Electronic Supplementary Information for

Insights into the Catalytic Mechanism of *meta*-Cleavage Product Hydrolase BphD: A Quantum Mechanics/Molecular Mechanics Study

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Keywords

Meta-cleavage product hydrolase, Quantum mechanics/molecular mechanics, Polychlorinated biphenyl metabolites, Electrostatic influence

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Contains additional details on the methods, five Tables, two Schemes, three Figures, and the coordinates of the QM atoms for all the optimized structures

Table S1 Key distances of the reactants during the substrate-assisted acylation (R-1) and deacylation pathway (R-5) at 6, 9, 12 ns. D1~D12 are labelled in Scheme 1. The unit is in Å.

Table S2 Relative energies of substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation at B3LYP/cc-pVTZ//CHARMM22 level in three different snapshots (6 ns, 9 ns, and 12 ns). The unit is in kcal mol^{-1}.

Table S3 Relative energies of substrate-assisted acylation (Ser112 involved) at B3LYP/cc-pVTZ//CHARMM22 level in three different snapshots (6 ns, 9 ns, and 12 ns) for wt BphD and BphD-H265A mutant. The unit is in kcal mol^{-1}.

Table S4 Key distances along the substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation pathway (acy-6 and dea-6). The unit is in Å.

Table S5 Key charges along the substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation pathway (acy-6 and dea-6). The unit is in e.

Scheme S1 Core atoms used (in red color) during microiterative TS optimizations of wt BphD acylation system, BphD-H265A acylation system, and deacylation system.

Scheme S2 The itinerary of the substrate-assisted acylation (Ser112 involved) for both wt BphD and BphD-H265A mutant.

Figure S1 Locations of the three water molecules in the X-ray data (PDB code 3V1N, resolution 1.59 Å) and in our QM/MM models, the unit for bond distances is in Å.

Figure S2 Spatial locations of seventeen residues studied during electrostatic influence analysis. a, Gly41, Gly42, Gly43, Ile153, Leu156, Phe175, Arg190, Phe239, Trp266; b, Asn51, Met113, Met135, Pro137, Gly138, Gly139, Leu213, Trp216. QM atoms are labeled in yellow.

Figure S3 Overlay of residues Gly42, Phe239, and Trp266 in structure R-5 (green) and TS-5-6 (red). The unit for bond distances is in Å.

Additional details on the methods

The protonation states of ionizable residues were determined on the basis of the pKa values obtained via the PROPKA procedure and were manually verified through visual inspection, especially for the residues around the active site. The pH value used (pH 7.5) during pKa calculation is same as experimentally used pH value in determining the k_{cat} (1). The protonation states of the ionizable residues (Glu, Asp, Arg, Cys, Lys, and His residues) are all set in the standard state, except for Lys69, a neutrally charged residue which is more than 15 Å away from the active site. For ten histidine residues of enzyme BphD, the protonation states are listed as follows: Hsd26, Hsd40, Hse107, Hse200, Hse244, Hse258, Hsd265, Hse271, and Hsd285. This was carefully determined based on the manual visual inspection and the results given by MolProbity software (*http://molprobity.biochem.duke.edu/*), especially for the active site residue Hsd265. Note that we follow the nomenclature in CHARMM. Important CHARMM simulation parameters are listed as follows (for explanation of the nomenclatures, see *http://www.charmm.org/documentation/c34b1/dynamc.html*):

The relevant codes for cutoff: "update group noextend fswitch cdie vdw vswitched eps 1.0 cutnb 14.0 ctofnb 13.0 ctonnb 12.0 vgroup WMIN 1.2 inbf 25"; time step for dynamics in picoseconds: timestp 0.001; the frequency for checking whether an atom is in the

Langevin region: ilbfrq 50; a Gaussian distribution of velocities: iasvel 1; simulation temperature: 298.15 K.

Optimization parameters for QM/MM calculations are listed as follows (most are set in default; for explanation of the nomenclatures, see *http://yfaat.ch.huji.ac.il/chemshell-31/manual/hdlcopt.html*):

Optimization parameters for reactants, intermediates, and products: Memory=100; mode=1; contyp=0; reghdl=60; cfact=0.5; recalc=0; toler=0.00045; printl=0; maxfun= 100000; update_procedure=hdlcopt_update; theory=hybrid. Optimization parameters for transition states: Memory=100; contyp=0; ctfirst=1; reghdl=200; cfact=1; maxfun= 100000; toler=0.00045; mode=1; lockon= 0; update_procedure=hdlcopt_update; theory=hybrid.

For QM/MM calculations of acylation system, each residue of the protein, each water molecule, and substrate HOPDA are defined as HDLC residues. For QM/MM calculations of deacylation system, each residue of the protein (including the acylated Ser112) and each water molecule are defined as HDLC residues.

References:

1. A. C. Ruzzini, S. Ghosh, G. P. Horsman, L. J. Foster, J. T. Bolin, and L. D. Eltis, *J. Am. Chem. Soc.*, 2012, **134**, 4615–4624.

Table S1 Key distances of the reactants during the substrate-assisted acylation (R-1) and deacylation pathway (R-5) at 6, 9, 12 ns. D1~D12 are labelled in Scheme 1. The unit is in Å.

Structures	R-1			R-5		
	6 ns	9 ns	12 ns	6 ns	9 ns	12 ns
D1	1.33	1.34	1.34			
D2	1.37	1.37	1.37			
D3	1.43	1.43	1.43			
D4	1.37	1.37	1.37			
D5	1.46	1.46	1.46			
D6	1.24	1.24	1.24	1.22	1.21	1.22
D7	0.98	0.97	0.98			
D8	2.14	2.64	2.40			
D9	3.90	3.76	3.69			
D10	0.97	0.97	0.97			
D11	3.00	2.92	3.04	1.36	1.36	1.37
D12	2.06	2.25	2.07			
D13	4.38	4.47	4.36			
D14	4.70	5.14	4.87			
D15	1.04	1.03	1.04	1.05	1.05	1.05
D16	1.76	1.96	1.71	1.81	1.78	1.74
D17				1.88	1.92	1.85
D18				0.98	1.98	1.00
D19				3.14	3.12	3.12
D20				3.02	3.04	3.17

Table S2 Relative energies of substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation at B3LYP/cc-pVTZ//CHARMM22 level in three different snapshots (6 ns, 9 ns, and 12 ns). The unit is in kcal/mol.

Mechanism	Structure	6 ns	9 ns	12 ns
Substrate-assisted acylation	R-1	0.0	0.0	0.0
	TS-1-2	2.3	0.2	3.9
	IM-2	2.0	1.3	3.4
	TS-2-3-T	15.4	8.5	14.8
	TS-2-3-H	30.1	26.6	32.1
	IM-3	-6.2	-8.3	-4.9
	TS-3-4	7.3	7.0	12.9
	IM-4	6.3	5.6	11.9
	TS-4-5	14.5	10.2	15.5
	IM-5	-11.5	-16.4	-11.2
Deacylation	R-5	0.0	0.0	0.0
	TS-5-6	18.9	26.2	23.5
	IM-6	14.8	22.8	20.9
	IM-6-7	16.3	25.1	23.5
	P-7	0.1	-1.7	1.4

Table S3 Relative energies of substrate-assisted acylation (Ser112 involved) at B3LYP/cc-pVTZ//CHARMM22 level in three different snapshots (6 ns, 9 ns, and 12 ns) for wt BphD and BphD-H265A mutant. The unit is in kcal/mol.

