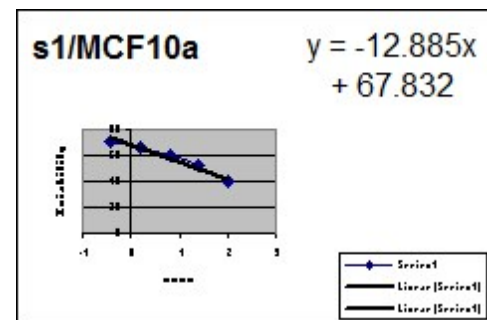
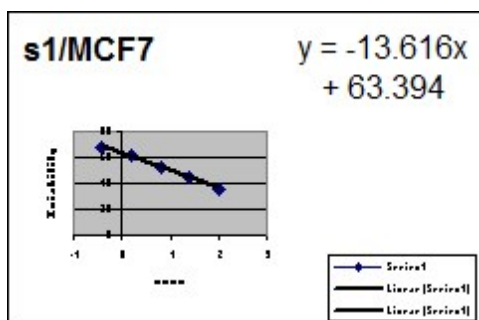
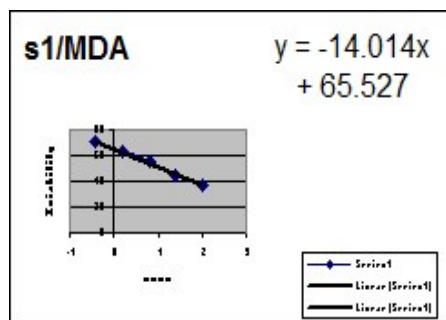
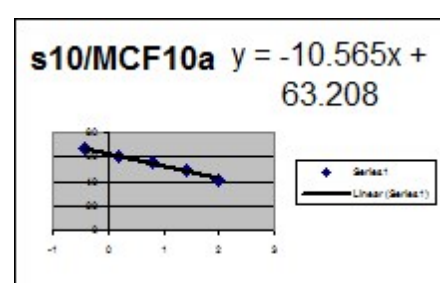
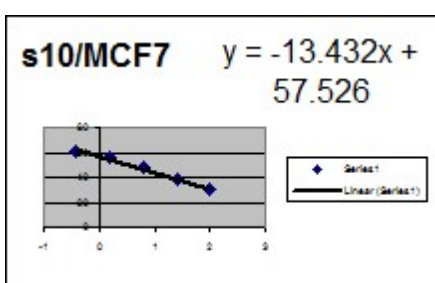
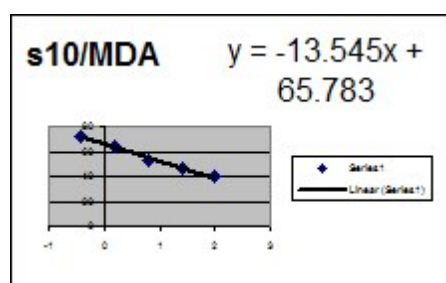


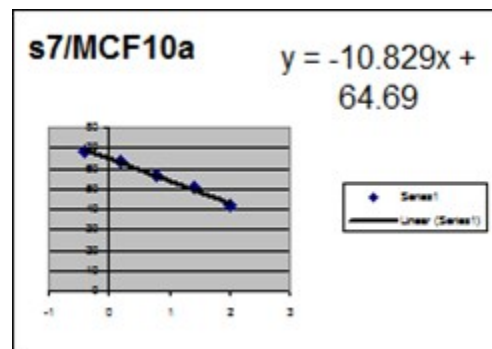
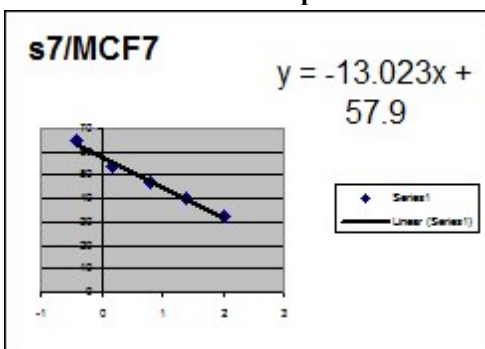
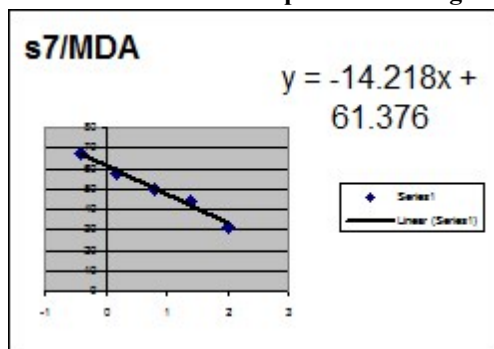
Fig S1: Curves of proliferation against the three cell lines of all the synthesized compounds.



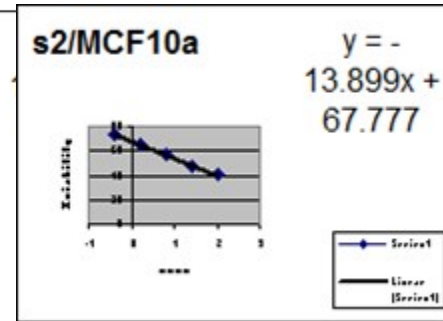
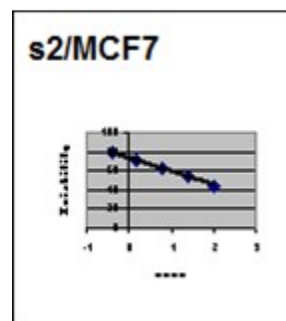
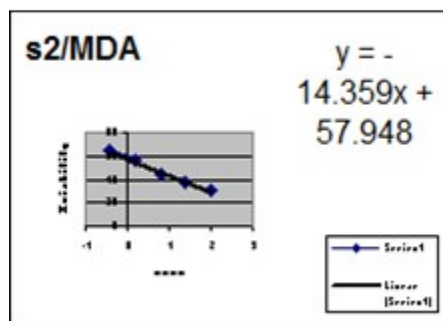
Curves of proliferation against the three cell lines of compound 4a.



