FINAL TECHNICAL REPORT

Awardee: Stanford University

Project Title: Selective Catalytic Oxidations: Opportunities and Challenges for Selective Conversion of Renewable Resources

DOE Award Number: DE-SC0018168

Project Period: 08/15/2017 - 08/14/2021

Yearly Budget: YR 1: $127,216, YR 2: $185,240, YR 3: $237,544

Project PI: Robert M. Waymouth,
Department of Chemistry,
Stanford University, Stanford CA 94305-5080.
Telephone: (650) 723-4515.
Email: waymouth@stanford.edu

Project History, Research Goals and Summary Accomplishments

The goal of this DOE-funded project was to investigate the fundamental science related to selective catalytic oxidation reactions for converting renewable polyhydroxylated bio-feedstocks into new classes of value-added chemicals. The focus was on selective oxidation catalysis, specifically the mechanisms and origin of chemoselectivity for the selective Pd-catalyzed aerobic oxidations of biomass-derived polyols and carbohydrates.

Specific Objectives for this project were to: (1) Investigate the basic science, mechanistic pathways and reactive intermediates generated in the aerobic oxidation of polyols and sugars with highly selective cationic Pd catalysts $[L1Pd(OAc)]_2[OTf]_2$. (**1,** L1 = neocuproine), (2) Investigate the mechanistic origin of the competitive oxidative degradation of **1** and to use these insights to extend catalyst lifetimes and turnover numbers, (3) Investigate the origin of high chemoselectivities for the oxidation of vicinal diols, polyols and unprotected carbohydrates, and (4) Investigate the scope and mechanism of catalytic strategies for the selective catalytic oxidation of diols, polyols and carbohydrates. In the last grant period, significant progress was made on objectives (1), (2), and (4); less progress was made on objective (3) due to an intentional effort to focus on new ligand designs, catalysts, concepts and strategies for selective oxidation reactions. Accomplishments and activities included:

(1) *Extension of catalyst lifetimes and improvement of turnover number for aerobic oxidation of alcohols with cationic Pd neocuproine complexes:*[1] The cationic Pd complex **1** $[L1Pd(\mu\text{-}OAc)]_2[OTf]_2$ (**L1** = neocuproine),[1-10] is an exceptionally chemoselective catalyst for the oxidation of primary and secondary alcohols, vicinal diols, and complex polyols such as carbohydrates.[10-13] This catalyst exhibits high selectivity for the oxidation of secondary alcohols in vicinal diols[3,6-7] and carbohydrates[10-13] to generate α-hydroxyketones.[14-19] The selective oxidation of unprotected polyhydroxylated substrates and carbohydrates provides an alternative to multi-step protection and deprotection strategies,[13,20] and has been used by us[6-7,10] and others[11-13,21-25] for the expedient synthesis of natural products,[25] chemical intermediates[6-7,26] and rare sugars.[10-13,21-23] Catalytic oxidation of α,ω-diols to lactones[27] with **1** provides an expedient synthesis of monomers for ring-opening polymerization.[28-29] Our group has invested effort into examining the wide scope of reactions possible[30-31] with this Pd catalyst and also the mechanistic pathways and reactive intermediates involved in catalysis.[8-9] With Pd catalyst **1**, both air and benzoquinone can be used as terminal oxidants, but aerobic oxidations are accompanied by oxidative degradation of the neocuproine ligand, thus necessitating high Pd loadings. In the last grant period, strategies to improve aerobic catalyst lifetimes were devised, guided by mechanistic studies of catalyst deactivation.[1] Kinetic and mechanistic studies of alcohol oxidation with **1** are consistent with the mechanism outlined in Figure 1.[1] These studies revealed the oxidative degradation of the neocuproine ligand occurs when O_2 or air is used as the terminal oxidant.[2] Several strategies were employed to illuminate the pathways for the oxidative degradation of the neocuproine during aerobic oxidations with the goal of increasing turnover numbers and enabling lower catalyst loadings.[1]

In-operando mass spectrometry studies, in collaboration with the Zare group at Stanford, revealed several ions (**D** and **E**, Figure 1) whose intensities increased in an inverse correlation with the decrease in rate of the aerobic oxidation reactions.[9] These studies collectively revealed that H atom abstraction from the benzylic methyl groups of the neocuproine ligand initiates catalyst degradation.