Enzyme	Structure	6 ns	9 ns	12 ns
	R-S-2	0.0	0.0	0.0
	TS1-S-2	20.9	30.9	27.8
wt BphD	IM-S-2	-10.7	3.5	8.6
	TS2-S-2	-8.2	5.5	14.7
	P-S-2	-18.5	-4.0	9.7
	R-M-2	0.0	0.0	0.0
	TS1-M-2	19.5	23.7	24.9
BphD-H265A mutant	IM-M-2	-4.6	2.4	7.8
	TS2-M-2	-1.2	6.4	6.3
	P-M-2	-20.2	-3.6	1.3

Table S4 Key distances of the substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation pathway (acy-6 and dea-6). The unit is in Å.

| Distance	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20
R-1	1.33	1.37	1.43	1.37	1.46	1.24	0.98	2.14	3.90	0.97	3.00	2.06	4.38	4.70	1.04	1.76				
TS-1-2	1.28	1.41	1.40	1.39	1.44	1.25	1.30	1.21	3.78	0.97	3.14	2.04	3.85	4.08	1.04	1.72				
IM-2	1.26	1.43	1.39	1.41	1.43	1.26	1.65	1.06	3.71	0.98	3.13	2.03	4.29	3.69	1.05	1.66				
TS-2-3-T	1.23	1.47	1.35	1.47	1.46	1.25	3.81	1.25	3.10	1.30	3.32	1.33	3.18	1.25	1.05	1.60				
TS-2-3-H	1.23	1.46	1.35	1.46	1.47	1.25	3.98	1.36	2.76	0.97	2.89	2.34	1.45	2.83	1.05	1.65				
IM-3	1.23	1.48	1.34	1.50	1.53	1.23	4.43	1.85	3.62	2.79	2.79	1.09	3.10	0.99	1.04	1.68				
TS-3-4	1.23	1.47	1.34	1.48	1.54	1.26	4.29	1.10	3.14	2.65	1.99	1.10	3.01	1.57	1.06	1.69				
IM-4	1.23	1.47	1.34	1.48	1.55	1.28	4.18	1.05	3.11	2.62	1.75	1.10	2.96	1.80	1.08	1.50				
TS-4-5	1.26	1.43	1.38	1.41	2.03	1.26	2.03	1.03	4.48	2.95	1.44	1.09	3.93	3.95	1.07	1.58				
IM-5	1.35	1.36	1.44	1.34	3.00	1.22	0.98	2.09	4.40	3.16	1.35	1.09	3.92	4.83	1.04	1.75				
R-5						1.22					1.36				1.05	1.81	1.88	0.98	3.14	3.02
TS-5-6						1.25					1.46				1.07	1.73	1.07	1.60	1.71	3.02
IM-6						1.26					1.60				1.09	1.56	1.08	2.37	1.49	1.52
TS-6-7						1.24					1.70				1.07	1.64	1.12	2.34	1.48	1.41
P-7						1.21					2.98				1.05	1.73	1.70	2.67	1.36	0.99

Table S5 Key charges of substrate-assisted acylation (Ser112-His265-Asp237 involved) and deacylation pathway (acy-6 and dea-6). The unit is in e.

Distance	C1	C2	C3	C4	C5	C6	C7	O1	O2	O3	O4	O5	O6	N1	N2	H1	H2	H3	H4	H5	H6	H7
R-1	0.76	0.34	-0.39	-0.13	-0.43	0.53		-0.68	-0.65	-0.77	-0.88			-0.62	-0.56	0.52	0.24	0.27	0.50	0.47		
TS-1-2	0.75	0.40	-0.42	-0.15	-0.48	0.50		-0.70	-0.70	-0.78	-0.87			-0.58	-0.54	0.49	0.23	0.25	0.50	0.49		
IM-2	0.74	0.42	-0.41	-0.16	-0.49	0.48		-0.69	-0.74	-0.78	-0.87			-0.55	-0.53	0.49	0.22	0.24	0.50	0.49		
TS-2-3-T	0.73	0.44	-0.38	-0.11	-0.65	0.57		-0.60	-0.70	-0.81	-0.87			-0.57	-0.55	0.50	0.24	0.24	0.43	0.47		
TS-2-3-H	0.73	0.44	-0.37	-0.13	-0.65	0.55		-0.60	-0.69	-0.75	-0.88			-0.57	-0.55	0.39	0.24	0.24	0.49	0.47		
IM-3	0.73	0.46	-0.35	-0.10	-0.58	0.64		-0.59	-0.64	-0.80	-0.88			-0.60	-0.56	0.27	0.25	0.24	0.52	0.47		
TS-3-4	0.73	0.47	-0.35	-0.09	-0.56	0.59		-0.63	-0.78	-0.77	-0.87			-0.55	-0.54	0.26	0.22	0.25	0.49	0.48		
IM-4	0.73	0.47	-0.35	-0.09	-0.54	0.59		-0.63	-0.87	-0.72	-0.86			-0.54	-0.54	0.25	0.21	0.25	0.49	0.48		
TS-4-5	0.74	0.42	-0.41	-0.12	-0.58	0.71		-0.71	-0.83	-0.61	-0.86			-0.54	-0.53	0.48	0.20	0.24	0.23	0.49		
IM-5	0.77	0.27	-0.37	-0.24	-0.47	0.85		-0.72	-0.69	-0.54	-0.89			-0.62	-0.56	0.52	0.24	0.24	0.22	0.47		
R-5						0.85	-0.32		-0.64	-0.57	-0.83	-0.69	-1.00	-0.63	-0.56					0.47	0.51	0.49
TS-5-6						0.84	-0.31		-0.80	-0.65	-0.83	-0.70	-0.92	-0.53	-0.54					0.48	0.49	0.48
IM-6						0.84	-0.31		-0.83	-0.69	-0.82	-0.71	-0.83	-0.53	-0.55					0.48	0.50	0.49
TS-6-7						0.84	-0.31		-0.80	-0.71	-0.83	-0.71	-0.82	-0.54	-0.55					0.47	0.50	0.49
P-7						0.86	-0.30		-0.63	-0.83	-0.82	-0.70	-0.72	-0.60	-0.56					0.47	0.51	0.52

