

Supporting Information

QM/MM Calculations and MD Simulations on Acetolactate Decarboxylase to Reveal Substrate R/S-Acetolactate Binding Mode and Stereoselective Catalytic Mechanism

Can-Bo Zhuang^b, Qing-Chuan Zheng^{a,b}.*

^aKey Laboratory for Molecular Enzymology and Engineering of the Ministry of Education, Jilin University, Changchun 130023, People's Republic of China.

^bLaboratory of Theoretical and Computational Chemistry, Institute of Theoretical Chemistry, Jilin University, Changchun 130023, People's Republic of China.

*E-mail: zhengqc@jlu.edu.cn

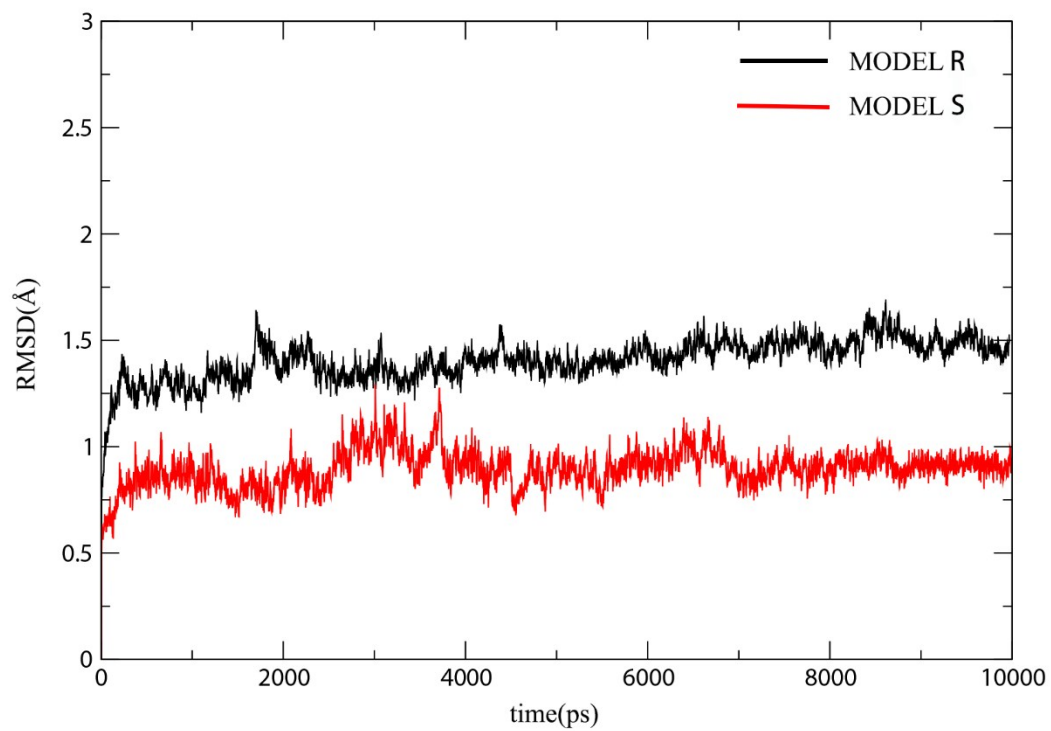


Figure S1. The RMSD results of the backbone of MODEL R and MODEL S.

