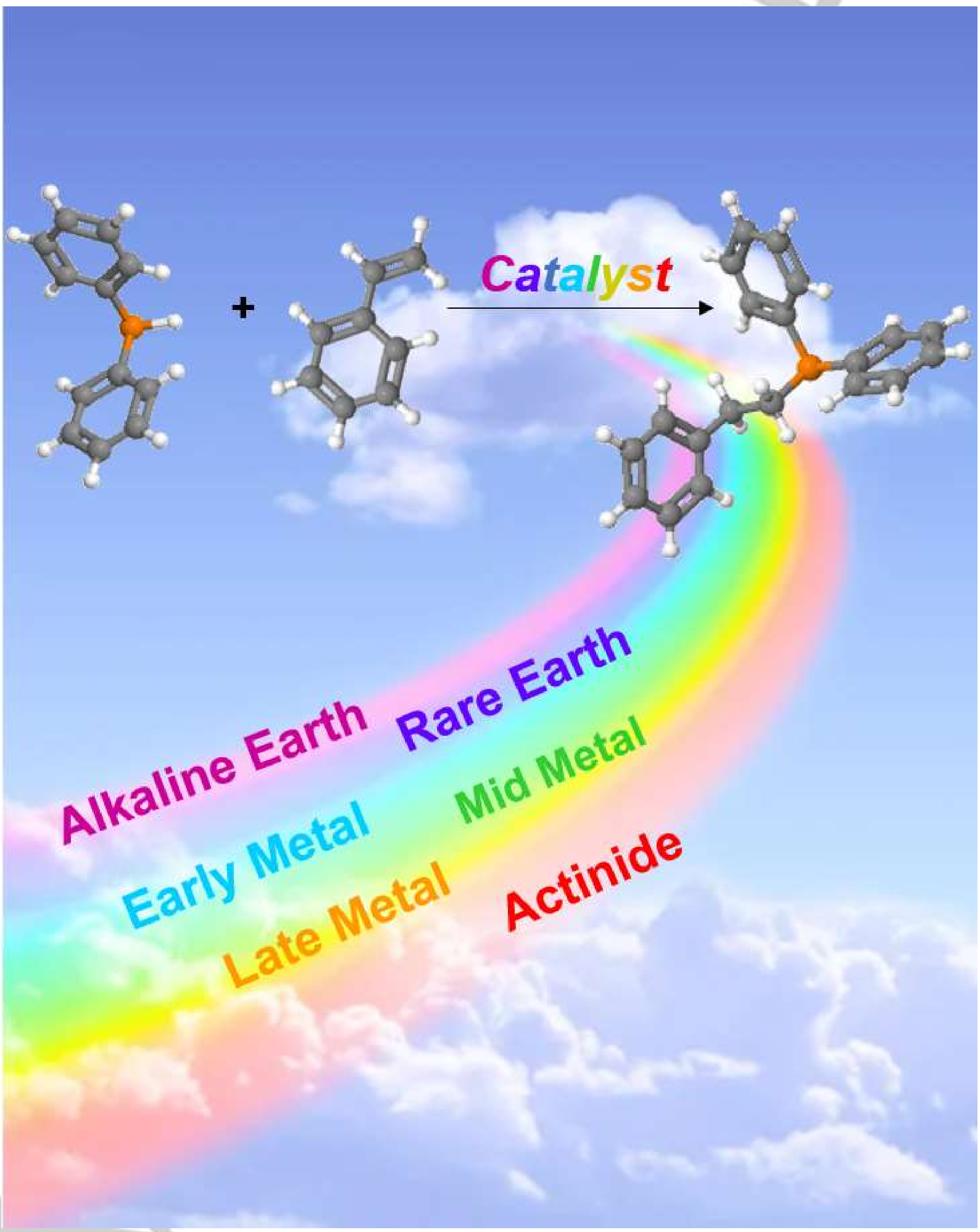
Metal-Catalyzed Hydrophosphination

Bryan T. Novas[a] and Rory Waterman*[a]



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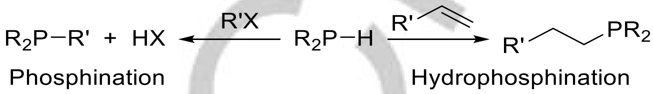
Abstract: Organophosphines have garnered attention from many avenues ranging from agriculture to fine chemicals. One-time use of phosphate resources has made sustainable use of phosphorus overall imperative. Hydrophosphination serves as an efficient method to selectively prepare P–C bonds, furnishing a range of phosphorus-containing molecules while maximizing the efficient use of phosphorus. Since the first report in 1958, a wide array of catalysts have appeared for hydrophosphination, a reaction that is spontaneous in some instances. This review presents a representative view of the literature based on known catalysts through mid-2022, highlighting extensions to unique substrates and advances in selectivity. While several excellent reviews have appeared for aspects of this transformation, this review is meant as a comprehensive guide to reported catalysts.

1. Introduction

Phosphorus-containing molecules are prevalent in many important areas of everyday life including biochemistry, materials, medicine, industry, and agriculture.[1] Though the primary use of phosphorus is in food production,[2] organophosphorus compounds, also known as phosphines, are capable of a wide breadth of chemical reactivity. Tertiary phosphines have ubiquitous use as ligands for catalysis.[3] Primary and secondary phosphines, which bear one or two reactive P–H bonds, respectively, also attract interest as synthons that can undergo several transformations to furnish unique phosphorus containing compounds.[4] Additionally, phosphorus-containing materials have become prevalent owing to their interesting electronic properties, resulting in major growth of that field.[5]

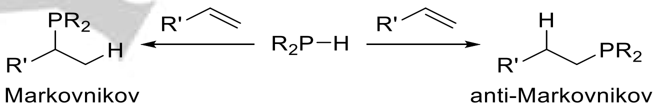
Estimates on the rate of phosphorus consumption have only increased based on chemical needs and increasing global population such that demand has remained high.[1] As a result, sustainable production of phosphorus-containing molecules is critical when dealing with a diminishing supply, arguably a dangerously limited supply of phosphorus resource.[1-2]

