

# Supporting Information

## Fundamental Reaction Mechanism and Free Energy Profile for (-)-Cocaine Hydrolysis Catalyzed by Cocaine Esterase

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**Supporting Information Available.** Absolute QM/MM energies (in Hartree) calculated at the QM/MM(MP2/6-31+G\*:AMBER) level, coordinates of QM part of the geometries optimized at the QM/MM(B3LYP/6-31G\*:AMBER) level, and complete citations of references 45 and 48. This material is available free of charge *via* the Internet at <http://pubs.acs.org>.

Table S1. Absolute QM/MM energies (in Hartree) calculated at the QM/MM(MP2/6-31+G\*:AMBER) level (single-point energy calculations) using the geometries optimized at the QM/MM(B3LYP/6-31G\*:AMBER) level.

State	QM/MM	State	QM/MM	State	QM/MM
ES	-1735.597344	INT1'	-1735.586793	TS3	-1143.272341
TS1	-1735.582760	TS2'	-1735.586642	INT3	-1143.277382
INT1	-1735.592940	INT2	-1735.595766	TS4	-1143.270944
TS2	-1735.583555	INT2'	-1143.308383	PD	-1143.282906

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Coordinates of the QM part of the geometries optimized at the QM/MM(B3LYP/6-31G\*:AMBER) level. Atom “F” represents the one-free-valence boundary atom described by pseudopotential in QM subsystem.

ES

F	0.313496	2.523484	4.068776
C	-0.237452	1.782143	2.856556
H	0.159462	0.751370	2.804528
H	-1.339948	1.709827	2.908642
O	0.083934	2.419748	1.659001
H	0.752248	1.876671	1.167784
F	8.439599	-0.617652	-1.196511
C	7.869420	-0.729460	0.225048
H	8.212368	-1.659779	0.733853
H	8.215793	0.087717	0.888734
C	6.348306	-0.823288	0.363525
O	5.738642	-1.381098	-0.598392
O	5.856086	-0.400531	1.437532
F	2.331472	-3.825727	-1.255190
C	1.877480	-2.500738	-1.939916
H	2.447351	-2.388548	-2.875387
H	0.821856	-2.542452	-2.248390
C	2.004111	-1.272775	-1.099905
N	3.133259	-0.930422	-0.378369
H	4.127697	-1.276535	-0.462363
C	2.838735	0.163641	0.356290
H	3.562412	0.594337	1.033962
N	1.590718	0.570886	0.162048
C	1.068633	-0.322198	-0.747810
H	0.054454	-0.232916	-1.104069
C	-1.977920	2.218524	0.104943
O	-1.871867	0.940572	-0.385006

C	-2.999570	0.084015	-0.189168
C	-2.830836	-0.994993	0.926113
C	-1.528033	-1.791709	0.911973
O	-0.711458	-1.486705	1.891968
C	0.511318	-2.264853	1.994085
H	0.273673	-3.211956	2.484540
H	0.935457	-2.429090	1.005741
H	1.189083	-1.667258	2.597226
O	-1.300507	-2.688173	0.099940
H	-2.887767	-0.489509	1.893116
C	-4.029515	-1.986730	0.823181
N	-3.977179	-2.652001	-0.550255
C	-4.757593	-3.925738	-0.650306
H	-4.800196	-4.222212	-1.699731
H	-4.238774	-4.690402	-0.071296
H	-5.759992	-3.780436	-0.251087
H	-2.985711	-2.868626	-0.745139
C	-4.466766	-1.539906	-1.464269
C	-5.707424	-1.020014	-0.710123
C	-5.409714	-1.294261	0.795281
H	-5.397026	-0.379309	1.391260
H	-6.165199	-1.949816	1.232114
H	-6.608222	-1.546031	-1.036196
H	-5.867059	0.040753	-0.913799
H	-4.680006	-1.971293	-2.443052
C	-3.329588	-0.517448	-1.559070
H	-2.436219	-0.976261	-1.996298
H	-3.628975	0.286120	-2.239572
H	-3.939586	-2.764756	1.582441
H	-3.825942	0.712250	0.148620
O	-2.740597	2.464468	1.029489