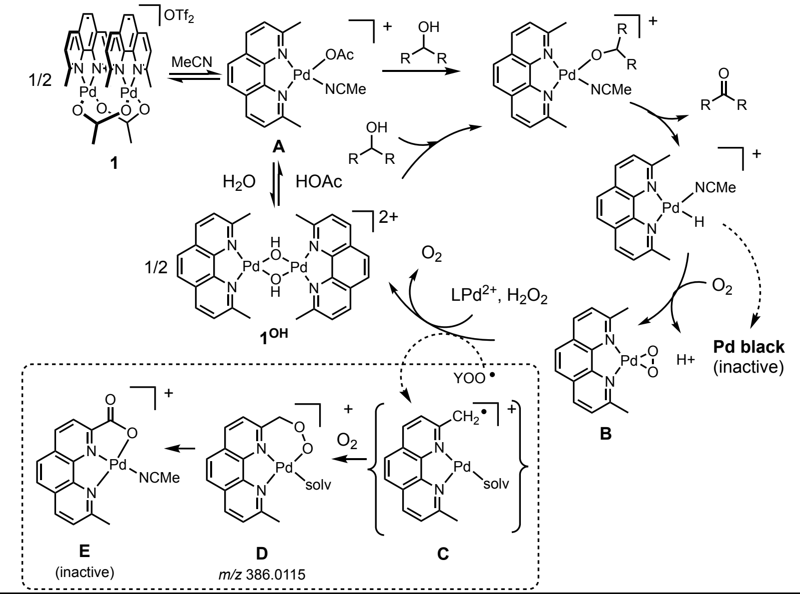

Figure 1. Mechanism of alcohol oxidation with $[L1Pd(\mu\text{-}OAc)]_2[OTf]_2$ and proposed catalyst deactivation pathways. YOO• represents a reactive partially reduced oxygen species.

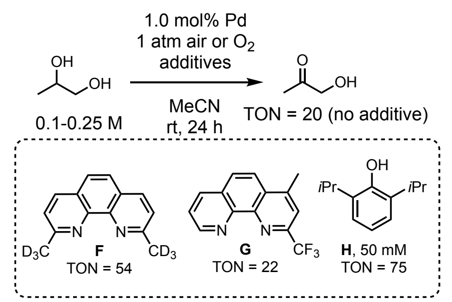

Figure 2. Ligand and additive strategies to increase catalyst turnover numbers (TON).

Guided by this hypothesis, we prepared the d_6-ligand **F**[1,32] and CF_3-substituted ligand **G**,[4] both of which resulted in modest increases in catalyst turnover numbers (from 20 to 54 mole ketone/mole Pd, Figure 2).[1] Sacrificial reductants were also investigated. Phenol anti-oxidants **H** proved a particularly useful additive for mitigating oxidative degradation of the catalyst and styrene additives proved to improve catalyst lifetimes by intercepting Pd hydrides, mitigating the formation of Pd black.[1,10] These insights enabled us to modify our aerobic oxidation protocols for the aerobic oxidation of a variety of polyols on a multigram scale with catalyst loadings as low as 0.25 mol % Pd.[1] Nevertheless, the requirements for stoichiometric additives are not optimal and motivated us to investigate alternative ligand designs.

(2) *New Ligand Designs.* Prior studies revealed that 2,9-substituents on the neocuproine were critical to activity,[2,4] but benzylic hydrogens are oxidative liabilities. To eliminate the vulnerable benzylic C(sp3)-H bonds near the catalyst active site, we prepared 2H-dibenzophenanthroline (**L2**), 2,2'-biquinoline (**L3**, Fig. 3) and the corresponding cationic Pd complexes $[LPd(\mu\text{-}OAc)]_2[OTf]_2$. Catalytic aerobic oxidation of 1,2-propanediol with all three catalysts revealed higher turnover numbers(TON) for catalysts ligated by **L2** and **L3** relative to that with neocuproine **L1**. Aerobic oxidation of 1,2-propane diol (Fig 2) with Pd complex **1** (L1) at 1.0 mol % Pd yielded a TON of 20, whereas Pd complexes **2** (**L2**) and **3** (**L3**) gave TONs of 43 and 84, respectively. Nevertheless, the rate of oxidation of polyol substrates by the new oxidatively robust ligands **L2** and **L3** is substantially reduced compared to the neocuproine system, limiting their synthetic utility. For example, catalytic aerobic oxidation of 1,2-propane diol with the biquinoline ligated Pd complex **3** $[L_3Pd(\mu\text{-}OAc)]_2[OTf]_2$ (**L3** = biquinoline) required > 3 days to reach full conversion at < 2.5 mol% Pd loading. Mechanistic investigations and in-situ mass spectrometry studies suggest that reaction rates with **L3** may be limited due to buildup of a poorly soluble trimeric species $[(LPd)_3(\mu\text{-}O)_2]^{2+}$ (L = 2,2'-biquinoline). Further ligand modifications and mechanistic studies are described in the Project Narrative (Specific Objective 1).

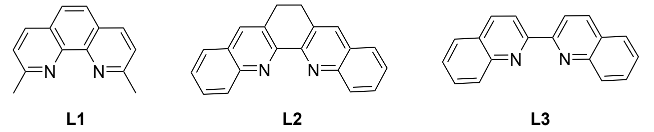

Figure 3. New Ligands L2 and L3.