One hindrance to efficient use is the limited number of efficient routes to synthesizing organophosphines.[4] Two major routes emerge for the functionalization of P–H bonds to generate organophosphines: Phosphination and hydrophosphination (Scheme 1). Both methods are able to produce P–C bonds from a wide range of substrates, and the pair of reactions thus leverage the array of common organic precursors available to the synthetic chemist. In some instances, both reactions rely on the enhanced nucleophilicity of the phosphorus in an M–P bond. There have been substantial developments in phosphination, and despite the reliability of such synthetic techniques, the products are burdened with stoichiometric waste. Hydrophosphination is attractive because of the atom economy, reduced waste, and potentially simplified purification.[4, 6] Though the atom efficiency is attractive, hydrophosphination is regarded as more difficult, where some accounts even identify the reaction as thermodynamically unfavorable.[4, 6a] Therefore, it would be inaccurate to consider these reactions competitors; they are complementary and jointly augment the organophosphorus chemist's toolbox.



Scheme 1. Examples of synthetic routes to value-added tertiary phosphines from a secondary phosphine.

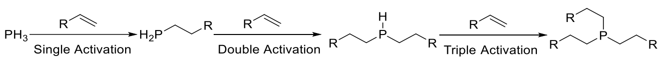
In some cases, hydrophosphination does not require a catalyst to occur.[6] If no catalyst is present, these reactions proceed thermally or photochemically, but radical initiation has also been described.[4] The advantages of catalysis are, of course, reduced activation energy, but a broader substrate scope has also been realized with catalytic reactions. Additionally, the selectivity that is potentially imparted by a catalyst is significant for the preparation of value-added molecules, where product selectivity is difficult to control by spontaneous P–H bond addition across an unsaturated substrate.[6a] In the case of the hydrophosphination of alkenes, the 1,2-addition vs. the 2,1-addition across unsaturation can yield Markovnikov or anti-Markovnikov products but selectivity for the former is less well known with catalysis (Scheme 2).[6a, 7]



Scheme 2. Distinguishing between Markovnikov and anti-Markovnikov hydrophosphination products.

Catalysts have demonstrated enhanced selectivity for these potential stereochemical outcomes.[6] Anti-Markovnikov addition is most common for intermolecular hydrophosphination catalysts,[6a, 7] but examples of Markonikov-selective hydrophosphination catalysts are known, though more rare.[8] It is clear that catalysts are available that can provide suitable regioselectivity for desired hydrophosphination products.

Products of hydrophosphination can vary based on the number of organic substituents at phosphorus. Phosphine can be activated up to three times, as has been seen (Scheme 3).[6a, 9] Primary phosphines can be activated up to twice, and secondary phosphines only once. Having control over activation events in catalytic hydrophosphination can be of value. For example, the selective single activation of a primary phosphine allows for further functionalization of a preserved P–H bond, maximizing the ability to tune steric and electronic properties of the final product.

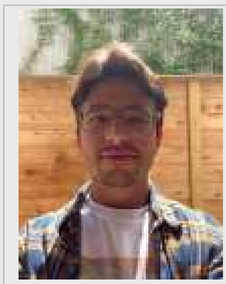


Scheme 3. Single, double, and triple activation of PH_3.

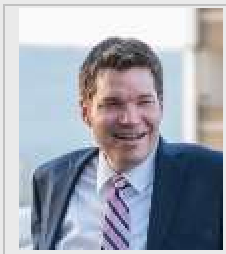
The first reported instance of metal-catalyzed hydrophosphination was described in a patent by Reuter and Orthner in 1958, with the platinum catalyzed hydrophosphination of formaldehyde.[10] Pringle and Smith followed up several decades later with the zero-valent nickel, palladium, and platinum catalyzed hydrophosphination of formaldehyde with PH_3.[11] The first catalytic hydrophosphionation of an alkene was reported shortly thereafterwhere by Pringle with the hydrophosphination of acrylonitrile with PH_3 mediated by a platinum salt.[12]

Since these initial reports, hydrophosphination catalysis has experienced tremendous growth, specifically in the areas of catalyst and substrate, which are the major developments that will be detailed throughout this review. This review primarily focuses on the development of catalysts across the periodic table. There have been an abundance of reviews on hydrophosphination,[6-7, 13] and of these, some have focused on specific issues such as mechanism[7, 14] or are perspective-type accounts.[13e] This review explores the breadth of catalysts that have been reported. The catalysts are sorted by position on the periodic table, broken down by element if there has been more study (e.g., platinum) or group where the literature has provided some natural relationships among catalysts (e.g., alkaline earth). In general, these sections are roughly organized chronologically, though following an intellectual thread will take priority over a strictly historical account. The aim is to provide a reader with a sense of the systems used for hydrophosphination and the successes that this global community of investigators have achieved with these catalysts. As appropriate, we direct the reader to reviews and therefore minimize the coverage of topics that have seen attention in the secondary literature already.

Bryan Novas is an organometallic chemist who received his B.Sc. from the University of Connecticut while studying the catalytic activity of heterogeneous transition metal compounds in Dr. Steven Suib's lab. He received his Ph.D. from the University of Vermont while in Dr. Rory Waterman's lab, where he explored the generality photocatalytic hydrophosphination with a variety of zirconium complexes.