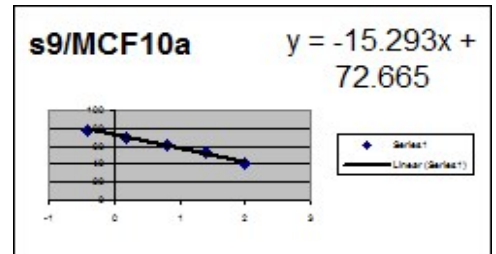
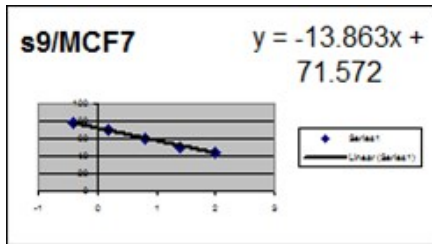
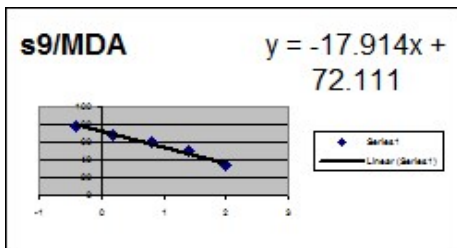
Curves of proliferation against the three cell lines of compound 4b.



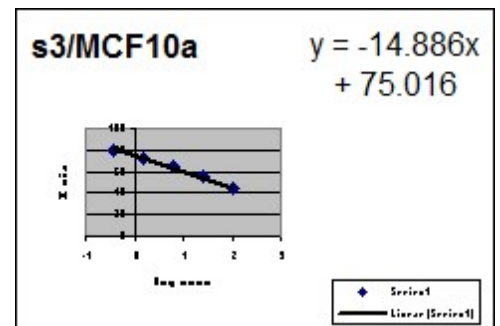
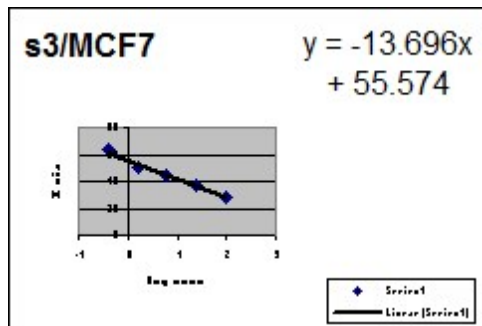
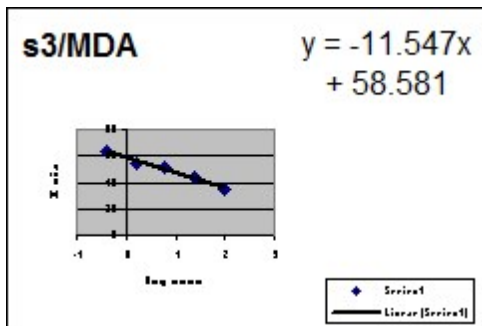
Curves of proliferation against the three cell lines of compound 4c.



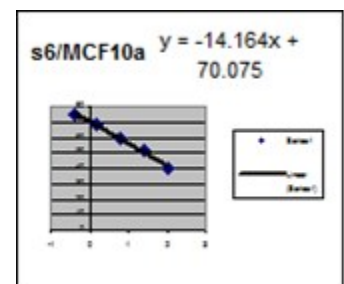
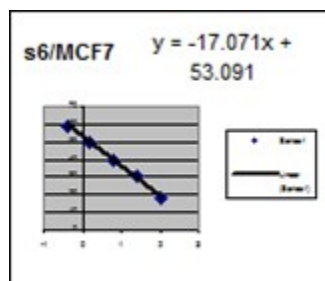
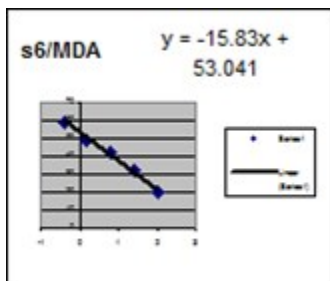
Curves of proliferation against the three cell lines of compound 4e.



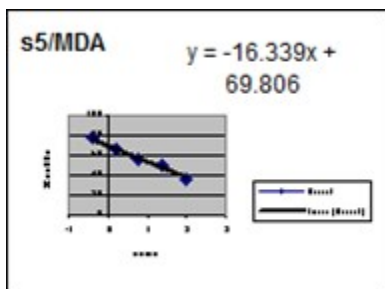
Curves of proliferation against the three cell lines of compound 4f.



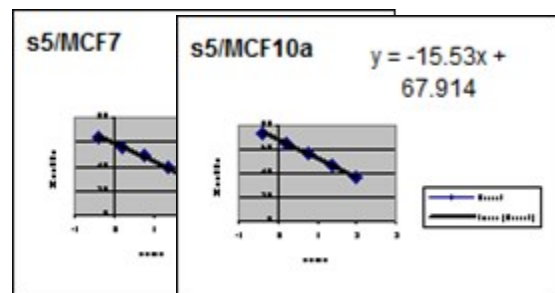
Curves of proliferation against the three cell lines of compound 4g.

