Supporting information for "Catalytic Mechanism of 4-Oxalocrotonate Tautomerase: Significances of Protein-Protein Interactions on Proton Transfer Pathways"

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I. Supporting figures

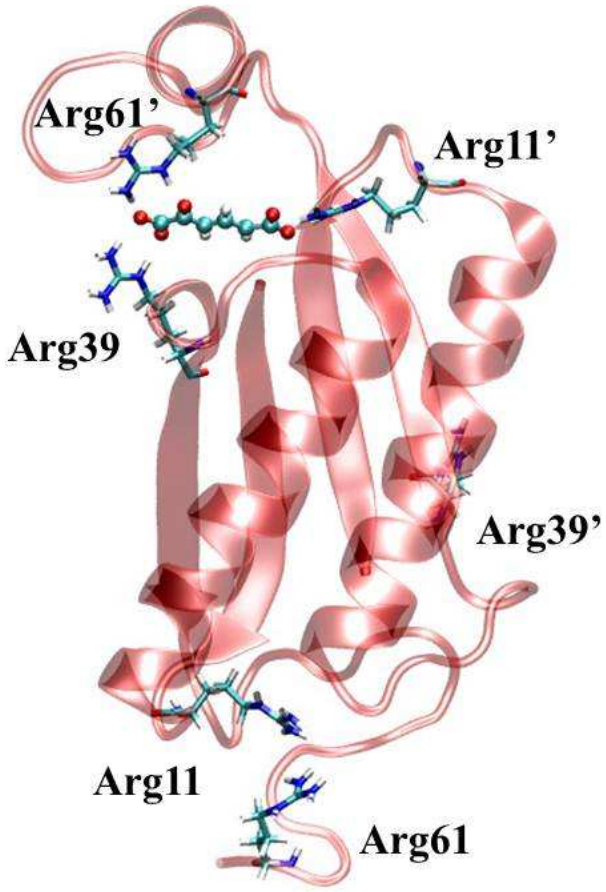


Figure S1: One typical snapshot of 1D1S from the classical MM MD simulation using the intermediate substrate. Large structural fluctuations for Arg39 and the active site were observed.

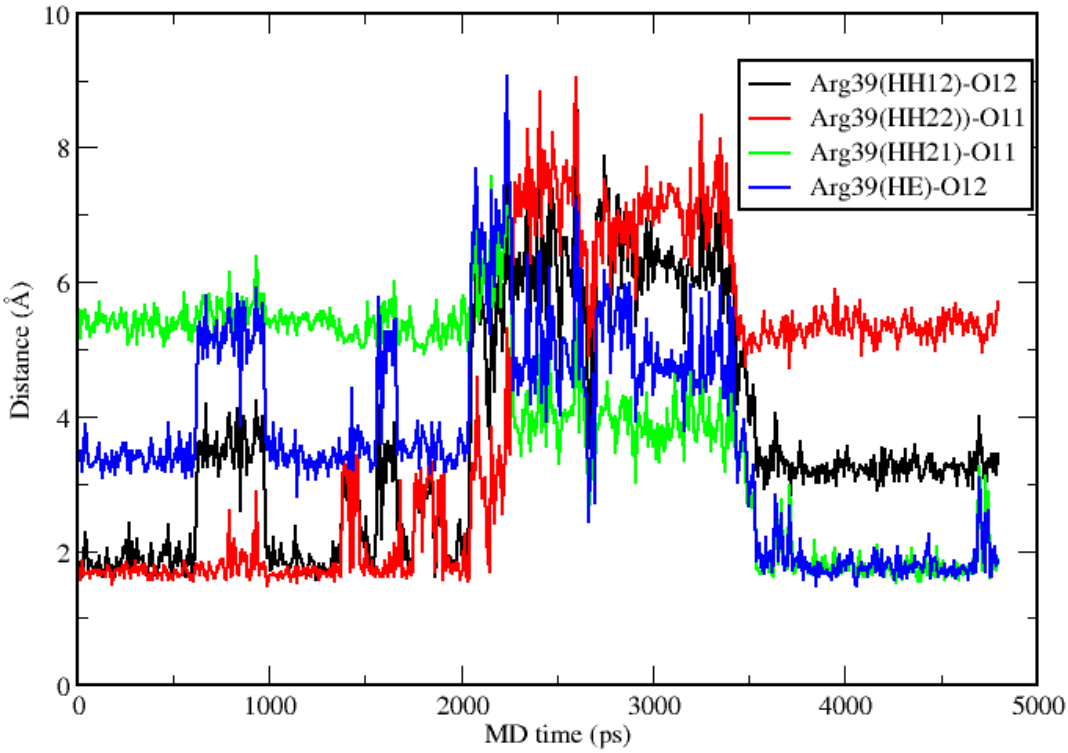


Figure S2: Four distances between four hydrogen atoms (HH12, HH22, HH21, HE) of Arg39 and the 1-carboxyl group of deprotonated 2HM during MD simulations.

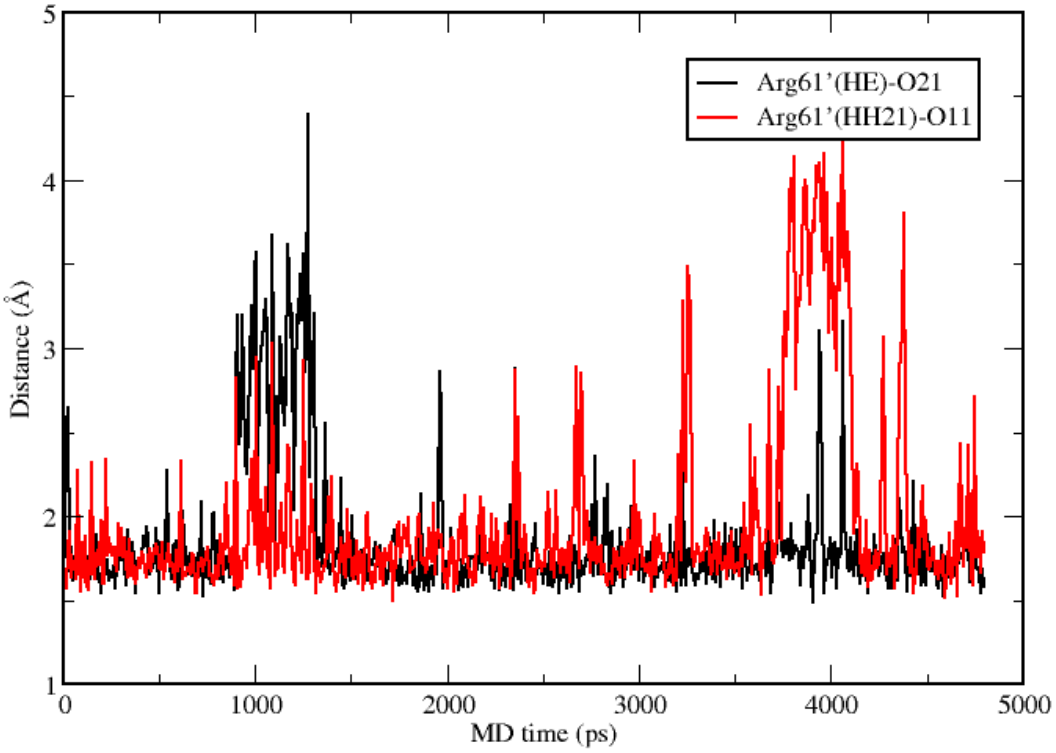


Figure S3: Two distances between two hydrogen atoms (HH21 and HE) of Arg61' and the 1-carbonyl group of deprotonated 2HM during MD simulations.