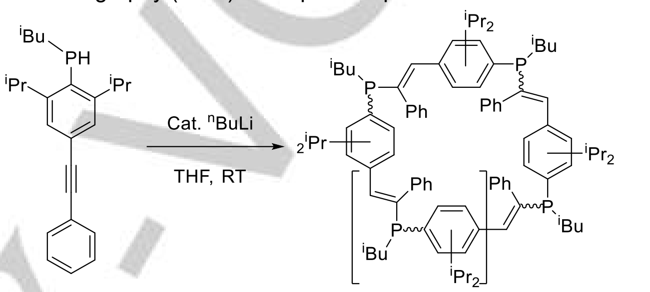
Rory Waterman is an inorganic chemist with interests in organometallic chemistry, materials science, and catalysis. Since his start at the University of Vermont in 2006, he has a particular focus on catalytic reactions that form bonds between main group elements, leading to interesting molecules and materials. Waterman has received awards and followships in recognition of his work, most recently awarded a Japan Society for promotion of Science Research Fellowship.



2. Alkali Metals

Hydrophosphination catalysis with alkali metals is fraught because common sources of group 1 cations are bases, and hydrophosphination is known to be base catalyzed. This situation overlaps the possibility of group 1 metal catalysis with described base catalysis, a circumstance that needs some reconciliation. However, there have been interesting reports focused on a variety of bases, and potassium bases are often at the forefront of these studies.[15] The prevalence of potassium and some comparative analysis of group 1 cations performed by Webster,[15a] suggest that the group 1 cation itself may be the catalyst or a key co-catalyst with the base. Further testing and refinement of this hypothesis are needed to better understand the role of the base in the catalytic reaction.

Stephan and coworkers devised a methodology to prepare phosphorus-containing oligomers/polymers through catalytic hydrophosphination (Scheme 4).[5b] The main aim of the work was to broaden the synthetic routes to P(III)-containing polymers and related materials, which are less common than paths towards P(V)-containing polymers. The synthesis of bifunctional monomers containing P–H and alkyne units was described along with their subsequent hydrophosphination as route to polymer products. This was the first report of the synthesis of P(III)-based oligomers and polymers via this method. The polymerization of the monomer was achieved by treatment with 0.2 equiv. of *n*-butyllithium (^{n}BuLi) in tetrahydrofuran (THF) at room temperature (RT) overnight. Consumption of the monomer was determined by disappearance of an alkyne precursor stretch at 2320 cm^{-1} in the infrared (IR) spectrum. The product retained a broad ^{31}P nuclear magnetic resonance (NMR) signal at δ = -20 ppm. No resonance for phosphorus containing end groups were observed in the NMR spectrum, suggesting the products were cyclic. The main oligomer shown in Scheme 4 was determined by gel permeation chromatography (GPC) with up to 8 repeat units.



Scheme 4. Alkyl lithium catalyzed hydrophosphination/polymerization.

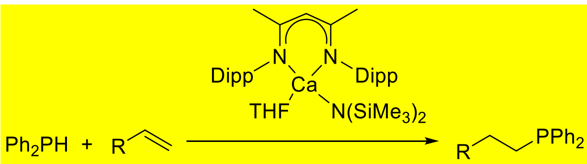
3. Alkaline Earth

Alkaline earth elements have demonstrated excellent potential in catalytic hydrophosphination, which is only complemented by the low toxicity of some prominent catalysts in the series and high relative abundance of these elements. Key contributions have been made in alkaline earth catalyzed heterofunctionalization reactions, in general, by the groups of Hill, Carpentier, and Sarazin, who have concisely described that broader body of work in respective comprehensive accounts.[13b, 16] Efforts in hydrophosphination catalysis has focused primarily on calcium, but strontium, barium, and even magnesium has been utilized for this transformation. Many developments have been made in substrate scope and catalyst development, which suggest that additional improvements and discoveries are yet to occur.

There is high similarity between alkaline earth and rare earth, and a reader should be cautious not to see the section in a vacuum with respect to the other. Some of this similarity should be evident by publications that study both classes of metals.

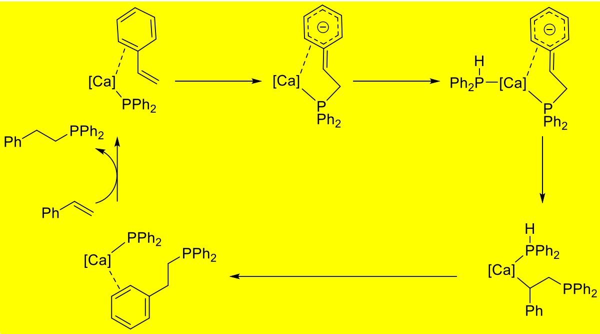
3.1. Calcium

The first example of alkaline earth hydrophosphination catalysis was reported by Barrett and Hill in 2007.[17] In this study, a β-diketiminate-supported calcium precatalyst bearing a protonation-labile hexamethyldisilazide was the focus. The calcium catalyst was utilized for the hydrophosphination of styrene derivatives, dienes, and diphenylacetylene upon heating (Scheme 5).



Scheme 5. Calcium-catalyzed intermolecular hydrophosphination of alkenes.

An unsuccessful reaction with 2-vinylpyridine indicated that competitive insertion into the Ca–C bond can compete with product-liberating reactions involving diphenylphosphine, demonstrating a limit of potential substrates but support for insertion-based catalysis. Hill further expanded on this work a year later with the hydrophosphination of carbodiimides using the same β-diketiminate catalyst, alongside hexamethyl disilazide alkaline earth complexes.[18] Compounds of the general formulation $Ae(N(SiMe_3)_2)_2(THF)_2$ (Ae = Ca, Sr, and Ba) were found to be successful catalysts for the hydrophosphination of carbodiimides. Multiple catalytic intermediates were identified via *in situ* ^1H NMR experiments and stoichiometric reactions, which led to a well-supported proposed catalytic cycle. Westerhausen reported the hydrophosphination of diphenylethyne and diphenylbutadiyne using $(THF)_4Ca(PPh_2)_2$ that same year.[19] One of these products, 1,4-diphenyl-1,4-bis(diphenylphosphanyl)buta-1,3-diene was isolated and characterized by single crystal X-ray diffraction. The crystal structure helped determine that *cis*-addition of Ph_2PH to the C–C triple bond of diphenylbutadiyne results in the formation of the *trans*/*trans* isomer. In all of these reports, mechanisms were suggested to be insertion-based. However, it was later suggested in a computational investigation by Ward and Hunt that alkene insertion proceeds via an outer sphere conjugative addition mechanism, where there is no direct interaction between the calcium atom and the unsaturated portion of the substrate (Scheme 6).[20]



Scheme 6. Calcium catalyzed outer sphere conjugate addition of diphenylphosphine to styrene.

