Cooperative Strategies for Catalytic Hydrogenation of Unsaturated Hydrocarbons

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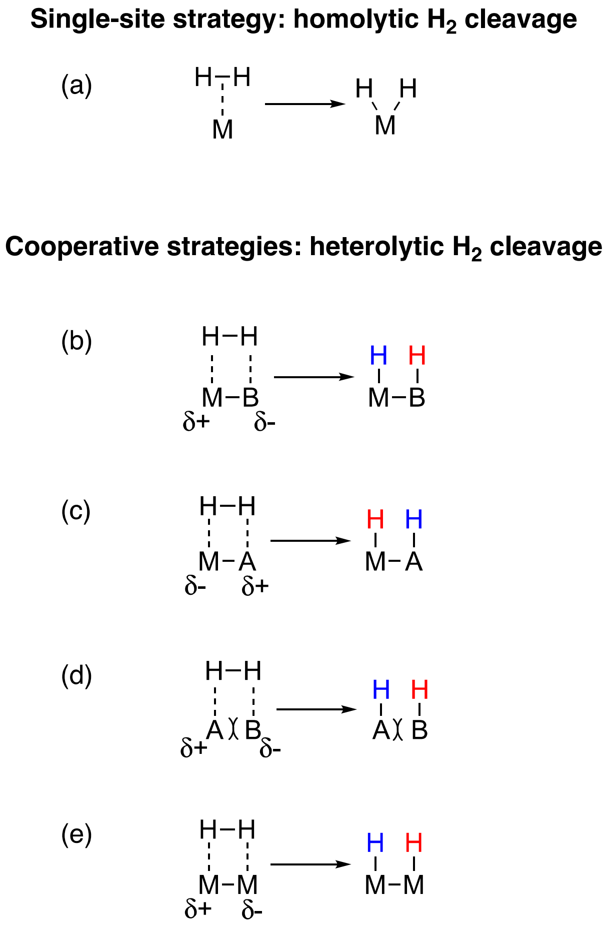
ABSTRACT. This Perspective discusses catalytic hydrogenation reactions of alkenes, alkynes, and other unsaturated C-C substrates in which the catalyst design involves cooperative strategies that enable bifunctional H_2 activation and delivery. These approaches complement the more traditional use of single-site precious metal systems for such hydrogenation reactions in homogeneous catalysis. Strategies included in this Perspective are cooperation between (a) a catalytic metal site and a basic ligand residue, (b) a catalytic metal site and an acidic ligand residue, (c) frustrated acid/base pairs, and (d) two co-catalytic metal sites. Unique reactivity and selectivity patterns with non-precious elements that have emerged from successful implementation of these strategies in catalytic transformations are emphasized.

KEYWORDS. Hydrogenation, cooperative, bifunctional, heterolytic cleavage, alkene, alkyne, hydrogen

Introduction

Hydrogenation catalysis represents a unique confluence in organometallic chemistry of industrial utility and fundamental interest. Catalytic hydrogenation is utilized industrially on enormous scales to produce bulk, commodity, and fine chemicals.[1] Asymmetric hydrogenation is one of the landmark contributions of homogeneous catalysis to industrial chemical production, as marked by the 2001 Nobel Prize in Chemistry. In terms of fundamental science, catalytic hydrogenation has played a crucial role in providing the intellectual framework for catalytic mechanisms more generally. In part, this is because hydrogenation catalysis inherently relies on activation of H_2, which not only is the simplest of all molecules but also features a non-polar (and thus relatively inert) bond. Fundamental understanding of how well-defined catalysts cleave the H_2 molecule and deliver it to substrates, therefore, provides a working model that can be extrapolated for bond cleavage processes and inert substrate activation reactions in arenas beyond just hydrogenation itself.

This Perspective focuses on innovative strategies for catalytic hydrogenation of C-C multiple bonds. As discussed below, much of the homogeneous catalysis literature regarding hydrogenation reactions involves precious metal catalysts with a single reactive site. Recent innovations beyond this dominant paradigm that employ cooperative behavior of two reactive sites are the focus here. The promise of pursuing such novel strategies include the potential for non-precious metal catalysis to be enabled, and more importantly for the potential emergence of unique reactivity and selectivity patterns that complement those of single-site precious metal catalysis. However, a challenge in this area derives from the heterolytic H_2 cleavage processes inherent to most of the cooperative design strategies. The resultant polarization of the non-polar H_2 into protic and hydridic entities within the catalyst is well suited for hydrogenation of polar bonds (e.g. C=O, C=N) but ill-suited for hydrogenation of non-polar bonds (e.g. C=C). To focus the discussion on this challenge inherent to bifunctional catalysis, this Perspective omits catalytic hydrogenation of polar substrates and focuses only on hydrogenation of C-C multiple bonds. Also omitted are catalytic transfer hydrogenation where H_2 is not the stoichiometric reductant, multimetallic catalysis with cluster compounds where mechanism is not well defined or well understood,[2] and the vast area of heterogeneous catalysis. Because cooperative design strategies are frontier areas in active catalysis research, this Perspective on cooperative strategies that enable bifunctional delivery of H_2 to non-polar hydrocarbon substrates is of timely value.

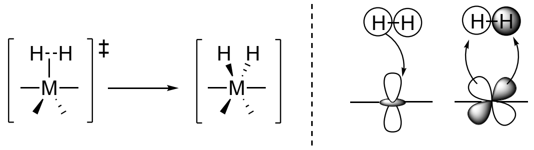


Scheme 1. Catalyst design strategies for H_2 activation and delivery. Here and in subsequent schemes, protic hydrogens are colored red and hydridic hydrogens are colored blue. M = metal, B = base, A = acid.

In this Perspective, after providing a brief overview of single-site catalysts involving homolytic H_2 oxidative addition (Scheme 1a), multiple cooperative strategies to enable bifunctional H_2 activation and delivery are discussed. Two strategies involve cooperation between a catalytic metal site and a reactive ligand residue within the metal coordination sphere. More commonly, an acidic metal site cooperates with a basic ligand residue to induce H_2 heterolysis (Scheme 1b). Less commonly, H_2 heterolysis is induced through the reversed polarity: an acidic ligand residue cooperating with a basic metal site (Scheme 1c). The two other permutations, then, are cooperation between spatially separated acid/base pairs (Scheme 1d), and between two co-catalytic metal sites (Scheme 1e). Upon considering these cooperative strategies and the unique reactivity patterns that they enable, an outlook on this approach to catalyst design is presented.

