Supporting Information

Dependence of Vibronic Coupling on Molecular Geometry and Environment: Bridging Hydrogen Atom Transfer and Electron-Proton Transfer

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Phenoxyl/Phenol System

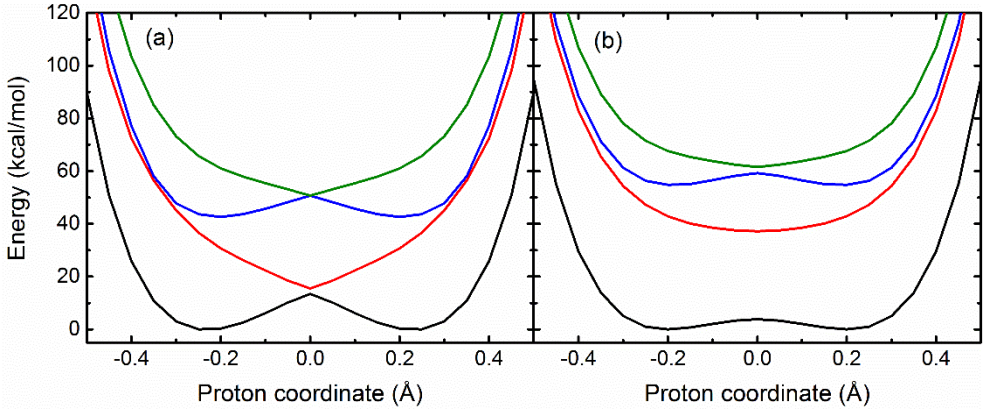

Figure S1. Four-state averaged CASSCF proton potential energy curves for the (a) open and (b) stacked geometries of the phenoxyl-phenol system. The results shown in this figure were generated with the 6-31G basis set using Molpro.

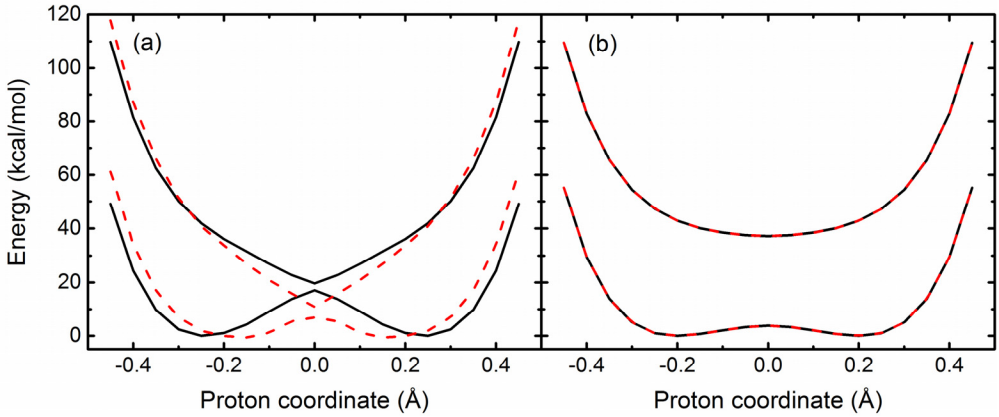

Figure S2. CASSCF (solid black lines) and CASPT2 (dashed red lines) proton potential energy curves for the (a) open and (b) stacked geometries of the phenoxyl-phenol system. The results shown in this figure were generated with the 6-31G basis set using Molcas.

Transition state geometries for phenoxyl-phenol from M06-2X/6311+G calculations**

Coordinates given in Angstroms.

Open TS: E = –614.2129158 Hartrees

C	-0.39280033	-2.06860660	0.00000000
O	-0.82873155	-0.84774822	0.00000000
H	0.00000000	0.00000000	0.00000000
C	0.99420344	-2.37493095	0.00000000
C	1.40978980	-3.68741611	0.00000000
C	0.47933002	-4.72950621	0.00000000
C	-0.88734752	-4.44184144	0.00000000
C	-1.32551216	-3.13697647	0.00000000
H	1.70350816	-1.55865867	0.00000000
H	2.46707498	-3.91338506	0.00000000
H	0.81637527	-5.75608459	0.00000000
H	-1.60578419	-5.24969308	0.00000000
H	-2.37707620	-2.88788567	0.00000000
O	0.82873155	0.84774822	0.00000000
C	0.39280033	2.06860660	0.00000000
C	1.32551216	3.13697647	0.00000000
C	0.88734752	4.44184144	0.00000000
C	-0.47933002	4.72950621	0.00000000
C	-1.40978980	3.68741611	0.00000000
C	-0.99420344	2.37493095	0.00000000
H	2.37707620	2.88788567	0.00000000
H	1.60578419	5.24969308	0.00000000

H	-0.81637527	5.75608459	0.00000000
H	-2.46707498	3.91338506	0.00000000
H	-1.70350816	1.55865867	0.00000000

Stacked TS: E = –614.2194541 Hartrees

C	1.46355300	0.97546600	-0.18858600
O	1.18607200	2.23246600	-0.02615000
H	0.00002600	2.36859100	-0.00009100
C	0.95674400	0.24412100	-1.29826100
C	1.19267900	-1.11073800	-1.40758000
C	1.95332700	-1.77115700	-0.44525500
C	2.49992400	-1.05924800	0.63007700
C	2.25736200	0.28625900	0.76859600
H	0.38076400	0.78189400	-2.03850700
H	0.78294900	-1.66219100	-2.24251300
H	2.13549100	-2.83267000	-0.53621300
H	3.10290200	-1.57721000	1.36309000
H	2.64663100	0.85665100	1.60046500
O	-1.18602200	2.23251500	0.02617000
C	-1.46351500	0.97550800	0.18857400
C	-0.95679400	0.24417400	1.29829100
C	-1.19281400	-1.11066600	1.40765000
C	-1.95343600	-1.77108300	0.44529900
C	-2.49987000	-1.05920100	-0.63013000
C	-2.25723600	0.28629300	-0.76867300
H	-0.38066600	0.78190700	2.03845200

