

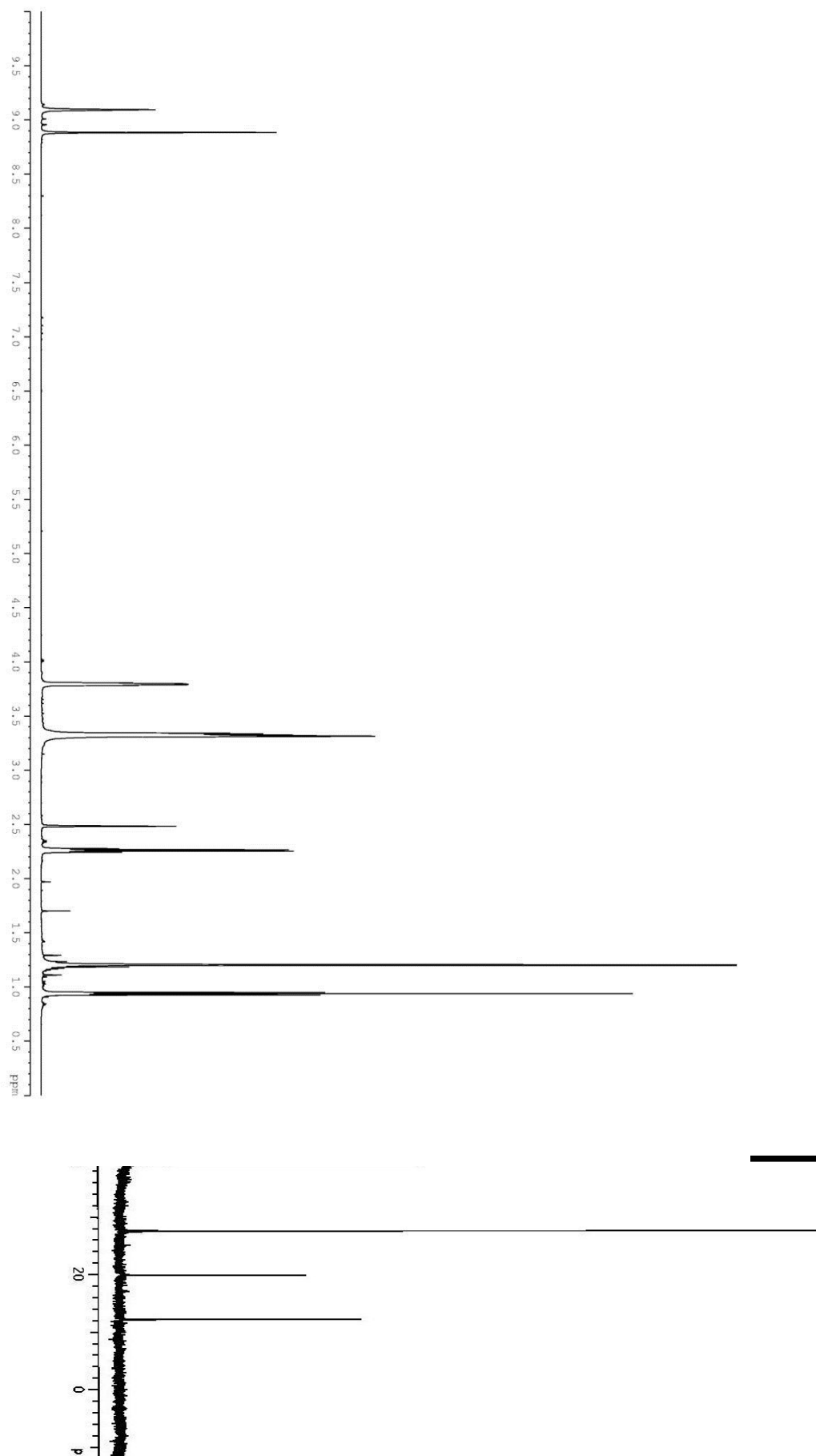
## SUPPORTING INFORMATION

1. Reagents and general experimental procedure	S2
2. <sup>1</sup> H NMR spectrum (DMSO) of <b>17</b>	S3
3. <sup>13</sup> C NMR spectrum (DMSO) of <b>17</b>	S4
4. COSY spectrum of (DMSO) of <b>17</b>	S5
5. HSQC spectrum of (DMSO) of <b>17</b>	S6
6. HMBC spectrum of (DMSO) of <b>17</b>	S7
7. ESI mass spectrum of <b>17</b>	S8
8. <sup>1</sup> H NMR spectrum (DMSO) of <b>20</b>	S9
9. <sup>13</sup> C NMR spectrum (DMSO) of <b>20</b>	S10
10. COSY spectrum of (DMSO) of <b>20</b>	S11
11. HSQC spectrum of (DMSO) of <b>20</b>	S12
12. HMBC spectrum of (DMSO) of <b>20</b>	S13
13. ESI mass spectrum of of <b>20</b>	S14
14. <sup>1</sup> H NMR spectrum (DMSO) of <b>18</b>	S15
15. <sup>13</sup> C NMR spectrum (DMSO) of <b>18</b>	S16
16. ESI mass spectrum of of <b>18</b>	S17
17. <sup>1</sup> H NMR spectrum (DMSO) of <b>21</b>	S18
18. <sup>13</sup> C NMR spectrum (DMSO) of <b>21</b>	S19
19. <sup>1</sup> H ESI mass spectrum of of <b>21</b>	S20
20. <sup>1</sup> H NMR spectrum (DMSO) of <b>19</b>	S21
21. <sup>13</sup> C NMR spectrum (DMSO) of <b>19</b>	S22
22. ESI mass spectrum of of <b>19</b>	S23
23. <sup>1</sup> H NMR spectrum (DMSO) of <b>22</b>	S24
24. <sup>13</sup> C NMR spectrum (DMSO) of <b>22</b>	S25
25. ESI mass spectrum of of <b>22</b>	S26
26. Purity criteria for tested compounds	S27
27. Table 1SI	S28
28. Table 2SI	S29
29. Table 3SI	S30
30. Figure 1SI	S31
31. Figure 2SI	S32
32. Figure 3SI	S33

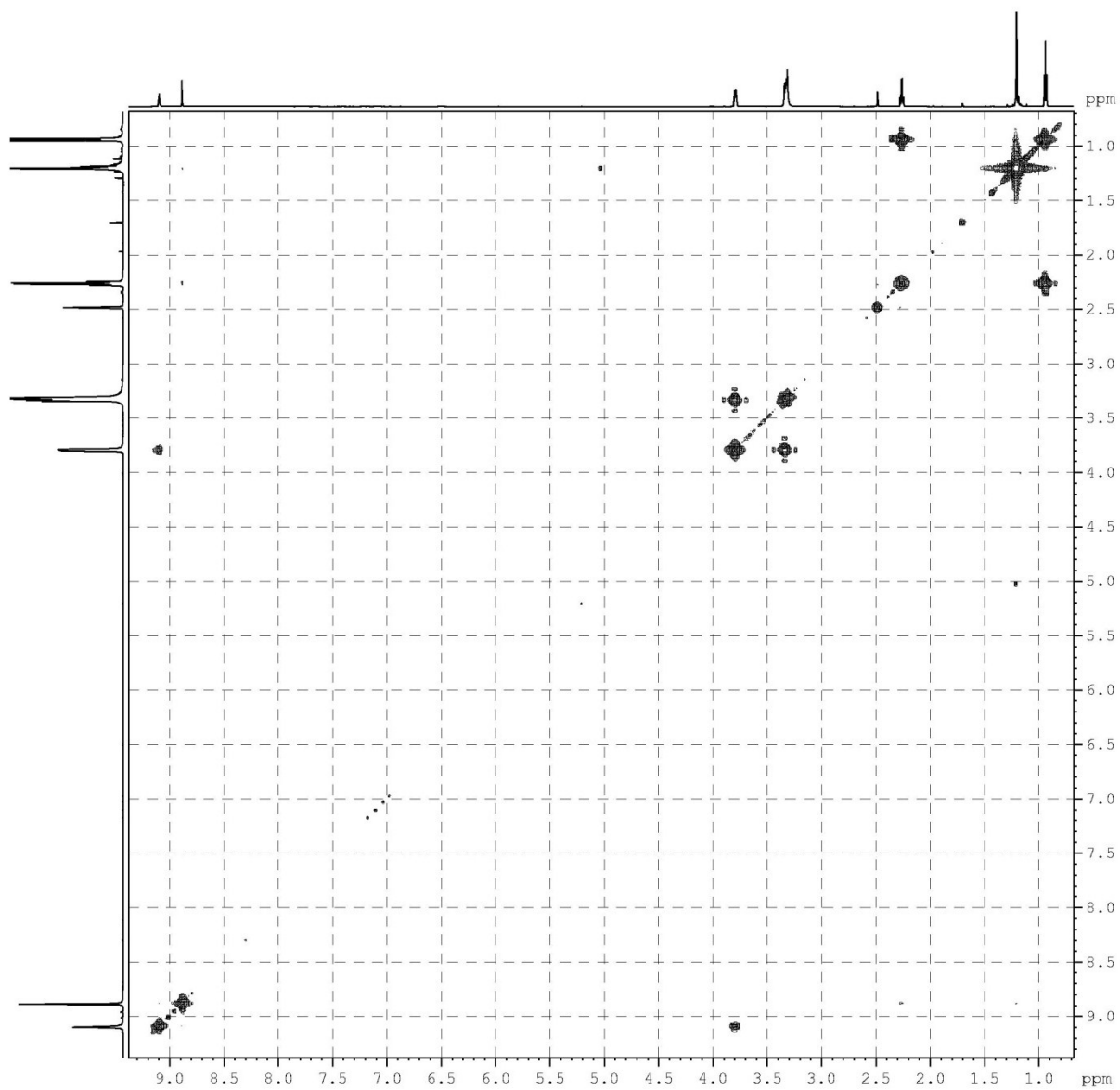
## Reagents and general experimental procedure

Commercial reagents: Sigma–Aldrich. Solvents: Carlo Erba. TLC: Silica Gel 60 F254 (plates 5 x 20, 0.25 mm) Merck. Preparative TLC: Silica Gel 60 F254 plates (20 x 20, 2 mm). Spots revealed by UV lamp then by spraying with 2 N sulfuric acid and heating at 120 °C. ‘Acidic’ silica gel was prepared by treating Silica Gel 60 Merck with 1 N HCl for 24 h, washing with water until the chlorine test was negative, activating for 48 h at 120 °C, then equilibrating with 10% of water. Anhydrous solvents: Sigma–Aldrich or prepared by distillation according to standard procedures. ESI mass spectra were performed on a hybrid quadrupole-TOF mass spectrometer, dissolving the sample in MeOH. The spectra were recorded by infusion into the ESI source using MeOH as the solvent. EI mass spectra were obtained on GC-MS HP 5890, HP 5971A Mass selective detector.  $^1\text{H}$  (700 MHz) and  $^{13}\text{C}$  (175 MHz) NMR spectra were recorded on a Varian INOVA spectrometer respectively; chemical shifts were referenced to the residual solvent signal ( $\text{CDCl}_3$ :  $\delta_{\text{H}}=7.26$ ,  $\delta_{\text{C}}=77.0$ ). For an accurate measurement of the coupling constants, the one-dimensional  $^1\text{H}$  NMR spectra were transformed at 64 K points (digital resolution: 0.09 Hz). Homonuclear ( $^1\text{H}$ -  $^1\text{H}$ ) and heteronuclear ( $^1\text{H}$ - $^{13}\text{C}$ ) connectivities were determined by COSY and HSQC experiments, respectively. Two and three bond  $^1\text{H}$ - $^{13}\text{C}$  connectivities were determined by gradient 2D HMBC experiments optimized for a  $^{2,3}J$  of 8 Hz. Routine  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded with a Varian Gemini 200 MHz or a Varian Mercury 300 MHz or a Bruker Avance 400 MHz. High performance liquid chromatography (HPLC) separations were achieved on a Knauer 501 apparatus equipped with an RI detector.

