Water as biocatalyst in cytochrome P450

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Supporting Information

Survey of tables and figures provided:

1. Substrates and procedures

The following *substrates* were studied:

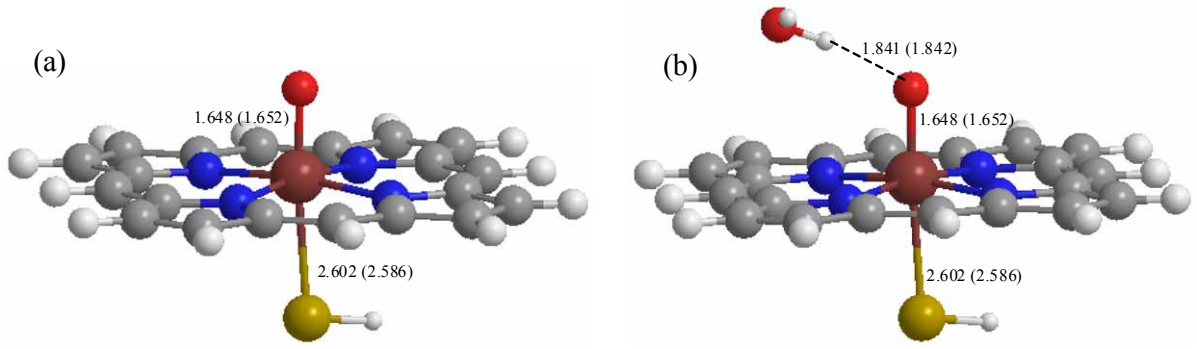
(**1**) ethane
(**2**) propane: **2n** (**2i**) denotes hydrogen abstraction from the primary (secondary) carbon atom in propane
(**3**) phenylethane: **3n** (**3b**) denotes hydrogen abstraction from the primary (benzylic) carbon atom in phenylethane
(**4**) Me-probe (*trans*-methyl-phenyl-cyclopropane)
(**5**) camphor
(**6**) propene
(**7**) toluene
(**8**) iPr-probe (*trans*-isopropyl-phenyl-cyclopropane)
(**9**) N,N-dimethylaniline

The computational *procedures* are described in the manuscript which also contains the pertinent references. For convenience, we repeat some specifications in the following.

QM method: unrestricted density functional theory using the hybrid density functional B3LYP with VWN5-LDA correlation as implemented in the Turbomole code.

Basis sets:
B1 = standard basis, LACVP on iron and 6-31G basis set on the remaining atoms.
B2W = Wachters' all-electron basis on iron, 6-31+G* on the six atoms coordinated to iron and the O atom of W_{903}, 6-31++G** on the migrating H atom and the H atoms of W_{903}, and 6-31G on the remaining atoms.
B3 = TZVP all-electron basis set on all atoms.
B4 = dzpdf polarized double-ξ quality all-electron basis set on iron, 6-31G* on first-row atoms, and 6-31G on all H atoms.

Geometry optimizations: performed at the B3LYP/B1 level for **1**-**9** and at the B3LYP/B4 level for **1**, **4**, **5**, and **9.**



^{2}CpdI (^{4}CpdI) ^{2}CpdI' (^{4}CpdI')

Figure S1: B3LYP/B1 optimised geometries for (a) ^{2,4}Cpd I without and (b) ^{2,4}Cpd I' of P450 with water W_{903}.

Table S1a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 without water W_{903}.

	Energy	ΔE
^{2}CpdI	-1584.772350	0.08
^{4}CpdI	-1584.772486	0.00

Table S1b: Group spin densities and group charges for ^{2,4}Cpd I of P450 without water W_{903}.

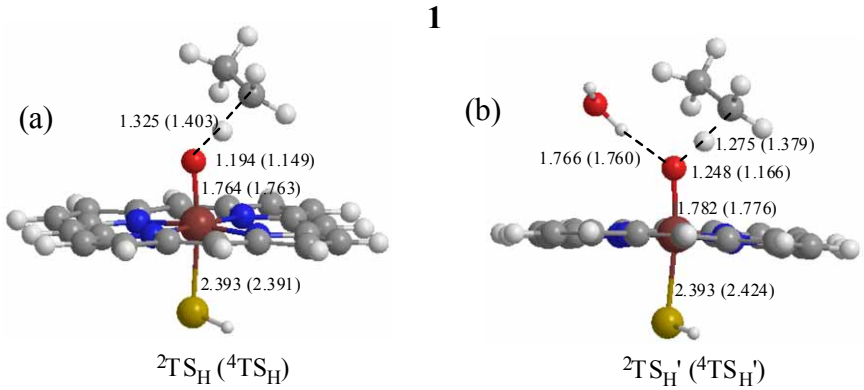
	Spin Density (ρ)				Charge (Q)			
	Fe	O	Por	SH	Fe	O	Por	SH
^{2}CpdI	1.17	0.92	-0.50	-0.60	0.51	-0.31	-0.13	-0.06
^{4}CpdI	1.05	0.98	0.43	0.55	0.50	-0.32	-0.12	-0.06

Table S1c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I' of P450 with water W_{903}.

	Energy	ΔE
^{2}CpdI'	-1661.137152	-0.02
^{4}CpdI'	-1661.137116	0.00

Table S1d: Group spin densities and group charges for ^{2,4}Cpd I of P450 with water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	W_{903}	Fe	O	Por	SH	W_{903}
^{2}CpdI'	1.29	0.82	-0.56	-0.56	0.01	0.50	-0.40	-0.05	-0.05	0.00
^{4}CpdI'	1.14	0.88	0.47	0.50	0.01	0.49	-0.40	-0.04	-0.05	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S2: B3LYP/B1 optimised TS geometries for ethane hydroxylation (a) without and (b) with water W_{903}.

Table S2a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation without water W_{903}.

	Energy	ΔE
ethane	-79.747541	-
^{2}CpdI+ ethane	-1664.519891	0.08
^{4}CpdI+ ethane	-1664.520027	0.00
^2TS_H	-1664.487513	20.32
^4TS_H	-1664.486112	21.28

Table S2b: Group spin densities and group charges for ethane hydroxylation without water W_{903}.

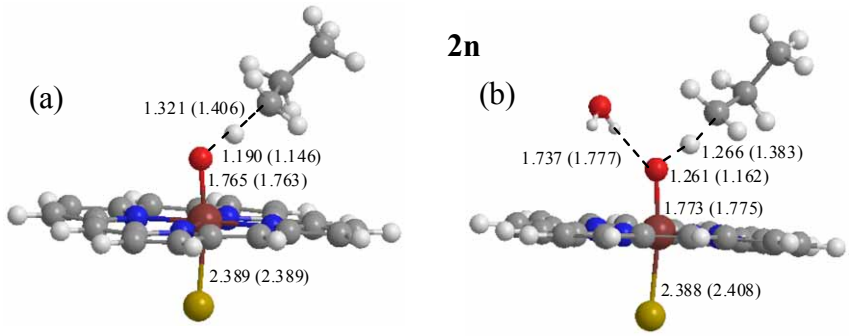
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.83	-0.05	-0.18	-0.11	0.03	-0.52	0.45	-0.51	-0.28	0.00	0.34	0.01
^4TS_H	1.26	0.65	0.13	0.39	-0.04	0.61	0.44	-0.52	-0.29	0.03	0.36	-0.03

Table S2c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation with water W_{903}.

	Energy	ΔE
ethane	-79.747541	-
^{2}CpdI'+ ethane	-1740.884693	-0.02
^{4}CpdI'+ ethane	-1740.884657	0.00
^2TS_H'	-1740.855762	18.13
^4TS_H'	-1740.854844	18.71

Table S2d: Group spin densities and group charges for ethane hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.92	-0.14	-0.20	-0.15	0.03	-0.46	0.00	0.46	-0.56	-0.23	0.03	0.31	-0.01	0.00
^4TS_H'	1.11	0.58	0.30	0.44	-0.04	0.60	0.01	0.45	-0.59	-0.21	0.03	0.35	-0.05	0.01



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S3: B3LYP/B1 optimised TS geometries for propane (2n) hydroxylation (a) without and (b) with water W_{903}.

Table S3a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propane (2n) hydroxylation without water W_{903}.

	Energy	ΔE
propane	-119.022435	-
^{2}CpdI+ propane	-1703.794785	0.08
^{4}CpdI+ propane	-1703.794921	0.00
^2TS_H	-1703.762308	20.47
^4TS_H	-1703.760462	21.62

Table S3b: Group spin densities and group charges for propane (2n) hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.82	-0.06	-0.18	-0.10	0.03	-0.51	0.45	-0.51	-0.28	0.01	0.33	0.01
^4TS_H	1.28	0.65	0.12	0.38	-0.04	0.61	0.44	-0.52	-0.29	0.03	0.36	-0.03

Table S3c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propane (2n) hydroxylation with water W_{903}.

	Energy	ΔE
propane	-119.022435	-
^{2}CpdI'+propane	-1780.159587	-0.02
^{4}CpdI'+ propane	-1780.159551	0.00
^2TS_H'	-1780.129174	19.06
^4TS_H'	-1780.127155	20.33

Table S3d: Group spin densities and group charges for propane (2n) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.87	-0.14	-0.19	-0.13	0.02	-0.44	0.01	0.45	-0.54	-0.25	0.03	0.30	0.01	-0.01
^4TS_H'	1.18	0.58	0.24	0.43	-0.04	0.60	0.01	0.44	-0.58	-0.22	0.04	0.35	-0.02	-0.01

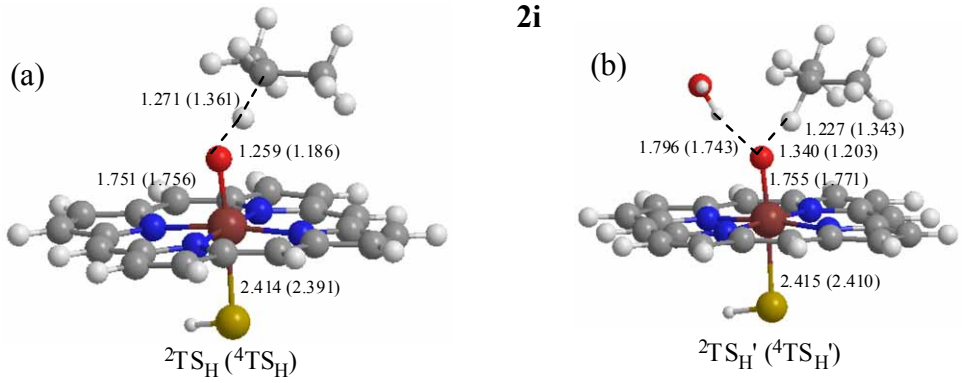


Figure S4: B3LYP/B1 optimised TS geometries for propane (2i) hydroxylation (a) without and (b) with water W_{903}.

Table S4a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propane (2i) hydroxylation without water W_{903}.

	Energy	ΔE
propane	-119.022435	-
^{2}CpdI+ propane	-1703.794785	0.08
^{4}CpdI+ propane	-1703.794921	0.00
^2TS_H	-1703.766210	18.02
^4TS_H	-1703.764222	19.26

Table S4b: Group spin densities and group charges for propane (2i) hydroxylation without water W_{903}.

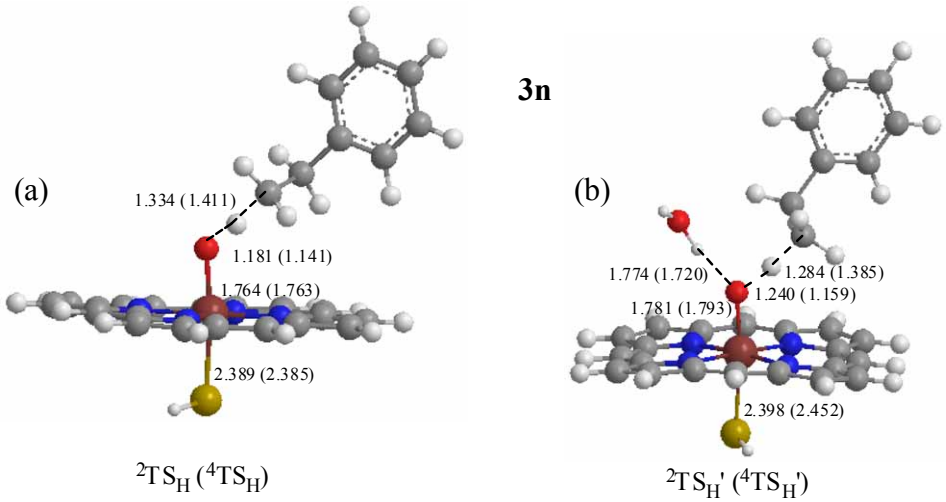
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.84	-0.03	-0.21	-0.20	0.02	-0.44	0.46	-0.50	-0.28	0.40	0.31	0.00
^4TS_H	1.34	0.68	0.09	0.36	-0.03	0.56	0.45	-0.51	-0.30	0.03	0.34	-0.01

Table S4c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propane (2i) hydroxylation with water W_{903}.

	Energy	ΔE
propane	-119.022435	-
^{2}CpdI'+ propane	-1780.159587	-0.02
^{4}CpdI'+ propane	-1780.159551	0.00
^2TS_H'	-1780.133086	16.61
^4TS_H'	-1780.133047	16.63

Table S4d: Group spin densities and group charges for propane (2i) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.90	-0.08	-0.25	-0.23	0.01	-0.36	0.00	0.49	-0.54	-0.23	0.01	0.28	-0.01	-0.01
^4TS_H'	1.26	0.59	0.21	0.42	-0.03	0.55	0.01	0.46	-0.59	-0.23	0.05	0.34	-0.03	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S5: B3LYP/B1 optimised TS geometries for phenylethane (3n) hydroxylation (a) without and (b) with water W_{903}.

Table S5a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for phenylethane (3n) hydroxylation without water W_{903}.

	Energy	ΔE
phenylethane (PhEth)	-310.597944	-
^{2}CpdI+ PhEth.	-1895.370294	0.08
^{4}CpdI+ PhEth.	-1895.370423	0.00
^2TS_H	-1895.338924	19.96
^4TS_H	-1895.336709	21.16

Table S5b: Group spin densities and group charges for phenylethane (3n) hydroxylation without water W_{903}.

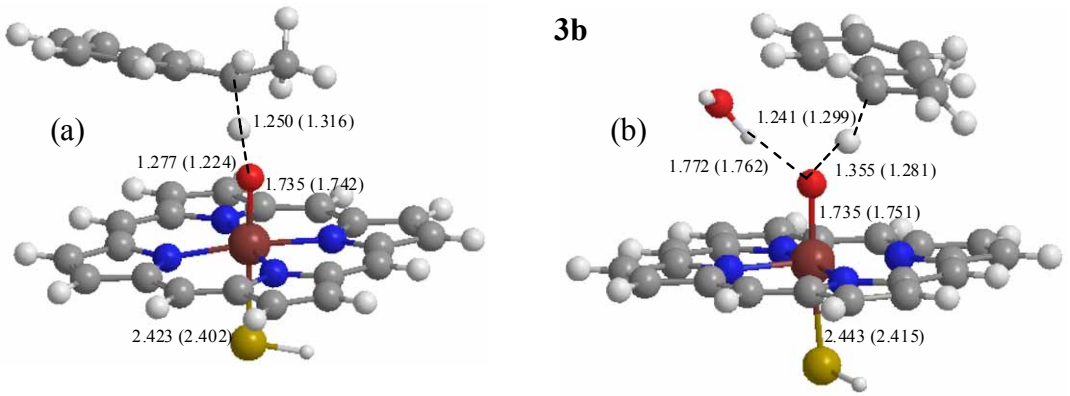
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.81	-0.04	-0.17	-0.09	0.03	-0.53	0.46	-0.52	-0.29	0.00	0.34	0.01
^4TS_H	1.31	0.64	0.11	0.37	-0.04	0.62	0.45	-0.53	-0.28	0.03	0.37	-0.03

Table S5c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for phenylethane (3n) hydroxylation with water W_{903}.

