Supplementary Information (SI) for Physical Chemistry Chemical Physics.

Supporting Information

Chalcogen bond interactions involving sulphur atoms of methionine or cysteine residues and backbone carbonyl oxygen atoms in protein structures

Prathvi Singh,[a] Venkatnarayan Ramanathan[b] and Ramasubbu Sankararamakrishnan[*a,c]

[a]*Department of Biological Sciences and Bioengineering, Indian Institute of Technology Kanpur, Kanpur 208016, Uttar Pradesh, India*

[b]*Department of Chemistry, Indian Institute of Technology (BHU) Varanas, Varanasi 221005, Uttar Pradesh, India*

[c]*Mehta Family Center for Engineering in Medicine, Indian Institute of Technology Kanpur, Kanpur 208016, Uttar Pradesh, India*

*Author for Correspondence
Email: rsankar@iitk.ac.in
Tel: +91 512 259 4014
Fax: +91 512 259 4010

Figure S1:

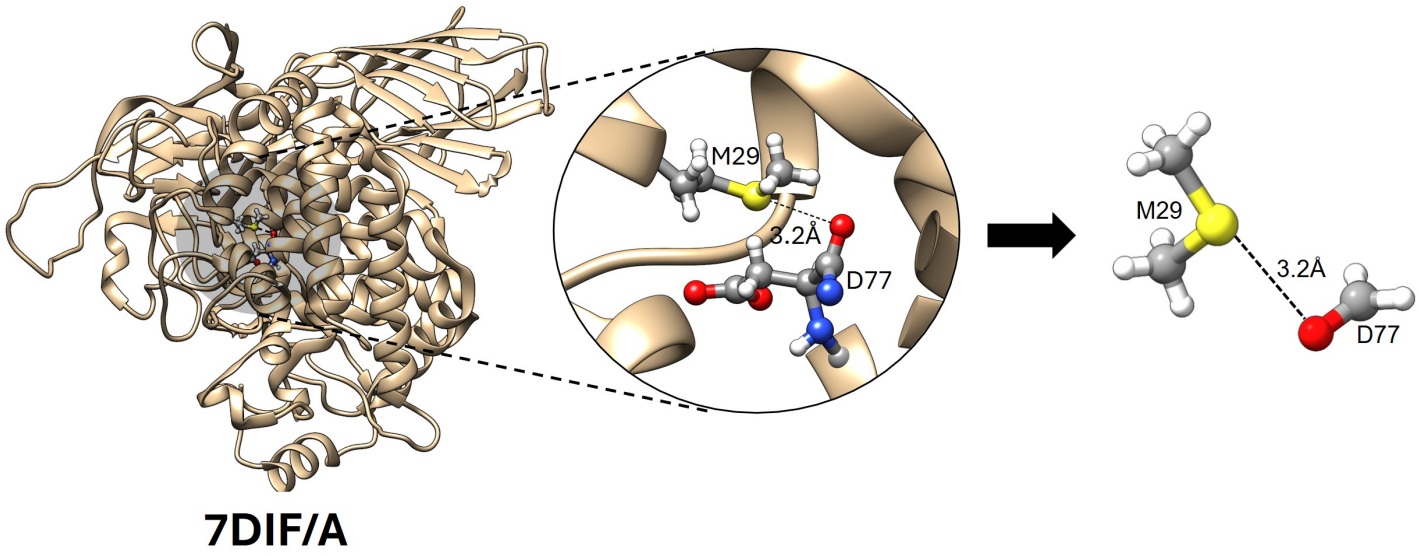

Fig. S1: A representative example of chalcogen bond between Met sulphur and backbone carbonyl oxygen atoms found in a hydrolase structure (PDB ID: 7DIF). The residues participating in chalcogen bond interaction are zoomed in with ball-and-stick representation. Standard colours are used to represent the atoms. Distance between the sulphur and carbonyl oxygen atom is shown. The arrow indicates the model compounds generated without altering the conformations of the residues found in the protein structure retaining the geometry of ChB interaction.

