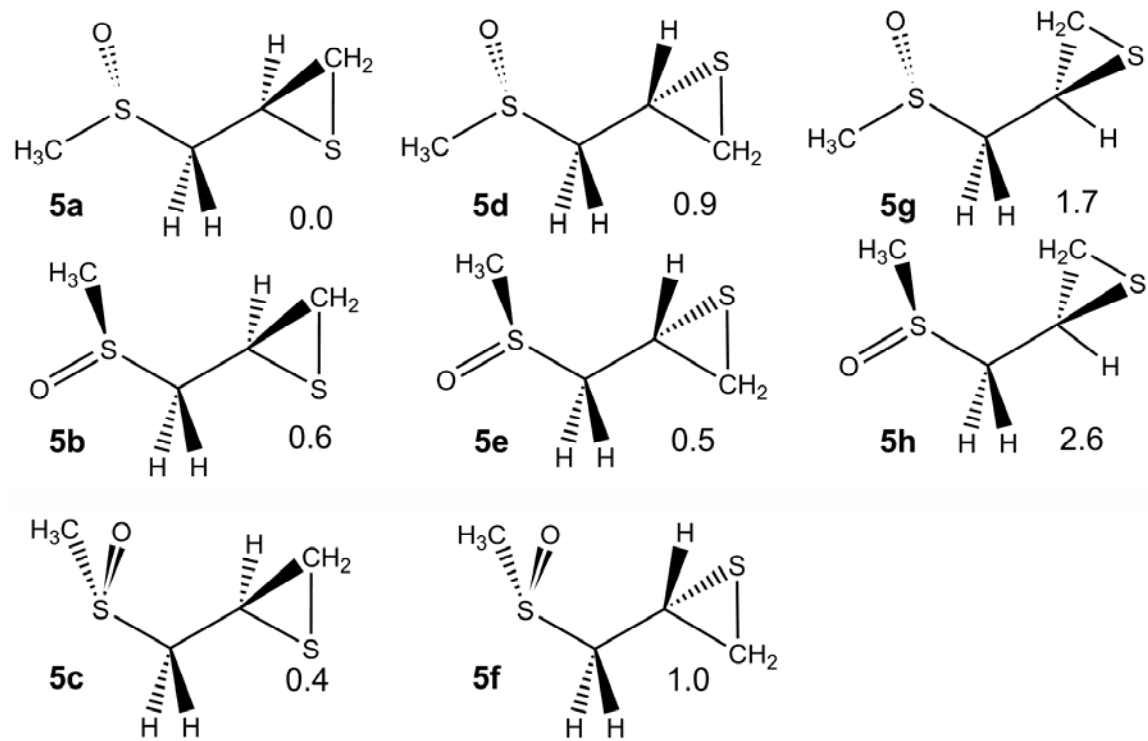
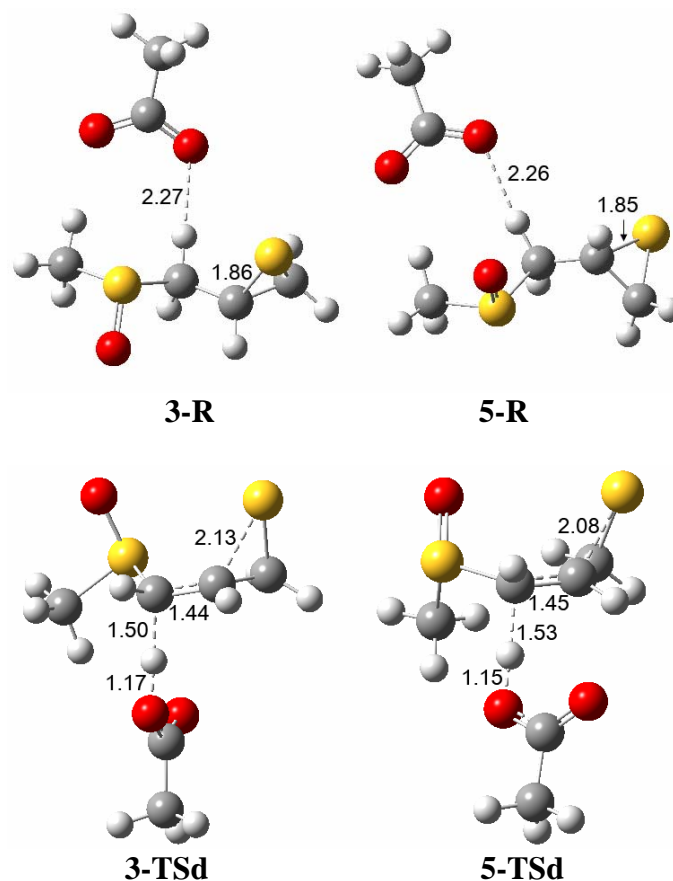


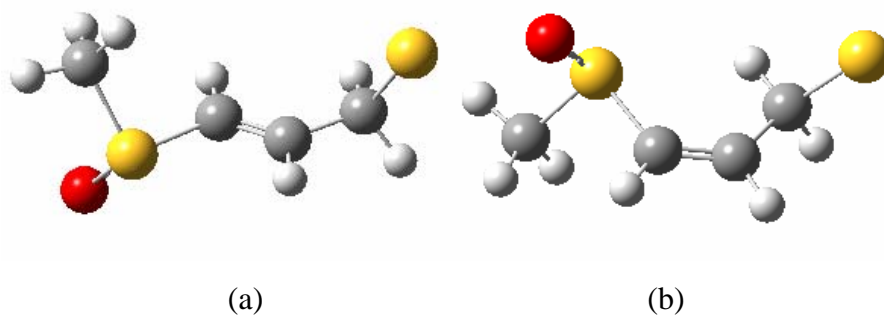
**SCHEME S1: (*S,R*)-2-(Methylsulfinylmethyl)thiirane<sup>a</sup>**



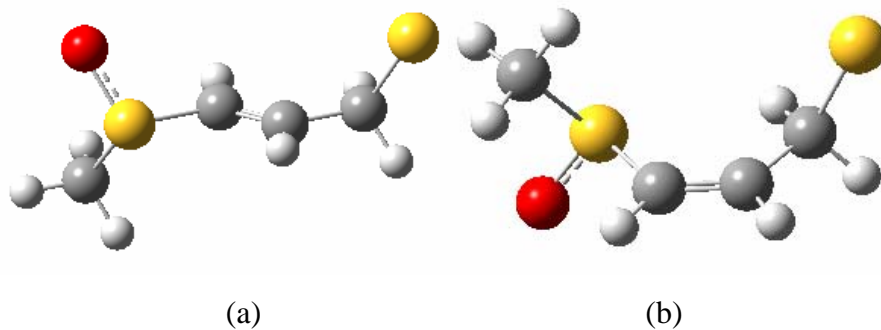
<sup>a</sup> Relative energies in kcal/mol.



