

Supporting Information

The Lactate Racemase Nickel-Pincer Cofactor Operates by a Proton-Coupled Hydride Transfer Mechanism

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Figure S1. Pyruvate analysis by LC-MS.

Table S1. Crystal statistics for the LarA structure.

Table S2. Absolute energies of reactants and transition states for large models

Table S3. Atomic coordinates for Model F, reactants

Table S4. Atomic coordinates for Model F, transition state

Table S5. Atomic coordinates for Model E, reactants

Table S6. Atomic coordinates for Model E, transition state

Table S7. Absolute energies of small models with and without bound hydride

Table S8. Atomic coordinates for Small Model, with protonated His200

Table S9. Atomic coordinates for Small Model, C4-bound hydride, with protonated His200

Table S10. Atomic coordinates for Small Model, with neutral His200

Table S11. Atomic coordinates for Small Model, C4-bound hydride, with neutral His200

Table S12. Atomic coordinates for Small Model, without His200

Table S13. Atomic coordinates for Small Model, C4-bound hydride, without His200

Table S14. Atomic coordinates for Small Model, Ni-bound hydride, without His200

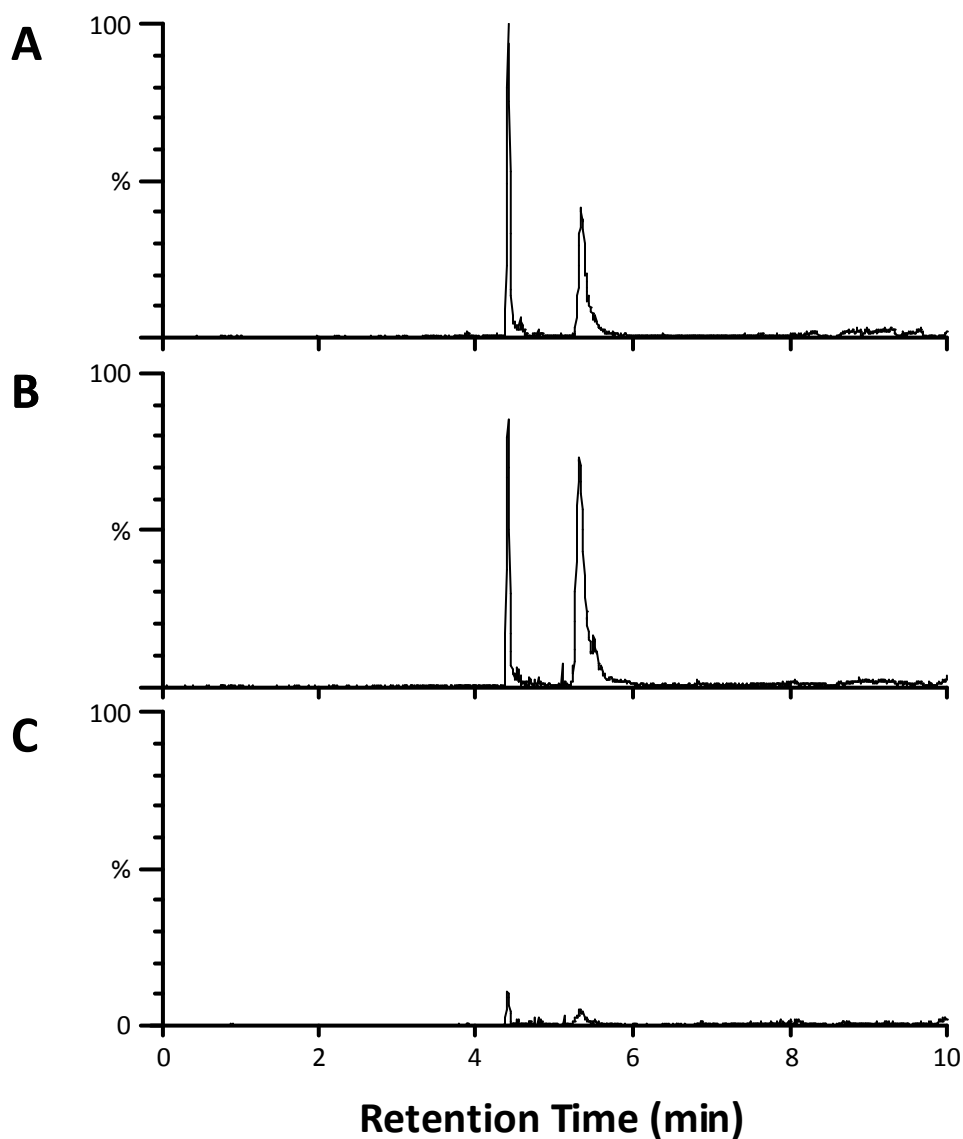


Figure S1. Analysis of DNPH-derivatized pyruvate by liquid chromatography-mass spectrometry. (A) LarA (4.4 mg/mL, 93 μ M) was incubated with sodium D-lactate, precipitated with perchloric acid, derivatized with DNPH, extracted into organic solvent, dried, dissolved in methanol, and analyzed by liquid chromatography-mass spectrometry. (B) A standard of 10 μ M sodium pyruvate was treated as in A. (C) Non-protein control. The profiles result from monitoring m/z of 267.04 ± 0.01 . The y-axes are on the same scale.

Table S1. Crystal statistics for the LarA structure.