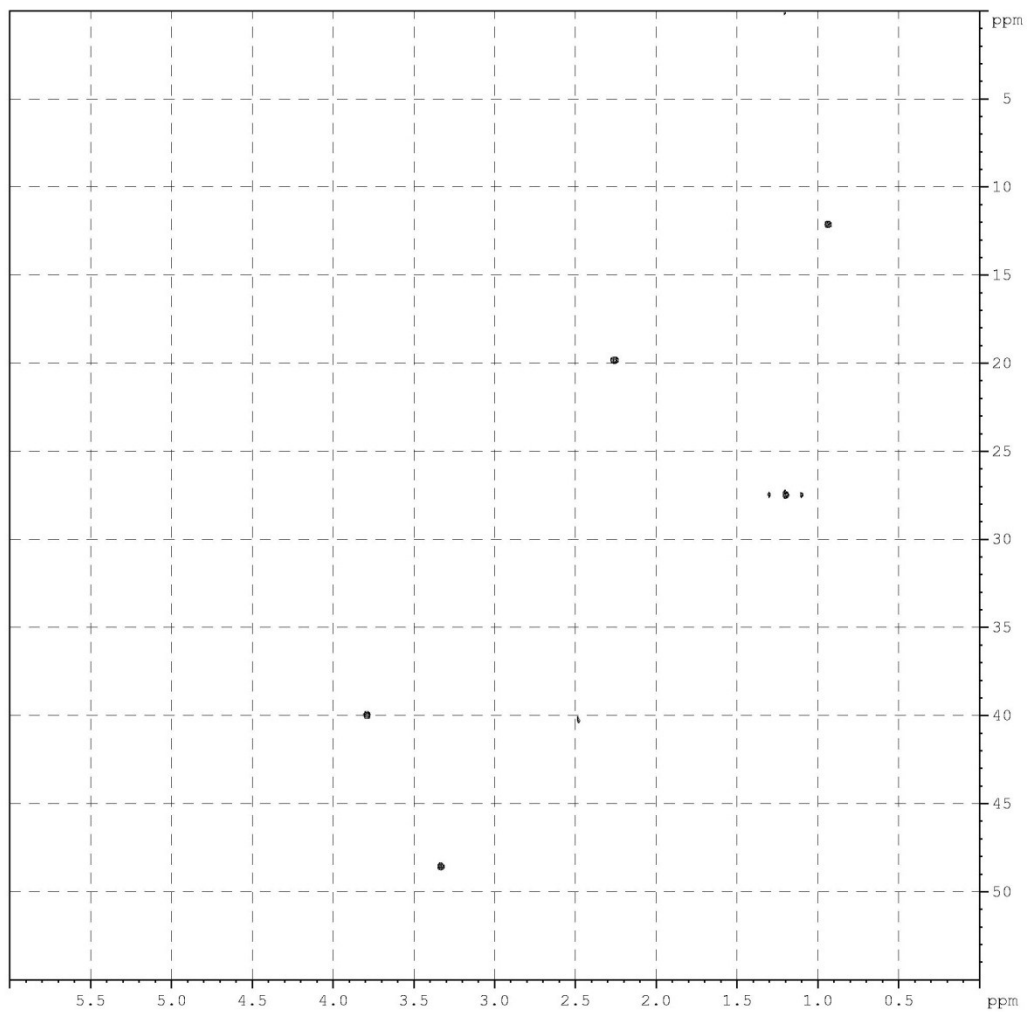
$^1\text{H}$  NMR in DMSO of 17



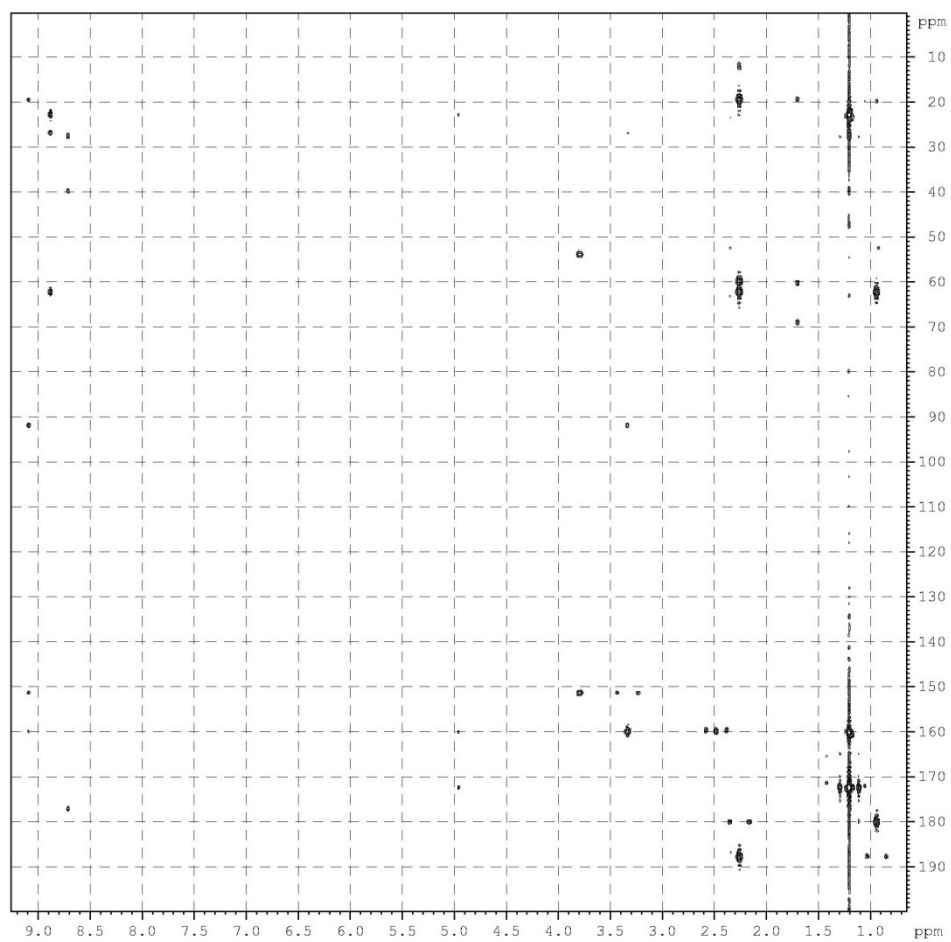
COSY in DMSO of 17



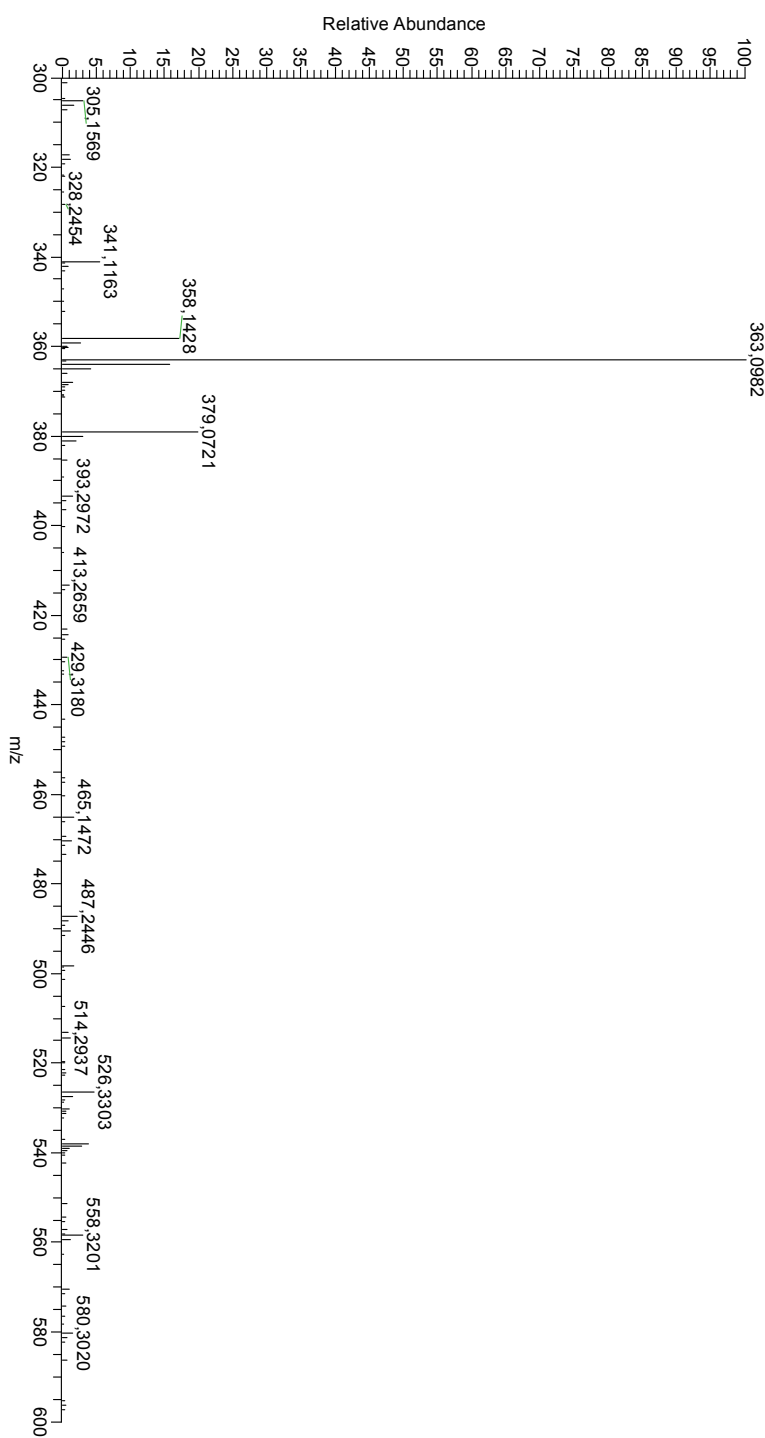
# HSQC in DMSO of 17



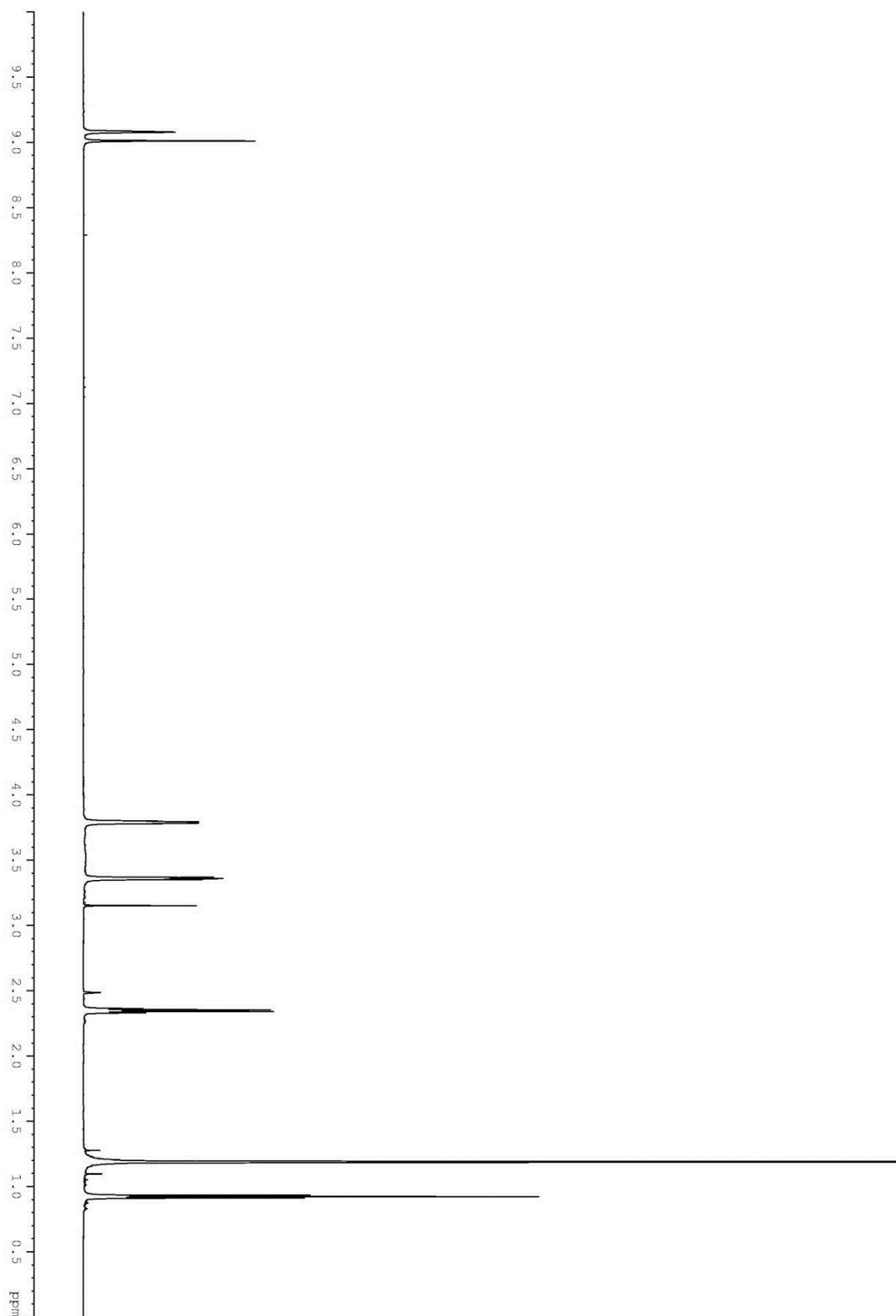
# HMBC in DMSO of 17



# ESI mass spectrum of 17

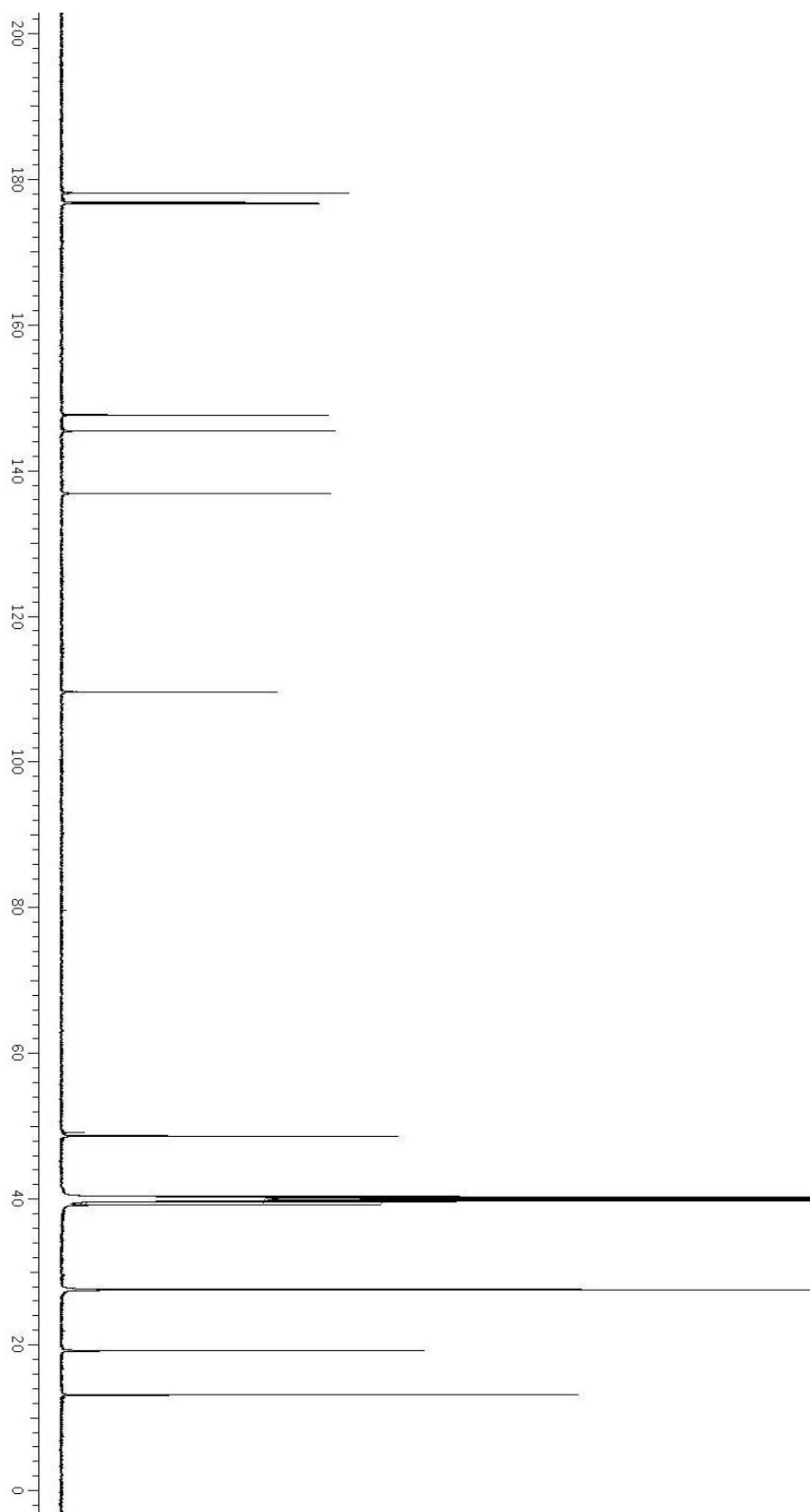


$^1\text{H}$  NMR in DMSO of **20**

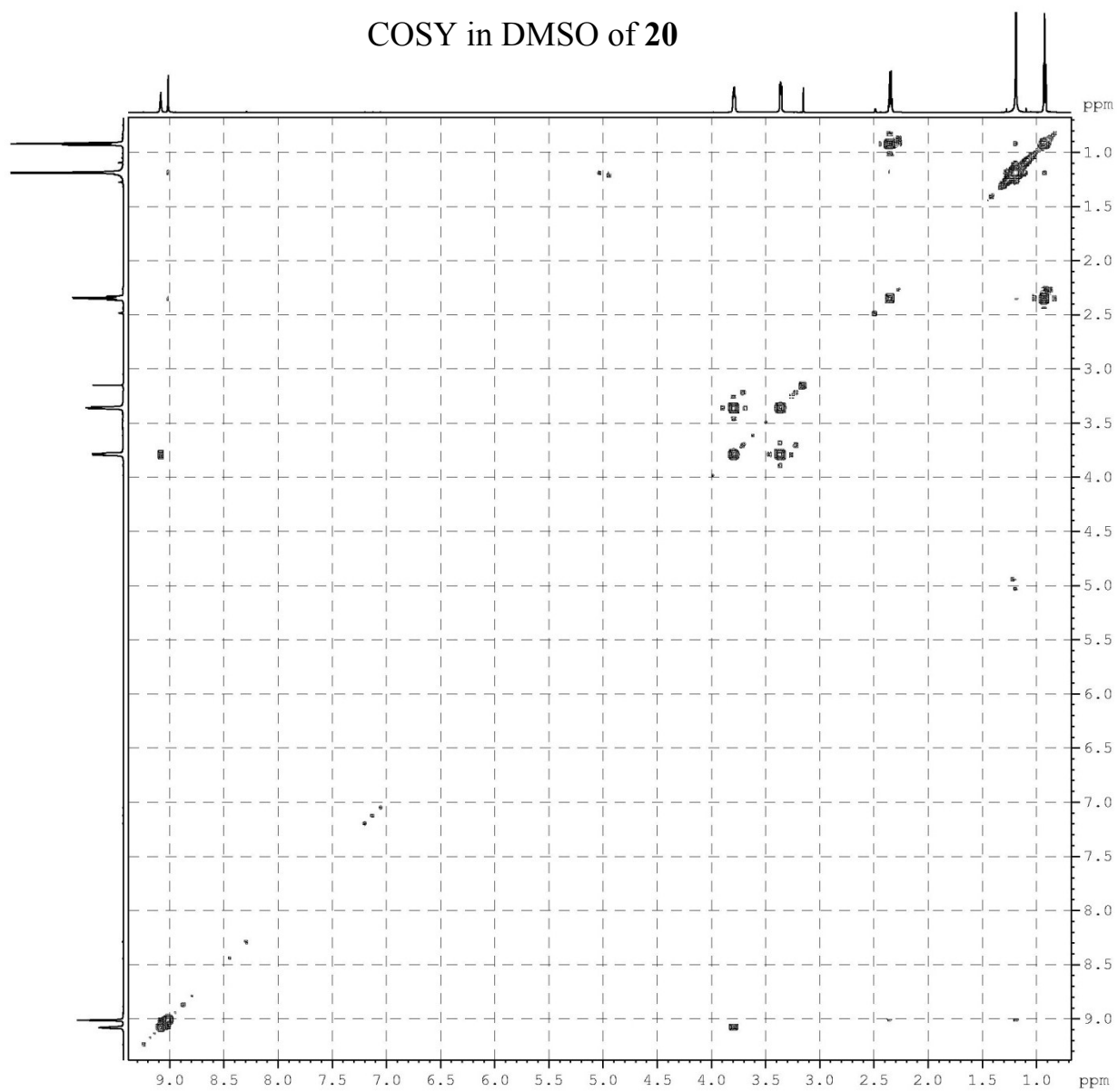




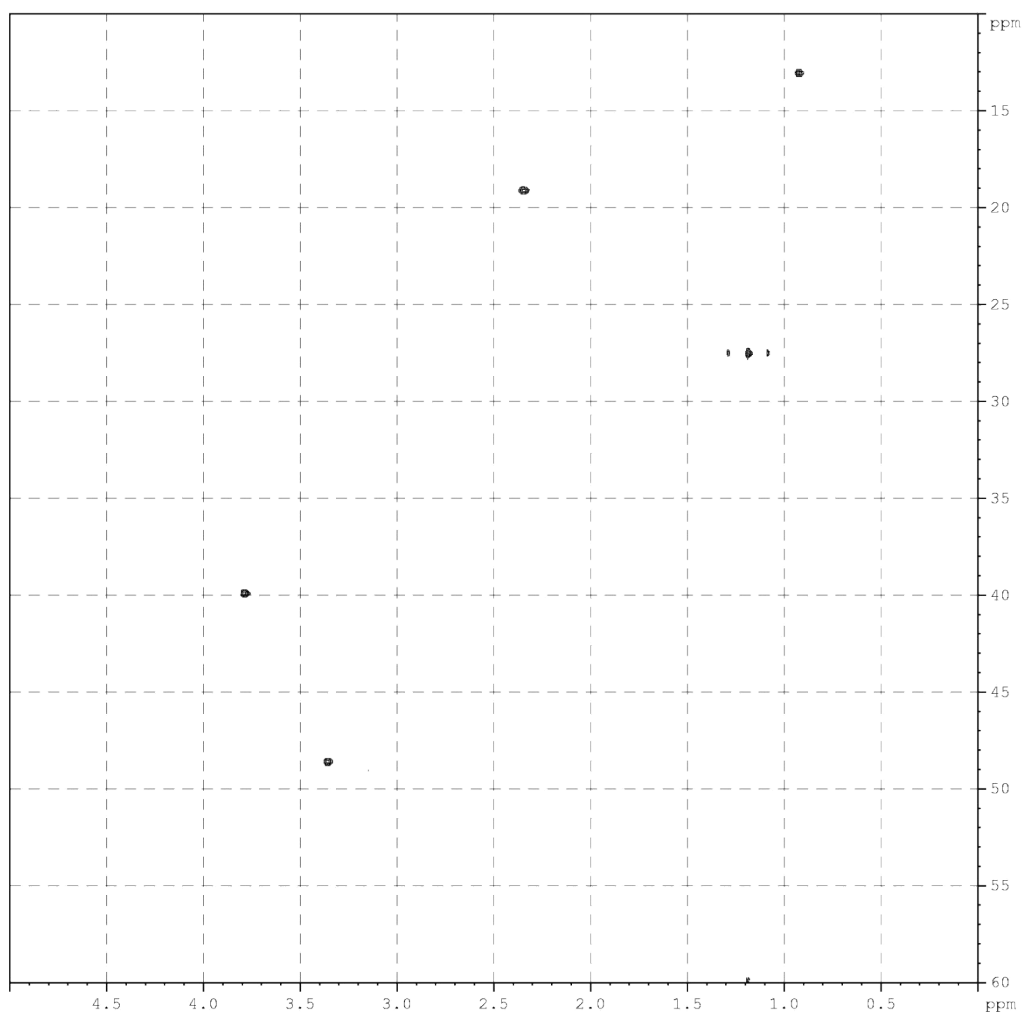
$^{13}\text{C}$  NMR in DMSO of **20**



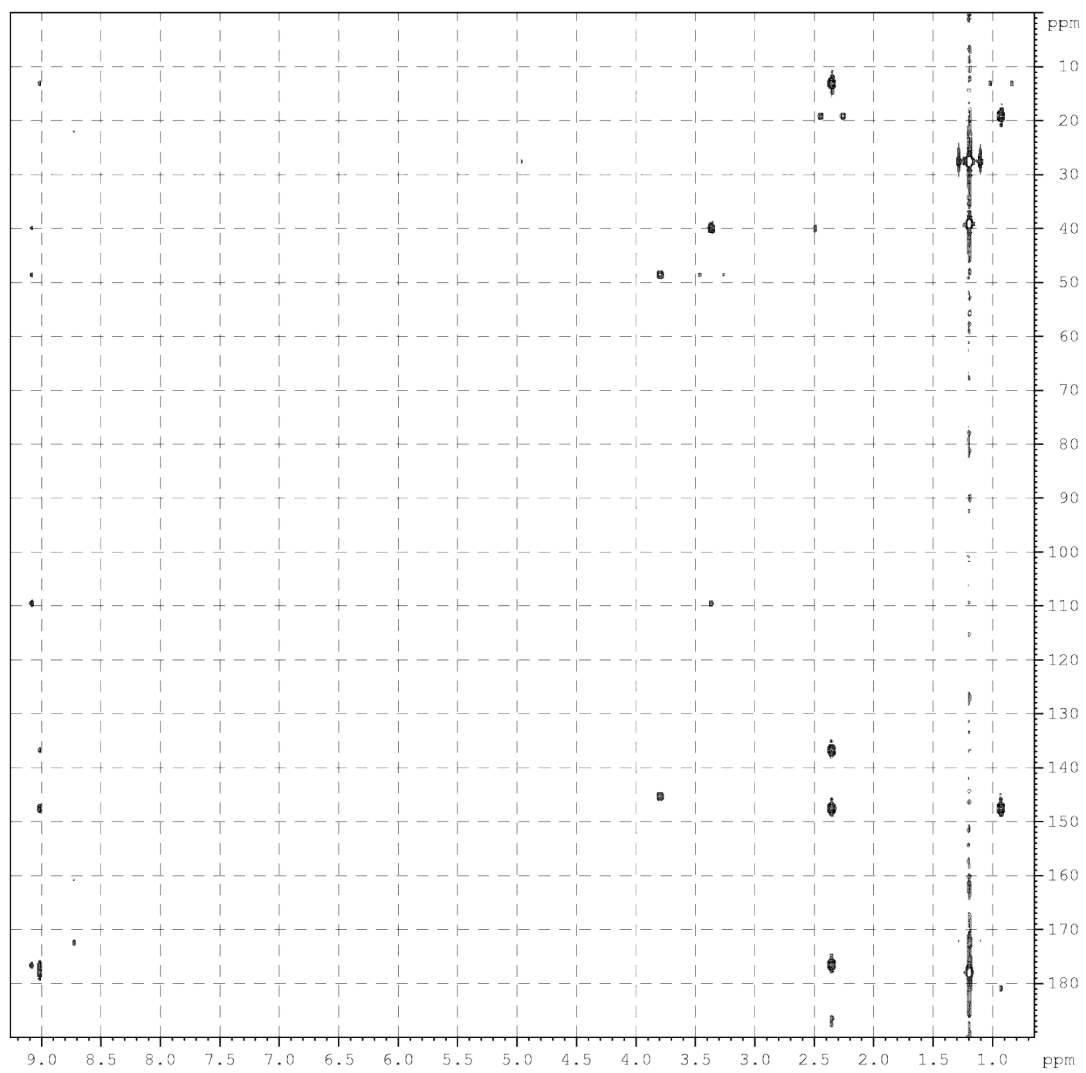
COSY in DMSO of 20



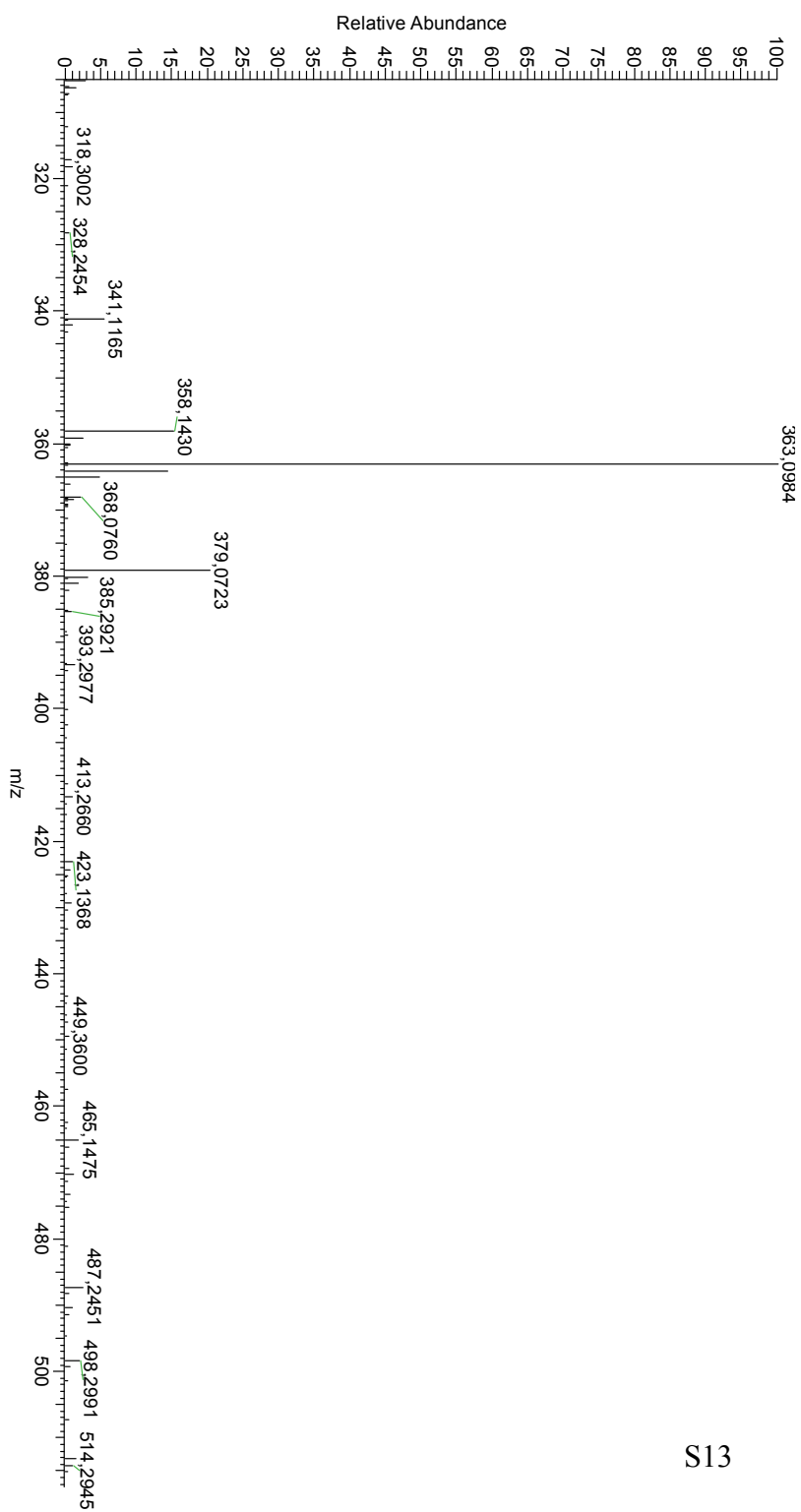
# HSQC in DMSO of **20**



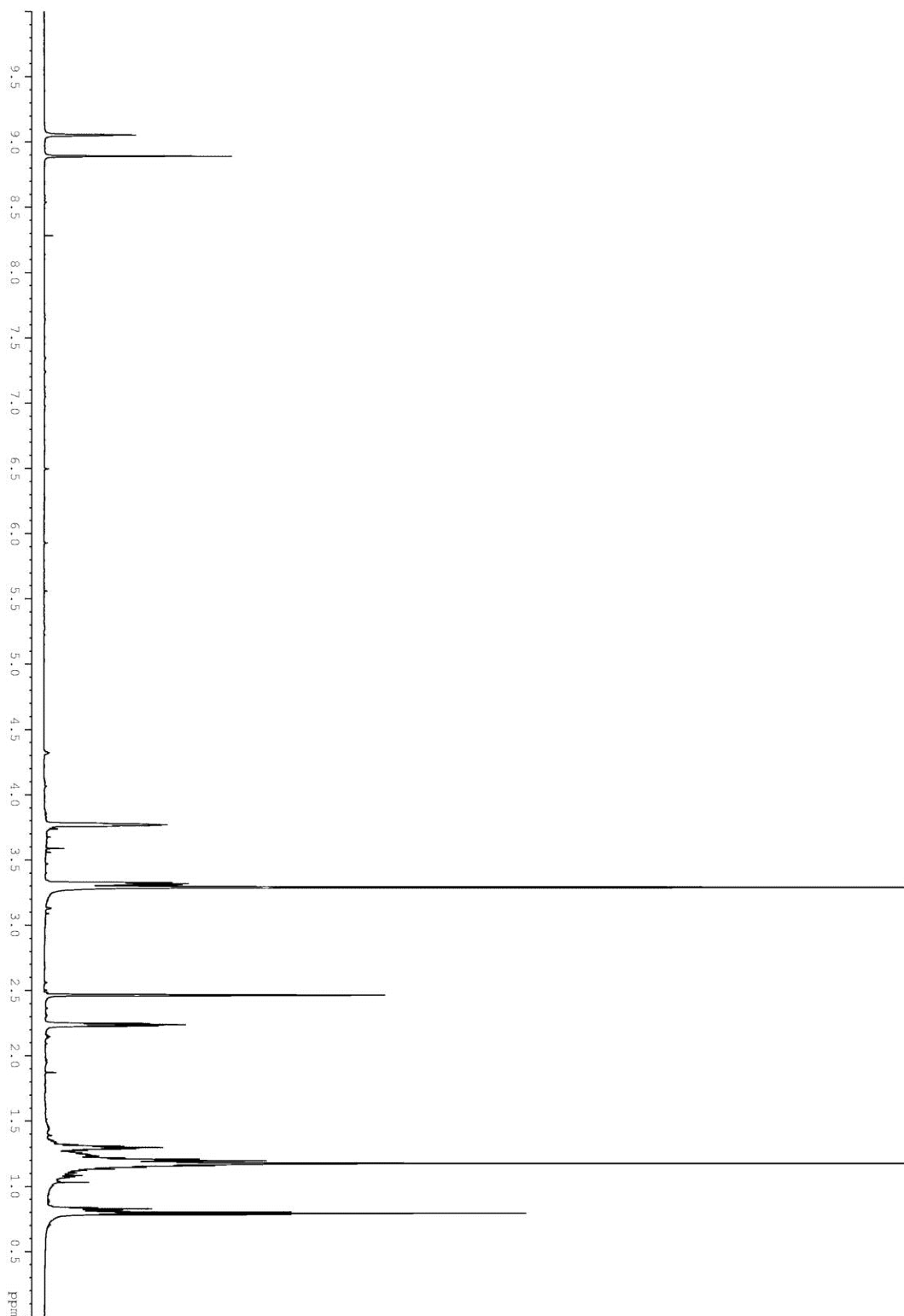
# HMBC in DMSO of 20



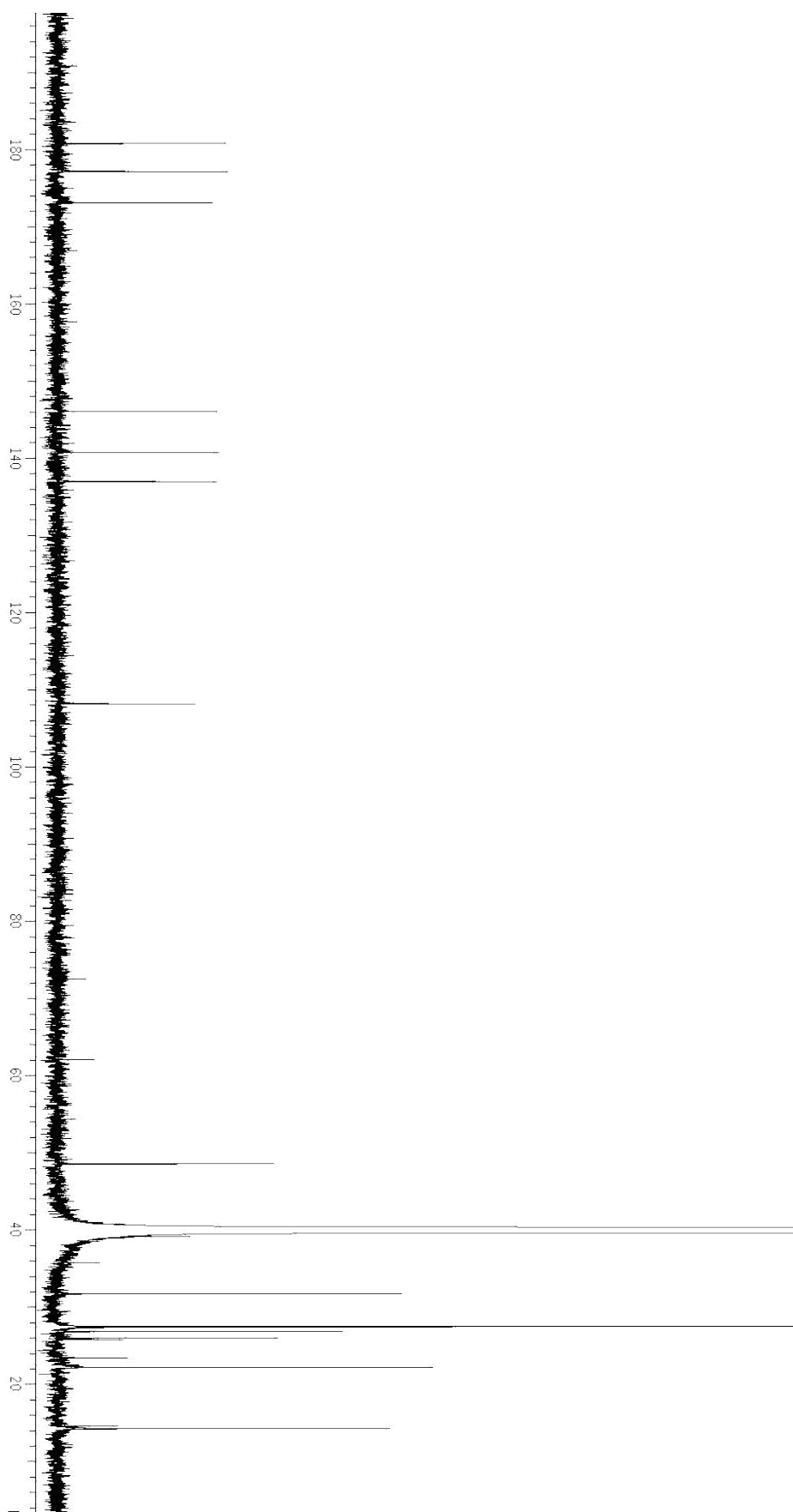
# ESI mass spectrum of **20**



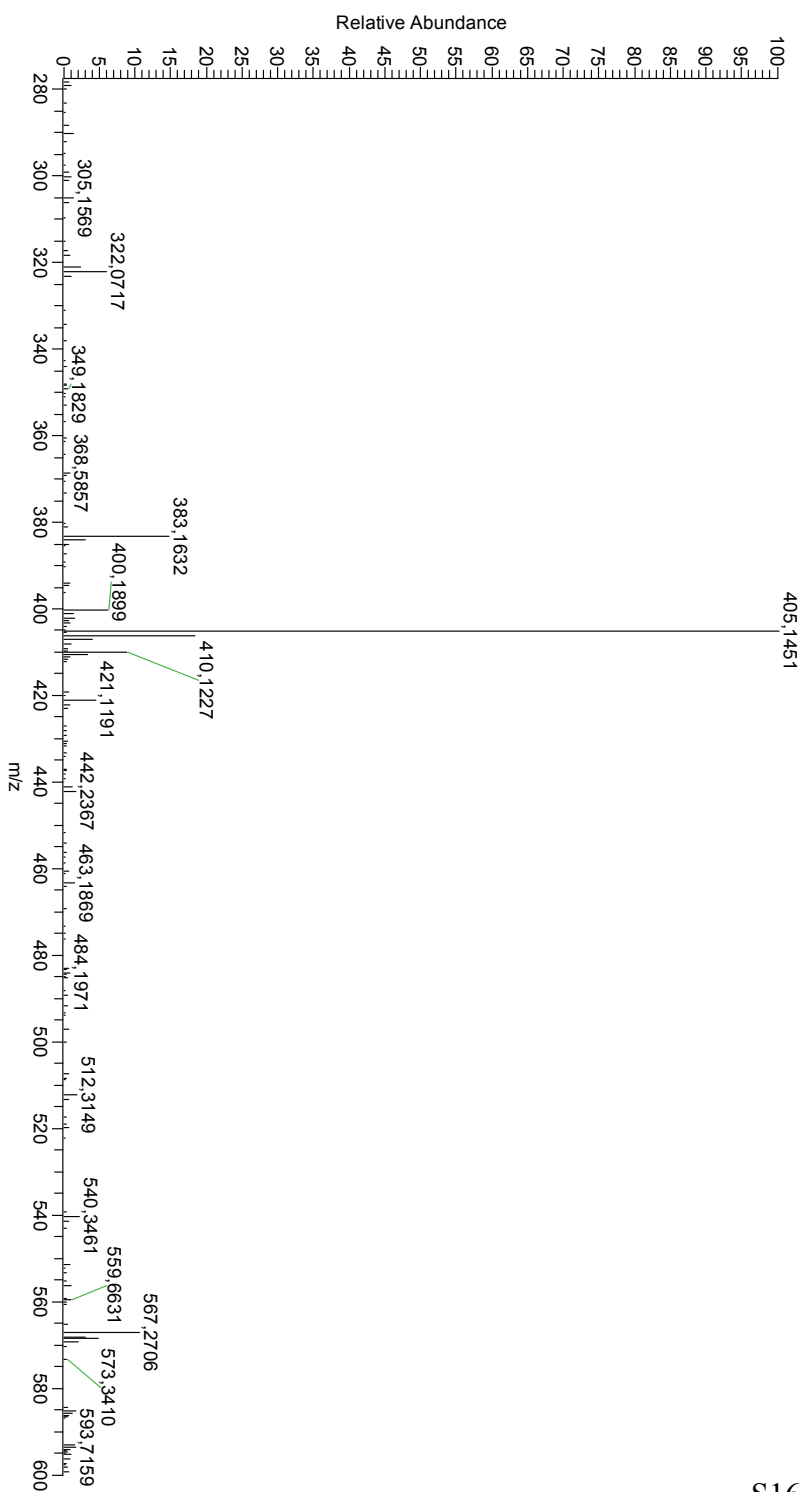