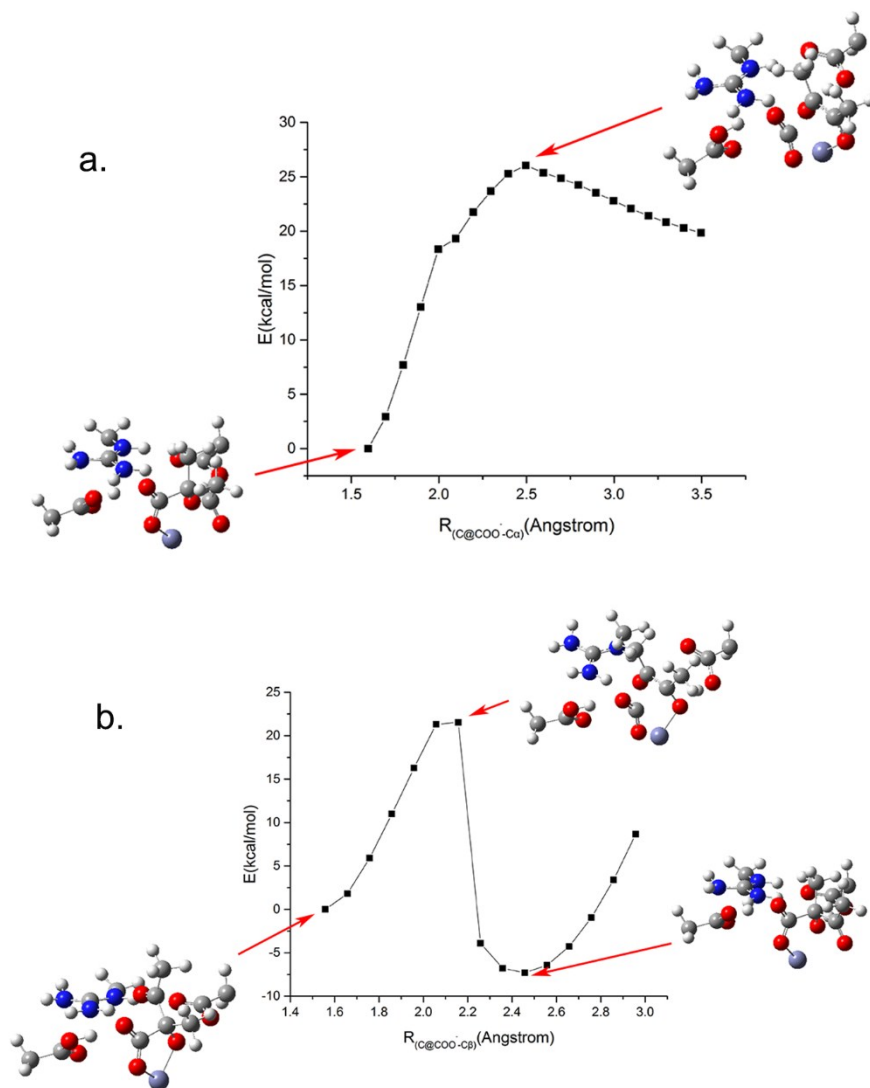


Figure S2. Flexible scanning of the distance between carboxyl and α/β -C of acetolactate in MODEL R.

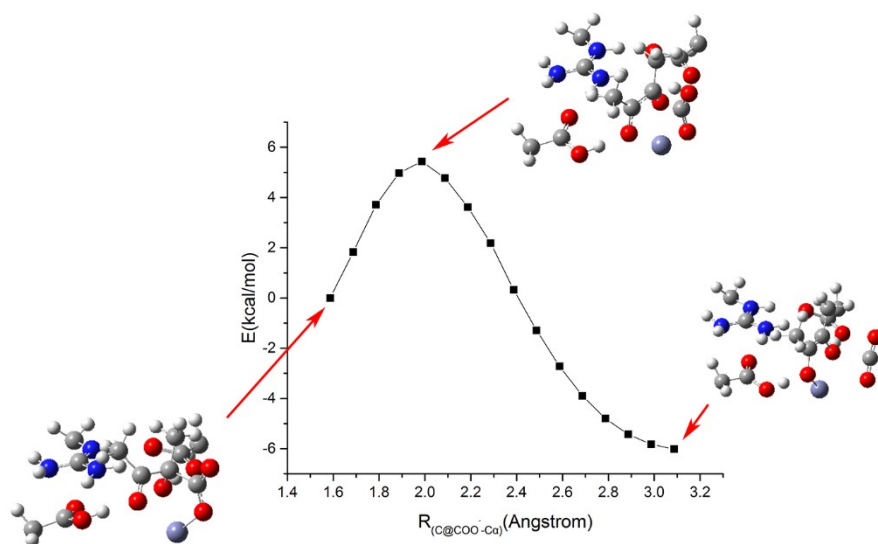


Figure S3. Flexible scanning the distance between carboxyl and α -C of acetolactate in MODEL S.

Table S1. Charges variation of ALDC catalyzing acetolactate. The optimized QM part was extracted and calculated.

