Supplementary Material

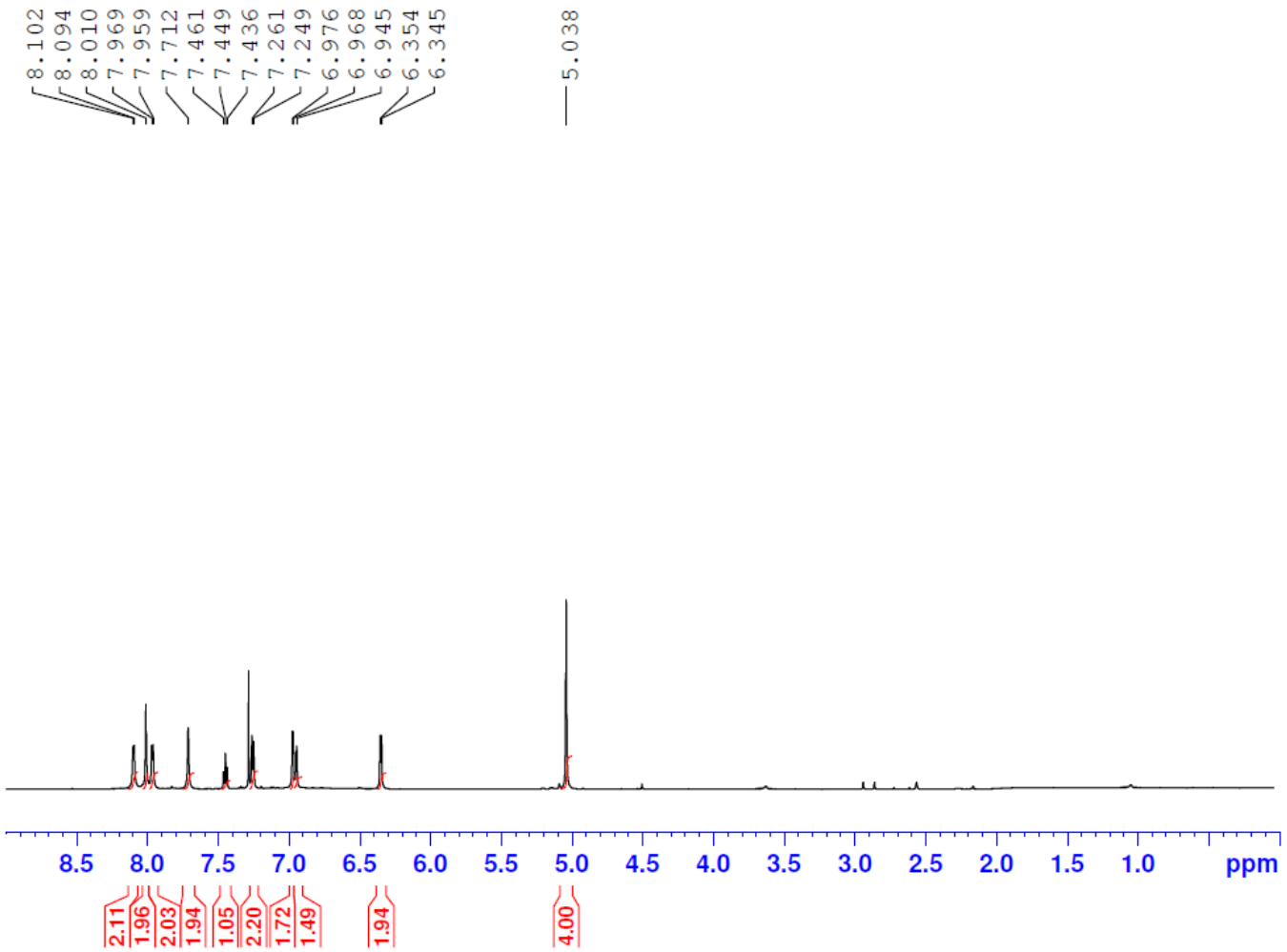
New isomeric dipyridothiazine dimers - synthesis, structural characterization and cytotoxicity screening