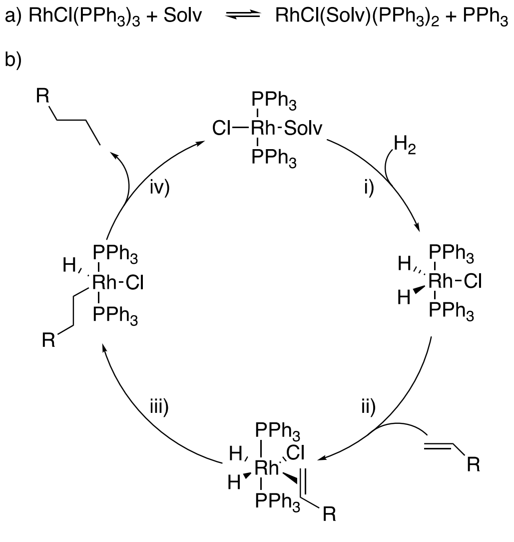
A Brief History of Single-Site Catalysts

Precious metals have long been utilized as single-site hydrogenation catalysts in homogeneous systems due to the identification of species that readily activate H_2 by oxidative addition. Classical oxidative addition of H_2 at single transition metal sites occurs via σ-complex formation, followed by a concerted homolysis of H_2 to generate two adjacent hydride ligands and a two-unit increase in formal oxidation state of the metal. This H_2 bond cleavage is brought forth by the donation of electron density from the σ_{HH} orbital into an empty *d*-orbital of the metal and back-donation from a filled metal *d*-orbital into the σ^*_{HH} orbital (Scheme 2).



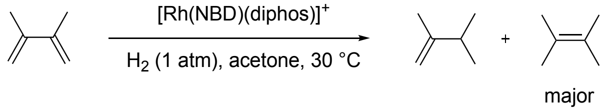
Scheme 2. Oxidative addition of H_2 at a single metal site.

Homogeneous catalytic hydrogenation of unsaturated C-C bonds was first introduced by Halpern and co-workers in 1961 using chlororuthenate(II) complexes.[3] A significant advance was then made with the development of the Wilkinson's catalyst, $RhCl(PPh_3)_3$, first reported in 1966.[4] The accepted mechanism of this single-site Rh catalyst has been studied vigorously over the years.[5] The catalytic cycle is thought to operate by Rh(I)/Rh(III) redox cycling (Scheme 3) and provides the conceptual basis for many other catalytic transformations that employ oxidative addition/reductive elimination cycling. It is interesting to note that the sequence of steps in the generally accepted mechanism for Wilkinson's catalyst: H_2 addition occurs first, followed by the alkene addition.



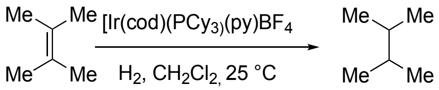
Scheme 3. Alkene hydrogenation by Wilkinson's catalyst: (a) catalyst activation; (b) catalytic cycle consisting of i) H_2 oxidative addition, ii) alkene coordination, iii) migratory insertion, iv) reductive elimination.

Another important advance was made with the Schrock-Osborn catalyst which was developed in 1977.[6] Here, a cationic Rh species, $[Rh(NBD)(diphos)]^+$ was used in place of a neutral one through use of a bulky, chelating diphosphine supporting ligand. The cationic catalyst is more active than Wilkinson's catalyst due to its enhanced electrophilicity, which facilitates the coordination of even unreactive alkenes during the rate determining step. Mechanistic studies have shown that in Schrock-Osborn catalysts featuring bidentate ligands, alkene coordination can precede H_2 addition in the catalytic cycle.[7] Selective hydrogenations were also demonstrated in converting dienes to monoenes (Scheme 4).[6a] Alkyne semi-hydrogenations were also achieved, yielding the *cis*-olefin product.[6c] The incorporation of bidentate ligands in Rh catalysts also opened the door to asymmetric hydrogenation reactions, which were ultimately developed using chiral diphosphine ligands.[8]



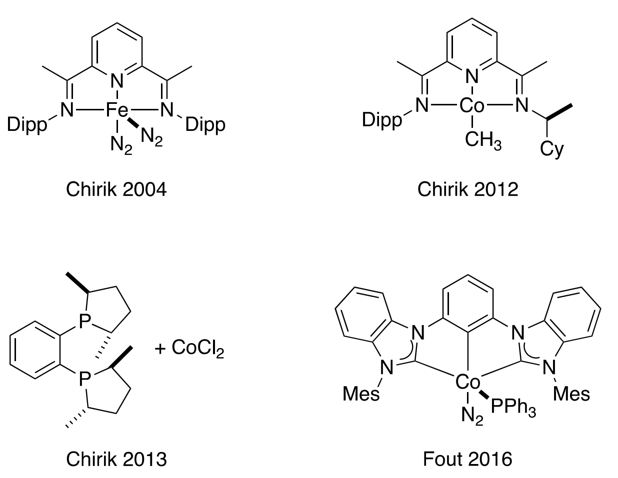
Scheme 4. Diene hydrogenation by the Schrock-Osborn catalyst.

Another important catalyst in the history of hydrogenation is the Crabtree's catalyst, $[Ir(cod)(PCy_3)(py)]^+$.[9] This cationic Ir catalyst exhibited even high activity than previous Rh analogues and enabled catalytic hydrogenation of hindered alkenes. For example, tetra-substituted olefins, which were unsuitable substrates for the Wilkinson and Schrock-Osborn systems, could be hydrogenated using the Crabtree system (Scheme 5). The catalyst is also well known for its substrate-directed hydrogenation behavior, which is a prominent feature in some Rh systems as well.[10]



Scheme 5. Hydrogenation of a tetra-substituted alkene using Crabtree's catalyst.

Since these seminal reports, in the decades that followed an array of single-site precious metal catalysts have been developed for the catalytic hydrogenation of unsaturated C-C bonds.[11,12] More recently, non-precious metal catalysts have been highly sought after for this and a variety of other catalytic transformations. For hydrogenation of unsaturated hydrocarbons, only a handful of single-site non-precious metal catalysts have been reported that operate by single-site H_2 activation mechanisms (Chart 1).[13] While H_2 activation occurs at a single Fe or Co site in all these systems, in some cases redox non-innocence of the supporting ligand is thought to be crucial for two-electron redox cycling of the catalyst. Further examples of non-precious metal catalysts have been obtained by cooperative strategies, which will be the focus of the remainder of this Perspective.



Chirik 2004

Chirik 2012

Chirik 2013

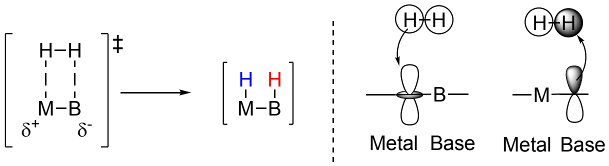
Fout 2016

Chart 1. Selected examples of non-precious metal catalysts that employ single-site H_2 activation mechanisms.

Cooperative Strategy 1: Metal-Ligand Cooperation

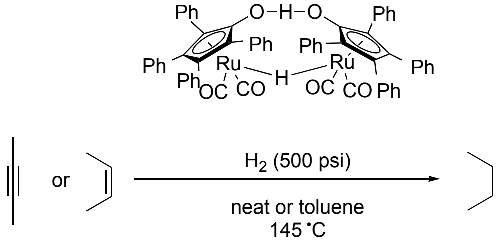
All the examples discussed so far involve H_2 activation at a single metal, with the ligands in its coordination sphere tuning reactivity/selectivity properties indirectly while being innocent with respect to direct participation in reaction chemistry. One set of cooperative strategies that employ bifunctional H_2 activation involve a catalytic metal site cooperating with a ligand residue in its primary or secondary coordination sphere that is non-innocent with respect to participating directly in acid/base reaction chemistry.

