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Supporting Information

Formation of the Active Species of Cytochrome P450 Using Iodosylbenzene: A Case for Spin-Selective Reactivity

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Supporting information

Methods: Comments about the Accuracy of B3LYP

Part 1: Reaction between Heme and Iodosylbenzene

Part 2: Reaction between H_2O-Heme and Iodosylbenzene

Part 3: Reaction between Heme and *N*,*N*-dimethylaniline-*N*-oxide

Part 4: Theoretical KIE calculations

Part 5: Experimental section

Methods

Optimizations have been done on B3LYP/LACVP level, and single point LACV3P*+ on the optimized geometry where indicated (ERMLER2*+ on iodine). Frequency and single point solvent calculations were also done on the optimized geometry using LACVP. Spin and charge values are taken from big basis set calculations. $<S^2>$ values are from LACVP calculations.

Remarks about the accuracy of B3LYP

As can be seen from the extensive data in the text and elsewhere in the literature, UB3LYP predicts the correct ground state for *the systems of this study*. Here are a few additional comments:

- Plenty of results show that B3LYP does as well as good level CI calculations and accords with experiment, as long as one includes **the environment effect** (solvent, enzyme, etc). To mention but a few results:

    a. B3LYP gives spin states ordering for Compound I in line with experimental results for chloroperoxidase (Green, M. T. *JACS* **1999**, *121*, 7939). We recently showed that the method does extremely well for the state ordering and spectroscopic parameters Cpd I of HRP (Shaik, S. et al, *JACS* **2005**, 127, 13611). Thiel and coworkers have shown that B3LYP for Compound I of P450 gives results at pair with good CI calculations (J. Schöneboom et al, *JACS* **2005**, *127*, 5840). To cite from this later work, "DDCI2 calculations [of Cpd I] yields doublet quartet splitting of [Cpd I of P450],… *which is in excellent agreement with the B3LYP value*".

    b. Furthermore, B3LYP does very well for the spin states of the pentaocordinated complexes of P450, for both Fe(II) and Fe(III) electromers. The performance of B3LYP in these complexes is so good, that the results allow to assign the electronic structure of the Fe(II)-pentacoodinated complex with great confidence in terms of spin state and a specific orbital occupancy (Altun, A.; Thiel, W. *JPC B.* **2005**, *109*, 1268); to quote the

authors, "*B3LYP correctly predicts the experimental ground state of the pentacoordinated complex*".

c. B3LYP predicts correctly the spin-state ordering of the resting state of P450 and the spin-equilibrium between the various spin states (Thiel, W. et al, *JPC B*, **2004**, 108, 7468, see also Shaik, S. et al *JACS*. **2005**, *127*, 13007). The same applies to the product state during camphor hydroxylation (Thiel et al, *JPC B*, **2004**, *108*, 10083; see also Shaik, S. et al *JACS* **2005**, *127*, 13007); here too, B3LYP does well, predicting small gaps between the low-spin and the high spin states, in accord with experiment.

d. A review on spin state ordering in a variety of iron porphyrins and related compound shows that "the B3LYP,.., and t-HCTH-hybrid functionals are able to provide a satisfactory description of all the systems considered" (M.-S. Liao, *J. Comput. Chem.* **2006**, *27*, 1577. A recent experimental-B3LYP theoretical verification of spin state ordering in a ferric complex: Gomes-Galleno et al, *Inorg. Chem.* **2006**, *45*, 5321.

Part 1

Reaction between Heme and Iodosylbenzene

In this summary, the five different stages of the reaction are named as below:

Heme + OIPh: Heme and Iodosylbenzene, uncomplexed.
1: Heme and Iodosylbenzene, complexed.
TS1: Transition state between 1 and 2.
2: Compound I and Iodobenzene, complexed.
Cpd I + IPh: Compound I and Iodobenzene, uncomplexed.

Structures

Heme + OIPh: Heme and Iodosylbenzene, uncomplexed.

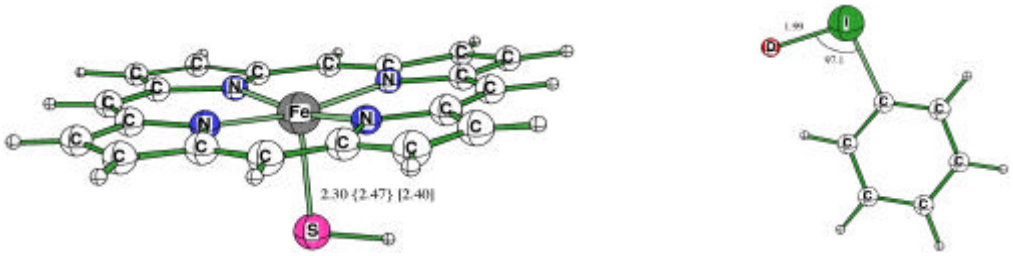


Figure S1: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S1: Valence orbitals of heme and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \sigma^*_{z^2}, \pi^*_{yz})$	$\alpha(\delta, \sigma^*_{xy}, \pi^*_{yz}, \pi^*_{xz}, \sigma^*_{z^2})$
<S^2>	0.98	3.79	8.77

Table S2: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.32	2.58	4.11	-0.01	-0.14	0.08
Porphyrin	-0.18	-0.05	0.44	-0.02	0.23	-0.07
S	-0.15	0.47	0.45	-0.07	-0.21	-0.14

Table S3: Coordinates in xyz-format.

39
Doublet Heme
Fe 0.029101 -0.289864 -0.013422
N -0.015310 0.008973 1.968029
N 2.007337 0.050991 -0.020650
N -1.976384 -0.248239 -0.027560
N 0.045497 -0.192432 -2.016361
C -1.129398 0.047105 2.804124
C 2.858333 0.131421 -1.119438
C 1.086905 0.070372 2.815541
C 2.836954 0.104124 1.094789
C -2.839407 -0.181655 1.064156
C 1.147542 -0.074543 -2.859268
C -2.794981 -0.436094 -1.137013
C -1.046380 -0.379680 -2.858638
C -0.713482 0.146291 4.183540
C 4.230046 0.248917 -0.681239
C 0.652237 0.154199 4.190799
C 4.217651 0.225329 0.683595
C -4.208502 -0.321058 0.625921
C 0.732860 -0.172243 -4.239525
C -4.180594 -0.484272 -0.729713
C -0.618349 -0.366958 -4.239104
H -1.388961 0.199263 5.024852
H 5.078951 0.335738 -1.343360
H 1.317531 0.218451 5.039297
H 5.054871 0.291777 1.362785
H -5.066943 -0.296683 1.281185
H 1.400294 -0.101570 -5.085745
H -5.012327 -0.617045 -1.405922
H -1.278722 -0.485003 -5.085658
C -2.445523 -0.031999 2.382708
C 2.457427 0.085379 -2.442963
C -2.361826 -0.512276 -2.449727
C 2.410827 0.096476 2.411198
H -3.220706 0.004411 3.140291
H 3.224197 0.160466 -3.206241
H -3.114315 -0.651458 -3.218493
H 3.169748 0.149555 3.184258
S 0.183036 -2.582999 0.129418
H -0.805174 -2.780125 1.075767

39
Quartet heme
Fe 0.030024 -0.311003 -0.006536
N -0.006419 -0.001584 1.979090
N 2.005671 0.108259 -0.005872
N -1.986453 -0.193554 -0.032320
N 0.034374 -0.201858 -2.012288
C -1.124635 -0.006490 2.810798
C 2.852810 0.141156 -1.108774
C 1.092520 0.119672 2.827589
C 2.834139 0.218964 1.106326
C -2.838804 -0.167729 1.066901
C 1.147383 -0.137839 -2.846360
C -2.812615 -0.325398 -1.143779
C -1.062136 -0.344135 -2.858432
C -0.713829 0.099743 4.188559
C 4.222924 0.292644 -0.676736
C 0.651874 0.174419 4.199256
C 4.211762 0.337762 0.688186
C -4.212579 -0.267324 0.631282
C 0.737351 -0.247689 -4.224880
C -4.196064 -0.367096 -0.730592
C -0.623718 -0.377340 -4.232164
H -1.391845 0.119353 5.029002
H 5.071455 0.349548 -1.342697
H 1.310503 0.268039 5.050313
H 5.049124 0.440227 1.362838
H -5.066151 -0.265143 1.293287
H 1.412487 -0.224614 -5.067740
H -5.033350 -0.462567 -1.406122
H -1.282269 -0.480681 -5.082095
C -2.441580 -0.083261 2.389490
C 2.457793 0.023946 -2.429477
C -2.385781 -0.408444 -2.457152
C 2.414197 0.212827 2.424669
H -3.214877 -0.077285 3.149583
H 3.228205 0.058785 -3.191672
H -3.140912 -0.518511 -3.227440
H 3.170857 0.302064 3.196206
S 0.218104 -2.769818 0.042064
H 0.202745 -2.921563 1.415428

39
Sextet heme
Fe 0.043194 -0.495198 0.002414
N -0.014337 0.068769 2.018493
N 2.045075 0.066794 -0.010701
N -2.027426 -0.247538 -0.030375
N 0.023331 -0.163113 -2.064976
C -1.135282 0.067187 2.837073
C 2.877899 0.104548 -1.122823
C 1.086340 0.238343 2.846929
C 2.857043 0.233913 1.104733
C -2.867187 -0.205453 1.077550
C 1.139717 -0.090651 -2.886533
C -2.846618 -0.325098 -1.151364
C -1.082639 -0.253069 -2.898992
C -0.723611 0.241860 4.215639
C 4.246453 0.283267 -0.688773
C 0.640372 0.346890 4.221554
C 4.233567 0.362799 0.678431
C -4.242916 -0.281398 0.637247
C 0.719428 -0.136642 -4.272635
C -4.230121 -0.354171 -0.730836
C -0.645014 -0.235899 -4.280516
H -1.397747 0.281206 5.059008
H 5.098587 0.346887 -1.349643
H 1.293052 0.488057 5.070850
H 5.073107 0.503669 1.343276
H -5.101285 -0.268466 1.293217
H 1.388081 -0.094219 -5.119942
H -5.075689 -0.412463 -1.400509
H -1.302952 -0.290141 -5.135713
C -2.449285 -0.072895 2.399731
C 2.456033 0.019461 -2.447307
C -2.404784 -0.338861 -2.472592
C 2.410447 0.301417 2.422159
H -3.224059 -0.055739 3.159267
H 3.226119 0.064127 -3.210600
H -3.166153 -0.403430 -3.243206
H 3.166170 0.435077 3.189340
S 0.283213 -2.878745 0.141760
H -1.061106 -3.194900 0.144133

13
PhIO
C 1.415409 0.120265 0.004033
C 0.782171 1.372081 0.005360
C -0.608723 1.395945 0.006898
C -1.393847 0.251012 0.006828
C -0.745443 -0.991273 0.005825
C 0.653989 -1.055311 0.004433
H 2.499551 0.070310 0.002652
H 1.370352 2.284324 0.005060
H -2.478269 0.350579 0.007460
H -1.333536 -1.903329 0.006127
H 1.151801 -2.019380 0.003613
I -1.749918 3.249734 0.009598
O -3.557073 2.426989 -0.003127

1: Heme and Iodosylbenzene, complexed.

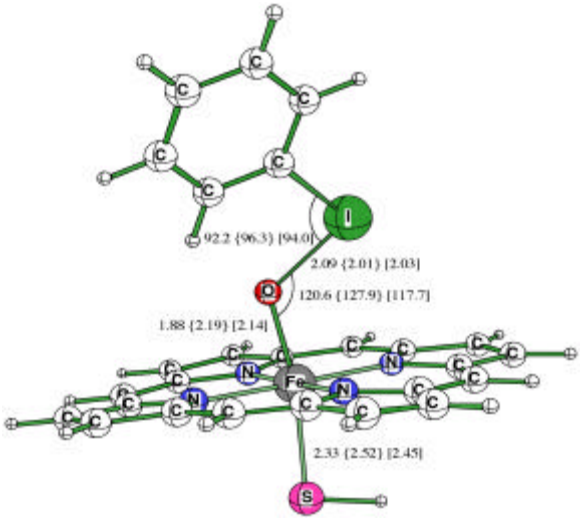


Figure S2: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S4: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{yz}, \pi^*_{xz}, \sigma^*_{z^2}, \sigma^*_{xy})$
<S^2>	0.81	3.82	8.78

Table S5: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.07	2.63	4.13	-0.05	0.04	0.16
O	0.06	0.02	0.07	-0.22	-0.21	-0.16
S	0.03	0.42	0.43	-0.25	-0.29	-0.27
Porphyrin	-0.12	-0.09	0.37	-0.05	-0.16	-0.27
I	-0.04	0.03	0.00	0.40	0.44	0.33
Ph	0.00	0.00	0.00	0.08	0.09	0.09

Table S6: Coordinates in xyz-format.

52			
Doublet			
Fe	0.026950	1.840844	-0.260725
N	0.449029	1.530855	1.694523
N	1.963811	1.625646	-0.761422
N	-1.917015	2.095377	0.244575
N	-0.385137	2.208178	-2.193211
C	-0.435076	1.487144	2.758386
C	2.521940	1.597299	-2.032245
C	1.708965	1.319651	2.225756
C	3.002420	1.370840	0.122433
C	-2.488152	1.974211	1.498512
C	0.470543	2.093523	-3.289888
C	-2.943689	2.424561	-0.619047
C	-1.646152	2.488023	-2.718537
C	0.290398	1.244392	3.989795
C	3.941210	1.331863	-1.939531
C	1.612305	1.147513	3.663061
C	4.238440	1.200509	-0.612668
C	-3.913044	2.232145	1.417373
C	-0.264274	2.334543	-4.509644
C	-4.193575	2.515340	0.112751
C	-1.562775	2.583934	-4.158188
H	-0.167318	1.162914	4.964954
H	4.608223	1.257247	-2.786271
H	2.453038	0.965662	4.317088
H	5.196821	0.993624	-0.158527
H	-4.591029	2.199586	2.257995
H	0.166633	2.308679	-5.500185
H	-5.148003	2.758474	-0.331071
H	-2.400430	2.798745	-4.806149
C	-1.806066	1.674786	2.667570
C	1.825257	1.804119	-3.214299
C	-2.818686	2.613611	-1.987950
C	2.889697	1.253020	1.500236
H	-2.384133	1.606985	3.582987
H	2.379893	1.742438	-4.144426
H	-3.722611	2.846941	-2.541010
H	3.802091	1.060446	2.055414
O	0.250323	3.639461	0.228968
S	-0.348260	-0.449982	-0.497288
H	-0.115006	-0.542264	-1.856765
C	2.963098	6.105546	2.595367
C	3.713825	7.244266	2.280913
C	3.687071	7.767431	0.982638
C	2.909073	7.154747	-0.009295
C	2.174785	6.021994	0.337563
C	2.178002	5.477907	1.617410
H	2.981963	5.698315	3.600871
H	4.317697	7.723905	3.044064
H	4.267684	8.649940	0.734527
H	2.888627	7.561241	-1.014949
I	0.954942	5.040111	-1.153559
H	1.584638	4.596070	1.833848

52			
Quartet			
Fe	0.053785	1.724344	-0.301513
N	0.441979	1.508946	1.660020
N	2.035661	1.710181	-0.699087
N	-1.918157	1.853214	0.097109
N	-0.318309	2.145161	-2.253292
C	-0.490043	1.379577	2.679175
C	2.633835	1.778747	-1.949898
C	1.690276	1.383930	2.252779
C	3.063054	1.538649	0.214796
C	-2.524123	1.674600	1.329332
C	0.603303	2.141892	-3.292180
C	-2.937200	2.117382	-0.805855
C	-1.562709	2.345193	-2.837682
C	0.191897	1.176661	3.938694
C	4.067688	1.645556	-1.811202
C	1.533180	1.184933	3.677682
C	4.332456	1.502472	-0.478037
C	-3.958601	1.811794	1.191998
C	-0.077765	2.361978	-4.548056
C	-4.212391	2.090405	-0.121135
C	-1.410678	2.493121	-4.268335
H	-0.303683	1.043892	4.889425
H	4.767025	1.660414	-2.633945
H	2.351003	1.054303	4.372366
H	5.290965	1.374594	0.004000
H	-4.664051	1.712371	2.004133
H	0.410277	2.403558	-5.510947
H	-5.167242	2.261467	-0.597536
H	-2.225489	2.661466	-4.958114
C	-1.865705	1.440866	2.527589
C	1.972905	1.968791	-3.153498
C	-2.776495	2.351379	-2.163474
C	2.906885	1.400661	1.587223
H	-2.473562	1.317289	3.417061
H	2.574272	1.988992	-4.056005
H	-3.673104	2.524029	-2.748891
H	3.805144	1.270336	2.182055
O	0.137441	3.830915	0.294322
S	-0.128022	-0.752925	-0.701156
H	-1.323680	-0.721592	-1.394055
C	3.677260	5.741537	2.200343
C	4.427250	6.868913	1.843864
C	4.096718	7.602114	0.697522
C	3.009541	7.215269	-0.099145
C	2.284691	6.091356	0.289148
C	2.586381	5.338703	1.417653
H	3.934114	5.170871	3.086947
H	5.268223	7.175026	2.456464
H	4.678045	8.474426	0.417651
H	2.752129	7.784476	-0.986852
I	0.567755	5.425825	-0.856290
H	1.984061	4.469988	1.667057

52			
Sextet			
Fe	0.074744	1.635852	-0.330530
N	0.505692	1.399858	1.678420
N	2.063916	1.287569	-0.829653
N	-1.870753	2.228861	0.149468
N	-0.241977	2.348471	-2.290277
C	-0.391183	1.519540	2.723628
C	2.637984	1.368229	-2.083034
C	1.724437	0.998348	2.194362
C	3.044838	0.898211	0.063794
C	-2.415382	2.221334	1.420455
C	0.646647	2.202334	-3.350674
C	-2.845181	2.662079	-0.728388
C	-1.478498	2.694486	-2.827990
C	0.295461	1.180022	3.959369
C	4.036923	0.990037	-1.981942
C	1.589704	0.860026	3.635409
C	4.286243	0.702106	-0.665282
C	-3.803525	2.641884	1.334153
C	-0.042401	2.524857	-4.584544
C	-4.067558	2.909811	0.016053
C	-1.341552	2.823722	-4.265524
H	-0.160742	1.182723	4.939558
H	4.731176	0.960205	-2.809507
H	2.383220	0.552242	4.302371
H	5.221310	0.391293	-0.220730
H	-4.478130	2.724065	2.175225
H	0.408856	2.502854	-5.566368
H	-4.995900	3.252314	-0.416957
H	-2.142970	3.089525	-4.939854
C	-1.734499	1.885216	2.596725
C	1.973876	1.777396	-3.244727
C	-2.661579	2.856890	-2.102258
C	2.880450	0.757163	1.446427
H	-2.313160	1.925859	3.515500
H	2.546941	1.749973	-4.166534
H	-3.535861	3.160601	-2.669348
H	3.756917	0.437845	2.003239
O	0.706296	3.537400	0.412683
S	-0.567971	-0.688209	-0.741584
H	-1.816449	-0.652318	-0.151017
C	3.181956	6.537628	2.463360
C	3.471824	7.870875	2.150223
C	2.982995	8.438087	0.967142
C	2.203915	7.673548	0.086807
C	1.938787	6.347946	0.425429
C	2.404455	5.757455	1.595611
H	3.558316	6.098058	3.381382
H	4.076385	8.467216	2.825869
H	3.202005	9.472739	0.724285
H	1.824357	8.114909	-0.829058
I	0.779014	5.087277	-0.897899
H	2.157704	4.723027	1.811799

TS1: Transition state between **1** and **2**.

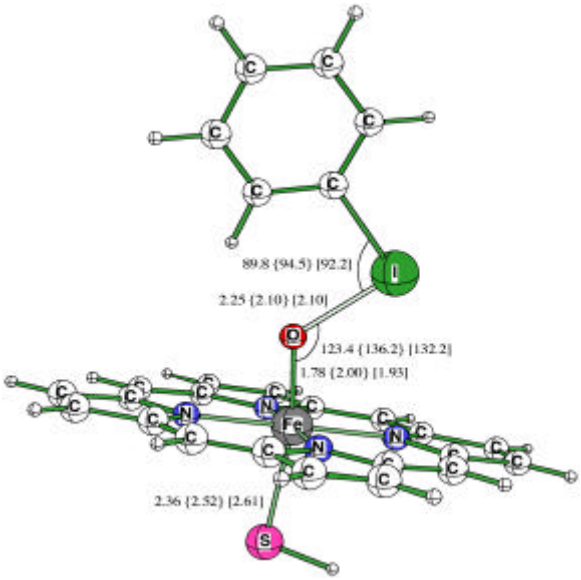


Figure S3: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S7: Valence orbitals, imaginary frequencies and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
Frequency	i103.43 cm^{-1}	i223.79 cm^{-1}	i184.58 cm^{-1}
<S^2>	0.90	3.86	8.88

Table S8: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.26	2.49	4.08	0.06	0.09	0.32
O	0.11	0.11	0.08	-0.31	-0.23	-0.24
S	-0.03	0.38	0.55	-0.26	-0.31	-0.29
Porphyrin	-0.16	-0.12	0.42	0.05	-0.07	-0.33

	Spin			***Charge***		
I	-0.19	0.14	-0.13	0.26	0.35	0.37
Ph	0.00	0.00	0.00	0.09	0.08	0.06

Comments: In the case of the sextet, the product after the **TS1** has the S....Fe bond broken. All attempts to obtain a product with the Fe....S bond intact failed.

Table S9: Coordinates in xyz-format.

52			
Doublet			
Fe	0.158334	1.758669	-0.269477
N	0.591052	1.352812	1.672892
N	2.025303	1.232188	-0.822889
N	-1.734011	2.226489	0.276657
N	-0.270720	2.156122	-2.180663
C	-0.251731	1.470755	2.764428
C	2.560696	1.216835	-2.100434
C	1.807201	0.911745	2.162501
C	3.031402	0.793215	0.023524
C	-2.263475	2.212008	1.554966
C	0.560417	2.000198	-3.293780
C	-2.758614	2.618939	-0.562758
C	-1.513812	2.541218	-2.687482
C	0.459240	1.101070	3.972957
C	3.933626	0.759483	-2.054337
C	1.727144	0.756952	3.602503
C	4.223679	0.499381	-0.745669
C	-3.657634	2.607598	1.513029
C	-0.166887	2.328005	-4.497250
C	-3.963686	2.857832	0.206940
C	-1.440146	2.659841	-4.124936
H	0.027286	1.103493	4.963231
H	4.574930	0.654983	-2.917516
H	2.540988	0.420947	4.228763
H	5.150745	0.139086	-0.323583
H	-4.301466	2.675212	2.377958
H	0.251243	2.293924	-5.492935
H	-4.907993	3.172348	-0.213065
H	-2.266746	2.950489	-4.757001
C	-1.579977	1.864079	2.710536
C	1.878928	1.573898	-3.254812
C	-2.658064	2.765065	-1.938426
C	2.934763	0.649484	1.399518
H	-2.129842	1.897699	3.645187
H	2.411516	1.503001	-4.197206
H	-3.551078	3.068024	-2.474848
H	3.817003	0.295241	1.922842
O	0.690802	3.381114	0.229448
S	-0.482592	-0.509228	-0.432076
H	-0.274564	-0.657127	-1.791555
C	2.594949	6.414774	2.675029
C	3.121302	7.685702	2.417470
C	3.074971	8.212899	1.121682
C	2.502568	7.473078	0.078109
C	1.985448	6.209529	0.365061
C	2.017710	5.659411	1.644013
H	2.628909	6.001739	3.678012
H	3.565543	8.263243	3.221512
H	3.481504	9.197680	0.915357
H	2.467540	7.883365	-0.924971
I	1.096001	5.054531	-1.224594
H	1.605502	4.672201	1.819068

52			
Quartet			
Fe	0.041487	1.799100	-0.208413
N	0.398662	1.515340	1.739030
N	2.025558	1.735736	-0.594699
N	-1.938374	1.805665	0.139378
N	-0.314954	2.193074	-2.187348
C	-0.545480	1.375646	2.746078
C	2.638917	1.865758	-1.833785
C	1.639989	1.356941	2.342659
C	3.039185	1.527224	0.323141
C	-2.562570	1.628519	1.363188
C	0.626934	2.266802	-3.200737
C	-2.949160	2.044969	-0.784223
C	-1.549920	2.370215	-2.787870
C	0.121469	1.146588	4.010723
C	4.070668	1.726172	-1.682021
C	1.464070	1.137100	3.763300
C	4.317639	1.519315	-0.353221
C	-3.995694	1.731411	1.200099
C	-0.034848	2.515675	-4.464898
C	-4.233322	1.989854	-0.121111
C	-1.376066	2.582045	-4.210519
H	-0.386939	1.003295	4.953116
H	4.781220	1.781560	-2.494021
H	2.272648	0.980870	4.462726
H	5.269753	1.371103	0.135414
H	-4.712862	1.625364	2.001082
H	0.471982	2.613161	-5.414150
H	-5.183704	2.135359	-0.614095
H	-2.183265	2.742972	-4.910560
C	-1.918673	1.418832	2.575053
C	1.996260	2.114438	-3.038058
C	-2.773752	2.308766	-2.134930
C	2.862827	1.360176	1.691868
H	-2.538416	1.288811	3.455645
H	2.615695	2.189342	-3.925614
H	-3.666715	2.464905	-2.731061
H	3.750975	1.202783	2.294681
O	0.098790	3.749348	0.221496
S	0.025168	-0.656190	-0.793908
H	-1.338045	-0.804710	-0.971599
C	3.728762	5.557267	1.990988
C	4.477686	6.691755	1.656940
C	4.076882	7.511340	0.594829
C	2.923534	7.202316	-0.140124
C	2.201903	6.066334	0.220619
C	2.571921	5.231821	1.268937
H	4.037676	4.918887	2.812185
H	5.371255	6.937645	2.221164
H	4.655790	8.390839	0.332308
H	2.613494	7.836966	-0.963407
I	0.401376	5.525031	-0.849793
H	1.972454	4.357060	1.500169

52			
Sextet			
Fe	0.293523	1.786890	-0.249379
N	0.742007	1.371752	1.706173
N	2.017315	0.831419	-0.885826
N	-1.559642	2.570467	0.311340
N	-0.203435	2.198677	-2.273375
C	-0.046226	1.670606	2.803742
C	2.456636	0.704611	-2.191349
C	1.873053	0.714922	2.154641
C	2.962428	0.260196	-0.058897
C	-2.000187	2.703570	1.612723
C	0.553874	1.840113	-3.375594
C	-2.516629	3.123809	-0.521994
C	-1.380654	2.765519	-2.732539
C	0.633336	1.201319	4.001348
C	3.735179	0.012974	-2.184360
C	1.805685	0.616136	3.604487
C	4.044590	-0.260375	-0.877967
C	-3.299163	3.354559	1.601915
C	-0.161995	2.231144	-4.579193
C	-3.616031	3.611550	0.293334
C	-1.346981	2.796628	-4.185477
H	0.249542	1.297499	5.007032
H	4.312424	-0.228698	-3.065493
H	2.555351	0.148348	4.226651
H	4.920696	-0.765859	-0.497481
H	-3.884911	3.582328	2.481118
H	0.192141	2.073811	-5.588189
H	-4.506969	4.088253	-0.090248
H	-2.135002	3.185482	-4.814829
C	-1.300062	2.283577	2.752569
C	1.783191	1.172389	-3.325015
C	-2.430250	3.203519	-1.917343
C	2.886990	0.206544	1.339002
H	-1.794228	2.447781	3.705653
H	2.259245	0.971795	-4.280605
H	-3.282635	3.644715	-2.425996
H	3.709787	-0.288821	1.845830
O	1.186993	3.488404	-0.030281
S	-0.871444	-0.491652	-0.739208
H	-2.188318	-0.090845	-0.607646
C	1.777052	6.732272	2.820145
C	1.896557	8.118282	2.664690
C	1.845396	8.689525	1.387503
C	1.674509	7.878042	0.257129
C	1.559324	6.502496	0.448289
C	1.605873	5.903216	1.702135
H	1.816882	6.287380	3.808994
H	2.029157	8.752407	3.535046
H	1.937015	9.763620	1.263116
H	1.634066	8.321005	-0.732200
I	1.295474	5.193372	-1.254330
H	1.509962	4.825459	1.788049

2: Compound I and Iodobenzene, complexed.

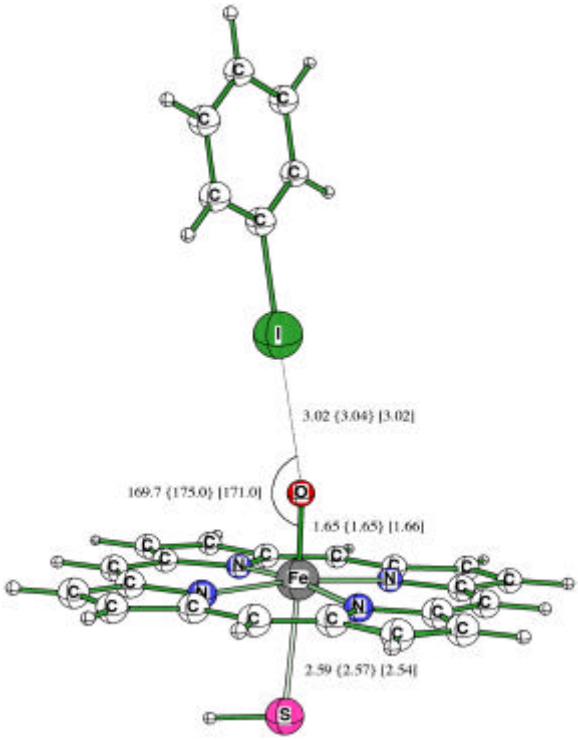


Figure S4: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S10: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{xz}, \pi^*_{yz})\beta(a_{2u})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, a_{2\upsilon})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, a_{2\upsilon}, \sigma^*_{xy})$
<S^2>	1.79	3.80	8.86

Table S11: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.28	1.16	3.19	0.09	0.06	0.14
O	0.84	0.88	0.63	-0.28	-0.27	-0.29
S	-0.60	0.57	0.39	-0.20	-0.18	-0.21
Porphyrin	-0.54	0.40	0.81	0.30	0.30	0.26

	Spin			***Charge***		
I	0.00	0.00	0.00	0.07	0.07	0.07
Ph	0.00	0.00	0.00	-0.08	-0.08	-0.08

Comments: It should be noted that strictly speaking, structure **2** is difficult to obtain as a product after the transition state. All trials, in all the different states, where the **TS1** was relaxed toward the product resulted in a state where the O....I bond was not kept. However, the resulting structure did not deviate too much from **2** in terms of energy, reflecting the very weak nature of the O....I bond at the product stage. Here, **2** was obtained simply by putting the structures there and let the structure relax.

