

New metallophthalocyanines bearing 2-methylimidazole moieties – potential photosensitizers against bacteria

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Poland

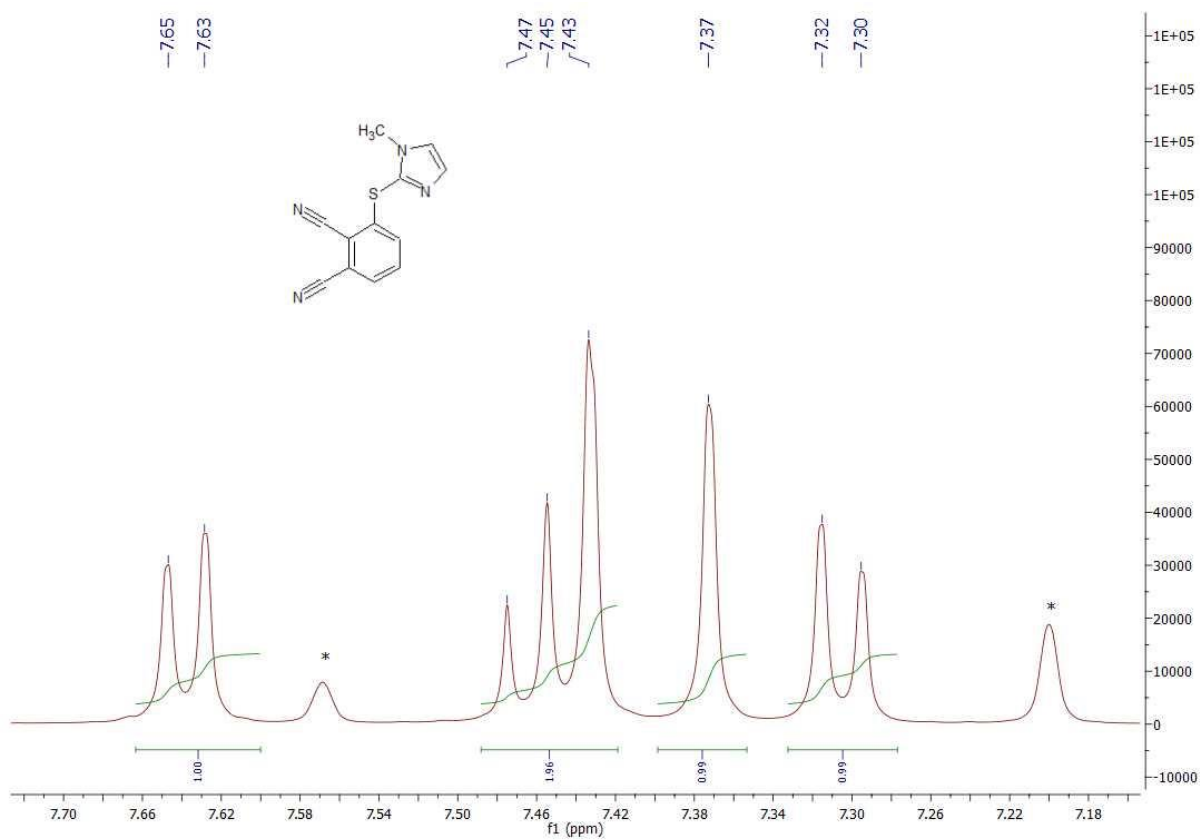
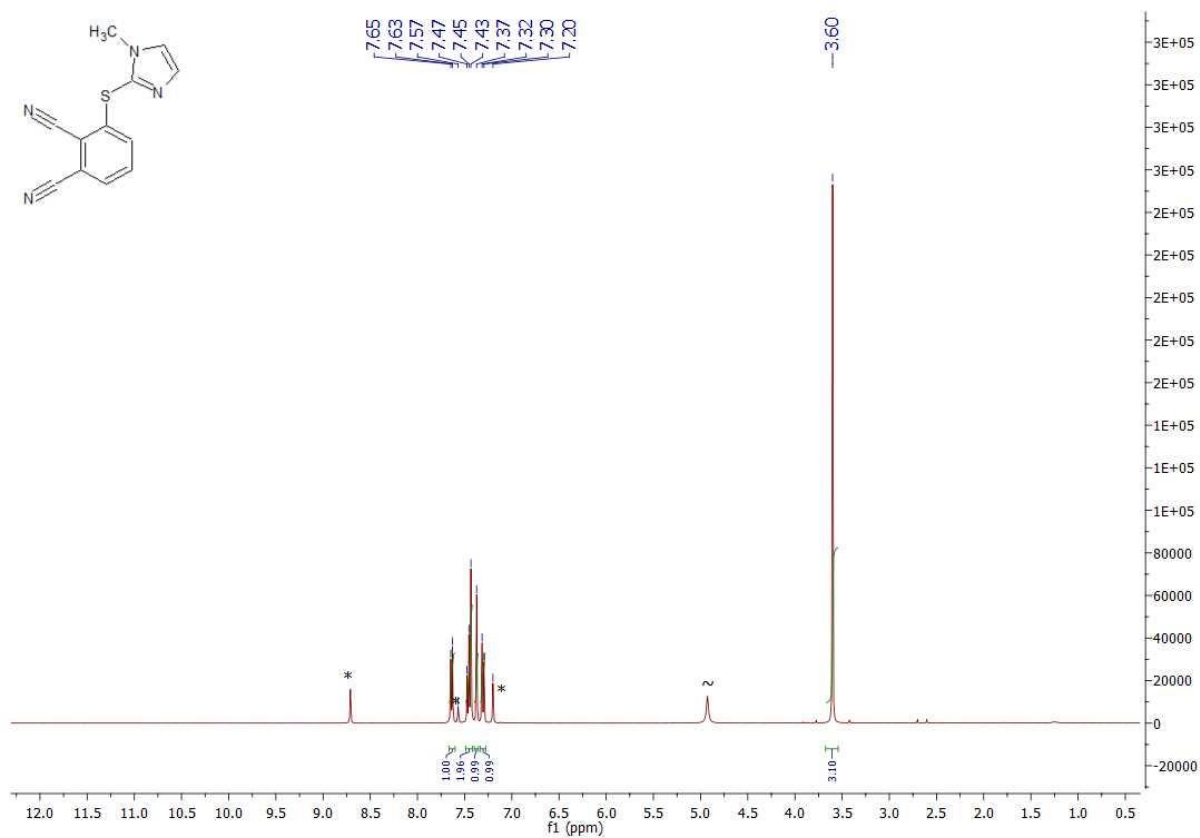
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Sciences, Swieczickiego 4, 60-781 Poznan, Poland

Supporting Information

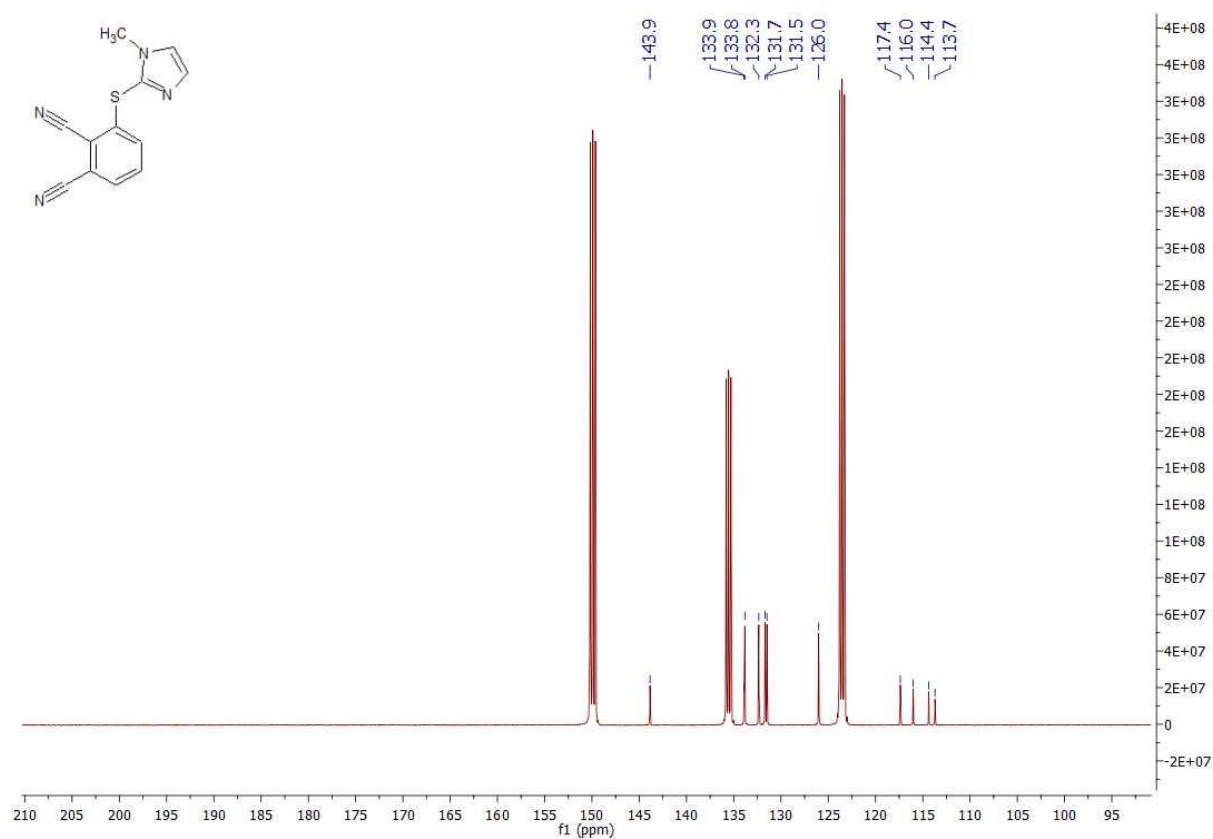
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1. NMR data

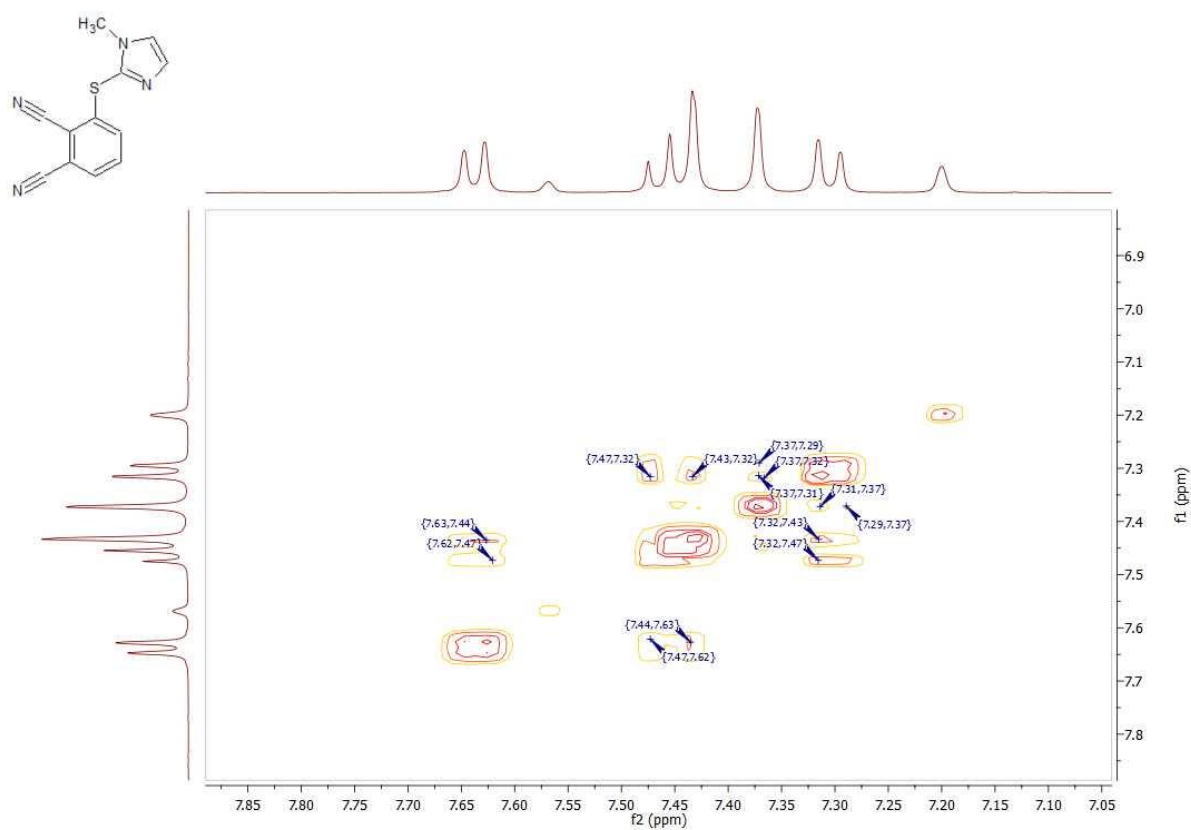
^1H NMR spectrum of **1** in pyridine- d_5



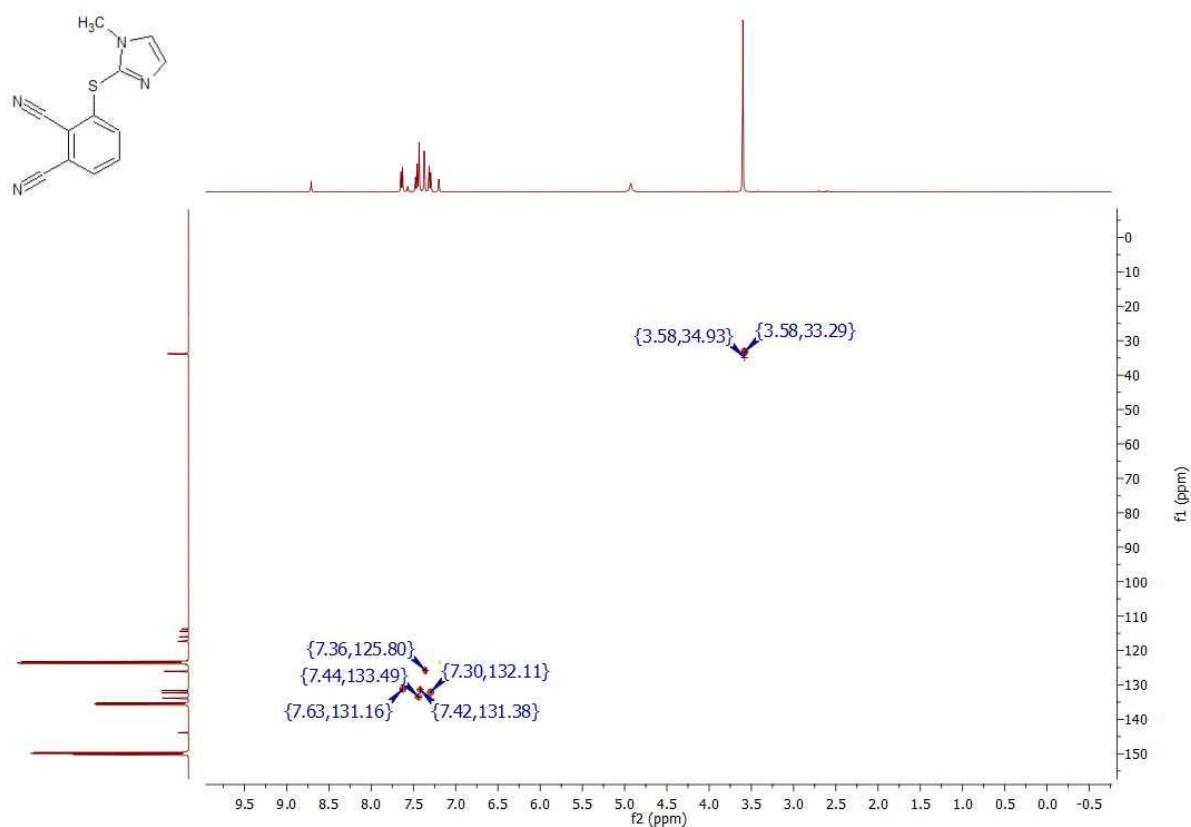
^{13}C NMR spectrum of **1** in pyridine- d_5



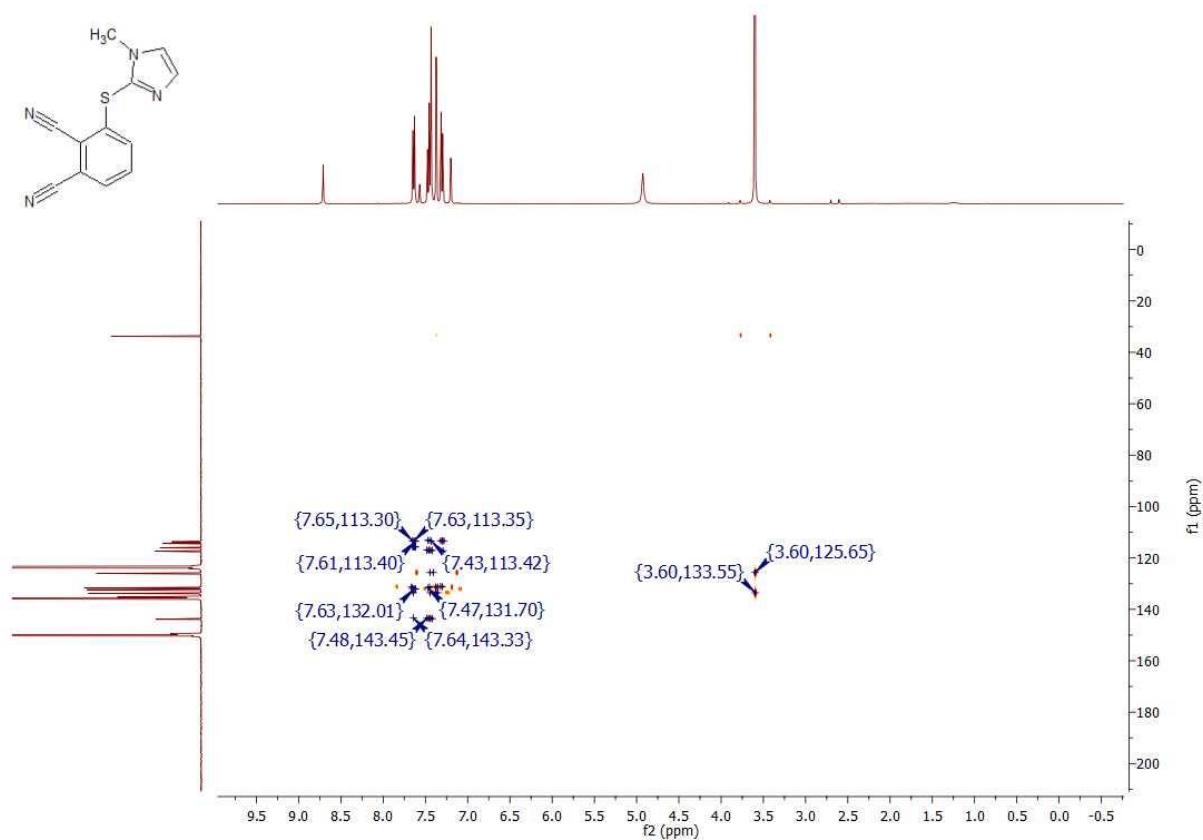
^1H - ^1H COSY spectrum of **1** in pyridine- d_5



