New alkaloids with unusual spermidine moieties from the seeds of Orychophragmus violaceus and their cytoprotective properties

Nailiang Zhu,[1,a] Haifeng Wu,[1,a] Ziqian Xu,[b] Chenqi Liu,[a] Yu Tian, [a] Meigeng Hu, [a] Zhong Hao Sun, [a] Pengfei Li,[a] Guoxu Ma[a,*]and Xudong. Xu[a,*]

[a] *Key Laboratory of Bioactive Substances and Resource Utilization of Chinese Herbal Medicine, Ministry of Education, Institute of Medicinal Plant Development, Peking Union Medical College and Chinese Academy of Medical Sciences，Beijing 100193, China*

[b] *School Public Health, Peking University, Beijing 100191, China.*

Table S1. NMR Data (600 MHz, in DMSO) for Compounds **1-3**

Position	**1**		**2**		**3**	
	δ_C, type	δ_H(*J* in Hz)	δ_C, type	δ_H(*J* in Hz)	δ_C, type	δ_H(*J* in Hz)
1	144.8, C		144.7, C		145.8, C	
2						
3	145.4, C		145.3, C		145.4, C	
4	151.3, C		150.9, C		145.2, C	
5	112.3, CH	7.38, d (1.2)	112.0, CH	7.36, d (1.2)	115.5, CH	6.19, d (1.2)
6	132.0, C		131.6, C		132.5, C	
7	138.2, CH	7.44, d (15.6)	137.7, CH	7.43, d (15.6)	28.7, CH_2	2.66, m
8	122.4, CH	6.77, d (15.6)	122.1, CH	6.68, d (15.6)	35.3, CH_2	2.15, m
9	165.4, C		165.1, C		170.9, C	
10		8.37, brs		8.43, brs		7.55, brs
11	37.1, CH_2	3.28, m	37.2, CH_2	3.28, m	37.5, CH_2	2.64, m
12	24.1, CH_2	1.57, m	24.4, CH_2	1.58, m	29.3, CH_2	1.40, m
13	21.3, CH_2	1.60, m	44.8, CH_2	2.70, m	47.3, CH_2	2.32, m
14	45.9, CH_2	2.80, m		8.40, brs		8.32, brs
15		8.26, brs	46.5, CH_2	2.51, m	48.7, CH_2	2.48, m
16	44.1, CH_2	2.58, m	23.3, CH_2	1.56, m	25.8, CH_2	1.48, m
17	25.6, CH_2	1.56, m	26.6, CH_2	1.51, m	26.0, CH_2	1.53, m
18	36.1, CH_2	2.61, m	36.3, CH_2	2.61, m	38.3, CH_2	3.22, m
19		7.82, brs		7.73, brs		8.60, brs
20	171.1, C		170.7, C		165.3, C	
21	36.1, CH_2	2.09, m	35.5, CH_2	2.13, m	122.9, CH	6.55, d (15.6)
22	29.0, CH_2	2.62, m	28.6, CH_2	2.65, m	137.6, CH	7.36, d (16.2)
23	132.2, C		132.0, C		131.9, C	
24	122.7, CH	6.62, dd (7.8, 1.2)	122.6, CH	6.65, dd (7.8, 1.2)	120.1, CH	7.13, dd (8.4, 1.2)
25	116.1, CH	6.75, d (7.8)	115.9, CH	6.76, d (7.8)	120.9, CH	6.81, d (8.4)
26	145.9, C		145.5, C		151.1, C	
27	114.9, CH	6.08, d (1.2)	114.9, CH	6.14, d (1.2)	112.3, CH	7.33, d (1.2)
28	121.8, CH	6.89, d (8.4)	121.2, CH	6.87, d (7.8)	116.3, CH	6.76, d (7.8)
29	120.7, CH	7.18, dd (8.4, 1.2)	120.1, CH	7.17, dd (7.8, 1.2)	123.3, CH	6.65, dd (7.8, 1.2)
-OCH_3	55.7, CH_3	3.80, s	55.4, CH_3	3.80, s	55.7, CH_3	3.80, s

Table S2. NMR Data (600 MHz, in DMSO) for Compounds **4-5**

Position	**4**		**5**	
	δ_C, type	δ_H(*J* in Hz)	δ_C, type	δ_H(*J* in Hz)
1	146.5, C		146.5, C	
2				
3	145.3, C		145.3, C	
4	151.8, C		151.8, C	
5	112.4, CH	7.35, d (1.2)	112.4, CH	7.35, d (1.2)
6	132.5, C		132.4, C	

7	138.4, CH	7.45, d (15.6)	138.3, CH	7.45, d (15.6)
8	122.4, CH	6.65 d (15.6)	122.3, CH	6.65, d (15.6)
9	165.6, C		165.6, C	
10		8.08, brs		8.08, brs
11	37.8, CH_2	3.27, m	37.5, CH_2	3.24, m
12	24.8, CH_2	1.37, m	24.6, CH_2	1.45, m
13	24.3, CH_2	1.48, m	48.4, CH_2	3.13, m
14	45.1, CH_2	3.13, m		
15			46.2, CH_2	3.00, m
16	43.6, CH_2	2.94, m	23.5, CH_2	1.42, m
17	27.9, CH_2	1.35, m	28.9, CH_2	1.39, m
18	36.7, CH_2	2.53, m	36.3, CH_2	2.54, m
19		7.52, brs		7.55, brs
20	170.9, C		171.1, C	
21	35.7, CH_2	2.10, m	35.7, CH_2	2.10, m
22	28.7, CH_2	2.64, m	28.8, CH_2	2.64, m
23	132.5, C		132.6, C	
24	122.6, CH	6.59, dd (7.8, 1.2)	122.6, CH	6.60, dd (7.8, 1.2)
25	116.0, CH	6.72, d (7.8)	116.1, CH	6.73, d (7.8)
26	144.7, C		144.7, C	
27	114.5, CH	6.05, d (1.2)	114.5, CH	6.05, d (1.2)
28	122.7, CH	6.95, d (8.4)	122.7, CH	6.94, d (8.4)
29	120.8, CH	7.17, dd (8.4, 1.2)	120.8, CH	7.17, dd (8.4, 1.2)
4-OCH_3	55.8, CH_3	3.78, s	55.8, CH_3	3.77, s
15-C=O	169.1, C			
15-C=O-CH_3	21.2, CH_3	1.92, s		
14-C=O			169.1, C	
14-C=O-CH_3			21.4, CH_3	1.89, s

Table S3. NMR Data (600 MHz, in DMSO) for Compounds **6-8**

Position	**6**		**7**		**8**	
	δ_C, type	δ_H(J in Hz)	δ_C, type	δ_H(J in Hz)	δ_C, type	δ_H(J in Hz)
1	143.7, C		144.0, C		127.0, C	
2					126.8, C	
3	157.5, C		157.4, C		154.2, C	
4	117.5, CH	6.71, dd (8.4, 1.8)	117.3, CH	6.71, dd (8.4, 1.8)	128.7, CH	6.96, d (1.2)
5	130.3, CH	7.04, dd (8.4, 1.8)	130.4, CH	7.04, dd (8.4, 1.8)	131.2, C	
6	135.6, C		135.5, C		30.9, CH_2	2.76, m
7	31.0, CH_2	2.80, m	31.0, CH_2	2.80, m	37.7, CH_2	2.35, m
8	37.9, CH_2	2.37, m	37.8, CH_2	2.37, m	171.9, C	
9	173.9, C		173.9, C			7.80, brs
10					37.5, CH_2	2.98, m
11	44.4, CH_2	2.98, m	44.4, CH_2	2.98, m	30.3, CH_2	1.25, m
12	25.6, CH_2	1.19, m	28.3, CH_2	1.40, m	26.2, CH_2	1.15, m

13	27.2, CH_2	1.26, m	37.1, CH_2	2.95, m	46.8, CH_2	2.35, m
14	45.9, CH_2	3.07, m				8.36, brs
15			45.9, CH_2	3.07, m	44.2, CH_2	2.29, m
16	37.2, CH_2	2.95, m	26.4, CH_2	1.29, m	30.9, CH_2	1.52, m
17	29.5, CH_2	1.48, m	27.2, CH_2	1.19, m	35.3, CH_2	3.09, m
18	47.3, CH_2	3.02, m	47.3, CH_2	3.02, m		8.21, brs
19					173.4, C	
20	174.1, C		174.1, C		36.6, CH_2	2.47, m
21	38.1, CH_2	2.31, m	38.2, CH_2	2.31, m	30.3, CH_2	2.77, m
22	31.4, CH_2	2.70, m	31.4, CH_2	2.70, m	130.9, C	
23	133.3, C		133.4, C		132,0, CH	6.98, dd (7.8, 1.2)
24	125.8, CH	6.74, dd (7.8, 1.8)	125.9, CH	6.74, dd (7.8, 1.8)	116.9, CH	6.74, d (7.8)
25	117.8, CH	6.77, d (7.8)	117.9, CH	6.77, d (7.8)	154.2, C	
26	148.0, C		148.0, C		127.8, CH	6.97, d (1.2)
27	122.0, CH	6.66, d (1.8)	122.3, CH	6.66, d (1.8)	117.0, CH	6.76, d (7.8)
28	117.5, CH	6.71, d (8.4, 1.8)	117.3, CH	6.71, d (8.4, 1.8)	131.6, CH	6.95, dd (7.8, 1.2)
29	130.3, CH	7.04, dd (8.4, 1.8)	130.3, CH	7.04, dd (8.4, 1.8)		
15-C=O	172.4, C					
15-C=O-CH_3	21.3, CH_3	1.94, s				
14-C=O			172.3, C			
14-C=O-CH_3			21.4, CH_3	1.88, s		

Table S4. In Vitro Cytoprotective Activity of Compounds **1-3**

Group/ Compounds	**1** Viability（%）	**2** Viability（%）	**3** Viability（%）
normal	96±1.67	96±1.67	96±1.67
model（200μmol/ml）	60.68±2.66##	60.68±2.66##	60.68±2.66##
25μg/ml	69.72±1.49**	69.45±1.27**	68.84±2.36**
50μg/ml	73.89±1.09**	70.13±2.11**	69.58±2.32**
100μg/ml	73.43±2.54**	72.21±1.78**	71.02±2.15**
200μg/ml	67.13±2.62	66.21±4.74	63.30±2.99
400μg/ml	64.95±3.25	62.12±2.55	61.34±2.60

Table S5. In Vitro Cytoprotective Activity of Compounds **4-8**

Group/ Compounds	**4/5** Viability（%）	**6/7** Viability（%）	**8** Viability（%）
normal	96±1.67	96±1.67	96±1.67
model（200μmol/ml）	60.68±2.66##	60.68±2.66##	60.68±2.66##
25μg/ml	69.11±1.34**	68.75±2.27**	68.77±2.75**
50μg/ml	70.66±2.45**	69.98±1.67**	69.33±2.18**
100μg/ml	72.19±2.08**	71.82±2.33**	71.47±1.78**
200μg/ml	65.43±4.77	64.26±4.31	63.55±2.65

400μg/ml	62.78±2.69	62.07±3.01	61.76±2.46

Experimental

General experimental procedures

Optical rotation data were obtained using a Perkin-Elmer 341 digital polarimeter. UV data were recorded with a Shimadzu UV2550 spectrometer. IR data were recorded using a FTIR-8400S spectrometer. NMR spectra were obtained using a Bruker AVⅢ 600 NMR spectrometer (chemical shift values are presented as δ values with TMS as an internal standard). HRESIMS was performed using an LTQ-Obitrap XL spectrometer. HPLC separation was conducted using a Lumiere K-1001 pump, a Lumiere K-2501 single λ absorbance detector and a Kromasil (250 × 21.2 mm) preparative column packed with C_{18} (5 μm). Sephadex LH-20 (Pharmacia, Uppsala, Sweden), MCI gel (CHP 20P, 75-150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan), C-18 reversed-phase silica gel (40-63 μm, Merck, Darmstadt, Germany) and silica gel (100～200 and 300～400 mesh, Qingdao Marine Chemical plant, Qingdao, People's Republic of China) were used for CC, and precoated silica gel GF_{254} plates (Zhi Fu Huang Wu Pilot Plant of Silica Gel Development, Yantai, China) were used for TLC. All solvents employed were of analytical grade (Beijing Chemical Plant, China).

Plant material

Seeds of *Orychophragmus violaceus* were collected in Beijing, China in August 2015 and identified by Prof. Wan-Long Ding of the Institute of Medicinal Plant Development, Peking Union Medical College and Chinese Academy of Medical Sciences. A voucher specimen (NO. 150811) was deposited at the Institute of

Medicinal Plant Development.

Extraction and isolation

The air-dried and powdered seeds of *Orychophragmus violaceus* (20.0 kg) were extracted three times with Water (3×40 L, 2h each). The Water extract was concentrated to the small volume (3 L), and applied on a D-101 macroporous adsorptive resin (20 Kg, 20 cm×200 cm), eluting with H_2O (60 L) and 10% EtOH (80 L). The 10% EtOH fraction was concentrated under reduced pressure, and the residue (400 g) was subjected to column chromatography (CC) on silica gel (100～200 mesh, 15 × 60 cm) eluting with a stepwise gradient of CH_2Cl_2/CH_3OH (10:1 to 1:1, 5 L) to obtain eight fractions (Fr. A–Fr. H). Fr. F (30 g) was subjected to chromatography using ODS MPLC elution with MeOH-H_2O (10:90; 30:70; 50:50), yielding three fractions (Fr. F1-3). Fr. F1 (5.7 g) was separated by a Sephadex LH-20 column (5 × 80 cm), eluted with MeOH, and then purified by preparative HPLC affording compounds **1** (15.6 mg)，**2** (10.2 mg) and **3** (11.8 mg). Fr. F2 (4.6 g) was separated via reverse-phase chromatography over C-18 silica gel, eluted with MeOH-H_2O (10:90; 30:70), and then purified through preparative HPLC elution using a MeOH-H_2O (25:75) system and a Kromasil RP-18 column. Finally, compounds **4**, **5** (15.3 mg), **6**, **7** (12.8 mg), and **8** (11.1 mg) were obtained .

Orychophragmuspine A (**1**), amorphous white solid; UV (MeOH) λ_{max} (log ε): 287.6 (3.20) nm, 233.6 (2.89) nm; IR (film) ν_{max}: 3301, 3250 (OH, NH) cm^{-1}, 1652 (β-unsaturated amide) cm^{-1}, 1588, 1537, 1504 (aromatic ring) cm^{-1}. ESIMS: *m/z* 468

[M+H] $^{+}$, *m/z* 490 [M+Na]$^{+}$, HRESIMS: *m/z* 468.2483 [M+H]$^{+}$ (calcd. for 468.2498); ^{1}H, ^{13}C NMR, see Table 1.

Orychophragmuspine B (**2**), amorphous white solid; UV (MeOH) λ_{max} (log ε): 285.1 (3.34) nm, 233.6 (3.30) nm; IR (film) ν_{max}: 3310, 3256 (OH, NH) cm^{-1}, 1651 (β-unsaturated amide) cm^{-1}, 1580, 1539, 1504 (aromatic ring) cm^{-1}. ESIMS: *m/z* 468 [M+H]$^{+}$, *m/z* 490 [M+Na]$^{+}$, HRESIMS: *m/z* 468.2487 [M+H]$^{+}$ (calcd. for 468.2498); ^{1}H, ^{13}C NMR, see Table 1.

Orychophragmuspine C (**3**), amorphous white solid; UV (MeOH) λ_{max} (log ε): 285.1 (3.34) nm, 233.6 (3.30) nm; IR (film) ν_{max}: 3310, 3256 (OH, NH) cm^{-1}, 1651 (β-unsaturated amide) cm^{-1}, 1580, 1539, 1504 (aromatic ring) cm^{-1}. ESIMS: *m/z* 468 [M+H]$^{+}$, *m/z* 490 [M+Na]$^{+}$, HRESIMS: *m/z* 468.2481 [M+H]$^{+}$ (calcd. for 468.2498); ^{1}H, ^{13}C NMR, see Table 1.

Orychophragmuspine D (**4**) and E (**5**), amorphous white solid; UV (MeOH) λ_{max} (log ε): 282.0 (3.39) nm, 215.3 (3.60) nm; IR (film) ν_{max}: 3272, 3095 (OH, NH) cm^{-1}, 1645 (β-unsaturated amide) cm^{-1}, 1558, 1540, 1507 (aromatic ring) cm^{-1}. ESIMS: *m/z* 510 [M+H]$^{+}$, *m/z* 532 [M+Na]$^{+}$, HRESIMS: *m/z* 532.2413 [M+Na]$^{+}$ (calcd. for 532.2424); ^{1}H, ^{13}C NMR, see Table 1.

Orychophragmuspine F (**6**) and G (**7**), amorphous white solid; UV (MeOH) λ_{max} (log

ε): 287.6 (3.26) nm, 222.6 (3.83) nm; IR (film) ν_{max}: 3256, 3043 (OH, NH) cm^{-1}, 1601, 1534, 1504 (aromatic ring) cm^{-1}. ESIMS: *m/z* 482 $[M+H]^+$, *m/z* 504 $[M+Na]^+$, HRESIMS: *m/z* 504.2461 $[M+Na]^+$ (calcd. for 504.2474); ^1H, ^{13}C NMR, see Table 1.

Orychophragmuspine H(**8**), amorphous white solid; UV (MeOH) λ_{max} (log ε): 288.2 (3.23) nm, 220.8 (3.73) nm; IR (film) ν_{max} : 3317, 3150 (OH, NH) cm^{-1}, 1600, 1520, 1503 (aromatic ring) cm^{-1}. ESIMS: *m/z* 440 $[M+H]^+$, *m/z* 462 $[M+Na]^+$, HRESIMS: *m/z* 440.2537 $[M+H]^+$ (calcd. for 440.2549); ^1H, ^{13}C NMR, see Table 1.

Cytoprotective assay

The cytoprotective of compounds **1**-**8** was assessed via the MTT method using the $HepG_2$ cell lines. Preliminary experiments were conducted to standardize the number of cells to be seeded onto the 96 well plates. 10×10^4 cells were seeded to each well. Five different concentrations of each compound dissolved in dimethyl sulfoxide (DMSO) were subsequently added to the wells. The cells were grown in DMEM supplemented, cells were allowed to attach (for 12 h). 200 μmol/L H_2O_2 was added to the cell medium and the mixture was further incubated at 37 ℃for 2 h. After the drug treatment, the medium containing the drug was removed, washed with 150 μL of the MTT stock (0.5 mg/mL) was added to each of the 96 wells. After 4 h of incubation at 37 ℃ in a 5% CO_2 incubator, the solution was removed and 150 μL of DMSO was added to each well. After 5-10 min of incubation at 37 ℃, the wells were read on an ELISA plate reader (Tecan, Austia) at 570 nm wavelength. The data was recorded

using the software package Magellan 6.3. The viability (%) was calculated as follows:

$$\text{Viability} / \% = \frac{A_1 - A_0}{A_2 - A_0} \times 100$$

A_0: Blank wells OD A_1: Test wells OD A_2: control wells OD

(OD = optical density; Test wells = treated wells)

Measurement of lactate dehydrogenase (LDH) release

The cell damage was determined by the release of lactate dehydrogenase (LDH) into the incubation medium using the assay kit (Nanjing Jiancheng Bioengineering Institute, China) according to the manufacturer's instructions. Briefly, after the treatment, the cells in 6-well plate were centrifuged at 1000g for 4 min, 1 mL culture supernatants were collected from each well; 3.4 mL reaction buffer supplied in the kit was then added. 30 min after mixing at room temperature, the release of LDH was assessed using a microplate reader at a test wavelength of 340 nm and expressed as a percentage (%) of total LDH activity (LDH in the medium +LDH in the cell), according to the equation % LDH released = (LDH activity in the medium/total LDH activity) × 100. Each experiment was performed for four times.

