Supporting Online Material for

Insights into the Binding of Pyridines to the Iron-Sulfur Enzyme IspH

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Supplementary Figures

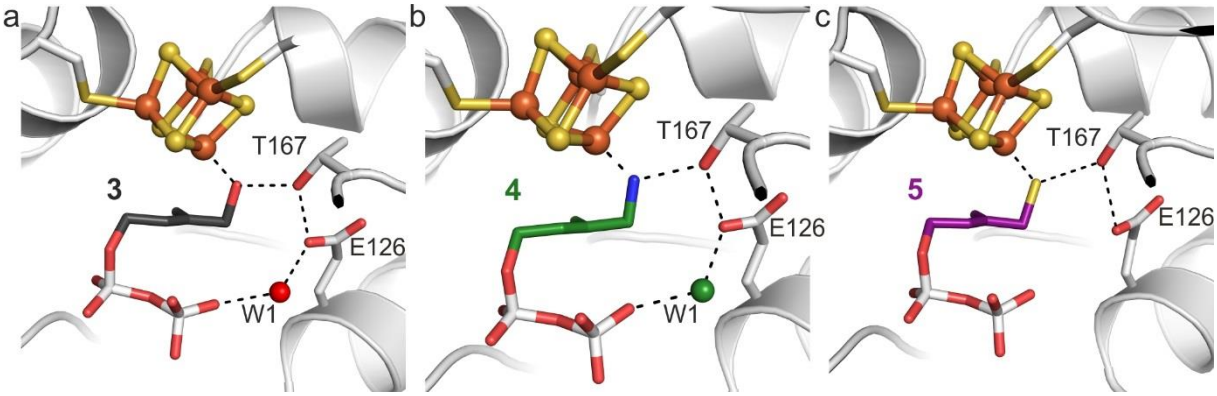

Figure S1. Structure of *E. coli* IspH bound to (a) (*E*)-1-hydroxy-2-methylbut-2-enyl 4-diphosphate (**3**)[1], (b) the amino-substituted substrate **4**[2] and (c) the thiol-substituted substrate **5**[2]. The protein is displayed as a cartoon model the cofactors as ball-and-stick models, ligands as well as amino acid side chains as stick models, and water molecules as spheres. The dotted lines indicate metal coordination or hydrogen bonding.

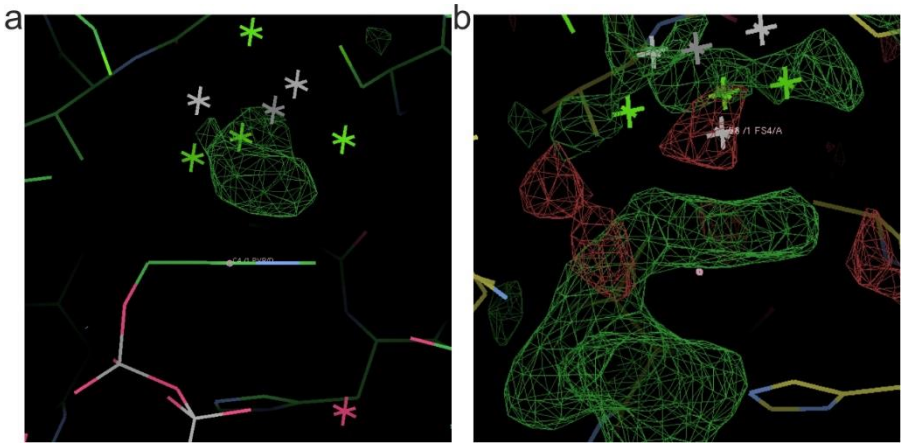

Figure S2. F_O-F_C map of the IspH-**10** structure with (a) the apical iron omitted from the refinement and (b) the ligand **10** excluded from the refinement.

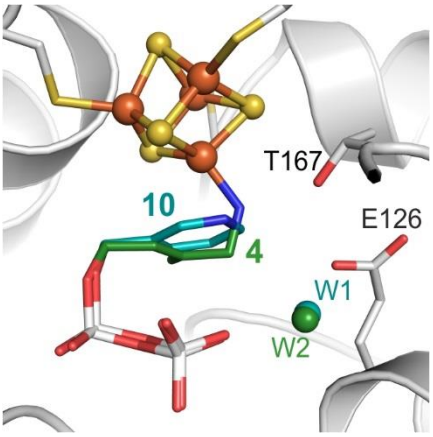

Figure S3. Structural superposition of the IspH-**10** complex compared to the amino-derivative of the HMBPP substrate, **4**.

Supplementary Tables

Table S1. Data collection and refinement statistics for the crystal structures of IspH in complex with **10**, **11**, **12**, and **13**.

	IspH:10	**IspH:11**	**IspH:12**	**IspH:13**
Data collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, *b*, *c* (Å)	69.78, 80.82, 111.25	70.19, 80.46, 111.89	69.47, 80.80, 111.49	70.13, 80.90, 111.89
α, β, γ (°)	90.0, 90.0,90.0	90.0, 90.0,90.0	90.0, 90.0,90.0	90.0, 90.0,90.0
Resolution (Å)	40-1.7 (1.8-1.7)	40-1.8 (1.9-1.8)	30-1.9 (2.0-1.9)	30-1.9 (2.0-1.9)
R_{sym} (%)	5.2 (57.4)	8.8 (41.6)	9.0 (42.1)	7.3 (50.3)
I / σ (I)	14.44 (2.38)	8.92 (2.81)	11.37 (2.82)	16.87 (4.68)
Completeness (%)	95.3 (95.2)	99.0 (99.4)	98.7 (95.6)	99.9 (100.0)
Redundancy	5.3	3.9	6.9	8.9
Refinement				
Resolution (Å)	10-1.7	10-1.8	15-1.9	15-1.9
No. reflections	62840	55376	46969	48176
R_{work} / R_{free}	0.203 / 0.247	0.177 / 0.224	0.218 / 0.256	0.215 / 0.249
No. atoms				
Protein	4802	4789	4789	4789
Ligand/ion	32	32	32	34
Water	242	539	246	190
B-factors				
Protein	41.4	25.8	36.6	34.9
Ligand/ion	27.5	27.0	22.3	28.4
Water	38.6	38.0	34.2	30.6
R.m.s. deviations				
Bond lengths (Å)	0.010	0.008	0.010	0.009
Bond angles (°)	1.3	1.3	1.4	1.4
Ramachandran plot (%)	99.2 / 0.8 / 0.0	99.2 / 0.8 / 0.0	98.7 / 1.3 / 0.0	98.9 / 1.1 / 0.0
PDB ID	4MUX	4MUY	4MV0	4MV5

Table S2. Comprehensive analysis of the occupancy of the apical iron site in the [Fe_4S_4] cluster of IspH.

Occupancy [%]	Rwork/Rfree	B-factor Fe1	B-factor Fe2	B-factor Fe3	B-factor Fe4	Difference electron density
100	0.214/0.277	26,7	25,1	64,6	28,85	positive
90	0.212/0.278	26,75	25,25	73,4	29	little positive
80	0.212/0.278	26,75	25,3	70,45	29	little positive
70	0.212/0.278	26,8	25,3	66,95	29,1	none
60	0.212/0.278	26,8	25,3	62,65	29,1	none
50	0.212/0.276	26,8	25,1	57,85	29	none
40	0.212/0.276	26,8	25,1	52,9	29	little negative
30	0.212/0.276	26,8	25,1	47,25	29,05	negative
20	0.212/0.276	26,8	25,1	43,95	29,05	negative
10	0.212/0.279	26,8	25,35	39,85	29,1	negative
0	0.213/0.279	26,85	25,35	n/a	29,2	negative

Table S3. Geometric and spectroscopic properties in various QM models.

