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

Ni(II)-catalyzed vinylic C-H functionalization of 2-acetamido-3-arylacrylates to access isotetronic acids

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Supporting Information

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1. General experimental details:

Addition of all the reagents and solvents were performed under air for GP-I and GP-II. Glassware used in the reactions was thoroughly oven-dried. All commercial grade reagents were used without further purification and solvents were dried prior to use following standard protocol. Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F254 pre-coated plates (0.25 mm) and the spots were visualized by exposure to UV light and/or by dipping into $KMnO_4$ solution. Silica gel of particle size 230–400 mesh and petroleum ether/ethyl acetate as eluent were used for column chromatographic purification. ^{1}H and ^{13}C NMR spectra for all the compounds were recorded at 400/600 and 100/150 MHz (BrukerUltrashield™ 400, Ascend™ 600), respectively. The spectra were recorded in deuterochloroform ($CDCl_3$) and deuterated dimethyl sulfoxide (DMSO-d_6) as solvent at room temperature. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$: δ_H = 7.26, δ_C = 77.16 ppm and DMSO-d_6: δ_H = 2.5, δ_C = 39.52 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublet q: quartet, dt: doublet of triplets, br: broad.), coupling constant (Hz), integration. Data for ^{13}C NMR are reported as chemical shift. HRMS spectra using ESI (+ ve) 70 eV for amidoacrylates and 10eV, were recorded for isotetronic acid derivatives on an ESI-FTMS mass spectrometer.

2. General procedure (GP-1) for the synthesis of acetamidoacrylates (10a-10x):

To a suspension of *N*-acetylglycine (1 equiv) in dry benzene (5mL/mmol) containing Et_3N (1.5 equiv), ethyl chloroformate (1.1 equiv) was added at 0 °C and the mixture was stirred at room temperature until the *N*-acetylglycine crystals disappeared and triethylamine hydrochloride separated. The aldehyde (0.5 equiv) was added to the mixture and heated under reflux at 80 °C for 2h.[1] After cooling to room temperature, triethylamine hydrochloride was removed by suction filtration and washed twice with dry benzene. The combined solution was concentrated and dried under reduced pressure. The residue was then dissolved in methanol (HPLC grade, 5mL/mmol), Et_3N (1.5 equiv) was added and refluxed at 65 °C for 3h. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure.[2,3] Purification of the residue by silica gel flash column chromatography using EtOAc/Hexanes as eluent or trituration afforded the desired acetamidoacrylates (**10a-10x**).

2.1. Experimental Details and Yield of the known amidoacrylates (10, 13, 14, 15):

All the starting materials has been synthesized by following literarure known procedure.[1-4] Spectral data were in complete agreement with reported values.[1-4] Yield of the individual compounds are given below.

(Z)-methyl 2-acetamido-3-phenylacrylate (10a):[2]

The titled compound 10a was synthesized from benzaldehyde (5 g, 47.17 mmol) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (8.057 g, 36.8 mmol, yield = 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 – 7.48 (m, 2H), 7.44 – 7.33 (m, 4H), 7.01 (s, 1H), 3.87 (s, 3H), 2.16 (s, 3H).

(Z)-methyl 2-acetamido-3-(2-methoxyphenyl)acrylate (10b):[2]

The titled compound 10b was synthesized from 2-anisaldehyde (500 mg, 3.67 mmol) according to GP-1. The crude product was dissolved in $CHCl_3$ and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (641 mg, 2.57 mmol, yield = 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.41 – 7.43 (m, 1H), 7.34 – 7.37 (m, 2H), 6.94 – 6.98 (m, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 2.07 (s, 3H).

(Z)-methyl 2-acetamido-3-(3-methoxyphenyl)acrylate (10c):[2]

The titled compound 10c was synthesized from 3-anisaldehyde (500 g, 3.67 mmol) according to GP-1. The crude product was dissolved in $CHCl_3$ and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (622 mg 2.5 mmol, yield = 68%). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.29 (m, 3H), 7.09 – 6.94 (m, 2H), 6.85 (d, *J* = 6.6 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 2.07 (s, 3H).

(Z)-methyl 2-acetamido-3-(4-methoxyphenyl)acrylate (10d):[3a]

The titled compound 10d was synthesized from 4-anisaldehyde (5 g, 47.17 mmol) by following the previous reports from our group.[3a] The crude product was dissolved in $CHCl_3$ and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (638 mg, 2.57 mmol, yield = 70%).

(Z)-methyl 2-acetamido-3-(2-bromophenyl)acrylate (10e):[2]

The titled compound 10e was synthesized from 2-bromobenzaldehyde (500 mg, 2.7 mmol) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (658 mg, 2.21 mmol, yield = 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.9 Hz, 1H), 7.42 (s, 2H), 7.27 (dd, *J* = 9.3, 5.2 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.11 (s, 1H), 3.86 (s, 3H), 2.02 (s, 3H).

(Z)-methyl 2-acetamido-3-(4-bromophenyl)acrylate (10f):[3b]

The titled compound 10f was synthesized from 4-bromobenzaldehyde (500 mg, 2.7 mmol) according to the literature known procedure.[3b] The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (640 g, 2.16 mmol, yield = 80%).

(Z)-methyl 2-acetamido-3-(4-fluorophenyl)acrylate (10g):[2]

The titled compound 10g was synthesized from 4-fluorobenzaldehyde (430 mg, 3.467 mmol) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (583 mg, 2.46 mmol, yield = 71%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.42 (m, 2H), 7.37 (s, 1H), 7.05 (t, *J* = 8.3 Hz, 2H), 3.84 (s, 3H), 2.12 (s, 3H).

(Z)-methyl 2-acetamido-3-(4-chlorophenyl)acrylate (10h):[3b]

The titled compound 10h was synthesized from 4-chlorobenzaldehyde (500 mg, 3.57 mmol) according to GP-1. Purification was done by flash column chromatography using 25% ethyl acetate in hexane as eluent to afford white solid product (657 mg, 2.6 mmol, yield = 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 5H), 3.82 (s, 3H), 2.09 (s, 3H).

(Z)-methyl 2-acetamido-3-(o-tolyl)acrylate (10j):[4a]

The titled compound 10j was synthesized by following literature known procedure.[4a]. Purification was done by flash column chromatography using 25% ethyl acetate in hexane as eluent to afford white solid product (677 mg, 2.91 mmol, yield = 70%).

(Z)-methyl 2-acetamido-3-(p-tolyl)acrylate (10k):[2]

The titled compound 10k was synthesized from *p*-tolualdehyde (500 mg, 4.16 mmol) according to GP-1. Purification was done by flash column chromatography using 25% ethyl acetate in hexane as eluent to afford white solid product (631 mg, 2.70 mmol, yield = 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.36 (m, 2H), 7.24 – 7.06 (m, 3H), 3.81 (s, 3H), 2.34 (s, 3H), 2.10 (s, 3H).

(Z)-methyl 2-acetamido-3-(3-nitrophenyl)acrylate (10q):[3a]

The titled compound 10q was synthesized from 3-nitrobenzaldehyde (500 mg, 3.31 mmol) by following the previous reports from our group.[3a] Purification was done by flash column chromatography using 30% ethyl acetate in hexane as eluent to afford yellowish white solid product (524 mg, 1.986 mmol, yield = 60%).

(Z)-methyl 2-acetamido-3-(4-nitrophenyl)acrylate (10r):[3b]

The titled compound 10r was synthesized from 4-nitrobenzaldehyde (500 mg, 3.31 mmol) according to the literature known procedure.[3b] Purification was done by flash column chromatography using 30% ethyl acetate in hexane as eluent to afford yellowish white solid product (585 mg, 2.21 mmol, yield = 67%).

4-(4-hydroxy-5-oxo-2,5-dihydrofuran-3-yl)benzonitrile (10t):[4b]

The titled compound 10t was synthesized from 4-Cyanobenzaldehyde (500 mg, 3.81 mmol) according to GP-1. Purification was done by flash column chromatography using 30% ethyl acetate in hexane as eluent to afford yellowish white solid product (680 mg, 2.78 mmol, yield = 73%).

^{1}H NMR (400 MHz, DMSO) δ 9.83 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 3.72 (s, 3H), 2.00 (s, 3H).

(Z)-methyl 2-acetamido-3-(pyridin-4-yl)acrylate (10u):[4c]

The titled compound 10u was synthesized from 4-Pyridinecarboxaldehyde (532 mg, 4.97 mmol) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (690 mg, 3.13 mmol, yield = 63%). ^{1}H NMR (600 MHz, DMSO) δ 9.85 (s, 1H), 8.62 (d, *J* = 5.2 Hz, 2H), 7.53 (d, *J* = 5.6 Hz, 2H), 7.05 (s, 1H), 3.74 (s, 3H), 2.02 (s, 3H).

(Z)-methyl 2-acetamidobut-2-enoate (10v):[3a]

The titled compound 10v was synthesized from L-threonine (960 mg, 8.05 mmol) by following the previous reports from our group.[3a] Purification was done by flash column chromatography using 15% ethyl acetate in hexane as eluent to afford brown gummy product (606 mg, 3.864 mmol, yield = 48%).

(2Z,4E)-methyl 2-acetamido-5-phenylpenta-2,4-dienoate (10w):[4d]

The titled compound 10w was synthesized from Cinnamaldehyde (650 mg, 4.92 mmol) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered

and dried in vacuo. The pure product was obtained as a white solid (470 mg, 1.92 mmol, yield = 39%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 6.5 Hz, 2H), 7.24-7.35 (m, 4H), 7.13 (s, 1H), 6.90 (s, 2H), 3.83 (s, 3H), 2.22 (s, 3H).

(Z)-methyl 2-benzamido-3-phenylacrylate (13a): [4e]

The titled compound 13a was synthesized from benzaldehyde (2 g, 18.86 mmol) and Hippuric acid (instead of N-acetylglycine) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (4.56 g, 16.22 mmol, yield = 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.5 Hz, 2H), 7.75 (s, 1H), 7.56-7.60 (m, 1H), 7.54 – 7.44 (m, 5H), 7.32-7.37 (m, 3H), 3.88 (s, 3H).

(Z)-methyl 2-benzamido-3-(4-methoxyphenyl)acrylate (13b):[4e]

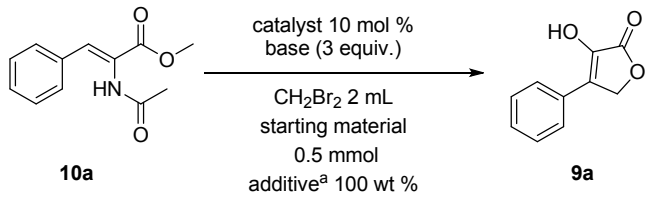
The titled compound 13b was synthesized from 2-anisaldehyde (545 mg, 4 mmol) and Hippuric acid (instead of N-acetylglycine) according to GP-1. The crude product was dissolved in acetone and triturated with hexane. The mixture was filtered and dried in vacuo. The pure product was obtained as a white solid (1g, 3.28 mmol, yield = 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.4 Hz, 2H), 7.72 (s, 1H), 7.56-7.60 (m, 1H), 7.48-7.50 (m, 5H), 6.87 (d, *J* = 8.6 Hz, 2H), 3.86 (s, 3H), 3.81 (s, 3H).

(Z)-methyl 2-(N-methylacetamido)-3-phenylacrylate (14):[4f] The titled compound 14 was synthesized from methyl 2-(N-methylacetamido)acrylate (320 mg, 2 mmol) by following literature known procedure.[4f] The pure product was obtained as a semisolid (246 mg, 1.06 mmol, yield = 48%).

(Z)-2-acetamido-3-phenylacrylic acid (15):[4g]

The titled compound 15 was synthesized from benzaldehyde (500 mg, 4.72 mmol) by following literature known procedure.[4g] The pure product was obtained as a white solid (696 mg, 3.39 mmol, yield = 72%).

3. Table S1: optimization of reaction



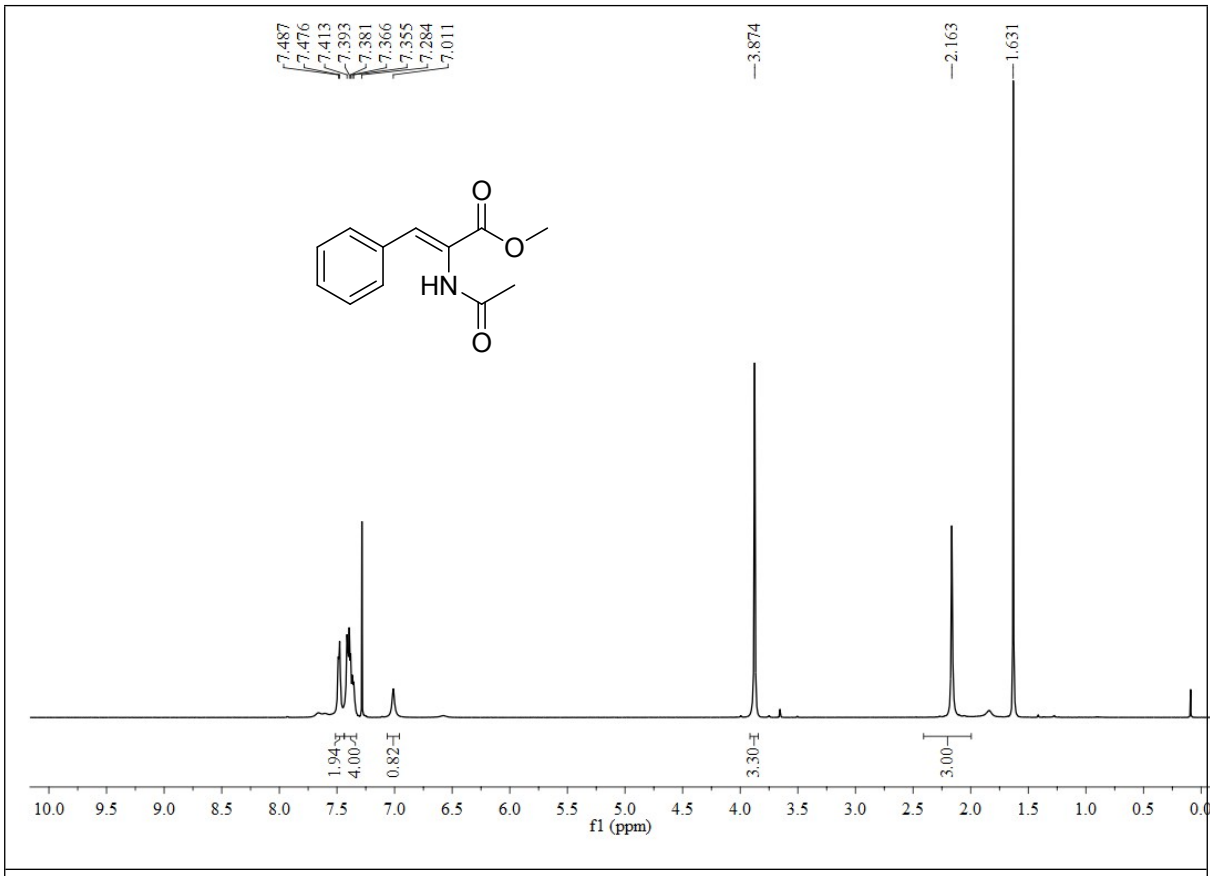
10a **9a**

Entry	Base	Catalyst	Temp °C	Time (h)	Yield[b] 9/10a (%)
1[c,d]	K_2HPO_4	$Pd(OAc)_2$	120	72	10/60
2	K_2CO_3	$Pd(OAc)_2$	120	72	11/68
3	K_2CO_3	$Pd(OAc)_2$	135	72	12/65
4	Cs_2CO_3	$Pd(OAc)_2$	135	72	12/57
5	KOAc	$Pd(OAc)_2$	135	48	22/55
6	KOAc	$Pd(OAc)_2$ (15 mol%)	135	48	21/55
7	NaOAc	$Pd(OAc)_2$	135	48	20/48
8	CsOAc	$Pd(OAc)_2$	140	48	17/50
9	KOAc (5equiv.)	$Pd(OAc)_2$	140	48	21/45
10	-	$Pd(OAc)_2$	135	48	0/91
11	KOAc	-	135	48	0/87
12[e]	KOAc	$Pd(OAc)_2$	135	48	trace
13[f]	KOAc	$Pd(OAc)_2$	135	48	-
14[g]	KOAc	$Pd(OAc)_2$	135	48	-
15[h]	KOAc	$Pd(OAc)_2$	135	48	26/23
16	$Li(OAc).2H_2O$	$Pd(OAc)_2$	140	48	41/35
17	$Li(OAc).2H_2O$	$Pd(OAc)_2$	140	48	49/35
18[i]	$Li(OAc).2H_2O$	$Pd(OAc)_2$	140	48	-
19	$Li(OAc).2H_2O$	$Ni(PCy_3)_2Cl_2$	140	48	62/19
20	$Li(OAc).2H_2O$	$Ni(PCy_3)_2Cl_2$	150	48	69/8
21	$Li(OAc).2H_2O$	$Ni(PCy_3)_2Cl_2$	160	48	42/-
22	$Li(OAc).2H_2O$	$Ni(PCy_3)_2Cl_2$	150	36	70/5
23	$Li(OAc).2H_2O$	$Ni(PCy_3)_2Cl_2$	150	36	58/18
24	$Li(OAc).2H_2O$	$Ni(OAc)_2.4H_2O$	150	36	72/6
25	$Li(OAc).2H_2O$	$Ni(OAc)_2.4H_2O$ (5 mol %)	150	22	76/0
26	$Li(OAc).2H_2O$	$Ni(OAc)_2.4H_2O$ (2 mol %)	150	22	76/0
27	$Li(OAc).2H_2O$	$Ni(OAc)_2.4H_2O$ (1 mol %)	150	22	51/15
28[j]	$Li(OAc).2H_2O$	$Ni(OAc)_2.4H_2O$ (2 mol %)	150	15	**81**/0
29[j]	$Li(OAc).2H_2O$	$Ni(Cl)_2.6H_2O$ (2 mol %)	150	22	72/0
30[j]	$Li(OAc).2H_2O$	$Ni(NO_3)_2.4H_2O$ (2 mol %)	150	22	70/0

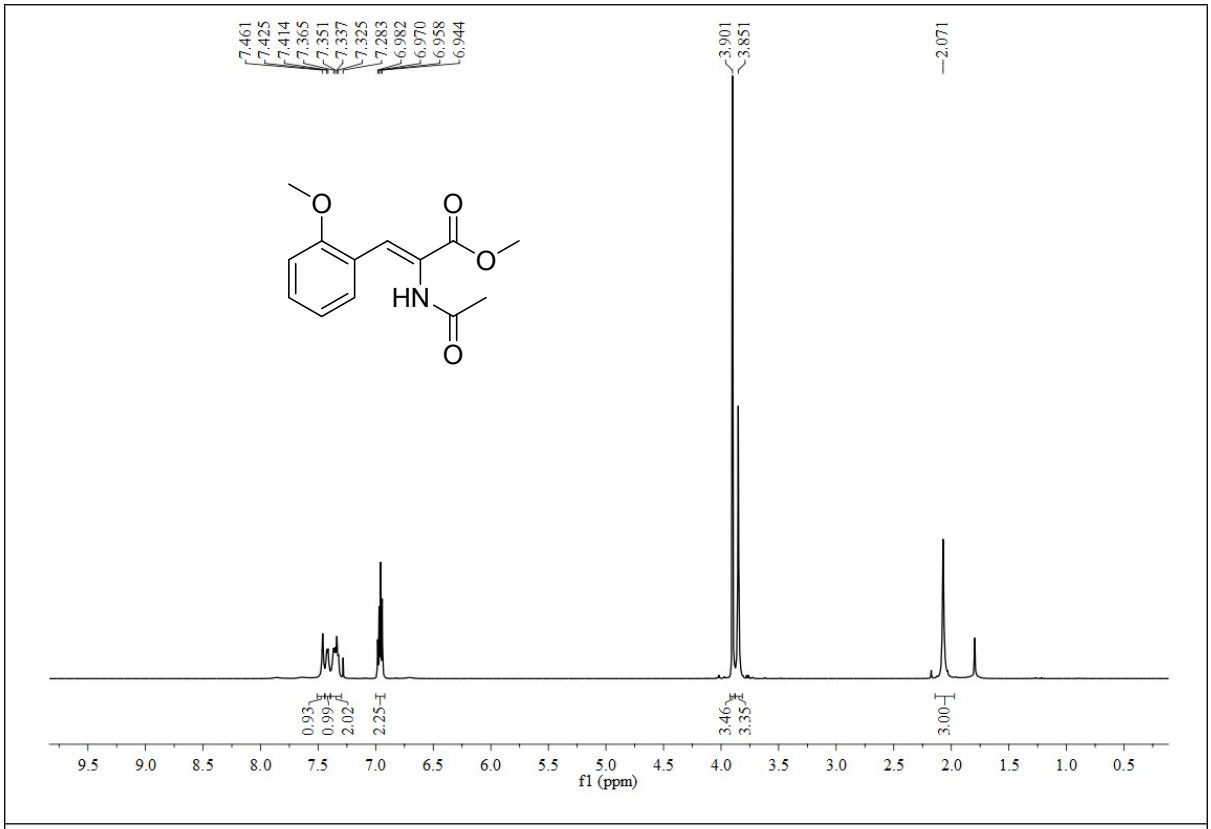
[a]100 wt % molecular sieve dust was used entries 17 to 30 except 23. [b]Yield was determined after column chromatographic purification. [c]All the compounds were added under nitrogen atmosphere. [d]All the compounds were added under air. [e](1mL/1mL) CH_2Br_2/H_2O was added as solvent. [f](1mL/1mL) CH_2Br_2/CH_3CN was added as

solvent. [g](1mL/1mL) CH_2Br_2:dioxane was added as solvent. [h](1mL/1mL) CH_2Br_2/DMF was added as solvent. [i]DCM (2 mL) was added as solvent. [j](2mL/0.5mL) CH_2Br_2/DMF was added as solvent.

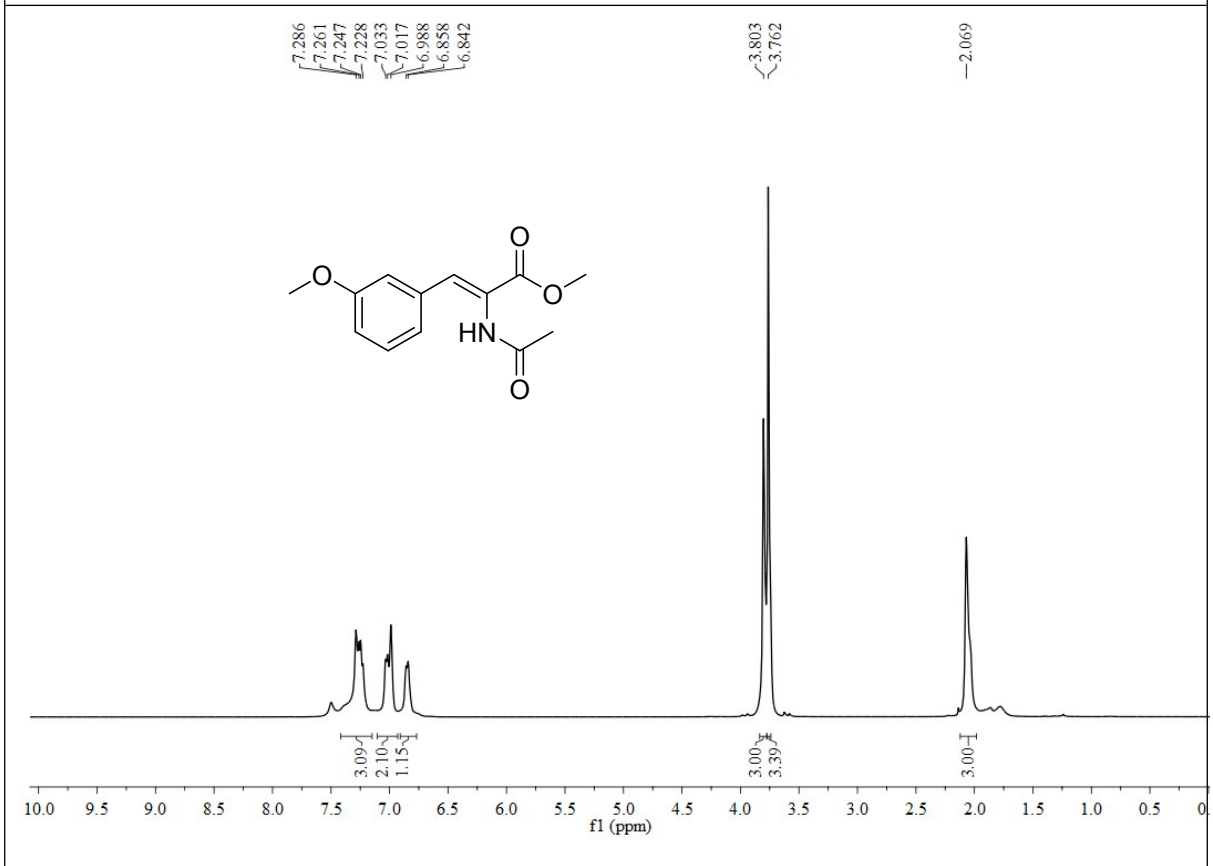
4. ^{1}H and ^{13}C NMR spectra of amidoacrylates:



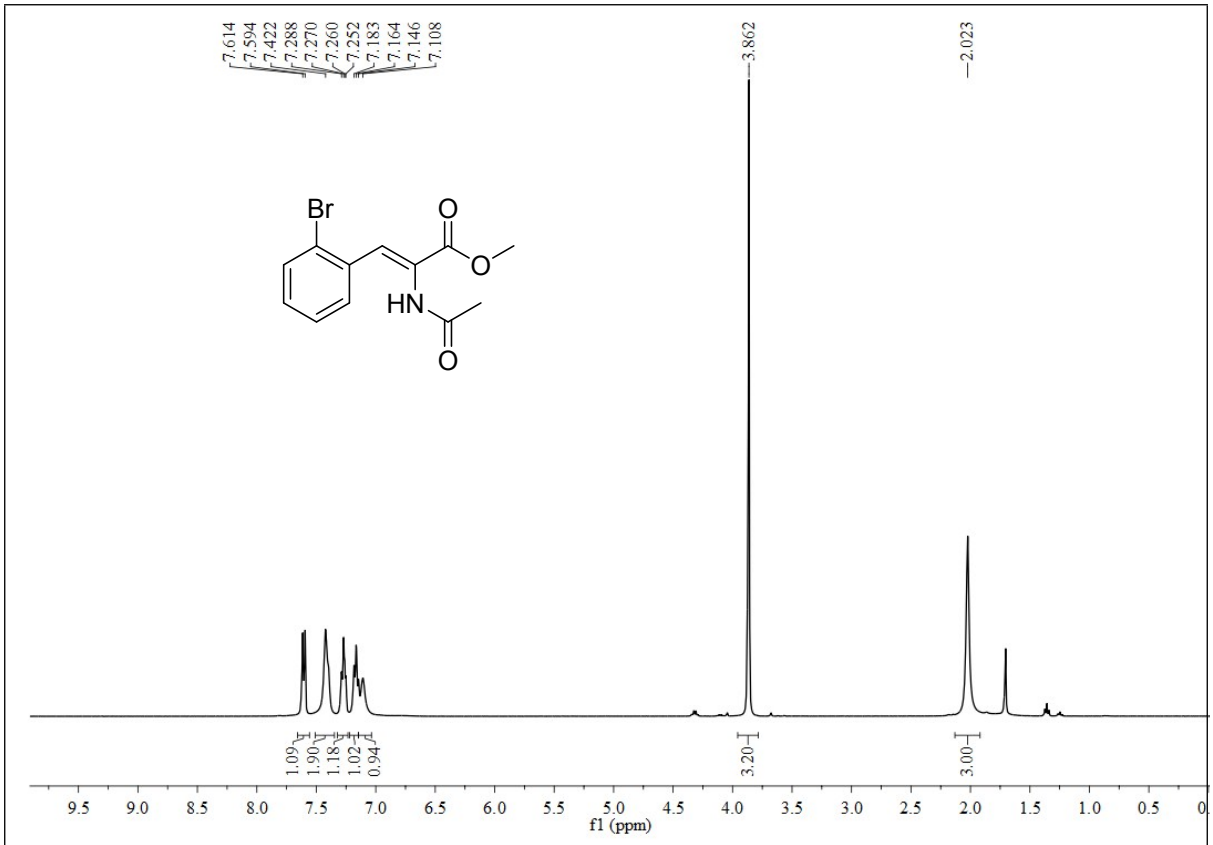
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **10a**



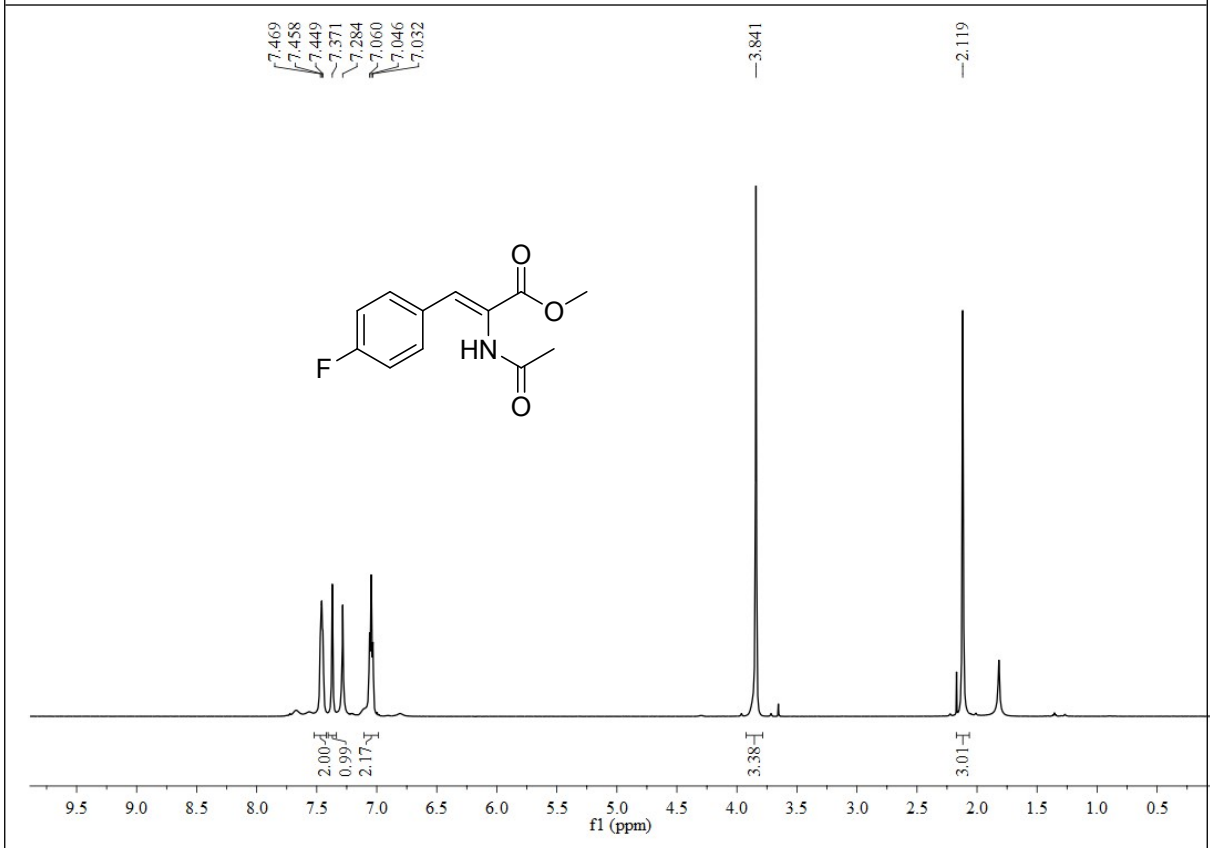
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **10b**



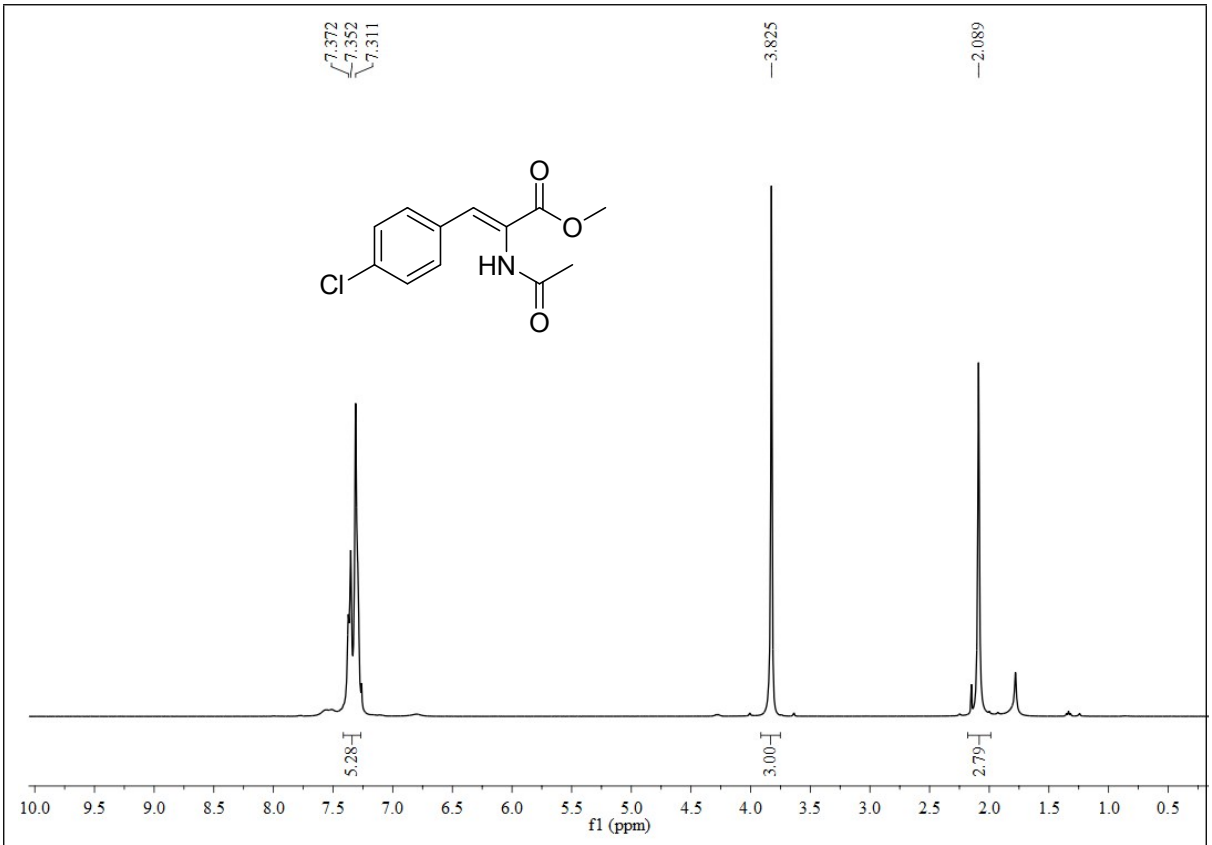
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10c**