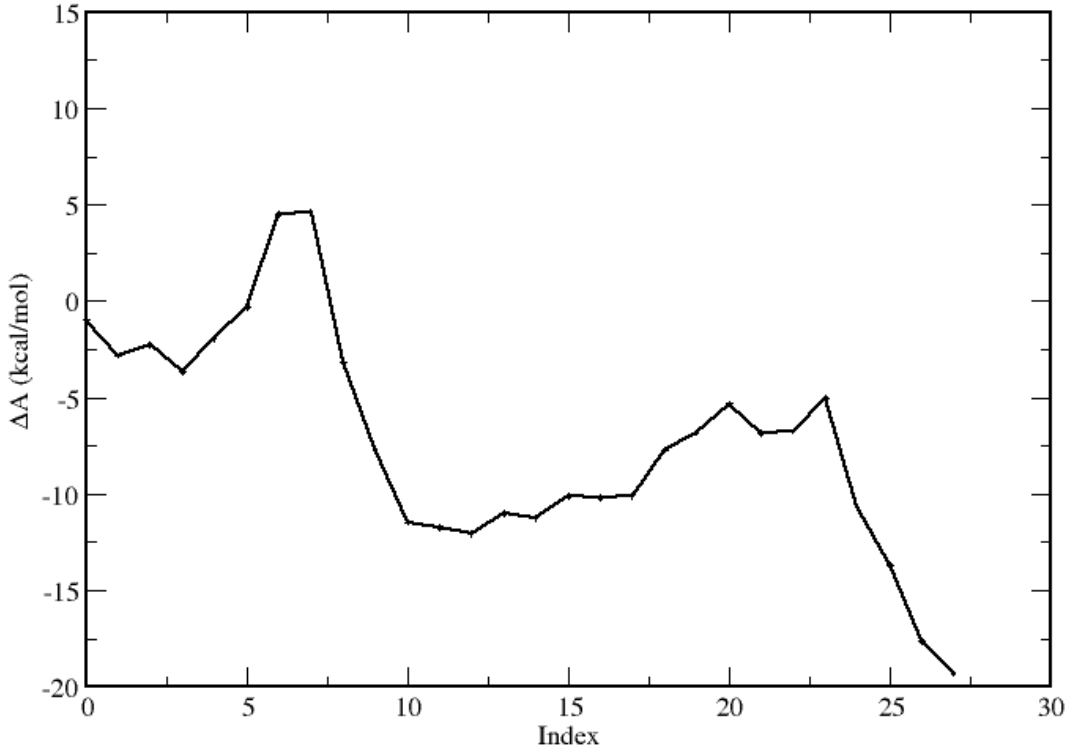


Figure S4: The reaction path of second proton transfer process optimized by QM/MM-MFEP in 1D1S model.

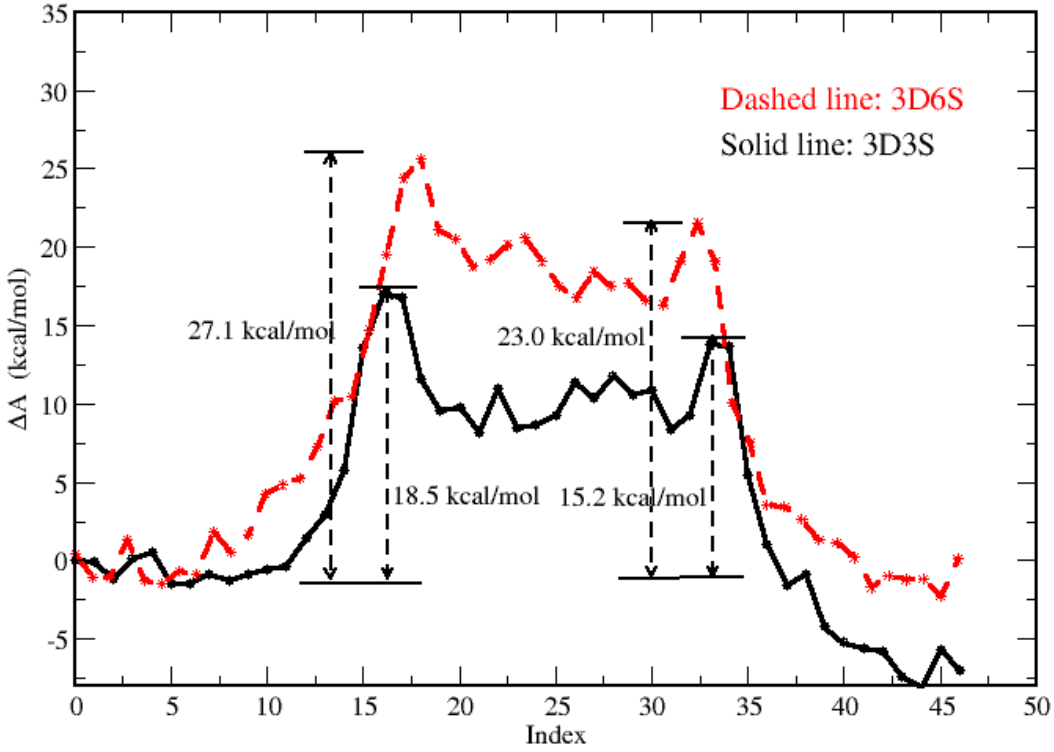


Figure S5. The free energy profiles for 3D3S (solid) and 3D6S (dashed). The blue circle points represent the first proton transfer process. The red square points indicate the second proton transfer process.

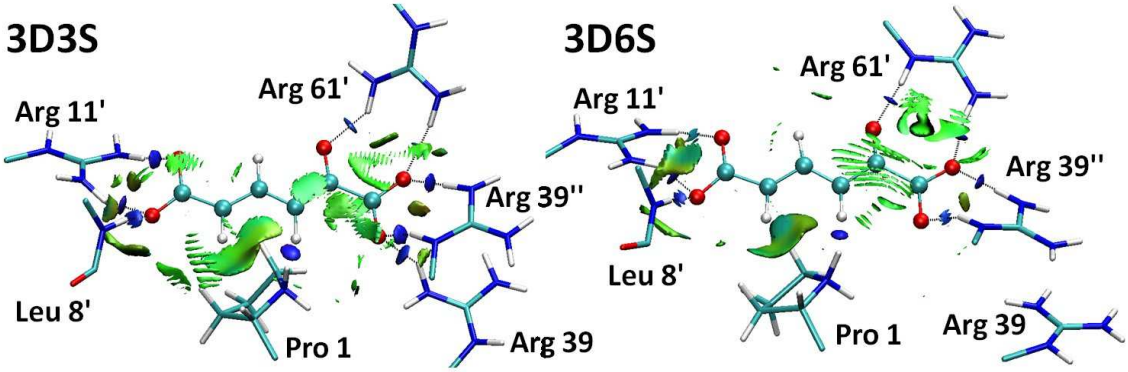


Figure S6: NCI topologies of the 3D3S and 3D6S systems.

