

## Supplementary Material

### **A Computational Investigation of the Uncatalysed and Water-Catalysed Acyl Rearrangements in Ingenol Esters**

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**Table S1.** Comparison between the reaction profile (DSD-PBEP86-D3/Def2-TZVPP,  $\Delta H_{298}$ ,  $\text{kJ mol}^{-1}$ ) for the uncatalysed concerted I5E to I20E acyl rearrangements using SMD(water)-B3LYP-D3/6-31G(2df,p) and SMD(water)-B3LYP-D3/Def2-TZVPP reference geometries (see also Figure 3 of the main text). As can be seen the choice of the reference geometry has a very small effect on the relative energies of the species along the reaction coordinate (typically of  $\sim 1 \text{ kJ mol}^{-1}$ ).

Specie	6-31G(2df,p)	Def2-TZVPP	Diff.
I3E	0.0	0.0	0.0
I5E	1.2	0.7	0.5
TS2	190.6	191.9	-1.3
I20E	-10.5	-9.7	-0.8

**Table S2.** Cartesian coordinates for all the local minima and transition structures considered in this work (SMD(water)-B3LYP-D3/6-31G(2df,p), Å)

I3E

C	1.289742	2.160117	-0.067684
C	0.005597	2.209004	0.297178
C	-0.956626	1.031355	0.464526
C	1.942688	0.853010	-0.406675
C	-0.656452	-0.445379	-0.005171
C	1.680440	-0.022478	0.806356
C	0.699093	-1.102966	0.491588
H	1.879893	3.072408	-0.081946
C	-1.756963	-1.334129	0.713561
C	-1.024825	-2.086907	1.771586
C	0.290308	-1.932564	1.670322
H	1.032359	-2.366668	2.328637
H	-2.571099	-0.737069	1.126177
H	-1.185659	0.976303	1.538514
O	2.235507	0.127644	1.877563
H	1.382434	0.443797	-1.249318
C	3.420578	0.726556	-0.763463
H	4.034002	0.875643	0.131282
C	3.632760	-0.680754	-1.359004
H	4.706368	-0.869803	-1.461358
C	3.006537	-1.870543	-0.588610
H	3.373987	-2.782773	-1.068820
H	3.389897	-1.900311	0.438379
O	-2.138161	1.436058	-0.256501
O	-0.760039	-0.496609	-1.408790
H	-1.376153	0.212290	-1.654752
O	-2.351117	-2.276559	-0.215872
C	-3.377089	-1.830754	-0.933934
C	-0.620806	3.539015	0.660631
H	-1.189208	3.434597	1.597133
H	0.167632	4.277008	0.828260

O	-1.457330	4.070831	-0.371879
H	-2.086012	3.360861	-0.565852
C	1.456308	-1.980353	-0.582579
H	1.074391	-1.739203	-1.574432
H	3.710325	1.487572	-1.494339
H	3.216403	-0.686855	-2.374405
H	1.186126	-3.019255	-0.380847
H	-1.547846	-2.670488	2.518507
O	-3.878389	-0.728216	-0.857948
H	-3.731846	-2.618576	-1.608798
H	-2.857494	0.791960	-0.136377

### ISE

C	0.172672	-2.228006	0.140526
C	1.204273	-1.467874	0.527194
C	1.212849	0.059654	0.632099
C	-1.116688	-1.610876	-0.311954
C	0.167709	0.987698	-0.072250
C	-1.497548	-0.680520	0.831465
C	-1.326218	0.744902	0.434171
H	0.251623	-3.309304	0.214847
C	0.436442	2.467038	0.387332
C	-0.511650	2.670798	1.530493
C	-1.465730	1.742513	1.547404
H	-2.286125	1.684813	2.252292
H	1.484066	2.614819	0.646396
H	1.157027	0.291351	1.701008
O	-1.913714	-1.070711	1.904979
H	-0.876000	-0.998546	-1.182428
C	-2.351956	-2.422350	-0.686967
H	-2.801913	-2.856124	0.212111
C	-3.329132	-1.459360	-1.393781
H	-4.293979	-1.959377	-1.527047
C	-3.588930	-0.093489	-0.708665
H	-4.402317	0.384528	-1.263468
H	-3.973095	-0.247775	0.306802
C	-2.425302	0.937390	-0.683487
H	-1.929584	0.947735	-1.656662
O	2.529677	0.562312	0.267622
O	0.351118	0.876223	-1.462018
H	0.294462	1.788078	-1.800288
C	2.452229	-2.142317	1.059410
H	2.837804	-1.599363	1.927352
H	2.191897	-3.157255	1.381335
O	3.534973	-2.188486	0.122697
H	3.210352	-2.660043	-0.654467
C	2.997028	0.257993	-0.953084
O	4.010975	0.770900	-1.363770

O	0.191294	3.367363	-0.702834
H	-0.766290	3.483877	-0.777884
H	-0.425312	3.511369	2.207605
H	-2.855724	1.929584	-0.530444
H	-2.089874	-3.245754	-1.358108
H	-2.939833	-1.258471	-2.400060
H	2.397942	-0.464117	-1.511729

## I20E

C	-1.491452	0.916068	-0.756671
C	-1.633437	-0.396790	-0.560009
C	-0.559981	-1.413017	-0.149941
C	-0.144998	1.563872	-0.616849
C	0.964740	-1.113392	-0.304618
C	0.374465	1.090850	0.732026
C	1.490491	0.120136	0.557508
H	-2.354795	1.530999	-0.989340
C	1.754406	-2.323862	0.313530
C	2.132124	-1.850388	1.683769
C	1.976393	-0.536191	1.816751
H	2.190530	0.044389	2.706006
H	1.136611	-3.221844	0.321343
H	-0.733892	-1.642890	0.909070
O	-0.065206	1.481352	1.797100
H	0.482974	1.126711	-1.394598
C	0.070436	3.071795	-0.697949
H	-0.301909	3.553460	0.212373
C	1.585646	3.304633	-0.876557
H	1.803431	4.371270	-0.758992
C	2.533628	2.515212	0.061848
H	3.541453	2.904798	-0.112885
H	2.303971	2.745289	1.109481
C	2.621983	0.975186	-0.132082
H	2.639114	0.744104	-1.199603
O	-0.823876	-2.632498	-0.853048
H	-0.466137	-2.494510	-1.742064
O	1.212286	-1.024431	-1.690820
H	2.093064	-1.417668	-1.815955
C	-2.990392	-1.060969	-0.652994
H	-3.133639	-1.558325	-1.612710
H	-3.110423	-1.800560	0.141752
C	-4.367268	0.352761	0.642855
O	-3.805265	0.045248	1.667575
O	2.935109	-2.575119	-0.465995
H	2.762155	-3.347482	-1.017263
O	-4.078928	-0.112089	-0.575246
H	2.511802	-2.527010	2.439643
H	1.849157	3.044268	-1.909694

H	-0.473922	3.499461	-1.545502
H	3.571788	0.631667	0.283153
H	-5.205004	1.058751	0.575558

RC I3E

C	1.441657	2.211917	-0.172681
C	0.157653	2.226008	0.199481
C	-0.786675	1.032904	0.387230
C	2.147924	0.916776	-0.448250
C	-0.403827	-0.449840	-0.004469
C	1.914587	0.115952	0.818457
C	0.958469	-1.004574	0.583176
H	1.995967	3.145242	-0.223976
C	-1.466036	-1.389691	0.682553
C	-0.775218	-1.922655	1.894345
C	0.535873	-1.714999	1.834821
H	1.263312	-2.017101	2.577505
H	-2.406347	-0.892635	0.900938
H	-1.071074	1.023406	1.447352
O	2.478734	0.342300	1.872030
H	1.602035	0.435679	-1.261124
C	3.628699	0.815820	-0.797598
H	4.237696	1.052048	0.081224
C	3.884866	-0.626842	-1.284013
H	4.963753	-0.786497	-1.381001
C	3.307100	-1.777147	-0.419520
H	3.709766	-2.708248	-0.830515
H	3.694769	-1.712256	0.603977
O	-1.939920	1.350568	-0.412437
O	-0.451043	-0.548771	-1.409291
H	-1.165278	0.057069	-1.671044
O	-1.746531	-2.524033	-0.190490
C	-2.716231	-2.410786	-1.087755
C	-0.515394	3.548884	0.501331
H	-1.095398	3.462475	1.433074
H	0.244173	4.320500	0.651409
O	-1.355052	4.003302	-0.565324
H	-1.903586	3.230177	-0.771687
C	1.762697	-1.953620	-0.394720
H	1.372167	-1.829503	-1.405078
H	3.894201	1.526257	-1.586305
H	3.463092	-0.725506	-2.292412
H	1.539413	-2.977744	-0.087957
H	-1.311203	-2.435590	2.682541
O	-3.490548	-1.485910	-1.216447
H	-4.263935	-0.214170	-0.065695
H	-2.739383	-3.309914	-1.716272
O	-4.342348	0.537449	0.549177