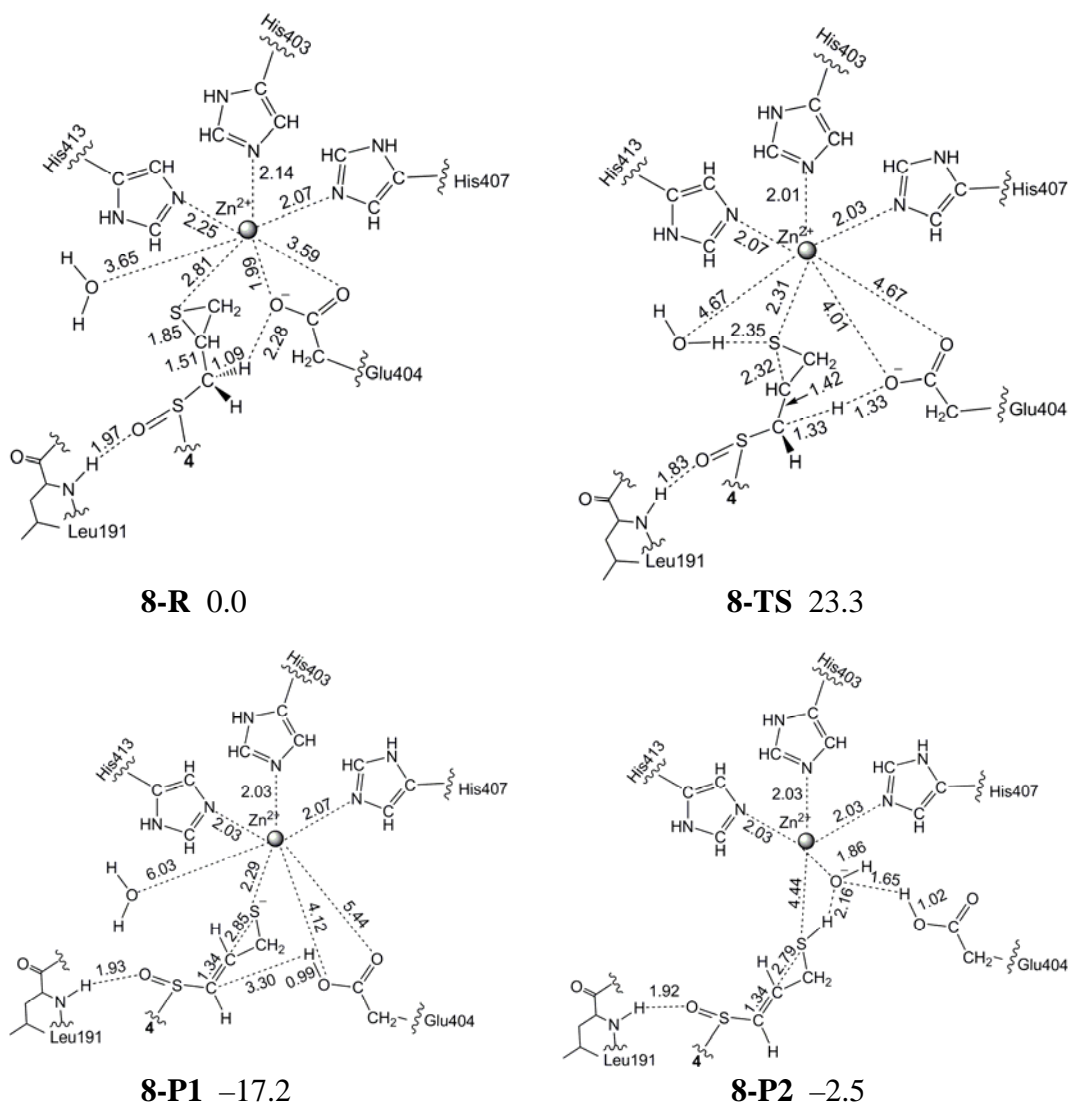
**Figure S1.** Reactant complexes (**3-R**, **5-R**) and TS complexes (**3-TSd**, **5-TSd**) of 2-(methylsulfinylmethyl)thiirane and acetate optimized at the IEF-PCM/B3LYP/6-31+G(d) level of theory in methanol. Distances are in Å. Atoms are colored according to atom types (H, C, O, and S shown in white, grey, red, and yellow, respectively). The same color scheme is also used in Figure S2 and S3.



**Figure S2.** Ring-opening products of **3** optimized at the IEF-PCM/B3LYP/6-31+G(d) level of theory in methanol. (a). (*E*)-3-(methylsulfinyl)prop-2-ene-1-thiolate, (b) (*Z*)-3-(methylsulfinyl)prop-2-ene-1-thiolate.

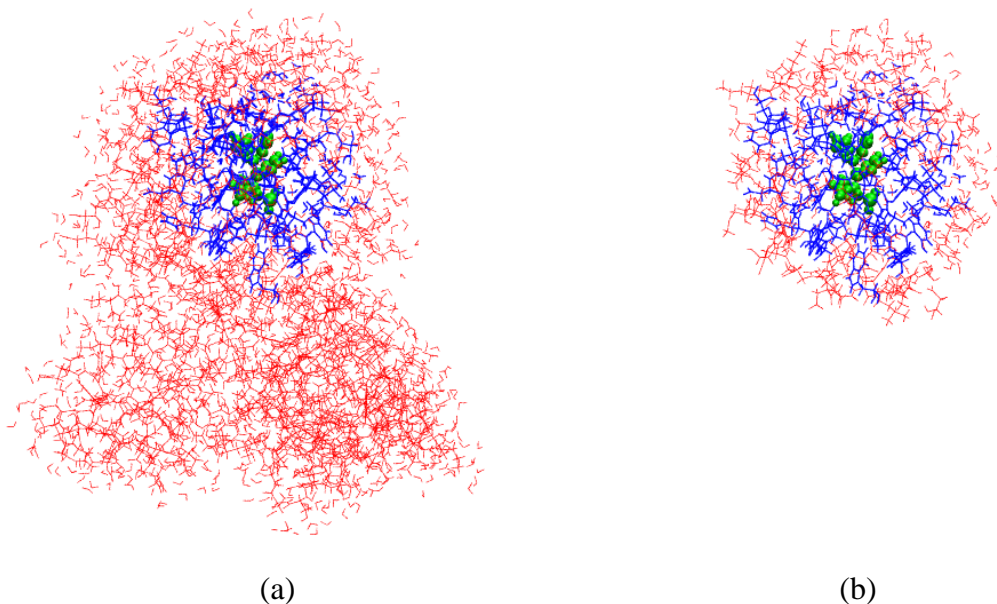


**Figure S3.** Ring-opening products of **5** optimized at the IEF-PCM/B3LYP/6-31+G(d) level of theory in methanol. (a). (*E*)-3-(methylsulfinyl)prop-2-ene-1-thiolate, (b) (*Z*)-3-(methylsulfinyl)prop-2-ene-1-thiolate.