Caspase-3 activity determination

Cells were harvested by centrifugation and the media removed. A volume of 50 μl of 10 μM substrate solution (PhiPhilux is a unique class of substrates for caspase-3) was added to the cell pellet (1×10^5 cells per sample); the cells were not vortex mixed. Cells were incubated at 37℃ for 60 minutes, then washed once by adding 1 ml of ice-cold PBS and were re-suspended in 1 ml fresh PBS. Cells were analyzed with a flow cytometer (Becton-Dickinson) equipped with an argon ion laser at 488 nm wavelength. Caspase-3 activity was determined and analyzed.

Measurement of intracellular ROS

The intracellular ROS level was measured using DCFH-DA. DCFH-DA is a non-

fluorescent compound that is enzymatically converted to the strongly fluorescent compound DCF in the presence of ROS. Briefly, PC12 cells were seeded into a 6-well culture plate at a density of 6 _ 105 cells/well. At the end of treatment, the cells were washed with PBS and incubated with DCFH-DA at a final concentration of 10 μM for 30 min at 37℃ in darkness. The cells were then washed 3 times with PBS to remove the extracellular DCFH-DA, and the fluorescence intensity of the DCF was measured with a fluorescent microplate reader at an excitation wavelength of 485 nm and an emission wavelength of 538 nm, and the intracellular ROS levels were expressed as percentage of control.

SOD assay

After the treatment, the cells were washed with ice-cold PBS twice, harvested by centrifugation at 1000g for 4 min, pooled in 0.5 mL PBS, and homogenized. The homogenate was centrifuged at 4000g for 15 min, and the supernatant was collected for SOD assay by using commercial kits (Nanjing Jiancheng Bioengineering Institute, Nanjing, China). All procedures complied with the manufacturer's instructions. The assay of total SOD was based on its ability to inhibit the oxidation of oxymine by the xanthine-xanthine oxidase system at 550 nm. The calculation: SOD activity (U/mg prot) = (absorbance of control tube-absorbance of test tube)/absorbance of control tube/50% ×dilution multiple/protein level (mg prot/mL).

