Electronic Supplementary Material (ESI) for New Journal of Chemistry.
This journal is © The Royal Society of Chemistry and the Centre National de la Recherche Scientifique 2023

Supportive Data

A synthesis and spectral characterization of 4-methylthiazole derivatives: DFT approach and biological activities

Pakkirisamy Sivakumar[1], Sarangapani Bharanidharan[2], Rajaram Rajamohan[3*], Balasubramaniyan Anandhan[4], Thangavelu Sumathi[4], Subramaniyan Kamatchi[4*]

[1] Department of Chemistry, Saraswathy College of Engineering and Technology, Olakkur, Tindivanam- 604 305, Tamil Nadu, India.

[2] Department of Physics, Panimalar Engineering College, Chennai - 600 123, Tamil Nadu, India.

[3*] Organic Materials Synthesis Lab, School of Chemical Engineering, Yeungnam University, Gyeongsan 38541, Republic of Korea.

[4*] PG & Research Department of Chemistry, Government Arts College, Chidambaram - 608 102, Tamil Nadu, India.

Correspondance :rajmohanau@yu.ac.kr, drskgaccdmchem@gmail.com

Anti-inflammation activity (albumin denaturation method)

To evaluate the anti-inflammatory activity of the synthesized molecules and standard diclofenac sodium, a modified albumin denaturation inhibition method was employed. The standard drug and MTs were diluted with phosphate buffer and dissolved in a small amount of DMF, with DMF present at a final concentration of less than 2.5% in all solutions. In the test solution (2.5 mL), different amounts of the drug were combined with 1 mL of a 1 mM Bovine Serum Albumin (BSA) solution in phosphate buffer. The mixture was then incubated at 37.0 °C for 10 minutes. Denaturation was induced by placing the reaction mixture in a water bath maintained at 70.0 °C for 10 minutes. The resulting turbidity was measured at 660.0 nm after cooling. The percentage of denaturation inhibition was determined by comparing it to the control, which did not have any drug added. The percentage inhibition of denaturation was calculated using the provided method.

$$\% \text{ of Inhibition} = 100 \times [A_c\text{-}A_t/A_c]$$

A_t: Absorbance of test

A_c: Absorbance of control

Anti-diabetic activity (α-amylase inhibition method)

The anti-diabetic activity of the synthesized molecules, MTs, was evaluated using the α-amylase inhibition technique. A solution of α-amylase (0.2%) was treated with samples (in 1.5 mL), standard drug acarbose, or without any treatment for 10 minutes at 25.0 °C. This assessment was performed in a 0.2M phosphate buffer solution with a pH of 6.9. After the pre-incubation, a 1% starch solution (0.5 mL) was added, and the reaction mixture was incubated for 30 minutes at 25.0 °C. To stop the enzymatic reaction, a coloring reagent called DNSA reagent (0.5 mL) was added, and the mixture was incubated for approximately 90 minutes in a boiling water bath. The absorbance of the samples was measured at 540.0 nm using a UV-Visible spectrophotometer. Prior to measurement, the samples were diluted with 2.5 mL of distilled water and allowed to settle to room temperature. The absorbance of the samples was compared to the absorbance of the control experiment. By applying the provided formula, the percentage of inhibition was calculated based on the absorbance values obtained.

