Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Copper/Ruthenium Relay Catalysis for Stereodivergent Construction of 1,4-Nonadjacent Stereocenters: Mechanistic Investigation Using DFT Calculations

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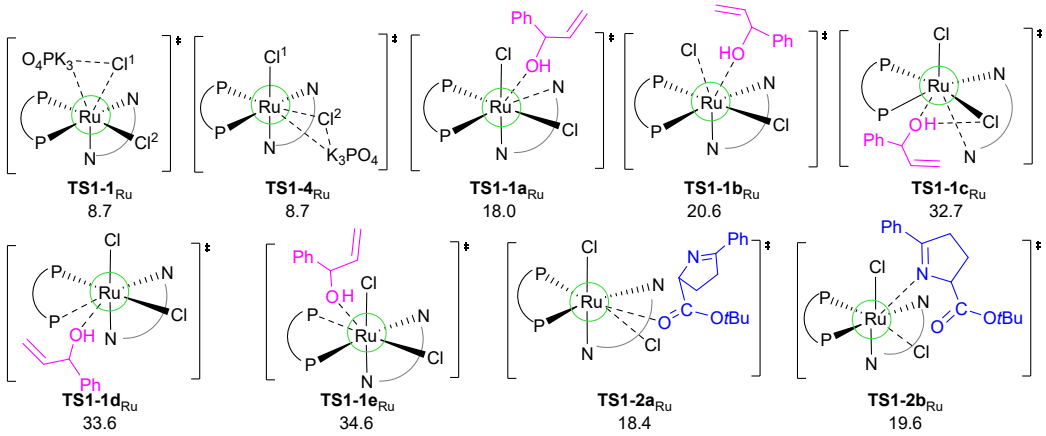
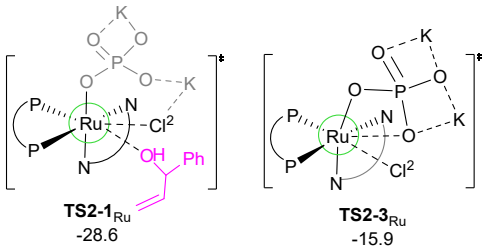
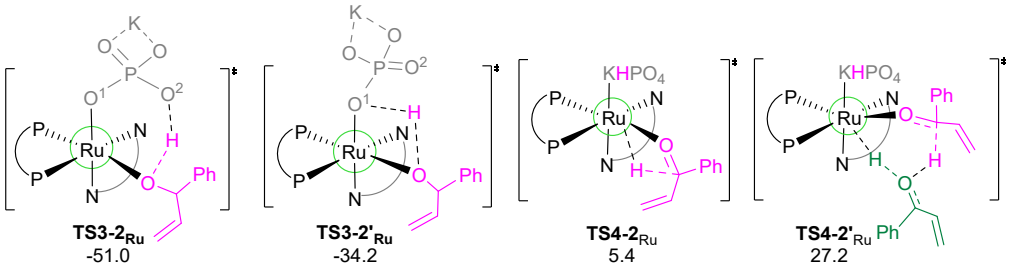
Section 1. Other Possible Isomers



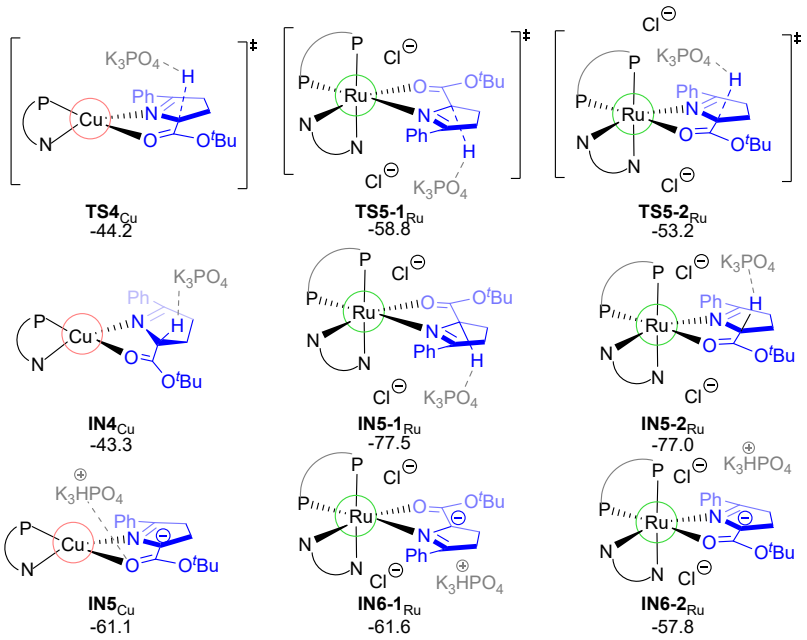
Scheme S1 Other possible isomers of transition states **TS1-1$_{Ru}$** and **TS1-2$_{Ru}$**. Values shown are relative free energies in kcal/mol.



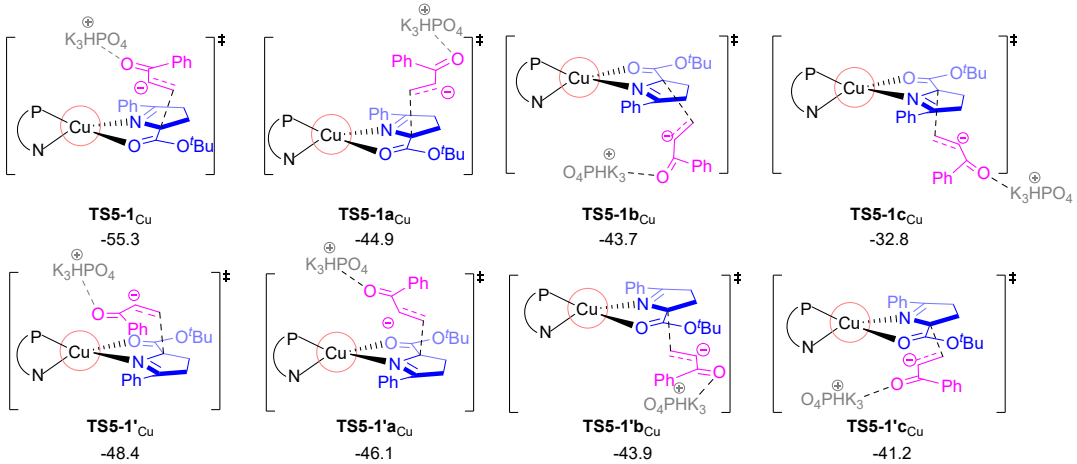
Scheme S2 Other possible isomers of transition states **TS2-1$_{Ru}$**. Values shown are relative free energies in kcal/mol.