Figure S1. HRESIMS spectrum of compound **1**

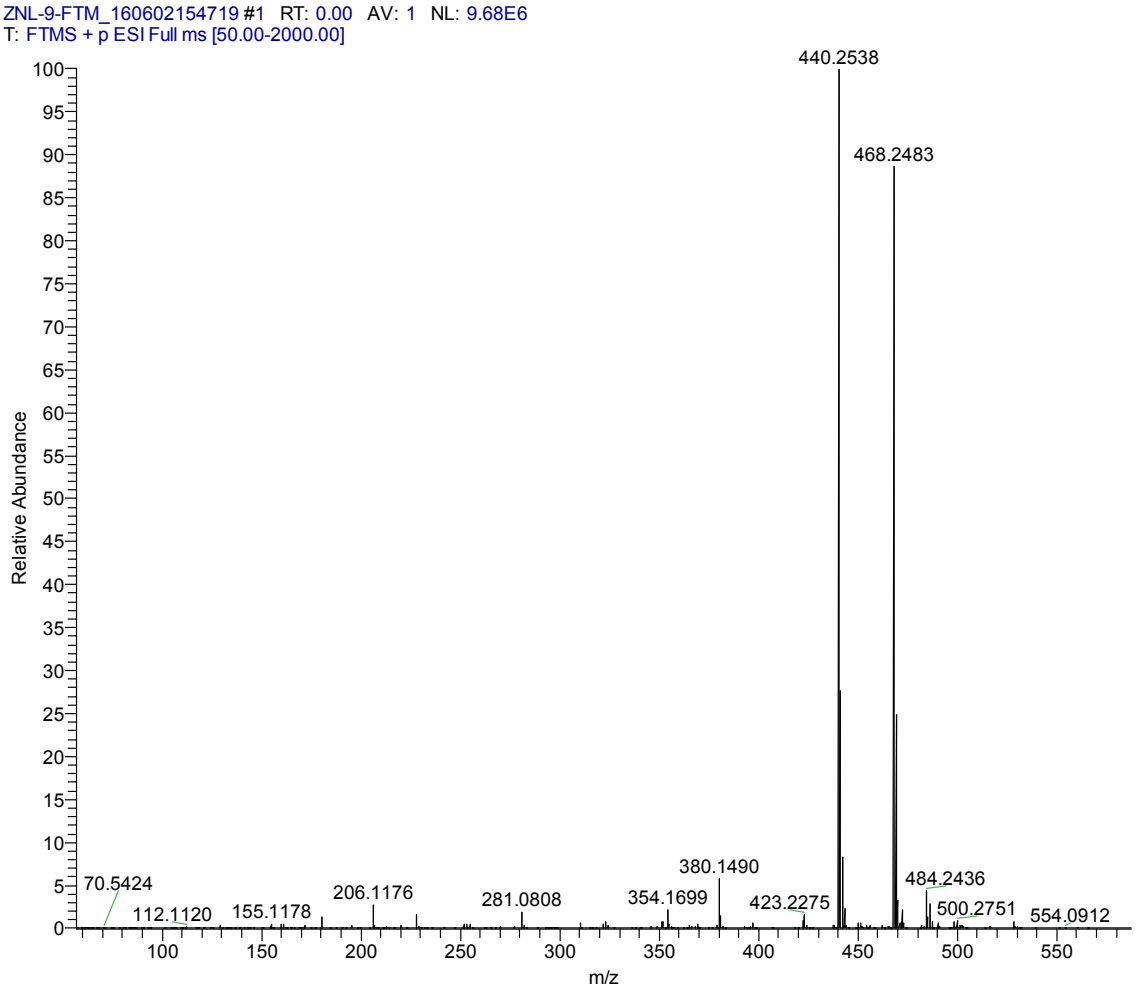

Figure S2. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **1**

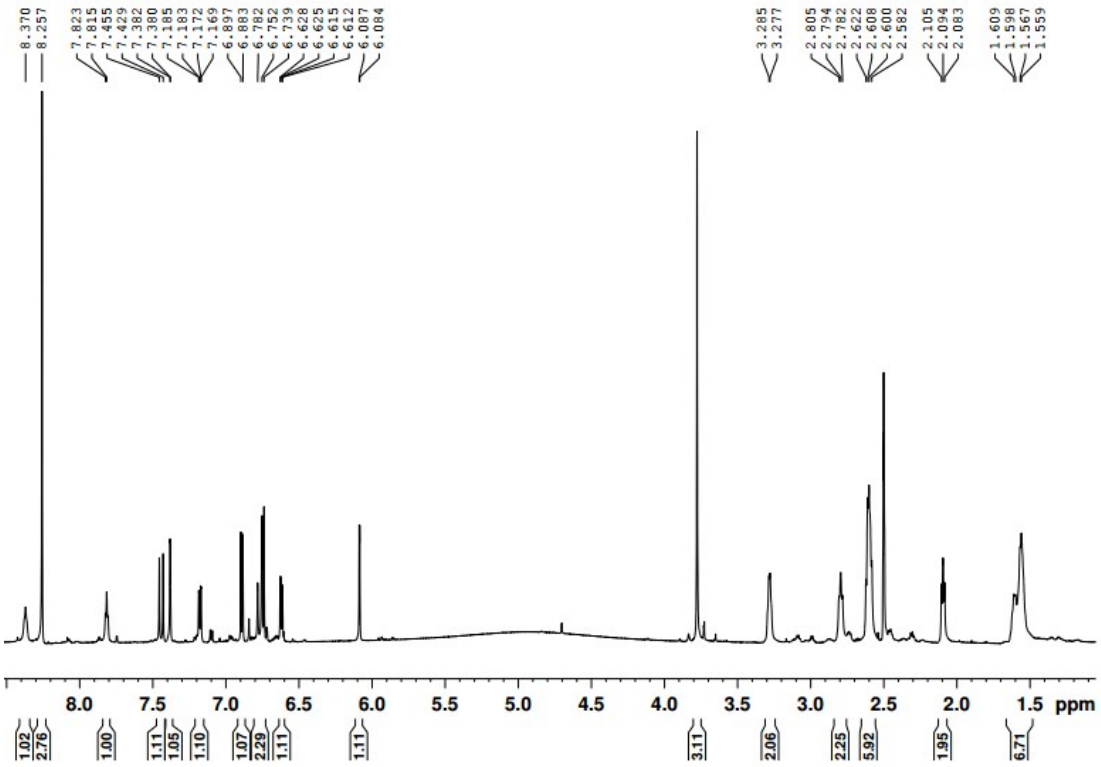

Figure S3. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **1**

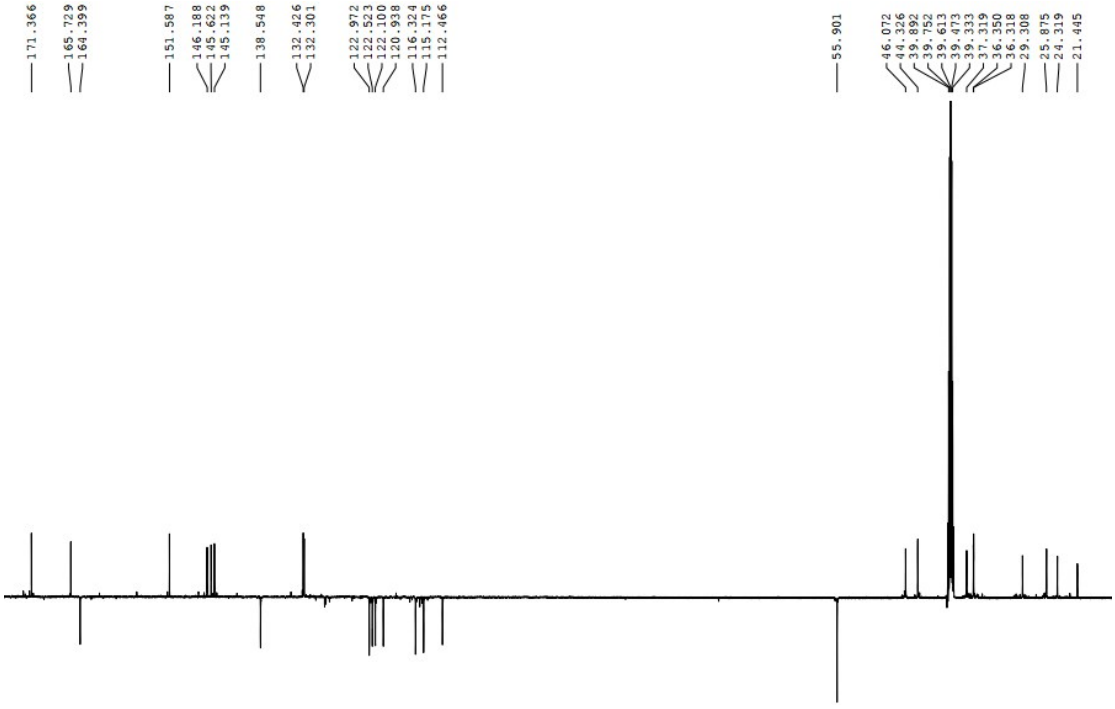

Figure S4. HSQC spectrum of the new compound **1**

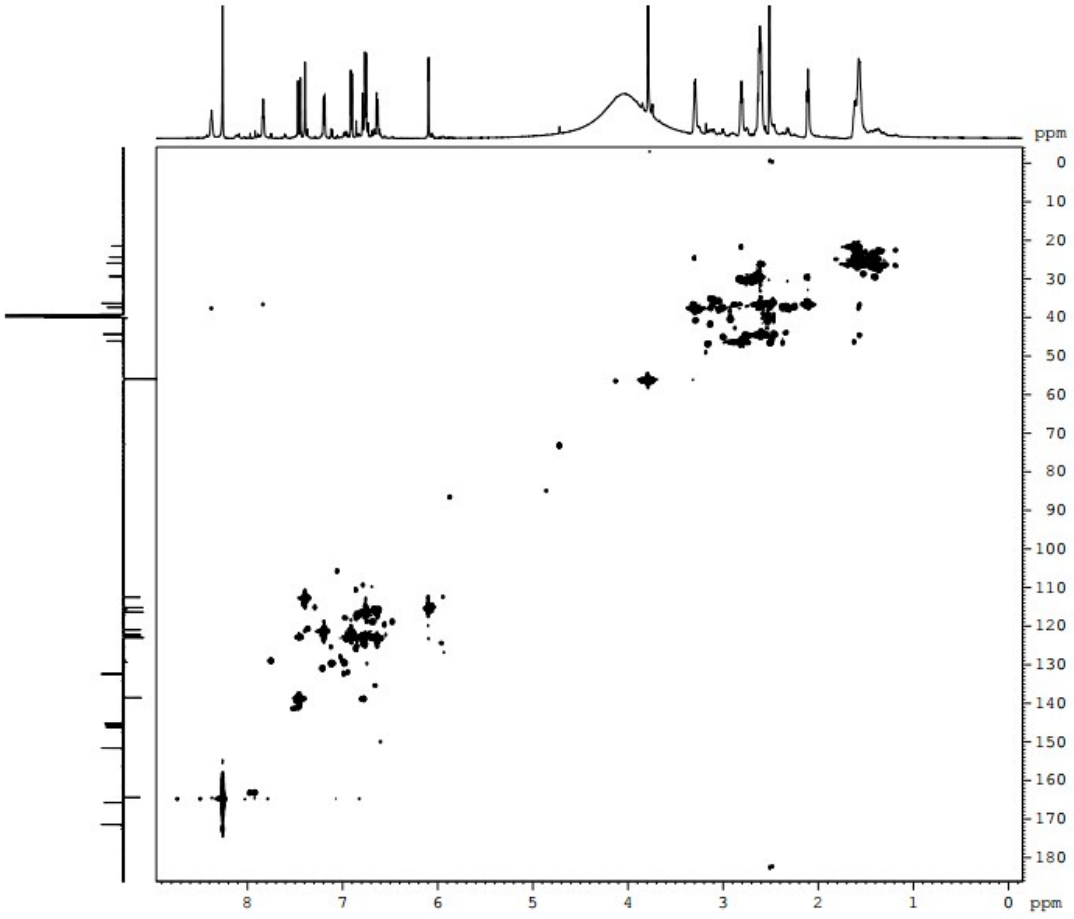

Figure S5. HMBC spectrum of the new compound **1**

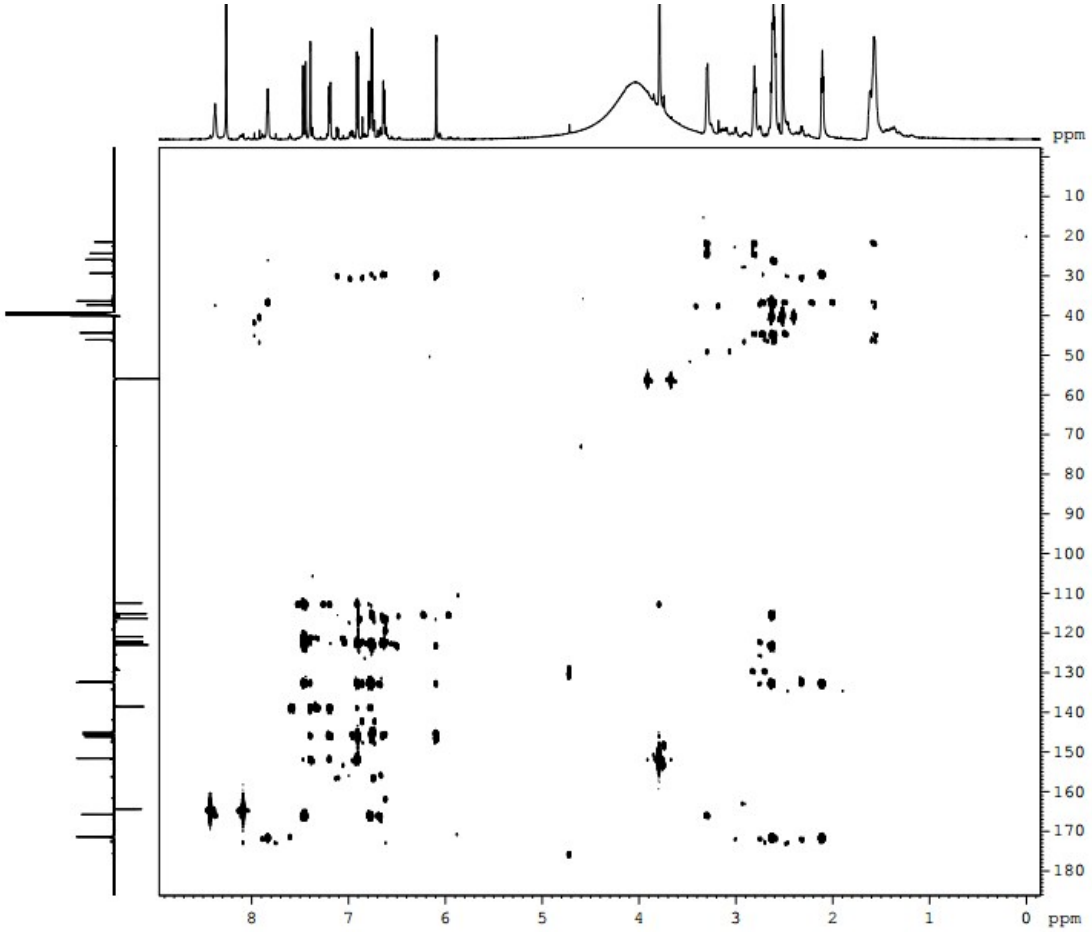

Figure S6. ^{1}H-^{1}H COSY spectrum of the new compound **1**

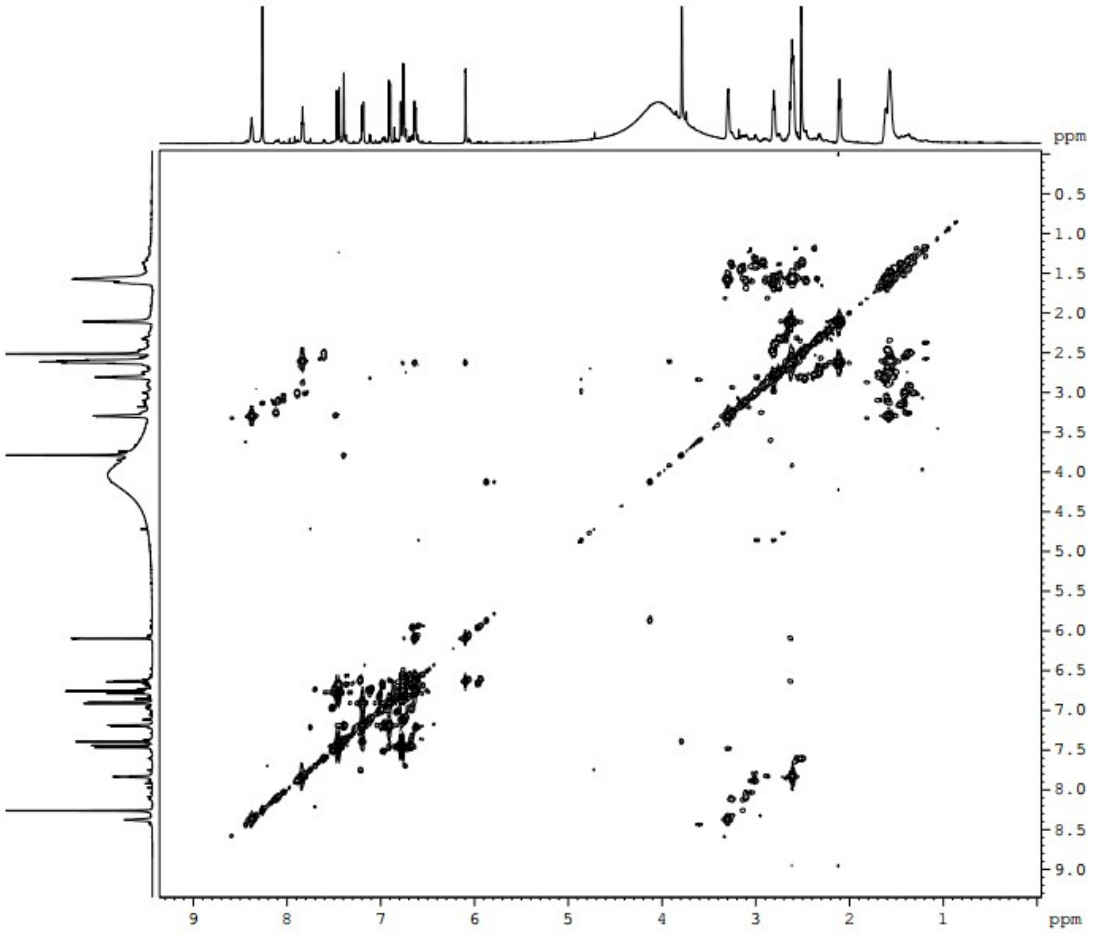

Figure S7. NOESY spectrum of the new compound **1**

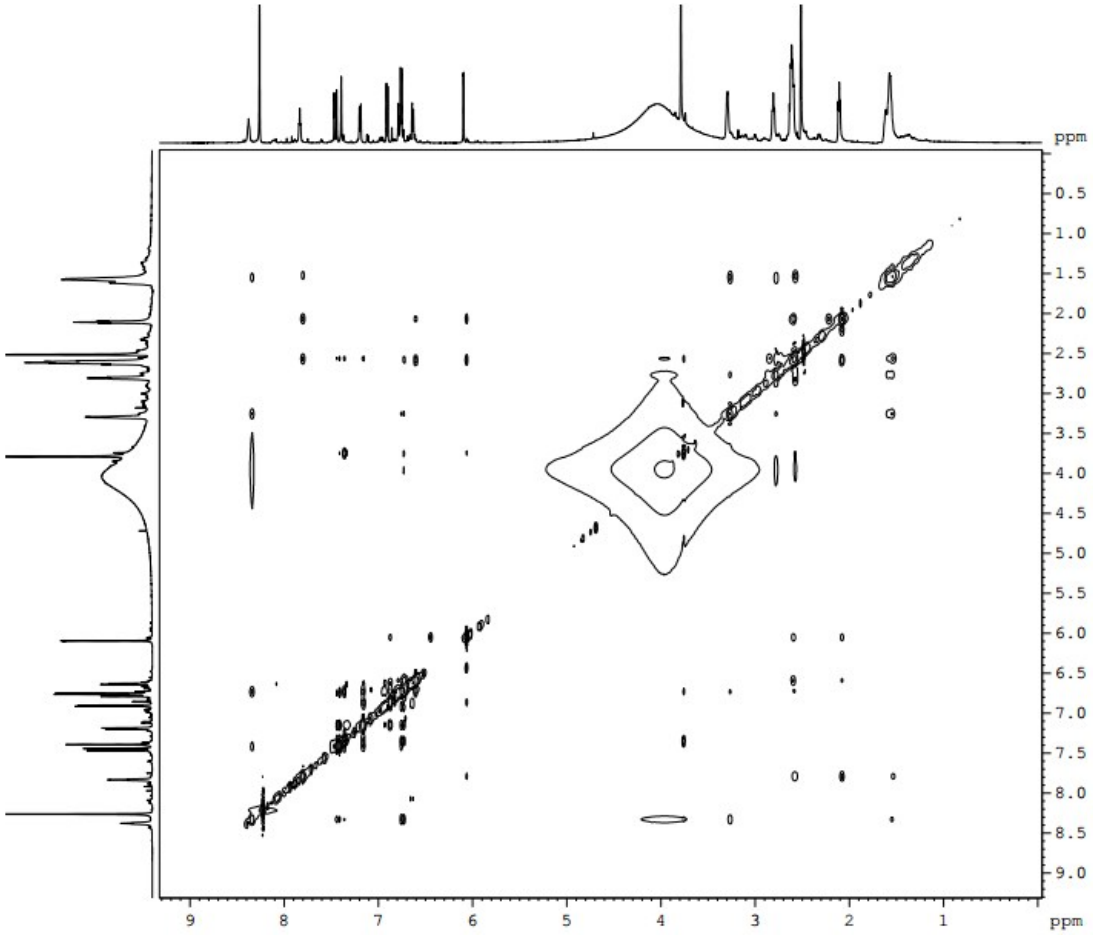

