ELECTRIFICATION AND DECARBONIZATION OF CHEMICAL SYNTHESIS

KARTHISH MANTHIRAM

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA

Synthetic paradigms, such as total synthesis, biosynthesis, and semi-synthesis, have driven significant progress toward synthetic routes with fewer steps. My group is developing a synthetic paradigm in which organic molecules are synthesized and functionalized with CO_2, N_2, and H_2O, using renewable electricity at ambient conditions (Fig. 1). In some cases, the carbon, hydrogen, nitrogen, and oxygen atoms derived from just these three precursors (CO_2, N_2, and H_2O) can be converted into useful products; in other cases, these three precursors can be used to sustainably functionalize petroleum-based and bio-based feedstocks. This paradigm makes use of increasingly available and cheap sources of renewable electricity, providing energy for sustainably driving synthetic steps at mild conditions; this electrification of chemical synthesis, along with the use of CO_2 as a precursor, provides a pathway toward decarbonizing chemical synthesis [1]. Given that the energy and feedstocks required are ubiquitous, the processes are conducive to distributed production of chemicals, close to where they are needed.

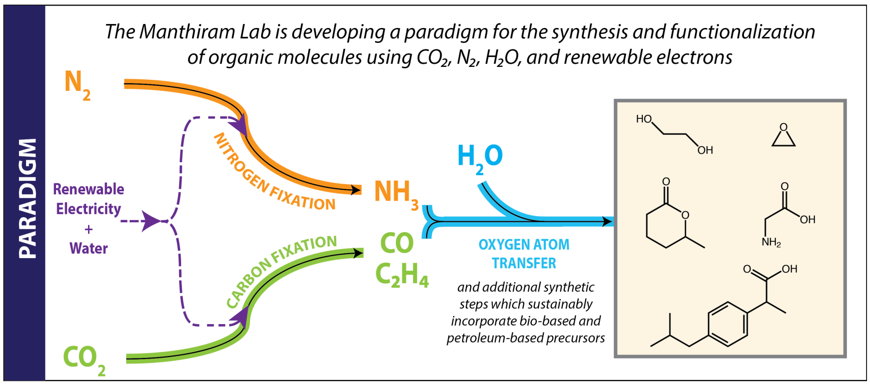

Figure 1. My group is developing a paradigm for the synthesis and functionalization of organic molecules using CO_2, N_2, H_2O, and renewable electrons.

Ammonia synthesis at ambient conditions

The Haber-Bosch process, which involves reacting nitrogen and hydrogen gas at 150-250 bar and 400-500 °C, has served as the dominant method of fixing atmospheric nitrogen to produce ammonia for over a century; ammonia serves as the gateway molecule through which nitrogen functionality is ultimately introduced into diverse molecules. The use of high temperature and pressure limits modularity of the Haber-Bosch process, requiring centralized ammonia synthesis at large scales, which does not match the distributed availability of renewable electricity, such as solar and wind. Electrochemical polarization can allow for overcoming both the use of temperature for improving kinetics and pressure for shifting the equilibrium [1], as well as replacing methane as the hydrogen source with water. My lab has advanced the use of a one-pot lithium-mediated process for ammonia synthesis which operates at ambient conditions (Fig. 2a,b) [2]. Lithium is attractive due to its intrinsic chemical reactivity with nitrogen, which leads to breaking of the nitrogen-nitrogen triple bond through formation of lithium nitride. The lithium nitride can react with protons to generate ammonia and lithium ions; the catalytic cycle is closed by electrochemically reducing lithium ions to produce lithium metal. Through mechanistic studies, we have put forth a coupled kinetic-transport model that quantitatively predicts reactivity, enabling the identification of more selective reaction conditions [2]. This model led to the first recognition of transport limitations in lithium-mediated nitrogen fixation, due to the poor solubility of nitrogen in the electrolyte. Typically, such transport limitations would be overcome through use of a gas diffusion electrode; however, a long-standing challenge in electrochemical architectures has been that commonly-used gas diffusion electrodes based on carbon fibers are easily flooded by non-aqueous solvents due to favorable surface interactions. My lab has developed non-aqueous gas diffusion electrodes based on metal meshes (Fig. 2c), which have less favorable surface interactions with the non-aqueous electrolyte, avoiding flooding and leading to effective contacting of the gas and liquid reactants. This method may be broadly applicable for non-aqueous electrosynthesis involving sparingly soluble reagents [3]. Our approach has led to record Faradaic efficiencies of up to 45% for one-pot ammonia synthesis at higher rates than those previously achieved at ambient conditions in the literature [3]. Cryogenic electron microscopy, typically used in structural biology, has been applied to image the reactive interface between lithium metal and the electrolyte, providing an unprecedented atomic-scale view of how electrolyte composition controls transport of critical reagents through the solid-electrolyte interface. We are developing methods by which the ammonia made through our electrochemical route can then be electrochemically activated [4] for use in downstream synthesis.