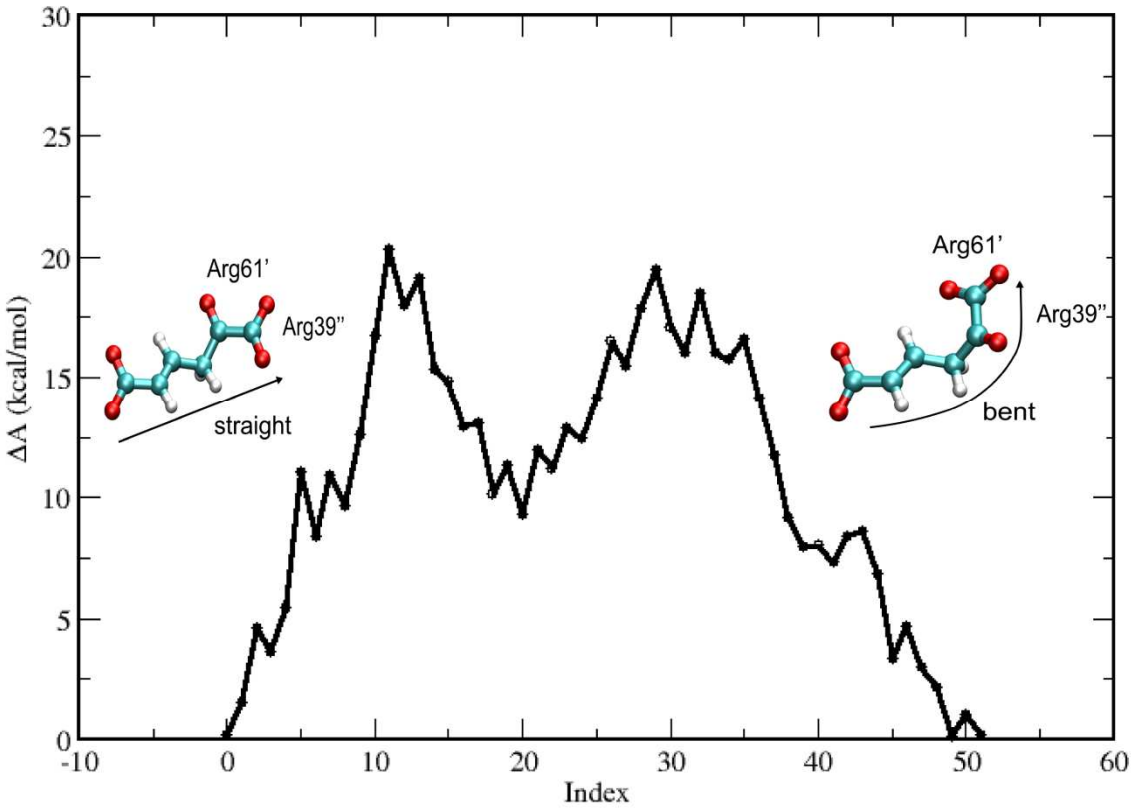


Figure S7: Free energy profiles of 2o4hex in 4-OT from “straight” to “bent” conformations.

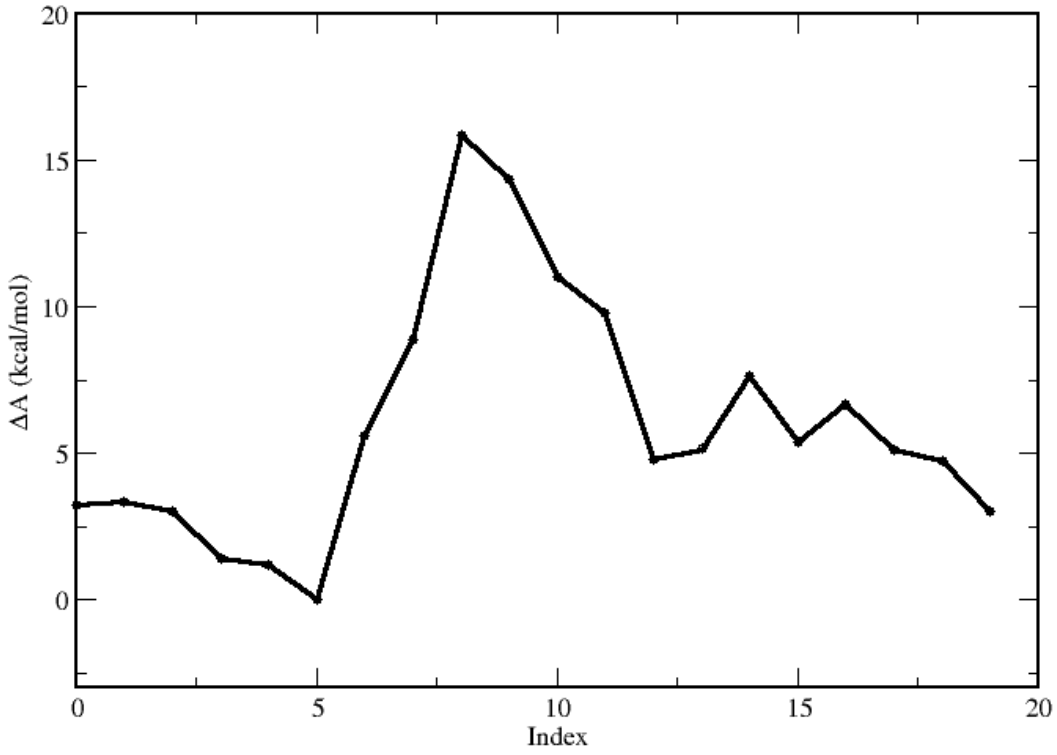


Figure S8: Reaction profile of 2o4hex with the bent conformation as reactant for the first proton transfer step.

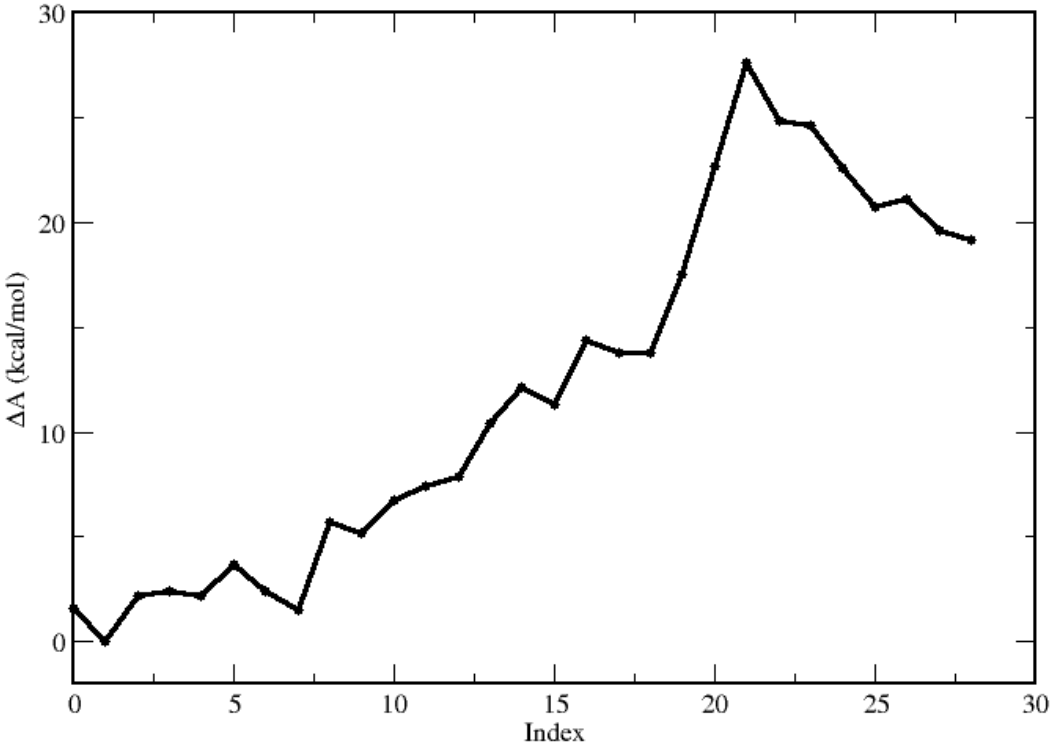


Figure S9: Reaction profile of protonated 2HM as a reactant for the first reaction step.