Table S12: Coordinates in xyz-format.

52
Doublet
Fe 0.147042 -0.157309 0.009732
N 0.118390 -0.248314 2.026981
N 2.151284 -0.337400 0.041238
N -1.871488 -0.269617 -0.004482
N 0.159803 -0.340871 -1.997026
C -0.996169 -0.191254 2.849421
C 2.995820 -0.399764 -1.054153
C 1.216424 -0.247450 2.876181
C 2.973031 -0.321248 1.152236
C -2.719213 -0.204869 1.093663
C 1.274377 -0.398412 -2.816533
C -2.697664 -0.253570 -1.124127
C -0.933316 -0.314036 -2.843590
C -0.586954 -0.166411 4.237581
C 4.374967 -0.424286 -0.617344
C 0.776575 -0.202355 4.254149
C 4.360826 -0.373939 0.747010
C -4.096435 -0.175747 0.652428
C 0.868533 -0.414468 -4.204985
C -4.083239 -0.206725 -0.712072
C -0.495856 -0.360365 -4.221868
H -1.267147 -0.127660 5.075404
H 5.227686 -0.473862 -1.278368
H 1.437543 -0.198334 5.108169
H 5.199014 -0.374597 1.427951
H -4.949530 -0.133903 1.313513
H 1.549039 -0.459806 -5.042497
H -4.923318 -0.194416 -1.390559
H -1.156674 -0.352843 -5.075910
C -2.312013 -0.160242 2.416580
C 2.589824 -0.432535 -2.379421
C -2.261399 -0.270271 -2.437506
C 2.539184 -0.277554 2.470871
H -3.085441 -0.103896 3.175040
H 3.365332 -0.480933 -3.136565
H -3.018576 -0.249645 -3.214143
H 3.298819 -0.269007 3.245166
O 0.153199 1.494683 -0.034779
S -0.157082 -2.714132 0.236629
H -1.117668 -2.899481 -0.739345
C 0.106928 8.773848 -1.180007
C -1.114298 9.327282 -0.779434
C -2.111702 8.496989 -0.256007
C -1.892165 7.119103 -0.131642
C -0.667919 6.571592 -0.533352
C 0.333632 7.396807 -1.058644
H 0.887115 9.409769 -1.587406
H -1.286946 10.394655 -0.874118
H -3.062680 8.916926 0.057568
H -2.668259 6.480806 0.275563
I -0.325625 4.464577 -0.339355
H 1.282157 6.973795 -1.369930

52
Quartet
Fe 0.054009 -0.170165 0.007880 -6.489845
N 0.044632 -0.245315 2.024359 8.397119
N 2.070861 -0.202672 0.027579 -0.600718
N -1.946398 -0.428125 0.004283 -0.604788
N 0.070024 -0.361322 -2.000161 -0.602438
C -1.065921 -0.247352 2.852369 1.283981
C 2.909827 -0.197515 -1.072880 0.278709
C 1.146402 -0.174085 2.866790 0.276774
C 2.894926 -0.127684 1.133741 0.275333
C -2.792236 -0.407950 1.107752 0.283186
C 1.182619 -0.333698 -2.825003 0.277004
C -2.777844 -0.503903 -1.110965 0.267056
C -1.025393 -0.431038 -2.840995 0.267827
C -0.651772 -0.185526 4.237767 -0.138162
C 4.289900 -0.117170 -0.644532 -0.139075
C 0.711964 -0.144660 4.246858 -0.136103
C 4.280470 -0.072584 0.720094 -0.139666
C -4.168748 -0.499247 0.674054 -0.137470
C 0.772027 -0.391844 -4.210981 -0.139071
C -4.159782 -0.562921 -0.689396 -0.135908
C -0.592311 -0.449958 -4.221363 -0.139878
H -1.328633 -0.178579 5.079163 5.147492
H 5.139717 -0.098544 -1.310915 0.146919
H 1.376109 -0.095733 5.097274 0.147903
H 5.120438 -0.010192 1.395984 0.147125
H -5.019396 -0.511189 1.339521 0.148352
H 1.449860 -0.387313 -5.051668 0.147260
H -5.001775 -0.635926 -1.361954 0.147967
H -1.255429 -0.502749 -5.072269 0.146999
C -2.383814 -0.307421 2.426185 -5.133957
C 2.498961 -0.264203 -2.395730 -0.137404
C -2.350324 -0.498686 -2.426715 -0.142723
C 2.466368 -0.120102 2.454976 -0.136628
H -3.155688 -0.290168 3.187889 5.145054
H 3.271122 -0.254811 -3.157586 0.145596
H -3.111088 -0.552311 -3.198183 0.145717
H 3.227631 -0.061746 3.225687 0.146288
O -0.019933 1.481271 -0.056933 -7.350490
S -0.084595 -2.722742 0.232854 -8.085095
H -0.895514 -2.979127 -0.856177 15.028762
C 0.368009 8.785200 -1.076332 -5.113614
C -0.846697 9.396445 -0.746340 -0.129358
C -1.919181 8.612174 -0.307279 -0.113596
C -1.781470 7.222427 -0.197798 -0.104480
C -0.563559 6.617101 -0.529483 -0.375652
C 0.513337 7.396133 -0.968944 -0.104139
H 1.206182 9.385119 -1.417723 5.126760
H -0.956339 10.472996 -0.830214 0.126021
H -2.865620 9.077203 -0.048467 0.126640
H -2.615781 6.619833 0.143185 0.141144
I -0.344182 4.491916 -0.358814 -5.730267
H 1.457101 6.928049 -1.225226 6.141554

52
Sextet
Fe 0.075555 -0.128330 0.040284
N 0.073041 -0.302345 2.113245
N 2.152040 -0.261867 0.050508
N -1.990178 -0.380381 0.039897
N 0.073572 -0.332175 -2.029400
C -1.040844 -0.316337 2.927945
C 2.965278 -0.265411 -1.062365
C 1.188677 -0.278407 2.931922
C 2.963738 -0.238563 1.160577
C -2.809336 -0.383122 1.156809
C 1.192336 -0.318919 -2.838864
C -2.809966 -0.401233 -1.079644
C -1.034021 -0.348343 -2.848261
C -0.612472 -0.304265 4.316278
C 4.353823 -0.240336 -0.634439
C 0.755209 -0.283555 4.318619
C 4.352977 -0.222868 0.734309
C -4.194497 -0.424787 0.722852
C 0.768998 -0.333492 -4.228022
C -4.194897 -0.437743 -0.644769
C -0.600149 -0.349873 -4.234169
H -1.277557 -0.313522 5.167521
H 5.206179 -0.238246 -1.298124
H 1.417331 -0.271578 5.172127
H 5.204249 -0.203975 1.399230
H -5.046862 -0.440716 1.386172
H 1.436405 -0.329944 -5.077278
H -5.047750 -0.465405 -1.306819
H -1.260277 -0.362602 -5.089250
C -2.364087 -0.340405 2.478036
C 2.514891 -0.296476 -2.385884
C -2.361533 -0.378180 -2.399527
C 2.510406 -0.246712 2.486272
H -3.132877 -0.336959 3.244802
H 3.283363 -0.297087 -3.153348
H -3.128361 -0.389028 -3.168294
H 3.276531 -0.228106 3.255758
O 0.051244 1.531363 0.005243
S -0.078772 -2.656374 0.195058
H -0.824921 -2.876883 -0.947487
C 0.318665 8.795657 -1.075821

C	-0.935110	9.381456	-0.868917	C	0.485461	7.412147	-0.933354	H	-2.714524	6.575000	-0.102037
C	-2.025278	8.577254	-0.518516	H	1.170786	9.411141	-1.347987	I	-0.355807	4.496366	-0.356461
C	-1.866284	7.192941	-0.374354	H	-1.061303	10.453792	-0.979487	H	1.459369	6.963905	-1.094271
C	-0.609194	6.613327	-0.581954	H	-3.002111	9.022512	-0.355782				

Cpd I + IPh: Compound I and Iodobenzene, uncomplexed.

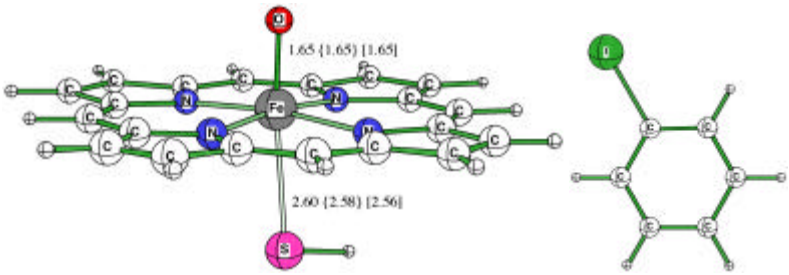


Figure S5: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S13: Valence orbitals of Cpd I and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{xz}, \pi^*_{yz})\beta(a_{2u})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, a_{2u})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, a_{2u}, \sigma^*_{xy})$
<S^2>	1.78	3.80	8.85

Table S14: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.25	1.11	3.16	0.24	0.23	0.25
O	0.87	0.92	0.64	-0.18	-0.19	-0.17
S	-0.63	0.60	0.42	-0.25	-0.23	-0.26
Porphyrin	-0.50	0.38	0.80	0.08	0.08	0.07
I	0.00			-0.01		

Table S15: Coordinates in xyz-format.

40
Doublet Cpd I
Fe -0.004220 0.000531 0.004963 -6.483393
N -0.004808 0.010954 2.016654 8.394721
N 2.014700 0.009213 0.011452 -0.606165
N -2.001691 -0.281895 0.003721 -0.607372
N 0.023199 -0.306004 -1.994974 -0.601589
C -1.112737 -0.010353 2.845678 1.278063
C 2.852070 0.016211 -1.091180 0.282048
C 1.089132 0.160356 2.848172 0.276324
C 2.840094 0.160576 1.116789 0.276055
C -2.840048 -0.262966 1.107191 0.275272
C 1.134508 -0.257040 -2.830890 0.285108
C -2.827872 -0.396487 -1.100131 0.267742
C -1.080938 -0.418933 -2.836899 0.268159
C -0.702109 0.127413 4.226535 -0.140121
C 4.228239 0.166484 -0.668182 -0.140076
C 0.659188 0.233364 4.227924 -0.140588
C 4.220888 0.253588 0.693629 -0.137402
C -4.218298 -0.379002 0.682996 -0.139925
C 0.716850 -0.371464 -4.210702 -0.137725
C -4.211131 -0.459174 -0.680394 -0.142067
C -0.644294 -0.472178 -4.214606 -0.136027
H -1.377195 0.139823 5.069620 5.146021
H 5.075066 0.198070 -1.337917 0.146533
H 1.322888 0.349888 5.072008 0.146220
H 5.060232 0.372072 1.362878 0.146610
H -5.066630 -0.393787 1.351468 0.146340
H 1.390451 -0.369043 -5.055063 0.147608
H -5.052249 -0.553524 -1.351463 0.145866
H -1.306069 -0.568375 -5.062864 0.146976
C -2.427976 -0.142430 2.425158 -5.140537
C 2.443183 -0.099279 -2.411806 -0.136213
C -2.399642 -0.456401 -2.420973 -0.144996
C 2.412048 0.227996 2.431435 -0.139454
H -3.197639 -0.142072 3.189835 5.144168
H 3.212067 -0.067568 -3.176353 0.143730
H -3.162100 -0.540716 -3.188093 0.143928
H 3.170354 0.349906 3.197701 0.144650
O -0.127732 1.638294 -0.134705 -7.321654
S 0.305561 -2.577048 -0.151070 -8.087179
H -0.902656 -2.880456 -0.750023 15.030366

40
Quartet Cpd I
40

Fe -0.001588 -0.000069 0.001152 -6.493209
N 0.000009 -0.000949 2.017440 8.399064
N 2.016272 0.005399 0.008486 -0.606036
N -2.001246 -0.271684 0.001549 -0.605847
N 0.021251 -0.291751 -1.995535 -0.602631
C -1.106763 -0.031243 2.846781 1.278749
C 2.854016 0.005573 -1.093514 0.281645
C 1.094741 0.138845 2.848861 0.275911
C 2.843283 0.143116 1.114814 0.276424
C -2.836699 -0.267175 1.107660 0.276160
C 1.133913 -0.263061 -2.831340 0.285485
C -2.830135 -0.373564 -1.101201 0.267062
C -1.083611 -0.402002 -2.837494 0.268105
C -0.694824 0.092319 4.228959 -0.140376
C 4.231503 0.141856 -0.670378 -0.139822
C 0.666472 0.197606 4.230173 -0.140438
C 4.224897 0.223809 0.691785 -0.137736
C -4.216040 -0.379232 0.685283 -0.140184
C 0.715922 -0.387620 -4.209990 -0.137776
C -4.212382 -0.442636 -0.678947 -0.141680
C -0.646280 -0.472681 -4.214056 -0.136123
H -1.369155 0.095771 5.072721 5.145964
H 5.078674 0.166543 -1.339950 0.146577
H 1.331250 0.303953 5.074862 0.146188
H 5.065461 0.329955 1.361569 0.146667
H -5.062644 -0.403685 1.355639 0.146358
H 1.390260 -0.402713 -5.053630 0.147730
H -5.054969 -0.531389 -1.348933 0.145884
H -1.308320 -0.571389 -5.061813 0.147064
C -2.422104 -0.162633 2.426069 -5.140317
C 2.443611 -0.111753 -2.413617 -0.136221
C -2.402856 -0.427681 -2.422574 -0.144397
C 2.417333 0.203566 2.430539 -0.139005
H -3.190439 -0.174456 3.191845 5.144192
H 3.212399 -0.091496 -3.178488 0.143831
H -3.165543 -0.505900 -3.190088 0.144104
H 3.177674 0.313255 3.196624 0.144791
O -0.130240 1.643658 -0.092975 -7.317006
S 0.288949 -2.561677 -0.142281 -8.088917
H -0.919517 -2.865656 -0.740249 15.029788

40
Sextet Cpd I
Fe -0.019224 0.019911 -0.007227 -6.329327
N -0.009759 -0.002759 2.070694 8.352053
N 2.062281 -0.060313 0.009223 -0.636712
N -2.074242 -0.297503 0.010285 -0.641475
N 0.015446 -0.342096 -2.054879 -0.650256
C -1.130344 -0.000810 2.882974 1.282505
C 2.887688 -0.080100 -1.106861 0.273066
C 1.094554 0.134483 2.884668 0.286640
C 2.873545 0.082653 1.125161 0.290033
C -2.891470 -0.254459 1.116279 0.281719
C 1.125269 -0.312314 -2.871868 0.271326
C -2.877139 -0.461233 -1.097485 0.283291
C -1.095366 -0.494007 -2.863704 0.280399
C -0.708652 0.140606 4.265852 -0.138244
C 4.267990 0.035461 -0.670417 -0.136102
C 0.656899 0.224424 4.267103 -0.139631
C 4.259158 0.134504 0.693508 -0.137586
C -4.274134 -0.394750 0.691366 -0.140736
C 0.701595 -0.457873 -4.253036 -0.141680
C -4.265189 -0.524303 -0.671364 -0.140079
C -0.662740 -0.572944 -4.247550 -0.140496
H -1.376263 0.169589 5.114579 5.146520
H 5.123786 0.041538 -1.329534 0.146793
H 1.314560 0.334423 5.117078 0.146384
H 5.106375 0.236802 1.356038 0.147411
H -5.127808 -0.397298 1.353499 0.145920
H 1.365549 -0.472619 -5.104967 0.145733
H -5.110400 -0.652281 -1.331959 0.145713
H -1.321529 -0.698187 -5.094584 0.146237
C -2.447395 -0.116459 2.437172 -5.139894
C 2.447163 -0.184730 -2.424656 -0.144464
C -2.417141 -0.556419 -2.414832 -0.141298
C 2.419856 0.180892 2.438926 -0.137369
H -3.216978 -0.099634 3.203127 5.143438
H 3.215675 -0.175721 -3.191746 0.142845
H -3.176896 -0.686192 -3.179846 0.142830
H 3.180953 0.300371 3.204066 0.142403
O -0.143682 1.663180 -0.156457 -7.347088
S 0.405558 -2.487253 0.313980 -8.089684
H 0.930979 -2.756947 -0.935761 15.029080

12
PhI
C 1.007336 0.814445 0.000000 0.884330
C 0.312079 2.030825 0.000001 -0.093241
C -1.086139 2.018974 0.000002 -0.345815
C -1.795553 0.814017 0.000001 -0.093219
C -1.089727 -0.396255 0.000002 -0.115672
C 0.310200 -0.399551 0.000000 -0.123912
H 2.092071 0.822214 0.000001 0.136065
H 0.854920 2.968337 0.000003 0.149197
I -2.159641 3.878322 -0.000001 0.182481
H -2.878892 0.812707 0.000000 0.149201
H -1.638783 -1.331790 0.000003 0.136009
H 0.852416 -1.338745 -0.000001 0.134576

Geometries (all in Å)

Table S16: C-I distances.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	2.18	2.16	2.16	2.14	2.15
Quartet		2.17	2.16	2.14	
Sextet		2.16	2.16	2.14	

Table S17: I-O distances.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	1.99	2.09	2.25	3.02	----
Quartet		2.01	2.10	3.04	
Sextet		2.03	2.10	3.02	

Table S18: O-Fe distances.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	----	1.88	1.78	1.65	1.65
Quartet		2.19	2.00	1.65	1.65
Sextet		2.14	1.93	1.66	1.65

Table S19: Fe-S distances.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	2.30	2.33	2.36	2.59	2.60
Quartet	2.47	2.52	2.52	2.57	2.58
Sextet	2.40	2.45	2.61	2.54	2.56

Energies

All energies are in kcal mol^{-1}, with the reference point as marked in **bold**.

Basis set test

Table S20: I_2 bond.

	***LACV3P*+*[1]	***ERMLER2*+ (SP)*[2]	***ERMLER2*+ (OPT)*[3]	***Experimental*[4]
Energy (kcal mol^{-1})	60.7	21.4	39.5	36.1
I-I distance (Å)	3.4	3.4	2.8	2.7

Conclusion: ERMLER2*+ is a good basis set for iodine.

Table S21: IO· bond.

	***LACV3P*+*[1]	***ERMLER2*+ (SP)*[2]	***ERMLER2*+ (OPT)*[3]	***Experimental*[4]
Energy (kcal mol^{-1})	46.1	53.5	54.4	59.5
I-I distance (Å)	2.01	2.01	1.95	----

Conclusion: LACVP optimization is sufficient for I-O bond geometry.

Table S22: PhI-O bond.

	***LACV3P*+*[1]	***ERMLER2*+ (SP)*[2]	***ERMLER2*+ (OPT)*[3]
Energy (kcal mol^{-1})	13.3	27.3	29.0
I-I distance (Å)	1.99	1.99	1.91

Final conclusion: LACVP optimization should produce good geometries. Single point energy calculations should be done with ERMLER2*+ on iodine since LACV3P*+ fail to produce correct energies.

1. On iodine, this basis set is the same as LACVP.
2. Single point calculation on the LACVP geometry
3. Optimized with ERMLER2*+ on iodine and LACV3P*+ on rest.
4. Kerr, J. A., In *CRC Handbook of Chemistry and Physics 1999-2000 : A Ready-Reference Book of Chemical and Physical Data (CRC Handbook of Chemistry and Physics, 81st edition*, Lide, D. R.(ed.), CRC Press, Boca Raton, Florida, USA, 2000

Table S23: Energy, LACVP.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	22.48	**0.00**	0.34	-17.78	-15.94
Quartet	21.10	10.33	10.41	-17.92	-15.90
Sextet	22.63	11.77	13.63	-3.58	-1.48

Table S24: Energy, LACV3P*+ (ERMLER2*+ on I).

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	13.55	**0.00**	4.11	-5.66	-2.90
Quartet	11.43	7.04	10.78	-5.64	-2.72
Sextet	8.23	4.52	11.10	5.35	8.51

Table S25: Energy, LACVP including solvation.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	12.12	**0.00**	2.69	-13.73	-16.72
Quartet	8.53	5.13	9.32	-14.14	-16.66
Sextet	6.42	6.02	10.82	-3.47	-2.24

Table S26: Energy, LACVP including zero-point vibration energy.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	21.85	**0.00**	0.11	-17.87	-16.25
Quartet	19.85	9.14	8.86	-18.09	-16.18
Sextet	20.36	9.65	11.00	-5.19	-3.19

Table S27: Total Energy, LACV3P*+ (ERMLER2*+ on I) including solvation and Z_0.

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Doublet	7.15	**0.00**	5.06	-5.44	-3.98

	Heme+OIPh	***1***	***TS1***	***2***	***Cpd I + IPh***
Quartet	2.95	2.11	7.72	-5.75	-3.75
Sextet	-0.18	2.10	7.91	3.39	5.74

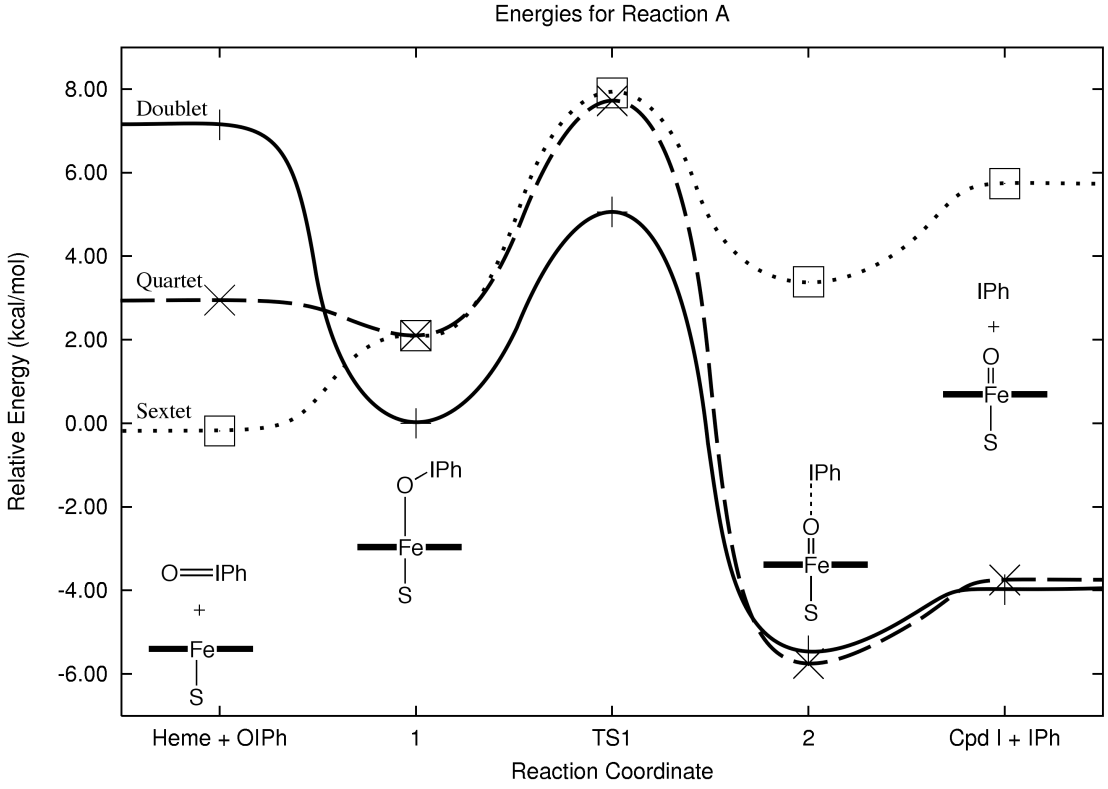


Figure S6: Graph of Table S27.

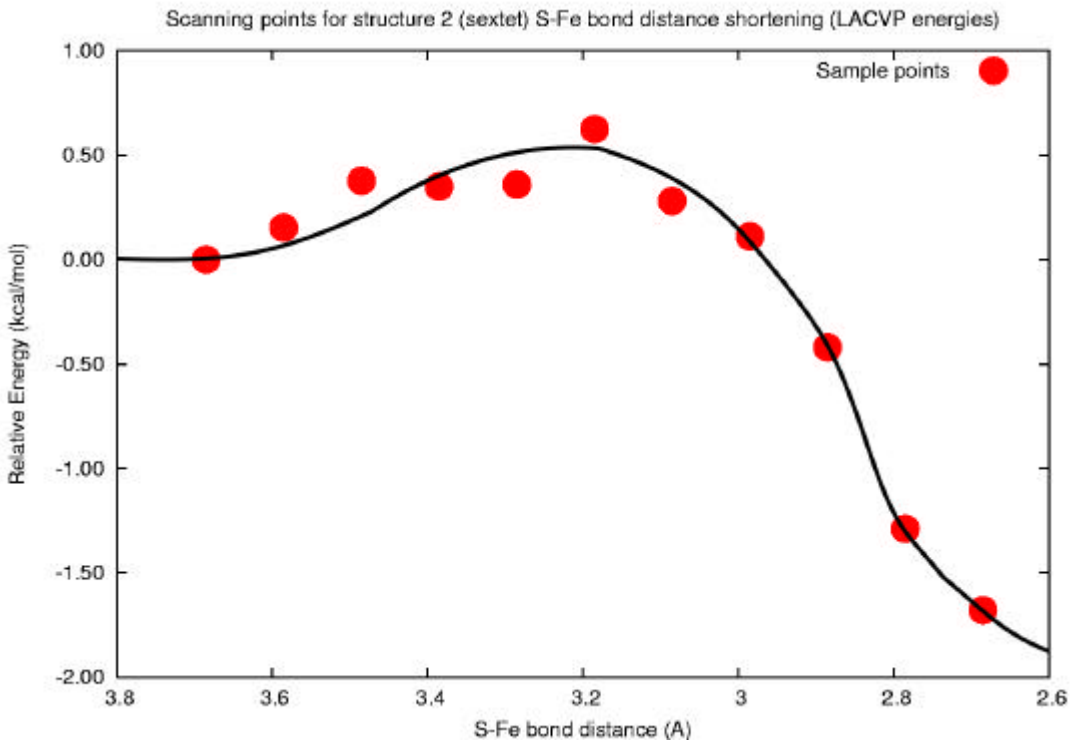


Figure S7: Scanning points for $^{6}2$ S-Fe bond formation (x-axis reversed).

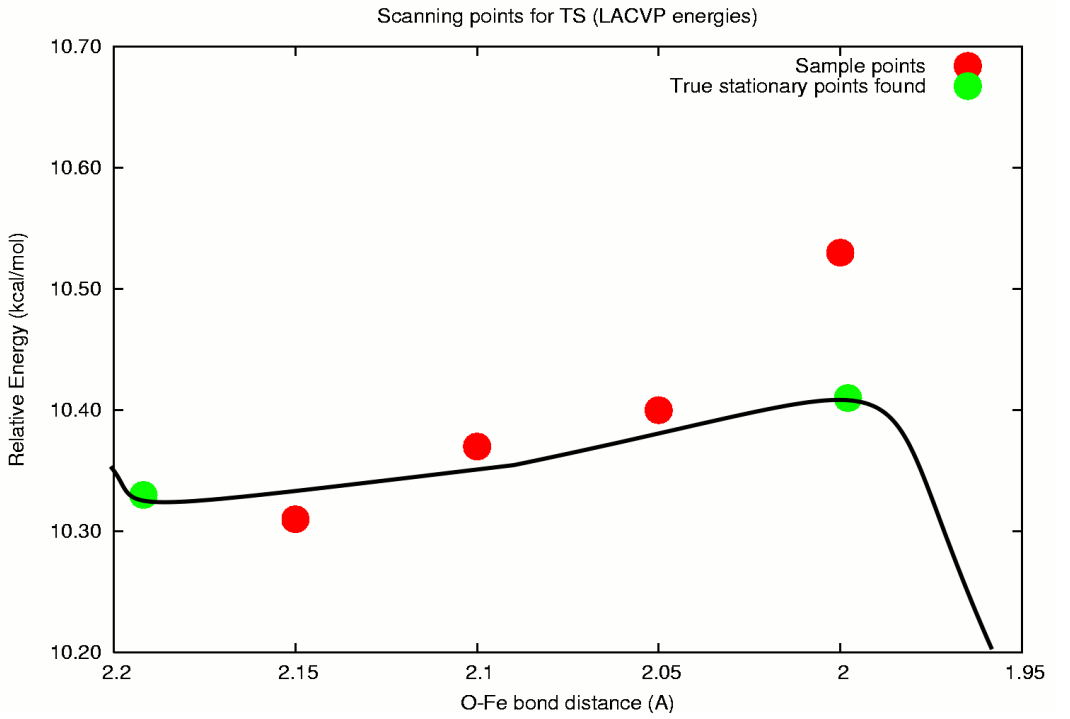


Figure S8: Scanning points in search for TS (Quartet, LACVP).

Table S28: Free Energy DG, component by component.

	A	B	C	D	E	F	A+B+C+D+E+F
Heme + OIPh							
Doublet	22.48	-8.94	-5.76	-0.63	-0.44	-14.42	**-7.70**
Quartet	21.10	-9.67	-7.23	-1.25	-0.09	-16.24	**-13.38**
Sextet	22.63	-14.40	-6.14	-2.27	+0.09	-16.93	**-17.02**
1							
Doublet	**0.00**	**+0.00**	**+0.00**	**+0.00**	**+0.00**	**+0.00**	**0.00**
Quartet	10.33	-3.29	-3.73	-1.19	+0.66	-3.24	**-0.47**
Sextet	11.77	-7.25	-0.30	-2.12	+1.23	-5.43	**-2.10**
TS1							
Doublet	0.34	+3.77	+1.18	-0.22	+0.21	-1.73	**3.54**
Quartet	10.41	+0.37	-1.51	-1.55	+0.89	-4.63	**3.98**
Sextet	13.63	-2.54	-0.55	-2.63	+0.32	-2.01	**6.22**
2							
Doublet	-17.78	+12.12	+0.32	-0.09	+0.42	-3.73	**-8.75**
Quartet	-17.92	+12.28	+0.06	-0.17	-0.15	-1.71	**-7.61**
Sextet	-3.58	+8.92	-0.34	-1.62	+0.66	-5.71	**-1.66**
IPh + Cpd I							
Doublet	-15.94	+13.05	-0.78	-0.31	-0.59	-13.55	**-18.12**
Quartet	-15.90	+13.18	-0.76	-0.28	-0.63	-13.85	**-18.24**
Sextet	-1.48	+9.99	-1.06	-1.70	-0.35	-14.57	**-9.18**

A=LACVP relative energy; B=LACV3P*+ (ERMLER2*+) correction; C=Solvent correction; D=Z_0 correction; E=Enthalpy correction F=Entropy correction; A+B+C+D+E+F=? G

Part 2

Reaction between H_2O-Heme and Iodosylbenzene

In this summary, the five different stages of the reaction are named as below:

[H_2O-Heme] + OIPh: [H_2O-Heme] and Iodosylbenzene, uncomplexed.
0: [H_2O-Heme] and Iodosylbenzene, complexed
TS0: Transition state between **0** and **1**.
1: Heme and Iodosylbenzene, complexed.
TS1: Transition state between **1** and **2**.
2: Compound I and Iodobenzene, complexed.
[H_2O-Cpd I] + IPh: Compound I and Iodobenzene, uncomplexed.