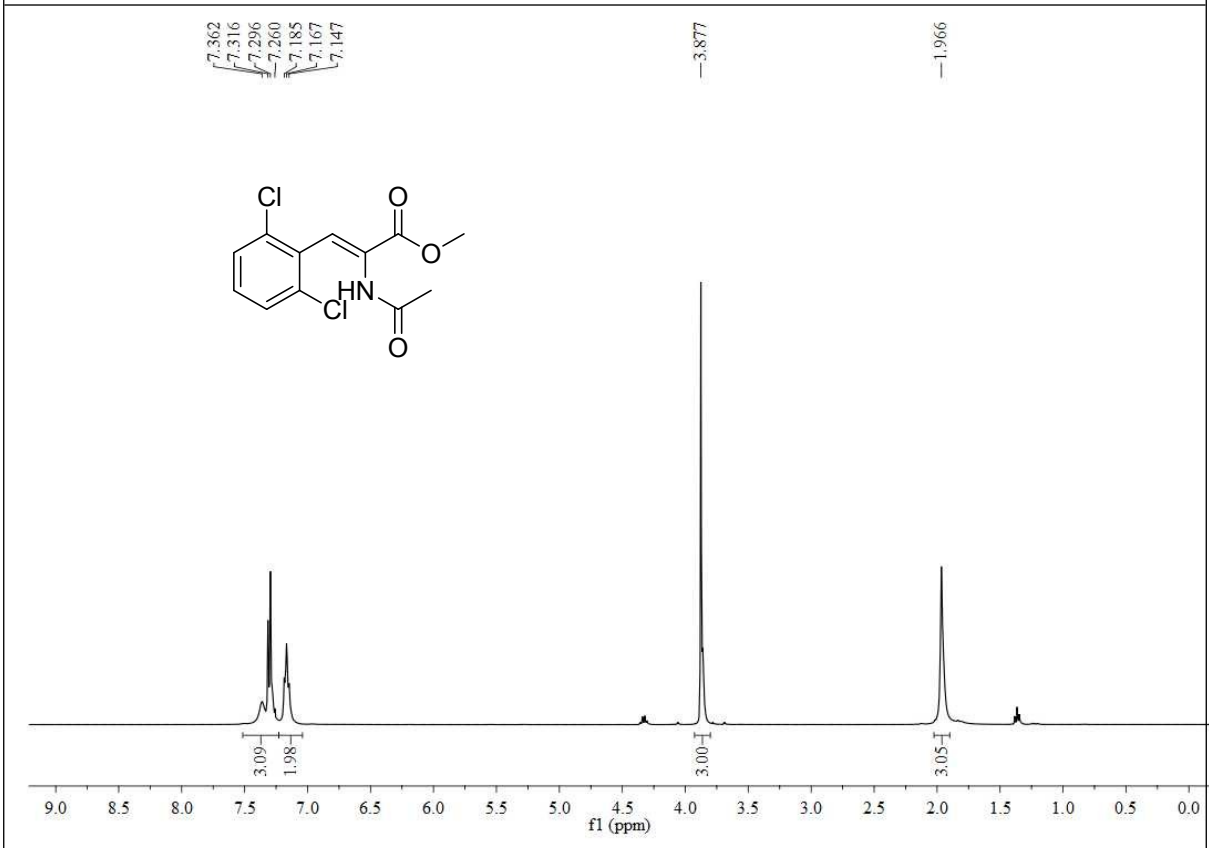
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10e**



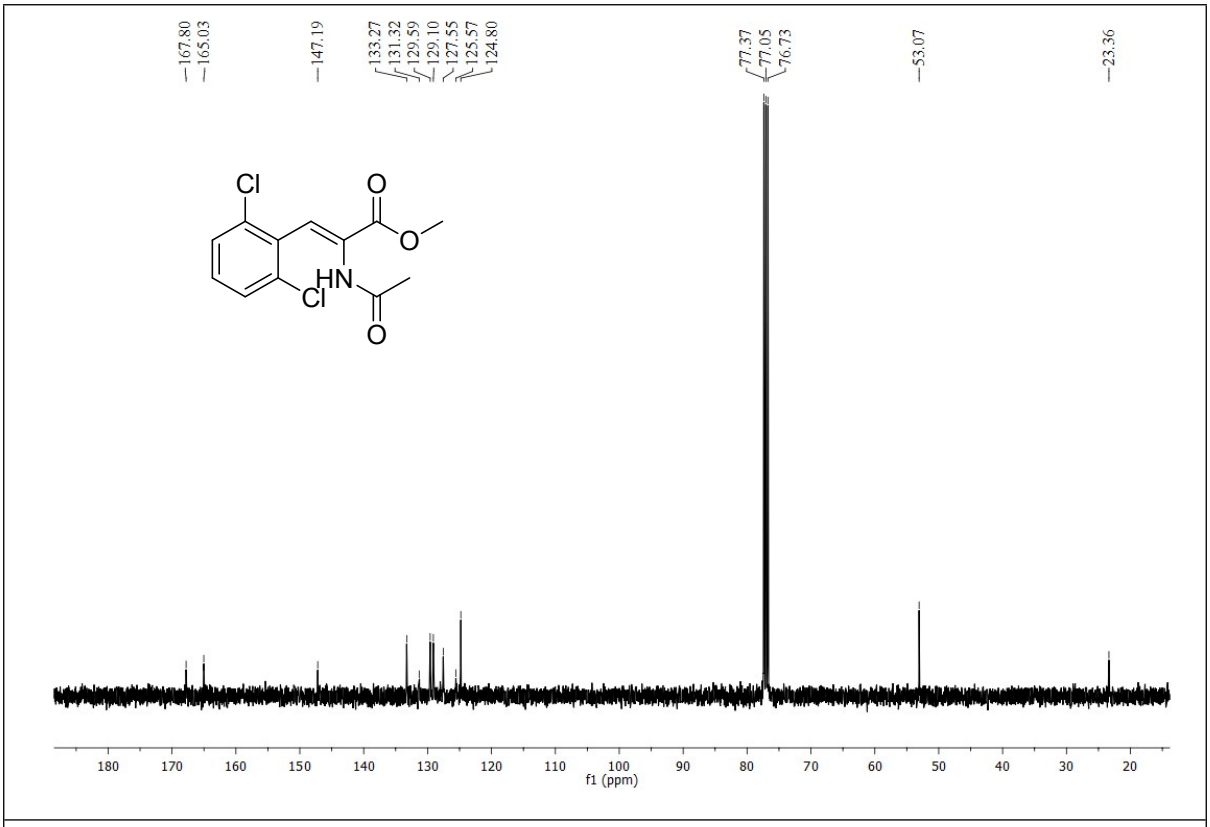
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **10g**



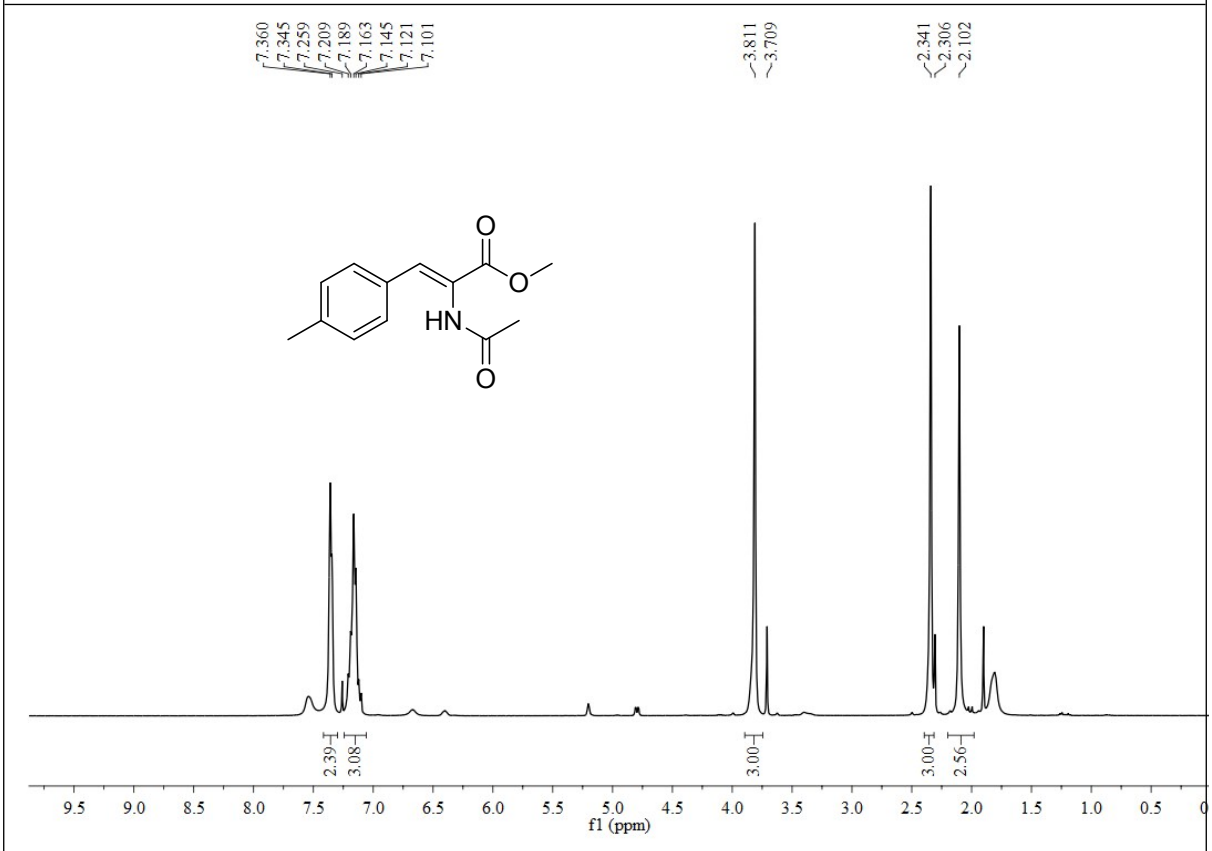
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10h**



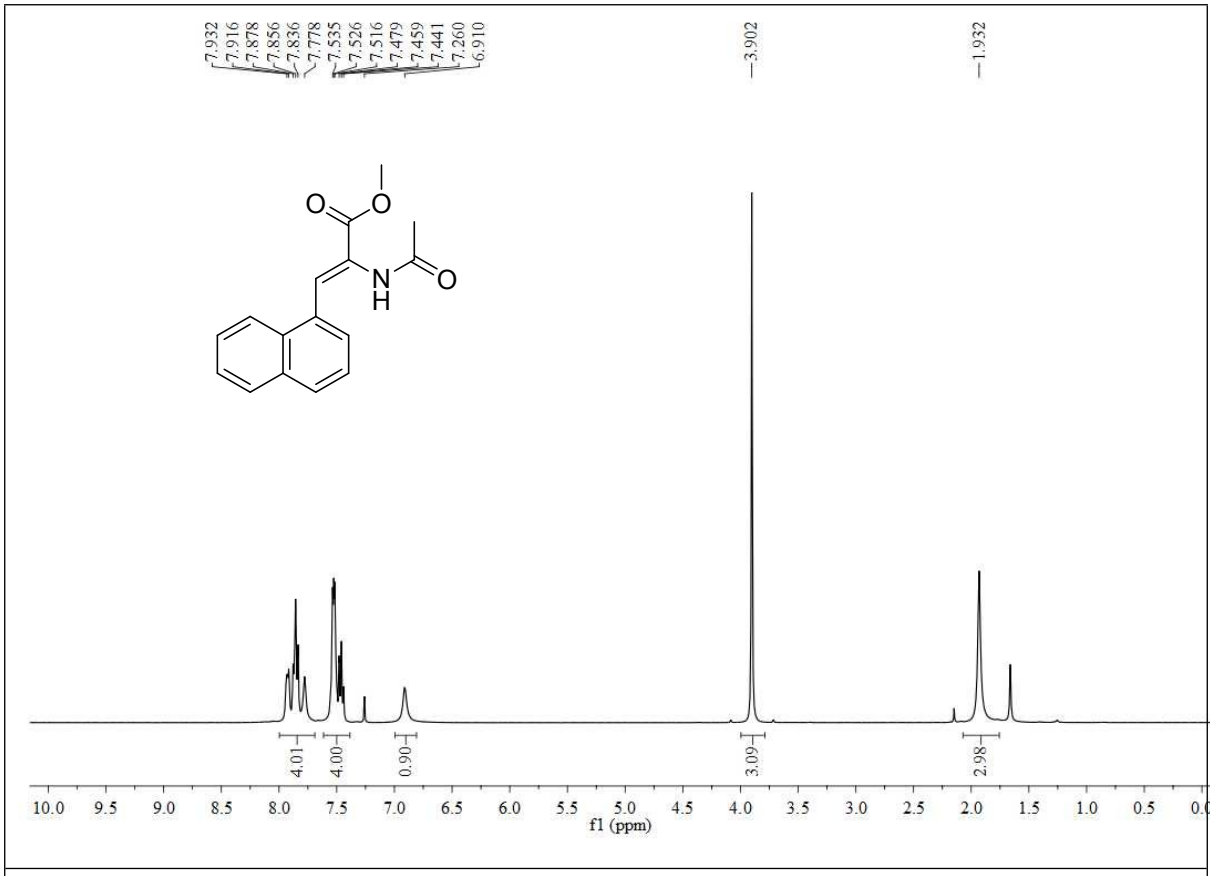
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10i**



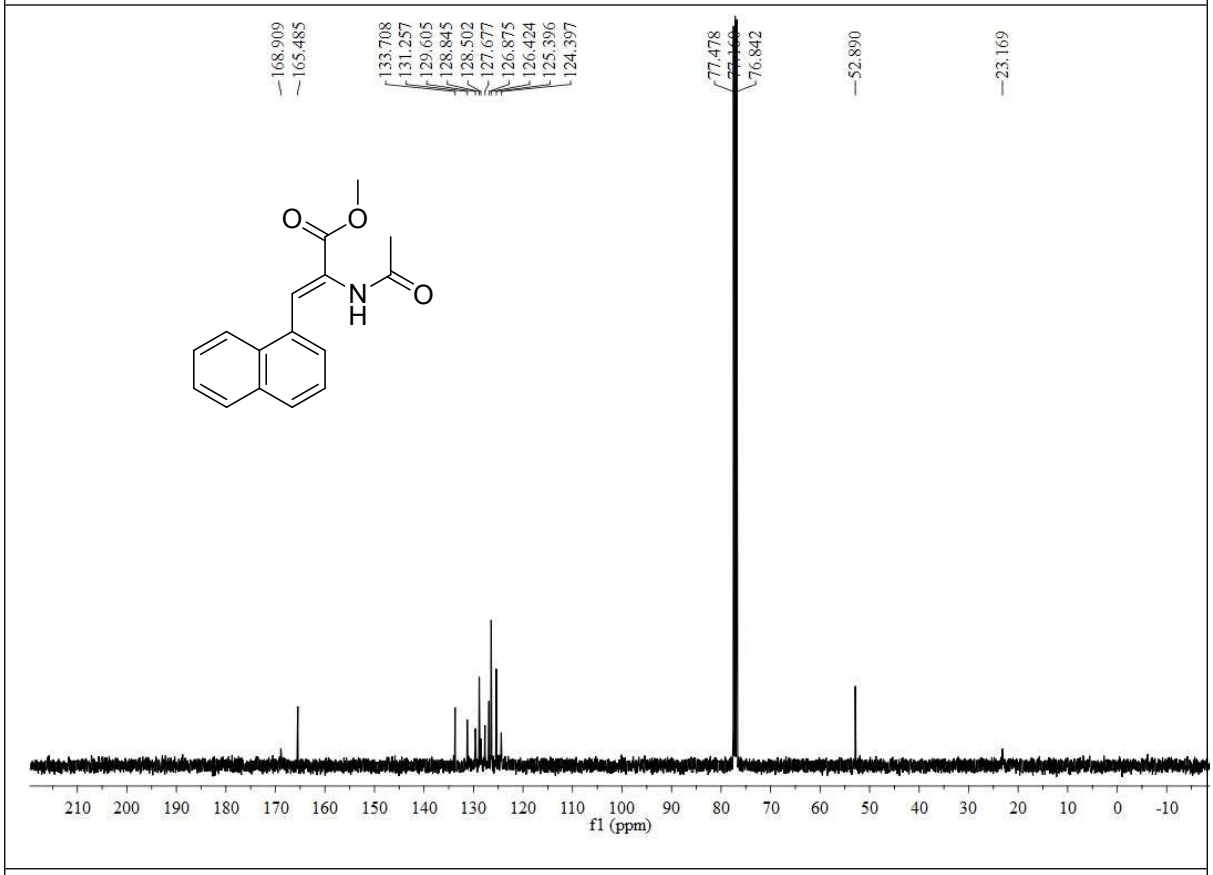
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) spectrum of compound **10i**



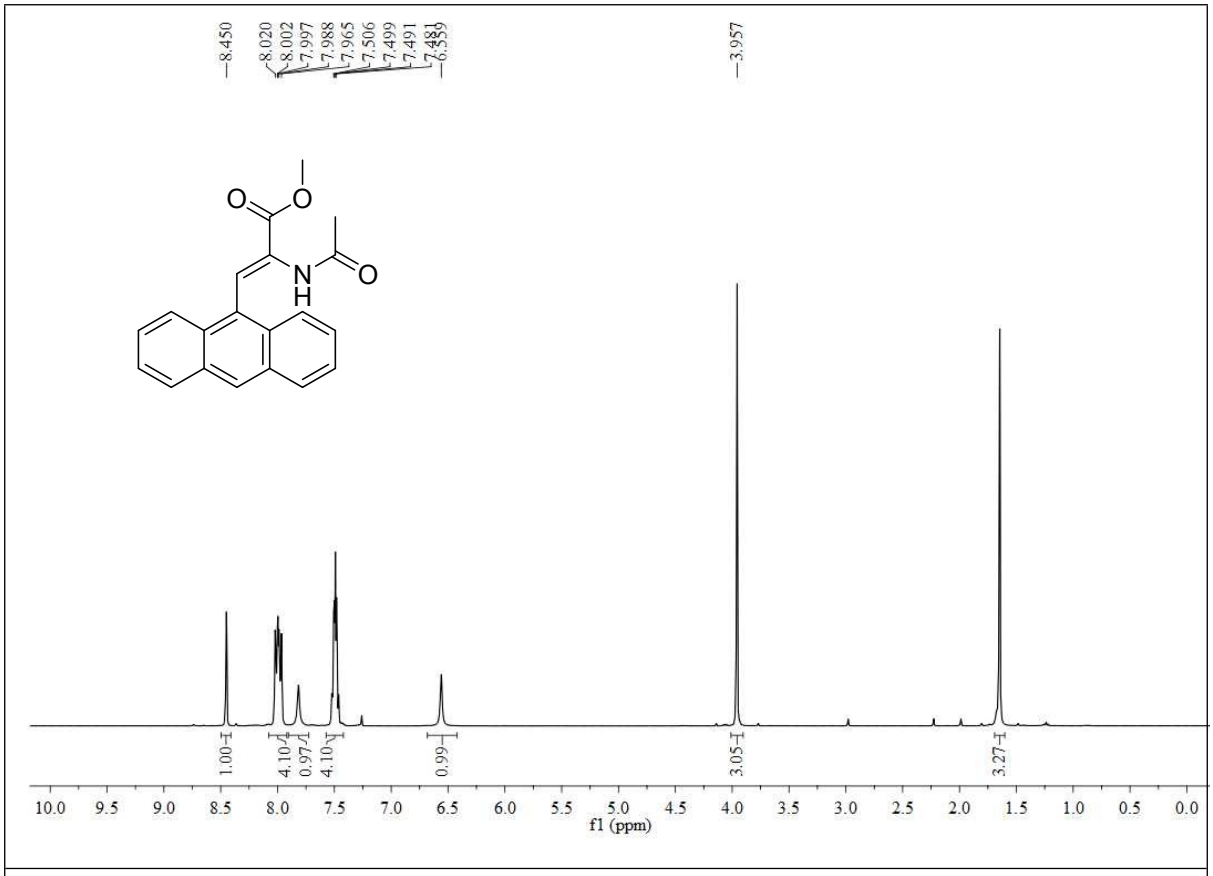
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10k**



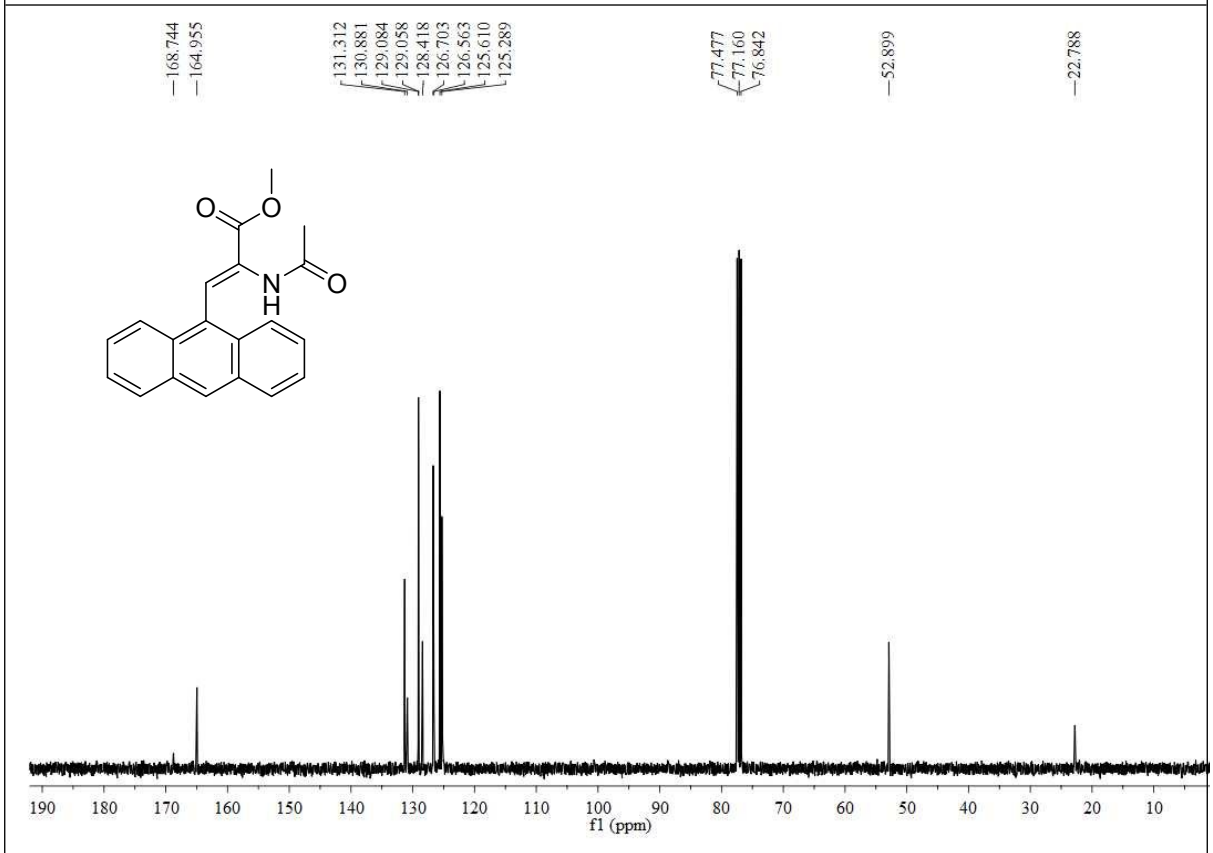
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10l**



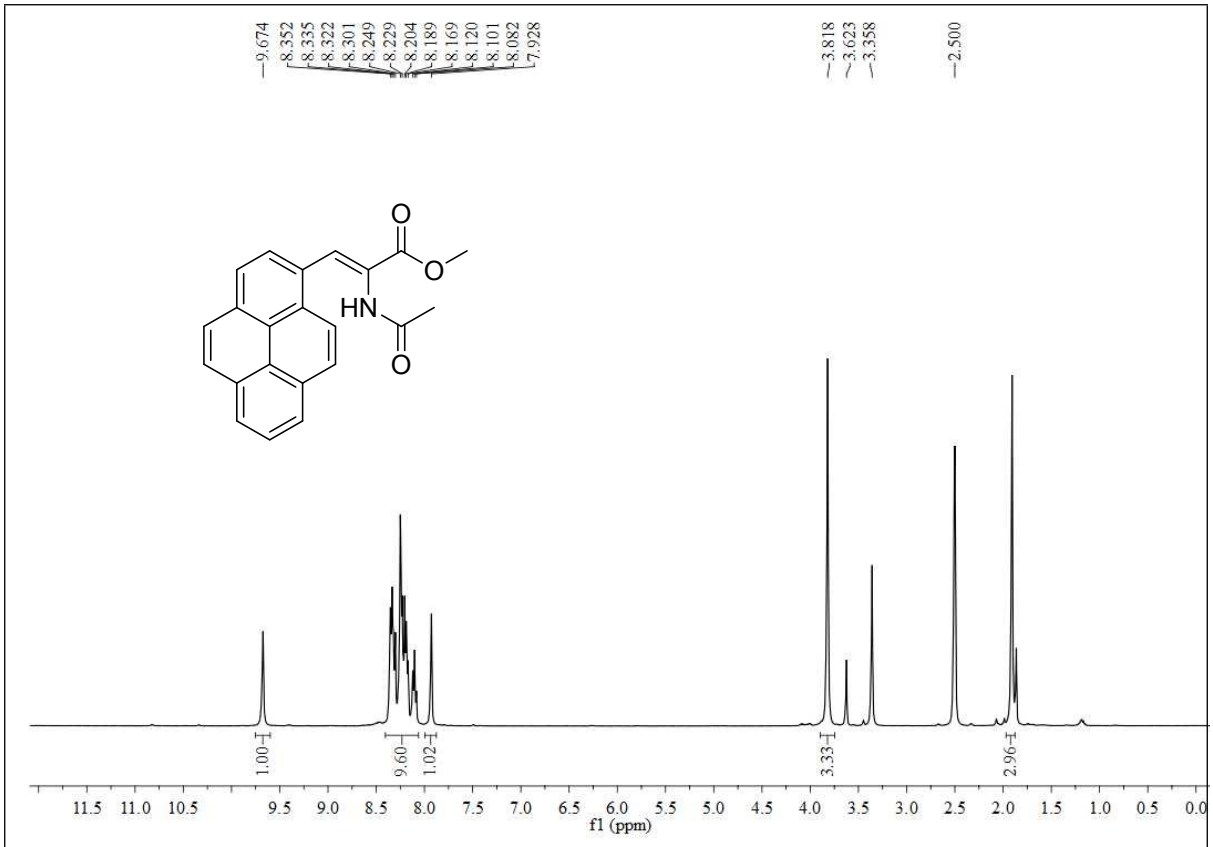
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **10l**



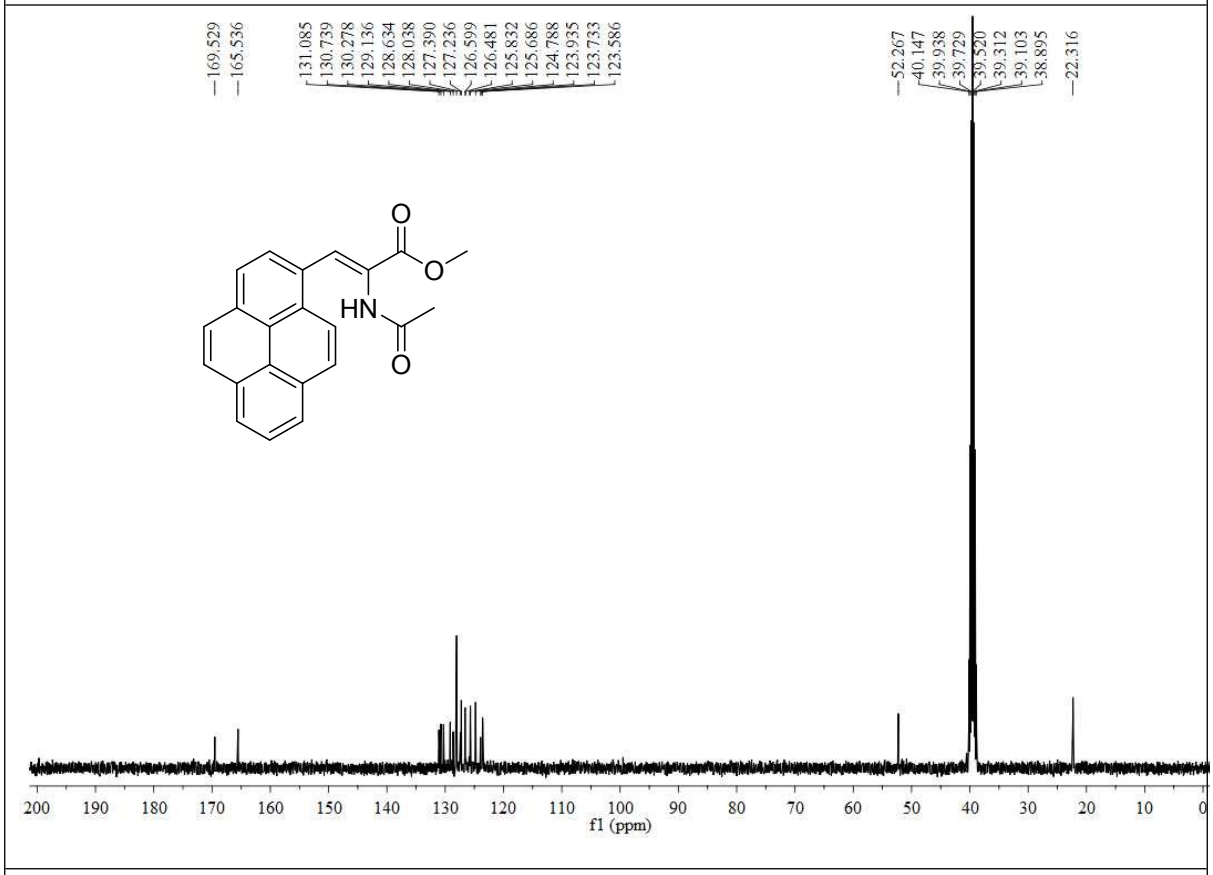
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10m**



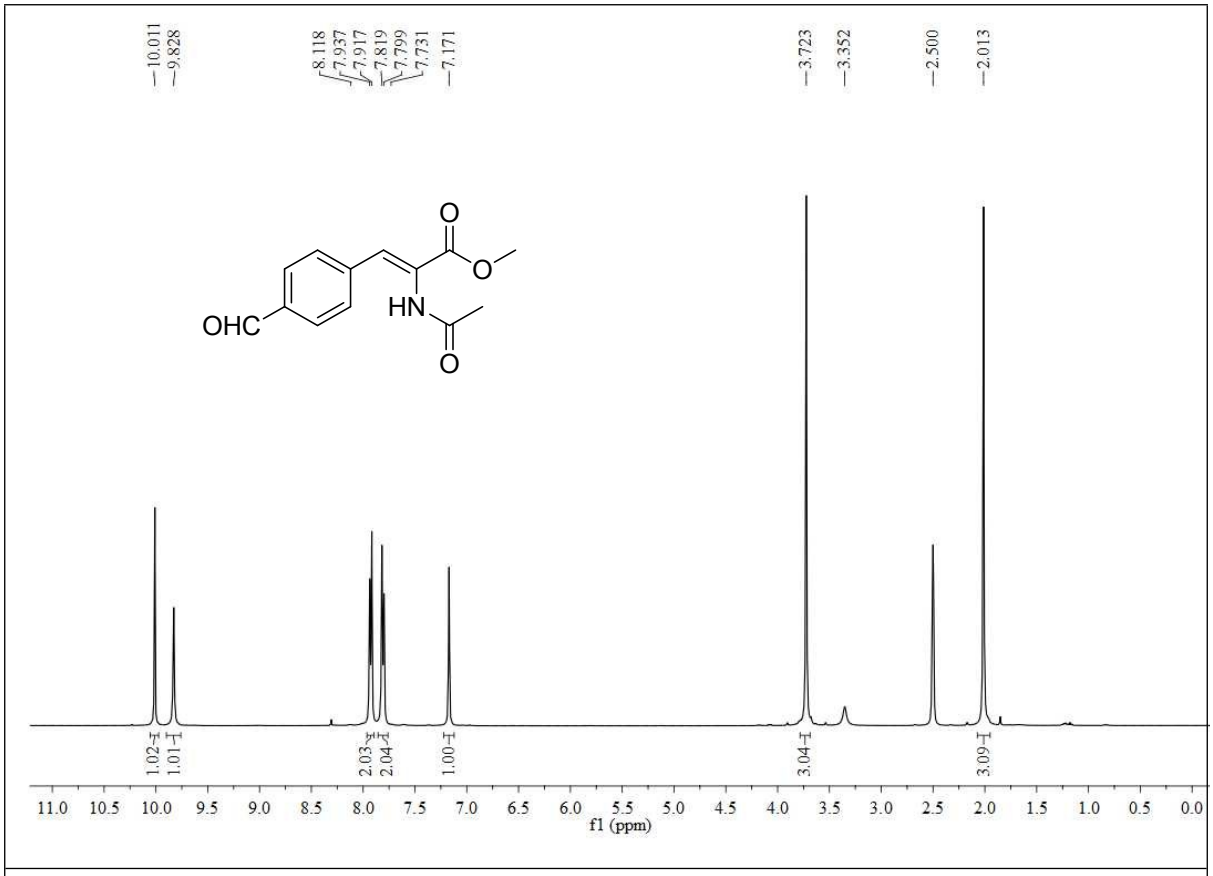
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **10m**