H	-2.774687	1.092052	0.042182
H	-4.932654	1.156381	0.100777

RC I5E

C	0.742289	2.327083	-0.175157
C	-0.513001	1.953066	0.093999
C	-0.980363	0.525981	0.395075
C	1.837515	1.316985	-0.335802
C	-0.246318	-0.733533	-0.152314
C	1.735301	0.408130	0.879633
C	1.202796	-0.929669	0.496789
H	0.970518	3.383320	-0.287712
C	-1.007765	-2.031460	0.330482
C	-0.235212	-2.484810	1.530559
C	0.939273	-1.871275	1.634051
H	1.675397	-2.028573	2.413013
H	-2.046961	-1.816774	0.581888
H	-1.055924	0.414149	1.480931
O	2.064235	0.745118	2.000599
H	1.560595	0.733603	-1.215808
C	3.305642	1.688366	-0.521946
H	3.732598	2.021494	0.429695
C	4.026430	0.430855	-1.052297
H	5.108476	0.595680	-1.024717
C	3.725827	-0.907420	-0.330706
H	4.413333	-1.649219	-0.748811
H	3.984491	-0.829550	0.732504
O	-2.342944	0.440609	-0.140380
O	-0.258821	-0.641759	-1.557841
H	-0.227271	-1.559627	-1.874710
O	-0.986153	-3.019020	-0.698178
C	-3.363324	0.288126	0.713028
C	-1.590459	3.009418	0.215017
H	-2.234970	2.801990	1.080681
H	-1.119930	3.981300	0.378765
O	-2.375561	3.152461	-0.974680
H	-2.756532	2.285511	-1.159026
C	2.297282	-1.501946	-0.483350
H	1.961153	-1.373878	-1.514761
H	3.412255	2.508256	-1.238709
H	3.756055	0.305731	-2.108560
H	2.350750	-2.576677	-0.298583
H	-0.620914	-3.240515	2.203875
O	-3.279908	0.208034	1.913414
H	-2.519549	-1.022137	-2.000033
H	-4.300041	0.248495	0.143451
O	-3.042745	-1.827638	-2.126569
H	-1.774257	-2.836135	-1.251516

H -3.749582 -1.736264 -1.475142

PC I20E

C -0.025153 -2.163363 0.128337  
C 0.982432 -1.290080 0.239605  
C 0.928724 0.236956 0.116413  
C -1.419102 -1.686227 -0.152334  
C -0.337645 1.016084 -0.383629  
C -1.669822 -0.655878 0.936792  
C -1.690284 0.727037 0.379567  
H 0.155914 -3.221074 0.299250  
C -0.089948 2.541758 -0.090831  
C -0.862899 2.789138 1.173262  
C -1.730258 1.812025 1.418107  
H -2.425268 1.763877 2.247429  
H 0.979754 2.749023 0.021255  
H 1.164221 0.632857 1.113017  
O -1.866702 -0.946641 2.101155  
H -1.377785 -1.166316 -1.110483  
C -2.632854 -2.607470 -0.208555  
H -2.877023 -2.966352 0.796739  
C -3.797242 -1.790535 -0.808956  
H -4.725479 -2.362479 -0.708317  
C -4.041938 -0.374365 -0.226535  
H -4.981013 -0.017352 -0.660983  
H -4.219134 -0.435804 0.853782  
C -2.983158 0.722419 -0.531903  
H -2.681287 0.642917 -1.576716  
O 1.966649 0.604724 -0.798287  
O -0.459361 0.805983 -1.782051  
H 0.456497 0.742536 -2.101060  
C 2.343366 -1.807248 0.621789  
H 2.853245 -1.138663 1.315209  
H 2.266418 -2.801172 1.063143  
C 4.352640 -1.351367 -0.607238  
O 4.839903 -0.647627 0.253946  
O -0.613193 3.341883 -1.152709  
H -0.648912 2.738746 -1.913252  
O 3.188549 -1.979200 -0.561144  
H -2.431653 -3.482525 -0.833874  
H -3.614247 -1.679527 -1.885398  
H -3.454835 1.699375 -0.407389  
H -0.734222 3.687756 1.764624  
H 4.850018 -1.573289 -1.560288  
H 2.588890 1.202580 -0.328490  
O 3.742202 1.911413 0.764730  
H 4.282808 2.478797 0.200828  
H 4.227563 1.068495 0.782517

TS1 concerted

C	0.638927	2.278398	0.367247
C	-0.639057	1.908872	0.252062
C	-1.042198	0.454098	0.298028
C	1.756982	1.296382	0.157809
C	-0.282608	-0.763384	-0.325921
C	1.579218	0.007894	0.978360
C	1.206243	-1.125065	0.063040
H	0.886328	3.327626	0.503306
C	-1.133724	-1.959409	0.257550
C	-0.130460	-3.071971	0.425750
C	1.092851	-2.555691	0.545258
H	1.985052	-3.104926	0.822347
H	-1.349714	-1.705284	1.310126
H	-1.168346	0.243443	1.362412
O	1.689195	-0.044816	2.185869
H	1.625313	1.026564	-0.889172
C	3.223985	1.716707	0.273564
H	3.558906	1.638271	1.313053
C	4.040538	0.799592	-0.658086
H	5.108223	0.916831	-0.445913
C	3.698850	-0.708841	-0.614229
H	4.419158	-1.215738	-1.263340
H	3.877348	-1.105224	0.393999
O	-2.407286	0.276495	-0.304777
O	-0.453020	-0.625766	-1.723175
H	-0.325468	-1.493492	-2.130165
O	-2.344558	-2.053147	-0.441620
C	-3.445518	-0.619896	0.530754
O	-4.561590	-0.554302	0.157958
C	-1.773390	2.899601	0.327673
H	-2.492648	2.594685	1.101313
H	-1.376871	3.879693	0.602115
O	-2.437609	3.068372	-0.928447
H	-2.858793	2.223031	-1.128340
C	2.280197	-1.128339	-1.088019
H	1.960720	-0.519748	-1.934957
H	-2.302267	-0.637093	-0.885862
H	3.346505	2.760231	-0.031896
H	3.886471	1.143175	-1.688757
H	2.330206	-2.154451	-1.458394
H	-0.411528	-4.098087	0.630294
H	-3.004677	-0.827888	1.506316

TS2 concerted



C	0.089151	-2.233934	-0.152520
C	1.168813	-1.460722	-0.004590
C	1.253385	0.079100	0.019000
C	-1.273010	-1.612971	-0.258456
C	0.050843	0.991565	-0.387762
C	-1.343171	-0.637405	0.904850
C	-1.283129	0.776311	0.431743
H	0.192130	-3.316005	-0.168545
C	0.449757	2.468230	-0.029311
C	-0.232660	2.708616	1.287033
C	-1.169401	1.796698	1.529105
H	-1.821139	1.761111	2.393541
H	1.538886	2.565956	0.028271
H	1.529099	0.370851	1.045270
O	-1.464650	-0.986421	2.063392
H	-1.260566	-1.036549	-1.185359
C	-2.570011	-2.415671	-0.271684
H	-2.776844	-2.810027	0.728604
C	-3.690541	-1.462833	-0.740934
H	-4.659934	-1.951363	-0.597961
C	-3.755481	-0.064704	-0.073508
H	-4.683084	0.402458	-0.418845
H	-3.862395	-0.169682	1.012929
C	-2.615926	0.941188	-0.399817
H	-2.383592	0.885736	-1.464141
O	2.309650	0.445978	-0.869368
O	-0.152705	0.867883	-1.787241
H	0.734478	0.715437	-2.153267
C	2.511786	-2.124645	0.185374
H	2.869705	-2.059502	1.214512
H	2.506444	-3.163453	-0.139748
C	3.941955	-0.057381	0.054721
O	-0.054901	3.370068	-1.016422
H	-0.153093	2.823001	-1.812884
O	3.533774	-1.444240	-0.637875
H	-2.495722	-3.266606	-0.955592
H	-3.574740	-1.309272	-1.821480
H	-2.982040	1.951428	-0.205328
H	0.005958	3.556759	1.917538
O	3.900597	0.033469	1.239007
H	2.906956	-0.796398	-1.231302
H	4.601206	0.403572	-0.677617

