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SULFUR-OXIDATION ENHANCES NITRILE HYDRATION IN
BIOINSPIRED RUTHENIUM COMPLEXES: CATALYTIC, KINETIC,
AND DFT INVESTIGATIONS

By

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A Dissertation

Submitted to the Faculty of the

College of Arts and Sciences of the University of Louisville

in Partial Fulfillment of the Requirements

for the Degree of

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Department of Chemistry
University of Louisville
Louisville, Kentucky

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By

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A Dissertation Approved on

March 31, 2015

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DEDICATION

This dissertation is dedicated to my father Sh. Janak Raj and mother Smt. Parkash Devi
and Late grandparents

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ABSTRACT

SULFUR-OXIDATION ENHANCES NITRILE HYDRATION IN BIOINSPIRED RUTHENIUM COMPLEXES: CATALYTIC, KINETIC, AND DFT INVESTIGATIONS

Davinder Kumar

March 31, 2015

The current dissertation focuses on the effects of sulfur–oxidation on nitrile hydration activity of a series of ruthenium(II) complexes inspired by nitrile hydratase (NHase). NHase catalytically hydrates nitriles to amides at a low spin non–heme Fe(III) or non–corrin Co(III) metal center. The active–site employs a N_2S_3X type donor set using two carboxamido nitrogens and three cofacial cysteinic sulfurs that are present in distinct oxidation states as sulfinate (RSO_2^-), sulfenate (RSO^-), and thiolate (RS^-). The apical site is occupied by substrate or solvent. A lack of sulfur–oxidation renders the enzyme inactive.

Three precatalysts, L^nRuPPh_3 ($n = 1-3$), are employed to assess S-oxidation effects on benzonitrile hydration that are derived from pentadentate ligand 4,7-bis(2'-methyl-2' -mercaptopropyl)-1-thia-4,7-diazacyclononane. Catalytic assays were performed in biphasic, pH neutral conditions. For L^1RuPPh_3 188 ± 32 TONs are observed with an associated TOF of 10 ± 2 h⁻¹. On S-oxidation to L^2RuPPh_3 , TON increases to 238 ± 23 with TOF reaching to 13 ± 1 h⁻¹. Further S-oxidation to

L^3RuPPh_3 results in statistically similar TON (242 ± 23) and TOF ($13 \pm 1 \text{ h}^{-1}$). The results suggest that S-oxidation enhances nitrile hydration at low nitrile:water ratio and also reduces inhibition offered by the product benzamide.

Homogeneous kinetic studies were conducted using DMF as the solvent. The kinetic results suggest that S-oxidation enhances the nitrile hydration rate constant (k_3) by *four-folds* from 0.37 ± 0.01 to $1.59 \pm 0.12 \text{ M}^{-1}\text{h}^{-1}$ for L^1RuPPh_3 to L^3RuPPh_3 , whereas the water-nitrile exchange equilibrium constant (K_2) exhibits an alternating behavior with values of 21 ± 1 , 9.0 ± 0.9 , and 23 ± 3 for L^1RuPPh_3 , L^2RuPPh_3 , and L^3RuPPh_3 . The enthalpy of activation ($\Delta H^\ddagger$) decreases by 26.8 kJ/mol concomitant with S-oxidation from L^1RuPPh_3 to L^2RuPPh_3 . The $\Delta H^\ddagger$ for precatalyst L^3RuPPh_3 is statistically same as that of L^2RuPPh_3 . Interestingly, S-oxidation increases the entropic barrier ($\Delta S^\ddagger$) by 65 J/(mol.K) from L^1RuPPh_3 to $L^{2-3}RuPPh_3$. DFT calculations predict a similar decrease in the enthalpic barrier with S-oxidation as observed experimentally. As suggested by DFT studies, S-oxidation switches the ligand affinity from water to nitrile, and a nitrile-bound mechanism is proposed for $L^{1-3}RuPPh_3$ complexes as corresponding water-bound intermediate is catalytically inactive.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS.....	iv
ABSTRACT	vi
LIST OF FIGURES.....	xi
LIST OF TABLES.....	xvi
Chapter 1	1
Introduction of Nitrile Hydratase and Review of Model Complexes.....	1
1.1 Scope of dissertation	1
1.2 Nitriles in the environment.....	3
1.3 History and the active-site structure of nitrile hydratase	5
1.4 Co-NHase	8
1.5 Applications of NHase	9
1.6 Proposed mechanistic pathways	9
1.7 Ligand centered mechanism	11
1.8 Other mechanisms	12
1.8.1 First Shell mechanism.....	12
1.8.2 Thiolate Mediated Nitrile Hydration	13
1.9 Role of second/outer coordination sphere in modulating the	
NHase activity	13
1.10 Synthetic modeling of the enzyme and challenges.....	14
1.11 Key structural and spectroscopic models.....	15
1.11.1 Fe-Model Complexes from the Kovacs Laboratory	16
1.11.2 Co-Model Complexes from the Kovacs Laboratory	18
1.11.3 Fe-model complexes from Mascharak Lab	21
1.11.4 Co-model complexes from Mascharak Lab	23
1.11.5 Fe-model complexes from Chottard laboratory	25
1.11.5 Co-model complexes from Chottard lab	26
1.11.6 Fe-model complexes from Chottard and Artaud lab.....	27
1.11.7 Fe-model complexes from Artaud lab.....	28
1.11.8 Co-model complexes from Artaud lab	29
1.11.9 Co-model complexes from Masuda lab.....	30
1.11.10 Co-metallopeptide mimics from Shearer lab	32
1.12 Summary of Functional Models of NHase.....	32
1.13 Model Complexes from Grapperhaus Group	34
1.13.1 Fe-model complexes from Grapperhaus lab	34
1.13.1 Ru-model complexes from Grapperhaus lab	36
Chapter 2	40
Experimental Methods	40

2.1 Experimental methods for catalytic assays	40
2.1.1 Materials and reagents.....	40
2.1.2 Synthetic methods	41
2.1.2.1 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}RuPPh_3$	41
2.1.2.2 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}RuPPh_3$ in presence of excess triphenylphosphine	41
2.1.2.3 Typical procedure for catalytic benzonitrile hydration using L^1RuPPh_3 in the presence of oxidant ferrocenium hexafluorophosphate	42
2.1.2.4 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}RuPPh_3$ in the presence of excess benzamide	43
2.1.2.5 Typical procedure for catalytic benzonitrile hydration using L^1RuPPh_3 saturated with air	43
2.1.3 Electrochemical methods	44
2.1.3.1 Square wave voltammetry	44
2.1.4 GC-MS Methods.....	45
2.1.4.1 Calibration curve to determine TONs and TOFs and sample calculation	45
2.1.5 UV-visible spectroscopy	46
2.2 Experimental Methods for Homogeneous Kinetic and Thermodynamic Studies	47
2.2.1 Materials and reagents.....	47
2.2.2 Synthetic Methods.....	47
2.2.3 GC-MS methods.....	47
2.2.3.1 Introduction to Gas Chromatography-Mass spectrometry (GC-MS).....	48
2.2.3.2 Choosing the Internal Standard (IS) and Response Factor (RF).....	52
2.2.3.3 Quantification of the product formation using internal standard technique..	53
2.2.3.4 Derivation of the Rate Law for $L^{1-2}RuPPh_3$ and extraction of K_2 and k_3	55
2.2.3.5 Derivation of the Rate Law for L^3RuPPh_3 and extraction of K_2 and k_3	56
2.3 Methods for DFT studies	57
2.3.1 Importance of computational chemistry	57
2.3.2 Computational methodology	61
2.3.3 Setting-up calculation at the Cardinal Research Cluster (CRC).....	62
Chapter 3	70
Catalytic and Mechanistic Studies under Biphasic Conditions	70
3.1 Overview of the Ru catalysts that catalyze nitrile hydration.....	71
3.1.1 Water-insoluble Ru complexes for nitrile hydration.....	71
3.1.3 Water soluble Ru nitrile hydration catalysts	75
3.3 Catalytic benzonitrile hydration assays with $L^{1-3}RuPPh_3$ (48-50)	78
Chapter 4	91
Kinetic and Thermodynamic Studies in Homogeneous Medium	91
4.1 Chemical kinetics.....	92
4.2 Temperature dependence of the reaction rate constant and kinetic barrier	93
4.3 Different methods to measure reactions rates	94
4.4 Kinetic studies on NHase	94
4.5 Kinetic studies using $L^{1-3}RuPPh_3$ precatalysts	95
4.6 Reaction mechanism and rate law	95

4.7	Activation parameters for $L^{1-3}RuPPh_3$	101
4.8	Full catalytic cycle	105
4.9	Relevance to enzyme nitrile hydratase	106
Chapter 5		110
DFT modeling of the catalytic nitrile hydration cycle		110
5.1	Literature overview of DFT studies on enzyme nitrile hydratase	111
5.2	DFT studies on the first-and second-shell mechanism	111
5.3	Nitrile vs. water binding affinity using metallopeptide mimics	115
5.4	Sulfenate (RSO^-) as the nucleophile and the disulfide switch	116
5.5	Effect of sulfur-oxidation on substrate/product binding to $L^{1-3}Ru$	117
5.5.1	Computational methodology	117
5.5.2	Free energies for ligand binding	118
5.6	Modeling the mechanistic cycle.....	119
5.8	Transition state structures	122
5.9	Sulfur-oxidation effect on Ru-O, Ru-N, and C-N bond distances in water-, nitrile-bound complexes in $L^{1-3}RuX$	125
Chapter 6		128
Conclusions and Future Directions.....		128
6.1	Nitrile hydratase and sulfur oxidation	129
6.1.1	Sulfur-oxidation effect on catalytic benzonitrile hydration under biphasic conditions employing $L^{1-3}RuPPh_3$	130
6.1.2	Catalytic nitrile hydration using weakly coordinating phosphines	131
6.1.3	Tuning the catalytic activity of L^1RuPPh_3 using Lewis acids.....	133
6.1.4	Cobalt and rhodium analogue of the precatalysts $L^{1-3}RuPPh_3$	134
6.2	Homogeneous kinetic and thermodynamic studies	135
6.2.1	Kinetic effects of sulfur-oxidation on catalytic nitrile hydration and activation barrier	135
6.2.2	Isolation of the intermediates of the reaction: substrate- and product-bound species.....	137
6.2.3	Substrate-bound intermediates: Nitrile-and water-bound complexes.....	138
6.2.4	Alternate way to access substrate and product-bound intermediates	140
6.2.5	Lowering the activation barrier with Ru(III) analogues of $L^{1-3}RuPPh_3$	141
6.2.6	$L^{1-3}RuPPh_3$ as mimics of metalloenzyme Thiocyanate Hydrolase (SCNase) 142	
6.3	Density functional theory studies.....	142
6.3.1	Sulfur-oxidation effects on kinetic barriers from DFT and binding affinities of substrates	142
REFERENCES.....		144
APPENDIX-A		162
APPENDIX-B		175
APPENDIX-C.....		236
CURRICULUM VITAE.....		240

LIST OF FIGURES

Figure 1.1. Nitriles found in plants	4
Figure 1.2. Nitrile assimilation by different enzymes.....	4
Figure 1.3. Active site structure of Fe-NHase where X = solvent, substrate, or NO molecule.....	7
Figure 1.4. Proposed mechanisms of nitrile hydration	11
Figure 1.5. Ligand-centered nitrile hydration pathway	12
Figure 1.6. Nitrile hydration pathway with sulfenate as the local base	12
Figure 1.7. Thiolate-mediated nitrile hydration.....	13
Figure 1.8. $[\text{Fe}(\text{ADIT})_2]\text{Cl}$ and its corresponding sulfenate complex	17
Figure 1.9. Complexes $[\text{Fe}^{\text{III}}(\text{tame-N}_3\text{S}_2^{\text{Me}_2})]_+$, $[\text{Fe}^{\text{III}}(\text{Et-N}_2\text{S}_2^{\text{Me}_2})(\text{py})]^{1-}$ and $[\text{Fe}^{\text{III}}(\text{tame-N}_2\text{S})\text{S}_2^{\text{Me}_2}]^{2-}$	18
Figure 1.10. $[\text{Co}(\text{III})\text{S}_2^{\text{Me}_2}\text{N}_3(\text{Pr},\text{Pr})]^+$ and its sulfur-oxidized derivatives.....	20
Figure 1.11. Cobalt based substrate and intermediate analogue of NHase catalytic cycle.....	21
Figure 1.12. $(\text{Et}_4\text{N})[\text{Fe}(\text{PyPS})]$ (13) and its derivatives 14-16.....	22
Figure 1.13. $\text{NEt}_4 [(\text{Cl}_2\text{PhPepS})\text{Fe}(\text{NO})(\text{DMAP})]$ and its bis-sulfinate derivative	23
Figure 1.14 $(\text{Et}_4\text{N})_2[\text{Co}(\text{PyPS})(\text{CN})]$ and its sulfur-oxidized derivatives developed by Mascharak group.....	25
Figure 1.15. $(\text{NEt}_4)_2[\text{Fe}^{\text{III}}(\text{L-O}_2)]$ complex with apical binding of sulfinate via O-atom... ..	26
Figure 1.16. $\text{Na}[\text{CoL-N}_2\text{S}_2]$ and its corresponding sulfenate, and sulfinate derivatives .	27
Figure 1.17. $[\text{Fe}(\text{N}_2\text{S}_2)\text{Cl}](\text{NEt}_4)_2$ and its NO derivative	28
Figure 1.18. Complex $(\text{Et}_4\text{N})_2[\text{Fe}(\text{N}_2\text{S}_2\text{Cl}_2)\text{Cl}]$ and its corresponding bis-sulfinate derivative.....	29
Figure 1.19. $(\text{Et}_4\text{N})[\text{Co}(\text{N}_2\text{S}_2)]$ and its bis-sulfinate derivative with different axial ligands	30
Figure 1.20. N_2S_2 donor set based Co-NHase mimics by Ozawa and Masuda group	31
Figure 1.21. N_2S_3 donor set based Co-NHase mimics developed by Masuda.....	31

Figure 1.22. Metallopeptide based mimics of Co-NHase developed by Shearer group...	32
Figure 1.23. N ₂ S ₃ donor set based Fe-NHase mimic developed by Grapperhaus group..	36
Figure 1.24. Spin-dependent reactivity of L ¹ FeCl and L ¹ FeCN with dioxygen.....	36
Figure 1.25. Series of sulfur-oxygenates obtained from L ¹ RuPPh ₃ using dioxygen	38
Figure 2.1 GC-MS and its various parts	49
Figure 2.2. The picture showing log in information to connect to CRC	63
Figure 2.3 The picture showing terminal once connected to CRC successfully	64
Figure 3.1. Stoichiometric nitrile hydration with ruthenium complex	72
Figure 3.2. Proposed mechanism for nitrile hydration by RuH ₂ (PPh ₃) ₄ [Ru]	73
Figure 3.3. The catalyst [RuH(η ⁵ -C ₉ H ₇)(dppm)] (left) and the proposed transition state showing H-bonding promoted hydration (right).....	74
Figure 3.4. Effect of ancillary ligand in second coordination sphere to promote nitrile hydration	75
Figure 3.5 Role of H-atom acceptor ancillary ligand in promoting nitrile hydration.....	76
Figure 3.6. General scheme of Ru-arene catalysts with water-soluble phosphines.....	77
Figure 3.7. Nitrile hydration catalyst [RuCl ₂ (C ₆ Me ₆){P(NMe ₂) ₃ }] operating via H-bonding through ancillary ligands	77
Figure 3.8. Cyanohydrin hydration using H-bonding via ancillary ligands with [RuCl ₂ (C ₆ Me ₆){P(NMe ₂) ₃ }]	78
Figure 3.9. Catalysts L ¹⁻³ RuPPh ₃ and increase in Ru-P bond distance as a function of sulfur-oxidation.....	79
Figure 3.10. Calibration curve using various concentrations (w/v%) of benzamide.....	80
Figure 3.11. Equilibrium between precatalyst and active catalyst for L ¹ RuPPh ₃ at elevated temperature	82
Figure 3.12. Shift of equilibrium with excess phosphine in reaction mixture for L ¹ RuPPh ₃	83
Figure 3.13. Oxidation of L ¹ RuPPh ₃ with FcPF ₆ and dioxygen	84
Figure 4.1. Concentration dependence of rate vs precatalyst L ¹ RuPPh ₃ (top), PhCN (middle), and H ₂ O (bottom).....	98
Figure 4.2. Double reciprocal plot for precatalyst L ¹ RuPPh ₃ and extraction of K ₂ and k ₃	99
Figure. 4.3. Arrhenius plot for precatalyst L ¹ RuPPh ₃ for calculation of activation energy	102

Figure 4.4. Eyring plot for L^1RuPPh_3 for calculation of enthalpic and entropic barriers	102
Figure 4.5. Proposed nitrile hydration catalytic cycle for L^nRuPPh_3 ($n = 2 - 3$). (R = Phenyl, L^n ligand abbreviated as $L\sim SO_2$ for clarity)	106
Figure 5.1. Proposed pathway for first-shell mechanism for NHase-catalyzed nitrile hydration	113
Figure 5.2. Proposed second-shell mechanism for nitrile hydration	114
Figure 5.3. Alternative proposed second-shell mechanism for NHase-catalyzed nitrile hydration with sulfenate as the nucleophile	114
Figure 5.4. Co(III) metallopeptides and ligand affinity as a function of sulfur-oxidation as determined by DFT studies	116
Figure 5.5. Proposed nitrile hydration reaction mechanism via sulfenate as nucleophile and involving the disulfide formation	117
Figure 5.6. Catalytically active nitrile- and inactive water-bound complexes for $L^{1-3}RuPPh_3$	120
Figure 5.7. Calculated energetics of the nitrile-bound pathway for benzonitrile hydration for precatalysts L^1RuPPh_3 (black), L^2RuPPh_3 (blue), and L^3RuPPh_3 (red) using B3LYP hybrid functional and LanL2DZ basis set for Ru atom and 6-31G(d) for all other atoms under standard conditions (298K). Enthalpies (kJ/mol) are given for gas phase and for DMF solvent phase in parentheses [TS=Transition State].	122
Figure 5.8. Gas phase transition state structures for L^nRuTS ($n = 1 - 3$).	123
Figure 5.9. Nitrile-bound complexes for precatalysts $L^{1-3}RuPPh_3$ and effect of sulfur-oxidation on nitrile polarization	125
Figure 6.1. Series of precatalysts employed in the current studies and effect of sulfur-oxidation on catalytic benzonitrile hydration activity (average TONs and TOFs are listed)	131
Figure 6.2. Proposed syntheses of different precatalysts with different phosphines at the exogenous position	133
Figure 6.3 Proposed syntheses of Co and Rh analogues	134
Figure 6.4. Schematic of overall effect of sulfur-oxidation	137
Figure 6.5. General scheme for synthesis of nitrile-and water, and amide-bound complexes	139
Figure 6.6. Syntheses of intermediates from NO analogues of $L^{2-3}RuPPh_3$	141

List of Figures: Appendix A

Figure A1. Kinetic traces for L^1RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$ and $[Cat.] = 0.21mM$ (A), $0.42mM$ (B), and $0.84 mM$ (C)	162
Figure A2. Kinetic traces for L^1RuPPh_3 under conditions: $[PhCN] = 0.97M$, and $[H_2O] = 2.8M$ (A), $8.3M$ (B), $11M$ (C), $14M$ (D), and $17M$ (E), and $[Cat.] = 0.21mM$	163
Figure A3. Kinetic traces for L^1RuPPh_3 under conditions: $[PhCN] = 0.12M$ (A), $0.49M$ (B), $0.97M$ (C), 1.9 (D), and $4.0M$ (E), $[H_2O] = 11M$ and $[Cat.] = 0.42mM$	164
Figure A4 Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$, and $[Cat.] = 0.056mM$ (A), $0.084mM$ (B), and $0.112 mM$ (C)	165
Figure A5. Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 0.97M$, $[H_2O] = 2.8M$ (A), $5.5M$ (B), $11M$ (C), $14M$ (D), and $17M$ (E), and $[Cat.] = 0.056mM$	166
Figure A6. Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 0.49M$ (A), $0.97M$ (B), $1.9M$ (C), $2.9M$ (D), and $4.0M$ (E), $[H_2O] = 11M$ and $[Cat.] = 0.056mM$	167
Figure A7. Plots for L^2RuPPh_3 showing linear dependence of rate vs $[Cat.]$ and k_{obs}^{-1} vs $[PhCN]^{-1}$ and $[H_2O]^{-1}$	168
Figure A8. Arrhenius plot for L^2RuPPh_3 in the temperature range 368–398K under conditions: $[Cat.] = 0.056mM$, $[PhCN] = 2.9M$, and $[H_2O] = 11M$ equation: $y = -5457.4x + 15.8$	169
Figure A9. Eyring plot for L^2RuPPh_3 in the temperature range 368–398K under conditions: $[Cat.] = 0.056mM$, $[PhCN] = 2.9M$, and $[H_2O] = 11M$ equation: $y = -5074.8x + 8.88$	169
Figure A10. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$, and $[Cat.] = 0.112mM$ (A), $0.168M$ (B), and $0.224mM$ (C).....	170
Figure A11. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 0.97M$, $[H_2O] = 2.8M$ (A), $8.3M$ (B), $11M$ (C), $17M$ (D), and $19M$ (E), and $[Cat.] = 0.112mM$	171
Figure A12. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 0.24M$ (A), $0.49M$ (B), $0.97M$ (C), $1.4M$ (D), and $2.9M$ (E), and $[H_2O] = 11M$, and $[Cat.] = 0.112mM$...	172
Figure A13. The plots for L^3RuPPh_3 showing linear dependence of rate vs $[Cat.]$ and k_{obs}^{-1} vs $[PhCN]^{-1}$ and k_{obs} vs $[H_2O]$	173
Figure A14. Arrhenius plot for the catalyst L^3RuPPh_3 in the temperature range 368–398K under conditions: $[Cat.] = 0.112mM$, $[PhCN] = 1.9M$, and $[H_2O] = 11M$ equation: $y = -5170.4x + 15.9$	174

Figure A15. Eyring plot for L^3RuPPh_3 in the temperature range 368–398K under conditions $[Cat.] = 0.112mM$, $[PhCN] = 1.9M$, and $[H_2O] = 11M$ equation: $y = -4787.9x + 8.94$ 174

LIST OF TABLES

Table 3.1. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L^1RuPPh_3 (48) at 124 °C in neat substrate mixtures at neutral pH.	81
Table 3.2. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L^2RuPPh_3 (49) at 124 °C in neat substrate mixtures at neutral pH.	85
Table 3.3. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L^3RuPPh_3 (50) at 124 °C in neat substrate mixtures at neutral pH.	86
Table 3.4. Summary of final benzamide concentrations achieved for the three catalysts $L^{1-3}RuPPh_3$ under different substrate ratio.....	87
Table 3.5. Product inhibition assays for the catalysts $L^{1-3}RuPPh_3$ (48-50) under neat substrate mixtures and neutral pH at 124 °C	89
Table 4.1. Water-nitrile equilibrium constant (K_2) and hydration rate constant (k_3) for L^nRuPPh_3 ($n = 1 - 3$) in DMF solvent at 398 K.	100
Table 4.2. Nitrile hydration activation parameters for L^nRuPPh_3 ($n = 1 - 3$) in DMF determined over a temperature range of 368 – 398 K and Co-NHase.....	103
Table 5.1. Relative free energies (kJ/mol) for L^nRuPPh_3 ($n = 1 - 3$) upon substitution of PPh_3 with H_2O , benzonitrile ($PhCN$), and benzamide ($PhC(O)NH_2$) from gas phase (and DMF) DFT computations using the B3LYP hybrid functional with the LanL2DZ basis set for Ru and 6–31G(d) all other atoms	119
Table 5.2. Summary of NPA charges for Ru, and C, and N (from nitrile) calculated for nitrile-bound complexes $L^{1-3}RuNCPh$	124
Table 5.3. Sulfur-oxidation effect on Ru-O ($Ru-OH_2$), Ru-N ($Ru-NCPh$), and C-N ($Ru-NCPh$) bond lengths in gas and DMF phase calculated by DFT studies	126

List of Tables: Appendix B

Table B1 Optimized coordinates for Benzonitrile (gas phase).....	175
Table B2 Optimized coordinates for Water (gas phase).....	175
Table B3 Optimized coordinates for Benziminol (gas phase).....	175
Table B4 Optimized coordinates for Benzamide (gas phase).....	176
Table B5 Optimized coordinates for Transition State for Benzonitrile Hydration with water (gas phase).....	176
Table B6 Optimized coordinates for PPh ₃ (gas phase).....	176
Table B7 Optimized coordinates for L ¹ RuPPh ₃ (gas Phase)	177
Table B8 Optimized coordinates for L ¹ Ru(PhCN) (gas phase).....	179
Table B9 Optimized coordinates for L ¹ Ru(H ₂ O) (gas phase)	180
Table B10 Optimized coordinates for L ¹ Ru (gas phase)	181
Table B11 Optimized coordinates for L ¹ Ru(PhCONH ₂) (gas phase).....	182
Table B12 Optimized coordinates for L ¹ Ru(PhC(OH)NH) (gas phase)	183
Table B13 Optimized coordinates for L ¹ RuTS (gas phase).....	184
Table B14 Optimized coordinates for L ² RuPPh ₃ (gas phase):.....	186
Table B15 Optimized coordinates for L ² Ru(PhCN) (gas phase):.....	187
Table B16 Optimized coordinates for L ² Ru(H ₂ O) (gas phase):	189
Table B17 Optimized coordinates for L ² Ru (gas phase)	190
Table B18 Optimized coordinates for L ² Ru(PhCONH ₂) (gas phase).....	191
Table B19 Optimized coordinates for L ² Ru(PhC(OH)NH) (gas phase):	192
Table B20 Optimized coordinates for L ² RuTS (gas phase).....	193
Table B21 Optimized coordinates for L ³ RuPPh ₃ (gas phase)	195
Table B22 Optimized coordinates for L ³ Ru(PhCN) (gas phase).....	198
Table B23 Optimized coordinates for L ³ Ru(H ₂ O) (gas phase)	199
Table B24 Optimized coordinates for L ³ Ru (gas phase)	200
Table B25 Optimized coordinates for L ³ Ru(PhCONH ₂) (gas phase):.....	201
Table B26 Optimized coordinates for L ³ Ru(PhC(OH)NH) (gas phase)	202
Table B27 Optimized coordinates for L ³ RuTS (gas phase).....	204
Table B28 Optimized coordinates for benzonitrile (DMF phase)	205

Table B29 Optimized coordinates for water (DMF phase)	205
Table B30 Optimized coordinates for benziminol (DMF phase)	206
Table B31 Optimized coordinates for benzamide (DMF phase)	206
Table B32 Optimized coordinates for transition state for benzonitrile hydration with Water (DMF phase)	206
Table B33 Optimized coordinates for PPh ₃ (DMF phase).....	208
Table B34 Optimized coordinates for L ¹ RuPPh ₃ (DMF phase)	209
Table B35 Optimized coordinates for L ¹ Ru(PhCN) (DMF phase)	210
Table B36 Optimized coordinates for L ¹ Ru(H ₂ O) (DMF phase)	211
Table B37 Optimized coordinates for L ¹ Ru (DMF phase).....	212
Table B38 Optimized coordinates for L ¹ Ru(PhCONH ₂) (DMF phase)	213
Table B39 Optimized coordinates for L ¹ Ru(PhC(OH)NH) (DMF phase)	215
Table B40 Optimized coordinates for L ¹ RuTS (DMF phase)	216
Table B41 Optimized coordinates for L ² RuPPh ₃ (DMF phase)	217
Table B42 Optimized coordinates for L ² Ru(PhCN) (DMF phase)	219
Table B43 Optimized coordinates for L ² Ru(H ₂ O) (DMF phase)	220
Table B44 Optimized coordinates for L ² Ru (DMF phase).....	221
Table B45 Optimized coordinates for L ² Ru(PhCONH ₂) (DMF phase)	222
Table B46 Optimized coordinates for L ² Ru(PhC(OH)NH) (DMF phase)	224
Table B47 Optimized coordinates for L ² RuTS (DMF phase):	225
Table B48 Optimized coordinates for L ³ RuPPh ₃ (DMF phase)	226
Table B49 Optimized coordinates for L ³ Ru(PhCN) (DMF phase)	228
Table B50 Optimized coordinates for L ³ Ru(H ₂ O) (DMF phase)	229
Table B51 Optimized coordinates for L ³ Ru (DMF phase).....	230
Table B52 Optimized coordinates for L ³ Ru(PhCONH ₂) (DMF phase)	231
Table B53 Optimized coordinates for L ³ Ru(PhC(OH)NH) (DMF phase)	233
Table B54 Optimized coordinates for L ³ RuTS (DMF phase)	234

CHAPTER 1

INTRODUCTION OF NITRILE HYDRATASE AND REVIEW OF MODEL COMPLEXES

1.1 Scope of dissertation

This dissertation presents the extensive assays performed to assess the effect of sulfur-oxidation to modulate the catalytic nitrile hydration activity in bioinspired ruthenium(II) mimics of metalloenzyme nitrile hydratase (NHase). The overall study is basically divided into four parts: catalytic, kinetic, thermodynamic, and density functional theory (DFT) investigations. The current studies are performed using a battery of techniques including anaerobic syntheses, electrochemistry, electron paramagnetic resonance (EPR), nuclear magnetic resonance (NMR), mass spectrometry (MS), single crystal X-ray diffraction (XRD), gas chromatography-mass spectrometry (GC-MS), and density functional theory (DFT) studies. The collection of former techniques is critical for the preparation and characterization of the metal complexes employed as catalysts. GC-MS is a valuable tool to analyze the sample both qualitatively and quantitatively and has proven to be very handy in rate quantification studies. Finally, DFT studies have provided the insights into the nature of transition state and intermediates for the three catalysts employed in the studies.

Chapter 1 of this dissertation introduces the metalloenzyme nitrile hydratase including its atypical active site, proposed mechanistic aspects for NHase-mediated hydration, and a review of synthetic model complexes prepared to provide valuable insights into NHase. Chapter 2 contains the experimental details including catalytic protocols under biphasic and homogeneous conditions, rate law derivations, an introduction to GC-MS and DFT, and computational details.

In Chapter 3, results of catalytic hydration assays performed under biphasic reaction conditions are reported for a series of complexes with varied sulfur-oxidation levels. These mimics are discussed in light of non-covalent interactions proposed to operate in the enzyme. In Chapter 4, homogeneous reaction conditions are developed allowing quantification of rate data, which is presented as a function of catalyst, nitrile, and water concentration for three catalysts. Rate constants are extracted according to the rate law developed in Chapter 2. Additionally, activation parameters for all three catalysts calculated from the Arrhenius and Eyring plots are summarized, and the results are discussed with respect to sulfur-oxidation.

Chapter 5 of the dissertation discusses a DFT study that has been utilized to calculate the nitrile hydration catalytic cycle and determine the activation barrier to complement the experimentally measured values. It also provides intricate details of the transitions state for all catalysts and intermediates of the catalytic cycle of nitrile hydration, and the relevance of these results to NHase is discussed. Chapter 6 summarizes the conclusions and provides future directions in terms of sulfur-oxidation and improving the catalytic nitrile hydration.

1.2 Nitriles in the environment

Nitriles are released in the environment from many different sources. Nitrile-containing compounds are essential components in the metabolic cycle of higher plants and many soil microorganisms.¹ Nitriles are widely dispersed in plants where they serve as growth hormones during plant germination (Fig. 1.1 **A**), natural products of plant metabolites, and constituents of the immune system that guard plants from herbivores. For example, a family of cyanoglycosides present in select plants release cyanide under mild conditions as a protection against herbivores (Figure 1.1 **B**). Plants are also known to contain cyanoalkaloids and cyanolipids whose functions are not known (Fig. 1.1 **C**). The subsequent release of nitriles from plants into the soil provide a niche for microorganisms that evolved to use nitriles as sole source of carbon and nitrogen for syntheses of DNA, RNA, and other essential biomolecules.

Other sources of nitriles are industrial as organic nitriles are precursors for plastics, fibres, pesticides, and fine chemicals.²⁻⁴ Chemical manufacturing produces significant quantities of nitrile-containing waste that is difficult to handle because of the huge quantity and low concentrations. The NHase enzyme can provide insight on the treatment of these toxic nitriles.

The metalloenzyme nitrile hydratase (NHase) performs the nitrile hydration to the amide at a very unusual active site. Due to intriguing active site of nitrile hydratase and given the industrial as well as academic importance of amides, it has attracted the attention of both chemists and biochemists to study this enzyme. Based on the metal center, these can broadly be classified into two categories: Fe-NHases and Co-NHases depending upon the type of metal ion present at the active site.

1.3 History and the active-site structure of nitrile hydratase

The metalloenzyme nitrile hydratase [EC 4.2.1. 84] is found in soil bacteria which is found near the root of plants.^{1,4-5,10} It was first discovered from the bacterium *Arthobacter sp. J-1* and named as “nitrile hydratase”. NHase catalyzes the conversion of nitriles to amides through either non-corrin cobalt (III) or non-heme iron(III) active site under the ambient conditions of temperature, pressure, and physiological pH. The optimum temperature for maximum activity of NHase is usually < 25°C but some Co-NHases are robust and can survive upto 60°C. The NHases exhibit optimum activity near neutral pH (6.5-8.5). NHase generally is a heterodimer with α and β subunits and mass of each subunit is in range ~ 23-29 kDa. The primary coordination sphere at the active site is found to be conserved and consists of –C-S-L-C-S-C- motif in a conserved manner. EPR studies on Fe-NHase have revealed the metal center maintains its low spin, Fe(III) oxidation state throughout the catalytic cycle and has a variable coordination site for substrate interaction. These studies are consistent with the hypothesis that the hydration is a redox-inactive process that is unusual compared to other non-heme

centers widespread in biology.¹¹⁻¹³ Few Fe-NHases when cultured in dark at low temperature result in loss of the enzyme activity. This is due to binding of NO at the sixth site. The source of NO was found to be enzyme NO synthase.⁵ This is independently tested with loss of EPR signal, when NHase is exposed to NO, gas due to loss of radical character of Fe(III). However, exposure to light leads to loss of nitric oxide and restores the activity. So, a photo-regulatory type mechanism is found for some Fe-NHase.¹⁴ Very recently it has been found that only α subunit is sufficient to have NHase activity.¹⁵

Initial X-ray crystallographic studies on Fe-NHase isolated from *Brevibacterium* R312 at 2.66 Å resolution finds the metal ion in a N_2S_3X primary coordination sphere consisting of deprotonated carboxamido nitrogens donors (Ser-113 and Cys-114) and cysteine sulfur donors (Cys-110, Cys-113, Cys-115).¹⁶ The sixth-ligand binding site is occupied by an O-atom from water or hydroxide. However, a higher resolution structure (1.7 Å) of NO-inactivated Fe-NHase from *Rhodococcus* sp *N-771* reveals post-translational modification of two cysteine donors resulting in three distinct oxidation states for the sulfur donors. While cys-109 is in the typical thiolate oxidation state (RS^- ; ox. state = 2-), cys-114 has been oxidized to a sulfenate (RSO^- ; ox. state = 0) and cys-112 is present as a sulfinate (RSO_2^- ; ox. state = 2+).¹⁷ The oxidized sulfur donors are co-facial with the substrate binding site, while the thiolate sulfur sits in the trans position to the labile site (Fig. 1.3). There is loss of enzymatic activity when cultured under anaerobic conditions. That suggests that sulfur-oxidation is crucial to the enzyme activity.¹⁸ While S-oxidation is critical for NHase activity, over oxidation

deactivates the enzyme. Odaka and coworkers prepared over-oxidized NHase mutants that show no activity towards nitrile hydration.¹⁹ Therefore it seems logical that asymmetric sulfur-oxidation is essential for the NHase activity. However, very recently Song and coworkers have found that bis-sulfinate coordination at the Fe-NHase active site that exhibits NHase activity. However, the manuscript doesn't report the activity on isolated crystal.²⁰ In addition to NO and over-oxidation of sulfur, Fe-NHases are also inactivated by N_3^- , CN^- , Hg^{2+} , and Ag^+ .²¹ The active-site structure of NHase is quite identical to enzyme thiocyanate hydrolase (SCNase) that employs Co(III) metal center and converts the thiocyanate into carbonyl sulfide (COS), ammonia (NH_3) and hydroxide (OH^-).²²⁻²⁴ SCNase is found in the cyanide containing waste-water from coal gasification factories and SCN^- is generated as a byproduct of cyanide detoxification process by enzyme thiosulfate transferase.²⁵ Recently, Odaka and coworkers have shown that NHase can also convert isonitriles into corresponding amine, at a slower rate though.²⁶

Figure 1.3. Active site structure of Fe-NHase where X = solvent, substrate, or NO molecule

1.4 Co-NHase

The Co-NHase active site is very similar to Fe-NHase and also maintains the conserved active site sequence.²⁷ Therefore it is presumed to operate by a mechanism very similar to the Fe-NHase. In spite of the fact that both types of enzymes are very similar to each other there are a few key differences between Fe-NHase and Co-NHase. First, Co-NHase has a broader substrate scope and greater activity than Fe-NHase.⁴ Second, Co-NHase has a tryptophan residue in place of a tyrosine, which is present in Fe-NHase, near the active site that accounts for the robust nature of Co-NHase.²⁸ Third, Fe-NHase preferentially hydrates aliphatic nitriles and Co-NHase shows preference to aromatic nitriles.⁴ Lastly, nitric oxide binds exclusively to Fe-NHase and has no affinity for Co-NHase.

The presence of Co(III) at the active-site of NHase has intrigued the chemists and biochemists because of its kinetically inert nature as compared to iron(III). Still, it hydrates nitriles with a similar rate as Fe-NHase in terms of specific activity. However, the result from Kovacs and Mascharak group have shown that thiolate moiety in the axial position trans to solvent/substrate binding site can make the substrate readily undergo exchange reaction that is perhaps the reason why trans thiolate is there and remains unmodified.²⁹⁻³⁰

Interestingly, a recent report shows the active-site of NHase to contain one Co, two Cu and one Zn per functional molecule of the enzyme. However, the pattern of four metal ions in holoenzyme is still unknown.^{4,31}

1.5 Applications of NHase

Given the clean NHase-mediated hydration of nitriles to amides and the usefulness of amides in the daily life (as lubricants, dyes, soap, drugs, polymers, rubber and paper industry).³² Currently, NHase is being used industrially to carry out the acrylonitrile hydration to acrylamide producing nearly 95 ktons of acrylamide annually that accounts for more than 25% of total world output. It also represents the first application of the biotechnology to petroleum industry.³³ Also, few other amides including benzamide, nicotinamide, and 5-cyanovaleramide are also produced on industrial scale and few other amides are produced on batch scale using NHase mediated hydration.^{34 35-40}

1.6 Proposed mechanistic pathways

During the initial stage of modeling studies, it was not very clear that whether the nitrile hydration follows a water-bound or nitrile-bound pathway by binding to the metal or does the metal ion even participates in the reaction. Therefore, different mechanistic proposals have been put forward by different groups based upon their observations that include inner-sphere and outer-sphere, and second outer-sphere pathways (Fig. 1.4) as proposed by Nelson and coworkers.^{1,16}

Apart from these traditional mechanisms, a few other pathways have been proposed including a ligand-centered catalytic nitrile hydration (Fig. 1.5) proposed by Chottard *et al.*⁴¹ A very recent proposal with sulfenate as the nucleophile has been proposed using both experimental studies by Holz⁴² and coworkers and using DFT studies on NHase by Hopmann⁴³. Since one of the three sulfur donors

remains unmodified, it was also proposed that nitrile hydration is carried out by unmodified sulfur since thiols (e. g. mercaptoethanol) are known to accelerate nitrile hydration by three orders of magnitude.⁵ Infact, enzyme nitrilases employ cysteine residue to hydrolyze nitriles without using metal ion.

Inner-sphere mechanism (nitrile-bound): In the first postulated mechanism the nitrile substrate is exchanged with hydroxide bound to the metal center and the metal-bound nitrile undergoes hydration by a water molecule. The reaction generates a metal-bound iminol intermediate that rearranges to the amide product and then the amide is released to regenerate the active specie (Fig. 1.4).

Outer-sphere mechanism (water-bound): This mechanism involves the nucleophilic attack of the metal-bound hydroxide generated by local base activation of water onto the nitrile substrate in the vicinity of the active site. The reaction generates iminolate species that is O-bonded to the metal center. This species then rearranges to amide and is released as product to complete the catalytic cycle (Fig. 1.4).

Second outer-sphere mechanism: This mechanism involves the deprotonation of a free water molecule near the active site by the water molecule bound to metal center. The newly generated hydroxide then carries out the hydration of the nitrile substrate. The eventual rearrangement of the intermediate leads to the amide product. This mechanism is distinct from other two mechanisms in the way that product amide when generated through this pathway is not bound to metal center (Fig. 1.4).

Figure 1.4. Proposed mechanisms of nitrile hydration

1.7 Ligand centered mechanism

In this type of mechanism, metal-bound sulfenate acts as a nucleophile and catalytically hydrates the nitrile. The sulfenate moiety is regenerated through attack of water on sulfur. (Fig. 1.5). This mechanism can be described as the ligand-centered outer sphere mechanism.

Figure 1.5. Ligand-centered nitrile hydration pathway

1.8 Other mechanisms

1.8.1 First Shell mechanism

In the other mechanism based on DFT investigation by Himo and coworkers,⁴⁴ they found that barrier of the reaction drops significantly when sulfenate acts a local base to activate water. (Fig. 1.6). This pathway is described as the first shell mechanism.

Figure 1.6. Nitrile hydration pathway with sulfenate as the local base

A very recent postulated proposal is based on the experimental and DFT studies where sulfenate acts as the nucleophile and presumably a disulfide bond formation takes place between the unmodified sulfur and sulfenyl sulfur.⁴²⁻⁴³ In this catalytic cycle, the sulfenate moiety is proposed to be regenerated every turnover from water molecule and is discussed in detail in Chapter 5.

1.8.2 Thiolate Mediated Nitrile Hydration

The other mechanism is proposed to be mediated by the unmodified sulfur (Fig. 1.7) that acts as the nucleophile to attack the electrophilic carbon of the nitrile and thioimide is formed as the intermediate which undergoes hydrolysis to give the product amide and regenerates the thiol catalyst.

Figure 1.7. Thiolate-mediated nitrile hydration

1.9 Role of second/outer coordination sphere in modulating the NHase activity

The role of non-covalent interactions is well known to affect the enzymatic activity.^{17,20,45-46} It is true in the case of NHase too. Around the Co-NHase active site, serine, tyrosine, and tryptophan residues form a triad and are proposed to act as the base/bases that are critical to NHase activity.^{28,46-47} The mutant studies by Holz and coworkers suggest that k_{cat} decreases by 17-folds on tyrosine (Tyr) replacement with phenylalanine (Phe) and K_{m} is found to increase by > 10-folds

that indicate that Tyr residue helps in nitrile positioning and binding at the active site. This result delineates the role of residues in second coordination sphere in tuning the activity of NHase. Additionally, the loss of complete activity by replacement of arginine residues,⁴⁸ which is in H-bonding distances with modified sulfurs, near the active site is noted elsewhere which is accounted due to role of arginine in the proton shuttling and probably protonating a transition state. Also, the experimental and molecular dynamics simulations suggest that a channel is responsible for the substrate/product transportation.^{16,20,49-50}

1.10 Synthetic modeling of the enzyme and challenges

The synthetic analogue approach employs small molecules to mimics key active site features. This may include structural, electronic, and/or functional aspects of the metalloenzyme.⁵¹⁻⁵³ An advantage of the synthetic analogue approach is synthetic flexibility allowing the tuning of chemical features to match desired properties of the enzyme by variation in ligand donor type, geometrical preferences, and/or choice of metal ion. Additionally, small molecule mimics are typically easier to manipulate and thoroughly characterized than metalloenzymes. A common disadvantage of small molecule mimics is the lack of second-coordination interactions. Proposed roles for S-oxidation of cysteine in the active site of NHase include non-covalent, second-coordination sphere interactions with substrates, intermediates, and products.^{28,43-44,47,54} Small molecule mimics with variable S-oxidation levels provide an attractive method to address these interactions.

However, there are significant challenges associated with synthesis of NHase model complexes. Several of these have been overcome by various groups in the field. For example, no small molecule complex with carboxamide nitrogen as a donor to Fe(III) was known prior to modeling studies. Under basic conditions, the iron(III) is more prone to form iron hydroxide and cluster.^{10,55} Also, prior to model studies, it was presumed based on earlier studies that Fe(III) with thiolate (RS^-) donors were unstable with respect to reduction/oxidation leading to Fe(II) and disulfide reaction products. In fact, no complex of iron(III) with thiolate, and/or sulfinate/sulfenate was known before NHase modeling studies. So, it was quite a challenge to synthesize the Fe(III) complex combining both carboxamido nitrogens and thiolato donors. Therefore chemist used wide variety of N-donors to mimic the NHase active site.

1.11 Key structural and spectroscopic models

The modeling studies of NHase have been performed by various groups across the world and work by Prof. Craig Grapperhaus (USA), Prof. Pradip Mascharak (USA), Prof. Julie Kovacs (USA), Prof. Jean-Claude Chottard (France), Prof. Isabelle Artaud (France), Prof. Jason Shearer (USA), and Prof. Hideki Masuda and Prof. Tomohiro Ozawa (Japan) has provided significant insights into the structure and functioning of enzyme NHase. Earlier models employed coordinatively saturated iron and cobalt complexes with and without sulfur-modification that provided unique insights into the atypical active site of the

NHase and provided the impetus for preparation of next generation models. In this section, key non-functional models are discussed.

The oxidation of thiolate donors were achieved through various O-atom transfer reagents including dioxygen, hydrogen peroxide, hydrogen peroxide•urea, N-sulfonyloxaziridine, (1S)-(+)-(10-camphorsulfonyl)oxaziridine. However, selective oxidation to a sulfinato/sulfenato mixed donor set proved very difficult and to date only one complex with asymmetric oxidation combined with variable ligand binding site has been reported as a NHase mimic.