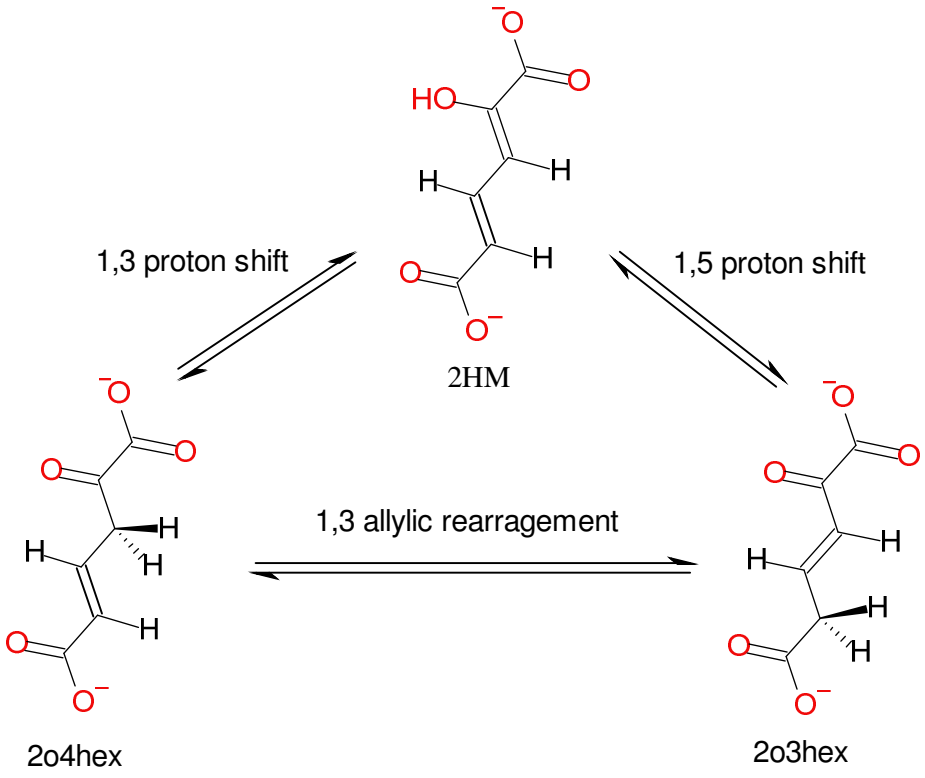


Figure S10: All the possible chemical reaction channels involved in 4-OT. 1,3 proton shift occurs quickly between 2HM and 2o4hex in aqueous solution. Presumably, 4-OT can either open a new channel of the 1,3 allylic rearrangement to convert 2o4hex to 2o3hex or directly converts 2HM to 2o3hex by 1,5 proton shift.

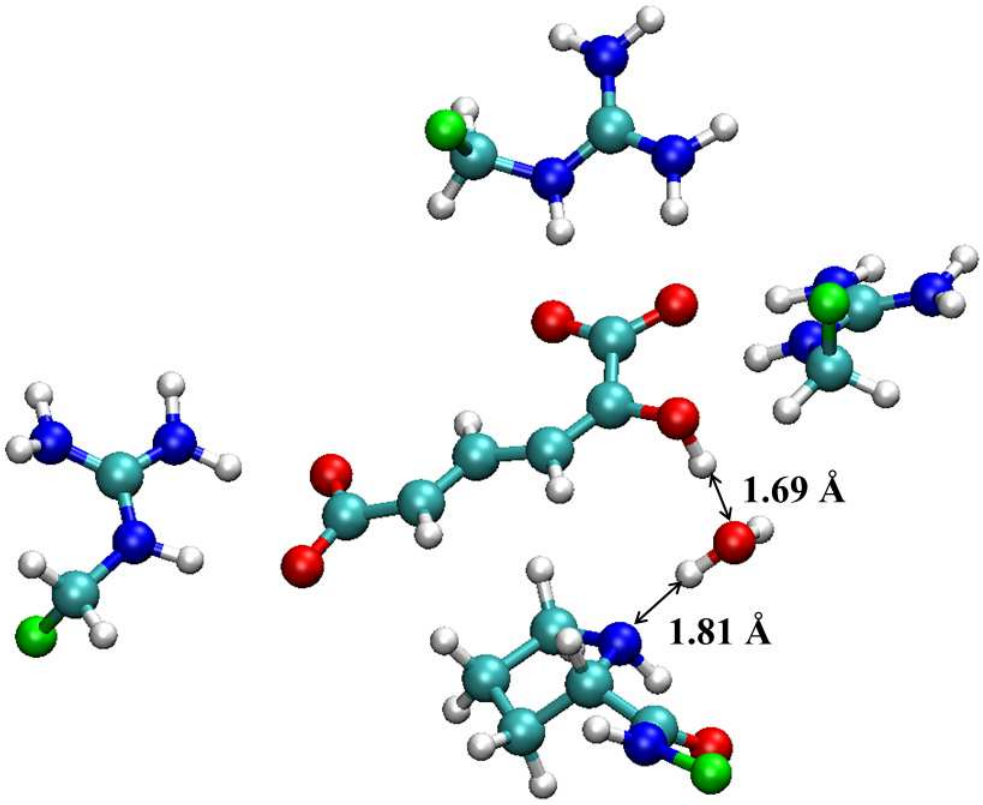
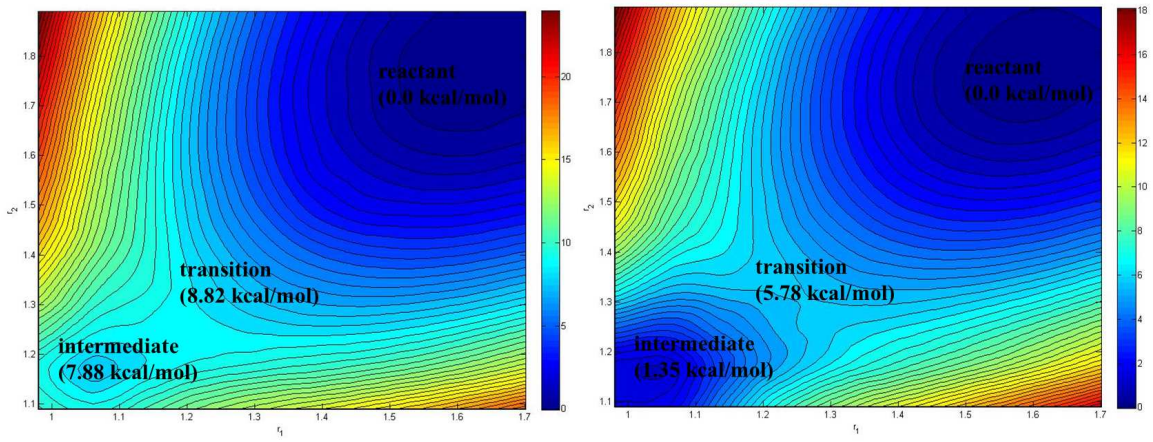


Figure S11. The optimized reactant structure with 2HM, Pro1, one water molecule, Arg39'', Arg61', and Arg11'. (carbon: cyan; oxygen: red; hydrogen: white; nitrogen: blue; and pseudoatom: green)



(a) gas phase (b) implicit solvent model (CPCM)

Figure S12. Two-dimension energy surface for the first proton transfer reaction with 2HM as reactant via water mediate reaction mechanism. The reaction coordinates are chosen as: r_1 represents distance between 2-hydroxyl hydrogen and water oxygen; r_2 represents distance between water hydrogen and proline nitrogen.

