Supplementary Material

Table S1: Anisotropic displacement parameters obtained from the SHADE3 server developed by Madsen *et al.*[21]

Atom	U11	U22	U33	U12	U13	U23
Piroxicam (1)						
H(2A)	0.030229	0.015605	0.024116	-0.004709	-0.006316	-0.000555
H(3A)	0.031921	0.017334	0.024358	0.000222	-0.008900	-0.000808
H(4)	0.041997	0.016338	0.033134	-0.008230	-0.007307	0.003249
H(5)	0.042970	0.024221	0.028314	-0.002603	-0.005825	0.013402
H(6)	0.033045	0.032495	0.018320	-0.002360	-0.007710	0.002375
H(7)	0.032764	0.019567	0.025718	-0.007363	-0.004583	-0.001470
H(11)	0.039047	0.019799	0.029023	0.002138	-0.007330	-0.001122
H(12)	0.042949	0.034530	0.025351	-0.000266	-0.010467	-0.009069
H(13)	0.038778	0.041994	0.023251	0.002663	-0.013967	0.005275
H(14)	0.044089	0.024341	0.033375	0.002804	-0.010314	0.008395
H(15A)	0.019425	0.044636	0.031657	0.001122	-0.005979	-0.010220
H(15B)	0.039187	0.016156	0.047325	0.001415	0.007148	-0.005402
H(15C)	0.035420	0.039477	0.023294	0.010225	0.005904	0.009442
Saccharin (2)						
H(1A)	0.023896	0.018248	0.028420	-0.008167	0.001341	0.005313
H(2)	0.024280	0.034050	0.027655	-0.012082	-0.004087	-0.002570
H(3)	0.033672	0.025973	0.042315	-0.018743	0.008340	0.003197
H(4)	0.020225	0.026743	0.030225	-0.004993	0.005891	0.013243
H(5)	0.029766	0.030994	0.021406	-0.004687	-0.004126	0.004017
Piroxicam – Saccharin (3)						
H(1A)	0.029700	0.031090	0.030083	0.017421	-0.008658	-0.012672
H(2)	0.041252	0.047994	0.027916	0.022095	-0.004808	-0.020159

H(3)	0.041325	0.040351	0.049676	0.027759	-0.015901	-0.020262
H(4)	0.057623	0.036282	0.036100	0.022000	-0.021367	-0.003857
H(5)	0.054255	0.045223	0.019517	0.017643	-0.008959	-0.010262
H(2A')	0.025048	0.029726	0.021210	0.014398	-0.003658	-0.010669
H(3A')	0.031127	0.031494	0.022935	0.016899	-0.007681	-0.009511
H(4')	0.040579	0.022921	0.025620	0.011911	-0.004558	-0.008047
H(5')	0.038191	0.037282	0.025580	0.013080	-0.000180	-0.016636
H(6')	0.030942	0.035304	0.016442	-0.000485	0.000029	-0.006971
H(7')	0.034379	0.020742	0.023666	0.002401	-0.009037	-0.004016
H(11')	0.027835	0.031900	0.024231	0.014740	-0.004399	-0.010836
H(12')	0.032787	0.029650	0.024512	0.011053	-0.012042	-0.004057
H(13')	0.034437	0.035171	0.015486	0.003338	-0.003890	-0.006244
H(14')	0.032210	0.037210	0.025160	0.014501	-0.001868	-0.014621
H(15A)	0.031102	0.045727	0.036598	0.009895	-0.010921	-0.025013
H(15B)	0.037515	0.030241	0.046267	0.015167	-0.023385	-0.007245
H(15C)	0.026407	0.043745	0.023423	-0.004496	-0.002168	-0.000811

Table S2: Comparison of bond lengths for Piroxicam (**1**) between IAM refinement, Kojic-Prodic *et al.*[27] and Gaussian OPT analysis.

Bond Lengths (Å)			
Atoms	EXP	Theoretical (OPT)	Kojic- Prodic *et al.*[27]
C(1)-C(2)	1.371(1)	1.372	1.369
C(1)-C(9)	1.469(1)	1.469	1.463
C(2)-C(3)	1.468(1)	1.471	1.462
C(3)-C(4)	1.399(1)	1.401	1.399
C(3)-C(8)	1.405(1)	1.405	1.397
C(4)-C(5)	1.391(1)	1.391	1.380
C(5)-C(6)	1.394(1)	1.395	1.374

C(6)-C(7)	1.394(1)	1.394	1.387
C(7)-C(8)	1.387(1)	1.388	1.376
C(10) - C(11)	1.399(1)	1.401	1.387
C(11) - C(12)	1.386(1)	1.389	1.381
C(12) - C(13)	1.394(1)	1.393	1.361
C(13) - C(14)	1.391(1)	1.392	1.376
N(1)-C(1)	1.436(1)	1.436	1.427
N(1)-C(15)	1.486(1)	1.483	1.479
N(2) - C(9)	1.356(1)	1.362	1.353
N(2) - C(10)	1.406(1)	1.405	1.408
N(3)-C(14)	1.341(1)	1.334	1.340
N(3)-C(10)	1.337(1)	1.337	1.320
S(1)-N(1)	1.646(1)	1.701	1.641
S(1)-C(8)	1.749(1)	1.795	1.749
S(1)-O(1)	1.436(1)	1.458	1.425
S(1)-O(2)	1.432(1)	1.455	1.427
O(3)-C(2)	1.336(1)	1.332	1.341
O(4)-C(9)	1.249(1)	1.246	1.238

Table S3: Comparison of angles for Piroxicam (**1**) between IAM refinement, Kojic-Prodic *et al.*[27] and Gaussian OPT analysis.

Angles (°)			
Atoms	EXP	Theoretical (OPT)	Kojic- Prodic *et al.*[27]
O(1)-S(1)-C(8)	108.46(2)	109.2	108.6
O(2)-S(1)-C(8)	109.85(2)	109.2	109.4
O(1)-S(1)-N(1)	108.27(2)	108.1	108.2
O(2)-S(1)-N(1)	108.16(2)	107.4	108.4
O(2)-S(1)-O(1)	119.05(2)	120.9	119.3
N(1)-S(1)-C(8)	101.60(2)	100.0	101.4

C(1)-N(1)-S(1)	112.75(2)	112.9	113.0
C(1)-N(1)-C(15)	115.72(3)	115.5	116.4
C(15)-N(1)-S(1)	115.16(3)	115.8	115.5
C(9)-N(2)-C(10)	128.88(3)	129.7	129.6
C(10)-N(3)-C(14)	117.50(4)	118.1	117.0
C(2)-C(1)-N(1)	121.20(3)	121.7	120.4
N(1)-C(1)-C(9)	118.04(3)	118.4	118.6
C(2)-C(1)-C(9)	120.75(3)	119.9	121.0
O(3)-C(2)-C(3)	115.37(3)	114.9	115.3
O(3)-C(2)-C(1)	122.59(4)	122.7	122.1
C(1)-C(2)-C(3)	122.04(3)	122.4	122.6
C(4)-C(3)-C(8)	118.09(4)	118.1	118.1
C(8)-C(3)-C(2)	120.47(3)	121.0	120.4
C(4)-C(3)-C(2)	121.42(3)	120.9	121.5
C(5)-C(4)-C(3)	119.80(3)	120.3	119.6
C(4)-C(5)-C(6)	120.95(3)	120.6	121.0
C(5)-C(6)-C(7)	120.28(4)	120.1	120.6
C(8)-C(7)-C(6)	118.19(3)	118.9	118.4
C(7)-C(8)-C(3)	122.65(3)	122.0	122.2
C(3)-C(8)-S(1)	116.40(3)	117.7	116.4
C(7)-C(8)-S(1)	120.92(2)	120.3	121.4
N(2)-C(9)-C(1)	115.33(3)	120.9	120.8
O(4)-C(9)-N(2)	124.14(4)	123.6	123.7
N(2)-C(9)-C(1)	115.33(3)	115.5	115.5
N(3)-C(10)-N(2)	112.44(3)	112.6	112.7
N(2) - C(10) - C(11)	123.88(3)	124.0	123.5
N(3)-C(10)-C(11)	123.68(4)	123.4	123.7
C(10) - C(11) - C(12)	117.60(4)	117.4	117.5

C(11) - C(12) - C(13)	119.85(4)	119.9	120.0
C(12) - C(13) - C(14)	117.79(5)	117.8	118.1
N(3)-C(14)-C(13)	123.58(4)	123.4	123.6

Table S4: Comparison of bond lengths for Saccharin (**2**) between IAM refinement, Bart[9] and Gaussian OPT analysis.

Bond lengths (Angstroms)	**EXP**	**Bart[9]**	**OPT**
C(1)-C(2)	1.387(1)	1.383(3)	1.385
C(1)-C(6)	1.390(1)	1.385(3)	1.391
C(1)-S(1)	1.757(1)	1.761(2)	1.793
C(2)-C(3)	1.399(1)	1.365(3)	1.397
C(3)-C(4)	1.399(1)	1.391(3)	1.398
C(4)-C(5)	1.395(1)	1.382(3)	1.395
C(5)-C(6)	1.388(1)	1.368(3)	1.390
C(6)-C(7)	1.479(1)	1.48(3)	1.494
C(7)-N(1)	1.372(1)	1.375(2)	1.389
O(3)-C(7)	1.224(1)	1.22(2)	1.209
N(1)-S(1)	1.668(1)	1.663(2)	1.718
S(1)-O(1)	1.434(1)	1.427(2)	1.456
S(1)-O(2)	1.433(1)	1.428(2)	1.456

Table S5: Comparison of angles for Saccharin (**2**) between IAM refinement, Bart[9] and Gaussian OPT analysis.

Bond angles (degrees)	**EXP**	**Bart[9]**	**OPT**
C(2)-C(1)-C(6)	122.54(3)	122.2(21)	122.8
C(2)-C(1)-S(1)	127.58(2)	128.1(15)	126.5
C(6)-C(1)-S(1)	122.54(3)	109.8(15)	110.7
C(1)-C(2)-C(3)	116.61(3)	116.7(21)	117.0
C(4)-C(3)-C(2)	121.43(3)	121.7(21)	121.0

C(5)-C(4)-C(3)	120.86(3)	121(21)	120.9
C(6)-C(5)-C(4)	117.93(3)	117.7(21)	118.4
C(5)-C(6)-C(1)	120.63(2)	120.8(21)	119.8
C(5)-C(6)-C(7)	126.77(2)	126.6(21)	126.2
C(1)-C(6)-C(7)	112.60(2)	112.6(21)	114.0
O(3)-C(7)-N(1)	124.41(2)	123.7(18)	124.9
O(3)-C(7)-C(6)	125.89(2)	126.5(18)	126.9
N(1)-C(7)-C(6)	109.69(2)	109.8(18)	108.2
C(7)-N(1)-S(1)	115.254(19)	115(15	116.7
O(2)-S(1)-O(1)	117.442(18)	117.4(10)	119.2
O(2)-S(1)-N(1)	109.356(16)	109.1(10)	109.8
O(1)-S(1)-N(1)	110.095(16)	110.3(10)	109.9
O(2)-S(1)-C(1)	112.902(16)	112.8(10)	112.0
O(1)-S(1)-C(1)	111.645(15)	111.8(10)	111.8
N(1)-S(1)-C(1)	92.570(12)	92.7(10)	90.4

Table S6: List of bond critical points (BCP's) found from topological analysis of experimental and theoretical models of **1**, **2** and **3** respectively

Piroxicam (1)

	ρ (e Å^{-3})			$\nabla^2\rho$ (e Å^{-5})			ε		
Atoms	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**
S(1) - O(1)	2.39	2.38	2.05	1.48	1.65	28.93	0.17	0.16	0.01
S(1) - O(2)	1.96	1.96	2.05	15.86	15.99	29.77	0.21	0.20	0.03
S(1) - N(1)	1.58	1.58	1.62	-10.92	-10.91	-8.00	0.35	0.32	0.11
S(1) - C(8)	1.39	1.39	1.51	-7.25	-7.42	-11.85	0.15	0.13	0.06
O(3) - C(2)	2.06	2.06	2.09	-18.00	-18.05	-11.27	0.15	0.14	0.01
O(3) - H(3A)	2.25	2.03	2.38	-24.80	-25.70	-61.45	0.01	0.01	0.01
O(4) - C(9)	2.62	2.59	2.58	-28.28	-27.67	-10.74	0.09	0.11	0.06
N(1) - C(1)	1.76	1.75	1.83	-9.32	-9.32	-16.90	0.09	0.10	0.07
N(1) - C(15)	1.62	1.61	1.65	-8.58	-8.32	-13.59	0.12	0.11	0.03
N(2) - C(9)	2.12	2.12	2.18	-21.42	-21.63	-22.60	0.17	0.18	0.13
N(2) - C(10)	2.08	2.07	1.94	-19.74	-19.54	-19.44	0.17	0.18	0.10
N(2) - H(2A)	2.35	2.05	2.30	-23.31	-23.75	-42.56	0.07	0.06	0.05
N(3) - C(10)	2.26	2.25	2.34	-17.88	-18.44	-25.85	0.17	0.17	0.17
N(3) - C(14)	2.39	2.37	2.25	-22.93	-22.74	-22.35	0.16	0.16	0.10