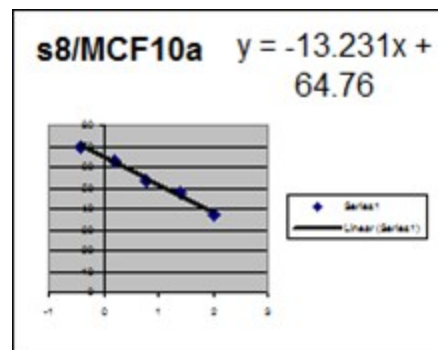
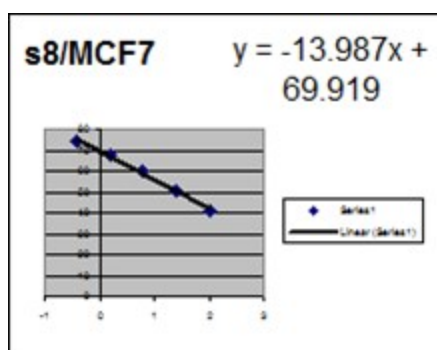
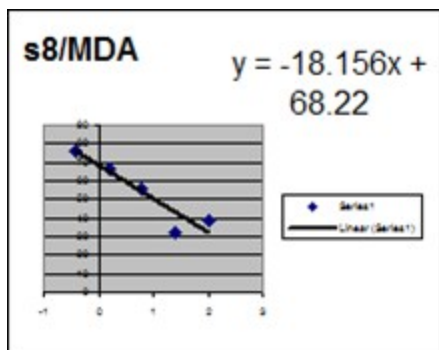


Curves of proliferation against the three cell lines of compound 4h.



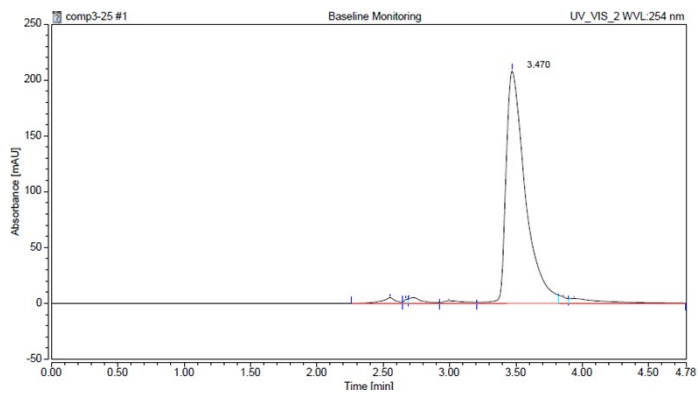
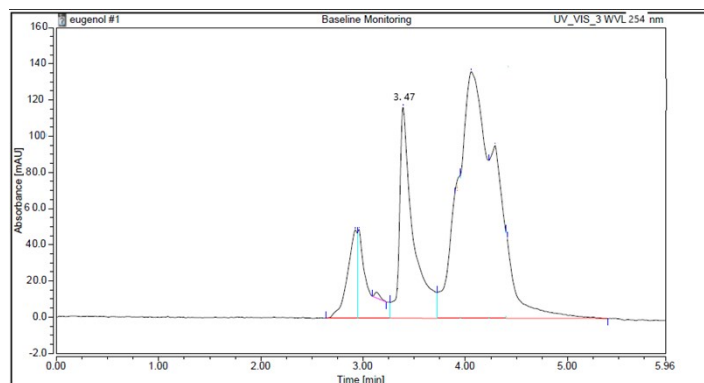
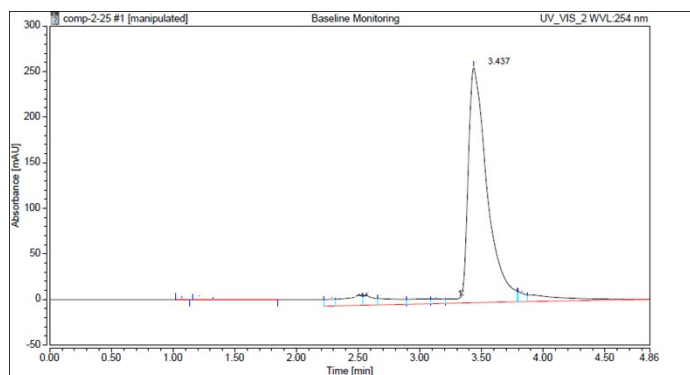
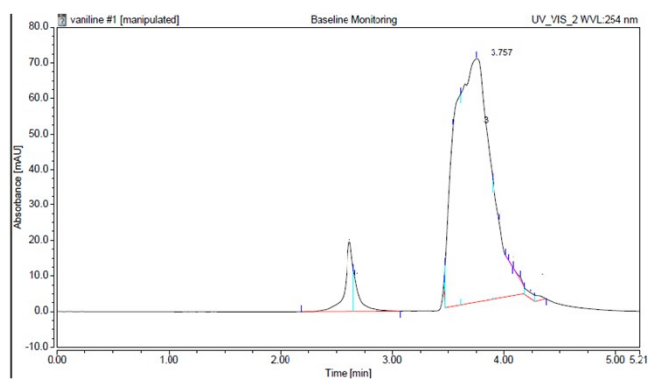
curves of proliferation against the three cell lines of compound 4i.





curves of proliferation against the three cell lines of compound 4j.

**Fig S2: The cellular uptake of compounds 4e and 4h by MDA-MB-231 cancer cell lines.**

**A****B****C****D**

**HPLC chromatogram of (A) : compound 4e, (B) cellular uptake of compound 4e by MDA-MB-231 cancer cell line, (C): compound 4h, (D): cellular uptake of compound 4h by MDA-MB-231 cancer cell line.**

**Table S1: IC<sub>50</sub> of carbonic anhydrase IX enzyme inhibition of all the synthesized derivatives.**

<b>Compound No.</b>	<b>CA IX IC<sub>50</sub> (nM)±S.D.</b>
<b>4a</b>	<b>338±16.5</b>
<b>4b</b>	<b>203.3±9.93</b>
<b>4c</b>	<b>31.68±1.55</b>
<b>4d</b>	<b>135.8±6.63</b>
<b>4e</b>	<b>10.93±0.53</b>
<b>4f</b>	<b>122.14±4.08</b>
<b>4g</b>	<b>16.96±0.83</b>
<b>4h</b>	<b>25.56±1.25</b>
<b>4i</b>	<b>39.51±1.93</b>
<b>4j</b>	<b>76.1±3.71</b>
<b>Dorzolamide</b>	<b>8.83±0.43</b>
<b>SLC-0111</b>	<b>4.5<sup>18</sup></b>