$$\% \text{ of Inhibition} = 100 \times [A_c\text{-}A_t/A_c]$$

A_t: Absorbance of test

A_c: Absorbance of control

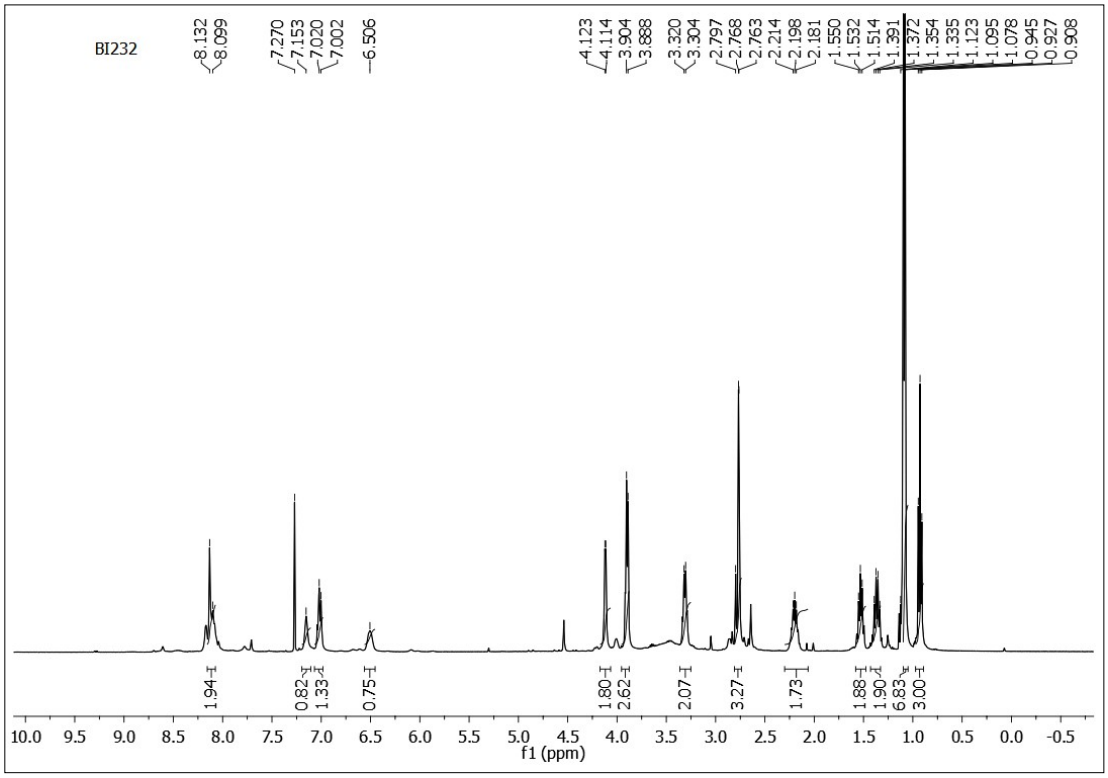

Figure S1. [1]H NMR spectrum of compound **6**

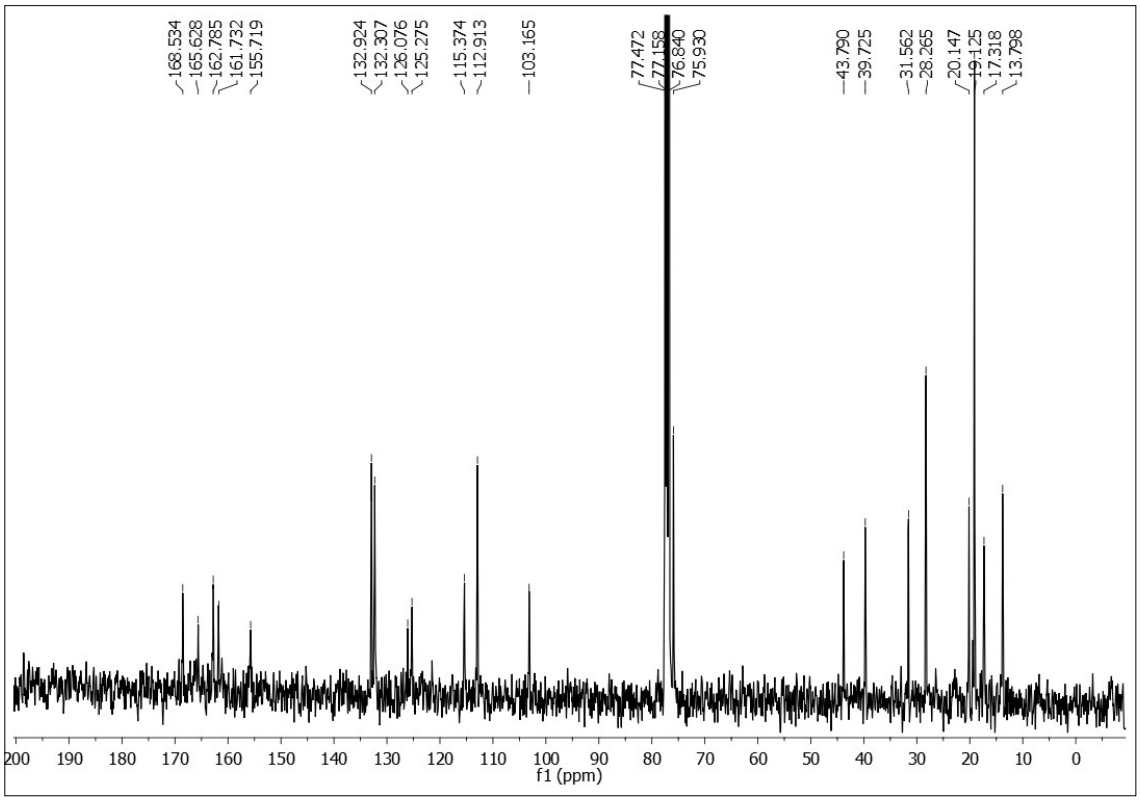

Figure S2.[13]C NMR spectrum of compound **6**

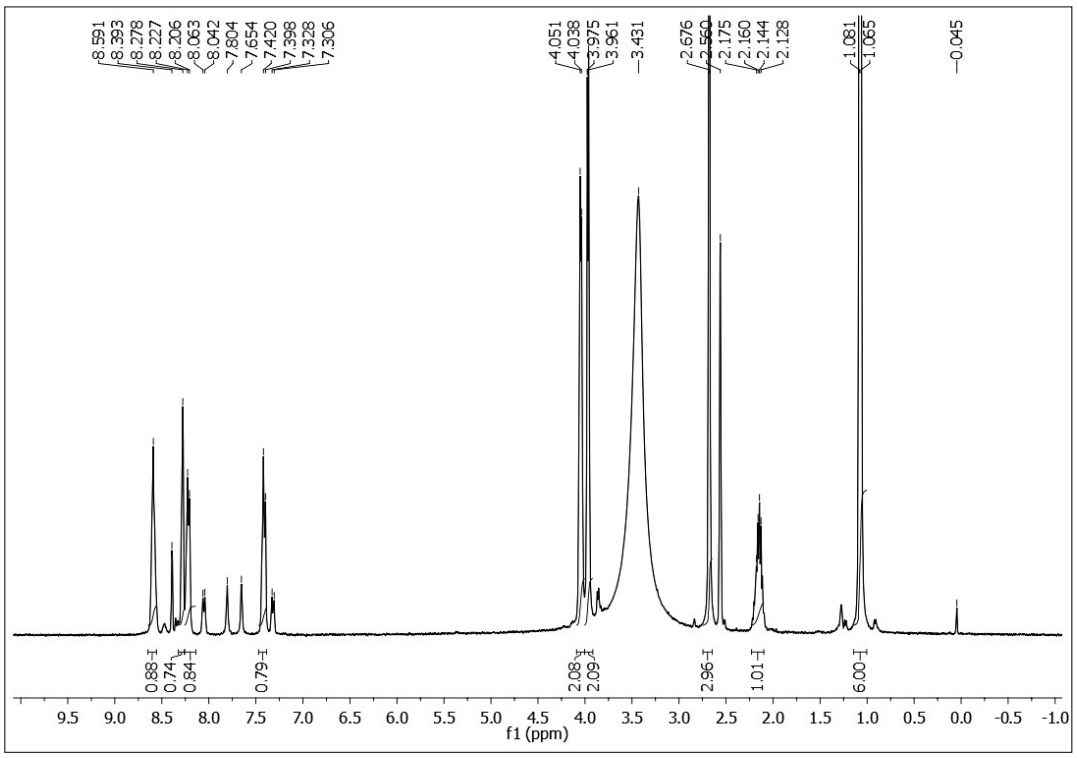

Figure S3. ^{1}H NMR spectrum of compound **7**