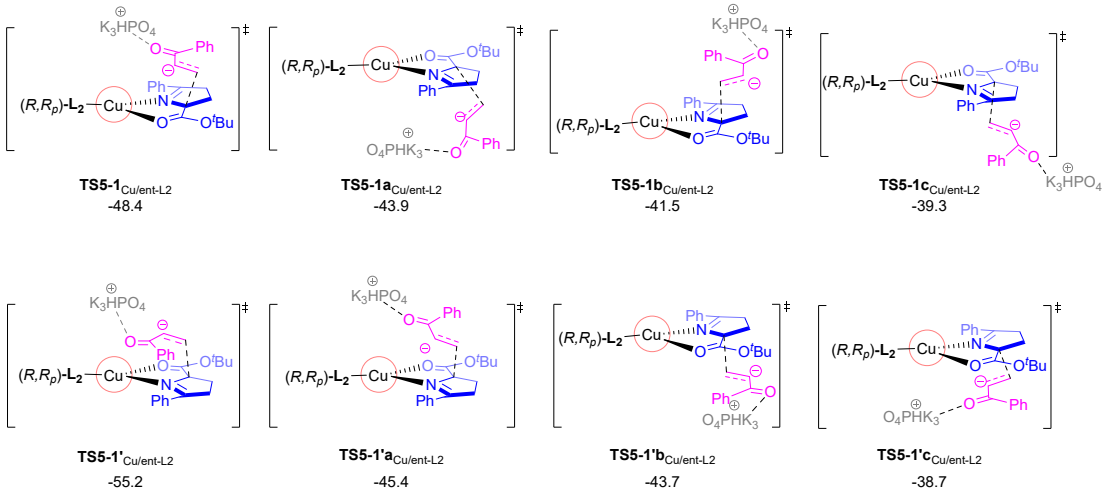
Scheme S3 Other possible isomers of transition states **TS3-2$_{Ru}$** and **TS4-2$_{Ru}$**. Values shown are relative free energies in kcal/mol.



Scheme S4 Other possible isomers of transition state $\mathbf{TS4_{Cu}}$ and their corresponding intermediates. Values shown are relative free energies in kcal/mol.



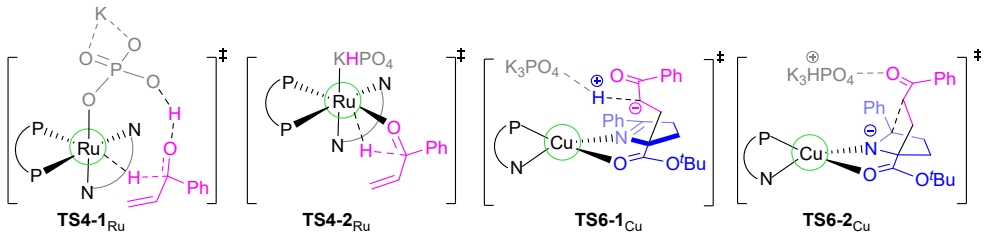
Scheme S5 Other possible isomers of transition states $\mathbf{TS5\text{-}1_{Cu}}$ and $\mathbf{TS5\text{-}1'_{Cu}}$. Values shown are relative free energies in kcal/mol.



Scheme S6 Other possible isomers of transition states **TS5-1$_{Cu/ent-L2}$** and **TS5-1'$_{Cu/ent-L2}$**. Values shown are relative free energies in kcal/mol.

Section 2. Optimization with BP86 and M06L Methods

Table S1. Relative Gibbs energies (in kcal/mol) for the important transition states with BP86 and M06L methods.



Species	ΔΔ*G*(B3LYP)	ΔΔ*G*(BP86)	ΔΔ*G*(M06L)
TS4-1$_{Ru}$	0.0	0.0	0.0
TS4-2$_{Ru}$	36.3	32.3	17.3
TS6-1$_{Cu}$	0.0	0.0	0.0
TS6-2$_{Cu}$	4.6	4.3	7.7

Section 3. Alternative Pathways for Stage I

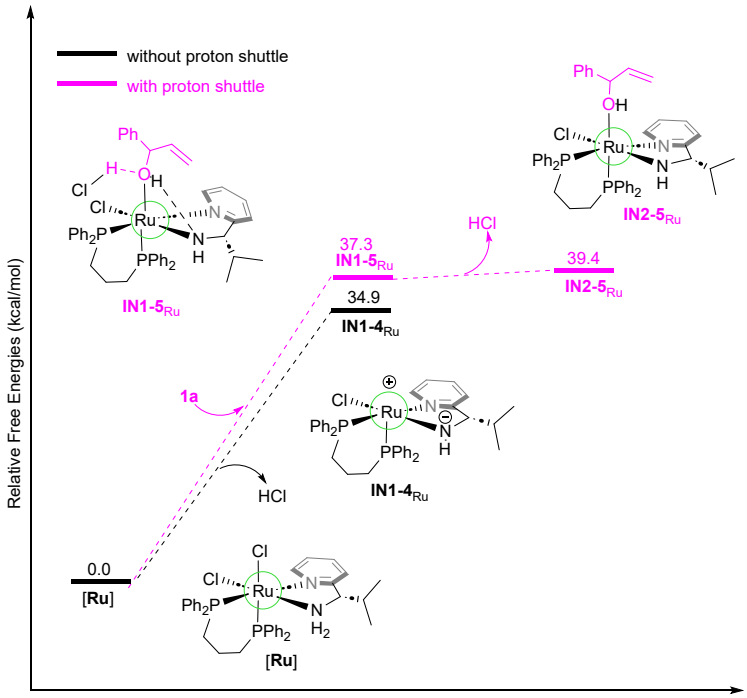


Fig. S1 Calculated energy profiles for the HCl elimination process with and without proton shuttle in Stage I. Values shown are relative free energies in kcal/mol.