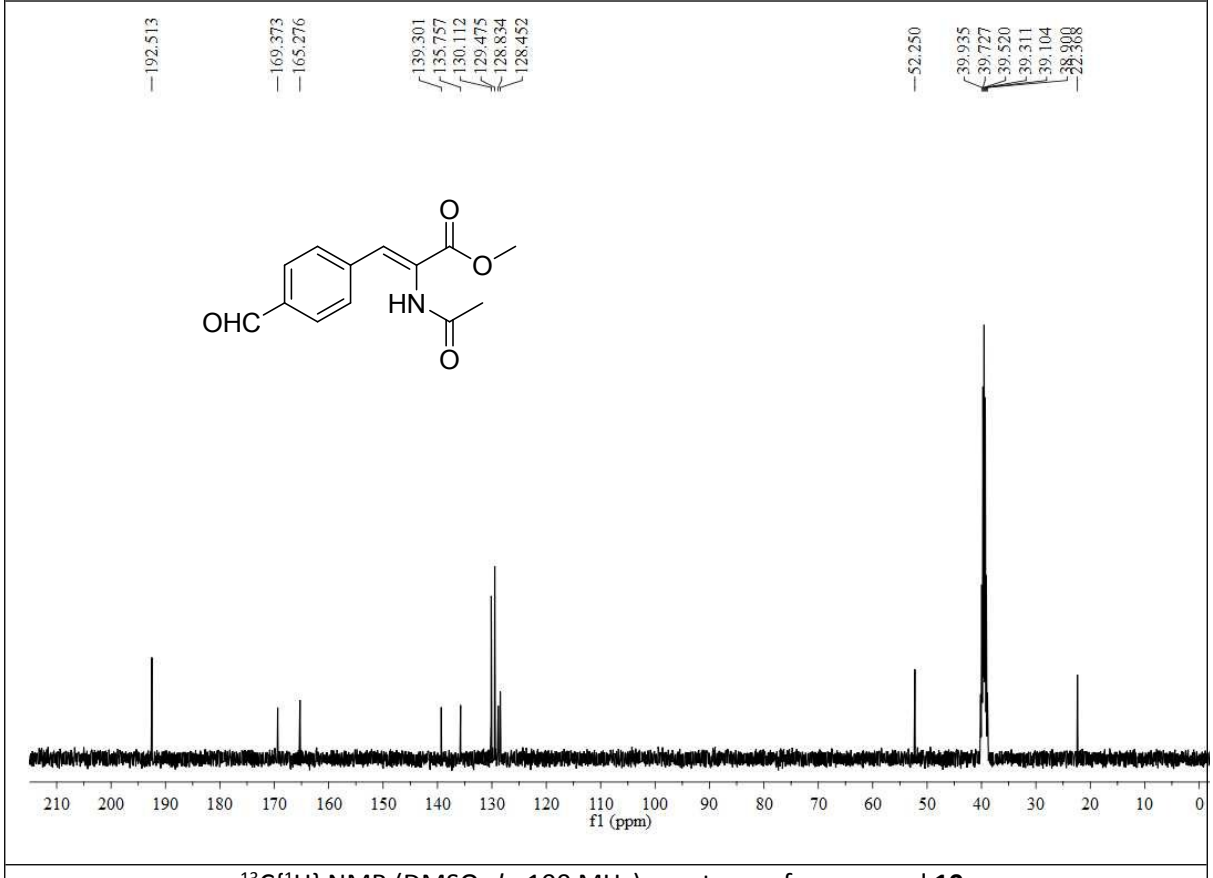
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **10n**



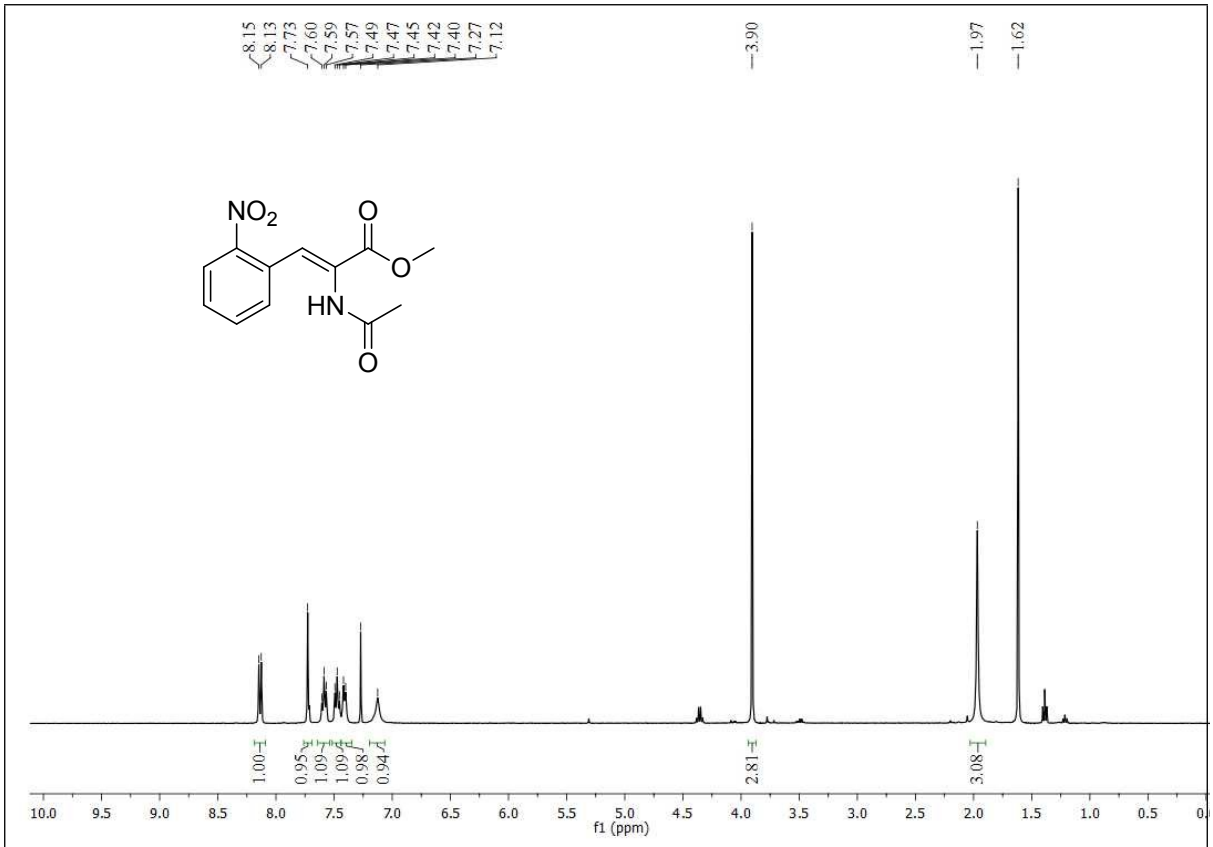
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **10n**



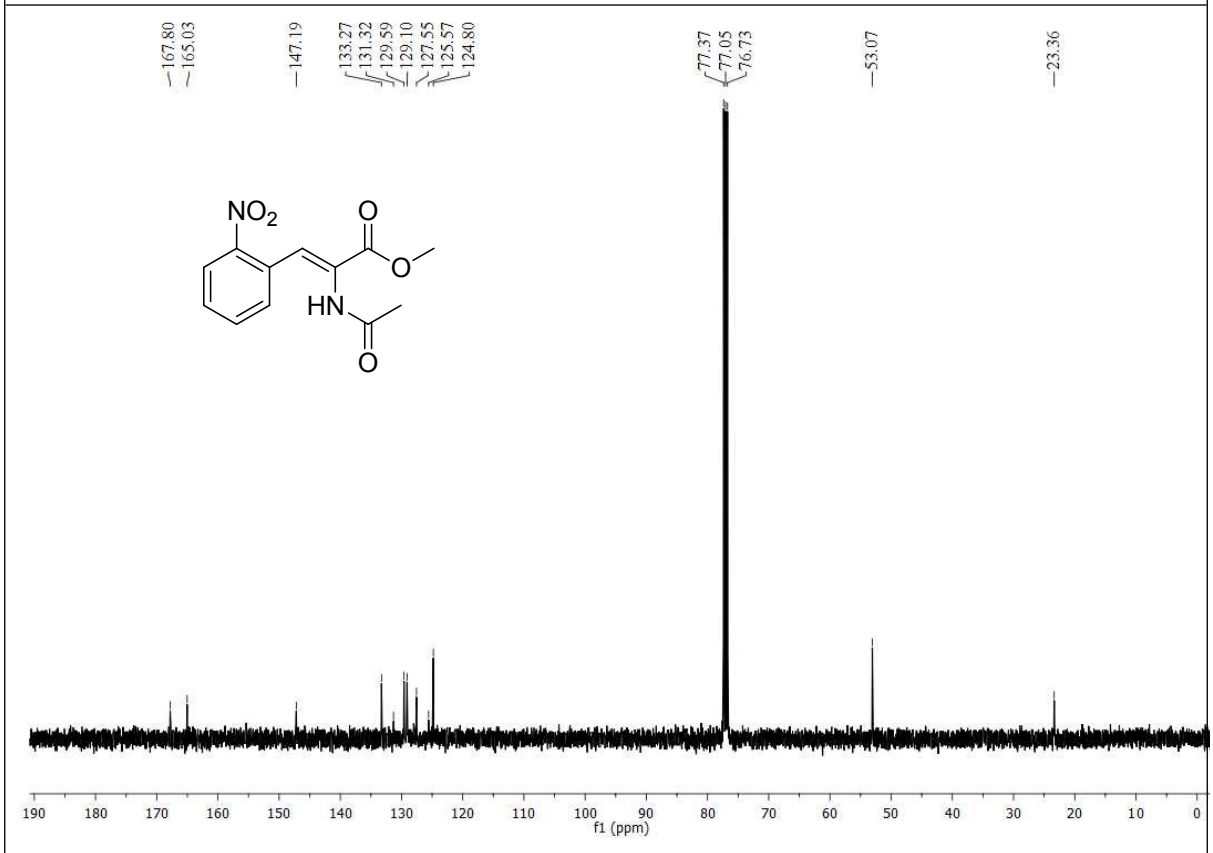
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **10o**



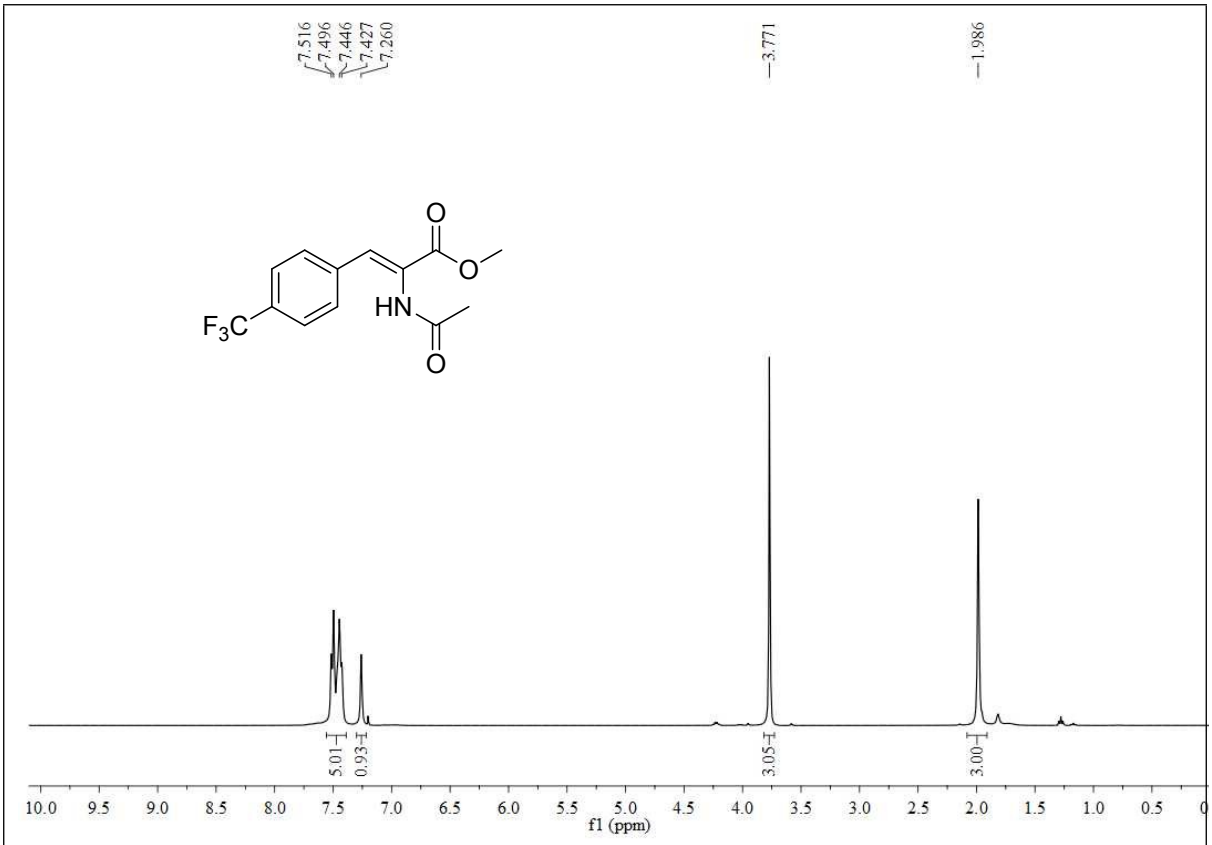
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **10o**



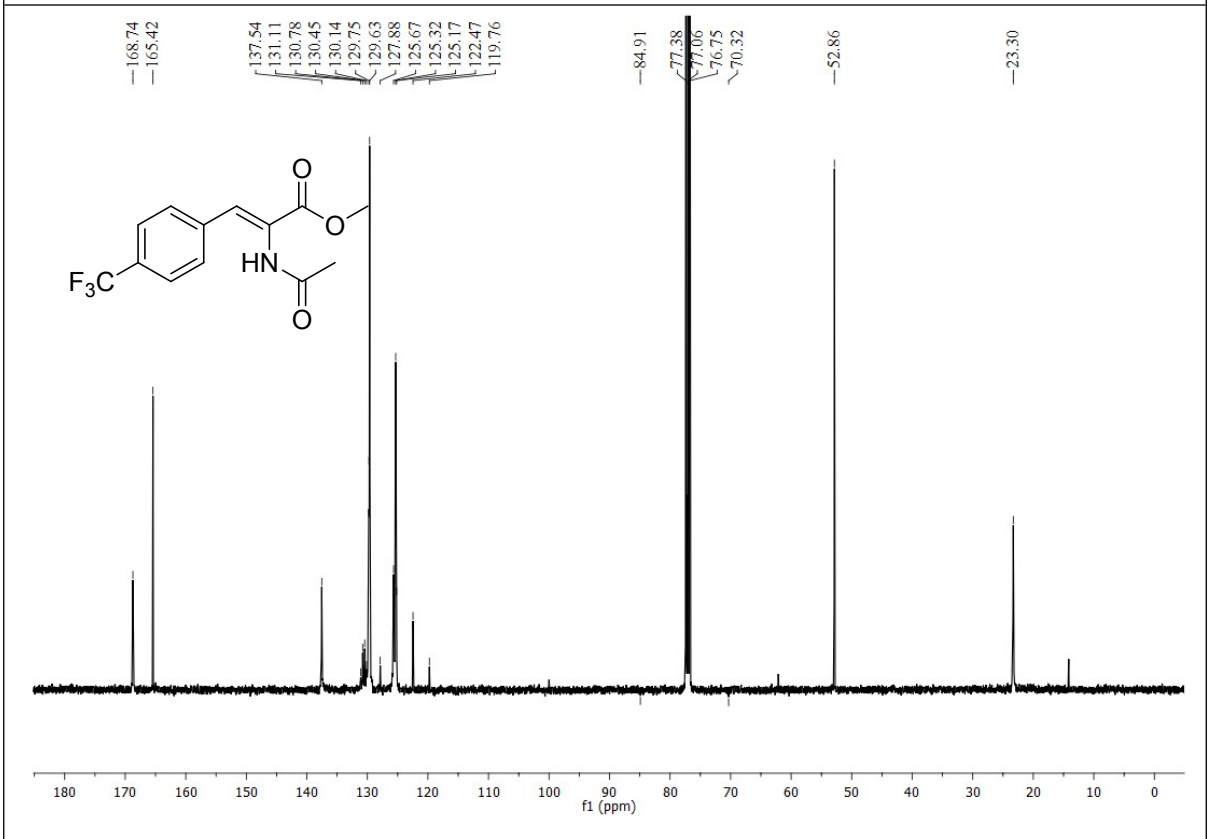
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **10p**



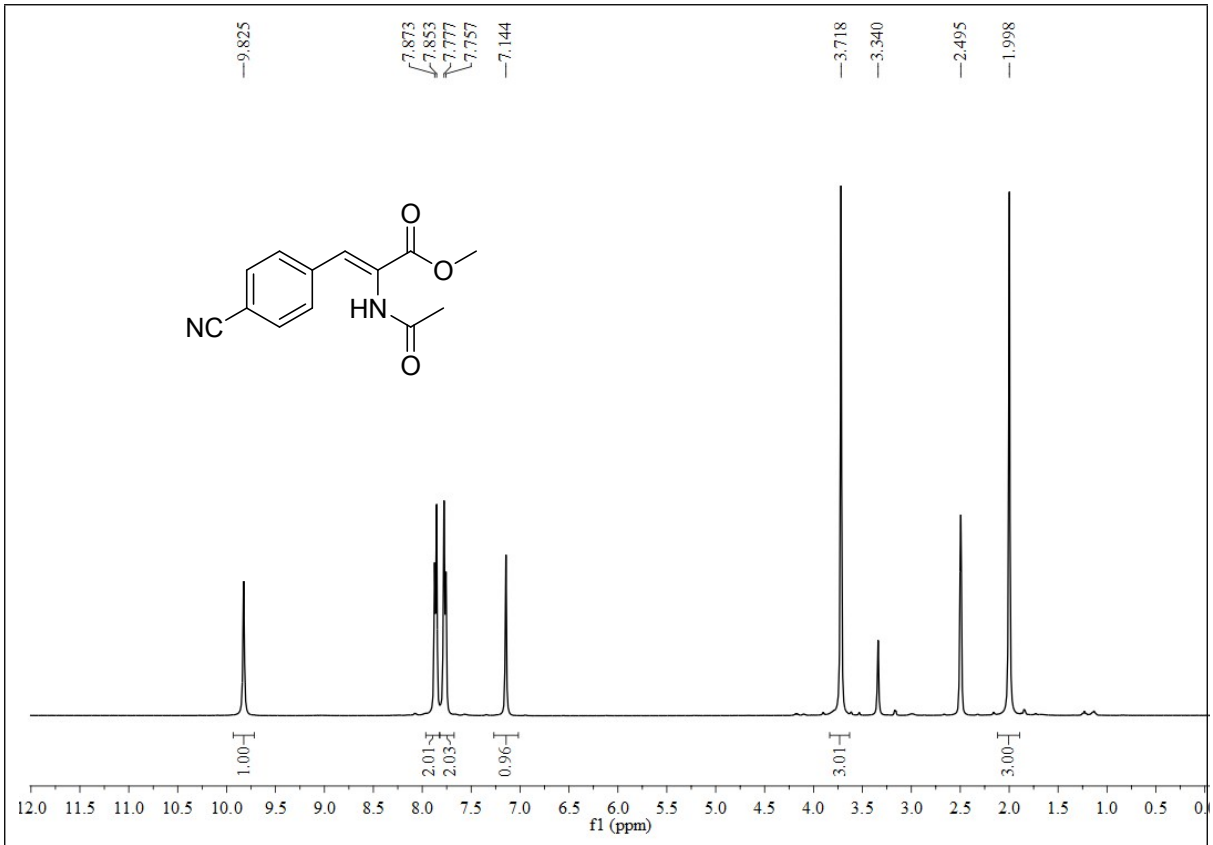
^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) spectrum of compound **10p**



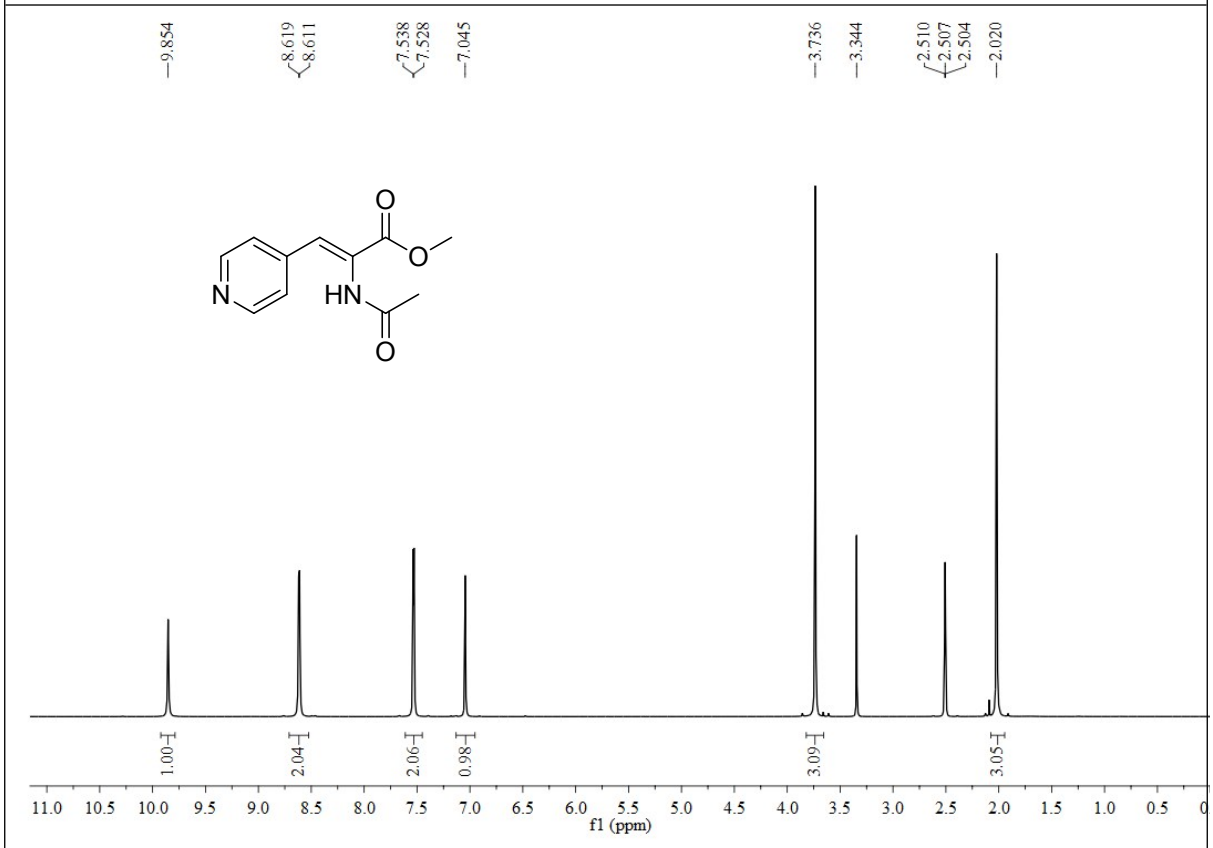
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10s**



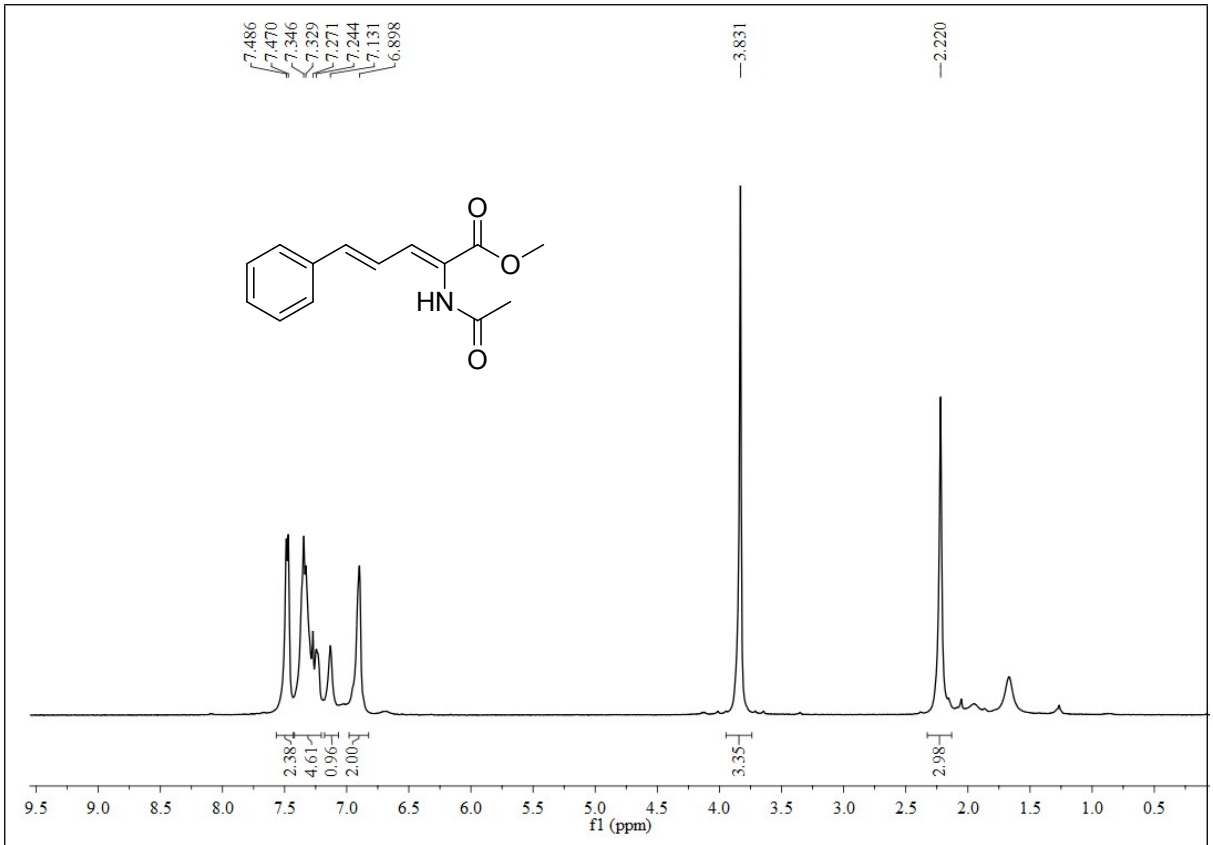
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) spectrum of compound **10s**



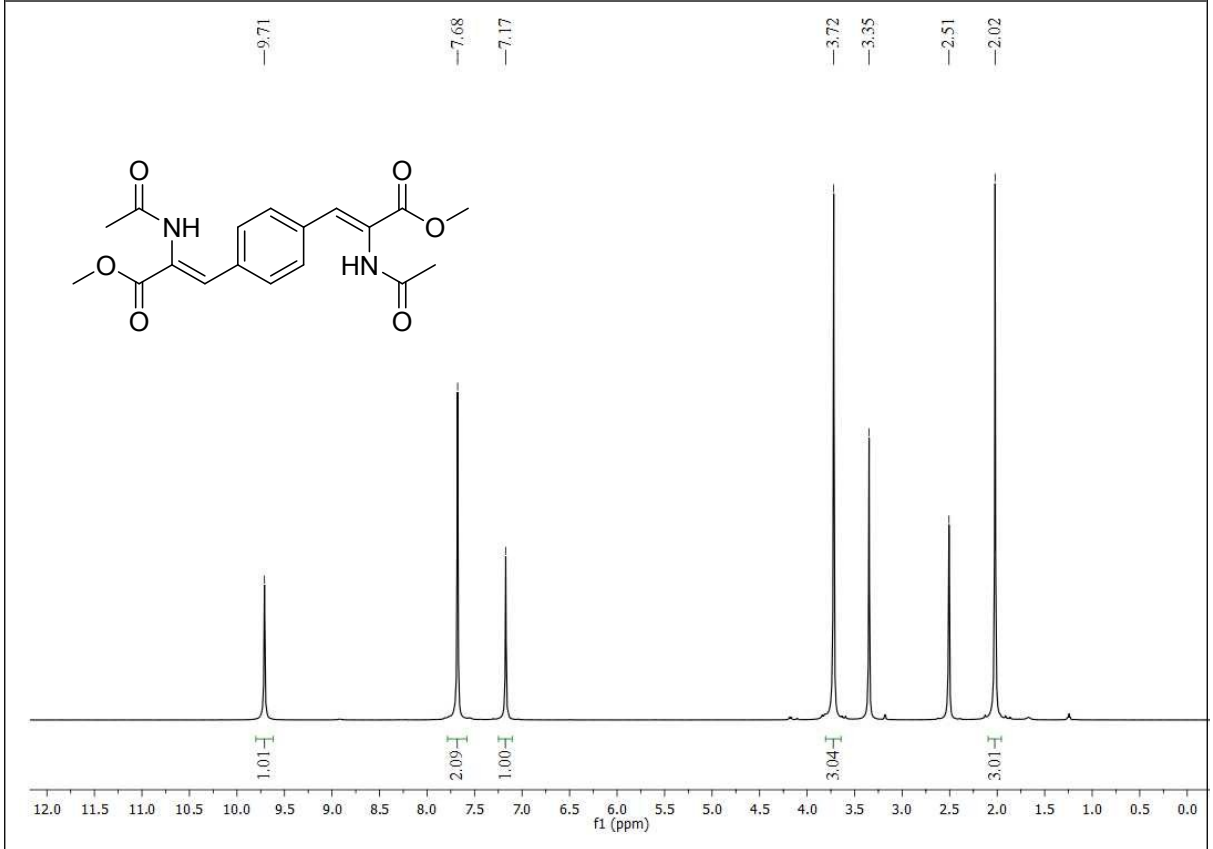
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **10t**



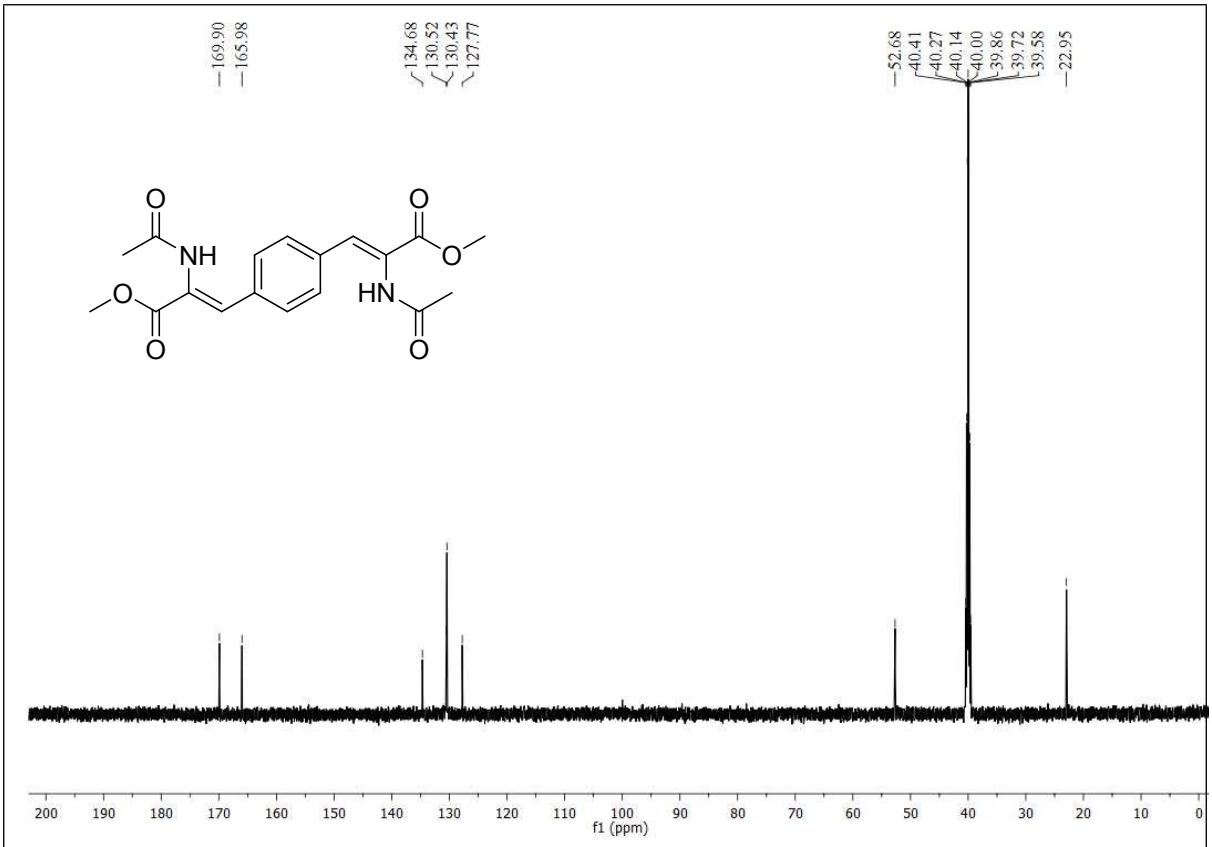
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **10u**



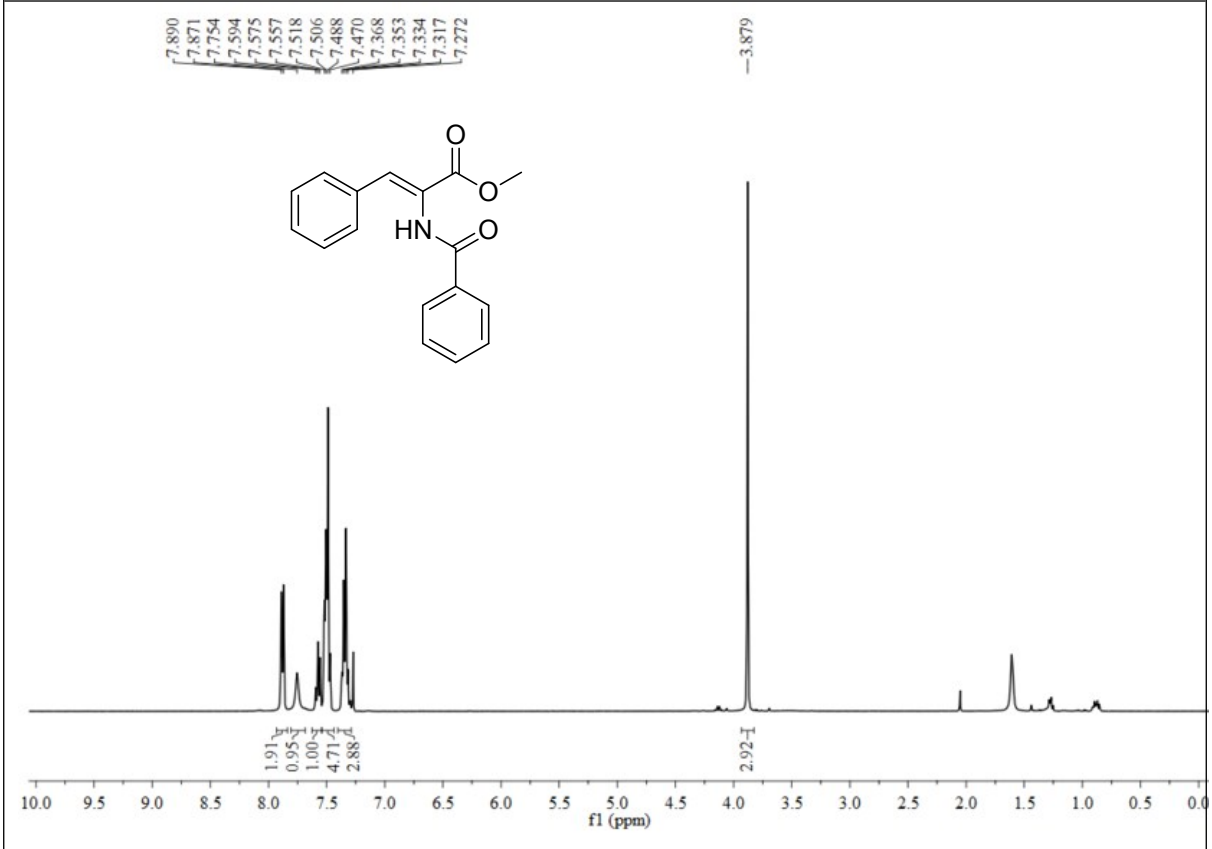
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **10w**