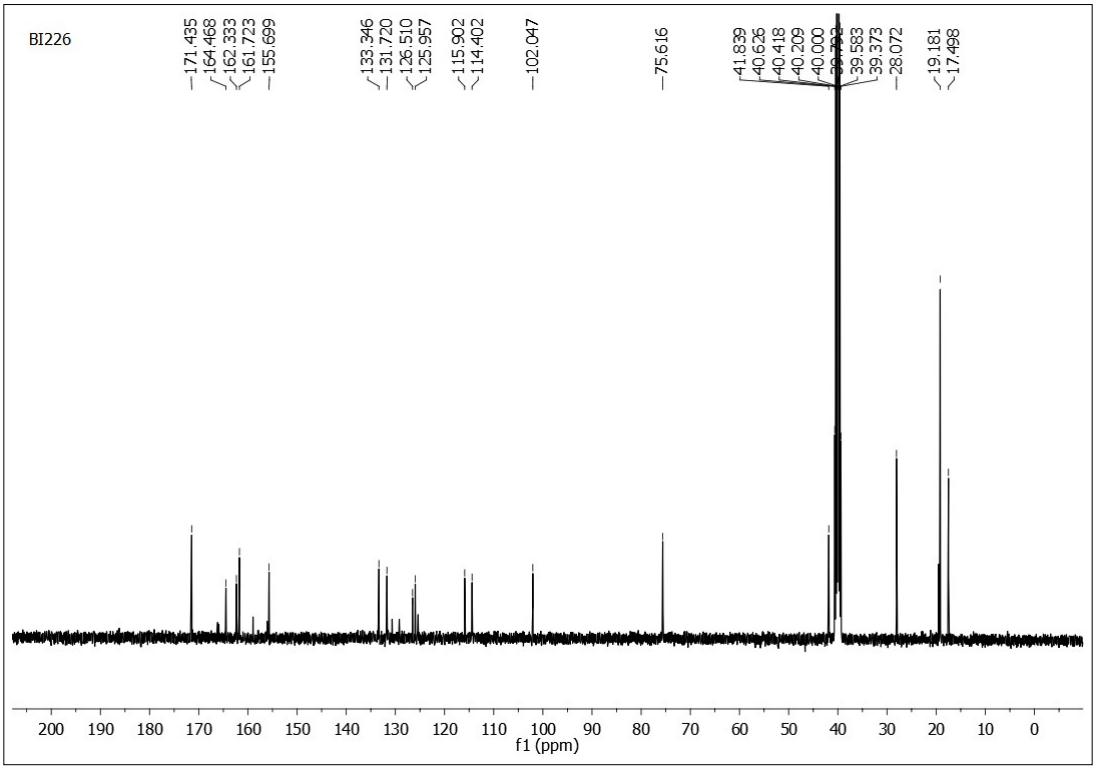

Figure S4. ^{13}C NMR spectrum of compound **7**

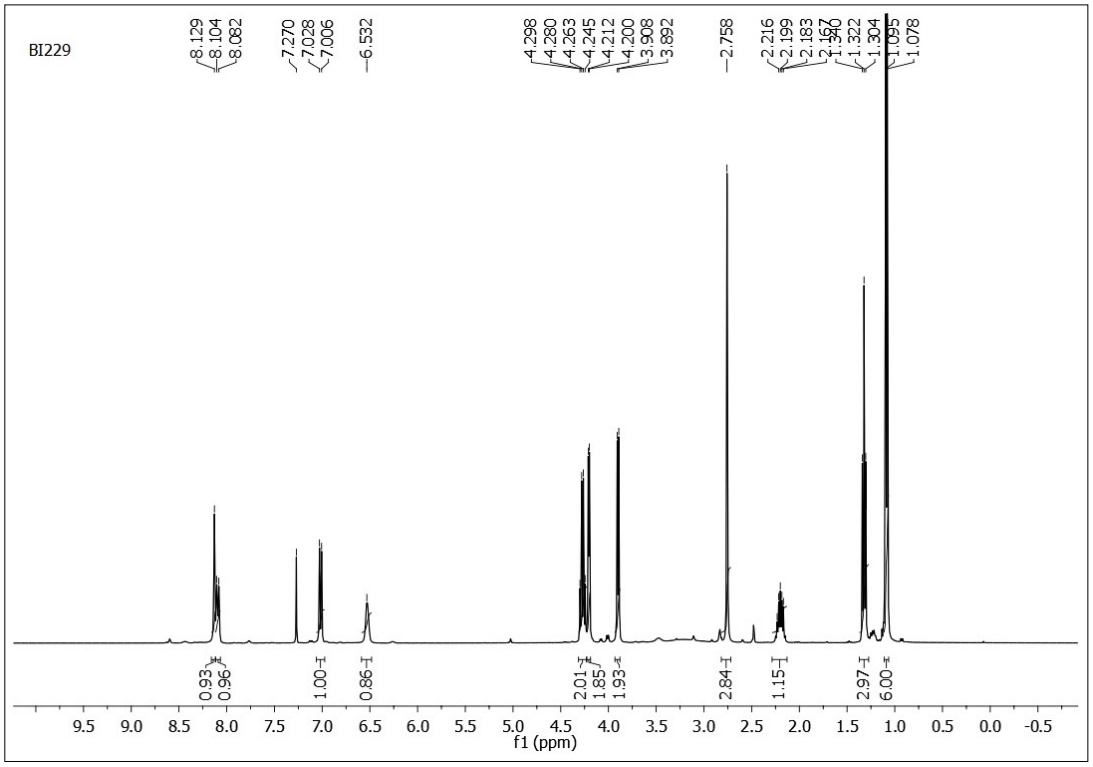

Figure S5. 1H NMR spectrum of compound **9**

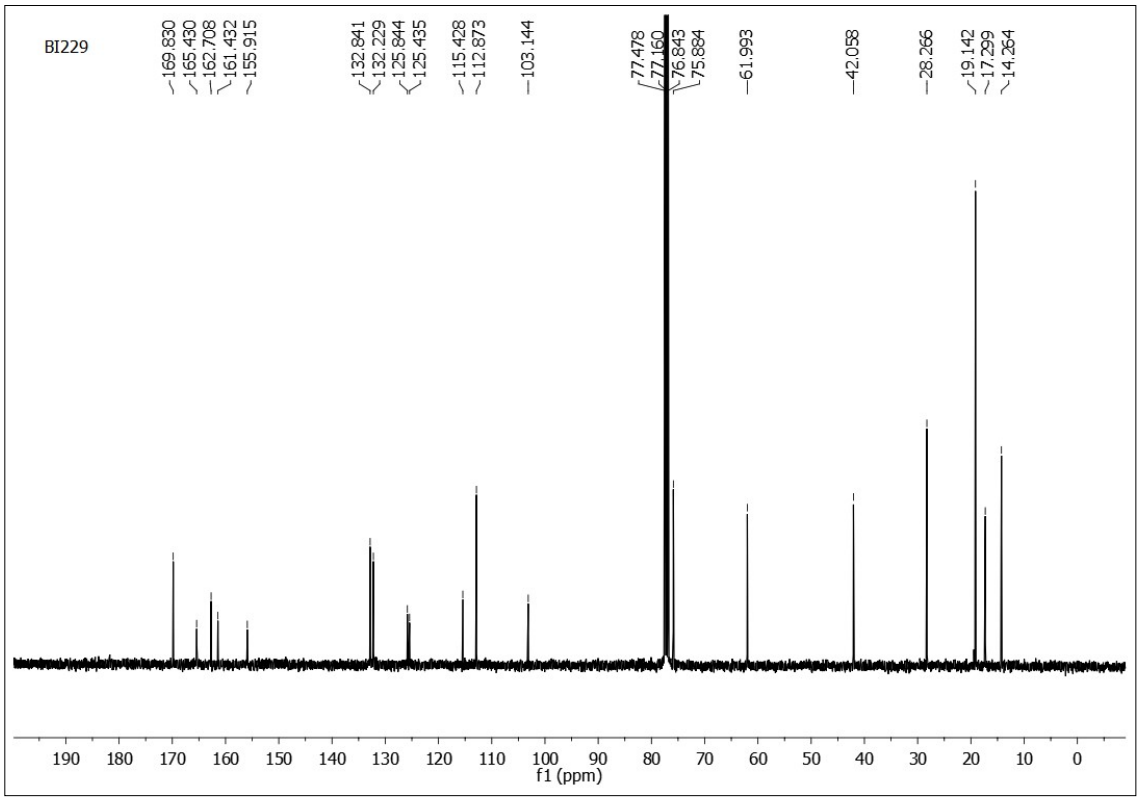

Figure S6. ^{13}C NMR spectrum of compound **9**

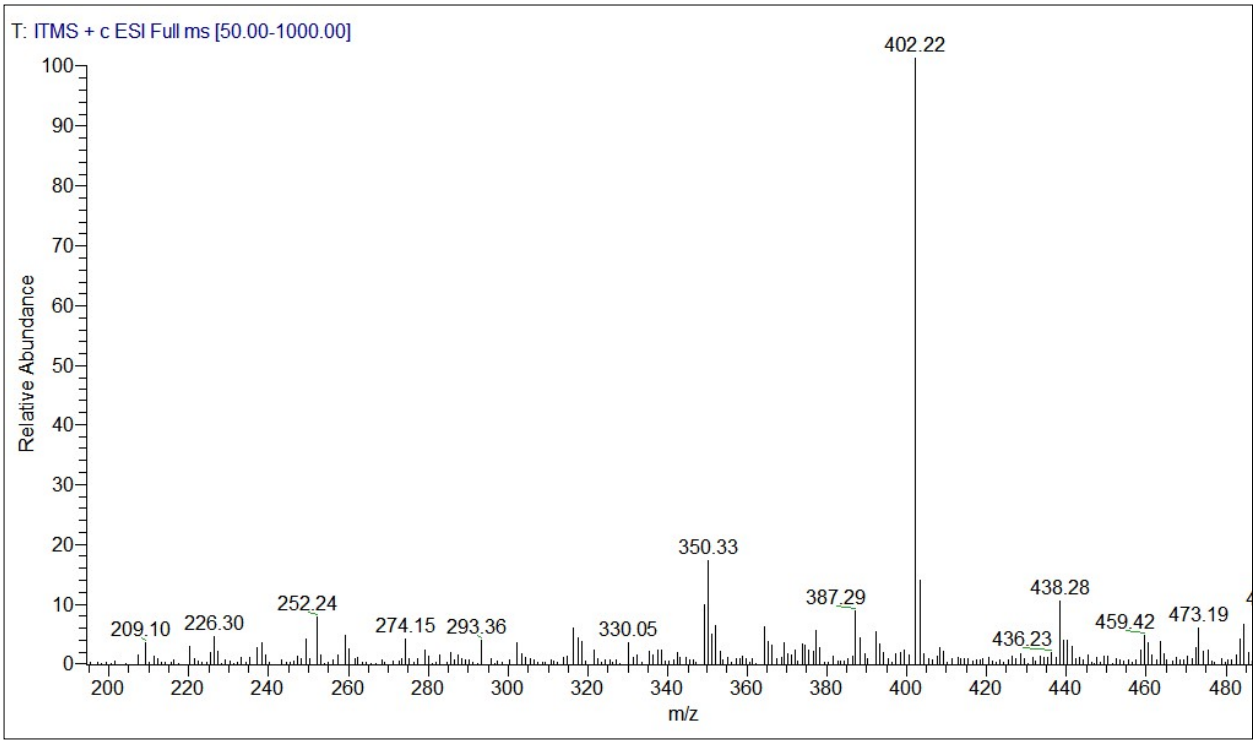

Figure S7. ESI-Mass spectrum of compound **6**

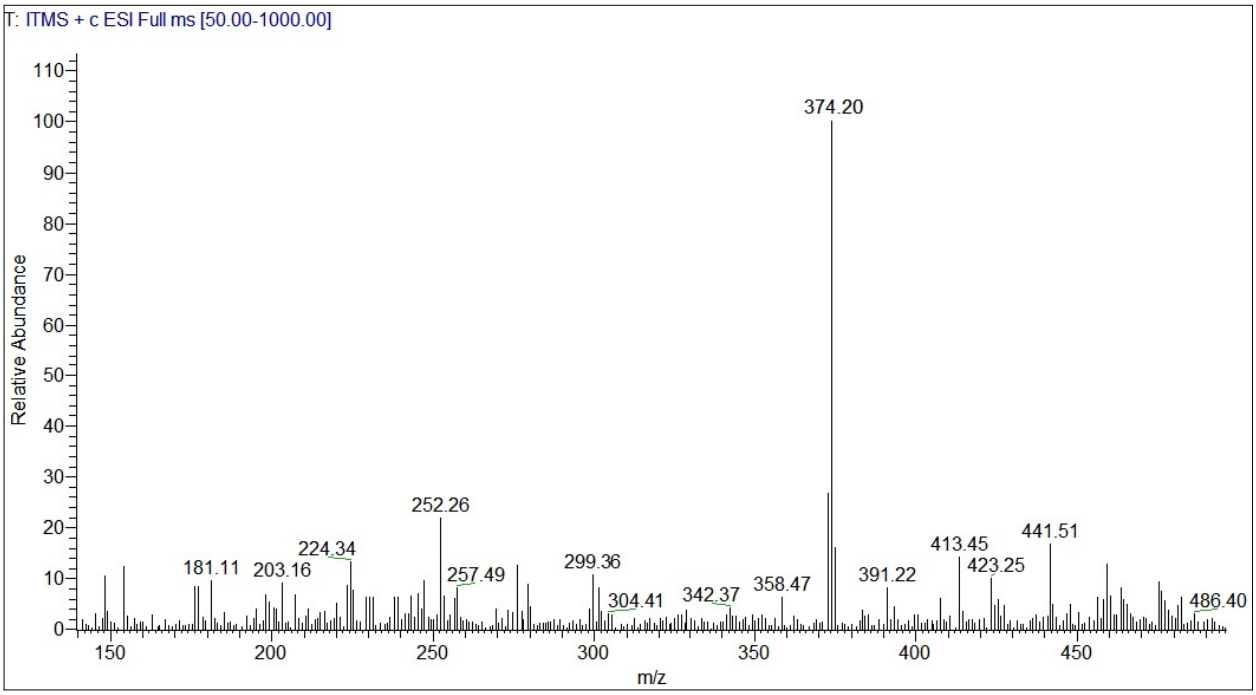

