Designing Biomimetic NADH-Analogs for Artificial Photosynthesis

ΒY

STEFAN ILIC

B.Sc., University of Belgrade, 2013

M.Sc., Bowling Green State University, 2017

THESIS

Submitted as partial fulfillment of the requirements

for the degree of Doctor of Philosophy of Chemistry

in the Graduate College of the

University of Illinois at Chicago, 2019

Chicago, Illinois

Defense Committee:

Ksenija D. Glusac, Chair and Advisor Neal P. Mankad Michael Trenary Preston T. Snee Karen L. Mulfort, Argonne National Laboratory



"The Science of Today is the Technology of Tomorrow." - Edward Teller

Acknowledgements

I am known as a person of few words, but the words written here are heartfelt and sincere. I am truly grateful for the opportunities that I was given during my research journey at University of Illinois at Chicago (UIC), Argonne National Laboratory (ANL) and Bowling Green State University. This thesis would not have been realized without the encouragement and active support from a number of people that I wish to acknowledge here.

I simply cannot start without expressing my eternal gratitude to my supervisor, Dr. Ksenija Glusac, without whom all of this would've been impossible. Her careful guidance, enthusiasm, selflessness and endless patience made working on this thesis enjoyable, even when the things were not going smoothly. Apart from being an excellent research advisor, Dr. Glusac has been a true role model. Her scientific curiosity and commitment to research continues to amaze and inspire me.

I would like to extend my sincere thanks to my committee members: Dr. Neal Mankad, Prof. Michael Trenary, Dr. Preston Snee and Dr. Karen Mulfort for going out of the way and take time off their busy schedule to review this thesis and provide feedback and suggestions for how to improve it.

To the current group members Marija, Ravindra, Nik, Jon, Varun, Erik, Nikita and former members Usha, Xiaoxiao, Janitha, Yun and Xin, thank you for sharing experiences and struggles in the lab and office. This journey would've not been as enjoyable without you.

I would also like to thank my dear collaborators, Prof. Musgrave and his students Aziz and Chern, Prof. Hynes, Prof. Maldonado and his former student Betsy, Dr. Keith

iii

and his student Yasemin, Dr. Poluektov and Dr. Niklas, for constructive discussions and for sharing their knowledge and ideas. Also, a big thank you to the Solar Energy Conversion group at ANL for allowing me to attend their meetings and learn about their exciting projects.

Many thanks to the entire staff of the Department of Chemistry for their help and assistance during my stay at UIC: Gloria, Yonilo, Shirley, Dan, Jennifer, Tanya, and especially Rhonda. I also had great pleasure of working with Tory and Dan from Chemical Science Engineering division at ANL.

I would like to thank my new and old friends. I am delighted that friends that I've made during my PhD studies (Eric, Imelda, Dasha, Ilnur, Chao, Mina, Vanessa and many others) have supported me throughout this long journey in Illinois and Ohio. Special thanks to my roommate, labmate and a friend Marija for keeping up with me and being there for me in the good times and the bad times.

Lastly, thanks to my parents, Ljubica and Milijan, and grandma Jelka for their love and encouragement.

iv

Contribution of Authors

Several parts of this thesis are reproduced from previously published articles co-authored with collaborators, who contributed significantly to the presented work.

Chapter 2 is adapted and reproduced in part from the published manuscript, *Thermodynamic and Kinetic Hydricities of Metal-Free Hydrides*, Ilic, S.; Alherz, A.; Musgrave, C.B.; Glusac, K.D. Chem. Soc. Rev. **2018**, 47(8), 2809-2836, DOI: 10.1039/C7CS00171A. S. Ilic was the primary author of this article and A. Alherz, Prof. C. B. Musgrave and Prof. K. D. Glusac contributed to the preparation of the manuscript.

Chapter 3 is adapted and reproduced in part from the published manuscript, *Benzimidazoles as Metal-Free and Recyclable Hydrides for CO*₂ *Reduction to Formate*, Lim, C.-H.; Ilic, S.; Alherz, A.; Worrell, B.T.; Bacon, S.S.; Hynes, J.T.; Glusac, K.D.; Musgrave, C.B. J. Am. Chem. Soc. **2019**, 141(1), 272-280, DOI: 10.1021/jacs.8b09653. S. Ilic was one of the co-authors of this article and conducted all of the cyclic voltammetry, preparative electrolysis experiments and calculations regarding hydride regeneration studies. Dr. C.-H. Lim designed the hydride donors and performed all of the CO₂ reduction experiments with help of Dr. B. T. Worrell and S. S. Bacon. The calculations were performed by Dr. C.-H. Lim and A. Alherz, while Prof. J. T. Hynes, Prof. K. D. Glusac and Prof. C. B. Musgrave contributed to the preparation of the manuscript.

Chapter 4 is adapted and reproduced in part from the published manuscript, Importance of proton-coupled electron transfer in cathodic regeneration of organic hydrides, Ilic, S.*; Alherz, A.*; Musgrave, C.B.; Glusac, K.D. Chem. Commun. **2019**, 55, 5583-5586, DOI: 10.1039/C9CC00928K. *In this work, S. Ilic and A. Alherz contributed

۷

equally to the manuscript. All of the synthesis, electrochemical and spectroscopy measurements were done by S. Ilic, while A. Alherz performed all of the calculations. Prof. C. B. Musgrave and Prof. K. D. Glusac contributed to the preparation of the manuscript.

Table of Contents

| | Table of Contents |
|----|--|
| Η | APTER |
| | Introduction |
| | 1.1 Why CO ₂ Reduction? |
| | 1.2 Previous Efforts On Homogenous CO2RR Electrocatalysts |
| | 1.2a Ruthenium- Polypyridyl Complexes |
| | 1.2b Rhenium- and Manganese- Bipyridyl Complexes |
| | 1 2c Fe-Porphyrin Complexes |
| | 1 2d Formate-Producing Electrocatalysts |
| | 1.3 Our Biomimetic Approach |
| | Thermodynamic And Kinetic Hydricities Of Metal-Free Hydrides |
| | 2.1 Introduction |
| | 2.2 Experimental Methods |
| | 2 2a The Potential-nKa Method |
| | 2.24 The Foldmar production Method |
| | 2.20 The Hydride Hansler Method |
| | 2 3 Computational Methods |
| • | 2 3a The Direct Annroach |
| | 2 3h Indirect Approaches |
| | 2 3c Calculated Nucleophilicity |
| | 2.30 Calculated Nucleophilicity |
| 4 | 2 /a Carbon-Based Hydride Donors |
| | 2.4a Calbon-Based Tryunde Donors |
| | |
| | 2.40 Δ GH- VS. Δ HH |
| | 2.40 Kinetic Aspects of Hydride Transfers |
| , | 2.40 Solvation Ellects |
| 4 | 2.5 Relevance To Calarysis |
| 4 | 2.0 Conclusions And Future Outlook |
| | Benzimidazoles As Metal-Free And Recyclable Hydrides For CO ₂ |
| | |
| | 2. Computational Matheda |
| 2 | 3.2 Computational Methods |
| | 3.3 Experimental Section. |
| 5 | 3.4 Results And Discussion |
| | 3.5 Conclusions |
| | mportance Of Proton-Coupled Electron Transfer In Cathodic |
| I | Regeneration Of Organic Hydrides |
| 2 | 1.1 Introduction |
| 2 | 1.2 Computational Details |
| Ζ | 4.3 Experimental Details |
| 4 | 4.4 Results And Discussion |
| | 4.4 Conclusions |
| | General Conclusions And Future Outlook |
| e | d Literature |
| | Α |
| ņ | vright Permissions |
| ۲. | |

List of Tables

Table 1. Standard potentials of several CO2 reductions in aqueous solutions at**3**1.0 atm and 25 °C.

Table 2. Comparison of main properties of homogeneous vs. heterogenous4catalysts.

Table 3. Standard reduction potentials (in acetonitrile) relevant for CO2RR with6metal-based electrocatalysts.

Table 4. Summary of different $G(H^-)$ values obtained computationally via various **38** approaches and levels of theory in MeCN.

Table 5. A list of the experimental and calculated (in parentheses) values for ΔG_{H-} **42** (kcal/mol) and ΔH_{H-} (kcal/mol) of the metal-free hydride donors reviewed here. Energies are for hydride transfers in acetoniotrile, unless otherwise noted. Hydridic hydrogens are shown in red.

Table 6. Mayr's kinetic parameters (s_N and N) as defined in equation 2 and **46** measured for different metal-free hydride donors in DCM, MeCN or DMSO solvents.

Table 7. Predicted thermochemical properties of CO2 reduction by reductants 1a-**76**d with their corresponding experimental formate yields.

 Table 8. Reaction of species 1c or 1d with CO₂ under various experimental
 79

 conditions.

viii

Table 9. Experimentally determined pKa values of organic acids in DMSO.³²⁶ The**94**second column contains pKa values calculated using DFT calculations and usingequations 3 and 4 shown above.

Table 10. Model R-H compounds and their calculated acidities, reduction and**98**hydride donor ability constants in DMSO as solvent.

List of Figures

Figure 1. Relationship between global climate change and increased emission of
CO₂: a) concentration of greenhouse gases vs. time; b) anthropogenic CO₂
emission vs. time; c) surface temperature changes vs. time; d) sea-level changes
vs. time. Adapted from IPCC AR5 (2014).

Figure 2. Electrochemical reduction with Ru-bpy complexes: a) cyclic **8** voltammograms of [Ru(bpy)₂(CO)CI]⁺ in DMF under nitrogen (solid) and CO₂ (dashed); adapted with permission from ref. 1. Copyright 1987 American Chemical Society. b) mechanism proposed by Tanaka et al., see ref. 1; c) mechanism proposed by Meyer *et al.*, see ref. 2.

Figure 3. Electrochemical CO2RR to CO using the Re-based catalyst: a) oneand two- electron reduction pathways for the activation of the catalyst proposed
by Meyer *et al.* in ref. 3; b) electrocatalytic cycles proposed by Carter *et al.* in ref.
4; c) schemastic representation of the potential energy surface for H⁺ and CO₂
additions calculated by Carter *et al.* in ref. 5.

Figure 4. Electrochemical CO2RR to CO with the Mn-bipyridine catalyst: a) the **13** mechanism for catalyst activation proposed by Deronzier and coworkers in ref. 62; b) suggested intermediate structure responsible for the more favorable 'protonation-first' mechanism; adapted with permission from ref. 6. Copyright 2017 American Chemical Society. c) schematic comparison of 'protonation-first' mechanisms.

Figure 5. Electrochemical CO2RR to CO using the Fe-porphyrin catalyst: a) cyclic **15** voltammograms of iron-tetraphenylporphyrin [Fe(TPP)]⁺ under argon (blue line)

х

and CO₂ (red line); adapted with permission from ref. 7. Copyright 2013 American Chemical Society. b) schematic representation of Lewis acid- and Brønsted acidpromoted catalytic cycles.

Figure 6. Importance of second coordination sphere in CO2RR electrocatalysis **17** with FeTPP: a) a phenol proton handle enables 'protonation-first' mechanism; b) linear sweep of several substituted FeTPP catalysts showcasing the influence of inductive effect and local Coulombic stabilization on catalysis; adapted with permission from ref. 8. Copyright 2016 American Chemical Society.

Figure 7. Electrochemical CO2RR to formate with the Ir – pincir complexe: a) **19** cyclic voltammograms of [Ir(PCP)(MeCN)(H₂)] (top) and [Ir(PCP)(MeCN)(H)]⁺ (bottom) in the Ar (black line) and CO₂ (red line); adapted with permission from ref. 9. Copyright 2012 American Chemical Society. b) schematic representation of the mechanism postulated from electrochemical measurements and DFT calculations.

Figure 8. Calculated versus experimental hydricities: (a) free energy and (b) **41** enthalpic hydricities in DMSO and MeCN. Data is reported in Table 5. Some computationally obtained hydricities are from references cited in Table 5. The rest have been calculated using Muckerman's scaling approach at the B3LYP/6-311++G(d,p)/CPCM level of theory.¹⁰⁻¹⁵ The 45° red line represents perfect agreement between experiment and theory, with a slope of unity and a y-intercept at 0. The dashed line is the correlation between calculated and experimental hydricities. Both fits were determined to have insignificant deviations from experiment with 95% confidence using the paired-t test, as is appropriate for such

xi

statistical analyses.¹⁶ A p-value of 0.76 is obtained for (a) and 0.14 for (b), indicating that the mean hypothesized difference between experimental and computational methods is 0. The confidence intervals are (-1.29, 0.94) for (a) and (-0.09, 0.61) for (b). The inclusion of 0 in both intervals further supports the insignificance of the errors between the experimental and computational hydricities.

Figure 9. The comparison between ΔH_{H-} and ΔG_{H-} at 298 K for hydrides tabulated in Table 5 for: (a) carbon-based and (b) other hydride donors. The red dashed lines represent the condition $\Delta H_{H-} = \Delta G_{H-}$ at which $T\Delta S_H = 0$. The data all lie above this line, indicating that $\Delta H_{H-} - \Delta G_{H-} = T\Delta S_{H-}$ is positive for metal-free hydride donors. The average $T\Delta S_{H-}$ contributions for different classes of hydrides at room temperature are as follows: carbon- fluorenes (12 kcal/mol), diphenylmethanes (9 kcal/mol), triphenylmethanes (7 kcal/mol), tricyclic heterocycles (7 kcal/mol), bicyclic heterocycles (5 kcal/mol), dihydropyridines (4 kcal/mol) and five-membered (5 kcal/mol); boron- (8 kcal/mol), silicon- (8 kcal/mol), nitrogen- (7 kcal/mol), oxygen- (7 kcal/mol), phosphorus- (8 kcal/mol) and germanium-based donors (6 kcal/mol).

Figure 10. Linear free energy relations expressed with respect to the kinetic **57** nucleophilicity parameter *N* and the thermodynamic hydricity (in kcal/mol) for boranes, silanes, and other subgroups of carbon-based hydrides. *N* values for borohydrides are measured in DMSO, while all other values are obtained in dichloromethane. Caution must be exercised when comparing *N* values because

xii

boranes are reported in a more polar solvent relative to others. All ΔG_{H-} values are reported in MeCN.

Figure 11. The scaling relationships between the thermodynamic hydricity ΔG_{H-} **60** and the first electron reduction potential E_1 of the oxidized form for metal-free (orange) and metal-based hydrides (blue). The ΔG_{H-} value for dihydrogen $\Delta G_{H-}(H_2) = 76$ kcal/mol and carbon dioxide $\Delta G_{H-}(CO_2) = 44$ kcal/mol along with reduction potentials $E(H^+/H_2) = 0.46$ V and $E(CO_2/HCO_2-) = -0.23$ V (both vs. NHE) are presented as black circles. The dashed gray line helps to estimate the overpotential.

Figure 12. (a) The difference in the first and second reduction potentials (E_1 - E_2) **62** as a function of the thermodynamic hydricity (ΔG_{H-}) for metal-free and metalbased hydrides. (b) The illustrative comparison of the energy profiles required for hydride catalyst recovery for metal-catalyst (Ni-complex) and for a metal-free hydride donor (2OH) possessing similar ΔG_{H-} .

Figure 13. ¹³C-NMR spectra of species 1c reacted with ¹³CO₂ in DMSO-*d*₆. **78** Reaction conditions: [1c] = 0.10 M, [KBr] = 0.20 M, $P_{CO2} = \sim 20$ psig, T = 50°C and t = 16 h. 0.05 M 1,3,5-trimethoxybenzene was introduced as an internal standard. ¹³C-formate appeared at 165.70 ppm; dissolved ¹³CO₂ appeared at 124.18 ppm.¹⁷

Figure 14. Electrochemical regeneration of 1c from 2c. (a) Cyclic voltammograms **86** at scan rates of 100 mV/s of 1 mM 2c in DMSO with (maroon solid) and without (blue solid) 100 eq. of phenol, baseline scan (blue dashed line) and a scan of a 100 mM solution of phenol in DMSO (maroon dashed line). Scan directions: +0.1 $V \rightarrow -2.3 V \rightarrow +0.75 V \rightarrow +0.1 V$. Inset: the oxidation of authentic 1 mM solution

of 1c (green); (b) Experimental (baseline subtracted, gray) and simulated (orange dashed) CVs of 1 mM solution of 2c in the presence of phenol at a scan rate of 100 mV/s. Simulation parameters: K(PT) = 100 and $k_f(PT) = 10^4$ s⁻¹ gave the closest match to experimental values.

Figure 15. ¹H-NMR spectra of catholyte DMSO- d_6 solution of 1 mM 2c in the **88** presence of 150 equiv of phenol and 1,3,5-trimethoxybenzene as an internal reference, before (a) and after (b) bulk electrolysis on carbon fiber paper as the working electrode at $E_{app} = -1.91$ V vs. NHE.

Figure 16. Attempted electrochemical CO₂ reduction with **2c** on glassy carbon **89** and tin electrodes.

Figure 17. $(G_{A^-} - G_{AH})$ computed using wB97XD/6-311+G(d,p) level of theory **95** versus experimentally determined pKa values reported in Table 9. Black round dots represent the experimental data set. The black dashed line is the linear regression performed on the experimental data set, with an adjusted R²_{adj} value of 0.950. The red triangles represent pK_a values of radical cation intermediates discussed in this work.

Figure 18. Cyclic voltammograms of: a) 2 mM A_2^+ in the presence of $0 \rightarrow 60$ eq **100** AcOH in DMSO; b) 5 mM A_2^+ in the presence of $0 \rightarrow 1$ eq TfOH in MeCN; c) 2 mM B_3^+ in the presence of $0 \rightarrow 60$ eq AcOH in DMSO; d) 2 mM B_2^+ in the presence of 0-60 eq AcOH in DMSO. Arrows indicate the direction of peak changes with the addition of acid, while black dashed curves represent baseline scans.

Figure 19. a) NMR spectra in DMSO-d₆ for catholyte before and after electrolysis **101** of A_2^+ in the presence of AcOH, at applied potential of -2.0 V vs. Fc/Fc⁺. b)

xiv

Comparison of catholyte solution before and after electrolysis with the authentic samples for A_2^+ and A_2H .

Figure 20. a) NMR spectra in MeCN-d₃ for catholyte before and after electrolysis **101** of A_2^+ in the presence of HBF₄, at applied potential of -1.2 V vs. Fc/Fc⁺. b) Comparison of catholyte solution before and after electrolysis with the authentic samples for A_2^+ and A_2^+ .

Figure 21. Cyclic voltammograms of B₈⁺ in the presence of: a) acetic acid, AcOH; 103
b) d-acetic acid, AcOD.

Figure 22. EEP and EPE reaction coordinate diagram for B_3H (blue, **104** benzimidazole) and A_5H (green, acridine). B_3 .^{/H+} and A_5 .^{/H+} structures with angles below to show geometric changes.

Figure 23. Acidity constant for RH⁺·, $pK_a(RH^+\cdot)$, as a function of $E^{0}_{R^+/R^+}$ for **106** benzimidazoles.

List of Schemes

Scheme 1. Schematic representation of the generalized CO2RR catalysis with
metal-based electrocatalysts. The scheme depicts possible pathways that lead to
the formation of most observed reduction products (carbon monoxide, hydrogen,
formate).

Scheme 2. Artificial photosynthesis. *left:* In natural photosynthesis, the reduction **22** of CO₂ to carbohydrates is performed by NADH, which is regenerated from photodriven water oxidation. *right:* Our biomimetic approach includes a photoelectrochemical cell for selective CO₂ reduction. Active hydrides are designed to have favorable thermodynamic parameters for hydride transfer to CO₂ and easy photoelectrochemical regeneration with semiconductor and water oxidation.

Scheme 3. a) Some examples of metal-free hydride donors. Metalloids are 26 shown in orange, while nonmetals are shown in blue. Hydridic hydrogens are shown in red and electronegativity values are represented by " χ ". The selected examples of each group are presented as follows, from top left: boron (lithium triethylborohydride, Super hydride^{™ 18}), carbon (NADPH,¹⁹ R = adenine dinucleotide phosphate), nitrogen (FADH₂,²⁰ R = adenine dinucleotide), oxygen Q_{10}^{21}), (coenzyme silicon (triphenylsilane²²), phosphorus (2-Hdiazaphospholene²³), germanium (tributylgermane²⁴) and tellurium (sodium hydrogen telluride²⁵). b) Thermodynamic and kinetic hydricity scales used to evaluate hydride donor ability and reactivity of metal-free hydride donors.

xvi

Scheme 4. Illustrative description of the methods used to obtain thermodynamic **29** and kinetic hydricities. The desired values obtained as outcomes from these methods are represented in red; measured parameters are represented in green and reference values are represented in blue.

Scheme 5. Carbon-based hydride donors: a) arylmethanes and b) dihydro- **48** heterocycles.

Scheme 6. Representations of FAD and hydroquinone N-H (a) and O-H hydrides 52
(b). Hydridic bonds are shown in red, whereas the negatively charged heteroatoms are shown in blue. The dashed lines of the hydroquinones represent a substitution or the presence of another phenyl ring.

Scheme 7. Reduction of CO₂ to formate anion by benzimidazole-based organo- **69** hydrides.

Scheme 8. Sequential regeneration pathways for electrochemical conversion of85species 2c to hydride-active species 1c.

Scheme 9. Activation of CO₂ for hydride transfer reaction with organic bases. The **110** adduct formation (activation) is a slightly unfavorable process (ΔG_{act}) which makes the hydride transfer to the adduct more favorable ($\Delta G_{aHT} = \Delta G_{dHT} - \Delta G_{act}$). Also shown, few activator structures and some calculated adduct formation ΔG_{act} .

Scheme 10. New generation of metal-free hydride donors. 111

Scheme 11. New generation of NAD⁺ bearing 'proton handles' as a strategy to **112** lower the overpotential for hydride regenerations.

Summary

Research efforts covered with this thesis focus on the design of metal-free hydride donors (NADH analogs) for possible application in CO₂ reduction (electro)catalysis.

Chapter 1 consists of a brief introduction on importance of the CO₂ reduction and highlights homogeneous electrocatalysis as one of the methods to produce carbonneutral fuels. An overview on several classes of metal-based electrocatalysts for CO₂ reduction is given to highlight the importance of considering mechanistic aspects in improving the catalyst performance.

In Chapter 2, the hydride donor ability of several classes of metal-free hydride donors is described with thermodynamic (hydricity) and kinetic (nucleophilicty) parameters. Different experimental and computational methods used to obtain these parameters are discussed in more detail. The hydricity and nucleophilicity values are tabulated and discussed in terms of structure-property relationships. Based on the presented data, benzimidazole-based hydrides have been identified as promising candidates due to their favorable thermodynamic and kinetic properties that rival those of precious metal hydrides. This work provides insights on structural and electronic features that contribute to hydride donor ability of metal-free hydrides, relevance to catalysis and contemporary limitations for replacing metal-based catalysts.

In Chapter 3, benzimidazole-based hydride donors have been tested for chemical reduction of CO₂. The selective reduction to formate is achieved in the absence of enzymes or activators. Contrary to boron- and silicon-based hydrides, the oxidized benzimidazolium form is quantitatively recovered upon the reduction, establishing the recyclability of benzimidazole hydrides. Furthermore, the active hydride form is

xviii

electrochemically regenerated in quantitative yield. This work serves as a proof of concept for selective CO₂ reduction using metal-free renewable hydride donors.

In Chapter 4, electrochemical regeneration of two classes of organic hydrides (acridines and benzimidazoles) from their oxidized forms has been explored. While the previous efforts have been hindered by the rapid dimerization of organic radicals (firstelectron products), we utilized proton-coupled electron transfer (PCET) to achieve quantitative electrochemical regeneration. It is found that PCET can determine the mechanism for the electrochemical conversions. However, the required applied potential remains consistent regardless of the mechanism of the conversion. This work gives mechanistic insights for the application of organic hydrides in electro- and photocatalytic processes.

In Chapter 5, a summary is presented with the key findings from the mechanistic studies deliberated in this thesis. Remaining challenges that prevent application of NADH analogs in catalytic application will be discussed along with the future outlook on possible ways how to overcome these obstacles.

Chapter 1. Introduction

1.1 Why CO₂ Reduction?

Modern civilization relies heavily on the energy obtained from carbon-rich fossil fuels, such as coal, oil and natural gas. In addition to the fact that fossil fuels will be inevitably depleted in near future, their mass consumption induces a high production of greenhouse gasses (particularly CO_2) that are being emitted in the atmosphere (Figure 1a).²⁶ The atmospheric CO_2 concentration has increased up to 400 ppm,²⁷ (Figure 1b), which exceeds the amount of CO_2 that is naturally recycled by photoautotrophic organisms.²⁸ The increased anthropogenic CO_2 emission has been associated with the 'climate change' phenomenon that include the trends of increasing temperature, rising sea-level, shifts in floral blooming, and greater instances of extreme weather events (Figure 1c and d).²⁶



Figure 1. Relationship between global climate change and increasing emissions of CO₂: a) concentration of greenhouse gases vs. time; b) anthropogenic CO₂ emission vs. time;

c) surface temperature changes vs. time; d) sea-level changes vs. time. Adapted from IPCC AR5 (2014).

However, atmospheric carbon dioxide can be utilized as a feedstock for renewable source of energy, which would address both growing energy demands and alarming concern about its increased emission. Specifically, the chemical reduction of carbon dioxide leads to the formation of carbon-neutral fuels where the energy is stored in chemical bonds.²⁹ A myriad of CO₂ reduction reaction (CO2RR) products can serve as fuels, such as C₁-compounds (formate, carbon monoxide, formaldehyde, methanol) or C₂, C₃ or higher-order compounds (oxalate, ethane, ethanol, propanol, etc.). The more desired ones are those that have higher energy content, usually evidenced by more C-H bonds and those that can be stored and transported more easily (such as liquid fuels).³⁰ Out of these, methanol appears to be the desired candidate that compromises relative synthetic ease, high energy density with three energy-carrying C-H bonds (~22 MJ/kg), low toxicity, and straightforward handling.³¹

Conversion of carbon dioxide to any type of fuel can be achieved using various methods: thermal hydrogenation, electrochemical, photochemical and enzymatic methods.³²⁻³⁵ While all methods have their advantages and drawbacks, the focus of this thesis is on electrochemical CO2RR. Furthermore, electrochemical CO2RR can be coupled to a renewable source of energy (i.e. solar energy) to give continuous, cost-effective replacement of fossil fuels.³⁶ During (photo)electrochemical CO2RR processes, multiple electron and proton transfers take place. Stepwise single-electron transfers are usually undesired since they produce high-energy radical intermediates, as represented with very negative reduction potential for one electron reduction of CO₂ to the radical

2

anion CO₂⁻⁻ (Table 1).³⁷ These open-shell intermediates can be bypassed through a sequence of proton-coupled electron transfers, which is reflected by significantly less negative potentials (Table 1). However, channeling multiple electron and proton equivalents toward one specific product is challenging and comes with a high kinetic cost.³⁸ In addition, it is difficult to circumvent the hydrogen evolution reaction (HER), which occurs at a similar thermodynamic potential as CO₂ reduction products (Table 1). Thus, electrochemical CO2RR require a catalyst to perform the conversion on a reasonable timescale by navigating electrons and protons toward a single product and avoiding the undesirable HER.

| Table 1. | Standard | potentials | of several | CO ₂ | reductions | in a | aqueous | solutions | at | 1.0 | atm |
|----------|----------|------------|------------|-----------------|------------|------|---------|-----------|----|-----|-----|
| and 25 ° | C. | | | | | | | | | | |

| electrochemical half-reaction | E ⁰ (V vs. SHE) |
|--|----------------------------|
| $\text{CO}_2(g) + e^- \rightarrow \text{CO}_2^{}$ | -1.92 |
| $CO_2 (g) + 2e^- + 2H^+ \rightarrow CO (g) + H_2O (I)$ | -0.11 |
| $CO_2 (g) + 2e^- + 2H^+ \rightarrow HCOOH (I)$ | -0.25 |
| $\text{CO}_2(\text{g}) + 4e^- + 4\text{H}^+ \rightarrow \text{CH}_2\text{O}(\text{I}) + \text{H}_2\text{O}(\text{I})$ | -0.07 |
| $\text{CO}_2(\text{g}) + 6e^- + 6\text{H}^+ \rightarrow \text{CH}_3\text{OH}(\text{I}) + \text{H}_2\text{O}(\text{I})$ | +0.02 |
| $CO_2(g) + 8e^- + 8H^+ \rightarrow CH_4(g) + 2H_2O(I)$ | +0.17 |
| $2CO_2 (g) + 2e^- + 2H^+ \rightarrow H_2C_2O_4 (aq)$ | -0.50 |
| $2CO_2 (g) + 12e^- + 12H^+ \rightarrow C_2H_4 (G) + 4H_2O (I)$ | +0.06 |
| $2H^{+} + 2e^{-} \rightarrow H_{2}(g)$ | 0.00 |

Over the past few decades, there have been tremendous scientific efforts and many reports on homogenous and heterogenous electrocatalysts that perform CO2RR to

produce various different products.³⁹⁻⁴¹ Both classes of catalysts exhibit different advantages (Table 2),³⁹ but for this work, only homogeneous systems will be discussed. While the most of the industrial, large-scale catalysis is heterogeneous due to their cost effectiveness, the apparent advantages of using homogenous molecular catalysts include the availability of advanced experimental and computational techniques for their syntheses and characterization, and the tunability of the active sites to achieve the selective and efficient conversion.³⁹ In addition, lessons learned from the studies on homogenous catalysts can be implemented in design of heterogenous catalysts. When evaluating the CO2RR catalyst's performance, there are several properties considered: activity, energy efficiency, robustness and selectivity. An ideal catalyst should be selective toward a single product, operate efficiently at low overpotentials and exhibit long-term stability. However, it is often difficult to compare different catalysts' performances due to variations in experimental setups. The following session outlines the current state of the homogenous CO2RR electrocatalysis field.

| Property | Homogeneous | Heterogeneous |
|---|-------------------|--------------------|
| Active site | majority of atoms | only surface atoms |
| Mechanism | defined | poorly defined |
| Selectivity | tunable/high | not tunable |
| Durability | poor | fair |
| Reaction conditions (temperature, pressure) | mild | often elevated |

Table 2. Comparison of main properties of homogeneous vs. heterogenous catalysts.³⁹

1.2 Previous Efforts on Homogenous CO2RR Electrocatalysts

The area of homogenous CO2RR electrocatalysis has been flourishing from its beginning in 1980s, which resulted in reports of numerous molecular catalysts.^{39-40, 42-43} The field has been dominated by studies on organometallic catalysts. Originally, the research was focused on complexes with late transition metals such as Ru, Re and Ir, while more recently there are more reports emerging on earth-abundant complexes such as Mn, Fe and Co. The majority of reported electrocatalysts generate 2e⁻ reduced products, CO and formate. In general, the catalyst serves as a multiple-electron carrier between the electrode and CO_2 , which enables catalysis to occur at the reduction potential of the catalyst rather than the potential for direct CO₂ reduction. Upon reduction of the catalyst, the low valent metal center binds either CO₂ to form a metallo-carboxylate, carbon monoxide-route, or a proton to form a hydride, formate-route (Scheme 1). It is not always clear whether the metal-center will have more tendency towards CO₂-binding or protonbinding, and often both products are observed, albeit in different yields. In addition, production of hydrogen is a very common side reaction when CO2RR electrocatalysts are employed in the presence of proton source because it is more thermodynamically favored over two-electron CO₂ reductions (Table 3).⁴⁴⁻⁴⁵ Since the product distribution primarily depends on the reaction mechanism and experimental conditions,⁴⁶ the mechanistic aspects of a few selected metal-complexes will be discussed in more detail; an exhaustive list of molecular electrocatalysts can be found elsewhere.³⁹

Scheme 1. Schematic representation of the generalized CO2RR catalysis with metalbased electrocatalysts. The scheme depicts possible pathways that lead to the formation of most observed reduction products (carbon monoxide, hydrogen and formate).



 Table 3. Standard reduction potentials in acetonitrile relevant for CO2RR with metalbased electrocatalysts.

| reduction reaction | E ⁰ (V vs. Fc ⁺ /Fc ⁰) | E ⁰ (V vs. SCE) |
|--------------------------------------|--|----------------------------|
| $CO_{2}(g) / HCO_{2}^{-}(s)$ | -0.77 | -0.39 |
| CO ₂ (g) / CO (g) | -0.12 | +0.26 |
| 2H ⁺ / H ₂ (g) | -0.03 | +0.35 |

1.2a Ruthenium – Polypyridyl Complexes

Polypyridyl complexes are one of the most often reported classes of molecular catalysts for photo- and electrocatalytical CO2RR for several reasons.⁴³ First, the easy synthesis and fairly approachable electronic and steric tunability have enabled development of a series of electrocatalysts. Second, polypyridyl ligands are redox active and their reduction often occurs at less negative potentials than for metals enabling multi-electron transformations. Lastly, the ligand can tune both the geometry and electronic structure of the metal centers, that are analogous to catalytic sites in enzymes.

The polypyridyl complexes of ruthenium have been extensively studied in electrocatalytic CO2RR. First introduced by Tanaka, the $[Ru(bpy)_2(CO)CI]^+$ complex (bpy – 2,2'-bipyridine) showed catalytic activity at -1.50 V vs. SCE potential in water/DMF mixture. The product distribution was found to depend on the pH (Figure 2).^{1, 47-48} Slightly acidic conditions (pH = 6) favored production of CO and H₂, while more formate was produced under basic conditions (pH = 9.5). The insights about the mechanism of the electrochemical transformation were obtained from the cyclic voltammetry of the complex in the presence and absence of CO₂ and product distribution. The voltammetric profile of the complex in the absence of CO₂ displays a reversible reduction peak at -1.24 V vs. SCE and an irreversible reduction peak at -1.48 V vs. SCE (Figure 2a). These two peaks were assigned to the reduction of two bpy-ligands according to DFT calculations.⁴⁹ The loss of reversibility at second electron reduction is explained by the reductive dehalogenation which results in the formation of five-coordinate species [Ru(bpy)₂(CO)]⁰ (Figure 2b).



Figure 2. Electrochemical reduction with Ru-bpy complexes: a) cyclic voltammograms of [Ru(bpy)₂(CO)CI]⁺ in DMF under nitrogen (solid) and CO₂ (dashed); adapted with permission from ref. 1. Copyright 1987 American Chemical Society. b) mechanism proposed by Tanaka et al., see ref. 1; c) mechanism proposed by Meyer *et al.*, see ref. 2.

Upon the formation of the neutral $[Ru(bpy)_2(CO)]^0$, there is a nucleophilic attack of the metal center to CO₂ to yield the metallocarboxyallato complex. Once this complex is protonated, it vields the critical selectivity-determining intermediate [Ru(bpy)₂(CO)(COOH)]⁺. In acidic condition, this intermediate undergoes additional protonation to initiate H₂O release and yield [Ru(bpy)₂(CO)₂]. Upon two-electron reduction, CO is being released which recovers the active catalyst [Ru(bpy)₂(CO)]⁰. Under basic conditions, [Ru(bpy)₂(CO)(COOH)]⁺ reacts with a proton and two electrons to produce formate and recover the active $[Ru(bpy)_2(CO)]^0$. It is interesting to note that authors propose that the process does not generate the hydride species during the conversion.

8

The study on electrocatalytic activity of $[Ru(bpy)_2(CO)H]^+$ in acetonitrile by Meyer *et al.* revealed an alternative, hydride mechanism.² By using controlled potential electrolysis of cis- $[Ru(bpy)_2(CO)H]^+$ and FTIR spectroscopy, several intermediates such as $[Ru(bpy)_2(CO)(OCHO)]^+$ and $[Ru(bpy)_2(CO)(MeCN)]$ were identified. This helped authors elucidate the mechanism. The catalytic cycle involves bpy-based one-electron reduction of the $[Ru(bpy)_2(CO)H]^+$ complex, followed by CO_2 insertion into the Ru-H bond to yield formato-complex $[Ru(bpy)_2(CO)(OCHO)]^+$. A subsequent electron transfer causes a loss of formate and recovery of the complex $[Ru(bpy)_2(CO)(MeCN)]$ that upon protonation recovers the starting complex.

Despite being structurally very similar, proposed mechanism for the catalysis with [Ru(bpy)₂(CO)CI]⁺ and [Ru(bpy)₂(CO)H]⁺ are very different, probably due to the different experimental conditions. While many detailed experimental and computational methods have been employed to explore the mechanism, the relationship between the structure of the catalyst or experimental conditions and reactivity remains empirical. Also, molecular Ru(bpy)-based complex generally display lower catalytic activity and poor selectivity than the corresponding Re- and Mn- analogs (*vide infra*). Furthermore, they undergo reductive electro-polimerization reaction which is initiated by bpy-ligand dissociation and the resulting film acts as a heterogenous catalysts for CO2RR.⁵⁰⁻⁵¹ A new generation of Rupolypyridyl complexes prevents the electro-polymerization by implementing ligands such as 2,2':6',2''-terpyridine and 1-methylbenzimidazol-2-ylidene.^{49, 52-55} In addition, these ligands enhance the catalytic activity and improve the selectivity towards CO by suppressing the formation of the heterogenous catalyst that produces both CO and formate.⁵⁶

1.2b Rhenium- and Manganese- Bipyridyl Complexes

First reports on CO2RR catalysis with Re-complex [Re(bpy)(CO)₃Cl] date back in 1980s, where it was shown that the bipyridyl-complex can act as both a photo- and electrocatalyst for the reduction to CO.^{3, 57} The mechanism for the electrochemical conversion is well studied experimentally and computationally and has found to depend on the experimental conditions, such as applied potential, solvent, etc.. ^{3-4, 57} Specifically, there are two oneelectron reduction events taking place under an inert atmosphere, assigned to reversible reduction of the bpy-ligand (at -1.35 V vs. SCE) and the irreversible metal-centered reduction (at -1.71 V vs. SCE).³ Upon the two-electron reduction, a loss of the chloride ligand takes place, followed by the intramolecular ligand-to-metal electron transfer that creates an active site for the CO₂ binding, similar to the Ru-based catalyst (Figure 3a). Ligand release also takes place at the catalyst's first reduction potential in weakly coordinating solvents, except on a much longer time scale (Figure 3a).⁵⁸ Once CO₂ is bound, the catalysts proceeds through several proton and electron transfers before releasing CO as the sole product (Figure 3b). DFT calculations revealed that the high selectivity toward CO production is achieved due to a practically barrier-less CO₂ binding, whereas the binding of a proton is not kinetically favorable (ΔG^{\ddagger} = 21.6 kcal/mol, Figure 3c).⁵ The protonation of the pentacoordinate metal-complex $[Re(bpy)(CO)_3]^-$ becomes more competitive in the presence of strong acids or in aqueous solutions, which then favors production of H_2 and formate (Scheme 1).



Figure 3. Electrochemical CO2RR to CO using the Re-based catalyst: a) one- and twoelectron reduction pathways for the activation of the catalyst proposed by Meyer *et al.* in ref. 3; b) electrocatalytic cycles proposed by Carter *et al.* in ref. 4; c) schemastic representation of the potential energy surface for H⁺ and CO₂ additions calculated by Carter *et al.* in ref. 5.

In addition to hydride formation, there is another side reaction occurring o that leads to the deactivation of the catalyst. Namely, the pentacoordinate Re-complex [Re(bpy)(CO)₃]⁻ undergos a slow dimerization reaction to form a Re-Re bond in the [Re(bpy)(CO)₃]₂ dimer that incapacitates the further reduction.⁵⁹ The same inactive dimer has been observed in photochemical catalysis by Rieger and collaborators.⁶⁰ The undesired dimerization reaction can be suppressed by the modification of the bipyridine-

ligand. In specific, a tert-butyl derivative showed an improved catalytic activity by inhibiting the formation of the dimer due to the steric constraints.⁶¹

Despite being superior in the CO₂-to-CO conversion, rhenium is one of the least abundant elements. As a result, the recent studies have shifted towards bipyridyl complexes of more earth abundant elements, such as manganese. The first study from 2011 on the $[Mn(bpy)(CO)_3Br]$ complex reported electrocatalytic activity for the CO2RR to CO at overpotentials lower than for the Re analog.⁶² The catalysis mechanism was studied experimentally and computationally,^{5, 62} and it was found to slightly differ from rhenium electrocatalysis. Under inert atmosphere, the cyclic voltammogram of [Mn(bpy)(CO)₃Br] display two irreversible reduction peaks at -1.26 V and -1.50 V vs. SCE. The first irreversible reduction (at -1.26 V vs. SCE) has been associated with halide dissociation and consequent rapid radical dimerization (Figure 4a). The formation of the dimer was previously confirmed using UV/Vis and IR spectroelectrochemistry.⁶³ The dimer is then further reduced at -1.50 V vs. SCE to produce the active penta-coordinate complex. Unlike the Re-complex, the CO₂ binding takes place only in the presence of a proton donor, which is rationalized by calculated endergenic ΔG value for CO₂ addition (Figure 3c).⁵ From there, the reaction mechanism proceeds similarly to Re-catalyst with multiple proton-electron transfers that lead to CO production (Figure 3b).