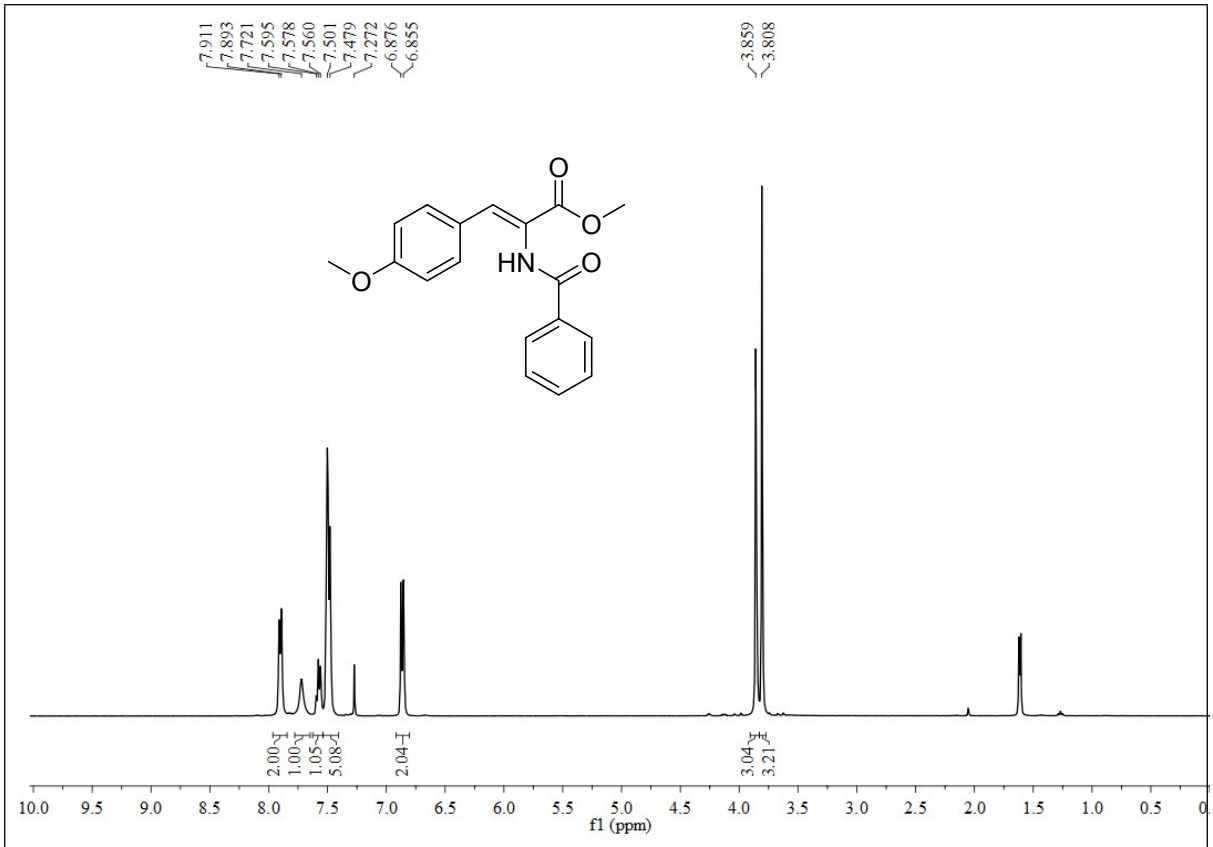
^{1}H NMR (DMSO-d_6, 600 MHz) spectrum of compound **10x**



$^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 150 MHz) spectrum of compound **10x**

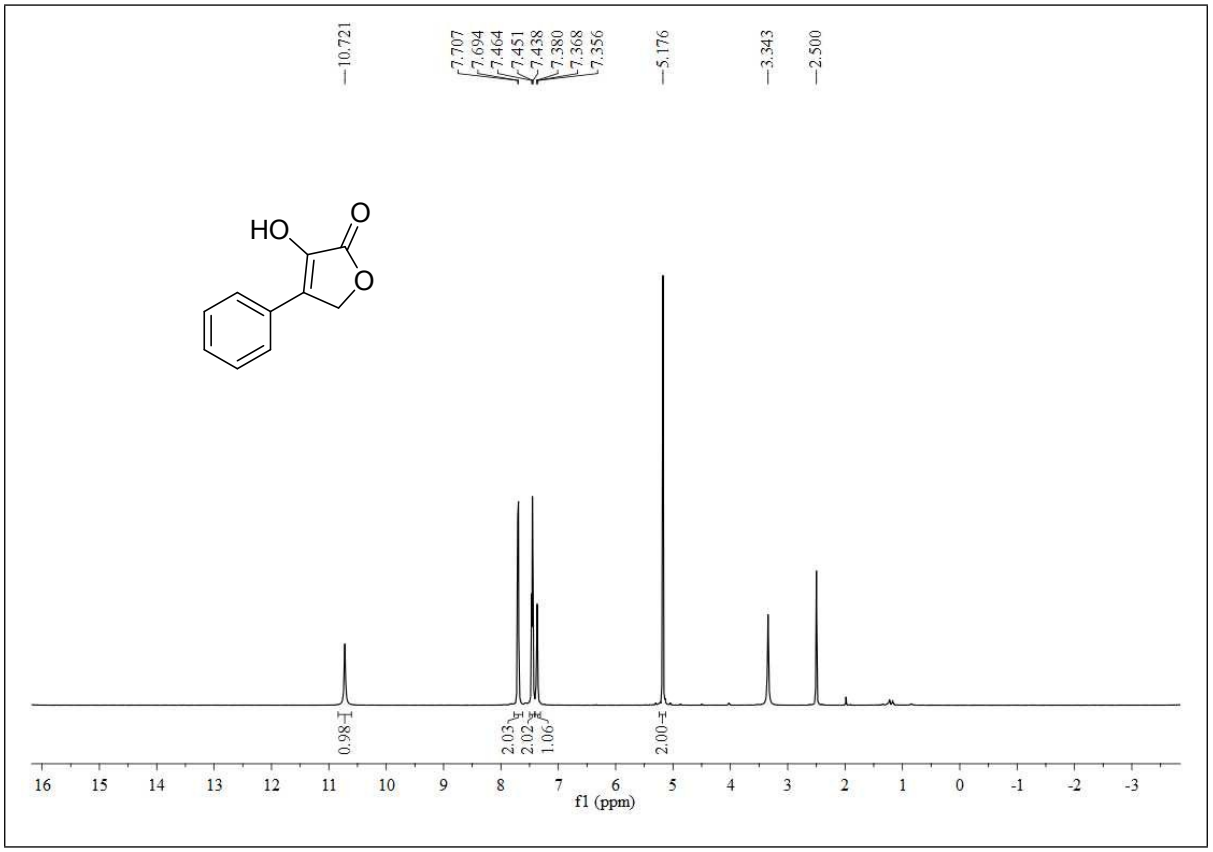


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **13a**

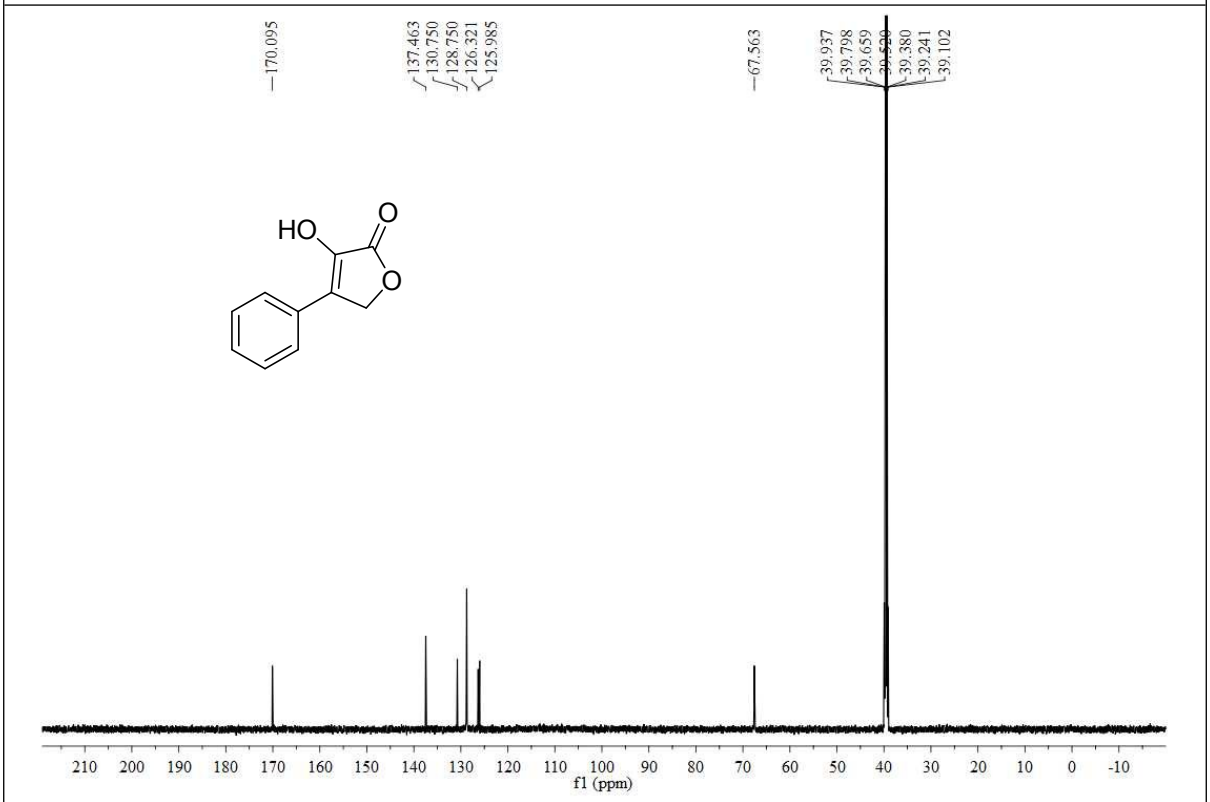


^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **13b**

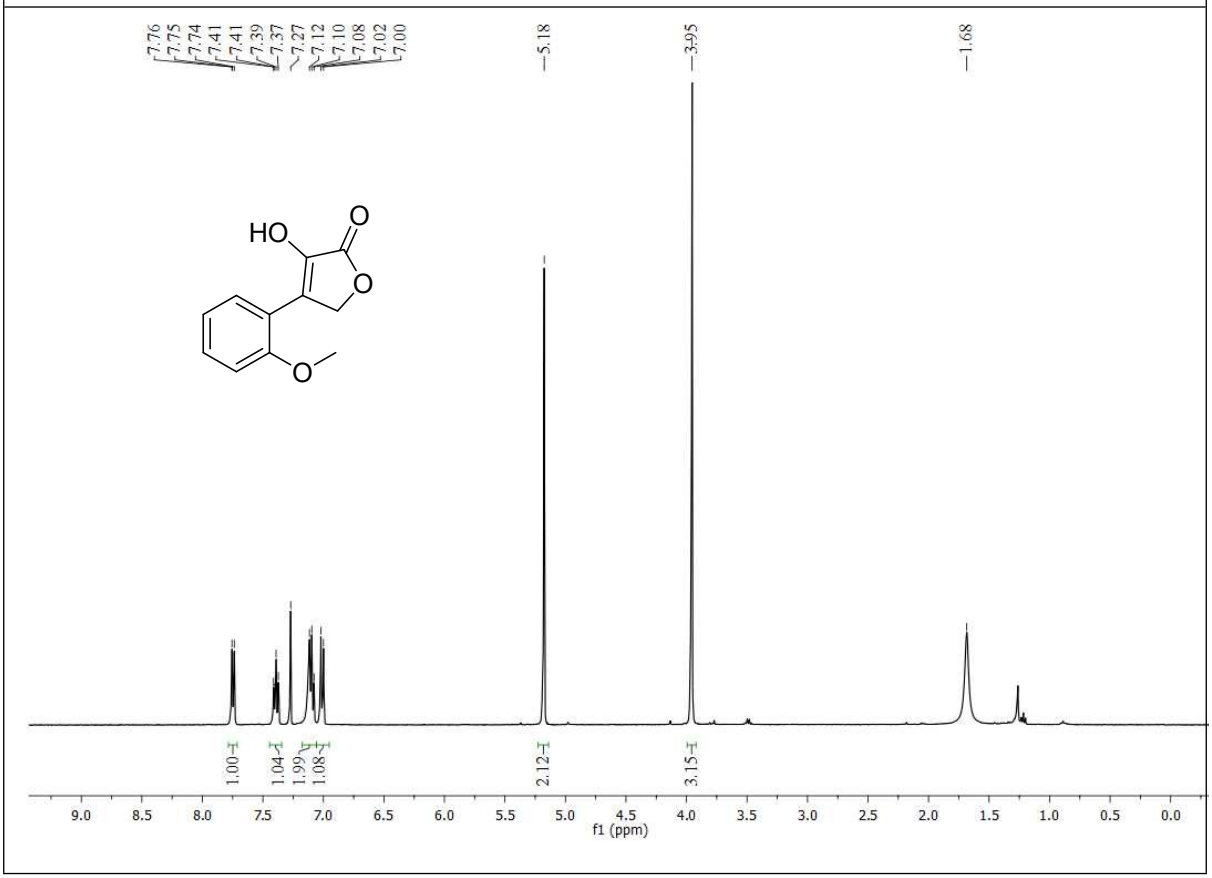
5. ^{1}H and ^{13}C NMR spectra of isotetronic acids:



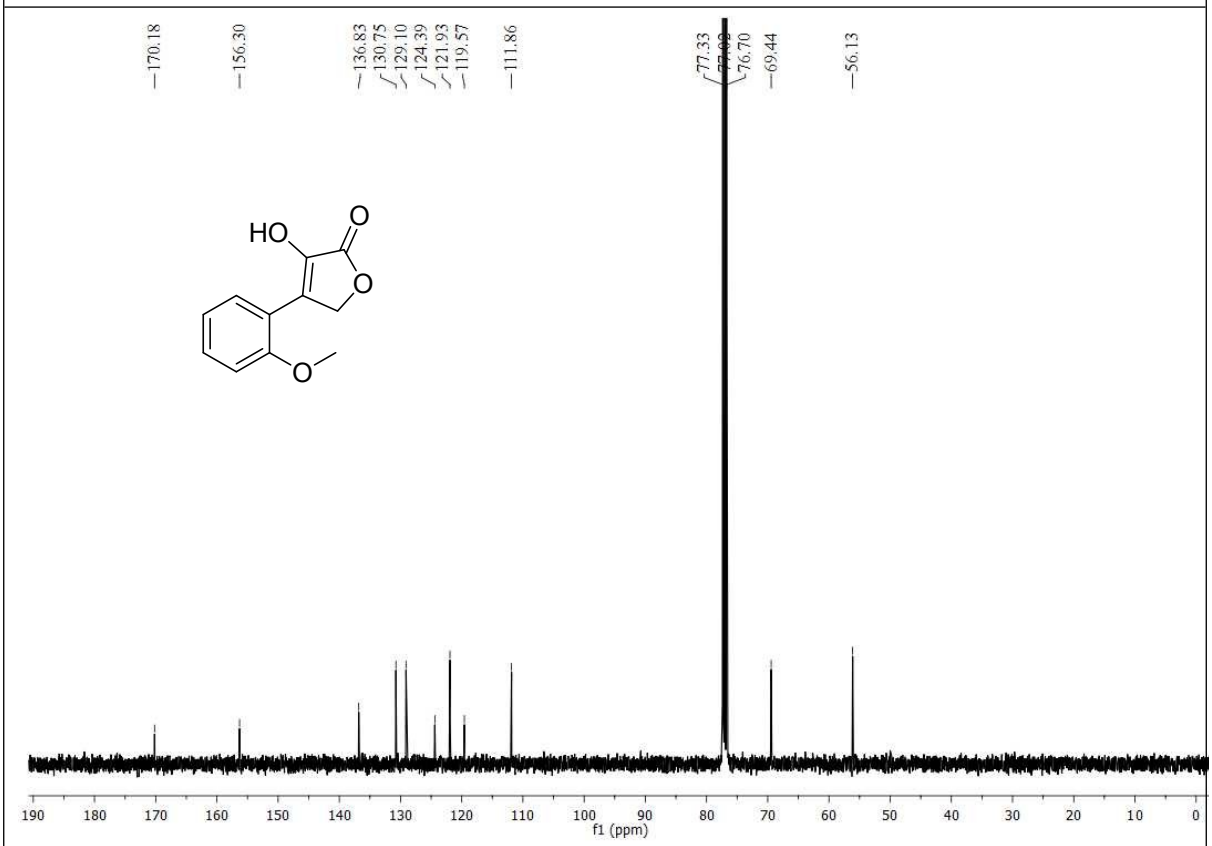
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9a**



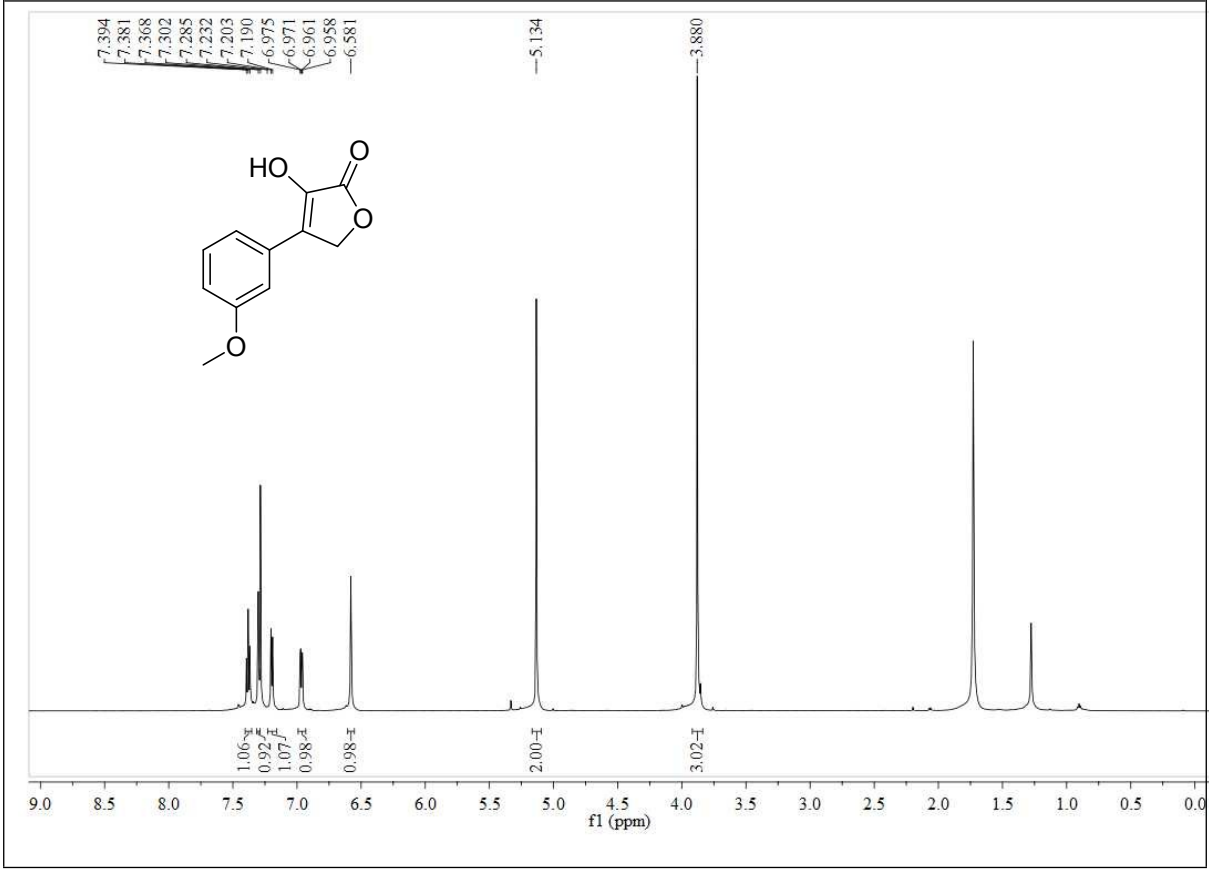
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9a**



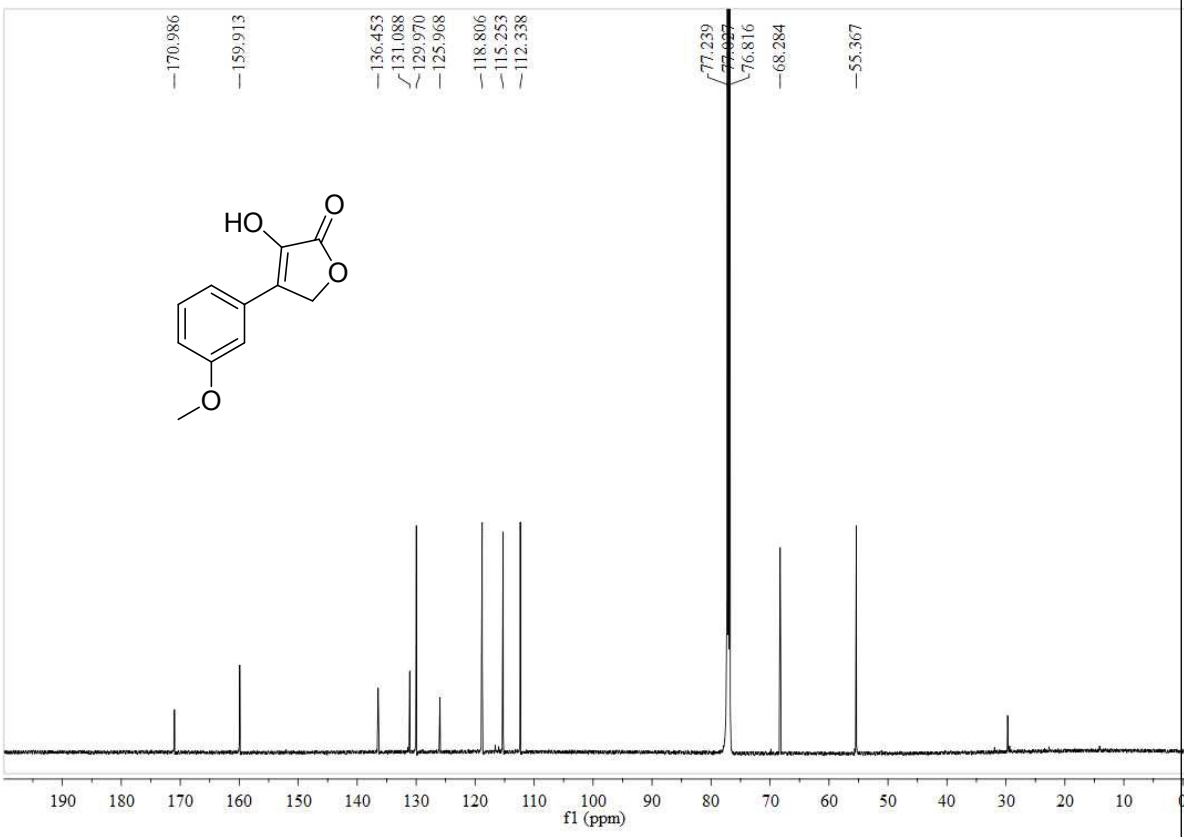
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9b**



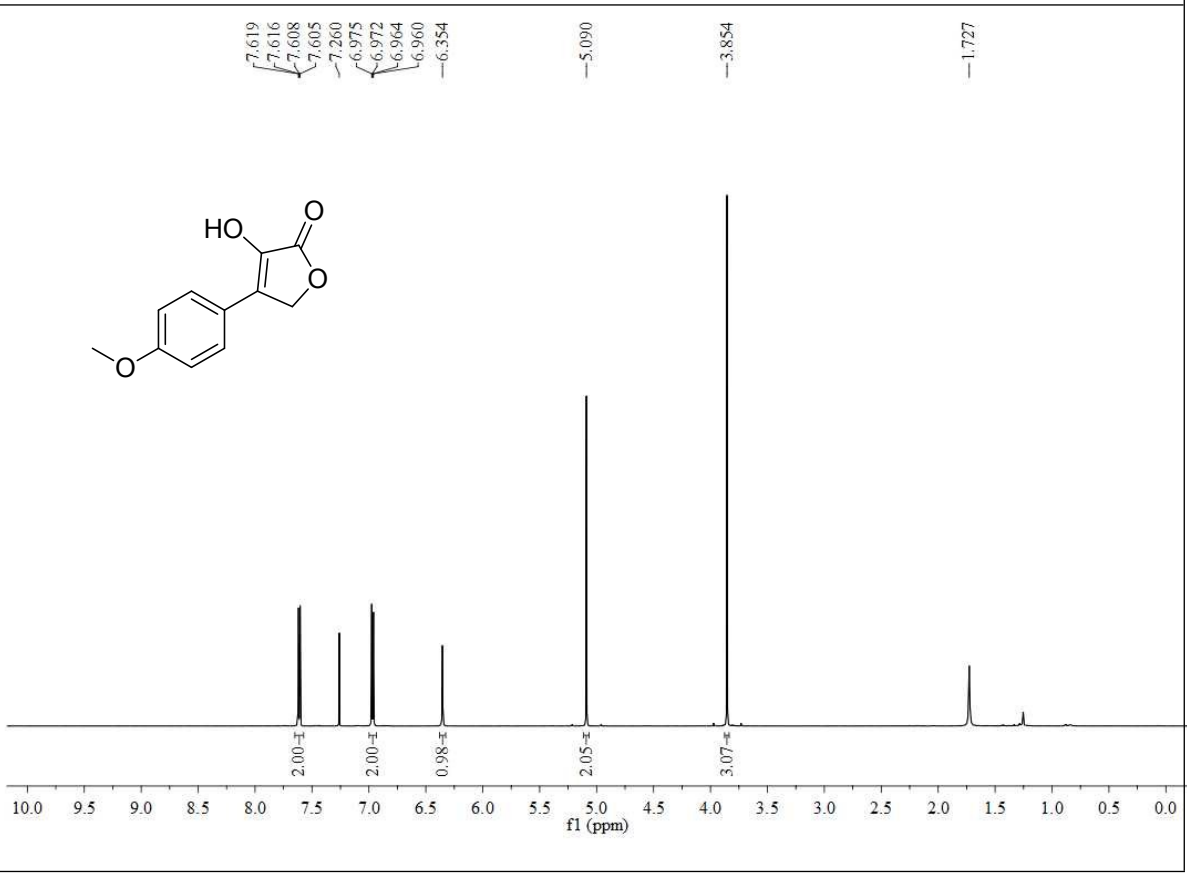
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **9b**



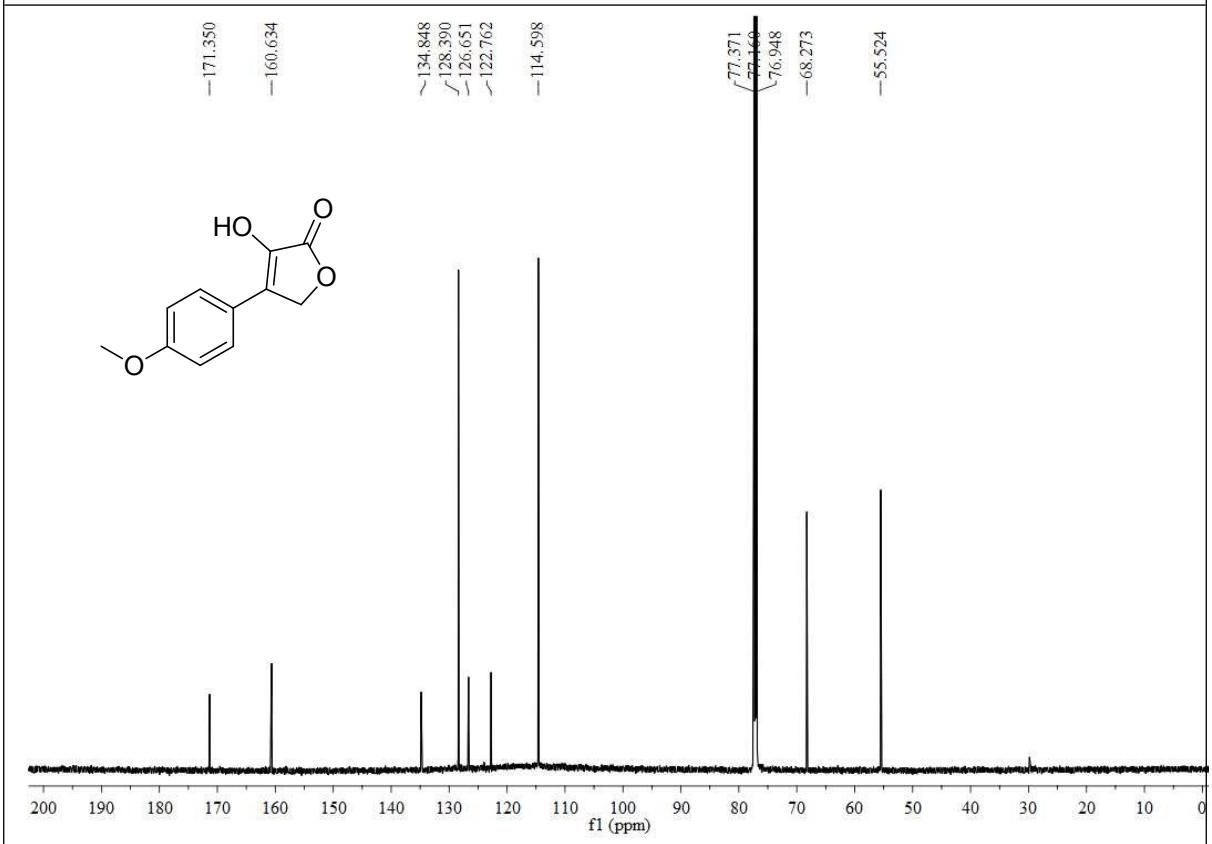
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **9c**



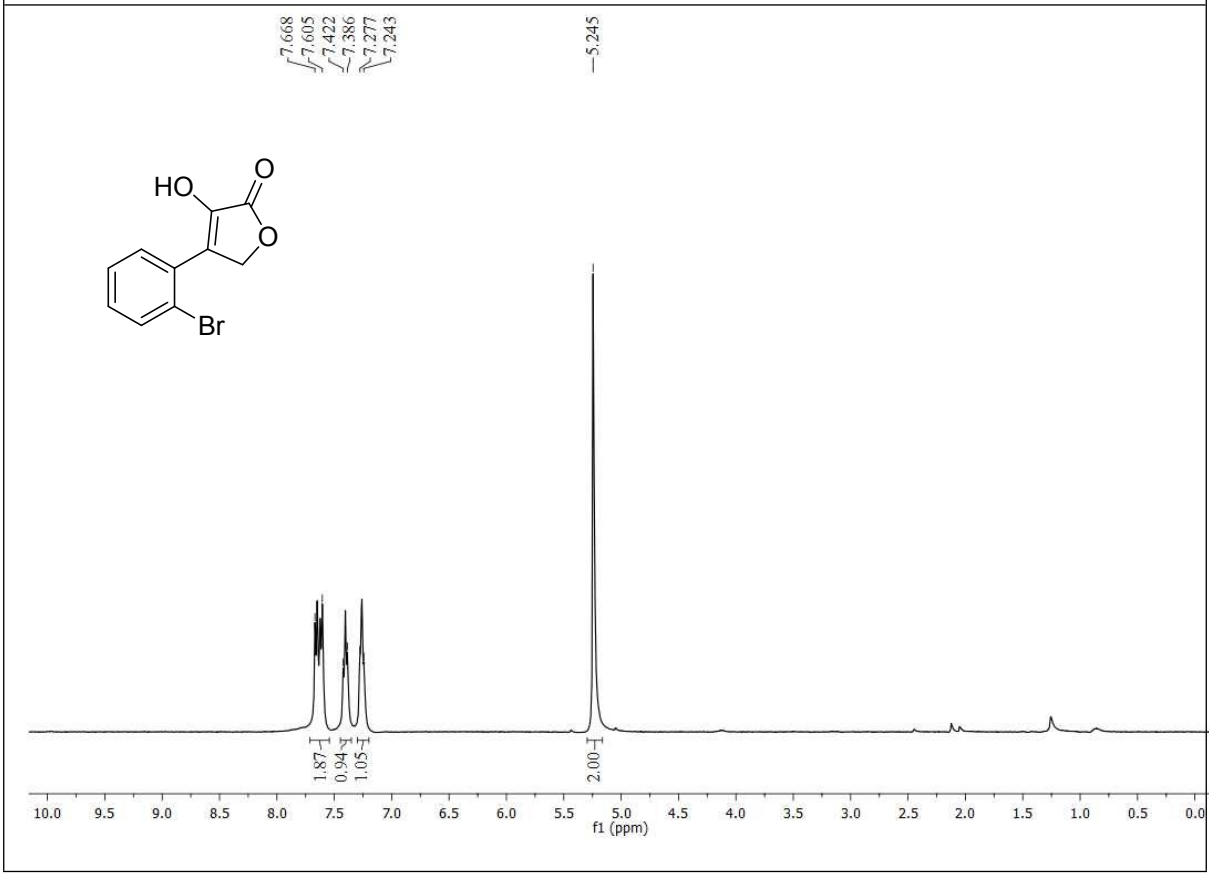
^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) spectrum of compound **9c**



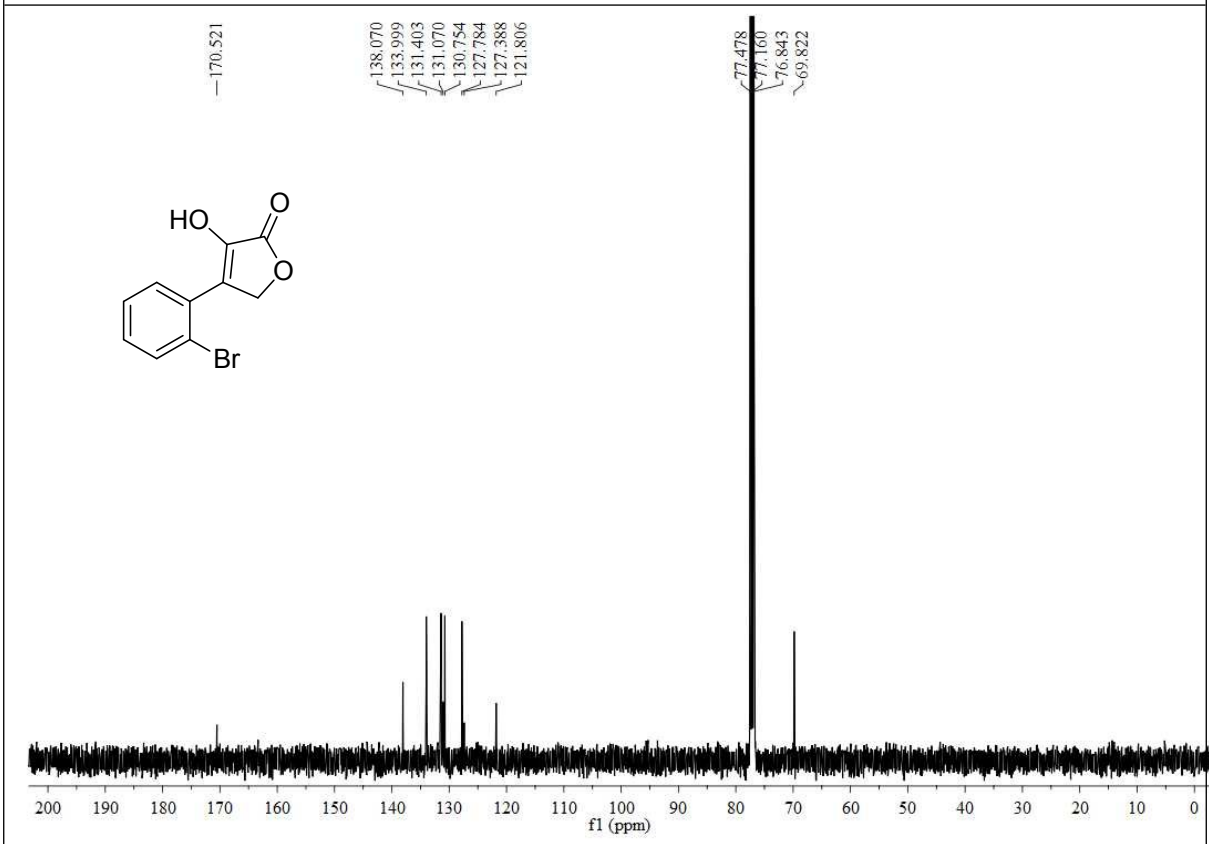
^{1}H NMR ($CDCl_3$, 600 MHz) spectrum of compound **9d**