C	-1.227075	3.217575	-0.688487
C	-1.082117	4.509834	-0.159801
H	-1.437422	4.705418	0.843112
C	-0.458544	5.506738	-0.899723
H	-0.360077	6.505665	-0.486160
C	0.037064	5.223335	-2.177135
H	0.522091	6.003855	-2.756362
C	-0.095037	3.936969	-2.703110
H	0.290911	3.713510	-3.692650
C	-0.720935	2.931454	-1.965045
H	-0.810967	1.932573	-2.376803

TS1

F	0.220403	2.430515	4.012603
C	-0.389549	1.638592	2.829174
H	-0.005452	0.597508	2.869748
H	-1.488359	1.586358	2.932007
O	-0.110669	2.118085	1.549678
H	0.736855	1.297999	0.839809
F	8.445358	-0.538649	-1.162602
C	7.829449	-0.659898	0.237321
H	8.117091	-1.616553	0.726988
H	8.193819	0.125792	0.928003
C	6.301499	-0.679426	0.348028
O	5.668842	-1.160741	-0.645648
O	5.813570	-0.280667	1.431460
F	2.387006	-3.747348	-1.311860
C	1.943420	-2.407108	-1.977020
H	2.557608	-2.243559	-2.875376
H	0.908295	-2.464414	-2.341958
C	1.983865	-1.192984	-1.096231

N	3.082613	-0.762195	-0.364199
H	4.121811	-1.032159	-0.465926
C	2.702149	0.259204	0.417261
H	3.366201	0.750564	1.113023
N	1.407718	0.530892	0.228841
C	0.955562	-0.364521	-0.719132
H	-0.065460	-0.348781	-1.050964
C	-1.710359	2.215481	0.481391
O	-1.674757	0.859251	-0.030767
C	-2.876674	0.118832	-0.019485
C	-2.820424	-1.088814	0.980536
C	-1.516426	-1.873458	0.936373
O	-0.703839	-1.620067	1.938772
C	0.527732	-2.378520	1.990453
H	0.318979	-3.353050	2.438031
H	0.942761	-2.496801	0.991851
H	1.204403	-1.800928	2.614882
O	-1.251938	-2.703857	0.065800
H	-2.917773	-0.686682	1.991476
C	-4.010959	-2.050745	0.721996
N	-3.897188	-2.571259	-0.706981
C	-4.671595	-3.826777	-0.955446
H	-4.627445	-4.059968	-2.018836
H	-4.208650	-4.632310	-0.383999
H	-5.705463	-3.698450	-0.640051
H	-2.901161	-2.776518	-0.882976
C	-4.338193	-1.361958	-1.521892
C	-5.612169	-0.918457	-0.778264
C	-5.385510	-1.348462	0.702059
H	-5.395158	-0.498128	1.386468
H	-6.162360	-2.039882	1.034447

H	-6.496020	-1.405521	-1.199247
H	-5.761445	0.158125	-0.875988
H	-4.504130	-1.690615	-2.549470
C	-3.191678	-0.341951	-1.458751
H	-2.298249	-0.770972	-1.928597
H	-3.463473	0.530639	-2.062024
H	-3.962788	-2.905034	1.398822
H	-3.677095	0.769121	0.345149
O	-2.650185	2.522559	1.228547
C	-1.129338	3.174450	-0.531424
C	-1.088464	4.537133	-0.204714
H	-1.433622	4.847483	0.774646
C	-0.611874	5.476032	-1.116904
H	-0.604485	6.530207	-0.856216
C	-0.158325	5.067122	-2.375717
H	0.205086	5.799460	-3.091550
C	-0.190751	3.712759	-2.705778
H	0.170292	3.377070	-3.674252
C	-0.677539	2.771114	-1.794326
H	-0.702794	1.724936	-2.074592

INT1

F	0.140179	2.464412	3.966170
C	-0.518861	1.669435	2.822024
H	-0.058881	0.666614	2.773659
H	-1.598182	1.555067	2.976340
O	-0.343188	2.229807	1.527991
H	0.825414	1.243359	0.632350
F	8.447490	-0.450460	-1.126049
C	7.819705	-0.556156	0.271087
H	8.112262	-1.502555	0.776655