1.11.1 Fe-Model Complexes from the Kovacs Laboratory

Studies by the Kovacs group include the tridentate N₂S ligand (ADIT = 6-amino-2,3-dimethyl-4-azahex-3-ene-2-thiolate). The ADIT ligand employs amine and imine N-donors with aliphatic thiolate leading to isolation of the coordinatively saturated, low-spin iron(III) complex [Fe(ADIT)₂]Cl (**1**) (Fig. 1.8).⁵⁶ The oxygenation of iron complex with tert-butyl N-sulfonyloxaziridine afforded the corresponding sulfenato complex [Fe(ADIT)(ADIT-O)]Cl (**2**) which was the first reported Fe-sulfenato complex. Oxidation of one thiolate donor to a sulfenato resulted in tighter binding of the remaining thiolate. Interestingly, protonation of the sulfenato led to even more shortening of the unmodified Fe-SR bond. This result was seen in the light of the role of unmodified thiolate in modulation of substrate binding and/or pK_a of the bound water. However, the pK_a of the Fe-sulfenato complex was not quantified.

Figure 1.8. $[\text{Fe}(\text{ADIT})_2]\text{Cl}$ and its corresponding sulfenate complex

Kovacs and coworkers also reported a series of Fe-based pentacoordinate complexes, with variable charge density as Fe–NHase mimics. The complexes $[\text{Fe}^{\text{III}}(\text{tame-N}_3)\text{S}_2^{\text{Me}_2}]^+$ (**3**), $[\text{Fe}^{\text{III}}(\text{Et-N}_2\text{S}_2^{\text{Me}_2})(\text{py})]^{1-}$ (**4**) and $[\text{Fe}^{\text{III}}(\text{tame-N}_2\text{S})\text{S}_2^{\text{Me}_2}]^{2-}$ (**5**) (tame = 1,1,1-tris(aminomethyl)ethane) contain an N_2S_2 donor set in the basal plane with a varied apical ligand.⁵⁷ The charge on complex depends on the nitrogen donor type and the nature of the apical ligand (Fig. 1.9). Each complex displayed a square pyramidal geometry with intermediate spin ($S = 3/2$). The iron atom sits 0.293 Å above the basal N_2S_2 plane in complex **3**, whereas it is 0.404 and 0.408 Å above the plane in the case of complex **4** and **5**, respectively. These observations revealed a weaker interaction to the amine donor in **3** as compared to the pyridine in **4** and thiolate in **5**.

Figure 1.9. Complexes $[\text{Fe}^{\text{III}}(\text{tame-N}_3\text{S}_2^{\text{Me}_2})]^{+}$, $[\text{Fe}^{\text{III}}(\text{Et-N}_2\text{S}_2^{\text{Me}_2})(\text{py})]^{1-}$ and $[\text{Fe}^{\text{III}}(\text{tame-N}_2\text{S})\text{S}_2^{\text{Me}_2}]^{2-}$

EPR studies on complexes **3** – **5** in methanol revealed that **4** and **5** maintain an intermediate spin-state in both solid and solution state and over a temperature range of 4 to 300 K. Complex **3** tends to binds solvent at low temperature near 7 K. Electrochemical measurements confirm the charge build-up from complex **1** (charge = 1+) to **4** (charge = 1–) and **5** (charge = 2–). The $\text{Fe}^{\text{III/II}}$ reduction potential shift negatively from –650 mV for **3**, to –1340 mV for **4**, to <–1800 mV for **5**. All potentials are reported versus saturated calomel electrode (SCE). This clearly shows the higher negative charge stabilizes the +3 oxidation state of iron consistent with the incorporation of five anionic ligands at the NHase active site.

Since the coordination sphere of **5** mimics the donor types and charge of the unmodified NHase active site ligand environment, the authors further studied its dioxygen reactivity. Exposure of CH_3CN solution of **5** to dioxygen resulted in oxidation of apical thiolate to corresponding sulfinate binding through *O*-atom whereas in enzyme sulfurs in the equatorial plane are oxidized. These studies suggested that perhaps protein scaffold around the active-site play a role in protecting the axial thiolate against unwanted reactivity.

1.11.2 Co-Model Complexes from the Kovacs Laboratory

During their initial efforts in preparing mimics of Co–NHase, the Kovacs group prepared cobalt(III) based mimics using a pentadentate ligand with N_3S_2 donor set with imine nitrogens and aliphatic thiolates. The complex $[\text{Co}(\text{III})\text{S}_2^{\text{Me}_2}\text{N}_3(\text{Pr},\text{Pr})]^{+}$ (**6**) was synthesized and its structure revealed trigonal

bipyramidal around the cobalt metal centre (Fig. 1.10).⁵⁸ The complex displayed intermediate spin ($S = 1$). The electrochemical measurements showed a $\text{Co}^{\text{III/II}}$ reduction potential at -460 mV vs SCE. Complex **6** exhibited strong binding affinity towards N_3^- and SCN^- ligands, at the apical site. Oxygenation of **6** with dioxygen after a period of 3 days led to formation of $[\text{Co}(\text{III})\text{S}^{\text{Me}}(\text{S}^{\text{O}_2})\text{N}_3(\text{Pr},\text{Pr})]^+$ (**7**) with concomitant change in geometry from trigonal bipyramidal to square pyramidal. The bond lengths of complex **6** were similar to that of complex **7** except the Co–S bond distances that were little short in the former complex. Complex **7** was found to possess a low-spin state ($S = 0$). The reduction potential for complex **7** appeared at -380 mV vs SCE indicating that S-oxygenation makes the +2 oxidation state of cobalt more easily accessible. However, complex **7** did not show any affinity towards azide or thiocyanate ligands. Interestingly, the addition of H_2O_2 to a solution of complex **7** resulted in the oxidation of the remaining thiolate to a sulfenato moiety producing the complex $[\text{Co}(\text{III})(\eta^2\text{-SO})(\text{S}^{\text{O}_2})\text{N}_3(\text{Pr},\text{Pr})]^+$ (**8**). Complex **8** possessed a η^2 -coordination with coordination of both sulfur and oxygen simultaneously. Electrochemical investigations on complex **8** revealed that the further sulfur oxidation shifted the reduction event negatively to -775 mV vs SCE. This suggests that post-translational modification in NHase stabilizes the higher oxidation state, which is retained throughout the catalytic cycle. Further, it was suggested that in NHase, the sixth site is remains occupied with substrate, product, or solvent to avoid side-on coordination of the sulfenato donor which would potentially lead to deactivation of the enzyme.

Figure 1.10. $[\text{Co(III)S}_2^{\text{Me}_2}\text{N}_3(\text{Pr,Pr})]^+$ and its sulfur-oxidized derivatives

Further, the Kovacs group reported a series of cobalt(III) complexes $[\text{Co}^{\text{III}}(\text{S}^{\text{Me}_2}\text{N}_4(\text{tren}))(\text{MeCN})](\text{PF}_6)_2$, $[\text{Co}^{\text{III}}(\text{S}^{\text{Me}_2}\text{N}_4(\text{tren}))(\text{NHC}(\text{O})\text{CH}_3)](\text{PF}_6)$, $[\text{Co}^{\text{III}}(\text{O}^{\text{Me}_2}\text{N}_4(\text{tren}))(\text{MeCN})](\text{OTf})_2$ and $\text{Co}^{\text{III}}(\text{O}^{\text{Me}_2}\text{N}_4(\text{tren}))(\text{NHC}(\text{OH})\text{CH}_3)(\text{OTf})_2$ **9-12**, respectively (Fig. 1.11).⁵⁴ The ligands consisted of $\text{N}_4\text{S}/\text{N}_4\text{O}$ environment with one imine nitrogen donor and three amino nitrogen donors in combination with either a thiolato or an alkoxide donor. Complex **9** readily transformed to **10** upon addition of OH^- nucleophile. However, **10** failed to release amide, even in the presence of an external proton source. Furthermore, when alkoxide donor was implanted in place of thiolate donor as in **11**, the nitrile of **11** was readily hydrated even with water acting as nucleophile to give **12** where cobalt–iminol complex was isolated as the product. Complex **12** also failed to release amide product. These results suggested that inclusion of moiety which is capable of forming H-bonding network activates the water that further attacks the nitrile carbon and produces the iminol product. This result signifies the importance of neighboring residues near the active site lies that are capable of forming H-bonding network and may help to activate water thereby triggering the hydration cycle.

Figure 1.11. Cobalt based substrate and intermediate analogue of NHase catalytic cycle

1.11.3 Fe-model complexes from Mascharak Lab

Fe-based models from Mascharak lab employed PyPS^{4-} ligand with N_2S_3 donor set (corresponding Fe complex shown in Fig. 1.12, **13**). Model complexes $(\text{Et}_4\text{N})[\text{Fe}(\text{PyPS})]$ (**13**) and $(\text{Et}_4\text{N})_2[\text{Fe}(\text{PyPS})(\text{CN})]$ (**14**) were synthesized and characterized (Fig. 1.12).⁵⁹ Complex **13** displayed distorted trigonal bipyramidal geometry and **14** possessed distorted octahedral geometry. Complex **13** readily formed adducts with various neutral and anionic ligands including water but it did not display reactivity towards nitrile even at very low temperatures. The pK_a of bound water was determined to be 6.3 ± 0.4 which is even lower than the corresponding cobalt complex (8.3)²⁹ suggesting that iron bound water would deprotonate easily and that further can trigger the hydration as observed in cobalt complexes. But the water bound complex was too unstable to be employed as nitrile hydration catalyst. Oxygenation of **13** and **14** with various reagents afforded bis-sulfinate product that was O-bound (**15**) in former case and S-bound in latter (**16**).

Figure 1.12. $(\text{Et}_4\text{N})[\text{Fe}(\text{PyPS})]$ (**13**) and its derivatives **14**-**16**

More recently, the Mascharak group reported complexes addressing how S-oxidation is crucial for photoregulatory activity as observed in some Fe-NHase. The complex $\text{NEt}_4[(\text{Cl}_2\text{PhPepS})\text{Fe}(\text{NO})(\text{DMAP})]$ (**17**) was isolated as a red powder (Fig. 1.13).⁶⁰⁻⁶¹ Complex **17** is an Fe-NO complex according to the Enemark-Feltham notation. It displayed a NO stretch at $\nu_{\text{NO}} = 1849 \text{ cm}^{-1}$, which is quite similar to the value of 1852 cm^{-1} observed in NO inactivated FeNHase. The Fe-N-O angle in **17** was found to be $173.2(8)^\circ$ as compared to 158.6° (av. 165°) in case of enzyme. Furthermore, authors found that in coordinating solvents NO was labile in **17** whereas in non-coordinating solvents NO in **17** was not labile even under photolytic conditions. Oxidation of **17** in CHCl_3 using 4 equivalents of (1S)-(+)-(10-camphorsulfonyl)oxaziridine afforded the bis-sulfinate derivative $[(\text{Cl}_2\text{PhPep}(\text{SO}_2)_2)\text{Fe}(\text{NO})(\text{DMAP})]^-$ (**18**) as a pale-orange powder. The ν_{NO}

shifted to a higher wavenumber (1854 cm^{-1}) as compared to **17** and ν_{SO} was observed in range from $1000\text{--}1100\text{ cm}^{-1}$. Interestingly, complex **18** exhibited NO lability when photolyzed using visible light. The quantum yield of the reaction was determined to be 0.55, which was very similar to that of enzyme (0.48). These studies supported the hypothesis that S-oxygenation imparts lability to NO molecule that further accounts for the observed catalytic activity in NHase.

Figure 1.13. $\text{NEt}_4 [(\text{Cl}_2\text{PhPepS})\text{Fe}(\text{NO})(\text{DMAP})]$ and its bis-sulfinate derivative

1.11.4 Co-model complexes from Mascharak Lab

The first complex that employed both carboxamido nitrogen donor and thiolato sulfur was reported by Mascharak group and is described herein. Their group reported the cobalt complex $(\text{Et}_4\text{N})_2[\text{Co}(\text{PyPS})(\text{CN})]$ (**19**) derived from the

pentacoordinate ligand PyPSH₄ (Fig. 1.14).⁶² The ligand is an N₃S₂ chelate with one pyridine nitrogen donor, two carboxamido nitrogens, and aromatic thiolates. The X-ray crystal structure of **19** revealed a distorted octahedral geometry with the cyano group occupying the position *trans* to one of the thiolates. The cyanide of **19** exchanged with water at room temperature to form relatively unstable (Et₄N)₂[Co(PyPS)(H₂O)][−], which suggests a strong *trans* effect of thiolate. At pH values above 9, the proposed (Et₄N)₂[Co(PyPS)(OH)]^{2−} species is relatively stable and interestingly was shown to display moderate NHase activity. These results suggested a metal-bound hydroxide may be relevant in the NHase mechanism.

The pK_a of water-bound to metal in **19** was found to be 8.3.²⁹ The related sulfinato complex **20** was obtained using H₂O₂ as oxidant. The pK_a of the sulfinato complex dropped to 7.2, suggesting that S-oxidation may tune the acidity of bound water molecule at the NHase active site. The reported hydration activity of **20** was reported to be 3 times higher than **19**. Surprisingly, the corresponding sulfinato/sulfonate complex **21** did not exchange cyanide ligand and hence no activity was observed in that case. These results suggested that unmodified thiolate is crucial for the lability of the exogenous ligand.

Figure 1.14 $(\text{Et}_4\text{N})_2[\text{Co}(\text{PyPS})(\text{CN})]$ and its sulfur-oxidized derivatives developed by Mascharak group

1.11.5 Fe-model complexes from Chottard laboratory

The Chottard group employed both N_2S_3 and N_2S_2 type ligands in their studies. The N_2S_3 ligand (carboxamido donors and aliphatic thiolates) was synthesized by the condensation of diethyl 2-methyl-2-benzylthiomethyl malonate with 2-methyl-2-(benzylthio)propylamine followed by reductive deprotection of the thiol group. The complex $(\text{NEt}_4)_2[\text{Fe}^{\text{III}}(\text{L}-\text{O}_2)]$ (**22**) was prepared by carrying out deprotonation of ligand in DMF and followed by complexation of the ligand with FeCl_3 afforded a deep red powder (Fig. 1.15).⁶³ Attempts to isolate the complex without sulfur-oxidation proved unsuccessful owing to air-sensitivity of the complex. The structure of complex revealed penta-coordinate complex with the two nitrogens and two thiolates in one plane and the sulfinyl oxygen occupying the apical position. The oxidized sulfur was coordinated to iron through oxygen giving Fe–O coordination. The preferential oxidation of apical thiolate as compared to equatorial thiolate probably signifies the role of outer sphere in protecting the axial

thiolate in enzyme from participating in side reactions which probably is crucial to activity of enzyme as noted in studies by the Kovacs group.⁵⁷

Figure 1.15. $(\text{NEt}_4)_2[\text{Fe}^{\text{III}}(\text{L-O}_2)]$ complex with apical binding of sulfinate via O-atom

1.11.5 Co-model complexes from Chottard lab

The N_2S_2 -Co(III) complex $\text{Na}[\text{CoL-N}_2\text{S}_2]$ (**23**) was prepared by addition of CoCl_2 to the ligand followed by air oxidation to Co(III) (Fig. 1.16).⁴¹ Complex **23** was air-stable deep green solid in square planar geometry. It is also air stable in solution, but when reacted with excess of H_2O_2 •urea or H_2O_2 , it resulted into decomposition of the complex. Complex **23** showed high affinity towards CN^- and $^t\text{BuNC}$ as determined using UV-visible and EXAFS studies. The treatment of **23** with H_2O_2 •urea in the presence of excess $^t\text{BuNC}$ resulted in the S-oxygenation product $\text{Na}[\text{CoL-N}_2\text{SOSO}(^t\text{BuNC})_2]\cdot\text{urea}\cdot 2\text{H}_2\text{O}$ (**24**) where two thiolate donors are oxidized to sulfenates. Further, S-oxidation of **23** with 50% H_2O_2 in excess amounts of $^t\text{BuNC}$ and one equivalent of Me_4NCl afforded bis-sulfinate $\text{Me}_4\text{N}[\text{CoL-N}_2\text{SO}_2\text{SO}_2(^t\text{BuNC})_2]$ (**25**) as a yellow powder. The bis-sulfinate complex was catalytically active and hydrated CH_3CN to acetamide as described under the section of functional models.

Figure 1.16. Na[CoL-N₂S₂] and its corresponding sulfenate, and sulfinate derivatives

1.11.6 Fe-model complexes from Chottard and Artaud lab

The mixed N₂S₂ donor set ligand consisting of carboxamido nitrogens and thiolato sulfur was derived from (2-mercapto-isobutyryl)-*o*-phenylene diamine. The ligand was complexed to Fe(III) center using FeCl₃ in DMF at -15 °C producing [Fe(N₂S₂)Cl](NEt₄)₂ (**26**) (Fig. 1.17) as a brown orange powder.⁶⁴ The iron sits 0.44 Å above the N₂S₂ basal plane. Electrochemical investigations in DMF revealed an oxidation event at + 275 mV and a reduction event at -1300 mV vs. SCE. The large negative value of the reduction event suggested the stabilization of +3 oxidation state by carboxamido nitrogen donors of iron in the complex. Further electrochemical studies indicated that the chloro ligand could be exchanged with water/OH⁻/solvent.

The corresponding NO derivative, [Fe(N₂S₂)NO](NEt₄) (**27**), was obtained by purging NO in a DCM solution of **26** at 0 °C. The metal complex **27** was a {Fe-NO}⁶ according to Enemark-Feltham notation. The structure of **27** was very similar to that of **26** except the position of iron 0.513 Å above the plane as compared to 0.44 Å in **26**. The Fe-NO moiety is almost linear with an angle of

177.5° for Fe–N–O and Fe–NO distance is 1.633 Å. The low energy stretch due to NO at 1780 cm⁻¹ suggested a longer N–O bond length than in NO inactivated NHase due to back-bonding. The NO–adduct exhibited a reduction event at –480 mV and an irreversible oxidation at +750 mV vs. SCE. Complex **27** was EPR silent consistent with the diamagnetism exhibited by the complex in magnetic measurements between 10 and 293 K.

Figure 1.17. [Fe(N₂S₂)Cl](NEt₄)₂ and its NO derivative

1.11.7 Fe-model complexes from Artaud lab

Continuing their efforts to understand features of nitrile hydrates, authors employed a similar ligand with a dichloro substituted aromatic ring. The metal complex (Et₄N)₂[Fe(N₂S₂Cl₂)Cl] (**28**) (Fig. 1.18).⁶⁵ It was found to have intermediate iron (III) center (S = 3/2) as suggested by EPR studies at 20K in frozen acetonitrile with g values 4.58 and 1.96. In the presence of additional one equivalent of NEt₄CN the cyano analogue of complex of **28** afforded S–oxygenated product producing green color bis–sulfinate complex (Et₄N)₃[Fe(N₂Cl₂{SO₂}₂)(CN)₂] (**29**). The Fe–N_{avg} (1.959 Å) bond distance for **29** is statistically different from Fe–N_{avg} (2.07 Å) for NHase whereas the Fe–S_{avg} (2.2521 Å) bond distances matches well to Fe–S_{avg} (2.30 Å) of NHase.

Figure 1.18. Complex $(\text{Et}_4\text{N})_2[\text{Fe}(\text{N}_2\text{S}_2\text{Cl}_2)\text{Cl}]$ and its corresponding bis-sulfinate derivative

1.11.8 Co-model complexes from Artaud lab

Initial efforts with Co(III) from Artaud's laboratory employed an N_2S_2 chelate with carboxamido nitrogens and aliphatic thiolates. The square planar complex $(\text{Et}_4\text{N})[\text{Co}(\text{N}_2\text{S}_2)]$ **30** reacted with dioxygen in the presence of tert-butyl isocyanides to yield the bis-sulfinate $(\text{Et}_4\text{N})[\text{Co}(\text{N}_2(\text{SO}_2)_2(\text{CNtBu})_2)]$ (**31**) (Fig. 1.19) complex.⁶⁶ The isocyanide ligands of **31** were strongly bound showing no exchange activity. Complex **31** displays strong stretches at 1210 and 1070 cm^{-1} in the IR spectrum corresponding to asymmetrical and symmetrical SO stretches.

Complex **30** reacted with air in presence of one equivalent of CN^- to give a trinuclear cluster ($\text{Co}^{\text{III}}\text{-Co}^{\text{II}}\text{-Co}^{\text{III}}$). The room temperature magnetic measurements ($\mu = 4.73$ BM) suggested the presence of three unpaired electrons, which is consistent with the inclusion of high spin Co(II) ($S = 3/2$) in the cluster as suggested by the EPR studies. Furthermore, Co(II) was trapped using chelex chromatography from the cluster using aqueous HCl yielding the six-coordinate mononuclear complexes $(\text{Na}_3)[\text{Co}(\text{N}_2(\text{SO}_2)_2(\text{CN})(\text{Cl}))]$ **32** and

(Et₄N)₂[Co(N₂(SO₂)₂(CN)(H₂O))] **33**. Complex **32** was characterized via various spectroscopic techniques whereas **33** was characterized using NMR only. The p^{K_a} of the bound water molecule in **33** was determined to be 10.1 using p^H-metric titrations. Complex **33** proved to be functional mimic of NHase as summarized below.

Figure 1.19. (Et₄N)[Co(N₂S₂)] and its bis-sulfinate derivative with different axial ligands

1.11.9 Co-model complexes from Masuda lab

Masuda and coworkers employed N₂S₂ and N₂S₃ type ligands in their study, Fig. 1.20 and Fig. 1.21. The N₂S₂ ligand is similar to the one developed by Chottard *et al.* with ^tBuNC ligands in the axial position. Oxygenation of the parent complex led to corresponding bis-sulfenate and bis-sulfinate derivatives **35** and **36**.⁶⁷⁻⁶⁸ Interestingly, the bis-sulfenate complex showed nitrile hydration activity as summarized in next section.⁶⁹ This result further supported the requirement of the sulfenate group for the catalytic activity of NHase.

Figure 1.20. N_2S_2 donor set based Co-NHase mimics by Ozawa and Masuda group

The Masuda group also employed N_2S_3 chelates with a thioether, aliphatic thiolate, and carboxamido N-donors (Fig. 1.21). Attempted isolation of the corresponding cobalt complex failed due to its extreme air-sensitive nature. The sulfur-oxidized products **37** and **38** were isolated but no crystal structures have been reported.⁸ Complexes **37** and **38** are reported to be bis-sulfinate and sulfinate/sulfenate, respectively. Interestingly, the complexes **37** and **38** convert ${}^t\text{BuNC}$ to ${}^t\text{BuNH}_2$, an activity exhibited by NHase.

Figure 1.21. N_2S_3 donor set based Co-NHase mimics developed by Masuda

1.11.10 Co-metallopeptide mimics from Shearer lab

Shearer and coworkers employed metallopeptides with an N_2S_3 (carboxamido nitrogens and three thiolato donors) environment to mimic the active site of nitrile hydratase. The peptide NHase-m1 (AcNH-CCDLP-CGVYD-PA-COOH) was metallated using $CoCl_2$.⁷⁰ On exposure to air the product was oxidized to $[Co^{III}NHase-m1]$. Further air exposure led to formation of sulfinato and sulfenato products as determined using FT-IR, gel permeation chromatography, electron spray ionization (ESI-MS), and extended X-ray absorption spectroscopy. The sulfinato/sulfenic acid form of the metallopeptide proved to be a functional model of the enzyme hydrating acrylonitrile to acrylamide. The complexes **39-41** were spectroscopically characterized whereas **42** was used in computational chemistry but was not experimentally observed (Fig. 1.22).

Figure 1.22. Metallopeptide based mimics of Co-NHase developed by Shearer group

1.12 Summary of Functional Models of NHase

Until today, no *functional* model of NHase employing iron(III) has been reported. Only five functional models have been reported that incorporate cobalt (III) as the metal center.^{29,41,62,66,69-70} However, these functional models exhibit low

activity and produce only upto 69 TON over the long time periods. Activity is pH dependent for all catalysts.

The first functional model was complex **20** reported by Mascharak and coworkers. The N_3S_2 complex hydrated acetonitrile (CH_3CN) to produce acetamide product (pH = 9.5, 50 °C, 4 h, 18 TON, and CH_3CN). The corresponding sulfinato complex **21** was reported to be 3 times more active than the dithiolate complex. These mimics were proposed to follow a water-bound pathway.^{29,62}

The second model that exhibited NHase activity was the bis-sulfenato complex **24** reported by Chottard group.⁴¹ The coordinatively saturated complex with an N_2S_2 chelate and aial tert-butylisonitrile was active toward nitrile hydration (pH = 4.5, 4 °C, 144 h, 50 TON, CH_3CN). The sulfenato O-atom was shown to be labile under catalytic conditions. This result invoked a ligand centered mechanism where sulfenato acts as the nucleophile. The corresponding bis-sulfinato was inactive consistent with the proposed role of the sulfenato donor in hydration.

The third functional model of NHase was reported the isolated a water-bound cobalt complex **33** reported by Artaud and coworkers.⁶⁶ The bis-sulfinato complex has a tetradentate \ N_2S_2 donor set that was shown to be active towards nitrile hydration producing acetamide from acetonitrile with low activity (pH = 7.0, 50 °C, 24 h, 14 TON, CH_3CN).

The metallopeptides of Shearer exhibited NHase activity towards acrylonitrile substrate (pH = 8, 25 °C, 18 h, 58 TON, CH_2CHCN).⁷⁰ Computational data suggested that nitrile binding is preferred over water in the case of

sulfinate/sulfenic acid form of metallopeptide, whereas the mono-sulfinate form prefers to be five coordinated specie and the bis-sulfinate complex favors water binding. Therefore it appears that SO₂/SOH modification is required for preferential binding of nitrile (**40**).

The fifth functional model bis-sulfenate complex **35** reported by Ozawa and Masuda. The coordinatively saturated cobalt(III) complex exhibited nitrile hydration activity in both homogeneous and heterogeneous phase (complex encapsulated in mesoporous silica).⁶⁹ The complex was able to hydrate CH₃CN, CH₂CHCN, CH₃CH₂CN, and PhCN. The bis-sulfenate complex showed higher activity towards acrylonitrile. Under optimized homogeneous conditions they reported 69 TON for CH₃CN after 24 h at 4°C under acidic conditions (pH = 4.8).

Very recently, a Co(III) based NHase mimic is reported to stoichiometrically hydrate acetonitrile (1.25 TON) and benzonitrile (1.20 TON).⁷¹ Notably, the corresponding Fe(III) mimic did not exhibit any activity.

1.13 Model Complexes from Grapperhaus Group

1.13.1 Fe-model complexes from Grapperhaus lab

The Grapperhaus group employed a pentadentate N₂S₃ ligand 4,7-bis-(2-methyl-2-mercaptopropyl)-1-thia-4,7-diazacyclononane abbreviated as (H₂(bmmp-TASN)), which contains tertiary amine, thioether, and aliphatic thiolates.⁷² The first generation models employed iron(III) as the metal center. The two thiolates are positioned in a cis-fashion and in facial manner with the exogenous ligand X. The ligand forms a N₂S backbone and this arrangement of ligand around the metal

center is structurally similar to enzyme. The corresponding six-coordinate complex (bmmp-TASN)FeCl or $L^1\text{FeCl}$ (**43**) was synthesized as a blue solid in a distorted octahedral geometry from the metal precursor $\text{Bu}_4\text{NFeCl}_4$ and the deprotonated ligand $(\text{bmmp-TASN})^{2-}$ in ethanolic solution.⁷³ The resulting chloro complex **43** was a high-spin complex. Metathesis with CN^- afforded a low-spin complex $L^1\text{FeCN}$ (**44**). The $[L^1\text{FeNO}]^+$ (**45**) was also prepared from $L^1\text{FeCl}$ by bubbling NO(g) through its acetonitrile solution. The $[L^1\text{FeNO}]^+$ complex displayed spectroscopic properties that were very similar to enzyme and hence served as a good spectroscopic model of the NO-inactivated NHase.⁷⁴ The metathesis reaction of the chloro complex with thallium triflate produced the five-coordinate iron(III) complex $L^1\text{FeOTf}$ (**46**) with weakly coordinating triflate anion in the sixth position. Metathesis reactions with silver triflate failed due to preferential $\text{Ag}\cdots\text{S}$ interactions that obstructed the reaction.⁷⁵⁻⁷⁶ Complex **46** compound was found to bind both water and nitrile, although it preferentially binds water over nitrile.⁷⁷ It was the first complex that exhibited binding for nitrile, amide and water and in order:

Figure 1.23. N₂S₃ donor set based Fe-NHase mimic developed by Grapperhaus group

Complexes **43** and **44** complexes exhibited distinct reactivities towards dioxygen due to difference in their spin-states and Fe-S bond covalency.⁷⁸ Introduction of dioxygen to a solution of **43** led to formation of iron-oxo cluster and disulfide,⁷⁹ whereas **44** underwent sulfur-oxidation all the way to bis-sulfonate (Fig. 1.24). The difference in reactivity of **43** (high-spin) and **44** (low-spin) complexes laid down the path to pursue the further modeling studies with low-spin metal complexes either by tuning the electronic properties of ligand or by changing the metal-center. Our group chose to work with ruthenium(II) as a surrogate low-spin d⁶ metal-center that will lead to low-spin complexes as the mimics of Co-NHase.

Figure 1.24. Spin-dependent reactivity of L¹FeCl and L¹FeCN with dioxygen

1.13.1 Ru-model complexes from Grapperhaus lab

Inspired from the spin-dependent oxygenation described above, the Grapperhaus and co-workers reported the ruthenium–dithiolate complex

L^1RuPPh_3 (**48**).⁸⁰ The complex is synthesized via metalation of ligand (bmmp-TASN)²⁻ with $RuCl_2(PPh_3)_3$. Complex **48** was obtained as an orange solid in a distorted octahedral geometry. The x-ray crystal structure of **48** revealed a Ru–P bond distance to be 2.2911 Å. As expected, the complex was EPR silent, consistent with a low-spin metal center. The complex **48** has a reduction potential ($Ru^{III/II}$) of –0.85 V vs. ferrocene in acetonitrile. Complex **48** is air-stable as a solid, but is highly sensitive to air when present in solution. The controlled oxygenation of **48** in methanol led to development of family of complexes including L^2RuPPh_3 (**49**), L^3RuPPh_3 (**50**), L^4RuPPh_3 (**51**).⁸¹ The various levels of sulfur-oxygenation include one derivative that has same level of sulfur oxygenation as that of the NHase active site (Fig. 1.25). The complex L^2RuPPh_3 possessed thiolate sulfurs modified to sulfinato/thiolate, whereas in **50** both of them were modified to yield a mixed sulfinato/sulfenato complex, while in **51** both sulfur donors were modified to yield the bis-sulfinato moiety.

Electrochemical studies of **49** and **50** revealed that the $Ru^{III/II}$ reduction potential shifted positively as a result of S-oxidation with a value of –0.39 and –0.26 V vs ferrocene in acetonitrile respectively. The Ru–P bond distance in complexes L^2RuPPh_3 and L^3RuPPh_3 were found to be 2.3519 Å and 2.3790 Å, respectively. Notably, the Ru–P bond distance was found to elongate with increase in the level of oxygenation. This suggested the potential exchange of substrate for the phosphine donor with possible catalytic activity. The EXAFS and DFT studies also confirmed the elongation of Ru–P bond distance as a function of sequential S-oxidation.⁸² It was suggested that hardness of Ru metal increases as the oxygen

atoms are added to form dithiolato/sulfinato, and sulfenato/sulfinato metal complexes. Concomitant of that, the interaction between the soft phosphine and hard metal–center decreases which accounts for the elongation of Ru–P bond distance.

Figure 1.25. Series of sulfur-oxygenates obtained from L^1RuPPh_3 using dioxygen

Preliminary studies using acetonitrile as substrate showed that complex **48** did not hydrate the nitrile, whereas with both **49** and **50** sub-stoichiometric activity was noticed.⁸¹ These results further inspired detailed studies to determine effect of sulfur-oxidation, temperature, inhibitor, substrate ratio, and metal-centered oxidation state on catalytic activity that are the focus of Chapter 3 in this

dissertation. Chapter 4 extends the study to include kinetic assays and Chapter 5 includes DFT studies.

CHAPTER 2

EXPERIMENTAL METHODS

2.1 Experimental methods for catalytic assays

2.1.1 Materials and reagents

All reagents were obtained from commercially available sources and used as received unless otherwise noted. All solvents were dried and freshly distilled using standard techniques under an atmosphere of inert nitrogen gas or argon gas and degassed using the freeze-pump-thaw method. Reactions were conducted using standard Schlenk techniques under a nitrogen/argon atmosphere or in an argon-filled glove-box unless otherwise noted. The ligand $\text{H}_2(\text{bmmp-TASN})$ and precatalysts $\text{L}^{2-3}\text{RuPPh}_3$ were prepared as described in the literature and precatalyst L^1RuPPh_3 was prepared through a slight modification to the procedure reported in literature.^{74,80-81,83} Ferrocenium hexafluorophosphate (FcPF_6) was recrystallized from ethanol/acetone mixture as described by Geiger *et. al.*⁸⁴ before use. Purity of precatalysts were determined through square wave voltammetry, prior to use. Deuterated solvents were obtained from Cambridge Isotope Laboratories, Inc. and were used as received.

2.1.2 Synthetic methods

2.1.2.1 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}RuPPh_3$

A 0.500 mL aliquot of stock solution of $L^{1-3}RuPPh_3$ in benzonitrile ($5.4 \times 10^{-4} M$), measured using an automatic micropipette was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile and water to make a total volume of 2.000 mL. The vial was capped using an air-tight teflon screw cap under argon atmosphere. The reaction mixture was heated at 124°C in an oil bath for 18 hours. After the reaction, the nitrile and water were removed under reduced pressure with the assistance of a water bath at 50°C. The metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide which was then subjected to GC-MS analysis, with required dilution using diethyl ether, to determine turnover number (TON).

2.1.2.2 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}RuPPh_3$ in presence of excess triphenylphosphine

A 0.500 mL aliquot of stock solution of $L^{1-3}RuPPh_3$ in benzonitrile ($5.4 \times 10^{-4} M$), measured using an automatic micropipette was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile containing 105 equivalents of PPh_3 and water to make a total volume of 2.000 mL. The vial was sealed with air-tight teflon screw cap under argon atmosphere. The reaction mixture was heated at 124°C in an oil bath for 18 hours. After the reaction, nitrile and water were removed under reduced pressure using a water bath at 50°C. The crude product

was washed with hexanes to remove excess phosphine and then metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide which was then subjected to GC-MS analysis, with required dilution using diethyl ether, to determine turnover number (TON).

2.1.2.3 Typical procedure for catalytic benzonitrile hydration using L^1RuPPh_3 in the presence of oxidant ferrocenium hexafluorophosphate

A 0.500 mL aliquot of stock solution of L^1RuPPh_3 in benzonitrile (5.4×10^{-4} M), measured using an automatic micropipette was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile containing 1 equivalent of ferrocenium hexafluorophosphate and water to make a total volume of 2.000 mL. The vial was sealed with an air-tight teflon screw cap under argon atmosphere. The reaction mixture was heated at 124°C in an oil bath for 18 hours. After the reaction, nitrile and water were removed under reduced pressure using a water bath at 50°C . The crude product was washed with hexanes to remove ferrocene and then metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide which was then subjected to GC-MS analysis, with required dilution using diethyl ether, to determine turnover number (TON).

2.1.2.4 Typical procedure for catalytic benzonitrile hydration using $L^{1-3}\text{RuPPh}_3$ in the presence of excess benzamide

A 0.500 mL aliquot of stock solution of $L^{1-3}\text{RuPPh}_3$ in benzonitrile ($5.4 \times 10^{-4} \text{ M}$), measured using an automatic micropipette was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile and water to make a total volume of 2.000 mL. Then the required amount of benzamide was transferred to the reaction mixture. The vial was capped using an air-tight teflon screw cap under argon atmosphere. The reaction mixture was heated at 124°C in an oil bath for 18 hours. After the reaction, the nitrile and water were removed under reduced pressure with the assistance of a water bath at 50°C . The metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide which was then subjected to GC-MS analysis, with required dilution using diethyl ether, to determine turnover number (TON).

2.1.2.5 Typical procedure for catalytic benzonitrile hydration using $L^1\text{RuPPh}_3$ saturated with air

A 0.500 mL aliquot of stock solution of $L^1\text{RuPPh}_3$ in benzonitrile ($5.4 \times 10^{-4} \text{ M}$), measured using an automatic micropipette was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile and water to make a total volume of 2.000 mL. The vial was capped using an air-tight teflon screw cap under argon atmosphere. After the sample preparation under inert conditions, the reaction vial was allowed to saturate with air. Following that, the reaction mixture was heated at 124°C in an oil bath for 18 hours. After the reaction, the nitrile and water were

removed under reduced pressure with the assistance of a water bath at 50°C. The metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide which was then subjected to GC-MS analysis, with required dilution using diethyl ether, to determine turnover number (TON).

2.1.3 Electrochemical methods

All electrochemical measurements were performed by using a PAR 273 potentiostat/galvanostat with a standard three-electrode cell (glassy carbon or platinum mesh as working electrode (WE), platinum wire/mesh as counter electrode (CE), and Ag/AgCl as pseudo reference electrode (RE)). All reported potentials are referenced to ferrocenium/ferrocene event.

2.1.3.1 Square wave voltammetry

For square wave voltammetry measurements to test the purity of catalysts, Dr. Bob's cell was used as a three-electrode cell with a 6.5 mm diameter glassy carbon working electrode (area = 0.071 cm²), a platinum wire counter electrode, and an Ag/AgCl reference electrode. The Dr. Bob's cell kit was purchased from Gamry Instruments. The Dr. Bob's cell can be used with solvent volumes from 2.0 mL to 50 mL and usually the experiments were performed with 5.0 mL volume. Prior to the addition of analyte, a background voltammogram was collected using 5.0 mL of dry, degassed acetonitrile (CH₃CN) with 0.1 M tetrabutylammonium hexafluorophosphate (TBAHFP) as the supporting electrolyte. Nitrogen gas was bubbled through to the solution for 5 minutes to remove dissolved oxygen, and

then the solution was allowed to settle for 2 minutes without disturbance under a nitrogen gas atmosphere. The initial, switching and final potentials were set between the solvent limits of -1.5 V to +1.5 V versus the reference.

2.1.4 GC-MS Methods

The GC-MS instrument utilized to perform the studies was obtained from Agilent Technologies augmented with 7820A GC system and 5975 series MSD using Helium as a carrier gas at a flow rate of 1mL/min. The oven and column temperature were set to 180 °C and 300 °C, respectively. The column used was poly (5% diphenyl, 95% dimethylsiloxane) with length 30 m, 250 µm inner diameter and 0.25 µm thickness. The samples were detected by thermal conductivity detector (TCD). A split ratio of 100:1 was employed in the studies. The isolated product, benzamide, was validated against an authentic sample of benzamide obtained from commercial source.

2.1.4.1 Calibration curve to determine TONs and TOFs and sample calculation

A calibration curve was created by preparing different benzamide standards with various concentrations (w/v %) that was utilized to quantify the amount of benzamide product formed after the catalytic trials. The product benzamide isolated after the assay was diluted with known volume of diethylether and then subjected to GC-MS analysis. The benzamide peak area was then converted to mass of benzamide using equation from calibration curve, following that

associated TONs and TOFs were calculated. A sample calculation is provided below.

Arbitrary benzamide peak area after dilution with 20.00 mL of ether = 10, 500,000

Arbitrary moles of catalyst = 2.0×10^{-7}

Reaction time = 18 hours

Equation from calibration curve: $y = 10^9 x - 10^6$ (1)

where y is the peak area of benzamide and x is the concentration (w/v %)

Placing the benzamide area in (1) and solving for x

$x = 0.025 \%$

Total benzamide isolated = $(0.025 / 100) \times 20.00 = 0.005 \text{ g}$

Moles of benzamide = $0.005 / 121.14 = 4.12 \times 10^{-5}$

$\text{TON} = \frac{\text{moles of product}}{\text{moles of catalyst}} = (4.12 \times 10^{-5}) / (2.0 \times 10^{-7}) = 206$

$\text{TOF} = \frac{\text{TON}}{\text{time}} = 206 / 18 = 11 \text{ h}^{-1}$

2.1.5 UV-visible spectroscopy

Electronic absorption spectra were recorded with an Agilent 8453 diode array spectrometer with air free 1 cm path length quartz cell. Samples were prepared under inert conditions using degassed solvents.

2.2 Experimental Methods for Homogeneous Kinetic and Thermodynamic Studies

2.2.1 Materials and reagents

The precatalysts $L^{1-3}RuPPh_3$ were synthesized as described in the earlier section. The nitriles (benzonitrile, *p*-chlorobenzonitrile), water, and amides (benzamide, *p*-chlorobenzamide, *p*-toluamide) were obtained from commercial sources.

2.2.2 Synthetic Methods

Typical procedure for kinetic studies:

The reactions were carried out in 8 mL glass vial, open top closure sealed with PTFE septa, equipped with a magnetic stir bar. A typical run included 500 μ L of catalyst stock solution in DMF, 500 μ L of benzonitrile, 500 μ L of H_2O , and 1000 μ L of DMF solvent, keeping a total volume of 2.500 mL. The samples were prepared under inert conditions and were placed in an oil bath at 398 K. The concentration of catalyst was changed using different volumes of stock solution and similarly PhCN, and H_2O concentration were varied. The volume of DMF was adjusted to keep the total reaction volume 2.500 mL. The aliquots were removed periodically depending upon the catalyst and then internal standard was added to the aliquots and the samples were subjected to GC-MS analysis.

2.2.3 GC-MS methods

The GC-MS instrument used in the studies was obtained from Agilent Technologies augmented with 7820A GC system and 5975 series MSD using

Helium as a carrier gas at a flow rate of 1.00 mL/min. The oven and inlet temperature were set to and 180 °C and 300 °C, respectively. The column used was poly (5% diphenyl, 95% dimethylsiloxane) with length 30m, 250µm inner diameter and 0.25µm thickness. The samples were detected by thermal conductivity detector (TCD). A split ratio of 20:1 was employed in the kinetic studies.

2.2.3.1 Introduction to Gas Chromatography-Mass spectrometry (GC-MS)

GC-MS is a hyphenated technique that combines gas chromatography (GC) with mass spectroscopy (MS). In GC part, the sample mixture is separated into its different constituents and then the separated compounds are fed into mass analyzer where they undergoes fragmentation and then the charged ions are separated based upon their mass to charge (m/z) ratio. The GC part gives rise to gas chromatograph and the MS part produces the mass spectrum of the individual compound separated. Therefore, with GC-MS technique, mixtures are first separated and then analyzed. The GC-MS is a powerful technique for both qualitative and quantitative analysis. The schematic diagram of GC/MS with typical components is provided below and the components and their function is discussed in order first GC and then MS part.⁸⁵ The schematic of GC-MS instrument with labeled parts are shown in Figure 2.1.

Figure 2.1 GC-MS and its various parts

Main Components of GC and their function:

1. Carrier Gas: Carrier gas is also called the mobile phase in gas chromatography since the carrier gas transports the analyte through the long packed column to the detector. The common carrier gases used are helium (He), nitrogen (N₂), hydrogen (H₂). He is the most commonly used carrier gas in gas chromatography.
2. Interface: An interface is the one that connects the GC part with MS part of the GC-MS instrument. It allows the analyte to travel to mass spectrometer for ionization. Usually, this part is kept at high temperature in order to prevent condensation of the sample.
3. Pneumatic Controls: The gas travels at a certain pressure (flow rate) in the column and flow rate does effect the separation of compounds in sample. The electronic pneumatic pressure controls takes care of the flow rate of the gas. Usually, a flow rate of 1.00 mL/min is standard.

4. Oven: The oven temperature are also electronically controlled. The typical range of GC oven is from 5 °C to 400 °C. Usually, a temperature ramp can also be employed if the compounds in the sample mixture vary widely in their boiling point. In the current studies, 180 °C is employed for the analyte with 280 °C boiling point.
5. Column: The column is mainly responsible for the separation of sample mixture to its individual components. Depending upon the type of analyte, a polar/non-polar column could be employed for separation. It is also called the stationary phase in chromatographic terminology. The stationary phase is usually coated onto the inner wall of the column which is usually polymer with two types of monomers with different fractions: dimethylsiloxane and diphenylsiloxane.
6. Injector: The injector acts as the interface between the user and GC-MS instrument. This is where sample is fed into the instrument for separation and analysis. The sample is first volatilized in the injector part and then travels to column part. The injector/inlet temperature should be at least 20 °C above the boiling point of the analyte. In current studies, inlet temperature of 300 °C is employed.

Main Components of MS and their function

1. Control electronics: From this panel, the MS parameters can be controlled. However, these could also be controlled with the software which is used to start the data collection.

2. Detector: Detector perform the job of detecting the ions produced from fragmentation of the sample. The detector transforms the detection into a signal which is read on the computer. Thermal conductivity detector (TCD) is known as the universal detector that is also employed in these studies.
3. Vacuum system: High vacuum is necessary to proper functioning of the GC-MS. Usually a forline of 58-63 is indicative of a good vacuum and a pressure of 10^{-6} Torr.
4. Mass analyzer: The function of a mass analyzer is to separate the ions produced from fragmentation process which is usually based on the m/z ratio of ions. Various different types of mass analyzers are: Quadrupole, ion trap, time of flight (TOF), and magnetic sector mass analyzer.
5. Ion source: The ion source is used to produce ions of sample which are then separated and detected. Two types of ionisation processes are discussed below.
 - I. Electron ionisation (EI): In this ionisation process, the source of ionisation are high energy electron beams that on collision with analyte subsequently produce radical cation of analyte by removal of electron. This is the most common type of ionization employed in the GC-MS.
 - II. Chemical ionisation (CI): In chemical ionisation, external gases, at high pressure, are used to produce radical cations/anions of the

species which are then detected further. The common gases employed for the purpose are: methane, isobutene, ammonia.

Merits of GC-MS

1. Provide a very quick analysis of the analyte as separation could be achieved very easily by changing various parameters such as flow rate, type of column, and temperature.
2. Very sensitive to the concentration and a concentration of 1 ng/mL can easily be detected
3. Excellent for qualitative and quantitative analysis
4. Broad range of analytes could be detected

Demerits of GC-MS

1. This technique requires the sample to have significant vapor pressure between 30 °C and 300 °C. Any sample with boiling point above the temperature range of column is difficult to analyze. Analyte boiling point should not exceed 400 °C and upper limit for molar mass of analyte is 500 Da.