			Coordination Mode	R_{FeN} (Å)	R_{FeC} (Å)	A_{iso}^{N} (MHz)	$NQCC^{N}$ (MHz)
Expt[a)]	Red/Ox		η^2	2.3	2.4		
Expt[b)]	Red					7.4	3.0
Small-Fopt	Ox	pyr	η^1	2.1	3.0	-	3.0
		$pyrH^+$	η^2	2.1	2.0	-	2.3
	Red	pyr	η^1	2.1	3.0	9.6	2.2
		$pyrH^+$	η^2	2.1	2.0	2.3	2.8
Small-Popt1	Ox	pyr	η^1	2.2	2.7	-	-0.5
		$pyrH^+$	η^2	2.1	2.1	-	2.3
	Red	pyr	η^2	2.0	2.1	6.9	3.6
		$pyrH^+$	η^2	2.0	2.0	2.1	2.8
Small-Popt2	Ox	pyr	η^2	2.1	2.3	-	4.2
		$pyrH^+$	η^2	2.0	2.1	-	2.3
	Red	pyr	η^2	2.0	2.1	6.6	3.5
		$pyrH^+$	η^2	2.0	2.1	1.1	2.8
Big-Popt	Ox	pyr	η^1	2.1	3.0	-	3.0
		$pyrH^+$	η^2	2.1	2.1	-	1.7
	Red	pyr	η^2	2.0	2.2	6.6	3.5
		$pyrH^+$	η^2	2.1	2.0	1.2	2.4

[a)] This work; [b)] [3].

Table S4. Coordinates of the optimized structure of Small-Fopt model for Ox/pyr.

C	5.37463000	-3.72874100	-7.64167200
S	4.13724400	-4.35660100	-8.85963000
C	-2.65212300	-1.34019600	-9.74218300
S	-1.59579500	-1.62831700	-8.25543800
C	2.52801300	2.78512800	-7.12553200
S	3.84335500	1.83018500	-8.00654800
Fe	2.87397100	-2.58570900	-9.35766300
S	2.06209500	-1.54285700	-7.46339300
Fe	0.50503200	-1.40047200	-9.00779900
S	1.09028300	-2.99887400	-10.62000200
Fe	1.97253500	-0.95536500	-11.20324200
S	4.04401400	-0.92720300	-10.44608100
Fe	2.68277200	0.14014500	-8.92838000
S	0.82189400	0.67298500	-10.04842800
C	1.85420500	-1.56279900	-15.46592300
C	1.61258500	-0.29142300	-16.00065800
C	1.41356700	0.77384800	-15.11459700
C	1.89206900	-1.72380100	-14.08323200
N	1.70953100	-0.69152900	-13.22067200
C	1.46663800	0.53771200	-13.74272800
H	4.86845100	-3.32012000	-6.75417600
H	5.99896100	-2.94136500	-8.09060500
H	-2.46065100	-0.34281100	-10.16738400
H	-2.45740200	-2.10201100	-10.51298400
H	2.02619000	2.15898900	-6.37230200
H	1.77530300	3.16199700	-7.83448700
H	1.57549000	-0.13575700	-17.08281800
H	1.21413700	1.78575300	-15.47746500
H	2.06611900	-2.69900800	-13.62019400
H	1.30894800	1.33510000	-13.01111800
H	3.00462000	3.63884000	-6.61637600
H	6.01955900	-4.56859300	-7.33566200
H	-3.70992200	-1.40307200	-9.43786400
H	2.00956800	-2.43124800	-16.11165800

Table S5. Coordinates of the optimized structure of Small-Fopt model for Ox/pyrH^+.

C	5.48007400	-3.72228400	-7.88296800
S	4.30451400	-4.21588400	-9.21044800
C	-2.54115800	-1.44281400	-10.27396300
S	-1.47490000	-1.93575300	-8.85247800
C	2.29915100	2.62889800	-7.31496100
S	3.69153100	1.60184400	-7.95685100
Fe	3.03960800	-2.50278900	-9.66489400
S	2.06735400	-1.74389700	-7.80897400
Fe	0.59885400	-1.56891100	-9.47854500
S	1.42143100	-2.93495400	-11.08291800
Fe	2.25794200	-0.89720300	-11.54714400
S	4.22905500	-0.82851800	-10.48634400
Fe	2.69958700	-0.00474200	-9.08506600
S	0.94035700	0.50417900	-10.31328900
C	1.50512700	-1.51361900	-14.34977800
C	0.52142000	-0.64955800	-14.75592900
C	0.62032800	0.74817800	-14.43365400
C	2.61020200	-1.07735700	-13.53886900
N	2.63809100	0.32152200	-13.19971100
C	1.66932500	1.21280100	-13.70561800
H	4.93212600	-3.40132200	-6.98520300
H	6.13200200	-2.90582000	-8.22649100
H	-2.39530900	-0.38034500	-10.51926300
H	-2.32267900	-2.05817800	-11.15940400
H	1.65999300	2.04091400	-6.64044000
H	1.69120400	3.03094900	-8.13812200
H	-0.32060400	-1.00995600	-15.35115600
H	-0.13506800	1.45523200	-14.78226200
H	3.58871800	-1.55812700	-13.64296300
H	1.81716800	2.25731300	-13.42976900
H	2.74303800	3.46272600	-6.74899000
H	6.09608100	-4.60155000	-7.63923200
H	-3.58912600	-1.60334200	-9.97696600
H	1.48069000	-2.57108300	-14.62435200
H	3.55808100	0.72974700	-13.02047200

Table S6. Coordinates of the optimized structure of Small-Fopt model for Red/pyr.

C	5.45238700	-3.71813800	-7.85147700
S	3.90857000	-4.38811900	-8.61934100
C	-2.70332200	-1.05744100	-10.04250000
S	-1.82140600	-1.29983900	-8.43618900
C	2.74654700	2.68622800	-6.77557100
S	3.94117900	1.86668500	-7.92971800
Fe	2.72044600	-2.53913000	-9.18833700
S	1.86144900	-1.35682800	-7.37423500
Fe	0.38975700	-1.19639300	-9.02658200
S	0.96520600	-2.90741200	-10.53968700
Fe	1.96530300	-0.89769800	-11.13268900
S	4.02342700	-0.99927700	-10.29581200
Fe	2.67339700	0.23164300	-8.86750500
S	0.87630400	0.85655700	-10.08772100
C	2.21137900	-1.61502800	-15.39299800
C	1.48294100	-0.57346900	-16.00912800
C	0.90973100	0.40067700	-15.15998800
C	2.33952900	-1.64676900	-14.01249600
N	1.78485000	-0.70265800	-13.18631800
C	1.07498000	0.30238300	-13.78577200
H	5.21560800	-3.13664300	-6.94626400
H	5.98281900	-3.05999300	-8.55785000
H	-2.43303800	-0.08780500	-10.49077200
H	-2.44245300	-1.85724000	-10.75405700
H	2.34078900	1.95911900	-6.05403500
H	1.90611400	3.13358700	-7.33048900
H	1.36213600	-0.52689500	-17.09562600
H	0.33225200	1.23759400	-15.56719800
H	2.89401100	-2.44145000	-13.50552800
H	0.64245700	1.03381200	-13.09648800
H	3.27024900	3.48395200	-6.21889500
H	6.11421900	-4.55763700	-7.57265400
H	-3.79365300	-1.07827900	-9.86696800
H	2.68172300	-2.40528500	-15.98800600

Table S7. Coordinates of the optimized structure of Small-Fopt model for Red/pyrH^+.

