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Supporting Information

Oxidative Sulfonamidomethylation of Imidazopyridines Utilizing Methanol as the Main C1 Source

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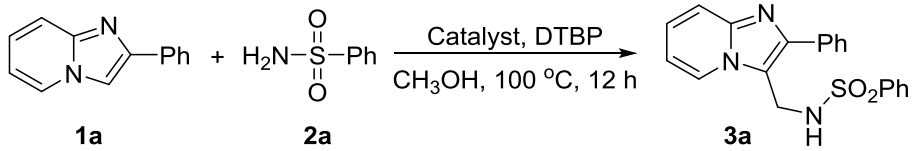
Experimental Section

1.1 Optimization of reaction conditions

Table S1. Optimization of catalysts[a]

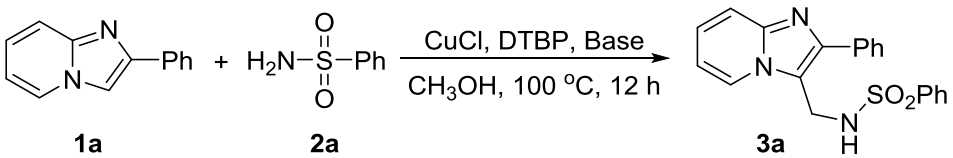


1a **2a** **3a**

Entry	Catalyst	Yield[b] [%]
1	CuCl	18
2	CuBr	Trace
3	CuI	Trace
4	Cu_2O	Trace
5	$[(MeCN)_4Cu]\ PF_6$	N.R.
6	$[(MeCN)_4Cu]\ BF_4$	N.R.
7	$CuCl_2 \cdot 2H_2O$	Trace
8	$Cu(OAc)_2$	Trace
9	$Cu(NO_3)_2 \cdot 3H_2O$	Trace
10	$Cu_2(OH)_2CO_3$	Trace
11	CuO	Trace
12	$Cu(OTf)_2$	Trace
13	$FeCl_2$	N.R.
14	$NiCl_2$	N.R.
15	$NiBr_2$	N.R.
16	$Ni(OT_f)_2$	N.R.
17	-	N.R.
18[c]	CuCl	19
19[d]	**CuCl**	**26**
20[e]	CuCl	24

[a]Reaction conditions:**1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (15 mol %), DTBP (2 equiv), CH_3OH (2 mL), under air, 100 °C, 12 h. [b]Isolated yields. [c]CuCl (0.3 equiv). [d]CuCl (0.5 equiv). [e]CuCl (1 equiv).

Table S2. Optimization of bases[a]



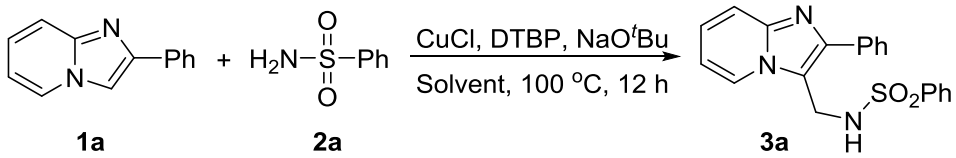
1a **2a** **3a**

Entry	Base	Yield[b] [%]

1	K_2CO_3	10
2	Na_2CO_3	10
3	Cs_2CO_3	9
4	Li_2CO_3	Trace
5	$KHCO_3$	25
6	**NaO^{t}Bu**	**33**
7	KO^{t}Bu	28
8	DABCO	29
9	DBU	19

[a]Reaction conditions:**1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), DTBP (2 equiv), base (1 equiv), CH_3OH (2 mL), under air, 100 °C, 12 h. [b]Isolated yields.

Table S3. Optimization of solvents[a]

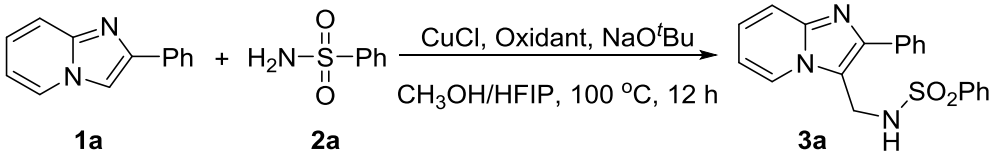


1a **2a** **3a**

Entry	Solvent	Yield[b] [%]
1	DMF	Trace
2	DMSO	Trace
3	DCE	N.R.
4	Toluene	N.R.
5	THF	N.R.
6	CH_3COOH	N.R.
7	PEG400	N.R.
8	CH_3OH	33
9	HFIP	21
10	CH_3CH_2OH	Trace
11[c]	**CH_3OH/HFIP**	**38**
12[d]	CH_3OH/HFIP	31
13[e]	CH_3OH/HFIP	34

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), DTBP (2 equiv), NaO^{t}Bu (1 equiv), solvent (2 mL), under air, 100 °C, 12 h. [b]Isolated yield, [c]CH_3OH/HFIP (v/v = 1/1, 2 mL). [d]NaO^{t}Bu (0.5 equiv). [e]NaO^{t}Bu (2 equiv).

Table S4. Optimization of oxidants[a]

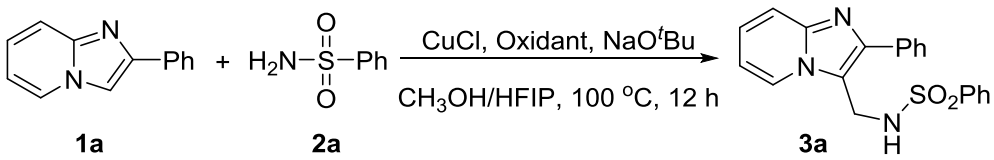


1a **2a** **3a**

Entry	Oxidant	Yield[b] [%]
1	DTBP	38
2	TBHP	47
3	$K_2S_2O_8$	Trace
4	DDQ	N.R.
5	Ag_2O	54
6	Ag_2CO_3	31
7	AgOAc	N.R.
8	$Mn(OAc)_2$	Trace
9	**$KMnO_4$**	**68**
10[c]	$KMnO_4$	30
11[d]	$KMnO_4$	52
12[e]	$KMnO_4$	70

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), oxidant (2 equiv), NaO^{t}Bu (1 equiv), CH_3OH/HFIP (v/v = 1/1, 2 mL), under air, 100 ^{o}C, 12 h. [b]Isolated yield. [c]$KMnO_4$ (0.5 equiv). [d]$KMnO_4$ (1 equiv). [e]$KMnO_4$ (3 equiv).

Table S5. Optimization of ratio of oxidant combinations[a]

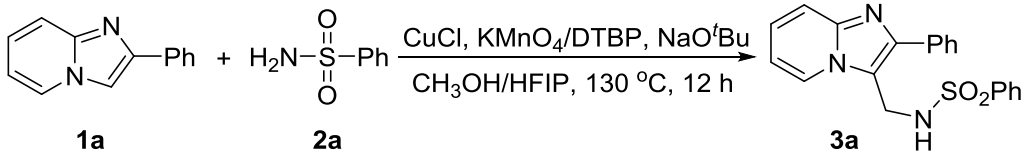


1a **2a** **3a**

Entry	Oxidant	Ratio	Yield[b] [%]
1	$KMnO_4$/DTBP	2/1	78
2	$KMnO_4$/ Ag_2O	2/1	79
3	$KMnO_4$/TBHP	2/1	66
4	$KMnO_4$/DTBP	1/1	56
5	$KMnO_4$/DTBP	1/2	65
6[c]	$KMnO_4$/DTBP	1/2	74
7[d]	**$KMnO_4$/DTBP**	**1/2**	**79**
8[e]	$KMnO_4$/DTBP	1/2	79

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), oxidant (3 equiv), NaO^{t}Bu (1 equiv), CH_3OH/HFIP (v/v = 1/1, 2 mL), under air, 100 ^{o}C, 12 h. [b]Isolated yield. [c]120 ^{o}C. [d]130 ^{o}C, [e]140 ^{o}C.

Table S6. Optimization of ratio of Solvents[a]

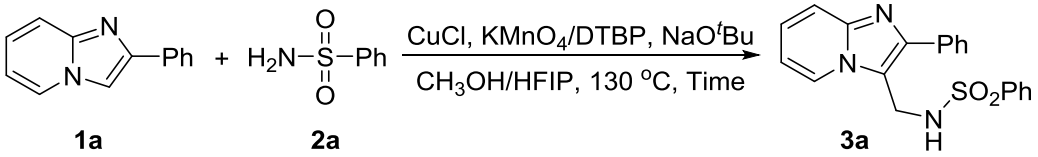


1a **2a** **3a**

Entry	Solvent	Ratio	Yield[b] [%]
1	CH_3OH/HFIP	1/9	42
2	CH_3OH/HFIP	2/8	43
3	CH_3OH/HFIP	3/7	47
4	CH_3OH/HFIP	4/6	58
5	CH_3OH/HFIP	5/5	79
6	CH_3OH/HFIP	6/4	83
7	CH_3OH/HFIP	7/3	82
8	CH_3OH/HFIP	8/2	85
9	**CH_3OH/HFIP**	**9/1**	**87**

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), DTBP (2 equiv), $KMnO_4$ (1 equiv), NaO^{t}Bu (1 equiv), CH_3OH/HFIP (2 mL), under air, 130 ^{o}C, 12 h. [b]Isolated yield.

Table S7. Optimization of reaction time[a]

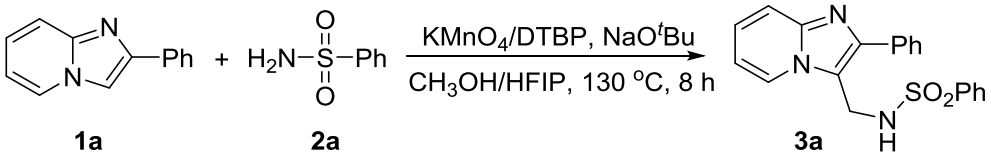


1a **2a** **3a**

Entry	Time (h)	Yield[b] [%]
1	10	85
2	**8**	**85**
3	6	80
4	4	71
5	2	65
6[c]	8	85

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), CuCl (0.5 equiv), DTBP (2 equiv), $KMnO_4$ (1 equiv), NaO^{t}Bu (1 equiv), CH_3OH/HFIP (v/v = 9/1, 2 mL), under air, 130 ^{o}C. [b]Isolated yield. [c]Without CuCl.

Table S8. Optimization of ratio of reactants[a]



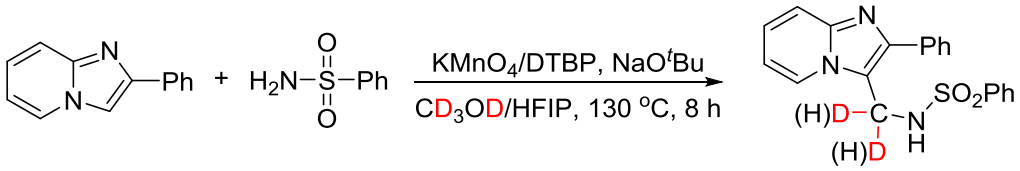
1a **2a** **3a**

Entry	**1a** (equiv)	**2a** (equiv)	Yield[b] [%]
1	1	1	74
2	1	1.5	78
3	**1**	**2**	**85**
4	1	2.5	86
5	1	3	86

[a]Reaction conditions: **1a** (0.1 mmol), **2a**, DTBP (2 equiv), $KMnO_4$ (1 equiv), NaO^tBu (1 equiv), CH_3OH/HFIP (v/v = 9/1, 2 mL), air atmosphere, 130 [o]C, 8 h. [b]Isolated yield.

1.2 Control experiments and mechanistic studies

a) Isotopic labeling experiment



1a **2a**

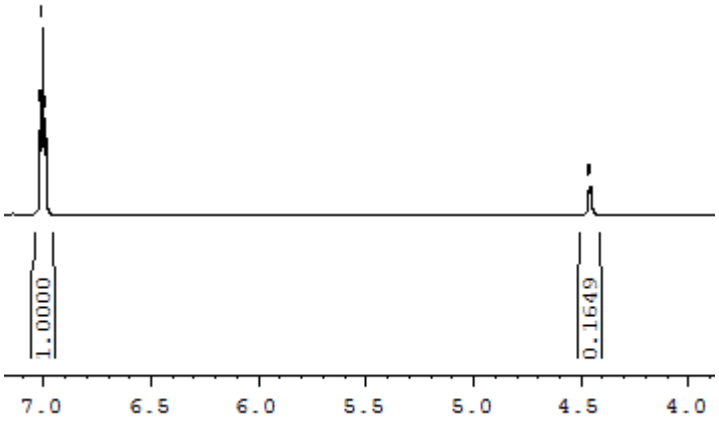
3a-d_2, 66% (D% = 92%)

w/o DTBP 50% (D% = 100%)

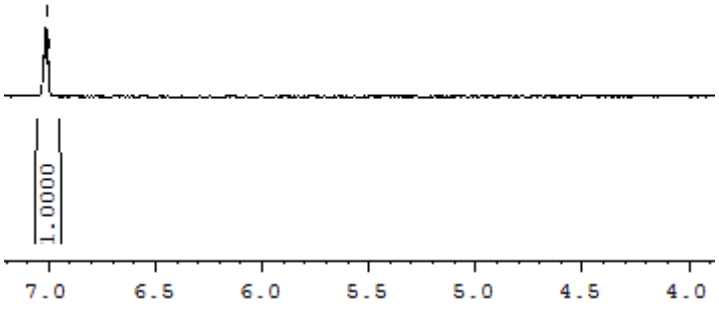
w/o $KMnO_4$ 14% (D% = 72%)

To a 15 mL sealed tube were added imidazo[1,2-α]pyridine **1a** (0.1 mmol, 19.4 mg), benzenesulfonamide **2a** (0.2 mmol, 31.4 mg), NaO^tBu (0.1 mmol, 9.6 mg), and oxidant: {$KMnO_4$ (0.1 mmol, 15.8 mg) and DTBP (0.2 mmol, 24.2 mg); or $KMnO_4$ (0.1 mmol, 15.8 mg); or DTBP (0.2 mmol, 24.2 mg)} in CD_3OD/HFIP (v/v = 9/1, 2 mL) under air. The reaction mixture was stirred at 130 ℃ for 8 h and then cooled to room temperature. After removal of solvent under reduced pressure, the residue was purified by preparative TLC on silica gel plates using petroleum ether/EtOAc as the eluent to give the corresponding products **3a**-d_2 in 66% (D% = 92%), 50% (D% = 100%), or 14% (D% = 72%) yield.

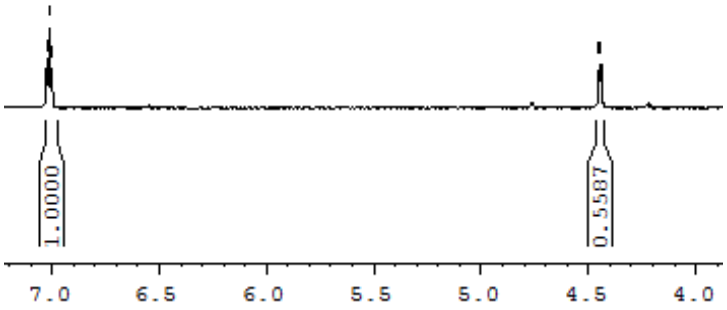
^{1}H NMR (600 MHz, DMSO-d_6) δ 8.26 (d, J = 5.2 Hz, 2H), 7.79 (d, J = 7.7 Hz, 2H), 7.65 (dd, J = 13.0, 7.1 Hz, 3H), 7.58 (dd, J = 17.7, 9.1 Hz, 3H), 7.42 – 7.29 (m, 4H), 7.00 (t, J = 6.7 Hz, 1H), 4.46 (d, J = 5.0 Hz, 0.16H or 0H or 0.56H). ^{13}C{H} NMR (101 MHz, DMSO-d_6) δ 144.2, 143.7, 139.5, 133.8, 132.6, 129.1, 128.4, 128.1, 127.7, 126.4, 125.3, 124.6, 116.7, 114.8, 112.3.



Using $KMnO_4$/DTBP (1)

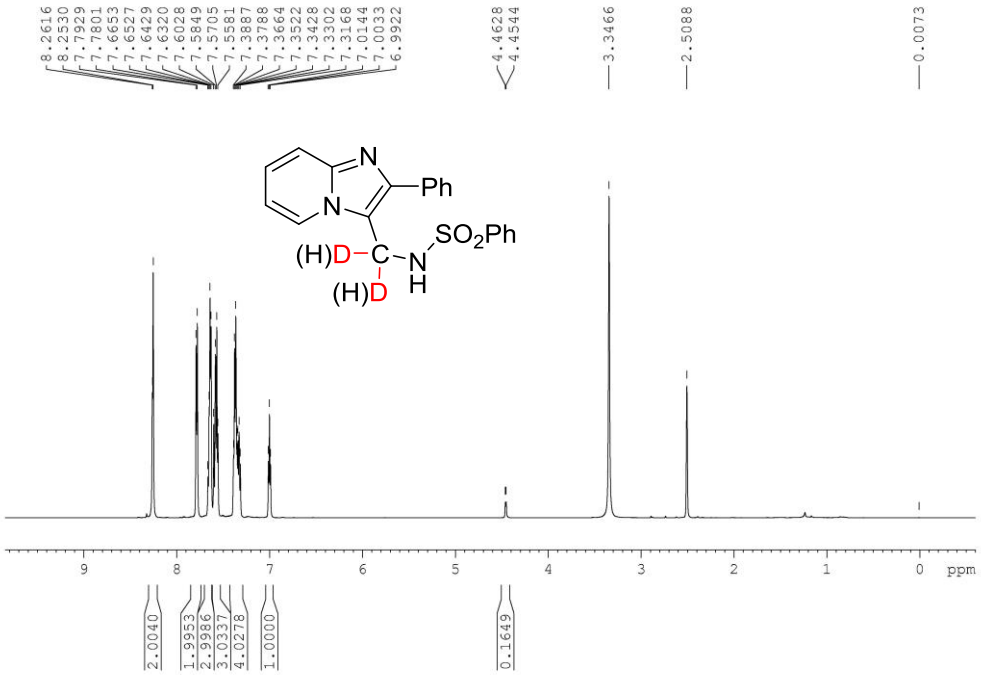


Using $KMnO_4$ (2)

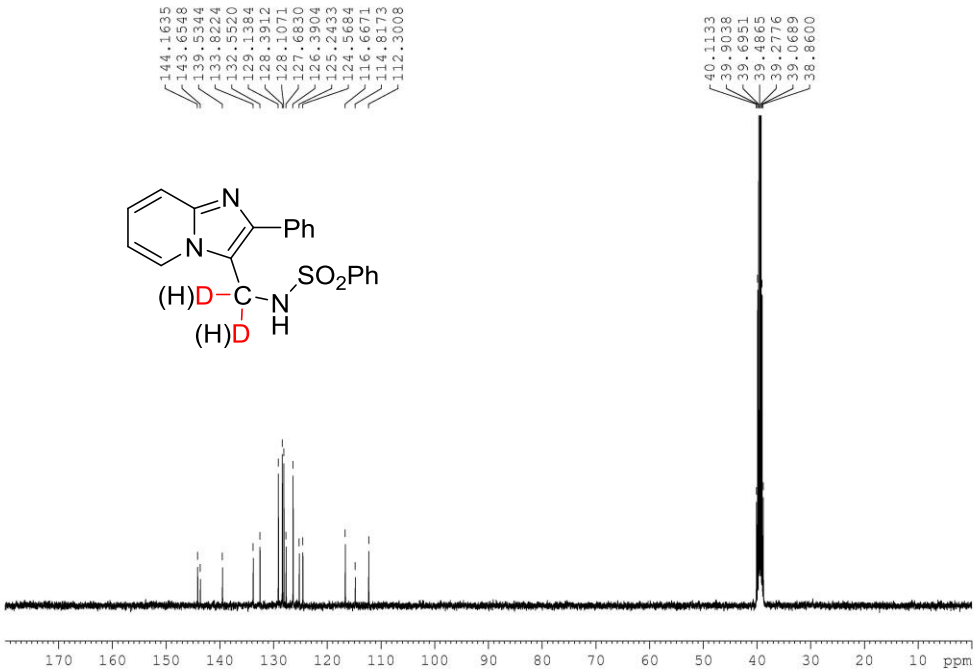


Using DTBP (3)

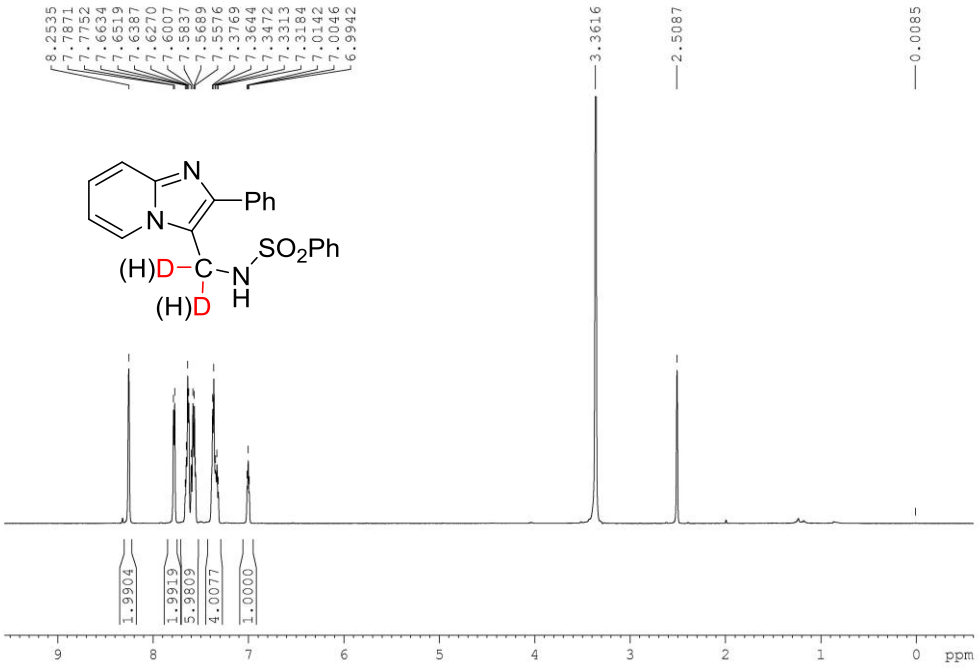
^{1}H NMR of compound **3a**-d_2 (Using both $KMnO_4$/DTBP as oxidant)



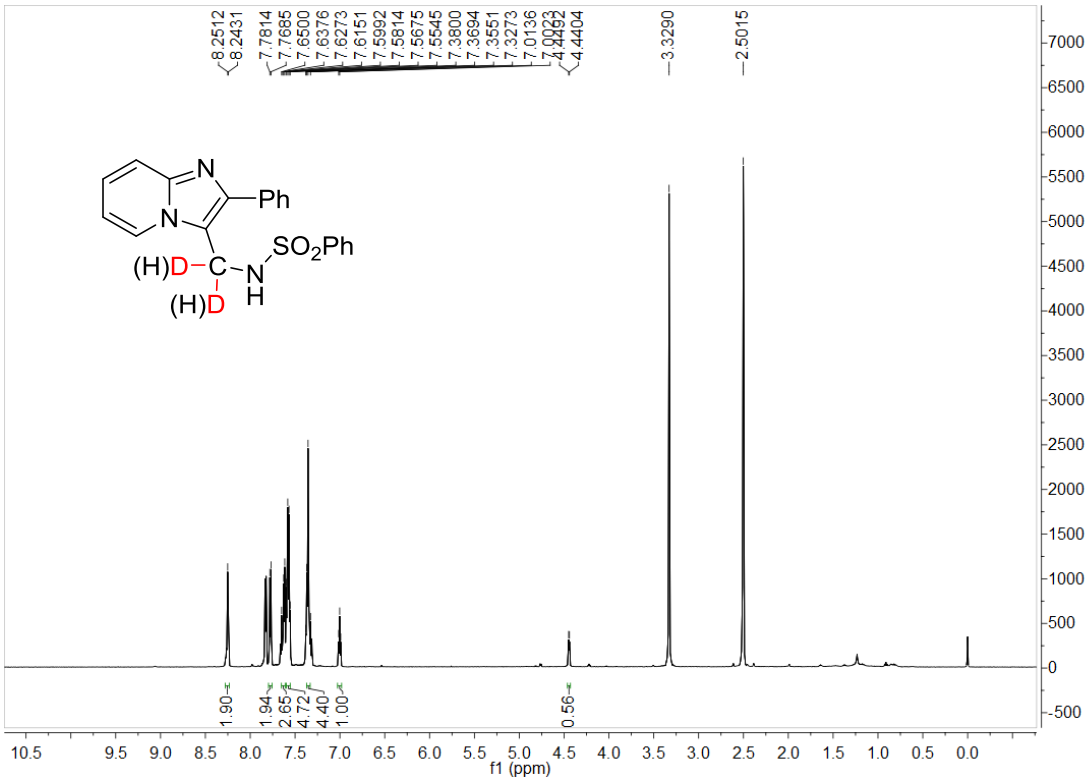
^{13}C NMR of compound **3a**-d_2 (Using both $KMnO_4$/DTBP as oxidant)



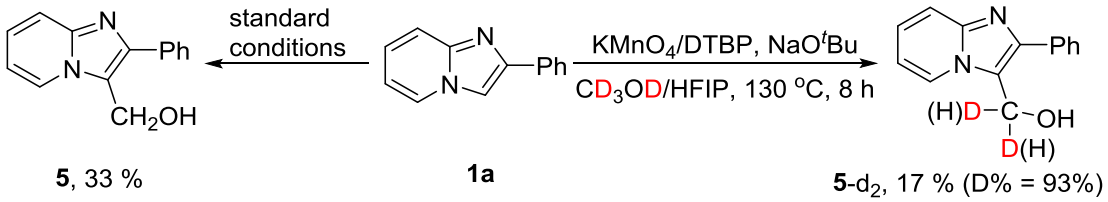
^{1}H NMR of compound **3a**-d_2 (Using $KMnO_4$ as oxidant)



^{1}H NMR of compound **3a**-d_2 (Using DTBP as oxidant)



b) Synthesis of 5 and 5-d_2

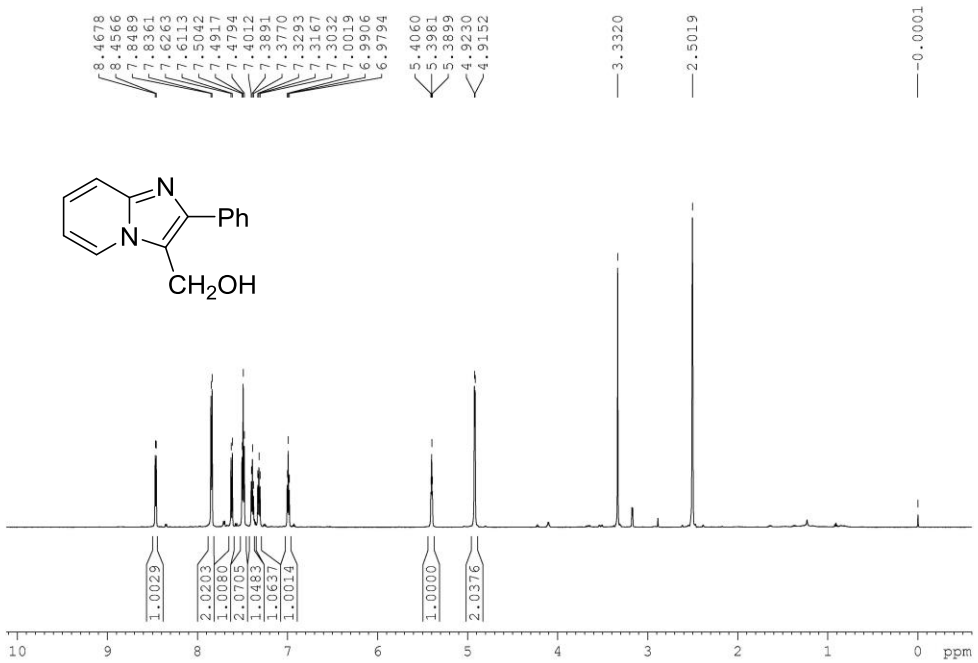


5, 33 % **1a** **5**-d_2, 17 % (D% = 93%)

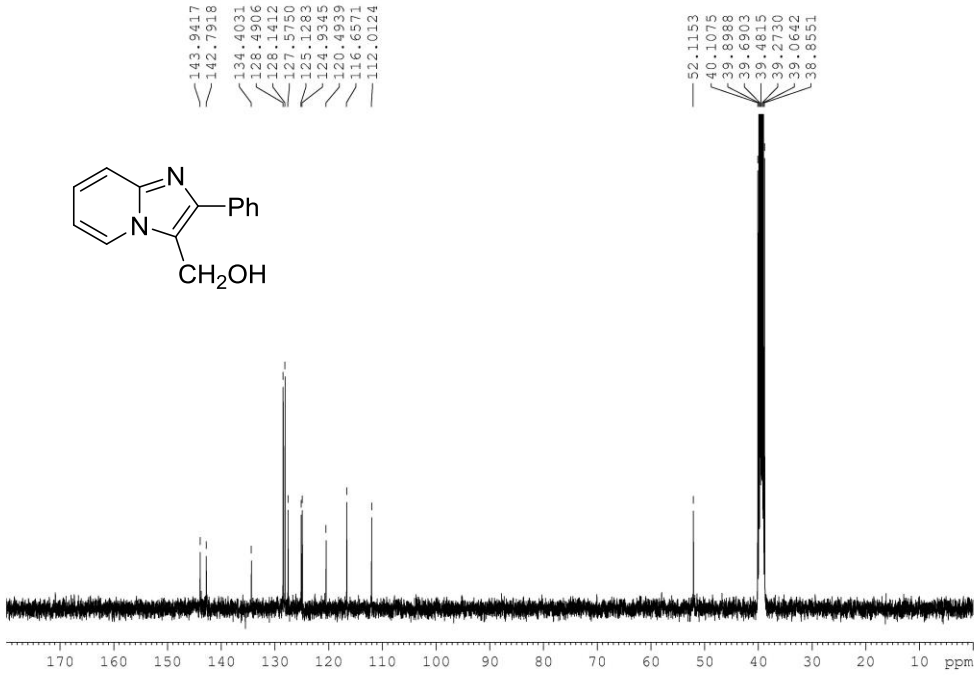
Characterization of **5**: ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.46 (d, J = 6.8 Hz, 1H), 7.84 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 9.0 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.34 – 7.28 (m, 1H), 6.99 (t, J = 6.7 Hz, 1H), 5.40 (t, J = 4.8 Hz, 1H), 4.92 (d, J = 4.7 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 143.9, 142.8, 134.4, 128.5, 128.1, 127.6, 125.1, 124.9, 120.5, 116.7, 112.0, 52.1.

