

Accessing Reactive Metal Hydrides Through Designed Heterometallic Bridges

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Abstract Methodology to access reactive hydride moieties is highly desired yet limited. Multimetallic hydride fragments have been notable in their heightened reactivity and catalysis but deliberate access to these species is lacking. In this highlight, we discuss recent developments by our group in the design of a new heterometallic complex which invokes architectures designed to provide modular access to reactive hydride moieties by leveraging metal hydrides in combination with pendant donors to the model heterotrimetallic Ni-(Al-H)₂ complex (**1**). An amplification of insertion-based reactivity was examined in the hydrofunctionalization of quinolines, and complex **1** substantially outperforms the parent aluminum hydride LAIH. Potential rationale for the dramatically increased reactivity and further examination of these motifs and methodology in catalysis are also discussed.

1. Introduction
2. Heterometallic Hydride Design and Characterization
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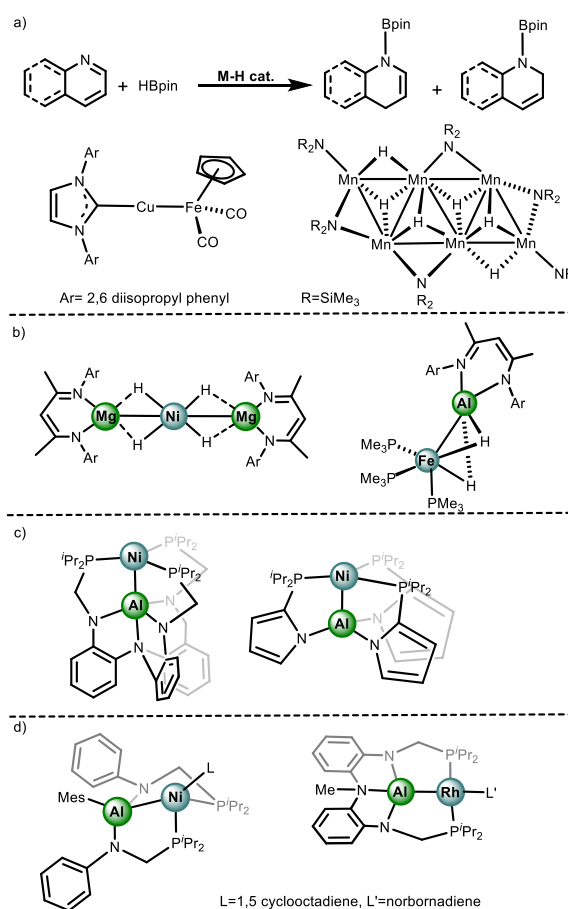
Key words Heterometallics, Cooperativity, Hydrofunctionalization, hydride, Lewis Acids, base metal

Introduction

Inspired by Nature and heterogenous systems, facile access to diverse sets of multimetallic complexes has been of long-standing interest, with overarching goals of sustainable molecular catalysis.¹ The current reliance of precious metals in homogenous catalysis has served as a major impetus in the development of catalytically competent multimetallic systems incorporating more abundant metal elements.² The past few decades have demonstrated increasing reports of transition metal-mediated catalysis operating via multimetallic assemblies through both *in-situ* generation as well as well-defined species.³

Transition metal hydrides are prominent moieties in catalysis due to their prevalence in a plethora of insertion-based transformations.⁴ Furthermore, multimetallic hydride complexes have demonstrated impressive bond transformations generally inaccessible by monometallic species, including skeletal rearrangements of aromatic species,⁵ single component multielectron reduction of dinitrogen,⁶ and others.⁷ The heightened reactivity of the multimetallic hydride, in both homometallic and heterometallic systems, has been postulated to

be the result of a more nucleophilic nature within the hydride moiety. Cooperative reactivity invoking Earth-abundant multimetallic hydrides has also been demonstrated catalytically through transformation of *N*-heterocycles. Mankad et al. demonstrated that a heterometallic Cu-Fe complex can hydrofunctionalize *N*-heterocycles via *in-situ* generation of a