Data collection	LarA
Beamline	GM/CA 23-ID-D
Wavelength (Å)	0.979
Space group	P2 ₁ 2 ₁ 2 ₁
Unit cell a, b, c (Å); α, β, γ (°)	69, 158, 159; 90, 90, 90
^a Resolution (Å)	40.00 – 2.40 (2.49 – 2.40)
Unique reflections	68,698 (6,669)
^a Redundancy	13.2 (11.3)
^a Completeness (%)	99.2 (97.7)
^a I/σI	17.3 (1.5)
^{a,b} R _{merge}	0.103 (-)
^{a,c} R _{pim}	0.043 (0.484)
^d CC _{1/2}	0.998 (0.797)
Data refinement	
Protein atoms	10,046
H ₂ O molecules	109
Ni atoms	3
SO ₄ molecules	16
SO ₃ molecules	1
4EY: P2TMN	2
ENJ: reduced P2TMN	1
^e R _{work} /R _{free}	0.206/0.263
B-factors (Å ²)	53.9
Protein atoms	53.9
H ₂ O molecules	48.3
Ni atoms	61.9
SO ₄ molecules	66.7
SO ₃ molecules	57.6
4EY: P2TMN	46.7
ENJ: reduced P2TMN	48.8
R.m.s. deviation in bond lengths (Å)	0.008
R.m.s. deviation in bond angles (°)	0.940
Ramachandran plot (%) favored	96.7
Ramachandran plot (%) outliers	0
Rotamer outliers	0
PDB ID	6C1W

^aHighest resolution shell is shown in parentheses.

^b $R_{merge} = \sum_{hkl} \sum_j |I_j(hkl) - \langle I(hkl) \rangle| / \sum_{hkl} \sum_j I_j(hkl)$, where I is the intensity of reflection.

^c $R_{pim} = \sum_{hkl} [1/(N-1)]^{1/2} \sum_j |I_j(hkl) - \langle I(hkl) \rangle| / \sum_{hkl} \sum_j I_j(hkl)$, where N is the redundancy of the dataset.

^dCC_{1/2} is the correlation coefficient of the half datasets.

^e $R_{work} = \sum_{hkl} ||F_{obs}| - |F_{calc}|| / \sum_{hkl} |F_{obs}|$, where F_{obs} and F_{calc} is the observed and the calculated structure factor, respectively. R_{free} is the cross-validation R factor for the test set of reflections (10% of the total) omitted in model refinement.

Table S2. Absolute energies of reactants and transition states for large models.

	Reactants (hartree)	Transition State (hartree)	Energy Barrier (kcal/mol)
Model F			
Yu & Chen, 97 atoms	-5164.699495	-5164.676233	14.6
Model E			
Zhang & Chung, 98 atoms	-5165.1764307	-5165.137388	24.5

Table S3. Atomic coordinates for Model F, reactants (Yu & Chen, 97 atoms)

(Optimized coordinates of the six capping H atoms are in blue; Cartesian coordinates in Å)

C	6.0	-43.11629868	26.19799995	-37.24240112
N	7.0	-42.87789917	25.43260002	-36.01480103
C	6.0	-41.71409988	24.90399933	-35.60549927
N	7.0	-40.68700027	24.68820000	-36.44010162
N	7.0	-41.57320023	24.59810066	-34.31079865
C	6.0	-46.30989838	22.51589966	-30.95219994
N	7.0	-46.11000061	23.30529976	-32.07350159
C	6.0	-45.05189896	22.11779976	-30.56240082
C	6.0	-44.77439880	23.35790062	-32.31159973
N	7.0	-44.09939957	22.64669991	-31.41950035
C	6.0	-38.80519867	18.96030045	-37.70690155
N	7.0	-39.92179871	19.46170044	-36.87799835
C	6.0	-38.04439926	15.02989960	-30.72739983
N	7.0	-37.98360062	14.61919975	-32.05099869
C	6.0	-38.76010132	16.20339966	-30.76379967
C	6.0	-38.63779831	15.52480030	-32.82059860
N	7.0	-39.12509918	16.49810028	-32.06790161
C	6.0	-42.18140030	27.05879974	-31.67709923
O	8.0	-43.01559830	27.96050072	-31.60330009
N	7.0	-42.49309921	25.74020004	-31.53300095
Ni	28.0	-40.34889984	17.91519928	-32.80699921
C	6.0	-42.42169952	20.23600006	-35.58259964
C	6.0	-41.39649963	19.56539917	-34.93270111
C	6.0	-43.04190063	18.87949944	-31.59659958
C	6.0	-41.58000183	19.08749962	-33.60770035
C	6.0	-42.78829956	19.42779922	-32.97560120

C	6.0	-43.78129959	20.10899925	-33.65290070
O	8.0	-44.06320190	19.09040070	-30.97410011
O	8.0	-41.36420059	23.75469971	-39.04479980
P	15.0	-41.78110123	22.33160019	-39.27280045
O	8.0	-41.81340027	22.02070045	-40.88859940
O	8.0	-41.04800034	21.15780067	-38.64540100
O	8.0	-43.35889816	22.22360039	-38.85400009
C	6.0	-44.14059830	21.06310081	-39.14250183
C	6.0	-45.22779846	20.91749954	-38.07910156
O	8.0	-44.73590088	20.12610054	-36.95859909
C	6.0	-45.69260025	22.25000000	-37.47560120
O	8.0	-47.04470062	22.10650063	-37.09469986
C	6.0	-44.75659943	22.36660004	-36.24319839
O	8.0	-45.12469864	23.25370026	-35.24309921
C	6.0	-44.76810074	20.89949989	-35.78279877
N	7.0	-43.60409927	20.46170044	-34.95520020
C	6.0	-40.15060043	19.14879990	-35.61989975
S	16.0	-39.07770157	18.18440056	-34.68140030
S	16.0	-41.73450089	17.79719925	-31.05540085
H	1.0	-43.31420135	27.24130058	-36.95930099
H	1.0	-42.21709824	26.18370056	-37.86270142
H	1.0	-43.66429901	25.43779945	-35.35580063
H	1.0	-39.76309967	24.50099945	-36.02000046
H	1.0	-40.86679840	24.44930077	-37.41999817
H	1.0	-42.19549942	24.97890091	-33.60789871
H	1.0	-40.87179947	23.90299988	-34.01490021
H	1.0	-44.76319885	21.48159981	-29.73920059
H	1.0	-46.84769821	23.71179962	-32.67190170
H	1.0	-44.36489868	23.90250015	-33.14559937
H	1.0	-39.06179810	16.84510040	-29.95009995
H	1.0	-37.51699829	13.79329967	-32.39260101
H	1.0	-38.73310089	15.45909977	-33.89319992
H	1.0	-43.42770004	25.50180054	-31.23030090
H	1.0	-41.76910019	25.01959991	-31.45159912
H	1.0	-38.33169937	18.13330078	-37.17250061
H	1.0	-38.07479858	19.76829910	-37.82659912
H	1.0	-42.37540054	20.55349922	-36.61800003
H	1.0	-44.73500061	20.33539963	-33.18880081
H	1.0	-43.51739883	20.16069984	-39.15549850
H	1.0	-44.60300064	21.18510056	-40.13079834
H	1.0	-46.08580017	20.38199997	-38.49840164
H	1.0	-45.54330063	23.08620071	-38.16590118
H	1.0	-47.34759903	22.97249985	-36.73509979
H	1.0	-43.74850082	22.61960030	-36.58909988
H	1.0	-46.06529999	23.54680061	-35.33440018
H	1.0	-45.66210175	20.71010017	-35.17890167