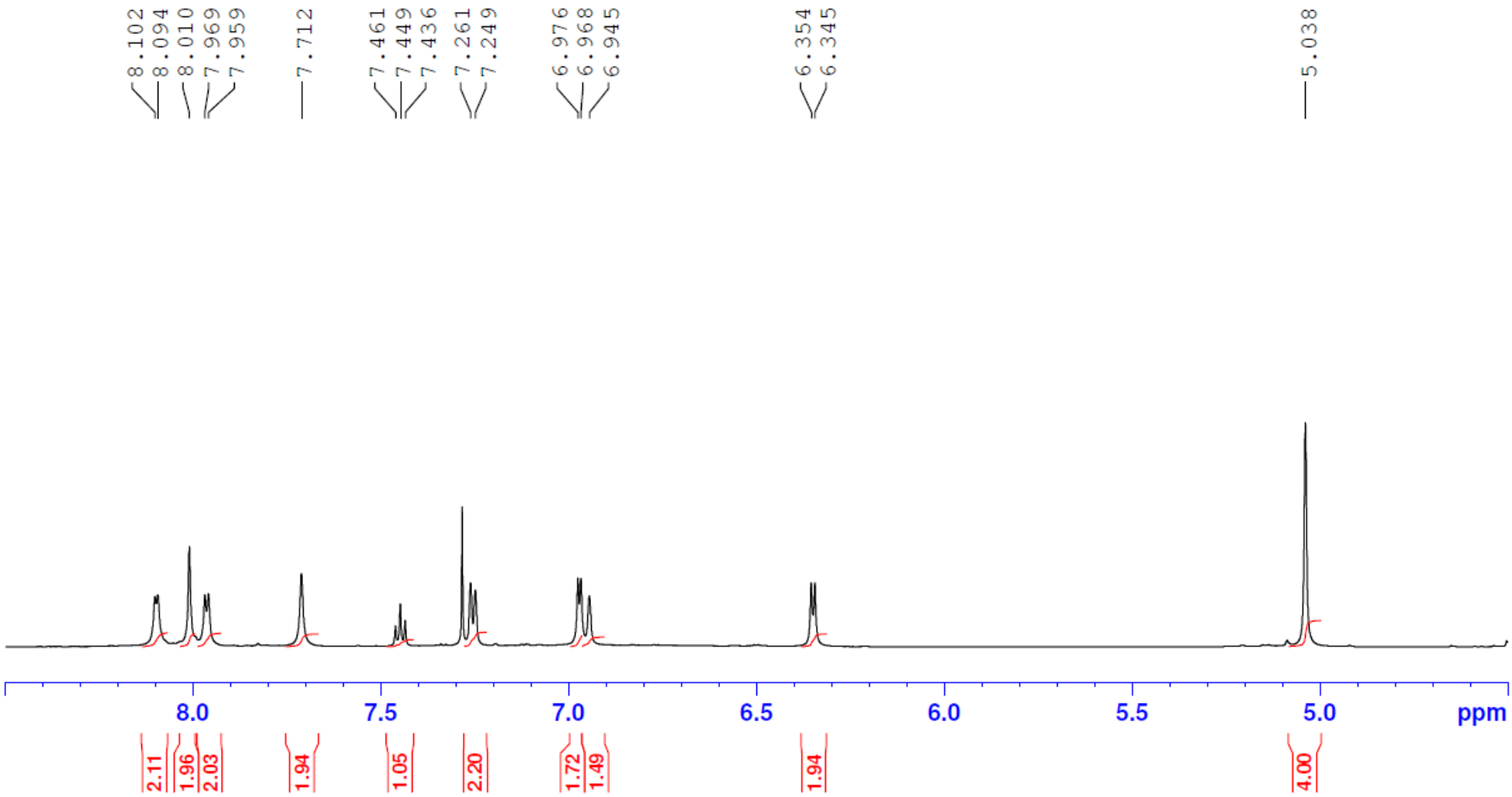
Emilia Martula[1], Beata Morak-Młodawska[2]*, Małgorzata Jeleń[2], Paulina Strzyga-Łach[3], Marta Struga[3], Katarzyna Żurawska[4] , Anna Kasprzycka[4,5]

[1] Doctoral School of The Medical University of Silesia, Poland, d201074@365.sum.edu.pl
[2] Department of Organic Chemistry, Faculty of Pharmaceutical Sciences, The Medical University of Silesia, Jagiellońska 4, 41-200 Sosnowiec, Poland; bmlodawska@sum.edu.pl(B.M.M.); manowak@sum.edu.pl (M.J.)
[3] Chair and Department of Biochemistry, Medical University of Warsaw, 02-097 Warsaw, Poland, paulina.strzyga-lach@wum.edu.pl (P.S.Ł), marta.struga@wum.edu.pl (M.S.),
[4] Biotechnology Centre, The Silesian University of Technology, Krzywoustego Street 8, 44-100 Gliwice, Poland katarzyna.hopko@polsl.pl
[5] Department of Organic Chemistry, Bioorganic Chemistry and Biotechnology, Faculty of Chemistry, Silesian University of Technology, Krzywoustego Street 4, 44-100 Gliwice, Poland, anna.kasprzycka@sum.edu.pl