Figure S8. ESI-Mass spectrum of compound **7**

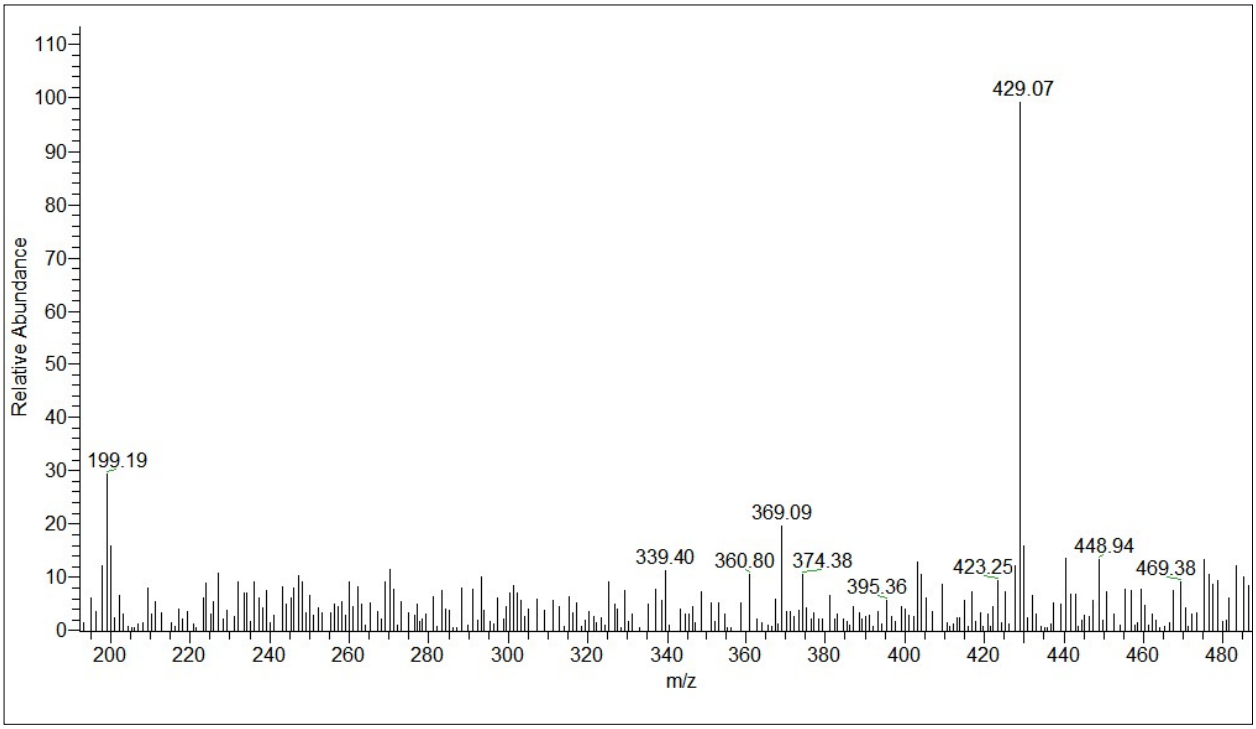

Figure S9. ESI-Mass spectrum of compound **9**

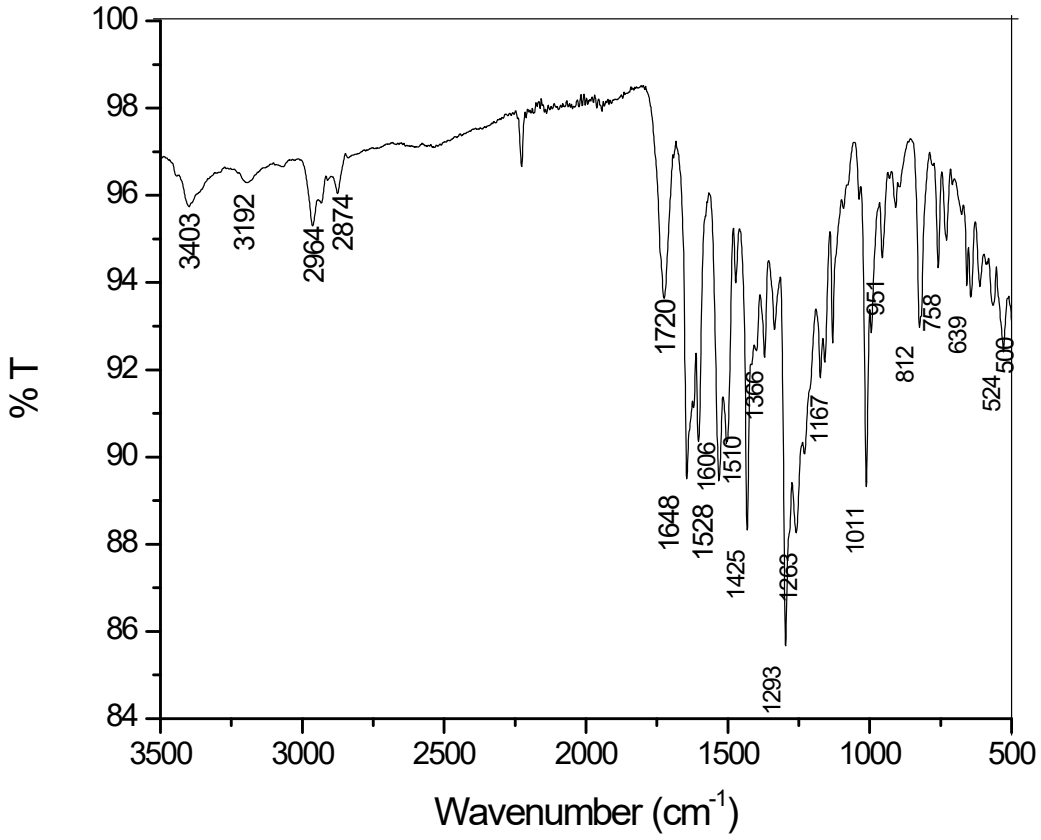

Figure S10. FT-IR spectrum of compound **6**

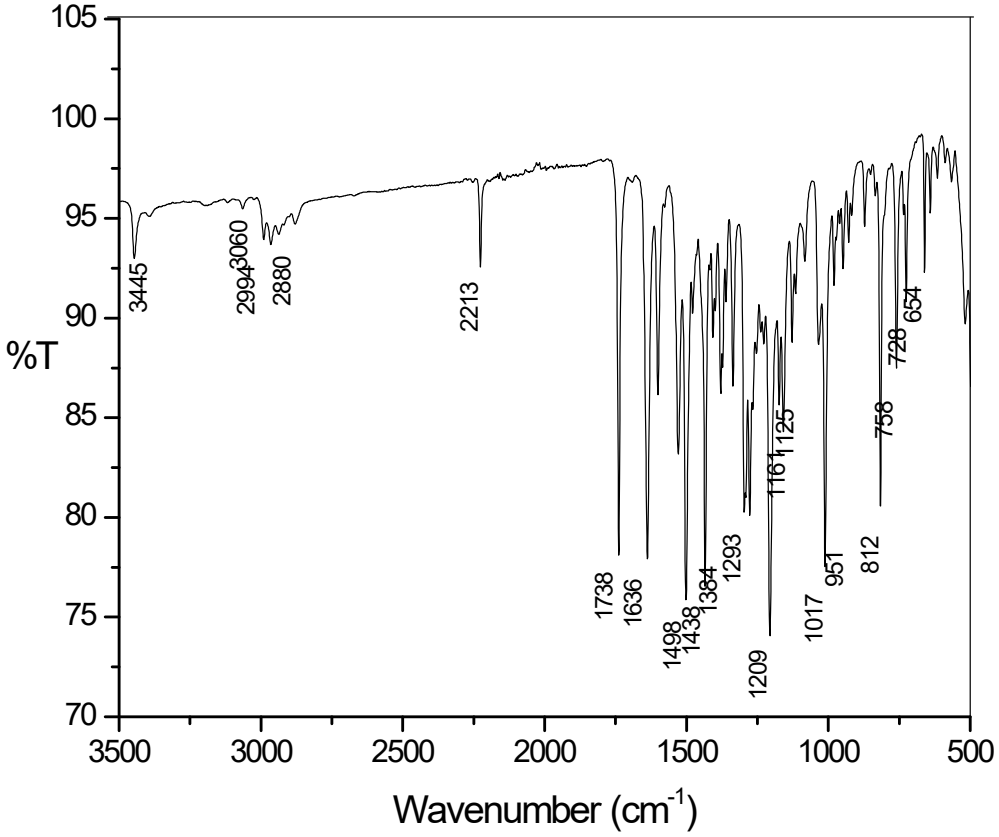

Figure S11. FT-IR spectrum of compound **7**

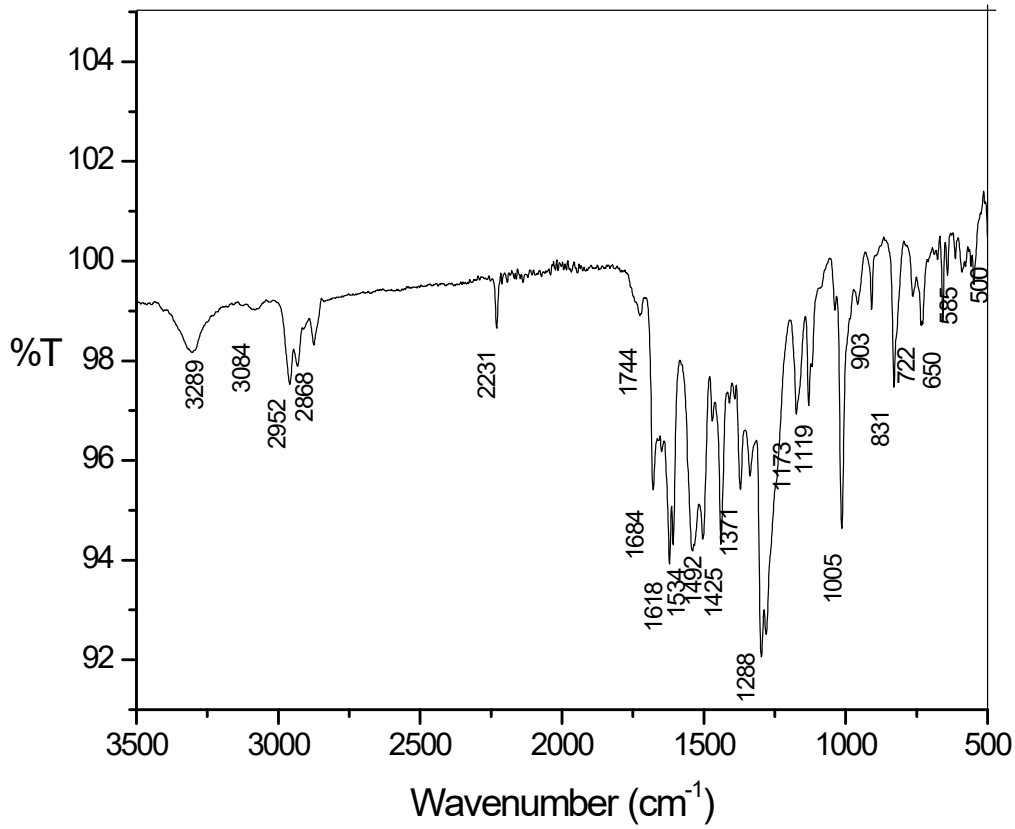

Figure S12. FT-IR spectra of compound **9**.