(3) *Scope and Utility of Chemoselective Catalytic Oxidations:* The fundamental investigations to improve the scope of the Pd-catalyzed alcohol oxidations inspired the development of improved protocols for the oxidation of a variety of diols, polyols and sugars.[1] The new oxidation protocols and additives were used to scale up the aerobic oxidations of diols (Fig. 4a) and glycosides (Fig 4b) with low Pd loadings.[1] The selectivity for secondary alcohols provides a more atom-economical route than the Swern oxidation used for the selective oxidation of the vinyl diol (Fig. 4c) to the keto-aldehyde, a key synthon in the Wender synthesis of Bryostatin 1.[33] Lactones accessed via the Pd- catalyzed oxidative lactonization of α-ω diols provide a new class of monomers (Fig. 4d) which can be polymerized to functional polyesters of precise molecular weight and low polydispersity.[28-29,34]

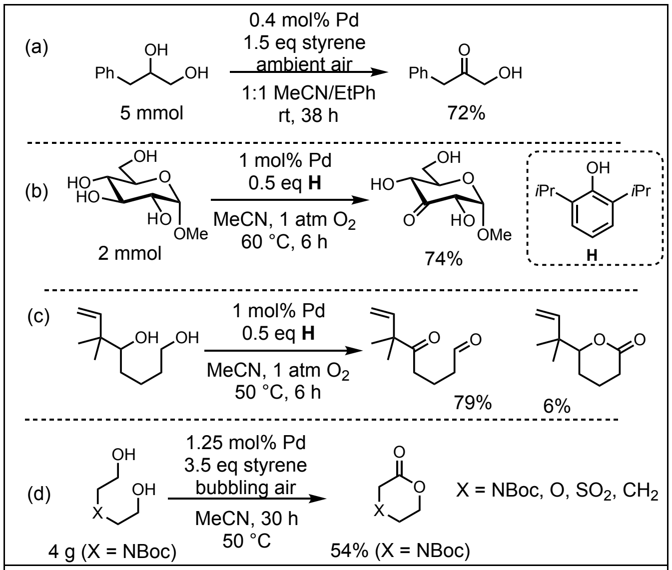

Figure 4. Improved catalytic aerobic oxidations.

(4) *Investigations of other coordination complexes and alternative oxidative strategies for selective alcohol oxidation catalysts.*[35] While these selective catalytic aerobic oxidation reactions with the Pd complexes have proven quite useful, these and other aerobic oxidation systems can suffer from complications due to safety concerns (explosion hazards of O_2 in organic solvents),[36] unselective reactivity from partially-reduced active oxygen species,[1,9] as well as mass transport limitations[37] resulting from the use of gaseous reagents. During the last grant period, we initiated studies to investigate other alcohol oxidation strategies that would avoid O_2 as a terminal oxidant.

We focused on several different coordination complexes and alternative alcohol oxidation strategies, including transfer hydrogenation,[38] acceptorless alcohol dehydrogenation (AAD - the catalytic elimination of H_2 from alcohols),[39-40] as well as electrocatalytic strategies.[24,41-53] We initially targeted a class of Co(II) pincer complexes reported by Hanson[54] that were reported to be effective for the acceptorless alcohol dehydrogenation (AAD) of benzylic alcohols,[55-56] but in-situ investigations by electrospray mass spectrometry (ESI-MS) revealed that vicinal diols bound avidly to the Co complexes and did not turnover readily. Moreover, the Co catalysts precursors/intermediates proved strongly basic, resulting in considerable enolization of aliphatic ketones, extensive deuterium scrambling and competitive aldol reactions.

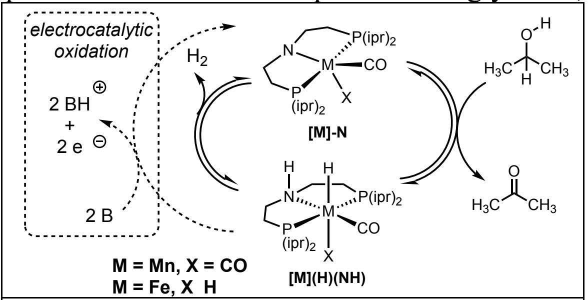

Figure 5. A. Mn and Fe PNP complexes for catalytic acceptorless alcohol dehydrogenation (AAD) and electro-catalytic isopropanol oxidation.

To evaluate whether electrocatalytic oxidations might provide an alternative to aerobic oxidations as a strategy for selective alcohol oxidation reactions, we initiated investigations of a class of Mn[57-59] and Fe[60-63] pincer complexes (PNH$_x$P)Fe(CO)(H)(X) (**[Fe](H)(NH), 6a**: x = 1, X = H; **[Fe]-N 6b** : x = 0, X = 0; PNHP = bis[2-(diisopropylphosphino)ethyl]amine) (Fig. 5) that were reported to be highly active for the acceptorless dehydrogenation (AAD) of alcohols to ketones/aldehydes. As acceptorless alcohol dehydrogenation is a close chemical analog of electrocatalytic alcohol oxidation, we targeted these complexes to evaluate whether electrochemical oxidations might provide an alternate pathway for selective oxidation reactions.[35] While considerable mechanistic and computational investigations of these systems had been carried out,[60-66] little was known of the electrochemical behavior of the Mn and Fe PNP pincer systems.