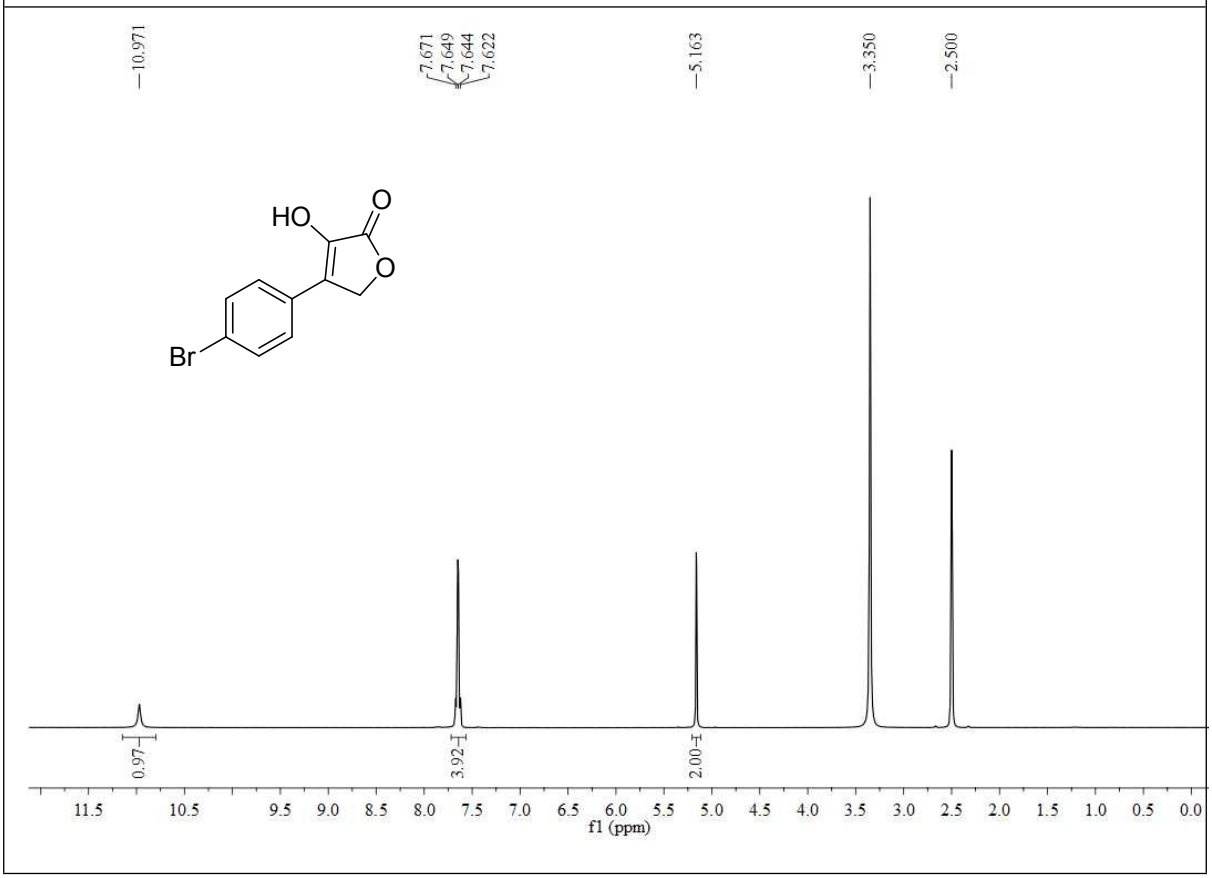
^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) spectrum of compound **9d**



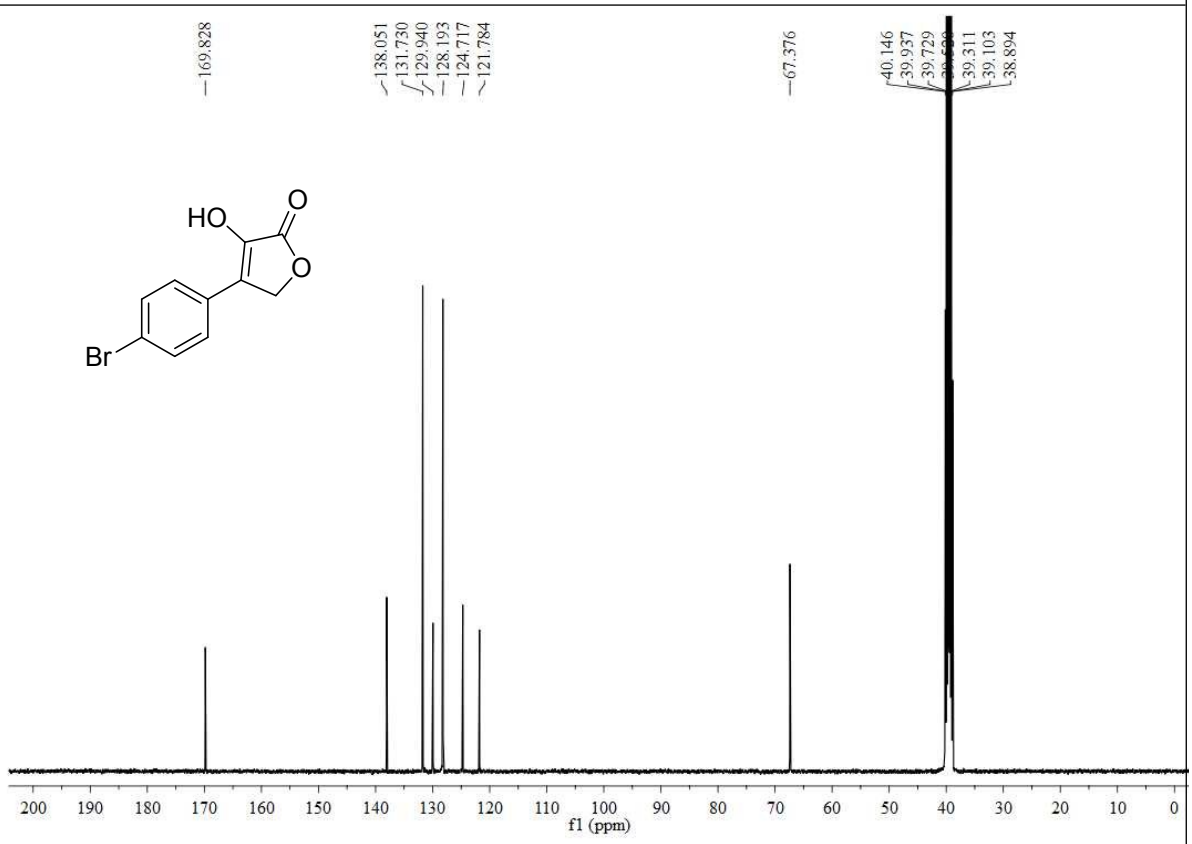
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9e**



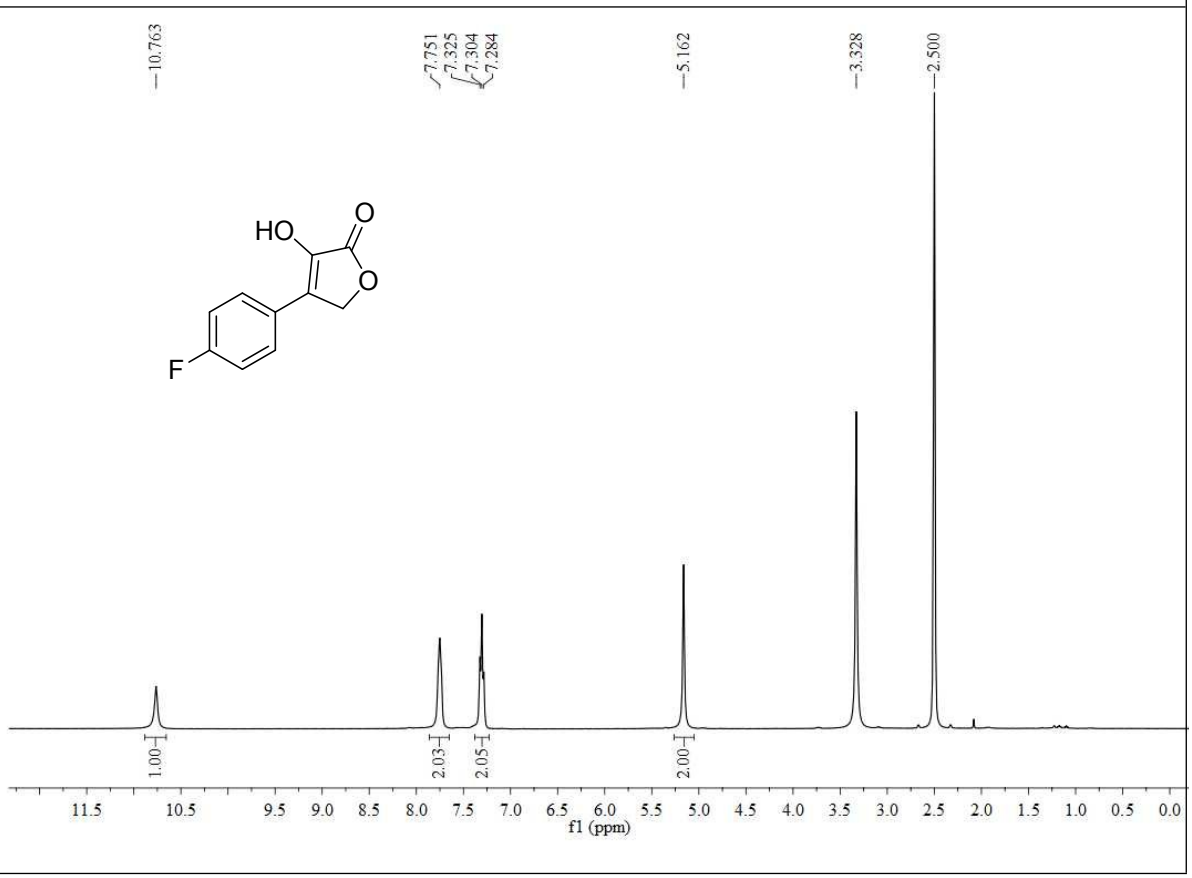
$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) spectrum of compound **9e**



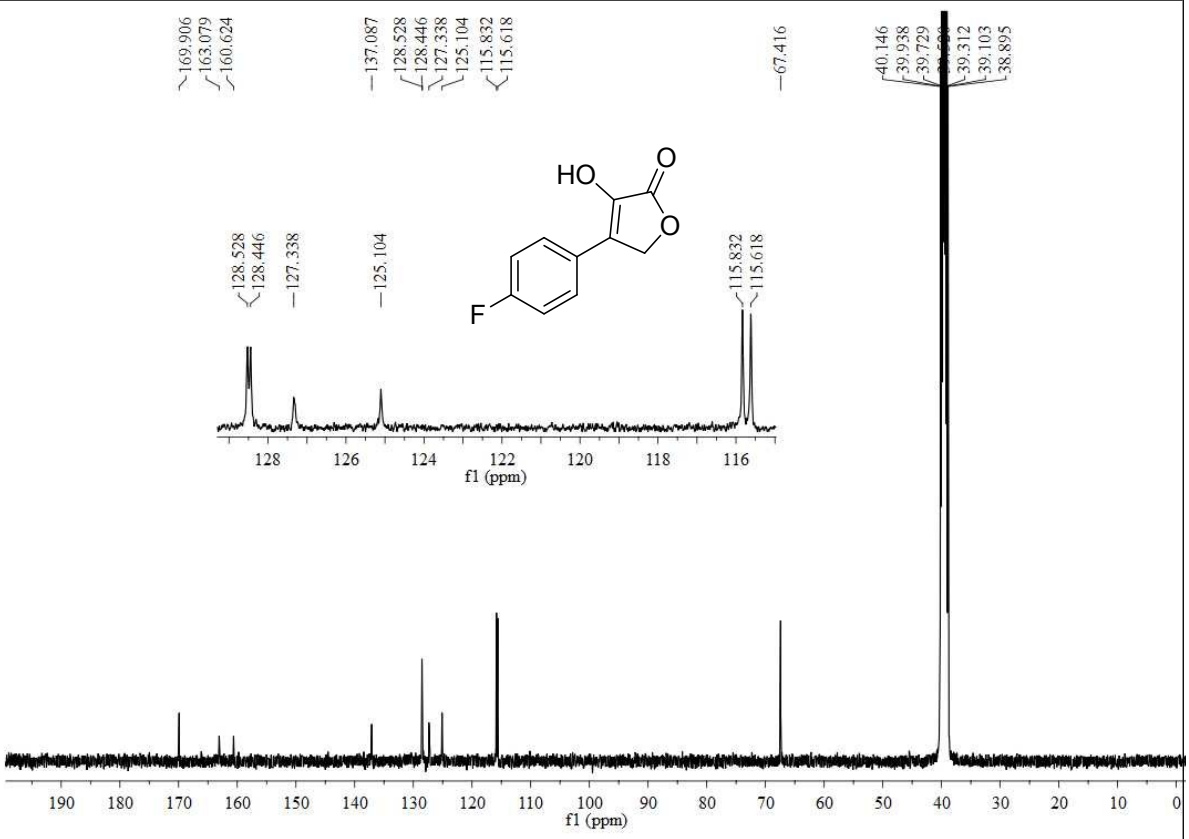
^{1}H NMR (DMSO-d_6, 600 MHz) spectrum of compound **9f**



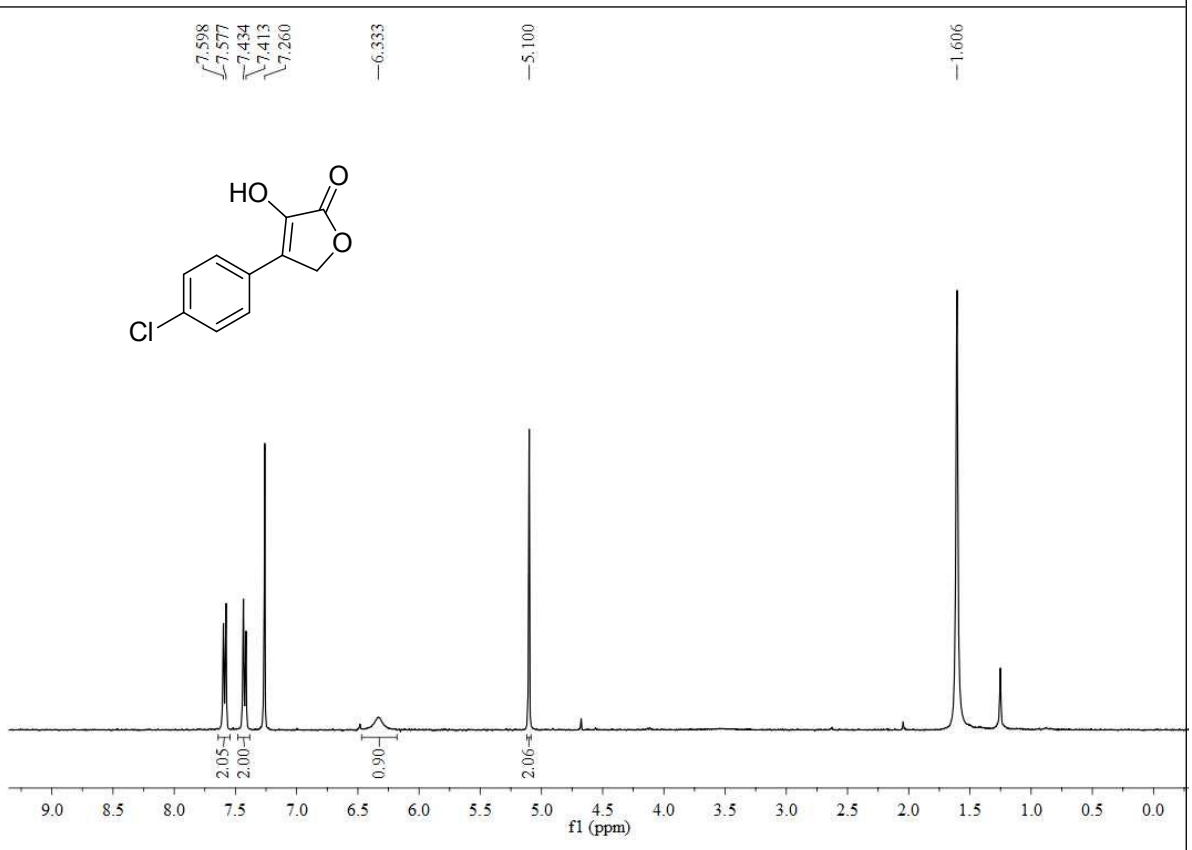
^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz) spectrum of compound **9f**



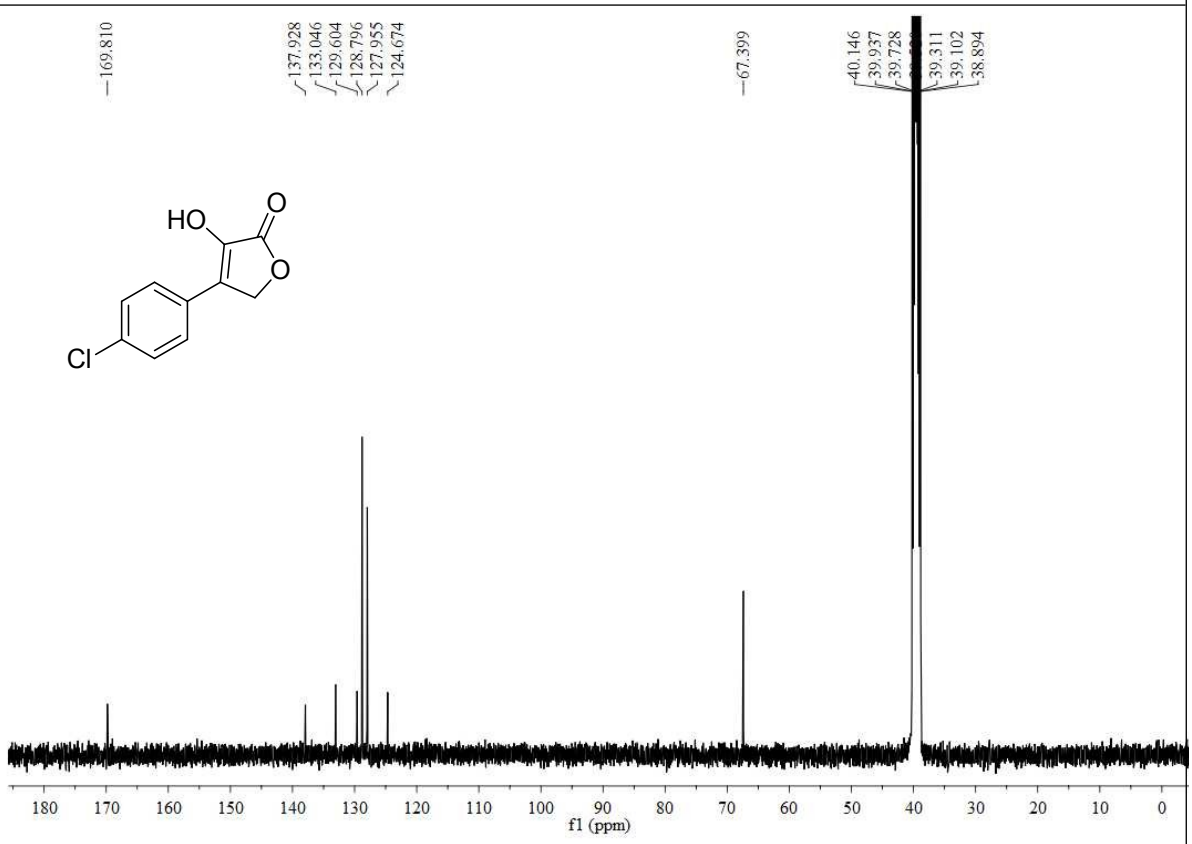
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9g**



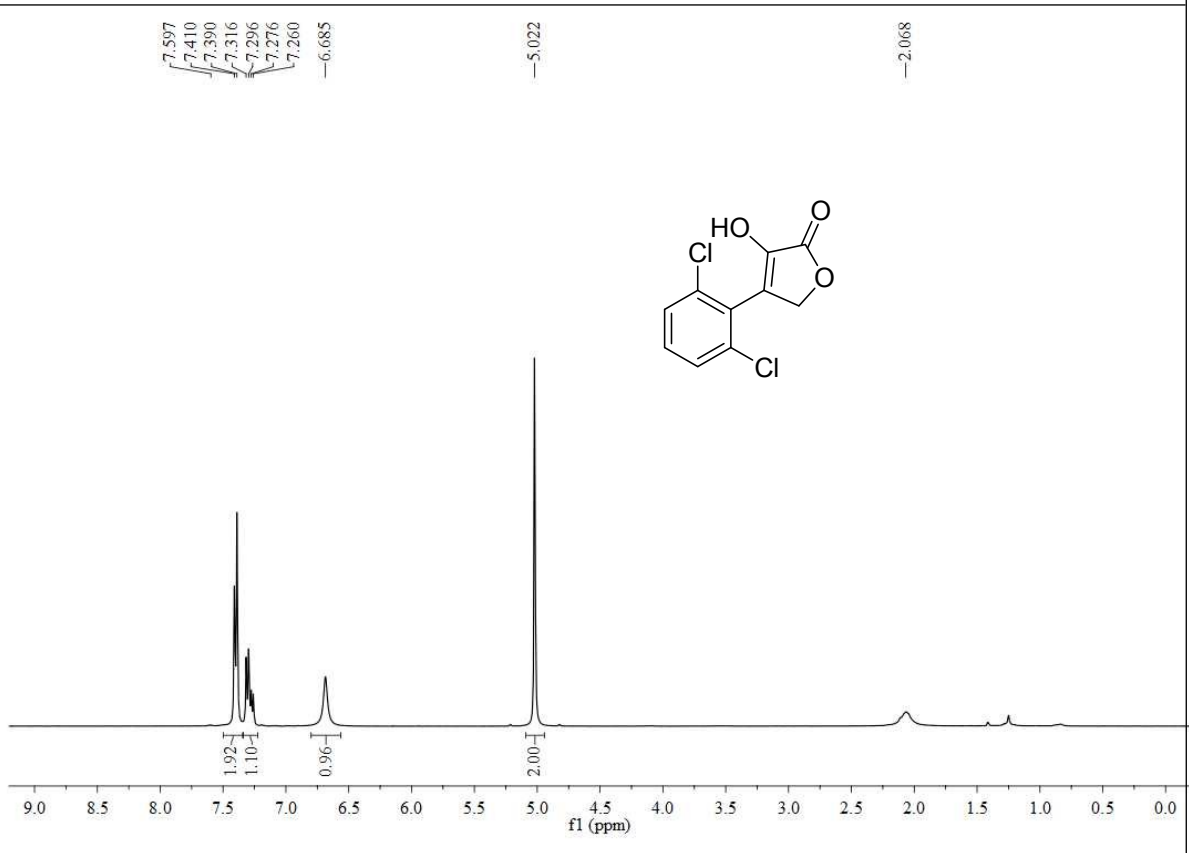
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9g**



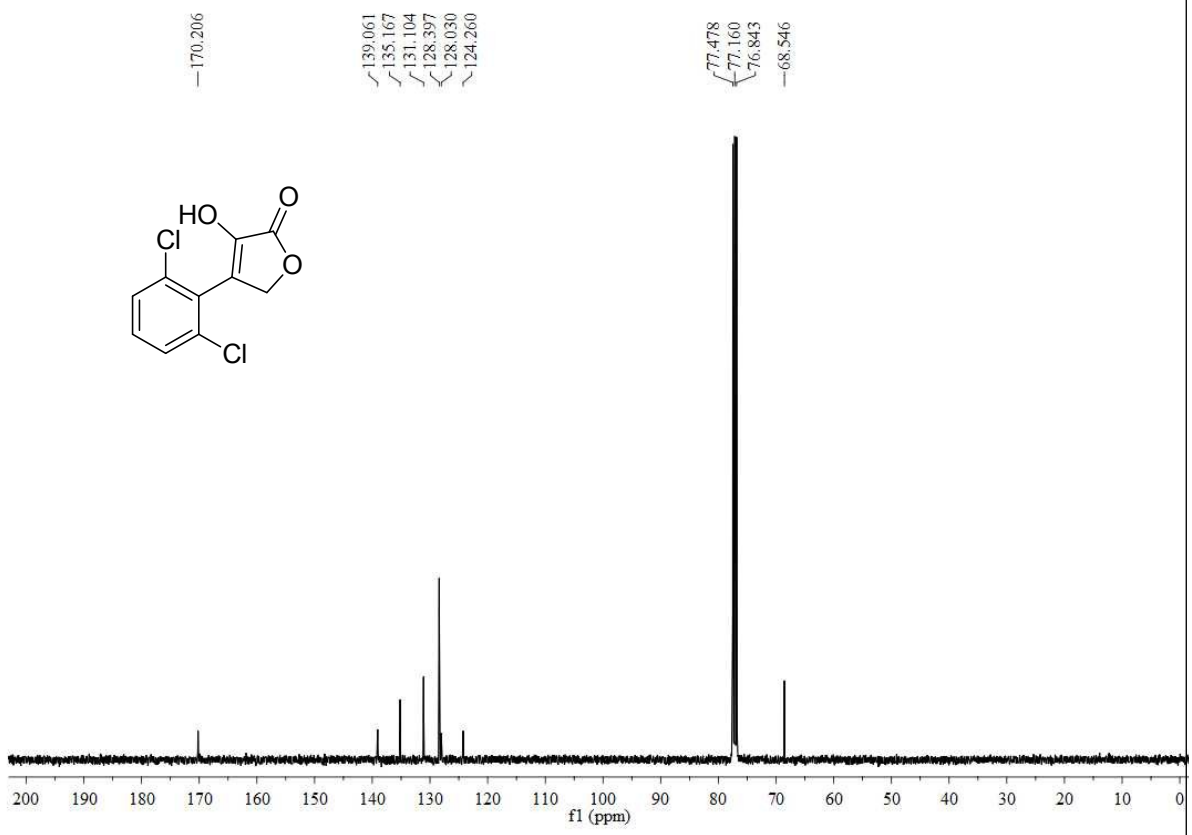
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9h**



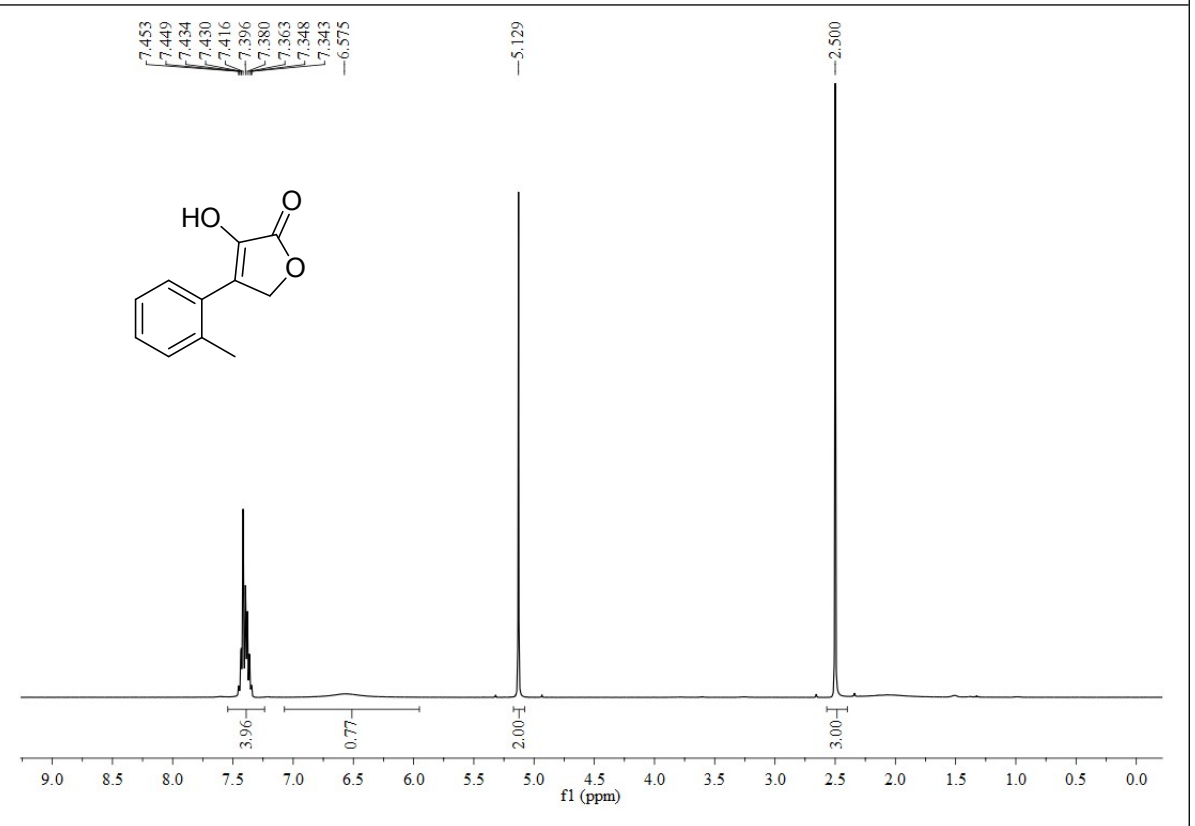
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **9h**



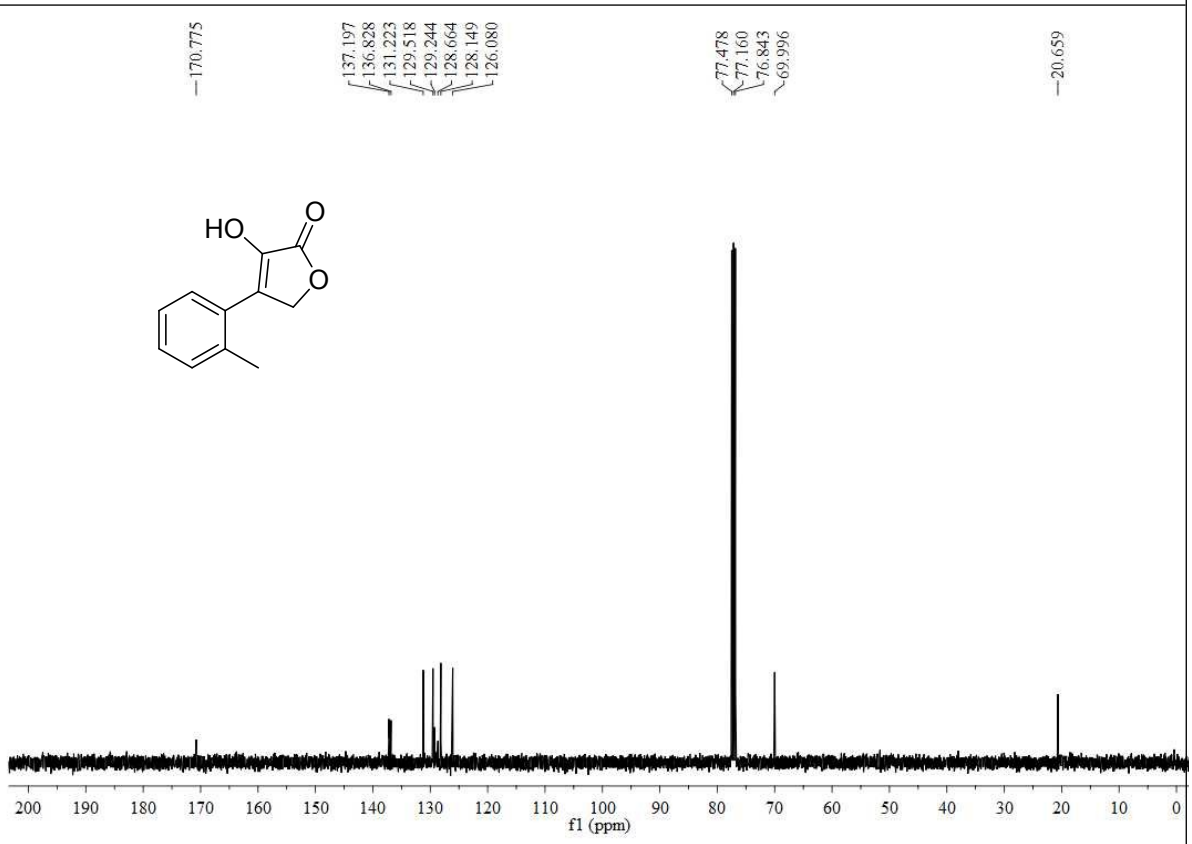
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9i**