TS1 stepwise (pathway a)

C	0.898362	2.292455	0.296829
C	-0.415069	2.057640	0.313639
C	-1.081731	0.681449	0.323251
C	1.868847	1.183844	0.012311

C	-0.439585	-0.646671	-0.242387
C	1.586536	0.001280	0.936203
C	1.013424	-1.143513	0.154415
H	1.275840	3.305108	0.414237
C	-1.361403	-1.759917	0.414332
C	-0.478723	-2.878473	0.814080
C	0.783688	-2.456937	0.851360
H	1.619252	-3.020924	1.248907
H	-1.877664	-1.381574	1.294026
H	-1.241589	0.490719	1.398058
O	1.789626	0.012909	2.133957
H	1.613513	0.874856	-1.001734
C	3.380378	1.417233	0.000272
H	3.771958	1.392810	1.022798
C	4.017286	0.320352	-0.874779
H	5.103892	0.329730	-0.739993
C	3.510970	-1.123641	-0.646541
H	4.130045	-1.779047	-1.266769
H	3.701632	-1.429862	0.390303
O	-2.345625	0.726647	-0.342064
O	-0.544599	-0.622817	-1.646228
H	-1.317080	-0.057415	-1.820806
O	-2.418234	-2.040584	-0.570528
C	-3.370898	-1.169407	-0.553722
C	-1.400671	3.188259	0.486833
H	-2.036907	2.998771	1.366455
H	-0.867726	4.127878	0.657664
O	-2.210625	3.360028	-0.680993
H	-2.526047	2.450641	-0.851737
C	2.030798	-1.415379	-1.015024
H	1.748096	-0.863477	-1.910805
H	3.609740	2.403513	-0.415032
H	3.829807	0.574148	-1.925815
H	1.938893	-2.473987	-1.268232
H	-0.856860	-3.817168	1.198173
O	-3.951832	-0.756939	0.548012
H	-3.872443	-1.038481	-1.512959
H	-3.549302	0.188371	0.559578

TS2 stepwise (pathway a)

C	0.652321	2.289987	0.371163
C	-0.634321	1.937908	0.332492
C	-1.123471	0.507779	0.269617
C	1.730259	1.299989	0.053741
C	-0.394904	-0.799923	-0.283744
C	1.568443	0.063471	0.939736
C	1.102078	-1.107415	0.128240
H	0.921153	3.321986	0.578557

C	-1.228179	-1.979756	0.371993
C	-0.191608	-3.001197	0.755688
C	1.022078	-2.460522	0.789531
H	1.924668	-2.943935	1.145758
H	-1.614838	-1.616129	1.335543
H	-1.457646	0.283072	1.284671
O	1.799253	0.058136	2.132042
H	1.507465	1.002482	-0.970806
C	3.208840	1.688497	0.055952
H	3.598159	1.672636	1.079224
C	3.952788	0.686461	-0.848607
H	5.032635	0.796949	-0.705632
C	3.586796	-0.806555	-0.669960
H	4.265864	-1.377973	-1.310095
H	3.806306	-1.127470	0.356614
O	-2.354038	0.532880	-0.589866
O	-0.530798	-0.874794	-1.682912
H	-1.298096	-1.468635	-1.808563
O	-2.305936	-2.320929	-0.458715
C	-3.280706	-0.350127	-0.474449
C	-1.724193	2.961707	0.562603
H	-2.470423	2.569285	1.267368
H	-1.283793	3.859744	1.001367
O	-2.356702	3.386601	-0.649428
H	-2.806469	2.616948	-1.017451
C	2.140513	-1.225339	-1.051733
H	1.805120	-0.671117	-1.927984
H	3.337272	2.704586	-0.329366
H	3.745785	0.954743	-1.892323
H	2.148889	-2.276973	-1.345599
H	-0.458662	-3.991134	1.107379
O	-3.719984	-0.811788	0.660443
H	-3.421232	-1.808005	0.434185
H	-3.856918	-0.491699	-1.388938

### TS3 stepwise (pathway a)

C	0.065755	-2.244682	-0.380891
C	1.159521	-1.477445	-0.380326
C	1.215324	0.012462	-0.020874
C	-1.293013	-1.621123	-0.243111
C	0.085541	0.959792	-0.504810
C	-1.217317	-0.638896	0.915778
C	-1.208752	0.769959	0.422343
H	0.148791	-3.308637	-0.586300
C	0.473373	2.451673	-0.222461
C	-0.085083	2.718601	1.143153
C	-0.999675	1.812292	1.483181
H	-1.570982	1.799934	2.403505

H	1.548033	2.602240	-0.303665
H	1.265432	0.104455	1.068521
O	-1.175702	-0.979737	2.081880
H	-1.411570	-1.038506	-1.159550
C	-2.588456	-2.414875	-0.097256
H	-2.694834	-2.783090	0.928268
C	-3.741275	-1.460611	-0.477641
H	-4.697223	-1.925121	-0.214641
C	-3.714993	-0.039009	0.140881
H	-4.661490	0.437020	-0.133497
H	-3.722915	-0.105350	1.235999
C	-2.587778	0.931831	-0.313747
H	-2.428034	0.836209	-1.390919
O	2.463153	0.518715	-0.549185
O	-0.112670	0.752014	-1.881327
H	-0.334464	1.628931	-2.238809
C	2.490070	-2.060551	-0.780846
H	2.496498	-3.146146	-0.674096
H	2.717895	-1.809103	-1.821835
C	3.568166	0.073374	0.136397
O	3.552430	0.020935	1.457950
O	-0.102369	3.299849	-1.228382
H	-1.036519	3.422927	-1.009474
O	3.597988	-1.544008	-0.009759
H	-2.590602	-3.282762	-0.763658
H	-3.738743	-1.347092	-1.569208
H	-2.926273	1.954590	-0.132439
H	0.206197	3.582590	1.727431
H	4.454632	0.443180	-0.384627
H	3.465092	-1.245164	1.130961

TS4 stepwise (pathway a)

C	0.247659	-2.156247	0.146709
C	1.247241	-1.294446	0.367604
C	1.203974	0.245192	0.366635
C	-1.126252	-1.662188	-0.190965
C	-0.003852	1.038574	-0.244197
C	-1.446878	-0.656291	0.900812
C	-1.428035	0.737610	0.372399
H	0.425789	-3.224592	0.236337
C	0.208567	2.557320	0.103370
C	-0.683336	2.779444	1.290661
C	-1.569199	1.797917	1.427843
H	-2.342170	1.731745	2.183788
H	1.263283	2.757674	0.315671
H	1.267519	0.546784	1.424758
O	-1.709875	-0.972087	2.045361
H	-1.018207	-1.119111	-1.131499

C	-2.337618	-2.574169	-0.355641
H	-2.661043	-2.947297	0.621660
C	-3.446518	-1.739355	-1.031853
H	-4.384984	-2.302857	-1.007863
C	-3.720291	-0.326971	-0.453293
H	-4.618205	0.046336	-0.955682
H	-3.982985	-0.398797	0.609110
C	-2.625939	0.758541	-0.656655
H	-2.230008	0.683251	-1.670375
O	2.345845	0.743624	-0.322078
O	0.028255	0.856222	-1.651768
H	0.975809	0.790996	-1.862113
C	2.601673	-1.855563	0.690179
H	3.085983	-1.373676	1.540442
H	2.578399	-2.933336	0.829113
C	3.925678	-0.451471	-0.654060
O	4.453602	0.248002	0.318743
O	-0.216350	3.376154	-0.989259
H	-0.157287	2.791795	-1.762881
O	3.446833	-1.651347	-0.504158
H	-2.093165	-3.440505	-0.977726
H	-3.182037	-1.618502	-2.090156
H	-3.094904	1.740868	-0.569702
H	-0.614596	3.664758	1.911448
H	4.185160	-0.228405	-1.689946
H	3.529928	0.840954	0.393597