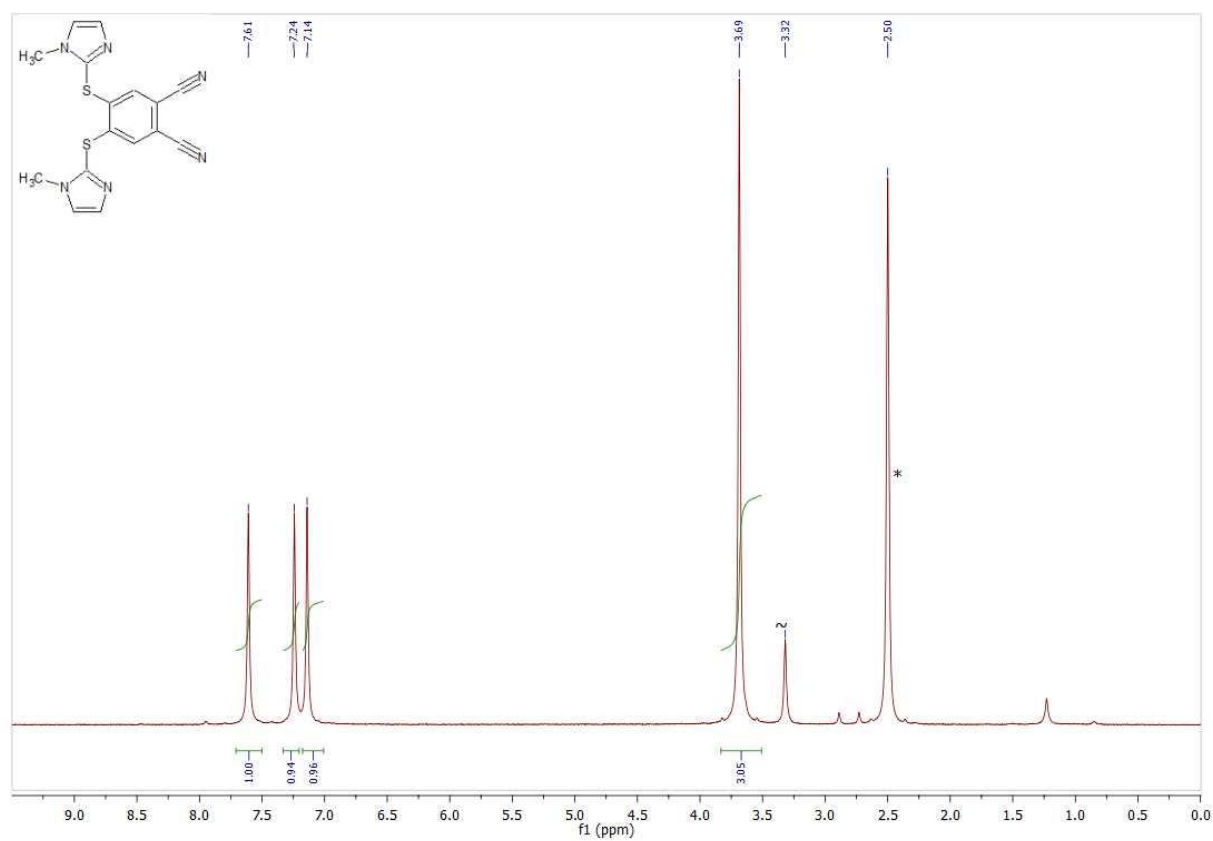
HSQC spectrum of **1** in pyridine-*d*₅



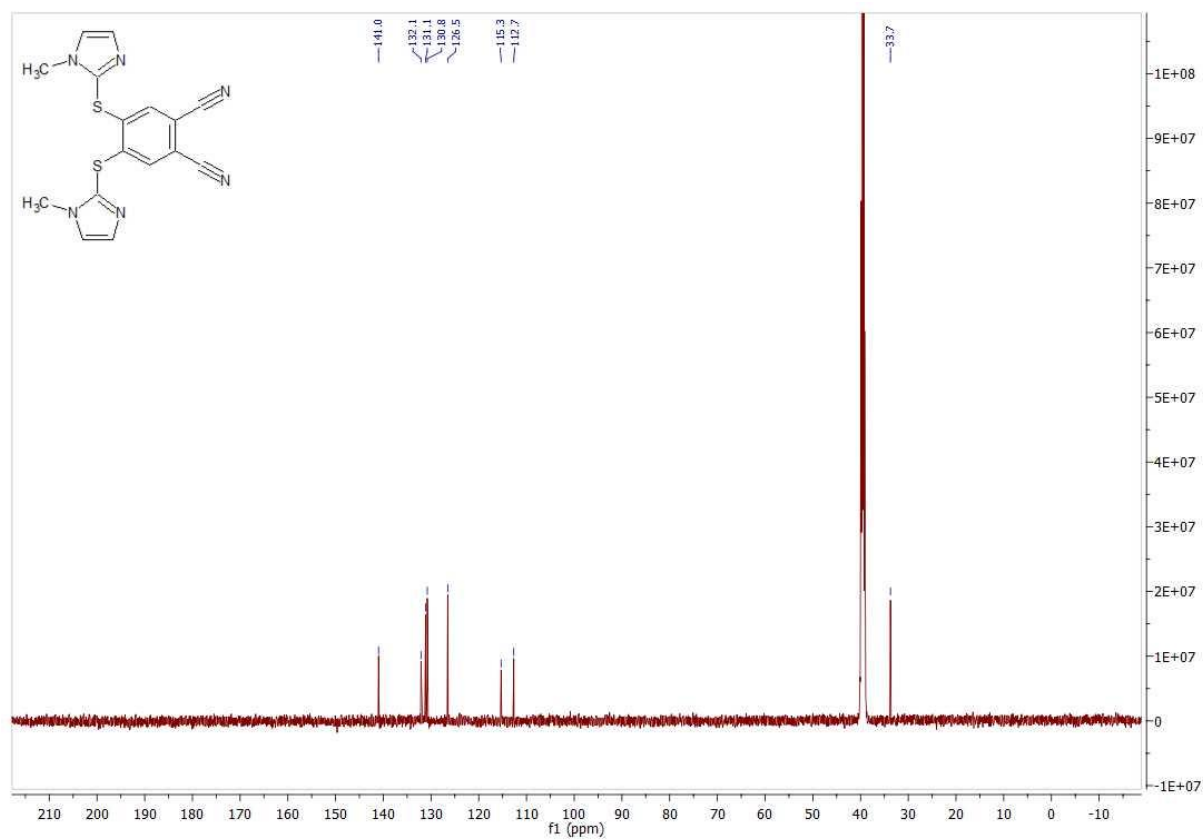
HMBC spectrum of **1** in pyridine-*d*₅



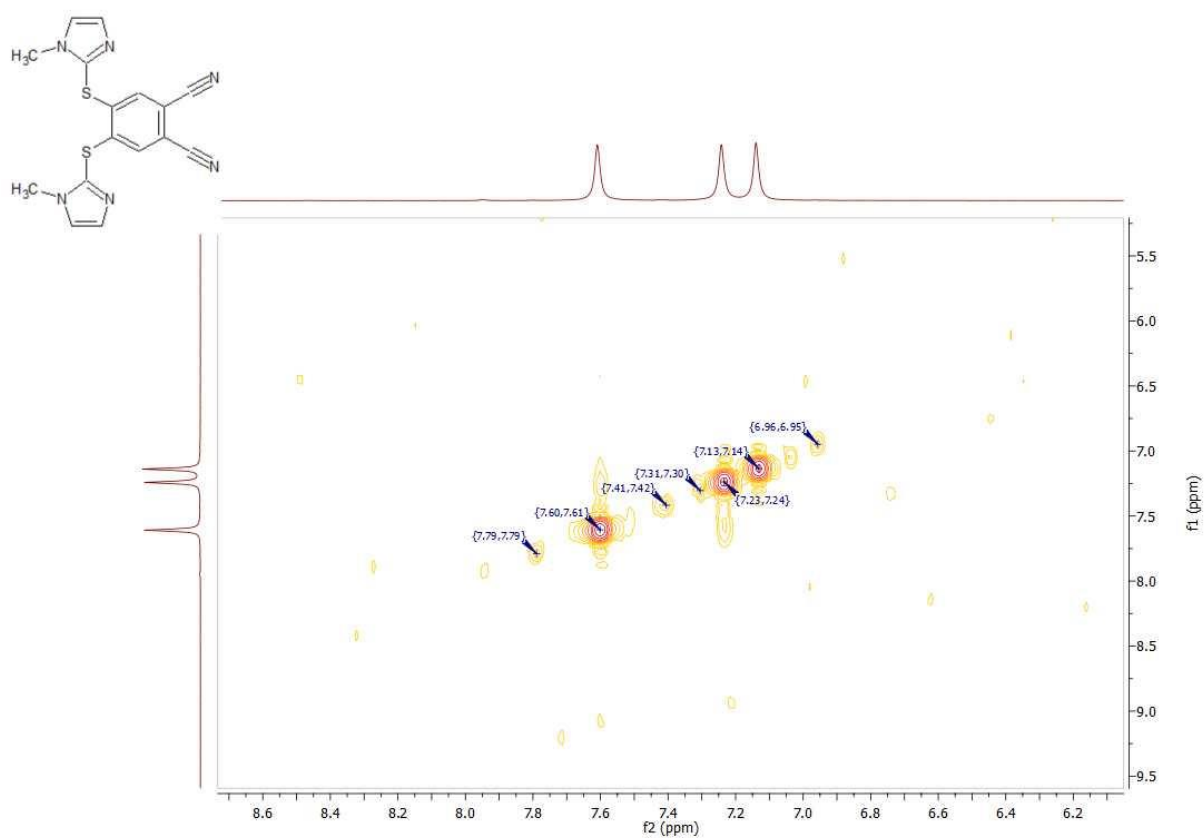
^1H NMR spectrum of **2** in $\text{DMSO}-d_6$



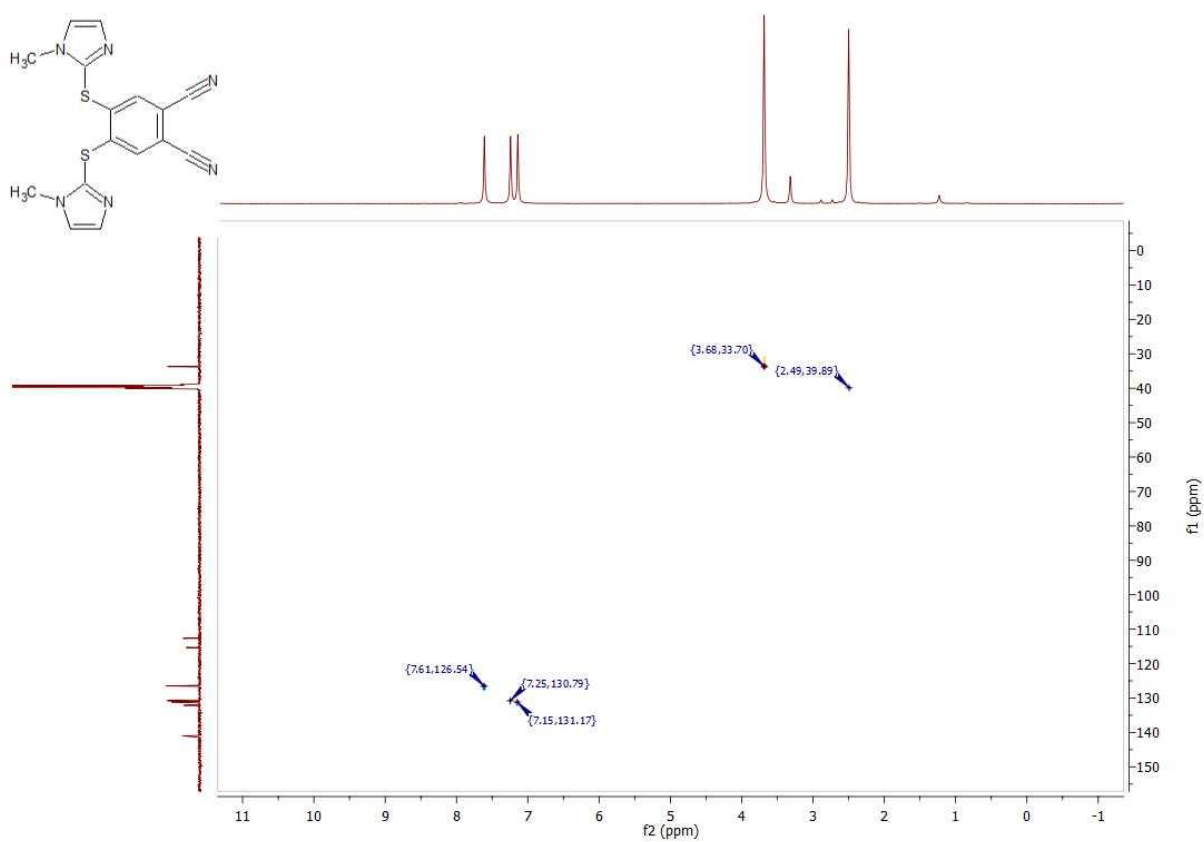
^{13}C NMR spectrum of **2** in $\text{DMSO}-d_6$



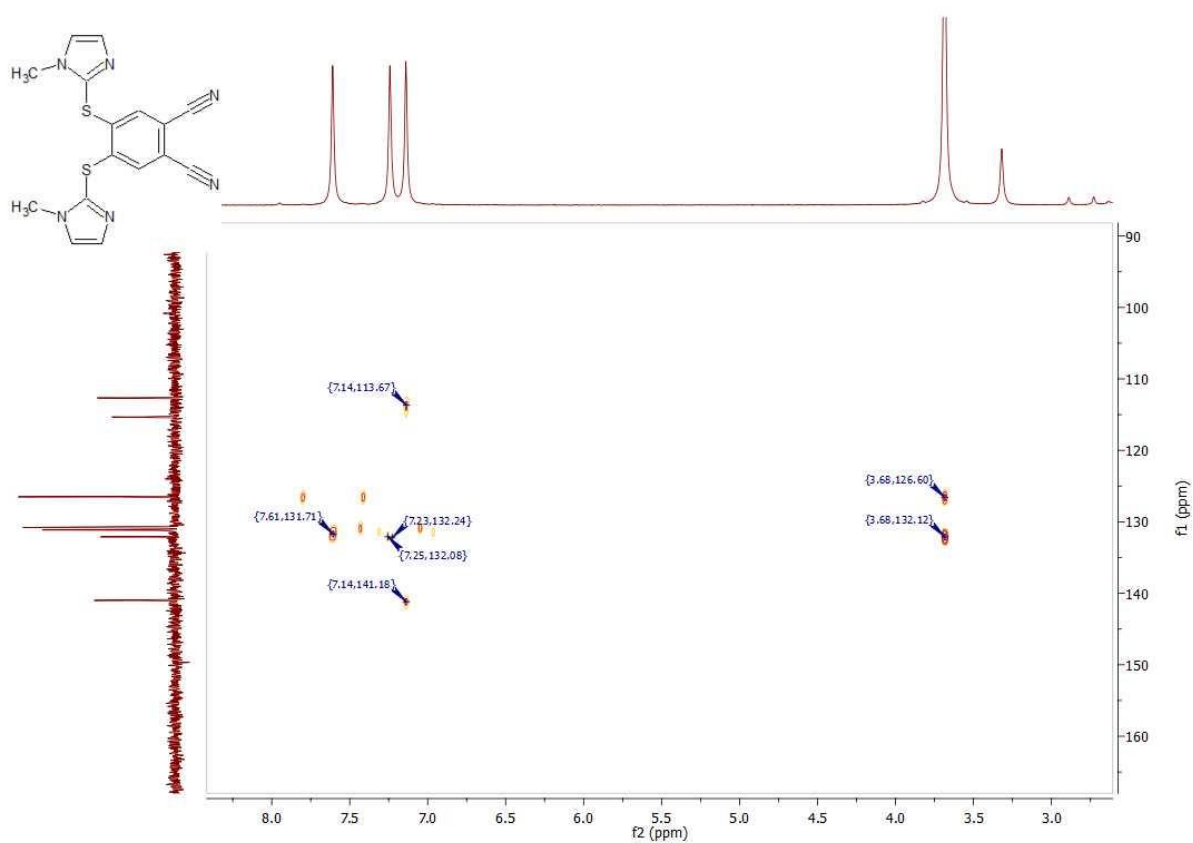
^1H - ^1H COSY spectrum of **2** in $\text{DMSO}-d_6$