	Energy	ΔE
phenylethane (PhEth)	-310.597944	-
^{2}CpdI'+ PhEth.	-1971.735096	-0.02
^{4}CpdI'+ PhEth.	-1971.735060	0.00
^2TS_H'	-1971.706854	17.70
^4TS_H'	-1971.705897	18.30

Table S5d: Group spin densities and group charges for phenylethane (3n) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.94	-0.12	-0.20	-0.17	0.02	-0.47	0.01	0.47	-0.57	-0.24	0.03	0.32	-0.01	0.00
^4TS_H'	1.02	0.55	0.43	0.43	-0.05	0.61	0.01	0.45	-0.60	-0.13	0.00	0.35	-0.06	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S6: B3LYP/B1 optimised TS geometries for phenylethane (3b) hydroxylation (a) without and (b) with water W_{903}.

Table S6a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for phenylethane (3b) hydroxylation without water W_{903}.

	Energy	ΔE
phenylethane (PhEth)	-310.597944	-
^{2}CpdI+ PhEth.	-1895.370294	0.08
^{4}CpdI+ PhEth.	-1895.370423	0.00
^2TS_H	-1895.347625	14.30
^4TS_H	-1895.347196	14.57

Table S6b: Group spin densities and group charges for phenylethane (3b) hydroxylation without water W_{903}.

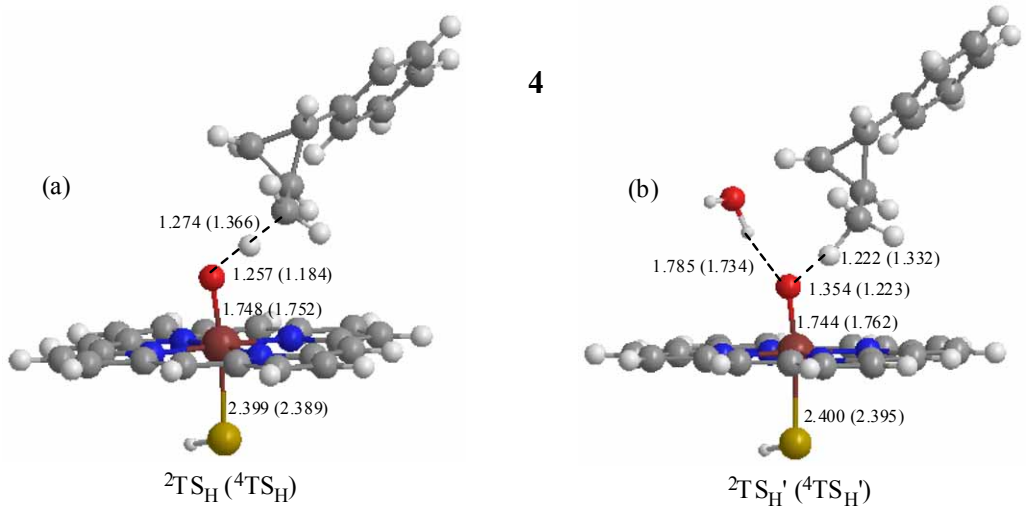
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.78	0.10	-0.25	-0.22	0.01	-0.41	0.47	-0.50	-0.27	0.02	0.33	-0.01
^4TS_H	1.31	0.69	0.14	0.37	-0.03	0.53	0.47	-0.51	-0.28	0.01	0.35	-0.04

Table S6c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for phenylethane (3b) hydroxylation with water W_{903}.

	Energy	ΔE
phenylethane (PhEth)	-310.597944	-
^{2}CpdI'+ PhEth.	-1971.735096	-0.02
^{4}CpdI'+ PhEth.	-1971.735060	0.00
^2TS_H'	-1971.718276	10.53
^4TS_H'	-1971.717820	10.81

Table S6d: Group spin densities and group charges for phenylethane (3b) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.82	0.14	-0.33	-0.28	0.00	-0.35	0.01	0.51	-0.56	-0.21	-0.01	0.31	-0.04	0.00
^4TS_H'	1.30	0.63	0.20	0.40	-0.03	0.50	0.01	0.48	-0.57	-0.23	0.03	0.33	-0.05	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S7: B3LYP/B1 optimised TS geometries for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation (a) without and (b) with water W_{903}.

Table S7a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
Me-probe	-387.909621	-
^{2}CpdI+ Me-probe	-1972.681971	0.08
^{4}CpdI+ Me-probe	-1972.682107	0.00
^2TS_H	-1972.654326	17.43
^4TS_H	-1972.652685	18.46

Table S7b: Group spin densities and group charges for Me-probe hydroxylation without water W_{903}.

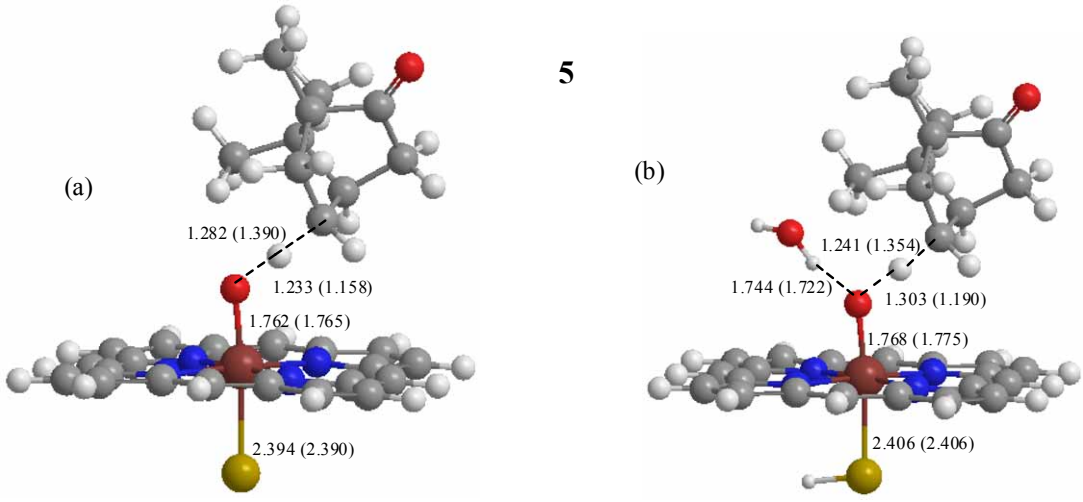
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.78	-0.02	-0.20	-0.12	0.02	-0.46	0.45	-0.49	-0.29	-0.01	0.33	0.01
^4TS_H	1.32	0.68	0.09	0.37	-0.03	0.59	0.45	-0.51	-0.30	0.02	0.36	-0.02

Table S7c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
Me-probe	-387.909621	-
^{2}CpdI'+ Me-probe	-2049.046773	-0.02
^{4}CpdI'+ Me-probe	-2049.046737	0.00
^2TS_H'	-2049.024111	14.20
^4TS_H'	-2049.023071	14.85

Table S7d: Group spin densities and group charges for Me-probe hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.80	-0.02	-0.24	-0.16	-0.40	-0.41	0.00	0.48	-0.54	-0.26	0.00	0.30	0.01	0.00
^4TS_H'	1.31	0.60	0.15	0.39	-0.02	0.57	0.00	0.48	-0.58	-0.26	0.04	0.34	-0.01	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S8: B3LYP/B1 optimised TS geometries for camphor hydroxylation (a) without and (b) with water W_{903}.

Table S8a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation without water W_{903}.

	Energy	ΔE
camphor	-465.490073	-
^{2}CpdI+Cam.	-2050.262423	0.08
^{4}CpdI+Cam.	-2050.262559	0.00
^2TS_H	-2050.235335	17.08
^4TS_H	-2050.233753	18.08

Table S8b: Group spin densities and group charges for camphor hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.84	-0.08	-0.19	-0.12	0.03	-0.48	0.45	-0.51	-0.27	0.01	0.33	0.00
^4TS_H	1.27	0.64	0.13	0.39	-0.04	0.61	0.43	-0.53	-0.27	0.04	0.36	-0.04

Table S8c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation with water W_{903}.

	Energy	ΔE
camphor	-465.490073	-
^{2}CpdI'+Cam.	-2126.627225	-0.02
^{4}CpdI'+Cam.	-2126.627183	0.00
^2TS_H'	-2126.605469	13.63
^4TS_H'	-2126.603634	14.78

Table S8d: Group spin densities and group charges for camphor hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.92	-0.11	-0.23	-0.21	0.02	-0.40	0.00	0.48	-0.56	-0.23	0.03	0.31	-0.05	0.03
^4TS_H'	1.20	0.58	0.23	0.44	-0.04	0.58	0.01	0.44	-0.60	-0.22	0.06	0.35	-0.06	0.02

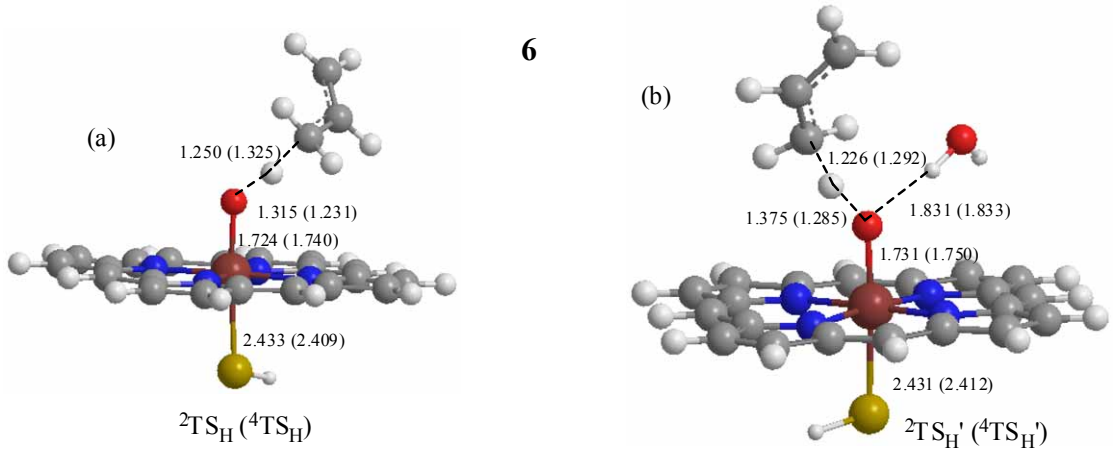


Figure S9: B3LYP/B1 optimised TS geometries for propene hydroxylation (a) without and (b) with water W_{903}.

Table S9a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propene hydroxylation without water W_{903}.

	Energy	ΔE
propene	-117.795017	-
^{2}CpdI+ propene	-1702.567367	0.08
^{4}CpdI+ propene	-1702.567503	0.00
^2TS_H	-1702.543068	15.33
^4TS_H	-1702.543577	15.01

Table S9b: Group spin densities and group charges for propene hydroxylation without water W_{903}.

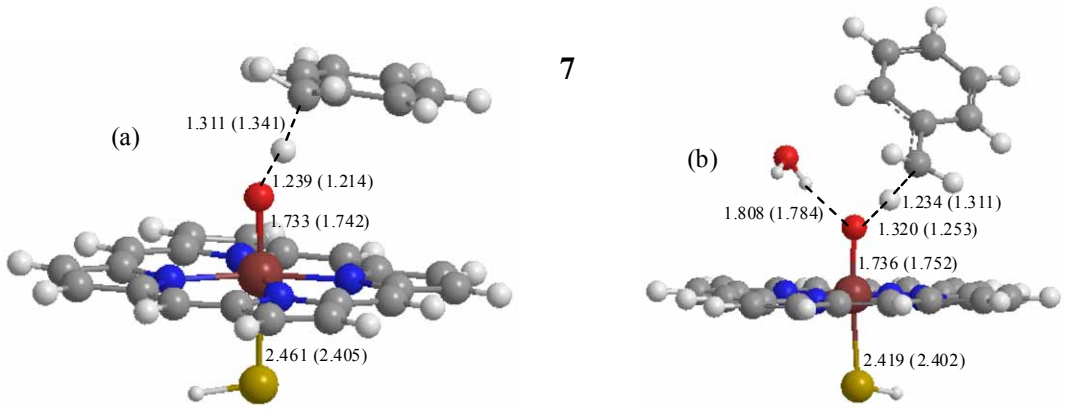
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.76	0.14	-0.30	-0.24	0.02	-0.38	0.47	-0.48	-0.23	-0.03	0.33	-0.06
^4TS_H	1.22	0.72	0.18	0.40	-0.04	0.52	0.45	-0.49	-0.26	0.01	0.36	-0.07

Table S9c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for propene hydroxylation with water W_{903}.

	Energy	ΔE
propene	-117.795017	-
^{2}CpdI'+ propene	-1778.932169	-0.02
^{4}CpdI'+ propene	-1778.932133	0.00
^2TS_H'	-1778.911084	13.21
^4TS_H'	-1778.911951	12.66

Table S9d: Group spin densities and group charges for propene hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.80	0.12	-0.31	-0.25	0.01	-0.37	0.01	0.49	-0.54	-0.23	-0.02	0.31	-0.03	0.01
^4TS_H'	1.22	0.67	0.20	0.42	-0.04	0.52	0.01	0.46	-0.54	-0.25	0.03	0.33	-0.04	0.01



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S10: B3LYP/B1 optimised TS geometries for toluene hydroxylation (a) without and (b) with water W_{903}.

Table S10a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for toluene hydroxylation without water W_{903}.

	Energy	ΔE
toluene	-271.323418	-
^{2}CpdI+Tol.	-1856.095768	0.08
^{4}CpdI+ Tol.	-1856.095904	0.00
^2TS_H	-1856.070754	15.78
^{4} TS_H	-1856.071762	15.15

Table S10b: Group spin densities and group charges for toluene hydroxylation without water W_{903}.

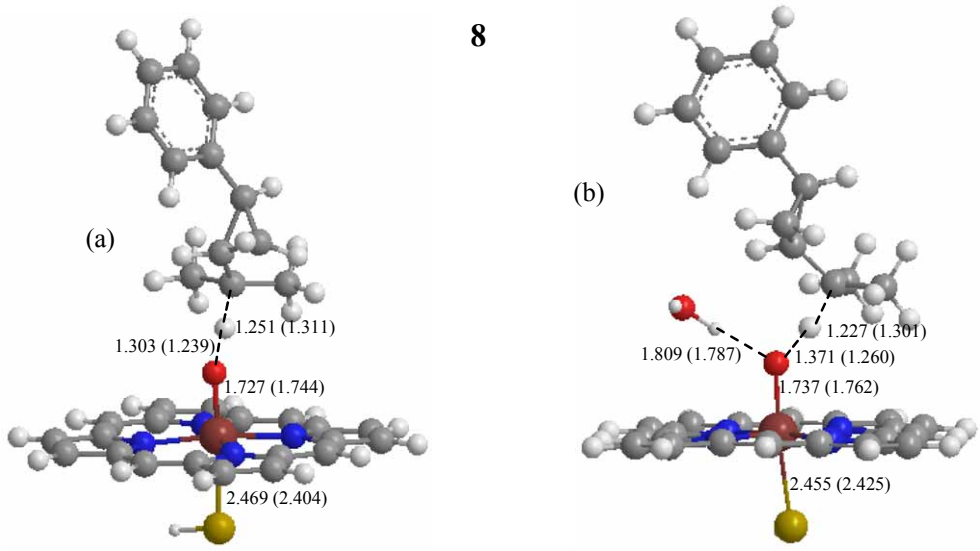
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.83	0.20	-0.29	-0.32	0.01	-0.44	0.51	-0.53	-0.26	-0.04	0.35	-0.04
^4TS_H	1.24	0.70	0.16	0.39	-0.04	0.54	0.45	-0.50	-0.27	0.01	0.37	-0.07

Table S10c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for toluene hydroxylation with water W_{903}.

	Energy	ΔE
toluene	-271.323418	-
^{2}CpdI'+ Tol.	-1932.460570	-0.02
^{4}CpdI'+ Tol.	-1932.460534	0.00
^2TS_H'	-1932.441795	11.76
^{4} TS_H'	-1932.441336	12.05

Table S10d: Group spin densities and group charges for toluene hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.80	0.09	-0.29	-0.22	0.01	-0.39	0.01	0.48	-0.54	-0.24	-0.01	0.32	-0.02	0.01
^{4} TS_H'	1.27	0.64	0.18	0.40	-0.03	0.54	0.01	0.45	-0.56	-0.24	0.04	0.35	-0.05	0.01



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S11: B3LYP/B1 optimised TS geometries for iPr-probe (*trans*-iso-propyl-phenyl-cyclopropane) hydroxylation (a) without and (b) with water W_{903}.

