The Influence of Intramolecular Proton Relays on Catalysis

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<thead>
<tr>
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</tr>
</thead>
<tbody>
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The Influence of Intramolecular Proton Relays on Catalysis

A dissertation presented
by
Daniel John Graham
to
The Department of Chemistry and Chemical Biology
in partial fulfillment of the requirements
for the degree of
Doctor of Philosophy
in the subject of
Chemistry
Harvard University
Cambridge, Massachusetts
March 2015
The Influence of Intramolecular Proton Relays on Catalysis

Abstract

Global energy demand is predicted to increase at an alarming rate over the next century; in order to meet this demand while also limiting the effects of runaway climate change, society will need to shift toward renewable sources of energy. Many of the fundamental chemical transformations that store renewable energy as fuel require the addition or removal of protons. Optimization of catalysts that carry out these transformations can be achieved with proton management at the molecular level.

Deliberate construction of molecular catalysts with an intramolecular proton relay is one strategy for controlling the movement of protons during catalysis. These so-called “hangman” catalysts have been shown to increase the rate of catalysis in the cases of hydrogen evolution, oxygen reduction, hydrogen peroxide dismutation, and olefin epoxidation. A new class of hangman porphyrins is now available on the gram scale and can easily be further modified, allowing for unprecedented control the strength and character of pendant proton relays. Using iron complexes of these new hangman porphyrins, the level of control over proton management is demonstrated with the variation in the rates of hydrogen evolution electrocatalysis depending on the nature of the proton relay in the second coordination sphere.

Understanding the fundamental electron transfer reactions of reactive oxygen species (ROS) is important in the chemistry of renewable energy storage, but also in a biological context. Hydrogen bond donors are known to affect the electron transfer
reactivity of ROS, with the strength of the hydrogen bond determining the nature of oxygen-oxygen bond activation. The catalytic performance of iron corroles towards peroxide dismutation is markedly enhanced by the presence of a pendant hydrogen bond donor which is also capable of transferring protons to bound substrates. Contrary to hangman corroles, the six hydrogen bond donors in hexacarboxamide cryptand do not readily transfer protons, allowing it to facilitate the chemically reversible two-electron reduction of dioxygen to “naked” peroxide dianion. Using electrochemical techniques and computational modeling, it is possible to use cryptand-encapsulated peroxide as a model for the electron transfer reactions within lithium-oxygen batteries.
# Table of Contents

Title Page i
Copyright Page ii
Abstract iii
Table of Contents v
List of Figures and Schemes viii
List of Tables xiii
List of Abbreviations xv
Dedication xvii
Acknowledgements xviii

## Chapter 1 — Introduction

1.1 Background 1
1.2 Energy Storage Molecules 4
1.3 Proton Management in H–H and O–O bond forming or breaking 4
1.4 O–O Bond Cleavage 5
1.5 Controlling the Extent of O₂ Reduction 6
1.6 The Hangman Effect 7
1.7 Summary of Chapters 9
1.8 References 13

## Chapter 2 — Hangman Effect on Hydrogen Peroxide Dismutation by Fe^{III}–Corroles

2.1 Introduction 16
2.2 Results and Discussion 17
2.3 Conclusion 24
2.4 Experimental Section 25
2.5 References 28
Chapter 3 — Gram Scale Synthesis of Post-synthetically Modifiable Hangman Porphyrins

3.1 Introduction
3.2 Results and Discussion
  3.2.1 Scaffold Synthesis
  3.2.2 Porphyrin Construction
  3.2.3 Hanging Group Attachment
3.3 Conclusion
3.4 Experimental Section
3.5 References

Chapter 4 — Electrocatalytic H₂ Evolution by Proton–Gated Hangman Iron Porphyrins

4.1 Introduction
4.2 Results and Discussion
  4.2.1 Synthesis of HPDFe Complexes
  4.2.2 Cyclic Voltammetry
  4.2.3 Foot–of–the–Wave Analysis
  4.2.4 Mechanistic Study
4.3 Conclusion
4.4 Experimental Section
4.5 References

Chapter 5 — Electron Transfer Behavior of Peroxide Dianion in a Hydrogen Bond–Rich Molecular Capsule

5.1 Introduction
5.2 Results and Discussion
  5.2.1 Chemistry of the Cryptand
  5.2.2 Electrochemical Studies of O₂ in the Presence of Cryptand
  5.2.3 Computational Modeling of Electrochemical Studies
5.3 Conclusion
5.4 Experimental Section 109
5.5 References 111

Chapter 6 — Future Prospects for Electrocatalysis Employing Hangman Macrocycles 115

6.1 Introduction 115
6.2 Results and Discussion 115
   6.2.1 Synthesis of HPDCo Complexes 115
   6.2.2 Synthesis of HPDNi Complexes 117
   6.2.3 Electrochemical Studies of HPDCo Complexes 119
   6.2.4 Electrochemical Studies of HPDNi Complexes 125
   6.2.5 Comparing Fe, Co, and Ni Porphyrins 131
6.3 Conclusion and Future Work 134
6.4 Experimental Section 135
6.5 References 144
List of Figures and Schemes

Figure 2.1. Fe$^{III}$-corroles employed in this chapter. 17

Figure 2.2. Titration of pyridine, 0 (—), 4.1, 8.3, 12.4, 16.6, 20.7 and 41 (—) mM, into a 15 μM solution of 2 in THF, monitored by UV–vis. 19

Figure 2.3. Absorption spectra of 2–py in pentane (——) and in THF (—). 20

Figure 2.4 Turnover number for catalytic H$_2$O$_2$ disproportionation by Fe corroles: 1–py (■), 2 (▲), 3 (◄), 1–Cl (●), 2–Cl (▼) and 3–Cl (►). TON measured over the first 2 min of the reaction. TON determined from volumetric measurement of O$_2$ produced. 21

Scheme 2.1. Proposed catalytic cycle for [Fe$^{III}$(Corr)]–catalyzed H$_2$O$_2$ dismutation. 24

Scheme 3.1. Synthesis of 2 from dibenzofuran 33

Scheme 3.2. Synthesis of hangman porphyrin precursor 4 by the statistical reduction and subsequent oxidation of 2. 34

Scheme 3.3. Attempted selective reduction of 2 by DIBAL–H. 34

Scheme 3.4. Formation for the porphyrin from pyrrole, TMB, and 4. 36

Scheme 3.5. Post–synthetic modification of hanging group with isolated yields for each hangman porphyrin derivative. 37

Figure 3.1. Solid state molecular structure of HPD–Ph with 50% ellipsoids. All carbon–bound hydrogens removed for clarity. Carbon atoms are grey, oxygen atoms are red, nitrogen atoms are blue, and hydrogen atoms are white. 39

Scheme 4.1. Method for Fe insertion to furnish the Fe–porphyrins used in this study 61

Figure 4.1. EPR spectrum of A$_4$Fe in toluene measured at 4 K. 62
Figure 4.2. Cyclic voltammograms of 0.5 mM solutions of HPDFe–Ph (blue), HPDFe–DMA (red), HPDFe–3SA (green), A₄Fe (purple) in CH₃CN (0.1 M [TEA⁺][TsO⁻]) with 40 mM PPh₃ at 50 mV/s.

Figure 4.3. Cyclic voltammograms of 0.5 mM solutions of (a) HPDFe–Ph, (b) HPDFe–DMA, (c) HPDFe–3SA, and (d) A₄Fe in the presence of 0 mM (blue), 5 mM (green), 10 mM (yellow), 15 mM (orange), and 20 mM (red) of H⁺ (from added HBF₄). Conditions: 40 mM PPh₃ in CH₃CN (0.1 M [TEA⁺][TsO⁻]) at a scan rate of 50 mV/s.

Scheme 4.2. Proposed catalytic mechanism.

Figure 4.4. Foot–of–the–wave analyses of (a) HPDFe–Ph, (b) HPDFe–DMA, (c) HPDFe–3SA, and (d) A₄Fe using the CVs displayed in Figure 3. Concentrations of H⁺ (from added HBF₄) are 5 mM (green), 10 mM (yellow), 15 mM (orange), and 20 mM (red).

Figure 4.5. Values of k determined from CVs of A₄Fe (0.5 mM) with 20 mM PPh₃ and 5 mM (green), 10 mM (yellow), 15 mM (orange), and 20 mM (red) of [TsOH•OTs⁻] (generated in situ by addition of HBF₄) in CH₃CN (0.1 M [TEA⁺][TsO⁻]) at scan rates from 50 mV/s to 2 V/s.

Figure 4.6. Plots of log(k) vs. log([TsOH•OTs⁻]) for HPDFe–Ph (blue), HPDFe–DMA (red), HPDFe–3SA (green), A₄Fe (purple) in CH₃CN (0.1 M [TEA⁺][TsO⁻]) with 40 mM PPh₃ at 50 mV/s A₄Fe.

Figure 5.1. Thermal ellipsoid plot at 50% probability level of K₂(DMF)₅[(O₂²⁻)ₓmBDCA–5t–H₆] peroxide adduct. Tertiary–butyl groups, potassium ions, non hydrogen–bonded hydrogen atoms, and DMF molecules have been omitted for clarity.

Figure 5.2. Encapsulation of O₂²⁻ through disproportionation of O₂⁻ (top) or in situ reduction of O₂ by CoCp₂ (bottom). Treatment of the product complex with DDQ oxidatively liberates O₂.
**Figure 5.3.** Cyclic voltammograms measure of O₂-saturated (4.8 mM) DMF (0.1 M [TBA⁺][ClO₄⁻]) in the presence of 0.0 mM $m$BDCA–5t–H₆ (red), 4.8 mM $m$BDCA–5t–H₆ (green) and 9.6 mM $m$BDCA–5t–H₆ (blue) at a scan rate of 10 mV/s.

**Figure 5.4.** Rotating ring disk electrode measurements of 4.8 mM $K_2$DMF₅[(O₂²⁻)⊂mBDCA–5t–H₆] in DMF (0.1 M [TBA⁺][ClO₄⁻]). (Left, top) Potential of disk electrode vs. time. (Left, Bottom) Observed current on disk (black) and ring (red) while fixed at −2.0 V vs. Ag⁺/Ag, a potential sufficient to reduce O₂ in solution. (Right, top) Potential of disk electrode vs. time. (Right, bottom) Observed current on disk (black) and ring (red) when fixed to −1.0 V vs. Ag⁺/Ag, a potential which is unable to reduce O₂ in solution.

**Figure 5.5.** Cyclic voltammogram of argon–saturated DMF (0.1 M [TBA⁺][ClO₄⁻]) in the presence of 4.8 mM $K_2$(DMF)₅[(O₂²⁻)⊂mBDCA–5t–H₆] displaying the release of O₂ upon oxidation (at a scan rate of 100 mV/s).

**Scheme 5.1.** Proposed mechanism of the reversible cryptand–facilitated O₂ reduction to encapsulated O₂²⁻.

**Figure 5.6.** Cyclic voltammogram of 9.6 mM solution of $m$BDCA–5t–H₆ in O₂–saturated DMF (0.1 M [TBA⁺][PF₆⁻]) (black), simulated cyclic voltammogram (red) using the mechanistic steps described in Scheme 1.

**Figure 5.7.** Experimental CVs (black) and simulated CVs (red) of 0.5 mM $[TBA^+]_2[(O_2^{2-})_{⊂}mBDCA–5t–H_6]$ in DMF (0.1 M [TBA⁺][PF₆⁻]) at (a) 50 mV/s, (b) 100 mV/s, (c) 250 mV/s, and (d) 500 mV/s. The first sweep is in the positive direction.

**Scheme 6.1.** Insertion of Co into porphyrins.

**Figure 6.1.** UV–vis spectra of 5 µM solutions of HPDCo–Ph (blue), HPDCo–DMA (red), HPDCo–3SA (green), and A₄Co (purple) in CH₃CN.

**Scheme 6.2.** Insertion of Ni into porphyrins.
Figure 6.2. Solid state molecular structure of $A_4Ni$. Hydrogen atoms and co-crystallized molecule of EtOAc removed for clarity. The central nickel atom is purple, nitrogen atoms are blue, oxygen atoms are red, and carbon atoms are gray.

Figure 6.3. CVs of HPDCo–Ph (▬ blue), HPDCo–DMA (▬ red), HPDCo–3SA (▬ green), and $A_4Co$ (▬ purple) in CH$_3$CN (0.1 M [TEA$^+$$]$$][TsO^-]$] at a glassy carbon electrode with a scan rate of 50 mV/s.

Figure 6.4. CVs of HPDCo–Ph (a), HPDCo–DMA (b), HPDCo–3SA (c), and $A_4Co$ (d) in CH$_3$CN (0.1 M [TEA$^+$$]$$][TsO^-]$] with H$^+$ concentrations (from added HBF$_4$) of 0 mM (▬ black), 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red).

Figure 6.5. Hangman cobalt porphyrins used in previous work from our group to study the mechanism of electrocatalytic H$_2$ generation.

Figure 6.6. CVs of 0.8 mM solutions of HPXCo–CO$_2$H (▬ black) and HPXCo–Br (▬ red) in CH$_3$CN (0.1 M [TBA][PF$_6$–]) in the presence of 10 mM TsOH.

Scheme 6.3. A possible mechanism for the multi-electron, multi-proton reduction of Co$^{II}$–porphyrin to Co$^I$–chlorin.

Figure 6.7. CVs of HPDNi–Ph (▬ blue), HPDNi–DMA (▬ red), HPDNi–3SA (▬ green), and $A_4Ni$ (▬ purple) in CH$_3$CN (0.1 M[TEA$^+$$]$$][TsO^-]$] at a scan rate of 50 mV/s.

Figure 6.8. CVs of HPDNi–Ph (▬ blue), HPDNi–DMA (▬ red), HPDNi–3SA (▬ green), and $A_4Ni$ (▬ purple) in CH$_3$CN (0.1 M[TEA$^+$$]$$][TsO^-]$] at a scan rate of 50 mV/s.

Figure 6.9. CVs of HPDNi–Ph (a), HPDNi–DMA (b), HPDNi–3SA (c), and $A_4Ni$ (d) in CH$_3$CN (0.1 M [TEA$^+$$]$$][TsO^-]$] with H$^+$ concentrations (from added HBF$_4$) of 0 mM (▬ black), 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red).
**Figure 6.10.** CVs of $\text{A}_4\text{Ni}$ in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) in the presence of 20 mM H$^+$ (from added HBF$_4$) at scan rates of 50 mV/s (■ black), 100 mV/s (■ purple), 250 mV/s (■ blue), 500 mV/s (■ green), 1 V/s (■ yellow), 1.5 V/s (■ orange), and 2 V/s (■ red).

**Figure 6.11.** CVs of $\text{A}_4\text{Fe}$ (■ red), $\text{A}_4\text{Co}$ (■ blue), and $\text{A}_4\text{Ni}$ (■ green) in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) in the presence of 20 mM H$^+$ (from added HBF$_4$) at a scan rate of 50 mV/s. The CV of $\text{A}_4\text{Fe}$ was collected in the presence of 40 mM PPh$_3$. 
List of Tables

Table 2.1. TON and TOF of catalytic H$_2$O$_2$ dismutation. The extent of reaction determined from volumetric measurement of O$_2$ produced. $^a$ calculated after 2 min. $^b$ determined from first 20 sec of the reaction.

Table 4.1. Values of log($k$) for all catalysts at different H$^+$ concentrations. Values were obtained from the foot–of–the–wave slope per Eq. (5). $^a$ H$^+$ concentration from added HBF$_4$ (to generate TsOH and its homoconjugate in situ). All experiments were conducted under an atmosphere of N$_2$ in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) containing 0.5 mM Fe–porphyrin. All scans were performed at 50 mV/s.

Table 4.2. Values for log(TOF$_0^{(2)}$) at different H$^+$ concentrations. Values were obtained from Eq. (7). $^a$ H$^+$ concentration from added HBF$_4$ (to generate TsOH and its homoconjugate in situ). All experiments were conducted under an atmosphere of N$_2$ in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) containing 0.5 mM Fe porphyrin. All scans were performed at 50 mV/s.

Table 5.1. Reactions and parameters used for simulation reactions i–iv (Scheme 1) of the CV of O$_2$ reduction in DMF (0.1M [TBA$^+$][ClO$_4$$^-$]) in the presence of 9.6 mM mBDCA–5t–H$_6$ at 10 mV/s (Figure 5). $E^0$ is the standard reduction potential, $k_s$ is the electron transfer rate constant, $\alpha$ is the transfer coefficient, K$_{eq}$ is the equilibrium constant for the reaction, and $k_f$ is the forward rate constant. L represents mBDCA–5t–H$_6$, [LO$_2^-$] and [LO$_2^{2^-}$] represent cryptand complexes of O$_2^-$ and O$_2^{2^-}$, respectively.

Table 5.2. Diffusion coefficients obtained from the fitting the CV of O$_2$ reduction in DMF (0.1M [TBA$^+$][ClO$_4$$^-$]) in the presence of 9.6 mM mBDCA–5t–H$_6$ at 10 mV/s (Figure 5). L represents mBDCA–5t–H$_6$, [LO$_2^-$] and [LO$_2^{2^-}$] represent cryptand complexes of O$_2^-$ and O$_2^{2^-}$, respectively.
Table 5.3. Reactions and parameters used for simulation reactions i–iv (Scheme 1) of the CV of O₂ reduction in DMF (0.1 M [TBA⁺][PF₆⁻]) in the presence of 0.5 mM \textit{mBDCA–5t–H₆} at different scan rates (Figure 6). \( E^0 \) is the standard reduction potential, \( k_s \) is the electron transfer rate constant, \( K_{eq} \) is the equilibrium constant for the reaction, and \( k_f \) is the forward rate constant. \( L \) represents \textit{mBDCA–5t–H₆}, \([LO_2^{-}\] and \([LO_2^{2-}]\) represent cryptand complexes of \( O_2^{2-} \) and \( O_2^{2-} \), respectively.

Table 5.4. Diffusion coefficients obtained from the fitting the CV of O₂ reduction in DMF (0.1 M [TBA⁺][PF₆⁻]) in the presence of 0.5 mM \textit{mBDCA–5t–H₆} at the various scan rates (Figure 6). \( L \) represents \textit{mBDCA–5t–H₆}, \([LO_2^{-}\] and \([LO_2^{2-}]\) represent cryptand complexes of \( O_2^{2-} \) and \( O_2^{2-} \), respectively.
<table>
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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>bdt</td>
<td>1,2-benedithiolate</td>
</tr>
<tr>
<td>$C_{\text{H}^+}$</td>
<td>Bulk concentration of acidic protons</td>
</tr>
<tr>
<td>CoCp$_2$</td>
<td>Cobaltocene</td>
</tr>
<tr>
<td>CV</td>
<td>Cyclic Voltammogram</td>
</tr>
<tr>
<td>D</td>
<td>Diffusion Coefficient</td>
</tr>
<tr>
<td>DCM</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>DDQ</td>
<td>2,3-dichloro-5,6-dicyano-1,4-benzoquinone</td>
</tr>
<tr>
<td>DIBAL–H</td>
<td>Diisobutylaluminum hydride</td>
</tr>
<tr>
<td>DMAP</td>
<td>N,N–dimethylaminopyridine</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N–dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethylsulfoxide</td>
</tr>
<tr>
<td>E</td>
<td>Electrode potential</td>
</tr>
<tr>
<td>$E^0$</td>
<td>Standard reduction potential for a given redox couple</td>
</tr>
<tr>
<td>$E_p$</td>
<td>Peak potential, potential at which a feature in a CV reaches a peak</td>
</tr>
<tr>
<td>EPR</td>
<td>Electron paramagnetic resonance</td>
</tr>
<tr>
<td>ET</td>
<td>Electron transfer</td>
</tr>
<tr>
<td>F</td>
<td>Faraday’s constant</td>
</tr>
<tr>
<td>FcOTf</td>
<td>Ferrocenium trifluoromethanesulfonate</td>
</tr>
<tr>
<td>FOWA</td>
<td>Foot–of–the–wave analysis</td>
</tr>
<tr>
<td>GC</td>
<td>Gas chromatography</td>
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<td>HCX</td>
<td>Hangman corrole with xanthene scaffold</td>
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<tr>
<td>HER</td>
<td>Hydrogen evolution reaction</td>
</tr>
<tr>
<td>HPD</td>
<td>Hangman porphyrin with dibenzofuran scaffold</td>
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<td>Hangman porphyrin with xanthene scaffold</td>
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<tr>
<td>$i$</td>
<td>Current</td>
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<tr>
<td>$i_p$</td>
<td>Peak current, current measured at the peak of a feature in a CV</td>
</tr>
<tr>
<td>$i_p^0$</td>
<td>Peak current of a catalyst’s redox feature in the absence of substrate</td>
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<tr>
<td>$k$</td>
<td>Apparent rate constant, in the context of FOWA</td>
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<td>$K_{\text{eq}}$</td>
<td>Equilibrium constant</td>
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<tr>
<td>Symbol</td>
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<tr>
<td>$k_f$</td>
<td>Forward rate constant</td>
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<td>$k_s$</td>
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<tr>
<td>MS</td>
<td>Mass spectrometry</td>
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<tr>
<td>$n$-BuLi</td>
<td>$n$-Butyllithium</td>
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<tr>
<td>NCHB</td>
<td>Normal charged hydrogen bond</td>
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<tr>
<td>NEt$_3$</td>
<td>Triethylamine</td>
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<td>NMR</td>
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<td>Proton–coupled electron transfer</td>
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<td>PPh$_3$</td>
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<td>Reactive Oxygen Species</td>
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<td>[TBA$^+$]</td>
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<td>[TEA$^+$]</td>
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<td>TEMPO</td>
<td>2,2,6,6–tetramethylpiperadinyloxy</td>
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<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TMB</td>
<td>3,4,5–trimethoxybenzaldehyde</td>
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<td>TMEDA</td>
<td>Tetramethylethylenediamine</td>
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<tr>
<td>TsCl</td>
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<td>[TsO$^-$]</td>
<td>4-Toluenesulfonate anion</td>
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<tr>
<td>[TsOH•OTs$^-$]</td>
<td>Homo–dimer of 4-toluenesulfonate and 4-toluenesulfonic acid</td>
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<td>$\alpha$</td>
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<td>Reorganization energy</td>
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<tr>
<td>$\nu$</td>
<td>Scan rate</td>
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for Vanessa
Acknowledgements

I could not have gotten to where I am today if it wasn’t for the physical, technical, and emotional support of many people with whom I was fortunate enough to interact during my education, and I will attempt to give thanks to all of them. To Ms. Phillips, Ms. Sagendorf, and Mr. Phillips at Schenectady High School for laying the groundwork that caused me to entertain the thought of pursuing a career in science. As a student at BrandX, my interest in chemistry was rewarded with entertaining, informative lectures and experiences in research labs. To Tim Rose, for reinforcing my passion for the chemistry behind environmental issues. To Milos Dolnik, for unrelenting questions and meticulous attention to detail during labs and presentations. To Jason Pontrello, for advice over the years. To Bruce Foxman, my mentor, confidant, and friend, whose teaching performance was a source of inspiration. To Oleg Ozerov, for taking the time and effort to assign me classic papers to read, ask tough questions, treat me like an adult, and give me opportunities to grow as a chemist. To Christine Thomas, for taking me in when Oleg moved to Texas, and allowing me to develop independent research skills.

One of the reasons that I joined the Nocera group was the diversity of the projects and backgrounds of the members. To Bob McGuire, for introducing me to electrochemistry. To Dilek Doğutan, for walking me through my first hangman porphyrin synthesis. To Yogi Surandranath, Kwabena Bediako, and Andrew Ullman, for always being there when I needed to discuss any aspect of electrochemistry. To Chris Lemon, for answering all my questions about pyrrolic macrocycles. To Tom Teets, Matt Chambers, and Mike Marshak, for being yourselves. To Manos, for the olive oil. To Charlie, for the laughs. To Andrew Maher and Bryce Anderson, for being good gym buddies (for the two months that I went)
who also put up with my bothering them with unrelated discussions during the day. To Seung Jun Hwang, my group meeting partner. To Cassandra Cox, for guidance. To Guillaume Passard, who significantly expanded my knowledge of electrochemistry in just a few months. To Tom Kempa, for the big-picture discussions. To Dave Powers, for the career discussions and advice. To Arturo Pizano, for keeping it real. To Yi Liu, my favorite office mate, thank you for the companionship. To Lisa Olshansky, for the great albeit brief times we've spent hanging out, I only hope to have a life 1/10 as exciting as yours. To Bon Jun Koo, for all the dinner parties and birthday cards.

To Carl Brožek, who was always there when I needed to vent and organized many great extra-lab activities. To Miller Li, for being a great friend and introducing me to the Miller Screwdriver. To Jon Axtell, who has never been anything but courteous and a joy to be around. To Joe Elias, with whom I had many good conversations. To Dan Kozera, who doesn’t have an amoral bone in his body, for his friendship during our time at MIT. To Jim Colombe, I wish we hung out more, because I always had a good time with you. To Matt Nava and Julia Stauber, you guys are the chillest and really smart, thanks for the good times. To Jon, Monica, Adam, Tim, Nikki, Jake, Katya, Eric, Kevin, Rox, and anyone else who I shared laughs with, thanks for the memories, you made my time in Boston lively and interesting, I will always remember our good times together.

To Mike Huynh, I can’t thank you enough for all the help you’ve given me over the years. You are easily the most disciplined person in the lab, who somehow managed to perform experiments and serve as the groups one man IT department. Bon Jun can attest to the fact that I literally paid Mike a visit at least a few times every week to ask for help connecting to the computing cluster, discussing python, asking for help to install the
correct software, knowing which bin folders to put my unzipped tarballs into, and help
with my window's virtual machine. Mike is also a great friend and was always there when I
wanted to discuss a potential startup idea, which was a welcome distraction during slumps
in my lab work.

To Robert Halbach, thank you for introducing me to Tito's and offering me your
hand in marriage for Canadian citizenship as a worst case Ontario. I thought about it. A lot.
Thanks for being one of the only people who enjoys watching deranged cartoons with me.
Stay in school buddy, one day you'll wake up and bringo! You'll be a real rocket appliance.
Know'm say'n? To Nancy Li, thank you for offering me your hand in marriage for Canadian
citizenship. I thought about it for quite a while, but not as long as I thought about being
Robert's husband.

To my mom Robin, I may not have acted like I appreciated your praise, but I did. I
try to make you proud and I literally owe my life to you. Thank you for all the love and
support over my 27 years, I can't even imagine what you had to go through when I was a
little brat. You gave me the drive to become who I am today. To my sister Ariel, we've had
some good times together and I expect them to only increase in frequency. I am very proud
of your efforts on the ground in the developing world, I've often thought about how little
impact my work has compared to yours, you should be proud. To my bubbe Shirley, for
giving me the "Sacks gene" which is no doubt the basis of whatever intelligence I have.
Everyone should be so lucky to have three strong women like yourselves in their lives.

To Nazario Lopez, I miss you buddy. Thanks for all the great times, I look forward to
visiting you. Stay safe, hermano. To Chao and Tofan, who along with Nazario made the
absolute greatest crew to hang out with at D.B.'s Golden Banana.

xx
To Jose’s Food Truck, Momogoose, and Al’s Sandwich Shop for all the delicious, inexpensive food that sustained me.

To Jose Salvador Monterrozza, mi amigo, conversations with you were a welcome break from the day. I will honor you by celebrating Jose Day every December with relaxation and tequila.

To Chris Perry, my hero, my idol, I aspire to be like you one day. Thanks for organizing softball and being a generally chill dude.

To my advisor Dan Nocera, I don’t know how I can possibly begin to thank you. I can honestly say I am better off for having met you. Thanks for putting up with me, sorry about all the damage to the lab.

To Kit Cummins, for being an excellent pseudo-co-advisor. You gave me opportunities to experience the non-academic working world through our collaborations.

To Ted Betley and Mircea Dincă, for being on my thesis committee.

To my wife Vanessa, who somehow put up with my long hours and mental preoccupation, yet still managed to be so mentally strong that I drew inspiration from it. “I love you” is too cliché, I don’t have the people-words to express my feelings toward you. I would have given up a long time ago if you were not there to support me and I hope I can partially make it up to you in our many happy years to come.
Chapter 1 – Introduction

1.1 Background

Although humans have long known about the consequences of incessantly releasing carbon dioxide (CO₂) into the atmosphere, we have consciously increased CO₂ emissions for the sake of continuous economic growth. In order to drive this growth in the most cost effective way possible, nations rely on inexpensive fossil fuel energy sources and hesitate to invest heavily in cleaner, renewable alternatives. For developing nations, this can be a choice between remaining poor spectators in the global economy and raising their national standard of living. While there have been piecemeal international deals and promises to curb emissions, the most current report from the International Energy Agency projects that even if world governments comply with their current policy plans to wean themselves off of fossil fuels, there will be a 0.5% annual increase in demand for coal, a 50% rise in natural gas output, and a 15% increase in world oil supply. Despite the projected rise in renewable electricity generation, fossil fuel use will result in a 20% rise of carbon emissions and a 3.6 °C increase in global temperatures over the long term.¹

The inexpensive nature of fossil fuels is due to an existing infrastructure for fossil fuels that is amortized and its portability, energy density, and natural availability, but also due to the fact there is rarely ever a cost associated with the societal impact of fossil fuel waste. This commonly acknowledged market failure can be addressed by placing a carbon tax on fossil fuel use, but this policy would be hard to implement given the political influence of fossil fuel companies and the general aversion of most consumers...
to new taxes. Given the profitability of the fossil fuel industry and the recent Supreme Court decisions in *Citizens United v. Federal Election Commission*\textsuperscript{2} and *McCutcheon v. Federal Election Commission*,\textsuperscript{3} large campaign donations will continue to influence political decisions concerning our energy use for many years to come. This political reality is unlikely to usher in the magnitude of policy changes that are necessary for humans to avoid runaway global climate instability and the displacement of billions of people within this century. Additionally, previous assumptions that fossil fuels will become more difficult to extract with time have had to be rethought with the technological advances in horizontal drilling and hydro-fracking which have instead resulted in an increase in the total amount of economically viable fossil fuel deposits. Therefore, the only path for a global shift away from fossil fuel usage must come from technological advances that out-compete traditional “dirty” energy sources not only according to the rules and regulations of our current state of free market capitalism, but also with the undeniable presence of corporate political influence.