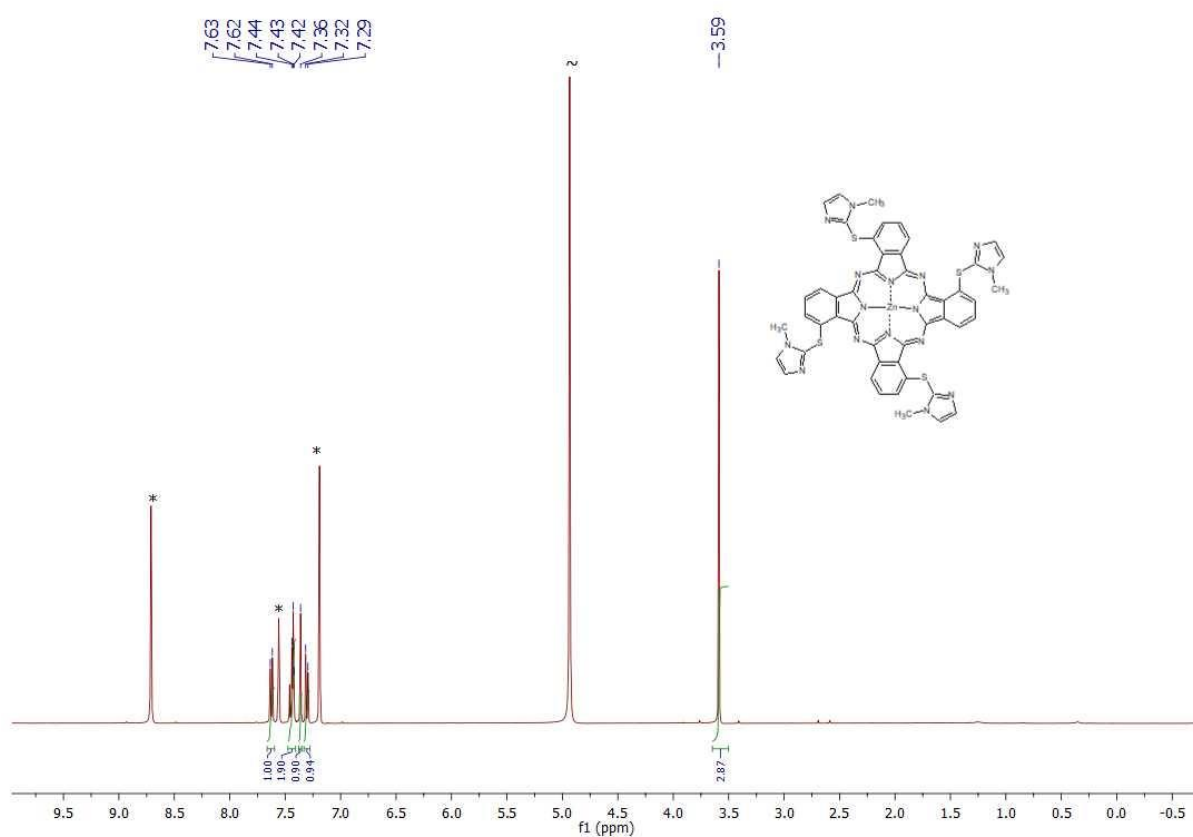
HSQC spectrum of **2** in $\text{DMSO}-d_6$



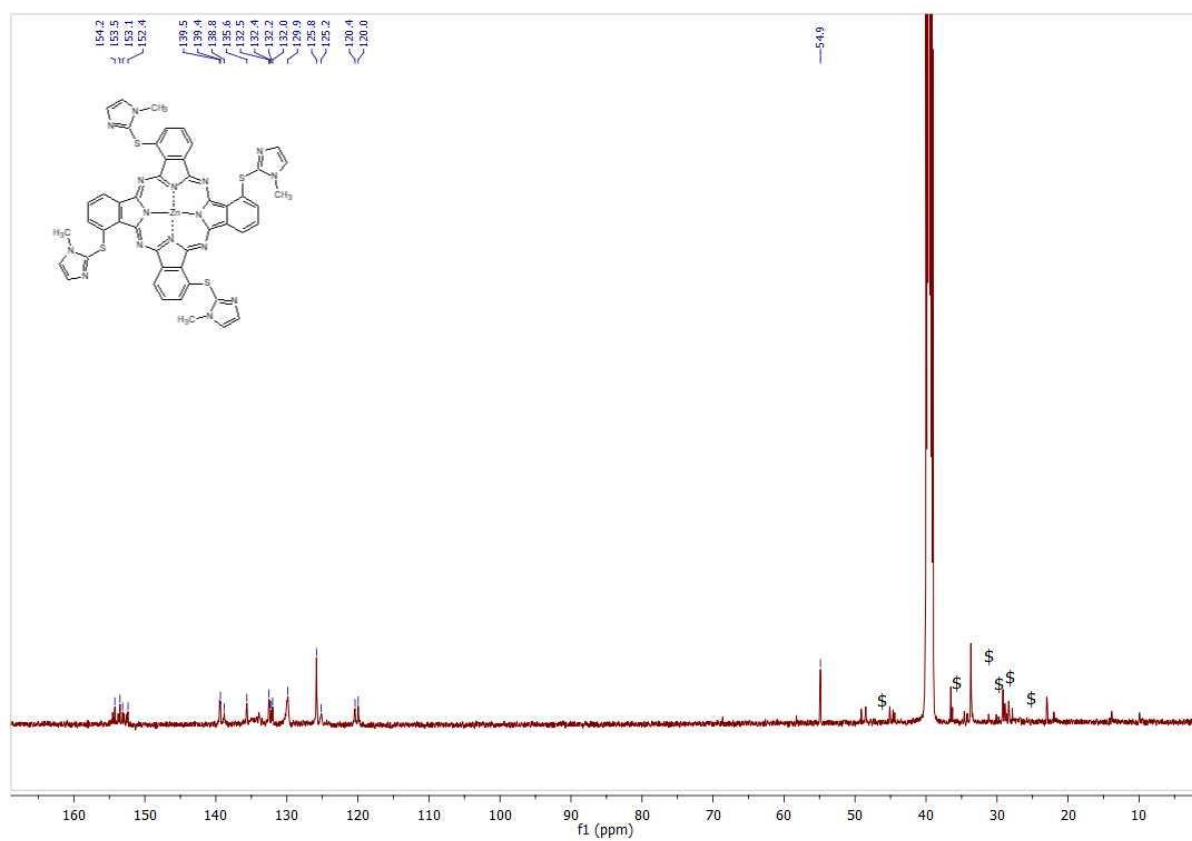
HMBC spectrum of **2** in DMSO- d_6



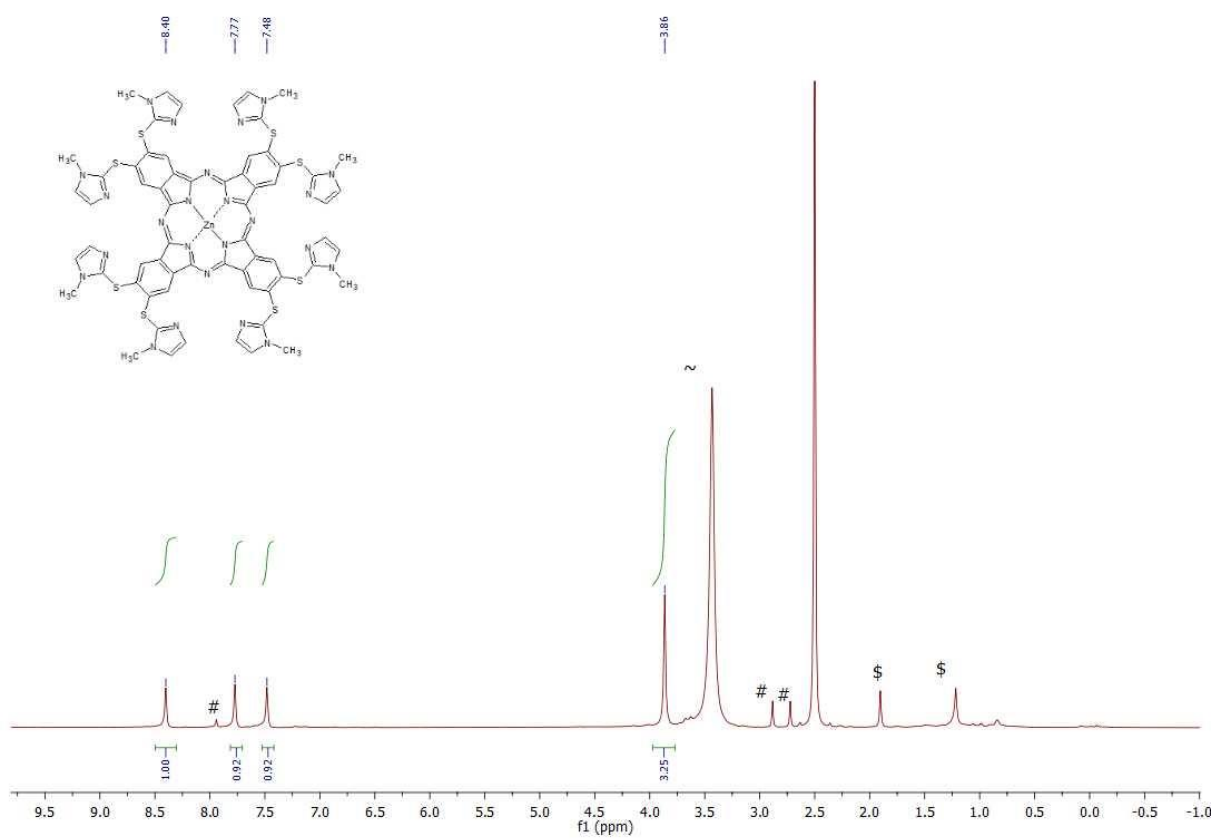
^1H NMR spectrum of **3** in DMSO- d_6



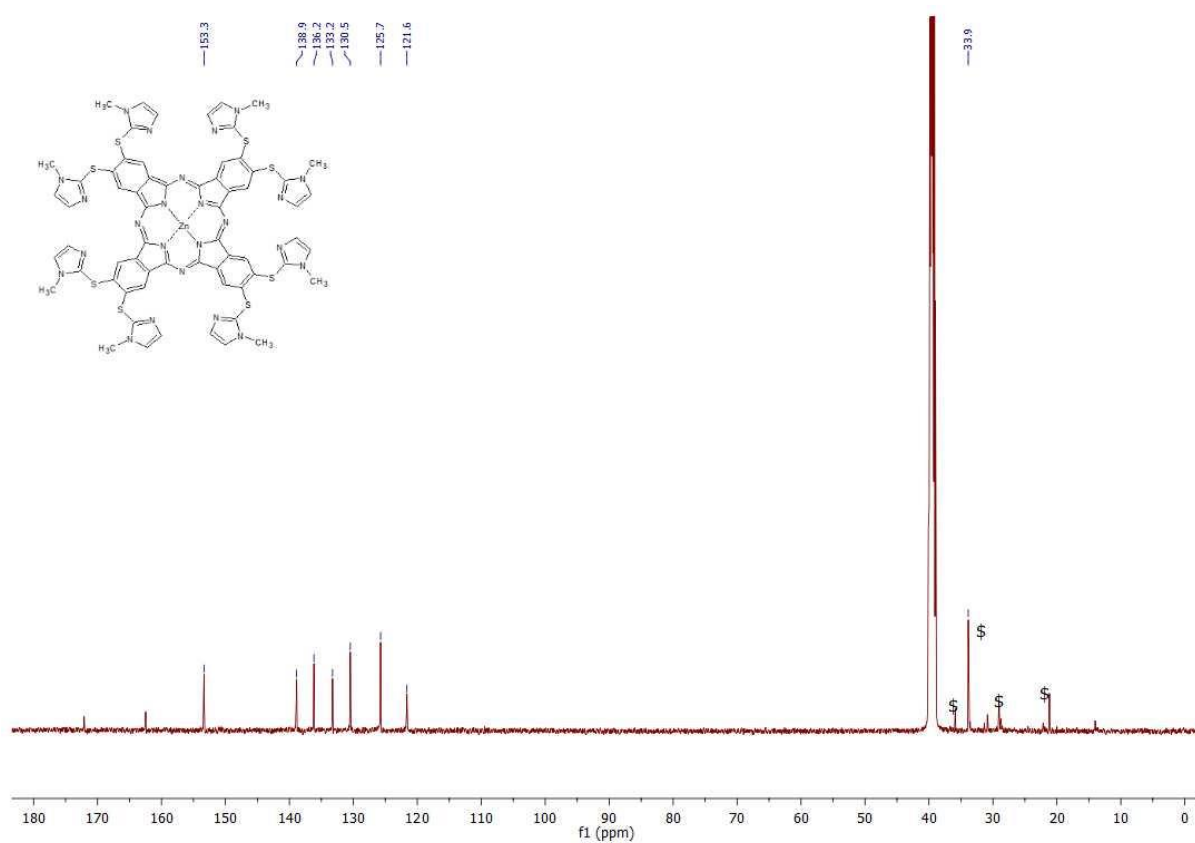
^{13}C NMR spectrum of **3** in $\text{DMSO}-d_6$



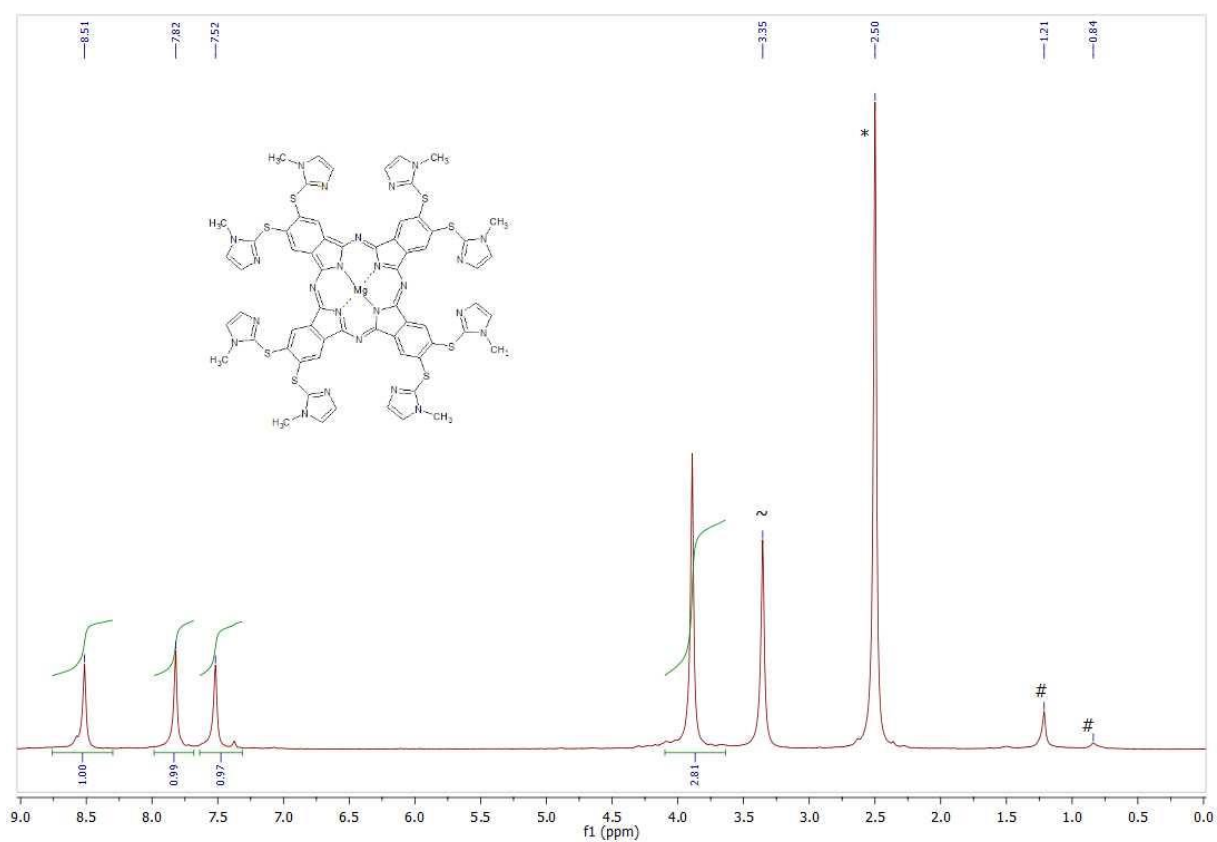
^1H NMR spectrum of **6** in $\text{DMSO}-d_6$



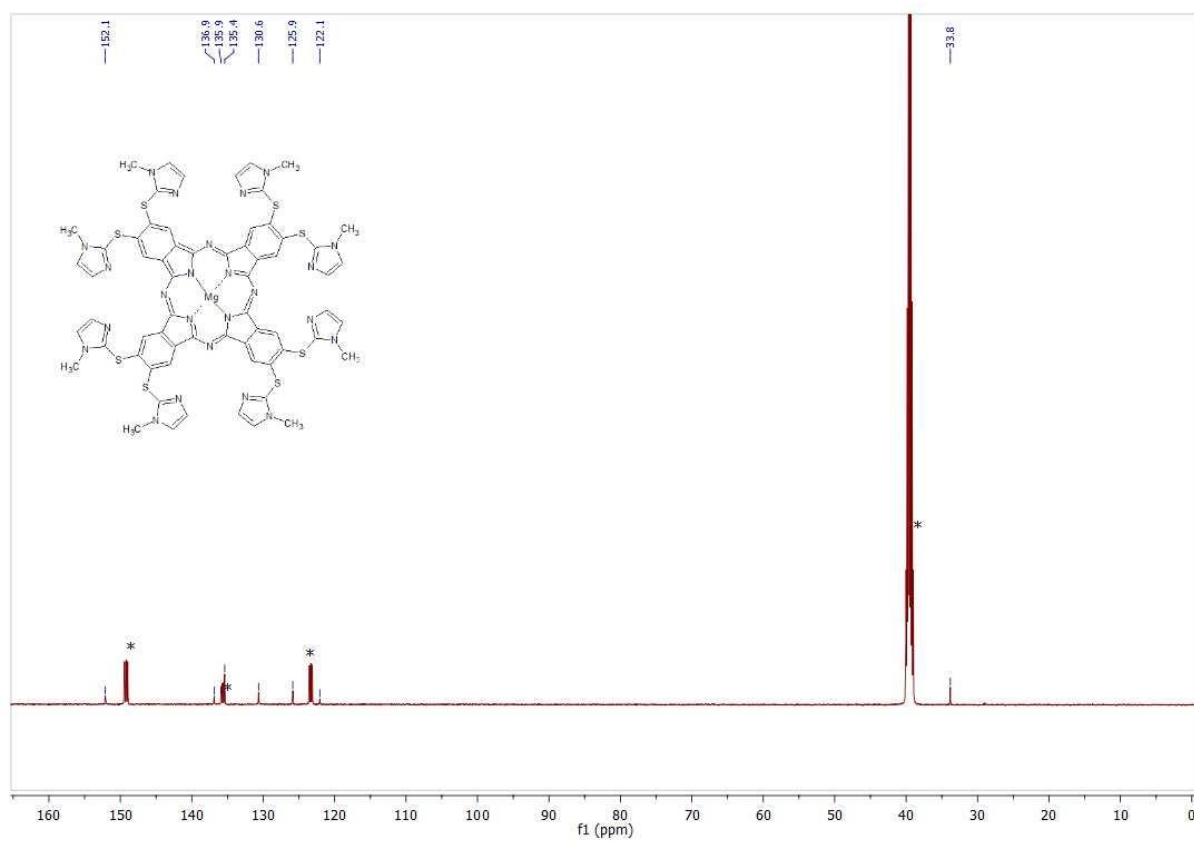
^{13}C NMR spectrum of **6** in $\text{DMSO}-d_6$