Structures

[H_2O-Heme] + OIPh: [H_2O-Heme] and Iodosylbenzene, uncomplexed.

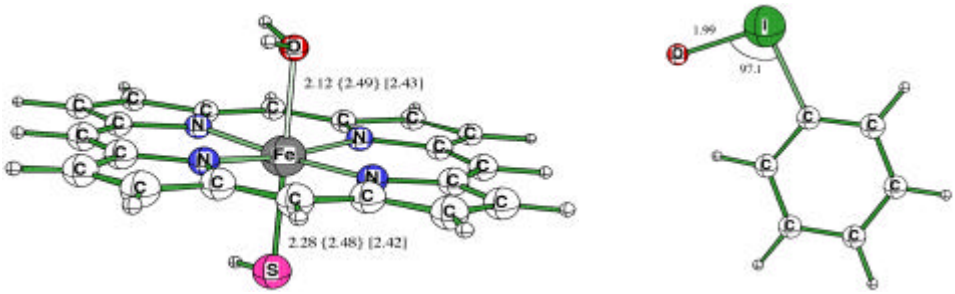


Figure S9: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S29: Valence orbitals of H_2O-heme and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{yz}, \pi^*_{xz}, \sigma^*_{z^2}, \sigma^*_{xy})$
<S^2>	0.80	3.80	8.76

Table S30: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.06	2.63	4.15	0.11	0.09	0.15
Porphyrin	-0.09	-0.07	0.40	-0.26	-0.07	-0.23
S	0.03	0.44	0.45	-0.14	-0.25	-0.20

Table S31: Coordinates in xyz-format.

43
Doublet Heme + H2O

Fe	1.171554	2.123437	-0.507502
N	0.911589	1.060636	1.176464
N	2.774894	0.987499	-0.970328
N	-0.578182	3.067993	-0.183535
N	1.275543	2.982800	-2.337231
C	-0.088474	1.229591	2.117984
C	3.592944	1.113996	-2.080290
C	1.752212	0.088170	1.686169
C	3.369668	0.023881	-0.168767
C	-1.374969	2.968772	0.945150
C	2.298997	2.836193	-3.268486
C	-1.162909	4.042933	-0.974491
C	0.437128	3.972020	-2.845478
C	0.129513	0.340905	3.237953
C	4.714392	0.205459	-1.976754
C	1.269950	-0.360784	2.973938
C	4.575930	-0.468151	-0.798096
C	-2.483156	3.890949	0.853382
C	2.076905	3.726043	-4.386515
C	-2.352055	4.556413	-0.331474
C	0.930950	4.423149	-4.127495
H	-0.510985	0.279746	4.104955
H	5.494390	0.108232	-2.717497
H	1.751986	-1.112401	3.581598
H	5.221064	-1.226171	-0.378713
H	-3.249337	4.004888	1.605891
H	2.724044	3.797363	-5.248319
H	-2.992117	5.321722	-0.745442
H	0.454724	5.178846	-4.734793
C	-1.151245	2.112845	2.010749
C	3.377530	1.979004	-3.142728
C	-0.690352	4.463106	-2.210933
C	2.893249	-0.396288	1.061047
H	-1.856315	2.146477	2.833779
H	4.108662	1.975683	-3.944003
H	-1.251440	5.239572	-2.719821
H	3.460974	-1.159605	1.582120
O	2.082587	3.302607	0.214484
S	-0.084618	0.396396	-1.945330
H	-1.157783	1.186306	-2.311120
O	1.105738	4.632420	2.461562
H	0.831094	5.468653	2.041783
H	1.598204	4.111240	1.783675

43
Quartet Heme + H2O

Fe	1.187386	2.118523	-0.521511
N	0.920731	1.039614	1.159993
N	2.788166	0.985757	-0.983128
N	-0.567589	3.045077	-0.198737
N	1.331711	3.044603	-2.310191
C	-0.083537	1.196380	2.099282
C	3.602186	1.111585	-2.096259
C	1.752111	0.050520	1.657814
C	3.370333	0.004601	-0.198501
C	-1.372466	2.934188	0.925063
C	2.340808	2.888586	-3.246616
C	-1.150293	4.033450	-0.983796
C	0.496781	4.026904	-2.815134
C	0.124439	0.288704	3.207424
C	4.709910	0.186157	-2.009313
C	1.257100	-0.420002	2.934116
C	4.566102	-0.498638	-0.836851
C	-2.486983	3.847921	0.829854
C	2.130039	3.789786	-4.359042
C	-2.350589	4.526295	-0.347034
C	0.990916	4.492467	-4.093026
H	-0.520752	0.217646	4.070216
H	5.485701	0.085979	-2.754000
H	1.726716	-1.190732	3.526978
H	5.200581	-1.271531	-0.428739
H	-3.258576	3.950941	1.578186
H	2.775342	3.858981	-5.222339
H	-2.991796	5.292217	-0.757850
H	0.514995	5.252570	-4.694860
C	-1.144888	2.080183	1.992295
C	3.395849	1.996874	-3.143842
C	-0.653618	4.489792	-2.194387
C	2.889059	-0.428910	1.028273
H	-1.853726	2.109771	2.812380
H	4.118621	1.985719	-3.952773
H	-1.214426	5.268693	-2.700344
H	3.449452	-1.206729	1.535974
O	2.087948	3.274484	0.263252
S	-0.168966	0.352408	-1.743254
H	-1.396593	0.985780	-1.767154
O	0.962445	4.893853	2.227175
H	0.821476	5.700346	1.697392
H	1.494926	4.271464	1.676793

43
Sextet Heme + H2O

Fe	1.197789	2.146626	-0.513860
N	0.909127	1.023545	1.214846
N	2.831215	0.957947	-0.995832
N	-0.630323	3.083410	-0.203410
N	1.316598	3.061179	-2.383449
C	-0.110990	1.185508	2.126815
C	3.614637	1.076019	-2.124639
C	1.758248	0.056243	1.706623
C	3.407517	0.001004	-0.186057
C	-1.422823	2.953174	0.918930
C	2.317509	2.867203	-3.314835
C	-1.188893	4.070344	-0.995720
C	0.476028	4.040711	-2.873208
C	0.103775	0.281662	3.245087
C	4.729824	0.150867	-2.025860
C	1.254662	-0.410994	2.988108
C	4.604812	-0.507000	-0.831886
C	-2.534826	3.879675	0.823167
C	2.096358	3.760797	-4.439178
C	-2.390094	4.568392	-0.351482
C	0.967479	4.483973	-4.166759
H	-0.543454	0.199793	4.105611
H	5.500294	0.029540	-2.773261
H	1.725822	-1.167850	3.598089
H	5.254570	-1.265359	-0.419914
H	-3.312234	3.987622	1.565140
H	2.726273	3.817603	-5.314736
H	-3.030430	5.340913	-0.751785
H	0.501163	5.242916	-4.777929
C	-1.177305	2.076724	1.981564
C	3.369604	1.957559	-3.183381
C	-0.668688	4.505793	-2.219360
C	2.908418	-0.403126	1.057081
H	-1.895028	2.101659	2.795607
H	4.082438	1.929290	-4.002186
H	-1.225963	5.288976	-2.725089
H	3.478513	-1.168370	1.575511
O	2.097119	3.317771	0.272691
S	-0.083309	0.383543	-1.742493
H	-1.282842	1.057546	-1.866606
O	0.984573	4.701063	2.415080
H	0.786351	5.546481	1.970830
H	1.519391	4.158945	1.786660

13
PhIO

C	1.415409	0.120265	0.004033
C	0.782171	1.372081	0.005360
C	-0.608723	1.395945	0.006898
C	-1.393847	0.251012	0.006828
C	-0.745443	-0.991273	0.005825
C	0.653989	-1.055311	0.004433
H	2.499551	0.070310	0.002652
H	1.370352	2.284324	0.005060
H	-2.478269	0.350579	0.007460
H	-1.333536	-1.903329	0.006127
H	1.151801	-2.019380	0.003613
I	-1.749918	3.249734	0.009598
O	-3.557073	2.426989	-0.003127

0: [H_2O-Heme] and Iodosylbenzene, complexed.

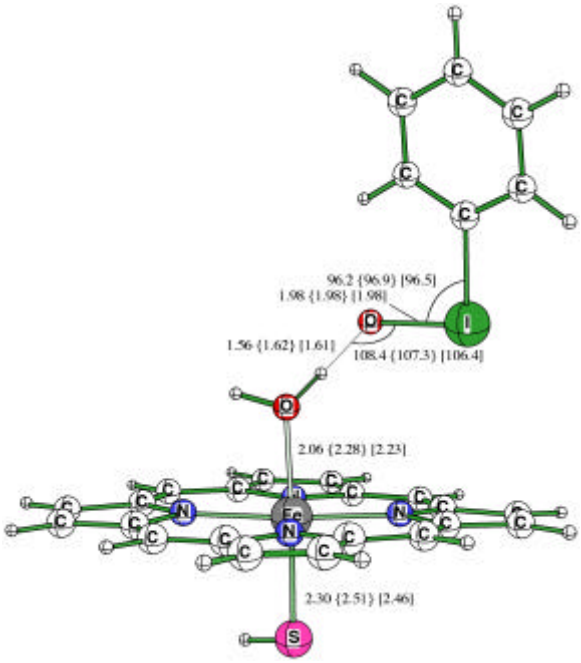


Figure S10: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S32: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
<S^2>	0.81	3.80	8.77

Table S33: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.07	2.66	4.16	0.06	0.11	0.24
O	0.00	0.00	0.00	-0.53	-0.56	-0.54
S	0.03	0.42	0.44	-0.15	-0.26	-0.19
Porphyrin	-0.09	-0.09	0.38	-0.26	-0.09	-0.35

	Spin			***Charge***		
I	0.00	0.00	0.00	0.54	0.54	0.54
Ph	0.00	0.00	0.00	0.05	0.05	0.05

Table S34: Coordinates in xyz-format.

55			
Doublet			
Fe	0.389081	1.700738	-0.434927
N	0.816011	1.345448	1.506027
N	2.368532	1.655410	-0.844895
N	-1.576441	1.877226	-0.001401
N	-0.028750	2.142800	-2.357206
C	-0.103115	1.219036	2.530758
C	2.941232	1.762051	-2.104800
C	2.061834	1.150121	2.077290
C	3.405965	1.378764	0.031771
C	-2.160179	1.644557	1.236917
C	0.886793	2.204593	-3.397115
C	-2.620333	2.144197	-0.878709
C	-1.269906	2.398676	-2.919535
C	0.584254	0.941366	3.778305
C	4.373980	1.567133	-2.008003
C	1.919110	0.900960	3.498853
C	4.659225	1.331471	-0.689253
C	-3.597817	1.780469	1.131166
C	0.200263	2.507126	-4.636847
C	-3.880879	2.090137	-0.169612
C	-1.127122	2.629823	-4.342515
H	0.093251	0.798846	4.730252
H	5.054391	1.583288	-2.847980
H	2.741279	0.716372	4.175334
H	5.619468	1.122726	-0.239052
H	-4.287037	1.651564	1.953354
H	0.686360	2.612024	-5.596163
H	-4.846929	2.263297	-0.621562
H	-1.944839	2.852144	-5.012899
C	-1.479854	1.347264	2.408405
C	2.256026	2.020833	-3.285969
C	-2.477595	2.403932	-2.234414
C	3.268840	1.163876	1.396792
H	-2.073474	1.207132	3.305651
H	2.841983	2.086535	-4.197057
H	-3.377733	2.605559	-2.805047
H	4.170538	0.969303	1.967959
O	1.840180	5.337335	-1.513910
S	0.212640	-0.562642	-0.830395
H	-0.929494	-0.531644	-1.609424
C	3.061714	9.172376	0.363826
C	4.254349	9.545931	0.995228
C	5.336390	8.658463	1.040577
C	5.234470	7.389842	0.451761
C	4.035390	7.053327	-0.170795
C	2.942241	7.908641	-0.230521
H	2.222631	9.859441	0.330881
H	4.340802	10.525567	1.453261
H	6.259197	8.944671	1.534431
H	6.071726	6.700432	0.493125
I	3.772069	5.121976	-1.122931
H	2.029989	7.584587	-0.723566
O	0.490548	3.718635	-0.014732
H	-0.426690	4.033318	0.085430
H	1.040056	4.347624	-0.609890

55			
Quartet			
Fe	0.404076	1.625477	-0.429973
N	0.829848	1.398137	1.525812
N	2.383667	1.633970	-0.857599
N	-1.566720	1.847542	0.029021
N	-0.016294	1.969507	-2.374467
C	-0.080603	1.318134	2.568085
C	2.955371	1.691627	-2.121835
C	2.086002	1.256880	2.092897
C	3.425064	1.432234	0.034803
C	-2.146635	1.685631	1.278525
C	0.887695	1.996949	-3.425674
C	-2.608727	2.054651	-0.863206
C	-1.270130	2.173244	-2.930999
C	0.623906	1.111773	3.815572
C	4.391028	1.539763	-2.012574
C	1.957956	1.076915	3.523407
C	4.679411	1.382450	-0.683090
C	-3.584288	1.812322	1.167373
C	0.181323	2.211684	-4.669561
C	-3.868451	2.041180	-0.150134
C	-1.146356	2.323507	-4.364768
H	0.146554	1.011259	4.779518
H	5.073117	1.529212	-2.850903
H	2.788249	0.939694	4.201080
H	5.643872	1.222017	-0.222409
H	-4.273186	1.728825	1.995467
H	0.652681	2.271989	-5.639804
H	-4.835573	2.180195	-0.610931
H	-1.975079	2.491083	-5.037251
C	-1.458468	1.442879	2.457946
C	2.264170	1.862205	-3.313810
C	-2.471247	2.216963	-2.234632
C	3.291375	1.274374	1.406786
H	-2.042082	1.345303	3.367036
H	2.844734	1.888963	-4.229911
H	-3.375713	2.373625	-2.812373
H	4.197459	1.129908	1.985475
O	1.738980	5.628440	-1.580033
S	0.169305	-0.860727	-0.722959
H	-0.737297	-0.840670	-1.766959
C	3.153697	9.104219	0.823296
C	4.413765	9.406955	1.352852
C	5.494287	8.540263	1.143041
C	5.321284	7.362296	0.402336
C	4.053711	7.094187	-0.108349
C	2.962498	7.931941	0.078951
H	2.318052	9.775038	0.986852
H	4.555057	10.315589	1.928610
H	6.471573	8.772602	1.554143
H	6.158498	6.689645	0.242860
I	3.669168	5.299719	-1.262886
H	1.999625	7.666033	-0.348101
O	0.430774	3.884449	-0.103623
H	-0.479050	4.167361	0.091083
H	0.914353	4.557100	-0.686930

55			
Sextet			
Fe	0.408402	1.595241	-0.393844
N	0.827140	1.279871	1.609805
N	2.445594	1.637517	-0.808875
N	-1.611893	1.903162	0.083508
N	-0.004694	2.110359	-2.368730
C	-0.103205	1.187222	2.628515
C	3.009414	1.768326	-2.067655
C	2.079412	1.073110	2.156818
C	3.458671	1.346038	0.085031
C	-2.184605	1.683473	1.323439
C	0.922093	2.192435	-3.391139
C	-2.629949	2.160650	-0.817561
C	-1.253857	2.363934	-2.904184
C	0.593939	0.899089	3.870361
C	4.445532	1.573909	-1.954439
C	1.931289	0.829939	3.581632
C	4.719568	1.316106	-0.634288
C	-3.625512	1.831983	1.202773
C	0.224134	2.493685	-4.628577
C	-3.898113	2.124954	-0.107707
C	-1.108975	2.600500	-4.330228
H	0.116515	0.770715	4.831153
H	5.141533	1.603021	-2.781326
H	2.746575	0.633299	4.263344
H	5.680807	1.101855	-0.188380
H	-4.328621	1.717314	2.015445
H	0.698011	2.611955	-5.592348
H	-4.864673	2.292971	-0.560657
H	-1.923048	2.820475	-5.006101
C	-1.484148	1.364191	2.490777
C	2.303811	2.028060	-3.248757
C	-2.456825	2.382967	-2.187539
C	3.285965	1.097038	1.451117
H	-2.078012	1.237802	3.391055
H	2.894491	2.106037	-4.156675
H	-3.356610	2.580094	-2.762327
H	4.185517	0.890415	2.023358
O	1.737347	5.490712	-1.547070
S	0.112522	-0.810373	-0.811894
H	-0.637872	-0.719128	-1.968034
C	3.125791	9.257679	0.371338
C	4.325894	9.562948	1.025311
C	5.365277	8.625545	1.066296
C	5.213134	7.375198	0.450335
C	4.008640	7.107090	-0.194316
C	2.956380	8.012798	-0.249607
H	2.319766	9.983362	0.341756
H	4.451036	10.527934	1.504760
H	6.293144	8.858165	1.578491
H	6.016233	6.646098	0.488675
I	3.667767	5.210348	-1.184398
H	2.035792	7.738935	-0.757814
O	0.491414	3.789641	0.015497
H	-0.402916	4.078038	0.268046
H	0.944524	4.457355	-0.603076

TS0: Transition state between **0** and **1**.

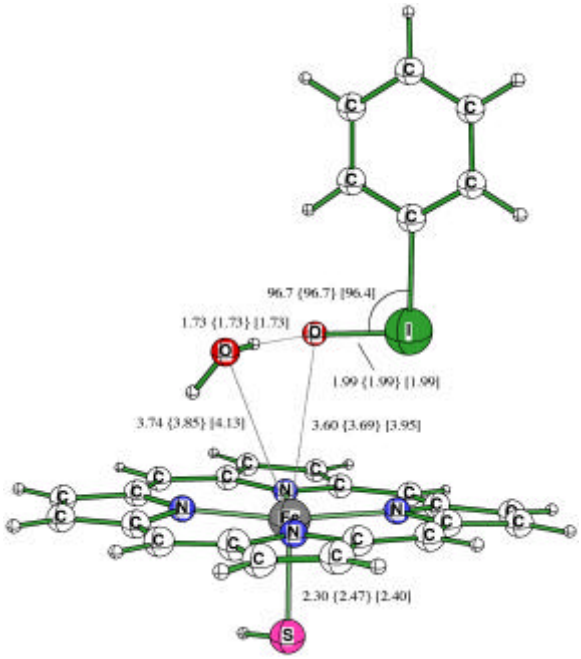


Figure S11: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S35: Valence orbitals, imaginary frequencies and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
Frequency	i33.0 cm^{-1}	i27.7 cm^{-1}	i25.9 cm^{-1}
<S^2>	1.01	3.79	8.77

Table S36: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.27	2.59	4.10	-0.06	-0.05	-0.01
O	0.00	0.00	0.00	-0.52	-0.52	-0.53
S	-0.12	0.47	0.47	-0.17	-0.28	-0.22
Porphyrin	-0.16	-0.06	0.43	0.05	0.13	0.03

	Spin			*Charge*		
I	0.00	0.01	0.00	0.46	0.47	0.48
Ph	0.00	0.00	0.00	0.07	0.07	0.05

Comments: This TS lies on a very flat surface (see the last graph), hence the small imaginary frequencies. Strictly speaking, if relaxing the structure, it may not go to **0** or **1**, but instead it may get stuck in one of the shallow minima at the flat surface. However, the energy should give a proper representation of the barrier between **0** and **1**.

Table S37: Coordinates in xyz-format.

55
Doublet
Fe 0.534014 1.652103 -0.784510 -6.652272
N 0.901136 1.361543 1.164197 8.369438
N 2.516074 1.558001 -1.128672 -0.647287
N -1.378098 2.079581 -0.377573 -0.643844
N 0.220761 2.207315 -2.682836 -0.631981
C -0.049445 1.276793 2.173458 1.284650
C 3.129134 1.581440 -2.381204 0.264214
C 2.118756 1.084116 1.777240 0.271889
C 3.523435 1.212535 -0.227645 0.243741
C -2.024924 1.874181 0.839535 0.253620
C 1.155057 2.192004 -3.710794 0.285036
C -2.373650 2.482510 -1.265153 0.262451
C -0.970143 2.621983 -3.268392 0.271238
C 0.585709 0.951965 3.432187 -0.133404
C 4.534419 1.279055 -2.249967 -0.142817
C 1.922915 0.837780 3.188906 -0.137921
C 4.778916 1.057516 -0.922346 -0.148670
C -3.434357 2.163852 0.706478 -0.137094
C 0.534392 2.594904 -4.954321 -0.140265
C -3.647608 2.544089 -0.588285 -0.138519
C -0.774155 2.866774 -4.680054 -0.137903
H 0.061865 0.838114 4.369932 5.145252
H 5.231725 1.239869 -3.074288 0.144062
H 2.715052 0.606879 3.886048 0.142360
H 5.713740 0.795710 -0.448063 0.142388
H -4.152678 2.090005 1.509872 0.146654
H 1.050700 2.667005 -5.900489 0.143136
H -4.575541 2.839537 -1.055620 0.145057
H -1.546330 3.203598 -5.356115 0.143522
C -1.408051 1.495407 2.020453 -5.146833
C 2.496521 1.877740 -3.576931 -0.148309
C -2.180274 2.753747 -2.608718 -0.152139
C 3.341251 1.016362 1.131759 -0.156227
H -2.034072 1.389963 2.899798 5.140387
H 3.104221 1.886219 -4.475488 0.136868
H -3.039692 3.072526 -3.188376 0.139257
H 4.212271 0.762718 1.726504 0.136836
O 1.379787 5.117780 -1.242937 -7.677100
S 0.176254 -0.582028 -1.180954 -8.024140
H -0.824932 -0.439865 -2.123549 15.034798
C 2.719561 9.212486 -0.122079 -5.118819
C 3.937611 9.678166 0.387892 -0.116423
C 4.980782 8.781607 0.649710 -0.119603
C 4.812609 7.411575 0.403089 -0.103798
C 3.588995 6.982494 -0.104671 -0.407216
C 2.534899 7.846514 -0.375108 -0.078623
H 1.909592 9.906314 -0.321574 5.144433
H 4.074064 10.736650 0.583229 0.138122
H 5.924969 9.140628 1.046339 0.138813
H 5.621133 6.717210 0.608835 0.137994
I 3.215831 4.889161 -0.516007 -5.042480
H 1.602266 7.451240 -0.767822 6.202950
O 0.044183 4.840808 1.101094 -7.794274
H -0.663274 4.174819 1.048050 7.368002
H 0.422018 4.977675 0.188910 0.400713

55
Quartet
Fe 0.518927 1.593347 -0.794814 -6.465163
N 0.888370 1.347296 1.161079 8.337400
N 2.514343 1.542974 -1.145631 -0.666337
N -1.381766 2.100653 -0.361871 -0.662843
N 0.217511 2.166010 -2.693633 -0.661667
C -0.049776 1.325650 2.187250 1.291335
C 3.136083 1.605182 -2.392186 0.263876
C 2.104799 1.030789 1.757653 0.280045
C 3.511186 1.168976 -0.246739 0.256585
C -2.017937 1.964399 0.869534 0.257168
C 1.156678 2.187703 -3.719262 0.289484
C -2.376617 2.473450 -1.259569 0.273595
C -0.984800 2.551588 -3.276103 0.280513
C 0.590091 0.988279 3.435965 -0.131737
C 4.539864 1.299270 -2.258319 -0.141270
C 1.918071 0.807075 3.171586 -0.136660
C 4.771535 1.032695 -0.936616 -0.146031
C -3.423329 2.271486 0.735853 -0.133767
C 0.524687 2.570739 -4.959395 -0.138912
C -3.643459 2.586734 -0.574994 -0.136591
C -0.794426 2.797909 -4.685771 -0.136552
H 0.078481 0.910639 4.383926 5.148805
H 5.243791 1.283731 -3.077615 0.146471
H 2.709218 0.548598 3.860046 0.146101
H 5.701393 0.752142 -0.463395 0.145451
H -4.135202 2.246867 1.547772 0.149303
H 1.038272 2.661553 -5.905279 0.146298
H -4.571824 2.869754 -1.049024 0.147854
H -1.575421 3.110912 -5.363078 0.147075
C -1.400644 1.600703 2.053843 -5.146320
C 2.506825 1.910178 -3.586830 -0.150344
C -2.193853 2.688326 -2.614489 -0.149283
C 3.323612 0.940639 1.106217 -0.154009
H -2.016140 1.540713 2.944331 5.142969
H 3.116556 1.942900 -4.482971 0.139025
H -3.057125 2.986001 -3.199153 0.140363
H 4.189930 0.661890 1.696019 0.138331
O 1.368605 5.157188 -1.259154 -7.678750
S 0.114183 -0.814034 -1.160983 -8.197279
H -0.515635 -0.704394 -2.386668 15.026049
C 2.706813 9.231531 -0.070646 -5.118987
C 3.928772 9.691588 0.435064 -0.116263
C 4.976096 8.793219 0.673059 -0.119852
C 4.808367 7.426798 0.406556 -0.103581
C 3.580735 7.003797 -0.096316 -0.405635
C 2.522308 7.869311 -0.343385 -0.076980
H 1.893657 9.926676 -0.251540 5.144860
H 4.065123 10.747151 0.645558 0.138541
H 5.923351 9.147994 1.066179 0.139198
H 5.620224 6.730963 0.593324 0.138067
I 3.205946 4.916600 -0.540151 -5.047696
H 1.586749 7.478292 -0.733490 6.203063
O 0.038351 4.911940 1.097927 -7.799094
H -0.670829 4.246753 1.058989 7.364531
H 0.418676 5.029554 0.184314 0.399478

55
Sextet
Fe 0.490434 1.390843 -0.837780 -6.259351
N 0.920088 1.348887 1.188885 8.287427
N 2.558366 1.515752 -1.181024 -0.704064
N -1.419690 2.064885 -0.374499 -0.706292
N 0.209782 2.125348 -2.758723 -0.707504
C -0.017853 1.370204 2.212605 1.288825
C 3.166368 1.592339 -2.430715 0.260933
C 2.147684 1.069775 1.774432 0.275906
C 3.554572 1.175443 -0.271414 0.252815
C -2.026885 1.970510 0.872217 0.254009
C 1.157566 2.170267 -3.772410 0.284397
C -2.403816 2.442084 -1.275174 0.274083
C -0.997446 2.519127 -3.321743 0.281220
C 0.640369 1.086297 3.470325 -0.131498
C 4.579631 1.313200 -2.292775 -0.139836
C 1.969796 0.901353 3.201532 -0.135858
C 4.818316 1.058637 -0.967744 -0.145288

C	-3.433326	2.297890	0.744856	-0.133153
C	0.519873	2.575304	-5.007607	-0.137143
C	-3.663943	2.588612	-0.573313	-0.136092
C	-0.802575	2.791818	-4.730463	-0.136662
H	0.144179	1.044753	4.428978	5.148298
H	5.289161	1.309204	-3.107646	0.145697
H	2.763715	0.677764	3.899308	0.145285
H	5.758530	0.804319	-0.499733	0.144517
H	-4.140011	2.309455	1.561887	0.148890
H	1.028136	2.691414	-5.953822	0.145516
H	-4.595705	2.880787	-1.035421	0.147099
H	-1.578979	3.117332	-5.407500	0.146454
C	-1.376044	1.641369	2.059270	-5.151468
C	2.514409	1.899325	-3.621490	-0.153945
C	-2.204513	2.647839	-2.637412	-0.153092
C	3.359423	0.976736	1.094020	-0.157874
H	-1.982705	1.618271	2.958608	5.141576
H	3.126343	1.950565	-4.516279	0.137561
H	-3.067584	2.954587	-3.219299	0.138933
H	4.235345	0.727181	1.684315	0.136614
O	1.237737	5.246824	-1.260262	-7.683782
S	0.110793	-0.960387	-1.167318	-8.173642
H	-0.513657	-0.871106	-2.396426	15.042214
C	2.749632	9.236828	-0.048385	-5.118869
C	3.980377	9.638013	0.485478	-0.116788
C	4.979636	8.691089	0.741436	-0.119754
C	4.754514	7.334927	0.464921	-0.104612
C	3.520134	6.970600	-0.066420	-0.406518
C	2.508858	7.885682	-0.331628	-0.077482
H	1.973501	9.969652	-0.243160	5.143550
H	4.160769	10.685378	0.703994	0.137245
H	5.933453	9.000248	1.156690	0.137756
H	5.528733	6.601322	0.666475	0.136750
I	3.054156	4.906483	-0.531612	-5.046118
H	1.565475	7.538264	-0.744132	6.202950
O	-0.077514	4.982097	1.112979	-7.804675
H	-0.740682	4.270197	1.089678	7.359699
H	0.282473	5.113091	0.193414	0.395165

1: Heme and Iodosylbenzene with water displaced.

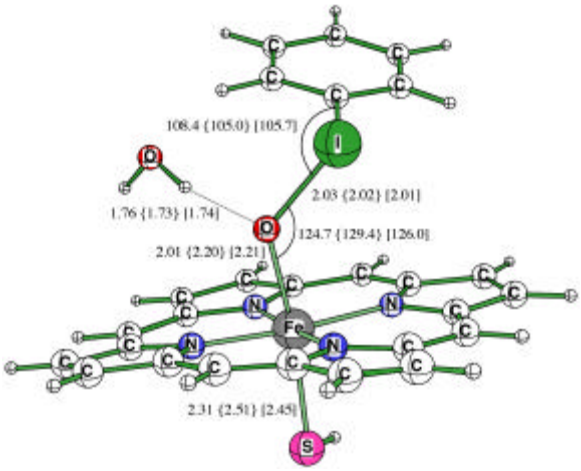


Figure S12: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S38: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
<S^2>	0.81	3.82	8.78

Table S39: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.07	2.62	4.15	0.13	0.08	0.16
O	0.00	0.01	0.02	-0.43	-0.37	-0.33
S	0.03	0.42	0.45	-0.23	-0.29	-0.24
Porphyrin	-0.10	-0.08	0.39	-0.23	-0.17	-0.35
I	0.01	0.03	0.00	0.47	0.48	0.47
Ph	0.00	0.00	0.00	0.12	0.08	0.09

Table S40: Coordinates in xyz-format.