In order to address this challenge, we first need to understand the projections that outline the goals and restrictions of energy supply and demand. There is a 95% probability that global population will be between 9.3 and 13.2 billion by the end of the century.\textsuperscript{4} This rise in population will result in an increase in demand for energy for heating, cooking, and transportation. If we are to stand a chance at decreasing our carbon emissions as the number of individual consumers increases, this energy will need to come in the form of electricity generated by renewable sources. Photovoltaics, concentrated solar-thermal, and wind turbines are by far the most promising methods of renewable electricity generation. The most commonly cited potential pitfall of these
methods is the intermittency of sunshine and wind, meaning that these power sources alone are not capable of directly providing baseload power for large groups of consumers. The storage of excess energy that is generated when there is insufficient demand is one strategy for transforming solar and wind farms into reliable sources of baseload power. Despite the fact that the current research is showing that intermittency is not as limiting of an issue as once thought, large scale energy storage will still be necessary.

Advances in long-distance power transmission and management may decrease the required storage capacity, but the need for capacity to buffer the intermittent behavior of the ideal renewable energy sources will still be needed in the near term. Batteries are a common mode of energy storage, but technological advances in that realm are needed in order to decrease the cost before gigawatt hours of capacity can be built. Electrons can also be stored in chemical bonds within molecules that we generally refer to as “fuels.” Ideal fuels are stable, portable, compatible with our current methods of fuel distribution infrastructure, and can be interfaced with developed engines or fuel cells. Fossil fuels are fuels by this definition, but the energy they hold was initially captured by the organisms that stored solar energy in the form of carbohydrates millions of years ago. In the same way that plants take energy from the sun to form fuels, there are various methods of forming simple, energy storage molecules from renewable electricity.
1.2 Energy Storage Molecules

For such simple molecules, hydrogen (H\textsubscript{2}) and oxygen (O\textsubscript{2}) are relevant to a wide range of scientific studies addressing the future of carbon-free sustainable energy. H\textsubscript{2} has been a popular topic in the energy community for decades, eliciting visions of energy storage via direct production of H\textsubscript{2} from water (H\textsubscript{2}O). After it is produced, H\textsubscript{2} can be burned directly for heat or used in a fuel cell in order to generate electricity. The other fuel cell input is O\textsubscript{2}, which combines with two molecules of H\textsubscript{2} to form water, cleaving their O–O bond in the process. O\textsubscript{2} has recently become a topic in a different subset of the energy storage sciences with increased interest in lithium-air or lithium-oxygen (Li–O\textsubscript{2}) batteries, which are theoretical energy densities exceeding currently available batteries.\textsuperscript{6}

1.3 Proton Management in H–H and O–O bond forming or breaking

With electron transfer reactions involving H\textsubscript{2} and O\textsubscript{2} specifically, proton management is essential. During hydrogen fuel cell operation, for example, the hydrogen ion or “proton” (H\textsuperscript{+}) must be shuttled away from the electrode (anode) into which the H\textsubscript{2} molecule deposits its electrons, thereby forming H\textsuperscript{+}, through a selective membrane, to another electrode where O\textsubscript{2} reduction is occurring (cathode).\textsuperscript{7} Proton management is equally essential for rapid, complete four-electron reduction of O\textsubscript{2} to H\textsubscript{2}O. During the course of fuel cell operation, H\textsuperscript{+} is depleted in the vicinity of the cathode which serves to limit both the rate at which O\textsubscript{2} is reduced, as well as the product into which it is transformed; the two resulting reduction products of O\textsubscript{2} in the presence of protons are either one equivalent of hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}), which results from two electron
reduction, or H₂O, which results from four electron reduction. The product distribution of oxygen reduction depends on the availability of protons in the immediate vicinity of the O₂ molecules as well as the duration of time that the partially reduced oxygen species remain near the cathode, the source of the reducing equivalents. Similarly, generation of H₂ from soluble acids depletes the availability of protons near the cathode. Attaching acid/base functionalities with appropriate pKₐ’s to the catalyst is one way to ensure that the effective concentration of protons remains high near the active site.

1.4 O–O Bond Cleavage

In addition to fuel cells, O–O bond cleavage is a subject of interest in the biology in the context of catalysts which serve to decompose reactive oxygen species (ROS), and there is a library of molecular compounds, both synthesized by nature and by scientists, that scavenges ROS and converts them to harmless molecules. H₂O₂ is one of these ROS, and nature uses enzymes called peroxidases to prevent the buildup of dangerous concentrations of H₂O₂. Some of these enzymes employ functionalized Fe-porphyrin (heme) active sites. The exact mechanism of peroxidase activity is unknown, but several hydrogen bonding moieties are contained in the second coordination sphere above the Fe center. These hydrogen bond donors are amino acid side chains that can stabilize reactive intermediates and play a role in the management of protons during the course of catalysis. H₂O₂ dismutation is interesting because it involves the transition metal-assisted cleavage of an O–O bond. The role of proton management in this process is a subject of study in the fields of molecular catalysis and enzyme modeling, with the hope that breakthroughs could provide insight into the
mechanism of peroxidases and the development of treatments to scavenge ROS in the human body.

1.5 Controlling the Extent of O₂ Reduction

In contrast to fuel cells and ROS scavenging, Li–O₂ batteries are one specific application for the rapid yet selective two-electron reduction of O₂. As opposed to traditional lithium batteries, which employ solid anodes like lithium cobaltate, Li–O₂ batteries employ oxygen gas as the sink into which electrons from Li metal are deposited, with the eventual goal of using O₂ from the air as opposed to a tank of pure gas, resulting in a battery that can theoretically deliver the same amount of energy while weighing much less than alternative batteries.

The first step during Li–O₂ battery discharge is the one electron reduction of O₂ to form superoxide (O₂⁻). Lithium ions (Li⁺) in solution then drive the production of lithium peroxide (Li₂O₂) by forming a lithium superoxide (LiO₂⁻) intermediate that deposits on the electrode and undergoes a slow disproportionation reaction to give Li₂O₂ and O₂. Over time and at large negative voltages, some of the Li₂O₂ is further reduced to the unwanted byproduct lithium oxide (Li₂O), which requires extra energy to return to gaseous O₂ upon battery recharge.

Li–O₂ batteries are far from commercialization for many reasons, but two of them are the slow nature of LiO₂ and the fact that Li₂O₂ cakes the cathode, retarding further electron transfer and physically damaging the electrode. There is clearly a need for a technological advance that will (1) drive the two electron reduction of O₂ in aprotic
solvents, (2) prevent further reduction of Li$_2$O$_2$, and (3) prevents deposition of Li$_2$O$_2$ on the cathode.

Like Li$^+$, protons are known to drive the multi–electron reduction of O$_2$. In protic solvents, O$_2$•$^-$ can react with a proton to form the neutral hydrosuperoxide (HO$_2$•) and eventually disproportionate into H$_2$O$_2$ and O$_2$. Brønsted-Lowry acids and protic solvents are incompatible with the idea of a Li–O$_2$ battery, so the use of hydrogen bond-donors must be chosen so that they are not deprotonated by O$_2$•$^-$ or O$_2^{2-}$. Hexacarboxamide cryptand, which was previously studied in our group,$^{13,14}$ has demonstrated the ability to carry out all three of the aforementioned tasks. Employing strong N-H bonds, the hexacarboxamide cryptand can tame O$_2^{2-}$ without being deprotonated, essentially becoming a soluble source of O$_2^{2-}$. This provides us with a unique opportunity to study the electron transfer properties of reduced oxygen species, which may hold importance in the field of Li-O$_2$ batteries.

1.6 The Hangman Effect

The Nocera group has a long history of studying catalytic transformations of small molecules that require the addition or removal of protons, and specifically the effect of placing a proton donor/acceptor in the secondary coordination sphere. Ligands that can participate in multiple hydrogen bonding interactions are known to bind more favorably to metal centers that have pendant acid/base functionalities in the secondary coordination sphere, a phenomenon that is known in the context of biochemistry and substrate binding selectivity in enzyme active sites. C. K. Chang studied molecular analogs of these enzyme active sites and found that exhibited similar preferential
behavior.\textsuperscript{15–17} Inspired by this finding, our group adopted the practice of designing ligands with “hanging” hydrogen bonding moieties, which were fittingly named “hangman ligands.” Following the first two publications in 2003, the Nocera group has produced a steady stream of studies investigating the difference in performance of metal complexes of hangman ligands and their non–hangman congeners under conditions of catalysis. In nearly every instance, the presence of an acid/base functionality in the secondary coordination sphere enhanced the catalyst's performance in carrying out transformations that required the addition or removal of protons, a phenomenon that is now referred to as the “hangman effect.”

Throughout the years, our group has studied the hangman effect in the context of H\textsubscript{2}O\textsubscript{2} dismutation,\textsuperscript{18–26} H\textsubscript{2} generation,\textsuperscript{27, 28} H\textsubscript{2}O oxidation,\textsuperscript{29, 30} and O\textsubscript{2} reduction.\textsuperscript{30–36} The broader concept of using the secondary coordination sphere to influence activity of redox reactions involving protons has subsequently been generalized to a variety of metal centers and secondary coordination sphere environments.\textsuperscript{37}

Our hangman ligands can be described as three separate sections that are combined to form the molecule; the transition metal and the atoms coordinated to it, the hangman scaffold on which the acid/base moiety is appended, and the acid/base moiety itself. The beauty of the hangman system lies in the control that one has over several different properties of the ligand through the modification of each of the aforementioned sections. Varying the pK\textsubscript{a} of the acid/base functionality will affect the movement of protons during catalysis. Changing the ligand in the immediate vicinity of the metal center will affect the behavior of the active site. And using different scaffolds will change the distance of the acid/base functionality from the metal center. Another
variable property of hangman metal complexes is of course the metal atom itself, which can be chosen for a desired task.

Researchers in the Nocera group have shown that simple changes in molecular construction have profound effects on catalyst performance. Our studies of proton management on molecular analogs of catalyst active sites strive to give insight into strategies that enhance the performance of larger systems that deal with the formation or cleavage of bonds in small molecules that will play a large role in the sustainable economy of the future. A complete understanding these simple, fundamental processes of chemical transformations are necessary for development of efficient energy systems that we need to ensure a sustainable future.

1.7 Summary of Chapters

Chapter 2: Hangman Effect on Hydrogen Peroxide Dismutation by Fe\textsuperscript{III}-Corroles. Iron (Fe) metallocycles are known H\textsubscript{2}O\textsubscript{2} dismutation catalysts, anyone who has cleaned a cut with H\textsubscript{2}O\textsubscript{2} will know this from the appearance of bubbles (O\textsubscript{2}) which are produced from catalysis by heme groups (Fe porphyrins) in red blood cells. This chapter describes the follow–up work to a study on the ability of Fe-corroles to catalyze H\textsubscript{2}O\textsubscript{2} dismutation and the effect that a pendant acid/base group in the second coordination sphere has on the rate of catalysis.

The first study employed Fe-corroles that were in the formal Fe\textsuperscript{IV} oxidation state, but is most likely a Fe\textsuperscript{III} ion ligated by a corrole lacking one electron from its \( \pi \)-system (Fe\textsuperscript{III}(Corr\textsuperscript{\cdot+})).\textsuperscript{38} Redox active ligands like corrole are known to aid in catalysis by reducing the demand from the transition metal center. This is especially true with first
row transition metals like Fe, where single electrons transfers are favored over two electron transfers. In the case of H₂O₂ dismutation, catalysis is thought to proceed through an Fe-oxo (Fe(=O)) intermediate, which represents a two electron oxidation. It was realized however, that Fe³⁺(Corr•⁺) might be outperformed by the synthetically feasible Fe-corrole complex consisting of an Fe³⁺ core ligated by a neutral corrole ligand.

When Fe³⁺(Corr•⁺) is used as a catalyst, as was previously done, a two electron oxidation would result in an intermediate of the form Fe⁵⁺(=O)(Corr•⁺), whereas the same oxidation using Fe³⁺Corr would pass through an Fe⁴⁺(=O)(Corr•⁺) intermediate. One would expect the difference in energy of these intermediates to have a significant effect on the rate of catalysis. This effect, as well as the consequence of placing a pendant acid/base functionality in the second coordination sphere a.k.a. “the hangman effect,” are demonstrated in this chapter.

Chapter 3: Synthesis of Hanging Porphyrin Dibenzo furans (HPDs) on the Gram Scale. Our group has had a long history of studying ligands that can be modified not only to change the electronic properties of the transition metal center, but also the environment around the transition metal. By engineering this space, which is too far from the transition metal to interact with it directly, we can influence the behavior of the catalyst after small molecule substrates bind. If the second coordination sphere contains a proton donor or acceptor, we can control the multistep processes that involve proton transfers. In cases where catalysis proceeds at the fastest possible rate, the intramolecular nature of the proton transfers on our ligand scaffolds containing pendant acid/base functionalities, a.k.a. “hangman ligands” consistently outperform molecules with identical electronic properties but lacking an internal proton relay.
Historically, our group has used xanthene most often to serve as the scaffold on which the acid/base is appended. Furthermore, the acid/base functionality has almost exclusively been a carboxylic acid. Early in my graduate career, I noticed the wide range of potential proton relays that had yet to be studied, and set out to design a new scaffold on which to append them. After meditating on the subject, I came to the conclusion that the geometric orientation of the xanthene scaffold limited the types of acids that could be attached following ligand synthesis. Upon evaluating other hangman scaffolds, it became clear that dibenzofuran was an attractive target, as it was inexpensive, rigid, and provided the required space to attach a hanging proton relay. This chapter details the synthetic journey toward dibenzofuran-functionalized porphyrins (HPDs) and one in particular than could be synthesized in an abnormally impressive yield for porphyrins.

**Chapter 4: Electrocatalytic H₂ Generation by Proton-Gated Hangman Porphyrins.** Fe porphyrins are known electrocatalysts for the reduction of protons and carbon dioxide (CO₂). Past studies have employed weak acids and catalysis is thought to commence with reduction to a formal “Fe⁰” oxidation state, which had the required basicity to accept a proton from a strong base. We succeeded in using Fe porphyrins as electrocatalysts in a solution containing a stronger proton donor, which resulted in initiation of catalysis from the Fe¹ oxidation state, without any noticeable degradation over the course of hours of controlled potential electrolysis.

This chapter details the use of Fe complexes of the HPD ligand (HPDFe) to electrocatalytically reduce protons to H₂ in organic solvents. A series of different HPDFe molecules are synthesized and characterized electrochemically. They are found to be competent proton reduction catalysts. The HPDFe series are nearly identical in terms of
the electronic properties of the Fe center, but differ in the identity of their pendant proton relay. Using different hanging groups (or the lack thereof) in conjunction with a new method for characterizing the intrinsic rate of electrocatalysis known as foot-of-the-wave analysis (FOWA), we are able to quantify the differences in rates of catalysis that can be attributed directly to the differences of hanging groups.

Chapter 5: Electron Transfer Behavior of Peroxide Dianion and Superoxide in a Hydrogen Bond-Rich Molecular Capsule. The hexacarboxamide cryptand project was initially conceived as the synthesis of a “hangman-like” ligand that could contain a transition metal within a cage that dangled three NH bonds at a distance where they can interact with bound substrates. It was discovered that the transition metal-free cryptand was capable of driving the disproportionation of $O_2^-$ and encapsulating a soluble, molecular form of peroxide dianion ($O_2^{2-}$). This remarkable molecule has been shown to oxidize phosphines and carbon monoxide (CO), and even to store carbon dioxide (CO$_2$) as carbonate (CO$_3^{2-}$) inside the cryptand.

While much work has been undertaken to detail the various reactions of cryptand-encapsulated peroxide, my interest regarded the electron transfer behavior of $O_2^{2-}$ and $O_2^*$ inside the cryptand. This chapter details the mechanistic modeling of $O_2$ reduction at an electrode in the presence of free cryptand, as well as the oxidation of the encapsulated $O_2^{2-}$. Using computational modeling in conjunction with stopped flow spectroscopy and electrochemical studies, we were able to interrogate the electron transfer behavior of a reduced oxygen species in the presence of cryptand.

Chapter 6: Future Prospects for Electrocatalytic Reductions with Hangman Metalloporphyrins. In addition to Fe, Cobalt (Co) and Nickel (Ni) macrocycles have
been identified as competent electrocatalysts for proton reduction. Notably, Co and Ni
porphyrins have been shown by our group to act as electrocatalysts for the reduction of
protons to H₂ in organic solvents. Other groups have demonstrated the ability of Co and
Ni macrocycles to reduce CO₂ electrocatalytically. With this knowledge, we wondered
how an analogous set of HPD metal complexes would behave as reduction
electrocatalysts. This chapter outlines the synthesis and electrochemical
characterization of HPD complexes of Ni (HPDNi) and Co (HPDCo), as well as a
comparison against the activity of HPDFe, which was detailed in Chapter 4. The
possibility that these complexes may facilitate the electrocatalytic transformation of CO₂
to CO or formic acid (HCO₂H) is discussed.

1.8 References
234.
Lett., 1, 2193.


Chapter 2 – Hangman Effect on Hydrogen Peroxide

Dismutation by Fe$^{III}$–Corroles

Portions of this chapter have been published:
DOI: 10.1039/C2CC30580A

2.1 Introduction

The strategic placement of an acidic or basic functionality in the secondary coordination sphere of transition metal complexes is known to facilitate catalysis and stabilize energetic intermediates during O–O bond formation or cleavage.$^{1-3}$ With the installation of acid–base groups on functionalized xanthene moieties featuring porphyrin, corrole, or salen ligands,$^{4,5}$ the so-called “hangman effect” has proven beneficial in the catalytic reduction of $O_2$,$^{6}$ production of $H_2$,$^7$ oxidation of $H_2O$,$^8$ epoxidation of olefins,$^9$ and disproportionation of $H_2O_2$.,$^{10-14}$ In every case, the hangman effect manifests itself in a lowered overpotential and/or significant increase in rate of catalysis.

Metallo–corroles can promote a variety of transformations, including atom efficient aziridination and cyclopropanations.$^{15}$ Accounts of Fe–corrole (Fe$^{III}$(Corr)) catalyzed decomposition of reactive nitrogen and oxygen containing species in biology and the pertinence of such a reaction chemistry to disease,$^{15-17}$ motivated us to investigate the role of the hangman effect on corrole $H_2O_2$ dismutation activity.

Mahammed and Gross have previously shown that Fe$^{III}$(Corr) complexes are active $H_2O_2$
dismutation catalysts, but quizzically, our experiments suggested that the presence of the hanging group decreased both the lifetime and activity of the catalyst. We tentatively ascribed the deterioration in performance of the hangman system to the oxidation state of the pre-catalyst, which is most accurately described as an Fe^{III}Cl center complexed by a corrole radical cation ([Fe^{III}Cl(Corr•+)]). In this case, H_{2}O_{2} dismutation would necessarily pass through a Fe^{V}(=O)(Corr•+) intermediate, which is thermodynamically challenging to access and prone to decomposition, thus obscuring any hangman effect. If this contention is correct, a pronounced hangman effect should be observed for H_{2}O_{2} dismutation from a hangman corrole resting state residing one redox level lower, Fe^{III}(Corr). As described in this chapter, this simple oxidation state change leads to superior rates of catalytic H_{2}O_{2} disproportionation by xanthene modified hangman corrole (HCXFe^{III}(Corr)) as compared to HCXFe^{III}Cl(Corr•+) and non-hangman congeners (Figure 1).

Figure 2.1. Fe^{III}-corroles employed in this chapter.

2.2 Results and Discussion

The systematic tuning of the steric and electronic properties of corrole metal complexes may be achieved through macrocycle meso-substituent variation. Given
that the electron rich and redox active corrole π-system is prone to reaction with O\textsubscript{2} resulting in macrocycle decomposition, corroles bearing electron-withdrawing pentafluorophenyl meso-substituents were chosen for this study. These electron-poor corroles display superior stability towards O\textsubscript{2}, with accordingly high turnover numbers (TONs) for O\textsubscript{2}-producing reactions relative to corroles with electron-releasing meso-substituents.\textsuperscript{19} Beginning with the free base hangman corrole,\textsuperscript{6} the standard method of refluxing in DMF or pyridine with excess FeCl\textsubscript{2}, followed by purification with diethyl ether (Et\textsubscript{2}O) delivered the pyridine or Et\textsubscript{2}O adducts 2-py and 3-Et\textsubscript{2}O.\textsuperscript{26} Isolation of 3-Et\textsubscript{2}O was desired so as to avoid any deleterious acid–base chemistry of the hanging carboxylic acid with pyridine. 2-py was isolated in high yield (94.6%) as the pyridine adduct owing to its enhanced resistance to oxidation and ease of handling. With Fe\textsuperscript{III}(Corr) complexes in hand, their one-electron oxidized congeners are easily obtained by employing the methods of Gross.\textsuperscript{26} Washing dichloromethane (DCM) solutions of 1-py, 2-py, and 3-Et\textsubscript{2}O with dilute HCl in H\textsubscript{2}O delivered the corresponding Fe\textsuperscript{III}Cl(Corr\textsuperscript{•+}) complexes 1-Cl, 2-Cl, and 3-Cl quantitatively.

The coordination environment of 1-py, 2-py, and 3-Et\textsubscript{2}O differs from 1-Cl, 2-Cl, and 3-Cl only in the nature of the axial ligand. The Fe centers in 1-Cl\textsuperscript{26} and HCXFe\textsuperscript{III}Cl(Corr\textsuperscript{•+})\textsuperscript{19} are known to be five-coordinate, with one Cl\textsuperscript{-} bound axially, though the coordination environments of 2-py and 3-Et\textsubscript{2}O are not certain without crystallographic evidence. Nonetheless, \textsuperscript{1}H NMR spectra are consistent with the presence of only one axial ligand. The xanthene scaffold imposes an asymmetry and axial ligands can reside on the syn and anti face of the corrole macrocycle and consequently two distinct sets of axial ligand NMR shifts would be observed for a six-coordinate
hangman complex. However, the $^1$H NMR spectrum of $2$-$\text{py}$ and $3$-$\text{Et}_2\text{O}$ display only one unique set of axial ligand NMR shifts in the $^1$H NMR spectra.

Although pre–catalysts $1$-$\text{py}$, $2$-$\text{py}$, and $3$-$\text{Et}_2\text{O}$ differ in the identity of their axial ligands, experimental conditions were such that the Fe coordination environments were identical immediately preceding catalysis. The labile nature of the pyridine ligand on Fe–corroles has been established by $^1$H NMR experiments.\textsuperscript{27} We provide further support for pyridine exchange upon dissolution of $2$-$\text{py}$ in tetrahydrofuran (THF) with the UV–vis titration data provided in Figure 2.

![Absorption Spectrum](image)

**Figure 2.2.** Titration of pyridine, 0 (—), 4.1, 8.3, 12.4, 16.6, 20.7 and 41 (– – –) mM, into a 15 μM solution of $2$ in THF, monitored by UV–vis.

An absorption spectrum of $2$-$\text{py}$ in pentane displayed the expected Soret band at 407 nm and a prominent Q–band at 556 nm (Figure 3). Upon changing the solvent to
THF, a shoulder at 333 nm increased in intensity, a shoulder at 368 nm was replaced by a shoulder at 385 nm, and a Q-band at 758 nm was blue-shifted to 737 nm. We ascribe these changes to displacement of the pyridine by THF to produce the THF adduct, 2. The spectra shown in Figure 2 for the titration of 2 with pyridine in THF confirm this contention. The final absorption spectrum of $2$–py in the presence of excess pyridine is identical to that of 2 in pentane. The similarities observed in the absorption spectra obtained upon dissolving $2$–py and $3$–Et\(_2\)O in THF suggest that the coordinated Et\(_2\)O molecule in $3$–Et\(_2\)O is also displaced promptly upon dissolution to form 3, and furthermore that the coordination environments of 2 and 3 in THF are similar.

**Figure 2.3.** Absorption spectra of $2$–py in pentane (— —) and in THF (—).

The dismutation chemistry of the THF adducts 1, 2, and 3 was compared to their one-electron oxidized congeners $1$–Cl, $2$–Cl, and $3$–Cl. The hydrophobicity of 1–3
together with their tendency to be instantaneously oxidized in chlorinated solvents led us to employ a 3:1 THF:MeOH solvent system for dismutation experiments. Figure 4 plots the TON for each of the compounds employed in this study. In each experiment, a 0.50 mM solution of catalyst in 2 mL 3:1 THF:MeOH was exposed at once to an excess (1000 equiv.) of H$_2$O$_2$ and the amount of generated O$_2$ was quantified using an apparatus described in the experimental section. In order to avoid initial O$_2$–induced catalyst decomposition, all solvents and reagents were thoroughly purged with argon prior to each experiment. As shown in Table 1, the Fe$^{III}$(Corr) systems 1–3 clearly exhibit enhanced activity over their one electron–oxidized analogues in the given solvent system.

**Figure 2.4.** Turnover number for catalytic H$_2$O$_2$ disproportionation by Fe–corroles: 1–py (■), 2 (▲), 3 (▲), 1–Cl (●), 2–Cl (▼) and 3–Cl (►). TON measured over the first 2 min of the reaction. TON determined from volumetric measurement of O$_2$ produced.
<table>
<thead>
<tr>
<th>Compound</th>
<th>TON&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TOF (min&lt;sup&gt;-1&lt;/sup&gt;)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95.7</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>79.0</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>83.2</td>
<td>170</td>
</tr>
<tr>
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<tr>
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<td>58</td>
</tr>
<tr>
<td>3–Cl</td>
<td>55.7</td>
<td>77</td>
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</tbody>
</table>

Table 2.1. TON and TOF of catalytic H<sub>2</sub>O<sub>2</sub> dismutation. The extent of reaction determined from volumetric measurement of O<sub>2</sub> produced. <sup>a</sup> calculated after 2 min. <sup>b</sup> determined from first 20 sec of the reaction.

The total amount of O<sub>2</sub> generated by 2 and 3 (1.9 mL and 2.0 mL, respectively) was less than the amount generated by 1 (2.3 mL); this is reflected in the reduced TONs. The total amount of O<sub>2</sub> generated by 2 and 3 were approximately equal, suggesting that they decompose at similar rates with respect to O<sub>2</sub> concentrations, and faster than that observed for 1. We attribute this observation to the greater stability of 1 as compared to 2 and 3. The presence of a third pentafluorophenyl meso–substituent on the macrocycle of 1 as compared to 2 and 3 serves to decrease electron density in the corrole π–system, thereby increasing catalyst lifetime by retarding oxidation by O<sub>2</sub> and subsequent μ–O formation. Introduction of the electron releasing xanthene backbone shortens the catalyst lifetime and TON. Notwithstanding, the clear benefit of the hangman effect is evident in the initial rate of O<sub>2</sub> production for 3, which far surpasses the initial rates displayed by both 1 and 2.
1-Cl, 2-Cl and 3-Cl display inferior catalytic activity compared to 1, 2, and 3. The similarity between TONs of 1-Cl, 2-Cl and 3-Cl may be explained by the facile formation of catalytically inactive μ-O complexes, known to result from the reaction of FeII\textsubscript{III}Cl(Corr\textsuperscript{•+}) and two OH\textsuperscript{−}.\textsuperscript{26} The inferior activity of the FeII\textsubscript{III}Cl(Corr\textsuperscript{•+}) may be understood within the context of the prevailing mechanistic understanding of H\textsubscript{2}O\textsubscript{2} dismutation at the metal cofactors, which include the Fe porphyrin centers of catalase enzymes.\textsuperscript{28–31} Dismutation is believed to initiate with the coordination of peroxide to the Fe\textsuperscript{(n)} center to form a Fe\textsuperscript{(n)}−OOH adduct. Subsequent addition of H\textsuperscript{+} and loss of water raises the formal oxidation state by two levels to furnish [Fe\textsuperscript{(n+2)}(=O)]. Reaction with another molecule of H\textsubscript{2}O\textsubscript{2} results in the release of O\textsubscript{2}, H\textsubscript{2}O, and regenerates the Fe\textsuperscript{(n+2)}. The presence of an acid–base moiety in the secondary coordination sphere of the metal, as provided in a hangman motif, facilitates the protonation of the hydroperoxy species and formation of the oxo as has been observed by stopped-flow spectroscopy.\textsuperscript{32,33} For the studies described here, the redox non–innocence of the corrole ligand provides a mechanism for redox levelling of the potential required for dismutation by avoiding a high energy [Fe\textsuperscript{V}(=O)] intermediate (Scheme 1). In the protonation of the initial hydroperoxyl group to form the oxo, only Fe\textsuperscript{IV} is needed with the participation of the corrole ligand. Conversely, with a Fe\textsuperscript{III}Cl(Corr\textsuperscript{•+}) pre–catalytic state, oxo formation must proceed through the Fe\textsuperscript{V} formal oxidation state even with the participation of the corrole. Considering the dramatically different reduction potentials for [Fe\textsuperscript{IV}(=O)] as compared to [Fe\textsuperscript{V}(=O)], driving dismutation from a Fe\textsuperscript{III}(Corr) resting state permits the thermodynamically costly [Fe\textsuperscript{V}(=O)] to be circumvented.
Scheme 2.1. Proposed catalytic cycle for [Fe\textsuperscript{III}–corr]–catalyzed H\textsubscript{2}O\textsubscript{2} dismutation.

