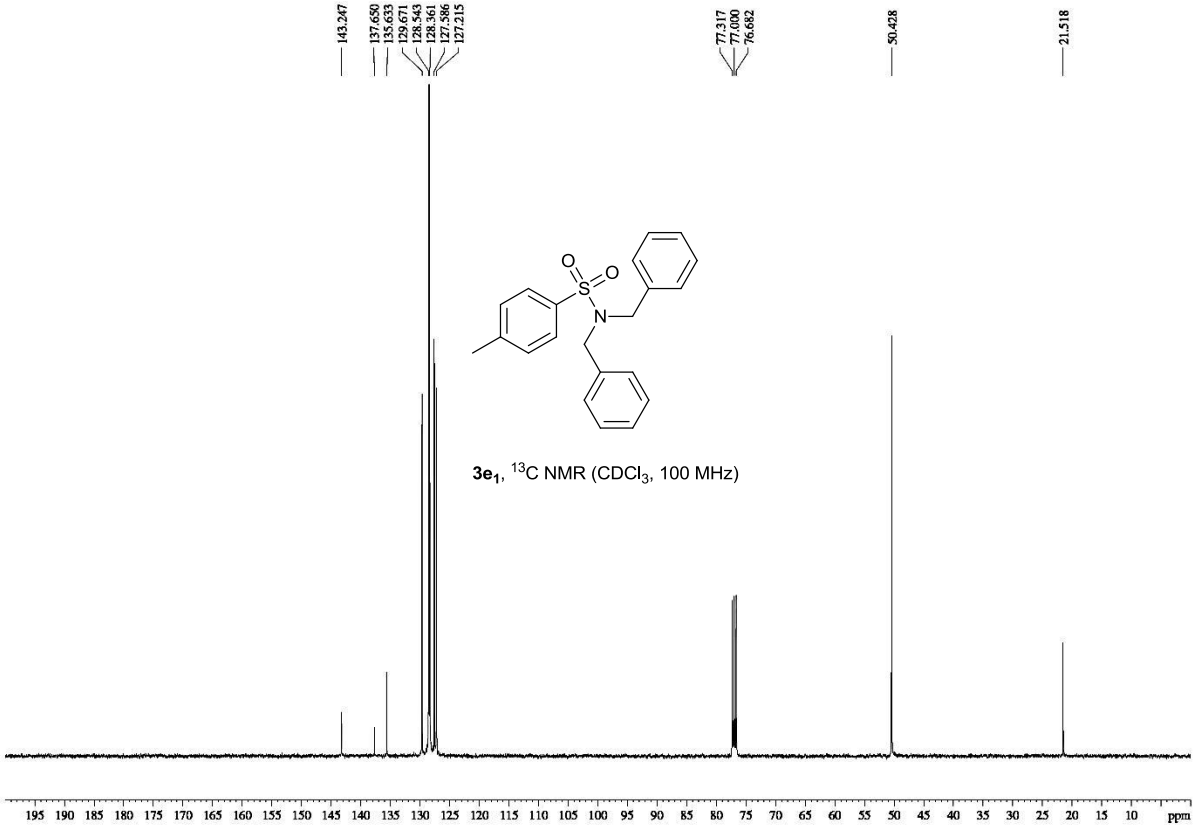


$3d_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N,N*-dibenzyl-4-methylbenzenesulfonamide ($3e_1$).**

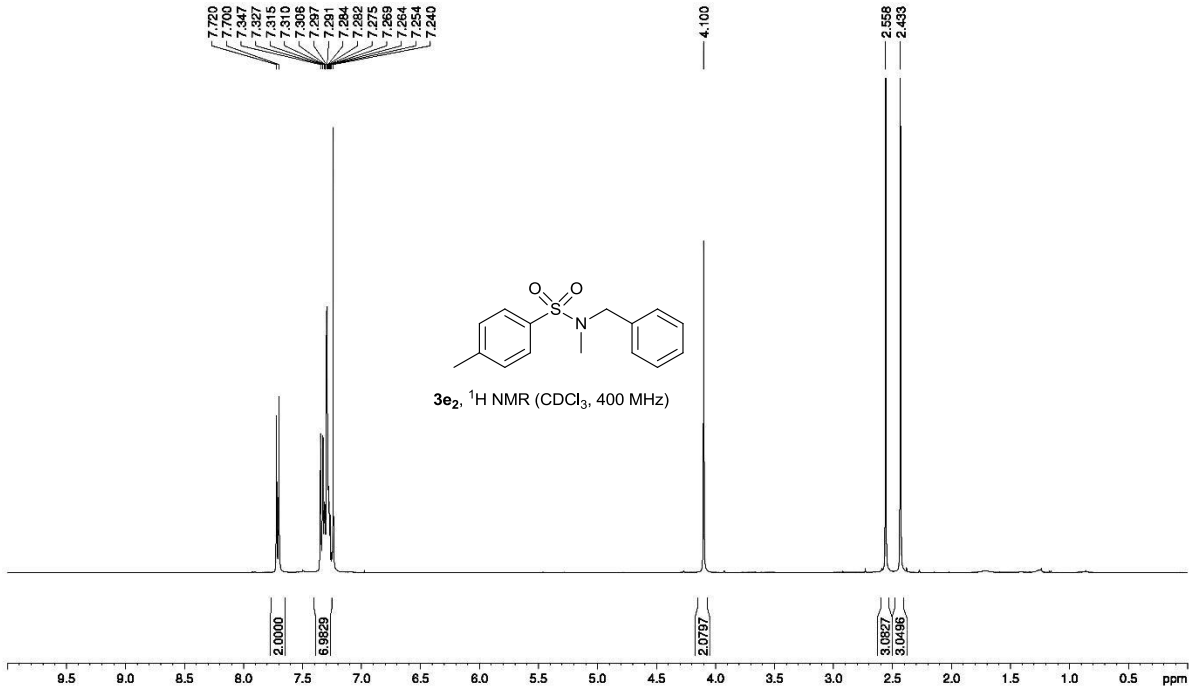


3e$_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

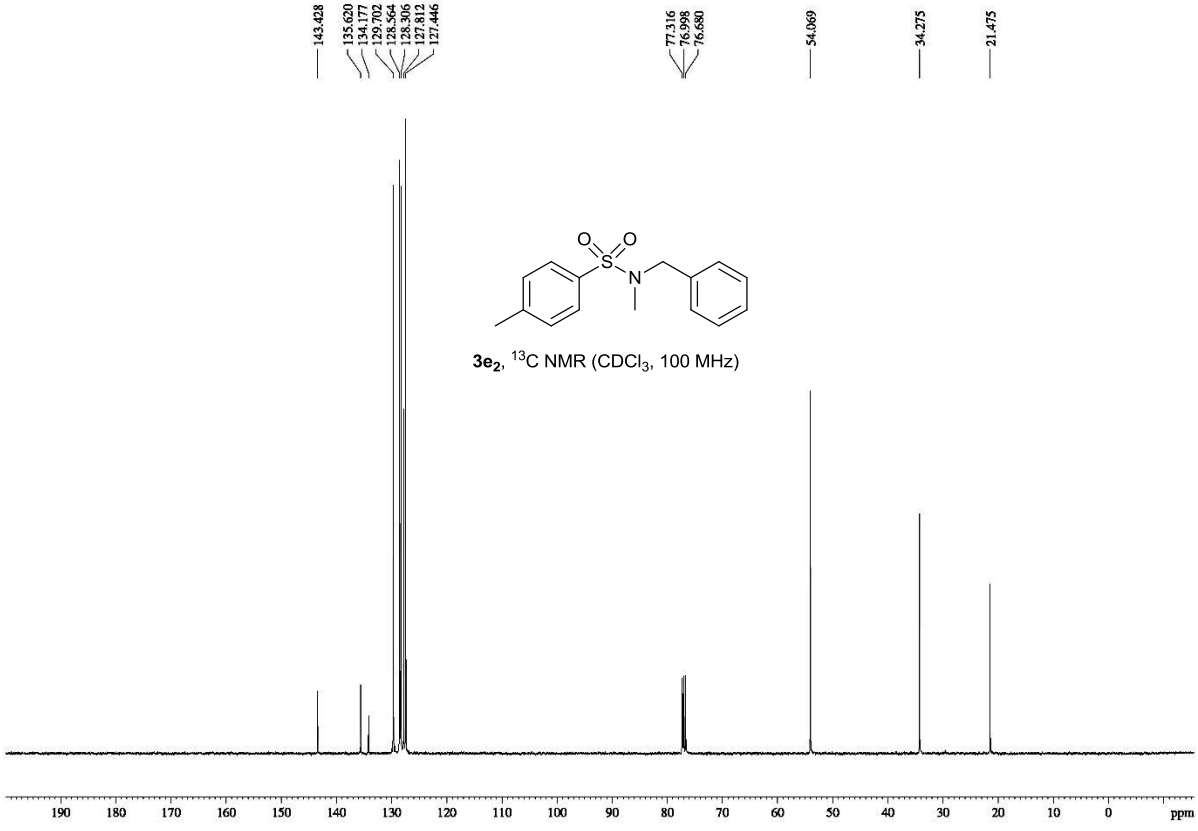


3e$_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N*-benzyl-*N*,4-dimethylbenzenesulfonamide ($3e_2$).**

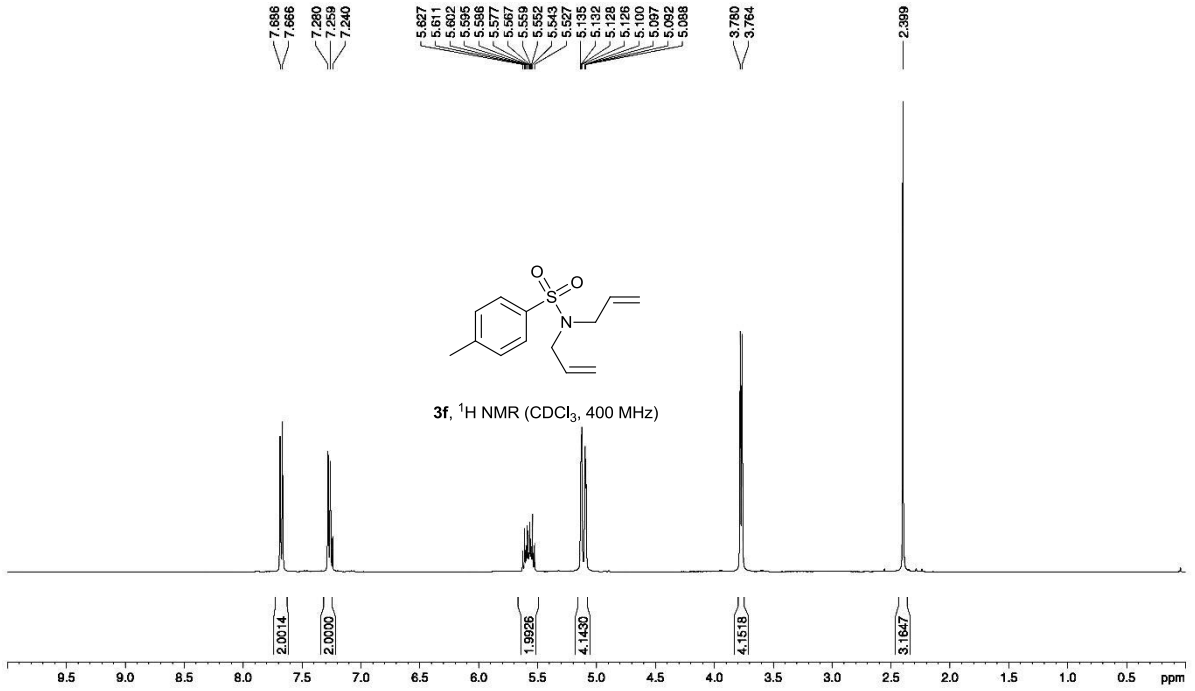


3e$_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

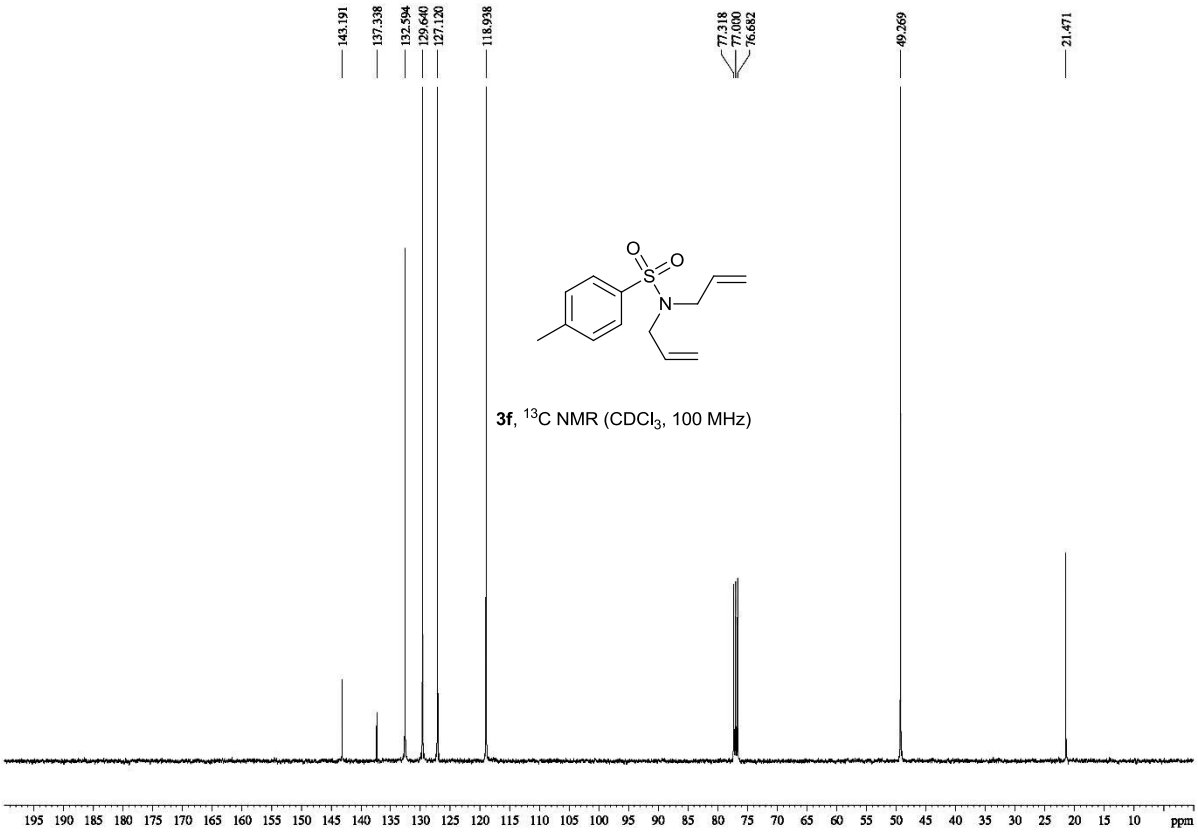


3e$_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N,N*-diallyl-4-methylbenzenesulfonamide (3f).**