Cyclic voltammetry of the **[Fe]-N, 6** and **[Fe](H)(NH), 6-H** (Fig. 6) complexes in tetrahydrofuran with $[Bu_4N][BF_4]$ as supporting electrolyte revealed a one-electron irreversible oxidation with an onset at –0.34 V versus ferrocene/ferrocenium ($Fc^{0/+}$) for **[Fe]-N 6** and a one-electron irreversible oxidation with an onset at –0.74 V versus $Fc^{0/+}$ for the corresponding iron hydride **6-H** (Fig. 7). In the presence of a strong base P2 (P2 = (P_2-Et, Et-N=P_2(dma)$_5$,[67] 3 mM) electrochemical oxidation of Fe hydride **6-H** at –0.74 V afforded the Fe amide **[Fe]-N 6**, indicating that the electrocatalytic oxidation of isopropanol might be feasible. Controlled potential electrolysis of isopropanol in the presence of P2 and a catalytic amount FeN at –0.74 V versus $Fc^{0/+}$ reveals acetone to be the two-electron oxidation product, generated with a high Faradaic efficiency (100 ± 15%),[35] but under the conditions of bulk electrolysis (4 h, 25°C, E = -0.74 V, vs. $Fc^{+/0}$) the Fe complex decomposed, leading to low conversions and turnover numbers (TON ~ 2). Thus, while these studies reveal that AAD catalysts are promising candidates as electrocatalysts, the stability of the Fe complexes under conditions of bulk electrolysis provides a limitation to large-scale electrocatalytic alcohol oxidation reactions. These insights will be used to guide the development more stable and long-lived chemoselective alcohol oxidation electrocatalysts.

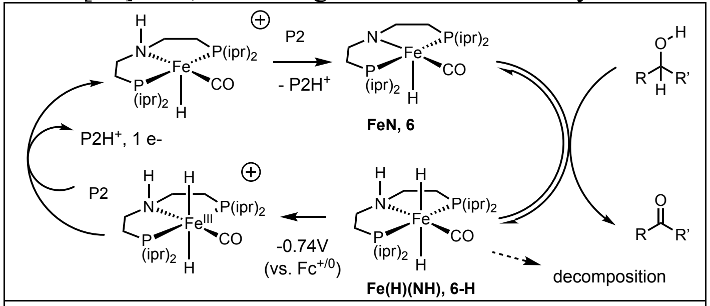

Figure 6. A. Mn and Fe PNP complexes for catalytic acceptorless alcohol dehydrogenation (AAD). Chemoselective AAD with Fe PNP complexes.

List of Publications during last reporting period intellectually driven by DOE Award.

1. Ho, W. C., Chung, K.; Ingram, A. J., Waymouth, R. M. "Pd-Catalyzed Aerobic Oxidation Reactions: Strategies to Increase Catalyst Lifetimes", J. Am. Chem. Soc., **2018**, *140*, 748-757. doi: 10.1021/jacs.7b11372.
2. McLoughlin, E. A.; Matson, B. D.; Sarangi, R.; Waymouth, R. M. “Electrocatalytic Alcohol Oxidation with Iron-Based Acceptorless Alcohol Dehydrogenation Catalyst” *Inorg. Chem.*. **2020**, *59*, 1453-1460. doi: 10.1021/acs.inorgchem.9b03230
3. Wilson C. Ho "Mechanistic Investigation and Optimization of Aerobic Palladium Catalysts and Base-Triggered Degrading Poly(aminoester)s". Ph.D. Thesis, Stanford University, December 2018.

Jointly funded by DOE Award and other grants.

1. Zhang, X.; Fevre, M.; Jones, G. O.; Waymouth, R. M. "Catalysis as an Enabling Science for Sustainable Polymers" *Chem. Rev.* **2018**, *118*, 839-885. doi: 10.1021/acs.chemrev.7b00329.
2. Benner, N. L.; Near, K. E.; Bachmann, M. H.; Contag, C. H.; Waymouth, R. M.; Paul A. Wender, P. A. "Functional DNA Delivery Enabled by Lipid-Modified Charge-Altering Releasable Transporters (CART)s", *Biomacromolecules,* **2018**, *19*, 2812-2824. doi: 10.1021/acs.biomac.8b00401
3. McKinlay, C.J.; Benner, N.L.; Haabeth, O.A.; Waymouth, R. M.; Wender, P.A. "Enhanced mRNA delivery into lymphocytes enable by lipid-varied libraries of Charge-Altering Releasable Transporters" *Proc. Nat. Acad. Sci.*, **2018**, *115(26)*, E5859-E5866. doi: 10.1073/pnas.1805358115
4. Katherine L. Walker, "Mechanisms, Mass Spectrometry & Microdroplets: Using High Resolution Mass Spectrometry to Elucidate Organometallic Reaction Mechanisms" Ph.D. Thesis, March 2018.
5. Colin J. McKinlay, "Organocatalytic Ring Opening Polymerization to Access Functional Nanomaterials for the Delivery of Therapeutically Relevant Molecules and Gene Therapy Targets", Ph.D. Thesis, Stanford, June 2018.