C	6.0	-40.50680161	21.40460014	-31.35009956
H	1.0	-40.45159912	20.54759979	-32.03200150
C	6.0	-39.43410110	21.24839973	-30.27669907
H	1.0	-39.64199829	20.34980011	-29.68580055
H	1.0	-38.44649887	21.14590073	-30.74139977
H	1.0	-39.43140030	22.12070084	-29.61660004
O	8.0	-41.78079987	21.40469933	-30.70439911
H	1.0	-42.48300171	21.95910072	-31.14889908
C	6.0	-40.27230072	22.67280006	-32.19820023
O	8.0	-40.43460083	23.79500008	-31.64539909
O	8.0	-39.93870163	22.49230003	-33.41159821
H	1.0	-40.51340103	20.14730072	-37.38479996
H	1.0	-41.84880066	22.86940002	-41.34999847
C	6.0	-38.21649933	25.47030067	-33.78519821
N	7.0	-38.14490128	24.41290092	-34.82220078
H	1.0	-39.24190140	25.44879913	-33.41790009
H	1.0	-38.06269836	26.44379997	-34.27299881
H	1.0	-37.19150162	24.30330086	-35.16310120
H	1.0	-38.43119812	23.53269958	-34.38399887
H	1.0	-47.29999924	22.31275940	-30.55195808
H	1.0	-39.19749069	18.65723419	-38.68603897
H	1.0	-41.10318375	27.23536682	-31.89751053
H	1.0	-43.95489883	25.77912140	-37.81644821
H	1.0	-37.51514816	25.35237694	-32.93946075
H	1.0	-37.58365631	14.47813320	-29.91346741

Table S4. Atomic coordinates for Model F, transition state (Yu & Chen, 97 atoms)
(Optimized coordinates of the six capping H atoms are in blue; Cartesian coordinates in Å)

C	6.0	1.69379997	-4.82189989	2.02200007
N	7.0	1.85630000	-3.49889994	1.40419996
C	6.0	1.57529998	-2.32620001	2.00799990
N	7.0	0.67009997	-2.23860002	2.98130012
N	7.0	2.27329993	-1.23979998	1.61790001
C	6.0	2.99950004	0.69749999	-4.25519991
N	7.0	3.03279996	-0.36170000	-3.35200000
C	6.0	2.33459997	1.71290004	-3.61800003
C	6.0	2.41770005	0.01190000	-2.21830010
N	7.0	1.98930001	1.26329994	-2.35700011
C	6.0	-5.54199982	-0.85140002	1.97280002
N	7.0	-4.30700016	-0.79030001	1.16659999
C	6.0	-6.10879993	6.28149986	-1.47959995
N	7.0	-7.00000000	5.22690010	-1.34480000
C	6.0	-4.86719990	5.70319986	-1.36269999
C	6.0	-6.29330015	4.08330011	-1.15190005
N	7.0	-4.99690008	4.34019995	-1.16050005

C	6.0	5.15670013	1.66460001	1.13520002
O	8.0	6.31629992	1.96290004	0.86420000
N	7.0	4.19910002	1.44430006	0.18009999
Ni	28.0	-3.61780000	2.87789989	-1.12070000
C	6.0	-2.19429994	-1.02470005	-0.82160002
C	6.0	-2.75300002	0.17850000	-0.45530000
C	6.0	-1.40129995	2.36940002	-3.25720000
C	6.0	-2.38549995	1.41700006	-1.13730001
C	6.0	-1.58449996	1.21870005	-2.32640004
C	6.0	-1.07190001	-0.00230000	-2.64720011
O	8.0	-0.61320001	2.36199999	-4.19199991
O	8.0	-1.33879995	-4.33979988	2.82209992
P	15.0	-2.37450004	-4.44880009	1.73660004
O	8.0	-3.24710011	-5.82900000	1.96179998
O	8.0	-3.38129997	-3.34500003	1.48370004
O	8.0	-1.58609998	-4.77099991	0.33610001
C	6.0	-2.33260012	-5.15819979	-0.82440001
C	6.0	-1.63259995	-4.65220022	-2.08080006
O	8.0	-2.04800010	-3.29279995	-2.36610007
C	6.0	-0.10270000	-4.61959982	-1.96770000
O	8.0	0.44769999	-4.86159992	-3.25020003
C	6.0	0.12870000	-3.16339993	-1.50259995
O	8.0	1.41470003	-2.64319992	-1.66059995
C	6.0	-0.91900003	-2.44320011	-2.36450005
N	7.0	-1.34230006	-1.11590004	-1.88859999
C	6.0	-3.87360001	0.26260000	0.49370000
S	16.0	-4.65089989	1.80250001	0.59119999
S	16.0	-2.54500008	3.69479990	-2.91100001
H	1.0	2.48530006	-4.97109985	2.77279997
H	1.0	0.73250002	-4.87029982	2.53290009
H	1.0	2.57890010	-3.43079996	0.68589997
H	1.0	0.56449997	-1.35660005	3.51740003
H	1.0	-0.04900000	-2.96230006	3.05839992
H	1.0	2.93339992	-1.39520001	0.86360002
H	1.0	1.81369996	-0.30689999	1.59270000
H	1.0	2.04089999	2.69400001	-3.95199990
H	1.0	3.40070009	-1.31750000	-3.54740000
H	1.0	2.25939989	-0.62599999	-1.36670005
H	1.0	-3.89150000	6.15859985	-1.43509996
H	1.0	-8.00510025	5.29489994	-1.36909997
H	1.0	-6.73159981	3.10990000	-0.99790001
H	1.0	4.42740011	1.79750001	-0.73900002
H	1.0	3.20830011	1.48010004	0.42919999
H	1.0	-6.16730022	-0.00060000	1.68939996
H	1.0	-5.27479982	-0.74910003	3.03119993
H	1.0	-2.44819999	-1.97060001	-0.35800001