**Substrate-assisted acylation
(wt BphD)**

**Substrate-assisted acylation
(BphD-H265A mutant)**

Deacylation

Scheme S1

Wild BphD

R-S-2   IM-S-2   P-S-2

H265A mutant

R-M-2   IM-M-2   P-M-2
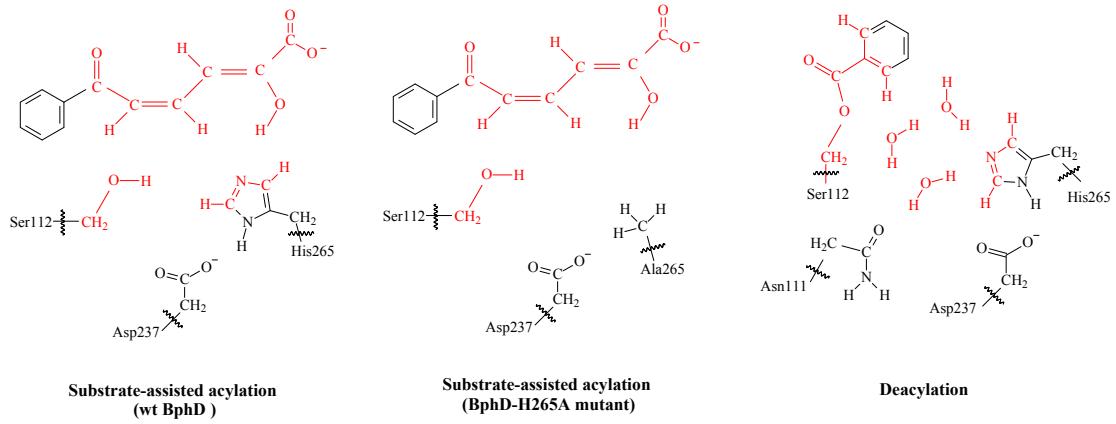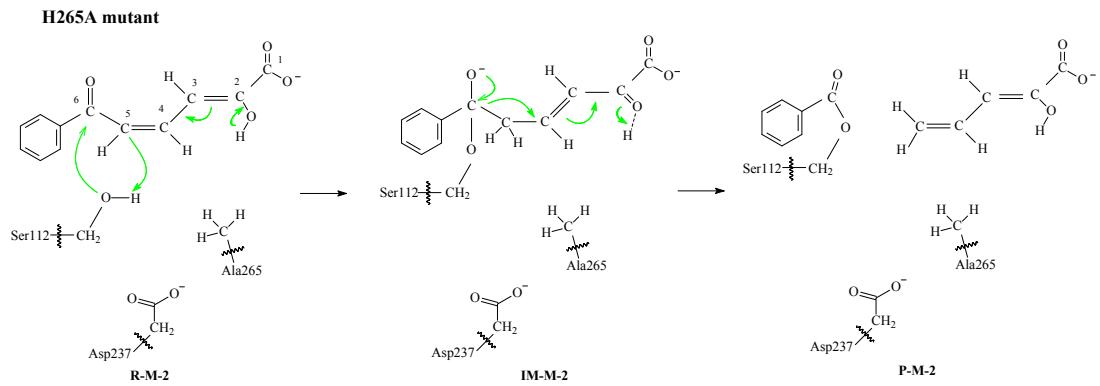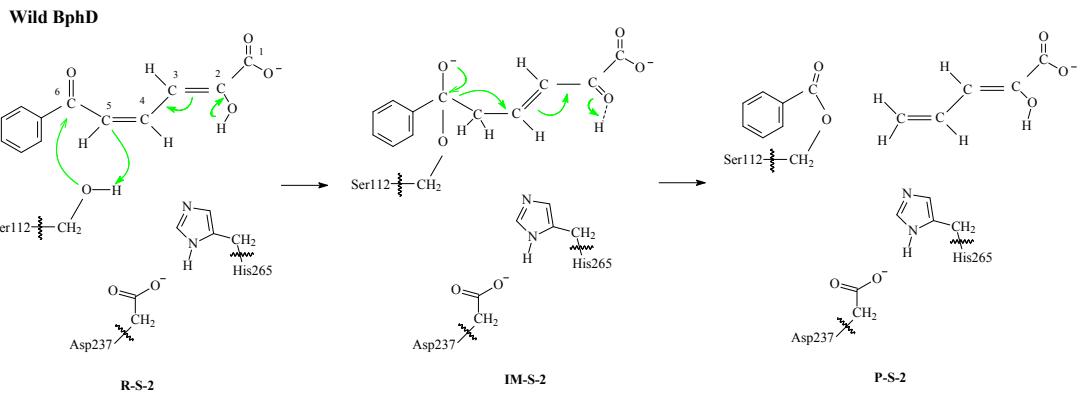
Scheme S2
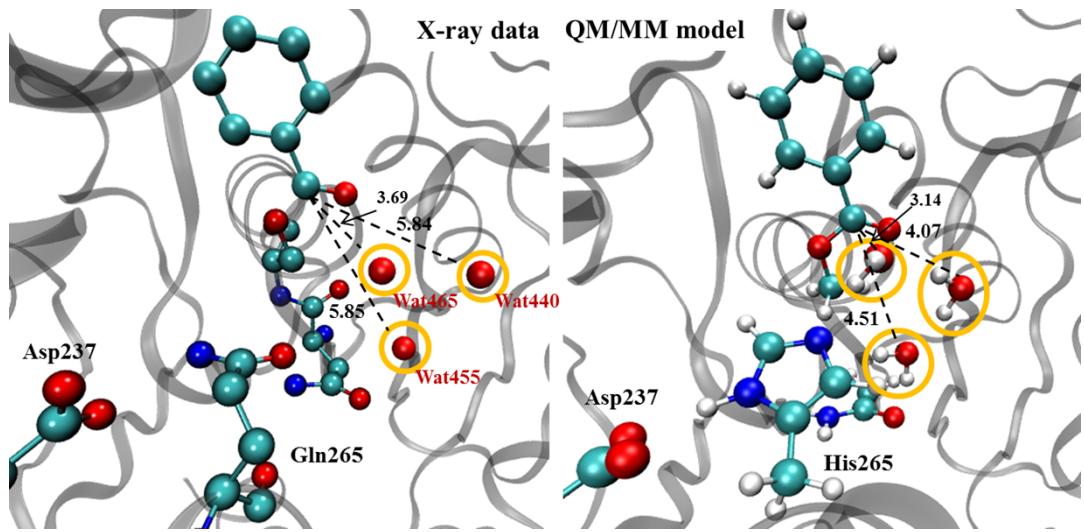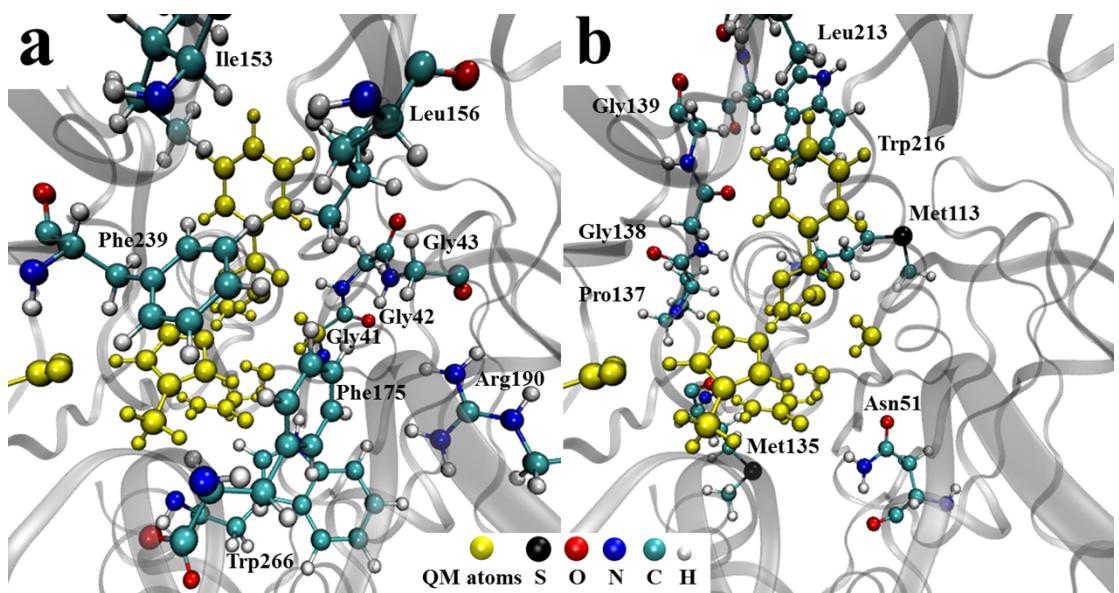
Figure S1

Figure S2
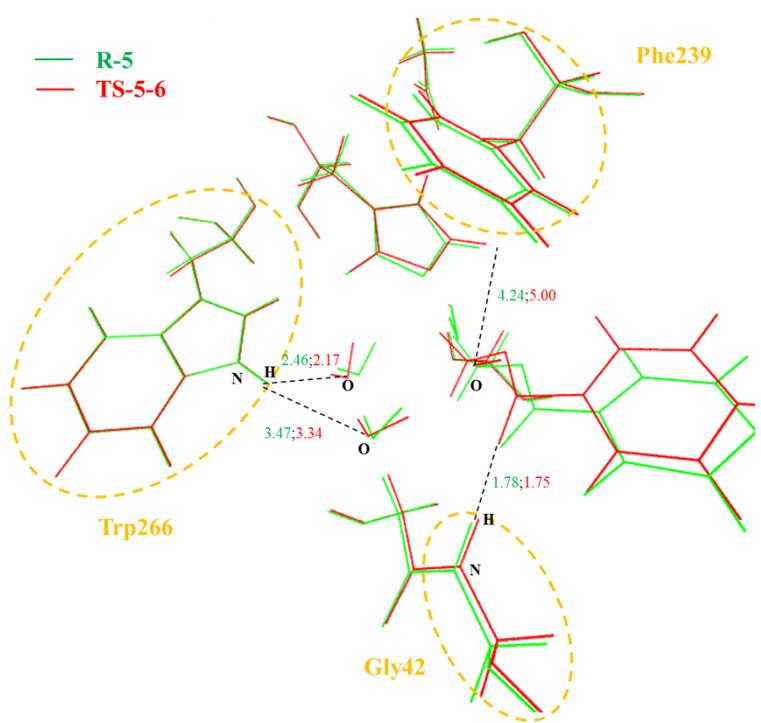
Figure S3

R-1

C	2.404122	-3.02676	2.775882
H	2.595802	-3.6839	1.919036
H	2.682459	-2.00624	2.459086
O	3.070107	-3.45634	3.944402
H	3.997109	-3.59282	3.694506
C	6.572653	-11.5925	0.050289
H	6.294936	-11.245	-0.94908
H	5.878581	-12.3911	0.322954
C	6.431732	-10.422	1.050536
O	6.872023	-9.29877	0.693599
O	5.900077	-10.6856	2.175039
C	6.959032	-7.21775	-1.63303
H	7.638871	-7.78335	-0.99207
H	7.526298	-6.48891	-2.21961
N	5.643204	-6.89919	0.49663
H	6.036613	-7.76834	0.906582
C	5.94441	-6.50497	-0.79016
C	4.7371	-6.02481	0.995395
H	4.310495	-6.11807	1.984796
N	4.428822	-5.07919	0.110204
C	5.170822	-5.39115	-1.01194
H	5.087727	-4.79406	-1.90582
C	6.751472	-0.22456	-0.47925
O	6.861971	-0.29001	-1.73273
O	7.04303	0.751447	0.260745
C	6.248685	-1.48543	0.235823
O	5.856723	-2.45379	-0.59491
H	5.388971	-3.17871	-0.13118
C	6.262178	-1.58211	1.604007
H	6.447528	-0.67075	2.153301
C	6.16923	-2.81754	2.3123
H	6.336618	-3.72082	1.724782
C	5.981273	-3.02925	3.656539
H	6.135296	-4.04007	4.017374
C	5.60442	-2.01938	4.642558
O	5.350834	-0.84451	4.340035
C	5.498863	-2.42787	6.086279
C	5.674256	-1.43207	7.060778
H	5.899489	-0.4238	6.727238
C	5.576405	-1.74075	8.415467
H	5.741988	-0.96911	9.162774
C	5.07292	-4.0392	7.856405
H	4.816556	-5.04769	8.163541
C	5.200446	-3.73591	6.500761
H	5.021668	-4.51951	5.771168
C	5.265502	-3.04343	8.816341
H	5.178728	-3.28495	9.871922
h	1.327636	-3.07361	2.940348
h	7.543091	-12.0729	-0.07423
h	6.549973	-7.96385	-2.31426
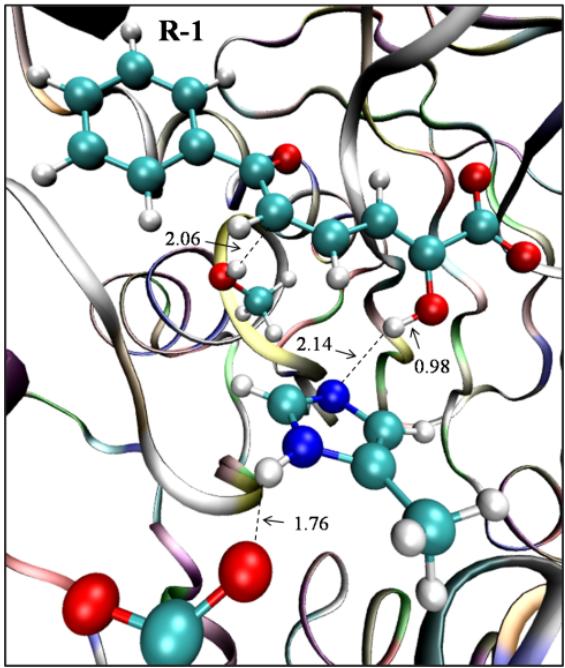
TS-1-2