6. Blake, T. R.; Ho, W. C.; Turlington, C.R.; Zhang, X.; Huttner, M. A.; Wender, P. A.; Waymouth, R. M. "Synthesis and Mechanistic Investigations of Rapid Base-Triggered Immolative Cationic Polyesters" *Chem. Sci.*, **2020**, *11,* 2951-2966. doi: 10.1039/c9sc05267d.

References Cited:

1. Ho, W. C.; Chung, K.; Ingram, A. J.; Waymouth, R. M., Pd-Catalyzed Aerobic Oxidation Reactions: Strategies To Increase Catalyst Lifetimes. *J. Am. Chem. Soc.* **2018,** *140* (2), 748-757.
2. Conley, N. R.; Labios, L. A.; Pearson, D. M.; McCrory, C. C. L.; Waymouth, R. M., Aerobic alcohol oxidation with cationic palladium complexes: Insights into catalyst design and decomposition. *Organometallics* **2007,** *26* (23), 5447-5453.
3. Painter, R. M.; Pearson, D. M.; Waymouth, R. M., Selective Catalytic Oxidation of Glycerol to Dihydroxyacetone. *Angew. Chem., Int. Ed.* **2010,** *49* (49), 9456-9459.
4. Pearson, D. M.; Conley, N. R.; Waymouth, R. M., Oxidatively Resistant Ligands for Palladium-Catalyzed Aerobic Alcohol Oxidation. *Organometallics* **2011,** *30* (6), 1445-1453.
5. Simon, J.; Olsson, J. V.; Kim, H.; Tenney, I. F.; Waymouth, R. M., Semicrystalline Dihydroxyacetone Copolymers Derived from Glycerol. *Macromolecules* **2012,** *45* (23), 9275-9281.
6. Chung, K.; Banik, S. M.; De Crisci, A. G.; Pearson, D. M.; Blake, T. R.; Olsson, J. V.; Ingram, A. J.; Zare, R. N.; Waymouth, R. M., Chemoselective Pd-Catalyzed Oxidation of Polyols: Synthetic Scope and Mechanistic Studies. *J. Am. Chem. Soc.* **2013,** *135* (20), 7593-7602.
7. De Crisci, A. G.; Chung, K.; Oliver, A. G.; Solis-Ibarra, D.; Waymouth, R. M., Chemoselective Oxidation of Polyols with Chiral Palladium Catalysts. *Organometallics* **2013,** *32* (7), 2257-2266.
8. Ingram, A. J.; Solis-Ibarra, D.; Zare, R. N.; Waymouth, R. M., Trinuclear Pd3O2 Intermediate in Aerobic Oxidation Catalysis. *Angew. Chem., Int. Ed.* **2014,** *53* (22), 5648-5652.
9. Ingram, A. J.; Walker, K. L.; Zare, R. N.; Waymouth, R. M., Catalytic Role of Multinuclear Palladium–Oxygen Intermediates in Aerobic Oxidation Followed by Hydrogen Peroxide Disproportionation. *J. Am. Chem. Soc.* **2015,** *137* (42), 13632-13646.
10. Chung, K.; Waymouth, R. M., Selective Catalytic Oxidation of Unprotected Carbohydrates. *ACS Catalysis* **2016,** *6* (7), 4653-4659.
11. Jager, M.; Hartmann, M.; de Vries, J. G.; Minnaard, A. J., Catalytic Regioselective Oxidation of Glycosides. *Angew. Chem., Int. Ed.* **2013,** *52* (30), 7809-7812.
12. Eisink, N.; Witte, M. D.; Minnaard, A. J., Regioselective Carbohydrate Oxidations: A Nuclear Magnetic Resonance (NMR) Study on Selectivity, Rate, and Side-Product Formation. *Acs Catalysis* **2017,** *7* (2), 1438-1445.
13. Eisink, N. N. H. M.; Minnaard, A. J.; Witte, M. D., Chemo- and Regioselective Oxidation of Secondary Alcohols in Vicinal Diols. *Synthesis* **2017,** *49* (04), 822-829.
14. Hoyos, P.; Sinisterra, J.-V.; Molinari, F.; Alcántara, A. R.; Domínguez de María, P., Biocatalytic Strategies for the Asymmetric Synthesis of α-Hydroxy Ketones. *Acc. Chem. Res.* **2010,** *43* (2), 288-299.
15. Bøgevig, A.; Sundén, H.; Córdova, A., Direct Catalytic Enantioselective α-Aminoxylation of Ketones: A Stereoselective Synthesis of α-Hydroxy and α,α′-Dihydroxy Ketones. *Angew. Chem., Int. Ed.* **2004,** *43* (9), 1109-1112.
16. Trost, B. M.; Ito, H.; Silcoff, E. R., Asymmetric Aldol Reaction via a Dinuclear Zinc Catalyst: α-Hydroxyketones as Donors. *J. Am. Chem. Soc.* **2001,** *123* (14), 3367-3368.
17. Plietker, B., The RuO4-Catalyzed Ketohydroxylation. Part 1. Development, Scope, and Limitation. *J. Org. Chem.* **2004,** *69* (24), 8287-8296.