II. Supporting tables

Table S1: Average dihedral angles defined by Pro1-N, Pro1-CA, Pro1-CD, and substrate-C4 in 3D3S and 3D6S from 2.4 ns MD simulations

	3D3S	3D6S
Mean Value	-62.41	-59.62
RMSD	5.70	7.35

Table S2: Average dihedral angles defined by Pro1-N, Pro1-CA, Pro1-CD, and substrate-C4 from 32 ps direct QM/MM MD simulations in 3D3S

MD Runs	1	2	3	4	5
Mean Value	-91.74	-103.95	-98.23	-72.30	-76.05
RMSD	15.83	20.87	19.88	19.09	19.33

Table S3: Average distances between *Pro-R* proton at C3 site in 2o4hex and Pro-N from five independent 32 ps direct QM/MM MD simulations (unit Å)

MD Runs	1	2	3	4	5
Mean Value	3.40	4.87	3.74	3.52	3.26
RMSD	0.36	0.78	0.71	0.61	0.59

Table S4: Average distances between the proton on 2-keto oxygen in 2HM and Pro-N from five independent 32 ps direct QM/MM MD simulations (unit Å)

MD Runs	1	2	3	4	5
Mean Value	5.24	5.28	4.69	5.07	4.74
RMSD	0.50	0.47	0.59	0.43	0.60

III Non-Covalent Index (NCI) analysis details

The Non Covalent Interaction (NCI) analysis is a newly defined index based on the study of the density and the reduced density gradient. As previously described [Jonhson, E. *et al*, J. Am. Chem. Soc., 132, 6498 (2010), Contreras-Garcia, J. *et al*. J. Chem. Theory. Comput., 7, 625 (2011)] it is possible to link the non-covalent interaction to the low reduce density gradient/low density area, the different local minima of the reduced gradient being named NCI Critical Point of Interaction (CPI). In addition, as previously stated, it is possible to link the density at the NCI CPI to the strength of the interaction [Contreras-Garcia, J., *et al*, J. Phys. Chem. A, 115, 12983 (2011)]. The NCI analyses were performed with NCIPLOT software using promolecular densities. The geometries were extracted from typical MD simulation snapshot. The ligand keyword was used in order to visualize only the interactions between the ligand (deprotonated 2HM) and the protein within 5Å of the ligand, with a grid interval 0.2, 0.2, 0.2 Å along each dimension. In Figure S6, the color ranges for densities from -0.04 to 0.04 au and the surfaces correspond to a reduced density gradient lower or equal to 0.3.

IV. Direct QM/MM MD computational details.

The initial crystal structure is taken from PDB: 1BJP, with the inhibitor substituted by the 2o4hex/2HM reactant. The QM subsystem in this direct MD simulation only includes one substrate. The other two substrates (2o4hex) are modeled with the classical force field. The integration step for short, medium and long distance interactions are 1, 4, and 8 fs, respectively.

The pair list is updated every 8 fs. This system is solvated in a rectangular box $90 \times 90 \times 90\ \text{Å}^3$ with 21,477 TIP3P water molecules. Energy minimization and series constraints were added to warm up the system to 300K. Five independent computations are carried out. The trajectories are saved at each 32 fs and 1000 snapshots were generated in the total 32 ps simulations.

V. 2HM vs 2o4hex: an experimental view

With the stereochemistry study of YwhB, a 4-OT homologue, Johnson, W.H. *et al* [Biochemistry, 46, 11919 (2007)] proposed that "the conversion of 2o4hex and 2HM may not be enzyme-catalyzed, and this observation could further suggest that 4-OT does not catalyze a 1,3-allylic rearrangement of 2o4hex to 2o3hex, but instead, may simply catalyze the conversion of 2HM to 2o3hex". To clarify the reactant issue in 4-OT, we list all the possible reaction channels in Figure S10. We think Johnson's stereochemistry argument cannot rule out the 1,3 allylic rearrangement of 2o4hex to 2o3hex because *the deprotonated 2HM, not protonated 2HM, is the intermediate state in 4-OT. Therefore, the inter-conversion between 2o4hex and 2o3hex does not go through the protonated 2HM.* We think some of experimental studies did not realize two different protonation states of 2HM. Even if interconversion of 2o4hex and 2HM may not be enzyme-catalyzed, this cannot prove that 4-OT does not catalyze 1,3-allylic rearrangement between 2o4hex and 2o3hex. Furthermore, since the tail part (6-carboxyl group) of substrate is anchored strongly by Arg11' and Leu8', the abstracted proton can only be transferred to the *Si* face. With the racemate 2o4hex substrate, a stereospecific 2o3hex can also be generated. The arguments from experimental studies about the reactant state are thus rendered ineffective by the

fast conversion between 2HM and 2o4hex. Based on our theoretical studies, 2o4hex is still a plausible reactant.

VI. 2HM as reactant: simulation details

The force field parameters for 2HM are generated using MATCH program. The molecular dynamics simulations preparations are same as in 3D3S model. Three independent 640 ps simulations are carried out for both straight and bent conformation, and 200 snapshots are taken during each trajectory, with a 3.2 ps interval.

After the 640 ps MD simulation, a structure is taken out for further QM/MM MFEP optimization. In this QM/MM calculation, besides previous QM active site (Pro1 and substrate), three arginine residues (Arg39'', Arg61', Arg11') side chains are also included in the QM region. The pseudo-atom for three arginine residues are the CG atoms, and pseudo-atom basis parameters is taken from Ref.28. The QM active site model is constructed based on the QM part of QM/MM optimization, with all arginine pseudo-atoms replaced by hydrogen atoms, and the Pro1 is terminated with methyl group. Total atom number in the QM active site model is 74. In QM calculation, we fixed all protein residue side chain carbon atoms, and the QM calculation is carried out in Gaussian 09, with B3LYP/6-31G(d) level, within gas phase and implicit solvent model (CPCM). Two reactions coordinate, distance between 2-hydroxyl hydrogen – water oxygen and hydrogen on water – Pro-N, were chosen to scan the 2-D reaction energy profile.

VII. Structure coordinates for reactant, intermediate, and product states

Reactant state:

```
ATOM      1  N   PRO     1      -2.514   0.069 -15.109
ATOM      2  HN1 PRO     1      -1.503   0.084 -15.215
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ATOM      4  CD  PRO     1      -3.098  -0.780 -16.178
ATOM      5  CA  PRO     1      -2.871  -0.495 -13.795
ATOM      6  HA  PRO     1      -3.531   0.204 -13.262
ATOM      7  HD1 PRO     1      -4.056  -0.362 -16.503
ATOM      8  HD2 PRO     1      -2.433  -0.787 -17.047
ATOM      9  CB  PRO     1      -3.661  -1.814 -14.085
ATOM     10  HB1 PRO     1      -4.729  -1.592 -14.001
ATOM     11  HB2 PRO     1      -3.428  -2.616 -13.377
ATOM     12  CG  PRO     1      -3.299  -2.158 -15.539
ATOM     13  HG1 PRO     1      -4.080  -2.739 -16.036
ATOM     14  HG2 PRO     1      -2.363  -2.730 -15.586
ATOM     15  C   PRO     1      -1.609  -0.625 -12.938
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ATOM    607  HG2 ARG    39       3.627   2.935 -13.163
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ATOM    619 HH22 ARG    39       1.826   6.855 -15.701
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ATOM   1102  HB2 LEU    70     -10.217   0.451 -14.281
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ATOM   1104  HG  LEU    70      -8.325   2.039 -13.044
ATOM   1105  CD1 LEU    70      -9.511   2.946 -14.586
ATOM   1106 HD11 LEU    70      -9.283   2.201 -15.414
ATOM   1107 HD12 LEU    70      -8.744   3.814 -14.700
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ATOM   1927 HH12 ARG   123      -4.591   4.826 -18.786
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ATOM   3552 HH21 ARG   225      -2.033   7.531 -16.967
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ATOM   5872  O62 HMI   373      -6.768  -0.564 -14.032
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ATOM   5874  C5  HMI   373      -5.760   1.426 -14.780
ATOM   5875  H2  HMI   373      -5.369   1.710 -16.829
ATOM   5876  C4  HMI   373      -5.129   1.993 -15.809
ATOM   5877  H3  HMI   373      -4.033   3.464 -14.664
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ATOM   5883  O12 HMI   373      -2.923   5.459 -15.168
```