H	8.169545	0.242722	0.954429
C	6.292316	-0.586986	0.375441
O	5.669894	-1.103397	-0.610509
O	5.789452	-0.164384	1.441664
F	2.432536	-3.750255	-1.277256
C	1.985218	-2.430676	-1.971535
H	2.600499	-2.276899	-2.870258
H	0.951456	-2.498520	-2.335935
C	2.017138	-1.202317	-1.114572
N	3.110779	-0.745688	-0.385306
H	4.172935	-1.004714	-0.466655
C	2.729064	0.288660	0.367010
H	3.377375	0.804725	1.059366
N	1.431690	0.534436	0.147797
C	0.974949	-0.382815	-0.772719
H	-0.054230	-0.380008	-1.077137
C	-1.603265	2.273686	0.678177
O	-1.582235	0.770412	0.120209
C	-2.800430	0.102082	0.041723
C	-2.811589	-1.144739	1.009598
C	-1.503181	-1.914426	0.967100
O	-0.691273	-1.655527	1.974862
C	0.541581	-2.404519	2.027927
H	0.341815	-3.382602	2.472527
H	0.963003	-2.521129	1.031507
H	1.214643	-1.828052	2.658117
O	-1.212628	-2.731655	0.089765
H	-2.931816	-0.768639	2.027771
C	-3.993730	-2.095149	0.700520
N	-3.842186	-2.578394	-0.737018
C	-4.604475	-3.828555	-1.034565

H	-4.484576	-4.069672	-2.089585
H	-4.192184	-4.634876	-0.426135
H	-5.658446	-3.691765	-0.799738
H	-2.842136	-2.777832	-0.889920
C	-4.258224	-1.344825	-1.532455
C	-5.550079	-0.917759	-0.811097
C	-5.365895	-1.390225	0.661782
H	-5.392511	-0.558273	1.367655
H	-6.152782	-2.089821	0.952334
H	-6.424532	-1.388490	-1.269660
H	-5.690009	0.161908	-0.881101
H	-4.400409	-1.650983	-2.571026
C	-3.109363	-0.330081	-1.415920
H	-2.213466	-0.756697	-1.885280
H	-3.365143	0.557324	-2.004416
H	-3.968008	-2.968100	1.355198
H	-3.591897	0.772816	0.403248
O	-2.670349	2.554026	1.292620
C	-1.161824	3.160996	-0.497234
C	-1.169974	4.547486	-0.285359
H	-1.521314	4.925124	0.668690
C	-0.733634	5.431240	-1.271440
H	-0.760082	6.501563	-1.089708
C	-0.277804	4.944434	-2.501132
H	0.059135	5.631363	-3.273082
C	-0.278216	3.568794	-2.727720
H	0.082636	3.167560	-3.671714
C	-0.721499	2.685345	-1.737624
H	-0.718878	1.621899	-1.939506

TS2



F	0.400595	2.423470	3.772665
C	-0.439108	1.676945	2.750662
H	-0.073484	0.644734	2.610443
H	-1.500100	1.629160	3.006403
O	-0.303409	2.285902	1.475080
H	0.305293	0.824518	0.573967
F	8.056299	-0.990851	-1.457423
C	7.947459	-0.906956	0.077348
H	8.009840	-1.913193	0.542697
H	8.760654	-0.328895	0.538406
C	6.618942	-0.333139	0.548038
O	5.603510	-0.859273	-0.017693
O	6.631530	0.572436	1.410049
F	3.093704	-3.598725	-1.418960
C	2.727063	-2.173533	-1.898053
H	3.591969	-1.691783	-2.381833
H	1.939231	-2.204488	-2.664988
C	2.270734	-1.203861	-0.885826
N	3.098146	-0.536479	0.006992
H	4.206817	-0.638389	0.103833
C	2.362810	0.342235	0.683761
H	2.722111	1.035497	1.431124
N	1.096737	0.255520	0.262440
C	1.014535	-0.694158	-0.717922
H	0.089654	-0.914224	-1.220559
C	-1.493627	2.544204	0.806295
O	-1.605370	0.620924	0.149848
C	-2.841691	0.069135	0.103706
C	-2.928750	-1.256863	0.983324
C	-1.708310	-2.131353	0.771014
O	-0.902641	-2.214207	1.826796