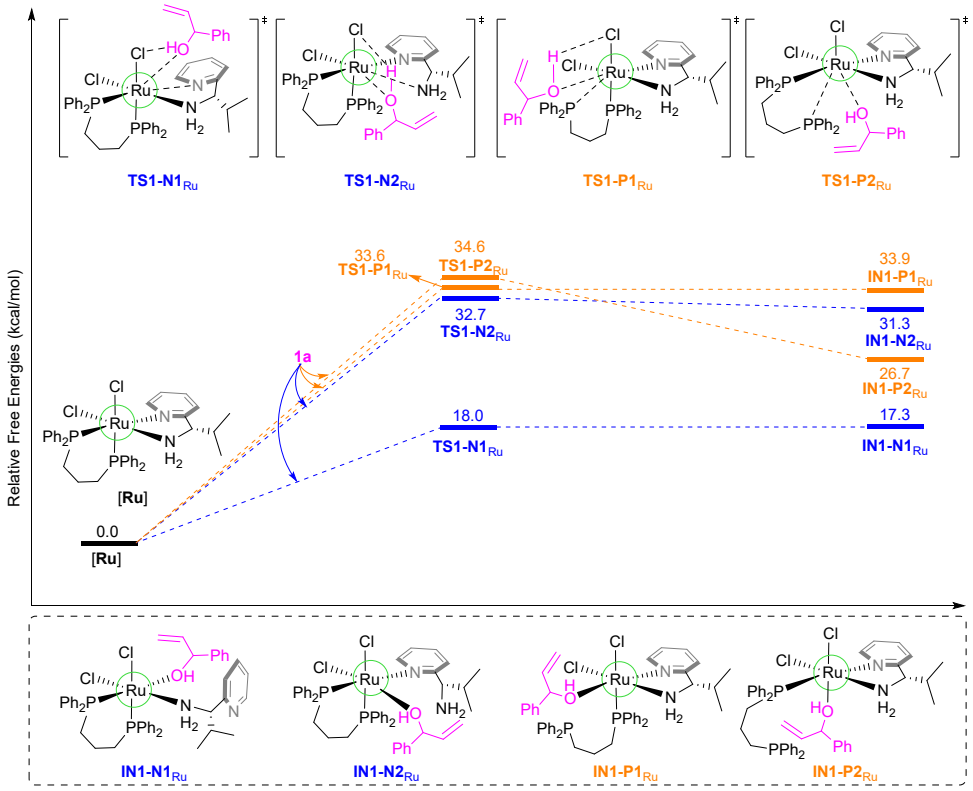


Fig. S2 Calculated energy profiles for the partial decoordination of the bidentate

ligand. Values shown are relative free energies in kcal/mol.

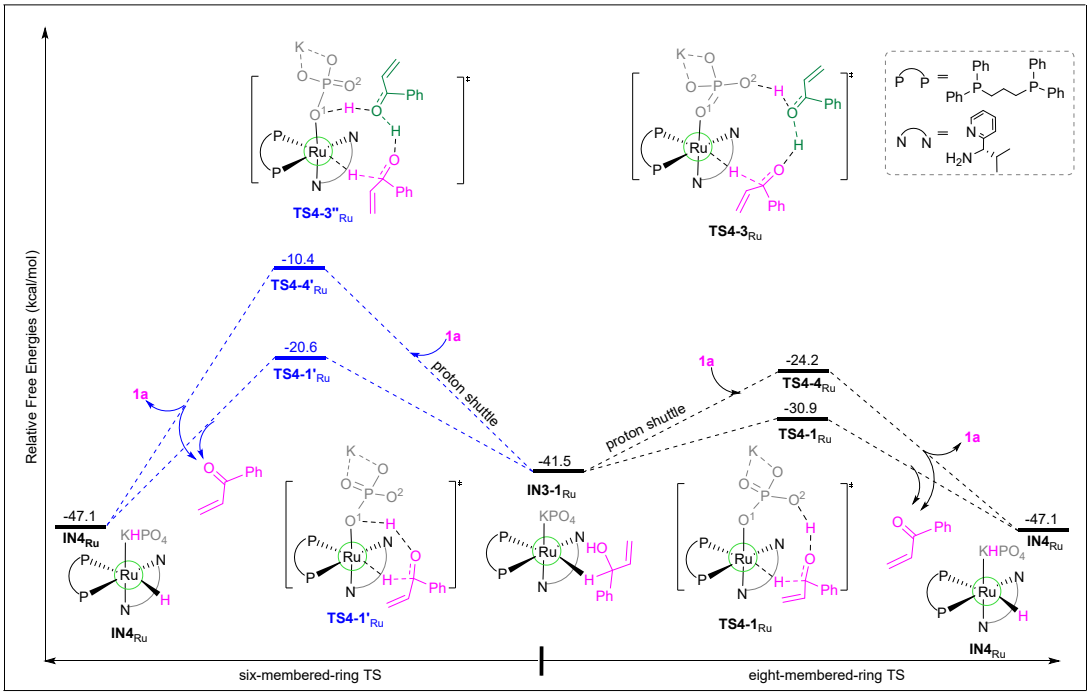


Fig. S3 Calculated energy profiles for the BDHT of **1a** using a proton shuttle mechanism. Values shown are relative free energies in kcal/mol.

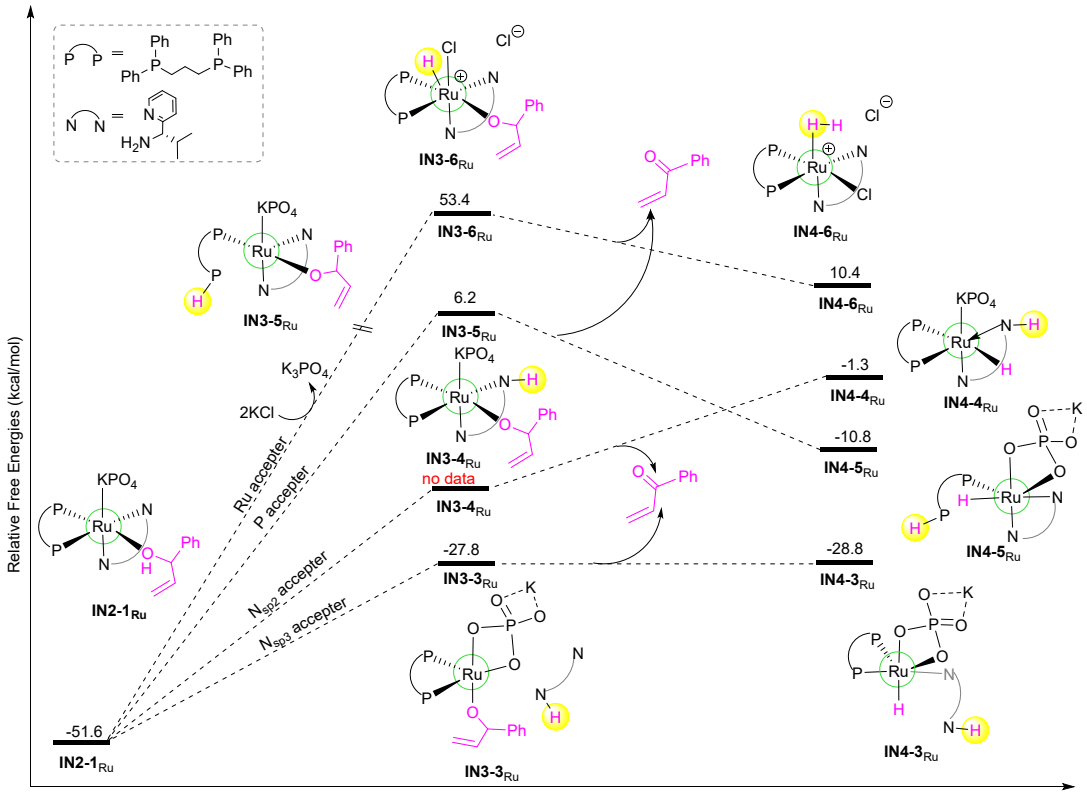


Fig. S4 Calculated energy profiles for the other possible alcohol-dehydrogenation

processes. Values shown are relative free energies in kcal/mol.