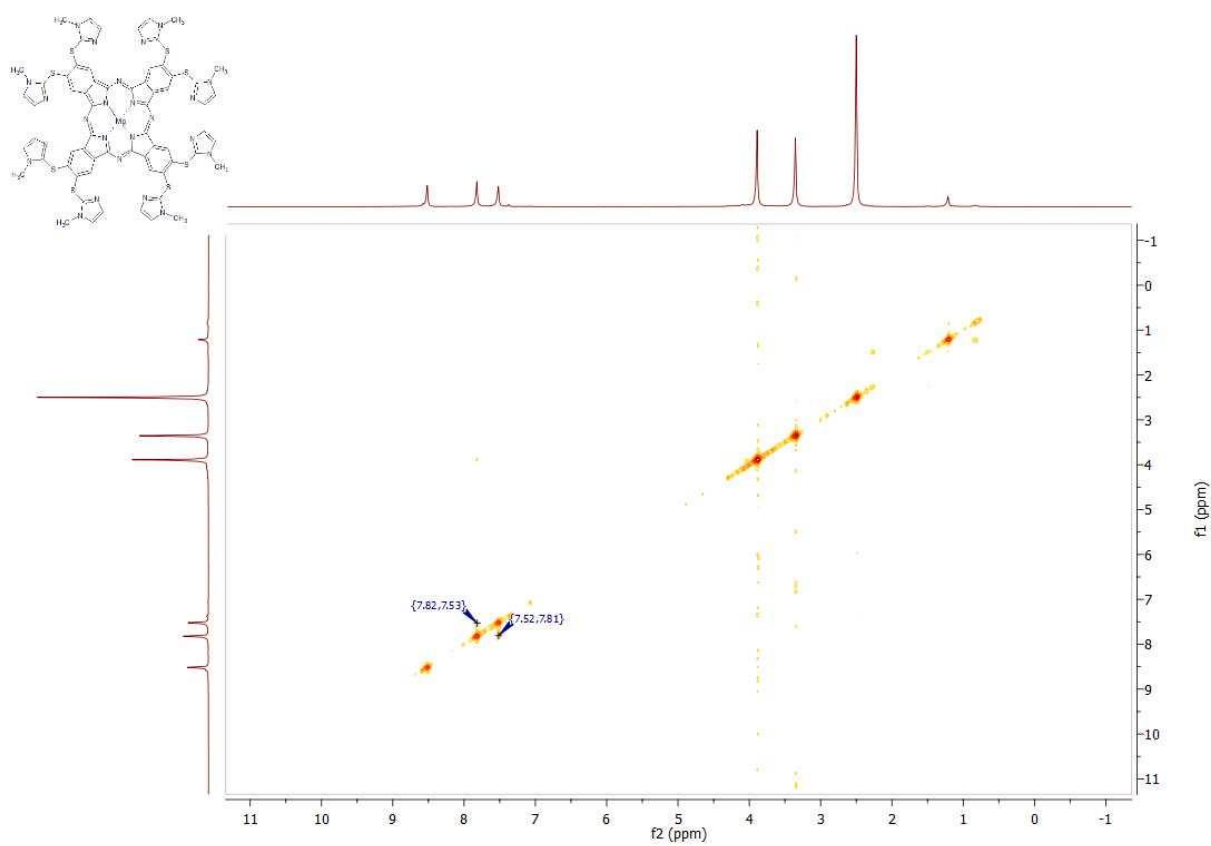
^1H NMR spectrum of **7** in $\text{DMSO}-d_6$



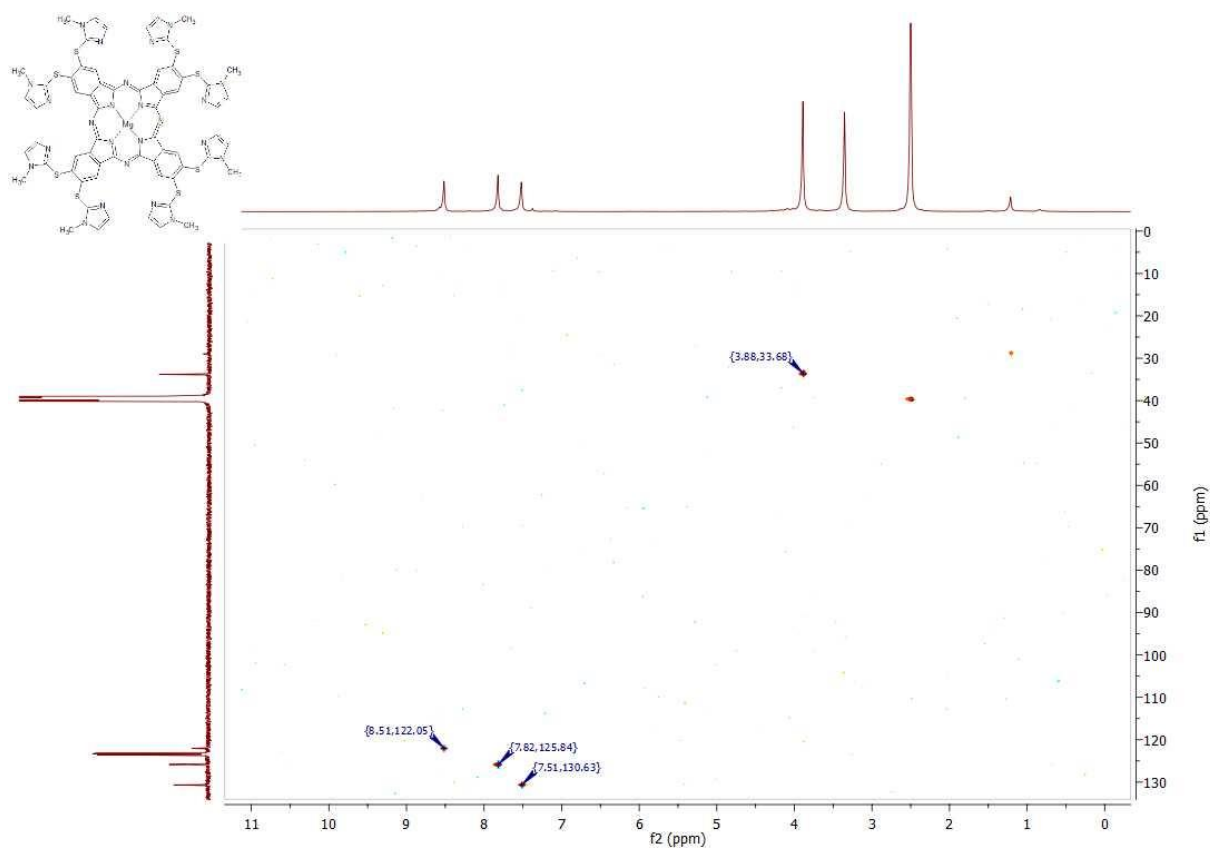
^{13}C NMR spectrum of **7** in pyridine- d_5



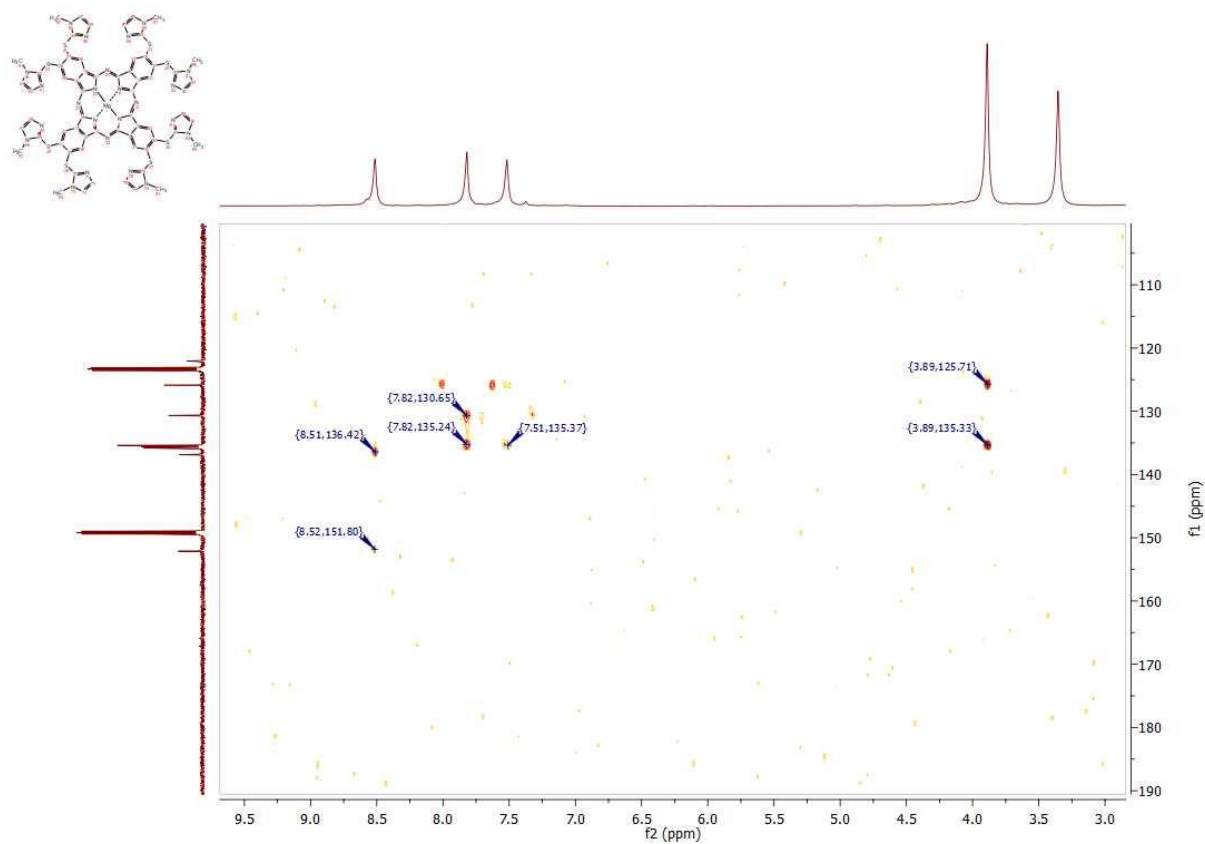
^1H - ^1H COSY spectrum of **7** in $\text{DMSO}-d_6$