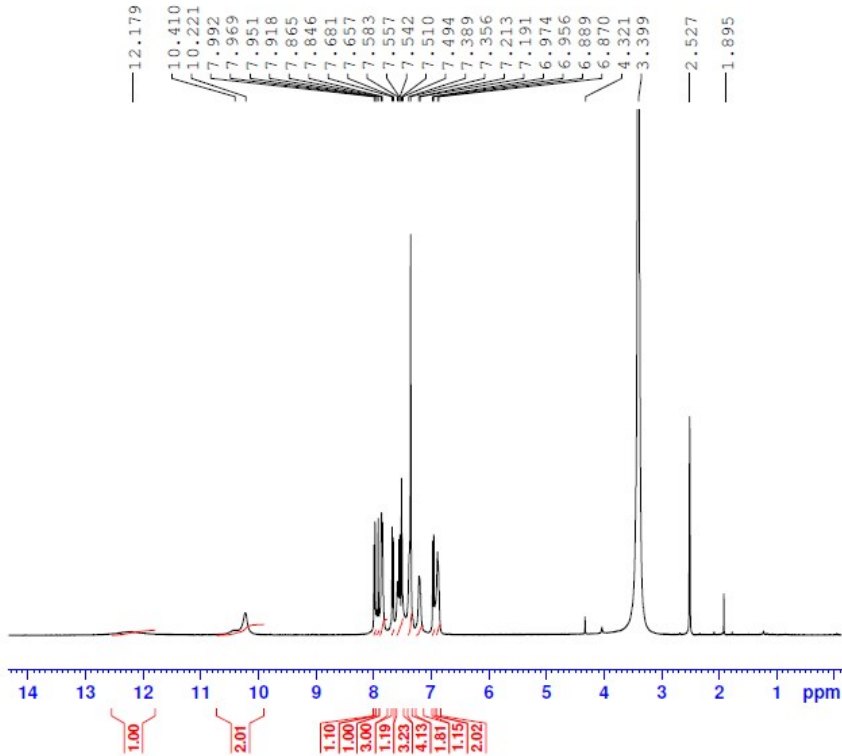
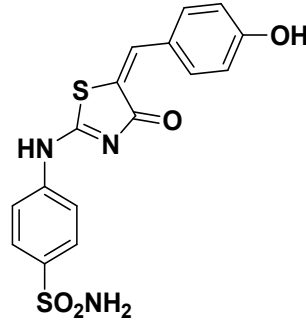
**S.D.** : Standard Deviation

Table	Property	Compound	Compound	Compound	S2:
		4e	4g	4h	
ADMET	<b>Lipophilicity</b> (Log p)	2.859	2.324	2.130	
	<b>Absorption</b>				
	Water Solubility (log mol/L)	-3.867	-4.323	-3.496	
	Caco2 permeability (log Papp in 10 <sup>-6</sup> cm/s)	0.222	0.045	0.176	
	Intestinal absorption (%)	73.743	81.72	77.04	
	Skin permeability (log Kp)	-2.752	-2.749	-2.916	
	P-glycoprotein substrate	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	
	P-glycoprotein I	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	
	P-glycoprotein II	<b>No</b>	<b>No</b>	<b>No</b>	
	<b>Distribution</b>				
	VDss (log L/kg)	0.047	-0.642	-0.21	
	Fraction unbound (Fu)	0.069	0	0.102	
	BBB permeability (log BB)	-1.154	-1.047	-1.134	
	CNS permeability (log PS)	-2.579	-2.561	-2.648	
	<b>Metabolism</b>				
	CYP2D6 substrate	<b>No</b>	<b>No</b>	<b>No</b>	
	CYP3A4 substrate	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	
	CYP1A2 inhibitor	<b>No</b>	<b>No</b>	<b>No</b>	
	CYP2C19 inhibitor	<b>Yes</b>	<b>No</b>	<b>No</b>	
	CYP2C9 inhibitor	<b>Yes</b>	<b>No</b>	<b>No</b>	
	CYP2D6 inhibitor	<b>No</b>	<b>No</b>	<b>No</b>	
	CYP3A4 inhibitor	<b>No</b>	<b>Yes</b>	<b>No</b>	
	<b>Excretion</b>				
	Total Clearance (log ml/min/kg)	-0.373	-0.477	-0.366	
	Renal OCT2 substrate	<b>No</b>	<b>No</b>	<b>Yes</b>	
	<b>Toxicity</b>				
	AMES toxicity	<b>No</b>	<b>No</b>	<b>No</b>	
Max. tolerated dose (log mg/kg/day)	-0.473	-0.339	-0.539		
hERG I inhibitor	<b>No</b>	<b>No</b>	<b>No</b>		
hERG II inhibitor	<b>Yes</b>	<b>No</b>	<b>No</b>		
Oral Rat Acute Toxicity (LD50) (mol/kg)	2.517	2.258	1.985		
Oral Rat Chronic Toxicity (LOAEL) (mol/kg_bw/day)	1.523	1.316	2.221		
Hepatotoxicity	<b>Yes</b>	<b>No</b>	<b>No</b>		

properties of the synthesized compounds.

Skin Sensitisation	<b>No</b>	<b>No</b>	<b>No</b>
<i>T.Pyriformis</i> toxicity (log µg/L)	0.369	0.347	0.606
Minnow toxicity (log mM)	0.205	0.091	0.514