Section 4. Alternative pathways for Stage II

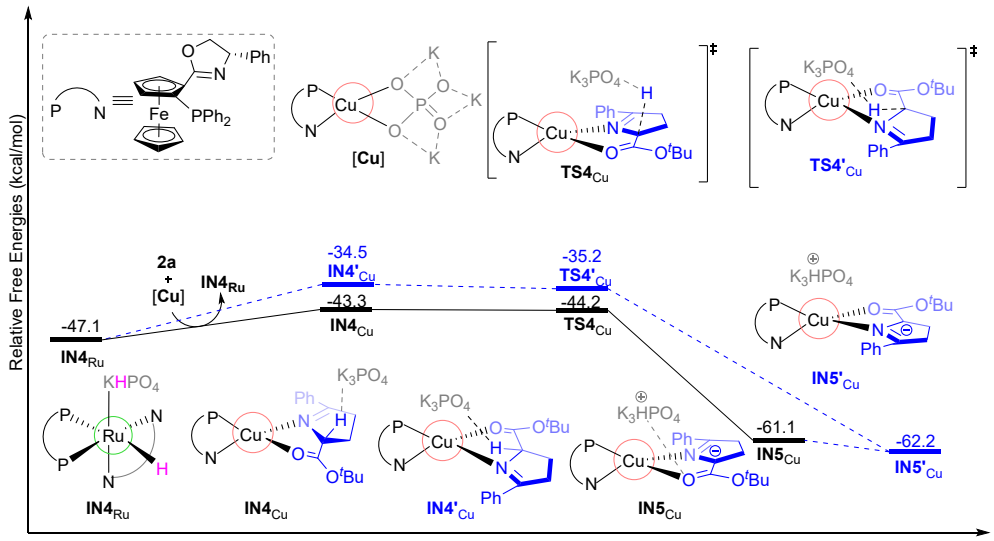


Fig. S5 Calculated energy profiles for the alternative pathways to form **IM5'$_{Cu}$**. Values shown are relative free energies in kcal/mol.

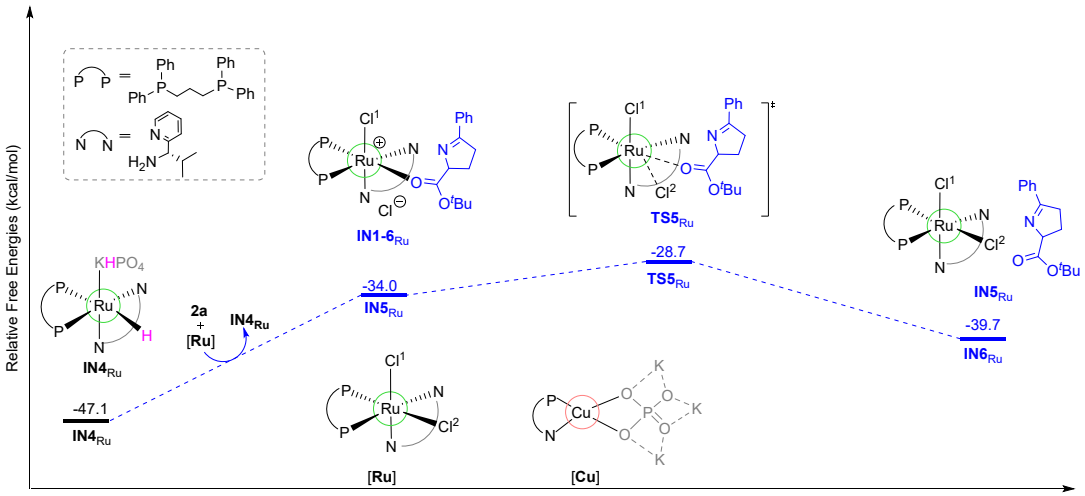


Fig. S6 Calculated energy profiles for the ligand-exchange process of Stage II catalyzed by ruthenium. Values shown are relative free energies in kcal/mol.

Section 5. Alternative pathways in Stage III

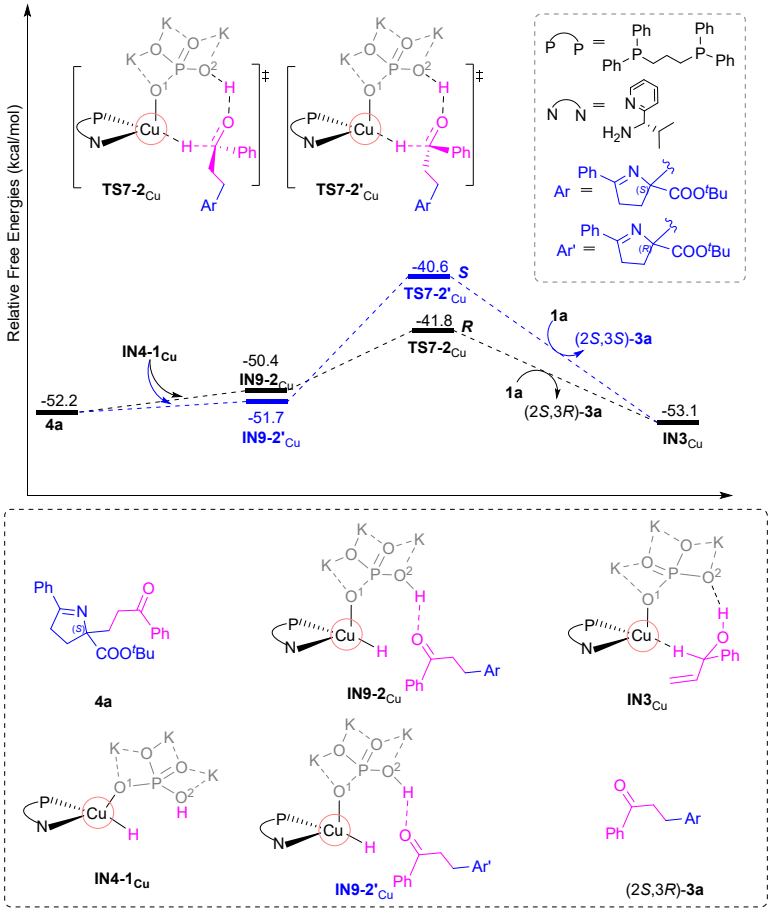


Fig. S7 Calculated energy profiles for Stage III catalyzed by copper. Values shown are relative free energies in kcal/mol.