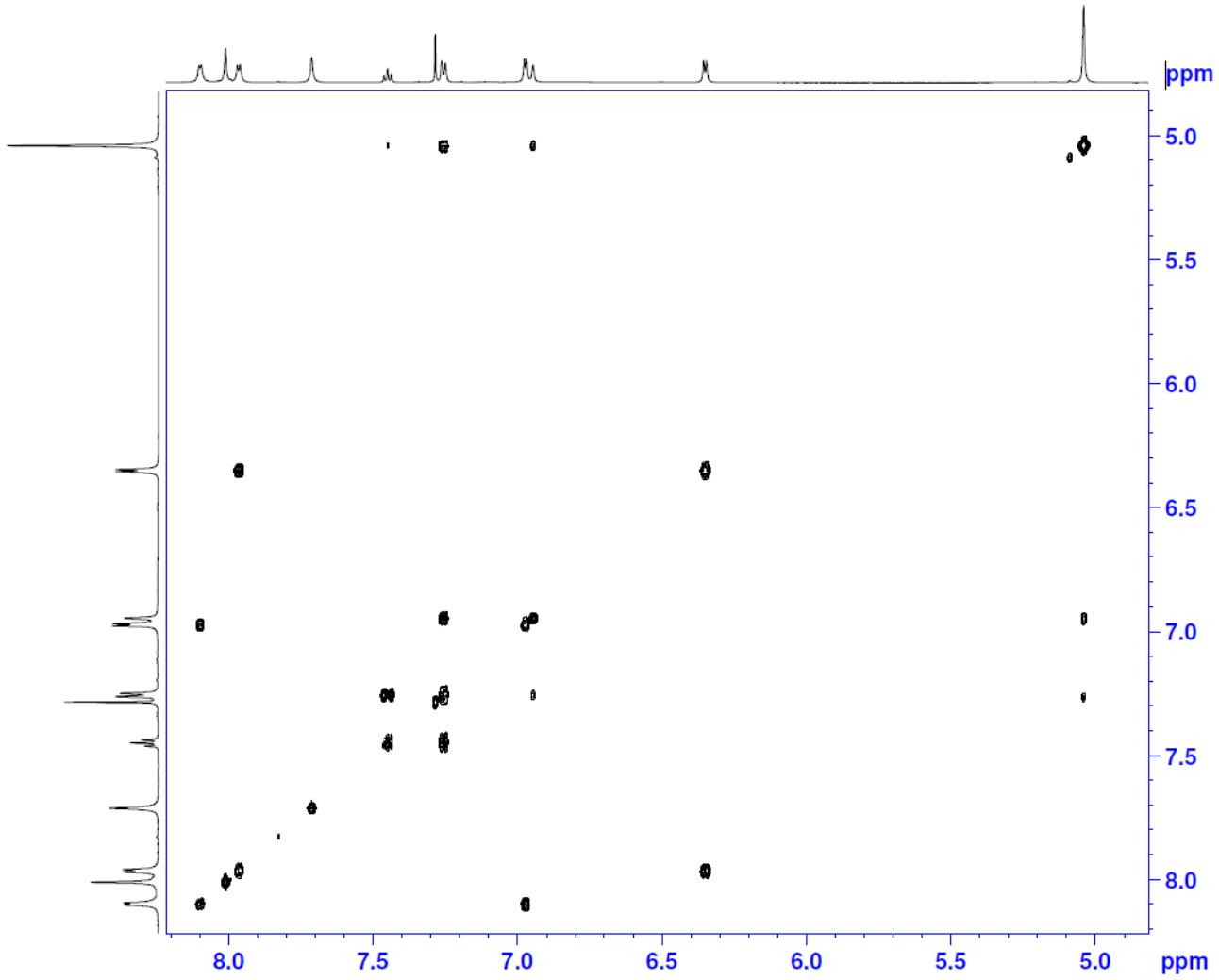
Content

[1]H NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)

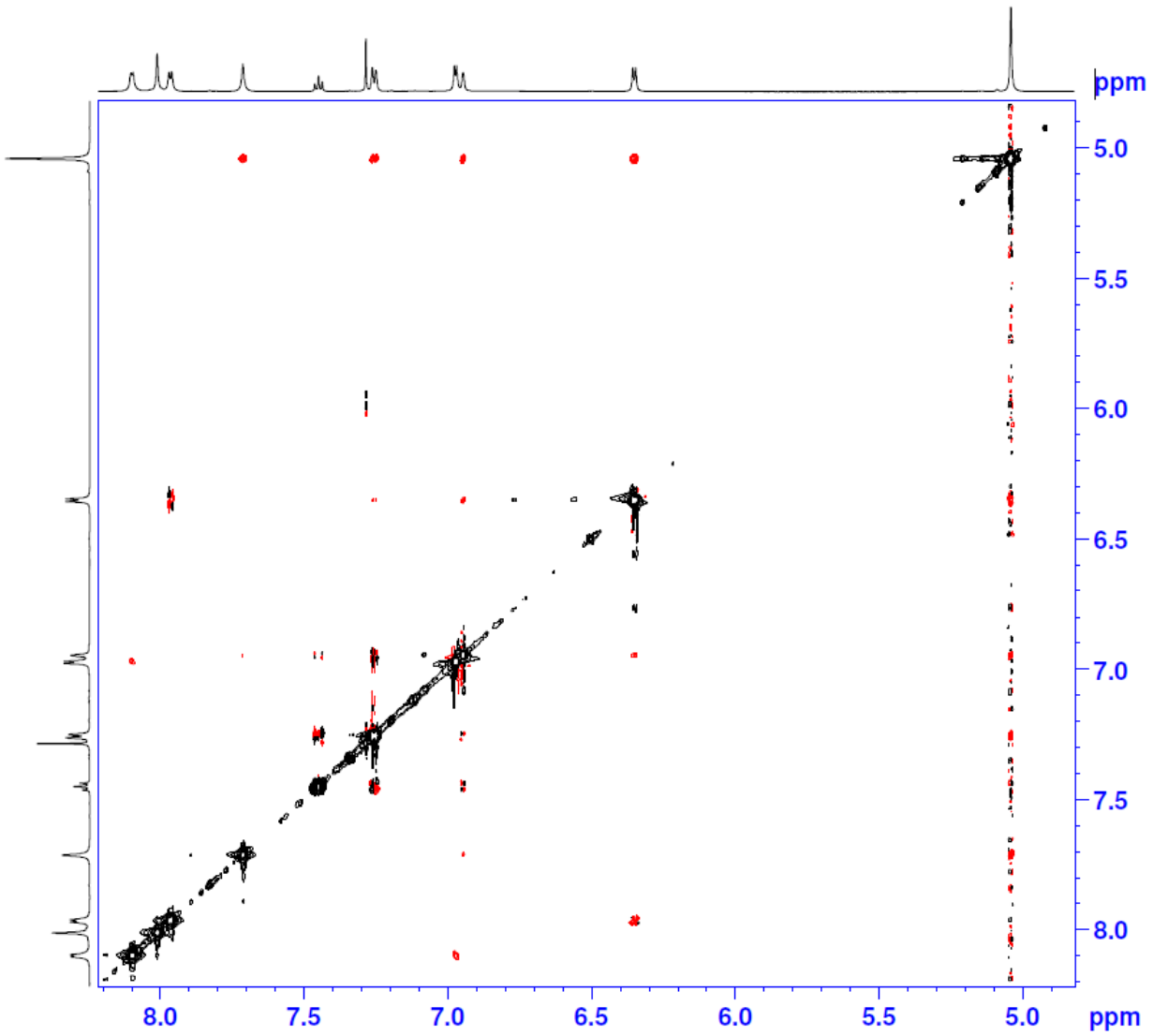



8.102
8.094
8.010
7.969
7.959
7.712
7.461
7.449
7.436
7.261
7.249
6.976
6.968
6.945
6.354
6.345
5.038
8.0
7.5
7.0
6.5
6.0
5.5
5.0
ppm
2.11
1.96
2.03
1.94
1.05
2.20
1.72
1.49
1.94
4.00