Figure S8. HRESIMS spectrum of compound **2**

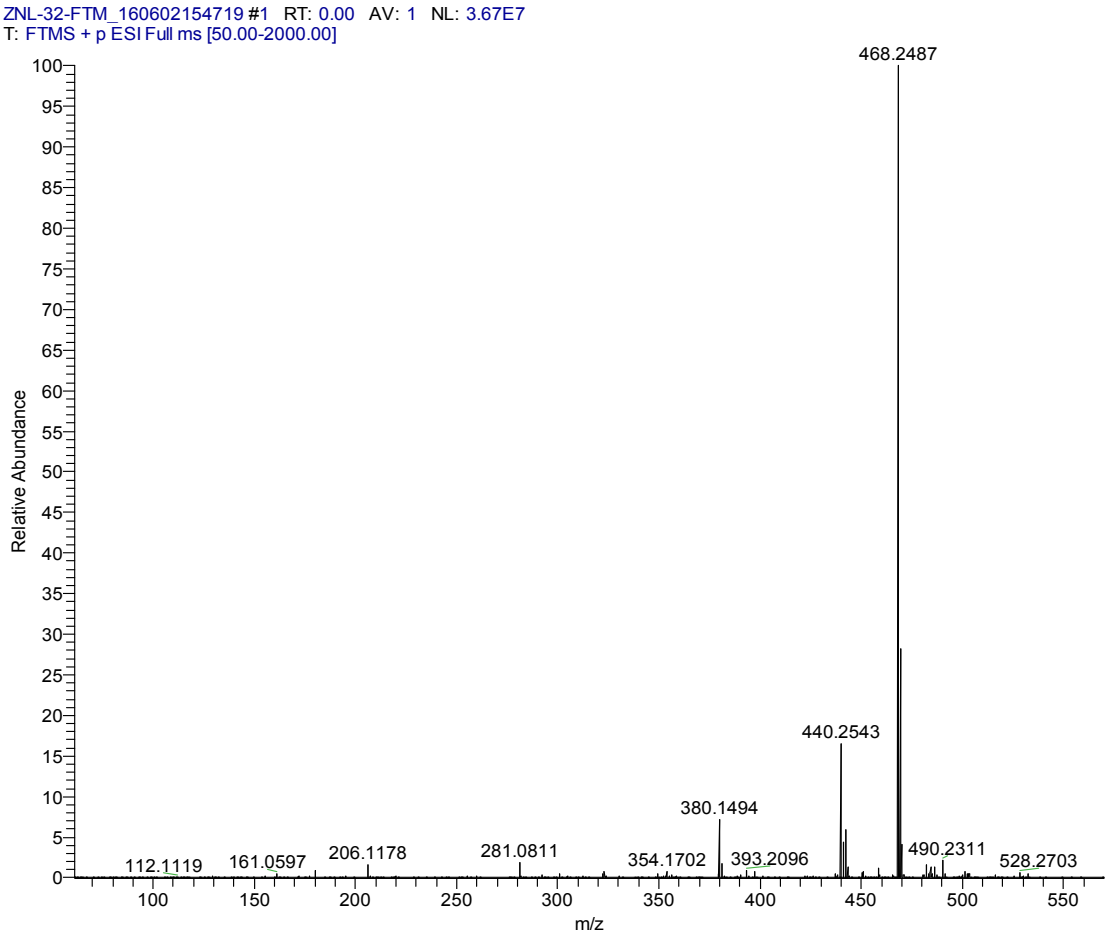

Figure S9. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **2**

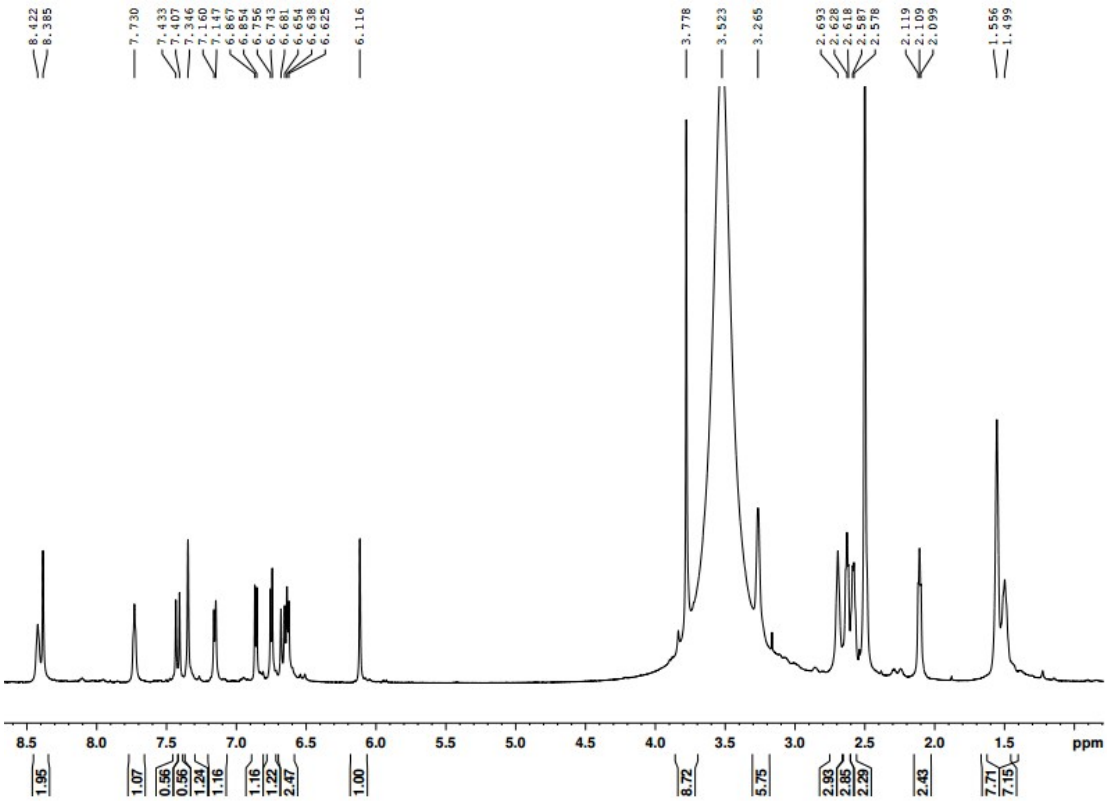

Figure S10. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **2**

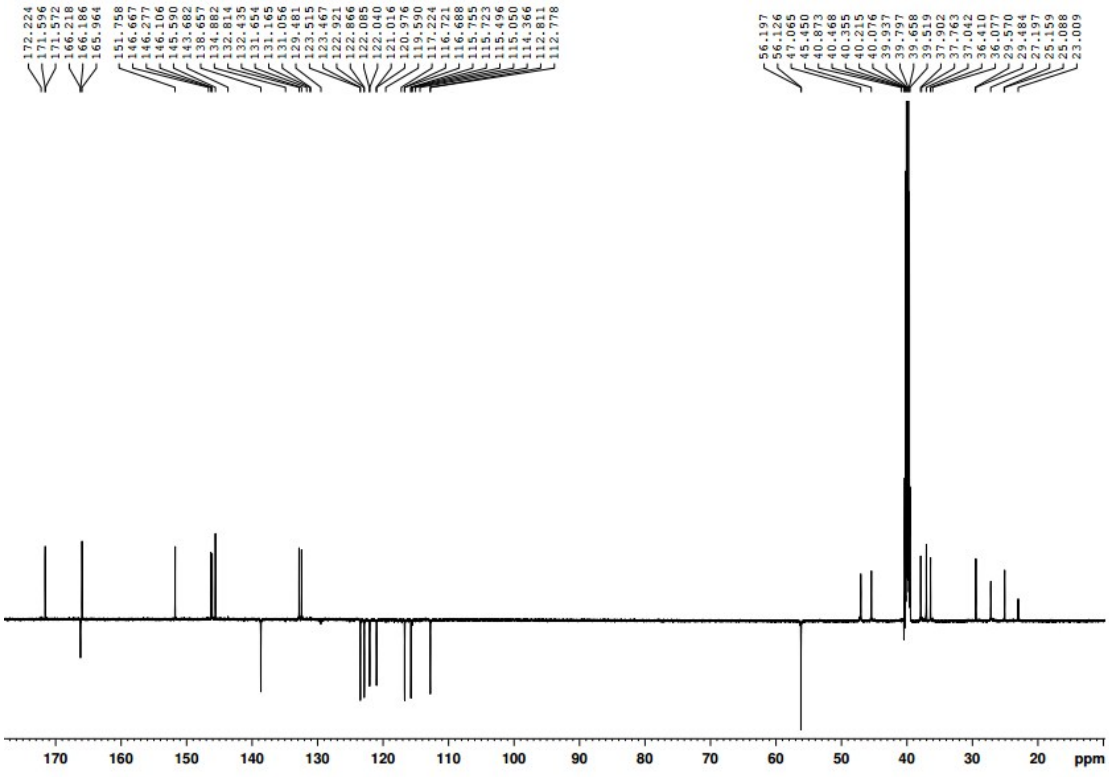

Figure S11. HSQC spectrum of the new compound **2**

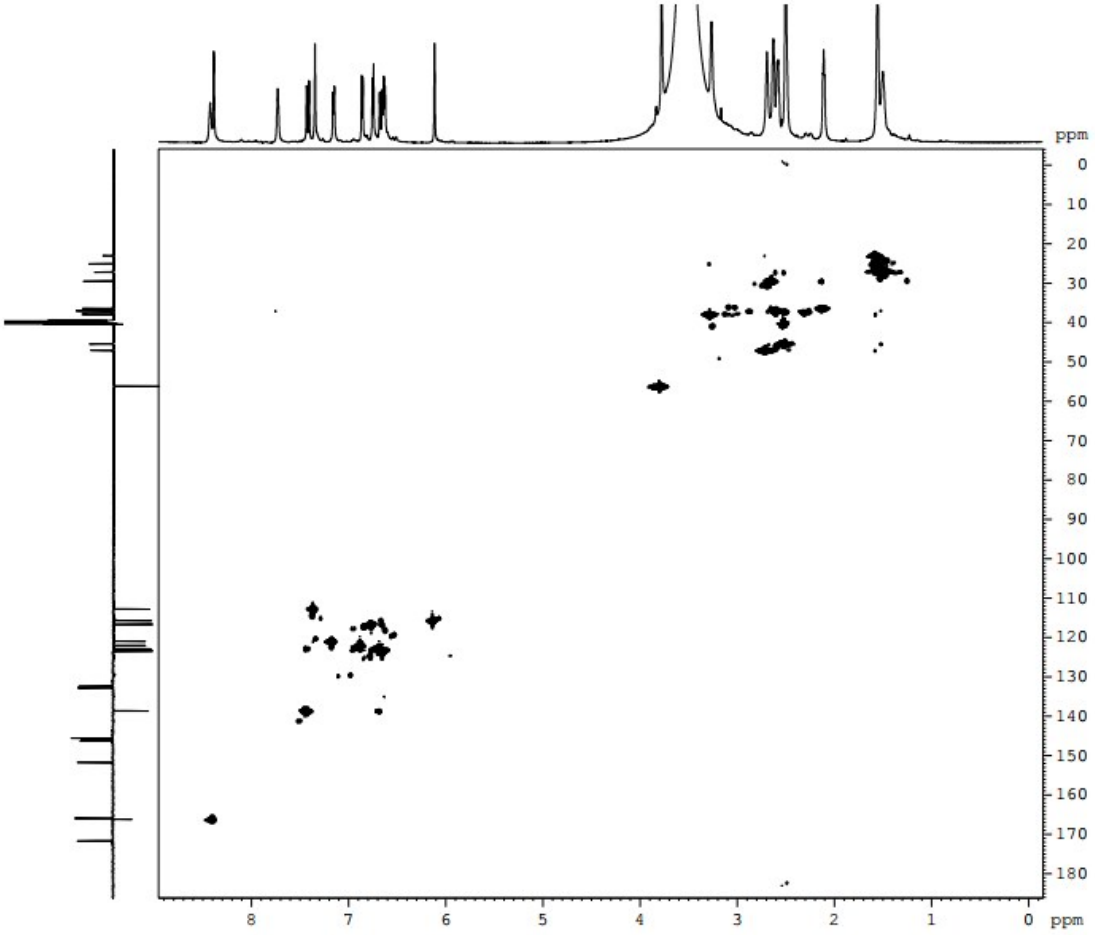

Figure S12. HMBC spectrum of the new compound **2**

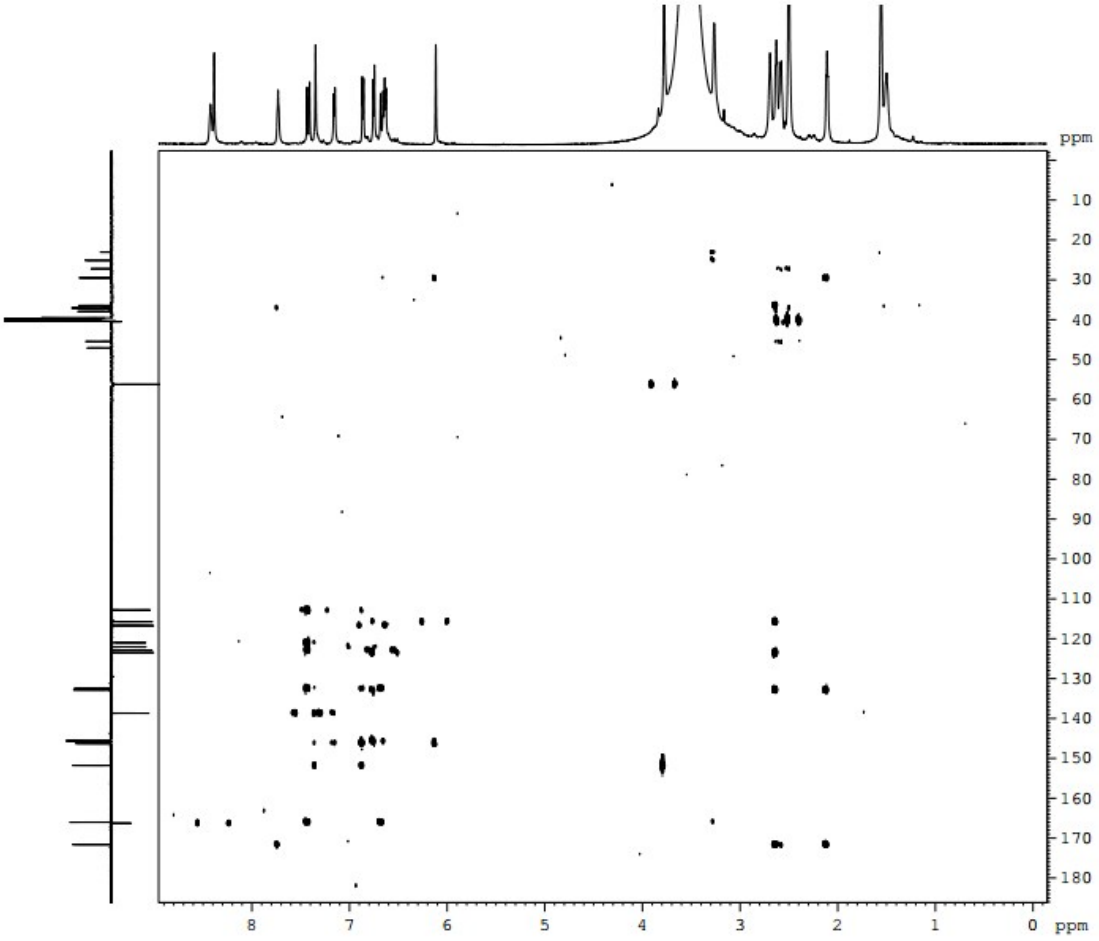

Figure S13. ^{1}H-^{1}H COSY spectrum of the new compound **2**

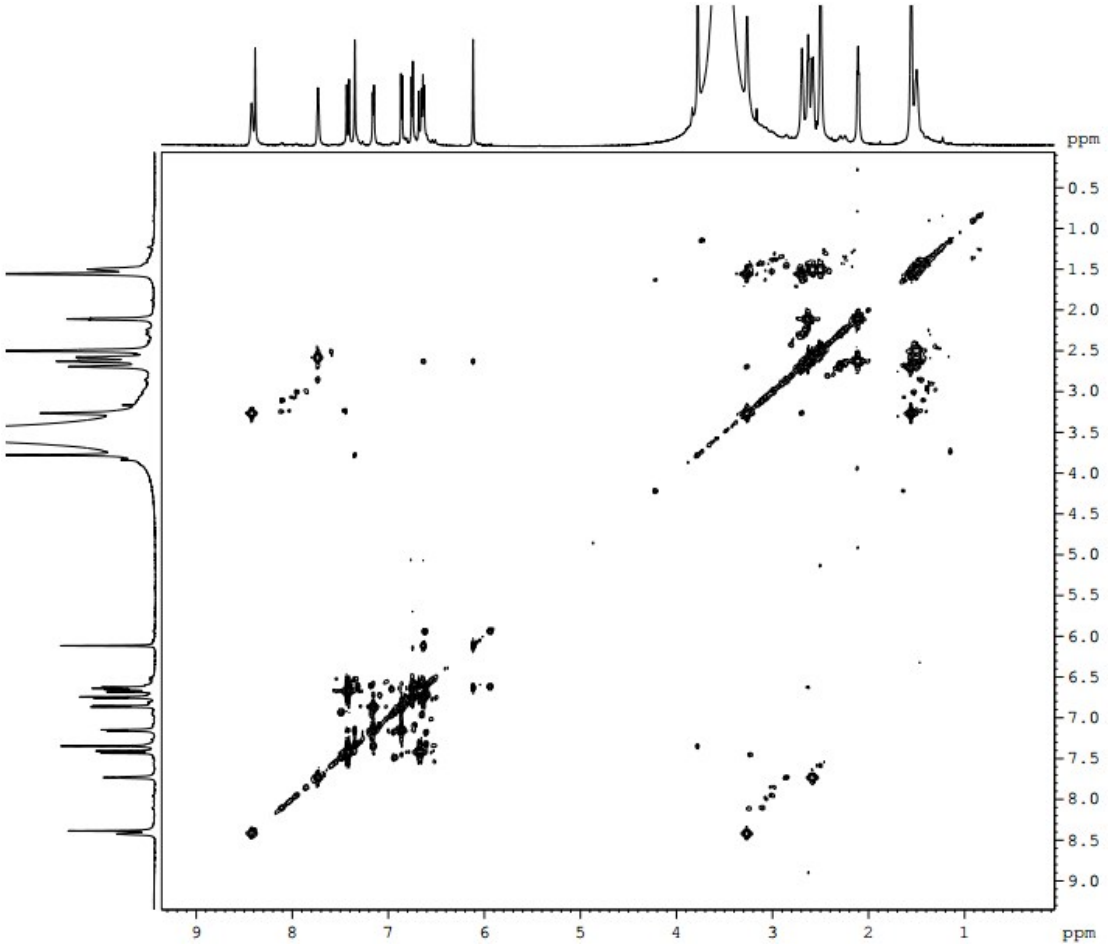

Figure S14. NOESY spectrum of the new compound **2**

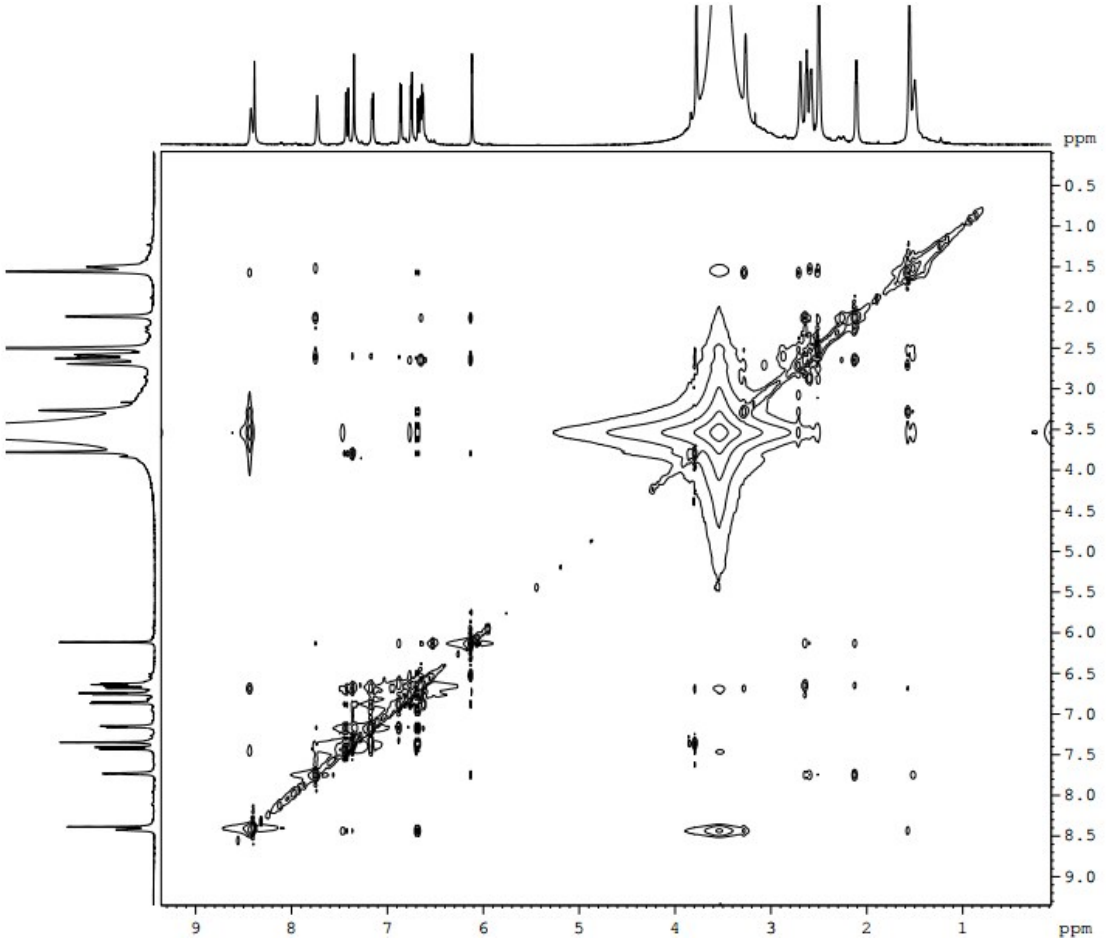

Figure S15. HRESIMS spectrum of compound **3**