55			
Doublet			
Fe	1.130737	2.031714	-0.607634
N	0.965433	1.161281	1.196091
N	2.817263	0.967679	-0.942806
N	-0.499514	3.153224	-0.242524
N	1.384208	3.011131	-2.346684
C	-0.082130	1.317874	2.090175
C	3.571468	0.967801	-2.105079
C	1.832398	0.243699	1.774057
C	3.430671	0.072831	-0.085150
C	-1.348384	3.029002	0.846297
C	2.332472	2.718177	-3.321197
C	-1.040510	4.151704	-1.040321
C	0.590646	4.022350	-2.875422
C	0.138573	0.485680	3.256168
C	4.681695	0.045105	-1.971088
C	1.320748	-0.168240	3.064980
C	4.598420	-0.501359	-0.722456
C	-2.445450	3.968204	0.723967
C	2.141040	3.581976	-4.464785
C	-2.250933	4.665085	-0.434264
C	1.072436	4.389315	-4.188062
H	-0.530692	0.425966	4.101936
H	5.420411	-0.143119	-2.736897
H	1.810252	-0.872793	3.721232
H	5.252217	-1.228785	-0.263744
H	-3.248807	4.069061	1.439588
H	2.747611	3.557869	-5.358592
H	-2.863711	5.448472	-0.856293
H	0.629475	5.150658	-4.813705
C	-1.165127	2.167656	1.920338
C	3.338670	1.768902	-3.213124
C	-0.525966	4.568475	-2.258267
C	2.982824	-0.254313	1.187188
H	-1.919470	2.176025	2.700582
H	4.011030	1.659311	-4.057645
H	-1.055003	5.355735	-2.784296
H	3.561338	-0.977201	1.752412
O	2.262064	3.263165	0.505877
S	-0.135128	0.382403	-1.617656
H	-0.974789	1.204281	-2.346141
C	0.746198	8.151236	0.619346
C	0.744364	8.881742	-0.575384
C	1.462248	8.421370	-1.686052
C	2.192448	7.228402	-1.605891
C	2.201607	6.542056	-0.389126
C	1.481144	6.962299	0.729815
H	0.176197	8.500599	1.473919
H	0.177630	9.804590	-0.644824
H	1.449204	8.977633	-2.617674
H	2.724561	6.850875	-2.471662
I	3.413848	4.763636	-0.236065
H	1.464122	6.364975	1.643360
O	1.308014	4.564524	2.709554
H	0.381891	4.314310	2.878723
H	1.671512	3.944133	2.021305

55			
Quartet			
Fe	1.088529	1.998497	-0.613640
N	0.948762	1.135973	1.200496
N	2.781240	0.963189	-0.984747
N	-0.552211	3.094000	-0.215549
N	1.365932	3.041809	-2.334015
C	-0.084665	1.281087	2.114326
C	3.545919	1.002770	-2.142175
C	1.816008	0.196258	1.739591
C	3.386093	0.039851	-0.148881
C	-1.387847	2.968103	0.884844
C	2.325119	2.795095	-3.307008
C	-1.101447	4.092080	-1.010892
C	0.551201	4.045294	-2.836784
C	0.150089	0.423778	3.257101
C	4.645332	0.069870	-2.030327
C	1.322343	-0.237798	3.029549
C	4.550373	-0.518785	-0.799724
C	-2.492699	3.892909	0.765513
C	2.119622	3.683363	-4.429730
C	-2.312624	4.588425	-0.398277
C	1.030388	4.457067	-4.138139
H	-0.506314	0.348039	4.111462
H	5.388236	-0.098098	-2.796583
H	1.813579	-0.964740	3.659525
H	5.198591	-1.264622	-0.362891
H	-3.291916	3.989715	1.486094
H	2.727989	3.693169	-5.322444
H	-2.936686	5.364905	-0.816389
H	0.570903	5.222325	-4.746976
C	-1.179844	2.117757	1.964047
C	3.331828	1.845019	-3.223746
C	-0.586167	4.543343	-2.217224
C	2.947704	-0.308222	1.121920
H	-1.924925	2.116404	2.752628
H	4.011077	1.759952	-4.065117
H	-1.131049	5.328802	-2.729292
H	3.523720	-1.051028	1.662947
O	2.291218	3.407248	0.566240
S	-0.248922	0.223233	-1.785792
H	-1.398564	0.961634	-1.996847
C	0.622657	8.095293	0.387812
C	0.762766	8.836428	-0.791669
C	1.673643	8.431745	-1.775205
C	2.451736	7.282859	-1.582054
C	2.307412	6.582691	-0.382635
C	1.400583	6.949549	0.611610
H	-0.092475	8.402158	1.143965
H	0.158689	9.724157	-0.948922
H	1.773851	8.995805	-2.696786
H	3.135375	6.947531	-2.353980
I	3.554011	4.848519	-0.058538
H	1.282299	6.352042	1.518843
O	1.159883	4.646824	2.692476
H	0.254287	4.320053	2.840740
H	1.596241	4.057644	2.014547

55			
Sextet			
Fe	1.047626	1.966594	-0.674845
N	0.940411	1.142646	1.222764
N	2.842940	0.973110	-1.015908
N	-0.598809	3.160963	-0.238273
N	1.384892	3.104458	-2.397876
C	-0.082869	1.324734	2.134132
C	3.624508	1.054237	-2.154533
C	1.813619	0.204983	1.745192
C	3.431882	0.062262	-0.160808
C	-1.398279	3.051769	0.885573
C	2.360172	2.853303	-3.350327
C	-1.134664	4.149028	-1.046870
C	0.541629	4.078680	-2.905448
C	0.158366	0.468764	3.283675
C	4.745600	0.142464	-2.016355
C	1.320481	-0.213716	3.046793
C	4.628511	-0.464022	-0.792465
C	-2.493991	3.997134	0.770379
C	2.136771	3.726783	-4.488260
C	-2.330525	4.671195	-0.412682
C	1.023914	4.479421	-4.215433
H	-0.482071	0.404742	4.151502
H	5.518414	-0.005312	-2.757027
H	1.803180	-0.939844	3.684760
H	5.287475	-1.199191	-0.352858
H	-3.279445	4.124693	1.501311
H	2.746101	3.745571	-5.380693
H	-2.957176	5.450236	-0.822649
H	0.557026	5.224440	-4.844665
C	-1.163752	2.194048	1.968302
C	3.387971	1.913844	-3.231911
C	-0.607060	4.564250	-2.272759
C	2.952374	-0.286977	1.106597
H	-1.895516	2.215067	2.770604
H	4.082231	1.849178	-4.064073
H	-1.156478	5.339373	-2.797937
H	3.528208	-1.028727	1.651282
O	2.239191	3.333842	0.588053
S	-0.264662	0.237094	-1.812556
H	-1.435107	0.955732	-1.954528
C	0.677098	8.084948	0.434935
C	0.793204	8.806040	-0.760166
C	1.655606	8.364088	-1.770309
C	2.408839	7.196538	-1.590047
C	2.291036	6.516869	-0.375421
C	1.432181	6.921994	0.647084
H	-0.001761	8.421158	1.211973
H	0.207227	9.707238	-0.908612
H	1.735645	8.912528	-2.702454
H	3.051774	6.830591	-2.382590
I	3.502507	4.754379	-0.070928
H	1.333360	6.338252	1.566204
O	1.192408	4.619342	2.735873
H	0.273497	4.338459	2.896077
H	1.588293	4.007994	2.053041

TS1: Transition state between **1** and **2**.

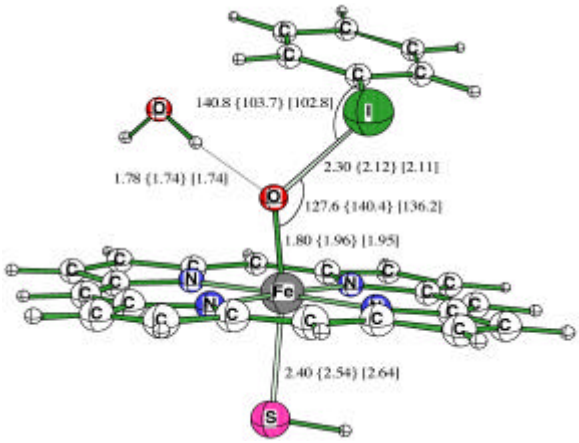


Figure S13: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S41: Valence orbitals, imaginary frequencies and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
Frequency	i161.24 cm^{-1}	i251.22 cm^{-1}	i209.12 cm^{-1}
<S^2>	1.11	3.84	8.89

Table S42: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.43	2.43	4.09	0.07	0.28	0.39
O	0.12	0.09	0.04	-0.44	-0.48	-0.39
S	-0.13	0.40	0.57	-0.25	-0.32	-0.29
Porphyrin	-0.21	-0.09	0.44	0.03	-0.13	-0.42
I	-0.20	0.15	-0.13	0.34	0.41	0.44
Ph	-0.01	0.01	0.00	0.07	0.07	0.09

Comments: As in the water free case, the sextet **TS1** relaxes to a product structure that has the Fe-S bond broken.

Table S43: Coordinates in xyz-format.

55				
Doublet				
Fe	1.042251	2.088170	-0.484289	-6.550230
N	0.889217	0.946127	1.184610	8.412379
N	2.776361	1.207053	-0.978004	-0.614665
N	-0.744274	2.924550	-0.017152	-0.593247
N	1.150079	3.162534	-2.169886	-0.618106
C	-0.141100	0.922528	2.109467	1.273765
C	3.538656	1.392301	-2.124200	0.255517
C	1.831488	0.041059	1.633558	0.289468
C	3.441839	0.247746	-0.226226	0.281253
C	-1.559792	2.638606	1.065256	0.249106
C	2.114543	3.097782	-3.169581	0.254490
C	-1.376749	3.929615	-0.725376	0.273502
C	0.231586	4.118219	-2.588368	0.278375
C	0.166542	-0.021937	3.165798	-0.136833
C	4.706552	0.540423	-2.082871	-0.140810
C	1.385113	-0.561238	2.875930	-0.141008
C	4.650342	-0.159672	-0.911268	-0.146296
C	-2.729134	3.493801	1.037853	-0.156315
C	1.794290	4.032563	-4.225301	-0.145934
C	-2.613003	4.294765	-0.064062	-0.146789
C	0.639049	4.665562	-3.864261	-0.139745
H	-0.475386	-0.227782	4.009797	5.144453
H	5.460118	0.494600	-2.855652	0.142313
H	1.941154	-1.300952	3.433223	0.143232
H	5.348259	-0.894104	-0.536117	0.144158
H	-3.525781	3.468020	1.767108	0.145805
H	2.384634	4.173043	-5.119238	0.140449
H	-3.296849	5.053771	-0.415311	0.143563
H	0.096839	5.428631	-4.403430	0.142711
C	-1.289182	1.695522	2.046616	-5.139174
C	3.226104	2.268594	-3.152184	-0.157621
C	-0.919118	4.489185	-1.910002	-0.143879
C	3.016532	-0.274353	0.986155	-0.147824
H	-2.020426	1.572604	2.838400	5.141808
H	3.902531	2.314349	-3.999096	0.137047
H	-1.529841	5.264527	-2.360555	0.137330
H	3.654895	-1.015936	1.455130	0.137919
O	1.782686	3.293131	0.625346	-7.544755
S	-0.165132	0.348464	-1.603521	-8.057953
H	0.516285	0.405293	-2.805412	15.020729
C	1.108949	8.291020	-0.277545	-5.133836
C	1.588388	8.874289	-1.456102	-0.117693
C	2.614199	8.253476	-2.179075	-0.122966
C	3.168494	7.050574	-1.723554	-0.079800
C	2.685734	6.502230	-0.531746	-0.398015
C	1.653198	7.090431	0.202325	-0.102840
H	0.307389	8.765644	0.279421	5.140974
H	1.162556	9.806479	-1.813345	0.135569
H	2.983359	8.696402	-3.098508	0.136151
H	3.953230	6.560947	-2.288248	0.148458
I	3.568120	4.683265	0.199362	-5.422466
H	1.264593	6.615597	1.104148	6.236176
O	0.468414	5.068646	2.280639	-7.777877
H	-0.485722	4.987399	2.097226	7.359303
H	0.939056	4.338185	1.798148	0.430886

55				
Quartet				
Fe	1.032068	2.006681	-0.535668	-6.386299
N	0.907202	1.062120	1.218261	8.354461
N	2.766328	1.032084	-0.947369	-0.627173
N	-0.695069	2.952071	-0.162042	-0.641054
N	1.168007	2.965122	-2.330077	-0.624589
C	-0.135082	1.132226	2.132437	1.290684
C	3.506581	1.104974	-2.118596	0.281386
C	1.838709	0.183171	1.757649	0.287726
C	3.433927	0.152908	-0.117025	0.273396
C	-1.523912	2.769236	0.935677	0.260487
C	2.138908	2.778383	-3.302468	0.276480
C	-1.296992	3.929170	-0.947633	0.275303
C	0.312577	3.939546	-2.813329	0.264472
C	0.154112	0.285051	3.268941	-0.136076
C	4.665256	0.242812	-2.014829	-0.145989
C	1.370303	-0.292265	3.041858	-0.140527
C	4.624084	-0.339195	-0.779014	-0.143140
C	-2.671082	3.644108	0.831832	-0.149842
C	1.879101	3.656577	-4.423761	-0.149438
C	-2.526809	4.362206	-0.322788	-0.142619
C	0.757920	4.377396	-4.119340	-0.143903
H	-0.497325	0.161187	4.121585	5.144375
H	5.403368	0.111358	-2.792732	0.141772
H	1.909237	-0.986456	3.670062	0.144219
H	5.319954	-1.043709	-0.347008	0.142973
H	-3.473327	3.691529	1.553980	0.143889
H	2.482693	3.703750	-5.318645	0.140527
H	-3.188961	5.112417	-0.730247	0.142447
H	0.262359	5.128991	-4.716752	0.140398
C	-1.273892	1.909868	1.996925	-5.167363
C	3.214967	1.906620	-3.211914	-0.154908
C	-0.826322	4.398635	-2.164258	-0.154605
C	3.012258	-0.230298	1.150149	-0.151411
H	-2.012404	1.861796	2.789804	5.137028
H	3.891261	1.859680	-4.058912	0.134340
H	-1.410970	5.164861	-2.662016	0.134248
H	3.634590	-0.933283	1.693324	0.135867
O	2.019240	3.446861	0.361801	-7.640902
S	-0.124098	0.128112	-1.793565	-8.159292
H	-1.022835	0.918801	-2.486558	15.019745
C	0.899199	8.305910	0.260436	-5.133185
C	1.217087	9.069710	-0.868787	-0.115122
C	2.192003	8.622553	-1.768717	-0.123652
C	2.856387	7.410439	-1.541364	-0.082499
C	2.533943	6.682391	-0.393283	-0.409037
C	1.557263	7.093712	0.515396	-0.095894
H	0.137180	8.647429	0.953497	5.143872
H	0.704095	10.008513	-1.050904	0.138188
H	2.434124	9.206277	-2.650896	0.139116
H	3.599560	7.053361	-2.245197	0.150223
I	3.578814	4.838746	-0.009382	-5.262544
H	1.300609	6.480415	1.381573	6.240549
O	0.899691	4.748877	2.472430	-7.783179
H	-0.047879	4.537199	2.552175	7.356437
H	1.298618	4.145418	1.784313	0.429661

55				
Sextet				
Fe	1.130297	2.084441	-0.494941	-6.176907
N	0.919023	1.066120	1.278599	8.305129
N	2.834864	0.970408	-0.953591	-0.676440
N	-0.669912	3.056037	-0.170796	-0.687523
N	1.276915	3.024531	-2.375717	-0.660148
C	-0.117519	1.206419	2.183677	1.292299
C	3.590753	1.057116	-2.109701	0.281023
C	1.788789	0.109703	1.773092	0.291222
C	3.417518	0.027129	-0.133779	0.281394
C	-1.471431	2.917062	0.948080	0.266572
C	2.265658	2.810411	-3.320196	0.277238
C	-1.251368	4.005625	-0.995147	0.274861
C	0.404871	3.969852	-2.880494	0.264954
C	0.119094	0.313346	3.306344	-0.139164
C	4.702030	0.126124	-2.008546	-0.146859
C	1.285767	-0.356368	3.055628	-0.141336
C	4.595999	-0.505561	-0.797068	-0.144677
C	-2.608330	3.812356	0.821610	-0.150118
C	2.009387	3.668776	-4.465248	-0.150382
C	-2.471965	4.479796	-0.367897	-0.143835
C	0.869580	4.380053	-4.195712	-0.146330
H	-0.529928	0.214142	4.164483	5.141994
H	5.455008	-0.023678	-2.769115	0.139828
H	1.764797	-1.104274	3.671102	0.142266
H	5.246345	-1.265376	-0.387694	0.141237
H	-3.403359	3.909302	1.547263	0.141111
H	2.618174	3.707888	-5.357403	0.138664
H	-3.134627	5.222583	-0.788758	0.139800
H	0.377504	5.106086	-4.827247	0.137997
C	-1.213555	2.058970	2.025423	-5.181206
C	3.327276	1.909642	-3.186862	-0.158730
C	-0.750032	4.423112	-2.232509	-0.157971
C	2.933272	-0.357344	1.123834	-0.153891
H	-1.948877	2.053733	2.824570	5.133725
H	4.019208	1.855345	-4.022256	0.131099
H	-1.334827	5.171886	-2.758583	0.130795
H	3.503823	-1.120092	1.645363	0.132977
O	2.146565	3.477499	0.414582	-7.672269
S	-0.080536	0.221696	-1.915067	-8.151872
H	-1.120746	1.000407	-2.389233	15.022799
C	0.775862	8.236483	0.346117	-5.133004
C	0.955397	9.002471	-0.811768	-0.114290
C	1.868425	8.593890	-1.791478	-0.124246
C	2.610293	7.418815	-1.615270	-0.080657
C	2.426782	6.690719	-0.437324	-0.410126
C	1.514293	7.061561	0.551425	-0.093719
H	0.060130	8.546790	1.100400	5.145546
H	0.381609	9.912446	-0.954426	0.139134
H	2.001919	9.178248	-2.696014	0.140089
H	3.303423	7.088726	-2.380546	0.152297
I	3.600560	4.910831	-0.134154	-5.238197
H	1.362864	6.446360	1.440904	6.240171
O	1.120074	4.725727	2.598083	-7.780102
H	0.186648	4.467117	2.705535	7.356955
H	1.522840	4.140962	1.897457	0.430616

2: [H_2O-Cpd I] and Iodobenzene, complexed.

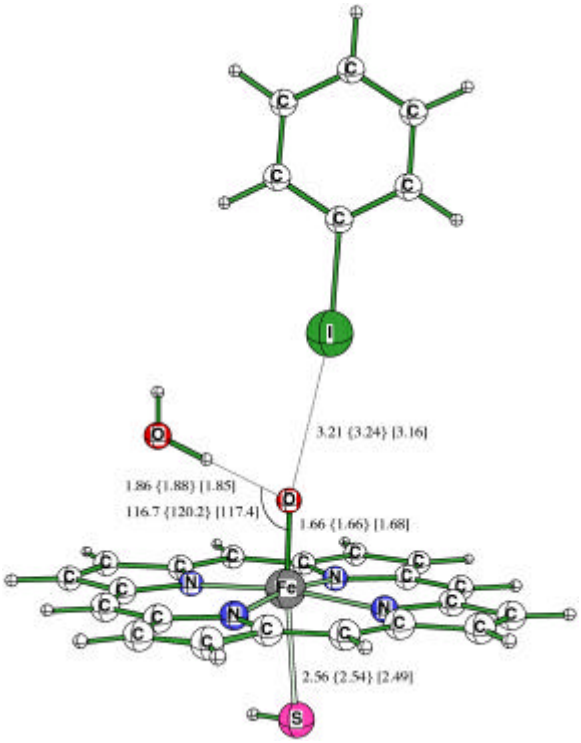


Figure S14: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S44: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{xz}, \pi^*_{yz})\beta(a_{2u})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, a_{2u})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, a_{2u}, \sigma^*_{xy})$
<S^2>	1.79	3.80	8.88

Table S45: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.40	1.25	3.26	0.13	0.13	0.22
O	0.74	0.80	0.59	-0.41	-0.40	-0.42
S	-0.56	0.52	0.19	-0.22	-0.21	-0.25
Porphyrin	-0.60	0.44	0.97	0.37	0.34	0.30

	Spin			***Charge***		
I	0.00	0.00	0.00	0.03	0.03	0.03
Ph	0.00	0.00	0.00	-0.05	-0.04	-0.05

Table S46: Coordinates in xyz-format.

55			
Doublet			
Fe	-0.041020	-0.180080	0.173480
N	-0.049612	-0.454910	2.165209
N	1.977154	-0.145183	0.196454
N	-2.030255	-0.495461	0.120635
N	-0.002854	-0.199060	-1.848470
C	-1.156621	-0.643045	2.973948
C	2.820848	0.007781	-0.891244
C	1.037578	-0.399399	3.018487
C	2.795452	-0.129060	1.316538
C	-2.870438	-0.672464	1.207405
C	1.113597	-0.038029	-2.662808
C	-2.853206	-0.449228	-0.992562
C	-1.101173	-0.195592	-2.704182
C	-0.753882	-0.705469	4.360677
C	4.192778	0.110452	-0.443859
C	0.602433	-0.552498	4.388925
C	4.176841	0.026404	0.918041
C	-4.243740	-0.751480	0.763488
C	0.704455	0.035800	-4.047194
C	-4.234179	-0.609392	-0.595181
C	-0.657151	-0.058878	-4.072875
H	-1.432179	-0.840091	5.189719
H	5.043267	0.230913	-1.098676
H	1.259597	-0.542111	5.245913
H	5.011143	0.064191	1.602560
H	-5.091581	-0.888897	1.418232
H	1.383372	0.151782	-4.878852
H	-5.071780	-0.613485	-1.276949
H	-1.314247	-0.035960	-4.929907
C	-2.465187	-0.751499	2.530304
C	2.419609	0.062980	-2.218078
C	-2.421660	-0.301934	-2.304507
C	2.360039	-0.244375	2.625333
H	-3.236231	-0.882704	3.281120
H	3.192623	0.195738	-2.967183
H	-3.180938	-0.279113	-3.078935
H	3.112314	-0.215926	3.406207
O	-0.186983	1.471946	0.257910
S	0.304754	-2.676615	-0.282966
H	-0.886701	-2.924725	-0.940599
C	0.440885	8.823052	-1.523105
C	-0.754719	9.443657	-1.145573
C	-1.800923	8.673701	-0.623914
C	-1.655659	7.288267	-0.478020
C	-0.456255	6.675875	-0.857583
C	0.594894	7.437983	-1.380549
H	1.258400	9.412241	-1.927491
H	-0.869684	10.517153	-1.255389
H	-2.731974	9.146198	-0.326630
H	-2.468241	6.697860	-0.070031
I	-0.222960	4.559232	-0.611377
H	1.524571	6.962655	-1.671610
O	-2.104303	2.472077	2.060771
H	-2.504904	3.178199	1.521349
H	-1.316029	2.144316	1.568968

55			
Quartet			
Fe	-0.063807	-0.186886	0.144324
N	-0.058243	-0.408315	2.148806
N	1.951110	-0.102911	0.161050
N	-2.046759	-0.548149	0.109885
N	-0.033847	-0.251851	-1.870623
C	-1.158026	-0.598665	2.965606
C	2.789145	0.032249	-0.933048
C	1.028817	-0.301389	2.995633
C	2.773148	-0.043651	1.278027
C	-2.876423	-0.719565	1.205482
C	1.076819	-0.099644	-2.694263
C	-2.875167	-0.554704	-0.999851
C	-1.133317	-0.310280	-2.722864
C	-0.750295	-0.610013	4.352936
C	4.160546	0.169276	-0.493534
C	0.601723	-0.423530	4.372198
C	4.150456	0.123080	0.870230
C	-4.248872	-0.846082	0.771263
C	0.663480	-0.089913	-4.079292
C	-4.249480	-0.739684	-0.590850
C	-0.695298	-0.218385	-4.097181
H	-1.422897	-0.736208	5.187945
H	5.006745	0.284373	-1.154372
H	1.260893	-0.371570	5.226158
H	4.986298	0.192852	1.550437
H	-5.089290	-0.989773	1.433766
H	1.338018	0.007334	-4.916875
H	-5.089931	-0.785218	-1.267456
H	-1.354255	-0.247589	-4.952458
C	-2.464178	-0.752276	2.528359
C	2.382243	0.041448	-2.258644
C	-2.449945	-0.436339	-2.317019
C	2.345913	-0.130426	2.591520
H	-3.229497	-0.883830	3.284776
H	3.150206	0.163470	-3.014686
H	-3.210128	-0.459227	-3.090404
H	3.101038	-0.065071	3.367414
O	-0.260347	1.460946	0.230204
S	0.329785	-2.674349	-0.204407
H	-0.831846	-2.968063	-0.892973
C	0.544428	8.868150	-1.388447
C	-0.653183	9.492810	-1.023822
C	-1.717707	8.722181	-0.542478
C	-1.588779	7.332030	-0.423787
C	-0.387312	6.715872	-0.790889
C	0.682009	7.478304	-1.273629
H	1.376267	9.457762	-1.761371
H	-0.755568	10.569555	-1.112193
H	-2.650390	9.197708	-0.254998
H	-2.414693	6.740808	-0.045133
I	-0.181703	4.591650	-0.587457
H	1.612734	6.999256	-1.554901
O	-2.298402	2.460721	1.909814
H	-2.851644	2.896468	1.233660
H	-1.452813	2.203653	1.472218

55			
Sextet			
Fe	-0.039672	-0.142994	0.151181
N	-0.056799	-0.470941	2.210111
N	2.038049	-0.118883	0.189649
N	-2.081589	-0.523976	0.079349
N	0.010135	-0.148664	-1.930820
C	-1.176102	-0.659135	2.989693
C	2.868981	0.039612	-0.900358
C	1.033901	-0.432851	3.048760
C	2.831606	-0.138445	1.320889
C	-2.907089	-0.697490	1.170521
C	1.137710	0.014117	-2.715693
C	-2.878915	-0.491296	-1.046764
C	-1.085621	-0.184424	-2.775570
C	-0.776333	-0.738649	4.383932
C	4.243679	0.121430	-0.439146
C	0.584416	-0.599044	4.420773
C	4.220599	0.011360	0.924947
C	-4.280953	-0.791398	0.713570
C	0.735316	0.073714	-4.109935
C	-4.264442	-0.663093	-0.649754
C	-0.626939	-0.048834	-4.146829
H	-1.453283	-0.876367	5.214077
H	5.104273	0.244681	-1.080329
H	1.229910	-0.605010	5.286722
H	5.058293	0.028623	1.606624
H	-5.137022	-0.929244	1.357603
H	1.413071	0.194013	-4.942509
H	-5.104322	-0.681102	-1.328601
H	-1.269343	-0.047996	-5.015096
C	-2.481949	-0.761412	2.501652
C	2.443448	0.110029	-2.231212
C	-2.409641	-0.331031	-2.356564
C	2.360726	-0.278991	2.629306
H	-3.261496	-0.890827	3.245454
H	3.222175	0.245192	-2.976101
H	-3.163448	-0.329521	-3.138197
H	3.113324	-0.272741	3.412434
O	-0.226462	1.517199	0.305517
S	0.314839	-2.588458	-0.181378
H	-0.866109	-2.862985	-0.843858
C	0.388821	8.759234	-1.716009
C	-0.733150	9.433364	-1.221288
C	-1.721161	8.721065	-0.532582
C	-1.591314	7.340109	-0.337265
C	-0.466252	6.673484	-0.835560
C	0.526601	7.378201	-1.525068
H	1.161215	9.303588	-2.250558
H	-0.836124	10.503399	-1.369949
H	-2.594719	9.235079	-0.143535
H	-2.358939	6.794545	0.199684
I	-0.259393	4.561415	-0.525122
H	1.398971	6.861381	-1.908452
O	-2.144097	2.422383	2.155712
H	-2.514592	3.211901	1.720167
H	-1.373729	2.123286	1.617340

[H_2O-Cpd I] + IPh: Compound I and Iodobenzene, uncomplexed.

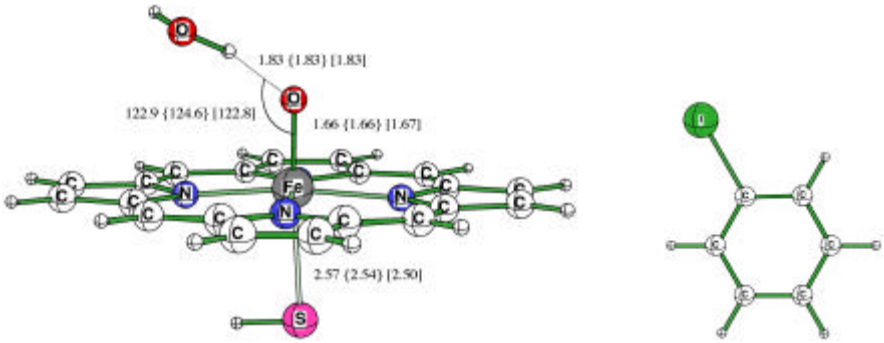


Figure S15: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S47: Valence orbitals of H_2O-Cpd I and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{xz}, \pi^*_{yz})\beta(a_{2u})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, a_{2u})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, a_{2u}, \sigma^*_{xy})$
<S^2>	1.79	3.81	8.87

Table S48: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.36	1.18	3.21	0.17	0.05	0.22
O	0.77	0.85	0.62	-0.32	-0.30	-0.25
S	-0.59	0.39	0.18	-0.25	-0.33	-0.32
Porphyrin	-0.57	0.58	0.98	0.25	0.43	0.20
I	0.00			-0.01		

Table S49: Coordinates in xyz-format.