Table S11a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for iPr-probe (*trans*-iso-propyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
iPr-probe	-466.457525	-
^{2}CpdI+ iPr-probe	-2051.229875	0.08
^{4}CpdI+ iPr-probe	-2051.230011	0.00
^2TS_H	-2051.208204	13.68
^4TS_H	-2051.207172	14.33

Table S11b: Group spin densities and group charges for iPr-probe hydroxylation without water W_{903}.

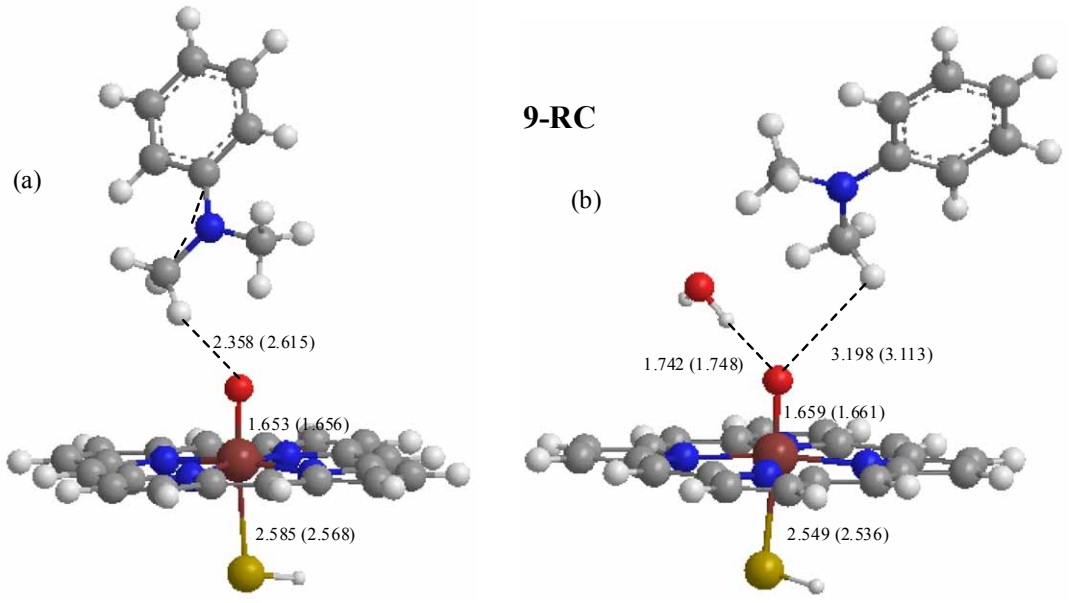
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.82	0.17	-0.27	-0.34	0.00	-0.38	0.49	-0.50	-0.28	-0.03	0.32	0.00
^4TS_H	1.32	0.72	0.09	0.37	-0.02	0.52	0.45	-0.50	-0.30	0.02	0.34	-0.01

Table S11c: B3LYP/B1 B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for iPr-probe (*trans*-iso-propyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
iPr-probe	-466.457525	-
^{2}CpdI'+ iPr-probe	-2127.594677	-0.02
^{4}CpdI'+ iPr-probe	-2127.598641	0.00
^2TS_H'	-2127.578057	12.92
^4TS_H'	-2127.577307	13.39

Table S11d: Group spin densities and group charges for iPr-probe hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.86	0.11	-0.31	-0.32	0.00	-0.35	0.01	0.49	-0.55	-0.22	-0.01	0.30	-0.02	0.01
^4TS_H'	1.25	0.63	0.20	0.43	-0.02	0.50	0.01	0.45	-0.57	-0.23	0.04	0.33	-0.03	0.01



^{2}RC (^{4}RC) ^{2}RC' (^{4}RC')

Figure S12: B3LYP/B1 optimised TS geometries for reactant cluster of dimethylaniline (a) without and (b) with water W_{903}.

Table S12a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for reactant cluster of dimethylaniline without water W_{903}.

	Energy	ΔE
dimethylaniline	-365.883358	-
^{2}CpdI+Me2Anil.	-1950.655708	0.08
^{4}CpdI+ Me2Anil.	-1950.655844	0.00
^{2}RC	-1950.662540	-4.15
^{4} RC	-1950.662618	-4.25

Table S12b: Group spin densities and group charges for reactant cluster of dimethylaniline without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	**O**	**Por**	**SH**	**R**	**Fe**	**O**	**Por**	**SH**	**R**
^{2}RC	1.23	0.87	-0.48	-0.56	-0.06	0.52	-0.37	-0.14	-0.05	0.04
^{4}RC	1.08	0.94	0.43	0.50	0.04	0.51	-0.35	-0.11	-0.06	0.02

Table S12c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for dimethylaniline with water W_{903}.

	Energy	ΔE
dimethylaniline	-365.883358	-
^{2}CpdI'+ Me2Anil.	-2027.020510	-0.02
^{4}CpdI'+ Me2Anil.	-2027.020474	0.00
^{2}RC'	-2027.030682	-6.41
^{4} RC'	-2027.030332	-6.19

Table S12d: Group spin densities and group charges for reactant cluster of dimethylaniline with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**R**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**R**	**W_{903}**
^{2}RC'	1.30	0.81	-0.43	-0.50	-0.18	0.01	0.49	-0.43	-0.16	-0.06	0.12	0.04
^{4} RC'	1.18	0.85	0.34	0.45	0.18	0.01	0.48	-0.43	-0.15	-0.06	0.11	0.04

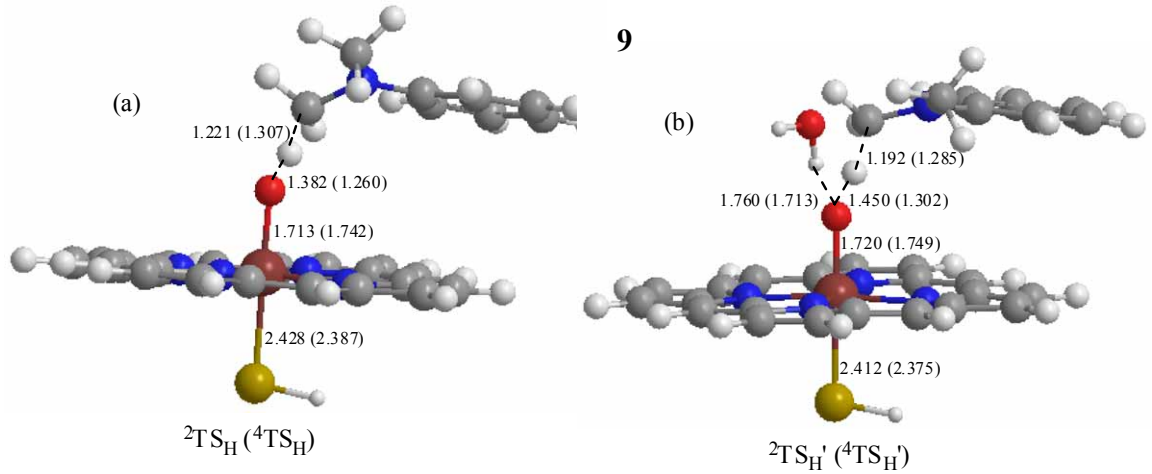


Figure S13: B3LYP/B1 optimised TS geometries for dimethylaniline hydroxylation (a) without and (b) with water W_{903}.

Table S13a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation without water W_{903}.

	Energy	ΔE	ΔE[a]
dimethylaniline	-365.883358	-	-
^{2}CpdI+Me2Anil.	-1950.655708	0.08	-
^{4}CpdI+ Me2Anil.	-1950.655844	0.00	-
^2TS_H	-1950.645763	6.33	10.58
^{4} TS_H	-1950.643425	7.79	12.04

[a] relative energy with respect to ^{4}RC.

Table S13b: Group spin densities and group charges for dimethylaniline hydroxylation without water W_{903}.

		Fe	O	Por	SH	H'	Me2-H'	N	phenyl
^2TS_H	ρ	1.62	0.27	-0.22	-0.16	0.00	-0.19	-0.24	-0.09
	Q	0.45	-0.49	-0.35	-0.08	0.35	0.20	-0.37	0.28
^{4} TS_H	ρ	1.43	0.69	-0.01	0.26	-0.01	0.31	0.25	0.09
	Q	0.46	-0.52	-0.38	-0.02	0.37	0.31	-0.55	0.34

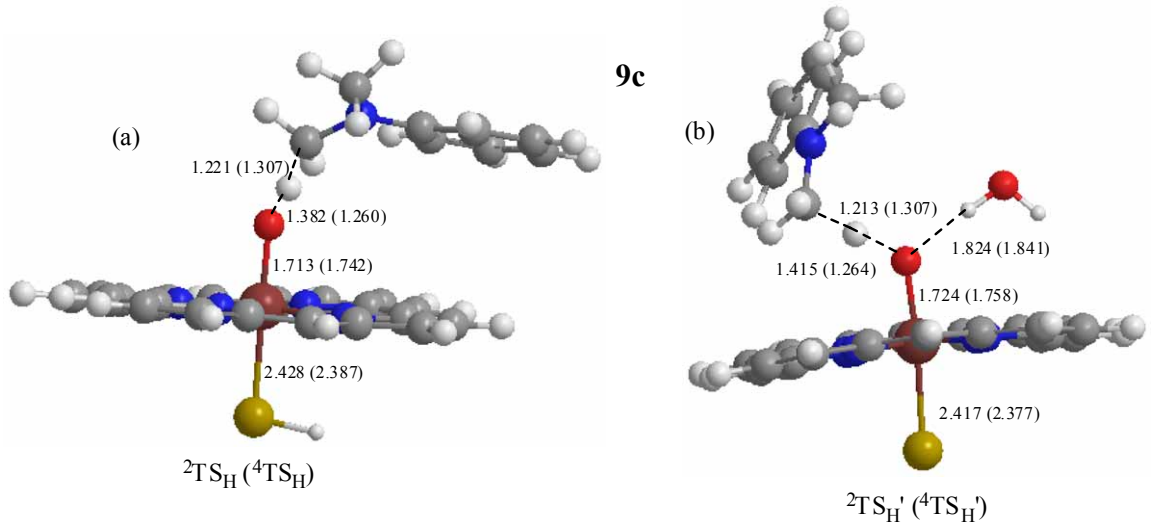
Table S13c: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE	ΔE[a]	ΔΔE[a]
dimethylaniline	-365.883358	-	-	-
^{2}CpdI'+ Me2Anil.	-2027.020510	-0.02	-	-
^{4}CpdI'+ Me2Anil.	-2027.020474	0.00	-	-
^2TS_H'	-2027.022979	-1.57	4.62	5.96
^{4} TS_H'	-2027.016857	2.27	8.46	3.58

[a] relative energy with respect to ^{4}RC'.

Table S13d: Group spin densities and group charges for dimethylaniline hydroxylation with water W_{903}.

		Fe	O	Por	SH	H'	Me2-H'	N	phenyl	W_{903}
^2TS_H'	ρ	1.62	0.29	-0.20	-0.11	-0.03	-0.11	-0.36	-0.12	0.01
	Q	0.45	-0.55	-0.36	-0.07	0.32	0.33	-0.53	0.40	0.00
^{4} TS_H'	ρ	1.55	0.59	-0.06	0.21	0.01	0.26	0.32	0.11	0.01
	Q	0.47	-0.60	-0.38	-0.01	0.36	0.33	-0.54	0.36	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S14: B3LYP/B1 optimised TS geometries for dimethylaniline hydroxylation with constrained dihedral angle: oxygen of W_{903} *trans* with respect to nitrogen of aniline.

Table S14a: B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with constrained dihedral angle: oxygen of W_{903} *trans* with respect to nitrogen of aniline.

	Energy	ΔE	ΔE[a]
dimethylaniline	-365.883358	-	-
^{2}CpdI'+ Me2Anil.	-2027.020510	-0.02	-
^{4}CpdI'+ Me2Anil.	-2027.020474	0.00	-
^2TS_H'	-2027.015095	3.38	9.58
^{4} TS_H'	-2027.012060	5.28	11.47

[a] relative energy with respect to ^{4}RC'.

Table S14b: Group spin densities and group charges for dimethylaniline hydroxylation with constrained dihedral angle: oxygen of W_{903} *trans* with respect to nitrogen of aniline.

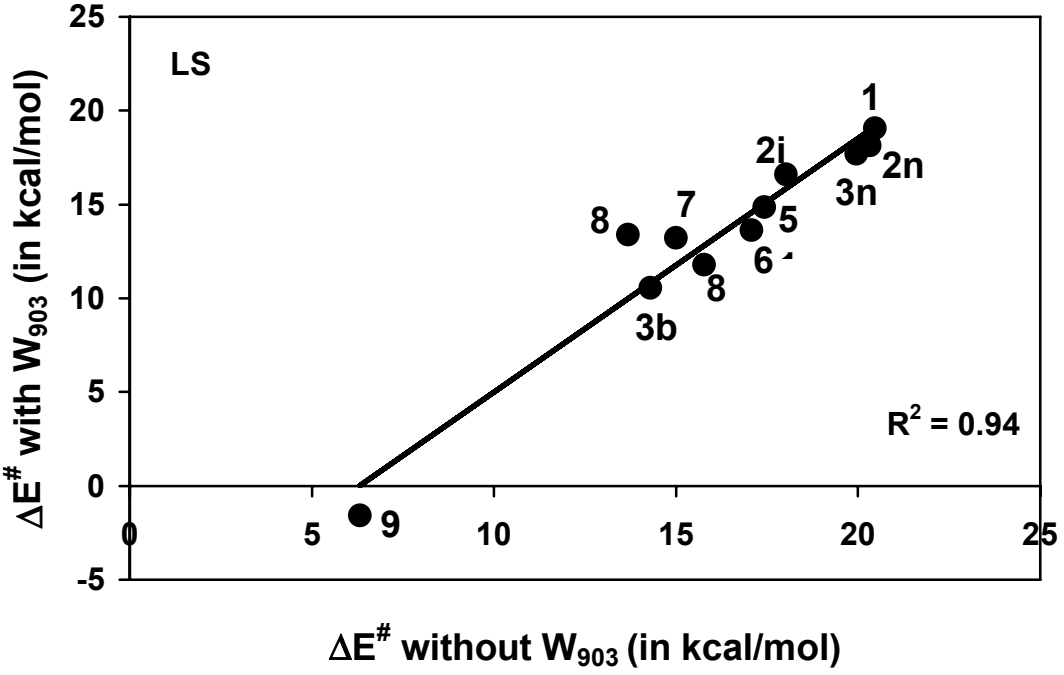
		Fe	O	Por	SH	H'	Me2-H'	N	phenyl	W_{903}
^2TS_H'	**ρ**	1.62	0.25	-0.21	-0.13	-0.02	-0.14	-0.32	-0.11	0.01
	Q	0.46	-0.55	-0.35	-0.05	0.33	0.33	-0.55	0.40	-0.02
^{4} TS_H'	**ρ**	1.53	0.62	-0.05	0.19	0.01	0.29	0.30	0.11	0.01
	Q	0.44	-0.58	-0.36	0.00	0.38	0.31	-0.54	0.38	-0.02

Table S15: Effect of water W_{903} on B3LYP/B1 hydrogen abstraction barriers (in kcal/mol).

		spin	$\Delta E^{\#}$ without W_{903}	$\Delta E^{\#}$ with W_{903}	$\Delta\Delta E^{\#}$
1	ethane	D	20.32	18.13	2.19
		Q	21.28	18.71	2.57
2n	propane	D	20.47	19.06	1.41
		Q	21.62	20.33	1.29
2b	propane	D	18.02	16.61	1.41
		Q	19.26	16.63	2.63
3n	phenylethane	D	19.96	17.70	2.26
		Q	21.16	18.30	2.86
3b	phenylethane	D	14.30	10.53	3.77
		Q	14.57	10.81	3.76
4	Me-probe	D	17.43	14.85	2.58
		Q	18.46	14.20	4.26
5	camphor	D	17.08	13.63	3.45
		Q	18.08	14.78	3.30
6	propene	D	15.01	13.60	1.37
		Q	15.33	13.21	1.80
7	toluene	D	15.78	12.66	2.67
		Q	15.15	12.05	3.01
8	iPr-probe	D	13.68	13.39	0.29
		Q	14.33	12.92	1.41
9	dimethylaniline	D	6.33	-1.57	7.90
		Q	7.79	2.27	5.52
9c	dimethylaniline **(constrained)**	D	6.33	3.38	2.95
		Q	7.79	5.28	2.51

Figure S15: Correlation of B3LYP/B1 hydrogen abstraction barriers without and with water W_{903} in the (a) doublet spin state and (b) quartet spin state.