Metal-base cooperativity. Catalytic hydrogenation using cooperation between a metal site and a basic ligand residue is initiated by heterolytic cleavage of H_2 across those two moieties. While the electron donation from the σ_{HH} orbital to an empty metal *d*-orbital occurs as in a single-site mechanism, back-donation into the σ^*_{HH} orbital is now done by a filled *p*-orbital in the basic residue rather than by a filled metal-based orbital (Scheme 6). This brings about heterolytic H_2 cleavage in which the metal does not undergo a change in formal oxidation state.



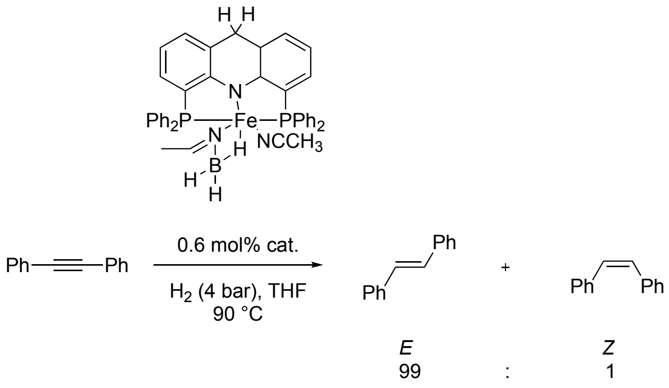
Scheme 6. Bifunctional H_2 activation by metal-base cooperativity.

Shvo's catalyst, first reported in 1985, was the first hydrogenation catalyst using metal-base cooperativity with activity towards C-C multiple bonds (Scheme 7).[14] Both alkenes and alkynes were successfully hydrogenated. The catalyst showed unique reactivity by adding H_2 across the metal center and the non-innocent cycopentadienone ligand. Similar bifunctional mechanistic features were observed in Noyori's[15] and Morris's[16] catalysts in the hydrogenation of C-O and C-N multiple bonds, but their application in the hydrogenation of C-C bonds remains underdeveloped.



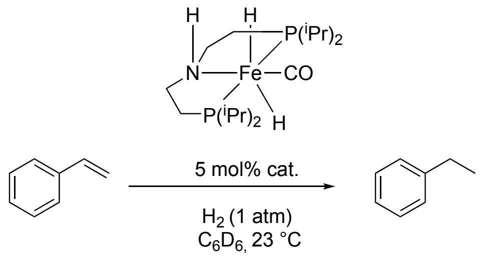
Scheme 7. Hydrogenation reactivity using Shvo's catalyst.

A prominent non-precious metal-containing bifunctional catalyst is Milstein's acridine-based PNP iron complex capable of *E*-selective semi-hydrogenation of alkynes (Scheme 8).[17] The reaction occurs with no added base and under mild conditions. While the intimate details of H_2 activation were not revealed by this study, it is likely that cooperation between the Fe center and the acridine ligand is operative based on previous work by Milstein's group in related systems.[18]



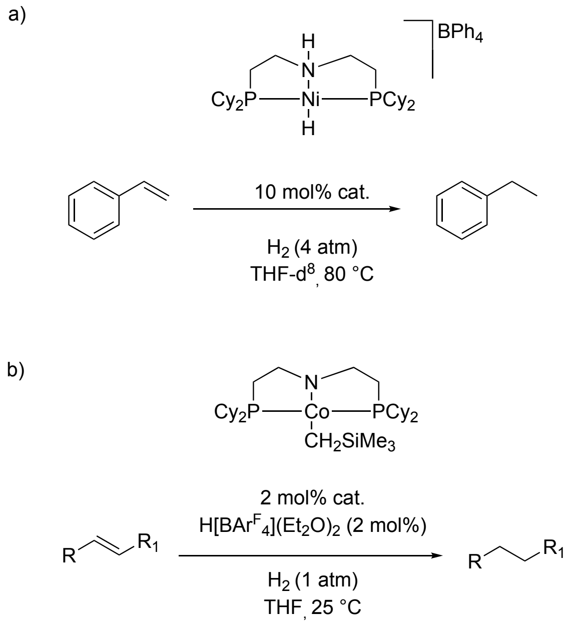
Scheme 8. *E*-selective alkyne semi-hydrogenation by Milstein's catalyst.

Another Fe-based system was reported by Jones recently for the hydrogenation of polar alkene substrates such as styrenes (Scheme 9).[19] Experimental and computational data were consistent with bifunctional H_2 activation by the Fe center cooperating with the basic bis(phosphino)amine pincer ligand.



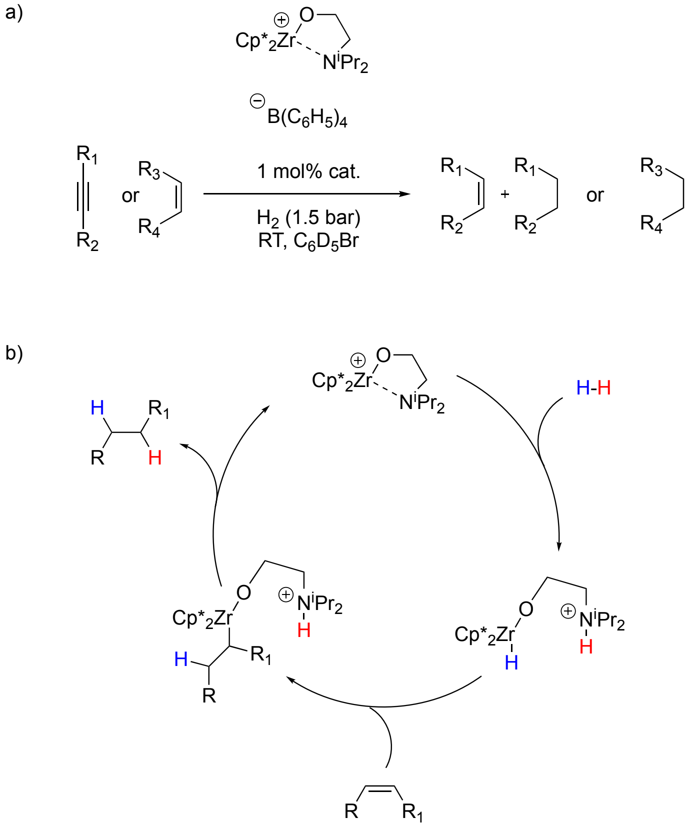
Scheme 9. Hydrogenation of styrene by an Fe catalyst developed by Jones.