Figure S2:

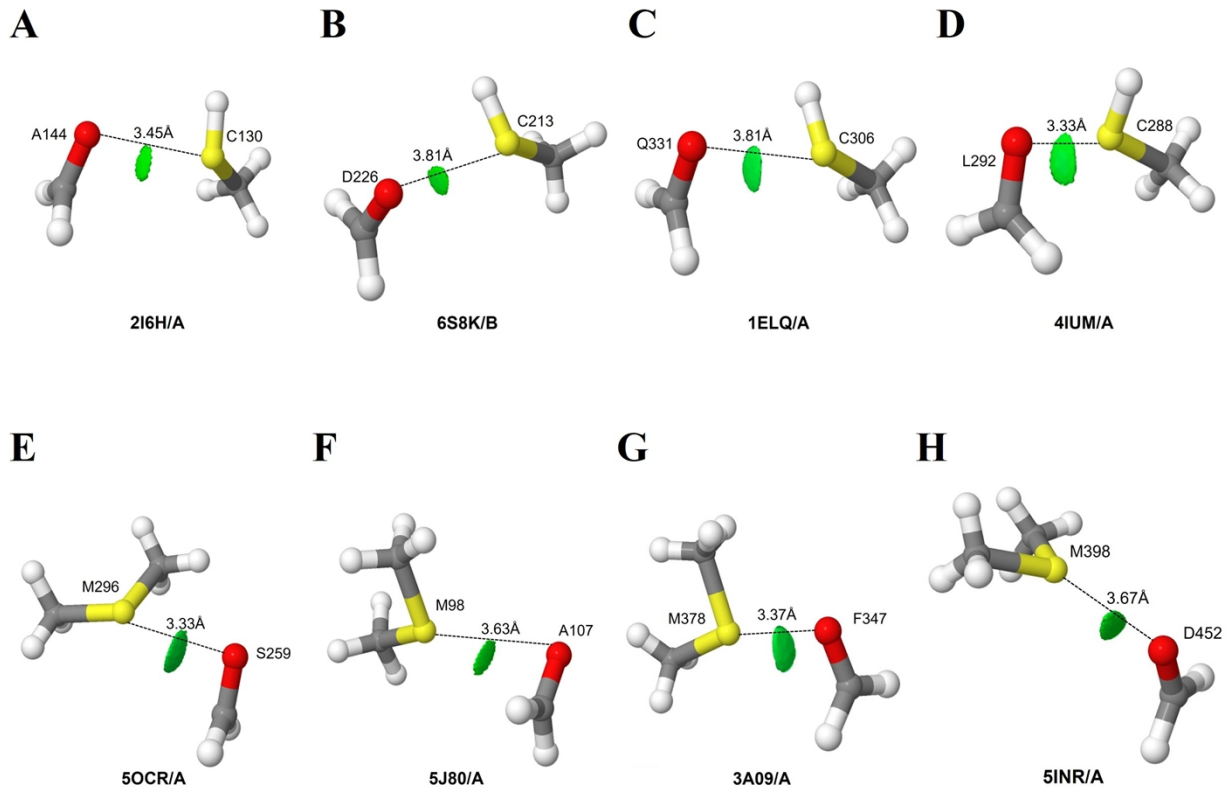

Fig. S2: NCIPLOT isosurfaces of representative examples for the model systems with S...O=C contacts. All the examples show weak interactions due to the formation of chalcogen bond interactions. Four-letter unique PDB IDs/Chain IDs are given. Molecules representing the model systems are shown in ball-and-stick representation with standard colors. Cys and Met residues participating in chalcogen bond interactions with *d*(S…O) distances are indicated.

Figure S3:

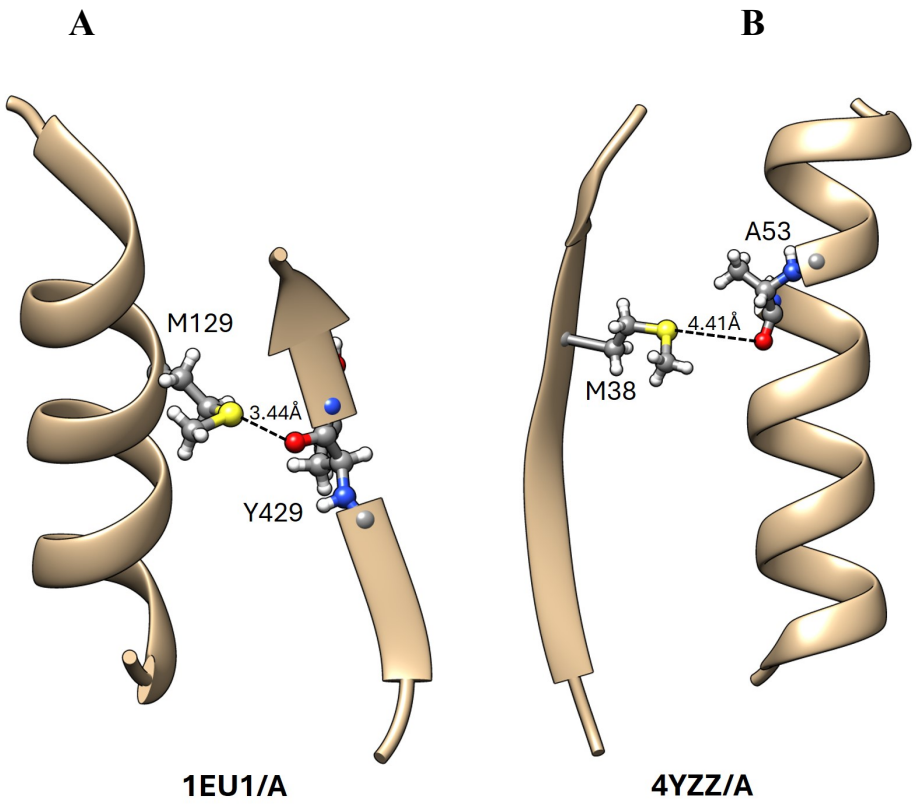

Fig. S3: Representative examples of chalcogen bonds stabilizing two secondary structural elements namely (A) helix-strand and (B) strand-helix. Residues participating in chalcogen bond interaction are shown in ball-and-stick representation with standard atom colors. For each example, the PDB IDs/Chain IDs and *d*(S…O) distances are provided.

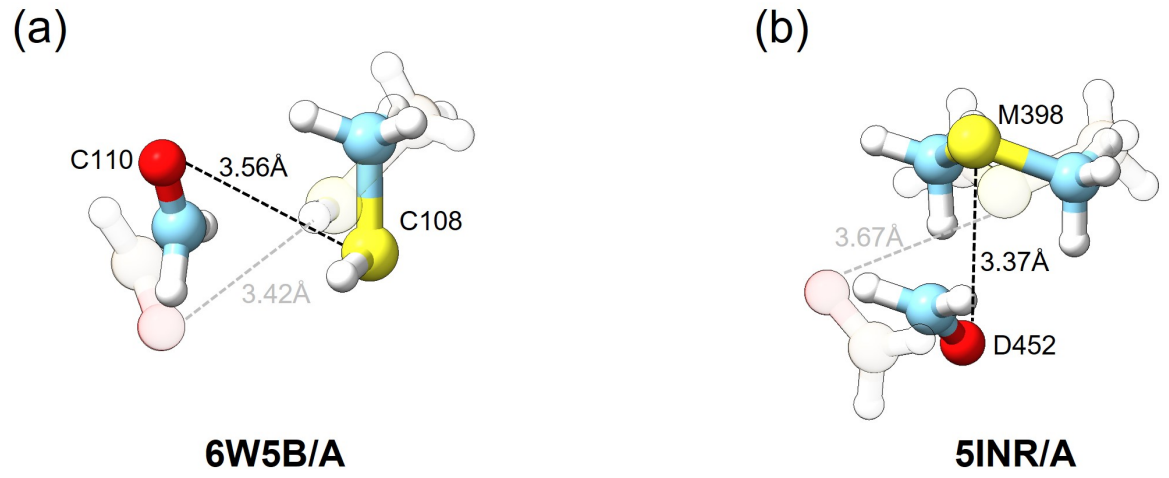

Fig. S4: Two representative examples of model systems with S…O=C contacts from (A) Cys and (b) Met before and after full optimization. The model systems with conformations as found in the protein structures are shown as ghost images. The structures after full optimization are superposed on the structures before optimization. It is clear that the model compounds after full optimization significantly deviated from the initial structures. The atoms for the fully optimized structures are shown in standard colors. The PDB IDs/Chain IDs and the *d*(S…O) distances are displayed for each example. The θ(C-S…O) angle deviated from the initial 161º before optimization to ~67º (Cys) and ~73º (Met) after optimization. Full optimization also improved the interaction energies from -1.19 to 4.32 kcal/mol for Cys and from -1.27 to -6.01 kcal/mol for Met.

