"Supporting Information"

Discovery and Structure-Based Optimization of 2-Ureidothiophene-3-Carboxylic Acids as Dual Bacterial RNA Polymerase and Viral Reverse Transcriptase Inhibitors

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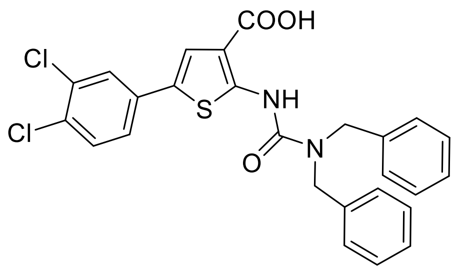
Chemistry

Synthesis and experimental data of compounds **1**–**9** and **22**–**26** were described in a previous work[1] and references therein. Compounds **21** and **27** are commercially available.

2-(3,3-Dibenzylureido)-5-(3,4-dichlorophenyl)thiophene-3-carboxylic acid (10)



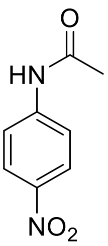
Synthesis of compound **10** was performed as described previously for **9**.[1]

Yield 90%; beige solid; ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 12.91 (br s, 1H), 10.99 (br s, 1H), 7.87 (d, J = 1.0 Hz, 1H), 7.58 (m, 3H), 7.34 (m, 10H), 4.67 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d$_6$) δ 166.70, 153.17, 151.30, 136.89 (2C), 134.26, 131.85, 131.05, 129.11, 128.60 (4C), 127.85, 127.39 (2C), 127.14 (4C), 126.14, 124.72, 121.86, 112.22, 50.34 (2C); m/z (ESI+) 510 [M]$^+$; t$_R$ = 16.01 min.

General procedure for synthesis of *N*-(substituted)-4-nitroanilines 29, 30, 33–35 and 39

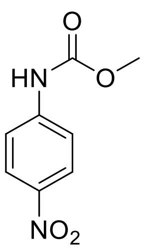
To a stirred solution of 4-nitroaniline **27** (1.38 g, 10 mmol), and pyridine (0.9 mL, 11 mmol) in DCM (50 mL), the appropriate acyl/sulfonyl/sulfamoyl chloride (11 mmol) was added drop wise. The reaction mixture was stirred at room temperature overnight then solvent was removed by vacuum distillation. The obtained material was triturated with cold 1 N HCl (50 mL) and collected by filtration, washed with cold 1 N HCl, water then *n*-hexane.

***N*-(4-Nitrophenyl)acetamide (29)**



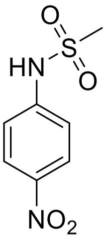
Yield 94%; greenish yellow solid; ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 9.73 (br s, 1H), 7.94 (d, J = 9.1 Hz, 2H), 7.60 (d, J = 9.1 Hz, 2H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d$_6$) δ 169.03, 144.65, 142.13, 124.14 (2C), 118.33 (2C), 23.87; m/z (ESI+) 181 [M + H]$^+$; t$_R$ = 9.52 min.

Methyl (4-nitrophenyl)carbamate (30)



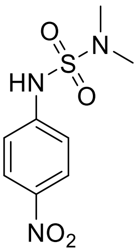
Yield 93%; greenish yellow solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.37 (br s, 1H), 8.19 (d, *J* = 9.2 Hz, 2H), 7.68 (d, *J* = 9.2 Hz, 2H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 153.82, 145.75, 141.74, 125.14 (2C), 117.71 (2C), 52.28; m/z (ESI+) 197 $[M + H]^+$; t_R = 8.95 min.

***N*-(4-Nitrophenyl)methanesulfonamide (33)**



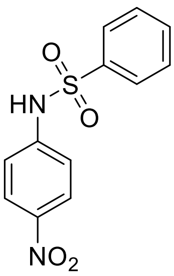
Yield 75%; greenish yellow solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.73 (br s, 1H), 8.22 (d, *J* = 9.2 Hz, 2H), 7.37 (d, *J* = 9.2 Hz, 2H), 3.18 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 145.38, 143.28, 126.28 (2C), 118.64 (2C), 40.78; m/z (ESI+) 216 $[M]^+$; t_R = 7.77 min.

***N*,*N*-Dimethyl-*N*'-(4-nitrophenyl)sulfamide (34)**



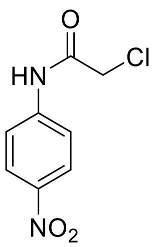
Yield 70%; yellow solid.

***N*-(4-Nitrophenyl)benzenesulfonamide (35)**



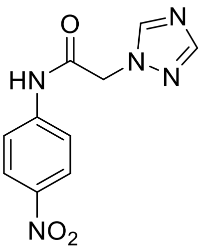
Yield 92%; yellow crystal; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.44 (br s, 1H), 8.04 (d, *J* = 9.1 Hz, 2H), 7.87 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.50 (m, 3H), 7.29 (d, *J* = 9.1 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 143.80, 142.85, 139.02, 132.82, 128.81 (2C), 126.70 (2C), 124.76 (2C), 117.88 (2C); m/z (ESI+) 278 $[M]^+$; t_R = 12.32 min.

2-Chloro-*N*-(4-nitrophenyl)acetamide (39)



Yield 98%; greenish yellow solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.87 (br s, 1H), 8.23 (d, J = 9.2 Hz, 2H), 7.83 (d, J = 9.2 Hz, 2H), 4.33 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.57, 144.56, 142.61, 125.02 (2C), 119. 08 (2C), 43.56; m/z (ESI+) 214 $[M]^+$; t_R = 10.63 min.

***N*-(4-Nitrophenyl)-2-(1*H*-1,2,4-triazol-1-yl)acetamide (40)**



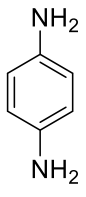
To a stirred mixture of 1,2,4-triazole (1.04 g, 15 mmol) and K_2CO_3 (2.42 g, 17.5 mmol) in DMF (40 mL), 2-chloro-*N*-(4-nitrophenyl)acetamide **39** (3.22 g, 15 mmol) was added. The reaction was stirred at 70 °C for 1 h and at room temperature for further 1 h, then it was poured onto ice cooled water (50 mL). The precipitate was collected by filtration, washed with cold water then *n*-hexane.

Yield 96%; yellow solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.00 (br s, 1H), 8.57 (s, 1H), 8.24 (d, J = 9.2 Hz, 2H), 8.01 (s, 1H), 7.82 (d, J = 9.2 Hz, 2H), 5.22 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.64, 151.43, 145.65, 144.49, 142.60, 125.08 (2C), 119.03 (2C), 51.86; m/z (ESI+) 248 $[M + H]^+$; t_R = 8.84 min.

General procedure for synthesis of *N*-((un)substituted)-1,4-phenylenediamines 28, 31, 32, 36–38 and 41

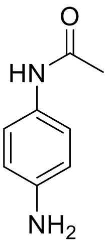
To a stirred solution of 4-nitroaniline **27** or derivatives (5 mmol) in EtOH (30 mL), iron powder (1.40 g, 25 mmol) was added at 55 °C followed by NH_4Cl (133 mg, 2.5 mmol) solution in water (15 mL). The reaction was heated at 90 °C for 1 h, then iron was filtered while hot and the filtrate was concentrated *in vacuo*. The residue was diluted with water (15 mL) and basified by $NaHCO_3$ (saturated aqueous solution) to pH 7–8. The mixture was extracted with EtOAc (3 × 20 mL). The combined organic extract was washed with brine, dried over anhydrous $MgSO_4$, and the solvent was removed by vacuum distillation. The obtained material was triturated with *n*-hexane, and collected by filtration.

1,4-Phenylenediamine (28)



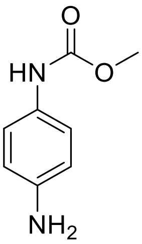
Yield 65%; pink crystals; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.58 (s, 4H), 3.33 (br s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.54 (2C), 116.69 (4C); m/z (ESI+) 150 $[M + H + MeCN]^+$; t_R = 0.88 min.

_N_-(4-Aminophenyl)acetamide (31)



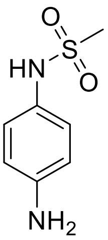
Yield 86%; buff solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.98 (br s, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.52 (d, *J* = 8.6 Hz, 2H), 3.89 (br s, 2H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 167.83, 142.94, 129.19, 121.18 (2C), 114.36 (2C), 23.41; m/z (ESI+) 151 $[M + H]^+$; t_R = 1.08 min.

Methyl (4-aminophenyl)carbamate (32)



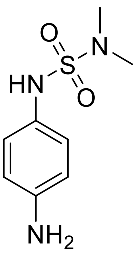
Yield 82%; pink solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (br s, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 6.49 (br s, 1H), 3.75 (s, 3H), 3.58 (br s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.53, 142.74, 129.15, 121.03 (2C), 115.54 (2C), 52.16; m/z (ESI+) 167 $[M + H]^+$; t_R = 4.58 min.

_N_-(4-Aminophenyl)methanesulfonamide (36)



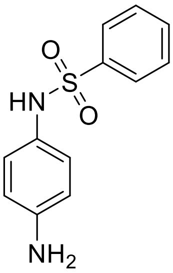
Yield 85%; reddish solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.90 (br s, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 5.01 (br s, 2H), 2.80 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 146.68, 125.99, 124.83 (2C), 114.11 (2C), 38.16; m/z (ESI+) 187 $[M + H]^+$; t_R = 2.50 min.

_N_'-(4-Aminophenyl)-_N_,_N_-dimethylsulfamide (37)



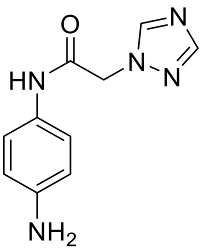
Yield 68%; beige crystals; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.90 (br s, 1H), 6.91 (d, *J* = 6.5 Hz, 2H), 6.48 (d, *J* = 6.5 Hz, 2H), 4.41 (br s, 2H), 2.64 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 144.92, 126.99, 123.59 (2C), 114.21 (2C), 37.72 (2C); m/z (ESI+) 216 $[M + H]^+$; t_R = 2.11 min.

_N_-(4-Aminophenyl)benzenesulfonamide (38)



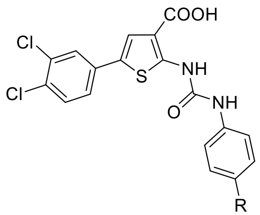
Yield 90%; pink solid; ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 9.11 (br s, 1H), 7.62 (m, 2H), 7.43 (m, 1H), 7.34 (m, 2H), 6.72 (d, J = 8.6 Hz, 2H), 6.40 (d, J = 8.6 Hz, 2H), 4.02 (br s, 2H); ^{13}C NMR (75 MHz, DMSO-d$_6$) δ 145.00, 139.47, 131.77, 128.20 (2C), 126.59 (2C), 126.33, 124.60 (2C), 114.47 (2C); m/z (ESI+) 249 [M + H]$^+$; t_R = 8.27 min.

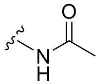
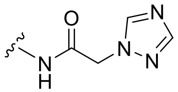
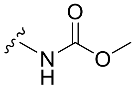
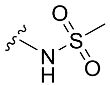
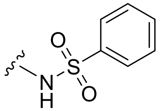
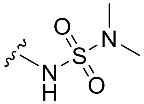
_N_-(4-Aminophenyl)-2-(1_H_-1,2,4-triazol-1-yl)acetamide (41)



Yield 75%; pale grey solid; ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 9.82 (br s, 1H), 8.36 (s, 1H), 7.84 (s, 1H), 7.21 (s, 2H), 6.52 (s, 2H), 4.98 (s, 2H), 4.39 (br s, 2H); ^{13}C NMR (75 MHz, DMSO-d$_6$) δ 162.93, 150.92, 144.72, 144.27, 127.77, 120.90 (2C), 114.01 (2C), 51.71; m/z (ESI+) 218 [M + H]$^+$; t_R = 0.91 min.

Table S1. Substituent Constants[2] and Molecular Descriptors of Compounds **11–20**[a]



Compound	R	RT IC_{50} (μM)	pIC_{50} (-log IC_{50})	π	σ	KierFlex	PC^+	Vsa_don	SMR
11	H	1.2	5.92	0.00	0.00	5.0488	4.7140	11.3652	10.5818
12	F	0.7	6.15	0.14	0.06	5.2057	4.7540	11.3652	10.5776
13	OMe	0.8	6.10	-0.02	-0.27	5.7827	4.9260	11.3652	11.2370
14	NH_2	20.0	4.70	-1.23	-0.66	5.2823	5.4640	29.1076	11.0230
15		0.6	6.22	-0.97	0.00	6.1130	5.8310	17.0477	12.0121
16		0.8	6.10	-	-	6.6457	5.8310	17.0477	13.4674
17		0.3	6.52	-0.52	-0.17	6.6264	6.1110	17.0477	12.1845
18		0.1	7.00	-1.18	0.03	7.2103	6.6210	19.4404	12.4284
19		0.9	6.05	0.45	0.01	7.4366	6.5160	19.4404	14.3068
20		0.6	6.22	-	-	7.9895	6.5160	19.4404	13.2047

[a]π: Lipophilicity constant; σ: Hammett constant; KierFlex: Kier molecular flexibility index[3]; PC^+: total positive partial charge; vsa_don: approximation to the sum of van der Waals surface areas of pure hydrogen bond donors; SMR: molecular refractivity including implicit hydrogens.

Binding and Mechanistic Studies of the Compounds

To perform binding studies, RT labeled with Alexa488 at position 69 in the finger subdomain of p66, was titrated with increasing concentrations of a model p/t duplex, where the template oligonucleotide sequence was labeled by carboxytetramethylrhodamine (TAMRA) at 7 nt away from the 3′-OH end of the primer (Figure S1A). The FRET efficiency is also sensitive to RT orientation on the duplex, with high FRET being obtained when RT is bound in polymerase orientation (polymerization site is towards 3′-OH end of primer). Binding affinities were obtained by fitting the FRET efficiency at different concentrations of p/t duplexes (Figure S1B) to eq 3, by assuming a single binding site for RT on the p/t.

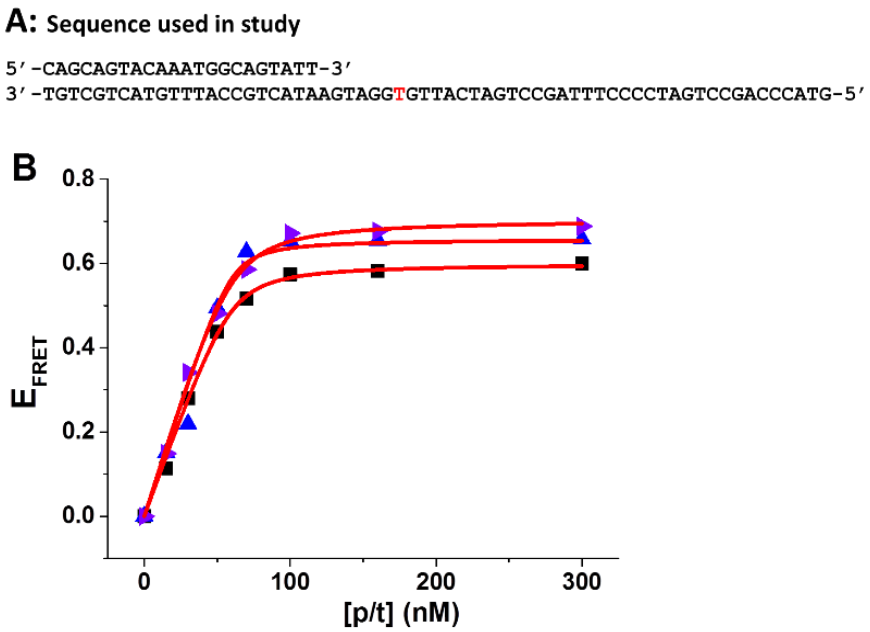


Figure S1. Effect of compounds **4** and **17** on the binding of RT to p/t duplex: (A) Sequence of the p/t duplex used in this study. The FRET acceptor fluorophore, TAMRA, is attached to the Thr residue in red in the template sequence; (B) The FRET efficiencies for 60 nM Alexa488-labelled RT are plotted against increasing concentrations of TAMRA-labeled p/t duplex in the absence (black squares) and in the presence of compound **4** (blue triangle) or compound **17** (violet triangle). FRET efficiencies were calculated as described in the methods section. Red lines represent the best fits of the experimental data to eq 3 and the values given in Table S2.

Table S2. Binding and Kinetic Parameters of the Interaction between RT and p/t Duplex in the Presence of the Inhibitors

Sample	K_d (nM)[a]	Kinetic rate constants, k_{obs} (s^{-1}), × 10^3[b]
RT	2.6 (±0.2)	--
RT + NVP	3.5 (±0.2)	223 (±10)
RT + **4**	3.0 (±0.3)	67 (±5)
RT + **11**	2.2 (±0.2)	41 (±10)
RT + **12**	3.4 (±0.1)	52 (±6)
RT + **13**	1.9 (±0.2)	60 (±7)
RT + **15**	3.1 (±0.3)	76 (±8)
RT + **16**	3.7 (±0.4)	49 (±6)
RT + **17**	3.5 (±0.4)	87 (±5)
RT + **18**	2.9 (±0.3)	97 (±10)
RT + **19**	3.3 (±0.4)	50 (±5)
RT + **20**	2.8 (±0.4)	47 (±9)

[a]Binding parameters were obtained as described in the materials and methods section. RT was labeled at position 69 of the p66 domain with alexa488 dye. Experiments were repeated at least 3 times; [b]A RT mutant doubly labeled at positions 24 and 287 with bodipy dyes was used. Rate constants are calculated by using eq 2.

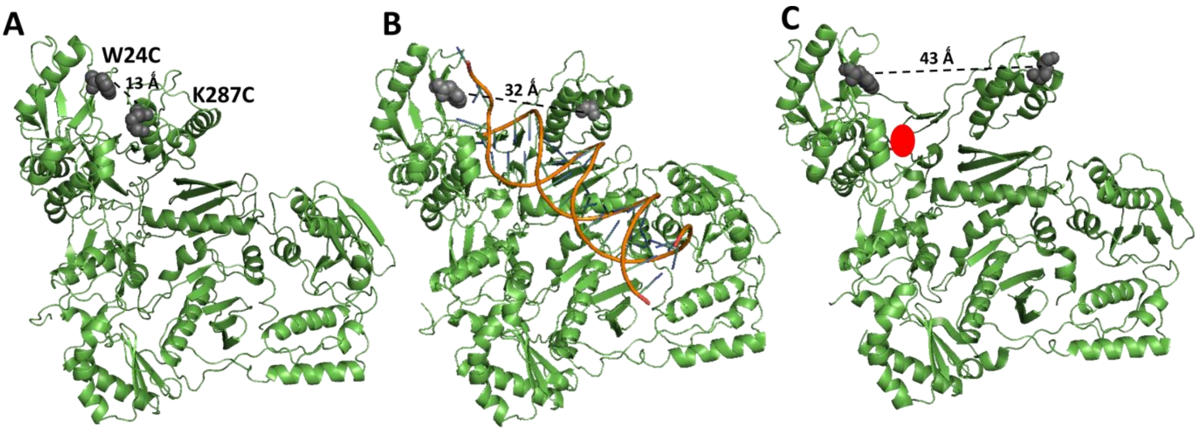


Figure S2. Distance changes between thumb and finger subdomains of RT: 3D structure of HIV-1 RT in the absence (A) and presence of either DNA/DNA p/t (B) or nevirapine (red oval) (C). The recombinantly engineered cysteines in thumb and finger are shown by gray spheres. The average distance between finger and thumb varies from ~ 13 Å (in the absence of duplex) to ~ 43 Å (in the presence of NVP). The figures were prepared by using structures in protein data bank (PDB ID: 1DLO, 1R0A and 1S1U).