C	5.65794500	-3.42018600	-8.24602500
S	4.09354100	-4.11691000	-8.93195200
C	-2.69191900	-1.38626300	-10.40129100
S	-1.74149800	-1.63343500	-8.83650200
C	2.50310600	2.42717200	-6.83653100
S	3.65180700	1.78586500	-8.13697400
Fe	2.81080200	-2.40427600	-9.49050100
S	1.84413800	-1.39795500	-7.72632300
Fe	0.39845000	-1.34784000	-9.42462900
S	1.18881800	-2.88661900	-10.91801700
Fe	2.08588600	-0.89345000	-11.50104000
S	4.04819500	-0.82962100	-10.40392200
Fe	2.55122100	0.17214000	-9.13659000
S	0.82547800	0.66301300	-10.41659000
C	1.53346300	-1.69746200	-14.27248100
C	0.61719300	-0.84822000	-14.83577000
C	0.74687800	0.57380900	-14.63687500
C	2.59676800	-1.23281700	-13.41506600
N	2.63123700	0.20062700	-13.18628200
C	1.74765900	1.06834400	-13.86307600
H	5.44943500	-2.79363400	-7.36571100
H	6.17630600	-2.80916300	-9.00123500
H	-2.52772500	-0.37454600	-10.80326100
H	-2.39521400	-2.12597100	-11.16104300
H	2.31286600	1.65484500	-6.07543000
H	1.54357900	2.74057600	-7.27554200
H	-0.20408100	-1.23924800	-15.44193900
H	0.04316400	1.26904600	-15.10065200
H	3.57362100	-1.72699900	-13.45887900
H	1.89912200	2.12898200	-13.65756800
H	2.97711900	3.29779300	-6.35237000
H	6.30941900	-4.25732100	-7.94505400
H	-3.76481300	-1.51348700	-10.18092300
H	1.47930600	-2.77691300	-14.43878800
H	3.54293500	0.59642200	-12.95265800

Table S8. Coordinates of the optimized structure of Small-Popt1 model for Ox/pyr.

C	4.82299100	-4.25499600	-8.24801900
S	3.67715100	-4.21818900	-9.69106500
C	-2.61100000	-1.46299700	-10.41500400
S	-2.12081900	-2.08251200	-8.75109900
C	2.91901000	2.68199500	-7.06700300
S	2.81199000	1.05028700	-6.20878900
Fe	2.46230300	-2.36086900	-9.43039300
S	1.42660600	-2.18440300	-7.36298900
Fe	0.01532100	-1.45904600	-8.87997300
S	0.81435500	-2.26107900	-10.89460300
Fe	1.61409600	-0.09839700	-10.57261100
S	3.60672200	-0.35397400	-9.61481000
Fe	2.02703000	-0.05398700	-7.98348400
S	0.25284400	0.85947100	-9.02251300
C	2.54497700	-1.37692900	-14.16694100
C	1.62880900	-0.96441500	-15.14582800
C	0.83841800	0.17538700	-14.92297800
C	2.62435300	-0.60801600	-13.01154400
N	1.78011100	0.41947100	-12.72625200
C	0.91302200	0.83492700	-13.69203400
H	4.25533200	-4.29319000	-7.30599400
H	5.47209000	-3.36595000	-8.23605800
H	-2.34680200	-0.40078300	-10.53184300
H	-2.11368800	-2.04492800	-11.20556700
H	1.91632100	3.05990300	-7.31724900
H	3.51326700	2.60395700	-7.99049300
H	1.52939000	-1.51872100	-16.08456900
H	0.13886700	0.52663100	-15.68701600
H	3.36697500	-0.83797100	-12.24304100
H	0.25534500	1.66649700	-13.42542900
H	3.41619400	3.40119300	-6.39370400
H	5.45351900	-5.15615600	-8.32351700
H	-3.70419400	-1.56780000	-10.52682000
H	3.19261400	-2.24582900	-14.29912500

Table S9. Coordinates of the optimized structure of Small-Popt1 model for Ox/pyrH^+.

C	4.82292600	-4.25500900	-8.24803600
S	3.64273400	-4.39615800	-9.64726200
C	-2.61098800	-1.46299600	-10.41498700
S	-1.64147100	-1.66877600	-8.86332900
C	2.91905500	2.68196300	-7.06707600
S	3.85651500	1.11217100	-7.29164800
Fe	2.72471300	-2.43389100	-9.76407000
S	1.84635200	-1.87567200	-7.79619200
Fe	0.44222700	-1.22844200	-9.39472300
S	1.11759400	-2.34863100	-11.22588400
Fe	2.28110200	-0.42656500	-11.32695200
S	4.18524500	-0.83597200	-10.25220800
Fe	2.72458900	-0.05764700	-8.76835900
S	1.07885400	0.90096100	-9.88039000
C	2.54483000	-1.37641800	-14.16674200
C	1.31303300	-1.30405300	-14.76313300
C	0.48530400	-0.16017800	-14.51247400
C	3.00820300	-0.38234400	-13.24696300
N	2.15067000	0.74585400	-13.01523000
C	0.91317700	0.83446000	-13.69215900
H	4.28340100	-4.05918400	-7.30976800
H	5.54683900	-3.44677900	-8.42781700
H	-2.52807600	-0.43552600	-10.80021800
H	-2.26706900	-2.17174600	-11.18297300
H	1.91072100	2.48269100	-6.67712700
H	2.84275300	3.23578600	-8.01359500
H	0.97125400	-2.09168700	-15.43761100
H	-0.49196100	-0.06019600	-14.98940400
H	4.07866900	-0.17269400	-13.17050700
H	0.34030600	1.73656200	-13.47339100
H	3.47356300	3.28972100	-6.33498700
H	5.36404000	-5.21037700	-8.16008000
H	-3.66700700	-1.67093100	-10.18233500
H	3.21913700	-2.21355600	-14.36597800
H	2.59912300	1.64393800	-12.81549000

Table S10. Coordinates of the optimized structure of Small-Popt1 model for Red/pyr.

C	4.82297500	-4.25500400	-8.24801600
S	3.51920100	-4.53001200	-9.52418800
C	-2.61099300	-1.46301600	-10.41499200
S	-1.80387400	-1.33538000	-8.75832400
C	2.91900500	2.68200600	-7.06702500
S	4.11473500	1.49630700	-7.81872800
Fe	2.65322800	-2.43456700	-9.73765300
S	1.84480000	-1.67843000	-7.71597200
Fe	0.39441800	-0.98659500	-9.28394200
S	0.94301100	-2.26629600	-11.13005100
Fe	2.17405400	-0.29850400	-11.31976400
S	4.13667700	-0.80674700	-10.29728900
Fe	2.73214900	0.06144300	-8.80394200
S	1.08604200	1.12132900	-9.85346600
C	2.54490900	-1.37683100	-14.16693900
C	1.34596100	-1.26102800	-14.83881900
C	0.52658800	-0.10143900	-14.63290700
C	2.95677200	-0.31586100	-13.29311300
N	2.10819200	0.76846000	-13.01959100
C	0.91310500	0.83484600	-13.69202800
H	4.37448000	-3.89036200	-7.31031300
H	5.55849000	-3.51058600	-8.59279400
H	-2.46134400	-0.54293100	-11.00248300
H	-2.19135100	-2.30786600	-10.98245100
H	2.22238600	2.16951300	-6.38359400
H	2.32937200	3.17642700	-7.85526600
H	0.99913200	-2.06136600	-15.50266500
H	-0.41849800	0.01848300	-15.17339600
H	4.02536200	-0.13423200	-13.12919700
H	0.27329200	1.68228400	-13.41707100
H	3.47282900	3.44999000	-6.49448100
H	5.34647900	-5.20696800	-8.04638200
H	-3.69578500	-1.62275900	-10.27922100
H	3.18570400	-2.25697400	-14.28360200

Table S11. Coordinates of the optimized structure of Small-Popt1 model for Red/pyr.