**Figure S4.** Reactant, transition state and products for the (*R,R*) sulfoxide analogue of SB-3CT (**4**) in the MMP2 active site (**8**) optimized at the ONIOM(B3LYP/6-31G(d):AMBER) level of theory. Energies (in kcal/mol) were calculated at ONIOM(B3LYP/6-311+G(d,p):AMBER) using electronic embedding with the reactant complex used as reference state. The sulfoxide group of **4** forms hydrogen bond with the backbone NH of Leu191. Complex **8-P1** is the unprotonated ring-opening product. In complex **8-P2**, the ring-opening product thiolate is protonated by a water molecule, and the resulting hydroxide anion coordinates with the zinc. Key bond lengths are in Å. Ball-and-stick representation of QM region and cartoon representation of protein are shown in Figure 2.





**Figure S6.** Illustration of full and partial QM/MM models. (a) full size QM/MM model, (b) partial QM/MM model. The QM region is shown in green. Residues allowed to move during optimization are in blue. Frozen residues are in red. Partial models were built for both **8-TS** and **9-TS** and subject to full vibrational frequency and IRC calculations. The animations available: vibrational normal mode and IRC path of **8-TS** and vibrational normal mode and IRC path of **9-TS**.

Cartesian coordinates of conformers for **3**:

**3a**

C	-1.118244	-0.033828	0.555534
H	-1.137279	0.012683	1.642811
C	-1.772674	1.081787	-0.164773
H	-2.193613	1.897027	0.417540
H	-1.377802	1.366310	-1.136409
C	0.086341	-0.730016	-0.027813
H	0.186452	-1.745841	0.368156
H	0.047873	-0.762802	-1.121562
C	2.802973	-0.989125	-0.370941
H	2.551048	-1.077815	-1.431458
H	3.803856	-0.567498	-0.252942
H	2.748775	-1.960461	0.128915
S	1.644631	0.168560	0.441248
O	1.671313	1.467141	-0.380090
S	-2.769018	-0.473037	-0.161647

**3b**

C	1.067754	0.437857	-0.098438
H	0.948937	1.481576	-0.379385
C	1.841180	0.176167	1.138792
H	2.192703	1.025853	1.717818
H	1.593468	-0.706520	1.723947
C	-0.058238	-0.478181	-0.509762
H	-0.294821	-0.397835	-1.575630
H	0.174653	-1.520888	-0.275235
C	-2.077283	1.446281	-0.337322
H	-2.105634	1.343884	-1.425780
H	-3.065688	1.713261	0.044369
H	-1.351984	2.205874	-0.032162
S	-1.643319	-0.159623	0.417010
O	-2.644331	-1.180474	-0.148822
S	2.794727	-0.165012	-0.402447



**3c**

C	-0.907027	-0.188609	0.337602
H	-0.655855	-0.594591	1.314903
C	-1.612314	1.113821	0.320167
H	-1.801194	1.614153	1.266508
H	-1.448455	1.778663	-0.524421
C	0.041865	-0.582536	-0.766355
H	-0.002807	-1.658426	-0.960281
H	-0.160656	-0.052728	-1.703101
C	1.803380	1.500126	-0.049160
H	1.146584	1.722027	0.795132
H	2.829595	1.789391	0.189324
H	1.474206	2.020174	-0.953309
S	1.836743	-0.300650	-0.363513
O	2.096440	-0.971208	0.995746
S	-2.718516	-0.318463	-0.039253

**3d**

C	-1.140102	0.074134	0.666138
H	-1.023395	-0.672930	1.447956
C	-2.443863	0.775923	0.615721
H	-3.185150	0.537643	1.373874
H	-2.461877	1.804877	0.264289
C	0.124336	0.816460	0.312069
H	-0.050045	1.555191	-0.476694
H	0.532680	1.312096	1.201963
C	2.760959	0.891778	-0.474250
H	2.925009	1.395431	0.482459
H	3.658856	0.346142	-0.773517
H	2.487469	1.608440	-1.254158
S	1.427065	-0.344277	-0.300072
O	1.802814	-1.233774	0.896565
S	-2.246693	-0.491127	-0.709726

**3e**

C	-1.142711	-0.655995	-0.418742
H	-1.093821	-0.855895	-1.487516
C	-2.433241	-0.972856	0.239685
H	-3.220358	-1.418983	-0.362569
H	-2.415082	-1.291398	1.279281
C	0.145395	-0.904156	0.329808
H	0.085894	-0.614571	1.383627
H	0.396683	-1.970296	0.269125
C	1.434537	1.585511	0.261137
H	1.408429	1.531277	1.353054
H	2.301791	2.161406	-0.070703
H	0.518413	2.034743	-0.130017
S	1.631853	-0.094038	-0.425238
O	2.838417	-0.710659	0.303000
S	-2.176425	0.831161	-0.020363

**3f**

C	0.970710	-0.658258	0.236085
H	0.679222	-0.996003	1.227562
C	2.382399	-0.935641	-0.138942
H	2.999414	-1.483493	0.568575
H	2.607973	-1.126562	-1.185696
C	-0.097543	-0.750219	-0.824175
H	0.253537	-0.332084	-1.772389
H	-0.382357	-1.796743	-0.994943
C	-2.231757	-0.811433	0.992848
H	-1.516681	-0.672738	1.807486
H	-3.203268	-0.402854	1.280853
H	-2.338035	-1.869030	0.735514
S	-1.701284	0.125204	-0.485557
O	-1.393153	1.549231	-0.002232
S	2.070194	0.825981	0.282807

**3g**

C	1.284430	-0.756525	0.619375
H	1.826569	-1.184318	1.461037
C	1.901221	-0.958349	-0.711508
H	2.811537	-1.548785	-0.774424
H	1.250401	-1.028602	-1.580362
C	-0.215174	-0.795047	0.833999
H	-0.558470	-1.832840	0.752096
H	-0.486940	-0.409548	1.822311
C	-2.746150	-0.735771	-0.228039
H	-3.038789	-0.819764	0.822422
H	-3.504958	-0.185232	-0.788747
H	-2.598184	-1.723287	-0.674478
S	-1.196805	0.225911	-0.365995
O	-1.477509	1.571729	0.321252
S	2.120114	0.751132	-0.052307

**3h**

C	-1.267835	-0.944537	0.300507
H	-1.788915	-1.891209	0.175677
C	-2.036588	0.107159	1.005220
H	-3.015986	-0.153645	1.397974
H	-1.496608	0.844745	1.594070
C	0.232296	-1.130030	0.462500
H	0.529249	-1.108788	1.517398
H	0.527594	-2.097547	0.047126
C	1.241921	1.501471	0.630417
H	2.006259	2.199747	0.280292
H	0.253701	1.952057	0.513774
H	1.436835	1.220573	1.669053
S	1.370555	0.027694	-0.442714
O	2.771418	-0.550923	-0.176149
S	-1.973195	0.362123	-0.818413

**3i**

C	1.228847	-0.536397	0.766244
H	1.897570	-0.799884	1.585871
C	1.694815	-0.944122	-0.580109
H	2.618651	-1.512791	-0.650216
H	0.941409	-1.157179	-1.331433
C	-0.211430	-0.616794	1.239154
H	-0.386582	-1.650199	1.564327
H	-0.372786	0.026145	2.111452
C	-1.596306	1.546814	0.026036
H	-0.659454	1.871245	-0.428384
H	-2.451248	1.841687	-0.587633
H	-1.709543	1.955486	1.034390
S	-1.657085	-0.278502	0.124091
O	-1.352678	-0.817622	-1.284068
S	1.922576	0.857843	-0.232451