H	1.0	-0.47909999	-0.14600000	-3.54290009
H	1.0	-3.34759998	-4.74690008	-0.79060000
H	1.0	-2.39540005	-6.25339985	-0.85079998
H	1.0	-1.92359996	-5.27540016	-2.93379998
H	1.0	0.26019999	-5.33860016	-1.22979999
H	1.0	1.42139995	-4.90780020	-3.14569998
H	1.0	-0.15790001	-3.08430004	-0.44980001
H	1.0	1.97950006	-3.23200011	-2.21219993
H	1.0	-0.51139998	-2.30029988	-3.37210011
C	6.0	-0.33730000	2.63229990	0.04070000
H	1.0	-1.42799997	2.06310010	-0.30010000
C	6.0	-0.89770001	3.92350006	0.63990003
H	1.0	-1.39040005	4.49119997	-0.15459999
H	1.0	-1.60850000	3.69970012	1.43830001
H	1.0	-0.07000000	4.52180004	1.04139996
O	8.0	0.40070000	2.78449988	-1.03919995
H	1.0	1.34949994	1.81659997	-1.66530001
C	6.0	0.15360001	1.60730004	1.09780002
O	8.0	1.37000000	1.23160005	1.00310004
O	8.0	-0.67769998	1.24230003	1.96010005
H	1.0	-3.77099991	-1.67180002	1.17439997
H	1.0	-2.75510001	-6.38719988	2.57850003
C	6.0	1.77470005	0.96410000	4.68830013
N	7.0	0.47040001	0.29429999	4.49139977
H	1.0	2.35019994	0.76249999	3.78270006
H	1.0	2.30150008	0.46849999	5.51630020
H	1.0	-0.12729999	0.41319999	5.30660009
H	1.0	-0.01050000	0.71929997	3.68670011
H	1.0	-6.43124962	7.30650663	-1.63937354
H	1.0	-6.03566217	-1.81588459	1.79686224
H	1.0	1.73565865	-5.59528923	1.24524355
H	1.0	1.72975600	2.05383945	4.87047529
H	1.0	4.79189444	1.50080466	2.17658162
H	1.0	3.43386054	0.63175339	-5.24846888

Table S5. Atomic coordinates for Model E, reactants (Zhang and Chung, 98 atoms)
(Proton removed in the 97-atom model is in red; Cartesian coordinates in Å)

C	6.0	-5.10467005	2.28796005	1.90693998
N	7.0	-4.86967993	0.95380002	2.40964007
C	6.0	-3.63591003	0.43564999	2.47043991
N	7.0	-2.55034995	1.21131003	2.39512992
N	7.0	-3.48211002	-0.87103999	2.72224998
H	1.0	-5.59921980	0.25295001	2.25123000
H	1.0	-2.53583002	-1.22481000	2.55634999
H	1.0	-4.24504995	-1.46424997	2.39138007

H	1.0	-4.57662010	3.03428006	2.51401997
H	1.0	-4.78761005	2.39178991	0.85759002
H	1.0	-1.70552003	0.68392998	2.14148998
H	1.0	-2.61698008	2.13677001	1.97469997
C	6.0	-4.07692003	-4.87506008	0.30689999
C	6.0	-3.15170002	-5.00840998	1.30449998
H	1.0	-4.46282005	-3.10309005	-0.88909000
H	1.0	-2.66160989	-1.97109997	0.42370999
C	6.0	-2.96679997	-3.00476003	0.57156003
N	7.0	-3.94983006	-3.58623004	-0.14514001
N	7.0	-2.46256995	-3.83166003	1.46783996
H	1.0	-2.93418002	-5.87903023	1.91090000
C	6.0	4.08700991	1.85037005	-1.79486001
N	7.0	2.78388000	1.27282000	-1.51324999
H	1.0	4.38662004	1.61335003	-2.82343006
H	1.0	4.84071016	1.44442999	-1.10604000
C	6.0	5.57305002	-5.17593002	0.62435001
C	6.0	4.30752993	-5.00620985	0.15166000
H	1.0	7.28329992	-3.94773006	0.22272000
H	1.0	5.87975979	-2.65590000	-1.37764001
C	6.0	5.52874994	-3.50766993	-0.81014001
N	7.0	6.33782005	-4.22318983	-0.01140000
N	7.0	4.28375006	-3.95245004	-0.74557000
H	1.0	3.41031003	-5.56271982	0.39014000
C	6.0	-0.79518002	0.40577000	5.06827021
H	1.0	-1.90058005	-1.14154005	5.77657986
O	8.0	0.01635000	0.87774998	4.27699995
N	7.0	-1.19263995	-0.86712998	5.11049986
H	1.0	-0.89963001	-1.56770003	4.40697002
C	6.0	2.02312994	2.35291004	2.55541992
N	7.0	0.80146003	1.88463998	1.86738002
H	1.0	1.74766004	3.08357000	3.32116008
H	1.0	2.70401001	2.81633997	1.83536994
H	1.0	0.99900001	0.96437001	1.38720000
H	1.0	0.10979000	1.65307999	2.59389997
Ni	28.0	2.67079997	-3.00019002	-1.26859999
P	15.0	0.38598999	4.23181009	-1.35397995
O	8.0	1.23927999	3.33085990	-0.47275999
O	8.0	-0.35135001	5.33212996	-0.39837000
O	8.0	0.96291000	4.89410019	-2.55676007
C	6.0	-0.20764001	-4.04089022	-1.36546004
C	6.0	-2.30972004	0.29776001	-2.36299992
N	7.0	-1.09341002	-0.49019000	-2.07115006
C	6.0	0.09218000	0.14148000	-1.88274002
C	6.0	-2.83316994	0.98711002	-1.09886003
O	8.0	-1.22841001	-4.67097998	-1.51769996