2.3 Conclusion

The oxidation state of the pre–catalyst plays a substantial role in determining the catalytic activity of Fe–corrole catalyzed H\textsubscript{2}O\textsubscript{2} dismutation reactions, consistent with observations made for other Fe–corrole catalyzed reactions\textsuperscript{34}. Fe\textsuperscript{III}(Corr) is nearly twice as active towards H\textsubscript{2}O\textsubscript{2} dismutation as their related Fe\textsuperscript{III}Cl(Corr\textsuperscript{•+}) complexes. Presumably, this is due to their ability to avoid high energy Fe(=O)intermediates by relying on the redox chemistry of the corrole to redox level the metal by contributing an oxidizing equivalent to the overall dismutation transformation. Whereas the hangman effect is obscured from a Fe\textsuperscript{III}Cl(Corr\textsuperscript{•+}) resting state, it is prevalent for a Fe\textsuperscript{II}(Corr) resting state. Other systems that study the hangman effect have demonstrated that proton transfer from the hanging group can be extremely fast (>10\textsuperscript{6} s\textsuperscript{-1})\textsuperscript{35}. Such a facile
proton transfer to a peroxy intermediate is greatly beneficial to promoting dismutation, and hence is undoubtedly at the origin of the enhanced catalytic activity of the hangman system.

2.4 Experimental Section

**General Considerations.** $^1$H NMR spectra were recorded at ambient temperature on a Varian Mercury 300 MHz spectrometer. All $^1$H NMR spectra were referenced to deuterated benzene ($C_6D_6$) as an internal standard (measured values for $\delta$ are given in parts per million (ppm) and for $J$ in Hertz (Hz)). $^{19}$F NMR spectra were referenced to CFCl$_3$ in CDCl$_3$. Electrospray ionization mass spectra (ESI–MS) were obtained using a Bruker Daltonics APEXIV 4.7 T FT–ICR–MS instrument at the DCIF facility of MIT. UV–vis spectra were recorded at room temperature in 10 mm path length quartz cuvettes on compound dissolved in anhydrous THF or pentane on a Varian Cary 5000 UV–vis–NIR spectrophotometer employing the software Cary WinUV. In a glovebox, the quartz cuvette was filled with 3.0 mL of solvent. From a stock solution, Fe$^{III}$–corrole was added to the cuvette, which was sealed and removed from the glovebox.

THF (anhydrous), DMF (anhydrous), pyridine (anhydrous), methanol (anhydrous), diethyl ether (anhydrous), pentane (anhydrous), 30 wt % H$_2$O in H$_2$O and pyridine were reagent grade and were used as received. 4–Formyl–5–bromo–2,7–di–tert–butyl–9,9–dimethylxanthene,$^{37}$ 5–pentafluorophenyl–dipyrro–methane,$^{38}$ 5,10,15–tris(pentafluorophenyl)corrole,$^{39}$ and $^1$–py$^{40}$ were prepared as described in the literature. ESI–MS data was measured on corroles in argon–saturated EtOAc. The
procedure to measure H$_2$O$_2$ disproportionation is as follows. 1 μmol of the iron corrole was placed in an oven-dried vial containing magnetic stirbar and 1,5-dicyclohexyl-imidazole (6.0 mg, 26 μmol). Under an inert atmosphere, dry THF (1.5 mL) was added, and the vial was sealed with a septum and secured with a plastic zip-tie. A cannula needle was inserted into the vial and was purged thoroughly with argon. The cannula needle was removed and argon-saturated MeOH (0.5 mL) was added, followed by argon-saturated H$_2$O$_2$ (0.11 mL, 30% wt in H$_2$O, 1.0 mmol) at time = 0, the syringe plunger was retracted to 0.11 mL and removed. The increase in headspace volume due to the generation of O$_2$ was measured through insertion of one end of the cannula needle into a 25 mL graduated pipette, which had been filled with water, inverted and submerged in water. Volume was converted to moles with the ideal gas law. Turnover frequencies were calculated from the amount of O$_2$ evolved after 20 seconds.

**Synthesis.** 10–(4–(5-bromo–2,7-di–tert–butyl–9,9–dimethyl–xanthene)–5,15–bis(pentafluoro–phenyl)corrolatoiron(III) pyridine adduct (2–py). Following published procedures for Fe insertion into corroles,$^{40}$ 10–(4–(5–Bromo–2,7–di–tert–butyl–9,9–dimethyl–xanthenyl))–5,15–bis(pentafluorophenyl) corrole (20.0 mg, 19.4 μmol) was dissolved in dry pyridine (10 mL) in a 100 mL 3-necked round bottom flask. After thorough purging with argon, anhydrous FeCl$_2$ (40 mg, 0.31 mmol, 16 mole equiv.) was added under strong argon flow, and the solution was immediately refluxed in a pre-heated 125 °C oil bath. After 30 min the flask was removed from the oil bath and volatiles were removed in vacuo. The flask was transferred to a glovebox and the solids were filtered through a celite plug with Et$_2$O. The volatiles were removed in vacuo and the resulting solids were filtered through a celite plug with pentane. The volatiles were
removed in vacuo to afford 2-py as a dark red solid (21.3 mg, 94.6% yield). $^1$H NMR (300 MHz, C$_6$D$_6$, 20 °C): δ = 31.80 (br, py–H), 22.16 (br, py–H), -2.057 (corrole β–H, 2H), -59.79 (br, corrole β–H, 2H H), -65.58 (br, corrole β–H, 2H), -125.42 (br, corrole β–H, 2H). Hangman backbone $^1$H resonances unidentifiable. $^{19}$F NMR (300 MHz, C$_6$D$_6$, 20 °C): δ = -95.4 (ortho–F, 2F), -111.8 (ortho–F, 2F), -150.8 (para–F, 2F), -156.3 (meta–F, 2F), -156.9 (meta–F, 2F). M = C$_{54}$H$_{36}$BrF$_{10}$FeN$_4$O: 1081.1262, (M + pyridine): 1160.1684; Found for ESI–MS: ((M + H)$^+$ + pyridine): 1162.1630; ((M–Br)$^+$ + pyridine) = 1181.25. 

$\lambda_{\text{max,abs}}$/nm ($\varepsilon \times 10^{-3}$) (pentane) = 407 (24), 556 (8.1), 758 (1.4), $\lambda_{\text{max,abs}}$/nm ($\varepsilon \times 10^{-3}$) (THF) = 406 (24), 556 (8.5), 737 (1.7)


Following published procedures for Fe insertion into corroles, 40 10–(4–(5–hydroxycarbonyl–2,7–di–tert–butyl–9,9–dimethylxanthenyl))–5,15–bis(pentafluorophenyl)corrole (27.4 mg, 27.4 μmol) was dissolved in dry DMF (10 mL) in a 100 mL 3–necked round bottom flask. After purging with argon, anhydrous FeCl$_2$ (60 mg, 0.50 mmol, 20 equiv.) was added under strong argon flow. The solution was immediately placed in a pre–heated 150 °C oil bath and brought to reflux. After 30 min the flask was removed from the oil bath and volatiles were removed in vacuo. The flask was transferred to a glovebox and the solids were filtered through a celite plug with Et$_2$O. The volatiles were removed in vacuo and the resulting solids were filtered through a celite plug with pentane to afford 3–Et$_2$O as a dark red solid (29.5 mg, 96.0%). $^1$H NMR (300 MHz, C$_6$D$_6$, 20 °C): δ = 13.90 (br, corrole β–H, 2H), 9.72 (br, corrole β–H, 2H), -59.27, (br, corrole β–H, 2H), -112.8 (br, corrole β–H, 2H). Hangman backbone $^1$H
resonances unidentifiable. $^{19}$F NMR (300 MHz, C$_6$D$_6$, 20 °C): δ = -92.4 (ortho–F, 2F), -106.6 (ortho–F, 2F), -148.0 (para–F, 2F), -153.6 (meta–F, 2F), -154.3 (meta–F, 2F). M = C$_{55}$H$_{37}$F$_{10}$FeN$_4$O$_3$: 1047.2055, (M + Et$_2$O): 1121.2787; Found for ESI–MS: ((M – H) + Et$_2$O): 1120.28 λ$_{max,abs}$/nm (ε $\times 10^{-3}$) (THF) = 406 (31), 556 (11), 737 (1.9).

10–(4–(5–Bromo–2,7–di–tert–butyl–9,9–dimethylxanthenyl))–5,15–bis(pentafluorophenyl)corrolatoiron(III) chloride (2–Cl). Following the published procedure,$^{40}$ in a scintillation vial, 2–py (1.2 mg, 1.0 μmol) was dissolved in DCM and washed with 4% HCl in H$_2$O (10 mL). The organic layer was dried over Na$_2$SO$_4$ and evaporated to dryness.

10–(4–(5–Hydroxycarbonyl–2,7–di–tert–butyl–9,9–dimethylxanthenyl))–5,15–bis–(pentafluorophenyl)corrolatoiron(III) chloride (3–Cl). Following the published procedure,$^{40}$ 3–Et$_2$O (1.1 mg, 1.0 μmol) was placed in an oven dried scintillation vial and dissolved in DCM and washed with 4% HCl (10 mL) in H$_2$O. The organic layer was dried over Na$_2$SO$_4$ and evaporated to dryness.

2.5 References


Chapter 3 – Gram Scale Synthesis of Post-synthetically Modifiable Hangman porphyrins

*Portions of this chapter have been published:*


10.1002/cssc.201402242

3.1 Introduction

Ligand design for the purpose of controlling the secondary coordination sphere of a metal site is a popular strategy to enhance catalytic activity. The placement of a pendant acid/base moiety in the second coordination sphere of metallocycles affects ligand binding,\(^1\)–\(^3\) as well as on the catalytic transformations of peroxide dismutation,\(^4\)–\(^12\) \(\text{H}_2\) generation,\(^13,14\) \(\text{H}_2\text{O}\) oxidation,\(^15,16\) and \(\text{O}_2\) reduction.\(^16\)–\(^22\) The concept of using the secondary coordination sphere to influence activity of redox reactions involving protons has subsequently been generalized to a variety of metal centers and secondary coordination spheres.\(^23\) The strategy has been especially important for promoting the hydrogen evolution reaction (HER), which involves coupling the reduction of a metal center to proton transfer.\(^24\)–\(^29\) In our hangman approach, xanthene has been a preferred scaffold for the assembly of macrocycles such as porphyrins or salens with a pendant acid/base group, which has often been a carboxylic acid. We have sought to expand the hangman methodology to include more sterically imposing pendant groups that not only assist in proton transfer, but also shield the metal center from bulk solution and effectively create a substrate binding pocket. In order to accommodate larger hanging
groups, we have turned our attention to the dibenzofuran scaffold. The dibenzofuran precursor that is needed for macrocyclic construction can be synthesized on the gram scale from inexpensive starting materials. Whereas this dibenzofuran spacer has been employed in the construction of Pacman complexes,\textsuperscript{30,31} the use of dibenzofuran as a platform for appending acid/base functionalities above a single transition metal complex has been largely unexplored and limited to hanging carboxylic acids.\textsuperscript{4,32} Building on our experience with hangman ligands containing carboxylic acids, we chose to pursue a modification strategy to post-synthetically attach hanging groups via carboxamide formation. This chapter details the high yielding synthesis of greater than one gram of hanging porphyrin dibenzofuran with a pendant carboxylic acid (HPD–CO$_2$H) using a modified Lindsey method\textsuperscript{33} and 3,4,5-trimethoxybenzaldehyde (TMB) as the second aldehyde. HPD–CO$_2$H can be cleanly isolated with minimal purification and post-synthetically modified through carboxamide formation with any primary amine, allowing for rapid generation of a library of hangman porphyrins with systematic variation of proton donor properties and/or steric hindrance.

3.2 Results and Discussion

3.2.1 Scaffold Synthesis

The synthesis of HPD–CO$_2$H requires an asymmetric dibenzofuran containing an aldehyde functionality and a pendant methyl ester, which can be subsequently hydrolysed after porphyrin formation to yield the free carboxylic acid. The synthesis of methyl 6-formyl-dibenzofuran-4-carboxylate (4) is carried out in 4 steps on the multigram scale. First, dibenzofuran was selectively deprotonated at the 4 and 6
positions using the combination of \(n\)-butyl lithium (\(n\)-BuLi) and tetramethylethlenediamine (TMEDA) in refluxing petroleum ether. The resulting lithium salt was quenched with \(\text{CO}_2\) at \(-78^\circ\text{C}\), yielding 4,6-dibenzofuran dicarboxylic acid (1) after acidic workup. Impure 1 was often used directly in the next step after removal of excess water \textit{in vacuo}. 1 was converted to dimethyl-4,6-dibenzofuran-dicarboxylate (2) by acid-catalysed esterification in refluxing methanol (MeOH) with trimethyl orthoformate as a dehydrating agent (Scheme 1). 2 is easily isolated by precipitation upon addition of excess water followed by drying \textit{in vacuo}. Column chromatography yields analytically pure 2. Notwithstanding, it was found that impure 2 could be used in the following step after sufficient drying \textit{in vacuo}.

![Scheme 3.1. Synthesis of 2 from dibenzofuran](image)

Following published methods,34 selective reduction of 2 was accomplished by treatment with sodium borohydride (NaBH₄) in a refluxing tetrahydrofuran (THF)/MeOH solution to yield 6-(hydroxy-methyl)dibenzofuran-4-carboxylate methyl ester (3). Subsequent oxidation of 3 with TEMPO and bis(acetoxy)iodosylbenzene in dichloromethane (DCM) gave the desired porphyrin precursor (4) in 38% overall yield starting from dibenzofuran (Scheme 2).
Scheme 3.2. Synthesis of hangman porphyrin precursor 4 by the statistical reduction and subsequent oxidation of 2.

In an attempt to synthesize the desired asymmetric aldehyde in three steps, 2 was treated with 1 equivalent of DIBAL–H. Curiously, regardless of solvent, reaction time, or temperature, only starting material was recovered. An additional equivalent of DIBAL–H resulted in a 1:1 mixture of 2 and fully reduced dialcohol, 4,6-di(hydroxymethyl)dibenzofuran (5) (Scheme 3).

Scheme 3.3. Attempted selective reduction of 2 by DIBAL–H.

The reason for this behavior is unknown, but our best hypothesis posits that the di-methylester 2 may serve as a ligand for DIBAL–H, forming a 6-coordinate Al complex that is incapable of transferring a hydride to the ester. Further equivalents of DIBAL–H reduce one ester and activate the bound DIBAL–H toward reducing the other ester on
one dibenzofuran. Loss of 2 equivalents of Al\textsubscript{2}Bu\textsubscript{2}OMe would generate a di-aldehyde, which is much more prone to hydride reduction than esters.

### 3.2.2 Porphyrin Construction

Porphyrons are notoriously difficult to synthesize on a large scale, especially those featuring multiple meso-substituents. Whereas all previous reported syntheses of hanging dibenzofuran ligands have employed Pd-catalysed cross coupling, we decided to attempt statistical porphyrin formation with 4 because the product of Pd cross-coupling reactions retain minute amounts of Pd that is capable of driving the HER catalytically.\textsuperscript{35} Our most common means of hangman porphyrin synthesis employs the Lindsey method in a highly dilute solution containing excess pyrrole and non-hangman aldehyde in order to maximize the yield of hangman porphyrin.\textsuperscript{36,37} Following this published strategy, treatment of a 0.53 mM solution of 4, containing an overall 1:15:16 ratio of 4:TMB:pyrrole, with BF\textsubscript{3}•OEt\textsubscript{2} resulted in an unusually high combined yield of tetrakis(3,4,5-trimethoxyphenyl)porphyrin (A\textsubscript{4}) and hanging porphyrin dibenzofuran methyl ester (A\textsubscript{3}B, HPD–CO\textsubscript{2}Me) with few other byproducts. Given the surprising ability of TMB and 4 to form porphyrin rings in a respectably selective fashion, statistical synthesis was attempted by subjecting a 2.1 mM solution of 4 in chloroform (CHCl\textsubscript{3}), with a 1:7:8 ratio of 4:TMB:pyrrole, to the Lindsey method (Scheme 4). The higher reagent concentrations resulted in more non-porphyrinic byproducts, but still gave remarkably high yields of porphyrin. Notably, this method gives relatively poor yields of porphyrin when other aldehydes, such as pentafluorobenzaldehyde (10%),
mesitylaldehyde (12%) or 2,4,6-trimethoxybenzaldehyde (7%), were used in the same ratios in conjunction with 4.

**HPD–CO₂Me** is difficult to separate from other porphyrinic byproducts due to similar elution properties, but hangman porphyrin could be isolated cleanly by carrying the entire porphyrin mixture directly through to the next step and hydrolysing the hanging methyl ester (Scheme 4). After filtering off a majority of the pyrrolic byproducts, microwave-assisted basic hydrolysis³⁷ converted **HPD–CO₂Me** to the corresponding **HPD–CO₂H**, which is easily separated from unreacted **HPD–CO₂Me** and **A₄** porphyrin on a silica column. Starting with a 2.1 mM solution of 4 in 1.5 L of CHCl₃, **HPD–CO₂H** was isolated in 33% over two steps on a gram scale. The yield of **HPD–CO₂H** increased to 41% if performed on a smaller scale in 560 mL of CHCl₃, keeping all reagent concentrations the same.

**Scheme 3.4.** Formation of the porphyrin from pyrrole, TMB, and 4.

In addition to **HPD–CO₂H**, 1.64 g (30% yield with respect to total available TMB) of **A₄** was isolated and identified by ¹H NMR. Even though it is a byproduct, the yield of **A₄** is similar to its synthesis by published methods.³⁸,³⁹
3.2.3 Hanging Group Attachment

The presence of 3,4,5-trimethoxyphenyl meso-substituents on HPD–CO₂H precludes the use of thionyl chloride in carboxamide formation.⁴⁰,⁴¹ Instead, a combination of p-toluenesulfonyl chloride (TsCl) and N,N-dimethylaminopyridine (DMAP) was employed to prepare the acyl transfer reagent. Treatment of HPD–CO₂H with 2–5 equiv. of TsCl and DMAP followed by addition of excess aryl amine gave the functionalized hangman porphyrins, which were easily purified and isolated in good yield (Scheme 5).

![Diagram of hangman porphyrin structure]

**Scheme 3.5.** Post-synthetic modification of hanging group with isolated yields for each hangman porphyrin derivative.

<table>
<thead>
<tr>
<th>R'</th>
<th>Cmpd</th>
<th>% Yield</th>
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Crystals suitable for X-ray diffraction studies were grown from slow evaporation of an acetonitrile (CH$_3$CN) solution of HPD-Ph. The porphyrin crystallized as a dimer and displayed the expected connectivity (Figure 1). The center of the hanging phenyl ring is positioned 4.474(2) Å above the mean porphyrin plane. The porphyrin ring is slightly saddled, which has the effect of tilting the hangman scaffold inward and decreasing the distance between the hanging group and the porphyrin plane. The presence of an intramolecular NH–O hydrogen bond is apparent between the carboxamide NH and the central dibenzofuran O, with an N–O distance of 2.791(3) Å and N–H–O bond angle of 141.90(1)°. This hydrogen bond may provide an anchor to prevent rotation around the C–C(O)NHR bond and maintain the desired second coordination sphere.
3.3 Conclusion

Hanging dibenzofuran porphyrins with 3,4,5-trimethoxyphenyl meso-substituents can be synthesized from inexpensive starting materials and isolated on a gram scale with minimal purification. Using these hangman porphyrins as ligands for transition metals allows one to control the nature of the secondary coordination sphere. Subsequent functionalization of HPD–CO$_2$H allows for the installation of any pendant group with tuneable steric, electronic, and/or proton donating properties. The origin of this unusually high yield for a porphyrin compound is presumably due to similar electronic properties of TMB and dibenzofuran aldehyde.
3.4 Experimental Section

**General Considerations.** $^1$H NMR spectra were recorded at ambient temperature on a Varian Mercury 500 MHz spectrometer. $^{13}$C NMR spectra were collected at ambient temperature on a Varian Inova 400 MHz spectrometer. All spectra were referenced to trace protonated chloroform (7.26 ppm ($^1$H), 77.16 ppm($^{13}$C)), acetonitrile (1.94 ppm), or dimethylsulfoxide (2.5 ppm) as an internal standard (measured values for $\delta$ are given in parts per million (ppm) and for $J$ in Hertz (Hz)). Elemental analysis was performed by Midwest Microlab Laboratories, IN. Electrospray ionization (ESI) mass spectra were obtained using a Bruker micrOTOF-QII. Absorption spectral measurements were made on CH$_3$CN solutions of each porphyrin using a Cary 5000 UV-vis-NIR spectrometer from Varian employing the software Cary WinUV. Quartz cells with a 10 mm path length were used.

THF, MeOH, pentane, CH$_3$CN, and DCM were purified by passage through alumina.$^{43}$ The following chemicals were used as received: ethyl acetate (EtOAc), CHCl$_3$, DMAP, TsCl, NaBH$_4$, TMEDA, sodium chloride (NaCl), sodium bicarbonate (NaHCO$_3$), 2,3-dichloro-5,6-dicyano-1,4-benzooquinone (DDQ), petroleum ether, $n$-BuLi, pyrrole, trimethylorthoformate, 3,4,5-trimethoxybenzaldehyde, 2,6-diaminopyridine, aniline, 2-aminopyridine, 3-aminopyridine, dibenzofuran, sulfuric acid from Sigma Aldrich; chloroform–d (CDCl$_3$, acetonitrile–d (CD$_3$CN), dimethylsulfoxide–d (DMSO–d$_6$) from Cambridge Isotope Laboratories; 5-aminopyrimidine from Matrix Scientific; 3-aminobenzenesulfonic acid, 2-aminobenzenesulfonic acid from TCI. 2-aminopyrimidine, $N,N$-dimethylamino–1,3-phenylenediamine dihydrochloride from Alfa Aesar.
X-Ray Crystallography. Data from a crystal mounted on a diffractometer was collected at 100 K. The intensities of the reflections were collected by means of a Bruker APEX II CCD diffractometer (MoKα radiation, λ = 0.71073 Å), and equipped with an Oxford Cryosystems nitrogen flow apparatus. The collection method involved 0.5° scans in ω at 28° in 2θ. Data integration down to 0.82 Å resolution was carried out using SAINT V7.46 A with reflection spot size optimization. Absorption corrections were made with the program SADABS. The structure was solved by the direct methods procedure and refined by least-squares methods again F² using SHELXS–97 and SHELXL–97 with OLEX 2 interface. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table 1, geometric parameters are shown in Table 2, and hydrogen–bond parameters are listed in Table 3. Figure 1 was produced with Olex2 program.

Synthesis. 4,6-dibenzofuran dicarboxylic acid (1) Dibenzofuran (10.0 g, 59.5 mmol) was dissolved in 250 mL petroleum ether in an oven–dried, 500 mL Schlenk flask. TMEDA (30 mL, 23.3 g, 200 mmol, 3.4 equiv.) and n-BuLi (2.5 M in hexanes, 75 mL, 187 mmol, 3.2 equiv.) were added to the solution under N₂ via syringe, a reflux condenser was affixed and the solution was heated to reflux for 30 min until solids were observed and the solution turned yellow. The solution was cooled and placed in a dry ice/acetone bath for 20 min to ensure that the solution cooled to the temperature of the bath, as unwanted byproducts formed if the solution was exposed to CO₂ without being allowed to cool. Anaerobic grade CO₂ gas was blown through a CaSO₄ drying column and over the
vigorously stirring solution for 2 h at −78 °C. The solution was quenched with excess HCl/H₂O and the solids were collected by vacuum filtration, washed with water, and dried in vacuo overnight and carried on in the synthesis yielding 15.6 grams of tan solid. Crude ¹H NMR (DMSO–d₆) showed that desired product was the dominant product.

**Dimethyl–4,6–dibenzofuran dicarboxylate (2).** Impure 1 (15.6 g) was dissolved in 200 mL MeOH in an oven–dried, 500 mL Schlenk flask under an atmosphere of N₂. Sulfuric acid (8 mL) and trimethylorthoformate (8 mL) were added via syringe and the solution was heated to reflux for 4 h. The solution was allowed to cool and 150 mL sat. NaHCO₃/H₂O was added, causing precipitation of the product, which was collected by vacuum filtration. The solids were washed with water and dried in vacuo, yielding 13.0 g of tan material. The product was suitably pure by NMR standards and could be used in the next step without further purification. Analytically pure 2 could be isolated after elution through a silica column with 1:9 EtOAc:DCM. Yield = 13.0 g (45.8 mmol) (77% over two steps). ¹H NMR (500 MHz, CDCl₃, δ): 4.11 (s, 3H, OCH₃), 7.47 (t, 2H, ArH, J = 7.7 Hz), 8.18 (d, 2H, ArH, J = 7.7 Hz), 8.18 (d, 2H, ArH, J = 7.7 Hz). ¹³C NMR (400 MHz, CDCl₃, δ): 52.6, 115.7, 123.1, 124.9, 125.4, 130.1, 155.0, 165.2. Anal. Calcd (Found) for C₁₆H₁₂O₅: C, 67.60 (67.67); H, 4.25 (4.02).

**6–(hydroxymethyl)dibenzofuran–4–carboxylate methyl ester (3).** Under N₂, 2 (5.0 g, 17.6 mmol) was dissolved in a 10:1 mixture of dry THF:MeOH (250 mL:25 mL) in an oven–dried 500 mL Schlenk flask. NaBH₄ (900 mg, 24.6 mmol, 1.4 equiv.) was added at once to the stirring mixture, a condenser was affixed, and the flask was lowered into a hot oil bath. The reaction was allowed to proceed for exactly 30 min after refluxing was observed. The flask was removed from the oil bath and excess HCl/H₂O
was added, taking care to avoid overflow from the generated H$_2$ gas. The organic solvent was removed \textit{in vacuo} and the solids were transferred to a separatory funnel containing ethyl acetate. The organic layer was washed with H$_2$O/HCl (1 × 100 mL), H$_2$O (1 × 100 mL), and brine (1 × 100 mL), before being dried over Na$_2$SO$_4$. The volatiles were removed \textit{in vacuo}, the resulting solids were dissolved in minimal DCM and loaded onto a 50 g Biotage column and eluted with 100% DCM which was increased to 1:1 DCM:EtOAc over 10 column volumes. Unreacted 2 eluted first, followed by 3 (at 30:70 DCM:EtOAc), and 4,6-di(hydroxymethyl)-dibenzofuran (5) could be collected from the top of the column as a white paste. Yield (of 3) = 2.57 g (57%). $^1$H NMR (500 MHz, CDCl$_3$, δ): 2.44 (s, 1H, OH), 4.04 (s, 3H, OCH$_3$), 5.16 (s, 2H, ArCH$_2$OH), 7.38 (t, 1H, Ar$H$, J = 7.5 Hz), 7.42 (t, 1H, Ar$H$, J = 7.7 Hz), 7.54 (d, 1H, Ar$H$, J = 7.3 Hz), 7.90 (d, 1H, Ar$H$, J = 7.7 Hz), 8.11 (dd, 1H, Ar$H$, J = 7.7 Hz, 1.3 Hz), 8.14 (d, 1H, Ar$H$, J = 7.7 Hz, 1.3 Hz) $^{13}$C NMR (400 MHz, CDCl$_3$, δ): 52.5, 60.2, 115.1, 119.8, 122.5, 123.0, 123.4, 125.5, 125.6, 126.0, 126.9, 129.2, 154.1, 154.8, 165.9. Anal. Calcd (Found) for C$_{15}$H$_{12}$O$_4$: C, 70.31 (70.22); H, 4.72 (4.75).

**Methyl 6-formyl-4-dibenzofurancarboxylate (4).** 3 (2.25 g, 8.79 mmol) was dissolved in DCM under N$_2$. TEMPO and BAIB were added and the solution stirred for 2 h. The volatiles (including TEMPO) were removed \textit{in vacuo}. The solids were dissolved in dry DCM and loaded onto a 50 g KP-SIL Biotage column and eluted with DCM at first, which was changed to 4:6 EtOAc:DCM over 7 column volumes. Yield (of 4) = 2.05 g (91.8%). $^1$H NMR (500 MHz, CDCl$_3$, δ): 4.09 (s, 3H, OCH$_3$), 7.50 (t, 1H, Ar$H$, J = 7.9 Hz), 7.53 (t, 1H, Ar$H$, J = 7.7 Hz), 8.04 (d, 1H, Ar$H$, J = 7.5 Hz), 8.20 (d, 2H (accidental overlap), Ar$H$, J = 7.5 Hz), 8.23 (d, 1H, Ar$H$, J = 7.7 Hz), 10.77 (s, 1H, C(O)H). $^{13}$C NMR (400 MHz,
CDCl₃, δ): 52.6, 115.9, 121.4, 123.4, 123.6, 124.7, 124.9, 125.6, 126.7, 127.0, 130.3, 155.2, 156.6, 165.0, 187.8. Anal. Calcd (Found) for C₁₅H₁₀O₄: C, 70.86 (70.70); H, 3.96 (4.02).