(a)



(b)

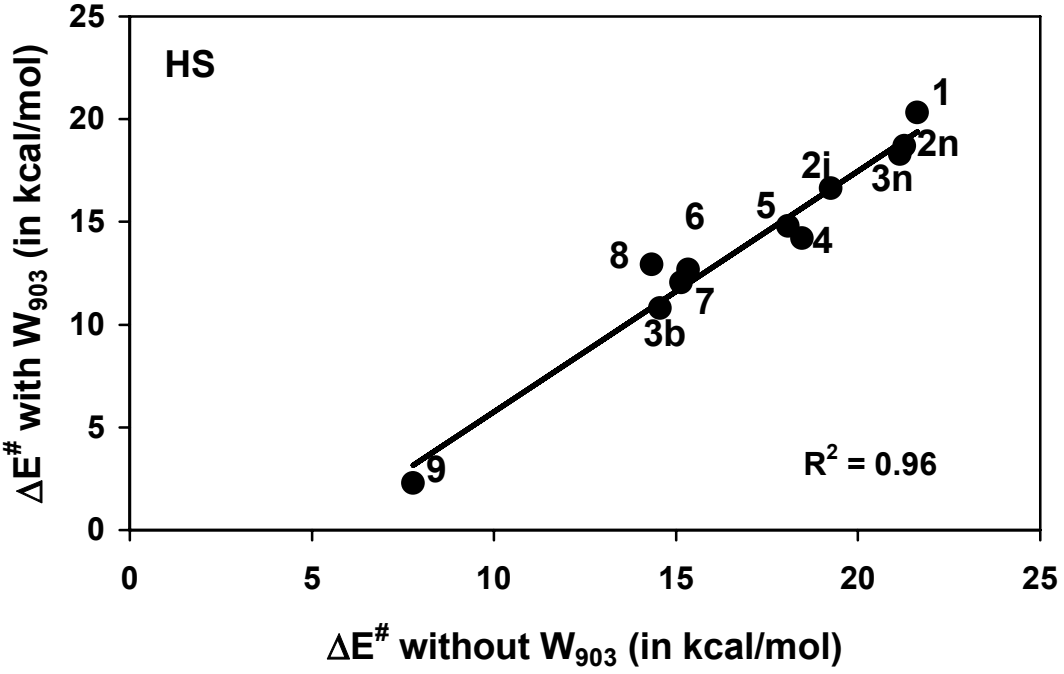


Table S16a: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 without water W_{903}.

	Energy	ΔE
^{2}CpdI	-2725.701470	-0.15
^{4}CpdI	-2725.701225	0.00

Table S16b: Group spin densities and group charges for ^{2,4}Cpd I of P450 without water W_{903}.

	Spin Density (ρ)				Charge (Q)			
	Fe	O	Por	SH	Fe	O	Por	SH
^{2}CpdI	1.24	0.87	-0.46	-0.64	0.23	-0.24	0.08	-0.08
^{4}CpdI	1.13	0.92	0.35	0.60	0.23	-0.23	0.09	-0.09

Table S16c: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I' of P450 with water W_{903}.

	Energy	ΔE
^{2}CpdI'	-2802.134617	-0.14
^{4}CpdI'	-2802.134388	0.00

Table S16d: Group spin densities and group charges for ^{2,4}Cpd I' of P450 with water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	W_{903}	Fe	O	Por	SH	W_{903}
^{2}CpdI'	1.36	0.77	-0.52	-0.06	0.01	0.23	-0.31	0.17	-0.08	-0.01
^{4}CpdI'	1.23	0.83	0.39	0.55	0.01	0.22	-0.31	0.18	-0.08	-0.01

Table S17a: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
Me-probe	-388.130159	-
^{2}CpdI+ Me-probe	-3113.831629	-0.15
^{4}CpdI+ Me-probe	-3113.831384	0.00
$^{2}TS_H$	-3113.806799	15.43
$^{4}TS_H$	-3113.804753	16.71

Table S17b: Group spin densities and group charges for Me-probe hydroxylation without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	Me-Pr.	Fe	O	Por	SH	Me-Pr.
$^{2}TS_H$	1.85	-0.07	-0.20	-0.11	-0.47	0.12	-0.30	0.06	-0.15	0.27
$^{4}TS_H$	1.57	0.59	-0.04	0.26	0.61	0.14	-0.30	0.00	-0.10	0.26

Table S17c: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
Me-probe	-388.130159	-
^{2}CpdI'+ Me-probe	-3190.264776	-0.14
^{4}CpdI'+ Me-probe	-3190.264547	0.00
$^{2}TS_H$'	-3190.242524	13.82
$^{4}TS_H$'	-3190.239607	15.65

Table S17d: Group spin densities and group charges for Me-probe hydroxylation with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	O	Por	SH	Me-Pr.	W_{903}	Fe	O	Por	SH	Cam.	Me-Pr.
$^{2}TS_H$'	1.88	-0.10	-0.23	-0.14	-0.42	0.00	0.14	-0.38	0.09	-0.13	0.29	-0.01
$^{4}TS_H$'	1.60	0.53	-0.01	0.28	0.60	0.00	0.14	-0.41	0.60	-0.08	0.30	-0.02

Table S18a: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation without water W_{903}.

	Energy	ΔE
dimethylaniline	-366.095150	-
^{2}CpdI+Me2Anil.	-3091.766620	-0.15
^{4}CpdI+ Me2Anil.	-3091.796375	0.00
$^{2}TS_{H}$	-3091.786532	6.18
$^{4}TS_{H}$	-3091.784702	7.32

Table S18b: Group spin densities and group charges for dimethylaniline hydroxylation without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	**O**	**Por**	**SH**	**Me2Anil.**	**Fe**	**O**	**Por**	**SH**	**Me2Anil.**
$^{2}TS_{H}$	1.74	0.15	-0.21	-0.14	-0.54	0.13	-0.34	0.00	-0.20	0.42
$^{4}TS_{H}$	1.60	0.61	-0.08	0.20	0.68	0.14	-0.34	-0.05	-0.14	0.39

Table S18c: B3//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE
dimethylaniline	-366.095150	-
^{2}CpdI'+ Me2Anil.	-3168.229767	-0.14
^{4}CpdI'+ Me2Anil.	-3168.229538	0.00
$^{2}TS_{H}$'	-3168.226419	1.96
$^{4}TS_{H}$'	-3168.222642	4.33

Table S18d: Group spin densities and group charges for dimethylaniline hydroxylation with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**Me2Anil.**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**Me2Anil.**	**W_{903}**
$^{2}TS_{H}$	1.74	0.18	-0.21	-0.11	-0.62	0.01	0.14	-0.44	-0.03	-0.19	0.51	0.01
$^{4}TS_{H}$	1.68	0.53	-0.11	0.16	0.73	0.00	0.16	-0.45	-0.03	-0.13	0.47	-0.02

Table S19a: B2W//B1 single-point energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 without water W_{903}.

	Energy	ΔE
^{2}CpdI	-2725.315605	-0.15
^{4}CpdI	-2725.315363	0.00

Table S19b: Group spin densities and group charges for ^{2,4}Cpd I of P450 without water W_{903}.

	Spin Density (ρ)				Charge (Q)			
	Fe	O	Por	SH	Fe	O	Por	SH
^{2}CpdI	1.31	0.84	-0.52	-0.63	1.27	-0.44	-0.78	-0.05
^{4}CpdI	1.14	0.89	0.58	0.38	1.25	-0.43	-0.06	-0.77

Table S19c: B3//B1 single-point B3LYP/B1 energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I' of P450 with water W_{903}.

	Energy	ΔE
^{2}CpdI'	-2801.721600	-0.08
^{4}CpdI'	-2801.721468	0.00

Table S19d: Group spin densities and group charges for ^{2,4}Cpd I' of P450 with water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	W_{903}	Fe	O	Por	SH	W_{903}
^{2}CpdI'	1.42	0.74	-0.57	-0.59	0.01	0.76	-0.35	-0.43	-0.05	0.07
^{4}CpdI'	1.23	0.80	0.43	0.53	0.01	0.75	-0.34	-0.43	-0.05	0.07

Table S20a: B2W//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
Me-probe	-388.010259	-
^{2}CpdI+ Me-probe	-3113.325864	-0.15
^{4}CpdI+ Me-probe	-3113.355622	0.00
$^{2}TS_H$	-3113.302751	14.35
$^{4}TS_H$	-3113.300473	15.78

Table S20b: Group spin densities and group charges for Me-probe hydroxylation without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	Me-Pr.	Fe	O	Por	SH	Me-Pr.
$^{2}TS_H$	1.73	-0.06	-0.14	-0.07	-0.46	-0.44	-0.04	0.23	-0.08	0.33
$^{4}TS_H$	1.49	0.59	0.04	0.27	0.61	-0.25	-0.05	-0.04	-0.02	0.36

Table S20c: B2W//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
Me-probe	-388.010259	-
^{2}CpdI'+ Me-probe	-3189.731859	-0.08
^{4}CpdI'+ Me-probe	-3189.731727	0.00
$^{2}TS_H$'	-3189.711042	12.98
$^{4}TS_H$'	-3189.708923	14.31

Table S20d: Group spin densities and group charges for Me-probe hydroxylation with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	O	Por	SH	Me-Pr.	W_{903}	Fe	O	Por	SH	Cam.	Me-Pr.
$^{2}TS_H$'	1.79	-0.07	-0.19	-0.12	-0.42	0.01	-0.56	0.11	0.22	-0.08	0.25	0.05
$^{4}TS_H$'	1.50	0.54	0.07	0.28	0.61	-0.01	-0.43	-0.12	0.23	-0.01	0.31	0.03

Table S21a: B2W//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation without water W_{903}.

	Energy	ΔE
dimethylaniline	-365.980536	-
^{2}CpdI+Me2Anil.	-3091.296141	-0.15
^{4}CpdI+ Me2Anil.	-3091.295899	0.00
$^{2}TS_H$	-3091.287879	5.03
$^{4}TS_H$	-3091.285966	6.23

Table S21b: Group spin densities and group charges for dimethylaniline hydroxylation without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	**O**	**Por**	**SH**	**Me2Anil.**	**Fe**	**O**	**Por**	**SH**	**Me2Anil.**
$^{2}TS_H$	1.65	0.16	-0.17	-0.11	-0.54	-0.76	0.18	0.19	-0.12	0.51
$^{4}TS_H$	1.51	0.61	-0.01	0.21	0.68	-0.28	0.11	-0.08	-0.07	0.54

Table S21c: B2W//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE
dimethylaniline	-365.980536	-
^{2}CpdI'+ Me2Anil.	-3167.702136	-0.08
^{4}CpdI'+ Me2Anil.	-3167.702004	0.00
$^{2}TS_H$'	-3167.700542	0.92
$^{4}TS_H$'	-3167.696532	3.43

Table S21d: Group spin densities and group charges for dimethylaniline hydroxylation with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**Me2Anil.**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**Cam.**	**Me2Anil.**
$^{2}TS_H$'	1.65	0.20	-0.16	-0.08	-0.61	0.01	-1.15	0.02	0.51	-0.07	0.60	0.09
$^{4}TS_H$'	1.55	0.55	-0.03	0.18	0.75	-0.01	-0.47	-0.10	0.10	-0.06	0.53	0.01

Table S22: Comparison of the effect of water W_{903} on hydrogen abstraction barriers for Me-probe and dimethylaniline in B3//B1, B2W//B1, and B4//B1 single-point calculations. Energies are in kcal/mol. Detailed B4//B1 single-point results are listed in tables S23-S36.

		B3//B1 single-point	B2W//B1 single-point	B4//B1 single-point
Me-probe	**$^{2}TS_H$**	1.61	1.37	1.61
	$^{4}TS_H$	1.06	1.47	1.73
dimethylaniline	**$^{2}TS_H$**	4.22	4.11	6.14
	$^{4}TS_H$	2.99	2.80	3.40

Table S23a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 without water W_{903}.

	Energy	ΔE
^{2}CpdI	-2725.311622	-0.01
^{4}CpdI	-2725.311465	0.00

Table S23b: Group spin densities and group charges for ^{2,4}Cpd I of P450 without water W_{903}.

	Spin Density (ρ)				Charge (Q)			
	Fe	O	Por	SH	Fe	O	Por	SH
^{2}CpdI	1.24	0.86	-0.51	-0.59	0.76	-0.46	-0.18	-0.12
^{4}CpdI	1.12	0.92	0.42	0.55	0.75	-0.46	-0.17	-0.13

Table S23c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 with water W_{903}.

	Energy	ΔE
^{2}CpdI'	-2801.694463	-0.19
^{4}CpdI'	-2801.694168	0.00

Table S23d: Group spin densities and group charges for ^{2,4}Cpd I of P450 with water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	O	Por	SH	W_{903}	Fe	O	Por	SH	W_{903}
^{2}CpdI'	1.34	0.77	-0.56	-0.55	0.01	0.75	-0.53	-0.10	-0.12	0.00
^{4}CpdI'	1.20	0.83	0.46	0.50	0.01	0.74	-0.53	-0.10	-0.12	0.00

Table S24a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation without water W_{903}.

	Energy	ΔE
ethane	-79.763799	-
^{2}CpdI+ ethane	-2805.075421	-0.10
^{4}CpdI+ ethane	-2805.075264	0.00
$^{2}TS_H$	-2805.043923	19.67
$^{4}TS_H$	-2805.040913	21.56

Table S24b: Group spin densities and group charges for ethane hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	O	Por	SH	H'	R-H'	Fe	O	Por	SH	H'	R-H'
$^{2}TS_H$	1.85	-0.11	-0.18	-0.07	0.04	-0.54	0.68	-0.62	-0.31	-0.12	0.39	-0.02
$^{4}TS_H$	1.52	0.60	0.01	0.27	-0.04	0.64	0.69	-0.64	-0.34	-0.09	0.41	-0.03

Table S24c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation with water W_{903}.

	Energy	ΔE
ethane	-79.763799	-
^{2}CpdI'+ ethane	-2881.458262	-0.10
^{4}CpdI'+ ethane	-2881.457967	0.00
$^{2}TS_H$'	-2881.428331	18.60
$^{4}TS_H$'	-2881.424602	20.94

Table S24d: Group spin densities and group charges for ethane hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	O	Por	SH	H'	R-H'	W_{903}	Fe	O	Por	SH	H'	R-H'	W_{903}
$^{2}TS_H$'	1.93	-0.20	-0.19	-0.11	0.04	-0.48	0.00	0.69	-0.65	-0.27	-0.10	0.36	-0.04	0.00
$^{4}TS_H$'	1.50	0.54	0.06	0.31	-0.03	-0.03	0.01	0.71	-0.70	-0.30	-0.08	0.41	-0.05	0.02

Table S25a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propane (2n) hydroxylation without water W_{903}.

	Energy	ΔE
propane	-119.047698	-
^{2}CpdI+ propane	-2844.359320	-0.10
^{4}CpdI+ propane	-2844.359163	0.00
$^{2}TS_H$	-2844.327675	19.76
$^{4}TS_H$	-2844.324526	21.74

Table S25b: Group spin densities and group charges for propane (2n) hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.84	-0.12	-0.17	-0.06	0.04	-0.53	0.69	-0.62	-0.31	-0.12	0.39	-0.02
$^{4}TS_H$	1.53	0.60	0.00	0.26	-0.04	0.64	0.69	-0.65	-0.33	-0.09	0.41	-0.03

Table S25c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propane (2n) hydroxylation with water W_{903}.