Characterization of **5**-d_2: ^{1}H NMR (600 MHz, DMSO) δ 8.47 (d, J = 6.8 Hz, 1H), 7.85 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 9.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 7.00 (t, J = 6.7 Hz, 1H), 5.37 (s, 1H), 4.92 (d, J = 5.2 Hz, 0.14H). ^{13}C NMR (151 MHz, DMSO) δ 144.5, 143.3, 134.9, 129.0, 128.6, 128.1, 125.6, 125.43, 121.0, 117.2, 112.5.

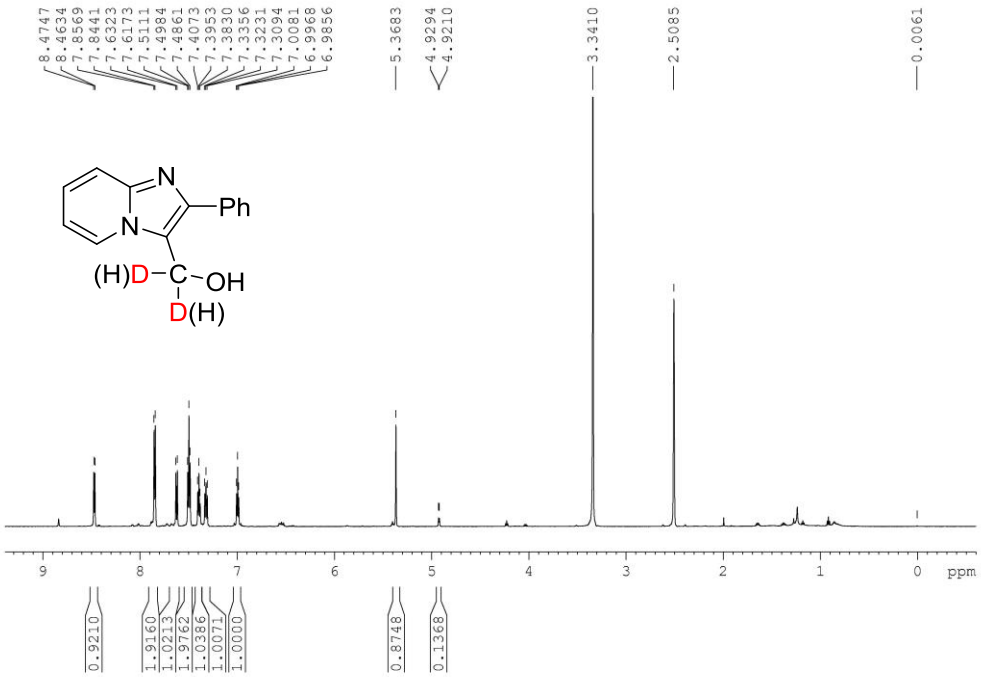
^{1}H NMR of compound **5**



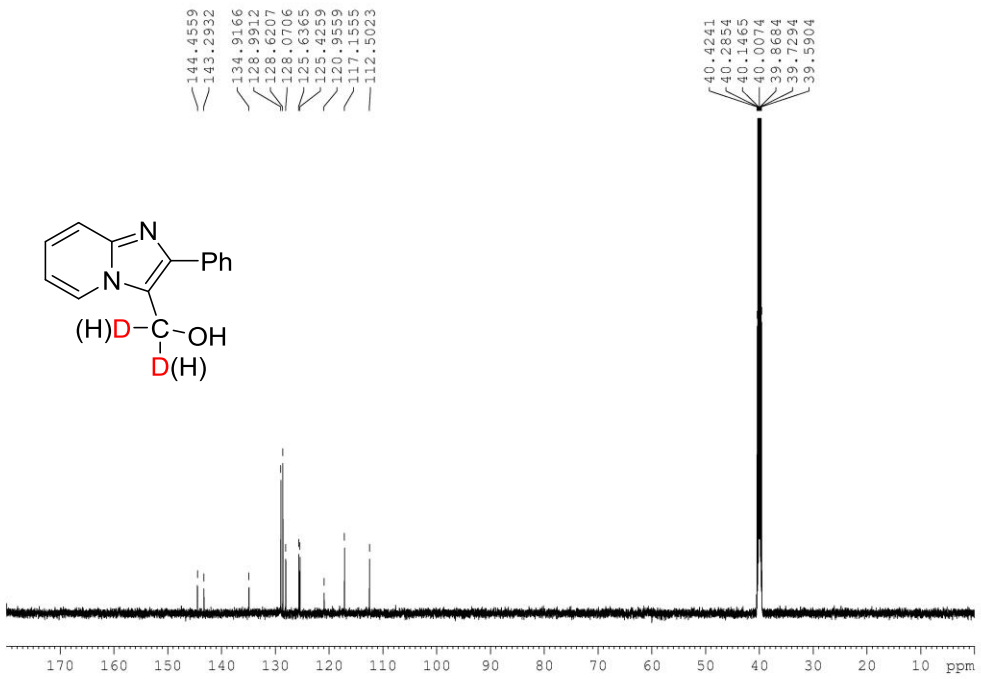
^{13}C NMR of compound **5**



^{1}H NMR of compound **5**-d_2



^{13}C NMR of compound **5**



1.3 X-Ray data of 3a

Table S9. Crystal data and structure refinement of **3a**

Identification code	201806282
Empirical formula	$C_{20}H_{17}N_3O_2S$
Formula weight	363.42
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.3160(2)
b/Å	19.1755(5)
c/Å	12.7269(5)
α/°	90
β/°	103.311(4)
γ/°	90
Volume/Å^3	1737.47(10)
Z	4
ρ_{calc}g/cm^3	1.389
μ/mm^{-1}	1.820
F(000)	760.0

Crystal size/mm^3	0.18 ×0.15 ×0.13
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.5 to 134.138
Index ranges	-6 ≤ h ≤ 8, -22 ≤ k ≤ 22, -15 ≤ l ≤ 15
Reflections collected	6661
Independent reflections	3094 [R_{int} = 0.0256, R_{sigma} = 0.0350]
Data/restraints/parameters	3094/6/287
Goodness-of-fit on F^2	1.015
Final R indexes [I>=2σ (I)]	R_1 = 0.0913, wR_2 = 0.1988
Final R indexes [all data]	R_1 = 0.0971, wR_2 = 0.2019
Largest diff. peak/hole / e Å^{-3}	0.35/-0.28

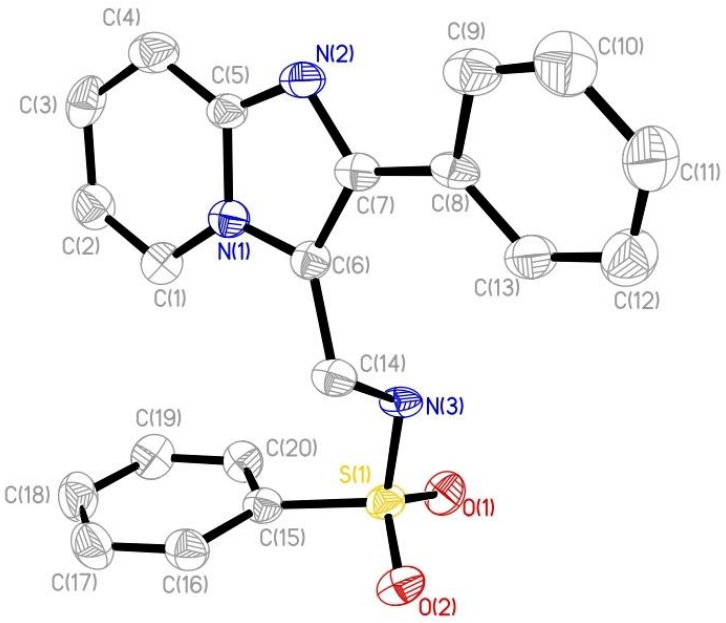
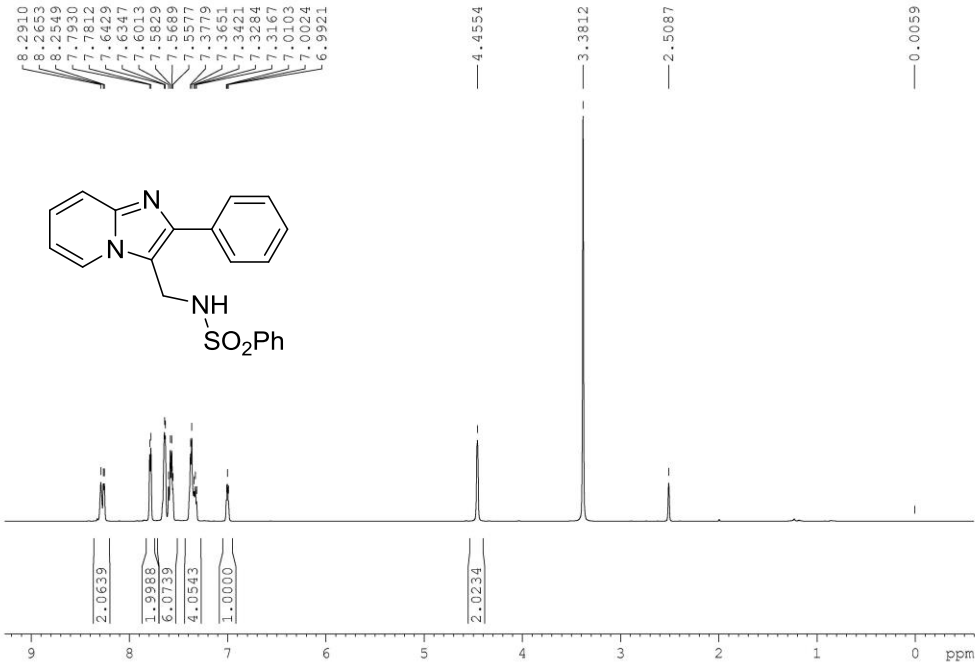


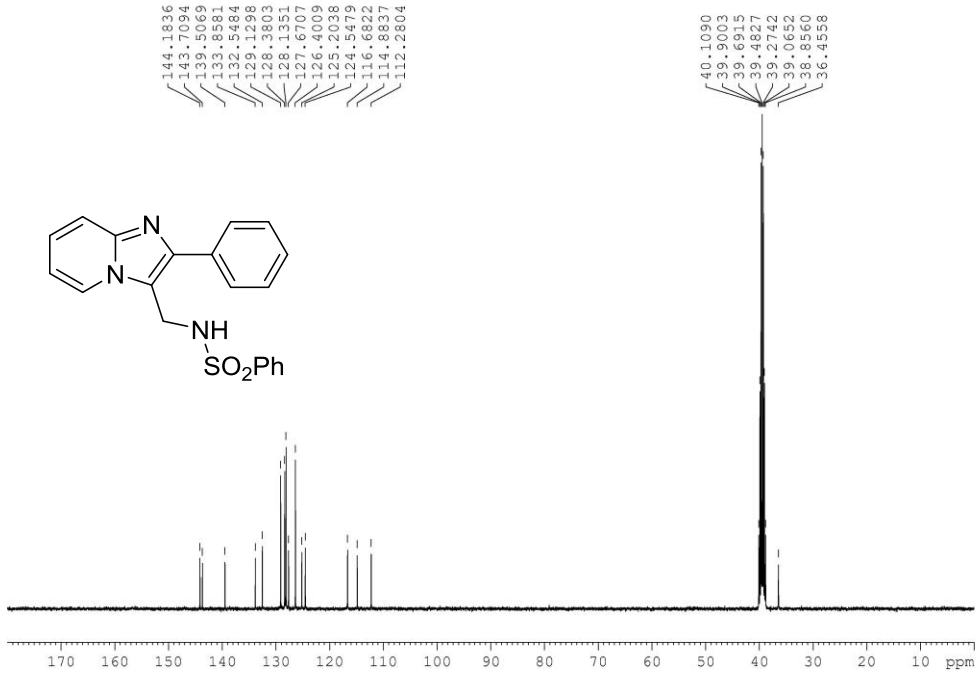
Figure S1. ORTEP views of the molecular structures of **3a** with ellipsoids drawn at the 30% probability level

NMR spectra of synthesized compounds

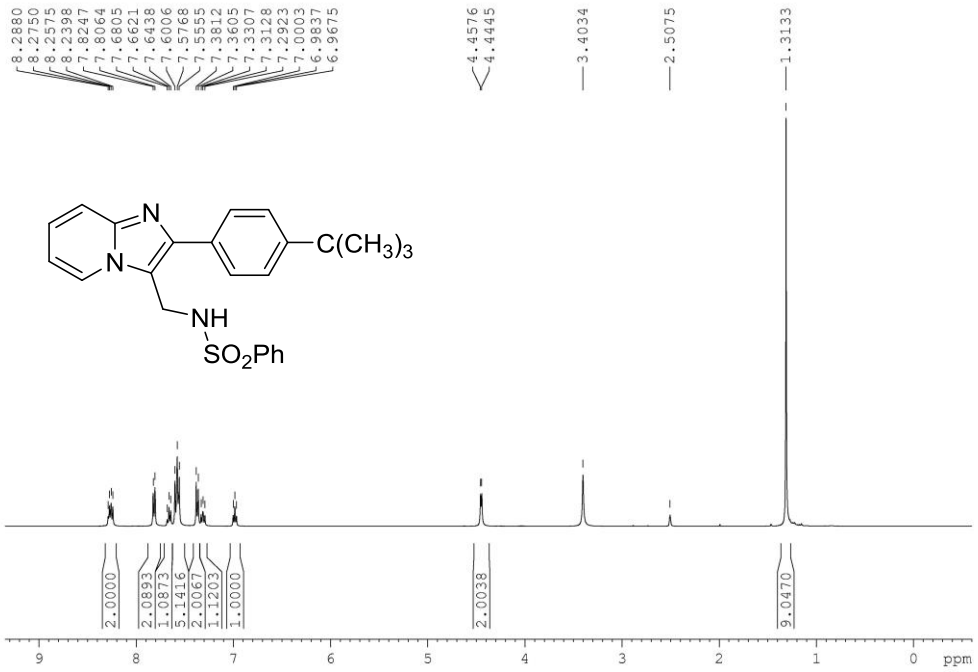
^{1}H NMR of compound **3a**



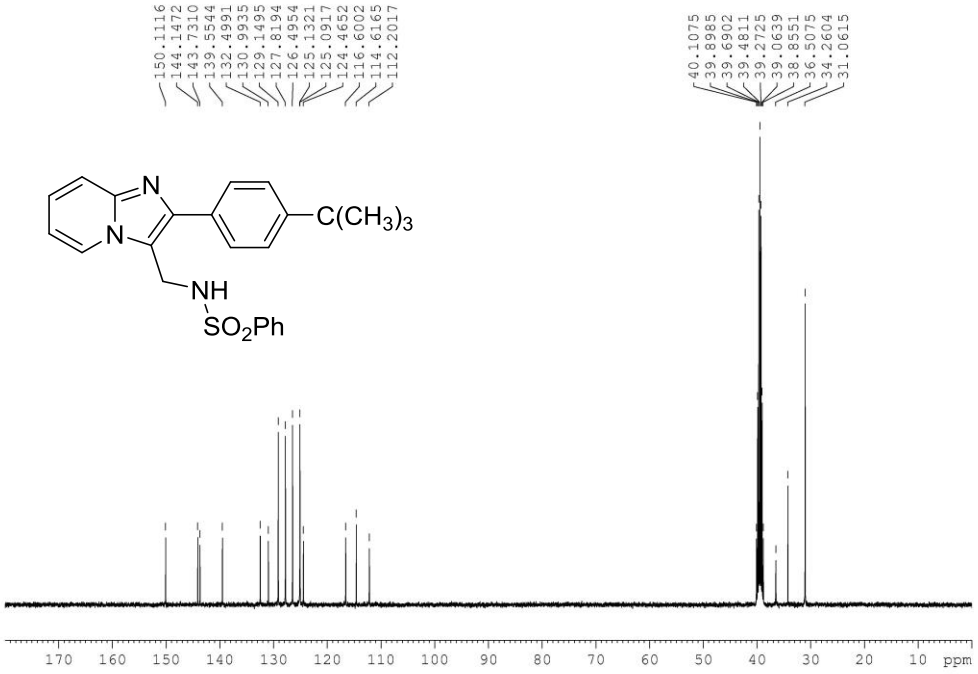
^{13}C NMR of compound **3a**



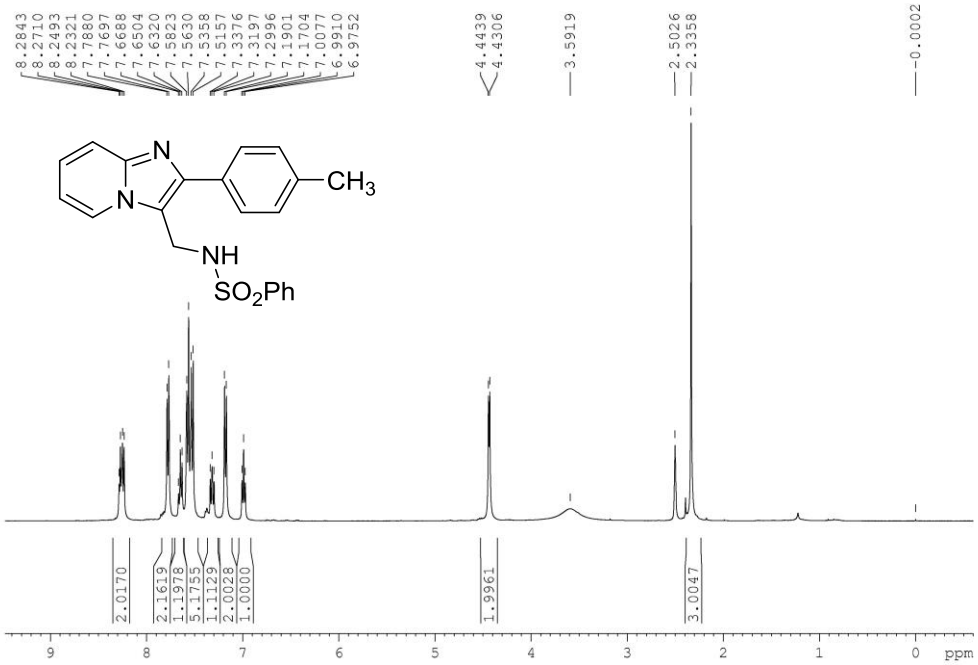
^{1}H NMR of compound **3b**



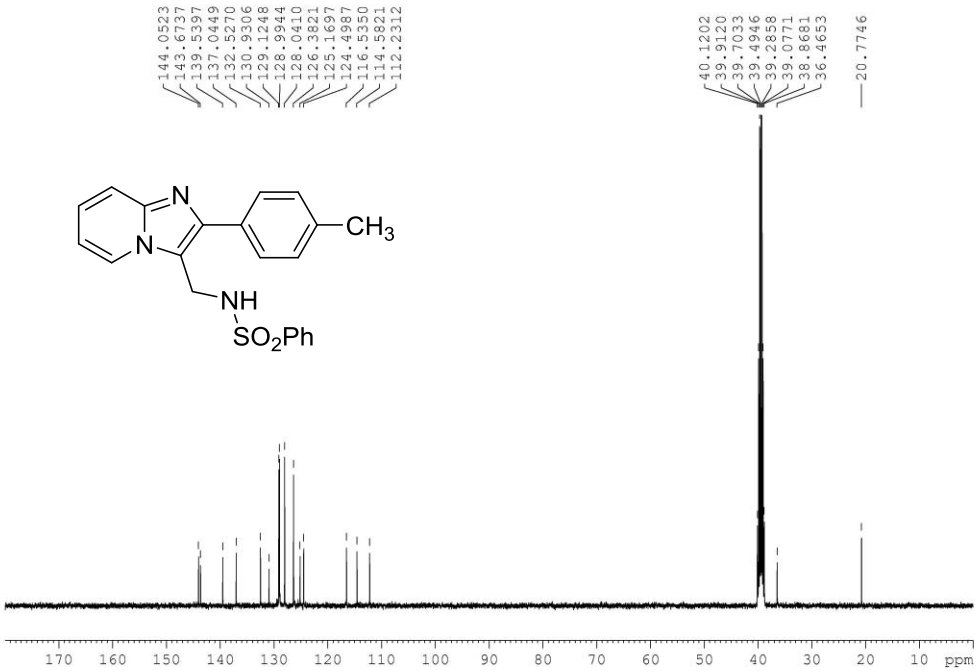
^{13}C NMR of compound **3b**



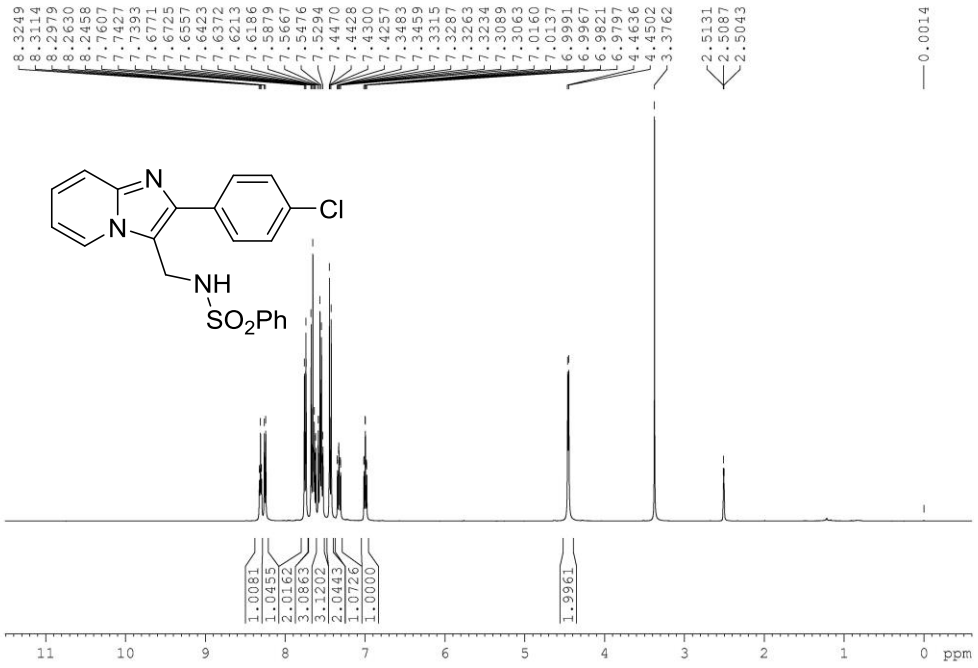
^{1}H NMR of compound **3c**



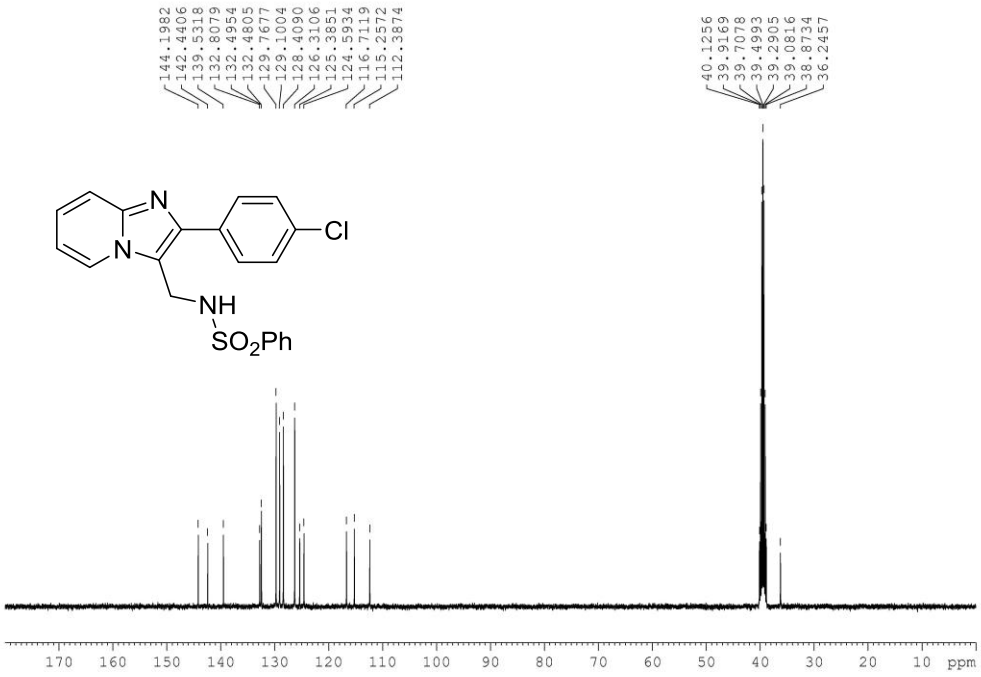
^{13}C NMR of compound **3c**



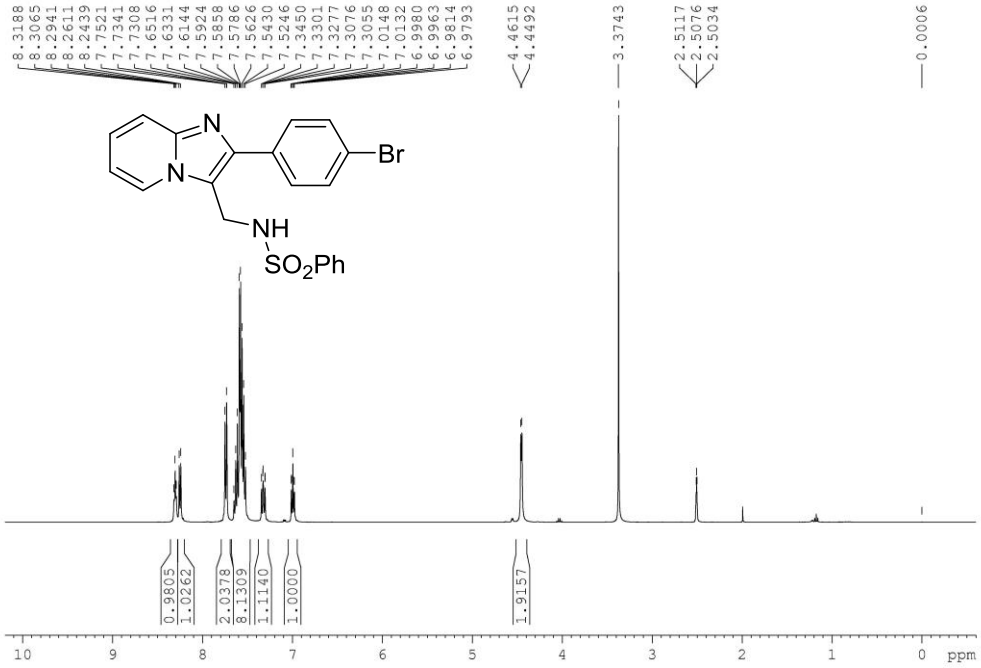
^{1}H NMR of compound **3d**



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



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



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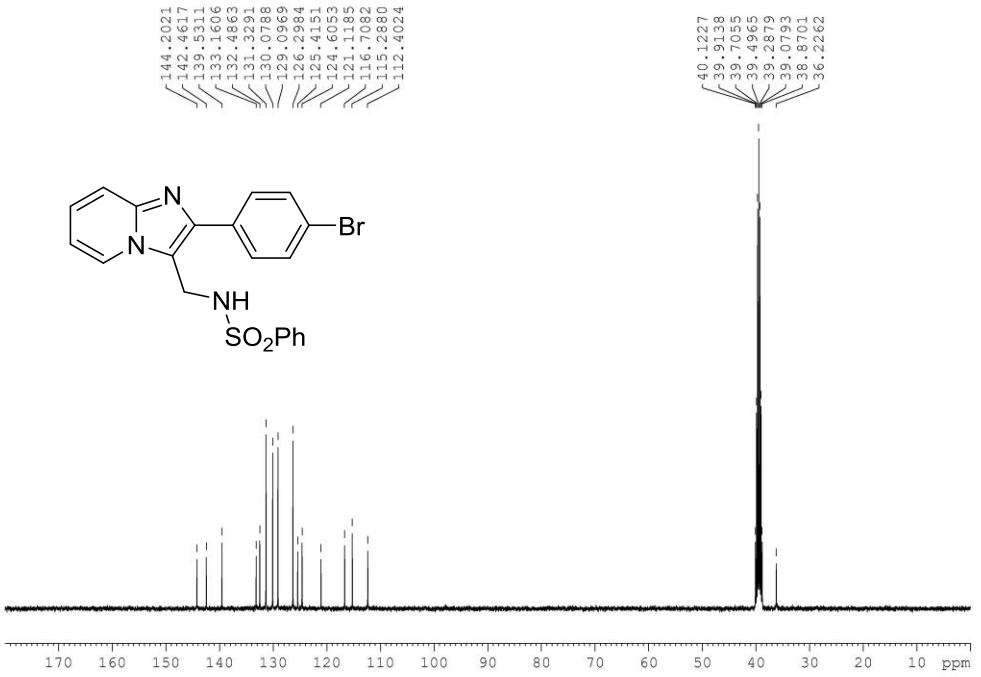
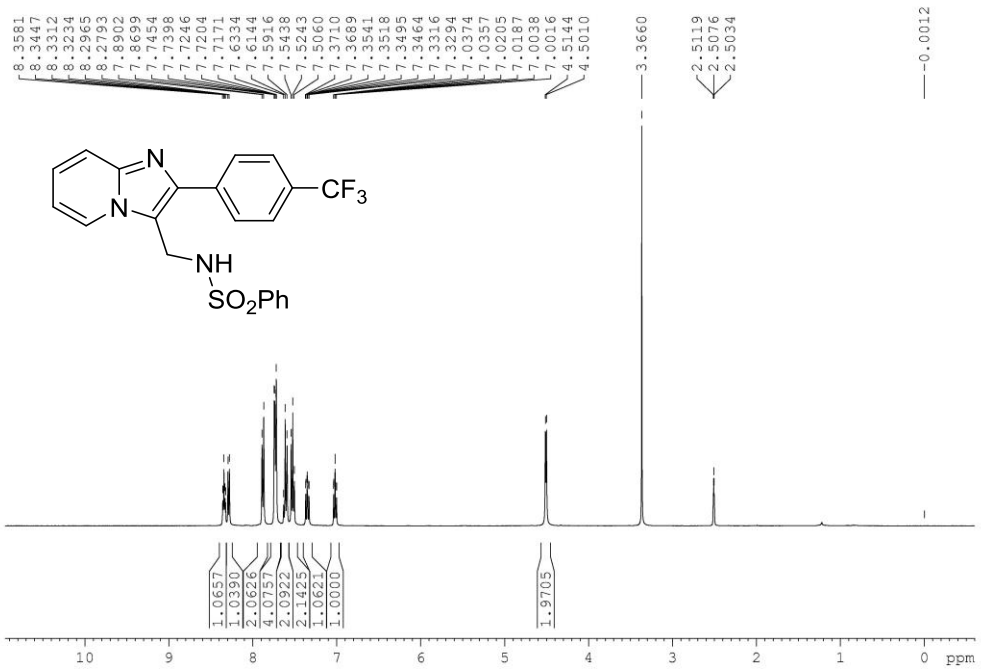