C	2.544026	-3.04977	2.542083
H	2.656724	-3.47511	1.532621
H	2.872349	-2.00312	2.477733
O	3.245429	-3.79813	3.510943
H	4.168988	-3.48676	3.507968
C	6.45033	-11.6935	0.047446
H	6.144993	-11.3789	-0.95442
H	5.805945	-12.5267	0.33867
C	6.230452	-10.5237	1.034088
O	6.459815	-9.36088	0.611003
O	5.822994	-10.8153	2.200619
C	7.286721	-7.42468	-1.5003
H	7.850846	-8.09691	-0.85112
H	7.973106	-6.80865	-2.07559
N	5.678222	-6.84804	0.404942
H	5.717736	-7.82114	0.780075
C	6.44207	-6.49804	-0.69414
C	5.118016	-5.73134	0.913691
H	4.479403	-5.69481	1.786021
N	5.485032	-4.68234	0.176513
C	6.317233	-5.14472	-0.81759
H	6.799987	-4.45392	-1.48837
C	6.635627	-0.06381	-0.43836
O	6.777875	-0.17737	-1.68811
O	6.921399	0.943874	0.261429
C	6.136397	-1.31297	0.328877
O	5.849719	-2.34348	-0.37663
H	5.487081	-3.47137	0.146602
C	6.078073	-1.27957	1.73354
H	6.059565	-0.31297	2.214751
C	6.198702	-2.44032	2.50915
H	6.581243	-3.31453	1.98212
C	5.99238	-2.64028	3.87266
H	6.407609	-3.54437	4.305792
C	5.281796	-1.77097	4.770112
O	4.666671	-0.73601	4.430181
C	5.269753	-2.16175	6.225388
C	5.453544	-1.15819	7.187813
H	5.586186	-0.13422	6.849883
C	5.491321	-1.47936	8.544105
H	5.663983	-0.69971	9.282108
C	5.076422	-3.80048	8.011514
H	4.903772	-4.82438	8.329166
C	5.078693	-3.48556	6.651481
H	4.893343	-4.26669	5.919171
C	5.29546	-2.79925	8.96012
H	5.310685	-3.04708	10.01756
h	1.473888	-3.10147	2.742581
h	7.441947	-12.1274	-0.08084
h	6.788965	-8.08653	-2.20901
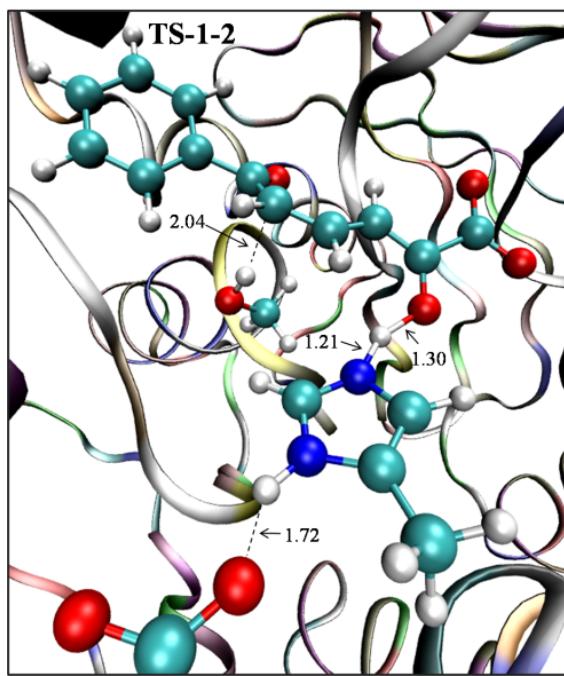
IM-2

C	2.545233	-3.05721	2.468814
H	2.613347	-3.37828	1.41711
H	2.915716	-2.02631	2.505971
O	3.26013	-3.92682	3.323218
H	4.162123	-3.56335	3.416215
C	6.464641	-11.7065	0.055973
H	6.160327	-11.3938	-0.9464
H	5.817709	-12.5373	0.348654
C	6.243797	-10.5346	1.035858
O	6.467925	-9.37155	0.602462
O	5.838936	-10.8158	2.20358
C	7.251629	-7.45263	-1.53418
H	7.828393	-8.1201	-0.89088
H	7.920996	-6.81708	-2.10723
N	5.61638	-6.93091	0.36138
H	5.699303	-7.91149	0.735856
C	6.387015	-6.54936	-0.72529
C	4.998367	-5.85033	0.862508
H	4.346287	-5.81548	1.725955
N	5.346309	-4.79591	0.117822
C	6.218505	-5.20314	-0.86075
H	6.685482	-4.47982	-1.50612
C	6.621888	-0.08764	-0.52679
O	6.792339	-0.19601	-1.77472
O	6.907845	0.911131	0.185441
C	6.06368	-1.33047	0.215575
O	5.749748	-2.34008	-0.4703
H	5.212069	-3.75024	0.198927
C	5.982639	-1.29138	1.640406
H	5.916171	-0.32696	2.120404
C	6.134337	-2.43466	2.411101
H	6.527489	-3.30341	1.880557
C	5.933964	-2.64471	3.788139
H	6.411112	-3.51756	4.220949
C	5.162972	-1.83556	4.67522
O	4.484094	-0.82843	4.344472
C	5.137191	-2.25866	6.123888
C	5.210742	-1.27348	7.119735
H	5.276806	-0.23252	6.815797
C	5.218041	-1.62824	8.468908
H	5.305677	-0.8595	9.232481
C	4.997988	-3.95554	7.863874
H	4.889556	-4.99679	8.150813
C	5.028422	-3.60299	6.513933
H	4.929726	-4.37737	5.758725
C	5.103111	-2.96849	8.845832
H	5.094475	-3.24205	9.896759
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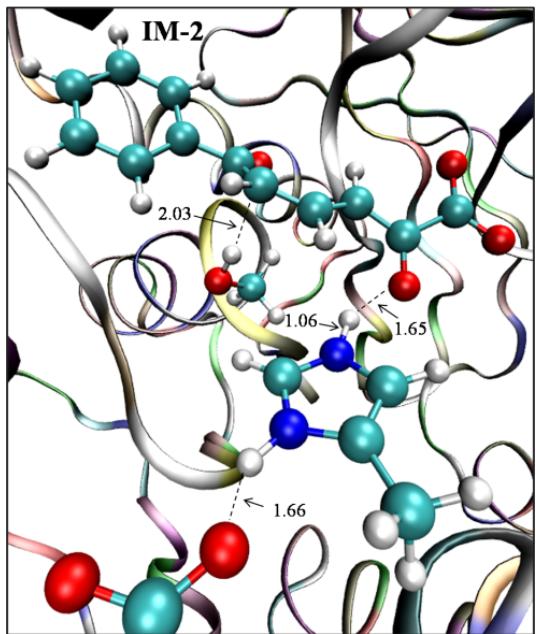
TS-2-3