C	4.82299100	-4.25500100	-8.24800400
S	3.45888900	-4.44409200	-9.46741500
C	-2.61099700	-1.46300300	-10.41499700
S	-1.70464600	-1.37099100	-8.80971900
C	2.91900300	2.68200000	-7.06700500
S	4.08128500	1.50140000	-7.87085100
Fe	2.64820400	-2.40260300	-9.68841700
S	1.87663500	-1.57967700	-7.73914200
Fe	0.43690700	-1.01550300	-9.35880900
S	1.01873700	-2.30968400	-11.14452800
Fe	2.23615400	-0.41523500	-11.35416600
S	4.15687500	-0.90190500	-10.30690300
Fe	2.79686800	0.06596600	-8.90274800
S	1.14910900	1.06878100	-9.99566600
C	2.54496000	-1.37692400	-14.16697500
C	1.31705000	-1.30214100	-14.77559600
C	0.48900100	-0.15664900	-14.51891200
C	3.01017200	-0.39458100	-13.23957300
N	2.15742200	0.75065200	-13.01633200
C	0.91304300	0.83492800	-13.69201800
H	4.44040300	-3.84165000	-7.30227100
H	5.60599800	-3.58513300	-8.63615600
H	-2.53848900	-0.51417000	-10.96962500
H	-2.20576800	-2.27298900	-11.04043600
H	2.25943800	2.16453000	-6.35292700
H	2.29590300	3.18335400	-7.82367300
H	0.96493400	-2.10063300	-15.43245700
H	-0.50009700	-0.06674300	-14.97497700
H	4.08156400	-0.18681700	-13.16999500
H	0.32666400	1.72152900	-13.44611800
H	3.50511400	3.44129700	-6.52065300
H	5.26441800	-5.24675500	-8.05259600
H	-3.67370600	-1.66906000	-10.20473300
H	3.20965100	-2.22647500	-14.35009300
H	2.61076900	1.64837800	-12.82884100

Table S12. Coordinates of the optimized structure of Small-Popt2 model for Ox/pyr.

C	4.82299200	-4.25499900	-8.24801500
S	3.72215100	-4.41135900	-9.72555100
C	-2.61100100	-1.46299800	-10.41500100
S	-1.66727800	-1.46169100	-8.82837600
C	2.91899300	2.68201600	-7.06700400
S	4.06600700	1.28293500	-7.41824700
Fe	2.71188500	-2.42674500	-9.89204300
S	1.88388300	-1.78839000	-7.84826800
Fe	0.47406900	-1.08059000	-9.38381500
S	1.02387900	-2.20546700	-11.29934500
Fe	2.25503200	-0.19703600	-11.37097400
S	4.16484700	-0.75118400	-10.41133900
Fe	2.79746500	0.07684700	-8.80511700
S	1.12433600	1.09411100	-9.85106500
C	2.54501300	-1.37700800	-14.16699900
C	1.25288400	-1.34120500	-14.69617900
C	0.44596900	-0.19808000	-14.50535100
C	3.01101100	-0.22371300	-13.50448000
N	2.18034500	0.82906600	-13.18251400
C	0.91297200	0.83502400	-13.69200800
H	4.22591200	-4.05343200	-7.34621500
H	5.54754700	-3.43835500	-8.38696800
H	-2.57251300	-0.47626700	-10.90259000
H	-2.20288500	-2.21807300	-11.10361600
H	1.97058100	2.32077200	-6.64282400
H	2.70419000	3.25288300	-7.98204700
H	0.85585700	-2.20348900	-15.23975200
H	-0.56373700	-0.15348200	-14.92306400
H	4.07036400	-0.08001100	-13.28072700
H	0.28525200	1.67712000	-13.38625300
H	3.40076600	3.34885900	-6.33184600
H	5.36937900	-5.20337700	-8.11954400
H	-3.66249400	-1.70751900	-10.19220300
H	3.19742500	-2.24445400	-14.29010800

Table S13. Coordinates of the optimized structure of Small-Popt2 model for Ox/pyrH^+.

C	4.82301200	-4.25500700	-8.24798400
S	3.63596300	-4.24700600	-9.65621600
C	-2.61098300	-1.46300600	-10.41498200
S	-1.62073500	-1.41760800	-8.86050400
C	2.91901000	2.68197500	-7.06699200
S	4.05441300	1.32174900	-7.55001100
Fe	2.73804900	-2.26303600	-9.77921600
S	1.87995000	-1.62436000	-7.81736800
Fe	0.46263400	-0.97127100	-9.41097900
S	1.11228800	-2.14852800	-11.22025600
Fe	2.25488400	-0.19692400	-11.37110400
S	4.18559700	-0.67428000	-10.34695700
Fe	2.76855700	0.13663300	-8.86827900
S	1.11192700	1.14581500	-9.93205300
C	2.54502700	-1.37703900	-14.16698600
C	1.29309000	-1.33316300	-14.72170400
C	0.46064300	-0.19666700	-14.45349000
C	3.02172100	-0.34103300	-13.29633500
N	2.19620700	0.81799100	-13.10785800
C	0.91305100	0.83500200	-13.69195300
H	4.29689200	-4.05492600	-7.30314200
H	5.60943800	-3.50028000	-8.39541100
H	-2.59567400	-0.48773000	-10.92446300
H	-2.22698500	-2.23849800	-11.09396000
H	2.01396800	2.29091800	-6.58024400
H	2.63225500	3.28634000	-7.93945900
H	0.93159900	-2.14127900	-15.36062200
H	-0.55087900	-0.13537600	-14.86049700
H	4.09455300	-0.14770800	-13.22941600
H	0.32900700	1.73094800	-13.47598700
H	3.45637200	3.32087100	-6.34757700
H	5.28274400	-5.25426300	-8.20452500
H	-3.64951300	-1.70519900	-10.14135700
H	3.22143200	-2.21530400	-14.35255100
H	2.65663300	1.72944400	-13.02418900

Table S14. Coordinates of the optimized structure of Small-Popt2 model for Red/pyr.

