Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supplementary Information

DFT study on the effect of proximal residues on the *Mycobacterium tuberculosis* catalase-peroxidase (katG) heme Compound I intermediate and its bonding interaction with Isoniazid.

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Table S1. Energy of the CpdI models calculated using different functionals and basis sets and the difference between their quartet and doublet spin states.

Functional/Basis	Model	$E_{Quartet}$ (kcal/mol)	$E_{Doublet}$ (kcal/mol)	$E_{Quart-Doub}$ (kcal/mol)
UB3LYP/BS2	HemeA	-780090.52648	-780080.73950	-9.78698
	HemeH	-911194.71115	-911185.16175	-9.54941
	HemeHD	-1054929.16641	-1054929.15865	-0.00776
	HemeHW	-1163813.60226	-1163813.60994	0.00768
	HemeHDW	-1307560.13253	-1307560.13896	0.00642
UM06-L/BS1	HemeA	-780306.33838	-780306.25301	-0.08537
	HemeH	-911444.03252	-911443.91394	-0.11858
	HemeHD	-1055192.61859	-1055192.59960	-0.01899
	HemeHW	-1164132.58579	-1164132.59071	0.00492
	HemeHDW	-1307893.19202	-1307893.21207	0.02005
UM06-L/BS2	HemeA	-780463.83451	-780463.78726	-0.04725
	HemeH	-911627.62135	-911627.54592	-0.07544
	HemeHD	-1055412.27155	-1055412.16096	-0.11060
	HemeHW	-1164371.22932	-1164371.24079	0.01148
	HemeHDW	-1308168.01559	-1308168.03624	0.02065

Table S2. NBO population analysis of the isolated CpdI models at the UB3LYP/BS2 level of theory.

Model		Fe^{4+}	O^{2-}	Por^{1-}	$*His/NH_3^0$	Asp^0	Trp^{1-}
^{2}HemeA	Partial Charge	0.994	-0.401	0.224	0.183	-	-
	Spin Density	1.122	0.938	-1.019	-0.041	-	-
^{4}HemeA	Partial Charge	0.993	-0.399	0.224	0.182	-	-
	Spin Density	1.092	0.935	0.954	0.019	-	-
^{2}HemeH	Partial Charge	1.005	-0.398	0.230	0.163	-	-
	Spin Density	1.125	0.931	-1.023	-0.033	-	-
^{4}HemeH	Partial Charge	1.004	-0.396	0.229	0.163	-	-
	Spin Density	1.097	0.929	0.956	0.018	-	-
^{2}HemeHD	Partial Charge	1.005	-0.402	0.222	0.141	0.033	-
	Spin Density	1.129	0.931	-1.021	-0.038	0.000	-
^{4}HemeHD	Partial Charge	1.004	-0.400	0.224	0.138	0.033	-
	Spin Density	1.099	0.928	0.953	0.020	0.000	-
^{2}HemeHW	Partial Charge	1.024	-0.456	-0.690	0.136	-	-0.014
	Spin Density	1.189	0.857	-0.041	-0.018	-	-0.987
^{4}HemeHW	Partial Charge	1.024	-0.456	-0.690	0.136	-	-0.014
	Spin Density	1.189	0.857	-0.040	0.007	-	0.987
^{2}HemeHDW	Partial Charge	1.024	-0.458	-0.691	0.122	-0.059	0.062
	Spin Density	1.190	0.857	-0.041	-0.034	0.002	-0.974
^{4}HemeHDW	Partial Charge	1.024	-0.458	-0.691	0.122	-0.059	0.062
	Spin Density	1.189	0.857	-0.040	0.022	-0.002	0.974

*Classical total formal charges are written as superscript to the column headers

Table S3. NBO population analysis of the isolated CpdI models at the UM06-L/BS1 level of theory.

Model		Fe^{4+}	O^{2-}	Por^{1-}	$*His^0$	Asp^0	Trp^{1-}
^{2}HemeA	Partial Charge	0.974	-0.403	0.243	0.186	-	-
	Spin Density	1.132	0.929	-1.014	-0.047	-	-
^{4}HemeA	Partial Charge	0.973	-0.402	0.244	0.185	-	-
	Spin Density	1.102	0.927	0.953	0.018	-	-
^{2}HemeH	Partial Charge	0.984	-0.400	0.250	0.166	-	-
	Spin Density	1.133	0.923	-1.017	-0.039	-	-
^{4}HemeH	Partial Charge	0.983	-0.399	0.251	0.165	-	-
	Spin Density	1.105	0.922	0.956	0.018	-	-
^{2}HemeHD	Partial Charge	0.984	-0.403	0.240	0.140	0.039	-
	Spin Density	1.136	0.923	-1.013	-0.046	0.000	-
^{4}HemeHD	Partial Charge	0.984	-0.401	0.242	0.137	0.039	-
	Spin Density	1.111	0.922	0.946	0.021	0.000	-
^{2}HemeHW	Partial Charge	0.999	-0.450	-0.668	0.137	-	-0.017
	Spin Density	1.177	0.865	-0.035	-0.023	-	-0.985
^{4}HemeHW	Partial Charge	0.999	-0.450	-0.668	0.136	-	-0.017
	Spin Density	1.177	0.865	-0.034	0.007	-	0.985
^{2}HemeHDW	Partial Charge	0.999	-0.452	-0.669	0.122	-0.055	0.055
	Spin Density	1.178	0.866	-0.036	-0.046	0.003	-0.964
^{4}HemeHDW	Partial Charge	0.999	-0.452	-0.669	0.121	-0.054	0.055
	Spin Density	1.178	0.866	-0.035	0.029	-0.003	0.964

