Electronic Supplementary Material (ESI) for RSC Advances.
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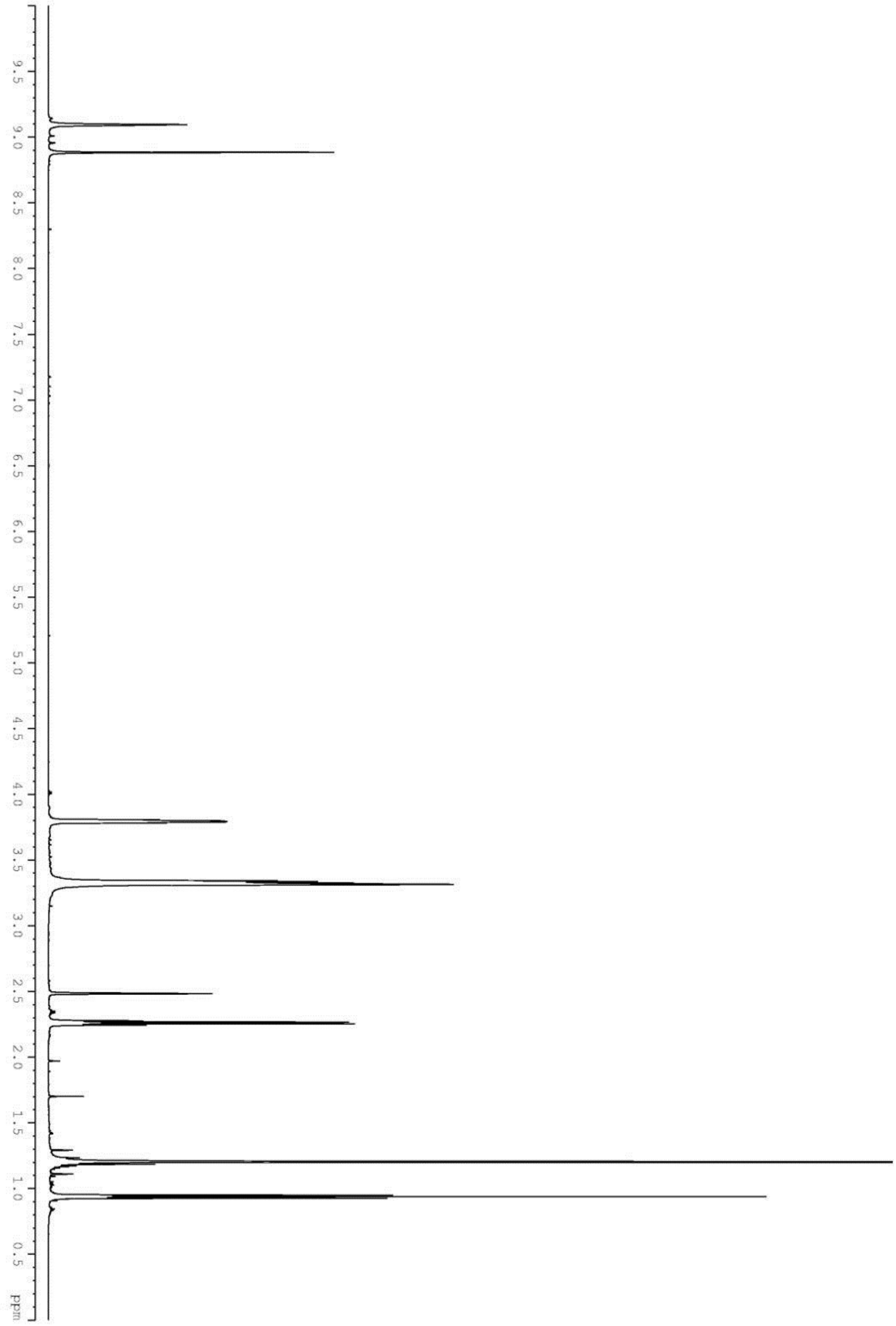
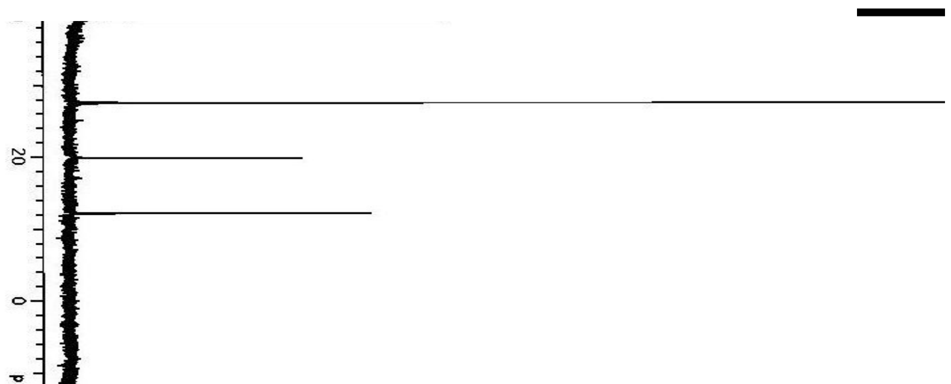
SUPPORTING INFORMATION

Reagents and general experimental procedure

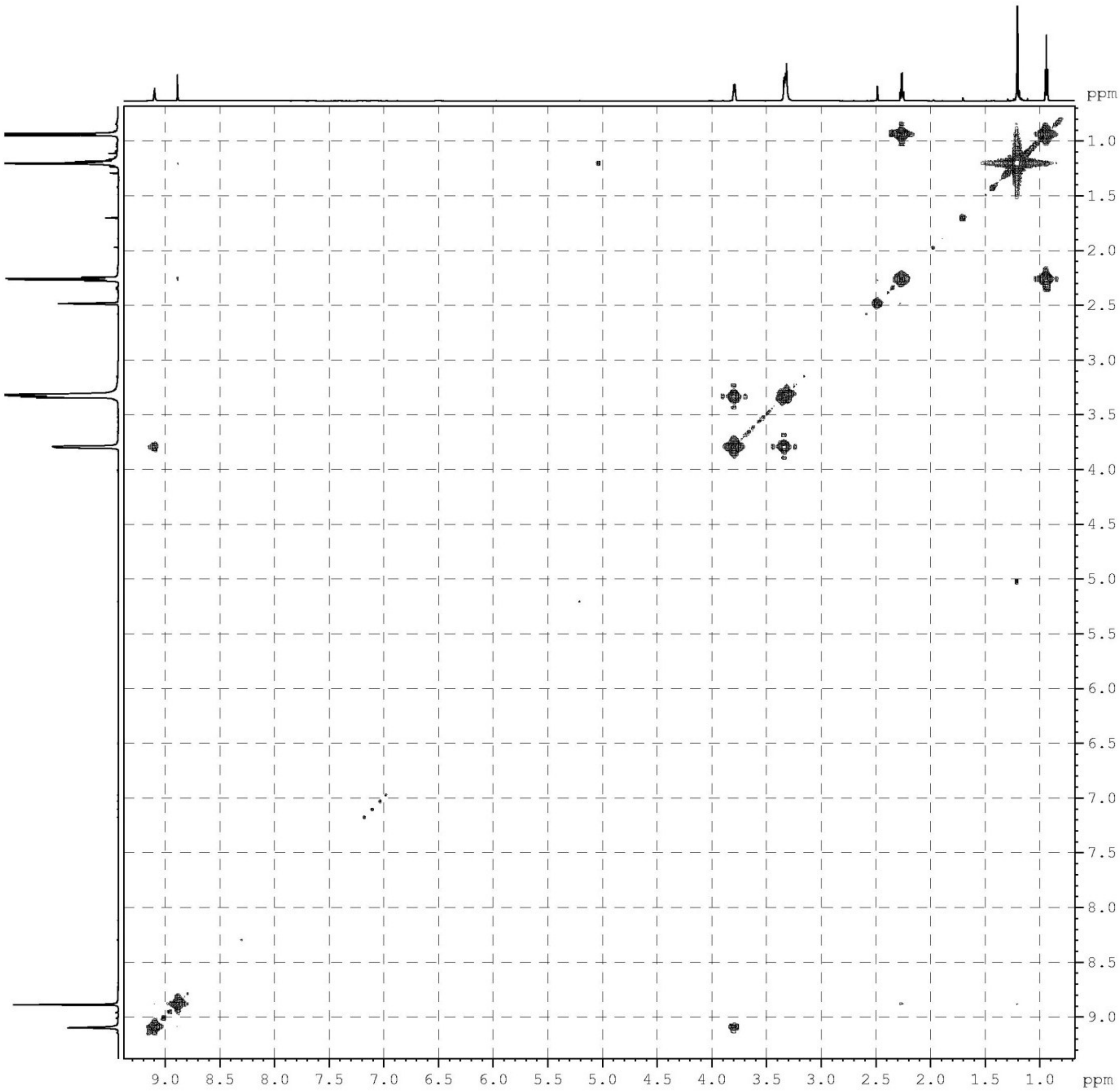
Commercial reagents: Sigma–Aldrich. Solvents: Carlo Erba. TLC: Silica Gel 60 F254 (plates 5 x 20, 0.25 mm) Merck. Preparative TLC: Silica Gel 60 F254 plates (20 x 20, 2 mm). Spots revealed by UV lamp then by spraying with 2 N sulfuric acid and heating at 120 °C. 'Acidic' silica gel was prepared by treating 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}H (700 MHz) and ^{13}C (175 MHz) NMR spectra were recorded on a Varian INOVA spectrometer respectively; chemical shifts were referenced to the residual solvent signal ($CDCl_3$: δ_H=7.26, δ_C=77.0). For an accurate measurement of the coupling constants, the one-dimensional ^{1}H NMR spectra were transformed at 64 K points (digital resolution: 0.09 Hz). Homonuclear (^{1}H- ^{1}H) and heteronuclear (^{1}H-^{13}C) connectivities were determined by COSY and HSQC experiments, respectively. Two and three bond ^{1}H-^{13}C connectivities were determined by gradient 2D HMBC experiments optimized for a $^{2,3}J$ of 8 Hz. Routine ^{1}H and ^{13}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}H NMR in DMSO of **17**