C	4.82298700	-4.25500200	-8.24799900
S	3.54886100	-4.45650700	-9.56797200
C	-2.61100500	-1.46300200	-10.41500200
S	-1.74605500	-1.25403900	-8.79423300
C	2.91899300	2.68200300	-7.06699200
S	4.16067900	1.55679400	-7.83294200
Fe	2.71924300	-2.34460400	-9.78119000
S	1.89629700	-1.58983100	-7.76894000
Fe	0.44906000	-0.88957000	-9.34327900
S	1.01258200	-2.16873200	-11.17606100
Fe	2.25507100	-0.19699700	-11.37100000
S	4.21331500	-0.72297800	-10.35242100
Fe	2.80130200	0.13518100	-8.86145100
S	1.16130200	1.21678500	-9.90667900
C	2.54500600	-1.37701800	-14.16700100
C	1.31558500	-1.29598900	-14.78560100
C	0.49202900	-0.13944600	-14.57741300
C	2.98706200	-0.27870900	-13.35393700
N	2.14599800	0.81449600	-13.08794300
C	0.91294900	0.83501600	-13.69200500
H	4.35976700	-3.89192600	-7.31683300
H	5.59665300	-3.53297900	-8.55506200
H	-2.55447000	-0.54357400	-11.02011700
H	-2.15633100	-2.28479400	-10.98930800
H	2.22107300	2.12454900	-6.42142800
H	2.33469700	3.19152400	-7.84942000
H	0.94449000	-2.12456500	-15.39966400
H	-0.48445400	-0.05372100	-15.06592900
H	4.06033500	-0.08730600	-13.23849600
H	0.27636000	1.68416900	-13.41536400
H	3.43758700	3.44148000	-6.45105400
H	5.30358000	-5.23012700	-8.05124800
H	-3.67397700	-1.69788600	-10.22807100
H	3.18681900	-2.25726000	-14.27603800

Table S15. Coordinates of the optimized structure of Small-Popt2 model for Red/pyr.

C	4.82303300	-4.25500900	-8.24795500
S	3.44768400	-4.31475500	-9.47691700
C	-2.61099000	-1.46300400	-10.41498500
S	-1.69190300	-1.14082500	-8.84327800
C	2.91899700	2.68199100	-7.06697300
S	4.14881400	1.58233700	-7.86743200
Fe	2.66929800	-2.24996400	-9.70791900
S	1.89075200	-1.39461000	-7.76920300
Fe	0.45949800	-0.78986700	-9.38927000
S	1.03140400	-2.10449500	-11.15659000
Fe	2.25489700	-0.19697700	-11.37116700
S	4.18134200	-0.75398200	-10.35297900
Fe	2.84215500	0.21637600	-8.94546400
S	1.21776700	1.29509100	-10.01116900
C	2.54496800	-1.37700800	-14.16699200
C	1.29846200	-1.33006400	-14.73428800
C	0.46469900	-0.19142400	-14.46230500
C	3.02043100	-0.35638200	-13.27513800
N	2.19792300	0.81992900	-13.09996900
C	0.91309500	0.83500700	-13.69192900
H	4.46535600	-3.85235500	-7.28798100
H	5.64881100	-3.62444400	-8.61258400
H	-2.59438100	-0.58244800	-11.07630500
H	-2.17174300	-2.31897900	-10.94910500
H	2.22323200	2.10319400	-6.44009100
H	2.33812700	3.22812600	-7.82600400
H	0.93102000	-2.14534200	-15.36160500
H	-0.55472200	-0.13833800	-14.85244000
H	4.09436900	-0.16054300	-13.22261200
H	0.31778500	1.71739200	-13.45046700
H	3.44477600	3.41143900	-6.42487900
H	5.19512600	-5.28090000	-8.09212700
H	-3.65825100	-1.69530100	-10.16074700
H	3.21346000	-2.22563600	-14.33861500
H	2.66325500	1.72971000	-13.03418200

Table S16. Coordinates of the optimized structure of Big-Popt model for Ox/pyr.

C	5.09747400	-5.63275500	-7.69991000
C	4.25830000	-4.36314800	-7.85221800
S	2.91867100	-4.59542800	-9.11488900
C	-4.05307500	-1.83360200	-10.40294600
C	-3.35752200	-0.63088800	-9.76252700
S	-2.33735800	-1.10640700	-8.28469500
C	2.73780200	5.86859200	-10.97354300
C	1.90462100	4.77911500	-10.30213500
O	1.55390300	3.83446000	-11.32581500
C	0.64716900	5.34302700	-9.62460500
C	3.56395600	3.85365600	-6.28484100
C	2.71834600	2.60711300	-6.55250000
S	3.70841700	1.34390800	-7.48372900
Fe	1.98266500	-2.58219800	-9.34391800
S	1.22393600	-1.66637800	-7.35862000
Fe	-0.19032800	-1.07830300	-8.93719800
S	0.25404600	-2.49704100	-10.72838700
Fe	1.51858400	-0.57619000	-10.98905500
S	3.48931100	-1.02841000	-10.12068200
Fe	2.21358600	0.05145500	-8.54666300
S	0.52999300	1.02807500	-9.68197500
O	4.60284300	-2.14589100	-15.15975900
C	3.79567000	-1.25020000	-15.91094800
C	2.62975500	-0.64722500	-15.14478800
C	1.60735500	0.05890200	-15.80091100
C	0.57351600	0.61782800	-15.04721900
C	2.55629900	-0.76052300	-13.75635800
N	1.53948500	-0.24533500	-13.02125200
C	0.56760900	0.44222300	-13.66376600
H	3.78564400	-4.09071700	-6.89479700
H	4.88978200	-3.51607700	-8.16454600
H	5.88814200	-5.48595600	-6.94062300
H	-4.10202400	0.10544100	-9.41299600
H	-2.71041700	-0.12060200	-10.49319000
H	-3.30938100	-2.56498400	-10.75831700
H	2.52936000	4.27735000	-9.53512200
H	0.06145800	4.53222000	-9.16041000
H	0.90480600	6.07280000	-8.83606900
H	0.00782500	5.84466200	-10.37198100

H	1.26581000	3.01037800	-10.87246500
H	3.05557300	6.63060200	-10.24199600
H	2.37783600	2.15934200	-5.60415800
H	1.82210300	2.86651600	-7.13815700
H	2.98652900	4.60211900	-5.71009400
H	3.40928000	-1.72382200	-16.83962900
H	4.48170200	-0.44466300	-16.22609100
H	1.62275600	0.17130600	-16.89079600
H	-0.23354200	1.18138600	-15.52252900
H	3.33642600	-1.27534300	-13.19078000
H	-0.22660700	0.84906400	-13.03319900
H	4.47302000	-6.48561200	-7.38465900
H	5.58253700	-5.90354800	-8.65273700
H	4.46866300	3.60079800	-5.70645600
H	3.88978300	4.31940000	-7.22929900
H	2.14793200	6.36612300	-11.76330300
H	3.63484700	5.42929000	-11.43843500
H	-4.70729100	-2.34380000	-9.67632600
H	-4.67286700	-1.51768100	-11.26436700
H	4.04032300	-2.88563700	-14.85893600

Table S17. Coordinates of the optimized structure of Big-Popt model for Ox/pyrH^+.

C	5.09700800	-5.63200000	-7.70099900
C	4.79252300	-4.18695100	-8.10303000
S	3.86146800	-4.13325700	-9.70899600
C	-4.05300800	-1.83400700	-10.40300600
C	-2.66008200	-1.24529500	-10.64908500
S	-1.53839300	-1.60723400	-9.21343200
C	2.73801000	5.86800900	-10.97300500
C	2.50367300	4.94899800	-12.17869900
O	2.96188400	3.59055700	-11.91499500
C	3.24677100	5.41344000	-13.42577800
C	3.56400000	3.85499600	-6.28399700
C	2.78595300	2.69078700	-6.90483700
S	3.95782400	1.53957800	-7.77257000
Fe	2.91436100	-2.18689400	-9.99032000
S	1.92733600	-1.59800100	-8.07883500
Fe	0.53570200	-1.08973000	-9.74464300
S	1.34691800	-2.23462000	-11.52254500
Fe	2.37076600	-0.23900400	-11.65408900
S	4.27940700	-0.51379100	-10.53303700
Fe	2.75886300	0.23642700	-9.08892400
S	1.06645800	1.06742800	-10.25152800
O	4.60299000	-2.14699800	-15.15999300
C	3.19634700	-2.30387500	-14.93694200
C	2.47997900	-1.01369300	-14.58216300
C	1.25931200	-0.70016300	-15.13459300
C	0.58322300	0.50818200	-14.76815000
C	3.06940600	-0.13328900	-13.60258400
N	2.37285400	1.06820200	-13.26673200
C	1.14286800	1.36947200	-13.87511300
H	4.17592600	-3.68718400	-7.34020100
H	5.71889900	-3.60330600	-8.22668100
H	5.65931400	-5.64423100	-6.75071900
H	-2.71377600	-0.15218000	-10.77980700
H	-2.21135500	-1.67616900	-11.55829200
H	-4.00594500	-2.92840500	-10.28452900
H	1.41522800	4.91792500	-12.39288000
H	3.06630300	4.72839400	-14.27000200
H	2.90998300	6.41931600	-13.72408900
H	4.33166900	5.44856200	-13.23382900