H	-0.78320800	-1.66210300	2.24265400
H	-2.13569000	-2.83257600	0.53630600
H	-3.10277100	-1.57717000	-1.36320100
H	-2.64637900	0.85666700	-1.60061400

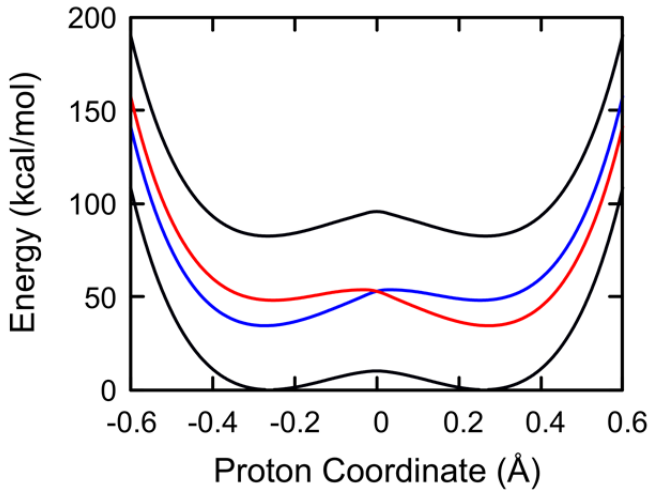

Figure S3. Diabatic (blue and red) and adiabatic (black) proton potential energy curves obtained from two-state averaged CASSCF calculations with the 6-31G** basis set and (3,6) active space for the stacked benzyl-toluene structure given in Ref. 13 of the main paper. The semiclassical parameters for this structure are calculated as: V^{el} = 14,965 cm^{-1}, τ_p = 3.55 fs, τ_e = 0.35 fs, and p = τ_p / τ_e = 10.0. The vibronic couplings are calculated as: $V^{(ad)}$ =50.9 cm^{-1}, $V^{(sc)}$ = 50.5 cm^{-1}, $V^{(na)}$ = 157 cm^{-1}, and $V^{(full)}$ = 50.8 cm^{-1}. These results indicate that the stacked benzyl-toluene system is electronically adiabatic. Note that a four-state averaged CASSCF calculation may provide more quantitatively accurate results for this system.

Soybean lipoxynase system

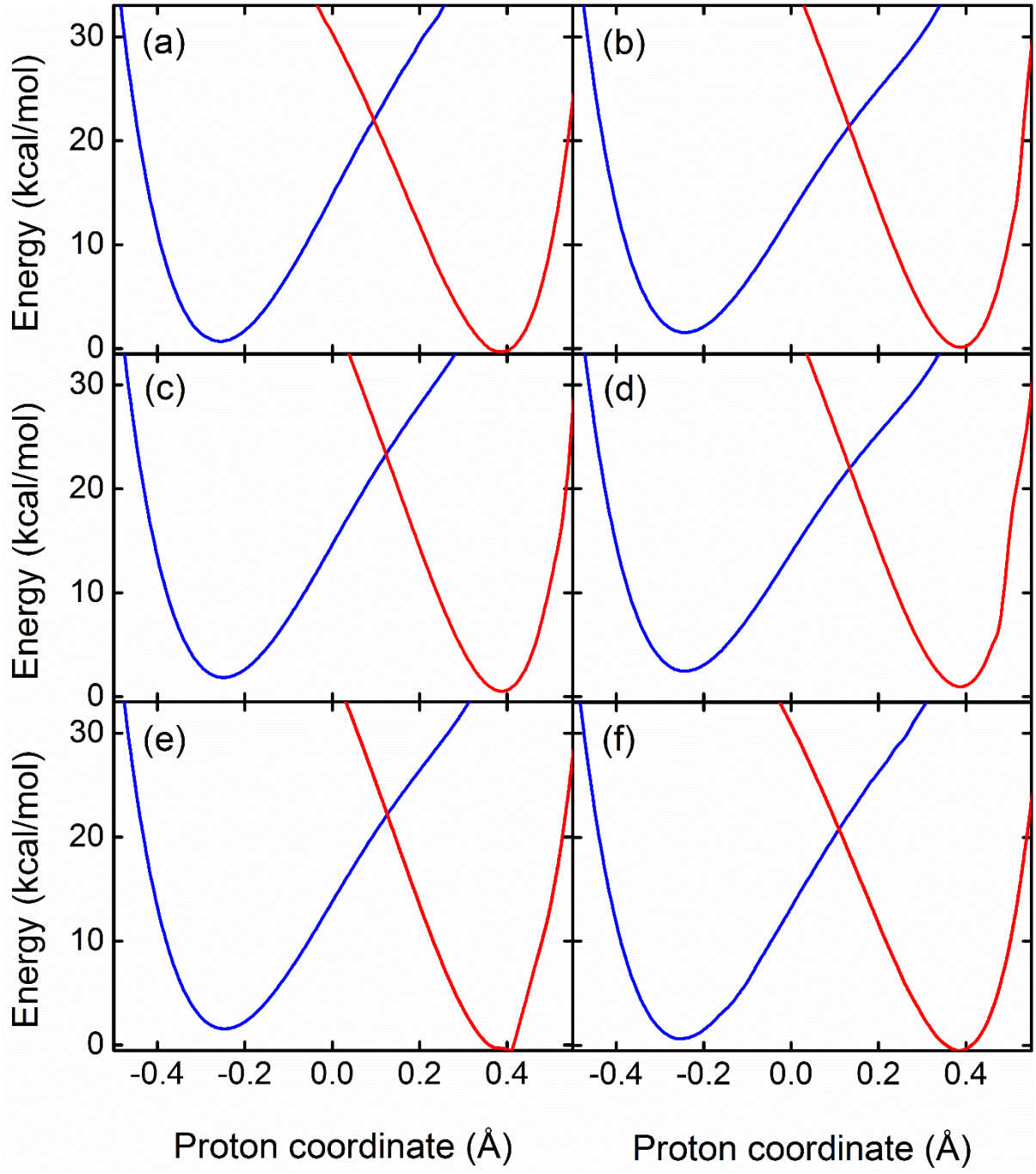

Figure S4. Diabatic proton potential energy curves for the SLO system calculated with QM/MM CDFT-CI/ωB97X/6-31G** for a configuration obtained by QM/MM geometry optimization with the donor-proton and acceptor-proton distances constrained to be 1.32 Å and 1.38 Å, respectively, for (a), (b), and (c) and both constrained to be 1.35 Å for (d), (e), and (f). The diabatic states were shifted to ensure that the ground proton vibrational energy levels are degenerate. Part (f) is also shown in the main paper.