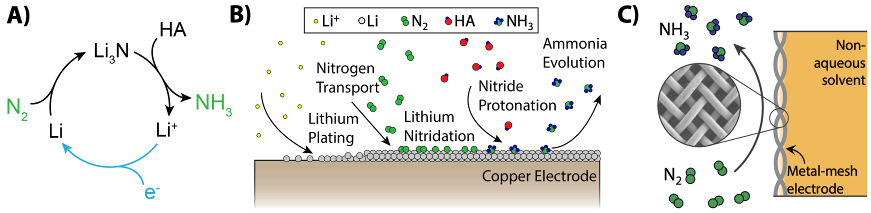

Figure 2. (A) Lithium-mediated reaction network for conversion of N_2 to NH_3 under ambient conditions, involving a proton donor (HA), which is typically ethanol. (B) Schematic of surface processes which occur continuously on the surface of the cathode. (C) Metal mesh-based cell architecture developed in my lab which enhances transport of sparingly soluble gases in non-aqueous solvents.

Electrochemical carboxylation for carbon chain extension

Broader efforts in the field on the electrochemical utilization of carbon dioxide have been focused on reduction of carbon dioxide to relatively simple products, such as carbon monoxide, ethylene, or formic acid. It is important to establish a broader toolkit through which carbon dioxide can be used to synthesize and functionalize more complex organic molecules. To this end, my group has been advancing electrochemical routes for carboxylation.

We have developed an electrochemical route for carboxylation of benzylic C-N bonds using carbon dioxide [5], which can be used to sustainably produce surfactants and pharmaceuticals, such as ibuprofen. This procedure does not require stoichiometric metals, external reducing agents, or sacrificial anodes, which are needed in conventional methods, making column chromatography unnecessary for product purification.

We have extended this methodology to aliphatic halides, dramatically expanding the substrate scope [6]. Importantly, the addition of inorganic salts such as magnesium chloride to the electrolyte allows for stabilization of the carboxylate product over other competing side products, in part by suppressing the nucleophilicity of the carboxylate product. In ongoing work, we have established design principles for solvents involved in carboxylation chemistry, moving beyond the typical screening-based selection of solvents in organic electrosynthesis.

Electrochemical oxygen atom transfer from water

Epoxidation reactions are a subset of oxygen atom transfer reactions in which an olefin is partially oxidized. An epoxidation agent, such as meta-chloroperbenzoic acid or tert-butylhydroperoxide, reacts with the olefin to generate an epoxide and a stoichiometric side product, in this case the corresponding benzoic acid and alcohol, respectively. These epoxidation agents are highly hazardous, and the resulting side products must be separated and dealt with. Other epoxidation methods, such as the direct oxidation of olefins with oxygen, can only be used with a small number of olefins, such as ethylene, and lead to large CO_2 footprints arising from over-oxidation; in fact, the production of epoxides is one of the top five contributors to CO_2 emissions from chemical manufacturing worldwide.

My group has developed a reaction in which *water* is a sustainable O-atom source for olefin epoxidation at ambient conditions; this reaction generates no stoichiometric waste products, involves no hazardous reagents, and operates at ambient conditions [7]. My lab elucidated the mechanism through which a hypothesized metal-oxo species generated from activation of water at a manganese oxide nanoparticle electrocatalyst drives epoxidation. While supporting high rates of epoxidation, our process simultaneously generates hydrogen at the cathode. In a typical water electrolyzer, the oxygen generated at the anode is simply vented; our approach provides a new paradigm through which the oxygen can instead be used for high-volume oxidative functionalization reactions. We have recently developed next generation catalysts for this reaction, involving single atoms of iridium deposited on manganese oxide, which are more selective for electrochemical olefin epoxidation, as the iridium promotes the generation of electrophilic oxygens on the surface [8].

