NADH-TYPE HYDRIDE STORAGE ON A FUNCTIONAL LIGAND AND ITS APPLICATION IN HYDROGEN TRANSFER CATALYSIS

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NADH is an important cofactor that plays a critical role in most oxidoreduction enzymatic processes relying on reversible storage of the hydride on the nicotinamide moiety (Fig. 1a). However, NADH is limited in its industrial application by its stoichiometric utilization resulting in high cost of the process. To tackle this challenge and diminish the overall price, several cofactor regeneration systems were developed based on enzymatic or transition metals hydride transfer catalysis for in-situ regeneration of NADH (Fig. 1b). However, the increasing complexity of the system makes this reaction less effective and less convenient.[1],[2]

Our group recently published an iridium complex bearing a pyridylidene-amines (PYEs) ligand that was successfully applied in the dehydrogenation of formic acid.[3] Interestingly, ligand optimization showed a unique functional ligand-type reactivity where the hydride is stored on the heterocycle ring, **^{Ir}PYEH**, mimicking an NADH-type reactivity (Fig. 1c). We studied herein the reactivity of **^{Ir}PYEH** with different electrophiles and acids to generate **^{Ir}PYE^{+}**, and its in-situ reversible regeneration by sequential addition of formate. The hydride and deuteride transfer mechanism were investigated using deuterated formate source, deuterated catalyst, and low temperature ^{1}H NMR spectroscopy. **^{Ir}PYE(H)** is a highly active and robust hydride transfer catalyst for aldehydes and ketones reduction (TON of 100,000), in mild condition (40 °C) where **^{Ir}PYE(H)** is transferring the hydride directly to the substrate and is self-regenerated in solution (Figure 1d). Unlike known metal–Hydride catalyst, minimal scrambling was observed in presence of water that allowed selective isotope labeling using equimolar amount of Deuteride offering a green, cost-efficient, and simple alternative to known system.

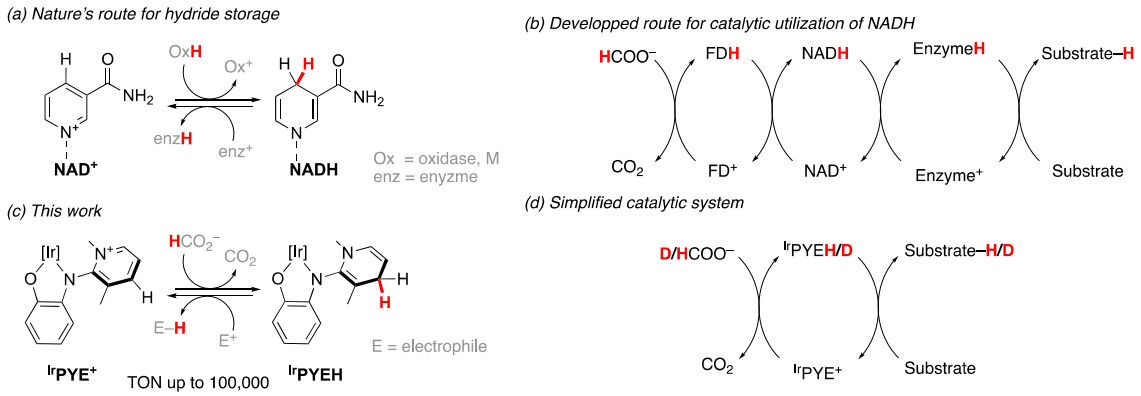

Figure 1.

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[1] L. Sellés Vidal, C. L. Kelly, P. M. Mordaka and J. T. Heap, *Biochim Biophys Acta Proteins Proteom*, **2018**, 1866(2), 327–347.

[2] H. Wu, C. Tian, X. Song, L. Chuang, D. Yang and Z. Jiang, *Green Chem.* **2013**, *15*, 1773–1789.

[3] N. Lentz and M. Albrecht, *ACS Catal.* **2021**, *12*, *20*, 12627–12631.