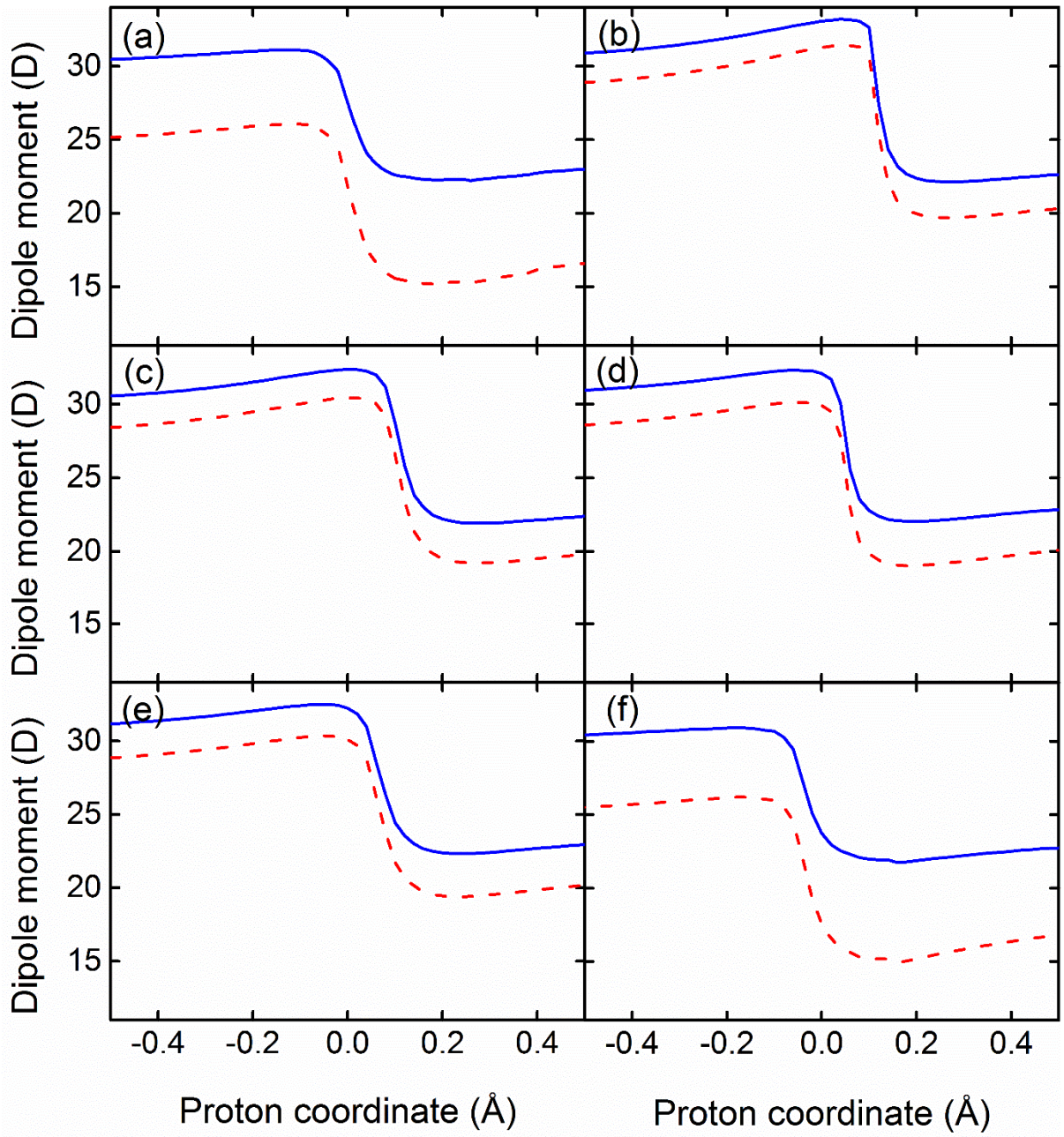

Figure S5. Dipole moment as the proton transfers from the donor to the acceptor for an SLO configuration obtained by QM/MM geometry optimization with the donor-proton and acceptor-proton distances constrained to be 1.32 Å and 1.38 Å, respectively, for (a), (b), and (c) and both distances constrained to be 1.35 Å for (d), (e), and (f). The magnitude of the total dipole moment vector (solid blue line) and the dipole moment vector projected onto the axis connecting the donor carbon and the Fe (dashed red line) were calculated for the QM region in the field of MM point charges for the QM/MM DFT/ωB97X/6-31G** ground adiabatic electronic state as the proton moves along the proton donor-acceptor axis. Part (f) is also shown in the main paper.