12



Figure 4. Electrochemical CO2RR to CO with the Mn-bipyridine catalyst: a) the mechanism for catalyst activation proposed by Deronzier and coworkers in ref. 62; b) suggested intermediate structure responsible for the more favorable 'protonation-first' mechanism; adapted with permission from ref. 6. Copyright 2017 American Chemical Society. c) schematic comparison of 'protonation-first' and 'reduction-first' mechanisms.

Significant improvements to the activity and stability can be achieved with the incorporation of bulky substituents in 5, 5' positions of the bpy-ligand, such as tert-butyl and mesityl groups.⁶⁴ Similar to Re-catalysts, bulky substituents inhibit the dimer formation while improving the catalytic activity. The overpotential can also be lowered by the substituents that alter the reaction mechanism. Specifically, incorporation of dimethoxyphenyl substituent favors the "protonation first" mechanism through a

hydrogen-bonding interaction and electronic substituent effect with the Mn(I)-COOH intermediate (Figure 4b), which enables a more facile C-OH bond cleavage.⁶ The reduction of the resulting intermediate [Mn(bpy)(CO)₄]⁺ is more thermodynamically favorable compared to Mn(I)-COOH intermediate: -1.3 V vs. SCE for the 'protonation-first' mechanism and -1.6 V vs. SCE for the 'reduction-first' mechanism (Figure 4c). As a consequence, methoxy-catalysts operates at more positive applied potentials than the catalyst with structurally similar ligands that cannot form hydrogen bonds, i.e. mesityl groups, 'reduction-first' pathway.

1.2c Fe-Porphyrin Complexes

The most noticable advancements in CO2RR electrocatalysis with first row transition metals have been achieved with iron porphyrin complexes. These biomimetic models of heme coenzymes are homogeneous electrocatalysts for CO₂-to-CO reduction with superior selectivity, reasonable stability, and remarkable rates. The first report on catalysis by iron-tetraphenylporphyrins FeTPP (Figure 5a) was by Saveant and co-workers in the 1980s.⁶⁵ In the absense of CO₂, the [Fe^{III}(TPP)]⁺ complex exhibit three reversible peaks, which were assigned to clear Fe^(III / II), Fe^(II / I), and Fe^(I / 0) couples.⁶⁶⁻⁶⁷ Under 1 atm of CO₂, there is a new catalytic peak rising at the Fe^(I / 0) potential, indicating that Fe⁰ acts as an active species that readily reacts with CO₂ to initiate the catalysis.⁷ In a =dry solvent, another molecule of CO₂ is proposed to act as the oxide acceptor thereby generating CO_3^{2-} (Figure 5b, scenario 1). The catalysis in anhydrous conditions proceeds with only few catalytic turnovers due to the catalyst deactivation by carboxylation of the TPP ligand.⁶⁵ The catalyst performance can be boosted by the addition of Lewis acids

(such as Mg²⁺), where Mg²⁺ promotes decomposition of the Fe-COO⁻ adduct into $[Fe^{II}(TPP)(CO)]$ and MgCO₃.^{66,68} Nonetheless, this is not very practical since the prolonged production of MgCO₃ in the form of precipitate covers the electrode surface and inhibits further catalysis. Alternatively, the dehydration of the metallocarboxylic complex $[Fe^{II}(TPP)(COOH)]^-$ can be accelerated by the addition of Brønsted acids (Figure 5b, scenario 2).⁶⁹⁻⁷⁰ However, the choice of the acid is critical because the stronger acids facilitate the dehydration of the $[Fe^{II}(TPP)(COOH)]^-$ but also promote the formation of the hydride, which favors the production of H₂ and formate.



Figure 5. Electrochemical CO2RR to CO using the Fe-porphyrin catalyst: a) cyclic voltammograms of iron-tetraphenylporphyrin [Fe(TPP)]⁺ under argon (blue line) and CO₂ (red line); adapted with permission from ref. 7. Copyright 2013 American Chemical

Society. b) schematic representation of Lewis acid- and Brønsted acid-promoted catalytic cycles.

A major breakthrough in FeTPP catalysis was realized by modifying second coordination sphere around the metal center. Specifically, the incorporation of phenol handles in the ortho position of the TPP ligand significantly improved CO₂ to CO kinetics by providing a local proton source.⁷¹ According to DFT calculations, the role of the proton handle is to stabilize [Fe^{II}(TPP)(CO₂)]²⁻ adduct through intramolecular H-bonding (Figure 6a).⁷² The prepositioned proton source alters the mechanism by initiating 'protonation first' pathway (Figure 6a), analogously to the intermediate observed in the methoxysubstituted Mn-bipyridine catalyst (Figure 4b). As a consequence, the overall catalysis occurs at more positive ~0.2 V applied potential. Alternatively, further improvement of the iron-porphyrin catalysts can be achieved by altering the electronic environment in the second coordination sphere. The work done by Saveant and coworkers showed that addition of charged substituents in para position of phenyl groups reduced the catalysis overpotential (Figure 6b) by lowering the reduction potential of the Fe^(1/0) couple through the inductive effect.^{8,73} However, the catalytic activity simultaneously declined presumably by decreasing the electron density around Fe⁰ center, which lowered its nucleophilicity for the reaction with CO2. The biggest improvement in terms of overpotential, to only 0.2 V from thermodynamic, has been achieved when a positively charged ammonium-substituent was placed in the ortho position.⁸ The ortho substitution also improved the catalytic activity (Figure 6b), most likely by Coulombic stabilization of the initial Fe- CO₂ adduct. Presently, the catalyst FeTPP-oA+ shown in Figure 6b is

16

considered the most efficient and highly selective homogenous electrocatalyst for the CO₂-to-CO reduction. However, the superior catalytic activity of FeTPP-oA+ is overshadowed by its synthetically challenging preparation, where the overall yield for the ligand synthesis is reported to be only 9%.



Figure 6. Importance of second coordination sphere in CO2RR electrocatalysis with FeTPP: a) a phenol proton handle enables 'protonation-first' mechanism; b) linear sweep of several substituted FeTPP catalysts showcasing the influence of inductive effect and local Coulombic stabilization on catalysis; adapted with permission from ref. 8. Copyright 2016 American Chemical Society.

1.2d Formate-Producing Electrocatalysts

The majority of catalysts perform electrochemical CO2RR to CO, where production of formate often occurs only as a side product. While certain catalysts show remarkable
selectivity towards CO production, this gaseous product is highly toxic and difficult to store and transfer. Formate, on the other hand, represent a more desired energy carrier candidate, due to its low toxicity and straightforward handling. The production of formate likely happens through a metal-hydride intermediate that is being formed mostly in the presence of strong acids or lower CO₂ concentrations. Under such conditions, hydride transfer to available protons (protonolysis) becomes a competing process yielding both formate and hydrogen gas as the major products. While the early studies performed by Meyer,⁷⁴ Deronzier⁷⁵ and Tanaka⁷⁶ showed comparable yields of formate and hydrogen gas, more recent studies lead by Brookhart,^{9, 77} Meyer^{9, 77} and Berben⁷⁸⁻⁸⁴ demonstrate catalysts that produce formate in predominant yields.

Unlike other precious metals, iridium has been mostly associated with the hydridebased catalysis. Iridium pincer complexes, studied by Brookhart,⁹ Meyer and coworkers, have been tested with regard to their selectivity for reduction of CO₂ to formate.⁹ A preparative electrolysis of iridium-hydride [Ir(PCP)(MeCN)(H₂)] under CO₂ atmosphere in MeCN/water mixture produced a high yield of formate, whereas H₂ was observed in significantly less yield. The mechanism was postulated based on the cyclic voltammetry, preparative electrolysis and DFT calculations.⁸⁵ In the absence of CO₂, cyclic voltammogram of the hydride show no cathodic signals (Figure 7a, top). In the presence of CO₂, a new catalytic wave appears at -1.64 V vs. SCE, indicating that [Ir(PCP)(MeCN)(H₂)] serves as active species for CO2RR. DFT calculations and cathodic scans of the oxidized form [Ir(PCP)(MeCN)(H)]⁺ confirmed that the active hydride is regenerated at this potential (Figure 7a, bottom).^{9, 85} In addition, a control experiment showed a quantitative CO2RR by [Ir(PCP)(MeCN)(H₂)] yielding [Ir(PCP)(MeCN)(H)]⁺ and

HCOO⁻ as sole products. Based on these findings, the authors proposed the mechanism depicted in Figure 7b. According to the DFT calculations, the lower yield for proton reduction is a consequence of the Ir-H bond being kinetically inert towards protonolysis under the given conditions due to an activation barrier of 25 kcal/mol.⁸⁶



Figure 7. Electrochemical CO2RR to formate with the Ir – pincir complexe: a) cyclic voltammograms of $[Ir(PCP)(MeCN)(H_2)]$ (top) and $[Ir(PCP)(MeCN)(H)]^+$ (bottom) in the argon (black line) and CO₂ (red line); adapted with permission from ref. 9. Copyright 2012 American Chemical Society. b) schematic representation of the mechanism postulated from electrochemical measurements and DFT calculations.

Another interesting group of metal catalysts that perform CO2RR to formate via a similar mechanism is the class of iron carbonyl clusters studied by Berben et al.⁷⁸⁻⁸⁴ These acid-resistant clusters achieve remarkable selectivity in both aqueous and in organic media. In the absence of CO₂, these iron clusters show catalytic activity in proton reduction,⁸⁷ indicating that the formation of formate is kinetically favored over protonolysis.⁷⁸ With regard to CO2RR, the reduction mechanism is suggested to proceed via hydride transfer based on cyclic voltammetry studies and spectroscopic measurements.⁸⁸ Similar to the Ir-hydride study, the reduction of CO₂ to formate with the pre-prepared hydride confirmed a hydride transfer mechanism. Efforts to increase overall kinetics by improving the hydride donor ability or by providing a local proton handle (as was demonstrated with Co-complexes with pendant amines; not discussed here) have resulted in diminishing of formate production and enhancing the hydrogen evolution.⁸⁹ Based on their studies, the authors suggest that the hydride donor ability of metal hydride for CO₂-to-formate conversions should be sufficiently high to drive hydride transfer reaction to CO₂, but not too high to undergo protonolysis.⁸⁴

In summary, organometallic electrocatalysts have come a long way since the initial discovery. Impressive progress has been achieved by mechanistic understanding of the catalytic systems obtained from electroanalytical techniques, spectroscopy and computational chemistry. Modifications to the primary and secondary coordination sphere have significantly improved catalyst activity and selectivity, even with the first-row transition metals. However, the vast majority of reported electrocatalysts catalyze CO2RR only to two electron products; the catalysis presumably terminates at the stage of CO and

formate due to their high stability.⁹⁰ Very recently, the reduction of CO₂ beyond twoelectron reduction products has been achieved by an iron electrocatalyst with the aid of an additive that prevented formate formation.⁹¹ Another major concern associated with utilization of electrocatalysts for CO2RR is their durability. Even the most durable catalysts suffer from deactivation after several hours or days. One of the approaches that aims to address stability issues is incorporating molecular catalysts into heterogenous systems. Such heterogenization process increases durability and catalytic activity of molecular catalysts while synergistically improving the selectivity of the heterogenous moiety.⁹²⁻⁹⁶ Further research in this area might result in a suitable candidate to replace fossil fuels.

1.3 Our Biomimetic Approach

Our group performs fundamental mechanistic studies on metal-free systems that are relevant for solar fuels and other energy storage applications.⁹⁷⁻¹⁰² We often draw inspiration from natural systems and cofactors that are pivotal for the enzymatic activity. For this project, the major source of inspiration comes from natural photosynthesis, where the critical step of CO₂ reduction to carbohydrates is performed by the organic cofactor nicotinamide adenine dinucleotide phosphate (NADPH). The NADPH cofactor, a medium strength hydride donor, selectively reduced an activated CO₂ molecule in form of ester, 1,3-bisphosphoglycerate to the aldehyde through a hydride transfer mechanism (Scheme 2, left). The active hydride form of NADPH is then regenerated by the electrons supplied from the photo-driven water oxidation reaction.

Scheme 2. Our approach. *left:* In natural photosynthesis, the reduction of CO_2 to carbohydrates is performed by NADH, which is regenerated from photo-driven water oxidation. *right:* Our biomimetic approach includes a photoelectrochemical cell for selective CO_2 reduction. Active hydrides are designed to have favorable thermodynamic parameters for hydride transfer to CO_2 and easy photoelectrochemical regeneration with a semiconductor and electrons from water oxidation.



In our approach (Scheme 2, right), the reduction of CO₂ is realized by biomimetic NADH-analog electrocatalysts that are covalently attached to a semiconductor surface that acts as a photocathode. The metal-free NADH analogs are designed to be capable of reducing CO₂ to methanol through a sequence of proton-coupled hydride transfers, as opposed to metal-based hydride catalysts that favor production of formate and hydrogen gas. This can be achieved based on the fact that metal-free NADH analogs are not efficient in hydrogen evolution catalysis.⁹⁷ Similar to natural photosynthesis, the

regeneration of NADH analogs from these NAD⁺-forms occurs by light-induced charge transfers from the photocathode with electrons obtained from the water oxidation part of the photoelectrochemical cell. The apparent advantages of using such system are:

- the reduction of CO₂ occurs in a selective manner accomplished by hydride transfer reactions;
- the reduction can be directed towards methanol as a final product through a sequence of proton-coupled hydride transfer steps, thus, avoiding gaseous products such as CO and H₂;
- (iii) the biomimetic NADH electrocatalysts are built from earth-abundant elements (carbon, nitrogen, oxygen) and can serve as inexpensive, non-toxic materials for industrial application.

The performance of the proposed photoelectrochemical cell depends on the hydride donor ability of the metal-free hydrides (often described using "*hydricity*") and the ease of the (photo)electrochemical regeneration of the active hydride form. This thesis consists of fundamental studies on NADH analogs in terms of their thermodynamic and kinetic hydricities, applicability in CO₂ reduction via hydride transfer, and electrochemical requirements for hydride regeneration. The experimental and computational data in this work outline structural motifs that afford better metal-free hydride donors, provide insights on their application in catalysis and current limitations for replacing metal-based catalysts.

Chapter 2. Thermodynamic and Kinetic Hydricities of Metal-Free Hydrides

Adapted in part from Ref. 241 with permission from Ilic, S.; Alherz, A.; Musgrave, C.B.; Glusac, K.D. Chem. Soc. Rev. **2018**, 47(8), 2809-2836, DOI: 10.1039/C7CS00171A.

© 2018 The Royal Society of Chemistry

2.1 Introduction

Hydride donors are powerful reducing reagents. By transferring a hydride ion to the appropriate substrate, hydride donors achieve a two-electron, proton-coupled reduction in a concerted fashion, without the formation of high energy, often unstable, intermediates. Transition metal hydrides, particularly those made of the noble metals Rh, Pd and Pt, are generally excellent hydride donors and can often be used in catalytic amounts through either electrochemical or chemical regeneration of the hydride donor from its conjugate hydride acceptor.¹⁰³⁻¹⁰⁵ However, due to the low abundance and high toxicity of transition metal-based hydrides,¹⁰⁶ recent scientific efforts have investigated metal-free hydride donors and their utilization in catalytic reduction processes.

Initial interest in metal-free hydride donors (Scheme 3a) was motivated by their close resemblance to enzymatic cofactors, nicotinamide adenine dinucleotide phosphate (NADPH) and flavin adenine dinucleotide (FADH₂). Natural systems often utilize these organic hydride donors to drive a myriad of reduction reactions. For example, the critical step in CO₂ reduction in photosynthetic systems is a hydride transfer from reduced NADP (NADPH),¹⁰⁷ a carbon-based hydride donor with moderate hydride donating ability. Inspired by natural cofactors, several synthetic analogs were investigated, such as Hantzsch esters, and applied as mild hydride sources in various asymmetric transformations, often activated by the presence of a metal ion in a similar fashion as in natural enzymatic systems.¹⁰⁸ Furthermore, stronger hydride donors (e.g. Super hydride[™], lithium triethylborohydride, Scheme 3a) are often used as stoichiometric reagents for reductions of numerous functional groups, such as C=O, C=N and C=C bonds in organic synthesis.^{18, 109} More recently, significant progress has been made

towards the catalytic use of metal-free hydride donors. Specifically, frustrated Lewis pairs, made of sterically-hindered hydride and proton acceptors, have emerged as a promising class of metal-free catalysts for hydrogen activation.¹¹⁰⁻¹¹¹

Scheme 3. a) Some examples of metal-free hydride donors. Metalloids are shown in orange, while nonmetals are shown in blue. Hydridic hydrogens are shown in red and electronegativity values are represented by " χ ". The selected examples of each group are presented as follows, from top left: boron (lithium triethylborohydride, Super hydride^{TM18}), carbon (NADPH,¹⁹ R = adenine dinucleotide phosphate), nitrogen (FADH₂,²⁰ R = adenine dinucleotide), oxygen (coenzyme Q₁₀²¹), silicon (triphenylsilane²²), phosphorus (2-H-diazaphospholene²³), germanium (tributylgermane²⁴) and tellurium (sodium hydrogen telluride²⁵). b) Thermodynamic and kinetic hydricity scales used to evaluate hydride donor ability and reactivity of metal-free hydride donors.



The hydridic H-atom in metal-free hydrides is bound either to a nonmetal - carbon, nitrogen, oxygen or phosphorus - or a metalloid - boron, silicon, germanium or tellurium (Scheme 3). In general, the hydride donating ability of metal-free hydrides can be tuned over a wide range by varying the donor's electronic and/or structural parameters, such as

the polarization of the hydridic bond of the hydride donor or the extent of positive charge delocalization in the conjugate hydride acceptor. The selection of appropriate hydride donors for various desired applications is usually made by considering thermodynamic and kinetic hydricity parameters. The thermodynamic hydricity (ΔG_{H-}) is defined as the standard Gibbs free energy change for the dissociation of a hydride donor R-H into a conjugate hydride acceptor R⁺ and a hydride anion H⁻:

$$R - H \rightarrow R^+ + H^- \Delta G_{H-}$$
(1)

 ΔG_{H-} values are always positive because spontaneous heterolytic dissociation of the hydride does not occur and lower values for ΔG_{H-} indicate a better hydride donor (Scheme 3b). Based on their ΔG_{H-} values in acetonitrile (MeCN) and dimethyl sulfoxide (DMSO), hydrides can be divided into weak ($\Delta G_{H-} > 80$ kcal/mol), moderate (50-80 kcal/mol) and strong (< 50 kcal/mol) donors. The Gibbs free energy associated with the reverse of process (1) is defined as the hydride affinity of R⁺, where this parameter is relevant for oxidation reactions involving abstraction of hydride ions from relevant substrates. Naturally, the ΔG_{H-} of the hydride donor and the hydride affinity of the conjugate hydride acceptor have the same value, but with opposite signs.

Kinetic hydricity of metal-free hydride donors is often defined in terms of a nucleophilicity factor *N*, which is a purely empirical parameter obtained from experimental rates for hydride transfer reactions with reference acceptors. The *N* value of the hydride donor can be correlated directly with the activation free energy for the hydride transfer reaction with an acceptor.¹¹²⁻¹¹³ Therefore, *N* can be used to quantify the kinetic strength of a hydride donor, where stronger hydride donors are defined to possess larger *N* values

(Scheme 3b). Hydride donors can be divided into slow reacting (N < 0), moderately reactive (0 – 10) and highly reactive (> 10).

A number of exhaustive reviews have covered metal-free hydride motifs and their application in organic synthesis and photoelectrocatalysis.^{108, 111, 114-115} Here, we approach metal-free hydrides from the mechanistic perspective; we review the literature reports of thermodynamic and kinetic hydricities of metal-free hydride donors. The first two sections summarize different experimental and computational methods for their determination, as well as a description of the advantages and disadvantages of each approach. The reported hydricity parameters are then tabulated, and the data used to derive structure-property relationships of the hydrides, with a focus on trends that govern the thermodynamic and kinetic properties for different classes of metal-free hydride donors. In the last section, we analyze the tabulated hydricities and other electrochemical properties to evaluate the applicability of metal-free hydrides to catalytic processes, such as solar fuels generation.

2.2 Experimental Methods

Several different experimental approaches are utilized to evaluate hydride donating abilities of metal-free hydrides. The Gibbs free energy ΔG_{H-} is the most accurate parameter to evaluate the thermodynamic driving forces for hydride transfer reactions. Two main experimental approaches are used to obtain ΔG_{H-} for metal-free hydride donors: the "potential-pKa" and "hydride transfer" methods (Scheme 4). However, both methods are often experimentally challenging. To avoid these challenges, one can resort to obtaining the experimental enthalpy change (ΔH_{H-}) and assume that the entropic

contributions to the hydride transfer processes are insignificant. Although this assumption is not always valid, the determination of ΔH_{H-} is experimentally simple, which enables one to screen a large number of model compounds. In addition to these thermodynamic parameters, a kinetic nucleophilicity scale was developed by Mayr,¹¹²⁻¹¹³ in which the nucleophilicity *N* of metal-free hydrides is derived from experimental rates for the relevant hydride transfer reactions. Although the nucleophilicity scale does not provide absolute activation barriers because it is expressed relative to the electrophilicities of reference hydride acceptors, it provides valuable information regarding the relative reactivity of various hydrides. The governing principles, as well as the advantages and disadvantages of each method are discussed below. Additionally, this section provides an exhaustive tabulation of the previously reported experimental hydricity parameters for metal-free donors.

Scheme 4. Illustrative description of the methods used to obtain thermodynamic and kinetic hydricities. The desired values obtained as outcomes from these methods are represented in red; measured parameters are represented in green and reference values are represented in blue.



2.2a The Potential-pK_a Method

The "potential-pKa" method is based on a thermochemical cycle that treats the free energy of hydride transfer as the net free energy of two electron transfers and a proton transfer, where the $\Delta G_{H^{-}}$ values are obtained from the relevant one-electron reduction potentials E_1 (for R⁺/R⁻) and E_2 (for R⁻/R⁻), and pK_a value of R-H (Scheme 4). To close the thermochemical cycle, the standard two-electron reduction potential of a proton ($\Delta G_{H+/H-}$) needs to be evaluated using the reduction potentials $E(H^+/H)$ and $E(H/H^-)$ (Scheme 4). The proton reduction potential $\Delta G_{H^+/H^-}$ in MeCN and DMSO have been estimated previously by Parker ($\Delta G_{H+/H-}$ (MeCN) = 54.7 kcal/mol, $\Delta G_{H+/H-}$ (DMSO) = 69.9 kcal/mol),¹¹⁶ and these values were used to derive experimental thermodynamic hydricities of both metal-based¹¹⁷⁻¹²⁹ and metal-free^{116, 130-135} hydride donors. However, it is important to emphasize that the evaluation of $\Delta G_{H^+/H^-}$ requires a number of assumptions associated with the solvation of a proton, hydrogen atom and hydride ion. For example, the solvation free energy of a proton is derived from its aqueous value and the free energy to transfer the proton from water to the solvent of interest, while the solvation of a hydrogen atom is approximated as the solvation free energy of helium.¹³⁶ Furthermore, $E(H/H^{-})$ is estimated using its aqueous value and the free energy to transfer a hydride from water to an organic solvent, which is obtained from linear correlations of halide ions.¹³¹

The potential-pK_a approach has been applied by $us^{134-135}$ and others^{116, 130-133} to obtain the thermodynamic hydricities of relatively weak organic hydride donors, such as arylmethanes, anthracene, fluorenes, quinones and acridines (Table 5). However, a number of experimental challenges have limited the broader use of the "potential-pK_a"

method. For instance, the standard reduction potentials E_1 and E_2 cannot always be practically obtained experimentally, either because the reduction peaks are chemically irreversible on cyclic voltammetry timescales or because the reduction processes occur outside the solvent electrochemical stability window. The latter issue is particularly important for species associated with strong hydride donors, because there is a linear correlation between the first reduction potential and thermodynamic hydricity, as discussed in Relevance to Catalysis section. For cases where chemical irreversibility is an issue, some researchers approximate the standard reduction potentials using the cathodic peak potentials, which introduces an ~0.3 V error in the estimated reduction potentials (assuming that the irreversibility occurs at the 100 mV/s sweep rate due to a subsequent chemical reaction with a rate constant of 10¹⁰ s⁻¹).¹³⁷⁻¹³⁹ In some cases, square-wave voltammetry is used to obtain a more accurate approximation of the standard reduction potentials.¹⁴⁰⁻¹⁴³ In cases where the first reduction is chemically irreversible, the second reduction process does not occur and will not be observed in the cyclic voltammograms. In such cases, the second reduction potential can be obtained by performing the one-electron oxidation of the deprotonated hydride, R⁻.¹⁴⁴ Alternatively, hydride donor ability of metal-free hydrides can be experimentally evaluated using the standard reduction potential for proton-coupled conversion of R to RH2.145-147

Another challenge associated with the potential-pK_a method is that metal-free hydrides tend be very weak acids, and the determination of their pK_a values is often hindered by the pK_a of solvent ($pK_a(DMSO) = 35$,¹⁴⁸ $pK_a(ACN) = 33^{149}$). On average, metal-free hydride donors are weaker acids than metal-based hydrides. For example, the pKa values of [Ni^{II}-H]⁺ hydride donors in acetonitrile are in the 13-24 range,¹⁵⁰ while the

pKa values of acridine-based hydrides are in the 27-50 range.¹³⁴⁻¹³⁵ For hydrides that are more basic than the solvent, the relevant pK_a values can be obtained using extrapolation techniques.¹⁴⁸

2.2b The Hydride Transfer Method

In cases where the potential-pK_a method cannot be applied, the "hydride transfer" method provides an excellent alternative approach. This method involves the determination of the equilibrium constant for the hydride transfer (HT) reaction between a donor of interest (R-H) and a reference acceptor with known hydride affinity (A⁺, Scheme 4). The equilibrium concentrations are readily obtained using NMR or UV/Vis absorption spectroscopy, and the "hydride transfer" method has been successfully applied to a series of metal-free hydride donors: NADH analogs,^{135, 151-152} imidazole analogs,¹³⁴⁻¹³⁵ acridine analogs¹³⁴⁻¹³⁵, ¹⁵¹ and triethylborohydride.¹⁵³ It is important to mention that the accuracy of this method requires that the equilibrium of the hydride transfer reaction is reached before the concentrations are measured. This condition implies that the $\ \Delta G_{H-}$ of A-H needs to be within 2-3 kcal/mol of the thermodynamic hydricity of R-H, indicating that usually several hydride acceptors A⁺ need to be tested before the appropriate reagent is identified. To ensure that equilibrium has been obtained, a second equilibrium of the reaction mixture should be obtained by adding products to the equilibrated system and the equilibrium constant re-measured.¹⁰³ In some cases, equilibrium is reached only after several weeks, increasing the probability that an undesired side reaction will occur. Alternatively, the equilibrium constant for the hydride transfer reaction can be obtained by measuring the rate constants for the forward and reverse reactions between a hydride of interest and a reference hydride. This approach has been particularly utilized in early studies on hydride transfer between NADH analogs.^{146, 154-156}

2.2c Nucleophilicity

In addition to the thermodynamic parameters discussed above, Mayr developed a nucleophilicity scale, which evaluates the relative kinetic reactivity of hydride donors.^{113, 157-161} This method involves the experimental determination of rate constants (*k*) for a reaction between a hydride donor of interest and a series of hydride acceptors with known electrophilicities (*E*). The results are fit to the following expression:

$$\log k = s_N (N + E) \tag{2}$$

which enables the determination of the parameters *N* and s_N . The nucleophilicity parameter (*N*) describes the rate of hydride transfer by a hydride donor. The experimentally obtained *N* values for metal-free hydrides range between –5 and 15, where the larger values indicate a more kinetically active hydride donor. The parameter s_N is the sensitivity parameter of a donor whose values range between 0.5 and 1.2. The sensitivity parameter depends on the structural characteristics of hydride donors and is expected to be similar over the same class of compounds.

The nucleophilicity parameter is set to a relative scale where the values are defined using bis(p-methoxyphenyl)methyl cation as a reference electrophile, whose *E* parameter is set to 0, and a reference nucleophile (2-methyl-1-pentene), whose s_N parameter is set to 1.^{112, 162} Furthermore, the nucleophilicity scale is highly empirical and does not provide direct information about the thermodynamic and kinetic parameters related to the hydride transfer process. Despite these drawbacks, the nucleophilicity scale provides valuable

information about the relative nucleophilicities of hydride donors that can guide the selection of a metal-free hydride that will be most suitable for a reaction of interest.

2.3 Computational Methods

Computational quantum chemical methods are a fast and inexpensive alternative to experimental approaches for determining hydricity that also provide a fundamental and detailed description of the phenomena involved in the hydride transfer process. The calculated hydricity parameters often accurately correlate with the experimental results, thus enabling their quantum chemical prediction for species whose empirical values are not known. This is especially useful when the hydrides of interest include species that are difficult to synthesize, expensive or in cases where the hydricity of a species has been measured in one solvent, but has not yet been measured in the solvent of interest. The thermodynamic hydricities of a wide variety of metal-free hydrides have been calculated in MeCN and DMSO, and representative values are listed in Table 5. The ΔG_{H-} values are calculated using one of two approaches: (i) the direct approach, where thermodynamic hydricity is calculated from absolute Gibbs free energies of individual species (G_{R-H} , G_{R+} and G_{H-});¹⁶³⁻¹⁶⁵ and (ii) indirect approaches, which are analogous to the experimental "hydride transfer" and "potential-pKa" methods,¹⁶⁶⁻¹⁷¹ described in the Experimental methods section. In addition to the thermodynamic hydricities, the kinetic nucleophilicity parameter N can also be derived computationally from transition state energies for hydride transfer reactions.¹⁷² This section describes each computational method in detail, including a discussion of the advantages and challenges associated with each approach.

2.3a The Direct Approach

In the direct approach, ΔG_{H-} values of hydrides (R-H) are determined from absolute Gibbs free energies using the following equation:

$$\Delta G_{H^{-}} = G(R^{+}) + G(H^{-}) - G(RH)$$
(3)

Gibbs free energies of the solvated hydride donor, G(RH), and the corresponding cation, $G(R^+)$, can be calculated with exquisite accuracy using quantum chemical methods.¹⁷³⁻¹⁷⁵ However, the Gibbs energy associated with the solvated hydride ion, $G(H^{-})$, represents a computational challenge. Most commonly employed implicit solvation models, which describe the solvent as a continuous polarizable medium, only account for electrostatic interactions and neglect dispersion and repulsion, as well as hydrogen-bonding between the solute and solvent molecules,^{15, 176-179} thus yielding inaccurate solvated hydride ion energies. These inaccuracies are especially significant for the solvated hydride ion modeled by some polarizable continuum models (PCM) based on united-atom force field methods as they do not assign cavities for hydrogen atoms.¹⁷⁶ For example, Papai and coworkers reported obtaining a free energy of -387.8 kcal/mol for the solvated hydride in an implicit MeCN solvent model, which they determined was inaccurate compared to their empirically derived value of -404.7 kcal/mol.¹⁸⁰ The solution to this problem is to treat solvents explicitly by directly including solvent molecules in the model. This still requires an approximation for the solvent environment as only a relatively small number of solvent molecules can be explicitly included in the quantum mechanical model. A further improvement on the model involves using a hybrid implicit/explicit approach, where the solute is solvated by a shell of quantum-mechanically treated solvent molecules embedded in implicit solvent.^{176, 181-183} Both of these approaches reduce the errors that

arise from solvation by more correctly describing the solute-solvent interactions, but require considerably more computationally expensive calculations as the number of electrons increases with additional quantum-mechanically described solvent molecules in the model.¹⁸⁴ To the best of our knowledge, explicit solvent models have not yet been used to predict ΔG_{H-} or hydride ion solvation energies. As we discuss below, other approaches are more efficient in predicting thermodynamic hydricities.

The challenge associated with calculating the solvation energy of the hydride ion can be circumvented by providing a semi-empirical value for G(H) in the solvent of interest. The hydride ion has not yet been observed in common solvents such as water, MeCN, or DMSO, because of its tendency to react with protons to evolve molecular hydrogen. Consequently, the experimental value for $G(H^{-})$ must be obtained using indirect methods. One such method is the scaling approach, in which $G(H^{-})$ is obtained from equation (1), using experimental ΔG_{H} and the calculated absolute Gibbs free energies for R⁺ and R-H.^{165, 180, 185-186} The $G(H^-)$ value is obtained as an intercept of the linear fit of experimental hydricities ΔG_{H-} with respect to the sum defined as ΔG_{HHR} = $G(R^+)$ - G(R-H). According to the equation $\Delta G_{H-} = \Delta G_{HHR} + G(H^-)$, the slope of the line is expected to be unity. With a slope of unity, Papai and Nimlos were able to obtain values of G(H) that minimize the errors in the predicted thermodynamic hydricities.^{180, 187} However, the results of Muckerman et al. show that the best linear fit provides a slope that deviates slightly from 1, and they associate this deviation to deficiencies in the implicit solvation model.¹⁶⁵ Nevertheless, the non-unity slope reproduced experimentally determined ΔG_{H-} more accurately compared to the linear fit constrained to have unity slope. The scaling approach has been successfully utilized for calculations of several transition metal hydrides^{185-186, 188} and a metal-free dihydropyridine.¹⁸⁹ The advantage of the scaling approach is that it reduces systematic error because the fit is generated using multiple data points. A drawback of this approach is that the quality of the linear fit depends on it spanning a wide range of ΔG_{H-} hydricities.

 $G(H^-)$ can also be obtained by computing the hydride ion gas-phase free energy $G(H^-)_{gas}$ and then accounting for solvation effects using derived solvation energies for the hydride ion (ΔG_{sol}):^{134-135, 164}

$$G(H^{-}) = G(H^{-})_{gas} + \Delta G_{sol} \tag{4}$$

The solvation energy ΔG_{sol} can be extracted from the experimental standard reduction potential for the hydride ion described in the Experimental methods section. The experimental reduction potentials ($E_{H/H-}$) are available for a range of solvents,¹¹⁶ enabling the evaluation of hydride solvation energies in MeCN, DMSO and water. This approach was shown to reproduce the experimental thermodynamic hydricities of several dihydroacridines.^{134-135, 164} Table 4 lists absolute Gibbs free energies for the hydride ion $G(H^-)$ in MeCN obtained using the semi-empirical methods described above. While Table 1 lists a large spread of values ranging from -400.7 to -412.7 kcal/mol in MeCN, the calculated hydricities ΔG_{H-} for model hydrides were all within 3 kcal/mol of the experimental values.^{134-135, 164-165, 180, 187} Creutz et al. estimated that $G(H^-)$ is expected to be 16 – 22 kcal/mol lower in water than in MeCN.¹¹⁸ **Table 4.** Summary of different $G(H^-)$ values obtained computationally via various approaches and levels of theory in MeCN.

| LEVEL OF THEORY | APPROACH | GH- (kcal/mol) | REF |
|--|--------------------------------------|----------------|-----------------|
| B3LYP/6-31+G(d,p)*/PCM | Scaling with non-unity slope | -412.7 | 165 |
| B3LYP/6-31+G(d,p)*/PCM | Scaling with unity slope | -406.6 | 165 |
| B3LYP/SDDP/PCM-UA0 | Scaling | -404.7 | 180 |
| wB97X-D/6-311+G(2df,p)/CPCM | Experimental Solvation Correction | -402.9 | 134-135, 164 |
| B3LYP/SDD+631G(d)**// BLYP/SDD+6-31G(d) [PCM-UA0] | Scaling | -400.7 | 187 |

2.3b Indirect Approaches

Indirect methods do not require knowledge of the absolute Gibbs energy of the hydride ion. For example, the isodesmic approach is similar to the experimental "hydride transfer" method and involves the calculation of ΔG_{HT} for a hydride transfer reaction between the donor of interest and a reference acceptor, with known affinity.¹⁶⁶⁻¹⁶⁷

 $RH + A^{+} \rightarrow R^{+} + AH \qquad \Delta G_{HT} = -RTlnK_{HT}$ $A^{+} + H^{-} \rightarrow AH \qquad -\Delta G_{H-}(AH)$ $RH \rightarrow R^{+} + H^{-} \qquad \Delta G_{H-}(RH)$

The isodesmic approach has been used extensively to determine the thermodynamic hydricities and affinities of metal-free hydride donors, such as arylcarbeniums, quinones, boranes and other main group hydrides.^{167-171, 190} This indirect method is relatively simple because energies of the solvated hydride donors (R-H and A-H) and corresponding hydride acceptors (R⁺ and A⁺) can be readily obtained using quantum chemical calculations. However, because the isodesmic approach depends on the thermodynamic hydricity of the single reference hydride, any error in the ΔG_{H-} of the reference is

systematically propagated to the ΔG_{H-} calculated via this approach. Another drawback of this method is that ΔG_{H-} can only be calculated for solvents which have a reliable reference molecule for which the hydricity has been determined. For instance, this approach is currently limited to only MeCN and DMSO solvents.

2.3c Calculated Nucleophilicity

Computational methods are also utilized to calculate the kinetic parameters, such as the nucleophilicity *N* discussed in the Experimental Methods section. Specifically, Alherz et al. showed that the kinetic nucleophilicity parameter of hydrides can be determined computationally via a linear fit between the activation free energy of a hydride transfer from a hydride donor to a hydride acceptor and the experimental nucleophilicity, as indicated by equations (5-6).¹⁷²

$$k = \frac{k_{\rm B}T}{h} \exp(-\Delta G^{\ddagger}/RT) \tag{5}$$

$$N = -\frac{1}{2.3RTs_N} \Delta G^{\ddagger} + N_0$$
 (6)

The transition state theory-based equation (5) is combined with Mayr's equation (2) to obtain equation (6).¹¹²⁻¹¹³ The linear relation between *N* and the activation free energy ΔG^{\ddagger} only holds if, 1) the hydride acceptor or 'electrophile' is constant for the hydrides considered and 2) the sensitivity parameter *s*_N is constant, which is a valid assumption within a class of hydrides.¹¹³ The constancy of the electrophile can be ensured by examining the same hydride acceptor species for all HT reactions considered.¹⁷² The limitations of the Mayr equation are described in more detail by Bentley.¹⁹¹⁻¹⁹² In accordance with the Bell-Evans-Polanyi principle, the free energies and enthalpies of reaction for HTs have also been shown by Alherz et al. to exhibit a linear correlation with

the nucleophilicity within a class of hydride donors.^{172, 193-194} Others, such as Pratihar and Kiyooka,¹⁹⁵⁻¹⁹⁶ have developed empirical relationships that utilize thermodynamic properties, such as the chemical hardness and electron affinity, to predict the nucleophilicities and electrophilicities of various nucleophiles and electrophiles. These values can be used to predict the kinetic properties of hydride donors and hydride acceptors.

Table 5 summarizes calculated thermodynamic hydricities for a range of metalfree donors, including carbon-, boron-, nitrogen- and silicon-based hydrides. In general, very good agreement is observed between the reported experimental and calculated values obtained from various methods, as shown in Figure 8. The mean absolute deviation (MAD) between experimental and calculated ΔG_{H} was found to be 3.4 kcal/mol, and the root-mean-square error (RMSE) is 5 kcal/mol (MAD = 3.0, RMSE = 3.7, ignoring the two outliers). The MAD and RMSE for enthalpic hydricities were determined to be 1.4 and 1.8 kcal/mol, respectively.



Figure 8. Calculated versus experimental hydricities: (a) free energy and (b) enthalpic hydricities in DMSO and MeCN. Data is reported in Table 5. Some computationally obtained hydricities are from references cited in Table 5. The rest have been calculated using Muckerman's scaling approach at the B3LYP/6-311++G(d,p)/CPCM level of theory.¹⁰⁻¹⁵ The 45° red line represents perfect agreement between experiment and theory, with a slope of unity and a y-intercept at 0. The dashed line is the correlation between calculated and experimental hydricities. Both fits were determined to have insignificant deviations from experiment with 95% confidence using the paired-t test, as is appropriate for such statistical analyses.¹⁶ A p-value of 0.76 is obtained for (a) and 0.14 for (b), indicating that the mean hypothesized difference between experimental and computational methods is 0. The confidence intervals are (-1.29, 0.94) for (a) and (-0.09, 0.61) for (b). The inclusion of 0 in both intervals further supports the insignificance of the errors between the experimental and computational hydricities.

The experimental and computational methods described above provide thermodynamic and kinetic parameters for various metal-free hydrides (Table 5 and 6), which are exceptionally valuable for the evaluation of their structure-property relationships and applicability in catalysis. Sections IV and V provide an in-depth perspective regarding these parameters, including the structural and electronic factors that lead to stronger hydride donors, comparison with metal-based hydrides and applicability in stoichiometric and catalytic hydride transfer processes.