^{1}H NMR of compound **3f**



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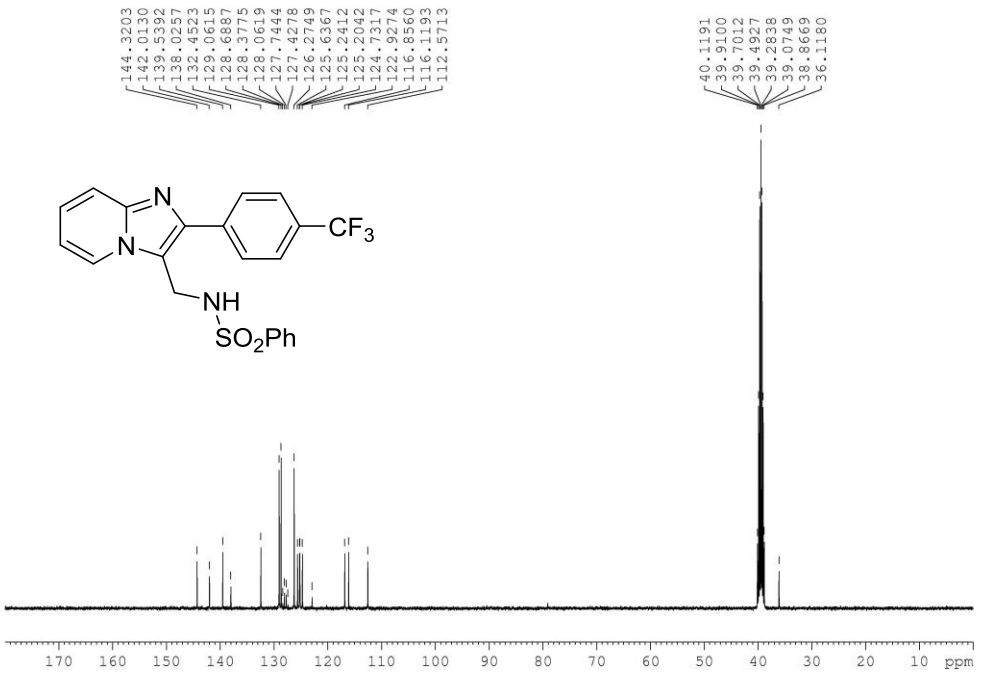
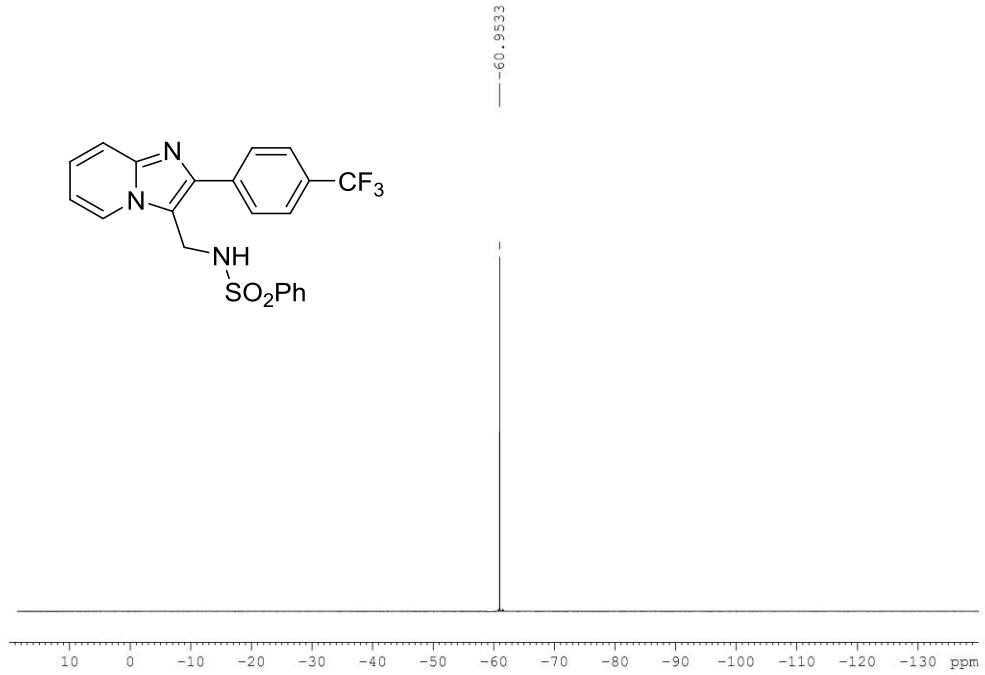
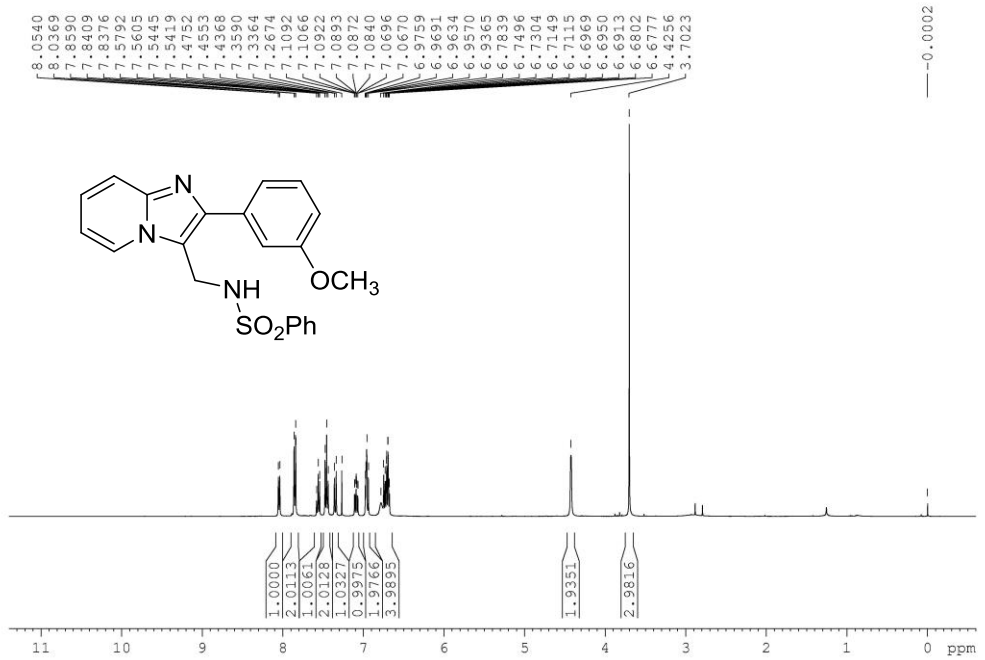


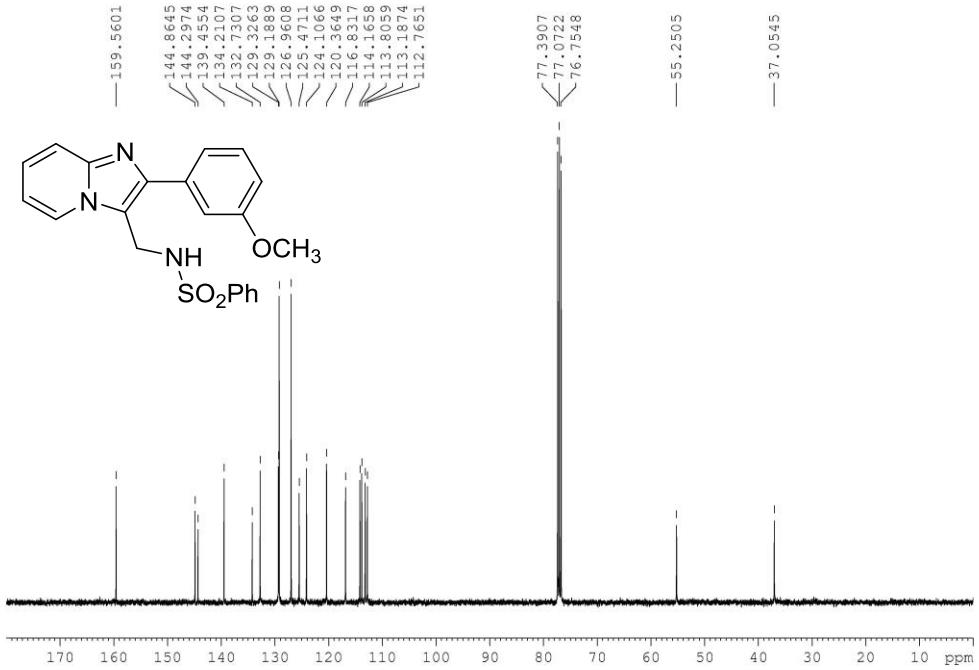
^{19}F NMR of compound **3f**



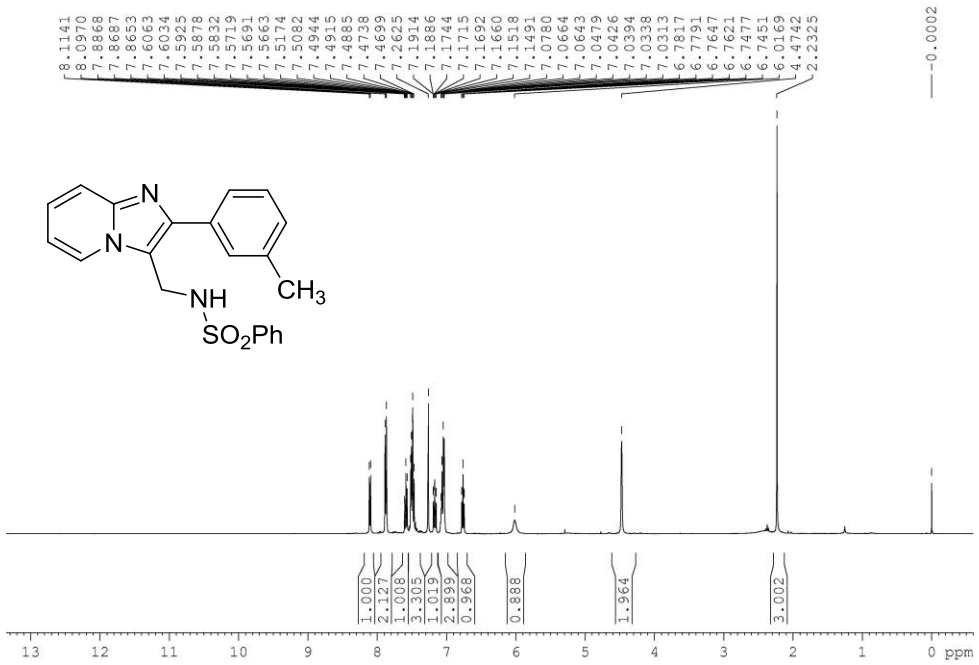
^{1}H NMR of compound **3g**



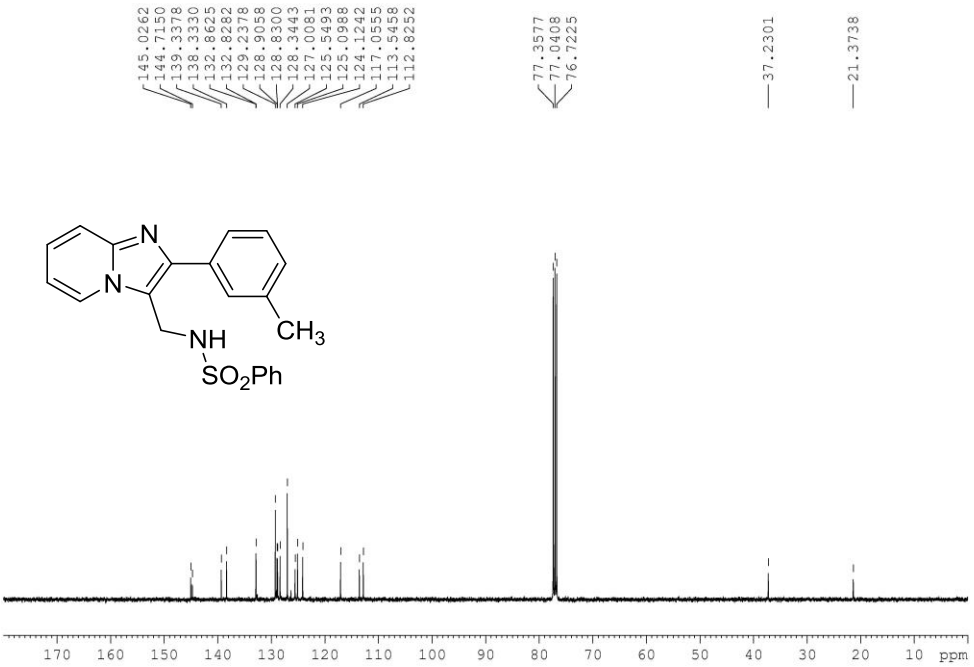
^{13}C NMR of compound **3g**



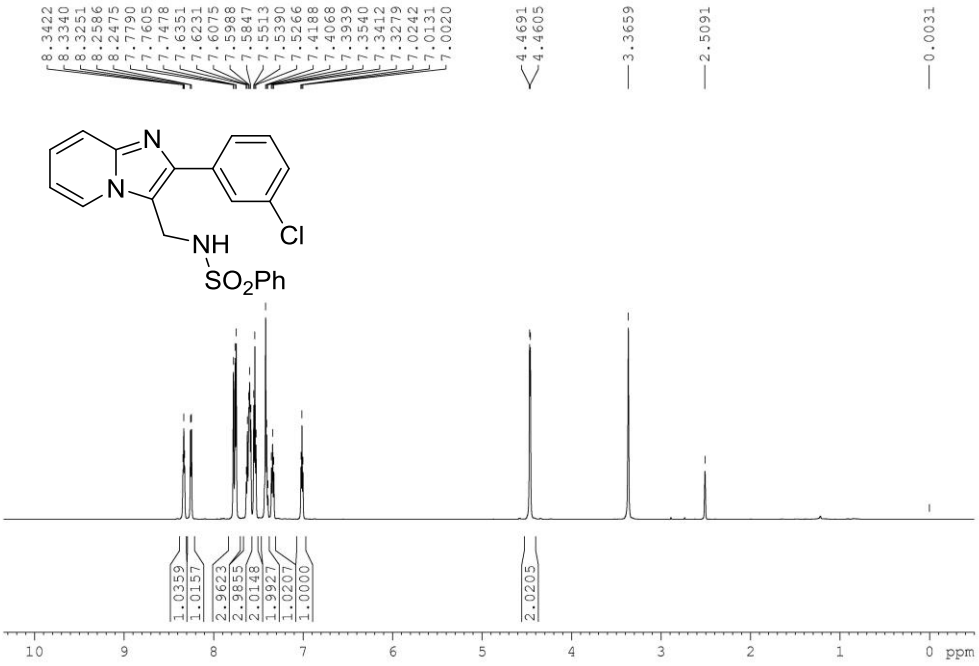
^{1}H NMR of compound **3h**



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



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



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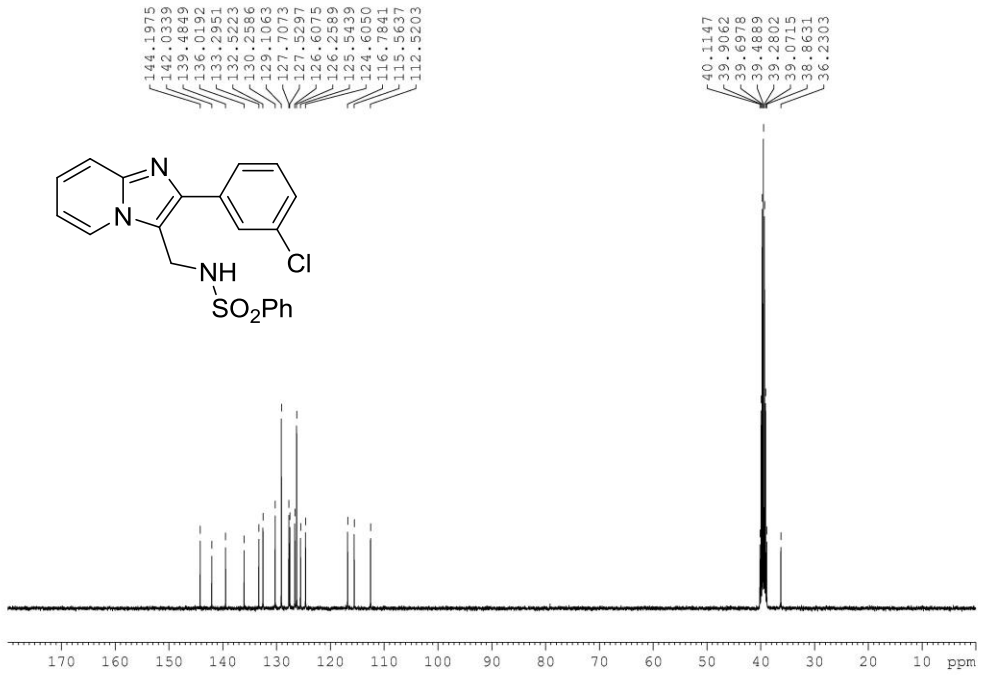

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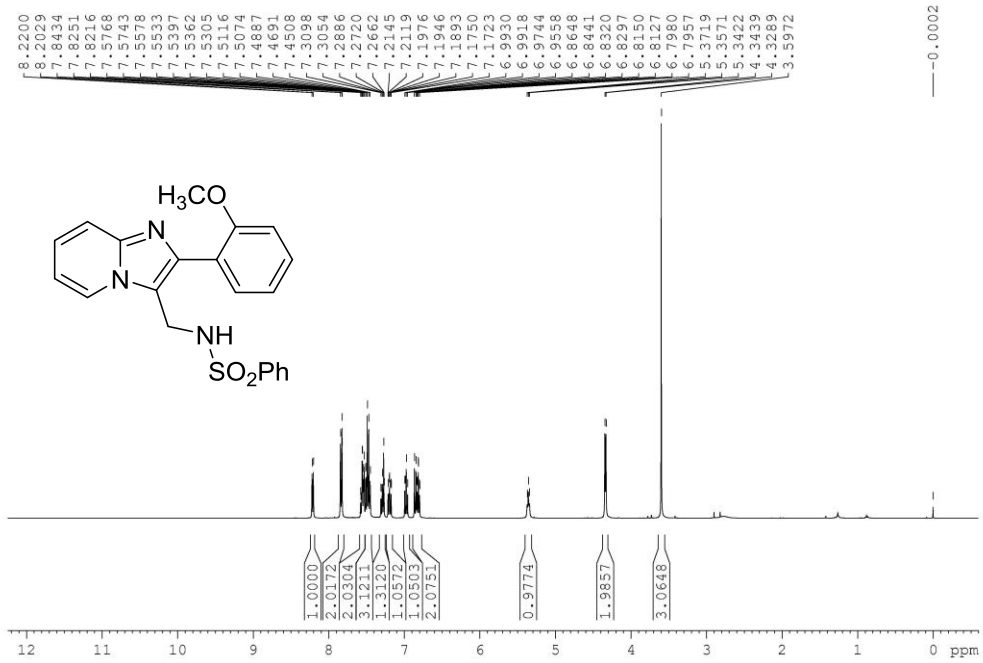

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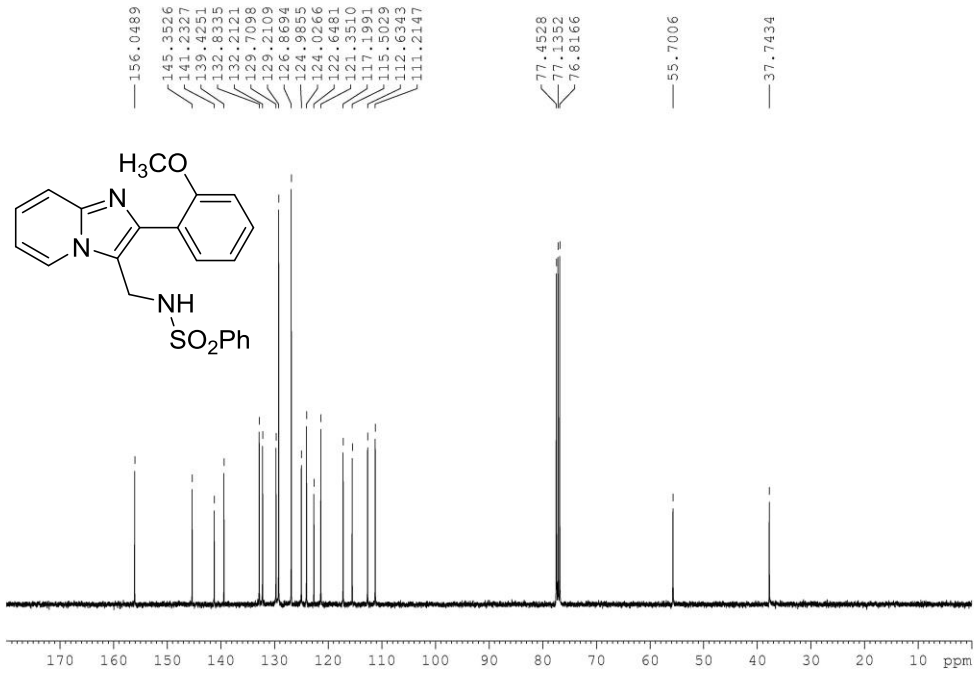
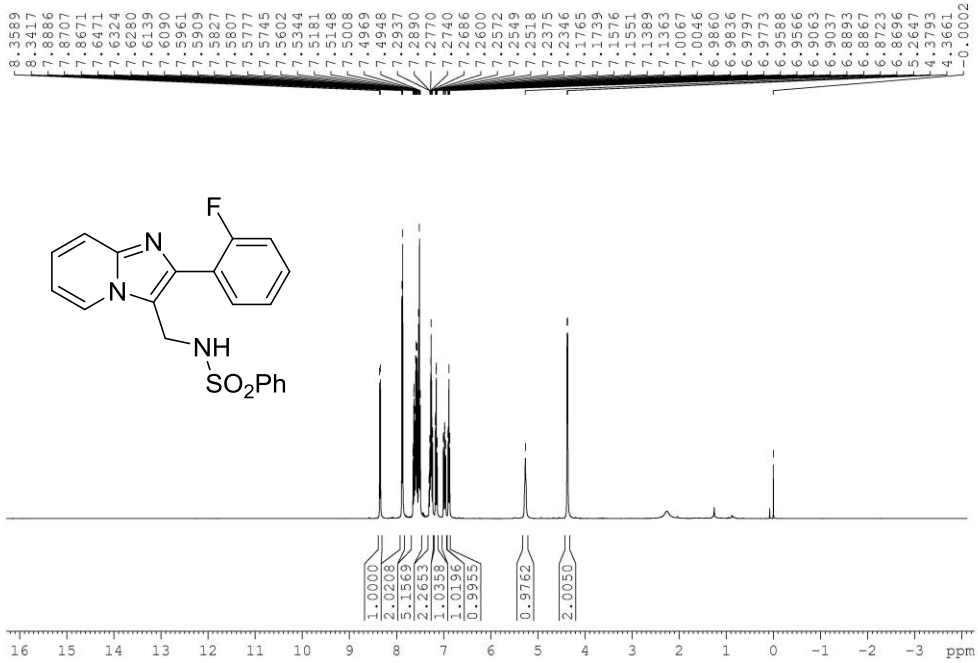


^{1}H NMR of compound **3k**



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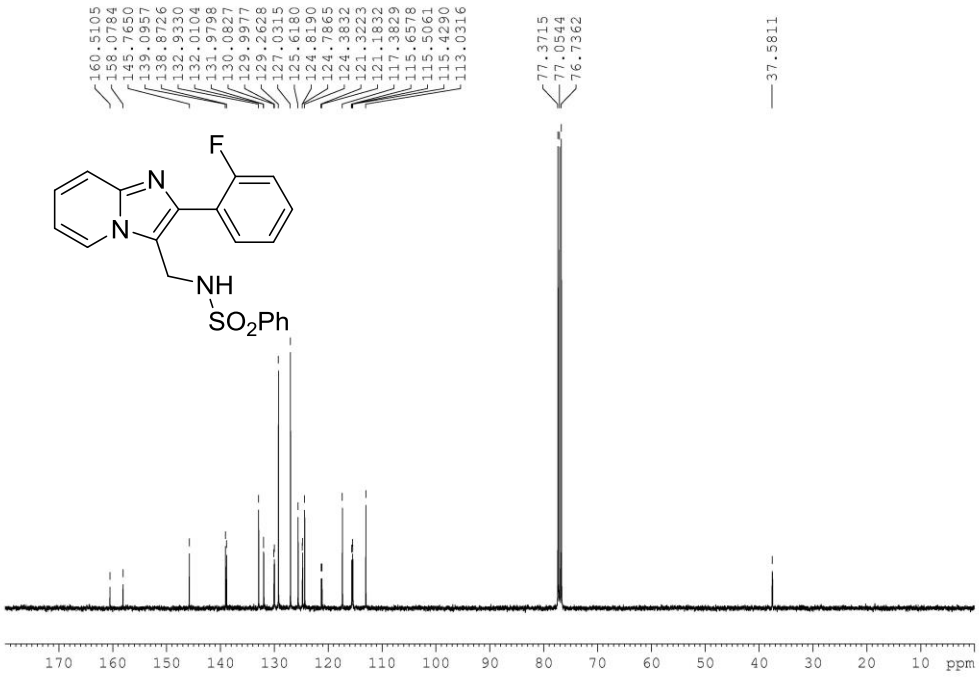
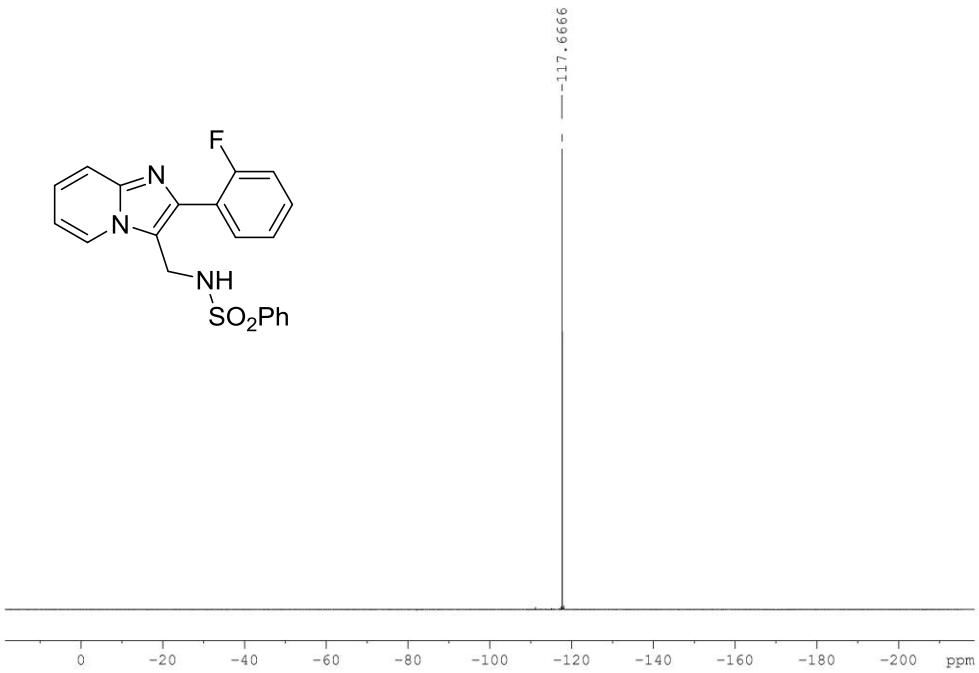