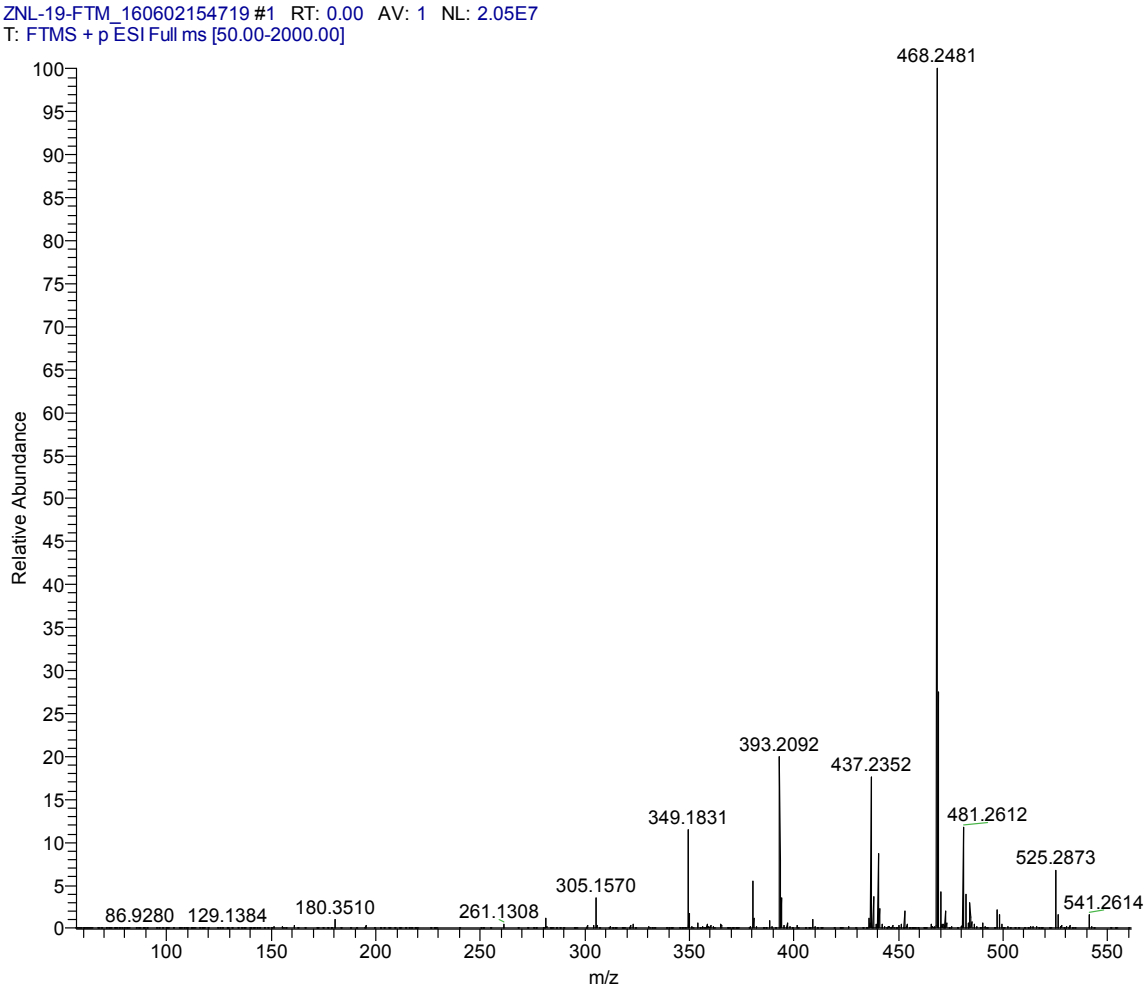

Figure S16. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **3**

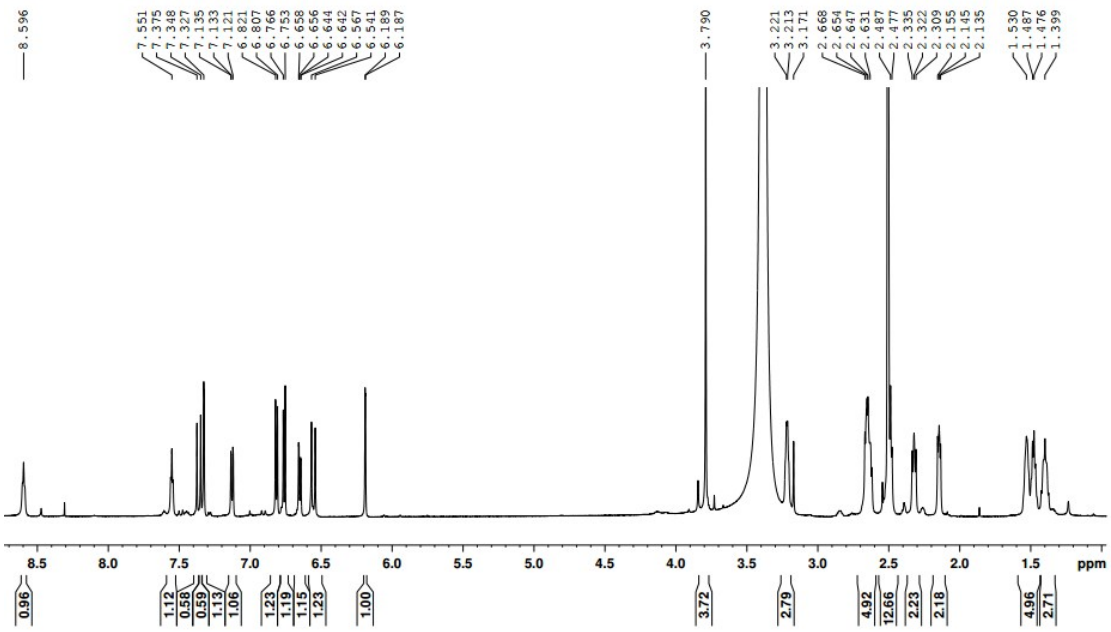

Figure S17. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **3**

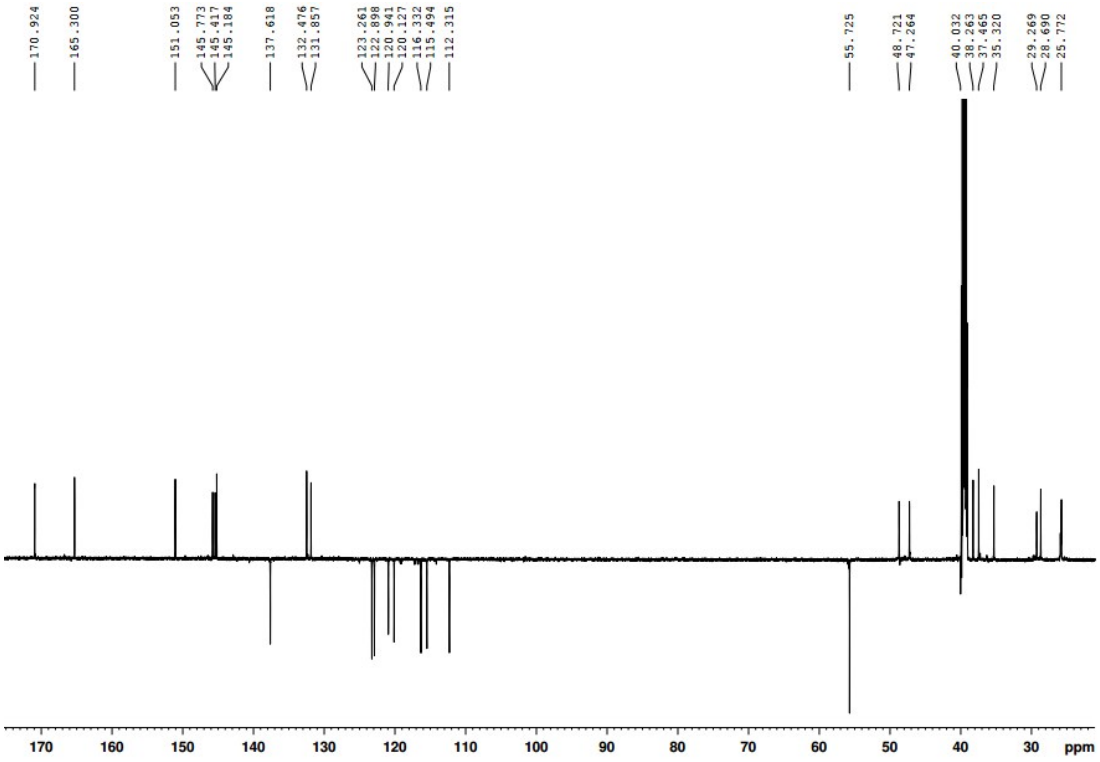

Figure S18. HSQC spectrum of the new compound **3**

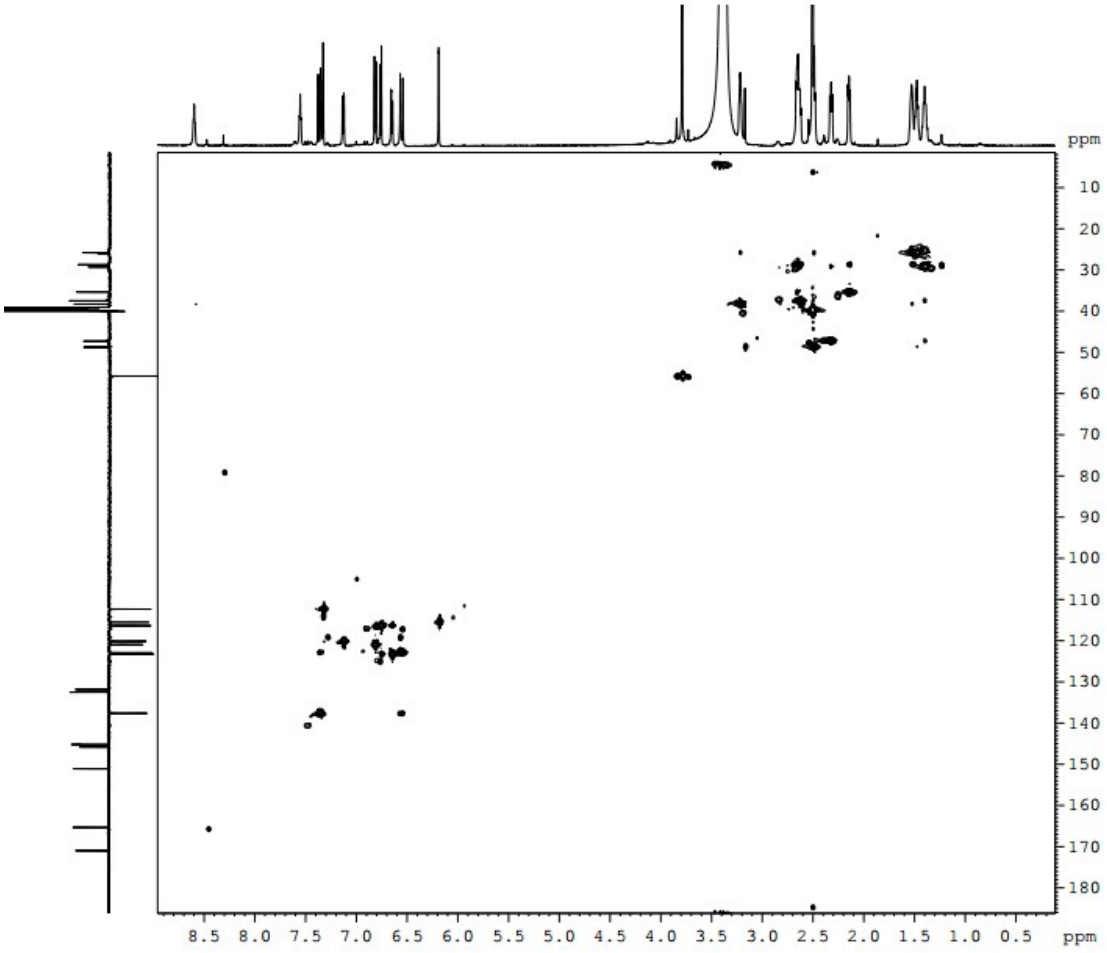

Figure S19. HMBC spectrum of the new compound **3**

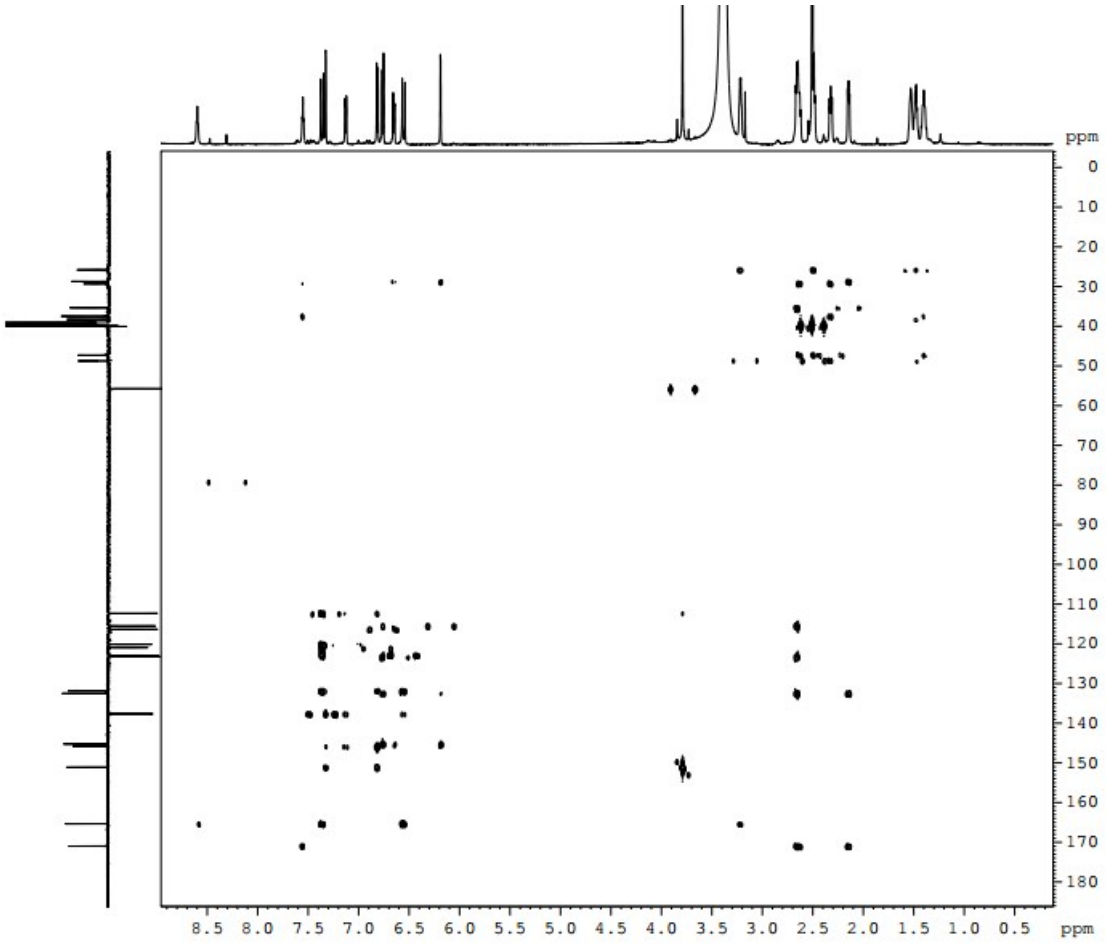

Figure S20. ^{1}H-^{1}H COSY spectrum of the new compound **3**

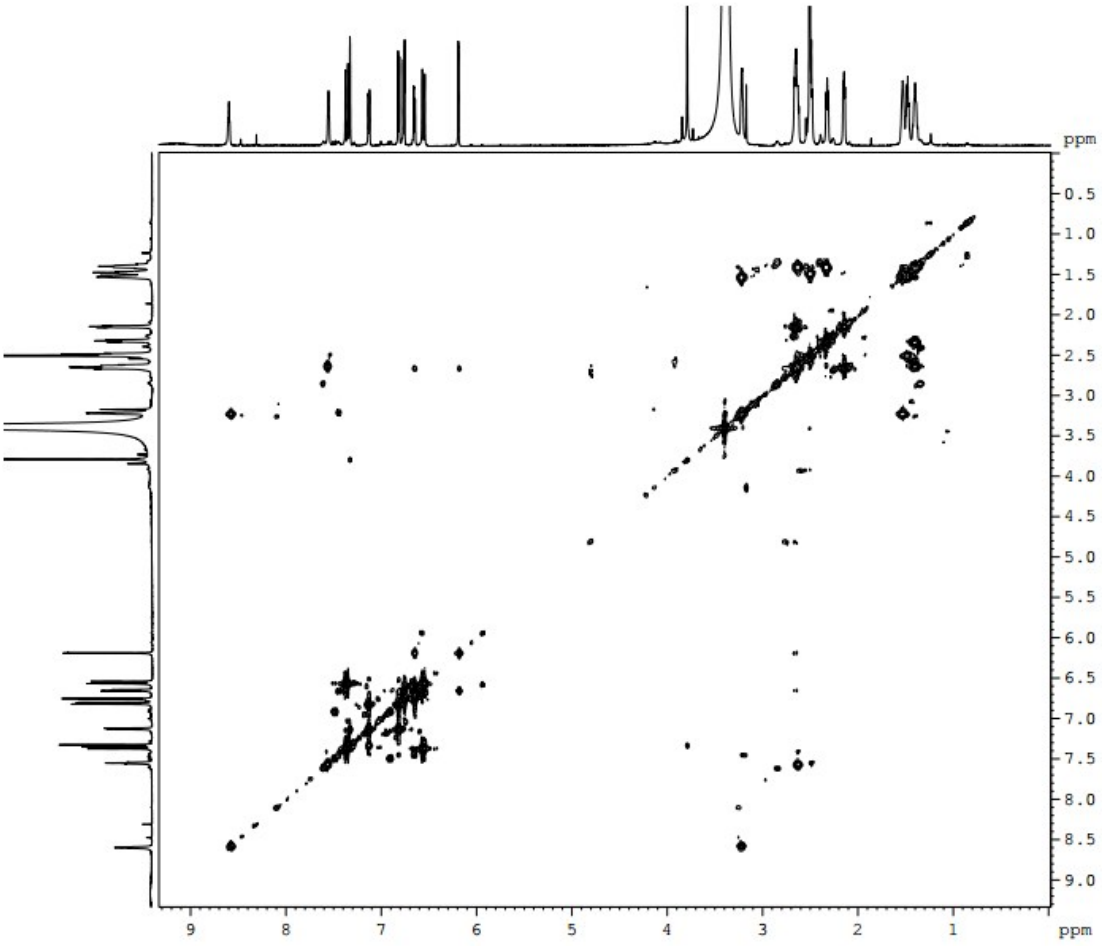

Figure S21. NOESY spectrum of the new compound **3**

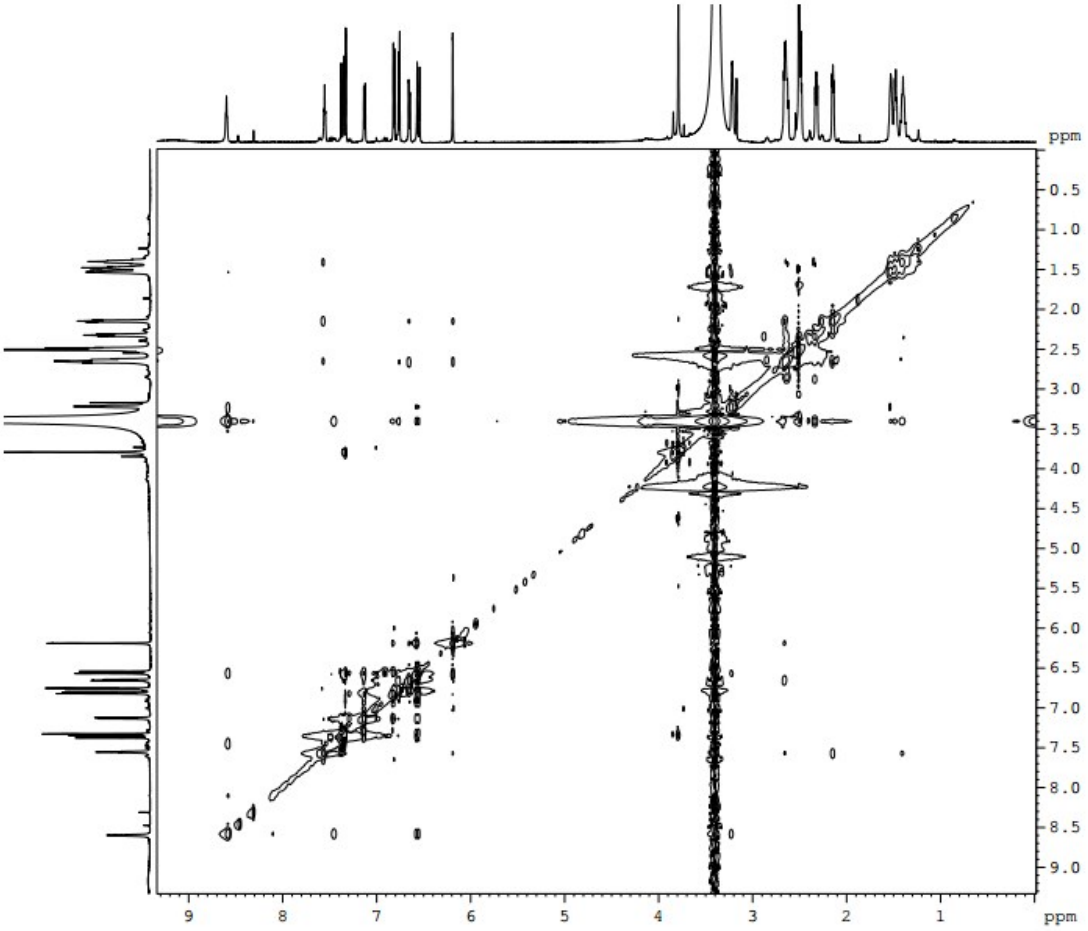

Figure S22. HRESIMS spectrum of compound **4** and **5**