Carpentier and Sarazin have shown that heteroleptic alkaline earth complexes of calcium, strontium, and barium are competent precatalysts for the hydrophosphination of styrene with Ph_2PH and dicyclohexylphosphine with low catalyst loadings (Figure 1).[21] Similar to Hill's study, β-diketiminate ligands were explored along with congested imino anilide and tetradentate amino-ether phenolate ligands.

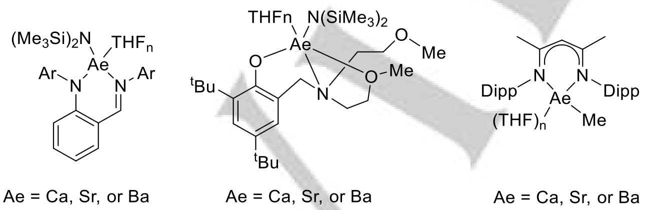


Figure 1. Alkaline earth hydrophosphination catalysts.

It was discovered that barium was more active than strontium, which was faster than calcium for the hydrophosphination of styrene neat at 60 °C. The barium β-diketiminate complex facilitated the hydrophosphination of styrene with Ph_2PH in only 15 min to 96% conversion.

Carpentier and Sarazin later describe a cationic calcium fluoroalkoxide complex that was extensively characterized and utilized for the anti-Markovnikov hydrophosphination of styrene (Figure 2).[22]

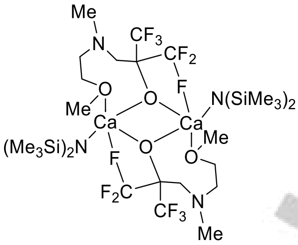


Figure 2. Carpentier and Sarazin's cationic calcium fluoroalkoxide hydrophosphination catalyst.

In a later report by Carpentier, Panda, and Sarazin, calcium complexes with imino-phosphinanilido chalcogenide ligands were used for the hydrophosphination of styrene (Figure 3).[23]

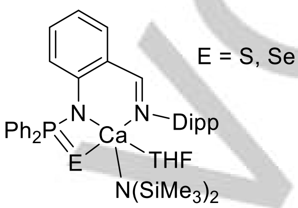
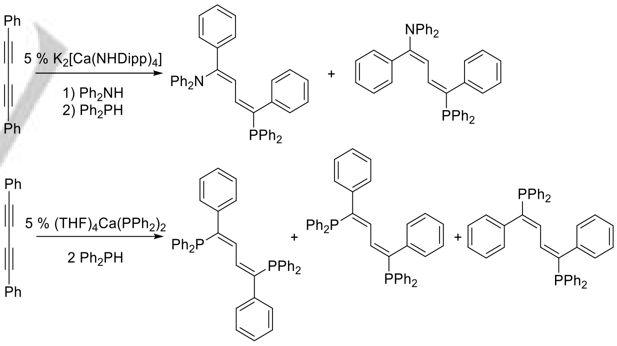


Figure 3. Carpentier, Panda, and Sarazin's calcium imino-phosphinanilido hydrophosphination catalyst.

Introducing a new class of hydrophosphination substrates, Westerhausen reported a calcium-mediated synthesis of 1-(diorganylamino)-1,4-diphenyl-4-(diphenylphosphanyl)buta-1,3-dienes that strictly produced the *Z,E* and *E,E* conformations of the product (Scheme 7).[24] This was achieved using a tetrakis(amino)calciate complex that catalyzed both the hydroamination and hydrophosphination of diphenylbutadiyne in a one-pot, sequential process that selected for the specific isomers.



Scheme 7. Calcium-catalyzed hydrophosphination of internal diynes.

In the proposed mechanism, hydroamination occurs prior to hydrophosphination where the hydrophosphination always selects the *E*-addition to the alkyne. Neither the amines nor phosphines react with the alkene double bonds in any intermediates or the product.

Trifonov reported well-defined calcium amido complexes bearing tridentate amidinate ligands for the hydrophosphination of styrenes and phenylacetylene with both diphenylphosphine and phenylphosphine (Figure 4).[25] This report is the first example of primary phosphine substrates in hydrophosphination with an alkaline earth catalyst.

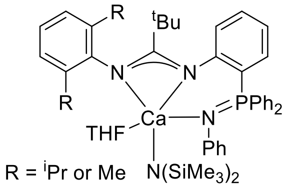


Figure 4. Trifonov's tridentate amidinate calcium hydrophosphination catalyst.

3.2. Strontium

Harder demonstrated that strontium and barium siloxide/amide clusters could participate in a metal-ligand cooperative (MLC) hydrophosphination of styrene derivatives where deprotonation of the phosphine is performed by the amine ligand (Figure 5).[26]

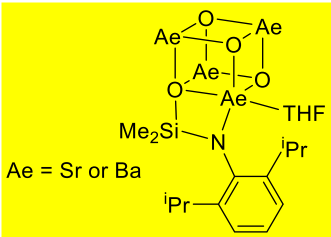


Figure 5. Harder's strontium and barium siloxide/amide cluster hydrophosphination catalyst.

