Electronic Supplementary Material (ESI) for RSC Advances.

Synthesis of Dimeric 1,2-Benzothiazine 1,1-Dioxide scaffolds: Molecular Structures, Hirshfeld Surface Analysis, DFT and Enzyme Inhibition Studies

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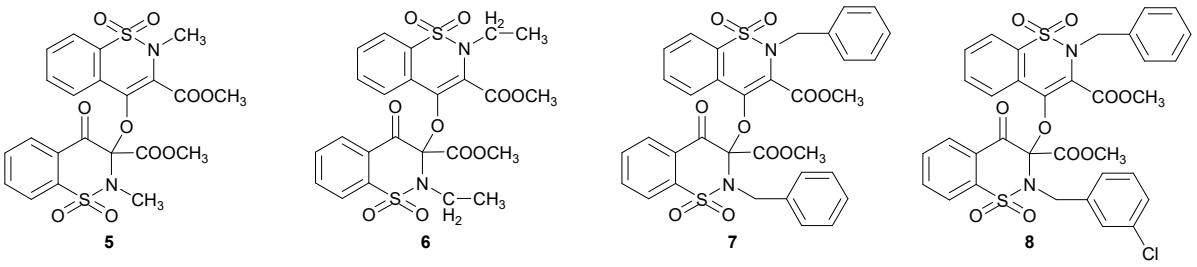

`Figure S1. Structures of the targeted compounds (**5-8**).

Table S1. Experimental and computed chemical shift (δ) in ppm for the compounds (**5-8**).

Protons	**Chemical shift (δ) in ppm**							
	5		**6**		**7**		**8**	
	Exp.	**Calc.**	**Exp.**	**Calc.**	**Exp.**	**Calc.**	**Exp.**	**Calc.**
H-5	8.11-8.04	7.75	8.06	7.73	8.09	7.80	8.09	7.26
H-6	7.97-7.92	7.90	8.03	7.87	7.88	7.88	7.88	7.29
H-5′, H-6′, H-7′, H-8′	7.88-7.62	8.21-7.01	7.83-7.65	8.31-7.26	7.74-7.65 7.42, 7.29	7.24-6.90	7.74-7.65, 7.42, 7.29	7.89-7.49
H-7, H-8	7.59-7.50	7.63-7.67	7.94-7.82	7.62-7.59	7.80-7.75	7.62-7.55	7.80-7.75	7.73-6.79
H-12/ H-12′	3.88/3.77	3.51-3.07/3.85-3.42	3.94/3.80	3.52-3.08/3.93-3.44	3.93/2.77	4.88-4.43/4.45-3.60	3.96/2.91	4.32-3.42/4.36-4.09
H-13/ H-13′	3.05/2.99	3.30-2.01/3.45-1.87	3.58, 3.54/ 3.52, 3.50	3.36-3.35/3.48-3.39	5.27, 4.94/ 4.67, 4.59	2.80-1.20/4.21-3.52	5.24, 4.88/ 4.74, 4.64	3.99-3.66/2.87-1.58
H-14/ H-14′	-	-	1.32-1.25/ 0.82-0.76	0.64-0.11/0.35-0.05	-	-	-	-
15-19	-	-	-	-	7.27-7.15	7.76-7.11	7.24-7.15	7.06-6.43
15′-19′	-	-	-	-	7.05-6.84	6.89-6.61	7.74-7.74	7.36-6.74