Scheme 1: a) Select examples of multimetallic quinoline dearomatization. b) Heterometallic hydride complexes with non-tethered ligands c) Heterometallics in caged architectures. d) Tethered heterometallics with more coordinatively open systems.

reactive Cu-H species.⁸ Hexanuclear Mn-H complexes have also been demonstrated to be competent hydrofunctionalization catalysts with wide scope (Scheme 1a).⁹ Towards development of a more thorough understanding of the heightened reactivity, facile and modular access to multimetallic hydrides is needed. Unfortunately, the synthetic methods are often non-selective in the formation sought-after multimetallic complexes. This is especially true when aiming to install hydride or alkyl groups on metal centers as they often undergo protonolysis or elimination-based reactivity.¹⁰

The use of heterometallic species, especially the combination of Lewis acidic and Lewis basic metals, is desirable from demonstrated synergistic effects in bond activation.¹¹ Early examples stem from olefin oligomerization studies where Ni salts and aluminum activators yielded selective formation of α -olefins, labelled as “the Nickel effect”.¹² Since these seminal findings, Al-based activators have been featured prominently in olefin oligomerization/polymerization studies in concert with transition metal catalysts. The use of Lewis acidic additives has observed continued growth in catalysis and has led to more sophisticated ligand design, interrogated in catalytically-relevant processes including modulating redox-potential, hydroformylation, hydrofunctionalization, polymerization chemistry, etc.¹³ Recently, examples of well-defined heterometallic complexes with bridging hydrides have emerged and demonstrate exciting reactivity including hydrogenation and C-H bond activation (Scheme 1b).¹⁴ Further work is needed to identify methodology to access reactive hydride moieties in a modular manner.

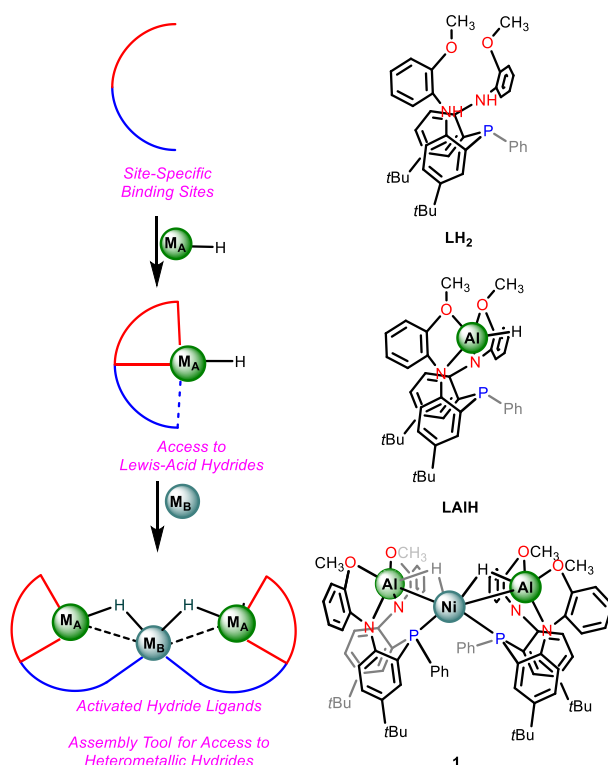
In the interest of developing heterometallic species to carefully interrogate systems with an appended σ -accepting LA, systems with site-specific binding sites have been developed by the groups of Iwasawa, Lu, Ozerov, among others.¹⁵ While these examples demonstrate the utility of site-specific binding sites in structure and reactivity, the nature of the ligand design impedes the ability for the LA to bind to incoming substrates and participate directly in bond-breaking or bond-making steps (Scheme 1c). The strategy of utilizing multiple metal centers in a more coordinatively unsaturated mode is highly sought after, but building the necessary motifs is a continued challenge due to the propensity for unsaturated LA complexes to form oligomeric species. Progress in this area has been made with recent examples from Nakao, who reported a Rh-Al scaffold with an Al center able to coordinate to incoming substrates, and Lu similarly demonstrated evidence of substrate binding with Ni and Al (Scheme 1d).¹⁶ Sterically-accessible heterometallic units with well-defined hydride moieties remain a synthetic challenge.