C	0.224548	-3.109470	1.704755
H	-0.122384	-4.114259	1.455206
H	0.915299	-2.757820	0.937819
H	0.704316	-3.114138	2.679788
O	-1.498929	-2.757139	-0.269332
H	-2.956680	-0.961691	2.035112
C	-4.203342	-2.080339	0.676004
N	-4.147200	-2.454651	-0.802620
C	-5.000171	-3.618062	-1.174259
H	-4.924836	-3.776996	-2.250900
H	-4.635482	-4.503130	-0.652940
H	-6.035300	-3.426066	-0.893029
H	-3.154209	-2.692550	-1.000444
C	-4.515767	-1.134383	-1.473656
C	-5.720881	-0.653716	-0.637939
C	-5.513851	-1.276927	0.770954
H	-5.443923	-0.516093	1.549538
H	-6.342429	-1.938692	1.036696
H	-6.666594	-0.981073	-1.080044
H	-5.741429	0.436011	-0.594709
H	-4.766186	-1.351158	-2.516868
C	-3.284522	-0.230425	-1.362447
H	-2.442660	-0.681878	-1.902263
H	-3.497202	0.723629	-1.856508
H	-4.229105	-3.004198	1.251357
H	-3.597495	0.745053	0.553095
O	-2.523247	2.747772	1.460601
C	-1.137161	3.275694	-0.466437
C	-1.179426	4.674099	-0.390783
H	-1.580047	5.145384	0.501624
C	-0.678258	5.456315	-1.430599

H	-0.693941	6.537155	-1.339989
C	-0.144654	4.848457	-2.569738
H	0.261102	5.458629	-3.372195
C	-0.134359	3.454726	-2.663640
H	0.273028	2.965433	-3.544996
C	-0.620995	2.669503	-1.616856
H	-0.603855	1.589646	-1.678085

INT1'

F	0.489210	2.457283	3.784942
C	-0.313776	1.775630	2.692960
H	0.081683	0.772759	2.487695
H	-1.381144	1.691273	2.908405
O	-0.147211	2.461938	1.451324
H	-0.183284	0.311668	0.438241
F	7.994239	-1.255171	-1.424244
C	7.824191	-1.155487	0.102649
H	7.774853	-2.163096	0.569575
H	8.672414	-0.660309	0.597541
C	6.541788	-0.451975	0.549349
O	5.489172	-0.766290	-0.095068
O	6.639120	0.359863	1.497217
F	2.990206	-3.741990	-1.386291
C	2.780386	-2.285686	-1.878067
H	3.735971	-1.820490	-2.170051
H	2.147328	-2.270326	-2.777136
C	2.187664	-1.342907	-0.922028
N	2.893960	-0.628345	0.034521
H	3.977003	-0.621705	0.134583
C	2.032313	0.146453	0.701577
H	2.302616	0.843041	1.483309

N	0.801945	-0.052603	0.210106
C	0.884867	-0.960743	-0.808465
H	0.021496	-1.256108	-1.379210
C	-1.246564	2.989214	0.887336
O	-1.627383	0.588920	0.174288
C	-2.844573	0.026239	0.112281
C	-2.981062	-1.301281	0.989998
C	-1.789945	-2.208141	0.777322
O	-0.967727	-2.287686	1.821095
C	0.144274	-3.202327	1.697887
H	-0.225715	-4.211529	1.504234
H	0.812578	-2.895416	0.892870
H	0.659445	-3.171771	2.654419
O	-1.601929	-2.844596	-0.261320
H	-3.001049	-1.006414	2.042296
C	-4.287715	-2.063914	0.672717
N	-4.236614	-2.449198	-0.803182
C	-5.137624	-3.575321	-1.173821
H	-5.076001	-3.731776	-2.251572
H	-4.805429	-4.476523	-0.658623
H	-6.162147	-3.343157	-0.884425
H	-3.253576	-2.730320	-0.992116
C	-4.540225	-1.118845	-1.485904
C	-5.733839	-0.583854	-0.666617
C	-5.561046	-1.199010	0.750899
H	-5.460297	-0.432305	1.520580
H	-6.420175	-1.818800	1.020340
H	-6.687050	-0.882793	-1.112819
H	-5.715940	0.506631	-0.637323
H	-4.788327	-1.330809	-2.530735
C	-3.272863	-0.269510	-1.360824