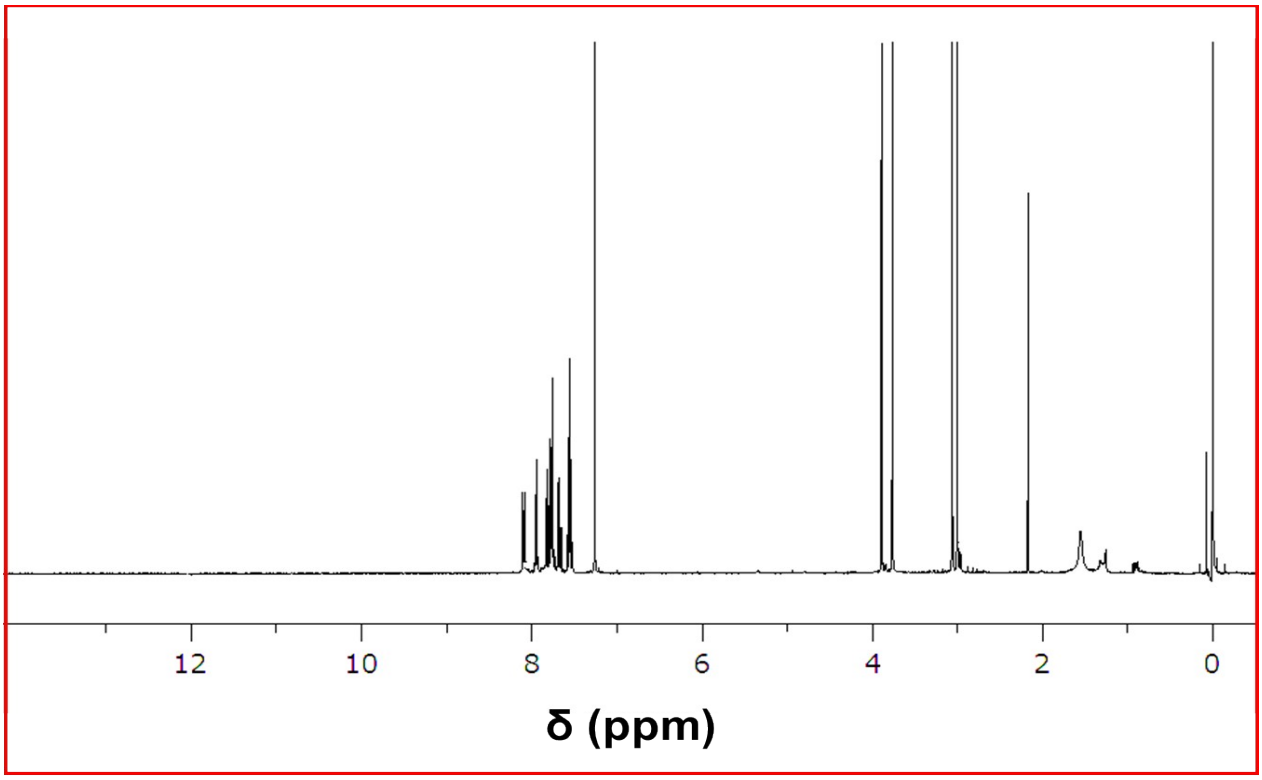

Figure S2. ^{1}H NMR spectrum of the compounds **5**

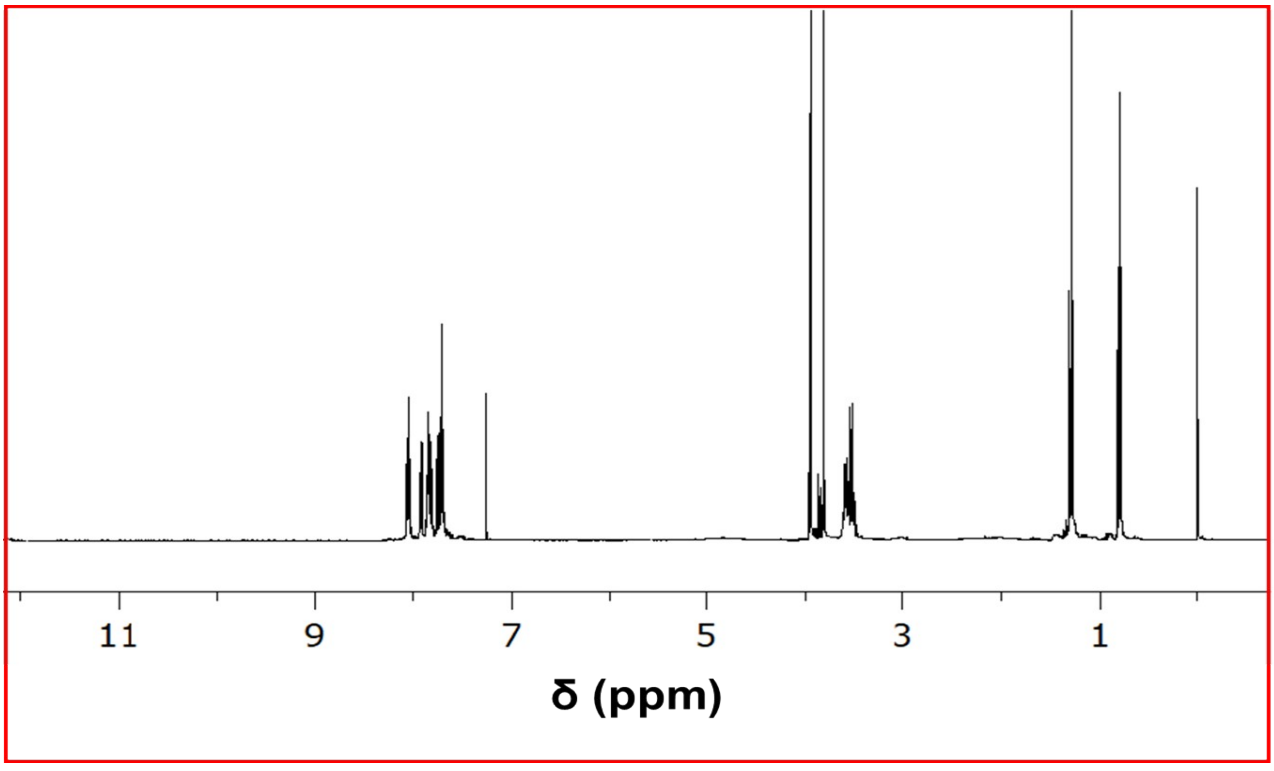

Figure S3. ^{1}H NMR spectrum of the compounds **6**

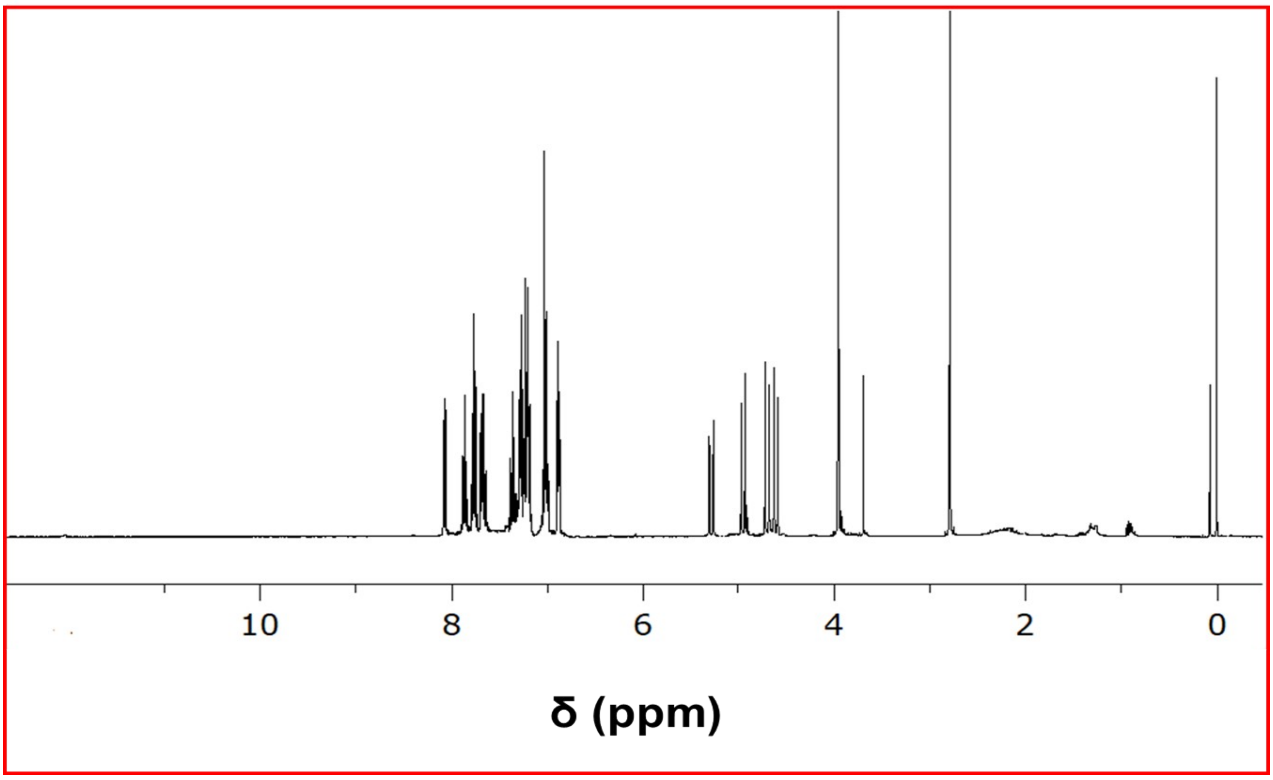

Figure S4. ^{1}H NMR spectrum of the compounds **7**

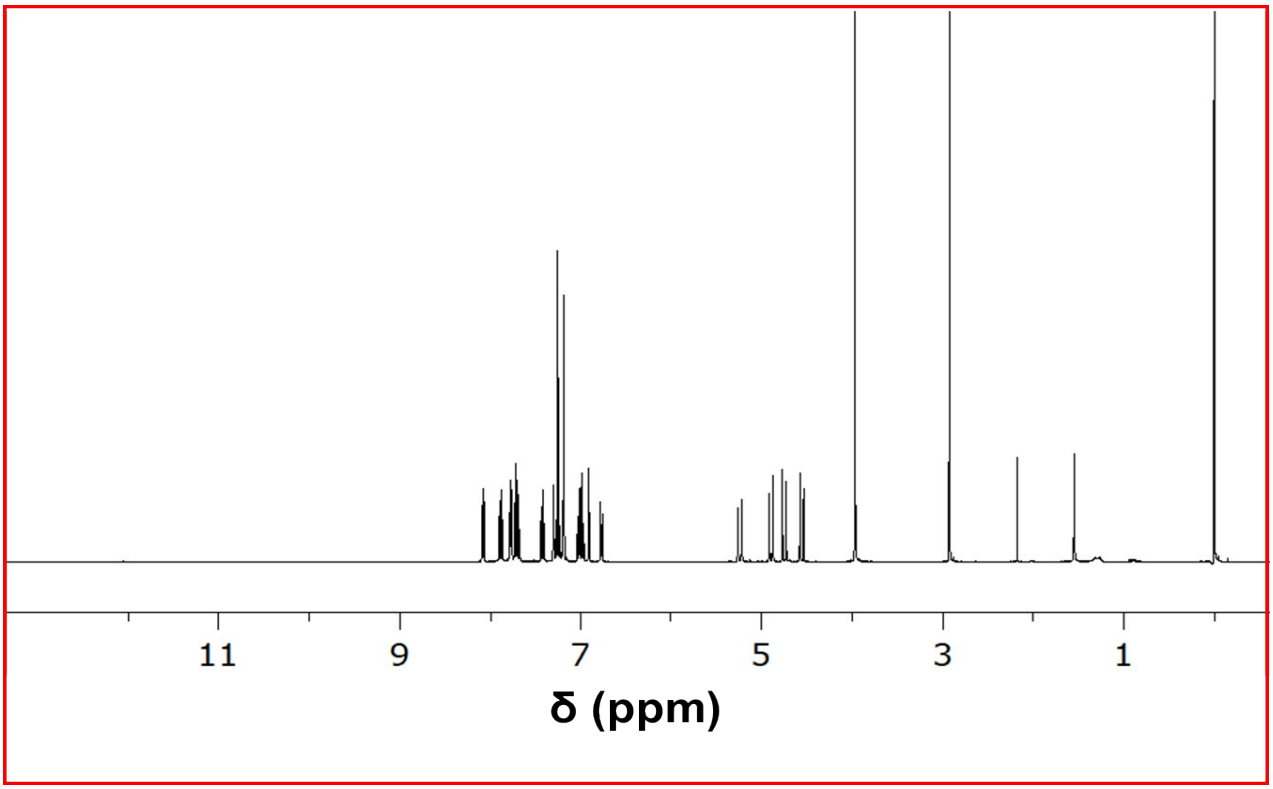

Figure S5. ^{1}H NMR spectrum of the compounds **8**

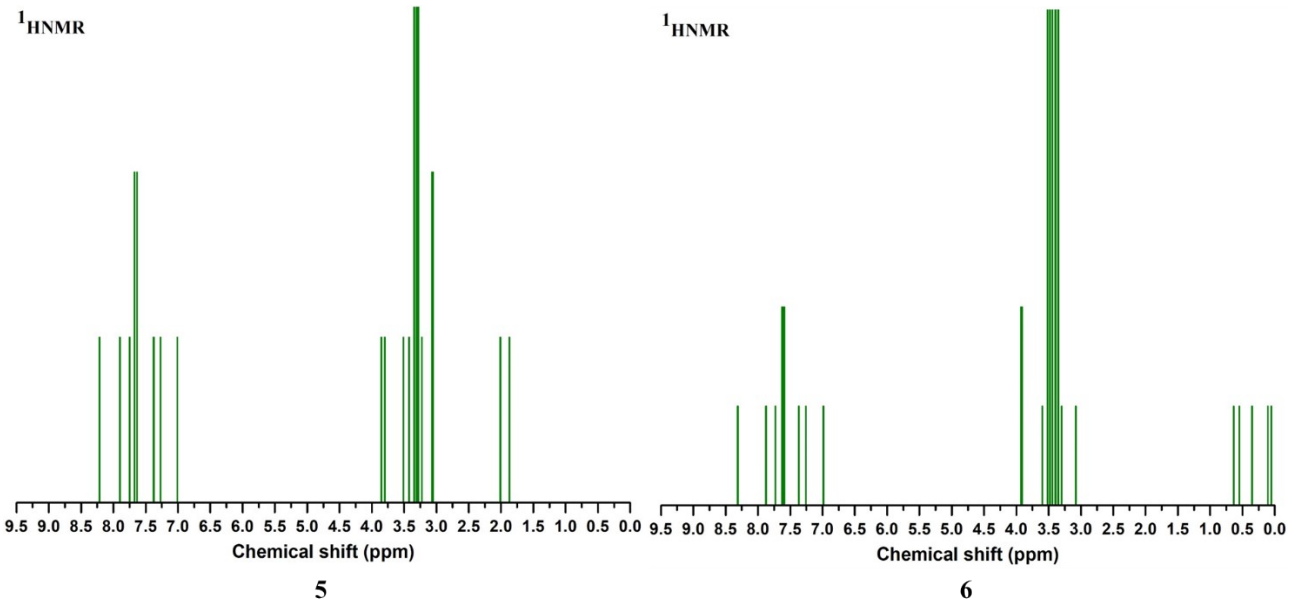

Figure S6. Computed ^{1}H NMR spectra of the compounds **5, 6**

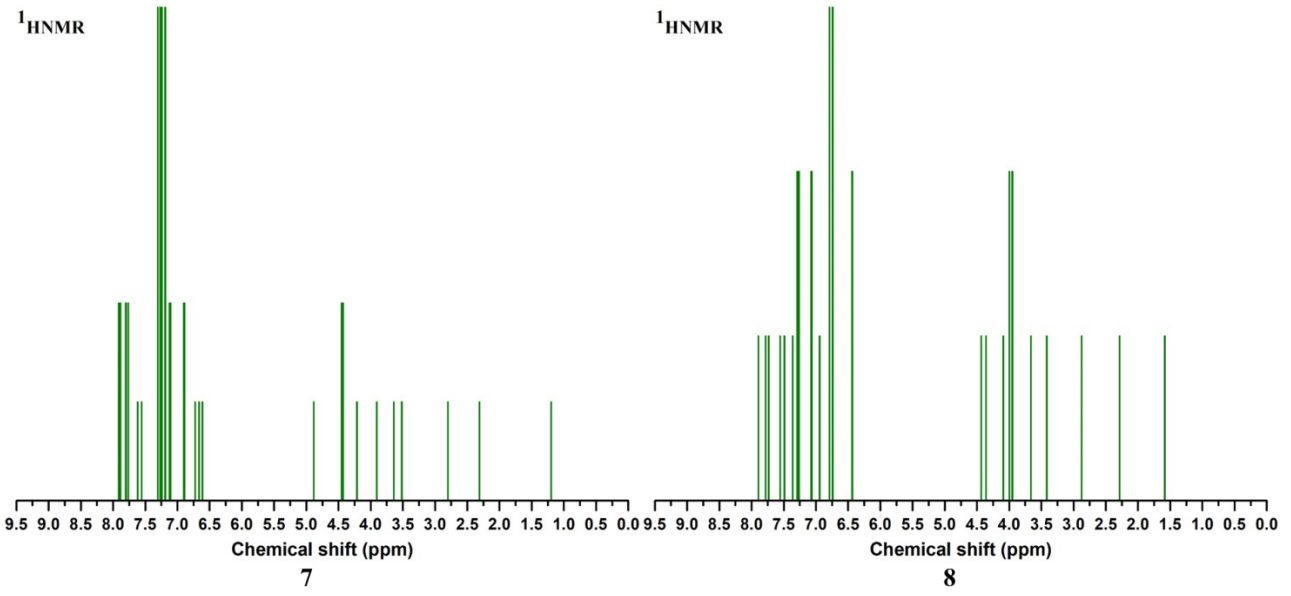

Figure S7. Computed ^{1}H NMR spectra of the compounds **7, 8**

Table S2. Experimental and computed wavenumber in cm^{-1} for the compounds **5-8**.

Group	5		6		7		8	
	Exp.	**Comp.**	**Exp.**	**Comp.**	**Exp.**	**Comp.**	**Exp.**	**Comp.**
C-H	3008, 2956	3060	3005, 2948,	3073	3031, 2952	3070	3031, 2928	3071
C=O	1778, 1745, 1663	1716, 1671	1774, 1705	1710, 1667, 1647,	1777, 1735, 1646	1719, 1656, 1650	1771, 1726, 1698	1712, 1670, 1647
C-H	1440	1471	1318, 1245	1470	1442	1472	1438	1473
SO_2	1328, , 1160	1325, 1305, 1123	1162, 1140	1365, 1283, 1219, 1122	1346, 1267, 1168	1327, 1259, 1218, 1185	1331, 1292, 1164	1327, 1287, 1197
C-O-C	1265	1238,	1240	1237	1238	1227	1245	1239
C-O	1048	1024	1047	1062	1023	1024	1023	1024