^{19}F NMR of compound **3k**



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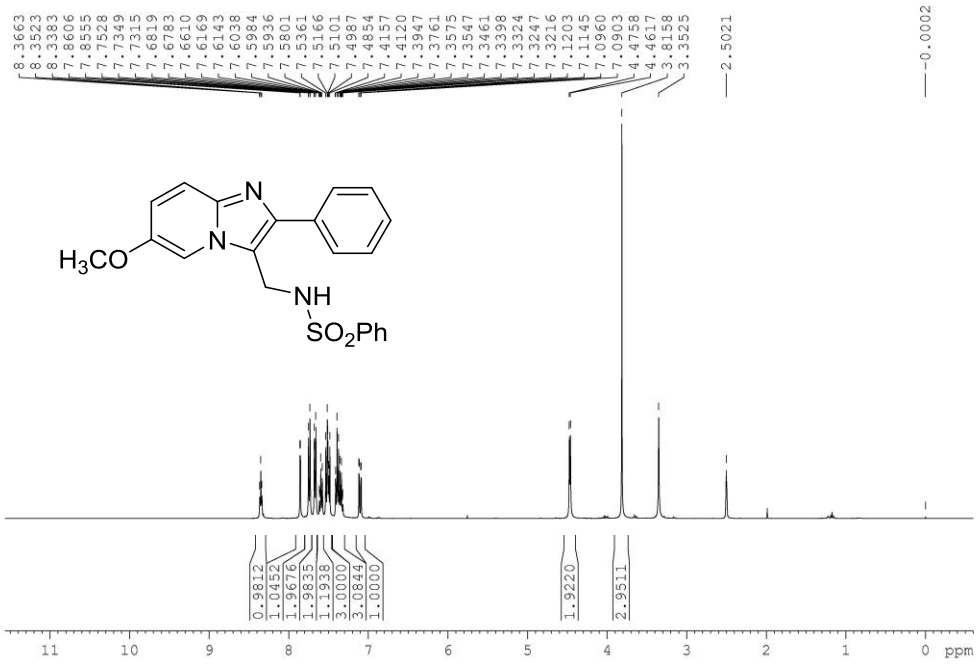

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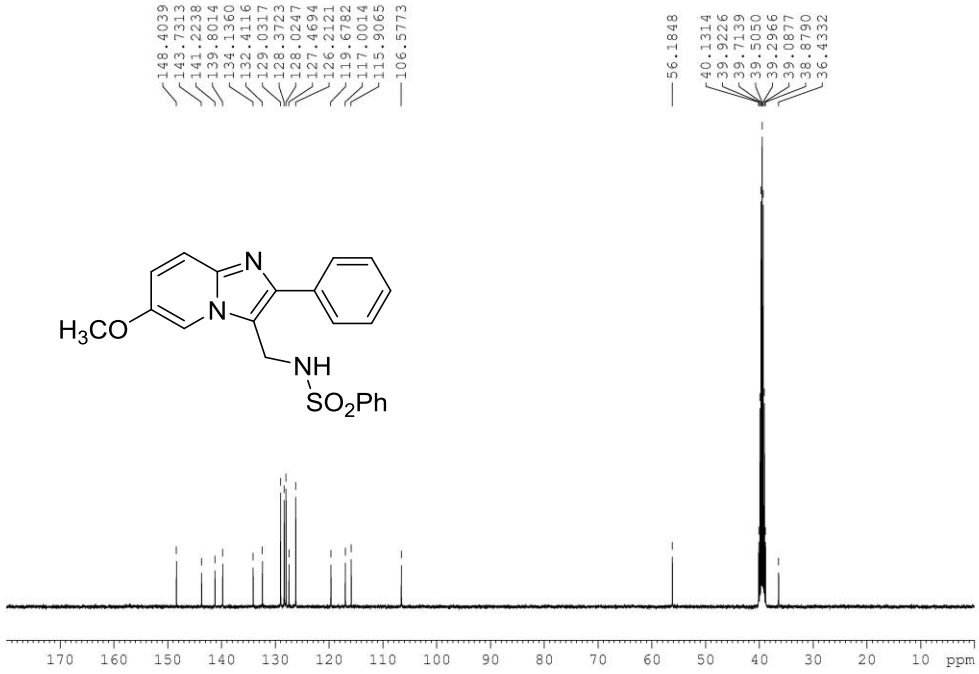
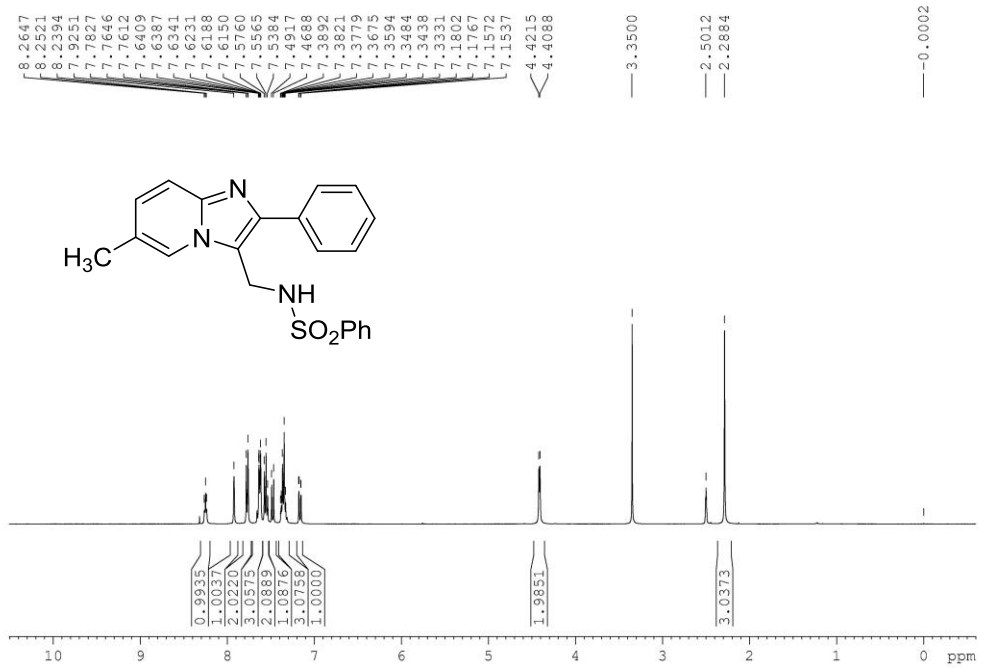
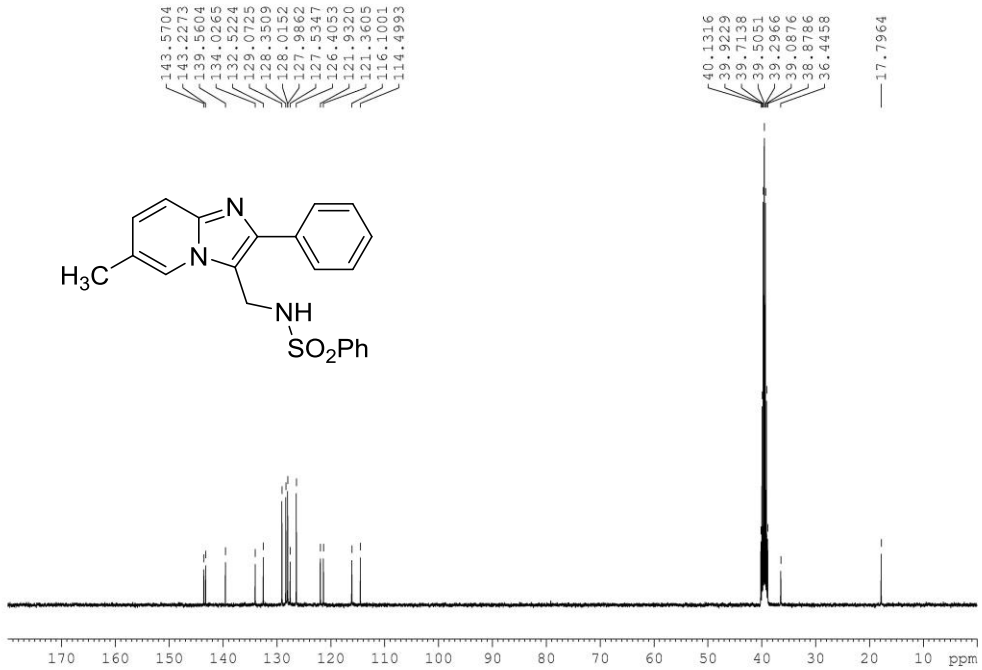


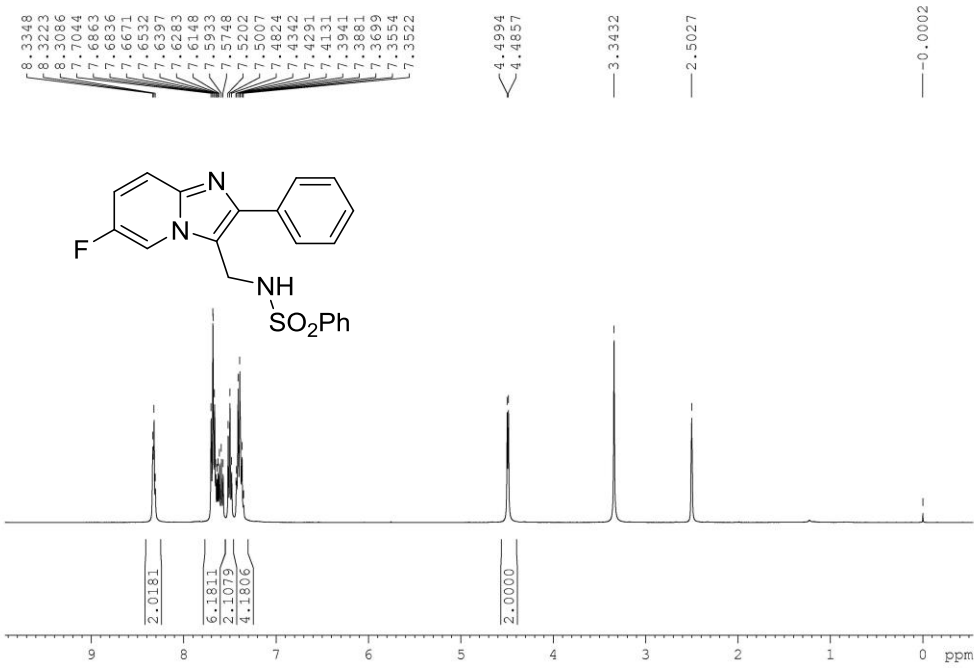
^{1}H NMR of compound **3m**



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



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



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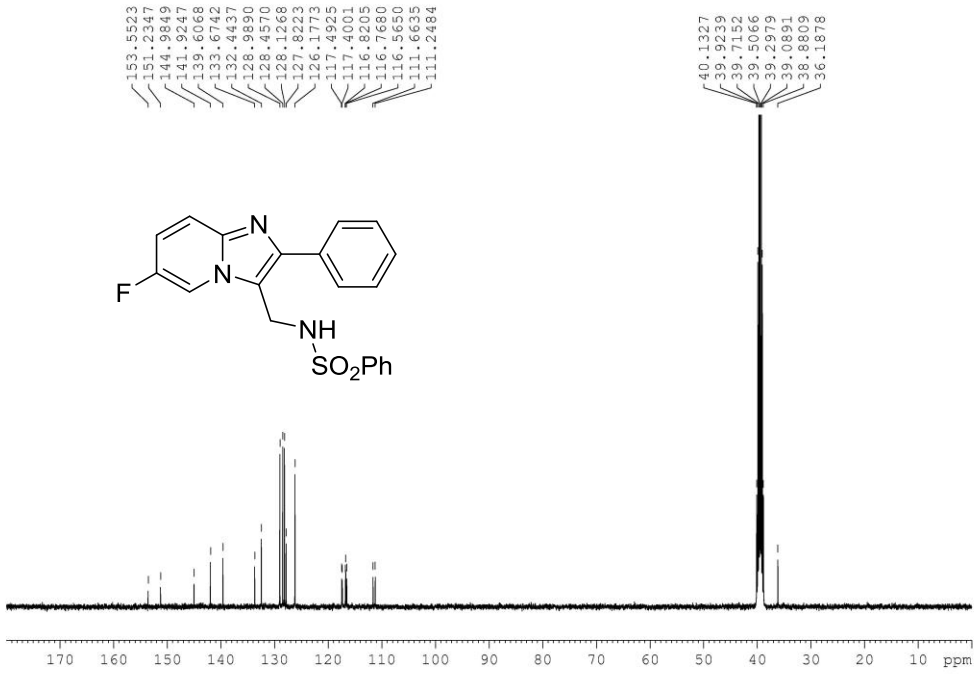
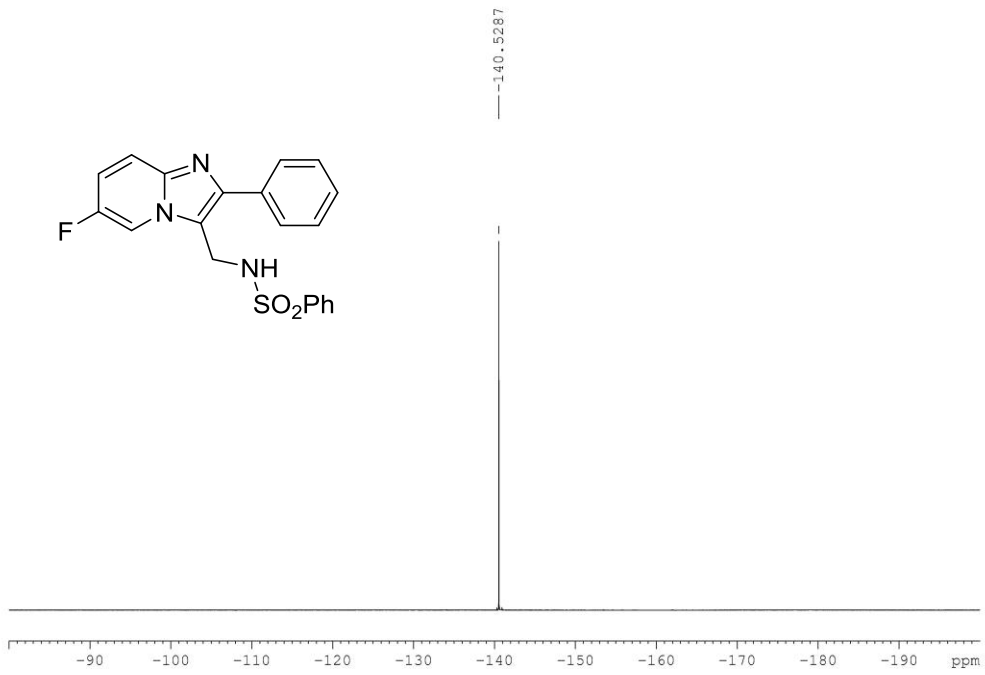
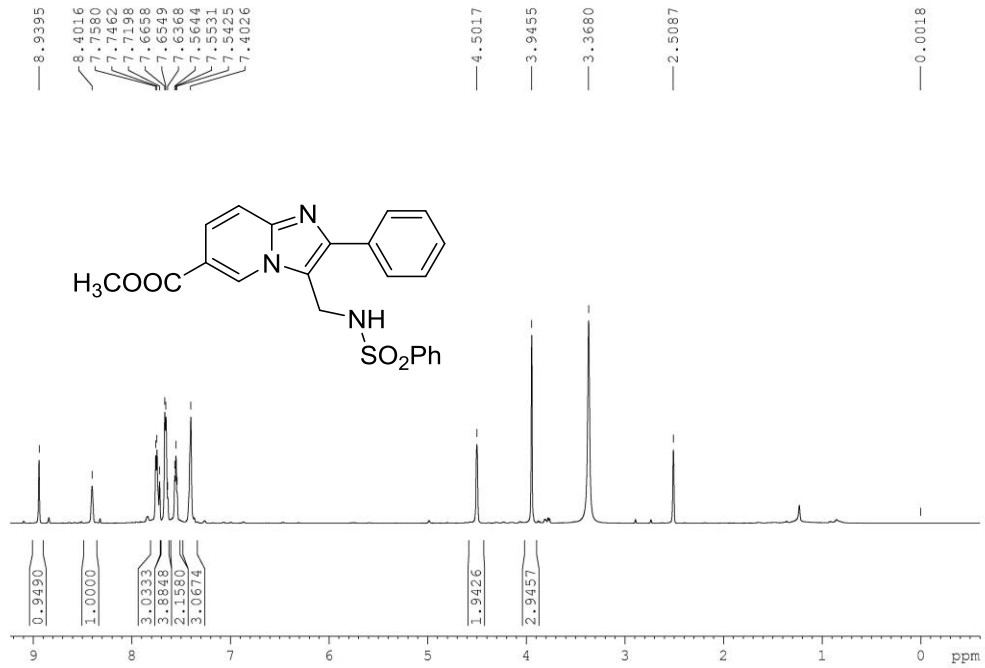