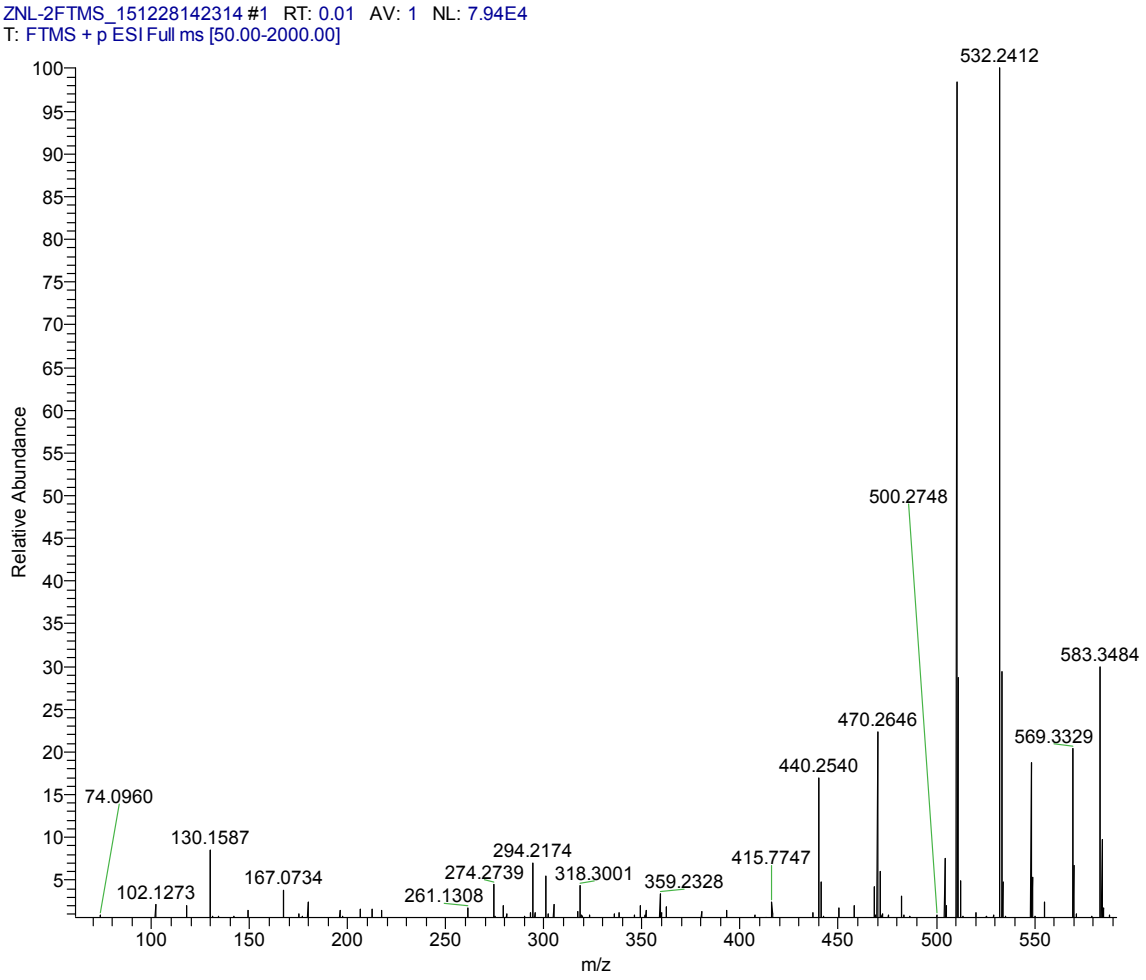

Figure S23. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **4** and **5**

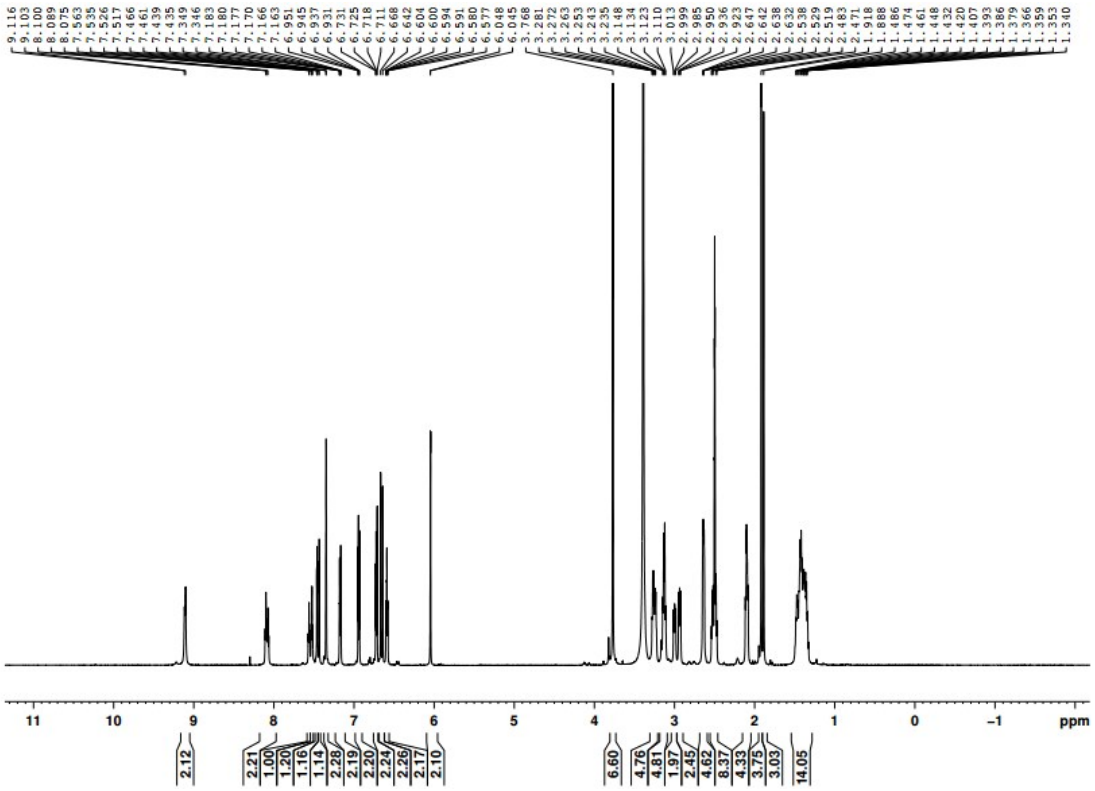

Figure S24. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **4** and **5**

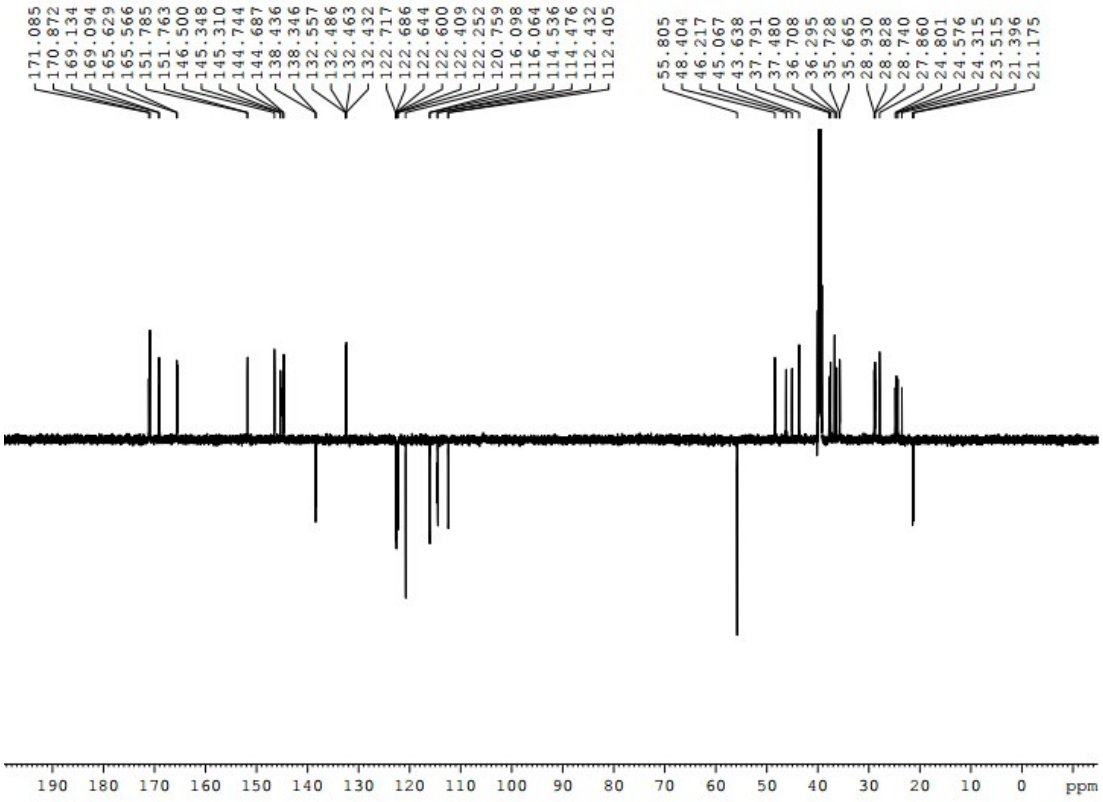

Figure S25. HSQC spectrum of the new compound **4** and **5**

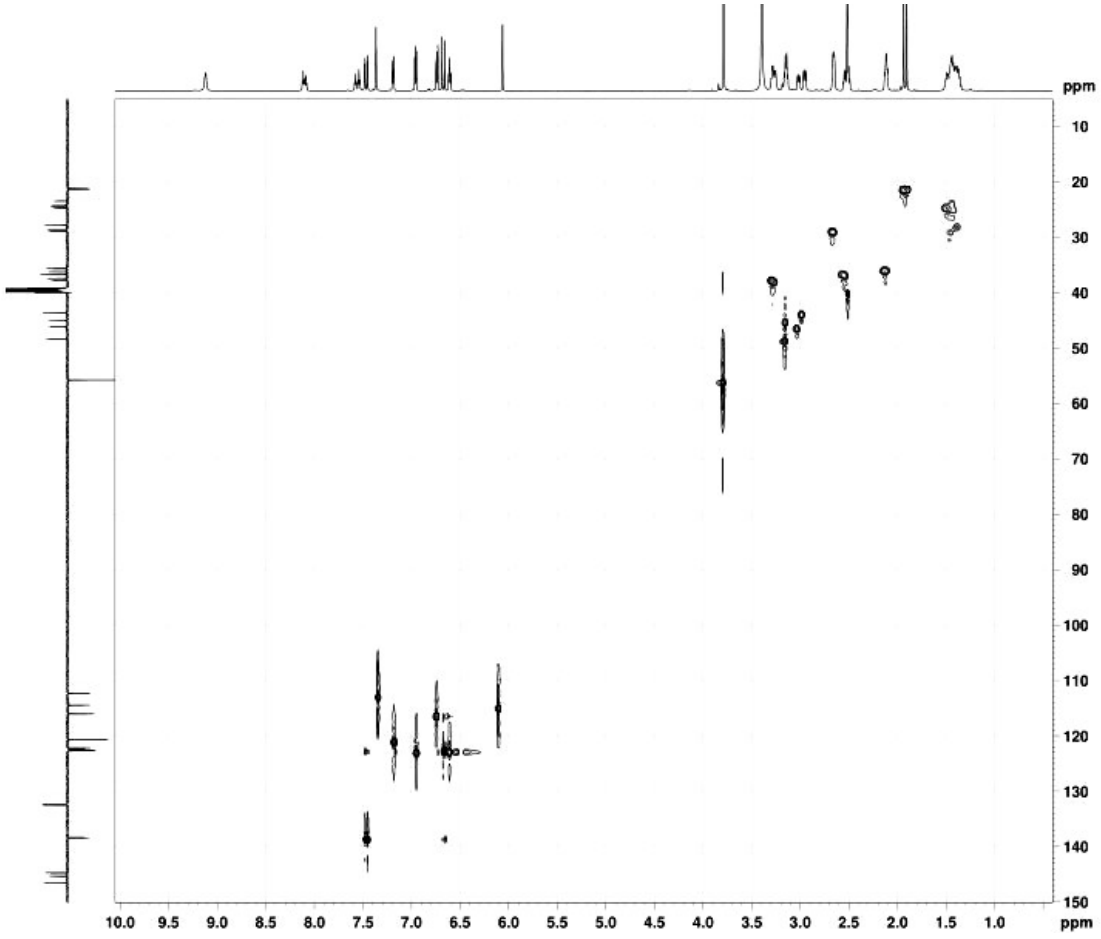

Figure S26. HMBC spectrum of the new compound **4** and **5**

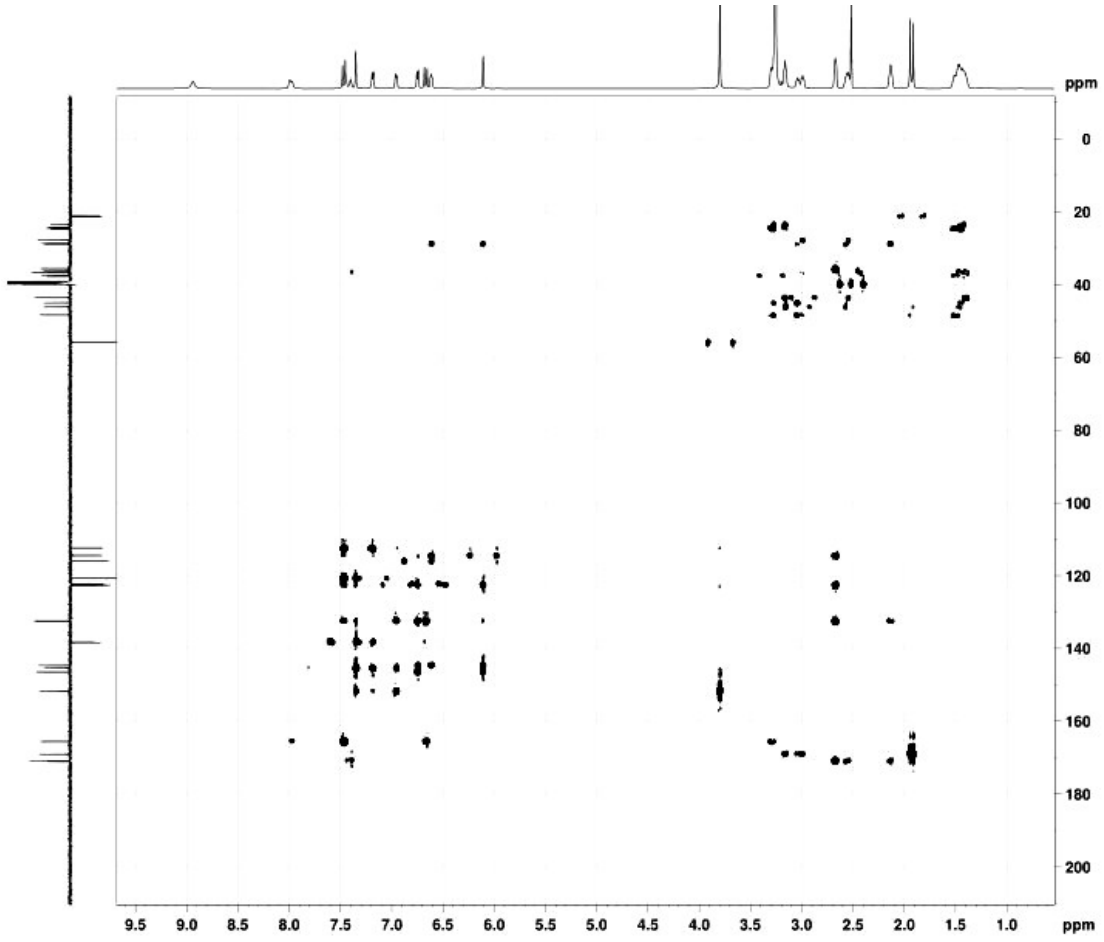

Figure S27. ^{1}H-^{1}H COSY spectrum of the new compound **4** and **5**

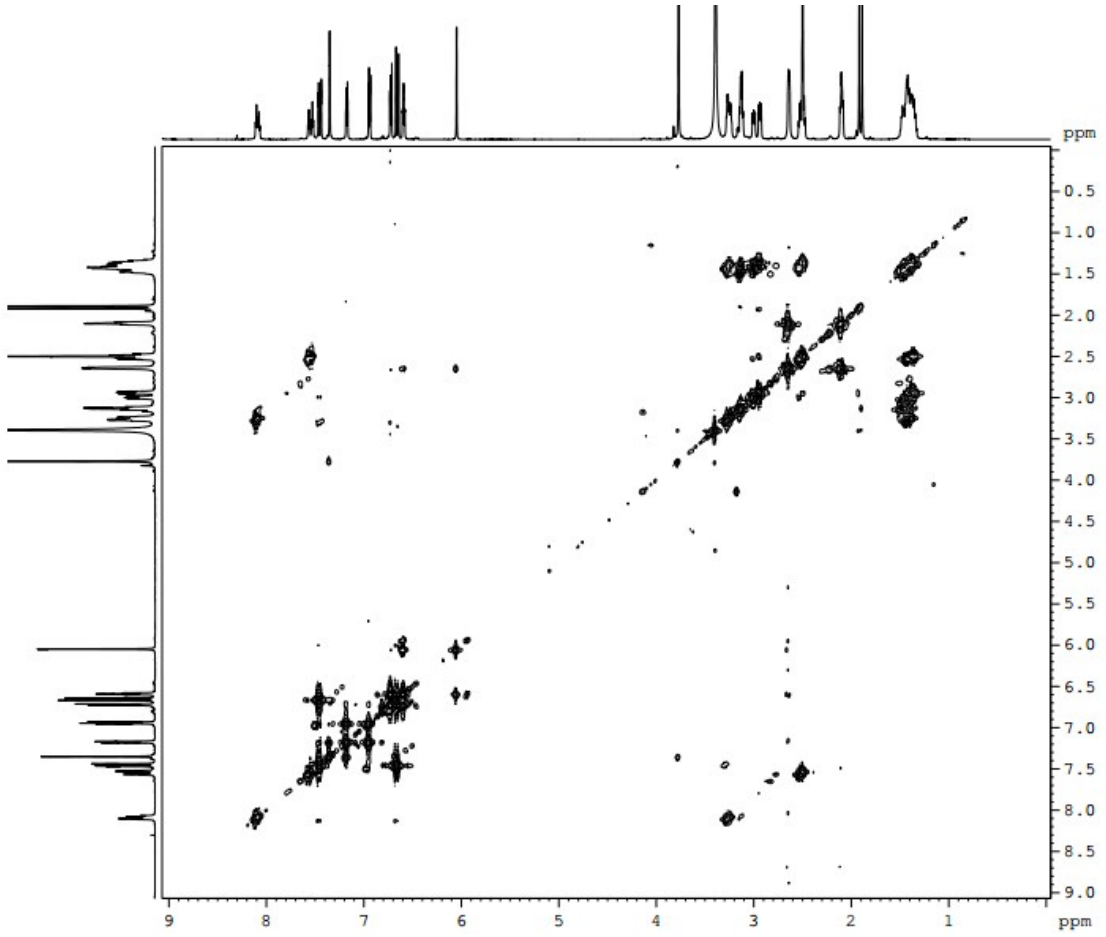

Figure S28. NOESY spectrum of the new compound **4** and **5**

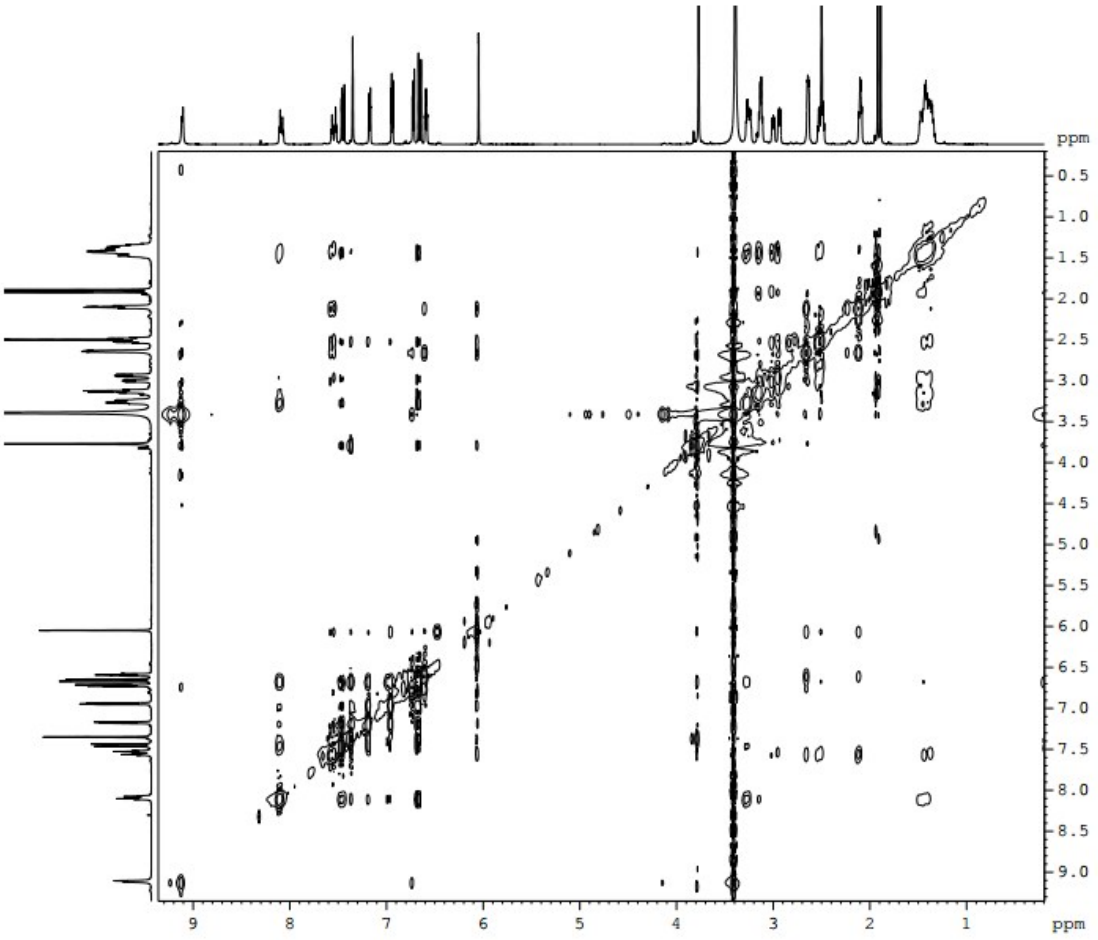