Section 6. Alternative Pathways for the Reduction of 1-Phenylprop-2-en-1-one and Ketimine Ester

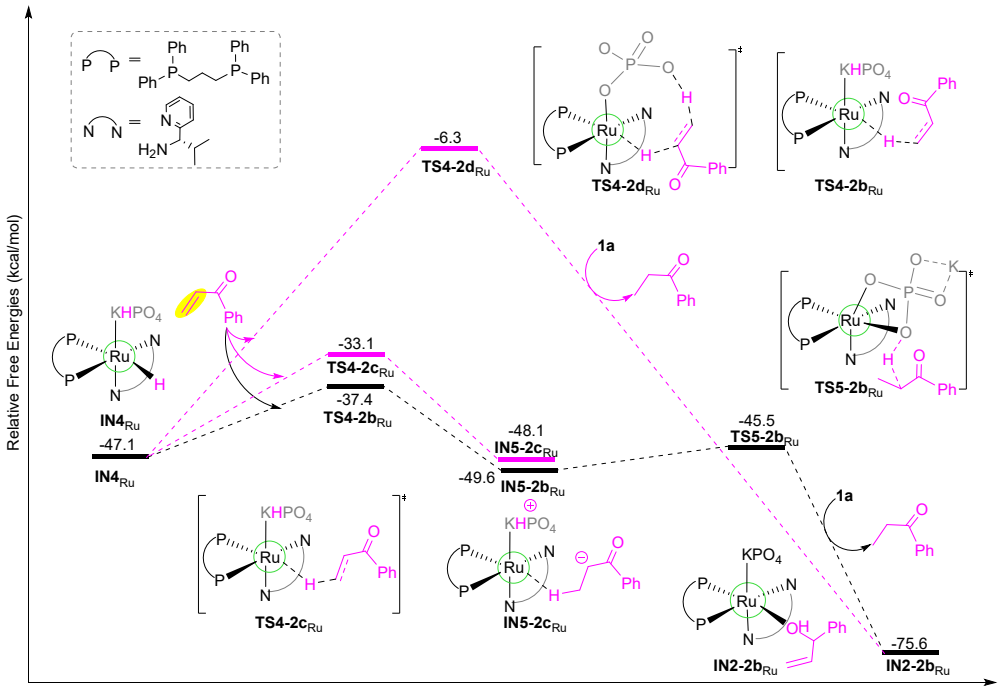


Fig. S8 Calculated energy profiles for alternative reduction pathways of 1-phenylprop-2-en-1-one. Values shown are relative free energies in kcal/mol.

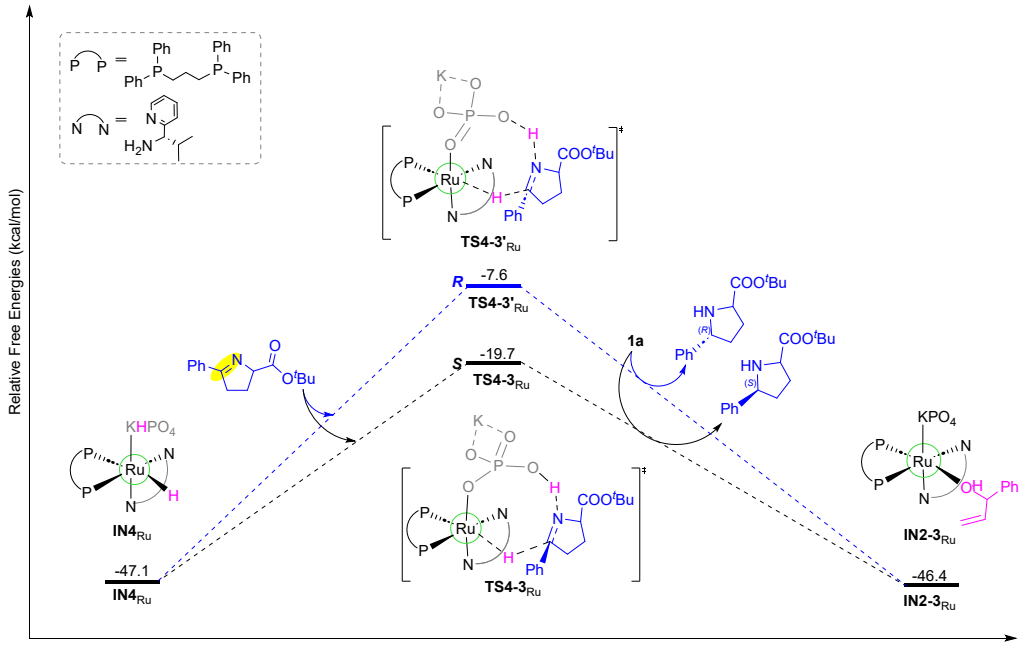
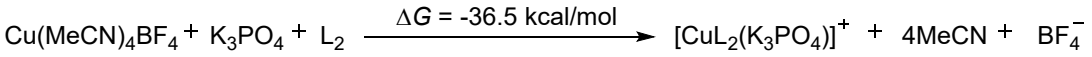


Fig. S9 Calculated energy profiles for alternative reduction pathways of ketimine ester. Values shown are relative free energies in kcal/mol.

Section 7. Supplementary Data: Other Findings



Scheme S7 Activation of the original catalyst $Cu(MeCN)_4BF_4$.