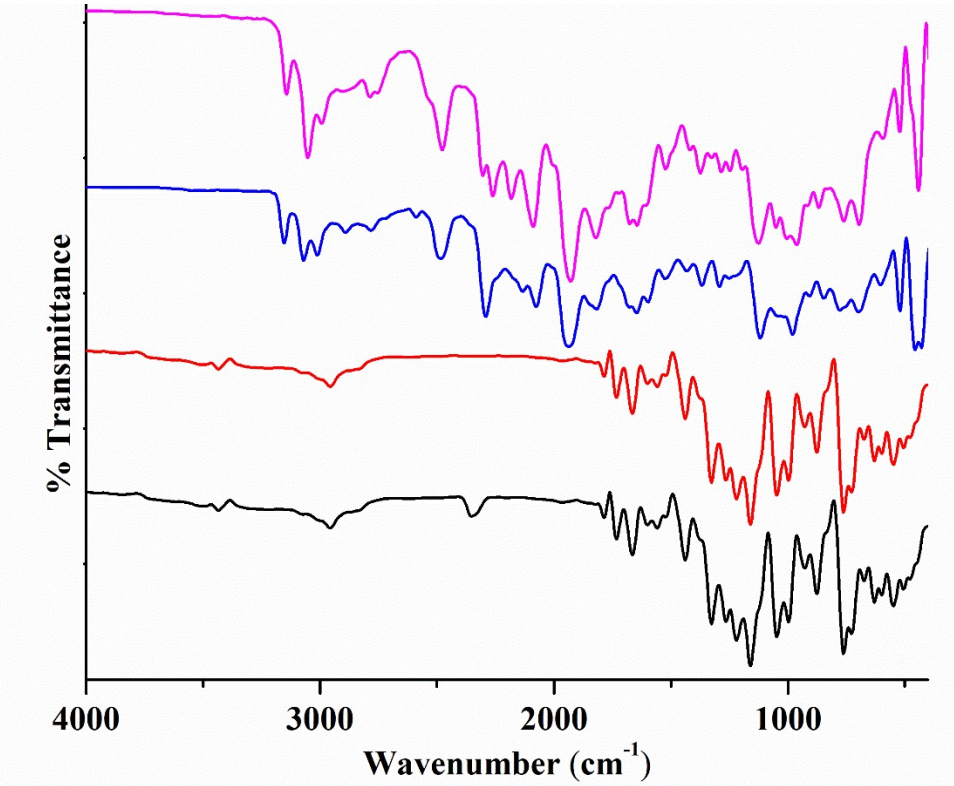

Figure S8. FT-IR spectra of the compounds **5-8**

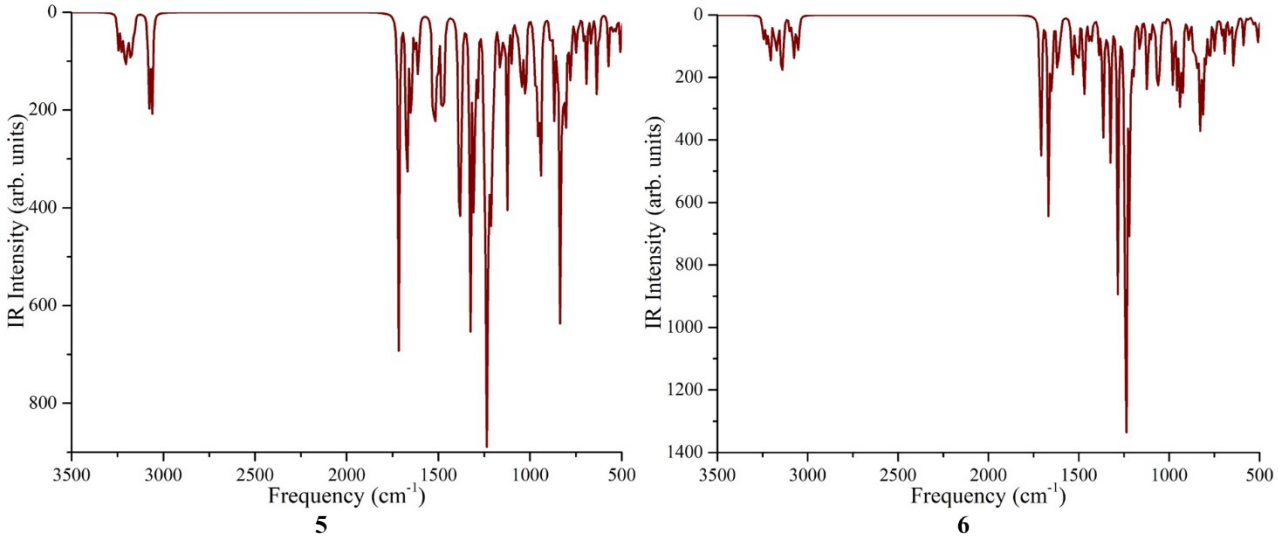

Figure S9. Computed FT-IR spectra of the compounds **5, 6**

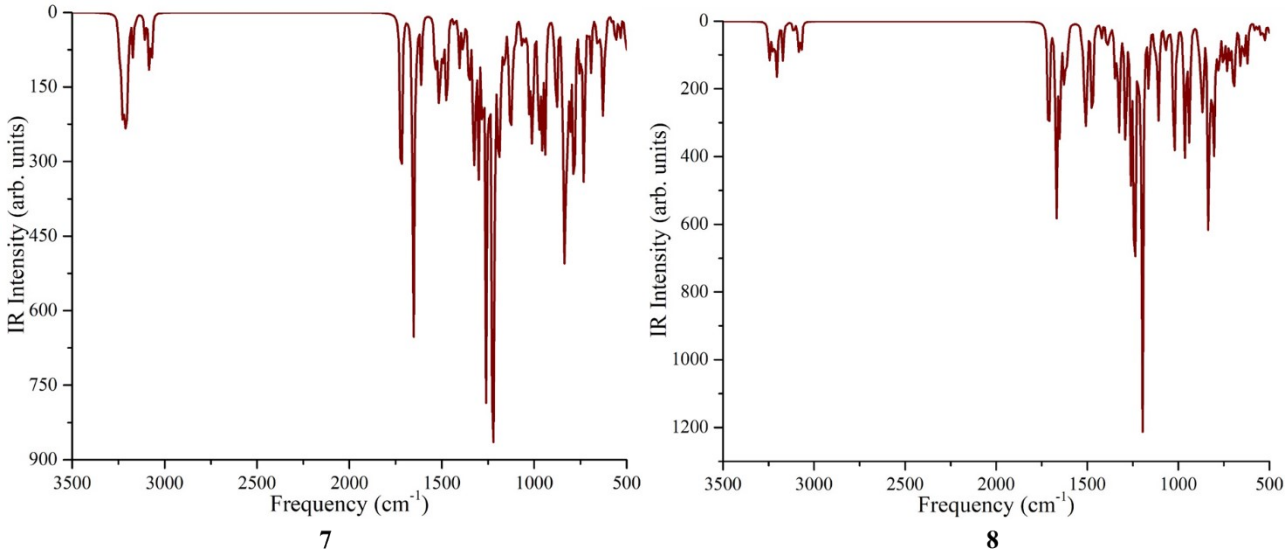

Figure S10. Computed FT-IR spectra of the compounds **7, 8**

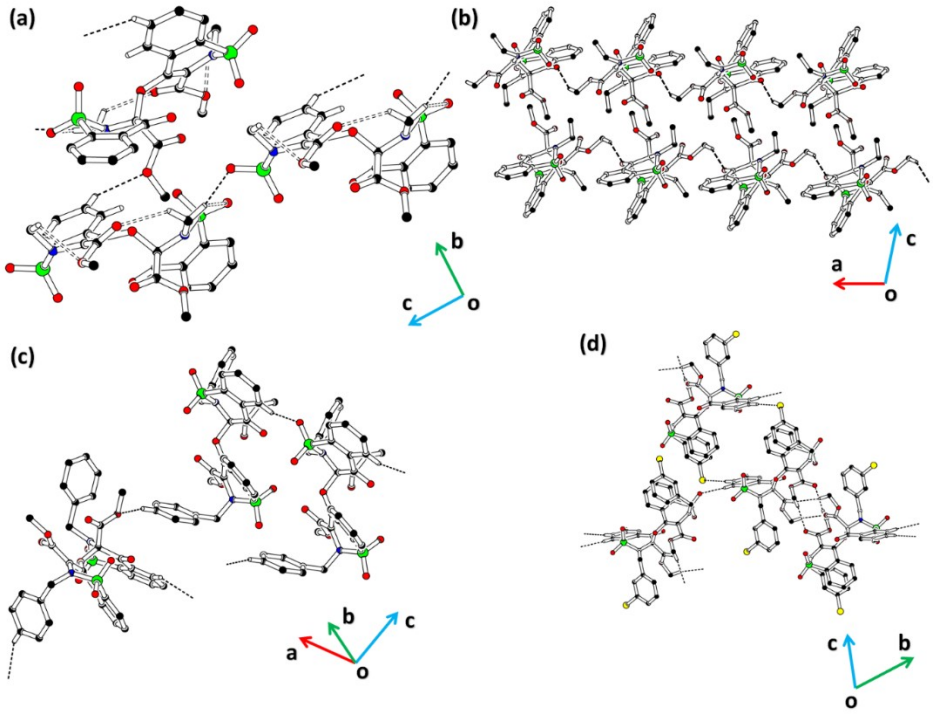

Figure S11. Packing diagram of compound **(a) 5**, **(b) 6**, **(c) 7**, **(d) 8**. Selected H-atoms are shown for clarity.