Pincer ligands have been employed for the development of hydrogenation catalysts with other transition metals as well.[20] In 2012, Hanson and co-workers achieved alkene hydrogenation using cationic and neutral PNP nickel hydride complexes (Scheme 10a).[21] Later they expanded their work to acquire the same feat using a cationic PNP cobalt(II)-alkyl complex (Scheme 10b).[22]



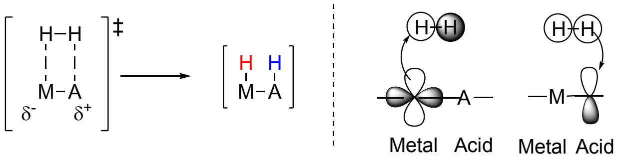
Scheme 10. Pincer-supported hydrogenation catalysts developed by Hanson.

Organometallic frustrated Lewis pairs (FLPs) are another class of metal-base catalysts in which the metal acts as a Lewis acid in sync with a basic ligand residue. Erker and co-workers recently reported two systems based on cationic zirconium Lewis acids with pendant nitrogen or phosphorous bases. These organometallic FLPs were found to catalyze hydrogenations of alkenes and alkynes with good activity under mild conditions.[23] The proposed catalytic mechanism (Scheme 11) is an excellent illustration that single-site catalysis can be mimicked by metal-base cooperativity, but using a redox-inactive metal center. The H_2 activation and alkane elimination steps are present here as in the classical Wilkson's catalyst mechanism, but now with participation from a d^0 metal center that would typically not participate in oxidative addition reactivity.



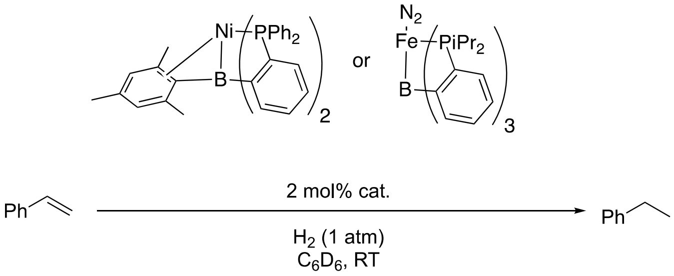
Scheme 11. a) Hydrogenation catalysis and b) catalytic mechanism of Zr(IV)-based organometallic FLPs developed by Erker.

Metal-acid cooperativity. Heterolytic H_2 cleavage also can be achieved through use of a Lewis acidic ligand residue cooperating with a Lewis basic, electron-rich metal center. It is typically thought that bifunctional H_2 activation occurs by the electron donation from the σ_{HH} orbital into the empty *p*-orbital of the ligand residue and the back-donation from a filled metal *d*-orbital into the σ^*_{HH} orbital (Scheme 12), although alternative models have been proposed including an empty metal *d*-orbital acting as the electron acceptor.[24]



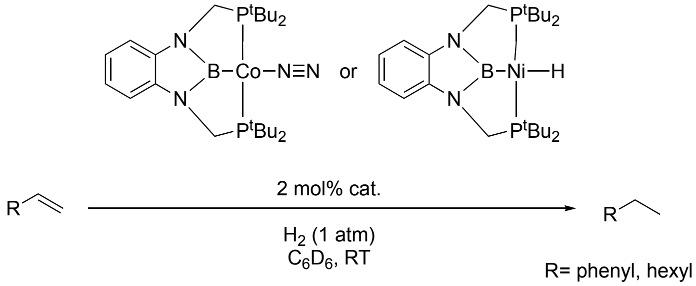
Scheme 12. Bifunctional H_2 activation by metal-acid cooperativity.

The first report of the metal-acid cooperation strategy was from Peters and coworkers, who employed a nickel-borane bifunctional catalyst in which the borane Lewis acid was incorporated into a chelating multidentate ligand.[25] The [Ni-B] unit was found to activate H_2 reversibly to provide a hydridonickel borohydride intermediate that could deliver the activated H_2 to styrene. Catalytic hydrogenations of both styrene and norbornene were achieved (Scheme 13). Related chemistry was later reported by the same group using an iron boratrane system,[26] where again a Lewis acidic borane moiety was held in proximity to an electron-rich metal center by chelation and generated observable metal borohydride intermediates relevant to catalytic hydrogenation of styrene, ethylene, and phenylacetylene (Scheme 13).



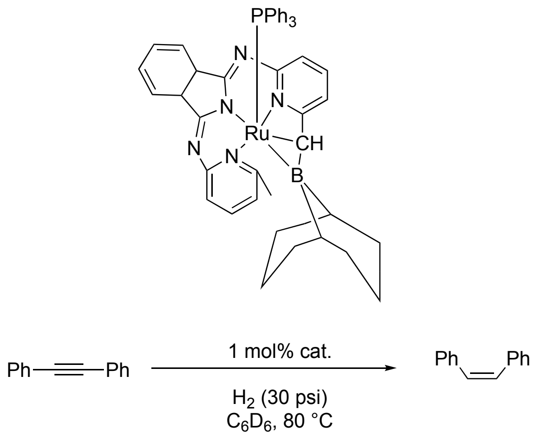
Scheme 13. Catalytic styrene hydrogenation using metal-borane complexes developed by Peters.

In addition to these chelated metal-borane catalysts, the Peters group also reported the use of chelated metal-boryl complexes as catalysts for olefin hydrogenation. A borylcobalt(I) catalyst was found to add two equivalents of H_2 to yield a dihydridoboratocobalt(III) dihydride intermediate relevant to catalytic hydrogenation of styrene.[27] This borylcobalt catalyst and a related borylnickel catalyst were later reported to catalyze hydrogenation reactions of styrene and some unactivated alkenes,[28] with turnover frequencies exceeding those of related systems lacking the metal-acid cooperative effect (Scheme 14). Unlike the metal-borane systems, relatively little is known about the key orbital interactions involved in H_2 cleavage at these metal-boryl reaction centers.



Scheme 14. Catalytic alkene hydrogenation using metal-boryl complexes developed by Peters.

Selective alkyne semi-hydrogenation was observed by the Szymczak group in 2016 using ruthenium-borane complexes.[29] These bifunctional metal-acid catalysts semi-hydrogenated internal and terminal alkynes at high pressures of H_2 to provide *Z*-alkene products selectively, with high conversions and high reaction rates (Scheme 15).

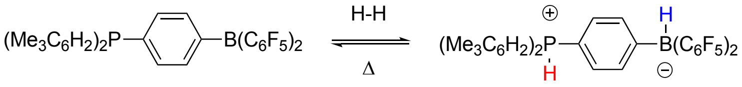


Scheme 15. *Z*-selective alkyne semi-hydrogenation catalyzed by Szymczak's ruthenium-borane complex.

Cooperative Strategy 2: Lewis Acid/Base Pairs

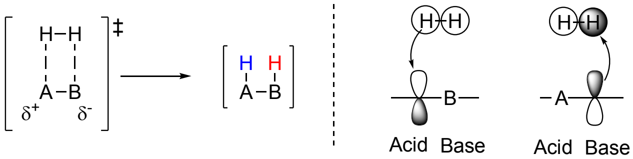
The strategies discussed thus far involved a catalytic metal site cooperating with a non-innocent ligand residue, either by metal-base cooperation or metal-acid cooperation. The two other possible permutations, then, are acid-base cooperation and metal-metal cooperation. Because many relevant examples of bimetallic H_2 chemistry involve bifunctional systems pairing together acidic and basic metals, both strategies are grouped together here under Lewis acid/base pairs.