H	2.62408300	3.30388900	-11.04177600
H	2.38086000	6.88758700	-11.19310800
H	2.25433300	2.11658200	-6.12936100
H	2.03727400	3.05425400	-7.62627800
H	2.87100600	4.52968400	-5.75060900
H	3.00021100	-3.04072100	-14.13340200
H	2.75734700	-2.70792000	-15.86502800
H	0.80478400	-1.36719800	-15.87268500
H	-0.37799900	0.76478200	-15.21866500
H	4.15915600	-0.06940900	-13.53995700
H	0.70107100	2.31544600	-13.56358200
H	4.16997000	-6.21002500	-7.55882200
H	5.70652200	-6.14299300	-8.46406400
H	4.31247100	3.49331700	-5.56064800
H	4.09099800	4.44013600	-7.05487000
H	3.81154000	5.91670500	-10.72643900
H	2.19160300	5.50906800	-10.08379800
H	-4.50928500	-1.41183800	-9.49301200
H	-4.71642400	-1.60757400	-11.25674800
H	5.07435500	-2.49624400	-14.38278600
H	2.88293200	1.90696700	-12.92100900

Table S18. Coordinates of the optimized structure of Big-Popt model for Red/pyr.

C	5.09703500	-5.63203000	-7.70096000
C	4.84431100	-4.18679200	-8.14716700
S	4.03058400	-4.14006800	-9.81138400
C	-4.05303300	-1.83400100	-10.40301000
C	-2.65090800	-1.23084700	-10.52798300
S	-1.63889100	-1.53612200	-9.00336300
C	2.73800900	5.86805200	-10.97298900
C	1.81874800	4.70286500	-10.60928900
O	1.42696500	4.07831000	-11.84124300
C	0.57899400	5.16202600	-9.82563800
C	3.56399800	3.85497700	-6.28402600
C	3.00201100	2.51750600	-6.79192200
S	3.96198700	1.88845600	-8.25752300
Fe	2.97202500	-2.13951000	-10.10487200
S	2.09219400	-1.41747500	-8.12342700
Fe	0.49269500	-1.07405200	-9.66470600
S	1.18441700	-2.41747800	-11.40820800
Fe	2.00376100	-0.30461200	-11.82749000
S	4.09583800	-0.33069800	-10.94803300
Fe	2.71625300	0.36908400	-9.31920400
S	0.87148800	1.09067800	-10.34713700
O	4.60299200	-2.14699800	-15.16001500
C	3.26125700	-2.63006400	-14.95336200
C	2.22199300	-1.55065100	-14.76042200
C	0.95278600	-1.65879500	-15.28957300
C	-0.03917500	-0.68013700	-14.97533000
C	2.52422300	-0.40250300	-13.94174100
N	1.54050200	0.52218900	-13.59338700
C	0.28164900	0.33127100	-14.09177400
H	4.18985000	-3.67168700	-7.42592000
H	5.79492500	-3.62763700	-8.18932200
H	5.59409600	-5.66238800	-6.71090100
H	-2.71558200	-0.14288400	-10.69934800
H	-2.12568300	-1.67031400	-11.39135500
H	-3.99544100	-2.92585300	-10.25445700
H	2.38671300	3.98326700	-9.98803200
H	-0.04946700	4.29195500	-9.57541300
H	0.85639900	5.66836300	-8.88233600
H	-0.02020200	5.86111600	-10.43750600

H	1.28707300	3.12347600	-11.64585400
H	3.07163400	6.41066500	-10.07091000
H	3.03596000	1.75907400	-5.99078300
H	1.94669300	2.63801100	-7.08663300
H	2.99239000	4.21957600	-5.40809000
H	3.23485600	-3.31002700	-14.07651700
H	3.02000500	-3.23056800	-15.84766800
H	0.69365400	-2.51537800	-15.92455400
H	-1.04834800	-0.74669000	-15.39372600
H	3.54958600	-0.01642600	-13.92468200
H	-0.46732000	1.05025200	-13.73942400
H	4.14652800	-6.18717100	-7.62963800
H	5.74035100	-6.16185000	-8.42528200
H	4.62193500	3.74919300	-5.98615000
H	3.51552300	4.62329800	-7.07406100
H	2.21064000	6.57906400	-11.63538300
H	3.62596500	5.49297300	-11.50644000
H	-4.59097700	-1.40676000	-9.53849500
H	-4.65306700	-1.63876500	-11.31387300
H	4.91945900	-1.84487700	-14.28714000

Table S19. Coordinates of the optimized structure of Big-Popt model for Red/pyrH^+.

C	5.09700200	-5.63199800	-7.70100100
C	4.96254100	-4.17659000	-8.15786500
S	4.21568100	-4.08982800	-9.85317000
C	-4.05300200	-1.83400400	-10.40300300
C	-2.61682000	-1.36900900	-10.67288600
S	-1.46787300	-1.93526200	-9.32819400
C	2.73800600	5.86799200	-10.97300100
C	1.91867100	4.66573900	-10.52167800
O	2.02326000	3.65995000	-11.55135800
C	0.44907200	5.02409300	-10.26489000
C	3.56400000	3.85500600	-6.28399700
C	2.88750800	2.54374600	-6.71369800
S	3.86224400	1.74259700	-8.07865200
Fe	3.11199000	-2.17797500	-10.13167500
S	2.07183700	-1.64517200	-8.21335200
Fe	0.61259100	-1.31353100	-9.87962300
S	1.53763800	-2.38569200	-11.67908200
Fe	2.35346700	-0.28329200	-11.78242700
S	4.27865200	-0.35812200	-10.64958800
Fe	2.71993600	0.23510300	-9.20107300
S	0.93695100	0.89044100	-10.36843100
O	4.60299500	-2.14699600	-15.15999800
C	3.16640900	-2.17484100	-15.13327800
C	2.51616700	-0.86039600	-14.74621600
C	1.35944600	-0.41981200	-15.34107100
C	0.75855700	0.82192200	-14.93198600
C	3.11856900	-0.10804600	-13.66754800
N	2.48562100	1.13137300	-13.29089800
C	1.32710100	1.58159300	-13.95906200
H	4.31645100	-3.61171900	-7.46828500
H	5.94690900	-3.67990300	-8.17935400
H	5.55751200	-5.68169100	-6.69657600
H	-2.57185300	-0.26904400	-10.73217600
H	-2.25892000	-1.77006700	-11.63534700
H	-4.10798600	-2.93428700	-10.35314700
H	2.36145900	4.26134800	-9.58996300
H	-0.11803200	4.13233800	-9.95117300
H	0.35656000	5.78483200	-9.46915400
H	-0.01366700	5.42256300	-11.18478900