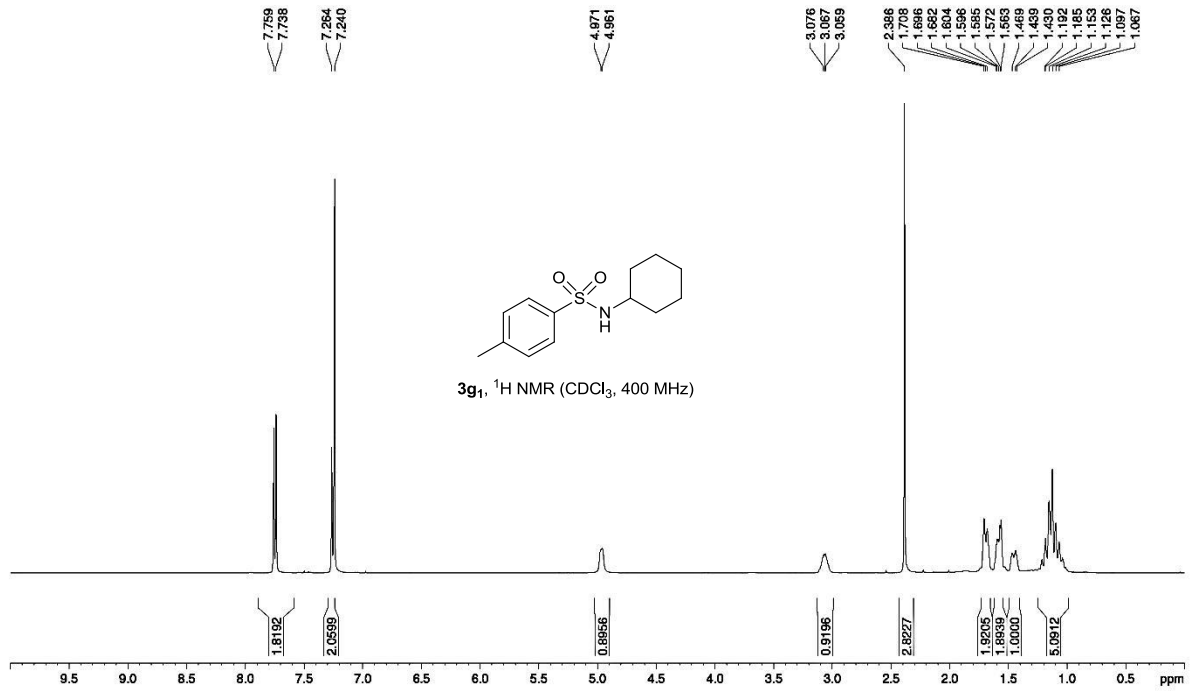


3f, ^{1}H NMR ($CDCl_3$, 400 MHz)

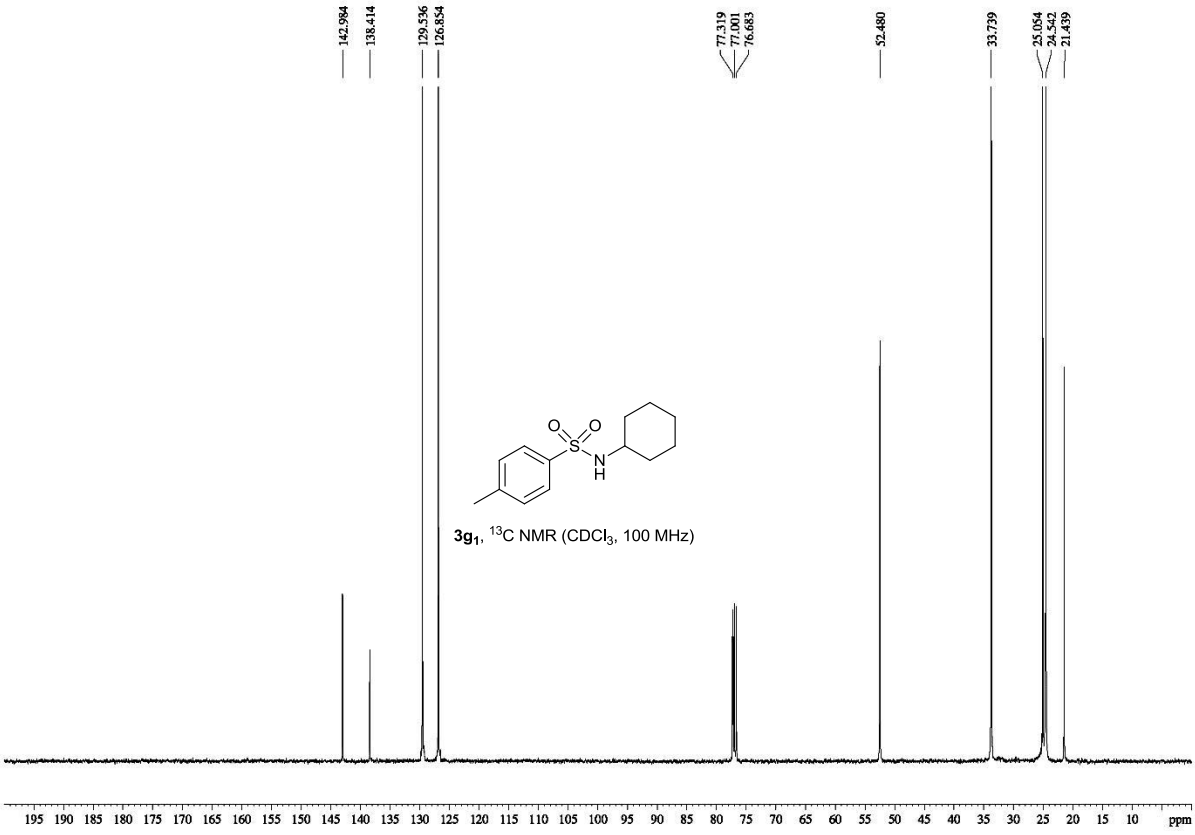


3f, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N*-cyclohexyl-4-methylbenzenesulfonamide ($3g_1$).**

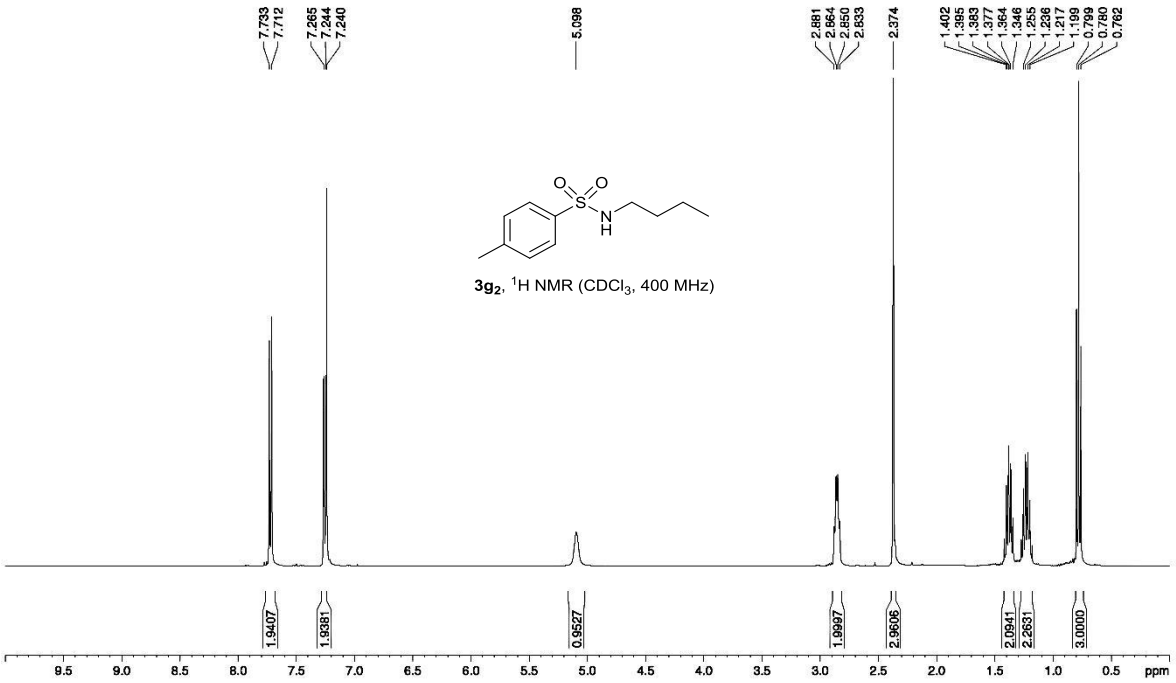


$3g_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

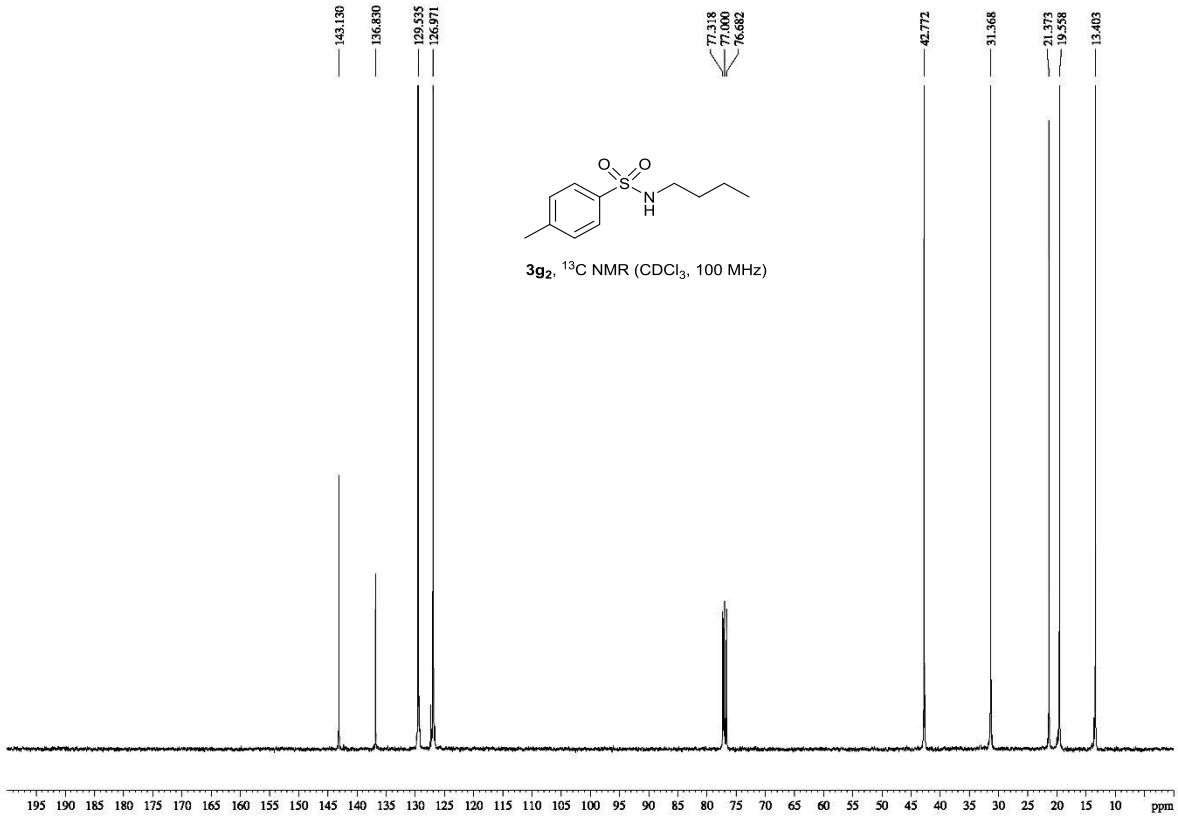


$3g_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N*-butyl-4-methylbenzenesulfonamide ($3g_2$).**