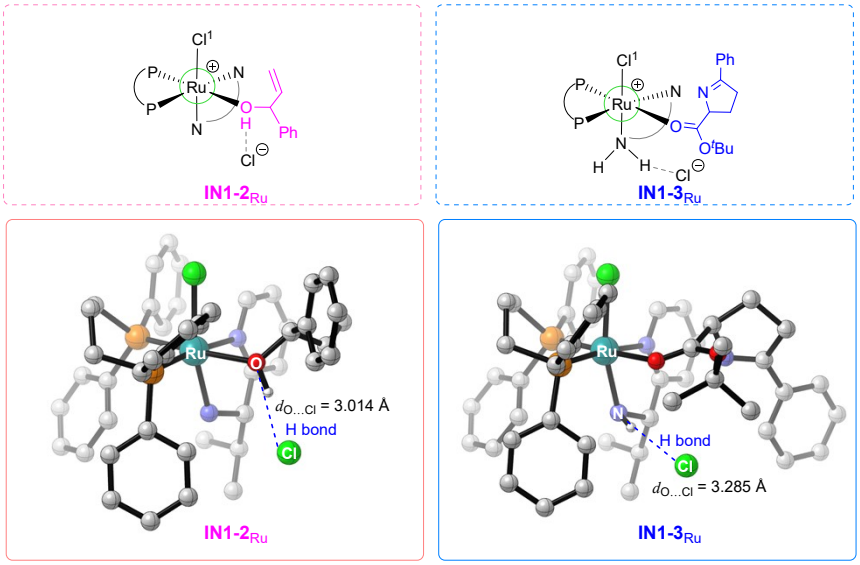


Fig. S10 Optimized geometries, selected bond lengths in angstroms (Å) of intermediate **IN1-2$_{Ru}$** and **IN1-3$_{Ru}$**

Section 8. Energies (in Hartree) of all TSs and Intermediates

Geometry	E_0	E	$H_{293.15}$	$G_{293.15}$	$E_{(sol,B3LYP)}$
[Ru]	-3203.0694	-3203.029074	-3203.028146	-3203.140617	-3204.339178
TS1-1$_{Ru}$	-3930.563971	-3930.513235	-3930.512307	-3930.647998	-3932.01626
IN1-1$_{Ru}$	-3930.63735	-3930.585168	-3930.584239	-3930.725564	-3932.08638
TS1-2$_{Ru}$	-3627.082222	-3627.031767	-3627.030838	-3627.168474	-3628.655604
IN1-2$_{Ru}$	-3627.115927	-3627.065635	-3627.064707	-3627.199389	-3628.685715
TS1-3$_{Ru}$	-3991.035257	-3990.977085	-3990.976157	-3991.128779	-3992.859972
IN1-3$_{Ru}$	-3991.057966	-3990.99983	-3990.998901	-3991.150104	-3992.872686
TS2-1$_{Ru}$	-4354.680057	-4354.618877	-4354.617949	-4354.778907	-4356.424137
IN2-1$_{Ru}$	-4354.673397	-4354.611962	-4354.611034	-4354.772754	-4356.412971
TS2-2$_{Ru}$	-4718.62969	-4718.560176	-4718.559248	-4718.737974	-4720.622482
IN2-2$_{Ru}$	-4718.645618	-4718.575813	-4718.574884	-4718.752584	-4720.641221
IN1-4$_{Ru}$	-2742.211492	-2742.172795	-2742.171867	-2742.28176	-2743.41836
IN1-5$_{Ru}$	-3627.044974	-3626.995662	-3626.994734	-3627.129516	-3628.602733
IN2-5$_{Ru}$	-3166.249207	-3166.200799	-3166.199871	-3166.331646	-3167.753019
TS1-N1$_{Ru}$	-3627.081091	-3627.030263	-3627.029335	-3627.167796	-3628.646311
IN1-N1$_{Ru}$	-3627.086353	-3627.035077	-3627.034149	-3627.172099	-3628.649166
TS1-N2$_{Ru}$	-3627.058272	-3627.007401	-3627.006472	-3627.142902	-3628.624672
IN1-N2$_{Ru}$	-3627.058722	-3627.006945	-3627.006016	-3627.144817	-3628.625177
TS1-P1$_{Ru}$	-3627.051088	-3627.000693	-3626.999765	-3627.136286	-3628.62232
IN1-P1$_{Ru}$	-3627.054047	-3627.003298	-3627.00237	-3627.138919	-3628.624582
TS1-P2$_{Ru}$	-3627.046941	-3626.995794	-3626.994866	-3627.135972	-3628.616055
IN1-P2$_{Ru}$	-3627.061439	-3627.010273	-3627.009345	-3627.149757	-3628.631942
TS1-4$_{Ru}$	-3930.566386	-3930.515403	-3930.514475	-3930.651596	-3932.014096
TS1-1a$_{Ru}$	-3627.081091	-3627.030263	-3627.029335	-3627.167796	-3628.646311
TS1-1b$_{Ru}$	-3627.068938	-3627.018861	-3627.017932	-3627.153771	-3628.64494
TS1-1c$_{Ru}$	-3627.058272	-3627.007401	-3627.006472	-3627.142902	-3628.624672
TS1-1d$_{Ru}$	-3627.051088	-3627.000693	-3626.999765	-3627.136286	-3628.62232
TS1-1e$_{Ru}$	-3627.046941	-3626.995794	-3626.994866	-3627.135972	-3628.616055
TS1-2a$_{Ru}$	-3991.035257	-3990.977085	-3990.976157	-3991.128779	-3992.859972
TS1-2b$_{Ru}$	-3991.039191	-3990.981809	-3990.980881	-3991.129938	-3992.862568
TS2-3$_{Ru}$	-3930.609786	-3930.558666	-3930.557738	-3930.695156	-3932.051223
IN3-3$_{Ru}$	-4354.676374	-4354.614535	-4354.613606	-4354.774848	-4356.413045
IN4-3$_{Ru}$	-4354.672144	-4354.609581	-4354.608653	-4354.772962	-4356.409368
IN4-4$_{Ru}$	-4354.625679	-4354.562853	-4354.561925	-4354.726946	-4356.362234
IN3-5$_{Ru}$	-4354.595554	-4354.533239	-4354.53231	-4354.696807	-4356.350068
IN4-5$_{Ru}$	-4354.634844	-4354.571235	-4354.570307	-4354.739775	-4356.373653
IN3-6$_{Ru}$	-3627.014766	-3626.964602	-3626.963673	-3627.098101	-3628.59055
IN4-6$_{Ru}$	-3204.21467	-3204.173533	-3204.172605	-3204.287022	-3205.519635
TS3-1$_{Ru}$	-4354.658538	-4354.596671	-4354.595743	-4354.759241	-4356.414943
IN3-1$_{Ru}$	-4354.684244	-4354.622573	-4354.621645	-4354.782365	-4356.433988