Table S2. RESP charges for linoliec acid

atom	charge	atom	charge
C18	-0.2913	C8	0.4234
H181	0.1044	H81	-0.0807
H182	0.1044	H82	-0.0807
H183	0.1044	C7	0.0648
C17	-0.2600	H71	-0.0212
H171	0.1430	H72	-0.0212
H172	0.1430	C6	-0.0710
C16	-0.4012	H61	-0.0094
H161	0.1692	H62	-0.0094
H162	0.1692	C5	0.0586
C15	-0.2933	H51	-0.0127
H151	0.1060	H52	-0.0127
H152	0.1060	C4	0.0702
C14	0.3801	H41	-0.0175
H141	-0.0463	H42	-0.0175
H142	-0.0463	C3	-0.5005
C13	-0.3707	H31	0.1341
H13	0.1287	H32	0.1341
C12	-0.0804	C2	0.0437
H12	0.1442	H21	-0.0101
C11	-0.4285	H22	-0.0101
H111	0.2234	C1	0.8041
H112	0.2234	O	-0.7944
C10	-0.1384	O2	-0.8429
H10	0.1599		
C9	-0.3975		
H9	0.1236		

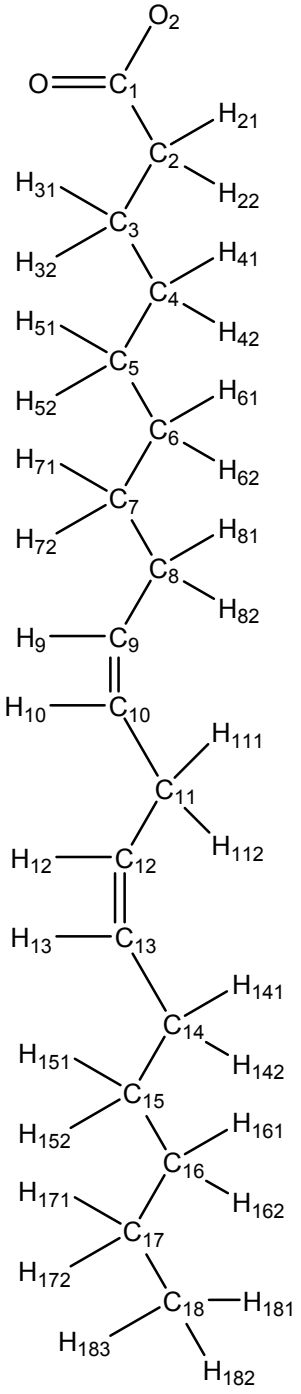

Table S3. Electronic couplings, semiclassical parameters, and nonadiabatic vibronic couplings for the SLO system

Geometry	V^{el} (cm^{-1})	τ_p (fs)	τ_e (fs)	$p = \tau_p / \tau_e$	$V^{(na)}$ (cm^{-1})
QM/MM I[a]	1532	0.22	3.46	0.06	2.0
QM/MM II	1918	0.28	2.77	0.10	3.6
QM/MM III	2358	0.31	2.30	0.13	3.1
gas phase model[b]	1607	0.22	3.30	0.07	1.8

[a] Geometries I, II, and III were obtained from QM/MM geometry optimization of three different snapshots from a classical MD trajectory. The QM/MM optimizations were conducted with the donor-proton and acceptor-proton distances constrained to be 1.32 Å and 1.38 Å, respectively. Results for three other geometries are provided in Table 2 of the main paper.
[b]This result was obtained by previous studies on a gas phase SLO-LA model system.

Computational details of classical MD simulations of soybean lipoxygenase system

To prepare the system, first the missing residues in the 3PZW structure were added using the Prime module in the Schrödinger package,[1] and the protonation states of the protein at pH = 9.0 were determined using the H++ database.[2,3] Then the linoleic acid (LA) was docked to the active site of SLO using the Glide module in the Schrödinger package.[4] The AMBER99 force field[5] was used to describe the protein. The partial charges of the atoms in the LA were determined by the RESP method,[6] where the LA was first optimized at the B3LYP/6-31G** level of theory, followed by the RESP fitting procedure at the MP2/6-31G* level of theory using Gaussian09.[7] These partial charges are provided in Table S1 of the Supporting Information. The parameters describing the Fe-ligand bonds and angles were identical to those used in previous studies[8] except the equilibrium Fe-O-C angle for the Ile839 ligand was chosen to be 132º based on the 3PZW crystal structure used herein.[9]

A careful equilibration procedure on the SLO-LA system was performed prior to data collection. First the positions of only the hydrogen atoms were optimized with the rest of the system fixed. Then the complex was immersed in a 134×90×80 $Å^3$ box of explicit water molecules, and the system was neutralized by adding sodium ions. The water and sodium ions were equilibrated at 303 K in the NVT ensemble for 100 ps. For the subsequent simulation of the full system, a restraining harmonic potential was applied to the proton donor-acceptor distance with an equilibrium distance of 2.7 Å, which was previously found to be the dominant hydrogen tunneling distance,[8] and a large force constant of 2000 kcal/mol $Å^2$. The full system was equilibrated by incrementally raising the temperature from 50 K to 100 K, 200 K, and 303 K, performing 40 ps of MD at each temperature in the NVT ensemble. Then 1 ns of MD was performed in the NPT ensemble at 303 K, followed by 20 ns of MD in the NVT ensemble at 303

K. The production MD trajectory was performed in the NVT ensemble for an additional 20 ns. Three snapshots separated by 50 ps near the end of the production trajectory were chosen for the subsequent QM/MM calculations.

Structures for QM regions of SLO-LA systems

Coordinates given in Angstroms.

First geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.35 Å during QM/MM optimization.