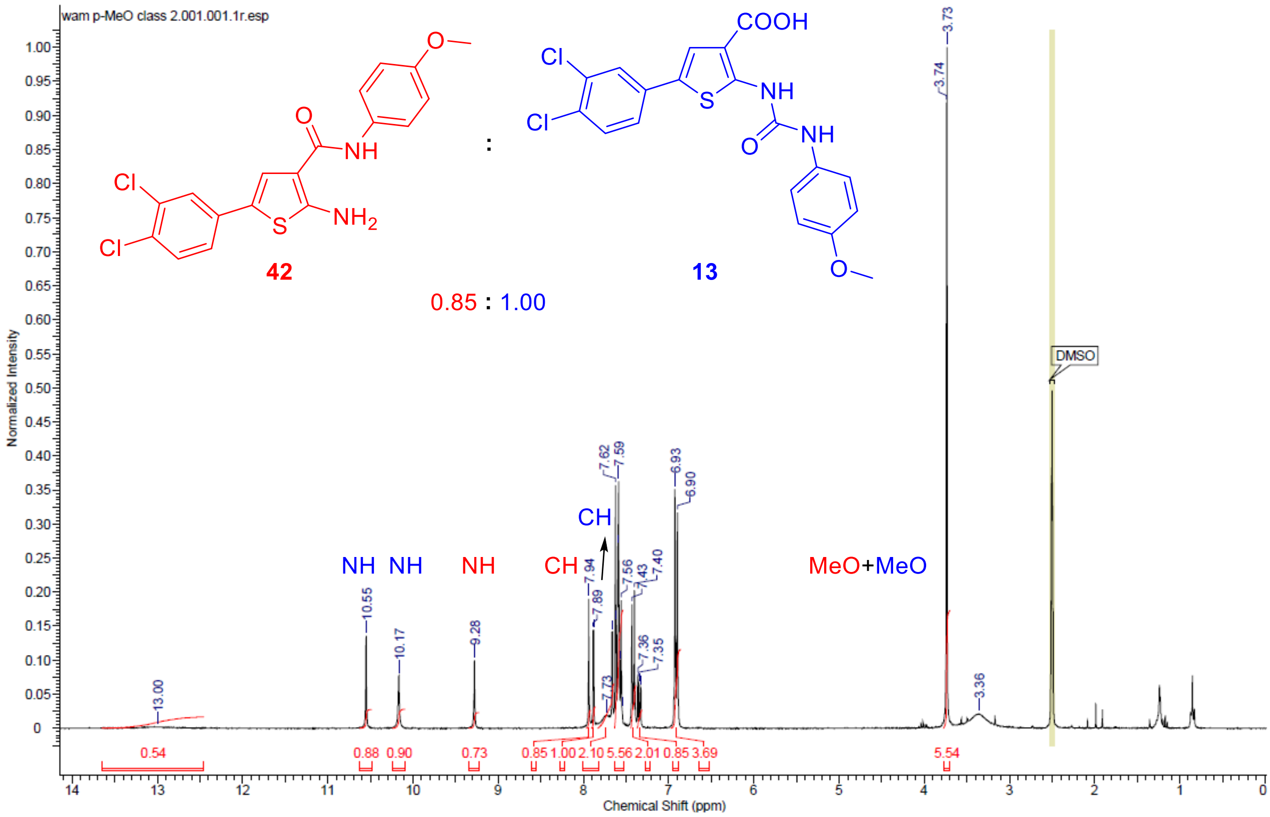


Figure S3. [1]H NMR spectrum (300 MHz, DMSO-d_6) indicating the formation of a mixture of the ureidothiophene **13** (blue) and the thiophenamide **42** (red) in 1.00:0.85 ratio, respectively from the reaction of compound **26** with *p*-anisidine in absence of TEA.

REFERENCES

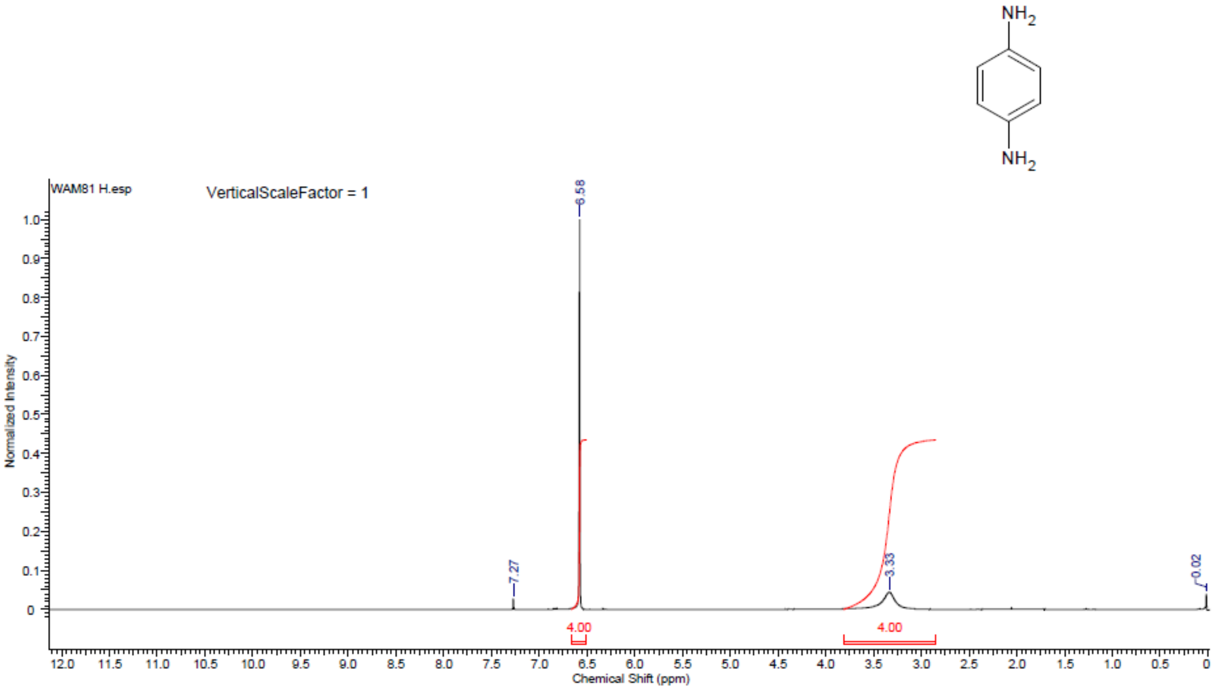
(1) Elgaher, W. A. M.; Fruth, M.; Groh, M.; Haupenthal, J.; Hartmann, R. W. Expanding the Scaffold for Bacterial RNA Polymerase Inhibitors: Design, Synthesis and Structure–Activity Relationships of Ureido-Heterocyclic-Carboxylic Acids. *RSC Adv.* **2014**, *4*, 2177–2194.

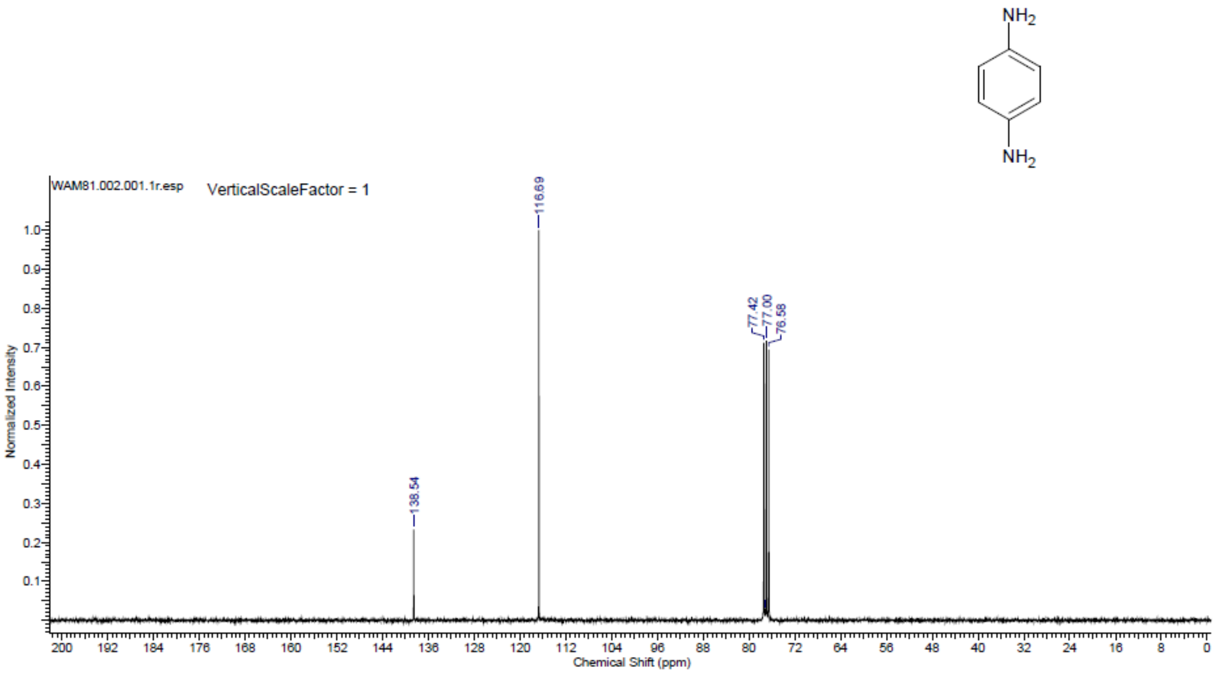
(2) Abraham, D. J.; Burger, A. *Burger's medicinal chemistry and drug discovery. Vol. 1, Drug discovery*; Wiley: Hoboken, N.J., Chichester, 2003.

(3) Kier, L. B. An Index of Molecular Flexibility from Kappa Shape Attributes. *Quant. Struct.-Act. Relat.* **1989**, *8*, 221–224.

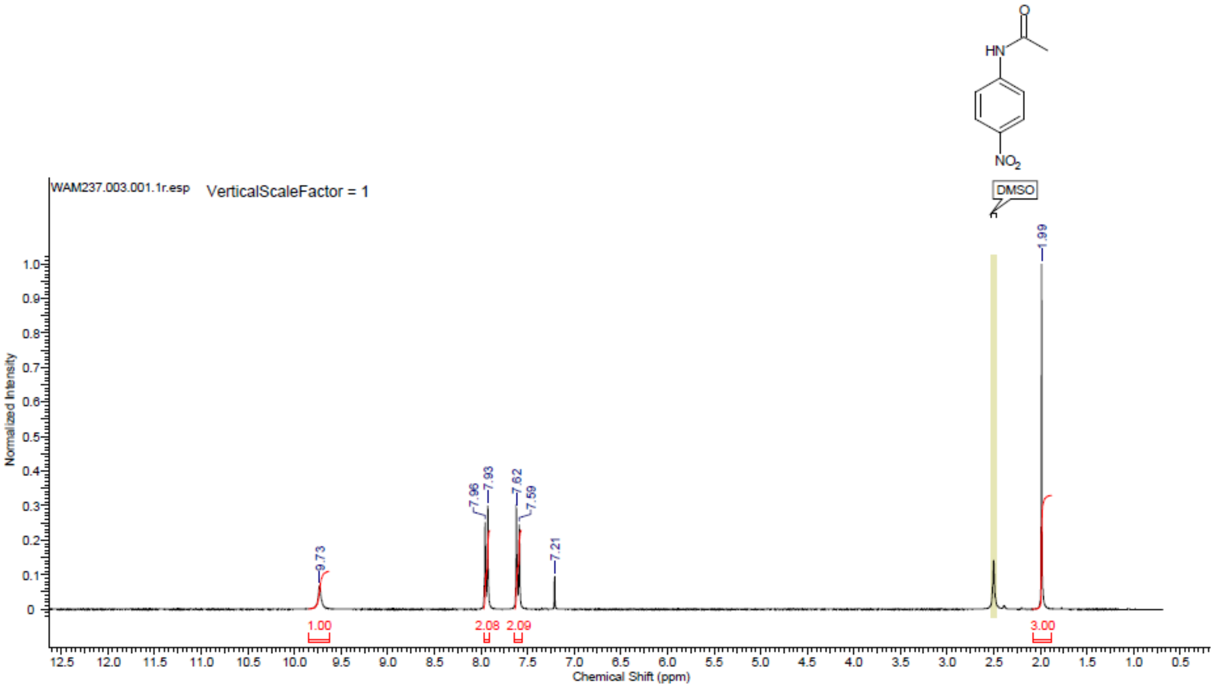
[1]H and [13]C NMR Spectra of the Described Compounds

Compound **28**

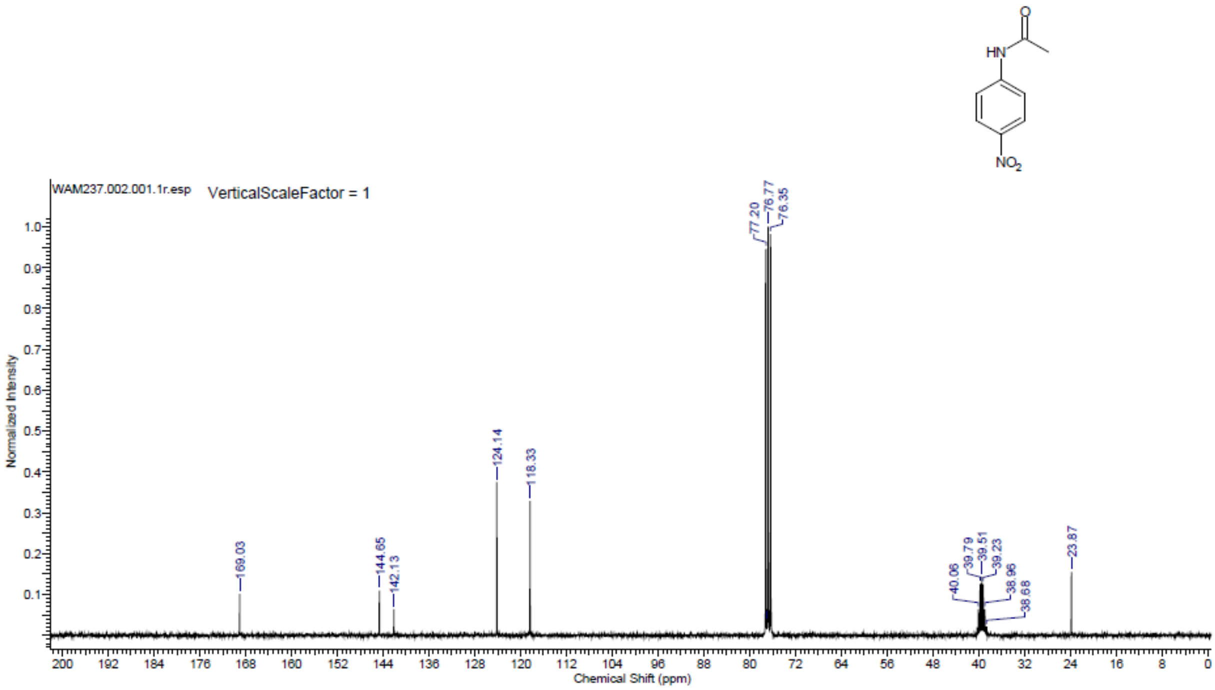




Compound **29**

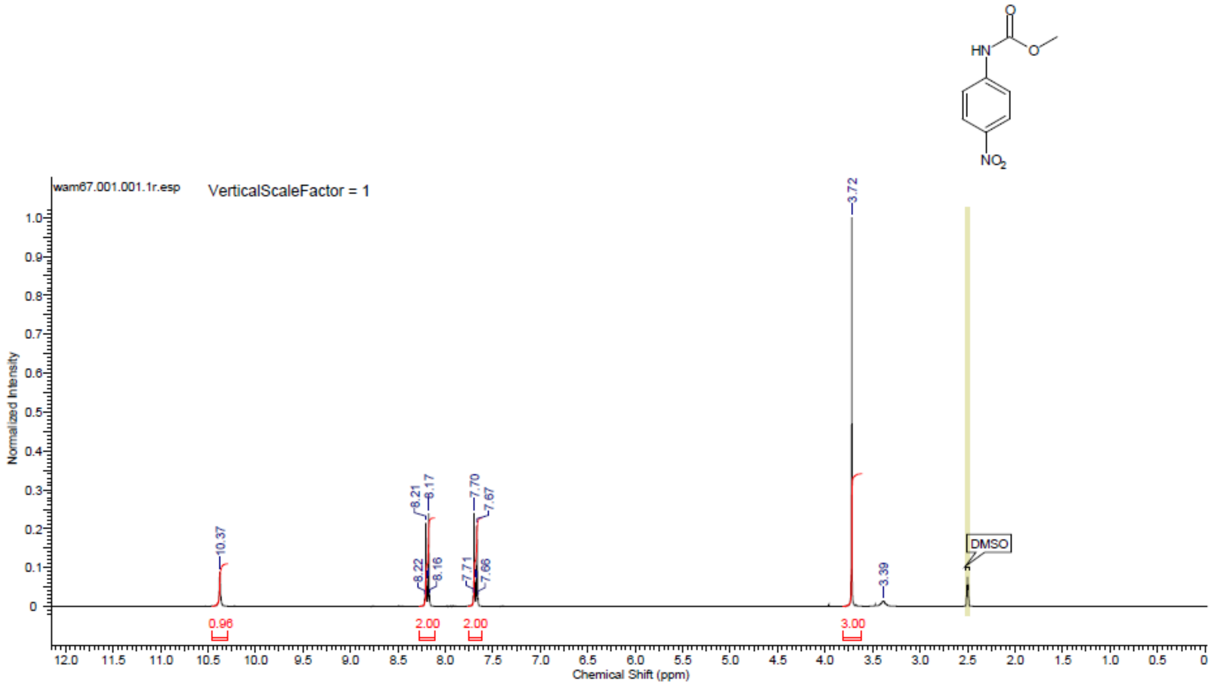


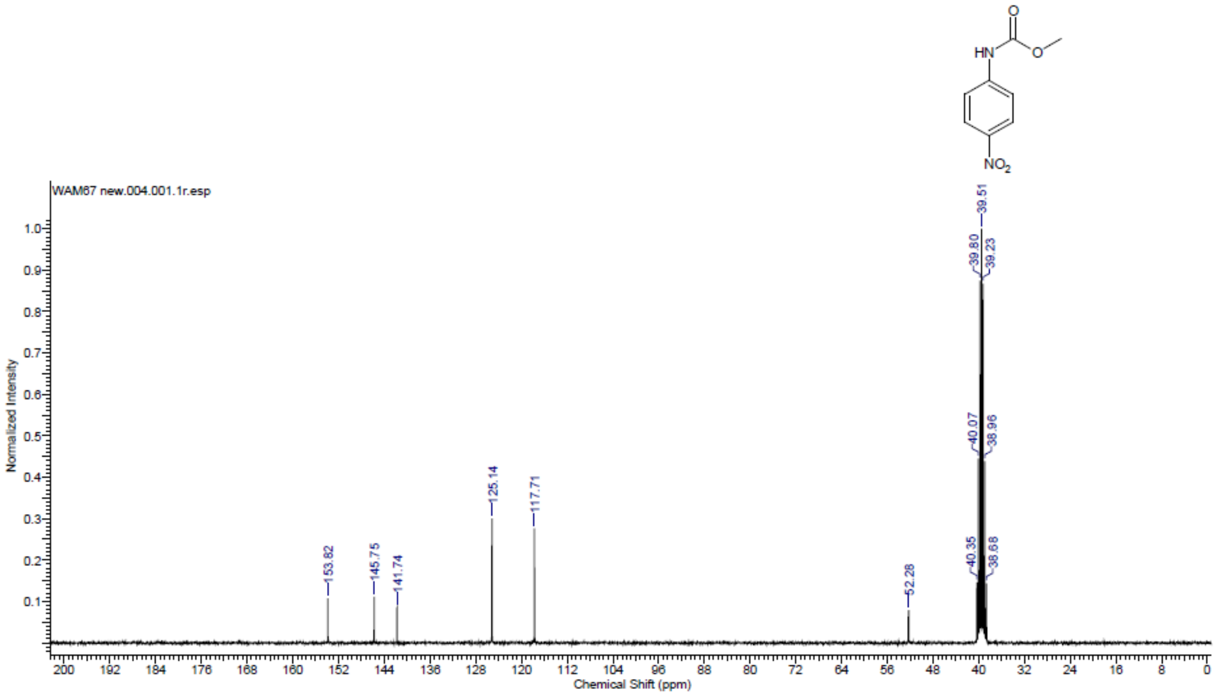
HN
O
NO_2
WAM237.003.001.1r.esp
VerticalScaleFactor = 1
DMSO
Normalized Intensity
Chemical Shift (ppm)
9.73
7.96
7.93
7.62
7.59
7.21
1.99
1.00
2.08
2.09
3.00