$^1\text{H}$  NMR in DMSO of **18**



$^{13}\text{C}$  NMR in DMSO of **18**

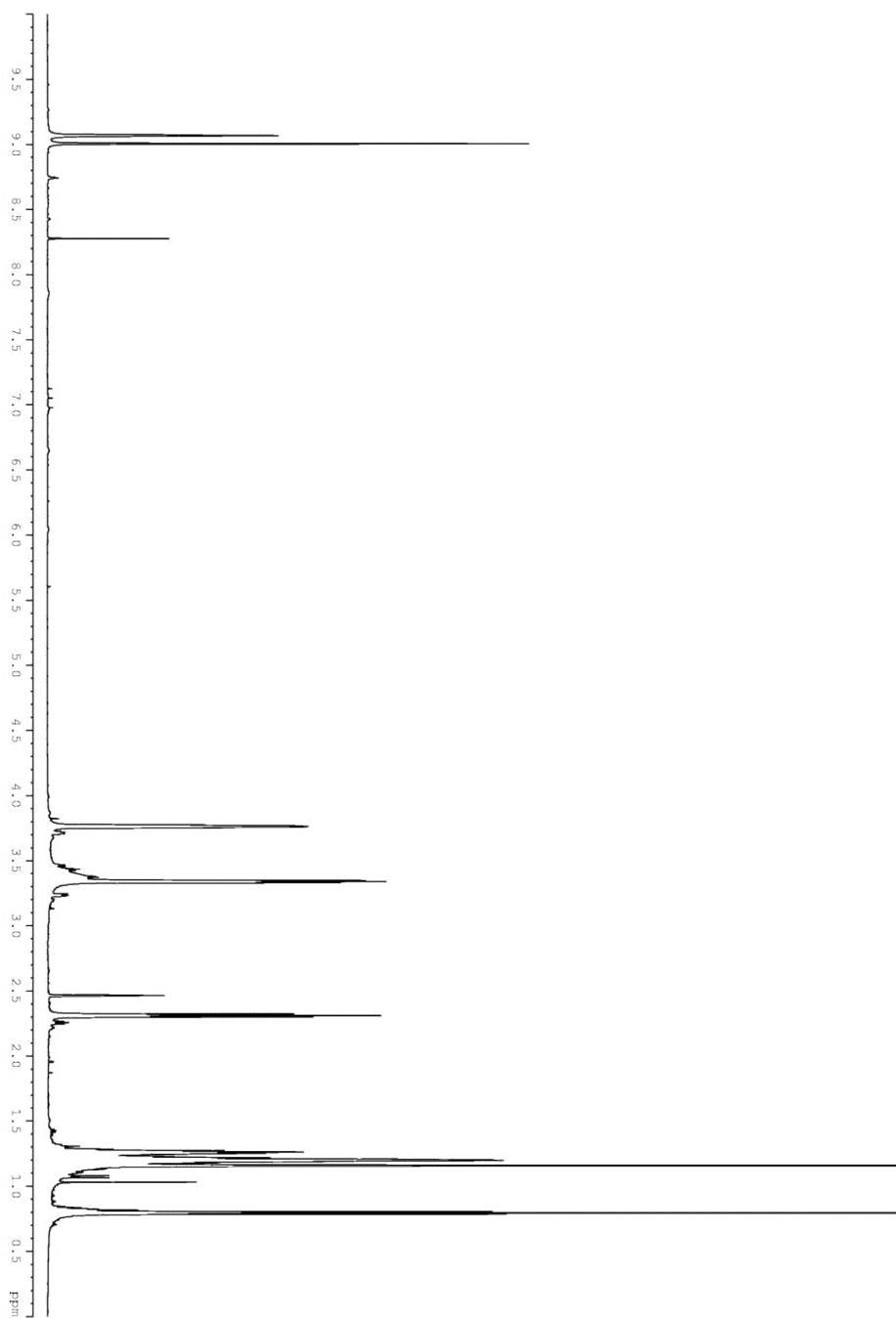


# ESI mass spectrum of 18

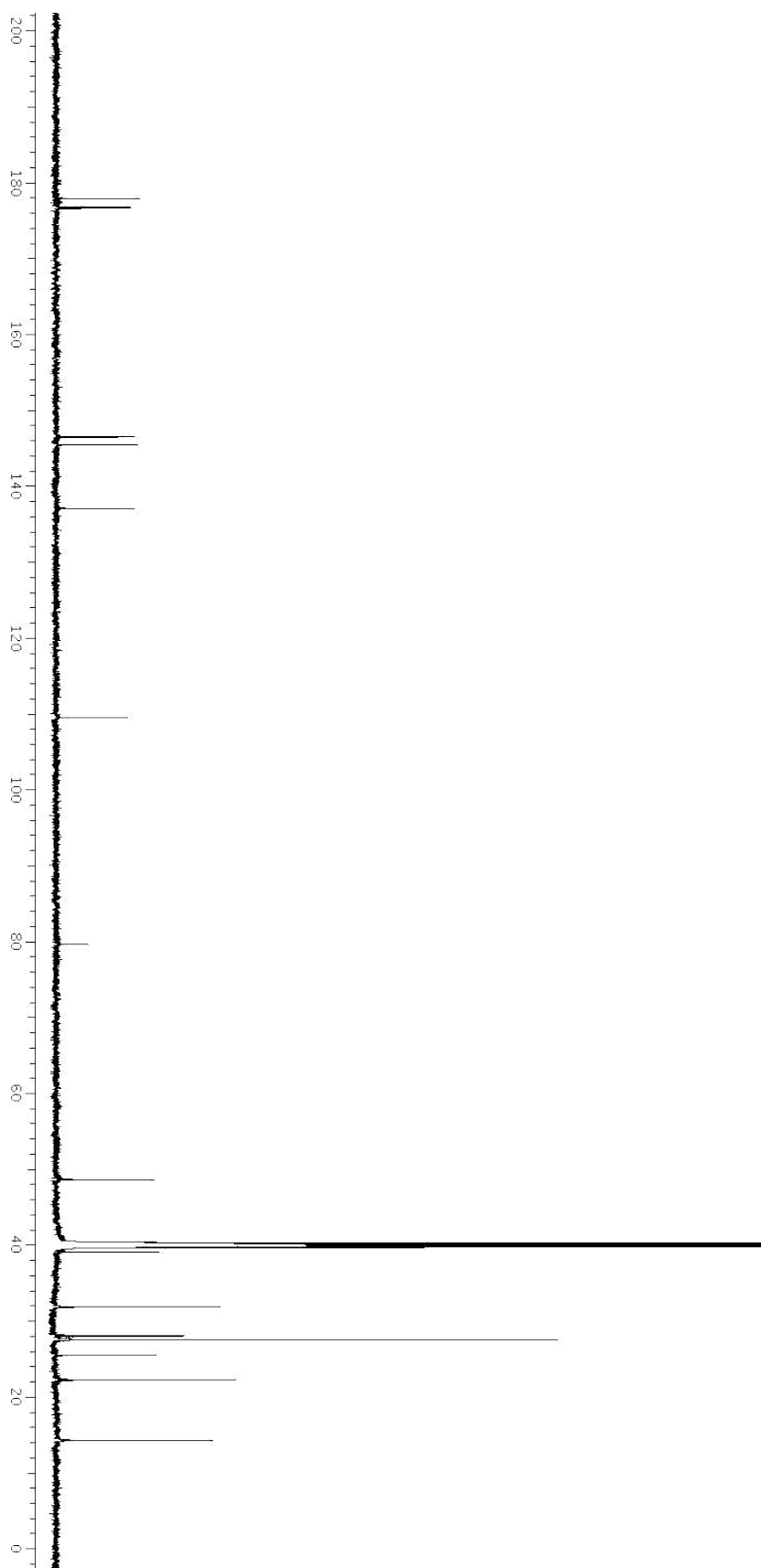




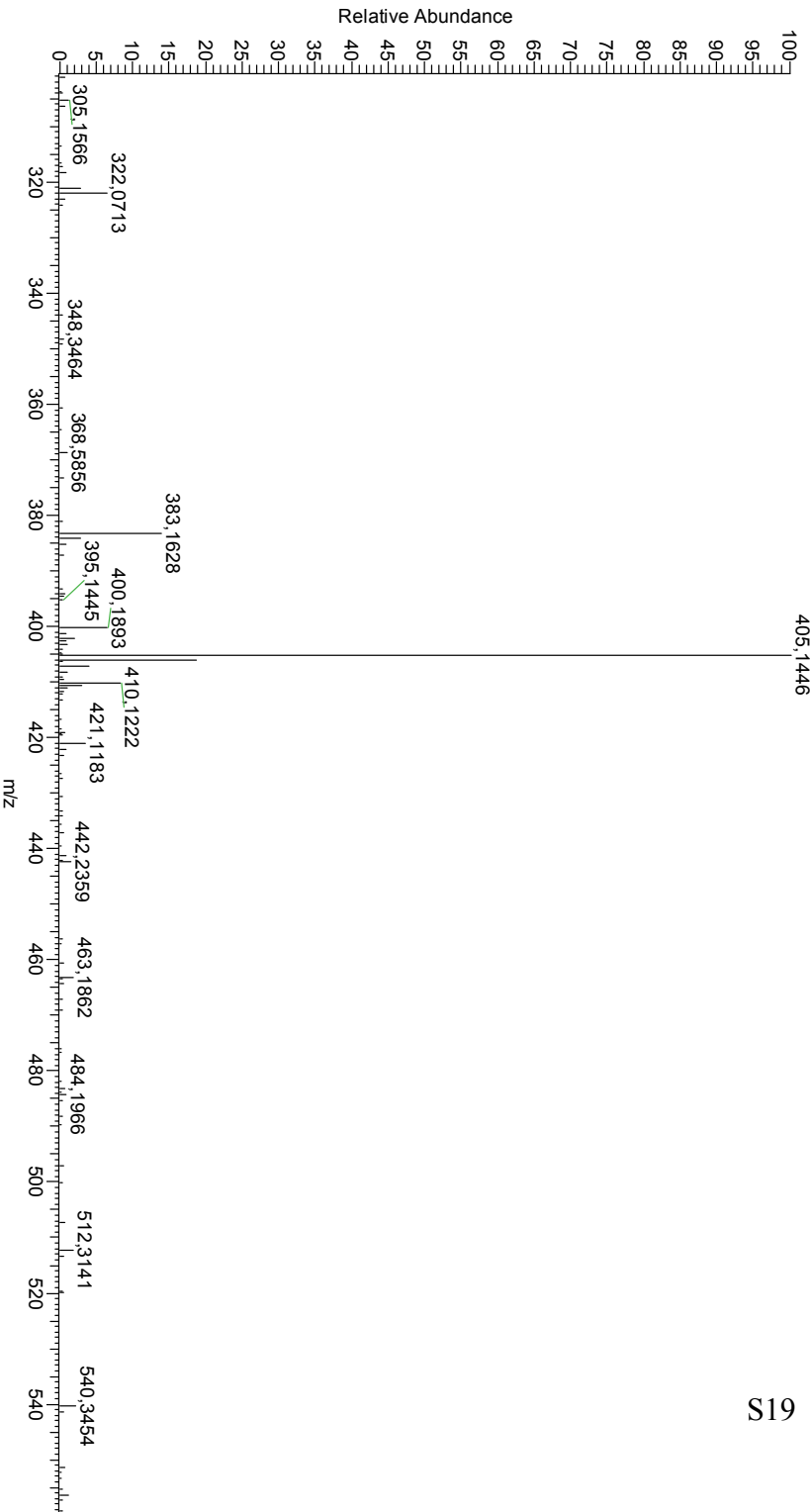
$^1\text{H}$  NMR in DMSO of **21**



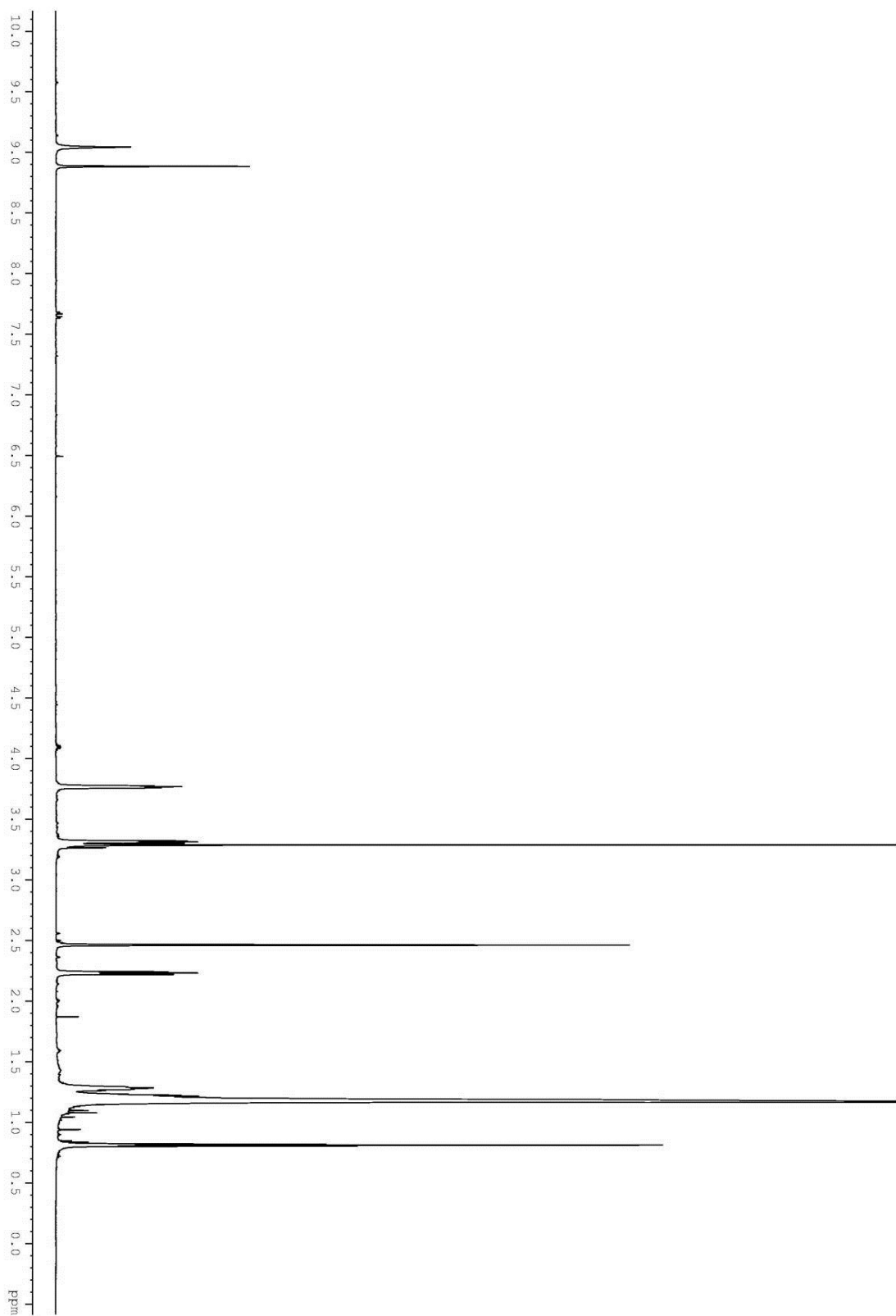
$^{13}\text{C}$  NMR in DMSO of **21**



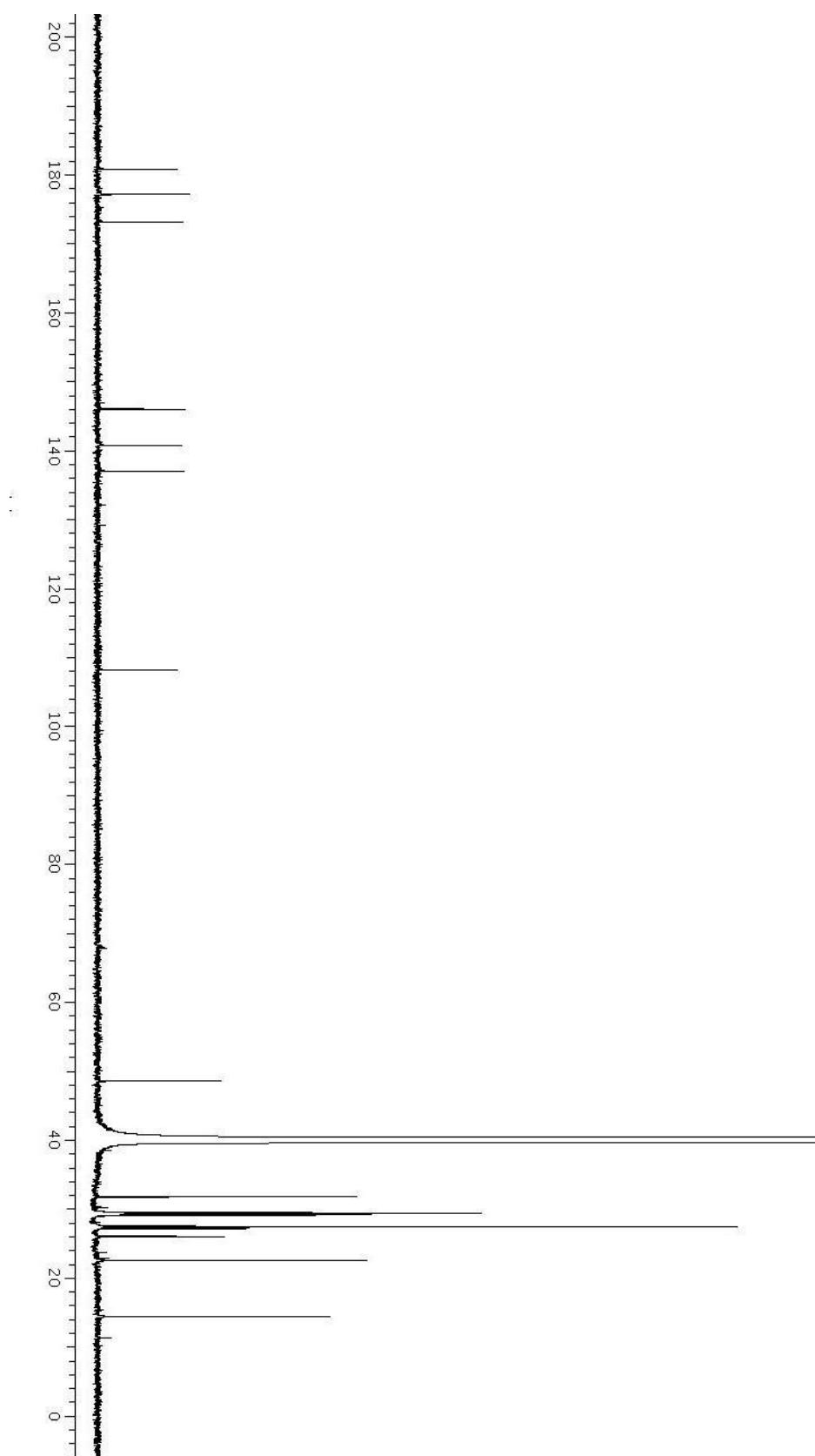
# ESI mass spectrum of 21



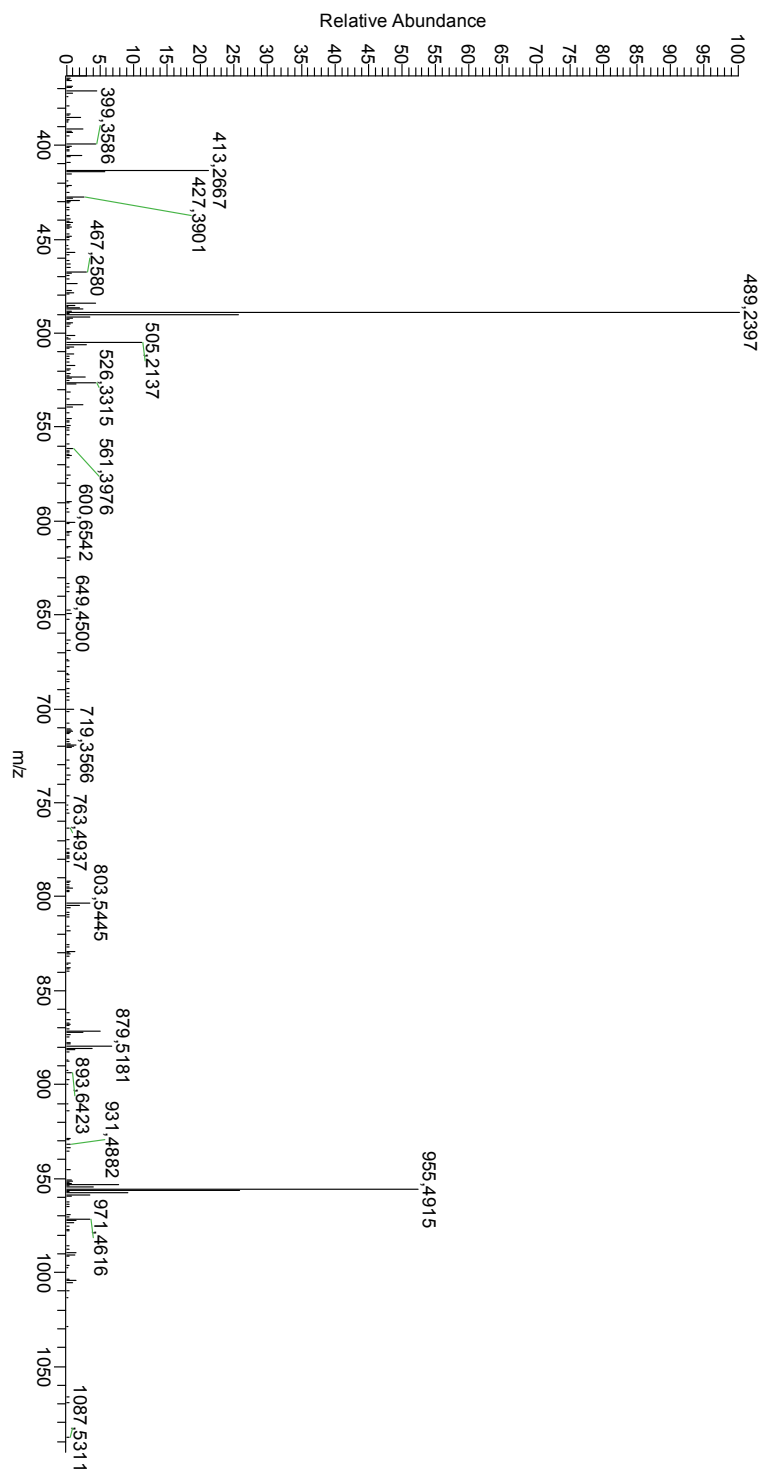
$^1\text{H}$  NMR in DMSO of **19**



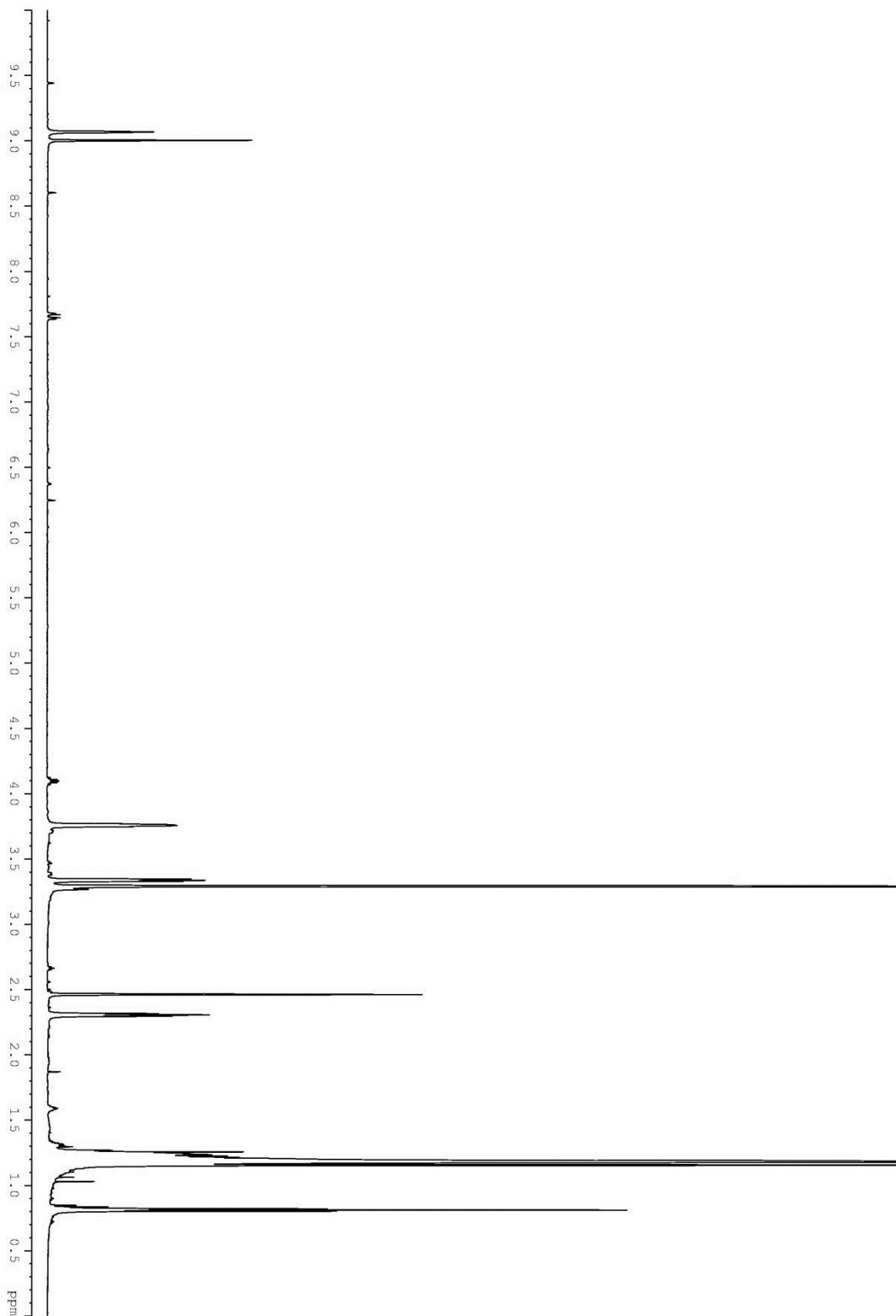
$^{13}\text{C}$  NMR in DMSO of **19**



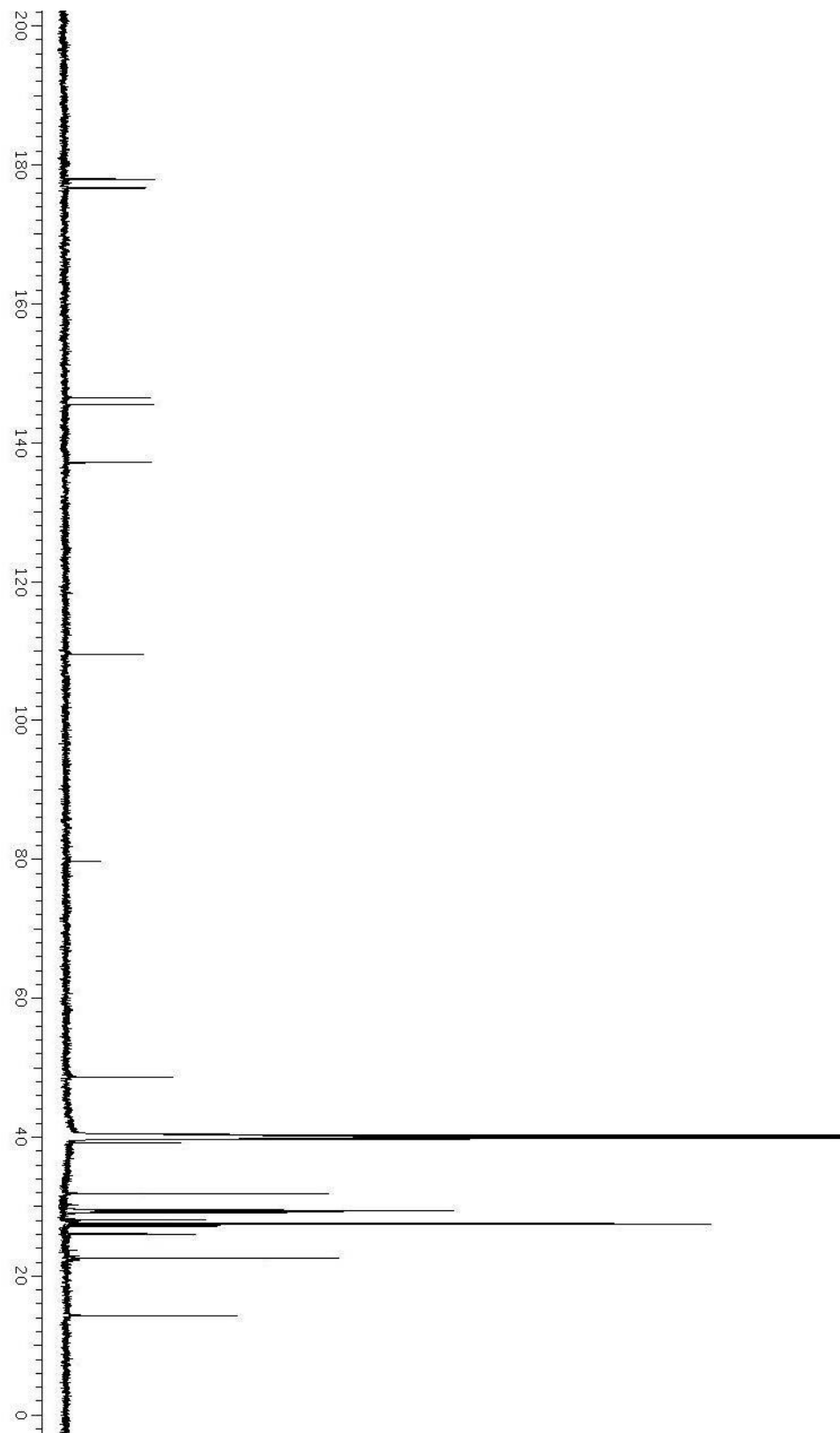
# ESI mass spectrum of 19



$^1\text{H}$  NMR in DMSO of **22**

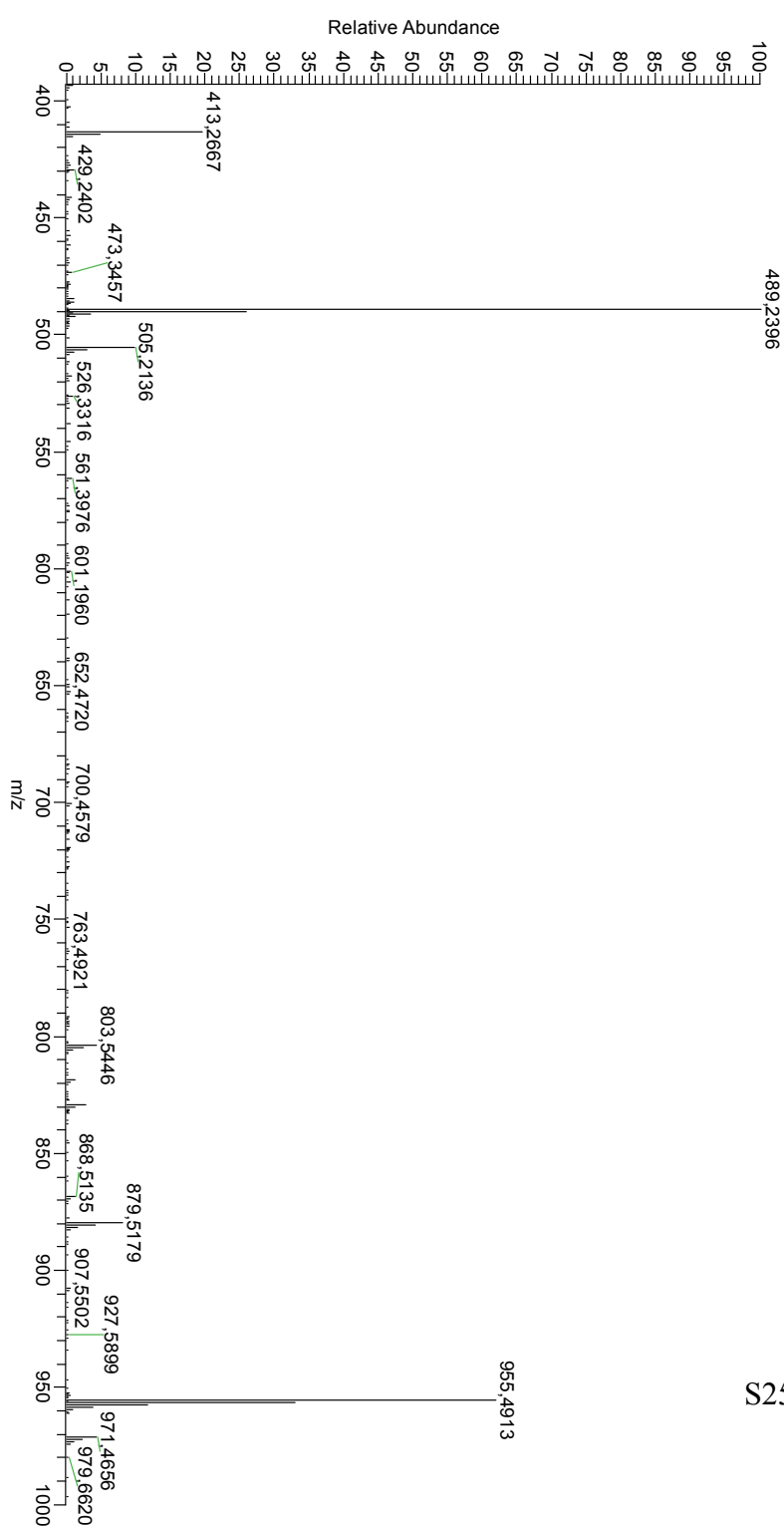


$^{13}\text{C}$  NMR in DMSO of **22**





# ESI mass spectrum of 22



S25