Frustrated Lewis Pairs. The ability of main-group Lewis acid/base pairs to cooperate requires sufficient steric crowding that the acidic and basic sites do not irreversibly associate and quench reactivity prior to substrate activation. Such systems are typically referred to as frustrated Lewis pairs (FLPs) and have come to represent a prominent strategy for transition-metal free chemistry.[30] In 2006, Stephan and co-workers reported the reversible activation of H_2 using a phosphine/borane FLP where both Lewis acidic and basic components comprised only of main group elements (Scheme 16).[31] This landmark discovery demonstrated that Lewis acid/base pairs of the main group are capable of bifunctional H_2 activation without requiring the presence of any transition metal. As described below, many FLP systems either are intermolecular in nature or position the intramolecular acid/base pair in spatial orientations well suited for catalytic small molecule chemistry.



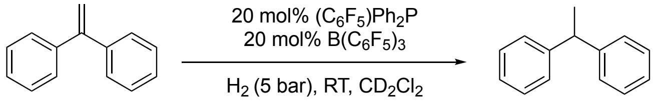
Scheme 16. Reversible H_2 activation using an FLP originally discovered by Stephan.

Heterolytic H_2 cleavage in FLP systems is thought to occur by electron donation from the σ_{HH} orbital to an empty *p*-orbital in the Lewis acid and back-donation from a filled *p*-orbital in the Lewis base into the σ^*_{HH} orbital (Scheme 17).[32] For intermolecular FLPs, this requires the three components (acid, base, and H_2) to encounter each other in solution simultaneously. For certain intramolecular FLPs, the engagement of H_2 by these two orbital interactions is facilitated by the spatial orientation of the catalyst design.



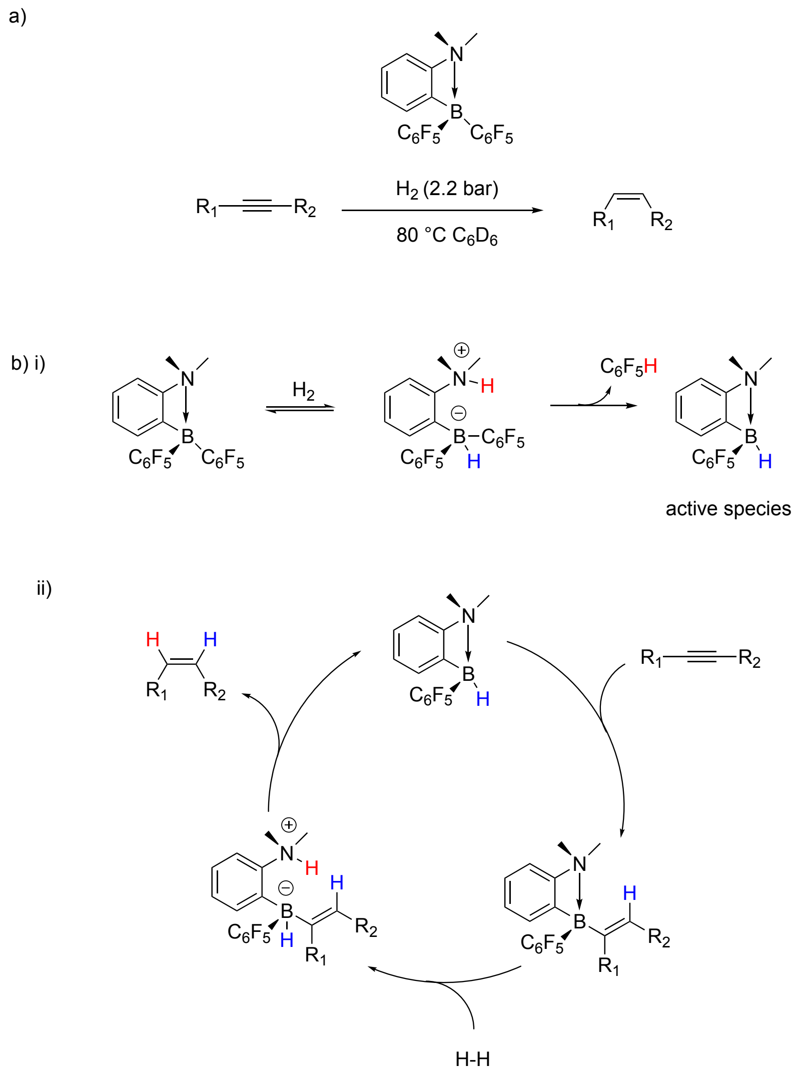
Scheme 17. Bifunctional H_2 activation by main group FLP systems.

Due to the heterolytic nature of H_2 activation with FLPs, catalytic hydrogenation was initially pursued successfully for polar substrates with C=O and C=N bonds.[33] Hydrogenation of non-polar C-C multiple bonds was first reported by Paradies, Stephan, Grimm and co-workers in 2012, with the activation of olefin substrates at low temperatures (Scheme 18).[34] More examples for olefin hydrogenation surfaced in the following years with modified FLPs,[35] including the more recent discovery of electrophilic phosphonium cations as co-catalysts in place of boranes.[36]



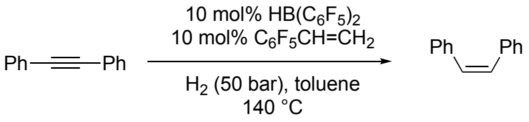
Scheme 18. FLP-catalyzed olefin hydrogenation developed by Paradies, Stephan, and Grimm.

Semi-hydrogenation of alkynes with FLPs were reported for the first time by Repo and co-workers in 2013.[37] Selective formation of *cis*-alkenes was observed under mild conditions (Scheme 19a). They later switched the C_6F_5 groups in the catalyst with Cl and H atoms while retaining catalytic activity.[38] In the reaction mechanism, the activation of the pre-catalyst by H_2 forms the active catalytic species, which then engages in reactivity mimicking transition metal-catalyzed processes. (Scheme 19b).