5–{(dibenzo[furan–6–carboxylic acid])–10,15,20–tri(3,4,5–trimethoxyphenyl)–porphyrin (HPD–CO₂H)}. 1.5 L of CHCl₃ was added to an oven–dried 2 L flask and sparged with dry N₂ for 45 min. The reaction flask was covered in tin foil. Pyrrole (1.77 mL, 1.71 g, 25.5 mmol) was filtered through basic alumina to remove any colored decomposition products and added to the stirring CHCl₃, sparging continued for another 45 min. 3,4,5–trimethoxybenzaldehyde (4.33 g, 22 mmol) and 4 (800 mg, 3.14 mmol) were added and sparging continued for another 45 min. The sparging needle was raised above the solution and boron trifluoride etherate (BF₃•OEt₂) (270 µL, 2.1 mmol, 0.6 equiv.) was added dropwise, the solution slowly turned pink. After 1 hour, the reaction was quenched with DDQ (4.3 g, 19 mol, 6.0 equiv.) and the solution stirred for 30 minutes. 2 mL of NEt₃ was added and the solution stirred for 15 more minutes before the volatiles were removed under reduced pressure. The solids were dissolved in DCM and transferred to a separatory funnel where the organic layer was washed with 1 M NaOH/H₂O (3 × 100 mL). The solution was filtered through Na₂SO₄, concentrated under reduced pressure, and loaded onto a silica column. 1:9 EtOAc:DCM was run through the silica column, all red fluorescence was collected and the volatiles were removed. The resulting solids were dissolved in 35 mL THF, divided into two portions, and each placed in a separate 35 mL microwave tube, each containing 10 mL 6 M NaOH/H₂O. The solutions were microwaved at 75 °C for 1.5 h. The contents of the tube were transferred to a separatory funnel containing H₂O and EtOAc. The organic layer was washed with 1 M HCl/H₂O until a faint green color (protonated porphyrin) was observed in the organic
layer, and then washed with H$_2$O (1 × 100 mL), and brine (1 × 100 mL), dried over Na$_2$SO$_4$, and dried under reduced pressure. The solids were dissolved in DCM and loaded onto a silica column (packed with DCM). 1:9 EtOAc:DCM removed the A$_4$ porphyrin. 1:9 MeOH:EtOAc removed HPD–CO$_2$H. After the solvent had been removed from the fraction containing HPD–CO$_2$H, the solids were dissolved in DCM, filtered through filter paper and dried overnight under reduced pressure. The resulting solids were sonicated and washed in pentane and dried under vacuum at 80 °C. Yield (HPD–CO$_2$H) = 1.06 g (33%). $^1$H NMR (500 MHz, CDCl$_3$, δ): –2.69 (s, 2H, NH), 3.90 (s, 6H, OCH$_3$), 3.95 (s, 6H, OCH$_3$), 3.97 (s, 3H, OCH$_3$), 3.99 (s, 3H, OCH$_3$), 4.14 (s, 6H, OCH$_3$), 4.19 (s, 3H, OCH$_3$), 7.37 (t, 1H, ArH, J = 7.8 Hz), 7.45 (s, 2H, 10,20–meso–ArH), 7.47 (s, 1H, 15–meso–ArH), 7.48 (s, 2H, 10,20–meso–ArH), 7.50 (s, 1H, 15–meso–ArH), 7.80 (d, 1H, ArH, J = 7.2 Hz), 7.83 (t, 1H, ArH, J = 7.7 Hz), 8.27 (d, 1H, ArH, J = 7.3 Hz), 8.35 (d, 1H, ArH, J = 7.8 Hz), 8.39 (d, 1H, ArH, J = 7.7 Hz), 8.74 (d, 2H, pyrrole–βH, J = 4.6 Hz), 8.90 (d, 2H, pyrrole–βH, J = 4.7 Hz), 8.98 (m, 4H, pyrrole–βH). $^{13}$C NMR (400 MHz, CDCl$_3$, δ): 56.5, 56.5, 61.4, 61.5, 112.7, 112.9, 113.0, 114.4, 120.3, 120.6, 120.7, 121.0, 121.1, 122.5, 122.7, 122.9, 123.0, 123.0, 123.2, 126.0, 126.5, 126.9, 129.9, 130.3, 131.4 (br), 134.8, 137.6, 137.7, 137.8, 137.9, 138.0, 151.4, 151.5, 151.5, 155.0, 156.7, 165.7. Anal. Calcd (Found) for C$_{60}$H$_{50}$N$_4$O$_{12}$: C, 70.72 (70.69); H: 4.95 (5.39); N: 5.50 (5.39). Mass spectrometry (m/z) 1019.3542. 

$\lambda_{\text{max,abs}}$/nm ($\varepsilon$ (M$^{-1}$ cm$^{-1}$)) (CH$_3$CN) = 419 (3.0 × 10$^5$), 513 (1.6 × 10$^4$), 548 (6.4 × 10$^3$), 588 (5.3 × 10$^3$), 645 (3.1 × 10$^3$).

**General Procedure for Carboxamide Formation.** DMAP and TsCl were dissolved in DCM under N$_2$. Solid HPD–CO$_2$H (1 equiv.) was sprinkled into the solution over the course of 5 min. The solution stirred for 2 h before the amine was added at once
and the solution stirred overnight under N₂. In the morning, the volatiles were removed and the solids were dissolved in EtOAc and transferred to a separatory funnel. The organic layer was washed with 1 M HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL), before being filtered through Na₂SO₄ and dried in vacuo. The solids were then purified by column chromatography, the major red fluorescent band was collected, the volatiles were removed, the solids were dissolved in benzene and filtered through filter paper, the volatiles were removed and the solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo.

5–(6–(dibenzofuran–4–N–(phenyl)carboxamide))–10,15,20-tri(3,4,5–trimethoxy–phenyl)porphyrin (HPD–Ph). HPD–CO₂H (100 mg, 98.2 µmol) was added to a stirring DCM solution of TsCl (57 mg, 300 µmol, 3 equiv.) and DMAP (72 mg, 600 µmol, 6 equiv.) and was allowed to stir under N₂ for 2 h. Aniline (0.45 mL, 5.0 mmol, 50 equiv.) was added via syringe and the solution stirred overnight. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL) before being dried over Na₂SO₄, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt₃) and loaded onto a silica column packed with DCM (2% NEt₃), and eluted with DCM (2% NEt₃). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et₃NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo. Yield = 80.2 mg (73 %). ¹H NMR (500 MHz, CDCl₃, δ): −2.53 (s, 2H, NH), 3.67 (s, 6H, OCH₃), 3.98 (s, 6H,
OCH₃), 3.99 (s, 3H, OCH₃), 4.04 (s, 3H, OCH₃), 4.13 (s, 6H, OCH₃), 4.21 (s, 3H, OCH₃), 5.06 (t, 2H, hanging–PhH, J = 7.6 Hz), 5.17 (d, 2H, hanging–PhH, J = 7.3 Hz), 6.01 (t, 1H, hanging–PhH, J = 7.3 Hz), 7.12 (br s, 2H, meso–ArH), 7.49 (s, 2H, meso–ArH), 7.49 (s, 1H, meso–ArH), 7.59 (s, 1H, meso–ArH), 7.60 (t, 1H, ArH, J = 7.9 Hz), 7.98 (t, 1H, ArH, J = 7.6 Hz), 8.29 (dd, 1H, ArH, J = 7.6 Hz, 1.2 Hz), 8.38 (dd, 1H, ArH, J = 8.0 Hz, 1.2 Hz), 8.47 (s, 1H, NH), 8.48 (dd, 1H, ArH, J = 7.1 Hz, 1.2 Hz), 8.50 (dd, 1H, ArH, J = 7.4 Hz, 1.0 Hz), 8.92 (m, 4H, pyrrole–βH), 8.98 (d, 2H, pyrrole–βH, J = 4.2 Hz), 9.04 (d, 2H, pyrrole–βH, J = 4.2 Hz). Mass spectrometry [M+H]+ (m/z) Calcd (Found): 1094.40 (1094.3852). λmax,abs/nm (ε (M⁻¹ cm⁻¹)) (CH₃CN) = 420 (1.8 × 10⁵), 514 (8.8 × 10³), 550 (3.8 × 10³), 589 (2.8 × 10³), 645 (1.6 × 10³).

5-(6-(dibenzofuran–4–N-(pyridin–2–yl)carboxamide))–10,15,20-tri(3,4,5-trimethoxy–phenyl)porphyrin (HPD–2AP). HPD–CO₂H (100 mg, 98.2 µmol) was added to a stirring, 100 mL DCM solution of TsCl (38 mg, 200 µmol, 2 equiv.) and DMAP (48 mg, 400 µmol, 4 equiv.) and was allowed to stir under N₂ for 2 h. 2–aminopyridine (500 mg, 5.2 mmol, 50 equiv.) was added and the solution stirred overnight under N₂. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL) before being dried over Na₂SO₄, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt₃) and loaded onto a silica column packed with DCM (2% NEt₃), and eluted with DCM (2% NEt₃). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et₃NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of
pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo.

Yield = 72.4 mg (67 %). ¹H NMR (500 MHz, CDCl₃, δ): −2.56 (s, 2H, NH), 3.71 (s, 6H, OCH₃), 3.98 (s, 6H, OCH₃), 3.99 (s, 3H, OCH₃), 4.05 (s, 3H, OCH₃), 4.13 (s, 6H, OCH₃), 4.21 (s, 3H, OCH₃), 4.30 (d, 1H, hanging–pyH, J = 3.8 Hz), 5.84 (ddd, 1H, hanging–pyH, J = 7.3 Hz, 4.9 Hz, 0.76 Hz), 6.95 (d, 1H, meso–ArH, J = 8.0, 1.8 Hz), 7.16 (br s, 2H, meso–ArH), 7.49 (d, 1H, meso–ArH, J = 1.8 Hz), 7.51 (d, 2H, meso–ArH, J = 1.7 Hz), 7.61 (d, 1H, meso–ArH, J = 1.8 Hz), 7.62 (t, 1H, ArH, J = 7.6 Hz), 7.62 (d, 1H, hanging–pyH, J = 8.0 Hz), 7.98 (t, 1H, ArH, J = 7.5 Hz), 8.29 (dd, 1H, ArH, J = 7.6 Hz, 1.2 Hz), 8.41 (dd, 1H, ArH, J = 7.8 Hz, 1.3 Hz), 8.48 (dd, 1H, ArH, J = 7.9 Hz, 1.1 Hz), 8.49 (dd, 1H, ArH, J = 7.4 Hz, 1.0 Hz), 8.90 (m, 4H, pyrrole–βH), 8.98 (s, 1H, NH), 8.98 (d, 2H, pyrrole–βH, J = 5.8 Hz), 9.02 (d, 2H, pyrrole–βH, J = 5.8 Hz). Mass spectrometry [M+H]⁺ (m/z) Calcd (Found): 1095.39 (1095.3923). \( \lambda_{\text{max,abs}} \) (nm (ε (M⁻¹ cm⁻¹)) (CH₃CN) = 421 (2.6 × 10⁵), 516 (1.4 × 10⁴), 551 (6.3 × 10³), 589 (4.9 × 10³), 645 (2.9 × 10³).

5-(6–(dibenzofuran–4–N–(pyridin–3–yl)carboxamide))–10,15,20-tri(3,4,5-trimethoxy–phenyl)porphyrin (HPD–3AP). HPD–CO₂H (100 mg, 98.2 µmol) was added to a stirring, 100 mL DCM solution of TsCl (57 mg, 300 µmol, 3 equiv.) and DMAP (72 mg, 600 µmol, 6 equiv.) and was allowed to stir under N₂ for 2 h. 3–aminopyridine (500 mg, 5.2 mmol, 50 equiv.) was placed in a vial, which was sealed with a septum and purged with N₂ for 30 min. 10 mL of dry DCM was added, mixed thoroughly and removed again with dissolved 5–aminopyrimidine. The 5–aminopyrimidine solution was then added and the solution stirred overnight under N₂. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 48
100 mL) before being dried over Na₂SO₄, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt₃) and loaded onto a silica column packed with DCM (2% NEt₃), and eluted with DCM (2% NEt₃). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et₃NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo. Yield = 88.5 mg (82 %).

1H NMR (500 MHz, CDCl₃, δ): –2.57 (s, 2H, NH), 3.73 (s, 6H, OCH₃), 3.97 (s, 6H, OCH₃), 3.98 (s, 3H, OCH₃), 4.04 (s, 3H, OCH₃), 4.13 (s, 6H, OCH₃), 4.20 (s, 3H, OCH₃), 4.31 (dd, 1H, hanging-pyH, J = 7.9 Hz, 3.9 Hz), 7.19 (s, 2H, meso–ArH), 7.37 (d, 1H, hanging–pyH, J = 5.2 Hz), 7.47 (s, 2H, meso–ArH), 7.47 (s, 1H, meso–ArH), 7.58 (d, 1H, meso–ArH, J = 1.5 Hz), 7.62 (t, 1H, ArH, J = 7.6 Hz), 7.98 (s, 1H, hanging–pyH), 7.99 (t, 1H, ArH, J = 7.5 Hz), 8.28 (d, 1H, ArH, J = 7.8 Hz), 8.40 (br s, 1H, hanging–pyH), 8.41 (d, 1H, ArH, J = 7.8 Hz, 1.3 Hz), 8.48 (d, 2H, ArH, J = 7.5 Hz), 8.93 (m, 4H, pyrrole–βH), 8.98 (d, 2H, pyrrole–βH, J = 4.0 Hz), 9.03 (s, 1H, NH), 9.03 (d, 2H, pyrrole–βH, J = 3.9 Hz). Mass spectrometry [M+H]+ (m/z) Calcd (Found): 1095.39 (1095.3946). λmax,abs/nm (ε (M⁻¹ cm⁻¹)) (CH₃CN) = 420 (3.1 × 10⁵), 515 (1.4 × 10⁴), 550 (6.1 × 10³), 590 (4.7 × 10³), 646 (2.9 × 10³).

5–(6–(dibenzofuran–4–N–(pyrimidin–2–yl)carboxamide))–10,15,20-tri(3,4,5–tri–methoxyphenyl)porphyrin (HPD–2APym). HPD–CO₂H (188 mg, 185 µmol) was added to a stirring DCM solution of TsCl (176 mg, 923 µmol, 5 equiv.) and DMAP (225 mg, 1.85 mmol, 10 equiv.) and was allowed to stir under N₂ for 2 h. 2–aminopyrimidine (350 mg, 3.69 mmol, 20 equiv.) was added and the solution stirred overnight under N₂. The volatiles were removed and the solids were dissolved in EtOAc
and transferred to the separatory funnel. The organic layer was washed with HCl/H2O (2 × 100 mL), H2O (1 × 100 mL), and brine (1 × 100 mL) before being dried over Na2SO4, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt3) and loaded onto a silica column packed with DCM (2% NEt3), and eluted with DCM (2% NEt3). The first porphyrinic band to elute was determined to be an undesired product. The second major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et3NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo. Yield = 130 mg (63 %). 1H NMR (500 MHz, CDCl3, δ): -2.60 (s, 2H, NH), 3.78 (s, 6H, OCH3), 3.97 (s, 6H, OCH3), 4.00 (s, 3H, OCH3), 4.05 (s, 3H, OCH3), 4.14 (s, 6H, OCH3), 4.21 (s, 3H, OCH3), 5.78 (t, 1H, hanging–pymH, J = 4.9 Hz), 6.15 (d, 2H, hanging–pymH, J = 4.9 Hz), 7.19 (s, 2H, meso–ArH), 7.48 (d, 2H, meso–ArH, J = 1.5 Hz), 7.51 (d, 1H, meso–ArH, J = 1.5 Hz), 7.58 (d, 1H, meso–ArH, J = 1.6 Hz), 7.60 (t, 1H, ArH, J = 7.7 Hz), 7.99 (t, 1H, ArH, J = 7.8 Hz), 8.32 (dd, 1H, ArH, J = 7.6 Hz, 1.2 Hz), 8.40 (dd, 1H, ArH, J = 7.9 Hz, 1.2 Hz), 8.48 (dd, 1H, ArH, J = 7.9 Hz), 8.53 (dd, 1H, ArH, J = 7.2 Hz, 1.1 Hz), 8.90 (d, 2H, pyrrole–βH, J = 4.7 Hz), 8.92 (d, 2H, pyrrole–βH, J = 4.6 Hz), 8.99 (d, 2H, pyrrole–βH, J = 4.1 Hz), 9.03 (d, 2H, pyrrole–βH, J = 4.1 Hz), 9.04 (s, 1H, NH). Mass spectrometry [M+H]+ (m/z) Calcd (Found): 1096.39 (1096.3802). \( \lambda_{\text{max,abs}}/\text{nm} \) (ε (M⁻¹ cm⁻¹)) (CH3CN) = 420 (4.7 × 10⁵), 515 (2.3 × 10⁴), 551 (9.2 × 10³), 590 (7.4 × 10³), 645 (4.5 × 10³).

5-((6-((dibenzofuran-4-4-(pyrimidin-5-yl)carboxamide))-10,15,20-tri(3,4,5-tri-methoxyphenyl)porphyrin (HPD-5APym). HPD-CO₂H (100 mg, 98.2
µmol) was added to a stirring, 100 mL DCM solution of TsCl (57mg, 300 µmol, 3 equiv.) and DMAP (72 mg, 600 µmol, 6 equiv.) and was allowed to stir under N₂ for 2 h. 5-aminopyrimidine (95 mg, 1.0 mmol, 10 equiv.) was placed in a vial, which was sealed with a septum and purged with N₂ for 30 min. 5 mL of dry DCM was added, mixed thoroughly and removed again with dissolved 5-aminopyrimidine. The 5-aminopyrimidine solution was then added and the solution stirred overnight under N₂. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL) before being dried over Na₂SO₄, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt₃) and loaded onto a silica column packed with DCM (2% NEt₃), and eluted with DCM (2% NEt₃). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et₃NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo.

Yield = 95 mg (88 %). ¹H NMR (500 MHz, CDCl₃, δ): -2.61 (s, 2H, NH), 3.79 (s, 6H, OCH₃), 3.96 (s, 3H, OCH₃), 3.97 (s, 6H, OCH₃), 4.03 (s, 3H, OCH₃), 4.14 (s, 6H, OCH₃), 4.20 (s, 3H, OCH₃), 7.06 (s, 2H, meso–ArH), 7.41 (1H, meso–Ar–H), 7.42 (d, 2H, meso–ArH, J = 1.6 Hz), 7.50 (d, 1H, hanging–pymH, J = 1.5 Hz), 7.60 (d, 2H, meso–ArH, J = 1.5 Hz), 7.64 (t, 1H, meso–ArH, J = 7.8 Hz), 7.79 (t, 1H, ArH, J = 7.8 Hz), 8.07 (s, 1H, hanging–pymH), 8.28 (d, 1H, ArH, J = 7.5 Hz), 8.38 (d, 1H, ArH, J = 7.5 Hz), 8.45 (d, 1H, ArH, J = 7.7 Hz), 8.47 (s, 1H, NH), 8.49 (d, 1H, ArH, J = 7.9 Hz), 8.93 (d, 2H, pyrrole–βH, J = 4.7 Hz), 8.98 (d, 4H, pyrrole–βH), 9.01 (d, 2H, pyrrole–βH, J = 4.1 Hz). Mass spectrometry [M+H]+ (m/z) Calcd (Found):
\[ \lambda_{\text{max,abs}} \text{/nm (}\varepsilon \text{ (M}^{-1}\text{ cm}^{-1})\text{)} = 420 (3.1 \times 10^5), 515 (1.3 \times 10^4), 551 (4.4 \times 10^3), 589 (3.1 \times 10^3), 645 (1.4 \times 10^3). \]

5-\{(dibenzo(furan-4-N-(3-aminophenyl)carboxamide))-10,15,20-tri(3,4,5-trimethoxyphenyl)porphyrin\} (HPD-DAP). HPD-CO\textsubscript{2}H (112.5 mg, 110.5 \mu\text{mol}) was added to a stirring, 100 mL DCM solution of TsCl (105 mg, 550 \mu\text{mol}, 5 equiv.) and DMAP (135 mg, 1.11 mmol, 10 equiv.) and was allowed to stir under N\textsubscript{2} for 2 h. Dry 2,6-diaminopyridine (602 mg, 5.53 mmol, 50 equiv.) was added and the solution stirred overnight under N\textsubscript{2}. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with HCl/H\textsubscript{2}O (2 \times 100 mL), H\textsubscript{2}O (1 \times 100 mL), and brine (1 \times 100 mL) before being dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and evaporated to dryness. The solids were dissolved in DCM (2% NEt\textsubscript{3}) and loaded onto a silica column packed with DCM (2% NEt\textsubscript{3}), and eluted with DCM (2% NEt\textsubscript{3}). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et\textsubscript{3}NH·Cl. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 \times 5 mL) and dried in vacuo. Yield = 104.5 mg (85.3%). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, \delta): -2.62 (s, 2H, NH), -0.64 (s, 2H, hanging-NH\textsubscript{2}), 3.72 (s, 6H, OCH\textsubscript{3}), 3.97 (s, 3H, OCH\textsubscript{3}), 4.00 (s, 6H, OCH\textsubscript{3}), 4.06 (s, 3H, OCH\textsubscript{3}), 4.14 (s, 6H, OCH\textsubscript{3}), 4.20 (s, 3H, OCH\textsubscript{3}), 5.03 (d, 1H, hanging-py\textsubscript{H}, J = 8.1 Hz), 6.79 (t, 1H, hanging-py\textsubscript{H}, J = 7.9 Hz), 7.15 (d, 1H, hanging-py\textsubscript{H}, J = 7.8 Hz), 7.19 (s, 2H, meso-Ar\textsubscript{H}), 7.37 (d, 1H, hanging-py\textsubscript{H}, J = 5.2 Hz), 7.42 (d, 1H, meso-Ar\textsubscript{H}, J = 1.8 Hz), 7.56 (d, 2H, meso-Ar\textsubscript{H}, J = 1.3 Hz), 7.60 (d, 1H, meso-Ar\textsubscript{H}, J = 1.8 Hz), 7.63 (t, 1H, Ar\textsubscript{H}, J = 7.7 Hz), 7.93 (t, 1H, Ar\textsubscript{H}, J = 7.8 Hz), 8.35 (d, 2H, overlapping Ar\textsubscript{H}, J = 7.5 Hz), 52
8.42 (dd, 1H, ArH, J = 7.6 Hz, 1.4 Hz), 8.47 (dd, 1H, ArH, J = 7.9 Hz, 1.0 Hz), 8.48 (d, 2H, ArH, J = 7.5 Hz), 8.90 (d, 2H, pyrrole–βH, J = 4.8 Hz), 8.92 (d, 2H, pyrrole–βH, J = 5.1 Hz), 8.94 (s, 1H, NH), 8.99 (d, 2H, pyrrole–βH, J = 4.4 Hz), 9.01 (d, 2H, pyrrole–βH, J = 4.4 Hz).

Mass spectrometry [M+H]+ (m/z) Calcd. (Found): 1096.39 (1110.4264). λmax,abs/nm (ε (M−1 cm−1)) (CH3CN) = 421 (2.6 × 10⁵), 516 (1.3 × 10⁴), 551 (6.1 × 10³), 589 (4.7 × 10³), 645 (2.6 × 10³).

5–(6–(dibenzofuran–4–N–(3–dimethylaminophenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin (HPD–DMA). HPD–CO₂H (50 mg, 49 µmol) was added to a stirring, 100 mL DCM solution of TsCl (29 mg, 150 µmol, 3 equiv.) and DMAP (36 mg, 300 µmol, 6 equiv.) and was allowed to stir under N₂ for 2 h. N,N–dimethyl–1,3–phenylenediamine hydrochloride (270 mg, 1.3 mmol, 13 equiv.) was placed in a vial, which was sealed with a septum and purged with N₂ for 30 minutes. 5 mL of dry DCM and 0.1 mL of dry pyridine were added to the vial via syringe, mixed thoroughly and removed again with dissolved N,N–dimethyl–1,3–phenylenediamine. The N,N–dimethyl–1,3–phenylenediamine solution was then added to the porphyrin solution and the resulting solution was stirred overnight under N₂. The volatiles were removed and the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with dilute HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL) before being dried over Na₂SO₄, filtered and evaporated to dryness. The solids were dissolved in DCM (2% NEt₃) and loaded onto a silica column packed with DCM (2% NEt₃), and eluted with DCM (2% NEt₃). The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene and filtered through filter paper to remove Et₃NH·Cl. The filtrate
was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried *in vacuo*. Yield = 52 mg (94%).

1H NMR (500 MHz, CDCl$_3$, δ): –2.55 (s, 2H, NH), 2.05 (s, 6H, hanging–N(CH$_3$)$_2$), 2.67 (d, 1H, hanging–ArH, $J$ = 7.0 Hz), 2.91 (s, 1H, hanging–ArH), 3.70 (s, 6H, OCH$_3$), 3.98 (s, 6H, OCH$_3$), 4.00 (s, 3H, OCH$_3$), 4.04 (s, 3H, OCH$_3$), 4.14 (s, 6H, OCH$_3$), 4.21 (s, 3H, OCH$_3$), 5.42 (dd, 1H, hanging–ArH, $J$ = 8.1 Hz, 2.2 Hz), 6.78 (t, 1H, hanging–ArH, $J$ = 2.0 Hz), 7.17 (d, 1H, meso–ArH, $J$ = 1.5 Hz), 7.50 (1H, meso–ArH), 7.50 (d, 2H, meso–ArH, $J$ = 1.8 Hz), 7.59 (d, 1H, meso–ArH, $J$ = 1.7 Hz), 7.61 (t, 1H, ArH, $J$ = 8.0 Hz), 7.96 (t, 1H, ArH, $J$ = 7.8 Hz), 8.31 (dd, 1H, ArH, $J$ = 7.8 Hz, 1.1 Hz), 8.38 (dd, 1H, ArH, $J$ = 7.8 Hz, 1.1 Hz), 8.45 (d, 1H, ArH, $J$ = 7.3 Hz), 8.47 (d, 1H, ArH, $J$ = 8.0 Hz), 8.49 (s, 1H, NH), 8.91 (br s, 4H, pyrrole–βH), 8.98 (d, 2H, pyrrole–βH, $J$ = 4.3 Hz), 9.02 (d, 2H, pyrrole–βH, $J$ = 4.1 Hz).

Mass spectrometry [M+H]$^+$ (m/z) Calcd. (Found): 1137.44 (1137.4372). $\lambda_{max,abs}$/nm (ε (M$^{-1}$ cm$^{-1}$)) (CH$_3$CN) = 421 (3.6 × 10$^5$), 515 (1.8 × 10$^4$), 551 (8.1 × 10$^3$), 590 (6.2 × 10$^3$), 646 (3.5 × 10$^3$).

5–(6–(dibenzofuran–4–(2–N–carboxamido)benzenesulfonic acid ))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin (HPD–2SA). HPD–CO$_2$H (50 mg, 49 µmol) was added to a stirring DCM solution of TsCl (57 mg, 300 µmol, 6 equiv.) and DMAP (72 mg, 600 µmol, 12 equiv.) and was allowed to stir under N$_2$ for 2 h. 2–Aminobenzenesulfonic acid (425 mg, 2.4 mmol, 50 equiv.) was weighed out in a vial which was sealed with a septum and purged with N$_2$. 5 mL of dry pyridine was added to the vial and mixed thoroughly. The pyridine solution was then added via syringe and added to the solution, which stirred overnight under N$_2$. The volatiles were removed, the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic
layer was washed with saturated NaHCO$_3$/H$_2$O (1 × 100 mL), dilute HCl/H$_2$O until a faint green color (from protonated porphyrin) was observed, H$_2$O (2 × 100 mL), and brine (1 × 100 mL) before being dried over Na$_2$SO$_4$, filtered and evaporated to dryness. The solids were dissolved in EtOAc and loaded onto a silica column packed with EtOAc, and eluted with EtOAc. The major red fluorescent band was collected and the fraction was evaporated to dryness. The solids were dissolved in benzene. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo. The $^1$H NMR shifts were all very broad, presumably due to rapid proton transfers. Yield = 41 mg (71.2%).

$^1$H NMR (500 MHz, CD$_3$CN, δ): –2.79 (s, 2H, NH), 3.79 (br s, 6H, OCH$_3$), 3.89 (br, 9H, OCH$_3$), 3.92 (s, 3H, OCH$_3$), 3.96 (s, 6H, OCH$_3$), 4.03 (s, 3H, OCH$_3$), 6.59 (br s, 2H), 7.37 (s, 2H), 7.50 (s, 2H), 7.54 (s, 2H), 7.70 (br, 1H), 7.79 (br, 1H), 8.20 (br, 1H), 8.36 (br, 1H), 8.73 (br s, 2H, pyrrole–βH), 8.94 (br s, 2H, pyrrole–βH), 9.00 (br s, 4H, pyrrole–βH). Mass spectrometry [M+H]$^+$ (m/z) Calcd. (Found): 1137.34 (1174.3535).

$\lambda_{\text{max, abs}}$/nm ($\varepsilon$ (M$^{-1}$ cm$^{-1}$)) (CH$_3$CN) = 419 (3.2 × 10$^5$), 513 (1.4 × 10$^4$), 548 (4.6 × 10$^3$), 588 (4.1 × 10$^3$), 644 (2.2 × 10$^3$).