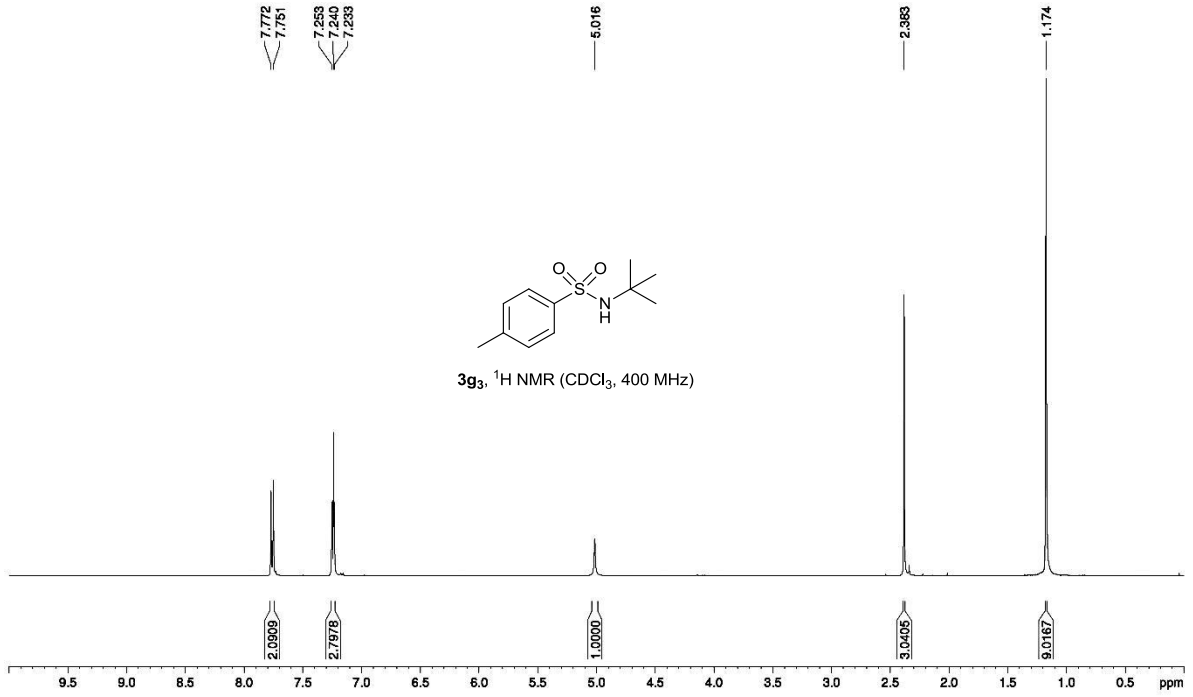


$3g_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

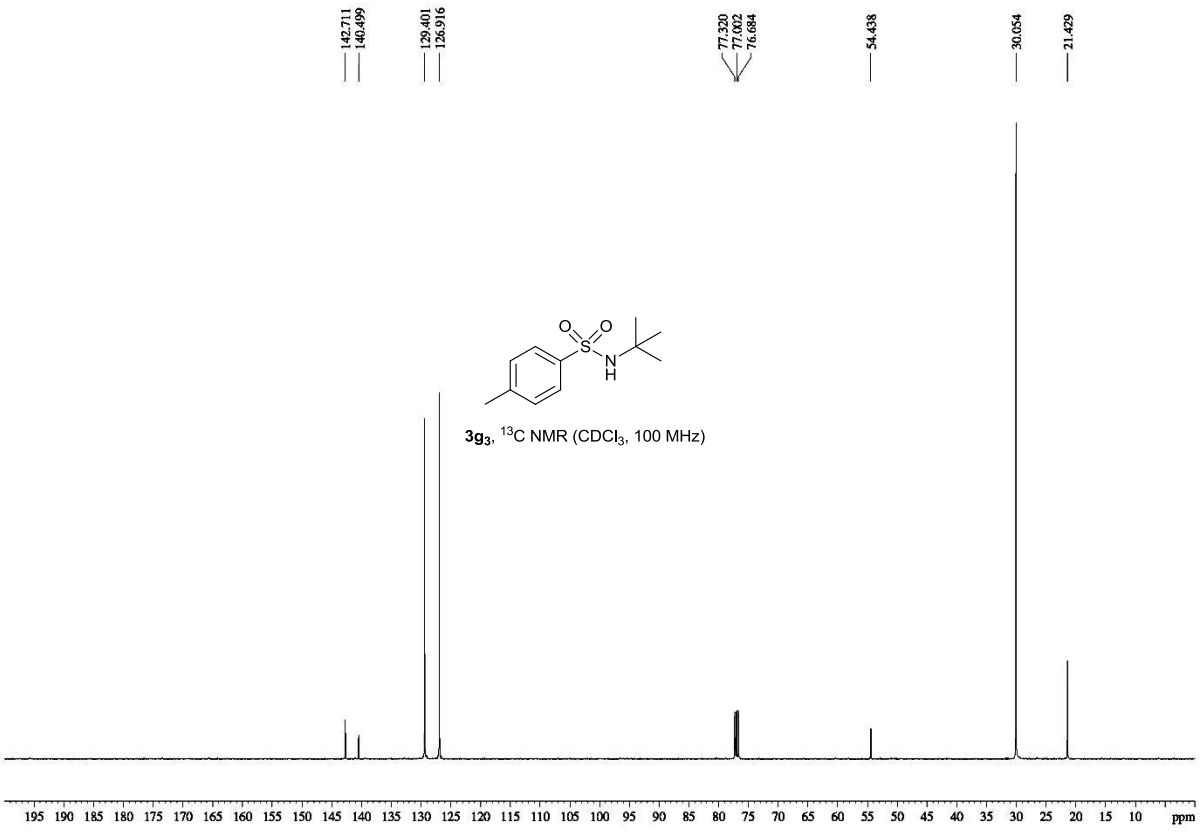


$3g_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

***N*-(tert-butyl)-4-methylbenzenesulfonamide (3g$_3$).**

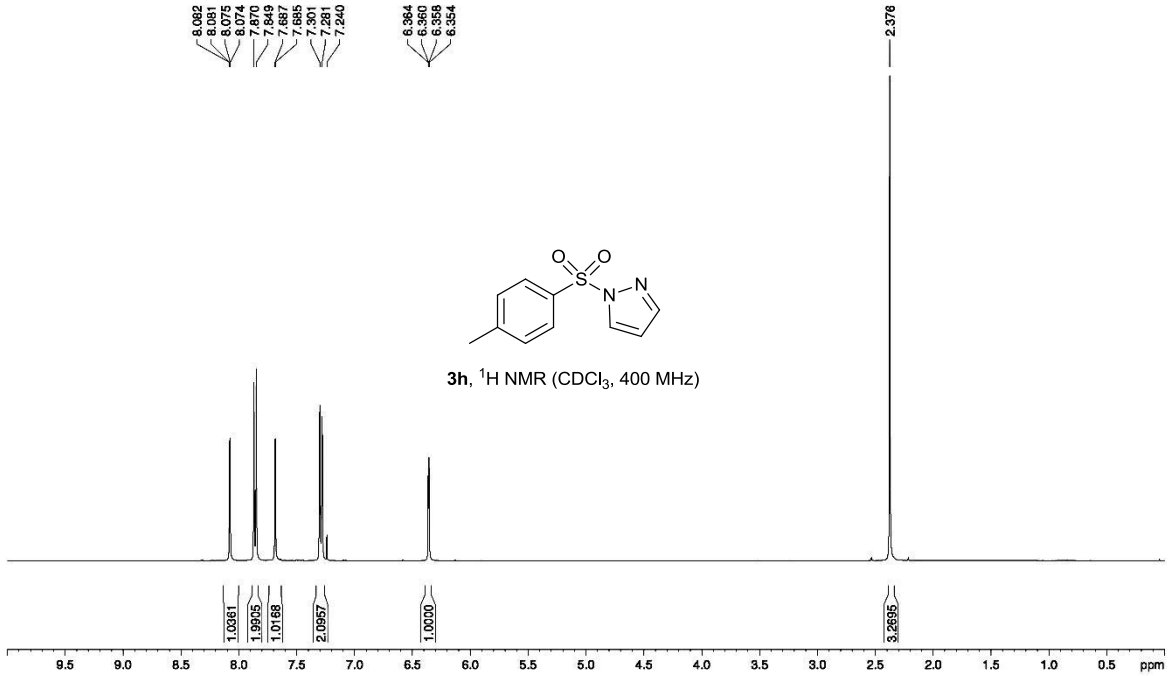


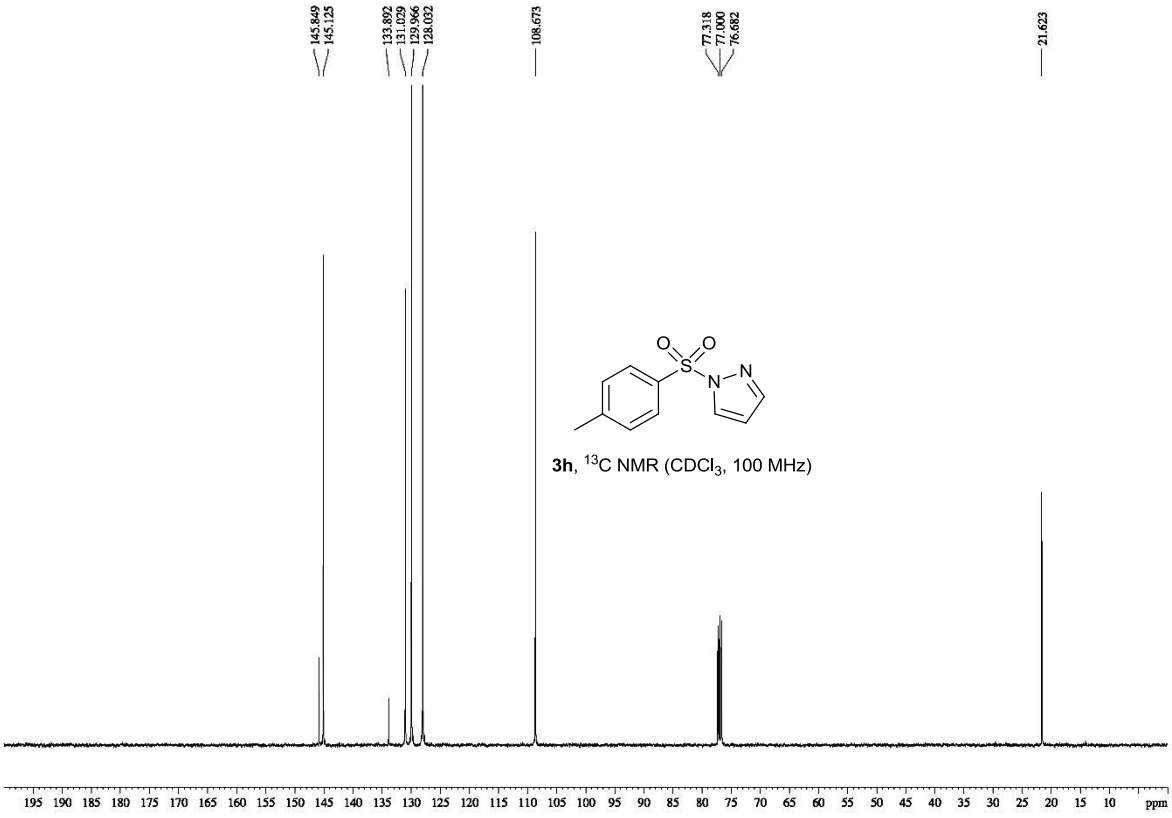
3g$_3$, ^{1}H NMR (CDCl$_3$, 400 MHz)



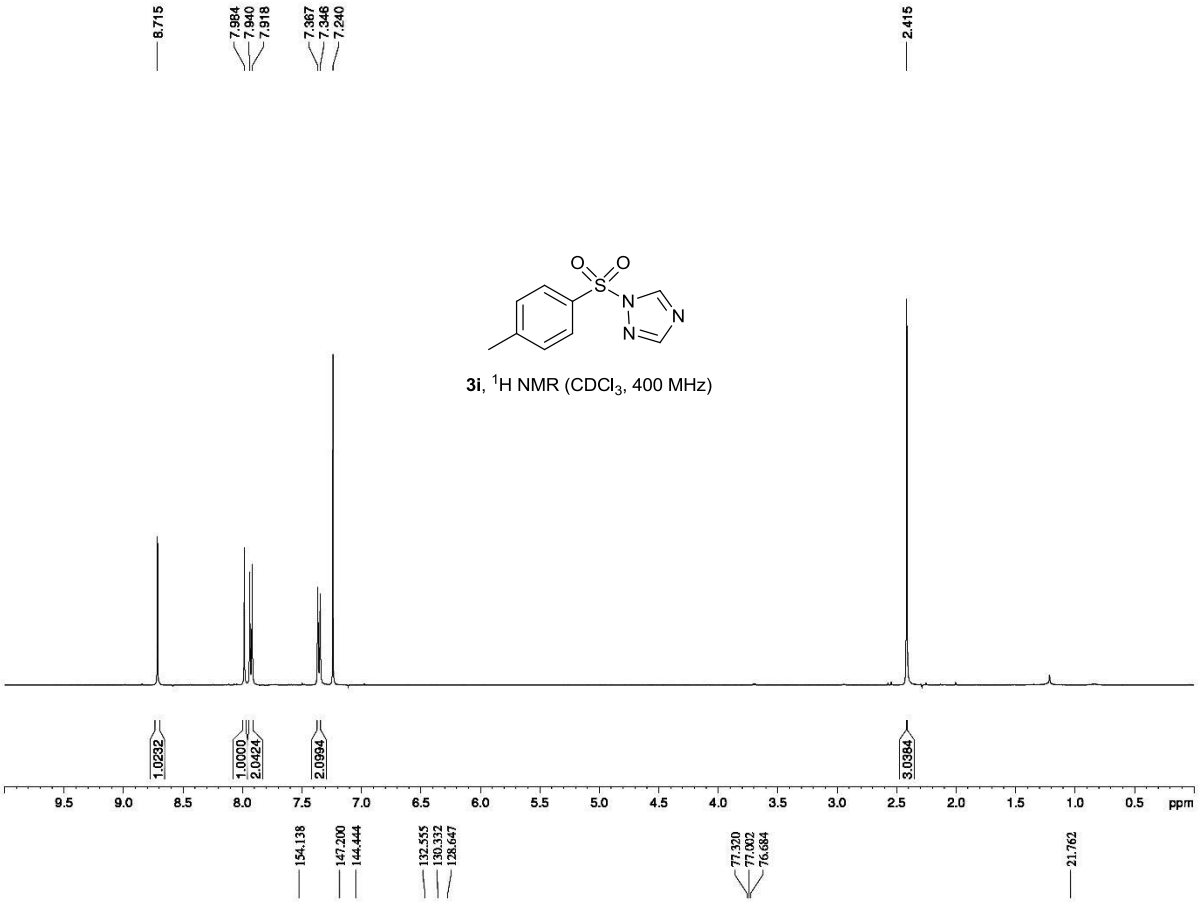
3g$_3$, ^{13}C NMR (CDCl$_3$, 100 MHz)

1-tosyl-1*H*-pyrazole (3h).