Our group has taken a keen interest in identifying approaches in synthesizing activated heterometallic hydrides relevant to catalysis. We sought to develop methodology to access reactive metal hydride moieties through the design of new heterometallics. Despite select examples outlining the described design elements, the effectiveness of the 3-center-2-electron leveraged in the synthesis of multimetallic complexes warrants further exploration. We set on utilizing metal-hydride ligand as a building block in the assembly of heterometallic motifs and simultaneously serving to activate hydride moieties. This methodology would be integrated into catalytic studies and serve

as a springboard to interrogate varying LA properties and gain insight to LA-H bonds as donors.¹⁷

Heterometallic Hydride Design and Characterization

Our group began development of a heterotrimetallic NiAl₂ hydride system following the rationale of metalloligand design with site-specific binding sites: utilizing soft neutral donors for late metals and hard anionic donors for Lewis-acidic metals (Scheme 2; top). The incorporation of the coordination site for LAs are present within the functionalized aryl groups on the phosphine ligand which hinder coordination of the LA to the phosphorous center while encouraging interaction with a transition metal center (**LH₂**). Furthermore, the eventual dianionic nature of the “hard” binding site positions group 3 and 13 metal hydride moieties to generate a LA-H metalloligand (Scheme 2; middle). The weak methoxy donors are incorporated to offer a degree of stabilization to the incoming LA. Assembling the hard donors on the functionalized aryl groups of the phosphine ligand allows the remaining hydride in group 13 metals such as Al to have a hydride directed towards an incoming metal center. Indeed, metalation of Al demonstrates coordination to anionic amide donors, forming **LAIH**. This system is then poised to interact with the uncoordinated phosphorous center and to be further stabilized by the metal hydride. Metalation with Ni(COD)₂ results in the formation of the heterotrimetallic hydride species **1** (Scheme 2; bottom), adding



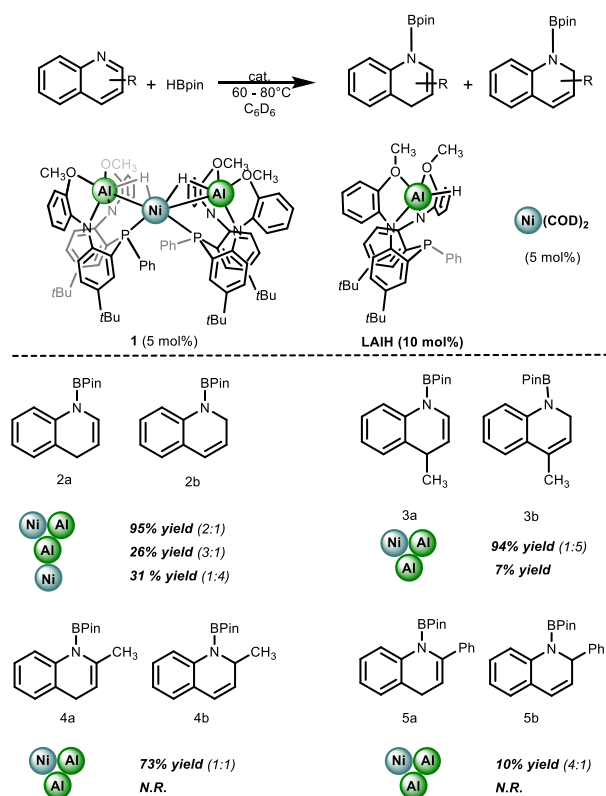
Scheme 2: Methodology for modular access to heterometallic hydrides using site specific-ligand binding and a platform to encourage 3-center-2-electron bonding motifs.