#### Intermediate 1 (pathway a)

C	0.618217	2.281542	0.386823
C	-0.662917	1.935511	0.239868
C	-1.114171	0.491691	0.217843
C	1.722868	1.286144	0.167604
C	-0.328193	-0.737889	-0.370328
C	1.514730	-0.005036	0.972799
C	1.145099	-1.126189	0.039089
H	0.881755	3.320206	0.567032
C	-1.178213	-1.889275	0.259220
C	-0.239468	-3.038841	0.415751
C	0.998740	-2.554112	0.521104
H	1.874450	-3.125800	0.803955
H	-1.453667	-1.614296	1.280749
H	-1.308111	0.272466	1.272704
O	1.607538	-0.072984	2.181001
H	1.598482	1.029041	-0.883418
C	3.193518	1.685612	0.308593
H	3.509219	1.600003	1.353670
C	4.017236	0.762194	-0.609952
H	5.082060	0.869084	-0.378461

C	3.659066	-0.742414	-0.574077
H	4.388532	-1.257571	-1.206450
H	3.809329	-1.140661	0.438043
O	-2.384595	0.382615	-0.496602
O	-0.391986	-0.726356	-1.778662
H	-1.249308	-0.346429	-2.016426
O	-2.402576	-1.986353	-0.474231
C	-3.138323	-0.806082	-0.267958
C	-1.777300	2.946194	0.344133
H	-2.486666	2.642498	1.128452
H	-1.364215	3.919189	0.620881
O	-2.464526	3.132713	-0.897827
H	-2.832503	2.266535	-1.118611
C	2.247588	-1.141946	-1.083623
H	1.959761	-0.525936	-1.935156
H	3.334167	2.728595	0.008582
H	3.884753	1.108436	-1.642800
H	2.293147	-2.167145	-1.457249
H	-0.554729	-4.050945	0.635804
O	-3.641623	-0.834297	1.035899
H	-3.928161	-0.781958	-1.022145
H	-4.087017	0.009347	1.192890

#### Intermediate 2 (pathway a)

C	-0.164257	-2.311197	-0.295007
C	0.992880	-1.648519	-0.261468
C	1.202928	-0.150505	-0.023373
C	-1.460725	-1.551865	-0.250482
C	0.145637	0.892656	-0.474637
C	-1.334353	-0.583092	0.915783
C	-1.170562	0.819218	0.433009
H	-0.173718	-3.393017	-0.398707
C	0.685191	2.331728	-0.159995
C	0.120878	2.644649	1.193272
C	-0.886088	1.831362	1.505260
H	-1.477840	1.870806	2.411820
H	1.772747	2.358246	-0.205839
H	1.343973	0.004607	1.055428
O	-1.375115	-0.926837	2.081668
H	-1.479134	-0.964199	-1.170318
C	-2.831448	-2.215746	-0.156891
H	-3.006655	-2.578937	0.861158
C	-3.875347	-1.153543	-0.563184
H	-4.879259	-1.529781	-0.340675
C	-3.738291	0.250906	0.078774
H	-4.627908	0.816257	-0.215931
H	-3.786303	0.170914	1.171856
C	-2.514147	1.119122	-0.329108

H	-2.337786	1.025446	-1.403422
O	2.419561	0.190929	-0.715140
O	-0.065426	0.732937	-1.856392
H	-0.179307	1.635639	-2.200054
C	2.325321	-2.340338	-0.412971
H	2.292267	-3.363250	-0.036014
H	2.637726	-2.369739	-1.465615
C	3.578937	-0.366475	-0.146322
O	4.115254	0.400506	0.885468
O	0.239463	3.252936	-1.167233
H	-0.678406	3.482109	-0.966225
O	3.321368	-1.652132	0.359241
H	-2.895153	-3.075250	-0.831163
H	-3.823334	-1.027339	-1.652141
H	-2.760503	2.165941	-0.136558
H	0.482040	3.472278	1.791187
H	4.322206	-0.379367	-0.951213
H	3.554200	0.281751	1.665568

TS1 stepwise (pathway b)

C	0.699479	2.310931	0.221544
C	-0.586756	1.974372	0.350399
C	-1.036878	0.536271	0.525805
C	1.750102	1.279900	-0.073084
C	-0.375664	-0.728861	-0.117259
C	1.661007	0.103455	0.908391
C	1.128555	-1.107059	0.196345
H	0.990896	3.357162	0.257346
C	-1.194979	-1.866001	0.597165
C	-0.214726	-2.942103	0.914029
C	1.018703	-2.437628	0.899042
H	1.909138	-2.954647	1.237184
H	-1.578853	-1.506197	1.557750
H	-1.010339	0.380031	1.611879
O	1.968241	0.174666	2.080066
H	1.460897	0.904395	-1.055096
C	3.225701	1.660928	-0.203824
H	3.687543	1.715414	0.787540
C	3.906282	0.597761	-1.087574
H	4.993320	0.714877	-1.029645
C	3.557844	-0.878333	-0.781090
H	4.192294	-1.494324	-1.425602
H	3.848332	-1.128800	0.247476
O	-2.438627	0.393195	0.157798
O	-0.597330	-0.707794	-1.510579
H	-1.328195	-1.315495	-1.699805
O	-2.340802	-2.124486	-0.223528
C	-3.263837	-1.093093	-0.053554

O	-3.814212	-0.646596	-1.143819
C	-1.639341	3.027372	0.604611
H	-2.163599	2.814124	1.546270
H	-1.149295	3.999032	0.705735
O	-2.583770	3.162368	-0.462985
H	-3.173872	2.402547	-0.402100
C	2.090972	-1.321845	-1.033123
H	1.693556	-0.837870	-1.924763
H	-2.983771	0.284435	-0.938750
H	3.324154	2.647675	-0.666557
H	3.624955	0.793717	-2.129990
H	2.086527	-2.393374	-1.244081
H	-0.508644	-3.909893	1.300031
H	-3.821841	-1.180036	0.882608

TS2 stepwise (pathway b)

C	0.740818	2.290321	0.355914
C	-0.558078	1.983238	0.369043
C	-1.077729	0.561854	0.428520
C	1.781117	1.255526	0.038524
C	-0.386866	-0.743346	-0.148344
C	1.634771	0.011670	0.923138
C	1.126115	-1.139239	0.098874
H	1.052103	3.323999	0.478885
C	-1.142551	-1.828467	0.676196
C	-0.217822	-2.993832	0.783623
C	1.028329	-2.533200	0.678773
H	1.927560	-3.105190	0.872817
H	-1.284013	-1.472526	1.700714
H	-1.229122	0.392500	1.500248
O	1.871041	-0.006409	2.113284
H	1.517552	0.961358	-0.976555
C	3.269023	1.609416	-0.021562
H	3.709723	1.555488	0.979340
C	3.943490	0.620577	-0.992320
H	5.031507	0.699242	-0.899205
C	3.548104	-0.867759	-0.843750
H	4.174602	-1.433984	-1.539497
H	3.815175	-1.230041	0.157707
O	-2.376361	0.504175	-0.226007
O	-0.631804	-0.855167	-1.531477
H	-1.443264	-0.360474	-1.720370
O	-2.498709	-1.936561	0.209790
C	-3.275713	-0.548596	0.056268
O	-3.933474	-0.940824	-1.006084
C	-1.614553	3.042354	0.571541
H	-2.261077	2.773418	1.419745
H	-1.132725	3.994640	0.805626



O	-2.403261	3.265544	-0.601748
H	-2.833843	2.421074	-0.789156
C	2.072083	-1.238521	-1.152509
H	1.693646	-0.647490	-1.985815
H	-3.015640	-1.921244	-0.846328
H	3.401720	2.633505	-0.383499
H	3.693349	0.927698	-2.015622
H	2.038464	-2.278597	-1.483931
H	-0.522267	-3.978140	1.113977
H	-3.776161	-0.393273	1.017277

TS3 stepwise (pathway b)