O	8.0	-3.56510997	0.15764999	-0.26223001
S	16.0	1.39549994	-4.74441004	-1.04493999
C	6.0	1.19981003	-0.58052999	-1.50143003
C	6.0	-3.59105992	2.16560006	-1.71750998
O	8.0	-4.85356998	1.78217995	-2.18364000
C	6.0	1.14602995	-1.98495996	-1.32042003
C	6.0	-2.73987007	2.50144005	-2.94187999
O	8.0	-2.01964998	1.29895997	-3.27852011
C	6.0	-0.12367000	-2.55741000	-1.46376002
C	6.0	-1.74970996	3.62467003	-2.77039003
O	8.0	-0.88817000	3.28538990	-1.69600999
C	6.0	-1.20518005	-1.82626998	-1.89482999
C	6.0	2.55176997	-0.02143000	-1.55736995
S	16.0	3.79064989	-1.16185999	-1.80145001
H	1.0	2.03365993	1.93370998	-1.24854004
H	1.0	0.08179000	1.21278000	-2.07856989
H	1.0	-2.17290998	-2.28127003	-2.11016011
H	1.0	-1.97412002	1.37839997	-0.52458000
H	1.0	-4.08384991	-0.50138003	-0.79799998
H	1.0	-3.64292002	3.02182007	-1.01675999
H	1.0	-5.34329987	1.28445995	-1.49658000
H	1.0	-3.41421008	2.74334002	-3.77558994
H	1.0	-1.16313004	3.76080990	-3.68888998
H	1.0	-2.28238010	4.56518984	-2.55326009
H	1.0	0.63650000	-3.34347010	1.61369002
C	6.0	0.55707002	-2.60483003	2.43649006
C	6.0	0.40335000	-1.23622000	1.76564002
C	6.0	1.80844998	-2.67685008	3.28781009
H	1.0	1.82886004	-1.85371995	4.01742983
H	1.0	1.82923996	-3.62786007	3.83092999
H	1.0	2.70777988	-2.60501003	2.66593003
O	8.0	1.46381998	-0.65783000	1.37193000
O	8.0	-0.75002003	-0.76915002	1.61192000
H	1.0	-3.05307007	-0.41813001	-2.74951005
O	8.0	-0.55172998	-2.91637993	3.24592996
H	1.0	-1.26620996	-3.28245997	2.65794992
H	1.0	5.99160004	-5.87751007	1.33103001
H	1.0	4.02461004	2.93436003	-1.66942000
H	1.0	-4.78599024	-5.56903982	-0.12307000
H	1.0	-6.17406988	2.50209999	1.96991003
H	1.0	-1.26501000	1.03433001	5.85305977
H	1.0	0.44830999	2.56851006	1.18060005
H	1.0	2.48951006	1.49120998	3.04227996
H	1.0	0.06787000	6.21586990	-0.51683003

Table S6. Atomic coordinates for Model E, transition state (Zhang and Chung, 98 atoms)
(Proton removed in the 97-atom model is in red; Cartesian coordinates in Å)

C	6.0	-5.03569984	2.42569995	1.75000000
N	7.0	-4.80810022	1.13999999	2.37369990
C	6.0	-3.58769989	0.59410000	2.42580009
N	7.0	-2.48530006	1.31630003	2.21790004
N	7.0	-3.46149993	-0.69260001	2.78979993
H	1.0	-5.56489992	0.45400000	2.33570004
H	1.0	-2.53349996	-1.09280002	2.64129996
H	1.0	-4.26119995	-1.28110003	2.55229998
H	1.0	-4.56409979	3.23300004	2.32500005
H	1.0	-4.65010023	2.45040011	0.72000003
H	1.0	-1.68379998	0.73060000	1.91740000
H	1.0	-2.56200004	2.22959995	1.77010000
C	6.0	-4.00540018	-4.75209999	0.28940001
C	6.0	-2.87220001	-4.94630003	1.01760006
H	1.0	-4.69780016	-2.89809990	-0.64719999
H	1.0	-2.69970012	-1.77559996	0.35980001
C	6.0	-2.95600009	-2.82660007	0.46910000
N	7.0	-4.03919983	-3.41510010	-0.03670000
N	7.0	-2.24320006	-3.72979999	1.12580001
H	1.0	-2.44729996	-5.84740019	1.43429995
C	6.0	4.10550022	1.62189996	-1.32690001
N	7.0	2.80159998	0.99860001	-1.20260000
H	1.0	4.48579979	1.50759995	-2.34949994
H	1.0	4.82420015	1.17830002	-0.62610000
C	6.0	5.77650023	-5.85680008	-0.19340000
C	6.0	4.50369978	-5.38219976	-0.09460000
H	1.0	7.33010006	-5.19169998	-1.50250006
H	1.0	5.67320013	-3.49349999	-2.41650009
C	6.0	5.46920013	-4.21850014	-1.63839996
N	7.0	6.37580013	-5.10780001	-1.18130004
N	7.0	4.32359982	-4.35790014	-0.99949998
H	1.0	3.69610000	-5.70830011	0.54790002
C	6.0	-0.65120000	-0.80500001	4.92780018
H	1.0	-1.19089997	-2.75040007	5.14720011
O	8.0	-0.11410000	0.10400000	4.31169987
N	7.0	-0.78969997	-2.07540011	4.51189995
H	1.0	-0.40669999	-2.43319988	3.62150002
C	6.0	1.46120000	2.84319997	3.20869994
N	7.0	0.34450001	2.20359993	2.48460007
H	1.0	1.06789994	3.51329994	3.97869992
H	1.0	2.08049989	3.40820003	2.50449991
H	1.0	0.71980000	1.43910003	1.84749997
H	1.0	-0.25729999	1.70299995	3.15389991
Ni	28.0	2.71700001	-3.31640005	-1.17739999