C(1) - C(2)	2.23	2.24	2.18	-21.42	-21.50	-21.72	0.42	0.44	0.41
C(1) - C(9)	1.91	1.90	1.85	-14.88	-14.97	-16.69	0.29	0.30	0.21
C(2) - C(3)	1.95	1.95	1.85	-16.25	-16.26	-17.22	0.24	0.23	0.12
C(3) - C(4)	2.05	2.06	2.06	-18.06	-18.03	-20.34	0.27	0.26	0.19
C(3) - C(8)	1.90	1.90	2.03	-15.07	-15.00	-19.46	0.18	0.18	0.20
C(4) - C(5)	2.16	2.18	2.09	-20.37	-20.44	-21.01	0.28	0.27	0.19
C(5) - C(6)	1.99	2.00	2.08	-18.04	-17.84	-20.84	0.19	0.21	0.19
C(6) - C(7)	2.09	2.11	2.08	-18.64	-18.85	-20.78	0.21	0.20	0.19
C(7) - C(8)	2.14	2.14	2.09	-18.67	-18.78	-20.57	0.24	0.23	0.20
C(10) - C(11)	2.08	2.05	2.07	-18.54	-18.33	-20.56	0.28	0.30	0.22
C(11) - C(12)	2.19	2.18	2.11	-20.30	-20.35	-21.26	0.21	0.22	0.20
C(12) - C(13)	2.01	2.00	2.09	-16.42	-16.59	-20.88	0.19	0.22	0.19
C(13) - C(14)	2.14	2.13	2.11	-18.44	-19.64	-21.29	0.23	0.04	0.22
C(4) - H(4)	1.65	1.70	1.92	-15.25	-15.40	-23.94	0.07	0.06	0.01
C(5) - H(5)	1.79	1.86	1.91	-18.87	-19.12	-23.69	0.07	0.06	0.01
C(6) - H(6)	1.75	1.75	1.91	-16.30	16.55	-23.69	0.10	0.09	0.02
C(7) - H(7)	1.71	1.68	1.92	-14.99	-14.77	-23.94	0.06	0.05	0.01
C(11) - H(11)	1.85	1.75	1.92	-17.45	-16.58	-23.98	0.06	0.05	0.02

C(12) - H(12)	1.76	1.78	1.92	-16.19	-16.08	-23.81	0.04	0.04	0.01
C(13) - H(13)	1.79	1.78	1.90	-16.61	-16.48	-23.32	0.08	0.07	0.02
C(14) - H(14)	1.88	1.73	1.94	-18.44	-16.17	-24.39	0.08	0.06	0.03
C(15) - H(15A)	1.78	1.77	1.94	-15.21	-14.90	-24.20	0.10	0.06	0.03
C(15) - H(15B)	1.74	1.80	1.92	-16.37	-16.64	-23.71	0.05	0.03	0.03
C(15) - H(15C)	1.78	1.78	1.92	-15.30	-15.08	-23.74	0.05	0.04	0.03

Saccharin (2)									
	ρ (e Å^{-3})			$\nabla^2\rho$ (e Å^{-5})			ε		
Atoms	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**
S(1) - O(1)	2.26	2.26	2.01	-5.47	-5.25	32.43	0.08	0.08	0.07
S(1) - O(2)	2.27	2.27	2.02	-7.71	-7.48	32.65	0.06	0.06	0.07
S(1) - N(1)	1.40	1.40	1.51	-5.86	-5.92	-6.87	0.06	0.06	0.07
S(1) - C(1)	1.32	1.32	1.49	-5.15	-5.12	-11.94	0.02	0.02	0.05
O(3) - C(7)	2.97	2.97	2.73	-39.32	-39.66	-1.93	0.15	0.15	0.10
N(1) - C(7)	2.14	2.14	2.11	-20.21	-20.45	-22.77	0.23	0.23	0.08
C(1) - C(2)	2.21	2.20	2.10	-17.77	-17.87	-20.45	0.26	0.26	2.20
C(1) - C(6)	2.19	2.19	2.13	-17.04	-17.21	-21.33	0.22	0.22	0.19
C(2) - C(3)	2.09	2.09	2.08	-17.32	-17.50	-20.00	0.20	0.22	0.19
C(3) - C(4)	2.11	2.11	2.09	-18.87	-19.07	-20.45	0.23	0.23	0.18
C(4) - C(5)	2.15	2.15	2.11	-18.54	-18.52	-20.81	0.24	0.25	0.19
C(5) -C(6)	2.20	2.20	2.12	-17.39	-17.44	-21.02	0.21	0.22	0.18
C(6) -C(7)	1.84	1.84	1.86	-13.25	-13.37	-17.42	0.19	0.19	0.10
N(1) - H(1A)	2.04	2.10	2.27	-21.30	-20.85	-43.61	0.07	0.06	0.04

C(2) - H(2)	1.84	1.81	1.94	-17.66	-17.26	-25.78	0.06	0.06	0.01
C(3) - H(3)	1.84	1.78	1.94	-16.62	-15.73	-25.59	0.06	0.05	0.01
C(4) - H(4)	1.67	1.69	1.94	-17.35	-17.28	-25.57	0.06	0.06	0.01
C(5) -H(5)	1.85	1.85	1.95	-15.68	-15.52	-26.05	0.05	0.04	0.01

Co-crystal (3)									
	ρ (e Å^{-3})			$\nabla^2\rho$ (e Å^{-5})			ε		
Atoms	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**	**EXP**	**SH_D**	**SP**
Piroxicam									
S(1') - O(1')	2.31	2.29	2.00	-7.75	-6.37	32.2	0.07	0.07	0.03
S(1') - O(2')	2.31	2.30	1.98	-0.62	0.12	32.1	0.19	0.19	0.01
S(1') - N(1')	1.46	1.45	1.66	-4.56	-4.10	-4.5	0.64	0.63	0.14
S(1') - C(8')	1.38	1.38	1.51	-8.34	-8.61	-12.3	0.13	0.14	0.05
O(3') - C(2')	2.44	2.43	2.23	-27.06	-26.69	-4.8	0.17	0.17	0.04
O(4') - C(9')	2.61	2.56	2.68	-30.19	-29.65	-4.8	0.06	0.05	0.11
N(1') - C(1')	1.95	1.94	1.87	-15.10	-14.95	-19.5	0.13	0.14	0.06
N(1') - C(15)	1.59	1.54	1.67	-6.80	-5.52	-15.7	0.06	0.01	0.04
N(2') - C(9')	2.00	1.99	2.06	-18.33	-18.03	-23.8	0.22	0.23	0.13
N(2') - C(10')	2.36	2.36	2.15	-23.99	-23.77	-21.3	0.24	0.25	0.11
N(3') - C(10')	2.20	2.18	2.31	-23.76	-23.23	-28.3	0.12	0.13	0.16
N(3') - C(14')	2.26	2.27	2.21	-22.76	-22.72	-24.5	0.18	0.19	0.10

C(1') - C(2')	1.95	1.95	2.12	-15.47	-15.65	-19.7	0.45	0.43	0.43
C(1') - C(9')	1.93	1.93	1.96	-16.03	-16.25	-19.0	0.29	0.29	0.16
C(2') - C(3')	1.75	1.75	1.80	-12.45	-12.52	-15.5	0.16	0.16	0.14
C(3') - C(4')	2.04	2.04	2.10	-17.81	-18.07	-20.2	0.14	0.14	0.19
C(3') - C(8')	2.06	2.07	2.07	-17.15	-17.47	-19.6	0.27	0.26	0.19
C(4') - C(5')	2.16	2.15	2.13	-20.67	-20.54	-20.9	0.15	0.16	0.20
C(5') - C(6')	2.11	2.12	2.13	-19.41	-19.74	-21.1	0.24	0.24	0.19
C(6') - C(7')	1.98	1.98	2.12	-16.40	-16.80	-20.8	0.22	0.21	0.19
C(7') - C(8')	2.13	2.12	2.10	-20.27	-20.29	-20.2	0.17	0.17	0.20
C(10') - C(11')	2.01	2.00	2.10	-18.68	-18.18	-20.5	0.28	0.28	0.22
C(11') - C(12')	2.23	2.22	2.17	-21.95	-21.71	-21.6	0.27	0.27	0.23
C(12') - C(13')	2.03	2.01	2.07	-16.97	-16.88	-19.9	0.17	0.18	0.18
C(13') - C(14')	2.24	2.24	2.25	-21.41	-21.58	-23.6	0.31	0.32	0.23
N(2') - H(2A')	1.76	1.86	2.34	-25.35	-24.40	-44.7	0.02	0.02	0.04
N(3') - H(3A')	1.90	2.00	2.34	-23.04	-23.22	-44.7	0.05	0.05	0.04
C(4') - H(4')	1.71	1.78	1.93	-14.92	-15.75	-25.0	0.05	0.05	0.01
C(5') - H(5')	1.87	1.82	1.94	-17.92	-16.70	-25.4	0.05	0.03	0.01
C(6') - H(6')	1.81	1.75	1.94	-17.06	-16.17	-25.5	0.04	0.04	0.01

C(7') - H(7')	1.73	1.76	1.95	-15.51	-15.85	-26.0	0.07	0.07	0.01
C(11') - H(11')	1.76	1.79	1.92	-17.24	-17.27	-24.3	0.06	0.06	0.02
C(12') - H(12')	1.78	1.76	1.95	-17.35	-17.05	-25.9	0.04	0.03	0.01
C(13') - H(13')	1.83	1.78	1.93	-16.59	-15.88	-24.8	0.08	0.07	0.02
C(14') - H(14')	1.73	1.77	1.94	-17.03	-17.64	-25.6	0.03	0.01	0.03
C(15) - H(15A)	1.79	1.71	1.96	-14.42	-12.96	-25.8	0.14	0.11	0.03
C(15) - H(15B)	1.75	1.73	1.96	-14.54	-13.82	-26.4	0.11	0.11	0.04
C(15) - H(15C)	1.74	1.72	1.95	-15.72	-14.90	-25.0	0.05	0.08	0.04
Saccharin									
S(1) - O(1)	1.90	1.88	2.02	25.44	26.86	32.8	0.38	0.37	0.07
S(1) - O(2)	2.38	2.37	2.02	-10.38	-9.85	32.1	0.09	0.10	0.07
S(1) - N(1)	1.37	1.37	1.56	-5.63	-5.70	-4.0	0.36	0.36	0.07
S(1) - C(1)	1.40	1.40	1.49	-7.15	-7.24	-11.8	0.12	0.12	0.06
O(3) - C(7)	2.93	2.91	2.78	-37.88	-37.72	0.2	0.10	0.10	0.10
N(1) - C(7)	2.21	2.21	2.09	-24.01	-24.05	-22.8	0.21	0.22	0.07
C(1) - C(2)	1.91	1.88	2.09	-16.52	-16.19	-20.2	0.35	0.38	0.20
C(1) - C(6)	2.06	2.05	2.15	-18.73	-18.89	-20.8	0.26	0.26	0.20
C(2) - C(3)	2.12	2.11	2.10	-19.49	-19.31	-20.4	0.17	0.17	0.19

C(3) - C(4)	2.16	2.16	2.10	-19.19	-19.14	-20.4	0.10	0.11	0.19
C(4) - C(5)	1.98	1.96	2.12	-16.80	-16.24	-20.8	0.25	0.28	0.19
C(5) - C(6)	2.21	2.21	2.13	-21.57	-21.56	-21.1	0.28	0.28	0.18
C(6) - C(7)	1.66	1.66	1.85	-11.74	-11.81	-17.0	0.15	0.16	0.11
N(1) - H(1A)	1.80	1.87	2.27	-22.20	-21.28	-43.7	0.05	0.05	0.04
C(2) - H(2)	1.80	1.74	1.95	-15.94	-14.87	-25.8	0.05	0.03	0.01
C(3) - H(3)	1.82	1.77	1.95	-16.89	-15.75	-26.0	0.03	0.02	0.01
C(4) - H(4)	1.79	1.76	1.97	-16.10	-15.12	-26.6	0.03	0.02	0.01
C(5) - H(5)	1.74	1.76	1.92	-16.62	-16.73	-25.2	0.03	0.02	0.01

Table S7: List of ring critical points (RCPs) found from topological analysis of experimental and theoretical models of complexes 1, 2 and 3.