to the short list of bridged hydrides between Al and Ni centers.¹⁸

To compare hydride bearing species **LAIH** and complex **1**, NMR spectroscopy is highly instructive. The ³¹P{¹H} NMR chemical shift provides a method to track the coordination of the

phosphorus center and demonstrates that the metalloligand features an Al that participates in minimal interaction with the phosphorous center, while complex **1** has a chemical shift consistent with a bound phosphorous center. Intriguingly, the hydride chemical shift in the ^1H NMR spectrum bears a dramatic change between **LAIH** and **1** moving from approximately 5.2 ppm to -1.5 ppm. This finding is consistent with nickel silane/silyl hydride species where the chemical shift strongly suggests the interaction of both metals to the hydride in a 3-center-2-electron motif.¹⁹

The solid-state structure of the complex showed that the Ni center takes a distorted tetrahedral symmetry with respect to the phosphines and hydride ligands with a τ_4 value of ~ 1.0 . The



Scheme 3: Catalysis results in dearomatization of quinolines. Evidence of cooperative impact by using complex **1** in comparison to **LAIH** as well as $\text{Ni}(\text{COD})_2$.

geometry suggests that complex **1** lies closer to the neutral alane side of the continuum of sigma bonding in comparison to an anionic alumanyl designation. The treatment of the alane moieties as neutral donors to a $\text{Ni}(0)$ species would render the species a tetrahedral 18 electron $\text{Ni}(0)$ species, the formality of oxidation states of systems invoking Lewis-acidic atoms bound to transition metal centers have been deliberated elsewhere.²⁰ The proximal distance between Ni and Al suggests a Z' based designation of the Al-H moiety to Ni similar to B-Ph fragments of Peters' nickel borane systems;²¹ albeit further studies are needed to gain insights into the electronic structure.

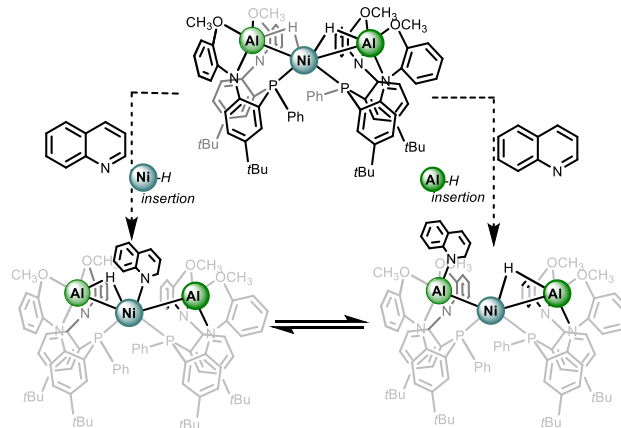
The formal assignment withstanding, the change in the hydride chemical shift between **LAIH** and **1** along with structural evidence of close interactions within the Al-H-Ni subunit

demonstrates an electronic interaction between the three units poised for exploration.

Catalysis

To demonstrate the impact of the tailored heterometallic hydride in **1**, we chose a model reaction to compare the **LAIH** and the **1**. Quinoline hydrofunctionalization represents an important transformation relevant to pharmaceuticals, agrichemicals, and functional materials and is a reaction both main group hydrides and Ni are capable of catalyzing.²² In our work we presented catalysis carried out by **1** which demonstrated significantly higher rate of consumption for quinoline during hydroboration in comparison to its metal hydride precursor **LAIH** (Scheme 3). We tested both complexes by performing hydroboration with quinoline variants with sterically differentiating profiles and found that complex **1** handily outperformed **LAIH**. In the hydroboration of quinoline, **1** demonstrated a k_{obs} of quinoline decay more than 400x greater than **LAIH**. To compare to Ni based precursors, $\text{Ni}(\text{COD})_2$ and the combination of $\text{Ni}(\text{COD})_2$ and phosphine donors were also tested and also showed low yield tested under similar conditions. In the cases with more sterically encumbering quinolines, **LAIH** showed no formation of hydroborated species while complex **1** showed good yield for 2-methyl quinoline and low yield for 2-phenyl quinoline, which was previously not reported. For all examples, complex **1** demonstrated an amplification in catalytic ability, potentially attributed to a more active hydride species with a more facile insertion step. Ongoing studies towards providing more evidence of this synergistic amplification of hydrofunctionalization ability have provided additional insight.