2.2.3.2 Choosing the Internal Standard (IS) and Response Factor (RF)

Numerous internal standards could be employed to quantify the product formation via GC-MS with time. However, there are few requirements for an ideal candidate for internal standard that would lead to more accurate, and precise results.

- I. It should have the same functional group as that of the analyte under study.
- II. It should have similar retention time as compared to the analyte.
- III. It should have similar boiling point as that of the analyte.

Furthermore, depending upon the reactions conditions, IS could be added to reaction mixture itself or addition of IS can be done after removing aliquots from the reaction mixture. In current studies, *p*-toluamide was employed as the IS and was added externally to the aliquots removed periodically. The reason behind doing external addition is that the complexes under study are prone to inhibition by the amide binding that would interfere with the kinetic measurements.

The response factor (RF) accounts for the variation in detector's response to that of analyte and IS. The RF is calculated by injection a mixture solution with known concentrations of analyte and IS. The RF between benzamide (analyte) and *p*-toluamide (IS) was measured to be 1.62 that is required in calculation of analyte concentration.

2.2.3.3 Quantification of the product formation using internal standard technique

Sample calculation:

Response Factor (analyte benzamide and IS *p*-toluamide) = 1.62

Total reaction mixture volume = 2.500 mL

Benzamide (analyte) area = 36 %

Internal Standard (IS) area = 63 %

Total moles of IS added to aliquot (40 μL) = 7.36×10^{-7}

Moles of catalyst used = 2.10×10^{-6}

Volume of aliquot removed = 50 μL = 50×10^{-6} mL

Number of moles of analyte in sample (90 μL) analyzed = $\left(\frac{\text{analyte area}}{\text{IS Area}} \right)$ (RF)
(moles of IS)

Number of moles of analyte in 90 μL of sample analyzed =

$$(36/63) (1.62) (7.36 \times 10^{-7}) = 6.81 \times 10^{-7}$$

Moles of product in reaction flask:

$$= \left(\frac{\text{moles of analyte in } 90 \mu\text{L}}{\text{volume of sample analyzed (0.09 mL)}} \right) (\text{volume of reaction mixture left}) \quad (2)$$

$$= (6.81 \times 10^{-7} / 0.09 \text{ mL}) (2.500 \text{ mL}) = 1.85 \times 10^{-5}$$

It is to be noted that in (2) second term changes after each aliquot removed from reaction mixture. From the moles of product, concentration (Molarity) can be obtained which when plotted versus time ultimately leads to rate of reaction. Further, TONs and TOFs can also be calculated as described earlier in this Chapter.

2.2.3.4 Derivation of the Rate Law for $L^{1-2}RuPPh_3$ and extraction of K_2 and k_3

$$\text{Rate} = \frac{d[PhCONH_2]}{dt} = k_3 [ES] [R] \quad (5)$$

Applying Steady-State approximation to [ES] and under reaction conditions $k_1 \gg k_{-1}$:

$$\frac{d[ES]}{dt} = k_2 [E] [S] - k_{-2} [ES] [R] - k_3 [ES] [R] = 0 \quad (6)$$

$$\text{Also, } [E] = [E_T] - [ES] \quad (7) \quad \text{where } [E_T] = \text{total concentration of catalyst}$$

Combining (6), and (7) and separation of variables to extract [ES] gives:

$$[ES] = \frac{k_2 [E_T] [S]}{(k_{-2} + k_3) [R] + k_2 [S]} \quad (8)$$

Placing the value of [ES] from (8) in (5), the Rate can be written as:

$$\text{Rate} = \frac{k_2 k_3 [E_T] [S] [R]}{(k_{-2} + k_3) [R] + k_2 [S]} \quad (9)$$

Assuming, $k_{-2} \gg k_3$

$$\text{Rate} = \frac{k_2 k_3 [E_T] [S] [R]}{k_{-2} [R] + k_2 [S]} = k_{\text{obs}} [E_T] \quad (10)$$

The equation (10) can be rewritten as (11) and (12), to extract k_3 and K_2 from slopes when $1/k_{\text{obs}}$ is plotted vs. $(1/R)$ and $(1/S)$, respectively :

$$\frac{1}{k_{\text{obs}}} = \frac{1}{K_2 k_3 [S]} + \frac{1}{k_3} \left(\frac{1}{[R]} \right) \quad \text{slope gives } k_3 \quad (11)$$

$$\frac{1}{k_{\text{obs}}} = \frac{1}{K_2 k_3} \left(\frac{1}{[S]} \right) + \frac{1}{k_3 [R]} \quad \text{slope gives } K_2 \quad (12)$$

2.2.3.5 Derivation of the Rate Law for L³RuPPh₃ and extraction of K₂ and k₃

$$\text{Rate} = \frac{d[\text{PhCONH}_2]}{dt} = k_3 [\text{ES}] [\text{R}] \quad (5)$$

Applying Steady-State approximation to [ES] and under reaction conditions $k_1 \gg k_{-1}$:

$$\frac{d[\text{ES}]}{dt} = k_2 [\text{E}] [\text{S}] - k_{-2} [\text{ES}] [\text{R}] - k_3 [\text{ES}] [\text{R}] = 0 \quad (6)$$

$$\text{Also, } [\text{E}] = [\text{E}_T] - [\text{ES}] \quad (7) \quad \text{where } [\text{E}_T] = \text{total concentration of catalyst}$$

Combining (6), and (7) and separation of variables to extract [ES] gives:

$$[\text{ES}] = \frac{k_2 [\text{E}_T] [\text{S}]}{(k_{-2} + k_3) [\text{R}] + k_2 [\text{S}]} \quad (8)$$

Placing the value of [ES] from (8) in (5), the Rate can be written as:

$$\text{Rate} = \frac{k_2 k_3 [\text{E}_T] [\text{S}] [\text{R}]}{(k_{-2} + k_3) [\text{R}] + k_2 [\text{S}]} \quad (9)$$

Assuming, $k_{-2} \gg k_3$

$$\text{Rate} = \frac{k_2 k_3 [\text{E}_T] [\text{S}] [\text{R}]}{k_{-2} [\text{R}] + k_2 [\text{S}]} = k_{\text{obs}} [\text{E}_T] \quad (10)$$

Since for L³RuPPh₃, a linear dependence of rate was observed for [H₂O] only, that means $k_2[\text{S}] > k_{-2}[\text{R}]$. Therefore (10) can be rewritten to extract k_3 from (11).

The K₂ was calculated from the double-reciprocal plot (12).

$$\text{Rate} = \frac{k_2 k_3 [\text{E}_T] [\text{S}] [\text{R}]}{k_2 [\text{S}]} = k_3 [\text{E}_T] [\text{R}] \quad (11)$$

$$\frac{1}{k_{\text{obs}}} = \frac{1}{K_2 k_3} \left(\frac{1}{[\text{S}]} \right) + \frac{1}{k_3 [\text{R}]} \quad \text{slope gives } K_2 \quad (12)$$

2.3 Methods for DFT studies

2.3.1 Importance of computational chemistry

Computational chemistry is the branch of chemistry that uses the computers to assist in studying the chemical problems. The various codes are incorporated into the programs that allows to calculate the structure and properties of the system. Using the available packages (Gaussian⁸⁶, ORCA⁸⁷ etc.), various properties such as absolute and relative energies, geometry optimization, electronic charge distribution, dipole and higher multipole moments, vibrational frequencies, NMR shifts, electronic transitions and numerous other spectroscopic data can be calculated. Also, reaction modeling using theoretical chemistry can provide insights into the reaction mechanism and therefore can enhance our understanding of a system. Overall, these theoretical methods could be broadly divided into four categories and are discussed below.

2.3.2 Various theoretical methods

***ab-initio* method:** The term *ab-initio* means from the beginning. In this method, a complete Hamiltonian is developed for the system and its solution is derived and no experimental data is fitted to obtain the solution of the Schrödinger equation.⁸⁸ Only constant employed in these method are the physical constants. The simplest method of this type is Hartree-Fock (HF) method. It is usually used to solve time-independent Schrödinger equation for many-electron systems. This method is not complete either as it uses many approximations that includes (i) Born-Oppenheimer approximation (ii) The relativistic effects are not taken into

consideration (iii) The specific interaction of an electron to other is neglected and mean field of electrons is taken into account. The Hamiltonian for a system with M point charges (nuclei) and N electrons can be written as shown in equation 1.

$$H = - \underbrace{\sum_{i=1}^N \frac{1}{2} \nabla_i^2}_{T_e} - \underbrace{\sum_{A=1}^M \frac{1}{2M_A} \nabla_A^2}_{T_n} - \underbrace{\sum_{i=1}^N \sum_{A=1}^M \frac{Z_A}{r_{iA}}}_{V_{en}} + \underbrace{\sum_{i=1}^N \sum_{j>i}^N \frac{1}{r_{ij}}}_{V_{ee}} + \underbrace{\sum_{A=1}^M \sum_{B>A}^M \frac{Z_A Z_B}{R_{AB}}}_{V_{nn}} \quad (1)$$

Where T_e = the operator electronic kinetic energy

T_n = the operator for nuclear kinetic energy

V_{en} = the operator for coulomb interaction between electron and nuclei

V_{nn} = the operator for coulomb interaction between nuclei

V_{ee} = the operator for coulomb interaction between electrons

Z = atomic charge on nuclei

M_A = ratio of mass of atom to the that of electron

With Born Oppenheimer approximation, electronic Hamiltonian can be written as:

$$H_{elec} = - \sum_{i=1}^N \frac{1}{2} \nabla_i^2 - \sum_{i=1}^N \sum_{A=1}^M \frac{Z_A}{r_{iA}} + \sum_{i=1}^N \sum_{j>i}^N \frac{1}{r_{ij}} \quad (2)$$

And the total energy of system is given by

$$E_{tot} = E_{elec} + \sum_{A=1}^M \sum_{B>A}^M \frac{Z_A Z_B}{R_{AB}} \quad (3)$$

The various other *ab-initio* methods are Møller Plesset (MP), Coupled Cluster (CC), Multi-configurational self-consistent field, Multi-reference configuration interaction etc. This type of method is practical to small molecules only.

Semi-empirical methods: In this method, a simpler Hamiltonian is employed and it uses parameters whose values are adjusted to fit to the results of *ab-initio* calculations or the experimental data. These calculations are faster than the *ab-initio* calculations, so larger systems could also be studied with semi-empirical method. However, one needs to be careful about choosing the molecule to parametrize the method. If the molecule is not similar to the molecule used to parametrize the method, the results could deviate significantly.

Molecular Mechanics (MM): It is not a quantum-mechanical method since it does not use Hamiltonian, wave function or electron density. The molecule is treated as the set of atoms held together by bonds and molecular energy is expressed in form of the force constants and bond stretching, bending, out-of-plane bending, and torsion. This method can be used for very large systems with many thousand atoms.

Density functional methods (DFT):

Density functional method is an approach for the description of ground-state of metals, semiconductors, insulators. The basic difference between the DFT⁸⁹ and other theoretical methods is that it does not take into account the calculation of wave-function (Φ) for many-body system rather it calculates the energy of the system in terms of the electron density (ρ). Therefore, system is now very easy to

deal with as we have now only three variables instead of having $3N$ degrees of freedom for a system with N electrons. So, expressing energy in form of electron density reduces the computational complexity. This is actually the underlying principle (theorem) of the DFT. A lot of knowledge about the chemical properties of the system can be obtained using DFT. The basic principles (Theorems) of the DFT are described below.

First Hohenberg-Kohn (H-K) Theorem: It states that electron density of the system determines the ground-state properties of the system. This means $E = E[\rho]$ where ρ is the ground state electron density of the system.

Second Hohenberg-Kohn (H-K) Theorem: It states that there exists a variational principle for the energy density functional, $E[\rho]$. This means $E[\rho'] > E[\rho]$ where ρ' is not the actual electron density of the system.

In the Kohn-Sham⁹⁰ approach the interacting electrons in the system are treated as the non-interacting particles in an effective potential such that actual electron density is not affected.

Therefore energy functional of the system can be written as,

$$E[\rho] = T[\rho] + E_{\text{ext}}[\rho] + E_{\text{coul}}[\rho] + E_{\text{xc}}[\rho] \quad (4)$$

In DFT, the fourth term in (4), exchange-correlational functional, is not known exactly and approximation to that is employed which then results into numerous density functional methods and some common functional are listed below.

1. Local Density Approximation (LDA): This approximation assumes that the electron density does not vary much and it can be calculated using a homogeneous electron gas functional which in reality is inhomogeneous.
2. Generalized Gradient Approach⁹¹: The DFT methods are further improved by taking into account the inhomogeneous nature of electron density. Therefore, a gradient for electron density is considered in this type of exchange-correlation functional.
3. Hybrid Methods: In this type of functional, both exchange and correlation are taken care of. One of the most common type of hybrid functional is B3LYP⁹²⁻⁹⁵ where B3 stands for three parameter Becke exchange correlation functional (gradient corrected) and LYP is Lee-Yang-Parr correlational function. B3LYP functional is one of the commonly used functional by inorganic, organic, and organometallic chemists for carrying out their computations and is more reliable than gradient corrected functional.

2.3.2 Computational methodology

The DFT calculations were carried out at the B3LYP level of theory using 6-31G(d) basis set for C, H, N, S, O, and P atoms and LanL2DZ basis set for Ru atom with effective core potential. The initial coordinates for precatalyst L^1RuPPh_3 were obtained from the crystal structure and for L^2RuPPh_3 , and L^3RuPPh_3 coordinates were generated from L^1RuPPh_3 by addition of required number of oxygen atoms. The initial coordinates for derivatives of precatalyst L^1RuPPh_3

(benzonitrile/water at the place of PPh_3 etc.) were obtained by substituting the phosphine with the corresponding group and then it was optimized. Similar methodology was undertaken for derivatives of precatalysts L^2RuPPh_3 , and L^3RuPPh_3 . The optimized coordinates are listed for all the compounds. The calculations were carried out in gas phase as well as in solution phase, using N, N'-dimethylformamide (DMF) solvent. The polarity effect of bulk solvent was evaluated by the conductor-like polarized continuum model (CPCM) at the same level of theory. The frequency calculations were performed at the aforementioned level of theory to identify the nature of all stationary points and the transition states were identified as the one with only single negative frequency. All the reported enthalpies and free energies of reactions have been corrected for zero-point energies. All quantum-chemical calculations were performed with *Gaussian09* program package. The chemcraft software was utilized for visualization.

2.3.3 Setting-up calculation at the Cardinal Research Cluster (CRC)

In this section, details are provided how to connect computer to CRC of University of Louisville and set-up the computational job. Thereafter, commands (keywords) for geometry optimization, frequency calculation, and transition state (TS) calculations are listed and a complete sample input file for computational job is provided and discussed.

First of all, to connect the computer to the CRC, a user interface namely PuTTY, available free of charge, needs to be installed. With required information filled into

the PuTTY (Figure 2.2), then one is able to connect to CRC and the required information is provided below.

Host Name: username@crc.hpc.louisville.edu

Port: 22

Connection Type: SSH

Figure 2.2. The picture showing log in information to connect to CRC

Once the aforementioned information is filled in, then click on load and open icons, respectively. The above information can also be saved and a nick name could be given which saves some time next time one wants to connect to CRC.

This action should lead to connection to CRC which results into a different black screen that would require the password to finally log in to CRC (Figure 2.3). Once in CRC, directories could be made using the following command: `mkdir directory name`. The files can be transferred to the particular directory using software called WinSCP which connects the computer to CRC and is used to transfer file either download or upload.

Figure 2.3 The picture showing terminal once connected to CRC successfully

Input file has .com extension and a sample contents of input file are described below. The input file can be generated from the crystal structure by removing the solvent molecule using Mercury software, if any. The file in mercury can be saved with .xyz extension. Furthermore, when transferred to CRC, its extension should be .com. The two commands for that are used to convert the file into unix format and then to move the contents from the xyz file to com file are given below:

```
dos2unix filename.xyz
```

```
mv filename.xyz filename.com
```

Sample input file for Gaussian for a metal complex:

%mem=1000MB (memory used to store) (Line1)

%nproc=8 (number of processors used) (Line2)

%chk=file name (check point file) (Line3)

#p B3LYP/Gen Pseudo=Read opt (Job type) (Line4)

Empty line (needed as per syntax) (Line5)

Title of calculation (just for you to remind) (Line6)

Empty line (needed as per syntax) (Line7)

0, 1 (charge on complex, spin multiplicity) (Line8)

Coordinates of complex (Line9-14)

Empty line (need as per syntax) (Line15)

C H N S O P O (Line16)

6-31G(d) (basis sets used for C, H, N, S, and O atoms in complex) (Line16)

Ru 0	(Line17)	
LANL2DZ	(basis set used for Ru atom with core potential)	(Line18)
*****	(Line19)	
Empty line	(needed as per syntax)	(Line20)
Ru 0		(Line21)
LANL2		(Line22)
Empty line	(needed as per syntax)	(Line23)
Empty line	(needed as per syntax)	(Line24)
Empty line	(needed as per syntax)	(Line25)
Empty line	(needed as per syntax)	(Line26)
End of file		

Line by line explanation of the input file:

Line1: Defines the memory used to store data. For a typical metal complex with ~ 100 atoms 1000MB is fine.

Line2: Defines the number of processors used to run the job which is 8 here and are maximum.

Line3: This command creates a check point file which in case if you need to restart the calculation, if it doesn't optimize in the end, then final geometry from check point file serves as the input geometry/coordinates.

Line4: This line is the command line that defines the type of calculation and functional, basis set to be used in the job. In this particular calculation, B3LYP functional is used to perform the geometry optimization and basis set is defined by using Gen keyword that means we are using different basis sets for different atoms and those are defined in the end of input file (Line15-22).

Line5: It should be left empty and is required as per syntax.

Line6: This describes the title of the job to help one recall what type of calculation we are running. It is for us only and is not read by program while running the job.

Line7: It should be left empty and is required as per syntax.

Line8: This describes the charge and spin multiplicity ($2S+1$) of the system under study.

Line9-14: These lines contain the coordinates of the system under study and can be longer depending upon the size of the system.

Line15: It should be left empty and is required as per syntax.

Line16-19: It defines the basis sets used for different atoms.

Line20: It should be left empty as per syntax.

Line 21-23: This line defines the core potential for the Ru atom.

Line 24-26: As per syntax, 4-5 lines should be left empty after defining the basis set.

Whenever a different calculation is need to be performed with same functional and basis set the only thing that changes is the Line4 in the sample input file and that too just the keyword. The different keywords and their function is discussed below. Just a reminder, spaces and empty lines are very critical to run a smooth calculation otherwise syntax errors show up all the time.

Different keyword for different jobs:

Opt performs geometry optimization to locate the global minima (gas phase)

Opt freq optimization followed by frequency calculation to ensure it is either intermediate or a transition state. If in frequency calculation, an imaginary frequency is there, this means it is not a stable structure and is near or a transition state. Frequency calculation is also called the thermodynamic calculation since it calculates the thermodynamic parameters like enthalpy, free energy and others that can used to form a potential energy surface for reaction modeling

Opt scrf=(solvent=water) performs geometry optimization in solvent water.

Opt freq scrf=(solvent=water) optimization, frequency calculation in solvent water

Opt=(calcfc, TS, noeigentest) freq locates transition state calculation in gas phase

Opt=(calcfc, TS, noeigentest) scrf=(solvent=water) freq locates transition
state calculation in solvent phase

Before one can run the calculation, a script file (.sh extension) is needed and a sample script file is provided below:

```
#!/bin/bash -l
```

```
module load g09
```

```
cd /home/username/directory name
```

```
g09 filename.com
```

The g09 represents that the job will run with the Gaussian 09 software if you want you can run with g03 too which is Gaussian 03 version.

The command used to run the calculation is provided below:

```
qsub -q short -l nodes=1:ppn=8,walltime=24:00:00 filename.sh
```

This means the job will run under short queue for which maximum time set is 24 hours if you think that your job may take more than 24 h you can change the queue from short to long that can go upto 168 hours (7 days).

The progress of job can be checked by looking at the log file with same file name which is created as soon as the job starts to run. In the next Chapter, catalytic assays with $L^{1-3}RuPPh_3$ are described with varying conditions to assess the effect of sulfur-oxidation on nitrile hydration.

CHAPTER 3

CATALYTIC AND MECHANISTIC STUDIES UNDER BIPHASIC CONDITIONS

This Chapter summarizes the catalytic nitrile hydration activity of complexes L^1RuPPh_3 (**48**), L^2RuPPh_3 (**49**), and L^3RuPPh_3 (**50**) in biphasic mixtures under pH neutral conditions. Reactions were performed neat without the use of external base or solvent. Reaction optimization has been carried out via assays under various substrate ratios. The effect of sulfur-oxidation has been assessed by comparing the turnover number (TON) for these series of catalysts. Further insights into the function of these catalysts have been probed via inhibition assays using different reaction temperatures or by addition of excess phosphine or benzamide product. The effect of metal-centered oxidation on catalytic activity was also probed via one-electron oxidation of the Ru(II) to Ru(III) using one equivalent of ferrocenium hexafluorophosphate ($FcPF_6$). All catalytic assays were carried out using the *very low loading (ppm level)* of catalysts.

3.1 Overview of the Ru catalysts that catalyze nitrile hydration

3.1.1 Water-insoluble Ru complexes for nitrile hydration

Typical nitrile hydration reactions in the absence of metal catalysts require the use of harsh conditions, such as high temperature and/or pressure in highly acidic/basic media, because of the highly inert nature of the nitrile (CN) functional group.^{2-3,96} However, the use of metal complexes eases the reaction conditions through the interaction of the nitrile nitrogen with the metal, which lowers the reaction barrier by polarization of the nitrile carbon and/or via metal activation of the water or hydroxide nucleophile. The use of metal complexes provides an attractive method to carry out catalytic nitrile hydration under relatively milder conditions with accelerated rates of the order of $10^6 - 10^9$. To date, many examples of metal complexes that catalyze nitrile hydration to amides under both homogeneous and heterogeneous conditions have been reported in the literature. These complexes employ metals such as Pt,⁹⁷⁻⁹⁹ Ni,¹⁰⁰⁻¹⁰¹ Os,¹⁰²⁻¹⁰³ Hg,¹⁰⁴⁻¹⁰⁶ Co,^{104,107} Rh,¹⁰⁸ Mo,¹⁰⁹⁻¹¹⁰ Ir,¹¹¹ Pd,⁹⁸ Au,¹¹²⁻¹¹³ Zn,¹⁰¹ W¹¹⁴, and Ru¹¹⁵⁻¹²² under homogeneous conditions as mononuclear as well as multi-nuclear¹²³ metal complexes. Given the focus of this dissertation on Ru-based complexes, typical examples of nitrile hydration catalysts that employ Ru are summarized in the following section.

The first example of stoichiometric nitrile hydration by a Ru complex was reported by Taube and coworkers in 1970's.¹⁰² The simple complex pentaamminechlororuthenium(III) chloride $[\text{Ru}(\text{NH}_3)_5\text{Cl}][\text{Cl}]_2$ (**52**) coupled with Ag_2O and trifluoroacetic acid and zinc amalgam led to hydration of aliphatic,

aromatic, and vinyl nitriles in high yields (64-95%) at 40-50 °C in dichloromethane solvent. (Fig. 3.1)

Figure 3.1. Stoichiometric nitrile hydration with ruthenium complex

The first example of catalytic nitrile hydration was reported by Murahashi and coworkers where they used PPh_3 as the ligand. The ruthenium-dihydride complex $[\text{Ru}(\text{H})_2(\text{PPh}_3)_4]$ (**53**) was able to hydrate various type of nitriles catalytically to amides at elevated temperatures producing excellent yields under pH neutral conditions in 1, 2-dimethoxyethane (DME) solvent (Fig. 3.2).¹²⁰⁻¹²¹ An inner-coordination sphere mechanism was proposed in which the nitrile first binds, displacing one of the phosphine. Then, nucleophilic attack by water leads to formation of an iminol intermediate that rearranges to the product-bound species. Further, the amide is replaced by the substrate nitrile to complete the catalytic cycle. However, the TOF ($\sim 2 \text{ h}^{-1}$) was low.

Mechanism:

Figure 3.2. Proposed mechanism for nitrile hydration by RuH₂(PPh₃)₄ [Ru]

An interesting application of the catalyst RuH₂(PPh₃)₄ is the conversion of δ -ketonitriles to corresponding ene-lactams through a tandem process. The process was used in the synthesis of the alkaloid (–)-pumiliotoxin C, which is found in the skin of poison dart frogs and interferes with muscle contraction causing paralysis.

Lau and coworkers reported the complex [RuH(η^5 -C₉H₇)(dppm)] (**54**) as the nitrile hydration catalyst.¹¹⁷ This work signified a pivotal role for the hydride ligand in tuning catalytic activity.

Proposed Transition State:

Figure 3.3. The catalyst $[\text{RuH}(\eta^5\text{-C}_9\text{H}_7)(\text{dppm})]$ (left) and the proposed transition state showing H-bonding promoted hydration (right).

As shown in Figure 3.3, a proposed H-bonding interaction between the coordinated hydride and incoming water promotes hydration. This system can also be regarded as a bi-functional catalyst where the metal and ligand cooperate to extensively lower the activation barrier. A TON of 865 and TOF of 12 h⁻¹ was observed for **54**.

Another example of a bi-functional catalyst for nitrile hydration was reported by Oshiki and co-workers. The series of catalysts based on *cis*- $[\text{Ru}(\text{acac})_2(\text{PPh}_2\text{py})_2]$ (**55**) (Fig. 3.4) stress the role of ancillary ligands to tunes catalyst activity.¹²⁴ The corresponding triphenylphosphine, and other phosphine derivatives that lack H-bonding functional groups, are less active towards nitrile hydration. A temperature dependent activity was noticed for **55**.

TOF = 20900 h⁻¹ @ 180 °C

TOF = 222 h⁻¹ @ 150 °C

Figure 3.4. Effect of ancillary ligand in second coordination sphere to promote nitrile hydration

3.1.3 Water soluble Ru nitrile hydration catalysts

The role of the ligand in modulating the catalytic activity of Ru complexes was further explored through ligands that also enhanced water-solubility. The aim was to develop *green catalysts* that would function in water without the requirement of the organic solvent. In 2010, Cadierno and coworkers reported a series of catalysts with the general formula [RuCl₂{κ¹(P)-3-PPh₂C₆H₄CH₂NHR}(η⁶-arene)] (arene = benzene or cymene) (Fig. 3.5). The catalysts functioned in neat water and were able to hydrate benzonitrile and other substituted nitriles. These catalysts were proposed to function through protonation of the aminoarylphosphines (that acted as Brønsted bases) to generate nucleophilic hydroxide in the solution. The hypothesis was further validated when reaction rate was enhanced with the use of external amines (PhCH₂NHR) with PPh₃.

Figure 3.5 Role of H-atom acceptor ancillary ligand in promoting nitrile hydration

To enhance the reactivity and solubility of Ru complexes in the water, various types of water-soluble phosphines (PTA, PTA-Bn, DAPTA, THPA) have been employed by various research groups as summarized in Fig. 3.6.¹²⁵⁻¹²⁶ All these phosphine have multiple N atoms that provide a chassis for the H-bond acceptor from water and hence improve the solubility of the complex in water even better than the sulfonated phosphines. Hence, various complexes are reported to perform nitrile hydration efficiently in water using these phosphines.

Figure 3.6. General scheme of Ru-arene catalysts with water-soluble phosphines

The ligand cooperativity effect was utilized by Cadierno and coworkers to enhance nitrile hydration. The complex [RuCl₂(C₆Me₆){P(NMe₂)₃}] (**61**) is a highly active water-soluble nitrile hydration catalyst with TOF up to 11,400 h⁻¹ when heated under microwave (MW) radiations. (Fig. 3.7).¹¹⁸

Figure 3.7. Nitrile hydration catalyst [RuCl₂(C₆Me₆){P(NMe₂)₃}] operating via H-bonding through ancillary ligands

Tyler and coworkers employed the concept of H-bonding for the hydration of difficult cyanohydrin substrates.¹²⁷ Glyconitrile and lactonitrile were efficiently hydrated at room temperature in the pH range of 3.5-8.5 (Fig. 3.8), while low-yield hydration of acetone cyanohydrin (a precursor to methyl methacrylate, which when polymerized gives poly(methylmethacrylate) PMMA) was also observed.

Figure 3.8. Cyanohydrin hydration using H-bonding via ancillary ligands with $[RuCl_2(C_6Me_6)\{P(NMe_2)_3\}]$

3.3 Catalytic benzonitrile hydration assays with $L^{1-3}RuPPh_3$ (**48-50**)

The X-ray crystal structures of $L^{1-3}RuPPh_3$ (**48-50**) displayed an elongation in the Ru-P bond distance as a function of sulfur-oxidation (Fig. 3.9).⁸⁰⁻⁸¹ Preliminary room temperature catalytic assays using acetonitrile as the substrate revealed no activity for complexes $L^{1-2}RuPPh_3$ with sub-stoichiometric nitrile hydration for L^3RuPPh_3 . We anticipated that elevated temperature would lead to phosphine dissociation opening a vacant site for substrate binding and promoting hydration activity. Therefore, we evaluated this series of complexes at elevated temperature for nitrile hydration activity.

Figure 3.9. Catalysts $L^{1-3}RuPPh_3$ and increase in Ru-P bond distance as a function of sulfur-oxidation.

Prior to catalytic assays, a calibration curve was prepared at benzamide concentrations of 0.21%, 0.10%, 0.050%, 0.010%, and 0.00050% (w/v) in diethyl ether using GC-MS (Fig. 3.10). Next, stock solutions of catalysts $L^{1-3}RuPPh_3$ were prepared in the degassed benzonitrile (PhCN) under an inert atmosphere. For each catalytic trial, an aliquot of the stock solution was diluted with the desired quantities of degassed benzonitrile and degassed water to obtain the targeted catalyst concentration and substrate ratio.

For trials 1-5 (Table 3.1) and trials 2-4 (Table 3.2) trial 2-6 (Table 3.3), a 0.500 mL aliquot of the L^1RuPPh_3 stock solution (5.4×10^{-4} M), measured using an automatic micropipette, was transferred to 3 mL screw-top vial containing the desired quantities of benzonitrile and water to make a total volume of 2.000 mL. For trials 1 (Table 3.2 and 3.3), with a nitrile:water ratio of 0.14, only 0.250 mL of stock solution was used with dilution to a total volume of 2.000 mL by addition of water. In each experiment, the vial was capped using an air-tight Teflon screw cap under an argon atmosphere. The reaction mixture was heated at 124°C in an oil

bath for 18 hours. After the reaction, the nitrile and water were removed under reduced pressure with the assistance of a water bath at 50°C. The metal complex was separated from benzamide by a short silica-gel column using diethyl ether as an eluent. Diethyl ether was removed in vacuo to isolate pure benzamide. GC-MS analysis of the product residue with proper dilution in diethyl ether was used to determine turnover number (TON). The product benzamide was validated against an authentic sample of benzamide. No hydrolysis to benzoic acid or other organic products were detected. The results obtained for the catalyst L^1RuPPh_3 are discussed below.

Figure 3.10. Calibration curve using various concentrations (w/v%) of benzamide

Table 3.1. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L¹RuPPh₃ (**48**) at 124 °C in neat substrate mixtures at neutral pH.

Entry	Catalyst (mol%)	V _{PhCN} /V _{H₂O}	TON	TOF (h ⁻¹)
1	0.0055	0.33	66 ± 1	3.7 ± 1
2	0.0027	1.00	91 ± 3	5.1 ± 2
3	0.0018	3.00	188 ± 32	10 ± 2
4	0.0017	4.00	176 ± 26	10 ± 1
5	0.0015	7.00	28 ± 4	1.5 ± 2

Table 3.1 summarizes TON and TOF (h⁻¹) of isolated benzamide product using L¹RuPPh₃ as catalyst. Each trial employ same molar quantity of catalyst. A TON of 66 ± 1 (Table 3.1, entry 1) was observed for catalyst L¹RuPPh₃ at the nitrile to water ratio of 0.33 with the corresponding TOF of 3.7 ± 1 h⁻¹.¹²⁸ Changing the substrate ratio to 1.00 (Table 3.1, entry 2) resulted in a slight increase in the TON to 91 ± 3 with the corresponding TOF of 5.1 ± 2. Further increase in the substrate ratio from 1.00 to 3.00 (Table 3.1, entry 3) raised the TON two-fold to 188 ± 32 with a TOF of 10 ± 2 h⁻¹. The increase in TON concomitant with change in substrate ratio is attributed to the balance between the substrate binding and product inhibition offered by binding of the benzamide. Increasing the substrate ratio to 4.00 did not further change the activity of the catalyst significantly (Table 3.1, entry 4). However, at a substrate ratio of 7.00 (Table 3.1, entry 5) the catalytic activity was greatly suppressed producing only 28 ± 4 TON and a TOF of 1.5 ± 2

h^{-1} . The decrease in catalytic activity at high nitrile to water ratio is attributed to the dilution of catalyst concentration. Catalytic assays with stirring of the mixture did not significantly alter the turnover. Attempts to recycle the catalyst led to irreproducible results attributed to difficulties in accurately quantifying the small amount (microgram quantity) of recovered catalyst.

After acquiring the catalytic assay data above, we designed assays to gain further insight into the functioning of the catalyst. We anticipated the high temperature ($124\text{ }^{\circ}\text{C}$) is required for the reaction to dissociate phosphine, which is entropically favored. Dissociation of the phosphine from L^1RuPPh_3 results into the formation of the pentacoordinate complex L^1Ru , which is the putative active catalyst (Fig. 3.11). The pentacoordinate complex now has an open binding site for the exogenous ligand such as nitrile or water and hence the catalytic activity is observed.

Figure 3.11. Equilibrium between precatalyst and active catalyst for L^1RuPPh_3 at elevated temperature

To test the aforementioned hypothesis, we first tried decreasing the temperature from the $124\text{ }^{\circ}\text{C}$ to $74\text{ }^{\circ}\text{C}$ at a substrate ratio of 1.0. We envisioned that lowering the reaction temperature would lead to decrease in the catalytic activity. Indeed, at $74\text{ }^{\circ}\text{C}$ a TON of only 28 ± 3 was observed, as compared to the TON of 91 ± 3

observed at 125 °C under the same substrate ratio. The observed TON at lower temperature are still higher than the background reaction at 125 °C, which produced 8 ± 2 TON. Thus the decrease in temperature by 50 °C led to a reduction in activity by 85 % that is attributed to poor phosphine lability at the lower temperature (Fig. 3.12). We further anticipated that excess phosphine would shift the equilibrium back to the parent six coordinate complex L^1RuPPh_3 decreasing catalytic activity. Catalytic assays carried out at substrate ratio 0.33 at 125 °C with an additional 105 equivalents of PPh_3 led to a decrease in the catalytic activity by 82 % (Fig. 3.12) producing only 11 ± 1 TON after 18 hours as compared to 66 ± 1 TON observed in the absence of PPh_3 . The TON produced with excess phosphine is statistically similar to the background reaction in absence of the catalyst that produced only 8 ± 2 TON.

Figure 3.12. Shift of equilibrium with excess phosphine in reaction mixture for L^1RuPPh_3

Additionally, we evaluated the tolerance of our catalyst to air exposure. Catalytic assays carried out with exposure to air lead to a decrease in activity. Under a substrate ratio of 0.33, a 50% reduction in TON was observed on air-exposure of the catalytic mixture. This is attributed to oxidation of Ru(II) to Ru(III) on the introduction of air. It was further confirmed that chemical oxidation of L^1RuPPh_3

(Fig. 3.13) with one equivalent of ferrocenium hexafluorophosphate (FcPF_6) led to an inactive complex and no benzamide product was detected.

We attribute the decreased activity of L^1RuPPh_3 upon of air exposure to catalyst inactivation via metal centered oxidation. As described in the Chapter 1, air exposure of methanolic solution of the L^1RuPPh_3 to air leads to formation of $\text{L}^{2-4}\text{RuPPh}_3$ via ligand-centered oxidation,^{3,80-81} whereas the introduction of air to benzonitrile solution proceeds through metal-centered oxidation to Ru(III). The lack of hydration activity of the Ru(III) derivative $[\text{L}^1\text{RuPPh}_3]^+$ is intriguing as it is known that the oxidation of $[\text{Ru}(\text{NH}_3)_5(\text{NCR})]^{2+}$ to $[\text{Ru}(\text{NH}_3)_5(\text{NCR})]^{3+}$ enhances the rate of nitrile hydration by six orders of magnitude.¹⁰⁸ However, the rate of hydration is not the only factor that determines the TON. The catalyst also needs to release product to turnover. The literature example of enhanced hydration with $[\text{Ru}(\text{NH}_3)_5(\text{NCR})]^{3+}$ is stoichiometric. We anticipate similar reactivity with our complex, although the Ru(III) derivative has not been fully characterized. Recently, Kovacs and coworkers reported Co(III) complexes that hydrate acetonitrile to give the corresponding iminol and amidate species, but without product release.⁵⁴

Figure 3.13. Oxidation of L^1RuPPh_3 with FcPF_6 and dioxygen

Table 3.2. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L^2RuPPh_3 (**49**) at 124 °C in neat substrate mixtures at neutral pH.

Entry	Catalyst (mol%)	V_{PhCN}/V_{H_2O}	TON	TOF (h^{-1})
1	0.0055	0.14	238 ± 23	13 ± 1
2	0.0055	0.33	88 ± 9	4.9 ± 0.5
3	0.0027	1.00	33 ± 8	1.8 ± 0.4
4	0.0018	3.00	0	0

As a next step, we moved to catalyst L^2RuPPh_3 to determine the effect of sulfur-oxidation to thiolato/sulfinato on catalytic nitrile hydration. Results are summarized in Table 3.2. High catalytic activity was observed at a substrate ratio of 0.14 (Table 3.2, entry 1) resulting in 238 ± 23 TON and a TOF of $13 \pm 1 h^{-1}$. Increase in substrate ratio to 0.33 (Table 3.2, entry 2) resulted in a drop of TON to 88 ± 9 with a corresponding TOF of $4.9 \pm 0.5 h^{-1}$. The decrease in catalytic activity is attributed to dilution of the catalyst. Comparing the catalyst L^1RuPPh_3 with L^2RuPPh_3 , sulfur-oxidation led to increased nitrile hydration activity when comparing the two catalysts under identical substrate ratio (Table 3.1, entry 1; Table 3.2, entry 2). Further increase in the substrate ratio led to a lower TON (Table 3.2, entry 3). However, no benzamide product was detected under a substrate ratio of 3.00 (Table 3.2, entry 4). Interestingly, the catalyst L^2RuPPh_3 exhibited maximum catalytic activity at the lower nitrile:water ratio.

After this, the catalyst L^3RuPPh_3 was employed for the catalytic assays. The results of catalytic assays are summarized in the Table 3.3. The catalyst L^3RuPPh_3 displayed activity very similar to L^2RuPPh_3 . The catalyst L^3RuPPh_3 exhibited maximum activity at the lower nitrile:water ratio of 0.14 (Table 3.3, entry 1) producing 242 ± 23 TON with an associated TOF of 13 ± 1 h⁻¹. The observed catalytic activity for L^3RuPPh_3 is statistically similar to what is observed for the catalyst L^2RuPPh_3 . Increasing the nitrile:water ratio resulted into lowering of the catalytic activity (Table 3.3, entry 2-6), a trend also observed for the catalyst L^2RuPPh_3 . The decrease in activity can be ascribed to the dilution effects that sequentially result into the lower catalyst concentration and thereby produce lower TON.

Table 3.3. Benzonitrile hydration turnover number (TON) and turnover frequency (TOF) values for catalyst L^3RuPPh_3 (**50**) at 124 °C in neat substrate mixtures at neutral pH.

Entry	Catalyst (mol%)	V_{PhCN}/V_{H_2O}	TON	TOF (h ⁻¹)
1	0.0055	0.14	242 ± 23	13 ± 1
2	0.0055	0.33	86 ± 11	4.8 ± 0.6
3	0.0027	1.00	38 ± 10	2.1 ± 0.5
4	0.0018	3.00	23 ± 7	1.3 ± 0.4
5	0.0017	4.00	2 ± 1	0.11 ± 0.05
6	0.0015	7.00	2 ± 1	0.11 ± 0.05

It is quite intriguing that the catalyst L^1RuPPh_3 exhibited optimum activity at the substrate ratio (3.0-4.0) where the dilution and product inhibition effects are balanced whereas the catalysts L^2RuPPh_3 and L^3RuPPh_3 displayed maximum activity at the lower substrate ratio (0.14). Careful inspection of results acquired for the catalytic assays led to the following hypothesis. The catalyst L^1RuPPh_3 stops turning over after reaching a product benzamide concentration ca. 32 ± 5 mM (except entry 5, Table 3.4, where dilution effects are predominant). For the L^2RuPPh_3 and L^3RuPPh_3 both achieve product concentrations up to 129 ± 12 mM. From these observations, we proposed that L^1RuPPh_3 is being inhibited by the product, whereas L^2RuPPh_3 and L^3RuPPh_3 are less prone to product inhibition and optimal TON are dictated by dilution effects.

Table 3.4. Summary of final benzamide concentrations achieved for the three catalysts $L^{1-3}RuPPh_3$ under different substrate ratio

Entry	V_{PhCN}/V_{H_2O}	L^1RuPPh_3 [benzamide] ^a mM	L^2RuPPh_3 [benzamide] ^a mM	L^3RuPPh_3 [benzamide] ^a mM
1	0.33	35.1 ± 0.5	129 ± 12	131 ± 12
2	1.00	24.6 ± 0.8	48 ± 5	46 ± 6
3	3.00	32 ± 5	9 ± 2	10 ± 3
4	4.00	32 ± 5	0 ^b	4 ± 1
5	7.00	4.2 ± 0.6	0 ^b	0.3 ± 0.2

^aFinal concentration of benzamide in the benzonitrile layer calculated from total moles of benzamide product and initial benzonitrile volume.

^bNo benzamide was detected

The aforementioned hypothesis was independently tested for each of three catalysts. The catalytic assays were carried out for $L^{1-3}RuPPh_3$ with the external addition of the benzamide commensurate to achieve the final benzamide concentration. Each reaction was run using the same protocol as above for 18 h. Product was isolated, yield quantified, and results compared to TON in the absence of added product. The summary of results is listed below in the Table 3.5. The results of these inhibition assays indicate that in the presence of the 36.3 mM benzamide L^1RuPPh_3 displayed only 19 % activity accounting only to 35 ± 2 TON. Therefore, benzamide greatly inhibits the activity of L^1RuPPh_3 by binding at the metal center. Interestingly, the sulfur-oxidized catalyst L^2RuPPh_3 displayed much better activity in the presence of benzamide. The catalyst L^2RuPPh_3 produced a final benzamide concentration of 73 ± 6 mM even with the addition of 51 mM of the benzamide. It accounted for the 50 % activity of the catalyst with the associated 41 ± 3 TON. Therefore, it is suggested that the sulfur-oxidation tunes the binding of the product at the metal center. A similar 50 % of the activity is achieved for L^3RuPPh_3 in the presence of 51 mM of the benzamide that accounts for 44 ± 5 TON. The results are consistent with reduced product inhibition for sulfur-oxidized catalysts $L^{2-3}RuPPh_3$ as compared to L^1RuPPh_3 .

This decreased product inhibition of the sulfur-oxidized catalysts may be due to participation of sulfinate/sulfenate moiety in non-covalent H-bonding interactions ($Ru-S-O \cdots H_2NC(O)Ph$) with benzamide. This could help in removal of the product. Alternately, increased steric interactions between the benzamide and sulfinate/sulfenate may contribute. This result can be directly related to the enzyme

NHase which selectively binds nitrile and exhibits activity only when the sulfurs are post-translationally modified. Therefore oxidized sulfurs could help in removal of amide product at the active site and also hydrating the nitrile efficiently, as suggested by our results, thereby tuning the activity of the enzyme.

Table 3.5. Product inhibition assays for the catalysts $L^{1-3}RuPPh_3$ (**48-50**) under neat substrate mixtures and neutral pH at 124 °C

Entry	Catalyst	[benzamide] _{initial} (mM)	[benzamide] _{final} (mM)	TON
1	L^1RuPPh_3	0	32 ± 5	188 ± 32
2	L^1RuPPh_3	36.3	42.6 ± 0.4	35 ± 2
3	L^2RuPPh_3	0	48 ± 5	88 ± 9
4	L^2RuPPh_3	51	73 ± 6	41 ± 3
5	L^3RuPPh_3	0	46 ± 6	86 ± 11
6	L^3RuPPh_3	51	75 ± 8	44 ± 5

Final benzamide concentrations in the absence (entries 1, 3, 5) and presence of added benzamide (entries 2, 4, 6). Calculated TON based on the difference between final and initial moles of benzamide.

Through these extensive catalytic assays performed on $L^{1-3}RuPPh_3$ we are able to produce high TON for benzonitrile hydration exclusively to benzamide under the neat substrate mixtures with very low loading of the catalysts at the *ppm levels*. Also, the catalytic activity is achieved without the assistance of external base or buffer and under pH neutral conditions. Overall, these results suggest that sulfur-oxidation enhances the nitrile hydration at the lower nitrile:water ratio and reduces the inhibition offered by the product.

The activity of the catalysts $L^{1-3}RuPPh_3$ was compared with the Co-NHase since Ru(II) is isoelectronic with the Co(III). The activity of enzyme is expressed in terms of specific activity ($U\ mg^{-1}$) and one unit of which is defined as the μ moles of the product per mg catalyst per minute. The Co-NHase isolated from the bacteria *Rhodococcus J1* has a specific activity of $120\ U\ mg^{-1}$ for benzonitrile substrate.^{4,129} Under the optimum conditions, L^2RuPPh_3 and L^3RuPPh_3 display a specific activity of $0.30\ U\ mg^{-1}$ whereas the catalyst L^1RuPPh_3 has associated specific activity of $0.24\ U\ mg^{-1}$. Therefore, specific activity of our system is 400 times lower than the enzyme. That could be due to various reasons since our complexes lack contribution from second/outer coordination sphere that are very crucial to the activity of the enzyme and Co(III) being more Lewis-acidic than Ru(II) can activate the nitrile better and lower the activation barrier. The studies discussed in this Chapter were published in *Chemical Communications* 2013, **49**, 294-296.