42

Doublet CpdI + H2O

Fe	0.397128	1.611873	-0.433664
N	0.804025	1.384602	1.531277
N	2.348387	1.587076	-0.882280
N	-1.550967	1.883797	0.046797
N	-0.014581	1.985776	-2.380815
C	-0.091209	1.333500	2.587627
C	2.935215	1.678077	-2.137909
C	2.059076	1.194635	2.083678
C	3.384345	1.364445	0.012879
C	-2.143551	1.735980	1.297937
C	0.880347	2.011656	-3.445872
C	-2.597253	2.060079	-0.854488
C	-1.276984	2.160478	-2.936655
C	0.621295	1.107771	3.829966
C	4.368445	1.522573	-2.020895
C	1.946844	1.022874	3.519583
C	4.644864	1.330590	-0.696803
C	-3.577715	1.856145	1.177566
C	0.162790	2.213379	-4.685258
C	-3.856971	2.056345	-0.145984
C	-1.164523	2.305258	-4.372253
H	0.152368	1.031301	4.800286
H	5.058454	1.555151	-2.851520
H	2.782513	0.862291	4.185241
H	5.605984	1.173936	-0.228877
H	-4.270108	1.784953	2.003903
H	0.626453	2.274685	-5.659084
H	-4.822758	2.180756	-0.613793
H	-2.000341	2.456238	-5.040178
C	-1.464893	1.492192	2.482164
C	2.256045	1.873188	-3.331975
C	-2.470098	2.199552	-2.229095
C	3.254152	1.186731	1.381929
H	-2.052679	1.412823	3.390355
H	2.843710	1.915623	-4.242731
H	-3.382561	2.336000	-2.800082
H	4.164202	1.024969	1.949770
S	0.186535	-0.647178	-0.664256
H	0.363762	-0.721810	-2.033135
O	0.554132	3.711602	-0.185826
H	-0.271866	3.980949	0.262710
H	0.604579	4.104503	-1.079222

42

Quartet CpdI + H2O

Fe	0.393509	1.563380	-0.431628
N	0.820352	1.372917	1.516058
N	2.370480	1.632264	-0.860262
N	-1.558730	1.887181	0.038331
N	-0.021821	1.978211	-2.362624
C	-0.085144	1.304691	2.566249
C	2.948747	1.723290	-2.119252
C	2.077536	1.200478	2.078109
C	3.415524	1.433459	0.029659
C	-2.140434	1.745236	1.291803
C	0.881078	2.002665	-3.422118
C	-2.607860	2.087632	-0.852194
C	-1.282523	2.158367	-2.925359
C	0.620497	1.065549	3.804461
C	4.386498	1.599996	-2.008493
C	1.952395	1.003468	3.504087
C	4.673854	1.424350	-0.684871
C	-3.574812	1.892686	1.185599
C	0.169884	2.194462	-4.662700
C	-3.862614	2.104021	-0.133604
C	-1.161019	2.291126	-4.357060
H	0.146662	0.966343	4.770160
H	5.071157	1.637272	-2.843330
H	2.783312	0.842863	4.175420
H	5.640239	1.288752	-0.221480
H	-4.260499	1.829069	2.017977
H	0.637582	2.248257	-5.635092
H	-4.829935	2.246638	-0.592649
H	-1.992127	2.438468	-5.031410
C	-1.458019	1.473872	2.466612
C	2.259826	1.888189	-3.310427
C	-2.480535	2.217219	-2.226466
C	3.282969	1.233116	1.393810
H	-2.040519	1.386109	3.377194
H	2.840906	1.929406	-4.225156
H	-3.387960	2.361353	-2.802638
H	4.189319	1.082090	1.969692
S	0.165242	-0.892274	-0.716308
H	-0.156738	-0.907536	-2.060381
O	0.520765	4.038307	-0.159476
H	-0.434578	4.240976	-0.177707
H	0.946797	4.380084	-0.968354

42

Sextet CpdI + H2O

Fe	0.389107	1.461255	-0.436552
N	0.825784	1.368320	1.573354
N	2.416230	1.619735	-0.878688
N	-1.606672	1.912158	0.049009
N	-0.031048	2.022726	-2.410256
C	-0.085398	1.345712	2.615269
C	2.981225	1.732235	-2.136994
C	2.090308	1.224512	2.118102
C	3.444413	1.425343	0.026222
C	-2.171977	1.768479	1.307906
C	0.884046	2.058919	-3.455336
C	-2.643263	2.106125	-0.853299
C	-1.294377	2.211403	-2.955793
C	0.632548	1.154286	3.860852
C	4.423779	1.611755	-2.017344
C	1.966476	1.081803	3.556126
C	4.707442	1.425108	-0.691229
C	-3.611564	1.905846	1.193803
C	0.168193	2.273946	-4.695704
C	-3.900394	2.111650	-0.129458
C	-1.165816	2.367768	-4.389913
H	0.171454	1.093634	4.836174
H	5.118514	1.662730	-2.843404
H	2.795321	0.950367	4.236753
H	5.677002	1.293871	-0.232599
H	-4.304413	1.842434	2.020611
H	0.629721	2.343287	-5.670207
H	-4.872183	2.247755	-0.581648
H	-1.990511	2.527955	-5.069639
C	-1.466020	1.515795	2.485752
C	2.269612	1.926792	-3.322493
C	-2.491208	2.250170	-2.233910
C	3.289057	1.242784	1.401484
H	-2.050994	1.448977	3.397715
H	2.852140	1.984498	-4.236669
H	-3.399402	2.398048	-2.809916
H	4.198737	1.106473	1.977740
S	0.141356	-0.927105	-0.749980
H	-0.160522	-0.913902	-2.097722
O	0.541428	3.868210	-0.135215
H	-0.417335	4.042286	-0.051580
H	0.866425	4.208088	-0.990866

12

PhI

C	1.007336	0.814445	0.000000	0.884330
C	0.312079	2.030825	0.000001	-0.093241
C	-1.086139	2.018974	0.000002	-0.345815
C	-1.795553	0.814017	0.000001	-0.093219
C	-1.089727	-0.396255	0.000002	-0.115672
C	0.310200	-0.399551	0.000000	-0.123912
H	2.092071	0.822214	0.000001	0.136065
H	0.854920	2.968337	0.000003	0.149197
I	-2.159641	3.878322	-0.000001	0.182481
H	-2.878892	0.812707	0.000000	0.149201
H	-1.638783	-1.331790	0.000003	0.136009
H	0.852416	-1.338745	-0.000001	0.134576

Geometries (all in Å)

Table S50: C-I distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	2.18	2.17	2.17	2.16	2.15	2.14	2.15
Quartet		2.17	2.17	2.16	2.15	2.14	
Sextet		2.17	2.17	2.16	2.15	2.14	

Table S51: I-O distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	1.99	1.98	1.99	2.03	2.30	3.21	----
Quartet		1.98	1.99	2.02	2.12	3.24	
Sextet		1.98	1.99	2.01	2.11	3.16	

Table S52: O-Fe distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	----	4.06	3.60	2.01	1.80	1.66	1.66
Quartet		4.37	3.69	2.20	1.96	1.66	1.66
Sextet		4.27	3.95	2.21	1.95	1.68	1.67

Table S53: H_2O-Fe distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	2.12	2.06	3.74	4.18	4.11	3.85	3.89
Quartet	2.49	2.28	3.85	4.24	4.07	3.89	3.91
Sextet	2.43	2.23	4.13	4.32	4.07	3.88	3.89

Table S54: H_2O-OI distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	----	1.56	1.73	1.76	1.78	1.86	1.83
Quartet		1.62	1.73	1.73	1.74	1.88	1.83
Sextet		1.61	1.74	1.74	1.74	1.85	1.83

Table S55: Fe-S distances.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	2.28	2.30	2.30	2.31	2.40	2.56	2.57
Quartet	2.48	2.51	2.47	2.51	2.54	2.54	2.54
Sextet	2.42	2.46	2.40	2.45	2.64	2.49	2.50

Energies

All energies are in kcal mol^{-1}, with the reference point as marked in **bold**.

Table S56: Energy, LACVP.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	21.78	2.82	16.81	**0.00**	-0.39	-14.20	-12.42
Quartet	27.00	10.13	16.04	7.32	7.93	-13.80	-11.42
Sextet	28.69	11.72	18.49	9.61	11.61	-0.12	2.44

Table S57: Energy, LACV3P*+ (ERMLER2*+ on I).

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	13.71	1.02	12.04	**0.00**	5.97	-2.48	-0.38
Quartet	17.96	7.28	10.36	6.12	10.54	-1.74	0.74
Sextet	15.30	4.93	7.01	4.08	11.02	8.21	10.88

Table S58: Energy, LACVP including solvation.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	15.57	2.13	14.27	**0.00**	0.38	-14.27	-14.23
Quartet	17.74	5.98	10.78	3.79	6.90	-14.29	-14.66
Sextet	22.05	10.50	15.03	9.13	11.83	-1.19	-1.09

Table S59: Energy, LACVP including zero-point vibration energy.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	21.18	3.35	16.49	**0.00**	-0.88	-14.86	-13.32
Quartet	24.68	9.31	15.10	6.57	6.71	-14.31	-12.80
Sextet	25.51	10.06	16.35	7.76	9.06	-2.39	-0.21

Table S60: Total Energy, LACV3P*+ (ERMLER2*+ on I) including solvation and Z_0.

	[H_2O-Heme]+ OIPh	***0***	***TS0***	***1***	***TS1***	***2***	***[H_2O-Cpd I]+ IPh***
Doublet	6.90	0.85	9.18	**0.00**	6.25	-3.21	-3.09
Quartet	6.37	2.32	4.17	1.84	8.29	-2.74	-3.88
Sextet	5.48	2.04	1.42	1.75	8.68	4.87	4.70

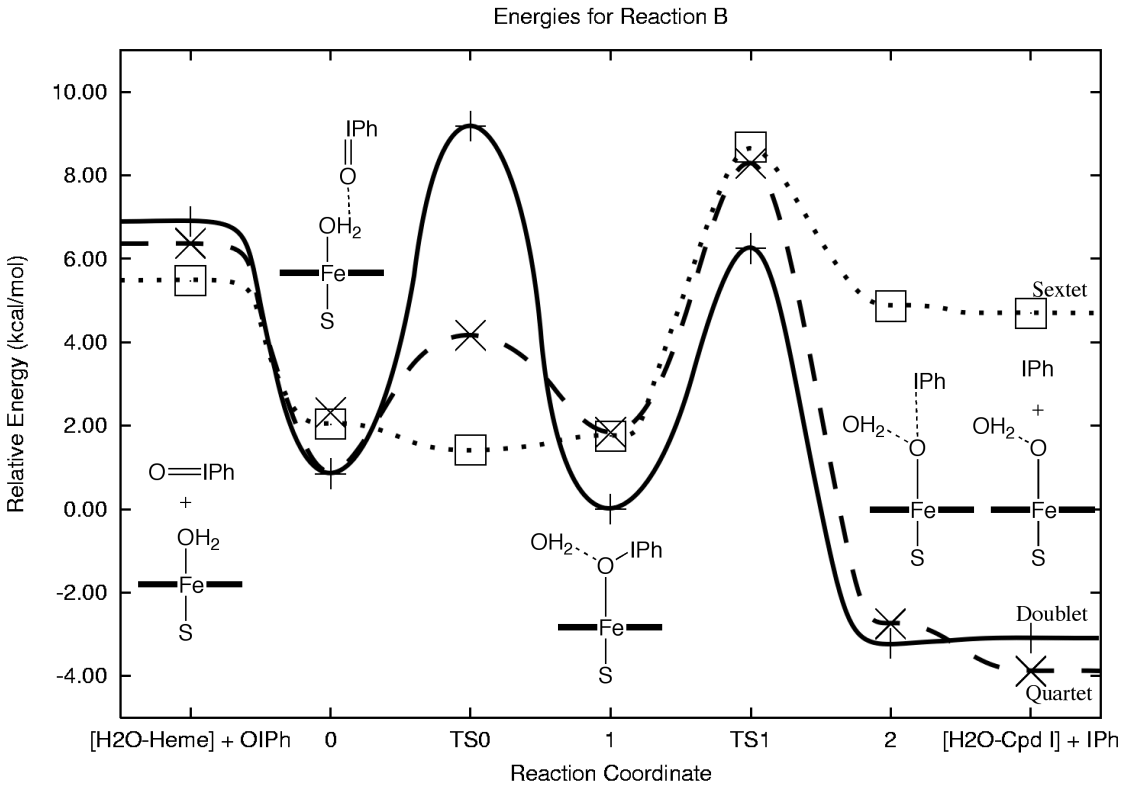


Figure S16: Graph of Table S60.

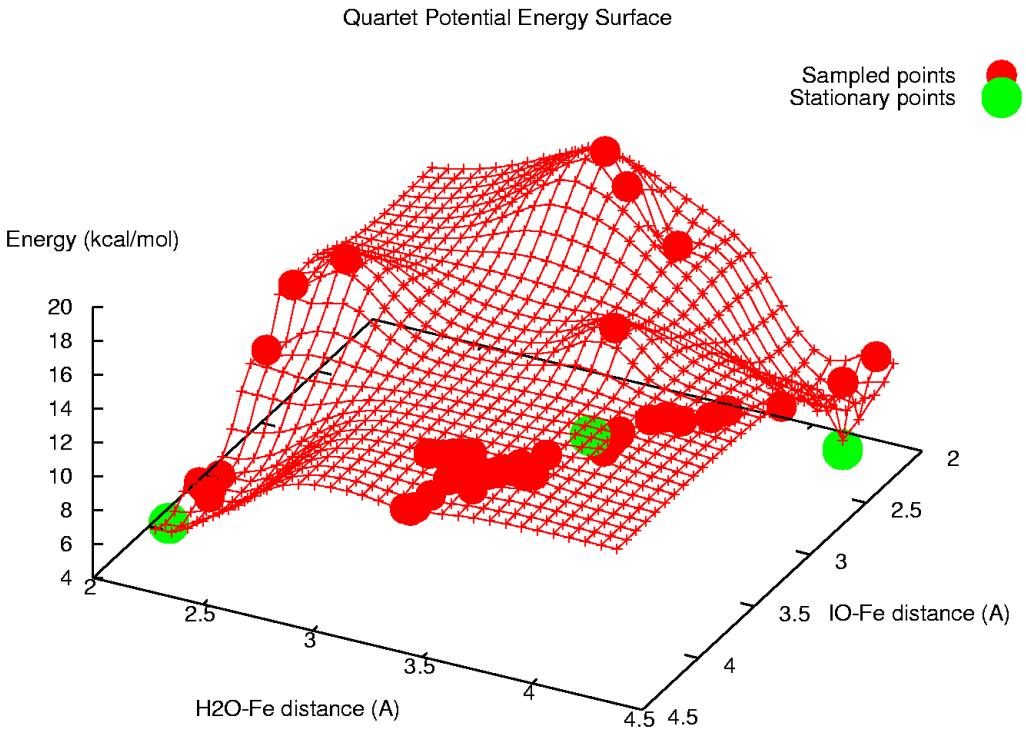


Figure S17: Scanning points in search for TS0 (Quartet, LACVP). The surface is a projected one with help of GNUPLOT and does in fact not necessarily reflect the actual potential energy surface except at the explicitly sampled points. The points sampled around the TS were obtained by constraining only one of the coordinates.

Table S61: Free Energy DG, component by component.

	A	B	C	D	E	F	A+B+C+D+E+F
[H_2O-Heme] + OIPh							
Doublet	21.78	-8.07	-6.21	-0.60	-0.51	-14.26	**-7.87**
Quartet	27.00	-9.04	-9.27	-2.32	-0.12	-16.32	**-10.06**
Sextet	28.69	-13.38	-6.64	-3.18	-0.11	-16.30	**-10.92**
0							
Doublet	2.82	-1.80	-0.69	0.52	0.09	-2.56	**-1.62**
Quartet	10.13	-2.85	-4.14	-0.82	0.30	-2.98	**-0.36**
Sextet	11.72	-6.79	-1.22	-1.66	0.86	-5.03	**-2.12**
TS0							
Doublet	16.81	-4.77	-2.54	-0.32	0.46	-3.86	**5.78**
Quartet	16.04	-5.67	-5.26	-0.94	0.81	-5.45	**-0.47**
Sextet	18.49	-11.48	-3.46	-2.13	1.14	-7.14	**-4.59**
1							
Doublet	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Quartet	7.32	-1.20	-3.53	-0.75	1.00	-4.48	**-1.64**
Sextet	9.61	-5.53	-0.48	-1.85	1.13	-5.22	**-2.34**
TS1							
Doublet	-0.39	6.36	0.77	-0.49	0.32	-2.58	**3.99**
Quartet	7.93	2.61	-1.04	-1.22	0.11	-1.35	**7.05**
Sextet	11.61	-0.60	0.21	-2.55	0.92	-4.58	**5.01**
2							
Doublet	-14.20	11.72	-0.07	-0.66	0.73	-5.15	**-7.63**
Quartet	-13.80	12.06	-0.49	-0.51	0.62	-5.32	**-7.44**
Sextet	-0.12	8.33	-1.07	-2.27	0.95	-6.31	**-0.49**
[H_2O-Cpd I] + IPh							
Doublet	-12.42	12.04	-1.80	-0.90	-0.19	-15.65	**-18.93**
Quartet	-11.42	12.16	-3.24	-1.38	-1.12	-14.04	**-19.04**
Sextet	2.44	8.44	-3.53	-2.65	0.09	-17.06	**-12.28**

A=LACVP relative energy; B=LACV3P*+ correction; C=Solvent correction; D=Z0 correction; E=Enthalpy correction F=Entropy correction; A+B+C+D+E+F=? G

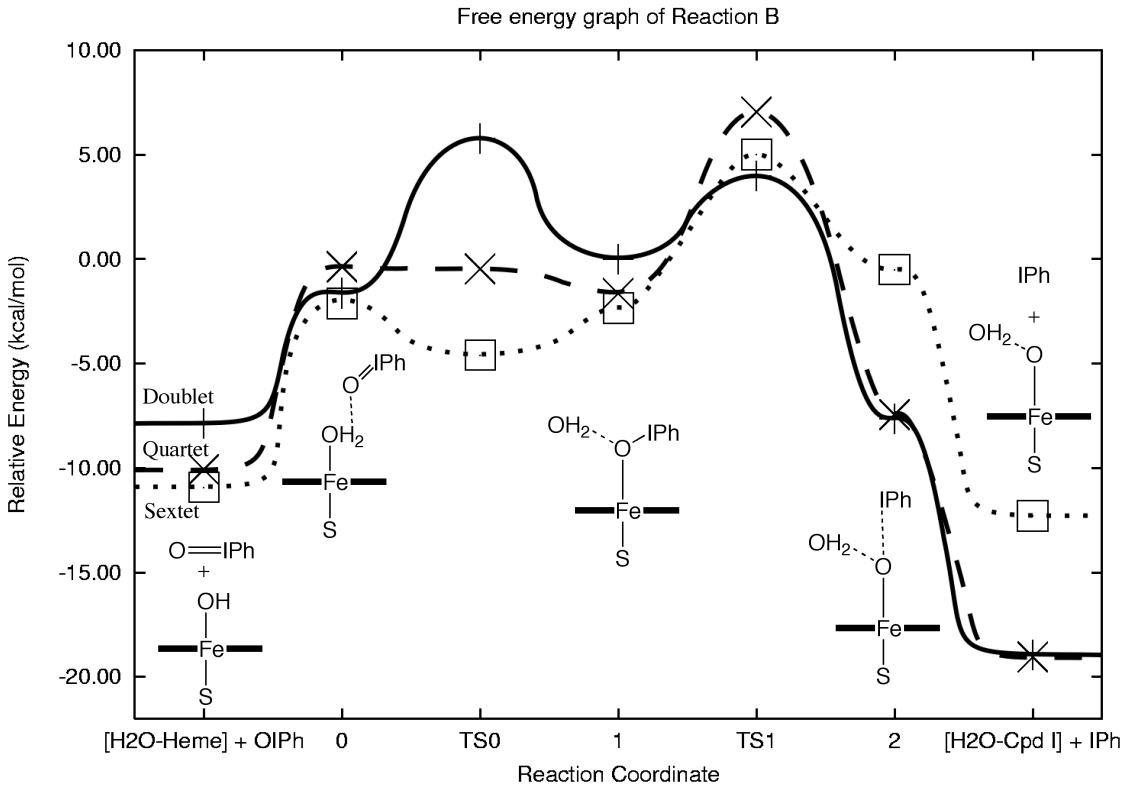


Figure S18: Free Energy Graph.

Table S62: Full energy profile (kcal mol^{-1}) from heme resting state with PhIO to Cpd I followed by H-abstraction from DMA (see Figure 8).

	Doublet	Quartet	Sextet
[H_2O-Heme] + OIPh	6.90	6.37	5.48
B0	0.85	2.32	2.04
BTS0	9.18	4.17	1.42
B1	**0.00**	1.84	1.75

BTS1	6.25	8.29	8.68
B2	-3.21	-2.74	4.87
[H_2O-Cpd I] + IPh	-3.09	-3.88	4.70
Cpd I + DMA	-4.10	-3.88	5.62
C2	-2.15	-2.60	6.61
TS_H	3.84	6.18	11.12

Part 3

Reaction between Heme and *N*,*N*-dimethylaniline-*N*-oxide

In this summary, the five different stages of the reaction are named as below:

1: Heme and *N*,*N*-dimethylaniline-*N*-oxide, complexed.
TS1: Transition state between **1** and **2**.
2: Compound I and *N*,*N*-dimethylaniline, complexed.

Structures

Heme + O: Heme and *N*,*N*-dimethylaniline-*N*-oxide, uncomplexed.

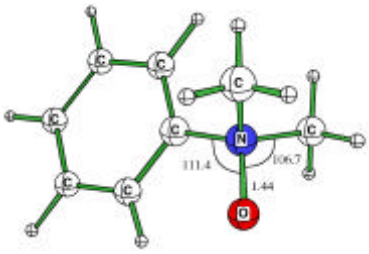


Figure S19: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet]. Heme is as described in Part 1.

Table S63: Charge distributions.

	Charge
N	-0.05
O	-0.40

Heme is as described in Part 1.

Table S64: Coordinates in xyz-format.

Heme is as described in Part 1.

21
N,N-dimethylaniline-N-oxide

N	-0.056651	-0.070112	-0.065845	-0.419418
O	-0.754969	-0.620939	1.061408	-0.485794
C	1.369518	0.161858	0.376681	-0.207171
C	-0.126594	-1.101651	-1.167755	-0.207116
C	-0.681754	1.226728	-0.521118	0.218152
H	0.415057	-0.778602	-2.061218	0.132367
H	0.294512	-2.017354	-0.755706	0.177523
H	-1.183321	-1.248830	-1.382405	0.185678
H	1.988832	0.550555	-0.436420	0.132360
H	1.322145	0.867202	1.204184	0.185724
H	1.738487	-0.798100	0.734383	0.177484
C	-0.163338	1.941748	-1.604985	-0.111932
C	-0.781214	3.138254	-1.986697	-0.148117
C	-1.901863	3.605586	-1.288525	-0.102937
C	-2.405362	2.873776	-0.206764	-0.147786
C	-1.795071	1.675932	0.182187	-0.104933
H	0.704552	1.587375	-2.151530	0.132773
H	-0.386452	3.701950	-2.825661	0.131194
H	-2.377448	4.534047	-1.587628	0.130281
H	-3.273384	3.233678	0.335950	0.135060
H	-2.129300	1.061591	1.008745	0.196496

1: Heme and *N*,*N*-dimethylaniline-*N*-oxide, complexed.

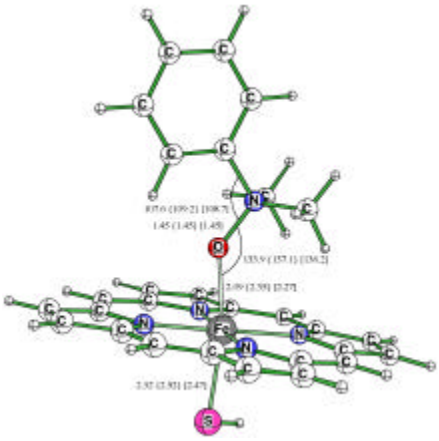


Figure S20: Values with two decimals are distances in Å. Values with one decimal are angles in °. The values are in order doublet, {quartet} and [sextet].

Table S65: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \sigma^*_{z^2}, \pi^*_{yz})$	$\alpha(\delta, \sigma^*_{xy}, \pi^*_{yz}, \pi^*_{xz}, \sigma^*_{z^2})$
<S^2>	0.82	3.80	8.77

Table S66: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.09	2.66	4.17	0.14	0.14	0.22
O	0.01	0.03	0.04	-0.16	-0.18	-0.16
S	0.00	0.41	0.44	-0.23	-0.33	-0.28
Porphyrin	-0.10	-0.10	0.35	-0.45	-0.29	-0.50
DMA	-0.00	0.00	0.00	0.57	0.53	0.54

Table S67: Coordinates in xyz-format.

60			
Doublet			
Fe	-0.022911	0.063683	0.044015
N	0.042826	-0.134841	2.061615
N	1.993485	0.028261	-0.047495
N	-0.085808	0.226386	-1.962441
N	-2.039470	0.048022	0.152781
C	-1.027178	-0.130592	2.951311
C	1.191887	-0.130337	2.843694
C	2.862381	-0.030711	1.028624
C	2.785060	0.092079	-1.181365
C	0.980324	0.262391	-2.841907
C	-1.230253	0.303460	-2.734272
C	-2.903587	0.156205	-0.925233
C	-2.836508	0.000380	1.286366
C	-0.534595	-0.157529	4.311685
C	0.830734	-0.157486	4.245462
H	-1.161780	-0.160986	5.191483
H	1.539845	-0.161684	5.060697
C	4.233498	-0.014322	0.555154
C	4.185065	0.059381	-0.807111
H	5.103998	-0.048967	1.194613
H	5.007750	0.097873	-1.506377
C	0.492236	0.371422	-4.203717
C	-0.870809	0.397591	-4.137552
H	1.122992	0.423570	-5.079386
H	-1.580400	0.474568	-4.948689
C	-4.274274	0.154270	-0.454541
C	-4.233095	0.060433	0.908168
H	-5.141859	0.227800	-1.094622
H	-5.059636	0.041505	1.604070
C	-2.368141	-0.083168	2.591331
C	2.495459	-0.101276	2.365526
C	2.318880	0.197865	-2.483087
C	-2.532761	0.269754	-2.257834
H	-3.102702	-0.092056	3.389685
H	3.294291	-0.119916	3.099913
H	3.055464	0.242244	-3.278394
H	-3.331063	0.344540	-2.989237
S	-0.014070	2.372384	0.228013
H	-0.783315	2.482514	1.371003
O	0.026804	-1.939992	-0.540496
N	-0.136155	-3.201315	0.166234
C	-1.426044	-3.178902	0.951917
C	-0.179724	-4.301463	-0.867235
C	1.061880	-3.376813	1.070312
H	-1.573680	-4.140276	1.448072
H	-1.357602	-2.372302	1.675547
H	-2.227124	-2.979523	0.243358
H	0.992607	-4.324554	1.608257
H	1.944073	-3.353282	0.433861
H	1.074689	-2.534277	1.756956
C	-0.291038	-5.633597	-0.452830
C	-0.332726	-6.646739	-1.415968
C	-0.263788	-6.326655	-2.777264
C	-0.152438	-4.989472	-3.171691
C	-0.108885	-3.965161	-2.217323
H	-0.345966	-5.895518	0.598306
H	-0.419121	-7.681188	-1.100483
H	-0.296607	-7.114966	-3.522105
H	-0.098574	-4.735483	-4.224971
H	-0.021558	-2.922419	-2.486364

60			
Quartet			
Fe	0.009747	-0.005865	-0.000283
N	0.012735	-0.054051	2.026618
N	2.025684	0.056318	0.013727
N	0.018311	-0.161487	-2.013072
N	-2.001511	-0.181885	0.004299
C	-1.103620	-0.021946	2.855432
C	1.117119	0.062243	2.862166
C	2.855534	0.133658	1.120840
C	2.855261	0.084389	-1.097338
C	1.127780	-0.114167	-2.838814
C	-1.082024	-0.291726	-2.842673
C	-2.826102	-0.298291	-1.105092
C	-2.836925	-0.155605	1.110685
C	-0.683907	0.085061	4.235329
C	0.682377	0.134184	4.239531
H	-1.357139	0.129497	5.079075
H	1.345454	0.228174	5.087320
C	4.235563	0.211536	0.693076
C	4.235075	0.183219	-0.673383
H	5.081517	0.283620	1.361149
H	5.081083	0.225721	-1.343990
C	0.711577	-0.216242	-4.222636
C	-0.649993	-0.327121	-4.225179
H	1.384323	-0.198082	-5.067605
H	-1.313447	-0.416857	-5.073346
C	-4.208277	-0.342654	-0.681026
C	-4.215548	-0.252583	0.683550
H	-5.052138	-0.427242	-1.350225
H	-5.066084	-0.249767	1.349940
C	-2.424019	-0.076192	2.434105
C	2.438656	0.133929	2.445100
C	2.443499	0.008365	-2.418972
C	-2.403394	-0.353028	-2.425842
H	-3.194079	-0.048644	3.197550
H	3.202173	0.218022	3.210952
H	3.211811	0.041743	-3.183859
H	-3.166668	-0.442510	-3.191604
S	-0.125575	2.509480	-0.098019
H	-1.332927	2.589176	-0.766204
O	0.145953	-2.322778	-0.348101
N	0.176095	-3.517855	0.467729
C	-1.079428	-3.535973	1.308763
C	0.224668	-4.730336	-0.429182
C	1.414732	-3.453693	1.331581
H	-1.103810	-4.425295	1.942806
H	-1.079354	-2.626477	1.905041
H	-1.920250	-3.526448	0.617980
H	1.483632	-4.337640	1.970048
H	2.265673	-3.394010	0.655963
H	1.346331	-2.543487	1.923027
C	0.252986	-6.014969	0.124499
C	0.298063	-7.123295	-0.727987
C	0.315358	-6.943007	-2.116591
C	0.287500	-5.650277	-2.650693
C	0.241767	-4.533303	-1.807710
H	0.240385	-6.167441	1.198522
H	0.319402	-8.122714	-0.306110
H	0.350226	-7.805041	-2.774715
H	0.301106	-5.505212	-3.725843
H	0.218363	-3.517035	-2.175754

60			
Sextet			
Fe	-0.001288	0.212400	0.115015
N	0.055392	-0.121448	2.183325
N	2.067621	0.093238	0.060613
N	-0.069323	0.247835	-1.959543
N	-2.079094	0.170839	0.193209
C	-1.036371	-0.080379	3.038374
C	1.201028	-0.128236	2.965148
C	2.918299	0.005336	1.145979
C	2.842570	0.149704	-1.084684
C	1.021267	0.266706	-2.802032
C	-1.210028	0.298742	-2.732105
C	-2.922789	0.239222	-0.901887
C	-2.861306	0.111840	1.331380
C	-0.557159	-0.108541	4.409466
C	0.811787	-0.137913	4.364466
H	-1.190040	-0.088269	5.285426
H	1.501427	-0.145648	5.196708
C	4.289077	0.011169	0.666729
C	4.242161	0.097723	-0.700678
H	5.165535	-0.043460	1.296835
H	5.073592	0.127940	-1.390609
C	0.547222	0.335688	-4.176884
C	-0.821201	0.355536	-4.134164
H	1.184087	0.369909	-5.049475
H	-1.509783	0.409282	-4.965524
C	-4.295960	0.232051	-0.429355
C	-4.258588	0.156856	0.939603
H	-5.168506	0.281381	-1.065340
H	-5.094610	0.131710	1.624224
C	-2.374404	0.006469	2.640527
C	2.513278	-0.092026	2.482536
C	2.358119	0.229765	-2.394359
C	-2.518745	0.301211	-2.240253
H	-3.115798	0.005699	3.434034
H	3.303567	-0.122746	3.226638
H	3.104904	0.262953	-3.182141
H	-3.312349	0.353891	-2.979553
S	0.080007	2.672380	0.312388
H	-1.281390	2.904178	0.342960
O	-0.085263	-1.974412	-0.506400
N	-0.106203	-3.253485	0.171939
C	-1.313064	-3.277448	1.081368
C	-0.203777	-4.348038	-0.862243
C	1.178584	-3.385732	0.956845
H	-1.375379	-4.233400	1.605742
H	-1.205504	-2.451447	1.780033
H	-2.185726	-3.120403	0.450779
H	1.208396	-4.345684	1.477266
H	1.994295	-3.304260	0.241358
H	1.214042	-2.555183	1.658157
C	-0.257643	-5.687672	-0.461505
C	-0.351065	-6.687064	-1.435976
C	-0.388812	-6.345252	-2.793366
C	-0.332966	-5.000245	-3.173530
C	-0.240432	-3.990640	-2.207800
H	-0.229567	-5.965278	0.586818
H	-0.395083	-7.727876	-1.132640
H	-0.461655	-7.123028	-3.546477
H	-0.361590	-4.729649	-4.223758
H	-0.198109	-2.940213	-2.458925

TS1: Transition state between **1** and **2**.