N	0.017000	2.277000	3.310000
C	0.398000	1.412000	4.309000
N	2.208000	2.149000	3.204000
C	1.762000	1.341000	4.225000
C	1.122000	2.687000	2.666000
H	-0.943000	2.489000	3.019000
H	2.445000	0.751000	4.810000
H	1.103000	3.343000	1.812000
H	-0.355000	1.006000	4.962000
N	6.536000	4.028000	5.367000
C	5.552000	3.406000	6.106000
N	5.264000	2.918000	3.949000
C	4.786000	2.710000	5.223000
C	6.318000	3.713000	4.065000
H	7.280000	4.607000	5.751000
H	3.938000	2.077000	5.422000
H	6.923000	4.069000	3.246000
H	5.526000	3.419000	7.175000
N	6.025000	-1.610000	2.034000
C	4.888000	-2.078000	2.660000
N	4.705000	0.140000	2.305000

C	4.085000	-0.981000	2.832000
C	5.870000	-0.282000	1.836000
H	6.840000	-2.160000	1.781000
H	3.109000	-0.931000	3.288000
H	6.593000	0.348000	1.345000
H	4.788000	-3.127000	2.889000
C	2.134000	-0.232000	-0.111000
C	2.899000	1.074000	-0.281000
O	2.797000	1.971000	0.595000
N	3.667000	1.277000	-1.340000
H	2.739000	-1.081000	-0.445000
H	1.963000	-0.351000	0.959000
H	4.238000	2.139000	-1.334000
H	3.852000	0.541000	-2.010000
H	1.134000	-0.273000	-0.591000
C	9.773000	3.305000	-0.043000
O	10.316000	4.405000	-0.108000
N	8.422000	3.110000	0.001000
C	7.371000	4.131000	-0.012000
C	7.515000	5.176000	-1.144000
C	7.554000	4.555000	-2.549000
C	6.439000	6.273000	-0.992000
C	6.671000	7.486000	-1.894000
C	6.036000	3.343000	-0.002000
O	5.193000	3.540000	-0.894000

O	5.928000	2.508000	0.971000
H	8.113000	2.187000	0.277000
H	7.393000	4.669000	0.947000
H	8.485000	5.654000	-0.961000
H	8.328000	3.783000	-2.622000
H	6.593000	4.104000	-2.806000
H	7.781000	5.322000	-3.298000
H	5.455000	5.844000	-1.201000
H	6.417000	6.599000	0.058000
H	6.007000	8.316000	-1.627000
H	7.704000	7.852000	-1.831000
H	6.473000	7.229000	-2.936000
H	10.366000	2.352000	-0.021000
Fe	4.149000	2.401000	2.134000
O	4.003000	4.457000	1.817000
H	3.614000	4.659000	0.950000
H	3.599000	5.431000	2.661000
C	4.063000	9.140000	1.868000
C	5.182000	9.014000	2.915000
C	5.259000	7.872000	3.897000
C	4.506000	6.772000	4.158000
C	3.235000	6.340000	3.590000
C	2.355000	5.483000	4.403000
C	1.059000	5.730000	4.680000
C	0.311000	7.003000	4.366000

C	-0.091000	7.146000	2.884000
H	3.699000	8.158000	1.552000
H	4.475000	9.612000	0.968000
H	6.132000	8.975000	2.367000
H	5.286000	9.943000	3.494000
H	6.156000	7.955000	4.513000
H	4.898000	6.111000	4.931000
H	2.711000	7.098000	3.014000
H	2.798000	4.563000	4.779000
H	0.503000	4.958000	5.209000
H	-0.580000	7.038000	5.004000
H	0.928000	7.864000	4.653000
H	0.778000	7.332000	2.244000
H	-0.569000	6.238000	2.511000
H	3.208000	9.755000	2.160000
H	-0.783000	7.973000	2.746000

Second geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.35 Å during QM/MM optimization.

N	-0.592000	5.023000	2.842000
C	-0.550000	3.661000	3.020000
N	1.318000	4.355000	1.992000
C	0.648000	3.264000	2.492000
C	0.531000	5.398000	2.204000
H	-1.347000	5.662000	3.126000
H	1.065000	2.274000	2.474000

H	0.739000	6.407000	1.894000
H	-1.284000	3.147000	3.620000
N	5.786000	5.556000	3.945000
C	4.820000	4.909000	4.688000
N	4.326000	4.730000	2.518000
C	3.927000	4.394000	3.796000
C	5.447000	5.426000	2.641000
H	6.603000	6.022000	4.328000
H	3.038000	3.815000	3.979000
H	6.026000	5.803000	1.814000
H	4.862000	4.851000	5.758000
N	4.519000	0.772000	-0.880000
C	3.605000	0.213000	-0.011000
N	3.541000	2.464000	0.164000
C	3.009000	1.272000	0.622000
C	4.449000	2.117000	-0.740000
H	5.227000	0.280000	-1.421000
H	2.241000	1.243000	1.374000
H	5.071000	2.809000	-1.283000
H	3.460000	-0.852000	0.089000
C	0.663000	2.831000	-2.011000
C	1.511000	4.074000	-1.807000
O	1.525000	4.631000	-0.685000
N	2.288000	4.520000	-2.789000
H	1.228000	2.080000	-2.566000

H	0.503000	2.432000	-1.009000
H	2.814000	5.381000	-2.620000
H	2.205000	4.155000	-3.731000
H	-0.339000	2.909000	-2.479000
C	8.339000	5.243000	-2.470000
O	9.029000	6.269000	-2.537000
N	6.995000	5.249000	-2.301000
C	6.244000	6.446000	-1.916000
C	6.226000	7.557000	-2.997000
C	5.486000	7.164000	-4.281000
C	5.735000	8.880000	-2.374000
C	6.105000	10.133000	-3.169000
C	4.851000	6.045000	-1.353000
O	3.853000	6.729000	-1.686000
O	4.825000	5.055000	-0.542000
H	6.533000	4.350000	-2.301000
H	6.784000	6.872000	-1.060000
H	7.283000	7.699000	-3.249000
H	4.415000	7.033000	-4.102000
H	5.609000	7.938000	-5.046000
H	5.888000	6.233000	-4.695000
H	4.653000	8.837000	-2.228000
H	6.177000	8.966000	-1.372000
H	5.929000	11.040000	-2.577000
H	7.164000	10.121000	-3.456000