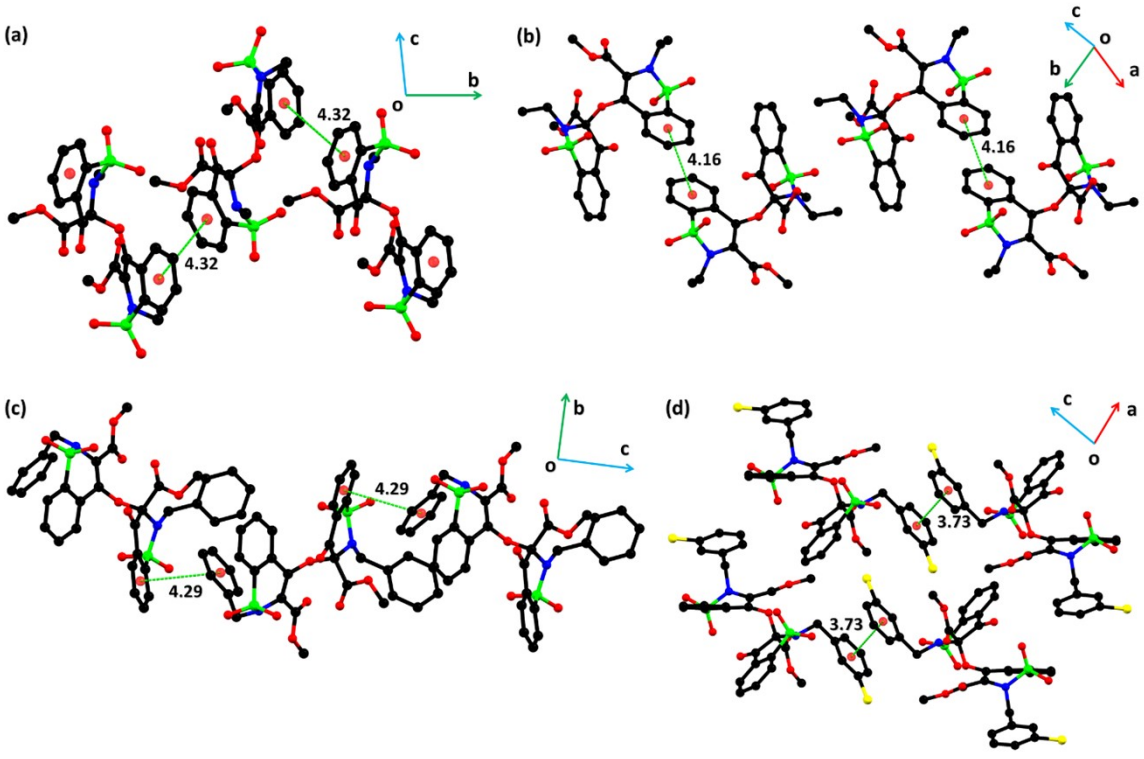

Figure S12. Graphical representation of π···π interactions in **(a) 5**, **(b) 6**, **(c) 7**, **(d) 8**.

Table S3. Particulars linked with SC-XRD.

Compound	**5**	**6**	**7**	**8**
CCDC	2295137	2295138	2295139	2295140
Chemical formula	$C_{22}H_{20}N_2O_{10}S_2$	$C_{24}H_{24}N_2O_{10}S_2$	$C_{34}H_{28}N_2O_{10}S_2$	$C_{34}H_{26}Cl_2N_2O_{10}S_2$
M_r	536.52	564.57	688.70	757.59
Crystal system, space group	Monoclinic, $P2_1$	Triclinic, $P\bar{1}$	Monoclinic, $P2_1/c$	Triclinic, $P\bar{1}$
Temperature (K)	296	296	296	296
a, *b*, *c* (Å)	9.1249 (17), 12.094 (2), 10.995 (2)	8.0501 (9), 11.7489 (15), 14.8904 (19)	8.112 (4), 17.079 (10), 22.560 (13)	8.4275 (7), 12.5962 (12), 17.3509 (16)
α, β, γ (°)	90, 108.971 (11), 90	107.833 (4), 102.961 (3), 97.540 (4)	90, 96.896 (17), 90	71.203 (5), 87.757 (4), 77.684 (5)
V (Å^3)	1147.5 (4)	1275.8 (3)	3103 (3)	1702.6 (3)
Z	2	2	4	2
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.30	0.27	0.24	0.38
Crystal size (mm)	0.34 × 0.28 × 0.16	0.38 × 0.34 × 0.26	0.38 × 0.24 × 0.10	0.38 × 0.26 × 0.22
Diffractometer	Bruker Kappa APEXII CCD	Bruker Kappa APEXII CCD	Bruker Kappa APEXII CCD	Bruker Kappa APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2007)	Multi-scan (*SADABS*; Bruker, 2007)	Multi-scan (*SADABS*; Bruker, 2007)	Multi-scan (*SADABS*; Bruker, 2007)
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7722, 5003, 3805	16181, 5994, 4302	5573, 5573, 2668	20015, 7525, 4577
R_{int}	0.042	0.044	0.148	0.063
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.661	0.658	0.606	0.644
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.055, 0.121, 1.02	0.048, 0.132, 1.04	0.100, 0.250, 1.01	0.059, 0.151, 1.01
No. of reflections	5003	5994	5573	7525
No. of parameters	329	347	412	453
No. of restraints	1	-	-	-
H-atom treatment	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.24, −0.34	0.28, −0.32	0.59, −0.58	0.58, −0.44

Table S4. Hydrogen-bond geometry (Å, º) for compounds **5-8**.

5	***D*—H···*A***	***D*—H**	**H···*A***	***D*···*A***	***<(D*—H···*A)*°**
	C11—H11*B*···O9	0.96	2.65	3.421 (7)	138
	C11—H11*C*···O3	0.96	2.34	2.847 (7)	112
	C22—H22*A*···O8	0.96	2.63	3.111 (8)	111
	C11—H11*C*···O7^{i}	0.96	2.31	3.158 (7)	147
	C15—H15···O4^{ii}	0.93	2.52	3.237 (6)	133.64
6	***D*—H···*A***	***D*—H**	**H···*A***	***D*···*A***	***<(D*—H···*A)*°**
	C22—H22*B*···O3^{iii}	0.96	2.65	3.549 (3)	156
	C23—H23*B*···O9	0.97	2.46	3.072 (3)	120
7	***D*—H···*A***	***D*—H**	**H···*A***	***D*···*A***	***<(D*—H···*A)*°**
	C5—H5···O2^{iii}	0.93	2.54	3.222 (9)	130.24
	C26—H26*A*···O1^{iv}	0.97	2.59	3.450 (7)	154.17
8	***D*—H···*A***	***D*—H**	**H···*A***	***D*···*A***	***<(D*—H···*A)*°**
	C10—H10*A*···O3^{v}	0.96	2.47	3.317 (4)	146
	C15—H15···O8^{vi}	0.93	2.62	3.549 (5)	175
	C20—H20*A*···O6^{vii}	0.96	2.47	3.410 (4)	165
	C26—H26···O1^{viii}	0.93	2.44	3.235 (4)	144

Symmetry codes. (i) *x*, *y*, *z*−1; (ii) −*x*, *y*+1/2, −*z*+1; (iii) *x*−1, *y*, *z*; (iv) *x*, −*y*+1/2, −*z*+1/2; (v) −*x*+1, −*y*+1, −*z*; (vi) −*x*+1, −*y*, −*z*+1; (vii) −*x*, −*y*+1, −*z*; (viii) *x*, *y*−1, *z*.