The results from biphasic catalytic assays in this Chapter suggest that sulfur-oxidation leads to increase in the catalytic activity. However, very little can be ascertained regarding the mechanism or reaction kinetics under these conditions. For example, does S-oxidation promote activity by enhancing nitrile binding or promoting nitrile hydration? To answer these questions additional kinetic assays under homogeneous conditions are needed. These studies are the subject of Chapter 4.

CHAPTER 4

KINETIC AND THERMODYNAMIC STUDIES IN HOMOGENEOUS MEDIUM

This Chapter describes kinetic assays on the series of catalysts $L^{1-3}RuPPh_3$ to determine the effect of sulfur-oxidation on catalytic benzonitrile hydration. The studies described in Chapter 3 were under heterogeneous conditions, which precluded detailed mechanistic investigations. In this Chapter, homogeneous conditions, using N, N'- dimethylformamide (DMF) solvent were developed allowing our kinetic study. In this Chapter, we propose a reaction mechanism, derive its rate law, and present kinetic data consistent with our proposal. The kinetic investigations suggest that sulfur-oxidation modulates the water-nitrile equilibrium constant (K_2) with alternating behavior and enhances the nitrile hydration rate constant (k_3) by four-fold. Additionally, temperature dependent studies show that sulfur-oxidation lowers the activation barrier (E_a and $\Delta H^\ddagger$) for the benzonitrile hydration. Interestingly, the entropic barrier rises concomitant with sulfur-oxidation. The net result is that S-oxidation affects the nitrile hydration in multiple ways by enhancing the rate-determining hydration rate constant concomitant with decrease in enthalpic barrier that occurs through a highly organized transition state.

4.1 Chemical kinetics

Introduction to reaction rate

The term chemical kinetics refers to reaction rates, which can be defined as the change of concentration of reactant/product per unit time. Typical units to describe the rate of reaction are $\text{mol L}^{-1} \text{s}^{-1}$. Overall chemical reactions may be broken into a series of elementary steps to describe the mechanism of a reaction. The individual rates of these elementary steps vary with some being relatively fast whereas others are relatively slow. The slowest step determines the rate of the overall reaction and is known as the rate-determining step. The number of molecules participating in the slowest-step is called the molecularity of the reaction. Accordingly, the reactions can be classified as the unimolecular, bimolecular, termolecular, and so on. The reactants are transformed into the products when collision takes place between the different ions/molecules. Since the probability of many different ions/molecules coming together in a collision is lower, consequently the reactions of higher molecularity are rare in nature and most commonly we encounter unimolecular, and bimolecular reactions. It should be noted that molecularity is different from order of the reaction and order of the reaction can be determined only experimentally.

Kinetic studies are very important as these provide insights into the reaction mechanism and unravel the mechanistic details. With the enough knowledge of the reaction mechanism, we can further design strategies to improve the system to function better. The kinetic and mechanistic investigations tell us about the nature

of rate-determining step and what other elementary reactions affect the overall reaction rate. Kinetic studies tell us that how many molecules are participating in the rate-limiting step and also order with respect to each reactant can be determined only through kinetic assays.

4.2 Temperature dependence of the reaction rate constant and kinetic barrier

Reaction rates are dependent of temperature as it can affect the collision frequency (A) and the fraction of molecules crossing over the reaction barrier. Both these factors directly affect the reaction rate. In many instances, increase in reaction temperatures by 10 °C leads to an increase in reaction rate (constant) by a factor of 1.5 – 1.6.¹³⁰ However, the effect of temperature on any given reaction must be determined experimentally. The temperature dependence of reaction rate (constant) is given by Arrhenius equation (eq. 1).^{108,131}

$$k = A e^{-\frac{E_a}{RT}} \quad (1)$$

Taking logarithm on both sides of eq. 1 and rearranging the terms:

$$\ln k = \ln A - \frac{E_a}{RT} \quad (2)$$

Therefore, a plot of $\ln k$ vs. $1/T$, should give a straight line with a slope equal to the activation energy (E_a) and an intercept equal to the collision frequency (A). Furthermore, using the Eyring equation (eq. 3) from the transition state theory, both enthalpic ($\Delta H^\ddagger$) and entropic barriers ($\Delta S^\ddagger$) for the reaction can be calculated.¹⁰⁸

$$\ln\left(\frac{k}{T}\right) = -\frac{\left(\frac{\Delta H^\ddagger}{R}\right)}{T} + \left(\ln(k_B/h) + \Delta S^\ddagger/R \right) \quad (3)$$

A plot of $\ln(k/T)$ vs. $1/T$ should give a straight line with a slope and an intercept that related to the enthalpic ($\Delta H^\ddagger$) and entropic barriers ($\Delta S^\ddagger$), respectively.

4.3 Different methods to measure reactions rates

Various spectroscopic techniques can be applied to measure the reaction rates depending upon the system. These techniques include UV–visible spectroscopy, NMR, FT–IR, and GC–MS. Since the studies described in this dissertation involve working at elevated temperature over extended time periods, therefore the use of NMR and UV-visible spectroscopy was disfavored. Therefore, GC–MS studies were utilized to perform rate quantification. In these studies a suitable internal standard (IS) is needed to quantify the benzamide product, in real time. The IS could be added directly to the reaction mixture externally to the isolated aliquots. Since, *p*-toluamide can potentially bind to Ru as an inhibitor it was employed externally.

4.4 Kinetic studies on NHase

There have been no kinetic investigations on NHase model complexes and even studies on the enzyme itself has been limited. Holz and coworkers very recently reported stopped-flow kinetic studies on Fe-NHase from *Rhodococcus equi* TG328-2 (ReNHase), using methacrylonitrile as substrate. They observed an Fe-bound nitrile intermediate via UV–vis spectroscopy.¹³² Related Fe based model complexes support the assignment. Kinetic studies suggested release of amide

product as the rate-determining step. A k_{cat} and K_M of 5 s^{-1} and $190 \text{ }\mu\text{M}$ were reported for the enzyme, respectively.

4.5 Kinetic studies using $\text{L}^{1-3}\text{RuPPh}_3$ precatalysts

Although previous results under biphasic conditions indicated that sulfur-oxidation enhances nitrile hydration at lower nitrile:water ratios,¹²⁸ additional insights into the effect of S-oxidation require the detailed kinetic investigations described in this Chapter. Reactions were conducted in N, N'-dimethylformamide (DMF) to allow complete mixing of the benzonitrile and water substrates with the precatalyst as a homogeneous solution. Preliminary studies under these conditions revealed a maximum turnover frequency (TOF) of 11 h^{-1} and 62 h^{-1} for precatalysts L^1RuPPh_3 and L^3RuPPh_3 , respectively.¹³³ As in the prior study, high reaction temperatures ($368 - 398\text{K}$) were maintained to ensure complete dissociation of the triphenylphosphine donor from the precatalysts L^nRuPPh_3 . Aliquots were removed at timed intervals for analysis by GC-MS with the external addition of *p*-toluamide as internal standard. Additional experimental details are provided under the experimental section in Chapter 2.

4.6 Reaction mechanism and rate law

Experimental kinetic data is consistent with the nitrile-bound hydration mechanism outlined in equations 4 – 7. The first step involves activation of the pre-catalyst via PPh_3 dissociation to form the aqua complex L^nRuOH_2 ($n = 1 - 3$) (eq. 4). Under the reaction conditions, PPh_3 dissociation is complete ($k_1 \gg k_{-1}$) such that $[\text{L}^n\text{RuPPh}_3]_{\text{initial}} = [\text{L}^n\text{RuOH}_2]_{\text{initial}}$. The aqua complex is in dynamic

equilibrium ($K_2 = k_2/k_{-2}$) with the nitrile complex L^nRuNCR (eq. 5). The kinetic data could be interpreted with either the L^nRuOH_2 or L^nRuNCR species as the catalytically competent intermediate. However, since the former is disfavored¹³³ based on density functional theory (DFT) calculations (discussed in detail in Chapter 5), we report the data based on a nitrile-bound route. Hydration of L^nRuNCR via an activated water molecule (eq. 6) yields the product complex $L^nRuNH_2C(O)R$. Under the conditions of low turnover ($[NH_2C(O)R] \ll [H_2O]$), the amide is quickly and effectively substituted by H_2O to complete the cycle (eq. 7). The rate law for the proposed mechanism (eq. 8) is derived assuming steady-state conditions for $LRuNCR$. Consistent with this mechanism, the reaction is first-order with respect to the L^1RuPPh_3 pre-catalyst (Fig. 4.1). Both the water and nitrile substrates display saturation kinetics for L^1RuPPh_3 (Fig. 4.1) and L^2RuPPh_3 . For L^3RuPPh_3 saturation behavior is observed with nitrile, while a linear dependence is maintained over the entire water concentration range tested indicative of relatively fast nitrile binding. A thermodynamic preference is also observed for nitrile substrate as suggested by DFT results (gas and DMF phase) that show that nitrile binding is favored over water by 11.6 kJ/mol and 19.5 kJ/mol, respectively.

$$Rate = \frac{k_2 k_3 [LRuPPh_3] [RCN] [H_2O]}{k_2 [RCN] + (k_3 + k_{-2}) [H_2O]} \quad (8)$$

$$\frac{1}{k_{obs}} = \frac{1}{k_3 [H_2O]} + \frac{1}{K_2 k_3 [RCN]} \quad (9)$$

The hydration rate constant k_3 and water-nitrile binding equilibrium constant K_2 are determined from the slopes of double reciprocal plots of k_{obs} versus water (Fig.4.2B) and nitrile concentrations (Fig. 4.2C) (with the exception of k_3 for L^3RuPPh_3 which is calculated from the normal plot of k_{obs} vs water concentration) according to eq. 8. All plots for $L^{1-3}RuPPh_3$ are provided in appendix 1.

Figure 4.1. Concentration dependence of rate vs precatalyst L^1RuPPh_3 (top), PhCN (middle), and H_2O (bottom)

Figure 4.2. Double reciprocal plot for precatalyst L¹RuPPh₃ and extraction of K₂ and k₃.

Numerical results are summarized in Table 4.1. Each experiment was performed in triplicate. Reported benzamide concentrations are the average of the three trials with error bars denoting the standard deviation. The errors in the measurement of rate and k_{obs} are determined from a least-squares-fit using the LINEST function in Excel. For $1/k_{\text{obs}}$, the error calculated using the law of error of propagation. The same technique is used for the calculation of error in K_2 and k_3 .

Table 4.1. Water-nitrile equilibrium constant (K_2) and hydration rate constant (k_3) for $L^n\text{RuPPh}_3$ ($n = 1 - 3$) in DMF solvent at 398 K.

Precatalyst	$K_2 = k_2/k_{-2}$	k_3 ($\text{M}^{-1} \text{h}^{-1}$)
$L^1\text{RuPPh}_3$	21 ± 1	0.37 ± 0.01
$L^2\text{RuPPh}_3$	9.0 ± 0.9	0.82 ± 0.07
$L^3\text{RuPPh}_3$	23 ± 3	1.59 ± 0.12

Interestingly, sulfur-oxidation results in a steady increase in the hydration rate constant k_3 . The sulfinate complex $L^2\text{RuNCR}$ hydrates at twice the rate of the thiolate precursor (Table 4.1). Further oxidation to the mixed sulfenate/sulfinate $L^3\text{RuNCR}$ again results in a doubling of the hydration rate constant. To our knowledge, these are first kinetic studies to show an increase in the nitrile hydration rate constant upon oxidation of sulfur donors. The influence of sulfur-oxidation on the nitrile/water binding preference (K_2) is less intuitive. All complexes display a small preference for nitrile coordination although with K_2 drops by a factor of 2 upon oxidation of $L^1\text{RuPPh}_3$ to $L^2\text{RuPPh}_3$ before rebounding

to its original value upon further oxidation to L^3RuPPh_3 . Density functional theory calculations (detailed in Chapter 5) reproduce the unexpected, alternating behavior of nitrile binding affinity.

Hydration reactions employing deuterium oxide (D_2O) display a secondary kinetic isotope effect for all three precatalysts with KIE (k_H/k_D) values of 1.08 ± 0.05 , 0.96 ± 0.04 , and 1.32 ± 0.21 for L^1 , L^2 , and L^3 , respectively. This suggests that O–H bond dissociation is relatively fast in each case and that some other step is kinetically limiting.¹³¹ Similar secondary KIEs were previously observed for other nitrile hydration catalysts.¹³¹ Further, the rate of hydration using *p*-chlorobenzonitrile substrate with pre-catalyst L^3RuPPh_3 is 2.5 times faster as compared to benzonitrile. This suggests the transition state is negatively charged, which is consistent with attack of water on metal-bound nitrile as the rate-determining step.

4.7 Activation parameters for $L^{1-3}RuPPh_3$

To gain further insight into the reaction mechanism, nitrile hydration activation parameters for L^nRuPPh_3 ($n = 1 - 3$) were calculated by performing the reactions over a temperature range of 368 – 398K. For each complex linear Arrhenius and Eyring plots were obtained (Fig. 4.3 and 4.4). The activation energy (E_a) and other parameters ($\Delta H^\ddagger$ and $\Delta S^\ddagger$) are summarized in Table 4.2 and are compared to Co-NHase.

Figure. 4.3. Arrhenius plot for precatalyst L^1RuPPh_3 for calculation of activation energy

Figure 4.4. Eyring plot for L^1RuPPh_3 for calculation of enthalpic and entropic barriers

Table 4.2. Nitrile hydration activation parameters for $L^n\text{RuPPh}_3$ ($n = 1 - 3$) in DMF determined over a temperature range of 368 – 398 K and Co-NHase

Precatalyst	E_a	$\Delta H^\ddagger$	$\Delta S^\ddagger$
	(kJ mol ⁻¹)	(kJ mol ⁻¹)	(J K ⁻¹ mol ⁻¹)
$L^1\text{RuPPh}_3$	72.0 ± 14.0	68.9 ± 14.0	-67.8 ± 18.7
$L^2\text{RuPPh}_3$	45.3 ± 3.7	42.1 ± 3.7	-123.7 ± 15.3
$L^3\text{RuPPh}_3$	43.0 ± 8.3	39.8 ± 8.3	-123.2 ± 35.2
Co-NHase	23.0 ± 1.2	18.0 ± 0.9	-146.0 ± 0.7

A summary of experimentally determined values for $L^n\text{RuPPh}_3$ is provided in Table 4.2 with values for Co-NHase provided for comparison. As expected, $L^1\text{RuPPh}_3$ exhibits the largest activation energy barrier, 72.0 ± 14.0 kJ mol⁻¹ for the benzonitrile hydration. The activation barrier is similar in magnitude to that observed by Hirano *et al.* using a dipalladium catalyst.¹³¹ Sulfur oxidation to the sulfinato complex $L^2\text{RuPPh}_3$ lowers the activation barrier by almost 27 kJ mol⁻¹ to 45.3 ± 3.7 kJ mol⁻¹. Further sulfur-oxidation to the sulfenato/sulfinato precatalyst $L^3\text{RuPPh}_3$ shows no statistical decrease in the hydration activation barrier. The same trend and magnitude of effect is observed in the enthalpy of activations ($\Delta H^\ddagger$) for $L^{1-3}\text{RuPPh}_3$.

The entropy of activation ($\Delta S^\ddagger$) sheds significant light on the effect of sulfur-oxidation on the nature of the transition state. Sulfur oxidation nearly doubles $\Delta S^\ddagger$ from the parent complex $L^1\text{RuPPh}_3$ to the sulfinato complex $L^2\text{RuPPh}_3$ (Table 4.2). As with the enthalpic contribution, further sulfur-oxidation to $L^3\text{RuPPh}_3$ results in

no further statistically significant changes. These results indicate that molecular motions are substantially more restricted in the transition state of the sulfur-oxidized catalysts. The increase in entropic barrier concomitant with sulfur-oxidation could be interpreted in the light of atoms participating crucially in transition state. For L^1RuTS there are 6 atoms whereas in $L^{2-3}RuTS$ there are 7 atoms that participate. Since it would take more energy to organize 7 atoms, hence $L^{2-3}RuTS$ exhibit higher entropic barrier than L^1RuTS . Interestingly, the $\Delta S^\ddagger$ for L^2RuPPh_3 and L^3RuPPh_3 are statistically similar to those observed for Co-NHase.²⁸

These results are interpreted as activation of the water molecule by the oxidized sulfur donors through H-bonding interactions for directed attack on the coordinated nitrile. This imposes the significant entropy of activation observed for L^2RuPPh_3 and L^3RuPPh_3 , and Co-NHase. However, this is more than offset by the substantial decrease in the enthalpy of activation upon S-oxidation. In addition to the activation of water through H-bonding with the oxidized sulfur donors, the enhanced Lewis acidity of the metal center upon sulfur-oxidation, as noted in electrochemical studies (positive shift of half potential as result of sulfur-oxidation) and XAS studies on L^nRuPPh_3 , is also expected to lower the enthalpic barrier.^{81,134} The further lowering of the enthalpy of activation of Co-NHase relative to L^2RuPPh_3 and L^3RuPPh_3 can be attributed to the greater Lewis acidity of Co(III) as compared to Ru(II).

4.8 Full catalytic cycle

A proposed mechanism consistent with the kinetic data for L^nRuPPh_3 ($n = 1 - 3$) is detailed in Figure 4.5. The six-coordinate L^nRuPPh_3 pre-catalysts undergo phosphine dissociation under reaction condition to give the catalytically inactive L^nRuOH_2 and catalytically active L^nRuNCR species in dynamic equilibrium. The latter undergoes nucleophilic attack by water (activated by H-bonding with the sulfinato ligand in the case of L^2 and L^3) to form the highly ordered transition state complex. The mechanistic studies and magnitude of entropic barrier suggest that attack of water is the rate-determining step.⁵⁴ Rearrangement affords the N-bound iminol intermediate which further tautomerizes to give the enthalpically preferred product-bound complex $L^nRuNH_2C(O)R$. Substitution of amide by either the water or nitrile substrate completes the catalytic cycle.

Figure 4.5. Proposed nitrile hydration catalytic cycle for L^nRuPPh_3 ($n = 2 - 3$). ($R = \text{Phenyl}$, L^n ligand abbreviated as $L\sim SO_2$ for clarity)

4.9 Relevance to enzyme nitrile hydratase

Mechanistic proposals based upon the synthetic models suggest nitrile-bound,^{26,28,42-44,54,132} water-bound²⁹ as well as ligand-centered nitrile hydration pathway.^{41,69} Mascharak's group supports a water-bound pathway²⁹ whereas the studies from Kovacs and coworkers indicate a nitrile-bound route⁵⁴ where they report intermediates of reaction too and they didn't observe any exchange reaction between the nitrile and water/hydroxide. However, Chottard's group as well as Masuda's group propose a ligand-centered pathway^{41,69} where only the bis-sulfenate complex was reported to be catalytically active. Therefore, they propose why oxidation to sulfenate is important for the enzymatic activity. Interestingly,

metallopeptide mimics of enzyme nitrile hydratase developed by Shearer⁷⁰ and coworkers also suggest a thermodynamic preference for nitrile as a result of sulfur-oxidation (discussed in more detail in Chapter 5).

Interestingly, our studies indicate that $L^{1-3}RuPPh_3$ precatalyst are able to bind both nitrile and water, based on DFT studies in gas as well as DMF phase studies.¹³³ Infact, it has been previously reported by our group that Fe(III) complexes of ligand L^1 bind both nitrile and water.⁷⁷ However, sulfur-oxidation to sulfinato favors water binding compared to nitrile. Interestingly, sulfur-oxidation to sulfinato/sulfenato switches the ligand binding and nitrile-binding is thermodynamically more preferred than water. Moreover, the nitrile-bound complex that is favored by sulfinato/sulfenato donor set is catalytically active too and that falls in line with the natural system in nitrile hydratase. Interestingly, in NHase both the thiolate and sulfinato derivative are inactive and only the mixed sulfenato/sulfinato donor set is catalytically active. This may be due, in part, to heightened affinity of nitrile over water for this sulfur-oxidation state. However, by maintaining some binding affinity for water, NHase would be able to protect against undesirable metal-binding/activation of oxygen or other small molecules, while maintaining a reservoir of catalyst ready for activation upon the introduction of nitrile substrate.

Increased nitrile binding affinity is not the only advantage of the mixed sulfenato/sulfinato donor set. Sulfur oxidation also promotes the activation of water and organization of the transition state through H-bonding. Both our oxidized pre-catalysts (L^2RuPPh_3 and L^3RuPPh_3) and Co-NHase show a large and

negative entropy of activation ($\Delta S^\ddagger$) of similar magnitude (Table 4.2).²⁸ The enthalpic barrier for L^2RuPPh_3 and L^3RuPPh_3 are lower relative to L^1RuPPh_3 , which approach the barrier observed for Co-NHase (Table 4.2), concomitant of sulfur-oxidation. Another interesting result from our studies is that our complexes $L^{2-3}RuPPh_3$ exhibit statistically similar entropic barrier as that of Co-NHase (Table 4.2), therefore exactly mimicking the effect of sulfur-oxidation as observed in enzyme. This result indicate that although sulfur-oxidation lowers down the enthalpic barrier but it raises the entropic barrier at the same time. Perhaps, the enthalpic factor outweighs the entropic factor and therefore reaction becomes spontaneous in NHase. While such decrease in enthalpic activation barrier has been long postulated, our series of complexes provided for the first experimental kinetic data to clearly demonstrate the anticipated enthalpic and entropic trends of sulfur-oxidation on nitrile hydration.

A significant difference between our complexes and the active site of NHase is the magnitude of effect observed upon sulfur-oxidation. In our complexes, a *four-fold* increase in hydration rate is observed, whereas in NHase the catalyst goes from inactive to highly active after sulfur-oxidation. One possible explanation is that Co(III) more strongly favors water coordination than our Ru(II) catalysts and that sulfur-oxidation is mandatory for significant nitrile coordination in the latter. It should be noted that alternate, ligand-centered nitrile hydration mechanism has been recently proposed for NHase based on experimental and DFT studies in which the sulfenato (RSO^-) ligand serves as the active nucleophile.⁴²⁻⁴³ While such a mechanism is inconsistent with the activity trends of L^nRuPPh_3 ($n = 1 - 3$), our

group is actively pursuing other model complexes to experimentally assess the validity of this mechanism.

At this point, we can anticipate that sulfur-oxidation perhaps engages in H-bonding that activates the water for nucleophilic attack and increased Lewis acidity of metal complexes concomitant with sulfur-oxidation might also work cooperatively to enhance nitrile hydration. However, that can't be confirmed on the basis of the aforementioned kinetic, and thermodynamic studies. Therefore, to further gain mechanistic insights we employed DFT studies in gas as well as DMF phase to answer some details about the proposed roles of sulfur-oxidation. Although, in the current studies; benzonitrile has been employed as the model substrate but a similar trend of reactivity is anticipated for other nitriles. These DFT studies are discussed in next Chapter. The results discussed in this Chapter were published in *Inorganic Chemistry* 2014, **53**, 12372-12377.

CHAPTER 5

DFT MODELING OF THE CATALYTIC NITRILE HYDRATION CYCLE

This Chapter describes the modeling of the nitrile hydration reaction mechanism using density functional calculations to assess the effect of sulfur-oxidation. An overview of DFT calculation on NHase and other model complexes is presented before moving into the detailed DFT studies on precatalysts $L^{1-3}RuPPh_3$. Free energies of binding are calculated for nitrile, water, and amide binding to active catalyst $L^{1-3}Ru$. Sulfur-oxidation to sulfinato/sulfenato switches the ligand binding preference from water to nitrile. A nitrile-bound pathway is proposed to occur in current system based on DFT calculations. The sulfur-oxidation to sulfinato/sulfenato mixed donor set lowers the enthalpic barrier by 36 kJ/mol in gas phase studies, and solvent phase studies follow a similar trend. These studies represent the first set of studies where extensive DFT calculations are performed to assess the effect of sulfur-oxidation on ligand binding affinity as well as activation barrier of the reaction and corroborate the experimental findings.

5.1 Literature overview of DFT studies on enzyme nitrile hydratase

Density functional theory calculations are a very valuable tool to compare and gain insight into reaction mechanism. Therefore, DFT modeling of the catalytic cycle of NHase can unravel the role of sulfur-oxidation in tuning the catalytic activity of NHase. Various groups (Richards, Himo, Hopmann, and Shearer) have employed DFT studies to study the enzyme NHase and have explored numerous roles of the unusual active site and mechanism of nitrile hydration. Outcomes of their studies have been summarized in this section.

5.2 DFT studies on the first-and second-shell mechanism

DFT studies on model complexes by Richards and coworkers were directed to understand the structural and spectroscopic features of the active site of NHase such as why the active-site employs low-spin Fe(III) center and possibility of high-spin Fe(III) was explored, and the origin of low energy electronic transition in Fe-NHase was determined.¹³⁵⁻¹³⁶ Himo and coworkers investigated the first-shell mechanism of the nitrile hydration using quantum chemical models of the Fe-NHase active site.¹³⁷ In a first-shell mechanism, as described in Chapter 1, nitrile substrate undergoes direct coordination to the metal center and following that nucleophilic attack by water leads to hydration to amide product. They employed acetonitrile as the substrate for the DFT calculation. In their calculations, they used two models **A** and **B** of the active site that serves as the smaller (truncated) and larger (with Arg 56 and Arg 141 residues in outer-sphere) models, respectively. For active site models a $\epsilon = 4$ was employed, and for acetonitrile hydration in

water a $\epsilon = 80$ was used. The reaction barrier reported in parentheses are obtained in solvent phase. A barrier of 58.1 (60.8) kcal/mol was calculated for direct acetonitrile hydration with water. Interestingly, the barrier was reduced to 37.8 (35.6) kcal/mol when a second molecule of water was introduced to assist in the acetonitrile hydration. These barriers are very high as compared to the barrier of 13 – 15 kcal/mol that is experimentally observed for NHase-catalyzed nitrile hydration. They proposed and tested two distinct ways in which NHase can lower down the barrier.

The nitrile hydration barrier can be lowered by the Lewis acidity of Fe(III) by activation of the coordinated acetonitrile for nucleophilic attack. However, DFT modelling studies with both smaller model **A** 45.0 (42.9) kcal/mol and larger model **B** 40.2 (38.7) kcal/mol led to barriers that were higher than the barrier corresponding to uncatalyzed acetonitrile hydration. Therefore, it was concluded that Fe(III) is too poor of a Lewis acid in the NHase active site environment to catalyze the reaction without additional assistance. Himo *et.al.* proposed that water activation achieved through a proximal base could lower the reaction barrier. The proximal sulfenate (RSO^-) was evaluated as the local base to play that role. The sulfenate activated water based mechanism led to reaction barrier of 23.6 (20.2) kcal/mol dropping the barrier dramatically by 15 kcal/mol (Fig. 5.1). However, it was still higher than what is observed for NHase. The authors attribute this discrepancy to the Tyr68 in Co-NHase in outer coordination sphere that is crucial to catalytic activity and can play similar role in Fe-NHase.

First-Shell Mechanism

Figure 5.1. Proposed pathway for first-shell mechanism for NHase-catalyzed nitrile hydration

In a subsequent paper by Himo group, they investigated an alternate hydration mechanism in which the nitrile does not coordinate to the metal center, but rather hydration is proposed to be mediated by a metal-bound hydroxide (Fig. 5.2). An activation barrier of 22.7 (18.3) kcal/mol for hydroxide mediated nitrile hydration was calculated. The barrier for second-shell mechanism is similar to barrier of first-shell mechanism.⁴⁴

Second-Shell Mechanism

Figure 5.2. Proposed second-shell mechanism for nitrile hydration

Interestingly, a similar barrier 23.5 (22.2) kcal/mol was also calculated for a second-shell route where the sulfenate itself acts as the nucleophile and ultimately leads to nitrile hydration. Therefore, it was suggested that sulfenate can also serve as nucleophile (Fig. 5.3).

Alternative Second-Shell Mechanism

Figure 5.3. Alternative proposed second-shell mechanism for NHase-catalyzed nitrile hydration with sulfenate as the nucleophile

5.3 Nitrile vs. water binding affinity using metallopeptide mimics

As detailed in Chapter 1, Co(III) metallopeptide mimics of NHase developed by Shearer *et. al.* were able to hydrate acrylonitrile to acrylamide producing 58 turnovers.⁷⁰ It was proposed that the catalytically active species contains a $\text{RSO}_2^-/\text{RSOH}$ environment similar to that of NHase. Furthermore, they employed DFT studies to probe the thermodynamics of substrate affinity as a function of sulfur-oxidation. Shearear reported that upon sulfur-modification to $\text{RSO}_2^-/\text{RSOH}$, Co(III) strongly favors nitrile binding (16.05 kcal/mol) over water (0.0 kcal/mol). In fact, for the $\text{RSO}_2^-/\text{RSOH}$ motif, water binding to Co(III) is an uphill process. In contrast, the sulfinate (RSO_2^-) species and over-oxidized bis-sulfinate ($\text{RSO}_2^-/\text{RSO}_2^-$) strongly favored five-coordinate and water-bound species, respectively (Fig. 5.4). Therefore, it provided a proof of concept that why sulfur-oxidation to $\text{RSO}_2^-/\text{RSOH}$ is crucial for catalytic activity of NHase. Additionally, Mayer bond order analysis of Co(III)- OH_2 species suggested that sulfur-oxidation results into tight binding of water with the exception of $\text{RSO}_2^-/\text{RSOH}$ motif that disrupts the non-covalent H-bonding interactions and hence leads to lowest bond order. However, recent QM/MM¹³⁸ studies suggest that sulfenate is not protonated to form sulfenic acid whereas XAS¹³⁹ studies support sulfenic acid formation at the active-site of NHase. Nevertheless, QM/MM studies support nitrile-bound pathway.¹³⁸

Figure 5.4. Co(III) metalloproteins and ligand affinity as a function of sulfur-oxidation as determined by DFT studies

5.4 Sulfenate (RSO^-) as the nucleophile and the disulfide switch

Quite recently, Hopmann *et. al.* reported DFT calculations on Fe-NHase with a different first-shell mechanism where sulfenate serves as the nucleophile and the sulfenyl O-atom is incorporated in product amide.⁴³ A cyclic disulfide formation is proposed to take place and attack of water regenerates the sulfenic motif. Nitrile exchange with water bound to Fe(III) center regenerates the catalytically active intermediate (Fig. 5.5). The total enthalpic barrier ($\Delta H^\ddagger$) calculated for the new mechanism is 13.8 kcal/mol which is lowest of all other proposed mechanism for nitrile hydration and matches very well with the experimentally determined barriers (13-15 kcal/mol) for Fe-NHase. It is to be noted that barrier for nitrile exchange with water is included in the barrier mentioned above and is 7.4 kcal/mol. This mechanism gained experimental supports as Holz and coworkers, very recently, reported that sulfenate can serve as the nucleophile in NHase.

Figure 5.5. Proposed nitrile hydration reaction mechanism via sulfenate as nucleophile and involving the disulfide formation

5.5 Effect of sulfur-oxidation on substrate/product binding to $L^{1-3}Ru$

5.5.1 Computational methodology

The DFT calculations were carried out at the B3LYP^{44,92-95} level of theory using 6-31G(d) basis set for C, H, N, S, O, and P atoms and LanL2DZ basis set for Ru atom with effective core potential. The initial coordinates for precatalyst L^1RuPPh_3 were obtained from the crystal structure and for L^2RuPPh_3 , and L^3RuPPh_3 coordinates were generated from L^1RuPPh_3 by addition of required number of oxygen atoms. The initial coordinates for derivatives of precatalyst L^1RuPPh_3 (benzonitrile/water at the place of PPh_3 etc.) were obtained by substituting the phosphine with the corresponding group and then it was optimized. Similar methodology was undertaken for derivatives of precatalyst L^2RuPPh_3 , and L^3RuPPh_3 . The optimized coordinates are listed for all the compounds. The calculations were carried out for the gas phase as well as for solution phase, using

N, N'-dimethylformamide (DMF) solvent. The polarity effect of bulk solvent was evaluated by the conductor-like polarized continuum model (CPCM)¹³⁷ at the same level of theory. The frequency calculations were performed at the aforementioned level of theory to identify the nature of all stationary points, and the transition state was identified as the one with only a single negative frequency. All the reported enthalpies and free energies of reactions have been corrected for zero-point energies. All quantum-chemical calculations were performed with *Gaussian09*¹⁴⁰ program package. Chemcraft software was utilized for visualization. The natural population analysis was performed using the NBO¹⁴¹ program included in the *Gaussian 09*.

5.5.2 Free energies for ligand binding

Since the Fe(III) derivative of L^1RuPPh_3 was previously reported to bind nitrile, water, and amide in experimental studies,⁷⁷ we first evaluated the relative free energies of L^nRuPPh_3 ($n = 1 - 3$) with water, benzonitrile, and benzamide coordinated in place of PPh_3 (Table 5.1). For all three series, substrate binding is thermodynamically preferred over product or PPh_3 coordination consistent with the observed catalysis. Pre-catalysts L^1RuPPh_3 and L^2RuPPh_3 display a preference for water over benzonitrile with the oxidized L^2 ligand more strongly favoring water coordination. Further oxidation to L^3RuPPh_3 switches binding preference to nitrile consistent with the alternating effects of S-oxidation on nitrile binding affinity noted experimentally, from water-nitrile equilibrium constant K_2 , as discussed in Chapter 4. Calculations in DMF solvent shows that each one of the ligands L^1 , L^2 ,

and L^3 favors nitrile binding over water where the nitrile coordination is much more pronounced for ligand L^3 .

Table 5.1. Relative free energies (kJ/mol) for L^nRuPPh_3 ($n = 1 - 3$) upon substitution of PPh_3 with H_2O , benzonitrile ($PhCN$), and benzamide ($PhC(O)NH_2$) from gas phase (and DMF) DFT computations using the B3LYP hybrid functional with the LanL2DZ basis set for Ru and 6-31G(d) all other atoms

Ligand	L^1RuPPh_3	L^2RuPPh_3	L^3RuPPh_3
PPh_3	0 (0)	0 (0)	0 (0)
H_2O	-29.4 (-33.3)	-45.8 (-49.5)	-30.7 (-30.4)
$PhCN$	-25.1 (-39.6)	-36.1 (-58.0)	-42.3 (-49.9)
$PhC(O)NH_2$	11.4 (5.0)	-13.1 (-4.6)	-10.3 (+1.9)

5.6 Modeling the mechanistic cycle

Given the relative energies of nitrile versus water binding for L^nRuPPh_3 ($n = 1 - 3$), we considered both nitrile-bound and water-bound catalytic hydration mechanisms. However, we could only locate a transition state for the former, using DFT, and the water-bound route was dismissed from further consideration (Fig. 5.6). The Ru-OH catalyzed hydration was also investigated for L^3RuPPh_3 precatalyst, but we were unable to locate the transition state metal-bound hydroxide attacking the nitrile. The calculated hydration mechanism involves nucleophilic attack of an associated water molecule on a metal-bound nitrile as the rate-controlling step. The

resulting iminol bound intermediate then rearranges to an N-bound amide product, which is readily displaced by water or nitrile completing the cycle.

Figure 5.6. Catalytically active nitrile- and inactive water-bound complexes for $L^{1-3}RuPPh_3$

The parent L^1RuNCR complex exhibits the largest enthalpic barrier that is calculated to be 81.7 kJ/mol in gas phase, which matches the experimentally measured barrier of 68.9 ± 14.0 kJ/mol. The energetics of nitrile hydration for precatalysts $L^{1-3}RuPPh_3$ is compared in Fig. 5.7. This barrier is significantly lower than the transition state enthalpy that is 203 kJ/mol as calculated for benzonitrile hydration in the absence of catalyst that serves as the blank reaction to compare the DFT calculated barriers. This indicated that active catalyst L^1RuNCR lowers down the reaction barrier dramatically by ~ 121 kJ/mol. Further oxidation to the sulfinato derivative L^2RuNCR reduces the enthalpic barrier by 21.7 kJ/mol to a barrier of 60.0 kJ/mol. The absolute decrease in calculated enthalpy matches the experimentally observed decrease of 26.8 kJ/mol remarkably well. Further sulfur-

oxidation to L^3RuNCR is predicted to lower the barrier by an additional 14.3 kJ/mol as estimated using DFT. However, the anticipated decrease in the enthalpic barrier for L^3RuPPh_3 compared to L^2RuPPh_3 as suggested by DFT studies, as a result of sulfur-oxidation to sulfenato, can neither be confirmed nor discounted due to experimental error associated with the experimentally determined barriers for precatalysts L^2RuPPh_3 and L^3RuPPh_3 . Calculated activation enthalpies in solvent DMF are higher than experimental results, but display the same trend upon sulfur-oxidation (Fig. 5.7). Further, our DFT results are consistent with prior reports by Himo and co-workers that note a reduction in the enthalpic barrier when sulfenate acts as a local base to activate water in NHase.¹³⁷ Interestingly, in these studies it is found that sulfinato can also play a role similar to sulfenate but comparison of their relative supremacy remains undetermined in these studies.

Figure 5.7. Calculated energetics of the nitrile-bound pathway for benzonitrile hydration for precatalysts L¹RuPPh₃ (black), L²RuPPh₃ (blue), and L³RuPPh₃ (red) using B3LYP hybrid functional and LanL2DZ basis set for Ru atom and 6-31G(d) for all other atoms under standard conditions (298K). Enthalpies (kJ/mol) are given for gas phase and for DMF solvent phase in parentheses [TS=Transition State].

5.8 Transition state structures

Examination of transition structures for LⁿRuTS ($n = 1 - 3$) confirm the high ordering foreshadowed by the entropic activation parameters (Fig. 5.8). For all three catalysts, the Ru-N-C bond angle in the transition state structure is bent indicating substantial imidate character. The transition state of L²RuPPh₃ displays a partial proton transfer from water to the sulfenato O with HO $\cdots$ H and SO $\cdots$ H distances of 1.318 and 1.143 Å, respectively. The corresponding distances in the transition state of L³RuPPh₃ (HO $\cdots$ H: 1.297 Å and SO $\cdots$ H: 1.161 Å) indicate slightly less transfer of the proton from the water. In L¹RuPPh₃, the proton is partially transferred to the thiolate donor with a slightly longer HO $\cdots$ H (1.331 Å) and an S $\cdots$ H distances of 1.561 Å. Taken together, these distances suggest lesser proton transfer is required in the transition state upon increased sulfur-oxidation. All these observations indicate that an early transition state is observed for

precatalyst with sulfur modification. An earlier transition state in the sulfur-oxidized complexes is also indicated by the C–OH distance that increases from 1.616 to 1.779 to 1.801 Å from L^1RuPPh_3 to L^3RuPPh_3 , with a corresponding decrease in the C–N distance due to additional triple bond character. The bond distance between Ru and N atom of nitrile ($Ru-N_{\text{nitrile}}$) is 2.068, 2.076 and 2.091 Å in transition state structures (gas phase) for L^1RuTS , and L^2RuTS , and L^3RuTS respectively. A similar elongation trend is observed for DMF phase transitions state for $L^{1-3}RuTS$. Therefore, it seems logical that early transition state formation for $L^{2-3}RuPPh_3$ precatalysts is responsible for observed decrease in enthalpic barrier.

Figure 5.8. Gas phase transition state structures for L^nRuTS ($n = 1 - 3$).

The exact features responsible for the lower barrier for sulfur-oxidized precatalysts $L^{2-3}RuPPh_3$ remained puzzling despite the calculated transition states. As discussed above, water appears to be less nucleophilic as seen through comparison of $HO\cdots H$ distances. Therefore, a metal-centered effect must contribute to the lower barriers. One possible factor is Lewis acidity of metal ion.

XAS and DFT studies on $L^{1-3}RuPPh_3$ reported earlier by our group in collaboration with Prof. Jason Shearer has shown that sulfur-oxidation renders the metal-center more Lewis acidic. Inspired by these results NPA charges for $L^{1-3}RuNCPh$ were calculated. The natural charges in gas phase $L^{1-3}RuNCPh$ suggest that sulfur-oxidation enhances the nitrile polarization, as the charges on C and N atoms of nitrile increased linearly with sulfur-oxidation (Table 5.2), that would lead to formation of early transition state as indicated by transition state calculations and decreased enthalpic barriers. A similar polarization trend is observed for natural charges calculated in DMF phase. For the first time it is seen directly, although it has been proposed earlier, that sulfur-oxidation can affect the nitrile coordinated to metal center.

Table 5.2. Summary of NPA charges for Ru, and C, and N (from nitrile) calculated for nitrile-bound complexes $L^{1-3}RuNCPh$

Atom type	$L^1RuNCPh$	$L^2RuNCPh$	$L^3RuNCPh$
Ru	- 0.504(-0.479)	- 0.624(-0.618)	- 0.671(-0.668)
C1	+ 0.373(+0.383)	+ 0.422(+0.413)	+ 0.423(+0.425)
N1	- 0.205(-0.230)	- 0.240(-0.242)	- 0.266(-0.287)

A pictorial presentation of effect of sulfur-oxidation on nitrile polarization is shown in Fig. 5.9.

Figure 5.9. Nitrile-bound complexes for precatalysts $L^{1-3}RuPPh_3$ and effect of sulfur-oxidation on nitrile polarization

5.9 Sulfur-oxidation effect on Ru-O, Ru-N, and C-N bond distances in water-, nitrile-bound complexes in $L^{1-3}RuX$

It was found that sulfur-oxidation increases the Ru-P bond distance in $L^{1-3}RuPPh_3$ as determined by single crystal crystallography and was further corroborated by DFT studies. To further determine the effect in aqua and nitrile-bound complex and see if the trend generalizes, in this section Ru-O and Ru-N bond distances are compared calculated by DFT studies.

In the aqua-bound complexes in gas phase, the Ru-O bond length was found to increase from 2.2611 Å in L^1RuOH_2 to 2.2664 Å in L^2RuOH_2 as a consequence of sulfur-oxidation to sulfinato motif (Table 5.3). On further oxidation to sulfinato/sulfenato in L^3RuOH_2 , the Ru-O bond length increased to 2.2999 Å. The increase in Ru-O bond distance is counter-intuitive as metal center that is rendered

harder as a consequence of sulfur-oxidation should prefer hard donors like water (O) and a decrease in bond length is expected. Nevertheless, the increase in bond length from L^1RuOH_2 to L^3RuOH_2 would lead to increase in pKa of water bound to Ru and hence decreased nucleophilicity of water that could be the reason why a transition-state corresponding to the water-bound pathway could not be located. A similar trend is found in DMF phase studies.

Ru-N bond distance is also found to increase linearly with sequential sulfur-oxidation in complexes $L^{1-3}RuNCPh$, in gas phase (Table 5.3). A similar trend is observed in DMF phase. At the same, C-N bond distance decreases both in gas and DMF phase. Since an early transition is observed for sulfur-oxidized complexes with nitrile-bound complex as catalytically active intermediate, it can be interpreted that sulfur-oxidation already sets the nitrile where less bond reorganization is required to reach transition state. The lessened bond reorganization leads to lower barrier as observed experimentally and by DFT studies.

Table 5.3. Sulfur-oxidation effect on Ru-O ($Ru-OH_2$), Ru-N ($Ru-NCPh$), and C-N ($Ru-NCPh$) bond lengths in gas and DMF phase calculated by DFT studies

Bond type	Metal complex	Bond length (Å)		
Ru-O	$L^{1-3}RuOH_2$	2.2611(2.2709)	2.2664(2.2566)	2.2999(2.2818)
Ru-N	$L^{1-3}RuNCPh$	1.9881(2.0083)	2.0233(2.0276)	2.0366(2.0445)
C-N	$L^{1-3}RuNCPh$	1.1672(1.1680)	1.1636(1.1653)	1.1646(1.1652)

In conclusion, through these extensive DFT calculations we have been able to show that sulfur-oxidation can modulate the ligand affinity from water to nitrile and it is the nitrile-bound intermediate that is catalytically active. Additionally, sulfur-oxidation is found to lower the reaction barrier by enhancing the nitrile polarization. Chapter 6 details the numerous ways to further lower the reaction barrier near or even lower than NHase and improving the catalytic activity of L^{-1} - $^3\text{RuPPh}_3$ and their potential use as mimic of enzyme of thiocyanate hydrolase (SCNase). The results discussed in this Chapter were published in *Inorganic Chemistry* 2014, **53**, 12372-12377.

CHAPTER 6

CONCLUSIONS AND FUTURE DIRECTIONS

This dissertation details the effect of sulfur-oxidation on catalytic nitrile hydration using bioinspired ruthenium(II) mimics ($L^{1-3}RuPPh_3$) of the active-site of metalloenzyme nitrile hydratase (NHase). The sulfur-oxidation effects on catalytic nitrile hydration have been quantified initially using catalytic assays under biphasic conditions, then by performing extensive kinetic studies under homogeneous conditions. The effect of sulfur-oxidation on the activation barriers have been determined for the series of precatalysts $L^{1-3}RuPPh_3$, and the results are further supported by density functional theory (DFT). The results are acquired by performing anaerobic syntheses, GC-MS, electrochemistry, and temperature-dependent assays.

The effect of sulfur-oxidation was quantified by performing the catalytic nitrile hydration assays under biphasic conditions using neat mixture of benzonitrile and water after 18 h. The sulfur-oxidation effect on catalytic hydration activity was probed by varying the substrate ratio (nitrile:water) using the same level of catalyst loading for the series of precatalysts. Furthermore, the reaction was mechanistically explored by designing assays in order to gain insight into the functioning of precatalysts. The effect of sulfur-oxidation was assessed as a

function of temperature, inhibitors, level of sulfur-oxidation, and metal-centered oxidation. A higher catalytic activity is observed as compared to other NHase mimics even in the absence of external base/buffer.

In the homogeneous kinetic studies, the DMF solvent was utilized to allow mixing of benzonitrile and water. The reaction was monitored via GC-MS using internal standard technique by periodically removing aliquots. The catalyst, benzonitrile, and water concentrations were varied; and a novel rate law was proposed and nitrile/water exchange equilibrium constant (K_2) and hydration rate constant (k_3) were extracted. Additionally, the activation parameters were obtained by performing the reaction at four different temperatures. The effect of sulfur-oxidation on the nitrile/water exchange equilibrium constant (K_2), hydration rate constant (k_3), and activation parameters is discussed in the light of NHase.