P	15.0	0.56389999	3.90140009	-1.25430000
O	8.0	1.23199999	3.12870002	-0.13740000
O	8.0	-0.25950000	5.16200018	-0.59549999
O	8.0	1.32379997	4.36870003	-2.44950008
C	6.0	-0.17039999	-4.35139990	-1.43439996
C	6.0	-2.22040009	0.04040000	-2.31940007
N	7.0	-1.03470004	-0.76069999	-2.00640011
C	6.0	0.15629999	-0.14530000	-1.74720001
C	6.0	-2.74440002	0.81489998	-1.10539997
O	8.0	-1.20969999	-4.97370005	-1.55359995
O	8.0	-3.56389999	0.06240000	-0.26560000
S	16.0	1.43400002	-5.08169985	-1.19330001
C	6.0	1.24810004	-0.86379999	-1.34979999
C	6.0	-3.41820002	2.01789999	-1.76740003
O	8.0	-4.70440006	1.70529997	-2.23009992
C	6.0	1.17270005	-2.28870010	-1.08770001
C	6.0	-2.53360009	2.25139999	-2.98970008
O	8.0	-1.91030002	0.99260002	-3.28889990
C	6.0	-0.08470000	-2.87459993	-1.47319996
C	6.0	-1.46440005	3.29909992	-2.81019998
O	8.0	-0.70520002	2.96490002	-1.65859997
C	6.0	-1.13150001	-2.12549996	-1.90380001
C	6.0	2.58540010	-0.29760000	-1.31169999
S	16.0	3.85870004	-1.43760002	-1.45140004
H	1.0	2.04060006	1.61220002	-0.87660003
H	1.0	0.17470001	0.92220002	-1.96000004
H	1.0	-2.06949997	-2.57319999	-2.23300004
H	1.0	-1.88520002	1.16219997	-0.50989997
H	1.0	-4.17679977	-0.49880001	-0.80739999
H	1.0	-3.41890001	2.89930010	-1.09599996
H	1.0	-5.25150013	1.34510005	-1.50390005
H	1.0	-3.17160010	2.53099990	-3.84030008
H	1.0	-0.81129998	3.33010006	-3.69300008
H	1.0	-1.93099999	4.29050016	-2.68280005
H	1.0	1.20340002	-2.45709991	0.30239999
C	6.0	0.98720002	-2.35770011	1.62479997
C	6.0	0.48220000	-0.91399997	1.54040003
C	6.0	2.40949988	-2.52370000	2.12310004
H	1.0	2.50600004	-2.08509994	3.12910008
H	1.0	2.62980008	-3.59549999	2.18359995
H	1.0	3.13930011	-2.04530001	1.46399999
O	8.0	1.35870004	-0.01270000	1.41359997
O	8.0	-0.76340002	-0.73310000	1.53989995
H	1.0	-2.98939991	-0.66860002	-2.67479992
O	8.0	0.15680000	-3.26270008	2.03649998
H	1.0	-1.26230001	-3.50799990	1.51040006

H	1.0	6.30019999	-6.64099979	0.33350000
H	1.0	3.99620008	2.68680000	-1.09790003
H	1.0	-4.76660013	-5.44360018	-0.04000000
H	1.0	-6.11159992	2.61030006	1.72049999
H	1.0	-1.09870005	-0.63990003	5.93139982
H	1.0	-0.20230000	2.86120009	1.90910006
H	1.0	2.04690003	2.05010009	3.68390012
H	1.0	0.11770000	6.02019978	-0.90149999

Table S7. Absolute energies of small models with and without bound hydride.

	Without bound hydride (hartree)	With bound hydride (hartree)
With His200		
34 atoms (protonated)	-3062.357911	-3063.092378
33 atoms	-3061.886510	-3062.592511
Without His200		
22 atoms (C4 bound)	-2797.110990	-2797.868924
22 atoms (Ni bound)	-2797.110990	-2797.855468

Table S8. Atomic coordinates for Small Model, with protonated His200
(Cartesian coordinates in Å)

C	6.0	-5.02164268	1.26245797	0.04452525
C	6.0	-3.63308215	1.33484483	0.09442662
C	6.0	-2.84809232	0.15021871	0.11858220
C	6.0	-3.56259584	-1.06436384	0.10122802
C	6.0	-4.94240952	-1.09072304	0.05016986
C	6.0	-2.86928391	2.59612513	0.11131589
N	7.0	-5.65587997	0.06686871	0.02113523
N	7.0	-3.46885967	3.78003383	0.13110240
S	16.0	-1.17534113	2.44853473	0.08201925
S	16.0	-1.02840221	-2.01734400	0.24993746
Ni	28.0	-0.99332792	0.19297892	0.16664065
N	7.0	0.96380597	0.23661913	0.21098191
N	7.0	3.03108907	0.65891057	0.80483031
C	6.0	1.72818220	0.90455770	1.06487095
C	6.0	1.81693387	-0.45987388	-0.62553561
C	6.0	3.12202358	-0.20673840	-0.27017024
C	6.0	4.42148924	-0.68414968	-0.82967854
H	1.0	-5.67822790	2.13462710	0.02302642
H	1.0	-5.50581694	-2.02715588	0.03895659
H	1.0	-2.91691232	4.63683224	0.15369463
H	1.0	-4.47707462	3.88324022	0.21732770
H	1.0	1.38306844	1.55291903	1.86882806
H	1.0	1.44187808	-1.10070908	-1.42089128
H	1.0	4.23981905	-1.37695587	-1.66645801
H	1.0	5.02069187	-1.21794856	-0.06891286
H	1.0	5.03178596	0.15636815	-1.20938766