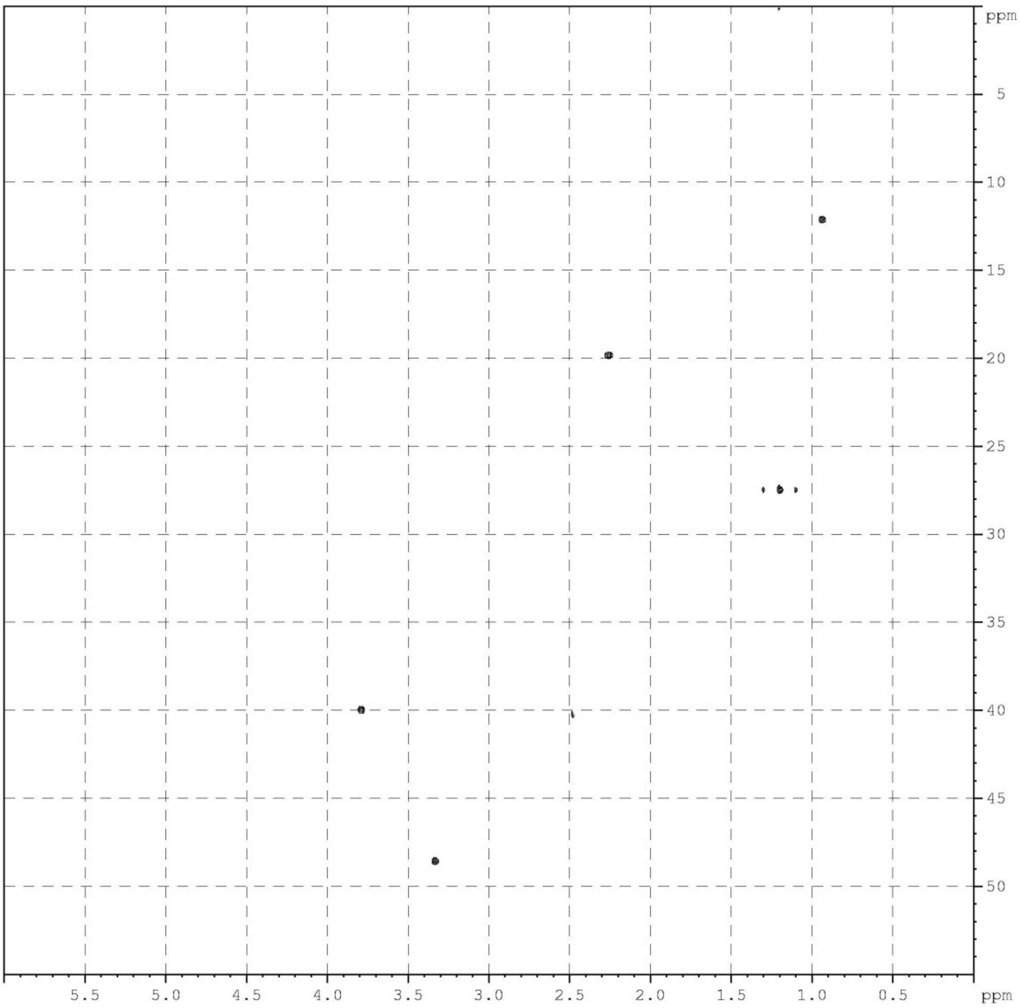




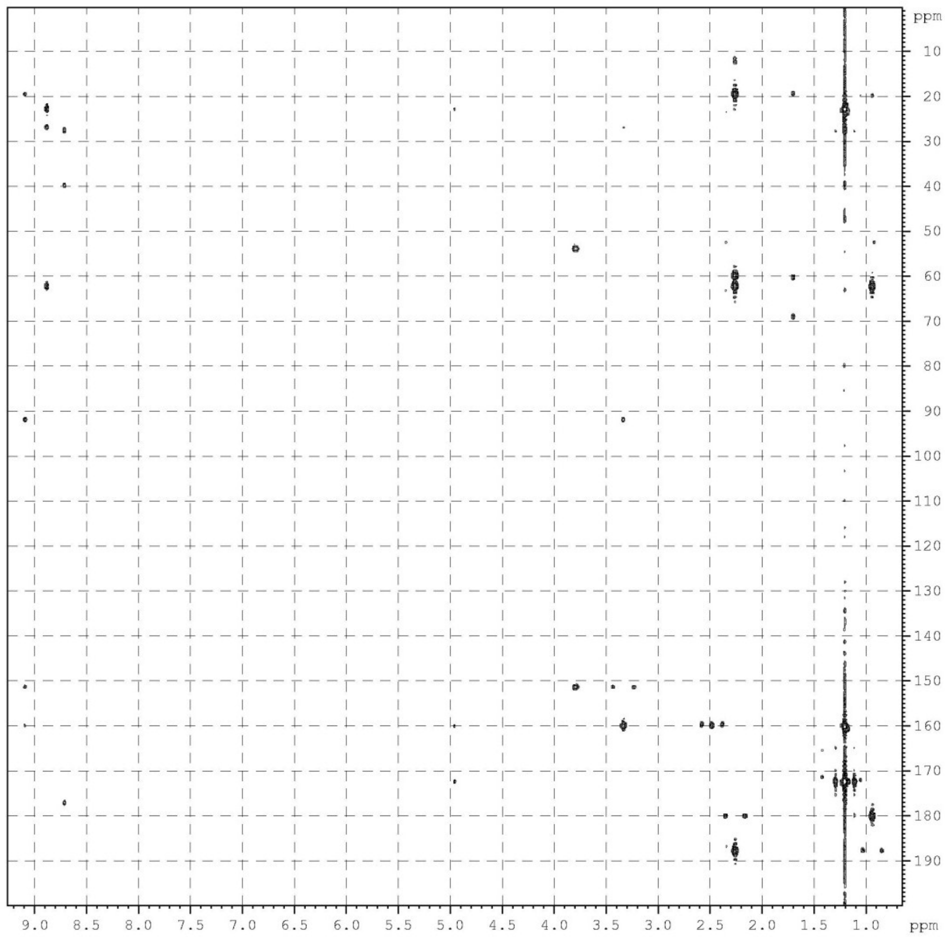
COSY in DMSO of 17



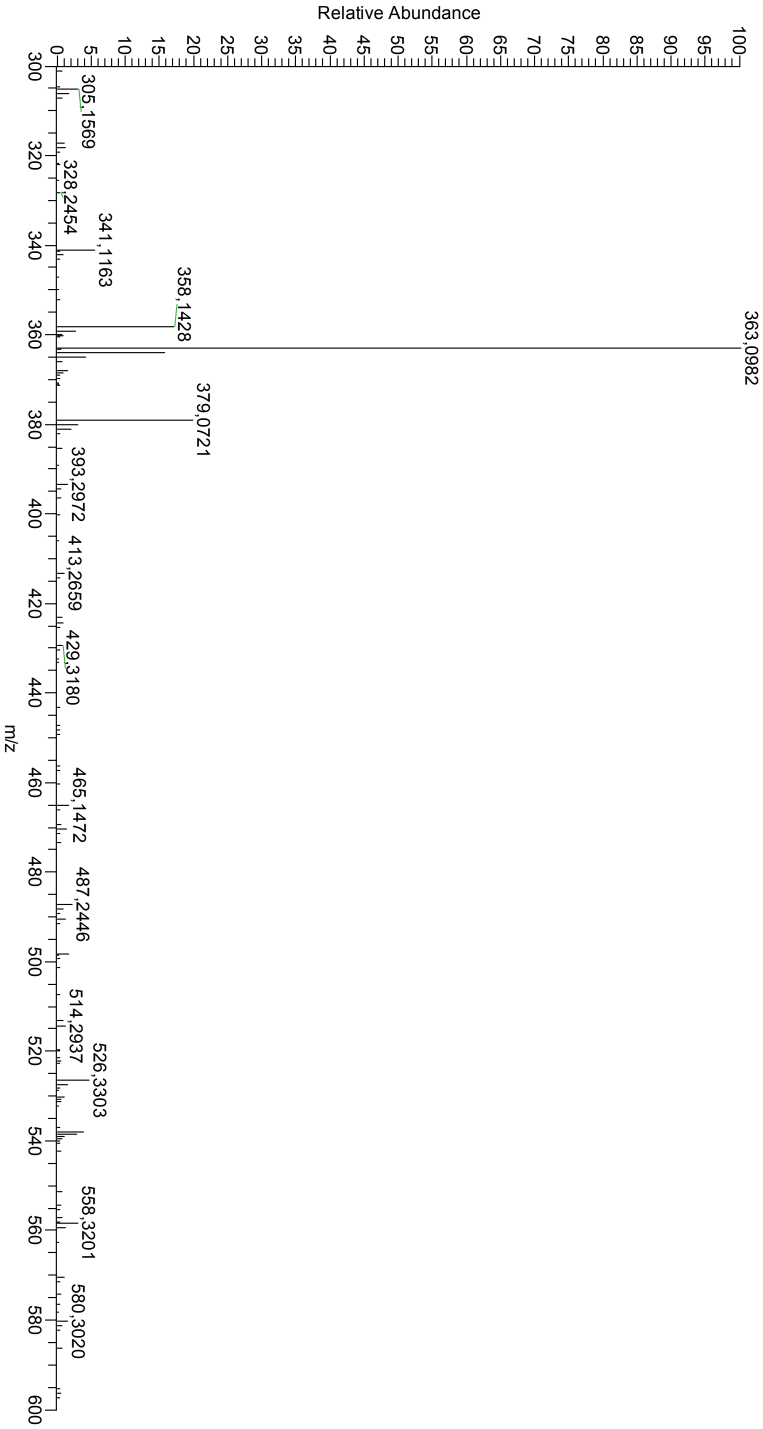
HSQC in DMSO of **17**



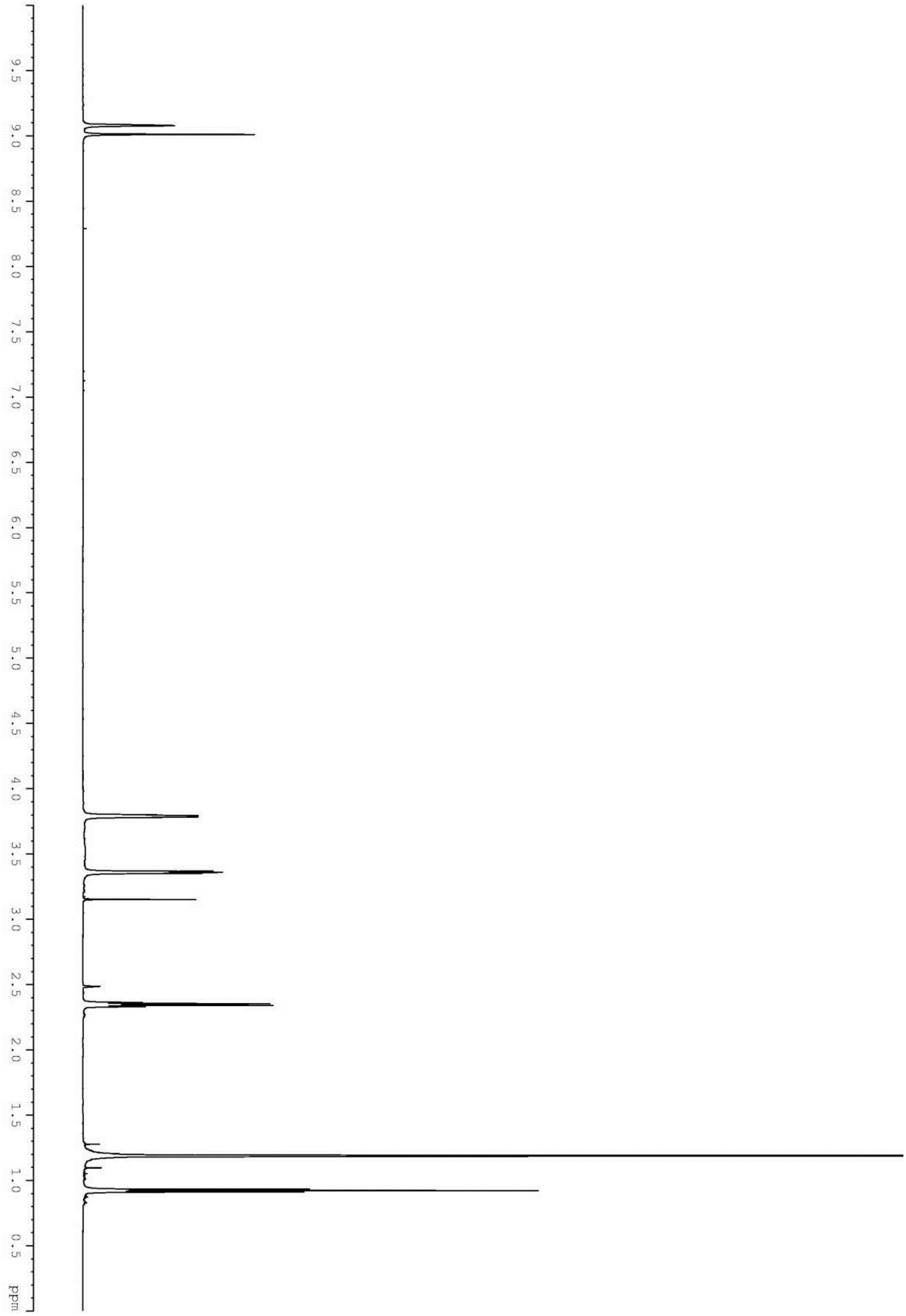
HMBC in DMSO of **17**



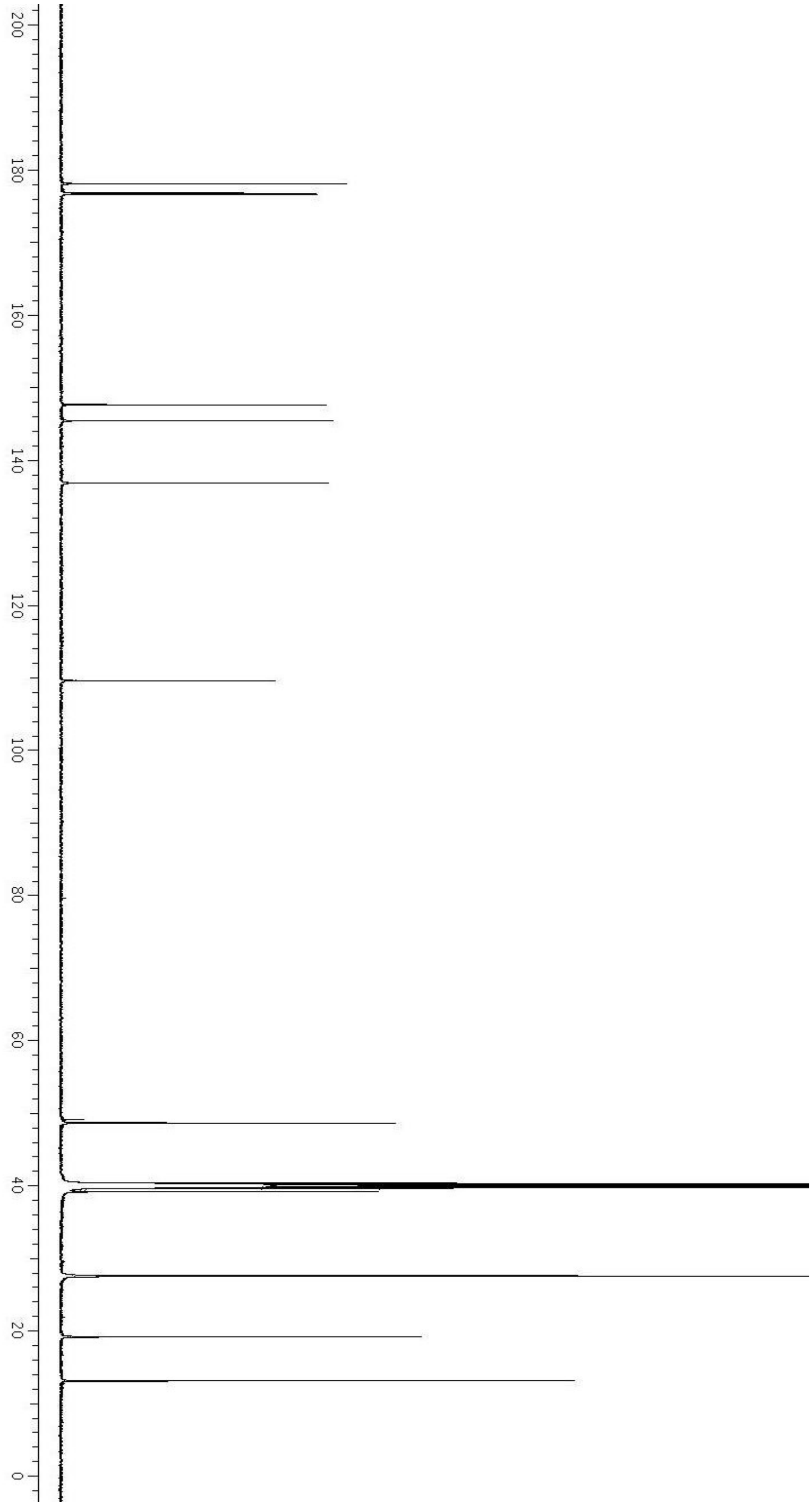
ESI mass spectrum of **17**



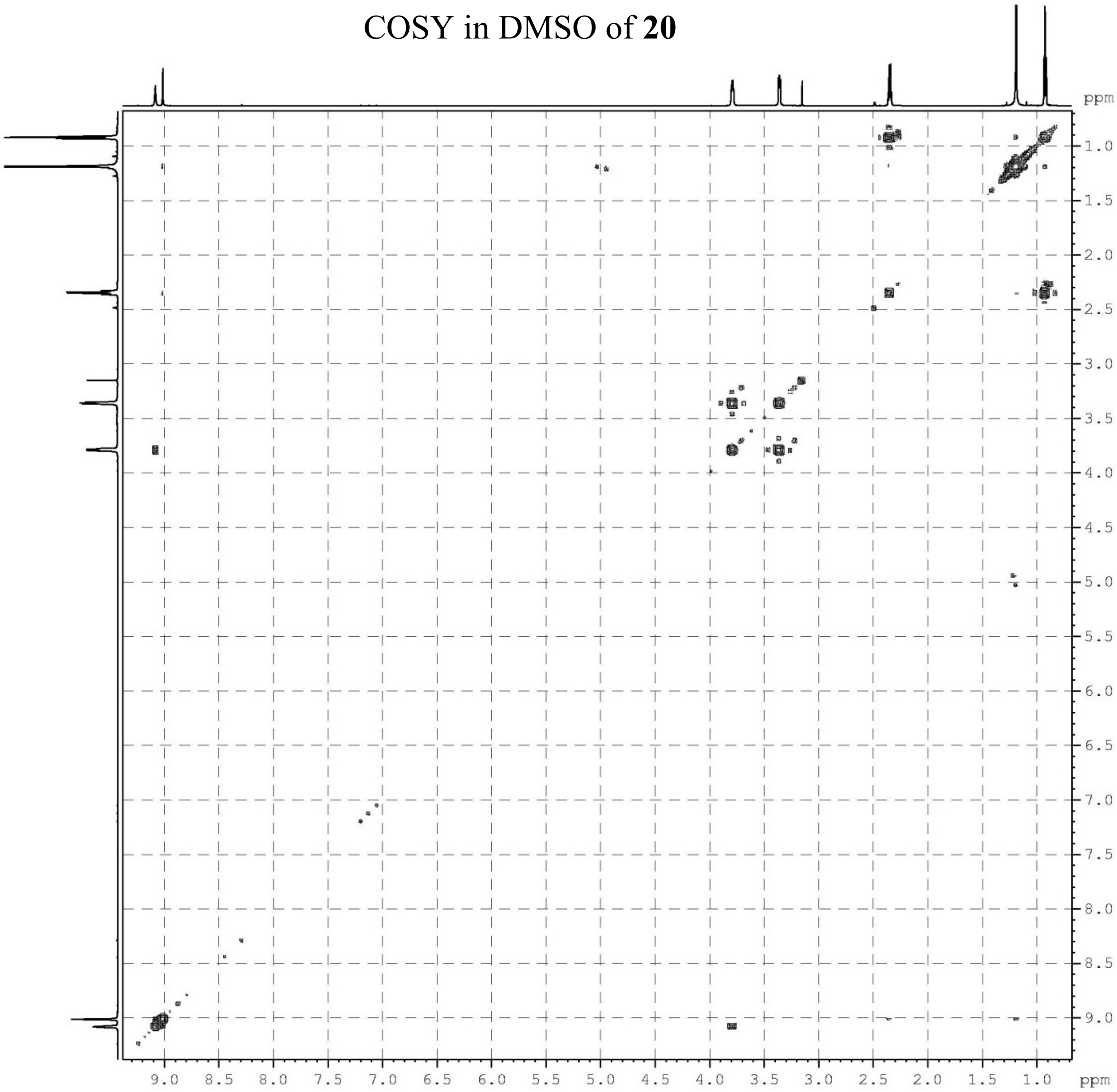
^{1}H NMR in DMSO of **20**



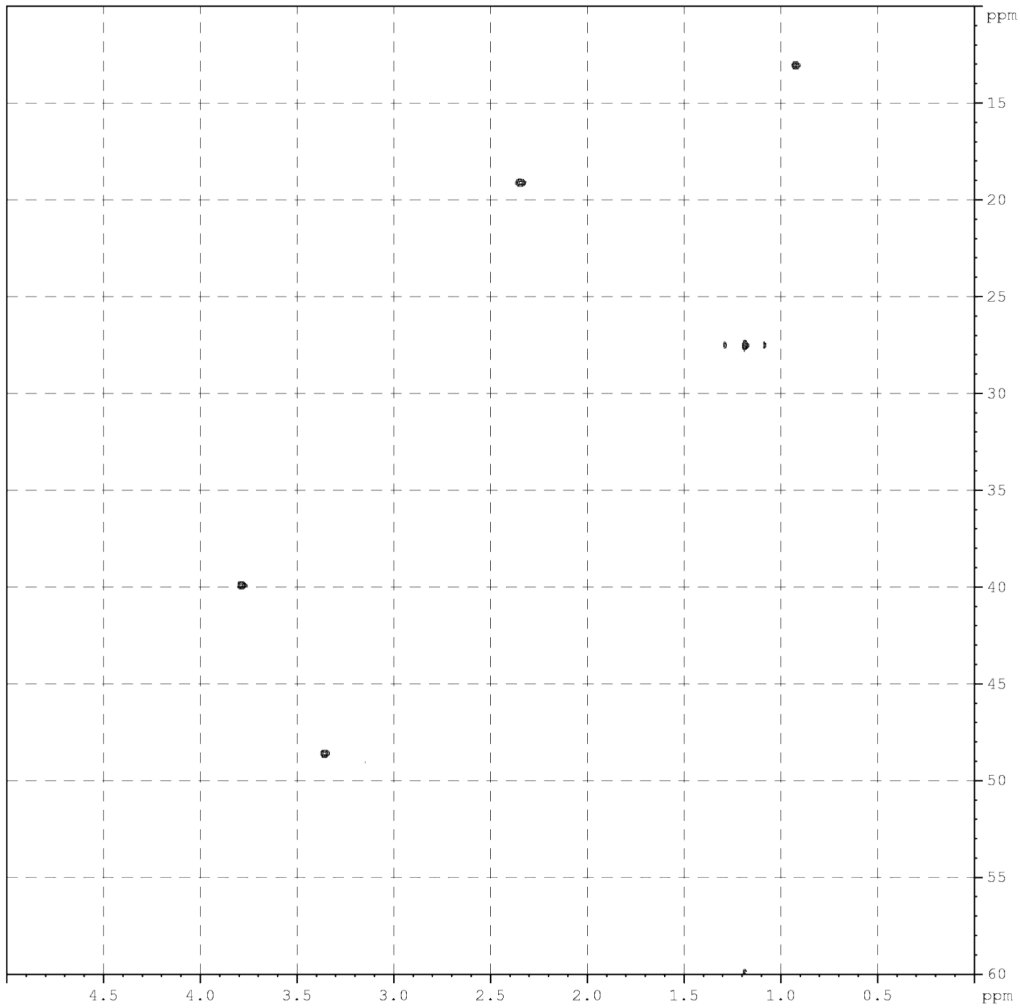
^{13}C NMR in DMSO of **20**



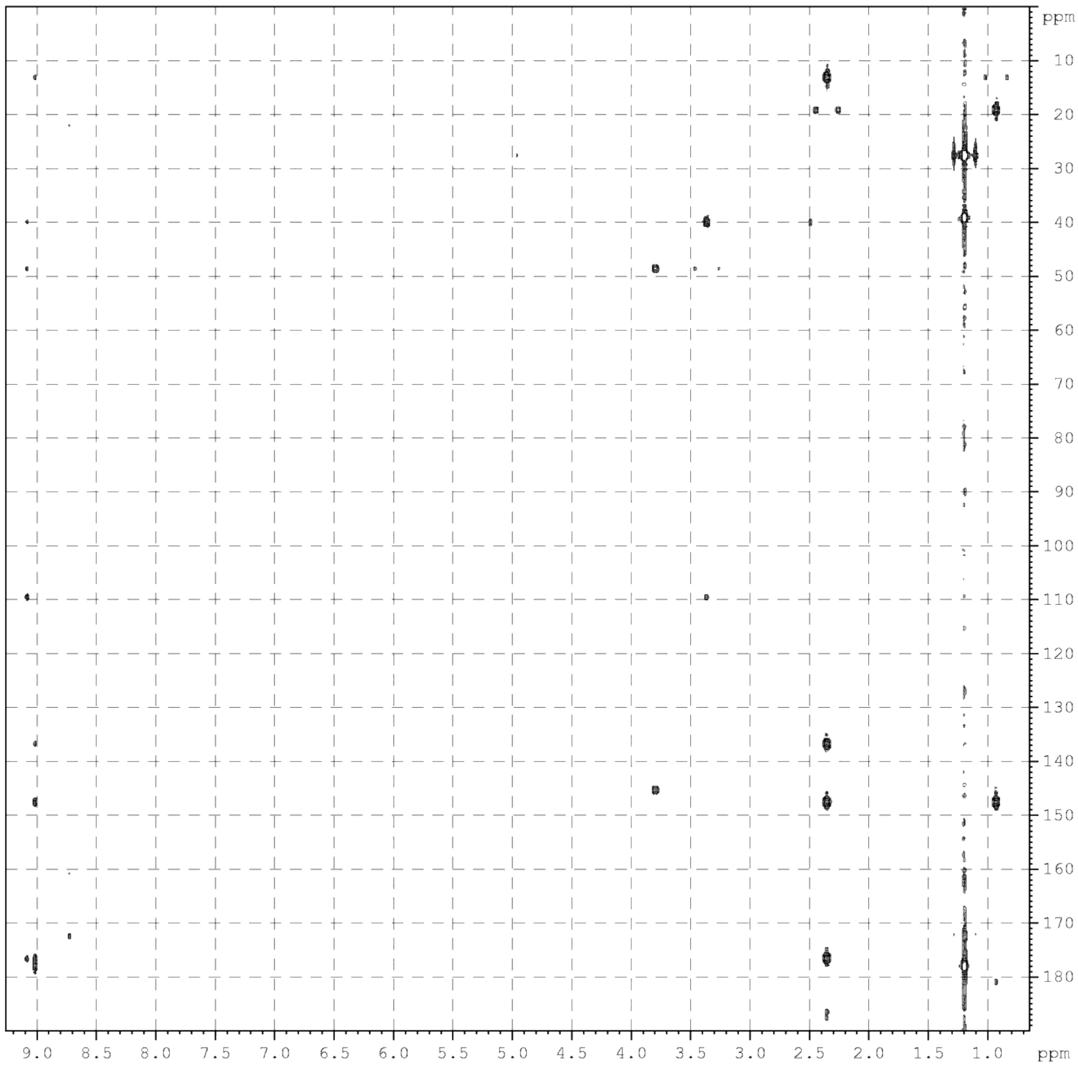