C	0.070921	-2.230829	-0.077370
C	1.124452	-1.469630	0.229812
C	1.198844	0.051428	0.288829
C	-1.265566	-1.598334	-0.342305
C	0.071914	0.987043	-0.240864
C	-1.473636	-0.669653	0.844576
C	-1.333814	0.761313	0.442956
H	0.166245	-3.313618	-0.069378
C	0.437683	2.453519	0.182707
C	-0.344818	2.651890	1.450630
C	-1.303869	1.739939	1.583030
H	-2.023359	1.678457	2.390082
H	1.519536	2.556734	0.324967
H	1.419188	0.353848	1.321888
O	-1.757154	-1.060123	1.960418
H	-1.137635	-0.987394	-1.236899
C	-2.554627	-2.387213	-0.544333
H	-2.880426	-2.824420	0.405137
C	-3.605781	-1.399385	-1.096061
H	-4.587821	-1.883467	-1.095034
C	-3.745811	-0.035240	-0.371302
H	-4.624165	0.456023	-0.801580
H	-3.982896	-0.192871	0.687484
C	-2.578434	0.983154	-0.508344
H	-2.236639	0.997276	-1.543786
O	2.327899	0.392993	-0.556693
O	-0.001467	0.884542	-1.652283
H	0.898008	0.714765	-1.969700
C	2.392702	-2.133330	0.709084
H	2.377914	-2.205210	1.802112
H	2.503343	-3.134160	0.290790
C	3.575688	0.126241	-0.023969
O	-0.003744	3.376931	-0.811493
H	0.015301	2.873470	-1.640951
O	3.602640	-1.400239	0.392504
H	-2.406027	-3.206046	-1.254643

H	-3.360005	-1.194058	-2.145787
H	-2.965910	1.979077	-0.284568
H	-0.151503	3.474267	2.128515
O	4.516918	-0.011602	-0.928855
H	4.220439	-1.278503	-0.598426
H	3.760586	0.690350	0.898554

TS4 stepwise (pathway b)

C	0.164249	-2.188367	-0.072909
C	1.198572	-1.385125	0.208979
C	1.227575	0.165073	0.205478
C	-1.196420	-1.614799	-0.334566
C	-0.002946	1.031507	-0.249108
C	-1.440717	-0.697420	0.854246
C	-1.386635	0.735175	0.448987
H	0.289739	-3.267513	-0.039982
C	0.302615	2.508138	0.186906
C	-0.488120	2.671745	1.453687
C	-1.401527	1.714465	1.588884
H	-2.115548	1.619693	2.397936
H	1.380119	2.647773	0.331187
H	1.456167	0.482444	1.235974
O	-1.684802	-1.105566	1.973722
H	-1.098432	-0.996930	-1.228586
C	-2.445320	-2.468124	-0.527237
H	-2.738618	-2.921657	0.425334
C	-3.553865	-1.540164	-1.068729
H	-4.507061	-2.078915	-1.060537
C	-3.761972	-0.187425	-0.339939
H	-4.671192	0.255278	-0.758854
H	-3.977372	-0.359721	0.721369
C	-2.650863	0.889355	-0.489525
H	-2.319367	0.917162	-1.528138
O	2.258411	0.516661	-0.700491
O	-0.075082	0.953292	-1.663023
H	0.854318	0.779517	-1.915464
C	2.456400	-2.068205	0.691698
H	2.650650	-1.858512	1.748181
H	2.422758	-3.141813	0.527754
C	3.918876	-0.384678	0.205057
O	-0.163377	3.421412	-0.808304
H	-0.159721	2.897200	-1.626664
O	3.667473	-1.620360	-0.054187
H	-2.259760	-3.278983	-1.238141
H	-3.328855	-1.319872	-2.120097
H	-3.087134	1.865082	-0.265592
H	-0.335246	3.502950	2.131641
O	4.583223	0.373414	-0.593783

H	3.557483	0.885294	-0.747814
H	3.660886	-0.026212	1.207566

Intermediate 1 (pathway b)

C	-0.928537	2.286443	-0.418001
C	0.354813	1.944563	-0.556125
C	0.791108	0.501809	-0.712484
C	-1.970758	1.271199	-0.040487
C	0.166104	-0.731352	0.036821
C	-1.909450	0.005602	-0.908686
C	-1.356896	-1.133163	-0.095907
H	-1.218043	3.333260	-0.455317
C	0.896405	-1.876542	-0.736716
C	-0.055382	-3.026972	-0.751496
C	-1.294132	-2.547895	-0.631015
H	-2.204068	-3.120198	-0.767282
H	0.984870	-1.586477	-1.793087
H	0.691199	0.303701	-1.788324
O	-2.231844	-0.029105	-2.078632
H	-1.651878	0.984800	0.961074
C	-3.444491	1.656271	0.109384
H	-3.951661	1.594382	-0.859138
C	-4.071709	0.697627	1.140460
H	-5.162021	0.795488	1.117938
C	-3.713649	-0.800523	0.994525
H	-4.304732	-1.341878	1.739567
H	-4.051572	-1.174014	0.018935
O	2.193423	0.399910	-0.366014
O	0.482850	-0.707845	1.406166
H	1.418952	-0.471612	1.539594
O	2.223413	-1.962159	-0.237971
C	2.902585	-0.796747	-0.697283
O	4.127639	-0.717350	-0.097021
C	1.427811	2.979067	-0.788164
H	1.944939	2.782393	-1.738332
H	0.969976	3.969238	-0.852435
O	2.378736	3.035598	0.283505
H	2.810089	2.169707	0.278128
C	-2.227811	-1.195752	1.214212
H	-1.788488	-0.602592	2.015477
H	3.314248	-0.224493	3.237642
H	-3.533838	2.688892	0.460619
H	-3.748625	1.018375	2.138968
H	-2.195244	-2.232051	1.557369
H	0.219418	-4.033057	-1.042704
H	3.023448	-0.857457	-1.786890
O	3.085647	0.000892	2.327430
H	3.003621	0.963211	2.312542

H 3.954443 -0.520953 0.851715

Intermediate 2 (pathway b)

C -0.754008 -2.350118 -0.104251  
C 0.444537 -1.897961 0.263087  
C 0.833807 -0.447511 0.524364  
C -1.864412 -1.378654 -0.386109  
C 0.075536 0.807126 -0.017843  
C -1.918245 -0.416176 0.794733  
C -1.439608 0.948017 0.404461  
H -0.928132 -3.417164 -0.215128  
C 0.796373 2.043823 0.665274  
C -0.243370 2.612588 1.584865  
C -1.406305 1.974928 1.499016  
H -2.291408 2.182849 2.088547  
H 1.666807 1.709250 1.233537  
H 0.915608 -0.322791 1.615262  
O -2.317824 -0.731181 1.898102  
H -1.531180 -0.817952 -1.261808  
C -3.293251 -1.825350 -0.687512  
H -3.788513 -2.139802 0.237129  
C -4.025535 -0.635116 -1.339810  
H -5.096347 -0.856712 -1.395153  
C -3.852555 0.747189 -0.663087  
H -4.534634 1.434349 -1.173138  
H -4.197649 0.704386 0.377426  
C -2.442325 1.396740 -0.727370  
H -2.000981 1.214590 -1.707409  
O 2.124581 -0.238189 -0.069350  
O 0.203288 0.864723 -1.425342  
H 1.097017 0.547023 -1.628344  
C 1.582454 -2.836962 0.589094  
H 1.745173 -2.864636 1.677606  
H 1.367296 -3.848078 0.242850  
C 3.131499 -1.125981 0.335004  
O 1.304245 2.960517 -0.307477  
H 0.832385 2.754122 -1.130790  
O 2.808235 -2.435314 -0.048701  
H -3.293110 -2.680935 -1.369719  
H -3.671088 -0.544028 -2.374419  
H -2.556498 2.478495 -0.629741  
H -0.017780 3.428334 2.261732  
O 4.285464 -0.761166 -0.326716  
H 3.033389 2.226191 -0.804119  
H 3.232664 -1.079068 1.434543  
O 3.888579 1.881795 -1.129764  
H 4.192273 0.195076 -0.555413  
H 3.704627 1.667519 -2.052969

TS1' catalysed (pathway a)