### Purity criteria for tested compounds.

Compounds	Purity <sup>a</sup>	t <sub>R</sub> <sup>b</sup>	Compounds	Purity <sup>a</sup>	t <sub>R</sub> <sup>b</sup>
<b>11</b>	95.8%	13.9	<b>17</b>	97.2%	9.1
<b>12</b>	96.8%	13.1	<b>18</b>	97.6%	7.4
<b>13</b>	97.1%	12.1	<b>19</b>	96.8%	5.7
<b>14</b>	96.5%	23.7	<b>20</b>	97.3%	22.3
<b>15</b>	95.8%	24.3	<b>21</b>	97.7%	18.3
<b>16</b>	95.5%	21.1	<b>22</b>	96.5%	14.5

<sup>a</sup> The degree of purity of compounds **11-22** was measured by silica gel high performance liquid chromatography (HPLC). The chromatography data were obtained on a SiO<sub>2</sub> column (Luna 3 μm, 150 x 4.60 mm) eluting with EtOAc/hexane 6:4 (v/v) the compounds **11-16** (flow rate of 1 mL/min) and eluting with EtOAc/hexane 7:3 (v/v) the compounds **17-22** (flow rate of 1 mL/min).

<sup>b</sup> Retention times (t<sub>R</sub>) are expressed in minutes

**Table 1. NMR data of compounds 18/21, 19/22.**

Pos.	18		21		19		22	
	$\delta_C$	$\delta_H$ , mult. (J in Hz)	$\delta_C$	$\delta_H$ , mult. (J in Hz)	$\delta_C$	$\delta_H$ , mult. (J in Hz)	$\delta_C$	$\delta_H$ , mult. (J in Hz)
<b>1</b>	-	-	-	-	-	-	-	-
<b>2</b>	48.8	3.34 m	48.6	3.33 m	48.8	3.34 m	48.7	3.33 m
<b>3</b>	40.0	3.80 m	39.9	3.76 m	40.0	3.80 m	39.5	3.76 m
<b>4</b>	-	9.05, brs	-	9.06, brs	-	9.05, brs	-	9.06, brs
<b>4a</b>	146.1	-	145.7	-	145.0	-	144.5	-
<b>5</b>	180.6	-	176.7	-	179.8	-	175.7	-
<b>6</b>	137.9	-	137.1	-	136.0	-	136.1	-
<b>7</b>	140.7	-	148.1	-	139.7	-	145.5	-
<b>8</b>	173.1	-	176.6	-	172.1	-	175.6	-
<b>8a</b>	108.4	-	109.6	-	107.2	-	108.5	-
<b>1'</b>	26.0	2.24, t (7.5)	25.5	2.31, t (7.5)	26.0	2.24, t (7.5)	25.5	2.31, t (7.5)