Figure S21: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S68: Valence orbitals, imaginary frequencies and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{yz})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, \sigma^*_{z^2}, \sigma^*_{xy})$
Frequency	i200.77cm^{-1}	i725.58cm^{-1}	i510.74cm^{-1}
<S^2>	1.37	3.81	9.09

Table S69: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.62	2.03	3.98	-0.01	0.12	0.44
O	0.11	0.39	0.10	-0.09	-0.11	-0.14
S	-0.14	0.37	0.78	-0.26	-0.30	-0.26
Porphyrin	-0.19	-0.10	0.41	-0.09	-0.18	-0.52
DMA	-0.30	0.23	-0.21	0.53	0.51	0.52

Comments: In the case of the sextet, the product after the **TS1** has the S....Fe bond broken. All attempts to obtain a product with the Fe....S bond intact failed.

Table S70: Coordinates in xyz-format.

60			
Doublet			
Fe	-0.018544	-0.044874	0.013701
N	-0.001566	-0.050162	2.022487
N	2.007412	-0.066339	0.003142
N	-0.026958	0.180490	-2.000554
N	-2.038954	0.115349	0.042653
C	-1.103565	0.013902	2.870363
C	1.117836	-0.101222	2.848160
C	2.847078	-0.144996	1.098079
C	2.822997	-0.027671	-1.113366
C	1.074734	0.181137	-2.834494
C	-1.139781	0.272119	-2.814213
C	-2.868758	0.221640	-1.060137
C	-2.861927	0.132691	1.153581
C	-0.661829	-0.008923	4.246557
C	0.703324	-0.080535	4.232974
H	-1.321291	0.034104	5.101354
H	1.380643	-0.107340	5.074446
C	4.228404	-0.171840	0.657412
C	4.212863	-0.099135	-0.705485
H	5.082141	-0.226230	1.317495
H	5.051804	-0.083415	-1.386176
C	0.640220	0.288909	-4.214228
C	-0.723166	0.344356	-4.201856
H	1.305592	0.318545	-5.064879
H	-1.399130	0.429788	-5.040376
C	-4.250759	0.288337	-0.626219
C	-4.246814	0.234975	0.738016
H	-5.097458	0.378998	-1.291391
H	-5.089091	0.272388	1.413737
C	-2.430681	0.082563	2.471033
C	2.437029	-0.165581	2.423007
C	2.396513	0.084220	-2.427468
C	-2.457805	0.287003	-2.382890
H	-3.185648	0.119771	3.249138
H	3.206360	-0.211034	3.186643
H	3.158686	0.104704	-3.199221
H	-3.229419	0.373378	-3.140822
S	0.094160	2.373868	-0.016180
H	0.118822	2.560447	1.353889
O	-0.088321	-1.719971	-0.390302
N	-0.232430	-3.526294	0.540570
C	-1.509239	-3.381232	1.268432
C	-0.225588	-4.343239	-0.632619
C	0.964268	-3.525508	1.396319
H	-1.732386	-4.303522	1.824614
H	-1.428443	-2.542736	1.956981
H	-2.316729	-3.175745	0.570474
H	1.060102	-4.472036	1.948512
H	1.847087	-3.360076	0.780410
H	0.878415	-2.702202	2.101969
C	0.769506	-5.316100	-0.837587
C	0.749434	-6.107264	-1.990666
C	-0.252145	-5.938457	-2.950824
C	-1.234236	-4.957898	-2.754363
C	-1.223874	-4.161961	-1.609986
H	1.551360	-5.472503	-0.105309
H	1.519544	-6.858687	-2.132218
H	-0.263449	-6.553286	-3.844595
H	-2.001724	-4.799310	-3.504884
H	-1.946224	-3.364652	-1.497170

60			
Quartet			
Fe	-0.002079	0.002934	-0.006270
N	-0.003573	-0.008843	2.047059
N	2.018253	0.010795	0.004866
N	0.003022	0.129243	-1.998280
N	-2.012780	0.197150	0.018375
C	-1.109319	-0.000561	2.878049
C	1.106858	-0.034925	2.872021
C	2.843136	-0.020883	1.119661
C	2.849990	-0.019638	-1.098116
C	1.109961	0.082784	-2.831782
C	-1.102269	0.263793	-2.824219
C	-2.840378	0.322949	-1.083469
C	-2.842914	0.174826	1.131925
C	-0.681166	-0.036383	4.262706
C	0.685371	-0.055170	4.258853
H	-1.348429	-0.030206	5.112445
H	1.357551	-0.068806	5.104826
C	4.228143	-0.065171	0.697089
C	4.232199	-0.067864	-0.669109
H	5.073632	-0.088375	1.369544
H	5.080948	-0.092828	-1.336989
C	0.683774	0.176090	-4.213453
C	-0.675846	0.291629	-4.208975
H	1.353000	0.165297	-5.061394
H	-1.342821	0.393785	-5.052829
C	-4.220768	0.390228	-0.653568
C	-4.222636	0.295912	0.709950
H	-5.065159	0.498372	-1.318670
H	-5.069456	0.314124	1.380969
C	-2.430340	0.072442	2.452987
C	2.427533	-0.041990	2.442827
C	2.430187	0.003494	-2.421481
C	-2.419413	0.358509	-2.406332
H	-3.201175	0.078655	3.216540
H	3.199458	-0.060864	3.205285
H	3.194285	-0.019491	-3.191087
H	-3.180854	0.466010	-3.171297
S	0.174217	2.520182	0.242380
H	-1.052143	2.732423	0.843586
O	-0.083356	-1.810936	-0.086505
N	-0.111087	-3.553727	0.543636
C	-1.332382	-3.532654	1.384871
C	-0.188972	-4.358652	-0.654321
C	1.142049	-3.610799	1.322862
H	-1.460229	-4.503434	1.883488
H	-1.230112	-2.736746	2.120179
H	-2.197877	-3.324105	0.760562
H	1.234510	-4.568286	1.854191
H	1.985027	-3.467814	0.648609
H	1.126020	-2.791649	2.039771
C	0.691780	-5.427539	-0.876849
C	0.571537	-6.195072	-2.041491
C	-0.417738	-5.903042	-2.983818
C	-1.287661	-4.825725	-2.761885
C	-1.175161	-4.051991	-1.607735
H	1.460600	-5.675160	-0.155171
H	1.253998	-7.022576	-2.205326
H	-0.505764	-6.499422	-3.885914
H	-2.042656	-4.575748	-3.499502
H	-1.799022	-3.179974	-1.461375

60				
Sextet				
Fe	-0.009670	-0.255785	-0.067363	-6.148016
N	0.010221	-0.054223	2.062584	8.349740
N	2.063301	0.054166	-0.023642	-0.672071
N	-0.006987	0.268719	-2.074946	-0.676705
N	-2.054640	0.230876	0.012188	-0.674639
C	-1.095770	0.004348	2.893581	1.241294
C	1.131916	-0.088466	2.872061	0.256849
C	2.886170	-0.015050	1.088643	0.274408
C	2.877360	0.165760	-1.134686	0.277517
C	1.106174	0.361123	-2.888599	0.286839
C	-1.121692	0.455939	-2.871207	0.284688
C	-2.874213	0.405113	-1.087540	0.269936
C	-2.865684	0.222921	1.135828	0.256117
C	-0.653049	-0.016073	4.278379	-0.147140
C	0.715029	-0.073715	4.264889	-0.147531
H	-1.306350	0.029202	5.138321	5.135986
H	1.386457	-0.083571	5.111833	0.136801
C	4.271947	0.042914	0.655643	-5.146567
C	4.266474	0.155894	-0.708661	-0.144183
H	5.127316	0.016906	1.315771	5.136275
H	5.116572	0.237570	-1.370980	0.137704
C	0.673183	0.586926	-4.259338	-5.142677
C	-0.692923	0.644887	-4.248757	-0.144013
H	1.336024	0.701226	-5.105181	5.137583
H	-1.356684	0.816461	-5.084175	0.136566
C	-4.253043	0.502890	-0.642069	-5.147523
C	-4.248121	0.389799	0.723151	-0.148442
H	-5.103872	0.650502	-1.292046	5.136903
H	-5.094050	0.428328	1.394916	0.135663
C	-2.419860	0.104104	2.455797	-5.174998
C	2.452304	-0.100862	2.413179	-0.165374
C	2.429921	0.293040	-2.453016	-0.154447
C	-2.438701	0.497126	-2.414005	-0.161141
H	-3.184369	0.131557	3.227070	5.128473
H	3.227821	-0.135110	3.172995	0.129092
H	3.196446	0.380784	-3.217225	0.129642
H	-3.208169	0.649072	-3.165260	0.128297
S	0.315198	2.829238	0.514699	*********
H	-0.900953	2.882031	1.174876	15.024150
O	-0.091470	-2.055497	-0.367915	-7.457403
N	-0.160171	-3.679240	0.448289	0.525354
C	-1.402380	-3.581304	1.255812	0.751719
C	-0.217553	-4.617066	-0.657325	0.272567
C	1.072156	-3.678384	1.264439	-0.249536
H	-1.536691	-4.494538	1.851117	5.146815
H	-1.322463	-2.711586	1.906167	0.203435
H	-2.252473	-3.448570	0.590184	0.189517
H	1.137827	-4.581426	1.886001	0.142534
H	1.932625	-3.609606	0.600587	0.200804
H	1.048651	-2.795822	1.901393	0.205412
C	0.626386	-5.735173	-0.713992	-5.120489
C	0.526595	-6.626962	-1.789441	-0.144465
C	-0.408487	-6.410132	-2.804485	-0.106302
C	-1.242206	-5.284492	-2.747248	-0.147313
C	-1.147671	-4.386660	-1.684001	-0.102428
H	1.352963	-5.926013	0.066174	5.134997
H	1.181492	-7.491513	-1.825862	0.131553
H	-0.482225	-7.102843	-3.636285	0.130387
H	-1.955553	-5.095309	-3.542674	0.134717
H	-1.741978	-3.482718	-1.662968	0.184566

2: Compound I and Iodobenzene, complexed.

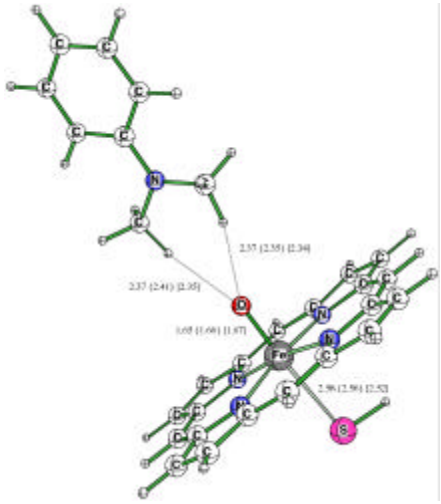


Figure S22: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet].

Table S71: Valence orbitals and expectation values of the spin operator (<S^2>).

	Doublet	***Quartet***	***Sextet***
Occupation	$\alpha(\pi^*_{xz}, \pi^*_{yz})\beta(a_{2u})$	$\alpha(\pi^*_{xz}, \pi^*_{yz}, a_{2\upsilon})$	$\alpha(\delta, \pi^*_{xz}, \pi^*_{yz}, a_{2\upsilon}, \sigma^*_{xy})$
<S^2>	1.78	3.79	8.86

Table S72: Spin and Charge distributions.

	Spin			***Charge***		
	Doublet	Quartet	Sextet	Doublet	Quartet	Sextet
Fe	1.28	1.17	3.21	0.15	0.04	0.24
O	0.83	0.88	0.62	-0.27	-0.21	-0.20
S	-0.62	0.56	0.31	-0.18	-0.19	-0.27
Porphyrin	-0.47	0.35	0.77	0.17	0.22	0.03
DMA	-0.03	0.03	0.06	0.34	0.34	0.38

Comments: It should be noted that when the **TS1** was relaxed toward the product, this resulted in a state where the O....I bond was not kept. However, the resulting

structure did not deviate too much from **2** in terms of energy, reflecting the very weak nature of the O....I bond at the product stage. Here, **2** was obtained simply by putting the structures there and let the structure relax.

Table S73: Coordinates in xyz-format.

60			
Doublet			
Fe	-0.043131	0.550149	0.070408
N	-0.006747	0.240046	2.063068
N	1.979158	0.621742	0.062031
N	-0.053066	1.123892	-1.865102
N	-2.041467	0.767629	0.138197
C	-1.103447	0.113244	2.900747
C	1.104084	-0.014750	2.847822
C	2.829194	0.318187	1.122473
C	2.801912	0.809360	-1.043458
C	1.041190	1.241878	-2.705171
C	-1.168459	1.350573	-2.658447
C	-2.885036	1.047068	-0.920661
C	-2.859831	0.579049	1.238254
C	-0.666790	-0.220296	4.238865
C	0.696010	-0.301930	4.205737
H	-1.327468	-0.369714	5.079935
H	1.374284	-0.530687	5.014378
C	4.203623	0.347767	0.673094
C	4.186514	0.648549	-0.658002
H	5.058228	0.156967	1.305282
H	5.024155	0.753104	-1.331626
C	0.603038	1.554265	-4.048859
C	-0.759456	1.623474	-4.019527
H	1.264325	1.700990	-4.889928
H	-1.437941	1.837856	-4.831921
C	-4.261701	1.032348	-0.476079
C	-4.246117	0.744555	0.858625
H	-5.113498	1.222664	-1.112043
H	-5.082848	0.651705	1.534982
C	-2.426133	0.278145	2.520978
C	2.422327	0.018514	2.410134
C	2.366637	1.088108	-2.326527
C	-2.481468	1.316978	-2.221410
H	-3.183969	0.155573	3.287295
H	3.194649	-0.204685	3.138355
H	3.121835	1.202252	-3.096598
H	-3.256918	1.517762	-2.952778
S	0.379146	3.055319	0.516592
H	0.960739	2.936879	1.764912
O	-0.086474	-1.064281	-0.282987
N	-0.243968	-4.959013	-0.832352
C	-1.456880	-4.146783	-0.935651
C	-0.294826	-6.330039	-1.044636
C	1.019333	-4.308770	-0.482119
H	-2.225360	-4.477286	-0.221507
H	-1.209675	-3.106228	-0.722062
H	-1.891355	-4.196687	-1.944814
H	1.433647	-4.709858	0.454730
H	1.774804	-4.444751	-1.269564
H	0.847036	-3.239407	-0.354760
C	0.869694	-7.135679	-0.933887
C	0.808429	-8.512007	-1.150577
C	-0.398223	-9.139846	-1.482967
C	-1.552819	-8.355517	-1.595158
C	-1.512853	-6.977702	-1.381932
H	1.819857	-6.684510	-0.678744
H	1.717406	-9.099851	-1.057881
H	-0.437601	-10.210969	-1.650565
H	-2.500417	-8.820457	-1.852632
H	-2.424876	-6.402830	-1.478828

60			
Quartet			
Fe	0.091609	-0.003219	0.034055
N	0.059112	-0.005601	2.050834
N	2.092609	0.246455	0.078345
N	0.109710	0.283642	-1.962536
N	-1.927057	0.010039	0.017948
C	-1.057413	-0.158592	2.869070
C	1.158693	-0.010154	2.902804
C	2.913135	0.203240	1.192399
C	2.939321	0.372242	-1.014066
C	1.220280	0.402247	-2.775717
C	-0.985802	0.306612	-2.806995
C	-2.745871	0.067392	-1.099438
C	-2.771615	-0.154016	1.101791
C	-0.644444	-0.233022	4.252992
C	0.716935	-0.142224	4.273454
H	-1.320692	-0.343576	5.087521
H	1.376558	-0.163263	5.128245
C	4.299683	0.310015	0.791296
C	4.315801	0.415653	-0.569361
H	5.136616	0.306070	1.473834
H	5.168816	0.515320	-1.224700
C	0.813876	0.498959	-4.161392
C	-0.550127	0.442207	-4.180656
H	1.493699	0.600547	-4.994302
H	-1.211953	0.486877	-5.032929
C	-4.131396	-0.056436	-0.702033
C	-4.147411	-0.196024	0.656575
H	-4.968647	-0.037360	-1.383978
H	-5.000225	-0.312484	1.309075
C	-2.366124	-0.237715	2.428189
C	2.480455	0.076148	2.504350
C	2.536615	0.443145	-2.336427
C	-2.310982	0.214283	-2.407456
H	-3.138685	-0.365740	3.178651
H	3.238577	0.049727	3.279541
H	3.310912	0.541433	-3.089539
H	-3.068527	0.249304	-3.183207
S	0.040571	2.514810	0.508255
H	-1.218607	2.585071	1.074065
O	0.177061	-1.651301	-0.103656
N	-0.580791	-5.510303	-0.424727
C	-1.524541	-4.503522	-0.910694
C	-0.876168	-6.862665	-0.530573
C	0.689967	-5.070223	0.152517
H	-2.503435	-4.603839	-0.420344
H	-1.131027	-3.510194	-0.690903
H	-1.681419	-4.582585	-1.997150
H	0.810508	-5.435452	1.182634
H	1.548766	-5.428183	-0.434399
H	0.716133	-3.979735	0.168255
C	0.032130	-7.852966	-0.070943
C	-0.276708	-9.208919	-0.177638
C	-1.485531	-9.634526	-0.741540
C	-2.386935	-8.666944	-1.202049
C	-2.097444	-7.305954	-1.103887
H	0.977508	-7.560699	0.367705
H	0.439457	-9.941335	0.184790
H	-1.718003	-10.691173	-0.821168
H	-3.330000	-8.972983	-1.646303
H	-2.816344	-6.586477	-1.474314

60			
Sextet			
Fe	-0.008180	-0.242573	0.198074
N	0.022895	0.135872	2.243327
N	2.071131	-0.227288	0.177161
N	-0.009699	-0.265374	-1.884942
N	-2.060796	0.104399	0.191866
C	-1.083440	0.291887	3.062835
C	1.145034	0.116452	3.053165
C	2.892442	-0.190038	1.284974
C	2.876006	-0.379624	-0.937224
C	1.089735	-0.414314	-2.697451
C	-1.126496	-0.228182	-2.692372
C	-2.877866	0.082193	-0.920233
C	-2.865611	0.258083	1.300912
C	-0.635159	0.390713	4.441228
C	0.728227	0.281855	4.435209
H	-1.285949	0.523975	5.293390
H	1.399055	0.309829	5.281327
C	4.273581	-0.322650	0.853069
C	4.263829	-0.436706	-0.510317
H	5.128926	-0.322070	1.512684
H	5.109859	-0.547657	-1.173074
C	0.650976	-0.482992	-4.081099
C	-0.712779	-0.368527	-4.077770
H	1.305174	-0.598904	-4.931780
H	-1.381877	-0.375468	-4.925167
C	-4.257583	0.233684	-0.493162
C	-4.250275	0.340116	0.872234
H	-5.110292	0.255920	-1.155564
H	-5.095573	0.466093	1.532904
C	-2.405772	0.339353	2.621449
C	2.456451	-0.044915	2.605527
C	2.417383	-0.466796	-2.252764
C	-2.440391	-0.066337	-2.241376
H	-3.165063	0.461249	3.387994
H	3.228582	-0.044371	3.368936
H	3.176898	-0.582399	-3.020319
H	-3.211621	-0.052798	-3.006015
S	0.316901	2.259595	0.147548
H	-0.838355	2.615842	0.816008
O	-0.152683	-1.897442	0.345446
N	-0.919975	-4.653998	-2.292635
C	-2.005991	-3.987815	-1.574778
C	-1.196883	-5.543255	-3.321411
C	0.463523	-4.357281	-1.918778
H	-2.681475	-4.715953	-1.105595
H	-1.582875	-3.350973	-0.797493
H	-2.603922	-3.352665	-2.245686
H	1.000269	-5.268036	-1.617379
H	1.016228	-3.895937	-2.750728
H	0.463607	-3.657321	-1.081925
C	-0.153327	-6.193841	-4.031823
C	-0.442235	-7.089387	-5.060311
C	-1.765546	-7.372084	-5.423092
C	-2.803472	-6.734343	-4.731108
C	-2.534507	-5.835230	-3.700059
H	0.879446	-5.998666	-3.777586
H	0.378650	-7.572514	-5.584075
H	-1.982203	-8.070694	-6.224180
H	-3.837753	-6.938099	-4.995827
H	-3.359563	-5.359589	-3.187487

Cpd I + IPh: Compound I and Iodobenzene, uncomplexed.

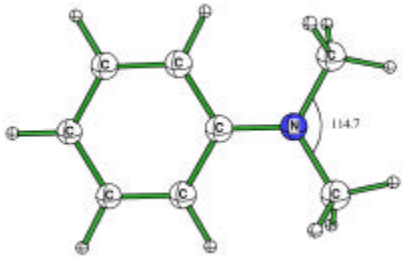


Figure S23: Values with two decimals are distances in Å. Values with one decimal are angles in º. The values are in order doublet, {quartet} and [sextet]. Cpd I is as described in Part 1.

Table S74: Spin and Charge distributions.

	Charge
N	0.18

Cpd I is as described in Part 1.

Table S75: Coordinates in xyz-format.

Cpd I is as described in Part 1.

20
N,N-dimethylaniline

H	-0.228810	-3.980313	-0.680553
C	-0.598929	-3.869859	-1.701406
H	-0.089592	-3.007071	-2.155183
H	-0.307669	-4.767004	-2.266306
N	-2.047754	-3.693430	-1.670501
C	-2.749935	-3.676259	-0.390688
H	-3.502024	-4.475812	-0.325462
H	-2.029803	-3.826364	0.415490
H	-3.261200	-2.718484	-0.214706
C	-2.757387	-3.529436	-2.859738
C	-2.097300	-3.538366	-4.114155
C	-4.163283	-3.348155	-2.855317
C	-2.816310	-3.374153	-5.299134
H	-1.024393	-3.672947	-4.166004
C	-4.864847	-3.185614	-4.050966
H	-4.709297	-3.333185	-1.920633
C	-4.204194	-3.196402	-5.284440
H	-2.280954	-3.385699	-6.244204
H	-5.941797	-3.048792	-4.013688
H	-4.756115	-3.069353	-6.209483

Geometries (all in Å)

Table S76: N-O distances.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	1.44	1.45	2.04	3.94	----
Quartet		1.45	1.85	3.95	
Sextet		1.45	1.82	3.89	

Table S77: O-Fe distances.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	----	2.09	1.72	1.65	As Part 1
Quartet		2.35	1.82	1.66	
Sextet		2.27	1.83	1.67	

Table S78: Fe-S distances.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	As Part 1	2.32	2.42	2.58	As Part 1
Quartet		2.52	2.54	2.56	
Sextet		2.47	3.16	2.52	

Energies

All energies are in kcal mol^{-1}, with the reference point as marked in **bold**.

Table S79: Energy, LACVP.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	16.01	**0.00**	19.02	5.23	9.91
Quartet	14.62	5.72	25.17	5.40	9.58
Sextet	16.15	7.71	28.43	19.52	23.89

Table S80: Energy, LACV3P*+.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	11.17	**0.00**	22.31	9.86	14.03
Quartet	9.05	5.52	31.01	9.91	13.41
Sextet	5.85	3.54	32.04	21.13	24.54

Table S81: Energy, LACVP including solvation.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	8.21	**0.00**	19.41	7.15	6.78
Quartet	5.35	2.82	24.26	6.87	6.51
Sextet	7.97	7.37	30.89	20.45	20.64

Table S82: Energy, LACVP including zero-point vibration energy.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	14.89	**0.00**	17.40	3.27	7.45
Quartet	12.88	4.51	23.17	3.39	7.26

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Sextet	13.40	5.49	24.28	16.04	20.18

Table S83: Total Energy, LACV3P*+ including solvation and Z_0.

	Heme + DMAO	***1***	***TS1***	***2***	***Cpd I + DMA***
Doublet	2.24	**0.00**	21.07	9.82	8.44
Quartet	-1.96	1.41	28.10	9.37	8.02
Sextet	-5.09	0.98	30.34	18.58	17.59

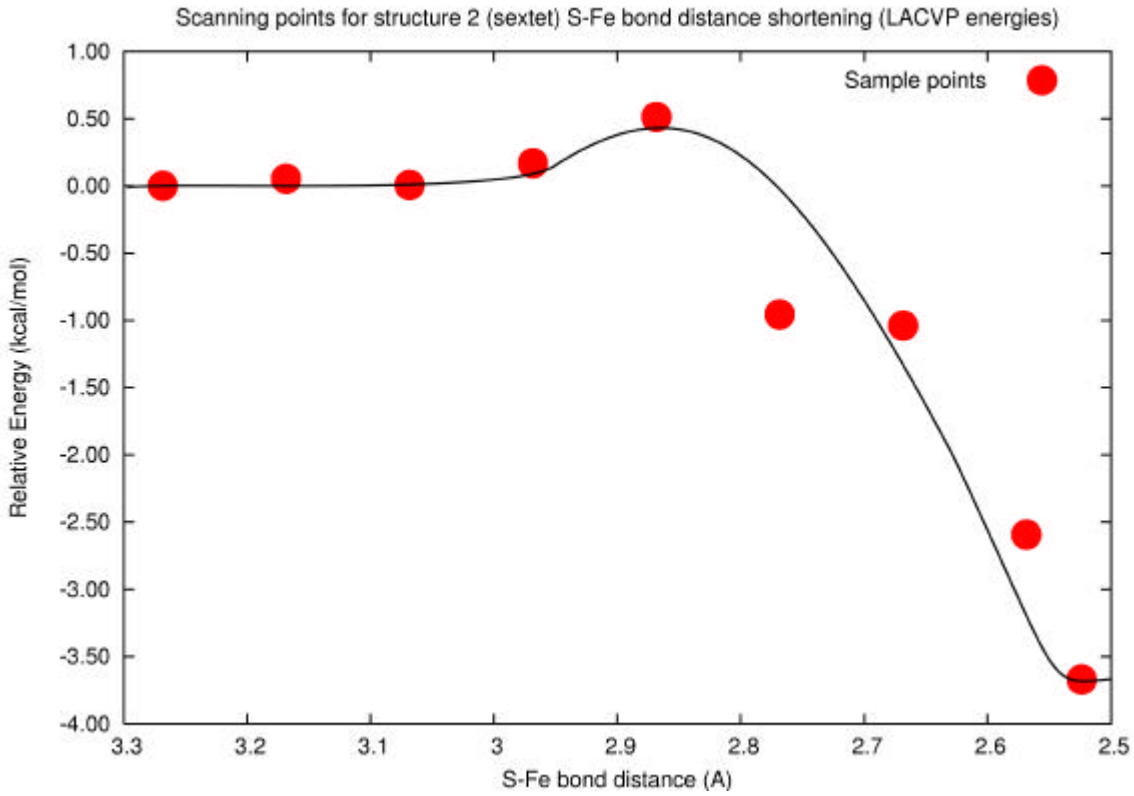


Figure S24: Scanning points for ^{6}2 S-Fe bond formation (x-axis reversed).

Table S84: Free Energy DG, component by component.

	A	B	C	D	E	F	A+B+C+D+E+F
DMAO + Heme							
Doublet	16.01	-4.84	-7.80	-1.12	-0.93	-12.44	**-11.13**
Quartet	14.62	-5.57	-9.27	-1.74	-0.59	-14.26	**-16.80**
Sextet	16.15	-10.30	-8.18	-2.76	-0.41	-14.94	**-20.44**
1							
Doublet	**0.00**	**+0.00**	**+0.00**	**+0.00**	**+0.00**	**+0.00**	**0.00**
Quartet	5.72	-0.20	-2.89	-1.21	+0.68	-3.15	**-1.06**
Sextet	7.71	-4.17	-0.33	-2.22	+0.73	-2.66	**-0.95**
TS1							
Doublet	19.02	+3.28	+0.39	-1.62	+0.27	-1.04	**20.30**
Quartet	25.17	+5.84	-0.91	-2.00	+0.39	-2.12	**26.37**
Sextet	28.43	+3.61	+2.46	-4.15	+1.16	-4.64	**26.86**
2							
Doublet	5.23	+4.63	+1.92	-1.96	+0.01	-1.03	**8.79**
Quartet	5.40	+4.51	+1.47	-2.02	+0.04	-2.46	**6.94**
Sextet	19.52	+1.61	+0.93	-3.48	+0.24	-1.54	**17.29**
DMA + Cpd I							
Doublet	9.43	+3.71	-2.97	-2.31	-0.32	-13.72	**-6.17**
Quartet	9.47	+3.84	-2.94	-2.28	-0.36	-14.02	**-6.29**
Sextet	23.89	+0.65	-3.25	-3.71	-0.08	-14.73	**2.77**

A=LACVP relative energy; B=LACV3P*+ correction; C=Solvent correction; D=Z_0 correction; E=Enthalpy correction F=Entropy correction; A+B+C+D+E+F=?G

Table S85: Full energy profile (kcal mol^{-1}) from heme resting state with DMAO to Cpd I followed by H-abstraction from DMA (see Figure 7).

	Doublet	Quartet	Sextet
BTS0	4.27	-0.04	-2.37
C1	**0.00**	1.41	0.98

CTS1	21.07	28.10	30.34
C2	9.82	9.37	18.58
$\boldsymbol{TS_H}$	15.81	18.15	23.09

Part 4

KIE calculations

Kinetic Isotope Effect (KIE) was calculated for the transition state of Cpd I - *N*,*N*-dimethylaniline proton abstraction, with and without a thiolate ligand present.

Cpd I with thiolate ligand present.

The coordinates for all the states were generated in this study according to "Computational Methods" in the text. In addition, while we initially used the geometries from reference 33 for the doublet and quartet, we re-optimized the structure according to our technical settings and applied the same methods as in the sextet case to be able to compare the energies accurately. Thus any discrepancies to the values in reference 33 should correspond to use of different protocol when generating the data.