Intermediate state:

```
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ATOM      4  CD  PRO     1      -3.051  -0.866 -16.174
ATOM      5  CA  PRO     1      -2.863  -0.455 -13.728
ATOM      6  HA  PRO     1      -3.528   0.230 -13.193
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```

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ATOM     11  HB2 PRO     1      -3.319  -2.561 -13.262
ATOM     12  CG  PRO     1      -3.135  -2.192 -15.429
ATOM     13  HG1 PRO     1      -3.861  -2.851 -15.911
ATOM     14  HG2 PRO     1      -2.163  -2.698 -15.430
ATOM     15  C   PRO     1      -1.524  -0.534 -12.996
ATOM     16  O   PRO     1      -0.451  -0.310 -13.559
ATOM    598  N   ARG    39       2.283  -0.067 -14.422
ATOM    599  HN  ARG    39       1.416   0.056 -13.971
ATOM    600  CA  ARG    39       3.392   0.327 -13.569
ATOM    601  HA  ARG    39       4.311   0.476 -14.068
ATOM    602  CB  ARG    39       3.227   1.544 -12.665
ATOM    603  HB1 ARG    39       4.120   1.789 -12.031
ATOM    604  HB2 ARG    39       2.273   1.460 -12.154
ATOM    605  CG  ARG    39       3.007   2.785 -13.576
ATOM    606  HG1 ARG    39       2.739   2.549 -14.631
ATOM    607  HG2 ARG    39       4.023   3.241 -13.732
ATOM    608  CD  ARG    39       1.931   3.815 -13.156
ATOM    609  HD1 ARG    39       1.979   3.930 -12.033
ATOM    610  HD2 ARG    39       0.906   3.490 -13.330
ATOM    611  NE  ARG    39       2.183   5.214 -13.761
ATOM    612  HE  ARG    39       2.828   5.789 -13.203
ATOM    613  CZ  ARG    39       1.832   5.650 -14.987
ATOM    614  NH1 ARG    39       1.023   4.959 -15.772
ATOM    615 HH11 ARG    39       0.656   4.099 -15.288
ATOM    616 HH12 ARG    39       0.892   5.226 -16.718
ATOM    617  NH2 ARG    39       2.420   6.723 -15.419
ATOM    618 HH21 ARG    39       3.068   7.259 -14.817
ATOM    619 HH22 ARG    39       2.190   7.096 -16.320
ATOM    620  C   ARG    39       3.638  -0.854 -12.648
ATOM    621  O   ARG    39       2.865  -1.123 -11.733
ATOM   1096  N   LEU    70      -8.397  -0.805 -12.030
ATOM   1097  HN  LEU    70      -7.761  -0.666 -12.760
ATOM   1098  CA  LEU    70      -9.622  -0.061 -12.063
ATOM   1099  HA  LEU    70      -9.842   0.380 -11.111
ATOM   1100  CB  LEU    70      -9.529   1.148 -13.060
ATOM   1101  HB1 LEU    70      -9.386   0.761 -14.075
ATOM   1102  HB2 LEU    70      -8.605   1.691 -12.767
ATOM   1103  CG  LEU    70     -10.727   2.130 -13.098
ATOM   1104  HG  LEU    70     -11.673   1.554 -13.294
ATOM   1105  CD1 LEU    70     -10.967   2.925 -11.787
ATOM   1106 HD11 LEU    70     -11.264   2.157 -11.009
ATOM   1107 HD12 LEU    70     -11.735   3.726 -11.869
ATOM   1108 HD13 LEU    70      -9.990   3.378 -11.490
ATOM   1109  CD2 LEU    70     -10.387   3.097 -14.266
ATOM   1110 HD21 LEU    70     -10.125   2.540 -15.240
ATOM   1111 HD22 LEU    70      -9.383   3.610 -14.040
ATOM   1112 HD23 LEU    70     -11.232   3.787 -14.517
ATOM   1113  C   LEU    70     -10.793  -0.928 -12.379
ATOM   1114  O   LEU    70     -10.671  -1.954 -13.076
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ATOM   1137  N   ARG    73     -13.744  -4.770 -14.983
ATOM   1138  HN  ARG    73     -14.013  -4.555 -13.994
ATOM   1139  CA  ARG    73     -13.076  -6.091 -15.281
ATOM   1140  HA  ARG    73     -13.042  -6.191 -16.343
ATOM   1141  CB  ARG    73     -11.663  -6.217 -14.686
ATOM   1142  HB1 ARG    73     -11.407  -7.284 -14.516
ATOM   1143  HB2 ARG    73     -11.704  -5.787 -13.693
ATOM   1144  CG  ARG    73     -10.483  -5.522 -15.356
ATOM   1145  HG1 ARG    73     -10.376  -6.174 -16.277
ATOM   1146  HG2 ARG    73      -9.424  -5.635 -14.865
ATOM   1147  CD  ARG    73     -10.635  -4.062 -15.843
ATOM   1148  HD1 ARG    73     -10.831  -3.324 -15.022
ATOM   1149  HD2 ARG    73     -11.392  -3.867 -16.616
ATOM   1150  NE  ARG    73      -9.293  -3.775 -16.469
ATOM   1151  HE  ARG    73      -9.226  -3.971 -17.452
ATOM   1152  CZ  ARG    73      -8.390  -2.926 -15.956
ATOM   1153  NH1 ARG    73      -8.359  -2.321 -14.777
ATOM   1154 HH11 ARG    73      -9.230  -2.327 -14.283
ATOM   1155 HH12 ARG    73      -7.592  -1.734 -14.472
ATOM   1156  NH2 ARG    73      -7.426  -2.464 -16.791
ATOM   1157 HH21 ARG    73      -7.509  -2.759 -17.810
ATOM   1158 HH22 ARG    73      -7.087  -1.565 -16.692
ATOM   1159  C   ARG    73     -13.939  -7.183 -14.773
ATOM   1160  O   ARG    73     -14.615  -7.072 -13.774
ATOM   1909  N   ARG   123     -10.681  10.056 -19.845
ATOM   1910  HN  ARG   123     -10.573   9.860 -18.847
ATOM   1911  CA  ARG   123     -10.670   8.926 -20.766
ATOM   1912  HA  ARG   123     -10.246   9.263 -21.717
ATOM   1913  CB  ARG   123      -9.785   7.767 -20.340
ATOM   1914  HB1 ARG   123      -9.865   6.932 -21.137
ATOM   1915  HB2 ARG   123     -10.242   7.343 -19.409
ATOM   1916  CG  ARG   123      -8.355   8.116 -20.036
ATOM   1917  HG1 ARG   123      -8.274   8.682 -19.124
ATOM   1918  HG2 ARG   123      -7.915   8.715 -20.869
ATOM   1919  CD  ARG   123      -7.588   6.766 -19.749
ATOM   1920  HD1 ARG   123      -7.587   5.979 -20.557
ATOM   1921  HD2 ARG   123      -8.045   6.316 -18.832
ATOM   1922  NE  ARG   123      -6.171   7.182 -19.420
ATOM   1923  HE  ARG   123      -5.899   8.119 -19.695
ATOM   1924  CZ  ARG   123      -5.239   6.351 -18.985
ATOM   1925  NH1 ARG   123      -5.480   5.103 -18.618
ATOM   1926 HH11 ARG   123      -6.403   4.847 -18.338