Table S1: Examples of chalcogen bonds identified from high-resolution crystal structures formed by Cys residues that are used for quantum chemical calculations

S.No.	PDB ID/ Chain ID	Cys residue number	Acceptor (O=C) residue number	*d*(S...O) (Å)	*θ*(S...O=C) (°)
1	1C0P/A	1259	1235	3.46	160.04
2	1D2N/A	590	629	3.43	157.89
3	1ELQ/A	306	331	3.82	152.83
4	1ELQ/A	367	169	3.99	163.39
5	1ERZ/A	278	189	3.75	152.97
6	1F9V/A	655	674	3.44	159.81
7	1GXM/A	510	528	4.02	157.61
8	1H0H/A	136	128	3.64	150.41
9	1JID/A	53	104	4.87	153.55
10	1LJ8/A	375	307	3.49	153.35
11	1LQT/A	395	386	4.16	164.42
12	1NS5/A	112	57	3.80	154.72
13	1OAI/A	588	599	3.71	159.57
14	1Q6Z/A	240	242	3.14	152.53
15	1QD1/A	33	57	3.19	163.01
16	1TBF/A	839	628	4.44	156.79
17	1UXO/A	74	69	3.54	153.81
18	1VPR/A	980	1137	3.43	160.67
19	1WKQ/A	80	103	3.43	159.83
20	1XFK/A	198	159	3.54	150.36
21	1YT3/A	183	102	4.20	158.74
22	2BF6/A	540	496	3.88	156.36
23	2BII/A	385	134	3.06	163.20
24	2BMO/A	149	35	3.14	155.37
25	2C5A/A	85	79	3.06	163.94
26	2CB9/A	146	57	3.64	150.49
27	2GF3/A	152	83	4.34	153.82
28	2I6H/A	130	144	3.45	151.56
29	2II2/A	219	202	4.05	160.11
30	2IMR/A	318	293	3.97	155.85
31	2IU5/A	147	104	4.33	154.22
32	2IZR/A	108	36	4.82	165.97
33	2J91/A	27	17	4.25	165.44

34	2JE8/A	639	641	3.48	156.99
35	2JE8/A	737	739	3.50	154.59
36	2JIS/A	44	445	4.95	162.01
37	2OLM/A	89	44	3.20	156.82
38	2P6W/A	177	182	3.75	164.67
39	2PS1/A	85	99	3.66	159.07
40	2QQ5/A	235	255	3.46	150.16
41	2R7G/A	706	752	4.29	159.79
42	2VFO/A	613	615	3.77	152.46
43	2WAW/A	129	113	4.49	154.64
44	2WK1/A	101	92	4.69	166.95
45	2WLV/A	140	64	3.56	160.93
46	2X5N/A	166	137	4.84	159.13
47	2XDW/A	526	518	3.36	161.74
48	2XE4/A	243	245	3.35	153.67
49	2Y3S/A	261	255	3.47	155.50
50	3A15/A	258	260	3.27	151.99
51	3ALJ/A	255	186	3.48	157.71
52	3BD1/A	42	37	4.72	152.21
53	3BFM/A	103	129	4.10	151.55
54	3BFM/A	166	70	3.92	150.24
55	3BOX/A	139	84	3.15	158.90
56	3BOX/A	306	308	3.63	155.27
57	3DB2/A	34	42	3.84	157.58
58	3EIN/A	201	162	4.98	158.57
59	3FF1/A	399	283	4.99	150.36
60	3FGV/A	47	49	3.30	155.46
61	3FPC/A	203	344	4.37	165.39
62	3G0T/A	183	128	4.16	166.20
63	3GD0/A	326	310	3.82	169.24
64	3GE3/A	492	350	4.19	150.72
65	3GKE/A	81	83	3.61	151.47
66	3HKW/A	521	457	3.75	154.39
67	3HN0/A	99	101	3.10	155.13
68	3ILS/A	1919	1946	4.08	156.77
69	3K1U/A	221	187	3.48	153.76
70	3K40/A	389	396	4.66	153.53
71	3KYA/A	271	273	3.42	155.88
72	3LXZ/A	107	121	4.70	159.93
73	3M0M/A	164	102	4.77	156.43