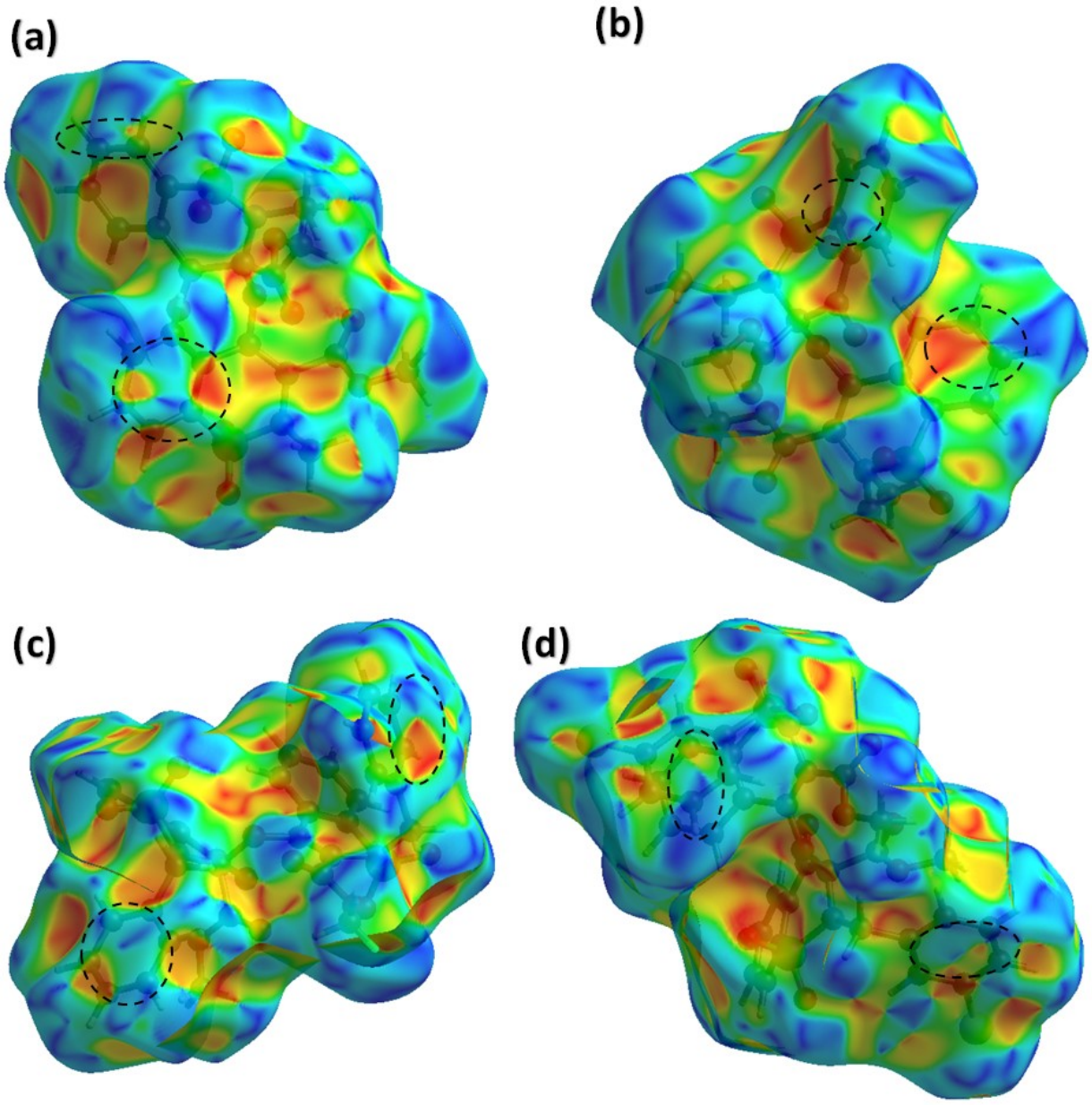

Figure S13. Hirshfeld surface plotted over shape index for compound **(a) 5**, **(b) 6**, **(c) 7**, **(d) 8**.

Table S5. Enrichment ratios for compound **5** with random contact greater than 0.98.

	Atom	**H**	**C**	**N**	**O**	**S**
Contact %	**H**	37.2	13.2	1.5	41.1	
	C	13.2	2.5		2.3	
	N	1.5				
	O	41.1	2.3		2.2	
	S					
Surface%		65.1	10.25	0.75	23.9	0

	Atom	H	C	N	O	S
Random contacts %	**H**	42.38				
	C	13.35	1.05			
	N	0.98	0.15	0.01		
	O	31.12	4.90	0.36	5.71	
	S	0.00	0.00	0.00	0.00	0.00
Enrichment ratio	**Atom**	**H**	**C**	**N**	**O**	**S**
	H	0.88				
	C	0.99	2.38			
	N					
	O	1.32	0.47		0.39	
	S					

Table S6. Enrichment ratios for compound **6** with random contact greater than 0.98.

	Atom	H	C	N	O	S
Contact %	**H**	41.8	13.2	0.5	41.1	0.1
	C	13.2	1.4		1.3	
	N	0.5				
	O	41.1	1.3		0.6	
	S	0.1				
Surface%		69.25	8.65	0.25	21.8	0.05
Random contacts %	**Atom**	**H**	**C**	**N**	**O**	**S**
	H	47.96				
	C	11.98	0.75			
	N	0.35	0.04	0.00		
	O	30.19	3.77	0.11	4.75	
	S	0.07	0.01	0.00	0.02	0.00
Enrichment ratio	**Atom**	**H**	**C**	**N**	**O**	**S**
	H	0.87				
	C	1.10				
	N					
	O	1.36			0.13	
	S					

Table S7. Enrichment ratios for compound **7** with random contact greater than 0.98.

	Atom	H	C	N	O	S
Contact %	**H**	49.7	14.7	0.5	30.8	0.1

	C	14.7	1.5		1.8	
	N	0.5				
	O	30.8	1.8		0.9	
	S	0.1				
Surface%		72.75	9.75	0.25	17.2	0.05
Random contacts %	**Atom**	**H**	**C**	**N**	**O**	**S**
	H	52.93				
	C	14.19	0.95			
	N	0.36	0.05	0.00		
	O	25.03	3.35	0.09	2.96	
	S	0.07	0.01	0.00	0.02	0.00
Enrichment ratio	**Atom**	**H**	**C**	**N**	**O**	**S**
	H	0.94				
	C	1.04				
	N					
	O	1.23	0.54		0.30	
	S					

Table S8. Enrichment ratios for compound **8** with random contact greater than 0.98.

Contact %	**Atom**	**H**	**C**	**N**	**O**	**S**	**Cl**
	H	34.3	11.4	0.4	33.3		12.8
	C	11.4	1.9		0.1		3.2
	N	0.4					
	O	33.3	0.1				2.3
	S						
	Cl	12.8	3.2		2.3		0.3
Surface%		63.25	9.25	0.2	17.85	0	9.45
Random Contacts %	**Atom**	**H**	**C**	**N**	**O**	**S**	**Cl**
	H	40.01					
	C	11.70	0.86				
	N	0.25	0.04	0.00			
	O	22.58	3.30	0.07	3.19		
	S	0.00	0.00	0.00	0.00	0.00	
	Cl	11.95	1.75	0.04	3.37	0.00	0.89
Enrichment ratio	**Atom**	**H**	**C**	**N**	**O**	**S**	**Cl**
	H	0.86					
	C	0.97					
	N						
	O	1.47	0.03		0.00		
	S						

	Cl	1.07	1.83		0.68		

Table S9. Interaction energies for compound **5**. **R** is the intermolecular distance.

	N	**Symop**	**R**	**E_ele**	**E_pol**	**E_dis**	**E_rep**	**E_tot**
	2	-x, y+1/2, -z	7.40	-14.7	-11.5	-83.0	37.7	-66.7
	2	x, y, z	11.79	-28.8	-7.8	-21.5	7.0	-48.0
	2	x, y, z	9.12	-1.8	-5.0	-41.0	15.4	-29.6
	2	-x, y+1/2, -z	10.68	-20.1	-5.4	-8.3	2.3	-29.6
	2	-x, y+1/2, -z	13.31	2.8	-0.7	-3.1	0.0	-0.4
	2	-x, y+1/2, -z	9.95	-6.2	-2.4	-12.8	4.4	-15.8
	2	x, y, z	11.00	-17.1	-8.5	-15.2	15.7	-24.0
	2	-x, y+1/2, -z	9.65	-19.7	-12.3	-29.1	12.2	-44.4

Table S10. Interaction energies for compound **6**. **R** is the intermolecular distance.

	N	**Symop**	**R**	**E_ele**	**E_pol**	**E_dis**	**E_rep**	**E_tot**
	1	-x, -y, -z	13.12	-12.2	-6.2	-14.7	0.0	-29.7
	1	-x, -y, -z	6.95	-1.8	-11.8	-80.0	43.3	-46.4
	1	-x, -y, -z	15.66	0.2	-0.0	-1.1	0.0	-0.8
	2	x, y, z	13.34	4.9	-2.3	-14.0	0.0	-9.1
	2	x, y, z	8.05	-15.9	-14.0	-35.9	11.6	-48.3
	1	-x, -y, -z	9.99	-16.4	-8.1	-31.4	11.8	-40.8
	1	-x, -y, -z	12.05	-12.8	-3.3	-11.5	0.0	-25.5
	2	x, y, z	11.75	-11.4	-6.0	-17.5	5.5	-26.8
	1	-x, -y, -z	8.94	-28.6	-9.3	-58.2	35.5	-58.8
	1	-x, -y, -z	8.82	-48.9	-12.8	-30.8	13.3	-75.1
	1	-x, -y, -z	9.91	-4.8	-5.0	-44.7	17.9	-33.9

Table S11. Interaction energies for compound **7**. **R** is the intermolecular distance.