Figure S29. HRESIMS spectrum of compound **6** and **7**

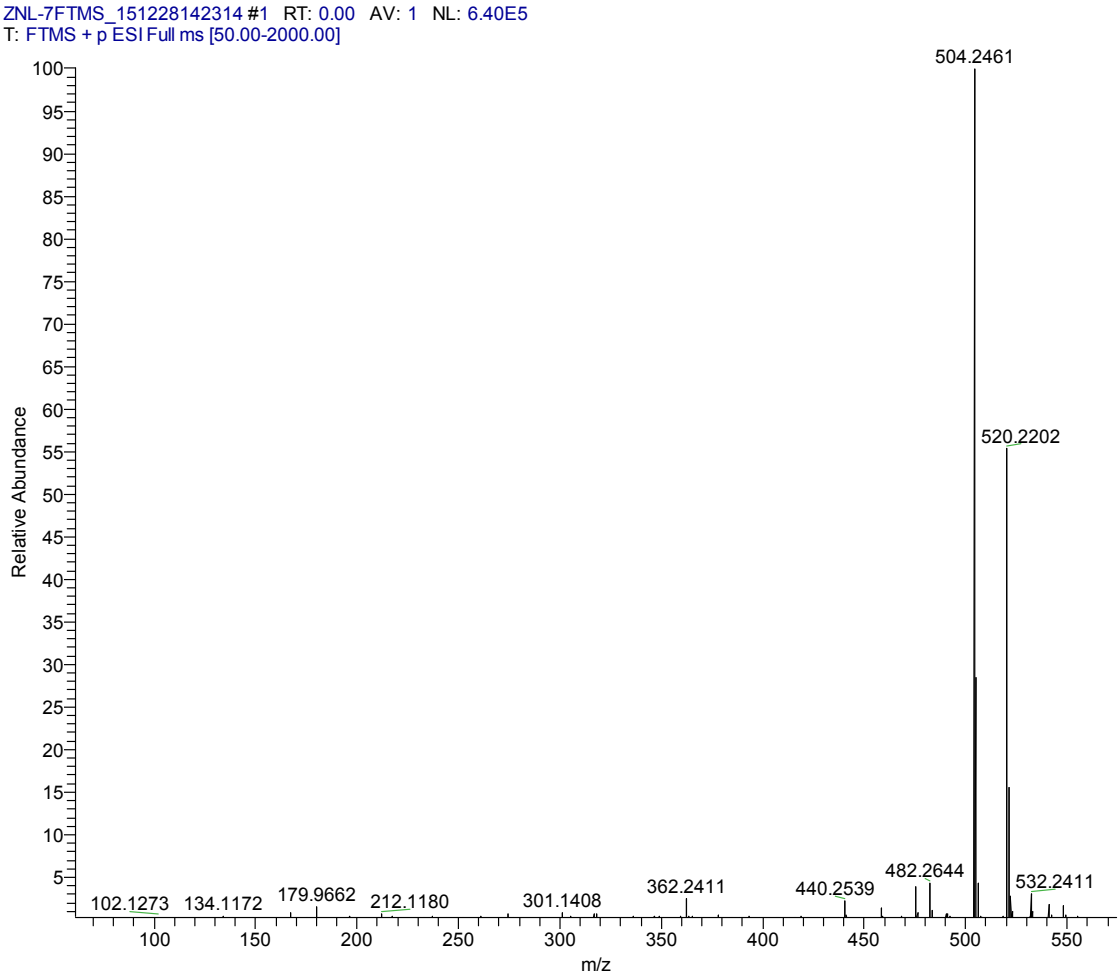

Figure S30. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **6** and **7**

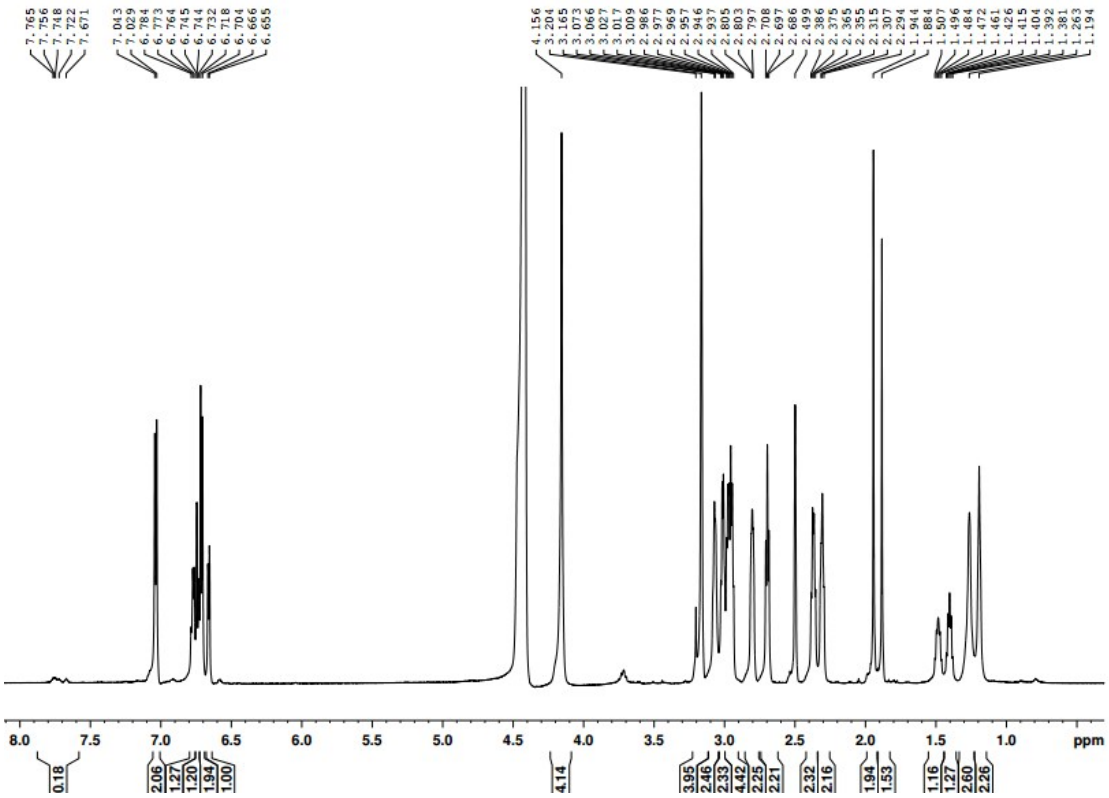

Figure S31. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **6** and **7**

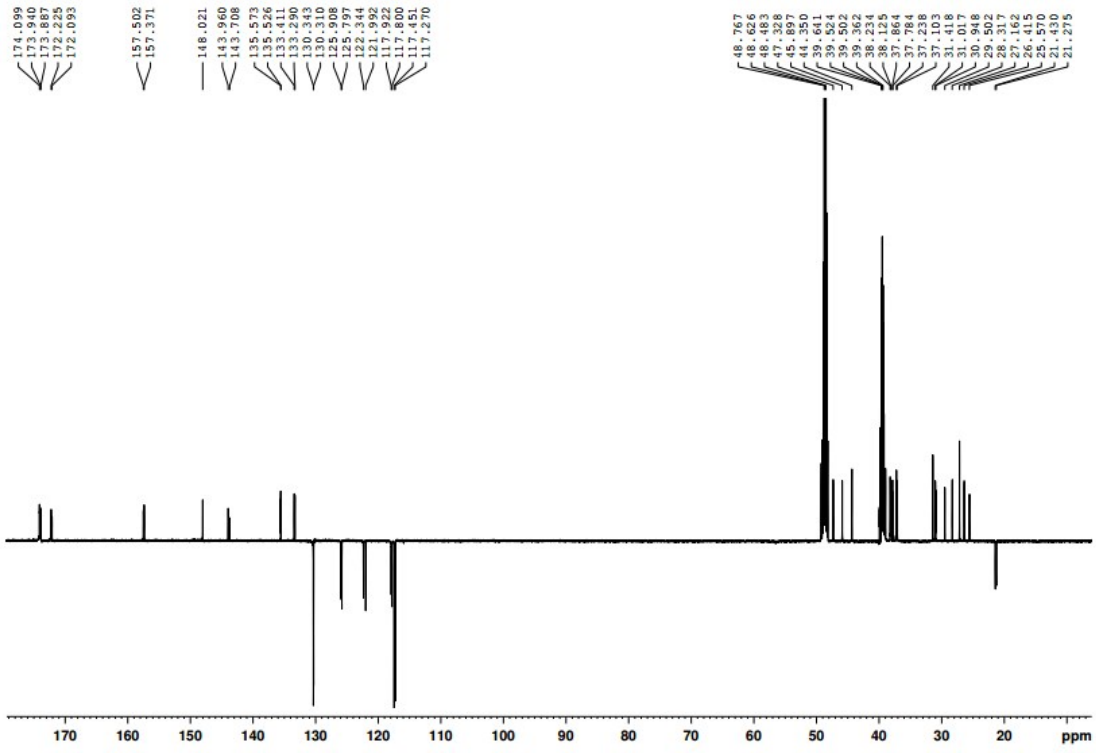

Figure S32. HSQC spectrum of the new compound **6** and **7**

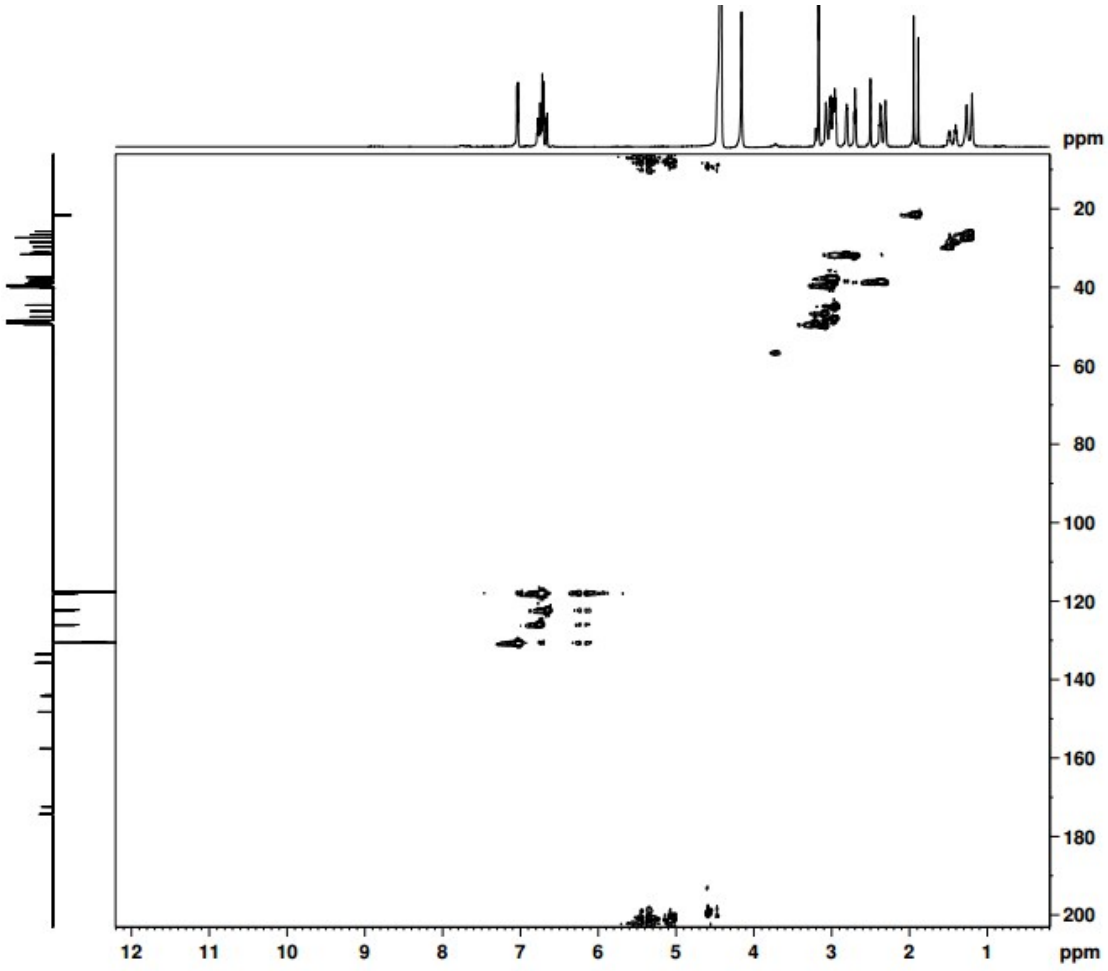

Figure S33. HMBC spectrum of the new compound **6** and **7**

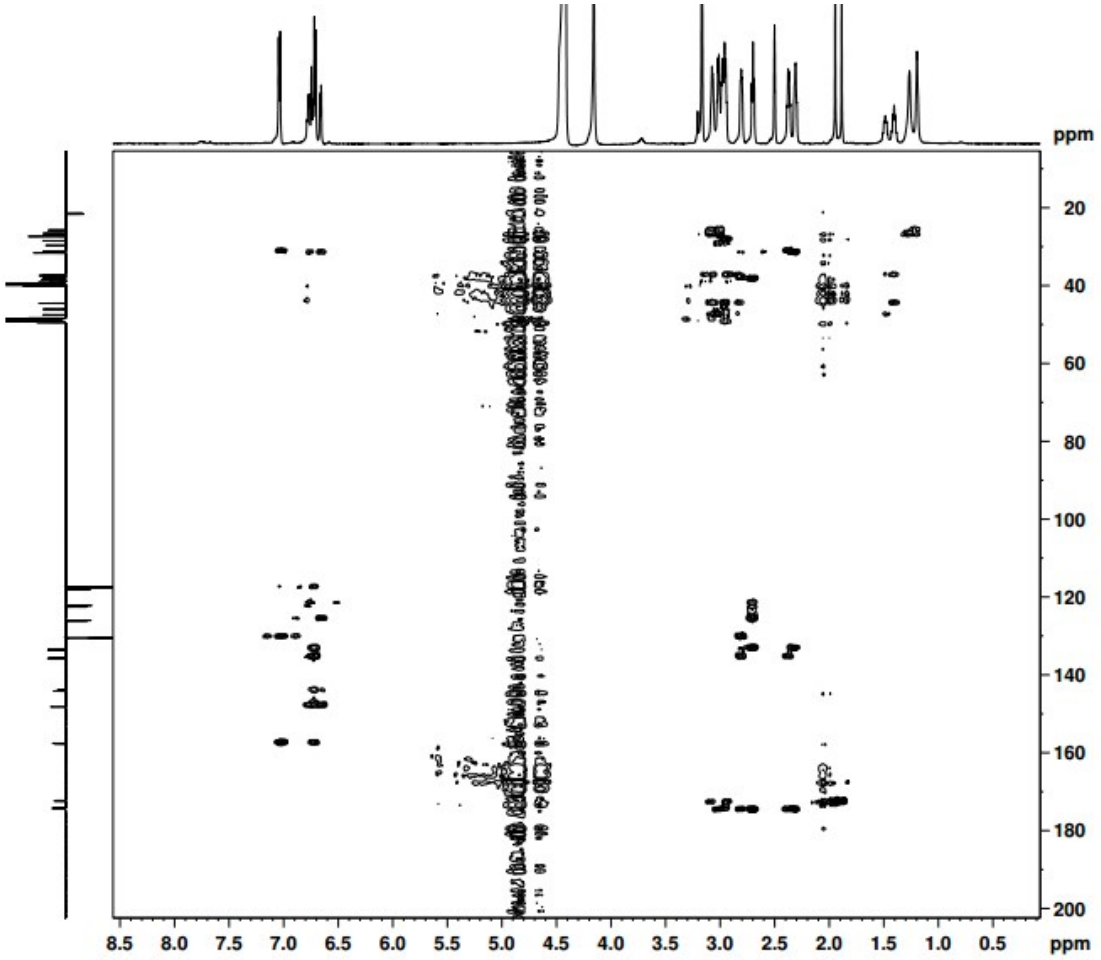

Figure S34. ^{1}H-^{1}H COSY spectrum of the new compound **6** and **7**

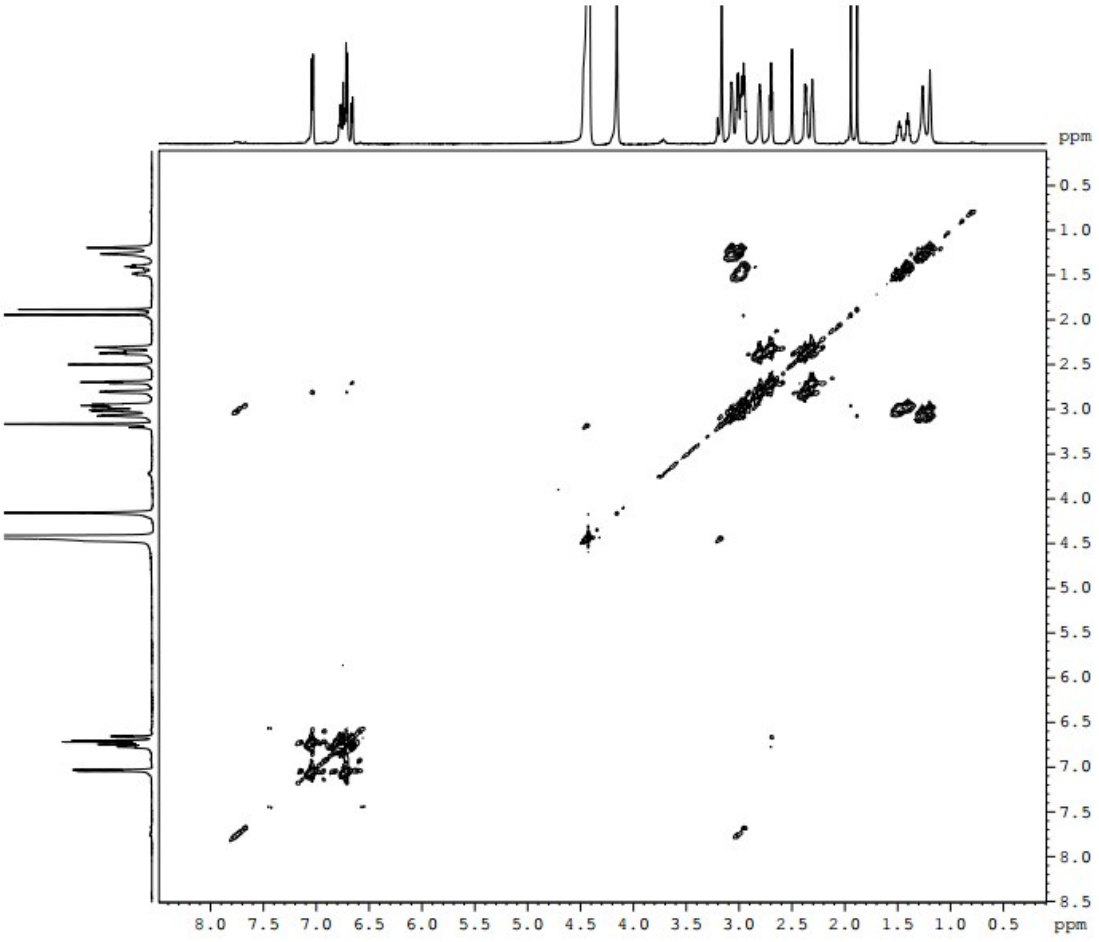

Figure S35. NOESY spectrum of the new compound **6** and **7**