H	5.504000	10.218000	-4.079000
H	8.815000	4.230000	-2.499000
Fe	3.084000	4.690000	0.727000
O	2.909000	6.706000	0.874000
H	2.965000	7.052000	-0.043000
H	2.608000	7.742000	1.685000
C	3.392000	11.130000	0.004000
C	4.582000	10.569000	0.797000
C	4.433000	10.189000	2.254000
C	3.491000	9.434000	2.864000
C	2.252000	8.894000	2.293000
C	1.164000	8.612000	3.236000
C	-0.137000	8.928000	3.057000
C	-0.725000	9.641000	1.864000
C	-2.038000	10.380000	2.174000
H	2.526000	10.466000	0.020000
H	3.697000	11.221000	-1.043000
H	4.921000	9.669000	0.262000
H	5.411000	11.282000	0.720000
H	5.270000	10.501000	2.877000
H	3.657000	9.198000	3.916000
H	1.913000	9.420000	1.403000
H	1.449000	8.134000	4.174000
H	-0.834000	8.673000	3.854000
H	0.016000	10.341000	1.457000

H	-0.911000	8.907000	1.065000
H	-2.835000	9.667000	2.379000
H	-1.946000	11.028000	3.051000
H	3.073000	12.117000	0.333000
H	-2.344000	11.010000	1.340000

Third geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.35 Å during QM/MM optimization.

N	0.130000	4.339000	2.439000
C	0.143000	2.978000	2.625000
N	2.042000	3.624000	1.622000
C	1.337000	2.551000	2.112000
C	1.279000	4.686000	1.824000
H	-0.597000	5.011000	2.711000
H	1.736000	1.551000	2.100000
H	1.508000	5.692000	1.520000
H	-0.626000	2.464000	3.176000
N	6.346000	4.935000	3.568000
C	5.428000	4.188000	4.279000
N	4.989000	4.013000	2.098000
C	4.599000	3.616000	3.361000
C	6.038000	4.805000	2.257000
H	7.121000	5.452000	3.977000
H	3.760000	2.962000	3.516000
H	6.594000	5.247000	1.449000
H	5.459000	4.113000	5.347000

N	5.340000	-0.015000	-1.099000
C	4.307000	-0.565000	-0.369000
N	4.232000	1.684000	-0.216000
C	3.639000	0.498000	0.177000
C	5.253000	1.329000	-0.987000
H	6.098000	-0.509000	-1.566000
H	2.775000	0.480000	0.818000
H	5.931000	2.024000	-1.455000
H	4.164000	-1.631000	-0.283000
C	1.155000	2.028000	-2.176000
C	2.082000	3.231000	-2.123000
O	2.196000	3.842000	-1.032000
N	2.825000	3.568000	-3.169000
H	1.703000	1.177000	-2.580000
H	0.946000	1.805000	-1.129000
H	3.399000	4.414000	-3.083000
H	2.643000	3.162000	-4.080000
H	0.169000	2.056000	-2.685000
C	8.984000	4.622000	-3.105000
O	9.563000	5.709000	-3.196000
N	7.639000	4.491000	-3.000000
C	6.822000	5.632000	-2.560000
C	6.706000	6.766000	-3.607000
C	6.021000	6.346000	-4.911000
C	6.081000	8.021000	-2.959000

C	6.445000	9.321000	-3.672000
C	5.478000	5.140000	-1.966000
O	4.425000	5.722000	-2.329000
O	5.533000	4.206000	-1.096000
H	7.285000	3.555000	-2.855000
H	7.361000	6.071000	-1.710000
H	7.747000	7.015000	-3.840000
H	6.516000	5.469000	-5.343000
H	4.967000	6.109000	-4.746000
H	6.077000	7.149000	-5.655000
H	4.995000	7.909000	-2.911000
H	6.425000	8.088000	-1.917000
H	5.930000	9.409000	-4.634000
H	6.170000	10.196000	-3.072000
H	7.524000	9.370000	-3.862000
H	9.592000	3.690000	-3.041000
Fe	3.800000	3.890000	0.281000
O	3.757000	5.909000	0.292000
H	3.681000	6.152000	-0.657000
H	3.377000	7.013000	0.971000
C	3.432000	11.200000	-0.216000
C	4.649000	10.260000	-0.120000
C	4.953000	9.772000	1.278000
C	4.225000	8.848000	1.942000
C	2.997000	8.227000	1.423000

C	1.904000	8.050000	2.395000
C	0.680000	8.608000	2.302000
C	0.160000	9.518000	1.215000
C	-1.368000	9.622000	1.249000
H	2.542000	10.740000	0.217000
H	3.211000	11.403000	-1.269000
H	4.471000	9.398000	-0.775000
H	5.528000	10.766000	-0.530000
H	5.812000	10.211000	1.785000
H	4.526000	8.565000	2.951000
H	2.660000	8.673000	0.487000
H	2.143000	7.496000	3.303000
H	-0.001000	8.449000	3.137000
H	0.614000	10.512000	1.342000
H	0.493000	9.173000	0.227000
H	-1.798000	8.665000	0.957000
H	-1.716000	9.855000	2.263000
H	3.578000	12.153000	0.286000
H	-1.784000	10.370000	0.576000

First geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.32 and 1.38 Å, respectively, during QM/MM optimization.

N	0.044000	2.258000	3.286000
C	0.411000	1.382000	4.278000
N	2.233000	2.100000	3.178000
C	1.776000	1.294000	4.198000

C	1.155000	2.659000	2.646000
H	-0.912000	2.491000	2.998000
H	2.449000	0.694000	4.782000
H	1.146000	3.327000	1.801000
H	-0.345000	0.978000	4.927000
N	6.512000	4.027000	5.337000
C	5.543000	3.386000	6.081000
N	5.263000	2.887000	3.924000
C	4.788000	2.672000	5.201000
C	6.301000	3.705000	4.038000
H	7.246000	4.621000	5.718000
H	3.954000	2.023000	5.402000
H	6.897000	4.075000	3.218000
H	5.521000	3.405000	7.152000
N	6.059000	-1.641000	2.030000
C	4.918000	-2.098000	2.656000
N	4.758000	0.122000	2.305000
C	4.125000	-0.994000	2.825000
C	5.914000	-0.313000	1.827000
H	6.869000	-2.198000	1.778000
H	3.145000	-0.938000	3.272000
H	6.635000	0.310000	1.327000
H	4.803000	-3.146000	2.884000
C	2.158000	-0.265000	-0.141000
C	2.921000	1.040000	-0.316000