# NMR Spectrum for compound 4b



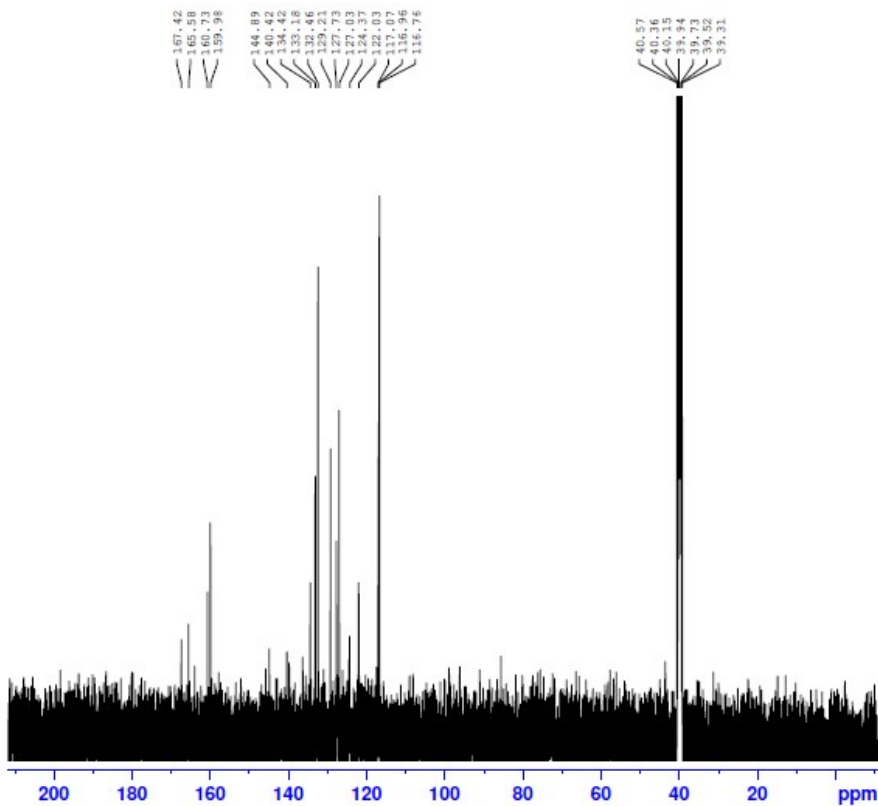
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 PROCNO 1

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 NS 61  
 DS 2  
 SWH 8012.820 Hz  
 FIDRES 0.122266 Hz  
 AQ 4.0894465 sec  
 RG 205.37  
 DW 62.400 usec  
 DE 6.50 usec  
 TE 300.0 K  
 D1 1.00000000 sec  
 TDO 1

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 NUC1 1H  
 P1 12.00 usec  
 PLW1 18.00000000 W

F2 - Processing parameters  
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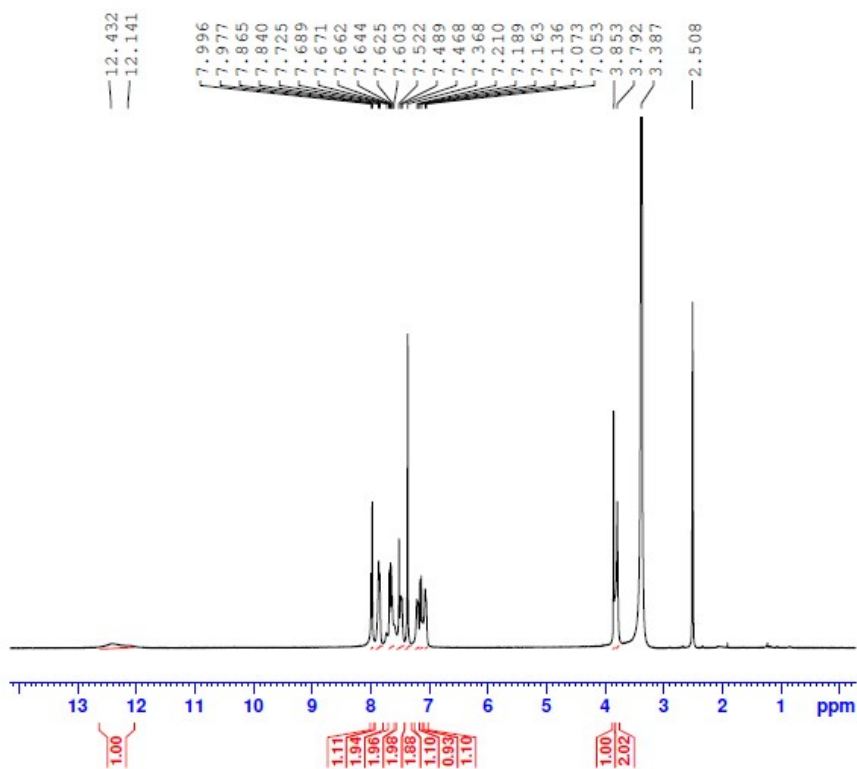
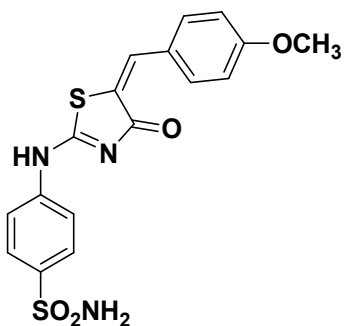
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 NS 1252  
 DS 4  
 SWH 24038.461 Hz  
 FIDRES 0.366798 Hz  
 AQ 1.3631488 sec  
 RG 205.37  
 DW 20.800 usec  
 DE 6.50 usec  
 TE 300.0 K  
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 D11 0.03000000 sec  
 TDO 1

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==== CHANNEL f2 =====  
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 PLW2 18.00000000 W  
 PLW12 0.34722000 W  
 PLW13 0.28125000 W