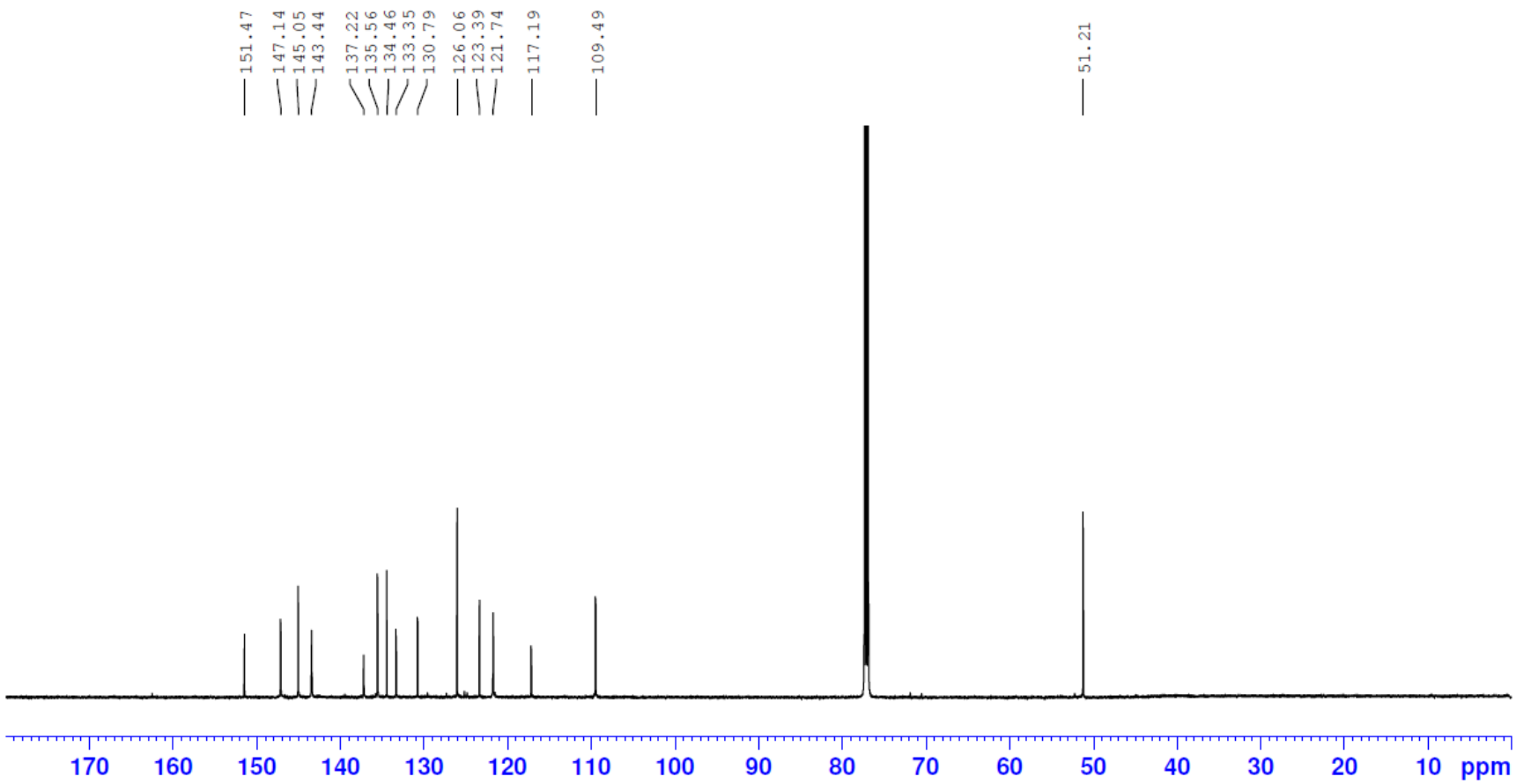
COSY NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)