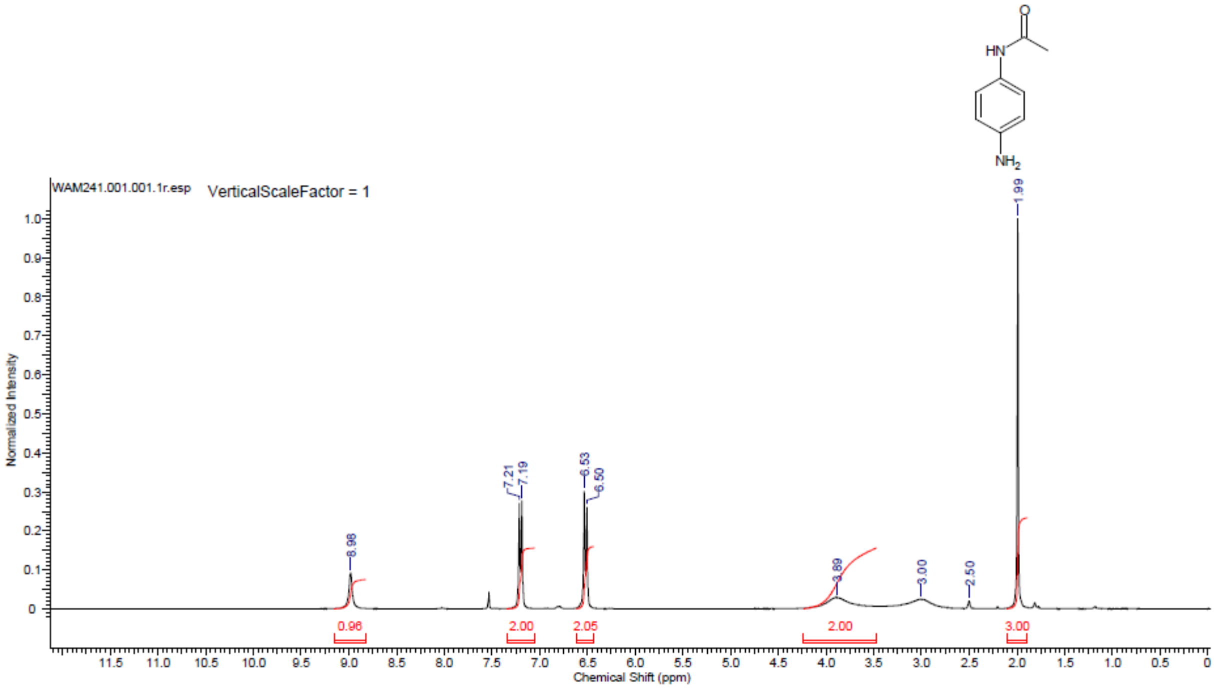
HN
O
NO_2
WAM237.002.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
169.03
144.65
142.13
124.14
118.33
77.20
76.77
76.35
40.06
39.79
39.51
39.23
38.96
38.68
23.87

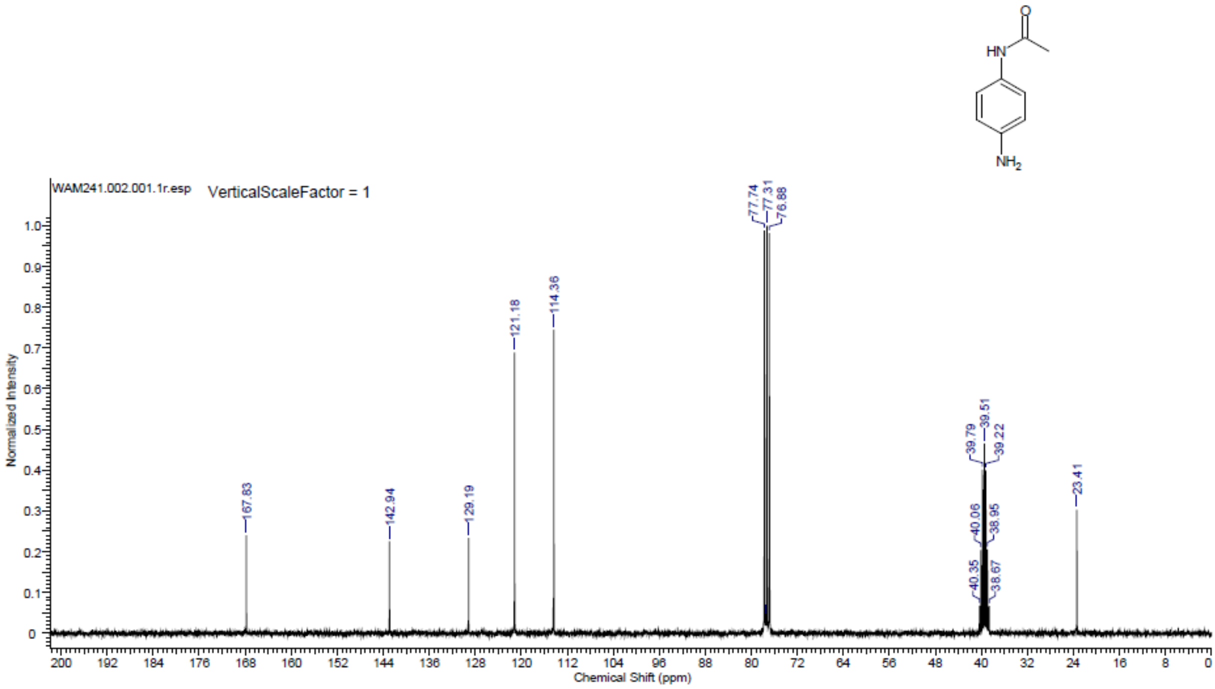
Compound **30**


wam67.001.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
10.37
8.22
8.21
8.17
8.16
7.71
7.70
7.67
7.66
3.72
3.39
DMSO
0.96
2.00
2.00
3.00
HN
O
O
NO2

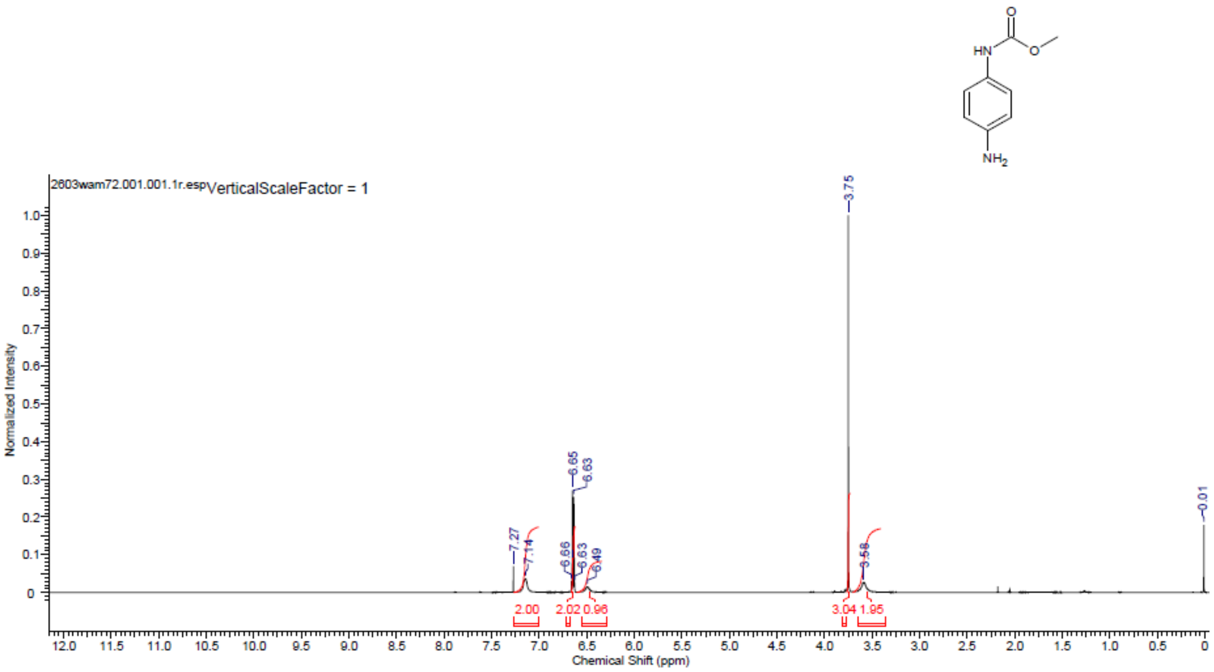

WAM67 new.004.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
153.82
145.75
141.74
125.14
117.71
52.28
40.35
40.07
39.80
39.51
39.23
38.96
38.68
HN
O
O
NO2