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 PC 1.40

# NMR spectrum for compound 4c

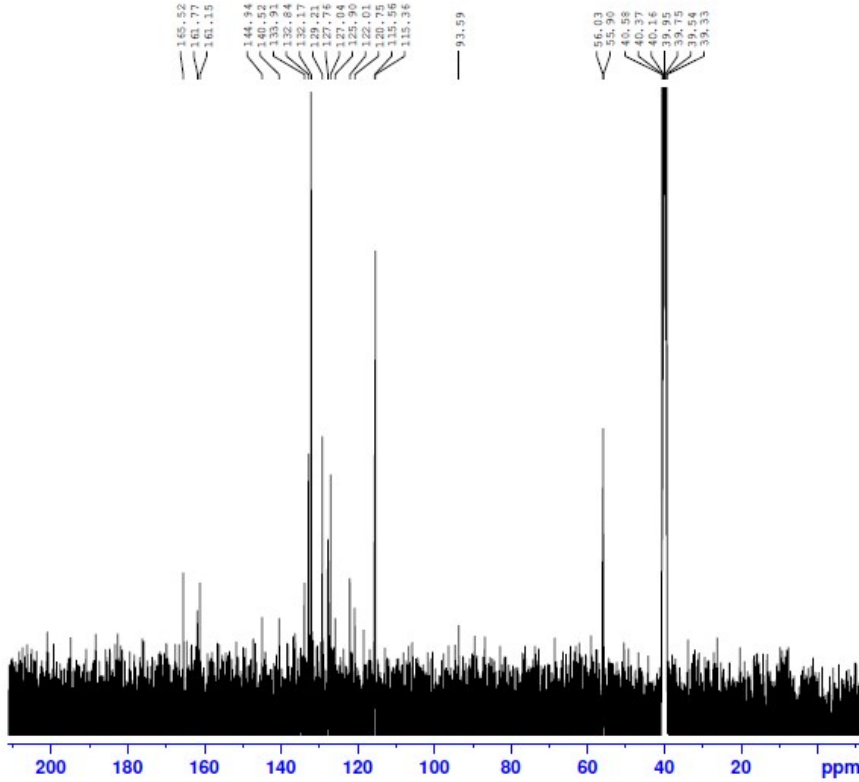


Current Data Parameters  
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 EXPNO 1  
 PROCNO 1

F2 - Acquisition Parameters  
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 SOLVENT DMSO  
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 DS 2  
 SWH 8012.820 Hz  
 FIDRES 0.122266 Hz  
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 RG 205.37  
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Current Data Parameters  
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PROCNO 1

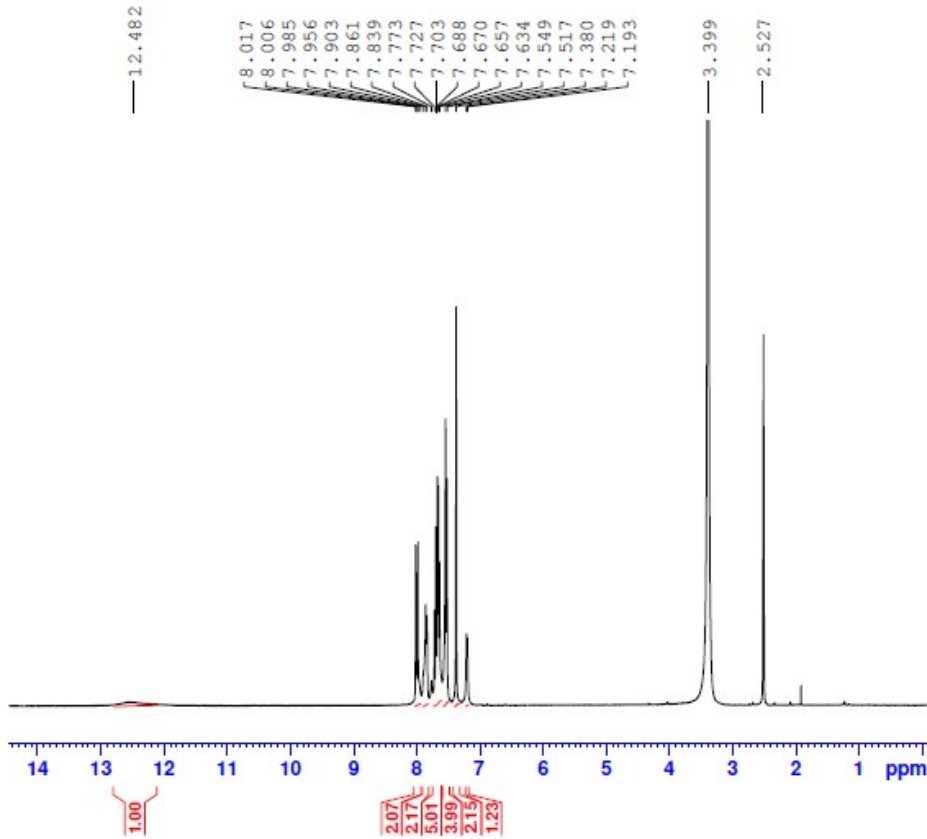
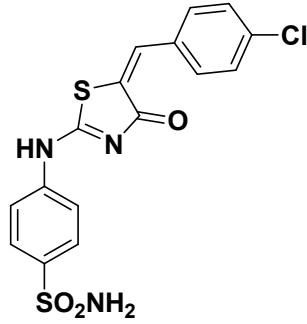
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SOLVENT DMSO  
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FIDRES 0.366798 Hz  
AQ 1.3631488 sec  
RG 205.37  
DW 20.800 usec  
DE 6.50 usec  
TE 300.0 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
TDO 1

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PLW1 47.00000000 W

==== CHANNEL f2 =====  
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NUC2 1H  
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PLW12 0.34722000 W  
PLW13 0.28125000 W

F2 - Processing parameters  
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# NMR Spectra for compound 4d