C	6.0	-2.76788712	-2.33801103	0.15006961
O	8.0	-3.28262258	-3.43800831	0.13122676
C	6.0	-7.12842846	0.00467316	-0.07733910
H	1.0	-7.55169582	0.97482252	0.21597362
H	1.0	-7.50027180	-0.77703410	0.60079706
H	1.0	-7.41962814	-0.22720528	-1.11454248
H	1.0	3.81318378	1.04898679	1.32480383

Table S9. Atomic coordinates for Small Model, C4-bound hydride, with protonated His200
(Cartesian coordinates in Å)

C	6.0	-4.99281263	1.26820385	0.06257334
C	6.0	-3.67698193	1.35935557	0.44722167
C	6.0	-2.89954209	0.13786003	0.87543869
C	6.0	-3.59833717	-1.10699272	0.43547273
C	6.0	-4.89508104	-1.10970473	0.04879747
C	6.0	-2.93318868	2.58481073	0.37726897
N	7.0	-5.64049149	0.07083896	-0.05104096
N	7.0	-3.50604606	3.80312705	0.36861768
S	16.0	-1.22476280	2.43165374	0.30038905
S	16.0	-1.06055844	-2.02767038	0.44737604
Ni	28.0	-1.00762904	0.19613077	0.48048437
N	7.0	0.96904236	0.25156698	0.29747015
N	7.0	3.08685136	0.76890576	0.58993918
C	6.0	1.81069350	1.01570225	0.97551948
C	6.0	1.73833430	-0.51293719	-0.55663341
C	6.0	3.07056260	-0.20719016	-0.39113075
C	6.0	4.30185270	-0.74163818	-1.04659617
H	1.0	-5.57731152	2.13658214	-0.25751719
H	1.0	-5.40389442	-2.02619863	-0.26157182
H	1.0	-2.93564725	4.63533878	0.25058901
H	1.0	-4.50063038	3.92786860	0.52767283
H	1.0	1.53750837	1.74465632	1.73709810
H	1.0	1.28638422	-1.24329495	-1.22514987
H	1.0	4.02415705	-1.48871207	-1.80773771
H	1.0	4.97295332	-1.23554552	-0.31861153
H	1.0	4.88164711	0.05469655	-1.54952133
C	6.0	-2.80576730	-2.36261392	0.37402949
O	8.0	-3.28747463	-3.48304534	0.26557401
C	6.0	-7.00978136	0.00033513	-0.54820418
H	1.0	-7.49875832	0.97775048	-0.41888875
H	1.0	-7.57884026	-0.75035214	0.02534160
H	1.0	-7.03844690	-0.27680874	-1.61939251
H	1.0	-2.79174685	0.13754381	1.98505902
H	1.0	3.91485834	1.22400320	0.96346062

Table S10. Atomic coordinates for Small Model, with neutral His200
(Cartesian coordinates in Å)

C	6.0	-5.01739645	1.25951874	0.08076264
C	6.0	-3.63023162	1.32524955	0.14904177
C	6.0	-2.84353065	0.13765945	0.12877284
C	6.0	-3.56638169	-1.07374406	0.05826504
C	6.0	-4.94421339	-1.09382987	-0.00399089
C	6.0	-2.86224651	2.58081937	0.22580189
N	7.0	-5.65614367	0.06732809	0.00422608
N	7.0	-3.45863795	3.76860070	0.30345246
S	16.0	-1.17209160	2.42816210	0.19348581
S	16.0	-1.04037035	-2.04662013	0.15358265
Ni	28.0	-0.98683369	0.17068580	0.16395622
N	7.0	0.93607175	0.22752090	0.16430886
N	7.0	3.04104733	0.88397861	0.65549785
C	6.0	1.74232173	1.08086467	0.85301262
C	6.0	1.81338036	-0.57771349	-0.53212702
C	6.0	3.10284948	-0.16894105	-0.22800498
C	6.0	4.40717697	-0.72760206	-0.71836877
H	1.0	-5.67005110	2.13505650	0.07383191
H	1.0	-5.50952339	-2.02751350	-0.06301605
H	1.0	-2.89946795	4.61758757	0.36580858
H	1.0	-4.46524525	3.87357521	0.39581773
H	1.0	1.34023356	1.85219610	1.51605153
H	1.0	1.46584451	-1.37982631	-1.18348622
H	1.0	4.24348307	-1.56865573	-1.41497850
H	1.0	5.02941895	-1.09881723	0.11953678
H	1.0	5.01052141	0.03718104	-1.24535418
C	6.0	-2.77750850	-2.35202479	0.05662921
O	8.0	-3.30586267	-3.44853163	0.00016428
C	6.0	-7.12504148	0.01224082	-0.11348087
H	1.0	-7.54789495	0.98346448	0.17766055
H	1.0	-7.51206303	-0.76903331	0.55758291
H	1.0	-7.40757275	-0.21571629	-1.15417266

Table S11. Atomic coordinates for Small Model, C4-bound hydride, with neutral His200
(Cartesian coordinates in Å)

C	6.0	-4.99320459	1.26974964	0.07546287
C	6.0	-3.67731786	1.35305429	0.45692226
C	6.0	-2.89809966	0.12932499	0.87652296
C	6.0	-3.60710216	-1.11303437	0.44595268
C	6.0	-4.90512371	-1.11216176	0.06388973
C	6.0	-2.92548203	2.57431149	0.37280968