74	3M0M/A	85	55	4.71	160.13
75	3MCX/A	195	174	3.35	170.33
76	3MFI/A	146	160	3.24	156.67
77	3MQD/A	46	48	3.54	156.42
78	3MVU/A	95	46	4.10	157.48
79	3MZ0/A	231	234	3.10	164.67
80	3NEH/A	201	229	3.32	152.21
81	3NKE/A	251	228	4.77	159.41
82	3NO2/A	113	145	3.11	163.93
83	3NOH/A	111	121	3.12	155.79
84	3OA5/A	424	54	3.87	153.83
85	3OF5/A	198	200	3.24	150.28
86	3OIS/A	241	243	3.77	153.60
87	3OOS/A	227	234	3.95	154.49
88	3PMO/A	268	283	3.15	169.87
89	3PT1/A	465	410	3.98	158.66
90	3QH6/A	114	116	3.27	150.13
91	3QP4/A	173	11	3.28	164.23
92	3QSJ/A	111	82	3.22	168.89
93	3R8Y/A	146	169	3.01	157.69
94	3SCY/A	126	180	3.47	152.10
95	3UR8/A	29	258	3.36	153.21
96	3UUW/A	126	238	3.73	153.26
97	3V4G/A	149	89	4.81	156.12
98	3V9J/A	95	73	3.80	164.59
99	3VBJ/A	48	63	3.00	159.34
100	3VU9/B	21	47	4.32	162.36
101	3VYG/B	76	112	3.69	161.69
102	3VZX/A	62	75	4.29	158.93
103	3WDN/A	37	83	4.28	160.99
104	3ZEU/B	298	293	3.55	153.89
105	3ZYL/A	230	222	3.76	158.43
106	4A37/A	273	320	3.44	150.03
107	4AT0/A	457	238	3.25	159.01
108	4B4U/A	109	75	4.10	153.70
109	4BQN/A	26	224	3.50	164.34
110	4BWR/A	163	155	4.14	153.93
111	4DK2/A	134	131	4.36	159.25
112	4DZ4/A	100	113	3.82	153.04
113	4E15/A	6	8	3.36	162.52

114	4EA9/A	29	97	3.05	161.90
115	4EYZ/A	151	139	3.41	154.34
116	4F6T/B	173	76	4.96	159.87
117	4FS7/A	136	110	3.12	162.94
118	4FS7/A	181	156	3.20	162.43
119	4FS7/A	204	178	3.02	168.89
120	4FS7/A	295	269	3.11	166.30
121	4FS7/A	316	292	3.14	162.47
122	4FS7/A	339	313	3.06	159.45
123	4FS7/A	362	336	3.00	164.53
124	4GMU/A	407	169	4.00	162.46
125	4H5I/A	87	71	3.10	160.99
126	4IA6/A	89	531	4.34	155.23
127	4IUM/A	288	292	3.33	164.46
128	4JN7/A	92	21	3.26	152.25
129	4L4E/A	85	90	4.27	151.93
130	4LAN/A	159	161	3.47	152.70
131	4LDV/A	125	223	4.64	161.20
132	4LER/A	59	424	4.21	151.54
133	4LPQ/A	300	282	3.37	157.76
134	4MC3/A	139	131	3.93	158.36
135	4OJ5/A	525	495	3.54	151.43
136	4PFO/A	236	421	3.81	150.21
137	4Q98/A	308	299	4.47	167.59
138	4QUS/A	100	102	3.34	156.44
139	4R9P/A	217	211	3.99	154.82
140	4RD8/A	134	77	3.70	155.81
141	4S28/A	443	402	3.80	159.64
142	4USK/A	155	81	3.58	150.56
143	4UWX/A	155	139	4.91	158.51
144	4V1S/A	109	84	4.26	159.89
145	4WU0/A	317	319	3.46	152.75
146	4XEM/A	187	173	4.01	163.68
147	4XY5/A	91	93	3.19	153.91
148	4Z9P/A	53	76	3.60	161.86
149	4ZSW/A	177	169	3.53	164.92
150	4ZSW/A	196	137	3.30	160.38
151	4ZSW/A	412	384	4.30	151.18
152	5AIZ/A	56	15	3.13	168.08
153	5AJJ/A	192	152	3.27	158.65