	Energy	ΔE
propane	-119.047698	-
^{2}CpdI'+ propane	-2920.742161	-0.19
^{4}CpdI'+ propane	-2920.741866	0.00
$^{2}TS_H$'	-2920.711288	19.19
$^{4}TS_H$'	-2920.707301	21.69

Table S25d: Group spin densities and group charges for propane (2n) hydroxylation with water W_{903}.

	Spin Density (ρ)						Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$'	1.89	-0.20	-0.19	-0.09	0.04	-0.46	0.01	0.69	-0.64	-0.29	-0.10	0.36	-0.02
$^{4}TS_H$'	1.51	0.55	0.05	0.30	-0.03	0.62	0.01	0.69	-0.69	-0.30	-0.07	0.41	-0.02

Table S26a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propane (2i) hydroxylation without water W_{903}.

	Energy	ΔE
propane	-119.047698	-
^{2}CpdI+ propane	-2844.359320	-0.10
^{4}CpdI+ propane	-2844.359163	0.00
$^{2}TS_H$	-2844.330411	18.04
$^{4}TS_H$	-2844.327071	20.14

Table S26b: Group spin densities and group charges for propane (2i) hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.86	-0.11	-0.20	-0.14	0.03	-0.46	0.71	-0.60	-0.31	-0.13	0.35	-0.02
$^{4}TS_H$	1.53	0.64	0.01	0.27	-0.03	0.58	0.70	-0.64	-0.34	-0.09	0.39	-0.02

Table S26c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propane (2i) hydroxylation with water W_{903}.

	Energy	ΔE
propane	-119.047698	-
^{2}CpdI'+ propane	-2920.742161	-0.19
^{4}CpdI'+ propane	-2920.741866	0.00
$^{2}TS_H$'	-2920.714025	17.47
$^{4}TS_H$'	-2920.711780	18.88

Table S26d: Group spin densities and group charges for propane (2i) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.92	-0.17	-0.23	-0.17	0.03	-0.38	0.0	0.73	-0.63	-0.27	-0.10	0.32	-0.04	-0.01
$^{4}TS_H$'	1.54	0.56	0.05	0.30	-0.03	0.57	0.01	0.71	-0.69	-0.30	-0.08	0.38	-0.03	0.01

Table S27a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for phenylethane (3n) hydroxylation without water W_{903}.

	Energy	ΔE
PhEth.	-310.661036	-
^{2}CpdI+ PhEth.	-3035.972658	-0.10
^{4}CpdI+ PhEth.	-3035.972501	0.00
$^{2}TS_H$	-3035.942330	18.93
$^{4}TS_H$	-3035.938855	21.11

Table S27b: Group spin densities and group charges for phenylethane (3n) hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.84	-0.09	-0.17	-0.06	0.04	-0.55	0.70	-0.63	-0.32	-0.12	0.40	-0.02
$^{4}TS_H$	1.56	0.59	-0.01	0.24	-0.03	0.65	0.70	-0.65	-0.34	-0.09	0.42	-0.04

Table S27c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for phenylethane (3n) hydroxylation with water W_{903}.

	Energy	ΔE
PhEth.	-310.661036	-
^{2}CpdI'+ PhEth.	-3112.355499	-0.19
^{4}CpdI'+ PhEth.	-3112.355204	0.00
$^{2}TS_H$'	-3112.326287	18.15
$^{4}TS_H$'	-3112.321723	21.01

Table S27d: Group spin densities and group charges for phenylethane (3n) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.94	-0.18	-0.19	-0.12	0.04	-0.50	0.00	0.7	-0.66	-0.28	-0.10	0.37	-0.04	0.01
$^{4}TS_H$'	1.42	0.51	0.15	0.34	-0.04	0.61	0.01	0.70	-0.70	-0.28	-0.09	0.41	-0.07	0.01

Table S28a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for phenylethane (3b) hydroxylation without water W_{903}.

	Energy	ΔE
PhEth.	-310.661036	-
^{2}CpdI+ PhEth.	-3035.972658	-0.10
^{4}CpdI+ PhEth.	-3035.972501	0.00
$^{2}TS_H$	-3035.948866	14.83
$^{4}TS_H$	-3035.946995	16.01

Table S28b: Group spin densities and group charges for phenylethane (3b) hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.82	0.00	-0.23	-0.17	0.03	-0.45	0.73	-0.61	-0.32	-0.14	0.37	-0.03
$^{4}TS_H$	1.48	0.65	0.06	0.29	-0.03	0.55	0.73	-0.63	-0.34	-0.10	0.39	-0.04

Table S28c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for phenylethane (3b) hydroxylation with water W_{903}.

	Energy	ΔE
PhEth.	-310.661036	-
^{2}CpdI'+ PhEth.	-3112.355499	-0.19
^{4}CpdI'+ PhEth.	-3112.355204	0.00
$^{2}TS_H$'	-3112.335435	12.41
$^{4}TS_H$'	-3112.333738	13.47

Table S28d: Group spin densities and group charges for phenylethane (3b) hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.87	0.04	-0.30	-0.24	0.01	-0.39	0.01	0.76	-0.66	-0.27	-0.13	0.34	-0.05	0.01
$^{4}TS_H$'	1.50	0.59	0.10	0.31	-0.03	0.52	0.01	0.75	-0.67	-0.31	-0.09	0.36	-0.05	0.01

Table S29a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
Newcomb probe	-387.994484	-
^{2}CpdI+New.	-3113.306106	-0.01
^{4}CpdI+ New.	-3113.305949	0.00
$^{2}TS_H$	-3113.278644	17.13
$^{4}TS_H$	-3113.275581	19.06

Table S29b: Group spin densities and group charges for Me-probe hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.81	-0.10	-0.19	-0.08	0.03	-0.48	0.70	-0.60	-0.32	-0.14	0.37	-0.01
$^{4}TS_H$	1.52	0.63	0.00	0.26	-0.03	0.62	0.70	-0.64	-0.35	-0.10	0.41	-0.02

Table S29c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
Newcomb probe	-387.994484	-
^{2}CpdI'+ New.	-3189.688947	-0.19
^{4}CpdI'+ New.	-3189.688652	0.00
$^{2}TS_H$'	-3189.663915	15.52
$^{4}TS_H$'	-3189.661039	17.33

Table S29d: Group spin densities and group charges for Me-probe hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.84	-0.11	-0.22	-0.12	0.02	-0.42	0.00	0.73	-0.63	-0.30	-0.12	0.34	-0.02	0.00
$^{4}TS_H$'	1.56	0.57	0.02	0.26	-0.02	0.60	0.01	0.73	-0.69	-0.34	-0.09	0.39	-0.01	0.00

Table S30a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation without water W_{903}.

	Energy	ΔE
camphor	-465.605785	-
^{2}CpdI+Cam	-3190.917407	-0.10
^{4}CpdI+Cam	-3190.917250	0.00
$^{2}TS_H$	-3190.890726	16.64
$^{4}TS_H$	-3190.887808	18.48

Table S30b: Group spin densities and group charges for camphor hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.87	-0.15	-0.18	-0.08	0.04	-0.50	0.70	-0.62	-0.31	-0.11	0.37	-0.03
$^{4}TS_H$	1.54	0.60	0.0	0.25	-0.04	0.64	0.69	-0.69	-0.33	-0.08	0.41	-0.04

Table S30c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation with water W_{903}.

	Energy	ΔE
camphor	-465.605785	-
^{2}CpdI'+Cam	-3267.300248	-0.19
^{4}CpdI'+Cam	-3267.299953	0.00
$^{2}TS_H$'	-3267.276202	14.90
$^{4}TS_H$'	-3267.272889	16.98

Table S30d: Group spin densities and group charges for camphor hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.94	-0.18	-0.21	-0.16	0.03	-0.42	0.00	0.73	-0.65	-0.10	-0.27	0.34	-0.08	0.03
$^{4}TS_H$'	1.54	0.55	0.04	0.29	-0.03	0.60	0.01	0.71	-0.70	-0.30	-0.06	0.40	-0.06	0.03

Table S31a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propene hydroxylation without water W_{903}.

	Energy	ΔE
propene	-117.817749	-
^{2}CpdI+ propene	-2843.129371	-0.10
^{4}CpdI+ propene	-2843.129214	0.00
$^{2}TS_H$	-2843.104379	15.58
$^{4}TS_H$	-2843.103257	16.29

Table S31b: Group spin densities and group charges for propene hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.82	-0.02	-0.24	-0.17	0.03	-0.42	0.72	-0.59	-0.29	-0.15	0.36	-0.06
$^{4}TS_H$	1.42	0.67	0.08	0.32	-0.04	0.55	0.71	-0.61	-0.32	-0.10	0.40	-0.07

Table S31c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for propene hydroxylation with water W_{903}.

	Energy	ΔE
propene	-117.817749	-
^{2}CpdI'+ propene	-2919.512212	-0.19
^{4}CpdI'+ propene	-2919.511917	0.00
$^{2}TS_H$'	-2919.488738	14.55
$^{4}TS_H$'	-2919.488217	14.87

Table S31d: Group spin densities and group charges for propene hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.86	-0.03	-0.26	-0.19	0.02	-0.41	0.01	0.73	-0.63	-0.26	-0.19	0.02	-0.41	0.01
$^{4}TS_H$'	1.44	0.64	0.08	0.33	-0.03	0.54	0.01	0.71	-0.64	-0.32	-0.08	0.37	-0.05	0.01

Table S32a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for toluene hydroxylation without water W_{903}.

	Energy	ΔE
toluene	-271.377423	-
^{2}CpdI+Tol.	-2996.689045	-0.10
^{4}CpdI+ Tol.	-2996.688888	0.00
$^{2}TS_H$	-2996.661920	16.92
$^{4}TS_H$	-2996.663129	16.16

Table S32b: Group spin densities and group charges for toluene hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.88	0.11	-0.26	-0.26	0.02	-0.48	0.75	-0.65	-0.31	-0.14	0.39	-0.04
$^{4}TS_H$	1.45	0.65	0.06	0.30	-0.04	0.57	0.70	-0.62	-0.32	-0.10	0.41	-0.06

Table S32c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for toluene hydroxylation with water W_{903}.

	Energy	ΔE
toluene	-271.377423	-
^{2}CpdI'+ Tol.	-3073.071886	-0.19
^{4}CpdI'+ Tol.	-3073.071591	0.00
$^{2}TS_H$'	-3073.050926	12.97
$^{4}TS_H$'	-3073.049086	14.12

Table S32d: Group spin densities and group charges for toluene hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.85	-0.03	-0.25	-0.17	0.02	-0.42	0.01	0.73	-0.64	-0.29	-0.13	0.35	-0.44	0.01
$^{4}TS_H$'	1.48	0.60	0.06	0.31	-0.03	0.57	0.01	0.70	-0.67	-0.31	-0.08	0.39	-0.05	0.02

Table S33a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for iPr-probe (*trans*-iso-propyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
dimethyl probe	-466.560131	-
^{2}CpdI+Me2Prob	-3191.871753	-0.01
^{4}CpdI+ Me2Prob	-3191.871596	0.00
$^{2}TS_H$	-3191.847285	15.26
$^{4}TS_H$	-3191.846103	15.99

Table S33b: Group spin densities and group charges for iPr-probe hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
$^{2}TS_H$	1.85	0.07	-0.24	-0.28	0.01	-0.41	0.73	-0.61	-0.31	-0.14	0.34	-0.01
$^{4}TS_H$	1.49	0.68	0.02	0.28	-0.02	0.54	0.70	-0.62	-0.34	-0.10	0.37	-0.01

Table S33c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for iPr-probe (*trans*-iso-propyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
dimethyl probe	-466.560131	-
^{2}CpdI'+ Me2Prob	-3268.254594	-0.19
^{4}CpdI'+ Me2Prob	-3268.254299	0.00
$^{2}TS_H$'	-3268.234849	12.21
$^{4}TS_H$'	-3268.232467	13.67

Table S33d: Group spin densities and group charges for iPr-probe hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
$^{2}TS_H$'	1.89	0.01	-0.27	-0.26	0.01	-0.38	0.00	0.73	-0.65	-0.27	-0.12	0.32	-0.03	0.01
$^{4}TS_H$'	1.50	0.60	0.07	0.32	-0.02	0.52	0.01	0.70	-0.67	-0.30	-0.08	0.36	-0.03	0.02

Table S34a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for reactant cluster of dimethylaniline without water W_{903}.

	Energy	ΔE
dimethylaniline	-365.964994	-
^{2}CpdI+M2Anil.	-3091.276617	-0.10
^{4}CpdI+ M2Anil.	-3091.276459	0.00
$^{2}RC_H$	-3091.281991	-3.47
$^{4}RC_H$	-3091.282435	-3.75

Table S34b: Group spin densities and group charges for reactant cluster of dimethylaniline without water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	**O**	**Por**	**SH**	**R**	**Fe**	**O**	**Por**	**SH**	**R**
$^{2}TS_H$	1.29	0.81	-0.50	-0.56	-0.04	0.77	-0.50	-0.18	-0.12	0.02
$^{4}TS_H$	1.15	0.88	0.43	0.50	0.03	0.77	-0.49	-0.16	-0.13	0.01

Table S34c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for reactant cluster of dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE
dimethylaniline	-365.964994	-
^{2}CpdI'+ M2Anil.	-3167.659457	-0.19
^{4}CpdI'+ M2Anil.	-3167.659162	0.00
$^{2}RC_H$'	-3167.666978	-4.91
$^{4}RC_H$'	-3167.666609	-4.67

Table S34d: Group spin densities and group charges for reactant cluster of dimethylaniline with water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**R**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**R**	**W_{903}**
$^{2}RC_H$'	1.35	0.76	-0.47	-0.50	-0.15	0.01	0.76	-0.56	-0.19	-0.13	0.08	0.04
$^{4}RC_H$'	1.24	0.81	0.36	0.44	0.15	0.01	0.75	-0.55	-0.18	-0.14	0.08	0.04

Table S35a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation without water W_{903}.

	Energy	ΔE	ΔE[a]
dimethylaniline	-365.964994	-	-
^{2}CpdI+M2Anil.	-3091.276617	-0.10	-
^{4}CpdI+ M2Anil.	-3091.276459	0.00	-
^2TS_H	-3091.265026	7.17	1092
^4TS_H	-3091.262435	8.80	12.55

[a] with respect to ^{4}RC.

Table S30b: Group spin densities and group charges for toluene hydroxylation without water W_{903}.

		Fe	O	Por	SH	H'	Me2-H'	N	phenyl
^2TS_H	**ρ**	1.70	0.14	-0.20	-0.12	0.00	-0.19	-0.24	-0.08
	Q	0.73	-0.60	-0.40	-0.19	0.35	0.20	-0.37	0.28
^4TS_H	**ρ**	1.55	0.64	-0.05	0.20	-0.01	0.32	0.24	0.09
	Q	0.71	-0.64	-0.42	-0.14	0.40	0.18	-0.37	0.27

Table S35c: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE	ΔE[a]
dimethylaniline	-365.964994	-	-
^{2}CpdI'+ M2Anil.	-3167.659457	-0.19	-
^{4}CpdI'+ M2Anil.	-3167.659162	0.00	-
^2TS_H'	-3167.657513	1.03	5.70
^4TS_H'	-3167.650565	5.40	10.07

[a] with respect to ^{4}RC'.

Table S35d: Group spin densities and group charges for dimethylaniline hydroxylation with water W_{903}.

		Fe	O	Por	SH	H'	Me2-H'	N	phenyl	W_{903}
^2TS_H'	**ρ**	1.70	0.18	-0.20	-0.09	-0.02	-0.14	-0.33	-0.12	0.01
	Q	0.74	-0.65	-0.41	-0.18	0.33	0.19	-0.34	0.31	0.01
^4TS_H'	**ρ**	1.63	0.57	-0.07	0.17	0.01	0.28	0.30	0.12	0.01
	Q	0.71	-0.69	-0.41	-0.13	0.38	0.20	-0.35	0.29	0.00

Table S36a: B4//B1 single-point energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with constraint dihedral angle: oxygen of water W_{903} *trans* with respect to nitrogen of aniline.