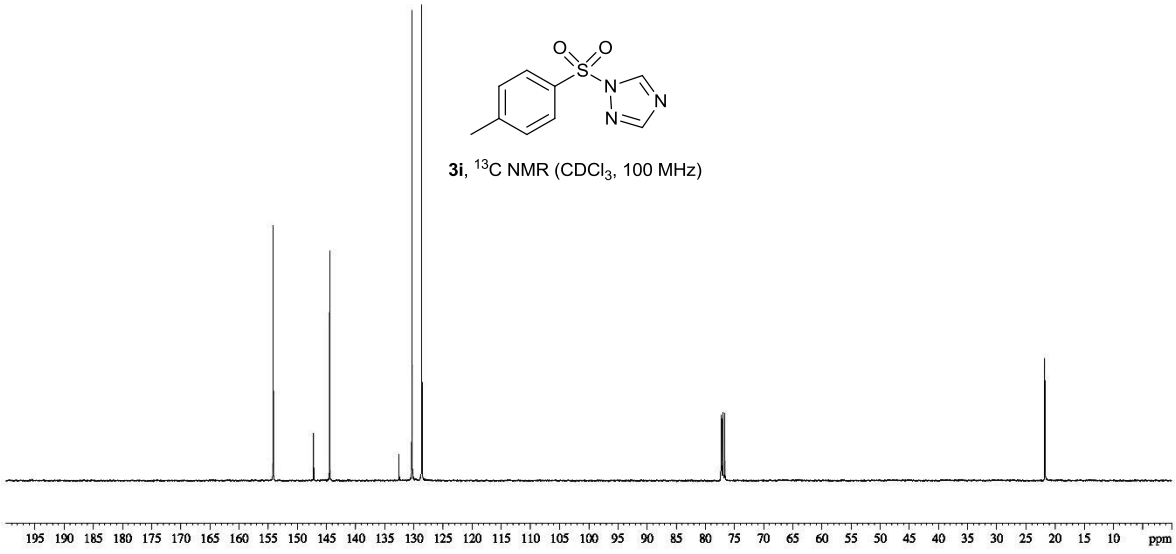




1-tosyl-1*H*-1,2,4-triazole (3i).

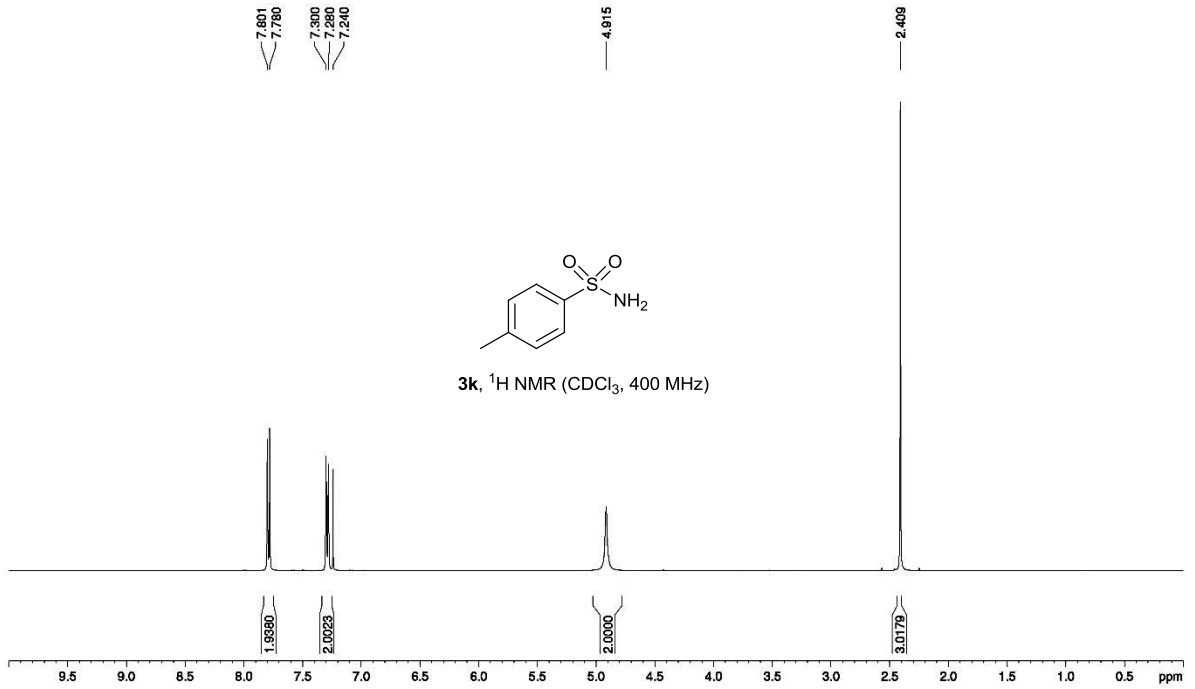


3i, ^{1}H NMR ($CDCl_3$, 400 MHz)

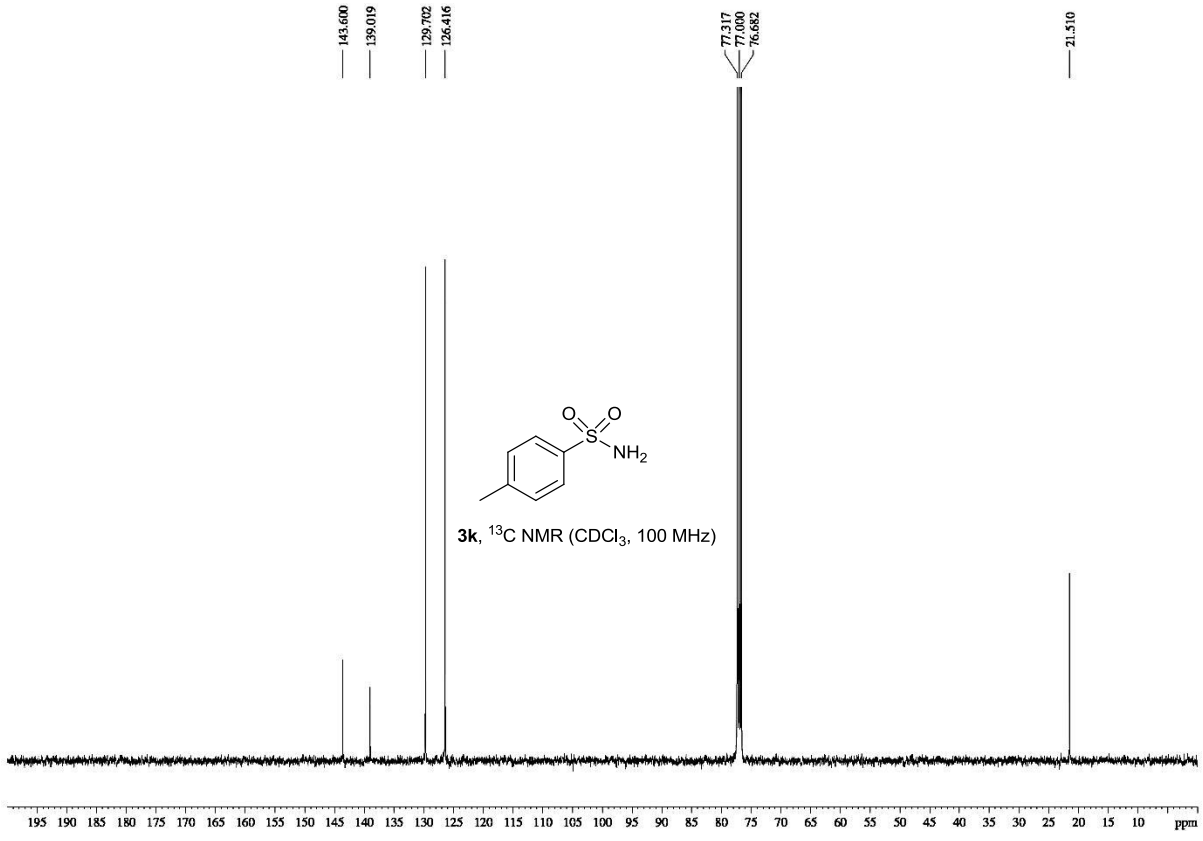


3i, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-methylbenzenesulfonamide (3k).

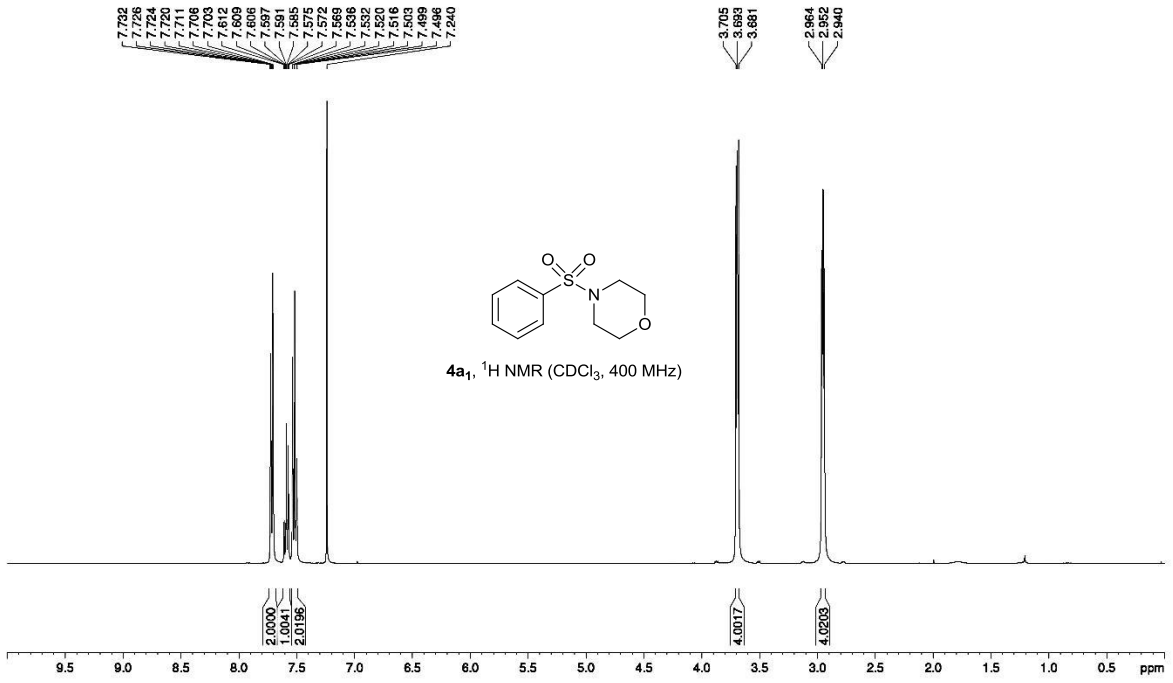


3k, ^{1}H NMR ($CDCl_3$, 400 MHz)

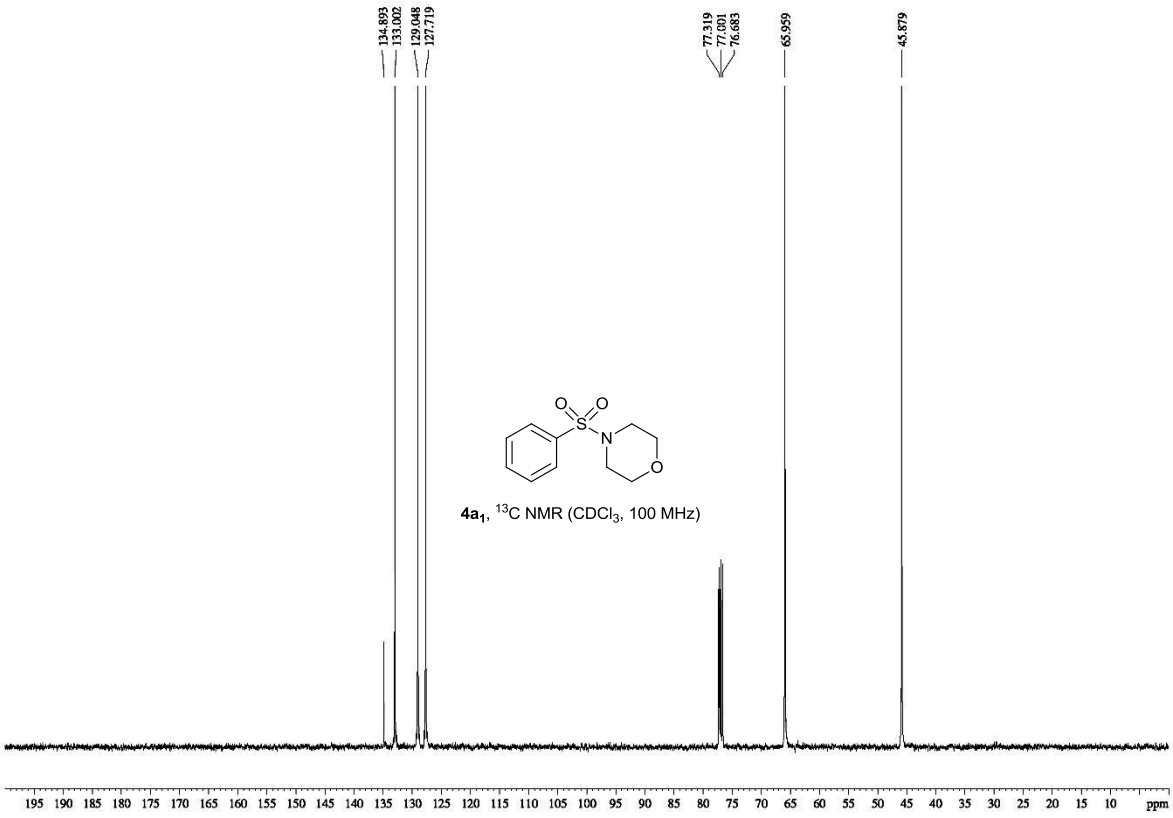


3k, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-(phenylsulfonyl)morpholine ($4a_1$).

