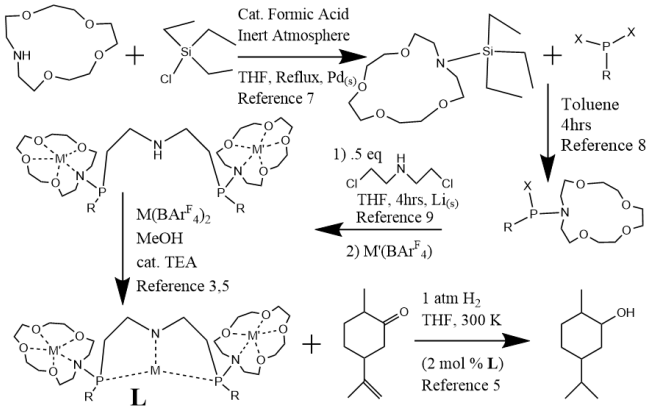
Motivation: Hydrogenation is an especially important industrial reaction that finds uses in pharmaceutical, agrochemical, fragrance, and fine chemical synthesis. 10-20% of chemical reactions at Roche (the world's third largest Biotech company) are catalytic hydrogenations[1], and hydrogenation of N_2 to NH_3 consumes an estimated 2% of the world's energy supply. Supramolecular chemistry utilizing adjustable hemilabile ligands that approximate enzymatic activity has been an extremely active area of research, and hydrogenation can be improved significantly with respect to its chemoselectivity by tuning the catalyst to minimize over-hydrogenation. Mirkin *et al.* have constructed elegant 'molecular tweezers' that take advantage of chloride binding and supramolecular interactions to create switchable on/off catalytic turnover[2]. Miller *et al.* have recently published a PCN (phosphorous-carbon-nitrogen donor atoms) pincer ligand that takes advantage of macrocycle-cation interactions to enable both switchable and tunable catalytic activity[2]; however, this ligand's catalytic potential has not yet been fully realized. Cation interaction with the macrocycle can speed the catalyzed reaction rate of olefin isomerization by over three orders of magnitude[3]. *In situ* control of catalytic activity via hemi-lability of crown ether/cation interactions will revolutionize homogenous hydrogenation catalysis. The ability to completely quench catalysis via addition of an anion, resulting in precipitation of a simple salt and re-coordination of the unoccupied crown-ether to the catalytic metal center, will give a new degree of control to hydrogenation catalysis. This will eliminate over-hydrogenation, a well-documented issue with isophorone, an essential polycarbonate precursor[4] as well as other feedstocks.

Enzymes are notable for their ability to use first-row transition metals to catalyze a wide variety of molecular transformations. These metals are generally more abundant, less toxic, and easier to dispose of than their heavier isoelectric counterparts. Replacing precious metals with 'greener' options is of vital importance to sustainable chemistry. Hanson *et al.* have reported an air- and water-stable Co(II) complex with a pincer ligand that is capable of hydrogenating alkenes, aldehydes, ketones, and imines at low pressures of gaseous hydrogen (1-4 atm) and low temperatures (>60°C)[5]. A Re complex with PNP was recently reported to activate N_2, but does not have switchable or tunable properties[6].

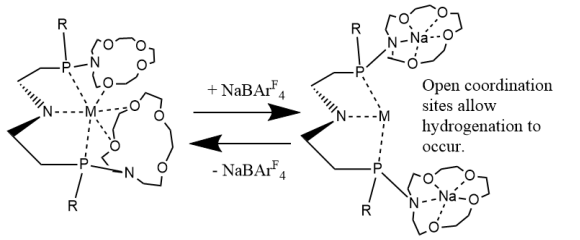


Scheme 1: Synthetic route for **L**. X= Halide; M= Co (II), Ir (II), Re (II), Rh (II); M'=Na^+, Li^+, Ca^{2+}; R=Ph, Me, Cy.