*Classical total formal charges are written as superscript to the column headers

Table S4. NBO population analysis of the isolated CpdI models at the UM06-L/BS2 level of theory.

Model		Fe^{4+}	O^{2-}	Por^{1-}	$*His/NH_3^0$	Asp^0	Trp^{1-}
^{2}HemeA	Partial Charge	0.983	-0.405	0.238	0.183	-	-
	Spin Density	1.129	0.930	-1.013	-0.046	-	-
^{4}HemeA	Partial Charge	0.982	-0.403	0.239	0.182	-	-
	Spin Density	1.099	0.929	0.955	0.018	-	-
^{2}HemeH	Partial Charge	0.992	-0.401	0.244	0.165	-	-
	Spin Density	1.130	0.925	-1.016	-0.039	-	-
^{4}HemeH	Partial Charge	0.991	-0.400	0.245	0.164	-	-
	Spin Density	1.102	0.923	0.957	0.018	-	-
^{2}HemeHD	Partial Charge	0.992	-0.404	0.234	0.147	0.032	-
	Spin Density	1.133	0.924	-1.011	-0.047	0.000	-
^{4}HemeHD	Partial Charge	0.992	-0.402	0.235	0.143	0.032	-
	Spin Density	1.108	0.924	0.947	0.022	0.000	-
^{2}HemeHW	Partial Charge	1.008	-0.452	-0.676	0.138	-	-0.018
	Spin Density	1.174	0.867	-0.033	-0.025	-	-0.983
^{4}HemeHW	Partial Charge	1.008	-0.452	-0.676	0.138	-	-0.018
	Spin Density	1.174	0.867	-0.033	0.008	-	0.984
^{2}HemeHDW	Partial Charge	1.008	-0.453	-0.677	0.131	-0.056	0.047
	Spin Density	1.175	0.868	-0.035	-0.048	0.003	-0.962
^{4}HemeHDW	Partial Charge	1.008	-0.453	-0.677	0.130	-0.056	0.047
	Spin Density	1.175	0.867	-0.033	0.030	-0.003	0.963