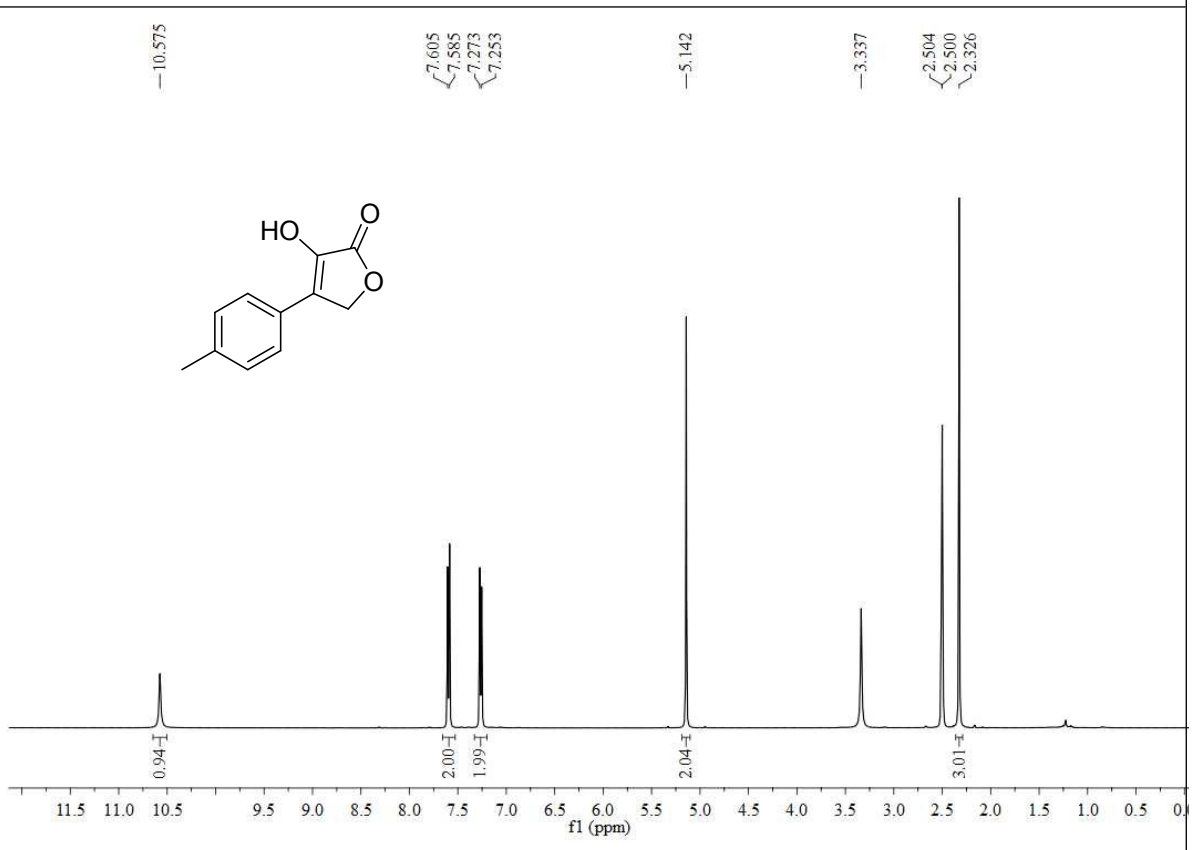
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **9i**



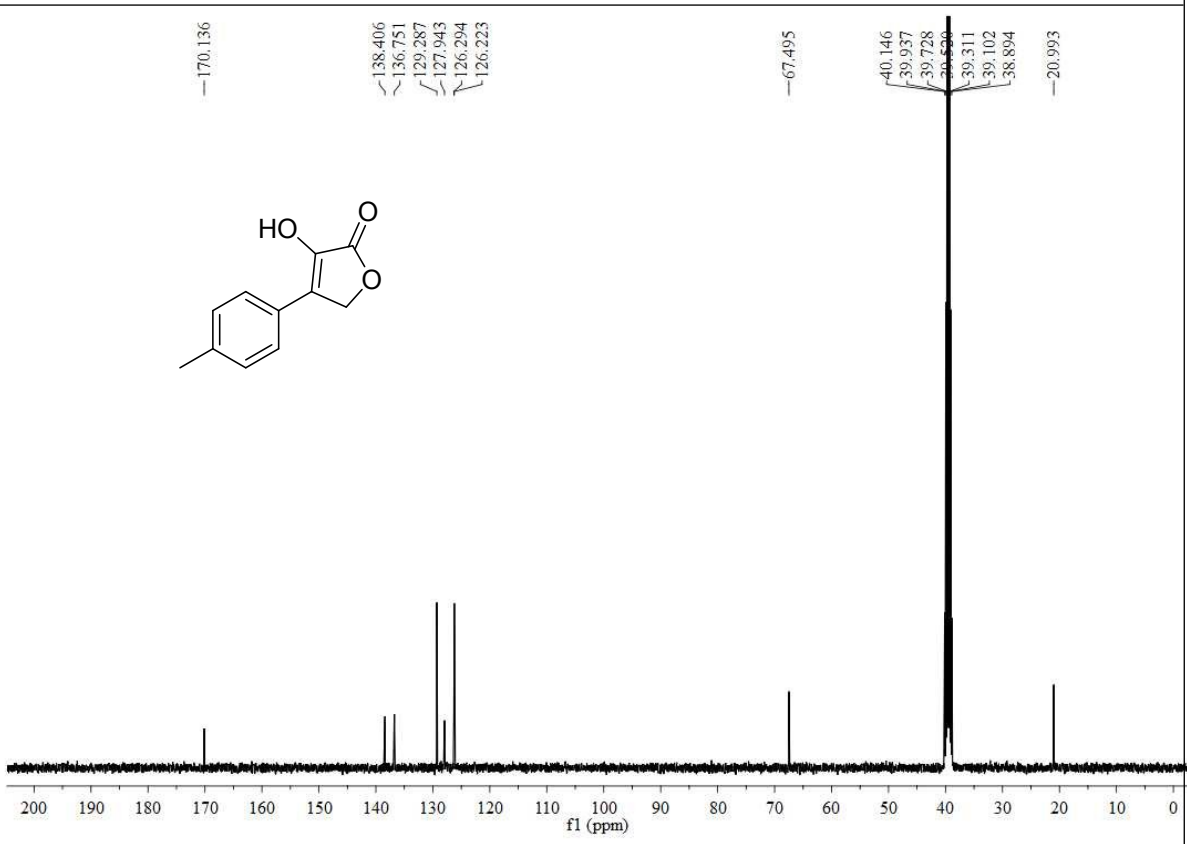
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9j**



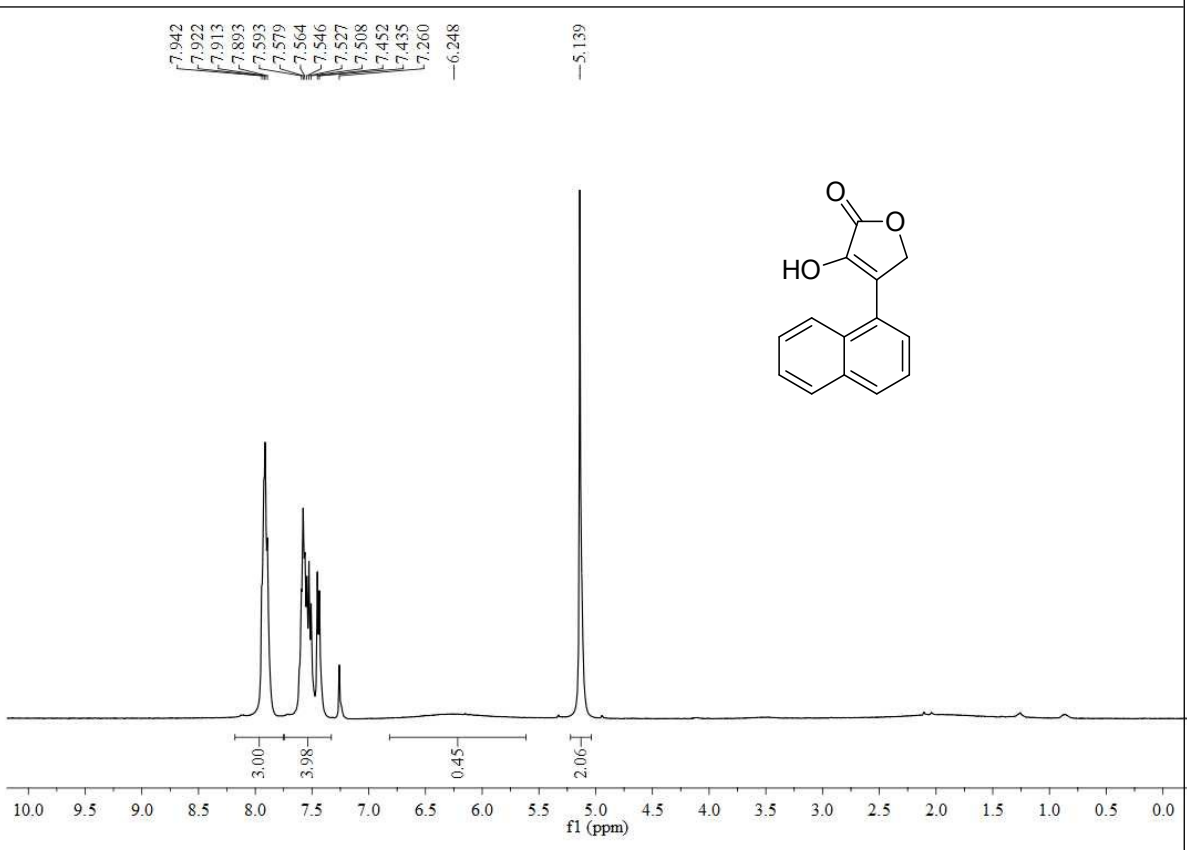
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **9j**



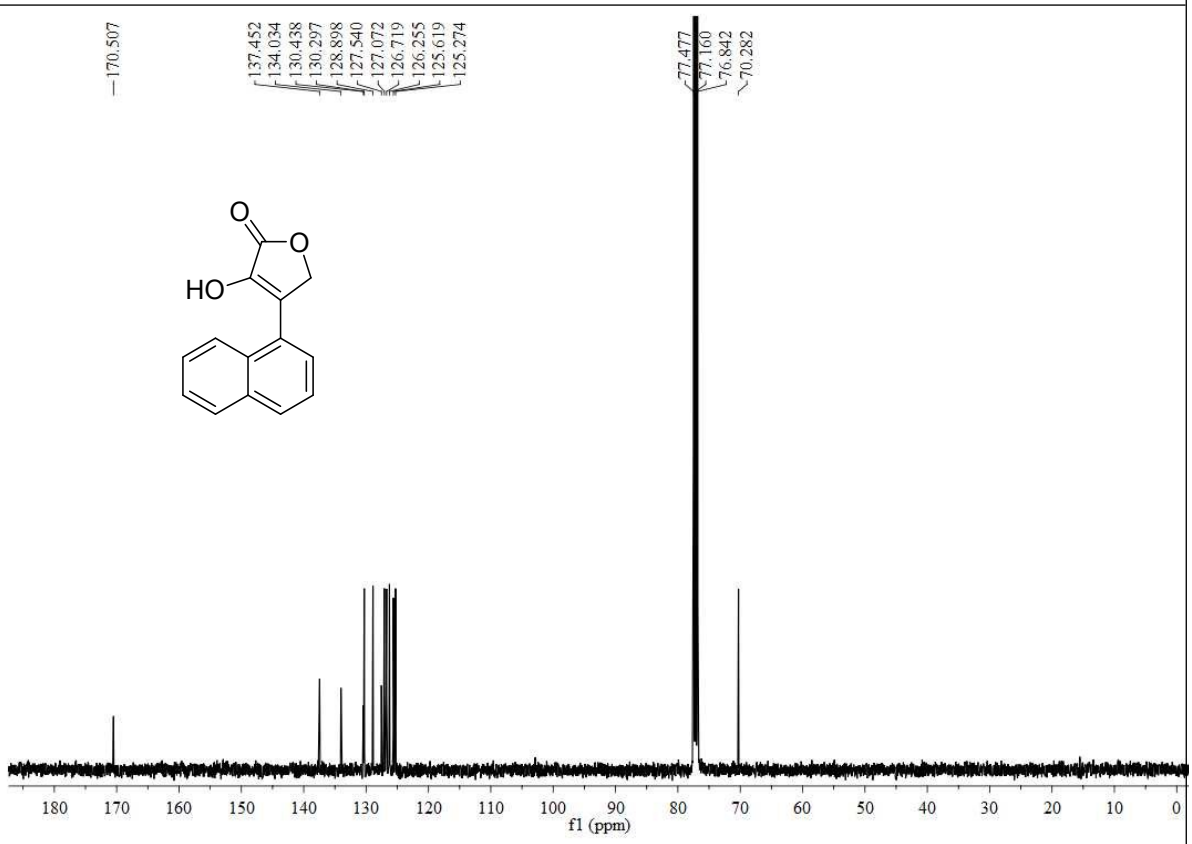
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9k**



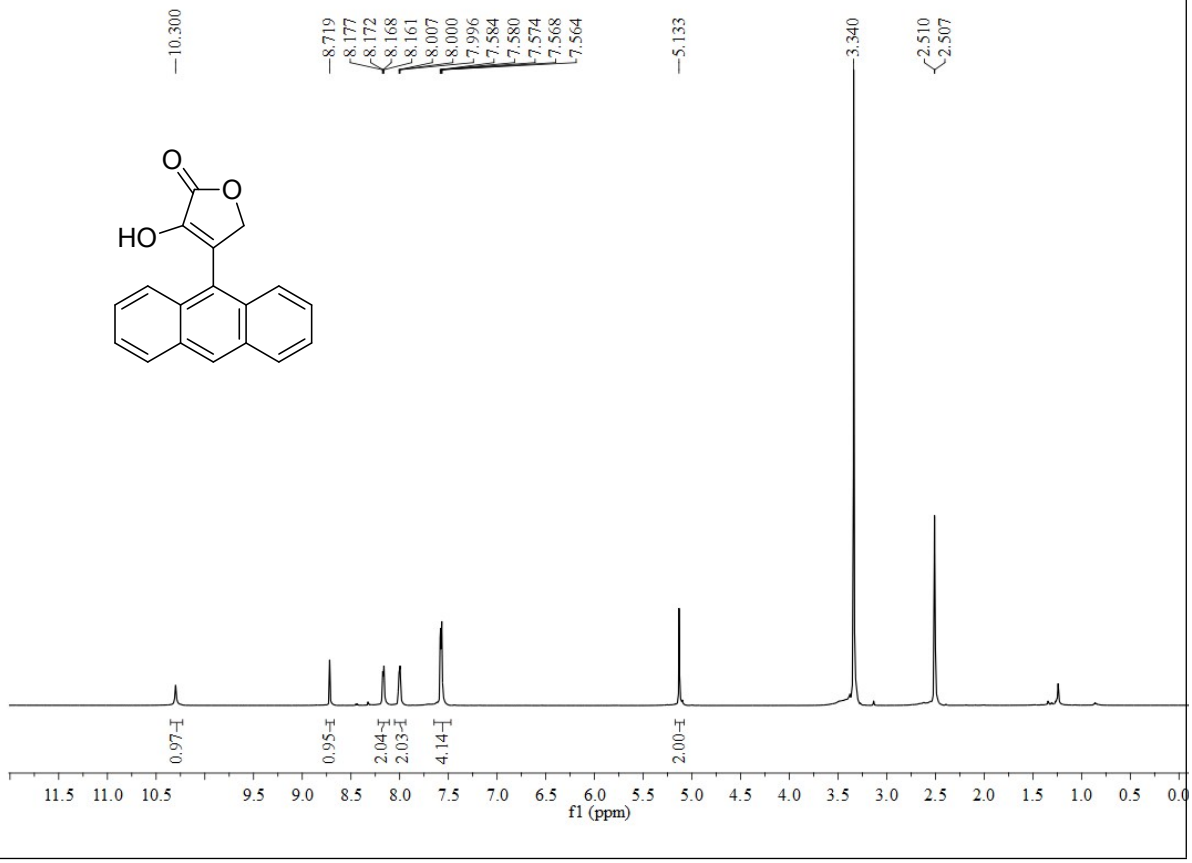
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9k**



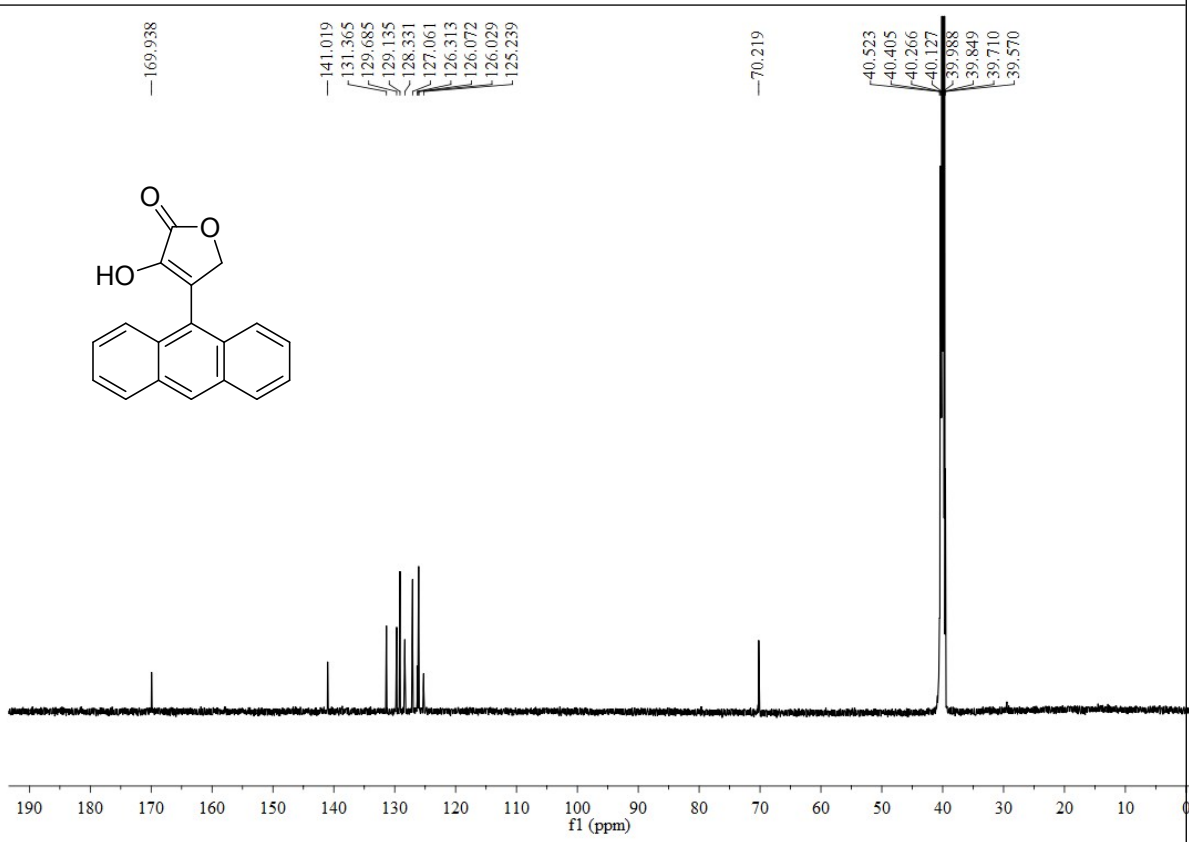
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9l**



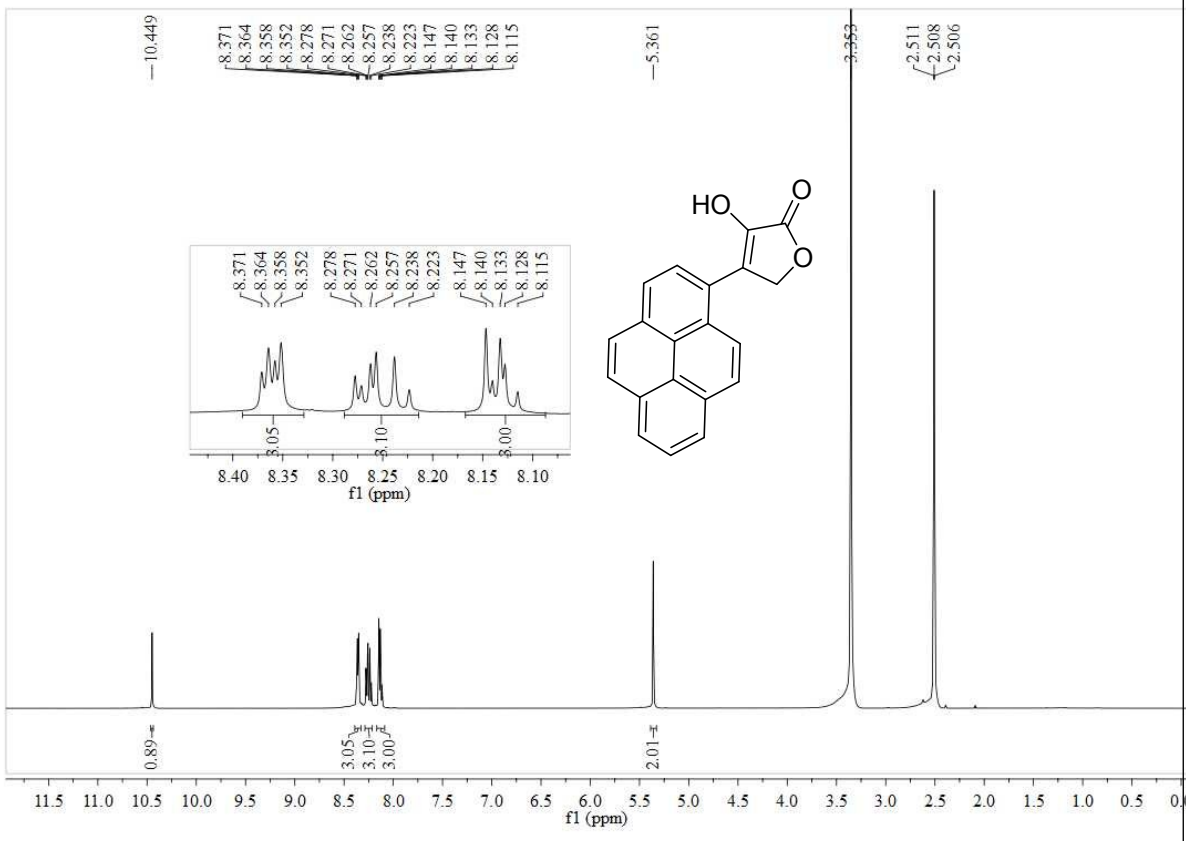
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **9l**



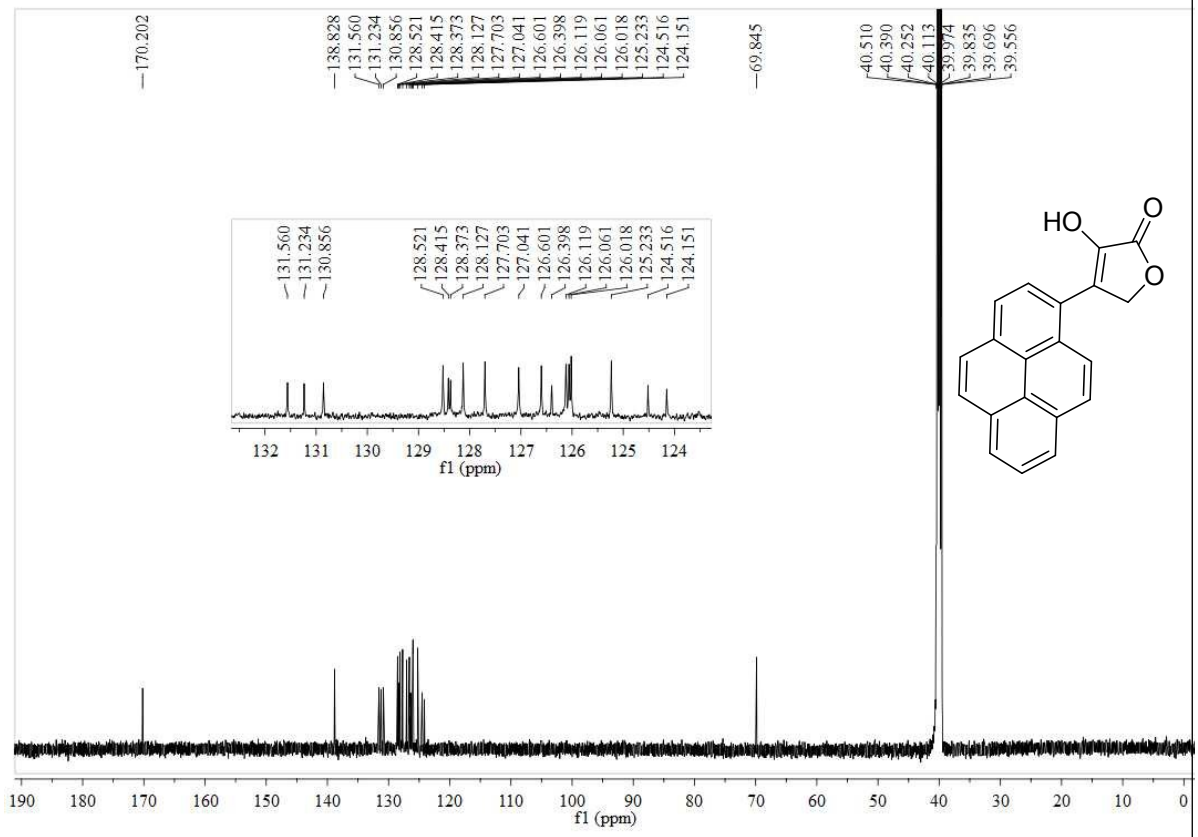
^{1}H NMR (DMSO-d_6, 600 MHz) spectrum of compound **9m**



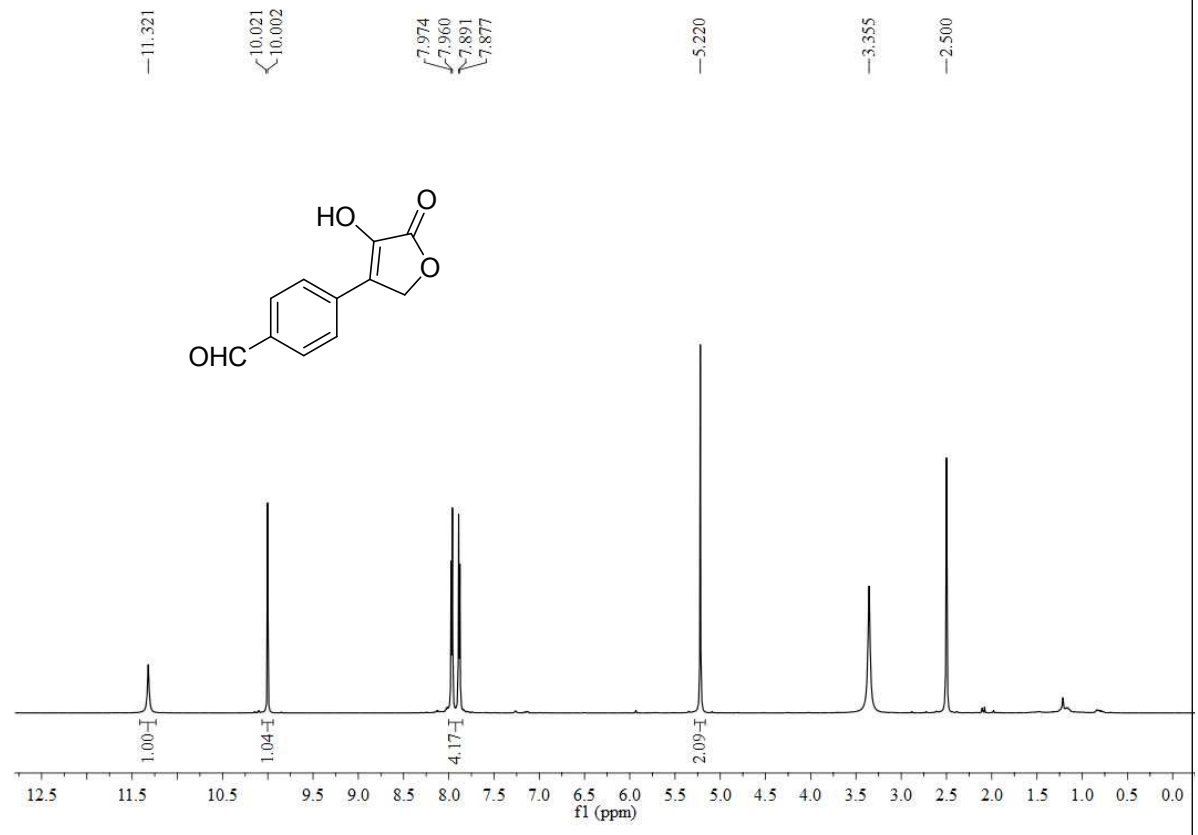
^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz) spectrum of compound **9m**



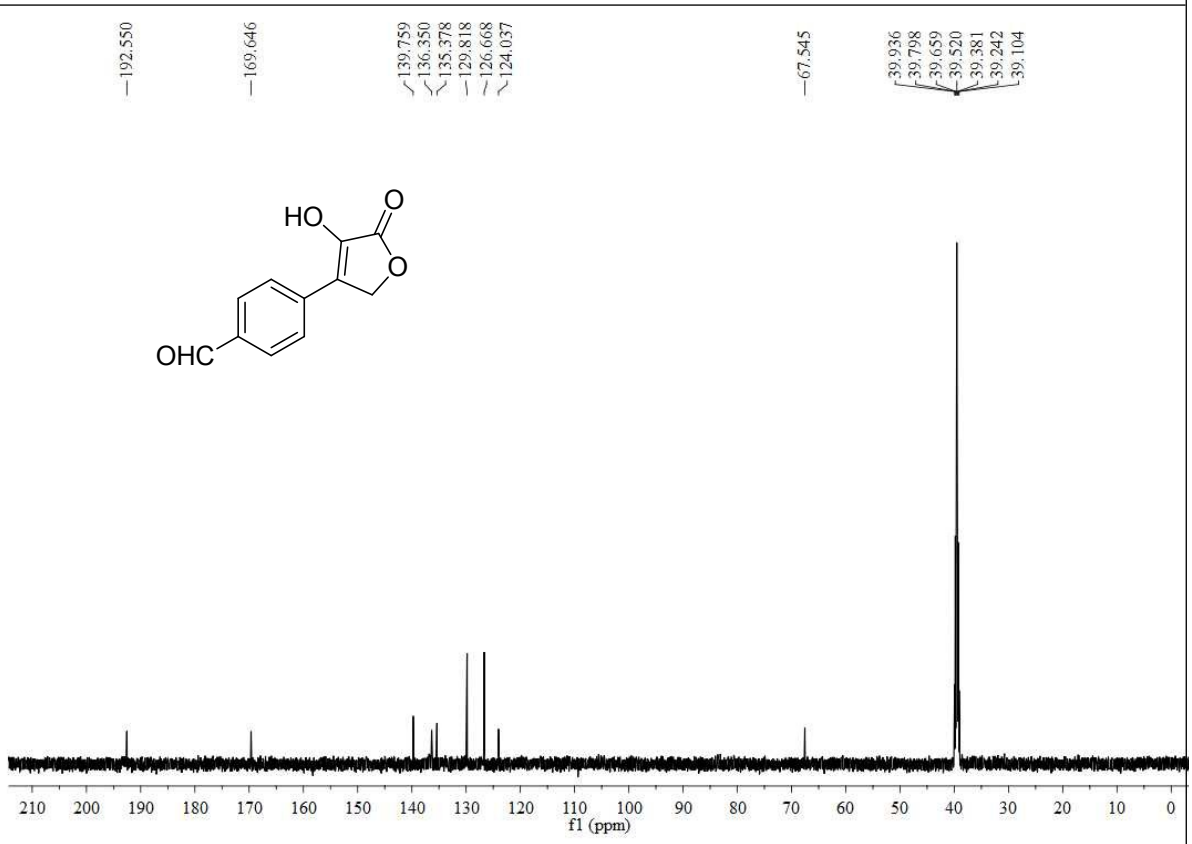
^{1}H NMR (DMSO-d_6, 600 MHz) spectrum of compound **9n**



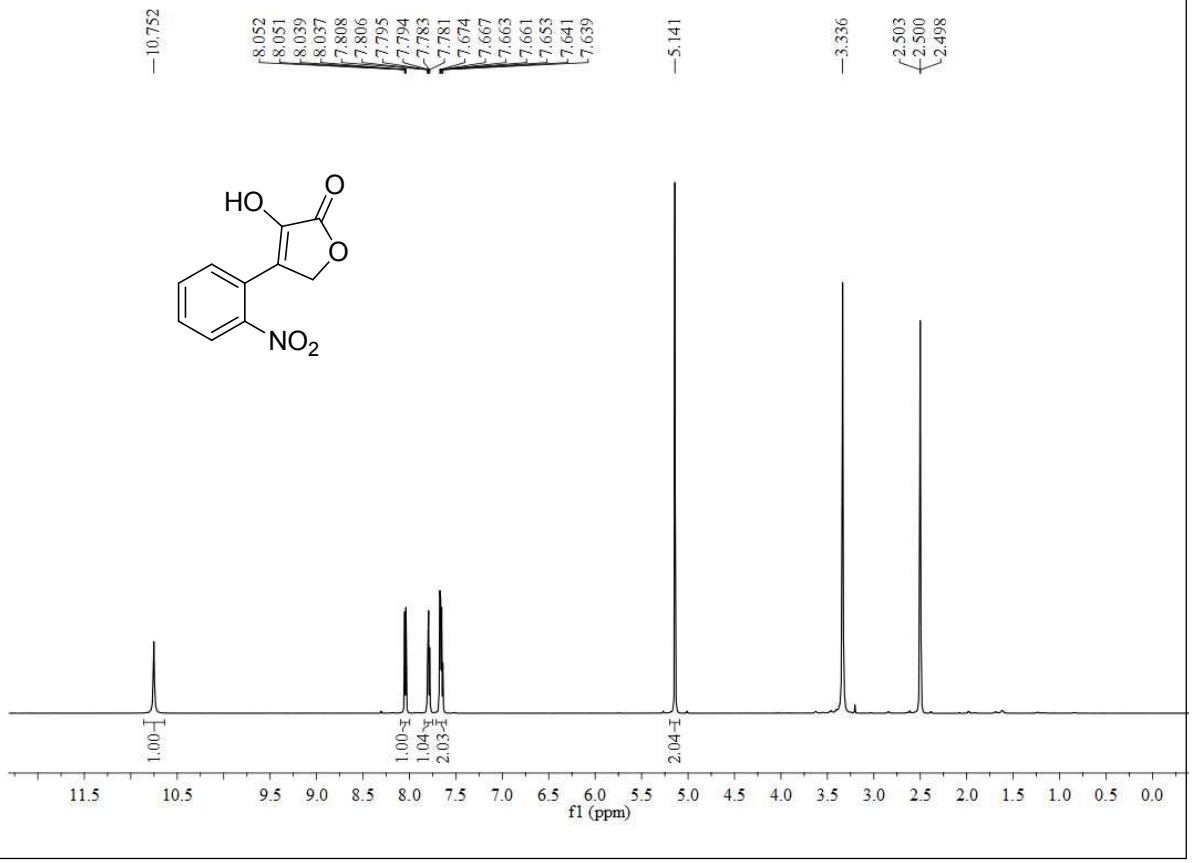
^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz) spectrum of compound **9n**