COSY in DMSO of **20**



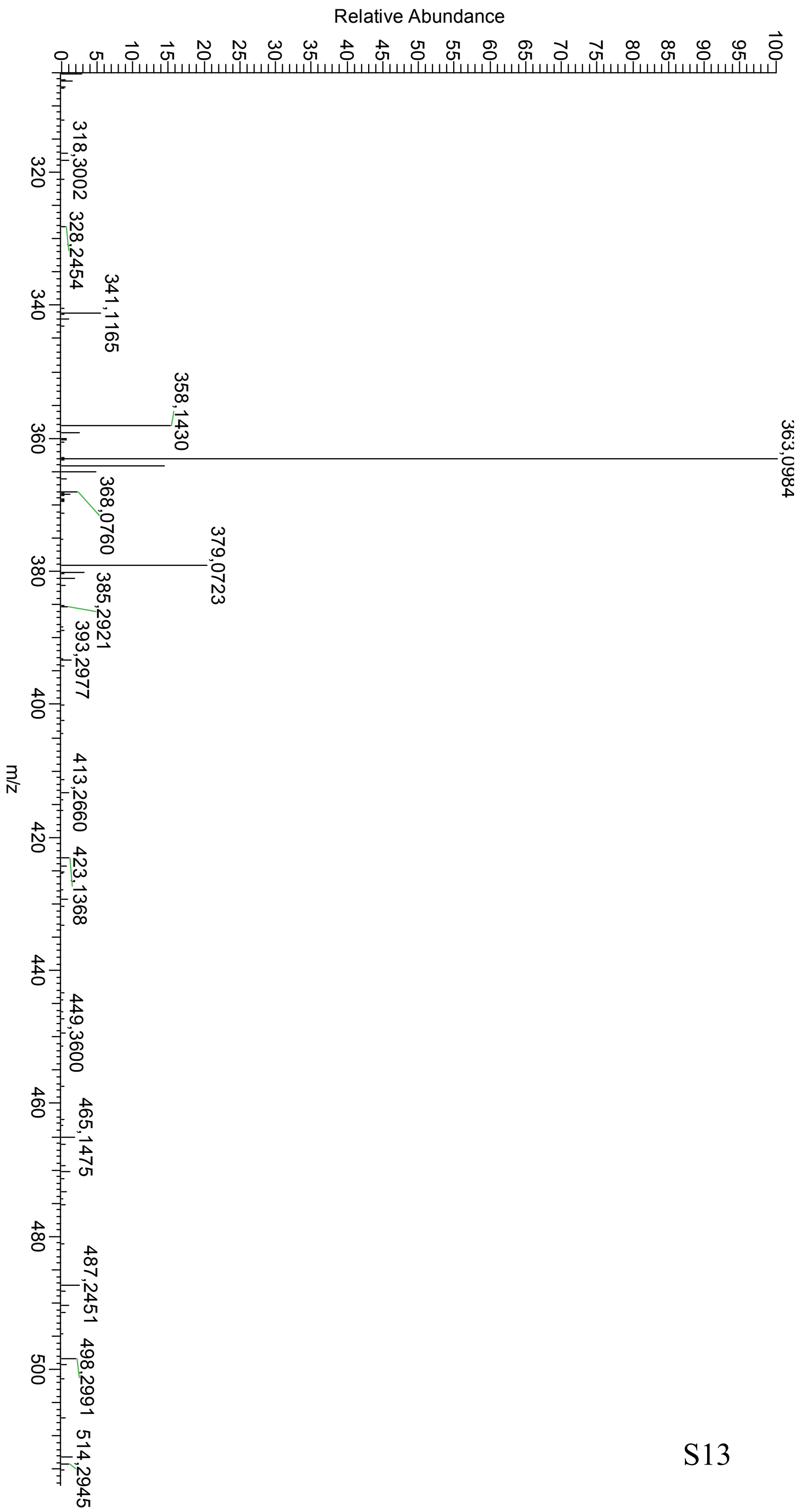
HSQC in DMSO of **20**



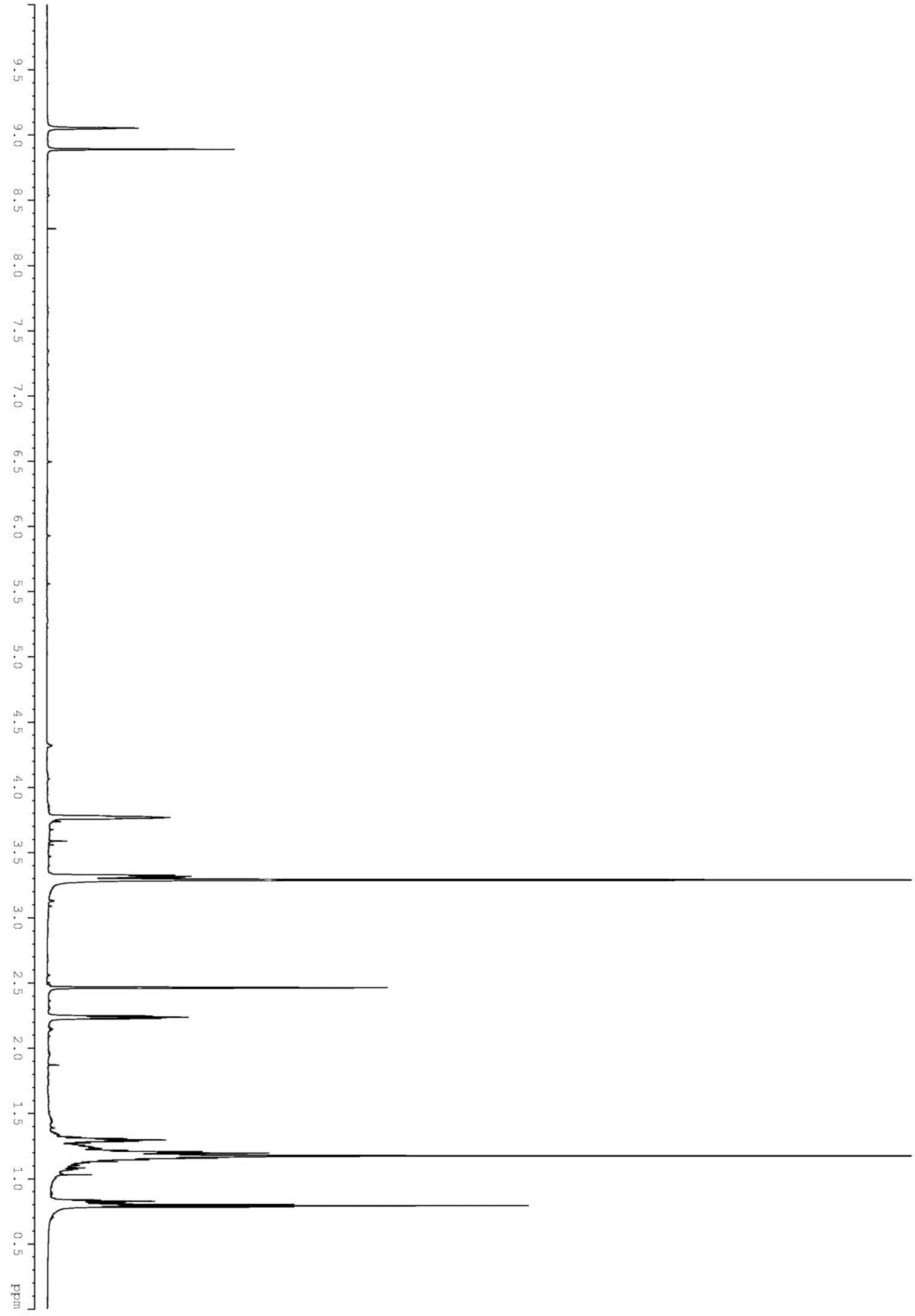
HMBC in DMSO of **20**



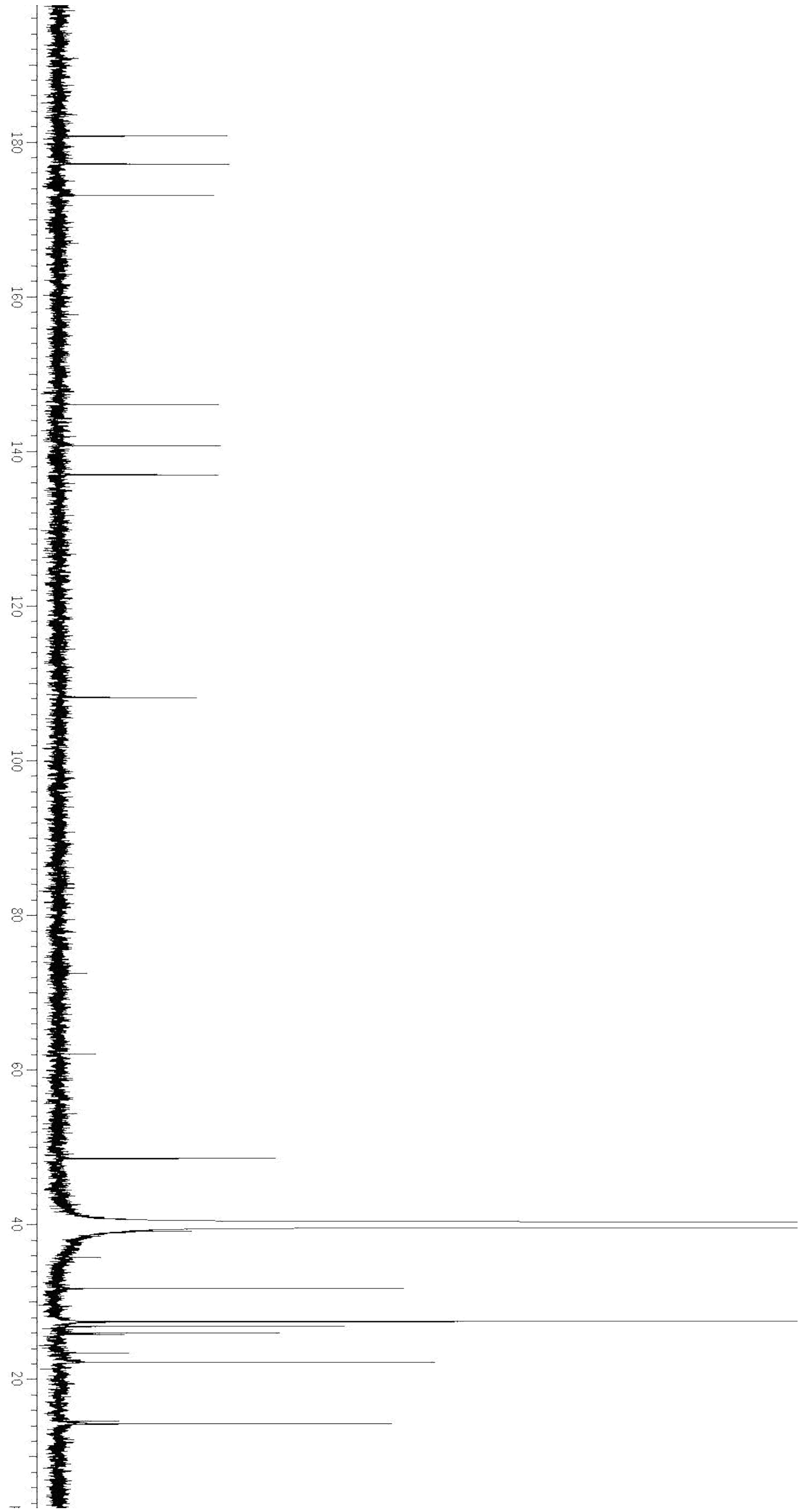
ESI mass spectrum of **20**



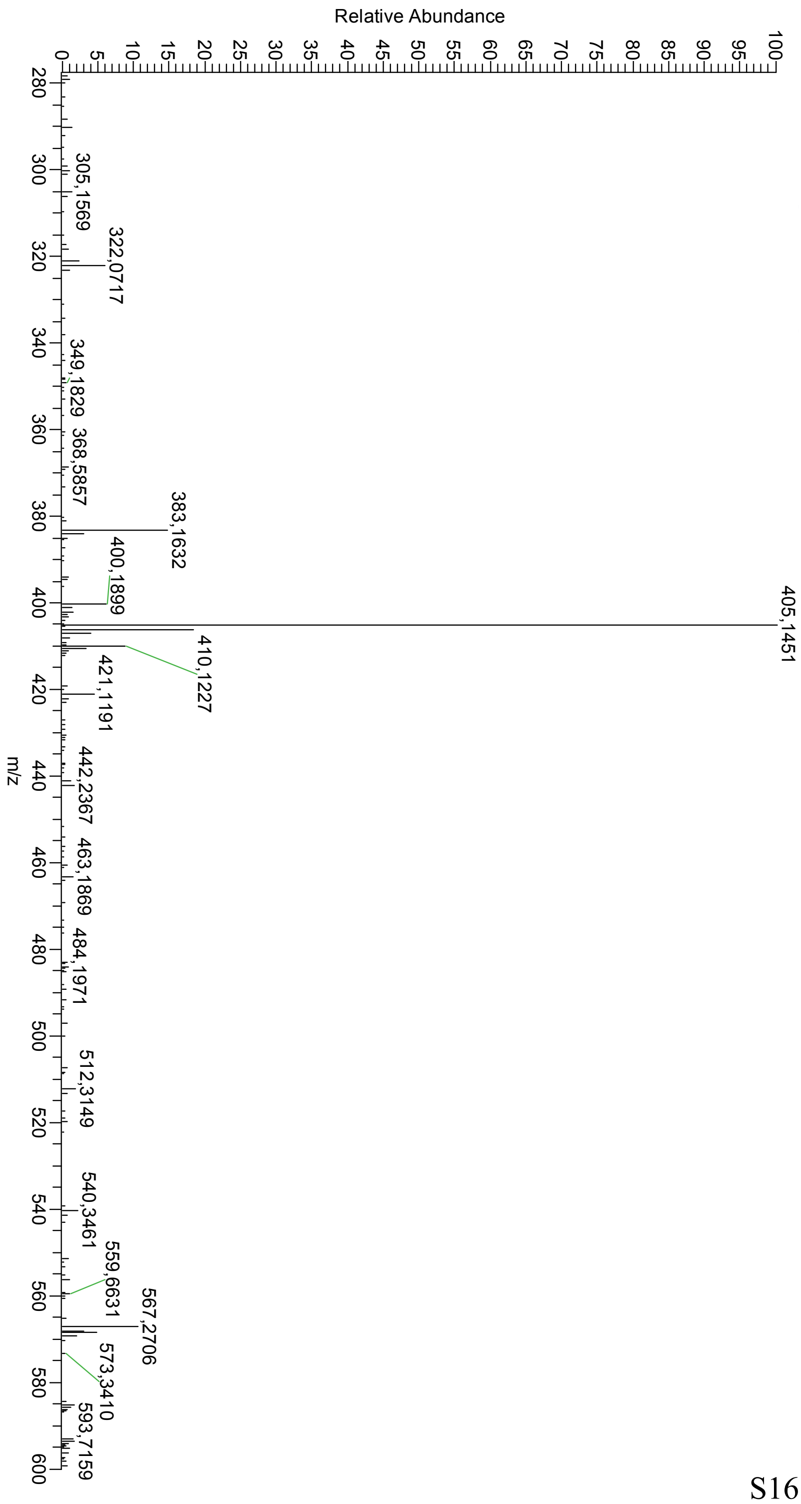
^{1}H NMR in DMSO of **18**



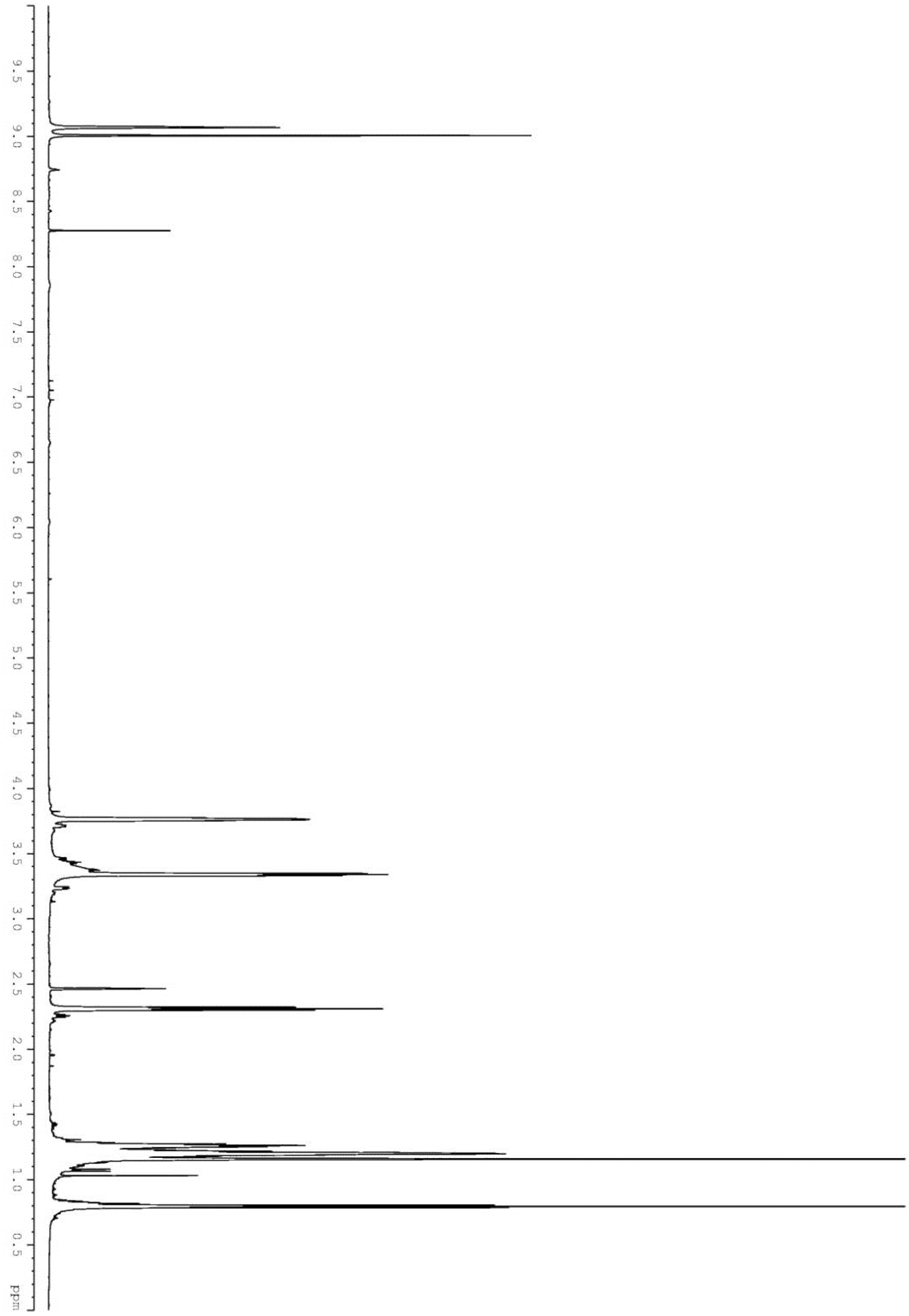
^{13}C NMR in DMSO of **18**



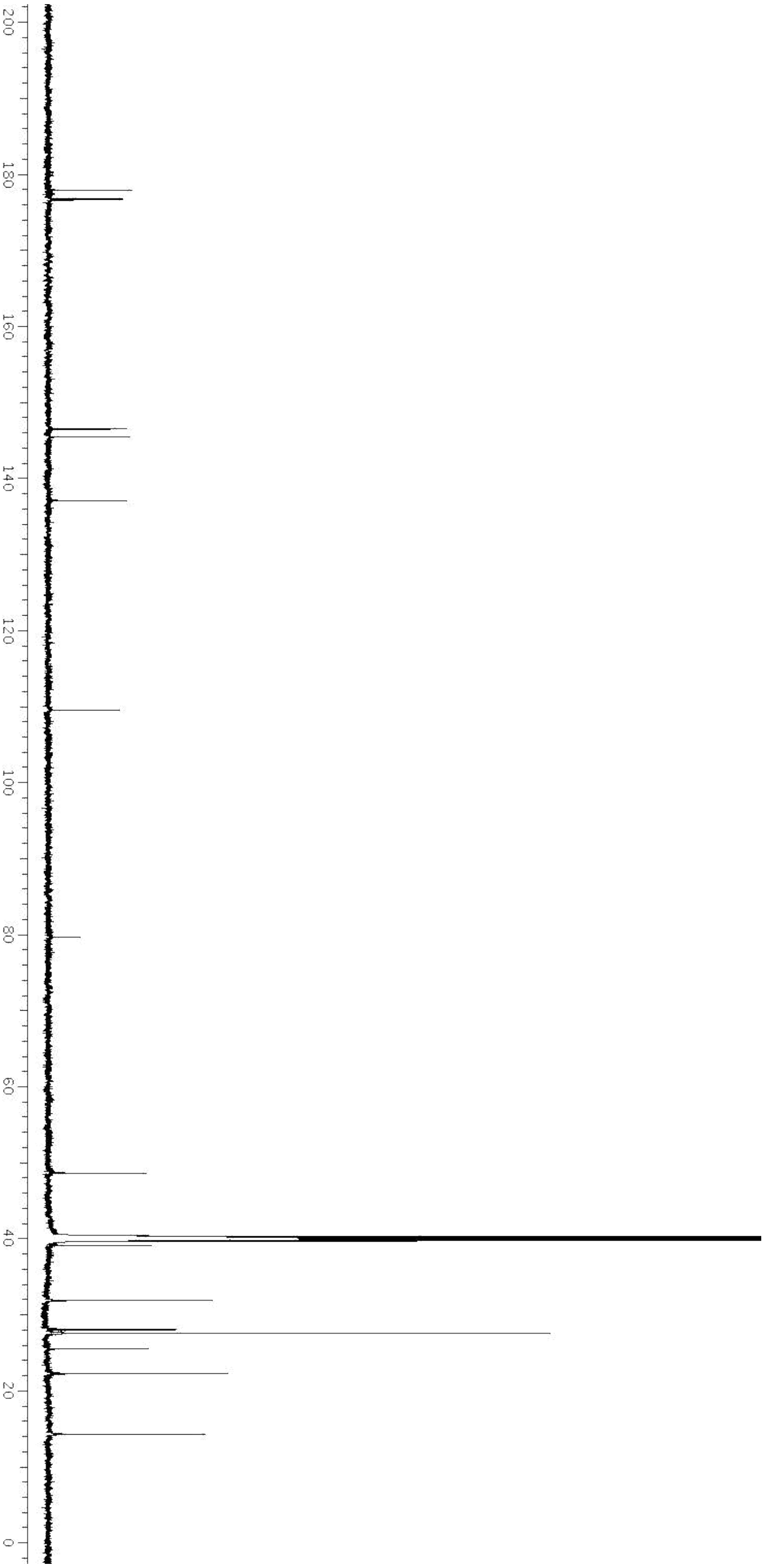
ESI mass spectrum of **18**



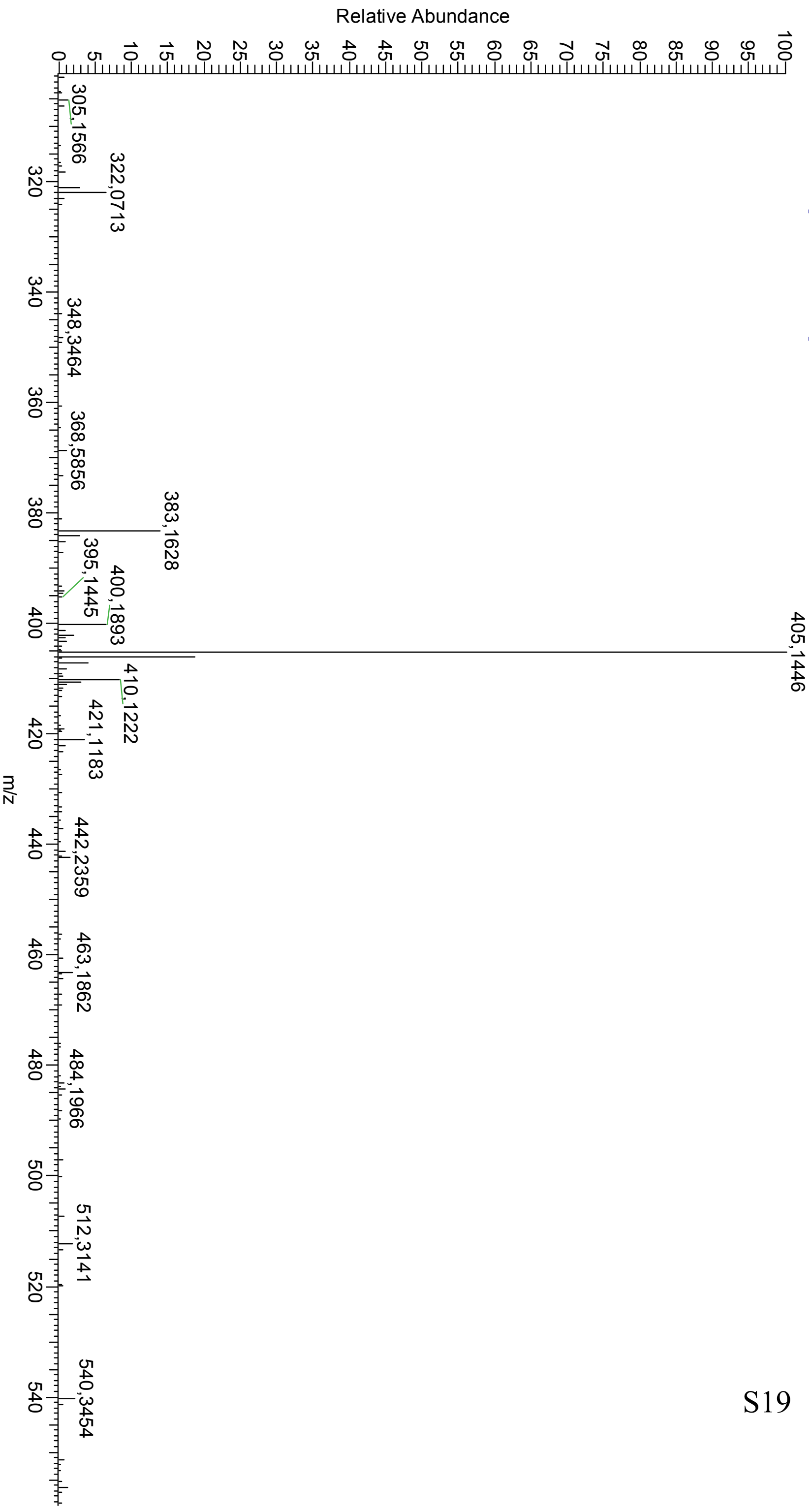
[1]H NMR in DMSO of **21**