HSQC spectrum of **7** in $\text{DMSO}-d_6$

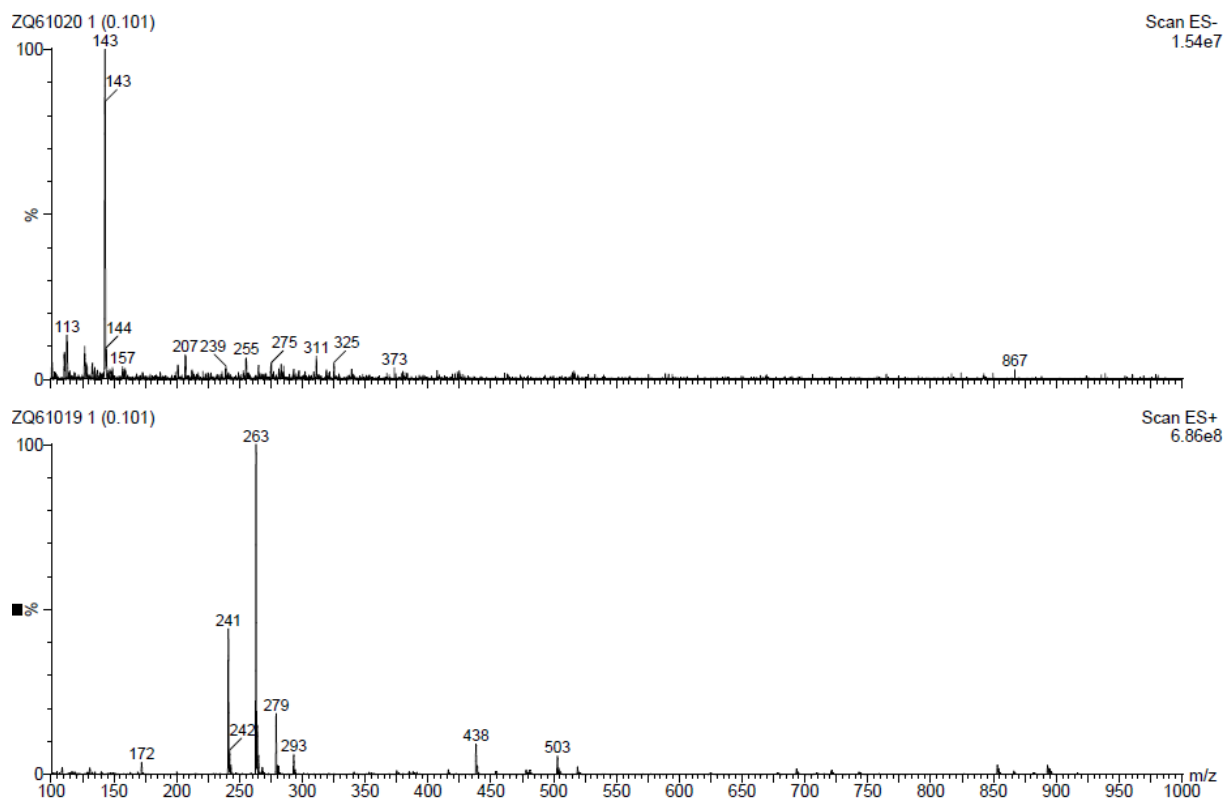


HMBC spectrum of **7** in $\text{DMSO}-d_6$

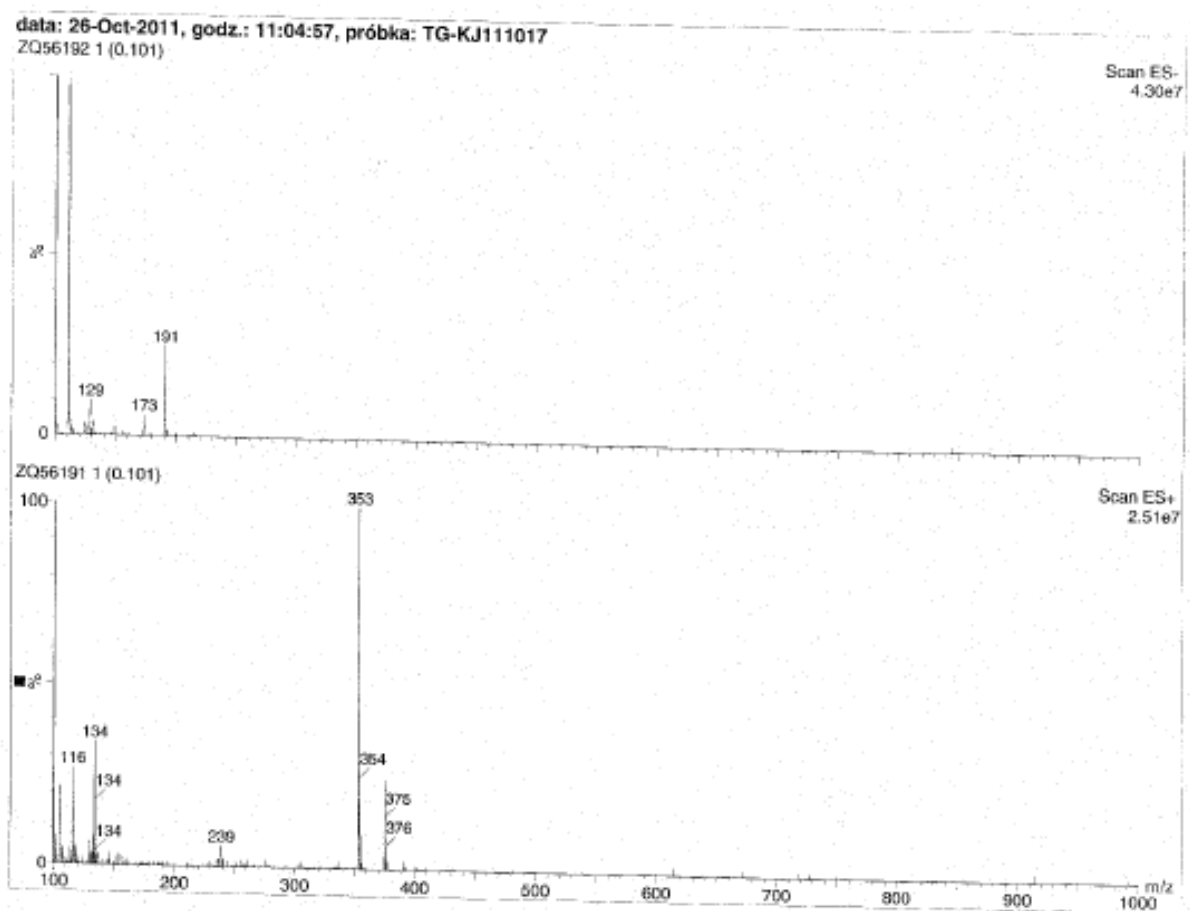


2. Mass spectra data

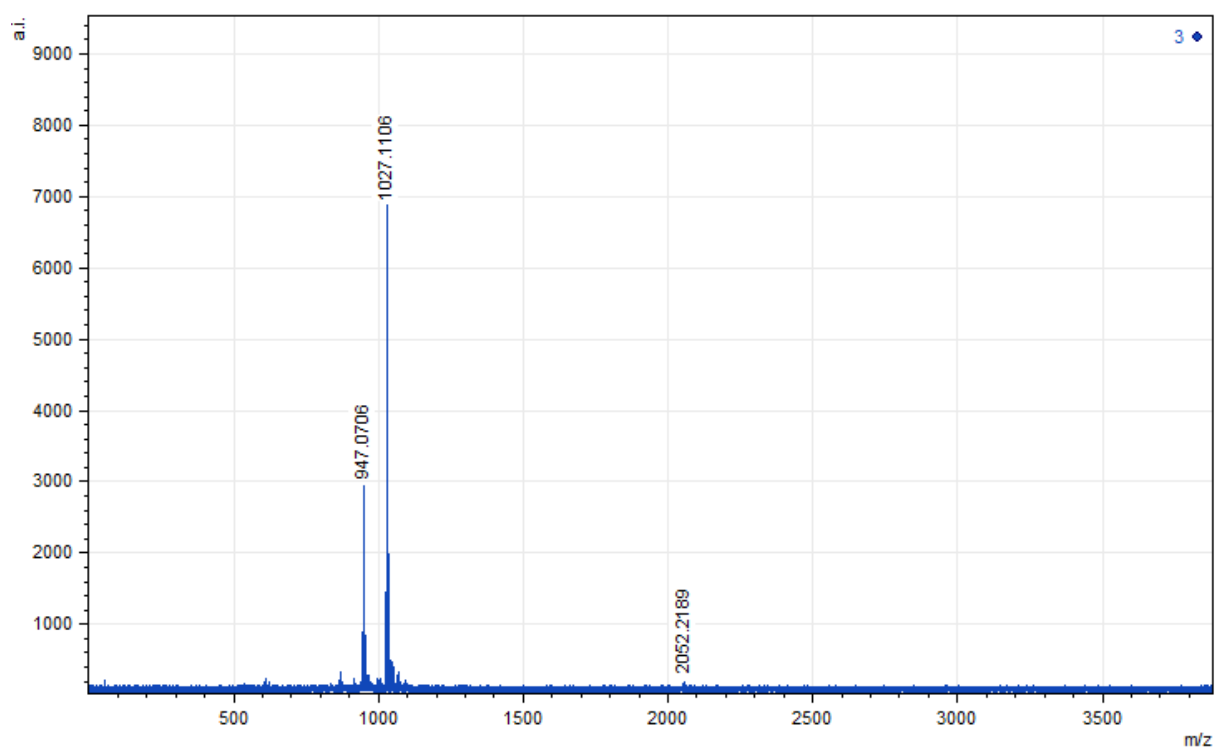
ESI spectra of compound 1.



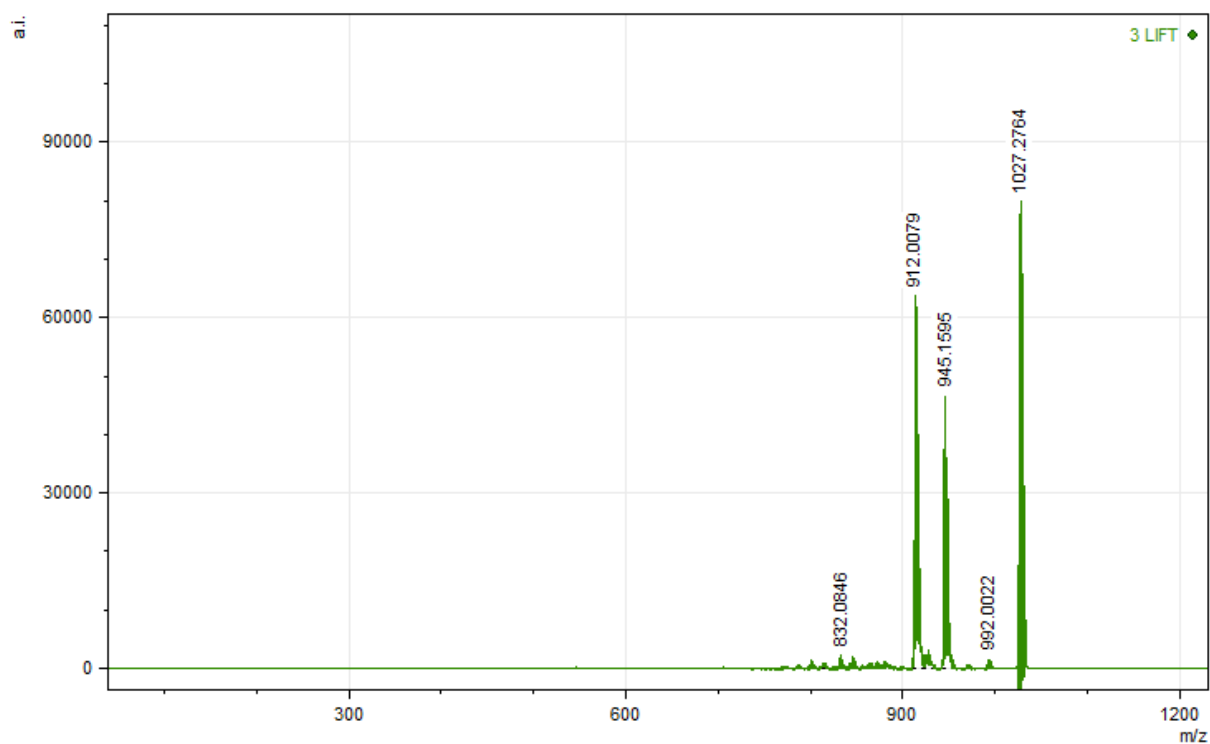
ESI spectra of compound 2



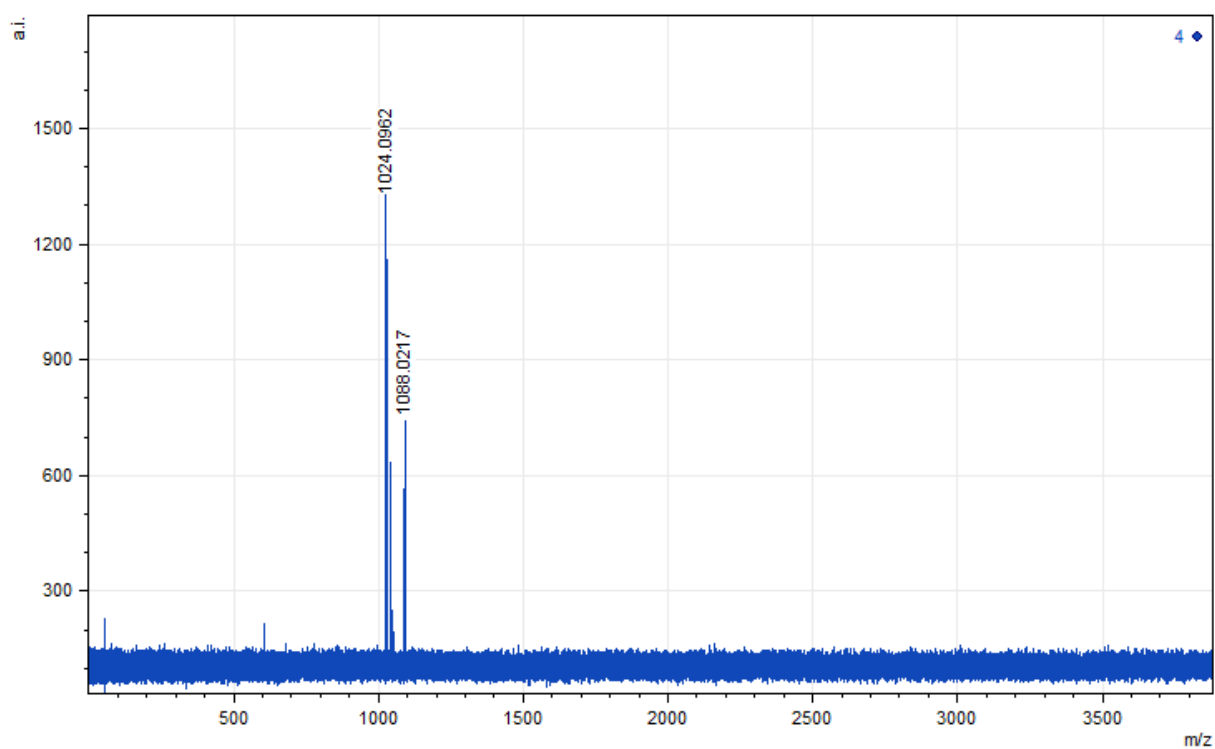
Maldi-TOF spectra of compound **3**



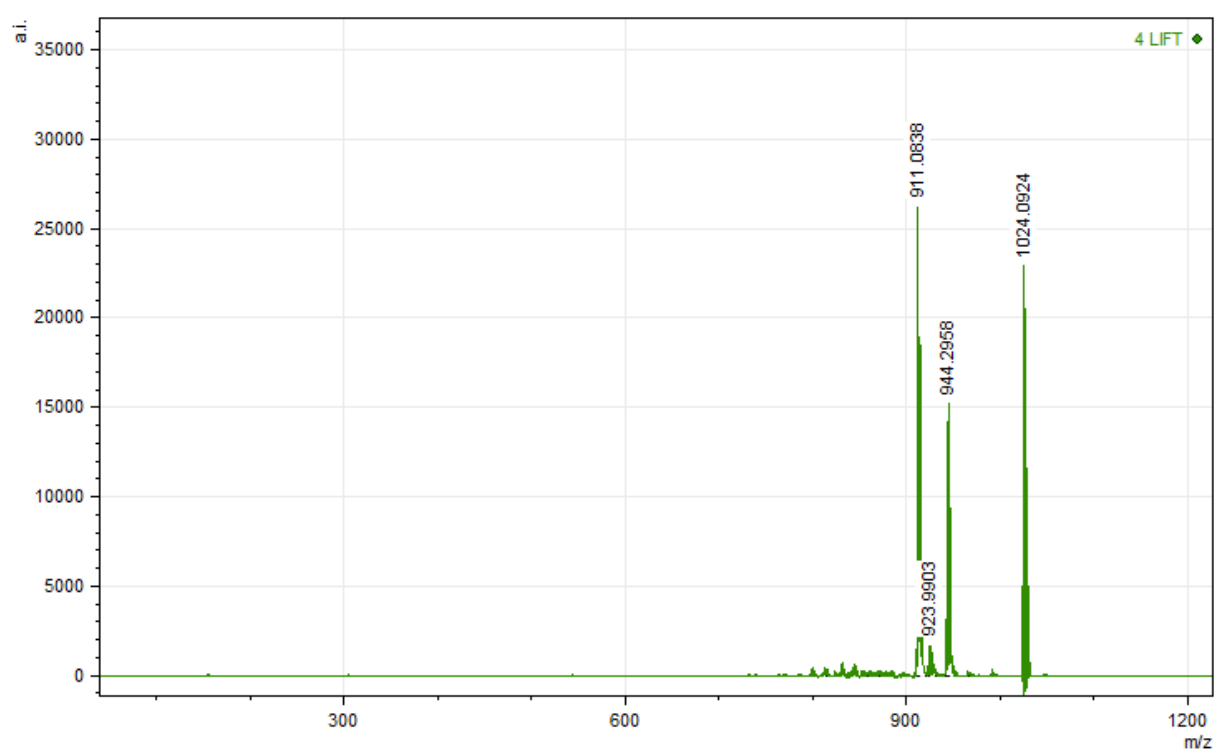
Maldi-TOF/TOF Lift spectra of compound **3**



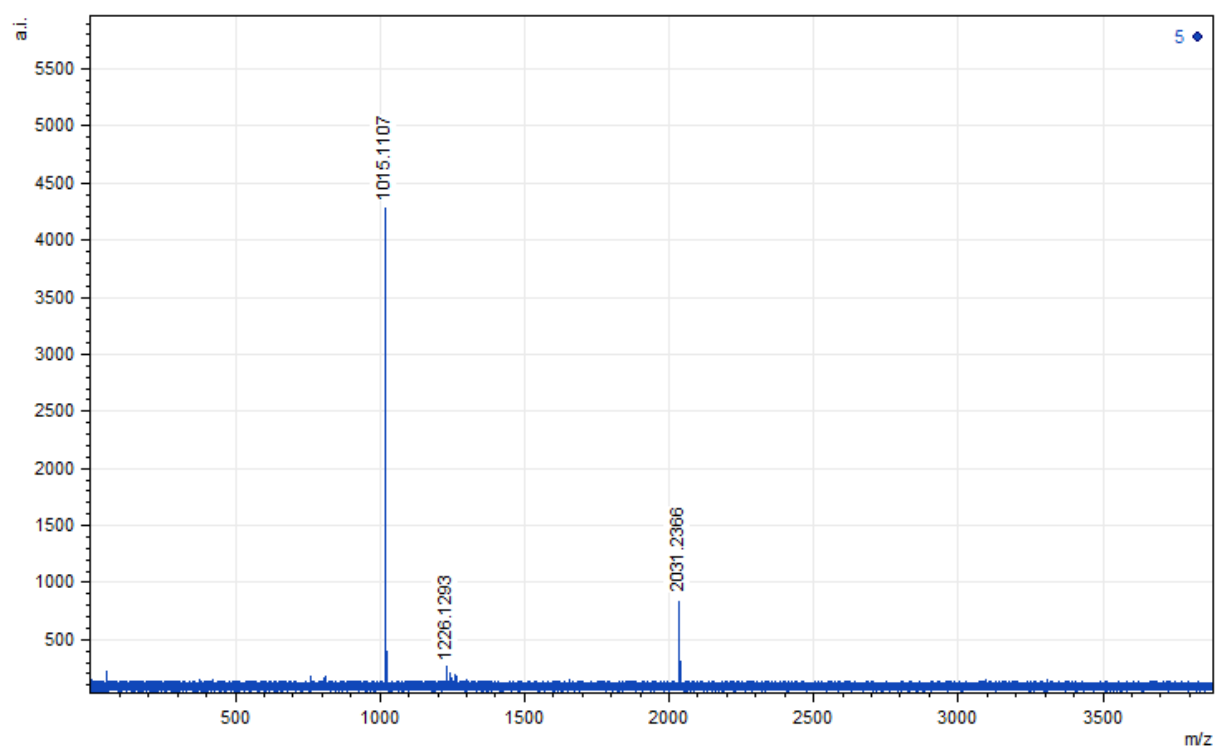
Maldi-TOF spectra of compound **4**



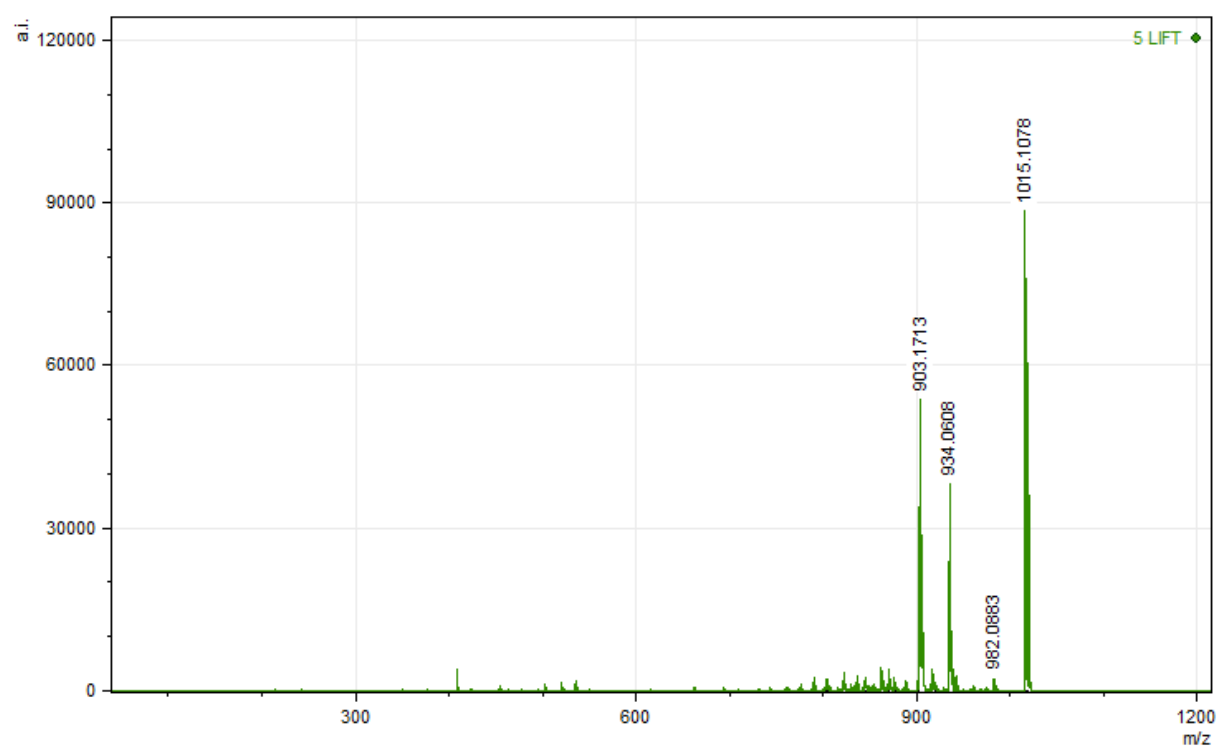
Maldi-TOF/TOF Lift spectra of compound **4**