	R-R	R-TS	R-P
Glu65	-0.62	-0.48	-0.48
Arg145	0.78	0.85	0.82
His194, His196, His207	0.92	0.75	0.54
Glu253	-0.04	-0.01	-0.02
ZN	0.61	0.65	0.71
substrate	-0.41	-0.74	-0.78

A. The charges distribution of ALDC catalyzing R-acetolactate.

	S-R	S-TS1	S-IM1-0
Glu65	-0.67	-0.70	-0.52
Arg145	0.79	0.81	0.84
His194, His196, His207	0.75	1.06	0.70
Glu253	-0.10	-0.22	-0.16
Zn	0.66	0.03	0.49
substrate	-0.43	0.01	-0.36

B. The charges distribution of ALDC catalyzing S-acetolactate by decarboxylation.

	S-IM1-1	S-TS2-1	S-P-1
Glu65	-0.69	-0.44	-0.43
Arg145	0.84	0.29	0.05
His194, His196, His207	0.72	0.49	0.59
Glu253	-0.09	-0.04	-0.02
ZN	0.50	0.93	0.81
substrate	-0.28	-0.23	-0.01

C. The charges distribution of ALDC catalyzing S-acetolactate by decarboxylation without a water molecule aid

	S-IM1-2	S-TS2-2	S-P-2
Glu65	-0.50	-0.42	-0.43
Arg145	0.82	0.49	0.36
His194, His196, His207	0.61	0.72	0.68
Glu253	-0.09	-0.06	-0.06
ZN	0.63	0.55	0.65
substrate	-0.41	-0.19	-0.01
H ₂ O	-0.06	-0.10	-0.19

D. The charges distribution of ALDC catalyzing S-acetolactate by decarboxylation with a water molecule aid.

Table S2. The frequencies of transition structures.

	frequencies
R-TS	-252.60
S-TS1	-209.84
S-TS2-1	-1294.66
S-TS2-2	-1007.25

Table S3. Activation and Reaction Energies Obtained for ALDC Catalyzing R/S-acetolactate.

functional	MODEL_R				MODEL_S				
	R-TS	R-P	S-TS1	S-IM1-0	S-TS2-1	S-P-1	S-TS2-2	S-P-2	(TS2-1)-(TS2-2)
B3LYP	23.3	5.6	5.3	-8.5	21.6	6.1	16.3	1.3	5.3
B3LYP-D3BJ	24.0	0.0	3.5	-6.8	21.7	10.6	17.3	0.9	4.4
X3LYP	23.7	0.0	5.5	-7.8	22.0	6.9	16.7	1.4	5.3
PBE1PBE	23.1	0.0	4.5	-4.8	21.1	8.3	16.1	3	5.0
BB1K	23.4	0.0	5.1	-4.9	25.1	7.3	20.0	-1.4	5.1
B972	22.5	0.0	5.2	-7.8	20.5	4.2	15.5	1.3	5.0
mPWB1K	23.9	0.0	5.3	-4.2	25.5	8.3	20.5	-1.3	5.0
M06-2X	24.8	-0.1	2.7	-6.5	24.6	11.4	19.4	-2.6	5.2
M05-2X	24.8	-0.1	2.7	-6.5	24.6	11.4	20.4	0.4	4.2

QM region is treated at the B3LYP, B3LYP-D3BJ, X3LYP, PBE1PBE, BB1K, B972, mPWB1K, M06-2X, and M05-2X density functionals, using the 6-311+g(2d,2p) basis set. All of the values are in kcal/mol.

Compared the energy barrier of proton transfer reaction. We can find that water-assist proton transfer reaction is more favor. The energy difference is about 4.2-5.3 kcal/mol. Our results suggest that the magnitude of the barrier is highly dependent on the HF exchange percentage in the hybrid functional. The reaction barrier is observed to increase with the increase of HF exchange as observed for the barrier calculated with BB1K, mPWB1K, M06-2X and M05-2X. For M06-2X, its HF exchange percentage is too high, and it is not recommended to calculate properties for compounds that contain transition metals.(Accounts of chemical research, 2008, 41, 157-167) The energy barrier calculated by hybrid functional with low HF exchange percentage, such as B3LYP, B3LYP-D3BJ, X3LYP, B972 and PBE1PBE, is more close to experimental result. Thus, B3LYP is suitable to illustrate the reaction.