Ring CPs					Eigenvalues		
Atoms involved	**Type of Analysis**	**Ring Number**	**ρ(e Å^{-3})**	**∇^2ρ(e Å^{-5})**	**λ1**	**λ2**	**λ3**
Co-crystal							
S(1') C(8') C(3') C(2') C(1')	EXP	1	0.158	2.3	-0.28	1.08	1.53

N(1')							
	SH_D		0.160	2.3	-0.25	1.12	1.44
	SP		0.124	2.8	-0.01	0.06	0.07
C(3') C(4') C(5') C(6') C(7') C(8')	EXP	2	0.156	2.9	-0.25	1.56	1.58
	SH_D		0.160	3.0	-0.23	1.57	1.67
	SP		0.140	3.9	-0.02	0.09	0.09
C(2') C(1') C(4) C(5) O(3')	EXP	3	0.023	0.3	-0.03	0.02	0.29
	SH_D		0.022	0.3	-0.03	0.02	0.27
	SP		0.018	0.2	0.00	0.00	0.01
C(1') C(19') N(2') C(4)	EXP	4					
	SH_D						
	SP		0.023	0.2	0.00	0.00	0.01
C(2') C(1') C(9') N(2') H(2A') O(3')	EXP	5	0.135	2.4	-0.28	0.99	1.70
	SH_D		0.133	2.4	-0.27	0.99	1.64
	SP		0.113	2.8	-0.01	0.05	0.08
S(1') N(1') C(15) C(4) H(4) O(2')	EXP	6					

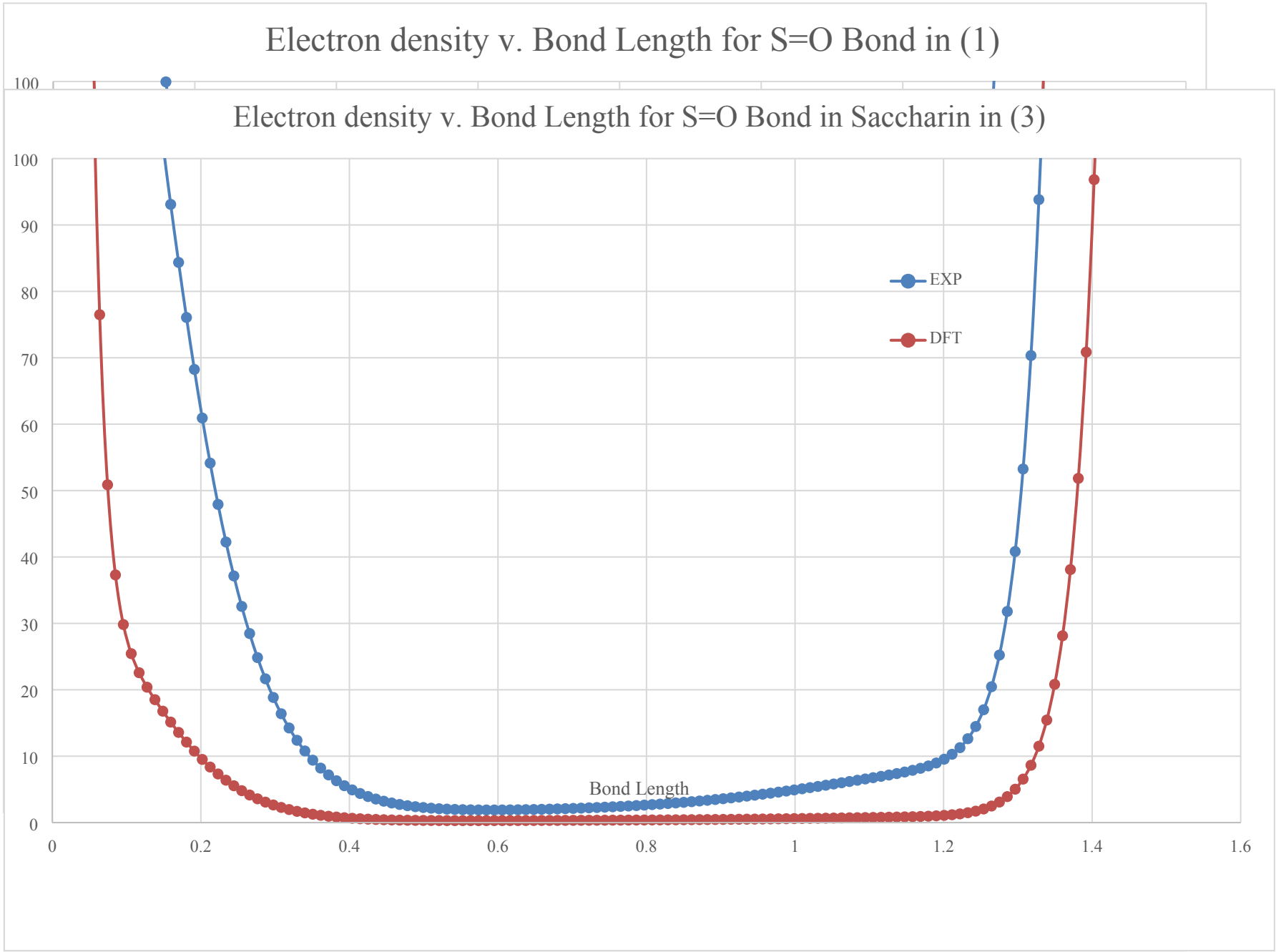
	SH_D		0.021	0.3	-0.04	0.09	0.24
	SP		0.022	0.3	0.00	0.00	0.01
C(9') O(4') N(3') C(10') N(2')	EXP	7	0.122	2.0	-0.33	0.55	1.82
	SH_D		0.127	2.1	-0.36	0.54	1.92
	SP		0.104	2.1	-0.01	0.03	0.07
O(3') H(2A') N(2') C(4) C(5)	EXP	8					
	SH_D						
	SP		0.019	0.3	0.00	0.00	0.01
C(10') C(11') C(12') C(13') C(14') N(3')	EXP	9	0.178	3.3	-0.32	1.66	1.92
	SH_D		0.176	3.3	-0.29	1.71	1.90
	SP		0.154	4.2	-0.02	0.09	0.11
N(2') C(10') C(11') C(2) C(3) C(4)	EXP	10	0.029	0.3	-0.05	0.01	0.37
	SH_D		0.028	0.3	-0.04	0.01	0.36
	SP		0.025	0.3	0.00	0.00	0.01
C(11') C(12') H(12') O(2) S(1) C(1) C(12)	EXP	11	0.026	0.3	-0.03	0.05	0.29
	SH_D		0.025	0.3	-0.03	0.05	0.27

	SP		0.023	0.3	0.00	0.00	0.01
S(1) C(1) C(6) C(7) N(1)	EXP	12	0.302	4.7	-0.80	2.39	3.11
	SH_D		0.289	4.6	-0.80	2.29	3.14
	SP		0.235	6.3	-0.03	0.13	0.16
C(1) C(2) C(3) C(4) C(5) C(6)	EXP	13	0.145	3.0	-0.12	1.33	1.84
	SH_D		0.163	3.1	-0.24	1.49	1.86
	SP		0.144	4.0	-0.02	0.08	0.10
O(3') C(2') C(1') C(9') N(2') H(2A') C(4) C(5)	EXP	14					
	SH_D						
	SP		0.018	0.2	0.00	0.00	0.01
Piroxicam							
S(1) N(1) C(1) C(2) C(3) C(8)	EXP	1	0.177	2.5	-0.35	1.31	1.51
	SH_D		0.182	2.5	-0.36	1.31	1.57
	SP		0.132	2.9	-0.01	0.06	0.07

C(3) C(4) C(5) C(6) C(7) C(8)	EXP	2	0.178	3.1	-0.29	1.65	1.74
	SH_D		0.190	3.2	-0.34	1.66	1.86
	SP		0.148	3.9	-0.02	0.08	0.09
C(2) C(1) C(9) O(4) H(3A) O(3)	EXP	3	0.159	2.7	-0.42	1.26	1.87
	SH_D		0.159	2.8	-0.41	1.21	1.96
	SP		0.141	3.1	-0.02	0.07	0.08
C(1) C(9) N(2) H(2A) N(1)	EXP	4					
	SH_D						
	SP		0.127	2.5	-0.02	0.01	0.11
C(9) N(2) C(10) C(11) H(11) O(4)	EXP	5	0.096	1.5	-0.27	0.48	1.24
	SH_D		0.094	1.4	-0.24	0.37	1.28
	SP		0.078	1.5	-0.01	0.02	0.05
C(10) C(11) C(12) C(13) C(14) N(3)	EXP	6	0.185	3.5	-0.32	1.70	2.10
	SH_D		0.193	3.6	-0.32	1.73	2.16
	SP		0.162	4.2	-0.02	0.09	0.10
Saccharin							

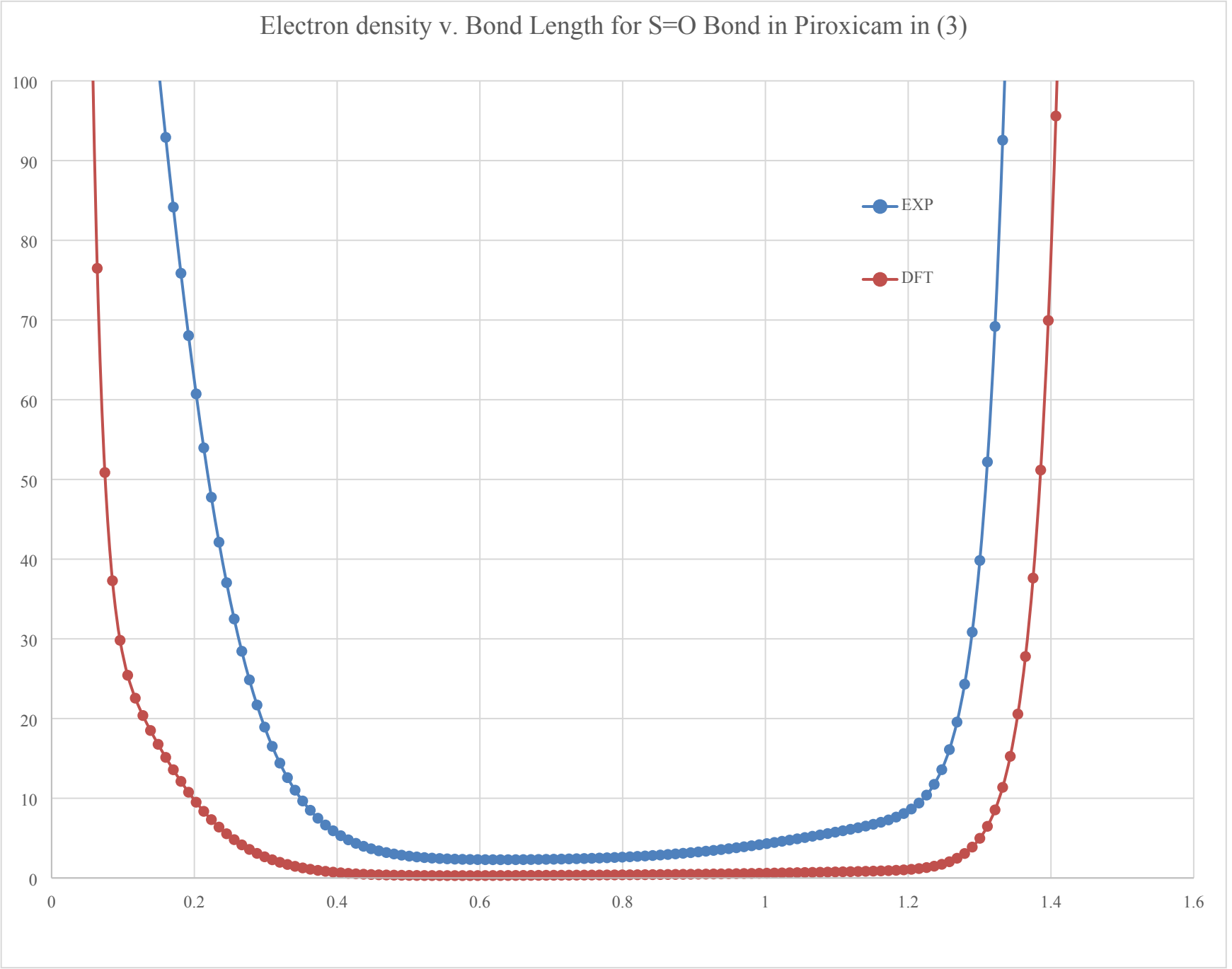
N(1) S(1) C(1) C(6) C(7)	EXP	1	0.319	4.700	-0.95	2.54	3.07
	SH_D		0.326	4.700	-0.98	2.60	3.04
	SP		0.241	5.924	-0.03	0.12	0.16
C(1) C(2) C(3) C(4) C(5) C(6)	EXP	2	0.189	3.300	-0.37	1.67	1.97
	SH_D		0.186	3.300	-0.32	1.58	2.00
	SP		0.150	3.887	-0.02	0.08	0.10