N	7.0	-5.64937830	0.07256424	-0.03240051
N	7.0	-3.50073743	3.79720950	0.35976273
S	16.0	-1.22363901	2.41411424	0.26919046
S	16.0	-1.07540131	-2.04816389	0.42641422
Ni	28.0	-1.00197852	0.17981245	0.44983685
N	7.0	0.94906056	0.24098280	0.24949230
N	7.0	3.10861659	0.85425085	0.55770892
C	6.0	1.82925296	1.05055928	0.88760507
C	6.0	1.74093318	-0.53547716	-0.56277531
C	6.0	3.06540799	-0.16027305	-0.36775327
C	6.0	4.30303907	-0.71891111	-1.01050556
H	1.0	-5.57039928	2.14075422	-0.25136921
H	1.0	-5.41699123	-2.02627945	-0.24896930
H	1.0	-2.91457963	4.62376547	0.28858238
H	1.0	-4.46898460	3.93016958	0.63430482
H	1.0	1.50050473	1.80088079	1.61339223
H	1.0	1.31642830	-1.30878997	-1.20445073
H	1.0	4.04595423	-1.47057104	-1.77886927
H	1.0	4.96868944	-1.21253216	-0.27348459
H	1.0	4.90676260	0.07114352	-1.49972939
C	6.0	-2.81812859	-2.37309790	0.38152146
O	8.0	-3.31450605	-3.49221730	0.28586119
C	6.0	-7.00605965	0.00853396	-0.55697638
H	1.0	-7.49960947	0.98345882	-0.42321351
H	1.0	-7.58728123	-0.75112486	-0.00730012
H	1.0	-7.01725674	-0.25200263	-1.63367379
H	1.0	-2.78469992	0.12894349	1.98635101

Table S12. Atomic coordinates for Small Model, without His200
(Cartesian coordinates in Å)

C	6.0	-5.03875923	1.28004694	0.06164420
C	6.0	-3.65107298	1.35634363	0.13805978
C	6.0	-2.87816334	0.16858120	0.07998190
C	6.0	-3.57820582	-1.04765177	-0.00803390
C	6.0	-4.95970726	-1.07004333	-0.05929429
C	6.0	-2.88356543	2.61197972	0.25803265
N	7.0	-5.67053795	0.08662982	-0.03433969
N	7.0	-3.47803736	3.78599477	0.40202484
S	16.0	-1.18885052	2.47540092	0.20742095
S	16.0	-1.02941763	-1.97559905	-0.03672492
Ni	28.0	-1.06903768	0.21532919	0.08698808
H	1.0	-5.69314957	2.15388989	0.06386662
H	1.0	-5.51893520	-2.00662661	-0.12805378
H	1.0	-2.92495608	4.63925791	0.48432583
H	1.0	-4.48647833	3.88674068	0.49407846

C	6.0	-2.77282906	-2.31190109	-0.06067912
O	8.0	-3.27386260	-3.41304421	-0.11728145
C	6.0	-7.14896917	0.04022636	-0.06379498
H	1.0	-7.52721548	0.92446721	-0.59540671
H	1.0	-7.53474855	0.02614772	0.96872348
H	1.0	-7.46541882	-0.86868203	-0.59295148

Table S13. Atomic coordinates for Small Model, C4-bound hydride, without His200
(Cartesian coordinates in Å)

C	6.0	-5.02265692	1.27903903	0.14739178
C	6.0	-3.66715050	1.36408556	0.36348552
C	6.0	-2.84824514	0.13317354	0.62470222
C	6.0	-3.59669948	-1.10251629	0.26397216
C	6.0	-4.93665218	-1.09249735	0.06500594
C	6.0	-2.93158150	2.59487200	0.20401748
N	7.0	-5.68047428	0.08633146	0.08056977
N	7.0	-3.49960947	3.80439806	0.32817432
S	16.0	-1.26517904	2.45533776	-0.17408487
S	16.0	-1.11462474	-1.99356127	-0.35715431
Ni	28.0	-1.19372690	0.20961958	-0.26296988
H	1.0	-5.63819599	2.15837264	-0.06355927
H	1.0	-5.48536825	-2.00430274	-0.18454157
H	1.0	-2.96049428	4.64606667	0.14310610
H	1.0	-4.44141150	3.92082381	0.69150841
C	6.0	-2.82070470	-2.34748650	0.01187743
O	8.0	-3.30520153	-3.46856976	0.01487629
C	6.0	-7.10716581	0.01698768	-0.22817343
H	1.0	-7.55413580	1.01752472	-0.13249636
H	1.0	-7.61241007	-0.66250253	0.47886866
H	1.0	-7.26968718	-0.35343018	-1.25685775
H	1.0	-2.44679451	0.09951234	1.65994978

Table S14. Atomic coordinates for Small Model, Ni-bound hydride, without His200
(Cartesian coordinates in Å)

C	6.0	-5.08287048	1.27360320	0.06910531
C	6.0	-3.70037103	1.34125495	0.18740545
C	6.0	-2.91692781	0.15219431	0.20848072
C	6.0	-3.62569571	-1.06341672	0.09902857
C	6.0	-4.99883413	-1.08816481	-0.01933601
C	6.0	-2.91811538	2.58490348	0.30622843
N	7.0	-5.71355295	0.07585140	-0.03072651
N	7.0	-3.50172615	3.78462291	0.30954760
S	16.0	-1.22745860	2.40615797	0.43732551
S	16.0	-1.07220078	-2.00372887	0.29726088

Ni	28.0	-1.06647909	0.18798235	0.37627625
H	1.0	-5.74316931	2.14395452	0.05143414
H	1.0	-5.56580591	-2.01886916	-0.10693531
H	1.0	-2.93908429	4.62878466	0.39435938
H	1.0	-4.50996780	3.89868093	0.26193190
C	6.0	-2.81158209	-2.32995248	0.12220592
O	8.0	-3.31917930	-3.43472195	0.02934098
C	6.0	-7.17702341	0.01794624	-0.18769833
H	1.0	-7.60961199	0.98802537	0.09377658
H	1.0	-7.58316183	-0.76351422	0.47222576
H	1.0	-7.43561649	-0.20864944	-1.23526061
H	1.0	0.47384486	0.22233823	0.52560937