Table 5. A list of the experimental and calculated (in parentheses) values for ΔG_{H-} (kcal/mol) and ΔH_{H-} (kcal/mol) of the metal-free hydride donors reviewed here. Energies are for hydride transfers in acetoniotrile, unless otherwise noted. Hydridic hydrogens are shown in red.

| STRUCTURE | # | COMPOUND | ⊿G _H . | ΔH_{H-} | # | COMPOUND | ΔG_{H-} | ΔH_{H-} |
|---------------------------------|----|------------------------|--|----------------------|----|---------------------------------------|--|-------------------------------|
| CARBON – BASED HYDRIDES | | | | | | | | |
| | | X = H, Ar = | | | | | | |
| | 1 | p-NO ₂ -Ph- | 129 ¹³¹ | - | 8 | p-Me-Ph- | 112 ¹³¹ | - |
| | 2 | m-CN-Ph- | $(127)^{108}$ 129 ¹³¹ | - | 9 | p-MeO-Ph- | $(113)^{108}$ 107^{131} $(106)^{168}$ | - |
| н | 3 | p-CN-Ph- | 122131 | - | | | () | |
| Ï . | | - | $(126)^{168}$ | | | | | |
| Ar | 4 | p-MeCO-Ph- | 124 ¹³¹ | - | | X = CN, Ar = | | |
| benzyl-hydrides | 5 | p-F-Ph- | 123^{131} | - | 10 | p-CN-Ph- | 129 ¹³³ | - |
| | 6 | p-Cl-Ph- | $(118)^{108}$ 123^{131} | - | 11 | Ph- | $(129)^{108}$ 120^{133} | - |
| | | | $(118)^{168}$ | | | | $(122)^{168}$ | |
| | 7 | Ph | $(118)^{168}$ | - | 12 | p-MeO-Ph- | $(108)^{168}$ | - |
| | , | 1 11- | 113 ^{133,b} | | | | (100) | |
| | | | • | | | | | |
| | | $Ar_1 = Ar_2 = Ph, Ar$ | 3 = | | | $Ar_1 = Ar_2 = Ar_3 =$ | 1 100 | |
| | 13 | H- | 105 ¹³¹ | $(116)^{a,b}$ | 23 | p-H-C ₆ F ₄ - | 116 ^{133,a} | - |
| | 14 | p-F-Ph- | $(104)^{a,b}$ 98 ¹³³ (97) ^b | (104) ^b | 24 | p- Br-C ₆ F ₄ - | 114 ^{133,a} | - |
| H | 15 | p-Ph-Ph- | $96^{131} (93)^{a,b} \\98^{133}$ | (102) ^{a,b} | 25 | p-NO ₂ -Ph- | 106 ^{135,a} | - |
| Ar ₁ Ar ₂ | 16 | p-PhCO-Ph- | 95 ¹³³ (97) ^{a,b} | (107) ^b | 26 | p-Cl-Ph- | 98 ¹³¹ (98) ^{a,b} | (108) ^{a,b} |
| triarylmethanes | 17 | p-NO ₂ -Ph- | 97 ¹³³ (98) ^{a,b} | (112) ^b | 27 | Ph- | $99^{133} (92)^{171} 96^{131} (94)^{a,b}$ | $(98)^{171}$ $(104)^{a,b}$ |
| | 18 | p-Me-Ph- | 96 ¹³³ (95) ^b | (101) ^b | 28 | p-Me-Ph- | 93 ¹³³ (89) ^b | (97) ⁶ |
| | 19 | p-MeS-Ph- | $95^{133}(93)^{b}$ | (98) ^b | 29 | p-MeO-Ph- | $86^{133}(83)^{b}$ | (88) ^b |
| | 20 | m-MeO-Ph- | 98133 (97) | (104)" | 30 | 0,0-(MeO)2-Ph- (6OH) | $(86)^{134-135}$ 84 (84) ¹³⁴⁻ 135,a | - |
| | 21 | p-MeO-Ph- | 94 ¹³³ (91) ^b | (97) ^b | 31 | p-Me ₂ N-Ph- | 74 ¹³³ (65) ^b | (69) ^b |

| | 22 | n-Me2N-Ph- | 83133 (81) | ^b (88) ^b | | | 76 ^{131,a} | |
|---|--|--|--|---|--|--|--|--|
| | | | | | | | | |
| | 32 | $R = MeCO_2$ - | 114 ¹³¹ (113 | $(132)^{a,b}$ | 37 | p-MeO-Ph- | 101^{133} | (106) ^{a,b} |
| C-R | 33 | H- | 109131 (111 |) ^{a,b} (127) ^{a,b} | 38 | Ph- | 97 ¹³¹ | (113) ^{a,b} |
| | 34 | t-Bu- | 108^{131} (105 | (120) ^{a,b} | 39 | PhS- | $(101)^{a,b}$ 97 ¹³¹ (98) ^{a,b} | (109) ^{a,b} |
| fluorenes | 35 | m-Cl-Ph- | 102^{131} (104 | $(116)^{a,b}$ $(116)^{a,b}$ | 40 | MeO- | $89^{131}(90)^{a,b}$ | $(99)^{a,b}$ |
| | 36 | Mes- | 101155 (101 | (115) ^{a,b} | 41 | Me ₂ N- | /0 ¹⁵⁵ (/4) ^{4,0} | (80) ^{4,0} |
| | | $X = C \cdot M \rho \cdot R$ | = | | | X = S R = | | |
| | 42 | NO ₂ - | 120 ^{131,a} | - | 50 | Ph- | 90 ¹³¹ (86) ^{a,b} | (93) ^{a,b} |
| | 43 44 | Cl- H- | 105 ^{131,a} 98 ^{131,a} | - | 51 | H- X = O, R = | (90) ^o | 94(93)° |
| | 45 | Me- | 95 ^{131,a} | - | 52 | CN- | 92 ¹³³ (94) ^{a,b} | (104) ^{a,b} |
| | 46 | MeO- $R = H X =$ | 91 ^{131,a} | - | 53 54 | H- Ph- | $90^{131} (87)^{a,b}$ $89^{131} (85)^{a,b}$ | $(95)^{a,b}$ $(92)^{a,b}$ |
| | 47 | C-CH ₂ OPh | 111 ^{131,a} | - | 55 | p-MeO-PH- | 87 ¹³³ (83) ^{a,b} | $(90)^{a,b}$ |
| | 48 49 | C-CH ₂ SPh C-CH ₂ OMe | $109^{131,a}$ $102^{131,a}$ | - | | X = N-Me, $R =$ | $76^{164}(75)^{16}$ | 4 – |
| dihydro- tricyclic heterocycles | | | | | 56 | Ph- | 74 ¹³⁴⁻¹³⁵ | |
| | | | | | 57 | Me ₂ N-Ph- | $(73)^{134-135,a}$ $70^{134-135}$ | _ |
| | | | | | | | (70) ^{134-135,a} | 107 1 |
| | | | | | 58 | H- | 70 ¹⁵¹ (72) ⁶ | 81 ¹⁹⁷ (79) ⁶ |
| | 59 60 | <i>R</i> = p-CN-Bz- p-CF ₃ -Bz- | 66.4 ¹⁵⁶ 65.6 ¹⁵⁶ | - | 62 63 | Me- H- (PheH ₂) | 61.4 ¹⁵⁶ (65.9) ^b | - |
| dihydro- | 61 | Bz- | 64.8150 | - | | | | |
| phenanthridines | | | | | | | | |
| · | | | | | | | | |
| | | $R = CH_2Ph X$ | / = | | | R = Me X = | | |
| H K K | 64 | $R = CH_2Ph, X$ CN-77 | $X = 1.7^{135, 156}$ | 83.9 ¹⁶⁷ (83.2) ^b | 67 | <i>R</i> = <i>Me</i> , <i>X</i> = CN- | 69.8 ¹⁵⁶ | 81.1 ¹⁶⁷ |
| | 64 | $R = CH_2Ph, X$ CN- 7 (7) NH ₂ CO- 60 | $X = 1.7^{135, 156}$ $(7.2)^{b}$ $(5.3)^{156} (71.4)^{b}$ | 83.9 ¹⁶⁷ (83.2) ^b 75.8 ¹⁴¹ (75.4) ^b | 67 | R = Me, X = CN- NH ₂ CO- | 69.8^{156} (76.3) ^b 65.4^{154} | 81.1 ¹⁶⁷ (80.5) ^b |
| H C C H C H X M dihydro- cuire lloco | 64 65 66 | R = CH ₂ Ph, X CN- 7 (7) NH ₂ CO- 60 H- 60 | $\begin{array}{c} 7 = \\ 1.7^{135, 156} \\ (7.2)^{b} \\ 6.3^{156} \\ (71.4)^{b} \\ \end{array}$ | 83.9 ¹⁶⁷ (83.2) ^b 75.8 ¹⁴¹ (75.4) ^b (70.1) ¹⁶⁷ | 67 68 | <i>R</i> = <i>Me</i> , <i>X</i> = CN- NH ₂ CO- | 69.8 ¹⁵⁶ (76.3) ^b 65.4 ¹⁵⁴ | 81.1 ¹⁶⁷ (80.5) ^b |
| dihydro- quinolines | 64 65 66 | R = CH ₂ Ph, X CN- 7 (7) NH ₂ CO- 66 H- 66 | $\begin{array}{c} 7 = \\ 1.7^{135, 156} \\ 77.2)^{b} \\ 6.3^{156} \\ 71.4)^{b} \\ \end{array}$ | 83.9 ¹⁶⁷ (83.2) ^b 75.8 ¹⁴¹ (75.4) ^b (70.1) ¹⁶⁷ | 67 68 | <i>R</i> = <i>Me</i> , <i>X</i> = CN- NH ₂ CO- | 69.8 ¹⁵⁶ (76.3) ^b 65.4 ¹⁵⁴ | 81.1 ¹⁶⁷ (80.5) ^b |
| H H H H H H H H H H H H H H H H H H H | 64 65 66 | $R = CH_2Ph, X$ CN- (7) (7) NH ₂ CO- (6) H- (7) (7) (7) (7) (7) (7) (7) (7) (7) (7) | $ \frac{7}{7} = \frac{1.7^{135, 156}}{5.3^{156} (71.4)^{b}} = \frac{1.7^{135, 156}}{1.7^{135, 156}} = \frac{1.7^{135, 156}}{1.7^{135, 156}} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ 3 = | 67 68 | $R = Me, X =$ CN- NH ₂ CO- $R_1 = CHO, R_2 =$ | $69.8^{156} (76.3)^{b} 65.4^{154}$ $= R_4 = R_5 = H, R_2$ | 81.1 ¹⁶⁷ (80.5) ^b |
| dihydro- quinolines | 64 65 66 69 | $R = CH_2Ph, X$ CN- 7 $CN- 17 (7) NH2CO- H- 66 H- R_1 = CN, R_2 = p -CN-Bz-$ | $\frac{7}{2} = \frac{1.7^{135, 156}}{6.3^{156} (71.4)^{b}}$ = $R_4 = R_5 = H, R_1$ (71.2) ^b | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ | 67 68 75 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- | $69.8^{156} (76.3)^{b} \\ 65.4^{154} \\ = R_4 = R_5 = H, R_2 \\ (68)^{b}$ | $81.1^{167} (80.5)^{b}$ $9 = 72.6^{141} (71.2)^{b}$ |
| dihydro- quinolines | 64 65 66 69 70 | $R = CH_2Ph$, X CN- 7 NH ₂ CO- 60 H- 7 $R_1 = CN, R_2 =$ P -CN-Bz- p-Cl-Bz- P -Cl-Bz- | $Z = \frac{1.7^{135, 156}}{(77.2)^{b}}$ $E = R_4 = R_5 = H, R.$ $(71.2)^{b}$ $(71.2)^{b}$ $(70.4)^{b}$ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ 72.4^{141} 72.4^{141} | 67 68 75 76 | $R = Me, X =$ CN- NH ₂ CO- $R_1 = CHO, R_2 =$ p-CN-Bz- p-F-Bz- | $= R_4 = R_5 = H, R_1$ (68) ^b (65.9) ^b | $81.1^{167} (80.5)^{b}$ $=$ $72.6^{141} (71.2)^{b} 70.6^{141} (71$ |
| dihydro- quinolines | 64 65 66 69 70 71 | $R = CH_2Ph, X$ $CN-$ 7: NH_2CO- 66 H- 67 $R_1 = CN, R_2 =$ p-CN-Bz- p-Cl-Bz- p-F-Bz- | $ \frac{7}{2} = \frac{1}{1.7^{135, 156}} + \frac{1}{1.7^$ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ 72.4^{141} $(73.9)^{b}$ 71.4^{141} | 67 68 75 76 77 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- | $= R_4 = R_5 = H, R_1$ (68) ^b (65.9) ^b (64.6) ^b | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $ |
| dihydro- quinolines | 64 65 66 70 71 72 | $R = CH_2Ph$, X CN- 7: (7) (7) NH ₂ CO- 60 H- 9 R ₁ = CN, R ₂ = p-CN-Bz- p-Cl-Bz- p-F-Bz- D- D- | | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (72.8)^{b}$ $71.6^{141} (72.8)^{b}$ | 67 68 75 76 77 78 | $R = Me, X =$ CN- NH ₂ CO- $R_1 = CHO, R_2 =$ p-CN-Bz- p-F-Bz- Bz- c Ma D= | $= R_4 = R_5 = H, R.$ (68) ^b (65.9) ^b (64.6) ^b (64.0) ^b | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $ |
| dihydro- quinolines | 64 65 66 70 71 72 | $R = CH_2Ph, X$ $CN-$ 7: NH_2CO- 66 H- 67 $R_1 = CN, R_2 =$ p -CN-Bz- p -Cl-Bz- p -F-Bz- Bz- | $\frac{7}{5} = \frac{1.7^{135, 156}}{5.3^{156} (71.4)^{b}}$ = $R_4 = R_5 = H, R_1$ (71.2) ^b (70.4) ^b (69.7) ^b (69.7) ^b (63 ¹⁵¹ (69.1) ^b | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ 72.4^{141} $(73.9)^{b}$ 71.4^{141} $(72.8)^{b}$ $71.6^{141} (73)^{b}$ | 67 68 75 76 77 78 | $R = Me, X =$ CN- NH ₂ CO- $R_{l} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- | $= R_4 = R_5 = H, R_1$ $(68)^{b}$ $(65.9)^{b}$ $(64.6)^{b}$ $(64.9)^{b}$ | $g = \frac{72.6^{141}}{(71.2)^{b}}$ $70.6^{141}}{(69.3)^{b}}$ $70.5^{141}}{(67.9)^{b}}$ $70.1^{141}}{(68.5)^{b}}$ |
| dihydro- quinolines | 64 65 66 70 71 72 73 | $R = CH_2Ph, X$ $CN-$ 7: NH_2CO- 60 $H-$ 60 $R_1 = CN, R_2 =$ p -CN-Bz- p -Cl-Bz- p -F-Bz- $Bz p$ -Me-Bz- | | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (73)^{b}$ | 67 68 75 76 77 78 79 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-Me-Bz- p-MeO-Bz- | $= R_4 = R_5 = H, R_1$ (68) ^b (65.9) ^b (64.6) ^b (65) ^b (65) ^b | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $ |
| $R_{1} \rightarrow R_{2} \rightarrow R_{5}$ | 64 65 66 70 71 72 73 74 | $R = CH_2Ph$, X CN- 7 NH ₂ CO- 60 H- 60 R ₁ = CN, R ₂ = p-CN-Bz- p-C1-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- p-MeO-Bz- | $Z = \frac{1.7^{135, 156}}{(77.2)^{b}}$ $E = R_4 = R_5 = H, R_1$ $(71.2)^{b}$ $(70.4)^{b}$ $(69.7)^{b}$ $(69.7)^{b}$ $(69)^{b}$ $(68.6)^{b}$ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (72.5)^{b}$ $70.2^{141} (71.9)^{b}$ | 67 68 75 76 77 78 79 | $R = Me, X =$ CN- NH ₂ CO- $R_1 = CHO, R_2 =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- | $= R_4 = R_5 = H, R_2$ (68) ^b (65.9) ^b (64.6) ^b (65) ^b (65) ^b | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ & \\ & \\ \end{array}$ |
| $\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$ | 64 65 66 70 71 72 73 74 80 | $R = CH_2Ph, X$ CN- T, T NH ₂ CO- H- $R_1 = CN, R_2 =$ p-CN-Bz- p-CI-Bz- p-F-Bz- Bz- p-Me-Bz- p-Me-Bz- p-MeO-Bz- $RI = COMe, I$ p CN Bz | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ 72.4^{141} $(73.9)^{b}$ 71.4^{141} $(72.8)^{b}$ $71.6^{141} (73)^{b}$ 70.6^{141} $(72.5)^{b}$ 70.2^{141} $(71.9)^{b}$ $H, R_{3} =$ $60^{141} (68.9)^{b}$ | 67 68 75 76 77 78 79 86 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $R1 = COOMe,$ P CN Bz | $= R_4 = R_5 = H, R_2$ $= R_4 = R_5 = H, R_3$ $= R_4 = R_5 = H, R_4$ $= R_4 = R_5 = H, R_5$ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ & \\ \end{array}$ |
| R_{2} | 64 65 66 70 71 72 73 74 80 81 | $R = CH_3Ph, X$ CN- 7: NH ₂ CO- 60 H- 60 P-CN-Bz- p -Cl-Bz- p-F-Bz- Bz- p-Me-Bz- p -MeO-Bz- $RI = COMe, I$ P -CN-Bz- P -CN-Bz- p -CN-Bz- P -CN-Bz- p -Cl-Bz- | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (73.5)^{b}$ $70.6^{141} (72.5)^{b}$ $70.2^{141} (71.9)^{b}$ $4. R_{3} =$ $69^{141} (68.9)^{b}$ 67.6^{141} | 67 68 75 76 77 78 79 86 87 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $R1 = COOMe,$ p-CN-Bz- p-CI-Bz- | $= R_4 = R_5 = H, R_1$ $= R_4 = R_5 = H, R_2$ $= (68)^{b}$ $(65.9)^{b}$ $(64.6)^{b}$ $(64.9)^{b}$ $(65)^{b}$ $= R_4 = R_5 = H_2$ $= R_4 = R_5 = H_2$ $= (65)^{b}$ $= (63.5)^{b}$ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ & \\ & \\ & \\ \end{array}$ |
| $\begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $ | 64 65 66 70 71 72 73 74 80 81 82 | $R = CH_2Ph$, X CN- 7: NH ₂ CO- 60 H- 60 P-CN-BZ- p-CN-BZ- p-F-BZ- BZ- p-Me-BZ- p-Me-BZ- p-CN-BZ- p-CO-BZ- p-Cl-BZ- p-CO-BZ- p-Cl-BZ- p-CN-BZ- p-Cl-BZ- p-Cl-BZ- | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (72.5)^{b}$ $70.2^{141} (71.9)^{b}$ $H, R_3 =$ $69^{141} (68.9)^{b}$ $67.6^{141} (67.5)^{b}$ $67.2^{141} (67)^{b}$ | 67 68 75 76 77 78 79 86 87 88 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $R1 = COOMe,$ p-CN-Bz- p-Cl-Bz- p-F-Bz- | $= R_4 = R_5 = H, R.$ $(68)^{b}$ $(65.9)^{b}$ $(64.6)^{b}$ $(64.9)^{b}$ $(65)^{b}$ $(65)^{b}$ $(65)^{b}$ $(65)^{b}$ $(63.5)^{b}$ $(63.5)^{b}$ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ & \\ & \\ & \\ \end{array}$ |
| $\begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $ | 64 65 66 70 71 72 73 74 80 81 82 83 | $R = CH_2Ph, X$ CN- 7: NH ₂ CO- 60 H- 60 R ₁ = CN, R ₂ = 9- p-CN-Bz- 9- p-F-Bz- Bz- p-Me-Bz- $P-CN-Bz-$ p-Cl-Bz- $P-CN-Bz-$ p-Cl-Bz- $P-CN-Bz-$ p-Cl-Bz- $P-CN-Bz-$ p-F-Bz- $Bz-$ Bz- $P-F-Bz-$ Bz- $P-F-Bz-$ Bz- $P-F-Bz Bz P-F-Bz Bz P-F-Bz-$ | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (73)^{b}$ $70.6^{141} (71.9)^{b}$ $70.2^{141} (68.9)^{b}$ $67.6^{141} (67.5)^{b}$ $67.2^{141} (67)^{b}$ 67.1^{141} | 67 68 75 76 77 78 79 86 87 88 88 89 | $R = Me, X =$ CN- NH ₂ CO- $R_{I} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $RI = COOMe,$ p-CN-Bz- p-CI-Bz- p-F-Bz- Bz- Bz- | $= R_4 = R_5 = H, R_5$ $= R_4 = R_5 = R_5$ $= R_4 = R_5 = R_5$ $= R_5 = $ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $ |
| $\begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $ | 64 65 66 70 71 72 73 74 80 81 82 83 84 | $R = CH_2Ph$, X CN- 7: (7) (7) NH ₂ CO- 60 H- 60 P-CN-BZ- p-CN-BZ- p-F-BZ- BZ- p-Me-BZ- p-Me-BZ- p-CN-BZ- p-CN-BZ- p-Cl-BZ- p-CN-BZ- p-CN-BZ- p-CN-BZ- p-Cl-BZ- p-CN-BZ- p-Ch-BZ- p-CN-BZ- p-Ch-BZ- p-Ch-BZ- p-F-BZ- BZ- p-K-BZ- p-F-BZ- | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (73.9)^{b}$ $70.2^{141} (71.9)^{b}$ $4, R_3 =$ $69^{141} (68.9)^{b}$ $67.6^{141} (67.5)^{b}$ $67.2^{141} (67.9)^{b}$ $67.1^{141} (66.8)^{b}$ 66.5^{141} | 67 68 75 76 77 78 79 86 87 88 88 89 90 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $R1 = COOMe,$ p-CN-Bz- p-Cl-Bz- p-F-Bz- Bz- p-F-Bz- Bz- p-Me-Bz- | $= R_4 = R_5 = H, R.$ $(68)^{b}$ $(65.9)^{b}$ $(64.6)^{b}$ $(64.9)^{b}$ $(65)^{b}$ $(65)^{b}$ $(65)^{b}$ $(65)^{b}$ $(63.5)^{b}$ $59.6^{156}(64.3)^{b}$ $59.5^{156}(63.3)^{b}$ $(62.8)^{b}$ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ & \\ & \\ & \\ & \\ \end{array}$ |
| $\begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $ | 64 65 66 70 71 72 73 74 80 81 82 83 84 84 85 | $R = CH_2Ph, X$ CN- T (7) NH ₂ CO- H- $R_1 = CN, R_2 =$ p-CN-Bz- p-CI-Bz- p-F-Bz- Bz- p-Me-Bz- p-Me-Bz- p-CI-Bz- p-CI-Bz- p-CI-Bz- p-F-Bz- Bz- p-F-Bz- Bz- p-Me-Bz- p-Me-Bz | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ 73.9^{141} $(75.4)^{b}$ 72.4^{141} $(73.9)^{b}$ 71.4^{141} $(72.8)^{b}$ $71.6^{141} (73)^{b}$ 70.6^{141} $(72.5)^{b}$ 70.2^{141} $(71.9)^{b}$ $4. R_{3} =$ $69^{141} (68.9)^{b}$ $67.2^{141} (67.5)^{b}$ $67.2^{141} (67.5)^{b}$ 67.1^{141} $(66.8)^{b}$ 66.5^{141} $(66.1)^{b}$ 66.2^{141} | 67 68 75 76 77 78 79 86 87 88 89 90 91 | $R = Me, X =$ CN- NH ₂ CO- $R_{1} = CHO, R_{2} =$ p-CN-Bz- p-F-Bz- Bz- p-Me-Bz- p-MeO-Bz- $R1 = COOMe,$ p-CN-Bz- p-Cl-Bz- p-F-Bz- Bz- p-Me-Bz- p-M | $= R_4 = R_5 = H, R_1$ $= R_4 = R_5 = H, R_2$ $= R_4 = R_5 = H, R_3$ $= (68)^{b}$ $= (64.6)^{b}$ $= (64.9)^{b}$ $= (65)^{b}$ $= (65)^{b}$ $= (65)^{b}$ $= (63.5)^{b}$ $= 59.6^{156}(64.3)^{b}$ $= 59.5^{156}(63.3)^{b}$ $= (62.8)^{b}$ $= (62.3)^{b}$ | $R_{3} = \frac{81.1^{167}}{(80.5)^{b}}$ $R_{3} = \frac{72.6^{141}}{(71.2)^{b}} \frac{70.6^{141}}{(69.3)^{b}} \frac{70.5^{141}}{(67.9)^{b}} \frac{70.1^{141}}{(68.5)^{b}} \frac{69.7^{141}}{(67.9)^{b}}$ $R_{4}R_{3} = \frac{67.9^{141}}{(67.9)^{b}} \frac{65.9^{141}}{(67.3)^{b}} \frac{65.9^{141}}{(67.3)^{b}} \frac{65.8^{141}}{(66.3)^{b}} \frac{65.2^{141}}{(66.3)^{b}} \frac{65.2^{141}}{(66.3)^{b}} \frac{64.0^{141}}{(66.3)^{b}} 64.0^{1$ |
| $\begin{array}{c} \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ $ | 64 65 66 70 71 72 73 74 80 81 82 83 84 85 | $R = CH_3Ph, X$ CN- 7: NH ₂ CO- 60 H- 60 R ₁ = CN, R ₂ = 60 p-CN-Bz- p -Cl-Bz- p-F-Bz- Bz- p-Me-Bz- p -Cl-Bz- p-Me-Bz- p -CN-Bz- p-Cl-Bz- p -Cl-Bz- p-CN-Bz- p -Cl-Bz- p-F-Bz- Bz - p-Me-Bz- p -Cl-Bz- p-F-Bz- Bz - p-Me-Bz- p -Cl-Bz- p-F-Bz- Bz - p-Me-Bz- p -Me-Bz- p-Me-Bz- p -Me-Bz- p-MeO-Bz- p -MeO-Bz- | $ \begin{array}{c} $ | $83.9^{167} (83.2)^{b}$ $75.8^{141} (75.4)^{b}$ $(70.1)^{167}$ $3 =$ $73.9^{141} (75.4)^{b}$ $72.4^{141} (73.9)^{b}$ $71.4^{141} (72.8)^{b}$ $71.6^{141} (73)^{b}$ $70.6^{141} (72.5)^{b}$ $70.6^{141} (72.5)^{b}$ $70.6^{141} (71.9)^{b}$ $4, R_3 =$ $69^{141} (68.9)^{b}$ $67.6^{141} (67.5)^{b}$ $67.2^{141} (67.5)^{b}$ $67.1^{141} (66.8)^{b}$ $66.5^{141} (66.1)^{b}$ $66.2^{141} (66.7)^{b}$ | 67 68 75 76 77 78 79 86 87 88 89 90 91 | $R = Me, X =$ CN-NH2CO- $R_I = CHO, R_2 =$ p-CN-Bz- p -F-Bz-Bz- p-Me-Bz- p -MeO-Bz- $RI = COOMe,$ p-CN-Bz- p-F-Bz- p -F-Bz-Bz- p-Me-Bz- p -Me-Bz- p -MeO-Bz- | $= R_4 = R_5 = H, R_1$ $= R_4 = R_5 = H, R_2$ $= R_4 = R_5 = H, R_3$ $= R_4 = R_5 = H, R_4$ $= R_4 = R_5 = H, R_5$ $= R_5 = H, R_5$ | $\begin{array}{c} 81.1^{167} \\ (80.5)^{b} \\ & - \end{array}$ $\begin{array}{c} 72.6^{141} \\ (71.2)^{b} \\ 70.6^{141} \\ (69.3)^{b} \\ 70.5^{141} \\ (67.9)^{b} \\ 70.1^{141} \\ (68.5)^{b} \\ 69.7^{141} \\ (67.9)^{b} \end{array}$ $\begin{array}{c} R_{3} = \\ 67.9^{141} \\ (67.9)^{b} \\ 65.9^{141} \\ (67.3)^{b} \\ 65.8^{141} \\ (66.3)^{b} \\ 65.2^{141} \\ (66.3)^{b} \\ 64.9^{141} \\ (66.4)^{b} \end{array}$ |

| | 92 | Me- (MeHEH) | 61.5 ¹³⁴ | 70 (65.7) ^b | 94 | -Br | (70) | 68.2 ¹⁴¹ (73.5) |
|-------------------------------|----------|---------------------------------|---|--|------------|-----------------------------|--|--|
| | 93 | H- (HEH) $R_1 = CONH_2, R_2$ | $(56)^{\circ}$ $(64.5)^{\circ}$ $p = R_4 = R_5 =$ | $69 (70.4)^{b}$ | 95 | -Me | (61.7) | 61.5 ¹⁴¹ (65.1) |
| | 96 | p-CF ₃ -Ph- | (68) ^b | 72.6 ¹⁹⁷ (72.6) ^b | 104 | p-CN-Bz- | (65) ^b | 66.3^{141} |
| | 97 98 | p-Br-Ph- p-Cl-Ph- | (66) ^b (66.1) ^b | 70.4 ¹⁹⁷ (70.4) ^b 70.2 ¹⁹⁷ (70.5) ^b | 105 106 | p-Cl-Bz- p-F-Bz- | (63.6) ^b 57 ¹⁵⁶ (62.7) ^b | (67.9) $65^{141} (66.4)^{b}$ 64.3^{141} |
| | 99 | Ph- (PNAH) | (64.6) ^b | 68.8 ¹⁹⁷ (68.9) ^b | 107 | Bz- (BNAH) | 59 ¹⁵¹ (62.6) ^b | $(65.3)^{\circ}$ 64.2 ¹⁴¹ (65.6) ^b |
| | 100 | p-Me-Ph- | (63.9) ^b | 67.5 ¹⁹⁷ (68) ^b | 108 | p-Me-Bz- | (62) ^b | 63.6^{141} |
| | 101 | p-MeO-Ph- | (63.7) ^b | 66.9 ¹⁹⁷ (67.2) ^b | 109 | p-MeO-Bz- | (62.5) ^b | $(64.3)^{2}$ 63.1^{141} $(64.7)^{b}$ |
| | 102 | Et- | (60.8) ^b | 61.5 ¹⁴¹ (63.8) ^b | 110 | iPr | (60.6) ^b | 61.3^{141} |
| | 103 | nBu- | (61.2) ^b | 61.4 ¹⁴¹ (63.8) ^b | 111 | nPr | (60.8) ^b | (63.2) ⁶ 60.8 ¹⁴¹ |
| | | | | | 112 | Me- | (61.9) ^b | $(63.8)^{\text{b}}$ 60.7^{141} |
| | | $R_2 = R_4 = R_5 = L$ | $H, R_3 = Ph-C$ | $CH_2, R_1 =$ | | | | (64.4)* |
| | 113 | -COOH | (65.4) ^b | 67.5 ¹⁴¹ | | | | |
| | 114 | -CONHPh | (62.6) ^b | $(68.9)^{\circ}$ 65.9 ¹⁴¹ (66) ^b | | | | |
| | 115 | -CONHEt | (60.9) ^b | 63.8^{141} (63.8) ^b | | | | |
| | 116 | -H | (50.7) ^b | $53^{141}(52.6)^{b}$ | | | | |
| | 117 | -Me | 43 ¹¹⁸ (49.4) ^в | 48 ¹⁴¹ (51.8) ⁶ | | | | |
| R ₁ R ₅ | | $R_4 = CONH_2, R_2$ | $R_1 = R_2 = R_5 =$ | $H, R_3 =$ | | | | |
| | 118 | p-Cl-Ph- | (61.3) ^b | 71.3^{198} | 124 | p-MeO-Ph- | (61.9) ^b | 66.8 ¹⁹⁸ |
| R ₃ H H | 119 | p-Br-Ph- | (60.9) ^b | $(67.9)^{\circ}$ 70.9 ¹⁹⁸ (68) ^b | | | | (65.6) |
| dihydropyridines | 120 | Ph- | (62.7) ^b | 69.5 ¹⁹⁸ | | $R_1 = R_2 = R_4 =$ | $R_5 = H, R_3 =$ | |
| | 123 | p-Me-Ph- | (61.9) ^b | $(67.3)^{6}$ 67.9 ¹⁹⁸ | 125 | H- (1,2-PyrH ₂) | (41.5)189 | - |
| | | | | (66.3) ^b | | | | |
| Λ H | | $X = S R_2 = R_2 =$ | $= H R_1 =$ | | | $X = O R_2 = R_2$ | $= H R_{I} =$ | |
| N-C-R1 | 126 | m-Cl-Ph- | (69.9) ^b | 76.9142 | 135 | p-Cl-Ph- | - 11, K ₁ - | 93.4 ¹⁴² |
| R ₂ | 127 | p-Br-Ph- | (69.7) ^b | $(74.7)^{b}$ 75.7 ¹⁴² (74.5) ^b | 136 | p-Br-Ph- | - | 93.2 ¹⁴² |
| five-membered | 128 | p-Cl-Ph- | (69.3) ^b | 75.6 ¹⁴² (74) ^b | 137 | Ph- | - | 91.2142 |
| neterocycles | 129 | m-MeO-Ph- | (67.1) ^b | 74.4^{142} (71.4) ^b | 138 | p-Me-Ph- | - | 89.3 ¹⁴² |
| | 130 | p-F-Ph- | (68.8) ^b | (71.4) 73.7 ¹⁴² (73.6) ^b | 139 | p-MeO-Ph- | - | 88.3142 |
| | 131 | Ph- | (68) ^b | 73 ¹⁴² (72.6) ^b | 1 | $X = N$ -Me, $R_1 =$ | $Ph, R_2 = H, R_3$ | = |
| | 132 | m-Me-Ph- | (66.4) ^b | 72.1^{142} | 140 | CF ₃ - | (55.7)⁵ | 61.9 ¹⁴² |
| | 133 | p-Me-Ph- | (67.2) ^b | (72.7) $71^{142} (71.5)^{b}$ | 141 | Cl- | (52.3) ^b | $58.2^{142}(56)^{b}$ |
| | 134 | p-MeO-Ph- | (66.3) ^b | 69.9 ¹⁴² | 142 | Me- | (48.2) ^b | 51 ¹⁴² (51.6) ^b |
| R ₁ | | | I | (70.6) | 143 | MeO- | (48.9) ^b | 49.7 ¹⁴² (52.1) ^b |
| <u> </u> | | $X = N$ - Me , $R_2 =$ | $R_3 = H, R_1 =$ | = | 1 | | | |
| five-membered | 144 | p-NO ₂ -Ph- | (53.3) ^b | 57.1 ¹⁴² | 158 | p-MeO-m-Br-P | h- (49.7) ^b | 54.6 ¹⁴² |
| heterocycles | 145 | m-NO ₂ -Ph- | (53.5) ^b | $(57.3)^{\circ}$ 56.9 ¹⁴² | 159 | Ph- | 50 ¹³⁴⁻¹³⁵ | $(53.2)^{\circ}$ 54.1 ¹⁴² |
| | | | | (57.2) ^b | | | (49) ^b | (52.8) ^b |
| | 146 | p-CN-Ph- | (52.6) ^b | 56.7^{142} (56.4) ^b | 160 | p,m,m-MeO ₃ -P | h- (50) ^b | 54 ¹⁴² (52.8) ^b |
| | 147 | p-Cl-m-Cl-Ph- | (52.6) ^b | 56.6 ¹⁴² | 161 | m-Me-Ph- | (47.1) ^b | 53.8 ¹⁴² |
| | 1 | 1 | 1 | (56.1) ⁰ | 1 | | | (52.8) ⁶ |

| | 149 | p-Cl-m-F-Ph- | (52.1) ^b | 56.4 | 4 ¹⁴² (56) ^b | 163 | p-MeO-m-MeO- | (48.9) ^b | 53.5 ¹⁴² |
|---------------------------------|------------|---|-------------------------------|------------------|--------------------------------------|----------|---|--|--|
| | 150 | p-F-m-Br-Ph- | (50.8) ^b | 56 ¹⁴ | ⁴² (55.6) ^b | 164 | Ph- p-Me-Ph- | (49.2) ^b | (51.9) ^b 53.4 ¹⁴² |
| | | pMeO-mNO2- | | 55.9 | 9 ¹⁴² | | | | $(51.9)^{b}$ 53.2 ¹⁴² |
| | 151 | Ph- | (52.4) ^b | (55 | .7) ^b | 165 | o-Cl-Ph- | (50.5) ^o | (52.5) ^b |
| | 152 | m-Br-Ph- | (49.8) | 55. (54 | 7 ¹⁴² .8) ^b | 166 | p-Me-m-Me-Ph- | (48.3) | 53.1 ¹⁴² (51.4) ^b |
| | 153 | p-F-m-F-Ph- | (52.1) ^b | 55. | 7 ¹⁴² 8) ^b | 167 | p-MeO-Ph- | (48.5) ^b | 52.9^{142} (51.5) ^b |
| | 154 | m-Cl-Ph- | (51.3) ^b | 55.0 | $6^{142} (56)^{b}$ | 168 | p-HO-Ph- | (48.9) ^b | 52.6^{142} |
| | 155 | p-Br-Ph- | (50.4) ^b | 55.2 | 2^{142} | 169 | o-Me-Ph- | (46.3) ^b | $51.4^{142} (50)^{\text{b}}$ |
| | 156 | p-Cl-Ph- | (50.6) ^b | 55.2 | 2^{142} | 170 | p-Me ₂ N-Ph- | (44.9) ^b | 50.6^{142} |
| | 157 | m-MeO-Ph- | (49) ^b | (54) | .2) ⁶ 6 ¹⁴² | 171 | H- | 45 ¹⁵¹ (47) ^b | (49.2) ⁶ 49.5 ¹⁴² |
| | | | | (52 | .6) ^b | | | | (49.4) [®] |
| | 172 | $X = N$ - Me , $R_1 = Ph$ Me- | $R_2 = R_3 = -$ | | 49 ¹⁴² | | | | |
| Г | | <i>V</i> – | | | | | | | |
| | 172 | NO ₂ - | 72116(79.3 |) ^b | (86.1) ^b | 176 | F- | 32 ¹¹⁶ (25.1) ^b | (23.7) ^b |
| | 173 | MeCO- | 50 ¹¹⁶ (51.6 |) ^b | $(55)^{b}$ | 177 | H- | $22^{116}(18.3)^{b}$ | $(17.3)^{b}$ |
| L" J | 174 | Cl- | 43 (45.8 37 ¹¹⁶ |) | (40.3) $(25.7)^{b}$ | 178 | MeO- | $19^{116}(18.2)^{b}$ | $(16.6)^{b}$ |
| | 100 | X = | 70116 | | | 107 | CI | 52116 | |
| | 180 | NO ₂ - CHO- | 63 ¹¹⁶ | | - | 185 | CI- Ph- | 52 ¹¹⁶ 50 ¹¹⁶ | - |
| | 182 | PhCO- | 62 ¹¹⁶ | | - | 187 | H- | 48 ¹¹⁶ | - |
| Radical-anion hydrides | 183 | CN- | 59 ¹¹⁶ | | - | 188 | Me- | 48 ¹¹⁶ | - |
| | 184 | PhS- | 54110 | | - | 189 | MeO- | 48110 | - |
| | | | | | | | | | |
| selected hydride donors | 190 | H,H,B,NH2 H,G,C,C,C,C,C,C,C,C,C,C,C,C,C,C,C,C,C,C, | - | | (77.1) ¹⁶⁷ | 193 | ₩ ₩ 40H | 70.2 (73.2) ¹³ | :4, a _ |
| | 191 | | (50) ¹⁷¹ | | (58) ¹⁷¹ | 194 | or HN → 2OH | 58.2 (61.1) ¹² 135, a 60.3(62.9) ¹³⁴ | 14- - 1 |
| | 192 | [∼] N ^I N ^K H M ^I N ^K H CAFH | (53.2) ¹³⁴ | | 57.6 ¹⁴³ | 195 | | $\begin{array}{c} 49.2 \ (48.7)^{13} \\ 135 \ (46.9)^{134, a} \end{array}$ | - |
| | · | I | OTHER H | YDR | IDES (N, C | , P, and | l Ge) | | |
| | 101 | $X = S, R_1 = R_3 = H$ | $R_2 =$ | 110 | 199 | 202 | $X = S, R_2 = R_3 = H,$ | $R_1 =$ | 111199 |
| R ₂ X R ₃ | 196 197 | Br- Cl- | - | 112 | 199 | 202 | Me- | - | 108 ¹⁹⁹ |
| N-neterocycles | 198 | H- | - | 110 | ¹⁹⁹ (108) | 204 | MeO- | - | 107 ¹⁹⁹ |
| | 199 | Me- | _ | 107 | 199 | | $X = S R_1 = H R_2 =$ | $R_3 =$ | 1 |
| | 200 | MeO- | - | 104 | 199 | 205 | Br- | - | 114 ¹⁹⁹ |
| | 201 | Me ₂ N- | (83) ^b | 95 ¹⁹ | ⁹⁹ (91) ^b | 206 | Cl- | - | 113 ¹⁹⁹ |
| | 202 | $R_1 = R_2 = R_3 = H, $ | X = | 100 | 199 | 207 | Me- | - (00)h | 105 ¹⁹⁹ |
| | 202 | 0 | - | (10) | 9) ¹⁶⁷ | 208 | MeO- | (90)- | 99 (98) |
| | 201 | N-Me | - | 91 ¹⁹ | ⁹⁹ (91) ¹⁶⁷ | 209 | Me ₂ N- | (72) ^b | 84 ¹⁹⁹ (78) ^b |
| HOCK OF | 210 | FMNH ₂ | - | (76 | .9) ¹⁶⁷ | 211 | | (58.4)° | - |
| | | $P_{i} = P_{i} = P_{i}$ | D | | | | P = P = P | | |
| | 212 | $K_2 = K_3 = K_4 = H,$ CN- (84) | $(K_1 = 4)^{169,a}$ | | - | 216 | $\kappa_1 = \kappa_2 = \kappa_3 = \kappa_4 =$ CN- | (113) ^{169,a} | - |



^cValues calculated here using Krylov's approach.¹³⁴

Table 6. Mayr's kinetic parameters (s_N and N) as defined in equation 2 and measured for different metal-free hydride donors in DCM, MeCN or DMSO solvents.

| STRUCTURE | SOLVENT | S_N | Ν |
|---------------------|------------|-------|-------|
| 7 | DCM | 1.32 | -4.47 |
| 53 ¹⁵⁹ | DCM | 0.97 | 0.64 |
| 58113 | DCM | 0.9 | 5.54 |
| 93 ¹⁵⁷ | DCM | 0.9 | 9 |
| 99 ¹⁵⁷ | DCM | 0.87 | 7.53 |
| 100157 | DCM | 0.95 | 7.68 |
| 101157 | DCM | 0.92 | 8.11 |
| | DCM | 0.82 | 8.67 |
| 107157 | MeCN | 0.7 | 9.8 |
| | W/MeCN=9/1 | 0.66 | 11.35 |
| 144 ¹⁶⁰ | MeCN | 0.71 | 8.36 |
| 148160 | MeCN | 0.71 | 8.74 |
| 154^{160} | MeCN | 0.71 | 9.38 |
| 159 ¹⁶⁰ | MeCN | 0.72 | 9.72 |
| 164 ¹⁶⁰ | MeCN | 0.7 | 10.14 |
| 167^{160} | MeCN | 0.72 | 10.01 |
| 235 ¹⁶² | DCM | 0.62 | 3.99 |
| $(nBu)_3Ge-H^{162}$ | DCM | 0.73 | 5.92 |

2.4 Structure-Property Relationships

The experimental and calculated hydricities tabulated in this review can be utilized to derive important structure-property relationships that affect the thermodynamic and kinetic reactivities of metal-free hydride donors. This section describes the structural parameters (such as the electronegativity of the atom directly bound to the hydridic H-atom, the type of molecular framework and the presence of electron-donating/withdrawing groups) that correlate with the hydricities of various metal-free hydrides.