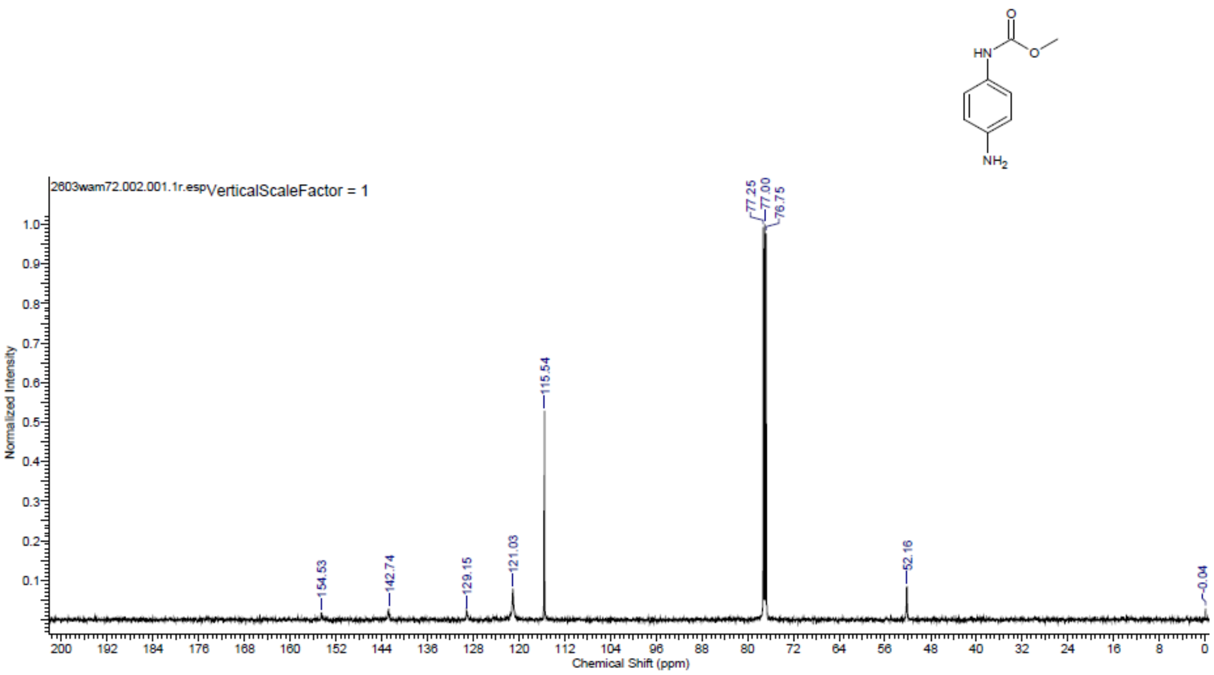
Compound **31**



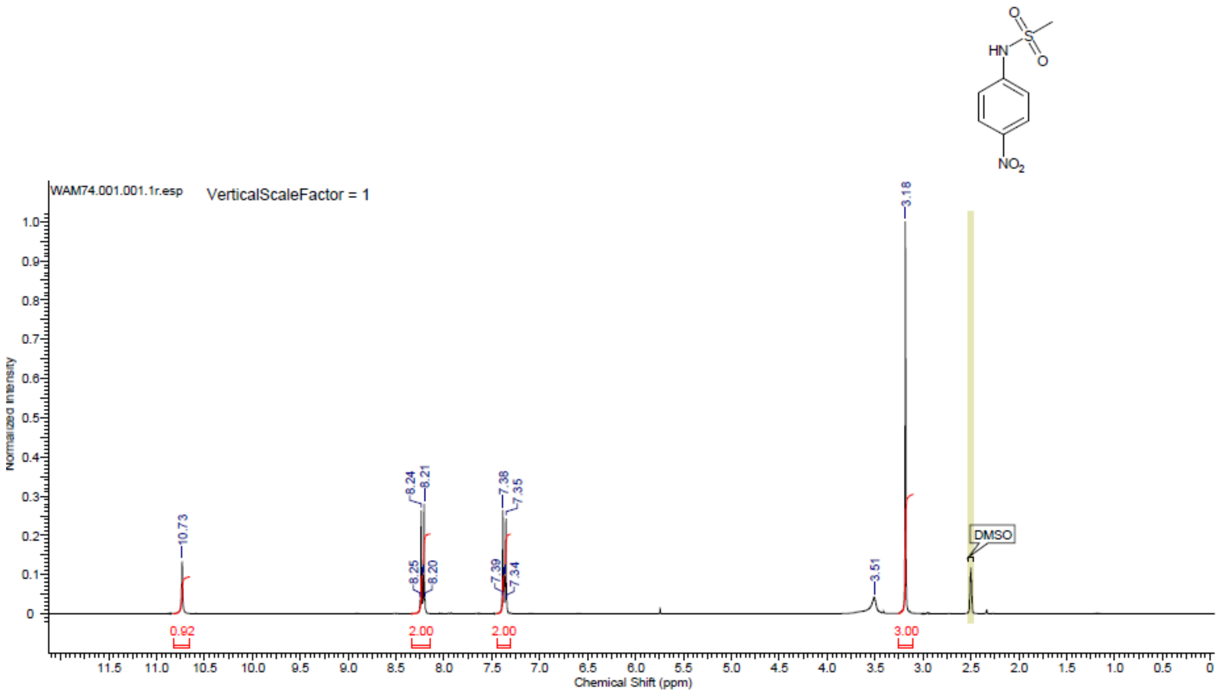


Compound **32**

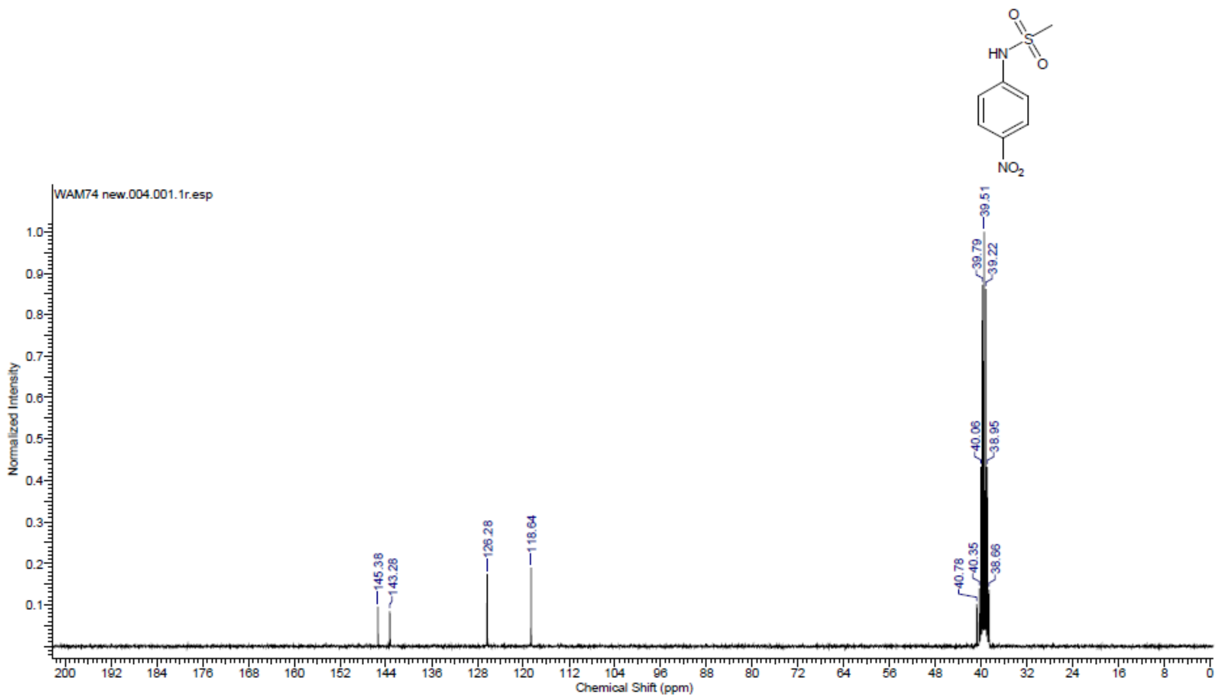




Compound **33**

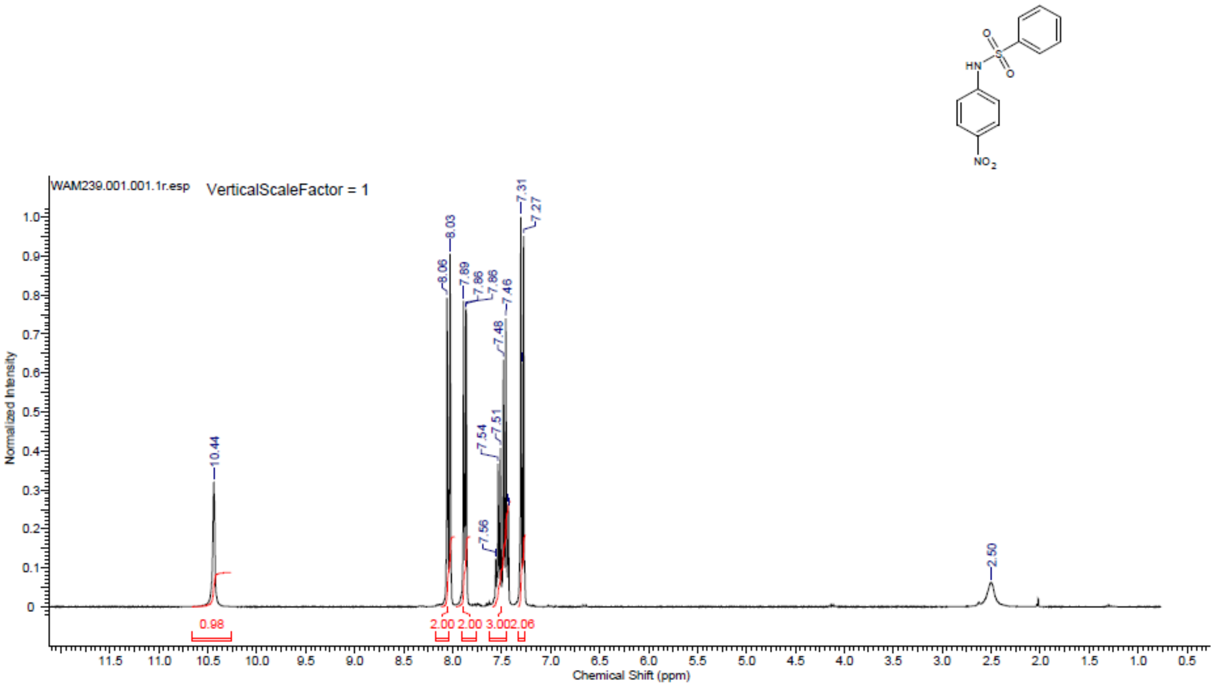


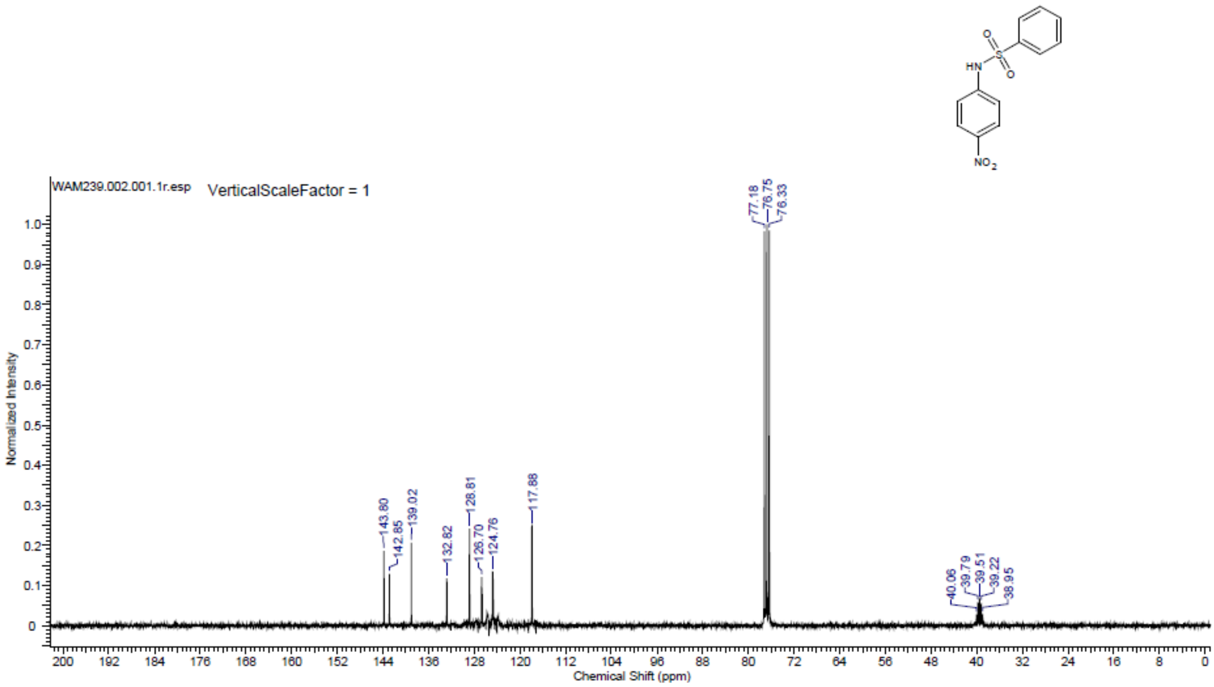
WAM74.001.001.1r.esp
VerticalScaleFactor = 1
DMSO
Normalized Intensity
Chemical Shift (ppm)



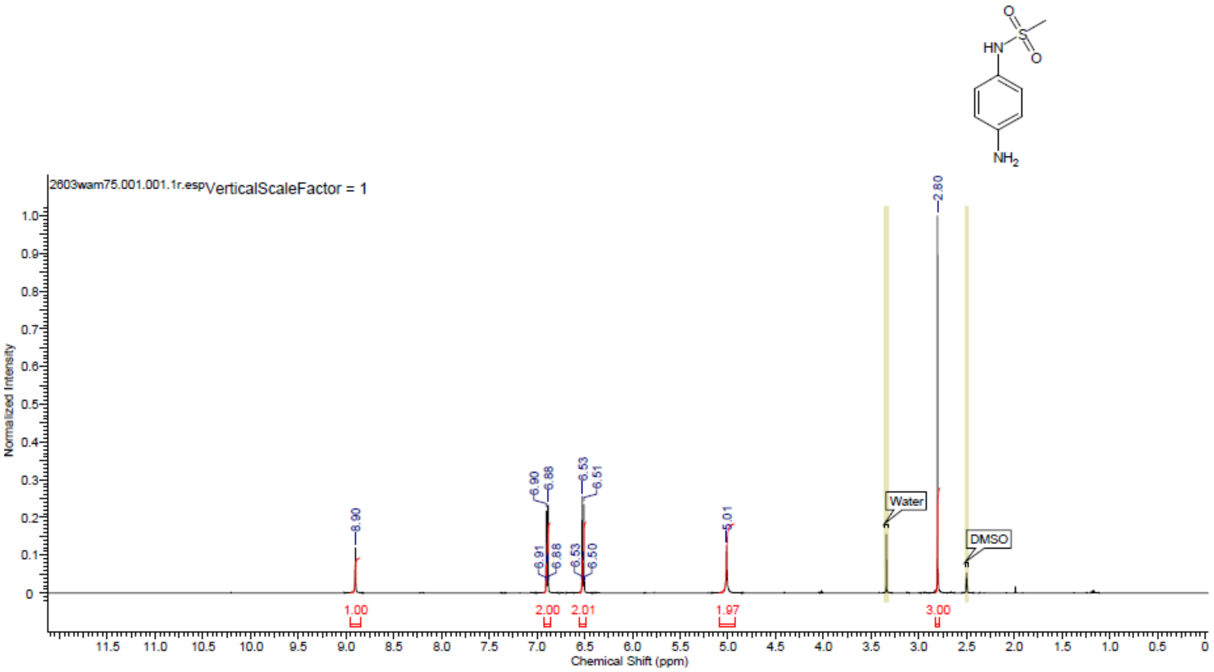
WAM74 new.004.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)

Compound **35**

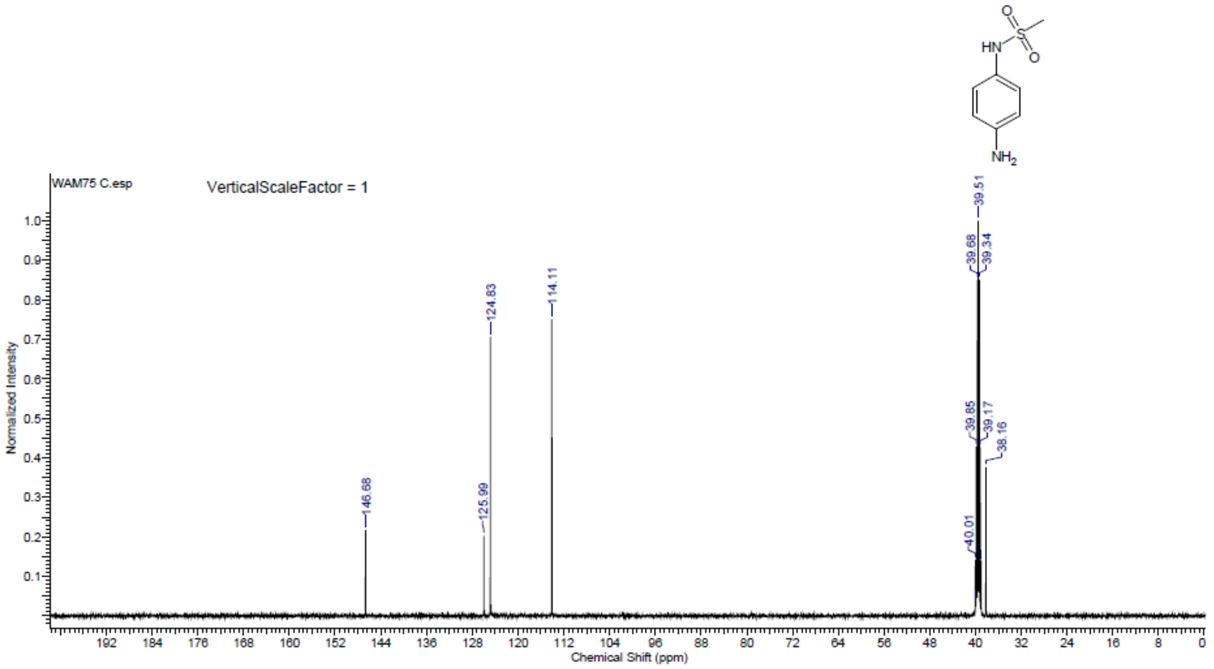

WAM239.001.001.1r.esp
VerticalScaleFactor = 1
10.44
8.06
8.03
7.89
7.86
7.86
7.56
7.54
7.51
7.48
7.46
7.31
7.27
2.50
0.98
2.00
2.00
3.00
2.06
Normalized Intensity
Chemical Shift (ppm)
HN
O
S
O
NO2


WAM239.002.001.1r.esp
VerticalScaleFactor = 1
143.80
142.85
139.02
132.82
128.81
126.70
124.76
117.88
77.18
76.75
76.33
40.06
39.79
39.51
39.22
38.95
Normalized Intensity
Chemical Shift (ppm)
HN
O
S
O
NO2

Compound **36**

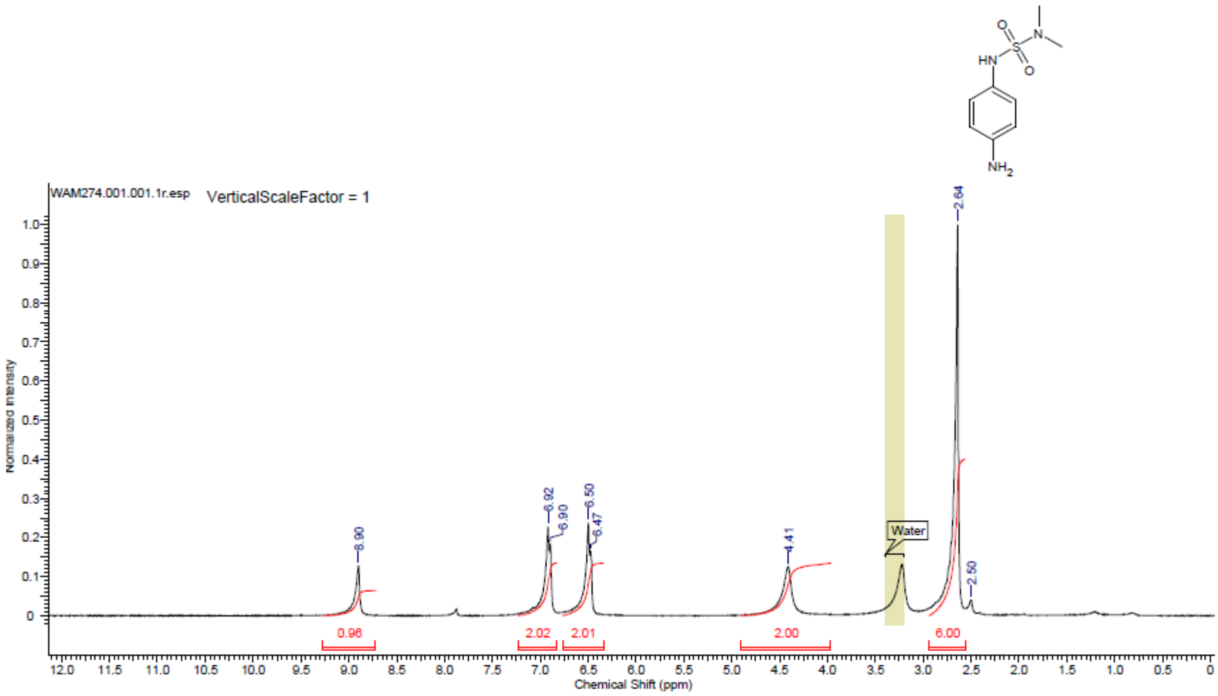


HN
O
S
O
NH2
2603wam75.001.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
8.90
6.90
6.88
6.91
6.88
6.53
6.51
6.53
6.50
5.01
Water
2.80
DMSO
1.00
2.00
2.01
1.97
3.00
Chemical Shift (ppm)

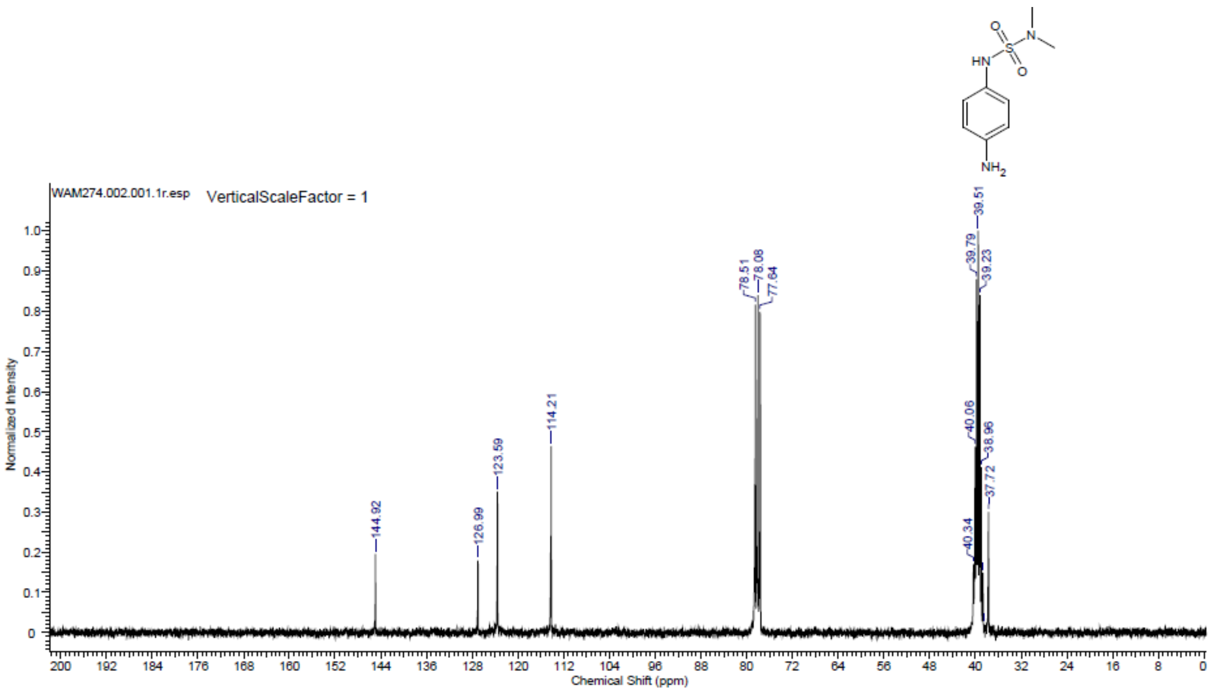


HN
O
S
O
NH2
WAM75 C.esp
VerticalScaleFactor = 1
Normalized Intensity
146.68
125.99
124.83
114.11
39.51
39.68
39.34
39.85
39.17
38.16
40.01
Chemical Shift (ppm)

Compound **37**

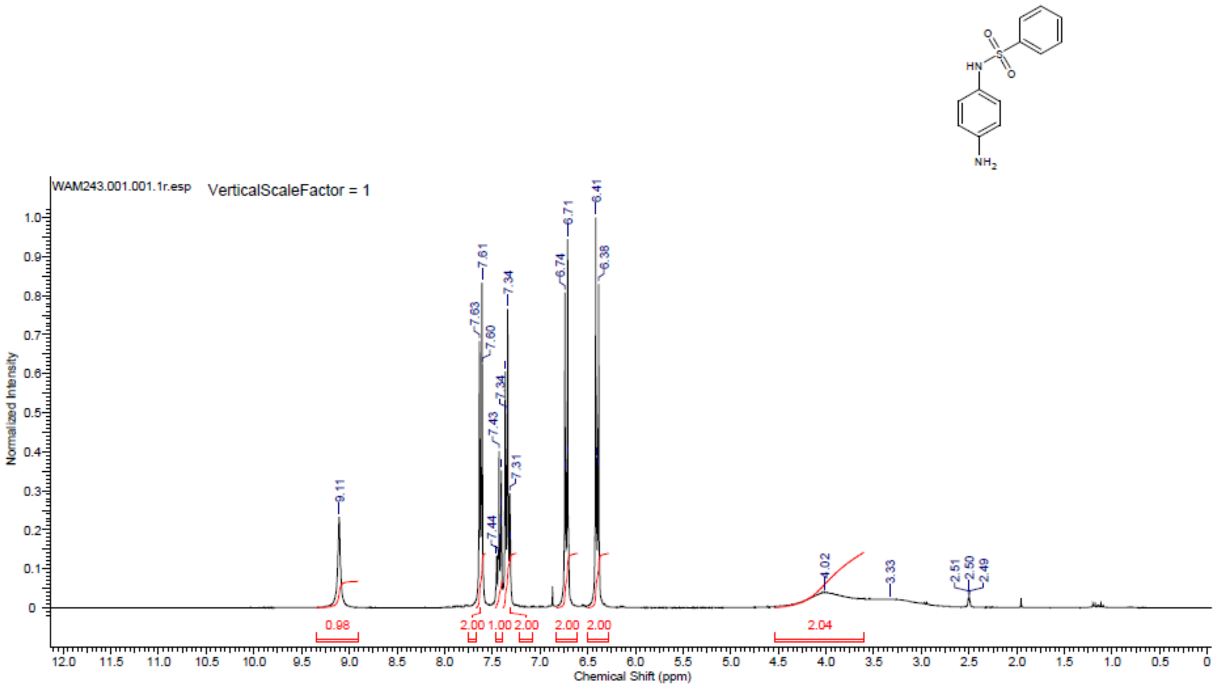


WAM274.001.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
Water

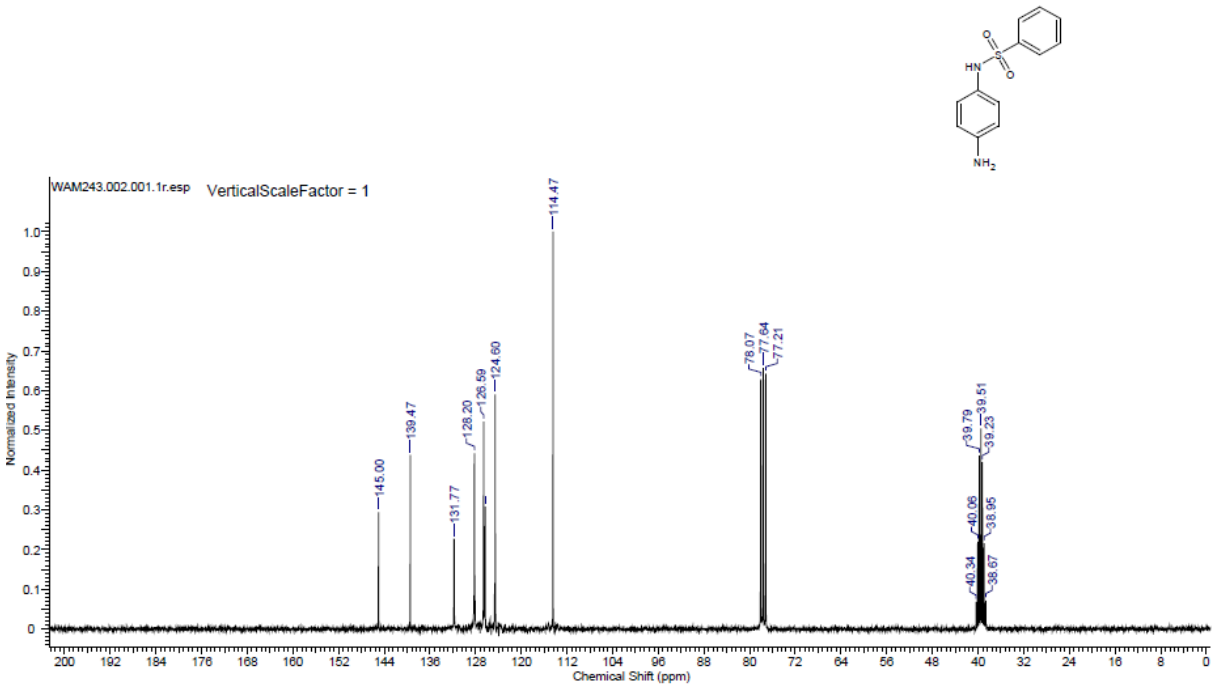


WAM274.002.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)