Cartesian coordinates of conformers for **5**:

**5a**

C	-1.094093	-0.364879	-0.236041
H	-0.982827	-1.236802	-0.876462
C	-1.894029	-0.547114	0.997434
H	-2.289372	-1.535333	1.216410
H	-1.638805	0.049130	1.870605
C	0.073687	0.589731	-0.264073
H	0.292221	0.928760	-1.281939
H	-0.098339	1.454486	0.384857
C	2.747970	1.141288	0.103273
H	2.463966	1.960710	0.769640
H	3.747679	0.783851	0.361332
H	2.715934	1.456106	-0.943545
S	1.604669	-0.261454	0.357538
O	1.967268	-1.321577	-0.695344
S	-2.789033	0.373802	-0.328894

**5b**

C	-1.080941	-0.080470	0.517551
H	-1.048135	-0.149281	1.603415
C	-1.755625	1.114781	-0.043454
H	-2.128712	1.868410	0.645189
H	-1.417427	1.498580	-1.002976
C	0.073286	-0.743071	-0.195687
H	0.090838	-1.819178	0.001266
H	0.048830	-0.581952	-1.278246
C	1.725552	1.522897	-0.238724
H	0.957286	2.106227	0.276300
H	2.709957	1.945706	-0.024094
H	1.549568	1.502624	-1.317777
S	1.738162	-0.180196	0.418981
O	2.757018	-0.961956	-0.426564
S	-2.775160	-0.417323	-0.152024

**5c**

C	-0.918570	-0.348858	0.300232
H	-0.731834	-1.020018	1.134616
C	-1.544165	0.950777	0.628523
H	-1.726507	1.187340	1.673317
H	-1.311402	1.804267	-0.002000
C	0.036047	-0.470974	-0.858598
H	0.119983	-1.501794	-1.218490
H	-0.275314	0.162284	-1.694806
C	2.186639	-1.078428	0.857861
H	2.076053	-2.107623	0.504215
H	3.229640	-0.889597	1.122512
H	1.544574	-0.885793	1.720682
S	1.781122	0.077783	-0.500810
O	1.707851	1.476999	0.129012
S	-2.727853	-0.257793	-0.114206

**5d**

C	-1.168091	-0.594668	-0.492980
H	-1.149464	-0.649034	-1.580119
C	-2.430533	-1.028551	0.154584
H	-3.226425	-1.410189	-0.479580
H	-2.371412	-1.485164	1.139927
C	0.151924	-0.893801	0.173967
H	0.103719	-0.767489	1.260652
H	0.453003	-1.922156	-0.063463
C	2.884987	-0.706695	0.366909
H	2.975481	-1.704310	-0.072007
H	3.794843	-0.133750	0.173771
H	2.696213	-0.766203	1.442550
S	1.518452	0.189612	-0.452223
O	1.402451	1.545813	0.258382
S	-2.213782	0.798768	0.133244

**5e**

C	1.123600	0.195402	0.666657
H	1.000556	1.170741	1.131828
C	2.461268	-0.426815	0.824256
H	3.203897	0.101000	1.416640
H	2.520201	-1.511431	0.873526
C	-0.106617	-0.677667	0.656282
H	0.120568	-1.678767	0.277565
H	-0.536507	-0.765479	1.661798
C	-1.913847	1.437367	0.461766
H	-1.095759	2.160492	0.400009
H	-2.798266	1.847067	-0.031930
H	-2.142045	1.187071	1.501733
S	-1.465548	-0.079352	-0.452999
O	-2.622998	-1.067678	-0.233751
S	2.173355	0.258165	-0.860434

**5f**

C	0.957261	-0.627809	0.262528
H	0.643035	-0.875663	1.274234
C	2.366715	-0.936425	-0.080358
H	2.984650	-1.419321	0.672312
H	2.598859	-1.209607	-1.107284
C	-0.112301	-0.816501	-0.784494
H	0.150090	-0.360731	-1.744650
H	-0.277684	-1.889185	-0.945229
C	-1.461317	1.586005	-0.153321
H	-1.084976	1.975684	-1.103217
H	-2.418904	2.054430	0.086451
H	-0.746203	1.757859	0.653677
S	-1.797738	-0.201990	-0.320821
O	-2.074752	-0.722267	1.100450
S	2.063176	0.859055	0.192319

**5g**

C	-1.243214	-0.783137	0.595150
H	-1.772245	-1.650971	0.986237
C	-1.829846	0.532532	0.938132
H	-2.708226	0.549194	1.578155
H	-1.159945	1.382156	1.034356
C	0.249608	-1.036702	0.517465
H	0.667104	-1.077249	1.531517
H	0.442151	-1.992016	0.017378
C	2.857024	-0.551204	-0.133209
H	2.886452	-1.529114	-0.622440
H	3.598533	0.110575	-0.586854
H	3.039196	-0.643424	0.941137
S	1.224512	0.222940	-0.421248
O	1.211416	1.519141	0.406907
S	-2.154873	0.010109	-0.806250

**5h**

C	1.300177	-0.640212	0.708000
H	1.871001	-0.911129	1.594694
C	1.928790	-0.978953	-0.588234
H	2.878863	-1.506549	-0.575675
H	1.288078	-1.211405	-1.435497
C	-0.193070	-0.741941	0.945690
H	-0.478338	-1.798829	1.005512
H	-0.481554	-0.253491	1.881000
C	-1.600941	1.571211	0.275804
H	-0.655640	2.110414	0.371841
H	-2.257616	2.088000	-0.428063
H	-2.094886	1.460059	1.245490
S	-1.275927	-0.087417	-0.417124
O	-2.598902	-0.864222	-0.284471
S	2.032900	0.817172	-0.172319

Cartesian coordinates of reactant complex **3-R**:

C	1.977018	-0.887604	0.538919
H	3.011809	-0.560364	0.611169
C	1.697463	-2.277937	0.966764
H	2.516710	-2.868769	1.368267
H	0.720866	-2.495860	1.392071
C	0.951221	0.190834	0.782345
H	-0.077947	-0.192164	0.737269
H	1.131696	0.654805	1.761247
C	-0.126279	2.664594	0.278940
H	0.205656	2.927832	1.288110
H	-0.159533	3.557843	-0.350365
H	-1.106169	2.169072	0.295434
S	1.088555	1.533036	-0.474888
O	2.479932	2.172262	-0.287021
S	1.708682	-2.072464	-0.866173
C	-3.037655	-0.237609	0.152566
C	-4.082084	-0.952328	-0.723999
H	-4.938373	-0.306149	-0.940517
H	-3.616006	-1.231066	-1.678764
H	-4.429167	-1.876353	-0.249061
O	-3.060945	1.030003	0.174327
O	-2.205666	-0.970726	0.768806