	N	Symop	R	E_ele	E_pol	E_dis	E_rep	E_tot
	2	-x, y+1/2, -z+1/2	10.79	-3.5	-5.8	-35.8	11.3	-30.5
	2	x, y, z	8.11	-46.2	-21.2	-69.4	28.5	-100.2
	2	x, -y+1/2, z+1/2	11.52	-8.8	-2.1	-34.8	11.4	-32.4
	2	x, -y+1/2, z+1/2	13.29	-7.8	-1.4	-23.0	0.0	-29.6
	1	-x, -y, -z	14.41	-2.3	-2.9	-13.5	0.0	-16.4
	2	-x, y+1/2, -z+1/2	10.02	-11.4	-8.3	-37.4	17.7	-36.3
	1	-x, -y, -z	9.47	-22.4	-17.9	-65.3	37.3	-63.0
	1	-x, -y, -z	13.02	-20.6	-5.2	-19.1	0.0	-41.6
	1	-x, -y, -z	13.54	-8.6	-1.0	-17.0	0.0	-24.8

Table S12. Interaction energies for compound **8**. **R** is the intermolecular distance.

	N	Symop	R	E_ele	E_pol	E_dis	E_rep	E_tot
	1	-x, -y, -z	12.94	-16.2	-3.2	-49.2	0.0	-62.9
	1	-x, -y, -z	10.44	-14.8	-6.5	-40.1	34.8	-27.2
	2	x, y, z	8.43	-25.6	-11.8	-66.2	27.3	-71.3
	1	-x, -y, -z	8.85	-49.3	-20.3	-43.6	19.6	-87.0
	1	-x, -y, -z	12.68	-19.8	-5.9	-33.9	0.0	-54.6
	2	x, y, z	12.60	-17.7	-7.0	-13.1	0.0	-34.5
	1	-x, -y, -z	12.15	63.6	-4.7	-59.1	0.0	8.5
	1	-x, -y, -z	10.04	-5.5	-4.6	-22.0	8.1	-21.9
	1	-x, -y, -z	10.19	-36.0	-15.4	-38.5	20.9	-64.4
	1	-x, -y, -z	14.07	16.3	-1.9	-35.4	0.0	-16.5

Table S13. Natural bond orbital (NBO) analysis of compound using B3LYP/LANL2DZ level of theory.

Compound 5						
Donor (i)	**Type**	**Acceptor (j)**	**Type**	**$E^{(2)a}$ [kcal/mol]**	**E(j)_E(i)[b] [a.u.]**	**F(i;j)[c] [a.u.]**
C18 - C20	π	C15 - C16	π*	23.23	0.27	0.071
C18 - C20	π	C22 - C24	π*	23.56	0.28	0.073
O11 - C48	π	C46 - C47	π*	3.21	0.4	0.034
O3 - C25	π	C22 - C24	π*	4.96	0.4	0.043
O6	LP2	O7 - C27	π*	51.16	0.3	0.111
O10	LP2	O11 - C48	π*	47.69	0.3	0.108
O6	LP2	C28 - H29	σ*	3.37	0.79	0.049
O11	LP1	C47 - C48	σ*	3.32	1.07	0.054
Compound 6						
C44 - C46	π	C39 - C48	π*	24	0.27	0.074
C22 - C24	π	C15 - C16	π*	23.92	0.27	0.072
O11 - C51	π	C49 - C50	π*	3.64	0.4	0.037
O5 - C25	π	C22 - C24	π*	5.04	0.4	0.044
O7	LP2	O6 - C27	π*	52.29	0.3	0.112
O12	LP2	O11 - C51	π*	47.17	0.31	0.108
O7	LP2	C 28 - H 29	σ*	3.36	0.79	0.049
O7	LP2	C 28 - H 31	σ*	3.37	0.8	0.049
Compound 7						
C22 - C24	π	C15 - C16	π*	23.89	0.27	0.073
C51 - C53	π	C46 - C55	π*	24.34	0.27	0.074
O5 - C25	π	C22 - C24	π*	4.88	0.4	0.043
O11 - C72	π	C56 - C57	π*	3.63	0.4	0.036
O7	LP2	O6 - C41	π*	52.5	0.3	0.112
O8	LP2	O7 - C29	π*	44.82	0.31	0.106
O12	LP2	C73 - H74	σ*	3.35	0.78	0.048
O7	LP2	C42 - H43	σ*	3.05	0.8	0.047
Compound 8						
C22 - C24	π	C17 - C26	π*	24.36	0.26	0.073
C54 - C55	π	C61 - C63	π*	23.98	0.27	0.072
O7 - C29	π	C27 - C28	π*	4.81	0.4	0.041
O14 - C53	π	C54 - C55	π*	5.04	0.4	0.044
O8	LP2	O7 - C29	π*	44.82	0.31	0.106
O11	LP2	O10 - C48	π*	54.04	0.3	0.113
O5	LP3	S3 - O6	σ*	3.02	0.38	0.031
O11	LP2	C49 - H50	σ*	3.14	0.8	0.047

[a]$E^{(2)}$ means energy of hyper conjugative interaction (stabilization energy).
[b]Energy difference between donor and acceptor i and j NBO orbitals.
[c]F(i;j) is the Fock matrix element between i and j NBO orbitals.

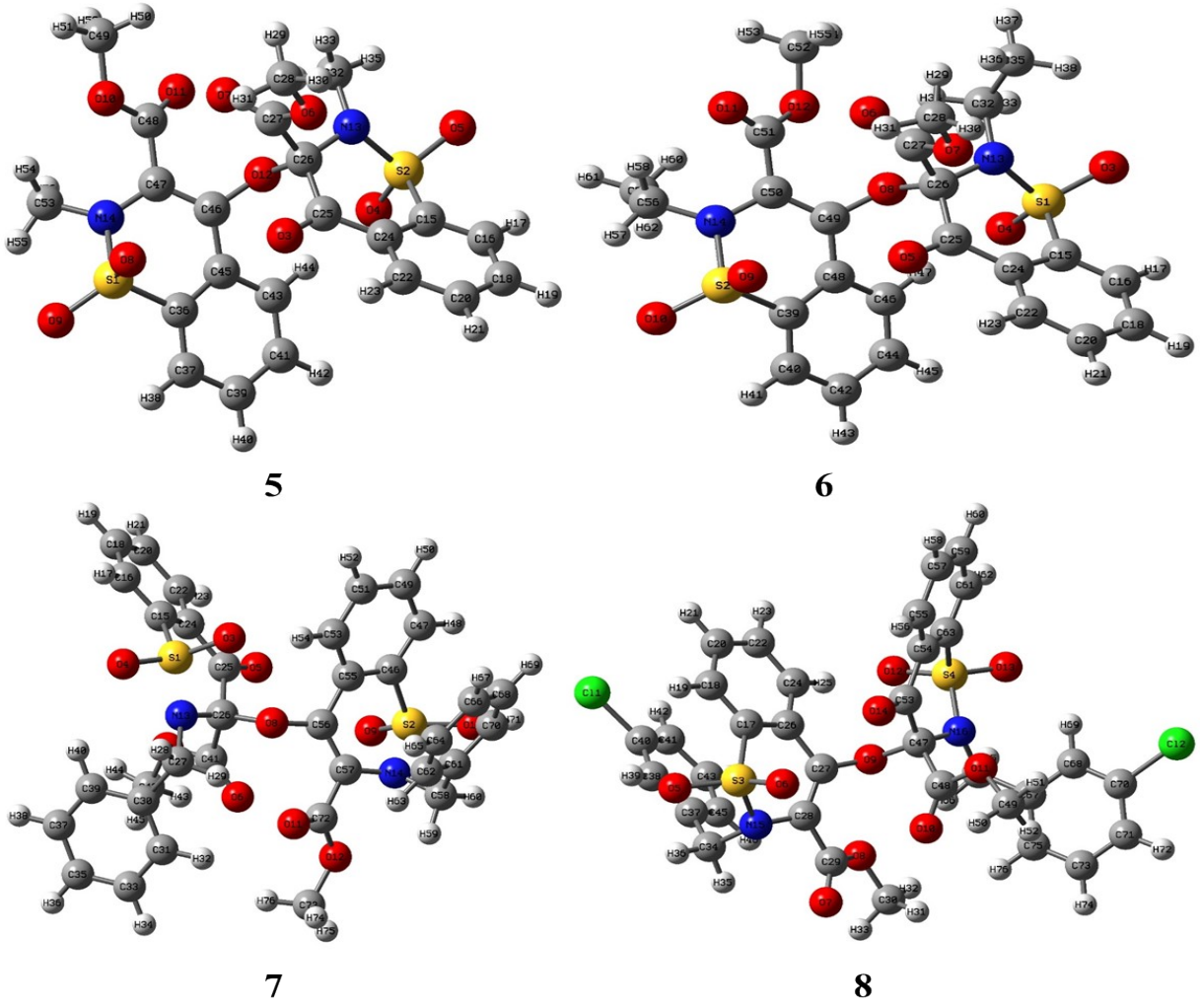

Figure S14. Optimized geometries for the compounds **(5-8)** using the B3LYP/LANL2DZ level of theory.