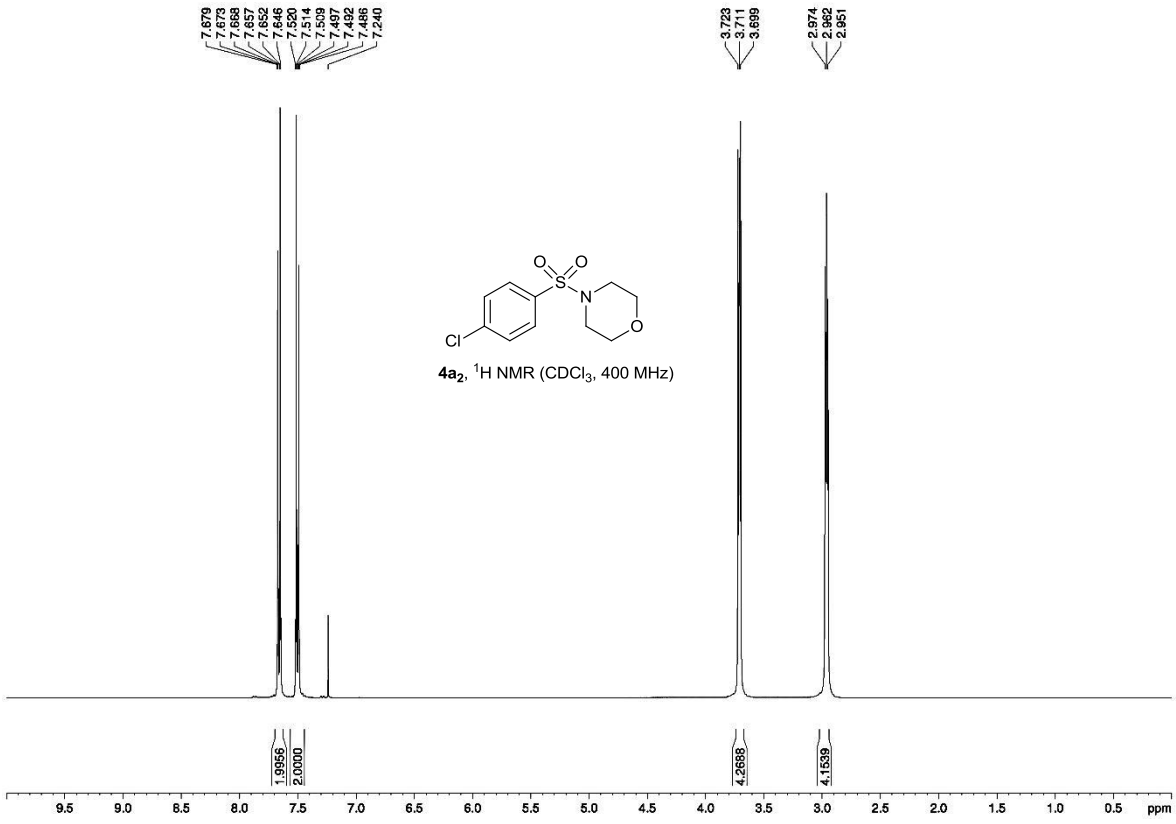


$4a_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

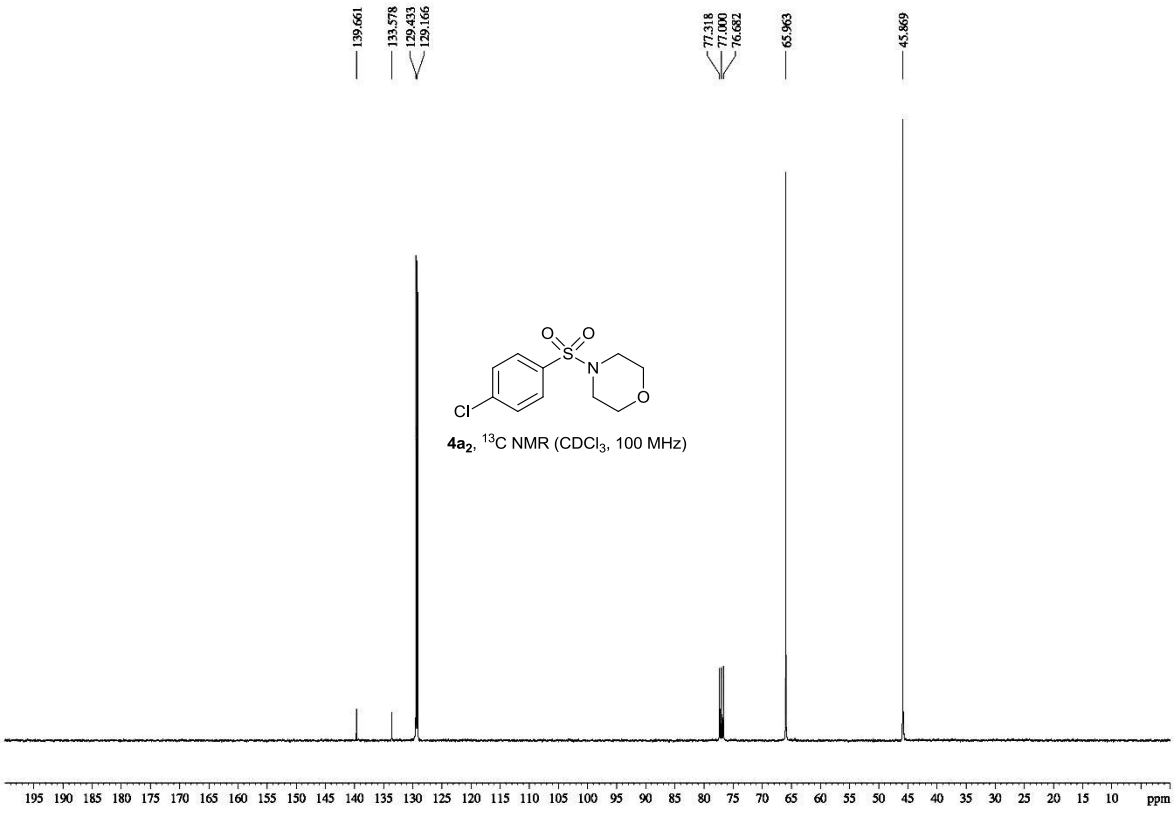


$4a_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-((4-chlorophenyl)sulfonyl)morpholine ($4a_2$).

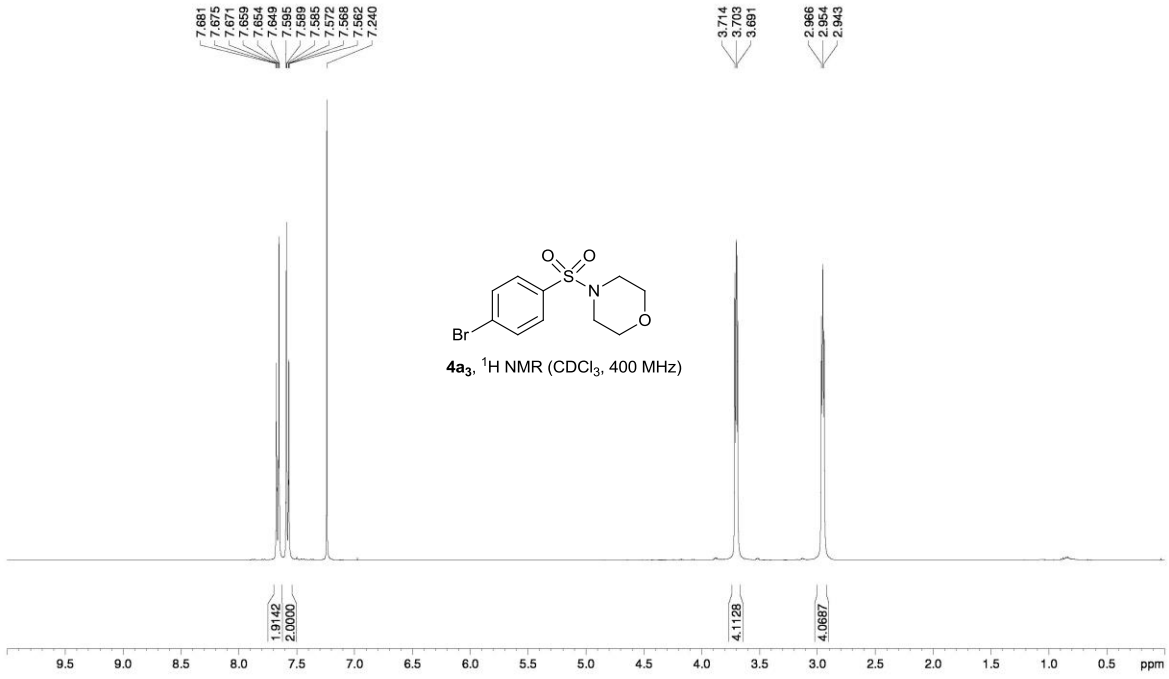


$4a_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

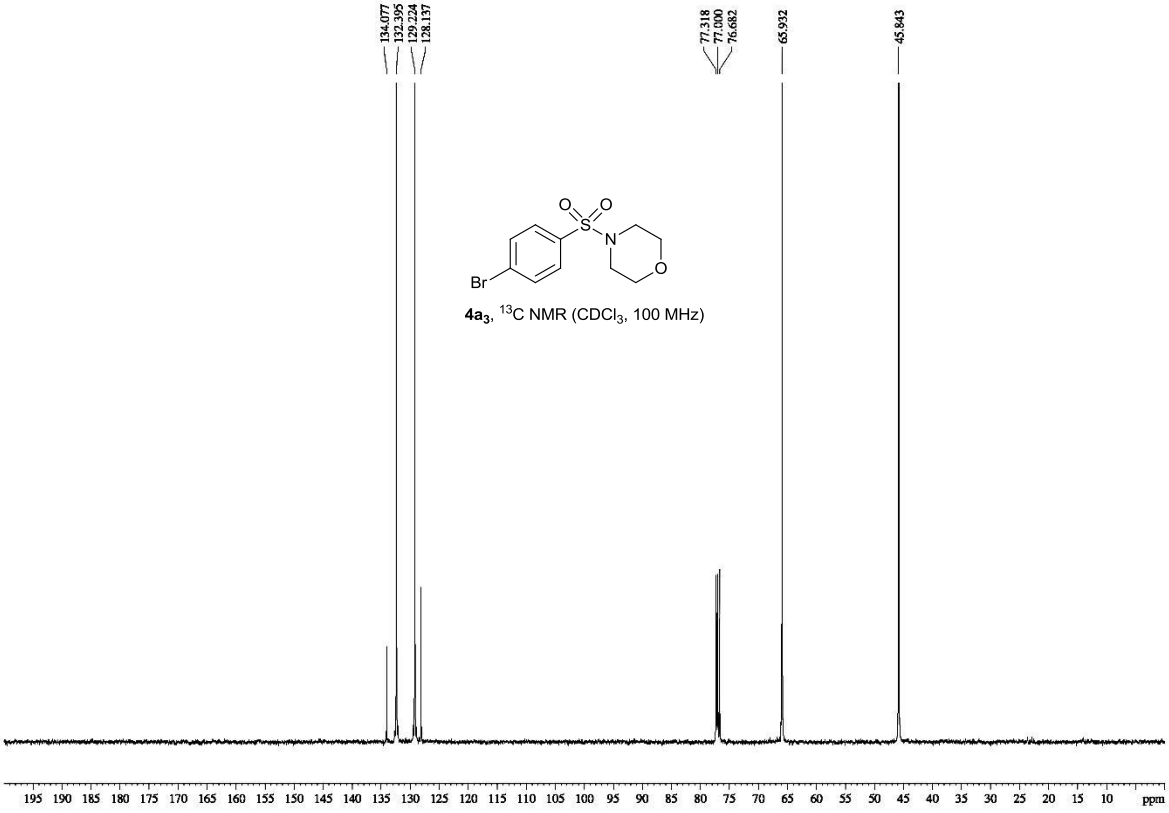


$4a_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-((4-bromophenyl)sulfonyl)morpholine ($4a_3$).