3.3. Barium

Sarazin explored barium catalyzed hydrophosphination with a well characterized crown-ether-functionalized amidinate and iminoanilide ligands (Figure 6) for the hydrophosphination of styrene with both primary and secondary phosphines.[27]

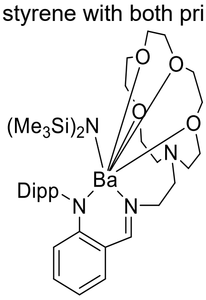
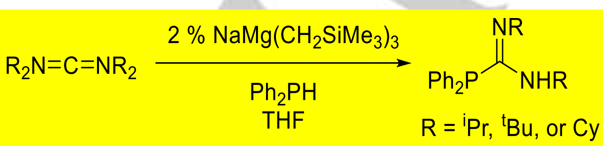


Figure 6. Sarazin's barium crown-ether-functionalized iminoanilide hydrophosphination catalyst.

3.4. Magnesium

Though less present than calcium in the hydrophosphination literature, magnesium catalysts have also been reported. The first example was described by Carrillo-Hermosilla and Hevia using a sodium magnesiate precatalyst (Scheme 8).[28]



Scheme 8. Sodium magnesiate catalyzed hydrophosphination of carbodiimides.

The study focused on the guanylation of amines, but the hydrophosphination of carbodiimides with Ph_2PH was also tested with success. Magnesium-catalyzed hydrophosphination was further expanded by the work of Harder, where Lewis acidic magnesium cation compounds bearing β-diketiminate ligands facilitated the hydrophosphination of phenylacetylene with perfect selectivity for the *Z*-isomer product.[29]

The future is bright for alkaline earth hydrophosphination catalysts. These results are also interesting in light of the following reports with rare earth catalysts. With great advances being made by several research groups, the increasing range of substrates and utilization of mild conditions promises a green avenue for P–C bond forming reactions alongside other heterofunctionalization chemistry also promoted by alkaline earth elements.

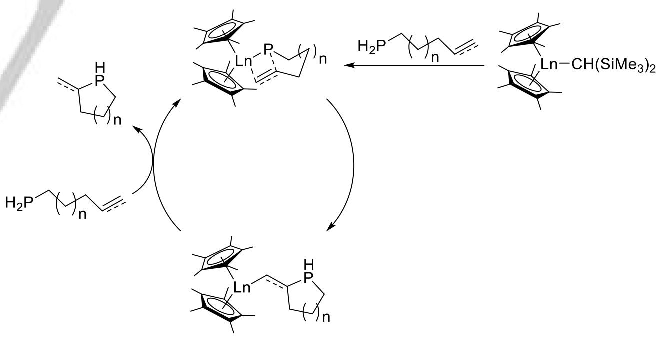
4. Rare Earth

The rare earth elements have garnered a great deal of attention as hydrophosphination catalysts since the turn of the century and continue to be the subject of active investigation. With many notable examples, rare earth catalysts have expanded the scope of hydrophosphination in the use of unusual and challenging unactivated substrates. Rare earth catalysts continue to grow in variety with a large library of compounds available. Trifonov has arguably been most active in this area with Marks and Takaki having made seminal contributions.[13a] The study of these metals remains a highly active area, and the groups of Carpentier, Cui, Sarazin, Schmidt, and others have made key contributions.

A casual reader starting at this section to engage rare earth chemistry is encouraged to consider the results presented in this section with the highly complimentary chemistry of the alkaline earth elements.

4.1. Yttrium

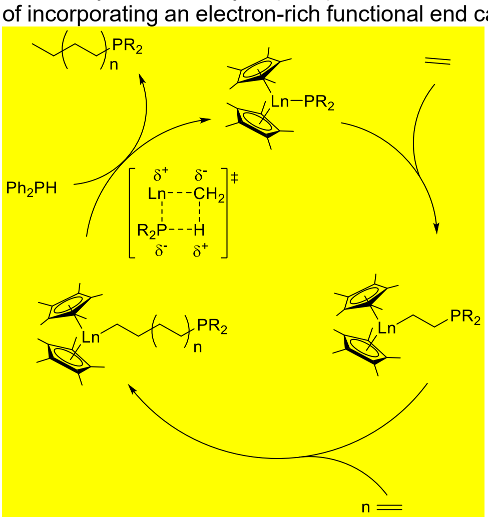
Marks and coworkers made the first report of hydrophosphination with a rare earth catalyst.[30] Primary and secondary alkenyl phosphines were cyclized by the lanthanide precatalyst $Cp^*_2LnCH(SiMe_3)_2$ (Ln = Y or La). The precatalyst would form the active catalyst upon interacting with an equivalent of phosphinoalkene. Alkenyl phosphines are known to cyclize upon UV-irradiation, selecting for the 1,2-insertion product. The catalysts confirmed the reverse selectivity providing 100% of the 2,1-insertion product (Scheme 9).



Scheme 9. Lanthanocene catalyzed hydrophosphination/cyclization of phosphinoalkenes.

A variety of phosphino alkenes/alkynes underwent hydrophosphination in quantitative yield between ambient temperature and 60 °C. Kinetic measurements suggest the turnover limiting step is insertion, consistent with lanthanide-catalyzed hydroamination. A greater study on scope, selectivity, and mechanism was later described by Marks and coworkers.[31] Additionally, lutetium catalysts were introduced, alongside those from the original report. It was determined that the identity of the lanthanide along with ancillary ligand structure impacts both the relative rate and selectivity. Metals with larger ionic radii lend themselves to more open ligand systems and lead to greater turnover frequency. Maximum turnover frequencies for phosphinoalkenes were identified when using intermediate-sized metal ions with Cp* ligands. Marks and coworkers also investigated homoleptic lanthanide alkyl and amide precatalysts for hydrophosphination/cyclization.[32] $Ln(CH(SiMe_3)_2)_3$ (Ln = La, Nd, Sm, Y, or Lu) and $Ln(N(SiMe_3)_2)_3$ (Ln = La, Nd, Sm, or Y) were prepared and tested for the intramolecular hydrophosphination of phosphinoalkenes/alkynes. Hydrophosphination with homoleptic lanthanides was found to be less stereoselective than was achieved with lanthanocene derivatives but at similar relative rates. The intermediate sized yttrium complexes were most active in these studies, followed by the larger, then smaller ions (Y > Sm > Lu > La).