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H	3.111476	-1.9124	2.580535
O	3.494391	-3.93701	2.557462
H	4.523348	-3.48185	3.212407
C	6.556744	-11.8782	0.037635
H	6.232078	-11.5956	-0.96897
H	5.924531	-12.7049	0.368353
C	6.384695	-10.6694	0.967981
O	6.821744	-9.5639	0.54639
O	5.83209	-10.8559	2.094331
C	6.883554	-7.11691	-1.44051
H	7.663825	-7.64885	-0.88778
H	7.3385	-6.28888	-1.99075
N	5.351841	-7.41394	0.52502
H	5.784948	-8.35245	0.722724
C	5.86369	-6.59342	-0.46358
C	4.502925	-6.70067	1.276215
H	3.956749	-7.08757	2.123972
N	4.431668	-5.44991	0.822538
C	5.287209	-5.36125	-0.26434
H	5.469145	-4.41745	-0.75676
C	6.791943	-0.06888	-0.54113
O	6.886162	-0.07569	-1.79731
O	7.106687	0.861891	0.248342
C	6.266633	-1.38077	0.108195
O	6.059794	-2.3571	-0.61319
H	3.916366	-4.61153	1.590885
C	6.058032	-1.38647	1.563211
H	5.918675	-0.43375	2.054123
C	6.056508	-2.55038	2.250805
H	6.327174	-3.43183	1.66922
C	5.64171	-2.87846	3.619901
H	6.223973	-3.68824	4.058443
C	5.158556	-1.89985	4.58745
O	4.640086	-0.80841	4.28183
C	5.204097	-2.26179	6.049207
C	5.335652	-1.22498	6.985568
H	5.403877	-0.20392	6.620696
C	5.397705	-1.50897	8.348768
H	5.525717	-0.70218	9.06657
C	5.117315	-3.86454	7.875813
H	5.001669	-4.8867	8.222248
C	5.100313	-3.58472	6.508566
H	4.964023	-4.39484	5.798251
C	5.279903	-2.82767	8.797503
H	5.312756	-3.04717	9.86055
h	1.643105	-2.98045	2.489343
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h	6.506826	-7.86133	-2.14192

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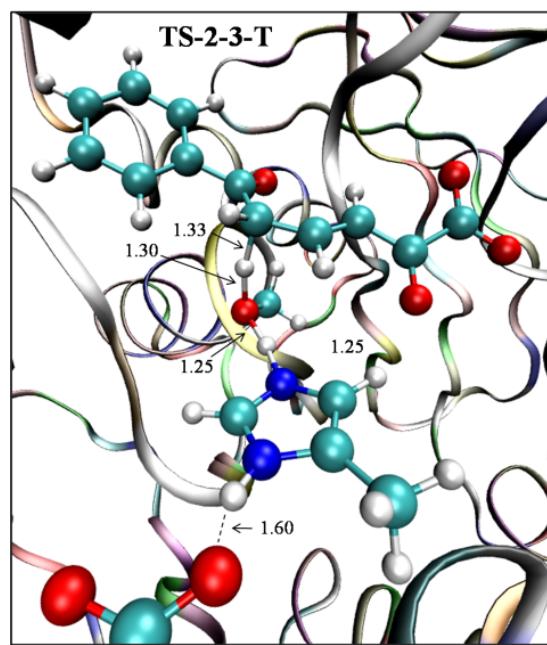
IM-3

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O	3.372003	-3.76506	3.084345
H	3.708626	-4.43405	2.432967
C	6.563357	-11.8474	0.052962
H	6.247639	-11.5364	-0.94777
H	5.918118	-12.6729	0.361089
C	6.405682	-10.657	1.013924
O	6.846233	-9.54705	0.620519
O	5.861369	-10.8744	2.142074
C	6.721743	-7.10382	-1.34297
H	7.503087	-7.64721	-0.80359
H	7.180716	-6.26735	-1.87807
N	5.266666	-7.41087	0.6801
H	5.712601	-8.32897	0.870358
C	5.715554	-6.59738	-0.34088
C	4.431459	-6.68877	1.456988
H	3.92095	-7.09836	2.318741
N	4.302281	-5.44591	1.008299
C	5.106354	-5.38061	-0.12136
H	5.218607	-4.45985	-0.67709
C	6.940892	-0.03231	-0.65857
O	7.131664	-0.05799	-1.89589
O	7.287719	0.855355	0.169939
C	6.182646	-1.24784	-0.06269
O	5.524771	-1.99393	-0.78368
H	6.086177	-3.83706	3.718186
C	6.335133	-1.43112	1.396603
H	6.886405	-0.65153	1.908856
C	5.893933	-2.52062	2.03572
H	5.374354	-3.28557	1.474947
C	6.093323	-2.76733	3.498011
H	7.080601	-2.39871	3.810854
C	5.113351	-2.0595	4.43261
O	4.507604	-1.04097	4.117834
C	5.071528	-2.54676	5.848161
C	5.147141	-1.58896	6.872359
H	5.213723	-0.53776	6.604332
C	5.174328	-1.98772	8.207398
H	5.265897	-1.24526	8.995985
C	4.976547	-4.29898	7.519473
H	4.880601	-5.34912	7.774298
C	4.990668	-3.90717	6.180504
H	4.886479	-4.64911	5.397634
C	5.079559	-3.3428	8.532243
H	5.079424	-3.65556	9.573804
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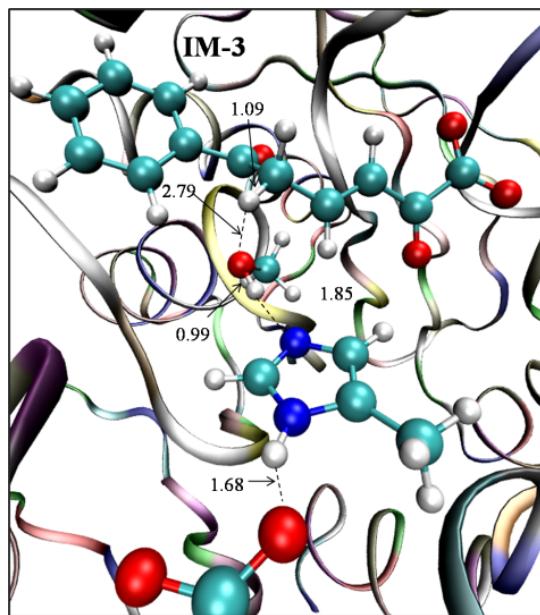
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H	2.51558	-3.25137	1.251184
H	2.731616	-1.85583	2.296538
O	3.456899	-3.6452	3.036236
H	4.018037	-4.66602	1.985071
C	6.561427	-11.8293	0.053485
H	6.24324	-11.5304	-0.94945
H	5.924703	-12.6594	0.364803
C	6.371521	-10.6381	1.003092
O	6.727087	-9.50618	0.57397
O	5.872444	-10.8588	2.147669
C	6.677311	-6.99382	-1.21887
H	7.472094	-7.54691	-0.70959
H	7.120516	-6.13488	-1.72939
N	5.223855	-7.38909	0.80055
H	5.652414	-8.34857	0.901516
C	5.699926	-6.51895	-0.16778
C	4.470784	-6.7143	1.672831
H	3.953324	-7.14162	2.518974
N	4.432006	-5.42996	1.31395
C	5.195247	-5.28293	0.160298
H	5.334776	-4.3201	-0.31331
C	7.101638	-0.02722	-0.80505
O	7.252322	-0.01263	-2.0488
O	7.481682	0.821982	0.045511
C	6.354323	-1.2428	-0.22045
O	5.631153	-1.95192	-0.92498
H	6.076082	-3.77174	3.412035
C	6.566372	-1.47508	1.217109
H	7.342647	-0.89563	1.703215
C	5.78947	-2.33838	1.87949
H	4.994104	-2.81127	1.316301
C	5.870177	-2.69915	3.315526
H	6.690603	-2.1633	3.812621
C	4.569887	-2.35538	4.070694
O	4.067307	-1.21768	3.90222
C	4.501196	-3.00051	5.439979
C	4.367675	-2.16096	6.552703
H	4.202601	-1.10254	6.376912
C	4.476424	-2.67001	7.849419
H	4.38531	-2.00815	8.70591
C	4.814835	-4.88225	6.943127
H	4.958384	-5.94631	7.100367
C	4.71055	-4.37077	5.650939
H	4.761737	-5.03544	4.795246
C	4.715246	-4.03034	8.048679
H	4.805187	-4.4358	9.051826
h	1.470668	-3.07014	2.603064
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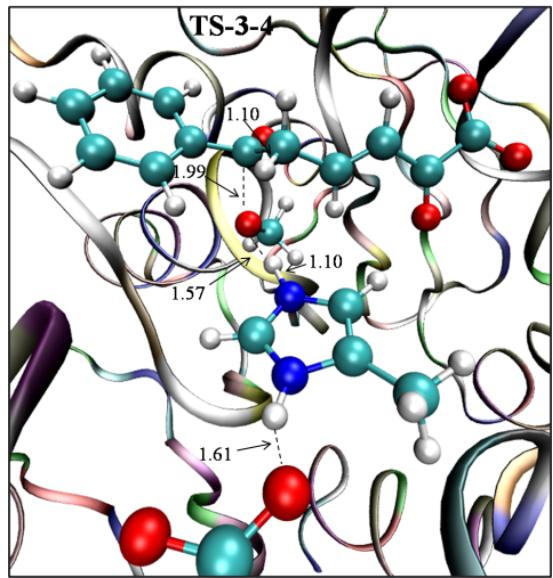
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C	2.492341	-2.91532	2.351375
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H	2.691096	-1.84047	2.275925
O	3.470616	-3.55712	3.116696
H	4.175643	-4.70187	1.919703
C	6.574331	-11.8465	0.027588
H	6.249854	-11.5645	-0.97904
H	5.941023	-12.6727	0.357287
C	6.382187	-10.6449	0.959827
O	6.72777	-9.51607	0.506629
O	5.883805	-10.8441	2.106122
C	6.808451	-6.96674	-1.28299
H	7.635753	-7.49442	-0.79641
H	7.214514	-6.10134	-1.81547
N	5.377317	-7.38516	0.744214
H	5.808966	-8.37325	0.813266
C	5.853628	-6.5007	-0.21071
C	4.631779	-6.72608	1.628444
H	4.110229	-7.1708	2.463099
N	4.604387	-5.43199	1.292553
C	5.367287	-5.26215	0.140003
H	5.492871	-4.29027	-0.31885
C	7.092226	-0.0782	-0.837
O	7.247765	-0.07203	-2.08075
O	7.454562	0.785284	0.00623
C	6.362764	-1.29818	-0.24014
O	5.663336	-2.03599	-0.94132
H	6.069328	-3.72439	3.435039
C	6.559054	-1.49869	1.20329
H	7.332559	-0.9122	1.684392
C	5.758887	-2.33232	1.877634
H	4.96112	-2.7915	1.303958
C	5.800679	-2.66642	3.323087
H	6.566508	-2.07577	3.840924
C	4.43277	-2.40014	4.001458
O	3.960894	-1.22111	3.859812
C	4.427186	-2.99774	5.412442
C	4.401128	-2.11286	6.494819
H	4.276035	-1.05614	6.27473
C	4.558255	-2.57688	7.804306
H	4.54719	-1.87359	8.633892
C	4.760728	-4.83355	6.970968
H	4.878207	-5.8959	7.160673
C	4.597737	-4.36625	5.666518
H	4.582972	-5.06424	4.835084
C	4.746412	-3.93856	8.046115
H	4.873282	-4.3084	9.059062
h	1.453362	-3.05375	2.650419
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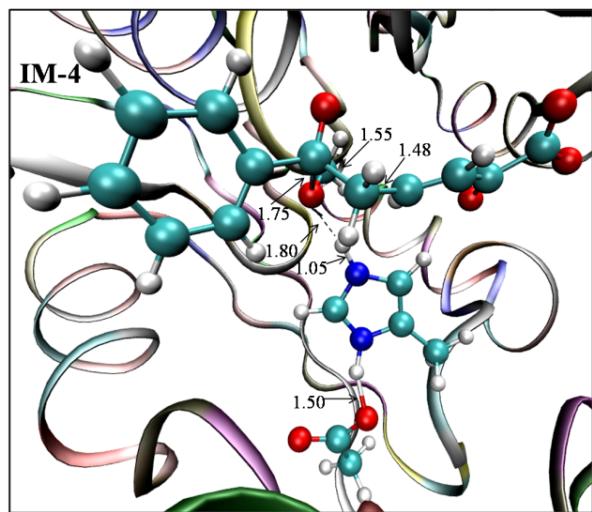
TS-4-5