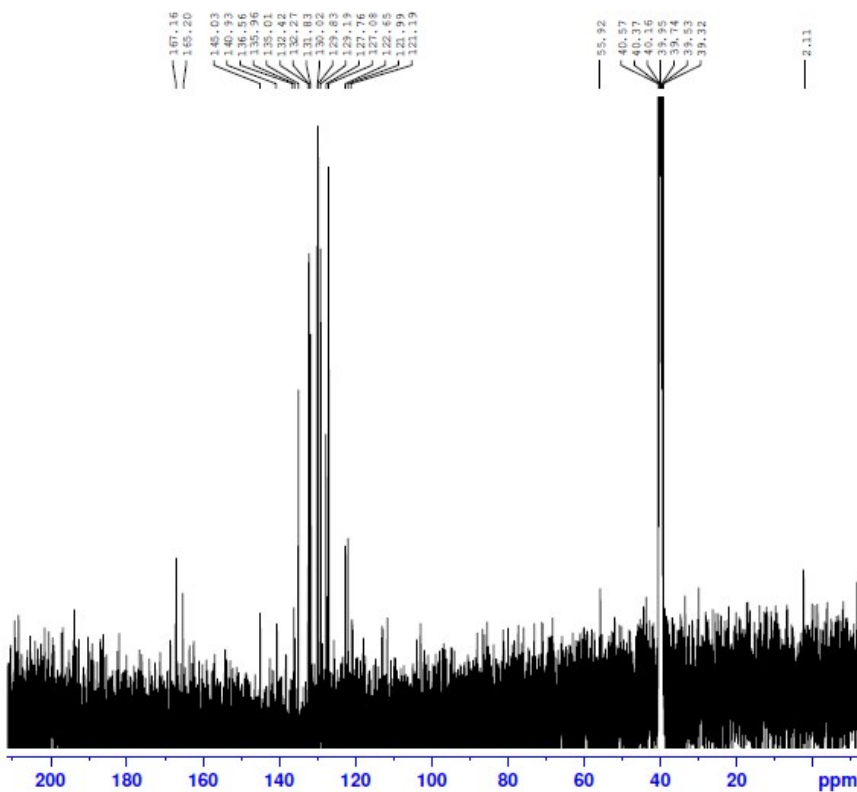


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 FIDRES 0.122266 Hz  
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 RG 205.37  
 DW 62.400 usec  
 DE 6.50 usec  
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 D1 1.0000000 sec  
 TDO 1

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 PLW1 18.00000000 W

F2 - Processing parameters  
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 PC 1.00



Current Data Parameters  
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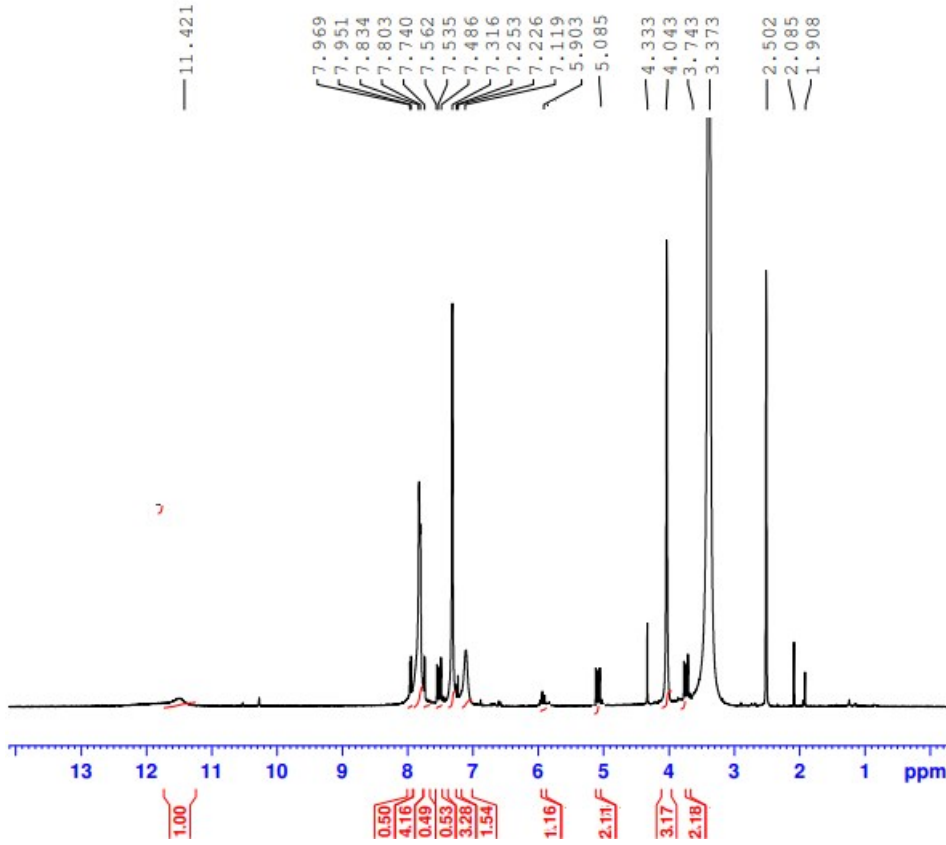
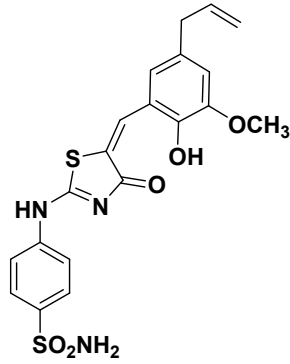
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 FIDRES 0.366798 Hz  
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 RG 205.37  
 DW 20.800 usec  
 DE 6.50 usec  
 TE 300.0 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1

==== CHANNEL f1 =====  
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 NUC1 13C  
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 PLW1 47.00000000 W

==== CHANNEL F2 =====  
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 NUC2 1H  
 CPDPRG[2] waltz16  
 PCPD2 90.00 usec  
 PLW2 18.00000000 W  
 PLW12 0.34722000 W  
 PLW13 0.28125000 W

F2 - Processing parameters  
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 WDW EM  
 SSB 0  
 LB 1.00 Hz  
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# NMR Spectra for compound 4e