Cartesian coordinates of reactant complex **5-R**:

C	-2.016724	-0.551828	0.404584
H	-1.870196	-0.551163	1.482303
C	-3.420190	-0.544709	-0.068895
H	-4.217849	-0.494661	0.667630
H	-3.640271	-0.058618	-1.016822
C	-0.926683	0.134905	-0.379297
H	0.065888	-0.281396	-0.158666
H	-1.122814	0.084756	-1.456014
C	0.554342	2.377351	-0.980475
H	0.264844	2.278436	-2.031741
H	0.784635	3.424014	-0.764083
H	1.406511	1.728359	-0.743225
S	-0.882008	1.938884	0.059026
O	-0.414508	2.025568	1.525115
S	-2.605016	-2.194676	-0.222804
C	3.146386	-0.773140	-0.036036
C	4.420803	-1.548749	0.347005
H	4.707422	-1.278349	1.372501
H	4.253044	-2.630482	0.323124
H	5.257471	-1.289884	-0.310205
O	3.300380	0.373400	-0.554805
O	2.033641	-1.324134	0.221483

Cartesian coordinates of transition states for **3**:

**3-TSa**

C	1.176441	1.301459	0.240870
H	1.339580	1.243983	1.315071
C	1.566593	2.565261	-0.385907
H	2.287279	3.185184	0.146951
H	1.748419	2.533959	-1.460200
C	0.916109	0.059847	-0.457060
H	-0.590462	-0.188215	-0.566551
H	1.220469	0.055664	-1.511198
C	-2.484363	-0.584704	0.166889
C	-3.935637	-0.774270	-0.235421
H	-4.557164	-0.955894	0.643837
H	-4.297136	0.116091	-0.761874
H	-4.024697	-1.619856	-0.926799
O	-2.111025	-0.649172	1.342833
C	0.865501	-2.658332	-0.667303
H	1.190518	-2.476677	-1.696483
H	1.265083	-3.610453	-0.310870
H	-0.224933	-2.656745	-0.601807
S	1.548692	-1.354473	0.416157
O	3.089938	-1.494407	0.247522
O	-1.685117	-0.353206	-0.851982
S	-0.194642	2.910202	0.074501

**3-TSb**

C	1.227010	1.112600	0.054606
H	1.585779	0.937755	1.066302
C	1.442786	2.456219	-0.479586
H	2.291741	3.007604	-0.073625
H	1.368855	2.552869	-1.563414
C	0.785467	-0.028112	-0.688963
H	-0.679283	-0.251510	-0.676441
H	0.899912	0.042218	-1.777136
C	-2.653899	-0.624205	0.011635
C	-4.070821	-0.891779	-0.469591
H	-4.736238	-1.080527	0.375506
H	-4.438432	-0.027077	-1.034225
H	-4.083592	-1.752051	-1.147731
O	-2.369190	-0.567959	1.213111
C	3.247894	-1.402925	-0.336428
H	3.583373	-0.580640	0.302147
H	3.725224	-2.338701	-0.031590
H	3.470929	-1.193890	-1.386793
S	1.433434	-1.620927	-0.142320
O	1.230247	-1.721327	1.387171
O	-1.796726	-0.458041	-0.969559
S	-0.144281	2.804162	0.414268



### 3-TSc

C	-1.903989	-0.269430	-0.069428
H	-2.298282	0.042905	0.893589
C	-2.613193	-1.390943	-0.687111
H	-3.679827	-1.459733	-0.468771
H	-2.403891	-1.546314	-1.746508
C	-0.892929	0.511970	-0.710695
H	0.409769	-0.084131	-0.689278
H	-1.015055	0.564536	-1.799693
C	2.295579	-0.798795	0.043562
C	3.630017	-1.396902	-0.375170
H	4.260197	-1.582894	0.497279
H	3.469113	-2.334626	-0.918435
H	4.146108	-0.710537	-1.056373
O	2.044173	-0.536569	1.228554
C	-0.225148	1.916519	1.610073
H	0.611837	1.212878	1.628613
H	0.056503	2.887200	2.027018
H	-1.080539	1.522327	2.166492
S	-0.716079	2.232810	-0.123486
O	0.535572	2.797350	-0.829756
O	1.475195	-0.595435	-0.954243
S	-1.575013	-2.437116	0.438626

### 3-TSd

C	1.050159	-1.161174	0.604898
H	0.939585	-1.846935	1.441307
C	1.337149	-1.789719	-0.685845
H	1.063444	-2.838700	-0.795695
H	1.116365	-1.204721	-1.577611
C	0.472888	0.141690	0.830746
H	-0.992760	-0.162892	0.795029
H	0.602113	0.527327	1.848750
C	-2.843321	-0.514819	-0.119477
C	-4.278672	-0.945511	0.125576
H	-4.833991	-0.986510	-0.813834
H	-4.296648	-1.930930	0.604537
H	-4.768135	-0.242729	0.809257
O	-2.417477	-0.261391	-1.253585
C	-0.571637	2.531069	0.017889
H	-0.609320	2.726315	1.093978
H	-0.402391	3.462524	-0.527822
H	-1.490888	2.052235	-0.326647
S	0.844525	1.438618	-0.349644
O	2.081786	2.250475	0.123830
O	-2.120195	-0.435535	0.973594
S	3.050496	-1.535655	-0.021899

**3-TSe**

C	-0.775232	-1.160441	-0.490971
H	-0.476441	-1.953362	-1.173513
C	-1.232200	-1.606639	0.826450
H	-0.858822	-2.572089	1.168457
H	-1.241499	-0.846818	1.603735
C	-0.299300	0.136045	-0.877676
H	1.156182	0.024528	-0.776701
H	-0.333812	0.341814	-1.953271
C	3.102172	-0.229578	0.061547
C	4.577803	-0.370036	-0.278097
H	5.176059	-0.467815	0.630497
H	4.728149	-1.255844	-0.906406
H	4.919519	0.497732	-0.852646
O	2.690540	-0.318967	1.225650
C	-2.464955	1.938675	-0.499345
H	-3.062521	1.094153	-0.149575
H	-2.779173	2.873020	-0.025574
H	-2.528470	2.033967	-1.587610
S	-0.706735	1.679849	-0.038110
O	-0.715017	1.455350	1.493020
O	2.338742	-0.018968	-0.982974
S	-2.834703	-1.739646	-0.106540

Cartesian coordinates of transition states for **5**:

**5-TSa**

C	1.302315	1.150800	-0.207237
H	2.206316	1.097151	0.393129
C	1.061988	2.446228	-0.848324
H	1.918428	3.105797	-0.985111
H	0.386397	2.442536	-1.703542
C	0.670064	-0.087354	-0.613799
H	-0.706390	-0.344030	0.017868
H	0.346654	-0.098088	-1.658941
C	-2.746074	-0.525697	-0.241072
C	-4.036300	-0.918279	0.455379
H	-4.213274	-0.257316	1.311409
H	-4.879853	-0.853262	-0.234937
H	-3.957623	-1.939869	0.843630
O	-1.687079	-0.608382	0.536728
C	1.532572	-1.585607	1.545713
H	0.497251	-1.616207	1.894115
H	2.070248	-2.477781	1.875550
H	2.038692	-0.690684	1.919305
S	1.554465	-1.595776	-0.284736
O	3.069022	-1.498990	-0.638250
O	-2.717305	-0.165643	-1.422342
S	0.212327	2.654234	0.783141