154	5AN4/A	140	253	4.29	152.22
155	5AO9/A	134	195	4.12	163.77
156	5BP8/A	484	519	3.86	154.15
157	5CIY/A	35	37	3.51	150.56
158	5FSV/A	188	175	3.15	156.10
159	5G3T/A	387	401	4.48	160.86
160	5HT2/A	283	248	4.04	151.42
161	5HZ2/A	459	290	3.42	160.51
162	5I2H/A	277	269	3.16	157.17
163	5I95/A	235	171	4.35	152.51
164	5I95/A	418	325	3.23	162.98
165	5IN4/A	142	94	3.58	163.31
166	5K7F/A	43	18	4.33	167.00
167	5KO5/A	231	163	3.53	154.24
168	5KPG/A	152	126	3.40	157.22
169	5KTN/A	199	229	3.76	154.01
170	5L9A/A	202	188	4.99	152.03
171	5NCB/A	54	48	3.35	155.24
172	5ONN/A	61	64	3.79	153.08
173	5QOV/A	140	129	3.62	163.34
174	5RL9/A	27	92	4.02	150.08
175	5RW1/A	316	362	3.35	153.37
176	5T39/A	224	220	3.14	157.58
177	5T3B/A	410	412	3.39	153.67
178	5TEE/A	371	373	3.42	150.29
179	5TQI/A	75	77	3.06	157.02
180	5UCS/A	90	102	3.86	150.99
181	5UKI/A	277	311	3.88	154.78
182	5XVT/A	121	162	3.27	150.30
183	5XWC/A	338	340	3.35	153.03
184	5YRV/A	330	297	4.97	150.41
185	6AON/A	32	11	3.36	152.28
186	6AU8/A	205	275	3.54	154.67
187	6B6U/A	358	464	3.76	158.23
188	6B9H/A	125	83	4.90	158.44
189	6COF/A	213	205	3.43	153.56
190	6CR0/A	221	18	3.79	168.49
191	6CXB/A	646	648	3.56	156.57
192	6D4K/A	215	193	4.00	158.61
193	6E43/A	335	200	3.07	157.00

194	6E85/A	102	78	4.73	158.24
195	6ECT/A	1066	1035	4.39	153.69
196	6EWH/A	276	217	3.86	158.74
197	6F0P/A	973	1056	3.28	158.24
198	6FJN/A	337	332	3.28	163.49
199	6FOP/A	555	610	4.96	159.52
200	6GDJ/A	229	213	4.53	164.20
201	6GG7/A	19	319	4.17	154.97
202	6GQD/A	180	182	3.27	152.97
203	6HCW/A	497	250	3.16	158.69
204	6HEM/A	931	893	3.25	162.91
205	6HFO/A	321	318	3.98	154.44
206	6HFZ/A	287	234	4.56	152.59
207	6HQD/A	50	52	3.38	162.27
208	6I18/A	80	68	3.41	151.88
209	6ILU/A	261	264	3.09	158.37
210	6J0Y/A	452	459	4.29	164.22
211	6JH7/A	246	2	3.27	162.51
212	6JY1/A	293	45	4.06	150.32
213	6KJH/A	325	71	3.44	156.02
214	6KQS/A	355	296	3.21	155.55
215	6LR3/A	57	48	3.86	154.93
216	6LXU/A	333	384	4.89	154.73
217	6N2H/A	31	26	4.78	152.23
218	6NYT/A	744	746	3.66	155.03
219	6OAL/A	608	629	3.81	169.87
220	6OAL/A	943	947	3.33	151.57
221	6OK1/A	31	63	4.83	165.26
222	6P2D/A	47	8	4.67	159.03
223	6P2L/A	520	524	3.32	165.37
224	6P2L/A	633	635	3.34	151.94
225	6QSP/A	212	345	3.40	159.33
226	6S8K/B	213	226	3.81	155.68
227	6SBQ/A	768	824	3.94	158.05
228	6TUO/A	197	222	3.78	150.36
229	6U1V/A	114	84	3.99	152.52
230	6W5B/A	108	110	3.43	160.98
231	6WRH/A	155	168	4.21	158.40
232	6YPF/A	118	120	3.56	156.18
233	7LD8/A	187	61	4.17	156.62

Table S2: Examples of chalcogen bonds identified from high-resolution crystal structures formed by Met residues that are used for quantum chemical calculations