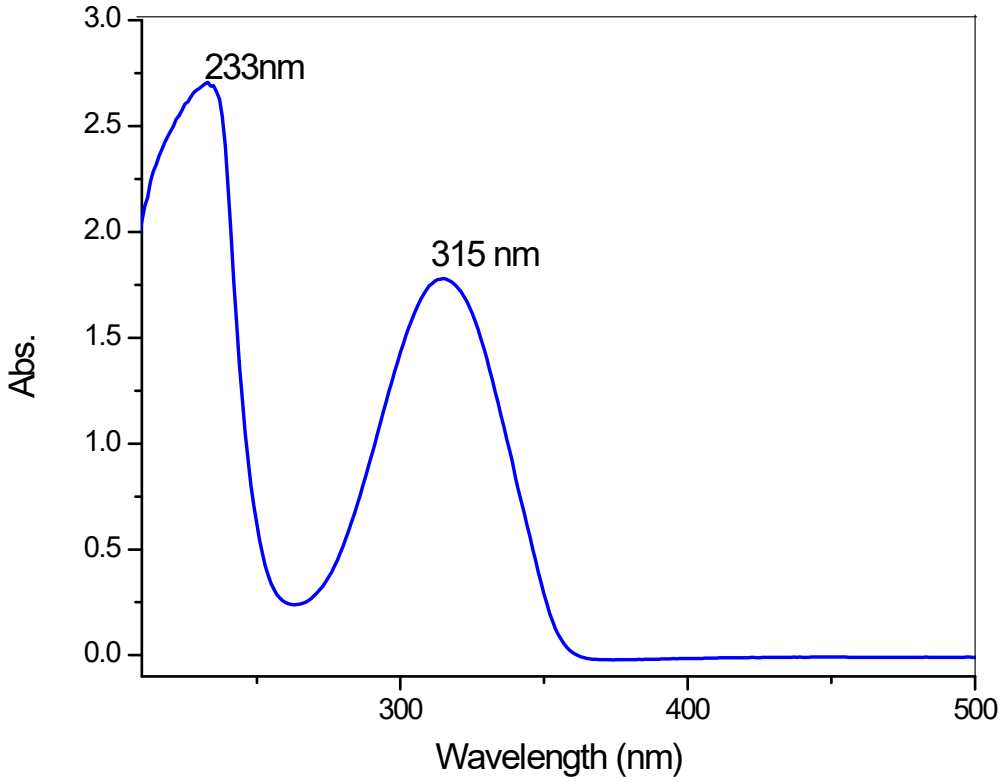

Figure S13. The UV-Visible spectrum of compound **6**

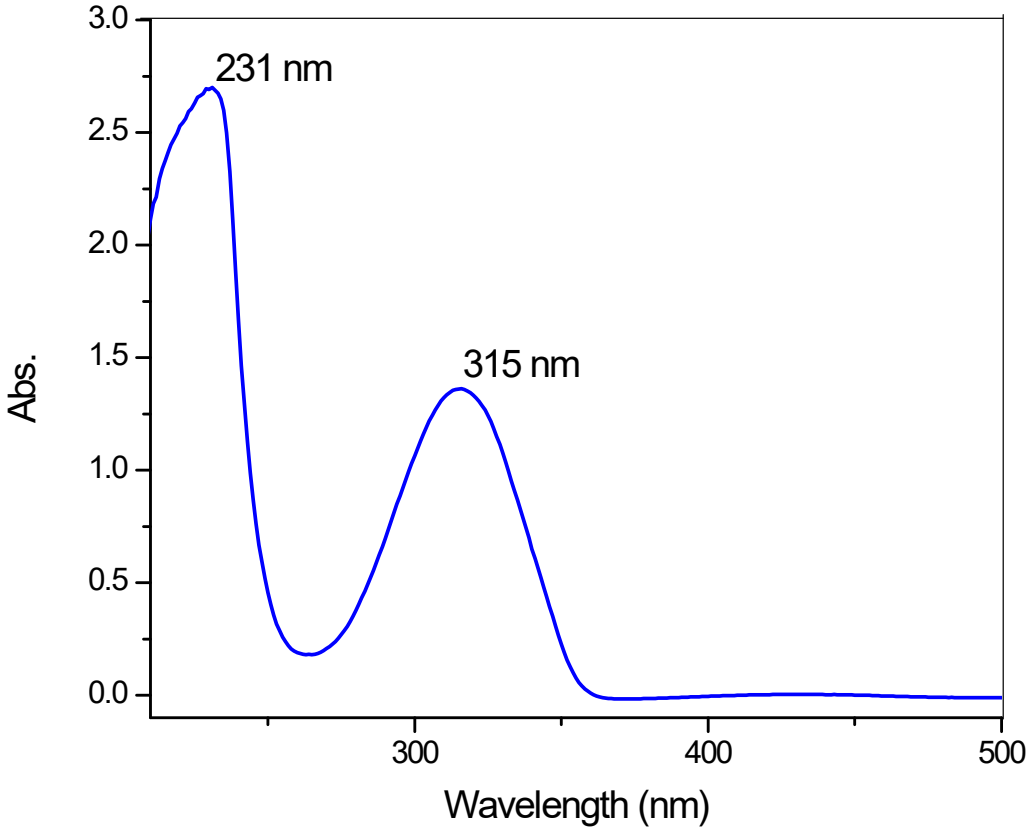

Figure S14. The UV-Visible spectrum of compound **7**

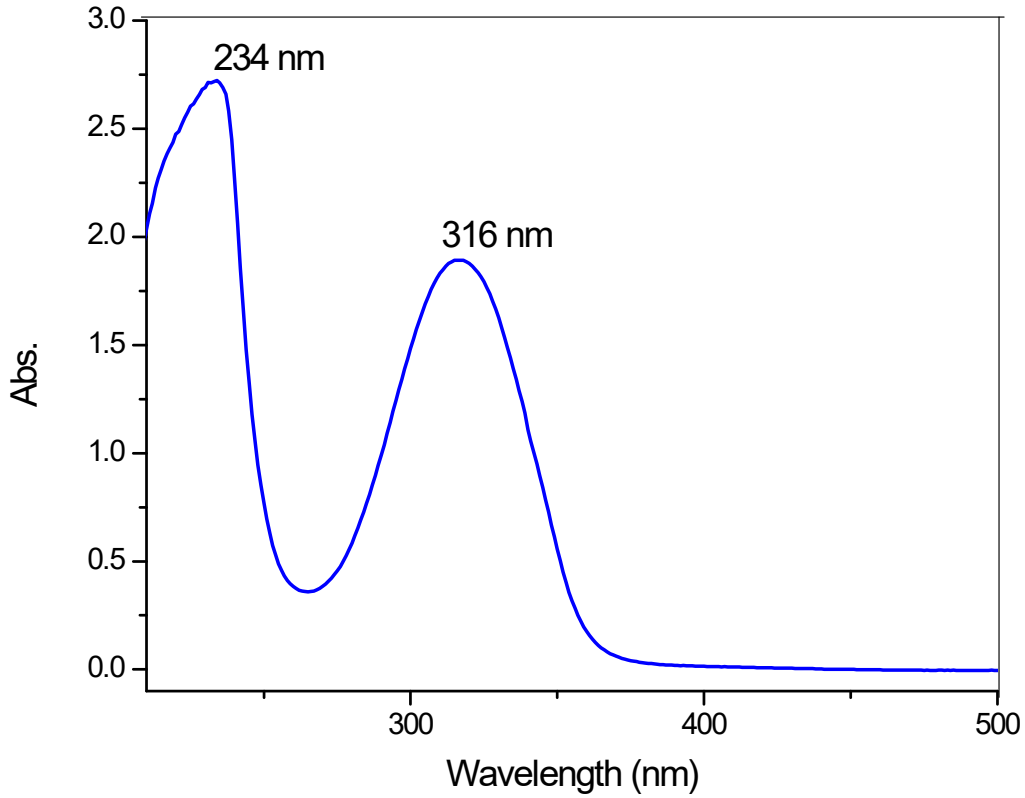

Figure S15. The UV-Visible spectrum of compound **9**

Table S1. The optimized bond parameters of the compounds **6, 7,** and **9**

Compound 6			
Bond Lengths (Å)	**DFT**	**Bond Lengths (Å)**	**DFT**
R(1,2)	1.3989	R(16,17)	1.368
R(1,6)	1.4122	R(16,19)	1.208
R(1,29)	1.0988	R(17,18)	1.4665
R(2,3)	1.4191	R(18,20)	1.513
R(2,7)	1.4495	R(18,35)	1.1041
R(3,4)	1.3787	R(18,36)	1.1057
R(3,30)	1.0939	R(20,37)	1.0965
R(4,5)	1.4234	R(20,38)	1.0984
R(4,31)	1.0914	R(20,39)	1.1008
R(5,6)	1.4127	R(21,40)	1.109
R(5,22)	1.3517	R(21,41)	1.1026
R(6,27)	1.4233	R(21,42)	1.1026
R(7,8)	1.322	R(22,23)	1.4694
R(7,11)	1.7802	R(23,24)	1.5403
R(8,9)	1.4142	R(23,43)	1.1013
R(9,10)	1.3832	R(23,44)	1.1024
R(9,21)	1.4752	R(24,25)	1.5298
R(10,11)	1.7306	R(24,26)	1.5302
R(10,12)	1.4613	R(24,45)	1.1225
R(12,13)	1.411	R(25,46)	1.096
R(12,14)	1.2227	R(25,47)	1.0975
R(13,15)	1.4723	R(25,48)	1.0957
R(13,32)	1.0212	R(26,49)	1.0971
R(14,40)	2.2555	R(26,50)	1.096
R(15,16)	1.5193	R(26,51)	1.0967
R(15,33)	1.1173	R(27,28)	1.1578
Bond Angles (º)	**DFT**	**Bond Angles (º)**	**DFT**
A(2,1,6)	121.2801	A(16,17,18)	118.27
A(2,1,29)	119.6232	A(17,18,20)	109.745
A(6,1,29)	119.0967	A(17,18,35)	108.435
A(1,2,3)	119.376	A(17,18,36)	100.528
A(1,2,7)	119.4228	A(20,18,35)	112.843
A(3,2,7)	121.1999	A(20,18,36)	113.408
A(2,3,4)	120.3819	A(35,18,36)	111.084
A(2,3,30)	120.2767	A(18,20,37)	111.533
A(4,3,30)	119.3392	A(18,20,38)	111.586
A(3,4,5)	120.2499	A(18,20,39)	111.307

A(3,4,31)	121.6081	A(37,20,38)	107.715
A(5,4,31)	118.1418	A(37,20,39)	107.449
A(4,5,6)	120.1866	A(38,20,39)	107.018
A(4,5,22)	110.9496	A(9,21,40)	111.597
A(6,5,22)	128.8636	A(9,21,41)	111.853
A(1,6,5)	118.5221	A(9,21,42)	111.398
A(1,6,27)	116.9743	A(40,21,41)	107.68
A(5,6,27)	124.5035	A(40,21,42)	107.566
A(2,7,8)	126.8695	A(41,21,42)	106.483
A(2,7,11)	120.977	A(5,22,23)	121.668
A(8,7,11)	112.1391	A(22,23,24)	102.255
A(7,8,9)	112.7726	A(22,23,43)	108.787
A(8,9,10)	114.2201	A(22,23,44)	108.03
A(8,9,21)	118.6231	A(24,23,43)	113.156
A(10,9,21)	127.154	A(24,23,44)	112.788
A(9,10,11)	110.3362	A(43,23,44)	111.255
A(9,10,12)	126.7593	A(23,24,25)	110.858
A(11,10,12)	122.8791	A(23,24,26)	109.222
A(7,11,10)	90.5088	A(23,24,45)	107.609
A(10,12,13)	115.6128	A(25,24,26)	111.477
A(10,12,14)	124.2235	A(25,24,45)	108.473
A(13,12,14)	120.0958	A(26,24,45)	109.105
A(12,13,15)	118.622	A(24,25,46)	111.262
A(12,13,32)	121.5628	A(24,25,47)	111.005
A(15,13,32)	114.9075	A(24,25,48)	112.178
A(13,15,16)	110.8592	A(46,25,47)	107.393
A(13,15,33)	109.6882	A(46,25,48)	107.18
A(13,15,34)	110.5299	A(47,25,48)	107.589
A(16,15,33)	109.3722	A(24,26,49)	110.898
A(16,15,34)	110.2719	A(24,26,50)	112.005
A(33,15,34)	105.9976	A(24,26,51)	112.047
A(15,16,17)	108.4074	A(49,26,50)	107.101
A(15,16,19)	128.1729	A(49,26,51)	106.909
A(17,16,19)	123.3899	A(50,26,51)	107.601
Dihedral Angles (º)	**DFT**	**Dihedral Angles (º)**	**DFT**
D(6,1,2,3)	-0.721	D(12,13,15,16)	110.998
D(6,1,2,7)	179.6816	D(12,13,15,33)	-128.12
D(29,1,2,3)	179.255	D(12,13,15,34)	-11.592
D(29,1,2,7)	-0.3424	D(32,13,15,16)	-44.626
D(2,1,6,5)	0.4569	D(32,13,15,33)	76.2617
D(2,1,6,27)	-179.4307	D(32,13,15,34)	-167.22

D(29,1,6,5)	-179.5193	D(13,15,16,17)	-164.16
D(29,1,6,27)	0.5932	D(13,15,16,19)	17.7974
D(1,2,3,4)	0.5454	D(33,15,16,17)	74.7668
D(1,2,3,30)	-178.9073	D(33,15,16,19)	-103.28
D(7,2,3,4)	-179.8646	D(34,15,16,17)	-41.42
D(7,2,3,30)	0.6827	D(34,15,16,19)	140.537
D(1,2,7,8)	17.6557	D(15,16,17,18)	179.212
D(1,2,7,11)	-160.8518	D(19,16,17,18)	-2.6297
D(3,2,7,8)	-161.9341	D(16,17,18,20)	-76.575
D(3,2,7,11)	19.5583	D(16,17,18,35)	47.0951
D(2,3,4,5)	-0.1153	D(16,17,18,36)	163.688
D(2,3,4,31)	-179.9574	D(17,18,20,37)	-170.76
D(30,3,4,5)	179.3425	D(17,18,20,38)	-50.239
D(30,3,4,31)	-0.4996	D(17,18,20,39)	69.2435
D(3,4,5,6)	-0.1495	D(35,18,20,37)	68.1875
D(3,4,5,22)	179.6878	D(35,18,20,38)	-171.29
D(31,4,5,6)	179.698	D(35,18,20,39)	-51.806
D(31,4,5,22)	-0.4647	D(36,18,20,37)	-59.237
D(4,5,6,1)	-0.0172	D(36,18,20,38)	61.287
D(4,5,6,27)	179.8612	D(36,18,20,39)	-179.23
D(22,5,6,1)	-179.8221	D(5,22,23,24)	-178.13
D(22,5,6,27)	0.0563	D(5,22,23,43)	-58.204
D(4,5,22,23)	178.4872	D(5,22,23,44)	62.6878
D(6,5,22,23)	-1.6934	D(22,23,24,25)	80.9699
D(2,7,8,9)	-179.1676	D(22,23,24,26)	-155.81
D(11,7,8,9)	-0.549	D(22,23,24,45)	-37.499
D(2,7,11,10)	179.8595	D(43,23,24,25)	-35.86
D(8,7,11,10)	1.1484	D(43,23,24,26)	87.3552
D(7,8,9,10)	-0.5678	D(43,23,24,45)	-154.33
D(7,8,9,21)	-179.9987	D(44,23,24,25)	-163.26
D(8,9,10,11)	1.4242	D(44,23,24,26)	-40.043
D(8,9,10,12)	179.6216	D(44,23,24,45)	78.2734
D(21,9,10,11)	-179.2026	D(23,24,25,46)	-174.85
D(21,9,10,12)	-1.0052	D(23,24,25,47)	-55.316
D(8,9,21,40)	-166.2421	D(23,24,25,48)	65.0877
D(8,9,21,41)	-45.5336	D(26,24,25,46)	63.2413
D(8,9,21,42)	73.5103	D(26,24,25,47)	-177.22
D(10,9,21,40)	14.4091	D(26,24,25,48)	-56.818
D(10,9,21,41)	135.1176	D(45,24,25,46)	-56.909
D(10,9,21,42)	-105.8386	D(45,24,25,47)	62.6282
D(9,10,11,7)	-1.4165	D(45,24,25,48)	-176.97