In the case of carbon and nitrogen-based hydride donors, the electronegativities of C and N tend to polarize the bond in a protic $X^{\delta-}-H^{\delta+}$ sense, which weakens their hydride donating abilities. Despite the protic nature of the active H-atom, appropriate design of the hydride's molecular framework and substituents can be utilized to derive group IV and V hydrides with a wide range of hydride donating abilities, as is evident from Table 5. It is thus not a surprise that the group IV (NADH) and group V (FADH₂) hydrides are common donors in enzymatic reduction reactions. In the following subsections we describe the structural and electronic effects that control the hydride donor abilities of metal-free hydrides, particularly those based on carbon, silicon, boron and nitrogen derivatives.

2.4a Carbon-based Hydride Donors

Carbon-based hydride donors (Scheme 5) can be grouped into two general classes of compounds: arylmethanes and dihydro-heterocycles (tricyclic, bicyclic, dihydropyridines and five-membered heterocycles). Arylmethanes are relatively weak hydride donors with thermodynamic hydricities in the ΔG_{H-} = 75 – 130 kcal/mol range (entries 1 – 31, Table

5).^{131, 133-135, 168, 171} Their ΔG_{H-} values decrease as R⁺ is stabilized through positive charge delocalization. For example, an increase in the number of aromatic rings lowers the ΔG_{H-} value, as exhibited by the following trend: PhCH₃ (entry 7, ΔG_{H-} = 118 kcal/mol in DMSO, Table 5), Ph₂CH₂ (entry 13, ΔG_{H-} = 105 kcal/mol in DMSO) and Ph₃CH (entry 27, ΔG_{H-} exp = 96 kcal/mol in DMSO).¹³¹ Similarly, the introduction of electron-donating groups lowers the ΔG_{H-} values, as exemplified by the DMSO values for the (p-X-Ph)₃CH series, which range from 106 kcal/mol for X=NO₂ (entry 25)¹³³ to 76 kcal/mol for X=Me₂N (entry 31, Table 5).¹³¹ Furthermore, the substituent effect is additive, as shown for successive additions of nitro-groups to triphenyl-methane (entries 17, 25, 27) which results in an increase of ΔG_{H-} values from 96 kcal/mol to 106 kcal/mol in DMSO, whereas the values drop from 99 kcal/mol to 74 kcal/mol in MeCN when multiple dimethyl amino-groups are introduced (entries 22, 27 and 31).^{131, 133}

Scheme 5. Carbon-based hydride donors: a) arylmethanes and b) dihydro-heterocycles. a) Arylmethanes



Generally, hydrides derived from heteroaromatic compounds are stronger donors than arylmethanes (ΔG_{H-} values range from 43 to 120 kcal/mol, Table 5), which is consistent with the stabilization of R⁺ provided by aromatization. For example, the ΔG_{H-} of dihydroanthracene is lower than that of diphenyl methane by 7 kcal/mol (entries 44 and 13, Table 5).¹³¹ The heteroatom plays a significant role in the stabilization of the R⁺ cation product, with strongly electron-donating atoms (such as nitrogen) forming stronger hydride donors. For example, the hydrides derived from tricyclic heteroaromatics have thermodynamic hydricity values decreased in anthracene > xanthene > acridine series from 98 kcal/mol to 70 kcal/mol in MeCN (entries 44, 53 and 58).^{131, 151} As the number of rings increases, two opposing factors control the stabilization of R⁺: (i) larger heteroaromatic structures exhibit lower aromatic stabilization, which decreases the stabilization of R⁺; (ii) the delocalization of the positive charge increases in larger, conjugated molecular frameworks, which increases the degree of R⁺ stabilization. Which factor prevails depends on the particular system of interest. For instance, the aromatic stabilization energy prevails in the acridine < quinoline < pyridine series (entries 58, 65) and 107), where the ΔH_{H_2} values decline from 81 kcal/mol to 64.2 kcal/mol in MeCN.^{141,} ¹⁹⁷ On the other hand, the effect of extended charge delocalization dominates in the 4OH > 2OH > 3NH series (entries 193, 194 and 195) with ΔG_{H-} decreasing from 73.2 kcal/mol to 46.9 kcal/mol in MeCN.¹³⁴⁻¹³⁵

Dihydropyridines and imidazoles are two types of carbon-based hydrides that are direct analogs of biologically relevant cofactors: NAD(P)H¹⁰⁷ (entry 190) and methylene tetrahydromethanopterin²⁰⁰ (H₄MPT, entry 191). The hydride-donating ability of NADH and other dihydropyridines is relatively high, where the aromatization of the forming

pyridinium ring is the main driving force for the hydride transfer reaction. Furthermore, the positive charge is efficiently stabilized through the inductive effect of electron-donating groups, as shown for differently meta-substituted pyridines for which ΔH_{H-} decreased from 71.6 kcal/mol to 48 kcal/mol in MeCN, in the following order: CN- > CHO- > COMe- > CO₂Me- > CONH₂- > H- > Me-, (entries 72, 77, 83, 89, 107, 116, and 117).¹⁴¹ The imidazole-based compounds (H₄MPT and its analogs) are quite strong hydride donors, with ΔH_{H-} values in the 49-57 kcal/mol range.^{134-135, 142, 151} Besides the aromatization of the imidazolium cation product, the hydride donating abilities of benzimidazoles are additionally facilitated by the anomeric effect. Namely, the lone pairs of neighboring nitrogen atoms are in hyperconjugation with the antibonding orbital of C-H bond. The ability of the nitrogen to donate its electron pair is demonstrated in the thiazole < oxazole < imidazole series where ΔH_{H-} ranges from 91.2 to 54.1 kcal/mol (entries 131, 137, and 159).¹⁴²

Interestingly, the thermodynamic hydricity of carbon-based hydrides R-H can be significantly improved (by 40 - 90 kcal/mol) upon one electron reduction to form R-H⁻ radical anions.¹¹⁶ For example, radical anions of benzyl-hydrides exhibit very low ΔG_{H-} values (as low as 19 kcal/mol, entries 178 and 179), making them the strongest carbon-based donors reported thus far. However, the potential applications of radical anion-based hydrides are limited by two drawbacks: (1) the potentials required for the hydride reduction are very negative ($E_{RH/RH^{-}} = -1$ to -3.24 V vs. NHE);¹¹⁶ (2) the bond dissociation energies of radical anions are also quite low (35 – 50 kcal/mol), making them comparatively good hydrogen atom donors.

2.4b Other Hydride Donors

Nitrogen- and oxygen-based hydrides are relatively weak, in accordance with the fact that N-H and O-H bonds are generally protic rather than hydridic. For example, nitrogencontaining tricyclic derivatives exhibit ΔH_{H_2} values in the 90-110 kcal/mol range.¹⁹⁹ The enthalpic hydricity sensitively depends on the co-heteroatom present in the structural backbone: weaker donors within the group are phenothiazine derivatives (S as coheteroatom, entry 198, $\Delta H_{H_{-}}$ = 110 kcal/mol), followed by phenoxazine (O as coheteroatom, entry 202, ΔH_{H-} = 108 kcal/mol) and phenazine (N as co-heteroatom, entry 203, ΔH_{H_2} = 91 kcal/mol).¹⁹⁹ This heteroatom effect is due to different electron donating abilities of the heteroatom, with nitrogen being the most electron-donating heteroatom. Interestingly, one of the most abundant biological cofactors for hydride transfer processes is a nitrogen-based structure, even though N-based hydride donors are relatively weak. Namely, the reduced forms of flavin-adenine dinucleotide (FADH₂) and flavin mononucleotide (FMNH₂) serve as hydride donors in enzymatic reduction processes (Scheme 6a).¹⁰⁷ The thermodynamic hydricity of flavins in enzymatic reactions is often strengthened by deprotonation to FADH⁻ or FMNH⁻ anions. The effect of deprotonation on ΔG_{H_2} can be observed by comparing ΔG_{H_2} values for FMNH₂ (entry 210, 76.9) kcal/mol)¹⁶⁷ and the deprotonated model compound (entry 211, ΔG_{H} = 58.4 kcal/mol).

Scheme 6. Representations of FAD and hydroquinone N-H (a) and O-H hydrides (b). Hydridic bonds are shown in red, whereas the negatively charged heteroatoms are shown in blue. The dashed lines of the hydroquinones represent a substitution or the presence of another phenyl ring.



Among oxygen-based hydrides, deprotonated hydroquinones are weak to mild hydride donors.^{132, 169} For instance, ortho-hydroquinone anion has a thermodynamic hydricity of ΔG_{H-} = 82 kcal/mol (entry 222), while para-hydroquinone anion is a stronger hydride donor, with ΔG_{H-} = 69 kcal/mol (entry 214) (Scheme 6b). The lower ΔG_{H-} of the *o*-isomer is caused by the stabilization of the hydride form due to the presence of the O-H---O hydrogen bond. In general, quinone-hydroquinone systems are better tuned for hydride abstraction rather than for hydride donation, because the aromaticity of hydroquinone is lost upon hydride release in contrast to the pyridine-based hydrides.¹⁶⁹ This effect can be observed by comparing the thermodynamic hydricities of hydroquinones with an expanding number of benzene rings: anthrahydroquinone > naphthahydroquinone > benzohydrophenone (entries 214, 227 and 229, Table 5). Thus,

it is not surprising that this group of hydrides participates in electron transfer rather than hydride transfer processes.

Hydrides of other metal-free elements (phosphorus, germanium and tellurium) have not been widely used as hydride donors and therefore have not been examined in terms of their hydricities. Because of the large differences in atomic sizes (poor orbital overlap) and the electronegativities of these elements are similar to hydrogen (χ (P) = 2.19, χ (Ge)= 2.01 and χ (Te) = 2.10), the bonds that these elements form with hydrogen are not sufficiently polarized for hydride transfer chemistry. However, the polarity of the X-H bond is tunable with substituents and reaction conditions. For example, Cl₃Ge-H acts as a proton donor, whereas Et₃Ge-H acts as a hydride donor in reactions with ketones.²⁰¹ In terms of thermodynamic hydricity, phosphorus-based hydrides are promising hydride donor candidates, with calculated values comparable to BH₄⁻.¹⁷¹ Organogermanes exhibit hydride donor abilities similar to organosilanes (ΔG_{H} ~80 kcal/mol and *N*= 3-6).^{113, 171}

2.4c ΔG_{H-} vs. ΔH_{H-}

Comparing the values obtained in ΔG_{H-} and ΔH_{H-} measurements indicates when entropic effects on hydride donation are significant. While experimental ΔH_{H-} values are simply obtained through calorimetry, the methods for determining ΔG_{H-} values are often challenging, as discussed in the Experimental Methods section. Consequently, significantly more ΔH_{H-} values are reported in the literature than ΔG_{H-} values, and it is often assumed that entropic contributions to the thermodynamic hydricity are negligible.^{140-143, 197-199, 202-203} To test the validity of this assumption, Figure 9 plots ΔH_{H-} and ΔG_{H-} values for the metal-free hydrides listed in Table 5. ΔS_{H-} is positive for all
hydrides, causing the room temperature ΔG_{H-} values to be ~6 kcal/mol lower than their corresponding ΔH_{H-} values. This relatively consistent offset suggests that ΔH_{H-} values can be used to compare the relative hydride donor abilities of compounds within a family of hydrides. However, entropic contributions should not be neglected, especially considering the large variations for different groups of hydride donors: from $T\Delta S_{H-}$ = 3.6 kcal/mol for dihydropyridines to 12.5 kcal/mol for fluorenes (at 298 K). Higher $T\Delta S_{H-}$ values were found for larger molecules, possibly due to a larger entropic contribution from a solvent¹⁵¹ or because hydride transfer significantly affected the low frequency skeletal modes of the larger molecules.



Figure 9. The comparison between ΔH_{H^-} and ΔG_{H^-} at 298 K for hydrides tabulated in Table 5 for: (a) carbon-based and (b) other hydride donors. The red dashed lines represent the condition $\Delta H_{H^-} = \Delta G_{H^-}$ at which $T\Delta S_H = 0$. The data all lie above this line, indicating that $\Delta H_{H^-} - \Delta G_{H^-} = T\Delta S_{H^-}$ is positive for metal-free hydride donors. The average $T\Delta S_{H^-}$ contributions for different classes of hydrides at room temperature are as follows:

carbon- fluorenes (12 kcal/mol), diphenylmethanes (9 kcal/mol), triphenylmethanes (7 kcal/mol), tricyclic heterocycles (7 kcal/mol), bicyclic heterocycles (5 kcal/mol), dihydropyridines (4 kcal/mol) and five-membered (5 kcal/mol); boron- (8 kcal/mol), silicon- (8 kcal/mol), nitrogen- (7 kcal/mol), oxygen- (7 kcal/mol), phosphorus- (8 kcal/mol) and germanium-based donors (6 kcal/mol).

2.4d Kinetic Aspects of Hydride Transfers

Early experimental studies performed by Kreevoy reveal that hydride transfer rates scale linearly with the driving force for hydride transfer reactions between NADH-analogs.¹⁵⁴⁻^{156, 204} His experimental data was fit based on the quadratic dependence predicted by Marcus theory for non-adiabatic electron transfer,²⁰⁵⁻²⁰⁶ as shown in eq (7):

$$\Delta G^{\ddagger} = \frac{(\lambda + \Delta G_0)^2}{4\lambda} \tag{7}$$

where λ is the reorganization energy associated with the electronic reorganization of the solute and configurational reorganization of the solvent, ΔG^{\ddagger} is the activation free energy, and ΔG_0 is the free energy of the hydride transfer reaction. However, the experimental results exhibit a linear rate dependence between the thermodynamic and kinetic parameters due to a large difference between the reorganization energies and respective reaction free energies ($\lambda \sim 80$ kcal/mol >> $\Delta G_0 = -10$ to 0 kcal/mol).

Warshel and coworkers²⁰⁷⁻²⁰⁸ provided a possible explanation for these experimental observations by modeling the adiabatic nature of S_N2 reactions (including hydride transfers) using a modified Marcus expression to calculate the activation free energy:

$$\Delta G^{\ddagger} = \frac{(\lambda + \Delta G_0)^2}{4\lambda} - H_{rp}(X^{\ddagger}) + \frac{H_{rp}^2(X_r^0)}{\lambda + \Delta G_0}$$
(8)

Here, $H_{rp}(X^{\ddagger})$ and $H_{rp}(X_r^0)$ are electronic coupling matrix elements at the transition-state and reactant geometries, respectively. Computing these matrices allows for the determination of the non-adiabatic reaction surface, which can be traced by calculating the energies along the reaction coordinate while freezing the electron density of the surroundings. This assumes that the hydride transfer occurs at rates much faster than reorganization. The adiabatic model yielded a larger reorganization energy for NADH analogs (λ = 236 kcal/mol) than those obtained using the non-adiabatic approach, which is consistent with the fact that the electronic coupling terms are significant for hydride transfer processes.²⁰⁷ Again, the larger reorganization energy (relative to the reaction free energy) further justifies the linear free energy relation for hydride donors observed in experiments.^{154-156, 204}

Recent studies of hydride transfer utilize linear relationships between thermodynamic and kinetic (*N*) parameters to describe the reactivity of hydride donors.¹⁷² Figure 10 shows a linear dependence between experimental *N* values and ΔG_{H} for structurally-related hydrides. Although only a few observations can be made due to the dearth of available data, some useful conclusions can be drawn about these linear relationships. Namely, the intercepts are correlated to the intrinsic activation energies (barriers) of the hydride transfer reactions.²⁰⁹ The intrinsic barriers for borohydrides and silanes are lower than those of carbon-based hydrides, possibly due to the role of their conjugate acceptors, which have higher Lewis acidities, in stabilizing the hydride transfer products. Furthermore, the slopes of the linear correlations represent the sensitivity of the kinetics to structural changes within each hydride donor class.¹⁶⁰ Smaller slopes in the

cases of borohydrides and silanes indicate that their nucleophilicity values are only slightly enhanced by the larger thermodynamic driving force (lower ΔG_{H-}) of a hydride donor. In contrast, carbon-based hydrides have steeper slopes, indicating that changes in their thermodynamic hydricities considerably alter the rates of hydride transfer.



Figure 10. Linear free energy relations expressed with respect to the kinetic nucleophilicity parameter *N* and the thermodynamic hydricity (in kcal/mol) for boranes, silanes, and other subgroups of carbon-based hydrides. *N* values for borohydrides are measured in DMSO, while all other values are obtained in dichloromethane. Caution must be exercised when comparing *N* values because boranes are reported in a more polar solvent relative to others. All ΔG_{H-} values are reported in MeCN.

2.4e Solvation Effects

Solvation plays a major role in determining the strength of a hydride donor, as demonstrated by ΔG_{H-} values in different solvents as shown in Table 5. Most hydrides

tend to be stronger (possess a lower ΔG_{H-} value) in more polar solvents, which can be attributed to more effective charge stabilization by the solvent molecules solvating the hydride ion. Most of the experimentally determined thermodynamic hydricities of metalfree species were obtained from measurements in MeCN and DMSO solvents, which have dielectric constants (ϵ) of 37.5 and 46.7, respectively. The results show that ΔG_{H-} are ~2 kcal/mol lower in DMSO relative to their values in the less polar solvent MeCN. While aqueous ΔG_{H-} values have not been evaluated for metal-free hydrides, transition metal hydrides are shown to be stronger in water (ϵ = 80) by at least 20 kcal/mol relative to their ΔG_{H-} values in MeCN.^{103, 210-211} Similar effects are also observed for nucleophilicity. Hydrides exhibit larger nucleophilicities in more polar solvents, as exemplified by 1-benzyl-1,4-dihydronicotinamide (entry 107, Table 6) when measured in DCM (N = 8.7), MeCN (N = 9.8), and a 9:1 water/MeCN mixture (N = 11.4).¹⁵⁷

2.5 Relevance to Catalysis

To efficiently utilize hydrides in catalytic reduction reactions, one needs to strike a balance between the hydride donating ability of R-H and the energy required to regenerate it from R⁺ to close the catalytic cycle. While the catalytic behavior of metal-based hydrides has been reported for many reduction reactions,^{104-105, 212} metal-free hydrides often behave only as stoichiometric reducing reagents rather than catalysts. This section describes the challenges associated with the use of metal-free hydrides in catalysis and outlines possible approaches to improve their performance.

Different thermodynamic arguments are considered for catalysis in which the recovery of the active hydride form is achieved using electrochemical or photochemical

methods. These approaches are particularly relevant to energy storage applications, where the ability of a hydride donor to form fuels, such as H₂ and CH₃OH, is defined by the thermodynamic hydricity of the fuel. For example, the ΔG_{H^-} values of H₂ and formate (the first intermediate in CO₂ reduction) in acetonitrile are 76 kcal/mol and 44 kcal/mol, respectively.^{136, 213} Competent hydride donors should have thermodynamic hydricities slightly below these limits in order to provide a finite driving force to make the thermodynamics of hydride transfer favorable. While having larger driving forces for hydride transfer seems desirable, larger driving forces are accompanied by higher overpotentials to drive recovery of the catalyst. Figure 11 and Table 5 show that most metal-free donors can serve as reductants for CO₂. However, successful CO₂ reduction could be performed using weaker hydride donors, if the hydride transfer is accompanied by a proton transfer.

For an ideal catalyst, electrochemical closure of the catalytic cycle should be achieved at a potential that is equal to the standard reduction potential for the fuel forming reactions (0.46 V vs. NHE for H⁺/H₂ and -0.23 V vs. NHE for CO₂/HCOO⁻). Thus, evaluation of ΔG_{H^-} values of hydride donors R-H and E_1 values of the conjugate hydride acceptors provides insight into metal-free hydride donors that should be screened for the target reduction process. Figure 11 compares these parameters for both metal-free and metal-based hydride donors,^{120-123, 125-126, 128, 130-131, 134, 136, 214-215} including those relevant to fuel-forming proton and CO₂ reduction processes. Interestingly, a scaling relationship is observed between the first reduction potential E_1 of the oxidized form (Scheme 4) and the ΔG_{H^-} values across different metal-free hydride donor groups. The existence of this

scaling relationship reflects the fact that bond dissociation energies (BDEs) of hydride donors are relatively similar to each other and that the intercept of the plot is directly related to these values. Most metal-free hydride donors have BDE values of approximately 75 kcal/mol, giving rise to the observed linearity. BDE values for the metal-based hydrides obtained from the correlation were found to be lower (~60 kcal/mol), which explains their higher activity.



Figure 11. The scaling relationships between the thermodynamic hydricity ΔG_{H-} and the first electron reduction potential E_1 of the oxidized form for metal-free (orange) and metal-based hydrides (blue). The ΔG_{H-} value for dihydrogen $\Delta G_{H-}(H_2) = 76$ kcal/mol and carbon dioxide $\Delta G_{H-}(CO_2) = 44$ kcal/mol along with reduction potentials $E(H^+/H_2) = 0.46$ V and $E(CO_2/HCO_2-) = -0.23$ V (both vs. NHE) are presented as black circles. The dashed gray line helps to estimate the overpotential.

The scaling relationship between E_1 and the thermodynamic hydricity has important consequences for the catalyst performance of the hydride donor. For example, it implies that the lowest possible overpotential that can be achieved for proton reduction using metal-free hydride donors is 0.3 V, while metal-based systems can operate at essentially zero overpotential. In the case of CO₂ reduction, both metal-free and metalbased systems contain sizeable overpotentials, ranging from 1.5 to 1.1 V (Figure 11). However, this overpotential is likely lower if CO₂ is reduced by a proton-coupled hydride transfer where the coupled proton transfer stabilizes the preceding hydride transfer.

The analysis shown in Figure 11 only considers E_1 values and thus fails to address the fact that recovery of the hydride catalysts requires two electron transfers. The potentials required for the second electron reduction E_2 (Scheme 4) tend to be more energetically demanding, often requiring more than 1 V energy input in addition to E_1 . In contrast, the second electron reduction of metal-based analogs is less demanding, where differences between two potentials ($\Delta E = E_1 - E_2$) are ~0.5 V (Figure 12a).^{120-123, 125-126, 128, ^{130-131, 134, 136, 214-215} The ability of metal complexes to screen the second incoming charge is possibly due to large structural changes that occur upon the first electron reduction.^{214, ²¹⁶ To illustrate the difference between the energy requirements for closure of the catalytic cycle, Figure 12b compares the well-known Dubois Ni-complex catalyst²¹⁷⁻²¹⁸ with a metal-free hydride donor of similar ΔG_{H-} (2OH).¹³⁴⁻¹³⁵ While the first electron transfers occur at comparable reduction potentials (-0.4 V vs. NHE for the Ni-complex and -0.5 V vs. NHE for 2OH), there is a significant difference in the second reduction potentials (-0.5 V vs. NHE for Ni-complex and -1.4 V vs. NHE for 2OH).^{134-135, 217}}}



Figure 12. (a) The difference in the first and second reduction potentials (E_1 - E_2) as a function of the thermodynamic hydricity (ΔG_{H-}) for metal-free and metal-based hydrides. (b) The illustrative comparison of the energy profiles required for hydride catalyst recovery for metal-catalyst (Ni-complex) and for a metal-free hydride donor (2OH) possessing similar ΔG_{H-} .

Very negative E_2 values of some metal-free hydrides are a likely reason why metalfree hydride donors are not often utilized in catalysis. These drawbacks of some metalfree models can be addressed by identifying approaches that enable catalyst recovery by lowering the reduction potentials without affecting their hydride donor ability. For example, the second reduction step can be achieved via a proton-coupled electron transfer mechanism, a tactic that is frequently used in many natural and artificial catalysts.²¹⁹⁻²²⁰ Specifically, the reduced forms of natural flavin-based cofactors are regenerated using such proton-coupled reduction steps, as discussed in the Selected Applications section. Proton-coupled reduction is often utilized in metal-based catalysis to achieve efficient recovery of the hydride form.¹⁵⁰ For example, a comparative study of the photochemical hydrogen evolution reaction by Fe, Co and Ni hydrides indicates that the Co-based photocatalyst performs much better than the Ni-based analog due to differences in the pKa values between $[Co^{III}-H]^{2+}$ (pKa=7) and $[Ni^{III}-H]^{2+}$ (pKa=-0.4).²²¹ An interesting approach, reported recently by Berben, involves the use of AI ion coordination to shift the reduction potentials of an imine-based ligand to less negative values.²²²

2.6 Conclusions and Future Outlook

In summary, the thermodynamic and kinetic hydricity parameters can in principle guide the design of hydride donors with desirable properties for specific chemical reductions. Analyzing trends between ΔG_{H} and other important properties, such as the nucleophilicity (*N*) and the first and second reduction potentials (E_1 and E_2), uncovers the principles that govern chemical reductions by hydride transfers to understand and enable the design of hydrides to perform desired reductions. For instance, structural and electronic features, such as rearomatization and hydride bond polarity, were found to considerably affect hydride transfer. Exploiting these effects systematically allows for the design of hydride donors that balance the energy efficiency and kinetics of hydride transfer reductions, including the ability to design for catalytic over stoichiometric mechanisms for chemical reductions.

A major challenge to utilizing metal-free hydrides for catalytic chemical reductions is the difficulty of recovering the active catalyst. Electrocatalysts require large negative reduction potentials to regenerate the hydride. Additionally, a significant tradeoff is

observed between the strength of the hydride donor and the first reduction potential as a consequence of the scaling relation between ΔG_{H} and E_1 . Breaking this scaling relation is key to synthesizing catalysts that can utilize less energy, require smaller over-potentials and yet be kinetically competent by maintaining the same reduction prowess. However, decoupling the strength of the hydride donor from the potential required for its recovery is a daunting challenge. In natural systems, high-energy intermediates are avoided by coupling proton and electron transfers as with the reduction of FAD to FADH₂. Another approach involves the incorporation of metal ions, where the role of the metal is to tune the reduction potential of the coordinated hydride donor.

Chapter 3. Benzimidazoles as Metal-Free and Recyclable Hydrides for CO₂

Reduction to Formate

Reproduced in part from Ref. 317 with permission from Lim, C.-H.; Ilic, S.; Alherz, A.; Worrell, B.T.; Bacon, S.S.; Hynes, J.T.; Glusac, K.D.; Musgrave, C.B. J. Am. Chem. Soc. **2019**, 141(1), 272-280, DOI: 10.1021/jacs.8b09653.

© 2019 American Chemical Society

3.1 Introduction

The chemical reduction of carbon dioxide (CO₂) to liquid fuels (e.g. methanol) powered by renewable energy would revolutionize the future energy landscape.²²³⁻²²⁴ Such a technology could effectively close the carbon cycle; however, despite progress in the reduction of CO₂ to valuable products, no process has effectively met the requirements for the practical conversion of CO₂ to utilizable fuels. Furthermore, the scientific community has not yet reached a consensus on a general approach to address this challenge.

The reduction of CO_2 via hydride (H⁻) transfer(s) stands as one of the most promising approaches to convert CO_2 to usable fuels,²²⁵⁻²²⁷ with several reports describing progress towards implementation of such a system.²²⁸⁻²³⁰ Of course, CO₂ cannot proceed directly to methanol by hydride transfers exclusively. An example is a recently proposed mechanism mediated by the organo-hydride dihydropyridine wherein CO₂ undergoes a series of three reductions, each one followed by a protonation: first, to generate formic acid (HCOOH), second, to produce methanediol — which converts to formaldehyde (CH₂O) with loss of water — and finally to generate methanol (CH₃OH).^{189,} ²³¹ This route may not always be effective, for example in cases where high activation barriers result in slow kinetics. A pteridine derivative is believed to undergo a similar pathway of CO₂ reduction, although the reduction by pteridines via this mechanism is not feasible due to slow kinetics.²³² In any event, the predicted mechanism of CO₂ reduction to methanol by hydride transfer we reported^{231,189} was somewhat complex. While the individual steps involved were relatively simple, the overall route was complicated in two senses: first, multiple steps, hydride transfers, and proton transfers were involved;

second, the preparation of the particular organic-hydride donor, dihydropyridine, involved electrode and photo-processes. This complexity suggests that an effective experimental scrutiny of the mechanism might focus on particular steps in the mechanism. Thus, in the present work we experimentally examined a fundamental but more limited CO₂ reduction; the key first reduction to formate by a chemically prepared (and different) organo-hydride donor that avoids the participation of proton transfer.

Before proceeding, we provide some perspective on CO₂ reduction via the use of other, non-organic hydrides. Transition metal (TM) hydrides are the most commonly studied hydrides and have proven effective for the reduction of CO₂, and thus merit discussion here. Some efforts have focused on determining the relative hydricity of TM hydrides, the thermodynamic property which quantifies their potency as hydride donors.^{165, 212, 233-234} Strong TM hydrides typically involve noble metals, such as $[Ru(tpy)(bpy)H]^+$ and $[Pt(depe)_2H]^+$; depe = 1,2-bis(diethylphosphino)ethane.²³³ Recent advances using non-precious metal species,^{88, 229} such as Co(dmpe)₂H, have been achieved in the reduction of CO₂ to HCOO⁻ (formate), but this requires a strong sacrificial base to form the requisite reducing complex in situ; dmpe = 1.2bis(dimethylphosphino)ethane.²²⁹ Beyond the realm of TM-catalyzed processes, only one example of a recycable organo-hydride has been experimentally demonstrated to reduce CO₂ to HCOO^{-.230} Yet, even here, the intermediacy of a transition metal center, specifically ruthenium, is required: a dihydropyridine organo-hydride (which ultimately acts as the reductant) forms part of a pbn (2-(pyridin-2-yl)benzo[b][1,5]naphthyridine)) ligand of a Ru(bpy)₂(pbnH₂)²⁺ complex. Moreover, in this system a stoichiometric quantity

of a Brønsted base is required to facilitate the transfer of the hydride from the pbn ligand of the Ru complex to CO_2 .²³⁵

While many transition metal-catalyzed and -coupled complexes effectively reduce CO₂ to formate (and beyond), the unfortunate fact remains that the high cost of homogeneous noble metal catalysts effectively hampers the development of economical processes catalyzed by these complexes for the production of utilizable fuels from CO₂. Furthermore, the selectivity of metal-based electrocatalysts is often limited because byproducts such as CO and/or H₂ are formed in addition to formate.^{37-39, 236} While CO and H₂ are difficult to store and transport, formate (and formic acid) represents a promising energy carrier candidate, due to its low toxicity, easy transportation and straightforward handling.²³⁷⁻²³⁹

Here we report what is to the best of our knowledge the first reduction of CO₂ to HCOO⁻ by a metal-free and recyclable organo-hydride derived from benzimidazoles (Scheme 7). Benzimidazoles, direct analogs to imidazole-based cofactors present in 5,10-methenyltetrahydromethanopterin (Hmd) hydrogenase,²⁴⁰ have been previously identified as promising hydride donors^{135, 142, 241} due to their characteristic conformation and an anomeric effect.²⁴² The choice of this hydride donor, the conception of the reduction's mechanism, and results of the reduction were further guided by quantum chemical calculations. An additional noteworthy aspect of the CO₂ reduction illustrated in Scheme 7 is that the reaction proceeds in the absence of biological enzymes,²⁴³ a sacrificial Lewis acid, or a base to activate the substrate or reductant.²⁴⁴ Specifically, we demonstrate that dihydrobenzimidazole organo-hydrides (1,3-dimethyl-2,3-dihydro-1H-benzimidazole derivatives, species 1a-d in Scheme 7) are capable of chemically reducing

 CO_2 to $HCOO^-$ in DMSO solvent. The choice of the solvent used was two-fold: (i) it is a polar solvent that helps stabilize the charged products (benzimidazolium cations and formate), while not possessing acidic protons (like methanol and water) prevents a possible hydrogen evolution reaction from the hydride; (ii) both benzimidazole-hydride and CO_2 are sufficiently soluble in DMSO.



Scheme 7. Reduction of CO₂ to formate anion by benzimidazole-based organo-hydrides.

While CO₂ reduction by metal-free hydrides has been previously achieved with organoboranes and organosilanes,²⁴⁵⁻²⁵⁵ the inability to regenerate their active hydride forms has restricted their use to only stoichiometric conditions;²⁴¹ notably, significant progress has been made to employ dihydrogen in sustainable CO₂ reduction processes catalyzed by Lewis acid and base pairs.²⁵⁶⁻²⁵⁸ In our attempt to identify a catalytic CO₂ reduction system, we have electrochemically transformed benzimidazolium cation (1,3-dimethyl-1H-benzimidazol-3-ium derivative 2c) to its corresponding organo-hydride 1c with quantitative yield. Thus, the present system serves as a proof of concept that organo-hydrides are capable of transferring a hydride ion to CO₂ and that the regeneration of the hydride can be achieved electrochemically.

3.2 Computational Methods

All stationary geometries (reactants, transition states and products) for the systems studied were computed using density functional theory based on the M06 density functional²⁵⁹ and 6-31+G** basis set.²⁶⁰ To account for the effect of solvent, the implicit polarized continuum solvation model (CPCM)²⁶¹⁻²⁶² was employed in all calculations to treat the solute-solvent electrostatic interactions in dimethyl sulfoxide (DMSO) solvent. Calculated values for relevant standard reduction potentials and pK_a values were obtained following the previously published procedure.¹³⁵ All reported energies were referenced to separated reactants in solution and calculations were performed using the GAUSSIAN 09 or 16 computational software packages.²⁶³

3.3 Experimental Section

General methods. Benzimidazole (98%), 5,6-dimethylbenzimidazole (\geq 99%), 2methylbenzimidazole (98%), iodomethane (99%), 1,3,5-trimethoxybenzene (\geq 99%), sodium borohydride (99%), ¹³CO₂ (99 atom % ¹³C, <3 atom % ¹⁸O), potassium iodide (\geq 99%), potassium bromide (\geq 99%), sodium iodide (\geq 99%), lithium bromide (\geq 99%) and potassium hexafluorophosphate (\geq 99%) were purchased from Sigma-Aldrich and used as received. Potassium nitrate (\geq 99%), potassium perchlorate (\geq 99%), and potassium tetrafluoroborate (98%) were purchased from Alfa Aesar and used as received. A ¹²CO₂ gas cylinder was purchased from Air Products (Bone Dry, 99.9%). DMSO- d_6 (d, 99.9%), MeCN- d_3 (d, 99.8%) and methanol- d_4 (d, 99.8%) were purchased from Cambridge Isotope Laboratories, Inc. DMF- d_7 (d, 99.5%) was purchased from Sigma-Aldrich. Glass tube reactors were purchased from Ace Glass Incorporated: Tube, 9 m L, 150 psig, 19 mm O.D., 10.2 cm long (part # 8648-62). ¹H and ¹³C NMR spectroscopies were performed in a Bruker Ascend 400 MHz spectrometer at the University of Colorado Boulder NMR facility. Chemical shifts are referenced to the internal solvent resonance (DMSO, 2.50 ppm) and reported as parts-per-million (ppm). ESI-MS analysis was performed with a Synapt G2 HDMS Qtof (Waters) at the University of Colorado Boulder mass spectrometry facility. The generalized synthetic procedures were modified from those already reported in the literature.^{142, 264}

General experimental procedure for the synthesis of benzimidazoliums (2). The method we describe here was used to synthesize species 2c and it generally applies to the synthesis of other benzimidazoliums (2). 60 mL of reagent grade methanol (0.83 M) was added to a 250 mL round bottom flask equipped with a magnetic stir bar, followed by the addition of 6.61 g (50.0 mmol, 1.00 equiv) of 2-methylbenzimidazole, 12.5 mL (28.5 g, 200 mmol, 4.00 equiv) of iodomethane, and, finally, 6.91 g (50.0 mmol, 1.00 equiv) of potassium carbonate (K₂CO₃). This suspension was subsequently heated at reflux for 18 hours. After cooling the reaction to room temperature, the solution was reduced in volume to ~30 mL in vacuo and the solids were filtered through a filter paper-topped Buchner filter. The filtered solids, which contained both residual K_2CO_3 and the desired product 1,2,3-trimethyl-1H-benzimidazol-3-ium iodide (species 2c) were added to a 250 mL round bottom flask containing 150 mL of reagent grade MeOH and heated to 60°C to dissolve most, but not all of the solids. The hot solution was then filtered through a Buchner funnel and the filtrate was collected and placed into a freezer (~ -20°C) for 4 hours. After this time the formed crystals were filtered from the supernatant, washed with additional

portions of reagent grade acetone (50 mL, 2 times), and dried under vacuum to give 10.9 g (76% yield) of the desired 1,2,3-trimethyl-1H-benzimidazole-3-ium iodide (2c) as a white solid which was used in the subsequent reaction with no further purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.03 – 7.94 (m, 2H), 7.68 – 7.59 (m, 2H), 4.00 (s, 6H), 2.87 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 152.25, 131.29, 125.81, 112.69, 31.72, 10.62. HRMS (ESI): C₁₀H₁₃N₂⁺ calculated at 161.1079; observed at 161.1078. General experimental procedure for the synthesis of dihydrobenzimidazoles (1). The method we describe here was used to synthesize species 1c and it generally applies to the synthesis of other dihydrobenzimidazoles (1). 40 mL of H₂O and 60 mL of reagent grade diethyl ether (1.0:1.5, v:v, 0.10 M total dilution) were added to a 250 mL round bottom flask equipped with a magnetic stir bar. Next, 2.88 g (10.0 mmol, 1.00 equiv) of 1,2,3-trimethyl-1Hbenzimidazole-3-ium iodide (2c) was added, followed by 1.13 g (30.0 mmol, 3.00 equiv) of sodium borohydride in small portions. This mixture was allowed to react under vigorous stirring for 1 hour at room temperature. After this time, the reaction mixture was placed into a separatory funnel and the organic layer was extracted, then washed with deionized water (50 mL, 2 times), and finally washed with brine (50 mL, 1 time). The organic solution was dried over MgSO₄, filtered, and concentrated under reduced pressure to yield 1.05 g (65% yield) of the compound (1c) as a clear liquid. The product was stored under argon in a ~ -20°C freezer until later use. We note that species 1c solidified in the freezer at ~ -20°C and is stable for months when stored at ~ -20°C even after repeated exposure to air. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.59 – 6.50 (m, 2H), 6.42 – 6.33 (m, 2H), 4.00 (q, J = 5.3 Hz, 1H), 2.61 (s, 6H), 1.39 (d, J = 5.3 Hz, 3H). ¹³C NMR (101 MHz, DMSO- d_6) δ 142.59, 118.68, 105.65, 86.13, 33.52, 18.13. HRMS (ESI): (C₁₀H₁₄N₂)Li⁺ calculated at

169.1317; observed at 169.1319. See SI section 4 for characterization of other dihydrobenzimidazoles (1).