(a)


Electron density v. Bond Length for S=O Bond in (1)
Electron density v. Bond Length for S=O Bond in Saccharin in (3)
100
90
80
70
60
50
40
30
20
10
0
EXP
DFT
Bond Length
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6

(b)

(c)


Electron density v. Bond Length for S=O Bond in Piroxicam in (3)
100
90
80
70
60
50
40
30
20
10
0
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
EXP
DFT

(d)

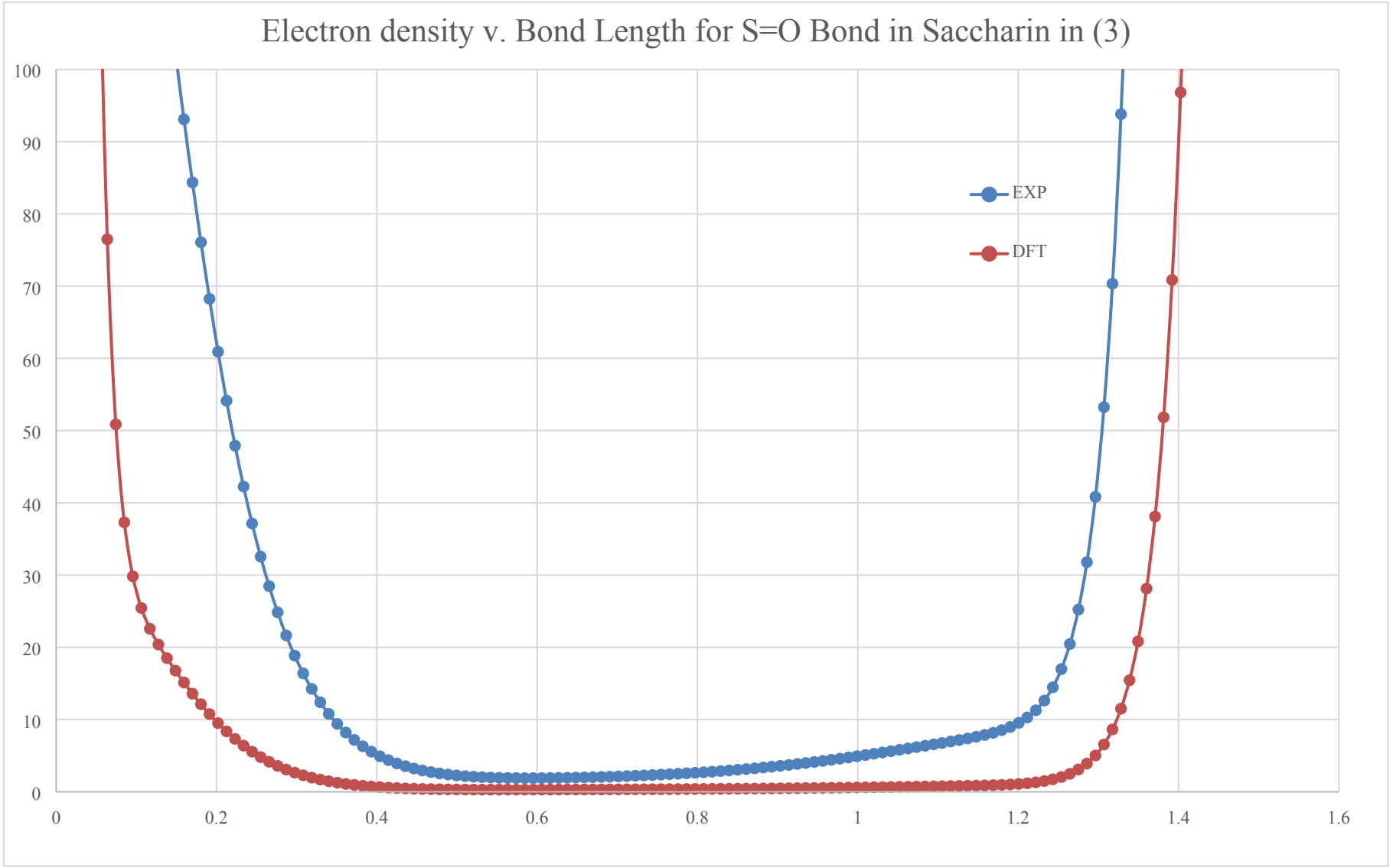
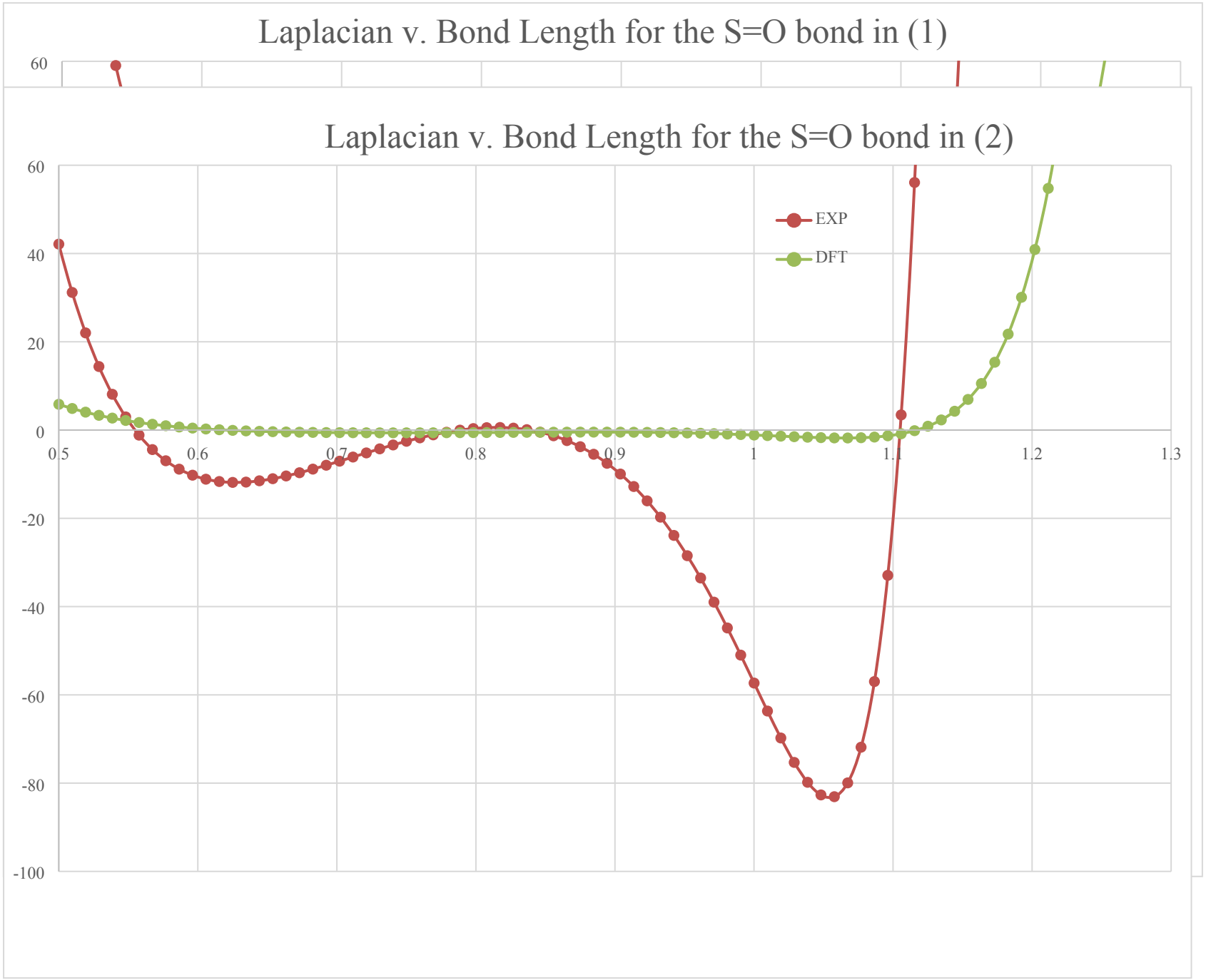

Electron density v. Bond Length for S=O Bond in Saccharin in (3)
100
90
80
70
60
50
40
30
20
10
0
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
EXP
DFT

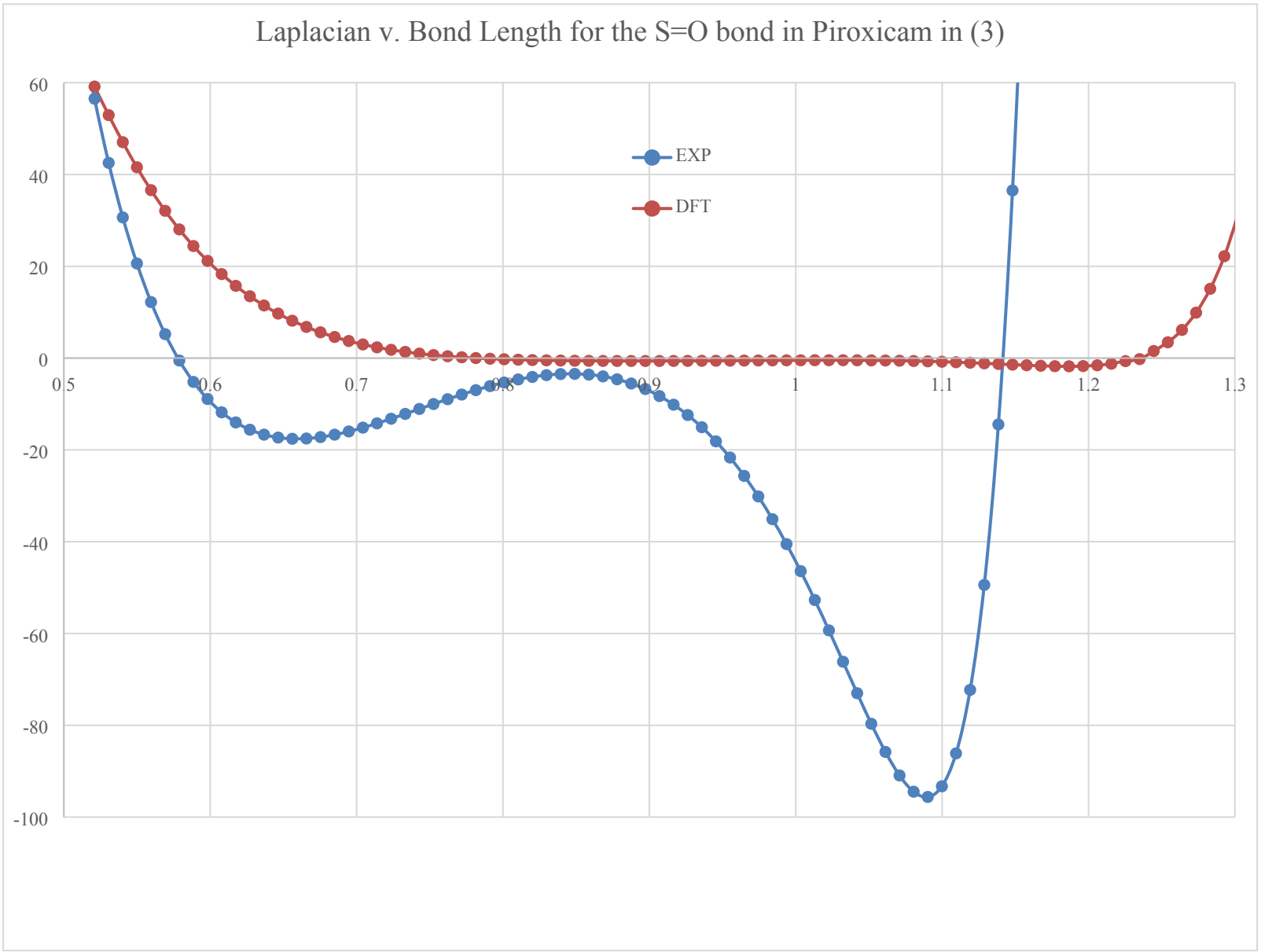
Figure S1: Electron density (ρ) y-axis, bond length (x-axis)plots along the S=O bonds in (a) (1), (b) (2), (c) piroxicam in (3) and (d) saccharin in (3)

(a)


Laplacian v. Bond Length for the S=O bond in (1)
60
Laplacian v. Bond Length for the S=O bond in (2)
60
40
20
0
-20
-40
-60
-80
-100
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
EXP
DFT

(b)

(c)


Laplacian v. Bond Length for the S=O bond in Piroxicam in (3)
60
40
20
0
-20
-40
-60
-80
-100
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
EXP
DFT

(d)