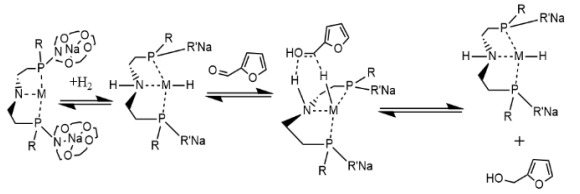
Research Plan: Pincer ligands are attractive due to their thermal and oxidative stability as well as ease of modification. I hypothesize that installing a hemi-labile macrocycle to a PNP ligand will allow significant switchable and tunable activity of an established homogenous hydrogenation catalyst. The synthesis of a novel ligand is shown in **Scheme 1** using commercially available starting materials and known methodology. The phosphine, macrocycle, secondary amine, and metal ions can all be varied to generate a large library of complexes for catalytic analysis. The double crown ether moieties are hypothesized to increase the tunability of catalysis even further than the published example by Miller *et. al.* Tunable steric bulk arising from the cation complexed crown-ethers, is hypothesized to allow for substrate specificity in hydrogenation.

Coordination of a vacant crown-ether to the catalytically active metal will block the association of H_2 that must take place for catalysis to occur; however, when a Group 1 or 2 cation

binds to the crown ether, it will detach from the Co(II) and allow H_2 to access and be activated by the transition metal (**Scheme 2**). My first goal will be to optimize of the synthesis and purification of **L**. Characterization of **L** will include single crystal XRD, mass spectrometry, and NMR. Determination of the stability of **L** to air and water, and its solubility, will be essential to further analysis of the complex.



Scheme 2: Showing the switchable activity of **L**.



Scheme 3: A proposed mechanism for the hydrogenation of furfural to furfuryl alcohol.

My second goal is to assess the ability of **L** to catalyze the selective hydrogenation of furfural. Furfural is a popular industrial feedstock that is a bio-based renewable building block for a wide range of polymers and fertilizers. Selective hydrogenation of furfural to furfuryl alcohol is a vitally important part of functionalization, and often requires the use of noble metals[10]. It is presumed that hydrogenation using Ir(II) will occur readily for a variety of alkenes, alkynes, imines, and carbonyls through redox pathways as there is significant precedent for this in literature. A mechanism showing the hypothesized hydrogenation is shown in **Scheme 3**. Besides furfural, it is hypothesized that this same mechanism should allow for selective hydrogenation of substituted benzaldehydes and cyclohexenes, two other classes of molecules that that are of high industrial importance. Screening multiple **L** complexes with an array of substrates, under varying reaction conditions will identify trends to investigate in further studies. Addition of anions to the reaction solution is hypothesized to result in a switchable activity. The identity of the cation used to dislodge the crown-ether from the active site, is also expected to result in tunable rates of reaction, with Group 2 likely exhibiting the fastest rate as the fit best within the crown ether.

I will then determine whether earth abundant Co(II) can substitute Ir(II) in the catalysis. Hanson *et al*. assert that the mechanism of hydrogenation proceeds through a Co(II) hydride intermediate, and that the coordination of a secondary amine to the metal center is essential[5]. It is hypothesized that although 3d catalytic pathways often favor one-electron processes due to size, as **L** still contains the secondary amine, hydrogenation via reductive elimination of the hydride intermediate can still occur. Use of deuterium-labeled H_2 and solvents to probe the catalytic mechanism will result in crucial fundamental research in this budding class of catalysis. Mechanistic study of catalytic cycles is an important area of fundamental research, and it is necessary to improve selectivity and turnover, or to design complementary catalysts.

Broader Impacts and Intellectual Merits: Earth abundant metals are cheaper, safer, and greener alternatives when used as catalysts, and this is an important aspect of establishing sustainable chemistry as well as increasing the long-term economic security of the U.S. by decreasing dependence on unstable sources of precious metals. The work will also contribute to our fundamental knowledge of switchable and tunable catalysis which is a relatively new and unexplored area.

1) *Curr Opin Drug Discov Devel.*, **2001**, 4(6), 745-755. 2) *Science*, **2010**, 330, 66-69. 3) *J. Am. Chem. Soc.*, **2014**, 136, 14519-14529. 4) *J. Am. Chem. Soc.*, **2015**, 137, 12121-12130. 5) *J. Am. Chem. Soc.*, **2013**, 135, 8668-8681. 6) *J. Am. Chem. Soc.*, **2018**, 140, 7922-7935. 7) *ACS Catal.*, **2017**, 7, 1720-1727. 8) *Russ. J. Gen. Chem.*, **1986**, 56(8), 1777-1781. 9) *J. Organomet. Chem.*, **2017**, 845, 82-89. 10) *Sci. Rep.*, **2016**, 6, 28558.