Density functional theory (DFT) calculations have been applied extensively, both in gas and DMF solvent phase, to corroborate the experimental findings. The DFT calculation on a series of precatalysts was employed to look at the preferred substrate for the pentacoordinate complex ($L^{1-3}Ru$), and the results are discussed in the light of NHase. Additionally, the catalytic cycle of nitrile hydration was modeled using the DFT studies, and the activation barriers were determined for precatalysts $L^{1-3}RuPPh_3$ which corroborate the experimental findings.

6.1 Nitrile hydratase and sulfur oxidation

As detailed in the Chapter 1, NHase catalyzes the transformation of nitriles to amides at an unusual low spin non-heme iron (III) or non-corrin cobalt(III) at its

active site, under the ambient conditions of temperature, pressure, and physiological pH.^{1,4-6,8,10} The coordination sphere includes a substrate binding site, two carboxamido nitrogens and three cysteine derived sulfurs in different oxidation states including a thiolate (RS^-), sulfenate (RSO^-), and sulfinato (RSO_2^-). The nitrogen donors, sulfenate, and sulfinato donors form the equatorial plane of the active site whereas the unmodified thiolate donor is present at the axial position trans to the substrate binding site.¹⁷ The unusual active site of NHase and its excellent catalytic nitrile hydration activity, which otherwise is a very challenging reaction, attracted the attention of scientists to study the enzyme and prepare structural, spectroscopic, and functional models.

6.1.1 Sulfur-oxidation effect on catalytic benzonitrile hydration under biphasic conditions employing $\text{L}^{1-3}\text{RuPPh}_3$

The modeling of NHase has been pursued by different groups to unravel the mechanistic details as well as the role of asymmetric sulfur oxidation.¹⁸ To date, numerous models of NHase have been prepared, but none of these complexes have been able to elaborate the exact role of sulfur-oxidation in tuning the catalytic activity of NHase partially due to lack of complexes with different level of sulfur-oxidation because of the difficulty in controlling the sulfur-oxidation. The modeling studies have shown that the modification of sulfur to sulfenate is crucial for catalytic activity as corresponding sulfinato complexes were not able to catalytically hydrate the nitrile.^{41,67} In the current studies, a series of precatalysts ($\text{L}^{1-3}\text{RuPPh}_3$) with different level of sulfur-oxidation is employed including one complex that mimics the exact level of sulfur-oxidation present in the enzyme, and

employing Ru(II) as the surrogate low spin d^6 metal. The complexes employed in this study show excellent NHase activity under biphasic conditions without the assistance of external base and under neutral pH conditions at ppm levels of catalyst loading, and higher TON and TOF were obtained compared to other mimics, using benzonitrile as the substrate, at elevated temperatures (125 °C).¹²⁸ The catalytic activity was optimized using different substrate ratios, and catalysts were also explored mechanistically. The catalysts possessing sulfur oxidation exhibited higher catalytic activity at lower nitrile to water ratio (Figure 6.1) and offered less product inhibition. However, it can not be stated at this time that whether the nitrile hydration followed a water-bound or nitrile-bound pathway.

Figure 6.1. Series of precatalysts employed in the current studies and effect of sulfur-oxidation on catalytic benzonitrile hydration activity (average TONs and TOFs are listed)

6.1.2 Catalytic nitrile hydration using weakly coordinating phosphines

The series of precatalysts employed in the current studies exhibit higher TONs and TOFs compared to other bioinspired NHase mimics. However, the catalytic

activity is achieved at elevated temperature (125 °C). In order to have these catalysts applications in academia and/or industry and to lower energy cost, it is best if catalysts can be tuned to function at lower temperature and in the best case scenario, at room temperature.

Mechanistic studies show that phosphine dissociation is required to observe the catalytic nitrile hydration in the employed precatalysts, $L^{1-3}RuPPh_3$; subsequently substrate binding and hydration take place. One such strategy is to employ a weakly coordinating phosphine in place of triphenylphosphine (PPh_3) that can come off at a lower temperature and hence reduce the energy cost. A weakly coordinating phosphine can be obtained from triphenylphosphine by placing different substituents at *ortho*, *meta*, and *para* positions of the phenyl groups which in turn introduces sterics and thereby alters the donor properties of the phosphine. The sterics can be tuned by having methyl, isopropyl, and tert-butyl groups at the phenyl ring. The new series of precatalyst (Figure 6.2) can function at a lower temperature or may even work at room temperature.

Figure 6.2. Proposed syntheses of different precatalysts with different phosphines at the exogenous position

6.1.3 Tuning the catalytic activity of L^1RuPPh_3 using Lewis acids

As discussed in the prior section, sulfur-oxidation is crucial to NHase activity¹⁸ and an enhanced nitrile hydration is observed in the precatalysts $L^{2-3}RuPPh_3$. The sulfur-oxidation enhances the nitrile hydration by removing the π -donor ability of sulfur donors^{56,81,142-144} and consequently, sulfenate/sulfinate acts more like an σ -donor. Concomitantly, the Lewis acidity of metal center is increased which in turn now polarizes the nitrile better. However, if the only function of post-translational modification of the sulfurs is to harden the metal center by removing the electron density from sulfur donors, an equivalent effect can be generated by addition of Lewis acid such as $Sc(OTf)_3$, $In(OTf)_3$, $Ga(OTf)_3$, $Y(OTf)_3$ to organic solutions of L^1RuPPh_3 that would lead to similar or better level

of catalysis as compared to $L^{2-3}RuPPh_3$. Furthermore, Zn, Ca, Ba, and Sr salts could also be explored for the aforementioned purposes.

6.1.4 Cobalt and rhodium analogue of the precatalysts $L^{1-3}RuPPh_3$

The current precatalysts employ ruthenium metal as a surrogate low-spin d^6 metal instead of cobalt which is actually present in the enzyme. Therefore, along the same lines; corresponding cobalt complexes could be synthesized and their reactivity with dioxygen or other O-atom transfer reagents can be explored to afford sulfur-oxygenated complexes, thereby mimicking the active site of enzyme NHase (Figure 6.3). These complexes could further be explored for nitrile hydration activity as Mascharak, Chottard, Artaud, and Masuda's group have shown that their cobalt complexes are active towards catalytic nitrile hydration. The cobalt(III) complexes are strong candidates as cobalt(III) is better Lewis acid than ruthenium(II) because of its smaller size and higher charge. Along the same lines, corresponding rhodium analogs could also be developed as mimics of NHase.

where $M = Co, Rh$

Figure 6.3 Proposed syntheses of Co and Rh analogues

6.2 Homogeneous kinetic and thermodynamic studies

The results discussed above were obtained in biphasic condition mixed by convection after 18 h time period. Although, these studies provided certain details about the functioning of catalyst and role of sulfur-oxidation in tuning the catalytic activity but these studies lack the real time monitoring the formation of the product which can lead to rate quantification and then fitting to rate law based on observations will unravel the effect of sulfur-oxidation on each step of the proposed mechanism. The rate quantification is achieved in the homogeneous medium by using DMF as the solvent that allows the mixing of nitrile and water substrates and kinetic barriers are extracted from Arrhenius and Eyring plots.

6.2.1 Kinetic effects of sulfur-oxidation on catalytic nitrile hydration and activation barrier

The kinetic studies, in homogeneous medium, were performed for precatalysts $L^{1-3}RuPPh_3$ by real time monitoring the formation of product benzamide by periodically removing the aliquots from the reaction mixture under anaerobic conditions which was further analyzed by GC-MS using the internal standard that was *p*-toluamide. The rate dependence on the concentration of precatalysts, benzonitrile, and water were determined by varying the concentration of one component systematically and keeping the concentrations of other components constant. In the case of all three precatalyst, the initial rate was found to increase linearly with precatalyst concentration whereas for both nitrile, and water substrates a saturation behavior was observed at higher concentration for all three precatalysts with the exception for precatalyst L^3RuPPh_3 in that case initial

rate was found to be have linear dependence on water concentration even upto a water concentration of 17M.¹³³ This observation indicates that L^3RuPPh_3 kinetically favors benzonitrile coordination over water even when the latter is present in very high concentration. This observation is consistent with the fact that enzyme nitrile hydratase is active only when sulfur donors are asymmetrically oxidized to sulfenate and sulfinic as in case of L^3RuPPh_3 . Moreover, the extraction of rate constant revealed that while nitrile/water exchange equilibrium constant (K_2) show alternating behavior concomitant of sequential sulfur oxidation from L^1RuPPh_3 to L^3RuPPh_3 whereas the hydration rate constant (k_3) quadruples from L^1RuPPh_3 to L^3RuPPh_3 . Furthermore, the activation energy (E_a) for L^1RuPPh_3 was determined to be 72.0 ± 14.0 kJ/mol which is reduced to 45.3 ± 3.7 kJ/mol for L^2RuPPh_3 as a consequence of sulfur oxidation to sulfinic. The precatalyst L^3RuPPh_3 possesses a similar activation energy for nitrile hydration as that of L^2RuPPh_3 . In nut shell, the sulfur oxidation was found to lower the activation energy by ~ 27 kJ/mol and similar trend was observed in case of enthalpy of activation ($\Delta H^\ddagger$). The activation energy observed for the L^3RuPPh_3 is almost half of what is observed for the Co-NHase. However, the entropic barrier ($\Delta S^\ddagger$) was found to increase by 65 J/(mol.K) concomitant with sulfur-oxidation from L^1RuPPh_3 to $L^{2-3}RuPPh_3$. Furthermore, the absolute value of entropic barrier ($\Delta S^\ddagger$) for L^3RuPPh_3 was found to be statistically similar to Co-NHase,²⁸ thereby proving itself to be excellent functional mimic of enzyme. An overall effect of sulfur-oxidation is summarized in the Figure 6.4.

Figure 6.4. Schematic of overall effect of sulfur-oxidation

6.2.2 Isolation of the intermediates of the reaction: substrate- and product-bound species

The catalytic assays performed on $\text{L}^{1-3}\text{RuPPh}_3$ indicate the binding of the product to the pentacoordinate complex and the fact that nitrile hydration takes place suggests that nitrile or water binds once the site is vacant after phosphine dissociation. Therefore, it would offer great advantage to have the nitrile-, water-, and amide-bound products for the series of precatalysts ($\text{L}^{1-3}\text{RuPPh}_3$). With these intermediates in hand, various types of studies can be initiated such as distinguishing between nitrile-bound and water-bound pathway, measuring the exchange equilibrium constant among the nitrile, water, and amide. Further, the determination of the activation parameters for the exchange reactions would offer minute details about the mechanistic aspects of the hydration reaction and XAS studies on these intermediates would provide new equations between sulfur-oxidation and substrates and products. Different proposed strategies to accomplish the aforementioned goals are discussed below.

6.2.3 Substrate-bound intermediates: Nitrile-and water-bound complexes

The substrate bound complexes can be achieved by heating the solution of precatalysts in the presence of a phosphine scavenger and required substrate or product. Various, phosphine scavengers could be utilized for this purpose such as HBF_4 ,⁵⁶ $\text{B}(\text{C}_6\text{F}_5)_3$, CuCl ,¹⁴⁵ and $\text{Ni}(\text{COD})_2$,¹⁴⁶ as shown in the Figure 6.5. The HBF_4 is used for protonation of phosphine but in these complexes it can protonate sulfur donors too. The reaction can be monitored by ^{31}P NMR spectroscopy. The nitrile could itself function as the solvent as all complexes are soluble in nitrile. Further, the water-bound complex could be accessed using a non-coordinating solvent such as chlorobenzene in the presence of water. In a similar way, heating the precatalyst solution in presence of amide would lead to amide-bound intermediate.

Figure 6.5. General scheme for synthesis of nitrile- and water-, and amide-bound complexes

6.2.4 Alternate way to access substrate and product-bound intermediates

Few Fe-NHases are also known to bind the nitrile oxide molecule (NO) that are inactive to hydrate nitriles. However, on photolysis NO molecule dissociates and the catalytic activity is reinstated.^{14,147} Mascharak group recently reported that sulfur-oxidation causes the exogenous NO molecule to dissociate on photolysis, in the Fe-NHase mimics.⁶⁰⁻⁶¹ In the Enemark-Feltham¹⁴⁸ notation these can be denoted as $\{\text{Fe-NO}\}^6$. So, to develop the synthesis of NO analogs of $\text{L}^{1-3}\text{RuPPh}_3$, the nitrile oxide precursor needed is $[\text{NO}][\text{BF}_4]$ in order to have complex with $\{\text{Ru-NO}\}^6$ configuration. The overall scheme to afford these complexes is presented in Figure 6.6. Photolysis of $[\text{L}^{1-3}\text{RuNO}][\text{BF}_4]$ in non-coordinating solvents and in excess presence of nitrile, water or amide can potentially lead to intermediates of the catalytic cycle.

Figure 6.6. Syntheses of intermediates from NO analogues of $\text{L}^{2-3}\text{RuPPh}_3$

6.2.5 Lowering the activation barrier with Ru(III) analogues of $\text{L}^{1-3}\text{RuPPh}_3$

As discussed in Chapter 3, the precatalysts $\text{L}^{1-3}\text{RuPPh}_3$ can be oxidized to corresponding Ru(III) analogues by one electron oxidation via ferrocenium hexafluorophosphates (FcPF_6).¹⁴⁹ The Ru(III) derivative would offer lower barrier to nitrile hydration as Ru(III) has higher Lewis acidity than Ru(II) due to higher charge and lower ionic radii. Additionally, lower or zero TONs were obtained with Ru(III) derivatives probably due to fact that reaction stops at the amido-bound form of the complexes as also noted by the Ford *et.al.* in their $[\text{Ru}(\text{NH}_3)_5(\text{PhCN})]^{3+}$ complexes.¹⁰⁸

6.2.6 $L^{1-3}RuPPh_3$ as mimics of metalloenzyme Thiocyanate Hydrolase (SCNase)

The active-site of enzyme nitrile hydratase is very similar to enzyme thiocyanate hydrolase that employs a cobalt(III) metal and it hydrolyzes thiocyanate ion (SCN^-) into carbonyl sulfide (COS), ammonia (NH_3), and hydroxide (OH^-).^{22-24,150} The enzyme is active only when sulfurs are posttranslationally modified. Therefore, the ruthenium based NHase mimics that show excellent functional activity could possibly be employed as mimics of SCNase too.

6.3 Density functional theory studies

In order to gain additional mechanistic insights into the nitrile hydration reaction, DFT calculations were employed to model the catalytic cycle. Additionally, the binding affinity of the different substrates such as PPh_3 , $PhCN$, H_2O , and $PhCONH_2$ to pentacoordinate complex $L^{1-3}Ru$ was explored derived from corresponding precatalysts $L^{1-3}RuPPh_3$. The calculations were performed in both gas as well as solvent DMF phase.

6.3.1 Sulfur-oxidation effects on kinetic barriers from DFT and binding affinities of substrates

As a first step, the binding affinities of the triphenylphosphine, benzonitrile, water, and benzamide to the pentacoordinate complex were calculated in gas phase and DMF phase. Benzonitrile and water binding were favored over the phosphine and benzamide for $L^{1-3}Ru$. Furthermore, although both benzonitrile and water coordination was energetically favored, the asymmetric sulfur oxidation favored

benzonitrile over water by 19.5 kJ/mol (DMF phase) and 11.6 kJ/mol (gas phase). DFT calculation performed by Shearer *et al.*⁷⁰ on the metalloprotein based NHase mimics also show that nitrile coordination is favored over water when sulfurs are asymmetrically oxidized. Both nitrile and water-bound pathway for hydration were considered but no transition state was observed in case of latter. Therefore, a nitrile-bound pathway is proposed for $L^{1-3}RuPPh_3$ complexes. The nitrile-bound pathway was modeled for the series of precatalysts and enthalpic barriers calculated from DFT studies matched very well with the experimentally measured barriers within the experimental error. In gas phase studies, the sulfur oxidation to sulfinic acid was found to bring down the barrier by ~ 22 kJ/mol as compared to catalyst with no sulfur oxidation whereas further oxidation to mixed sulfinic acid/sulfenic acid lowered the barrier by 36 kJ/mol. Similar trend in enthalpic barrier was observed for DMF phase studies. Calculations on nitrile hydrates from Himo *et al.*^{44,137} also show a decrease in barrier when sulfenic acid acts as a local base. A closer look into the transition state structures ($L^{1-3}RuTS$) revealed that an early transition state is observed for catalysts with sulfur modification thereby lower barriers are observed. Additionally, better polarization of nitrile is observed (calculated NPA charges) concomitant with sulfur oxidation that probably leads to enhanced nitrile hydration alone or in cooperative effect from the entropic effects.

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APPENDIX-A

Figure A1. Kinetic traces for L^1RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$ and $[Cat.] = 0.21mM$ (A), $0.42mM$ (B), and $0.84 mM$ (C)

Figure A2. Kinetic traces for L^1RuPPh_3 under conditions: [PhCN] = 0.97M, and [H₂O] = 2.8M (A), 8.3M (B), 11M (C), 14M (D), and 17M (E), and [Cat.] = 0.21mM

Figure A3. Kinetic traces for L^1RuPPh_3 under conditions: $[PhCN] = 0.12M$ (A), $0.49M$ (B), $0.97M$ (C), 1.9 (D), and $4.0M$ (E), $[H_2O] = 11M$ and $[Cat.] = 0.42mM$

Figure A4 Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$, and $[Cat.] = 0.056mM$ (A), $0.084mM$ (B), and $0.112 mM$ (C)

Figure A5. Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 0.97M$, $[H_2O] = 2.8M$ (A), $5.5M$ (B), $11M$ (C), $14M$ (D), and $17M$ (E), and $[Cat.] = 0.056mM$

Figure A6. Kinetic traces for L^2RuPPh_3 under conditions: $[PhCN] = 0.49M$ (A), $0.97M$ (B), $1.9M$ (C), $2.9M$ (D), and $4.0M$ (E), $[H_2O] = 11M$ and $[Cat.] = 0.056mM$

Figure A7. Plots for L^2RuPPh_3 showing linear dependence of rate vs [Cat.] and k_{obs}^{-1} vs $[PhCN]^{-1}$ and $[H_2O]^{-1}$.

Figure A8. Arrhenius plot for L^2RuPPh_3 in the temperature range 368–398 K under conditions: [Cat.]=0.056 mM, [PhCN]=2.9 M, and $[H_2O]=11$ M equation: $y = -5457.4x + 15.8$

Figure A9. Eyring plot for L^2RuPPh_3 in the temperature range 368–398 K under conditions: [Cat.]=0.056 mM, [PhCN]=2.9 M, and $[H_2O]=11$ M equation: $y = -5074.8x + 8.88$

Figure A10. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 4.0M$, $[H_2O] = 11M$, and $[Cat.] = 0.112mM$ (A), $0.168M$ (B), and $0.224mM$ (C)

Figure A11. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 0.97M$, $[H_2O] = 2.8M$ (A), $8.3M$ (B), $11M$ (C), $17M$ (D), and $19M$ (E), and $[Cat.] = 0.112mM$

Figure A12. Kinetic traces for L^3RuPPh_3 under conditions: $[PhCN] = 0.24M$ (A), $0.49M$ (B), $0.97M$ (C), $1.4M$ (D), and $2.9M$ (E), and $[H_2O] = 11M$, and $[Cat.] = 0.112mM$

Figure A13. The plots for L^3RuPPh_3 showing linear dependence of rate vs [Cat.] and k_{obs}^{-1} vs $[PhCN]^{-1}$ and k_{obs} vs $[H_2O]$

Figure A14. Arrhenius plot for the catalyst L^3RuPPh_3 in the temperature range 368–398K under conditions: [Cat.] = 0.112mM, [PhCN] = 1.9M, and $[H_2O]=11M$ equation: $y = -5170.4x + 15.9$

Figure A15. Eyring plot for L^3RuPPh_3 in the temperature range 368–398K under conditions [Cat.]=0.112mM, [PhCN]=1.9M, and $[H_2O]=11M$ equation: $y = -4787.9x + 8.94$

APPENDIX-B

Optimized coordinates for benzonitrile hydration with water in gas phase

Table B1 Optimized coordinates for Benzonitrile (gas phase)

Z	x	y	z
6	2.045308000	-0.000142000	-0.000032000
7	3.208636000	0.000074000	0.000036000
6	0.610563000	-0.000073000	-0.000017000
6	-0.091427000	-1.217654000	-0.000009000
6	-0.091292000	1.217586000	-0.000009000
6	-1.484259000	-1.211066000	0.000005000
1	0.458958000	-2.152990000	-0.000015000
6	-1.484124000	1.211153000	0.000005000
1	0.459198000	2.152861000	-0.000015000
6	-2.181209000	0.000082000	0.000012000
1	-2.026298000	-2.152234000	0.000011000
1	-2.026058000	2.152382000	0.000010000
1	-3.267607000	0.000143000	0.000023000

Table B2 Optimized coordinates for Water (gas phase)

Z	x	y	z
8	0.000000000	0.000000000	0.119426000
1	0.000000000	0.762617000	-0.477705000
1	0.000000000	-0.762617000	-0.477705000

Table B3 Optimized coordinates for Benziminol (gas phase)

Z	x	y	z
6	0.222894000	0.044184000	-0.001583000
6	-0.449127000	-1.184522000	0.087491000
6	-0.529300000	1.224510000	-0.097047000
6	-1.842922000	-1.226644000	0.096677000
1	0.127659000	-2.099806000	0.153933000
6	-1.921403000	1.180589000	-0.092287000
1	-0.027399000	2.183266000	-0.195253000
6	-2.582770000	-0.046087000	0.008035000
1	-2.351372000	-2.183926000	0.172202000
1	-2.489971000	2.102918000	-0.172166000
1	-3.668830000	-0.080516000	0.012528000
7	2.486324000	1.089426000	0.193710000
1	1.969562000	1.948647000	0.375641000
6	1.711143000	0.092508000	0.010124000
8	2.269174000	-1.127817000	-0.203325000
1	3.231610000	-0.981262000	-0.144720000

Table B4 Optimized coordinates for Benzamide (gas phase)

Z	x	y	z
6	-0.220410000	-0.021856000	-0.018298000
6	0.514969000	-1.208170000	0.106893000
6	0.460703000	1.197856000	-0.141013000
6	1.907220000	-1.174522000	0.134878000
1	-0.029119000	-2.144089000	0.179763000
6	1.855468000	1.230199000	-0.120383000
1	-0.091208000	2.122010000	-0.289548000
6	2.580420000	0.045434000	0.023970000
1	2.469066000	-2.098639000	0.239991000
1	2.375305000	2.178608000	-0.225486000
1	3.666700000	0.071989000	0.042155000
7	-2.421754000	1.024799000	0.201600000
1	-3.418495000	0.900620000	0.323595000
1	-1.998184000	1.771459000	0.733561000
6	-1.718503000	-0.136782000	-0.033912000
8	-2.287623000	-1.196065000	-0.266005000

Table B5 Optimized coordinates for Transition State for Benzonitrile Hydration with water (gas phase)

Z	x	y	z
6	1.533211000	-0.485193000	-0.000143000
7	2.485275000	-1.221780000	-0.000431000
6	0.120873000	-0.197369000	0.000043000
6	-0.769355000	-1.287312000	0.000126000
6	-0.370533000	1.114533000	-0.000055000
6	-2.141648000	-1.053519000	0.000135000
1	-0.376289000	-2.298835000	0.000181000
6	-1.745688000	1.336367000	-0.000061000
1	0.337340000	1.934162000	-0.000189000
6	-2.631370000	0.255946000	0.000040000
1	-2.829685000	-1.893920000	0.000205000
1	-2.126459000	2.353536000	-0.000145000
1	-3.703279000	0.433104000	0.000037000
1	2.813367000	1.982923000	0.000626000
8	2.664539000	1.017738000	0.000254000
1	3.198827000	-0.201136000	-0.000244000

Table B6 Optimized coordinates for PPh₃ (gas phase)

Z	x	y	z
15	-0.000077000	-0.000447000	-1.206677000
6	1.333534000	-1.005927000	-0.403239000
6	2.592019000	-1.007186000	-1.029335000
6	1.160232000	-1.781318000	0.753728000
6	3.653063000	-1.744235000	-0.503180000
1	2.738537000	-0.429069000	-1.938963000
6	2.219344000	-2.528952000	1.274262000
1	0.193864000	-1.804599000	1.248222000
6	3.468110000	-2.509795000	0.650493000
1	4.620036000	-1.729517000	-0.999409000
1	2.067112000	-3.126338000	2.169739000

1	4.290500000	-3.092886000	1.056613000
6	-1.537811000	-0.651328000	-0.402357000
6	-2.115314000	-0.120494000	0.761709000
6	-2.175688000	-1.732566000	-1.034534000
6	-3.292101000	-0.663417000	1.283125000
1	-1.647321000	0.722538000	1.261126000
6	-3.344660000	-2.282211000	-0.507829000
1	-1.754097000	-2.142652000	-1.949501000
6	-3.907434000	-1.746630000	0.653011000
1	-3.727495000	-0.238450000	2.184101000
1	-3.821378000	-3.120658000	-1.009058000
1	-4.823508000	-2.166773000	1.059885000
6	0.205071000	1.657035000	-0.403331000
6	-0.421087000	2.748241000	-1.030130000
6	0.960690000	1.893503000	0.755671000
6	-0.313948000	4.035267000	-0.502860000
1	-0.993019000	2.586792000	-1.941115000
6	1.077750000	3.184077000	1.277445000
1	1.462809000	1.067724000	1.250691000
6	0.438718000	4.256692000	0.652836000
1	-0.808656000	4.865907000	-0.999637000
1	1.669057000	3.350051000	2.174518000
1	0.531792000	5.260080000	1.060031000

Gas Phase DFT Studies optimized coordinates for Catalyst L^1RuPPh_3 and derivatives

Table B7 Optimized coordinates for L^1RuPPh_3 (gas Phase)

Z	x	y	z
44	-0.909135000	0.007027000	-0.134363000
16	-0.904598000	0.727003000	-2.415374000
16	-1.130681000	-1.212727000	1.990186000
16	-1.294225000	2.258329000	0.780950000
15	1.447272000	0.249855000	0.077742000
7	-3.155495000	0.061346000	-0.339194000
7	-1.262265000	-2.049765000	-0.980963000
6	-2.608575000	1.417672000	-2.450901000
1	-2.450684000	2.399121000	-1.997888000
1	-2.950190000	1.555788000	-3.483079000
6	-3.628491000	0.601359000	-1.658828000
1	-4.522137000	1.216701000	-1.496033000
1	-3.952814000	-0.242505000	-2.274658000
6	-3.573416000	-1.361222000	-0.209922000
1	-4.642548000	-1.484830000	-0.451569000
1	-3.414750000	-1.629391000	0.832269000
6	-2.742951000	-2.275570000	-1.101984000
1	-3.026535000	-2.134853000	-2.147695000
1	-2.977318000	-3.321032000	-0.867638000
6	-0.656477000	-2.099128000	-2.341545000
1	-0.917000000	-3.045042000	-2.848090000
1	0.426117000	-2.079926000	-2.217587000
6	-1.076946000	-0.934871000	-3.250118000

1	-2.104622000	-1.028113000	-3.612018000
1	-0.426510000	-0.926411000	-4.129679000
6	-3.708198000	0.808911000	0.840837000
1	-3.485212000	0.167387000	1.693790000
1	-4.805605000	0.872303000	0.734179000
6	-3.128511000	2.201835000	1.154958000
6	-0.921521000	-2.992384000	1.423779000
6	-0.614807000	-3.069048000	-0.095367000
1	0.455797000	-2.926145000	-0.235780000
1	-0.863564000	-4.078903000	-0.469429000
6	-2.144426000	-3.842975000	1.831444000
1	-1.974781000	-4.904570000	1.597082000
1	-3.075288000	-3.541295000	1.345928000
1	-2.304628000	-3.759368000	2.910863000
6	0.293838000	-3.595729000	2.161634000
1	0.093164000	-3.640607000	3.236624000
1	1.185575000	-2.979163000	2.025150000
1	0.508705000	-4.618729000	1.814542000
6	-3.331415000	2.432707000	2.667865000
1	-2.946473000	3.416832000	2.954072000
1	-2.797419000	1.677442000	3.251515000
1	-4.398517000	2.394887000	2.936940000
6	-3.848010000	3.343992000	0.410115000
1	-4.912949000	3.378848000	0.684748000
1	-3.783238000	3.256701000	-0.677695000
1	-3.399547000	4.304999000	0.681684000
6	2.459853000	-0.927049000	-0.964248000
6	2.739152000	-0.589173000	-2.301950000
1	2.471532000	0.394812000	-2.675334000
6	3.371862000	-1.491653000	-3.158911000
1	3.581703000	-1.199444000	-4.184919000
6	3.746808000	-2.756401000	-2.699619000
1	4.246014000	-3.456651000	-3.363980000
6	3.480384000	-3.107623000	-1.375859000
1	3.773043000	-4.084834000	-1.000166000
6	2.840461000	-2.205295000	-0.521213000
1	2.648874000	-2.501804000	0.504135000
6	2.214454000	0.162173000	1.768620000
6	3.488798000	-0.363730000	2.033111000
1	4.076192000	-0.811540000	1.238640000
6	4.027106000	-0.315966000	3.321627000
1	5.013588000	-0.733939000	3.506917000
6	3.305518000	0.271712000	4.360631000
1	3.724550000	0.310246000	5.363055000
6	2.044309000	0.812297000	4.103487000
1	1.474612000	1.274539000	4.905286000
6	1.496892000	0.753266000	2.821695000
1	0.513984000	1.172311000	2.631877000
6	2.217690000	1.857716000	-0.508425000
6	3.614128000	2.020414000	-0.442995000
1	4.237148000	1.222085000	-0.053105000
6	4.220474000	3.200275000	-0.867385000
1	5.301093000	3.302066000	-0.805994000
6	3.441867000	4.250116000	-1.363697000
1	3.913567000	5.173167000	-1.691260000

6	2.058078000	4.105514000	-1.425676000
1	1.438644000	4.918251000	-1.796303000
6	1.449943000	2.918346000	-1.002586000
1	0.370446000	2.837925000	-1.026100000

Table B8 Optimized coordinates for L¹Ru(PhCN) (gas phase)

Z	x	y	z
44	-0.466392000	-0.134680000	0.190615000
16	-0.964643000	-0.966484000	2.380610000
16	0.003008000	1.098676000	-1.875628000
16	-0.757402000	-2.353950000	-0.790024000
7	-2.626733000	0.005679000	-0.083325000
7	-0.723923000	1.885963000	1.044060000
6	-2.695301000	-1.472247000	2.016215000
1	-2.537187000	-2.443335000	1.542022000
1	-3.264396000	-1.612552000	2.942029000
6	-3.428389000	-0.509521000	1.082109000
1	-4.334249000	-1.000312000	0.704886000
1	-3.770025000	0.351847000	1.663888000
6	-2.866549000	1.471695000	-0.245946000
1	-3.944692000	1.701678000	-0.228963000
1	-2.464233000	1.736352000	-1.222569000
6	-2.154579000	2.294653000	0.831757000
1	-2.681270000	2.204722000	1.785310000
1	-2.203415000	3.355814000	0.560670000
6	-0.426345000	1.801234000	2.503842000
1	-0.651255000	2.759507000	3.003355000
1	0.648580000	1.627038000	2.596244000
6	-1.174730000	0.679032000	3.235587000
1	-2.243846000	0.884741000	3.334378000
1	-0.770678000	0.590094000	4.248738000
6	-2.961141000	-0.681813000	-1.382558000
1	-2.502588000	-0.050264000	-2.143914000
1	-4.055922000	-0.652803000	-1.522172000
6	-2.434880000	-2.120161000	-1.598057000
6	0.317245000	2.811327000	-1.163865000
6	0.258653000	2.806071000	0.386326000
1	1.233559000	2.478197000	0.754060000
1	0.092450000	3.834632000	0.754114000
6	-0.645304000	3.841130000	-1.792750000
1	-0.417590000	4.859229000	-1.442131000
1	-1.698221000	3.640705000	-1.578542000
1	-0.534390000	3.828547000	-2.881525000
6	1.750711000	3.244476000	-1.542084000
1	1.853663000	3.288776000	-2.630822000
1	2.487749000	2.528586000	-1.165957000
1	1.989600000	4.240767000	-1.137974000
6	-2.274550000	-2.299532000	-3.123287000

1	-1.930983000	-3.314514000	-3.347651000
1	-1.533984000	-1.598295000	-3.517989000
1	-3.229324000	-2.140700000	-3.649418000
6	-3.419700000	-3.198497000	-1.103652000
1	-4.376473000	-3.131933000	-1.643423000
1	-3.633036000	-3.129924000	-0.033266000
1	-3.001558000	-4.193906000	-1.283784000
7	1.502368000	-0.354213000	0.359853000
6	2.655552000	-0.532227000	0.329912000
6	4.060238000	-0.738905000	0.199655000
6	4.818016000	-1.253909000	1.268857000
6	4.692123000	-0.423755000	-1.020365000
6	6.188237000	-1.446664000	1.115543000
1	4.325137000	-1.502686000	2.203513000
6	6.063037000	-0.621474000	-1.157680000
1	4.096230000	-0.036250000	-1.840549000
6	6.813766000	-1.130916000	-0.093944000
1	6.769495000	-1.847029000	1.941377000
1	6.546885000	-0.380150000	-2.099845000
1	7.883164000	-1.284498000	-0.208271000

Table B9 Optimized coordinates for L¹Ru(H₂O) (gas phase)

Z	x	y	z
44	0.009235000	0.129626000	-0.614888000
16	0.914940000	2.290298000	-0.916580000
16	-1.316026000	-1.909440000	-0.319013000
16	2.087035000	-0.891014000	-1.388428000
7	0.948634000	0.130888000	1.295111000
7	-1.655749000	1.096548000	0.451103000
6	2.227636000	2.155571000	0.373119000
1	3.016901000	1.636189000	-0.174103000
1	2.588399000	3.146069000	0.671705000
6	1.775166000	1.359728000	1.595305000
1	2.652247000	1.064337000	2.183795000
1	1.179353000	2.013017000	2.239292000
6	-0.199242000	0.065839000	2.253444000
1	0.140606000	0.234112000	3.288746000
1	-0.598674000	-0.943290000	2.183673000
6	-1.298064000	1.078397000	1.910340000
1	-0.981071000	2.084433000	2.197439000
1	-2.185876000	0.857790000	2.515218000
6	-1.751183000	2.504312000	-0.040275000
1	-2.482947000	3.076061000	0.556393000
1	-2.128220000	2.453339000	-1.064686000
6	-0.418010000	3.262544000	-0.043068000
1	-0.070240000	3.501949000	0.965375000
1	-0.553701000	4.211357000	-0.571155000
6	1.737492000	-1.154314000	1.406111000
1	0.977013000	-1.934500000	1.433952000
1	2.265855000	-1.155222000	2.375197000
6	2.721967000	-1.512136000	0.263938000
6	-2.948305000	-1.165109000	0.259003000
6	-2.934038000	0.380417000	0.139329000

1	-3.145033000	0.633058000	-0.902704000
1	-3.748336000	0.803997000	0.753864000
6	-3.294665000	-1.659559000	1.678800000
1	-2.562712000	-1.367727000	2.435242000
1	-3.340190000	-2.752878000	1.685077000
1	-4.276528000	-1.278178000	1.996008000
6	-4.067851000	-1.669197000	-0.676985000
1	-4.123360000	-2.761536000	-0.642422000
1	-3.879484000	-1.377330000	-1.715021000
1	-5.048379000	-1.270118000	-0.376476000
6	2.802212000	-3.052516000	0.222795000
1	3.516154000	-3.370028000	-0.543847000
1	1.827707000	-3.483208000	-0.024326000
1	3.136128000	-3.463692000	1.188597000
6	4.142889000	-0.972223000	0.517594000
1	4.177505000	0.117141000	0.607049000
1	4.799330000	-1.247596000	-0.313759000
1	4.565906000	-1.400766000	1.438760000
1	-1.308754000	-0.958580000	-2.346326000
8	-0.955221000	-0.078030000	-2.649458000
1	-0.175564000	-0.307591000	-3.185654000

Table B10 Optimized coordinates for L¹Ru (gas phase)

Z	x	y	z
44	-0.045548000	0.054915000	-0.664603000
16	0.846587000	2.214777000	-1.092838000
16	-1.406314000	-1.828098000	-0.715982000
16	2.017932000	-0.990477000	-1.439262000
7	0.931959000	0.198655000	1.192458000
7	-1.714926000	1.080582000	0.342314000
6	2.182398000	2.188994000	0.179683000
1	2.980159000	1.660885000	-0.345313000
1	2.519702000	3.202817000	0.420599000
6	1.751028000	1.450025000	1.442065000
1	2.630597000	1.181961000	2.038450000
1	1.148065000	2.122055000	2.059623000
6	-0.210251000	0.150412000	2.163386000
1	0.140277000	0.372705000	3.184589000
1	-0.578569000	-0.872454000	2.149565000
6	-1.350976000	1.109503000	1.799415000
1	-1.077603000	2.134081000	2.067684000
1	-2.224006000	0.857821000	2.413791000
6	-1.803292000	2.474907000	-0.193522000
1	-2.527132000	3.068530000	0.390872000
1	-2.189772000	2.396553000	-1.212202000
6	-0.467865000	3.224136000	-0.236123000
1	-0.108794000	3.492981000	0.760788000
1	-0.606479000	4.157210000	-0.790914000
6	1.739167000	-1.075490000	1.358908000
1	0.988219000	-1.862664000	1.425540000
1	2.264838000	-1.018493000	2.327691000
6	2.716988000	-1.473367000	0.230715000
6	-2.991285000	-1.178815000	0.058820000

6	-3.004030000	0.366523000	0.047145000
1	-3.266693000	0.673050000	-0.968152000
1	-3.790426000	0.745593000	0.722901000
6	-3.212372000	-1.778207000	1.461647000
1	-4.176893000	-1.451018000	1.877133000
1	-2.433035000	-1.509324000	2.178512000
1	-3.225831000	-2.870528000	1.398989000
6	-4.165038000	-1.642831000	-0.829556000
1	-4.206221000	-2.736171000	-0.856033000
1	-4.045742000	-1.288146000	-1.858083000
1	-5.126876000	-1.277659000	-0.440139000
6	2.843743000	-3.011173000	0.291382000
1	3.550247000	-3.355800000	-0.470199000
1	1.879203000	-3.486750000	0.091769000
1	3.212235000	-3.348864000	1.273285000
6	4.127169000	-0.883023000	0.427763000
1	4.139070000	0.210025000	0.450912000
1	4.775437000	-1.192355000	-0.397973000
1	4.577337000	-1.245760000	1.364377000

Table B11 Optimized coordinates for L¹Ru(PhCONH₂) (gas phase)

Z	x	y	z
44	-0.639833000	0.001033000	-0.301690000
16	-1.581779000	-1.167689000	-2.139389000
16	0.520994000	0.820633000	1.697644000
16	-1.575173000	2.126167000	-1.074621000
7	-2.533546000	-0.244547000	0.662955000
7	-0.222213000	-1.982576000	0.578256000
6	-3.344263000	-0.877753000	-1.695582000
1	-3.510407000	0.118328000	-2.111451000
1	-4.001250000	-1.591791000	-2.204395000
6	-3.592802000	-0.905790000	-0.189241000
1	-4.562321000	-0.440537000	0.026005000
1	-3.675952000	-1.947933000	0.131527000
6	-2.242477000	-1.121977000	1.836991000
1	-3.175088000	-1.461618000	2.317042000
1	-1.691473000	-0.507654000	2.544627000
6	-1.399794000	-2.337191000	1.440354000
1	-2.016487000	-3.059274000	0.899732000
1	-1.060854000	-2.851111000	2.347901000
6	-0.095249000	-2.956252000	-0.548588000
1	-0.008220000	-3.986911000	-0.162619000
1	0.830457000	-2.713139000	-1.074925000
6	-1.254072000	-2.908981000	-1.553217000
1	-2.184977000	-3.320716000	-1.153036000
1	-0.984388000	-3.510812000	-2.426182000
6	-2.950540000	1.114484000	1.174219000
1	-2.217749000	1.343732000	1.947987000
1	-3.941126000	1.016511000	1.651306000
6	-2.957094000	2.302074000	0.180836000
6	1.249973000	-0.786964000	2.364816000
6	1.062602000	-1.940376000	1.347020000
1	1.842024000	-1.849077000	0.587663000
1	1.210257000	-2.910151000	1.855885000

6	0.683380000	-1.108493000	3.765261000
1	1.156150000	-2.012044000	4.178926000
1	-0.397248000	-1.260002000	3.785975000
1	0.900160000	-0.277164000	4.443297000
6	2.772202000	-0.610393000	2.551452000
1	3.228554000	-1.524744000	2.960709000
1	2.971210000	0.205937000	3.253038000
1	3.267278000	-0.369612000	1.608739000
6	-2.709449000	3.573354000	1.019641000
1	-2.728450000	4.457875000	0.374901000
1	-1.731263000	3.529693000	1.506792000
1	-3.483506000	3.700570000	1.792804000
6	-4.308200000	2.469812000	-0.541243000
1	-5.116482000	2.658486000	0.181261000
1	-4.586506000	1.596877000	-1.137966000
1	-4.261649000	3.323991000	-1.224128000
6	2.395394000	-0.124177000	-1.663102000
7	1.189929000	0.617870000	-1.600635000
1	0.686554000	0.537820000	-2.480937000
8	2.399077000	-1.210660000	-2.227883000
6	3.624411000	0.468155000	-1.058753000
6	4.843489000	-0.164860000	-1.355005000
6	3.621414000	1.620119000	-0.254643000
6	6.040890000	0.351845000	-0.870203000
1	4.825801000	-1.055058000	-1.974750000
6	4.824730000	2.129797000	0.233832000
1	2.688857000	2.082504000	0.053539000
6	6.033208000	1.503723000	-0.077044000
1	6.979691000	-0.139936000	-1.109555000
1	4.813335000	3.012564000	0.866485000
1	6.967895000	1.908567000	0.302052000
1	1.276848000	1.593737000	-1.329816000

Table B12 Optimized coordinates for $L^1Ru(PhC(OH)NH)$ (gas phase)

Z	x	y	z
44	-0.543736000	-0.080330000	-0.363933000
16	-2.030910000	-0.300759000	-2.217098000
16	0.865049000	-0.290753000	1.637216000
16	-0.503623000	2.355375000	-0.654157000
7	-2.328837000	0.353647000	0.810271000
7	-1.071195000	-2.175736000	0.124173000
6	-3.435591000	0.641852000	-1.492912000
1	-3.140861000	1.670871000	-1.709752000
1	-4.368698000	0.416823000	-2.021374000
6	-3.603436000	0.407227000	0.008172000
1	-4.254940000	1.187331000	0.421205000
1	-4.132905000	-0.538508000	0.156143000
6	-2.399897000	-0.783911000	1.776023000
1	-3.353931000	-0.776124000	2.329553000
1	-1.581824000	-0.634395000	2.479053000
6	-2.229771000	-2.137425000	1.081769000
1	-3.137578000	-2.391188000	0.528416000

1	-2.113425000	-2.918385000	1.842706000
6	-1.484246000	-2.849752000	-1.139700000
1	-1.871504000	-3.862927000	-0.934086000
1	-0.580290000	-2.966644000	-1.743488000
6	-2.532455000	-2.080416000	-1.955211000
1	-3.522197000	-2.100729000	-1.491736000
1	-2.631510000	-2.554457000	-2.936767000
6	-2.066860000	1.619471000	1.583093000
1	-1.276739000	1.346872000	2.283217000
1	-2.971714000	1.871197000	2.163822000
6	-1.580686000	2.860207000	0.795296000
6	0.883974000	-2.158395000	1.844134000
6	0.137770000	-2.859884000	0.682076000
1	0.828994000	-2.926642000	-0.160966000
1	-0.131727000	-3.889844000	0.978713000
6	0.341869000	-2.556681000	3.233409000
1	0.411650000	-3.644350000	3.387974000
1	-0.696596000	-2.259340000	3.398268000
1	0.938453000	-2.068886000	4.010668000
6	2.348064000	-2.643853000	1.777440000
1	2.413998000	-3.739716000	1.869247000
1	2.926541000	-2.201772000	2.594497000
1	2.818010000	-2.340793000	0.837595000
6	-0.735413000	3.698209000	1.778224000
1	-0.384157000	4.611756000	1.287382000
1	0.139610000	3.133842000	2.113448000
1	-1.322311000	3.993311000	2.662508000
6	-2.740786000	3.748992000	0.304615000
1	-3.332665000	4.123620000	1.153398000
1	-3.420727000	3.230170000	-0.376495000
1	-2.343618000	4.613746000	-0.236528000
6	2.399063000	-0.353775000	-1.795012000
7	1.125014000	-0.489208000	-1.646839000
1	0.779382000	-0.952912000	-2.489580000
8	2.942024000	-0.956630000	-2.902884000
1	3.822047000	-0.576977000	-3.061079000
6	3.357584000	0.366099000	-0.931681000
6	4.675906000	-0.116890000	-0.828789000
6	3.004979000	1.556554000	-0.278243000
6	5.626129000	0.576821000	-0.081012000
1	4.949398000	-1.060498000	-1.295785000
6	3.966853000	2.252931000	0.450093000
1	1.987510000	1.930943000	-0.348167000
6	5.273813000	1.769117000	0.553759000
1	6.635788000	0.184848000	0.006342000
1	3.687714000	3.178352000	0.945856000
1	6.014692000	2.317241000	1.130028000

Table B13 Optimized coordinates for L¹RuTS (gas phase)

Z	x	y	z
44	-0.545668000	-0.004680000	0.293486000
16	-1.146341000	-0.209236000	2.573114000
16	-0.042937000	0.592785000	-2.041729000
16	-0.709549000	-2.413275000	-0.013400000