**5-TSb**

C	-1.134147	1.380086	-0.174057
H	-1.682493	1.484294	-1.107815
C	-1.068189	2.584239	0.653997
H	-1.868028	3.313590	0.523859
H	-0.815104	2.426384	1.702736
C	-0.778986	0.049753	0.248910
H	0.567377	-0.296858	-0.201027
H	-0.699644	-0.090327	1.332339
C	2.560393	-0.787221	0.262296
C	3.892728	-1.222270	-0.327485
H	4.239553	-0.483983	-1.059059
H	4.642877	-1.338627	0.457754
H	3.770919	-2.173557	-0.858182
O	1.629035	-0.591596	-0.637208
C	-3.224903	-1.258773	0.635040
H	-3.732324	-0.289822	0.617039
H	-3.904239	-2.046092	0.296803
H	-2.854927	-1.482181	1.640548
S	-1.801904	-1.208940	-0.520454
O	-1.118829	-2.583248	-0.329683
O	2.402257	-0.644167	1.482368
S	0.399089	2.899839	-0.433360

**5-TSc**

C	-1.515322	1.132410	0.204408
H	-2.253167	1.096757	-0.593969
C	-1.370960	2.422098	0.877368
H	-2.282391	3.017290	0.952710
H	-0.828613	2.392755	1.823647
C	-0.868364	-0.079625	0.583637
H	0.387773	-0.222795	-0.044671
H	-0.587214	-0.139986	1.640362
C	2.510187	-0.279821	0.112762
C	3.811961	-0.528787	-0.633933
H	3.929793	0.220201	-1.425923
H	4.664588	-0.469367	0.046250
H	3.792203	-1.511910	-1.116547
O	1.440811	-0.448877	-0.621763
C	-0.568531	-2.826400	0.563145
H	-0.375984	-2.760135	1.638215
H	-1.003742	-3.800466	0.326094
H	0.346235	-2.658281	-0.009341
S	-1.815019	-1.569660	0.102287
O	-1.905764	-1.575514	-1.437466
O	2.499493	0.057310	1.305512
S	-0.313709	2.915494	-0.568001

**5-TSd**

C	-0.655973	-1.090826	0.115613
H	0.076500	-1.892323	0.052249
C	-1.592701	-1.195895	1.240186
H	-1.289336	-1.799784	2.094616
H	-2.143260	-0.301941	1.519170
C	-0.271092	0.087953	-0.636771
H	1.160746	0.349694	-0.167820
H	-0.042640	-0.117302	-1.686490
C	3.104345	-0.346243	-0.117988
C	4.529119	0.001689	0.272381
H	4.582924	0.209937	1.346844
H	5.206406	-0.818470	0.025262
H	4.848368	0.909886	-0.251175
O	2.234077	0.600096	0.164350
C	-0.662434	2.230749	1.117030
H	0.424779	2.307412	1.194199
H	-1.118739	3.216009	1.242461
H	-1.051864	1.544018	1.871720
S	-1.099411	1.666658	-0.572795
O	-2.654934	1.593503	-0.561466
O	2.809918	-1.422599	-0.649293
S	-2.430212	-2.160389	-0.102985

**5-TSe**

C	0.768551	-1.242588	0.180664
H	0.332458	-1.996791	0.831226
C	1.421570	-1.757185	-1.024226
H	1.116218	-2.748040	-1.359362
H	1.555703	-1.059428	-1.849643
C	0.276867	0.090752	0.412032
H	-1.090650	0.014809	-0.124699
H	0.097680	0.336342	1.463187
C	-3.137677	-0.342770	0.226242
C	-4.511326	-0.413025	-0.421034
H	-4.509081	-1.156770	-1.225808
H	-5.273190	-0.675924	0.316015
H	-4.759759	0.553923	-0.873183
O	-2.173824	-0.050885	-0.612608
C	2.236426	1.990182	0.902633
H	2.897714	1.158604	1.160394
H	2.816602	2.837036	0.526128
H	1.633477	2.295588	1.763553
S	1.112379	1.440282	-0.431483
O	0.099524	2.603045	-0.589990
O	-2.975988	-0.546755	1.437407
S	2.841288	-1.787456	0.171224

**5-TSf**

C	-1.001579	-1.181585	-0.197097
H	-0.620629	-2.071182	-0.692979
C	-1.821889	-1.423073	0.991114
H	-1.661727	-2.370774	1.505577
H	-1.931119	-0.586830	1.679121
C	-0.350173	0.035033	-0.582610
H	0.986171	-0.041027	0.035907
H	-0.100815	0.088703	-1.646737
C	2.982805	-0.680590	-0.073949
C	4.333613	-0.654171	0.621629
H	4.243049	-1.073915	1.629851
H	5.070563	-1.226128	0.053642
H	4.678506	0.380312	0.730441
O	2.049200	-0.010444	0.559499
C	0.129707	2.704869	-0.864581
H	0.111548	2.574494	-1.950470
H	-0.157585	3.728245	-0.611318
H	1.117691	2.471968	-0.459385
S	-1.120035	1.604715	-0.102683
O	-0.973340	1.779647	1.427220
O	2.808332	-1.287464	-1.139011
S	-3.157721	-1.512882	-0.298714

Active site coordinates (QM region) for MMP2 complex with **4 (8)**:

**8-R**

C	51.804911	38.188371	51.607687
N	52.406267	37.942271	52.822335
H	53.411591	37.935590	53.016483
C	51.435283	37.734446	53.742225
H	51.645828	37.532502	54.781058
N	50.233092	37.840742	53.185666
C	50.464661	38.140656	51.853088
H	49.626952	38.307731	51.201306
C	47.372907	38.461723	49.595440
H	48.244221	39.111149	49.713999
H	46.544331	39.070787	49.218752
C	46.925389	37.846219	50.935790
O	47.693271	38.127193	51.959900
O	45.906322	37.153835	50.988343
C	47.294256	33.486001	52.371128
N	47.475333	33.213991	53.711684
H	47.186822	32.392978	54.257947
C	47.751618	34.383253	54.335913
H	47.911487	34.456795	55.399928
N	47.808241	35.378717	53.461496
C	47.520763	34.820912	52.225758
H	47.373364	35.431506	51.355861
C	49.574024	35.956494	57.687029
N	48.511028	36.745406	58.074957
H	48.088672	36.845403	59.003839
C	48.025310	37.367009	56.974122
H	47.157995	38.007172	57.008208
N	48.728360	37.044983	55.894715
C	49.711055	36.169146	56.339855
H	50.424044	35.750964	55.646507
Zn	48.211701	37.386181	53.735241
C	45.020001	39.206423	53.520584
H	45.250927	38.612266	52.640760
H	43.990877	39.146497	53.863354
S	46.264209	39.055766	54.874006
C	45.748121	40.466092	53.789209
H	45.176375	41.202162	54.350166
C	46.758409	41.079151	52.852175
H	47.456623	40.334777	52.461466
H	46.265064	41.597251	52.022107
S	47.619812	42.397529	53.821999
O	46.801585	43.665443	53.686602
O	45.395947	36.308944	55.794994
H	45.120822	35.794249	55.000688
H	45.691593	35.595734	56.412486