*Classical total formal charges are written as superscript to the column headers

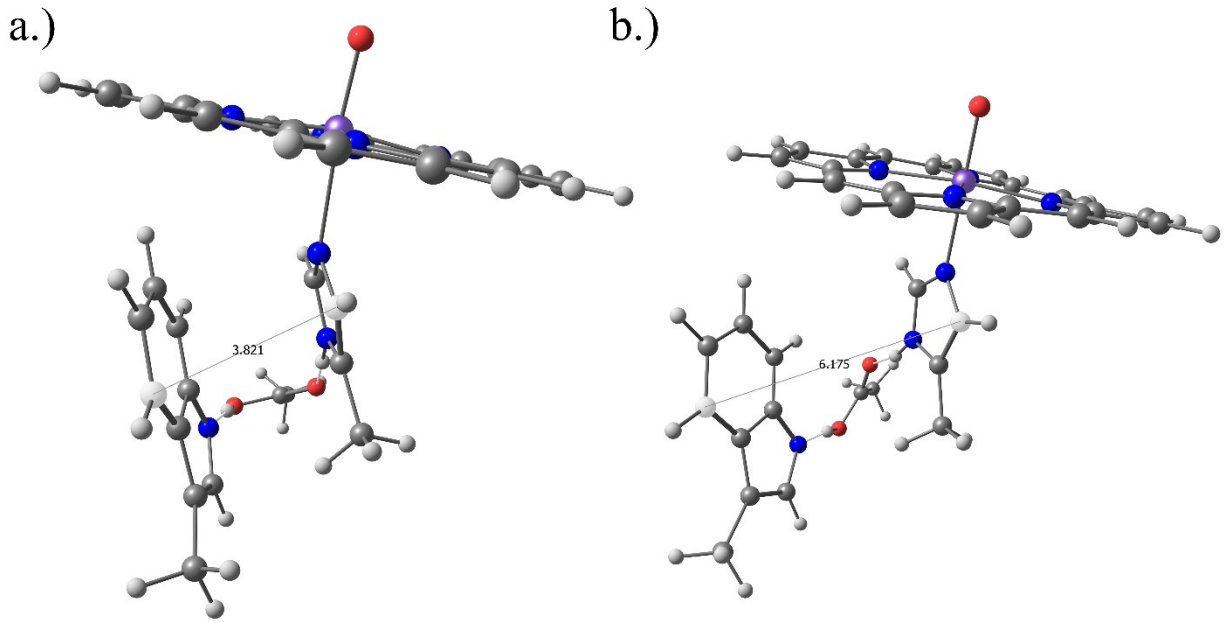

Fig. S1. Optimized geometry of the HemeHDW complex a) with and b) without dispersion correction.

Table S5. Binding energy of INH with M. tb. katG CpdI models using BS2.

CpdI Model	UB3LYP/BS2 (kcal/mol)	M06-L/BS2 (kcal/mol)
^{2}HemeH	-16.07068	-24.45192
^{4}HemeH	-16.15906	-24.44086
^{2}HemeHDW	-18.20999	-27.09545
^{4}HemeHDW	-18.21152	-27.09860

Table S6. NBO population analysis of the optimized complex of INH with HemeHDW and HemeH models at the UB3LYP/BS2 level of theory.

INH complex		INH^{0}	Fe^{4+}	O^{2-}	Por^{1-}	$His/NH_3{}^{0}$	Asp^{0}	Trp^{1-}
^{2}HemeH	Partial Charge	-0.018	1.033	-0.455	0.269	0.170	-	-
	Spin Density	0.004	1.212	0.843	-1.027	-0.031	-	-
^{4}HemeH	Partial Charge	-0.018	1.033	-0.454	0.270	0.169	-	-
	Spin Density	0.011	1.190	0.839	0.945	0.015	-	-
^{2}HemeHDW	Partial Charge	-0.043	1.060	-0.522	-0.632	0.124	-0.060	0.073
	Spin Density	0.008	1.291	0.753	-0.046	-0.023	0.002	-0.986
^{4}HemeHDW	Partial Charge	-0.043	1.061	-0.523	-0.633	0.124	-0.060	0.073
	Spin Density	0.008	1.291	0.753	-0.045	0.009	-0.002	0.986

Classical total formal charges are written as superscripts to the column header

Table S7. NBO population analysis of the optimized complex of INH with HemeHDW and HemeH models at the M06-L/BS1 level of theory.

INH complex		INH^{0}	Fe^{4+}	O^{2-}	Por^{1-}	$His/NH_3{}^{0}$	Asp^{0}	Trp^{1-}
^{2}HemeH	Partial Charge	-0.025	1.006	-0.438	0.284	0.174	-	-
	Spin Density	0.006	1.198	0.848	-1.016	-0.037	-	-
^{4}HemeH	Partial Charge	-0.032	1.005	-0.437	0.285	0.172	-	-
	Spin Density	0.012	1.178	0.846	0.943	0.015	-	-
^{2}HemeHDW	Partial Charge	-0.057	1.027	-0.494	-0.611	0.122	-0.055	0.068
	Spin Density	0.013	1.255	0.776	-0.036	-0.032	0.003	-0.979
^{4}HemeHDW	Partial Charge	-0.057	1.027	-0.494	-0.611	0.122	-0.055	0.068
	Spin Density	0.013	1.255	0.776	-0.036	-0.032	0.003	-0.979

Classical total formal charges are written as superscripts to the column header

Table S8. NBO population analysis of the optimized complex of INH with HemeHDW and HemeH models at the M06-L/BS2 level of theory.

INH complex		INH^{0}	Fe^{4+}	O^{2-}	Por^{1-}	$His/NH_3{}^{0}$	Asp^{0}	Trp^{1-}
^{2}HemeH	Partial Charge	-0.013	1.016	-0.451	0.276	0.173	-	-
	Spin Density	0.006	1.198	0.849	-1.014	-0.038	-	-
^{4}HemeH	Partial Charge	-0.013	1.015	-0.451	0.277	0.172	-	-
	Spin Density	0.017	1.177	0.846	0.944	0.015	-	-
^{2}HemeHDW	Partial Charge	-0.041	1.038	-0.509	-0.623	0.131	-0.057	0.061
	Spin Density	0.012	1.254	0.777	-0.034	-0.034	0.003	-0.978
^{4}HemeHDW	Partial Charge	-0.041	1.038	-0.510	-0.623	0.131	-0.057	0.061
	Spin Density	0.012	1.254	0.777	-0.033	0.014	-0.003	0.978

Classical total formal charges are written as superscripts to the column header