TS4-1$_{Ru}$	-4354.672516	-4354.611284	-4354.610355	-4354.769282	-4356.413989
IN4$_{Ru}$	-3931.830562	-3931.777523	-3931.776595	-3931.921516	-3933.297981
TS3-2$_{Ru}$	-4354.704409	-4354.643316	-4354.642387	-4354.801679	-4356.447406
IN3-2$_{Ru}$	-4354.702091	-4354.640629	-4354.639701	-4354.800131	-4356.447271
IN3-2'$_{Ru}$	-4354.67238	-4354.61047	-4354.609542	-4354.771682	-4356.420411
TS4-2$_{Ru}$	-4354.616665	-4354.555628	-4354.5547	-4354.711783	-4356.356875
TS3-2'$_{Ru}$	-4354.674438	-4354.613119	-4354.61219	-4354.7727	-4356.41955
TS4-2'$_{Ru}$	-4778.630214	-4778.559773	-4778.558844	-4778.736637	-4780.661523
TS4-4$_{Ru}$	-4778.69829	-4778.626544	-4778.625616	-4778.808263	-4780.749873
TS4-1'$_{Ru}$	-4354.647799	-4354.586526	-4354.585598	-4354.743493	-4356.399047
TS4-4'$_{Ru}$	-4778.682408	-4778.611313	-4778.610385	-4778.789868	-4780.71949
[Cu]	-2716.608371	-2716.567243	-2716.566315	-2716.685699	-2717.710917
IN4$_{Cu}$	-3504.608934	-3504.55004	-3504.549111	-3504.706119	-3506.257947
TS4$_{Cu}$	-3504.611647	-3504.553321	-3504.552393	-3504.707575	-3506.257306
IN5$_{Cu}$	-3504.639981	-3504.58057	-3504.579642	-3504.736974	-3506.28591
IN6-1$_{Cu}$	-3927.496276	-3927.426959	-3927.426031	-3927.607647	-3929.41422
TS5-1$_{Cu}$	-3927.487273	-3927.419153	-3927.418224	-3927.59792	-3929.411826
IN7-1$_{Cu}$	-3927.498786	-3927.430881	-3927.429952	-3927.608356	-3929.428819
IN5'$_{Cu}$	-3504.601862	-3504.542387	-3504.541458	-3504.701785	-3506.25827
IN6-1'$_{Cu}$	-3927.506271	-3927.436579	-3927.435651	-3927.617954	-3929.422887
TS5-1'$_{Cu}$	-3927.477967	-3927.410066	-3927.409138	-3927.587878	-3929.401768
IN7-1'$_{Cu}$	-3927.48847	-3927.420858	-3927.419929	-3927.596378	-3929.419799
TS6-1$_{Cu}$	-3927.491841	-3927.425144	-3927.424216	-3927.596273	-3929.410022
IN8-1$_{Cu}$	-3927.499746	-3927.432801	-3927.431873	-3927.604784	-3929.421718
TS6-2$_{Cu}$	-3927.477122	-3927.40959	-3927.408662	-3927.586245	-3929.400182
IN8-2$_{Cu}$	-3927.484331	-3927.416485	-3927.415556	-3927.595012	-3929.406787
4a	-1210.841771	-1210.816847	-1210.815919	-1210.897467	-1211.675651
IN4'$_{Cu}$	-3504.585942	-3504.526985	-3504.526056	-3504.685397	-3506.242544
TS4'$_{Cu}$	-3504.587473	-3504.528817	-3504.527889	-3504.686372	-3506.238964
IN5'$_{Cu}$	-3504.601862	-3504.542387	-3504.541458	-3504.701785	-3506.25827
IN5$_{Ru}$	-3991.057966	-3990.99983	-3990.998901	-3991.150104	-3992.872686
TS5$_{Ru}$	-3991.035257	-3990.977085	-3990.976157	-3991.128779	-3992.859972
IN6$_{Ru}$	-3991.052871	-3990.993772	-3990.992844	-3991.150121	-3992.875753
IN5-1$_{Ru}$	-4718.609264	-4718.53901	-4718.538082	-4718.716823	-4720.627068
TS5-1$_{Ru}$	-4718.581916	-4718.512937	-4718.512008	-4718.687823	-4720.596455
IN6-1$_{Ru}$	-4718.589464	-4718.520344	-4718.519416	-4718.69443	-4720.605762
IN5-2$_{Ru}$	-4718.626431	-4718.556021	-4718.555093	-4718.73271	-4720.627482
TS5-2$_{Ru}$	-4718.587735	-4718.519046	-4718.518117	-4718.692064	-4720.589413
IN6-2$_{Ru}$	-4718.590051	-4718.520861	-4718.519932	-4718.696304	-4720.59884
TS5-1a$_{Cu}$	-3927.471911	-3927.404325	-3927.403396	-3927.579959	-3929.399075
TS5-1b$_{Cu}$	-3927.466547	-3927.39847	-3927.397542	-3927.576869	-3929.393815
TS5-1c$_{Cu}$	-3927.441256	-3927.373095	-3927.372166	-3927.552237	-3929.375671
TS5-1'a$_{Cu}$	-3927.468504	-3927.4005	-3927.399571	-3927.578038	-3929.398807