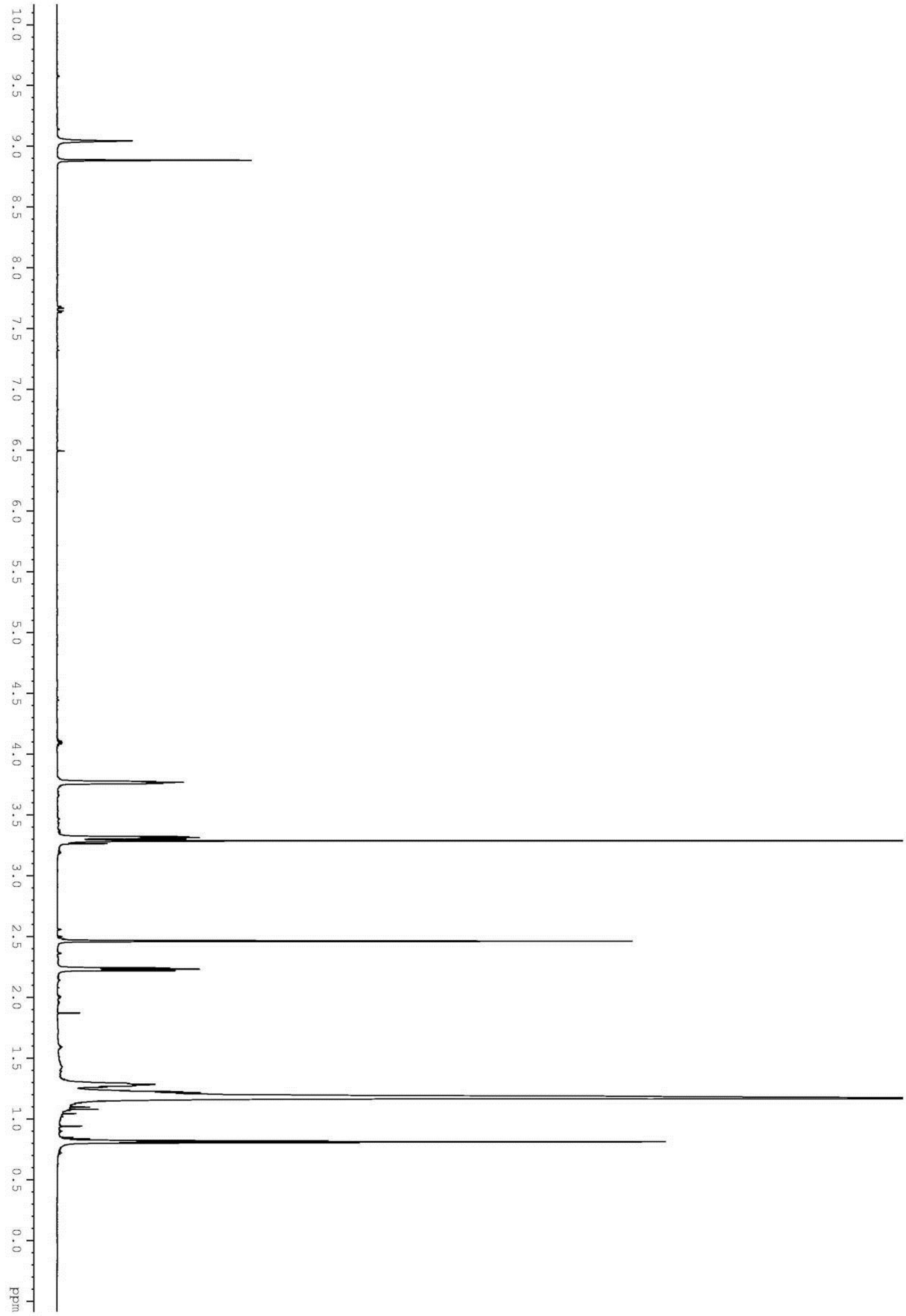
^{13}C NMR in DMSO of **21**



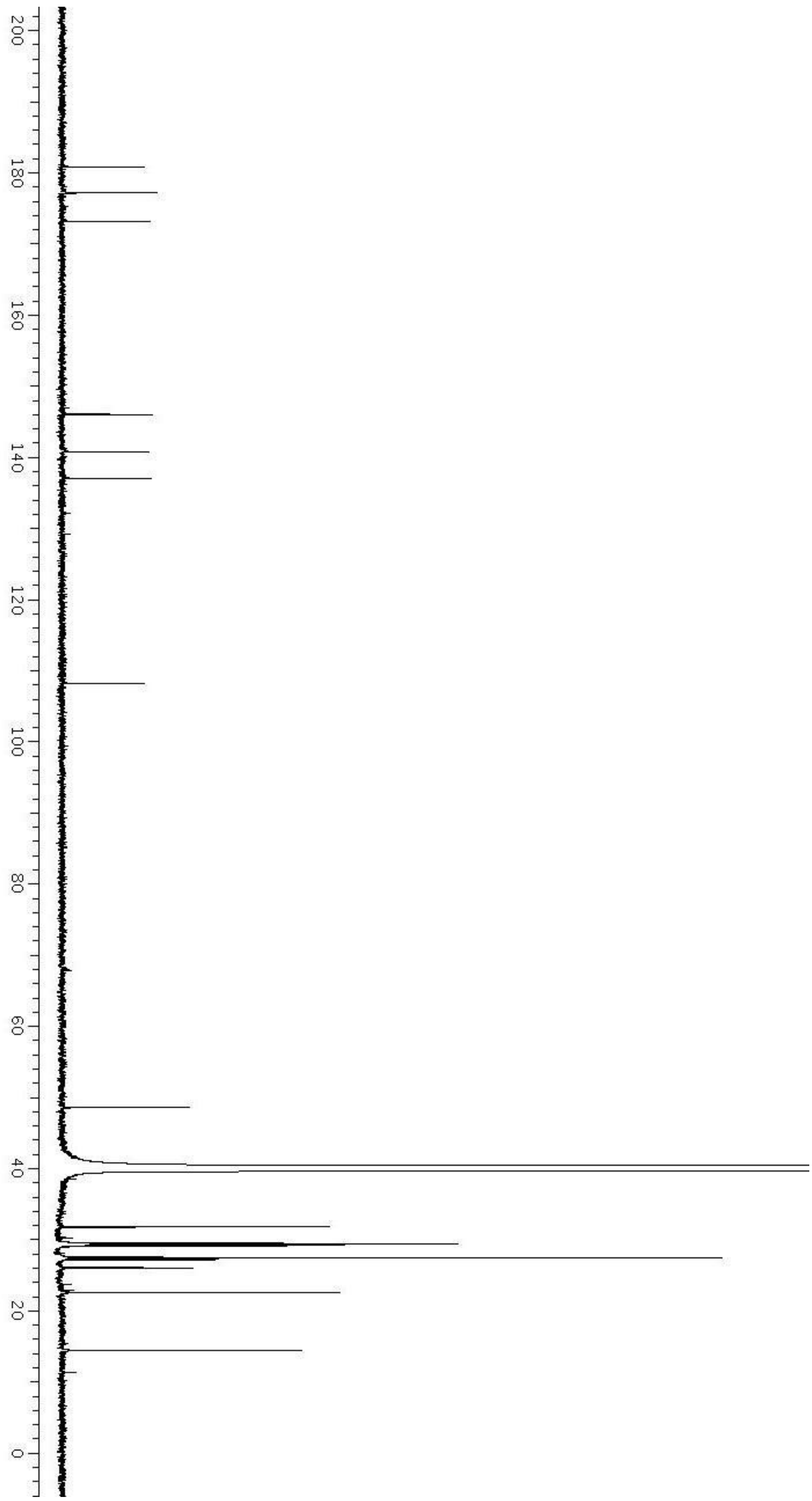
ESI mass spectrum of **21**



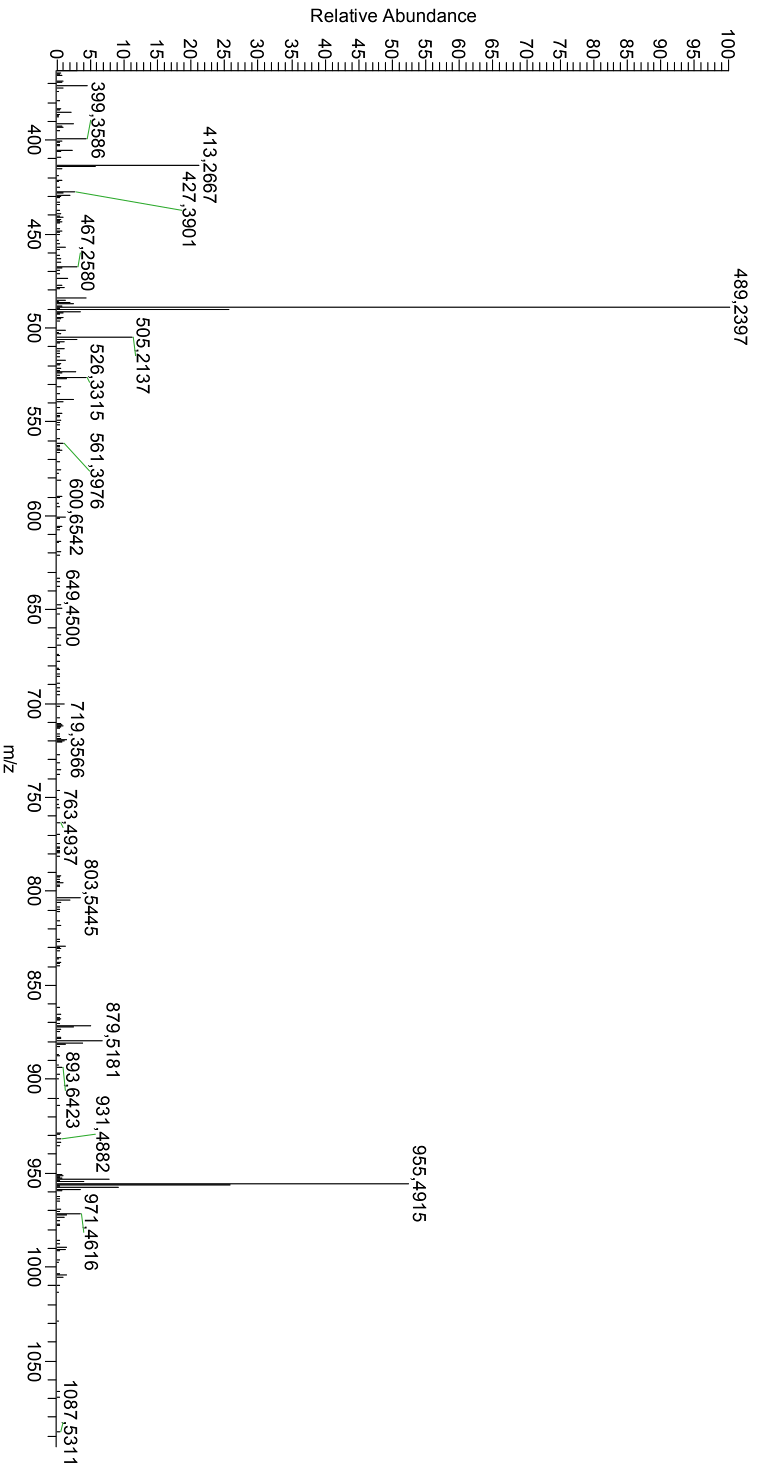
^{1}H NMR in DMSO of **19**



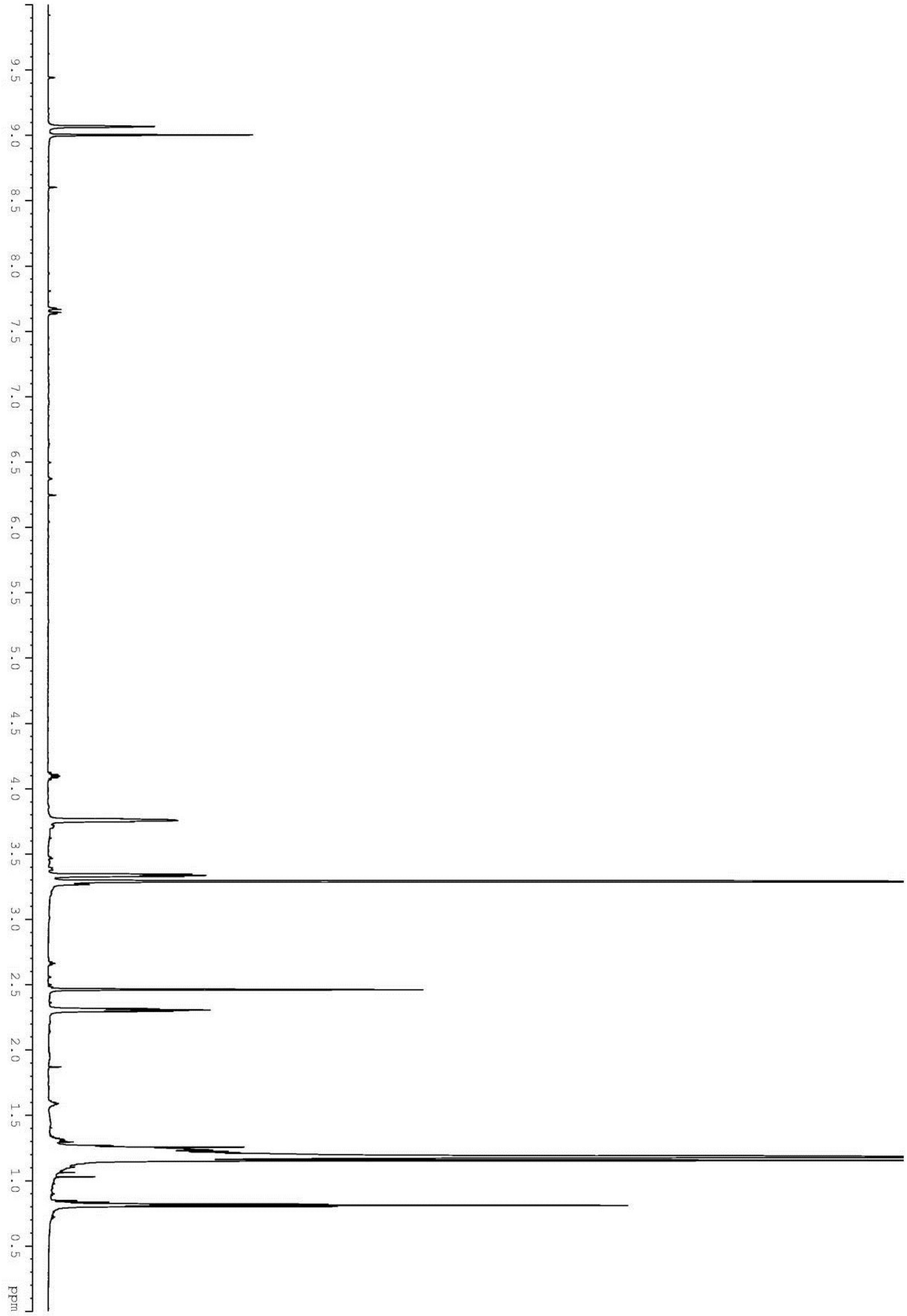
^{13}C NMR in DMSO of **19**



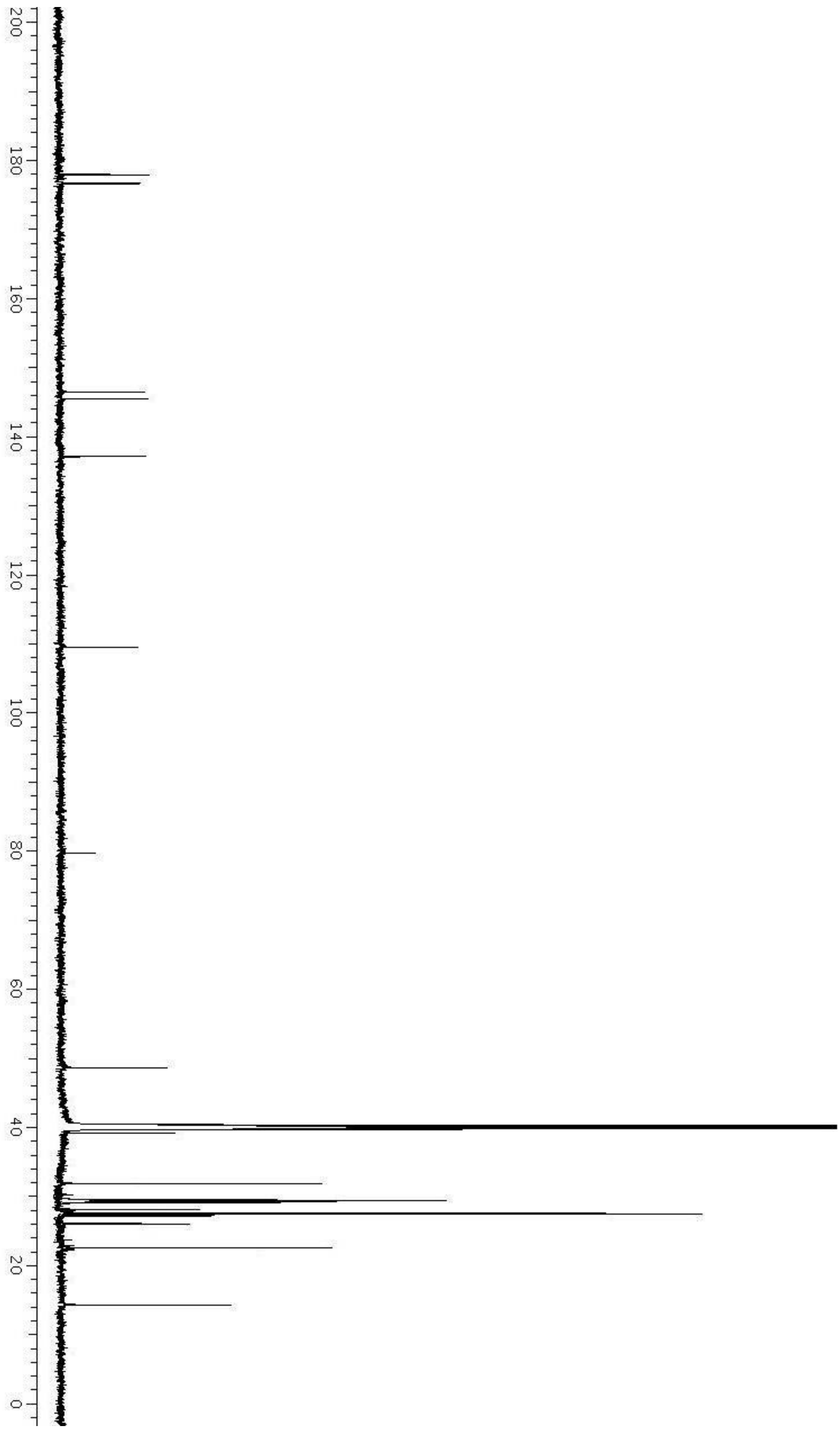
ESI mass spectrum of **19**



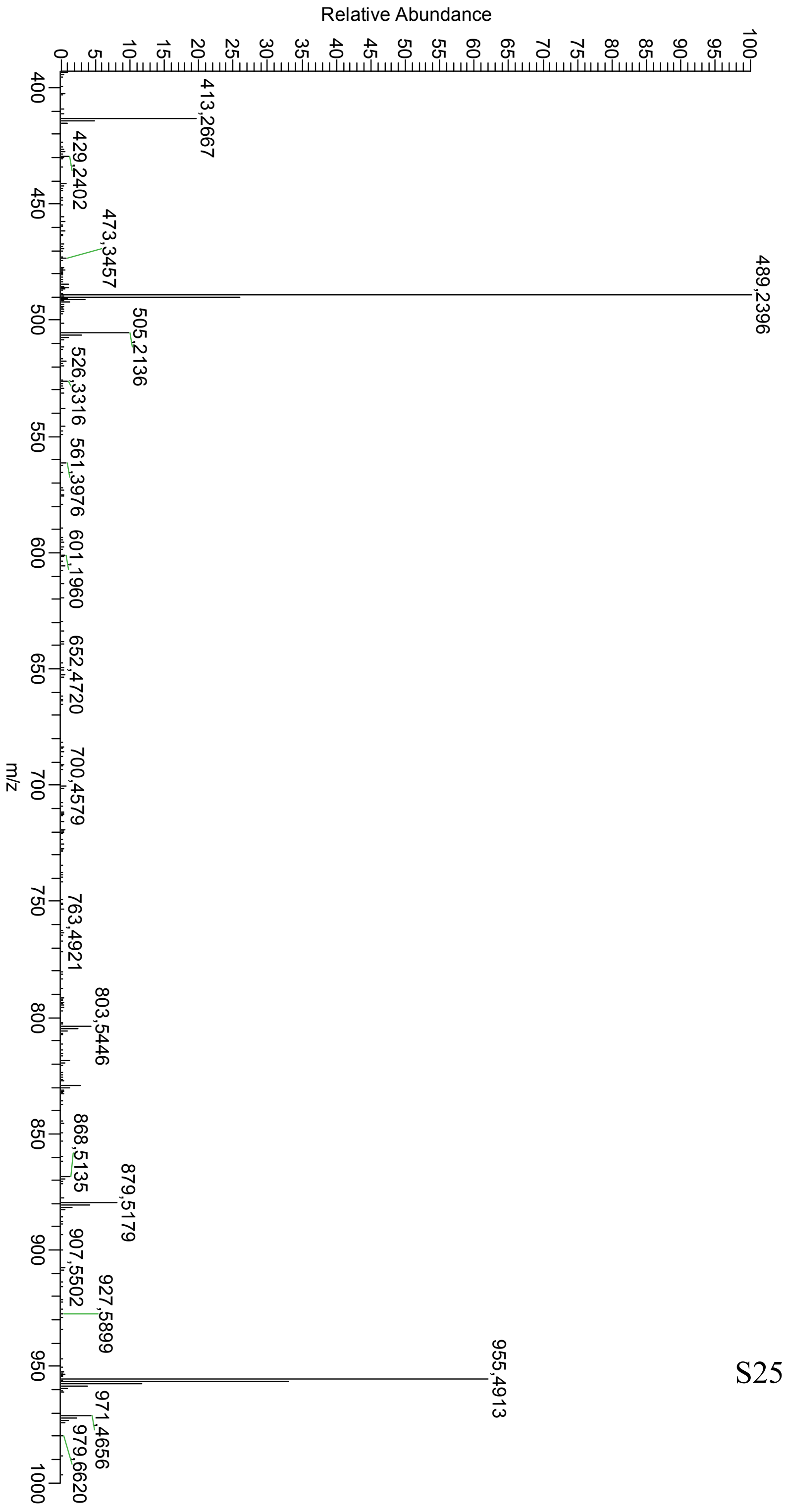
[1]H NMR in DMSO of **22**



^{13}C NMR in DMSO of **22**



ESI mass spectrum of **22**