Table S86: Calculated KIE for the doublet *N,N*-dimethylaniline proton abstraction by Cpd I.

N,N-(CD2H)2-aniline[a]		KIE_1[b]	KIE_2[c]
LS(gas)	1-H/4-D	3.54	3.77
	1-H/7-D	4.07	4.39
	2-H/6-D	3.53	3.77
	2-H/9-D	4.07	4.38
	3-H/5-D	3.53	3.77
	3-H/8-D	4.07	4.38
	Average[d]	3.79	4.06

[a] For details, see ref 33; [b] Eyring model; [c] Wigner correction with scaling frequency by scale factor 0.9704; [d] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S87: Parameter used in calculating Table S86.

Compound	Free energy (G, in Hartree)	Frequency (cm-1)	Aniline[a]
1H	-1951.253044	-707.6244	-365.998076
2H	-1951.253045	-707.9852	-365.998074
3H	-1951.253113	-707.6521	-365.998016
4D	-1951.251793	-633.4962	-365.998018
5D	-1951.251862	-633.5241	-365.997957
6D	-1951.251794	-633.8074	-365.998015
7D	-1951.251719	-621.6247	-365.998077
8D	-1951.251789	-621.6689	-365.998017
9D	-1951.251720	-621.9805	-365.998074
Doublet Cpd I[b]	-1585.280048		

[a] Values taken from ref 33.

[b] For coordinates, see Table S15.

Table S88: Coordinates of sextet Transition State used in calculating Table S87.

```
60
Doublet Transition State
Fe    -0.052970     0.084117     0.010317
 N    -0.112493     0.063018     2.033598
 N     1.946532    -0.181893     0.054358
 N     0.022337     0.216961    -1.995859
 N    -2.017708     0.559724    -0.023819
 C     2.275511    -0.326709     2.495902
 C     2.425037    -0.209565    -2.360787
 C    -2.335771     0.786219    -2.456636
 C    -2.518970     0.443965     2.388610
 C     0.957535    -0.151658     2.883953
 C     2.728292    -0.338259     1.185831
 C     2.799504    -0.300204    -1.029205
 C     1.135587     0.043367    -2.804476
 C    -1.033999     0.513199    -2.845444
 C    -2.789581     0.800796    -1.147160
 C    -2.876248     0.626284     1.061103
 C    -1.233356     0.184451     2.835878
 C    -0.855494     0.037028     4.227305
 C     0.493574    -0.167155     4.256953
 C     4.107740    -0.551846     0.799654
 C     4.151417    -0.531412    -0.564737
 C     0.760675     0.205097    -4.192393
 C    -0.574480     0.498048    -4.217124
 C    -4.162290     1.041858    -0.755153
 C    -4.216305     0.931070     0.604637
 H     3.011636    -0.473083     3.279055
 H     4.921673    -0.696945     1.495039
 H     5.008599    -0.653783    -1.210855
 H     3.201668    -0.318518    -3.110132
 H     1.445089     0.123626    -5.024563
 H    -1.200500     0.701717    -5.073821
 H    -3.057139     0.996968    -3.238744
 H    -4.965724     1.260258    -1.443484
 H    -5.072859     1.043607     1.253452
 H    -3.302850     0.525740     3.133887
 H    -1.544362     0.093308     5.057717
 H     1.131585    -0.313218     5.116430
 O    -0.379318    -1.595101     0.043116
 S     0.455449     2.453281     0.183285
 H    -0.692762     2.848382     0.841974
 H    -0.333018    -2.405900    -1.079914
 C    -0.311236    -3.202849    -2.000046
 H    -0.338461    -2.605890    -2.906880
 H     0.646993    -3.716867    -1.876915
 N    -1.414198    -4.092318    -1.864529
 C    -1.393493    -4.935469    -0.661702
 H    -1.931079    -5.868516    -0.842259
 H    -0.354469    -5.164788    -0.418125
 H    -1.833245    -4.412311     0.197120
 C    -2.600063    -3.965407    -2.610478
 C    -2.586295    -3.406616    -3.910632
 C    -3.832645    -4.421643    -2.087965
 C    -3.764470    -3.303793    -4.647046
 H    -1.655380    -3.077907    -4.354531
 C    -5.003718    -4.316918    -2.840326
 H    -3.884593    -4.832005    -1.087633
 C    -4.982665    -3.756558    -4.121813
 H    -3.728464    -2.878129    -5.644821
 H    -5.938617    -4.666844    -2.414533
 H    -5.895055    -3.676658    -4.702754
```

Table S89: Calculated KIE for the quartet *N,N*-dimethylaniline hydrogen abstraction by Cpd I.

N,N-(CD2H)2-aniline[a]		KIE_1[b]	KIE_2[c]
HS(gas)	1-H/4-D	5.47	7.32
	1-H/7-D	6.11	8.21
	2-H/6-D	5.46	7.32
	2-H/9-D	6.10	8.20
	3-H/5-D	5.46	7.32
	3-H/8-D	6.11	8.21
	Average[d]	5.78	7.75

[a] For details, see ref 33; [b] Eyring model; [c] Wigner correction with scaling frequency by scale factor 0.9704; [d] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S90: Parameter used in calculating Table S89.

Compound	Free energy (G, in Hartree)	Frequency (cm-1)	Aniline[a]
1H	-1951.251614	-1289.3837	-365.998076
2H	-1951.251603	-1289.4292	-365.998074
3H	-1951.251672	-1289.4110	-365.998016
4D	-1951.249952	-981.7215	-365.998018
5D	-1951.250010	-981.7291	-365.997957
6D	-1951.249941	-981.7712	-365.998015
7D	-1951.249907	-978.2132	-365.998077
8D	-1951.249965	-978.2256	-365.998017
9D	-1951.249896	-978.2681	-365.998074
Quartet Cpd I[b]	-1585.280680		

[a] Values taken from ref 33.

[b] For coordinates, see Table S15.

Table S91: Coordinates of quartet Transition State used in calculating Table S89.

```
60
 Quartet Transition State
Fe    -0.109545     0.071737    -0.011334
 N    -0.215030     0.034616     1.980307
 N     1.888754    -0.205783     0.079221
 N     0.004079     0.139427    -2.055608
 N    -2.063465     0.547539    -0.123151
 C     2.154250    -0.385029     2.519806
 C     2.420084    -0.254046    -2.333538
 C    -2.351197     0.629860    -2.577533
 C    -2.610812     0.531566     2.279218
 C     0.827783    -0.195862     2.864807
 C     2.644689    -0.383831     1.221155
 C     2.762137    -0.321951    -0.992301
 C     1.139765    -0.041765    -2.824764
 C    -1.038549     0.357860    -2.937430
 C    -2.819276     0.720339    -1.276419
 C    -2.939218     0.680329     0.939387
 C    -1.347548     0.225242     2.755592
 C    -1.009015     0.087941     4.158018
 C     0.328565    -0.171471     4.224896
 C     4.030828    -0.599399     0.862665
 C     4.102830    -0.561928    -0.500537
 C     0.795561     0.045982    -4.229462
 C    -0.547678     0.292276    -4.298668
 C    -4.194925     0.993200    -0.918150
 C    -4.268850     0.969160     0.445448
 H     2.864621    -0.542593     3.324066
 H     4.829193    -0.759263     1.572689
 H     4.972521    -0.684643    -1.129625
 H     3.219910    -0.369565    -3.057335
 H     1.502043    -0.053014    -5.041064
 H    -1.159161     0.433936    -5.178093
 H    -3.066306     0.790129    -3.377164
 H    -4.988069     1.171762    -1.629780
 H    -5.134507     1.124648     1.072993
 H    -3.404266     0.662306     3.007143
 H    -1.714542     0.189588     4.969913
 H     0.939297    -0.324761     5.102780
 O    -0.429136    -1.636517    -0.113186
 S     0.464225     2.386983    -0.082581
 H    -0.767730     2.890419    -0.454472
 H    -0.350788    -2.371781    -1.138629
 C    -0.310634    -3.297393    -2.060211
 H    -0.169501    -2.769579    -2.998320
 H     0.558905    -3.886300    -1.758357
 N    -1.525288    -4.018645    -1.971063
 C    -1.738616    -4.742554    -0.708353
 H    -2.416475    -5.584657    -0.862184
 H    -0.774904    -5.122073    -0.362162
 H    -2.135559    -4.076936     0.068118
 C    -2.607938    -3.801164    -2.847783
```

C	-2.379624	-3.449871	-4.198216	H	-4.146713	-4.191423	-1.368498
C	-3.940244	-3.953996	-2.404146	C	-4.771747	-3.406870	-4.620883
C	-3.451837	-3.253917	-5.066881	H	-3.255178	-2.994478	-6.102387
H	-1.366996	-3.360193	-4.571031	H	-6.021182	-3.871140	-2.923781
C	-5.004531	-3.758818	-3.286777	H	-5.602388	-3.256884	-5.302273

Table S92: Calculated KIE for the penta-radical sextet *N,N*-dimethylaniline hydrogen abstraction by Cpd I.

N,N-(CD2H)2-aniline[a]		KIE_1[b]	KIE_2[c]
5R-HHS(gas)	1-H/4-D	5.27	7.08
	1-H/7-D	5.92	8.01
	2-H/6-D	5.27	7.07
	2-H/9-D	5.91	8.00
	3-H/5-D	5.27	7.07
	3-H/8-D	5.91	8.00
	Average[d]	5.59	7.53

[a] For details, see ref 33; [b] Eyring model; [c] Wigner correction with scaling frequency by scale factor 0.9704; [d] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S93: Parameter used in calculating Table S92.

Compound	Free energy (G, in Hartree)	Frequency (cm-1)	Aniline[a]
1H	-1951.230092	1447.2129	-365.998076
2H	-1951.230144	1447.4085	-365.998074
3H	-1951.230093	1447.2710	-365.998016
4D	-1951.228464	1132.2479	-365.998018
5D	-1951.228465	1132.3127	-365.997957
6D	-1951.228516	1132.3715	-365.998015
7D	-1951.228414	1123.3726	-365.998077
8D	-1951.228416	1123.4425	-365.998017
9D	-1951.228466	1123.5040	-365.998074
Sextet Cpd I[b]	-1585.260743		

[a] Values taken from ref 33.

[b] For coordinates, see Table S15.

Table S94: Coordinates of sextet Transition State used in calculating Table S92.

```
60
 5R-Sextet Transition State
Fe    -0.020517    -0.069843     0.043918
 N     0.003444    -0.026852     2.096862
 N     2.044720    -0.053437    -0.008363
 N    -0.066136     0.026651    -2.063227
 N    -2.093929     0.203097     0.056981
 C     2.448314    -0.126491     2.424790
 C     2.368610    -0.053804    -2.459352
 C    -2.503267     0.219202    -2.383938
 C    -2.423545     0.155422     2.506149
 C     1.133303    -0.084563     2.889429
 C     2.872304    -0.111580     1.091980
 C     2.833949    -0.076550    -1.143485
 C     1.037761     0.002322    -2.887367
 C    -1.191019     0.126281    -2.855090
 C    -2.923068     0.247687    -1.050652
 C    -2.887530     0.217424     1.186412
 C    -1.098700     0.047005     2.927667
 C    -0.642148     0.013694     4.308715
 C     0.723004    -0.067087     4.285093
 C     4.251144    -0.166303     0.633836
 C     4.227387    -0.144805    -0.734684
 C     0.588365     0.069695    -4.270124
 C    -0.778534     0.144469    -4.250441
 C    -4.300782     0.310474    -0.594347
 C    -4.278972     0.292058     0.776749
 H     3.227661    -0.168505     3.179450
 H     5.114713    -0.214954     1.281626
 H     5.068154    -0.171889    -1.413097
 H     3.125325    -0.069031    -3.238067
 H     1.240915     0.070956    -5.131701
 H    -1.452442     0.215202    -5.092213
 H    -3.284167     0.272749    -3.136233
 H    -5.163682     0.368982    -1.242762
 H    -5.120705     0.327730     1.453901
 H    -3.178312     0.196332     3.285761
 H    -1.289473     0.055087     5.173112
 H     1.400177    -0.104525     5.126446
 O    -0.150756    -1.809375    -0.015330
 S     0.228694     2.332563    -0.057019
 H    -1.109511     2.656737    -0.179136
 H    -0.361951    -2.693408    -0.932093
 C    -0.600534    -3.722784    -1.646415
 H    -0.092392    -3.563603    -2.592977
 H    -0.140712    -4.504331    -1.034666
 N    -2.004171    -3.864975    -1.759044
 C    -2.731807    -3.988533    -0.485880
 H    -3.643202    -4.572959    -0.625539
 H    -2.085465    -4.493937     0.233728
 H    -2.977732    -3.000052    -0.079142
 C    -2.711965    -3.632261    -2.953861
 C    -2.105755    -3.871271    -4.208596
 C    -4.053884    -3.189680    -2.922255
 C    -2.818598    -3.658608    -5.387498
 H    -1.094668    -4.255629    -4.259107
 C    -4.756602    -2.987042    -4.110485
 H    -4.532230    -2.967790    -1.977028
 C    -4.147419    -3.216097    -5.350375
 H    -2.337616    -3.854611    -6.340262
 H    -5.783968    -2.639966    -4.065926
 H    -4.699006    -3.057928    -6.270739
```

Table S95: Calculated KIE for the penta-radical sextet *N,N*-dimethylaniline hydrogen abstraction by Cpd I.

N,N-(CD2H)2-aniline[a]		KIE_1[b]	KIE_2[c]
7R-HHS(gas)	1-H/4-D	2.29	2.29
	1-H/7-D	2.40	2.40
	2-H/6-D	2.28	2.29
	2-H/9-D	2.39	2.40
	3-H/5-D	2.29	2.29
	3-H/8-D	2.40	2.40
	Average[d]	2.34	2.34

[a] For details, see ref 33; [b] Eyring model; [c] Wigner correction with scaling frequency by scale factor 0.9704; [d] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S96: Parameter used in calculating Table S95.

Compound	Free energy (G, in Hartree)	Frequency (cm-1)	Aniline[a]
1H	-1951.252032	-146.5123	-365.998076
2H	-1951.252062	-146.5624	-365.998074
3H	-1951.252114	-146.6135	-365.998016
4D	-1951.251193	-144.5673	-365.998018
5D	-1951.251274	-144.6595	-365.997957
6D	-1951.251223	-144.6160	-365.998015
7D	-1951.251208	-143.8595	-365.998077
8D	-1951.251289	-143.9484	-365.998017
9D	-1951.251238	-143.9090	-365.998074
Sextet Cpd I[b]	-1585.260743		

[a] Values taken from ref 33.

[b] For coordinates, see Table S15.

Table S97: Coordinates of sextet Transition State used in calculating Table S95.

60			
7R-Sextet Transition State			
Fe	-0.157652	-0.017590	0.168830
N	0.111649	0.270486	2.236662
N	1.931063	-0.164609	0.016016
N	-0.185130	0.551551	-1.850679
N	-2.010303	0.955367	0.380649
C	2.475174	-0.428301	2.406935
C	2.141255	-0.024847	-2.438852
C	-2.530716	1.300724	-2.007726
C	-2.199536	0.897452	2.840337
C	1.243256	-0.090971	2.959648
C	2.803925	-0.445537	1.050528
C	2.651909	-0.259136	-1.163498
C	0.838418	0.362077	-2.760998
C	-1.294543	0.969067	-2.563819
C	-2.864223	1.301181	-0.654498
C	-2.715451	1.114441	1.560003
C	-0.898921	0.516506	3.159847
C	-0.378469	0.316317	4.498018
C	0.932630	-0.056431	4.375103
C	4.117609	-0.735891	0.503862
C	4.024674	-0.619376	-0.856041
C	0.352272	0.658347	-4.096299
C	-0.959685	1.032380	-3.974914
C	-4.150640	1.686182	-0.103620
C	-4.059972	1.570107	1.257044
H	3.268561	-0.681072	3.103575
H	4.990190	-0.981258	1.092070
H	4.806712	-0.753103	-1.589727
H	2.834966	-0.131815	-3.267410
H	0.946834	0.601331	-4.996915
H	-1.638545	1.339282	-4.757703
H	-3.308971	1.606536	-2.700271
H	-5.000611	2.007952	-0.688169
H	-4.821486	1.780715	1.994274
H	-2.877656	1.059056	3.672719
H	-0.947973	0.449064	5.406734
H	1.634213	-0.283804	5.164841
O	-0.630572	-1.681051	0.100771
S	0.875356	2.970619	1.017658
H	-0.372847	3.269301	1.537470
H	-1.056495	-3.057418	-0.019758
C	-1.261663	-4.199151	-0.248189
H	-0.522492	-4.454641	-1.013948
H	-1.058543	-4.744841	0.674296
N	-2.598250	-4.439947	-0.696114
C	-3.577548	-4.994705	0.242754
H	-4.503387	-4.410302	0.229261
H	-3.161914	-4.959285	1.250566
H	-3.820875	-6.039734	0.005442
C	-3.007615	-4.038879	-1.976559

C	-2.206726	-3.156977	-2.740223	H	-4.853704	-5.185872	-1.967043
C	-4.224528	-4.504162	-2.526438	C	-3.812187	-3.247609	-4.565110
C	-2.612466	-2.773532	-4.018516	H	-1.992224	-2.081958	-4.579767
H	-1.308863	-2.730637	-2.310995	H	-5.547402	-4.484047	-4.215927
C	-4.613647	-4.110021	-3.807330	H	-4.120939	-2.944387	-5.559994

Cpd I without thiolate ligand present.

According to the gas-phase calculations, the dissociation would create a thiolyl radical (SH•) and a reduced Cpd I, which in effect is a Compound II (Cpd II) species. For the sextet process, the so formed Cpd II would be in an initial quintet state. However, in the enzyme pocket, the cysteine could dissociate as an anion (or be protonated to form a neutral cysteine residue). In such an event, the bare Cpd I species would be cationic and in a sextet state if the dissociation is spin conserving. As such, we have calculated the KIE due to H-abstraction from *N*,*N*-dimethylaniline by PorFeO Cpd I and Cpd II species in all the multiplicities ranging from 1 to 6 (Table S89). In the case of Cpd I, there is an initial spontaneous electron transfer from *N*,*N*-dimethylaniline to Cpd I, followed by H^+ abstraction. The results of the KIE calculations show high KIE values for the lower spin states, and a low KIE for the quintet state, while the sextet state shows an intermediate value. We may therefore conclude that if the thiolate ligand dissociates in a spin-conserving manner, and if the thiolate-free Cpd I or Cpd II subsequently react with the *N*,*N*-dimethylaniline by H-abstraction, the resulting KIE values for the high spin states should be relatively low or intermediate. If however, the dissociation of the thiolate would occur with inversion of spin to the lowest spin states, then one would observe a large KIE value.

While under the fast sextet-to-quartet spin relaxation assumption this scenario also lead to a KIE jump as one changes from the "native route" to the "PhIO route", there is no evidence that substrate oxidation actually occurs from the dissociated Cpd I. In fact, since the experiments show both oxidation and heme dissociation in presence of PhIO, these processes must be competitive. We tend therefore to prefer the scenario whereby an intact Cpd I species in the quartet state reacts with the substrate.

Table S98. Theoretically calculated average KIE values for enzyme-free Cpd I(I) hydrogen abstraction from deuterium substituted *N*,*N*-$(CD_2H)_2$-aniline at T=298.15 K.

	Cpd I			Cpd II		
	Doublet	Quartet	Sextet	Singlet	Triplet	Quintet
KIE1[a]	5.42	5.83	4.36	5.63	6.40	2.62
KIE2[b]	6.63	7.58	4.95	7.14	8.31	2.63

[a] Eyring model; [b] Wigner correction with scaled frequency by scale factor 0.9704.

Table S99: Relative energies (LACVP, free energy, kcal mol^{-1}).

	[PorFeO]^{Z}	***Transition State***
Z=0 (Cpd II)		
Singlet	10.10	5.97
Triplet	**0.00**	**0.00**
Quintet	9.08	-2.17
Z=+1 (Cpd I)		
Doublet	**0.00**	**0.00**
Quartet	1.40	-0.87
Sextet	9.87	2.38

Table S100: Transition state for enzyme-free Cpd I + *N*,*N*-dimethylaniline, spin and charge.

	Doublet		***Quartet***		***Sextet***	
	Spin	Charge	Spin	Charge	Spin	Charge
Cpd I	1.74	0.22	2.22	0.15	4.15	0.19
H	-0.07	0.38	0.07	0.39	0.05	0.37
N,*N*-dimethylaniline (excl. one H)	-0.67	0.40	0.71	0.47	0.80	0.44
$<S^2>$	1.59		3.90		9.38	

Table S101: Transition state for enzyme-free Cpd II + *N,N*-dimethylaniline, spin and charge.

	Singlet		***Triplet***		***Quintet***	
	Spin	Charge	Spin	Charge	Spin	Charge
Cpd II	0.51	-0.34	2.55	-0.38	4.43	-0.34
H	0.04	0.34	0.01	0.38	0.00	0.33
N,N-dimethylaniline (excl. one H)	-0.55	0.00	-0.56	0.00	-0.43	0.01
$<S^2>$	1.21		2.62		6.57	

Table S102: KIE values of Cpd I (without axial ligand) proton abstraction from *N,N*-dimethylanile radical cation.

	Doublet		***Quartet***		***Sextet***	
	[a]KIE_1	[b]KIE_2	[a]KIE_1	[b]KIE_2	[a]KIE_1	[b]KIE_2
1H/4D	5.18	6.33	5.57	7.21	4.08	4.51
1H/7D	5.66	6.95	6.11	7.97	4.67	5.22
2H/6D	5.18	6.33	5.57	7.22	4.08	4.51
2H/9D	5.66	6.94	6.11	7.96	4.67	5.22
3H/5D	5.18	6.32	5.56	7.21	4.08	4.51
3H/8D	5.66	6.95	6.11	7.97	4.68	5.23
AvgH/AvgD[c]	5.42	6.63	5.83	7.58	4.36	4.95

[a] Eyring model; [b] Wigner correction with scaling frequency by scale factor 0.9704; [c] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S103: Free energies (in Hartree) used to calculate Table S102.

	Doublet	***Quartet***	***Sextet***
Transition State	-1552.294686	-1552.296066	-1552.290896
1H	-1552.308525	-1552.309917	-1552.304716
2H	-1552.308588	-1552.309977	-1552.304775
3H	-1552.308528	-1552.309895	-1552.304687
4D	-1552.306914	-1552.308238	-1552.303331
5D	-1552.306917	-1552.308216	-1552.303301
6D	-1552.306976	-1552.308297	-1552.303389
7D	-1552.306889	-1552.308209	-1552.303261
8D	-1552.306892	-1552.308187	-1552.303231
9D	-1552.306952	-1552.308269	-1552.303320
Cpd I	-1186.305090	-1186.302858	-1186.288399

Table S104: Frequencies (non-scaled, in cm^{-1}) used to calculate Table S102.

	Doublet	***Quartet***	***Sextet***
Transition State	-1090.0618	-1432.3411	-796.5833
1H	-1057.7528	-1404.2358	-757.7404
2H	-1057.6829	-1404.1900	-758.0150
3H	-1057.8320	-1404.2709	-757.9085
4D	-847.0748	-1127.7383	-644.2198
5D	-847.1500	-1127.7798	-644.3940

	Doublet	***Quartet***	***Sextet***
6D	-847.0052	-1127.6769	-644.4645
7D	-841.8688	-1121.6524	-632.2307
8D	-841.9623	-1121.7057	-632.4572
9D	-841.8118	-1121.5993	-632.5005

Table S105: Coordinates used to calculate Tables S103 and S104.

58

Transition State doublet

Fe	-0.090985	-0.029530	-0.119534
N	-0.296906	0.140885	1.866675
N	1.881958	-0.290045	0.147767
N	0.258096	0.297832	-2.063652
N	-1.890833	0.830288	-0.337244
C	1.954204	-0.544724	2.601488
C	2.641332	-0.337292	-2.199790
C	-1.981654	1.040020	-2.793686
C	-2.662069	0.819337	2.007039
C	0.635979	-0.212974	2.841329
C	2.534554	-0.572639	1.347798
C	2.851124	-0.474640	-0.842068
C	1.433022	0.019616	-2.769628
C	-0.678082	0.649295	-3.040115
C	-2.543123	1.130214	-1.536062
C	-2.852803	1.024366	0.654105
C	-1.470870	0.407861	2.570499
C	-1.261513	0.223478	3.986093
C	0.037407	-0.158943	4.153017
C	3.916379	-0.903257	1.102431
C	4.111799	-0.841902	-0.247156
C	1.217426	0.188722	-4.183138
C	-0.083704	0.577055	-4.350027
C	-3.900978	1.540442	-1.279285
C	-4.092289	1.473942	0.070382
H	2.578301	-0.789654	3.453202
H	4.633058	-1.143603	1.873516
H	5.020610	-1.021802	-0.801944
H	3.482060	-0.509077	-2.862370
H	1.976386	0.048581	-4.938610
H	-0.594961	0.823796	-5.268991
H	-2.599493	1.305742	-3.644021
H	-4.603764	1.840198	-2.042335
H	-4.982653	1.709360	0.634154
H	-3.499035	1.005690	2.670145
H	-2.016961	0.381101	4.741327
H	0.559554	-0.377704	5.072474
O	-0.552934	-1.648685	-0.255694
H	-0.522102	-2.282841	-1.337465
C	-0.476244	-3.083136	-2.374255
H	-0.647052	-2.417260	-3.213864
H	0.541171	-3.467661	-2.308246
N	-1.454709	-4.060829	-2.176609
C	-1.156340	-5.106242	-1.174522
H	-1.592767	-6.055961	-1.486208
H	-0.074924	-5.214643	-1.095032
H	-1.549954	-4.820795	-0.192801
C	-2.758726	-3.969717	-2.717589
C	-2.993642	-3.257954	-3.916520
C	-3.839740	-4.612722	-2.073564
C	-4.280550	-3.190036	-4.445503
H	-2.174631	-2.801095	-4.457505
C	-5.122312	-4.532673	-2.614026
H	-3.690494	-5.148010	-1.144867
C	-5.351841	-3.822542	-3.799279
H	-4.445976	-2.658000	-5.375828
H	-5.944983	-5.022163	-2.105106
H	-6.349931	-3.769609	-4.219066

58

Transition State quartet

Fe	-0.079768	0.154059	-0.354393
N	-0.381113	-0.089951	1.620343
N	1.885927	-0.145496	-0.044620
N	0.373920	0.964358	-2.137612
N	-1.890473	1.027008	-0.472495
C	1.837595	-0.934112	2.292476
C	2.769391	0.388158	-2.284767
C	-1.850390	1.786863	-2.818975
C	-2.765317	0.522853	1.777819
C	0.507220	-0.649358	2.537898
C	2.479563	-0.694040	1.093068
C	2.905860	-0.087462	-0.994288
C	1.591019	0.877629	-2.815776
C	-0.518673	1.510560	-3.062049
C	-2.486343	1.565758	-1.611610
C	-2.902343	0.994075	0.486325
C	-1.591463	0.017349	2.304258
C	-1.446887	-0.463352	3.656199
C	-0.152747	-0.875391	3.800032
C	3.875623	-0.962431	0.849331
C	4.138678	-0.587615	-0.436887
C	1.452734	1.384222	-4.158840
C	0.152538	1.772961	-4.310922
C	-3.868813	1.884338	-1.351271
C	-4.125031	1.532934	-0.057269
H	2.420583	-1.360086	3.101270
H	4.556189	-1.372949	1.580434
H	5.077348	-0.630526	-0.969142
H	3.647676	0.385227	-2.920408
H	2.257606	1.440592	-4.876687
H	-0.318621	2.211969	-5.177865
H	-2.431832	2.221734	-3.624142
H	-4.539976	2.328124	-2.071523
H	-5.047893	1.632368	0.494709
H	-3.634444	0.560959	2.424854
H	-2.237355	-0.467328	4.392008
H	0.327348	-1.283915	4.676879
O	-0.506256	-1.410352	-0.878886
H	-0.448448	-2.447478	-1.605776
C	-0.441267	-3.605491	-2.157395
H	-0.463294	-3.403995	-3.224140
H	0.503537	-4.020012	-1.803641
N	-1.563871	-4.294347	-1.664883
C	-1.511104	-4.664993	-0.235140
H	-2.156279	-5.520937	-0.043056
H	-0.482194	-4.924350	0.016747
H	-1.812178	-3.809631	0.380449
C	-2.770252	-4.410037	-2.380297
C	-2.764116	-4.440369	-3.796161
C	-4.002542	-4.512543	-1.690972
C	-3.962043	-4.559042	-4.494678
H	-1.829568	-4.422707	-4.342727
C	-5.192459	-4.627751	-2.405212
H	-4.034002	-4.469624	-0.609926
C	-5.181542	-4.650595	-3.807222
H	-3.945294	-4.598640	-5.577896
H	-6.131686	-4.693190	-1.867883
H	-6.110588	-4.746543	-4.357422

58

Transition State sextet

Fe	-0.092238	0.057353	-0.422290
N	-0.504641	-0.059350	1.641968
N	1.939240	-0.161327	0.098689
N	0.584847	1.090365	-2.126635
N	-1.855236	1.204243	-0.581453
C	1.661611	-0.941047	2.421080
C	2.963098	0.439304	-2.061292
C	-1.554314	2.066964	-2.870444
C	-2.853128	0.689783	1.613423
C	0.313178	-0.633546	2.603567
C	2.421870	-0.719920	1.272795
C	3.016317	-0.090494	-0.772059
C	1.849330	0.995483	-2.690723
C	-0.211760	1.738644	-3.059952
C	-2.318915	1.831863	-1.727887
C	-2.910467	1.204613	0.318330
C	-1.746662	0.110728	2.234978
C	-1.706017	-0.372913	3.600117
C	-0.436884	-0.831736	3.827203
C	3.835122	-1.007577	1.132147
C	4.201435	-0.619844	-0.127765
C	1.840769	1.591454	-4.010695
C	0.571159	2.049395	-4.238088
C	-3.699194	2.231758	-1.542023
C	-4.063641	1.845387	-0.281257
H	2.179310	-1.377945	3.269498
H	4.458629	-1.436164	1.902913
H	5.180496	-0.672075	-0.580794
H	3.890740	0.440188	-2.625241
H	2.698327	1.660074	-4.663732
H	0.196815	2.562619	-5.111624
H	-2.048390	2.582127	-3.688468
H	-4.297286	2.749931	-2.277066
H	-5.015596	1.988638	0.208431
H	-3.758139	0.768900	2.207851
H	-2.536663	-0.348000	4.290096
H	-0.035468	-1.252356	4.737453
O	-0.539866	-1.516661	-1.013985
H	-0.660685	-2.435271	-2.024664
C	-0.773670	-3.406037	-2.783866
H	-1.220469	-3.056909	-3.709976
H	0.255357	-3.753740	-2.908068
N	-1.574754	-4.348007	-2.080224
C	-0.999738	-4.820043	-0.805277
H	-1.446432	-5.767839	-0.509901
H	0.074538	-4.955061	-0.943498
H	-1.148777	-4.056346	-0.033658
C	-2.901333	-4.635800	-2.421639
C	-3.328933	-4.543012	-3.771229
C	-3.828108	-5.044031	-1.429140
C	-4.644200	-4.845965	-4.107375
H	-2.622630	-4.287613	-4.550936
C	-5.141763	-5.336983	-1.782397
H	-3.531492	-5.093273	-0.389472
C	-5.558809	-5.241085	-3.119006
H	-4.955733	-4.791211	-5.144255
H	-5.846352	-5.635229	-1.014383
H	-6.581918	-5.477950	-3.387861