We reported stoichiometric reactivity of **1** with quinoline resulting in a dearomatized quinoline, consistent with hydride transfer, which was unobserved in all other control studies supporting the occurrence of a cooperative insertion. Several aspects about the studied insertion step provide intrigue. One example is identifying, prior to insertion, if the hydride ligands retain the bridged nature or if there is a rearrangement in which anionic alumanyl centers are accessed. Whether or not the amplification is aided by potential access to alumanyl systems warrants further exploration. Sigma complexes of B-H to Ni which serve as a masked $\text{Ni}(\text{II})$ system with anionic boryls, are known.²³ Assuming retention of a heterotrimetallic core,



Scheme 4: Representative pathways of potential insertion.

pathways of hydride transfer can be simplified to a heterometallic Ni-H vs Al-H based insertion where the former requires the formally Ni(II) aluminyl support (Scheme 4). Characterizing and isolating intermediates would provide further support for the synergy of both metals, and current experiments in this realm are ongoing. In addition, exploring whether potential insertion complexes can access both alane and aluminyl designations interchangeably as depicted in the bottom of Scheme 4. An area of intrigue also involves exploring whether complex **1** retains the heterotrimetallic configuration or if there are fragmentation steps involved. To this end, investigating systems with more robust coordination to Ni, to hinder potential disassembly of components of the framework, can offer insight for the operative mechanisms.

Summary and Outlook

Our group has made strides towards the development of new methodology for amplifying reactivity of metal hydrides. Given the prevalence of metal hydrides in a number of catalytic transformations, identifying new ways to toggle and/or amplify activity is potentially transformative. The reactivity of the current complexes has been tested through hydrofunctionalization of *N*-heterocycles and has showed a greater than 400-fold increase in quinoline consumption. In the realm of catalysis, further reactivity and studies of expansion of scope are underway. Also exploring ways to potentially impact selectivity of reactivity is of great interest within our systems.

Access to complexes such as **1** has sparked new opportunities to gain direct insight towards amplification of hydride reactivity. Gaining a better understanding of electronic distribution within the Ni-H-Al subunits is crucial to aid in our cumulative understanding of the amplification. Exploring perturbation of electronic density within the Al-H-Ni subunit and examining the impact of catalytic insertion can also aid in identifying design elements conducive to more challenging catalytic insertion. Si-H-Ni systems benefit from coupling constant analysis²⁴ but the quadrupolar nature of Al obfuscates this level of assignment in our complex, therefore new quantitative experimental tools are needed to investigate these rare motifs. Lastly, leveraging the ligand motif in examination of varying Lewis-acidic metals can offer access to coordinative substrate binding in addition to further amplification of hydride ligands to ingress towards unprecedented reactivity transcending purely insertion-based mechanisms.

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Conflict of Interest

The authors declare no conflict of interest

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Biosketches



Manar M. Shoshani (middle) grew up in Ontario, Canada. He obtained his PhD at the University of Windsor under the guidance of Prof. Samuel Johnson. From 2018-2021 he conducted his postdoctoral research with Prof. Theodor Agapie at the California Institute of Technology. In 2021, he began his independent career at the University of Texas Rio Grande Valley, as an Assistant Professor in the Department of Chemistry.

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