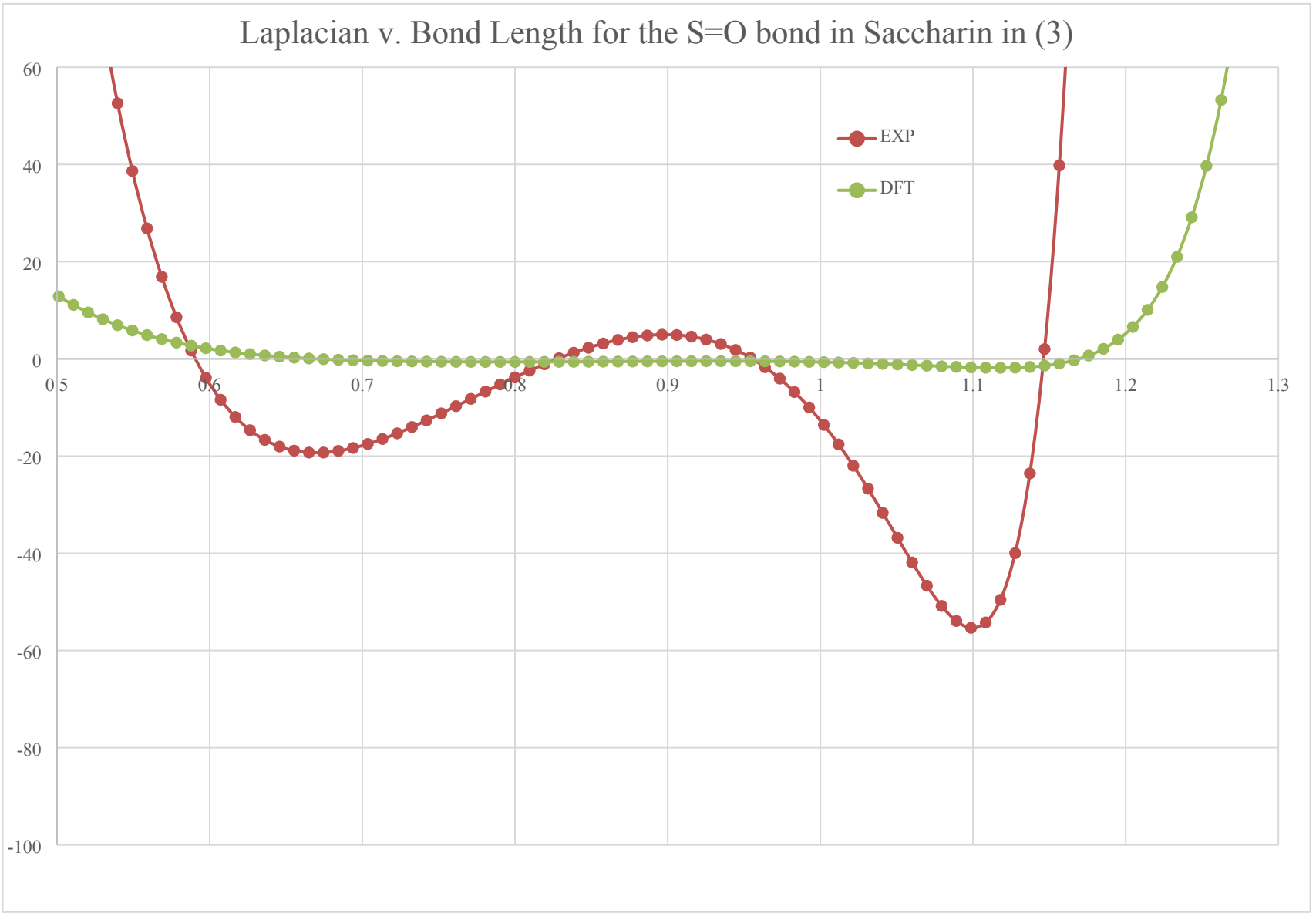

Laplacian v. Bond Length for the S=O bond in Saccharin in (3)
60
40
20
0
-20
-40
-60
-80
-100
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
EXP
DFT

Figure S2: Laplacian plots along the S=O bonds in (a) (1), (b) (2), (c) piroxicam in (3) and (d) saccharin in (3)

Table S8: Geometrical details for the hydrogen bonds found in complexes (1), (2) and (3)

	d1-2(Å)	d1-3 (Å)	DHA angle(°)
Intermolecular			
N(2)–H(2A) ··· O(2)	2.194	3.002	135.9
C(5) – H(5) ··· O(2)	2.363	3.130	126.4
C(5) – H(5) ··· O(1)	2.372	3.213	133.3
C(14) – H(14) ··· O(4)	2.558	3.631	170.7
C(15) – H(15A) ··· O(1)	2.469	3.455	150.7
C(15) – H(15B) ··· O(1)	2.660	3.464	130.6
Intramolecular			
N(2) - H(2A) ··· N(1)	2.226	2.728	130.7
O(3) - H(3A) ··· O(4)	1.668	2.563	152.2
C(11) - H(11) ···O(4)	2.244	2.893	116.4

Table S9: Topological details of the hydrogen bonds present in (1), (2) and (3)

	ρ / eÅ^{-3}	$\nabla^2\rho$ / eÅ^{-5}	G / E_h eÅ^{-3}	V / E_h eÅ^{-3}	H / E_h eÅ^{-3}	E_{HB} / kJ mol^{-1}
Intermolecular						
N(2)–H(2A) ··· O(2)	0.073	1.248	0.07	-0.05	0.02	19.45
Shade	0.072	1.151	0.06	-0.05	0.02	19.45
C(5) – H(5) ··· O(2)	0.049	0.750	0.04	-0.03	0.01	11.67
	0.053	0.798	0.04	-0.03	0.01	11.67
C(5) – H(5) ··· O(1)	0.045	0.739	0.04	-0.03	0.01	11.67
	0.048	0.789	0.04	-0.03	0.01	11.67
C(14) – H(14) ··· O(4)	0.012	0.437	0.02	-0.01	0.01	3.89
	0.025	0.530	0.03	-0.02	0.01	7.78
C(15) – H(15A) ··· O(1)	0.039	0.672	0.03	-0.02	0.01	7.78
	0.046	0.684	0.04	-0.03	0.01	11.67
C(15) – H(15B) ··· O(1)	0.047	0.743	0.04	-0.03	0.01	11.67
	0.054	0.770	0.04	-0.03	0.01	11.67
Intramolecular						
N(2) - H(2A) ··· N(1)	0.166	2.185	0.14	-0.13	0.01	50.57
Shade	0.157	2.072	0.13	-0.12	0.01	46.68
DFT						
O(3) - H(3A) ···	0.362	5.038	0.38	-0.41	0.01	159.51

O(4)						
	0.350	4.497	0.35	-0.38	-0.03	147.84
C(11) - H(11) ··· O(4)	0.119	1.606	0.10	-0.08	0.01	31.12
	0.118	1.556	0.10	-0.08	0.01	31.12
Close Contacts						
C(3)…C(12)	0.034	0.313	0.02	-0.01	0.00	3.89
Shade	0.034	0.312	0.02	-0.01	0.00	3.89
C(4)…C(10)	0.037	0.359	0.02	-0.01	0.01	3.89
	0.037	0.355	0.02	-0.01	0.00	3.89
C(5)…C(9)	0.036	0.343	0.02	-0.01	0.00	3.89
	0.035	0.345	0.02	-0.01	0.01	3.89
H(12)…H(6)	0.013	0.599	0.03	-0.02	0.01	7.78
H(11)…H(15C)	0.018	0.615	0.03	-0.02	0.01	7.78
	0.018	0.615	0.03	-0.02	0.01	7.78
	0.027	0.349	0.02	-0.01	0.01	3.89

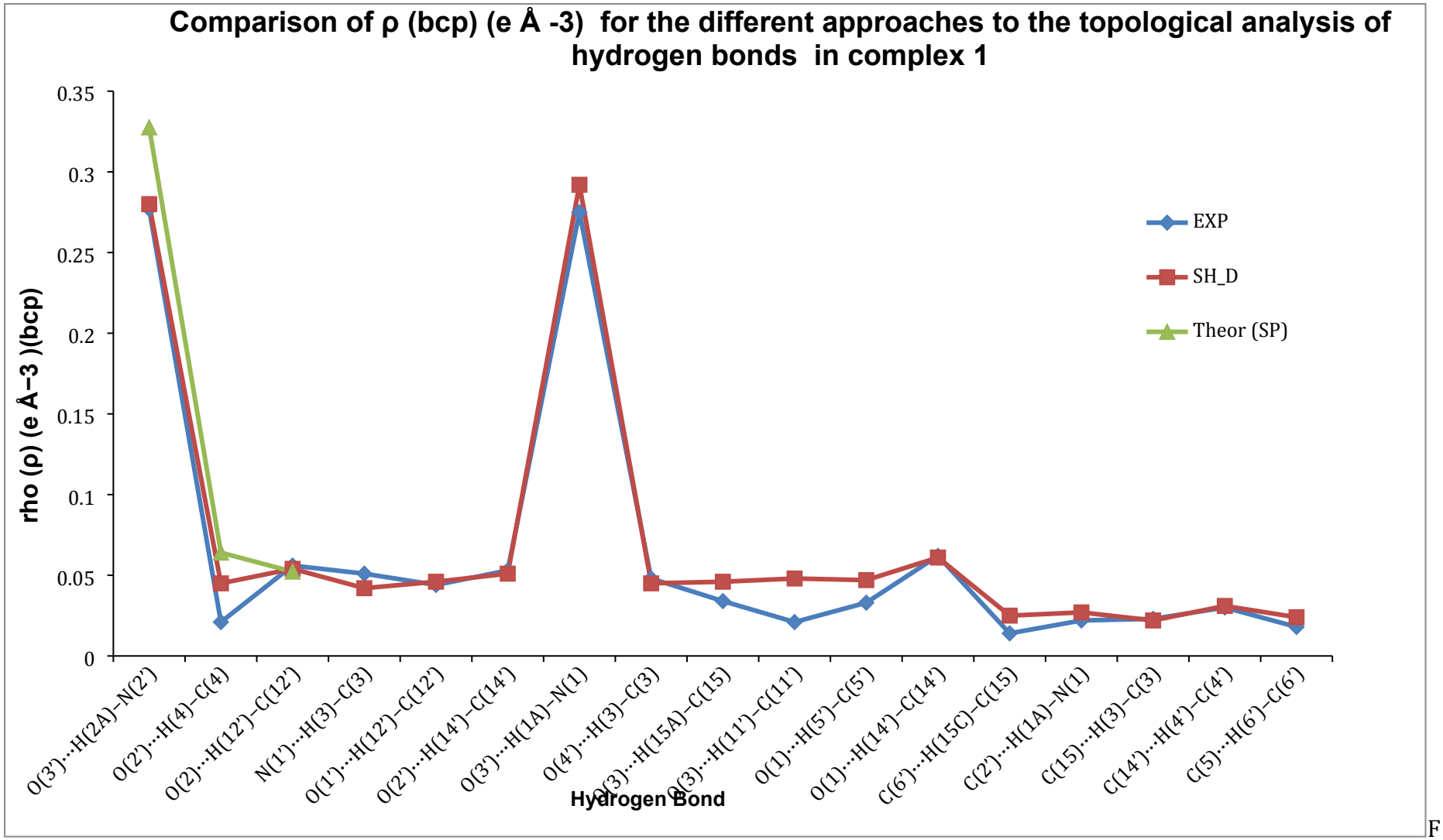


Figure S2 (a): A comparison of the ρ values from topological analysis of hydrogen bonds between EXP, SH_D and Theor (SP) analysis in complex 1