7	-2.706848000	-0.024627000	-0.132750000
7	-0.828257000	2.125737000	0.513512000
6	-2.875518000	-0.812120000	2.313168000
1	-2.728746000	-1.890892000	2.216541000
1	-3.484687000	-0.635496000	3.206894000
6	-3.570471000	-0.223280000	1.080328000
1	-4.427715000	-0.858203000	0.819228000
1	-3.987614000	0.750313000	1.353714000
6	-2.932253000	1.346217000	-0.691639000
1	-4.009178000	1.570760000	-0.773101000
1	-2.493638000	1.346473000	-1.688110000
6	-2.254712000	2.437098000	0.148472000
1	-2.814296000	2.598488000	1.073576000
1	-2.301692000	3.384924000	-0.401054000
6	-0.578020000	2.460814000	1.948368000
1	-0.794891000	3.525718000	2.139591000
1	0.488143000	2.294837000	2.118374000
6	-1.372658000	1.604689000	2.941517000
1	-2.442272000	1.833931000	2.945625000
1	-0.997438000	1.795797000	3.951497000
6	-2.914631000	-1.040610000	-1.220978000
1	-2.481406000	-0.578917000	-2.107768000
1	-3.996026000	-1.172121000	-1.395114000
6	-2.264023000	-2.452648000	-1.082354000
6	0.299122000	2.423532000	-1.821469000
6	0.187630000	2.836935000	-0.331422000
1	1.140692000	2.602555000	0.145225000
1	0.020330000	3.926059000	-0.254957000
6	-0.617548000	3.254654000	-2.742368000
1	-0.381893000	4.327107000	-2.667602000
1	-1.681537000	3.128383000	-2.523044000
1	-0.467825000	2.950478000	-3.783229000
6	1.757712000	2.702134000	-2.242340000
1	1.896495000	2.457812000	-3.300326000
1	2.449730000	2.086966000	-1.660670000
1	2.019605000	3.762874000	-2.101697000
6	-1.911043000	-2.941088000	-2.497146000
1	-1.495367000	-3.953562000	-2.461897000
1	-1.178584000	-2.278901000	-2.968302000
1	-2.808776000	-2.968019000	-3.131576000
6	-3.220807000	-3.463104000	-0.421560000
1	-4.137989000	-3.560836000	-1.017927000
1	-3.508670000	-3.166385000	0.592315000
1	-2.752788000	-4.450044000	-0.353724000
7	1.493123000	0.025383000	0.641930000
6	2.352027000	-0.703449000	0.147460000
6	3.827070000	-0.691373000	0.279060000
6	4.391812000	-0.065218000	1.405137000
6	4.686899000	-1.251289000	-0.680978000
6	5.772487000	-0.010709000	1.569469000
1	3.722996000	0.371698000	2.139625000
6	6.071879000	-1.191312000	-0.513573000
1	4.268706000	-1.704960000	-1.573399000
6	6.621060000	-0.576170000	0.611575000
1	6.190807000	0.471713000	2.449460000

1	6.721700000	-1.621889000	-1.271314000
1	7.699274000	-0.533365000	0.741463000
1	0.656462000	-2.174110000	-0.738518000
8	1.950503000	-1.878952000	-0.839064000
1	2.442459000	-2.673695000	-0.559647000

Gas Phase DFT Studies optimized coordinates for Catalyst L^2RuPPh_3 and derivatives

Table B14 Optimized coordinates for L^2RuPPh_3 (gas phase):

Z	x	y	z
44	-0.896504000	-0.109404000	-0.146344000
16	-0.932950000	0.504031000	-2.474724000
16	-1.046396000	-1.258773000	2.017900000
16	-1.435823000	2.049920000	0.587814000
15	1.510531000	0.254647000	0.065533000
7	-3.141365000	-0.264904000	-0.377513000
7	-1.092074000	-2.239922000	-0.927581000
6	-2.694809000	1.027492000	-2.568492000
1	-2.622800000	2.049957000	-2.191620000
1	-3.027401000	1.042988000	-3.612323000
6	-3.649999000	0.180382000	-1.726783000
1	-4.582181000	0.740713000	-1.586587000
1	-3.917243000	-0.716026000	-2.293285000
6	-3.447272000	-1.712795000	-0.200823000
1	-4.502671000	-1.921531000	-0.440906000
1	-3.275758000	-1.933744000	0.849734000
6	-2.544533000	-2.584770000	-1.059191000
1	-2.825479000	-2.490989000	-2.110288000
1	-2.701218000	-3.638909000	-0.798344000
6	-0.461910000	-2.297193000	-2.276227000
1	-0.646172000	-3.278315000	-2.747960000
1	0.613356000	-2.197506000	-2.139133000
6	-0.948224000	-1.200282000	-3.234057000
1	-1.955154000	-1.388584000	-3.616547000
1	-0.277295000	-1.174477000	-4.097593000
6	-3.783727000	0.461042000	0.773690000
1	-3.571700000	-0.164288000	1.640462000
1	-4.874490000	0.472004000	0.616745000
6	-3.295119000	1.883977000	1.103032000
6	-0.698733000	-3.040531000	1.524011000
6	-0.385275000	-3.167152000	0.009692000

1	0.673048000	-2.963391000	-0.135871000
1	-0.564128000	-4.208315000	-0.314667000
6	-1.852929000	-3.962389000	1.973598000
1	-1.593658000	-5.017336000	1.800882000
1	-2.799426000	-3.767319000	1.463920000
1	-2.031444000	-3.832702000	3.045545000
6	0.560360000	-3.509745000	2.285489000
1	0.365738000	-3.515939000	3.362437000
1	1.403182000	-2.835578000	2.113326000
1	0.850206000	-4.529966000	1.988969000
6	-3.373898000	2.072619000	2.624785000
1	-3.044112000	3.075532000	2.905032000
1	-2.739718000	1.352945000	3.149601000
1	-4.410335000	1.936814000	2.963942000
6	-4.101831000	2.985484000	0.403653000
1	-5.136744000	2.962425000	0.771639000
1	-4.120245000	2.879680000	-0.683425000
1	-3.681271000	3.970331000	0.620386000
6	2.502571000	-0.881059000	-1.041198000
6	2.737162000	-0.487492000	-2.372291000
1	2.436650000	0.502734000	-2.700327000
6	3.363894000	-1.343523000	-3.279557000
1	3.536835000	-1.008969000	-4.299372000
6	3.781541000	-2.614767000	-2.878218000
1	4.277131000	-3.278249000	-3.581797000
6	3.564311000	-3.019021000	-1.560907000
1	3.892318000	-4.000812000	-1.228998000
6	2.928355000	-2.164019000	-0.655842000
1	2.774935000	-2.504255000	0.362035000
6	2.302113000	0.107572000	1.740030000
6	3.560988000	-0.470183000	1.973529000
1	4.127530000	-0.911686000	1.161252000
6	4.119066000	-0.471402000	3.254657000
1	5.093198000	-0.927153000	3.414166000
6	3.434711000	0.118661000	4.316980000
1	3.869393000	0.119927000	5.313451000
6	2.194107000	0.716145000	4.088550000
1	1.657624000	1.190753000	4.905737000
6	1.625053000	0.708627000	2.814680000
1	0.669622000	1.195133000	2.650324000
6	2.261340000	1.872145000	-0.499488000
6	3.642067000	2.079754000	-0.320509000
1	4.246285000	1.330586000	0.179942000
6	4.253318000	3.246691000	-0.771321000
1	5.320606000	3.387286000	-0.619672000
6	3.495868000	4.234177000	-1.408636000
1	3.971392000	5.147971000	-1.756211000
6	2.128108000	4.041261000	-1.583087000
1	1.521728000	4.807055000	-2.059432000
6	1.510867000	2.867673000	-1.134268000
1	0.438852000	2.769583000	-1.247355000
8	-0.741664000	2.621993000	1.786494000
8	-1.525743000	3.004552000	-0.588338000

Table B15 Optimized coordinates for $L^2Ru(PhCN)$ (gas phase):

Z	x	y	z
44	-0.481900000	0.112700000	0.254412000
16	-0.959554000	-0.520365000	2.526951000
16	-0.197375000	1.131273000	-1.951840000
16	0.148240000	-2.055536000	-0.320683000
7	-2.507267000	-0.543017000	-0.202512000
7	-1.502318000	2.019480000	0.729737000
6	-2.364950000	-1.638895000	2.128681000
1	-1.823430000	-2.553423000	1.874144000
1	-2.981724000	-1.813401000	3.017187000
6	-3.239308000	-1.147011000	0.973861000
1	-3.855954000	-1.981290000	0.617670000
1	-3.936886000	-0.393938000	1.352060000
6	-3.202541000	0.715010000	-0.624255000
1	-4.287792000	0.550122000	-0.720313000
1	-2.796864000	0.972295000	-1.600799000
6	-2.946651000	1.869709000	0.349619000
1	-3.527727000	1.724241000	1.263419000
1	-3.316515000	2.800456000	-0.097141000
6	-1.376490000	2.248796000	2.198103000
1	-1.958033000	3.135252000	2.505363000
1	-0.322807000	2.463842000	2.392948000
6	-1.802292000	1.052956000	3.058832000
1	-2.883945000	0.893968000	3.051198000
1	-1.517500000	1.251622000	4.096695000
6	-2.430641000	-1.467218000	-1.395618000
1	-2.177619000	-0.812668000	-2.229674000
1	-3.433629000	-1.885425000	-1.578073000
6	-1.391047000	-2.614535000	-1.370842000
6	-0.547688000	2.926813000	-1.525375000
6	-0.798247000	3.116830000	-0.007023000
1	0.176013000	3.195448000	0.480677000
1	-1.334411000	4.067651000	0.163028000
6	-1.702016000	3.470398000	-2.393057000
1	-1.859151000	4.543813000	-2.209477000
1	-2.653183000	2.958814000	-2.223433000
1	-1.456270000	3.344042000	-3.452067000
6	0.709674000	3.756538000	-1.865503000
1	0.925990000	3.689040000	-2.936100000
1	1.582754000	3.378394000	-1.325492000
1	0.569273000	4.819519000	-1.614265000
6	-0.911108000	-2.847141000	-2.810460000
1	-0.184605000	-3.662830000	-2.842540000
1	-0.426685000	-1.956330000	-3.218980000
1	-1.761309000	-3.111862000	-3.454849000
6	-1.942782000	-3.923868000	-0.793508000
1	-2.731227000	-4.310797000	-1.453807000
1	-2.364349000	-3.809543000	0.207920000
1	-1.153085000	-4.675638000	-0.721206000
7	1.468435000	0.536715000	0.586683000
6	2.631331000	0.497880000	0.570138000
6	4.029425000	0.238714000	0.436869000
6	5.001480000	1.094574000	0.981417000
6	4.404354000	-0.922916000	-0.268167000
6	6.350032000	0.787910000	0.820146000

1	4.696067000	1.985405000	1.521829000
6	5.758347000	-1.212021000	-0.418192000
1	3.627676000	-1.565462000	-0.676544000
6	6.728670000	-0.362664000	0.122016000
1	7.106192000	1.445802000	1.238941000
1	6.056307000	-2.105351000	-0.959411000
1	7.782644000	-0.597105000	-0.000567000
8	0.101588000	-2.972629000	0.880185000
8	1.349306000	-2.247476000	-1.197282000

Table B16 Optimized coordinates for L²Ru(H₂O) (gas phase):

Z	x	y	z
44	-0.062470000	0.120528000	-0.518231000
16	0.743925000	2.308880000	-0.993915000
16	-1.320524000	-1.940234000	-0.057770000
16	1.994725000	-0.781552000	-0.897403000
7	0.595325000	0.444963000	1.489509000
7	-1.927570000	1.109182000	0.201760000
6	1.864689000	2.441075000	0.466267000
1	2.757614000	1.939866000	0.086701000
1	2.096256000	3.490503000	0.678148000
6	1.310943000	1.761147000	1.718781000
1	2.127572000	1.599809000	2.432664000
1	0.603884000	2.437484000	2.207144000
6	-0.670091000	0.431898000	2.293805000
1	-0.478878000	0.754607000	3.329709000
1	-1.010094000	-0.600613000	2.310758000
6	-1.758905000	1.317990000	1.676644000
1	-1.526808000	2.371817000	1.851416000
1	-2.705301000	1.128919000	2.197840000
6	-2.030478000	2.418679000	-0.506048000
1	-2.873146000	3.011118000	-0.108979000
1	-2.250907000	2.191953000	-1.552246000
6	-0.756706000	3.269363000	-0.446953000
1	-0.569050000	3.675823000	0.550486000
1	-0.875169000	4.121695000	-1.122912000
6	1.420984000	-0.768493000	1.879646000
1	0.686936000	-1.564192000	2.000228000
1	1.880404000	-0.571880000	2.860707000
6	2.508038000	-1.286667000	0.896131000
6	-3.050488000	-1.244004000	0.199105000
6	-3.108449000	0.263392000	-0.152658000
1	-3.196143000	0.347074000	-1.239113000
1	-4.020257000	0.707497000	0.285384000
6	-3.557044000	-1.555531000	1.623164000
1	-2.955871000	-1.101973000	2.414403000
1	-3.540356000	-2.636878000	1.789968000

1	-4.593557000	-1.210602000	1.750068000
6	-4.003028000	-1.963358000	-0.780626000
1	-4.004055000	-3.039795000	-0.584027000
1	-3.691934000	-1.814347000	-1.819498000
1	-5.034830000	-1.597733000	-0.670627000
6	2.526524000	-2.819719000	0.963043000
1	3.292436000	-3.220649000	0.293881000
1	1.564975000	-3.242402000	0.658829000
1	2.749720000	-3.154778000	1.985455000
6	3.902814000	-0.726905000	1.200419000
1	3.926998000	0.365644000	1.222513000
1	4.621162000	-1.044770000	0.440969000
1	4.242624000	-1.098506000	2.176965000
1	-1.098797000	-1.320217000	-2.244508000
8	-0.586239000	-0.558204000	-2.616219000
1	0.267905000	-0.988832000	-2.841818000
8	3.052030000	0.223465000	-1.286530000
8	1.958990000	-2.008334000	-1.769271000

Table B17 Optimized coordinates for L²Ru (gas phase)

Z	x	y	z
44	-0.142643000	0.040997000	-0.540623000
16	0.636105000	2.228131000	-1.142240000
16	-1.386727000	-1.911961000	-0.549336000
16	1.927007000	-0.889486000	-1.012738000
7	0.635403000	0.484641000	1.375081000
7	-1.978547000	1.057973000	0.192723000
6	1.831255000	2.452508000	0.242848000
1	2.712491000	1.944479000	-0.152626000
1	2.055548000	3.513819000	0.394209000
6	1.329455000	1.827312000	1.539736000
1	2.162317000	1.705050000	2.241243000
1	0.616967000	2.506715000	2.016047000
6	-0.596991000	0.459240000	2.234532000
1	-0.363624000	0.820597000	3.248760000
1	-0.894568000	-0.583552000	2.309312000
6	-1.758792000	1.279787000	1.658382000
1	-1.584073000	2.346209000	1.826657000
1	-2.666389000	1.029320000	2.221284000
6	-2.101502000	2.365769000	-0.522738000
1	-2.925432000	2.963324000	-0.096514000
1	-2.366357000	2.132193000	-1.556419000
6	-0.824268000	3.209153000	-0.530671000
1	-0.589128000	3.620844000	0.454368000
1	-0.972800000	4.058520000	-1.204635000
6	1.511125000	-0.685188000	1.788580000
1	0.812969000	-1.505356000	1.956102000
1	1.976986000	-0.433311000	2.754353000
6	2.582761000	-1.182182000	0.796531000
6	-3.066058000	-1.310910000	0.036943000
6	-3.183178000	0.220293000	-0.130318000
1	-3.379469000	0.406478000	-1.188637000
1	-4.049610000	0.599367000	0.438737000
6	-3.353881000	-1.794022000	1.471571000

1	-4.367568000	-1.503207000	1.783575000
1	-2.652357000	-1.401558000	2.211374000
1	-3.288612000	-2.885308000	1.515279000
6	-4.125061000	-1.947047000	-0.888405000
1	-4.091359000	-3.037676000	-0.804902000
1	-3.942852000	-1.686160000	-1.935635000
1	-5.138029000	-1.617949000	-0.615037000
6	2.736947000	-2.697201000	0.991603000
1	3.495350000	-3.089687000	0.310117000
1	1.803089000	-3.224579000	0.777783000
1	3.044548000	-2.922528000	2.022831000
6	3.944669000	-0.500348000	0.972603000
1	3.892640000	0.590265000	0.934862000
1	4.631517000	-0.810840000	0.181601000
1	4.378109000	-0.787426000	1.940816000
8	2.865686000	0.169125000	-1.542274000
8	2.007683000	-2.214139000	-1.691510000

Table B18 Optimized coordinates for L²Ru(PhCONH₂) (gas phase)

Z	x	y	z
44	-0.601451000	-0.127207000	-0.290990000
16	-1.883317000	-0.646342000	-2.242519000
16	0.791227000	-0.056704000	1.723905000
16	-1.134968000	2.094823000	-0.384681000
7	-2.431890000	-0.362467000	0.819549000
7	-0.455702000	-2.329851000	0.014720000
6	-3.523076000	-0.227867000	-1.515624000
1	-3.538979000	0.854810000	-1.663675000
1	-4.331321000	-0.687103000	-2.095096000
6	-3.652172000	-0.611717000	-0.040894000
1	-4.506281000	-0.077630000	0.392717000
1	-3.890064000	-1.676835000	0.026173000
6	-2.192427000	-1.561340000	1.683834000
1	-3.123856000	-1.880113000	2.178449000
1	-1.480332000	-1.247559000	2.443046000
6	-1.604309000	-2.730983000	0.890503000
1	-2.374414000	-3.188800000	0.264730000
1	-1.288086000	-3.511651000	1.593208000
6	-0.573000000	-2.969515000	-1.328121000
1	-0.612362000	-4.068829000	-1.234400000
1	0.337474000	-2.713757000	-1.876413000
6	-1.791373000	-2.503757000	-2.136887000
1	-2.737470000	-2.877586000	-1.735865000
1	-1.702808000	-2.889169000	-3.157138000
6	-2.563972000	0.850943000	1.717143000
1	-1.791226000	0.709142000	2.472125000
1	-3.546979000	0.810985000	2.212383000
6	-2.357753000	2.260870000	1.100743000
6	1.326072000	-1.859662000	1.854756000
6	0.877749000	-2.664420000	0.609115000
1	1.598893000	-2.481221000	-0.189778000

1	0.906213000	-3.744716000	0.838998000
6	0.849027000	-2.478911000	3.186315000
1	1.233866000	-3.503630000	3.296633000
1	-0.236626000	-2.519181000	3.297877000
1	1.233334000	-1.886179000	4.022240000
6	2.869129000	-1.910746000	1.882462000
1	3.226846000	-2.948876000	1.957941000
1	3.246895000	-1.361454000	2.750509000
1	3.302384000	-1.458940000	0.987998000
6	-1.698566000	3.153594000	2.161635000
1	-1.550086000	4.164044000	1.771732000
1	-0.722141000	2.763583000	2.460650000
1	-2.338588000	3.216943000	3.052537000
6	-3.662478000	2.904078000	0.614523000
1	-4.316193000	3.097496000	1.475972000
1	-4.210090000	2.278918000	-0.095380000
1	-3.461489000	3.853542000	0.112688000
6	2.433406000	-0.101787000	-1.592386000
7	1.183499000	0.575986000	-1.576663000
1	0.750975000	0.507711000	-2.495878000
8	2.521384000	-1.173297000	-2.178550000
6	3.586409000	0.551428000	-0.914023000
6	4.856579000	-0.006676000	-1.137419000
6	3.459965000	1.689357000	-0.098465000
6	5.987065000	0.566797000	-0.564291000
1	4.932076000	-0.885751000	-1.768878000
6	4.597845000	2.255347000	0.476195000
1	2.489149000	2.122997000	0.121220000
6	5.857951000	1.700790000	0.243947000
1	6.966853000	0.133986000	-0.746509000
1	4.494712000	3.129969000	1.111723000
1	6.739788000	2.150480000	0.692960000
1	1.223234000	1.555285000	-1.280233000
8	-1.978482000	2.471257000	-1.581803000
8	0.033309000	3.022935000	-0.152221000

Table B19 Optimized coordinates for L²Ru(PhC(OH)NH) (gas phase):

Z	x	y	z
44	0.541420000	-0.167780000	0.301116000
16	2.013430000	-0.474825000	2.191324000
16	-0.899159000	-0.347500000	-1.668092000
16	0.827717000	2.137823000	0.316936000
7	2.361175000	-0.195133000	-0.904822000
7	0.701131000	-2.380228000	0.042768000
6	3.536807000	0.137150000	1.366079000
1	3.407593000	1.215690000	1.484291000
1	4.428087000	-0.189683000	1.912794000
6	3.637680000	-0.282188000	-0.100127000
1	4.408957000	0.324891000	-0.589933000
1	3.990145000	-1.316274000	-0.147938000
6	2.225012000	-1.427158000	-1.743108000
1	3.162921000	-1.640121000	-2.281561000
1	1.442418000	-1.213015000	-2.469037000
6	1.828592000	-2.649058000	-0.910519000

1	2.686977000	-3.003917000	-0.335168000
1	1.561385000	-3.470280000	-1.585987000
6	1.004287000	-2.977344000	1.373420000
1	1.194879000	-4.060849000	1.281945000
1	0.106265000	-2.856429000	1.985382000
6	2.190213000	-2.326275000	2.096128000
1	3.147838000	-2.562900000	1.624802000
1	2.234552000	-2.714176000	3.118562000
6	2.327895000	1.001904000	-1.822633000
1	1.528734000	0.778590000	-2.530000000
1	3.278887000	1.045589000	-2.378478000
6	2.025847000	2.382251000	-1.198551000
6	-1.243868000	-2.194679000	-1.678261000
6	-0.619374000	-2.888800000	-0.442561000
1	-1.299571000	-2.740464000	0.399269000
1	-0.543325000	-3.975990000	-0.624854000
6	-0.797902000	-2.823032000	-3.015500000
1	-1.063369000	-3.890207000	-3.055446000
1	0.274461000	-2.737333000	-3.206079000
1	-1.308696000	-2.320177000	-3.842556000
6	-2.769652000	-2.406109000	-1.572555000
1	-3.025268000	-3.477307000	-1.559897000
1	-3.271807000	-1.950301000	-2.431408000
1	-3.170394000	-1.937988000	-0.669950000
6	1.284751000	3.217362000	-2.252839000
1	1.056373000	4.212078000	-1.862699000
1	0.339805000	2.749414000	-2.541145000
1	1.908545000	3.329265000	-3.151118000
6	3.275036000	3.142525000	-0.736339000
1	3.888160000	3.405445000	-1.609544000
1	3.899821000	2.574107000	-0.043816000
1	2.992051000	4.064644000	-0.222770000
6	-2.379533000	0.094181000	1.886984000
7	-1.123075000	-0.118448000	1.695571000
1	-0.716740000	-0.319483000	2.611274000
8	-2.845684000	-0.156469000	3.150069000
6	-3.395178000	0.568298000	0.924270000
6	-4.694311000	0.028001000	0.987286000
6	-3.108975000	1.599030000	0.018310000
6	-5.693204000	0.501142000	0.139034000
1	-4.912733000	-0.787823000	1.673140000
6	-4.123684000	2.079733000	-0.809778000
1	-2.115510000	2.038282000	-0.010974000
6	-5.407684000	1.534014000	-0.758014000
1	-6.688269000	0.066639000	0.179082000
1	-3.901524000	2.886851000	-1.501785000
1	-6.187667000	1.912533000	-1.413729000
8	1.667388000	2.562187000	1.501813000
8	-0.334550000	3.047137000	0.037755000
1	-3.716641000	0.263198000	3.247481000

Table B20 Optimized coordinates for L²RuTS (gas phase)

Z x y z

44	-0.490884000	0.115854000	0.108810000
16	-0.334625000	-0.788277000	2.335371000
16	-0.725792000	1.427366000	-1.936257000
16	-0.485665000	-1.833497000	-1.057957000
7	-2.665834000	-0.178553000	0.338700000
7	-0.903820000	2.026343000	1.103528000
6	-1.981428000	-1.594222000	2.387238000
1	-1.769022000	-2.559213000	1.924912000
1	-2.294241000	-1.773291000	3.422032000
6	-3.071893000	-0.820548000	1.640011000
1	-3.920253000	-1.493011000	1.459289000
1	-3.448192000	-0.032120000	2.297231000
6	-3.179678000	1.225146000	0.287713000
1	-4.250042000	1.267978000	0.550118000
1	-3.051393000	1.556296000	-0.741768000
6	-2.396387000	2.160516000	1.221023000
1	-2.674329000	1.969839000	2.261128000
1	-2.697298000	3.194457000	1.015817000
6	-0.272184000	2.015441000	2.454525000
1	-0.546493000	2.921839000	3.020265000
1	0.808148000	2.038471000	2.293287000
6	-0.618376000	0.782003000	3.293285000
1	-1.652643000	0.787719000	3.647767000
1	0.025733000	0.759631000	4.177240000
6	-3.142186000	-0.942105000	-0.864946000
1	-3.058762000	-0.236423000	-1.693172000
1	-4.206071000	-1.201196000	-0.738838000
6	-2.363572000	-2.222735000	-1.273106000
6	-0.565662000	3.155960000	-1.228050000
6	-0.257710000	3.108652000	0.286862000
1	0.812477000	2.924374000	0.395729000
1	-0.488010000	4.085808000	0.747532000
6	-1.809892000	4.001323000	-1.569446000
1	-1.692385000	5.035723000	-1.213229000
1	-2.736689000	3.603260000	-1.148001000
1	-1.943331000	4.035364000	-2.655320000
6	0.650799000	3.834348000	-1.895411000
1	0.486195000	3.922881000	-2.973804000
1	1.555111000	3.238681000	-1.743764000
1	0.815551000	4.846341000	-1.493515000
6	-2.592295000	-2.432513000	-2.780122000
1	-2.074660000	-3.329963000	-3.127042000
1	-2.222900000	-1.589384000	-3.367863000
1	-3.666532000	-2.555509000	-2.970606000
6	-2.779299000	-3.501575000	-0.535263000
1	-3.813694000	-3.749092000	-0.808475000
1	-2.731358000	-3.427117000	0.550951000
1	-2.138704000	-4.335986000	-0.830089000
7	1.576774000	0.289537000	0.035992000
6	2.509818000	-0.466768000	0.168589000
6	3.973286000	-0.380164000	0.052464000
6	4.526050000	0.896254000	-0.167915000
6	4.831419000	-1.486920000	0.136906000
6	5.902629000	1.059274000	-0.288124000
1	3.856842000	1.746260000	-0.250513000

6	6.210804000	-1.315999000	0.011273000
1	4.401287000	-2.467810000	0.289251000
6	6.752703000	-0.047220000	-0.197215000
1	6.313824000	2.051021000	-0.458409000
1	6.863448000	-2.183012000	0.073502000
1	7.827832000	0.080241000	-0.293820000
8	-0.012594000	-3.024587000	-0.087567000
8	0.134215000	-1.985892000	-2.398955000
1	2.143467000	-2.115271000	1.594125000
8	2.187044000	-2.172746000	0.624770000
1	1.022469000	-2.669231000	0.246639000

Gas Phase DFT Studies optimized coordinates for Catalyst L^3RuPPh_3 and derivatives

Table B21 Optimized coordinates for L^3RuPPh_3 (gas phase)

Z	x	y	z
44	-0.870029000	-0.075584000	-0.227489000
16	-0.733696000	0.769351000	-2.532695000
16	-1.049653000	-1.336618000	1.821651000
16	-1.403421000	2.023355000	0.691583000
15	1.567435000	0.238551000	0.103139000
7	-3.076469000	-0.127914000	-0.611002000
7	-1.034610000	-2.099823000	-1.232731000
6	-2.470666000	1.357261000	-2.627066000
1	-2.394533000	2.316735000	-2.109776000
1	-2.755780000	1.523905000	-3.671822000
6	-3.476923000	0.426979000	-1.954192000
1	-4.427565000	0.963282000	-1.844671000
1	-3.678455000	-0.416207000	-2.620427000
6	-3.416993000	-1.583043000	-0.557131000
1	-4.459761000	-1.746855000	-0.875377000
1	-3.328728000	-1.872354000	0.491887000
6	-2.490373000	-2.411279000	-1.436632000
1	-2.727151000	-2.252424000	-2.491385000
1	-2.670245000	-3.476396000	-1.247890000
6	-0.357549000	-2.041625000	-2.560169000
1	-0.536204000	-2.974738000	-3.121852000
1	0.713122000	-1.970573000	-2.375015000
6	-0.787534000	-0.856907000	-3.433872000

1	-1.790137000	-0.980931000	-3.851508000
1	-0.095896000	-0.785685000	-4.278496000
6	-3.802018000	0.528380000	0.539446000
1	-3.673620000	-0.168802000	1.368662000
1	-4.870990000	0.588380000	0.280530000
6	-3.306763000	1.902656000	1.022525000
6	-0.687243000	-3.121405000	1.131324000
6	-0.362155000	-3.128363000	-0.378808000
1	0.704916000	-2.958715000	-0.509454000
1	-0.577816000	-4.130676000	-0.790626000
6	-1.860498000	-4.037466000	1.504568000
1	-1.579421000	-5.080120000	1.302385000
1	-2.779137000	-3.824109000	0.955279000
1	-2.100778000	-3.939131000	2.565142000
6	0.558015000	-3.601151000	1.898921000
1	0.325788000	-3.721948000	2.961618000
1	1.383103000	-2.886421000	1.827213000
1	0.905796000	-4.572567000	1.517566000
6	-3.516434000	1.976391000	2.542719000
1	-3.139517000	2.922858000	2.937608000
1	-3.004292000	1.157545000	3.052953000
1	-4.589228000	1.905419000	2.769816000
6	-4.007487000	3.088464000	0.346700000
1	-5.070862000	3.075053000	0.621641000
1	-3.936548000	3.068496000	-0.743234000
1	-3.578796000	4.037240000	0.678147000
6	2.590246000	-0.778744000	-1.087316000
6	2.889509000	-0.229943000	-2.348784000
1	2.619106000	0.798717000	-2.564699000
6	3.545368000	-0.980201000	-3.326269000
1	3.767378000	-0.526986000	-4.289042000
6	3.930453000	-2.297304000	-3.065716000
1	4.450001000	-2.878246000	-3.822888000
6	3.649834000	-2.855352000	-1.818479000
1	3.951985000	-3.875385000	-1.595243000
6	2.982491000	-2.106793000	-0.844357000
1	2.778905000	-2.567734000	0.115218000
6	2.276677000	-0.106420000	1.784721000
6	3.491880000	-0.770722000	2.022502000
1	4.081292000	-1.158056000	1.199077000
6	3.976701000	-0.926071000	3.323415000
1	4.917751000	-1.445648000	3.485779000
6	3.263673000	-0.406165000	4.404211000
1	3.641849000	-0.525777000	5.416268000
6	2.069502000	0.278402000	4.175011000
1	1.512973000	0.701426000	5.006823000
6	1.572665000	0.426673000	2.879085000
1	0.654991000	0.985466000	2.717559000
6	2.367114000	1.894809000	-0.232289000
6	3.739638000	2.046419000	0.042054000
1	4.302412000	1.231337000	0.484967000
6	4.394819000	3.241936000	-0.239892000
1	5.454291000	3.339498000	-0.016835000
6	3.690434000	4.312767000	-0.798992000
1	4.200146000	5.248639000	-1.013915000

6	2.331162000	4.173487000	-1.065985000
1	1.765371000	5.002760000	-1.482072000
6	1.669054000	2.971606000	-0.787924000
1	0.602141000	2.911539000	-0.961913000
8	-0.781719000	2.423485000	1.996449000
8	-1.347558000	3.095750000	-0.381402000
8	-2.509702000	-1.434402000	2.370201000

Table B22 Optimized coordinates for L³Ru(PhCN) (gas phase)

Z	x	y	z
44	-0.457780000	0.099161000	0.297221000
16	-0.761270000	-0.597136000	2.629407000
16	-0.233140000	1.117464000	-1.866226000
16	0.142257000	-2.048892000	-0.369543000
7	-2.496203000	-0.565999000	-0.001812000
7	-1.433727000	1.988053000	0.920903000
6	-2.176062000	-1.714557000	2.281681000
1	-1.651558000	-2.612061000	1.945788000
1	-2.724729000	-1.934951000	3.203940000
6	-3.135903000	-1.173387000	1.221516000
1	-3.804525000	-1.983799000	0.905515000
1	-3.774802000	-0.411629000	1.676771000
6	-3.209129000	0.704719000	-0.369496000
1	-4.299245000	0.544540000	-0.395278000
1	-2.870935000	0.954642000	-1.378918000
6	-2.897470000	1.848704000	0.603628000
1	-3.434191000	1.704970000	1.545351000
1	-3.278624000	2.785319000	0.179371000
6	-1.230500000	2.166428000	2.388889000
1	-1.794847000	3.041513000	2.754262000
1	-0.167864000	2.377023000	2.533284000
6	-1.600468000	0.944898000	3.236953000
1	-2.678880000	0.771227000	3.272859000
1	-1.273177000	1.126115000	4.265555000
6	-2.526179000	-1.488605000	-1.204445000
1	-2.368892000	-0.823962000	-2.055694000
1	-3.534556000	-1.925325000	-1.275478000
6	-1.468700000	-2.618720000	-1.291299000
6	-0.519319000	2.962195000	-1.316231000
6	-0.760831000	3.114745000	0.202559000
1	0.211931000	3.214865000	0.689809000
1	-1.318425000	4.048913000	0.392618000
6	-1.655399000	3.539925000	-2.167753000
1	-1.753373000	4.615589000	-1.965901000
1	-2.620574000	3.064624000	-1.977522000
1	-1.447505000	3.402341000	-3.231115000
6	0.793532000	3.690384000	-1.654092000
1	0.973647000	3.677787000	-2.733486000
1	1.649337000	3.210283000	-1.165969000
1	0.759322000	4.740292000	-1.327986000
6	-1.112230000	-2.813979000	-2.772865000
1	-0.340351000	-3.579650000	-2.883867000
1	-0.744275000	-1.887363000	-3.219283000
1	-2.003249000	-3.133708000	-3.330724000
6	-1.941037000	-3.950373000	-0.694163000
1	-2.776247000	-4.338611000	-1.293101000
1	-2.278233000	-3.864334000	0.341788000
1	-1.135776000	-4.689344000	-0.706905000
7	1.521547000	0.522211000	0.523642000
6	2.684478000	0.465065000	0.497601000
6	4.081016000	0.199613000	0.369484000
6	5.050489000	1.046068000	0.934657000

6	4.458359000	-0.954974000	-0.345813000
6	6.399162000	0.736559000	0.783295000
1	4.742271000	1.930879000	1.483400000
6	5.812830000	-1.247156000	-0.485524000
1	3.684094000	-1.590311000	-0.769654000
6	6.780176000	-0.407171000	0.074984000
1	7.153442000	1.386670000	1.217562000
1	6.113666000	-2.134856000	-1.034069000
1	7.834382000	-0.643755000	-0.039749000
8	0.216015000	-2.976344000	0.821862000
8	1.277850000	-2.193044000	-1.339587000
8	-1.415451000	0.811620000	-2.839729000

Table B23 Optimized coordinates for L³Ru(H₂O) (gas phase)

Z	x	y	z
44	-0.052371000	0.236484000	-0.514775000
16	0.810494000	2.492231000	-0.850525000
16	-1.252655000	-1.806356000	-0.175454000
16	1.946294000	-0.736698000	-0.968930000
7	0.629961000	0.401608000	1.498381000
7	-1.875273000	1.238607000	0.272055000
6	1.953006000	2.415697000	0.591699000
1	2.805165000	1.886313000	0.158924000
1	2.265688000	3.424601000	0.881959000
6	1.364839000	1.684665000	1.799449000
1	2.172085000	1.473820000	2.511856000
1	0.669459000	2.352858000	2.314464000
6	-0.638407000	0.338089000	2.303708000
1	-0.439341000	0.578260000	3.360374000
1	-0.979931000	-0.698757000	2.241935000
6	-1.711560000	1.294389000	1.766109000
1	-1.474686000	2.325871000	2.041807000
1	-2.664664000	1.062795000	2.256596000
6	-1.946635000	2.615533000	-0.295786000
1	-2.766514000	3.187518000	0.172009000
1	-2.189924000	2.505933000	-1.356059000
6	-0.649863000	3.423536000	-0.176119000
1	-0.432006000	3.718455000	0.853648000
1	-0.759620000	4.345996000	-0.754776000
6	1.447896000	-0.844870000	1.805030000
1	0.703008000	-1.639576000	1.882908000
1	1.925792000	-0.704133000	2.786160000
6	2.518598000	-1.313249000	0.777269000
6	-3.042069000	-1.068920000	-0.021534000
6	-3.074828000	0.467618000	-0.180189000
1	-3.170009000	0.695717000	-1.244932000
1	-3.975414000	0.866964000	0.319297000
6	-3.648385000	-1.553529000	1.300227000
1	-3.152336000	-1.139554000	2.181317000
1	-3.571392000	-2.639764000	1.382769000
1	-4.709541000	-1.272139000	1.338740000
6	-3.825572000	-1.677245000	-1.198280000
1	-3.889782000	-2.764958000	-1.094823000
1	-3.335415000	-1.457852000	-2.153450000

1	-4.850190000	-1.279571000	-1.238029000
6	2.548870000	-2.849080000	0.784374000
1	3.270409000	-3.221901000	0.052030000
1	1.567509000	-3.266152000	0.548481000
1	2.846877000	-3.210569000	1.777855000
6	3.920587000	-0.758845000	1.059595000
1	3.944251000	0.331302000	1.134915000
1	4.617260000	-1.039438000	0.266065000
1	4.288559000	-1.173449000	2.007639000
1	0.136357000	-1.130323000	-2.667431000
8	-0.454632000	-0.331651000	-2.706892000
1	0.050123000	0.294015000	-3.253899000
8	3.030290000	0.214173000	-1.416434000
8	1.765198000	-1.937464000	-1.875819000
8	-0.996511000	-2.511138000	1.195885000

Table B24 Optimized coordinates for L³Ru (gas phase)

Z	x	y	z
44	-0.077912000	0.228793000	-0.618178000
16	0.758128000	2.530129000	-0.908652000
16	-1.246527000	-1.780768000	-0.442462000
16	1.973356000	-0.716858000	-1.081954000
7	0.578915000	0.326448000	1.382042000
7	-1.918894000	1.200891000	0.179562000
6	1.880172000	2.397667000	0.542506000
1	2.736966000	1.890635000	0.092326000
1	2.181184000	3.395443000	0.879688000
6	1.296727000	1.616439000	1.720774000
1	2.104090000	1.388683000	2.426281000
1	0.590435000	2.254168000	2.258197000
6	-0.693200000	0.230518000	2.175692000
1	-0.494405000	0.427454000	3.240692000
1	-1.030276000	-0.803011000	2.077045000
6	-1.762736000	1.208038000	1.672364000
1	-1.519445000	2.227011000	1.983510000
1	-2.718100000	0.965947000	2.153115000
6	-2.005925000	2.594213000	-0.347007000
1	-2.833571000	3.140888000	0.136297000
1	-2.248411000	2.514125000	-1.410517000
6	-0.718058000	3.413006000	-0.205055000
1	-0.505023000	3.682638000	0.832803000
1	-0.843763000	4.350483000	-0.755660000
6	1.406093000	-0.911883000	1.678156000
1	0.681058000	-1.728956000	1.673774000
1	1.816431000	-0.803710000	2.693824000
6	2.534466000	-1.279654000	0.688658000
6	-3.051607000	-1.112861000	-0.172263000
6	-3.106995000	0.424519000	-0.297816000
1	-3.200820000	0.677445000	-1.358351000
1	-4.017275000	0.798131000	0.202633000
6	-3.595456000	-1.649135000	1.156724000
1	-4.673651000	-1.449555000	1.217372000
1	-3.122010000	-1.206724000	2.035935000
1	-3.432472000	-2.726851000	1.223439000

6	-3.878630000	-1.709444000	-1.326116000
1	-3.909362000	-2.800844000	-1.249701000
1	-3.447445000	-1.456069000	-2.301506000
1	-4.913539000	-1.339276000	-1.302850000
6	2.662989000	-2.810437000	0.671138000
1	3.435204000	-3.119775000	-0.037910000
1	1.722633000	-3.283500000	0.380306000
1	2.943083000	-3.174159000	1.669575000
6	3.892368000	-0.651184000	1.024224000
1	3.856848000	0.435884000	1.128850000
1	4.621004000	-0.870118000	0.239990000
1	4.264407000	-1.070197000	1.969237000
8	2.990972000	0.333496000	-1.457358000
8	1.955432000	-1.935009000	-1.945343000
8	-0.965949000	-2.667652000	0.803628000

Table B25 Optimized coordinates for $L^3Ru(PhCONH_2)$ (gas phase):

Z	x	y	z
44	-0.595374000	-0.158688000	-0.327416000
16	-1.897805000	-0.729673000	-2.323019000
16	0.796609000	-0.000354000	1.614049000
16	-1.077946000	2.073211000	-0.503302000
7	-2.444972000	-0.302241000	0.756000000
7	-0.513629000	-2.354552000	0.023018000
6	-3.507226000	-0.225095000	-1.593817000
1	-3.481406000	0.854038000	-1.763466000
1	-4.335907000	-0.662554000	-2.161164000
6	-3.649996000	-0.575602000	-0.112204000
1	-4.509671000	-0.029890000	0.295773000
1	-3.892220000	-1.637930000	-0.021638000
6	-2.219600000	-1.463598000	1.679136000
1	-3.157559000	-1.746838000	2.183622000
1	-1.515406000	-1.109312000	2.434514000
6	-1.661617000	-2.683073000	0.935639000
1	-2.447028000	-3.155636000	0.339946000
1	-1.352442000	-3.435699000	1.670536000
6	-0.667632000	-3.045042000	-1.290956000
1	-0.741642000	-4.137022000	-1.148163000
1	0.246410000	-2.845809000	-1.856775000
6	-1.872232000	-2.575778000	-2.115748000
1	-2.827659000	-2.892388000	-1.689546000
1	-1.805283000	-3.022091000	-3.112647000
6	-2.586663000	0.952316000	1.598885000
1	-1.830482000	0.833377000	2.377718000
1	-3.586347000	0.943866000	2.059713000
6	-2.342471000	2.331212000	0.927552000
6	1.318609000	-1.869833000	1.791823000
6	0.821022000	-2.711353000	0.599418000
1	1.528670000	-2.595595000	-0.225019000
1	0.820086000	-3.779481000	0.881530000
6	0.858186000	-2.385110000	3.161996000
1	1.301833000	-3.373991000	3.340416000
1	-0.223775000	-2.478375000	3.265526000
1	1.187800000	-1.705798000	3.950895000

6	2.857939000	-1.888049000	1.775132000
1	3.233599000	-2.918518000	1.852752000
1	3.254725000	-1.321325000	2.623459000
1	3.264611000	-1.450484000	0.860221000
6	-1.697761000	3.258201000	1.969405000
1	-1.472902000	4.233419000	1.528935000
1	-0.772637000	2.829973000	2.361366000
1	-2.390104000	3.408599000	2.808892000
6	-3.614129000	2.979885000	0.366307000
1	-4.289409000	3.227146000	1.196334000
1	-4.155370000	2.335448000	-0.331107000
1	-3.375633000	3.901436000	-0.170367000
6	2.445864000	-0.192129000	-1.680300000
7	1.188627000	0.470654000	-1.679633000
1	0.729844000	0.331711000	-2.577770000
8	2.544289000	-1.286374000	-2.220375000
6	3.588082000	0.497255000	-1.018455000
6	4.861494000	-0.073280000	-1.189735000
6	3.448428000	1.673561000	-0.260342000
6	5.980964000	0.523776000	-0.620172000
1	4.946995000	-0.981148000	-1.777635000
6	4.576098000	2.261869000	0.312903000
1	2.477093000	2.129014000	-0.087601000
6	5.838445000	1.693661000	0.133428000
1	6.963076000	0.081389000	-0.761899000
1	4.462296000	3.165720000	0.903948000
1	6.712011000	2.160875000	0.580416000
1	1.224076000	1.468928000	-1.453583000
8	-1.864275000	2.408240000	-1.751152000
8	0.114332000	2.975813000	-0.282149000
8	0.031590000	0.310630000	2.942360000

Table B26 Optimized coordinates for $L^3Ru(PhC(OH)NH)$ (gas phase)

Z	x	y	z
44	-0.541495000	-0.186543000	-0.325679000
16	-2.003760000	-0.528946000	-2.301283000
16	0.887914000	-0.271723000	1.579739000
16	-0.788729000	2.126396000	-0.396748000
7	-2.393553000	-0.149492000	0.811528000
7	-0.753757000	-2.389285000	-0.056135000
6	-3.503375000	0.152692000	-1.496055000
1	-3.332562000	1.224852000	-1.619031000
1	-4.400660000	-0.142509000	-2.050910000
6	-3.640826000	-0.256045000	-0.030854000
1	-4.431693000	0.349814000	0.428930000
1	-3.987643000	-1.291938000	0.014558000
6	-2.281564000	-1.357365000	1.694240000
1	-3.234892000	-1.547438000	2.214219000
1	-1.523229000	-1.109922000	2.442107000
6	-1.887113000	-2.612393000	0.907378000
1	-2.743135000	-2.989299000	0.341786000
1	-1.623944000	-3.407345000	1.614585000
6	-1.066098000	-3.015835000	-1.372389000
1	-1.278814000	-4.091750000	-1.249439000