38

Cpd I doublet

Fe	-0.044420	0.022397	-0.048293
N	0.070887	-0.064164	1.950834
N	1.958247	0.048380	-0.129914
N	-0.096667	0.613681	-1.962343
N	-1.983507	0.501364	0.117982
C	2.495267	-0.426848	2.230826
C	2.289600	0.393985	-2.549981
C	-2.523421	0.955410	-2.246011
C	-2.319884	0.118398	2.531981
C	1.201294	-0.340193	2.710503

C	2.839672	-0.241822	0.904222
C	2.746046	0.129947	-1.271757
C	0.961944	0.623101	-2.862242
C	-1.228308	0.879009	-2.724004
C	-2.866357	0.781197	-0.917663
C	-2.773720	0.400223	1.256693
C	-0.990128	-0.093678	2.847407
C	-0.506674	-0.375702	4.196888
C	0.836858	-0.526277	4.112925
C	4.207479	-0.323377	0.397376
C	4.150053	-0.096180	-0.936790
C	0.480299	0.919944	-4.209097
C	-0.862440	1.076941	-4.124437
C	-4.232453	0.875713	-0.408671
C	-4.175594	0.642114	0.924366
H	3.286326	-0.650158	2.936241
H	5.072751	-0.527866	1.009679
H	4.958194	-0.074256	-1.652227
H	3.015380	0.429388	-3.353250
H	1.113777	0.993100	-5.079961
H	-1.565281	1.306332	-4.911092
H	-3.315650	1.169241	-2.952843
H	-5.095870	1.095243	-1.018366
H	-4.982346	0.628996	1.641308
H	-3.047983	0.066384	3.332243
H	-1.138964	-0.440725	5.069469
H	1.541510	-0.741227	4.901798
O	-0.242391	-1.574496	-0.313251

38

Cpd I quartet

Fe	-0.042624	0.034264	-0.045562
N	0.081529	-0.064035	1.955599
N	1.963234	0.058230	-0.138258
N	-0.107305	0.620809	-1.964155
N	-1.987166	0.502261	0.130029
C	2.505422	-0.421224	2.220874
C	2.278278	0.400468	-2.557839
C	-2.533624	0.954783	-2.233813
C	-2.309481	0.108621	2.541010
C	1.231852	-0.341809	2.712586
C	2.845059	-0.230101	0.873683
C	2.748164	0.138545	-1.300641
C	0.929527	0.632568	-2.864142
C	-1.259496	0.880827	-2.724737
C	-2.870277	0.782319	-0.883469
C	-2.775764	0.393652	1.287431
C	-0.958222	-0.101980	2.851335
C	-0.479053	-0.388360	4.193887
C	0.868912	-0.535767	4.109831
C	4.205902	-0.320198	0.369195
C	4.147354	-0.094469	-0.969297
C	0.450645	0.918279	-4.206948
C	-0.896801	1.069723	-4.122560
C	-4.230417	0.876465	-0.378380
C	-4.173769	0.634999	0.957441
H	3.308678	-0.646470	2.912617
H	5.071580	-0.529918	0.979006
H	4.955505	-0.079598	-1.685054
H	2.989969	0.434565	-3.374387
H	1.082070	0.988033	-5.079467
H	-1.599636	1.290513	-4.911596
H	-3.339286	1.162879	-2.928072
H	-5.094520	1.098526	-0.986047
H	-4.981869	0.618873	1.673017
H	-3.025160	0.046450	3.352412
H	-1.110577	-0.460228	5.066160
H	1.572386	-0.753611	4.899164
O	-0.232306	-1.561473	-0.314579

38

Cpd I sextet

Fe	-0.063224	-0.134165	-0.073796
N	0.086853	-0.062051	2.002060
N	2.009434	0.056281	-0.141098
N	-0.106996	0.637168	-2.008048
N	-2.029545	0.519560	0.135035
C	2.519692	-0.401558	2.231453
C	2.290988	0.436324	-2.562638
C	-2.538500	0.987810	-2.235695
C	-2.309298	0.153241	2.558929
C	1.240688	-0.327373	2.744730
C	2.881710	-0.217282	0.884576
C	2.780926	0.161751	-1.301818
C	0.942864	0.663787	-2.893894
C	-1.259462	0.913370	-2.748935
C	-2.899924	0.809088	-0.887881
C	-2.799307	0.427485	1.298068
C	-0.960835	-0.071280	2.890748
C	-0.468828	-0.340347	4.242813
C	0.877693	-0.498472	4.153928
C	4.251953	-0.280432	0.373720
C	4.190822	-0.050075	-0.963893
C	0.456082	0.974400	-4.238913
C	-0.891298	1.125711	-4.151169
C	-4.264705	0.915679	-0.369639
C	-4.203960	0.681201	0.967285
H	3.323439	-0.613149	2.927914
H	5.124994	-0.474500	0.978491
H	5.003716	-0.016911	-1.673822
H	3.008606	0.490942	-3.373766
H	1.082022	1.060914	-5.114316
H	-1.589673	1.361781	-4.940121
H	-3.340482	1.212944	-2.929964
H	-5.133737	1.142085	-0.968940
H	-5.013047	0.678004	1.682311
H	-3.025036	0.113665	3.372582
H	-1.090627	-0.393980	5.123778
H	1.579569	-0.706604	4.947614
O	-0.267694	-1.752787	-0.343194

Table S106: KIE values of Cpd II (without axial ligand) hydrogen abstraction from N,N-dimethylanile.

	Singlet		***Triplet***		***Quintet***	
	$^{a}KIE_1$	$^{b}KIE_2$	$^{a}KIE_1$	$^{b}KIE_2$	$^{a}KIE_1$	$^{b}KIE_2$
1H/4D	5.47	6.95	6.12	7.92	2.48	2.49
1H/7D	5.79	7.34	6.72	8.73	2.78	2.78
2H/6D	5.47	6.94	6.11	7.92	2.48	2.49
2H/9D	5.78	7.34	6.72	8.72	2.77	2.78
3H/5D	5.47	6.94	6.11	7.91	2.48	2.49
3H/8D	5.79	7.35	6.72	8.72	2.78	2.79

	Singlet		*Triplet*		*Quintet*	
AvgH/AvgD[c]	5.63	7.14	6.40	8.31	2.62	2.63

[a] Eyring model; [b] Wigner correction with scaling frequency by scale factor 0.9704; [c] KIE value calculated using average free energy and frequency of 1,2,3-H and 4,5,6,7,8,9-D.

Table S107: Free energies (in Hartree) used to calculate Table S106.

	Singlet	*Triplet*	*Quintet*
Transition State	-1552.497603	-1552.507114	-1552.510580
1H	-1552.511367	-1552.520899	-1552.524324
2H	-1552.511405	-1552.520960	-1552.524394
3H	-1552.511443	-1552.520893	-1552.524327
4D	-1552.509704	-1552.519131	-1552.523407
5D	-1552.509780	-1552.519126	-1552.523409
6D	-1552.509742	-1552.519192	-1552.523476
7D	-1552.509710	-1552.519101	-1552.523361
8D	-1552.509786	-1552.519096	-1552.523363
9D	-1552.509748	-1552.519162	-1552.523431
Cpd I	-1186.534107	-1186.550203	-1186.535730

Table S108: Frequencies (non-scaled, in cm^{-1}) used to calculate Table S106.

	Singlet	***Triplet***	***Quintet***
Transition State	-1097.425200	-1216.670000	-251.959100
1H	-1078.231600	-1200.438200	-235.380800
2H	-1078.296200	-1200.505200	-235.782900
3H	-1078.518300	-1200.497900	-235.835000
4D	-826.404200	-929.156500	-228.335300
5D	-826.595500	-929.211900	-228.750500
6D	-826.451200	-929.194900	-228.704800
7D	-827.606000	-925.979000	-227.653700
8D	-827.802000	-926.038900	-228.105100
9D	-827.662900	-926.022800	-228.032400

Table S109: Coordinates used to calculate Tables S107 and S108.

58

Transition State singlet

Fe	-0.263076	0.186049	-0.199218
N	-0.381337	0.286801	1.811691
N	1.592976	-0.573299	-0.039094
N	0.069663	0.479681	-2.164125
N	-1.889776	1.371719	-0.313257
C	1.625028	-1.021875	2.387916
C	2.310001	-0.523022	-2.399322
C	-2.054467	1.581805	-2.764694
C	-2.481589	1.546252	2.072475
C	0.451577	-0.361657	2.713073
C	2.167607	-1.096163	1.114702
C	2.498677	-0.838154	-1.062929
C	1.172444	0.078337	-2.913128
C	-0.834988	1.004046	-3.081533
C	-2.531209	1.773131	-1.478049
C	-2.711739	1.784437	0.727809
C	-1.404049	0.834858	2.573451
C	-1.196849	0.537194	3.975078
C	-0.057150	-0.208855	4.060346
C	3.447318	-1.692890	0.804397
C	3.655812	-1.525797	-0.536071
C	0.948960	0.355899	-4.314424
C	-0.291920	0.918159	-4.419129
C	-3.764340	2.459688	-1.156360
C	-3.870929	2.474651	0.204364
H	2.184217	-1.478925	3.197663
H	4.096840	-2.161312	1.529845
H	4.507884	-1.832909	-1.125330
H	3.098783	-0.787399	-3.095645
H	1.657465	0.144668	-5.102291
H	-0.798721	1.261139	-5.309582
H	-2.660701	1.953438	-3.584223
H	-4.442614	2.876536	-1.886875
H	-4.655719	2.902284	0.811349
H	-3.211518	1.920954	2.782169
H	-1.849174	0.860348	4.773390
H	0.413319	-0.616235	4.943568
O	-1.153414	-1.328601	-0.306809
H	-0.717188	-2.247294	-1.106629
C	-0.334506	-3.140744	-1.929848
H	-0.360627	-2.620771	-2.889810
H	0.683080	-3.378982	-1.620760
N	-1.164625	-4.291207	-1.904511
C	-0.750884	-5.448464	-1.104659
H	-0.440993	-6.290802	-1.738781
H	0.095646	-5.160237	-0.479848
H	-1.564945	-5.783878	-0.453090
C	-2.427613	-4.288373	-2.523280
C	-3.044044	-3.070752	-2.891866
C	-3.099411	-5.500826	-2.795777
C	-4.283063	-3.080189	-3.533209
H	-2.581417	-2.128808	-2.624547
C	-4.339365	-5.491036	-3.437873
H	-2.647118	-6.448945	-2.530182
C	-4.939319	-4.284725	-3.817017
H	-4.747120	-2.134543	-3.796825
H	-4.834680	-6.434421	-3.647278
H	-5.903209	-4.282522	-4.315167

58

Transition State triplet

Fe	-0.120753	-0.034692	-0.063264
N	0.099635	-0.132366	1.954886
N	1.901027	0.017826	-0.232893
N	-0.249937	0.690988	-1.957666
N	-2.054527	0.529756	0.228109
C	2.530585	-0.522775	2.089312
C	2.106844	0.469389	-2.648232
C	-2.677110	1.107625	-2.088056
C	-2.255147	0.107382	2.649788
C	1.265097	-0.433186	2.646405
C	2.823279	-0.306866	0.752638
C	2.630112	0.144665	-1.407265
C	0.769571	0.730805	-2.898998
C	-1.410804	1.023840	-2.643177
C	-2.972486	0.884133	-0.752466
C	-2.780277	0.428382	1.408083
C	-0.916426	-0.145194	2.901580
C	-0.373052	-0.452763	4.206643
C	0.971910	-0.630900	4.049178
C	4.151652	-0.377294	0.183568
C	4.032532	-0.099144	-1.148152
C	0.236231	1.101055	-4.191973
C	-1.107913	1.282618	-4.034075
C	-4.292522	1.005493	-0.173425
C	-4.173892	0.724455	1.158889
H	3.354449	-0.768568	2.750762
H	5.046882	-0.605631	0.743694
H	4.810694	-0.054269	-1.896308
H	2.796762	0.535964	-3.482651
H	0.826484	1.207488	-5.090585
H	-1.838290	1.566718	-4.777752
H	-3.496134	1.380651	-2.744888
H	-5.180467	1.281619	-0.723815
H	-4.945618	0.724040	1.915190
H	-2.940725	0.065434	3.489533
H	-0.956098	-0.514541	5.114197
H	1.709682	-0.868112	4.802008
O	-0.361140	-1.741320	-0.397640
H	-0.661668	-2.868159	-0.675938
C	-1.055142	-4.109304	-0.931555
H	-0.289551	-4.497258	-1.597245
H	-1.027235	-4.564311	0.061297
N	-2.356528	-4.080014	-1.486944
C	-3.413859	-3.594714	-0.590787
H	-4.375635	-4.033828	-0.866559
H	-3.168466	-3.898073	0.429333
H	-3.489314	-2.499501	-0.609023
C	-2.599429	-4.149537	-2.874377
C	-1.726432	-4.858460	-3.731628
C	-3.740075	-3.537567	-3.441549
C	-1.986690	-4.942243	-5.098721
H	-0.861562	-5.369240	-3.326671
C	-3.992540	-3.636735	-4.812010
H	-4.416910	-2.963566	-2.821564
C	-3.120818	-4.334868	-5.653498
H	-1.302610	-5.497264	-5.733431
H	-4.874305	-3.153988	-5.222552
H	-3.319452	-4.406615	-6.717512

58

Transition State quintet

Fe	-0.067219	-0.070917	-0.158677
N	0.026824	-0.162709	1.945586
N	2.031447	0.090331	-0.130970
N	-0.008750	0.965545	-1.992128
N	-2.014684	0.699186	0.081236
C	2.442723	-0.601925	2.201660
C	2.399062	0.737785	-2.484129
C	-2.410374	1.482258	-2.226946
C	-2.369006	0.135189	2.459043
C	1.138766	-0.526416	2.688029
C	2.860303	-0.309752	0.904544
C	2.839431	0.299851	-1.236791
C	1.088198	1.056682	-2.833692
C	-1.108759	1.396780	-2.716407
C	-2.830388	1.173777	-0.934191
C	-2.812130	0.558740	1.206937
C	-1.059147	-0.190465	2.806017
C	-0.613821	-0.585598	4.129601
C	0.736895	-0.792144	4.056958
C	4.231987	-0.354041	0.432371
C	4.219050	0.019975	-0.883629
C	0.661950	1.558825	-4.126899
C	-0.688021	1.767980	-4.054769
C	-4.182829	1.326645	-0.431887
C	-4.171593	0.948924	0.883859
H	3.211712	-0.899860	2.907716
H	5.084230	-0.627178	1.038156
H	5.058735	0.110545	-1.557902
H	3.154680	0.861667	-3.253776
H	1.318131	1.732849	-4.967722
H	-1.344825	2.145630	-4.825379
H	-3.168734	1.845459	-2.913791
H	-5.018955	1.689236	-1.012833
H	-4.996780	0.945415	1.581881
H	-3.113419	0.075124	3.247156
H	-1.255501	-0.678421	4.994262
H	1.408784	-1.086115	4.850722
O	-0.323859	-1.720227	-0.600362
H	-0.581738	-3.044874	-1.050888
C	-0.835601	-4.183527	-1.294682
H	-0.219504	-4.468651	-2.144381
H	-0.533910	-4.724049	-0.391434
N	-2.237211	-4.324410	-1.546731
C	-3.104328	-3.955384	-0.421605
H	-4.052726	-4.494492	-0.478444
H	-2.598481	-4.226292	0.507542
H	-3.293781	-2.873508	-0.397975
C	-2.776541	-4.426555	-2.841495
C	-2.043038	-5.026854	-3.892805
C	-4.083521	-3.962616	-3.119385
C	-2.598302	-5.149850	-5.165210
H	-1.053099	-5.425504	-3.708193
C	-4.629046	-4.099085	-4.397462
H	-4.664663	-3.474559	-2.347813
C	-3.894904	-4.689886	-5.431090
H	-2.016923	-5.619681	-5.952363
H	-5.632446	-3.729851	-4.585492
H	-4.322460	-4.791548	-6.422702

38

Cpd II singlet

Fe	-0.047303	-0.000106	-0.051934
N	0.069620	-0.075688	1.955353
N	1.962910	0.039589	-0.131110
N	-0.097793	0.605065	-1.970155
N	-1.990340	0.494410	0.116946
C	2.494738	-0.425783	2.230686
C	2.290236	0.402576	-2.547903
C	-2.522688	0.956890	-2.245298
C	-2.318227	0.126684	2.533073
C	1.202870	-0.344576	2.716062

C	2.845948	-0.241714	0.906433
C	2.752269	0.135425	-1.272626
C	0.964039	0.625197	-2.868529
C	-1.230554	0.877539	-2.730320
C	-2.872379	0.784048	-0.919115
C	-2.778641	0.406346	1.259873
C	-0.991833	-0.093772	2.854242
C	-0.510537	-0.360868	4.189707
C	0.842555	-0.516487	4.104092
C	4.199395	-0.305041	0.406331
C	4.141686	-0.072113	-0.937256
C	0.487438	0.929008	-4.197678
C	-0.865670	1.084389	-4.112339
C	-4.219915	0.893627	-0.411105
C	-4.162086	0.661006	0.932547
H	3.287937	-0.640349	2.938322
H	5.068403	-0.499723	1.017691
H	4.953682	-0.036850	-1.648551
H	3.018874	0.449887	-3.349660
H	1.119523	1.012347	-5.069496
H	-1.565663	1.320766	-4.900166
H	-3.314787	1.179805	-2.951578
H	-5.084512	1.123098	-1.016614
H	-4.969557	0.661163	1.649834
H	-3.046024	0.086778	3.335984
H	-1.138762	-0.415607	5.066741
H	1.546192	-0.725077	4.896539
O	-0.247074	-1.600114	-0.319553

38

Cpd II triplet

Fe	-0.046228	0.007269	-0.050659
N	0.070722	-0.065337	1.957327
N	1.964425	0.047456	-0.130991
N	-0.097427	0.612138	-1.969172
N	-1.990110	0.500076	0.117713
C	2.495027	-0.420945	2.230731
C	2.289446	0.397391	-2.549432
C	-2.522726	0.959495	-2.245272
C	-2.318982	0.123056	2.532204
C	1.203455	-0.337828	2.717423
C	2.846549	-0.239057	0.905861
C	2.752728	0.132070	-1.274157
C	0.963784	0.625365	-2.868912
C	-1.230367	0.882543	-2.730183
C	-2.872888	0.784339	-0.919373
C	-2.779834	0.403222	1.259158
C	-0.991758	-0.091773	2.854764
C	-0.511709	-0.368143	4.188873
C	0.842105	-0.519014	4.104196
C	4.198842	-0.316121	0.403834
C	4.141006	-0.087487	-0.940507
C	0.486455	0.923844	-4.199117
C	-0.866302	1.083336	-4.113494
C	-4.222381	0.881968	-0.413579
C	-4.164902	0.647356	0.929704
H	3.287509	-0.641282	2.937488
H	5.066888	-0.517756	1.014313
H	4.952280	-0.063398	-1.653316
H	3.016489	0.436168	-3.353137
H	1.117914	1.000936	-5.071925
H	-1.566454	1.317728	-4.901971
H	-3.315331	1.177972	-2.952440
H	-5.087962	1.104611	-1.020259
H	-4.973897	0.639028	1.645212
H	-3.047812	0.074704	3.333785
H	-1.141369	-0.432477	5.064229
H	1.544986	-0.731757	4.896152
O	-0.241618	-1.593017	-0.312098

38

Cpd II quintet

Fe	-0.064397	-0.139617	-0.075292
N	0.075137	-0.052967	2.006020
N	2.013667	0.062426	-0.130871
N	-0.098409	0.635267	-2.013759
N	-2.035912	0.520749	0.122653
C	2.507959	-0.382790	2.244191
C	2.300848	0.435779	-2.551451
C	-2.526675	1.000657	-2.246379
C	-2.322089	0.160454	2.545565
C	1.214760	-0.310675	2.754053
C	2.883436	-0.210200	0.914926
C	2.788898	0.161837	-1.277055
C	0.971331	0.660430	-2.897038
C	-1.234539	0.920509	-2.757461
C	-2.902671	0.820769	-0.918440
C	-2.809430	0.435990	1.271270
C	-0.992587	-0.064365	2.891457
C	-0.506196	-0.328585	4.231102
C	0.850362	-0.478889	4.146894
C	4.240691	-0.274653	0.410020
C	4.182571	-0.046705	-0.937142
C	0.491441	0.976055	-4.227767
C	-0.863763	1.137822	-4.141664
C	-4.253495	0.933498	-0.405360
C	-4.196222	0.696339	0.940059
H	3.302739	-0.588854	2.954250
H	5.114688	-0.466249	1.015630
H	5.000107	-0.016507	-1.642845
H	3.030318	0.489828	-3.353348
H	1.117981	1.065258	-5.103254
H	-1.556236	1.385127	-4.933261
H	-3.317933	1.235957	-2.951277
H	-5.122266	1.167770	-1.003425
H	-5.009168	0.699612	1.651467
H	-3.049248	0.127052	3.350699
H	-1.128483	-0.385359	5.112215
H	1.548195	-0.681576	4.946036
O	-0.254311	-1.768627	-0.328406

Table S110: Reactant state for Cpd I + N,N-dimethylaniline, spin and charge.

	Doublet		***Quartet***		***Sextet***	
	Spin	Charge	Spin	Charge	Spin	Charge
Cpd I	1.80	0.23	2.23	0.14	4.02	0.10
H	-0.06	0.36	0.07	0.39	0.02	0.31
N,*N*-dimethylaniline (excl. one H)	-0.74	0.42	0.70	0.47	0.96	0.59
$<S^2>$	1.70		3.90		9.27	

Part 5

Experimental results

Heme disappearance was monitored by UV absorbance and mass spectrometry upon addition of PhIO.

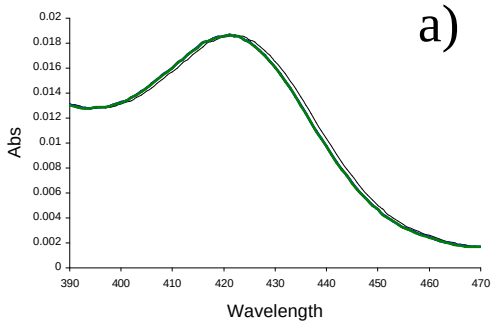
Preparation:

Heme disappearance by UV absorbance - The sample cuvette contained a mixture of 495 µL of sodium phosphate buffer (pH 7.4) and purified CYP3A4 (300 pmol) plus 0.6% methanol. Using a Carey 4000, a kinetic UV scan was programmed to scan from 390 to 465 every 20 seconds for 5 minutes at 10 °C. The scan rate was set to 600 nm/min with the spectral bandwidth of 2 nm. The spectra were overlaid to monitor loss of heme as a function of time. A second experiment was performed under the same conditions but with the addition of PhIO (5 µL, 100 nmol).

Heme disappearance determined by mass spectrometry - Selected ion monitoring of *m/z* 614 was measured to follow heme disappearance using a Finnigan LTQ. Separation of the heme was achieved using a Poros R2 chromatography as described previously.[S1] Aliquots of 100 µL were removed from the reaction in 20 second intervals and quenched according to Macdonald *et al*.[S2] The analysis was performed on a control, which excluded PhIO, in addition to the PhIO containing reaction. Only the first 30 seconds time point was used since no heme remained in that sample.

Results

The dissociation of heme from P450 has been observed experimentally[S3] and we confirmed these results by monitoring the disappearance of heme associated P450 at 420 nm over time after treatment with PhIO (Figure S25). However, it is not known from the experiment whether thee dissociated heme participates at all in oxidation. We therefore leave the result for future experimental research.



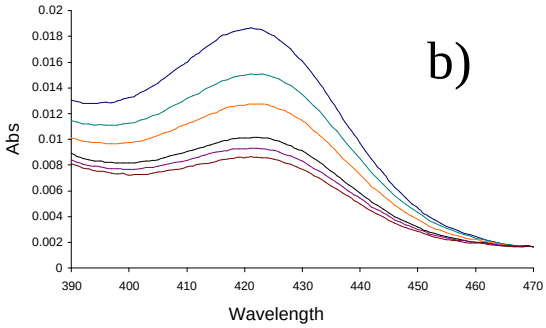


Figure S25. Absolute spectra of CYP3A4 measured in 20 sec intervals at 10 °C. a) Sample without PhIO, indicating no loss of heme; b) Same sample spiked with 5 µL of 50 mM PhIO. Final organic content was 0.5% methanol.

Further experiments confirmed that heme was lost from the protein by electrospray mass spectrometry. Upon subjecting the heme bound protein to chromatography the heme is lost from the protein and heme can be monitored by at m/z of 616. The data indicated that after incubation of P450 with PhIO almost all of the heme is dissociated from the enzyme (Figure S26). However, it is not known from the experiment whether thee dissociated heme participates at all in oxidation. We therefore leave the result for future experimental research.

The experimental heme dissociation lends indirect support to the computational finding that the sextet state shows loss of the thiolate ligand. It should however be emphasized that the experiments do not show whether the free heme (and presumably thiolate-free Cpd I) is responsible for the observed oxidation of *N*,*N*-dimethylaniline. Since this is nevertheless a possibility, it was deemed necessary to consider all the scenarios. Thus, by providing the results of the KIE calculations in the text both with and without thiolate ligand (Tables 5, S102 and S106), we cover the most obvious possibilities as outlined in the discussion section. In fact, the suggestion of Referee D that there is a heme degradation, and the experimental results of MacDonald *et al.*[S2] that "the rate of substrate oxidation with PhIO supported system are constant for short periods of time due to competing heme destruction…", mean that the substrate oxidation stops after the heme is released/destructed.

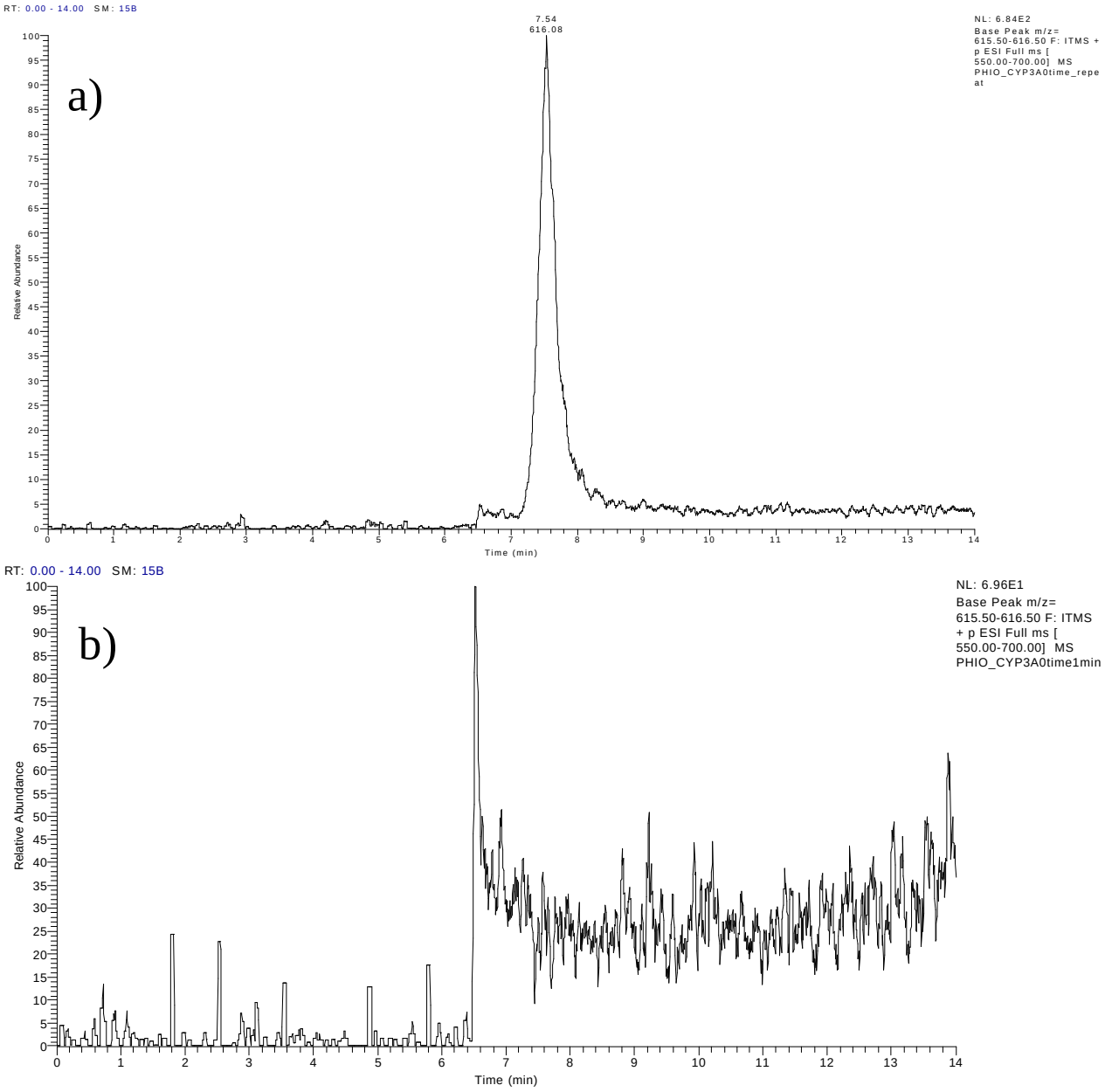


Figure S26. Mass Spectrometry of CYP3A4 before (a) and after (b) treatment with PhIO.

References

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(S2) Macdonald, T. L.; Gutheim, W. G.; Martin, R. B.; Guengerich, F. P. *Biochemistry*, **1989**, *28*, 2071-2077.

(S3) Guengerich, F. P.; Yun, C.-H.; Macdonald, T. L. *J. Biol. Chem.* **1996**, *271*, 27321-27329.