H	-2.439995	-0.756616	-1.883209
H	-3.434474	0.691744	-1.860165
H	-4.362311	-2.980804	1.251841
H	-3.627303	0.691565	0.539366
O	-2.307286	3.123445	1.484837
C	-0.890461	3.623492	-0.412348
C	-0.875436	5.021078	-0.432462
H	-1.240260	5.575069	0.427442
C	-0.328949	5.693496	-1.522721
H	-0.256345	6.772466	-1.487234
C	0.153262	4.976351	-2.619602
H	0.588334	5.505746	-3.462797
C	0.083014	3.579467	-2.620040
H	0.445778	3.010444	-3.472138
C	-0.416183	2.897315	-1.510854
H	-0.459640	1.815422	-1.479260

TS2'

F	0.489263	2.465041	3.791514
C	-0.306404	1.801533	2.683679
H	0.087250	0.803706	2.458494
H	-1.375393	1.714443	2.888194
O	-0.131154	2.510277	1.453331
H	-0.416866	0.227379	0.347659
F	7.984950	-1.266476	-1.404391
C	7.792715	-1.170726	0.120269
H	7.721104	-2.180448	0.580404
H	8.643515	-0.692804	0.627838
C	6.517089	-0.446237	0.562133
O	5.460156	-0.722518	-0.089695
O	6.632790	0.347513	1.525137

F	2.991350	-3.756379	-1.387436
C	2.802068	-2.298256	-1.883864
H	3.770976	-1.827251	-2.116530
H	2.222209	-2.283288	-2.818675
C	2.153020	-1.367773	-0.956349
N	2.812317	-0.636256	0.017957
H	3.879484	-0.601448	0.140152
C	1.903512	0.110071	0.661302
H	2.142837	0.811494	1.448237
N	0.687410	-0.118262	0.146719
C	0.837127	-1.021365	-0.870569
H	0.007457	-1.352799	-1.472608
C	-1.217695	3.057459	0.896114
O	-1.651735	0.622094	0.345937
C	-2.840238	-0.002588	0.186441
C	-2.982010	-1.346024	1.020006
C	-1.788621	-2.251404	0.802323
O	-0.973861	-2.345300	1.846322
C	0.154587	-3.238888	1.702394
H	-0.202560	-4.252356	1.505908
H	0.804982	-2.912677	0.890369
H	0.680859	-3.205490	2.652359
O	-1.594826	-2.865373	-0.249275
H	-3.021219	-1.081017	2.079670
C	-4.288242	-2.089208	0.651903
N	-4.203396	-2.443777	-0.829291
C	-5.110471	-3.550145	-1.244851
H	-5.016213	-3.693614	-2.322074
H	-4.809899	-4.463429	-0.731434
H	-6.140212	-3.305094	-0.986214
H	-3.219133	-2.735020	-0.998166

C	-4.471469	-1.095600	-1.490358
C	-5.684950	-0.568210	-0.694195
C	-5.556385	-1.214727	0.715040
H	-5.473192	-0.466052	1.504640
H	-6.426783	-1.833687	0.947426
H	-6.626132	-0.853088	-1.173646
H	-5.664580	0.521661	-0.644016
H	-4.688673	-1.278975	-2.547000
C	-3.199354	-0.259448	-1.307978
H	-2.356120	-0.742641	-1.816826
H	-3.338999	0.713778	-1.790072
H	-4.382993	-3.015585	1.211113
H	-3.648037	0.636828	0.592516
O	-2.285075	3.194859	1.480532
C	-0.860421	3.671302	-0.411207
C	-0.849968	5.067614	-0.456890
H	-1.216984	5.635712	0.392697
C	-0.299613	5.720040	-1.556366
H	-0.219590	6.797955	-1.532687
C	0.179217	4.984899	-2.642668
H	0.612909	5.500226	-3.495164
C	0.110998	3.588196	-2.618984
H	0.474115	3.004564	-3.460834
C	-0.380858	2.926201	-1.494463
H	-0.400669	1.844703	-1.442102