D(12,10,11,7)	-179.6969	D(23,24,26,49)	-178.71
D(9,10,12,13)	163.9633	D(23,24,26,50)	61.6962
D(9,10,12,14)	-19.0402	D(23,24,26,51)	-59.337
D(11,10,12,13)	-18.0494	D(25,24,26,49)	-55.866
D(11,10,12,14)	158.9471	D(25,24,26,50)	-175.46
D(10,12,13,15)	-175.6159	D(25,24,26,51)	63.5096
D(10,12,13,32)	-21.6776	D(45,24,26,49)	63.911
D(14,12,13,15)	7.2543	D(45,24,26,50)	-55.68
D(14,12,13,32)	161.1927	D(45,24,26,51)	-176.71
Compound 7			
Bond Lengths (Å)	**DFT**	**Bond Lengths (Å)**	**DFT**
R(1,2)	1.3991	R(15,31)	1.1182
R(1,6)	1.412	R(15,32)	1.128
R(1,27)	1.0989	R(16,17)	1.3724
R(2,3)	1.4191	R(16,18)	1.2066
R(2,7)	1.4491	R(17,33)	0.9961
R(3,4)	1.3786	R(18,30)	2.684
R(3,28)	1.0938	R(19,34)	1.1089
R(4,5)	1.4235	R(19,35)	1.1028
R(4,29)	1.0914	R(19,36)	1.1029
R(5,6)	1.4129	R(20,21)	1.4696
R(5,20)	1.3514	R(21,22)	1.5403
R(6,25)	1.4233	R(21,37)	1.1013
R(7,8)	1.3221	R(21,38)	1.1024
R(7,11)	1.7808	R(22,23)	1.5298
R(8,9)	1.4138	R(22,24)	1.5302
R(9,10)	1.3837	R(22,39)	1.1225
R(9,19)	1.4749	R(23,40)	1.096
R(10,11)	1.7306	R(23,41)	1.0975
R(10,12)	1.4598	R(23,42)	1.0957
R(12,13)	1.413	R(24,43)	1.0972
R(12,14)	1.2221	R(24,44)	1.096
R(13,15)	1.4706	R(24,45)	1.0967
R(13,30)	1.0202	R(25,26)	1.1578
Bond Angles (º)	**DFT**	**Bond Angles (º)**	**DFT**
A(2,1,6)	121.2852	A(16,15,31)	109.37
A(2,1,27)	119.621	A(16,15,32)	110.004
A(6,1,27)	119.0938	A(31,15,32)	105.894
A(1,2,3)	119.3652	A(15,16,17)	109.332
A(1,2,7)	119.4058	A(15,16,18)	129.916
A(3,2,7)	121.2277	A(17,16,18)	120.734

A(2,3,4)	120.3864	A(16,17,33)	112.907
A(2,3,28)	120.2863	A(9,19,34)	111.663
A(4,3,28)	119.3251	A(9,19,35)	111.888
A(3,4,5)	120.2574	A(9,19,36)	111.385
A(3,4,29)	121.6111	A(34,19,35)	107.688
A(5,4,29)	118.1313	A(34,19,36)	107.51
A(4,5,6)	120.1733	A(35,19,36)	106.435
A(4,5,20)	110.9591	A(5,20,21)	121.686
A(6,5,20)	128.8674	A(20,21,22)	102.247
A(1,6,5)	118.5292	A(20,21,37)	108.779
A(1,6,25)	116.98	A(20,21,38)	108.024
A(5,6,25)	124.4907	A(22,21,37)	113.161
A(2,7,8)	126.8873	A(22,21,38)	112.794
A(2,7,11)	120.991	A(37,21,38)	111.263
A(8,7,11)	112.1072	A(21,22,23)	110.859
A(7,8,9)	112.8173	A(21,22,24)	109.218
A(8,9,10)	114.2018	A(21,22,39)	107.611
A(8,9,19)	118.6472	A(23,22,24)	111.478
A(10,9,19)	127.1478	A(23,22,39)	108.474
A(9,10,11)	110.3418	A(24,22,39)	109.104
A(9,10,12)	126.7118	A(22,23,40)	111.26
A(11,10,12)	122.9211	A(22,23,41)	111.017
A(7,11,10)	90.5094	A(22,23,42)	112.18
A(10,12,13)	115.6086	A(40,23,41)	107.388
A(10,12,14)	124.483	A(40,23,42)	107.17
A(13,12,14)	119.8475	A(41,23,42)	107.591
A(12,13,15)	118.576	A(22,24,43)	110.897
A(12,13,30)	121.6624	A(22,24,44)	112.012
A(15,13,30)	115.2316	A(22,24,45)	112.051
A(13,15,16)	111.1614	A(43,24,44)	107.096
A(13,15,31)	109.8676	A(43,24,45)	106.901
A(13,15,32)	110.4052	A(44,24,45)	107.603
Dihedral Angles (º)	**DFT**	**Dihedral Angles (º)**	**DFT**
D(6,1,2,3)	-0.7137	D(11,10,12,13)	-18.438
D(6,1,2,7)	179.6907	D(11,10,12,14)	158.71
D(27,1,2,3)	179.2683	D(10,12,13,15)	-175.88
D(27,1,2,7)	-0.3272	D(10,12,13,30)	-20.898
D(2,1,6,5)	0.4597	D(14,12,13,15)	6.827
D(2,1,6,25)	-179.4253	D(14,12,13,30)	161.812
D(27,1,6,5)	-179.5225	D(12,13,15,16)	108.164
D(27,1,6,25)	0.5926	D(12,13,15,31)	-130.64

D(1,2,3,4)	0.536	D(12,13,15,32)	-14.205
D(1,2,3,28)	-178.9223	D(30,13,15,16)	-48.391
D(7,2,3,4)	-179.876	D(30,13,15,31)	72.8097
D(7,2,3,28)	0.6657	D(30,13,15,32)	-170.76
D(1,2,7,8)	17.124	D(13,15,16,17)	-165.64
D(1,2,7,11)	-161.3823	D(13,15,16,18)	15.9677
D(3,2,7,8)	-162.4638	D(31,15,16,17)	72.8727
D(3,2,7,11)	19.0299	D(31,15,16,18)	-105.52
D(2,3,4,5)	-0.1139	D(32,15,16,17)	-43.034
D(2,3,4,29)	-179.9507	D(32,15,16,18)	138.569
D(28,3,4,5)	179.3495	D(15,16,17,33)	-179.81
D(28,3,4,29)	-0.4873	D(18,16,17,33)	-1.2429
D(3,4,5,6)	-0.1407	D(5,20,21,22)	-178.14
D(3,4,5,20)	179.6978	D(5,20,21,37)	-58.216
D(29,4,5,6)	179.7017	D(5,20,21,38)	62.6776
D(29,4,5,20)	-0.4599	D(20,21,22,23)	81.0392
D(4,5,6,1)	-0.028	D(20,21,22,24)	-155.75
D(4,5,6,25)	179.8476	D(20,21,22,39)	-37.433
D(20,5,6,1)	-179.8342	D(37,21,22,23)	-35.779
D(20,5,6,25)	0.0414	D(37,21,22,24)	87.4357
D(4,5,20,21)	178.5013	D(37,21,22,39)	-154.25
D(6,5,20,21)	-1.6781	D(38,21,22,23)	-163.2
D(2,7,8,9)	-179.1697	D(38,21,22,24)	-39.982
D(11,7,8,9)	-0.5518	D(38,21,22,39)	78.3311
D(2,7,11,10)	179.8486	D(21,22,23,40)	-174.91
D(8,7,11,10)	1.138	D(21,22,23,41)	-55.37
D(7,8,9,10)	-0.5481	D(21,22,23,42)	65.0455
D(7,8,9,19)	-179.9483	D(24,22,23,40)	63.1901
D(8,9,10,11)	1.3974	D(24,22,23,41)	-177.27
D(8,9,10,12)	179.5973	D(24,22,23,42)	-56.856
D(19,9,10,11)	-179.2629	D(39,22,23,40)	-56.96
D(19,9,10,12)	-1.063	D(39,22,23,41)	62.5784
D(8,9,19,34)	-165.7721	D(39,22,23,42)	-177.01
D(8,9,19,35)	-44.9814	D(21,22,24,43)	-178.71
D(8,9,19,36)	74.0153	D(21,22,24,44)	61.7036
D(10,9,19,34)	14.9142	D(21,22,24,45)	-59.341
D(10,9,19,35)	135.7049	D(23,22,24,43)	-55.862
D(10,9,19,36)	-105.2984	D(23,22,24,44)	-175.45
D(9,10,11,7)	-1.396	D(23,22,24,45)	63.5052
D(12,10,11,7)	-179.6769	D(39,22,24,43)	63.9169
D(9,10,12,13)	163.5732	D(39,22,24,44)	-55.672

D(9,10,12,14)	-19.279	D(39,22,24,45)	-176.72
Compound 9			
Bond Lengths (Å)	**DFT**	**Bond Lengths (Å)**	**DFT**
R(1,2)	1.3948	R(17,37)	1.012
R(1,6)	1.3948	R(19,38)	1.113
R(1,31)	1.1	R(19,39)	1.113
R(2,3)	1.3949	R(19,40)	1.113
R(2,7)	1.337	R(20,21)	1.402
R(3,4)	1.3948	R(21,22)	1.523
R(3,32)	1.1	R(21,41)	1.113
R(4,5)	1.3948	R(21,42)	1.113
R(4,33)	1.1	R(22,23)	1.523
R(5,6)	1.3949	R(22,24)	1.523
R(5,20)	1.355	R(22,43)	1.113
R(6,29)	1.313	R(23,44)	1.113
R(7,8)	1.3152	R(23,45)	1.113
R(7,11)	1.7161	R(23,46)	1.113
R(8,9)	1.3813	R(24,47)	1.113
R(9,10)	1.3788	R(24,48)	1.113
R(9,19)	1.497	R(24,49)	1.113
R(10,11)	1.7154	R(25,26)	1.523
R(10,12)	1.351	R(25,50)	1.113
R(12,13)	1.369	R(25,51)	1.113
R(12,14)	1.208	R(26,27)	1.523
R(13,15)	1.45	R(26,52)	1.113
R(13,34)	1.012	R(26,53)	1.113
R(14,38)	1.7564	R(27,28)	1.523
R(15,16)	1.509	R(27,54)	1.113
R(15,35)	1.113	R(27,55)	1.113
R(15,36)	1.113	R(28,56)	1.113
R(16,17)	1.369	R(28,57)	1.113
R(16,18)	1.208	R(28,58)	1.113
R(17,25)	1.45	R(29,30)	1.158
Bond Angles (º)	**DFT**	**Bond Angles (º)**	**DFT**
A(2,1,6)	120.0029	A(38,19,40)	109.462
A(2,1,31)	119.9986	A(39,19,40)	109.52
A(6,1,31)	119.9985	A(5,20,21)	110.8
A(1,2,3)	119.9969	A(20,21,22)	109.5
A(1,2,7)	120.0015	A(20,21,41)	109.442
A(3,2,7)	120.0016	A(20,21,42)	109.462
A(2,3,4)	120.0002	A(22,21,41)	109.442