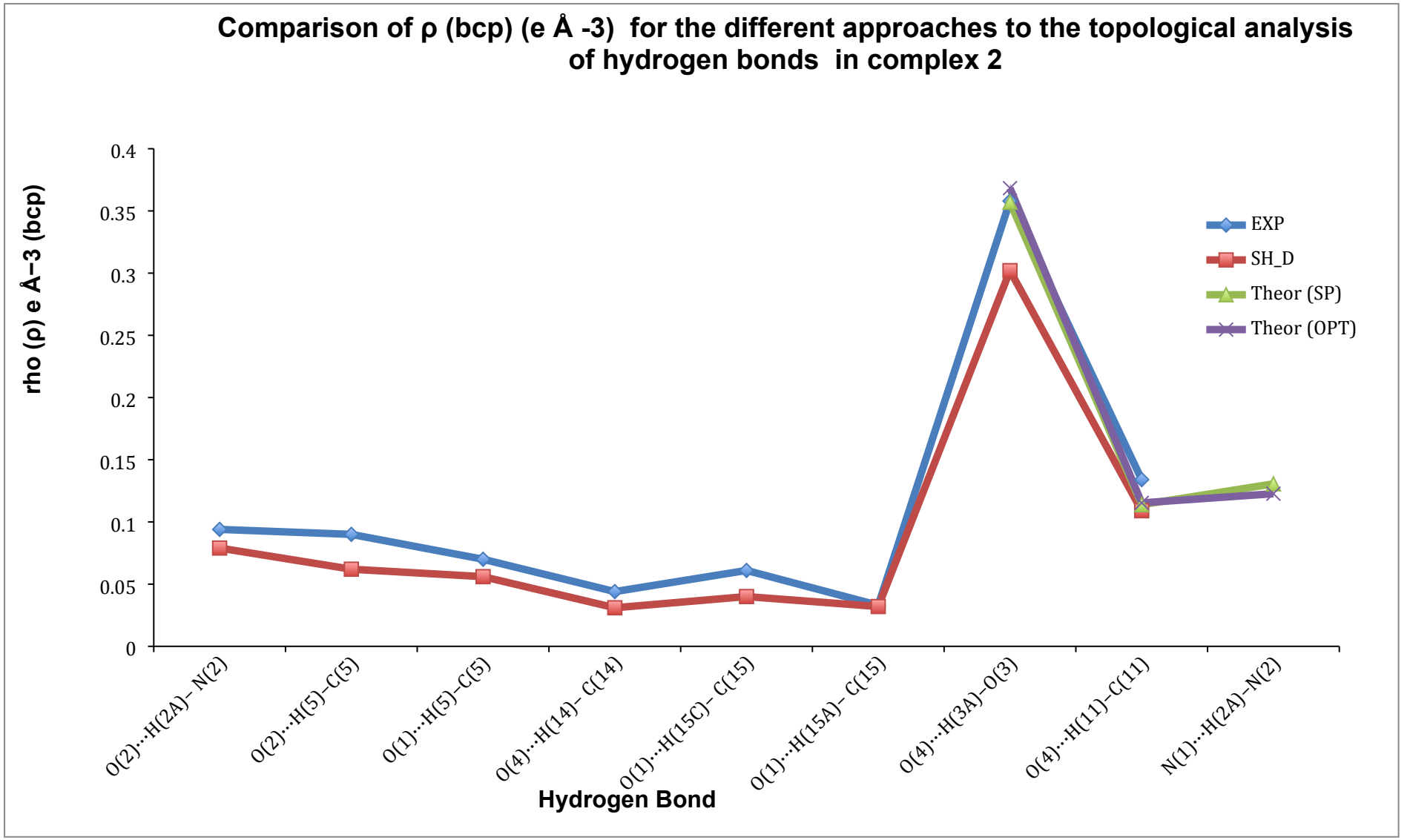


Figure S2 (b): A comparison of the ρ values from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex 2

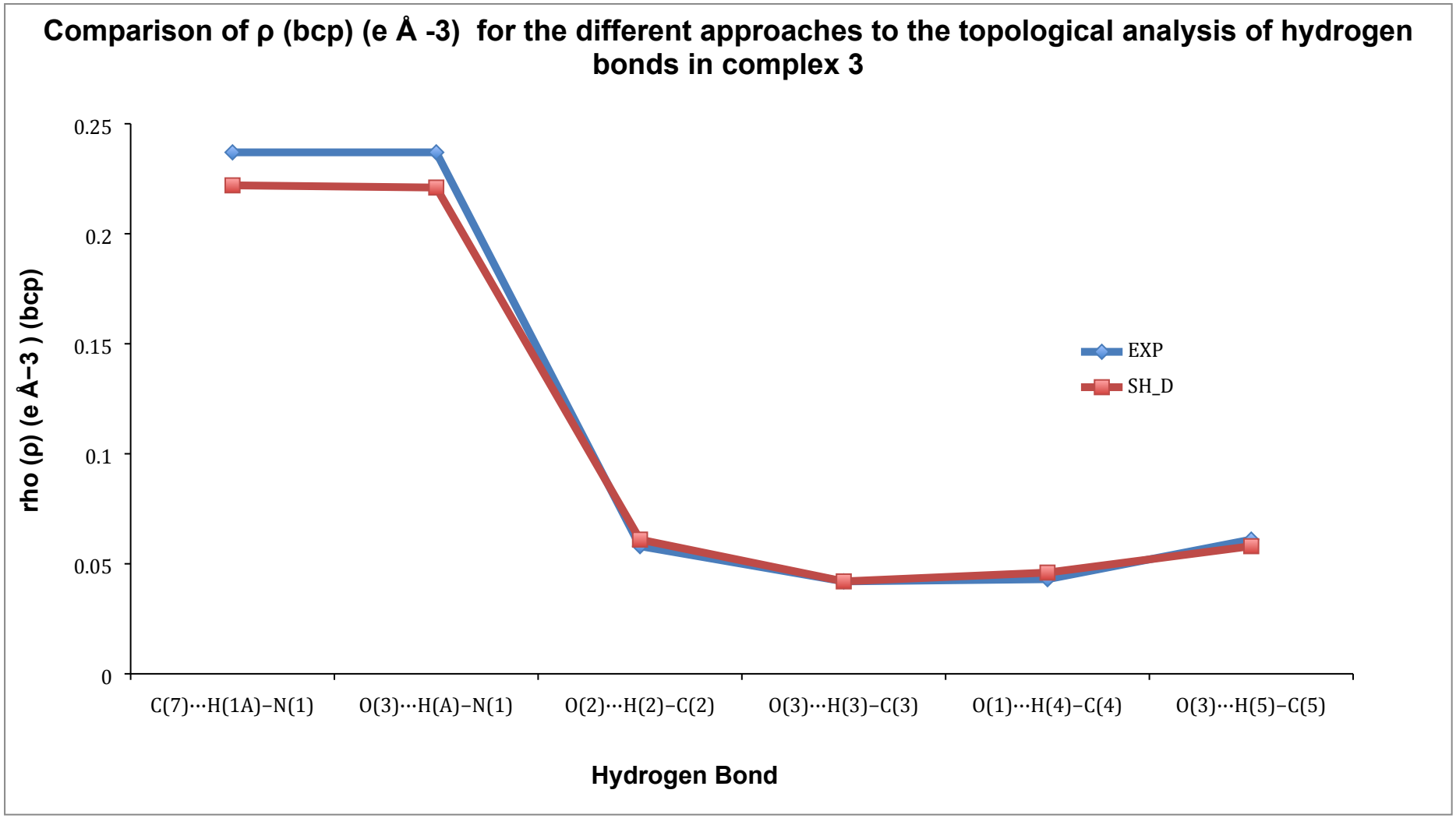


Figure S2 (c): A comparison of the ρ values from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex 3

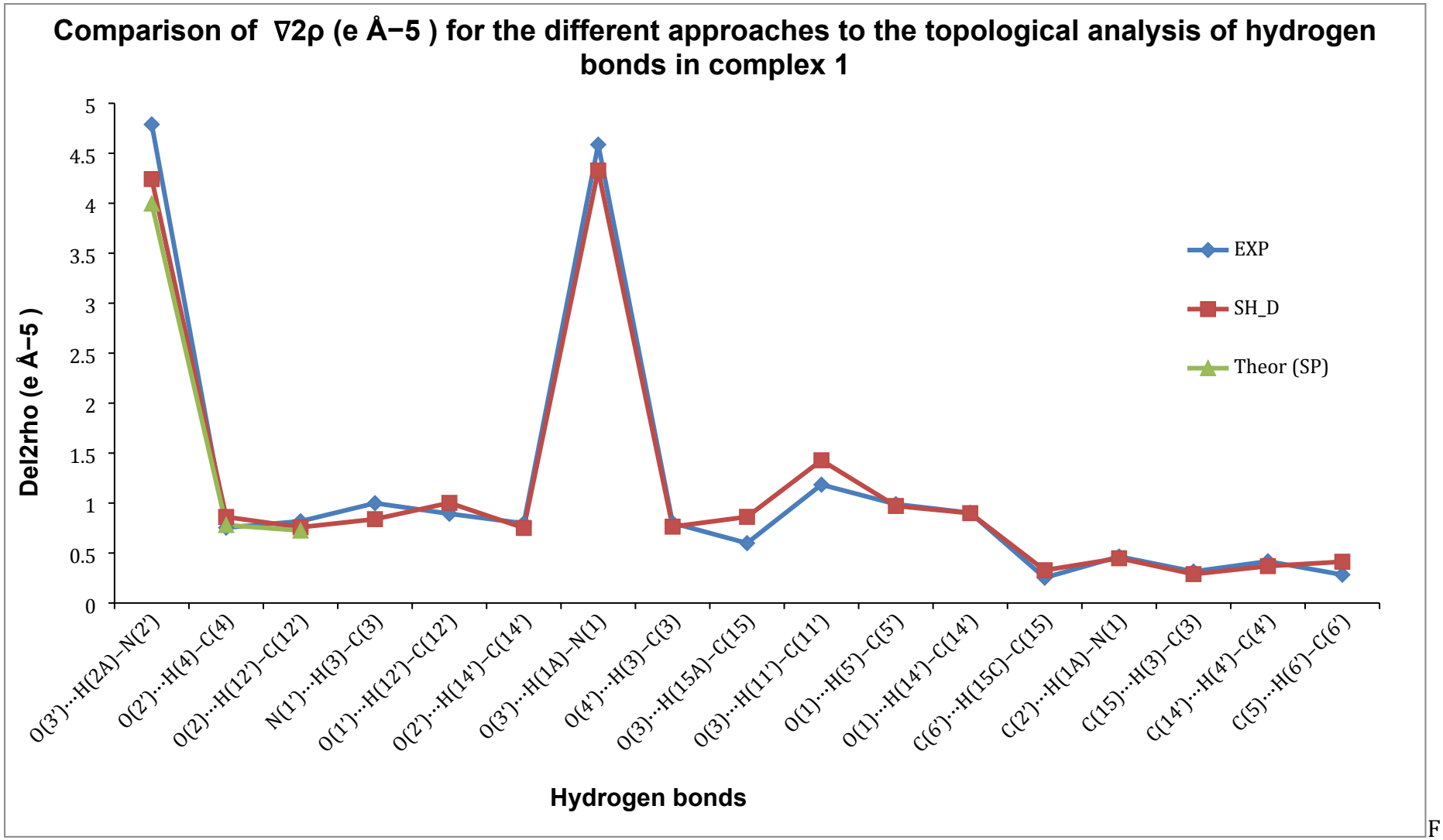


Figure S2 (d): A comparison of the $\nabla^2\rho$ values from topological analysis of hydrogen bonds between EXP, SH_D and Theor (SP) analysis in complex 1

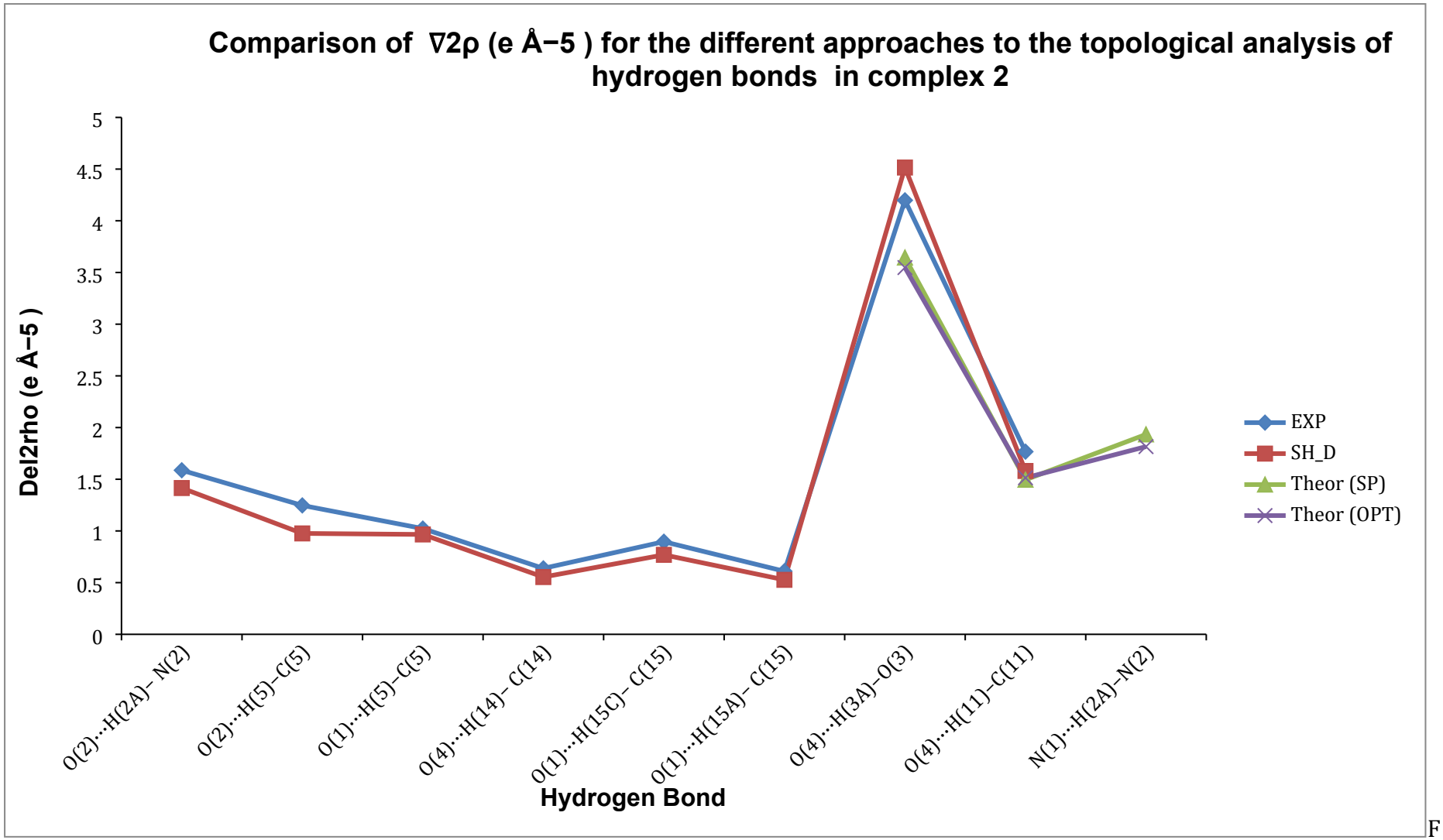


Figure S2(e): A comparison of the $\nabla^2\rho$ values from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex 2