H	1.69695800	2.81799400	-11.14310800
H	2.70653000	6.66950700	-10.21596800
H	2.82409000	1.84378300	-5.86370500
H	1.86089600	2.73424300	-7.06659000
H	3.00282900	4.33354300	-5.45971600
H	2.80612600	-2.95806500	-14.43641600
H	2.84250700	-2.45602400	-16.14900000
H	0.89277600	-1.00707600	-16.13836200
H	-0.15641400	1.17883300	-15.41098100
H	4.21064500	-0.09453800	-13.60887100
H	0.95164800	2.54154200	-13.60298500
H	4.10961600	-6.11951700	-7.65386600
H	5.72784100	-6.21191300	-8.39592000
H	4.59464100	3.67059700	-5.93733400
H	3.61561200	4.56590500	-7.12518800
H	2.34215200	6.27032400	-11.92225700
H	3.78907700	5.57765200	-11.13109800
H	-4.42345300	-1.43439900	-9.44408500
H	-4.73140300	-1.48977400	-11.20609500
H	4.91133600	-2.36545100	-14.26066900
H	3.07142300	1.88253900	-12.91035800

Table S20. Coordinates of the optimized structure of Big-Popt model for Ox/Pyr with pyridine ring flipped.

C	5.09699800	-5.63199200	-7.70100500
C	4.93077300	-4.23170500	-8.29735000
S	3.98875600	-4.28368300	-9.89869700
C	-4.05299600	-1.83399700	-10.40299700
C	-2.61650200	-1.31544300	-10.48670000
S	-1.63363100	-1.79995800	-8.98718000
C	2.73799900	5.86799600	-10.97300000
C	1.91843500	4.72963700	-10.37543700
O	1.60317400	3.82914600	-11.45341500
C	0.63557400	5.22920400	-9.69618000
C	3.56399900	3.85498300	-6.28401800
C	2.88318200	2.55821800	-6.73317600
S	3.96778400	1.64125500	-7.92916800
Fe	2.86385200	-2.36584300	-10.09904800
S	2.00706600	-1.75606500	-8.03449800
Fe	0.47523900	-1.30560400	-9.54147200
S	1.10955500	-2.44921500	-11.46712300
Fe	1.97134200	-0.33086400	-11.53338700
S	4.03440600	-0.49551400	-10.76012500
Fe	2.65944900	0.21484500	-9.06606300
S	0.77033400	0.95118300	-10.04842600
O	4.60300000	-2.14699100	-15.15998000
C	3.26276500	-2.13182000	-15.63664500
C	2.36417400	-1.12109500	-14.94476900
C	2.88876800	-0.07774500	-14.17570300
C	2.00169300	0.81689100	-13.53516400
C	0.96315600	-1.18896000	-15.07780800
N	0.09495300	-0.33956700	-14.51072100
C	0.61390900	0.63360200	-13.73655900
H	4.38585300	-3.57757600	-7.59982700
H	5.91324100	-3.77064200	-8.49199400
H	5.67701200	-5.58266100	-6.76070100
H	-2.60452000	-0.21606500	-10.56700900
H	-2.11248500	-1.72081600	-11.37837000
H	-4.07258800	-2.93461900	-10.33943500
H	2.54063000	4.19798400	-9.62723800

H	0.06039300	4.38364000	-9.28329900
H	0.86176400	5.92320600	-8.86691000
H	-0.00235300	5.75354000	-10.42886800
H	1.30663100	2.98715800	-11.03720100
H	3.02193800	6.59793700	-10.19633100
H	2.68574800	1.90495400	-5.86733500
H	1.91583300	2.77532000	-7.21324200
H	2.93200200	4.39309200	-5.55312000
H	2.79433600	-3.13610100	-15.57166100
H	3.34302900	-1.88486400	-16.71045400
H	3.97051300	0.04354000	-14.07618100
H	2.37041600	1.71797400	-13.02737500
H	0.51397700	-1.98633100	-15.68669400
H	-0.10161600	1.32213900	-13.27504500
H	4.11608100	-6.08275000	-7.47869600
H	5.62843600	-6.30312600	-8.39683700
H	4.53689300	3.64546800	-5.80863500
H	3.74604900	4.52310000	-7.14152900
H	2.15453400	6.39282700	-11.74967800
H	3.65596600	5.47410000	-11.43760300
H	-4.56932700	-1.43505100	-9.51360100
H	-4.62566300	-1.53001700	-11.29884400
H	4.58131200	-2.42220100	-14.22195700

Table S21. Coordinates of the optimized structure of Big-Popt model for Ox/PyrH$^+$ with pyridine ring flipped.

C	5.09700000	-5.63200000	-7.70099900
C	4.73474400	-4.19930400	-8.08788700
S	3.77006800	-4.17454100	-9.67240900
C	-4.05299800	-1.83399900	-10.40299900
C	-2.67858600	-1.21586300	-10.68326800
S	-1.54429700	-1.50771500	-9.24347600
C	2.73800000	5.86800000	-10.97300100
C	1.32751800	5.60765200	-11.51207500
O	1.14240300	4.21363000	-11.85334500
C	1.02720200	6.40162300	-12.77881300
C	3.56399800	3.85499700	-6.28400100
C	2.75497500	2.65885700	-6.78748400
S	3.90196300	1.33863200	-7.41010500
Fe	2.88190200	-2.19888900	-9.90796200
S	1.81121900	-1.66053600	-8.02900800
Fe	0.54511000	-1.00924400	-9.74187000
S	1.41421000	-2.09466700	-11.53171000
Fe	2.58039500	-0.15810900	-11.50194800
S	4.36715200	-0.58595600	-10.24994400
Fe	2.77443400	0.16953500	-8.89624000
S	1.21471900	1.13282600	-10.14367300
O	4.60300000	-2.14699900	-15.16000000
C	3.19617200	-2.19560500	-14.89055500
C	2.73523900	-0.84332600	-14.40935900
C	3.50816000	-0.16775000	-13.38678800
C	3.12527200	1.18414500	-13.03169100
C	1.59618200	-0.26398800	-14.89500700
N	1.18458400	0.97473700	-14.40250600
C	1.91092600	1.69025000	-13.51699400
H	4.11748600	-3.72483100	-7.30936800
H	5.63693900	-3.58237600	-8.22811900
H	5.67742100	-5.63246000	-6.76143000
H	-2.76420600	-0.12918400	-10.84831700
H	-2.22637400	-1.66452400	-11.58246400
H	-3.97306800	-2.92200500	-10.24883100
H	0.58651900	5.88438100	-10.73370900

H	0.01108300	6.17937200	-13.14136700
H	1.09959400	7.48401800	-12.58549500
H	1.74731800	6.14366500	-13.57390200
H	1.22287400	3.67358800	-11.04056400
H	2.86689900	6.92862900	-10.69758400
H	2.14681300	2.22461400	-5.97768400
H	2.07282900	2.95436800	-7.59920200
H	2.88655000	4.63036900	-5.88345600
H	2.96852400	-2.93175900	-14.09374000
H	2.63041600	-2.49438000	-15.79542800
H	4.54831300	-0.48012900	-13.27620800
H	3.80953100	1.87669900	-12.53418200
H	0.95441400	-0.71130300	-15.65451100
H	1.53013000	2.67574800	-13.22400500
H	4.19372200	-6.24350800	-7.54531400
H	5.70901300	-6.11722900	-8.47892100
H	4.25495200	3.55865300	-5.47809600
H	4.16133100	4.30281400	-7.09446700
H	3.49405600	5.61284400	-11.73465900
H	2.93947300	5.26244900	-10.07296700
H	-4.50981200	-1.39503700	-9.50129700
H	-4.73317500	-1.65457400	-11.25494400
H	4.98558000	-3.00683500	-14.91067500
H	0.29140500	1.35220200	-14.71330000

Table S22. Coordinates of the optimized structure of Big-Popt model for Red/Pyr with pyridine ring flipped.