In addition to electrocatalytically generating electrophilic oxygen atoms from water for use in epoxidation, my group has pursued the generation of nucleophilic oxygens from water for use in reactions such as lactonization [9]. Specifically, we have found that platinum can activate water for the conversion of cyclic ketones into branched lactones, providing unique selectivity patterns compared to the conventional Baeyer-Villiger reaction. In ongoing work, we are establishing how water's thermodynamic non-ideality in a blended electrolyte controls rates of oxygen atom transfer.

Outlook to future developments of research on Catalysis for Sustainable Chemistry

The research efforts described above lay a foundation for the effective utilization of CO_2, N_2, and H_2O in chemical synthesis. There are many opportunities for continuing to build on this foundation. For instance, ongoing efforts in my lab are focused on harnessing: 1) CO produced from CO_2 reduction for electrochemical hydroformylation of olefins, 2) NH_3 produced from N_2 reduction for electrochemical reductive amination, and 3) water as an oxygen atom source for C-H activation. These reactions and others will continue to expand the realm of chemical synthesis and functionalization which can be conducted with ubiquitous precursors. These new reactions need to be integrated into multistep syntheses through which one can make more complex monomers or building blocks. For instance, one could also envision routes through which amino acids could be generated abiotically from just carbon dioxide, nitrogen, and water, using the foundational methods developed in my group.

As the complexity of the target molecules increases, it will be important to implement enzyme-inspired design principles which allow for recognition of molecules at an electrode surface in order to direct selective oxidations and reductions at particular sites. This will be especially important for molecules that present sites with similar reactivity or for electrode reactions that otherwise have poor functional group tolerance. The field will also need to develop methods of discriminating molecules on the basis of their transport to an electrode surface as a means of imparting selectivity in reactions involving multi-component mixtures. Substrates can be discriminated in their transport based on size or charge; in a way, this will be a means of integrating separations with electrode reactions. Altogether, these approaches will provide greater fidelity over synthetic steps driven directly at electrode surfaces.

Acknowledgments

K.M. gratefully acknowledges support of work on oxygen atom transfer by the U.S. Department of Energy (DOE) Office of Science, Office of Basic Energy Sciences, Catalysis Science Program, under Award No. DE-SC0020999, work on ammonia synthesis supported by the National Science Foundation under grant no. 2204756, and efforts on carboxylation supported by the National Science Foundation under grant no. 2204757.

References and citations

1. Z. J. Schiffer, K. Manthiram, *Joule* **1**, 10 (2017).
2. N. Lazouski, Z. J. Schiffer, K. Williams, K. Manthiram, *Joule* **3**, 1127 (2019).
3. N. Lazouski, M. Chung, K. Williams, M. L. Gala, K. Manthiram, *Nat. Catal.* **3**, 463 (2020).
4. Z. J. Schiffer, N. Lazouski, N. Corbin, K. Manthiram, *J. Phys. Chem. C* **123**, 9713 (2019).
5. D. Yang, M. Zhu, Z. J. Schiffer, K. Williams, X. Song, X. Liu, K. Manthiram, *ACS Catal.* **9**, 4699 (2019).
6. N. Corbin, D. Yang, N. Lazouski, K. Steinberg, K. Manthiram, *Chem. Sci*. **37**, 12365 (2021).
7. K. Jin, J. H. Maalouf, N. Lazouski, N. Corbin, D. Yang, K. Manthiram, *J. Am. Chem. Soc.* **141**, 6413 (2019).
8. M. Chung, K. Jin, J. S. Zeng, T. Ton, K. Manthiram, *J. Am. Chem. Soc.*, accepted (DOI: 10.1021/jacs.2c04711).
9. J. H. Maalouf, K. Jin, D. Yang, A. Limaye, K. Manthiram, *ACS Catal.* **10**, 5750 (2020).