General experimental procedure for the reduction of CO_2 with a representative benzimidazole hydride. 31.5 mg (0.25 mmols, 20.00 equiv) of KBF₄ was added to an oven-dried 9 mL glass tube reactor equipped with a 9.5 × 4.7 mm egg-shaped magnetic stir bar purchased from VWR. This was then diluted with 500 µL of DMSO-*d*₆ containing 2.0 mg (0.0125 mmol, 1.00 equiv) of species 1c and 4.2 mg (0.025 mmol, 2.00 equiv) of 1,3,5-trimethoxybenzene (as the internal standard) using a calibrated pipette. The tube was then sealed and degassed under vacuum while under sonication for a total of 5 minutes. After degassing, the valve connected to the vacuum was closed and ¹²CO₂ at 20 psig (or ¹³CO₂ at ~20 psig) was then introduced to the reaction vessel. The reaction mixture temperature was maintained at 50°C in an oil bath for 18 hours while stirring at 800 rpm. After this time, species 1c was fully consumed and an additional 200 µL of DMSO-*d*₆ (in some cases methanol-*d*₄) was added to improve the solubility of the solution. The reaction solution was then analyzed by ¹H NMR spectroscopy (and in some cases ¹³C NMR spectroscopy).

Cyclic voltammetry and digital simulations. Cyclic and linear sweep voltammetries were performed using a BASi epsilon potentiostat in a VC-2 voltammetry cell (Bioanalytical Systems) using a glassy carbon (3 mm diameter, MF-2012, Bioanalytical Systems) or tin (3 mm diameter, custom made, Bioanalytical Systems) working electrode, a nonaqueous Ag/Ag⁺ reference electrode (MF-2062, Bioanalytical Systems) and a platinum wire (MW-4130, Bioanalytical Systems) as a counter electrode. The spectroscopic grade solvent DMSO and the electrolyte tetrabutylammonium perchlorate

(TBAP) were purchased from Sigma Aldrich and used as received. Electrochemical potentials were converted to NHE by adding 0.569 V to the experimental potentials.⁴⁵ For cyclic voltammetry (CV) measurements, the iodide salt of 2c was converted to perchlorate using a previously published procedure.²⁰⁴ The CV was simulated using DigiSim simulation software with the following parameters: (i) Electrode area: 0.07 cm², planar electrode geometry, scan rate: 100 mV/s, resistance uncompensated; (ii) Semi-infinite diffusion model, diffusion constants for all species calculated using a Stokes radius obtained from optimized structures ($D = 2.8 \cdot 10^{-6} \text{ cm}^2/\text{s}$), initial concentration of 2c: 1 mM; (iii) Mechanism: A + e⁻ \rightarrow B (E⁰ = -1.96 V); B = C (K and k_f for this process was varied, see SI); C + e⁻ \rightarrow D (E⁰ = 0.30 V); (iv) Electron transfer kinetics were simulated using the Butler-Volmer model with the parameters: $\alpha/\lambda=0.5 \text{ eV}$, ks=10 cm/s.

Controlled potential electrolysis. Bulk electrolysis was performed in a glovebox using a BASi EpsilonTM potentiostat in a VC-2 voltammetry cell (Bioanalytical Systems), with a carbon fiber paper working electrode (Freudenberg H23, Fuel Cell Store), a nonaqueous Ag/Ag⁺ reference electrode (MF-2062, Bioanalytical Systems) and a coiled platinum wire in an auxiliary electrode chamber (MW-1033 and MR1196, Bioanalytical Systems) as the counter electrode. The electrolysis was performed in deuterated DMSO- d_6 with 1,3,5-trimethoxybenzene (as the internal standard) while its progress was monitored using ¹H-NMR spectroscopy.

3.4 Results And Discussion

Benzimidazole organo-hydrides for CO₂ reduction to formate. A number of previous studies have suggested that benzimidazole-based organo-hydrides are potentially strong hydride donors.^{135, 142, 172, 226, 233, 241} We used density functional theory (DFT) to calculate the thermochemical properties of CO₂ reduction to HCOO⁻ by four different benzimidazole-based organo-hydrides (1a-d) in order to determine if such hydrides are competent for this reduction. Table 7 shows that species 1a (the simplest dihydrobenzimidazole considered, where R₁ = H and R₂ = H) is predicted to reduce CO₂ to HCOO⁻ with a calculated reaction free energy of ΔG^{0}_{rxn} = 4.2 kcal/mol, while regenerating species 2a. Species 1b, where R₁ = Me and R₂ = H, is predicted to be a stronger hydride donor relative to our base case 1a; ΔG^{0}_{rxn} is now lowered to 2.0 kcal/mol. We calculate that substitution of Me at R₂ further improves the hydride donation strength such that ΔG^{0}_{rxn} = 0.7 kcal/mol for 1c. Finally, 1d with Me substituted at both R₁ and R₂ is predicted to be the strongest hydride donor reducing CO₂ to HCOO⁻ with ΔG^{0}_{rxn} = -1.7 kcal/mol.

Table 7. Predicted thermochemical properties of CO₂ reduction by reductants 1a-d with their corresponding experimental formate yields.



| Hydride donor | Formate yield (%) ^a | ∆G [‡] _{HT} (298 K) (kcal/mol) ^d | ΔG^{0}_{rxn} (298 K) (kcal/mol) ^d | R _{C-H} (Å) ^e |
|---------------|-----------------------------------|--|---|--------------------------------------|
| 1a | 5 ^b | 23.1 | 4.2 | 1.37 |
| 1b | 4 ^b | 22.1 | 2.0 | 1.39 |
| 1c | 59 ^b (66) ^c | 20.6 | 0.7 | 1.38 |
| 1d | 51° | 21.1 | -1.7 | 1.39 |

^a Experimental yields determined by ¹H-NMR spectroscopy using 0.05 M of 1,3,5trimethoxybenzene as an internal standard and species 1 as the limiting reagent.

^b Reaction conditions: 0.50 ml DMSO-*d*₆, [hydride donor] = 0.10 M, [KBr] = 0.50 M, P_{CO2} = 30 psig, T = 50°C and t = 24 h (except t = 11 h for 1c). ^c Reaction conditions: 0.50 mL DMSO-*d*₆, [hydride donor] = 0.025 M, [KBF₄] = 1.00 M, P_{CO2} = 20 psig, T = 50°C and t = 18 h. ^d Theoretical activation free energies (ΔG^{\ddagger}_{HT}) and reaction free energies (ΔG^{0}_{rxn}) at standard conditions of 298 K and 1 atm, computed at the rM06/6-31+G(d,p) level of theory in implicitly described (CPCM) DMSO solvent. ^e Calculated bond distance between the transferring hydride (H⁻) and the carbon (C) of CO₂ at the transition state. The ball-andstick model shows the computed TS structure for reductant 1c. Our initial experimental results, reported in Table 7, are consistent with these calculations (except for the case of 1d). The hydride donor 1c produced the correspondingly highest yield of HCOO⁻ (59%) relative to weaker donors 1a and 1b (5% and 4%, respectively). These reactions were performed under mild conditions (T= 50°C and P_{CO2}= 30 psig) in DMSO-*d*₆ for 24 hours or less (11 hours for 1c); the addition of salts such as KBr was empirically discovered to significantly increase the yield of formate (*vide infra*). Modifying the reaction conditions resulted in an increase in HCOO⁻ yield by 1c to 66%, while 1d produced a lower yield of 51% despite it being predicted to be a stronger hydride donor. Both 1c and 1d suffer from parasitic side reactions in DMSO that prevents their quantitative HCOO⁻ yield;²⁶⁵ 1d is a stronger hydride donor and thus suffered more from non-productive side reactions, thus explaining its lower formate yield relative to 1c (*vide infra*).

The presumed formation of formate in our reaction was confirmed by its detection under synthetically relevant conditions via both ¹H-NMR spectroscopy and electrospray ionization mass spectrometry (ESI-MS). The ¹H-NMR spectra obtained after completion of the reaction exhibited a peak at 8.46 ppm, which was confirmed to be formate by comparison to the authentic sample. To further confirm formate's presence, ESI-MS in negative ion mode was employed. The formate anion was observed to complex with the added salts: for example, we observe the presence of the KBr·HCOO⁻ complex in the correct isotopic ratios with m/z = 162.9, 164.9, and 166.9. Thus, these two analytical methods confirm the presence of formate in our product solution.



Figure 13. ¹³C-NMR spectra of species 1c reacted with ¹³CO₂ in DMSO-*d*₆. Reaction conditions: [1c] = 0.10 M, [KBr] = 0.20 M, $P_{CO2} = \sim 20$ psig, T = 50 °C and t = 16 h. 0.05 M 1,3,5-trimethoxybenzene was introduced as an internal standard. ¹³C-formate appeared at 165.70 ppm; dissolved ¹³CO₂ appeared at 124.18 ppm.¹⁷

To further validate our proposed mechanism of reduction, we conducted experiments with isotopically enriched ¹³CO₂ gas (99 atom % ¹³C). Figure 13 confirms the presence of H¹³COO⁻ (appearing at 165.70 ppm) in the product solution after ¹³CO₂ reacted with hydride species 1c. The significant enhancement of H¹³COO⁻'s ¹³C-NMR signal relative to other species in the solution (peaks a-d) is apparent in Figure 13. In addition, the ¹³C nuclear spin splits the ¹H-NMR peak of H¹³COO⁻ into a doublet (at 8.27 and 8.72 ppm), further corroborating the presence of isotopically enriched H¹³COO⁻. These results demonstrate that the formate anion detected in the reaction mixture is derived from the chemical reduction of the carbon dioxide introduced to our solution.

Effect of salts and solvents. During the course of these studies, we empirically discovered that the addition of various salts to the reaction mixture greatly enhances the observed formation of the formate anion. A similar salt effect was reported for a

photochemically driven system involving the reduction of CO_2 by pyridine²⁶⁶ and in the catalytic formation of acrylate from ethene and CO_2 .²⁶⁷ Table 8 indicates that in the absence of salts, the HCOO⁻ yield by 1c was nearly undetectable (5%, entry 1). Alternatively, under various reaction conditions, the presence of salts (e.g. KBr, KI, LiBr and NaI) resulted in markedly higher yields of the reduced product (25-59%, entries 2-7). Of these salts, KBr produced the highest formate yield (59%, entry 3) relative to other salts under identical conditions.



 Table 8. Reaction of species 1c or 1d with CO2 under various experimental conditions.

| | ייי – ראין | , ι α [ιν ₁ – | | | | | 20(1 | √ 1 − Π _∫ , ∠ | | ſ |
|--------------------|------------------|---------------------------------|-------------------|-------------------|--|-------------|--------------------------------------|--|-----------------------------|-------------------------------------|
| Entry ^a | Hydride donor | [Hydride donor] (M) | Salt | [Salt] (M) | CO ₂ (psig) ^b | Time (h) | Consumption of 1 (%) ^c | Formation of 2 (%) ^c | Recovery of 2 (%) | Formate Yield (%) ^{c,d} |
| 1 | 1c | 0.100 | - | - | 30 | 24 | 69 | 69 | 100 | 5 |
| 2 | 1c | 0.100 | KBr | 0.20 | 30 | 11 | 86 | 86 | 100 | 40 |
| 3 | 1c | 0.100 | KBr | 0.50 | 30 | 11 | 92 | 91 | 99 | 59e |
| 4 | 1c | 0.100 | KI | 0.50 | 30 | 11 | 82 | 82 | 100 | 40 ^e |
| 5 | 1c | 0.100 | LiBr | 0.50 | 30 | 11 | 95 | 94 | 99 | 36 ^e |
| 6 | 1c | 0.100 | NaI | 0.50 | 30 | 11 | 87 | 86 | 99 | 25 ^e |
| 7 ^f | 1c | 0.100 | KBr | 0.50 | 30 | 24 | 79 | 77 | 97 | 33 |
| 8 | 1c | 0.050 | KBF ₄ | 0.50 | 20 | 18 | 97 | 96 | 99 | 57 |
| 9 | 1c | 0.025 | KBF ₄ | 0.50 | 20 | 18 | 100 | 99 | 99 | 61 |
| 10 | 1c | 0.025 | KBF ₄ | 1.00 ^g | 20 | 18 | 100 | 100 | 100 | 66 |
| 11 | 1c | 0.025 | KClO ₄ | 0.50 | 20 | 18 | 100 | 100 | 100 | 35 |
| 12 | 1c | 0.025 | KNO ₃ | 0.50 | 20 | 18 | 100 | 100 | 100 | 49 |
| 13 | 1c | 0.025 | KPF ₆ | 0.50 | 20 | 18 | 100 | 100 | 100 | 17 |
| 14 | 1d | 0.025 | KBF ₄ | 1.00 ^g | 20 | 18 | 100 | 100 | 100 | 51 |
| 15 | 1d | 0.025 | KNO ₃ | 1.00 | 20 | 18 | 100 | 99 | 99 | 53 |

^a All reactions were conducted in 0.50 mL of DMSO- d_6 solvent at 50 °C, unless

otherwise specified; the solution appeared slightly cloudy after reactions were completed,

0.20 mL of methanol- d_4 (entries 1-7) or 0.20 mL of DMSO- d_6 (entries 8-15) were added to the solution to improve solubility prior to acquiring NMR spectra. ^b Pressure of introduced CO₂ in psig. ^c Determined from ¹H-NMR spectroscopy using 0.05 M of 1,3,5trimethoxybenzene as an internal standard. ^d Yield based on species **1** as the limiting reagent. ^e Formate yield was determined from the average of three runs, with reproducibility of ±5%. ^f Reaction at 25 °C. ^g Salt not fully soluble.

We propose that adding salts creates a more polar environment that stabilizes ionic products (species 2c and HCOO⁻) by increasing the ionic strength of the solution, and thus biases the equilibrium towards the formation of ionic products. In fact, our calculations of a model including the salt KBr suggest that the salt effect significantly improves the thermodynamics of the hydride transfer reaction from $\Delta G^{0}_{rxn} = 0.7$ kcal/mol to $\Delta G^{0}_{rxn} = -7.1$ kcal/mol.

Although we first performed the CO₂ reductions at slightly elevated temperatures (50°C, entries 1-6), we anticipated that, in view of the predicted relatively low free energy activation barrier ΔG^{\ddagger}_{HT} (298 K) = 20.6 kcal/mol in Table 7, species 1c could still be capable of reducing CO₂ to HCOO⁻ at room temperature, T = 25°C. Indeed, species 1c was found to be effective as a reductant under ambient conditions, although lower yield of formate was obtained (33%, t = 24 h, entry 7), presumably due to the slower reaction rate. We also examined this reduction in several solvents: methanol-*d*₄, MeCN-*d*₃, and DMF-*d*₇ yielded essentially no formate. Mixed solvents comprising of DMSO-*d*₆ with methanol-*d*₄, MeCN-*d*₃, or DMF-*d*₇ in 1:1 ratios by volume produced lower formate yields relative to pure DMSO-*d*₆. D₂O was not examined as a solvent due to 1c's poor solubility

and tendency to react with water to form H₂, as mentioned below. We propose that the observed reduced activity in methanol- d_4 , MeCN- d_3 and DMF- d_7 solvents is caused by their lower polarities (their polarity index values are 5.1, 5.8, and 6.4, respectively, compared to 7.2 for DMSO- d_6).²⁶⁸ Just as was argued above in connection with the salt effect on the reaction, the lower solvent polarity is presumed to disfavor ionic product formation leading to reduced product yields.

Reaction optimization and side reactions. In an effort to further increase formate yield (beyond the 59% yield of entry 3 of Table 8), we varied 1c's concentration, types of potassium salts, salt concentration, CO₂ pressure, and length of reaction time (Table 8, entries 8-13). We found that by both lowering [1c] from 0.100 M to 0.025 M and increasing the reaction time from 11 h to 18 h, we were able to fully consume hydride donor 1c to quantitatively form 2c; however, not all 1c was consumed to form the desired formate product as some reacted in parasitic side reactions (*vide infra*). From the results reported in Table 8 we also determined that a CO₂ pressure of 20 psig produced a slight improvement over 30 psig while a higher CO₂ pressure of 40 psig yielded poorer results (*vide infra*). At the reaction conditions of [1c] = 0.025 M, P_{CO2} = 20 psig, t = 18 h and 0.50 M of KBF₄, formate yield improved to 61% (entry 9). Notably, KBF₄ gave a higher formate yield than the potassium salts KCIO₄, KNO₃ and KPF₆ under identical conditions (entries 11-13). When [KBF₄] was increased to 1.00 M or 40 equiv. relative to 1c, formate yield was further increased to 66% (entry 10).

Under these optimized conditions, we tested the performance of 1d. 1d was computationally predicted to be a slightly stronger hydride donor than 1c, due to the moderate electron-donating ability of the methyl groups at the 5 and 6 positions of the benzimidazole. As reported in Table 7, 1d was predicted to reduce CO_2 to formate with the following properties: $\Delta G^{\ddagger}_{HT} = 21.1$ kcal/mol, $\Delta G^{0}_{rxn} = -1.7$ kcal/mol, and $R_{C-H} = 1.39$ Å. However, despite being predicted as a stronger hydride donor, 1d produced formate yields of only 51% (1.00 M KBF₄, entry 14) and 53% (1.00 M KNO₃, entry 15), lower than the 66% (entry 10) produced by 1c (while 1d was fully reacted to generate 2d). As we describe next, the hydrides of 1c and 1d participated in parasitic reactions that limit their formate yields.

We have identified two potential channels for the non-productive consumption of hydride donors 1c and 1d. First, we anticipate that the hydride can react with trace water in DMSO (present due to its hygroscopic nature) to form H₂ and hydroxide OH^{-.269} Second, the hydride could also non-productively react with DMSO to form dimethyl sulfide²⁶⁵ and OH⁻. The OH⁻ generated from these two sources likely reacts with excess CO_2 in the solution to form bicarbonate (HCO_3^{-}); this anion may then complex with potassium cations present in the solution to form the less soluble KHCO₃ salt. Indeed, this may well explain the observed cloudiness of the solution after completion of the reaction. Furthermore, we observed that formate yield by 1c was significantly lowered to 12% at a higher CO₂ pressure of 40 psig. Following an argument similar to that above, we hypothesize that the larger excess of CO₂ increased OH⁻ consumption, which in turn increased the parasitic consumption of 1c and 1d, thereby resulting in lower formate yields. Given that 1d is a stronger hydride donor, the parasitic consumption of its hydride was presumably more severe, thus producing a lower formate yield than 1c. Future design of the hydrides will focus on improving the kinetics of CO₂ reduction, while preventing the parasitic loss of the hydrides.²⁷⁰

Connections to dihydropyridine. Interestingly, the benzimidazole-based hydride systems studied here closely resemble our previously studied dihydropyridines, whose NADPH analogue is used as a recyclable hydride in natural photosynthetic CO₂ fixation.^{189, 231} Although, as explained in the Introduction, the present study is deliberately restricted compared to dihydropyridines --- with a focus on examining the fundamental concept of CO₂ reduction by hydride transfer --- it is instructive to note key points of commonality.

Perhaps the most important among several key features in common between these two chemistries is a hydride bound to a carbon that neighbors a N atom of a ring that becomes aromatic upon transfer of the hydride; this provides an analogous source for the driving force for hydride transfer. The underlying dearomatization-aromatization cycle that creates the thermodynamic driving force for CO₂ reduction was previously uncovered in the pyridine system.^{271,189} Similarly, because the aromatic species 2 is dearomatized upon its reduction to compound 1, the proclivity of this latter species to rearomatic species 2. While ref. ¹⁸⁹ includes the next protonation step of formate to produce formic acid that is not addressed here, the experimental results we report confirm the reduction of CO₂ by 1, and support the proposed theoretical homogeneous hydride transfer mechanism for the reduction of CO₂ to methanol.^{189, 232} For an extended discussion and references, see ref. ²³¹.

Electrochemical regeneration. As determined by ¹H-NMR spectroscopy, 1 was consumed to quantitatively recover the oxidized and aromatic species 2 (Table 8), thereby establishing its potential to function as a recyclable organo-hydride. Here, we examine

the possibility of regenerating 1c from 2c electrochemically to achieve catalytic CO₂ reduction. Generally, the recovery of 1 from the oxidized species 2 requires a net transfer of two electrons and a proton. Three possible pathways for electrochemical regeneration are represented in Scheme 8. The first pathway (pathway i) involving the protonation of 2c followed by two successive electron transfers (ETs) has been discarded because of the inability to protonate the benzimidazolium species 2c due to its high free energy cost. In contrast, the other two pathways in Scheme 8 (ii and iii) include an initial ET which leads to the formation of a neutral radical 2c'. The fate of 2c' depends on experimental conditions (e.g. applied electrochemical potentials and the presence of acids). Even though the second ET is calculated to be feasible at applied potentials (pathway ii), a rapid dimerization of 2c' impedes further recovery of the dihydrobenzimidazole hydride species 1c.²⁷² Finally, in the presence of a proton source, the facile protonation of the hydride 1c (pathway iii).

Scheme 8. Sequential regeneration pathways for electrochemical conversion of species 2c to hydride-active species 1c.



Inspired by the favorable calculated thermodynamic parameters for the electrochemical regeneration, we performed cyclic voltammetry (CV) experiments in the presence (pathway iii) and absence (pathway ii) of acids. Specifically, Figure 14a shows CVs of 2c obtained with different scanning directions in the presence and absence of phenol acting as a weak proton donor. In both cases, the irreversible reduction peaks appear at –1.88 V vs. NHE, which is consistent with the calculated one-electron reduction potential for 2c/2c⁻ conversion. Interestingly, the current intensity doubled in the presence of phenol indicating a possible proton-coupled two-electron transfer process, as represented in pathway iii (Scheme 7). Similar behavior was observed when stronger acids (acetic, chloroacetic and tetrafluoroboronic acids) were employed.

Indeed, scanning to positive potentials from these reduction peaks (scan direction: -2.3 V to +0.75 V) resulted in the appearance of a peak at ~ +0.3 V vs. NHE only in the presence of the acid. The peak matches well with the calculated oxidation peak of species

1c (+0.30 V vs. NHE). To confirm this regeneration, we performed the electrochemical oxidation of an authentic sample 1c; this indeed exhibited an oxidation potential at +0.36 V vs. NHE supporting the electrochemical regeneration of 1c from 2c (Figure 14a, inset).

To evaluate the efficiency of electrochemical regeneration of 1c, the experimental CVs were compared with the simulation, which was computed assuming that 2c undergoes a proton-coupled two-electron reduction process to form 1c (Figure 14b). An excellent match was obtained between the experimental and simulated voltammograms, indicating a quantitative conversion of 2c to 1c and that no side reactions (e.g. dimerization) occur.



Figure 14. Electrochemical regeneration of 1c from 2c. (a) Cyclic voltammograms at scan rates of 100 mV/s of 1 mM 2c in DMSO with (maroon solid) and without (blue solid) 100 eq. of phenol, baseline scan (blue dashed line) and a scan of a 100 mM solution of phenol in DMSO (maroon dashed line). Scan directions: $+0.1 V \rightarrow -2.3 V \rightarrow +0.75 V \rightarrow +0.1 V$. Inset: the oxidation of authentic 1 mM solution of 1c (green); (b) Experimental (baseline subtracted, gray) and simulated (orange dashed) CVs of 1 mM solution of 2c in the

presence of phenol at a scan rate of 100 mV/s. Simulation parameters: K(PT) = 100 and $k_f(PT) = 10^4 \text{ s}^{-1}$ gave the closest match to experimental values.

To further confirm and quantify the electrochemical conversion of 2c to 1c, we performed a controlled potential electrolysis experiment using a carbon fiber paper working electrode in DMSO-*d*₆ and an excess of phenol. The electrolysis progress was monitored via ¹H-NMR spectroscopy, with 1,3,5-trimethoxybenzene as an internal standard. Over the course of 4 h, 2c was quantitatively transformed to hydride 1c (Figure 15) at an applied potential of $E_{app} = -1.91 V$ (vs. NHE). Specifically, after electrolysis, the ¹H-NMR spectra of the resulting product matched the authentic sample of 1c and the integration values (relative to 1,3,5-trimethoxybenzene at ~6.1 ppm) of the aromatic hydrogens were identical (0.56 in Figure 15a and 0.55 in Figure 15b). The full conversion required a slight excess of supplied charge due to the competing proton reduction (Figure 14a). This experiment rules out the possibility that 2c is involved in any side reactions (e.g. dimerization of the forming radical) in the course of electrolysis under the given experimental conditions, which has often prevented the regeneration of previously studied NADH-analogs.²⁷³⁻²⁷⁷



Figure 15. ¹H-NMR spectra of catholyte DMSO- d_6 solution of 1 mM 2c in the presence of 150 equiv of phenol and 1,3,5-trimethoxybenzene as an internal reference, before (a) and after (b) bulk electrolysis on carbon fiber paper as the working electrode at $E_{app} = -1.91$ V vs. NHE.

We note that the relatively slow hydride transfer kinetics (e.g. over hours, see Table 8) impedes the exploitation of the current system for electrocatalytic CO₂ reduction, as we attempted by electrochemical experiments on two different electrodes (glassy carbon and tin) in the presence of CO₂ (Figure 16). We suggest that the hydride transfer kinetics can be improved by tuning the thermodynamic hydricity of benzimidazole-based hydrides.^{135, 142, 241} In any event, the combined reduction of CO₂ to formate and complete electrochemical recovery of the active hydride form demonstrated here indicate that

improving the kinetic properties of the current system could plausibly result in the development of metal-free catalytic systems for solar energy to fuels applications.



Figure 16. Attempted electrochemical CO₂ reduction with **2c** on glassy carbon and tin electrodes.

3.5 Conclusions

In conclusion, we have demonstrated the unprecedented use of metal-free and recyclable benzimidazole-based organo-hydrides (1) for the chemical reduction of CO_2 to formate, a reaction driven by the dearomatization-aromatization^{231,189} of the dihydrobenzimidazole/benzimidazolium (1/2) redox couple. We further established the quantitative regeneration of 1 from 2 via controlled potential electrolysis as proof of concept for conceivable electrocatalytic CO_2 reduction with 1/2 redox couple.

This work demonstrates an accessible CO₂ reduction to formate by organohydrides, even in the absence of metal-centers. The present results suggest the possibility of completely metal-free hydride sources as alternatives to noble metal-based
hydride donors to reduce CO_2 efficiently to usable fuels in a catalytic fashion. This opens the door to future development of related organic species that are reduced to reactive hydrides electrochemically, photochemically or photoelectrochemically powered by renewable energy. In a more extended arena, we hope that the present work will inspire future research to incorporate an appropriate proton source into our proposed catalytic cycle to effect the reduction of CO_2 directly to methanol.

Chapter 4. Importance Of Proton-Coupled Electron Transfer In Cathodic

Regeneration Of Organic Hydrides

Reproduced in part from Ref. 100 with permission from Ilic, S.; Alherz, A.; Musgrave, C.B.; Glusac, K.D. Chem. Commun. **2019**, 55, 5583-5586, DOI: 10.1039/C9CC00928K

© 2019 The Royal Society of Chemistry

4.1 Introduction

Proton-coupled electron transfer (PCET) is a process where protons and electrons are transferred either simultaneously or concertedly. While prominent in many biological systems, PCET is also particularly important in fuel cells and artificial photosynthetic systems, because it enables multi-proton and multi-electron transfer processes required for the desired chemical transformation.²⁷⁸⁻²⁸⁰ Electrochemical fuel-forming processes, such as the hydrogen evolution reaction (HER) and CO₂ reduction to methanol, involve several proton and electron transfers. Hydrides are often used in such processes to catalyze the transfer of electrons in pairs, thus avoiding high energy open-shell intermediates obtained by single electron transfers.²⁸¹⁻²⁸³ As such, electrochemical regeneration of catalytic hydrides with optimal efficiency is essential to obtain a highperforming CO₂ reduction and HER.^{218, 284-290} Metal-based hydrides regenerate their hydridic form through stepwise transfers of electrons and protons, and the mechanism is controlled by metal-ligand complexes and experimental conditions (such as applied potentials, proton source, solvent, etc.).^{285, 291-295} PCET in the regeneration of metal-free hydrides has not been electrochemically explored significantly beyond flavins and quinones,²⁹⁶⁻³⁰⁰ despite the significance of NADH and similar hydride donors in natural and artificial hydride transfer processes.³⁰¹⁻³⁰⁶ While the enzymatic regeneration of NADH occurs through a hydride transfer,³⁰⁵ the electrochemical formation of NADH analogues is hindered by the difficulty of protonating the one-electron reduced NAD radical and its rapid dimerization.³⁰⁷⁻³¹²

Our groups examined the thermodynamic and kinetic hydride donor abilities of various organic NADH analogues³¹³⁻³¹⁶ and following a series of systematic studies,

recently achieved a selective CO₂ reduction to formate under mild conditions using a recyclable organic benzimidazole hydride.³¹⁷ Here electrochemical regeneration pathways are explored for two groups of organic hydrides (RH) – acridines and benzimidazoles from their respective cations (R⁺) as an essential step towards their potential utilization as catalysts. We achieved quantitative hydride regeneration by improving the stability of acridine-based radicals and by facilitating the protonation of benzimidazole-based radicals. This work also provides guiding principles for improving the photochemical regeneration of organic hydrides mediated by inorganic semiconductors that act as hole acceptors.³¹⁸⁻³¹⁹

4.2 Computational Details

Density functional theory calculations were performed based on the wB97XD functional^{263, 320} and the triple-zeta basis set 6-311+G(d,p)³²¹ implemented in Gaussian '16. Vibrational force constants at the wB97XD/6-311+G(d,p) level of theory were calculated to (a) validate that all geometries have only positive vibrational frequencies and (b) compute entropies, zero-point energies, and thermal corrections for the reported free energies at 298 K. Solvation effects of dimethyl sulfoxide (DMSO) were simulated using an implicit polarized continuum solvation model (CPCM).³²²⁻³²³ Hydricity values were calculated using methods developed in earlier studies.³¹³

Reduction Potential (E^0) *Calculations.* Reduction potentials E^0 versus the ferrocene electrode (vs. Fc/Fc⁺) in DMSO were calculated using the wB97XD/6-311+G(d,p) level theory according to the following equation:³²⁴

$$\Delta G_{red} = G_{RH} - G_{RH^+} \tag{9}$$

$$E^0 = -27.2114 \,\Delta G_{red} - 5.043 \,V \tag{10}$$

Acidity (pK_a) Calculations. Acidity values are essential to this work as they help determine the reaction route. pK_a values are calculated according to the following equation, following the work of Schlegel:³²⁵

$$pK_a = \frac{\Delta G}{2.303RT} \tag{11}$$

$$\Delta G = G_{A^{-}} - G_{AH} + G_{H^{+}} \tag{12}$$

In order to determine the free energy of a proton solvated in DMSO, a scaling approach is utilized where the value of G_{H} + is averaged for a set of experimentally studied acids, presented in Table 9.

Table 9. Experimentally determined pKa values of organic acids in DMSO.³²⁶ The second column contains pKa values calculated using DFT calculations and using equations 3 and 4 shown above.

| | р <i>К</i> а | p <i>K</i> a | | p <i>K</i> a | р <i>К</i> а |
|-----------------|--------------|--------------|--------------------|--------------|--------------|
| | exp't | predicted | | exp't | predicted |
| benzimidazole | 16.4 | 18.4 | NH_4^+ | 10.5 | 4.3 |
| CH₄ | 56 | 50.8 | Nicotinamide | 22 | 22.6 |
| HCI | 1.8 | -0.8 | Trimethyldioxane- | 7.4 | 11.9 |
| | | | dione | | |
| Cyclopentadiene | 18 | 20.6 | PhCO₂H | 11 | 8.7 |
| imidazoleH | 18.6 | 20.0 | Ph ₂ NH | 24.95 | 27.6 |
| MeCO₂H | 12.3 | 13.5 | PhSH | 10.3 | 11.4 |
| MeOH | 29 | 30.5 | PyNH₂ | 28.5 | 26.3 |
| NaphthNOH | 20.7 | 20.1 | $C_5H_5NNH_2$ | 26.5 | 27.7 |
| NH ₃ | 41 | 41.2 | | | |

Plotting the DFT-calculated expression ($G_{A^-} - G_{AH}$) versus the pKa data in Table 9 yields Figure 17. The mean absolute deviation between experimentally determined and computationally predicted pKa values is 2.25 pKa units. Using the expression ($G_{H^+} = -$

intercept/slope), we find that the free energy of the DMSO-solvated proton is $G_{H+} = -265.49$ kcal/mol.



 $G_{AH} - G_{A-}$

Figure 17. $(G_{A^-} - G_{AH})$ computed using wB97XD/6-311+G(d,p) level of theory versus experimentally determined pKa values reported in Table 9. Black round dots represent the experimental data set. The black dashed line is the linear regression performed on the experimental data set, with an adjusted R²_{adj} value of 0.950. The red triangles represent pK_a values of radical cation intermediates discussed in this work.

4.3 Experimental Details

General Methods. All chemicals were purchased from commercial suppliers and used without further purification. 10-Methyl-9-phenylacridinium perchlorate (A_2^+) and 10-methylacridinium perchlorate (A_1^+) were purchased from TCI America. Cations (A_6^+ ,³²⁷ A_3^+ ,³¹⁸ A_4^+ ,³¹⁸ A_5^+ ,³¹⁸ B_1^+ ,³²⁸ B_2^+ ,³¹⁸ B_3^+ ,³²⁸ B_4^+ ,³²⁹ B_5^{+330} and B_8^{+331}) and hydrides (A_2H ,³¹⁸ A_4H ,³¹⁸ B_1H ,³²⁸ B_2H ,³¹⁸ B_3H^{328} and B_5H^{330}) were synthesized according to the previously

published procedures. For cyclic voltammetry (CV) measurements, the iodide salt of NAD⁺ analogs was converted to perchlorate using a previously published procedure.²⁰⁴ Absorption spectra were measured with Ocean FX (Ocean Optics) spectrophotometer.

Choice of Solvent. DMSO was chosen as a solvent for experiments and calculations, due to good solubility of NAD⁺ analogues and CO₂, which is relevant for fuel-forming reduction catalysis. However, the high basicity of DMSO hinders the protonation of acridine-derivatives with strong acids (section 2B). Instead, these experiments were performed in acetonitrile.

Cyclic Voltammetry. Cyclic voltammetry was performed using a BASi epsilon potentiostat in a VC-2 voltammetry cell (Bioanalytical Systems) using a glassy carbon (3 mm diameter, MF-2012, Bioanalytical Systems), a nonaqueous Ag/Ag⁺ reference electrode (MF-2062, Bioanalytical Systems), and a platinum wire (MW-4130, Bioanalytical Systems) as a counter electrode. The spectroscopic grade solvents DMSO and MeCN and the electrolyte tetrabutylammonium perchlorate (TBAP) were purchased from Sigma-Aldrich and used as received. All cyclic voltammograms were obtained with the scan rate of 0.1 V/s. Electrochemical potentials were converted to vs. Fc/Fc⁺ by adding -37 mV to the experimental potentials.³³²

*Preparation of A*₂*-radical.* 50 mg of A_2^+ was dissolved in sufficient amount of deionized water (~10 mL) and 5 mL of diethyl ether was added. The solution was then purged with argon for 30 min and 20 mg of zinc was added to the mixture. The reaction was stirred for 30 min during which the deep red color was developed in the diethyl ether layer. The organic layer was extracted and washed with water. The prepared solution of A₂-radical was stable over 10 days under inert atmosphere.

4.4 Results and Discussion

In order to investigate the regeneration pathways for metal-free NADH-analogues and their applicability in electrochemical reductions of protons and CO₂, we calculated relevant hydricity values (ΔG_{H-}), reduction potentials (E⁰) and acidity constants in DMSO as solvent (Table 10). Our calculated ΔG_{H-} values indicate that benzimidazole hydrides act as strong hydride donors with hydricities that compete with noble-metal hydrides,³³³ whereas acridine hydrides have moderate reducing strengths, comparable to that of the NADH-cofactor.³¹⁴ However, the considerable hydride donor ability of benzoimidazoles is accompanied by a high energy cost for its regeneration due to the scaling relationship between $E^0(R^+/R^{\cdot})$ and ΔG_{H^-} .^{314, 316} Furthermore, their second reductions $E^0(R^+/R^-)$ often occur at potentials ~ 0.5 V more negative than their first reduction potenitals (Table 10). Here, we suggest utilizing PCETs to circumvent the scaling relationship by avoiding these high-energy intermediates. Another distinguishing characteristic between these two groups of hydrides is the remarkable difference in the acidity constants (pK_a) of their radical cationic intermediates (RH^{+}) that determine their regeneration pathways. We propose two distinct pathways for the electrochemical generation of organic hydrides: (a) sequential transfer of two electrons followed by a proton transfer (EEP) and (b) sequential electron-proton-electron (EPE) transfer. Our calculated pK_a values predict that all model compounds are reduced via the EEP pathway, while only the benzimidazoles can be reduced via EPE with a reasonable proton source. The computed acidity constants reported in Table 10 indicate the drastic difference in acidity values of the intermediates

of both classes. Indeed, this computational analysis corroborates our experimental findings discussed below.

Table 10. Model R-H compounds and their calculated acidities, reduction and hydride donor ability constants in DMSO as solvent.

| Hydride | pl RH⁺∙ | Ka RH | I R⁺/R∙ | E ⁰ (V cs Fc/F R·/R⁻ | [:] c⁺) RH⁺·/RH | ΔG_{H^-} | Hydride | pl RH+· | Ka RH | R⁺/R∙ | E ⁰ (V cs Fc/ R·/R ⁻ | ′Fc⁺) RH⁺·/RH | ΔG_{H^-} |
|---------------------|------------|-----------------|------------|------------------------------------|-----------------------------|------------------|---|------------|----------|-------|---|------------------|------------------|
| | -0.4 | 35.8 | -1.04 | -1.83 | 0.25 | 73.0 | B₁H CCT ^N N ^H | 15.2 | 63.9 | -2.56 | -3.38 | -0.52 | 47.0 |
| | -1.8 | 34.2 | -1.07 | -1.79 | 0.28 | 72.8 | | 12.4 | 48.2 | -2.30 | -2.53 | -0.44 | 48.6 |
| A ₃ H | -1.0 | 35.0 | -1.11 | -1.86 | 0.20 | 70.3 | B ₃ H (), ^{PhNMe₂} | 14.9 | 51.7 | -2.60 | -2.61 | -0.47 | 44.7 |
| A₄H | -3.4 | -3.4 34.0 -1.33 | -1.33 | -1.95 | 0.18 | 61.1 | B₄H | 13.6 | 53.8 | -2.70 | -2.81 | -0.45 | 41.7 |
| | | | | | | | B₅H | 15.4 | 50.0 | -2.66 | -2.55 | -0.54 | 45.2 |
| olio | -6.4 | 35.7 -1.80 | -1 80 | -2.15 | 0.28 | 46.9 | _{₿6} Ħ ᡘᡘᡘᢤ | 18.4 | 54.4 | -2.79 | -2.63 | -0.54 | 44.7 |
| A₅H ^{-N} € | | 00.1 | -1.00 | | | | B ₇ H [™] CÌL _N X ^H | 21.4 | 50.6 | -2.83 | -2.58 | -0.96 | 42.7 |
| | 1.7 | 41.0 | -1.44 | -2.21 | 0.01 | 61.5 | B ₈ H € ^N X ^{Ph(OMe)} ₃ | 16.3 | 54.1 | -2.70 | -2.81 | 0.01 | 41.9 |

The electrochemical behaviour of a representative acridine (A_2^+) in the absence of proton donors exhibits a reversible reduction peak at -0.97 V (vs. Fc/Fc⁺), which we assign to R⁺/R⁺ conversion based on its calculated E⁰_{R+/R} potentials (Figure 18, Inset 1). Similar reversible first-reduction properties have been observed for the acridine derivatives A_3^+ , A_4^+ and A_5^+ , which are less susceptible to dimerization due to functionalization at the 4-position, justifying the reversibility of the observed reduction.³⁰⁹ In contrast, unsubstituted A_1^+ and A_6^+ exhibit irreversible R⁺/R⁺ conversion due to radical dimerization, a behavior analogous to the natural NAD⁺-cofactor.³¹¹⁻³¹² Potentials associated with the second electron reduction (R⁺/R⁻) are shifted to significantly more negative values and exhibit quasi-reversible and irreversible characteristics. Such irreversible behavior is associated

with the protonation of the forming anion by the solvent, as confirmed by the appearance of the A₂H oxidation peak at +0.3 - 0.6 V (vs. Fc/Fc⁺) in the anodic scan (Figure 18a). Experiments with two acids of significantly different acidities were performed to investigate the electrochemical regeneration of acridine-based hydrides. In the presence of weak acids (i.e. acetic acid, $pK_{a, calc} = 12.7$, DMSO), a modest shift in the second reduction potential of +0.2 V was observed (Figure 18a). This shift and the partial loss of reversibility displayed in the first reduction peak were assigned to facilitated protonation of the anion to form a hydride, indicating regeneration via EEP. This likely occurs via a stepwise mechanism, due to a lack of a kinetic isotope effect when deuterated acetic acid was used. However, the shift was not further improved with higher acid concentrations nor slightly stronger acids. In contrast, the addition of a very strong triflic acid ($pK_{a,calc}$ = -8.6, DMSO) resulted in a concomitant increase in the current density at the first reduction potential and the disappearance of the second reduction peak (Figure 18), suggesting that strong acids facilitate the EPE mechanism.³³⁴ The formation of the hydride via EPE was confirmed by switching the cathodic potential at -1.2 V and monitoring the presence of the hydride oxidation peak (Figure 18, Inset 2). The radical protonation was further confirmed using UV-Vis absorption spectra of chemically produced A_2 and its reaction with HBF₄ acid.