Marks used $Cp^*_2LnCH(SiMe_3)_2$ and the hydride $(Cp^*_2LnH)_2$ (Ln = Lu, Y, Sm, or La) as precatalysts for ethylene polymerization.[33] The resulting polyethylene is terminated with a PPh_2 moiety through the continuous insertion of ethylene between the Ln–P bond that was generated by the treatment of $Cp^*_2LnCH(SiMe_3)_2$ with one equiv. of phosphine (Scheme 10). Catalytic activity based on the metal center was noted to proceed in the order Y > Sm, Lu > La, similar to typical hydrophosphination. This study illustrates hydrophosphination as an efficient method of incorporating an electron-rich functional end cap on a polymer.



Scheme 10. Lanthanocene catalyzed polymerization/hydrophosphination of ethylene.

Trifonov and coworkers studied metallacyclic yttrium alkyl and hydrido compounds for the hydrophopshination of terminal alkenes and diphenylacetylene (Figure 7).[34] Low catalyst loadings of 2 mol % were used with heating. Reactions with primary and secondary phosphines were tested, where products were formed upon heating, typically for 72 h.

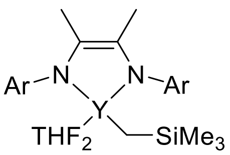
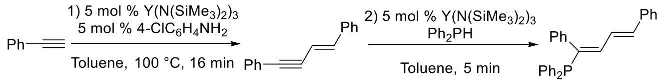


Figure 7. Trifonov's metallacyclic yttrium alkyl hydrophosphination catalyst.

Komeyama and Takaki furthered the utility of yttrium-catalyzed hydrophosphination in the dimerization of alkynes with subsequent hydrophosphination in a one-pot procedure (Scheme 11).[35] In this work, the catalyst was selective for *Z,E*-head-to-head and head-to-tail dimers, despite other products being possible. Thus, the regio- and stereoselective dimerization of terminal alkynes was successful in producing conjugated enynes followed by hydrophosphination. Yttrium catalysts were superior to those of samarium or lanthanum. Amine additives played a pivotal role in the efficiency and regioselectivity of products. For example, *Z*-head-to-head were selected with aniline derivatives and *Z*-head-to-tail dimers with $N(SiMe_3)_3$.[35] This enabled a highly efficient synthesis of 1-phosphinyl-1,3-butadienes.



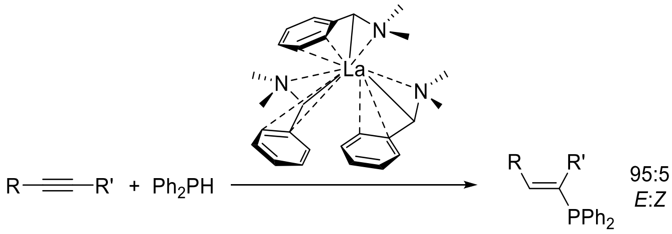
Scheme 11. Yttrium catalyzed dimerization/hydrophosphination of alkynes.

4.2. Lanthanum

A DFT study was conducted by Fragalà and Marks to compute the energetics of the proposed mechanism of lanthanum catalyzed hydrophosphination/cyclization.[36] The reaction was found to proceed in two discrete steps: Cyclization via C=C insertion into the Cp_2La–P bond of the phosphido to form La–C and C–P bonds, which is followed by La–C protonolysis. The insertion is thermoneutral in nature and proceeds through a highly organized, seven-membered chair-like cyclic transition state. The resulting alkyl complex then undergoes a turnover-limiting but exothermic protonolysis to yield a phosphine-phosphido complex, which is proposed to be the resting state of the catalyst. This is in sharp contrast to hydroamination/cyclization reactions, where C=C insertion is turnover-limiting and protonolysis is rapid. It was determined cyclized products compete with unconverted substrate for coordination at the metal and inhibit protonation, which is corroborated by experiments. The thermodynamic and kinetic parameters were in overall agreement with the experimental studies.

Schmidt and coworkers explored insertion reactions and catalytic hydrophosphination with heterocumulenes using α-metalated *N,N*-dimethylbenzylamine lanthanum and yttrium.[37] Both complexes were shown to undergo triple-insertion reactions to form homoleptic amidinate and phosphaguanidinate complexes. These are both useful catalyst precursors for the hydrophosphination of C=N bonds, with the lanthanum derivative demonstrating excellent activity at ambient temperature for a large library of heterocumulenes. A broad tolerance for electron donating and withdrawing substituents was observed on aryl isocyanates. The catalytic effectiveness was dependent on the acidity of the phosphine and the steric bulk of the heterocumulene. The authors proposed formation of phosphido intermediate at the onset of the reaction that then leads to insertion followed by protonation to yield the product. This study showed a great development in α-metalated *N,N*-dimethylbenzylamine rare earth catalysis.

Schmidt and coworkers continued to study lanthanum *N,N*-dimethylbenzylamine lanthanum complexes for the hydrophosphination of unactivated alkynes under mild conditions (Scheme 12).[38] Single addition hydrophosphination reactions to alkenes resulted in high regioselectivity, yielding only anti-Markonikov products. The hydrophosphination of alkynes with excess phosphine yielded the *E* isomer as the major product, except for when excess alkyne was used and the *Z* isomer was isolated as the major product.



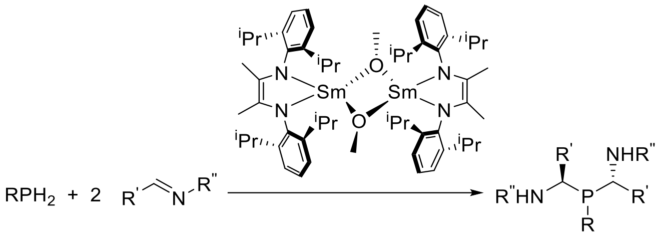
Scheme 12. Schmidt's *N,N*-dimethylbenzylamine lanthanum catalyzed hydrophosphination of alkynes.