<b>2'</b>	26.8	1.30	28.0	1.28	27.1	1.30	27.9	1.30
<b>3'</b>	31.7	1.20	31.8	1.20	29.0	1.20	29.0	1.20
<b>4'</b>	22.2	1.19	22.1	1.19	29.2	1.19	29.2	1.19
<b>5'</b>	14.2	0.80, t (7.5)	14.2	0.80, t (7.5)	29.3	1.19	29.3	1.19
<b>6'</b>	-	-	-	-	29.4	1.19	29.4	1.19
<b>7'</b>	-	-	-	-	31.7	1.19	31.8	1.19
<b>9'</b>	-	-	-	-	22.5	1.20	22.3	1.20
<b>10'</b>	-	-	-	-	14.4	0.81, t (7.5)	14.3	0.81, t (7.5)
<b>1''</b>	177.2	-	177.9	-	177.1	-	177.9	-
<b>2''</b>	39.1	-	39.0	-	39.1	-	39.0	-
<b>Me</b>	27.4	1.22	27.3	1.22	27.4	1.21	27.3	1.21
<b>NH</b>	-	8.90, brs	-	9.00, brs	-	8.88, brs	-	9.00, brs

**Table 2SI.** Prevalent ionic forms of new thiazinoquinones.

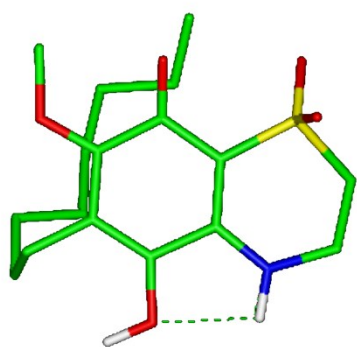
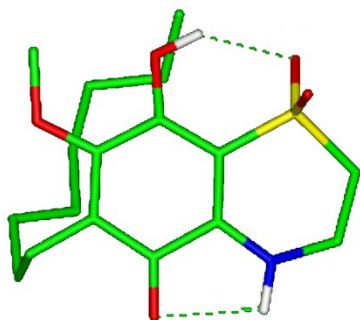
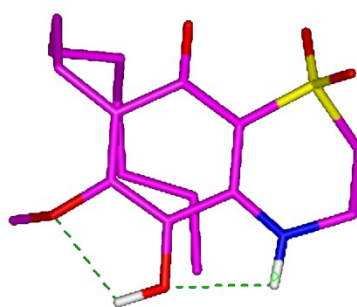
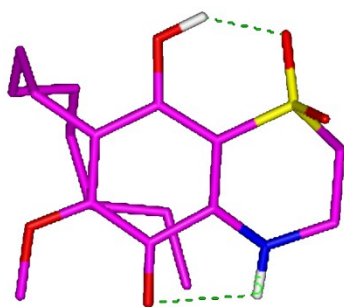
<b>Compounds</b>	<b>Prevalent ionic form (%)<sup>a</sup></b>	