5-(6-(dibenzofuran-4-(3-N-carboxamido)benzenesulfonic acid))–10,15,20-tri(3,4,5-trimethoxyphenyl)porphyrin (HPD–3SA). HPD–CO$_2$H (50 mg, 49 µmol) was added to a stirring DCM solution of TsCl (57 mg, 300 µmol, 6 equiv.) and DMAP (72 mg, 600 µmol, 12 equiv.) and was allowed to stir under N$_2$ for 2 h. 3-aminobenzenesulfonic acid (425 mg, 2.4 mmol, 50 equiv.) was weighed out in a vial which was sealed with a septum and purged with N$_2$. 5 mL of dry pyridine was added to the vial and mixed thoroughly. The pyridine suspension was then added via syringe and
added to the solution, which stirred overnight under N$_2$. The volatiles were removed, the solids were dissolved in EtOAc and transferred to the separatory funnel. The organic layer was washed with saturated NaHCO$_3$/H$_2$O (1 × 100 mL), dilute HCl/H$_2$O until a faint green color (from protonated porphyrin) was observed, H$_2$O (2 × 100 mL), and brine (1 × 100 mL) before being dried over Na$_2$SO$_4$, filtered and evaporated to dryness. The solids were dissolved in EtOAc and loaded onto a silica column packed with EtOAc, and eluted with EtOAc to remove a non–porphyrinic byproduct and HPD–CO$_2$H. The desired product was removed with 20% MeOH in EtOAc, and was collected and evaporated to dryness. The solids were dissolved in DCM and filtered through filter paper. The filtrate was concentrated and the product was precipitated with the addition of pentane. The solids were sonicated and washed in pentane (3 × 5 mL) and dried in vacuo. Yield = 29.6 mg (51.4%). $^1$H NMR (500 MHz, CD$_3$CN, δ): -2.67 (s, 2H, NH), 3.53 (br s, 6H, OCH$_3$), 3.90 (s, 6H, OCH$_3$), 3.94 (s, 3H, OCH$_3$), 3.95 (s, 3H, OCH$_3$), 3.97 (s, 6H, OCH$_3$), 4.06 (s, 3H, OCH$_3$), 7.07 (d, 2H, meso–ArH, J = 1.5 Hz), 7.53 (s, 2H, meso–ArH), 7.56 (s, 1H, meso–ArH), 7.58 (t, 1H, hanging–ArH, J = 7.3 Hz), 7.63 (s, 1H, meso–ArH), 8.00 (t, 1H, ArH, J = 7.0 Hz), 8.06 (br s, 1H, ArH), 8.25 (br s, 1H, ArH), 8.47 (d, 1H, ArH, J = 7.4 Hz), 8.54 (d, 1H, ArH, J = 7.0 Hz), 8.58 (d, 1H, ArH, J = 7.3 Hz), (s, 1H, NH), 8.91 (br s, 2H, pyrrole–βH), 8.92 (br s, 2H, pyrrole–βH), 8.99 (br s, 2H, pyrrole–βH), 9.05 (br s, 2H, pyrrole–βH). Mass spectrometry [M+H]$^+$ (m/z) Calcd. (Found): 1174.34 (1174.3383). $\lambda_{\text{max,abs}}$/nm (ε (M$^{-1}$ cm$^{-1}$)) (CH$_3$CN) = 421 (3.3 × 10$^3$), 515 (1.5 × 10$^4$), 550 (6.0 × 10$^3$), 590 (4.4 × 10$^3$), 645 (2.6 × 10$^3$).
3.5 References


42. Additional experimental information, including UV-vis spectra, NMR spectra, mass spectra, and X-ray crystallographic data, are available online from Graham DJ, Zheng S-L, Nocera DG (2014) *ChemSusChem.* **7**, 2449.


Chapter 4 – Electrocatalytic H₂ Evolution by Proton–Gated Hangman Iron Porphyrins

Portions of this chapter have been published:

Graham DJ, Nocera DG (2014) Organometallics, 33, 4994. DOI: 10.1021/om500300e

4.1 Introduction

The potential utility of hydrogen (H₂) as a form of renewable energy storage continues to drive the development of catalysts to promote its catalytic generation from acidic solutions. Earth–abundant transition metal complexes have been studied extensively as electrocatalysts for H₂ evolution and are of particular interest due to their non–criticality.¹⁻⁴ The placement of an acid/base moiety in the second coordination sphere of metal redox platforms has been shown by our group⁵⁻¹⁶ and others¹⁷⁻²⁷ to facilitate proton–coupled electron transfer (PCET) at the metal–bound substrate, especially in the context of electrocatalytic H₂ production.

Iron (Fe) porphyrins are competent and efficient electrocatalysts for the reduction of protons²⁸ and CO₂²⁹⁻³¹. We have recently synthesized a series of Fe complexes based on hanging dibenzofuran porphyrins (HPDs).³² These new HPDs allow for the modular installation of a wide range of pendant acid/base moieties, which are sterically imposing. In combination with a phosphine to occupy the “non–hangman” face of the reduced porphyrin, these hangman porphyrins channel protons from solution to the catalyst active site via the pendent acid/base group. In our study of the catalytic efficacy of these new hangman porphyrins, we have employed foot–of–the–wave analysis (FOWA),
developed by Costentin and Savéant.\textsuperscript{33} FOWA is a useful tool for evaluating the activity of a molecular, homogeneous electrocatalyst even when it is obscured by substrate consumption, catalyst decomposition, or product inhibition. As of yet, FOWA has only been used in a few cases to analyze the electrocatalytic reduction of CO\textsubscript{2} to CO,\textsuperscript{33–39} the reduction of oxygen gas (O\textsubscript{2}) to water,\textsuperscript{40} and the reduction of protons to H\textsubscript{2}.\textsuperscript{41} This chapter describes the application of FOWA to electrocatalytic proton reduction on Fe–hangman porphyrins in order to evaluate the turnover frequency (TOF), and the effect of a pendant proton donor.

4.2 Results and Discussion

4.2.1 Synthesis of HPDFe Complexes

Hangman porphyrins were synthesized from 3,4,5–trimethoxybenzaldehyde and dibenzofuran aldehyde.\textsuperscript{32} Fe insertion into freebase porphyrins was accomplished with microwave–assisted metellation (Scheme 1).

![Scheme 4.1. Method for Fe insertion to furnish the Fe–porphyrins used in this study.](image)
In contrast to standard methods that use N,N-dimethylformamide (DMF) as the reaction solvent,\textsuperscript{42,43} acetonitrile (CH\textsubscript{3}CN) containing a trace amount of triethylamine (NEt\textsubscript{3}) was an equally competent solvent system that delivered the desired product after 1 h of microwave irradiation (Scheme 1). Column chromatography, extensive washing with aqueous HCl, and rigorous drying at elevated temperatures \textit{in vacuo} furnished the Fe\textsuperscript{III}Cl porphyrins in moderate yields as brown powders. EPR of \textbf{A}_4\textbf{Fe} reveals an axially symmetric signal \((g_\parallel = 2.01, g_\perp = 5.87)\) consistent with reported, high–spin Fe\textsuperscript{III}–porphyrin complexes (Figure 1).\textsuperscript{44}

![EPR spectrum of \textbf{A}_4\textbf{Fe} in toluene measured at 4 K.](image)

\textbf{Figure 4.1.} EPR spectrum of \textbf{A}_4\textbf{Fe} in toluene measured at 4 K.

\textbf{4.2.2 Cyclic Voltammetry}

Cyclic voltammograms (CVs) of the Fe\textsuperscript{III}Cl porphyrins employed in this study display a quasi–reversible wave corresponding to Fe\textsuperscript{III}/II reduction and loss of Cl\textsuperscript{–}, and two reversible waves attributed to the Fe\textsuperscript{II}/I reduction and the Fe\textsuperscript{I}/0 reduction (Figure 2).
A fourth reversible reduction is apparent for the hangman porphyrins, and is most likely ligand based. All of the respective reduction potentials for the hangman Fe-porphyrin are within 120 mV of each other, which is expected for a homologous series of molecules that have similar redox centers. Moreover, the reduction potentials of the non-hangman $A_4$Fe are very similar to those of the hangman porphyrins, suggesting that dibenzofuran and 3,4,5-trimethoxyphenyl meso-substitutions have a similar electronic influence on the porphyrin.

Electrochemical experiments were conducted using CH$_3$CN as the solvent because the pK$_a$ values of many common acids are known in CH$_3$CN. Initial studies utilized tetraethylammonium tetrafluoroborate ([TEA$^+$][BF$_4^-$]) as the supporting electrolyte and $p$-toluenesulfonic acid (TsOH) as the proton source, but it was found that the
onset potential for direct reduction of TsOH at a glass–like carbon electrode occurred at potentials significantly positive of the Fe^{II/II} reduction potential. Replacing the [BF_4^{-}] supporting anion for p-toluenesulfonate ([TsO^{-}]) dramatically reduced the proton discharge current. The presence of 0.1 M [TsO^{-}] in solution suppresses the direct reduction of TsOH presumably through its ability to form hydrogen–bonded homoconjugate with an equilibrium constant of 790 M^{-1} (Eq. (1)).^{47-49} This equilibrium essentially transforms the proton source into a negatively charged entity ([TsOH•OTs^{-}]) and reduces the concentration of “free” TsOH to at most 2% of the total H^{+} concentration for these studies. The effective pK_{a} of the homoconjugate may be obtained by adding the free energy of homoconjugate formation to the free energy of acid dissociation of TsOH, both of which can be determined from their respective equilibrium constants, resulting in a pK_{a} of 11.5, nearly three pK_{a} units higher than TsOH.

\[
\begin{align*}
\text{TsO}^{-} + \text{TsOH} & \rightleftharpoons \text{TsOH•OTs}^{-} \\
K = 790 \text{ M}^{-1}
\end{align*}
\]

The addition of excess triphenylphosphine (PPh_3) was found to prevent additional, unwanted reduction events under acidic conditions and thus was present in excess at all times. Protonated PPh_3 is not expected to be present in any meaningful concentrations due to its pK_{a} in CH_3CN (7.6)^{46} being 1 pK_{a} unit lower than TsOH, competing homoconjugate formation, and the abundance of [TsO^{-}] in solution. With acid concentrations
higher than 20 mM, unwanted features in CVs of Fe–porphyrins were observed, even in
the presence of 40 mM PPh₃, putting an upper limit on the acid concentration for this
study. This upper limit is far below that needed to observe an S–shaped catalytic wave in
the CV, which permits the most straightforward determination of the pseudo–first order
rate constant for the catalysts. In the absence of the S–shaped CV, FOWA permits the rate
of catalysis at low concentrations of acid to be ascertained.

CVs of Fe–porphyrins in CH₃CN under these conditions display a catalytic wave
that grows from the FeⅡ/Ⅰ reduction wave upon addition of H⁺ to solution (Figure 3). As
acid concentration increases, the catalytic wave slightly shifts to more positive potential
as a consequence of facilitating protonation of the Fe center upon reduction. Such shifts
are with acid concentration are well established from previous investigations.¹⁶,⁴⁹ Gas
chromatographic analysis confirmed the presence of H₂ in the headspace of a two–
compartment cell following controlled potential electrolysis. Faradaic efficiencies were
notably similar between working solutions utilizing HPDFe–Ph (66%), HPDFe–DMA
(65%), HPDFe–3SA (65%), and A₄Fe (67%). The FOWA analysis allows for insight into
the catalytic H₂ evolving activity of these systems despite these nonideal Faradaic effi-
ciencies.
Figure 4.3. Cyclic voltammograms of 0.5 mM solutions of (a) HPDFe–Ph, (b) HPDFe–DMA, (c) HPDFe–3SA, and (d) A4Fe in the presence of 0 mM (▬ blue), 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red) of H⁺ (from added HBF₄). Conditions: 40 mM PPh₃ in CH₃CN (0.1 M [TEA⁺][TsO⁻]) at a scan rate of 50 mV/s.

The beneficial role of excess PPh₃ is thought to be threefold: (1) inducing a low spin d⁶ configuration of the Fe⁺, thus preventing any side reactions that may occur between H⁺ and intermediate or high spin Fe⁺–porphyrin, (2) physically blocking the “non-hangman” porphyrin face from acidic species in solution, and (3) providing a strong trans–influence to increase the reactivity of Fe⁺ and any resulting Fe–hydride.

Given the ability of Fe⁺ porphyrins to bind two axial phosphines, one would expect excess PPh₃ to hinder further reduction to five-coordinate Fe⁺, since it would require an additional chemical step (PPh₃ dissociation). CVs of A₄Fe in the presence of various con-
centrations of PPh\textsubscript{3} indicate that both the Fe\textsuperscript{III}/\textsuperscript{II} and Fe\textsuperscript{II}/\textsuperscript{I} half-wave potentials are hardly affected by increasing concentration of phosphine and remain electrochemically reversible, even when there is no obstruction to inhibit axial ligand binding. The probable explanation for this behavior is the existence of a fast equilibrium between five- and six-coordinate Fe\textsuperscript{II}. We posit that the presence of an imposing hanging group is likely to shift the equilibrium towards five coordinate Fe\textsuperscript{II}, with one PPh\textsubscript{3} on the non-hangman face of the porphyrin, consistent with previous observations of low-spin, five-coordinate Fe\textsuperscript{II} porphyrin where binding is disfavored on one porphyrin face.\textsuperscript{51}

In previous studies of the reduction of weak acids by Fe–porphyrins, catalysis was reported to occur upon reduction of the Fe–porphyrin unit to a formal “Fe\textsuperscript{0}” oxidation state.\textsuperscript{28} The nature of “Fe\textsuperscript{0}” has been studied crystallographically\textsuperscript{52} and by NMR techniques;\textsuperscript{53} the commonly accepted electronic configuration is a d\textsuperscript{7} Fe\textsuperscript{I} ion ligated by a porphyrin–based radical anion (Fe\textsuperscript{I}Porph\textsuperscript{–1}). This ligand–based radical anion can act as a nucleophile, resulting in decomposition or deactivation of the catalyst.\textsuperscript{54,55} Using strong acids that react with the Fe–porphyrin at the Fe\textsuperscript{I} oxidation state, our Fe–porphyrins generate H\textsubscript{2} at more positive potentials while bypassing deleterious porphyrin–based radicals.

Catalytic current at the Fe\textsuperscript{II}/Fe\textsuperscript{I} reduction potential suggests that Fe\textsuperscript{I} is the species that undergoes protonation. Yet the question remains as to whether the Fe\textsuperscript{I} species reacts via the metal center or the porphyrin ligand, as the electronic configuration of reduced metalloporphyrins is sensitive to a number of factors. Fe\textsuperscript{I} porphyrins may have ligand–based radical character in the solid state,\textsuperscript{52} but solution EPR studies suggest that
axially ligated Fe\(^{1}\) porphyrins are d\(^7\) species containing an unpaired electron in the Fe d\(_{z^2}\) orbital with no observed radical character on the porphyrin ring (provided there are only meso–substituents on the porphyrin periphery).\(^{56,57}\) The fact that extended controlled potential electrolysis did not result in a green solution (indicative of porphyrin ring reduction) leads us to believe that ligand–based reactions do not occur and direct protonation of Fe\(^{1}\) is the first chemical step during catalysis, as indicated in Scheme 2. The appearance of catalysis at the Fe\(^{II}/Fe^{1}\) suggests that Fe\(^{III}H\) may be hydridic enough to react with H\(^+\). Studies to measure the hydricity of a Fe\(^{III}H\) porphyrin are currently underway.

Scheme 4.2. Proposed catalytic mechanism.

4.2.3 Foot–of–the–Wave Analysis

All Fe–porphyrins in this study are catalytically active for the reduction of [TsOH•OTs\(^-\)] at the Fe\(^{II}/Fe^{1}\) reduction potential, but differences in catalytic behavior are not immediately apparent from CVs. FOWA allows one to quantify catalytic activity in the
absence of any catalyst decomposition or extensive substrate consumption that may occur.\textsuperscript{33} FOWA can be applied to electrocatalytic proton reduction by Fe–porphyrin if it is assumed that the process begins with a fast electron transfer (Eq. (2)), is followed by a combination of chemical steps (Eq. (3)) and regeneration of Fe\textsuperscript{II}–porphyrin by electron transfer from an Fe\textsuperscript{I}–porphyrin in solution (Eq. 4). Reduction of Fe\textsuperscript{III} by Fe\textsuperscript{I} in solution, rather than the electrode, is more likely when catalysis is relatively slow compared to electron transfer.

\[
\text{Fe}^{\text{II}} \rightleftharpoons \text{Fe}^{\text{I}} \quad (2)
\]

\[
\text{Fe}^{\text{I}} + 2 \text{H}^+ \rightarrow \text{Fe}^{\text{III}} + \text{H}_2 \quad (3)
\]

\[
\text{Fe}^{\text{I}} + \text{Fe}^{\text{III}} \rightarrow 2 \text{Fe}^{\text{II}} \quad (4)
\]

Since the Fe\textsuperscript{II}/I reduction is reversible and $E_{1/2}(\text{Fe}^{\text{II}}/\text{Fe}^{\text{I}})$ is known, the concentration of active catalyst (Fe\textsuperscript{I}) for every potential is given by the Nernst equation; additional current observed at potentials near $E_{1/2}(\text{Fe}^{\text{II}}/\text{Fe}^{\text{I}})$ is due to catalysis. The concentration of substrate at the electrode decreases as the scan progresses, thereby affecting the observed rate of catalysis. By analyzing the beginning (foot) of the catalytic wave, the activity of the catalyst may be ascertained before significant substrate consumption occurs.

In order to analyze the foot of the wave, a plot of the catalytic enhancement (current ($i$) as a fraction of the Fe\textsuperscript{II}/I reduction wave peak current in the absence of substrate ($i_p^0$)) as a function of $[1 + \exp\left(\frac{F}{RT} \left( E - E^0 \right) \right]^{-1}$ allows us to classify catalyst behavior (Figure 4).
Figure 4.4. Foot-of-the-wave analyses of (a) HPDFe-Ph, (b) HPDFe-DMA, (c) HPDFe-3SA, and (d) A₄Fe using the CVs displayed in Figure 3. Concentrations of H⁺ (from added HBF₄) are 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red).

Invoking the steady state approximation for the catalytic intermediates allows us to use Eq. (5) to determine the apparent rate constant, \( k \), representing the combination of the steps corresponding to Eq. (3).

\[
\frac{i}{i^\circ_p} = \frac{2.24 \frac{RT}{Fv} 2kC_{H^+}}{1 + \exp \frac{F}{RT} (E - E^0)} \tag{5}
\]

In the cases of HPDFe-DMA, HPDFe-3SA, and A₄Fe, FOWA shows a curve that deviates from the initial trajectory. This behavior is consistent with modeled examples of rapid substrate consumption near the electrode, which limits the catalytic current.³³
FOWA of HPDFe–Ph results in nearly linear plots, suggesting that this catalyst consumes H⁺ much slower than the other catalysts in this study.

Values of $k$ are obtained from linearizing the curves in Figure 4 at early points on the graph, which have slopes of $2.24 \frac{RT}{Fv} 2kC_{H^+}$ (Table 1).

<table>
<thead>
<tr>
<th>Compound</th>
<th>log($k$) (M⁻¹ s⁻¹)</th>
<th>5 mM a</th>
<th>10 mM a</th>
<th>15 mM a</th>
<th>20 mM a</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPDFe–Ph</td>
<td>3.74</td>
<td>3.72</td>
<td>3.69</td>
<td>3.66</td>
<td></td>
</tr>
<tr>
<td>HPDFe–DMA</td>
<td>4.25</td>
<td>4.43</td>
<td>4.48</td>
<td>4.53</td>
<td></td>
</tr>
<tr>
<td>HPDFe–3SA</td>
<td>5.06</td>
<td>5.44</td>
<td>5.81</td>
<td>6.12</td>
<td></td>
</tr>
<tr>
<td>A₄Fe</td>
<td>4.96</td>
<td>5.02</td>
<td>5.08</td>
<td>5.17</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1. Values of log($k$) for all catalysts at different H⁺ concentrations. Values were obtained from the foot–of–the–wave slope per Eq. (5).³ H⁺ concentration from added HBF₄ (to generate TsOH and its homoconjugate in situ). All experiments were conducted under an atmosphere of N₂ in CH₃CN (0.1 M [TEA⁺][TsO⁻]) containing 0.5 mM Fe–porphyrin. All scans were performed at 50 mV/s.

These values of $k$ show little to no variation over a range of scan rates (Figure 5).

When comparing the activity of the Fe–porphyrins in the presence of a 40–fold excess of H⁺, we see a clear trend between the proton donating ability and $k$. While no direct measurements of the hanging group pKₐ’s were made, we can approximate them from the pKₐ of related acids in CH₃CN. With their N–bound carboxamide, the sulfonic acid in HPDFe–3SA and N,N–dimethylanilinium in HPDFe–DMA should have pKₐ’s slightly higher than that of TsOH and N,N–dimethylanilinium (pKₐ(CH₃CN) = 8.6 and 11.5, respectively).⁴⁵ The apparent rate of catalysis is higher for hangman porphyrins that are able to transfer a proton to the metal center in an intramolecular fashion.
**Figure 4.5.** Values of $k$ determined from CVs of $\text{A}_4\text{Fe}$ (0.5 mM) with 20 mM PPh$_3$ and 5 mM (green), 10 mM (yellow), 15 mM (orange), and 20 mM (red) of [TsOH•OTs$^-$] (generated *in situ* by addition of HBF$_4$) in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) at scan rates from 50 mV/s to 2 V/s.

**HPDFe–3SA** is by far the highest performing catalyst, most likely due to its ability to undergo intramolecular, rather than intermolecular, H$^+$ transfer from a sulfonic acid, a phenomenon which has been studied computationally and shown that a reduced energetic barrier to proton transfer results when the proton is delivered intramolecularly.$^{58}$ In accordance with this result, the hangman effect results in a high local proton concentration that effectively requires an effective intermolecular concentration that is $10^3$ greater than that needed for the proton–assisted intramolecular concentration.$^{16}$ When intramolecular proton transfer is retarded by increasing the hanging group pK$_a$, as in the case of **HPDFe–DMA**, we observe a large decrease in $k$ compared to **HPDFe–3SA**. It is
noteworthy that the hanging group of \textbf{HPDFe-DMA} is more often protonated under our conditions, whereas the hanging group in \textbf{HPDFe-3SA} has a lower pK\textsubscript{a} and is less likely to be a protonated at any given time, yet \textbf{HPDFe-3SA} still operates faster than \textbf{HPDFe-DMA} and \textbf{A\textsubscript{4}Fe}. \textbf{HPDFe-Ph} is the slowest of the catalysts and is much slower than \textbf{A\textsubscript{4}Fe}, which also lacks a hanging acid/base moiety. This is expected only if direct protonation of \textbf{HPDFe-Ph} by H\textsuperscript{+} in solution is inhibited by both PPh\textsubscript{3} on one face and the hanging group on the other.

An accurate picture of a catalyst TOF is furnished from FOWA. The TOF varies with overpotential (\(\eta\)) according to Eq. 6.

\[
\log TOF^{(2)} = \log k - \frac{F}{RT\ln 10} \left( E_{HA}^{0} H_{2} - E_{Fe^{II}}^{0} Fe^{I} \right) - \frac{\eta F}{RT\ln 10}
\]  

(6)

This equation accounts for the slight differences in Fe\textsuperscript{II/1} reduction potentials and driving forces. By extrapolating the potential dependent TOF back to the standard reduction potential of the acid (\(E_{HA}^{0} H_{2}\)), we can determine the TOF at zero overpotential (\(TOF_{0}^{(2)}\)) for each electrocatalyst at different acid concentrations (Table 2). \(TOF_{0}^{(2)}\) can be thought of as the molecular catalyst’s exchange current, and can therefore be used to directly compare different electrocatalysts. \(TOF_{0}^{(2)}\) can also be calculated by dropping the last term of Eq. (6) (since \(\eta = 0\)) and rearranging to get Eq. (7),

\[
TOF_{0}^{(2)} = \frac{k}{1 + \exp \left( \frac{F}{RT} E_{HA}^{0} H_{2} - E_{Fe^{II}}^{0} Fe^{I} \right)}
\]  

(7)
<table>
<thead>
<tr>
<th>Compound</th>
<th>log(TOF₀⁽²⁾) (M⁻¹ s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 mMᵃ</td>
</tr>
<tr>
<td></td>
<td>10 mMᵃ</td>
</tr>
<tr>
<td></td>
<td>15 mMᵃ</td>
</tr>
<tr>
<td></td>
<td>20 mMᵃ</td>
</tr>
<tr>
<td>HPDFe–Ph</td>
<td>−8.41 −8.45 −8.50 −8.55</td>
</tr>
<tr>
<td>HPDFe–DMA</td>
<td>−8.52 −8.35 −8.29 −8.24</td>
</tr>
<tr>
<td>HPDFe–3SA</td>
<td>−9.17 −8.77 −8.41 −8.10</td>
</tr>
<tr>
<td>A₄Fe</td>
<td>−8.34 −8.31 −8.30 −8.32</td>
</tr>
</tbody>
</table>

Table 4.2. Values for log(TOF₀⁽²⁾) at different H⁺ concentrations. Values were obtained from Eq. (7).ᵃ H⁺ concentration from added HBF₄ (to generate TsOH and its homoconjugate in situ). All experiments were conducted under an atmosphere of N₂ in CH₃CN (0.1 M [TEA⁺][TsO⁻]) containing 0.5 mM Fe porphyrin. All scans were performed at 50 mV/s.

$E_{HA \ H₂}^0$ in our study has to be slightly modified from the standard reduction potential of TsOH since the acid source in this study is primarily a homoconjugate. Taking into account the free energy of [TsOH•OTs⁻] formation gives us an $E_{HA \ H₂}$ of −0.71 V vs Fc⁺/Fc (derived in Experimental Section), which results in the values aggregated in Table 2.

The TOF₀⁽²⁾ of HPDFe–3SA changes drastically as the acid concentration is increased from 5 mM, where it has to lowest TOF₀⁽²⁾, to 20 mM, where it outperforms all other catalysts. We attribute this behavior to the acid/base equilibrium between the hanging sulfonic acid on HPDFe–3SA and [TsOH•OTs⁻]. Even though the hanging N,N–dimethylanilinium in HPDFe–DMA is a weaker proton donor than the hanging sulfonate in HPDFe–3SA, it has an advantage at lower H⁺ concentrations because it effectively increases the local concentration of H⁺ near the Fe center, giving it a higher TOF₀⁽²⁾ than
HPDFe–3SA. As the concentration of H\(^+\) increases, the hanging sulfonate on HPDFe–3SA is more likely to be protonated and TOF\(_0^{(2)}\) increases.

In the presence of 5 mM H\(^+\), A\(_4\)Fe displays the highest TOF\(_0^{(2)}\) but shows little variation with increasing acid concentration. At 15 and 20 mM concentrations of acid, both HPDFe–DMA and HPDFe–3SA have higher values of TOF\(_0^{(2)}\), suggesting that when the hanging group is more likely to be protonated, it outperforms non–hangman porphyrins. Additionally, the ability of the hanging phenyl group in HPDFe–Ph to impede the approach of H\(^+\) sources may be discerned from its TOF\(_0^{(2)}\) at every acid concentration, which are consistently lower than A\(_4\)Fe. The TOF\(_0^{(2)}\) of HPDFe–Ph shows very little variation with increasing acid concentration suggesting that the combination of excess PPh\(_3\) and the steric profile of the hanging phenyl group is effective at shielding the Fe center from [TsOH•OTs\(^–\)] or TsOH in solution.

FOWA analysis of electrocatalytic H\(_2\) evolution using hydrogenase models [Fe\(_2\)(µ–bdt)(CO)\(_6\)] and [Fe\(_2\)(µ–bdt)P(OMe)\(_3\)–(CO)\(_5\)] (bdt = 1,2–benzenedithiolate) in CH\(_3\)CN\(^41\) yields lower rates of catalysis than observed here for the hangman Fe–porphyrins of this study. However, we note that [Fe\(_2\)(µ–bdt)(CO)\(_6\)] operates at a ~200 mV lower overpotential, which yields a higher intrinsic activity (\(\log \text{TOF}_0^{(2)} = -7.03\)) upon extrapolation back to the standard potential of the substrate. These results highlight the interplay between activity and overpotential, and the importance of using FOWA to compare catalysts.
4.2.4 Mechanistic Study

Analysis of CVs with varying concentrations of acid can lead to some insight into the movement of protons during electrocatalysis. Plotting the log of the acid concentration versus the log of the observed rate of catalysis should give linear fits with slopes that inform the rate determining step (Figure 6).

**Figure 4.6.** Plots of log($k$) vs. log([TsOH•OTs$^-$]) for HPDFe–Ph (blue), HPDFe–DMA (red), HPDFe–3SA (green), $A_4$Fe (purple) in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) with 40 mM PPh$_3$ at 50 mV/s $A_4$Fe.

One can see that in plotting log($k$) vs. log([TsOH•OTs$^-$]) for HPDFe–Ph, HPDFe–DMA, and $A_4$Fe, the slopes are approximately zero, which gives no meaningful information about the catalytic mechanism. This zero-order rate dependence is especially puzzling since it is observed with both HPDFe–DMA, which contains an intramolecular proton relay, as well as $A_4$Fe and HPDFe–Ph, which do not. One possible explanation for this behavior is an additional, rate limiting electron transfer to reduce Fe$^{III}$H(PPh$_3$)–.
porphyrin to Fe$^{II}$H(PPh$_3$)-porphyrin before reacting with another equivalent of H$^+$ to produce H$_2$, and investigations are currently underway. The same plot for HPDFe–3SA displays a slope of 1.73, very close to the slope of 2 which is indicative of an equilibrium preceding the rate limiting step. This behavior is consistent with the hypothesis that the proton transfer equilibrium favors protons in the electrolyte solution bound to [TsO$^-$] anions in the form of [TsOH•OTs$^-$] rather than the hanging sulfonate on the HPD ligand.