C	0.915094	2.309987	0.353049
C	-0.368348	1.956120	0.263400
C	-0.914836	0.526336	0.190082
C	2.005053	1.309705	0.105117
C	-0.098711	-0.746946	-0.325541
C	1.787914	0.070493	0.968681
C	1.386261	-1.094748	0.115256
H	1.185724	3.350648	0.513605
C	-0.916968	-1.942404	0.305787
C	0.061821	-2.993122	0.674396
C	1.276814	-2.455461	0.751638
H	2.158914	-2.951304	1.139479
H	-1.426081	-1.621871	1.213427
H	-1.165490	0.307180	1.242201
O	1.909620	0.058114	2.178053
H	1.842999	1.016315	-0.932002
C	3.484339	1.689535	0.192025
H	3.821574	1.654099	1.233454
C	4.272843	0.703320	-0.691240
H	5.344555	0.810295	-0.493552
C	3.899146	-0.791689	-0.555202
H	4.611029	-1.354448	-1.166862
H	4.064657	-1.127087	0.477106
O	-2.087741	0.474111	-0.608786
O	-0.164128	-0.746993	-1.731578
H	-1.001982	-0.272566	-1.904475
O	-1.972174	-2.290408	-0.644009
C	-3.027121	-1.521543	-0.508203
C	-1.455587	2.999203	0.343762
H	-2.186649	2.730692	1.121767
H	-1.028677	3.971282	0.605370
O	-2.116469	3.152959	-0.920601
H	-2.295930	2.232355	-1.186814
C	2.474291	-1.205346	-1.014291
H	2.179884	-0.641335	-1.898978
H	3.636238	2.712375	-0.166698
H	4.117740	0.989196	-1.739344
H	2.499919	-2.254051	-1.319300
H	-0.230848	-3.979522	1.011454
O	-3.594164	-1.399340	0.623599
H	-4.137887	-0.449979	0.655780
H	-3.549516	-1.286923	-1.433098
O	-4.314205	0.901674	0.598802
H	-3.425513	0.970476	0.108500
H	-4.992599	1.112594	-0.057164

TS2' catalysed (pathway a)

C	1.440466	2.158306	0.422931
C	0.112269	2.124612	0.296362
C	-0.693050	0.845497	0.190605
C	2.269010	0.938481	0.151744
C	-0.256336	-0.557722	-0.404203
C	1.748079	-0.247879	0.967352
C	1.084767	-1.248216	0.068395
H	1.938011	3.096022	0.654533
C	-1.399914	-1.519642	0.124813
C	-0.679820	-2.787962	0.496388
C	0.623587	-2.566399	0.641972
H	1.349190	-3.276319	1.022842
H	-1.764824	-1.129865	1.087292
H	-1.043792	0.662653	1.210327
O	1.865028	-0.335942	2.173229
H	2.066039	0.728142	-0.898373
C	3.793166	0.954870	0.276063
H	4.085362	0.812549	1.321749
C	4.345313	-0.168076	-0.624089
H	5.405435	-0.327561	-0.401482
C	3.619858	-1.533056	-0.548493
H	4.190693	-2.229327	-1.170545
H	3.675936	-1.932857	0.472430
O	-1.883583	1.149748	-0.634647
O	-0.312984	-0.523376	-1.811554
H	-1.217197	-0.850716	-1.999408
O	-2.449490	-1.503411	-0.795950
C	-3.012703	0.506207	-0.406211
C	-0.718688	3.374093	0.473334
H	-1.546936	3.181382	1.170192
H	-0.096139	4.165040	0.897984
O	-1.221037	3.885986	-0.766195
H	-1.789821	3.197141	-1.131432
C	2.149080	-1.575015	-1.045897
H	2.025007	-0.926274	-1.912781
H	4.192317	1.920953	-0.047939
H	4.292256	0.176498	-1.664623
H	1.928537	-2.586637	-1.393127
H	-1.205681	-3.695994	0.769156
O	-3.464087	0.379929	0.776353
H	-4.160862	-0.541519	0.776218
H	-3.667886	0.482967	-1.273738
O	-4.547706	-1.741105	0.568451
H	-3.749145	-1.883430	-0.075497
H	-5.346126	-1.726043	0.022335

TS3' catalysed (pathway a)

C	-0.017893	-2.170127	-0.216365
C	0.983197	-1.299284	-0.064069
C	0.900838	0.222013	0.027185
C	-1.436540	-1.683567	-0.296695
C	-0.368422	1.035957	-0.357005
C	-1.585998	-0.760435	0.902045
C	-1.659048	0.669581	0.479273
H	0.191485	-3.236369	-0.237381
C	-0.104110	2.533978	0.038278
C	-0.777466	2.666778	1.374833
C	-1.617106	1.662159	1.606253
H	-2.242326	1.538069	2.481854
H	0.971463	2.735765	0.081880
H	1.185683	0.520504	1.043073
O	-1.669056	-1.157671	2.048233
H	-1.492474	-1.077028	-1.202002
C	-2.650436	-2.606375	-0.325018
H	-2.804383	-3.054359	0.662163
C	-3.862695	-1.747540	-0.746211
H	-4.779834	-2.330007	-0.610411
C	-4.050231	-0.386501	-0.026862
H	-5.022042	0.002559	-0.346477
H	-4.133763	-0.540514	1.055662
C	-3.017677	0.737285	-0.325392
H	-2.800184	0.748741	-1.394018
O	1.890219	0.724322	-0.903042
O	-0.593711	0.926080	-1.753176
H	0.278674	0.840654	-2.166547
C	2.386354	-1.797430	0.163497
H	2.671652	-1.620477	1.208789
H	2.456863	-2.867389	-0.040183
C	3.219584	0.463594	-0.564795
O	3.618111	0.843811	0.604790
O	-0.715354	3.409503	-0.909673
H	-0.765297	2.887366	-1.726702
O	3.351259	-1.143452	-0.693191
H	-2.506181	-3.421176	-1.040955
H	-3.777644	-1.545509	-1.821609
H	-3.476023	1.697874	-0.081454
H	-0.605571	3.514139	2.027487
H	3.812641	0.743917	-1.446588
H	4.473429	-1.243397	-0.081489
O	5.295348	-0.946523	0.679945
H	6.114186	-0.750671	0.200424
H	4.781016	-0.031767	0.829698

TS4' catalysed (pathway a)

C	-0.350628	-2.276359	0.019999
C	0.791675	-1.606110	0.207919
C	1.042466	-0.084099	0.160868
C	-1.637284	-1.551677	-0.238013
C	-0.077599	0.923530	-0.305217
C	-1.718257	-0.558291	0.906207
C	-1.477995	0.830827	0.428464
H	-0.358728	-3.359412	0.111507
C	0.382928	2.385793	0.049134
C	-0.348643	2.694423	1.323369
C	-1.357234	1.852470	1.522644
H	-2.057737	1.871572	2.348457
H	1.466422	2.451266	0.169212
H	1.329578	0.214148	1.182110
O	-1.987199	-0.872608	2.050619
H	-1.490002	-0.994371	-1.164245
C	-2.991676	-2.241205	-0.356748
H	-3.315258	-2.603056	0.624777
C	-3.980754	-1.199561	-0.923116
H	-4.998513	-1.598456	-0.859868
C	-3.976275	0.206971	-0.269897
H	-4.825006	0.750647	-0.696795
H	-4.185778	0.125294	0.803353
C	-2.729207	1.106135	-0.501845
H	-2.421113	1.025774	-1.544904
O	2.118884	0.152786	-0.747063
O	-0.195554	0.788213	-1.713679
H	0.702301	0.516469	-1.985299
C	2.020707	-2.402210	0.551879
H	2.459880	-2.093064	1.503809
H	1.807428	-3.469281	0.579291
C	3.620093	-1.046482	-0.474472
O	4.155446	-0.617212	0.601367
O	-0.028454	3.285326	-0.984150
H	-0.097207	2.720746	-1.772196
O	3.014811	-2.235141	-0.499857
H	-2.936111	-3.104129	-1.027308
H	-3.762246	-1.069834	-1.990840
H	-3.019073	2.145134	-0.332511
H	-0.084595	3.533643	1.955574
H	4.035370	-0.784222	-1.448848
H	2.969681	1.239169	-0.309066
O	3.790770	1.695090	0.197682
H	4.368730	2.086253	-0.473426
H	4.188452	0.619146	0.480819

Intermediate 1 water complex (pathway a)