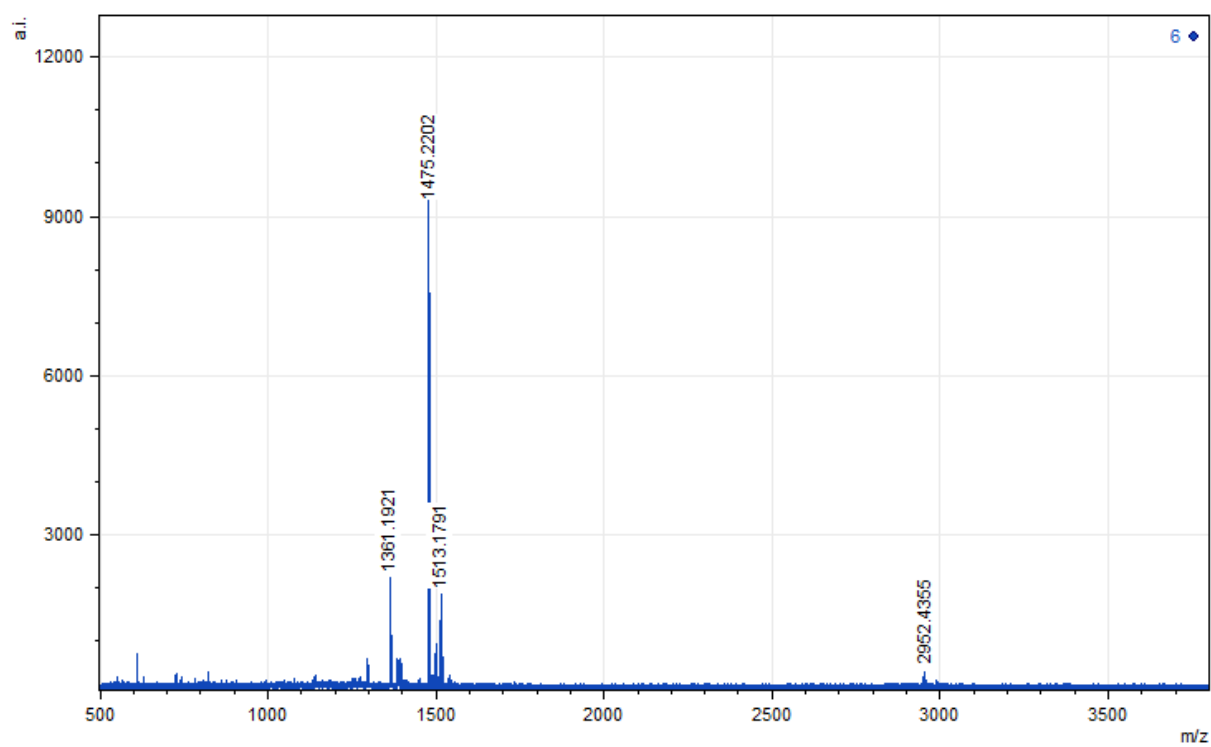
Maldi-TOF spectra of compound 5



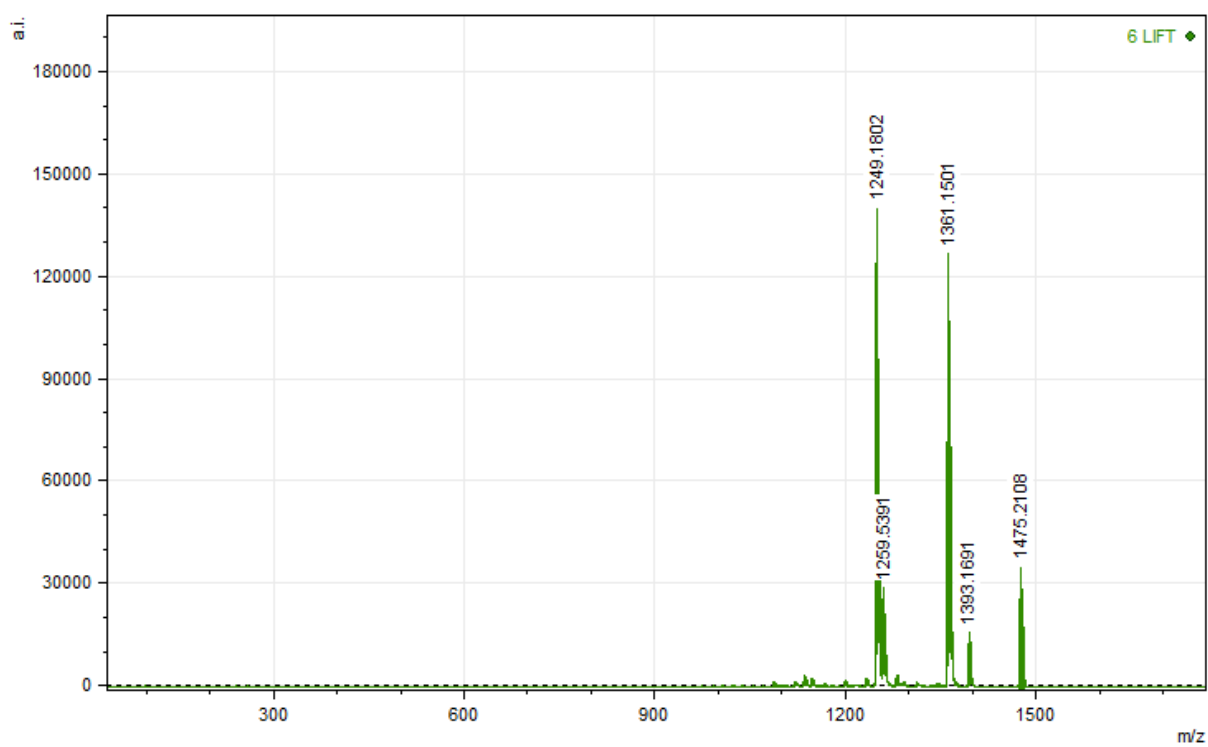
Maldi-TOF/TOF Lift spectra of compound 5



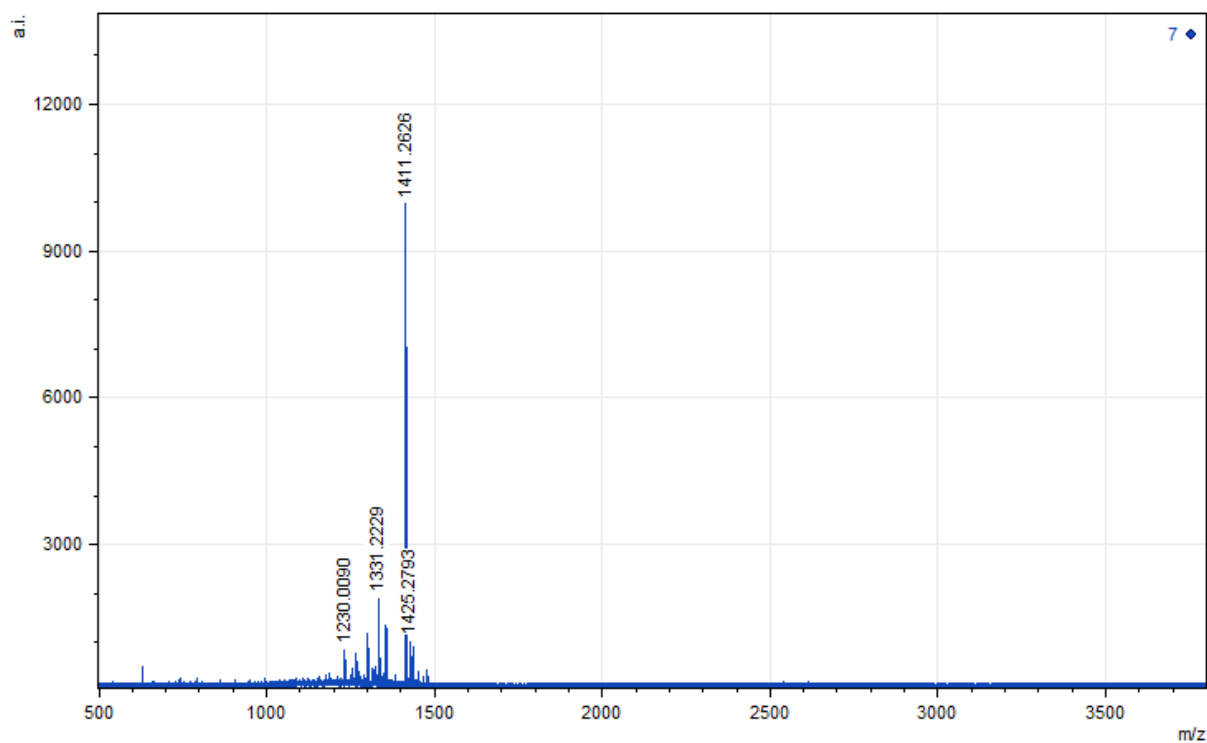
Maldi-TOF spectra of compound 6



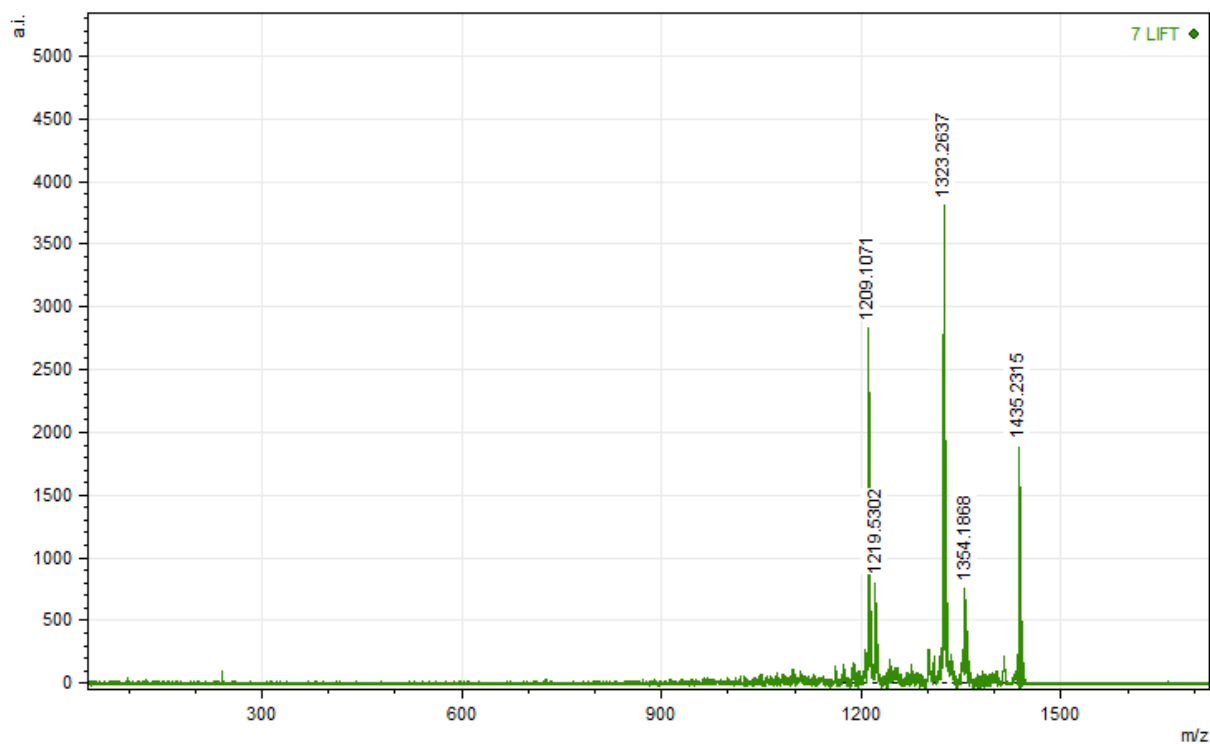
Maldi-TOF/TOF Lift spectra of compound 6