Figure 18. Cyclic voltammograms of: a) 2 mM A_2^+ in the presence of $0 \rightarrow 60$ eq AcOH in DMSO; b) 5 mM A_2^+ in the presence of $0 \rightarrow 1$ eq TfOH in MeCN; c) 2 mM B_3^+ in the presence of $0 \rightarrow 60$ eq AcOH in DMSO; d) 2 mM B_2^+ in the presence of 0-60 eq AcOH in DMSO. Arrows indicate the direction of peak changes with the addition of acid, while black dashed curves represent baseline scans.

Bulk electrolysis experiments of A_2^+ with acetic acid (which favors the EEP mechanism) and HBF₄ (which favors the EPE mechanism) both resulted in successful hydride regeneration of A_2H . A_2H regeneration using HBF₄ occurred at an applied potential of -1.2 V (vs. Fc/Fc⁺), while hydride formation using acetic acid required a more negative applied potential (-2.0 V vs. Fc/Fc⁺). Nevertheless, both routes yielded a quantitative hydride recovery due to the successful protonation of the radical (EPE route) and its high stability under anaerobic conditions (EEP route).



Figure 19. a) NMR spectra in DMSO-d₆ for catholyte before and after electrolysis of A_2^+ in the presence of AcOH, at applied potential of -2.0 V vs. Fc/Fc⁺. b) Comparison of catholyte solution before and after electrolysis with the authentic samples for A_2^+ and A_2 H.



Figure 20. a) NMR spectra in MeCN-d₃ for catholyte before and after electrolysis of A_2^+ in the presence of HBF₄, at applied potential of -1.2 V vs. Fc/Fc⁺. b) Comparison of catholyte solution before and after electrolysis with the authentic samples for A_2^+ and A_2H .

Cyclic voltammograms of benzimidazole-based derivatives B_3^+ and B_2^+ (Figure 18c and 18d) display irreversible peaks at the potentials predicted for the first electron reduction R^+/R_{\cdot} , as indicated in Table 10. The irreversibility of the first reduction peaks is caused by the tendency of unstable benzimidazole radicals to dimerize, as confirmed by the appearance of oxidation peaks in the reverse scan at potentials that match the calculated potentials of dimers ($-0.84 \text{ V vs. Fc/Fc}^+$ for B_3^+). The addition of acetic acid to B_3^+ prevents undesired dimerization, as indicated by the disappearance of the dimer oxidation peak at $-0.84 \text{ V vs. Fc/Fc}^+$ (Inset 3). Hydride B_3H is now indicated by the new peak at $-0.34 \text{ V vs. Fc/Fc}^+$ (Inset 3). Hydride formation was further confirmed with controlled-potential electrolysis, where B_3H was observed by NMR as the sole product. The protonation of B_2^+ , (and further hydride regeneration) was achieved only in the presence of a large excess of the acid which is consistent with the lower calculated acidity for for B_2H^+ .

The mechanism of hydride regeneration in benzimidazoles was investigated using compounds B_4H and B_8H with bulky substituents to impede radical dimerization. In the absence of a proton source, the cyclic voltammogram of B_8^+ exhibits electrochemical properties similar to those of the stable acridines with two well-separated reduction peaks. In contrast, upon addition of acetic acid the current density at the first reduction potential increases and the current density at the second reduction potential decreases, indicating a shift from the EEP to the EPE route. The EPE process presumably occurs via a stepwise mechanism consistent with the absence of a kinetic isotope effect when deuterated acetic acid is used (Figure 21). The stepwise mechanism likely results from the low tendency of carbon-based radicals to form hydrogen bonds. This behavior is unlike that observed in

nitrogen- and oxygen-based radicals, where hydrogen bonding occurs to pre-associate proton donors and acceptors and to facilitate the concerted reduction of flavins and quinones/phenols.^{297-300, 335-336}



Figure 21. Cyclic voltammograms of B_8^+ in the presence of: a) acetic acid, AcOH; b) d-acetic acid, AcOD.

Lastly, we address why benzimidazole radicals are drastically more reactive towards protons than acridines, although they are seemingly structurally similar (i.e. both are N-heterocyclic species). Electron-donating substituents decrease the acidity of radical cations,³¹⁵ as Table 10 indicates. However, the sensitivity of acidity to functionalization for both classes is limited to a few pK_a units. Various acridine-based radicals were only protonated by very strong acids, indicating that the radical cation remains extremely acidic regardless of functionalization. The large difference in the acidities of radical cations can be attributed to the stability of the radicals (Figure 22), where cyclopentyl radicals (benzimidazoles) are more destabilized by ring strain relative to cyclohexyl radicals

(acridines).³³⁷ This is further supported by our calculated 'strain energies' of two representative derivatives.³³⁸ Protonation of the singly-reduced radical intermediates R· of both classes requires reorganization of the molecular structure, as indicated by the angular differences between R· and RH⁺ (see Figure 22). Acridine-based compounds undergo a more pronounced structural relaxation upon protonation, whereas the reorganization associated with protonating benzimidazole radicals is minimal. The energy penalty of straining the geometry of the radical species is ~17 kcal/mol for the acridine derivative A₅· but only ~8 kcal/mol for the benzimidazole intermediate B₃·, indicating that protonation of acridine derivatives requires a larger driving force.



Figure 22. EEP and EPE reaction coordinate diagram for B_3H (blue, benzimidazole) and A_5H (green, acridine). B_3 .^{/H+} and A_5 .^{/H+} structures with angles below to show geometric changes.

The computed energy profiles for the regeneration of two representative hydrides with similar hydricities (A₅H and B₃H, $\Delta G_{H_2} = \sim 45-47$ kcal/mol, Table 10) reveals several

key principles for their electrochemical conversions (Figure 22). First, as evident from Figure 22 and supported by our experimental findings, acridines prefer the EEP route unless coupled with very strong acids (pKa << 0, DMSO). In contrast, benzimidazoles proceed facilely via the EPE path even with relatively weak acids. Second, the regeneration of both classes of hydrides necessitates an overpotential for their successful transformation. The "ideal" system would operate at the thermodynamic potential (-1.3 V vs. Fc/Fc^+),^{339,340} while the required applied potential (E_{app}) for generation of both representatives is slightly more negative. Specifically, the generation of A₅H is determined by $E^{0}_{R'/R}$ - due to the difficult radical protonation ($E_{app} = -2.4 \text{ V vs Fc/Fc}^{+}$), whereas B₃H is generated at $E^{0}_{R^{+}/R^{+}}$ with an appropriate proton donor ($E_{app} = -2.3 \text{ V vs Fc/Fc}^{+}$). We emphasize that the overpotential is not affected by the basicity of the radical species. Instead, it only depends on the first reduction potential $(E_{app} = E_{R+/R}^0)$ for benzimidazoles because they follow the EPE route, and the second reduction potential $(E_{app} = E^0_{R'/R-})$ for acridines, as they favour the EEP route. This outcome indicates that the structural factors that facilitate the radical protonation of benzimidazoles – as defined by $pK_a(RH^+)$ - also impede the first reduction process, as defined by $E^{0}_{R+/R}$, leading to an overall compensating effect on the thermodynamics of hydride generation (Figure 23).



Figure 23. Acidity constant for RH^+ , $pK_a(RH^+)$, as a function of $E^{0}_{R^+/R^+}$ for benzimidazoles.

While the mechanisms have no effect on the overall reaction free energy to generate the hydrides, we suggest that the EEP and EPE routes likely exhibit different kinetics. This is also true for the kinetics of undesirable side reactions, especially for those that involve the intermediates produced by the two mechanisms. Exploiting the differences in the kinetics of the two mechanisms can be highly advantageous. For example, the dimerization of open-shell radicals R· formed by the first electron transfer significantly lowers the efficiency of hydride regeneration via EEP mechanisms. However, rapid protonation of R· lowers its concentration and consequently the rate of the bimolecular dimerization reaction with $r_{dim} \propto [R \cdot]^2$. Indeed, our experiments clearly demonstrate that the EPE mechanism where protonation of the radical successfully outcompetes dimerization enables quantitative hydride recovery. Thus, the EPE

mechanism is likely more suitable for catalytic systems that involve reductions by organic hydrides.

4.4 Conclusions

To conclude, the experiments and calculations in this work support our hypothesis that the acidity of the radical cation (RH^+ ·) of organic hydrides is critical for determining the pathway of electrochemical hydride generation. A detailed analysis of the factors that determine radical stability (and correspondingly its basicity) demonstrates how structural modification can tune the hydride regeneration mechanism. In contrast, the different hydride generation pathways (EEP vs. EPE) do not affect the overall potential required for the complete regeneration, due to the opposing effects that radical stability plays on electrochemical potentials and pK_a values. Thus, despite its identical thermodynamic requirements, the EPE mechanism observed in benzimidazoles is likely more efficient due to the suppression of undesired radical dimerization. This work provides the groundwork for a more effective use of organic hydrides as catalyts.

Chapter 5. General Conclusions and Future Outlook

The apparent advantages of metal-based catalysts in energy conversion catalysis are overshadowed by their often low selectivity, poor sustainability, and high toxicity. Our approach is to utilize metal-free hydride donors NADH analogs as promising cost-effective replacements for selective CO₂ reduction, where the selectivity is achieved via sequence of hydride and proton transfers. In this work, the focus is on designing NADH analogs that can be applied in electrocatalysis.

The design of molecular catalyst for electrochemical CO2RR include tuning the hydricity for favorable hydride transfer to CO_2 and enabling an easy electrochemical regeneration of the active hydride form. A detailed analysis of a large number of metal-free hydride donors helped identifying structural and electronic features that contribute to better hydride donor ability. After evaluating their thermodynamic and kinetic hydricities, benzimidazoles have been recognized as promising candidates for selective CO_2 reduction. In our preliminary study, we have showed that benzimidazole-based hydrides are indeed capable of reducing CO_2 selectively to formate. In addition, the corresponding oxidized benzimidazolium forms (NAD⁺ analogs) are fully recovered upon the completion of the reaction, establishing their applicability in catalytic processes.

The regeneration of the NADH-form is very important for the closure of the catalytic cycle. Previous efforts on utilizing organic hydrides in catalysis have been hindered due to the rapid dimerization of radicals produced as the first intermediates of the electrochemical transformations. Our study in Chapter 4 showed that this side reaction can be circumvented with protonation that occurs on a much shorter timescale. In fact,

the proton coupled electron reductions enabled quantitative NADH regenerations from their corresponding oxidized NAD⁺ analogs. The principles that govern electrochemical transformations can serve as a groundwork for photoelectrochemical cells, where the choice of semiconductor with appropriate conduction band plays a pivotal role in reduction of NAD⁺ analogs.³¹⁸⁻³¹⁹

Collectively, preliminary results discussed in this thesis provide insights on the possibility of utilizing organic catalysts for selective CO₂ reduction. Nonetheless, several critical problems for eventual catalytic applications persist: (1) slow kinetics for hydride transfer reactions, and (2) large overpotentials for hydride regeneration. The slow hydride transfer rates for hydride transfer are associated with high kinetic barriers (> 20 kcal/mol, Table 7). We previously stated that the kinetics for these reactions linearly depend on the driving force (Chapter 2, section 2.4d). Improvement of the thermodynamics for hydride transfer to CO₂ can be achieved using few different strategies. First, we propose that the hydride transfer can be facilitated by increasing the hydride affinity of CO₂, which can be achieved with activators as cocatalysts (Scheme 9). The proposed activator B reversibly binds CO₂ to form an adduct B-CO₂ that is easier to reduce than the unbound CO₂. To make B-CO₂ more prone to reduction, the free energy for adduct formation should be slightly endergenic ($\Delta G_{act} > 0$, Scheme 9). Such activators, usually organic bases, have been reported previously.³⁴¹⁻³⁴² Few examples of the activators along with their calculated adduct formation free energies ΔG_{act} are shown in Scheme 9.

Scheme 9. Activation of CO₂ for hydride transfer reaction with organic bases. The adduct formation (activation) is a slightly unfavorable process (ΔG_{act}) which makes the hydride transfer to the adduct more favorable ($\Delta G_{aHT} = \Delta G_{dHT} - \Delta G_{act}$). Also shown, few activator structures and some calculated adduct formation ΔG_{act} .



Another approach includes the tuning of the thermodynamic hydricity in order to make stronger hydride donors. In Chapter 2, we identified structural factors that contribute to the improved hydride donor ability, such as stabilization of the positive charge of NAD⁺ through an inductive effect or increased conjugation, and destabilization of the NADH-form by anomeric effect or structural constrains. Exploiting these factors would result in strong hydride donors capable of reducing CO₂ at reasonable rates. Scheme 9 shows several proposed structures of new metal-free hydrides with their calculated ΔG_{H-} values that can serve in futures studies. Instalment of methyl groups on two of the best hydrides from Chapter 4 resulted in improvement of hydricity by ~2 kcal/mol, presumably through the inductive effect of methyl groups (5a and 5b in Scheme 9). Hydrides 5c,³⁴³ 5d and 5e are results of blending of two effects that contributed the most to the hydride donor ability:

anomeric effect and structural constrains. These constrained benzimidazoles display drastically lower calculated hydricity values (well below 44 kcal/mol). Hydrides 5f³⁴⁴ and 5g³⁴⁵ are derived from previously published oxidized NAD⁺ forms, while 5h represents a phosphorus-based hydride with fairly good hydride donor ability and high nucleophilicity.³⁴⁶



Scheme 9. New generation of metal-free hydride donors.

Having strong hydrides would certainly help hydride transfer rates, but the hydricity is closely correlated to the reduction potentials for the catalyst regenerations: stronger NADH hydride donors require larger overpotentials for successful electrochemical regeneration from NAD⁺, as shown in Figure 11 (section 2.5a in Chapter 2). In natural systems (O-H and N-H hydrides),^{297-300, 335-336} large overpotentials are avoided with a concerted PCET mechanism, that is facilitated by the pre-association of hydrogen-bonded proton donor and organic radical.³⁴⁷ Unfortunately, we observed only sequential PCET reactions in our studies in Chapter 4, likely due to the fact that carbon-based hydrides do not form hydrogen bonds. In addition to promising thermodynamic and kinetic

hydricities, phosphorus-based hydrides may be good candidates for concerted PCET processes, given that phosphorus compounds have been recently reported to form hydrogen bonds with alcohols.³⁴⁸ Alternatively, the overpotentials can be considerably improved by introducing a 'proton handle' in close proximity to the active center. This strategy has been utilized to improve both overpotentials and kinetics for metal complexes (Chapter 1). Scheme 10 shows proposed structural design of NAD⁺ for the new hydride donors that contain a prepositioned 'proton handle'.

Scheme 10. New generation of NAD⁺ bearing prepositioned 'proton handles' as a strategy to lower the overpotential for hydride regenerations.



With further improvements of metal-free hydrides, we anticipate the realization of a completely metal-free catalytic system for CO₂ reduction. Once a fully operational molecular catalyst is developed, these systems could serve as replacements for metal-based electrocatalyst and may be applicable and scalable for industrial applications.

Cited Literature

1. Ishida, H.; Tanaka, K.; Tanaka, T., Electrochemical CO₂ Reduction Catalyzed by Ruthenium Complexes $[Ru(bpy)_2(CO)_2]^{2+}$ And $[Ru(bpy)_2(CO)CI]^+$. Effect of pH on the Formation of CO and HCOO. *Organometallics* **1987**, *6* (1), 181-186.

2. Pugh, J. R.; Bruce, M. R.; Sullivan, B. P.; Meyer, T. J., Formation of a Metal-Hydride Bond and the Insertion of Carbon Dioxide. Key Steps in the Electrocatalytic Reduction of Carbon Dioxide to Formate Anion. *Inorg. Chem.* **1991**, *30* (1), 86-91.

3. Sullivan, B. P.; Bolinger, C. M.; Conrad, D.; Vining, W. J.; Meyer, T. J., One-and Two-Electron Pathways in the Electrocatalytic Reduction Of CO₂ by fac-Re(bpy)(CO)₃Cl (bpy= 2, 2'-Bipyridine). *J. Chem. Soc.* **1985**, (20), 1414-1416.

4. Keith, J. A.; Grice, K. A.; Kubiak, C. P.; Carter, E. A., Elucidation of the Selectivity of Proton-Dependent Electrocatalytic CO₂ Reduction by fac-Re(bpy)(CO)₃Cl. *J. Am. Chem. Soc.* **2013**, *135* (42), 15823-15829.

5. Riplinger, C.; Sampson, M. D.; Ritzmann, A. M.; Kubiak, C. P.; Carter, E. A., Mechanistic Contrasts between Manganese and Rhenium Bipyridine Electrocatalysts for the Reduction of Carbon Dioxide. *J. Am. Chem. Soc.* **2014**, *136* (46), 16285-16298.

6. Ngo, K. T.; Mckinnon, M.; Mahanti, B.; Narayanan, R.; Grills, D. C.; Ertem, M. Z.; Rochford, J., Turning on the Protonation-First Pathway for Electrocatalytic CO₂ Reduction by Manganese Bipyridyl Tricarbonyl Complexes. *J. Am. Chem. Soc.* **2017**, *139* (7), 2604-2618.

7. Costentin, C.; Drouet, S.; Passard, G.; Robert, M.; Savéant, J.-M., Proton-Coupled Electron Transfer Cleavage of Heavy-Atom Bonds in Electrocatalytic Processes.

Cleavage of a C–O Bond in the Catalyzed Electrochemical Reduction of CO₂. *J. Am. Chem. Soc.* **2013**, *135* (24), 9023-9031.

8. Azcarate, I.; Costentin, C.; Robert, M.; Savéant, J.-M., Through-Space Charge Interaction Substituent Effects in Molecular Catalysis Leading to the Design of the Most Efficient Catalyst of CO₂-to-CO Electrochemical Conversion. *J. Am. Chem. Soc.* **2016**, *138* (51), 16639-16644.

9. Kang, P.; Meyer, T. J.; Brookhart, M., Selective Electrocatalytic Reduction of Carbon Dioxide to Formate by a Water-Soluble Iridium Pincer Catalyst. *Chem. Sci.* **2013**, *4* (9), 3497-3502.

10. Lee, C.; Yang, W.; Parr, R. G., Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev B* **1988**, *37* (2), 785.

11. Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H., Results Obtained with the Correlation Energy Density Functionals of Becke And Lee, Yang And Parr. *Chem. Phys. Lett.* **1989**, *157* (3), 200-206.

12. Dunning Jr, T. H.; Hay, P. J., Gaussian Basis Sets for Molecular Calculations. In *Methods Of Electronic Structure Theory*, Springer: 1977; Pp 1-27.

13. Mclean, A.; Chandler, G., Contracted Gaussian Basis Sets for Molecular Calculations. I. Second Row Atoms, Z= 11–18. *J. Chem. Phys.* **1980**, *72* (10), 5639-5648.

Frisch, M. J.; Pople, J. A.; Binkley, J. S., Self-Consistent Molecular Orbital Methods
 Supplementary Functions for Gaussian Basis Sets. *J. Chem. Phys.* **1984**, *80* (7),
 3265-3269.

15. Cossi, M.; Rega, N.; Scalmani, G.; Barone, V., Energies, Structures, And Electronic Properties of Molecules in Solution with the C-PCM Solvation Model. *J. Comput. Chem.* **2003**, *24* (6), 669-681.

16. Montgomery, D. C.; Runger, G. C., *Applied Statistics And Probability For Engineers*. John Wiley & Sons: 2010.

17. O'Leary, M. H.; Jaworski, R. J.; Hartman, F. C., ¹³C Nuclear Magnetic Resonance Study of the CO₂ Activation of Ribulosebisphosphate Carboxylase from Rhodospirillum Rubrum. *PNAS* **1979**, *76* (2), 673-675.

18. Brown, H. C.; Kim, S.; Krishnamurthy, S., Selective Reductions. 26. Lithium Triethylborohydride as an Exceptionally Powerful and Selective Reducing Agent in Organic Synthesis. Exploration of the Reactions with Selected Organic Compounds Containing Representative Functional Groups. *J. Org. Chem.* **1980**, *45* (1), 1-12.

19. Visser, C. M., Evolutionary Roots of Catalysis by Nicotinamide and Flavins in CH Oxidoreductases and in Photosynthesis. *Orig. Life Evol. Biospheres* **1982**, *12* (2), 165-179.

20. Walsh, C., Naturally Occurring 5-Deazaflavin Coenzymes: Biological Redox Roles. *Acc. Chem. Res* **1986**, *19* (7), 216-221.

21. Li, R.; Bianchet, M. A.; Talalay, P.; Amzel, L. M., The Three-Dimensional Structure of NAD(P)H: Quinone Reductase, a Flavoprotein Involved in Cancer Chemoprotection and Chemotherapy: Mechanism of the Two-Electron Reduction. *PNAS* **1995**, *92* (19), 8846-8850.

22. L Larson, G.; L Fry, J., *Ionic and Organometallic-Catalyzed Organosilane Reductions*. Wiley Online Library: 2008.

 Burck, S.; Gudat, D.; Nieger, M.; Du Mont, W.-W., P-Hydrogen-Substituted 1,3,2-Diazaphospholenes: Molecular Hydrides. *J. Am. Chem. Soc.* 2006, *128* (12), 3946-3955.
 Quane, D.; Bottei, R. S., Organogermanium Chemistry. *Chem. Rev.* 1963, *63* (4), 403-442.

25. Osuka, A.; Shimizu, H.; Suzuki, H., Reduction of Aromatic and Aliphatic Nitro Compounds by Sodium Hydrogen Telluride. *Chem. Lett.* **1983**, *12* (9), 1373-1374.

26. Pachauri, R. K.; Allen, M. R.; Barros, V. R.; Broome, J.; Cramer, W.; Christ, R.; Church, J. A.; Clarke, L.; Dahe, Q.; Dasgupta, P., *Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II And III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. IPCC: 2014.

27. Monastersky, R., Global Carbon Dioxide Levels near Worrisome Milestone. *Nature News* **2013**, *4*97 (7447), 13.

28. Olah, G. A.; Prakash, G. S.; Goeppert, A., Anthropogenic Chemical Carbon Cycle for a Sustainable Future. *J. Am. Chem. Soc.* **2011**, *133* (33), 12881-12898.

29. Olah, G. A.; Goeppert, A.; Prakash, G. S., Chemical Recycling of Carbon Dioxide to Methanol and Dimethyl Ether: From Greenhouse Gas to Renewable, Environmentally Carbon Neutral Fuels and Synthetic Hydrocarbons. *J. Org. Chem.* **2008**, *74* (2), 487-498.

30. Singh, M. R.; Clark, E. L.; Bell, A. T., Thermodynamic and Achievable Efficiencies for Solar-Driven Electrochemical Reduction of Carbon Dioxide to Transportation Fuels. *PNAS* **2015**, *112* (45), E6111-E6118.

31. Bossel, U., The Physics of the Hydrogen Economy. *European Fuel Cell News* **2003**, *10* (2), 1-16.

32. Li, W.; Wang, H.; Jiang, X.; Zhu, J.; Liu, Z.; Guo, X.; Song, C., A Short Review of Recent Advances in CO₂ Hydrogenation to Hydrocarbons over Heterogeneous Catalysts. *RSC Adv.* **2018**, *8* (14), 7651-7669.

33. Windle, C. D.; Perutz, R. N., Advances in Molecular Photocatalytic and Electrocatalytic CO₂ Reduction. *Coord. Chem. Rev.* **2012**, *256* (21-22), 2562-2570.

34. Sakakura, T.; Choi, J.-C.; Yasuda, H., Transformation of Carbon Dioxide. *Chem. Rev.* **2007**, *107* (6), 2365-2387.

35. Sultana, S.; Sahoo, P. C.; Martha, S.; Parida, K., A Review of Harvesting Clean Fuels from Enzymatic CO₂ Reduction. *RSC Adv.* **2016**, *6* (50), 44170-44194.

36. Cook, T. R.; Dogutan, D. K.; Reece, S. Y.; Surendranath, Y.; Teets, T. S.; Nocera,
D. G., Solar Energy Supply and Storage for the Legacy and Nonlegacy Worlds. *Chem. Rev.* 2010, *110* (11), 6474-6502.

37. Qiao, J.; Liu, Y.; Hong, F.; Zhang, J., A Review of Catalysts for the Electroreduction of Carbon Dioxide to Produce Low-Carbon Fuels. *Chem. Soc. Rev.* **2014**, *43* (2), 631-675.

38. Costentin, C.; Robert, M.; Savéant, J.-M., Catalysis of the Electrochemical Reduction of Carbon Dioxide. *Chem. Soc. Rev.* **2013**, *42* (6), 2423-2436.

39. Francke, R.; Schille, B.; Roemelt, M., Homogeneously Catalyzed Electroreduction of Carbon Dioxide—Methods, Mechanisms, and Catalysts. *Chem. Rev.* **2018**, *118* (9), 4631-4701.

40. Savéant, J.-M., Molecular Catalysis of Electrochemical Reactions. Mechanistic Aspects. *Chem. Rev.* **2008**, *108* (7), 2348-2378.

41. Zhao, G.; Huang, X.; Wang, X.; Wang, X., Progress in Catalyst Exploration for Heterogeneous CO₂ Reduction and Utilization: A Critical Review. *J. Mater. Chem. A* **2017**, *5* (41), 21625-21649.

42. Elouarzaki, K.; Kannan, V.; Jose, V.; Sabharwal, H. S.; Lee, J. M., Recent Trends, Benchmarking, and Challenges of Electrochemical Reduction of CO₂ by Molecular Catalysts. *Adv. Energy Mater.* **2019**, 1900090.

43. Elgrishi, N.; Chambers, M. B.; Wang, X.; Fontecave, M., Molecular Polypyridine-Based Metal Complexes as Catalysts for the Reduction of CO₂. *Chem. Soc. Rev.* **2017**, *46* (3), 761-796.

44. Waldie, K. M.; Ostericher, A. L.; Reineke, M. H.; Sasayama, A. F.; Kubiak, C. P., Hydricity of Transition-Metal Hydrides: Thermodynamic Considerations for CO₂ Reduction. *ACS Catal.* **2018**, *8* (2), 1313-1324.

45. Pavlishchuk, V. V.; Addison, A. W., Conversion Constants for Redox Potentials Measured versus Different Reference Electrodes in Acetonitrile Solutions at 25 °C. *Inorganica Chim. Acta* **2000**, 298 (1), 97-102.

46. Iffland, L.; Khedkar, A.; Petuker, A.; Lieb, M.; Wittkamp, F.; Van Gastel, M.; Roemelt, M.; Apfel, U.-P., Solvent-Controlled CO₂ Reduction by a Triphos–Iron Hydride Complex. *Organometallics* **2019**, *38* (2), 289-299.

47. Ishida, H.; Tanaka, K.; Tanaka, T., The Electrochemical Reduction of CO₂ Catalyzed by Ruthenium Carbonyl Complexes. *Chem. Lett.* **1985**, *14* (3), 405-406.

48. Ishida, H.; Tanaka, H.; Tanaka, K.; Tanaka, T., Selective Formation of HCOO⁻ in the Electrochemical CO₂ Reduction Catalysed by [Ru(bpy)₂(CO)₂]²⁺ (bpy= 2, 2'-Bipyridine). *J. Chem. Soc.* **1987**, (2), 131-132.

49. Chen, Z.; Chen, C.; Weinberg, D. R.; Kang, P.; Concepcion, J. J.; Harrison, D. P.; Brookhart, M. S.; Meyer, T. J., Electrocatalytic Reduction of CO₂ to CO by Polypyridyl Ruthenium Complexes. *Chem. Comm.* **2011**, *47* (47), 12607-12609.

50. Collomb-Dunand-Sauthier, M.-N.; Deronzier, A.; Ziessel, R., Electrocatalytic Reduction of Carbon Dioxide with Mono-(bipyridine)-carbonylruthenium Complexes in Solution or as Polymeric Thin Flms. *Inorg. Chem.* **1994**, *33* (13), 2961-2967.

51. Chardon-Noblat, S.; Collomb-Dunand-Sauthier, M.-N.; Deronzier, A.; Ziessel, R.; Zsoldos, D., Formation of Polymeric [{Ru⁰(bpy)(CO)₂}N] Films by Electrochemical Reduction of [Ru(bpy)₂(CO)₂](PF₆)₂: Its Implication in CO₂ Electrocatalytic Reduction. *Inorg. Chem.* **1994**, 33 (19), 4410-4412.

52. White, T. A.; Maji, S.; Ott, S., Mechanistic Insights into Electrocatalytic CO₂ Reduction within [Ru^{II}(Tpy)(NN)X]N⁺ Architectures. *Dalton Trans.* **2014**, *43* (40), 15028-15037.

53. Johnson, B. A.; Maji, S.; Agarwala, H.; White, T. A.; Mijangos, E.; Ott, S., Activating a Low Overpotential CO₂ Reduction Mechanism by a Strategic Ligand Modification on a Ruthenium Polypyridyl Catalyst. *Angew. Chem. Int. Ed. Engl.* **2016**, *55* (5), 1825-1829.

54. Gonell, S.; Massey, M. D.; Moseley, I. P.; Schauer, C. K.; Muckerman, J. T.; Miller, A. J., The Trans Effect in Electrocatalytic CO₂ Reduction: Mechanistic Studies of Asymmetric Ruthenium Pyridyl-Carbene Catalysts. *J. Am. Chem. Soc.* **2019**, *141* (16), 6658-6671.

55. Meser Ali, M., Selective Formation Of HCO_2^- and $C_2O_4^{2-}$ in Electrochemical Reduction of CO₂ Catalyzed by Mono- and Di-Nuclear Ruthenium Complexes. *Chem. Comm.* **1998**, (2), 249-250.

56. Machan, C. W.; Sampson, M. D.; Kubiak, C. P., A Molecular Ruthenium Electrocatalyst for the Reduction of Carbon Dioxide to CO and Formate. *J. Am. Chem. Soc.* **2015**, *137* (26), 8564-8571.

57. Hawecker, J.; Lehn, J.-M.; Ziessel, R., Electrocatalytic Reduction of Carbon Dioxide Mediated by Re(bipy)(CO)₃Cl (bipy= 2, 2'-bipyridine). *J. Chem. Soc.* **1984**, (6), 328-330.

58. Johnson, F. P.; George, M. W.; Hartl, F.; Turner, J. J., Electrocatalytic Reduction of CO₂ using the Complexes [Re(bpy)(CO)₃L]^N (N=+ 1, L= P(OEt)₃, CH₃CN; N= 0, L= Cl-, OTf-; bpy= 2,2'-bipyridine; OTf-= CF₃SO₃) as Catalyst Precursors: Infrared Spectroelectrochemical Investigation. *Organometallics* **1996**, *15* (15), 3374-3387.

59. Benson, E. E.; Kubiak, C. P., Structural Investigations into the Deactivation Pathway of the CO₂ Reduction Electrocatalyst Re(bpy)(CO)₃Cl. *Chem. Comm.* **2012**, *48* (59), 7374-7376.

60. Meister, S.; Reithmeier, R. O.; Tschurl, M.; Heiz, U.; Rieger, B., Unraveling Side Reactions in the Photocatalytic Reduction of CO₂: Evidence for Light-Induced Deactivation Processes in Homogeneous Photocatalysis. *Chem. Cat. Chem.* **2015**, *7* (4), 690-697.

61. Smieja, J. M.; Kubiak, C. P., Re(bipy-tBu)(CO)₃Cl⁻ Improved Catalytic Activity for Reduction of Carbon Dioxide: IR-Spectroelectrochemical and Mechanistic Studies. *Inorg. Chem.* **2010**, *49* (20), 9283-9289.

Bourrez, M.; Molton, F.; Chardon-Noblat, S.; Deronzier, A., [Mn(bipyridyl)(CO)₃Br]:
 An Abundant Metal Carbonyl Complex as Efficient Electrocatalyst for CO₂ Reduction.
 Angew. Chem. Int. Ed. Engl. 2011, 50 (42), 9903-9906.

63. Hartl, F.; Rossenaar, B. D.; Stor, G. J.; Stufkens, D. J., Role of an Electron-Transfer Chain Reaction in the Unusual Photochemical Formation of Five-Coordinated Anions [Mn (CO)₃(A-Diimine)][−] From fac-[Mn(X)(CO)₃(A-Diimine)](X= Halide) at Low Temperatures. *Recl. Trav. Chim. Pays-Bas* **1995**, *114* (11-12), 565-570.

64. Sampson, M. D.; Nguyen, A. D.; Grice, K. A.; Moore, C. E.; Rheingold, A. L.; Kubiak, C. P., Manganese Catalysts with Bulky Bipyridine Ligands for the Electrocatalytic Reduction of Carbon Dioxide: Eliminating Dimerization and Altering Catalysis. *J. Am. Chem. Soc.* **2014**, *136* (14), 5460-5471.

65. Hammouche, M.; Lexa, D.; Savéant, J.; Momenteau, M., Catalysis of the Electrochemical Reduction of Carbon Dioxide by Iron ("0") Porphyrins. *J. Electroanal. Chem.* **1988**, *249* (1-2), 347-351.

66. Bhugun, I.; Lexa, D.; Savéant, J.-M., Catalysis of the Electrochemical Reduction of Carbon Dioxide by Iron(0) Porphyrins. Synergistic Effect of Lewis Acid Cations. *J. Phys. Chem.* **1996**, *100* (51), 19981-19985.

67. Costentin, C.; Robert, M.; Savéant, J.-M., Current Issues in Molecular Catalysis Illustrated by Iron Porphyrins as Catalysts of the CO₂-to-CO Electrochemical Conversion. *Acc. Chem. Res* **2015**, *48* (12), 2996-3006.

68. Hammouche, M.; Lexa, D.; Momenteau, M.; Saveant, J. M., Chemical Catalysis of Electrochemical Reactions. Homogeneous Catalysis of the Electrochemical Reduction of Carbon Dioxide by Iron("0") Porphyrins. Role of the Addition of Magnesium Cations. *J. Am. Chem. Soc.* **1991**, *113* (22), 8455-8466.

69. Bhugun, I.; Lexa, D.; Savéant, J.-M., Catalysis of the Electrochemical Reduction of Carbon Dioxide by Iron(0) Porphyrins: Synergystic Effect of Weak Brönsted Acids. *J. Am. Chem. Soc.* **1996**, *118* (7), 1769-1776.

70. Bhugun, I.; Lexa, D.; Saveant, J.-M., Ultraefficient Selective Homogeneous Catalysis of the Electrochemical Reduction of Carbon Dioxide by an Iron(0) Porphyrin Associated with a Weak Broensted Acid Cocatalyst. *J. Am. Chem. Soc.* **1994**, *116* (11), 5015-5016.

71. Costentin, C.; Drouet, S.; Robert, M.; Savéant, J.-M., A Local Proton Source Enhances CO₂ Electroreduction to CO by a Molecular Fe Catalyst. *Science* **2012**, *338* (6103), 90-94.

72. Costentin, C.; Passard, G.; Robert, M.; Savéant, J.-M., Pendant Acid–Base Groups in Molecular Catalysts: H-Bond Promoters or Proton Relays? Mechanisms of the Conversion of CO₂ to CO by Electrogenerated Iron(0) Porphyrins Bearing Prepositioned Phenol Functionalities. *J. Am. Chem. Soc.* **2014**, *136* (33), 11821-11829.

73. Azcarate, I.; Costentin, C.; Robert, M.; Savéant, J.-M., Dissection of Electronic Substituent Effects in Multielectron–Multistep Molecular Catalysis. Electrochemical CO₂-to-CO Conversion Catalyzed by Iron Porphyrins. *J. Phys. Chem. C* **2016**, *120* (51), 28951-28960.

74. Bolinger, C. M.; Story, N.; Sullivan, B. P.; Meyer, T. J., Electrocatalytic Reduction of Carbon Dioxide by 2,2'-bipyridine Complexes of Rhodium and Iridium. *Inorg. Chem.* **1988**, 27 (25), 4582-4587.

75. Caix, C.; Chardon-Noblat, S.; Deronzier, A., Electrocatalytic Reduction of CO₂ into Formate with $[(H_5-Me_5C_5)M(L)CI]^+$ Complexes (L= 2,2'-bipyridine Ligands; M= Rh (III) and Ir (III)). *J. Of Electroanal. Chem.* **1997**, *434* (1-2), 163-170.

76. Ishida, H.; Tanaka, H.; Tanaka, K.; Tanaka, T., Selective Formation of HCOO⁻ in the Electrochemical CO₂ Reduction Catalysed by $[Ru(bpy)_2(CO)_2]^{2+}$ (bpy= 2,2'-bipyridine). *J. Chem. Soc.* **1987**, (2), 131-132.

77. Kang, P.; Cheng, C.; Chen, Z.; Schauer, C. K.; Meyer, T. J.; Brookhart, M., Selective Electrocatalytic Reduction of CO₂ to Formate by Water-Stable Iridium Dihydride Pincer Complexes. *J. Am. Chem. Soc.* **2012**, *134* (12), 5500-5503.

78. Taheri, A.; Berben, L. A., Tailoring Electrocatalysts for Selective CO₂ or H⁺ Reduction: Iron Carbonyl Clusters as a Case Study. *Inorg. Chem.* **2015**, *55* (2), 378-385.

79. Taheri, A.; Thompson, E. J.; Fettinger, J. C.; Berben, L. A., An Iron Electrocatalyst for Selective Reduction of CO₂ to Formate in Water: Including Thermochemical Insights. *ACS Catal.* **2015**, *5* (12), 7140-7151.

80. Rail, M. D.; Berben, L. A., Directing the Reactivity of [HFe₄N(CO)₁₂]⁻ toward H⁺ or
CO₂ Reduction by Understanding the Electrocatalytic Mechanism. *J. Am. Chem. Soc.* **2011**, *1*33 (46), 18577-18579.

81. Taheri, A.; Berben, L. A., Making C–H Bonds with CO₂: Production of Formate by Molecular Electrocatalysts. *Chem. Comm.* **2016**, *52* (9), 1768-1777.

82. Cluff, D. B.; Arnold, A.; Fettinger, J. C.; Berben, L. A., Electrocatalytic Reduction of CO₂ into Formate with Glassy Carbon Modified by [Fe₄N(CO)₁₁(PPh₂Ph-Linker)]⁻. *Organometallics* **2018**, *38* (6), 1230-1235.

83. Taheri, A.; Carr, C. R.; Berben, L. A., Electrochemical Methods for Assessing Kinetic Factors in the Reduction of CO₂ to Formate: Implications For Improving Electrocatalyst Design. *ACS Catal.* **2018**, *8* (7), 5787-5793.

84. Loewen, N. D.; Neelakantan, T. V.; Berben, L. A., Renewable Formate from C–H
Bond Formation with CO₂: Using Iron Carbonyl Clusters as Electrocatalysts. *Acc. Chem. Res* 2017, *50* (9), 2362-2370.

85. Cao, L.; Sun, C.; Sun, N.; Meng, L.; Chen, D., Theoretical Mechanism Studies on the Electrocatalytic Reduction of CO₂ to Formate by Water-Stable Iridium Dihydride Pincer Complex. *Dalton Trans.* **2013**, *42* (16), 5755-5763.

86. Johnson, S. I.; Nielsen, R. J.; Goddard III, W. A., Selectivity for HCO₂⁻ over H₂ in the Electrochemical Catalytic Reduction of CO₂ By (POCOP)IrH₂. *ACS Catal.* **2016**, *6* (10), 6362-6371.

87. Nguyen, A. D.; Rail, M. D.; Shanmugam, M.; Fettinger, J. C.; Berben, L. A., Electrocatalytic Hydrogen Evolution from Water by a Series of Iron Carbonyl Clusters. *Inorg. Chem.* **2013**, *52* (21), 12847-12854.

88. Taheri, A.; Thompson, E. J.; Fettinger, J. C.; Berben, L. A., An Iron Electrocatalyst for Selective Reduction of CO₂ to Formate in Water: Including Thermochemical Insights. *ACS Catal.* **2015**, 7140-7151.

Loewen, N. D.; Thompson, E. J.; Kagan, M.; Banales, C. L.; Myers, T. W.;
 Fettinger, J. C.; Berben, L. A., A Pendant Proton Shuttle on [Fe₄N(CO)₁₂]⁻ Alters Product
 Selectivity in Formate vs. H₂ Production via the Hydride [H–Fe₄N(CO)₁₂]⁻. *Chem. Sci.* **2016**, 7 (4), 2728-2735.