C	0.556761	2.314250	0.173737
C	-0.653204	1.767974	0.030368
C	-0.876365	0.271728	0.043819
C	1.800838	1.481774	0.044127
C	0.127213	-0.865747	-0.376170
C	1.757024	0.257779	0.975759
C	1.605317	-0.993308	0.154584
H	0.654071	3.382573	0.345890
C	-0.600739	-2.074392	0.301775
C	0.481239	-3.049942	0.630340
C	1.625091	-2.376738	0.769869
H	2.547599	-2.784789	1.165115
H	-0.992503	-1.761434	1.273142
H	-1.152928	0.084491	1.085900
O	1.809882	0.328966	2.185996
H	1.748589	1.111381	-0.979183
C	3.185073	2.119067	0.183111
H	3.453965	2.199523	1.241732
C	4.191067	1.245572	-0.589800
H	5.211326	1.551443	-0.336175
C	4.071892	-0.282302	-0.383655
H	4.908564	-0.742585	-0.918007
H	4.221091	-0.533277	0.674771
O	-2.027271	-0.079223	-0.783312
O	0.170817	-0.983862	-1.780481
H	-0.711563	-0.753316	-2.103963
O	-1.738026	-2.412617	-0.497492
C	-2.650035	-1.337147	-0.468084
C	-1.906419	2.580049	0.244224
H	-2.376444	2.256014	1.185062
H	-1.652194	3.637769	0.344385
O	-2.873699	2.476088	-0.818663
H	-2.776417	1.579147	-1.175555
C	2.772567	-0.953942	-0.903062
H	2.449421	-0.483474	-1.830794
H	3.178434	3.132321	-0.230303
H	4.060847	1.445433	-1.660947
H	2.996126	-1.992905	-1.153859
H	0.300302	-4.075012	0.928485
O	-3.258423	-1.278875	0.772793
H	-3.847914	-0.481852	0.766045
H	-3.354395	-1.498229	-1.288191
O	-4.833404	0.933317	0.618429
H	-4.290116	1.577047	0.124429
H	-5.498791	0.651327	-0.021794

Intermediate 2 water complex (pathway a)

C	-0.846963	-2.347426	0.043213
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C	0.401366	-1.908827	0.191073
C	0.889524	-0.472169	0.158546
C	-1.940740	-1.350242	-0.218619
C	0.098501	0.811564	-0.268638
C	-1.819211	-0.300873	0.880258
C	-1.350467	1.013864	0.338714
H	-1.078952	-3.405114	0.132844
C	0.947977	2.015710	0.327491
C	0.018843	2.695452	1.286905
C	-1.170193	2.106982	1.351139
H	-1.986580	2.391743	2.004336
H	1.813261	1.626380	0.870057
H	1.265513	-0.268027	1.168056
O	-2.104228	-0.515466	2.042210
H	-1.686231	-0.876751	-1.169434
C	-3.409474	-1.755475	-0.315847
H	-3.795923	-1.986089	0.682537
C	-4.181127	-0.585592	-0.958021
H	-5.256432	-0.772686	-0.870933
C	-3.888858	0.829995	-0.403004
H	-4.608601	1.507370	-0.872853
H	-4.104299	0.867590	0.671997
C	-2.479762	1.418386	-0.687589
H	-2.172378	1.149821	-1.697871
O	1.996812	-0.439510	-0.773767
O	0.044931	0.893298	-1.679992
H	0.841428	0.443881	-2.005519
C	1.551474	-2.817186	0.543102
H	1.857953	-2.644334	1.583160
H	1.276385	-3.866286	0.428984
C	3.078274	-1.281022	-0.448993
O	3.698444	-0.841461	0.722079
O	1.477618	2.854718	-0.697921
H	1.007008	2.591644	-1.507353
O	2.686955	-2.613187	-0.322918
H	-3.520205	-2.655230	-0.928722
H	-3.951714	-0.574465	-2.031151
H	-2.547206	2.508156	-0.658370
H	0.340616	3.539685	1.885578
H	3.748961	-1.231899	-1.312547
H	3.288457	2.096438	-0.565470
O	4.142825	1.743963	-0.253389
H	4.404167	2.360486	0.441438
H	3.922937	0.100006	0.542460

TS1' catalysed (pathway b)

C	-0.964487	2.301306	-0.321096
C	0.319032	1.977404	-0.497057

C	0.827079	0.545856	-0.612325
C	-1.977503	1.266755	0.073919
C	0.177308	-0.739934	0.033006
C	-1.922916	0.066703	-0.879008
C	-1.345258	-1.121324	-0.166758
H	-1.281322	3.337187	-0.409940
C	0.934413	-1.854776	-0.763423
C	-0.049479	-2.959249	-0.959476
C	-1.284047	-2.472699	-0.839028
H	-2.195345	-3.009720	-1.075277
H	1.175981	-1.488541	-1.767555
H	0.787080	0.373500	-1.699295
O	-2.284922	0.106819	-2.037383
H	-1.626905	0.925466	1.047874
C	-3.449835	1.630266	0.274737
H	-3.965422	1.649275	-0.691303
C	-4.067505	0.585560	1.224261
H	-5.157894	0.685388	1.219386
C	-3.711024	-0.893926	0.945188
H	-4.299064	-1.499147	1.641908
H	-4.052268	-1.180862	-0.058083
O	2.197302	0.459304	-0.209197
O	0.490290	-0.800839	1.410886
H	1.281478	-1.353258	1.495006
O	2.181586	-2.082632	-0.108542
C	3.085914	-1.069101	-0.466017
O	4.119267	-0.984497	0.260701
C	1.324041	3.032053	-0.897775
H	1.729582	2.789430	-1.891937
H	0.822851	4.000792	-0.969822
O	2.395083	3.194418	0.037102
H	2.855489	2.343811	0.028459
C	-2.223739	-1.301328	1.128310
H	-1.787598	-0.773188	1.975445
H	3.770181	-0.304096	1.406826
H	-3.538899	2.629216	0.712848
H	-3.736439	0.817709	2.244434
H	-2.183947	-2.362648	1.383085
H	0.223295	-3.933242	-1.346084
H	3.168813	-0.974602	-1.554289
O	3.234918	0.449786	1.987594
H	2.544376	0.607708	1.195545
H	2.765823	0.019562	2.718733

TS2' catalysed (pathway b)

C	1.286831	2.276097	0.151933
C	-0.035230	2.144977	0.280711
C	-0.719764	0.813612	0.520686

C	2.160559	1.084161	-0.114538
C	-0.251444	-0.602944	0.006371
C	1.910297	-0.040396	0.897296
C	1.203877	-1.182648	0.223342
H	1.734771	3.266049	0.139354
C	-1.134797	-1.524413	0.915669
C	-0.332160	-2.769634	1.126930
C	0.957300	-2.485908	0.949621
H	1.785408	-3.146394	1.177791
H	-1.194601	-1.069244	1.913750
H	-0.784942	0.750893	1.613523
O	2.219500	0.023522	2.069833
H	1.794795	0.735243	-1.079547
C	3.674688	1.225516	-0.286540
H	4.167898	1.210238	0.691089
C	4.153677	0.065374	-1.180714
H	5.246736	0.007791	-1.152539
C	3.582699	-1.335335	-0.856220
H	4.087834	-2.045247	-1.518326
H	3.863641	-1.629113	0.163803
O	-2.073454	0.873865	-0.001205
O	-0.571560	-0.736303	-1.361307
H	-1.336549	-0.164949	-1.523238
O	-2.464862	-1.541153	0.444563
C	-3.067030	0.029285	0.574976
O	-4.169525	0.076468	-0.050775
C	-0.936321	3.346919	0.427250
H	-1.533662	3.259663	1.346867
H	-0.328248	4.251515	0.505359
O	-1.794466	3.528662	-0.704501
H	-2.323781	2.720553	-0.752431
C	2.055019	-1.533182	-1.052743
H	1.709639	-0.981760	-1.926704
H	-2.846262	-1.818389	-0.783078
H	3.915410	2.182422	-0.759895
H	3.879146	0.301897	-2.216558
H	1.867688	-2.587182	-1.269046
H	-0.738872	-3.676269	1.557363
H	-3.039398	0.115533	1.670913
O	-3.502201	-1.662463	-1.688181
H	-4.138108	-2.392689	-1.746275
H	-3.985208	-0.860235	-1.223760

TS3' catalysed (pathway b)

C	-0.045893	-2.168879	-0.009180
C	0.930161	-1.298090	0.262028
C	0.837910	0.231311	0.334299
C	-1.440255	-1.690461	-0.290314