4.3 Conclusion

We have quantified the enhancement of catalytic activity towards hydrogen evolution that accompanies the placement of a proton donor in the second coordination sphere of Fe–porphyrins during electrocatalysis. In the presence of excess PPh$_3$, the HPD ligand limits the exposure of the Fe center to solution to such an extent that it modulates the rate of electrocatalytic H$_2$ evolution by gating the flow of protons to the catalyst active site. The presence of an acid/base group in the second coordination sphere increases the rate of catalysis, with stronger pendant proton donors resulting in consistently faster proton reduction. When correcting for differences in Fe$^{II}$/I reduction potentials by determining the TOF$_0^{(2)}$, the higher performance as a result of the hangman effect is apparent at high concentrations of acid. Future studies will use recently published methods$^{59}$ to determine the mechanism of proton reduction on Fe–porphyrins and exploit our ability to modulate the effective rate of proton transfer to the catalysts active site. For instance, in cases where H$_2$ evolution represents a parasitic side reaction, such as carbon dioxide reduction,$^{60,61}$ nitrite reduction,$^{62–64}$ and olefin reduction$^{65}$ in the acidic
solutions, we wish to tailor the rate of proton transfer to the catalyst active site in order to minimize parasitic evolution of H₂.

4.4 Experimental Section

**General Considerations.** CH₃CN was purified by passage through alumina and was stored over activated 3Å molecular sieves under N₂. Tetraethylammonium p-toluenesulfonate ([TEA⁺][TsO⁻]) and tetraethylammonium tetrafluoroborate ([TEA⁺][BF₄⁻]) were purchased from Alfa Aesar and recrystallized prior to use. [TEA⁺][BF₄⁻] was purified by dissolving in CH₃CN, adding ethanol until saturation was achieved, and placing in refrigerator for recrystallization. The crystals were washed with cold ethanol, dried at 100 °C *in vacuo* overnight, and stored under nitrogen. [TEA⁺][TsO⁻] was purified by dissolving in minimal ethanol, adding ethyl acetate until saturation was achieved, and placing in refrigerator for recrystallization. The crystals were washed with cold ethyl acetate, dried at 100 °C *in vacuo* overnight, and stored under nitrogen. Tetrafluoroboric acid etherate were purchased from Alfa Aesar and used as received. NEt₃, methanol (MeOH), dichloromethane (DCM), benzene, ethanol, ethyl acetate, FeBr₂ (98%), and anhydrous FeCl₂ beads (99.99%) were purchased from Sigma Aldrich and were used as received. PPh₃ was purchased from Strem, recrystallized from hexanes, and dried *in vacuo* prior to use. All porphyrins were synthesized according to published procedures. The microwave-assisted reactions were performed inside the cavity of a CEM Discover microwave synthesis system equipped with infrared, pressure, and temperature sensors for monitoring the synthesis. The reaction vessels were 35 mL crimp-
sealed thick–wall glass tubes. The contents of each vessel were stirred with a magnetic stirrer. Absorption spectral measurements were made on 5 µM solutions of each Fe–porphyrin in CH$_3$CN using a Cary 5000 UV–vis–NIR spectrometer from Varian employing the software Cary WinUV. Quartz cells with a 10 mm path length were used. A perpendicular X–band EPR spectrum was collected at 4 K with a ca. 0.2 mM solution of $\text{A}_4\text{Fe}$ in toluene using a Bruker ElexSys E500 EPR spectrometer using a microwave frequency of 9.379 GHz. Electrospray ionization mass spectra (ESI–MS) were obtained using a Bruker microTOF–QII. Masses were generated using mMass.$^6$ Elemental analyses were not collected, as they provide little insight into the purity of hangman porphyrins. Due to their high molecular weights, we would expect many of the imaginable porphyrin–derived impurities in a sample of hangman Fe–porphyrin to have very similar elemental analysis results.

**Synthesis.** 5–(6–(dibenzofuran–4–N–(phenyl)carbox–amide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrinato iron(III) chloride (HPDFe–Ph). Freebase hangman porphyrin (5–(6–(dibenzofuran–4–N–(phenyl)carboxamide))–10,15,20–tri–(3,4,5–trimethoxyphenyl)porphyrin, 75 mg, 69 µmol) and freshly ground FeCl$_2$ (173 mg, 1.37 mmol, 20.0 equiv.) were dissolved in 15 mL CH$_3$CN and transferred to a 35 mL microwave reactor tube. A small amount of NEt$_3$ (0.05 mL) was added to the solution, the tube was capped, and microwave irradiation proceeded for 1 h at 70 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with 1 M HCl/H$_2$O (2 × 100 mL), H$_2$O (1 × 100 mL) and
brine (1 × 100 mL), filtered through Na$_2$SO$_4$, and dried in vacuo. The solids were dissolved in DCM (2% MeOH), loaded onto a silica column packed with DCM (2% MeOH) and eluted with DCM (2% MeOH). The major brown band was collected. The volatiles were removed, the solids were dissolved in DCM, which was covered in 1 M HCl/H$_2$O and the solution was stirred thoroughly for 4 h. The organic layer was dried over Na$_2$SO$_4$ and the volatiles were removed. The solids were dissolved in benzene, and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo. Yield = 45.6 mg (83.5%). ESI–MS [M – Cl]$^+$ (m/z) Calcd. (Found): 1147.31 (1147.3013). $\lambda_{\text{max,abs}}$/nm ($\varepsilon$/M$^{-1}$ cm$^{-1}$) (CH$_3$CN) = 380 (5.7 × 10$^4$), 423 (1.1 × 10$^5$), 577 (5.4 × 10$^5$).

5–(6–(dibenzofuran–4–N–(3–dimethylamino–phenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)–porphyrinato iron(III) chloride (HPDFe–DMA). Freebase hangman porphyrin (5–(6–(dibenzofuran–4–N–(3–dimethylamino–phenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin, 50.0 mg, 44.0 µmol) and freshly ground FeCl$_2$ (111 mg, 0.880 mmol, 20 equiv.) were dissolved in 15 mL CH$_3$CN and transferred to a 35 mL microwave reactor tube. A small amount of NEt$_3$ (0.05 mL) was added to the solution, the tube was capped, and microwave irradiation proceeded for 1 h at 70 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with 1 M HCl/H$_2$O (2 × 100 mL), H$_2$O (1 × 100 mL) and brine (1 × 100 mL), filtered through Na$_2$SO$_4$, and dried in vacuo. The solids were dissolved in DCM (2% MeOH, 2% NEt$_3$),
loaded onto a silica column packed with DCM (2% MeOH, 2% NEt₃), and eluted with DCM (2% MeOH, 2% NEt₃). The major brown band was collected. The volatiles were removed, the solids were dissolved in DCM, which was covered in 1 M HCl/H₂O and thoroughly stirred for 4 h. The organic layer was dried over Na₂SO₄ and the volatiles were removed. The solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo. Yield = 35.6 mg (66%). ESI–MS [M + H⁺]⁺ (m/z) Calcd. (Found): 1226.33 (1226.3250). [M – Cl⁻]⁺ (m/z) Calcd. (Found): 1190.35 (1190.3503). λmax,abs/nm (ε/M⁻¹ cm⁻¹) (CH₃CN) = 422 (1.5 × 10⁵), 573 (7.1 × 10³).

5–(6–(dibenzofuran–4–(3–N–carboxamido)–benzenesulfonic acid ))–10,15,20–tri(3,4,5–trimethoxyphenyl)–porphyrinato iron(III) chloride (HPDFe–3SA). Freebase hangman porphyrin (5–(6–(dibenzofuran–4–(3–N–carboxamido)–benzenesulfonic acid))–10,15,20–tri(3,4,5–trimethoxyphenyl)por–phyrin, 36.0 mg, 30.6 µmol) and freshly ground FeCl₂ (77.4 mg, 0.614 mmol, 20.0 equiv.) were dissolved in 15 mL CH₃CN and transferred to a 35 mL microwave reactor tube. A small amount of NEt₃ (0.05 mL) was added to the solution, the tube was capped, and microwave irradiation proceeded for 1 h at 70 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with 1 M HCl/H₂O (2 × 100 mL), H₂O (2 × 100 mL) and dried in vacuo. The solids were dissolved in DCM (10% MeOH), loaded onto a silica column packed with DCM (10% MeOH) and eluted with DCM (15% MeOH). The major brown band was collected. The volatiles were
removed, the solids were dissolved in DCM, which was covered in 1 M HCl/H₂O and the solution was stirred thoroughly for 4 h. The organic layer was filtered through filter paper, the volatiles were removed, and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo. Yield = 30.7 mg (79.3%). ESI−MS [M − Cl−]+ (m/z) Calcd. (Found): 1227.27 (1227.2618). λ_{max,abs}/nm (ε/M⁻¹ cm⁻¹) (CH₃CN) = 381 (7.4 × 10⁴), 423 (1.4 × 10⁵), 579 (6.8 × 10³).

**Tetrakis(3,4,5−trimethoxyphenyl)porphyrinato iron(III) chloride (A₄Fe).**

Freebase A₄ porphyrin (123 mg, 126 µmol) and FeBr₂ (318 mg, 2.52 mmol, 20.0 equiv.) were dissolved in 15 mL CH₃CN and transferred to a 35 mL microwave reactor tube. A small amount of NEt₃ (0.05 mL) was added to the solution, the tube was capped, and microwave irradiation proceeded for 1 h at 70 °C. The solution was analyzed by TLC, and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with 1 M HCl/H₂O (2 × 100 mL), H₂O (1 × 100 mL) and brine (1 × 100 mL), filtered through Na₂SO₄, and dried in vacuo. The solids were dissolved in DCM (2% MeOH), loaded onto a silica column packed with DCM (2% MeOH) and eluted with DCM (2% MeOH). The major brown band was collected. The volatiles were removed, the solids were dissolved in DCM, which was covered in 1 M HCl/H₂O and the solution was stirred thoroughly for 4 h. The organic layer was dried over Na₂SO₄ and the volatiles were removed. The solids were dissolved in benzene, and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo. Yield = 112 mg (83.5%). ESI−MS [M − Cl−]+ (m/z) Calcd. (Found): 1028.29
(1028.2819). $\lambda_{\text{max,abs}}/\text{nm} (\varepsilon /\text{M}^{-1} \text{cm}^{-1}))$ (CH$_3$CN) = 379 (6.3 \times 10^4), 422 (1.2 \times 10^5), 577 (4.8 \times 10^3).

**Cyclic Voltammetry.** All studies were conducted under a nitrogen atmosphere using a CHInstruments 730C potentiostat. All CVs were performed in an oven–dried conical glass cell purchased from BASi. Working solutions were prepared from 1 mL of a 1 mM Fe–porphyrin stock solution in CH$_3$CN (0.1 M electrolyte) was combined with 0.4 mL of 0.2 M stock solution of PPh$_3$ in CH$_3$CN (0.1 M electrolyte) and 0.6 mL of CH$_3$CN (0.1 M electrolyte) to make the 0.5 mM Fe–porphyrin solution. HBF$_4$ was added from a 0.2 M stock solution in CH$_3$CN (0.1 M electrolyte). The working electrode for cyclic voltammetry was a 0.7 cm$^2$ glass–like carbon disk, which was polished before each series of CVs with 50 nm alumina, sonicated in 18 MΩ water, and rinsed with methanol before being dried with compressed air. The pseudo–reference electrode was a polished Ag wire encased in a glass container immersed in CH$_3$CN containing a 0.1 M solution of the supporting electrolyte; the reference and working electrode compartments were separated by a vycor frit. The counter electrode was a Pt wire. All potentials were referenced to Fc$^+$/Fc.

In [TEA$^+$][TsO$^-$] solutions, acid titrations were carried out with the addition of HBF$_4$$\bullet$OEt$_2$, exploiting the large difference in pK$_a$’s of TsOH (8.6) and HBF$_4$ (0.1) in CH$_3$CN to generate TsOH and its homoconjugate in situ.

**Bulk Electrolysis.** 4 mL of CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) containing 20 mM PPh$_3$ and 10 mM [H$^+$] (added in the form of HBF$_4$) was placed in the auxiliary compartment of a small H–cell consisting of ca. 10 mL compartments separated by porous glass, which were custom made by James Glass (www.jamesglass.com). A Pt mesh counter electrode
and Ag wire pseudo–reference (in a glass compartment containing CH$_3$CN (0.1 M [TEA$^+$/TsO$^-$]) separated from the auxiliary solution by a vycor frit) were placed in the auxiliary compartment. 4 mL of CH$_3$CN (0.1 M [TEA$^+$/TsO$^-$]) containing 0.25 mM Fe–porphyrin, 20 mM PPh$_3$, and 10 mM [H$^+$] (added in the form of HBF$_4$) was placed in the working compartment. A glass–like carbon rod (connected to Cu wire which was inserted through a silicone 14/20 septum) and a stirbar were inserted into the working compartment. The working compartment was sealed with a silicone septum. The solution resistance was countered with iR compensation. A CV was collected, and controlled potential electrolysis was performed at the foot of the catalytic wave with vigorous stirring. After sufficient current was passed (2 – 4 C), the electrolysis was halted, and 50 µL of the headspace of the working electrode was injected into a gas chromatograph to detect the presence of H$_2$. The Faradaic efficiency was calculated using a calibration curve constructed using multiple injections of 1%, 3%, and 5% H$_2$ in N$_2$. The percentage of H$_2$ in the headspace of the working compartment after each bulk electrolysis was determined and the total amount of H$_2$ in the headspace of the working compartment was calculated. The headspace volume was calculated by subtracting the volume of the working solution from the volume of the working compartment containing the glass–like carbon disk electrode.

**Foot–of–the–Wave Analysis.** Data from the CVs of each Fe–porphyrin were analyzed by the methods developed by Costentin et. al.$^{33}$ Observed currents from the catalytic waves were baseline corrected by subtracting the diffusion limited current after the Fe$^{III/II}$ reduction (between –1.1 and –1.2 V vs. Fc$^+$/Fc), then divided by the peak current
of the Fe-porphyrins in the absence of H+ ($i_0$), which was baseline corrected in the same manner. Slopes at the foot of the wave were obtained from linear fits of all data

$1 < \frac{i}{i_0} < 3$ for HPDFe–Ph and HPDFe–DMA whereas slopes for HPDFe–3SA and A₄Fe were obtained from linear fits of all data $1 < \frac{i}{i_0} < 5$. The data over these ranges are good linear fits and are sufficient given the limited data in the $\frac{i}{i_0}$ direction. Due to the fact that the values of $k$ are reported on the log scale, any errors in linear fits make little to no difference in the values of log($k$), and error bars are not reported. Normalized current for catalytic enhancement was plotted vs. $[1 + \exp(\frac{F}{RT} E - E^0)]^{-1}$ where $E^0$ is the half-wave potential for the FeII/I reduction determined for each Fe-porphyrin in the absence of acid and $E$ was the applied potential.

**Derivation of $E_{HA} H_2$ for [TsOH•OTs]⁻.** $E_{[TsOH•TsO^-]} H_2$ was derived from the following thermodynamic cycle:

$$2 \text{H}^+ + 2 e^- \rightleftharpoons \text{H}_2$$

$$2 \text{TsOH} \rightleftharpoons 2 \text{H}^+ + 2 \text{[TsO]}^{-}$$

$$2 \text{TsOH} \cdot \text{TsO}^- \rightleftharpoons 2 \text{[TsO]}^{-} + 2 \text{TsOH}$$

$$2 \text{[TsOH} \cdot \text{TsO}^-] \rightleftharpoons \text{H}_2 + 4 \text{[TsO]}^{-}$$

$E_{H^+ H_2}$ in CH₃CN has been determined by Roberts et. al.⁶⁹ to be $-0.028$ V vs. Fc⁺/Fc. The potential may be converted to free energy,

$$\Delta G = -nFE$$

$$\Delta G = -(2)(96,485 \text{ J V}^{-1} \text{ mol}^{-1})(-0.028 \text{ V})$$

$$\Delta G = 5.4 \text{ kJ mol}^{-1}$$
Using the p$K_a$ of TsOH in CH$_3$CN (8.6),$^{45}$ the free energy of acid dissociation is:

\[
K_a = 10^{-8.6}
\]

\[
\Delta G = -RT\ln K_a
\]

\[
\Delta G = -8.314 \frac{J}{\text{mol K}} \times 298 \text{ K} \times \ln 10^{-8.6}
\]

\[
\Delta G = 49 \text{ kJ mol}^{-1}
\]

Using the inverse of the homoconjugation equilibrium constant, the free energy of homoconjugate dissociation is:

\[
K_a = 10^{-2.9}
\]

\[
\Delta G = -RT\ln K_a
\]

\[
\Delta G = -8.314 \frac{J}{\text{mol K}} \times 298 \text{ K} \times \ln 10^{-2.9}
\]

\[
\Delta G = 17 \text{ kJ mol}^{-1}
\]

Summing the free energy for each step and taking stoichiometry into account, the free energy of the net process is obtained.

\[
\Delta G_{\text{tot}} = 5.4 + 2 \times 49 + 2 \times 17 \text{ kJ mol}^{-1}
\]

\[
\Delta G_{\text{tot}} = 137 \text{ kJ mol}^{-1}
\]

Converting the additional free energy from homoconjugate dissociation and acid dissociation to potential yields,

\[
\Delta G_{\text{tot}} = -nFE_{\text{TSOH-TSO}^- \text{ H}_2}
\]

\[
-\frac{\Delta G}{nF} = E_{[\text{TSOH-TSO}^- \text{ H}_2]}
\]

\[
-137,000 \text{ J mol}^{-1} \div 2 \times 96,485 \text{ J V}^{-1}\text{mol}^{-1} = E_{[\text{TSOH-TSO}^- \text{ H}_2]}
\]

\[
-0.71 \text{ V} = E_{[\text{TSOH-TSO}^- \text{ H}_2]}
\]
4.5 References


66. Additional experimental information, including UV-vis spectra, cyclic voltamograms, gas chromatographs, mass spectra, and additional FOWA, are available online from Graham DJ, Nocera DG (2014) *Organometallics*, **33**, 4994.
Chapter 5 – Electron Transfer Behavior of Peroxide

Dianion in a Hydrogen Bond–Rich Molecular Capsule

Portions of this chapter have been published:


5.1 Introduction

Aerobic life is driven by the thermodynamic potential provided by oxygen gas \((O_2)\). In its ground state, \(O_2\) is kinetically stable with respect to the chemical bonds found in living organisms. The controlled activation of \(O_2\) in nature is mediated by electron transfer (ET) to produce its diatomic congener superoxide \((O_2^-)\) and peroxide dianion \((O_2^{2-})\).\(^1\) In non–aqueous environments, \(O_2^-\) is stable in the absence of electrophilic species such as protons or metal ions, and the anion exhibits reversible ET behavior; accordingly, the outer–sphere oxidation of \(O_2^-\) has been comprehensively studied using chemical and electrochemical techniques.\(^2\)-\(^4\) This chapter details the ET chemistry of \(O_2^{2-}\) as an isolated species, which was previously ill–defined because it is not readily available in a soluble form. \(O_2^{2-}\) is extremely unstable in non–aqueous conditions owing to its ability to act as a strong Brønsted–Lowry base.\(^5\) For example, the electrochemical reduction of \(O_2^-\) at a gold electrode in DMSO in the presence of tetraethylammonium
 perchlorate ([TEA+] [ClO$_4^-$]) results in the deprotonation–induced decomposition of the [TEA+] cation to form protonated peroxide (HO$_2^-$), which in turn, oxidizes DMSO to dimethyl sulfone. O$_2^{2-}$ is stabilized by coordination to a metal ion and hence the intrinsic oxidation–reduction properties of the isolated dianion are difficult to establish owing to metal–oxygen orbital mixing and electrostatic effects. Given the importance of O$_2^{2-}$ as a deleterious reactive oxygen species (ROS) in the biochemical reduction of O$_2$, as a valuable industrial feedstock, and, in particular, as a primary discharge product in non–aqueous lithium–air batteries, it is desirable to understand the basic ET properties of O$_2^{2-}$ uncoupled from the complicating effects of protons or metal ions.

Reduction of O$_2$ to O$_2^{2-}$ is typically accomplished in chemical and biological systems in the stabilizing coordination sphere of a transition metal. Such peroxide transition–metal complexes are important intermediates in natural oxidation processes, and they have long been employed as reagents for organic synthesis. Laboratory generation of soluble sources of O$_2^{2-}$ is a challenge in dioxygen chemistry. The reactivity of O$_2^{2-}$ renders its stabilization in organic media difficult. This chapter describes the chemically reversible reduction of O$_2$ to cryptand–encapsulated O$_2^{2-}$, which can be interrogated with computational modeling and electrochemical techniques to unveil the charge transfer behavior of O$_2^{•-}$ and O$_2^{2-}$ in the absence of metal ions. We discovered that a hexacarboxamide cryptand (mBDCA–5t–H$_6$) of a type introduced originally as receptors for halide ions, and investigated by us as binucleating ligands for transition–metal ions, form soluble 1:1 complexes with peroxide dianion wherein
O$_2^{2-}$ resides in a molecular interior surrounded by six carboxamide N–H hydrogen bond donors in a trigonal prismatic array (Figure 1).

A structural basis for O$_2^{2-}$ stabilization via hydrogen bonding as opposed to a metal ion has appeared in the context of sodium peroxide crystallization with 1,6-anhydro-β-maltose. The reported complex salt of formula [Na$_2$(1,6-anhydro-β-maltose)$_2$(H$_2$O)$_3$][O$_2^{2-}$] has a layered structure featuring six hydrogen bonds that encase each O$_2^{2-}$ ion, with sugar O–H groups acting as the hydrogen–bond donors. This O$_2^{2-}$ environment is reminiscent of that determined for Na$_2$O$_2$•8H$_2$O, in which chains of edge–connected [Na(OH$_2$)$_6$]$^+$ octahedra are linked together by O–H⋯O peroxide/water hydrogen bonds.
$O_2^{2-}$ is stabilized by strong hydrogen bonds to N–H groups from $m$BDCA–5t–$H_6$. Similar interactions have been observed in biological systems where peroxide is generated by reduction of dissolved oxygen and is stabilized by hydrogen bonding. The peroxide adducts of cryptand are stable at room temperature in dimethysulfoxide (DMSO) and $N,N$-dimethylformamide (DMF) and can be obtained in gram quantities from the cryptand–driven disproportionation reaction of potassium superoxide ($KO_2$) at room temperature. $m$BDCA–5t–$H_6$ stabilize peroxide dianion to such an extent that if it is present in the same solution, $O_2^{2-}$ undergoes disproportionation to form $O_2$ and encapsulated $O_2^{2-}$, thus coupling the anion receptor molecular recognition phenomenon to an oxidation–reduction process.

When encapsulated by $m$BDCA–5t–$H_6$, $O_2^{2-}$ does not interact with surrounding cations and $O_2$ is released upon exposure to chemical oxidants. This simple oxidative ET serves as a model for the desired half-reaction needed for a rechargeable lithium–oxygen (Li–O$_2$) battery, for which a large overpotential is required. This overpotential has been the subject of numerous studies$^{23-25}$ and remains a hurdle in the pursuit of a practical metal–air battery.$^{26}$ This chapter details the ET kinetics of chemical and electrochemical oxidation of $[(O_2^{2-})_{2}c_{m}$BDCA–5t–$H_6]$ by ET with the goal of providing insight into the inherent properties germane to oxidation of $O_2^{2-}$. Knowledge of the ET behavior from discrete $O_2^{2-}$ is useful not only for the design of metal–air batteries capable of recharging at lower overpotentials, but also for the informed use of cryptand–encapsulated $O_2^{2-}$ as an oxidant and/or atom transfer reagent, in chemical transformations.
5.2 Results and Discussion

5.2.1. Chemistry of the Cryptand

Observations of chemical reactivity can inform mechanistic studies. Encapsulation preferences of cryptand have emerged from studies by the Cummins and Bowman–James labs. For instance, the encapsulation of O$_2^{2-}$ by an empty cryptand is achieved starting from O$_2^{-}$, either by treating a cryptand solution with potassium superoxide (KO$_2$) or the combination of O$_2$ gas and a reductant capable or reducing O$_2$ in situ. Treatment of a slurry of mBDCA–5t–H$_6$ with 2.2 equivalent of KO$_2$ in DMF results in the formation of the O$_2^{2-}$ adduct K$_2$(DMF)$_5$[(O$_2^{2-}$)⊂mBDCA–5t–H$_6$] in 74% isolated yield. The [(O$_2^{2-}$)⊂mBDCA–5t–H$_6$] adduct can also be obtained by reducing O$_2$ in situ with 2 equivalents of cobaltocene (CoCp$_2$) in the presence of 1 equivalent of free cryptand in DMF. Vigorous bubbling was observed immediately after adding KO$_2$, which has been identified by mass spectrometry as O$_2$. Further evidence for O$_2^{2-}$ can be seen in the $^1$H nuclear magnetic resonance (NMR) spectrum, which indicates the formation of a O$_2^{2-}$ adduct in which the amide chemical shift is in the range of a normal charged hydrogen bond (NCHB) interaction.$^{27}$

K$_2$(DMF)$_5$[(O$_2^{2-}$)⊂mBDCA–5t–H$_6$] was characterized by X–ray diffraction studies using single crystals obtained by vapor diffusion of diethyl ether into DMF solutions. The O–O bond length of 1.504(2) Å for K$_2$(DMF)$_5$[(O$_2^{2-}$)⊂mBDCA–5t–H$_6$] is comparable to that in ribonucleotide reductase Ib (1.47 Å),$^{28}$ in 1,6–anhydro–β–maltose adduct (1.496(2) Å) (6), and in Na$_2$O$_2$ (1.49 Å),$^{29}$ are indicative of the peroxide character of the O$_2$ moiety. The complementarity of the six amide protons with the six lone pairs of
O$_2^{2-}$ results in N⋯O distances in the range of 2.64–2.73 Å for $K_2$(DMF)$_5$[(O$_2^{2-}$)$_{-}m$BDCA–5t–H$_6$]; these short distances are indicative of strong hydrogen bonds. The aryl protons pointing inside the cavity also interact with O$_2^{2-}$, with C⋯O distances ranging from 3.16 Å to 3.23 Å for $K_2$(DMF)$_5$[(O$_2^{2-}$)$_{-}m$BDCA–5t–H$_6$]; these distances are indicative of weak hydrogen bonds. Thus, O$_2^{2-}$ is stabilized by a combination of six strong hydrogen bonds to six amide protons and six weak hydrogen bonds to three aryl protons (Figure 1).

$K_2$(DMF)$_5$[(O$_2^{2-}$)$_{-}m$BDCA–5t–H$_6$] is stable in solution at room temperature for at least one month, and remains intact even after heating for 100 min at 50 °C. The molecular recognition of O$_2^{2-}$ is reversible. Attempts at oxidizing $K_2$(DMF)$_5$[(O$_2^{2-}$)$_{-}m$BDCA–5t–H$_6$] with 2 equivalents of ferrocenium trifluoromethanesulfonate (FcOTf) or 1 equivalent of the convenient two-electron oxidant, XeF$_2$, results in quantitative production of free cryptand as indicated by $^1$H NMR spectroscopy. Interestingly, no O$_2$ was observed when either XeF$_2$ or FcOTf were used as oxidants and the fate of O$_2^{2-}$ remains unknown. Gas chromatography (GC) revealed CO$_2$ and Xe in the headspace of the XeF$_2$ reaction and no gaseous products above the FcOTf reaction. This is most likely due to the fact that ferrocene (Fc) is known to react with O$_2$ and O$_2^{*}$, while XeF$_2$ might be strong enough of an oxidant to attack the solvent and provide a pathway for decomposition products that can react with O$_2^{*}$ or O$_2^{2-}$. O$_2$ was released in 88% yield as determined by GC and MS when the same oxidation was attempted with the slow addition of 1.1 equivalent of the two electron oxidant 2,3-dichloro–5,6–dicyano–1,4–
benzoquinone (DDQ). Thus, we can summarize the known reaction chemistry of O₂ and \textbf{mBDCA–5t–H₆} in Figure 2.

**Figure 5.2.** Encapsulation of O₂²⁻ through disproportionation of O₂⁻⁻ (top) or \textit{in situ} reduction of O₂ by CoCp₂ (bottom). Treatment of the product complex with DDQ oxidatively liberates O₂.

### 5.2.2 Electrochemical Studies of O₂ in the Presence of Cryptand

The observed chemical reactivity for reversible peroxide encapsulation is supported by the electrochemistry of the cryptand in the presence of O₂. The reduction of O₂ to O₂⁻⁻ solvated by large cations such as tetrabutyl ammonium ([TBA⁺]) is reversible in aprotic solvents.\(^{32}\) Whereas \textbf{mBDCA–5t–H₆} shows no redox features from 0.25 to –2.3 V vs Ag⁺/Ag, several new features are observed in the cyclic voltammograms of the cryptand in the presence of O₂ as shown in Figure 3a. Upon scanning to negative potentials, an additional sharp reduction wave appears positive of the O₂ reduction wave (Figure 3), while a new wave simultaneously appears on the positive sweep at ~ –0.7 V. The current associated with these new reduction and oxidation waves increases
with increasing concentration of the cryptand, while the oxidation associated with $O_2^{•-}$ decreases.

![Cyclic voltammograms measure of $O_2$-saturated (4.8 mM) DMF (0.1 M $[TBA^+][ClO_4^-]$) in the presence of 0.0 mM $mBDCA-5t-H_6$ (red), 4.8 mM $mBDCA-5t-H_6$ (green) and 9.6 mM $mBDCA-5t-H_6$ (blue) at a scan rate of 10 mV/s.](image)

**Figure 5.3.** Cyclic voltammograms measure of $O_2$-saturated (4.8 mM) DMF (0.1 M $[TBA^+][ClO_4^-]$) in the presence of 0.0 mM $mBDCA-5t-H_6$ (red), 4.8 mM $mBDCA-5t-H_6$ (green) and 9.6 mM $mBDCA-5t-H_6$ (blue) at a scan rate of 10 mV/s.