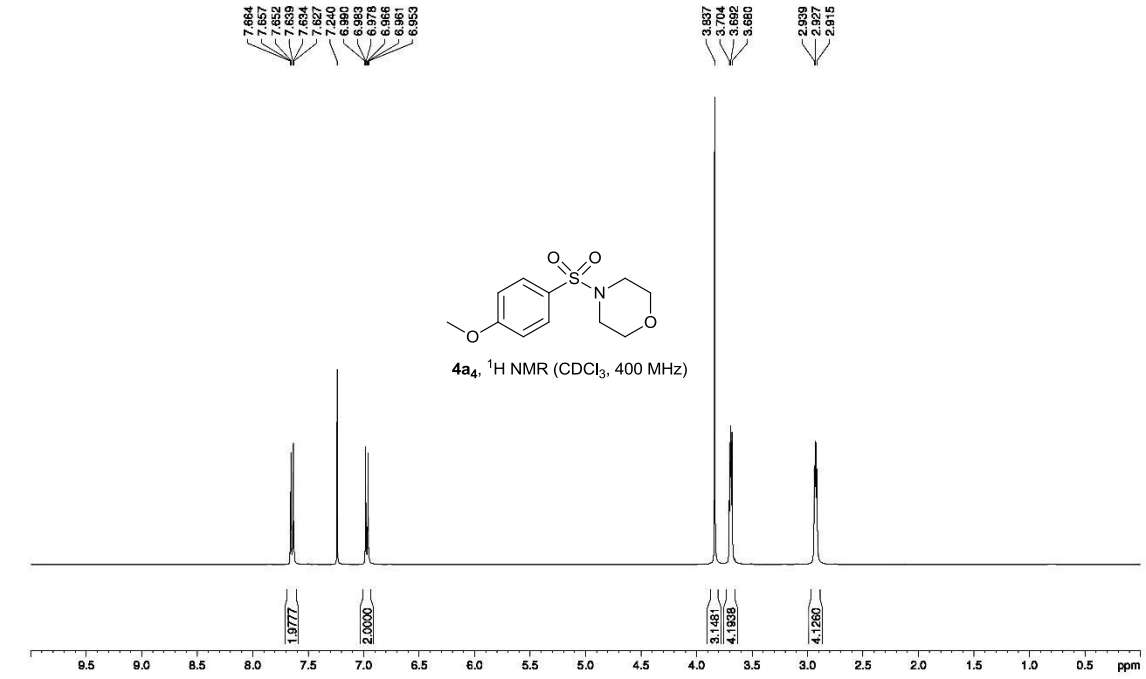


$4a_3$, ^{1}H NMR ($CDCl_3$, 400 MHz)

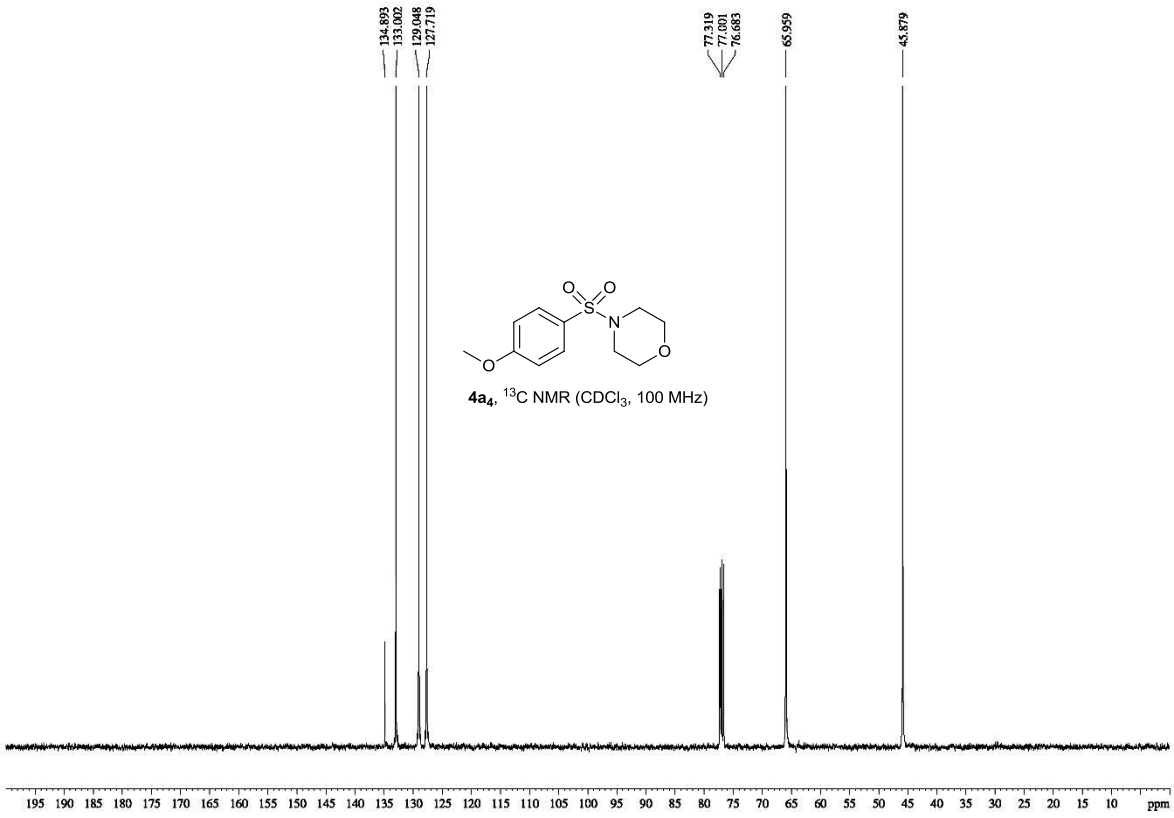


$4a_3$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-((4-methoxyphenyl)sulfonyl)morpholine ($4a_4$).

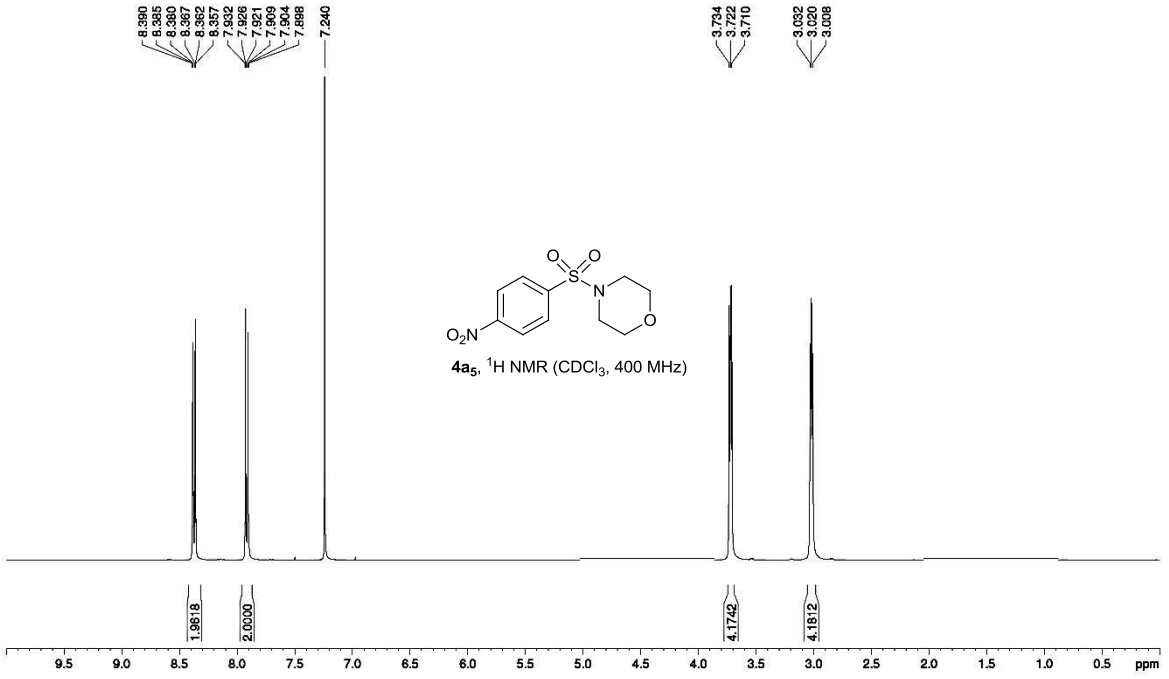


$4a_4$, ^{1}H NMR ($CDCl_3$, 400 MHz)

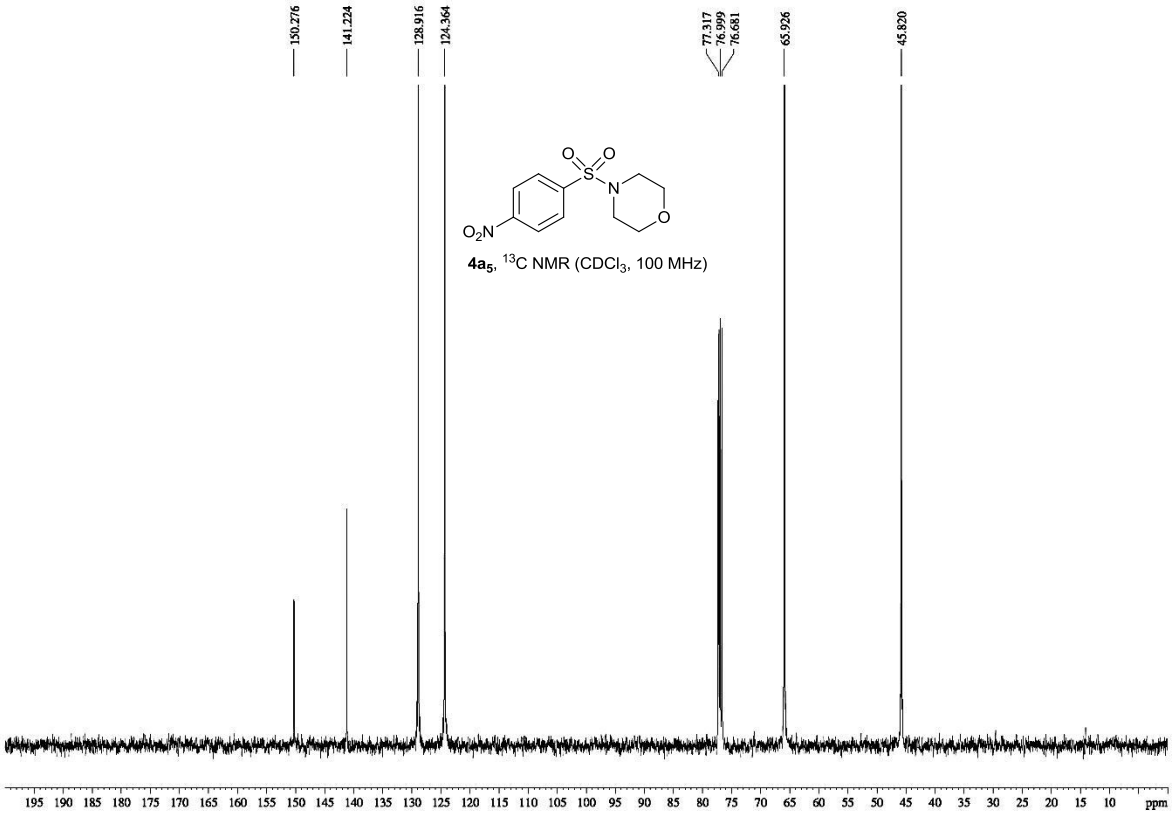


$4a_4$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-((4-nitrophenyl)sulfonyl)morpholine ($4a_5$).

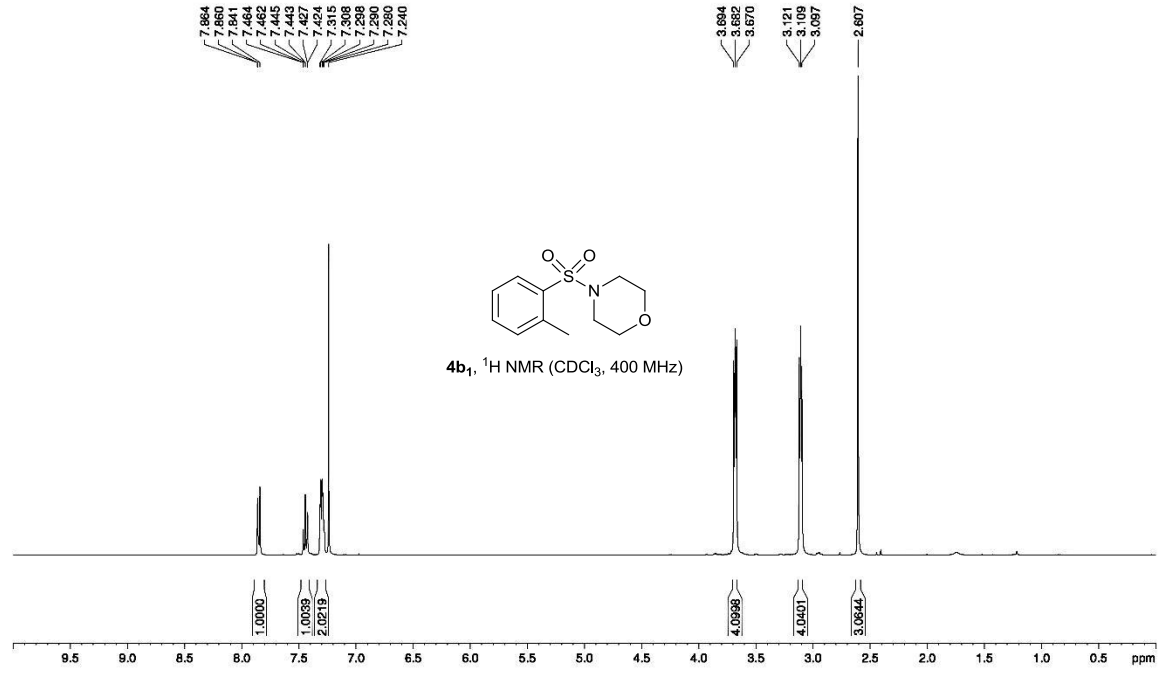


$4a_5$, ^{1}H NMR ($CDCl_3$, 400 MHz)