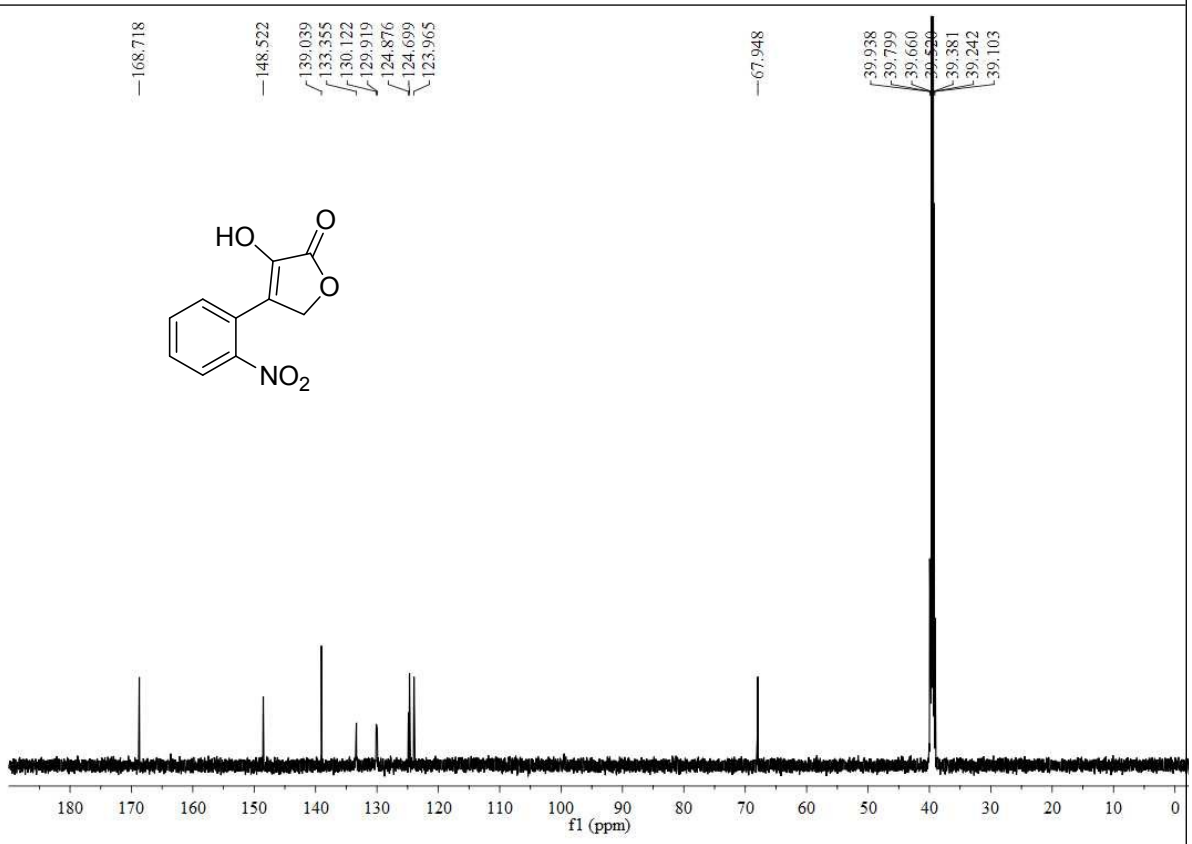
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9o**



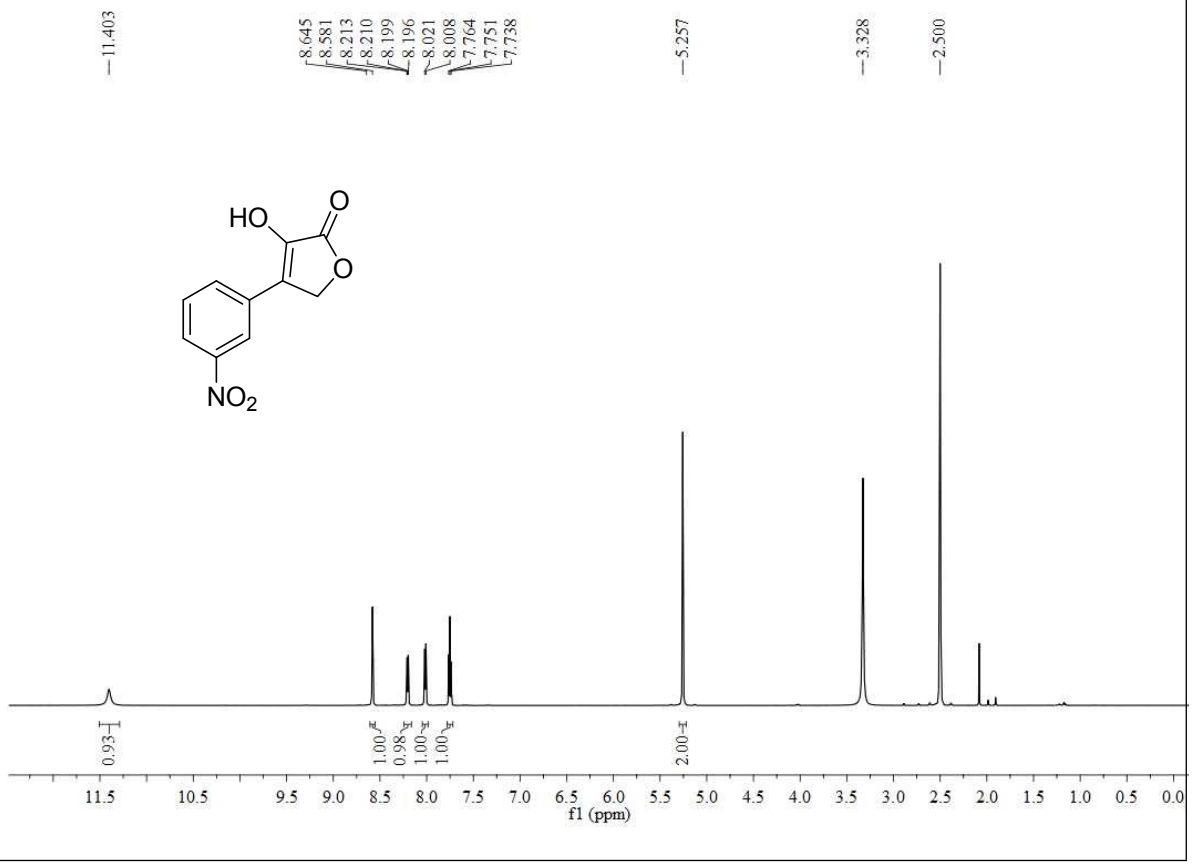
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9o**



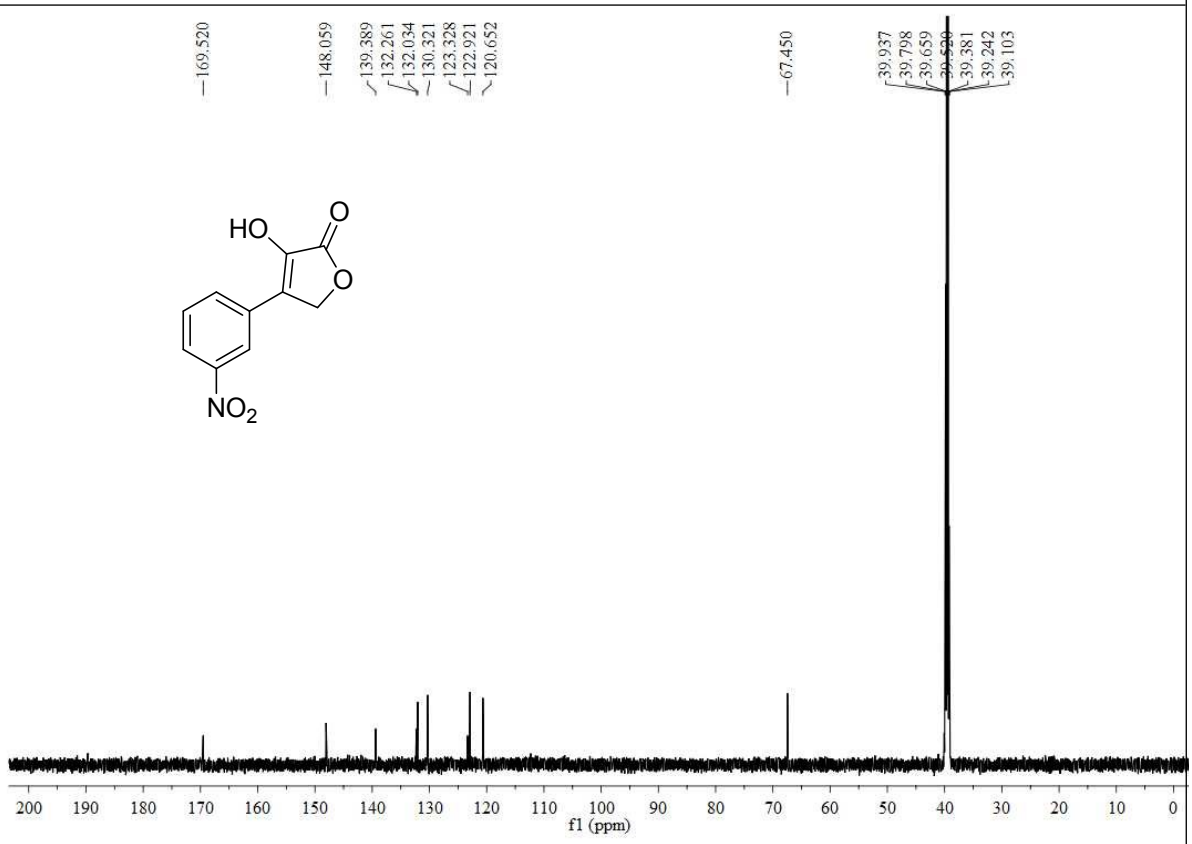
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9p**



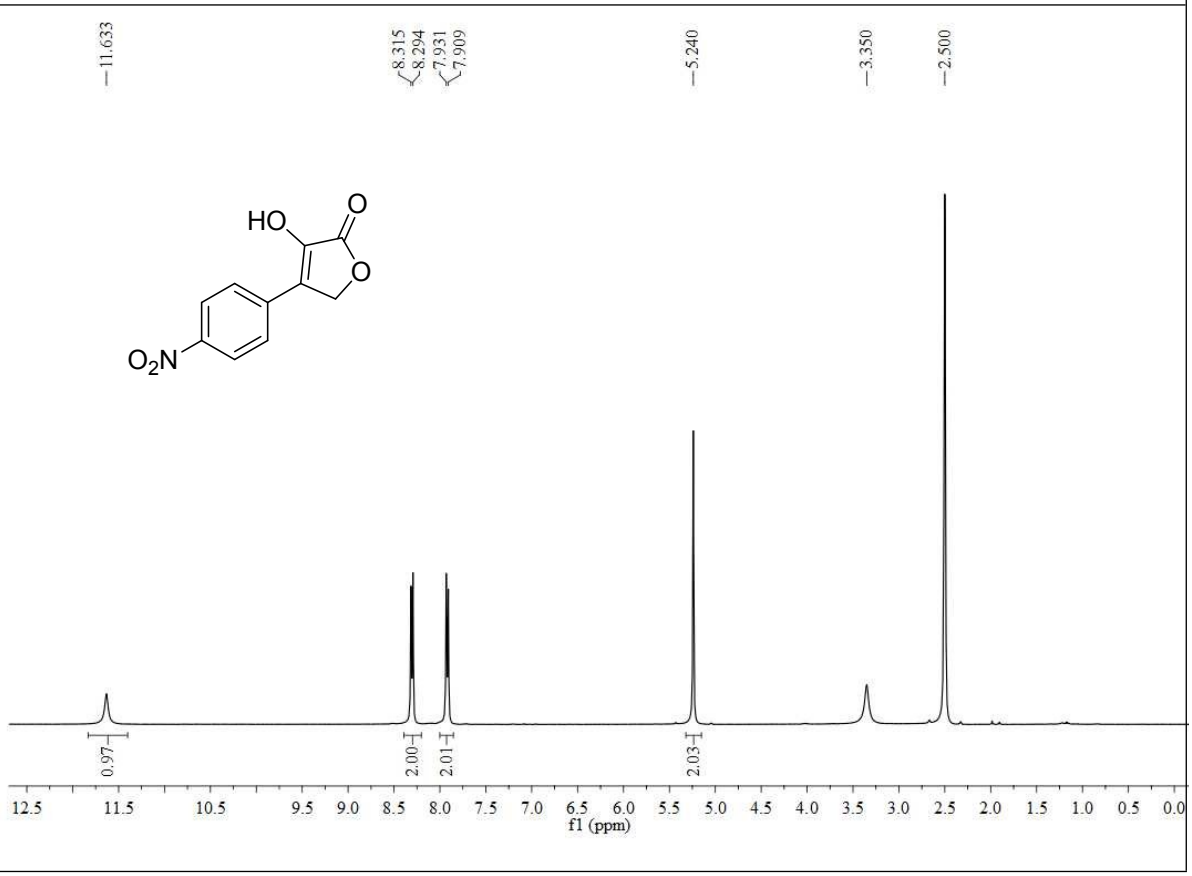
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9p**



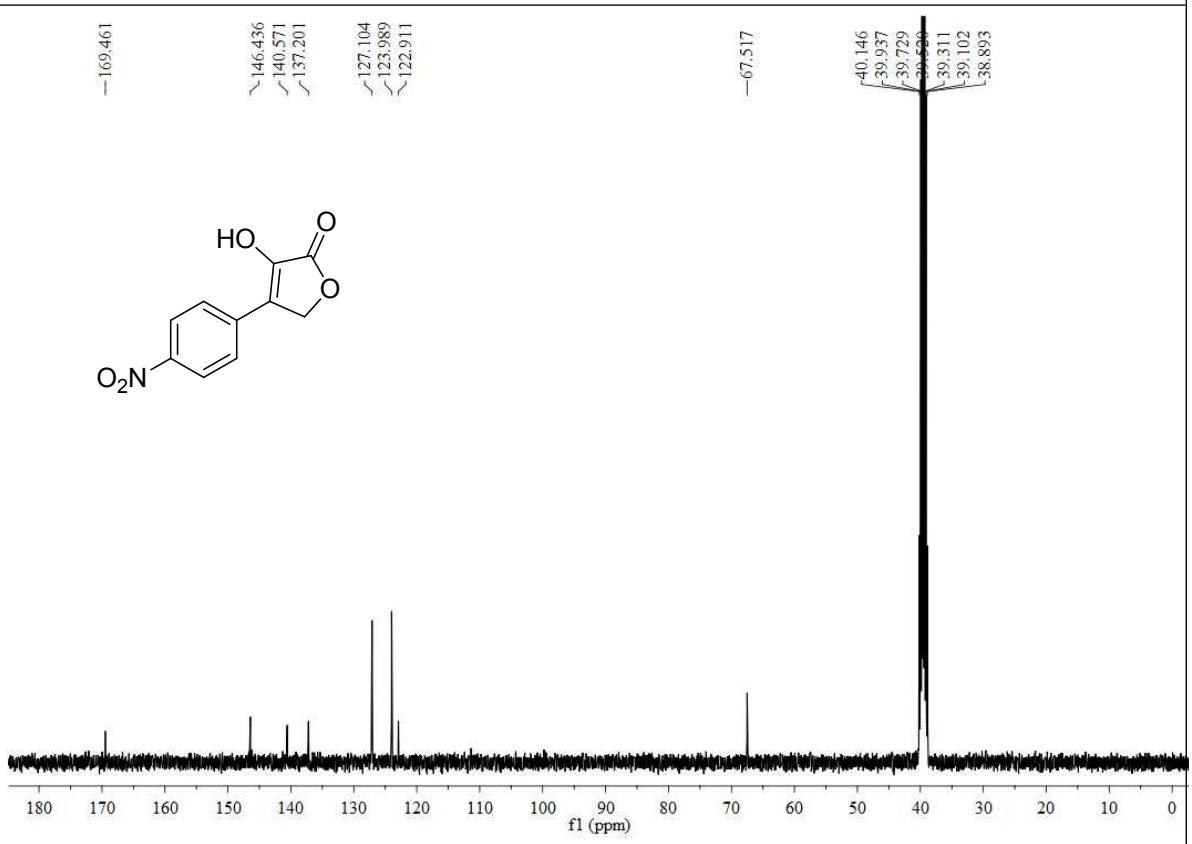
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9q**



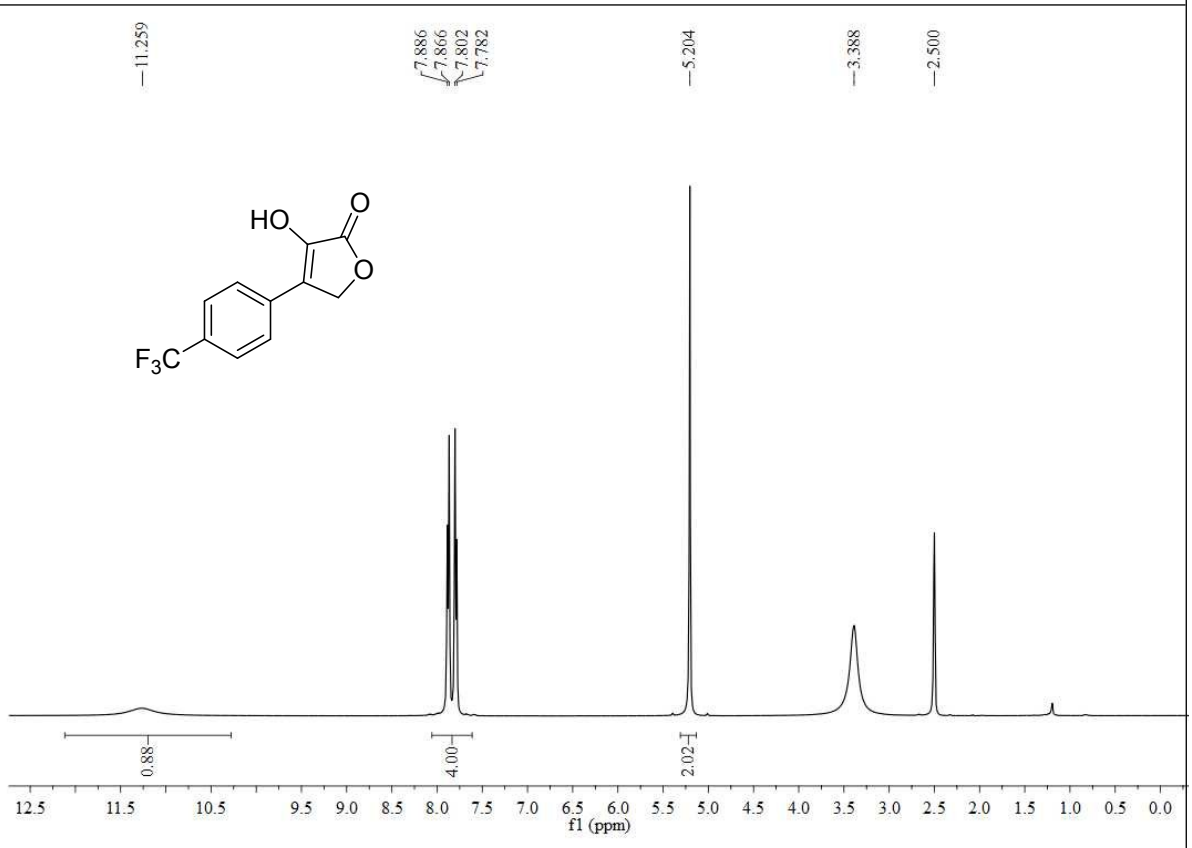
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9q**



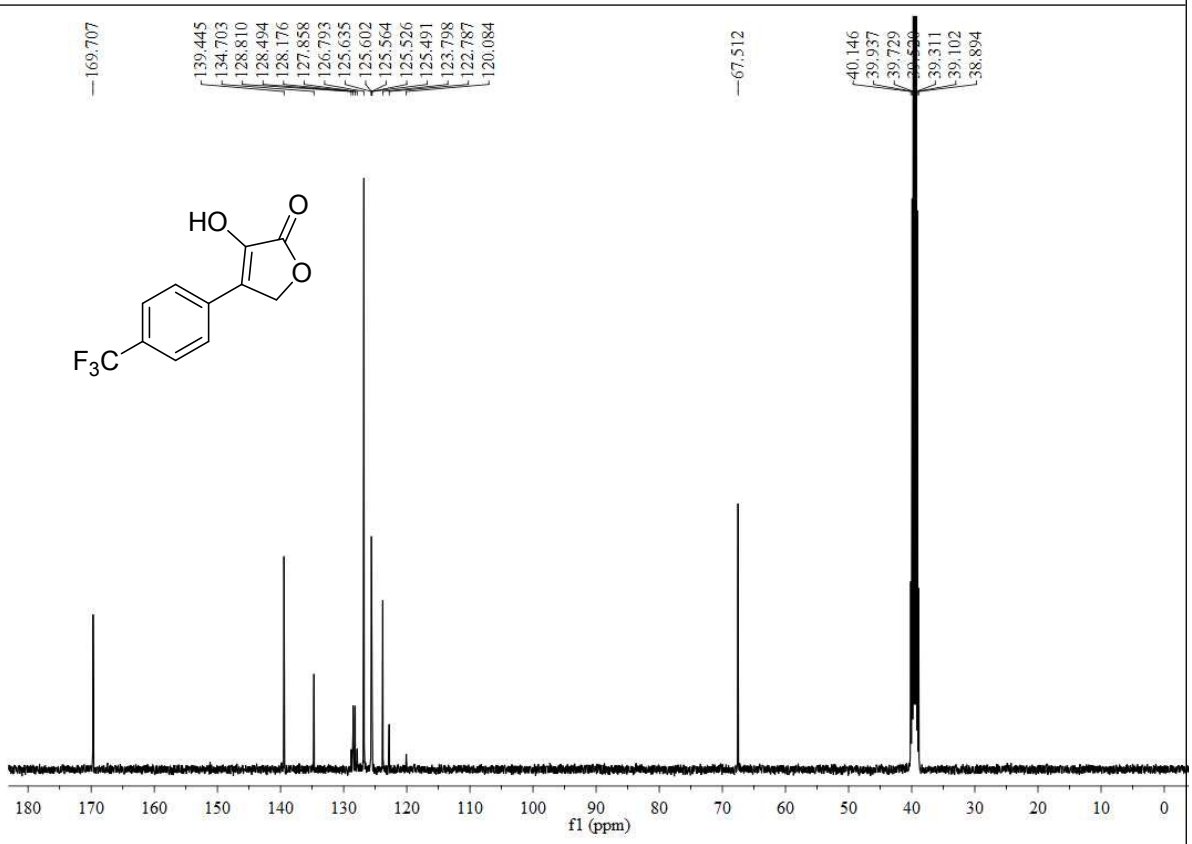
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9r**



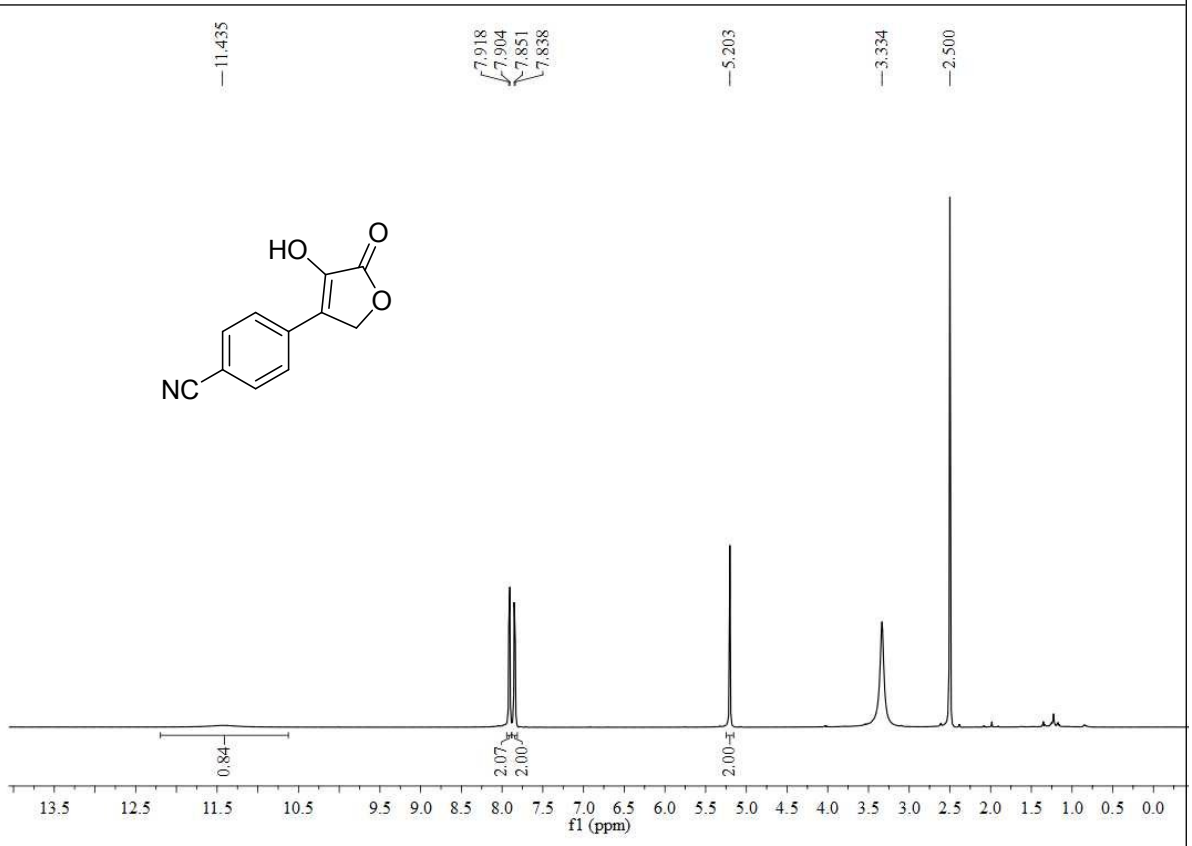
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9r**



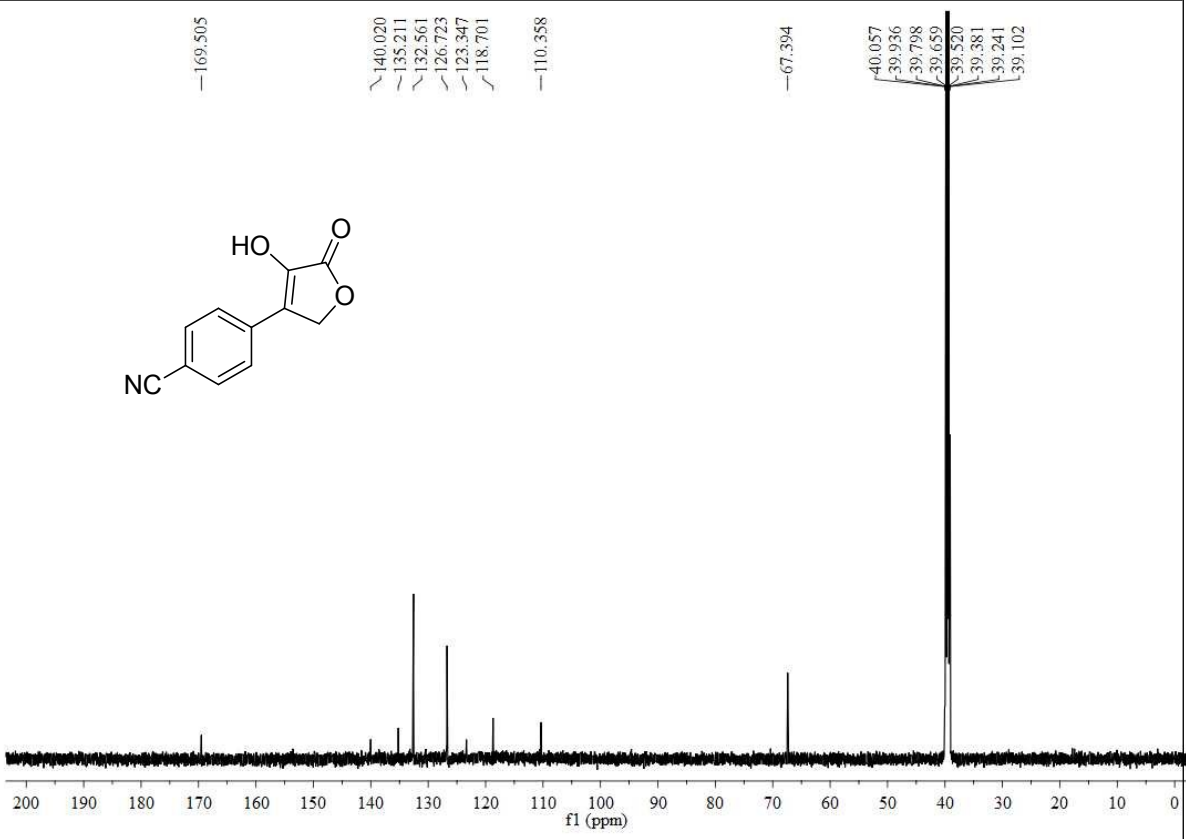
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9s**



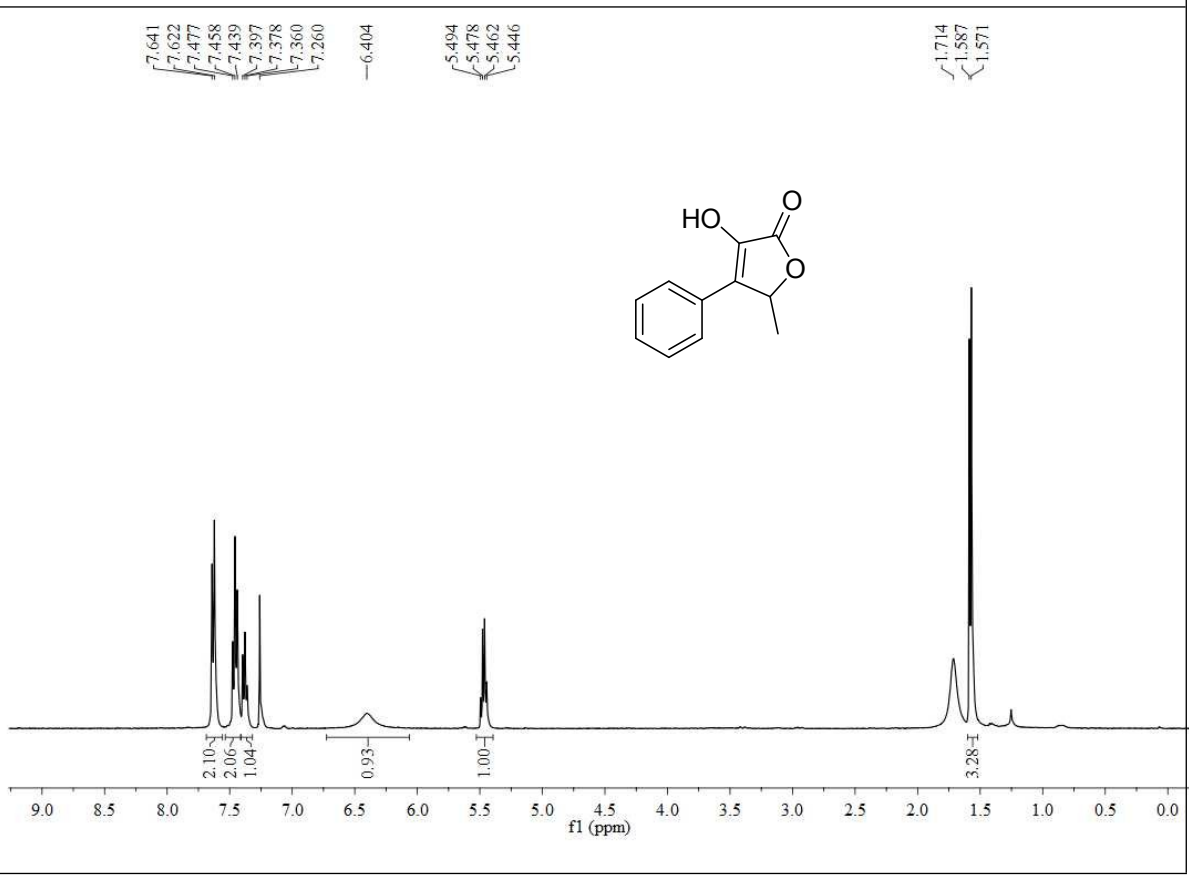
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9s**



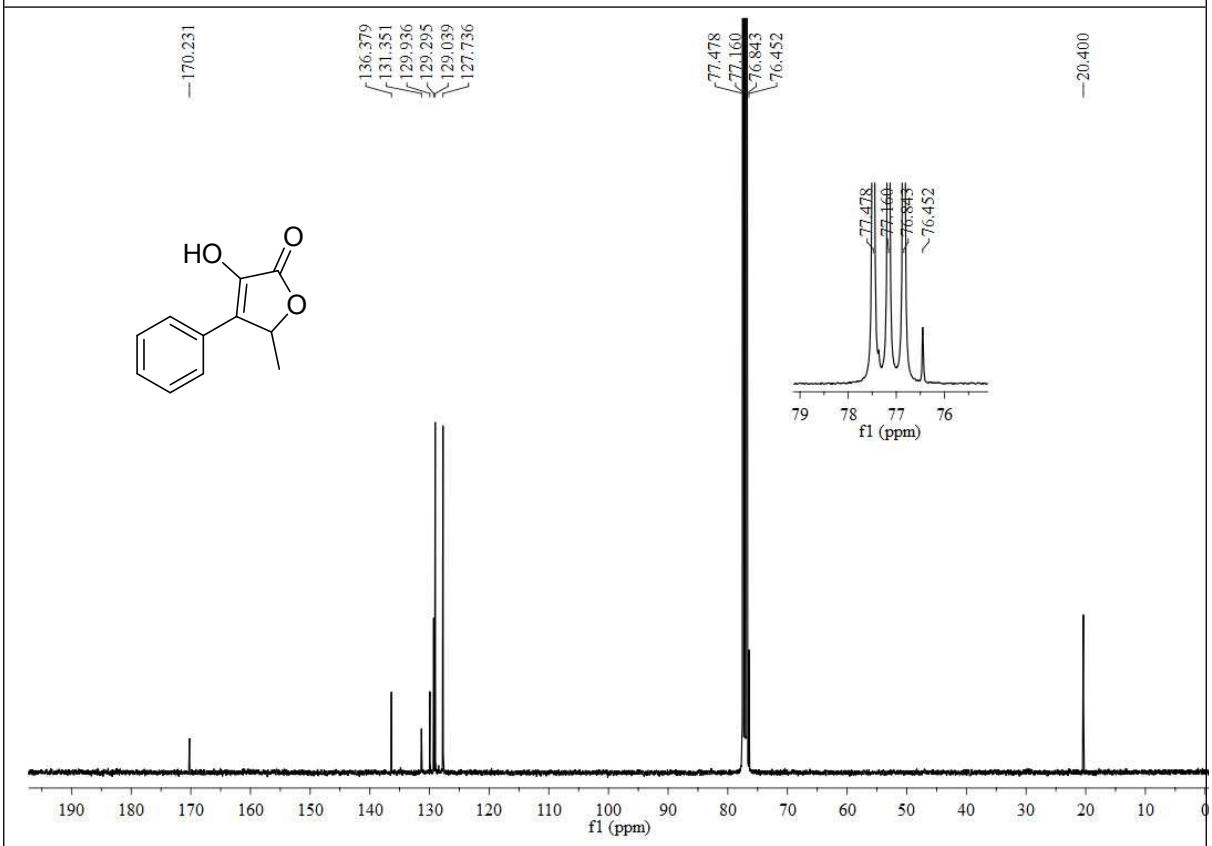
^{1}H NMR (DMSO-d_6, 400 MHz) spectrum of compound **9t**