S.No.	PDB ID/ Chain ID	Met residue number	Acceptor (O=C) residue number	*d*(S...O) (Å)	*θ*(S...O=C) (°)
1	1D2N/A	581	589	4.39	150.03
2	1EU1/A	129	429	3.44	157.11
3	1EVL/A	374	520	3.70	151.34
4	1EVL/A	509	334	4.91	158.76
5	1EVL/A	593	582	3.80	158.04
6	1FTR/A	20	250	3.25	156.43
7	1J7K/A	207	240	3.91	152.30
8	1JG8/A	285	143	4.12	152.36
9	1JL0/A	233	60	3.66	159.34
10	1KDK/A	107	129	4.49	153.18
11	1LC5/A	239	91	3.41	155.07
12	1M7Y/A	299	126	3.91	152.79
13	1MC2/A	1095	1071	3.77	158.21
14	1MJ5/A	253	133	3.02	163.66
15	1TBF/A	760	646	4.27	150.49
16	1UWK/A	396	188	4.09	157.07
17	1V6T/A	76	66	3.92	154.01
18	1VYI/A	232	266	4.74	153.76
19	1X0T/A	104	67	3.75	151.99
20	1XFI/A	7	289	4.92	154.22
21	2BII/A	283	278	3.78	151.88
22	2D1G/A	335	375	4.74	156.30
23	2E7Z/A	505	91	3.85	157.51
24	2EAB/A	436	379	3.54	155.72
25	2GSO/A	113	107	3.29	161.22
26	2NX4/A	162	185	4.67	153.74
27	2OVJ/A	458	442	4.05	154.80
28	2OVJ/A	477	528	4.86	153.44
29	2P6W/A	194	202	4.01	157.33
30	2Q35/A	111	120	4.58	152.06
31	2QKP/A	364	368	3.96	156.01
32	2RDQ/A	224	169	3.10	164.90
33	2RKV/A	343	312	4.76	150.99

34	2WAO/A	182	229	3.44	157.88
35	2WFP/A	119	126	4.40	157.91
36	2ZB4/A	158	171	3.83	164.30
37	2ZQ0/A	280	250	4.25	166.25
38	3A09/A	378	347	3.38	156.45
39	3AML/A	225	272	4.41	162.22
40	3B0X/A	1	40	4.90	150.51
41	3BMX/A	560	596	4.17	160.69
42	3BOX/A	299	288	3.64	153.85
43	3BOX/A	352	359	3.66	160.46
44	3BVX/A	1026	1006	3.33	155.46
45	3C7X/A	422	470	4.54	155.75
46	3CTP/A	66	105	4.18	156.74
47	3DO8/A	1	3	3.90	150.66
48	3FEG/A	122	265	3.84	154.43
49	3GZD/A	194	143	3.24	162.55
50	3H8G/A	393	444	3.64	156.28
51	3H9C/A	333	341	4.58	151.67
52	3I2K/A	16	93	3.63	161.27
53	3IT3/A	312	307	3.37	153.95
54	3MDM/A	316	469	4.48	157.13
55	3MFI/A	395	423	4.03	165.24
56	3NZN/A	26	35	3.43	161.41
57	3OND/A	396	247	4.34	157.04
58	3PV8/A	701	696	3.41	150.68
59	3R3Q/A	143	138	3.84	160.70
60	3S5M/A	734	1114	3.56	157.54
61	3S5M/A	819	829	3.72	161.65
62	3UW3/A	257	263	3.87	151.89
63	3ZSU/A	78	115	3.81	152.35
64	3ZXK/A	555	399	4.16	150.91
65	4AK2/A	611	655	3.43	155.12
66	4ATE/A	262	232	3.99	154.67
67	4AZ6/A	305	333	3.47	159.91
68	4C08/A	160	157	4.74	152.32
69	4CHI/A	308	241	3.89	157.24
70	4CJ0/A	281	519	3.73	156.70
71	4DNX/A	1	184	3.69	152.78
72	4DNX/A	344	329	4.37	157.61
73	4EAD/A	242	90	3.58	152.07