O	2.838000	1.928000	0.571000
N	3.664000	1.255000	-1.388000
H	2.758000	-1.114000	-0.485000
H	1.998000	-0.385000	0.930000
H	4.241000	2.114000	-1.382000
H	3.833000	0.528000	-2.072000
H	1.153000	-0.303000	-0.610000
C	9.790000	3.294000	-0.051000
O	10.327000	4.397000	-0.129000
N	8.440000	3.084000	-0.015000
C	7.378000	4.096000	-0.026000
C	7.528000	5.159000	-1.136000
C	7.589000	4.555000	-2.546000
C	6.446000	6.250000	-0.982000
C	6.642000	7.443000	-1.919000
C	6.052000	3.295000	-0.039000
O	5.217000	3.493000	-0.938000
O	5.943000	2.447000	0.925000
H	8.141000	2.161000	0.271000
H	7.373000	4.623000	0.941000
H	8.494000	5.638000	-0.936000
H	8.359000	3.777000	-2.612000
H	6.630000	4.113000	-2.827000
H	7.837000	5.329000	-3.279000
H	5.461000	5.809000	-1.159000

H	6.448000	6.600000	0.060000
H	5.980000	8.274000	-1.653000
H	7.674000	7.817000	-1.897000
H	6.417000	7.157000	-2.948000
H	10.383000	2.355000	-0.006000
Fe	4.172000	2.362000	2.103000
O	4.045000	4.365000	1.760000
H	3.674000	4.551000	0.880000
H	3.639000	5.399000	2.580000
C	4.015000	9.126000	1.704000
C	5.202000	8.955000	2.664000
C	5.246000	7.902000	3.744000
C	4.493000	6.815000	4.048000
C	3.251000	6.314000	3.449000
C	2.360000	5.494000	4.305000
C	1.099000	5.806000	4.648000
C	0.396000	7.117000	4.385000
C	-0.096000	7.307000	2.935000
H	3.604000	8.158000	1.400000
H	4.383000	9.601000	0.788000
H	6.077000	8.750000	2.030000
H	5.463000	9.914000	3.133000
H	6.124000	8.033000	4.379000
H	4.860000	6.210000	4.878000
H	2.718000	7.046000	2.847000

H	2.770000	4.546000	4.649000
H	0.528000	5.056000	5.194000
H	-0.449000	7.179000	5.081000
H	1.065000	7.945000	4.648000
H	0.692000	7.719000	2.297000
H	-0.404000	6.355000	2.490000
H	3.198000	9.759000	2.056000
H	-0.954000	7.973000	2.886000

Second geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.32 and 1.38 Å, respectively, during QM/MM optimization.

N	-0.548000	5.030000	2.771000
C	-0.507000	3.672000	2.972000
N	1.362000	4.342000	1.929000
C	0.687000	3.260000	2.444000
C	0.578000	5.392000	2.132000
H	-1.296000	5.676000	3.055000
H	1.102000	2.269000	2.440000
H	0.793000	6.398000	1.819000
H	-1.241000	3.171000	3.579000
N	5.797000	5.532000	3.895000
C	4.836000	4.877000	4.636000
N	4.348000	4.690000	2.466000
C	3.948000	4.355000	3.744000
C	5.462000	5.399000	2.591000
H	6.607000	6.011000	4.278000

H	3.062000	3.772000	3.927000
H	6.038000	5.785000	1.767000
H	4.877000	4.824000	5.706000
N	4.583000	0.734000	-0.872000
C	3.602000	0.188000	-0.071000
N	3.550000	2.440000	0.091000
C	2.979000	1.255000	0.519000
C	4.515000	2.080000	-0.748000
H	5.317000	0.235000	-1.372000
H	2.161000	1.240000	1.217000
H	5.177000	2.764000	-1.251000
H	3.451000	-0.878000	0.035000
C	0.658000	2.810000	-2.035000
C	1.526000	4.043000	-1.861000
O	1.574000	4.605000	-0.738000
N	2.287000	4.474000	-2.860000
H	1.206000	2.047000	-2.590000
H	0.517000	2.426000	-1.024000
H	2.840000	5.321000	-2.703000
H	2.178000	4.105000	-3.798000
H	-0.358000	2.882000	-2.481000
C	8.412000	5.219000	-2.461000
O	9.095000	6.250000	-2.511000
N	7.064000	5.217000	-2.317000
C	6.290000	6.402000	-1.941000

C	6.292000	7.525000	-3.009000
C	5.603000	7.134000	-4.322000
C	5.762000	8.833000	-2.387000
C	6.137000	10.099000	-3.158000
C	4.887000	5.977000	-1.427000
O	3.885000	6.630000	-1.802000
O	4.854000	4.996000	-0.602000
H	6.611000	4.315000	-2.352000
H	6.795000	6.821000	-1.061000
H	7.355000	7.684000	-3.223000
H	4.529000	6.982000	-4.182000
H	5.739000	7.920000	-5.072000
H	6.037000	6.216000	-4.733000
H	4.677000	8.772000	-2.273000
H	6.173000	8.914000	-1.371000
H	5.932000	10.997000	-2.562000
H	7.203000	10.105000	-3.418000
H	5.559000	10.185000	-4.084000
H	8.886000	4.204000	-2.475000
Fe	3.125000	4.664000	0.662000
O	3.005000	6.638000	0.800000
H	3.001000	6.982000	-0.119000
H	2.699000	7.700000	1.627000
C	3.383000	11.235000	0.004000
C	4.581000	10.642000	0.761000