Based on the reaction chemistry depicted in Figure 2, we propose that the new reduction wave in Figure 3 results from the ability of $mBDCA-5t-H_6$ to rapidly sequester $O_2^{•-}$, which is formed at the cathode and to facilitate subsequent transfer of a second electron from either the electrode or another molecule of $O_2^{•-}$. The sharp decrease in current responsible for the shape of the peak is indicative of the rapid depletion of free cryptand near the electrode, a phenomenon that is due to (i) the ease with which $mBDCA-5t-H_6$ reacts with $O_2^{•-}$ and (ii) the sluggish diffusion of $mBDCA-5t-H_6$ to the electrode relative to free $O_2$. As the working electrode potential decreases
further, one-electron reduction of $O_2$ produces a steady supply of $O_2^-$, which can react with $m$BDCA–5t–$H_6$ as it diffuses away from the electrode.

Evidence for the release of $O_2$ upon oxidation of $K_2$(DMF)$_5$[($O_2^{2-}$)$\subset m$BDCA–5t–$H_6$] at a glass–like carbon electrode was obtained from a 4.8 mM solution of cryptand peroxide adduct in DMF (0.1 M [TBA$^+$$][ClO_4^-]$) using a rotating ring disk electrode by scanning the potential of the disk and holding the ring potential constant (Figure 4). During a potential scan of the disk electrode, a collection current is observed only when the ring is fixed to a potential sufficient for $O_2$ reduction.

**Figure 5.4.** Rotating ring disk electrode measurements of 4.8 mM $K_2$DMF$_5$[($O_2^{2-}$)$\subset m$BDCA–5t–$H_6$] in DMF (0.1 M [TBA$^+$$][ClO_4^-]$). (Left, top) Potential of disk electrode vs. time. (Left, Bottom) Observed current on disk (black ■) and ring (red □) while fixed at $-2.0$ V vs. Ag$^+$/Ag, a potential sufficient to reduce $O_2$ in solution. (Right, top) Potential of disk electrode vs. time. (Right, bottom) Observed current on disk (black ■) and ring (red □) when fixed to $-1.0$ V vs. Ag$^+$/Ag, a potential which is unable to reduce $O_2$ in solution.
The release of O$_2$ can also be observed in cyclic voltammograms of the same solution where no features are observed during an initial scan to negative potentials, a reductive wave appears only after oxidation of [$(O_2^{2-})_{m}BDCA-5t-H_6$] at the electrode (Figure 4).

![Cyclic voltammogram](image)

**Figure 5.5.** Cyclic voltammogram of argon–saturated DMF (0.1 M [TBA$^+$][ClO$_4^-$]) in the presence of 4.8 mM $K_2(\text{DMF})_5[O_2^{2-}\subset mBDCA-5t-H_6]$ displaying the release of O$_2$ upon oxidation (at a scan rate of 100 mV/s).

This measurement of independently prepared $K_2(\text{DMF})_5[O_2^{2-}\subset mBDCA-5t-H_6]$ in argon–saturated solution show predominant oxidation at $\sim -0.7$ V and subsequent reduction at $\sim -1.4$ V, which supports observations indicating that these two features correspond to the oxidation of $[O_2^{2-}\subset mBDCA-5t-H_6]$ with concomitant release of O$_2$, and reformation of $mBDCA-5t-H_6$, respectively (Scheme 1).
**Scheme 5.1.** Proposed mechanism of the reversible cryptand–facilitated O₂ reduction to encapsulated O₂²⁻.

### 5.2.3 Computational Modeling of Electrochemical Studies

The proposed mechanism in Scheme 1 was modeled computationally in order to gain insight into the relative rates of each step. The optimized simulation of the CV is shown in Figure 5. Parameters obtained from the simulation are collected in Tables 1 and 2.
Figure 5.6. Cyclic voltammogram of 9.6 mM solution of mBDCA–5t–H₆ in O₂–saturated DMF (0.1 M [TBA⁺][PF₆⁻])(black —), simulated cyclic voltammogram (red —) using the mechanistic steps described in Scheme 1.

Table 5.1. Reactions and parameters used for simulation reactions i–iv (Scheme 1) of the CV of O₂ reduction in DMF (0.1 M [TBA⁺][ClO₄⁻]) in the presence of 9.6 mM mBDCA–5t–H₆ at 10 mV/s (Figure 5). E₀ is the standard reduction potential, kₛ is the electron transfer rate constant, α is the transfer coefficient, Kₑq is the equilibrium constant for the reaction, and k₉ is the forward rate constant. L represents mBDCA–5t–H₆, [LO₂⁺⁻] and [LO₂²⁻] represent cryptand complexes of O₂⁻⁻ and O₂²⁻, respectively.
Species & Diffusion Coefficient (cm$^2$ s$^{-1}$)
\hline
O$_2$ & 7.892 × 10$^{-5}$
O$_2$$^-$ & 2.475 × 10$^{-5}$
L & 3.505 × 10$^{-6}$
[LO$_2$$^-$] & 5.068 × 10$^{-6}$
[LO$_2$$^{2-}$] & 7.182 × 10$^{-7}$
\hline

Table 5.2. Diffusion coefficients obtained from the fitting the CV of O$_2$ reduction in DMF (0.1 M [TBA$^+$][ClO$_4^-$]) in the presence of 9.6 mM $m$BDCA–5t–H$_6$ at 10 mV/s (Figure 5). L represents $m$BDCA–5t–H$_6$, [LO$_2$$^-$] and [LO$_2$$^{2-}$] represent cryptand complexes of O$_2$$^-$ and O$_2$$^{2-}$, respectively.

Insight from the model suggests that an initial one–electron reduction of O$_2$ by the electrode is the means by which O$_2$$^-$ formation occurs. Our model suggests that rapid encapsulation of O$_2$$^-$ by free cryptand drives further one–electron reduction, either directly by the working electrode or through a disproportionation reaction with free or encapsulated O$_2$$^-$, resulting in the formation of [(O$_2$$^{2-}$)$_{m}$BDCA–5t–H$_6$] and decreasing the effective concentration of O$_2$$^-$ near the electrode. Since the reduction of O$_2$ is electrochemically reversible and the concentrations of O$_2$ and O$_2$$^-$ near the electrode obey the Nernst equation at all times during the potential sweep, sequestering O$_2$$^-$ perturbs that equilibrium and induces additional current to be drawn from the electrode to reduce O$_2$ until all $m$BDCA–5t–H$_6$ near the electrode has been converted to [(O$_2$$^{2-}$)$_{m}$BDCA–5t–H$_6$]. Using the steps displayed in Scheme 1, this sharp feature can be reproduced by the simulation when it is assumed that the diffusion coefficient of O$_2$ is much greater than that of the cryptand species (Table 2) in DMF containing 0.1 M [TBA$^+$][ClO$_4^-$]. An appropriate fit for the anodic sweep could only be accomplished by modeling the oxidation of [(O$_2$$^{2-}$)$_{m}$BDCA–5t–H$_6$] as a series of two, one–electron oxidations.
The foregoing simulation was completed with the assumption that the electron transfer obeys Butler–Volmer kinetic model of electron transfer. Further interrogation revealed that it was possible to study the charge transfer kinetics of cryptand–encapsulated peroxide with much greater detail by first collecting CVs of \([\text{O}_2^{2-}\subset\text{mBDCA–5t−H}_6]\) at a variety of different scan rates. (Figure 6).

**Figure 5.7.** Experimental CVs (black —) and simulated CVs (red —) of 0.5 mM \([\text{TBA}^+]_2[\text{O}_2^{2-}\subset\text{mBDCA–5t−H}_6]\) in DMF (0.1 M [TBA\(^+\)][PF\(_6^−\)]) at (a) 50 mV/s, (b) 100 mV/s, (c) 250 mV/s, and (d) 500 mV/s. The first sweep is in the positive direction.

The peak current \((i_p)\) of the feature corresponding the oxidation of \(\text{O}_2^{2-}\) was found to vary linearly with the square root of scan rate \((\nu)\), indicating well-defined Cottrell kinetics for a soluble diffusion controlled species. Interestingly, the peak potential \((E_p)\) of that same feature varied linearly with \(\log(\nu)\) at a rate of 95 mV/decade.
which is inconsistent with an electrochemically reversible electron transfer or an
electron transfer followed by a chemical step (30 mV/decade) according to Butler–
Volmer kinetics for $\alpha = 0.5$. This result together with the broadness of the oxidation
wave indicates that electron transfer attendant to the cryptand–peroxide oxidation
process is not an electrochemically or chemically facile process.

The broad oxidation wave may be modeled according to the Butler–Volmer
formalism using $\alpha = 0.38$ for the one electron oxidation of $[\text{TBA}^+]_2[(\text{O}_2^2-)\text{mBDCA–5t–H}_6]$. This contrasts typical values of $\alpha$, which are almost always very close to 0.5.

Accordingly, the data was analyzed with a more complete Marcus–Hush model of
electrode kinetics, using $\alpha = 0.38$ and varying the reorganization energy ($\lambda$). Figure 6
shows that a satisfactory representation of the data is achieved for all scan rates using
electrochemical simulation software, such as

<table>
<thead>
<tr>
<th>Reaction</th>
<th>$E^0$ (V vs. Ag$^+$/Ag)</th>
<th>$\lambda$ (eV)</th>
<th>$k_s$ (cm$^2$ s$^{-1}$)</th>
<th>$K_{eq}$</th>
<th>$k_f$ (M$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>i</td>
<td>$\text{O}_2 + e^- \rightleftharpoons \text{O}_2^{2-}$</td>
<td>-1.31</td>
<td>1.5</td>
<td>$9.3 \times 10^{-2}$</td>
<td></td>
</tr>
<tr>
<td>ii</td>
<td>$L + \text{O}_2^{2-} \rightleftharpoons [\text{LO}_2^{2-}]$</td>
<td>-0.85</td>
<td>0.79</td>
<td>$2.7 \times 10^{-5}$</td>
<td>$1.2 \times 10^6$</td>
</tr>
<tr>
<td>iii</td>
<td>$[\text{LO}_2^{2-}] + e^- \rightleftharpoons [\text{LO}_2^{2-}]$</td>
<td>-0.85</td>
<td>0.79</td>
<td>$2.7 \times 10^{-5}$</td>
<td>$1.2 \times 10^6$</td>
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<tr>
<td>iv</td>
<td>$[\text{LO}_2^{2-}] + \text{O}_2^{2-} \rightleftharpoons [\text{LO}_2^{2-}] + \text{O}_2$</td>
<td>-0.85</td>
<td>0.79</td>
<td>$2.7 \times 10^{-5}$</td>
<td>$1.2 \times 10^6$</td>
</tr>
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</table>

**Table 5.3.** Reactions and parameters used for simulation reactions i–iv (Scheme 1) of
the CV of O$_2$ reduction in DMF (0.1M [TBA$^+$][PF$_6^-$]) in the presence of 0.5 mM $\text{mBDCA–5t–H}_6$ at different scan rates (Figure 6). $E^0$ is the standard reduction potential, $k_s$ is the
electron transfer rate constant, $K_{eq}$ is the equilibrium constant for the reaction, and $k_f$ is the
forward rate constant. L represents $\text{mBDCA–5t–H}_6$, $[\text{LO}_2^{2-}]$ and $[\text{LO}_2^{2-}]$ represent
cryptand complexes of O$_2^{2-}$ and O$_2^{2-}$, respectively.
Table 5.4. Diffusion coefficients obtained from the fitting the CV of O$_2$ reduction in DMF (0.1M [TBA$^+][PF_6^-]$) in the presence of 0.5 mM $m$BDCA–5t–H$_6$ at the various scan rates (Figure 6). L represents $m$BDCA–5t–H$_6$, [LO$_2^+$] and [LO$_2^{2-}$] represent cryptand complexes of O$_2^+$ and O$_2^{2-}$, respectively.

DigiElch,\textsuperscript{34} with a reorganization energy $\lambda = 0.79$ eV, an electron transfer rate constant of $k_s = 2.7 \times 10^{-5}$ cm s$^{-1}$ and a standard reduction potential of $-0.85$ V vs. Fc$^+$/Fc for O$_2^+$/O$_2^{2-}$ within the cryptand (Tables 3 and 4). The poor fit at low scan rates of the reduction of free O$_2$ is ascribed to unwanted convection contributions to the current.

The electron transfer behavior of $[\text{[O}_2^{2-}\text{]mBDCA–5t–H}_6]$ was further interrogated in its reaction with a series of quinones. Chemical variations on the quinone ring change their reduction potential, which in turn changes the driving force of the overall electron transfer. Stopped–flow UV–vis monitoring of $[\text{[O}_2^{2-}\text{]mBDCA–5t–H}_6]$ oxidation by various quinones in rapidly–mixed THF solutions gave experimental values for the initial electron transfer from O$_2^{2-}$ within the cryptand as the driving force of the reaction is systematically varied. Using this data, it was possible to perform a complete Marcus analysis of the homogeneous electron transfer, the result of which gave a value 1.7 eV for the $\lambda$ associated with the self–exchange reaction of $[\text{[O}_2^{2-}\text{]mBDCA–5t–H}_6]$ and $[\text{[O}_2^{+}\text{]mBDCA–5t–H}_6]$. An estimate of $\lambda$ for the one–electron oxidation of $[\text{[O}_2^{2-}\text{]mBDCA–5t–H}_6]$ at an electrode can be obtained by taking one half
of the value of the bimolecular self-exchange $\lambda$. This estimate gives a $\lambda$ value of 0.85 eV, which is consistent with the $\lambda$ value obtained by computer modeling of 0.79 eV.

5.3 Conclusion

The electrochemistry of $m$BDCA–5t–H$_6$ in the presence of oxygen is consistent with reduction of oxygen by one electron to superoxide followed by incorporation into the cryptand cavity, in turn driving disproportionation to give the cryptand encapsulated peroxide adduct. Oxidation of peroxide dianion within the cavity restores oxygen and the free cryptand ligand. The proposed electrochemical mechanism in Scheme 1 maps on to the observed chemical reactivity of Figure 2; the combined chemical and electrochemical studies demonstrate encapsulation–driven chemically reversible two-electron reduction of O$_2$ to O$_2^{2-}$.

We have synthesized a molecular peroxide adduct by the use of the cavity of hexacarboxamide cryptands as a molecular recognition site. Reduction of O$_2$ in situ and stabilization of O$_2^{2-}$ is facilitated by hydrogen bonding within the cavity of the cryptand. This process mimics the structural characteristics of biological systems that utilize peroxide as an oxidant. The use of molecular recognition of an in situ generated reactive oxygen species has the potential to be incorporated into several technologies including Li–O$_2$ batteries because it is chemically reversible, prevents overreduction to lithium oxide, and imparts significant solubility in aprotic media.$^{35}$ In addition, because the O$_2^{2-}$ adducts can be obtained in high yield in a one-pot reaction and are stable in solution, they could be used as a soluble source of O$_2^{2-}$ for a variety of reactions.
The fact that $O_2^{2-}$ may be isolated within the cage of a hexacarboxamide cryptand allows for the electron transfer reactivity of $O_2^{2-}$ to be examined. The electron transfer reaction of the encapsulated $O_2^{2-}$ with quinones is consistent with outer sphere electron transfer owing to steric shielding of $O_2^{2-}$ from its reacting partner by $m$BDCA-$5t$-$H_6$.

These results correlate well with the heterogeneous electron transfer rate measurements, which exhibit an apparent transfer coefficient of $\alpha < 0.5$, but modeling the $[(O_2^{2-})\subset m$BDCA-$5t$-$H_6]$ electrochemical response within a Marcus theory framework yields a consistent set of results for the homogeneous and heterogeneous electron transfer reactions. The $\lambda$ obtained from the modeling of a heterogeneous electron transfer is consistent with that obtained in a homogeneous Marcus analysis. This is one of the few cases\textsuperscript{36,37} where a direct comparison between homogeneous and heterogeneous ET reactions for a given species has been made. Understanding the intrinsic parameters that govern the kinetics of electron transfer from this unique species will facilitate its development as a reagent for oxidations, reductions, and/or atom transfer chemistries.

The most fundamental reaction of all molecular oxygen species is electron transfer. Owing to our success in using a macro–bicyclic anion receptor\textsuperscript{38} to furnish an isolated $O_2^{2-}$ species that is soluble in aprotic organic media, the kinetics of the transfer of an electron from the $O_2^{2-}$ in the absence of an intimately bound proton or metal ion have now been established. Considering the importance of $O_2^{2-}$ as an intermediate in biochemical redox processes, as a valuable industrial feedstock, and as a primary discharge product in non–aqueous lithium–air batteries, the results reported herein
provide a basis for elucidating the chemistry of peroxide in a range of subjects pertaining to oxygen atom and electron transfer.

5.4 Experimental Section

General Considerations. All manipulations were performed either using Schlenk techniques or in a nitrogen–atmosphere glovebox. All reagents were purchased from Aldrich. Quinones were sublimed three times. Solvents (EMD Chemicals) were either used as received or purified on a Glass Contour Solvent Purification System built by SG Water USA, LLC. IR spectra were recorded on a Bruker Tensor 37 Fourier transform IR (FTIR) spectrometer. NMR solvents were obtained from Cambridge Isotope Laboratories, and ¹H and ¹³C{¹H} NMR spectra were obtained on a Varian 300 MHz or a Bruker 400 MHz spectrometer and are referenced to residual solvent signals. Elemental analyses were performed by Midwest Microlabs, LLC. mBDCA–5t–H₆,²⁰ [K₂(DMF)₅][(O₂⁻)⊂mBDCA–5t–H₆],²⁰ [TBA⁺]₂[(O₂⁻)⊂mBDCA–5t–H₆],⁴⁰ and [K(18–crown–6)]₂[(O₂⁻)⊂mBDCA–5t–H₆]⁴⁰ were synthesized according to the literature.

X–ray Crystallography. Low–temperature diffraction data were collected on a three–circle diffractometer coupled to a Bruker–AXS Smart Apex charged–coupled device (CCD) detector with graphite–monochromated Mo Kα radiation (λ= 0.71073 Å) for the structure of [K(18–crown–6)]₂[(O₂⁻)⊂mBDCA–5t–H₆], performing φ– and ω–scans. The structures were solved by direct methods using SHELXS and refined against F² on all data by full–matrix least squares with SHELXL–97 using established methods.⁴¹ All non–hydrogen atoms were refined anisotropically.⁴²
**Cyclic Voltammetry.** CVs were collected using a CH Instruments (Austin, Texas) 730C Potentiostat. For static solutions, the working electrode was a glass–like carbon button electrode with a 0.07 cm$^2$ area, the counter electrode was a Pt wire, and the Ag wire pseudoreference electrode was separated from the working solution by a vycor frit in a DMF solution containing 0.1 M tetrabutylammonium hexafluorophosphate ([TBA$^+$][PF$_6^-$]) or [TBA$^+$][ClO$_4^-$]. Rotating ring–disk electrode measurements used a glass–like carbon disk and platinum ring calibrated to a collection efficiency of 0.275 using in DMF. The reference electrode was a non–aqueous Ag/Ag$^{+}$ electrode from BASi, which consisted of a Ag wire immersed in 0.1 M [TBA$^+$][PF$_6^-$] from Sigma–Aldrich and 0.01 M AgNO$_3$ (BASi) in propylene carbonate:dimethoxy ethane (PC:DME) 1:2 v/v solution connected to the main compartment by a Vycor frit. Potentials were referenced to the Fc$^+/$/Fc reduction potential. The counter electrode was Ni foam or Pt wire. The electrolyte was either 0.1 M [TBA$^+$][ClO$_4^-$] or 0.1 M [TBA$^+$][PF$_6^-$] in anhydrous DMF (Sigma–Aldrich). The cryptand was dissolved in solution at various concentrations indicated in the text. When saturated, the concentration of oxygen in DMF is 4.8 mM.$^{43}$

For the scan rate dependence studies, solutions of 0.5 mM solutions of [TBA$^+$]$_2$[(O$_2$)$_2$–mBDCA–5t–H$_6$] in DMF (0.1 M [TBA$^+$][PF$_6^-$]) were prepared in a nitrogen glovebox. The cell was covered with a Teflon cap containing the electrodes and sealed with parafilm. It was then removed from the glovebox and immediately placed under a blanket of argon. The temperature was controlled by placing the cell in an ethylene glycol bath kept at 298 K. The working electrode was freshly polished glass–like carbon (area = 0.07 cm$^2$), the counter electrode was a Pt wire, and a fresh Ag wire in DMF (0.1 M [TBA$^+$][PF$_6^-$]) separated from the working solution by a vycor frit was used
as a pseudo-reference electrode. Prior to use, the DMF had been dried by passage through an alumina column followed by exposure to activated 4Å sieves overnight. At the conclusion of the experiments, ferrocene was added and all potentials were referenced to the Fc+/Fc couple.

**Electrochemical Modeling.** For the simulations probing peroxide oxidation in the cryptand at varying scan rates, the diffusion coefficient (D) and reduction potential (E°) of O₂ were determined from a CV of 4.6 mM (saturated) solution of O₂ in DMF (0.1 M [TBA⁺][PF₆⁻]). The diffusion coefficient (D) of O₂• was approximated as \( \frac{3}{4}D(O_2) \). The literature value for the heterogeneous rate constant (kₛ) of 0.093 cm s⁻¹ O₂ in DMSO (0.1 M [TBA⁺][ClO₄⁻]) was used. All other quantities were varied in the DigiElch software suite until a satisfactory fit to the experimental data was achieved with reasonable values.

### 5.5 References


Chapter 6 – Future Prospects for Electrocatalysis

Employing Hangman Macrocycles

6.1 Introduction

Through experimentation and optimization, electrocatalysis with HPDFe has been improved greatly after a new combination of electrolyte and additives was uncovered.¹ Cobalt (Co) and nickel (Ni) macrocycles are also known to be competent reduction catalysts in the cases of CO₂,² H⁺,³ and NO₂⁻.⁶ Since the HPD ligand can be synthesized on such a large scale and different hanging groups can be easily installed, a series of analogous HPD complexes of Co and Ni were also synthesized and characterized electrochemically.

6.2 Results and Discussion

6.2.1 Synthesis of HPDCo Complexes

The insertion of Co into porphyrins is a fairly straightforward procedure that generally involves elevated temperature and the presence of base. Our group has made strides using modern microwave reactor technology to decrease the necessary reaction time and side reactions.⁷

Insertion of Co followed the published procedure, where Co(OAc)₂ was employed as both the source of Co and the source of base. Microwaving at 60 °C for 6 hours in CHCl₃ resulted in a color change to deep red (Scheme 1). Thin layer chromatography was used to check for any remaining freebase porphyrin, which would fluorescence red
under UV light, and further purification by washing and column chromatography resulted in the isolation of various HPDCo complexes.

Scheme 6.1. Insertion of Co into porphyrins.

As opposed to the other porphyrins used in this chapter, HPDCo–3SA is difficult to isolate as a Co$^{II}$ species when the same procedures for metal insertion are used. This is due to the presence of O$_2$ and a strong intramolecular proton source in the form of a sulfonic acid. Co$^{II}$–porphyrins are known to reversibly bind O$_2$ to form a transient Co$^{III}$–superoxide complex. This Co–superoxo species may be trapped and protonated in the presence of an acid, resulting in the production of Co$^{III}$–porphyrin after dissociation of HO$_2^*$, which can disproportionate to H$_2$O$_2$ and O$_2$ in solution. The proton transfer should be aided by the presence of an intramolecular acid, as is the case in HPDCo–3SA.

The identity of Co$^{III}$–porphyrin is most apparent in the UV–vis spectra of all four Co–porphyrins. Even though O$_2$ was precluded from the HPDCo–3SA sample solution, its absorption maxima are red-shifted ~17 nm from all other Co–porphyrins in this
chapter (Figure 1). The mass spectrum of HPDCo–3SA does not show any evidence of an additional axial ligand, such as Cl⁻. Given that sulfonic acids and HCl have similar pKa’s in aprotic solvents such as CH₃CN, one would expect the intramolecular hanging sulfonate in HPDCo–3SA to have an advantage in terms of binding to Co⁺⁺. Therefore, until crystallographic evidence is obtained, HPDCo–3SA is assumed to be a Co⁺⁺ porphyrin with an intramolecular sulfonate serving as an axial ligand.

Figure 6.1. UV–vis spectra of 5 µM solutions of HPDCo–Ph (blue), HPDCo–DMA (red), HPDCo–3SA (green), and A₄Co (purple) in CH₃CN.

6.2.2 Synthesis of HPDNi Complexes

Ni insertions required excessive time for reaction completion. Prior methods employed a mixture of MeOH and CHCl₃, which sometimes required up to 24 hours for complete metal insertion. Acetonitrile (CH₃CN) has a higher boiling point than both MeOH and CHCl₃, allowing higher reaction temperatures to be achieved, leading to lower reaction times without the danger of explosion in the microwave. Triethylamine (NEt₃) is a strong base in CH₃CN, and as such it was used in combination as a reaction
solvent. Using Ni(OAc)$_2$(H$_2$O)$_4$ in excess as a source of Ni, the reaction time at 80 °C could be decreased to 4 hours and the resulting HPDNi complexes could be isolated cleanly after washing and column chromatography (Scheme 2).

Scheme 6.2. Insertion of Ni into porphyrins.

Crystals of A$_4$Ni suitable for single crystal x-ray diffraction were obtained from cooling a saturated EtOAc solution. The solid state structure of A$_4$Ni is a saddled porphyrin with a co-crystallized molecule of EtOAc (Figure 2).
6.2.3 Electrochemical Studies of HPDCo Complexes

The electrochemical analysis of HPDCo complexes were carried out in the same electrolyte solution as the HPDFe studies detailed in Chapter 4. They all display quasi-reversible Co^{III/II} waves at ~0.1 V vs. Fc^{+}/Fc, as expected for such a couple involving the gaining or loss of a ligand. The Co^{II/I} (~1.2 V vs. Fc^{+}/Fc) and Co^{I/I^{*}} (~2.3 V vs. Fc^{+}/Fc) waves are electrochemically reversible in the absence of H^{+} (Figure 3).
Figure 6.3. CVs of HPDCo–Ph (blue), HPDCo–DMA (red), HPDCo–3SA (green), and A₄Co (purple) in CH₃CN (0.1 M [TEA⁺][TsO⁻]) at a glassy carbon electrode with a scan rate of 50 mV/s.

In the presence of added HBF₄ (which generates [TsOH•OTs⁻] in situ), CVs of Co–porphyrins display an increase in current concomitant with the production of Co²⁻porphyrin (Figure 4).
Figure 6.4. CVs of HPDCo–Ph (a), HPDCo–DMA (b), HPDCo–3SA (c), and A4Co (d) in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) with H$^+$ concentrations (from added HBF$_4$) of 0 mM (▬ black), 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red).

Upon addition of acid, the increased current plateaus at ~3–4 times the peak current of the Co$^{II/III}$ reduction wave in the absence of H$^+$. If the Co$^I$ complex reacted with H$^+$ without inducing another electron transfer, the plateau current and the peak current of the Co$^{II/III}$ reduction wave in the absence of H$^+$ should be the same height. The plateau behavior at high acid concentrations suggests that the electro–generated Co$^I$ complex reacts with an equivalent of H$^+$, and then undergoes an additional reduction, in a so–called “ECE” mechanism. This process would account for the enhanced current that is observed.
Our group has previously investigated the mechanism of H₂ evolution in Co–porphyrins. Using hangman cobalt porphyrins with xanthene scaffolds and three pentafluorophenyl (C₆F₅) meso–substituents depicted in Figure 5, our group has shown that protonation of Co⁺ by a strong acid occurs at the metal center to generate a Co³⁺H species. This Co³⁺H intermediate is not hydridic enough to react with another equivalent of H⁺, however, and must be reduced by an additional electron to generate a Co²⁺H species before H₂ is released.

**Figure 6.5.** Hangman cobalt porphyrins used in previous work from our group to study the mechanism of electrocatalytic H₂ generation.

Co²⁺H–porphyrin is extremely reactive towards further protonation and release of H₂, owing to the partially filled dₓ² orbital on Co that results in a metal–hydride bond order of 0.5. If the proposed ECE mechanism for the Co–porphyrins described in this chapter proceeded through these steps, whereby the Co⁺ center is protonated and subsequently reduced to yield a Co²⁺H, one would expect to see much higher currents than are observed in Figure 4. In fact, even the CVs of Co–porphyrins used in the calculations are obviously different than those in Figure 4, in that the first feature at
1.0 V is a peak and not a plateau and the catalytic wave is much more pronounced (Figure 6).

Figure 6. CVs of 0.8 mM solutions of HPXCo–CO₂H (● black) and HPXCo–Br (● red) in CH₃CN (0.1 M [TBA][PF₆⁻]) in the presence of 10 mM TsOH.⁷

These observations suggest that the HPDCo complexes, along with A₄Co, behave differently than those used by the group for mechanistic studies. The key difference between these two classes of Co–porphyrins lies in the electronic effects imposed by the porphyrins meso–substituents; C₆F₅ groups are electron withdrawing and decrease the proton affinity of the porphyrin ring, whereas the 3,4,5–trimethoxyphenyl groups are electron releasing and have the opposite effect on the porphyrin ring. The Co¹ center itself is not particularly basic, and it is plausible that electron–rich carbons on the porphyrin ring are more easily protonated. The addition of two equivalents of H⁺ and two electrons to the β–pyrrole position on the porphyrin ring gives rise to a chlorin. During prolonged bulk electrolysis experiments with metalloporphyrins in the presence of H⁺, a gradual change of the working solution to green is often taken as a sign that the porphyrin ring itself is getting reduced and transforming into a chlorin, although
demetalated, protonated porphyrin is also green in color, so more analysis is needed before this conclusion can be definitively made. Indeed, bulk electrolysis experiments with HPDCo have resulted in green solutions.

These observations suggest that the porphyrin ring of HPDCo complexes described in this chapter are electron rich, leading to unwanted ring protonation and eventual reduction. Such chemistry accounts for the appearance of a plateau current in the presence of excess acid, as the reduction of Co$^{II}$–porphyrin to Co$^{I}$–chlorin requires the net transfer of three electrons from the electrode (Scheme 3).