A(2,3,32)	119.9999	A(22,21,42)	109.462
A(4,3,32)	119.9999	A(41,21,42)	109.52
A(3,4,5)	120.0033	A(21,22,23)	109.5
A(3,4,33)	119.9984	A(21,22,24)	109.442
A(5,4,33)	119.9983	A(21,22,43)	109.462
A(4,5,6)	119.9972	A(23,22,24)	109.442
A(4,5,20)	120.0014	A(23,22,43)	109.462
A(6,5,20)	120.0014	A(24,22,43)	109.52
A(1,6,5)	119.9996	A(22,23,44)	109.5
A(1,6,29)	120.0002	A(22,23,45)	109.442
A(5,6,29)	120.0002	A(22,23,46)	109.462
A(2,7,8)	121.8997	A(44,23,45)	109.442
A(2,7,11)	121.8996	A(44,23,46)	109.462
A(8,7,11)	116.2007	A(45,23,46)	109.52
A(7,8,9)	109.1722	A(22,24,47)	109.5
A(8,9,10)	115.6691	A(22,24,48)	109.442
A(8,9,19)	122.1655	A(22,24,49)	109.462
A(10,9,19)	122.1654	A(47,24,48)	109.442
A(9,10,11)	109.7076	A(47,24,49)	109.462
A(9,10,12)	125.1462	A(48,24,49)	109.52
A(11,10,12)	125.1462	A(17,25,26)	109.5
A(7,11,10)	89.2503	A(17,25,50)	109.442
A(10,12,13)	120	A(17,25,51)	109.462
A(10,12,14)	120	A(26,25,50)	109.442
A(13,12,14)	120	A(26,25,51)	109.462
A(12,13,15)	120	A(50,25,51)	109.52
A(12,13,34)	120	A(25,26,27)	109.5
A(15,13,34)	120	A(25,26,52)	109.442
A(13,15,16)	109.5	A(25,26,53)	109.462
A(13,15,35)	109.4419	A(27,26,52)	109.442
A(13,15,36)	109.4618	A(27,26,53)	109.462
A(16,15,35)	109.4418	A(52,26,53)	109.52
A(16,15,36)	109.4618	A(26,27,28)	109.5
A(35,15,36)	109.52	A(26,27,54)	109.442
A(15,16,17)	120	A(26,27,55)	109.462
A(15,16,18)	120	A(28,27,54)	109.442
A(17,16,18)	120	A(28,27,55)	109.462
A(16,17,25)	120	A(54,27,55)	109.52
A(16,17,37)	120	A(27,28,56)	109.5
A(25,17,37)	120	A(27,28,57)	109.442
A(9,19,38)	109.5	A(27,28,58)	109.462

A(9,19,39)	109.4418	A(56,28,57)	109.442
A(9,19,40)	109.4618	A(56,28,58)	109.462
A(38,19,39)	109.4418	A(57,28,58)	109.52
Dihedral Angles (º)	**DFT**	**Dihedral Angles (º)**	**DFT**
D(6,1,2,3)	0.0058	D(15,16,17,25)	180
D(6,1,2,7)	-179.9942	D(15,16,17,37)	0
D(31,1,2,3)	-179.9942	D(18,16,17,25)	0
D(31,1,2,7)	0.0058	D(18,16,17,37)	180
D(2,1,6,5)	-0.0012	D(16,17,25,26)	180
D(2,1,6,29)	179.9988	D(16,17,25,50)	-60.036
D(31,1,6,5)	179.9988	D(16,17,25,51)	59.9996
D(31,1,6,29)	-0.0012	D(37,17,25,26)	0
D(1,2,3,4)	-0.0058	D(37,17,25,50)	119.964
D(1,2,3,32)	179.9942	D(37,17,25,51)	-120
D(7,2,3,4)	179.9942	D(5,20,21,22)	180
D(7,2,3,32)	-0.0058	D(5,20,21,41)	-60.036
D(1,2,7,8)	22.2468	D(5,20,21,42)	59.9996
D(1,2,7,11)	-157.7532	D(20,21,22,23)	60
D(3,2,7,8)	-157.7532	D(20,21,22,24)	179.964
D(3,2,7,11)	22.2468	D(20,21,22,43)	-60
D(2,3,4,5)	0.0012	D(41,21,22,23)	-59.964
D(2,3,4,33)	-179.9988	D(41,21,22,24)	60
D(32,3,4,5)	-179.9988	D(41,21,22,43)	-179.96
D(32,3,4,33)	0.0012	D(42,21,22,23)	-180
D(3,4,5,6)	0.0034	D(42,21,22,24)	-60.036
D(3,4,5,20)	-179.9966	D(42,21,22,43)	60
D(33,4,5,6)	-179.9966	D(21,22,23,44)	-180
D(33,4,5,20)	0.0034	D(21,22,23,45)	-60.036
D(4,5,6,1)	-0.0034	D(21,22,23,46)	59.9996
D(4,5,6,29)	179.9966	D(24,22,23,44)	60.0364
D(20,5,6,1)	179.9966	D(24,22,23,45)	-180
D(20,5,6,29)	-0.0034	D(24,22,23,46)	-59.964
D(4,5,20,21)	180	D(43,22,23,44)	-60
D(6,5,20,21)	0	D(43,22,23,45)	59.964
D(2,7,8,9)	179.9979	D(43,22,23,46)	180
D(11,7,8,9)	-0.0021	D(21,22,24,47)	-180
D(2,7,11,10)	-179.9975	D(21,22,24,48)	60.0363
D(8,7,11,10)	0.0025	D(21,22,24,49)	-60
D(7,8,9,10)	0.0003	D(23,22,24,47)	-60.001
D(7,8,9,19)	-179.9997	D(23,22,24,48)	-179.96
D(8,9,10,11)	0.0015	D(23,22,24,49)	59.9997

D(8,9,10,12)	-179.9985	D(43,22,24,47)	59.9997
D(19,9,10,11)	-179.9985	D(43,22,24,48)	-59.964
D(19,9,10,12)	0.0015	D(43,22,24,49)	-180
D(8,9,19,38)	180	D(17,25,26,27)	-180
D(8,9,19,39)	-60.0364	D(17,25,26,52)	-60.036
D(8,9,19,40)	59.9995	D(17,25,26,53)	59.9996
D(10,9,19,38)	0	D(50,25,26,27)	60.0364
D(10,9,19,39)	119.9636	D(50,25,26,52)	-180
D(10,9,19,40)	-120.0005	D(50,25,26,53)	-59.964
D(9,10,11,7)	-0.0021	D(51,25,26,27)	-60
D(12,10,11,7)	179.9979	D(51,25,26,52)	59.9641
D(9,10,12,13)	180	D(51,25,26,53)	-180
D(9,10,12,14)	0	D(25,26,27,28)	180
D(11,10,12,13)	0	D(25,26,27,54)	-60.036
D(11,10,12,14)	-180	D(25,26,27,55)	59.9996
D(10,12,13,15)	180	D(52,26,27,28)	60.0363
D(10,12,13,34)	0	D(52,26,27,54)	180
D(14,12,13,15)	0	D(52,26,27,55)	-59.964
D(14,12,13,34)	180	D(53,26,27,28)	-60
D(12,13,15,16)	-180	D(53,26,27,54)	59.964
D(12,13,15,35)	-60.0363	D(53,26,27,55)	-180
D(12,13,15,36)	59.9997	D(26,27,28,56)	180
D(34,13,15,16)	0	D(26,27,28,57)	-60.036
D(34,13,15,35)	119.9636	D(26,27,28,58)	59.9996
D(34,13,15,36)	-120.0004	D(54,27,28,56)	60.0364
D(13,15,16,17)	-180	D(54,27,28,57)	-180
D(13,15,16,18)	0	D(54,27,28,58)	-59.964
D(35,15,16,17)	60.0363	D(55,27,28,56)	-60
D(35,15,16,18)	-119.9637	D(55,27,28,57)	59.964
D(36,15,16,17)	-59.9996	D(55,27,28,58)	180

Table S2. The NBO analysis of compound **6**

Type	Donor NBO (i)	ED/e	Acceptor NBO (j)	ED/e	$E^{(2)}$ KJ/mol	E(j)-E(i) a.u.	F(i, j) a.u.
π -π*	BD (2) C1-C2	1.62294	BD*(2) C3-C4	0.2877	207.02	0.47	0.14
			BD*(2) C7-N8	0.33342	187.36	0.44	0.127
π -π*	BD (2) C3-C4	1.68641	BD*(2) C1-C2	0.34202	122.97	0.49	0.107
			BD*(2) C5-C6	0.42484	221.46	0.46	0.144
π -π*	BD (2) C5-C6	1.62324	BD*(2) C1-C2	0.34202	221.04	0.5	0.146
π -π*	BD (2) C7-N8	1.83112	BD*(2) C1-C2	0.34202	54.56	0.58	0.081
			BD*(2) C9-C10	0.28805	187.28	0.58	0.149
π -π*	BD (2) C9-C10	1.82358	BD*(2) C7-N8	0.33342	62.47	0.49	0.08
			BD*(2) C12-O14	0.30172	210.2	0.55	0.153
π -π*	BD (2) C12-O14	1.9824	BD*(2) C9-C10	0.28805	28.41	0.65	0.064
			BD*(2) C12-O14	0.30172	5.06	0.67	0.027
n -σ*	LP (1) N8	1.92982	BD*(1) C9-C10	0.03463	26.32	1.38	0.084
n -σ*	LP (1) S11	1.98407	BD*(1) C7-N8	0.02181	15.27	1.59	0.068
n -π*	LP (2) S11	1.70801	BD*(2) C7-N8	0.33342	229.62	0.46	0.144
			BD*(2) C9-C10	0.28805	119.29	0.5	0.107
n -π*	LP (1) N13	1.79183	BD*(2) C12-O14	0.30172	386.77	0.54	0.205
n -σ*	LP (2) O14	1.88955	BD*(1) C10-C12	0.04502	73.68	1.33	0.139
			BD*(1) C12-N13	0.06109	153.22	1.12	0.183
n -π*	LP (2) O17	1.83346	BD*(2) C16-O19	0.17567	317.52	0.64	0.197
n -σ*	LP (2) O19	1.88379	BD*(1) C15-C16	0.04313	92.55	1.06	0.139
			BD*(1) C16-O17	0.07354	186.36	1.02	0.193
n -π*	LP (2) O22	1.85984	BD*(2) C5-C6	0.42484	209.2	0.61	0.168
n -σ*	LP (1) N28	1.96918	BD*(1) C6-C27	0.03493	46.36	1.71	0.123
π*-π*	BD*(2) C5-C6	0.42484	BD*(2) C1-C2	0.34202	1282.02	0.02	0.123
			BD*(2) C3-C4	0.2877	1326.5	0.02	0.124
π*-π*	BD*(2) C7-N8	0.33342	BD*(2) C1-C2	0.34202	588.31	0.03	0.106
			BD*(2) C9-C10	0.28805	454.05	0.04	0.106
π*-π*	BD*(2) C9-C10	0.28805	BD*(2) C12-O14	0.30172	1311.68	0.02	0.117