18. Hayashi, Y.; Yamaguchi, J.; Sumiya, T.; Shoji, M., Direct Proline-Catalyzed Asymmetric α-Aminoxylation of Ketones. *Angew. Chem., Int. Ed.* **2004,** *43* (9), 1112-1115.

19. Davis, F. A.; Chen, B. C., Asymmetric hydroxylation of enolates with N-sulfonyloxaziridines. *Chem Rev* **1992,** *92* (5), 919-934.

20. Stick, R. V., *Carbohydrates: The Sweet Molecules of Life*. Academic Press: London, 2001; Vol. Chapter 6.

21. Eisink, N. N. H. M.; Lohse, J.; Witte, M. D.; Minnaard, A. J., Regioselective oxidation of unprotected 1,4 linked glucans. *Org. Biomol. Chem.* **2016,** *14* (21), 4859-4864.

22. Jumde, V. R.; Eisink, N. N.; Witte, M. D.; Minnaard, A. J., C3 Epimerization of Glucose, via Regioselective Oxidation and Reduction. *J Org Chem* **2016,** *81* (22), 11439-11443.

23. Zhang, J.; Eisink, N.; Witte, M. D.; Minnaard, A. J., Regioselective Manipulation of GlcNAc Provides Allosamine, Lividosamine, and Related Compounds. *J. Org. Chem.* **2019,** *84* (2), 516-525.

24. Lybaert, J.; Tehrani, K. A.; De Wael, K., Mediated electrolysis of vicinal diols by neocuproine palladium catalysts. *Electrochim. Acta* **2017,** *247*, 685-691.

25. Wu, Z. T.; Jager, M.; Buter, J.; Minnaard, A. J., A protecting group-free synthesis of the Colorado potato beetle pheromone. *Beilstein Journal of Organic Chemistry* **2013,** *9*, 2374-2377.

26. Vu, N. D.; Guicheret, B.; Duguet, N.; Métay, E.; Lemaire, M., Homogeneous and heterogeneous catalytic (dehydrogenative) oxidation of oleochemical 1,2-diols to α-hydroxyketones. *Green Chem.* **2017,** *19* (14), 3390-3399.

27. Xie, X.; Stahl, S. S., Efficient and Selective Cu/Nitroxyl-Catalyzed Methods for Aerobic Oxidative Lactonization of Diols. *J. Am. Chem. Soc.* **2015,** *137* (11), 3767-3770.

28. Blake, T. R.; Waymouth, R. M., Organocatalytic Ring-Opening Polymerization of Morpholinones: New Strategies to Functionalized Polyesters. *J. Am. Chem. Soc.* **2014,** *136* (26), 9252-9255.

29. McKinlay, C. J.; Vargas, J. R.; Blake, T. R.; Hardy, J. W.; Kanada, M.; Contag, C. H.; Wender, P. A.; Waymouth, R. M., Charge-altering releasable transporters (CARTs) for the delivery and release of mRNA in living animals. *Proc. Natl. Acad. Sci.* **2017,** *114* (4), E448-E456.

30. Davis, D. C.; Walker, K. L.; Hu, C. H.; Zare, R. N.; Waymouth, R. M.; Dai, M. J., Catalytic Carbonylative Spirolactonization of Hydroxycyclopropanols. *J. Am. Chem. Soc.* **2016,** *138* (33), 10693-10699.

31. Walker, K. L.; Dornan, L. M.; Zare, R. N.; Waymouth, R. M.; Muldoon, M. J., Mechanism of Catalytic Oxidation of Styrenes with Hydrogen Peroxide in the Presence of Cationic Palladium(II) Complexes. *J. Am. Chem. Soc.* **2017,** *139* (36), 12495-12503.

32. Armenise, N.; Tahiri, N.; Eisink, N. N. H. M.; Denis, M.; Jager, M.; De Vries, J. G.; Witte, M. D.; Minnaard, A. J., Deuteration enhances catalyst lifetime in palladium-catalysed alcohol oxidation. *Chem. Commun.* **2016,** *52* (10), 2189-2191.

33. Wender, P. A.; Hardman, C. T.; Ho, S.; Jeffreys, M. S.; Maclaren, J. K.; Quiroz, R. V.; Ryckbosch, S. M.; Shimizu, A. J.; Sloane, J. L.; Stevens, M. C., Scalable synthesis of bryostatin 1 and analogs, adjuvant leads against latent HIV. *Science* **2017,** *358* (6360), 218-222.

34. Benner, N. L.; Near, K. E.; Bachmann, M. H.; Contag, C. H.; Waymouth, R. M.; Wender, P. A., Functional DNA Delivery Enabled by Lipid-Modified Charge-Altering Releasable Transporters (CARTs). *Biomacromolecules* **2018,** *19* (7), 2812-2824.