90. Goeppert, A.; Czaun, M.; Jones, J.-P.; Prakash, G. S.; Olah, G. A., Recycling of Carbon Dioxide to Methanol and Derived Products–Closing the Loop. *Chem. Soc. Rev.* **2014**, *43* (23), 7995-8048.

91. Bi, J.; Hou, P.; Liu, F. W.; Kang, P., Electrocatalytic Reduction of CO₂ to Methanol by Iron Tetradentate Phosphine Complex through Amidation Strategy. *ChemSusChem* **2019**, *12* (10), 2195-2201.

92. Shen, J.; Kortlever, R.; Kas, R.; Birdja, Y. Y.; Diaz-Morales, O.; Kwon, Y.; Ledezma-Yanez, I.; Schouten, K. J. P.; Mul, G.; Koper, M. T., Electrocatalytic Reduction of Carbon Dioxide to Carbon Monoxide and Methane at an Immobilized Cobalt Protoporphyrin. *Nature Comm.* **2015**, *6*, 8177.

Walsh, J. J.; Neri, G.; Smith, C. L.; Cowan, A. J., Electrocatalytic CO₂ Reduction with a Membrane Supported Manganese Catalyst in Aqueous Solution. *Chem. Comm.* **2014**, *50* (84), 12698-12701.

94. Walsh, J. J.; Smith, C. L.; Neri, G.; Whitehead, G. F.; Robertson, C. M.; Cowan, A.
J., Improving the Efficiency of Electrochemical CO₂ Reduction using Immobilized
Manganese Complexes. *Faraday Discussions* **2015**, *183*, 147-160.

Rosser, T. E.; Windle, C. D.; Reisner, E., Electrocatalytic and Solar-Driven CO₂
 Reduction to CO with a Molecular Manganese Catalyst Immobilized on Mesoporous TiO₂.
 Angew. Chem. Int. Ed. Engl. **2016**, *55* (26), 7388-7392.

96. Torralba-Peñalver, E. N.; Luo, Y.; Compain, J.-D.; Chardon-Noblat, S.; Fabre, B., Selective Catalytic Electroreduction of CO₂ at Silicon Nanowires (SiNWS) Photocathodes using Non-Noble Metal-Based Manganese Carbonyl Bipyridyl Molecular Catalysts in Solution and Grafted onto SiNWS. *ACS Catal.* **2015**, *5* (10), 6138-6147.
97. Ilic, S.; Zoric, M. R.; Kadel, U. P.; Huang, Y.; Glusac, K. D., Metal-Free Motifs for Solar Fuel Applications. *Annu. Rev. Phys. Chem.* **2017**, *68*, 305-331.

98. Mirzakulova, E.; Khatmullin, R.; Walpita, J.; Corrigan, T.; Vargas-Barbosa, N. M.; Vyas, S.; Oottikkal, S.; Manzer, S. F.; Hadad, C. M.; Glusac, K. D., Electrode-Assisted Catalytic Water Oxidation by a Flavin Derivative. *Nat. Chem.* **2012**, *4* (10), 794.

99. Zoric, M. R.; Kadel, U. P.; Glusac, K. D., Cocatalysis: Role of Organic Cations in Oxygen Evolution Reaction on Oxide Electrodes. *ACS Appl. Mat. Interfaces* **2018**, *10* (32), 26825-26829.

100. Ilic, S.; Alherz, A.; Musgrave, C. B.; Glusac, K. D., Importance of Proton-Coupled Electron Transfer in Cathodic Regeneration of Organic Hydrides. *Chem. Comm.* **2019**, *55* (39), 5583-5586.

101. Yang, X.; Walpita, J.; Mirzakulova, E.; Oottikkal, S.; Hadad, C. M.; Glusac, K. D., Mechanistic Studies of Electrode-Assisted Catalytic Oxidation by Flavinium and Acridinium Cations. *ACS Catal.* **2014**, *4* (8), 2635-2644.

102. Zoric, M. R.; Singh, V.; Zeller, M.; Glusac, K. D., Conformational Analysis of Diols:
Role of the Linker on the Relative Orientation of Hydroxyl Groups. *J. Phys. Org. Chem.*2019, E3975.

103. Wiedner, E. S.; Chambers, M. B.; Pitman, C. L.; Bullock, R. M.; Miller, A. J.; Appel,
A. M., Thermodynamic Hydricity of Transition Metal Hydrides. *Chem. Rev.* 2016, *116* (15),
8655-8692.

104. Dubois, D. L., Development of Molecular Electrocatalysts for Energy Storage. *Inorg. Chem.* **2014**, *53* (8), 3935-3960.

105. Kan, Y.; Zhang, Q., Transition Metal Complexes for Hydrogen Activation. In *Nanostructured Materials for Next-Generation Energy Storage and Conversion*, Springer: 2017; Pp 43-84.

106. Gordon, R. B.; Bertram, M.; Graedel, T. E., Metal Stocks and Sustainability. *PNAS***2006**, *103* (5), 1209-1214.

107. Berg, J. M.; Tymoczko, J. L.; Stryer, L., II. Transducing and Storing Energy. In *Biochemistry*, New York: WH Freeman: 2002.

108. Mcskimming, A.; Colbran, S. B., The Coordination Chemistry of Organo-Hydride Donors: New Prospects for Efficient Multi-Electron Reduction. *Chem. Soc. Rev.* **2013**, *42* (12), 5439-5488.

109. Brown, H. C.; Krishnamurthy, S., Forty Years of Hydride Reductions. *Tetrahedron* **1979**, *35* (5), 567-607.

110. Stephan, D. W.; Erker, G., Frustrated Lewis Pairs: Metal-Free Hydrogen Activation and More. *Angew. Chem. Int. Ed. Engl.* **2010**, *4*9 (1), 46-76.

111. Stephan, D. W.; Erker, G., Frustrated Lewis Pair Chemistry: Development and Perspectives. *Angew. Chem. Int. Ed. Engl.* **2015**, *54* (22), 6400-6441.

112. Mayr, H.; Patz, M., Scales of Nucleophilicity and Electrophilicity: A System for Ordering Polar Organic and Organometallic Reactions. *Angew. Chem. Int. Ed. Engl.* **1994**, 33 (9), 938-957.

113. Horn, M.; Schappele, L. H.; Lang-Wittkowski, G.; Mayr, H.; Ofial, A. R., Towards a Comprehensive Hydride Donor Ability Scale. *Chem.: Eur. J* **2013**, *19* (1), 249-263.

114. Zheng, C.; You, S.-L., Transfer Hydrogenation with Hantzsch Esters and Related Organic Hydride Donors. *Chem. Soc. Rev.* **2012**, *41* (6), 2498-2518.

115. Oh, Y.; Hu, X., Organic Molecules as Mediators and Catalysts for Photocatalytic and Electrocatalytic CO₂ Reduction. *Chem. Soc. Rev.* **2013**, *42* (6), 2253-2261.

116. Handoo, K. L.; Cheng, J. P.; Parker, V. D., Hydride Affinities of Organic Radicals in Solution. A Comparison of Free Radicals and Carbenium lons as Hydride Ion Acceptors. *J. Am. Chem. Soc.* **1993**, *115* (12), 5067-5072.

117. Matsubara, Y.; Hightower, S. E.; Chen, J.; Grills, D. C.; Polyansky, D. E.; Muckerman, J. T.; Tanaka, K.; Fujita, E., Reactivity of a fac-ReCl(A-Diimine)(CO)₃ Complex with an NAD⁺ Model Ligand Toward CO2 Reduction. *Chem. Comm.* **2014**, *50* (6), 728-730.

118. Matsubara, Y.; Fujita, E.; Doherty, M. D.; Muckerman, J. T.; Creutz, C., Thermodynamic and Kinetic Hydricity of Ruthenium(II) Hydride Complexes. *J. Am. Chem. Soc.* **2012**, *134* (38), 15743-15757.

119. Barrett, S. M.; Pitman, C. L.; Walden, A. G.; Miller, A. J., Photoswitchable Hydride Transfer from Iridium to 1-Methylnicotinamide Rationalized by Thermochemical Cycles. *J. Am. Chem. Soc.* **2014**, *136* (42), 14718-14721.

120. Berning, D. E.; Noll, B. C.; Dubois, D. L., Relative Hydride, Proton, and Hydrogen Atom Transfer Abilities of [HM(Diphosphine)₂]PF₆ Complexes (M= Pt, Ni). *J. Am. Chem. Soc.* **1999**, *121* (49), 11432-11447.

121. Yang, J. Y.; Smith, S. E.; Liu, T.; Dougherty, W. G.; Hoffert, W. A.; Kassel, W. S.; Dubois, M. R.; Dubois, D. L.; Bullock, R. M., Two Pathways for Electrocatalytic Oxidation of Hydrogen by a Nickel bis(Diphosphine) Complex with Pendant Amines in the Second Coordination Sphere. *J. Am. Chem. Soc.* **2013**, *135* (26), 9700-9712.

122. Curtis, C. J.; Miedaner, A.; Ellis, W. W.; Dubois, D. L., Measurement of the Hydride Donor Abilities of [HM(Diphosphine)₂]⁺ Complexes (M= Ni, Pt) by Heterolytic Activation of Hydrogen. *J. Am. Chem. Soc.* **2002**, *124* (9), 1918-1925.

123. Ciancanelli, R.; Noll, B. C.; Dubois, D. L.; Dubois, M. R., Comprehensive Thermodynamic Characterization of the Metal– Hydrogen Bond in a Series of Cobalt-Hydride Complexes. *J. Am. Chem. Soc.* **2002**, *124* (12), 2984-2992.

124. Estes, D. P.; Vannucci, A. K.; Hall, A. R.; Lichtenberger, D. L.; Norton, J. R., Thermodynamics of the Metal–Hydrogen Bonds in $(H_5-C_5H_5)M(CO)_2H$ (M= Fe, Ru, Os). *Organometallics* **2011**, *30* (12), 3444-3447.

125. Berning, D. E.; Miedaner, A.; Curtis, C. J.; Noll, B. C.; Rakowski Dubois, M. C.; Dubois, D. L., Free-Energy Relationships between the Proton and Hydride Donor Abilities of [HNi(diphosphine)₂]⁺ Complexes and the Half-Wave Potentials of Their Conjugate Bases. *Organometallics* **2001**, *20* (9), 1832-1839.

126. Raebiger, J. W.; Miedaner, A.; Curtis, C. J.; Miller, S. M.; Anderson, O. P.; Dubois,
D. L., Using Ligand Bite Angles to Control the Hydricity of Palladium Diphosphine
Complexes. J. Am. Chem. Soc. 2004, 126 (17), 5502-5514.

127. Yang, J. Y.; Bullock, R. M.; Shaw, W. J.; Twamley, B.; Fraze, K.; Dubois, M. R.; Dubois, D. L., Mechanistic Insights into Catalytic H₂ Oxidation by Ni Complexes Containing a Diphosphine Ligand with a Positioned Amine Base. *J. Am. Chem. Soc.* **2009**, *131* (16), 5935-5945.

128. Miedaner, A.; Raebiger, J. W.; Curtis, C. J.; Miller, S. M.; Dubois, D. L., Thermodynamic Studies of [HPt(etxantphos)₂]⁺ and [(H)₂Pt(etxantphos)₂]²⁺. *Organometallics* **2004**, 23 (11), 2670-2679.

129. Roberts, J. A.; Appel, A. M.; Dubois, D. L.; Bullock, R. M., Comprehensive Thermochemistry of W–H Bonding in the Metal Hydrides CpW(CO)₂(IMes)H, [CpW (CO)₂(IMes)H]^{*+}, and [CpW(CO)₂(IMes)(H)₂]⁺. Influence of an N-Heterocyclic Carbene Ligand on Metal Hydride Bond Energies. *J. Am. Chem. Soc.* **2011**, *133* (37), 14604-14613.

130. Parker, V., Hydridre Affinities of Organic Cations in Solution. *Acta Chem. Scand.***1992**, *46* (11), 1133-1134.

131. Cheng, J.; Handoo, K. L.; Parker, V. D., Hydride Affinities of Carbenium Ions in Acetonitrile and Dimethyl Sulfoxide Solution. *J. Am. Chem. Soc.* **1993**, *115* (7), 2655-2660.

132. Cheng, J.; Handoo, K. L.; Xue, J.; Parker, V. D., Free Energy Hydride Affinities of Quinones in Dimethyl Sulfoxide Solution. *J. Org. Chem.* **1993**, *58* (19), 5050-5054.

133. Zhang, X.-M.; Bruno, J. W.; Enyinnaya, E., Hydride Affinities of Arylcarbenium Ions and Iminium Ions in Dimethyl Sulfoxide and Acetonitrile. *J. Org. Chem.* **1998**, *63* (14), 4671-4678.

134. Ilic, S.; Pandey Kadel, U.; Basdogan, Y.; Keith, J. A.; Glusac, K. D., Thermodynamic Hydricities of Biomimetic Organic Hydride Donors. *J. Am. Chem. Soc.* **Submitted**.

135. Ilic, S.; Pandey Kadel, U.; Basdogan, Y.; Keith, J. A.; Glusac, K. D., Thermodynamic Hydricities of Biomimetic Organic Hydride Donors. *J. Am. Chem. Soc.* **2018**, *140* (13), 4569-4579

136. Wayner, D. D.; Parker, V. D., Bond Energies in Solution from Electrode Potentials and Thermochemical Cycles. A Simplified and General Approach. *Acc. Chem. Res* **1993**, *26* (5), 287-294.

137. Walpita, J.; Yang, X.; Khatmullin, R.; Luk, H. L.; Hadad, C. M.; Glusac, K. D., Pourbaix Diagrams in Weakly Coupled Systems: A Case Study Involving Acridinol and Phenanthridinol Pseudobases. *J. Phys. Org. Chem.* **2016**, *29* (4), 204-208.

 Parker, V. D.; Handoo, K. L.; Roness, F.; Tilset, M., Electrode Potentials and the Thermodynamics of Isodesmic Reactions. *J. Am. Chem. Soc.* **1991**, *113* (20), 7493-7498.
 Roth, H. G.; Romero, N. A.; Nicewicz, D. A., Experimental and Calculated Electrochemical Potentials of Common Organic Molecules for Applications to Single-Electron Redox Chemistry. *Synlett* **2016**, *27* (05), 714-723.

140. Zhu, X.-Q.; Zhang, J.-Y.; Cheng, J.-P., Negative Kinetic Temperature Effect on the Hydride Transfer from NADH Analogue BNAH to the Radical Cation of N-Benzylphenothiazine in Acetonitrile. *J. Org. Chem.* **2006**, *71* (18), 7007-7015.

141. Zhu, X.-Q.; Tan, Y.; Cao, C.-T., Thermodynamic Diagnosis of the Properties and Mechanism of Dihydropyridine-Type Compounds as Hydride Source in Acetonitrile with "Molecule ID Card". *J. Phys. Chem. B* **2010**, *114* (5), 2058-2075.

142. Zhu, X.-Q.; Zhang, M.-T.; Yu, A.; Wang, C.-H.; Cheng, J.-P., Hydride, Hydrogen Atom, Proton, and Electron Transfer Driving Forces of Various Five-Membered Heterocyclic Organic Hydrides and their Reaction Intermediates in Acetonitrile. *J. Am. Chem. Soc.* **2008**, *130* (8), 2501-2516.

143. Han, X.; Hao, W.; Zhu, X.-Q.; Parker, V. D., A Thermodynamic and Kinetic Study of Hydride Transfer of a Caffeine Derivative. *J. Org. Chem.* **2012**, 77 (15), 6520-6529.

144. Cheng, J.-P.; Lu, Y.; Zhu, X.; Mu, L., Energetics of Multistep Versus One-Step Hydride Transfer Reactions of Reduced Nicotinamide Adenine Dinucleotide (NADH) Models with Organic Cations and p-Quinones. *J. Org. Chem.* **1998**, 63 (18), 6108-6114.

145. Giesbrecht, P. K.; Nemez, D. B.; Herbert, D. E., Electrochemical Hydrogenation of a Benzannulated Pyridine to a Dihydropyridine in Acidic Solution. *Chem. Comm.* **2018**, *54* (4), 338-341.

146. Anne, A.; Moiroux, J., Redox Potentials and Acid-Base Equilibria of NADH/NAD⁺ Analogs in Acetonitrile. *J. Org. Chem.* **1990**, *55* (15), 4608-4614.

147. Saveant, J.-M.; Tard, C. D., Attempts to Catalyze the Electrochemical CO₂-to-Methanol Conversion by Biomimetic 2e⁻ + 2H⁺ Transferring Molecules. *J. Am. Chem. Soc.* **2016**, *138* (3), 1017-1021.

148. Bordwell, F. G., Equilibrium Acidities in Dimethyl Sulfoxide Solution. *Acc. Chem. Res* **1988**, *21* (12), 456-463.

149. Hammerich, O.; Speiser, B., *Organic Electrochemistry: Revised and Expanded*. CRC Press: 2015.

150. Morris, R. H., Brønsted–Lowry Acid Strength of Metal Hydride and Dihydrogen Complexes. *Chem. Rev.* **2016**, *116* (15), 8588-8654.

151. Ellis, W. W.; Raebiger, J. W.; Curtis, C. J.; Bruno, J. W.; Dubois, D. L., Hydricities of BzNADH, C₅H₅Mo(PMe₃)(CO)₂H, and C₅Me₅Mo(PMe₃)(CO)₂H in Acetonitrile. *J. Am. Chem. Soc.* **2004**, *126* (9), 2738-2743.

152. Ilic, S. Utilizing NAD⁺/NADH Analogs for the Solar Fuel Forming Reductions. Bowling Green State University, 2017.

153. Dubois, D. L.; Blake, D. M.; Miedaner, A.; Curtis, C. J.; Dubois, M. R.; Franz, J. A.; Linehan, J. C., Hydride Transfer from Rhodium Complexes to Triethylborane. *Organometallics* **2006**, *25* (18), 4414-4419.

154. Roberts, R.; Ostović, D.; Kreevoy, M., Hydride Transfer between NAD⁺ Analogues. *Faraday Discuss.* **1982**, *74*, 257-265.

155. Kreevoy, M. M.; Lee, I. S. H., Marcus Theory of a Perpendicular Effect on α for Hydride Transfer Between NAD⁺ Analogs. *J. Am. Chem. Soc.* **1984**, *106* (9), 2550-2553. 156. Kreevoy, M. M.; Ostovic, D.; Lee, I. S. H.; Binder, D. A.; King, G. W., Structure Sensitivity of the Marcus λ for Hydride Transfer between NAD⁺ Analogs. *J. Am. Chem. Soc.* **1988**, *110* (2), 524-530.

157. Richter, D.; Mayr, H., Hydride-Donor Abilities of 1,4-Dihydropyridines: A Comparison with π Nucleophiles and Borohydride Anions. *Angew. Chem. Int. Ed. Engl.* **2009**, *48* (11), 1958-1961.

158. Funke, M. A.; Mayr, H., Kinetics and Mechanism of the Reactions of Amine Boranes with Carbenium Ions. *Chem.: Eur. J* **1997,** *3* (8), 1214-1222.

159. Mayr, H.; Lang, G.; Ofial, A. R., Reactions of Carbocations with Unsaturated Hydrocarbons: Electrophilic Alkylation or Hydride Abstraction? *J. Am. Chem. Soc.* **2002**, *124* (15), 4076-4083.

160. Richter, D.; Tan, Y.; Antipova, A.; Zhu, X. Q.; Mayr, H., Kinetics of Hydride Abstractions from 2-Arylbenzimidazolines. *Chem. Asian J.* **2009**, *4* (12), 1824-1829.

161. Horn, M.; Mayr, H.; Lacôte, E.; Merling, E.; Deaner, J.; Wells, S.; Mcfadden, T.; Curran, D. P., N-Heterocyclic Carbene Boranes are Good Hydride Donors. *Org. Lett.* **2011**, *14* (1), 82-85.

162. Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G., Reference Scales for the Characterization of Cationic Electrophiles and Neutral Nucleophiles. *J. Am. Chem. Soc.* **2001**, *123* (39), 9500-9512.

163. Würthwein, E.-U.; Lang, G.; Schappele, L. H.; Mayr, H., Rate-Equilibrium Relationships in Hydride Transfer Reactions: The Role of Intrinsic Barriers. *J. Am. Chem. Soc.* **2002**, *124* (15), 4084-4092.

164. Yang, X.; Walpita, J.; Zhou, D.; Luk, H. L.; Vyas, S.; Khnayzer, R. S.; Tiwari, S. C.; Diri, K.; Hadad, C. M.; Castellano, F. N., Toward Organic Photohydrides: Excited-State Behavior of 10-Methyl-9-Phenyl-9, 10-Dihydroacridine. *J. Phys. Chem. B* **2013**, *117* (49), 15290-15296.

165. Muckerman, J. T.; Achord, P.; Creutz, C.; Polyansky, D. E.; Fujita, E., Calculation of Thermodynamic Hydricities and the Design of Hydride Donors for CO₂ Reduction. *PNAS* **2012**, *109* (39), 15657-15662.

166. Qi, X.-J.; Fu, Y.; Liu, L.; Guo, Q.-X., Ab Initio Calculations of Thermodynamic Hydricities of Transition-Metal Hydrides in Acetonitrile. *Organometallics* **2007**, *26* (17), 4197-4203.

167. Shi, J.; Huang, X.-Y.; Wang, H.-J.; Fu, Y., Hydride Dissociation Energies of Six-Membered Heterocyclic Organic Hydrides Predicted by ONIOM-G₄ Method. *J. Chem. Inf. Model.* **2011**, *52* (1), 63-75.

168. Zhu, X.-Q.; Wang, C.-H., Hydride Affinity Scale of Various Substituted Arylcarbeniums in Acetonitrile. *J. Phys. Chem. A* **2010**, *114* (50), 13244-13256.

169. Zhu, X.-Q.; Wang, C.-H.; Liang, H.; Cheng, J.-P., Theoretical Prediction of the Hydride Affinities of Various p- and o-Quinones in DMSO. *J. Org. Chem.* **2007**, *72* (3), 945-956.

170. Mock, M. T.; Potter, R. G.; Camaioni, D. M.; Li, J.; Dougherty, W. G.; Kassel, W. S.; Twamley, B.; Dubois, D. L., Thermodynamic Studies and Hydride Transfer Reactions from a Rhodium Complex to BX₃ Compounds. *J. Am. Chem. Soc.* **2009**, *131* (40), 14454-14465.

171. Heiden, Z. M.; Lathem, A. P., Establishing the Hydride Donor Abilities of Main Group Hydrides. *Organometallics* **2015**, *34* (10), 1818-1827.

172. Alherz, A.; Lim, C.-H.; Hynes, J. T.; Musgrave, C. B., Predicting Hydride Donor Strength via Quantum Chemical Calculations of Hydride Transfer Activation Free Energy. *J. Phys. Chem. B* **2018**, *122* (3), 1278-1288.

173. Zhao, Y.; Truhlar, D. G., Density Functionals with Broad Applicability in Chemistry. *Acc. Chem. Res* **2008**, *41* (2), 157-167.

174. Goerigk, L.; Grimme, S., A Thorough Benchmark of Density Functional Methods for General Main Group Thermochemistry, Kinetics, and Noncovalent Interactions. *Phys. Chem. Chem. Phys.* **2011**, *13* (14), 6670-6688.

175. Goerigk, L.; Grimme, S., Efficient and Accurate Double-Hybrid-Meta-GGA Density Functionals- Evaluation with the Extended GMTKN30 Database for General Main Group Thermochemistry, Kinetics, and Noncovalent Interactions. *J. Chem. Theory Comput.* **2010**, *7* (2), 291-309.

176. Tomasi, J.; Mennucci, B.; Cammi, R., Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105* (8), 2999-3094.

177. Miertuš, S.; Scrocco, E.; Tomasi, J., Electrostatic Interaction of a Solute with a Continuum. A Direct Utilizaion of AB Initio Molecular Potentials for the Prevision of Solvent Effects. *Chem. Phys.* **1981**, *55* (1), 117-129.

178. Tomasi, J.; Persico, M., Molecular Interactions in Solution: An Overview of Methods Based on Continuous Distributions of the Solvent. *Chem. Rev.* **1994**, *94* (7), 2027-2094.

179. Cramer, C. J.; Truhlar, D. G., Implicit Solvation Models: Equilibria, Structure, Spectra, and Dynamics. *Chem. Rev.* **1999**, *99* (8), 2161-2200.

180. Kovács, G.; Pápai, I., Hydride Donor Abilities of Cationic Transition Metal Hydrides from DFT-PCM Calculations. *Organometallics* **2006**, *25* (4), 820-825.

181. Nikitina, E.; Sulimov, V.; Grigoriev, F.; Kondakova, O.; Luschekina, S., Mixed Implicit/Explicit Solvation Models in Quantum Mechanical Calculations of Binding Enthalpy for Protein–Ligand Complexes. *Int. J. Quantum Chem.* **2006**, *106* (8), 1943-1963.

182. Thapa, B.; Schlegel, H. B., Density Functional Theory Calculation of pKa's of Thiols in Aqueous Solution using Explicit Water Molecules and the Polarizable Continuum Model. *J. Phys. Chem. A* **2016**, *120* (28), 5726-5735.

183. Wang, L.-P.; Van Voorhis, T., A Polarizable QM/MM Explicit Solvent Model for Computational Electrochemistry in Water. *J. Chem. Theory Comput.* **2012**, *8* (2), 610-617.

184. Kohn, W.; Sham, L. J., Self-Consistent Equations Including Exchange and Correlation Effects. *Phys. Rev* **1965**, *140* (4A), A1133.

185. Kang, S.-B.; Cho, Y.-S.; Hwang, S.-G., Density Functional Theoretical Study on the Hydricities of Transition Metal Hydride Complexes in Water. *Bull. Korean Chem. Soc.* **2009**, *30* (12), 2927-2929.

186. Mondal, B.; Neese, F.; Ye, S., Toward Rational Design of 3d Transition Metal Catalysts for CO₂ Hydrogenation Based on Insights into Hydricity-Controlled Rate-Determining Steps. *Inorg. Chem.* **2016**, *55* (11), 5438-5444.

187. Nimlos, M. R.; Chang, C. H.; Curtis, C. J.; Miedaner, A.; Pilath, H. M.; Dubois, D.
L., Calculated Hydride Donor Abilities of Five-Coordinate Transition Metal Hydrides
[HM(diphosphine)₂]⁺ (M= Ni, Pd, Pt) as a Function of the Bite Angle and Twist Angle of
Diphosphine Ligands. *Organometallics* **2008**, *27* (12), 2715-2722.

188. Cho, Y.-S.; Lee, J.-B.; Hwang, S.-G., Density Functional Theoretical Study on the Hydricities of $(H_5-C_5H_5)M(CO)_2H$ (M= Fe, Ru, And Os) in Acetonitrile. *Bull. Korean Chem. Soc.* **2012**, 33 (4), 1413-1415.

189. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Reduction of CO₂ to Methanol Catalyzed by a Biomimetic Organo-Hydride Produced from Pyridine. *J. Am. Chem. Soc.* **2014**, *136* (45), 16081-16095.

190. Skyner, R.; Mcdonagh, J.; Groom, C.; Van Mourik, T.; Mitchell, J., A Review of Methods for the Calculation of Solution Free Energies and the Modelling of Systems in Solution. *Phys. Chem. Chem. Phys.* **2015**, *17* (9), 6174-6191.

191. Bentley, T. W., Limitations of the S(E+N) and Related Equations: Solvent Dependence of Electrophilicity. *Angew. Chem* **2011**, *123* (16), 3688-3691.

192. Bentley, T. W., Nucleophilicity Parameters for Strong Nucleophiles in Dimethyl Sulfoxide. A Direct Alternative to the S(E+N) Equation. *J. Phys. Org. Chem.* **2011**, *24* (4), 282-291.

193. Bell, R. P., The Theory of Reactions Involving Proton Transfers. *Proc. Royal Soc. Lond.* **1936**, *154* (882), 414-429.

194. Evans, M.; Polanyi, M., Further Considerations on the Thermodynamics of Chemical Equilibria and Reaction Rates. *J. Chem. Soc. Faraday Trans* **1936**, *32*, 1333-1360.

195. Pratihar, S., Electrophilicity and Nucleophilicity of Commonly Used Aldehydes. *Org. Biomol. Chem.* **2014**, *12* (30), 5781-5788.

196. Kiyooka, S.-I.; Kaneno, D.; Fujiyama, R., Intrinsic Reactivity Index as a Single Scale Directed Toward Both Electrophilicity and Nucleophilicity using Frontier Molecular Orbitals. *Tetrahedron* **2013**, 69 (21), 4247-4258.

197. Zhu, X. Q.; Li, H. R.; Li, Q.; Ai, T.; Lu, J. Y.; Yang, Y.; Cheng, J. P., Determination of the C4-H Bond Dissociation Energies of NADH Models and Their Radical Cations in Acetonitrile. *Chem.: Eur. J* **2003**, *9* (4), 871-880.

198. Zhu, X. Q.; Cao, L.; Liu, Y.; Yang, Y.; Lu, J. Y.; Wang, J. S.; Cheng, J. P., Thermodynamics and Kinetics of the Hydride-Transfer Cycles for 1-Aryl-1,4-Dihydronicotinamide and Its 1,2-Dihydroisomer. *Chem.: Eur. J* **2003**, *9* (16), 3937-3945. 199. Zhu, X.-Q.; Dai, Z.; Yu, A.; Wu, S.; Cheng, J.-P., Driving Forces for the Mutual Conversions between Phenothiazines and Their Various Reaction Intermediates in Acetonitrile. *J. Phys. Chem. B* **2008**, *112* (37), 11694-11707.

200. Hiromoto, T.; Warkentin, E.; Moll, J.; Ermler, U.; Shima, S., The Crystal Structure of an [Fe]-Hydrogenase–Substrate Complex Reveals the Framework for H₂ Activation. *Angew. Chem. Int. Ed. Engl.* **2009**, *48* (35), 6457-6460.

201. Wilkinson, G.; Stone, F. G. A.; Abel, E. W., *Comprehensive Organometallic Chemistry*. Pergamon Press: 1982; Vol. 2.

202. Zhu, X. Q.; Zhang, M.; Liu, Q. Y.; Wang, X. X.; Zhang, J. Y.; Cheng, J. P., A Facile Experimental Method to Determine the Hydride Affinity of Polarized Olefins in Acetonitrile. *Angew. Chem. Int. Ed. Engl.* **2006**, *45* (24), 3954-3957.

203. Zhu, X.-Q.; Chen, X.; Mei, L.-R., Determination of Hydride Affinities of Various Aldehydes and Ketones in Acetonitrile. *Org. Lett.* **2011**, *13* (9), 2456-2459.

204. Lee, I.-S. H.; Jeoung, E. H.; Kreevoy, M. M., Marcus Theory of a Parallel Effect on A for Hydride Transfer Reaction between NAD⁺ Analogues. *J. Am. Chem. Soc.* **1997**, *119* (11), 2722-2728.

205. Marcus, R. A., Theoretical Relations Among Rate Constants, Barriers, and Brønsted Slopes of Chemical Reactions. *J. Phys. Chem.* **1968**, *72* (3), 891-899.

206. Marcus, R., Theory Of Rates of S_N2 Reactions and Relation to Those of Outer Sphere Bond Rupture Electron Transfers. *J. Phys. Chem. A* **1997**, *101* (22), 4072-4087. 207. Kong, Y. S.; Warshel, A., Linear Free Energy Relationships with Quantum Mechanical Corrections: Classical and Quantum Mechanical Rate Constants for Hydride Transfer between NAD⁺ Analogs in Solutions. *J. Am. Chem. Soc.* **1995**, *117* (23), 6234-6242.

208. Rosta, E.; Warshel, A., Origin of Linear Free Energy Relationships: Exploring the Nature of the Off-Diagonal Coupling Elements in $S_N 2$ Reactions. *J. Chem. Theory Comput.* **2012**, *8* (10), 3574-3585.

209. Bernasconi, C. F., Intrinsic Barriers of Reactions and the Principle of Nonperfect Synchronization. *Acc. Chem. Res* **1987**, *20* (8), 301-308.

210. Tsay, C.; Livesay, B. N.; Ruelas, S.; Yang, J. Y., Solvation Effects on Transition Metal Hydricity. *J. Am. Chem. Soc.* **2015**, *1*37 (44), 14114-14121.

211. Ceballos, B. M.; Tsay, C.; Yang, J. Y., CO₂ Reduction or HCO₂⁻ Oxidation? Solvent-Dependent Thermochemistry of a Nickel Hydride Complex. *Chem. Comm.* **2017**. 212. Huang, K.-W.; Han, J. H.; Musgrave, C. B.; Fujita, E., Carbon Dioxide Reduction by Pincer Rhodium H₂-Dihydrogen Complexes: Hydrogen-Binding Modes and Mechanistic Studies by Density Functional Theory Calculations. *Organometallics* **2007**, *26* (3), 508-513.

213. Dubois, D. L.; Berning, D. E., Hydricity of Transition-Metal Hydrides and Its Role in CO₂ Reduction. *Appl. Organomet. Chem.* **2000**, *14* (12), 860-862.

214. Price, A. J.; Ciancanelli, R.; Noll, B. C.; Curtis, C. J.; Dubois, D. L.; Dubois, M. R., HRh(dppb)₂, A Powerful Hydride Donor. *Organometallics* **2002**, *21* (22), 4833-4839.

215. Fang, M.; Wiedner, E. S.; Dougherty, W. G.; Kassel, W. S.; Liu, T.; Dubois, D. L.; Bullock, R. M., Cobalt Complexes Containing Pendant Amines in the Second Coordination Sphere as Electrocatalysts for H₂ Production. *Organometallics* **2014**, *33* (20), 5820-5833.

216. Bowyer, W. J.; Geiger, W. E., Structural Consequences of Electron-Transfer Reactions. 11. Electrochemically Induced Changes in Hapticity in Mixed-Sandwich Compounds of Iridium and Rhodium. *J. Am. Chem. Soc.* **1985**, *107* (20), 5657-5663.

217. Fraze, K.; Wilson, A. D.; Appel, A. M.; Rakowski Dubois, M.; Dubois, D. L., Thermodynamic Properties of the Ni-H Bond in Complexes of the Type [HNi(P₂RN₂R')₂](BF₄) and Evaluation of Factors that Control Catalytic Activity for Hydrogen Oxidation/Production. *Organometallics* **2007**, *26* (16), 3918-3924.

218. Helm, M. L.; Stewart, M. P.; Bullock, R. M.; Dubois, M. R.; Dubois, D. L., A Synthetic Nickel Electrocatalyst with a Turnover Frequency Above 100,000 s⁻¹ for H₂ Production. *Science* **2011**, 333 (6044), 863-866.

219. Carrillo, N.; Ceccarelli, E. A., Open Questions in Ferredoxin-NADP⁺ Reductase Catalytic Mechanism. *Eur J Biochem.* **2003**, *270* (9), 1900-1915.

220. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Catalytic Reduction of CO₂ by Renewable Organohydrides. *J. Phys. Chem. Lett.* **2015**, *6* (24), 5078-5092.

221. Call, A.; Codolà, Z.; Acuña-Parés, F.; Lloret-Fillol, J., Photo-And Electrocatalytic H₂ Production by New First-Row Transition-Metal Complexes Based on an Aminopyridine Pentadentate Ligand. *Chem.: Eur. J* **2014**, *20* (20), 6171-6183.

222. Thompson, E. J.; Berben, L. A., Electrocatalytic Hydrogen Production by an Aluminum (III) Complex: Ligand-Based Proton and Electron Transfer. *Angew. Chem. Int. Ed. Engl.* **2015**, *54* (40), 11642-11646.

223. Appel, A. M.; Bercaw, J. E.; Bocarsly, A. B.; Dobbek, H.; Dubois, D. L.; Dupuis, M.; Ferry, J. G.; Fujita, E.; Hille, R.; Kenis, P. J. A.; Kerfeld, C. A.; Morris, R. H.; Peden, C. H. F.; Portis, A. R.; Ragsdale, S. W.; Rauchfuss, T. B.; Reek, J. N. H.; Seefeldt, L. C.; Thauer,

R. K.; Waldrop, G. L., Frontiers, Opportunities, and Challenges in Biochemical and Chemical Catalysis of CO₂ Fixation. *Chem. Rev.* **2013**, *113* (8), 6621-6658.

224. Lewis, N. S.; Nocera, D. G., Powering the Planet: Chemical Challenges in Solar Energy Utilization. *PNAS* **2006**, *103* (43), 15729-15735.

225. Deno, N. C.; Peterson, H. J.; Saines, G. S., The Hydride-Transfer Reaction. *Chem. Rev.* **1960**, *60* (1), 7-14.

226. Horn, M.; Schappele, L. H.; Lang-Wittkowski, G.; Mayr, H.; Ofial, A. R., Towards a Comprehensive Hydride Donor Ability Scale. *Chem.: Eur. J* **2013**, *19* (1), 249-263.

227. Richter, D.; Mayr, H., Hydride-Donor Abilities of 1,4-Dihydropyridines: A Comparison with π Nucleophiles and Borohydride Anions. *Angew. Chem. Int. Ed. Engl.* **2009**, *48* (11), 1958-1961.

228. Moret, S.; Dyson, P. J.; Laurenczy, G., Direct Synthesis of Formic Acid from Carbon Dioxide by Hydrogenation in Acidic Media. *Nature Comm.* **2014**, *5*.

229. Jeletic, M. S.; Mock, M. T.; Appel, A. M.; Linehan, J. C., A Cobalt-Based Catalyst for the Hydrogenation of CO₂ under Ambient Conditions. *J. Am. Chem. Soc.* **2013**, *135* (31), 11533-11536.

230. Ohtsu, H.; Tanaka, K., An Organic Hydride Transfer Reaction of a Ruthenium NAD Model Complex Leading to Carbon Dioxide Reduction. *Angew. Chem. Int. Ed. Engl.* **2012**, *51* (39), 9792-9795.

231. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Catalytic Reduction of CO₂ by Renewable Organohydrides. *The Journal Of Physical Chemistry Letters* **2015**, 5078-5092.

232. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Dihydropteridine/Pteridine as a 2H⁺/2e⁻ Redox Mediator for the Reduction of CO₂ to Methanol: A Computational Study. *J. Phys. Chem. B* **2017**, *121* (16), 4158-4167.

233. Matsubara, Y.; Fujita, E.; Doherty, M. D.; Muckerman, J. T.; Creutz, C., Thermodynamic and Kinetic Hydricity of Ruthenium(II) Hydride Complexes. *J Am Chem Soc* **2012**, *134* (38), 15743-15757.

234. Dubois, D. L.; Berning, D. E., Hydricity of Transition-Metal Hydrides and Its Role in CO₂ Reduction. *Appl. Organomet. Chem.* **2000**, *14* (12), 860-862.

235. Ohtsu, H.; Tsuge, K.; Tanaka, K., Remarkable Accelerating and Decelerating Effects of the Bases on CO₂ Reduction using a Ruthenium NADH Model Complex. *J. Photochem. Photobiol.* **2015**, *313*, 163-167.

Zhu, D. D.; Liu, J. L.; Qiao, S. Z., Recent Advances in Inorganic Heterogeneous Electrocatalysts for Reduction of Carbon Dioxide. *Adv. Mater.* 2016, *28* (18), 3423-3452.
Sordakis, K.; Tang, C.; Vogt, L. K.; Junge, H.; Dyson, P. J.; Beller, M.; Laurenczy, G., Homogeneous Catalysis for Sustainable Hydrogen Storage in Formic Acid and Alcohols. *Chem. Rev.* 2017, *118* (2), 372-433.

238. Eppinger, J. R.; Huang, K.-W., Formic Acid as a Hydrogen Energy Carrier. ACS *Energy Lett.* **2016**, *2* (1), 188-195.

239. Mellmann, D.; Sponholz, P.; Junge, H.; Beller, M., Formic Acid as a Hydrogen Storage Material–Development of Homogeneous Catalysts for Selective Hydrogen Release. *Chem. Soc. Rev.* **2016**, *45* (14), 3954-3988.

240. Shima, S.; Pilak, O.; Vogt, S.; Schick, M.; Stagni, M. S.; Meyer-Klaucke, W.; Warkentin, E.; Thauer, R. K.; Ermler, U., The Crystal Structure of [Fe]-Hydrogenase Reveals the Geometry of the Active Site. *Science* **2008**, *321* (5888), 572-575.

241. Ilic, S.; Alherz, A.; Musgrave, C. B.; Glusac, K. D., Thermodynamic and Kinetic Hydricities of Metal-Free Hydrides. *Chem. Soc. Rev.* **2018**.

242. Brunet, P.; Wuest, J. D., Formal Transfers of Hydride from Carbon– Hydrogen Bonds. Generation of H₂ from Orthoformamides Designed to Undergo Intramolecular Protonolyses of Activated Carbon– Hydrogen Bonds. *J. Org. Chem.* **1996**, *61* (6), 2020-2026.