C	5.09700400	-5.63194000	-7.70103300
C	4.65496800	-4.23855500	-8.16175800
S	3.96366100	-4.27195400	-9.88563400
C	-4.05295700	-1.83397100	-10.40300400
C	-2.69973400	-1.14610000	-10.62840300
S	-1.51385600	-1.49147000	-9.23468400
C	2.73799700	5.86800000	-10.97300000
C	1.78057800	4.75233200	-10.55874600
O	1.30315300	4.13547900	-11.76849800
C	0.59904100	5.27447100	-9.72728800
C	3.56398200	3.85491600	-6.28404500
C	2.89049800	2.63907700	-6.93579300
S	3.89057800	2.02039700	-8.36807800
Fe	2.91350200	-2.25012900	-10.14574600
S	2.05029000	-1.36348900	-8.29683800
Fe	0.54547600	-1.12725500	-9.97063700
S	1.17484600	-2.42792900	-11.66493200
Fe	2.04800100	-0.34417900	-12.04619500
S	4.15522900	-0.46872300	-11.04384900
Fe	2.76537000	0.42367900	-9.54701700
S	0.82621100	0.98546500	-10.65890700
O	4.60297400	-2.14700500	-15.15991800
C	3.19183400	-2.41434600	-15.17448200
C	2.31660000	-1.20147100	-14.94070200
C	2.76942500	-0.14350300	-14.08442500
C	1.84899600	0.92773000	-13.82198300
C	1.04608500	-1.11862500	-15.48247800
N	0.15909800	-0.09510600	-15.26169900
C	0.56875200	0.87252800	-14.44945200
H	3.88256900	-3.83872300	-7.48565500
H	5.50830300	-3.54037500	-8.13319500
H	5.51494800	-5.59580800	-6.67554600
H	-2.83270800	-0.05427200	-10.71800500
H	-2.24440600	-1.50271000	-11.56604800
H	-3.92630700	-2.92797900	-10.33476800
H	2.34393200	4.00948000	-9.96045200

H	-0.06751500	4.44091400	-9.45034700
H	0.94138900	5.76097600	-8.79561200
H	0.01299800	6.00600200	-10.31304200
H	1.03217100	3.21922100	-11.52954600
H	3.13856300	6.39220600	-10.08829100
H	2.77718600	1.82342100	-6.20170700
H	1.87967100	2.90759900	-7.28523800
H	2.97255900	4.22532800	-5.42347000
H	2.94085100	-3.17784900	-14.40844900
H	2.97753400	-2.85331000	-16.16432300
H	3.84336000	0.00340300	-13.94200400
H	2.18775500	1.87893400	-13.39819800
H	0.68310000	-1.91317400	-16.15030900
H	-0.13809800	1.69571100	-14.27653200
H	4.24426300	-6.33233200	-7.70261100
H	5.86963700	-6.04438900	-8.37345200
H	4.57420000	3.59511100	-5.92326800
H	3.67149100	4.67829500	-7.01044600
H	2.21836100	6.60388600	-11.61377200
H	3.58176400	5.44671900	-11.54222700
H	-4.51886500	-1.49191200	-9.46196300
H	-4.75217600	-1.61627300	-11.23384900
H	4.84688900	-2.01897500	-14.22252800

Table S23. Coordinates of the optimized structure of Big-Popt model for Red/Pyr+ with pyridine ring flipped

C	5.09700100	-5.63199700	-7.70100200
C	4.97386900	-4.20327800	-8.23681000
S	4.01978500	-4.17571200	-9.82702500
C	-4.05300100	-1.83400100	-10.40300200
C	-2.62790700	-1.31379900	-10.62304400
S	-1.51915700	-1.80474800	-9.21865600
C	2.73800500	5.86797600	-10.97300400
C	1.81037500	4.80713800	-10.38986400
O	1.50119900	3.88297500	-11.44939800
C	0.52162600	5.40559100	-9.80948200
C	3.56400000	3.85501300	-6.28399100
C	2.90794900	2.51237500	-6.63090000
S	3.94212800	1.61376700	-7.88388600
Fe	3.01197200	-2.20791600	-10.04598100
S	2.00784400	-1.68193100	-8.09973300
Fe	0.57512200	-1.20542600	-9.74859000
S	1.43947800	-2.25326500	-11.59786900
Fe	2.38944400	-0.18699400	-11.62610400
S	4.29325100	-0.44151200	-10.48978600
Fe	2.75367100	0.18135500	-9.04421400
S	1.01431500	0.99582600	-10.17321600
O	4.60299600	-2.14699100	-15.16000000
C	3.18062700	-2.20002500	-14.97338000
C	2.58353200	-0.88617700	-14.51532100
C	3.28609500	-0.11386900	-13.50404300
C	2.75348600	1.19764200	-13.16805400
C	1.37388000	-0.45838600	-14.98388600
N	0.81258400	0.72433900	-14.49040300
C	1.46777200	1.52406400	-13.60713900
H	4.45140300	-3.56122500	-7.51082100
H	5.96951000	-3.76421700	-8.41621700
H	5.68287800	-5.64558300	-6.76282600
H	-2.62821600	-0.21403400	-10.70747500
H	-2.21265300	-1.72255800	-11.55918300
H	-4.06250400	-2.93429600	-10.33092500
H	2.35025700	4.26612800	-9.58796300

H	-0.12320600	4.60873100	-9.40360900
H	0.73756800	6.11970200	-8.99468800
H	-0.04010900	5.93459400	-10.59917200
H	1.30937100	3.01129000	-11.02099900
H	3.01065800	6.61881800	-10.21190600
H	2.80881300	1.88312600	-5.73022100
H	1.89770900	2.66780000	-7.04287200
H	2.97299000	4.39772800	-5.52236500
H	2.91382200	-2.98052500	-14.23284300
H	2.75103000	-2.49843000	-15.94423400
H	4.36665700	-0.25849900	-13.43869100
H	3.34752800	1.97939800	-12.68905500
H	0.76705000	-1.00356200	-15.70846700
H	0.97261100	2.45055700	-13.30951700
H	4.10235000	-6.05926600	-7.49344200
H	5.60184100	-6.28924200	-8.42934900
H	4.58157100	3.70456200	-5.88545800
H	3.64673800	4.49517500	-7.17768000
H	2.24381600	6.38836300	-11.81253200
H	3.66110400	5.40098400	-11.35132300
H	-4.47898700	-1.43214900	-9.46838900
H	-4.71358300	-1.53618100	-11.23927900
H	5.01107200	-2.31899200	-14.29155300
H	-0.15382900	0.94012500	-14.71912100

Table S24. Comparison of the B-factors of the ligand's ring atoms in the original structure as well as the structure with flipped ring atoms.

Atom number	Atom type	$B_{average}$ (IspH-10)	$B_{average}$ (ring flipped)
1	C	35,85	34,3
2	C	36,9	35,8
3	N	39,6	37
4	C	43,75	41,1
5	C	38,85	36,1
6	C	40,55	39,9

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