INT2

F	0.508978	2.473552	3.793908
C	-0.285578	1.835417	2.672515
H	0.092350	0.836399	2.431626
H	-1.358521	1.771003	2.864098

O	-0.083095	2.551199	1.445518
H	-0.875448	0.276733	0.377197
F	7.962630	-1.364299	-1.380066
C	7.775920	-1.262583	0.143991
H	7.686766	-2.270090	0.606509
H	8.636968	-0.799951	0.649377
C	6.513436	-0.513076	0.580623
O	5.461850	-0.752495	-0.087944
O	6.639396	0.265502	1.556656
F	2.942028	-3.806632	-1.384979
C	2.759040	-2.351780	-1.898189
H	3.732093	-1.891519	-2.135144
H	2.182129	-2.343913	-2.835941
C	2.113689	-1.414052	-0.978051
N	2.777182	-0.698643	0.000149
H	3.830488	-0.664693	0.126322
C	1.860543	0.050197	0.641559
H	2.119431	0.739204	1.434248
N	0.636833	-0.147296	0.140192
C	0.799652	-1.046520	-0.881429
H	-0.018631	-1.379377	-1.501820
C	-1.125874	3.169432	0.893553
O	-1.794625	0.702878	0.542143
C	-2.933395	-0.017823	0.261737
C	-3.038082	-1.370719	1.044956
C	-1.829111	-2.264754	0.813146
O	-1.024208	-2.372122	1.855530
C	0.129398	-3.236022	1.688736
H	-0.210180	-4.261190	1.521646
H	0.739824	-2.899798	0.850134
H	0.683599	-3.170771	2.620453



O	-1.638875	-2.856040	-0.251411
H	-3.094865	-1.142998	2.112483
C	-4.336206	-2.102935	0.625661
N	-4.215628	-2.418008	-0.860466
C	-5.119389	-3.508980	-1.323013
H	-4.995733	-3.631608	-2.399608
H	-4.838061	-4.433719	-0.819499
H	-6.154214	-3.261796	-1.087954
H	-3.227315	-2.712460	-1.010891
C	-4.462295	-1.053577	-1.492926
C	-5.698006	-0.546034	-0.716173
C	-5.605049	-1.227839	0.680858
H	-5.544802	-0.500771	1.493235
H	-6.480248	-1.851808	0.875977
H	-6.624436	-0.822465	-1.227176
H	-5.686245	0.543096	-0.642262
H	-4.644735	-1.203347	-2.560446
C	-3.196396	-0.218937	-1.249753
H	-2.333441	-0.686565	-1.738763
H	-3.322779	0.767514	-1.707289
H	-4.439193	-3.040117	1.161247
H	-3.759999	0.591362	0.647595
O	-2.204093	3.333599	1.451071
C	-0.741240	3.747599	-0.417720
C	-0.750301	5.140288	-0.514557
H	-1.138003	5.733695	0.307821
C	-0.180113	5.756227	-1.623252
H	-0.090652	6.831945	-1.622468
C	0.312183	4.988427	-2.680441
H	0.751784	5.478013	-3.545020
C	0.258858	3.592834	-2.607760

H	0.633877	2.982811	-3.424621
C	-0.226081	2.967252	-1.459832
H	-0.187678	1.888791	-1.357901
INT2'			
F	-2.428102	-0.720229	3.501962
C	-2.561661	-1.528138	2.211763
H	-1.673736	-2.138688	1.997599
H	-3.446264	-2.170093	2.171362
O	-2.573589	-0.633111	1.101895
C	-3.738234	-0.386331	0.489780
O	-4.771125	-0.992491	0.743930
C	-3.626718	0.798333	-0.387842
C	-4.765687	1.590071	-0.552420
H	-5.705916	1.255799	-0.128314
C	-4.668456	2.812678	-1.210419
H	-5.541954	3.443470	-1.304236
C	-3.437313	3.237557	-1.708778
H	-3.371397	4.186615	-2.229113
C	-2.294093	2.453043	-1.535453
H	-1.326249	2.811641	-1.868542
C	-2.387102	1.228054	-0.885856
H	-1.508685	0.611102	-0.738072
F	6.066461	2.199455	-0.651176
C	5.774573	2.043471	0.852747
H	6.436591	1.286793	1.326796
H	5.990839	2.954657	1.436837
C	4.362399	1.589835	1.244675
O	4.007947	1.866529	2.416005
O	3.683598	0.974159	0.369370
F	4.154334	-2.668117	-1.794563