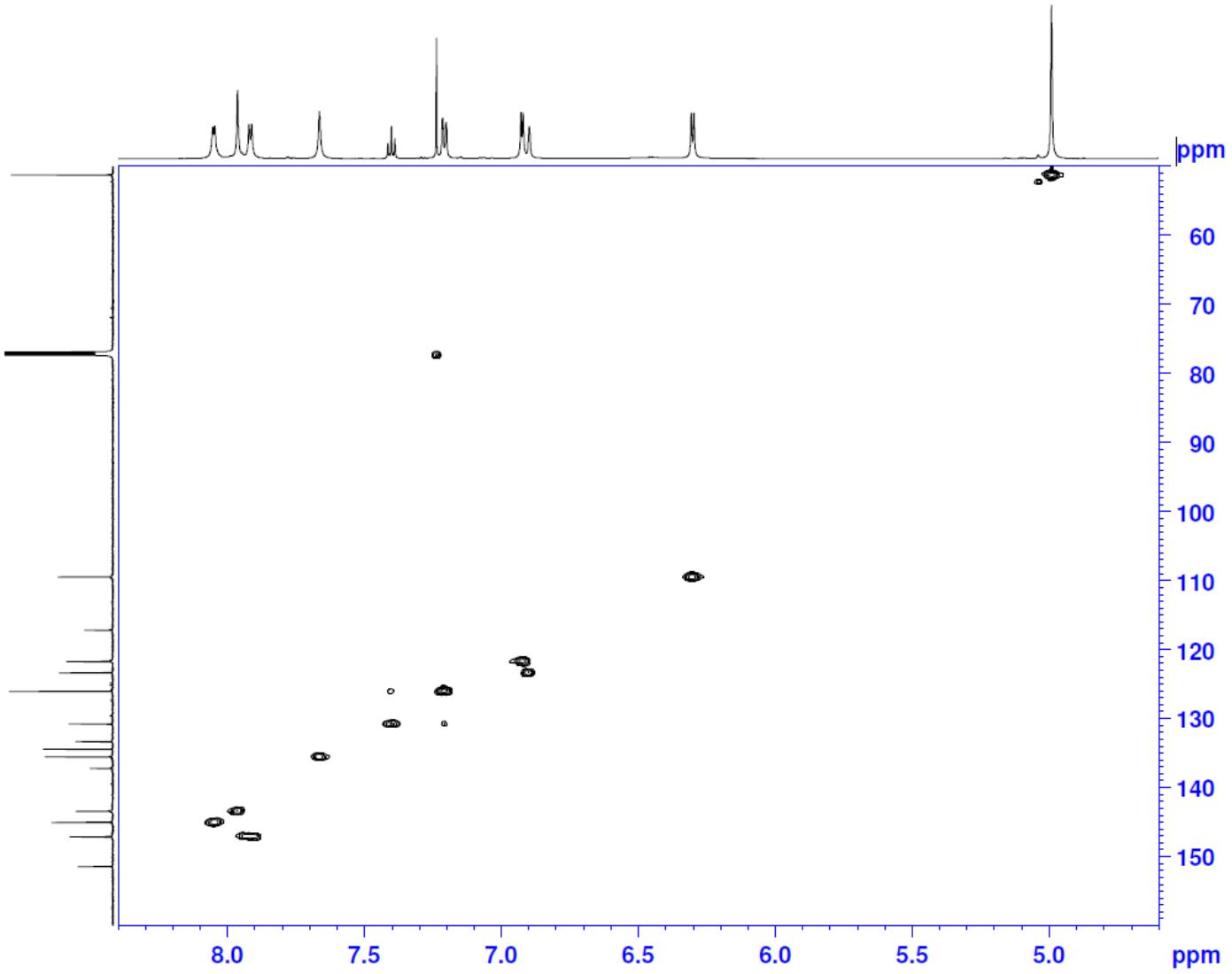
ROESY NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)



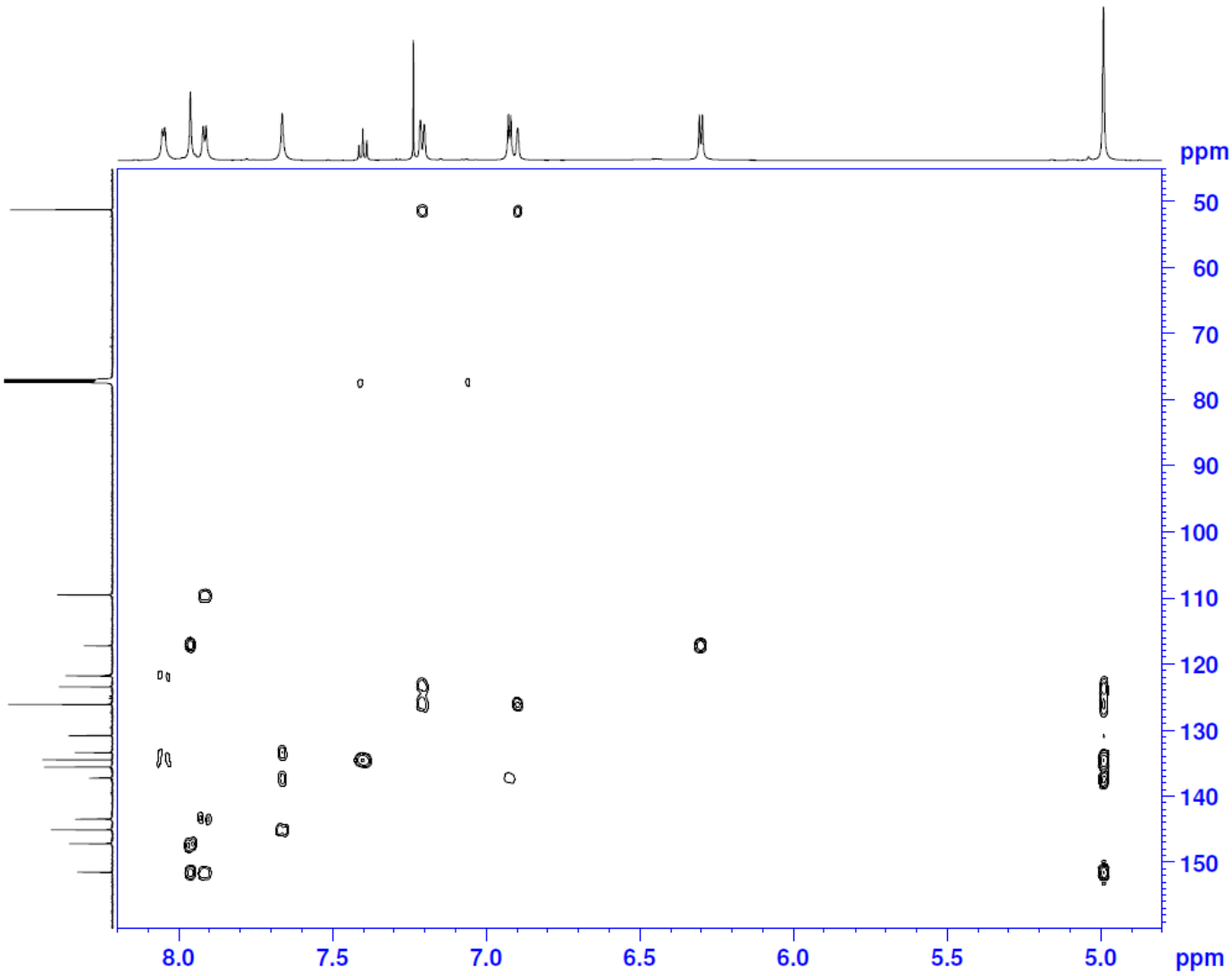
^{13}C NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)