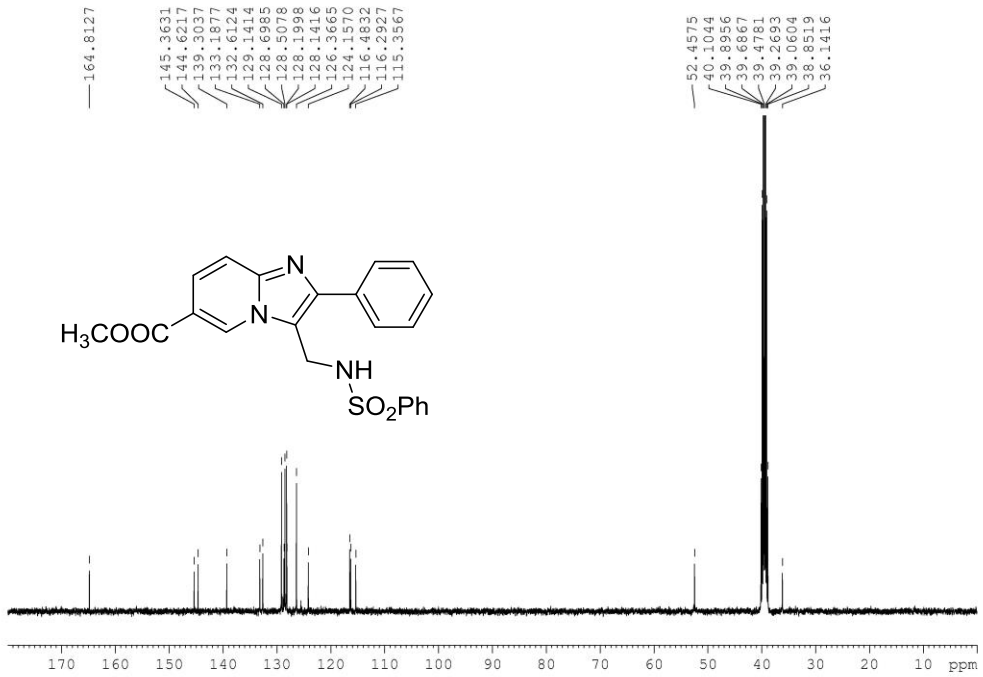
^{19}F NMR of compound **3n**



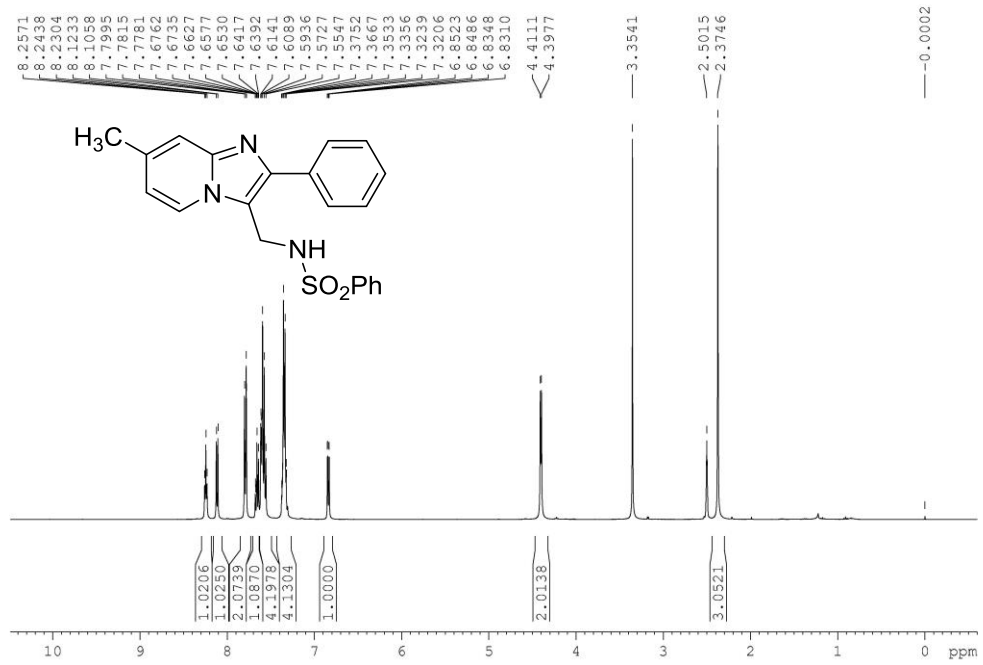
^{1}H NMR of compound **3o**



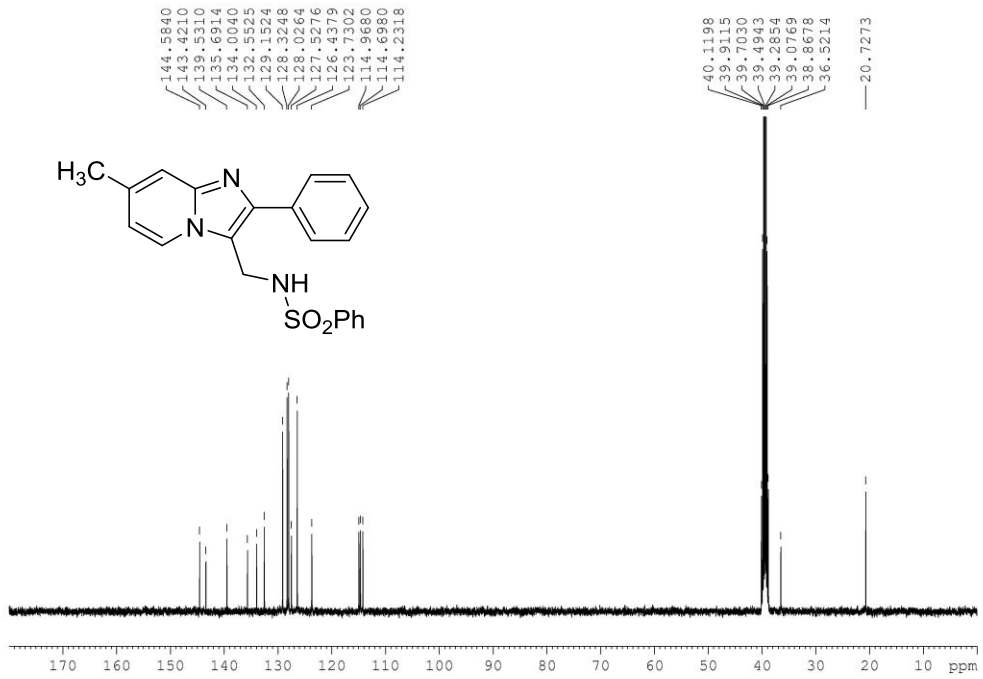
^{13}C NMR of compound **3o**



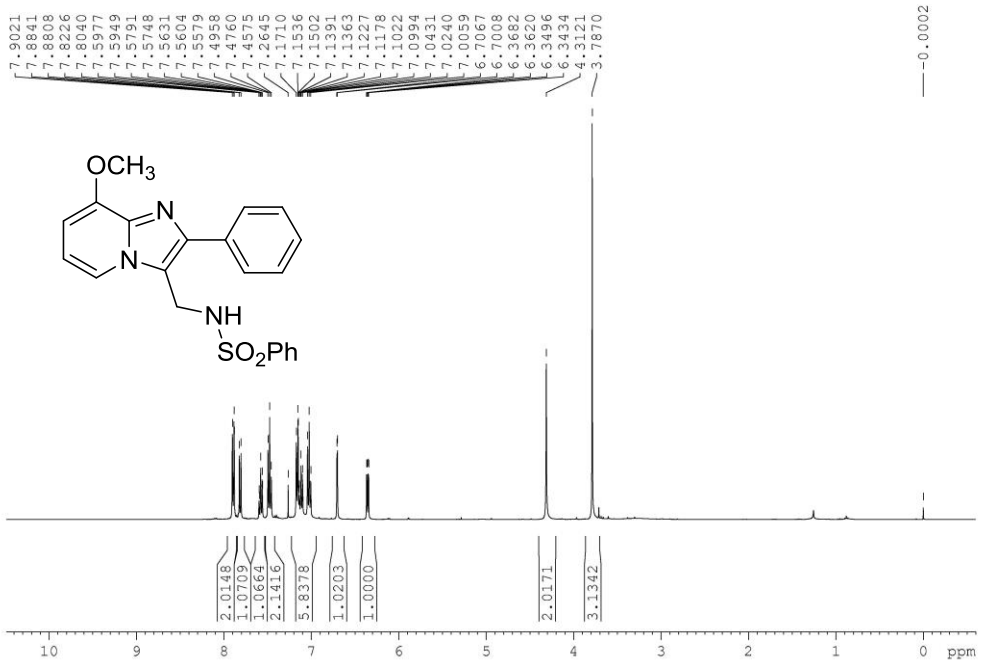
^{1}H NMR of compound **3p**



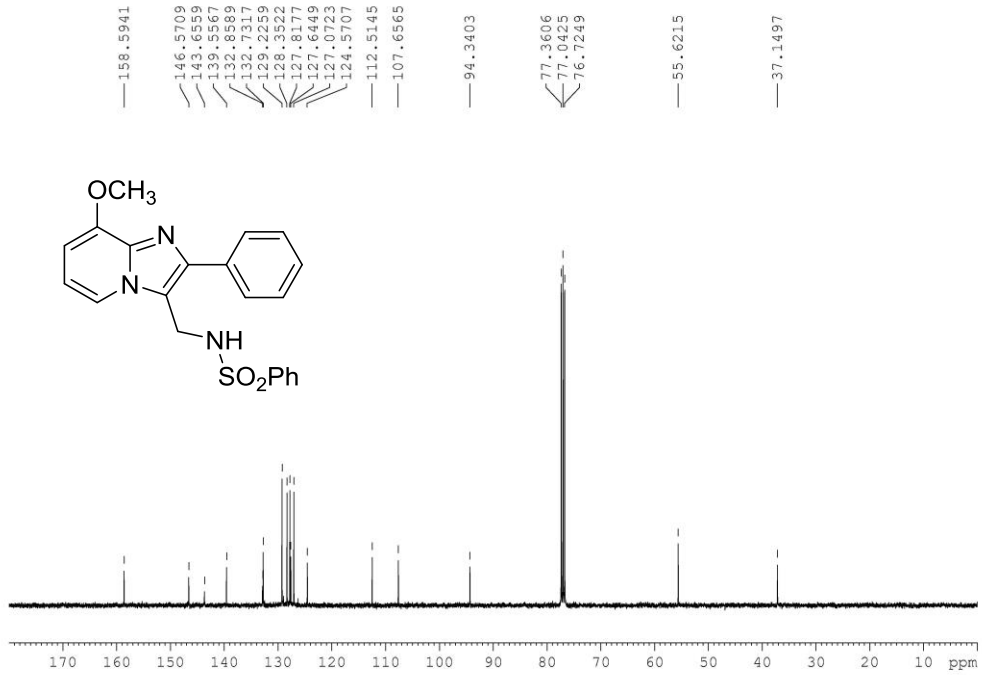
^{13}C NMR of compound **3p**



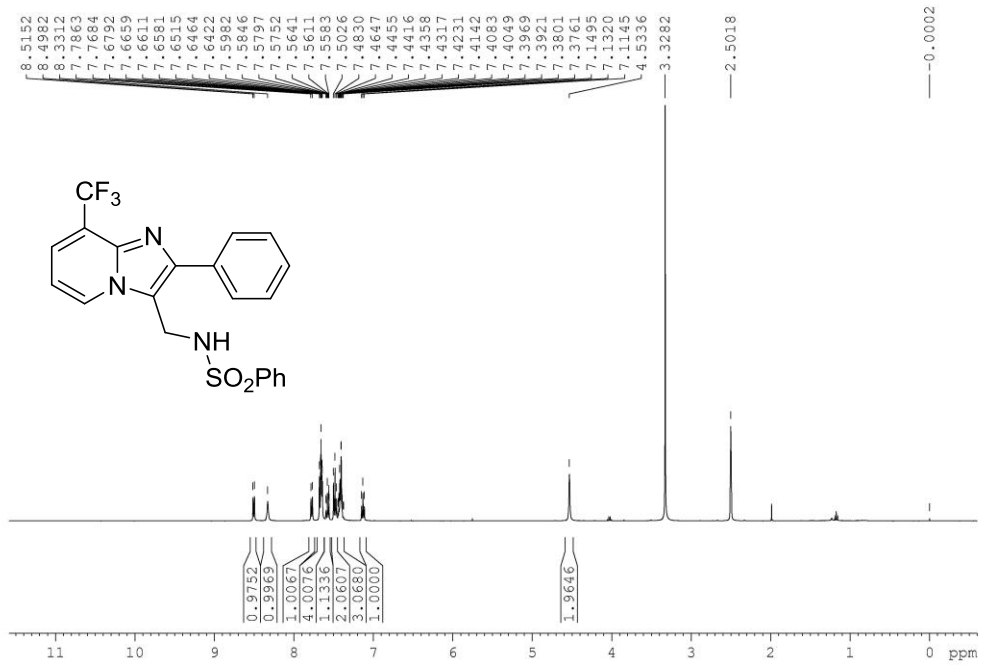
^{1}H NMR of compound **3q**



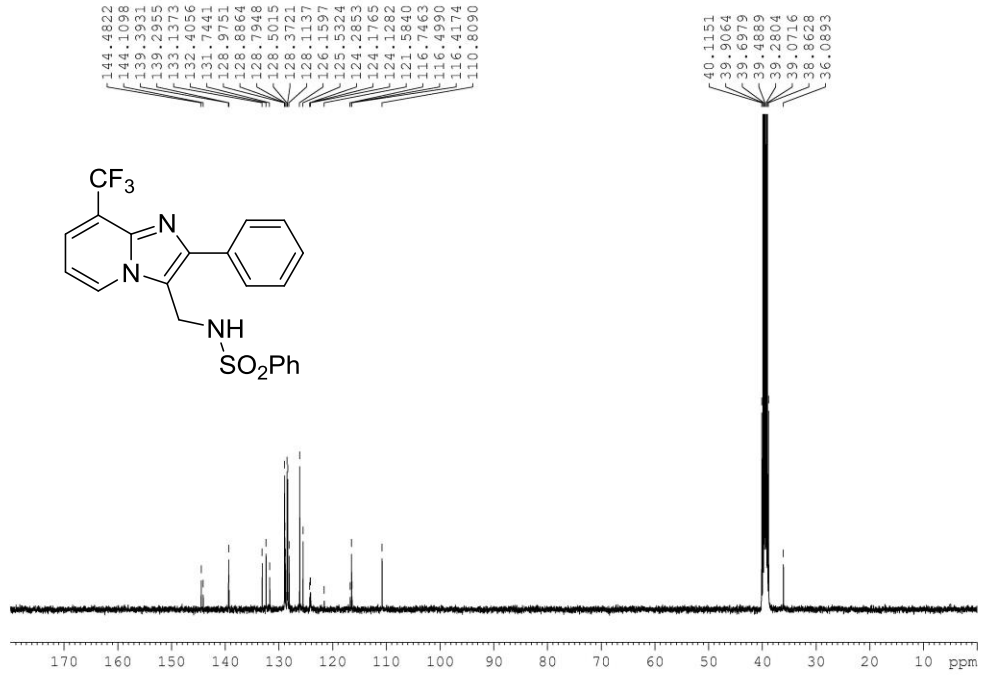
^{13}C NMR of compound **3q**



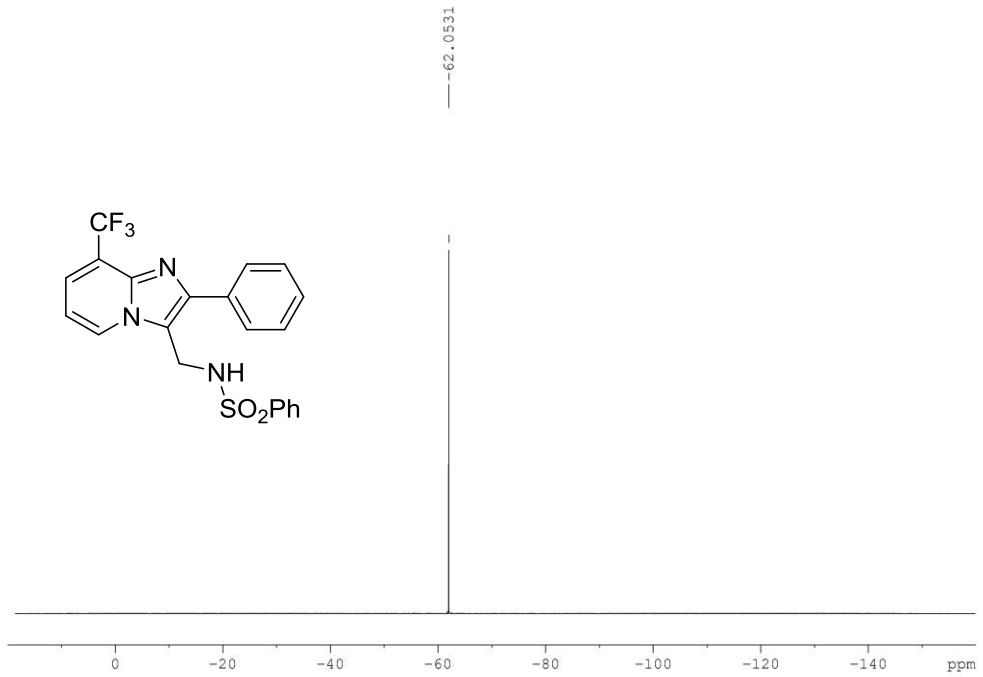
^{1}H NMR of compound **3r**



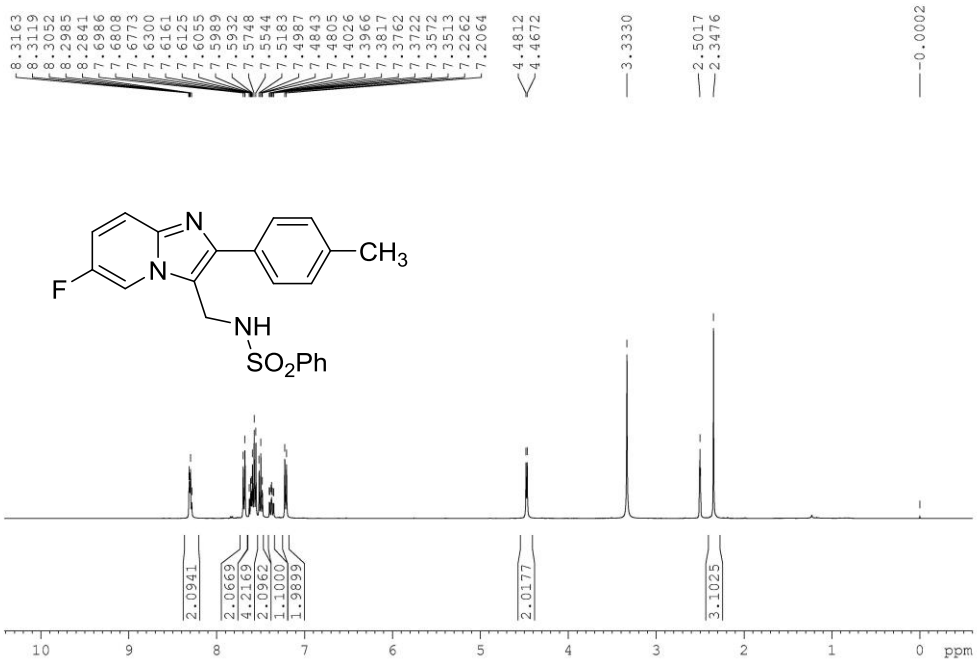
^{13}C NMR of compound **3r**



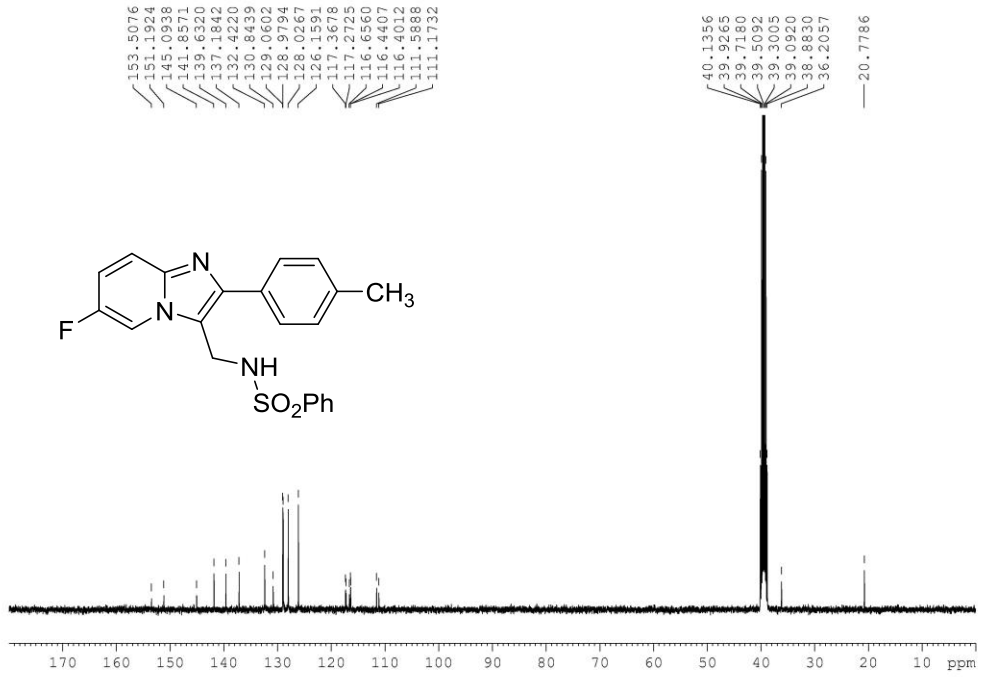
^{19}F NMR of compound **3r**



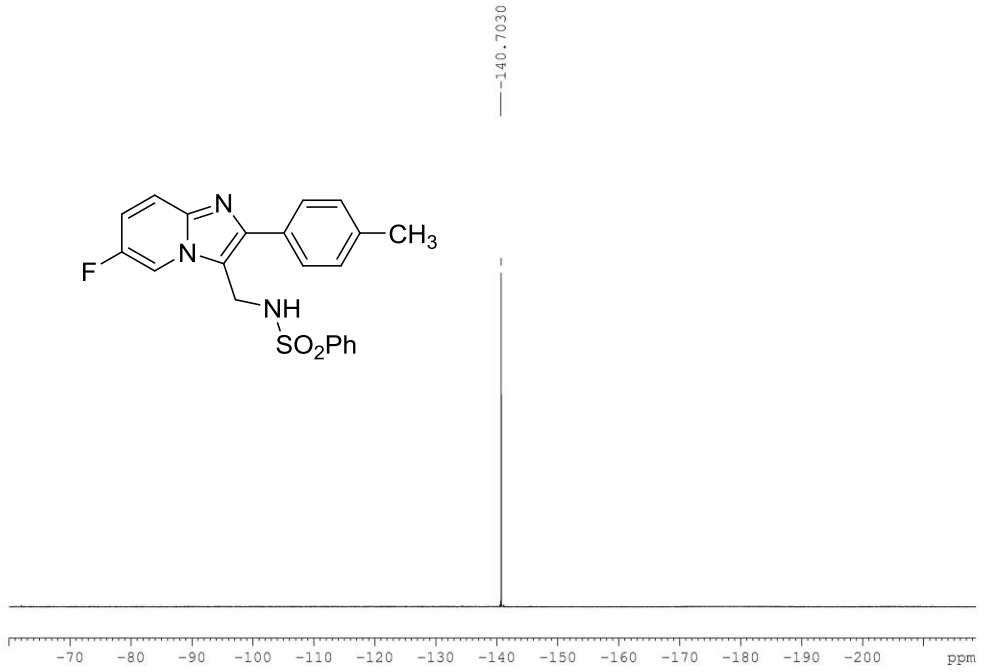
^{1}H NMR of compound **3s**



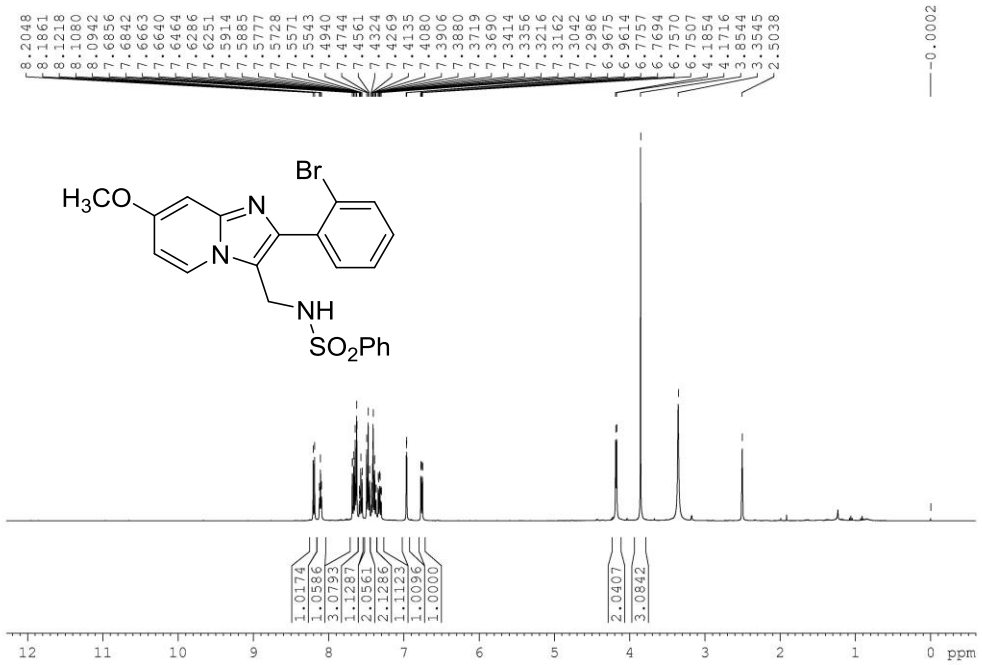
^{13}C NMR of compound **3s**



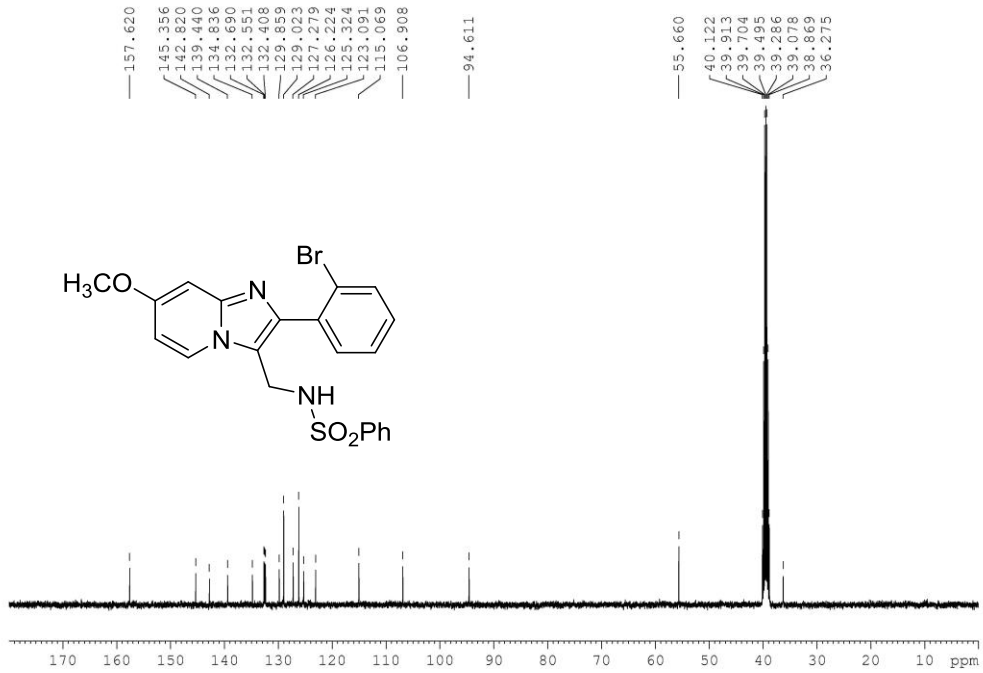
^{19}F NMR of compound **3s**



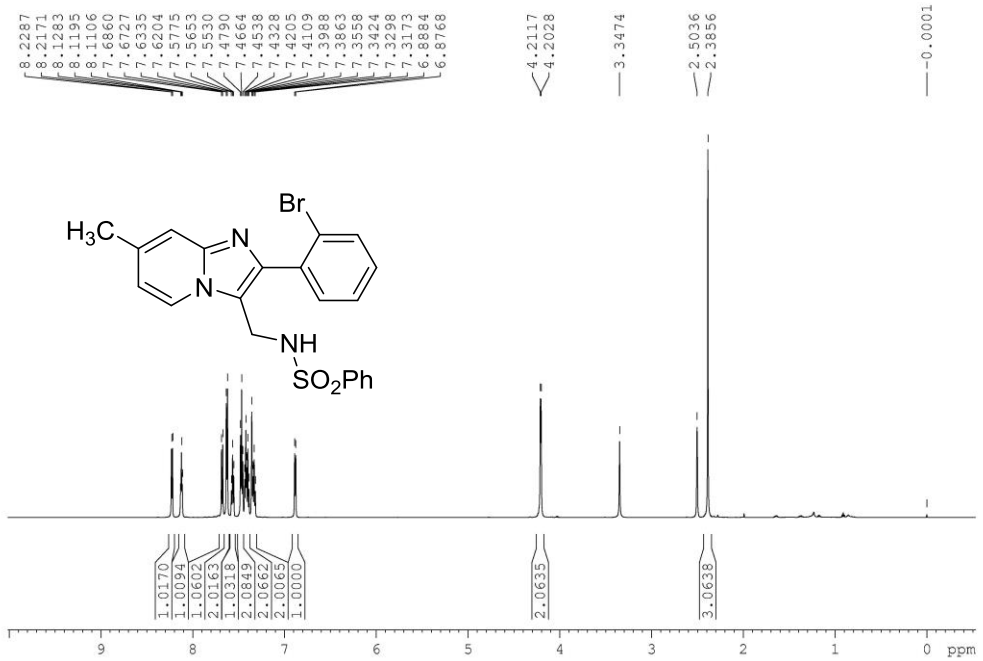
^{1}H NMR of compound **3t**



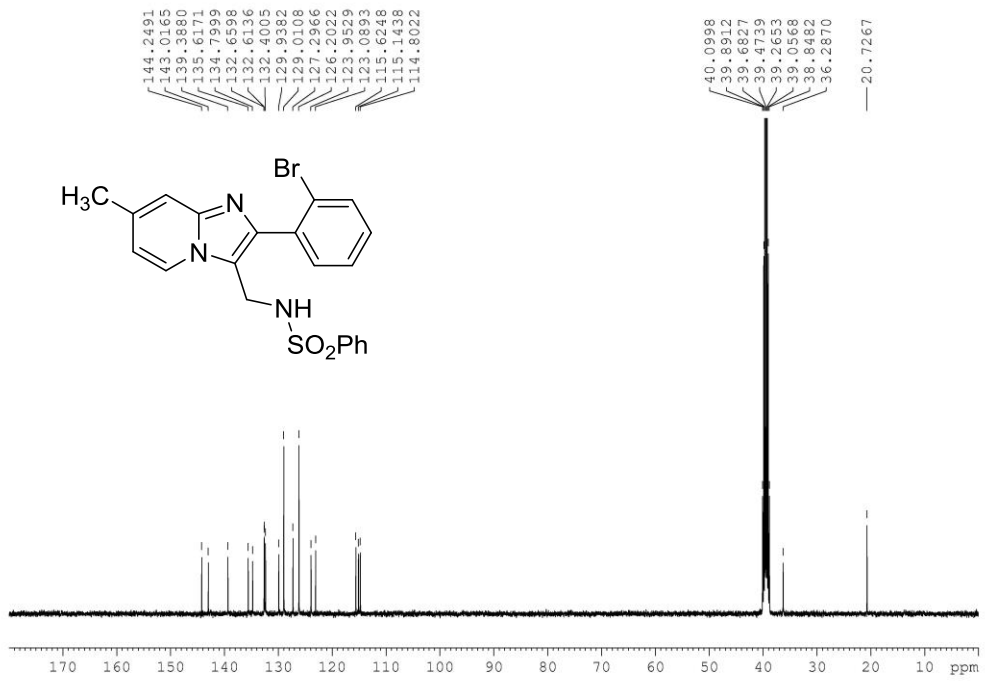
^{13}C NMR of compound **3t**



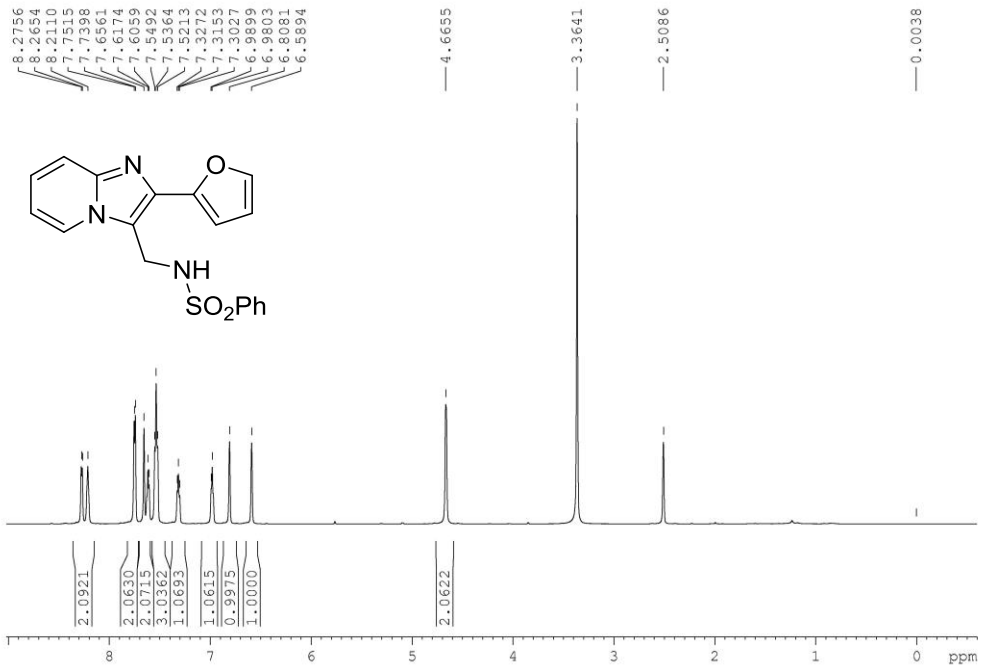