Maldi-TOF spectra of compound **7**

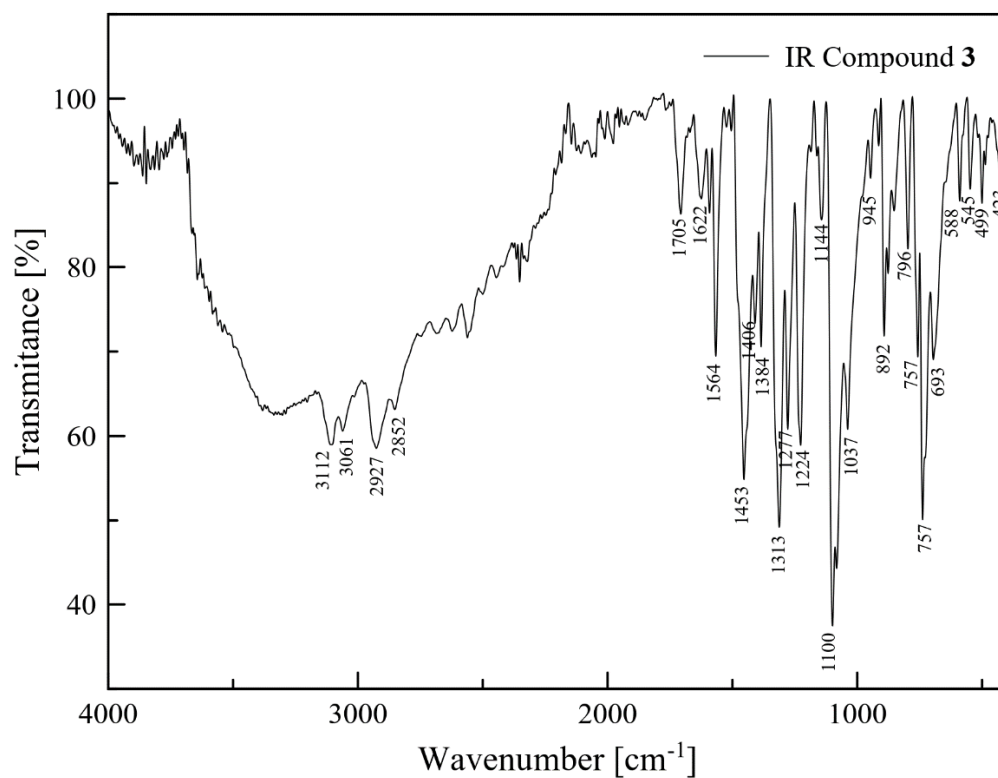


Maldi-TOF/TOF Lift spectra of compound **7**

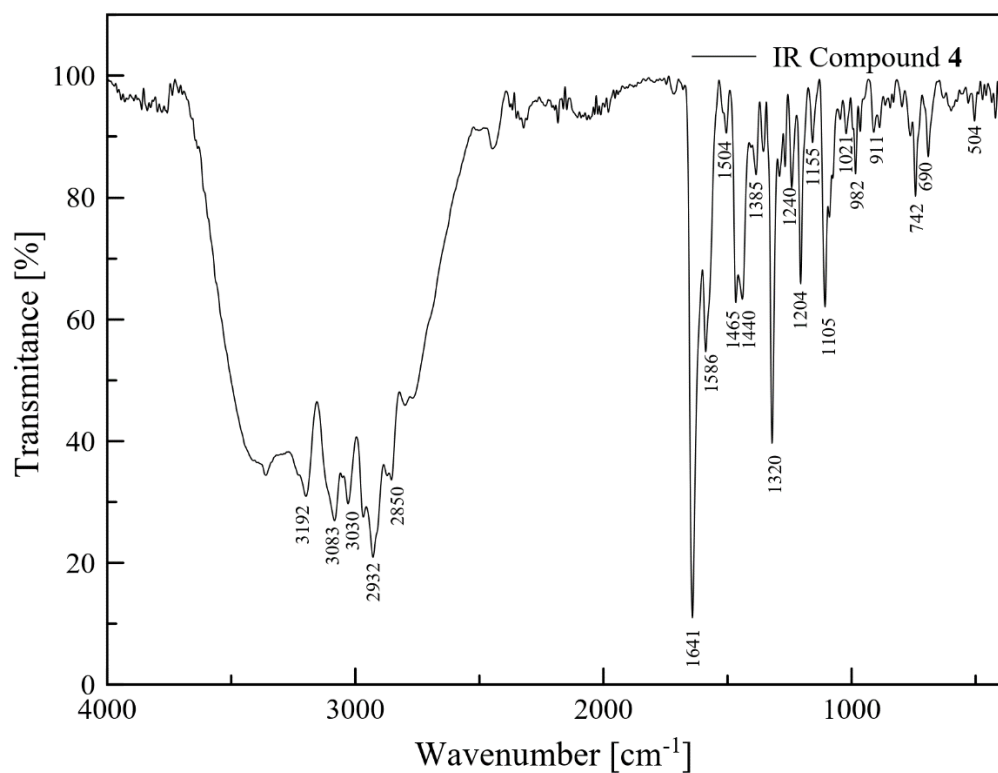


3. IR data

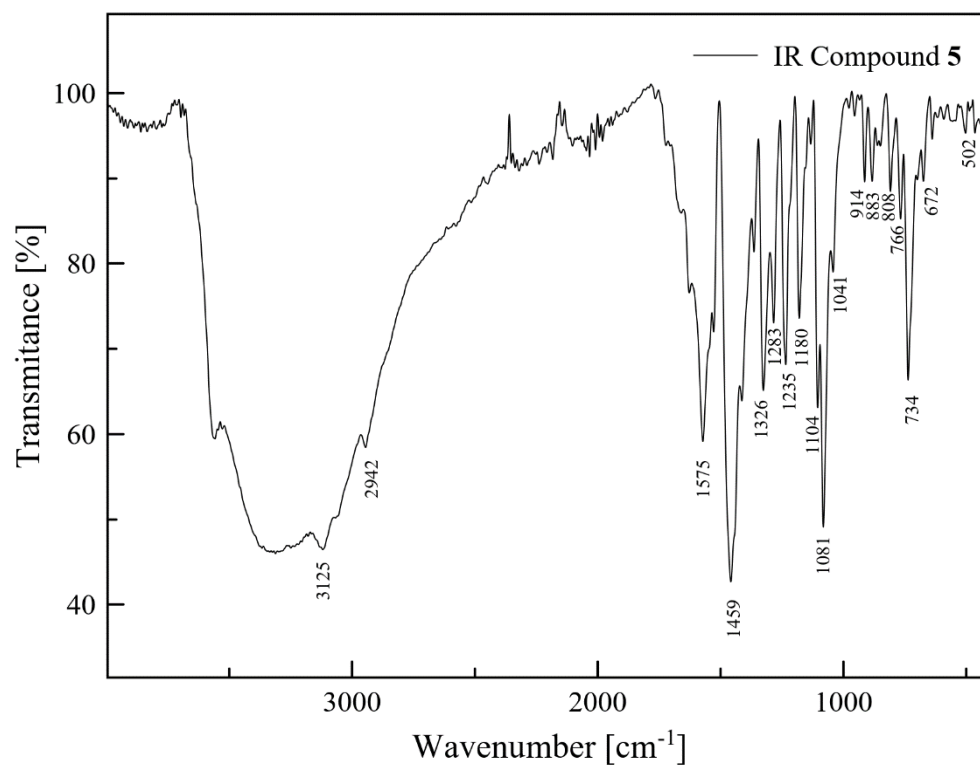
IR spectra of compound **3**



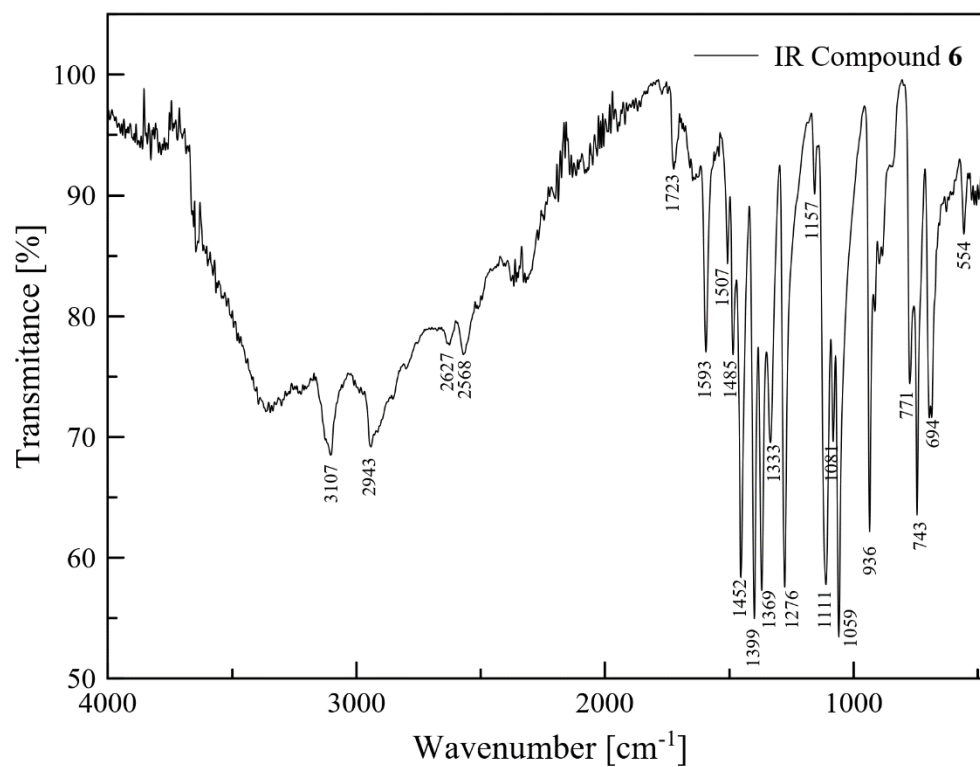
IR spectra of compound **4**



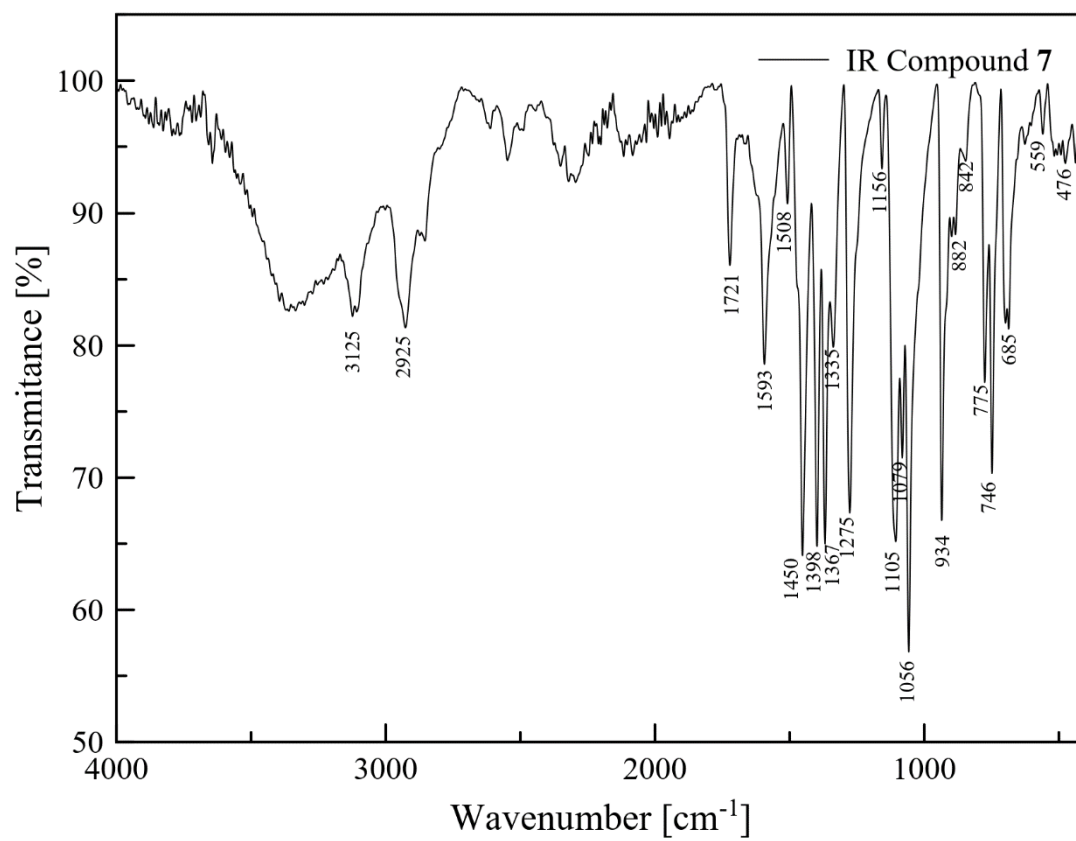
IR spectra of compound **5**



IR spectra of compound **6**



IR spectra of compound **7**

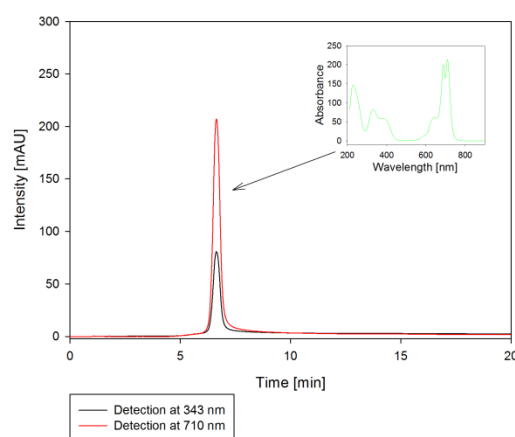


4. HPLC data

Compound 3

Analytical HPLC was carried out on an Agilent 1200 instrument equipped with an UV-DAD detector. The chromatographic separation was achieved on an octadecylsilane coated columns, 150 mm \times 4.6 mm, 5 μ m (Eclipse XDB-C18, Agilent), using isocratic and linear gradient conditions at a flow rate of 1.0 mL/min in three different phases configurations.

Phases configuration 1



Phase

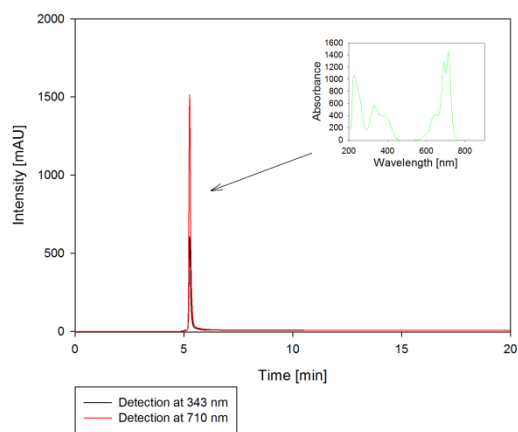
Time	MeOH	H ₂ O
0	85	15
2	85	15
3	99	1
20	99	1

Detection at 343 nm

Detection at 710 nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	6,64	1765,1	100,00	1	6,64	4711,8	100,00

Phases configuration 2



Phase

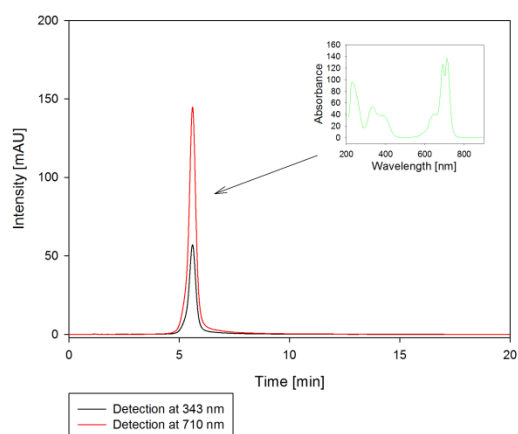
Time	MeOH	H2O	CH2Cl2
0	80	15	5
2	80	15	5
3	60	1	39
20	60	1	39

Detection at 343 nm

Detection at 710 nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	5,26	3800,8	100,00	1	5,26	8975,2	100,00

Phases configuration 3



Phase

MeOH	H2O	CH2Cl2
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70	15	15
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Detection at 343 nm

Detection at 710 nm

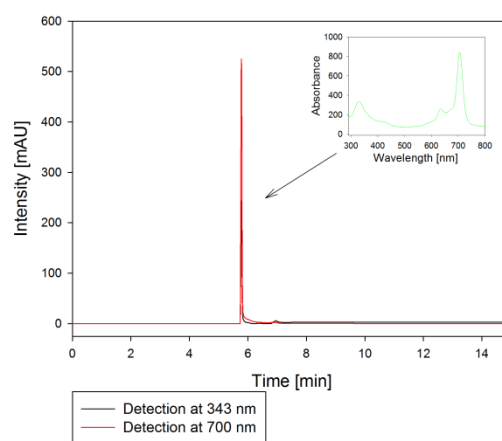
Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	5,60	1324,2	100,00	1	5,60	3424,7	100,00

Compound 4

Analytical HPLC was carried out on an Agilent 1200 instrument equipped with a UV-DAD detector. The chromatographic separation was achieved on hexaphenyl coated column, 150mm x 4.6 mm 5 μ m (Gemini C6-Phenyl, Phenomenex) using linear gradient at a flow rate of 1.0 mL/min in different phases configurations.

Phases configuration 1

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	CH ₂ Cl ₂	MeOH
0	100	0
3	100	0
4	0	100
15	0	100

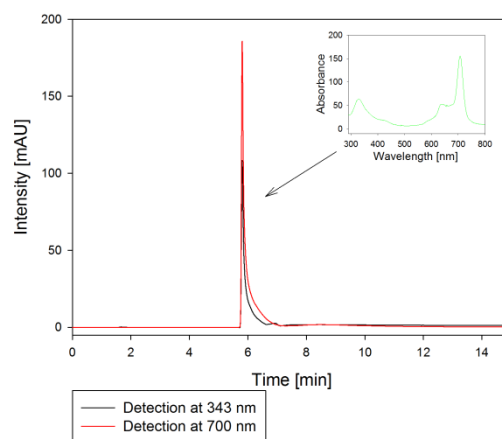
Detection at $\lambda = 343$ nm

Detection at $\lambda = 700$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	5,78	693,4	100,00	1	5,78	1562,6	100,00

Phases configuration 2

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	CH ₂ Cl ₂	isopropanol
0	100	0
3	100	0
4	0	100
15	0	100

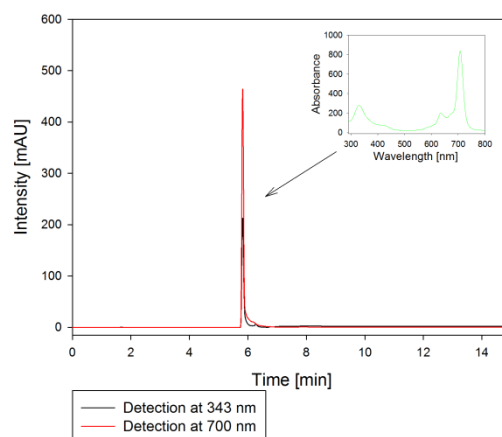
Detection at $\lambda = 343$ nm

Detection at $\lambda = 700$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	5,80	945,9	100,00	1	5,80	1749,1	100,00

Phases configuration 3

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	CH ₂ Cl ₂	isopropanol	MeOH
0	100	0	0
3	100	0	0
4	0	50	50
15	0	50	50

Detection at $\lambda = 343$ nm

Detection at $\lambda = 700$ nm

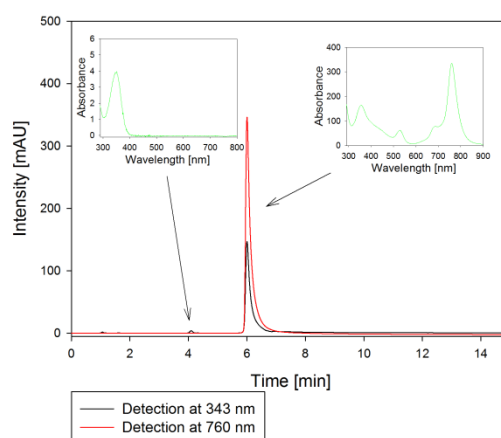
Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	5,82	1047,8	94,98	1	5,82	2338,7	100,00
2	6,27	55,4	5,02				

Compound 5

Analytical HPLC was carried out on an Agilent 1200 instrument equipped with a UV-DAD detector. The chromatographic separation was achieved on hexaphenyl coated column, 150mm x 4.6 mm 5 μ m (Gemini C6-Phenyl, Phenomenex) using linear gradient conditions at a flow rate of 1.0 mL/min in different configurations.

Phases configuration 1

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	MeOH	H ₂ O
0	50	50
3	50	50
4	100	0
15	100	0

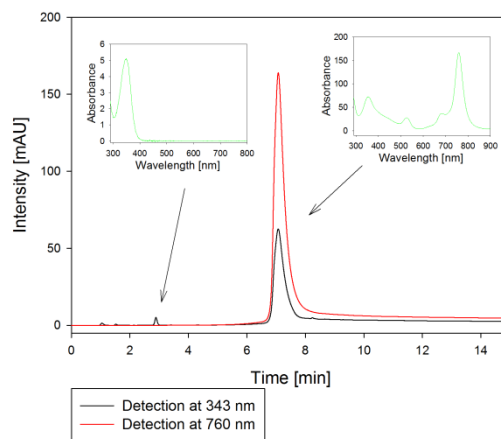
Detection at $\lambda = 343$ nm

Detection at $\lambda = 760$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	1,06	9,0	0,49	1	6,01	4471,2	100,00
2	4,09	29,0	1,57				
3	6,00	1812,8	97,94				

Phases configuration 2

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	MeOH	H ₂ O
0	60	40
4	60	40
5	100	0
15	100	0

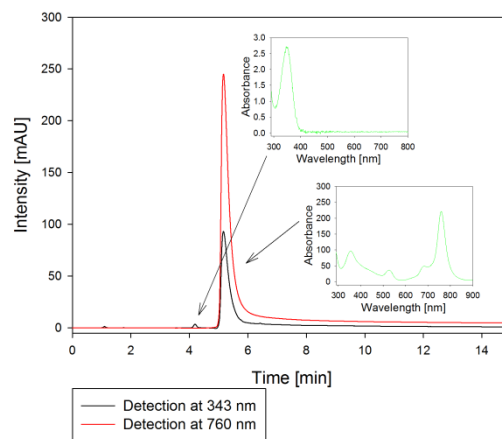
Detection at $\lambda = 343$ nm

Detection at $\lambda = 760$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	1,05	9,6	0,62	1	7,07	4178,5	100,00
2	2,89	28,1	1,83				
3	7,07	1500,4	97,55				

Phases configuration 3

Gemini C6-Phenyl, Phenomenex



Mobile phase

Time	MeOH	H ₂ O
0	50	50
2	50	50
3	99	1
15	99	1

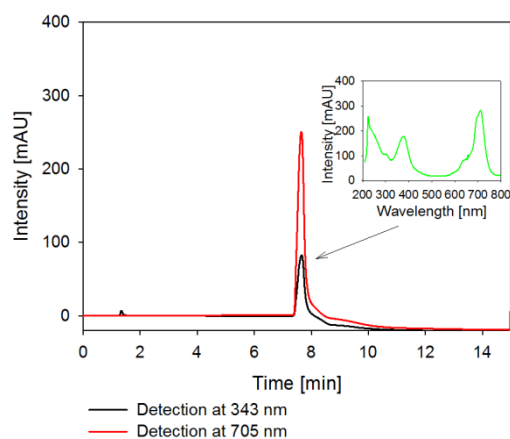
Detection at $\lambda = 343$ nm

Detection at $\lambda = 760$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	1,10	8,2	0,45	1	5,17	5038,9	100,00
2	4,19	28,0	1,55				
3	5,16	1769,8	98,00				