C	4.439000	10.258000	2.219000
C	3.533000	9.446000	2.803000
C	2.332000	8.831000	2.200000
C	1.228000	8.567000	3.149000
C	-0.057000	8.940000	2.986000
C	-0.613000	9.717000	1.813000
C	-1.975000	10.367000	2.102000
H	2.504000	10.589000	0.045000
H	3.659000	11.326000	-1.051000
H	4.889000	9.742000	0.210000
H	5.422000	11.339000	0.675000
H	5.242000	10.624000	2.858000
H	3.683000	9.223000	3.861000
H	1.984000	9.362000	1.316000
H	1.499000	8.052000	4.072000
H	-0.764000	8.693000	3.776000
H	0.116000	10.482000	1.511000
H	-0.711000	9.047000	0.946000
H	-2.741000	9.605000	2.239000
H	-1.953000	10.976000	3.012000
H	3.087000	12.224000	0.347000
H	-2.289000	11.015000	1.285000

Third geometry obtained with the donor-proton and acceptor-proton distances constrained to be 1.32 and 1.38 Å, respectively, during QM/MM optimization.

N	0.159000	4.319000	2.445000

C	0.161000	2.957000	2.626000
N	2.061000	3.594000	1.617000
C	1.351000	2.523000	2.106000
C	1.306000	4.661000	1.827000
H	-0.564000	4.996000	2.719000
H	1.743000	1.521000	2.091000
H	1.543000	5.668000	1.528000
H	-0.610000	2.449000	3.180000
N	6.355000	4.915000	3.552000
C	5.440000	4.170000	4.267000
N	4.998000	3.984000	2.089000
C	4.609000	3.594000	3.354000
C	6.047000	4.779000	2.242000
H	7.129000	5.437000	3.957000
H	3.769000	2.942000	3.514000
H	6.601000	5.219000	1.432000
H	5.471000	4.102000	5.336000
N	5.347000	-0.035000	-1.096000
C	4.308000	-0.580000	-0.375000
N	4.235000	1.669000	-0.229000
C	3.635000	0.486000	0.160000
C	5.261000	1.310000	-0.990000
H	6.108000	-0.532000	-1.556000
H	2.762000	0.470000	0.789000
H	5.945000	2.000000	-1.454000

H	4.167000	-1.645000	-0.283000
C	1.159000	2.016000	-2.197000
C	2.096000	3.210000	-2.131000
O	2.213000	3.813000	-1.034000
N	2.844000	3.552000	-3.170000
H	1.701000	1.163000	-2.606000
H	0.945000	1.787000	-1.152000
H	3.425000	4.392000	-3.076000
H	2.658000	3.161000	-4.088000
H	0.174000	2.057000	-2.705000
C	8.996000	4.590000	-3.072000
O	9.565000	5.683000	-3.146000
N	7.650000	4.446000	-2.974000
C	6.833000	5.590000	-2.538000
C	6.741000	6.735000	-3.578000
C	6.065000	6.335000	-4.891000
C	6.130000	7.998000	-2.927000
C	6.533000	9.298000	-3.623000
C	5.480000	5.114000	-1.960000
O	4.438000	5.713000	-2.322000
O	5.518000	4.170000	-1.095000
H	7.296000	3.508000	-2.849000
H	7.362000	6.021000	-1.678000
H	7.788000	6.969000	-3.798000
H	6.553000	5.456000	-5.326000

H	5.006000	6.110000	-4.741000
H	6.141000	7.144000	-5.626000
H	5.041000	7.909000	-2.897000
H	6.458000	8.049000	-1.880000
H	6.024000	9.414000	-4.585000
H	6.282000	10.172000	-3.011000
H	7.614000	9.320000	-3.809000
H	9.609000	3.668000	-3.017000
Fe	3.807000	3.872000	0.277000
O	3.759000	5.849000	0.296000
H	3.679000	6.110000	-0.649000
H	3.415000	6.984000	1.001000
C	3.413000	11.194000	-0.168000
C	4.646000	10.275000	-0.076000
C	4.958000	9.784000	1.320000
C	4.254000	8.835000	1.970000
C	3.043000	8.172000	1.440000
C	1.947000	8.006000	2.423000
C	0.729000	8.570000	2.348000
C	0.203000	9.494000	1.272000
C	-1.325000	9.596000	1.316000
H	2.532000	10.717000	0.266000
H	3.183000	11.395000	-1.219000
H	4.485000	9.415000	-0.737000
H	5.518000	10.800000	-0.481000

H	5.807000	10.238000	1.830000
H	4.561000	8.550000	2.977000
H	2.694000	8.632000	0.515000
H	2.186000	7.434000	3.321000
H	0.050000	8.402000	3.182000
H	0.657000	10.486000	1.405000
H	0.528000	9.157000	0.279000
H	-1.751000	8.635000	1.034000
H	-1.669000	9.836000	2.329000
H	3.545000	12.148000	0.337000
H	-1.747000	10.334000	0.636000

References

(1) *Prime;* version 3.9; Schrödinger, LLC, New York, NY,, 2015.

(2) Bashford, D.; Karplus, M. *Biochemistry* **1990**, *29*, 10219.

(3) Gordon, J. C.; Myers, J. B.; Folta, T.; Shoja, V.; Heath, L. S.; Onufriev, A. *Nucleic Acids Res* **2005**, *33*, W368.

(4) *Glide;* version 6.2; Schrödinger, LLC, New York, NY, 2014.

(5) Cornell, W. D.; Cieplak, P.; Bayly, C. I.; Gould, I. R.; Merz, K. M.; Ferguson, D. M.; Spellmeyer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 5179.

(6) Bayly, C. I.; Cieplak, P.; Cornell, W. D.; Kollman, P. A. *J. Phys. Chem.* **1993**, *97*, 10269.

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

(8) Hatcher, E.; Soudackov, A. V.; Hammes-Schiffer, S. *J. Am. Chem. Soc.* **2007**, *129*, 187.

(9) Chruszcz, M.; Wlodawer, A.; Minor, W. *Biophys. J.* **2008**, *95*, 1.