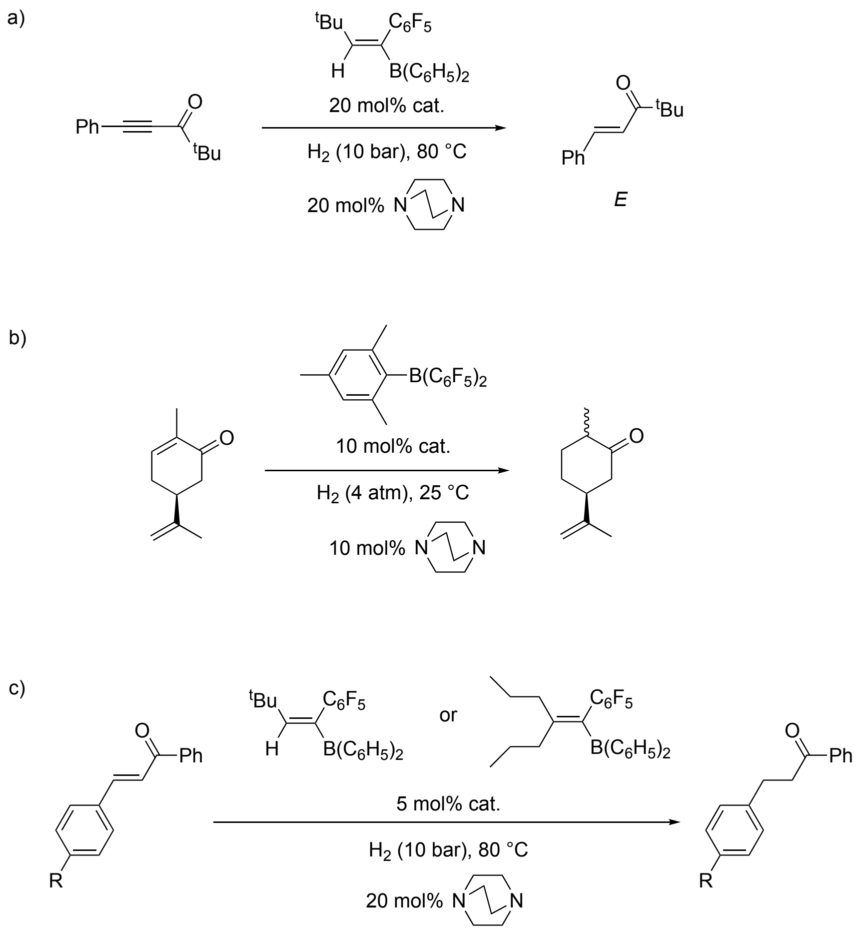
Scheme 19. a) *Z*-selective alkyne semi-hydrogen catalyzed by Repo's FLP; b) i) formation of the active catalyst, ii) proposed catalytic cycle.

In 2015, Du and co-workers showed that both *cis*- and *trans*-alkenes can be obtained with high selectivities from alkynes using high temperatures and pressures (Scheme 20).[39] Here, the cooperative role in catalysis is assumed by $HB(C_6F_5)_2$ and an alkene species interacting with a pentafluorophenyl group. Selective alkyne hydrogenation to produce *cis*-alkenes has been demonstrated by silica-supported FLP systems as well.[40]



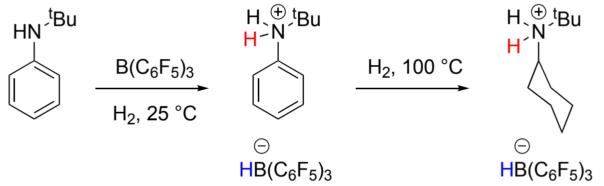
Scheme 20. *Z*-selective alkyne semi-hydrogenation developed by Du.

FLP catalysis also has been developed for selective C-C hydrogenation by conjugate addition to α,β-unsaturated ketone systems.[41] Erker and co-workers reported *trans*-selective catalytic hydrogenation of the C-C triple bonds in ynones in 2011 (Scheme 21a).[42] Soós and co-workers selectively hydrogenated the C-C double bond in carvones in 2012 (Scheme 21b).[30b] Similarly, C-C hydrogenation in nitroolefins, acrylates[43] and enones[30c] was achieved by Paradies and co-workers (Scheme 21c). It is noteworthy that Paradies proposed a mechanistic reversal in these reductions compared to the more typical FLP-catalyzed C=O and C=N reductions. While C=O and C=N reduction is thought to be initiated by protic activation of the heteroatom followed by hydride delivery, the proposed mechanism for the hydrogenation of polar C=C bonds involves initial hydride delivery followed by protonation.[30c]



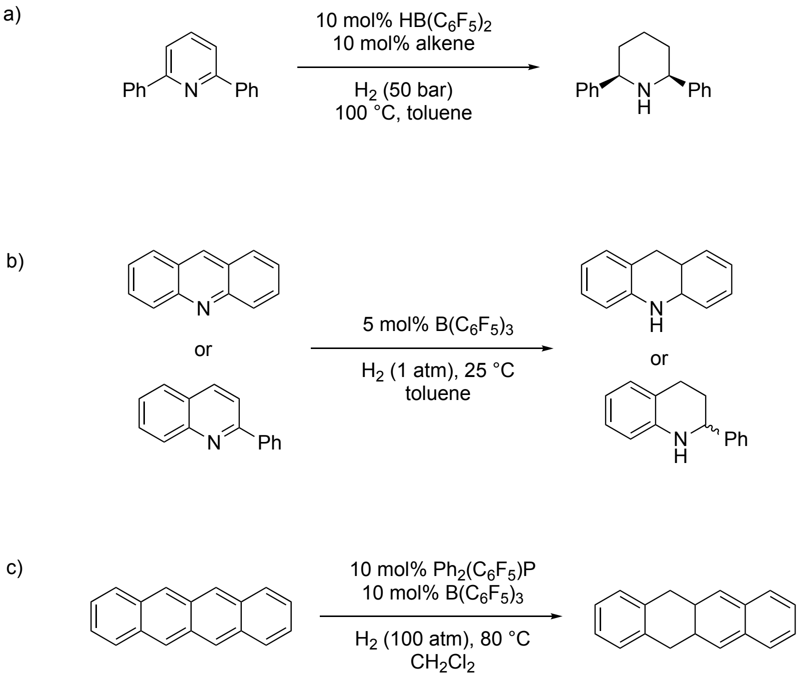
Scheme 21. Selective C-C hydrogenation catalysis by FLP systems developed by a) Erker, b) Soós, and c) Paradies.

In 2012, while studying H_2 activation reactions by different FLP combinations, Stephan and co-workers unexpectedly discovered that FLPs were capable of hydrogenating C-C double bonds in aromatic rings when their catalyst itself was hydrogenated (Scheme 22).[44]