74	4FZL/A	39	105	4.12	150.37
75	4G38/A	432	394	4.06	165.13
76	4GF0/A	136	105	3.49	156.66
77	4HHR/A	152	391	4.05	159.48
78	4I71/A	54	66	3.31	156.35
79	4LCL/A	85	207	4.36	158.10
80	4LDV/A	64	240	4.11	151.47
81	4LHD/A	154	972	3.86	152.42
82	4MAI/A	3	15	3.64	160.84
83	4MBO/A	553	499	3.46	156.88
84	4MLO/A	229	263	4.35	154.05
85	4ORD/A	87	62	3.78	156.63
86	4PWQ/A	170	146	4.79	150.64
87	4QGS/A	276	352	4.32	158.60
88	4R6H/A	62	80	3.80	152.28
89	4TJV/A	128	151	4.17	161.92
90	4UP3/A	72	14	4.46	151.28
91	4USA/A	366	833	4.39	150.44
92	4WBY/A	280	193	3.94	151.59
93	4WS6/A	217	183	3.46	154.26
94	4WVA/A	386	411	3.22	160.89
95	4XHF/A	203	215	4.12	151.78
96	4YAA/A	444	406	3.25	162.17
97	4YZZ/A	38	53	4.41	151.26
98	5BOI/A	346	301	3.90	162.58
99	5BXR/A	317	356	4.24	151.52
100	5C8Z/A	241	157	3.40	151.13
101	5CR5/A	78	93	4.44	153.20
102	5D16/A	524	391	4.49	150.27
103	5DCU/A	356	273	3.34	153.65
104	5DKX/A	910	841	4.24	158.43
105	5EB1/A	86	49	3.88	152.58
106	5EKY/A	192	155	4.91	154.06
107	5EU0/B	62	41	4.62	154.72
108	5EYN/A	162	134	4.32	152.52
109	5FQE/A	343	351	4.01	153.80
110	5HWN/A	192	168	3.54	150.37
111	5HZD/A	616	611	3.77	163.69
112	5I7I/A	178	234	3.83	153.90
113	5INR/A	398	452	3.67	161.30

114	5INR/A	407	351	3.50	159.68
115	5IY2/A	256	251	3.94	152.63
116	5J80/A	98	107	3.64	158.40
117	5J90/A	348	220	4.82	152.12
118	5JOV/A	915	910	3.94	161.74
119	5K3X/A	314	237	3.69	154.98
120	5LJW/A	146	16	4.29	157.48
121	5LTE/A	68	150	4.04	158.96
122	5LX8/A	492	434	4.79	154.12
123	5MC1/A	217	212	3.48	155.01
124	5OCR/A	296	259	3.34	155.80
125	5OL4/C	106	100	4.20	152.80
126	5TNV/A	123	173	4.82	156.03
127	5USB/A	118	107	4.35	158.17
128	5VIA/A	120	135	4.67	156.05
129	5WMK/A	364	307	3.14	150.19
130	5X8Z/A	41	107	3.74	162.78
131	5YQJ/A	787	799	4.00	150.95
132	5YSE/A	350	334	4.43	153.20
133	5YSE/A	364	340	4.72	153.30
134	6A2Q/A	161	209	4.01	150.94
135	6AD3/A	346	195	3.86	155.85
136	6DUB/A	274	100	3.78	166.73
137	6EE7/A	67	61	3.72	151.04
138	6F6M/A	143	158	3.71	151.27
139	6F8A/A	165	63	3.42	153.94
140	6HCW/A	54	147	3.66	153.76
141	6I8L/B	231	82	4.03	152.90
142	6I9W/A	27	239	4.45	151.13
143	6J4P/A	118	161	3.51	171.98
144	6JCH/A	360	355	3.90	151.08
145	6JZ2/A	447	434	4.06	150.55
146	6KO8/A	126	60	4.31	155.91
147	6KRI/A	537	405	4.46	150.94
148	6NOK/A	52	267	4.54	153.50
149	6OJL/A	543	566	4.15	157.95
150	6OMP/A	298	245	4.60	153.27
151	6Q10/A	81	147	3.92	152.70
152	6R09/A	174	171	3.18	166.55
153	6RS4/A	303	300	3.31	151.07

154	6RY0/A	89	107	4.74	153.89
155	6SUK/A	248	272	3.61	151.79
156	6TGU/A	138	219	4.32	151.90
157	6V4B/A	68	78	3.47	155.26
158	6WGM/A	323	115	3.24	161.06
159	6ZTU/A	168	163	3.28	158.54
160	7C3H/A	267	462	3.37	162.62
161	7DIF/A	29	77	3.22	156.50
162	7K7W/A	88	154	3.63	156.45