**8-TS**

C	51.712006	38.147972	51.588778
N	52.386824	37.868173	52.756422
H	53.400055	37.850814	52.894696
C	51.483275	37.672597	53.737130
H	51.751989	37.445643	54.757765
N	50.251294	37.818617	53.256178
C	50.384693	38.128078	51.909393
H	49.514209	38.397814	51.316045
C	47.666089	38.818959	48.471536
H	48.625993	39.336788	48.411589
H	46.940545	39.403203	47.895982
C	47.177270	38.757549	49.925037
O	46.135588	38.165554	50.219659
O	47.970309	39.376783	50.773434
C	47.629758	33.541326	52.345692
N	47.368423	33.324575	53.680005
H	46.891654	32.553067	54.163862
C	47.779254	34.404501	54.370495
H	47.650129	34.498080	55.438295
N	48.315541	35.301584	53.555405
C	48.236929	34.764332	52.280831
H	48.622115	35.298003	51.424611
C	49.677154	35.867809	57.940527
N	48.621560	36.676726	58.305036
H	48.166211	36.781243	59.218366
C	48.171601	37.314357	57.200286
H	47.298112	37.950125	57.208917
N	48.905718	36.973371	56.142327
C	49.852526	36.075350	56.601207
H	50.566763	35.637918	55.920995
Zn	48.533246	37.243703	54.119361
C	45.310194	38.866745	53.141718
H	45.501889	38.487487	52.132534
H	44.284048	38.729868	53.480196
S	46.431918	38.141681	54.444675
C	45.906649	40.167980	53.454875
H	45.669283	40.574746	54.434652
C	46.752983	40.890905	52.573644
H	47.466385	40.082249	51.784081
H	46.214745	41.232911	51.677563
S	47.479092	42.279386	53.513451
O	46.671016	43.547445	53.338171
O	45.076304	37.119081	57.253721
H	45.342653	37.248321	56.319702
H	45.428189	36.215109	57.439462

**8-P1**

C	51.801927	38.165706	51.237357
N	52.471943	37.997566	52.428425
H	53.482692	38.014907	52.591970
C	51.560842	37.811025	53.405392
H	51.830128	37.662214	54.439897
N	50.331996	37.855457	52.904116
C	50.471783	38.092193	51.545519
H	49.604933	38.228039	50.911098
C	47.641088	38.763679	47.755259
H	48.568962	39.328056	47.861078
H	46.985241	39.284659	47.052204
C	46.919971	38.628214	49.077902
O	47.720815	38.937421	50.134766
O	45.785006	38.240794	49.219741
C	47.805204	33.474903	52.185257
N	47.608492	33.253409	53.529838
H	47.077857	32.524816	54.024121
C	48.152404	34.285400	54.205903
H	48.096294	34.375393	55.280669
N	48.713295	35.148174	53.371113
C	48.507284	34.642485	52.100001
H	48.882375	35.156435	51.224033
C	49.654866	35.959619	57.597170
N	48.454550	36.586792	57.838630
H	47.790462	36.541739	58.620612
C	48.071623	37.201737	56.701105
H	47.124469	37.715247	56.598092
N	48.973696	37.032961	55.744138
C	49.979057	36.262693	56.301559
H	50.837529	35.976973	55.714966
Zn	48.611091	37.182648	53.751331
C	45.624442	38.870201	53.670292
H	44.865369	39.181878	52.951450
H	45.102195	38.501194	54.559221
S	46.510775	37.434688	52.875785
C	46.487170	40.033240	54.043900
H	46.911215	40.027644	55.050808
C	46.751735	41.080881	53.256279
H	47.208119	38.757834	50.960088
H	46.353668	41.202888	52.251045
S	47.600662	42.487722	53.975820
O	46.776676	43.725706	53.700004
O	45.959838	36.613248	59.131959
H	45.556387	37.334127	58.569974
H	45.822256	35.858140	58.486499



**8-P2**

C	51.875388	38.049114	51.378631
N	52.631548	37.981497	52.524964
H	53.643934	38.088164	52.631176
C	51.808755	37.756521	53.570348
H	52.156010	37.668120	54.588748
N	50.553468	37.686504	53.154284
C	50.581788	37.881825	51.782410
H	49.666633	37.949654	51.209622
C	47.434177	38.592163	48.373754
H	48.322622	39.227398	48.379747
H	46.637840	39.109043	47.831137
C	46.956184	38.310323	49.789403
O	47.812060	38.791558	50.713356
O	45.951343	37.693048	50.076111
C	47.727135	33.516824	52.306419
N	47.423534	33.313957	53.633806
H	46.915321	32.556998	54.107451
C	47.887580	34.365332	54.337737
H	47.753352	34.462880	55.404844
N	48.494125	35.227798	53.534842
C	48.403628	34.702404	52.257829
H	48.830359	35.220315	51.410199
C	49.712495	35.910581	57.880515
N	48.553764	36.602626	58.159333
H	48.034195	36.676188	59.039671
C	48.136978	37.205184	57.020036
H	47.218631	37.764407	56.933567
N	48.991779	36.957658	56.032530
C	49.981279	36.155132	56.563079
H	50.794795	35.814994	55.942065
Zn	48.792221	37.176949	54.023122
C	44.522800	39.506278	53.757837
H	44.708432	39.098127	52.763012
H	43.507331	39.916517	53.781057
S	44.541259	38.081580	54.940291
C	45.505211	40.574473	54.124236
H	45.450053	40.933795	55.151202
C	46.420662	41.124687	53.312993
H	47.506420	38.553305	51.652125
H	46.528258	40.882951	52.257770
S	47.384972	42.467621	54.033503
O	46.707015	43.792835	53.775915
O	47.402629	38.143709	53.247267
H	47.276281	39.021716	53.642509
H	45.663029	37.556669	54.383786

Active site coordinates (QM region) for MMP2 complex with **6 (9)**:

**9-R**

C	51.810650	38.274404	51.618934
N	52.426849	38.007949	52.821498
H	53.434347	37.992909	53.002975
C	51.468242	37.788863	53.750992
H	51.692716	37.573237	54.784029
N	50.259790	37.906931	53.212227
C	50.472586	38.228507	51.882128
H	49.624222	38.410498	51.247276
C	47.347648	38.519059	49.700112
H	48.214379	39.175711	49.812033
H	46.513041	39.121805	49.326059
C	46.907911	37.905774	51.046891
O	47.675846	38.210237	52.065821
O	45.901468	37.196613	51.099132
C	47.287005	33.503394	52.394966
N	47.488684	33.235809	53.733848
H	47.193007	32.421625	54.286312
C	47.784188	34.406417	54.346824
H	47.958250	34.483381	55.408374
N	47.833163	35.398737	53.468715
C	47.521170	34.836429	52.240288
H	47.361690	35.441642	51.368390
C	49.570833	35.996501	57.664511
N	48.502635	36.777934	58.054513
H	48.077886	36.870247	58.983557
C	48.008988	37.398518	56.957824
H	47.143310	38.040500	56.992365
N	48.716071	37.085650	55.877806
C	49.707274	36.215611	56.318755
H	50.423013	35.804319	55.624102
Zn	48.252975	37.416905	53.769650
C	44.971359	39.436438	53.695634
H	45.220629	38.938438	52.764221
H	43.941962	39.309483	54.019664
S	46.227617	39.264158	55.015261
C	45.648110	40.714196	54.046789
H	45.057347	41.386609	54.664689
C	46.609043	41.400133	53.112606
H	47.285010	40.679591	52.646993
H	46.071933	41.954454	52.332236
S	47.513936	42.721383	54.086793
O	47.895175	42.185108	55.453406
O	45.430475	36.381008	55.736194
H	45.143805	35.865847	54.945347
H	45.731267	35.666918	56.349349

**9-TS**

C	51.845515	38.253766	51.550521
N	52.513320	37.965822	52.721564
H	53.525829	37.935635	52.865537
C	51.602177	37.775399	53.696637
H	51.863770	37.543843	54.717996
N	50.373437	37.932289	53.209684
C	50.516090	38.245318	51.864539
H	49.646538	38.516585	51.268370
C	47.783039	38.949634	48.490395
H	48.761468	39.433645	48.453963
H	47.095719	39.542683	47.877913
C	47.238501	38.935295	49.930696
O	46.110959	38.480891	50.157448
O	48.058610	39.429496	50.821334
C	47.717107	33.583446	52.370785
N	47.471590	33.394163	53.712456
H	46.963298	32.649348	54.206106
C	47.944430	34.462861	54.381545
H	47.838248	34.573826	55.450101
N	48.507361	35.326277	53.546941
C	48.378822	34.776829	52.281145
H	48.771147	35.282017	51.409975
C	49.725208	35.934611	57.886582
N	48.651337	36.731043	58.227215
H	48.168253	36.818056	59.127898
C	48.231309	37.378842	57.115835
H	47.356346	38.011819	57.101322
N	49.002565	37.057633	56.079170
C	49.941619	36.162316	56.556579
H	50.679862	35.738055	55.893613
Zn	48.663504	37.317299	54.051875
C	45.418205	38.992454	53.154023
H	45.517032	38.740257	52.092008
H	44.390882	38.913293	53.517659
S	46.436195	37.896410	54.253531
C	46.096348	40.227289	53.545548
H	46.093096	40.509015	54.596515
C	46.816431	41.024594	52.622258
H	47.545100	40.320365	51.913215
H	46.176854	41.320661	51.776846
S	47.490120	42.527987	53.474417
O	47.760322	42.166282	54.927748
O	45.139684	37.190813	57.207925
H	45.396294	37.319466	56.270399
H	45.498411	36.288451	57.391333

**9-P1**

C	51.804238	38.301332	51.250614
N	52.462767	38.159829	52.451590
H	53.472290	38.180247	52.624548
C	51.542134	37.963924	53.418403
H	51.802292	37.826053	54.456536
N	50.318227	37.980122	52.902882
C	50.471124	38.201637	51.543130
H	49.608957	38.299102	50.896126
C	47.637138	38.806314	47.788354
H	48.558845	39.378633	47.902209
H	46.982946	39.323358	47.080543
C	46.906306	38.664803	49.105936
O	47.680686	39.018737	50.167014
O	45.782040	38.242515	49.237622
C	47.785701	33.547105	52.182368
N	47.592673	33.343305	53.530163
H	47.079472	32.608703	54.035773
C	48.114364	34.397373	54.190101
H	48.057834	34.499466	55.263776
N	48.655311	35.260446	53.342497
C	48.459705	34.730525	52.079426
H	48.825987	35.237088	51.195576
C	49.659723	35.990069	57.578262
N	48.480335	36.653215	57.833079
H	47.818226	36.610129	58.616840
C	48.107945	37.287074	56.702942
H	47.184741	37.842513	56.610505
N	48.997101	37.095968	55.738048
C	49.982688	36.291416	56.281683
H	50.828084	35.983149	55.687015
Zn	48.596794	37.300197	53.761042
C	45.523780	38.946635	53.772158
H	44.770720	39.273172	53.052289
H	44.995472	38.498172	54.620160
S	46.479618	37.588296	52.915926
C	46.334557	40.113087	54.238416
H	46.821328	40.050292	55.213583
C	46.488706	41.247056	53.554880
H	47.156942	38.841064	50.988379
H	46.047175	41.452026	52.582086
S	47.353300	42.632233	54.312643
O	47.874652	42.192528	55.667969
O	45.987772	36.637224	59.133343
H	45.576149	37.356679	58.573920
H	45.861838	35.886063	58.480424

**9-P2**

C	51.832330	38.171991	51.395802
N	52.591147	38.148399	52.543125
H	53.602577	38.267565	52.644213
C	51.774555	37.897334	53.588840
H	52.125072	37.828445	54.607497
N	50.524357	37.772618	53.173257
C	50.546587	37.951143	51.800025
H	49.632347	37.959966	51.223685
C	47.365865	38.569628	48.294039
H	48.228176	39.237324	48.234407
H	46.529352	39.026376	47.757351
C	46.957658	38.346379	49.743518
O	47.822420	38.912731	50.593921
O	45.987401	37.698430	50.095605
C	47.785567	33.561860	52.353655
N	47.490460	33.345044	53.681693
H	46.984345	32.581447	54.146367
C	47.937542	34.402641	54.390560
H	47.811452	34.490599	55.459274
N	48.523335	35.282780	53.592632
C	48.433857	34.764197	52.312724
H	48.845406	35.294824	51.465673
C	49.630901	35.969529	57.869827
N	48.538732	36.750070	58.190376
H	48.039991	36.832004	59.080678
C	48.129832	37.383810	57.064085
H	47.267442	38.033877	57.024006
N	48.920996	37.071783	56.046448
C	49.869027	36.197565	56.543533
H	50.631289	35.797778	55.893373
Zn	48.747515	37.291978	54.030239
C	44.070476	40.177263	54.423010
H	43.371423	40.812382	53.874398
H	43.574635	39.857449	55.342795
S	44.304129	38.622700	53.430886
C	45.338809	40.915681	54.757212
H	45.752750	40.761930	55.754113
C	45.974900	41.769415	53.951840
H	47.560920	38.713718	51.567407
H	45.681143	41.991765	52.928963
S	47.230355	42.842550	54.663076
O	47.732319	42.229853	55.958512
O	47.519177	38.261074	53.063368
H	46.654241	38.440618	53.467751
H	44.610485	39.297996	52.290455