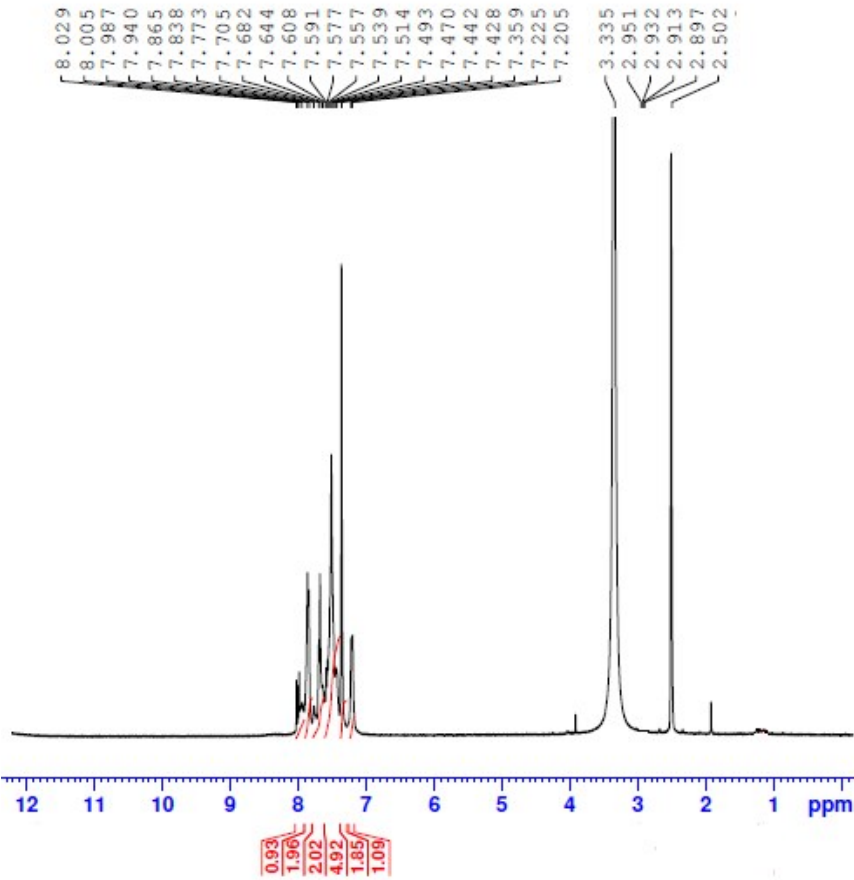
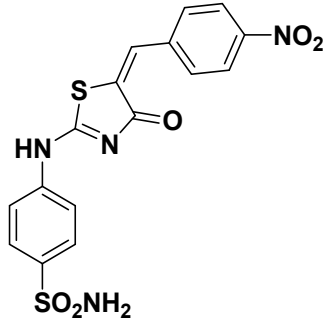
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 SOLVENT DMSO  
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 FIDRES 0.122266 Hz  
 AQ 4.0894465 sec  
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 DE 6.50 usec  
 TE 300.0 K  
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===== CHANNEL f1 =====  
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 NUC1 1H  
 P1 12.00 usec  
 PLW1 18.00000000 W

F2 - Processing parameters  
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 GB 0  
 PC 1.00

# NMR Spectra for compound 4g



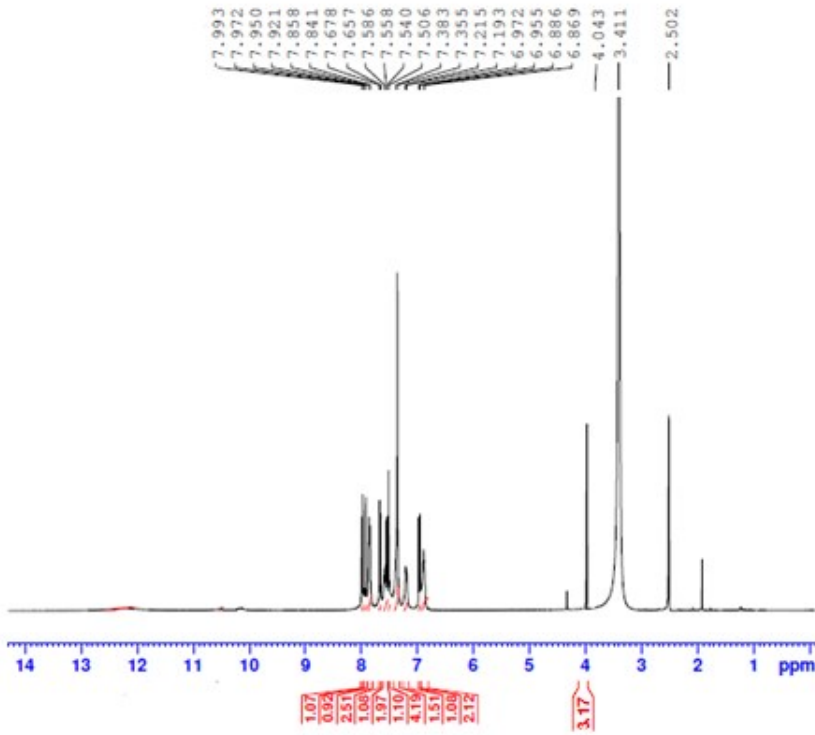
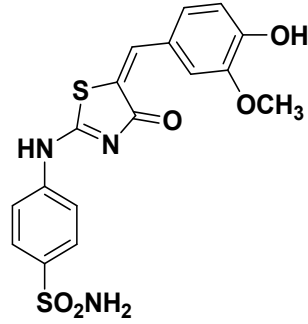
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 SWH 8012.820 Hz  
 FIDRES 0.122266 Hz  
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 DE 6.50 usec  
 TE 300.0 K  
 D1 1.0000000 sec  
 TDO 1

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 NUC1 1H  
 P1 12.00 usec  
 PLW1 18.0000000 W

F2 - Processing parameters  
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 PC 1.00

# NMR Spectra for compound 4h



```

Current Data Parameters
NAME      asmas-magd-4f
EXPNO    1
PROCNO   1

F2 - Acquisition Parameters
Date_    20200504
Time     14.08
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zg30
TD        65536
SOLVENT  DMSO
NS        128
DS        2
SWH       8012.820 Hz
FIDRES    0.122266 Hz
AQ         4.0894465 sec
RG         209.37
DM         62.400 usec
DE         6.50 usec
TE         300.0 K
D1         1.00000000 sec
TDO        1

===== CHANNEL f1 =====
SPD1      400.1524711 MHz
NUC1      1H
P1        12.00 usec
P1M1      18.00000000 M

F2 - Processing parameters
SI        65536
SF        400.1500000 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
    
```