^{1}H NMR of compound **3u**



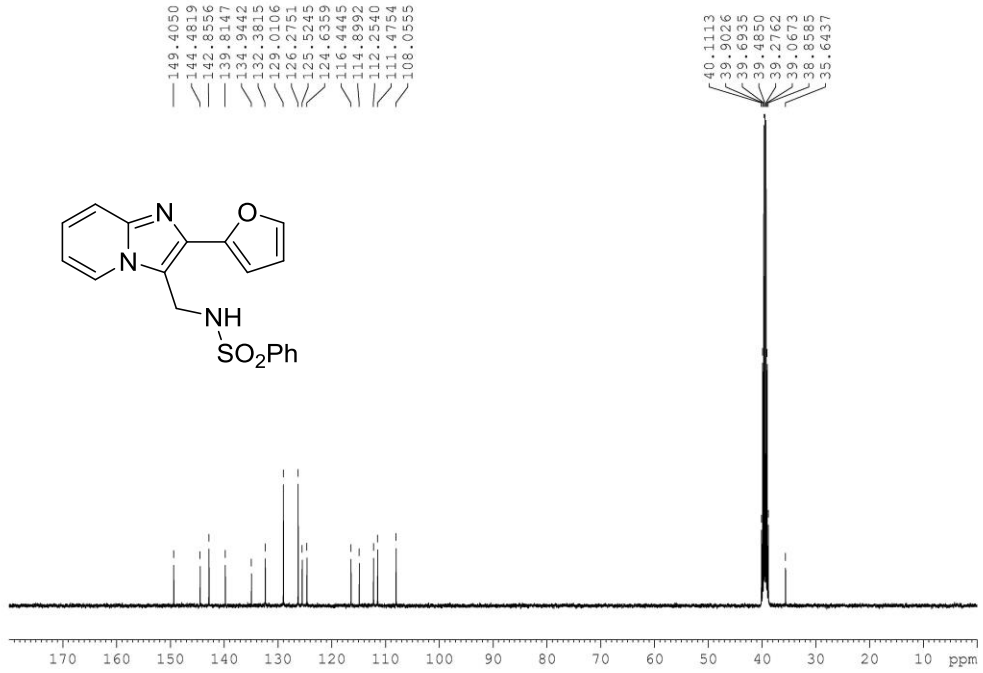
^{13}C NMR of compound **3u**



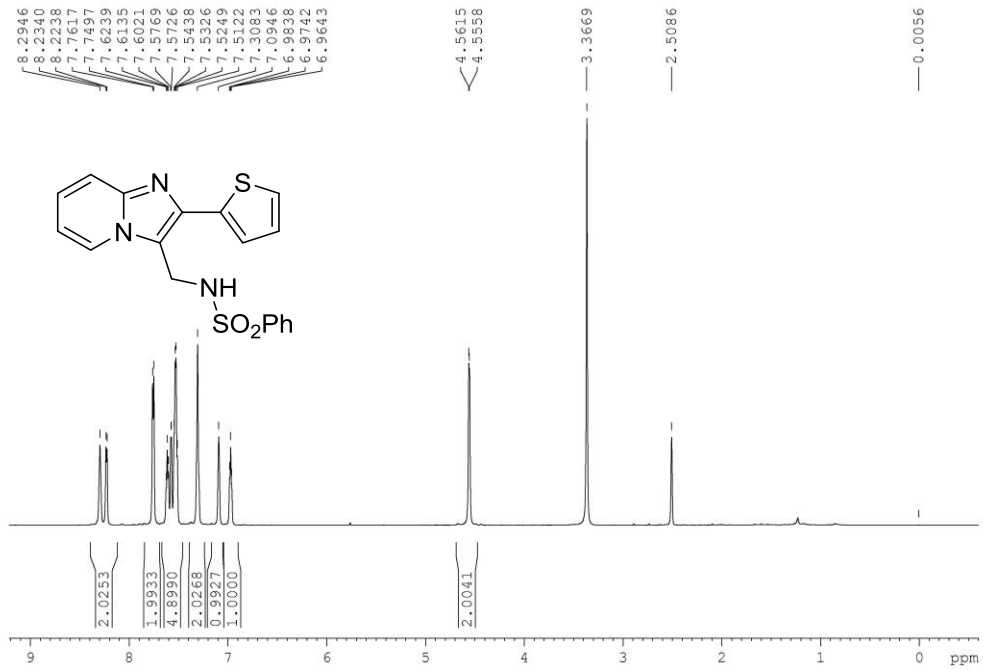
^{1}H NMR of compound **3v**



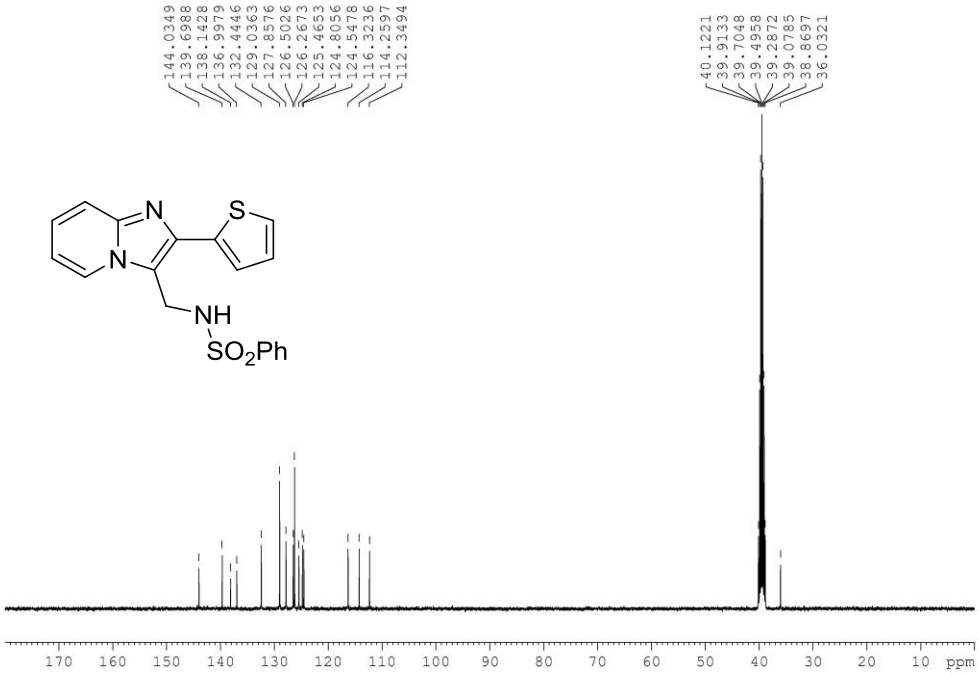
^{13}C NMR of compound **3v**



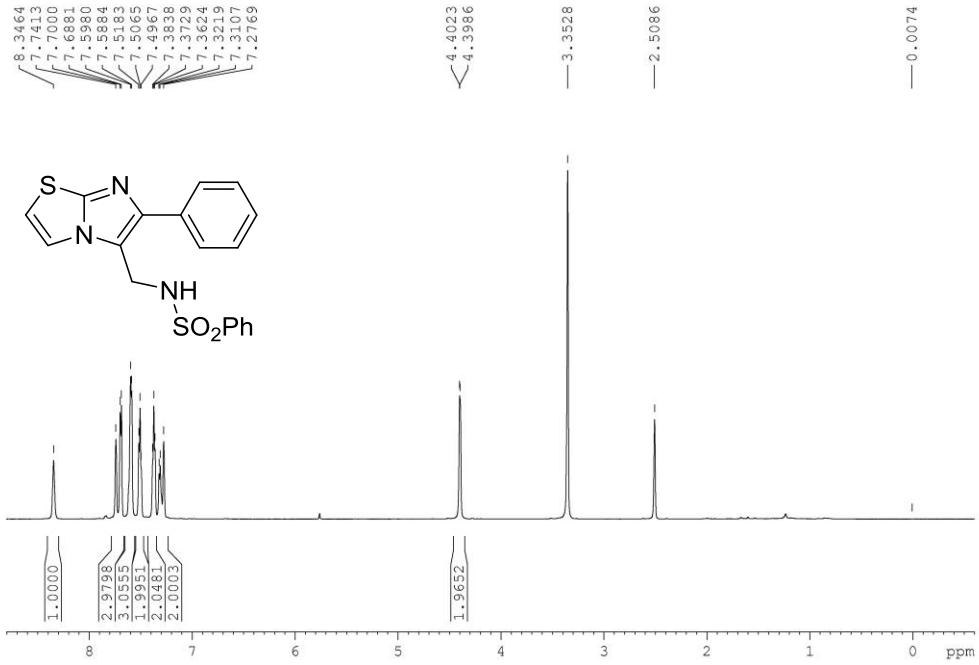
^{1}H NMR of compound **3w**



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



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



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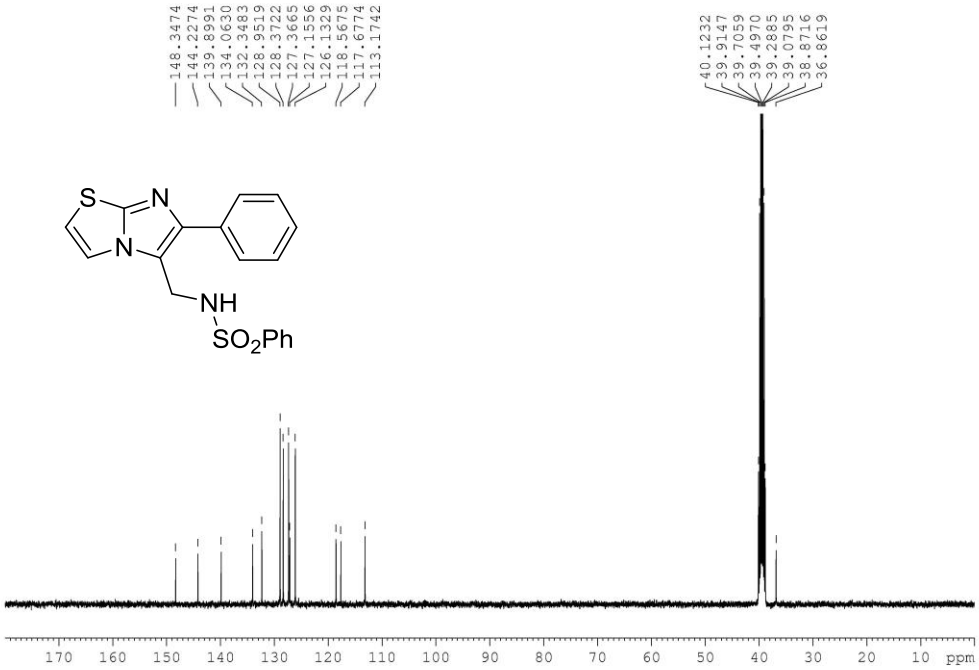
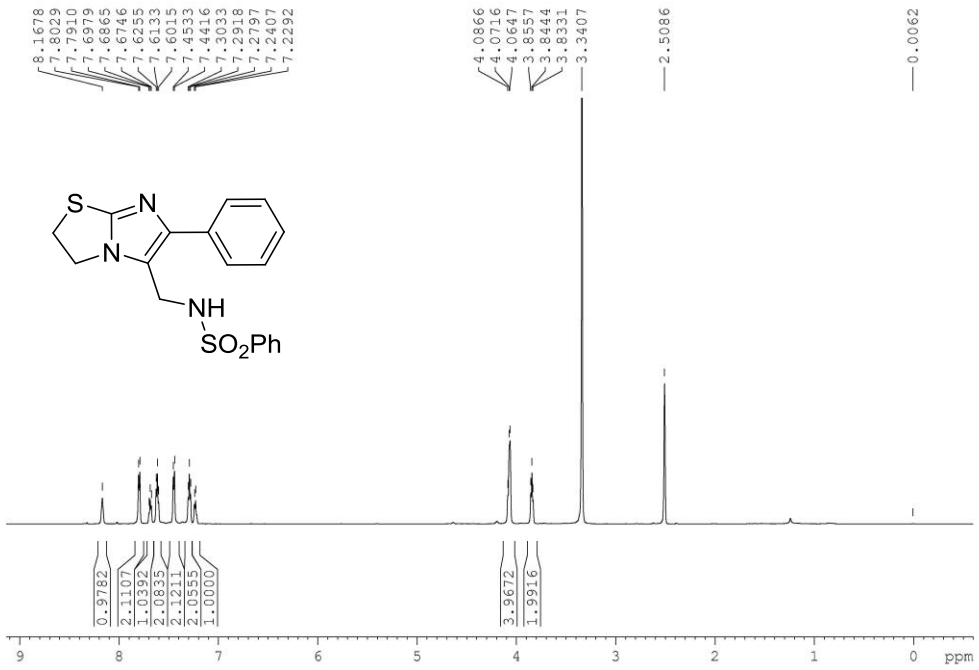
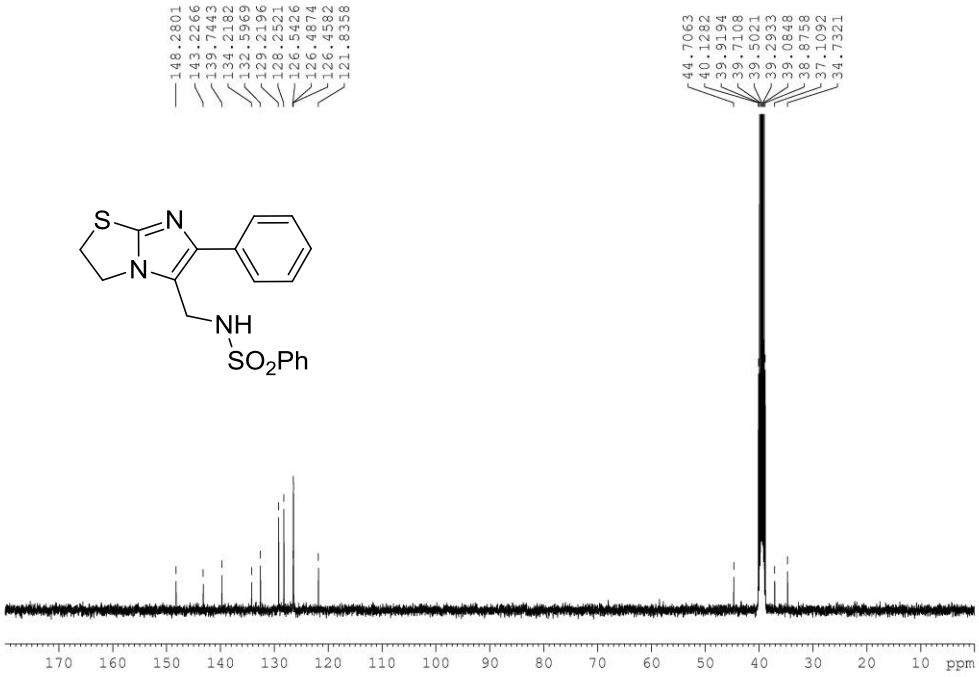


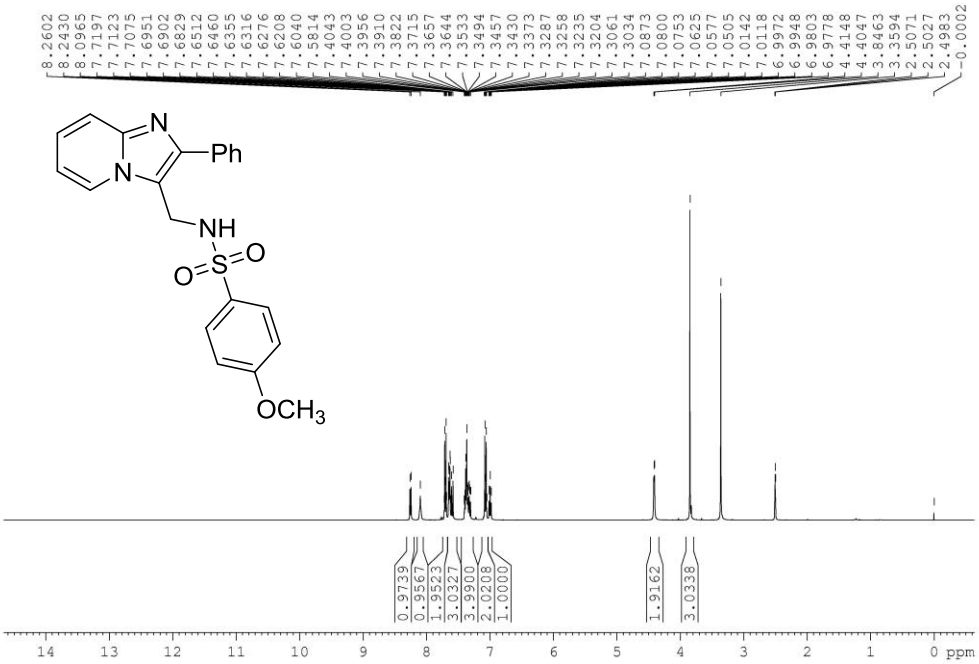
^{1}H NMR of compound **3y**



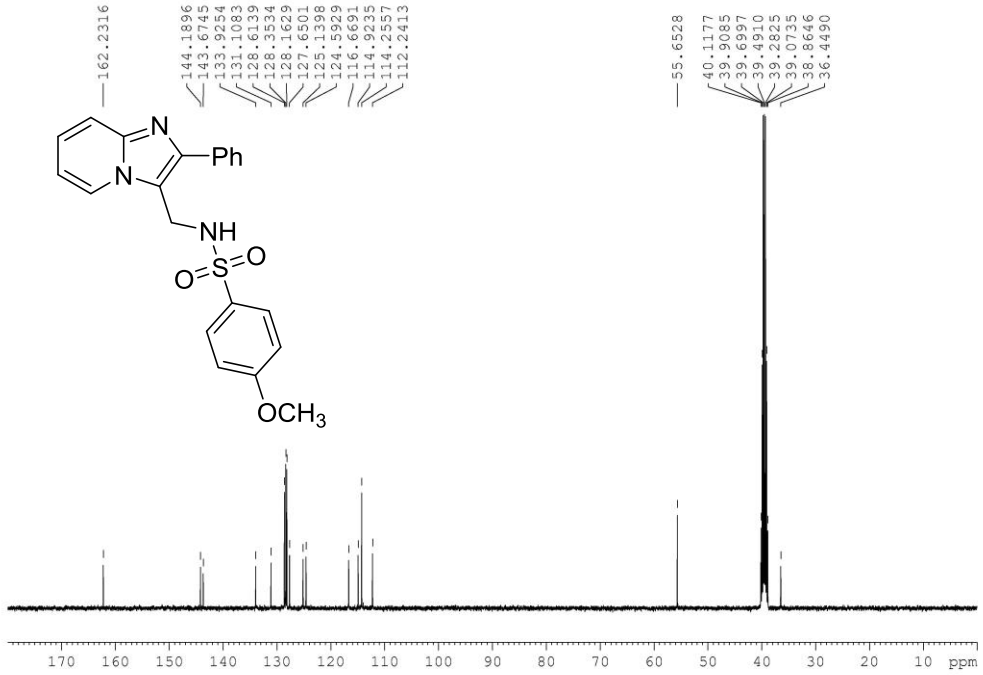
^{13}C NMR of compound **3y**



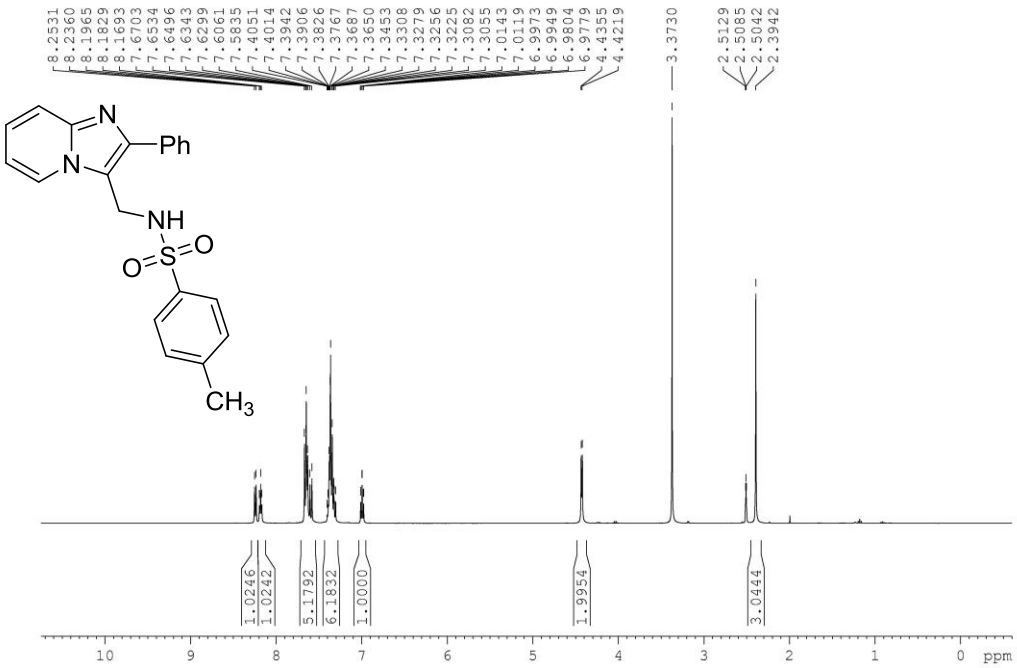
^{1}H NMR of compound **4a**



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



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



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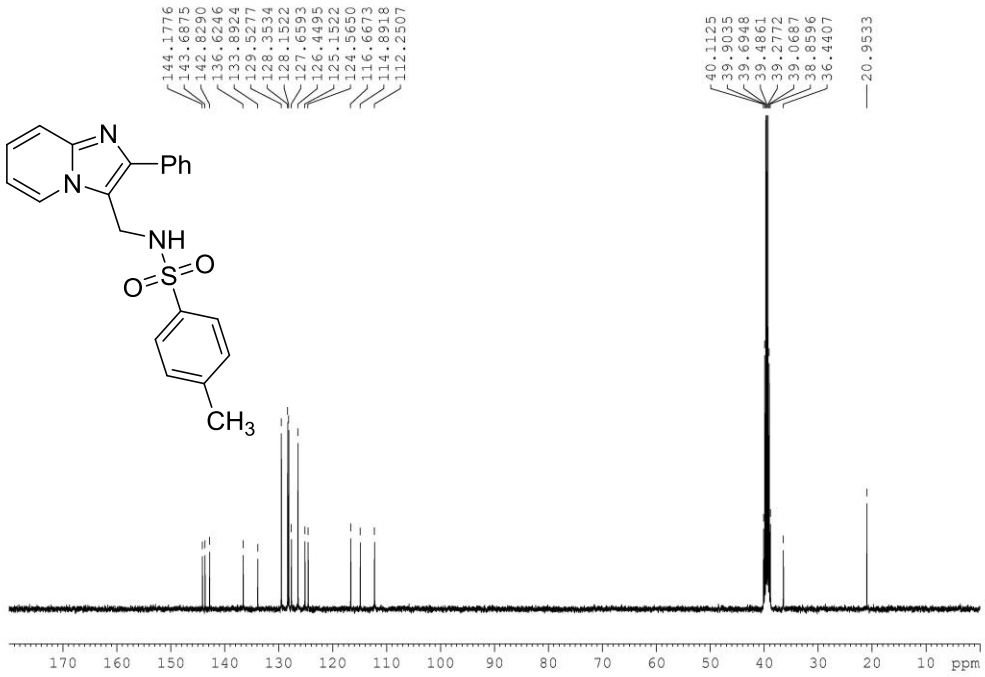
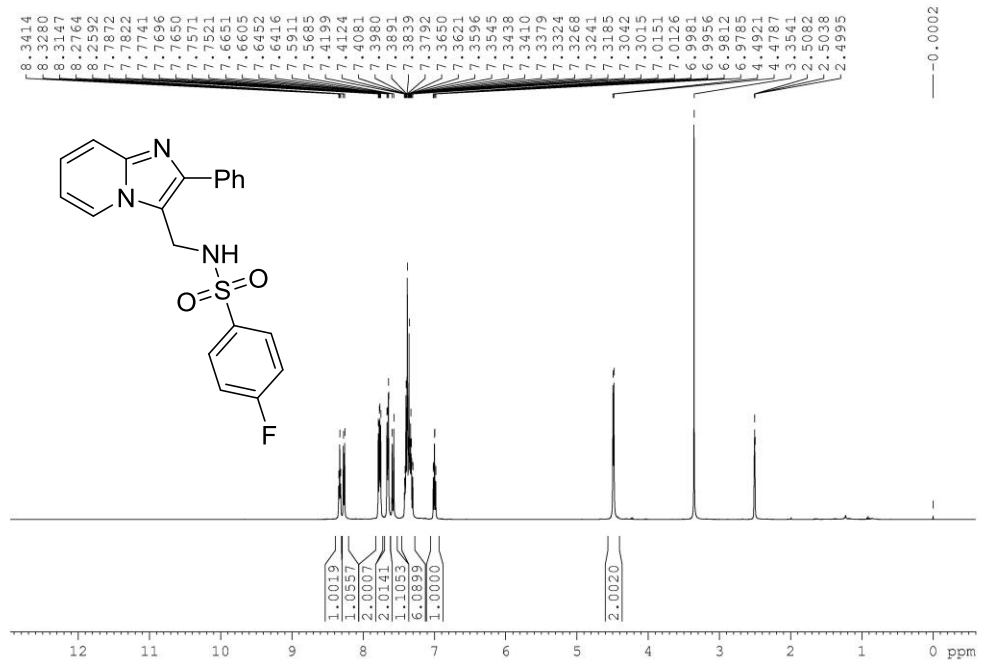
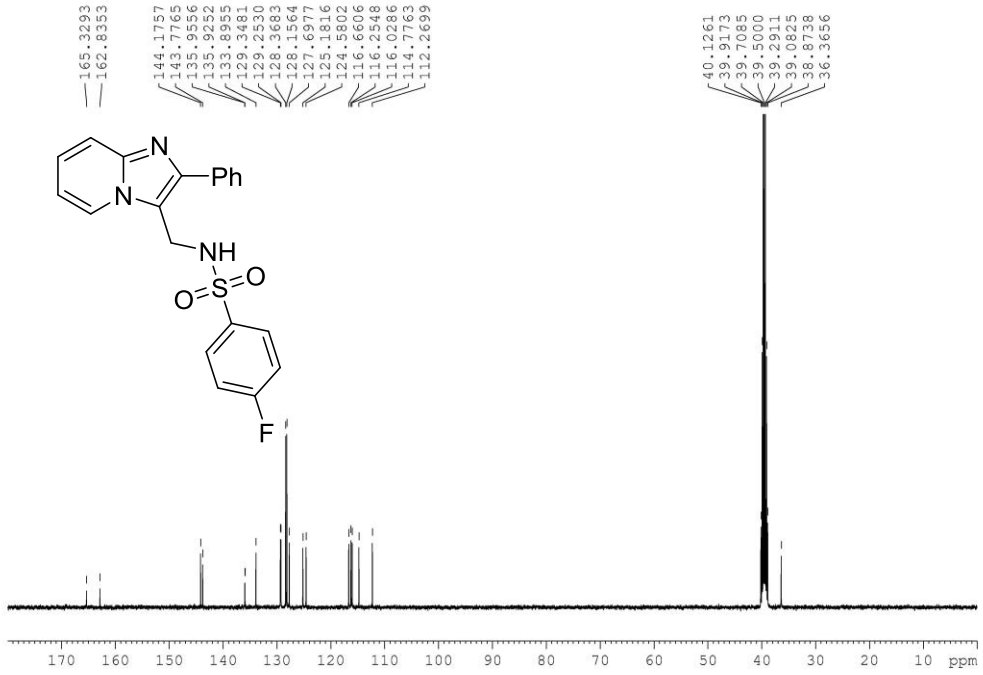