Scheme 6.3. A possible mechanism for the multi-electron, multi-proton reduction of Co$^{II}$–porphyrin to Co$^{I}$–chlorin.

When the potential scan is extended to more negative potentials, a larger increase in current is observed. We cannot confidently attribute this apparent catalytic
current to a species in solution, since we cannot rule out side reactions and catalyst decomposition. Unfortunately, due to the complicated nature of the electrochemical and chemical steps, H₂ generation by these HPDCo complexes is unavailable to study by foot-of-the-wave (FOWA).

If a Co^{III}H species resulted from the reaction of Co¹ with acid, one might expect a ligand containing an intramolecular proton donor to have the advantage in evolving hydrogen, but this is apparently not the case. Synthesized HPD ligands seem to provide little benefit. The fact that all the porphyrins have similar current potential traces in Figure 3 suggests that the hanging groups make very little difference in the rate of protonation and follow-up reactions.

6.2.4 Electrochemical Studies with HPDNi Complexes

CVs of the Ni porphyrins with 3,4,5-trimethoxyphenyl meso-substituents all display an electrochemically reversible Ni¹/I reduction wave which is followed by a reversible Ni⁰/I⁻ feature. (Figure 7).
As is the case with their Co and Fe analogues, these Ni complexes display very similar reduction potentials due to their similarities between the ligands near the metal centers. Additionally, the variation of $E_{1/2}$(Ni$^{II}$/I) and $E_{1/2}$(Ni$^{I}$/0) is negligible when comparing A$_4$Ni and the HPDNi complexes. This result is also observed in the case of analogous Fe and Co porphyrins owing to the similar electronic influence of dibenzofuran and 3,4,5-trimethoxyphenyl meso-substituents. The presence of an additional oxidation feature at $\sim$–0.7 V vs Fc$^+$/Fc on the return sweep indicates that the Ni$^{0}$ is not stable in solution, as this feature is not observed when the potential sweep direction is reversed before the Ni$^{I}$/0 reduction (Figure 8).
Figure 6.8. CVs of HPDNi–Ph (blue), HPDNi–DMA (red), HPDNi–3SA (green), and A4Ni (purple) in CH$_3$CN (0.1 M[TEA$^+$][TsO$^-$]) at a scan rate of 50 mV/s.

When exposed to acid in the form of [TsOH•OTs$^-$], an increase in current is observed to coincide with the Ni$^{II}$/I reduction, suggesting that the Ni$^I$ species is can be protonated by [TsOH•OTs$^-$] (Figure 9).
Figure 6.9. CVs of HPDNI–Ph (a), HPDNI–DMA (b), HPDNI–3SA (c), and A4Ni (d) in CH3CN (0.1 M [TEA]+[TsO]) with H+ concentrations (from added HBF4) of 0 mM (▬ black), 5 mM (▬ green), 10 mM (▬ yellow), 15 mM (▬ orange), and 20 mM (▬ red).

Curiously, the increase in current is barely significant, with peak currents of the feature coincident with reduction to NiI only 4–6 times as high as the peak current of the NiII/I reduction wave in the absence of H+. Additionally, while a large difference is observed in CVs of Ni-porphyrins in the presence of 5 mM H+ compared to those collected in the absence of acid, additional equivalents of acid do not result in a subsequent increase in peak current. In fact, after doubling and quadrupling the acid concentrations to 10 and 20 mM, respectively, a negligible increase in peak current is observed. This, in conjunction with the fact that the current continues to rise after the initial peak, suggests that this “proton reduction” is taking place at the onset of direct
reduction of the acid by the working electrode. This in turn gives rise to an uncertainty as to whether it is the Ni-porphyrin that is catalyzing the reduction of H\(^+\), or whether the reduction of [TsOH•OTs\(^-\)] to forms radical anion which in turn reacts with Ni-porphyrin to either transfer an electron or a hydrogen atom (H\(^+\)). Both of these instances would give rise to an increase in current near the Ni\(^{II/1}\) reduction potential, but reaction with a radical anion may result in decomposition. This suggests that for [TsOH•OTs\(^-\)] in CH\(_3\)CN, Ni-porphyrins are not optimal H\(_2\)–evolution catalysts, and these compounds may undergo deleterious side reactions.

The evidence for catalyst decomposition is apparent in the observation of a current crossover during the CV. As the potential returns in the positive direction following the “catalytic wave,” the current crosses over its own trace. As the scan rate of the CV is increased, the current ceases to cross over itself, implying that the deleterious reaction occurs at a rate which can compete with the scan rate of the potential sweep (Figure 10).
Figure 6.10. CVs of $\text{A}_4\text{Ni}$ in CH$_3$CN (0.1 M [TEA$^+$][TsO$^-$]) in the presence of 20 mM H$^+$ (from added HBF$_4$) at scan rates of 50 mV/s ( black), 100 mV/s ( purple), 250 mV/s ( blue), 500 mV/s ( green), 1 V/s ( yellow), 1.5 V/s ( orange), and 2 V/s ( red).

One plausible explanation for this observation of current crossover in the case of Ni–porphyrins is the slow reaction of Ni$^\text{I}$–porphyrin to produce another redox–active species that has a $E_{1/2}$ more positive of the $E_{1/2}(\text{Ni}^\text{II}/\text{I})$. The identity of this species is currently unknown, but could result from reaction with a proton to form either a Ni$^\text{III}$–hydride ($\text{Ni}^\text{III}H$) or a protonated porphyrin. Ni$^\text{III}H$ is isoelectronic with Co$^\text{II}H$, which is the proposed active species in Co–porphyrin proton reduction electrocatalysis. This $d^7$ species has a formal metal–hydrogen bond order of 0.5, owing to the presence of an electron in the $d_{z^2}$ orbital, which is $\sigma$ anti–bonding with hydrogen. One would expect this species to be extremely reactive and have a short lifetime in the presence of excess acid, which is not consistent with the current crossover.
The slight increase in current in the presence of acid is most likely due to protonation of the porphyrin periphery followed by another electron transfer, similar to what is observed in the case of the Co-porphyrins described in this chapter. It would not be unexpected for Ni⁺–porphyrins to have a significant contribution from the isoelectronic Ni⁺⁺–porphyrin⁺⁻, since a d⁹ Ni⁺ species is expected to contain an electron in the Ni x²–y² orbital, which is strongly σ anti–bonding to the porphyrin nitrogen atoms. Any presence of a porphyrin based anion would present an opportunity for protonation, but the extent of this porphyrin anion character depends on the electronic properties of the porphyrin ring itself, which is affected by the meso–substituents. Insight may be provided by EPR studies, which have yet to be undertaken. We note that a similar reaction between Ni⁺–porphyrins and nucleophiles such as methyl iodide to produce chlorin–type products has been reported in the literature.¹⁰

6.2.5 Comparing Fe, Co, and Ni Porphyrins

The comparison of Fe, Co, and Ni porphyrins is a quintessential “goldilocks” situation, where Fe porphyrins have a combination of basicity and hydricity that is “just right” to result in efficient H₂ evolution. Porphyrin ligands possess only axial coordination sites available for inner sphere electron transfers, meaning that metalloporphyrins cannot participate in oxidative addition/reductive elimination transformations that are common to H–H bond formation or cleavage. Successful H₂ evolution on metalloporphyrins therefore relies on two proton transfers; one proton transfer to the metal center itself, and the follow–up reaction in which the generated hydride reacts with another proton to release H₂. The first step requires a reduced metal
complex that is basic enough to react with a proton at the metal center, and the second requires a metal–hydride complex that is nucleophilic enough to react with H\(^+\) and release H\(_2\) in the presence of excess acid. If the electrocatalyst is not basic enough to react with a proton, then a subsequent reduction of the metal center provides one approach to increase basicity, but only if the orbital in which the added electron resides is metal-based. If the reduction is not metal-based, then reaction with a proton may lead to catalyst decomposition. The resulting metal hydride formed after metal reduction must also have enough electron density on the hydride ligand itself in order to complete the catalytic cycle. Again, reduction of the metal hydride by an additional electron is one way to “activate” a complex that is not basic enough. However, additional reduction comes with the risk of unwanted side reactions should the reduction be ligand-based.

In all cases, the porphyrin complexes are found to react with [TsOH•OTs\(^-\)] in the formal +1 oxidation state of the metal. However, their ability to turn over catalytically are vastly disparate. Figure 11 demonstrates this in the case of \(\text{A}_4\text{Fe}, \text{A}_4\text{Co},\) and \(\text{A}_4\text{Ni}\).
Figure 6.11. CVs of $A_4\text{Fe}$ (— red), $A_4\text{Co}$ (— blue), and $A_4\text{Ni}$ (— green) in CH$_3$CN (0.1 M [TEA$^+$][TsO–]) in the presence of 20 mM H$^+$ (from added HBF$_4$) at a scan rate of 50 mV/s. The CV of $A_4\text{Fe}$ was collected in the presence of 40 mM PPh$_3$.

The Co–porphyrins have a $M^{II/I}$ reduction potential that is at a more positive potential than analogous Fe and Ni complexes. While this could be an advantage in terms of minimizing overpotential, the reaction that occurs between Co$^I$ and H$^+$ likely results in reduction of the porphyrin ring as opposed to the continued reduction of protons. It should be noted, however, that even in the case when Co$^I$-porphyrins are protonated at the metal center,$^9$ the resulting metal hydride is not hydridic enough to react with another proton to release H$_2$. Ni–porphyrins have a $M^{II/I}$ reduction potential more negative than Co and Fe porphyrins, which should result in a more reactive species. Unfortunately, it most likely reacts at the macrocycle owing to the electron richness of the porphyrin periphery, which leads to decomposition.
The ability of the Fe–porphyrins to bind phosphine at all steps of the proposed catalytic cycle is paramount to its stability and activity. Fe–porphyrins have a $\text{M}^{II/І}$ reduction potential, lying between that of its Co and Ni analogues. Whereas a Ni–porphyrin may have electron density on the porphyrin ring, reduction of Fe$^{ІІ}$ to Fe$^{І}$ is a well–known metal based reduction$^{11,12}$ and it follows that reaction with a proton will take place at the metal. Additionally, the product of the reaction between Fe$^{І}$ and H$^{+}$ is hydridic enough to result in the formation of a H–H bond, possibly with the help of the strong trans influence of an axial phosphine.

6.3 Conclusion and Future Work

The identity of the metal in hangman metalloporphyrins determines whether the complex is competent at reducing H$^{+}$ without experiencing any decomposition. The combination of hangman Fe–porphyrins and bulky phosphines are the most active H$_2$ evolving molecular catalysts in this chapter. The differences between the abilities of the hanging acid/base functionalities to channel H$^{+}$ to the metal center is not immediately apparent by the CV traces of similar Fe–porphyrin complexes, but can be seen in the FOWA of the traces.$^{13}$ Co$^{І}$–porphyrins are basic enough to act as a Brønsted–Lowry base, but the electron–releasing trimethoxyphenyl meso–substituents likely facilitate protonation on the porphyrin ring and not at the metal center. Judging by the Ni$^{ІІ/І}$ reduction potentials, Ni$^{І}$–porphyrins are a higher energy species than Fe$^{І}$–porphyrins, but perhaps to the residence of an unpaired electron on the porphyrin ring itself, reaction with a proton most likely results in eventual catalyst decomposition. In the
cases of Co and Ni porphyrins, their electronic structures are not conducive to FOWA, and therefore any difference in proton transfer rates is obfuscated at the moment.

Future studies could focus on directing protonation towards the metal center of Co–porphyrins by decreasing the electron density of the porphyrin ring itself, a strategy that might also prove useful in the case of Ni-porphyrins. The HER activity of Co-porphyrins with pentafluorophenyl meso-substituents establishes the validity of this approach. This can be done using meso-substituents that are electron withdrawing, although the synthesis of these new ligands will likely not be as high yielding as that of the 3,4,5-trimethoxyphenyl HPD ligands. If protonation can be directed towards the metal center to generate a metal hydride, carrying out the experiment in the presence of CO₂ might allow for selective reduction of CO₂ into formic acid.

6.4 Experimental Section

General Considerations. Acetonitrile (CH₃CN) was purified by passage through alumina¹⁴ and was stored over activated 3Å molecular sieves under nitrogen. Tetraethylammonium p-toluenesulfonate ([TEA⁺][TsO⁻]) was purchased from Alfa Aesar and recrystallized prior to use. [TEA⁺][TsO⁻] was purified by dissolving in minimal ethanol, adding ethyl acetate until saturation was achieved, and placing in refrigerator for recrystallization. The crystals were washed with cold ethyl acetate, dried at 100 °C in vacuo overnight, and stored under nitrogen. Tetrafluoroboric acid etherate (HBF₄•OEt₂) was purchased from Alfa Aesar and used as received. Anaerobic grade CO₂ was purchased from Airgas and bubbled through CH₃CN in order to saturate the gas prior to introduction to the electrochemical cell. Triethylamine (NEt₃), methanol, benzene,
ethanol, ethyl acetate, Co(OAc)$_2$ and Ni(OAc)$_2$(H$_2$O)$_4$ were purchased from Sigma Aldrich and were used as received. All porphyrins were synthesized according to published procedures.$^{15}$ $^1$H NMR spectra were recorded at ambient temperature on a Varian Mercury 500 MHz spectrometer. All spectra were referenced to trace protonated chloroform (7.26) as an internal standard (measured values for $\delta$ are given in parts per million (ppm) and for $J$ in Hertz (Hz)). The microwave–assisted reactions were performed inside the cavity of a CEM Discover microwave synthesis system equipped with infrared, pressure, and temperature sensors for monitoring the synthesis. The reaction vessels were 35 mL crimp–sealed thick–wall glass tubes. The contents of each vessel were stirred with a magnetic stirrer. Absorption spectral measurements were made on 5 $\mu$M solutions of each metalloporphyrin in CH$_3$CN using a Cary 5000 UV–vis–NIR spectrometer from Varian employing the software Cary WinUV. Quartz cells with a 10 mm path length were used. Electrospray ionization mass spectra (ESI–MS) were obtained using a Bruker microTOF–QII. Masses were generated using mMass.$^{16}$ Elemental analyses were not collected, as they provide little insight into the purity of hangman porphyrins.

**Synthesis.** 5–(6–(dibenzofuran–4–N–(phenyl)carbox–amide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrinato–cobalt(II) (HPDCo–Ph). Following published procedure,$^{17}$ freebase hangman porphyrin (5–(6–(dibenzofuran–4–N–(phenyl)carboxamide))–10,15,20–tri–(3,4,5–trimethoxyphenyl)porphyrin, 60 mg, 55 $\mu$mol) and Co(OAc)$_2$ (49 mg, 270 $\mu$mol, 5.0 equiv.) were dissolved in 15 mL CHCl$_3$ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 6 h at 60 °C. The solution was analyzed by TLC and no red
fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with H₂O (2 × 100 mL) and brine (1 × 100 mL), filtered through Na₂SO₄, and dried in vacuo. The solids were dissolved in dichloromethane (DCM) (2% NEt₃), loaded onto a silica column packed with DCM (2% NEt₃) and eluted with DCM (2% NEt₃). The major red band was collected and the volatiles were removed in vacuo. The solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo and stored under N₂. Yield = 55.7 mg (88.2%). ESI–MS [M]+ (m/z) Calcd. (Found): 1150.31 (1150.2825). λ_{max,abs}/nm (ε/M–1 cm–1) (CH₃CN) = 418 (1.7 × 10⁵), 532 (1.7 × 10⁴).

5–(6–(dibenzofuran–4–N–(3–dimethylamino–phenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)–porphyrinato–cobalt(II) (HPDCo–DMA). Following published procedure,¹⁷ freebase hangman porphyrin (5–(6–(dibenzofuran–4–N–(3–dimethylamino–phenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin, 50 mg, 44 μmol) and Co(OAc)₂ (39 mg, 220 μmol, 5.0 equiv.) were dissolved in 15 mL CHCl₃ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 6 h at 60 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with H₂O (2 × 100 mL) and brine (1 × 100 mL), filtered through Na₂SO₄, and dried in vacuo. The solids were dissolved in dichloromethane (DCM) (2% NEt₃), loaded onto a silica column packed with DCM (2% NEt₃) and eluted with DCM (2% NEt₃). The major red band was collected and the
volatiles were removed *in vacuo*. The solids were dissolved in benzene, and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C *in vacuo* and stored under N$_2$. Yield = 44.2 mg (84.2%). ESI–MS [M$^+$] (m/z) Calcd. (Found): 1193.35 (1193.3261). $\lambda_{max,abs}$/nm ($\varepsilon$/M$^{-1}$ cm$^{-1}$) (CH$_3$CN) = 418 (2.0 × 10$^5$), 532 (1.9 × 10$^4$).

5-(6-(dibenzofuran-4-(3-N-carboxamido)benzenesulfonate))-10,15,20-tri(3,4,5-trimethoxyphenyl)porphyrinato-cobalt(III) (HPDCo-3SA). Following published procedure,$^{17}$ freebase hangman porphyrin (5-(6-(dibenzofuran-4-(3-N-carboxamido)benzenesulfonic acid))-10,15,20-tri(3,4,5-trimethoxyphenyl)porphyrin, 27 mg, 23 µmol) and Co(OAc)$_2$ (20 mg, 110 µmol, 5.0 equiv.) were dissolved in 15 mL CHCl$_3$ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 6 h at 60 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with H$_2$O (2 × 100 mL) and brine (1 × 100 mL), filtered through Na$_2$SO$_4$, and dried *in vacuo*. The solids were dissolved in dichloromethane (DCM) (5% MeOH), loaded onto a silica column packed with DCM (5% MeOH) and eluted with DCM (5% MeOH). The first major red band was collected and the volatiles were removed *in vacuo*. The solids were dissolved in benzene, and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C *in vacuo* and stored under N$_2$. Yield = 23 mg (81.2%). ESI–MS [M$^+$] (m/z) Calcd. (Found): 1230.26 (1230.2368). $\lambda_{max,abs}$/nm ($\varepsilon$/M$^{-1}$ cm$^{-1}$) (CH$_3$CN) = 435 (3.0 × 10$^5$), 549 (2.1 × 10$^4$).
**Tetrakis(3,4,5-trimethoxyphenyl)porphyrinato-cobalt(II) (A₄Co).** Following published procedure,¹⁷ freebase A₄ porphyrin (200 mg, 200 µmol) and Co(OAc)₂ (180 mg, 1.0 mmol, 5.0 equiv.) were dissolved in 15 mL CHCl₃ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 6 h at 60 °C. The solution was analyzed by TLC and no red fluorescence (indicative of freebase porphyrin) was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with H₂O (2 × 100 mL) and brine (1 × 100 mL), filtered through Na₂SO₄, and dried *in vacuo.* The solids were dissolved in EtOAc, loaded onto a silica column packed with EtOAc and eluted with EtOAc. The first major red band was collected and the volatiles were removed *in vacuo.* The solids were dissolved in benzene, and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C *in vacuo* and stored under N₂. Yield = 165 mg (78%). ESI−MS [M − Cl−]⁺ (m/z) Calcd. (Found): 1031.29 (1031.2768). λ_{max,abs}/nm (ε /M⁻¹ cm⁻¹) (CH₃CN) = 416 (2.5 × 10⁵), 532 (1.7 × 10⁴).

**5-(6-(dibenzofuran-4-N-(phenyl)carboxamide))–10,15,20-tri(3,4,5-trimethoxyphenyl)porphyrinato-nickel(II) (HPDNI–Ph).** Freebase hangman porphyrin 5–(6–(dibenzofuran–4–N–(phenyl)carboxamide))–10,15,20–tri–(3,4,5–trimethoxyphenyl)porphyrin, 33 mg, 30 µmol) and Ni(OAc)₂(H₂O)₄ (380 mg, 1.5 mmol, 50 equiv.) were dissolved in 15 mL CH₃CN containing 1 mL of NEt₃ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 4 h at 80 °C. The solution was analyzed by TLC and one major, new, fluorescent spot was detected. The solution was transferred to a separatory funnel
containing 100 mL EtOAc. The organic layer was washed with dilute HCl/H$_2$O (1 × 100 mL) saturated Na$_2$CO$_3$/H$_2$O (1 × 100 mL), H$_2$O (1 × 100 mL), and brine (1 × 100 mL), filtered through Na$_2$SO$_4$, and dried in vacuo. The solids were dissolved in DCM (2% MeOH), loaded onto a silica column packed with DCM (2% MeOH) and eluted with DCM (2% MeOH). The first major red band was collected and the volatiles were removed in vacuo. The solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo and stored under N$_2$. Yield = 31 mg (89%). $^1$H NMR (500 MHz, CDCl$_3$, δ): 3.70 (br, 6H, OCH$_3$), 3.90 (br, 6H, OCH$_3$) 3.97 (s, 6H, OCH$_3$), 4.08 (s, 6H, OCH$_3$), 4.16 (s, 3H, OCH$_3$), 5.30 (t, 2H, hanging–PhH, J = 8 Hz), 5.41 (d, 2H, hanging–PhH, J = 8.2 Hz), 6.14 (t, 1H, hanging–PhH, J = 7.4 Hz), 7.05 (br, 2H, meso–ArH), 7.12 (br, 2H, meso–ArH), 7.34 (s, 2H, meso–ArH), 7.58 (t, 2H, ArH, J = 7.7 Hz), 7.90 (t, 1H, ArH, J = 7.7 Hz), 8.27 (d, 1H, ArH, J = 7.7 Hz), 8.34 (d, 2H, ArH, J = 7.7 Hz), 8.42 (d, 1H, ArH, J = 7.7 Hz), 8.49 (s, 1H, amide–NH), 8.80 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.83 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.91 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.95 (d, 2H, pyrrole–βH, J = 4.9 Hz). ESI–MS [M$^+$] (m/z) Calcd. (Found): 1149.31 (1149.2900). $\lambda_{\text{max,abs}}$/nm ($\varepsilon$/M$^{-1}$ cm$^{-1}$) (CH$_3$CN) = 417 (6.5 × 10$^4$), 526 (5.1 × 10$^3$).


Freebase hangman porphyrin (5–(6–(dibenzofuran–4–N–(3–dimethylamino–phenyl carboxamide))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin, 52 mg, 46 µmol) and Ni(OAc)$_2$(H$_2$O)$_4$ (570 mg, 2.3 mmol, 50 equiv.) were dissolved in 15 mL CH$_3$CN containing 1 mL of NEt$_3$ and transferred to a 35 mL microwave reactor tube. The tube
was capped, and microwave irradiation proceeded for 4 h at 80 °C. The solution was analyzed by TLC and one major, new, fluorescent spot was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with dilute HCl/H2O (1 × 100 mL) saturated Na2CO3/H2O (1 × 100 mL), H2O (1 × 100 mL), and brine (1 × 100 mL), filtered through Na2SO4, and dried in vacuo. The solids were dissolved in DCM (2% MeOH), loaded onto a silica column packed with DCM (2% MeOH) and eluted with DCM (2% MeOH). The first major red band was collected and the volatiles were removed in vacuo. The solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo and stored under N2. Yield = 46 mg (84 %).

2.47 (s, 6H, hanging–N(CH3)2), 2.59 (d, 1H, hanging–ArH, J = 7.7 Hz), 3.70 (br, 6H, OCH3), 3.92 (br, 6H, OCH3), 4.08 (s, 6H, OCH3), 4.15 (s, 3H, OCH3), 5.51 (dd, 1H, hanging–ArH, J = 8.2, 2.2 Hz), 7.05 (br, 2H, meso–ArH), 7.18 (br, 2H, meso–ArH), 7.29 (t, 1H, hanging–ArH, J = 2.2 Hz), 7.34 (s, 2H, meso–ArH), 7.58 (t, 2H, ArH, J = 7.7 Hz), 7.88 (t, 1H, ArH, J = 7.4 Hz), 8.27 (d, 1H, ArH, J = 7.6 Hz), 8.28 (d, 1H, ArH, J = 7.6 Hz), 8.34 (d, 1H, ArH, J = 7.7 Hz), 8.41 (d, 1H, ArH, J = 7.7 Hz), 8.50 (s, 1H, amide–NH), 8.77 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.81 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.90 (d, 2H, pyrrole–βH, J = 4.9 Hz), 8.94 (d, 2H, pyrrole–βH, J = 4.9 Hz). ESI–MS [M+1] (m/z) Calcd. (Found): 1192.35 (1192.3392). λmax,abs/nm (ε/M–1 cm–1) (CH3CN) = 417 (2.4 × 105), 525 (1.7 × 104).


Freebase hangman porphyrin (5–(6–(dibenzofuran–4–(3–N–carboxamido)–benzenesulfonic acid ))–10,15,20–tri(3,4,5–trimethoxyphenyl)porphyrin, 42 mg, 36
and Ni(OAc)$_2$(H$_2$O)$_4$ (460 mg, 1.8 mmol, 50 equiv.) were dissolved in 15 mL CH$_3$CN containing 1 mL of NEt$_3$ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 4 h at 80 °C. The solution was analyzed by TLC and one major, new, fluorescent spot was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with dilute HCl/H$_2$O (1 × 100 mL), H$_2$O (1 × 100 mL), and brine (1 × 100 mL), and dried in vacuo. The solids were dissolved in DCM (5% MeOH), loaded onto a silica column packed with DCM (5% MeOH) and eluted with DCM (5% MeOH). A faint red band was collected. The rest of the material was eluted with DCM (10% MeOH). A major red band was collected and the volatiles were removed in vacuo. The solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C in vacuo and stored under N$_2$. Yield = 36.1 mg (82%). $^1$H NMR spectrum was uninterpretable as it contained many broad peaks as a result of acid base equilibria and multiple structural conformations. ESI–MS [M – H$^+$]– (m/z) Calcd. (Found): 1228.27 (1228.2765).

$\lambda_{\text{max,abs}}$/nm ($\varepsilon$/M$^{-1}$ cm$^{-1}$) (CH$_3$CN) = 417 (1.4 × 10$^5$), 525 (9.6 × 10$^3$).

**Tetrakis(3,4,5-trimethoxyphenyl)porphyrinato-nickel(II) (A$_4$Ni).** Freebase A$_4$ porphyrin (100 mg, 100 µmol) and Ni(OAc)$_2$(H$_2$O)$_4$ (460 mg, 1.0 mmol, 50 equiv.) were dissolved in 15 mL CH$_3$CN containing 1 mL of NEt$_3$ and transferred to a 35 mL microwave reactor tube. The tube was capped, and microwave irradiation proceeded for 4 h at 80 °C. The solution was analyzed by TLC and one major, new, fluorescent spot was detected. The solution was transferred to a separatory funnel containing 100 mL EtOAc. The organic layer was washed with dilute HCl/H$_2$O (1 × 100 mL) saturated Na$_2$CO$_3$/H$_2$O.
(1 × 100 mL), H₂O (1 × 100 mL), and brine (1 × 100 mL), filtered through Na₂SO₄, and dried \textit{in vacuo}. The solids were dissolved in DCM (2% MeOH), loaded onto a silica column packed with DCM (2% MeOH) and eluted with DCM (2% MeOH). The first major red band was collected and the volatiles were removed \textit{in vacuo}. Crystals suitable for single crystal x-ray diffraction could be grown from a saturated solution of A₄Ni in EtOAc, but the solids were dissolved in benzene and filtered through filter paper. The volatiles were removed and the solids were sonicated in pentane (3 × 5 mL) then dried at 80 °C \textit{in vacuo} and stored under N₂. Yield = 89.6 mg (85%). ¹H NMR (500 MHz, CDCl₃, δ): 3.93 (s, 24H, meta–OCH₃), 4.13 (s, 12H, para–OCH₃), 7.27 (s, 8H, ortho–ArH), 8.86 (s, 8H, pyrrole–βH). ESI–MS [M⁺]+ (m/z) Calcd. (Found): 1030.29 (1030.2771). λ\textsubscript{max,abs}/nm (ε /M⁻¹ cm⁻¹) (CH₃CN) = 415 (7.0 × 10⁴), 526 (1.2 × 10³).

**Cyclic Voltammetry.** All studies were conducted under a nitrogen atmosphere using a CHInstruments 660C potentiostat. All CVs were performed in an oven–dried conical glass cell purchased from BASi. Working solutions were prepared from 1 mL of a 1 mM iron porphyrin stock solution in CH₃CN (0.1 M [TEA⁺][TsO⁻]) was combined with 0.4 mL of 0.2 M stock solution of PPh₃ in CH₃CN (0.1 M [TEA⁺][TsO⁻]) and 0.6 mL of CH₃CN (0.1 M [TEA⁺][TsO⁻]) to make the 0.5 mM iron porphyrin solution. HBF₄ was added from a 0.2 M stock solution in CH₃CN (0.1 M [TEA⁺][TsO⁻]). The working electrode for cyclic voltammetry was a 0.7 cm² glass–like carbon disk, which was polished before each series of CVs with 50 nm alumina, sonicated in 18 MΩ water, and rinsed with methanol before being dried with compressed air. The pseudo–reference electrode was a polished Ag wire encased in a glass container immersed in CH₃CN (0.1 M [TEA⁺][TsO⁻]); the reference and working electrode compartments were separated by a vycor frit.
The counter electrode was a Pt wire. Fc was present at during every CV and was assumed to not interact with electron transfers and chemical steps, potentials were referenced to $E_{1/2}(\text{Fc}^+/\text{Fc})$ for each scan. Acid titrations were carried out with the addition of HBF$_4$•OEt$_2$, exploiting the large difference in pKa's of TsOH (8.6) and HBF$_4$ (0.1) in CH$_3$CN to generate TsOH and its homoconjugate in situ.

6.5 References