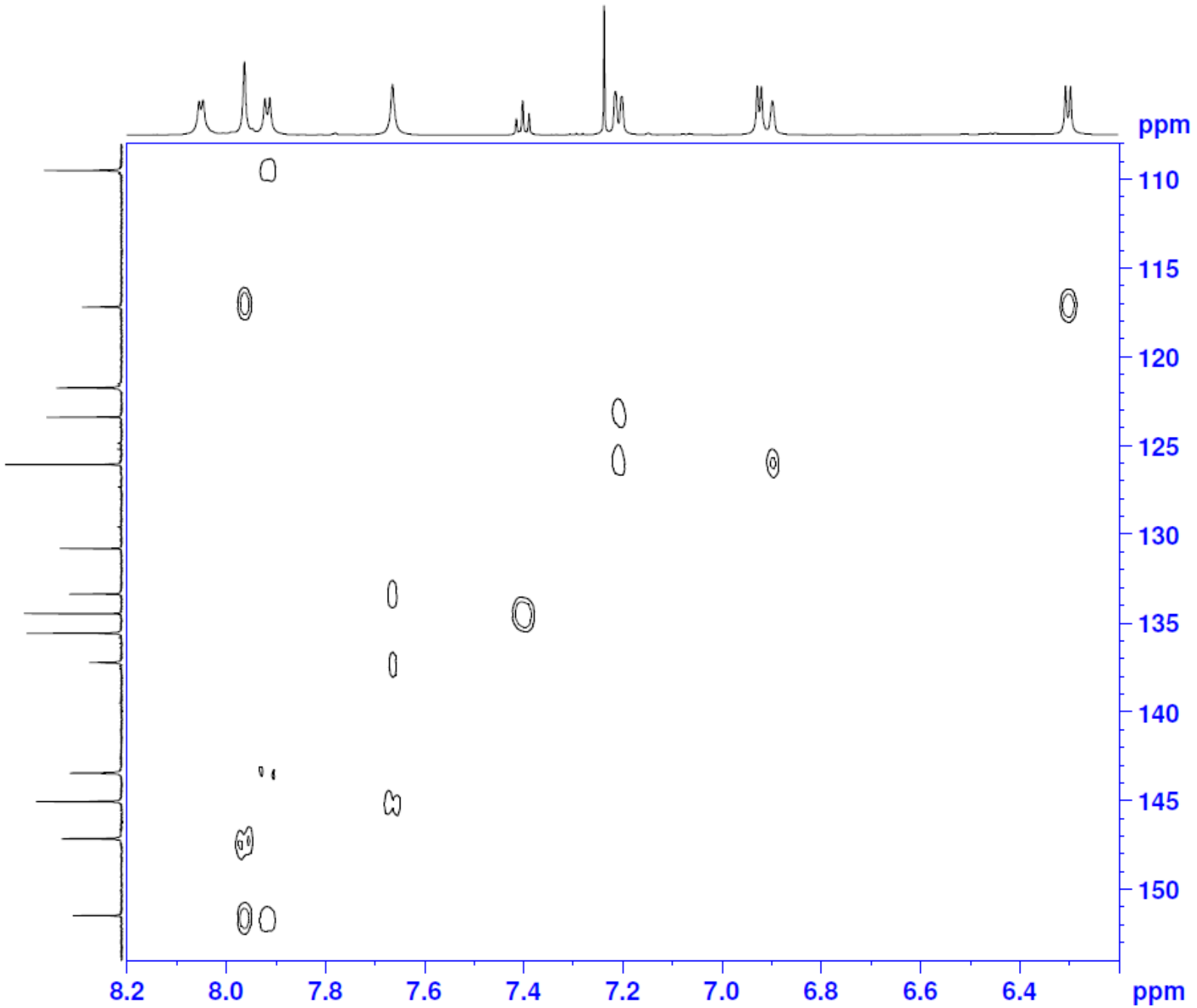


HSQC NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)



HMBC NMR of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)


ppm
50
60
70
80
90
100
110
120
130
140
150
8.0
7.5
7.0
6.5
6.0
5.5
5.0
ppm


ppm
110
115
120
125
130
135
140
145
150
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
ppm