	Energy	ΔE	ΔE[a]
dimethylaniline	-365.964994	-	-
^{2}CpdI'+ M2Anil.	-3167.659457	-0.19	-
^{4}CpdI'+ M2Anil.	-3167.659162	0.00	-
^2TS_H'	-3167.651434	4.85	9.52
^4TS_H'	-3167.647947	7.04	11.71

[a] with respect to ^{4}RC'.

Table S36b: Group spin densities and group charges for dimethylaniline hydroxylation with constraint dihedral angle: oxygen of water W_{903} *trans* with respect to nitrogen of aniline.

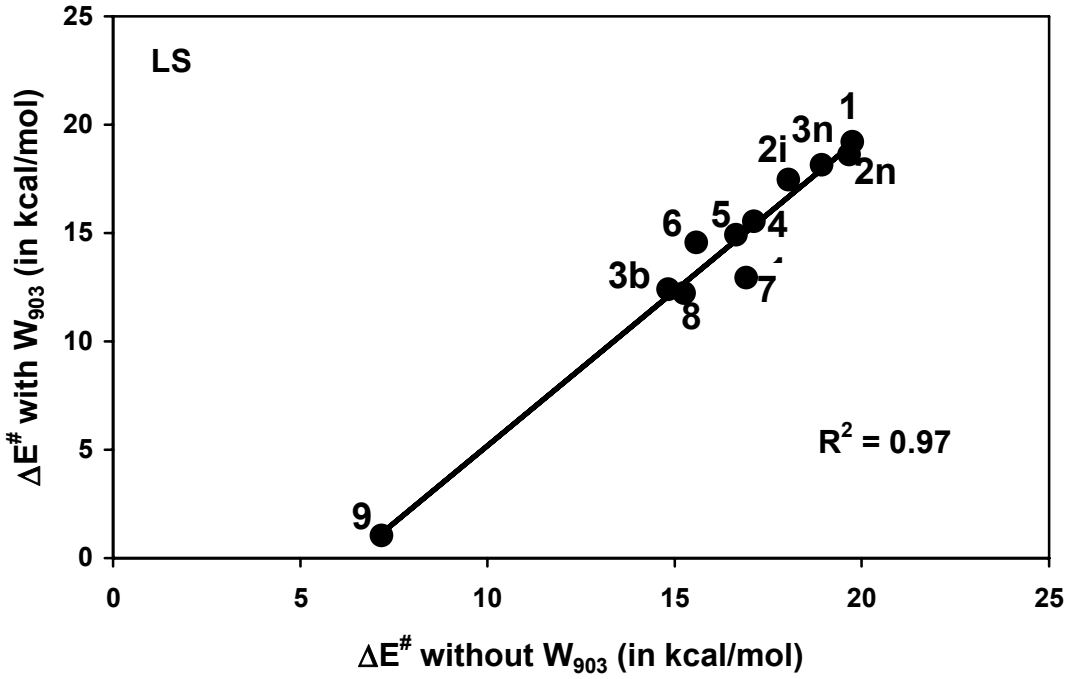
		Fe	O	Por	SH	H'	Me2-H'	N	phenyl	W_{903}
^2TS_H'	**ρ**	1.73	0.14	-0.20	-0.11	-0.01	-0.17	-0.27	-0.11	0.01
	Q	0.73	-0.65	-0.39	-0.17	0.35	0.19	-0.36	0.31	-0.02
^4TS_H'	**ρ**	1.63	0.59	-0.07	0.14	0.00	0.31	0.28	0.11	0.01
	Q	0.69	-0.68	-0.40	-0.12	0.40	0.19	-0.36	0.30	-0.02

Table S37: Effect of water W_{903} on B4//B1 single-point hydrogen abstraction barriers (kcal/mol).

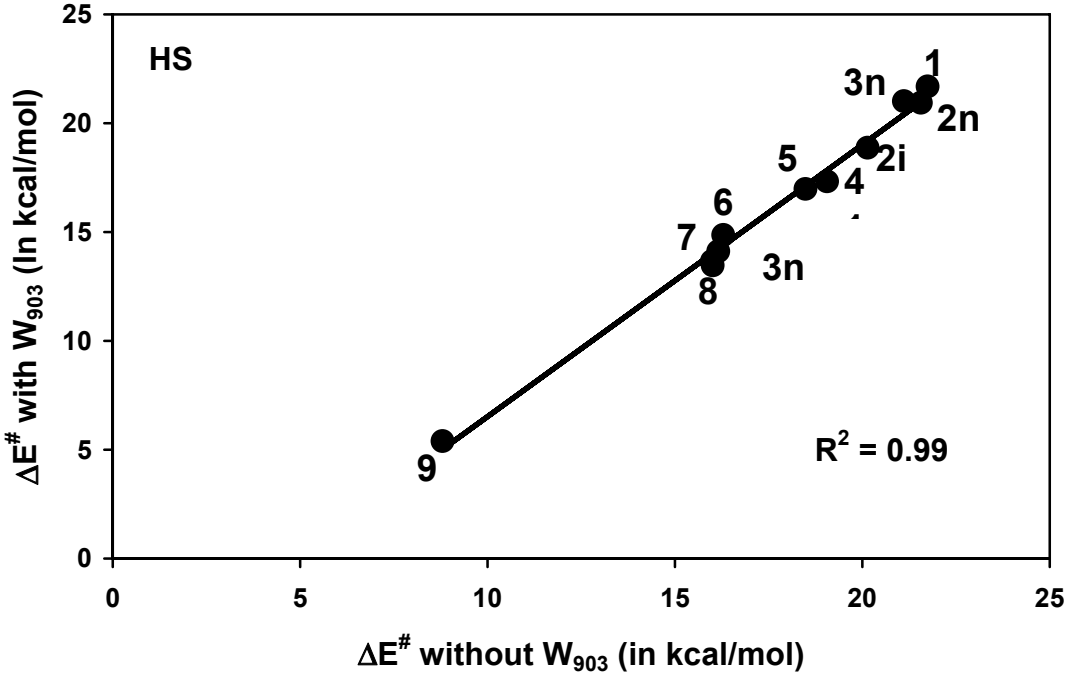
		spin	$\Delta E^{\#}$ without W_{903}	$\Delta E^{\#}$ with W_{903}	$\Delta\Delta E^{\#}$
1	ethane	D	19.67	18.60	1.07
		Q	21.56	20.94	0.62
2n	propane	D	19.76	19.19	0.57
		Q	21.74	21.69	0.05
2i	propane	D	18.04	17.47	0.57
		Q	20.14	18.88	1.26
3n	phenylethane	D	18.93	18.15	0.78
		Q	21.11	21.01	0.10
3b	phenylethane	D	14.83	12.41	2.42
		Q	16.01	13.47	2.54
4	Me-probe	D	17.13	15.52	1.61
		Q	19.06	17.33	1.73
5	camphor	D	16.64	14.90	1.74
		Q	18.48	16.98	1.50
6	propene	D	15.58	14.55	1.03
		Q	16.29	14.87	1.42
7	toluene	D	16.92	12.93	3.99
		Q	16.16	14.12	2.04
8	iPr-probe	D	15.26	12.21	3.05
		Q	15.99	13.67	2.32
9	dimethylaniline	D	7.17	1.03	6.14
		Q	8.80	5.40	3.40
9c	dimethylaniline (**constrained**)	D	7.17	4.85	2.32
		Q	8.80	7.04	1.76

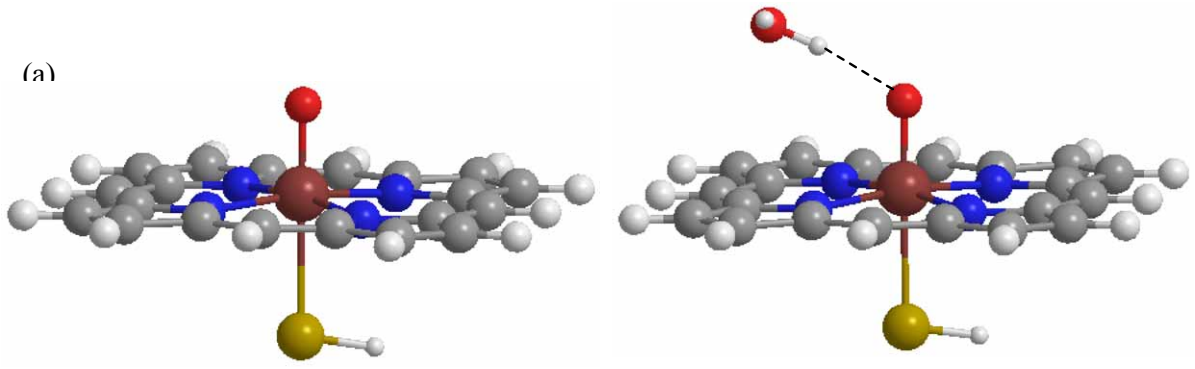
Figure S16: Correlation of B4//B1 single-point hydrogen abstraction barriers without and with water W_{903} in the (a) doublet spin state and (b) quartet spin state.

(a)



(b)





^{2}CpdI (^{4}CpdI) ^{2}CpdI' (^{4}CpdI')

Figure S17: B3LYP/B4 optimised TS geometries for (a) ^{2,4}Cpd I without and (b) ^{2,4}Cpd I' of P450 with water W_{903}.

Table S38a: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 without water W_{903}.

	Energy	ΔE
^{2}CpdI	-2725.314099	-0.14
^{4}CpdI	-2725.313879	0.00

Table S38b: Group spin densities and group charges for ^{2,4}Cpd I of P450 without water W_{903}.

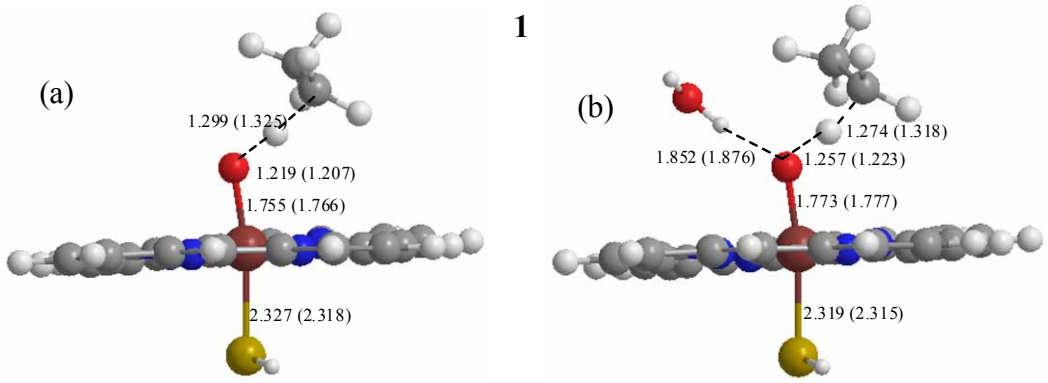
	Spin Density (ρ)				Charge (Q)			
	Fe	**O**	**Por**	**SH**	**Fe**	**O**	**Por**	**SH**
^{2}CpdI	1.24	0.85	-0.52	-0.57	0.75	-0.47	-0.16	-0.12
^{4}CpdI	1.13	0.90	0.43	0.53	0.75	-0.47	-0.15	-0.13

Table S38c: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for ^{2,4}Cpd I of P450 with water W_{903}.

	Energy	ΔE
^{2}CpdI'	-2801.697601	-0.18
^{4}CpdI'	-2801.697317	0.00

Table S38d: Group spin densities and group charges for ^{2,4}Cpd I' of P450 with water W_{903}.

	Spin Density (ρ)					Charge (Q)				
	Fe	**O**	**Por**	**SH**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**W_{903}**
^{2}CpdI'	1.33	0.77	-0.58	-0.53	0.01	0.74	-0.54	-.09	-0.12	0.00
^{4}CpdI'	1.21	0.82	0.48	0.48	0.01	0.73	-0.53	-0.08	-0.12	0.00



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S18: B3LYP/B4 optimised TS geometries for ethane hydroxylation (a) without and (b) with water W_{903}.

Table S39a: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation without water W_{903}.

	Energy	ΔE
ethane	-79.763799	-
^{2}CpdI+ ethane	-2805.077898	-0.14
^{4}CpdI+ ethane	-2805.077678	0.00
^2TS_H	-2805.046626	19.49
^4TS_H	-2805.043108	21.69

Table S39b: Group spin densities and group charges for ethane hydroxylation without water W_{903}.

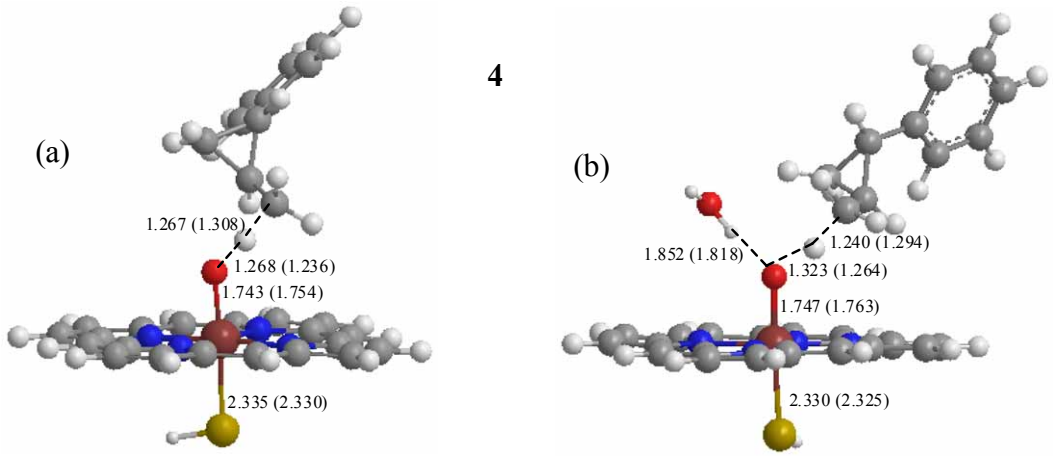
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.76	-0.16	-0.17	0.02	0.04	-0.50	0.64	-0.60	-0.30	-0.09	0.38	-0.03
^4TS_H	1.48	0.70	0.04	0.29	-0.05	0.54	0.65	-0.60	-0.32	-0.05	0.39	-0.06

Table S39c: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for ethane hydroxylation with water W_{903}.

	Energy	ΔE
ethane	-79.763799	-
^{2}CpdI'+ ethane	-2881.461400	-0.18
^{4}CpdI'+ ethane	-2881.461116	0.00
^2TS_H'	-2881.429208	18.10
^4TS_H'	-2881.429208	20.02

Table S39d: Group spin densities and group charges for ethane hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.82	-0.23	-0.18	0.01	0.04	-0.47	0.00	0.65	-0.63	-0.27	-0.06	0.36	-0.04	0.00
^4TS_H'	1.50	0.65	0.06	0.29	-0.04	0.53	0.01	0.65	-0.64	-0.29	-0.03	0.38	-0.07	0.02



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S19: B3LYP/B4 optimised TS geometries for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation (a) without and (b) with water W_{903}.

Table S40a: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation without water W_{903}.

	Energy	ΔE
Newcomb probe	-387.994716	-
^{2}CpdI+New.	-3113.308815	-0.14
^{4}CpdI+ New.	-3113.308595	0.00
^2TS_H	-3113.281528	16.99
^4TS_H	-3113.278077	19.15

Table S40b: Group spin densities and group charges for Me-probe hydroxylation without water W_{903}.