Compound 6

Phases configuration 1

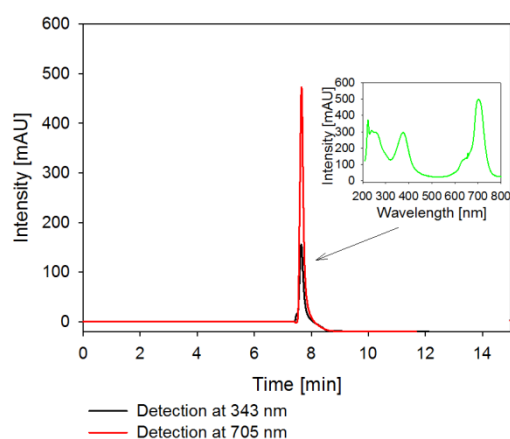


Mobile phase			
Time	MeOH	CH ₂ Cl ₂	
0	95	5	
5	95	5	
6	5	95	
15	5	95	

Flow 1.0 ml/min
 Temperature 25°C
 Column Agilent. Eclipse XDB-C18
 150 mm · 4.6 mm. 5 µm

Detection at λ=343 nm				Detection at λ=705 nm			
Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	1.34	40.8	2.36	1	7.65	4377.1	100
2	7.66	1684.6	97.64				

Phases configuration 2



Mobile phase							
Time	MeOH	CH ₂ Cl ₂	2-propanol		Flow	1.0 ml/min	
0	5	90	5		Temperature	25°C	
5	5	90	5		Column	Agilent. Eclipse XDB-C18	
6	45	10	45			150 mm · 4.6 mm. 5 µm	

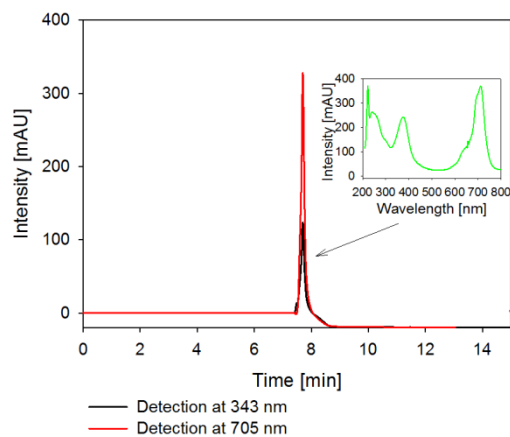
15	45	10	45
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Detection at $\lambda=343$ nm

Detection at $\lambda=705$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	7.65	2002.8	100	1	7.65	4377.1	100

Phases configuration 3



Mobile phase

Time	MeOH	CH ₂ Cl ₂	ACN	Flow	1.0 ml/min
0	98	1	1	Temperature	25°C
5	98	1	1	Column	Agilent. Eclipse XDB-C18
6	94	1	5		150 mm · 4.6 mm. 5 μ m
15	94	1	5		

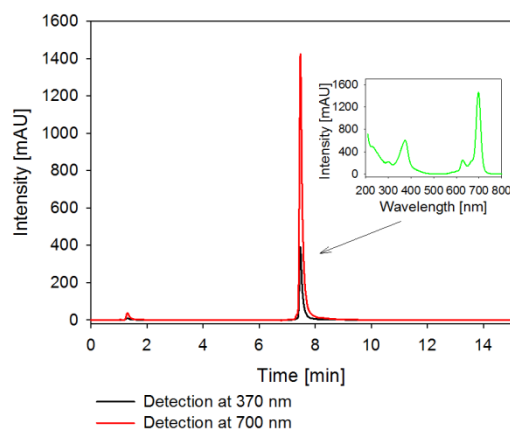
Detection at $\lambda=343$ nm

Detection at $\lambda=705$ nm

Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	7.7	1600.8	100	1	7.7	3229	100

Compound 7

Phases configuration 1



Mobile phase

Time	MeOH	H ₂ O
0	70	30
4	70	30
5	100	0
15	100	0

Flow	1.0 ml/min
Temperature	25°C
Column	Agilent, Eclipse XDB-C18
	150 mm · 4.6 mm, 5 µm

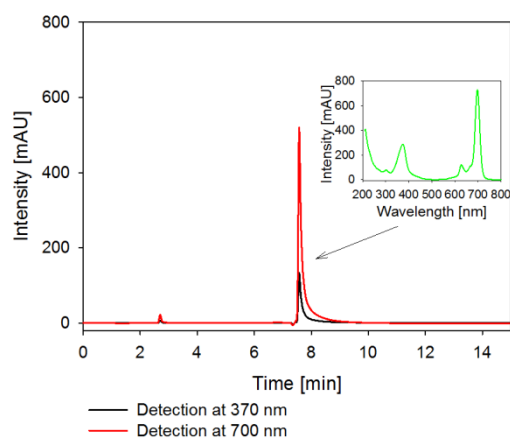
Detection at $\lambda=370$ nm

Signal	Retention time [min]	Area	Content [%]
1	1.3	83.09	2.71
2	7.47	2984.9	97.29

Detection at $\lambda=700$ nm

Signal	Retention time [min]	Area	Content [%]
1	1.3	363.98	3.01
2	7.47	11720.23	96.99

Phases configuration 2



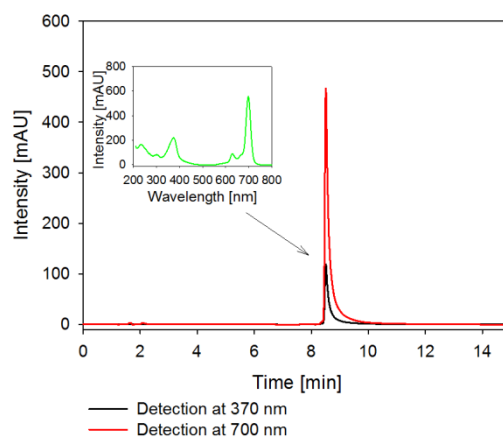
Mobile phase

Time	MeOH	H ₂ O
0	60	40
4	60	40
5	100	0
15	100	0

Flow	1.0 ml/min
Temperature	25°C
Column	Agilent, Eclipse XDB-C18
	150 mm · 4.6 mm, 5 µm

Detection at $\lambda=370$ nm				Detection at $\lambda=700$ nm			
Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	2.7	31.19	2.11	1	2.7	123.89	2.05
2	7.58	1446.92	97.89	2	6.82	150.92	2.5
				3	7.58	5765.54	95.45

Phases configuration 3



Mobile phase						
Time	MeOH	H ₂ O	ACN		Flow	1.0 ml/min
0	60	30	10		Temperature	25°C
5	60	30	10		Column	Agilent. Eclipse XDB-C18
6	0	0	100			150 mm · 4.6 mm. 5 μ m
15	0	0	100			

Detection at $\lambda=370$ nm				Detection at $\lambda=700$ nm			
Signal	Retention time [min]	Area	Content [%]	Signal	Retention time [min]	Area	Content [%]
1	8.51	1279.44	100	1	1.65	29.89	0.56
				2	2.08	49.25	0.92
				3	8.51	5254.71	98.52

5. Computational data

Table S1. Atom coordination of compound 7.

number	type	coordinate			number	type	coordinate		
		x	y	z			x	y	z
1	N	-0.15832000	-2.0020490	0.16467900	74	S	-8.20135300	-1.0696310	0.12129600
2	N	0.15832000	2.0020490	0.16467900	75	C	-8.89059900	-0.6115940	1.69073500
3	N	2.00204900	-0.1583200	0.16467900	76	N	-8.26154000	-0.6679610	2.85045300
4	N	-2.00204900	0.1583200	0.16467900	77	C	-9.19228100	-0.2730800	3.77777400
5	C	-1.34170600	-2.6975840	0.15817900	78	H	-8.94827000	-0.2125470	4.82932900
6	C	-0.89999000	2.8757930	0.15391400	79	C	-10.39394400	0.0000000	3.17049300
7	C	2.69758400	-1.3417060	0.15817900	80	H	-11.35210200	0.3123110	3.55719500
8	C	2.87579300	0.8999900	0.15391400	81	N	-10.19582600	-0.2073860	1.82244400
9	C	1.34170600	2.6975840	0.15817900	82	C	-11.19264100	-0.0387350	0.77071900
10	C	0.89999000	-2.8757930	0.15391400	83	H	-11.64427400	-0.9996940	0.50237700
11	C	-2.69758400	1.3417060	0.15817900	84	H	-10.73513500	0.4152190	-0.11243600
12	C	-2.87579300	-0.8999900	0.15391400	85	H	-11.97590100	0.6242550	1.14286400
13	C	0.37000400	-4.2384620	0.14073900	86	S	-2.33733400	-7.9558660	0.14452600
14	C	1.03369200	4.1253070	0.14876600	87	C	-2.23976600	-8.5787830	-1.51092400
15	C	4.23846200	0.3700040	0.14073900	88	N	-1.68262300	-9.7316400	-1.84576900
16	C	4.12530700	-1.0336920	0.14876600	89	C	-1.91334600	-9.8793940	-3.18764600
17	C	-0.37000400	4.2384620	0.14073900	90	H	-1.56281300	-10.7462000	-3.72991100
18	C	-1.03369200	-4.1253070	0.14876600	91	C	-2.61935200	-8.8054850	-3.67295300
19	C	-4.23846200	-0.3700040	0.14073900	92	H	-2.97682400	-8.5573190	-4.66099300
20	C	-4.12530700	1.0336920	0.14876600	93	N	-2.84094200	-7.9780050	-2.59641700
21	N	-2.57818100	-2.1991880	0.14972500	94	C	-3.56441600	-6.7158230	-2.62762700
22	N	-2.19918800	2.5781810	0.14972500	95	H	-2.87960600	-5.8661130	-2.70185600
23	N	2.19918800	-2.5781810	0.14972500	96	H	-4.15535700	-6.6136280	-1.71617200
24	N	2.57818100	2.1991880	0.14972500	97	H	-4.23449000	-6.7146570	-3.48878700
25	C	5.48792900	0.9851450	0.14979200	98	S	1.06963100	-8.2013530	0.12129600
26	C	5.26302600	-1.8387260	0.14146500	99	C	0.61159400	-8.8905990	1.69073500
27	C	-0.98514500	5.4879290	0.14979200	100	N	0.66796100	-8.2615400	2.85045300
28	C	-1.83872600	-5.2630260	0.14146500	101	C	0.27308000	-9.1922810	3.77777400
29	C	-5.48792900	-0.9851450	0.14979200	102	H	0.21254700	-8.9482700	4.82932900
30	C	-5.26302600	1.8387260	0.14146500	103	C	0.00000000	-10.3939440	3.17049300
31	C	0.98514500	-5.4879290	0.14979200	104	H	-0.31231100	-11.3521020	3.55719500
32	C	1.83872600	5.2630260	0.14146500	105	N	0.20738600	-10.1958260	1.82244400
33	C	6.63705200	0.1878850	0.14599700	106	C	0.03873500	-11.1926410	0.77071900
34	C	6.52249000	-1.2330800	0.11284200	107	H	0.99969400	-11.6442740	0.50237700
35	C	-0.18788500	6.6370520	0.14599700	108	H	-0.41521900	-10.7351350	-0.11243600
36	C	-1.23308000	-6.5224900	0.11284200	109	H	-0.62425500	-11.9759010	1.14286400
37	C	-6.63705200	-0.1878850	0.14599700	110	S	-7.95586600	2.3373340	0.14452600
38	C	-6.52249000	1.2330800	0.11284200	111	C	-8.57878300	2.2397660	-1.51092400
39	C	0.18788500	-6.6370520	0.14599700	112	N	-9.73164000	1.6826230	-1.84576900
40	C	1.23308000	6.5224900	0.11284200	113	C	-9.87939400	1.9133460	-3.18764600
41	Mg	0.00000000	0.0000000	0.19856800	114	H	-10.74620000	1.5628130	-3.72991100
42	H	-2.06466300	5.5754910	0.18870800	115	C	-8.80548500	2.6193520	-3.67295300
43	H	2.91903600	5.1730720	0.15143700	116	H	-8.55731900	2.9768240	-4.66099300
44	H	5.57549100	2.0646630	0.18870800	117	N	-7.97800500	2.8409420	-2.59641700
45	H	5.17307200	-2.9190360	0.15143700	118	C	-6.71582300	3.5644160	-2.62762700
46	H	2.06466300	-5.5754910	0.18870800	119	H	-5.86611300	2.8796060	-2.70185600
47	H	-2.91903600	-5.1730720	0.15143700	120	H	-6.61362800	4.1553570	-1.71617200
48	H	-5.57549100	-2.0646630	0.18870800	121	H	-6.71465700	4.2344900	-3.48878700
49	H	-5.17307200	2.9190360	0.15143700	122	S	7.95586600	-2.3373340	0.14452600
50	S	-1.06963100	8.2013530	0.12129600	123	C	8.57878300	-2.2397660	-1.51092400
51	C	-0.61159400	8.8905990	1.69073500	124	N	9.73164000	-1.6826230	-1.84576900
52	N	-0.66796100	8.2615400	2.85045300	125	C	9.87939400	-1.9133460	-3.18764600
53	C	-0.27308000	9.1922810	3.77777400	126	H	10.74620000	-1.5628130	-3.72991100
54	H	-0.21254700	8.9482700	4.82932900	127	C	8.80548500	-2.6193520	-3.67295300
55	C	0.00000000	10.3939440	3.17049300	128	H	8.55731900	-2.9768240	-4.66099300
56	H	0.31231100	11.3521020	3.55719500	129	N	7.97800500	-2.8409420	-2.59641700
57	N	-0.20738600	10.1958260	1.82244400	130	C	6.71582300	-3.5644160	-2.62762700
58	C	-0.03873500	11.1926410	0.77071900	131	H	5.86611300	-2.8796060	-2.70185600
59	H	-0.99969400	11.6442740	0.50237700	132	H	6.61362800	-4.1553570	-1.71617200
60	H	0.41521900	10.7351350	-0.11243600	133	H	6.71465700	-4.2344900	-3.48878700
61	H	0.62425500	11.9759010	1.14286400	134	S	8.20135300	1.0696310	0.12129600
62	S	2.33733400	7.9558660	0.14452600	135	C	8.89059900	0.6115940	1.69073500
63	C	2.23976600	8.5787830	-1.51092400	136	N	8.26154000	0.6679610	2.85045300
64	N	1.68262300	9.7316400	-1.84576900	137	C	9.19228100	0.2730800	3.77777400
65	C	1.91334600	9.8793940	-3.18764600	138	H	8.94827000	0.2125470	4.82932900
66	H	1.56281300	10.7462000	-3.72991100	139	C	10.39394400	0.0000000	3.17049300

67	C	2.61935200	8.8054850	-3.67295300	140	H	11.35210200	-0.3123110	3.55719500
68	H	2.97682400	8.5573190	-4.66099300	141	N	10.19582600	0.2073860	1.82244400
69	N	2.84094200	7.9780050	-2.59641700	142	C	11.19264100	0.0387350	0.77071900
70	C	3.56441600	6.7158230	-2.62762700	143	H	11.64427400	0.9996940	0.50237700
71	H	2.87960600	5.8661130	-2.70185600	144	H	10.73513500	-0.4152190	-0.11243600
72	H	4.15535700	6.6136280	-1.71617200	145	H	11.97590100	-0.6242550	1.14286400
73	H	4.23449000	6.7146570	-3.48878700	74	S	-8.20135300	-1.0696310	0.12129600

Summary of NMR spectra (SCF GIAO Magnetic shielding), Values of **7** for element C only
Degenerate peaks are condensed together (Degeneracy Tolerance 0.05)

Shielding (ppm) Degeneracy Atoms

```

22.4243000000    4.0000  5,7,9,11
22.7236000000    4.0000  6,8,10,12
29.7097000000    4.0000  33,35,37,39
30.3117000000    4.0000  51,75,99,135
34.3942000000    4.0000  63,87,111,123
34.8692000000    4.0000  34,36,38,40
36.1343000000    4.0000  13,15,17,19
36.6794000000    4.0000  14,16,18,20
43.2229000000    4.0000  26,28,30,32
44.5690000000    4.0000  25,27,29,31
48.6029000000    4.0000  53,77,101,137
49.4615000000    4.0000  65,89,113,125
51.5323000000    4.0000  67,91,115,127
53.8700000000    4.0000  55,79,103,139
147.1335500000    8.0000  58,82,106,142,70,94,118,130

```

6. Crystallographic data

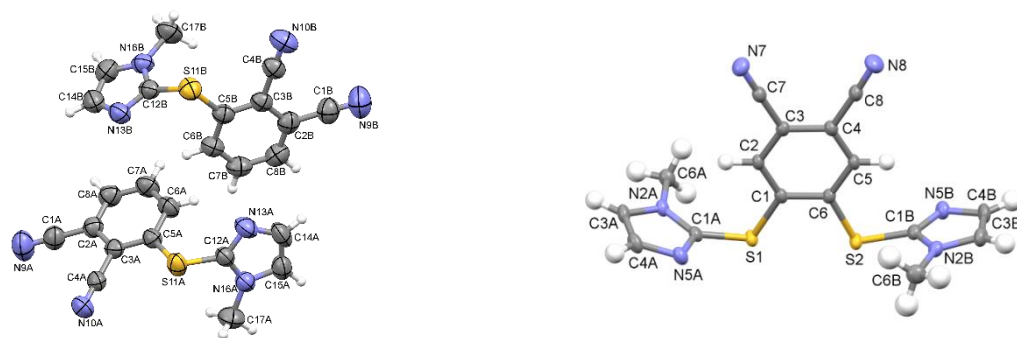


Figure S1. Anisotropic ellipsoid representation of **1** (left) and **2** (right), showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

7. Liposomes

Table S2. Size of liposomal formulation of studied phthalocyanines

Compound	Mean diameter [nm]	Dv10	Dv50	Dv90
3	152	94	131	248
4	155	100	148	199
5	265	133	240	422
6	141	85	139	191
7	160	110	155	200

8. Dark activity of PSs against *Staphylococcus aureus*

Table S3. Dark activity of PSs against *Staphylococcus aureus*

Compound	3	4	5	6	7
Concentration [M]	log reduction in bacterial growth				
10^{-4}	0.08	0.00	0.06	0.20	0.08
10^{-5}	0.02	0.07	0.03	0.11	0.11