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H	2.854349	-1.88634	2.486817
O	3.40411	-3.18079	4.016129
H	6.338771	-3.46316	4.207514
C	6.498378	-11.7019	-0.00107
H	6.199425	-11.3985	-1.00806
H	5.845916	-12.5249	0.299765
C	6.28745	-10.5179	0.961584
O	6.574222	-9.36505	0.52868
O	5.834797	-10.77	2.116246
C	7.194229	-7.2807	-1.57576
H	7.860288	-7.88716	-0.95818
H	7.773159	-6.56897	-2.16449
N	5.54925	-7.02403	0.35486
H	5.767578	-8.01414	0.68714
C	6.249926	-6.49875	-0.7225
C	4.803632	-6.06268	0.904785
H	4.164067	-6.16481	1.768971
N	4.996049	-4.93996	0.198266
C	5.908187	-5.17991	-0.80295
H	6.258994	-4.36599	-1.4144
C	6.710675	-0.19695	-0.6385
O	6.866693	-0.32608	-1.88506
O	7.052945	0.795561	0.060275
C	6.063927	-1.38322	0.131669
O	5.498862	-2.31086	-0.50113
H	4.722779	-3.96588	0.380134
C	6.205759	-1.34121	1.557791
H	6.5599	-0.41514	1.989638
C	6.043672	-2.45213	2.355449
H	5.839957	-3.39322	1.850415
C	6.083689	-2.49796	3.767719
H	6.579021	-1.6581	4.253541
C	4.225999	-2.09218	4.489753
O	3.906025	-0.92945	4.120801
C	4.578557	-2.34981	5.940677
C	4.966763	-1.2603	6.73003
H	4.963772	-0.27276	6.278933
C	5.347498	-1.45015	8.05859
H	5.655413	-0.59762	8.659754
C	4.932693	-3.81863	7.842001
H	4.901403	-4.81401	8.274875
C	4.577147	-3.63258	6.505036
H	4.279267	-4.47916	5.89383
C	5.32157	-2.72715	8.623776
H	5.60251	-2.87138	9.663576
h	1.567198	-2.99277	2.995609
h	7.488636	-12.1422	-0.11745
h	6.731334	-7.98835	-2.26353

TS-4-5
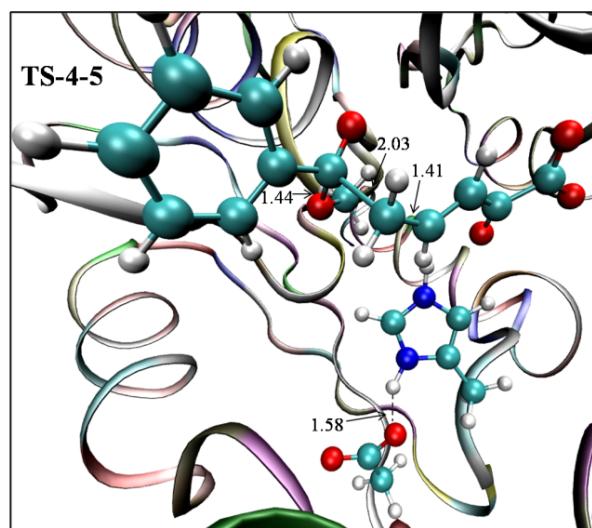
IM-5

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H	2.811622	-1.91231	2.571735
O	3.262548	-3.10234	4.236107
H	6.314982	-3.88957	3.968851
C	6.493068	-11.7314	0.040848
H	6.18074	-11.4234	-0.96153
H	5.853329	-12.5636	0.344568
C	6.291219	-10.5465	1.01127
O	6.591374	-9.40158	0.593614
O	5.833066	-10.8174	2.168002
C	7.124782	-7.25799	-1.573
H	7.783176	-7.84	-0.92327
H	7.712987	-6.54877	-2.15846
N	5.396315	-7.01428	0.273862
H	5.615428	-7.94789	0.664242
C	6.121649	-6.48691	-0.77443
C	4.555677	-6.04825	0.714934
H	3.865915	-6.20499	1.533635
N	4.686094	-4.92426	0.013758
C	5.675318	-5.19878	-0.91041
H	6.044859	-4.43682	-1.57501
C	6.807894	-0.09154	-0.56355
O	6.862761	-0.13129	-1.82586
O	7.194219	0.851876	0.17977
C	6.252477	-1.31907	0.140125
O	5.600106	-2.1665	-0.68872
H	5.167874	-2.8973	-0.20258
C	6.488891	-1.52419	1.460271
H	7.011511	-0.72018	1.966638
C	6.198483	-2.73472	2.190974
H	5.741275	-3.55833	1.646247
C	6.488921	-2.93156	3.489168
H	6.95808	-2.1576	4.08794
C	3.924866	-2.05293	4.776264
O	3.883636	-0.92922	4.291972
C	4.564917	-2.36906	6.075735
C	5.143543	-1.31362	6.796362
H	5.152524	-0.32211	6.35537
C	5.690004	-1.54855	8.055554
H	6.143864	-0.73339	8.611938
C	5.075525	-3.88685	7.891133
H	5.034269	-4.88199	8.319987
C	4.549905	-3.66137	6.620488
H	4.116488	-4.47717	6.051072
C	5.64188	-2.8307	8.610355
H	6.04683	-3.00845	9.602645
h	1.480698	-2.97361	3.112447
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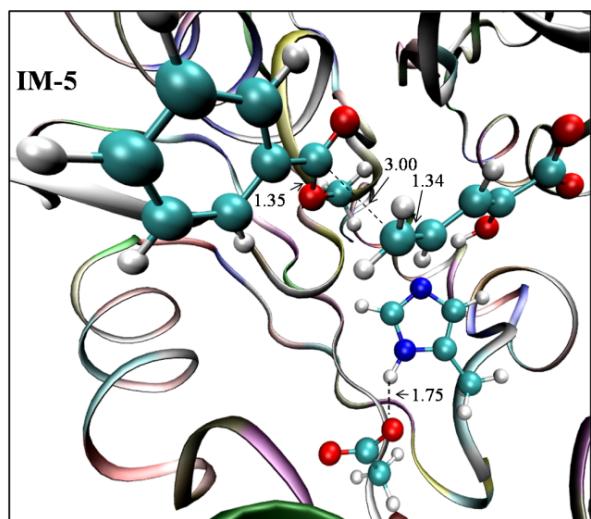
R-5