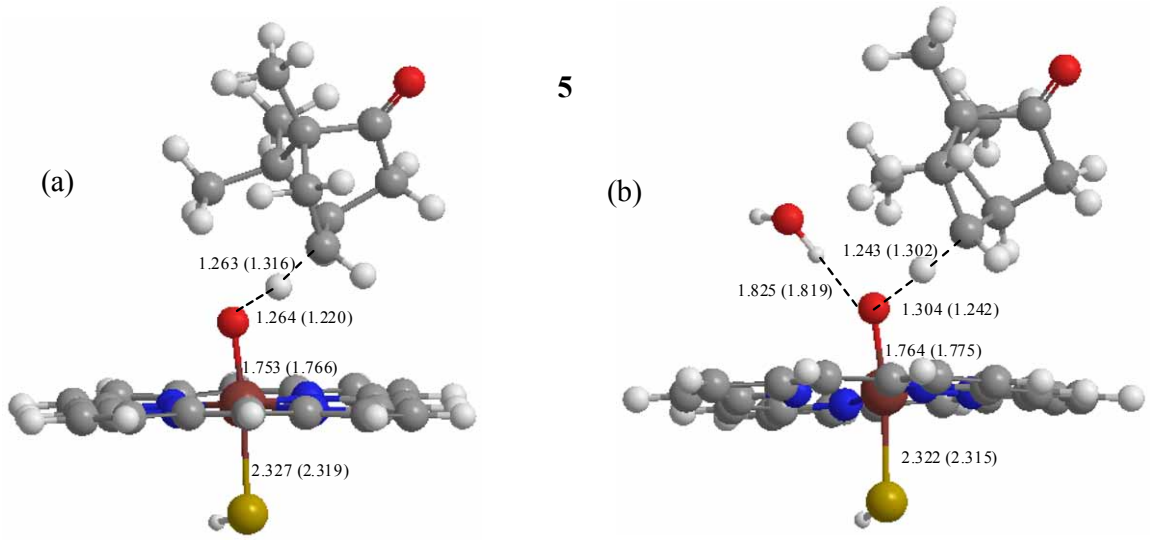
	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.74	-0.03	-0.18	0.01	0.04	-0.47	0.66	-0.59	-0.32	-0.11	0.36	-0.02
^4TS_H	1.45	0.71	0.04	0.29	-0.04	0.54	0.66	-0.60	-0.33	-0.06	0.38	-0.05

Table S40c: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for Me-probe (*trans*-methyl-phenyl-cyclopropane) hydroxylation with water W_{903}.

	Energy	ΔE
Newcomb probe	-387.994716	-
^{2}CpdI'+ New.	-3189.692317	-0.18
^{4}CpdI'+ New.	-3189.692033	0.00
^2TS_H'	-3189.668030	15.06
^4TS_H'	-3189.665218	16.83

Table S40d: Group spin densities and group charges for Me-probe hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.77	-0.14	-0.20	-0.02	0.03	-0.44	0.00	0.69	-0.63	-0.30	-0.08	0.35	-0.02	0.01
^4TS_H'	1.51	0.64	0.06	0.28	-0.03	0.53	0.00	0.69	-0.66	-0.31	-0.05	0.37	-0.05	0.01



^2TS_H (^4TS_H) $^2TS_H'$ ($^4TS_H'$)

Figure S20: B3LYP/B4 optimised TS geometries for camphor hydroxylation (a) without and (b) with water W_{903}.

Table S41a: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation without water W_{903}.

	Energy	ΔE
camphor	-465.606843	-
^{2}CpdI+Cam	-3190.920942	-0.14
^{4}CpdI+Cam	-3190.920722	0.00
^2TS_H	-3190.894510	16.45
^4TS_H	-3190.890911	18.71

Table S41b: Group spin densities and group charges for camphor hydroxylation without water W_{903}.

	Spin Density (ρ)						Charge (Q)					
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**
^2TS_H	1.78	-0.20	-0.18	0.02	0.05	-0.46	0.67	-0.59	-0.30	-0.08	0.35	-0.04
^4TS_H	1.48	0.70	0.05	0.29	-0.05	0.54	0.64	-0.61	-0.30	-0.04	0.38	-0.07

Table S41c: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for camphor hydroxylation with water W_{903}.

	Energy	ΔE
camphor	-465.606843	-
^{2}CpdI'+Cam	-3267.304444	-0.18
^{4}CpdI'+Cam	-3267.304160	0.00
^2TS_H'	-3267.281506	14.22
^4TS_H'	-3267.278156	16.32

Table S41d: Group spin densities and group charges for camphor hydroxylation with water W_{903}.

	Spin Density (ρ)							Charge (Q)						
	Fe	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**	**Fe**	**O**	**Por**	**SH**	**H'**	**R-H'**	**W_{903}**
^2TS_H'	1.82	-0.23	-0.20	-0.01	0.04	-0.43	0.00	0.69	-0.64	-0.28	-0.06	0.34	-0.07	0.02
^4TS_H'	1.51	0.65	0.06	0.28	-0.04	0.53	0.01	0.66	-0.66	-0.27	-0.03	0.37	-0.09	0.02

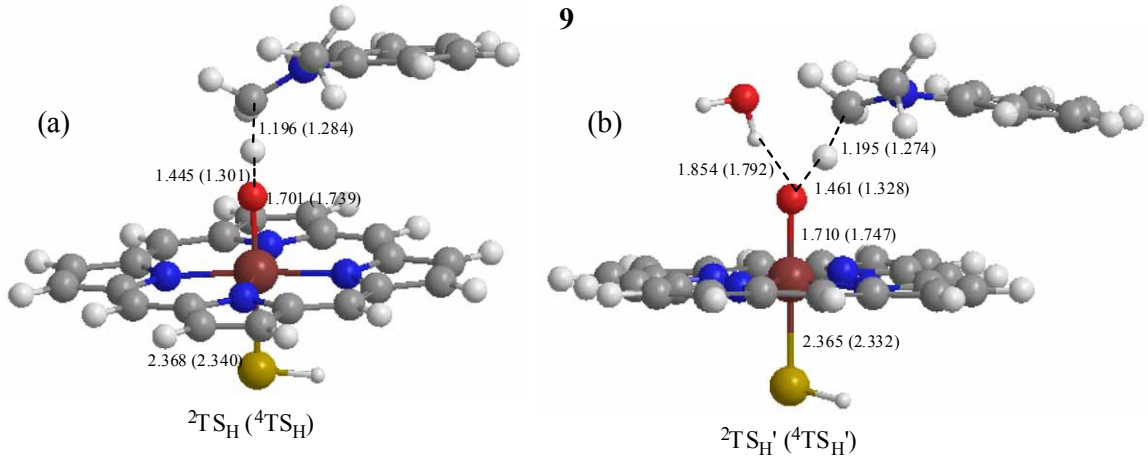


Figure S21: B3LYP/B4 optimised TS geometries for dimethylaniline hydroxylation (a) without and (b) with water W_{903}.

Table S42a: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation without water W_{903}.

	Energy	ΔE
dimethylaniline	-365.965221	-
^{2}CpdI+M2Anil.	-3019.279320	-0.14
^{4}CpdI+ M2Anil.	-3019.279100	0.00
^2TS_H	-3019.268275	6.79
^{4} TS_H	-3019.265126	8.77

Table S42b: Group spin densities and group charges for toluene hydroxylation without water W_{903}.

		Fe	O	Por	SH	H'	Me2-H'	N	phenyl
^2TS_H	ρ	1.63	0.12	-0.22	-0.05	0.00	-0.17	-0.24	0.09
	Q	0.70	-0.58	-0.38	-0.17	0.33	0.19	-0.37	0.27
^{4} TS_H	ρ	1.50	0.69	-0.03	0.23	-0.02	0.30	0.24	0.09
	Q	0.67	-0.62	-0.41	-0.11	0.38	0.18	-0.36	0.27

Table S42c: B3LYP/B4 energies (in hartree), relative energies (kcal/mol) for dimethylaniline hydroxylation with water W_{903}.

	Energy	ΔE
dimethylaniline	-365.965221	-
^{2}CpdI'+ M2Anil.	-3167.662822	-0.17
^{4}CpdI'+ M2Anil.	-3167.662538	0.00
^2TS_H'	-3167.661728	0.51
^{4} TS_H'	-3167.654217	5.22

Table S42d: Group spin densities and group charges for dimethylaniline hydroxylation with water W_{903}.

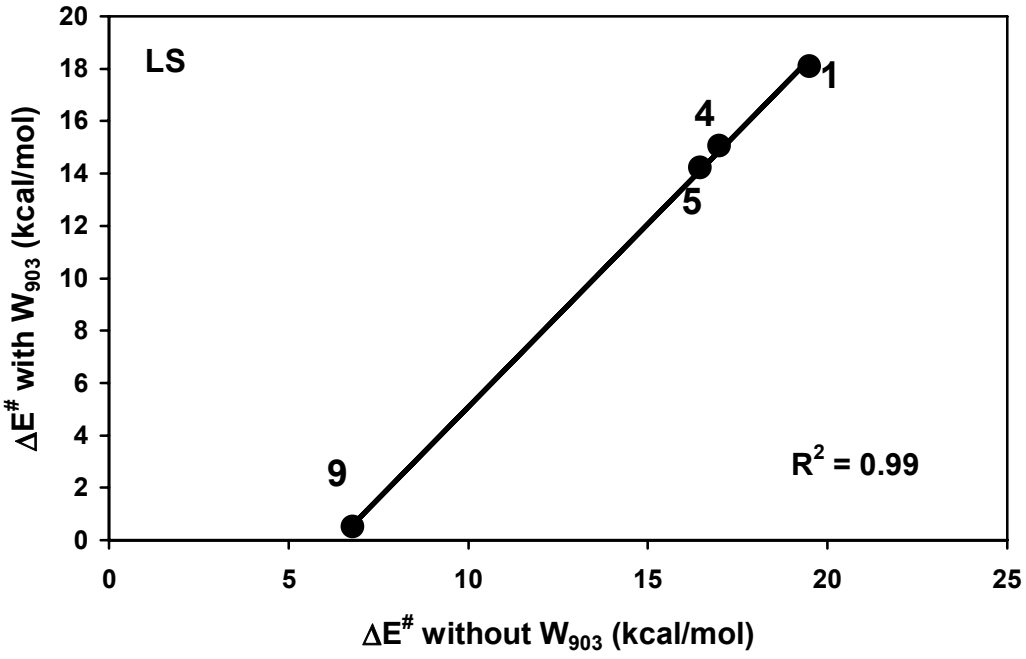
		Fe	O	Por	SH	H'	Me2-H'	N	phenyl	W_{903}
^2TS_H'	ρ	1.66	0.16	-0.19	-0.04	-0.01	-0.14	-0.31	-0.12	0.01
	Q	0.70	-0.63	-0.40	-0.16	0.33	0.18	-0.34	0.30	0.01
^{4} TS_H'	ρ	1.58	0.61	-0.07	0.19	0.00	0.27	0.29	0.12	0.00
	Q	0.68	-0.67	-0.41	-0.10	0.37	0.19	-0.35	0.29	0.00

Table S43: Effect of water W_{903} on B3LYP/B4 hydrogen abstraction barriers (in kcal/mol).

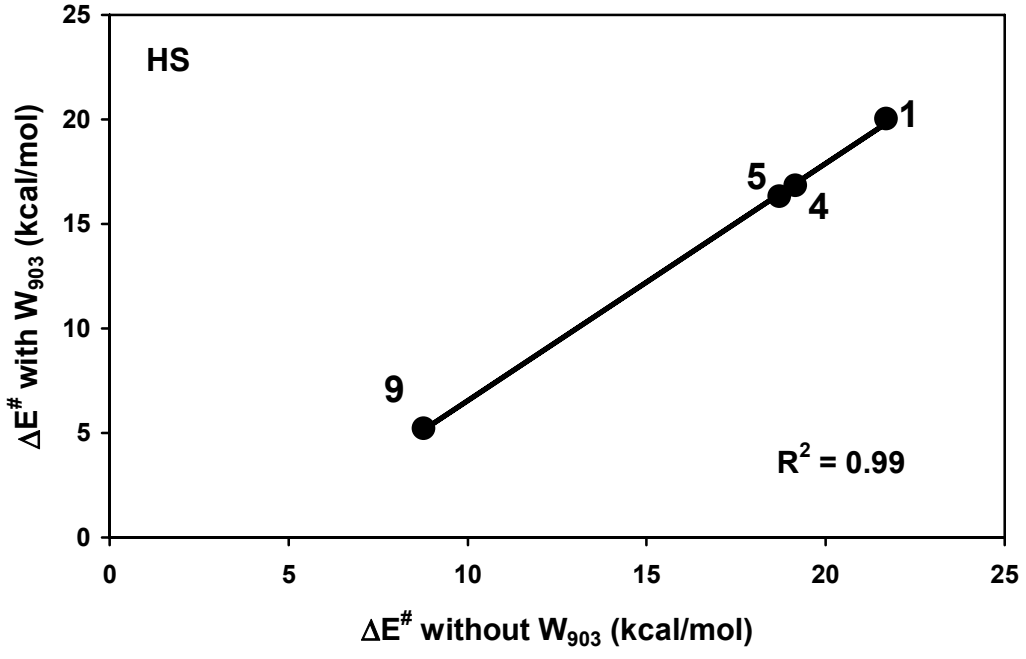
		spin	$\Delta E^{\#}$ without W_{903}	$\Delta E^{\#}$ with W_{903}	$\Delta\Delta E^{\#}$
1	ethane	D	19.49	18.10	1.39
		Q	21.69	20.02	1.67
4	Me-probe	D	16.99	15.06	1.93
		Q	19.15	16.83	2.32
5	camphor	D	16.45	14.22	2.23
		Q	18.71	16.32	2.39
9	dimethylaniline	D	6.79	0.51	6.28
		Q	8.77	5.22	3.55

Figure S22: Correlation of B3LYP/B4 hydrogen abstraction barriers without and with water W_{903} in the (a) doublet spin state and (b) quartet spin state.

(a)



(b)



The Source of Stabilization by W_{903}:

(a) Stabilization Energy by W_{903}:

The stabilization energy is defined as:

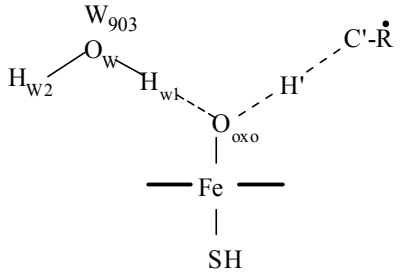
$$E_{stab} = [E_{R1w} - (E_{R1} + E_{w903})]$$

where E_{R1w} and E_{R1} are the total energies of the transition states with and without W_{903}, respectively, and E_{W903} is the total energy of an isolated water molecule.

(b) Electrostatic Interactions with W_{903}:

$$E_{el} = 332 \times \sum_{A,B} \frac{q_A \times q_B}{R_{AB}}$$

where the distance between two point charges R_{AB} is given in Å.



$^{4,2}\mathbf{TS}_{H'}$

We include the interactions between each atom of W_{903} and the oxo ligand (O_{oxo}), the migrating H (H') as well as the carbon atom (H') donating H.

These rough estimates of the electrostatic interaction energies are close to the full B3LYP computed interaction energies. According to the Mulliken charges, W_{903} is almost neutral and should thus exhibit relatively small long-range electrostatic interactions.

The analysis based on the equations given above in sections (a) and (b) are summarized in tables S44 and S45 using B3LYP/B1 and B3LYP/B4 data, respectively.

Table S44: B3LYP stabilization energies and electrostatic interactions of water W_{903} with O_{oxo}, H' and C' using B1 Mulliken charges.

	spin	E_{stab} (kcal/mol)	E_{el}: interaction W_{903} with O_{oxo} & H' (kcal/mol)
ethane	LS	-12.08	-9.47
	HS	-12.38	-10.45
propane (2n)	LS	-11.21	-7.86
	HS	-11.10	-9.05
propane (2i)	LS	-11.22	-8.86
	HS	-12.44	-10.18
phenylethane (3n)	LS	-11.88	-9.59
	HS	-12.67	-10.64
phenylethane (3b)	LS	-13.59	-9.97
	HS	-13.57	-10.11
Me-probe	LS	-13.04	-9.20
	HS	-13.42	-10.05
camphor	LS	-13.26	-11.70
	HS	-13.10	-12.18
propene	LS	-11.94	-8.19
	HS	-12.16	-8.10
toluene	LS	-13.83	-8.81
	HS	-12.91	-9.40
iPr-probe	LS	-13.09	-10.01
	HS	-13.26	-10.50
dimethylaniline	LS	-17.71	-10.03
	HS	-15.33	-10.71
dimethylaniline (**constrained**)	LS	-13.14	-8.70
	HS	-12.32	-8.57

Table S45: B3LYP stabilization energies and electrostatic interactions of water W_{903} with O_{oxo}, H' and C' using B4 Mulliken charges.

	spin	E_{stab} (kcal/mol)	E_{el}: interaction W_{903} with O_{oxo} & H' (kcal/mol)
ethane	LS	-9.89	-8.09
	HS	-10.17	-8.60
Me-probe	LS	-10.42	-11.47
	HS	-10.82	-12.18
camphor	LS	-10.73	-13.09
	HS	-10.89	-13.18
dimethylaniline	LS	-14.78	-12.02
	HS	-12.05	-12.76

Table S46: B3LYP/B1 optimized geometry parameters without water W_{903}.