TS5-1'b$_{Cu}$	-3927.46559	-3927.397509	-3927.396581	-3927.576077	-3929.394012
TS5-1'c$_{Cu}$	-3927.460203	-3927.392505	-3927.391577	-3927.569719	-3929.391326
TS5-1$_{Cu/ent-L2}$	-3927.477967	-3927.410066	-3927.409138	-3927.587878	-3929.401767
TS5-1a$_{Cu/ent-L2}$	-3927.46559	-3927.397509	-3927.396581	-3927.576077	-3929.394012
TS5-1b$_{Cu/ent-L2}$	-3927.466223	-3927.398739	-3927.39781	-3927.574093	-3929.39424
TS5-1c$_{Cu/ent-L2}$	-3927.456713	-3927.388578	-3927.38765	-3927.56592	-3929.387422
TS5-1'$_{Cu/ent-L2}$	-3927.487271	-3927.419152	-3927.418224	-3927.597911	-3929.411822
TS5-1'a$_{Cu/ent-L2}$	-3927.474466	-3927.406534	-3927.405606	-3927.582742	-3929.398618
TS5-1'b$_{Cu/ent-L2}$	-3927.466548	-3927.398471	-3927.397543	-3927.576875	-3929.393816
TS5-1'c$_{Cu/ent-L2}$	-3927.45237	-3927.384414	-3927.383486	-3927.563262	-3929.385665
IN9-1$_{Ru}$	-5142.746835	-5142.667264	-5142.666336	-5142.866825	-5145.027436
TS7-1$_{Ru}$	-5142.707648	-5142.629463	-5142.628535	-5142.824015	-5144.99305
IN9-1'$_{Ru}$	-5142.72936	-5142.649714	-5142.648786	-5142.84961	-5145.011296
TS7-1'$_{Ru}$	-5142.690976	-5142.61255	-5142.611622	-5142.80919	-5144.98104
IN9-2$_{Cu}$	-3928.66137	-3928.592396	-3928.591468	-3928.772176	-3930.60738
TS7-2$_{Cu}$	-3928.64431	-3928.576003	-3928.575075	-3928.754247	-3930.592617
IN9-2'$_{Cu}$	-3928.659922	-3928.590965	-3928.590037	-3928.770734	-3930.609616
TS7-2'$_{Cu}$	-3928.647614	-3928.579564	-3928.578636	-3928.755294	-3930.59368
IN3$_{Cu}$	-3140.635506	-3140.58319	-3140.582261	-3140.728796	-3142.036082
IN4-1$_{Cu}$	-3140.659613	-3140.608342	-3140.607413	-3140.749797	-3142.063982
TS7-1$_{Ru/ent-L2}$	-5142.685913	-5142.607541	-5142.606612	-5142.804953	-5144.97288
TS7-1'$_{Ru/ent-L2}$	-5142.686521	-5142.608121	-5142.607193	-5142.804901	-5144.976308
TS4-2a$_{Ru}$	-4354.644024	-4354.582501	-4354.581573	-4354.742842	-4356.382393
TS4-2b$_{Ru}$	-4354.68362	-4354.621862	-4354.620933	-4354.781195	-4356.423062
IN5-2b$_{Ru}$	-4354.699985	-4354.637796	-4354.636868	-4354.798769	-4356.447454
TS5-2b$_{Ru}$	-4354.699922	-4354.638191	-4354.637263	-4354.797527	-4356.438652
TS4-2c$_{Ru}$	-4354.673755	-4354.611994	-4354.611065	-4354.772594	-4356.41507
IN5-2c$_{Ru}$	-4354.693794	-4354.631984	-4354.631055	-4354.792053	-4356.444686
TS4-2d$_{Ru}$	-4354.622632	-4354.56062	-4354.559692	-4354.722332	-4356.369287
TS4-3'$_{Ru}$	-4719.774977	-4719.705414	-4719.704486	-4719.880093	-4721.7985598
TS4-3$_{Ru}$	-4719.793693	-4719.723764	-4719.722835	-4719.900356	-4721.815687
1a	-424.002934	-423.994097	-423.993169	-424.036858	-424.3169312
1a-2H	-422.831963	-422.823817	-422.822888	-422.864872	-423.1138688
2a	-787.96365	-787.947015	-787.946087	-788.009309	-788.5259682
3a	-1212.014521	-1211.988726	-1211.987798	-1212.071666	-1212.886041
K_3PO_4	-727.439651	-727.429813	-727.428884	-727.477428	-727.6643632
$Cu(MeCN)_4^+$	-2254.495734	-2254.455979	-2254.455051	-2254.572235	-2255.610282
MeCN	-132.706959	-132.703445	-132.702517	-132.729479	-132.8060109

E_0 = Sum of electronic and zero-point energies calculated by B3LYP-D3

E = Sum of electronic and thermal energies calculated by B3LYP-D3

$H_{293.15}$ = Sum of electronic and thermal enthalpies calculated by B3LYP-D3

$G_{293.15}$ = Sum of electronic and thermal free energies calculated by B3LYP-D3

$E_{(sol, B3LYP)}$ = Single point energies calculated by B3LYP-D3 in solvent

Section 9. Calculated Imaginary Frequencies of All Transition States

Species

Species	Frequency
TS1-1$_{Ru}$	-50.21
TS1-2$_{Ru}$	-60.6
TS1-3$_{Ru}$	-38.69
TS2-1$_{Ru}$	-46.08
TS2-2$_{Ru}$	-16.44
TS1-N1$_{Ru}$	-57.47
TS1-N2$_{Ru}$	-36.1
TS1-P1$_{Ru}$	-23.73
TS1-P2$_{Ru}$	-28.81
TS1-4$_{Ru}$	-85.47
TS1-1a$_{Ru}$	-57.47
TS1-1b$_{Ru}$	-57.67
TS1-1c$_{Ru}$	-36.1
TS1-1d$_{Ru}$	-23.73
TS1-1e$_{Ru}$	-28.81
TS1-2a$_{Ru}$	-38.69
TS1-2b$_{Ru}$	-19.82
TS2-3$_{Ru}$	-64.83
TS3-1$_{Ru}$	-41.02
TS4-1$_{Ru}$	-283.12
TS3-2$_{Ru}$	-399.79
TS4-2$_{Ru}$	-190.37
TS3-2'$_{Ru}$	-326.9
TS4-2'$_{Ru}$	-1215.68
TS4-4$_{Ru}$	-166.97
TS4-1'$_{Ru}$	-638.32
TS4-4'$_{Ru}$	-740.94
TS4$_{Cu}$	-350.92
TS5-1$_{Cu}$	-255.82
TS5-1'$_{Cu}$	-261.46
TS6-1$_{Cu}$	-1136.56
TS6-2$_{Cu}$	-312.63
TS4'$_{Cu}$	-828.9
TS5$_{Ru}$	-38.69
TS5-1$_{Ru}$	-715.45
TS5-2$_{Ru}$	-819.15
TS5-1a$_{Cu}$	-274.92
TS5-1b$_{Cu}$	-119.28

TS5-1c$_{Cu}$	-141.84
TS5-1'a$_{Cu}$	-208.87
TS5-1'b$_{Cu}$	-208.15
TS5-1'c$_{Cu}$	-201.88
TS5-1$_{Cu/ent-L2}$	-208.15
TS5-1a$_{Cu/ent-L2}$	-208.15
TS5-1b$_{Cu/ent-L2}$	-288
TS5-1c$_{Cu/ent-L2}$	-102.05
TS5-1'$_{Cu/ent-L2}$	-261.46
TS5-1'a$_{Cu/ent-L2}$	-194.49
TS5-1'b$_{Cu/ent-L2}$	-119.28
TS5-1'c$_{Cu/ent-L2}$	-195.83
TS7-1$_{Ru}$	-286.35
TS7-1'$_{Ru}$	-261.92
TS7-2$_{Cu}$	-220.99
TS7-2'$_{Cu}$	-138.88
TS3$_{Cu}$	-220.99
TS7-1$_{Ru/ent-L2}$	-373.51
TS7-1'$_{Ru/ent-L2}$	-443.68
TS4-2a$_{Ru}$	-340.48
TS4-2b$_{Ru}$	-383.25
TS5-2b$_{Ru}$	-1076.79
TS4-2c$_{Ru}$	-694.7
TS4-2d$_{Ru}$	-743.7
TS4-3'$_{Ru}$	-295.84
TS4-3$_{Ru}$	-372.56