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H	0.492258	-1.94873	-1.77126
C	1.397945	-3.83799	-2.02532
O	2.302157	-3.29838	-2.67618
N	1.460449	-5.1366	-1.65882
H	2.257506	-5.67508	-1.99194
H	0.701824	-5.63004	-1.18937
C	5.073474	-3.66286	5.96578
H	4.284511	-4.37005	5.741058
C	5.695773	-3.66955	7.213344
H	5.390286	-4.38796	7.966363
C	6.699947	-2.74133	7.497174
H	7.173965	-2.74545	8.474419
C	6.454874	-1.78785	5.28916
H	6.734372	-1.06539	4.530089
C	7.082522	-1.80372	6.532268
H	7.863847	-1.08197	6.75278
C	3.108035	-3.56527	2.243255
H	3.429428	-4.2904	1.499907
H	3.163278	-2.56556	1.816147
O	3.987025	-3.68741	3.389536
C	4.739085	-2.59864	3.697748
O	4.777343	-1.60645	2.997411
C	5.447028	-2.71976	4.999096
C	5.537966	-12.4821	-0.14738
H	4.921991	-12.5611	-1.05079
H	4.982518	-12.9768	0.65389
C	5.675354	-10.9693	0.16901
O	6.790524	-10.3944	0.07422
O	4.59306	-10.3884	0.506614
C	6.285443	-7.81253	-1.9384
H	6.896488	-8.6348	-1.54975
H	6.905735	-7.17012	-2.5683
N	5.003017	-7.57747	0.234334
H	4.810789	-8.60013	0.36278
C	5.736602	-7.0288	-0.80058
C	4.737127	-6.578	1.106672
H	4.170006	-6.72842	2.015429
N	5.246728	-5.41868	0.701596
C	5.877111	-5.70008	-0.4956
H	6.392635	-4.93066	-1.05546
O	6.555144	-1.32683	0.283444
H	5.782223	-1.73466	-0.14824
H	6.887545	-2.0435	0.858516
O	4.319559	-2.74552	-0.78869
H	4.475102	-3.63795	-0.44522
H	3.734785	-2.8676	-1.56152
O	7.09829	-3.61171	1.882126
H	6.358461	-4.19247	1.591982
H	7.883974	-4.14949	1.716034
h	-0.4152	-3.08105	-0.78092
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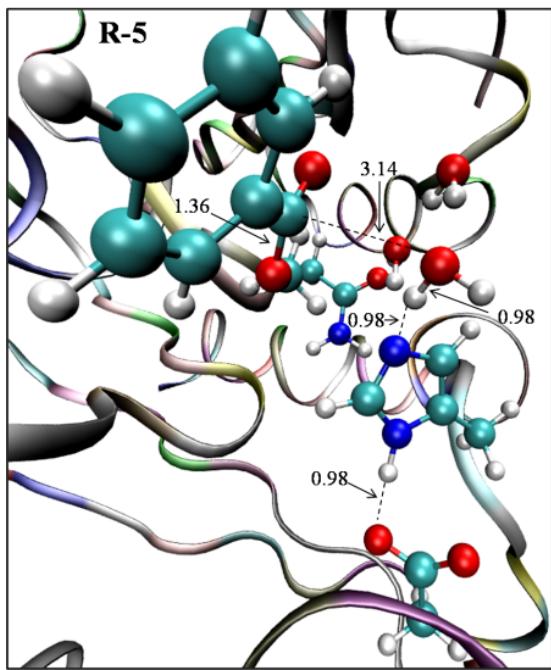
TS-5-6

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H	-0.67793	-3.06713	-2.53713
H	0.414583	-1.91456	-1.79863
C	1.277355	-3.81422	-2.11542
O	2.151138	-3.29787	-2.82786
N	1.359713	-5.10297	-1.72416
H	2.141419	-5.64449	-2.08356
H	0.621054	-5.59332	-1.22093
C	5.391687	-4.17841	5.409116
H	4.822122	-5.00145	4.991287
C	5.918067	-4.26355	6.700928
H	5.7542	-5.15865	7.294894
C	6.654822	-3.20323	7.231865
H	7.060046	-3.27194	8.237808
C	6.308323	-1.95922	5.186587
H	6.423751	-1.05637	4.594475
C	6.856388	-2.05151	6.465173
H	7.4298	-1.22061	6.868745
C	3.111412	-3.68183	1.96615
H	3.241323	-4.35824	1.113535
H	3.174636	-2.65023	1.61452
O	4.101929	-3.94627	2.949068
C	4.96703	-2.80969	3.256532
O	4.557024	-1.67312	2.955015
C	5.573443	-3.02251	4.642224
C	5.56089	-12.351	-0.15596
H	4.937757	-12.4329	-1.054
H	4.997751	-12.8218	0.654325
C	5.727638	-10.8338	0.128225
O	6.842549	-10.2711	-0.00383
O	4.65747	-10.2255	0.475744
C	6.358939	-7.68178	-1.95
H	7.021008	-8.48921	-1.61562
H	6.913442	-7.01786	-2.61711
N	5.188104	-7.48628	0.296886
H	4.922329	-8.5158	0.367765
C	5.916192	-6.92708	-0.74418
C	5.090073	-6.5808	1.280539
H	4.567681	-6.7128	2.215241
N	5.729817	-5.47053	0.916614
C	6.251289	-5.65848	-0.34479
H	6.844468	-4.89739	-0.83259
O	6.464019	-1.35339	0.158936
H	5.654473	-1.63967	-0.30186
H	6.459121	-1.89725	0.977434
O	4.244422	-2.63334	-1.0975
H	4.568151	-3.54425	-1.03442
H	3.53263	-2.68239	-1.77176
O	6.27814	-3.22124	2.233121
H	5.891805	-4.59825	1.514395
H	7.068171	-3.31414	2.790191
h	-0.49095	-3.05288	-0.81599
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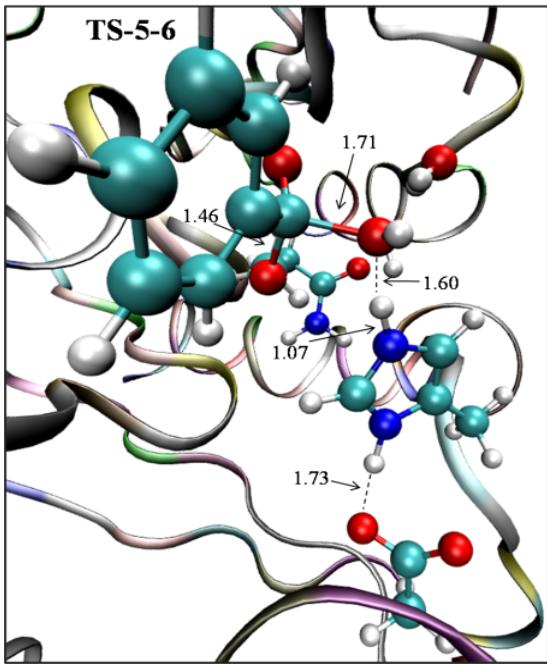
IM-6