Compound **38**

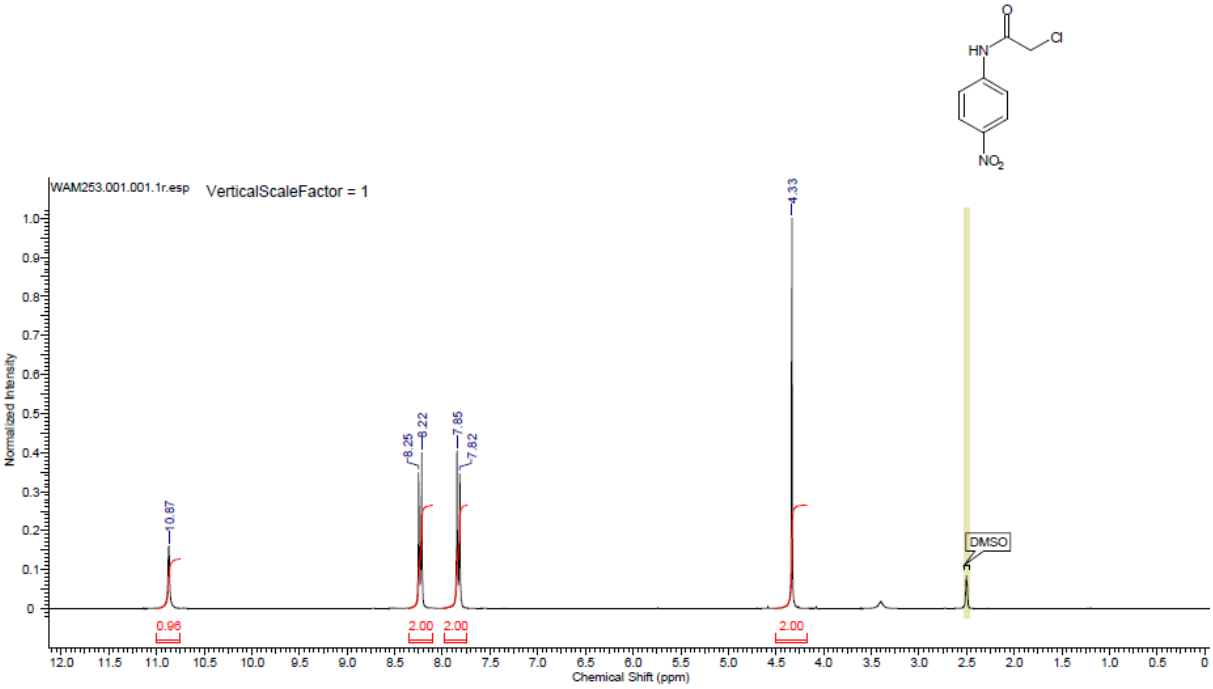


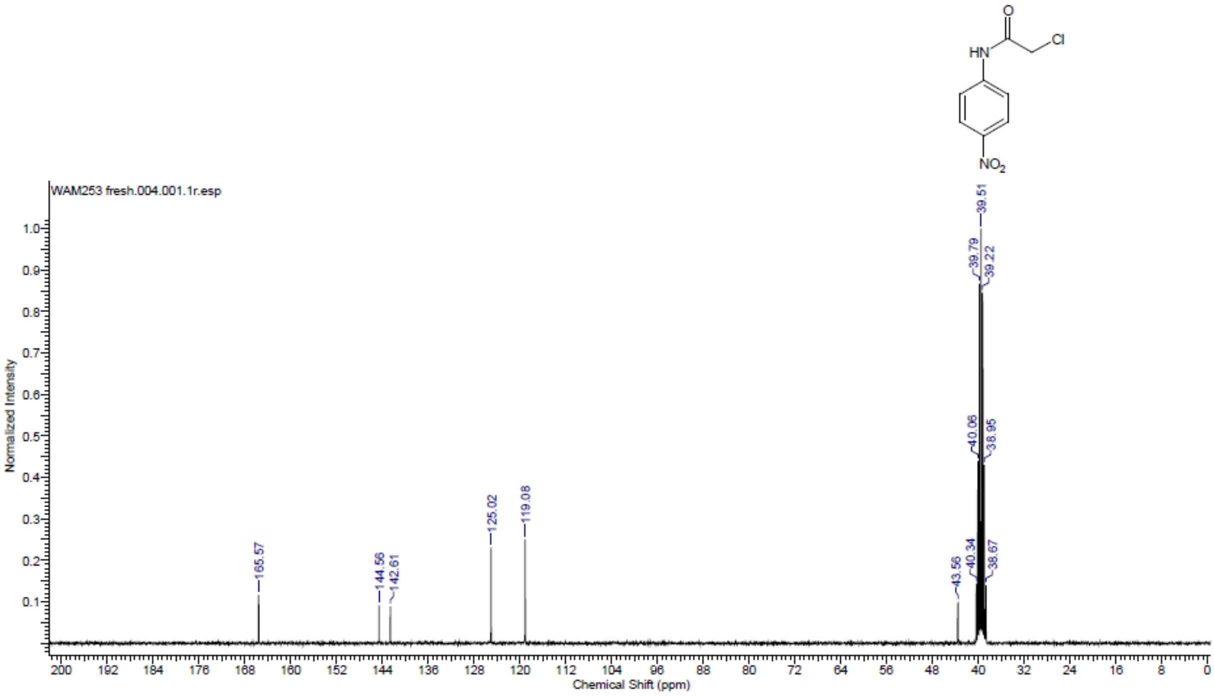
WAM243.001.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
HN
NH2



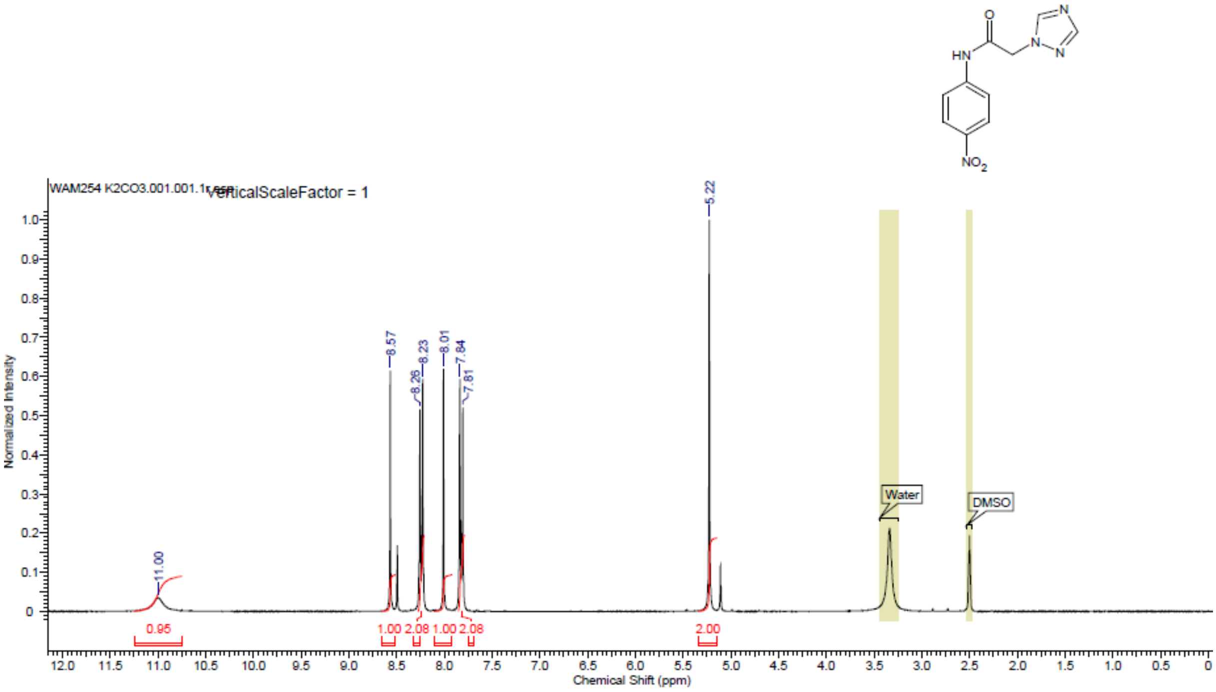
WAM243.002.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
HN
NH2

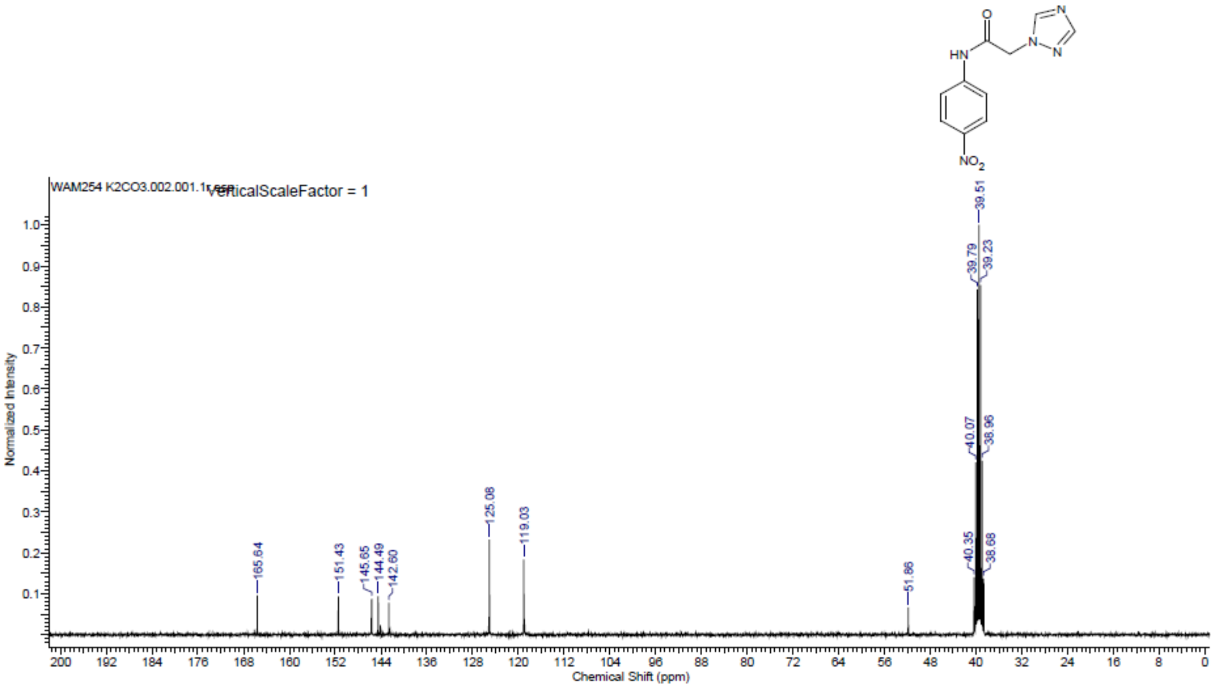
Compound **39**


WAM253.001.001.1r.esp
VerticalScaleFactor = 1
HN
O
Cl
NO2
4.33
8.25
8.22
7.85
7.82
10.87
DMSO
0.96
2.00
2.00
2.00
Normalized Intensity
Chemical Shift (ppm)

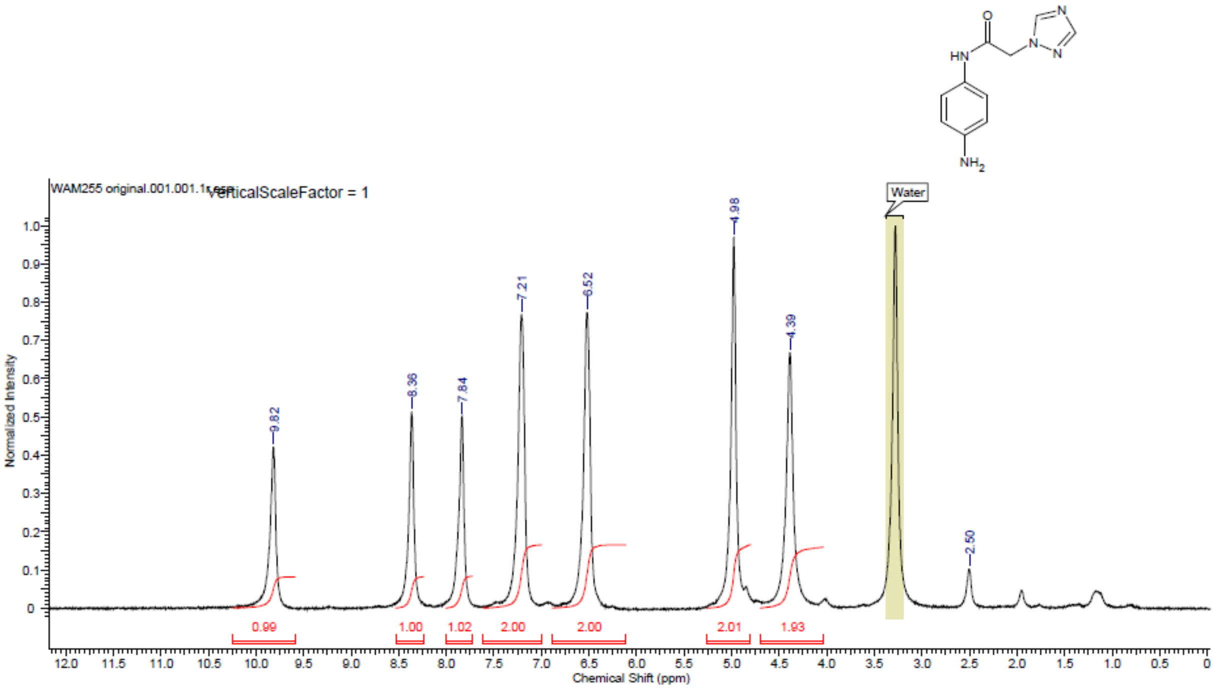

WAM253 fresh.004.001.1r.esp
HN
O
Cl
NO2
39.51
39.79
39.22
40.06
38.95
43.56
40.34
38.67
165.57
144.56
142.61
125.02
119.08
Normalized Intensity
Chemical Shift (ppm)

Compound **40**

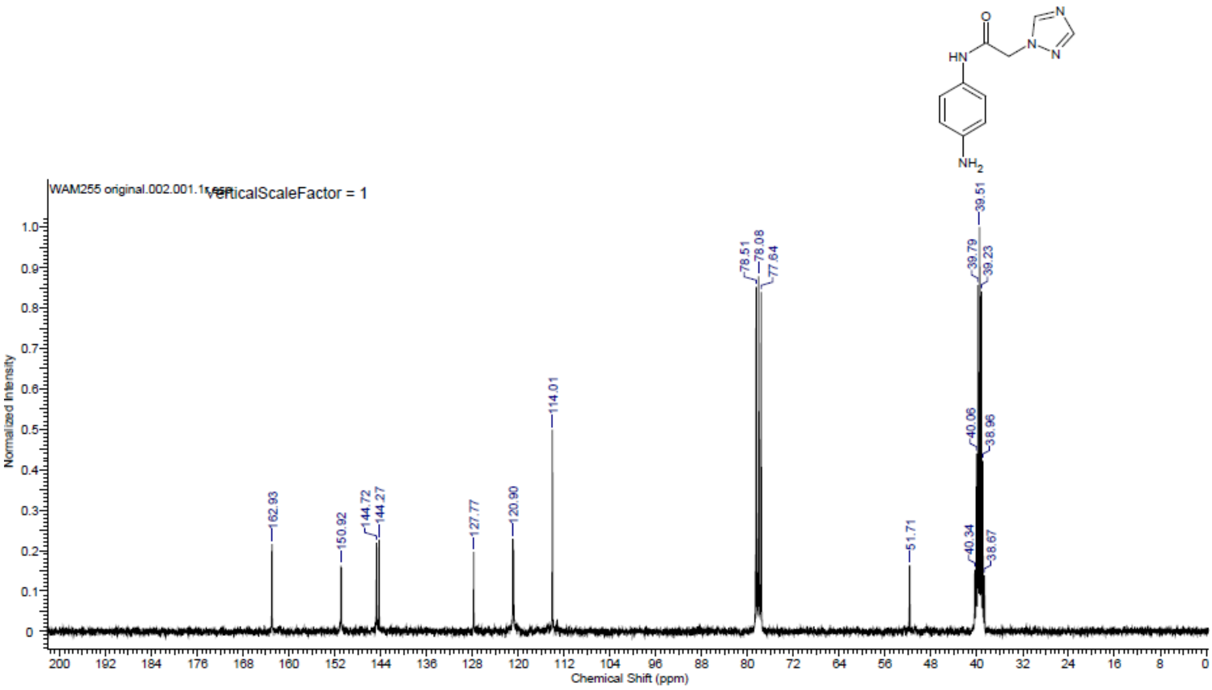




Compound **41**

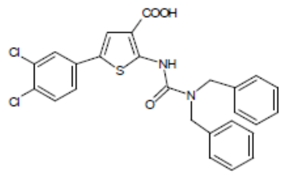


O
HN
N
N
N
NH2
WAM255 original.001.001.1r.esp
verticalScaleFactor = 1
Water
9.82
8.36
7.84
7.21
6.52
4.98
4.39
2.50
0.99
1.00
1.02
2.00
2.00
2.01
1.93
Normalized Intensity
Chemical Shift (ppm)

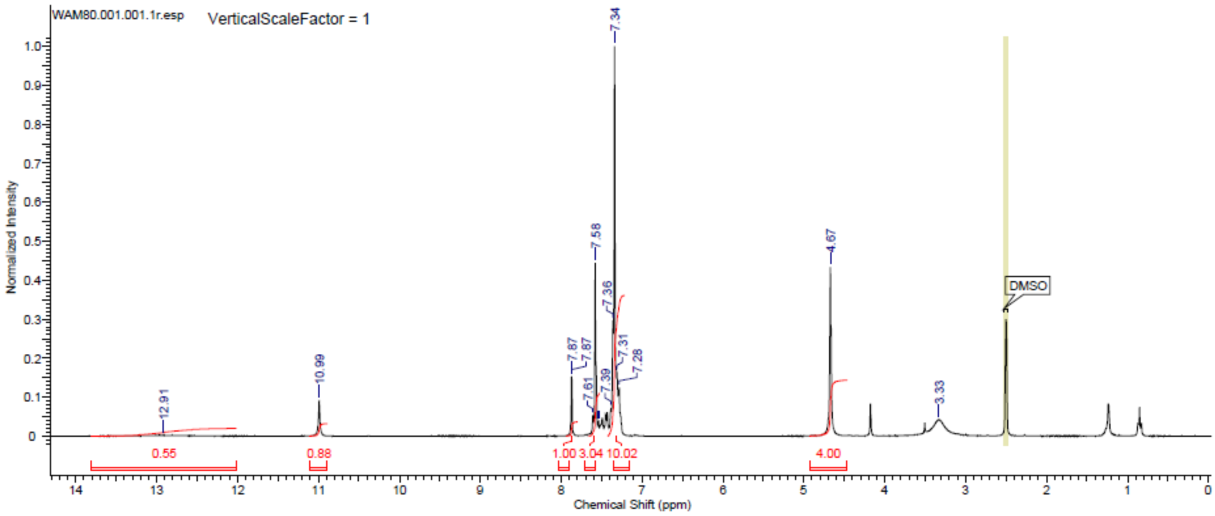


O
HN
N
N
N
NH2
WAM255 original.002.001.1r.esp
verticalScaleFactor = 1
162.93
150.92
144.72
144.27
127.77
120.90
114.01
78.51
78.08
77.64
51.71
40.34
40.06
39.79
39.51
39.23
38.96
38.67
Normalized Intensity
Chemical Shift (ppm)

