Supporting Information

Impact of Mutation on Proton Transfer Reactions in Ketosteroid Isomerase: Insights from Molecular Dynamics Simulations

Dhruva K. Chakravorty, and Sharon Hammes-Schiffer*

Department of Chemistry, 104 Chemistry Building, Pennsylvania State University, University Park, PA 16802; e-mail: shs@chem.psu.edu

Tables

Rate constants[a,b]	WT	D99L	Y14F	Y14F/D99L
k_1	1.7×10^5	6.1×10^2	1.3×10^2	10
k_{-1}	5.6×10^5	3.1×10^8	1.7×10^8	1.6×10^8
k_2	2.1×10^5	1.6×10^7	9.3×10^5	5.0×10^7
k_{-2}	40	0.93	8.0×10^{-3}	1.1×10^{-3}

Table S1: Rate constants obtained for the two proton transfer reactions catalyzed by WT and mutant forms of KSI for the second independent data set.

a) The EVB parameters used in all calculations for this table were V_{12} = 99.5 kcal/mol and Δ = 1.8 kcal/mol for the first step and V_{12} = 93.1 kcal/mol and Δ = -14.5 kcal/mol for the second step. These parameters were determining by fitting to the experimental rate constants for WT KSI.
b) All rate constants were calculated with Eq. (4) and are given in s^{-1}.

Figures

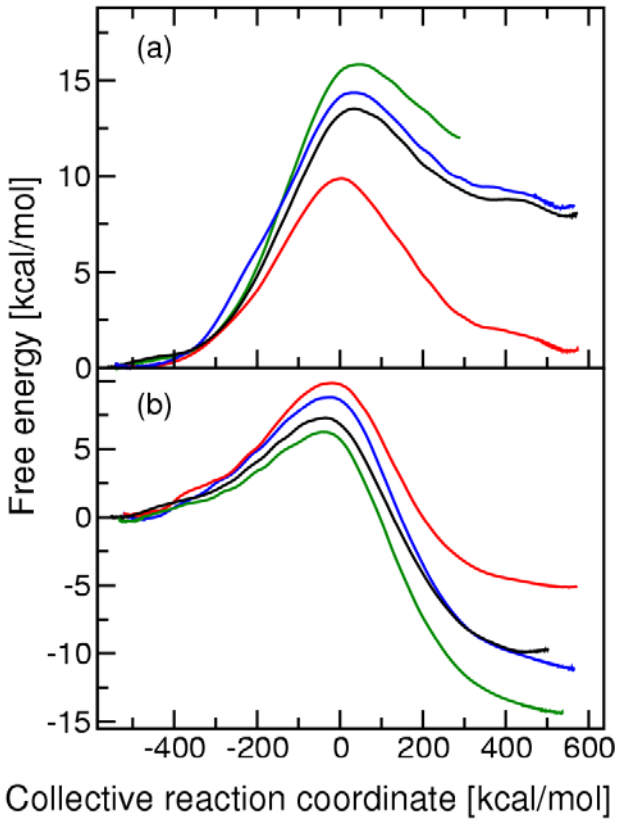

Figure S1: Potential of mean force (PMF) curves for (a) the first proton transfer step and (b) the second proton transfer step catalyzed by KSI, as obtained from the second independent data set. These profiles are depicted for the WT (red), D99L mutant (black), Y14F mutant (blue), and Y14F/D99L double mutant (green) forms of KSI. For both steps, all curves are shifted so that the reactant is at zero energy, although mechanistically the product of the first step is the same as the reactant of the second step, following rotation of the Asp38 carboxylate group.

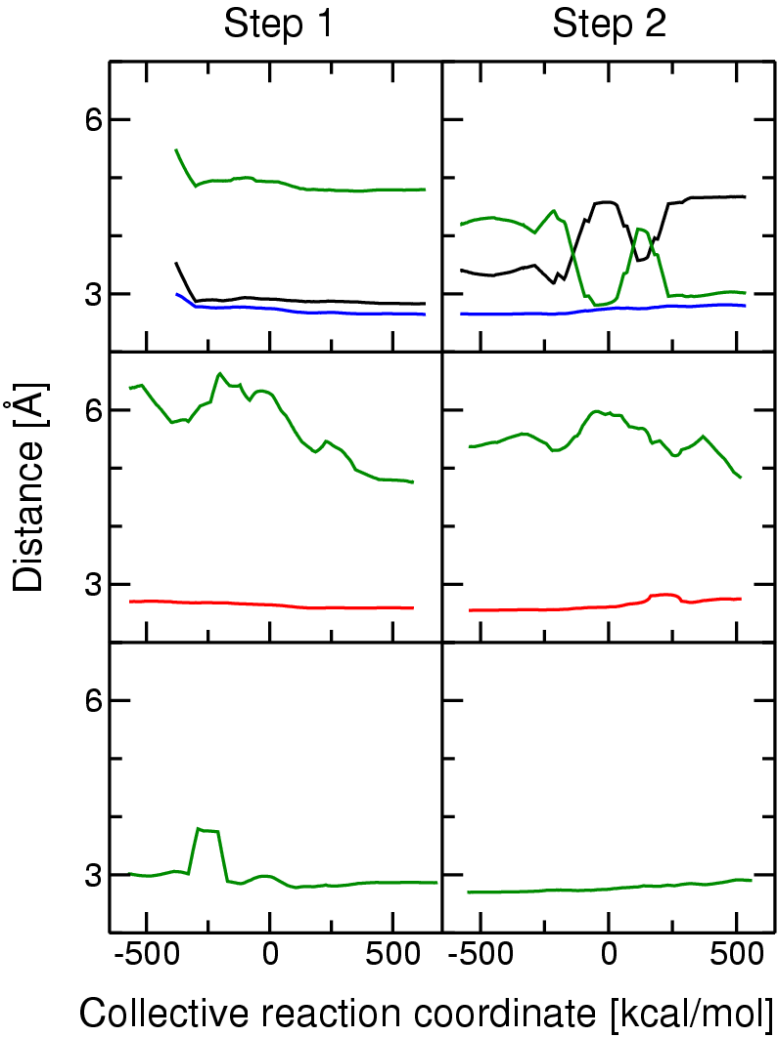

Figure S2: Thermally averaged distances calculated along the collective reaction coordinate for the first (left) and second (right) proton transfer reactions catalyzed by KSI, as obtained from the second independent data set. The results for the D99L, Y14F, and Y14F/D99L mutants are given from top to bottom. The thermally averaged hydrogen bond donor-acceptor distances between the substrate O3 atom and Tyr14 (blue), between the substrate O3 atom and Asp99 (red), between the substrate O3 atom and Tyr55 (green), and between Tyr14 and Tyr55 (black) are shown. The distances are not shown for the mutated residue. The color coding is depicted in Figure 3.