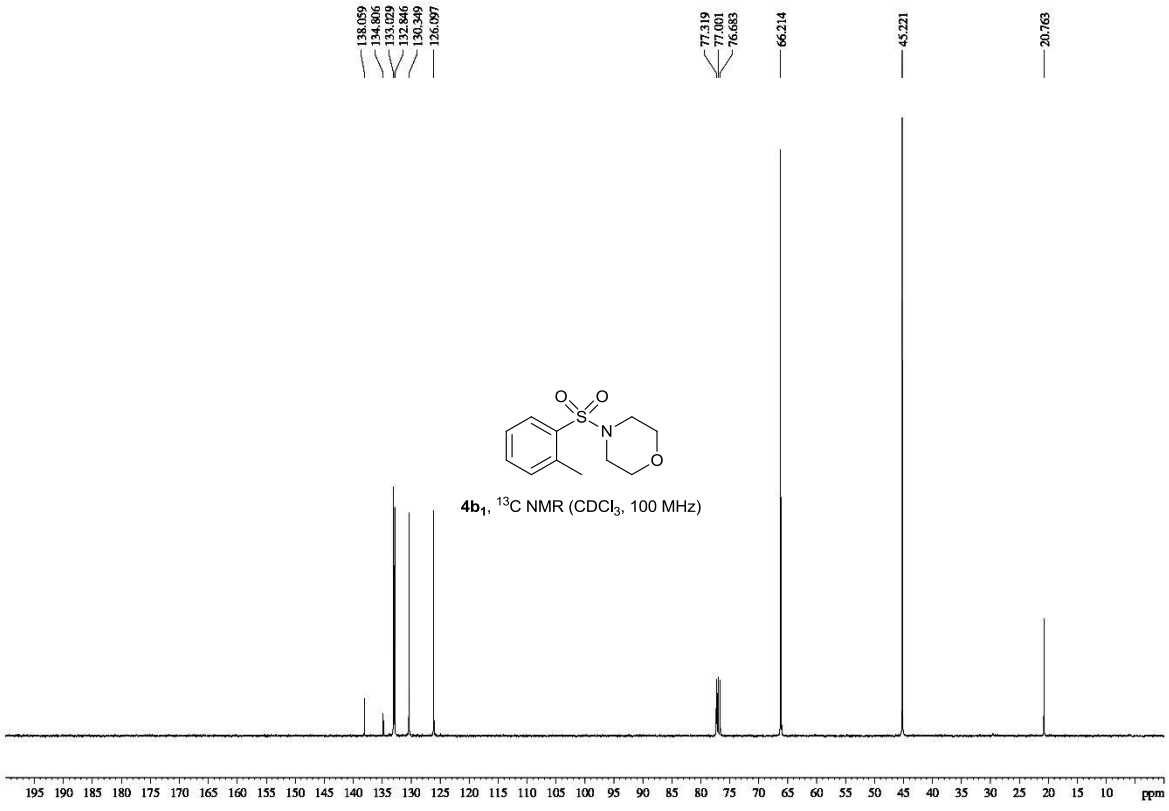


$4a_5$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-(*o*-tolylsulfonyl)morpholine ($4b_1$).

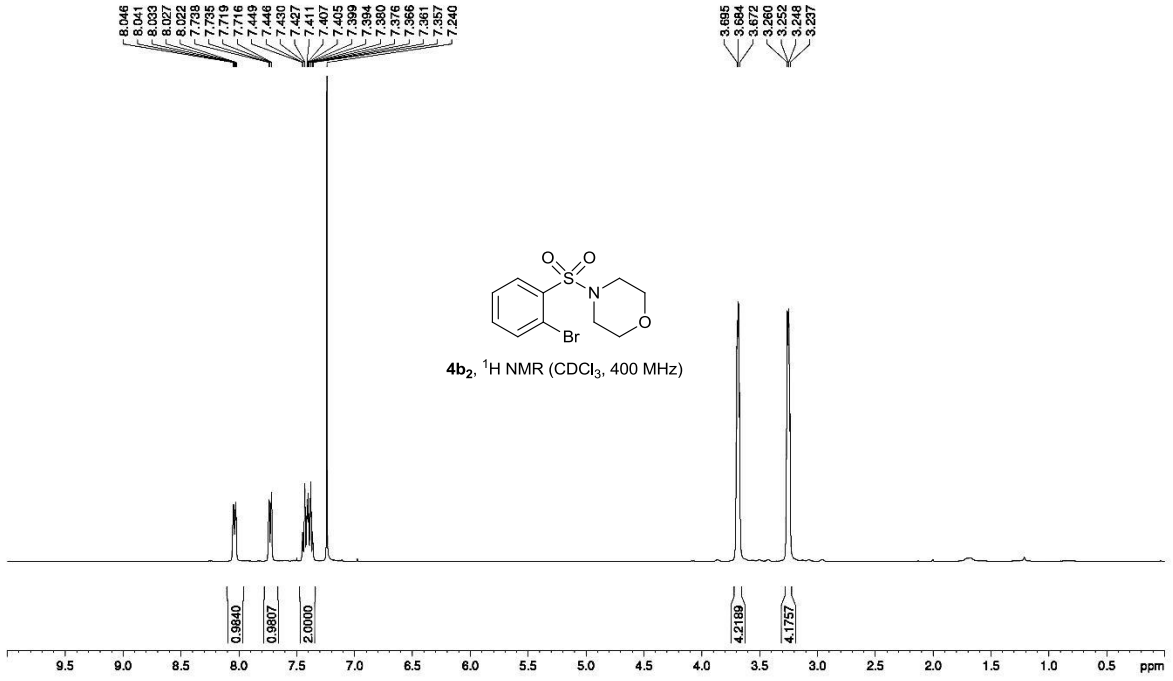


$4b_1$, ^{1}H NMR ($CDCl_3$, 400 MHz)

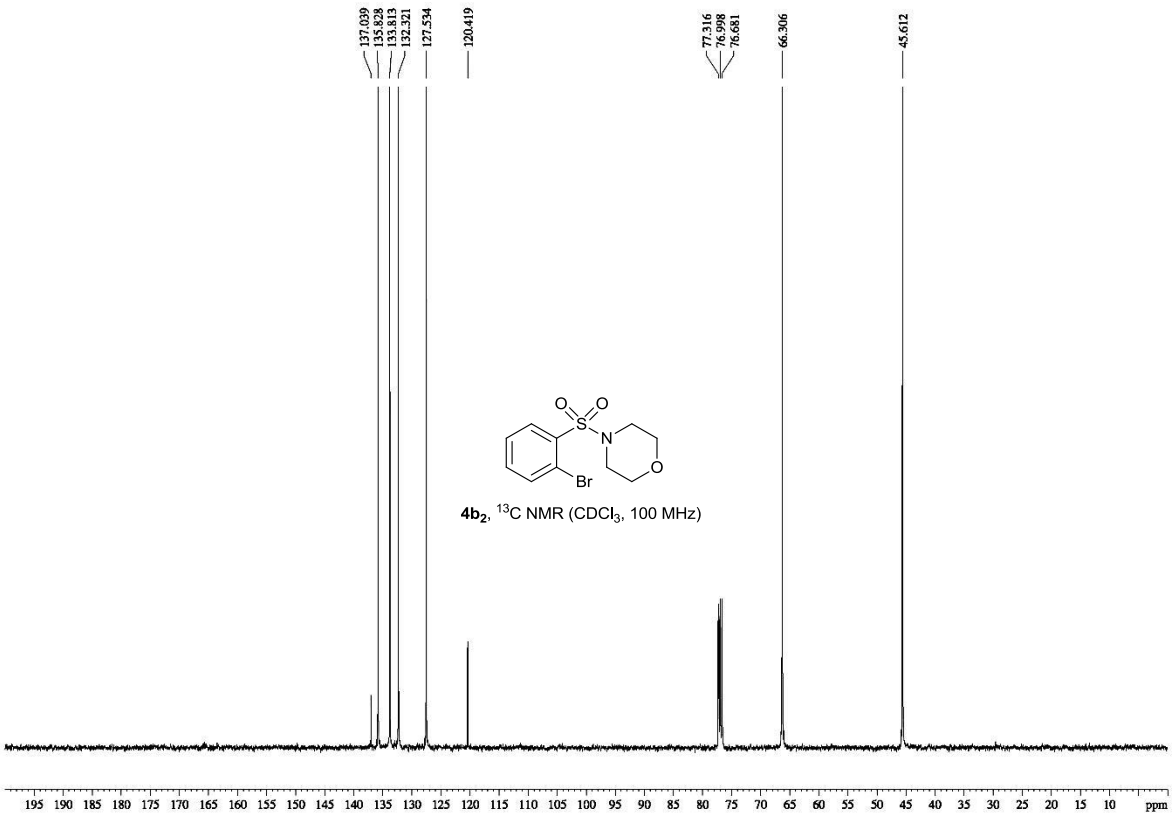


$4b_1$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-((2-bromophenyl)sulfonyl)morpholine ($4b_2$).

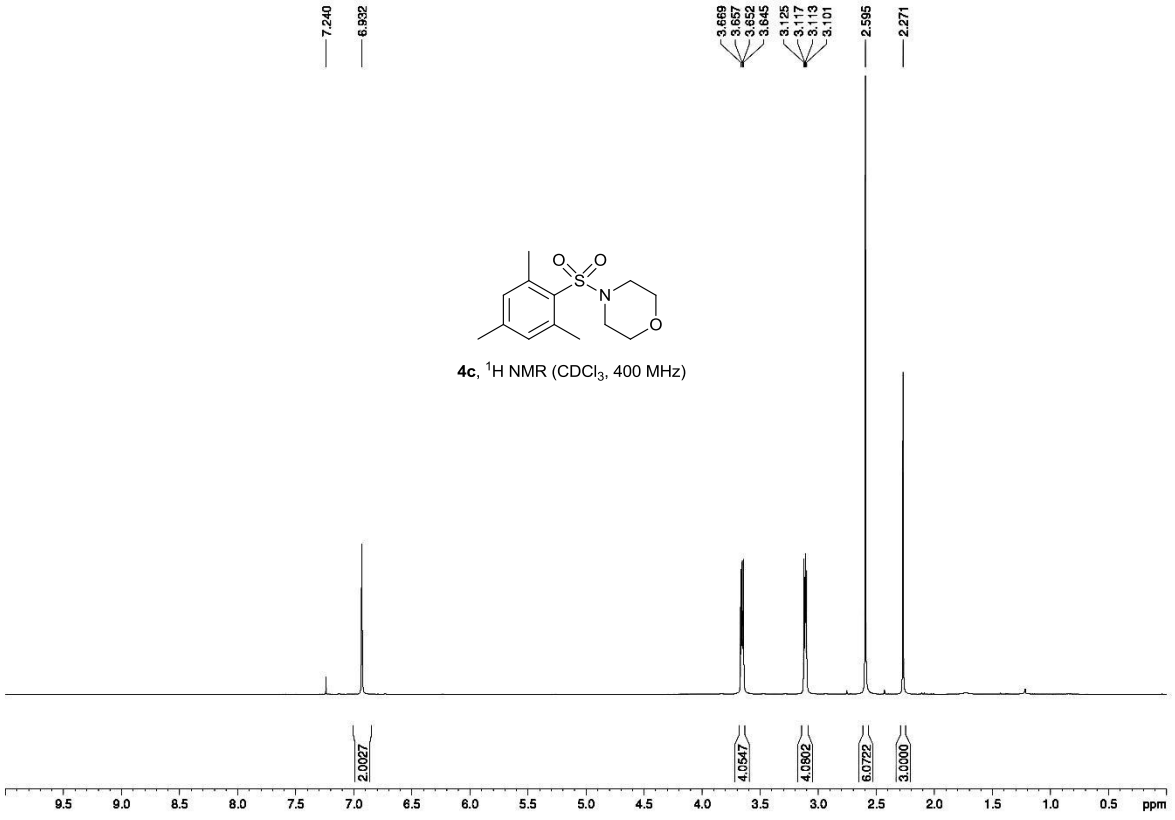


$4b_2$, ^{1}H NMR ($CDCl_3$, 400 MHz)

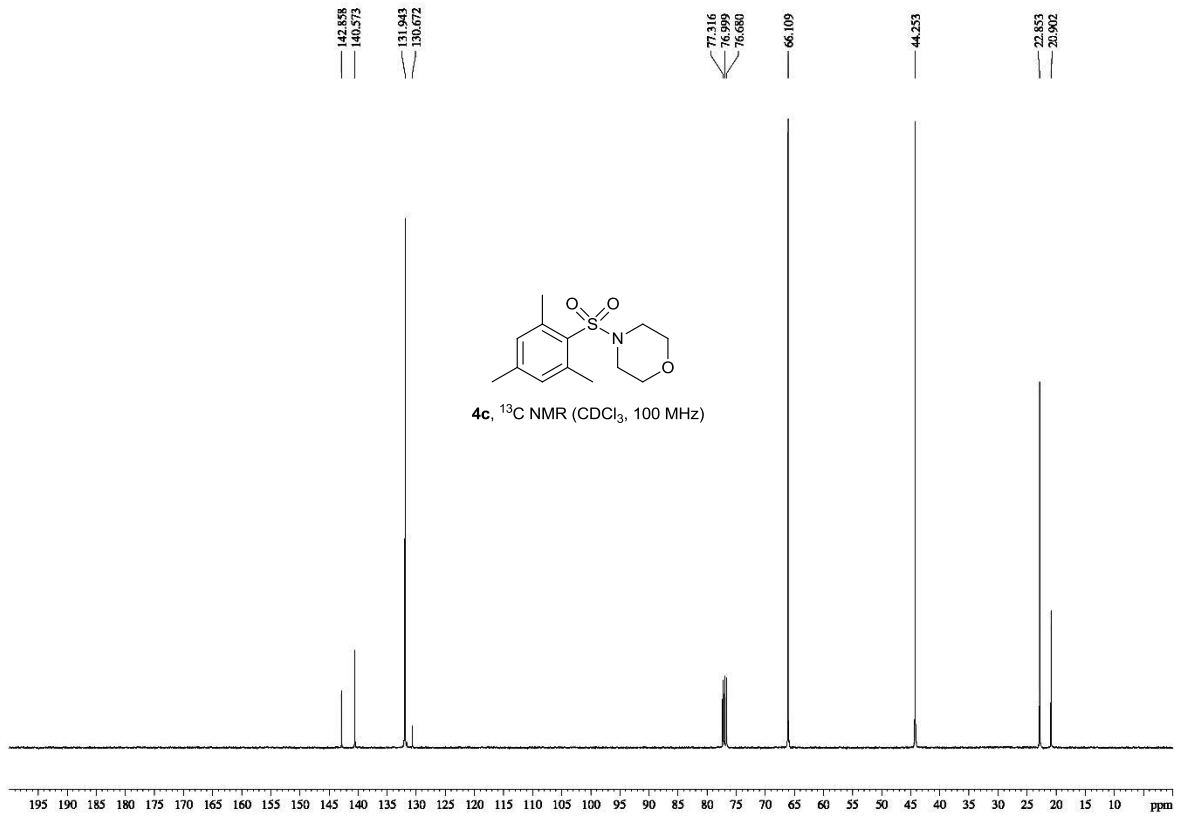


$4b_2$, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-(mesitylsulfonyl)morpholine (4c).