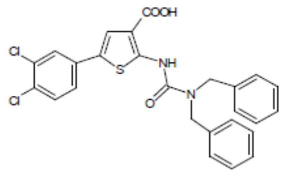
Compound **10**



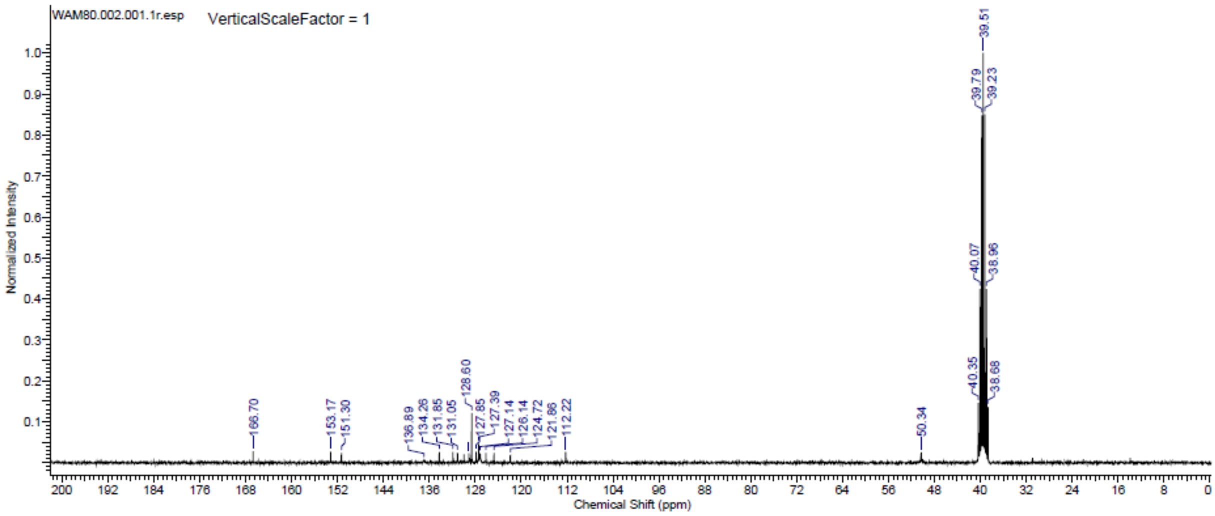
COOH
Cl
Cl
S
NH
O
N



WAM80.001.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
DMSO
12.91
10.99
7.87
7.87
7.61
7.58
7.39
7.36
7.34
7.31
7.28
4.67
3.33
0.55
0.88
1.00
3.04
10.02
4.00

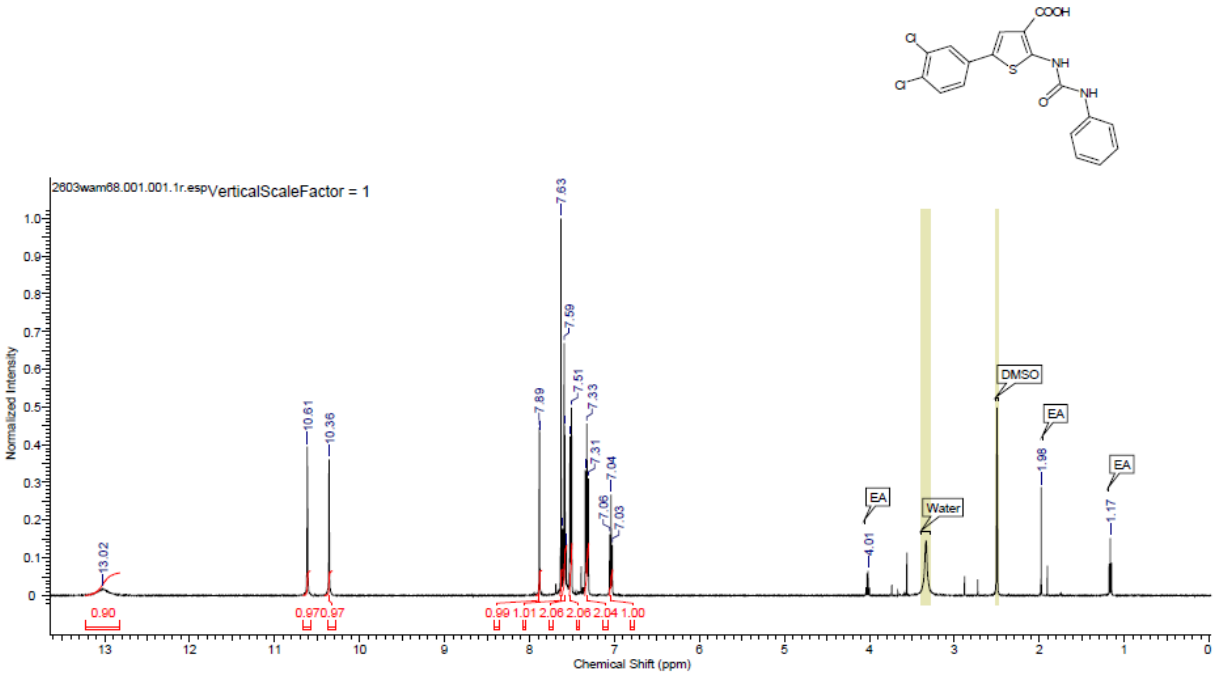


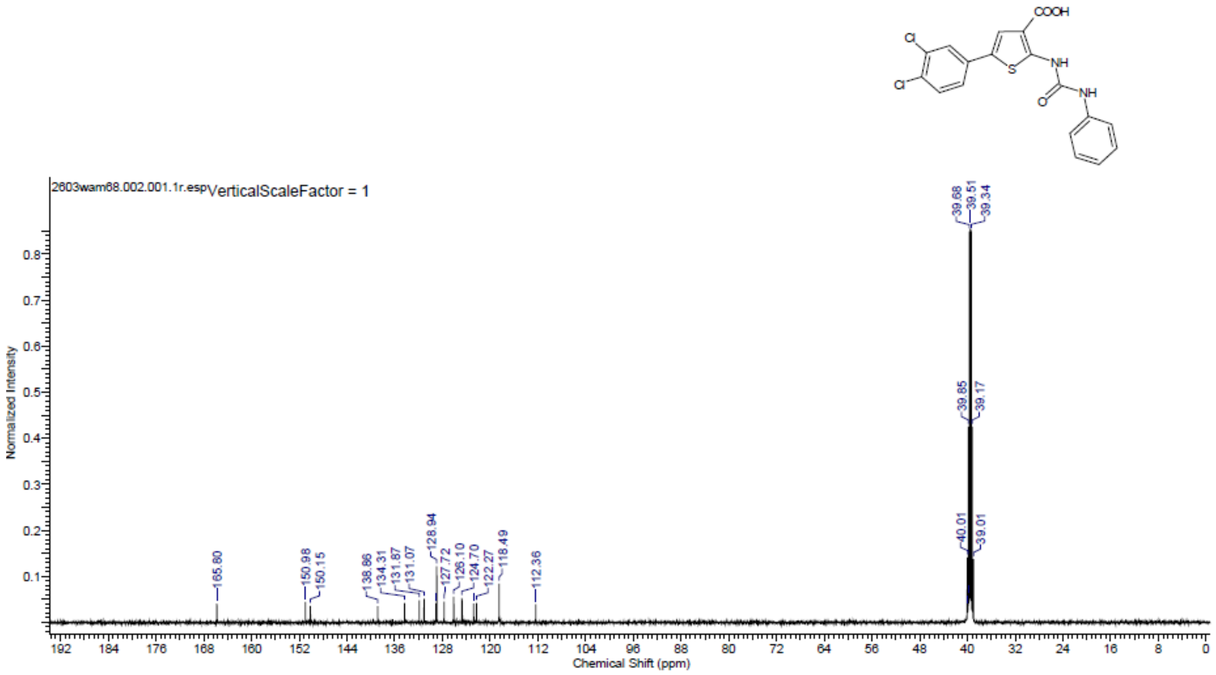
COOH
Cl
Cl
S
NH
O
N



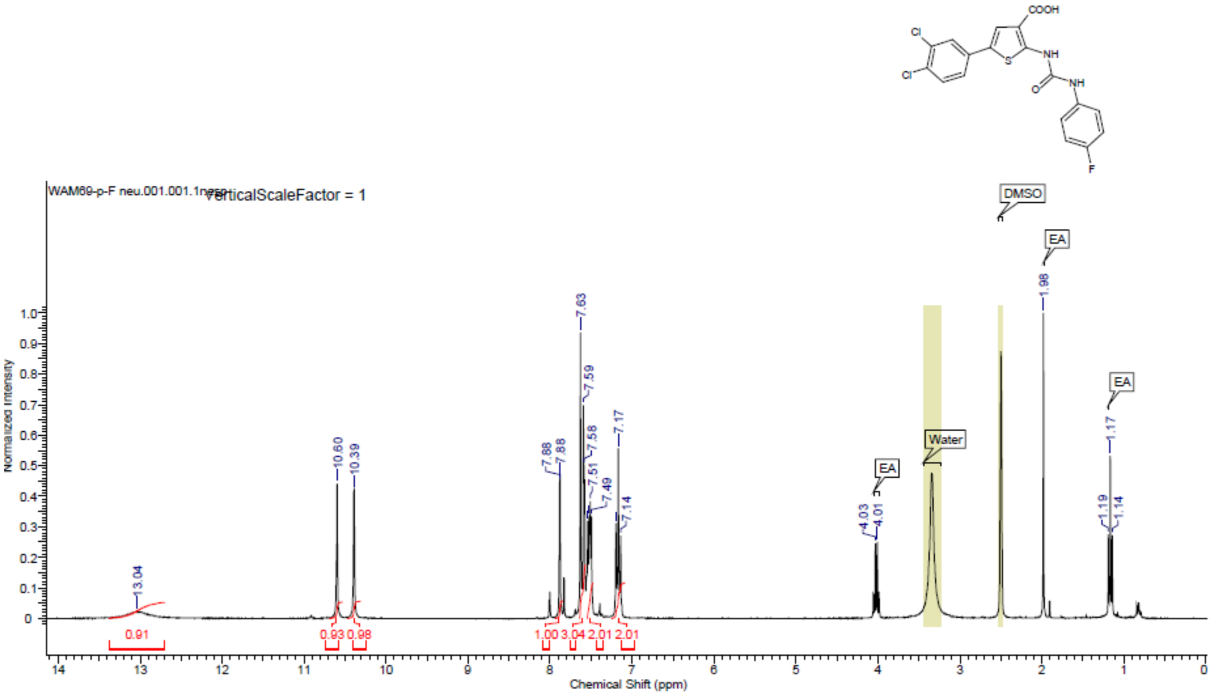
WAM80.002.001.1r.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
166.70
153.17
151.30
136.89
134.26
131.85
131.05
128.60
127.85
127.39
127.14
126.14
124.72
121.86
112.22
50.34
40.35
40.07
39.79
39.51
39.23
38.96
38.68