4.3. Cerium

Cerium hydrides, which were secondary building units in a porous metal-organic framework (MOF) prepared by Lin and coworkers, were a catalyst for hydrophosphination reactions.[39] The report was dominated by characterization of these compounds, but the catalytic hydrophosphination of aliphatic alkenes was explored with good conversion after 5 d at moderate heating. This is a relatively lengthy reaction time, but examples of unactivated alkenes as successful substrates are still quite limited. The multi-day reaction time was normative for the mid-2010s for these substrates, though reaction times have substantially improved with new catalysts.

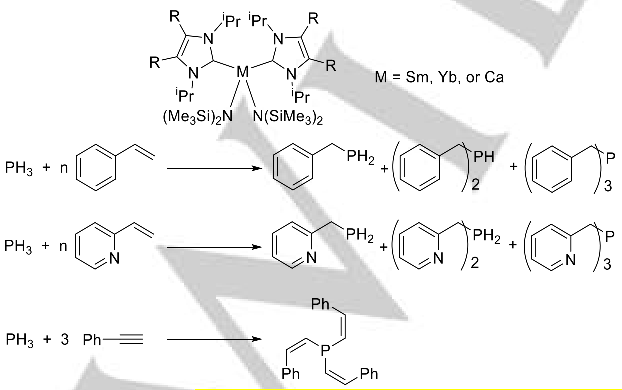
4.4. Samarium

Maron and Cui studied a dimeric ene-diamido samarium methoxide compound for the double P–H activation of primary phosphines with imines to prepare bis(α-amino)phosphines (Scheme 13).[40] Ideal conditions were found with 5 mol % of samarium precatalyst at ambient temperature. Under these conditions, quantitative conversion was realized to the double addition product, $[PhNHCH(Ph)]_2PPh$, where the highest dr values were observed in non-polar solvents such as benzene. Computational evidence explained the critical role of the ligand in controlling the activity and diastereoselectivity.



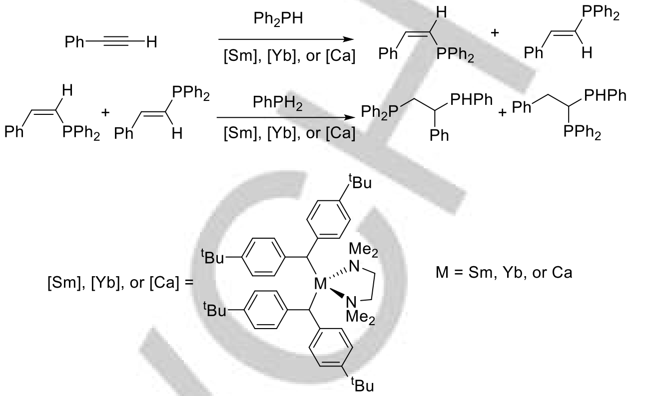
Scheme 13. Cui's samarium oxide catalyzed hydrophosphination of imines with phenylphosphine.

Trifonov returned to samarium, ytterbium, and calcium complexes, supported by bis(amido) N-heterocyclic carbene ligands for hydrophosphination with PH_3 (Scheme 14), which is uncommon among hydrophosphination reports.[9] Styrene, 2-vinylpyridine, and phenylacetylene were demonstrated as viable substrates with PH_3 in this study. Primary, secondary, and tertiary phosphines were produced in the hydrophosphination of styrene and 2-vinylpyridine from one or multiple P–H bond activations. Calcium and samarium catalysts favored the triple activation where the single and double addition predominated for ytterbium catalysts. When phenylacetylene was used as substrate, only the triple activation was realized in high conversions to exclusively yield tris(styryl)phosphine, strongly preferring the *Z* isomer. This study identified how catalyst can afford selectivity for the primary, secondary, and tertiary phosphine products. It was noticed that the catalytic activity of the catalysts was affected by the Lewis base coordination to the metal ion in the precatalyst.[9]



Scheme 14. Trifonov's rare earth and calcium bis(amido) NHC precatalysts for the hydrophosphination of unsaturated substrates with PH_3.

Trifonov and coworkers explored thermally stable calcium, ytterbium, and samarium bis(benzhydryl) complexes for hydrophosphination.[41] The facile hydrophosphination of stilbene, a typically challenging substrate, was achieved with quantitative conversion using $PhPH_2$. The first double sequential hydrophosphination of a triple bond was achieved using phenylacetylene with Ph_2PH and $PhPH_2$ facilitated by both calcium and ytterbium catalysts (Scheme 15).



Scheme 15. Samarium, ytterbium, and calcium catalyzed hydrophosphination of phenylacetylene with diphenylphosphine followed by phenylphosphine.

Trifonov also used ring-expanded NHC samarium and ytterbium compounds for hydrophosphination (Figure 8).[42] The activity of these catalysts were superior for styrene hydrophosphination compared to others present at the time. Unreactive terminal alkenes were also facile substrates. Excellent reactivity was attributed to the enhanced activity of σ-donating, ring expanded carbene ligands. The hydrophosphination of 1-cyclohexene resulted in 73% conversion and norbornene resulted in 89% conversion.