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_1-C_1
Cpd I	D	1.648	2.602	2.019	-	-	-
	Q	1.652	2.586	2.019	-	-	-
ethane	D	1.764	2.393	2.017	1.194	1.325	174.1
	Q	1.763	2.391	2.018	1.149	1.403	170.3
propane (2n)	D	1.765	2.389	2.017	1.190	1.321	174.2
	Q	1.763	2.389	2.018	1.146	1.406	169.6
propane (2i)	D	1.751	2.414	2.018	1.259	1.271	168.6
	Q	1.756	2.391	2.018	1.186	1.361	166.1
phenylethane (3n)	D	1.764	2.389	2.0188	1.181	1.334	174.8
	Q	1.763	2.385	2.018	1.141	1.411	171.8
phenylethane (3b)	D	1.735	2.423	2.017	1.277	1.250	164.9
	Q	1.742	2.402	2.018	1.224	1.316	163.3
Me-probe	D	1.748	2.399	2.018	1.257	1.274	174.9
	Q	1.752	2.389	2.018	1.184	1.366	170.2
camphor	D	1.762	2.394	2.017	1.233	1.282	173.2
	Q	1.765	2.390	2.018	1.158	1.390	170.5
propene	D	1.724	2.433	2.018	1.315	1.250	172.9
	Q	1.740	2.409	2.019	1.231	1.325	173.3
toluene	D	1.733	2.461	2.018	1.239	1.311	166.1
	Q	1.742	2.405	2.019	1.214	1.341	174.1
iPr-probe	D	1.727	2.469	2.019	1.303	1.251	174.1
	Q	1.744	2.404	2.019	1.239	1.315	169.4
dimethylaniline	D	1.713	2.428	2.020	1.382	1.221	171.3

	Q	1.742	2.387	2.020	1.260	1.307	170.6

table S46 cont. ...

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_1-C_1
dimethylaniline (**RC**)	D	1.653	2.586	2.019	2.407	-	-
	Q	1.656	2.568	2.018	2.615	-	-

Table S47: B3LYP/B1 optimized geometry parameters with water W_{903}.

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_{1W}	O-H_1-C_1
Cpd I'	D	1.656	2.578	2.018	-	-	1.841	-
	Q	1.658	2.557	2.018	-	-	1.842	-
ethane	D	1.782	2.393	2.015	1.248	1.275	1.766	170.1
	Q	1.776	2.424	2.017	1.166	1.379	1.760	167.8
propane (2n)	D	1.773	2.388	2.015	1.261	1.266	1.837	167.2
	Q	1.775	2.408	2.018	1.162	1.383	1.777	168.6
propane (2i)	D	1.755	2.415	2.017	1.340	1.227	1.796	163.6
	Q	1.771	2.410	2.016	1.203	1.343	1.743	162.7
phenylethane (3n)	D	1.781	2.398	2.027	1.240	1.284	1.774	171.5
	Q	1.793	2.452	2.018	1.159	1.385	1.720	168.1
phenylethane (3b)	D	2.443	1.735	2.017	1.355	1.241	1.24	1.772
	Q	2.415	1.751	2.019	1.281	1.299	1.762	162.1
Me-probe	D	1.744	2.400	2.017	1.354	1.222	1.785	165.0
	Q	1.762	2.395	2.017	1.223	1.332	1.734	164.9
camphor	D	1.768	2.406	2.017	1.303	1.241	1.744	171.0
	Q	1.775	2.406	2.018	1.190	1.354	1.722	169.3
propene	D	1.731	2.431	2.016	1.375	1.226	1.831	163.9
	Q	1.750	2.412	2.017	1.285	1.292	1.833	165.5

table S47 contd. ...

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_{1W}	O-H_1-C_1
toluene	D	1.736	2.419	2.016	1.320	1234	1.808	166.1
	Q	1.752	2.402	2.018	1.253	1.311	1.784	166.2
iPr-probe	D	1.737	2.455	2.014	1.371	1.227	1.809	167.2
	Q	1.762	2.425	2.019	1.260	1.301	1.787	166.6
dimethylaniline	D	1.720	2.412	2.021	1.450	1.192	1.760	168.8
	Q	1.749	2.375	2.021	1.302	1.285	1.713	164.4
dimethylaniline (**RC**)	D	1.659	2.549	2.019	3.198	-	1.742	-
	Q	1.661	2.536	2.018	3.113	-	1.748	-
dimethylaniline (**constrained**)	D	1.724	2.417	2.013	1.415	1.213	1.824	177.1
	Q	1.758	2.377	2.017	1.264	1.307	1.841	177.4

Table S48: B3LYP/B4 optimized geometry parameters without water W_{903}.

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_1-C_1
Cpd I	D	1.630	2.562	2.021	-	-	-
	Q	1.632	2.523	2.020	-	-	-
ethane	D	1.755	2.327	2.019	1.219	1.299	170.5
	Q	1.766	2.318	2.019	1.207	1.325	169.0
Me-probe	D	1.743	2.335	2.020	1.268	1.267	170.3
	Q	1.754	2.330	2.019	1.236	1.308	167.9
camphor	D	1.753	2.327	2.019	1.264	1.263	168.0
	Q	1.766	2.319	2.018	1.220	1.316	168.1
dimethylaniline	D	1.701	2.368	2.022	1.445	1.196	170.7
	Q	1.739	2.340	2.021	1.301	1.284	168.5

Table S49: B3LYP/B4 optimized geometry parameters with water W_{903}.

		Fe-O	Fe-S	Fe-N	O-H_1	H_1-C_1	O-H_{1W}	O-H_1-C_1
Cpd I'	D	1.638	2.544	2.020	-	-	1.880	-
	Q	1.640	2.533	2.020		-	1.879	-
ethane	D	1.773	2.319	2.017	1.257	1.274	1.852	168.4
	Q	1.777	2.315	2.017	1.223	1.318	1.876	168.4
Me-probe	D	1.747	2.330	2.018	1.323	1.240	1.852	164.0
	Q	1.763	2.325	2.017	1.264	1.294	1.818	164.8
camphor	D	1.764	2.322	2.017	1.304	1.243	1.825	172.9
	Q	1.775	2.315	2.017	1.242	1.302	1.819	171.0
dimethylaniline	D	1.710	2.365	2.022	1.461	1.195	1.854	171.2
	Q	1.747	2.332	2.022	1.328	1.274	1.792	163.3

Table S50: B3LYP energy lowerings (kcal/mol) and net charge of substrate in the transition state.

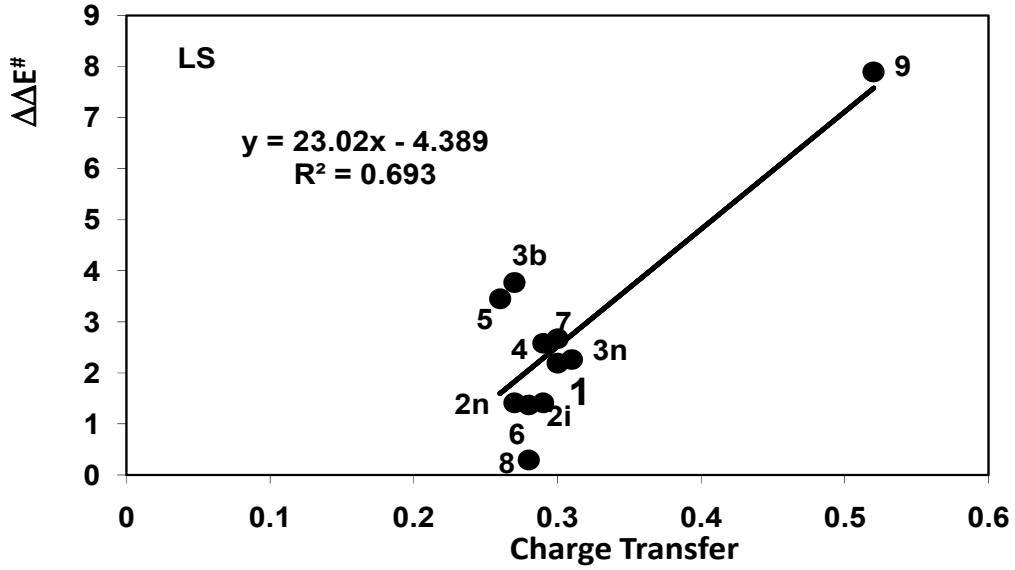
		B3LYP/B1		B3LYP/B4//B1		B3LYP/B4	
		$\Delta\Delta E^{\#}$	charge	$\Delta\Delta E^{\#}$	charge	$\Delta\Delta E^{\#}$	charge
1.Ethane	D	2.19	0.30	1.07	0.32	1.39	0.32
	Q	2.57	0.30	0.62	0.36	1.67	0.31
2n. Propane	D	1.41	0.29	0.55	0.34	-	-
	Q	1.29	0.33	0.05	0.41	-	-
2i. Propane	D	1.41	0.27	0.57	0.28	-	-
	Q	2.63	0.31	1.26	0.35	-	-
3n. Phenylethane	D	2.26	0.31	0.78	0.33	-	-
	Q	2.86	0.29	0.10	0.34	-	-
3b. Phenylethane	D	3.77	0.27	2.42	0.29	-	-
	Q	3.76	0.28	2.54	0.30	-	-
4. Me-Probe	D	2.58	0.29	1.61	0.32	1.93	0.33
	Q	4.26	0.33	1.73	0.38	2.32	0.32
5. Camphor	D	3.45	0.26	1.74	0.26	2.23	0.27
	Q	3.30	0.29	1.50	0.36	2.39	0.28
6. Propene	D	1.37	0.28	1.03	0.38	-	-
	Q	1.80	0.29	1.42	0.32	-	-
7. Toluene	D	2.67	0.30	3.99	0.32	-	-
	Q	3.01	0.30	2.04	0.34	-	-
8. iPr-probe	D	0.29	0.28	3.05	0.29	-	-
	Q	1.41	0.30	2.32	0.33	-	-
9. Dimethylaniline	D	7.90	0.52	6.14	0.50	6.28	0.48
	Q	5.52	0.51	3.40	0.52	3.55	0.50
9c. Dimethylaniline constrained	D	2.95	0.51	2.32	0.49	-	-
	Q	2.51	0.53	1.76	0.51	-	-

Table S51: B3LYP/B1 energy lowerings and ionization potentials of the substrates (kcal/mol).

		B1: LACVP	
		$\Delta\Delta E^{\#}$	IP
1.Ethane	D	2.19	265.1
	Q	2.57	
2n. Propane	D	1.41	251.1
	Q	1.29	
2i. Propane	D	1.41	251.1
	Q	2.63	
3n. Phenylethane	D	2.26	193.5
	Q	2.86	
3b. Phenylethane	D	3.77	193.5
	Q	3.76	
4. Me-probe	D	2.58	175.6
	Q	4.26	
5. Camphor	D	3.45	193.4
	Q	3.30	
6. Propene	D	1.37	215.9
	Q	1.80	
7. Toluene	D	2.67	195.0
	Q	3.01	
8. iPr-probe	D	0.29	173.3
	Q	1.41	
9. Dimethylaniline	D	7.90	156.0
	Q	5.52	

Figure S23: Correlation between the B3LYP/B1 barrier lowering for hydrogen abstraction in the presence of water W_{903} and the net charge on the substrate in the transition state of the (a) doublet and (b) quartet.

(a)



(b)

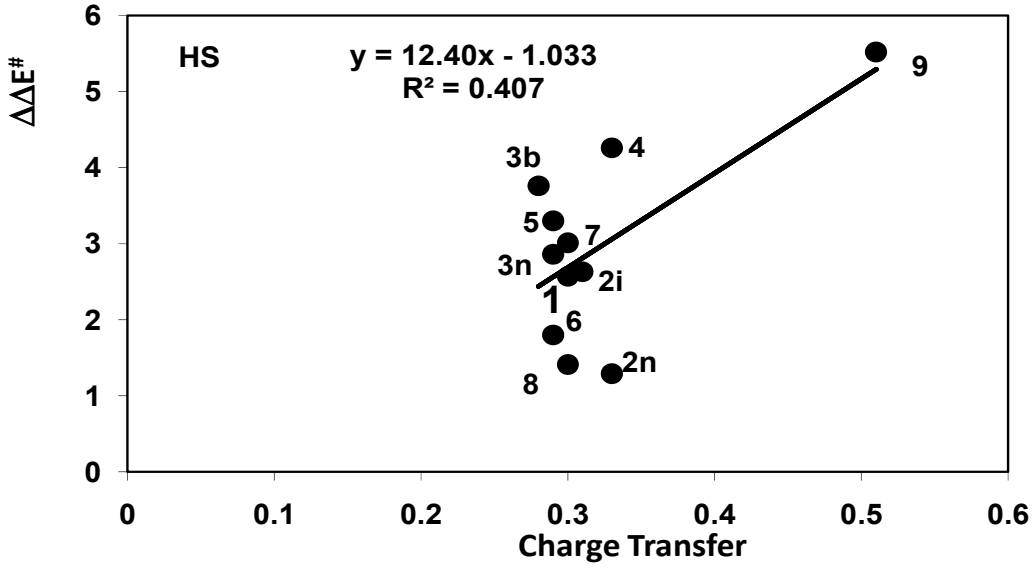
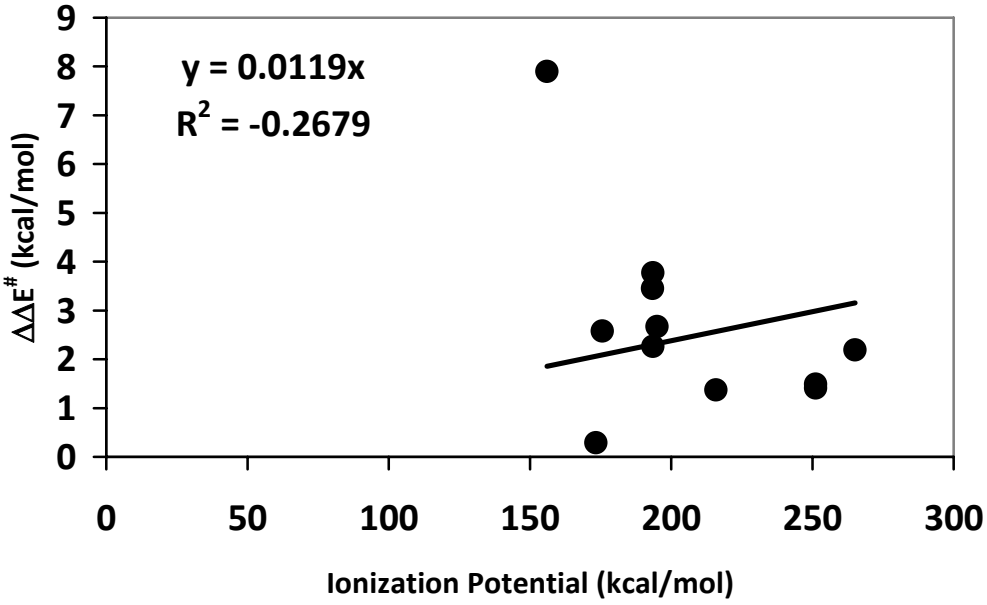


Figure S24: Correlation between the B3LYP/B1 barrier lowering for hydrogen abstraction in the presence of water W_{903} and the ionization potential of the substrate: (a) doublet and (b) quartet.

(a)



(b)