35. McCloughlin, E. A.; Matson, B. D.; Sarangi, R.; Waymouth, R. M., Electrocatalytic Alcohol Oxidation with Iron-Based Acceptorless Alcohol Dehydrogenation Catalysts. *Inorg. Chem.* **2020,** *59*, 1453-1460.

36. Osterberg, P. M.; Niemeier, J. K.; Welch, C. J.; Hawkins, J. M.; Martinelli, J. R.; Johnson, T. E.; Root, T. W.; Stahl, S. S., Experimental Limiting Oxygen Concentrations for Nine Organic Solvents at Temperatures and Pressures Relevant to Aerobic Oxidations in the Pharmaceutical Industry. *Organic Process Research & Development* **2015,** *19* (11), 1537-1543.

37. Lin, S.; Tagge, C. D.; Waymouth, R. M.; Nele, M.; Collins, S.; Pinto, J. C., Kinetics of Propylene Polymerization Using Bis(2-phenylindenyl)zirconium Dichloride/Methylaluminoxane. *J. Am. Chem. Soc.* **2000,** *122* (46), 11275-11285.

38. Wang, D.; Astruc, D., The Golden Age of Transfer Hydrogenation. *Chem. Rev.* **2015,** *115* (13), 6621-6686.

39. Balaraman, E.; Nandakumar, A.; Jaiswal, G.; Sahoo, M. K., Iron-catalyzed dehydrogenation reactions and their applications in sustainable energy and catalysis. *Catalysis Science & Technology* **2017,** *7* (15), 3177-3195.

40. Crabtree, R. H., Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev.* **2017,** *117* (13), 9228-9246.

41. Lybaert, J.; Trashin, S.; Maes, B. U. W.; De Wael, K.; Tehrani, K. A., Cooperative Electrocatalytic and Chemoselective Alcohol Oxidation by Shvo's Catalyst. *Adv. Synth. Catal.* **2017,** *359* (6), 919-925.

42. Bonitatibus, P. J.; Chakraborty, S.; Doherty, M. D.; Siclovan, O.; Jones, W. D.; Soloveichik, G. L., Reversible catalytic dehydrogenation of alcohols for energy storage. *Proceedings of the National Academy of Sciences of the United States of America* **2015,** *112* (6), 1687-1692.

43. Bonitatibus, P. J.; Rainka, M. P.; Peters, A. J.; Simone, D. L.; Doherty, M. D., Highly selective electrocatalytic dehydrogenation at low applied potential catalyzed by an Ir organometallic complex. *Chem. Commun.* **2013,** *49* (90), 10581-10583.

44. Bianchini, C.; Shen, P. K., Palladium-based electrocatalysts for alcohol oxidation in half cells and in direct alcohol fuel cells. *Chem. Rev.* **2009,** *109* (9), 4183-4206.

45. Bellini, M.; Filippi, J.; Miller, H. A.; Oberhauser, W.; Vizza, F.; He, Q.; Grutzmacher, H., Hydrogen and Chemicals from Renewable Alcohols by Organometallic Electroreforming. *Chemcatchem* **2017,** *9* (5), 746-750.

46. Serra, D.; Correia, M. C.; McElwee-White, L., Iron and Ruthenium Heterobimetallic Carbonyl Complexes as Electrocatalysts for Alcohol Oxidation: Electrochemical and Mechanistic Studies. *Organometallics* **2011,** *30* (21), 5568-5577.

47. Badalyan, A.; Stahl, S. S., Cooperative electrocatalytic alcohol oxidation with electron-proton-transfer mediators. *Nature* **2016,** *535* (7612), 406-410.

48. Weiss, C. J.; Wiedner, E. S.; Roberts, J. A. S.; Appel, A. M., Nickel phosphine catalysts with pendant amines for electrocatalytic oxidation of alcohols. *Chem. Commun.* **2015,** *51* (28), 6172-6174.

49. Waldie, K. M.; Flajslik, K. R.; McLoughlin, E.; Chidsey, C. E. D.; Waymouth, R. M., Electrocatalytic Alcohol Oxidation with Ruthenium Transfer Hydrogenation Catalysts. *J. Am. Chem. Soc.* **2017,** *139* (2), 738-748.

50. Buonaiuto, M.; De Crisci, A. G.; Jaramillo, T. F.; Waymouth, R. M., Electrooxidation of Alcohols with Electrode-Supported Transfer Hydrogenation Catalysts. *Acs Catalysis* **2015,** *5* (12), 7343-7349.

51. Lancaster, L.; Hickey, D. P.; Sigman, M. S.; Minteer, S. D.; Wheeldon, I., Bioinspired design of a hybrid bifunctional enzymatic/organic electrocatalyst for site selective alcohol oxidation. *Chem. Commun.* **2018,** *54* (5), 491-494.