ATOM   1927 HH12 ARG   123      -4.658   4.630 -18.255
ATOM   1928  NH2 ARG   123      -4.004   6.826 -18.866
ATOM   1929 HH21 ARG   123      -3.814   7.749 -19.108
ATOM   1930 HH22 ARG   123      -3.316   6.435 -18.196
ATOM   1931  C   ARG   123     -12.154   8.393 -21.100
ATOM   1932  O   ARG   123     -12.858   7.746 -20.308
ATOM   3532  N   ARG   225      -0.162   9.819 -10.065
ATOM   3533  HN  ARG   225       0.580   9.663  -9.449
ATOM   3534  CA  ARG   225      -1.370   9.120  -9.892
ATOM   3535  HA  ARG   225      -2.165   9.596 -10.484
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ATOM   3536  CB  ARG   225      -1.280   7.599 -10.164
ATOM   3537  HB1 ARG   225      -1.907   7.003  -9.554
ATOM   3538  HB2 ARG   225      -0.263   7.343  -9.838
ATOM   3539  CG  ARG   225      -1.712   7.164 -11.631
ATOM   3540  HG1 ARG   225      -2.745   7.519 -11.764
ATOM   3541  HG2 ARG   225      -1.673   6.059 -11.653
ATOM   3542  CD  ARG   225      -0.829   7.811 -12.670
ATOM   3543  HD1 ARG   225       0.246   7.595 -12.606
ATOM   3544  HD2 ARG   225      -0.937   8.874 -12.479
ATOM   3545  NE  ARG   225      -1.268   7.465 -14.016
ATOM   3546  HE  ARG   225      -1.960   6.694 -14.267
ATOM   3547  CZ  ARG   225      -0.970   8.285 -15.067
ATOM   3548  NH1 ARG   225      -0.158   9.343 -14.851
ATOM   3549 HH11 ARG   225       0.113   9.542 -13.967
ATOM   3550 HH12 ARG   225      -0.041   9.918 -15.625
ATOM   3551  NH2 ARG   225      -1.353   8.138 -16.356
ATOM   3552 HH21 ARG   225      -1.933   7.293 -16.555
ATOM   3553 HH22 ARG   225      -1.056   8.820 -17.041
ATOM   3554  C   ARG   225      -1.820   9.251  -8.462
ATOM   3555  O   ARG   225      -0.991   9.179  -7.520
ATOM   5870  C6  HMI   373      -6.307   0.184 -14.946
ATOM   5871  O61 HMI   373      -6.662  -0.069 -16.136
ATOM   5872  O62 HMI   373      -6.477  -0.625 -13.976
ATOM   5873  H1  HMI   373      -5.416   1.724 -13.664
ATOM   5874  C5  HMI   373      -5.573   1.420 -14.696
ATOM   5875  H2  HMI   373      -5.193   1.816 -16.741
ATOM   5876  C4  HMI   373      -5.015   2.129 -15.713
ATOM   5877  H3  HMI   373      -4.131   3.679 -14.501
ATOM   5878  C3  HMI   373      -4.177   3.243 -15.488
ATOM   5879  O51 HMI   373      -3.412   3.496 -17.718
ATOM   5880  C2  HMI   373      -3.496   3.883 -16.497
ATOM   5881  C1  HMI   373      -2.853   5.202 -16.124
ATOM   5882  O11 HMI   373      -2.376   5.878 -17.087
ATOM   5883  O12 HMI   373      -2.835   5.570 -14.923
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Product state:

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ATOM      1  N   PRO     1      -2.341  -0.159 -15.098
ATOM      2  HN1 PRO     1      -1.331  -0.147 -15.236
ATOM      3  HN2 PRO     1      -4.067   1.503 -14.299
ATOM      4  CD  PRO     1      -2.934  -0.943 -16.215
ATOM      5  CA  PRO     1      -2.624  -0.860 -13.825
ATOM      6  HA  PRO     1      -3.390  -0.305 -13.270
ATOM      7  HD1 PRO     1      -3.942  -0.589 -16.433
ATOM      8  HD2 PRO     1      -2.333  -0.802 -17.117
ATOM      9  CB  PRO     1      -3.235  -2.248 -14.215
ATOM     10  HB1 PRO     1      -4.312  -2.183 -14.042
ATOM     11  HB2 PRO     1      -2.835  -3.075 -13.619
ATOM     12  CG  PRO     1      -2.961  -2.394 -15.722
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ATOM     13  HG1 PRO     1      -3.732  -2.989 -16.223
ATOM     14  HG2 PRO     1      -1.991  -2.870 -15.903
ATOM     15  C   PRO     1      -1.342  -0.832 -12.988
ATOM     16  O   PRO     1      -0.219  -0.719 -13.476
ATOM    598  N   ARG    39       2.451   0.383 -14.124
ATOM    599  HN  ARG    39       1.474   0.208 -13.851
ATOM    600  CA  ARG    39       3.348   0.869 -13.053
ATOM    601  HA  ARG    39       4.174   1.344 -13.527
ATOM    602  CB  ARG    39       2.604   1.947 -12.224
ATOM    603  HB1 ARG    39       3.141   2.104 -11.266
ATOM    604  HB2 ARG    39       1.542   1.631 -12.030
ATOM    605  CG  ARG    39       2.514   3.347 -12.879
ATOM    606  HG1 ARG    39       3.521   3.707 -13.139
ATOM    607  HG2 ARG    39       2.102   3.991 -12.034
ATOM    608  CD  ARG    39       1.473   3.471 -14.024
ATOM    609  HD1 ARG    39       0.417   3.220 -13.811
ATOM    610  HD2 ARG    39       1.935   2.783 -14.771
ATOM    611  NE  ARG    39       1.633   4.875 -14.583
ATOM    612  HE  ARG    39       1.967   5.595 -13.929
ATOM    613  CZ  ARG    39       1.187   5.287 -15.798
ATOM    614  NH1 ARG    39       0.609   4.494 -16.693
ATOM    615 HH11 ARG    39       0.589   3.537 -16.468
ATOM    616 HH12 ARG    39       0.377   4.717 -17.641
ATOM    617  NH2 ARG    39       1.290   6.545 -16.057
ATOM    618 HH21 ARG    39       1.683   7.107 -15.401
ATOM    619 HH22 ARG    39       1.151   6.910 -16.964
ATOM    620  C   ARG    39       3.791  -0.284 -12.139
ATOM    621  O   ARG    39       2.911  -0.896 -11.512
ATOM   1096  N   LEU    70      -7.991  -0.862 -12.502
ATOM   1097  HN  LEU    70      -7.297  -0.656 -13.176
ATOM   1098  CA  LEU    70      -9.355  -0.349 -12.801
ATOM   1099  HA  LEU    70      -9.823   0.110 -12.020
ATOM   1100  CB  LEU    70      -9.377   0.743 -13.854
ATOM   1101  HB1 LEU    70     -10.391   0.873 -14.242
ATOM   1102  HB2 LEU    70      -8.736   0.378 -14.753
ATOM   1103  CG  LEU    70      -9.012   2.143 -13.287
ATOM   1104  HG  LEU    70      -8.210   2.023 -12.548
ATOM   1105  CD1 LEU    70      -8.608   3.143 -14.407
ATOM   1106 HD11 LEU    70      -7.648   2.907 -14.920