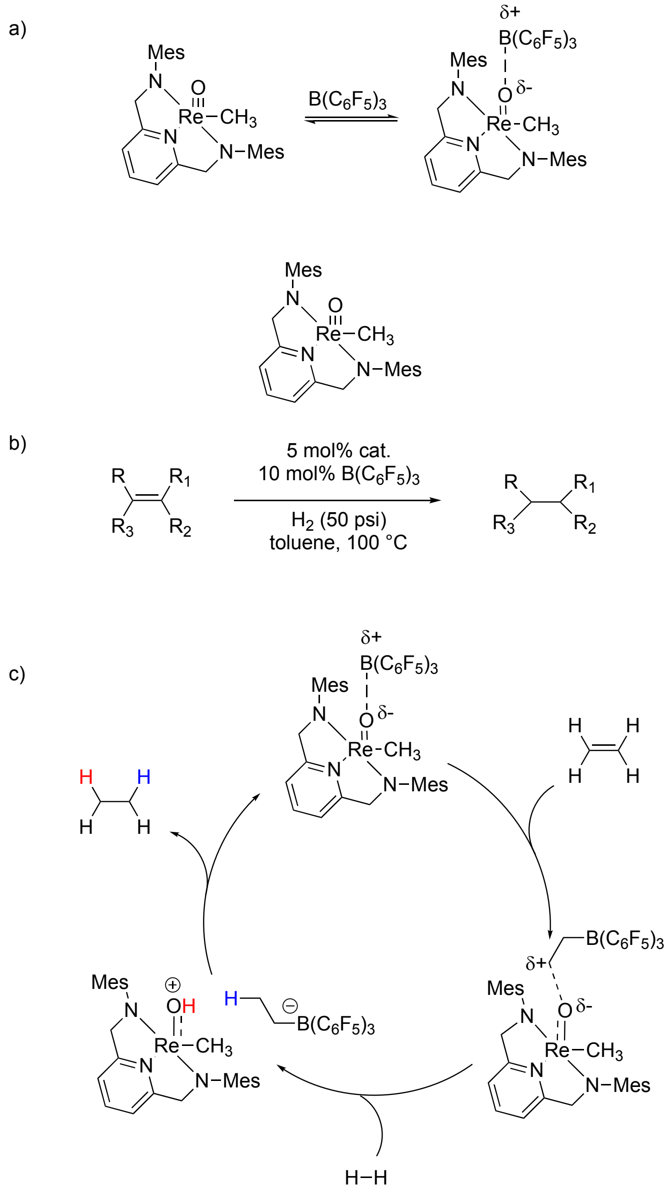
Scheme 22. Aniline hydrogenation discovered by Stephan.

Following upon the serendipitous discovery by Stephan, catalytic hydrogenation of aromatic systems was later extended to pyridine,[45] trisubstituted quinoline,[46] N-heterocycle,[47] and polyaromatic[48,70] substrates by the Stephan and Du groups (Scheme 23).



Scheme 23. Catalytic hydrogenation of aromatic substrates a) pyridines, b) *N*-heterocycles, and c) polyaromatics developed by the groups of Du and Stephan.

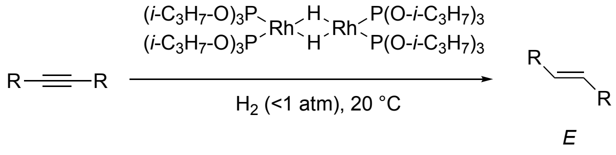
In a unique recent addition to the FLP literature, Ison and co-workers showed that the nucleophilic oxygen centers of oxorhenium complexes could act as the Lewis basic partners in FLP systems (Scheme 24a).[49] While technically an organometallic FLP, here the Re center does not participate directly in bond activation, bond formation, or any redox changes. These systems were shown to be capable of catalytic olefin hydrogenation (Scheme 24b). Interestingly, here the H_2 activation is preceded by alkene coordination in the mechanism elucidated by experimental and computational investigations (Scheme 24c).



Scheme 24. a) Ison's ReO-containing FLP system; b) catalytic olefin hydrogenation with this FLP; c) proposed mechanism in which alkene activation precedes H_2 cleavage.

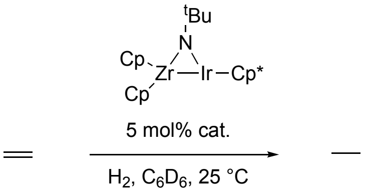
Bimetallic cooperativity. Beyond the metal/base, metal/acid, and acid/base combinations discussed thus far, the remaining permutation is metal/metal cooperation during hydrogenation catalysis. Stoichiometric activation of H_2 by homobimetallic complexes have rarely been reported,[50] which may reflect the symmetry-forbidden nature of the relevant transition state in many systems as calculated by Hoffmann.[51] Indeed, heterobimetallic H_2 activation reactions are significantly more common.[52] In these cases and others described below, heterolysis of H_2 occurs through cooperation of a Lewis acid metal center and a Lewis basic metal center. Thus, these heterobimetallic H_2 activation reactions are related conceptually to the FLP chemistry of the *p*-block. Despite these advances, successful applications of stoichiometric bimetallic H_2 activation reactions in catalysis have remained elusive. Catalytic hydrogenation of multiple C-C bonds also have been reported by some multimetallic complexes.[2] However, their reaction mechanisms are poorly understood and sometimes may even involve heterogeneous species as the active catalysts.

In 1982, Muetterteis, Williams and co-workers introduced a dinuclear rhodium catalyst capable of catalytic hydrogenation of alkynes to selectively form *trans*-olefins.[53] This system was the first homobimetallic catalyst to promote hydrogenation of C-C multiple bonds. The catalyst precursor is a bridged square-planer dimer with two adjacent reactive metal centers (Scheme 25). Bimetallic intermediates formed upon activation of H_2 and of alkyne were observed experimentally in this study, including a vinyl-bridged bimetallic intermediate exhibiting *trans* geometry consistent with the observed catalytic *E*-selectivity. In 1985, a related system studied by Bosnich and co-workers tethered dirhodium and diiridium reaction centers together using a binucleating ligand scaffold.[54]



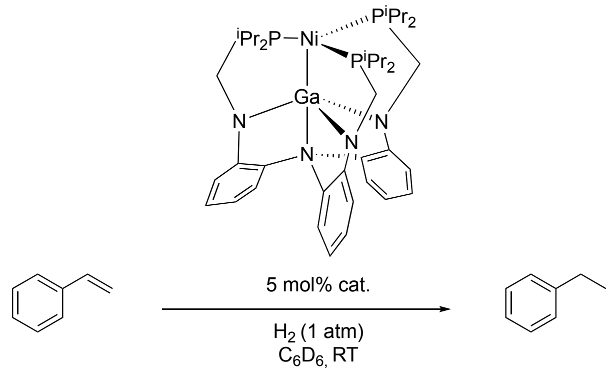
Scheme 25. *E*-selective alkyne semi-hydrogenation using a dirhodium catalyst developed by Muetterties.

Almost a decade later, Bergman and co-workers reported an early-late heterobimetallic complex showing catalytic reactivity towards alkene and alkyne hydrogenation.[55] This imido-bridged zirconium-iridium complex was capable of hydrogenating ethylene, propylene, butane, 1-phenyl-1-propyne, 3-hexyne and *N*-phenylbenzaldimine catalytically (Scheme 26). The intermediate formed upon H_2 activation was observed directly in this study and featured one terminal Zr-H moiety and one bridging hydride ligand. Related bis(methylene)-bridged iridium-tantalum complexes studied by Bergman have also shown activity towards alkene hydrogenations,[56] and a computational study of mechanism was recently published by Ess.[57]



Scheme 26. A heterobimetallic Zr/Ir catalyst for alkene hydrogenation studied by Bergman.