Purity criteria for tested compounds.

Compounds	Purity[a]	t_R[b]	Compounds	Purity[a]	t_R[b]
11	95.8%	13.9	**17**	97.2%	9.1
12	96.8%	13.1	**18**	97.6%	7.4
13	97.1%	12.1	**19**	96.8%	5.7
14	96.5%	23.7	**20**	97.3%	22.3
15	95.8%	24.3	**21**	97.7%	18.3
16	95.5%	21.1	**22**	96.5%	14.5

[a] 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_2 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).

[b] Retention times (t_R) are expressed in mintes

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

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

Table 2SI. Prevalent ionic forms of new thiazinoquinones.

Compounds	**Prevalent ionic form (%)[a]**	
	pH 7.2	**pH 5.5**
12	N(100)	N(100)
15	N(100)	N(100)
19	N(100)	N(100)
22	N(100)	N(100)

[a]Percentage of ionic form in brackets; N = neutral form.

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

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

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

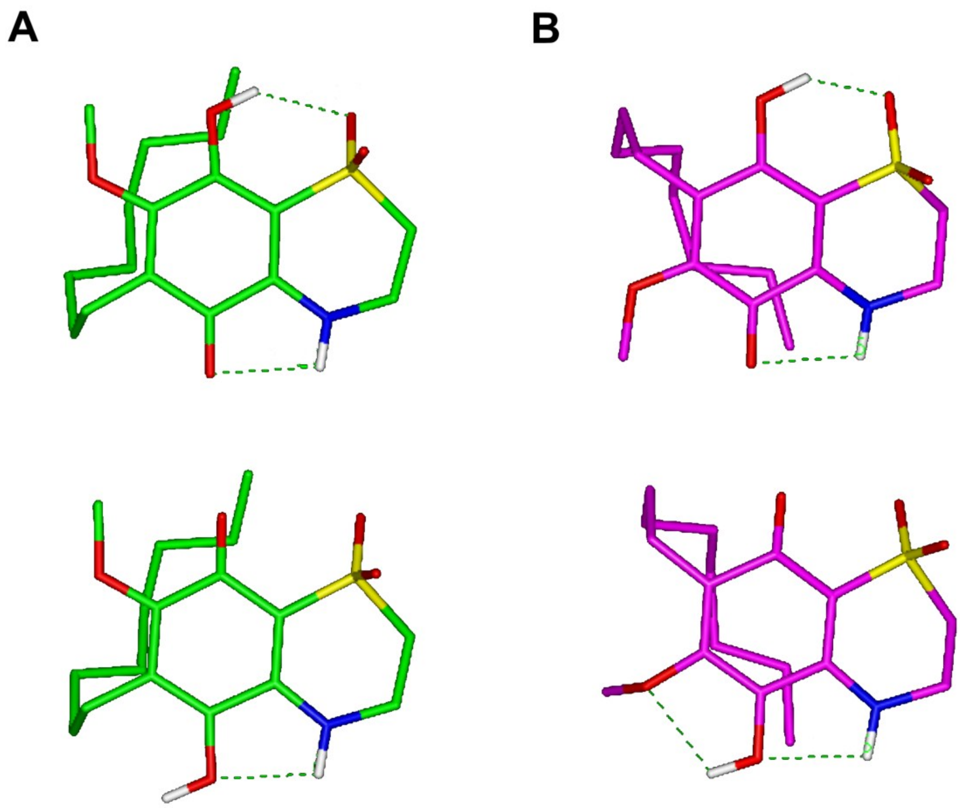