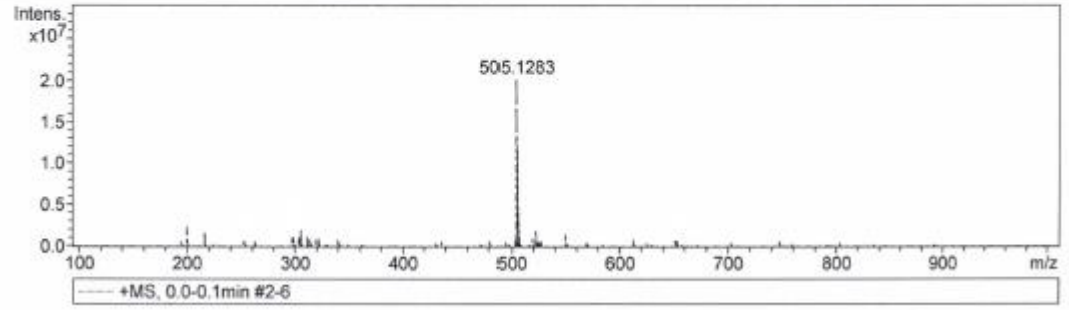
HR MS of 1,3-bis((10*H*-dipyrido[3,4-b:3',4'-e][1,4]thiazin-10-yl)methyl)benzene (**8**)

Analysis Info

Analysis Name	D:\Data\EM-1,6-mk.d	Acquisition Date	1/25/2024 11:34:37 AM
Method	low_mass_positive.m	Operator	KM
Sample Name	cf3	Instrument	impact II 1825265.10082
Comment			

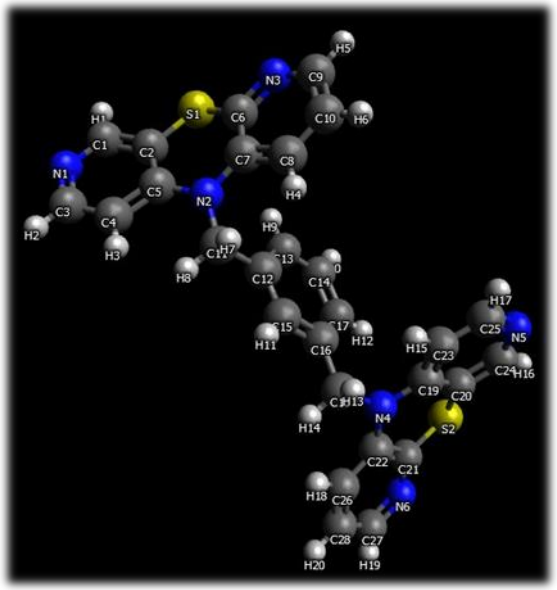
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	100 m/z	Set End Plate Offset	-500 V	Set Dry Gas	3.0 l/min
Scan End	1000 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C



#	m/z	Res.	S/N	I	I %	FWHM
1	505.1283	17250	17139.0	20377596	100.0	0.0293

Mulliken charges and bond length of compound **8**



	Mulliken charges	Mulliken charges with hydrogens summed into heavy atoms
N1	-0.427727	-0.427727
C1	0.015013	0.180829
C2	-0.152921	-0.152921
C3	0.045555	0.198507
C4	-0.191700	-0.056485
C5	0.352397	0.352397
S1	0.226982	0.226982
C6	0.056859	0.056859
C7	0.296058	0.296058
N2	-0.610680	-0.610680
C8	-0.127497	0.020032
N3	-0.476133	-0.476133
C9	0.050436	0.204382
C10	-0.152235	-0.012615
C11	-0.225222	0.128715
C12	0.133503	0.133503
H1	0.188323	
H2	0.165614	
C13	-0.163259	-0.006837
C14	-0.134315	0.010534
C15	-0.232908	-0.120546
C16	0.135397	0.135397
C17	-0.162392	-0.007165
C18	-0.226010	0.128266
N4	-0.610889	-0.610889
H3	0.186638	
H4	0.167638	
C19	0.332274	0.332274
C20	-0.154042	-0.154042
S2	0.227947	0.227947
C21	0.057054	0.057054
C22	0.316497	0.316497
C23	-0.178117	-0.040481
C24	0.013605	0.178961
N5	-0.428085	-0.428085
C25	0.044249	0.196072
C26	-0.141868	0.003138
N6	-0.473241	-0.473241
C27	0.050173	0.203738
C28	-0.149823	-0.010295
H5	0.139527	
H6	0.145007	
H7	0.153565	
H8	0.137636	
H9	0.151822	

H10	0.165356	
H11	0.156421	
H12	0.144849	
H13	0.155226	
H14	0.165816	
H15	0.152951	
H16	0.135215	
H17	0.153946	
H18	0.139621	
H19	0.147529	
H20	0.112362	