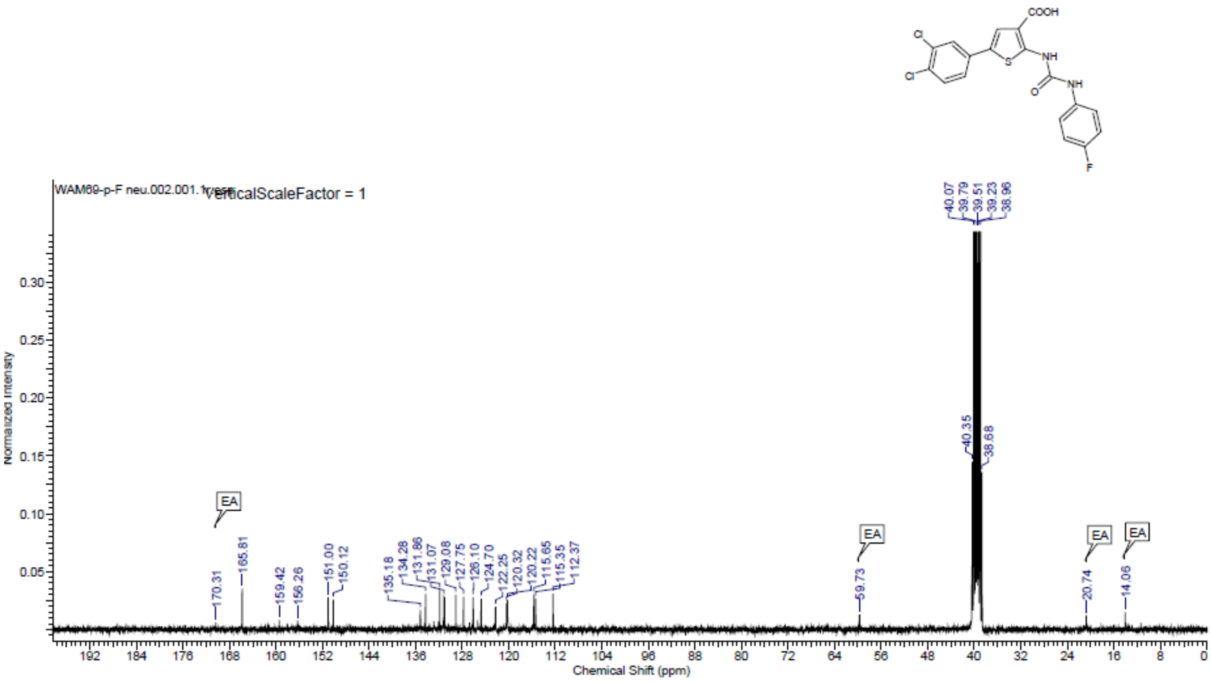
Compound **11**



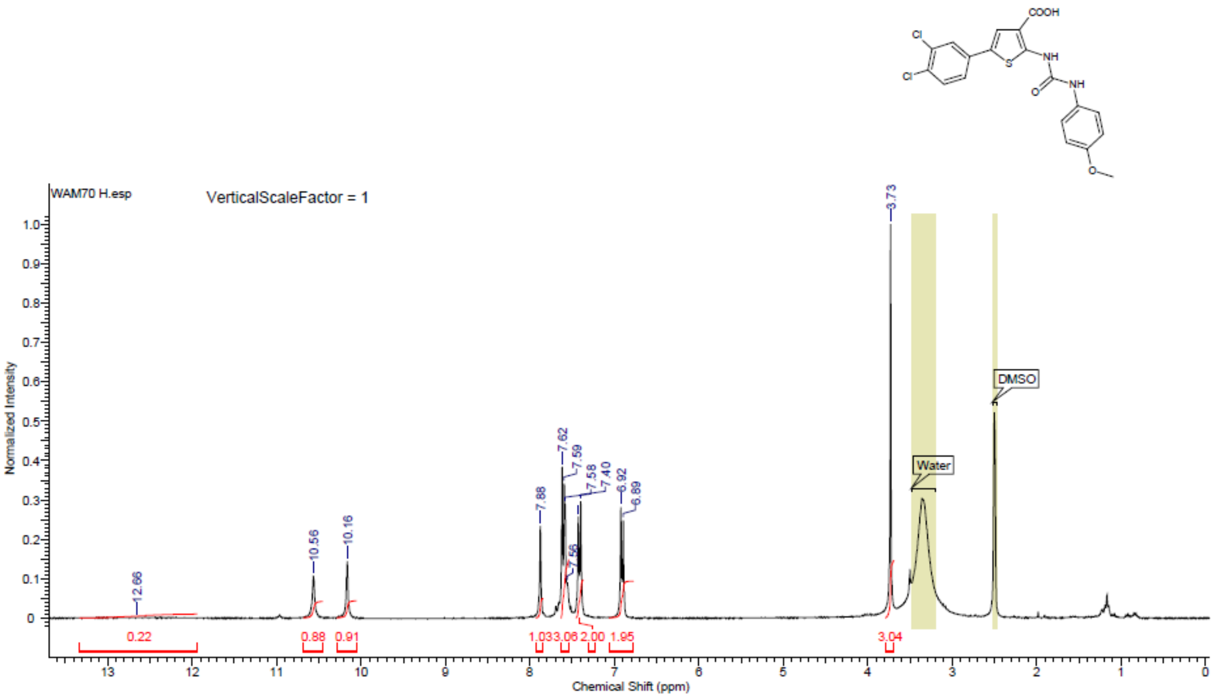


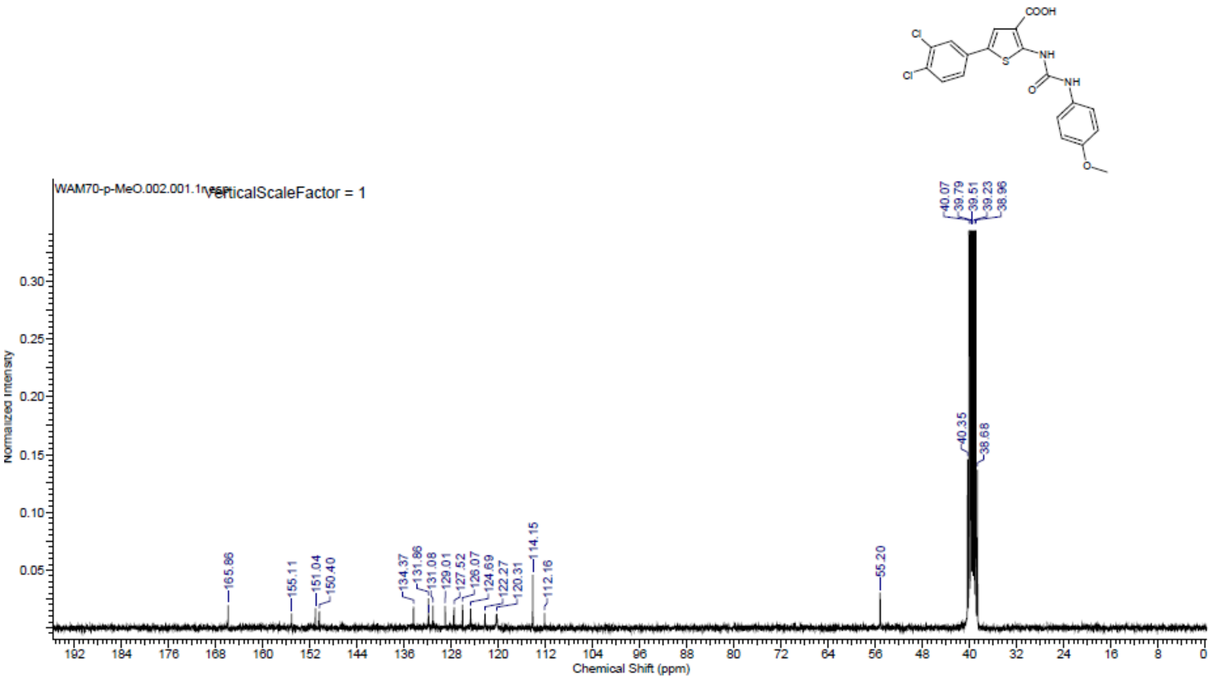
Compound **12**



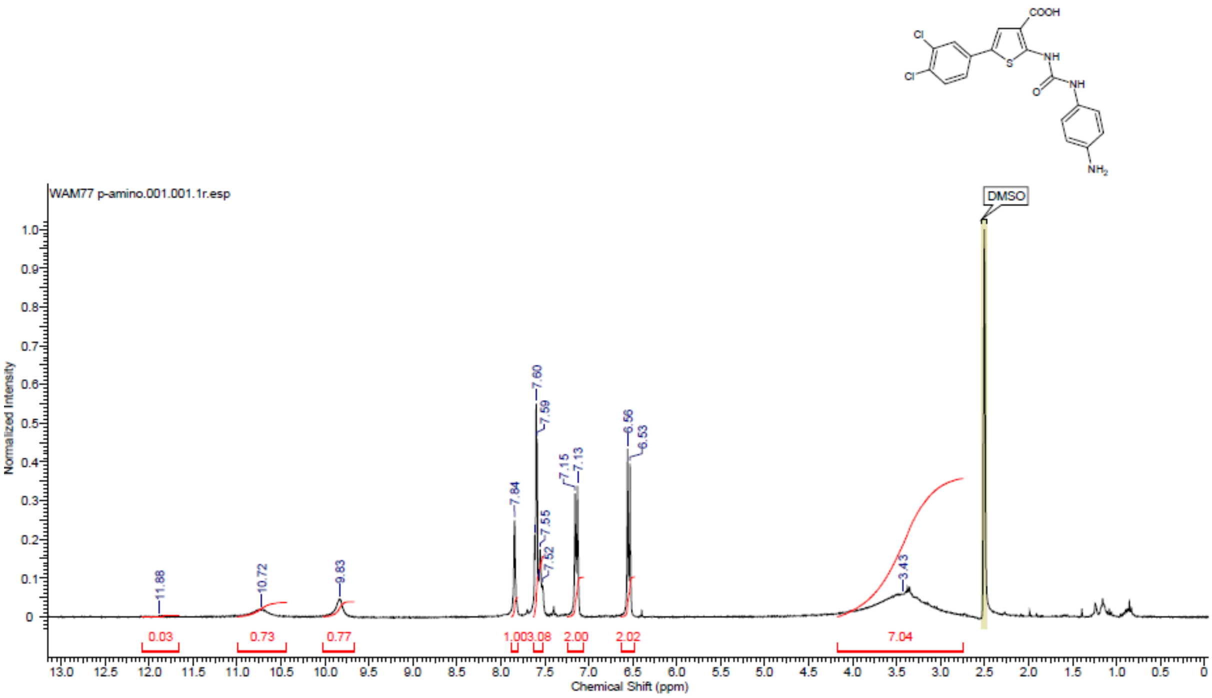


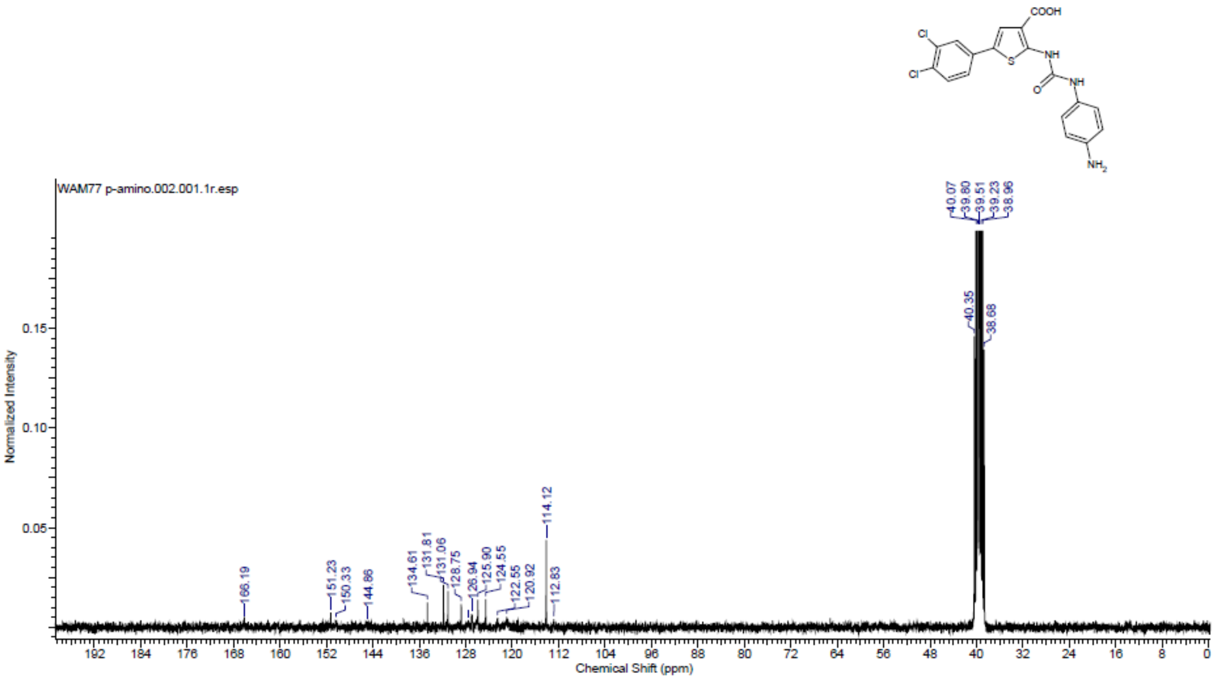
Compound **13**



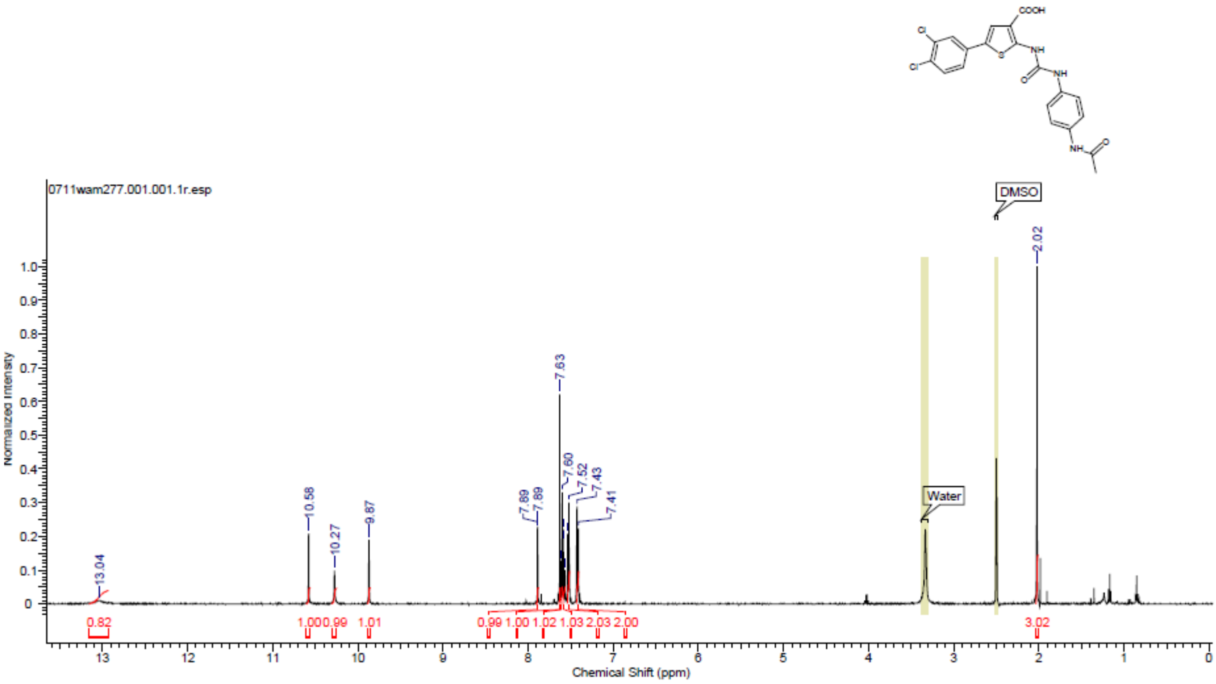


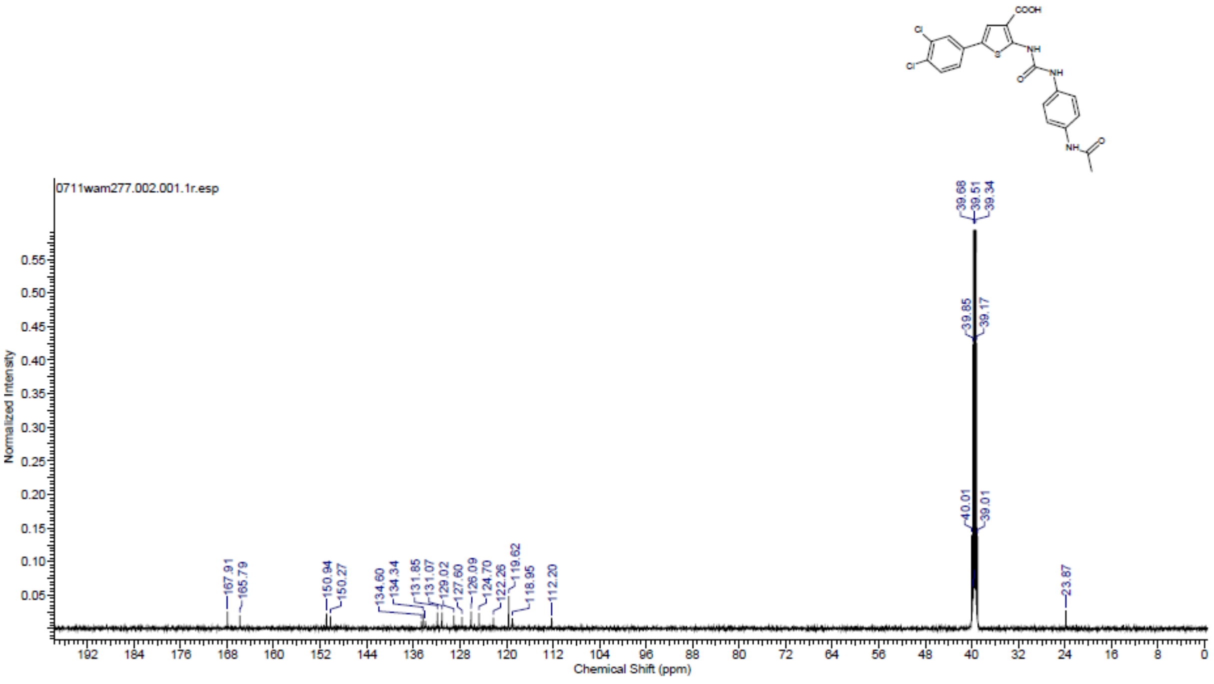
Compound **14**


COOH
Cl
Cl
S
NH
O
NH
NH_2
WAM77 p-amino.001.001.1r.esp
DMSO
Normalized Intensity
Chemical Shift (ppm)
11.88
10.72
9.83
7.84
7.60
7.59
7.55
7.52
7.15
7.13
6.56
6.53
3.43
0.03
0.73
0.77
1.00
3.08
2.00
2.02
7.04

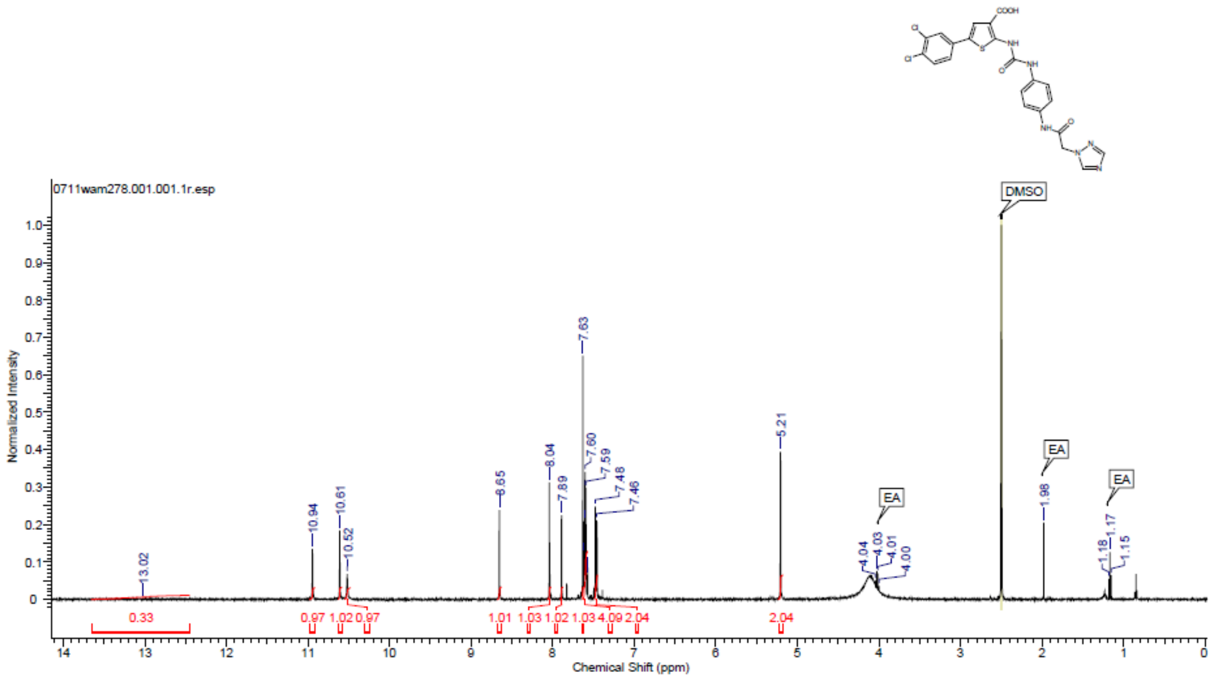

COOH
Cl
Cl
S
NH
O
NH
NH_2
WAM77 p-amino.002.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
40.07
39.80
39.51
39.23
38.96
40.35
38.68
166.19
151.23
150.33
144.86
134.61
131.81
131.06
128.75
126.94
125.90
124.55
122.55
120.92
114.12
112.83