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H	0.353671	-1.82098	-1.8506
C	1.221985	-3.71787	-2.18195
O	2.073234	-3.20242	-2.92363
N	1.328471	-5.0006	-1.77636
H	2.11388	-5.53492	-2.13686
H	0.61345	-5.48939	-1.24018
C	5.479089	-4.50371	5.08154
H	5.288583	-5.30835	4.378485
C	5.73183	-4.78908	6.424326
H	5.725927	-5.82039	6.768398
C	5.996114	-3.7563	7.328277
H	6.198085	-3.98232	8.372181
C	5.708467	-2.1495	5.542252
H	5.672916	-1.12707	5.178515
C	5.998114	-2.43503	6.877932
H	6.21765	-1.62845	7.572827
C	3.092686	-3.39582	1.856784
H	3.151749	-3.79591	0.839795
H	3.156749	-2.3066	1.790347
O	4.146993	-3.89669	2.653392
C	5.175253	-2.78125	3.171655
O	4.772609	-1.6117	2.959291
C	5.448217	-3.17835	4.629069
C	5.490279	-12.4914	-0.18995
H	4.877926	-12.5927	-1.09473
H	4.938772	-12.9872	0.615282
C	5.583948	-10.98	0.108854
O	6.681155	-10.3737	0.091263
O	4.456854	-10.419	0.35131
C	6.202449	-7.7293	-1.76174
H	6.84999	-8.54565	-1.42139
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N	4.72713	-7.79085	0.294508
H	4.566131	-8.86853	0.292769
C	5.572759	-7.10073	-0.56326
C	4.364263	-6.96259	1.278799
H	3.670313	-7.19637	2.072181
N	4.96254	-5.78502	1.114002
C	5.720107	-5.84124	-0.03622
H	6.333987	-5.00808	-0.34548
O	6.384776	-1.4625	0.039096
H	5.601769	-1.79556	-0.43066
H	6.349739	-1.92787	0.895137
O	4.219631	-2.80212	-1.20555
H	4.613923	-3.67205	-1.34737
H	3.512807	-2.74993	-1.88052
O	6.329072	-3.23237	2.342707
H	4.799861	-4.94428	1.772329
H	7.122954	-2.97161	2.829479
h	-0.52777	-2.96664	-0.8537
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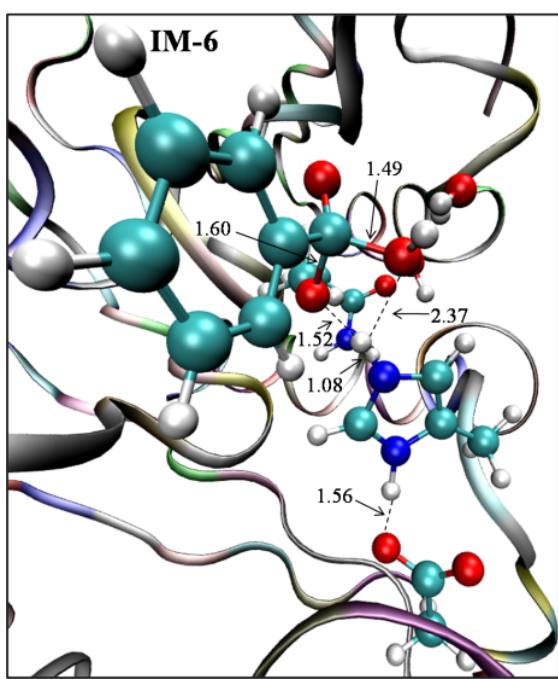
TS-6-7

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C	1.237398	-3.73337	-2.16246
O	2.095781	-3.21648	-2.89451
N	1.339397	-5.01586	-1.75899
H	2.126488	-5.55151	-2.11473
H	0.617436	-5.50609	-1.2331
C	5.481467	-4.42355	5.118989
H	5.225111	-5.24186	4.4534
C	5.759585	-4.6725	6.463763
H	5.717745	-5.68913	6.846779
C	6.099269	-3.62342	7.322201
H	6.321709	-3.82212	8.366878
C	5.833369	-2.06694	5.490613
H	5.833335	-1.05476	5.096934
C	6.145842	-2.31944	6.827292
H	6.418858	-1.49893	7.485853
C	3.094017	-3.43581	1.848461
H	3.13805	-3.84812	0.833506
H	3.165579	-2.34508	1.769262
O	4.147759	-3.93959	2.638895
C	5.228816	-2.73754	3.165718
O	4.785829	-1.59881	2.927483
C	5.503734	-3.11454	4.620967
C	5.507872	-12.5072	-0.18452
H	4.900521	-12.6107	-1.09072
H	4.958877	-13.0093	0.615938
C	5.593518	-10.9941	0.11599
O	6.68805	-10.3814	0.065309
O	4.472007	-10.4462	0.395335
C	6.208737	-7.7094	-1.75818
H	6.853535	-8.5232	-1.4076
H	6.813584	-6.9847	-2.308
N	4.741017	-7.75034	0.306187
H	4.580038	-8.80839	0.304553
C	5.582114	-7.06653	-0.56113
C	4.391608	-6.91775	1.295045
H	3.702018	-7.15059	2.092907
N	4.984739	-5.73968	1.123886
C	5.733722	-5.80648	-0.03267
H	6.346953	-4.97699	-0.35523
O	6.40196	-1.34834	0.078353
H	5.605097	-1.6381	-0.40373
H	6.359987	-1.85897	0.910559
O	4.229553	-2.61155	-1.20919
H	4.620854	-3.49456	-1.2933
H	3.491306	-2.62213	-1.85685
O	6.342039	-3.20614	2.318914
H	4.781852	-4.87572	1.804586
H	7.158176	-2.96473	2.788958
h	-0.52176	-2.98052	-0.84691
h	2.117561	-3.72547	2.236662
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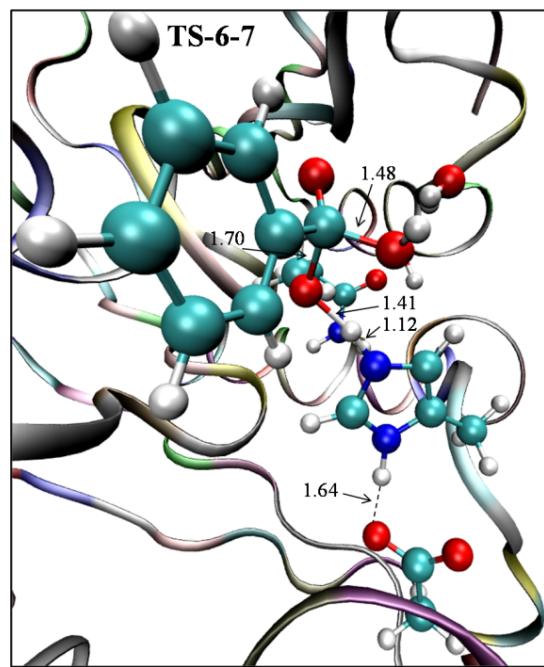
P-7

C	0.028023	-2.87216	-1.79802
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O	2.180951	-3.16537	-2.7563
N	1.34928	-5.00548	-1.73599
H	2.158855	-5.53519	-2.05134
H	0.607896	-5.49756	-1.24072
C	5.905872	-4.4436	5.188822
H	5.737845	-5.01112	4.277751
C	5.833706	-5.08277	6.42592
H	5.650722	-6.15299	6.475977
C	6.011811	-4.355	7.605541
H	5.990404	-4.86457	8.56377
C	6.263899	-2.32792	6.320473
H	6.417189	-1.25541	6.255818
C	6.229027	-2.97649	7.552371
H	6.358826	-2.41178	8.470987
C	2.933072	-3.57163	1.838821
H	2.984462	-4.12643	0.896592
H	2.954928	-2.50458	1.57602
O	3.965108	-3.9461	2.721144
C	6.172367	-2.28954	3.85484
O	5.872453	-1.11516	3.792799
C	6.118277	-3.0594	5.131601
C	5.516793	-12.4943	-0.16569
H	4.910048	-12.5754	-1.07569
H	4.958809	-13.0052	0.624372
C	5.618941	-10.9842	0.16628
O	6.726561	-10.3903	0.135994
O	4.508293	-10.4255	0.447733
C	6.244348	-7.72054	-1.80465
H	6.893835	-8.53871	-1.46993
H	6.836085	-7.01872	-2.39935
N	4.899802	-7.67279	0.340251
H	4.685077	-8.70386	0.362435
C	5.692856	-7.03798	-0.59553
C	4.674874	-6.7899	1.33868
H	4.044679	-7.00549	2.190603
N	5.280434	-5.62945	1.121306
C	5.919144	-5.77418	-0.09584
H	6.538504	-4.99179	-0.51753
O	6.411952	-1.35288	0.15539
H	5.706053	-1.85808	-0.29107
H	6.563015	-1.81243	0.991977
O	4.381638	-2.89468	-1.02183
H	4.651804	-3.82142	-0.96258
H	3.693694	-2.87546	-1.71845
O	6.665569	-2.89699	2.747464
H	4.592302	-4.4705	2.156628
H	6.777786	-3.85394	2.853436
h	-0.56505	-2.98754	-0.89082
h	1.946761	-3.80822	2.237921
h	6.433013	-13.0461	-0.37574
h	5.524977	-8.21472	-2.45761

P-7