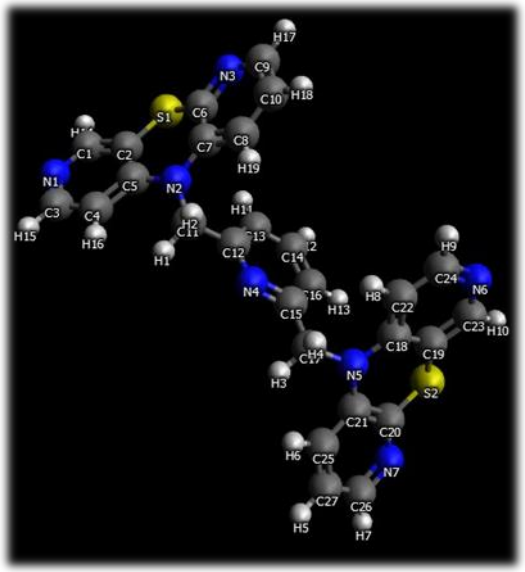
	Bond length
H12-C14	1.082536
S2-C21	1.777657
S2-C20	1.780656
N6-C27	1.352689
N6-C21	1.36038
H7-C27	1.081798
H10-C24	1.082544
H13-C17	1.080121
C27-C28	1.384542
C14-C17	1.394971
C14-C13	1.394959
C21-C22	1.41607
H14-C1	1.082619
H11-C13	1.080132
S1-C2	1.78099
S1-C6	1.77774
C17-C16	1.408731
C24-C20	1.401356

C24-N5	1.354548
C20-C19	1.411702
C13-C12	1.408718
C1-C2	1.401252
C1-N1	1.353435
C28-H5	1.082727
C28-C26	1.393256
C22-C26	1.422934
C22-N4	1.451335
C2-C5	1.41469
N1-C3	1.352089
C6-N3	1.360608
C6-C7	1.412828
C26-H6	1.075085
N5-C25	1.353056
N3-C9	1.353974
C19-N4	1.450773
C19-C23	1.420065
N4-C18	1.474973
C16-C18	1.520583
C16-C15	1.405454
C5-N2	1.451097
C5-C4	1.422406
C12-C15	1.405445
C12-C11	1.520558
C3-C4	1.39444
C3-H15	1.082175
H17-C9	1.081773
C9-C10	1.386227
C7-N2	1.450725
C7-C8	1.420274
N2-C11	1.47486

C18-H3	1.098364
C18-H4	1.109715
C4-H16	1.075286
C25-C23	1.393811
C25-H9	1.082018
C23-H8	1.078169
C15-H20	1.084335
C11-H1	1.098566
C11-H2	1.109779
C10-C8	1.392768
C10-H18	1.082556

C8-H19	1.078175

Mulliken charges and bond length of isomer with lutidine linker of compound **8**



	Mulliken charges	Mulliken charges with hydrogens summed into heavy atoms
N1	-0.427145	-0.427145
C1	0.015195	0.181291
C2	-0.153020	-0.153020
C3	0.045704	0.200081
C4	-0.192632	-0.052975
C5	0.351763	0.351763
S1	0.226860	0.226860
C6	0.056789	0.056789
C7	0.294820	0.294820
N2	-0.610996	-0.610996
C8	-0.133740	0.019396
N3	-0.475664	-0.475664
C9	0.050500	0.205199
C10	-0.152336	-0.011418
C11	0.209580	0.166439
C12	0.281152	0.281152
H1	0.197630	
H2	0.178389	
C13	-0.160940	0.001179
C14	-0.103189	0.051315
N4	-0.559045	-0.559045
C15	0.282848	0.282848
C16	-0.160077	0.000931
C17	-0.210322	0.166048
N5	-0.611086	-0.611086
H3	0.195979	
H4	0.180390	
C18	0.330886	0.330886
C19	-0.154002	-0.154002
S2	0.227613	0.227613
C20	0.057070	0.057070
C21	0.315746	0.315746
C22	-0.184507	-0.041120
C23	0.013551	0.179562
N6	-0.427495	-0.427495
C24	0.044361	0.197463
C25	-0.142581	0.006757
N7	-0.473135	-0.473135
C26	0.050528	0.204771
C27	-0.149863	-0.008877
H5	0.140986	
H6	0.149338	
H7	0.154243	
H8	0.143386	

H9	0.153102	
H10	0.166011	
H11	0.162118	
H12	0.154504	
H13	0.161008	
H14	0.166096	
H15	0.154376	
H16	0.139657	
H17	0.154698	
H18	0.140919	
H19	0.153136	

	Bond length
H12-C14	1.082487
S2-C20	1.777696
S2-C19	1.780705
N7-C26	1.352717
N7-C20	1.360384
H7-C26	1.0818
H13-C16	1.080239
H10-C23	1.082531
C14-C16	1.393761
C14-C13	1.393762
C26-C27	1.384579
C20-C21	1.41603
H14-C1	1.082615
H11-C13	1.080244
S1-C2	1.781004
S1-C6	1.777754
C16-C15	1.407115
C19-C23	1.401352
C19-C18	1.411706
C23-N6	1.354565

C13-C12	1.407103
C1-C2	1.401258
C1-N1	1.353448
C27-H5	1.082731
C27-C25	1.39325
C21-C25	1.422866
C21-N5	1.451259
C2-C5	1.414673
N1-C3	1.352104
C6-N3	1.360615
C6-C7	1.412843
C25-H6	1.07513
N3-C9	1.353976
N6-C24	1.353061
C18-N5	1.450701
C18-C22	1.420006
N5-C17	1.474971
C15-C17	1.515774
C15-N4	1.361722
C5-N2	1.45103
C5-C4	1.422356
C12-N4	1.361705
C12-C11	1.515743
C3-C4	1.394443
C3-H15	1.082173
C7-N2	1.450676
C7-C8	1.420237
N2-C11	1.474857
H17-C9	1.081781
C9-C10	1.386228
C4-H16	1.075307
C17-H3	1.098097

C17-H4	1.109297
C24-C22	1.393837
C24-H9	1.082016
C22-H8	1.078162
C11-H1	1.098285
C11-H2	1.109352
C8-C10	1.392785

C8-H19	1.078165
C10-H18	1.082559