	<b>pH 7.2</b>	<b>pH 5.5</b>
<b>12</b>	N(100)	N(100)
<b>15</b>	N(100)	N(100)
<b>19</b>	N(100)	N(100)
<b>22</b>	N(100)	N(100)

<sup>a</sup>Percentage of ionic form in brackets; N = neutral form.

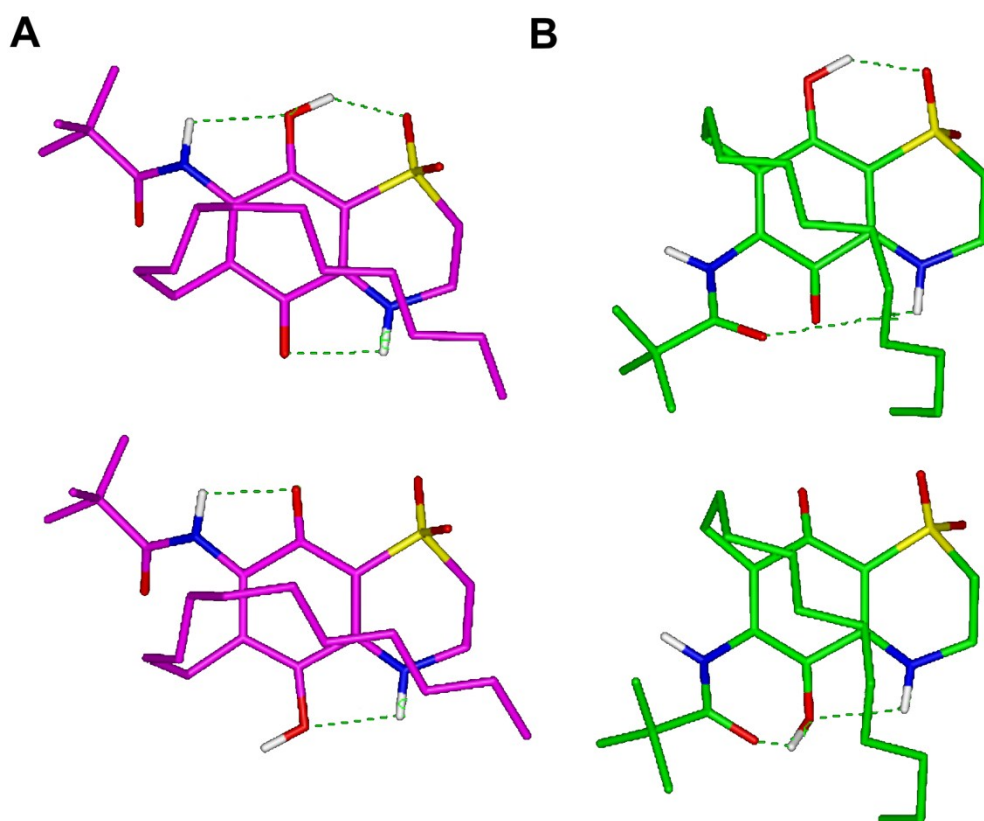
**Table 3SI.** Inhibition of BH formation by chloroquine and test compounds

<b>Compounds</b>	Hemin/ compound ratios	<b>% inhibition BH formation*</b>					
		1:0.5	1:1	1:2	1:4	1:8	1:16
<b>17</b>		0	1.01	1.78	3.57	14.6	19.15
<b>20</b>		0	0	1.04	8.91	13.68	25.31
<b>22</b>		0	0	1.12	7.47	12.15	
<b>CQ</b>		0	44.11	89.46	80.02	90.83	

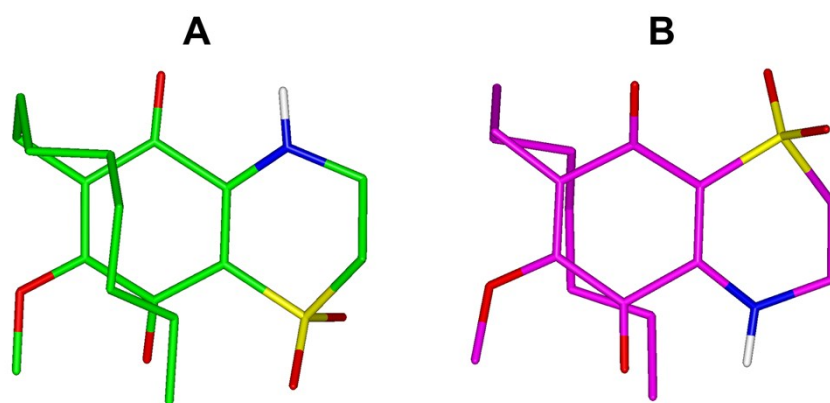
\*The data are the mean of the results from two experiments in duplicate

**A****B**

**Figure 1SI.**  $\text{QH}^{\bullet}_i$  (top) and  $\text{QH}^{\bullet}_{ii}$  (bottom) species of **12** GM (green; A) and **15** GM (magenta; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogen bonds are highlighted by green dashed lines. Hydrogens are omitted for the sake of clarity with the exception of those involved in hydrogen bonds.



**Figure 2SI.**  $\text{QH}^{\bullet}_i$  (top) and  $\text{QH}^{\bullet}_{ii}$  (bottom) species of 19 GM (magenta; A) and 22 GM (green; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogen bonds are highlighted by green dashed lines. Hydrogens are omitted for the sake of clarity with the exception of those involved in hydrogen bonds.



**Figure 3SI.** PM7 GM conformer of **12** (green; A); PM7 GM conformer of **15** (magenta; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogens are omitted for the sake of clarity with the exception of those of amine function.