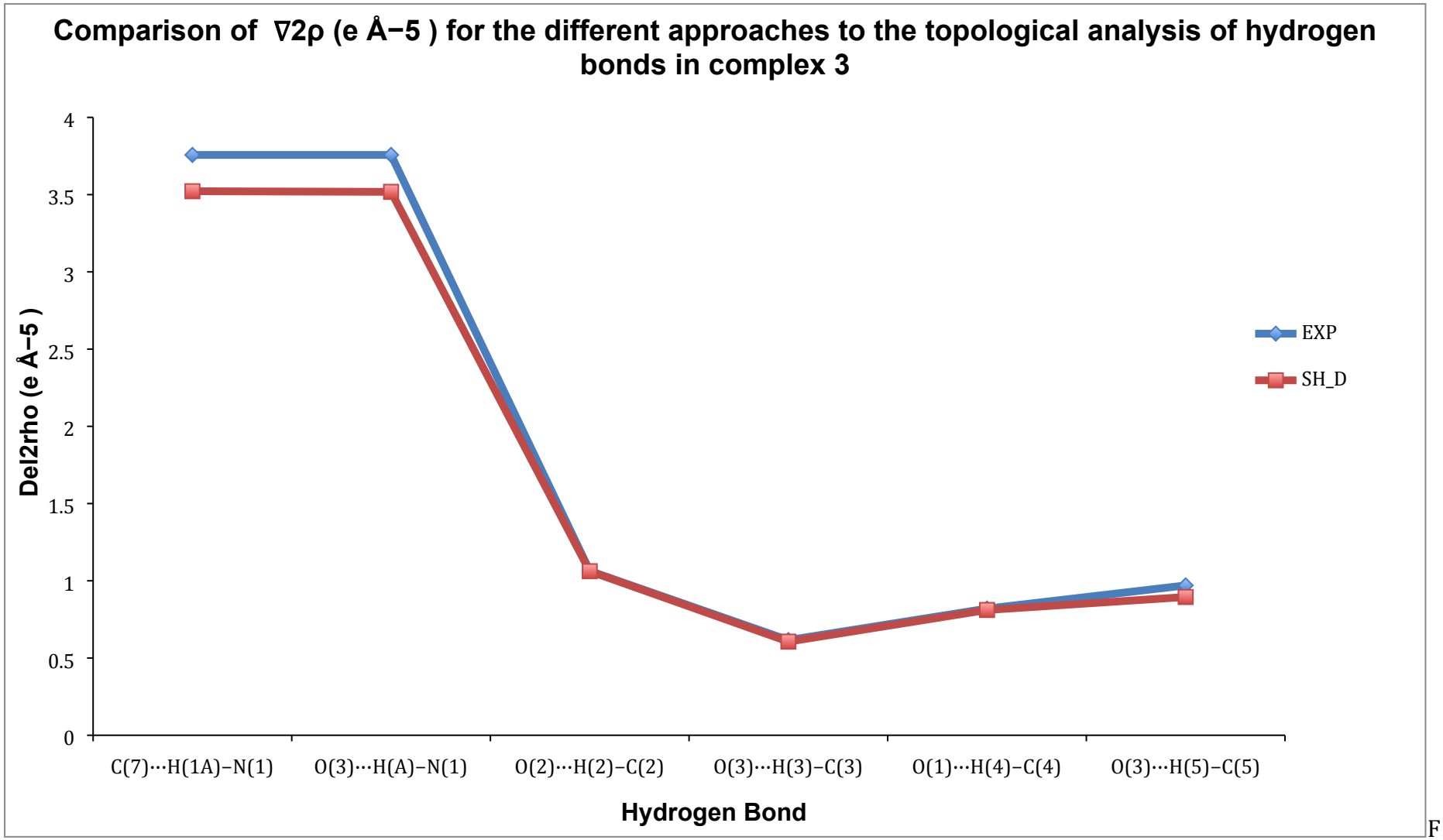


Figure S2(f): A comparison of the $\nabla^2\rho$ values from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex 3

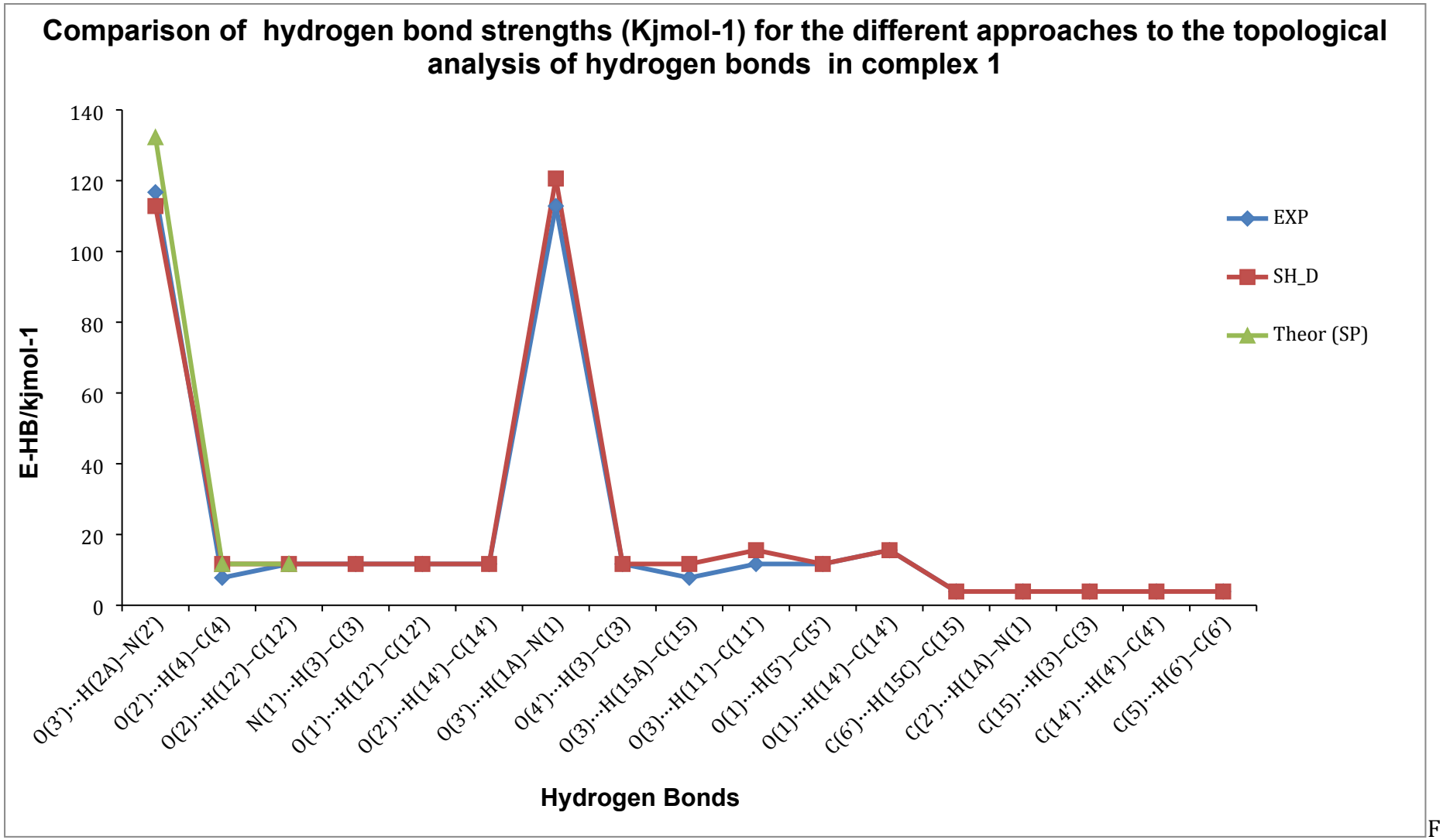


Figure S2 (g): A comparison of the hydrogen bond strengths E_{HB} (kjmol^{-1}) from topological analysis of hydrogen bonds between EXP, SH_D and Theor (SP) analysis in complex 1

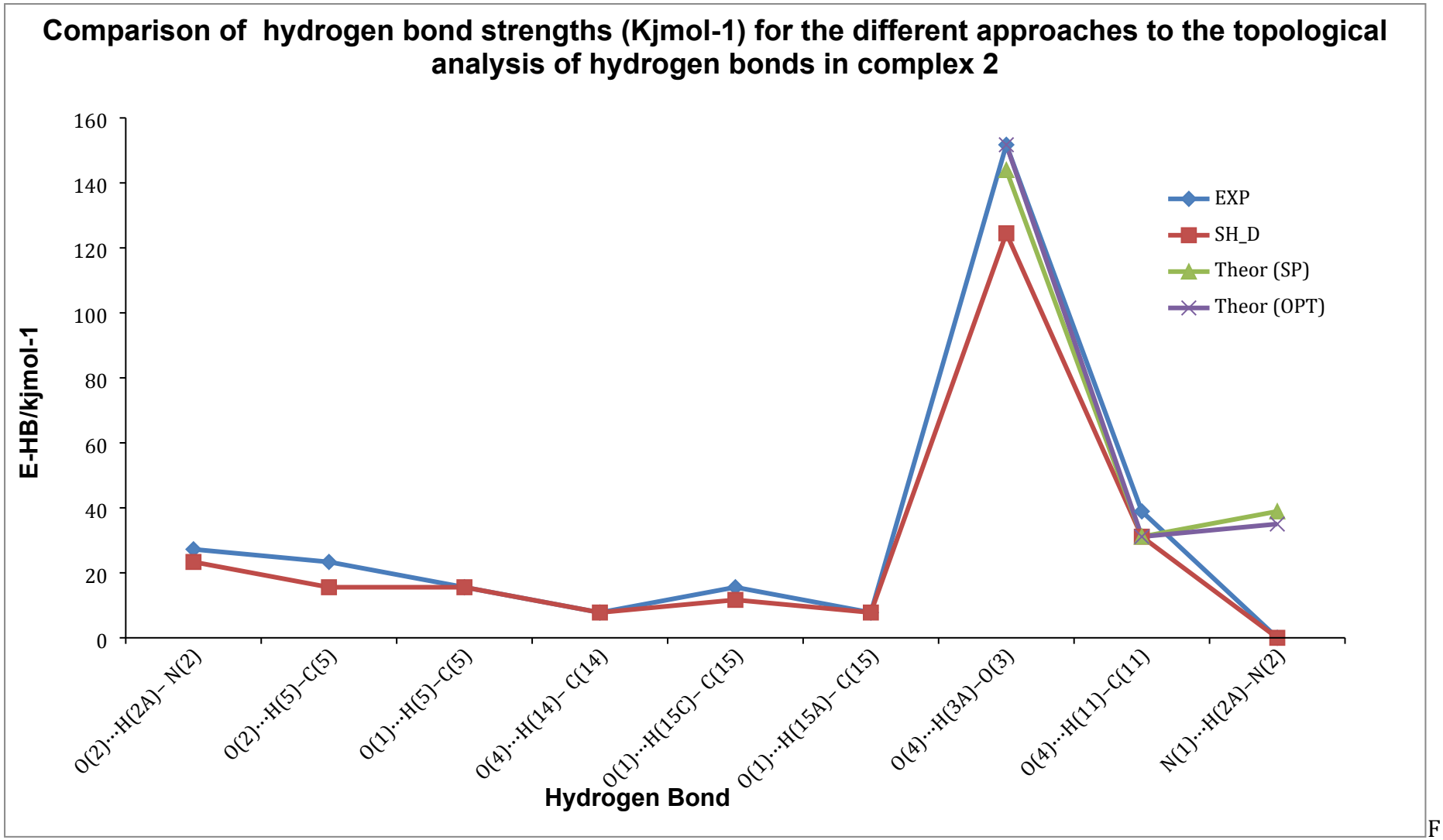


Figure S2 (h): A comparison of the hydrogen bond strengths E_{HB} (kjmol^{-1}) from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex 2