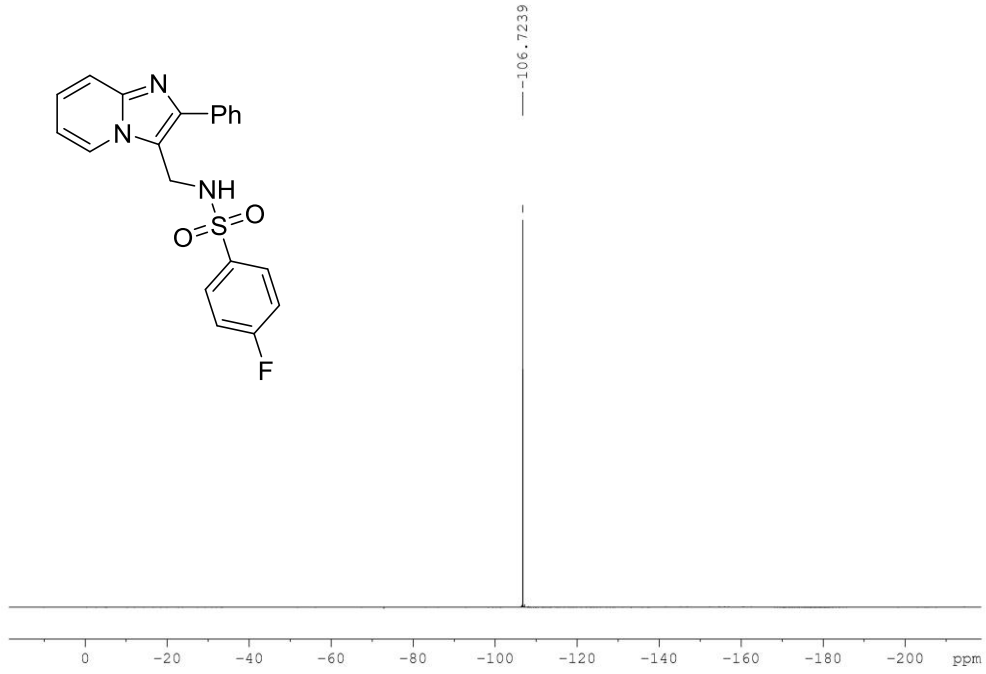
^{1}H NMR of compound **4c**



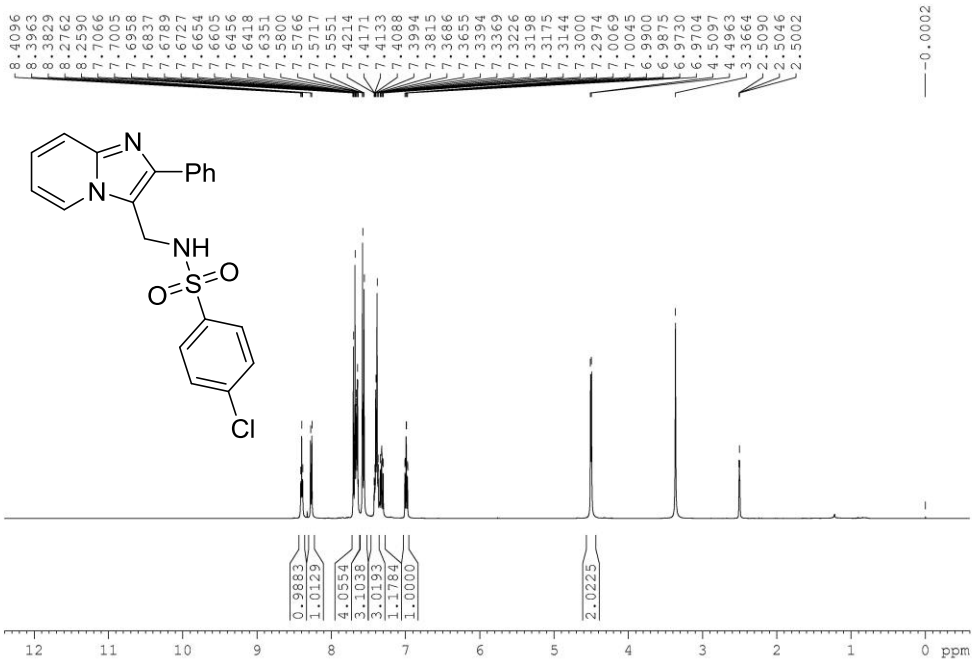
^{13}C NMR of compound **4c**



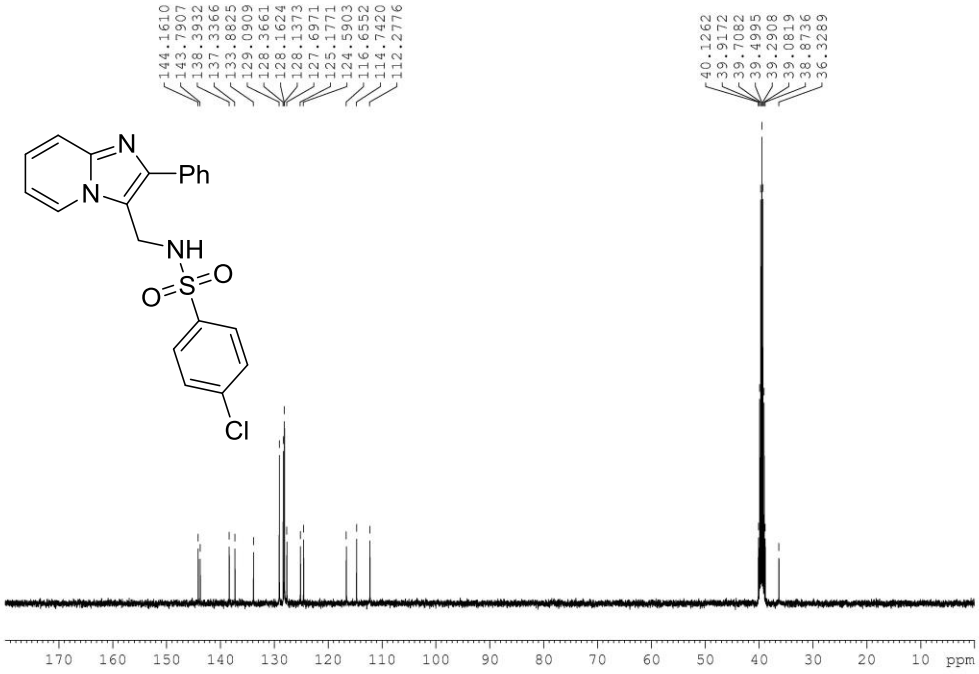
^{19}F NMR of compound **4c**



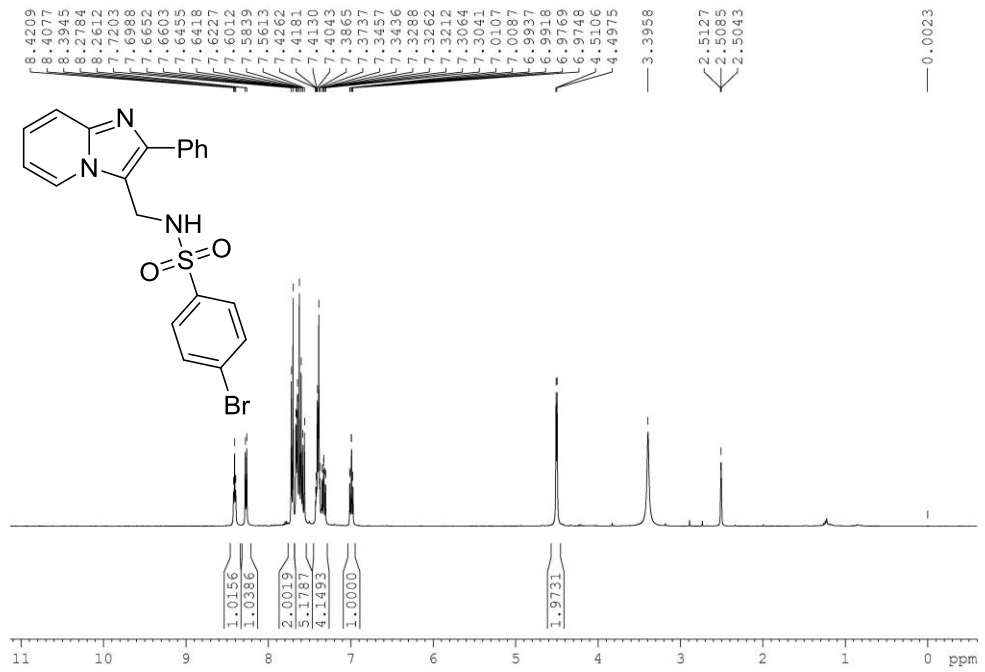
^{1}H NMR of compound **4d**



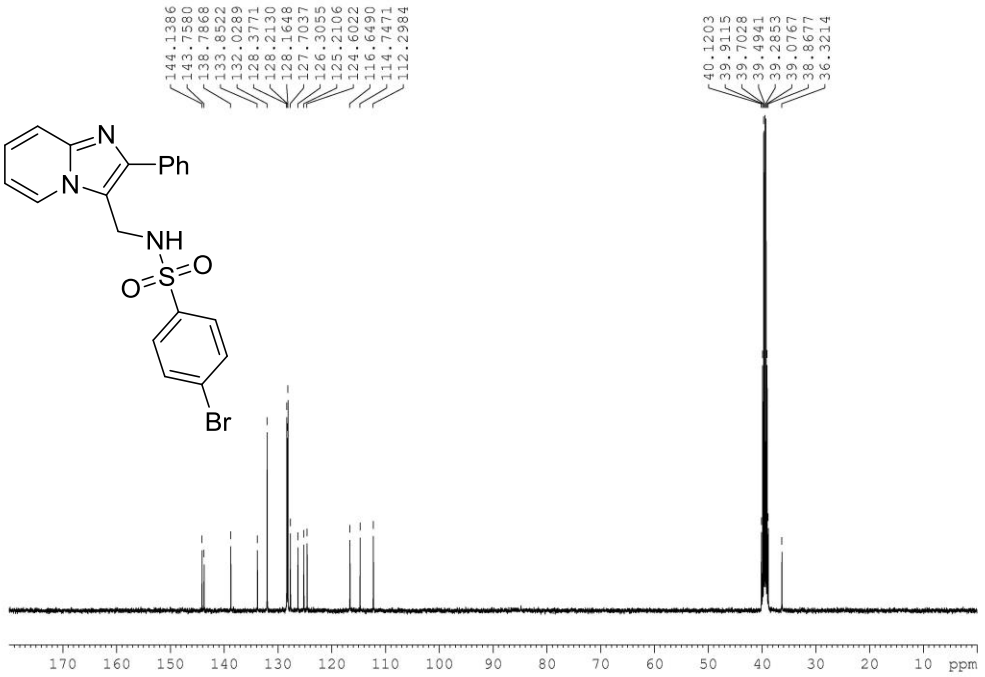
^{13}C NMR of compound **4d**



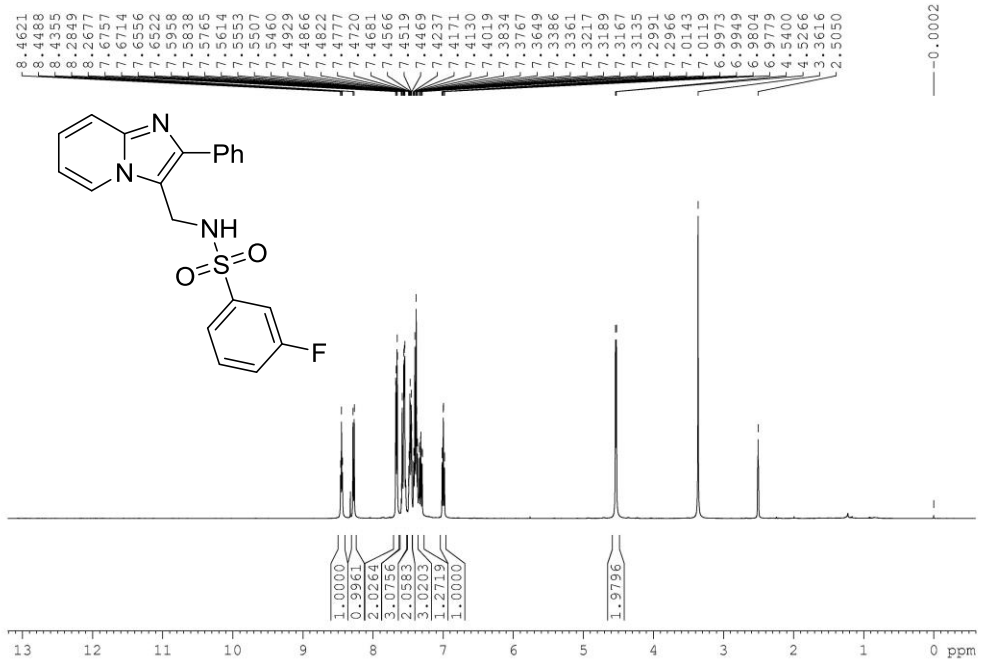
^{1}H NMR of compound **4e**



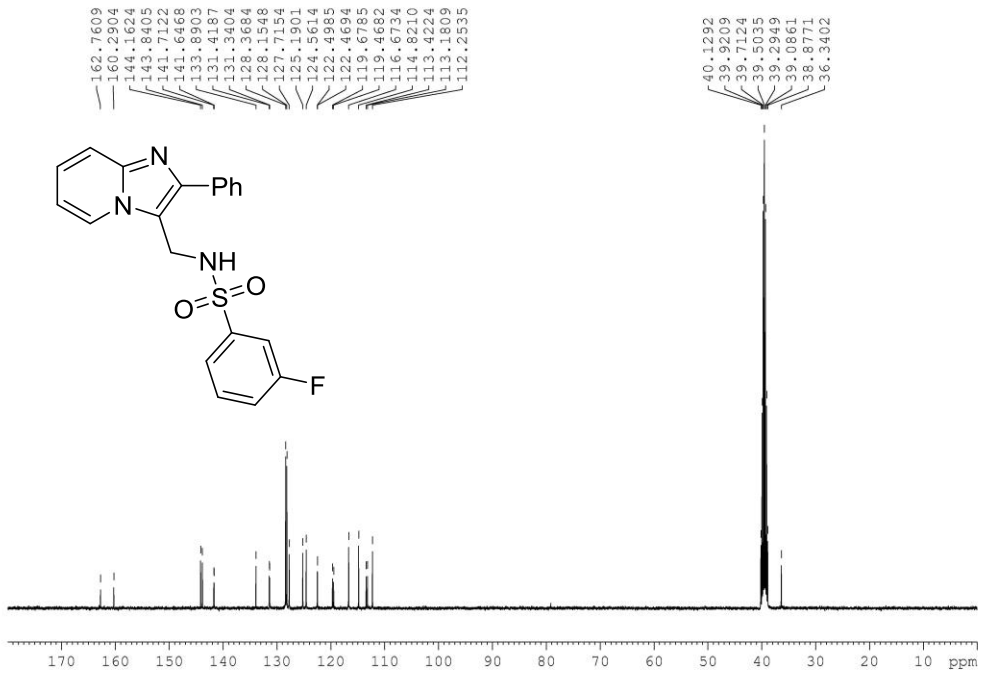
^{13}C NMR of compound **4e**



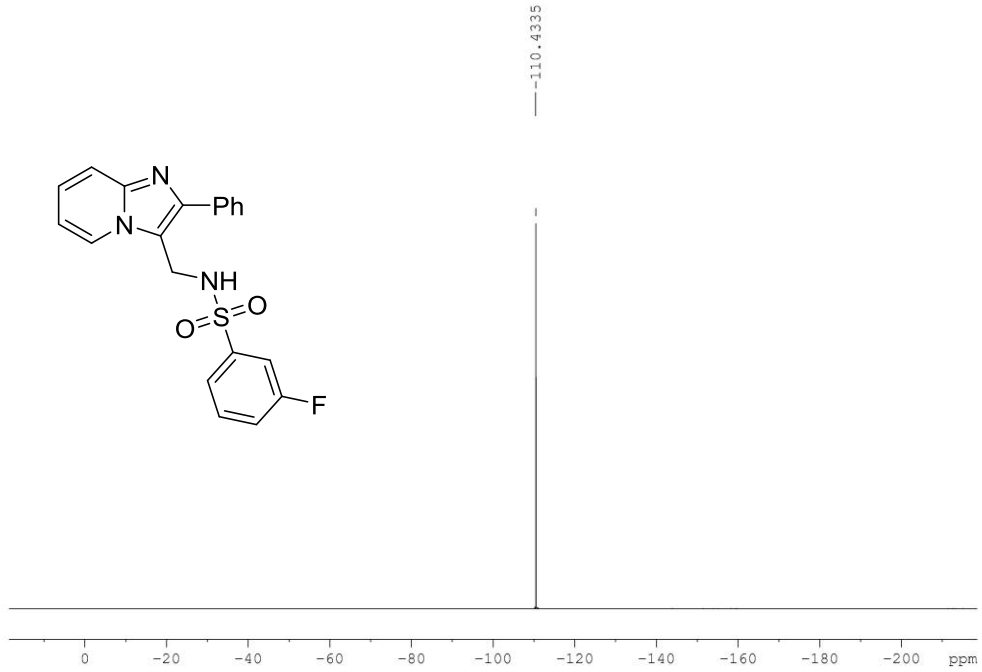
^{1}H NMR of compound **4f**



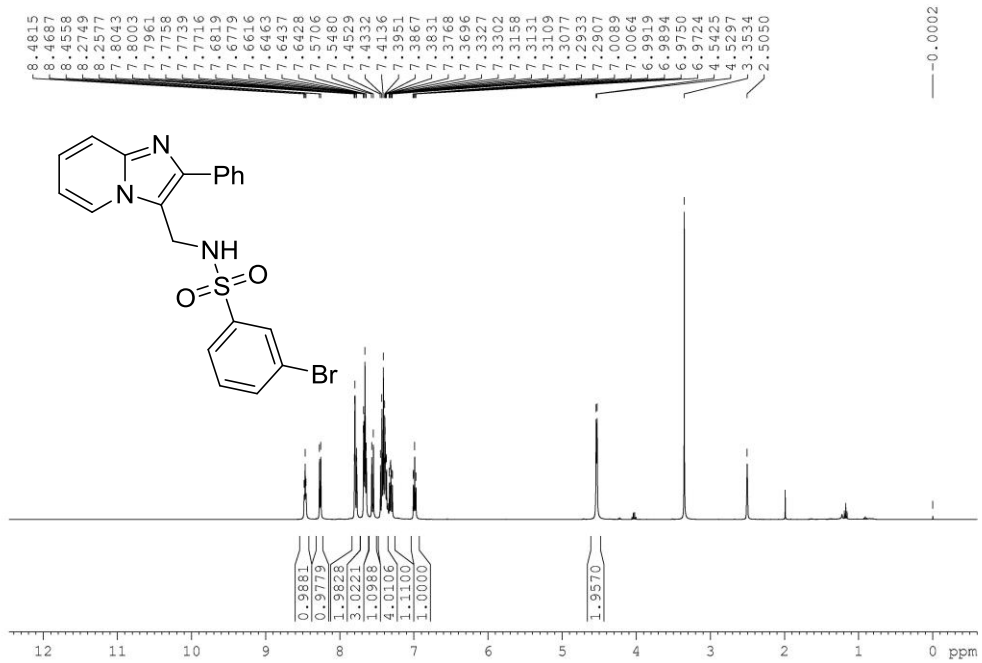
^{13}C NMR of compound **4f**



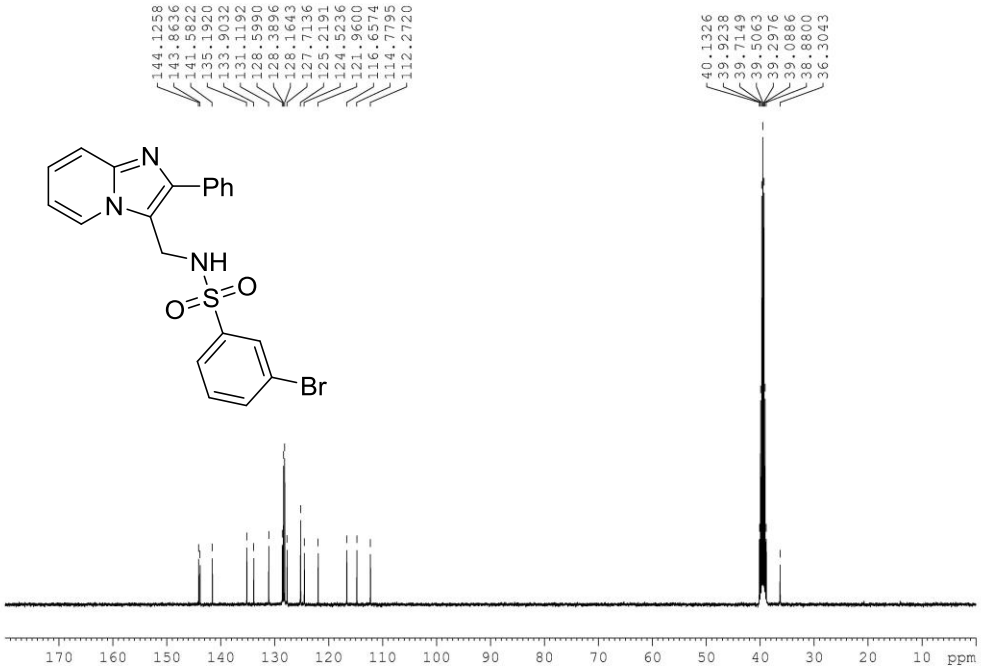
^{19}F NMR of compound **4f**



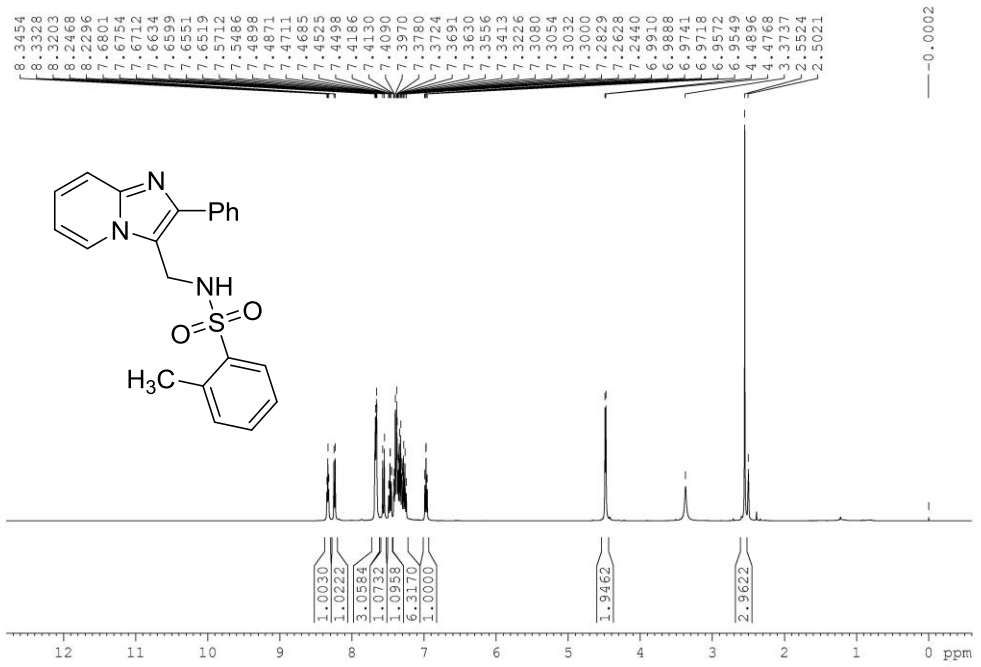
^{1}H NMR of compound **4g**



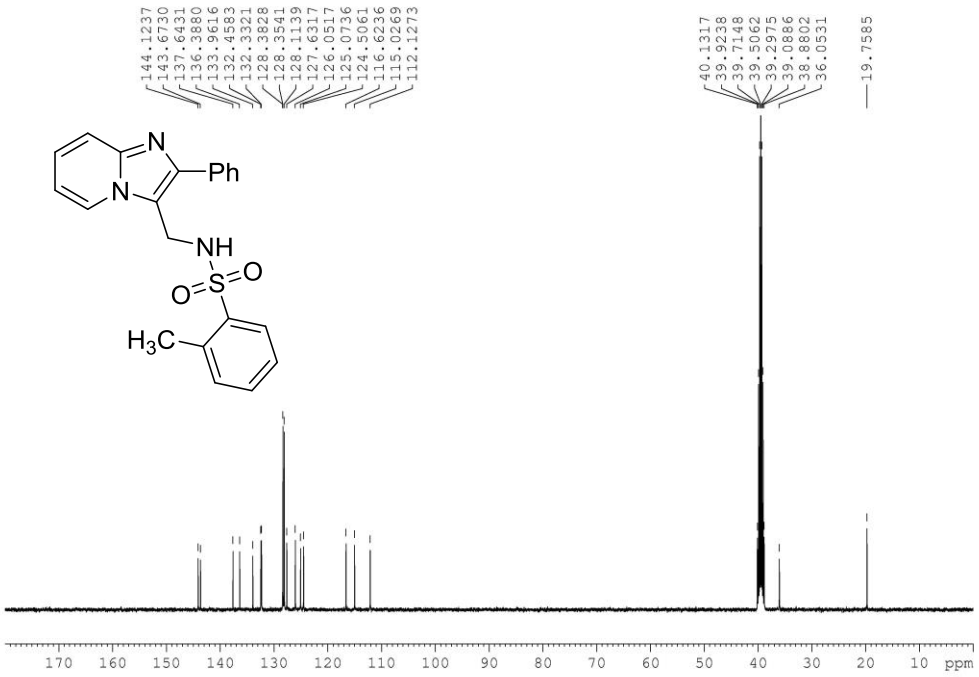
^{13}C NMR of compound **4g**



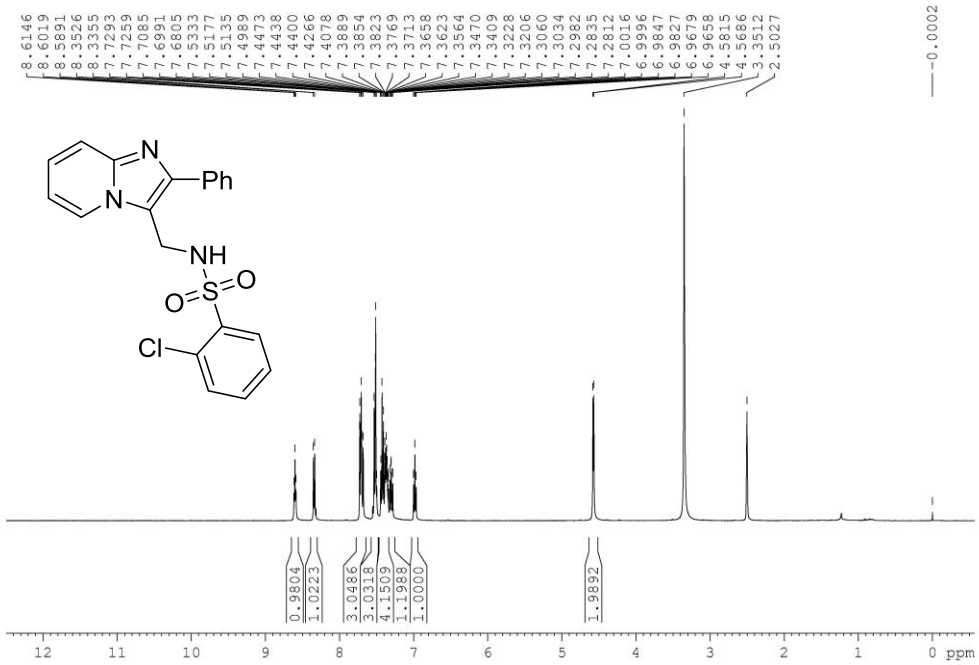
^{1}H NMR of compound **4h**



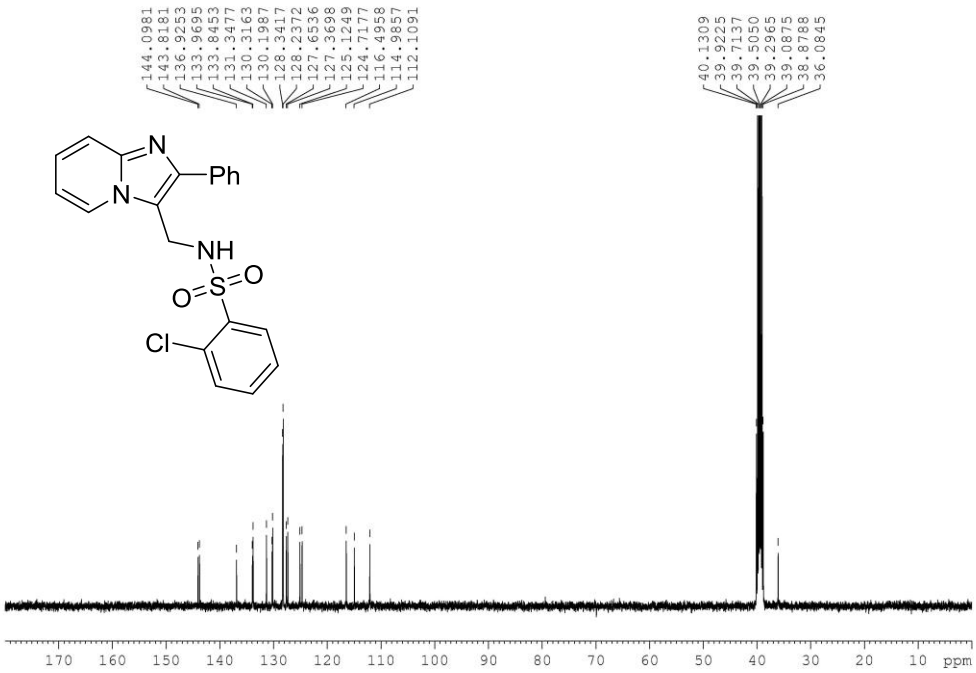
^{13}C NMR of compound **4h**



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



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



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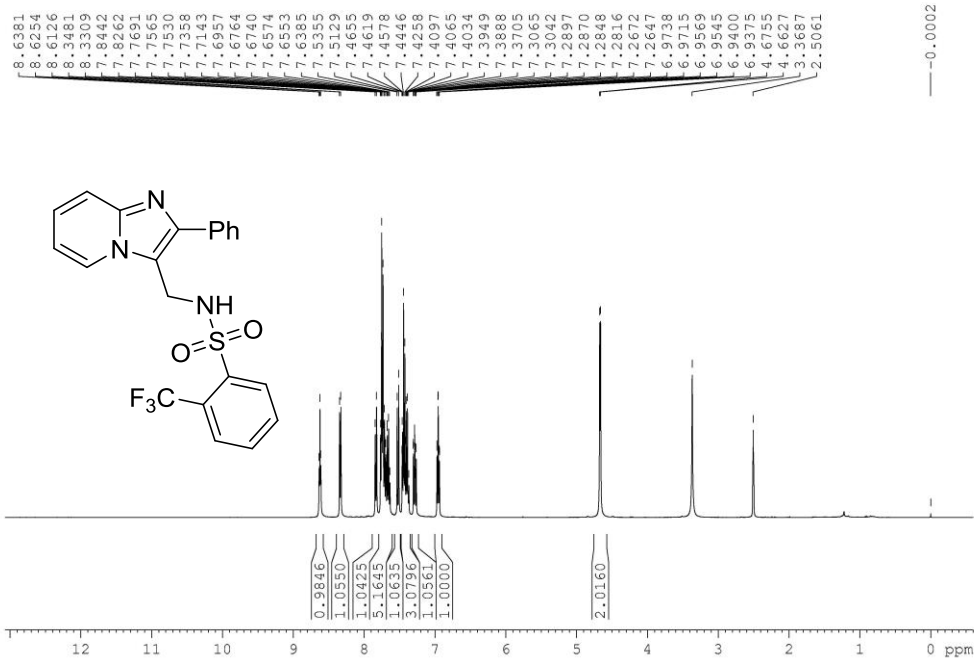

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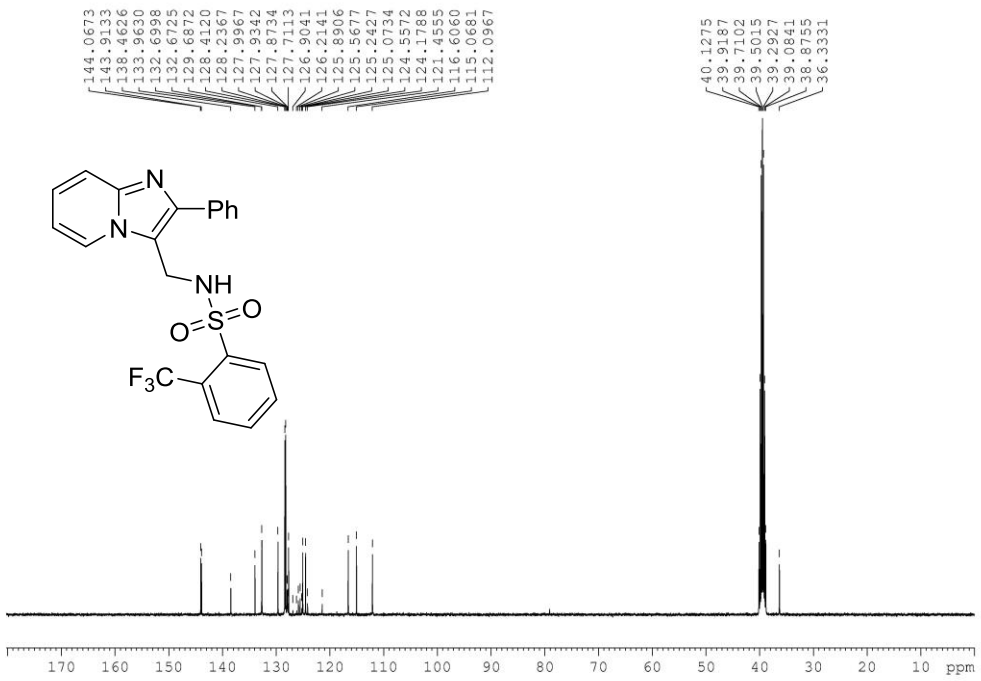
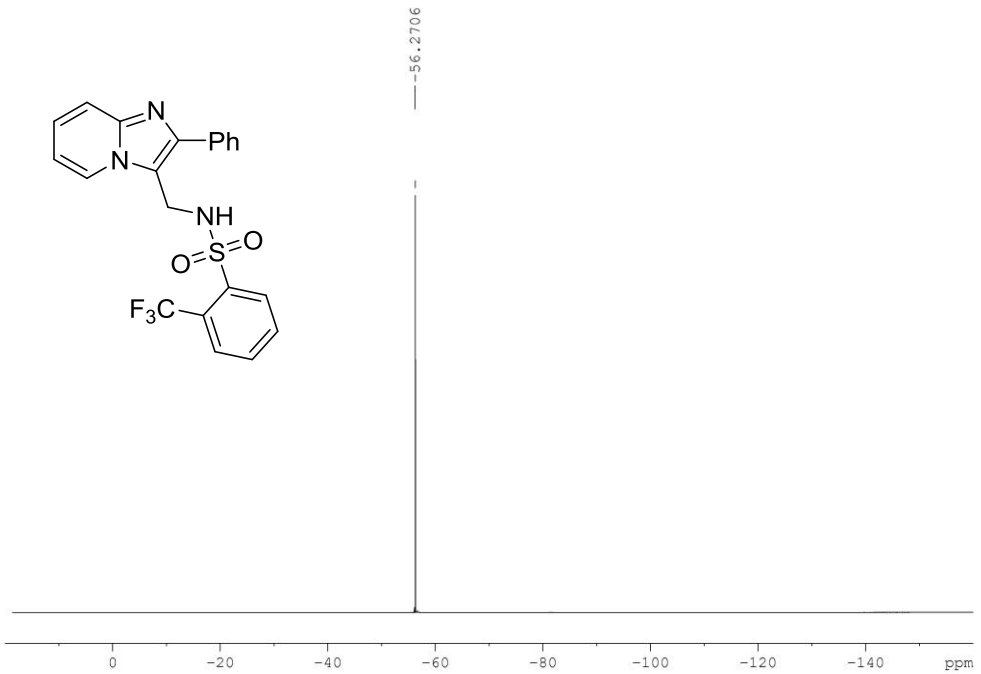


^{19}F NMR of compound **4j**



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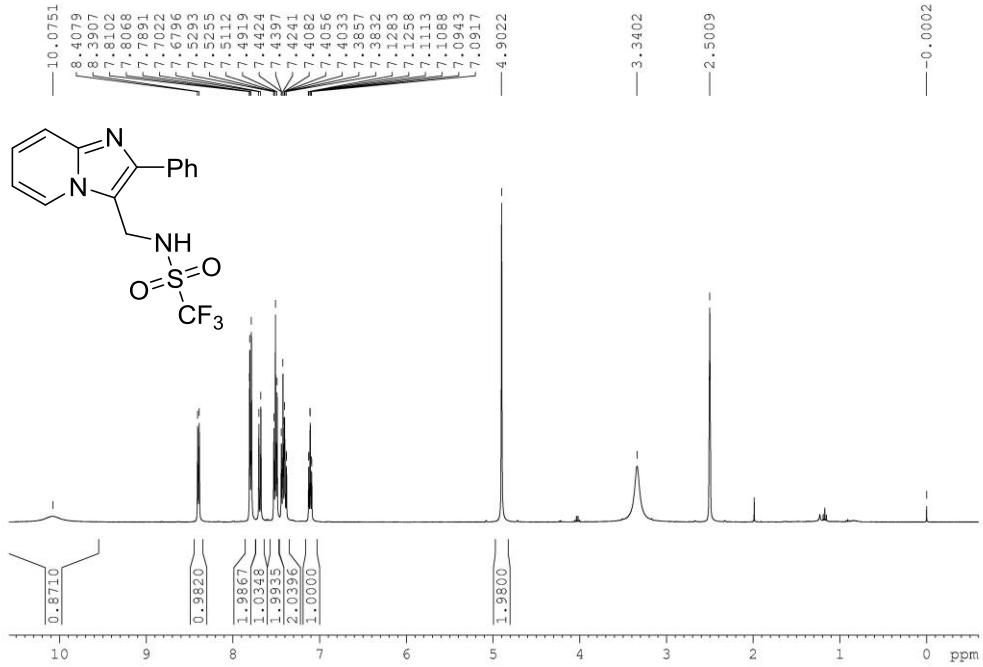

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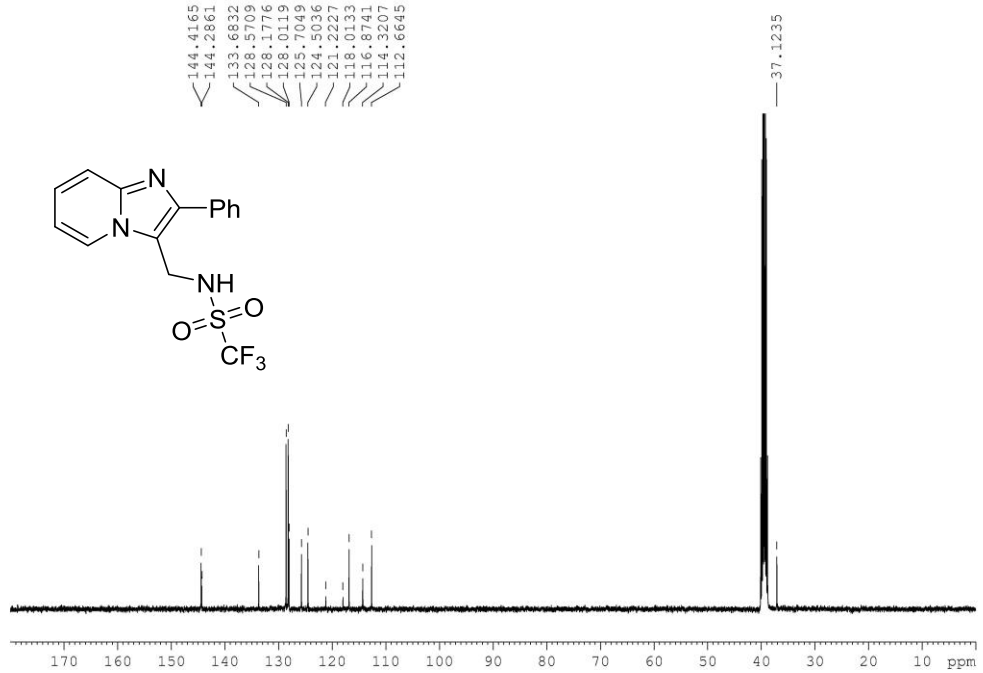