ATOM   1107 HD12 LEU    70      -8.448   4.092 -13.955
ATOM   1108 HD13 LEU    70      -9.412   3.279 -15.107
ATOM   1109  CD2 LEU    70     -10.261   2.755 -12.599
ATOM   1110 HD21 LEU    70     -10.274   2.437 -11.515
ATOM   1111 HD22 LEU    70     -11.217   2.481 -13.063
ATOM   1112 HD23 LEU    70     -10.301   3.860 -12.677
ATOM   1113  C   LEU    70     -10.331  -1.507 -13.199
ATOM   1114  O   LEU    70      -9.913  -2.494 -13.817
ATOM   1137  N   ARG    73     -12.178  -5.294 -16.716
ATOM   1138  HN  ARG    73     -11.734  -4.904 -15.892
ATOM   1139  CA  ARG    73     -11.708  -6.600 -17.132
ATOM   1140  HA  ARG    73     -11.799  -6.641 -18.136
ATOM   1141  CB  ARG    73     -10.179  -6.834 -16.868
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ATOM   1142  HB1 ARG    73      -9.977  -7.845 -17.336
ATOM   1143  HB2 ARG    73      -9.998  -6.837 -15.814
ATOM   1144  CG  ARG    73      -9.313  -5.707 -17.495
ATOM   1145  HG1 ARG    73      -9.789  -5.158 -18.337
ATOM   1146  HG2 ARG    73      -8.518  -6.309 -17.893
ATOM   1147  CD  ARG    73      -8.723  -4.703 -16.509
ATOM   1148  HD1 ARG    73      -8.048  -5.120 -15.786
ATOM   1149  HD2 ARG    73      -9.679  -4.228 -16.056
ATOM   1150  NE  ARG    73      -8.054  -3.628 -17.327
ATOM   1151  HE  ARG    73      -7.952  -3.747 -18.309
ATOM   1152  CZ  ARG    73      -7.254  -2.658 -16.797
ATOM   1153  NH1 ARG    73      -7.262  -2.456 -15.515
ATOM   1154 HH11 ARG    73      -8.149  -2.639 -15.039
ATOM   1155 HH12 ARG    73      -6.702  -1.709 -15.277
ATOM   1156  NH2 ARG    73      -6.615  -1.786 -17.560
ATOM   1157 HH21 ARG    73      -6.790  -1.663 -18.519
ATOM   1158 HH22 ARG    73      -6.420  -0.946 -17.063
ATOM   1159  C   ARG    73     -12.492  -7.680 -16.506
ATOM   1160  O   ARG    73     -12.950  -7.668 -15.350
ATOM   1909  N   ARG   123     -10.833   8.728 -19.907
ATOM   1910  HN  ARG   123     -11.026   8.634 -18.922
ATOM   1911  CA  ARG   123     -10.645   7.487 -20.625
ATOM   1912  HA  ARG   123     -10.099   7.721 -21.496
ATOM   1913  CB  ARG   123      -9.770   6.504 -19.857
ATOM   1914  HB1 ARG   123      -9.406   5.567 -20.387
ATOM   1915  HB2 ARG   123     -10.315   6.240 -18.903
ATOM   1916  CG  ARG   123      -8.386   7.191 -19.451
ATOM   1917  HG1 ARG   123      -7.887   6.449 -18.845
ATOM   1918  HG2 ARG   123      -8.606   7.978 -18.764
ATOM   1919  CD  ARG   123      -7.464   7.526 -20.679
ATOM   1920  HD1 ARG   123      -7.930   8.166 -21.431
ATOM   1921  HD2 ARG   123      -7.301   6.554 -21.172
ATOM   1922  NE  ARG   123      -6.245   8.167 -20.111
ATOM   1923  HE  ARG   123      -5.995   9.135 -20.272
ATOM   1924  CZ  ARG   123      -5.258   7.373 -19.617
ATOM   1925  NH1 ARG   123      -5.282   6.039 -19.451
ATOM   1926 HH11 ARG   123      -5.980   5.478 -19.838
ATOM   1927 HH12 ARG   123      -4.432   5.588 -19.158
ATOM   1928  NH2 ARG   123      -4.155   8.022 -19.392
ATOM   1929 HH21 ARG   123      -4.177   8.991 -19.684
ATOM   1930 HH22 ARG   123      -3.361   7.642 -18.854
ATOM   1931  C   ARG   123     -11.960   6.908 -21.095
ATOM   1932  O   ARG   123     -13.049   6.966 -20.469
ATOM   3532  N   ARG   225      -1.335  10.708 -10.304
ATOM   3533  HN  ARG   225      -0.548  10.485  -9.760
ATOM   3534  CA  ARG   225      -2.529   9.811 -10.122
ATOM   3535  HA  ARG   225      -3.342  10.215 -10.680
ATOM   3536  CB  ARG   225      -2.135   8.346 -10.588
ATOM   3537  HB1 ARG   225      -2.787   7.573 -10.132
ATOM   3538  HB2 ARG   225      -1.038   8.185 -10.355
ATOM   3539  CG  ARG   225      -2.264   8.203 -12.116
ATOM   3540  HG1 ARG   225      -3.238   8.558 -12.492
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ATOM   3541  HG2 ARG   225      -2.251   7.139 -12.366
ATOM   3542  CD  ARG   225      -1.328   8.857 -13.081
ATOM   3543  HD1 ARG   225      -0.217   8.671 -12.832
ATOM   3544  HD2 ARG   225      -1.452  10.007 -13.046
ATOM   3545  NE  ARG   225      -1.611   8.471 -14.509
ATOM   3546  HE  ARG   225      -2.183   7.631 -14.779
ATOM   3547  CZ  ARG   225      -0.983   9.110 -15.496
ATOM   3548  NH1 ARG   225      -0.253  10.209 -15.357
ATOM   3549 HH11 ARG   225      -0.104  10.607 -14.481
ATOM   3550 HH12 ARG   225       0.252  10.651 -16.107
ATOM   3551  NH2 ARG   225      -1.248   8.712 -16.738
ATOM   3552 HH21 ARG   225      -1.835   7.970 -16.917
ATOM   3553 HH22 ARG   225      -1.013   9.202 -17.570
ATOM   3554  C   ARG   225      -2.912   9.846  -8.653
ATOM   3555  O   ARG   225      -2.062   9.912  -7.747
ATOM   5870  C6  HMI   373      -5.766   0.543 -15.086
ATOM   5871  O61 HMI   373      -6.161   0.406 -16.274
ATOM   5872  O62 HMI   373      -5.911  -0.307 -14.166
ATOM   5873  H1  HMI   373      -5.548   2.412 -14.018
ATOM   5874  C5  HMI   373      -5.007   1.820 -14.761
ATOM   5875  H2  HMI   373      -4.329   2.081 -16.851
ATOM   5876  C4  HMI   373      -4.644   2.615 -15.958
ATOM   5877  H3  HMI   373      -4.797   4.528 -15.059
ATOM   5878  C3  HMI   373      -4.547   3.953 -15.939
ATOM   5879  O51 HMI   373      -3.628   4.192 -18.127
ATOM   5880  C2  HMI   373      -3.850   4.643 -16.998
ATOM   5881  C6  HMI   373      -3.262   6.016 -16.611
ATOM   5882  O11 HMI   373      -2.724   6.670 -17.549
ATOM   5883  O12 HMI   373      -3.329   6.354 -15.410
```

Complete reference for Ref. 51.

(51) Gaussian 09, Revision A.1, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.