C	3.039485	-1.613115	-1.984372
H	3.426692	-0.590367	-1.842401
H	2.656892	-1.654529	-3.016523
C	1.917780	-1.753532	-1.039814
N	1.843242	-1.025067	0.128695
H	2.507318	-0.259688	0.396067
C	0.733997	-1.430948	0.784256
H	0.427760	-0.996764	1.726682
N	0.082331	-2.388434	0.127234
C	0.829473	-2.593828	-1.012755
H	0.531253	-3.307593	-1.770787
O	-2.201197	-1.960630	-1.628447
H	-1.662951	-1.368880	-2.175312
H	-1.589190	-2.187493	-0.894644

TS3

F	-2.409061	-0.820376	3.572170
C	-2.574977	-1.530134	2.228908
H	-1.741758	-2.247245	2.047894
H	-3.508958	-2.094423	2.127615
O	-2.483172	-0.584908	1.202917
C	-3.511183	-0.622602	0.203568
O	-4.605819	-1.150604	0.516720
C	-3.431744	0.733570	-0.475392
C	-4.585026	1.511952	-0.549517
H	-5.515565	1.091839	-0.185280
C	-4.532317	2.810126	-1.061118
H	-5.433880	3.410462	-1.111731
C	-3.315438	3.342973	-1.481416
H	-3.279707	4.345894	-1.892121
C	-2.149373	2.581432	-1.379017

H	-1.187162	3.014463	-1.635257
C	-2.212203	1.275452	-0.903543
H	-1.304248	0.686137	-0.837099
F	6.167083	1.968686	-0.548399
C	5.897805	1.674205	0.944140
H	6.517947	0.827727	1.313787
H	6.183129	2.504390	1.610023
C	4.464740	1.271929	1.319342
O	4.066215	1.628489	2.453277
O	3.809484	0.600654	0.461995
F	4.063621	-2.634113	-1.893730
C	3.037404	-1.485898	-2.015928
H	3.497557	-0.528545	-1.722757
H	2.726079	-1.379042	-3.064205
C	1.815993	-1.574666	-1.195883
N	1.736520	-1.046904	0.083337
H	2.506548	-0.443887	0.495865
C	0.475055	-1.177401	0.516577
H	0.103590	-0.821109	1.465257
N	-0.263067	-1.785392	-0.419355
C	0.560689	-2.031171	-1.491815
H	0.191369	-2.468540	-2.407009
O	-2.714206	-1.636271	-0.956103
H	-3.258673	-2.435478	-0.865065
H	-1.421812	-1.801831	-0.542037

### INT3

F	-2.413653	-0.800478	3.559648
C	-2.581200	-1.530376	2.221001
H	-1.778358	-2.298302	2.085480
H	-3.537801	-2.055679	2.113858

O	-2.427078	-0.632757	1.169562
C	-3.495042	-0.665038	0.133271
O	-4.616458	-1.117368	0.523924
C	-3.399339	0.732399	-0.482543
C	-4.545475	1.522290	-0.539529
H	-5.474758	1.099462	-0.175314
C	-4.489629	2.824550	-1.040804
H	-5.388987	3.429523	-1.083360
C	-3.273329	3.355026	-1.466446
H	-3.234871	4.359718	-1.872565
C	-2.111869	2.585494	-1.377794
H	-1.148397	3.015866	-1.635126
C	-2.181015	1.273986	-0.916557
H	-1.273126	0.681987	-0.866639
F	6.154126	1.954427	-0.556177
C	5.879136	1.679983	0.938435
H	6.508763	0.849708	1.328130
H	6.147763	2.523739	1.594556
C	4.453351	1.259973	1.317013
O	4.061908	1.593655	2.458584
O	3.797347	0.594994	0.452459
F	4.037432	-2.670446	-1.894942
C	3.023429	-1.511598	-2.019550
H	3.493676	-0.555359	-1.737406
H	2.706126	-1.408221	-3.066219
C	1.807011	-1.576556	-1.189340
N	1.743480	-1.033382	0.086409
H	2.527367	-0.425230	0.487074
C	0.490035	-1.142165	0.536250
H	0.116388	-0.773559	1.479233
N	-0.253885	-1.754702	-0.393647