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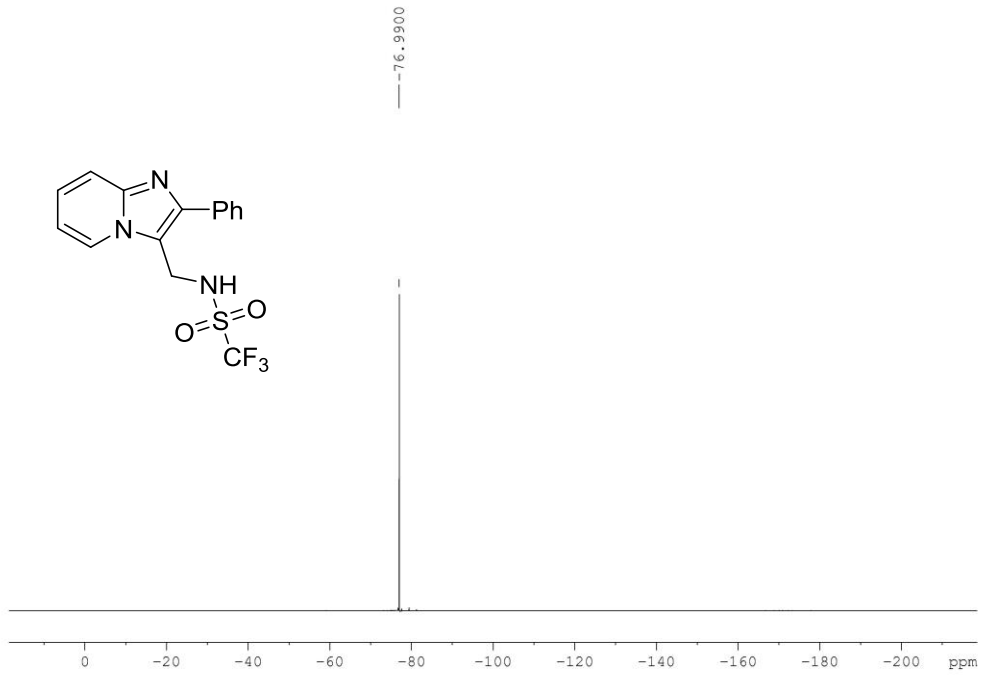
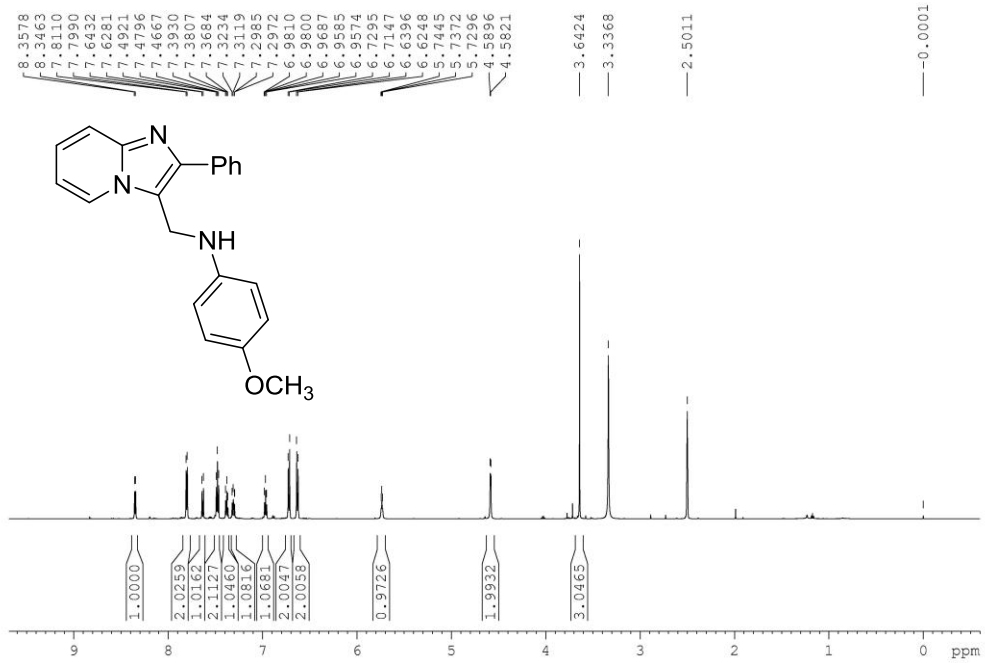
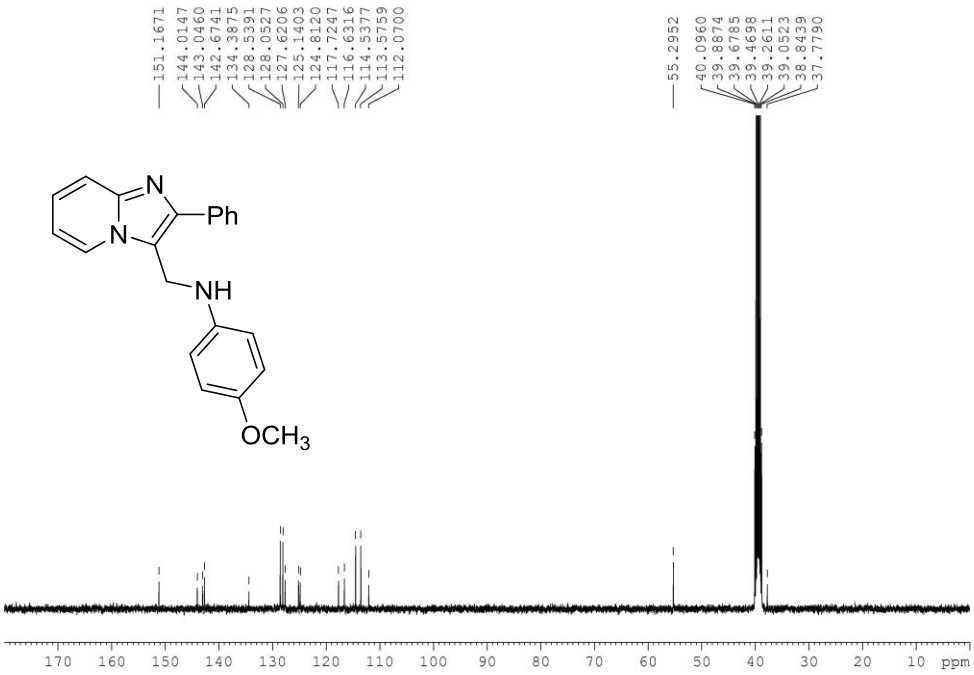


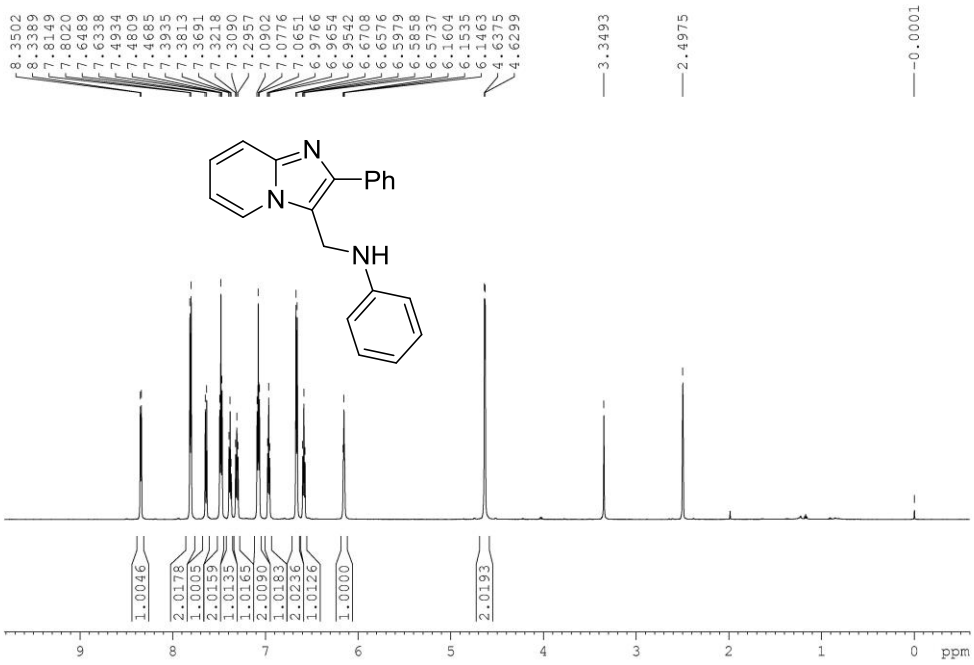
^{1}H NMR of compound **4l**



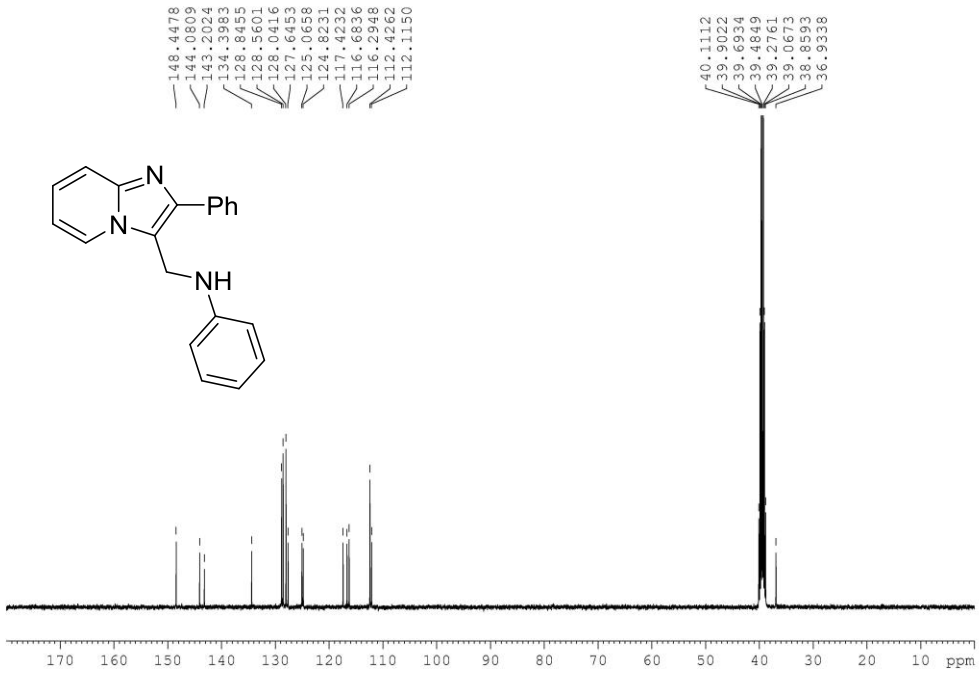
^{13}C NMR of compound **4l**



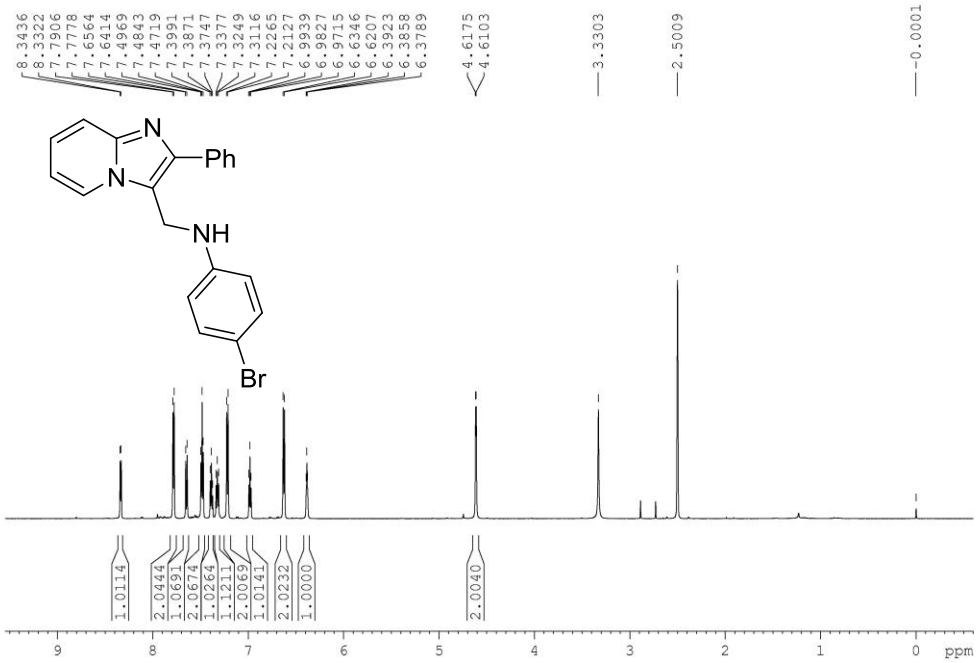
^{1}H NMR of compound **4m**



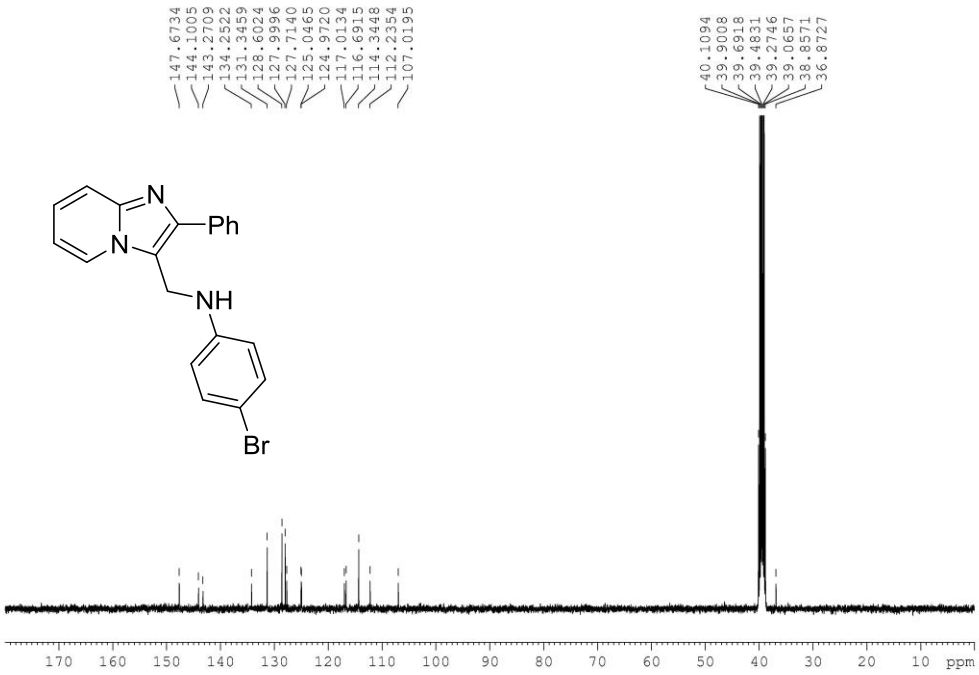
^{13}C NMR of compound **4m**



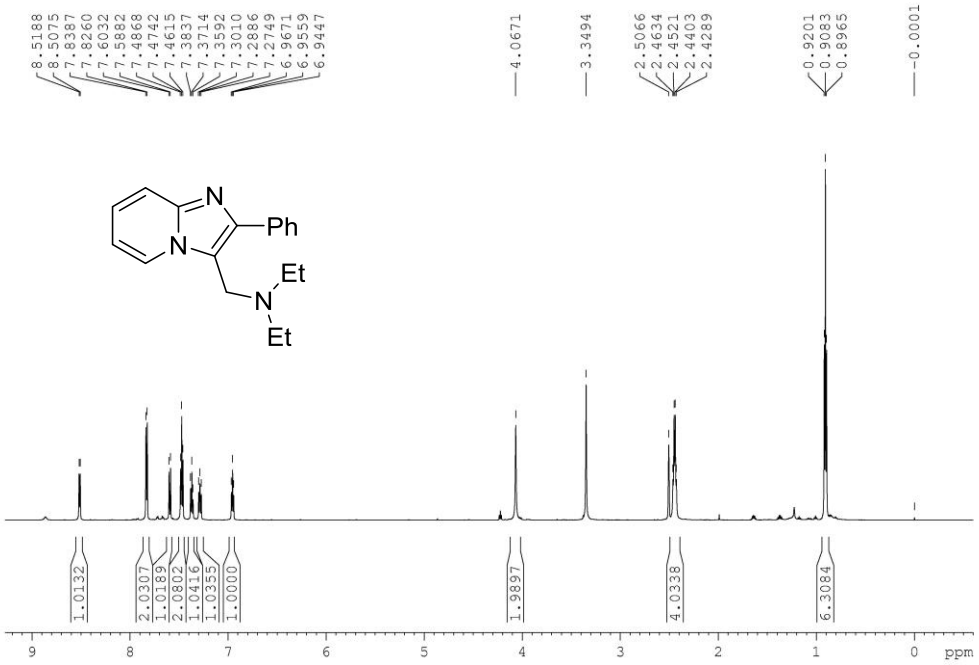
^{1}H NMR of compound **4n**



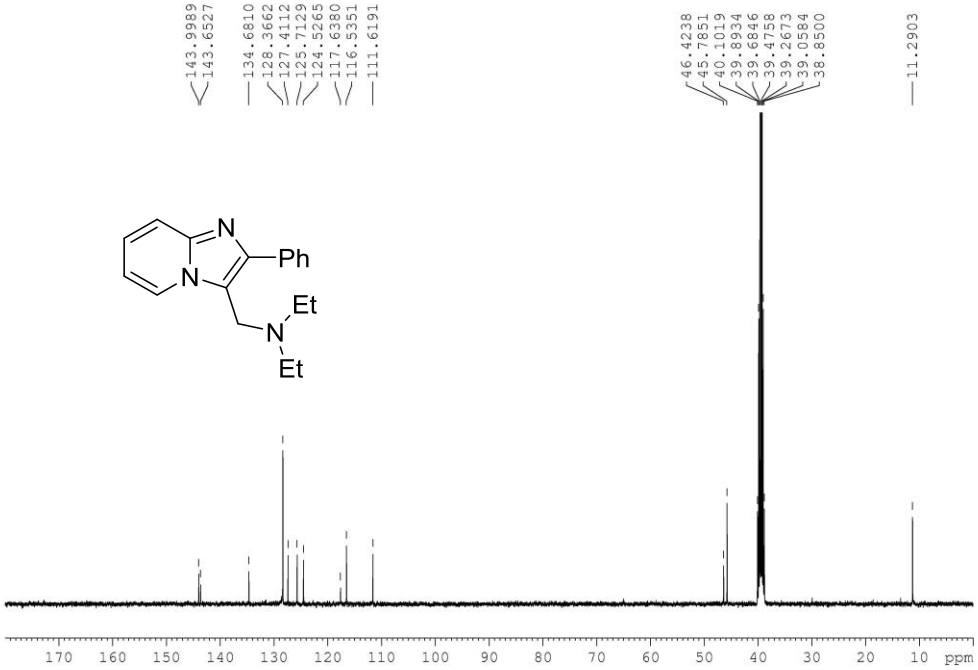
^{13}C NMR of compound **4n**



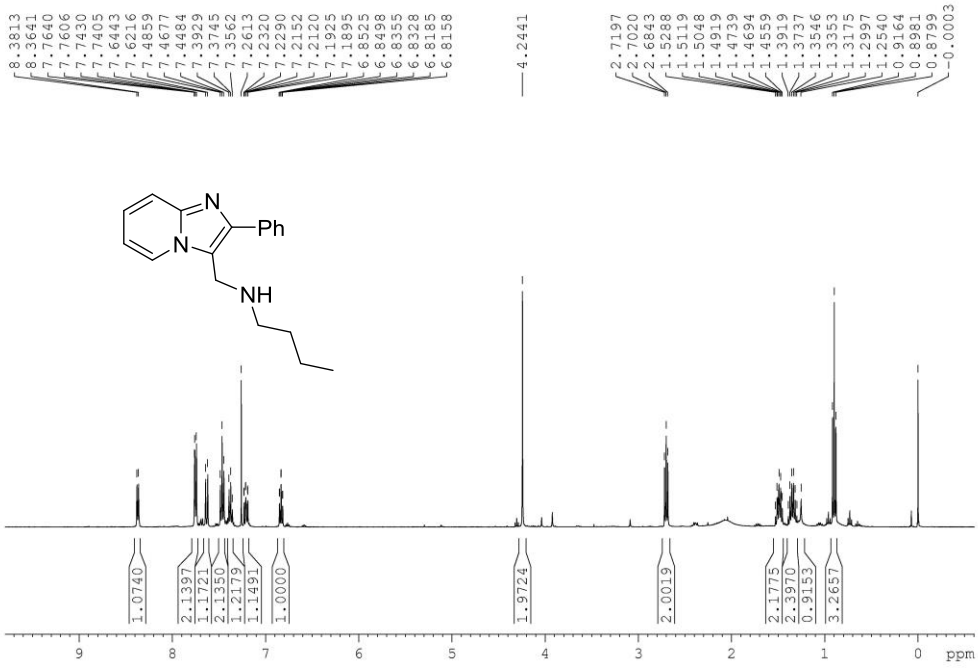
^{1}H NMR of compound **4o**



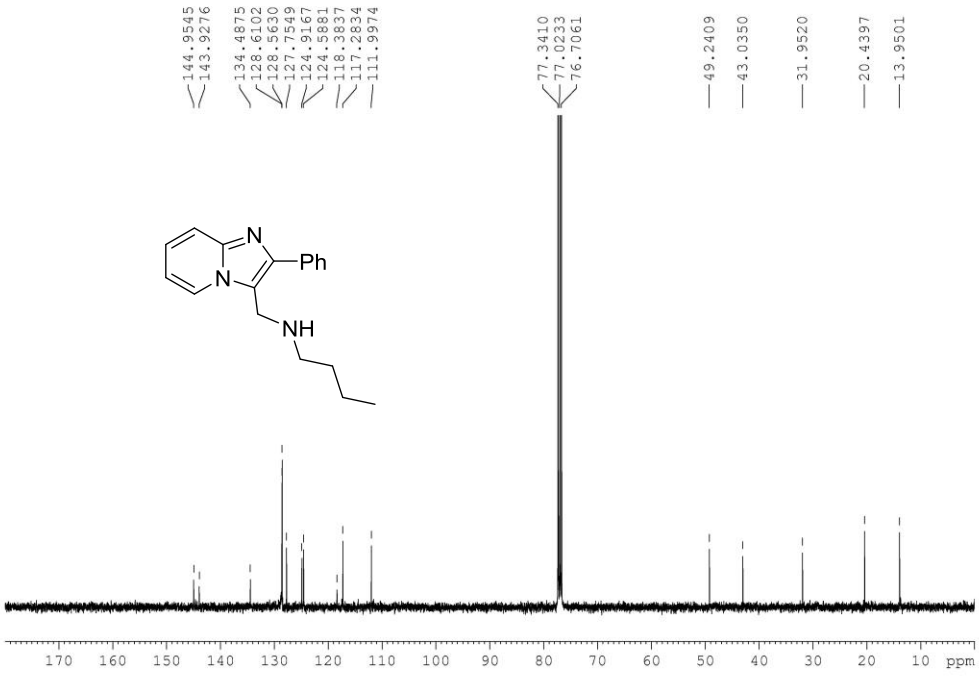
^{13}C NMR of compound **4o**



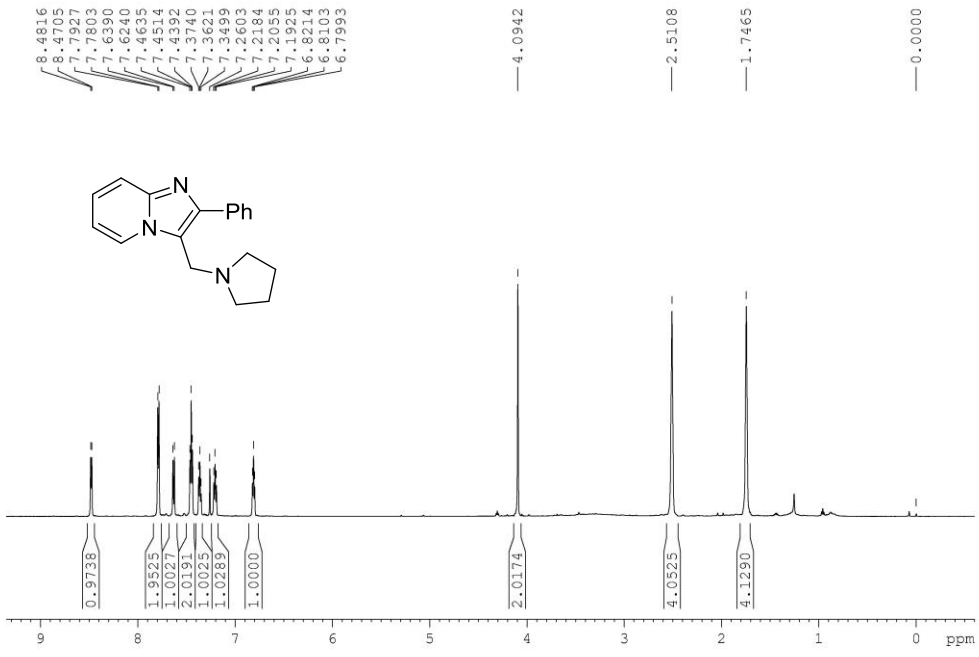
^{1}H NMR of compound **4p**



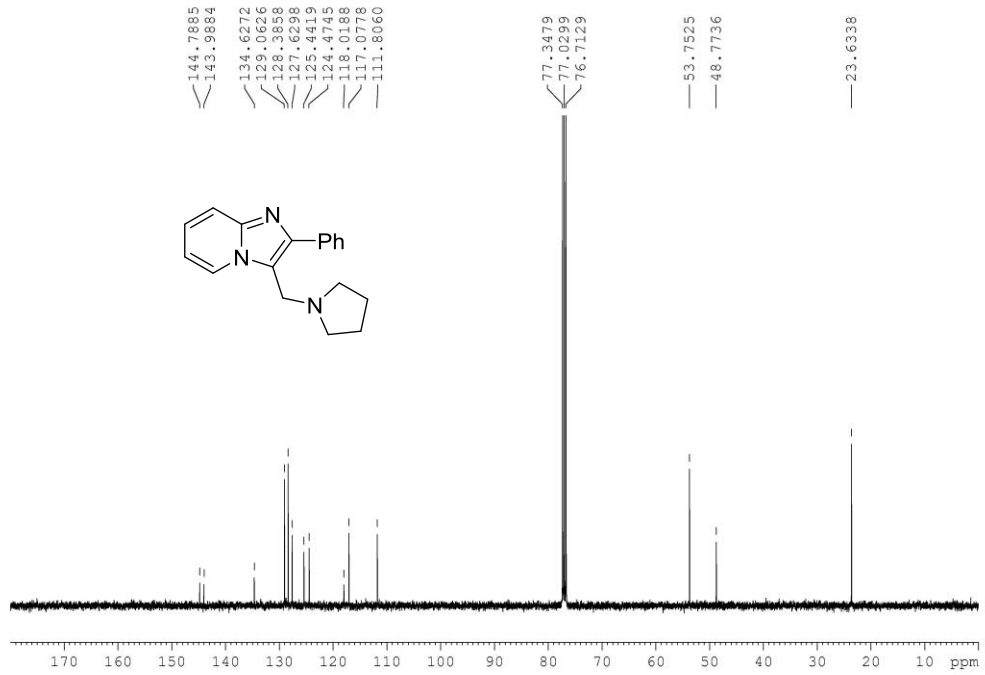
^{13}C NMR of compound **4p**



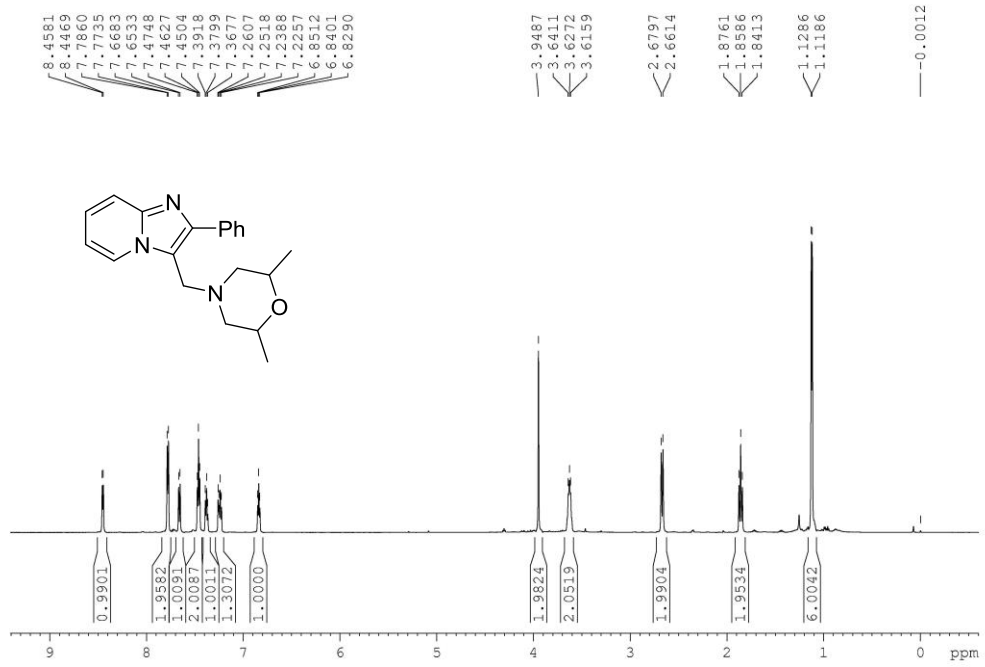
^{1}H NMR of compound **4q**



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



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



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