Table S14. The E_{HOMO}, E_{LUMO}, and energy gap (E_{LUMO}-E_{HOMO}) of the compounds **(5-8)**.

Complex	E_{HOMO} (eV)	E_{LUMO} (eV)	HOMO-LUMO gap (eV)
5	-7.50	-2.38	5.12
6	-7.48	-2.38	5.10
7	-6.84	-2.34	4.50
8	-6.99	-2.56	4.43

Table S15. Global reactivity descriptors for the compounds **5-8** in electron volts (eV).

Property		Calculated results (eV)			
		5	**6**	**7**	**8**
Ionization potential	*IP*	6.14	6.14	6.26	6.58
Electron affinity	*EA*	3.34	3.37	3.30	3.52
Electronegativity	χ	4.74	4.76	4.78	5.05
Chemical potential	μ	-4.74	-4.76	-4.78	-5.05
Global hardness	η	1.40	1.38	1.48	1.53
Global softness	*S*	0.36	0.36	0.34	0.33
Global electrophilicity	ω	7.99	8.17	7.73	8.34

Table S16. Linear polarizabilities with major contributing tensors (a.u.) and dipole moments (D) of the compounds **5-8**.

Dipole Moment				
	5	**6**	**7**	**8**
μ_x	-0.884	0.489	-2.276	-0.877
μ_y	-1.846	2.431	1.082	-2.489
μ_z	-1.274	0.932	-0.488	-0.078
$\boldsymbol{\mu_{total}}$	**2.412**	**2.649**	**2.567**	**2.640**
Polarizability				
	5	**6**	**7**	**8**
α_{xx}	376.595	316.382	459.083	402.162
α_{yy}	240.201	427.666	489.878	459.615
α_{zz}	371.898	308.59	354.999	479.778
$\boldsymbol{\langle\alpha\rangle}$	**329.564**	**350.879**	**434.653**	**447.185**

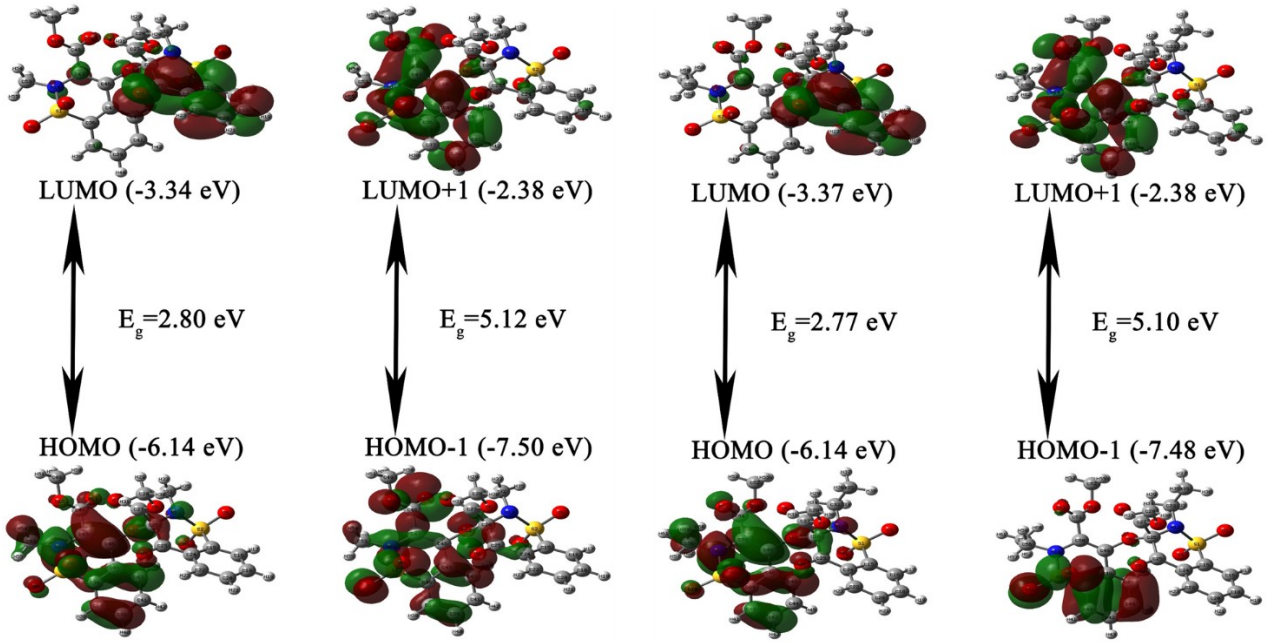

Figure S15. FMOs of the compounds **5** and **6**

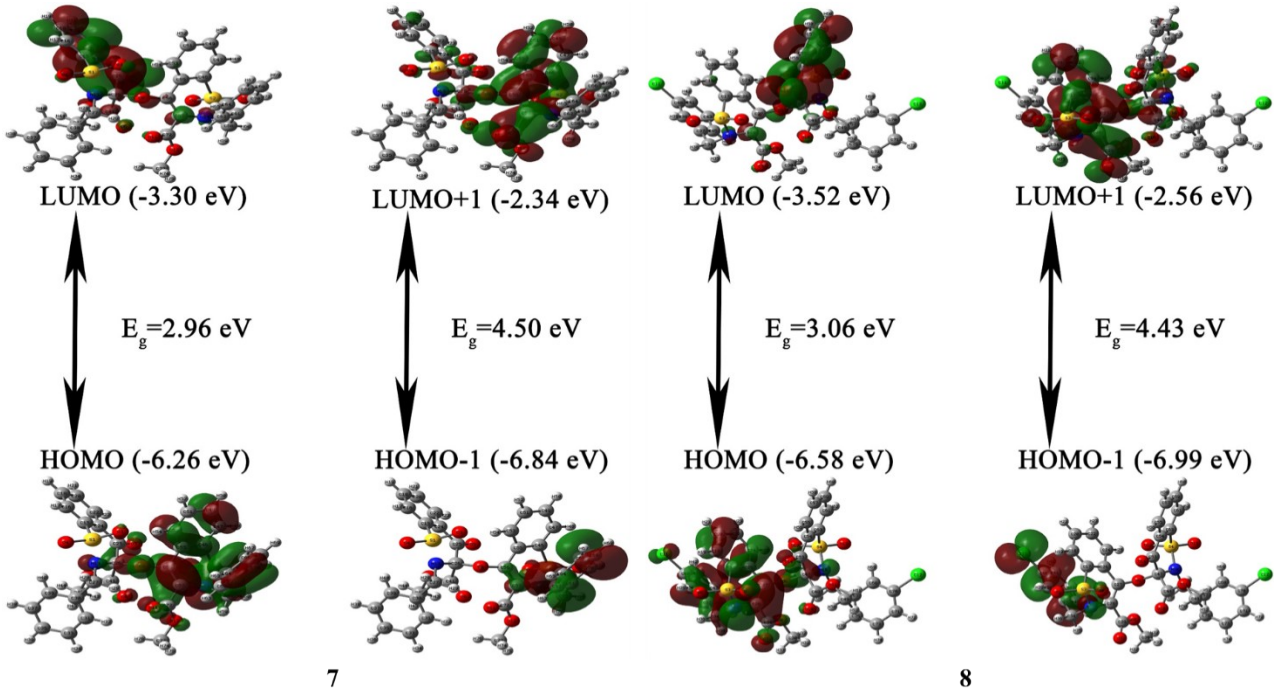

Figure S16. FMOs of the compounds **7** and **8**