1	-0.163102000	-2.933087000	-1.983899000
6	-2.230480000	-2.363854000	-2.126242000
1	-3.195209000	-2.555186000	-1.649447000
1	-2.281208000	-2.797051000	-3.130113000
6	-2.395300000	1.075384000	1.697791000
1	-1.629627000	0.863563000	2.446659000
1	-3.376120000	1.140488000	2.195578000
6	-2.049549000	2.434378000	1.049687000
6	1.220776000	-2.190317000	1.615630000
6	0.557346000	-2.919916000	0.430297000
1	1.226694000	-2.844567000	-0.430374000
1	0.448900000	-3.992959000	0.670173000
6	0.802301000	-2.731764000	2.987888000
1	1.117298000	-3.780786000	3.075964000
1	-0.272205000	-2.681981000	3.171896000
1	1.278174000	-2.156035000	3.784615000
6	2.744164000	-2.351728000	1.470784000
1	3.026346000	-3.414741000	1.444652000
1	3.260086000	-1.887433000	2.317015000
1	3.115060000	-1.878566000	0.556536000
6	-1.343411000	3.287582000	2.115062000
1	-1.049155000	4.255104000	1.700966000
1	-0.448578000	2.789135000	2.494447000
1	-2.025244000	3.461747000	2.959250000
6	-3.261485000	3.201991000	0.506451000
1	-3.909484000	3.495984000	1.343483000
1	-3.864491000	2.625237000	-0.198676000
1	-2.941169000	4.107308000	-0.015334000
6	2.384019000	0.030014000	-1.959896000
7	1.136367000	-0.192342000	-1.727701000
1	0.704631000	-0.422416000	-2.624555000
8	2.824296000	-0.244071000	-3.225237000
6	3.413261000	0.527709000	-1.022490000
6	4.707672000	-0.025936000	-1.079607000
6	3.141154000	1.584205000	-0.141562000
6	5.713973000	0.457801000	-0.247101000
1	4.915399000	-0.857595000	-1.749475000
6	4.163210000	2.070979000	0.674999000
1	2.153376000	2.040473000	-0.119841000
6	5.441368000	1.511734000	0.630090000
1	6.705343000	0.014695000	-0.282471000
1	3.950977000	2.895457000	1.349294000
1	6.227376000	1.896214000	1.274780000
8	-1.557015000	2.523916000	-1.638225000
8	0.384758000	3.014850000	-0.091656000
8	0.159054000	0.017896000	2.932596000
1	3.689063000	0.179991000	-3.353662000

Table B27 Optimized coordinates for L³RuTS (gas phase)

Z	x	y	z
44	-0.460013000	0.087294000	0.178495000
16	-0.233133000	-0.934200000	2.408486000
16	-0.652200000	1.415915000	-1.797291000
16	-0.471463000	-1.813738000	-1.073196000
7	-2.608735000	-0.248923000	0.460824000
7	-0.847360000	1.937052000	1.294367000
6	-1.863940000	-1.764860000	2.409446000
1	-1.645227000	-2.683623000	1.863448000
1	-2.161235000	-2.033702000	3.429192000
6	-2.971267000	-0.943250000	1.745424000
1	-3.833866000	-1.598408000	1.567387000
1	-3.312482000	-0.183471000	2.453794000
6	-3.135407000	1.156047000	0.469810000
1	-4.197319000	1.176713000	0.767325000
1	-3.052513000	1.510031000	-0.562060000
6	-2.343155000	2.067513000	1.420220000
1	-2.612286000	1.858151000	2.459436000
1	-2.642418000	3.106004000	1.237143000
6	-0.213127000	1.856053000	2.643591000
1	-0.485904000	2.734291000	3.252418000
1	0.867051000	1.887115000	2.482920000
6	-0.549954000	0.584693000	3.425704000
1	-1.586446000	0.562665000	3.771871000
1	0.086842000	0.538381000	4.314181000
6	-3.128846000	-0.970591000	-0.755997000
1	-3.092655000	-0.222335000	-1.551491000
1	-4.177736000	-1.259840000	-0.583268000
6	-2.346281000	-2.215338000	-1.259368000
6	-0.441601000	3.155735000	-0.973945000
6	-0.194237000	3.061776000	0.545508000
1	0.875209000	2.906013000	0.697670000
1	-0.467985000	4.017197000	1.026564000
6	-1.651908000	4.019101000	-1.346208000
1	-1.491583000	5.045515000	-0.988750000
1	-2.591349000	3.651403000	-0.927609000
1	-1.785746000	4.045917000	-2.430088000
6	0.827623000	3.747399000	-1.613087000
1	0.680560000	3.900975000	-2.686753000
1	1.681767000	3.074278000	-1.482200000
1	1.079877000	4.718491000	-1.162578000
6	-2.611338000	-2.331023000	-2.771356000
1	-2.073321000	-3.182273000	-3.195625000
1	-2.299239000	-1.429772000	-3.302774000
1	-3.686296000	-2.481820000	-2.935206000
6	-2.718728000	-3.544260000	-0.589872000
1	-3.753857000	-3.795059000	-0.856278000
1	-2.651008000	-3.530879000	0.498338000
1	-2.070207000	-4.348521000	-0.945500000
7	1.616716000	0.287450000	0.044752000
6	2.556011000	-0.466496000	0.133484000
6	4.016991000	-0.380767000	-0.004750000
6	4.574674000	0.904066000	-0.151046000

6	4.867682000	-1.496522000	-0.012536000
6	5.949423000	1.066045000	-0.292058000
1	3.912205000	1.763426000	-0.156799000
6	6.244907000	-1.326263000	-0.159186000
1	4.433931000	-2.482325000	0.088703000
6	6.791876000	-0.049827000	-0.295794000
1	6.364920000	2.064291000	-0.403112000
1	6.891954000	-2.199479000	-0.169143000
1	7.865484000	0.076778000	-0.408204000
8	0.049781000	-3.029960000	-0.167629000
8	0.127981000	-1.881545000	-2.432178000
1	2.195503000	-2.155212000	1.521943000
8	2.243030000	-2.190021000	0.551627000
1	1.099815000	-2.666598000	0.167712000
8	-2.107774000	1.411860000	-2.367055000

Optimized Coordinates for Solution Phase (N, N'-dimethylformamide (DMF))

DFT Studies for benzonitrile hydration with water(Å)

Table B28 Optimized coordinates for benzonitrile (DMF phase)

Z	x	y	z
6	2.042493000	-0.000372000	-0.000096000
7	3.206562000	0.000193000	0.000110000
6	0.608770000	-0.000182000	-0.000050000
6	-0.090308000	-1.220553000	-0.000027000
6	-0.089967000	1.220385000	-0.000027000
6	-1.483298000	-1.212573000	0.000015000
1	0.457824000	-2.156969000	-0.000044000
6	-1.482959000	1.212794000	0.000015000
1	0.458426000	2.156647000	-0.000044000
6	-2.179099000	0.000208000	0.000036000
1	-2.025711000	-2.153025000	0.000032000
1	-2.025110000	2.153397000	0.000031000
1	-3.265157000	0.000360000	0.000069000

Table B29 Optimized coordinates for water (DMF phase)

Z	x	y	z
8	0.000000000	0.000000000	0.120461000
1	0.000000000	0.759875000	-0.481845000
1	0.000000000	-0.759875000	-0.481845000

Table B30 Optimized coordinates for benziminol (DMF phase)

Z	x	y	z
6	0.224137000	0.042821000	-0.000490000
6	-0.448940000	-1.185422000	0.100490000
6	-0.526468000	1.224317000	-0.108244000
6	-1.843303000	-1.226934000	0.108875000
1	0.123299000	-2.102657000	0.180119000
6	-1.919347000	1.180176000	-0.105000000
1	-0.026321000	2.182660000	-0.214797000
6	-2.581973000	-0.045709000	0.006731000
1	-2.352273000	-2.182749000	0.194812000
1	-2.487007000	2.101768000	-0.194820000
1	-3.667797000	-0.079225000	0.010210000
7	2.480899000	1.091169000	0.219200000
1	1.948886000	1.937147000	0.421090000
6	1.712413000	0.091174000	0.011962000
8	2.270046000	-1.122501000	-0.231444000
1	3.235447000	-0.997653000	-0.165410000

Table B31 Optimized coordinates for benzamide (DMF phase)

Z	x	y	z
6	-0.221875000	-0.020521000	-0.013835000
6	0.514863000	-1.206711000	0.114833000
6	0.460387000	1.199191000	-0.141492000
6	1.907985000	-1.175050000	0.138660000
1	-0.022736000	-2.145317000	0.199168000
6	1.855735000	1.229554000	-0.125986000
1	-0.087084000	2.126433000	-0.283003000
6	2.581587000	0.044479000	0.019387000
1	2.468793000	-2.099006000	0.248260000
1	2.374767000	2.177677000	-0.233690000
1	3.667633000	0.070574000	0.034044000
7	-2.422051000	1.013250000	0.217432000
1	-3.424303000	0.917866000	0.319299000
1	-1.995877000	1.796668000	0.691515000
6	-1.720333000	-0.131019000	-0.031395000
8	-2.287117000	-1.197147000	-0.282331000

Table B32 Optimized coordinates for transition state for benzonitrile hydration with Water (DMF phase)

Z	x	y	z
6	-1.581536000	-0.409345000	-0.041586000
7	-2.492358000	-1.213809000	-0.111203000
6	-0.150943000	-0.158212000	-0.015831000
6	0.698869000	-1.278334000	0.050349000
6	0.390491000	1.134132000	-0.071085000
6	2.079208000	-1.096932000	0.063606000
1	0.269891000	-2.274377000	0.091642000

6	1.774214000	1.304198000	-0.058118000
1	-0.276602000	1.986440000	-0.128139000
6	2.618625000	0.192802000	0.009685000
1	2.734340000	-1.961274000	0.116756000
1	2.192597000	2.305203000	-0.101904000
1	3.696002000	0.329960000	0.020787000
1	-2.563714000	1.417655000	0.945770000
8	-2.554564000	1.077260000	0.028809000
1	-3.143059000	-0.054878000	-0.019089000

Table B33 Optimized coordinates for PPh₃ (DMF phase)

Z	x	y	z
15	-0.006942000	-0.004684000	-1.199961000
6	-1.612246000	-0.461851000	-0.396246000
6	-2.427300000	-1.382278000	-1.078014000
6	-2.068975000	0.066162000	0.822803000
6	-3.657950000	-1.778197000	-0.549434000
1	-2.099015000	-1.789328000	-2.031820000
6	-3.304149000	-0.323068000	1.348115000
1	-1.462318000	0.786533000	1.363843000
6	-4.099124000	-1.247796000	0.665679000
1	-4.273499000	-2.492367000	-1.089671000
1	-3.643279000	0.096931000	2.291542000
1	-5.060628000	-1.547115000	1.074728000
6	0.401033000	1.616052000	-0.400512000
6	1.193892000	1.757759000	0.749579000
6	-0.102706000	2.775242000	-1.017010000
6	1.468868000	3.024401000	1.272323000
1	1.599540000	0.877482000	1.238934000
6	0.161864000	4.039756000	-0.488638000
1	-0.704318000	2.687731000	-1.919216000
6	0.951889000	4.167241000	0.657544000
1	2.085876000	3.116339000	2.162475000
1	-0.239640000	4.923995000	-0.976537000
1	1.167410000	5.151156000	1.065084000
6	1.204866000	-1.164796000	-0.412613000
6	2.468663000	-1.273969000	-1.019934000
6	0.932297000	-1.954076000	0.715982000
6	3.441354000	-2.128694000	-0.499183000
1	2.693119000	-0.685812000	-1.907433000
6	1.901921000	-2.820123000	1.230103000
1	-0.038328000	-1.893323000	1.197365000
6	3.158811000	-2.906289000	0.627965000
1	4.414833000	-2.192843000	-0.977019000
1	1.674350000	-3.423719000	2.105365000
1	3.911966000	-3.578252000	1.030743000

Optimized Coordinates for Solution Phase (DMF) DFT Studies for Catalyst

L¹RuPPh₃ and derivatives

Table B34 Optimized coordinates for L¹RuPPh₃ (DMF phase)

Z	x	y	z
44	-0.919412000	-0.004576000	-0.111185000
16	-0.890722000	0.683823000	-2.399416000
16	-1.117062000	-1.235663000	2.033178000
16	-1.358201000	2.247640000	0.838097000
15	1.456910000	0.250537000	0.070257000
7	-3.154359000	0.030128000	-0.357493000
7	-1.225394000	-2.058878000	-0.938172000
6	-2.601083000	1.346002000	-2.499302000
1	-2.478201000	2.353922000	-2.098707000
1	-2.916021000	1.425025000	-3.544557000
6	-3.618429000	0.536009000	-1.701132000
1	-4.523358000	1.138421000	-1.563532000
1	-3.921023000	-0.325149000	-2.300274000
6	-3.560916000	-1.398347000	-0.215846000
1	-4.621738000	-1.533081000	-0.476529000
1	-3.424197000	-1.651940000	0.832167000
6	-2.705257000	-2.308457000	-1.084102000
1	-2.971877000	-2.181354000	-2.134144000
1	-2.926743000	-3.354730000	-0.847718000
6	-0.599867000	-2.129324000	-2.293929000
1	-0.851762000	-3.083946000	-2.782278000
1	0.480216000	-2.103462000	-2.154899000
6	-1.016857000	-0.985523000	-3.224312000
1	-2.033488000	-1.094291000	-3.608276000
1	-0.346866000	-0.971320000	-4.087792000
6	-3.755870000	0.786818000	0.789309000
1	-3.548734000	0.169133000	1.663465000
1	-4.849069000	0.826842000	0.651921000
6	-3.217249000	2.198180000	1.092763000
6	-0.919094000	-3.019251000	1.466978000
6	-0.582599000	-3.076207000	-0.045597000
1	0.489472000	-2.920425000	-0.161354000
1	-0.812053000	-4.083650000	-0.431198000
6	-2.156499000	-3.861462000	1.846372000
1	-1.999422000	-4.915519000	1.576897000
1	-3.080888000	-3.532371000	1.369310000
1	-2.315856000	-3.815247000	2.929015000
6	0.276069000	-3.648080000	2.215943000
1	0.066575000	-3.695255000	3.289952000
1	1.187676000	-3.060779000	2.080249000
1	0.466867000	-4.673748000	1.866917000
6	-3.528427000	2.477042000	2.579101000
1	-3.174125000	3.474029000	2.862577000
1	-3.042491000	1.744535000	3.231150000
1	-4.611777000	2.441291000	2.766378000
6	-3.899633000	3.309746000	0.270841000
1	-4.983875000	3.313670000	0.452708000

1	-3.740031000	3.212955000	-0.804691000
1	-3.507900000	4.288206000	0.569967000
6	2.490798000	-0.959748000	-0.904058000
6	2.760240000	-0.696264000	-2.260254000
1	2.460268000	0.250882000	-2.698130000
6	3.418214000	-1.632263000	-3.060683000
1	3.615523000	-1.400902000	-4.103972000
6	3.826751000	-2.855474000	-2.523199000
1	4.343338000	-3.582146000	-3.143861000
6	3.567162000	-3.133654000	-1.180327000
1	3.882568000	-4.078709000	-0.746597000
6	2.901873000	-2.198293000	-0.382362000
1	2.716060000	-2.439741000	0.658444000
6	2.248902000	0.275296000	1.758412000
6	3.546348000	-0.187374000	2.031393000
1	4.137876000	-0.660516000	1.255573000
6	4.102426000	-0.047845000	3.306640000
1	5.106131000	-0.419189000	3.496406000
6	3.376882000	0.570183000	4.326290000
1	3.810582000	0.681008000	5.316633000
6	2.090478000	1.047377000	4.062101000
1	1.517590000	1.533191000	4.848028000
6	1.528177000	0.895140000	2.793168000
1	0.525170000	1.260026000	2.595053000
6	2.196938000	1.847039000	-0.589656000
6	3.594765000	2.015012000	-0.608905000
1	4.244246000	1.217997000	-0.261853000
6	4.171462000	3.195878000	-1.073609000
1	5.253304000	3.299982000	-1.079725000
6	3.361339000	4.241518000	-1.528900000
1	3.809725000	5.162952000	-1.890794000
6	1.975745000	4.091140000	-1.510807000
1	1.334107000	4.897404000	-1.857217000
6	1.398636000	2.903141000	-1.045769000
1	0.320146000	2.810052000	-1.015898000

Table B35 Optimized coordinates for L¹Ru(PhCN) (DMF phase)

Z	x	y	z
44	-0.457102000	-0.161217000	0.077098000
16	-0.629104000	-1.373421000	2.127947000
16	-0.256138000	1.454847000	-1.782189000
16	-0.958714000	-2.135725000	-1.317249000
7	-2.625833000	0.009909000	0.182637000
7	-0.510673000	1.646262000	1.303820000
6	-2.410986000	-1.802028000	2.001470000
1	-2.385766000	-2.707117000	1.392893000
1	-2.811517000	-2.057810000	2.987168000
6	-3.254251000	-0.703262000	1.358169000
1	-4.214948000	-1.127549000	1.045831000
1	-3.489637000	0.044741000	2.117552000
6	-2.848496000	1.484175000	0.335409000
1	-3.900737000	1.699227000	0.573261000
1	-2.609511000	1.929905000	-0.627636000
6	-1.949389000	2.083685000	1.417292000

1	-2.312722000	1.805048000	2.407732000
1	-2.010881000	3.176046000	1.373750000
6	0.024985000	1.309274000	2.662872000
1	-0.097454000	2.164558000	3.344587000
1	1.095942000	1.130388000	2.544558000
6	-0.620327000	0.076215000	3.300294000
1	-1.645984000	0.253889000	3.630830000
1	-0.041301000	-0.209951000	4.182037000
6	-3.199640000	-0.426526000	-1.137737000
1	-2.861161000	0.330689000	-1.845286000
1	-4.298749000	-0.373479000	-1.081119000
6	-2.772567000	-1.804392000	-1.698345000
6	0.186783000	3.009897000	-0.816464000
6	0.373405000	2.691410000	0.689715000
1	1.388829000	2.314130000	0.827221000
1	0.283950000	3.621893000	1.273362000
6	-0.857137000	4.117119000	-1.071434000
1	-0.575506000	5.041595000	-0.547654000
1	-1.865955000	3.846834000	-0.752892000
1	-0.904473000	4.341771000	-2.142396000
6	1.544895000	3.544983000	-1.319691000
1	1.476957000	3.820561000	-2.377443000
1	2.331713000	2.791546000	-1.214758000
1	1.846751000	4.441834000	-0.758787000
6	-2.957403000	-1.727948000	-3.228955000
1	-2.686683000	-2.682634000	-3.692759000
1	-2.328721000	-0.946355000	-3.666231000
1	-4.004819000	-1.514481000	-3.488981000
6	-3.652303000	-2.964578000	-1.192854000
1	-4.703450000	-2.798863000	-1.468946000
1	-3.608787000	-3.101026000	-0.110750000
1	-3.331093000	-3.905303000	-1.653035000
7	1.538004000	-0.382993000	0.015884000
6	2.693313000	-0.546592000	-0.036523000
6	4.102682000	-0.760186000	-0.114946000
6	4.738607000	-1.617658000	0.805004000
6	4.857127000	-0.117938000	-1.117137000
6	6.112672000	-1.825610000	0.716852000
1	4.153008000	-2.111191000	1.573866000
6	6.230371000	-0.336298000	-1.191925000
1	4.362031000	0.540091000	-1.823832000
6	6.859967000	-1.187853000	-0.278468000
1	6.600924000	-2.487798000	1.425477000
1	6.810075000	0.158401000	-1.965379000
1	7.931143000	-1.354813000	-0.342675000

Table B36 Optimized coordinates for L¹Ru(H₂O) (DMF phase)

Z	x	y	z
44	0.002746000	0.124487000	-0.621051000
16	0.884060000	2.297386000	-0.901036000
16	-1.344626000	-1.922108000	-0.355639000
16	2.060839000	-0.972553000	-1.425455000
7	0.977566000	0.118100000	1.272423000
7	-1.639999000	1.068566000	0.466520000

6	2.208014000	2.192450000	0.375022000
1	3.029467000	1.732997000	-0.176077000
1	2.516230000	3.193934000	0.690009000
6	1.789635000	1.360395000	1.584363000
1	2.679037000	1.069366000	2.153781000
1	1.194451000	1.987744000	2.250603000
6	-0.161039000	0.033238000	2.246831000
1	0.192873000	0.193180000	3.275942000
1	-0.552593000	-0.978401000	2.173349000
6	-1.265223000	1.043594000	1.926346000
1	-0.950404000	2.048024000	2.215576000
1	-2.145503000	0.818103000	2.537780000
6	-1.767962000	2.486079000	-0.005081000
1	-2.493502000	3.032673000	0.616614000
1	-2.166703000	2.444598000	-1.021091000
6	-0.448834000	3.260511000	-0.020651000
1	-0.088099000	3.506284000	0.980376000
1	-0.596336000	4.203164000	-0.553904000
6	1.788768000	-1.148322000	1.379561000
1	1.047189000	-1.946636000	1.408763000
1	2.320088000	-1.144210000	2.344658000
6	2.780582000	-1.482461000	0.238200000
6	-2.958423000	-1.185621000	0.283901000
6	-2.929049000	0.359494000	0.173435000
1	-3.159889000	0.619416000	-0.862220000
1	-3.725961000	0.784365000	0.804743000
6	-3.262301000	-1.692468000	1.708354000
1	-2.498124000	-1.428402000	2.441417000
1	-3.342869000	-2.784577000	1.703034000
1	-4.220468000	-1.287468000	2.062685000
6	-4.111673000	-1.669751000	-0.621037000
1	-4.186189000	-2.761749000	-0.590278000
1	-3.957043000	-1.369798000	-1.662510000
1	-5.073427000	-1.257909000	-0.283284000
6	2.967610000	-3.014437000	0.259565000
1	3.682107000	-3.320119000	-0.512335000
1	2.021854000	-3.532516000	0.072586000
1	3.359981000	-3.350793000	1.230828000
6	4.170854000	-0.851205000	0.446555000
1	4.149422000	0.239828000	0.470161000
1	4.842495000	-1.146807000	-0.366656000
1	4.614145000	-1.199429000	1.390375000
1	-1.426371000	-0.857920000	-2.362089000
8	-1.073378000	0.033851000	-2.618788000
1	-0.372737000	-0.154448000	-3.266994000

Table B37 Optimized coordinates for L¹Ru (DMF phase)

Z	x	y	z
44	-0.039453000	0.070880000	-0.687078000
16	0.840420000	2.244887000	-1.061242000
16	-1.412083000	-1.861789000	-0.670602000
16	2.019536000	-1.044486000	-1.456035000
7	0.925285000	0.177044000	1.174663000
7	-1.702044000	1.063020000	0.321182000

6	2.158597000	2.221400000	0.225090000
1	2.995930000	1.752970000	-0.292971000
1	2.444367000	3.240962000	0.499569000
6	1.728310000	1.438371000	1.459525000
1	2.605053000	1.167696000	2.056473000
1	1.113674000	2.083972000	2.089447000
6	-0.223294000	0.108862000	2.145667000
1	0.127677000	0.314164000	3.166861000
1	-0.591275000	-0.913721000	2.114271000
6	-1.351004000	1.080011000	1.787166000
1	-1.073598000	2.099320000	2.063446000
1	-2.231767000	0.834069000	2.389653000
6	-1.814015000	2.469126000	-0.193785000
1	-2.544730000	3.035506000	0.403112000
1	-2.199979000	2.403023000	-1.213335000
6	-0.492624000	3.235951000	-0.216697000
1	-0.138923000	3.501204000	0.781662000
1	-0.631532000	4.167228000	-0.771634000
6	1.748271000	-1.081918000	1.343770000
1	1.012606000	-1.883467000	1.409044000
1	2.268406000	-1.021930000	2.312177000
6	2.747093000	-1.463861000	0.226688000
6	-3.008619000	-1.187764000	0.063049000
6	-2.994428000	0.356806000	0.018893000
1	-3.240094000	0.649592000	-1.004737000
1	-3.783564000	0.755964000	0.675267000
6	-3.256193000	-1.761116000	1.471982000
1	-4.208429000	-1.389427000	1.874989000
1	-2.471467000	-1.511942000	2.188527000
1	-3.316728000	-2.853329000	1.423874000
6	-4.177914000	-1.647884000	-0.832808000
1	-4.240711000	-2.741051000	-0.844231000
1	-4.049411000	-1.303027000	-1.863923000
1	-5.134755000	-1.261042000	-0.455122000
6	2.940453000	-2.992166000	0.324713000
1	3.656794000	-3.331476000	-0.431029000
1	1.996435000	-3.521427000	0.160961000
1	3.332756000	-3.279483000	1.311483000
6	4.132436000	-0.814052000	0.405769000
1	4.106227000	0.276363000	0.367125000
1	4.808201000	-1.151291000	-0.387475000
1	4.573731000	-1.106977000	1.368962000

Table B38 Optimized coordinates for L¹Ru(PhCONH₂) (DMF phase)

Z	x	y	z
44	-0.813837000	0.006333000	0.187874000
16	-1.439698000	-1.023458000	2.235473000
16	0.171810000	1.421046000	-1.430109000
16	-0.109753000	-2.135725000	-0.810822000
7	-2.734048000	-0.526478000	-0.479334000
7	-1.771523000	1.808292000	0.954007000
6	-2.849274000	-2.024803000	1.605021000
1	-2.362209000	-2.932366000	1.246762000
1	-3.527032000	-2.291589000	2.421191000

6	-3.607054000	-1.299851000	0.499230000
1	-4.217694000	-2.012995000	-0.063744000
1	-4.300889000	-0.590021000	0.952491000
6	-3.370830000	0.812142000	-0.742325000
1	-4.444025000	0.690494000	-0.946669000
1	-2.898484000	1.204198000	-1.639816000
6	-3.179644000	1.795043000	0.416072000
1	-3.860411000	1.554207000	1.234961000
1	-3.462505000	2.796435000	0.075006000
6	-1.793470000	1.742519000	2.454430000
1	-2.395360000	2.568331000	2.862251000
1	-0.764138000	1.885639000	2.790014000
6	-2.314790000	0.422462000	3.018365000
1	-3.389397000	0.292965000	2.875656000
1	-2.124021000	0.396507000	4.094265000
6	-2.585549000	-1.237835000	-1.806184000
1	-2.211646000	-0.474025000	-2.487780000
1	-3.588559000	-1.534129000	-2.149475000
6	-1.619666000	-2.443237000	-1.889269000
6	-0.446854000	3.113068000	-0.884811000
6	-0.986990000	3.029696000	0.560468000
1	-0.120456000	3.032542000	1.225996000
1	-1.582681000	3.927106000	0.789667000
6	-1.465716000	3.680874000	-1.891565000
1	-1.791658000	4.683293000	-1.581688000
1	-2.356532000	3.060988000	-2.005693000
1	-1.003043000	3.769658000	-2.879985000
6	0.759812000	4.074227000	-0.856572000
1	0.455244000	5.074805000	-0.519465000
1	1.187952000	4.175870000	-1.859290000
1	1.544362000	3.708497000	-0.186288000
6	-1.176821000	-2.541574000	-3.364401000
1	-0.502343000	-3.393527000	-3.501060000
1	-0.650028000	-1.635837000	-3.680957000
1	-2.042064000	-2.688716000	-4.027518000
6	-2.289113000	-3.780825000	-1.520435000
1	-3.138077000	-3.983494000	-2.188563000
1	-2.656947000	-3.810396000	-0.493181000
1	-1.571826000	-4.600639000	-1.633466000
6	3.869734000	-0.903274000	1.759445000
7	2.521352000	-0.974281000	1.567042000
1	1.969125000	-1.364412000	2.319725000
8	4.381109000	-1.165661000	2.851660000
6	4.702106000	-0.466936000	0.586715000
6	6.083831000	-0.696979000	0.656179000
6	4.167855000	0.166287000	-0.546299000
6	6.917956000	-0.320367000	-0.394775000
1	6.485375000	-1.175607000	1.543191000
6	5.005939000	0.549488000	-1.595050000
1	3.106649000	0.392246000	-0.613528000
6	6.379554000	0.303290000	-1.524552000
1	7.985861000	-0.510721000	-0.333685000
1	4.584392000	1.045475000	-2.464817000
1	7.028297000	0.600292000	-2.344007000
1	2.100415000	-0.997469000	0.646996000

Table B39 Optimized coordinates for L¹Ru(PhC(OH)NH) (DMF phase)

Z	x	y	z
44	-0.514792000	-0.063206000	-0.345151000
16	-1.888193000	-0.304830000	-2.277550000
16	0.820791000	-0.293195000	1.729856000
16	-0.517007000	2.414924000	-0.526767000
7	-2.385275000	0.293434000	0.722382000
7	-0.992881000	-2.169755000	0.068405000
6	-3.375217000	0.563285000	-1.636251000
1	-3.132374000	1.608453000	-1.833298000
1	-4.258880000	0.289516000	-2.220624000
6	-3.617547000	0.301717000	-0.152708000
1	-4.326777000	1.042393000	0.233886000
1	-4.108548000	-0.667612000	-0.048452000
6	-2.477623000	-0.866756000	1.664167000
1	-3.467172000	-0.903568000	2.144732000
1	-1.725118000	-0.699617000	2.430898000
6	-2.212775000	-2.194999000	0.955017000
1	-3.072681000	-2.468004000	0.341186000
1	-2.115600000	-2.990928000	1.700881000
6	-1.311512000	-2.851101000	-1.226083000
1	-1.684168000	-3.870436000	-1.041480000
1	-0.372890000	-2.948248000	-1.777739000
6	-2.333593000	-2.106493000	-2.090503000
1	-3.349078000	-2.166923000	-1.692906000
1	-2.349300000	-2.555292000	-3.087039000
6	-2.239409000	1.551013000	1.530034000
1	-1.477128000	1.309642000	2.271316000
1	-3.185642000	1.743887000	2.062007000
6	-1.782334000	2.835923000	0.798903000
6	0.844566000	-2.165738000	1.917469000
6	0.193788000	-2.843039000	0.686856000
1	0.941798000	-2.873176000	-0.108039000
1	-0.072319000	-3.883623000	0.936070000
6	0.203409000	-2.593699000	3.254654000
1	0.244177000	-3.686218000	3.373022000
1	-0.838250000	-2.284791000	3.359267000
1	0.757589000	-2.148792000	4.088277000
6	2.310505000	-2.650386000	1.955777000
1	2.362166000	-3.745656000	2.048357000
1	2.829419000	-2.218945000	2.818496000
1	2.853573000	-2.356004000	1.052866000
6	-1.116925000	3.730142000	1.867084000
1	-0.787682000	4.675474000	1.422179000
1	-0.243997000	3.238113000	2.307048000
1	-1.822721000	3.968919000	2.676650000
6	-2.951063000	3.642182000	0.198105000

1	-3.659244000	3.939843000	0.984705000
1	-3.509745000	3.094416000	-0.563483000
1	-2.571524000	4.556134000	-0.271777000
6	2.498318000	-0.410395000	-1.702788000
7	1.219291000	-0.515132000	-1.566651000
1	0.890618000	-1.094720000	-2.341789000
8	3.063184000	-1.151467000	-2.702718000
1	3.955914000	-0.818669000	-2.896554000
6	3.429854000	0.414501000	-0.903943000
6	4.744665000	-0.039625000	-0.690559000
6	3.046687000	1.670161000	-0.409889000
6	5.657018000	0.746908000	0.012780000
1	5.048977000	-1.022239000	-1.041387000
6	3.968264000	2.457741000	0.277722000
1	2.028308000	2.014851000	-0.554923000
6	5.272744000	2.001001000	0.492717000
1	6.664403000	0.378977000	0.184406000
1	3.665767000	3.432679000	0.650187000
1	5.985188000	2.618666000	1.032512000

Table B40 Optimized coordinates for L¹RuTS (DMF phase)

Z	x	y	z
44	-0.524146000	-0.018890000	0.280851000
16	-1.073768000	-0.396295000	2.552682000
16	-0.059206000	0.814376000	-2.019541000
16	-0.542820000	-2.417061000	-0.175084000
7	-2.676886000	-0.165172000	-0.103312000
7	-0.969426000	2.071599000	0.647344000
6	-2.756161000	-1.113774000	2.292820000
1	-2.539641000	-2.174294000	2.142294000
1	-3.351521000	-1.019251000	3.206132000
6	-3.510048000	-0.504603000	1.108492000
1	-4.319329000	-1.182796000	0.813212000
1	-3.995006000	0.413772000	1.446445000
6	-3.034039000	1.213101000	-0.569199000
1	-4.125704000	1.346460000	-0.609716000
1	-2.635831000	1.313007000	-1.575881000
6	-2.429919000	2.291379000	0.333941000
1	-2.975676000	2.332605000	1.277893000
1	-2.567521000	3.272142000	-0.133624000
6	-0.721371000	2.345384000	2.099266000
1	-1.034803000	3.369722000	2.354358000
1	0.358117000	2.277364000	2.248154000
6	-1.418621000	1.367085000	3.047500000
1	-2.500949000	1.507674000	3.093890000
1	-1.029145000	1.514784000	4.058176000
6	-2.846195000	-1.123708000	-1.248707000
1	-2.440988000	-0.592567000	-2.109240000

1	-3.919720000	-1.293896000	-1.426255000
6	-2.133496000	-2.507326000	-1.191388000
6	0.046091000	2.662883000	-1.679287000
6	-0.050286000	2.936792000	-0.158957000
1	0.936939000	2.761945000	0.272751000
1	-0.311657000	3.994908000	0.009528000
6	-1.009362000	3.431433000	-2.502532000
1	-0.922337000	4.513579000	-2.328429000
1	-2.037375000	3.139684000	-2.279595000
1	-0.846912000	3.252469000	-3.571034000
6	1.426491000	3.186020000	-2.132751000
1	1.553785000	3.034901000	-3.210120000
1	2.241356000	2.667656000	-1.618923000
1	1.524023000	4.263619000	-1.933064000
6	-1.804671000	-2.923199000	-2.634467000
1	-1.339388000	-3.914214000	-2.655059000
1	-1.123497000	-2.207798000	-3.105585000
1	-2.722307000	-2.969772000	-3.236755000
6	-3.011634000	-3.594324000	-0.544598000
1	-3.946253000	-3.703235000	-1.109422000
1	-3.271956000	-3.366002000	0.492818000
1	-2.496163000	-4.560076000	-0.552555000
7	1.537737000	0.024554000	0.608565000
6	2.422589000	-0.629288000	0.064951000
6	3.897007000	-0.618017000	0.213334000
6	4.445355000	-0.125293000	1.412836000
6	4.774501000	-1.043200000	-0.799677000
6	5.824793000	-0.067746000	1.594972000
1	3.770721000	0.206839000	2.195516000
6	6.157643000	-0.979776000	-0.615268000
1	4.375257000	-1.404099000	-1.741382000
6	6.689497000	-0.496007000	0.581263000
1	6.227908000	0.309483000	2.531175000
1	6.818721000	-1.306900000	-1.413410000
1	7.765622000	-0.451188000	0.724203000
1	0.781721000	-2.089522000	-0.932614000
8	2.049997000	-1.711826000	-1.075253000
1	2.585714000	-2.511316000	-0.911640000

Optimized Coordinates for Solution Phase (DMF) DFT Studies for Catalyst

L²RuPPh₃ and its' derivatives

Table B41 Optimized coordinates for L²RuPPh₃ (DMF phase)

Z	x	y	z
44	-0.910442000	-0.123331000	-0.135394000
16	-0.922977000	0.463607000	-2.468707000
16	-1.033766000	-1.268677000	2.046076000
16	-1.501863000	2.039298000	0.594050000
15	1.519175000	0.252492000	0.058462000
7	-3.134441000	-0.312947000	-0.395373000
7	-1.046827000	-2.242588000	-0.892392000

6	-2.687700000	0.968433000	-2.589923000
1	-2.642368000	1.995715000	-2.225170000
1	-3.002226000	0.970497000	-3.637893000
6	-3.635801000	0.106637000	-1.760777000
1	-4.584918000	0.640106000	-1.641113000
1	-3.868921000	-0.799218000	-2.322761000
6	-3.428624000	-1.766516000	-0.211527000
1	-4.472707000	-1.986090000	-0.478068000
1	-3.289062000	-1.977771000	0.844764000
6	-2.494640000	-2.626315000	-1.043610000
1	-2.760251000	-2.553581000	-2.098574000
1	-2.627378000	-3.679942000	-0.775303000
6	-0.402184000	-2.314777000	-2.239371000
1	-0.573836000	-3.304538000	-2.690389000
1	0.670177000	-2.200489000	-2.095413000
6	-0.898548000	-1.243859000	-3.216695000
1	-1.897078000	-1.450786000	-3.607372000
1	-0.219787000	-1.208967000	-4.072505000
6	-3.815388000	0.411667000	0.730232000
1	-3.596521000	-0.185639000	1.614724000
1	-4.902287000	0.385410000	0.562894000
6	-3.379942000	1.857794000	1.029757000
6	-0.674180000	-3.053478000	1.559600000
6	-0.335461000	-3.162969000	0.050503000
1	0.721597000	-2.941500000	-0.077262000
1	-0.491538000	-4.202383000	-0.281809000
6	-1.831667000	-3.980807000	1.987729000
1	-1.572203000	-5.029696000	1.787453000
1	-2.776634000	-3.772665000	1.483106000
1	-2.007684000	-3.881408000	3.064085000
6	0.574519000	-3.527082000	2.334647000
1	0.370164000	-3.538980000	3.410564000
1	1.427402000	-2.864576000	2.165081000
1	0.858966000	-4.547096000	2.037435000
6	-3.548216000	2.095404000	2.537431000
1	-3.274036000	3.119192000	2.803496000
1	-2.928073000	1.413010000	3.124860000
1	-4.597156000	1.935900000	2.819502000
6	-4.185901000	2.912723000	0.260223000
1	-5.238588000	2.843009000	0.562460000
1	-4.135219000	2.790817000	-0.823073000
1	-3.832171000	3.920468000	0.493336000
6	2.544725000	-0.893207000	-0.999817000
6	2.785502000	-0.538363000	-2.340583000
1	2.456894000	0.426825000	-2.713010000
6	3.448046000	-1.407831000	-3.209062000
1	3.620425000	-1.107267000	-4.238905000
6	3.893445000	-2.652399000	-2.756539000
1	4.413846000	-3.327058000	-3.430286000
6	3.666168000	-3.018839000	-1.429379000
1	4.010846000	-3.980800000	-1.060187000
6	2.994534000	-2.151160000	-0.563143000
1	2.832726000	-2.465210000	0.461658000
6	2.318808000	0.191895000	1.739489000
6	3.592274000	-0.343371000	1.993695000

1	4.164777000	-0.810775000	1.201089000
6	4.156135000	-0.272557000	3.271585000
1	5.141302000	-0.697334000	3.445196000
6	3.463254000	0.347228000	4.311896000
1	3.902511000	0.404360000	5.304334000
6	2.204370000	0.900594000	4.064137000
1	1.660244000	1.394848000	4.865120000
6	1.632094000	0.819631000	2.793228000
1	0.658231000	1.261819000	2.610481000
6	2.246855000	1.871631000	-0.547040000
6	3.625342000	2.109823000	-0.383741000
1	4.249975000	1.381372000	0.122230000
6	4.213163000	3.278311000	-0.864271000
1	5.278927000	3.439795000	-0.725478000
6	3.435054000	4.237521000	-1.521161000
1	3.892465000	5.149258000	-1.896113000
6	2.069471000	4.014262000	-1.684649000
1	1.451229000	4.754993000	-2.185564000
6	1.477422000	2.839437000	-1.203095000
1	0.407893000	2.711520000	-1.308265000
8	-0.860963000	2.613513000	1.839076000
8	-1.533923000	3.048785000	-0.544820000

Table B42 Optimized coordinates for L²Ru(PhCN) (DMF phase)

Z	x	y	z
44	-0.443677000	0.005262000	0.146205000
16	-0.578361000	-0.860124000	2.379741000
16	-0.248980000	1.288807000	-1.936917000
16	-0.971206000	-2.036267000	-0.865129000
7	-2.595910000	0.283664000	0.290001000
7	-0.396766000	1.993735000	1.084908000
6	-2.374489000	-1.243802000	2.356643000
1	-2.382759000	-2.227682000	1.885741000
1	-2.753864000	-1.338283000	3.378399000
6	-3.201204000	-0.217133000	1.586232000
1	-4.191402000	-0.636780000	1.377265000
1	-3.369649000	0.648332000	2.229493000
6	-2.772249000	1.773957000	0.226419000
1	-3.807245000	2.050970000	0.472167000
1	-2.572944000	2.064735000	-0.802248000
6	-1.812374000	2.501063000	1.169336000
1	-2.149614000	2.400849000	2.201928000
1	-1.838937000	3.573824000	0.951208000
6	0.177303000	1.846192000	2.460230000
1	0.116152000	2.800793000	3.004061000
1	1.234486000	1.601907000	2.336708000
6	-0.489898000	0.755014000	3.300877000
1	-1.497530000	1.021533000	3.626881000

1	0.106863000	0.589975000	4.201578000
6	-3.238369000	-0.321089000	-0.930138000
1	-2.940649000	0.331781000	-1.750757000
1	-4.331350000	-0.258437000	-0.824996000
6	-2.844442000	-1.766190000	-1.314244000
6	0.281202000	2.959325000	-1.248901000
6	0.503920000	2.885312000	0.283210000
1	1.508868000	2.494276000	0.453844000
1	0.469222000	3.901494000	0.707455000
6	-0.726189000	4.052242000	-1.660799000
1	-0.394984000	5.036771000	-1.301932000
1	-1.735320000	3.880025000	-1.281013000
1	-0.794439000	4.100812000	-2.752845000
6	1.642630000	3.335720000	-1.871109000
1	1.551327000	3.426505000	-2.958560000
1	2.398799000	2.574766000	-1.655668000
1	2.000426000	4.300699000	-1.483091000
6	-2.994059000	-1.898842000	-2.837140000
1	-2.744216000	-2.911614000	-3.164581000
1	-2.343143000	-1.200625000	-3.369492000
1	-4.032863000	-1.692905000	-3.126814000
6	-3.701774000	-2.843438000	-0.637394000
1	-4.738727000	-2.746648000	-0.983717000
1	-3.707148000	-2.779791000	0.451665000
1	-3.345104000	-3.841824000	-0.903469000
7	1.563001000	-0.278922000	0.085555000
6	2.713152000	-0.465043000	0.061523000
6	4.120768000	-0.705383000	0.031762000
6	4.763891000	-1.247381000	1.161588000
6	4.859763000	-0.402529000	-1.128309000
6	6.135985000	-1.481430000	1.123510000
1	4.187081000	-1.480092000	2.050742000
6	6.231189000	-0.642892000	-1.150161000
1	4.355854000	0.013090000	-1.994645000
6	6.869847000	-1.180797000	-0.028361000
1	6.632886000	-1.900068000	1.993296000
1	6.801916000	-0.410822000	-2.044073000
1	7.939567000	-1.366466000	-0.051932000
8	-0.988397000	-3.205370000	0.104077000
8	-0.285713000	-2.379365000	-2.166657000

Table B43 Optimized coordinates for $L^2Ru(H_2O)$ (DMF phase)

Z	x	y	z
44	-0.083992000	0.116038000	-0.515760000
16	0.682430000	2.317122000	-0.990757000
16	-1.320612000	-1.967166000	-0.129099000
16	1.969080000	-0.856126000	-0.943239000
7	0.643603000	0.431750000	1.467522000
7	-1.910786000	1.070874000	0.256836000
6	1.852040000	2.454601000	0.423261000
1	2.745337000	1.976472000	0.019147000
1	2.073842000	3.505208000	0.632173000
6	1.338990000	1.765724000	1.684440000
1	2.168558000	1.621241000	2.384569000

1	0.630188000	2.428216000	2.183541000
6	-0.597467000	0.397791000	2.314964000
1	-0.372713000	0.722018000	3.340737000
1	-0.917655000	-0.640300000	2.347781000
6	-1.712110000	1.271099000	1.735234000
1	-1.494724000	2.325740000	1.913618000
1	-2.643675000	1.064295000	2.272574000
6	-2.066219000	2.394246000	-0.428733000
1	-2.899334000	2.960245000	0.014979000
1	-2.326999000	2.180958000	-1.467773000
6	-0.808402000	3.264370000	-0.402540000
1	-0.590466000	3.673231000	0.586338000
1	-0.952299000	4.111758000	-1.077735000
6	1.504344000	-0.748219000	1.847946000
1	0.805119000	-1.577488000	1.954167000
1	1.952766000	-0.555017000	2.833258000
6	2.608701000	-1.190012000	0.857654000
6	-3.039111000	-1.288288000	0.246039000
6	-3.105913000	0.226429000	-0.071198000
1	-3.238770000	0.333284000	-1.150423000
1	-3.995685000	0.660587000	0.411764000
6	-3.462846000	-1.632811000	1.688274000
1	-2.809490000	-1.209703000	2.452824000
1	-3.461129000	-2.719191000	1.825014000
1	-4.482076000	-1.271547000	1.881638000
6	-4.045872000	-1.982823000	-0.696244000
1	-4.047085000	-3.063793000	-0.521519000
1	-3.797303000	-1.809067000	-1.748235000
1	-5.065258000	-1.613195000	-0.517112000
6	2.809253000	-2.703263000	1.026658000
1	3.597703000	-3.065692000	0.361350000
1	1.895408000	-3.259476000	0.802274000
1	3.105416000	-2.925946000	2.060106000
6	3.951262000	-0.481506000	1.080326000
1	3.883984000	0.606481000	1.031883000
1	4.682202000	-0.796711000	0.331197000
1	4.338783000	-0.750639000	2.071194000
1	-1.252474000	-1.174812000	-2.267488000
8	-0.900402000	-0.300227000	-2.577937000
1	-0.136800000	-0.527419000	-3.137282000
8	3.004377000	0.091836000	-1.525906000
8	1.960559000	-2.193993000	-1.649730000

Table B44 Optimized coordinates for L²Ru (DMF phase)

Z	x	y	z
44	-0.132091000	0.067850000	-0.564124000
16	0.625420000	2.275801000	-1.101786000
16	-1.368228000	-1.939452000	-0.486449000
16	1.933905000	-0.892074000	-1.008616000
7	0.612702000	0.455018000	1.365406000
7	-1.965661000	1.037115000	0.163193000
6	1.804027000	2.467337000	0.298208000
1	2.702886000	1.990096000	-0.093350000
1	2.011871000	3.525429000	0.480393000