C	0.547651	-2.023291	-1.476981
H	0.161179	-2.463031	-2.382978
O	-2.842794	-1.609043	-0.927653
H	-3.457434	-2.361009	-0.894794
H	-1.321537	-1.798452	-0.433586
TS4			
F	-2.396462	-0.878942	3.498233
C	-2.645576	-1.636589	2.169873
H	-2.033087	-2.573916	2.117504
H	-3.688116	-1.965216	2.046723
O	-2.292518	-0.891192	1.058915
C	-3.596947	-0.703045	-0.137502
O	-4.640356	-1.121891	0.408594
C	-3.416811	0.760370	-0.482462
C	-4.539392	1.585332	-0.406044
H	-5.468014	1.158232	-0.046195
C	-4.471241	2.918089	-0.811310
H	-5.355492	3.545379	-0.771105
C	-3.262727	3.439979	-1.266411
H	-3.221066	4.460949	-1.625523
C	-2.118446	2.640504	-1.282878
H	-1.159852	3.069144	-1.557961
C	-2.200005	1.298111	-0.922257
H	-1.314067	0.673934	-0.972986
F	6.146888	1.950282	-0.611974
C	5.920279	1.696303	0.891423
H	6.588683	0.899972	1.286308
H	6.159512	2.560757	1.532430
C	4.525015	1.214955	1.277398
O	4.117578	1.493857	2.426989

O	3.908982	0.552899	0.383522
F	3.906972	-2.678742	-2.033067
C	2.837981	-1.565462	-2.165133
H	3.308947	-0.575766	-2.037489
H	2.399398	-1.562369	-3.173525
C	1.738189	-1.570089	-1.173788
N	1.936124	-1.074419	0.106049
H	2.786531	-0.486987	0.403160
C	0.773287	-1.104266	0.753336
H	0.587361	-0.727059	1.748982
N	-0.171328	-1.617614	-0.034975
C	0.407947	-1.903000	-1.251815
H	-0.167085	-2.273575	-2.086362
O	-3.050677	-1.476028	-1.200300
H	-3.521732	-2.323733	-1.124784
H	-1.225451	-1.457220	0.308249

PD

F	-2.429838	-0.722778	3.653709
C	-2.791187	-1.226615	2.260434
H	-3.174152	-2.265942	2.267548
H	-3.558735	-0.577345	1.815313
O	-1.724999	-1.117938	1.372650
C	-3.099507	-0.777021	-0.862158
O	-3.860617	-1.672625	-0.524847
C	-3.410126	0.670876	-0.767712
C	-4.664308	1.051526	-0.272342
H	-5.311135	0.293333	0.154258
C	-5.087823	2.371455	-0.381071
H	-6.062142	2.672554	-0.008799
C	-4.259361	3.300539	-1.011843

H	-4.653840	4.280812	-1.246968
C	-2.954439	2.961828	-1.374895
H	-2.280933	3.716350	-1.772440
C	-2.521834	1.645346	-1.247277
H	-1.516723	1.361839	-1.537047
F	5.814235	2.512686	-0.873280
C	5.615207	2.280718	0.636010
H	6.331628	1.527273	1.032345
H	5.836973	3.172071	1.247456
C	4.251292	1.749856	1.091878
O	3.952673	1.989788	2.287088
O	3.561389	1.113281	0.239774
F	3.991337	-2.598323	-1.957328
C	2.740201	-1.691969	-2.065039
H	3.015806	-0.624640	-2.070583
H	2.209957	-1.870133	-3.014344
C	1.815926	-1.869947	-0.928855
N	1.904064	-1.080539	0.197890
H	2.511842	-0.232821	0.313886
C	1.052146	-1.585677	1.107510
H	0.846485	-1.099853	2.049281
N	0.413253	-2.667075	0.664192
C	0.889266	-2.843070	-0.618031
H	0.557551	-3.661678	-1.247304
O	-1.918462	-1.003169	-1.471027
H	-1.686524	-1.939812	-1.342413
H	-1.201471	-1.944732	1.288569



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