243. Calvin, M., Path of Carbon in Photosynthesis. Science **1962**, *135* (3507), 879-&.

244. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Roles of the Lewis Acid and Base in the Chemical Reduction of CO₂ Catalyzed by Frustrated Lewis Pairs. *Inorg. Chem.* **2013**, *52* (17), 10062-10066.

245. Park, S.; Bézier, D.; Brookhart, M., An Efficient Iridium Catalyst for Reduction of Carbon Dioxide to Methane with Trialkylsilanes. *J. Am. Chem. Soc.* **2012**, *134* (28), 11404-11407.

246. Ménard, G.; Stephan, D. W., Room Temperature Reduction of CO₂ to Methanol by
Al-Based Frustrated Lewis Pairs and Ammonia Borane. *J. Am. Chem. Soc.* 2010, 132
(6), 1796-1797.

247. Lu, Z.; Hausmann, H.; Becker, S.; Wegner, H. A., Aromaticity as Stabilizing Element in the Bidentate Activation for the Catalytic Reduction of Carbon Dioxide. *J. Am. Chem. Soc.* **2015**, *137* (16), 5332-5335.

248. Mukherjee, D.; Osseili, H.; Spaniol, T. P.; Okuda, J., Alkali Metal Hydridotriphenylborates [(L)M][HBPh₃] (M= Li, Na, K): Chemoselective Catalysts for Carbonyl and CO₂ Hydroboration. *J. Am. Chem. Soc.* **2016**, *138* (34), 10790-10793.

249. Chen, J.; Falivene, L.; Caporaso, L.; Cavallo, L.; Chen, E. Y.-X., Selective Reduction of CO₂ to CH₄ by Tandem Hydrosilylation with Mixed Al/B Catalysts. *J. Am. Chem. Soc.* **2016**, *138* (16), 5321-5333.

250. Matsuo, T.; Kawaguchi, H., From Carbon Dioxide to Methane: Homogeneous Reduction of Carbon Dioxide with Hydrosilanes Catalyzed by Zirconium–Borane Complexes. *J. Am. Chem. Soc.* **2006**, *128* (38), 12362-12363.

251. Courtemanche, M.-A.; Légaré, M.-A.; Maron, L.; Fontaine, F. D. R.-G., A Highly Active Phosphine–Borane Organocatalyst for the Reduction of CO₂ to Methanol using Hydroboranes. *J. Am. Chem. Soc.* **2013**, *135* (25), 9326-9329.

252. Berkefeld, A.; Piers, W. E.; Parvez, M., Tandem Frustrated Lewis Pair/Tris(Pentafluorophenyl)Borane-Catalyzed Deoxygenative Hydrosilylation of Carbon Dioxide. *J. Am. Chem. Soc.* **2010**, *132* (31), 10660-10661.

253. Chakraborty, S.; Zhang, J.; Krause, J. A.; Guan, H., An Efficient Nickel Catalyst for the Reduction of Carbon Dioxide with a Borane. *J. Am. Chem. Soc.* **2010**, *132* (26), 8872-8873.

254. Bontemps, S.; Vendier, L.; Sabo-Etienne, S., Ruthenium-Catalyzed Reduction of Carbon Dioxide to Formaldehyde. *J. Am. Chem. Soc.* **2014**, *136* (11), 4419-4425.

255. Zimmerman, P. M.; Zhang, Z. Y.; Musgrave, C. B., Simultaneous Two-Hydrogen Transfer as a Mechanism for Efficient CO₂ Reduction. *Inorg. Chem.* **2010**, *49* (19), 8724-8728.

256. Courtemanche, M.-A.; Pulis, A. P.; Rochette, É.; Légaré, M.-A.; Stephan, D. W.; Fontaine, F.-G., Intramolecular B/N Frustrated Lewis Pairs and the Hydrogenation of Carbon Dioxide. *Chem. Comm.* **2015**, *51* (48), 9797-9800.

257. Ye, J.; Johnson, J. K., Screening Lewis Pair Moieties for Catalytic Hydrogenation of CO₂ in Functionalized UiO-66. *ACS Catal.* **2015**, 5 (10), 6219-6229.

258. Ashley, A. E.; Thompson, A. L.; O'Hare, D., Non-Metal-Mediated Homogeneous Hydrogenation of CO₂ to CH₃OH. *Angew Chem Int Edit* **2009**, *48* (52), 9839-9843.

259. Zhao, Y.; Truhlar, D. G., The M06 Suite Of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Functionals. *Theor. Chem. Acc* **2008**, *120* (1-3), 215-241. 260. Hariharan, P. C.; Pople, J. A., The Influence of Polarization Functions on Molecular

Orbital Hydrogenation Energies. Theor. Chim. Acta 1973, 28 (3), 213-222.

261. Li, H.; Jensen, J. H., Improving The Efficiency and Convergence of Geometry Optimization with the Polarizable Continuum Model: New Energy Gradients and Molecular Surface Tessellation. *J. Comput. Chem.* **2004**, *25* (12), 1449-1462.

262. Li, H.; Pomelli, C. S.; Jensen, J. H., Continuum Solvation of Large Molecules Described by QM/MM: A Semi-Iterative Implementation of the PCM/EFP Interface. *Theor. Chem. Acc* **2003**, *109* (2), 71-84.

263. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.;

Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16 Rev. B.01*, Wallingford, CT, 2016.

264. Roberts, G. M.; Pierce, P. J.; Woo, L. K., Palladium Complexes with N-Heterocyclic Carbene Ligands as Catalysts for the Alkoxycarbonylation of Olefins. *Organometallics* **2013**, *32* (6), 2033-2036.

265. Wood, P. M., The Redox Potential for Dimethyl Sulphoxide Reduction to Dimethyl Sulphide: Evaluation and Biochemical Implications. *FEBS Lett.* **1981**, *124* (1), 11-14.

266. Boston, D. J.; Xu, C.; Armstrong, D. W.; Macdonnell, F. M., Photochemical Reduction of Carbon Dioxide to Methanol and Formate in a Homogeneous System with Pyridinium Catalysts. *J. Am. Chem. Soc.* **2013**, *135* (44), 16252-16255.

267. Lejkowski, M. L.; Lindner, R.; Kageyama, T.; Bódizs, G. É.; Plessow, P. N.; Müller, I. B.; Schäfer, A.; Rominger, F.; Hofmann, P.; Futter, C.; Schunk, S. A.; Limbach, M., The First Catalytic Synthesis of an Acrylate From CO₂ and an Alkene- A Rational Approach. *Chem.: Eur. J* **2012**, *18* (44), 14017-14025.

268. Snyder, L. R., Classification of the Solvent Properties of Common Liquids. *J. Chromatogr. A* **1974**, *92* (2), 223-230.

269. Hecht, S. M.; Adams, B. L.; Kozarich, J. W., Chemical Transformations of 7,9-Disubstituted Purines and Related Heterocycles. Selective Reduction of Imines and Immonium Salts. *J. Org. Chem.* **1976**, *41* (13), 2303-2311.

270. Schwarz, D. E.; Cameron, T. M.; Hay, P. J.; Scott, B. L.; Tumas, W.; Thorn, D. L., Hydrogen Evolution from Organic "Hydrides". *Chem. Comm.* **2005**, (47), 5919-5921.

271. Barton, E. E.; Rampulla, D. M.; Bocarsly, A. B., Selective Solar-Driven Reduction of CO₂ to Methanol using a Catalyzed p-GaP Based Photoelectrochemical Cell. *J. Am. Chem. Soc.* **2008**, *130* (20), 6342-6344.

272. De Robillard, G.; Devillers, C. H.; Kunz, D.; Cattey, H. L. N.; Digard, E.; Andrieu, J., Electrosynthesis of Imidazolium Carboxylates. *Org. Lett.* **2013**, *15* (17), 4410-4413.

273. Micheletti Moracci, F.; Liberatore, F.; Carelli, V.; Arnone, A.; Carelli, I.; Cardinali, M. E., Electrochemical Reduction of 1-Benzyl-3-Carbamoylpyridinium Chloride, A Nicotinamide Adenine Dinucleotide Model Compound. *J. Org. Chem.* **1978**, *43* (17), 3420-3422.

274. Carelli, I.; Cardinali, M. E.; Casini, A.; Arnone, A., Electrochemical Reduction of 3-Cyano-1-Methylpyridinium lodide, a Nicotinamide Adenine Dinucleotide Model Compound. *J. Org. Chem.* **1976**, *41* (25), 3967-3969.

275. Malinski, T.; Elving, P. J., Electrochemical Reduction of Nicotinamide Adenine Dinucleotide in Dimethylsulfoxide: Ion-Pair, Protonation, and Adsorption Effects. *J. Electrochem. Soc.* **1982**, *129* (9), 1960-1967.

276. Schmakel, C. O.; Santhanam, K.; Elving, P. J., Nicotinamide Adenine Dinucleotide (NAD⁺) and Related Compounds. Electrochemical Redox Pattern and Allied Chemical Behavior. *J. Am. Chem. Soc.* **1975**, *97* (18), 5083-5092.

277. Santhanam, K.; Elving, P. J., Electrochemical Redox Pattern for Nicotinamide Species in Nonaqueous Media. *J. Am. Chem. Soc.* **1973**, 95 (17), 5482-5490.

278. Meyer, T. J.; Huynh, M. H. V.; Thorp, H. H., The Possible Role of Proton-Coupled Electron Transfer (PCET) in Water Oxidation by Photosystem II. *Angew. Chem* **2007**, *4*6 (28), 5284-5304.

279. Huynh, M. H. V.; Meyer, T. J. J. C. R., Proton-Coupled Electron Transfer. *Chem. Rev.* **2007**, *107* (11), 5004-5064.

Weinberg, D. R.; Gagliardi, C. J.; Hull, J. F.; Murphy, C. F.; Kent, C. A.; Westlake,
B. C.; Paul, A.; Ess, D. H.; Mccafferty, D. G.; Meyer, T. J., Proton-Coupled Electron
Transfer. *Chem. Rev.* 2012, *112* (7), 4016-4093.

281. Zimmerman, P. M.; Zhang, Z.; Musgrave, C. B., Simultaneous Two-Hydrogen Transfer as a Mechanism for Efficient CO₂ Reduction. *Inorg. Chem.* **2010**, *49* (19), 8724-8728.

282. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Reduction of CO₂ to Methanol Catalyzed by a Biomimetic Organo-Hydride Produced from Pyridine. *J. Am. Chem. Soc.* **2014**, *136* (45), 16081-16095.

283. Lim, C.-H.; Holder, A. M.; Hynes, J. T.; Musgrave, C. B., Catalytic Reduction of CO₂ by Renewable Organohydrides. *J. Phys. Chem. Lett* **2015**, *6* (24), 5078-5092.

284. Hu, X.; Brunschwig, B. S.; Peters, J. C., Electrocatalytic Hydrogen Evolution at Low Overpotentials by Cobalt Macrocyclic Glyoxime and Tetraimine Complexes. *J. Am. Chem. Soc.* **2007**, *129* (29), 8988-8998.

285. Rountree, E. S.; Dempsey, J. L., Potential-Dependent Electrocatalytic Pathways: Controlling Reactivity with pKa for Mechanistic Investigation of a Nickel-Based Hydrogen Evolution Catalyst. *J. Am. Chem. Soc.* **2015**, *137* (41), 13371-13380.

286. Taheri, A.; Thompson, E. J.; Fettinger, J. C.; Berben, L. A., An Iron Electrocatalyst for Selective Reduction of CO₂ to Formate in Water: Including Thermochemical Insights. *ACS Catal.* **2015**, *5* (12), 7140-7151.

287. Roy, S.; Sharma, B.; Pécaut, J.; Simon, P.; Fontecave, M.; Tran, P. D.; Derat, E.; Artero, V., Molecular Cobalt Complexes with Pendant Amines for Selective Electrocatalytic Reduction of Carbon Dioxide to Formic Acid. *J. Am. Chem. Soc.* **2017**, *139* (10), 3685-3696.

288. Witt, S. E.; White, T. A.; Li, Z.; Dunbar, K. R.; Turro, C., Cationic Dirhodium (II, II) Complexes for the Electrocatalytic Reduction of CO₂ to HCOOH. *Chem. Comm.* **2016**, *52* (82), 12175-12178.

289. Loewen, N. D.; Thompson, E. J.; Kagan, M.; Banales, C. L.; Myers, T. W.; Fettinger, J. C.; Berben, L. A., A Pendant Proton Shuttle on $[Fe_4N(CO)_{12}]^-$ Alters Product Selectivity in Formate vs. H₂ Production via the Hydride $[H-Fe_4N(CO)_{12}]^-$. *Chem. Sci.* **2016**, 7 (4), 2728-2735.

290. Nguyen, A. D.; Rail, M. D.; Shanmugam, M.; Fettinger, J. C.; Berben, L. A., Electrocatalytic Hydrogen Evolution from Water by a Series of Iron Carbonyl Clusters. *Inorg. Chem* **2013**, *52* (21), 12847-12854.

291. Rountree, E. S.; Martin, D. J.; Mccarthy, B. D.; Dempsey, J. L., Linear Free Energy Relationships in the Hydrogen Evolution Reaction: Kinetic Analysis of a Cobaloxime Catalyst. *ACS Catal.* **2016**, *6* (5), 3326-3335.

292. Wiedner, E. S.; Brown, H. J.; Helm, M. L., Kinetic Analysis of Competitive Electrocatalytic Pathways: New Insights into Hydrogen Production with Nickel Electrocatalysts. *J. Am. Chem. Soc.* **2016**, *138* (2), 604-616.

293. Bediako, D. K.; Solis, B. H.; Dogutan, D. K.; Roubelakis, M. M.; Maher, A. G.; Lee, C. H.; Chambers, M. B.; Hammes-Schiffer, S.; Nocera, D. G., Role of Pendant Proton Relays and Proton-Coupled Electron Transfer on the Hydrogen Evolution Reaction by Nickel Hangman Porphyrins. *PNAS* **2014**, *111* (42), 15001-15006.

294. Muckerman, J. T.; Fujita, E., Theoretical Studies of the Mechanism of Catalytic Hydrogen Production by a Cobaloxime. *Chem. Comm.* **2011**, *47* (46), 12456-12458.

295. Elgrishi, N. M.; Kurtz, D. A.; Dempsey, J. L., Reaction Parameters Influencing Cobalt Hydride Formation Kinetics: Implications for Benchmarking H₂-Evolution Catalysts. *J. Am. Chem. Soc.* **2016**, *139* (1), 239-244.

296. Costentin, C., Electrochemical Approach to the Mechanistic Study of Proton-Coupled Electron Transfer. *Chem. Rev.* **2008**, *108* (7), 2145-2179.

297. Gupta, N.; Linschitz, H., Hydrogen-Bonding and Protonation Effects in Electrochemistry of Quinones in Aprotic Solvents. *J. Am. Chem. Soc.* **1997**, *119* (27), 6384-6391.

298. Breinlinger, E.; Niemz, A.; Rotello, V. M., Model Systems for Flavoenzyme Activity. Stabilization of the Flavin Radical Anion Through Specific Hydrogen Bond Interactions. *J. Am. Chem. Soc.* **1995**, *117* (19), 5379-5380.

299. Hammarström, L.; Styring, S., Proton-Coupled Electron Transfer of Tyrosines in Photosystem II and Model Systems for Artificial Photosynthesis: The Role of a Redox-

Active Link Between Catalyst and Photosensitizer. *Energy Environ. Sci.* **2011**, *4* (7), 2379-2388.

300. Johannissen, L. O.; Irebo, T.; Sjödin, M.; Johansson, O.; Hammarström, L., The Kinetic Effect of Internal Hydrogen Bonds on Proton-Coupled Electron Transfer from Phenols: A Theoretical Analysis with Modeling of Experimental Data. *J. Phys. Chem. B* **2009**, *113* (50), 16214-16225.

301. Solis, B. H.; Maher, A. G.; Dogutan, D. K.; Nocera, D. G.; Hammes-Schiffer, S., Nickel Phlorin Intermediate Formed by Proton-Coupled Electron Transfer in Hydrogen Evolution Mechanism. *PNAS* **2016**, *113* (3), 485-492.

302. Ohtsu, H.; Tanaka, K., An Organic Hydride Transfer Reaction of a Ruthenium NAD Model Complex Leading to Carbon Dioxide Reduction. *Angew. Chem* **2012**, *51* (39), 9792-9795.

303. Matsubara, Y.; Hightower, S. E.; Chen, J.; Grills, D. C.; Polyansky, D. E.; Muckerman, J. T.; Tanaka, K.; Fujita, E., Reactivity of a fac-ReCl(A-Diimine)(CO)₃ Complex with an NAD⁺ Model Ligand toward CO₂ Reduction. *Chem. Comm.* **2014**, *50* (6), 728-730.

304. Polyansky, D. E.; Cabelli, D.; Muckerman, J. T.; Fukushima, T.; Tanaka, K.; Fujita,
E., Mechanism of Hydride Donor Generation using a Ru (II) Complex Containing an NAD⁺
Model Ligand: Pulse and Steady-State Radiolysis Studies. *Inorg. Chem* 2008, 47 (10), 3958-3968.

305. Karplus, P. A.; Daniels, M. J.; Herriott, J. R., Atomic Structure of Ferredoxin-NADP⁺ Reductase: Prototype for a Structurally Novel Flavoenzyme Family. *Science* **1991**, *251* (4989), 60-66.

306. Solis, B. H.; Maher, A. G.; Honda, T.; Powers, D. C.; Nocera, D. G.; Hammes-Schiffer, S., Theoretical Analysis of Cobalt Hangman Porphyrins: Ligand Dearomatization and Mechanistic Implications for Hydrogen Evolution. *ACS Catal.* **2014**, *4* (12), 4516-4526.

307. Anne, A.; Fraoua, S.; Grass, V.; Moiroux, J.; Savéant, J.-M., The Role of Homolytic Bond Dissociation Energy in the Deprotonation of Cation Radicals. Examples in the NADH Analogues Series. *J. Am. Chem. Soc.* **1998**, *120* (12), 2951-2958.

308. Zielonka, J.; Marcinek, A.; Adamus, J.; Gebicki, J., Direct Observation of NADH Radical Cation Generated in Reactions with One-Electron Oxidants. *J. Phys. Chem. A* **2003**, *107* (46), 9860-9864.

309. Hermolin, J.; Levin, M.; Kosower, E. M., Stable Free Radicals. 12. New Aspects of the Behavior of 1-Alkyl-4-(Carboalkoxy)-and 1-Alkyl-4-Carbamidopyridinyl Radicals in Solution and in Thin Films. *J. Am. Chem. Soc.* **1981**, *103* (16), 4808-4813.

310. De Robillard, G.; Devillers, C. H.; Kunz, D.; Cattey, H.; Digard, E.; Andrieu, J., Electrosynthesis of Imidazolium Carboxylates. *Org. Lett.* **2013**, *15* (17), 4410-4413.

311. Anne, A.; Hapiot, P.; Moiroux, J.; Savéant, J.-M., Electrochemistry of Synthetic Analogues of NAD Dimers. *J. Electroanal. Chem.* **1992**, *331* (1-2), 959-970.

312. Hapiot, P.; Moiroux, J.; Saveant, J. M., Electrochemistry of NADH/NAD⁺ Analogs. A Detailed Mechanistic Kinetic and Thermodynamic Analysis of the 10-Methylacridan/10-Methylacridinium Couple in Acetonitrile. *J. Am. Chem. Soc.* **1990**, *112* (4), 1337-1343.

313. Ilic, S.; Pandey Kadel, U.; Basdogan, Y.; Keith, J. A.; Glusac, K. D., Thermodynamic Hydricities of Biomimetic Organic Hydride Donors. *J. Am. Chem. Soc.* **2018**, *140* (13), 4569-4579.

314. Ilic, S.; Alherz, A.; Musgrave, C. B.; Glusac, K. D., Thermodynamic and Kinetic Hydricities of Metal-Free Hydrides. *Chem. Soc. Rev.* **2018**, *47* (8), 2809-2836.

315. Alherz, A.; Lim, C.-H.; Kuo, Y.-C.; Lehman, P.; Cha, J.; Hynes, J. T.; Musgrave, C.
B., Renewable Hydride Donors for the Catalytic Reduction of CO₂: A Thermodynamic and Kinetic Study. *J. Phys. Chem. B* **2018**, *122* (44), 10179-10189.

316. Alherz, A.; Lim, C.-H.; Hynes, J. T.; Musgrave, C. B., Predicting Hydride Donor Strength via Quantum Chemical Calculations of Hydride Transfer Activation Free Energy. *J. Phys. Chem. B* **2018**, *122* (3), 1278-1288.

317. Lim, C.-H.; Ilic, S.; Alherz, A.; Worrell, B. T.; Bacon, S. S.; Hynes, J. T.; Glusac, K.
D.; Musgrave, C. B., Benzimidazoles as Metal-Free and Renewable Hydrides for CO₂
Reduction to Formate. *J. Am. Chem. Soc.* **2018**, *141* (1), 272-280.

318. Ilic, S.; Brown, E. S.; Xie, Y.; Maldonado, S.; Glusac, K. D., Sensitization of p-GaP with Monocationic Dyes: The Effect of Dye Excited-State Lifetime on Hole Injection Efficiencies. *J. Phys. Chem. C* **2016**, *120* (6), 3145-3155.

319. Hargenrader, G. N.; Weerasooriya, R. B.; Ilic, S.; Niklas, J.; Poluektov, O. G.; Glusac, K. D., Photoregeneration of Biomimetic Nicotinamide Adenine Dinucleotide Analogues via a Dye-Sensitized Approach. *ACS Appl. Energy Mater.* **2018**.

320. Chai, J.-D.; Head-Gordon, M., Long-Range Corrected Hybrid Density Functionals with Damped Atom–Atom Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2008**, *10* (44), 6615-6620.

321. Hariharan, P. C.; Pople, J. A., The Influence of Polarization Functions on Molecular Orbital Hydrogenation Energies. *Theor Chim Acta* **1973**, *28* (3), 213-222.

322. Li, H.; Pomelli, C. S.; Jensen, J. H., Continuum Solvation of Large Molecules Described by QM/MM: A Semi-Iterative Implementation of the PCM/EFP Interface. *Theor Chim Acta* **2003**, *109* (2), 71-84.

323. Li, H.; Jensen, J. H., Improving the Efficiency and Convergence of Geometry Optimization with the Polarizable Continuum Model: New Energy Gradients and Molecular Surface Tessellation. *J. Comput. Chem.* **2004**, *25* (12), 1449-1462.

324. Namazian, M.; Lin, C. Y.; Coote, M. L., Benchmark Calculations of Absolute Reduction Potential of Ferricinium/Ferrocene Couple in Nonaqueous Solutions. *J. Chem. Theory Comput.* **2010**, *6* (9), 2721-2725.

325. Thapa, B.; Schlegel, H. B., Density Functional Theory Calculation of pKa's of Thiols in Aqueous Solution using Explicit Water Molecules and the Polarizable Continuum Model. *J. Phys. Chem. A* **2016**, *120* (28), 5726-5735.

326. Bordwell, F. G., Equilibrium Acidities in Dimethyl Sulfoxide Solution. *Acc. Chem. Res.* **1988**, *21* (12), 456-463.

327. Wang, G.; Hu, W.; Hu, Z.; Zhang, Y.; Yao, W.; Li, L.; Fu, Z.; Huang, W., Carbene-Catalyzed Aerobic Oxidation of Isoquinolinium Salts: Efficient Synthesis of Isoquinolinones. *Green Chem.* **2018**.

328. Zhu, X.-Q.; Zhang, M.-T.; Yu, A.; Wang, C.-H.; Cheng, J.-P., Hydride, Hydrogen Atom, Proton, and Electron Transfer Driving Forces of Various Five-Membered Heterocyclic Organic Hydrides and Their Reaction Intermediates in Acetonitrile. *J. Am. Chem. Soc.* **2008**, *130* (8), 2501-2516.

329. Wright, A. G.; Weissbach, T.; Holdcroft, S., Poly(Phenylene) and M-Terphenyl as Powerful Protecting Groups for the Preparation of Stable Organic Hydroxides. *Angew. Chem* **2016**, *55* (15), 4818-4821.

330. Lim, C.-H.; Ilic, S.; Alherz, A.; Worrell, B. T.; Bacon, S. S.; Hynes, J. T.; Glusac, K.
D.; Musgrave, C. B., Benzimidazoles as Metal-Free and Renewable Hydrides for CO₂
Reduction to Formate. *J. Am. Chem. Soc.* **2018**, *Vol.*

331. Bin, Z.; Liu, Z.; Duan, L., Organic Radicals Outperform Lif as Efficient Electron-Injection Materials for Organic Light-Emitting Diodes. *J. Phys. Chem. Lett.* **2017**, *8* (19), 4769-4773.

332. Pavlishchuk, V. V.; Addison, A. W., Conversion Constants for Redox Potentials Measured versus Different Reference Electrodes in Acetonitrile Solutions at 25 ^oC. *Inorganica Chim. Acta* **2000**, 298 (1), 97-102.

333. Wiedner, E. S.; Chambers, M. B.; Pitman, C. L.; Bullock, R. M.; Miller, A. J.; Appel, A. M., Thermodynamic Hydricity of Transition Metal Hydrides. *Chem. Rev.* **2016**, *116* (15),

8655-8692.

334. the appearance of the irreversible peak at -1.3 v was due to the background proton reduction by the electrode.

335. Markle, T. F.; Rhile, I. J.; Mayer, J. M., Kinetic Effects of Increased Proton Transfer
Distance on Proton-Coupled Oxidations of Phenol-Amines. *J. Am. Chem. Soc.* 2011, *133*(43), 17341-17352.

336. Rhile, I. J.; Mayer, J. M., One-Electron Oxidation of a Hydrogen-Bonded Phenol
Occurs by Concerted Proton-Coupled Electron Transfer. *J. Am. Chem. Soc.* 2004, 126
(40), 12718-12719.

337. Zipse, H., Radicals in Synthesis I: Methods and Mechanisms. *To. In Curr. Chem* **2006**, *2*63, 163.

338. The strain energy is defined as the free energy difference between the relaxed geometry of the radical (r·) and the deprotonated cationic radical intermediates. larger strain energies correspond to larger acidities (lower pka values) since the radical (conjugate base) must undergo a more drastic structural change.

339. the ideal reduction potential for the hydride regeneration ($R^+ + 2e^- + H^+ -> RH$) was calculated using the hydricity dgh- 45 kcal/mol ($RH -> R^+ + H^-$) and dg for the reaction: $H^+ + 2e^- -> H^-$ (from ref 340).

340. Handoo, K. L.; Cheng, J. P.; Parker, V. D., Hydride Affinities of Organic Radicals in Solution. A Comparison of Free Radicals and Carbenium lons as Hydride Ion Acceptors. *J. Am. Chem. Soc.* **1993**, *115* (12), 5067-5072.

341. Lee, H. M.; Youn, I. S.; Saleh, M.; Lee, J. W.; Kim, K. S., Interactions of CO₂ with Various Functional Molecules. *Phys. Chem. Chem. Phys.* **2015**, *17* (16), 10925-10933.

342. Zhou, H.; Wang, G.-X.; Zhang, W.-Z.; Lu, X.-B., CO₂ Adducts of Phosphorus Ylides: Highly Active Organocatalysts for Carbon Dioxide Transformation. *ACS Catal.* **2015**, 5 (11), 6773-6779.

343. Villar, J. M.; Suárez, J.; Varela, J. S. A.; Saá, C., N-Doped Cationic Pahs by Rh(III)-Catalyzed Double C–H Activation and Annulation Of 2-Arylbenzimidazoles with Alkynes. *Org. Lett.* **2017**, *19* (7), 1702-1705.

344. Bower, J.; Ramage, G., Heterocyclic Systems Related to Pyrrocoline. Part I. 2: 3 A-Diazaindene. *J. Chem. Soc.* **1955**, 2834-2837.

345. Groves, B. R.; Crawford, S. M.; Lundrigan, T.; Matta, C. F.; Sowlati-Hashjin, S.; Thompson, A., Synthesis and Characterisation of the Unsubstituted Dipyrrin and 4, 4-Dichloro-4-Bora-3a, 4a-Diaza-S-Indacene: Improved Synthesis and Functionalisation of the Simplest BODIPY Framework. *Chem. Comm.* **2013**, *49* (8), 816-818.

346. Zhang, J.; Yang, J. D.; Cheng, J. P., A Nucleophilicity Scale for the Reactivity of Diazaphospholenium Hydrides: Structural Insights and Synthetic Applications. *Angew. Chem* **2019**, *131* (18), 6044-6048.

347. Markle, T. F.; Mayer, J. M., Concerted Proton–Electron Transfer in Pyridylphenols: The Importance of the Hydrogen Bond. *Angew. Chem. Int. Ed.* **2008**, *47* (4), 738-740.

348. Hansen, A. S.; Du, L.; Kjaergaard, H. G., Positively Charged Phosphorus as a Hydrogen Bond Acceptor. *J. Phys. Chem. Lett.* **2014**, *5* (23), 4225-4231.

VITA

EDUCATION

- 2019 **Ph.D.** Chemistry, Department of Chemistry, University of Illinois at Chicago
- 2017 M. Sc. Chemistry, Center for Photochemical Sciences, Bowling Green State University
- 2013 B. Sc. Chemistry, Department of Chemistry, University of Belgrade, Belgrade, Serbia

HONORS AND AWARDS

- 2017-8 Fund for Young Talents Studying Abroad Scholarship, Republic of Serbia
- 2016 DOE Travel Grant for Gordon Research Conference Poster Presentation
- 2016 BGSU Shanklin Colloquium Award for the Best Paper Presentation
- 2013 Serbian Chemical Society Award for Outstanding Success during Undergraduate Studies
- 2012-3 Fund for Young Talents of Republic of Serbia Scholarship

PUBLICATIONS

- (8) <u>S. Ilic;</u> A. Alherz; C. Musgrave; K. D. Glusac; *Chem. Comm.*, **2019**, 55, 5583-5586
- G. N. Hargenrader; R. B. Weerasooriya; <u>S. Ilic</u>; J. Niklas; O. G. Poluektov; K. D. Glusac; ACS Appl. Energy Mater., 2019, 2(1), 80-91
- (6) C. H. Lim; <u>S. Ilic</u>; A. Alherz; B. T. Worrell; S. S. Bacon; J. T. Hynes; K. D. Glusac; C. B. Musgrave; J. Am. Chem. Soc., 2019, 141(1), 272-280
- (5) <u>S. Ilic;</u> A. Alherz; C. Musgrave; K. D. Glusac; *Chem. Soc. Rev.*, **2018**, 47(8), 2809-2836,
- (4) <u>S. Ilic;</u> U. Pandey Kadel; Y. Basdogan; J. A. Keith; K. D. Glusac; *J. Am. Chem. Soc.*, **2018**, 140(13), 4569-4579
- (3) <u>S. Ilic;</u> M. Zoric; U. Pandey Kadel; Y. Huang; K. D. Glusac; *Annu. Rev. Phys. Chem.*, 2017, 68, 305-331
- (2) Y. Xie; <u>S. Ilic;</u> S. Skaro; V. Maslak; K. D. Glusac; *J. Phys. Chem A*, **2017**, 121, 448-457
- (1) <u>S. Ilic;</u> E. S. Brown; Y. Xie; S. Maldonado; K. D. Glusac; *J. Phys. Chem C*, **2016**, *120* (6), 3145–3155

CONFERENCE PRESENTATIONS

- 2019 International Conference on Photochemistry, Oral Presentation, "Toward Metal-Free Catalysis: Designing Organic Hydrides for Fuel-Forming Reductions"
- 2018 255th ACS National Meeting & Exposition, Oral Presentation, "Utilizing NAD⁺/NADH Analogs for Fuel Forming Photoreductions"
- 2018 Fusion Conferences: Frontiers in Photochemistry, Oral Presentation, "Utilizing NAD⁺/NADH Analogs for Fuel Forming Photoreductions"
- 2018 UIC Chemistry Graduate Student Symposium, Poster Presentation, "Biomimetic CO₂ Reduction by Metal-Free NADH Analogs"
- 2017 UIC Chemistry Graduate Student Symposium, Poster Presentation, "Designing a Semiconductor:Dye Co-Catalysts System for Solar Fuel Application"
- 2017 Telluride Science Research Center (TSRC), *Solar Solutions to Energy and Environmental Problems*, Oral Presentation, "Utilizing NAD⁺/NADH Analogs for Fuel Forming Photoreductions"
- 2017 Inter-American Photochemical Society (IAPS), Poster Presentation "Utilizing NAD⁺/NADH Analogs in Artificial Photosynthesis: Thermodynamic Hydricities of NADH"
- 2016 Ohio-Region Section APS conference (OSAPS), *Materials for Energy and Sustainability*, Poster Presentation "Photocatalytic Reductions using p-GaP Photoelectrode and NAD⁺/NADH Analogs"
- 2016 Gordon Research Conference, *Electron Donor-Acceptor Interactions*, Poster Presentation "Photocatalytic Reductions using p-GaP Photoelectrode and NAD⁺/NADH Analogs"
- 2016 Gordon Research Seminar, *Electron Donor-Acceptor Interactions*, Poster Presentation "Photocatalytic Reductions using p-GaP Photoelectrode and NAD⁺/NADH Analogs"
- 2015 Ohio Inorganic Weekend, Poster Presentation "Sensitization of p-GaP with Cationic Iminium Dyes: The Effect of Dye Excited-State Lifetime on Hole Injection Efficiencies"

Copyright Permissions

Figure 1

Figure SPM.1

You may freely download and copy the material contained on this website for your personal, non-commercial use, without any right to resell, redistribute, compile or create derivative works therefrom, subject to more specific restrictions that may apply to specific materials.

OOWNLOAD
SHARE
Figure 2 Copyright Clearance Center RightsLink[®]



LOGIN

If you're a copyright.com

copyright.com credentials.

Already a RightsLink user or want to learn more?

user, you can login to

RightsLink using your



Electrochemical CO2 reduction catalyzed by ruthenium complexes [Ru(bpy)2(CO)2]2 and [Ru(bpy)2(CO)CI] . Effect of pH on the formation of CO and HCOO-Hitoshi. Ishida, Koji. Tanaka,

Author: Hitoshi. Ishida, Koji. Tanaka Toshio. Tanaka

Publication: Organometallics

Publisher: American Chemical Society

Date: Jan 1, 1987

Copyright \circledast 1987, American Chemical Society

PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 <u>Copyright Clearance Center, Inc.</u> All Rights Reserved. <u>Privacy statement</u>. <u>Terms and Conditions</u>. Comments? We would like to hear from you. E-mail us at <u>customercare@copyright.com</u>

Figure 4 Copyright Clearance Center Center Clearance



ACS Publications Title:

Title:Turning on the Protonation-First
Pathway for Electrocatalytic CO2
Reduction by Manganese
Bipyridyl Tricarbonyl ComplexesAuthor:Ken T. Ngo, Meaghan McKinnon,
Bani Mahanti, et alPublication:Journal of the American
Chemical SocietyPublisher:American Chemical SocietyDate:Feb 1, 2017Copyright © 2017, American Chemical Society

LOGIN If you're a copyright.com user, you can login to RightsLink using your copyright.com credentials. Already a RightsLink user or want to learn more?

PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 <u>Copyright Clearance Center, Inc.</u> All Rights Reserved. <u>Privacy statement</u>. <u>Terms and Conditions</u>. Comments? We would like to hear from you. E-mail us at <u>customercare@copyright.com</u>

Figure 5



Proton-Coupled Electron Transfer Cleavage of Heavy-Atom Bonds in Electrocatalytic Processes. Cleavage of a C-O Bond in the Catalyzed Electrochemical Reduction of CO2 Cyrille Costentin, Samuel Author: Drouet, Guillaume Passard, et al Publication: Journal of the American **Chemical Society** Publisher: American Chemical Society Date: Jun 1, 2013 Copyright © 2013, American Chemical Society





LOGIN If you're a copyright.com user, you can login to RightsLink using your copyright.com credentials. Already a RightsLink user or want to learn more?

PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 Copyright Clearance Center, Inc. All Rights Reserved. Privacy statement. Terms and Conditions. Comments? We would like to hear from you. E-mail us at customercare@copyright.com

Figure 6 Copyright RightsLink Clearance Center ACS Publications Title: st Trusted, Most Cited, Most Read

Date:

Through-Space Charge Interaction Substituent Effects in Molecular Catalysis Leading to the Design of the Most Efficient Catalyst of CO2-to-CO **Electrochemical Conversion** Author: Iban Azcarate, Cyrille Costentin, Marc Robert, et al Publication: Journal of the American Chemical Society Publisher: American Chemical Society Dec 1, 2016

Create

Account

LOGIN

If you're a copyright.com

copyright.com credentials.

Already a RightsLink user or want to learn more?

user, you can login to

RightsLink using your

Home

Help

Copyright © 2016, American Chemical Society

PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 Copyright Clearance Center, Inc. All Rights Reserved. Privacy statement. Terms and Conditions. Comments? We would like to hear from you. E-mail us at customercare@copyright.com



PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 Copyright Clearance Center, Inc. All Rights Reserved. Privacy statement. Terms and Conditions. Comments? We would like to hear from you. E-mail us at customercare@copyright.com

Chapter 2

Thermodynamic and kinetic hydricities of metal-free hydrides

S. Ilic, A. Alherz, C. B. Musgrave and K. D. Glusac, *Chem. Soc. Rev.*, 2018, **47**, 2809 DOI: 10.1039/C7CS00171A

If you are not the author of this article and you wish to reproduce material from it in a third party non-RSC publication you must <u>formally request permission</u> using Copyright Clearance Center. Go to our <u>Instructions for</u> <u>using Copyright Clearance Center page</u> for details.

Authors contributing to RSC publications (journal articles, books or book chapters) do not need to formally request permission to reproduce material contained in this article provided that the correct acknowledgement is given with the reproduced material.

If the material has been adapted instead of reproduced from the original RSC publication "Reproduced from" can be substituted with "Adapted from".

In all cases the Ref. XX is the XXth reference in the list of references.

If you are the author of this article you do not need to formally request permission to reproduce figures, diagrams etc. contained in this article in third party publications or in a thesis or dissertation provided that the correct acknowledgement is given with the reproduced material.

If you are the author of this article you still need to obtain permission to reproduce the whole article in a third party publication with the exception of reproduction of the whole article in a thesis or dissertation.

Information about reproducing material from RSC articles with different licences is available on our <u>Permission Requests page</u>.

Chapter 3



ost Trusted, Most Cited, Most Read





ACS Publications Title: Benzimidazoles as Metal-Free and Recyclable Hydrides for CO2 Reduction to Formate Chern-Hooi Lim, Stefan Ilic, Author: Abdulaziz Alherz, et al Publication: Journal of the American **Chemical Society** Publisher: American Chemical Society Date: Jan 1, 2019 Copyright © 2019, American Chemical Society



PERMISSION/LICENSE IS GRANTED FOR YOUR ORDER AT NO CHARGE

This type of permission/license, instead of the standard Terms & Conditions, is sent to you because no fee is being charged for your order. Please note the following:

- Permission is granted for your request in both print and electronic formats, and translations.
- If figures and/or tables were requested, they may be adapted or used in part.
- Please print this page for your records and send a copy of it to your publisher/graduate school.
- Appropriate credit for the requested material should be given as follows: "Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (YEAR) American Chemical Society." Insert appropriate information in place of the capitalized words.
- One-time permission is granted only for the use specified in your request. No additional uses are granted (such as derivative works or other editions). For any other uses, please submit a new request.

If credit is given to another source for the material you requested, permission must be obtained from that source.



Copyright © 2019 Copyright Clearance Center, Inc. All Rights Reserved. Privacy statement. Terms and Conditions. Comments? We would like to hear from you. E-mail us at customercare@copyright.com

Chapter 4

Importance of proton-coupled electron transfer in cathodic regeneration of organic hydrides

S. Ilic, A. Alherz, C. B. Musgrave and K. D. Glusac, *Chem. Commun.*, 2019, **55**, 5583 DOI: 10.1039/C9CC00928K

If you are not the author of this article and you wish to reproduce material from it in a third party non-RSC publication you must <u>formally request permission</u> using Copyright Clearance Center. Go to our <u>Instructions for</u> <u>using Copyright Clearance Center page</u> for details.

Authors contributing to RSC publications (journal articles, books or book chapters) do not need to formally request permission to reproduce material contained in this article provided that the correct acknowledgement is given with the reproduced material.

If the material has been adapted instead of reproduced from the original RSC publication "Reproduced from" can be substituted with "Adapted from".

In all cases the Ref. XX is the XXth reference in the list of references.

If you are the author of this article you do not need to formally request permission to reproduce figures, diagrams etc. contained in this article in third party publications or in a thesis or dissertation provided that the correct acknowledgement is given with the reproduced material.

If you are the author of this article you still need to obtain permission to reproduce the whole article in a third party publication with the exception of reproduction of the whole article in a thesis or dissertation.

Information about reproducing material from RSC articles with different licences is available on our <u>Permission Requests page</u>.

 \sim