Figure 1SI. QH$^{\bullet}_{i}$ (top) and QH$^{\bullet}_{ii}$ (bottom) species of **12** GM (green; A) and **15** GM (magenta; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogen bonds are highlighted by green dashed lines. Hydrogens are omitted for the sake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

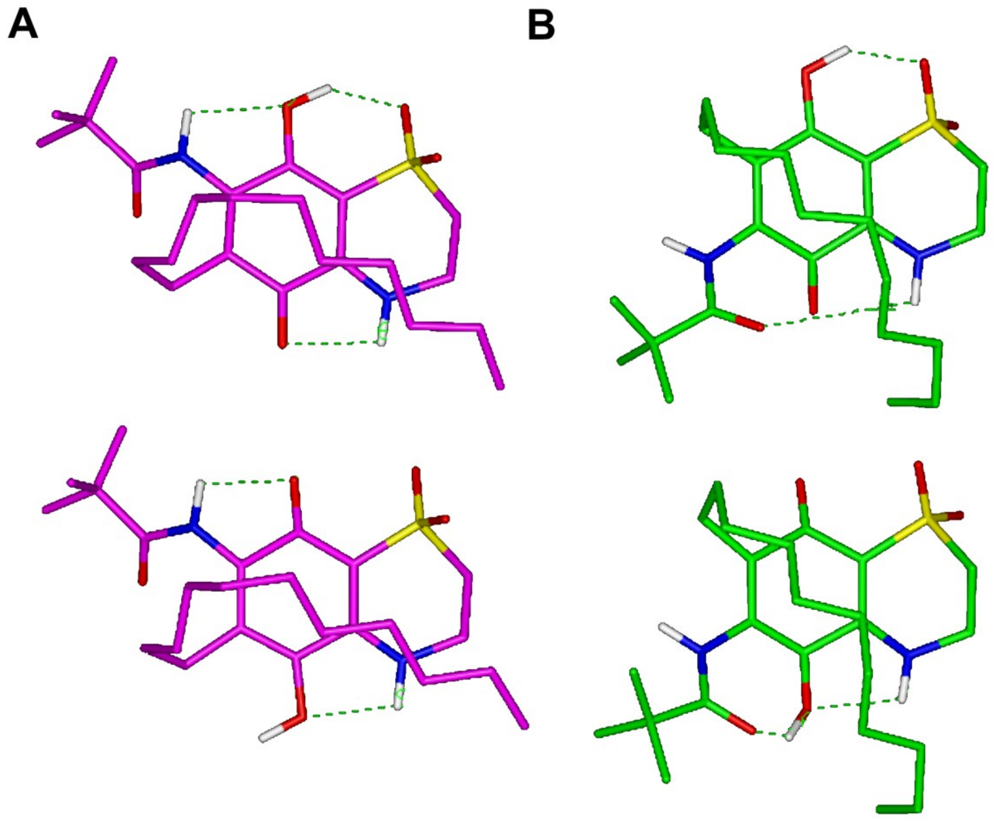


Figure 2SI. QH$^{\bullet}_{i}$ (top) and QH$^{\bullet}_{ii}$ (bottom) species of **19** GM (magenta; A) and **22** GM (green; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogen bonds are highlighted by green dashed lines. Hydrogens are omitted for the sake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

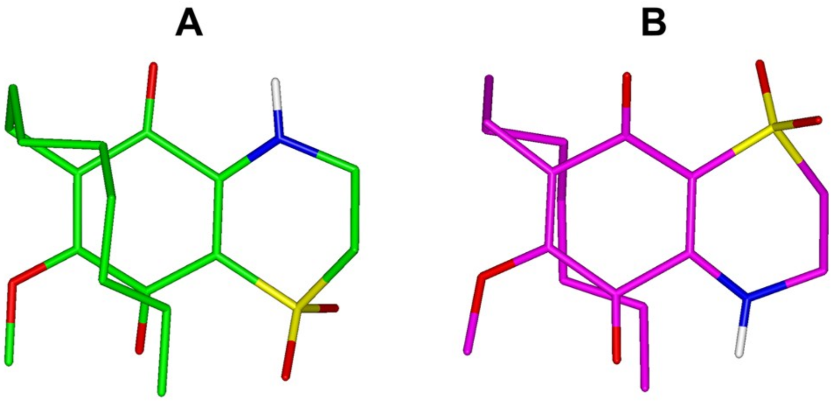


Figure 3SI. PM7 GM conformer of **12** (green; A); PM7 GM conformer of **15** (magenta; B). The ligands are colored by atom type (O = red, N = blue, S = yellow and H = white). Hydrogens are omitted for the sake of clarity with the exception of those of amine function.