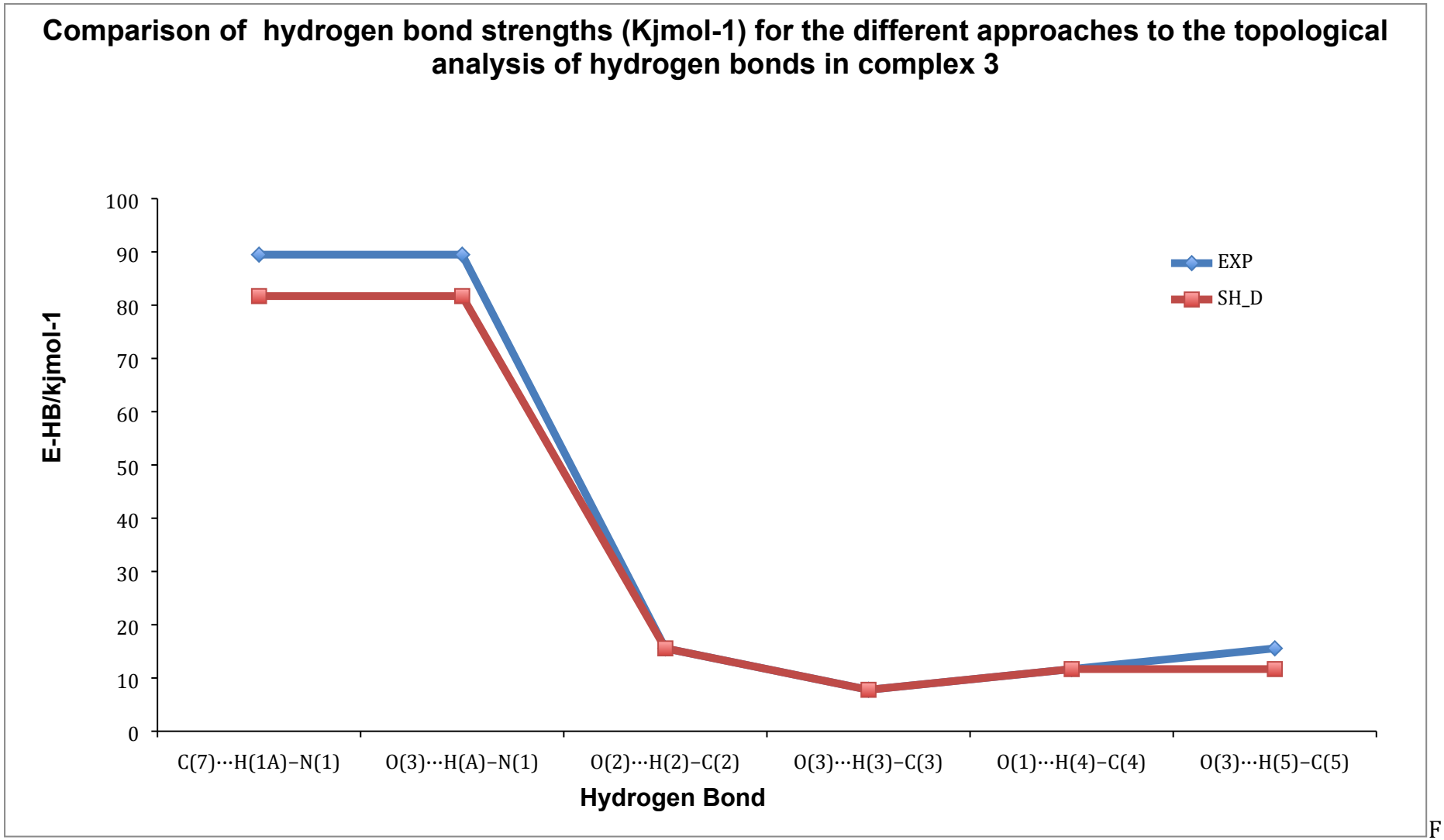


Figure S2(i): A comparison of the hydrogen bond strengths E_{HB} (kjmol^{-1}) from topological analysis of hydrogen bonds between EXP, SH_D, Theor (SP) and Theor (OPT) analysis in complex

Table S10: A comparison of the monopole electron populations (Pv) between complex 1 and complex 2 for piroxicam and complex 3 for saccharin

Atom	Pv	Pv	ΔPv
Piroxicam			
	Complex 1	Complex 2	
S(1')	15.44	14.74	0.70
O(1')	6.41	6.49	-0.08
O(2')	6.35	6.45	-0.10
O(3')	6.38	6.38	0.00
O(4')	6.21	6.40	-0.19
N(1')	5.29	5.22	0.08
N(2')	5.18	5.21	-0.03
N(3')	5.06	5.07	-0.01
C(1')	4.11	4.05	0.06
C(2')	3.93	3.98	-0.05
C(3')	4.02	3.88	0.14
C(4')	4.06	4.05	0.01
C(5')	3.95	3.96	-0.02
C(6')	3.90	4.00	-0.10
C(7')	4.01	4.02	-0.01
C(8')	4.15	4.04	0.11
C(9')	3.85	3.83	0.02
C(10')	3.89	3.93	-0.04
C(11')	4.02	3.91	0.12
C(12')	4.09	4.04	0.05
C(13')	4.15	3.99	0.16
C(14')	3.90	4.04	-0.14
C(15')	4.01	4.03	-0.01
H(2A')	0.58	0.86	-0.28

H(3A')	0.70	0.77	-0.08
H(4')	0.85	0.80	0.06
H(5')	1.07	0.87	0.20
H(6')	0.98	0.80	0.19
H(7')	0.83	0.86	-0.03
H(11')	0.83	0.96	-0.12
H(12')	0.84	0.83	0.01
H(13')	0.98	0.88	0.10
H(14')	0.88	1.01	-0.13
H(15A')	1.12	0.99	0.12
H(15B')	0.88	0.87	0.02
H(15C')	0.89	0.87	0.02
Saccharin			
Atom	Complex 1	Complex 3	Difference
S(1)	15.67	15.70	-0.04
O(1)	6.43	6.59	-0.16
O(2)	6.32	6.51	-0.19
O(3)	6.16	6.40	-0.25
N(1)	5.38	5.36	0.02
C(1)	4.19	4.29	-0.10
C(2)	3.94	3.99	-0.04
C(3)	3.89	3.83	0.06
C(4)	4.12	3.93	0.18
C(5)	3.96	4.12	-0.16
C(6)	3.88	4.18	-0.30
C(7)	3.93	3.69	0.24
H(1A)	0.64	0.83	-0.19
H(2)	0.99	0.92	0.07

H(3)	1.02	1.01	0.01
H(4)	0.88	0.75	0.13
H(5)	0.85	1.00	-0.15

Table S11: A comparison of the Bader charges in the experimental model between complex 1 and complex 2 for piroxicam and complex 3 for saccharin

Atom	**q(A)**		**Δ q(A)**
Piroxicam			
	Complex 1	Complex 2	
S(1')	1.17	2.84	1.67
O(1')	0.83	-1.50	-2.32
O(2')	-0.09	-1.44	-1.35
O(3')	-0.13	-1.21	-1.08
O(4')	-0.19	-1.06	-0.87
N(1')	0.44	-1.05	-1.49
N(2')	0.09	-1.18	-1.27
N(3')	0.63	-0.83	-1.46
C(1')	0.54	0.17	-0.37
C(2')	0.17	0.47	0.31
C(3')	-0.06	0.13	0.19
C(4')	0.03	-0.10	-0.13
C(5')	0.19	0.02	-0.17
C(6')	0.24	-0.05	-0.29
C(7')	0.20	-0.04	-0.24
C(8')	0.04	-0.14	-0.17
C(9')	0.17	1.21	1.04
C(10')	-0.10	0.70	0.80
C(11')	0.14	0.04	-0.10

C(12')	0.14	-0.06	-0.20
C(13')	2.82	0.00	-2.83
C(14')	-1.25	0.39	1.64
C(15')	-1.21	0.06	1.26
H(2A')	-0.97	0.44	1.41
H(3A')	-1.37	0.58	1.96
H(4')	-0.34	0.26	0.59
H(5')	0.03	0.15	0.12
H(6')	0.09	0.26	0.17
H(7')	-0.14	0.18	0.32
H(11')	0.07	0.08	0.01
H(12')	0.13	0.22	0.09
H(13')	1.26	0.15	-1.11
H(14')	0.54	-0.03	-0.58
H(15A')	0.02	0.07	0.05
H(15B')	0.03	0.11	0.09
H(15C')	0.14	0.17	0.02
Saccharin			
	Complex 1	Complex 3	
S(1)	2.93	2.86	-0.07
O(1)	-1.19	-1.27	-0.08
O(2)	-1.36	-1.19	0.17
O(3)	-1.35	-1.11	0.23
N(1)	-1.02	-1.11	-0.09
C(1)	-0.92	-0.33	0.59
C(2)	-1.19	-0.05	1.14
C(3)	-1.07	0.12	1.19

C(4)	-1.03	-0.02	1.01
C(5)	0.11	-0.17	-0.28
C(6)	0.73	-0.19	-0.93
C(7)	0.00	1.32	1.32
H(1A)	-0.09	0.44	0.52
H(2)	0.03	0.18	0.16
H(3)	0.12	0.05	-0.07
H(4)	0.02	0.33	0.30
H(5)	-0.34	0.06	0.40

Table S12: A comparison of the Bader charges in the theoretical model between complex 1 and complex 2 for piroxicam and complex 3 for saccharin

Atom	**q(A)**		**Δ q(A)**
Piroxicam			
	Complex 1	Complex 2	
S(1')	3.15	3.14	-0.01
O(1')	-1.36	-1.34	0.02
O(2')	-1.37	-1.36	0.01
O(3')	-1.19	-1.19	0.01
O(4')	-1.22	-1.21	0.02
N(1')	-1.33	-1.32	0.01
N(2')	-1.29	-1.28	0.00
N(3')	-1.35	-1.23	0.12
C(1')	0.27	0.32	0.05
C(2')	0.84	0.63	-0.20

C(3')	0.00	0.02	0.02
C(4')	0.02	0.02	0.00
C(5')	0.01	0.02	0.01
C(6')	0.01	0.02	0.01
C(7')	0.02	0.03	0.01
C(8')	-0.16	-0.16	0.00
C(9')	1.37	1.45	0.08
C(10')	1.03	0.94	-0.08
C(11')	0.05	0.02	-0.03
C(12')	0.05	0.02	-0.04
C(13')	0.04	-0.01	-0.05
C(14')	0.49	0.58	0.09
C(15')	0.42	0.41	-0.01
H(2A')	0.55	0.47	-0.08
H(3A')	0.55	0.66	0.11
H(4')	0.05	0.06	0.00
H(5')	0.01	0.02	0.01
H(6')	0.01	0.02	0.01
H(7')	0.05	0.06	0.01
H(11')	0.07	0.08	0.01
H(12')	0.08	0.02	-0.06
H(13')	0.05	0.02	-0.03
H(14')	0.07	0.02	-0.05
H(15A')	-0.03	0.01	0.04
H(15B')	0.03	0.04	0.01
H(15C')	0.00	-0.01	-0.02
Saccharin			
	Complex	Complex	

	1	3	
S(1)	3.13	3.11	-0.02
O(1)	-1.37	-1.33	0.03
O(2)	-1.34	-1.34	0.00
O(3)	-1.17	-1.17	0.00
N(1)	-1.44	-1.39	0.05
C(1)	-0.17	-0.16	0.01
C(2)	0.03	0.05	0.02
C(3)	0.01	0.02	0.01
C(4)	0.02	0.02	0.00
C(5)	0.04	0.03	-0.01
C(6)	0.01	0.01	0.01
C(7)	1.49	1.50	0.01
H(1A)	0.49	0.47	-0.02
H(2)	0.04	0.06	0.02
H(3)	0.03	0.03	0.00
H(4)	0.10	0.03	-0.07
H(5)	0.08	0.06	-0.02