C	-0.371022	1.029964	-0.239806
C	-1.754332	-0.751565	0.862295
C	-1.766524	0.670751	0.411661
H	0.164047	-3.235065	0.011087
C	-0.185220	2.540215	0.154783
C	-1.027968	2.686376	1.389773
C	-1.884927	1.678287	1.520020
H	-2.621662	1.559268	2.304841
H	0.871223	2.767903	0.326848
H	0.947953	0.519740	1.389891
O	-1.995566	-1.132301	1.991561
H	-1.370643	-1.097643	-1.203699
C	-2.636787	-2.618000	-0.473452
H	-2.926789	-3.051187	0.489410
C	-3.778575	-1.768443	-1.072690
H	-4.705929	-2.350296	-1.056446
C	-4.063274	-0.396255	-0.408268
H	-4.980545	-0.013400	-0.866502
H	-4.297156	-0.532608	0.654371
C	-2.997768	0.723738	-0.577975
H	-2.631883	0.716556	-1.605420
O	1.953132	0.778719	-0.409034
O	-0.388597	0.889127	-1.651319
H	0.536672	0.813736	-1.929922
C	2.300042	-1.804648	0.637613
H	2.503413	-1.616565	1.701399
H	2.389912	-2.875085	0.447213
C	3.219661	0.436597	0.088510
O	-0.691756	3.382064	-0.882168
H	-0.603541	2.853364	-1.691399
O	3.286402	-1.130381	-0.154976
H	-2.393171	-3.442992	-1.149639
H	-3.544694	-1.583227	-2.128849
H	-3.484121	1.688074	-0.418009
H	-0.950571	3.544420	2.046409
O	4.194986	0.987788	-0.538992
H	5.315141	-0.021702	-0.326230
H	3.201411	0.485637	1.195230
O	5.641045	-0.999544	-0.154715
H	4.515060	-1.325842	-0.049444
H	6.057330	-1.012253	0.720217

TS4' catalysed (pathway b)

C	-0.459418	-2.305954	-0.049014
C	0.672964	-1.691167	0.304216
C	0.953995	-0.182735	0.391011
C	-1.685512	-1.504578	-0.378458
C	-0.046952	0.907905	-0.125566

C	-1.847160	-0.571261	0.809235
C	-1.522351	0.836811	0.441406
H	-0.509667	-3.391720	-0.051503
C	0.465967	2.299915	0.403082
C	-0.423292	2.586723	1.578693
C	-1.489774	1.793932	1.597942
H	-2.290352	1.814304	2.327288
H	1.520571	2.242504	0.693402
H	1.141740	0.046631	1.452881
O	-2.230524	-0.940226	1.903247
H	-1.427059	-0.903408	-1.251893
C	-3.047624	-2.126208	-0.669296
H	-3.480189	-2.527030	0.253397
C	-3.938056	-1.016562	-1.268651
H	-4.970184	-1.377317	-1.327905
C	-3.949719	0.351253	-0.538572
H	-4.733215	0.950746	-1.012692
H	-4.265786	0.220379	0.503336
C	-2.654035	1.208130	-0.597946
H	-2.241078	1.162829	-1.606329
O	2.133064	0.023362	-0.378880
O	-0.021519	0.886180	-1.544351
H	0.862187	0.543185	-1.767194
C	1.848488	-2.522919	0.752892
H	2.057862	-2.342543	1.816162
H	1.650408	-3.584507	0.609057
C	3.519879	-0.988868	0.221042
O	0.311271	3.299883	-0.603866
H	0.269387	2.796832	-1.434248
O	3.051995	-2.243581	0.001384
H	-2.956501	-2.953335	-1.379884
H	-3.609952	-0.838723	-2.300770
H	-2.921224	2.249794	-0.407757
H	-0.205034	3.375966	2.288127
O	4.524197	-0.632021	-0.466970
H	2.917448	1.200521	-0.495166
H	3.409162	-0.655780	1.263806
O	3.864580	1.695493	-0.582070
H	4.401000	0.743580	-0.557522
H	3.931545	2.067867	-1.474642

Intermediate 1 water complex (pathway b)

C	-0.928537	2.286443	-0.418001
C	0.354813	1.944563	-0.556125
C	0.791108	0.501809	-0.712484
C	-1.970758	1.271199	-0.040487
C	0.166104	-0.731352	0.036821
C	-1.909450	0.005602	-0.908686

C	-1.356896	-1.133163	-0.095907
H	-1.218043	3.333260	-0.455317
C	0.896405	-1.876542	-0.736716
C	-0.055382	-3.026972	-0.751496
C	-1.294132	-2.547895	-0.631015
H	-2.204068	-3.120198	-0.767282
H	0.984870	-1.586477	-1.793087
H	0.691199	0.303701	-1.788324
O	-2.231844	-0.029105	-2.078632
H	-1.651878	0.984800	0.961074
C	-3.444491	1.656271	0.109384
H	-3.951661	1.594382	-0.859138
C	-4.071709	0.697627	1.140460
H	-5.162021	0.795488	1.117938
C	-3.713649	-0.800523	0.994525
H	-4.304732	-1.341878	1.739567
H	-4.051572	-1.174014	0.018935
O	2.193423	0.399910	-0.366014
O	0.482850	-0.707845	1.406166
H	1.418952	-0.471612	1.539594
O	2.223413	-1.962159	-0.237971
C	2.902585	-0.796747	-0.697283
O	4.127639	-0.717350	-0.097021
C	1.427811	2.979067	-0.788164
H	1.944939	2.782393	-1.738332
H	0.969976	3.969238	-0.852435
O	2.378736	3.035598	0.283505
H	2.810089	2.169707	0.278128
C	-2.227811	-1.195752	1.214212
H	-1.788488	-0.602592	2.015477
H	3.314248	-0.224493	3.237642
H	-3.533838	2.688892	0.460619
H	-3.748625	1.018375	2.138968
H	-2.195244	-2.232051	1.557369
H	0.219418	-4.033057	-1.042704
H	3.023448	-0.857457	-1.786890
O	3.085647	0.000892	2.327430
H	3.003621	0.963211	2.312542
H	3.954443	-0.520953	0.851715

Intermediate 2 water complex (pathway b)

C	-0.754008	-2.350118	-0.104251
C	0.444537	-1.897961	0.263087
C	0.833807	-0.447511	0.524364
C	-1.864412	-1.378654	-0.386109
C	0.075536	0.807126	-0.017843
C	-1.918245	-0.416176	0.794733
C	-1.439608	0.948017	0.404461

H	-0.928132	-3.417164	-0.215128
C	0.796373	2.043823	0.665274
C	-0.243370	2.612588	1.584865
C	-1.406305	1.974928	1.499016
H	-2.291408	2.182849	2.088547
H	1.666807	1.709250	1.233537
H	0.915608	-0.322791	1.615262
O	-2.317824	-0.731181	1.898102
H	-1.531180	-0.817952	-1.261808
C	-3.293251	-1.825350	-0.687512
H	-3.788513	-2.139802	0.237129
C	-4.025535	-0.635116	-1.339810
H	-5.096347	-0.856712	-1.395153
C	-3.852555	0.747189	-0.663087
H	-4.534634	1.434349	-1.173138
H	-4.197649	0.704386	0.377426
C	-2.442325	1.396740	-0.727370
H	-2.000981	1.214590	-1.707409
O	2.124581	-0.238189	-0.069350
O	0.203288	0.864723	-1.425342
H	1.097017	0.547023	-1.628344
C	1.582454	-2.836962	0.589094
H	1.745173	-2.864636	1.677606
H	1.367296	-3.848078	0.242850
C	3.131499	-1.125981	0.335004
O	1.304245	2.960517	-0.307477
H	0.832385	2.754122	-1.130790
O	2.808235	-2.435314	-0.048701
H	-3.293110	-2.680935	-1.369719
H	-3.671088	-0.544028	-2.374419
H	-2.556498	2.478495	-0.629741
H	-0.017780	3.428334	2.261732
O	4.285464	-0.761166	-0.326716
H	3.033389	2.226191	-0.804119
H	3.232664	-1.079068	1.434543
O	3.888579	1.881795	-1.129764
H	4.192273	0.195076	-0.555413
H	3.704627	1.667519	-2.052969



**Table S3. Full reference for references 59 (Gaussian09) and 60 (Gaussian16).**

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