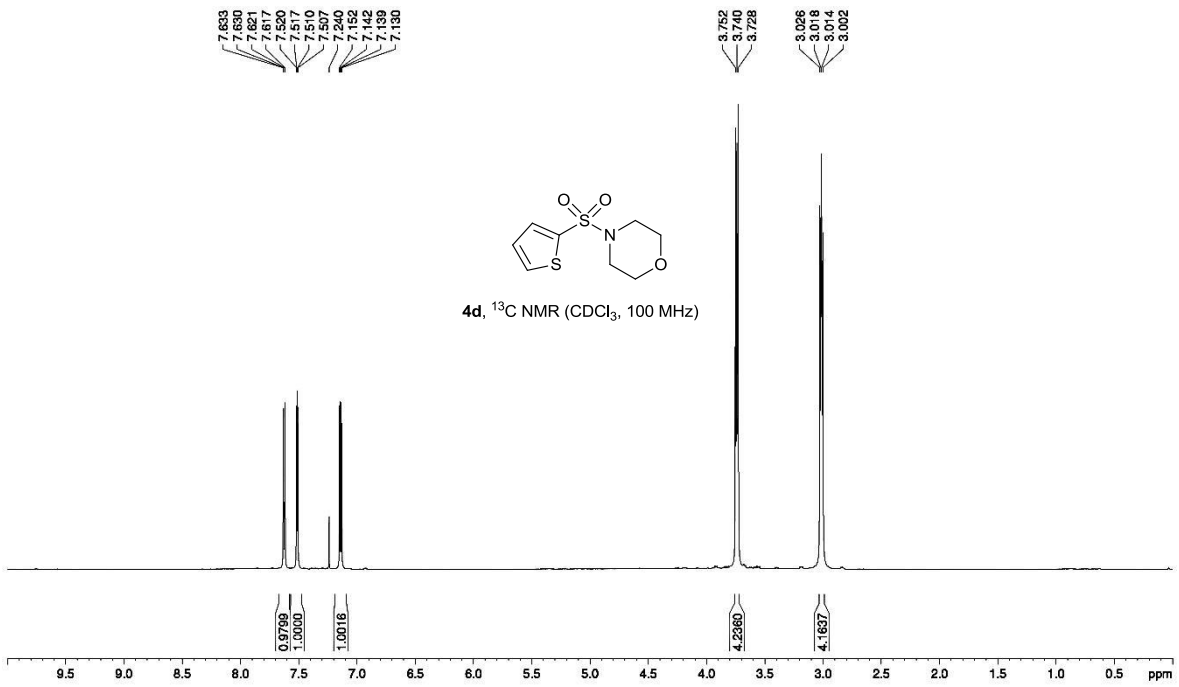


4c, ^{1}H NMR ($CDCl_3$, 400 MHz)

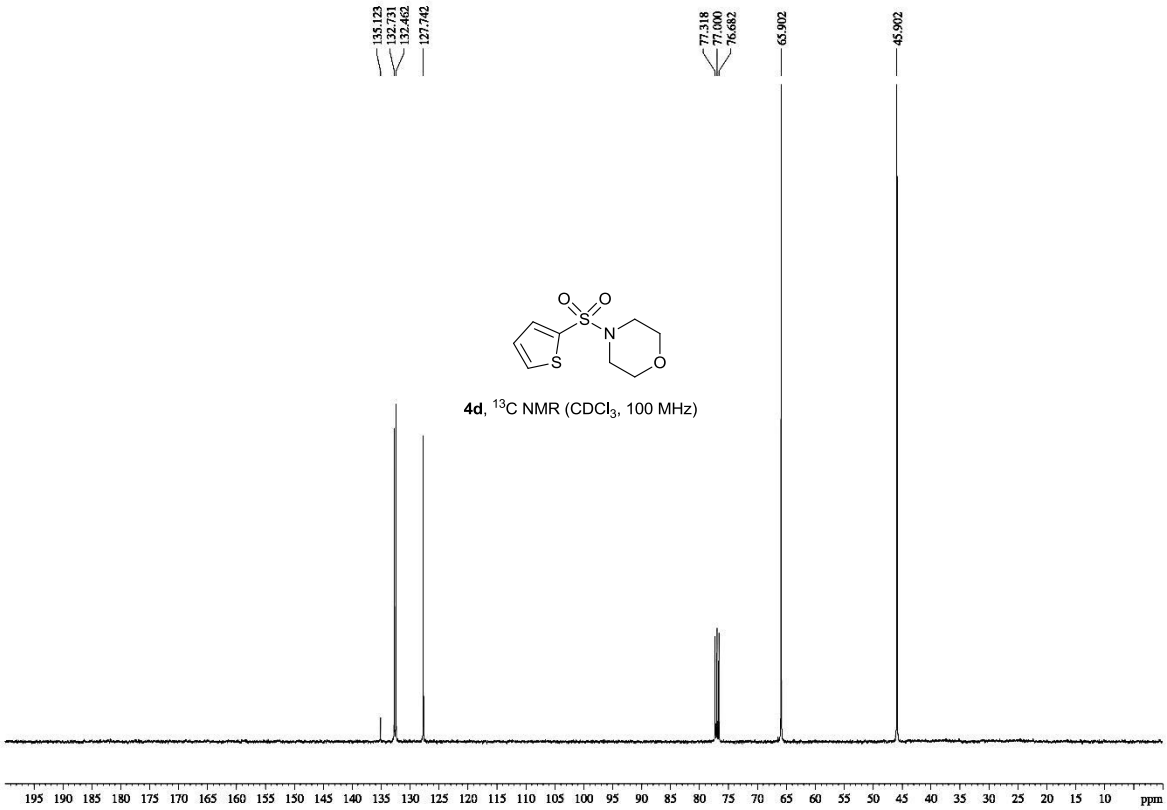


4c, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-(thiophen-2-ylsulfonyl)morpholine (4d).

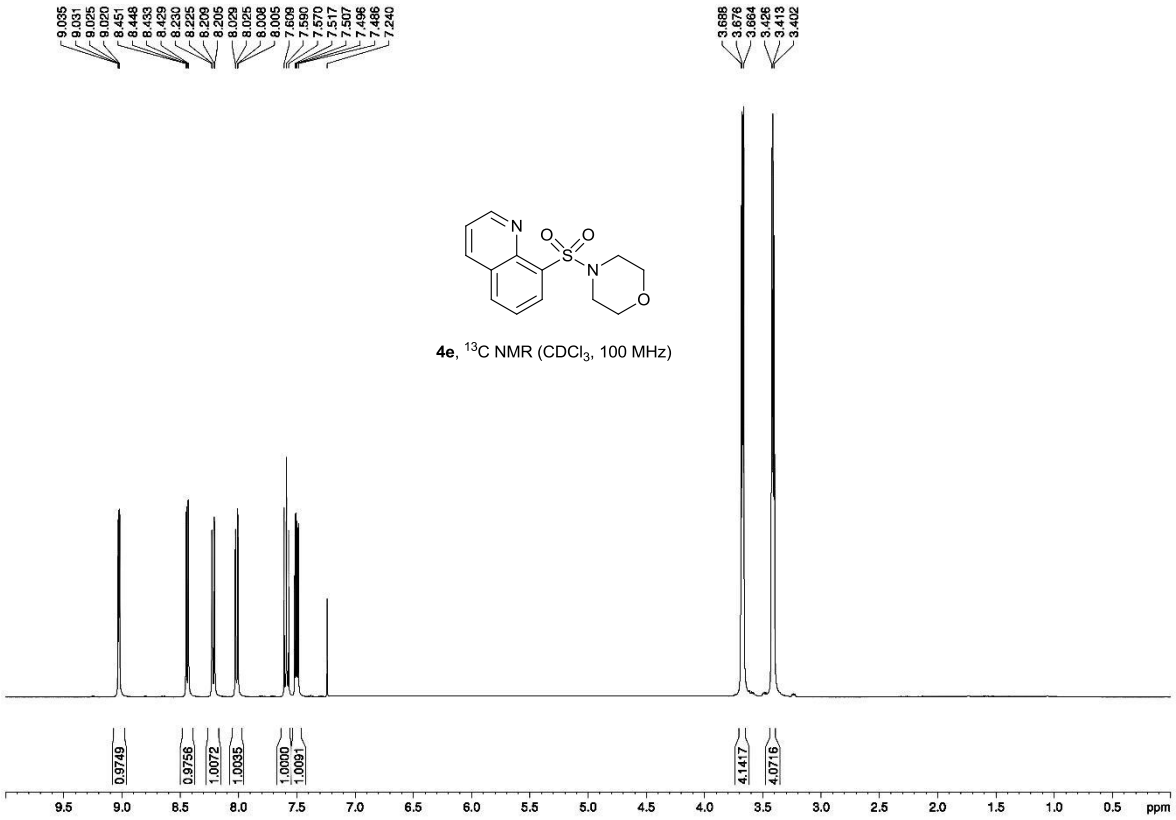


4d, ^{13}C NMR ($CDCl_3$, 100 MHz)

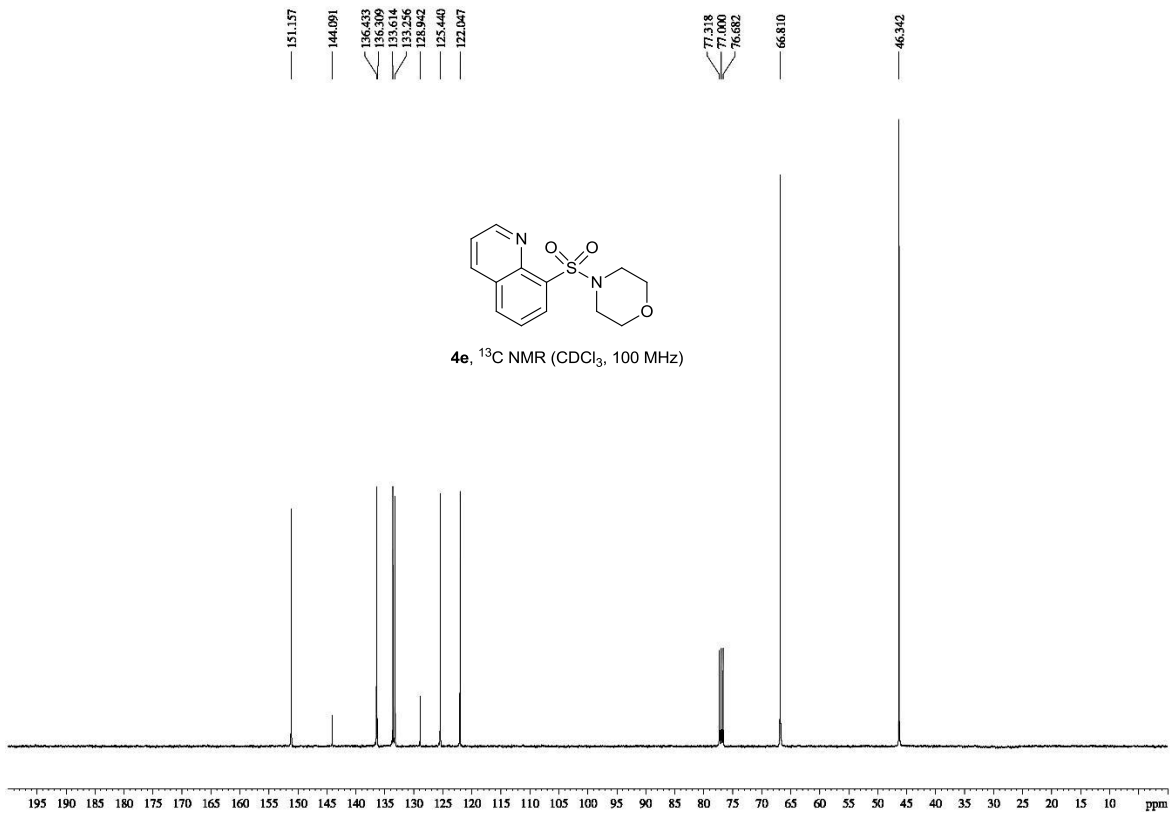


4d, ^{13}C NMR ($CDCl_3$, 100 MHz)

4-(quinolin-8-ylsulfonyl)morpholine (4e).



4e, ^{13}C NMR ($CDCl_3$, 100 MHz)



4e, ^{13}C NMR ($CDCl_3$, 100 MHz)