Table S3. The NBO analysis of compound **7**

Type	Donor NBO (i)	ED/e	Acceptor NBO (j)	ED/e	$E^{(2)}$ KJ/mol	E(j)-E(i) a.u.	F(i, j) a.u.
π -π*	BD (2) C1-C2	1.69982	BD*(2) C3-C4	0.30514	217.86	0.5	0.146
			BD*(2) C7-N8	0.30426	162.09	0.49	0.126
π -π*	BD (2) C3-C4	1.68251	BD*(2) C1-C2	0.35391	141.5	0.51	0.118
			BD*(2) C5-C6	0.43913	224.85	0.47	0.147
π -π*	BD (2) C5-C6	1.62456	BD*(2) C1-C2	0.35391	226.48	0.52	0.15
π -π*	BD (2) C7-N8	1.83757	BD*(2) C1-C2	0.35391	74.31	0.58	0.095
			BD*(2) C9-C10	0.27945	168.57	0.6	0.143
π -π*	BD (2) C9-C10	1.82707	BD*(2) C7-N8	0.30426	93.55	0.53	0.101
			BD*(2) C12-O14	0.24884	176.69	0.58	0.142
π -π*	BD (2) C12-O14	1.96998	BD*(2) C9-C10	0.27945	53.6	0.67	0.088
			BD*(2) C12-O14	0.24884	5.65	0.69	0.029
n -π*	LP (2) S11	1.73404	BD*(2) C7-N8	0.30426	188.2	0.5	0.135
			BD*(2) C9-C10	0.27945	129.7	0.52	0.114
n -π*	LP (1) N13	1.82773	BD*(2) C12-O14	0.24884	320.45	0.59	0.193
n -σ*	LP (2) O14	1.88753	BD*(1) C10-C12	0.04325	99.16	1.22	0.154
			BD*(1) C12-N13	0.07026	168.57	1.08	0.189
n -π*	LP (2) O17	1.86814	BD*(2) C16-O18	0.155	289.49	0.66	0.192
n -σ*	LP (2) O18	1.89042	BD*(1) C15-C16	0.05939	123.64	1	0.155
			BD*(1) C16-O17	0.07518	189.79	1.04	0.195
n -π*	LP (2) O20	1.8519	BD*(2) C5-C6	0.43913	223.59	0.58	0.17
π*-π*	BD*(2) C5-C6	0.43913	BD*(2) C1-C2	0.35391	908.18	0.03	0.122
			BD*(2) C3-C4	0.30514	783.41	0.04	0.123
π*-π*	BD*(2) C7-N8	0.30426	BD*(2) C9-C10	0.27945	833.66	0.02	0.107
π*-π*	BD*(2) C9-C10	0.27945	BD*(2) C12-O14	0.24884	742.91	0.03	0.116

Table S4. The NBO analysis of compound **9**

Type	Donor NBO (i)	ED/e	Acceptor NBO (j)	ED/e	$E^{(2)}$ KJ/mol	E(j)-E(i) a.u.	F(i, j) a.u.
π -π*	BD (2) C1-C2	1.62306	BD*(2) C3-C4	0.28792	207.02	0.47	0.14
			BD*(2) C7-N8	0.33411	186.23	0.44	0.126
π -π*	BD (2) C3-C4	1.68594	BD*(2) C1-C2	0.34156	123.18	0.49	0.107
			BD*(2) C5-C6	0.42548	221.79	0.46	0.144
π -π*	BD (2) C5-C6	1.62396	BD*(2) C1-C2	0.34156	220.16	0.5	0.146
			BD*(2) C3-C4	0.28792	103.05	0.49	0.101
π -π*	BD (2) C9-C10	1.82409	BD*(2) C7-N8	0.33411	63.14	0.49	0.08
			BD*(2) C12-O14	0.30403	208.07	0.55	0.152
n -σ*	LP (1) N8	1.93004	BD*(1) C7-S11	0.05137	80.17	0.93	0.12
			BD*(1) C9-C10	0.03463	26.28	1.38	0.084
n -π*	LP (2) S11	1.70624	BD*(2) C7-N8	0.33411	230.58	0.46	0.144
			BD*(2) C9-C10	0.28786	120.12	0.5	0.107
n -π*	LP (1) N13	1.78708	BD*(2) C12-O14	0.30403	394.72	0.54	0.206
n -σ*	LP (2) O14	1.88994	BD*(1) C10-C12	0.04507	73.72	1.33	0.139
			BD*(1) C12-N13	0.06057	152.09	1.13	0.183
n -π*	LP (1) N17	1.78446	BD*(2) C16-O18	0.2221	405.56	0.55	0.206
n -σ*	LP (2) O18	1.89048	BD*(1) C15-C16	0.0463	107.07	1.04	0.148
			BD*(1) C16-N17	0.0574	149.83	1.11	0.181
n -π*	LP (2) O20	1.86022	BD*(2) C5-C6	0.42548	208.7	0.61	0.168
π*-π*	BD*(2) C5-C6	0.42548	BD*(2) C1-C2	0.34156	1255.83	0.02	0.123
			BD*(2) C3-C4	0.28792	1305.45	0.02	0.124
π*-π*	BD*(2) C7-N8	0.33411	BD*(2) C1-C2	0.34156	597.89	0.03	0.106
			BD*(2) C9-C10	0.28786	450.49	0.04	0.106
π*-π*	BD*(2) C9-C10	0.28786	BD*(2) C12- O14	0.30403	1253.69	0.02	0.117

Table S5. The Mulliken atomic charges of **6, 7,** and **9**

6		**7**		**9**	
Atoms	**Charges**	**Atoms**	**Charges**	**Atoms**	**Charges**
1C	0.07456	1C	0.07627	1C	0.01854
2C	-0.1922	2C	-0.195	2C	-0.1063
3C	0.03105	3C	0.03198	3C	-0.0463
4C	-0.3398	4C	-0.3402	4C	-0.178
5C	0.41769	5C	0.41874	5C	0.15844
6C	-0.2764	6C	-0.2766	6C	-0.1432
7C	0.201	7C	0.20491	7C	-0.1687
8N	-0.3915	8N	-0.3923	8N	-0.1291
9C	0.37644	9C	0.38117	9C	0.03835
10C	-0.4886	10C	-0.493	10C	-0.459
11S	0.07982	11S	0.07859	11S	0.45261
12C	0.6742	12C	0.67734	12C	0.40262
13N	-0.4837	13N	-0.4879	13N	-0.3994
14O	-0.5489	14O	-0.5452	14O	-0.373
15C	-0.2232	15C	-0.2134	15C	-0.0301
16C	0.6022	16C	0.60285	16C	0.29587
17O	-0.4607	17O	-0.5241	17N	-0.401
18C	0.05562	18O	-0.499	18O	-0.3682
19O	-0.5145	19C	-0.5223	19C	-0.199
20C	-0.5261	20O	-0.3739	20O	-0.171
21C	-0.5211	21C	-0.0521	21C	-0.0728
22O	-0.3746	22C	-0.0029	22C	-0.1111
23C	-0.052	23C	-0.4949	23C	-0.2117
24C	-0.0029	24C	-0.5004	24C	-0.2084
25C	-0.4949	25C	0.11275	25C	-0.0092
26C	-0.5004	26N	-0.221	26C	-0.1815
27C	0.11341	27H	0.17791	27C	-0.1607
28N	-0.2222	28H	0.15731	28C	-0.2134
29H	0.17778	29H	0.19515	29C	-0.061
30H	0.15767	30H	0.28724	30N	-0.0688
31H	0.19491	31H	0.1879	31H	0.17359
32H	0.28798	32H	0.22392	32H	0.14924
33H	0.18492	33H	0.3447	33H	0.15984
34H	0.22002	34H	0.21143	34H	0.25297
35H	0.13257	35H	0.19394	35H	0.11134
36H	0.1391	36H	0.19233	36H	0.11121
37H	0.16614	37H	0.14459	37H	0.23206
38H	0.17352	38H	0.14163	38H	0.15766

39H	0.1805	39H	0.13935	39H	0.09787
40H	0.21144	40H	0.15666	40H	0.09868
41H	0.19306	41H	0.16096	41H	0.10904
42H	0.19106	42H	0.15578	42H	0.1067
43H	0.14444	43H	0.16233	43H	0.10002
44H	0.14152	44H	0.15617	44H	0.07689
45H	0.13931	45H	0.16038	45H	0.08522
46H	0.15648			46H	0.07613
47H	0.16103			47H	0.08044
48H	0.15566			48H	0.08213
49H	0.16217			49H	0.08422
50H	0.15612			50H	0.09373
51H	0.16029			51H	0.09398
				52H	0.08649
				53H	0.08647
				54H	0.08559
				55H	0.08574
				56H	0.07782
				57H	0.07463
				58H	0.07464

Table S6. Anti-inflammatory activity data of the synthesized compounds

Concentrations of the samples (µg/ml)	6	7	9	Std
20	26.30923	28.92768	32.29426	22.31920
40	33.41646	36.40898	40.02494	30.04988
80	46.75810	49.50125	52.36908	43.39152
200	59.47631	62.34414	64.46384	56.85786
400	78.92768	81.17207	84.41397	75.56110

Table S7. Anti-diabetic data of the synthesized compounds

Concentrations of the samples (µg/ml)	6	7	9	Std
20	29.47462	31.25557	23.41941	26.35797
40	45.41407	47.72930	40.96171	42.56456
80	58.59305	59.21638	54.31879	56.72306
200	81.21104	82.27961	75.60107	80.05343
400	88.42386	89.84862	83.43722	86.82102