Compound **15**

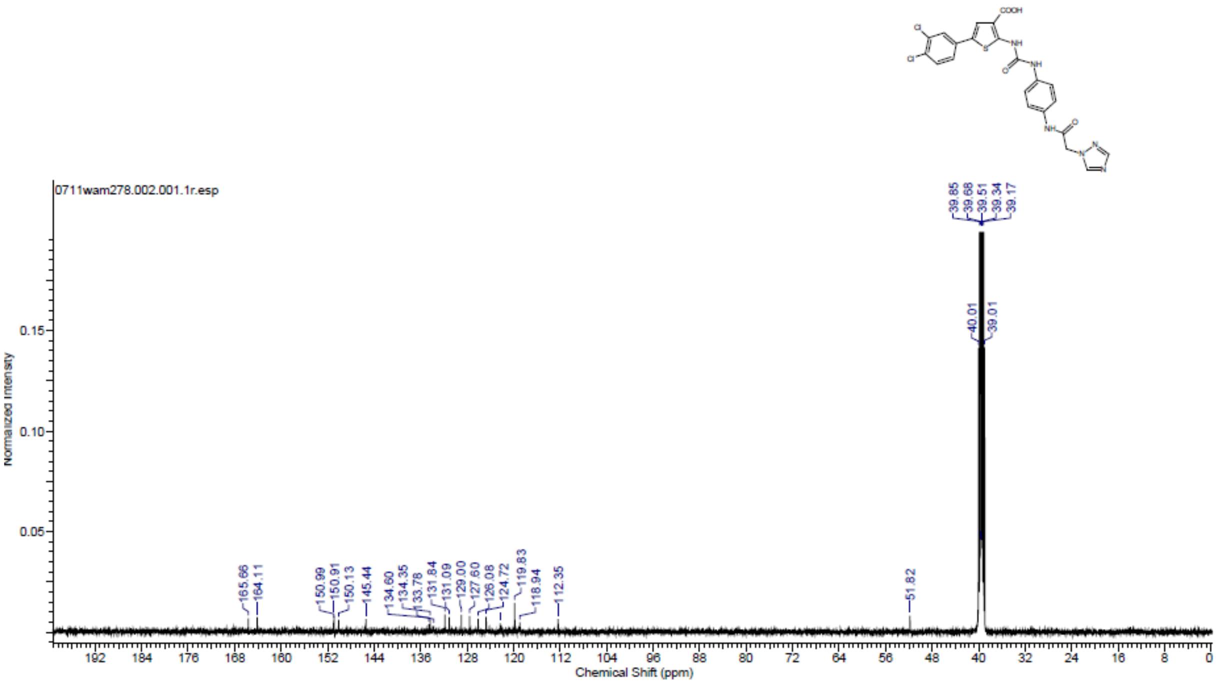




Compound **16**

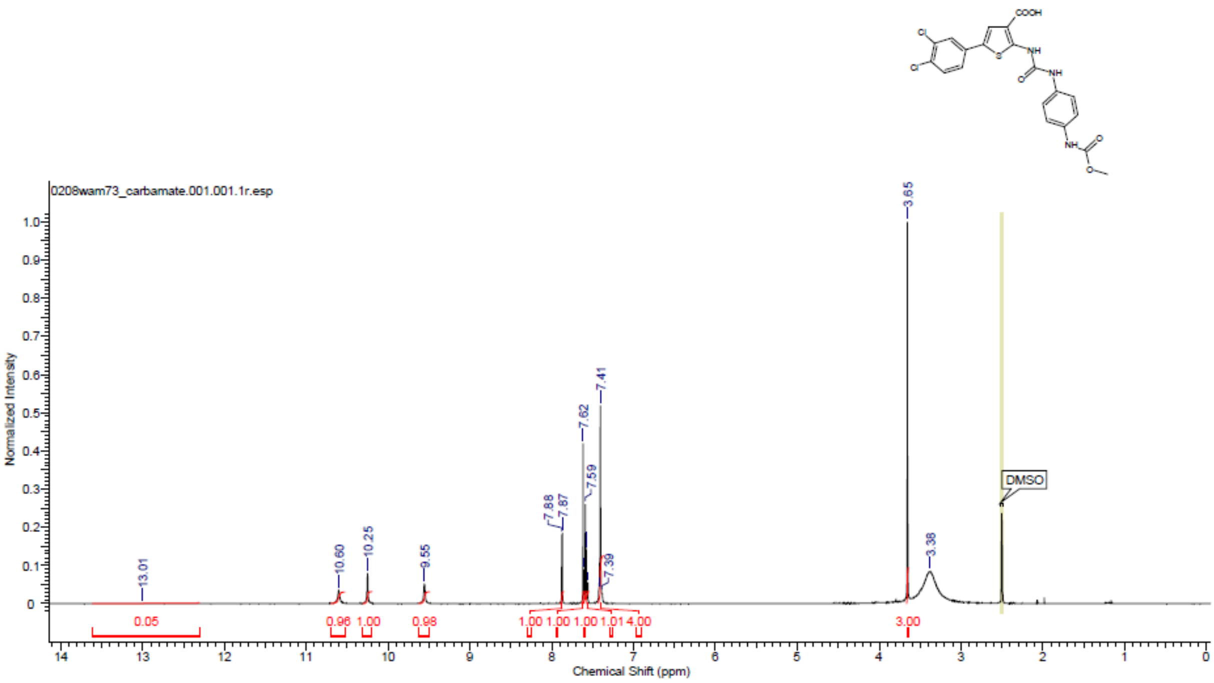


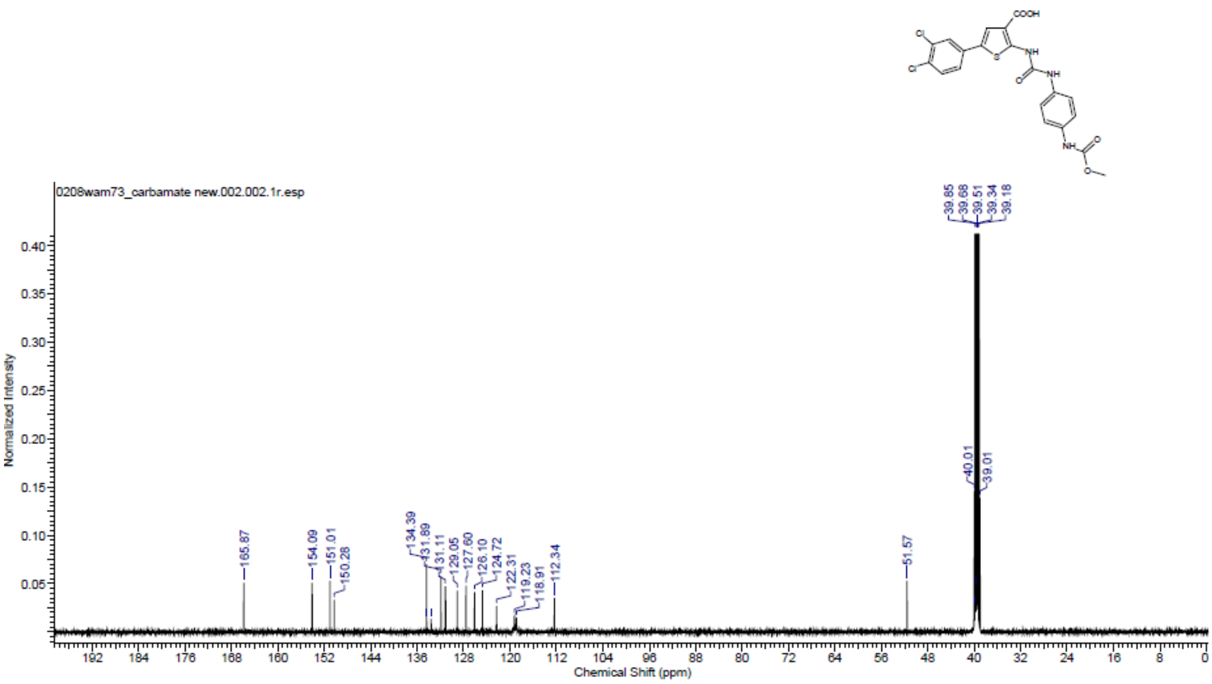
0711wam278.001.001.1r.esp
DMSO
EA
EA
EA
Normalized Intensity
Chemical Shift (ppm)
13.02
10.94
10.61
10.52
8.65
8.04
7.89
7.63
7.60
7.59
7.48
7.46
5.21
4.04
4.03
4.01
4.00
1.98
1.18
1.17
1.15
0.33
0.97
1.02
0.97
1.01
1.03
1.02
1.03
4.09
2.04
2.04



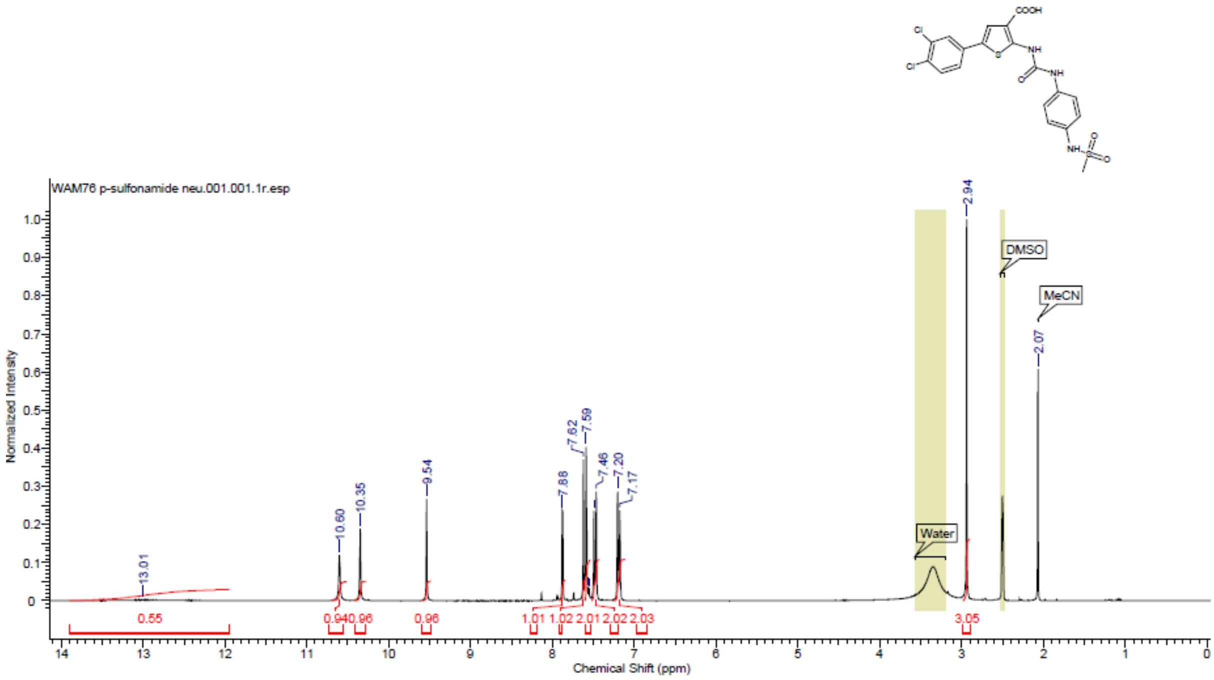
0711wam278.002.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
165.66
164.11
150.99
150.91
150.13
145.44
134.60
134.35
133.78
131.84
131.09
129.00
127.60
126.08
124.72
119.83
118.94
112.35
51.82
40.01
39.85
39.68
39.51
39.34
39.17
39.01

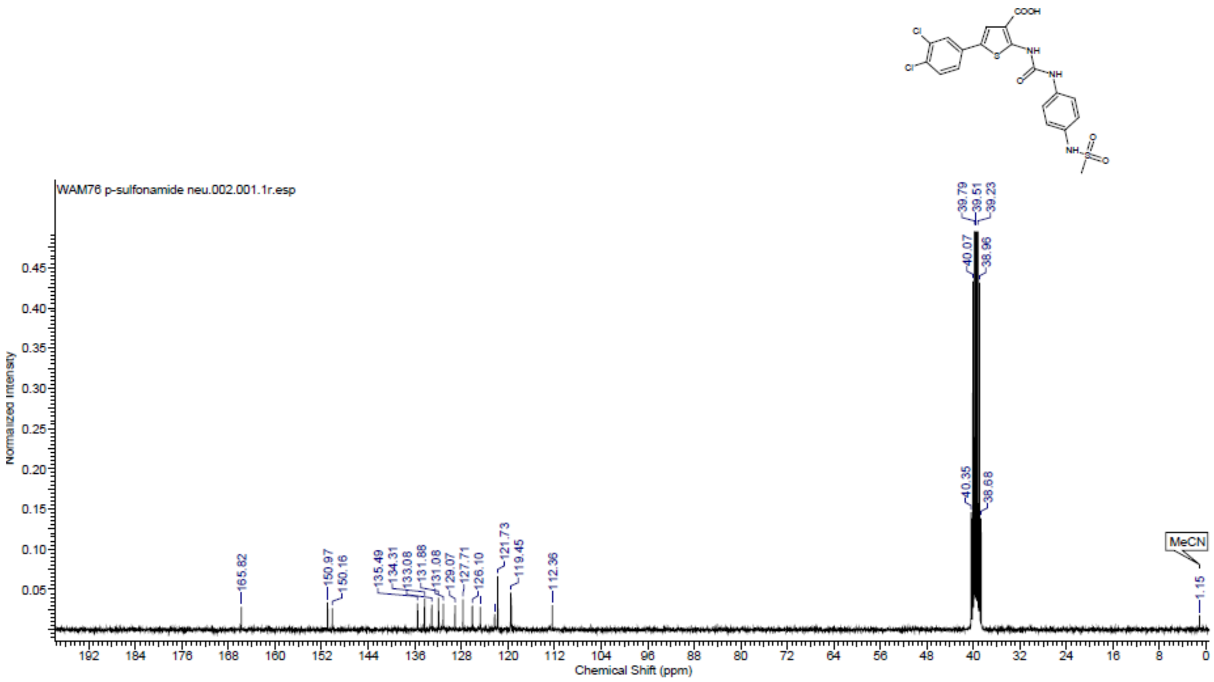
Compound **17**


0208wam73_carbamate.001.001.1r.esp
DMSO
Normalized Intensity
Chemical Shift (ppm)

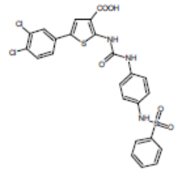

0208wam73_carbamate new.002.002.1r.esp
Normalized Intensity
Chemical Shift (ppm)

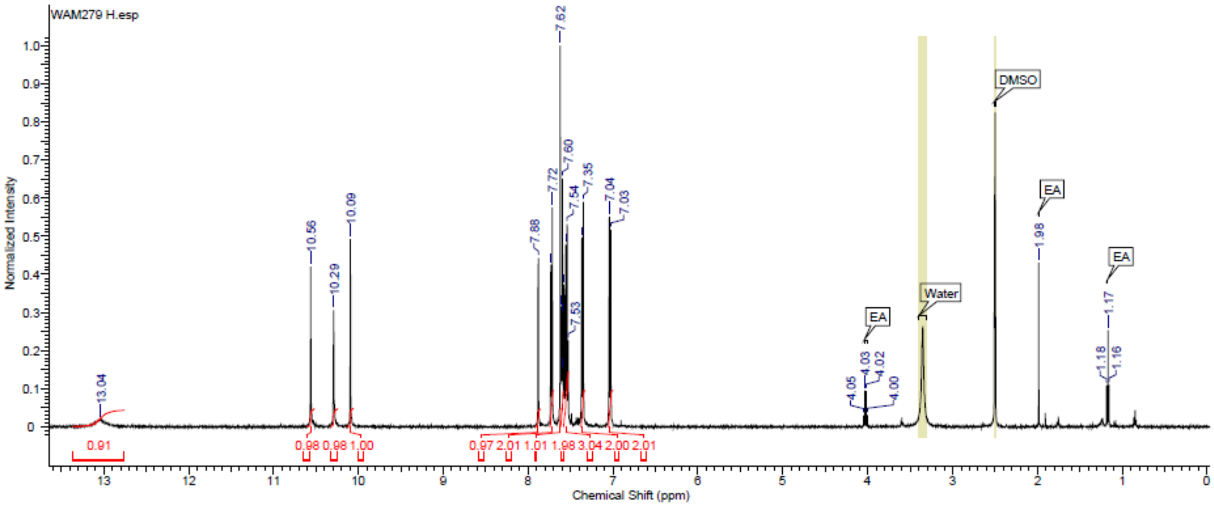
Compound **18**

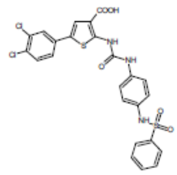


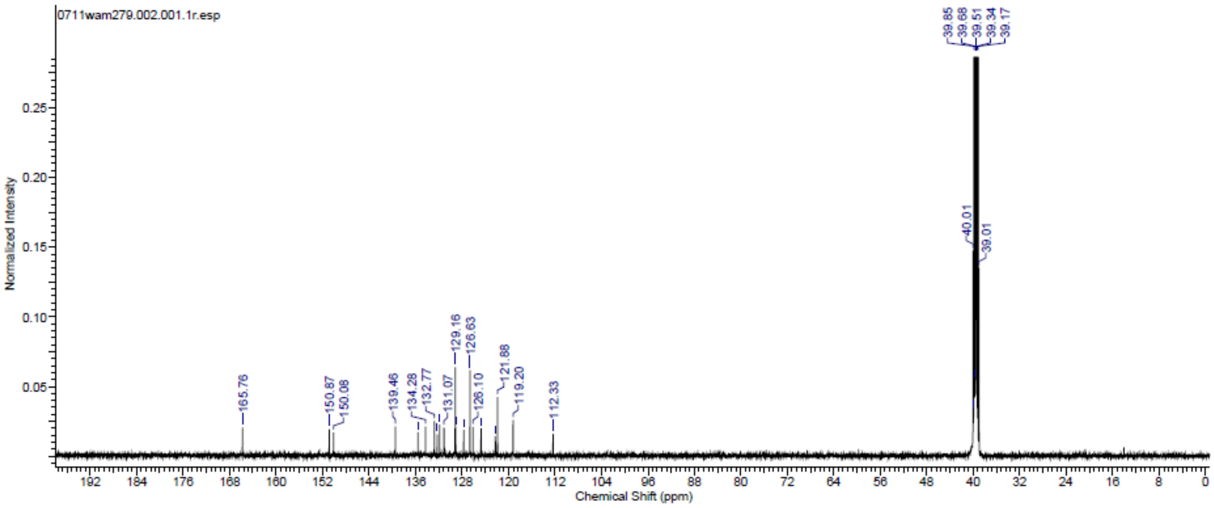


Compound **19**

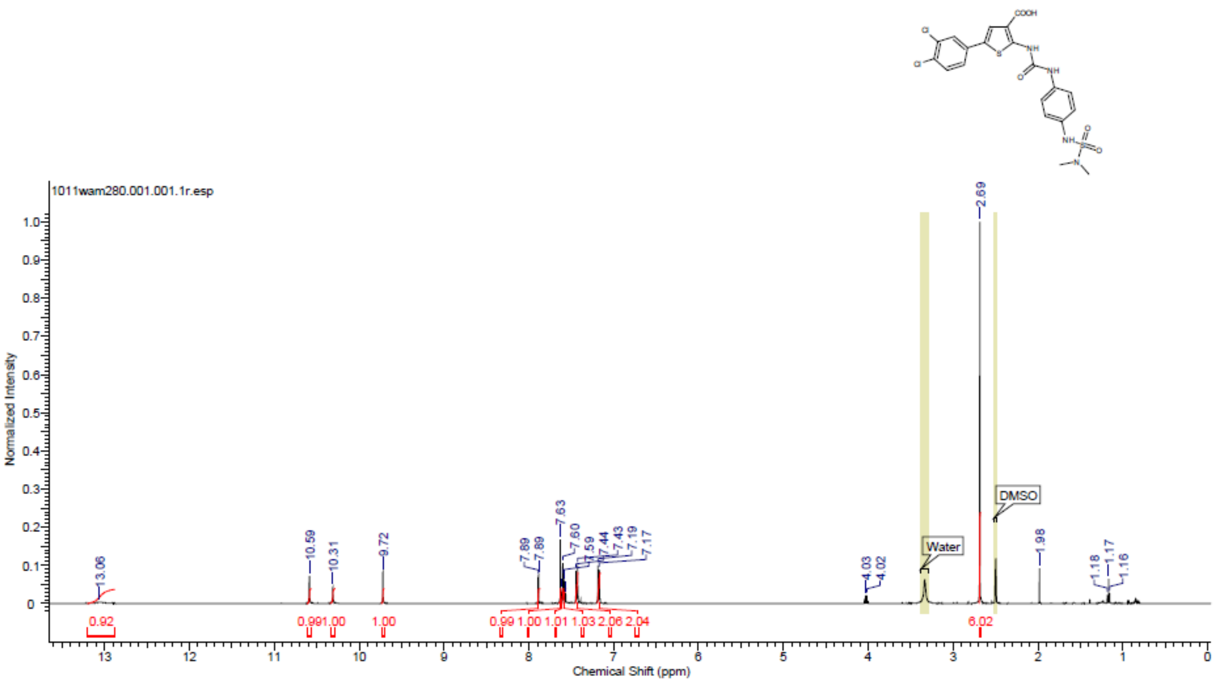

COOH
Cl
Cl
S
NH
NH
O
NH
S
O
O


WAM279 H.esp
Normalized Intensity
Chemical Shift (ppm)
13.04
10.56
10.29
10.09
7.88
7.72
7.62
7.60
7.54
7.53
7.35
7.04
7.03
4.05
4.03
4.02
4.00
1.98
1.18
1.17
1.16
EA
Water
DMSO
0.91
0.98
0.98
1.00
0.97
2.01
1.01
1.98
3.04
2.00
2.01

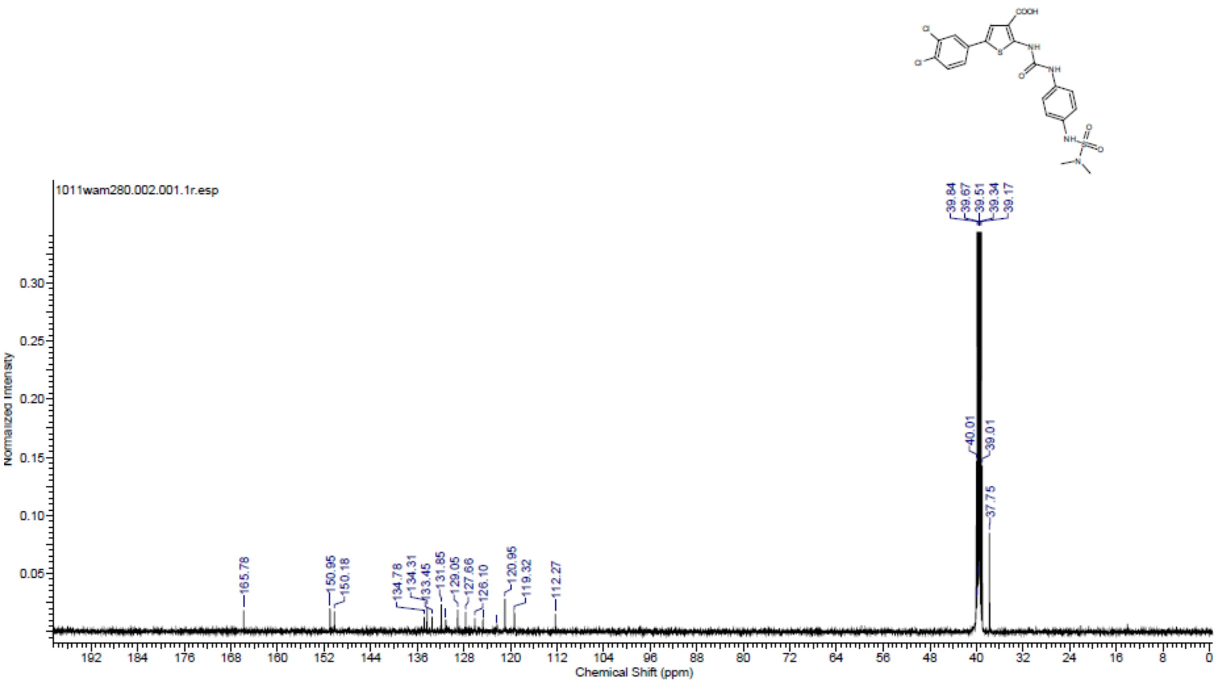

COOH
Cl
Cl
S
NH
NH
O
NH
S
O
O


0711wam279.002.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
165.76
150.87
150.08
139.46
134.28
132.77
131.07
129.16
126.63
126.10
121.88
119.20
112.33
39.85
39.68
39.51
39.34
39.17
40.01
39.01

Compound **20**



1011wam280.001.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Water
DMSO



1011wam280.002.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)