52. Quah, T.; Milton, R. D.; Abdellaoui, S.; Minteer, S. D., Bioelectrocatalytic NAD+/NADH inter-conversion: transformation of an enzymatic fuel cell into an enzymatic redox flow battery. *Chem. Commun.* **2017,** *53* (60), 8411-8414.
53. Macazo, F. C.; Hickey, D. P.; Abdellaoui, S.; Sigman, M. S.; Minteer, S. D., Polymer-immobilized, hybrid multi-catalyst architecture for enhanced electrochemical oxidation of glycerol. *Chem. Commun.* **2017,** *53* (74), 10310-10313.
54. Zhang, G.; Hanson, S. K., Cobalt-catalyzed transfer hydrogenation of C[double bond, length as m-dash]O and C[double bond, length as m-dash]N bonds. *Chem. Commun.* **2013,** *49* (86), 10151-10153.
55. Zhang, G. Q.; Hanson, S. K., Cobalt-Catalyzed Acceptorless Alcohol Dehydrogenation: Synthesis of Imines from Alcohols and Amines. *Org. Lett.* **2013,** *15* (3), 650-653.
56. Xu, R.; Chakraborty, S.; Yuan, H.; Jones, W. D., Acceptorless, Reversible Dehydrogenation and Hydrogenation of N-Heterocycles with a Cobalt Pincer Catalyst. *ACS Catalysis* **2015,** *5* (11), 6350-6354.
57. Nguyen, D. H.; Trivelli, X.; Capet, F.; Paul, J.-F.; Dumeignil, F.; Gauvin, R. M., Manganese Pincer Complexes for the Base-Free, Acceptorless Dehydrogenative Coupling of Alcohols to Esters: Development, Scope, and Understanding. *ACS Catalysis* **2017,** *7* (3), 2022-2032.
58. Anderez-Fernandez, M.; Vogt, L. K.; Fischer, S.; Zhou, W.; Jiao, H. J.; Garbe, M.; Elangovan, S.; Junge, K.; Junge, H.; Ludwig, R.; Beller, M., A Stable Manganese Pincer Catalyst for the Selective Dehydrogenation of Methanol. *Angew. Chem., Int. Ed.* **2017,** *56* (2), 559-562.
59. Perez, M.; Elangovan, S.; Spannenberg, A.; Junge, K.; Beller, M., Molecularly Defined Manganese Pincer Complexes for Selective Transfer Hydrogenation of Ketones. *Chemsuschem* **2017,** *10* (1), 83-86.
60. Werkmeister, S.; Junge, K.; Wendt, B.; Alberico, E.; Jiao, H.; Baumann, W.; Junge, H.; Gallou, F.; Beller, M., Hydrogenation of Esters to Alcohols with a Well-Defined Iron Complex. *Angew. Chem., Int. Ed.* **2014,** *53* (33), 8722-8726.
61. Chakraborty, S.; Brennessel, W. W.; Jones, W. D., A Molecular Iron Catalyst for the Acceptorless Dehydrogenation and Hydrogenation of N-Heterocycles. *J. Am. Chem. Soc.* **2014,** *136* (24), 8564-8567.
62. Chakraborty, S.; Dai, H.; Bhattacharya, P.; Fairweather, N. T.; Gibson, M. S.; Krause, J. A.; Guan, H., Iron-Based Catalysts for the Hydrogenation of Esters to Alcohols. *J. Am. Chem. Soc.* **2014,** *136* (22), 7869-7872.
63. Bielinski, E. A.; Lagaditis, P. O.; Zhang, Y.; Mercado, B. Q.; Wuertele, C.; Bernskoetter, W. H.; Hazari, N.; Schneider, S., Lewis Acid-Assisted Formic Acid Dehydrogenation Using a Pincer-Supported Iron Catalyst. *J. Am. Chem. Soc.* **2014,** *136* (29), 10234-10237.
64. Yang, X., A self-promotion mechanism for efficient dehydrogenation of ethanol catalyzed by pincer ruthenium and iron complexes: aliphatic versus aromatic ligands. *ACS Catalysis* **2013,** *3* (12), 2684-2688.
65. Jiao, H.; Junge, K.; Alberico, E.; Beller, M., A comparative computationally study about the defined m (II) pincer hydrogenation catalysts (m= fe, ru, os). *Journal of computational chemistry* **2016,** *37* (2), 168-176.
66. Chakraborty, S.; Lagaditis, P. O.; Forster, M.; Bielinski, E. A.; Hazari, N.; Holthausen, M. C.; Jones, W. D.; Schneider, S., Well-Defined Iron Catalysts for the Acceptor less Reversible Dehydrogenation-Hydrogenation of Alcohols and Ketones. *Acs Catalysis* **2014,** *4* (11), 3994-4003.

67. Kaljurand, I.; Rodima, T.; Pihl, A.; Mäemets, V.; Leito, I.; Koppel, I. A.; Mishima, M., Acid−Base Equilibria in Nonpolar Media. 4. Extension of the Self-Consistent Basicity Scale in THF Medium. Gas-Phase Basicities of Phosphazenes. *The Journal of Organic Chemistry* **2003,** *68* (26), 9988-9993.