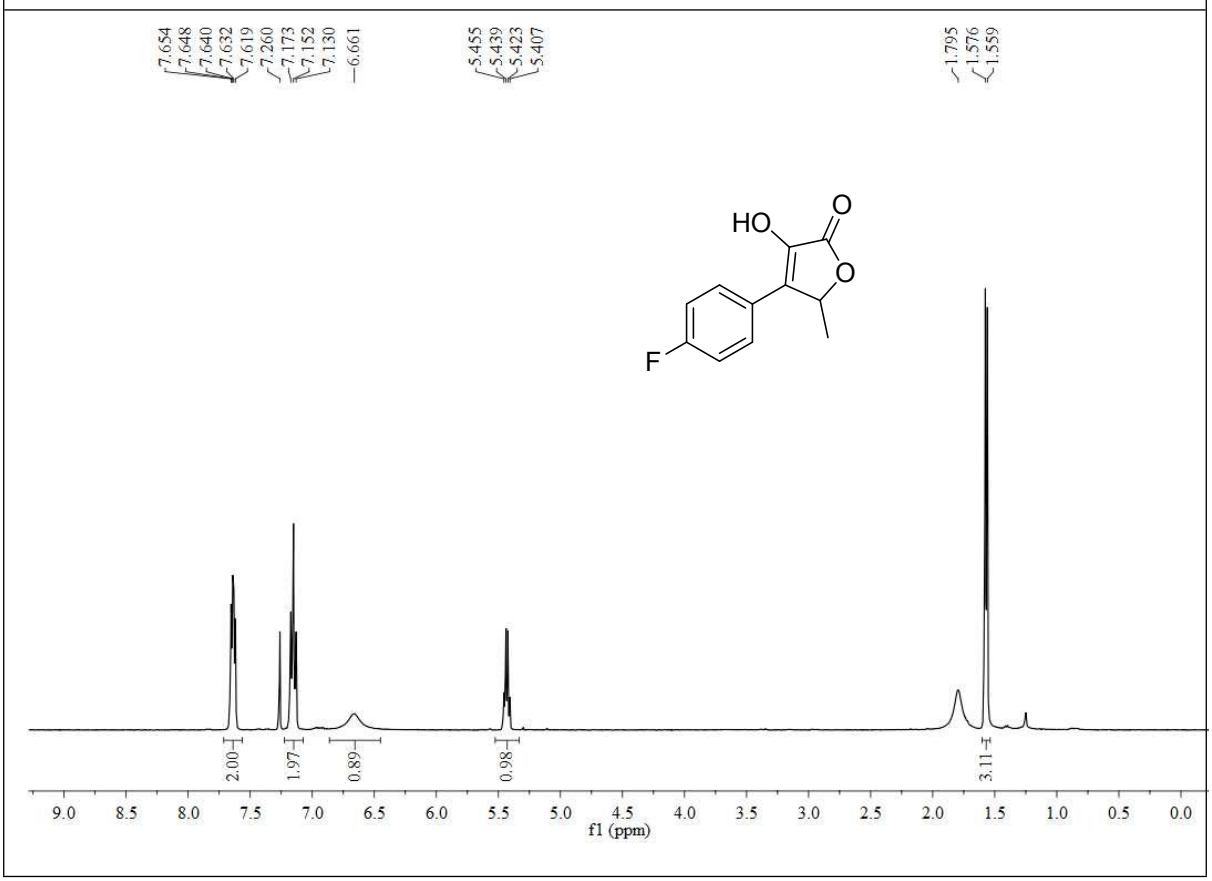
^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) spectrum of compound **9t**



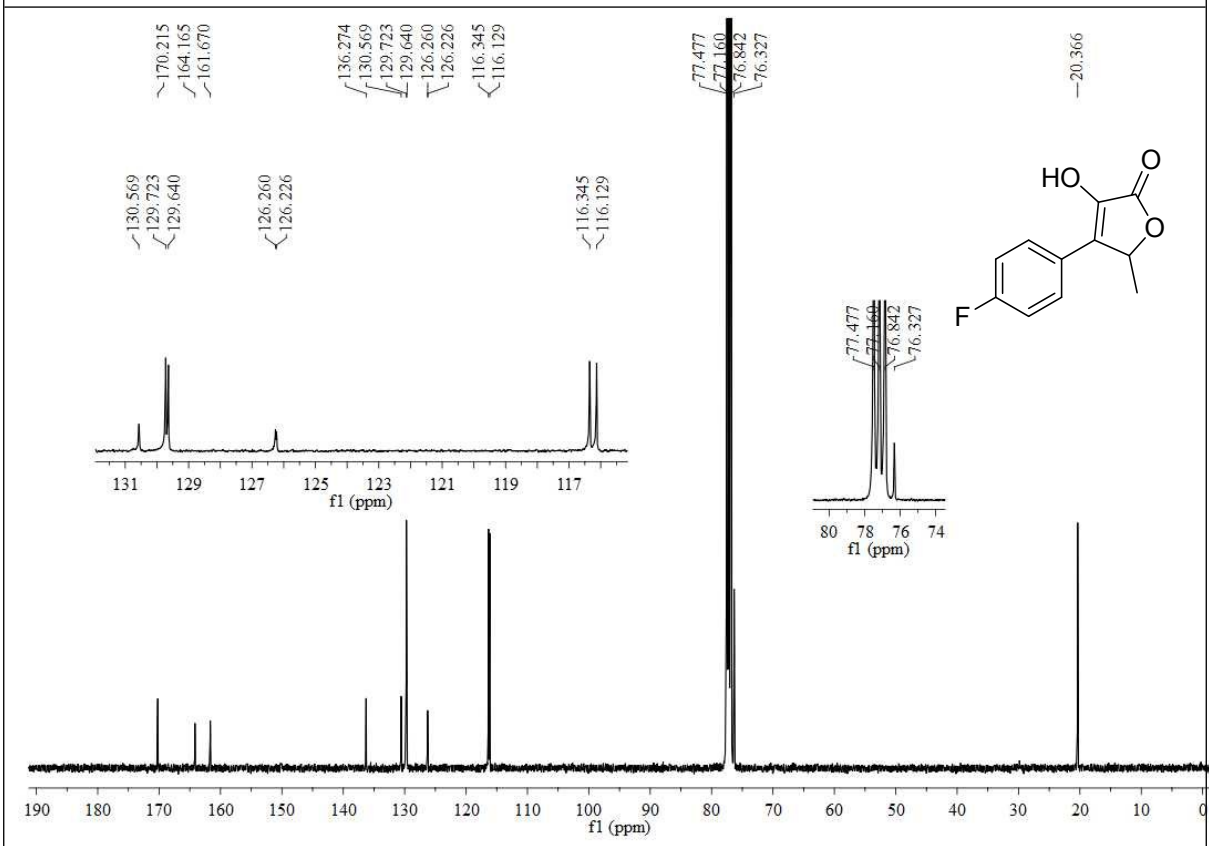
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **11a**



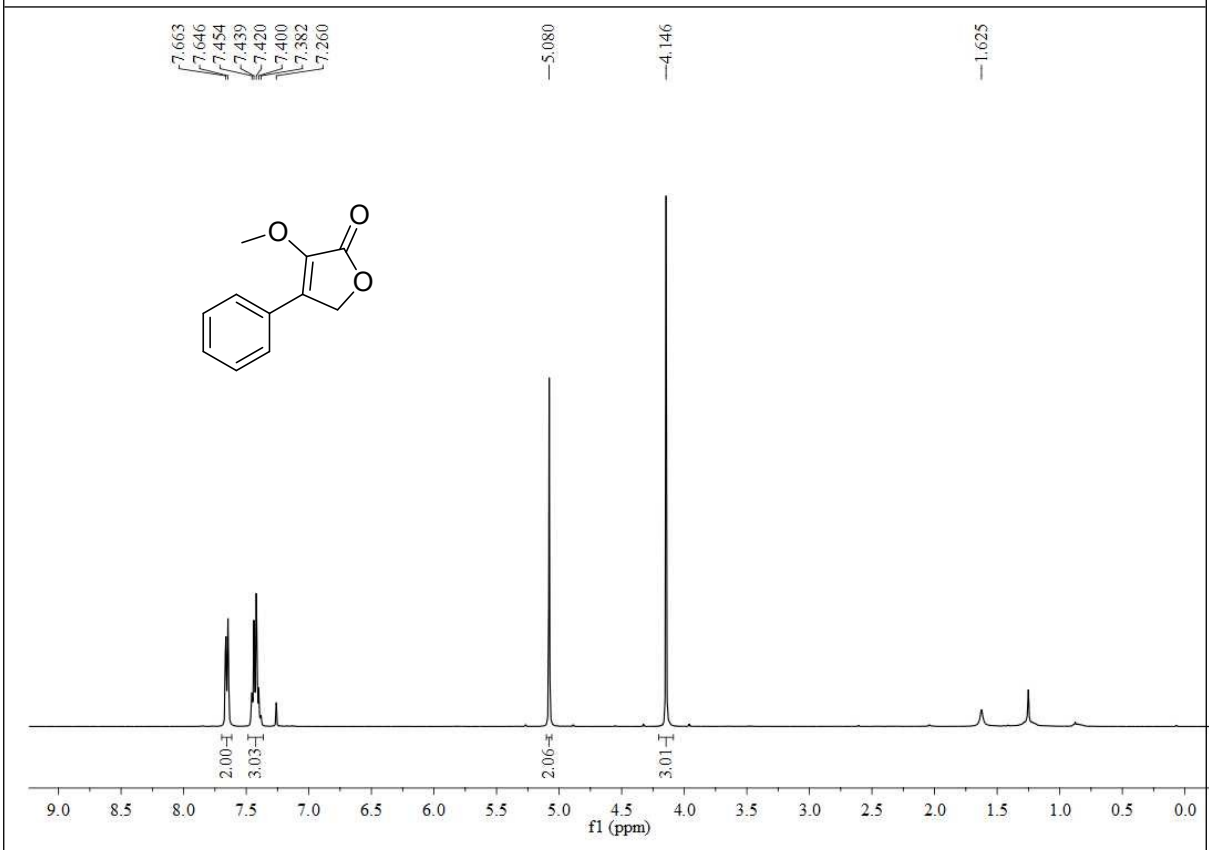
^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **11a**



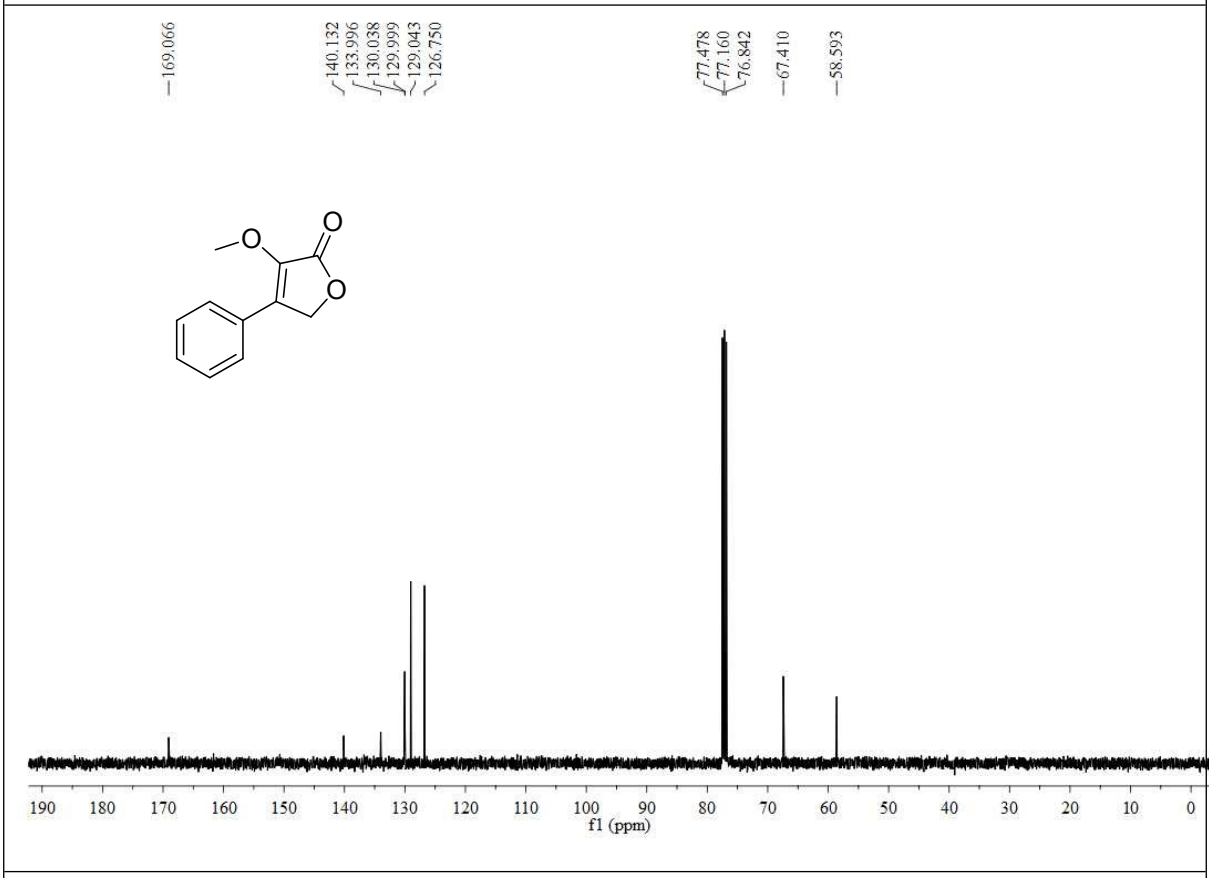
^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **11g**



^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **11g**



^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **12a**



^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) spectrum of compound **12a**

6. ORTEP diagram and crystal data

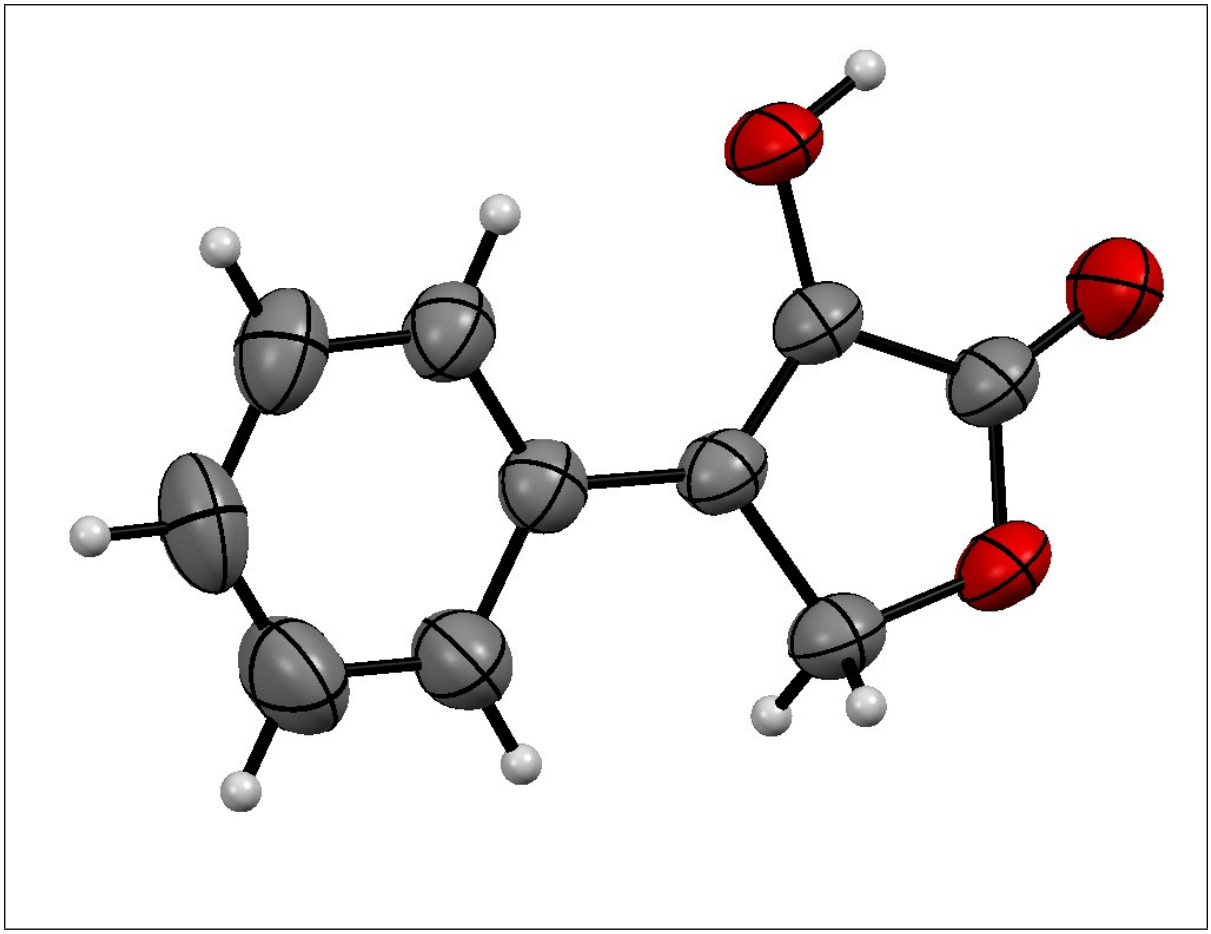
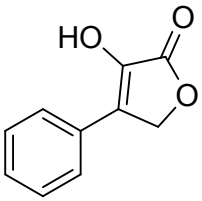


Fig. S1 ORTEP diagram of **9a** with 50% probability ellipsoids. (**CCDC:** 1872034)



Sample preparation: 3 mg of compound **9a** dissolved in $CHCl_3$ (~1 ml) followed by addition of 3-4 drops of HPLC hexane and the solution kept undisturbed until crystal growth.

Table S2 Crystal data and structure refinement for **9a**

Empirical formula	$C_{40}\ H_{32}\ O_{12}$
Formula weight	704.65
Crystal system	orthorhombic
Space group	*F*dd2
a[Å]	18.987(4)
b[Å]	25.021(6)

c[Å]	7.0870(18)
α[°]	90
β[°]	90
γ[°]	90
Volume[Å^3]	3366.9(14)
Z	4
Density (calculated) [Mg/m^3]	1.390
F(000)	1472
Goodness of fit ref	1.042
final R indices [I > 2σ(I)]	R_1 = 0.0466, wR_2 = 0.1106

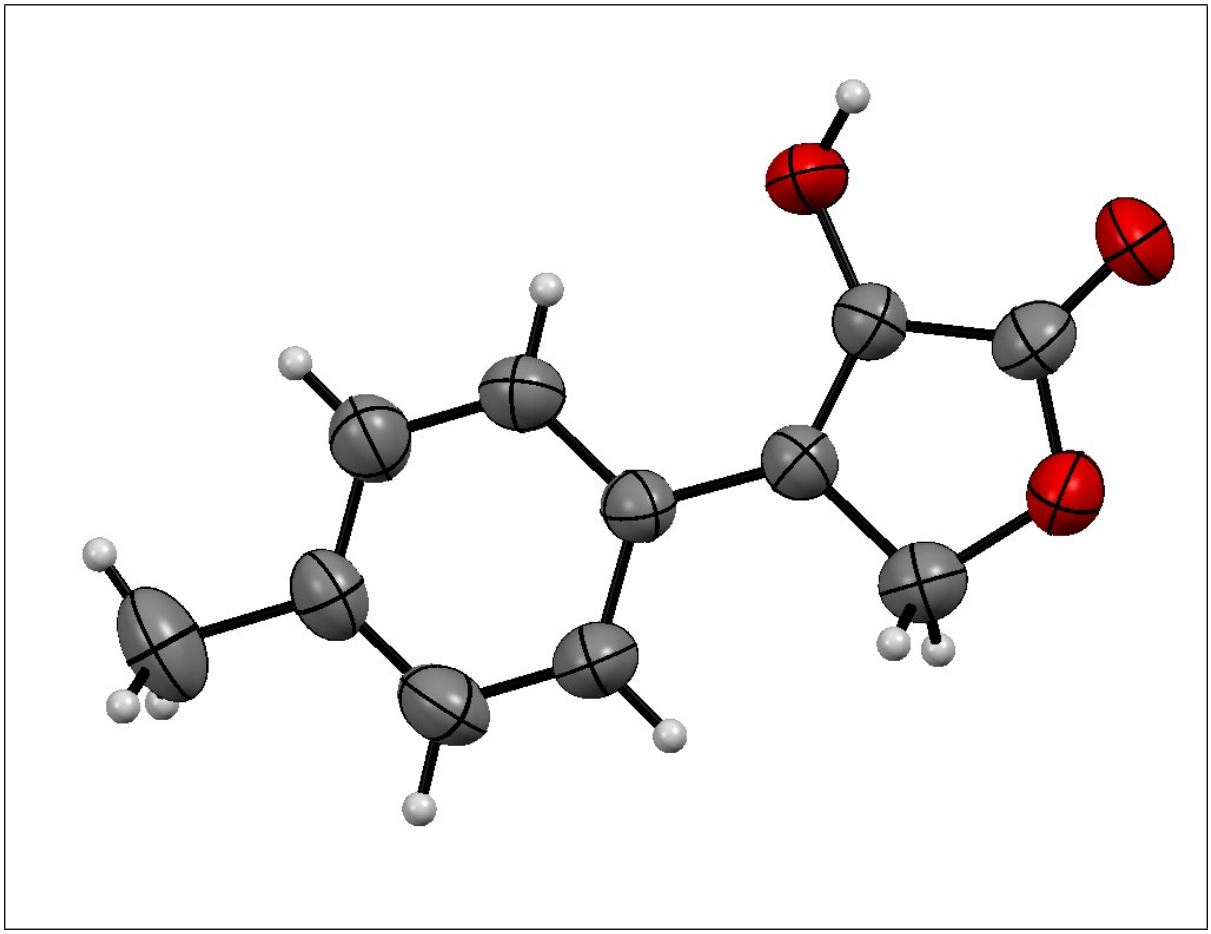
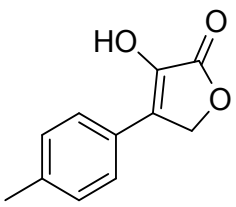


Fig. S2 ORTEP diagram of **9k** with 50% probability ellipsoids. (**CCDC:** 1872059)



Sample preparation: 2 mg of compound **9k** dissolved in acetone (~1 ml) followed by addition of 3-4 drops of HPLC hexane and then the solution kept undisturbed until crystal growth.

Table S3 Crystal data and structure refinement for **9k**

Empirical formula	$C_{44}\ H_{40}\ O_{12}$
Formula weight	760.76
Crystal system	monoclinic
Space group	*P*21
a[Å]	7.570(2)
b[Å]	9.753(2)
c[Å]	13.656(3)
α[°]	90.00(3)
β[°]	102.23(3)
γ[°]	90.00(3)
Volume[$Å^3$]	985.4(4)
Z	4
Density (calculated) [Mg/m^3]	1.282
F(000)	400
Goodness of fit ref	0.946
final R indices [I > 2σ(I)]	R_1 = 0.0568, wR_2 = 0.1306

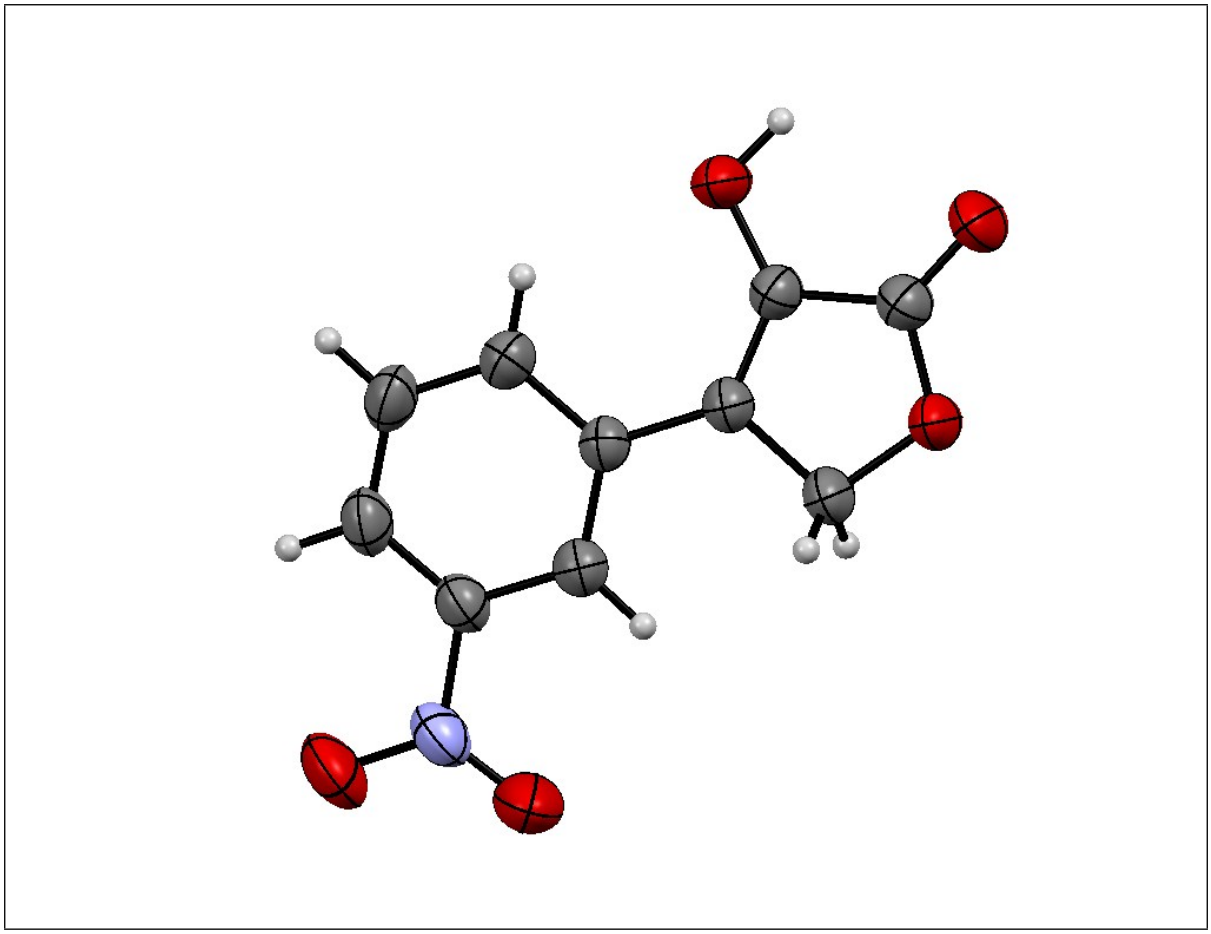
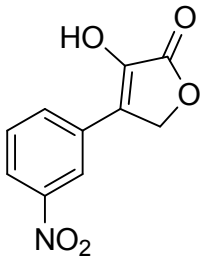


Fig. S3 ORTEP diagram of **9q** with 50% probability ellipsoids. (**CCDC:** 1872060)



Sample preparation: 3 mg of compound **9q** dissolved in acetone (~1 ml) followed by addition of 3-4 drops of HPLC hexane and then the solution kept undisturbed until crystal growth.

Table S4 Crystal data and structure refinement for **9q**

Empirical formula	$C_{80}\ H_{56}\ N_8\ O_{40}$
Formula weight	1769.32
Crystal system	monoclinic
Space group	*C*2/c
a[Å]	25.689(5)

b[Å]	10.003(2)
c[Å]	7.418(2)
α[°]	90.00(3)
β[°]	105.62(3)
γ[°]	90.00(3)
Volume[Å^3]	1835.8(8)
Z	8
Density (calculated) [Mg/m^3]	1.600
F(000)	912
Goodness of fit ref	1.019
final R indices [I > 2σ(I)]	R_1 = 0.0536, wR_2 = 0.1228

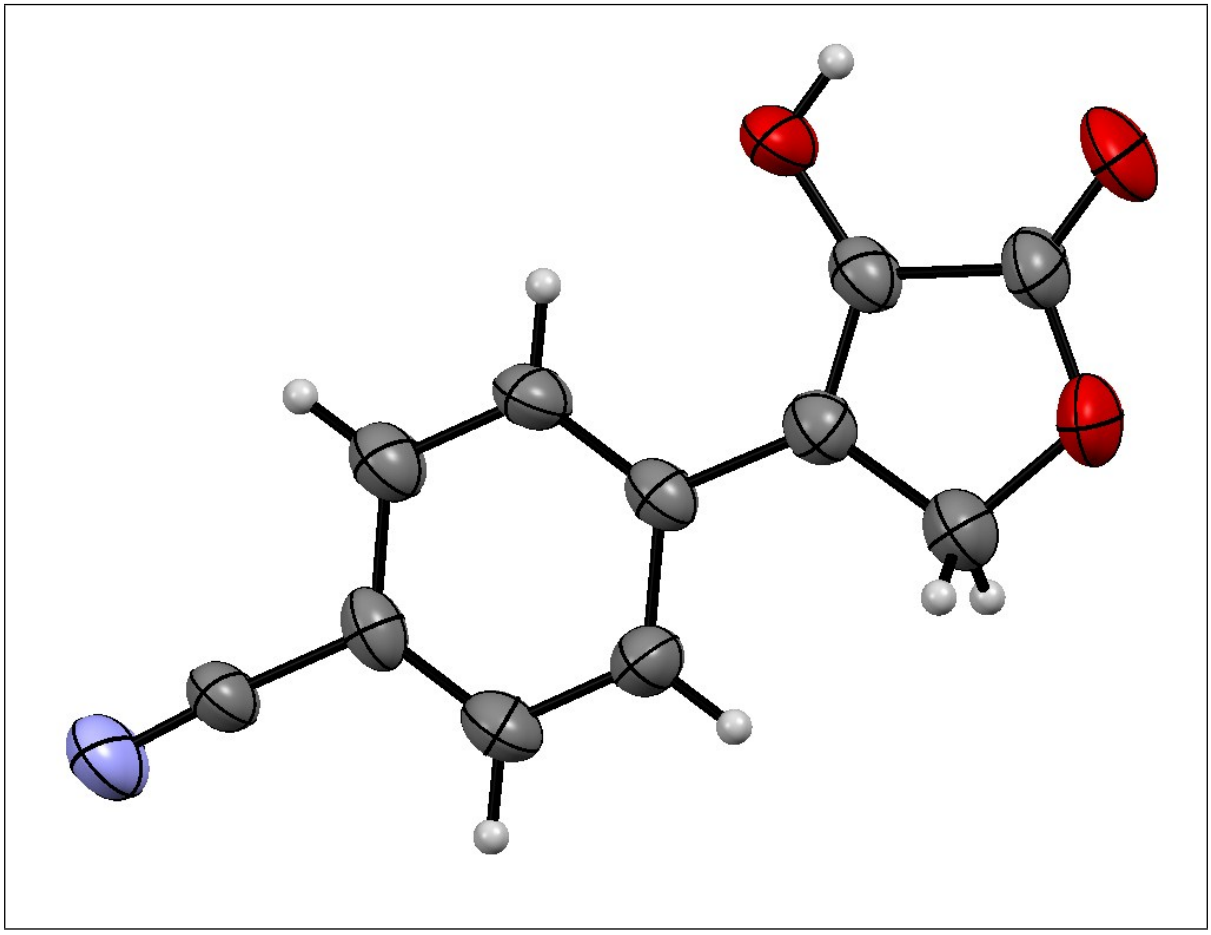
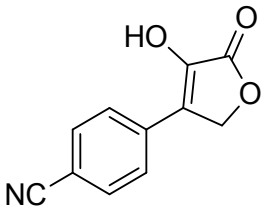


Fig. S4 ORTEP diagram of **9t** with 50% probability ellipsoids. (**CCDC:** 1872061)



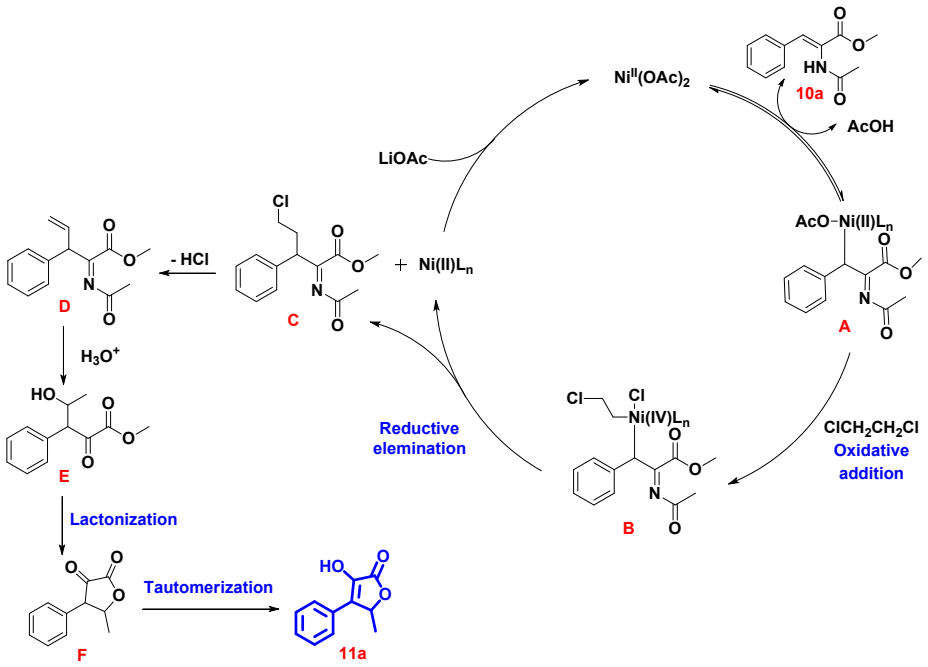
Sample preparation: 3 mg of compound **9t** dissolved in acetone (~1 ml) followed by addition of 3-4 drops of HPLC hexane and then the solution kept undisturbed until crystal growth.

Table S5 Crystal data and structure refinement for **9t**

Empirical formula	$C_{22}\ H_{14}\ N_2\ O_6$
Formula weight	402.35
Crystal system	triclinic
Space group	*P*-1
a[Å]	8.009
b[Å]	9.607
c[Å]	13.044
α[°]	94.77
β[°]	105.91
γ[°]	108.25
Volume[Å^3]	900.8
Z	2
Density (calculated) [Mg/m^3]	1.483
F(000)	416
Goodness of fit ref	1.030
final R indices [I > 2σ(I)]	R_1 = 0.0748, wR_2 = 0.1975

6. A plausible mechanistic pathway for 11a:

A plausible mechanistic pathway for the formation of 5-methyl substituted isotetronic acid is shown below.



Scheme S1: A plausible mechanistic pathway for **11a**.

The reaction mechanism of the formation of compound **11a** is quite similar to compound **9a**, except in this case we got a rearranged product. Initially, heteroatom-guided electrophilic nikelation with acetamidoacrylate derivative (**10a**) gives rise to intermediate **A**, which then undergoes oxidative addition with 1,2-dichloroethane to form nickel(IV)-intermediate **B**. Then reductive elimination from Ni(IV)-intermediate B furnish a primary chloro-derivative **C**. Dehydrohalogenation from intermediate **C** results an allyl substituted intermediate **D**. Next, **D** undergo hydration reaction by following Markovnikov's rule to form more stable secondary alcohol E where at the same time the imide moiety also get hydrolysed. Finally, lactonization followed by tautomerization gives isotetronic acid **11a**.

7. References:

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