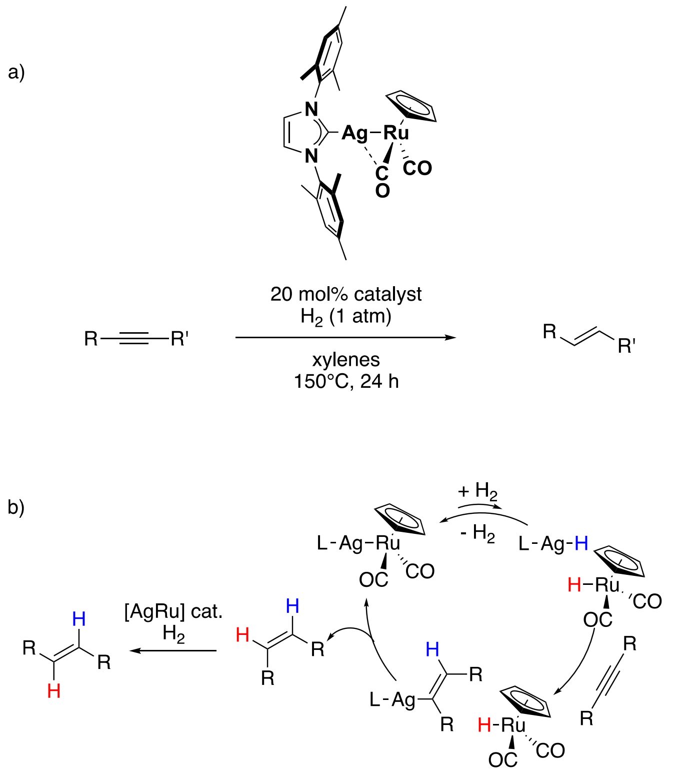
Lu and co-workers described a nickel-gallium heterobimetallic system demonstrating catalytic hydrogenation of olefins in high yields in 2015 (Scheme 27).[58] They also showed that the parallel nickel-indium system is active in olefin hydrogenation, but suffers from poor reactivity. The bifunctional H_2 activation that is operative in this system involves cooperation between an electron-rich Ni center and a Lewis acidic Ga center and, thus, is related conceptually to the metal/acid bifunctional catalysts developed by Peters (*vide supra*).[59]



Scheme 27. A Ni/Ga catalyst for alkene hydrogenation developed by Lu.

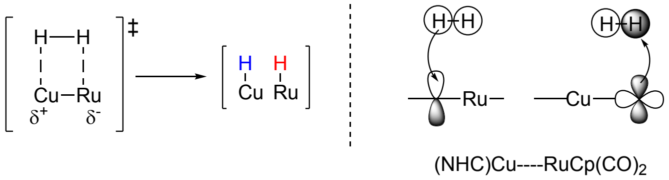
In 2015, we reported a series of (NHC)M-M'Cp(CO)$_2$ catalysts for *E*-selective alkyne semi-hydrogenation, where M = Cu or Ag and M' = Fe or Ru.[60] The optimal Ag/Ru heterobimetallic catalyst was active for generation of *trans*-alkenes from diarylalkyne substrates at low H_2 pressures and relatively high temperatures (Scheme 28). Based on analogies to previous work with dehydrogenative catalysis with related complexes,[61] the proposed mechanism for alkyne semi-hydrogenation involved bifunctional H_2 activation, *syn*-hydrometallation of the alkyne by the hydridic metal-hydride species, and *cis*-alkene release through protonolysis of the vinyl intermediate by the protic metal species. Subsequent isomerization to the observed *trans* product under the catalytic conditions, mediated by the same metal-hydride intermediates, was proposed.

Consistent with this proposed *cis*-hydrogenation/isomerization cascade, the catalyst was shown to mediate isomerization of *cis*-stillbene to the *trans* isomer under the same conditions.



Scheme 28. a) *E*-selective alkyne semi-hydrogenation by a Ag/Ru heterobimetallic catalyst; b) proposed catalytic mechanism.

In a subsequent computational study,[62] a transition state for H_2 cleavage by a (NHC)Cu-RuCp(CO)$_2$ model system was determined. Analysis of atomic and fragment charges over the calculated reaction coordinate verified the heterolytic nature of the H_2 activation process in this system. Furthermore, NBO analysis indicated two key charge transfer interactions being dominant over the calculated reaction coordinate (Scheme 29). Electron density transfer was calculated from the σ_{HH} orbital into an acceptor orbital on Cu, an empty 4*p* orbital that is energetically accessible due to the linear geometry at Cu. (In other bimetallic systems involving Lewis acidic metals with lower *d*-electron counts, one can imagine this acceptor orbital being an empty *d* orbital.) In addition, electron density transfer was identified from a filled Cu-Ru bonding orbital of predominantly Ru 5*d* character into the σ^*_{HH} orbital. The separation of the bonding and back-bonding electronic interactions over two reactive sites, one with Lewis acidic character and one with Lewis basic character, is reminiscent of the H_2 activation model conventially used to describe *p*-block FLP systems (*vide supra*). Indeed, we[62] and others[63] have proposed that many heterobimetallic catalysts can be thought of as the *d*-block analogues of FLPs in this regard.



Scheme 29. H_2 cleavage by a model Cu/Ru heterobimetallic catalyst.

Outlook

The pursuit of these cooperative strategies that allow for bifunctional H_2 activation and delivery to unsaturated hydrocarbon substrates has given rise to two advantages. First, while traditional hydrogenation catalysis relies on precious metals, the cooperative strategies described here have given rise to hydrogenation catalysis with non-precious metals and non-metals. This expansion of the periodic table that can access hydrogenation catalysis has included some elements (e.g., Zr, B, N, P) that are not capable of oxidative addition and reductive elimination processes individually. Thus, the cooperative paradigms allow these elements to mimic the canonical two-electron redox cycling elucidated for Wilkinson's catalyst and other precious metal systems. Second, novel modes of reactivity and selectivity have emerged, in some cases serendipitously, from the exploration of these novel mechanistic paradigms. These exciting results include hydrogenation of arene substrates and *E*-selective semi-hydrogenation of alkynes.

Based on these observations, the continued pursuit of these and other unique strategies in catalyst design should target several factors. Based on the mechanistic knowledge that has emerged from the studies described here, improvements to catalyst design should be implemented to improve catalytic activity of non-precious metal catalysts such that they can compete with established and highly active precious metal catalysts. In addition, asymmetric catalysis with bifunctional catalysts should be pursued, where appropriate, because of the established impact of asymmetric hydrogenation with precious metal systems. Most importantly, the continued emergence of new and surprising reactivity modes from the exploration of novel mechanistic paradigms can be expected. An especially significant impact of cooperative catalysis strategies can be realized if new reactivity not possible with traditional single-site catalysis can be developed successfully because of these explorations.

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ABBREVIATIONS

BAr^F_4, tetrakis[3,5-bis(trifluoromethyl)phenyl]borate; *t*Bu, *tert*-butyl; cat, catalyst; cod, 1,5-cyclooctadiene; Cy, cyclohexyl; DFT, density functional theory; diphos, 1,2-bis(diphenylphosphino)ethane; Dipp, 2,6-di-*iso*-propylphenyl; FLP, frustrated Lewis pair; *i*Pr, *iso*-propyl; Mes, mesityl; NBD, norbornadiene; NHC, *N*-heterocyclic carbene; Ph, phenyl; PNP, phorphorus-nitrogen-phosphorus; py, pyridine; RT, room temperature; THF, tetrahydrofuran.

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