6	1.291876000	1.804646000	1.570181000
1	2.113381000	1.676574000	2.281879000
1	0.567146000	2.464412000	2.049563000
6	-0.629099000	0.407063000	2.219372000
1	-0.399763000	0.749009000	3.237702000
1	-0.922828000	-0.638022000	2.270608000
6	-1.773309000	1.243401000	1.641472000
1	-1.594764000	2.304895000	1.823324000
1	-2.693638000	0.996867000	2.181031000
6	-2.114787000	2.359746000	-0.530616000
1	-2.949198000	2.927250000	-0.092123000
1	-2.372561000	2.142495000	-1.569425000
6	-0.858074000	3.228313000	-0.508821000
1	-0.636782000	3.636110000	0.479537000
1	-1.004481000	4.076160000	-1.182824000
6	1.493137000	-0.708198000	1.770496000
1	0.806160000	-1.544398000	1.899358000
1	1.934793000	-0.480278000	2.750559000
6	2.600603000	-1.157220000	0.791108000
6	-3.068758000	-1.328200000	0.034801000
6	-3.165468000	0.198609000	-0.179494000
1	-3.327807000	0.362389000	-1.247324000
1	-4.043388000	0.596206000	0.352863000
6	-3.403629000	-1.775363000	1.470878000
1	-4.419395000	-1.456384000	1.741156000
1	-2.720672000	-1.379682000	2.224434000
1	-3.365964000	-2.867371000	1.539174000
6	-4.106193000	-1.979869000	-0.903929000
1	-4.083882000	-3.069419000	-0.797218000
1	-3.906334000	-1.735081000	-1.952065000
1	-5.121071000	-1.639795000	-0.656267000
6	2.827203000	-2.660978000	1.007922000
1	3.624222000	-3.028356000	0.356062000
1	1.924696000	-3.240410000	0.796478000
1	3.123523000	-2.847254000	2.048417000
6	3.932275000	-0.420234000	0.981663000
1	3.845959000	0.664970000	0.912826000
1	4.657395000	-0.737625000	0.227765000
1	4.339295000	-0.662671000	1.971501000
8	2.926291000	0.076726000	-1.627200000
8	1.968403000	-2.251619000	-1.665625000

Table B45 Optimized coordinates for L²Ru(PhCONH₂) (DMF phase)

Z	x	y	z
44	0.566841000	-0.008022000	-0.179645000
16	1.198062000	0.432420000	-2.437215000
16	-0.401117000	-0.105854000	2.069839000
16	1.820409000	-1.935111000	0.006043000
7	2.358213000	1.034192000	0.386493000
7	-0.289742000	2.033856000	-0.185650000
6	2.978130000	0.747574000	-2.102830000
1	3.385322000	-0.264556000	-2.104420000
1	3.427721000	1.309455000	-2.926962000
6	3.224162000	1.473172000	-0.782379000

1	4.276970000	1.366637000	-0.500128000
1	3.057295000	2.540726000	-0.933457000
6	1.875021000	2.258974000	1.105555000
1	2.706552000	2.954969000	1.285907000
1	1.496192000	1.921292000	2.066419000
6	0.772158000	2.970466000	0.323907000
1	1.198919000	3.502955000	-0.527512000
1	0.321121000	3.740283000	0.959141000
6	-0.644420000	2.391505000	-1.595879000
1	-0.948646000	3.447682000	-1.659061000
1	-1.503163000	1.779860000	-1.876308000
6	0.482171000	2.144231000	-2.603158000
1	1.299547000	2.863960000	-2.518602000
1	0.075879000	2.234821000	-3.613735000
6	3.102013000	0.170498000	1.375280000
1	2.481456000	0.184397000	2.271365000
1	4.060945000	0.653016000	1.614038000
6	3.355075000	-1.311160000	1.006401000
6	-1.465360000	1.452244000	2.072015000
6	-1.533367000	2.066839000	0.651893000
1	-2.279786000	1.509211000	0.082022000
1	-1.889377000	3.107735000	0.721193000
6	-0.987167000	2.449251000	3.148769000
1	-1.653253000	3.322755000	3.182413000
1	0.029623000	2.814966000	2.999410000
1	-1.017497000	1.969781000	4.132900000
6	-2.907907000	1.058343000	2.454616000
1	-3.567060000	1.938619000	2.451171000
1	-2.927934000	0.633254000	3.463921000
1	-3.317029000	0.315990000	1.765719000
6	3.435228000	-2.110238000	2.315511000
1	3.639058000	-3.165345000	2.113045000
1	2.503581000	-2.047766000	2.883167000
1	4.249563000	-1.719635000	2.939459000
6	4.640139000	-1.543922000	0.201328000
1	5.505280000	-1.276137000	0.821078000
1	4.694544000	-0.958131000	-0.717219000
1	4.732821000	-2.596905000	-0.077388000
6	-2.276704000	-0.970194000	-1.547218000
7	-1.116387000	-1.455622000	-0.894515000
1	-0.530904000	-1.966682000	-1.553205000
8	-2.172042000	-0.486704000	-2.668033000
6	-3.583392000	-1.041385000	-0.833909000
6	-4.616943000	-0.206392000	-1.294183000
6	-3.840663000	-1.937880000	0.216740000
6	-5.874445000	-0.248112000	-0.699330000
1	-4.414607000	0.470189000	-2.117549000
6	-5.107068000	-1.988752000	0.799840000
1	-3.074312000	-2.617137000	0.575636000
6	-6.121630000	-1.140875000	0.348974000
1	-6.662703000	0.409676000	-1.053194000
1	-5.299881000	-2.691484000	1.604684000
1	-7.104657000	-1.179194000	0.809481000
1	-1.264331000	-2.000149000	-0.048091000
8	2.391488000	-2.430461000	-1.313234000

8 1.205466000 -3.059276000 0.813072000

Table B46 Optimized coordinates for L²Ru(PhC(OH)NH) (DMF phase)

Z	x	y	z
44	-0.530302000	-0.168049000	-0.286292000
16	-1.923558000	-0.535390000	-2.218866000
16	0.873117000	-0.291856000	1.725227000
16	-0.840015000	2.145990000	-0.322103000
7	-2.393262000	-0.198618000	0.843583000
7	-0.659405000	-2.355132000	0.000967000
6	-3.493882000	0.054357000	-1.473403000
1	-3.406746000	1.132560000	-1.614431000
1	-4.348632000	-0.314747000	-2.047930000
6	-3.641471000	-0.335011000	-0.005811000
1	-4.444162000	0.260183000	0.443607000
1	-3.970291000	-1.374115000	0.049315000
6	-2.273786000	-1.415115000	1.712309000
1	-3.230524000	-1.631591000	2.209176000
1	-1.532421000	-1.176021000	2.470964000
6	-1.824324000	-2.637566000	0.913606000
1	-2.650226000	-3.016543000	0.309799000
1	-1.568178000	-3.446692000	1.605200000
6	-0.895854000	-2.999446000	-1.328274000
1	-1.080020000	-4.077611000	-1.204870000
1	0.027068000	-2.891648000	-1.902691000
6	-2.056748000	-2.389543000	-2.118996000
1	-3.033947000	-2.644039000	-1.703744000
1	-2.030894000	-2.778550000	-3.140088000
6	-2.430534000	1.011182000	1.735768000
1	-1.649457000	0.831917000	2.475081000
1	-3.397323000	1.039794000	2.260337000
6	-2.156248000	2.387337000	1.090155000
6	1.218138000	-2.140767000	1.798410000
6	0.642274000	-2.854416000	0.550151000
1	1.357863000	-2.729451000	-0.265072000
1	0.553642000	-3.934456000	0.751760000
6	0.714344000	-2.739310000	3.128680000
1	0.959752000	-3.809144000	3.187938000
1	-0.361958000	-2.635751000	3.279306000
1	1.207611000	-2.238101000	3.968437000
6	2.745946000	-2.362248000	1.761164000
1	2.988163000	-3.435084000	1.786047000
1	3.218477000	-1.894357000	2.631427000
1	3.190220000	-1.928591000	0.861037000
6	-1.545444000	3.289813000	2.172840000
1	-1.346830000	4.289900000	1.778780000
1	-0.605067000	2.884371000	2.554782000
1	-2.247256000	3.385110000	3.011908000
6	-3.406023000	3.075607000	0.526503000
1	-4.097613000	3.296407000	1.349725000
1	-3.944436000	2.476396000	-0.208816000
1	-3.139711000	4.020302000	0.044923000
6	2.459202000	-0.088795000	-1.827669000

7	1.191160000	-0.239613000	-1.642046000
1	0.815345000	-0.620651000	-2.512469000
8	2.955467000	-0.564397000	-3.005159000
6	3.442702000	0.540324000	-0.920568000
6	4.757497000	0.040068000	-0.876788000
6	3.101599000	1.668476000	-0.161051000
6	5.717421000	0.656090000	-0.074458000
1	5.025877000	-0.848853000	-1.441891000
6	4.074738000	2.290356000	0.621457000
1	2.088719000	2.058951000	-0.190770000
6	5.378365000	1.788118000	0.671243000
1	6.725397000	0.253753000	-0.034659000
1	3.810926000	3.172540000	1.198600000
1	6.127842000	2.276336000	1.288198000
8	-1.552854000	2.621372000	-1.580371000
8	0.295830000	3.075614000	0.056835000
1	3.844873000	-0.202497000	-3.159788000

Table B47 Optimized coordinates for L²RuTS (DMF phase):

Z	x	y	z
44	-0.487722000	0.106871000	0.089908000
16	-0.223477000	-0.795728000	2.300405000
16	-0.787050000	1.461019000	-1.944173000
16	-0.560581000	-1.822371000	-1.097133000
7	-2.638425000	-0.190797000	0.431946000
7	-0.846365000	2.008010000	1.107034000
6	-1.867090000	-1.588096000	2.472051000
1	-1.695882000	-2.581531000	2.056919000
1	-2.115814000	-1.709916000	3.530514000
6	-2.990329000	-0.834841000	1.757048000
1	-3.834702000	-1.516667000	1.607969000
1	-3.354619000	-0.048875000	2.420014000
6	-3.167116000	1.212223000	0.419966000
1	-4.216206000	1.240306000	0.749022000
1	-3.117680000	1.552081000	-0.612044000
6	-2.334969000	2.134609000	1.318049000
1	-2.547054000	1.921589000	2.366846000
1	-2.648232000	3.171148000	1.156193000
6	-0.137222000	2.005689000	2.425776000
1	-0.394973000	2.907395000	3.001276000
1	0.931977000	2.044071000	2.207070000
6	-0.426152000	0.772855000	3.280737000
1	-1.428830000	0.775220000	3.713268000
1	0.284342000	0.738565000	4.110259000
6	-3.188624000	-0.949892000	-0.741358000
1	-3.161823000	-0.246245000	-1.574655000
1	-4.239687000	-1.211917000	-0.553410000
6	-2.437402000	-2.233899000	-1.193951000
6	-0.652051000	3.188772000	-1.218397000
6	-0.266928000	3.117220000	0.277783000
1	0.812387000	2.964774000	0.333362000
1	-0.496731000	4.078987000	0.764163000
6	-1.942145000	3.992200000	-1.482214000
1	-1.845730000	5.015151000	-1.092166000

1	-2.833788000	3.546748000	-1.036941000
1	-2.119602000	4.062700000	-2.560811000
6	0.499048000	3.933014000	-1.928834000
1	0.284610000	4.032954000	-2.998084000
1	1.444565000	3.393277000	-1.820406000
1	0.626481000	4.944555000	-1.516525000
6	-2.779493000	-2.465884000	-2.675289000
1	-2.287432000	-3.365920000	-3.052633000
1	-2.477081000	-1.623760000	-3.301462000
1	-3.863084000	-2.601987000	-2.773644000
6	-2.790099000	-3.504368000	-0.410261000
1	-3.857883000	-3.712886000	-0.547762000
1	-2.599464000	-3.437414000	0.659219000
1	-2.226116000	-4.358556000	-0.792975000
7	1.595222000	0.258108000	-0.058479000
6	2.530590000	-0.497265000	0.077246000
6	3.997613000	-0.393491000	-0.009388000
6	4.543690000	0.892963000	-0.192187000
6	4.867727000	-1.492680000	0.069973000
6	5.921160000	1.071591000	-0.287883000
1	3.872433000	1.743030000	-0.257163000
6	6.248128000	-1.307113000	-0.029424000
1	4.451135000	-2.481628000	0.206919000
6	6.781176000	-0.028952000	-0.206772000
1	6.324868000	2.070969000	-0.426091000
1	6.907937000	-2.168369000	0.032264000
1	7.856103000	0.110767000	-0.281565000
8	0.031150000	-3.057478000	-0.256120000
8	-0.028231000	-1.904559000	-2.498303000
1	2.171577000	-2.166144000	1.464788000
8	2.212064000	-2.197976000	0.492869000
1	1.041519000	-2.666591000	0.109618000

Optimized Coordinates for Solution Phase (DMF) DFT Studies for Catalyst

L^3RuPPh_3 and derivatives

Table B48 Optimized coordinates for L^3RuPPh_3 (DMF phase)

Z	x	y	z
44	-0.880377000	-0.083479000	-0.228374000
16	-0.739416000	0.780673000	-2.515079000
16	-1.023629000	-1.373310000	1.807254000
16	-1.452729000	1.994520000	0.746290000
15	1.577832000	0.235049000	0.096078000
7	-3.068509000	-0.164634000	-0.624151000
7	-0.995113000	-2.081900000	-1.244038000
6	-2.482131000	1.347170000	-2.624579000
1	-2.433614000	2.311896000	-2.117346000
1	-2.755713000	1.507020000	-3.671949000
6	-3.477617000	0.397920000	-1.966490000
1	-4.437114000	0.914886000	-1.854849000
1	-3.662601000	-0.439521000	-2.640957000
6	-3.391450000	-1.627147000	-0.590700000

1	-4.427545000	-1.798009000	-0.918479000
1	-3.307612000	-1.929158000	0.452655000
6	-2.445260000	-2.424631000	-1.471909000
1	-2.674526000	-2.257147000	-2.525000000
1	-2.602336000	-3.494912000	-1.301996000
6	-0.306683000	-2.011949000	-2.571398000
1	-0.475663000	-2.943545000	-3.132635000
1	0.761688000	-1.932163000	-2.379039000
6	-0.749255000	-0.832323000	-3.440543000
1	-1.743125000	-0.966815000	-3.872446000
1	-0.048740000	-0.732144000	-4.273450000
6	-3.811075000	0.461385000	0.526112000
1	-3.649913000	-0.227512000	1.356668000
1	-4.882761000	0.480975000	0.278464000
6	-3.368377000	1.855511000	0.999428000
6	-0.661851000	-3.145046000	1.104627000
6	-0.317176000	-3.117903000	-0.401592000
1	0.749447000	-2.933768000	-0.514089000
1	-0.512899000	-4.112517000	-0.833297000
6	-1.832533000	-4.075780000	1.448218000
1	-1.547262000	-5.106770000	1.203370000
1	-2.753276000	-3.847756000	0.909864000
1	-2.060760000	-4.026875000	2.515328000
6	0.579463000	-3.637951000	1.872031000
1	0.345058000	-3.773366000	2.933045000
1	1.410231000	-2.929096000	1.804101000
1	0.921149000	-4.604325000	1.476753000
6	-3.656176000	1.950118000	2.505538000
1	-3.351586000	2.922291000	2.901959000
1	-3.131783000	1.166437000	3.056381000
1	-4.734151000	1.832438000	2.678012000
6	-4.071619000	3.012702000	0.278333000
1	-5.147788000	2.951446000	0.484734000
1	-3.935430000	2.998366000	-0.804094000
1	-3.711428000	3.978610000	0.641629000
6	2.625543000	-0.739611000	-1.101179000
6	2.927899000	-0.166305000	-2.350479000
1	2.635511000	0.856993000	-2.562083000
6	3.609331000	-0.890947000	-3.330197000
1	3.829068000	-0.422814000	-4.285707000
6	4.014330000	-2.204509000	-3.081822000
1	4.550015000	-2.766438000	-3.841491000
6	3.727302000	-2.786902000	-1.846512000
1	4.040107000	-3.805628000	-1.635319000
6	3.035044000	-2.064853000	-0.870140000
1	2.825594000	-2.547640000	0.077253000
6	2.300202000	-0.109788000	1.775463000
6	3.528563000	-0.752733000	2.003717000
1	4.118837000	-1.129197000	1.176600000
6	4.025652000	-0.902954000	3.301844000
1	4.976211000	-1.406808000	3.454727000
6	3.312850000	-0.398640000	4.390548000
1	3.701130000	-0.513400000	5.398973000
6	2.102332000	0.263186000	4.172106000
1	1.545521000	0.670890000	5.011921000

6	1.594493000	0.403030000	2.878964000
1	0.659229000	0.932759000	2.722074000
6	2.333154000	1.920821000	-0.207537000
6	3.677498000	2.144408000	0.146368000
1	4.248825000	1.368044000	0.644002000
6	4.297154000	3.361427000	-0.131400000
1	5.335191000	3.512323000	0.152762000
6	3.586230000	4.382260000	-0.770901000
1	4.068677000	5.331664000	-0.987250000
6	2.254105000	4.172159000	-1.121965000
1	1.687355000	4.960377000	-1.610917000
6	1.629829000	2.949615000	-0.844425000
1	0.582567000	2.828021000	-1.084250000
8	-0.886525000	2.329942000	2.109489000
8	-1.344442000	3.159476000	-0.225072000
8	-2.465981000	-1.467621000	2.429001000

Table B49 Optimized coordinates for L³Ru(PhCN) (DMF phase)

Z	x	y	z
44	-0.423920000	0.001191000	0.222261000
16	-0.540608000	-0.699243000	2.560371000
16	-0.160235000	1.016308000	-1.938167000
16	-0.991660000	-2.109095000	-0.613405000
7	-2.556837000	0.308010000	0.375893000
7	-0.320774000	2.042024000	1.027690000
6	-2.341235000	-1.053871000	2.551282000
1	-2.364948000	-2.065115000	2.142849000
1	-2.724622000	-1.076601000	3.575497000
6	-3.152112000	-0.066382000	1.715299000
1	-4.154919000	-0.477541000	1.553699000
1	-3.291864000	0.851321000	2.289273000
6	-2.691942000	1.792336000	0.166797000
1	-3.722336000	2.117196000	0.372042000
1	-2.478215000	1.964112000	-0.888829000
6	-1.727262000	2.584556000	1.051182000
1	-2.072989000	2.589163000	2.086310000
1	-1.727537000	3.632195000	0.732866000
6	0.239783000	1.994600000	2.416682000
1	0.191002000	2.990971000	2.880346000
1	1.294015000	1.724772000	2.323053000
6	-0.447514000	0.985036000	3.337468000
1	-1.456022000	1.287753000	3.625845000
1	0.136975000	0.896587000	4.256798000
6	-3.233382000	-0.385916000	-0.780081000
1	-2.930612000	0.191970000	-1.655120000
1	-4.322062000	-0.297334000	-0.652901000
6	-2.867095000	-1.863627000	-1.051235000
6	0.434388000	2.767322000	-1.359444000
6	0.613112000	2.845176000	0.173751000
1	1.609665000	2.471993000	0.416720000
1	0.574562000	3.899242000	0.489901000

6	-0.521439000	3.827225000	-1.920098000
1	-0.119842000	4.823886000	-1.696038000
1	-1.530537000	3.769316000	-1.507377000
1	-0.610508000	3.728709000	-3.004523000
6	1.822971000	2.962082000	-1.997345000
1	1.747677000	2.978636000	-3.089362000
1	2.510034000	2.156643000	-1.715255000
1	2.266888000	3.913529000	-1.673952000
6	-3.040313000	-2.110151000	-2.558149000
1	-2.776976000	-3.139316000	-2.817261000
1	-2.417029000	-1.433036000	-3.146588000
1	-4.088878000	-1.944813000	-2.838610000
6	-3.723015000	-2.876168000	-0.280051000
1	-4.764806000	-2.789063000	-0.613793000
1	-3.707824000	-2.730880000	0.800980000
1	-3.387416000	-3.897715000	-0.477157000
7	1.595750000	-0.309561000	0.155420000
6	2.744343000	-0.504265000	0.129422000
6	4.150245000	-0.752895000	0.082774000
6	5.041004000	0.113557000	0.745569000
6	4.637712000	-1.863593000	-0.633138000
6	6.409769000	-0.135848000	0.687298000
1	4.656750000	0.967400000	1.294406000
6	6.009309000	-2.098676000	-0.681416000
1	3.943107000	-2.525094000	-1.140365000
6	6.894638000	-1.238244000	-0.023991000
1	7.099073000	0.530894000	1.196735000
1	6.387470000	-2.953998000	-1.232925000
1	7.963388000	-1.426799000	-0.066031000
8	-0.999752000	-3.186204000	0.457745000
8	-0.322556000	-2.566448000	-1.888744000
8	-1.494805000	1.261937000	-2.730251000

Table B50 Optimized coordinates for $L^3Ru(H_2O)$ (DMF phase)

Z	x	y	z
44	-0.056399000	0.242563000	-0.509874000
16	0.788593000	2.498359000	-0.827719000
16	-1.253742000	-1.809186000	-0.224669000
16	1.939730000	-0.755028000	-1.003700000
7	0.648931000	0.385732000	1.488008000
7	-1.856274000	1.215274000	0.291680000
6	1.942282000	2.430300000	0.604396000
1	2.810298000	1.933611000	0.167531000
1	2.227241000	3.443144000	0.903804000
6	1.378863000	1.673601000	1.805454000
1	2.194105000	1.456420000	2.504561000
1	0.685789000	2.324863000	2.340240000
6	-0.612158000	0.311918000	2.309164000
1	-0.398655000	0.542825000	3.362522000
1	-0.951951000	-0.722365000	2.244853000
6	-1.686650000	1.271504000	1.788105000

1	-1.443062000	2.299338000	2.063366000
1	-2.637428000	1.047182000	2.283253000
6	-1.958831000	2.600345000	-0.269382000
1	-2.778579000	3.149991000	0.217535000
1	-2.215882000	2.495592000	-1.326250000
6	-0.674968000	3.424194000	-0.155385000
1	-0.450404000	3.728492000	0.869120000
1	-0.791374000	4.337838000	-0.744002000
6	1.471164000	-0.852967000	1.778049000
1	0.737245000	-1.659935000	1.823730000
1	1.935738000	-0.736861000	2.767497000
6	2.558577000	-1.275332000	0.752447000
6	-3.032028000	-1.092586000	0.025342000
6	-3.058162000	0.441565000	-0.153385000
1	-3.150872000	0.654861000	-1.220827000
1	-3.956293000	0.847476000	0.338731000
6	-3.582903000	-1.563788000	1.376165000
1	-3.044451000	-1.157375000	2.234174000
1	-3.536009000	-2.652775000	1.451572000
1	-4.633314000	-1.257325000	1.459942000
6	-3.883752000	-1.704134000	-1.102740000
1	-3.948824000	-2.791564000	-0.991089000
1	-3.453747000	-1.486600000	-2.086505000
1	-4.905205000	-1.300333000	-1.080965000
6	2.667034000	-2.806888000	0.789111000
1	3.419583000	-3.160363000	0.077985000
1	1.709844000	-3.274830000	0.549673000
1	2.969682000	-3.131877000	1.793156000
6	3.936125000	-0.659909000	1.027267000
1	3.922288000	0.430691000	1.072805000
1	4.652630000	-0.946867000	0.253245000
1	4.306708000	-1.030952000	1.991408000
1	-0.105913000	-0.932108000	-2.823178000
8	-0.672419000	-0.146411000	-2.672340000
1	-0.299134000	0.541654000	-3.250184000
8	3.033779000	0.161963000	-1.522340000
8	1.790066000	-2.003936000	-1.858361000
8	-0.941163000	-2.637233000	1.075382000

Table B51 Optimized coordinates for L³Ru (DMF phase)

Z	x	y	z
44	-0.084740000	0.240621000	-0.615804000
16	0.735715000	2.530501000	-0.916412000
16	-1.257066000	-1.792448000	-0.446177000
16	1.959494000	-0.753569000	-1.080015000
7	0.582470000	0.351983000	1.371439000
7	-1.904866000	1.187019000	0.164203000
6	1.862986000	2.437126000	0.532024000
1	2.742300000	1.959576000	0.097143000
1	2.133018000	3.444417000	0.862134000
6	1.292343000	1.652402000	1.711271000
1	2.098691000	1.433109000	2.418656000
1	0.581487000	2.283447000	2.245822000
6	-0.687630000	0.259060000	2.177786000

1	-0.480001000	0.472018000	3.235298000
1	-1.018764000	-0.775899000	2.096001000
6	-1.759666000	1.222744000	1.662047000
1	-1.524026000	2.246408000	1.957359000
1	-2.715855000	0.986608000	2.140402000
6	-2.019618000	2.577106000	-0.383888000
1	-2.855031000	3.107720000	0.096571000
1	-2.259355000	2.478459000	-1.445571000
6	-0.750566000	3.418817000	-0.244791000
1	-0.541218000	3.713630000	0.785709000
1	-0.877615000	4.338386000	-0.821738000
6	1.414948000	-0.872696000	1.679215000
1	0.699939000	-1.698085000	1.667051000
1	1.818283000	-0.765420000	2.695950000
6	2.556968000	-1.229639000	0.700012000
6	-3.046112000	-1.133540000	-0.144336000
6	-3.090888000	0.400683000	-0.308473000
1	-3.171349000	0.625598000	-1.375386000
1	-4.001834000	0.788509000	0.173077000
6	-3.568705000	-1.638550000	1.205567000
1	-4.634106000	-1.391318000	1.291625000
1	-3.056092000	-1.209162000	2.067690000
1	-3.460042000	-2.723574000	1.272232000
6	-3.906464000	-1.745994000	-1.266223000
1	-3.945488000	-2.836035000	-1.169187000
1	-3.503317000	-1.506478000	-2.256565000
1	-4.935481000	-1.365518000	-1.217034000
6	2.747848000	-2.753327000	0.752300000
1	3.536004000	-3.069222000	0.063131000
1	1.825696000	-3.275978000	0.490323000
1	3.042173000	-3.052968000	1.766746000
6	3.894206000	-0.547153000	1.013200000
1	3.837223000	0.541962000	1.041260000
1	4.646428000	-0.814464000	0.266308000
1	4.250258000	-0.889344000	1.993335000
8	3.017370000	0.214610000	-1.580527000
8	1.927708000	-2.038427000	-1.876365000
8	-0.931928000	-2.731270000	0.766261000

Table B52 Optimized coordinates for L³Ru(PhCONH₂) (DMF phase)

Z	x	y	z
44	-0.598302000	-0.162154000	-0.326825000
16	-1.879430000	-0.752301000	-2.318439000
16	0.806148000	0.016499000	1.603245000
16	-1.078944000	2.083478000	-0.499938000
7	-2.451547000	-0.307478000	0.736533000
7	-0.508419000	-2.336753000	0.036743000
6	-3.508015000	-0.268510000	-1.618113000
1	-3.522705000	0.805239000	-1.810750000
1	-4.314540000	-0.742182000	-2.185573000
6	-3.657353000	-0.597022000	-0.134383000
1	-4.519458000	-0.051672000	0.265020000
1	-3.894873000	-1.656853000	-0.030979000
6	-2.237702000	-1.465860000	1.670279000

1	-3.181784000	-1.745469000	2.159270000
1	-1.548094000	-1.110294000	2.434541000
6	-1.666844000	-2.680733000	0.936672000
1	-2.440414000	-3.157759000	0.332753000
1	-1.359751000	-3.433299000	1.670499000
6	-0.639548000	-3.049189000	-1.274515000
1	-0.712168000	-4.135629000	-1.112939000
1	0.281635000	-2.855145000	-1.829169000
6	-1.834577000	-2.598441000	-2.117918000
1	-2.794682000	-2.925278000	-1.713189000
1	-1.742534000	-3.035785000	-3.115470000
6	-2.607694000	0.943002000	1.572478000
1	-1.839475000	0.846418000	2.342211000
1	-3.598796000	0.922341000	2.047723000
6	-2.399610000	2.318806000	0.887313000
6	1.299910000	-1.846660000	1.831912000
6	0.817546000	-2.692420000	0.634977000
1	1.538880000	-2.583392000	-0.177823000
1	0.811161000	-3.756037000	0.922873000
6	0.811229000	-2.348606000	3.197383000
1	1.220919000	-3.351523000	3.371778000
1	-0.272955000	-2.410573000	3.292781000
1	1.167424000	-1.689273000	3.992239000
6	2.840056000	-1.886558000	1.844595000
1	3.194542000	-2.922189000	1.936964000
1	3.231670000	-1.321404000	2.697000000
1	3.270120000	-1.465276000	0.932272000
6	-1.825445000	3.279813000	1.939304000
1	-1.636987000	4.265537000	1.504526000
1	-0.893154000	2.893099000	2.356685000
1	-2.546427000	3.400639000	2.758399000
6	-3.679764000	2.917704000	0.291855000
1	-4.395415000	3.105011000	1.102352000
1	-4.163140000	2.267640000	-0.439570000
1	-3.471214000	3.869976000	-0.203279000
6	2.494266000	-0.261671000	-1.659071000
7	1.222534000	0.372588000	-1.705478000
1	0.779126000	0.162782000	-2.598004000
8	2.621848000	-1.377339000	-2.147892000
6	3.617080000	0.474927000	-1.015346000
6	4.900591000	-0.087714000	-1.130668000
6	3.453254000	1.690688000	-0.327388000
6	6.003325000	0.553155000	-0.574065000
1	5.012979000	-1.024948000	-1.664916000
6	4.562411000	2.325563000	0.232244000
1	2.472884000	2.140711000	-0.199487000
6	5.834953000	1.762224000	0.109317000
1	6.991752000	0.114115000	-0.671949000
1	4.430561000	3.261309000	0.767295000
1	6.694441000	2.263859000	0.545008000
1	1.260116000	1.382310000	-1.567945000
8	-1.807079000	2.471000000	-1.776463000
8	0.087189000	3.015475000	-0.214144000
8	0.091151000	0.422296000	2.945438000

Table B53 Optimized coordinates for L³Ru(PhC(OH)NH) (DMF phase)

Z	x	y	z
44	-0.537978000	-0.197032000	-0.319173000
16	-1.948579000	-0.653513000	-2.293409000
16	0.886039000	-0.173769000	1.594836000
16	-0.828452000	2.121723000	-0.453844000
7	-2.406892000	-0.160530000	0.778332000
7	-0.689060000	-2.368561000	0.029663000
6	-3.493490000	-0.002085000	-1.553436000
1	-3.386604000	1.068842000	-1.729591000
1	-4.360775000	-0.370323000	-2.109493000
6	-3.644006000	-0.342595000	-0.073994000
1	-4.456387000	0.260395000	0.347225000
1	-3.963708000	-1.382072000	0.015485000
6	-2.280450000	-1.330806000	1.712195000
1	-3.236844000	-1.522798000	2.220582000
1	-1.544641000	-1.036602000	2.461350000
6	-1.841594000	-2.597019000	0.975760000
1	-2.674252000	-3.009578000	0.404074000
1	-1.575383000	-3.366593000	1.707283000
6	-0.949656000	-3.072686000	-1.265500000
1	-1.142007000	-4.141107000	-1.085537000
1	-0.032885000	-3.004343000	-1.855861000
6	-2.111012000	-2.492000000	-2.075495000
1	-3.085560000	-2.701332000	-1.629594000
1	-2.107356000	-2.947144000	-3.069197000
6	-2.460135000	1.091701000	1.613855000
1	-1.682716000	0.944773000	2.366358000
1	-3.438916000	1.140333000	2.114300000
6	-2.175862000	2.436261000	0.909874000
6	1.231360000	-2.074383000	1.752741000
6	0.618188000	-2.857839000	0.573250000
1	1.314042000	-2.806443000	-0.267019000
1	0.519059000	-3.919378000	0.851302000
6	0.770415000	-2.562846000	3.131840000
1	1.062994000	-3.613609000	3.253358000
1	-0.306196000	-2.492346000	3.290687000
1	1.250041000	-1.980787000	3.922579000
6	2.761107000	-2.233208000	1.672766000
1	3.041729000	-3.294987000	1.708332000
1	3.244643000	-1.729805000	2.516611000
1	3.165277000	-1.807703000	0.749457000
6	-1.581064000	3.384946000	1.962488000
1	-1.345365000	4.357802000	1.522865000
1	-0.669909000	2.972360000	2.400597000
1	-2.311679000	3.540620000	2.767379000
6	-3.409413000	3.103853000	0.288183000
1	-4.112521000	3.368970000	1.088107000
1	-3.941158000	2.471386000	-0.423476000
1	-3.130676000	4.022410000	-0.235583000
6	2.444091000	-0.167574000	-1.910113000
7	1.183244000	-0.327962000	-1.684616000
1	0.785277000	-0.735243000	-2.532564000

8	2.915378000	-0.663009000	-3.086543000
6	3.442117000	0.484336000	-1.033981000
6	4.750434000	-0.032951000	-0.980258000
6	3.120388000	1.641999000	-0.310822000
6	5.721252000	0.594189000	-0.201012000
1	5.003622000	-0.941612000	-1.520259000
6	4.104763000	2.272341000	0.451344000
1	2.115369000	2.053186000	-0.353920000
6	5.400545000	1.752714000	0.512222000
1	6.723932000	0.179971000	-0.152959000
1	3.855571000	3.175836000	1.001047000
1	6.159035000	2.248096000	1.111988000
8	-1.501231000	2.539512000	-1.753153000
8	0.313522000	3.049930000	-0.088521000
8	0.181171000	0.234130000	2.942874000
1	3.802226000	-0.306036000	-3.265977000

Table B54 Optimized coordinates for L³RuTS (DMF phase)

Z	x	y	z
44	-0.454947000	0.073252000	0.175259000
16	-0.172059000	-0.960223000	2.380662000
16	-0.661930000	1.447405000	-1.773397000
16	-0.537679000	-1.787264000	-1.128630000
7	-2.586617000	-0.245404000	0.523883000
7	-0.784057000	1.911333000	1.312198000
6	-1.818368000	-1.752753000	2.483934000
1	-1.652454000	-2.716324000	2.001839000
1	-2.074503000	-1.945669000	3.530029000
6	-2.933862000	-0.942980000	1.819989000
1	-3.792388000	-1.602168000	1.649393000
1	-3.275772000	-0.183406000	2.524728000
6	-3.104352000	1.165279000	0.563710000
1	-4.154325000	1.186315000	0.891951000
1	-3.054515000	1.533652000	-0.462003000
6	-2.275757000	2.046267000	1.506917000
1	-2.502692000	1.801078000	2.545779000
1	-2.575713000	3.091147000	1.375851000
6	-0.090019000	1.826690000	2.637687000
1	-0.341338000	2.701281000	3.255691000
1	0.981750000	1.861551000	2.431873000
6	-0.397929000	0.556745000	3.426183000
1	-1.409869000	0.538918000	3.835999000
1	0.293527000	0.487350000	4.269564000
6	-3.151928000	-0.946587000	-0.681362000
1	-3.113762000	-0.198303000	-1.476367000
1	-4.201453000	-1.213521000	-0.491302000

6	-2.411437000	-2.208673000	-1.207602000
6	-0.490404000	3.179144000	-0.944610000
6	-0.170496000	3.054030000	0.558790000
1	0.906207000	2.907541000	0.659596000
1	-0.427390000	3.996426000	1.067599000
6	-1.742053000	4.011329000	-1.245748000
1	-1.598195000	5.026643000	-0.854978000
1	-2.653778000	3.604779000	-0.805342000
1	-1.907613000	4.080145000	-2.323853000
6	0.724309000	3.841775000	-1.621155000
1	0.529481000	4.010031000	-2.685534000
1	1.618815000	3.216005000	-1.531892000
1	0.942055000	4.814347000	-1.159178000
6	-2.780699000	-2.361982000	-2.693300000
1	-2.278817000	-3.227396000	-3.133947000
1	-2.512320000	-1.474024000	-3.268417000
1	-3.863252000	-2.517395000	-2.774764000
6	-2.738593000	-3.522028000	-0.487077000
1	-3.809597000	-3.725760000	-0.605481000
1	-2.518364000	-3.516205000	0.578739000
1	-2.184823000	-4.352093000	-0.933271000
7	1.628701000	0.255304000	-0.015885000
6	2.564137000	-0.507924000	0.071715000
6	4.028641000	-0.407973000	-0.050436000
6	4.572267000	0.877479000	-0.246889000
6	4.898114000	-1.508565000	0.014002000
6	5.947692000	1.053657000	-0.371261000
1	3.901478000	1.728776000	-0.299020000
6	6.276440000	-1.325102000	-0.113302000
1	4.483746000	-2.496737000	0.162361000
6	6.807368000	-0.048088000	-0.304555000
1	6.350075000	2.051980000	-0.520134000
1	6.936233000	-2.186973000	-0.061950000
1	7.880765000	0.089886000	-0.401016000
8	0.098841000	-3.057474000	-0.387696000
8	-0.037245000	-1.757190000	-2.544847000
1	2.148075000	-2.189479000	1.415724000
8	2.246360000	-2.211080000	0.447497000
1	1.113567000	-2.664735000	0.008464000
8	-2.095844000	1.417431000	-2.417634000

APPENDIX-C

A	Collision frequency
Arg	Arginine
Av.	Average
Å	Angstrom
H	Hapticity
^t BuNC	tert-butyl isonitrile
^t BuNH ₂	tert-butylamine
CC	Coupled cluster
CE	Counter electrode
CI	Chemical ionization
Co-NHase	Cobalt type NHase
CRC	Cardinal research cluster
DFT	Density functional theory
DMF	N, N'-dimethylformaamide
E _a	Activation energy
EI	Electron ionization
EPR	Electron paramagnetic resonance
ESI-MS	Electron spray ionization-mass spectrometry

Fe-NHase	Iron type NHase
FT-IR	Fourier transform infrared spectroscopy
GC-MS	Gas chromatography-mass spectrometry
GGA	Generalized gradient approach
h^{-1}	per hour
HF	Hartree Fock
kJ	Kilo joules
k	rate constant
k_{obs}	first-order observed rate constant
K	Kelvin
K_2	Equilibrium constant
LDA	Local density approximation
m	meta
M	Molar
MB	Mega byte
mL	millilitre
μL	microlitre
MM	Molecular mechanics
MP	Møller Plesset

m/z	mass to charge ratio
NBO	Natural bonding orbital
NHase	Nitrile hydratase
NMR	Nuclear magnetic resonance
NPA	Natural population analysis
<i>o</i>	ortho
<i>p</i>	para
Phe	Phenylalanine
PTFE	poly(tetrafluoroethane)
RE	Reference electrode
RF	Response factor
SCNase	Thiocyanate hydrolase
Ser	Serine
TCD	Thermal conductivity detector
TON	Turnover number
TOF	Turnover frequency
TS	Transition state
Tyr	Tyrosine
UV-vis	Ultraviolet-visible spectroscopy

WE	Working electrode
w/v	weight by volume ratio
XAS	X-ray absorption spectroscopy
XRD	X-ray diffraction

CURRICULUM VITAE

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Education and Research Experience

University of Louisville, Louisville, KY, USA (GPA = 3.87/4.00)

2009 – 2015 Ph.D., Chemistry – Inorganic Chemistry (Spring 2015)

Dissertation: Sulfur-Oxidation Enhances Nitrile Hydration in Bioinspired Ruthenium Complexes: Catalytic, Kinetic, and DFT Investigations

Advisor: Prof. Craig A. Grapperhaus

Panjab University, Chandigarh, India (Grade: 70.0%)

2006 – 2008 M.Sc. (Honors School) Physical Chemistry

Thesis: Structure and Stability of Alkali and Alkaline Earth Metal Cluster: A DFT Study

Advisor: Prof. Neetu Gupta

Indian Institute of Technology, Kharagpur, West Bengal, India

May 2007 – July 2007 Summer Research Internship

Dissertation: To Solve the Time-Dependent Schrodinger Equation (TDSE) and Time-Independent Schrodinger Equation for a Particle in a 3D Spherically Symmetric Box & a 1D Box with Moving Boundaries

Advisor: Prof. P. K. Chattaraj

Kurukshetra University, Kurukshetra, India (Grade: 79.3%)

2003 – 2006 B.Sc. (Physics, Chemistry and Mathematics)

Research Skills

- Air-free and open to air organic and inorganic syntheses, photochemistry, crystallization, purification
- Spectroscopic analysis and interpretation, including UV-visible spectroscopy, FT-IR, electrochemistry, spectro-electrochemistry mass spectroscopy, electron paramagnetic resonance, multinuclear magnetic resonance, gas chromatography, GC-MS, and atomic absorption spectroscopy
- Microsoft office program suite, Chem Draw, Corel Draw, Mercury, Digisim (simulation software for electrochemistry), WebCSD, Scifinder, Reaxys, Origin, and Endnote
- Gaussian 98/03/09 program for DFT studies, Geometry optimization, Transition state calculation, Mechanistic investigations, NBO analysis, and Fortran 90 language
- Computer assisted analysis of DFT calculations by Gaussview, Chemcraft, and Jmol.
- Laboratory equipment maintenance including glove box, vacuum pumps, and schlenk line

Research Interests

Transition metal-mediated homogeneous and heterogeneous small molecule activation/transformation (CO₂ reduction, H₂O oxidation, H₂ oxidation and production, N₂ reduction), Electrocatalysis, Kinetics and Mechanism, Computational Chemistry

Publications

1. Bioinspired Catalytic Nitrile Hydration by Dithiolato, Sulfinato/Thiolato, and Sulfenato/Sulfinato Ruthenium Complexes

Davinder Kumar, César A. Masitas, Tho N. Nguyen, and Craig A. Grapperhaus
Chem. Commun. **2013**, 49, 294-296.

2. Addition of Polysubstituted Alkenes, Aromatic Alkynes, and Dienes to a Metal-Stabilized Thiyl Radical via Carbon-Sulfur Bond Formation: Electrochemical, Chemical, and Computational Investigations

Kagna Ouch Sampson, **Davinder Kumar**, Mark S. Mashuta, and Craig A. Grapperhaus
Inorg. Chim. Acta **2013**, 408, 1-8.

3. Kinetic Effects of Sulfur Oxidation on Catalytic Nitrile Hydration: Nitrile Hydratase Insights from Bioinspired Ruthenium(II) Complexes

Davinder Kumar, Tho N. Nguyen, and Craig A. Grapperhaus *Inorg. Chem.* **2014**, 53, 12372-12377.

4. Sulfur-Oxygenation and Functional Models of Nitrile Hydratase

Davinder Kumar and Craig A. Grapperhaus *Bioinspired Catalysis–Metal-Sulfur Complexes*, John Wiley and Sons, **2014**, 325-347. (Invited Minireview)

5. Homogeneous Ligand-Centered Hydrogen Evolution at a Mononuclear Metal-Thiolate Center

Andrew Z. Haddad, Rajat Chauhan, Kagna Ouch, **Davinder Kumar**, and Craig A. Grapperhaus (In preparation)

Invited Talks

“Sulfur-Oxidation Enhances Nitrile Hydration in Bioinspired Ruthenium (II) Complexes: Catalytic, Kinetic, and DFT Investigations” for post-doctoral position at University of Kentucky, Center for Applied Energy Research, March 13th, 2015

Presentations

1. César A. Masitas, **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus Gordon Research Seminar, Bioinorganic Chemistry, Jan. 2012 (**Poster**)

2. **Davinder Kumar**, César A. Masitas, Mark S. Mashuta, and Craig A. Grapperhaus Graduate Research Symposium, March 2012 at Univ. of Louisville, Louisville, KY (**Poster**)

3. **Davinder Kumar**, César A. Masitas, Mark S. Mashuta, and Craig A. Grapperhaus 244th ACS National Meeting Philadelphia, PA, Fall-2012 (**Poster**) (*Selected for online put-up of the poster on ACS website*)

4. Conor J. Young, Craig A. Grapperhaus, **Davinder Kumar**, and Tho N. Nguyen Undergraduate Summer Research Symposium, University of Louisville, Fall 2012 (**Poster**)

5. **Davinder Kumar**, César A. Masitas, Tho N. Nguyen, and Craig A. Grapperhaus Gordon Research Seminar, Bioinorganic Chemistry, Ventura, CA, Jan. 2013 (**Poster**)

6. **Davinder Kumar**, César A. Masitas, Tho N. Nguyen, and Craig A. Grapperhaus Gordon Research Conference, Metals in Biology, Ventura, CA, Jan. 2013 (**Poster**) (Joint session with Bioinorganic Chemistry)

7. **Davinder Kumar**, César A. Masitas, Tho N. Nguyen, and Craig A. Grapperhaus 246th ACS National Meeting, Indianapolis, IN, Fall-2013 (**Oral**)

8. **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus Oesper Symposium organized by ACS-Cincinnati section to honor Prof. Richard Eisenberg for his contribution to science for fifty years, University of Cincinnati, Cincinnati, OH, October 25th, 2013 (**Poster**)

9. **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus Ohio Inorganic Weekend, University of Dayton, Dayton, OH, November 15th -16th, 2013 (**Oral**)

10. **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus Gordon Research Conference, Metals in Biology, Ventura, CA, Jan. 2014 (**Poster**)

11. **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus 248th ACS National Meeting, San Francisco, CA, Fall-2014 (**Oral**)

12. **Davinder Kumar**, Tho N. Nguyen, and Craig A. Grapperhaus Tri-state Catalysis Society Symposium University of Louisville, Louisville, KY, Sept. 15th 2014 (**Oral**)

Workshops

1. Q-chem workshop, University of Louisville, KY, March 2010
2. Grant writing workshop, Gordon Conference, Ventura, CA, Jan. 2013 (by Michele McGuirl from NSF)
3. Organic Fluorine Chemistry: Basic concepts and application to materials and drug sciences by Professor Kenji Uneyama, Okayama University, Japan, University of Louisville, Oct. 2013

Professional Awards

University of Louisville, Louisville, KY, USA

Fall 2012	ACS–Division of Inorganic Chemistry Travel Award
Spring 2014	Graduate Student Council Travel Award
Fall 2014	Graduate Student Council Travel Award
Spring 2015	Doctoral Dissertation Completion Award from SIGS

Educational Awards

Panjab University, Chandigarh, India

Awarded Late Smt. Leela Mahant and Late Sh. Sampurna Mahant Scholarship in M.Sc. 2nd year

Summer Research Fellowship by The Summer Research Fellowship Programme jointly sponsored by IASc (Bangalore), INSA (New Delhi) and NASI (Allahabad)

Government Senior Secondary School, Tohana, Haryana, India

2003 Best Student Award

Teaching Experience

University of Louisville, Louisville, KY, USA

August 2009 – December 2014 Graduate Teaching Assistant

General Chemistry – I and II (Chem-201 and Chem-202) Lecture

General Chemistry – III and IV (Chem-209 and Chem-210) Lab

Chemistry for Non–Science Majors (Chem-103) Lab

Professional Memberships

American Chemical Society

American Chemical Society-Division of Inorganic Chemistry