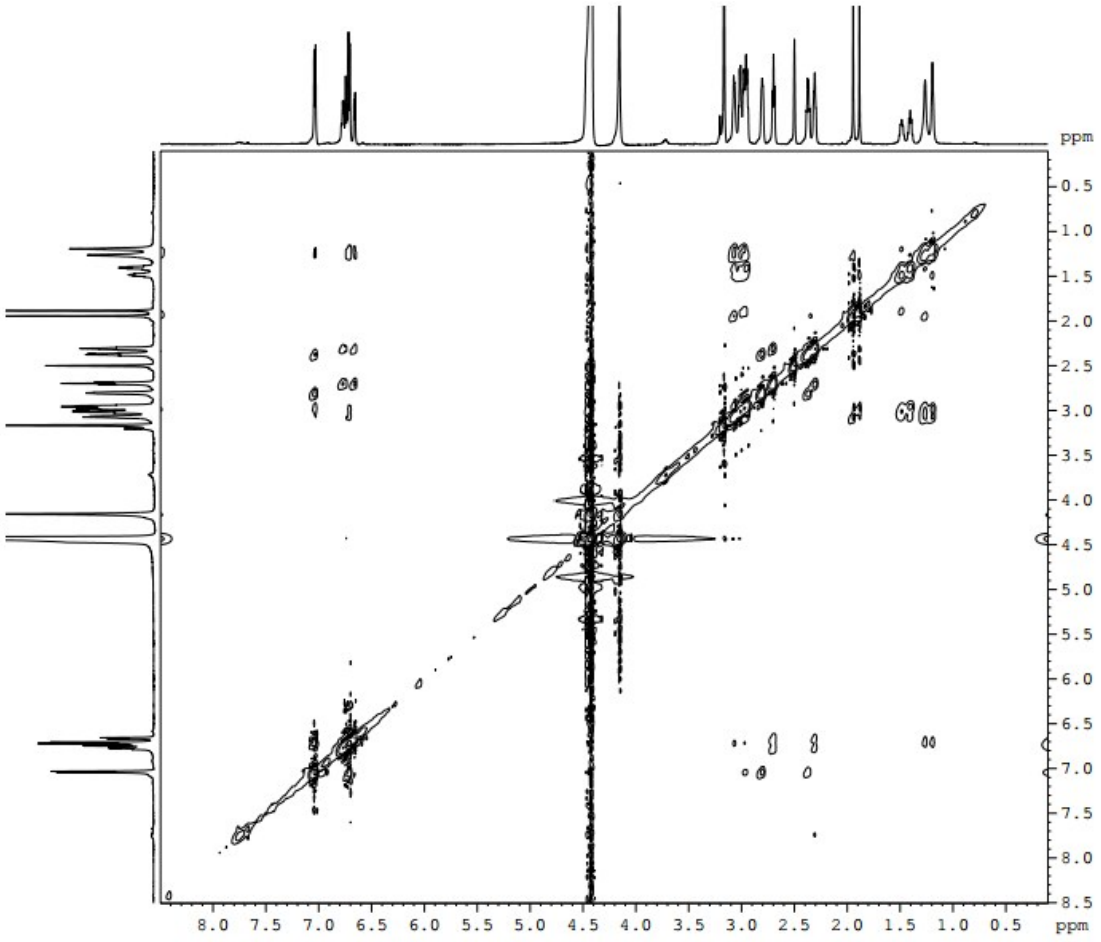

Figure S36. HRESIMS spectrum of compound **8**

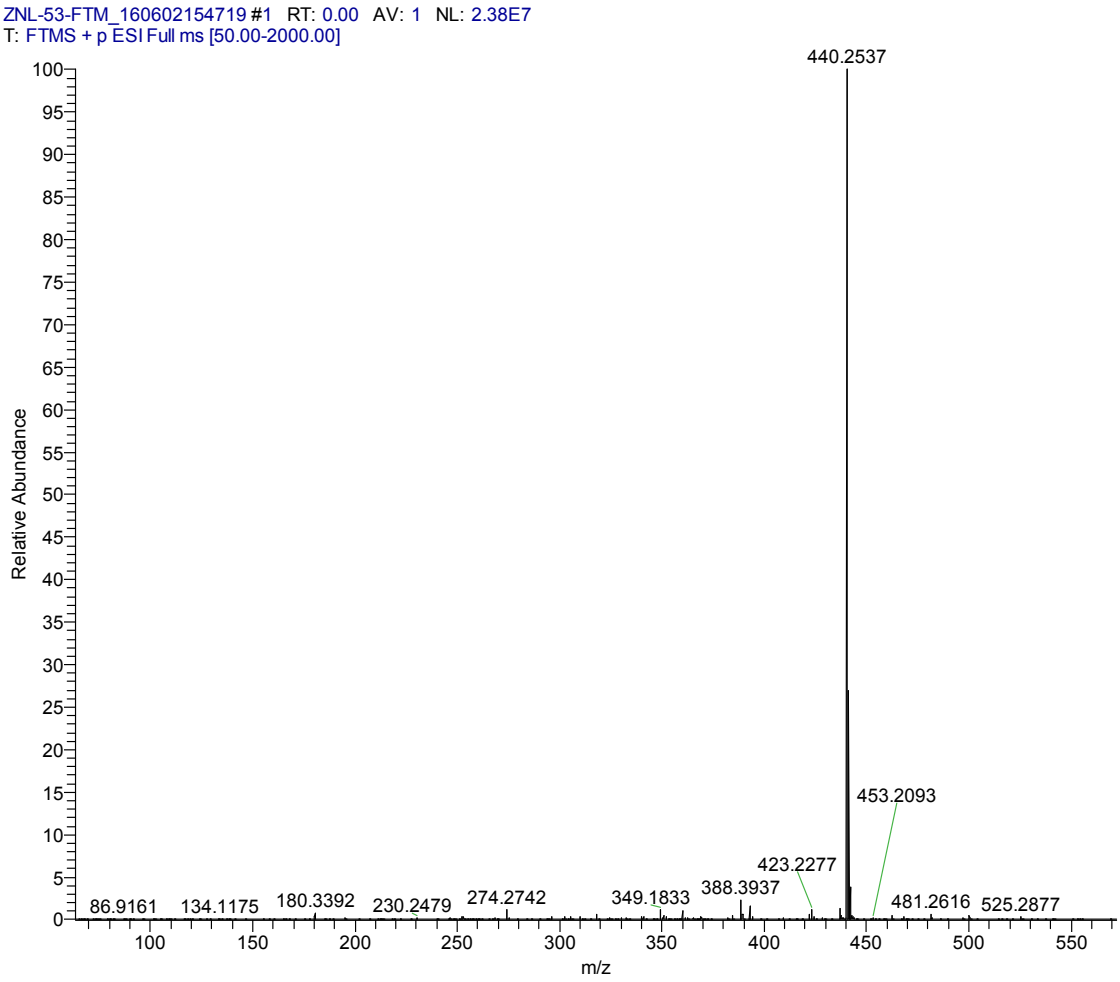

Figure S37. ^{1}H-NMR (600 MHz, DMSO) spectrum of the new compound **8**

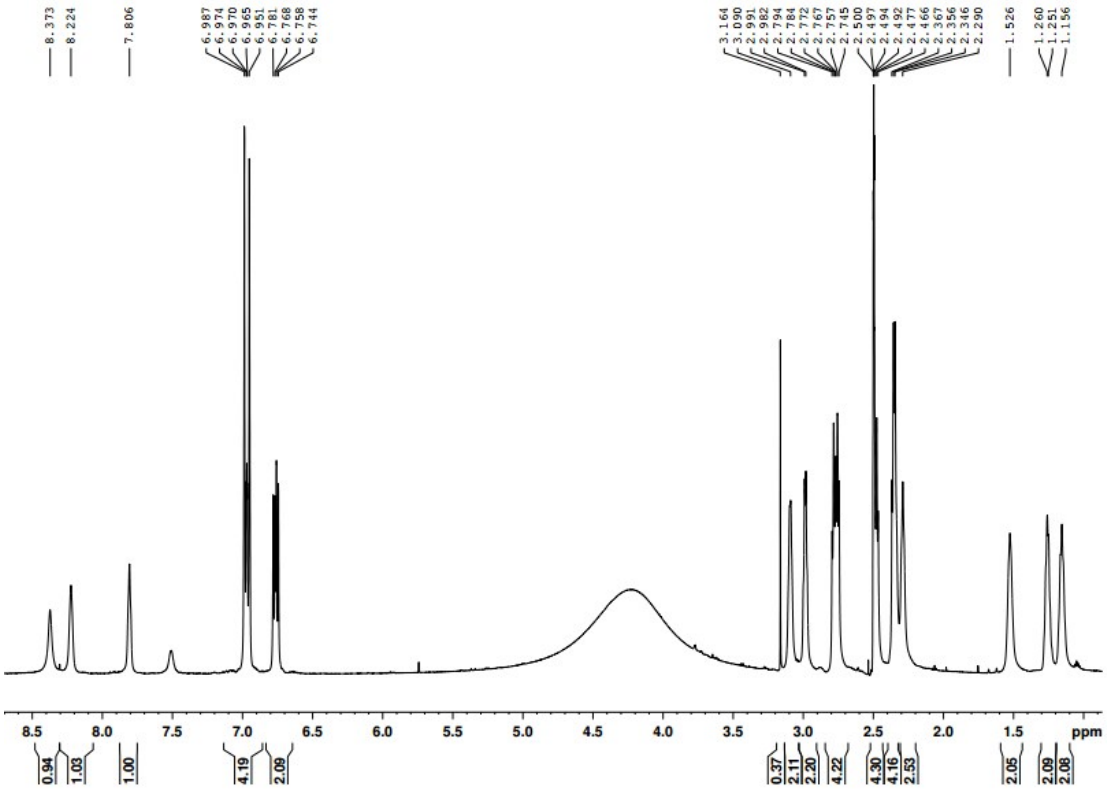

Figure S38. ^{13}C-APT (150 MHz, DMSO) spectrum of the new compound **8**

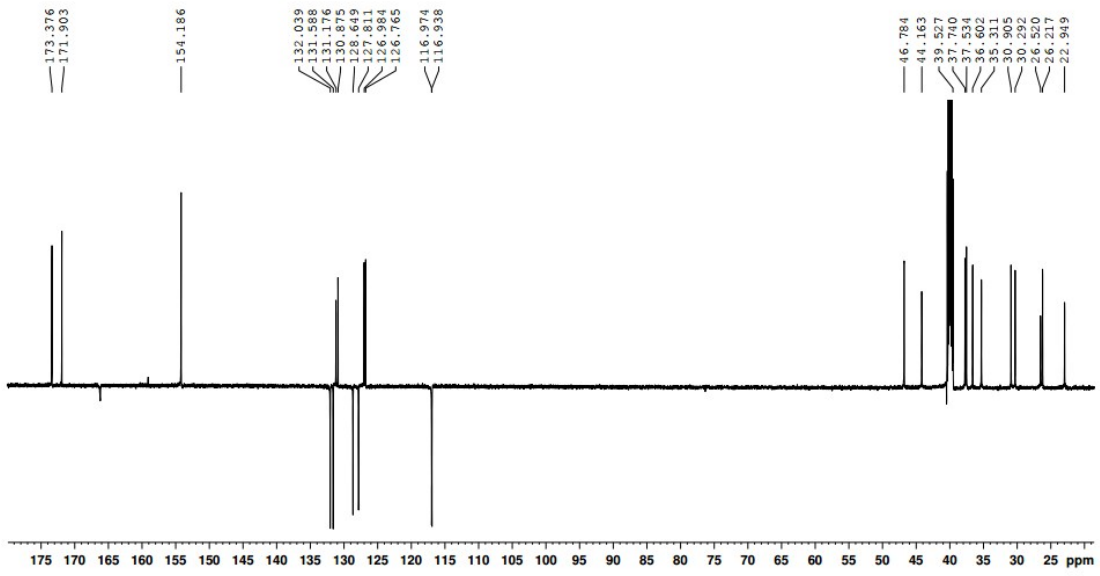

Figure S39. HSQC spectrum of the new compound **8**

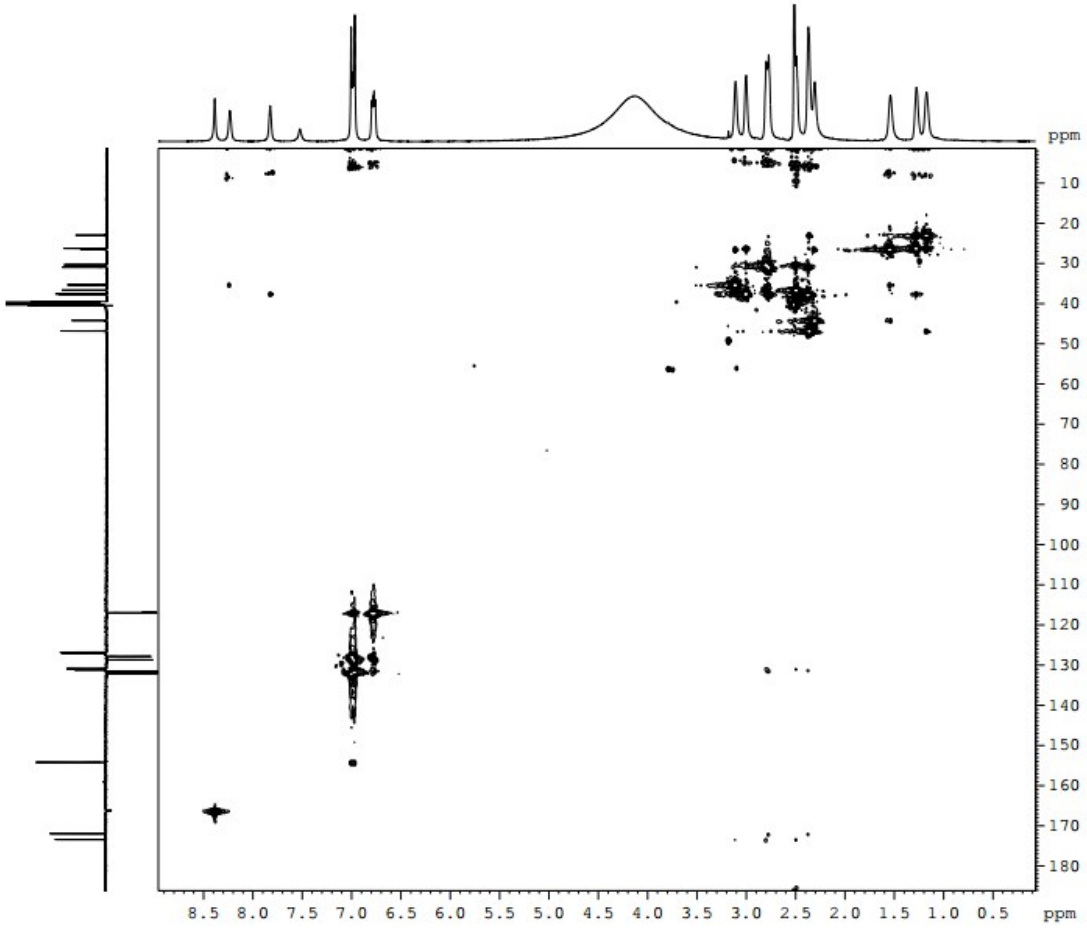

Figure S40. HMBC spectrum of the new compound **8**

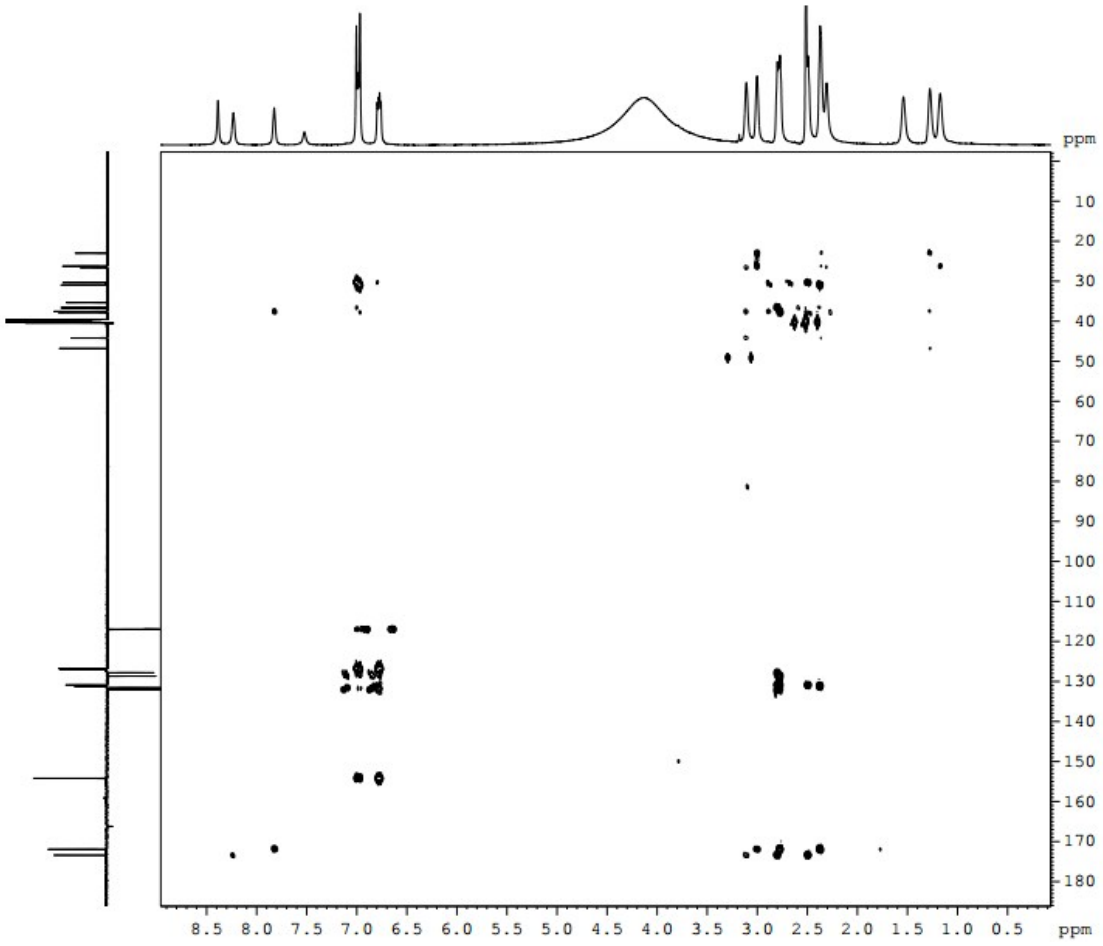

Figure S41. ^{1}H-^{1}H COSY spectrum of the new compound **8**

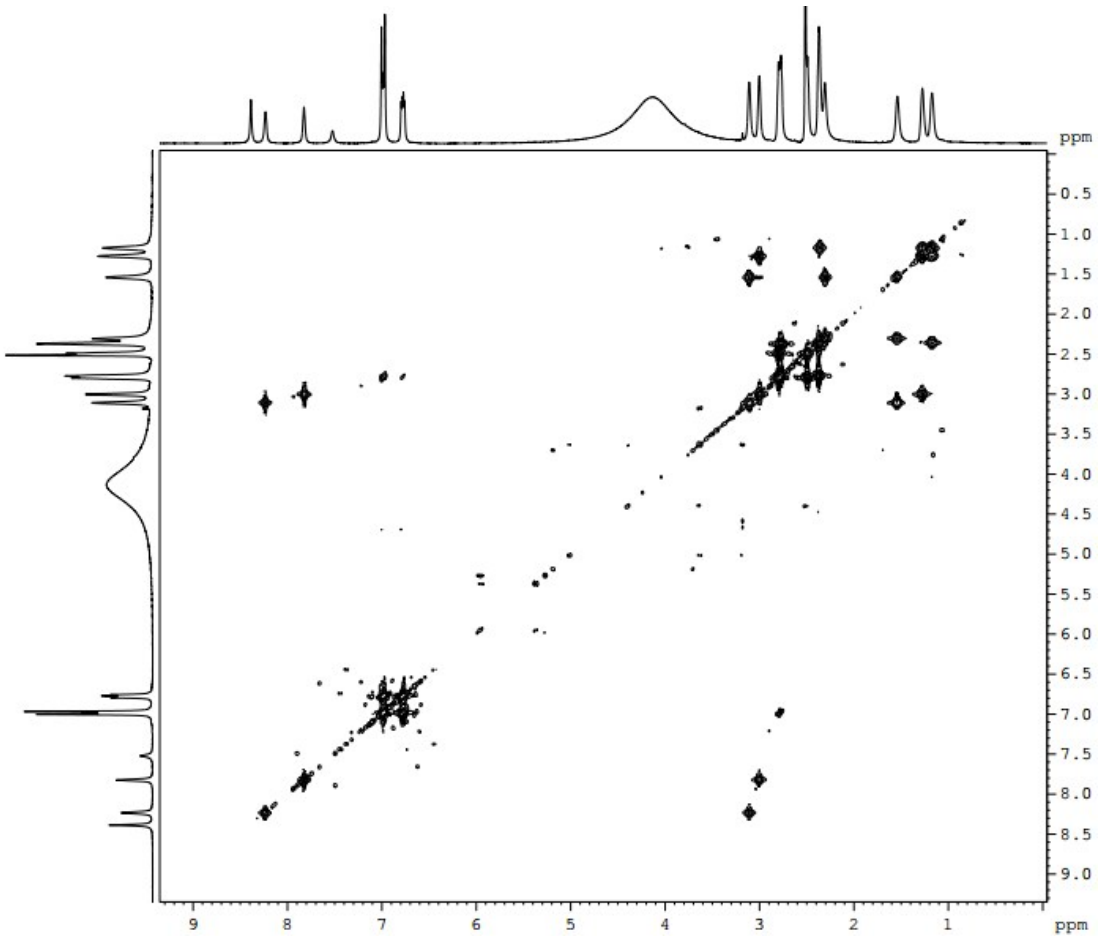

Figure S42. NOESY spectrum of the new compound **8**