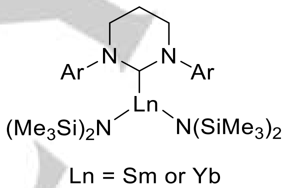
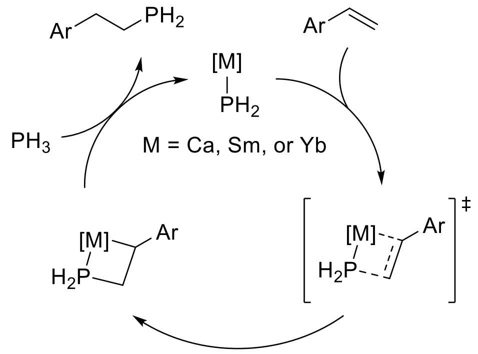


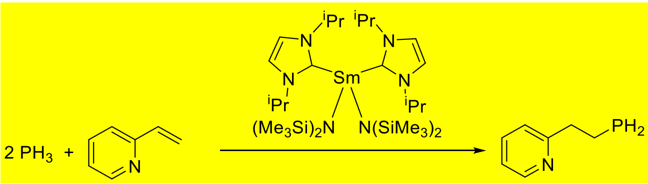
Figure 8. Trifonov's ring-expanded NHC rare earth hydrophosphination precatalyst.

In their most recent work, Trifonov and coworkers studied NHC-coordinated samarium, ytterbium, and calcium catalysts for the hydrophosphination of alkenes.[43] All complexes used started with the metal centers as cations in the +2 oxidation state. Primary phosphines were a common substrate in this study; however, it was found that all of the catalysts explored reacted with phosphine (PH_3) and multiple equivalents of styrene to selectively provide the double P–H activation product (secondary phosphine) at very low catalyst loading. This remarkable selectivity for the secondary phosphine allows for further functionalization via the remaining P–H bond. A tentative reaction mechanism is proposed where catalysis occurs through a metallacyclic intermediate containing a dative bond from the phosphine moiety (Scheme 16).



Scheme 16. Rare earth and calcium catalyzed hydrophosphination of vinylarenes with PH_3.

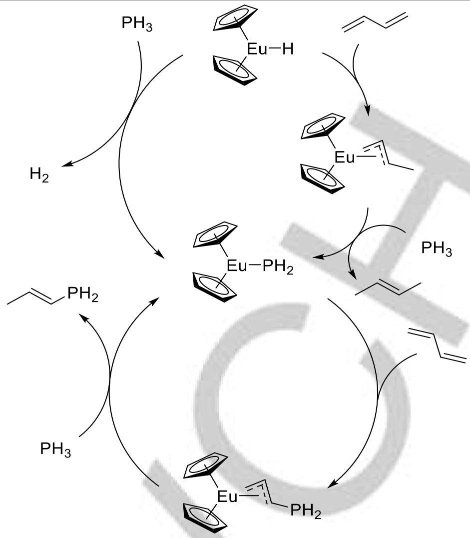
Most notably, Trifonov and coworkers demonstrated with one of their samarium NHC precatalysts the selective hydrophosphination of 2-vinylpyridine with phosphine (PH_3) to avail the primary phosphine product when two equiv. of phosphine are used with respect to vinyl pyridine (Scheme 17). This provides a new methodology to selectively prepare uncommon primary phosphines without the use of any chlorinated reagents.



Scheme 17. Samarium catalyzed hydrophosphination of 2-vinylpyridine with phosphine.

4.5. Europium

A theoretical study by Maron explored the capability of Cp_2EuH for the hydrophosphination of 1,3-butadiene using PH_3 (Scheme 18).[44] Cp_2EuH was the precatalyst that would form the active catalyst, Cp_2EuPH_2, in the presence of phosphine. Based on the computation, this occurs in two different ways: P–H bond activation of PH_3 with Cp_2EuH or a two-step reaction where the 1,4-insertion of 1,3-butadiene occurs into the Eu–H bond followed by P–H bond activation. The latter of the two mechanisms was calculated to be both thermodynamically and kinetically favorable. A catalytic cycle was proposed where the phosphido compound, Cp_2EuPH_2 reacts with 1,3-butadiene via a 1,4-insertion into the Eu–P bond followed by P–H activation. It is proposed that no side reactions can occur, leading to a very efficient process. Side products arise from isomerization of the phosphoallyl intermediate that forms upon insertion. Isomerization is only possible for 1,3-dienes. If non-conjugated dienes are used, 1,4-insertion would not occur, and no additional isomers are observed.

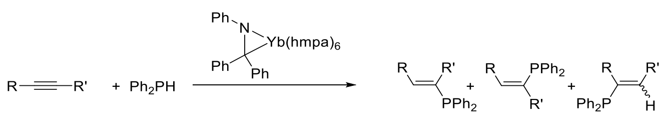


Scheme 18. Theoretical europium catalyzed hydrophosphination of 1,3-butadiene and phosphine.

Shen and coworkers synthesized divalent bridged bis(guanidinate) europium(II) compounds and employed them for the hydrophosphination of styrene derivatives and alkynes.[45] Excellent reactivity was observed with all reactions nearing completion in 12 h or less with a low catalyst loading of 1 mol %. *Anti*-addition products were predominant for the hydrophosphination of alkynes.

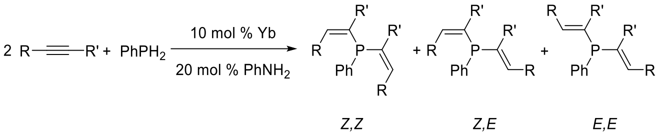
4.6. Ytterbium

Takaki and coworkers made the first report of the intermolecular functionalization of C–C multiple bonds using ytterbium-imine compounds (Scheme 19).[46] Internal and terminal alkynes were explored along with diynes and dienes. All products were obtained in high yield after oxidative workup. This catalysis was later extended to samarium, and ytterbium was also revisited in a later report.[47] These compounds were shown to facilitate others types of reactivity such as hydrosilylation and dehydrogenative silylation. Takaki later expanded on this work with a larger substrate scope.[48] Stereoselectivity of phosphinoalkenes products were deemed to be dependent on the alkyne substituents, where aliphatic alkynes preferred the *Z* product and aromatic alkynes preferred the *E* product. Diynes, dienes, allenes, and styrene derivatives were also utilized as substrates. The Yb-imine precatalyst reacts with Ph_2PH to form a Yb-phosphido species. Insertion of the unsaturated substrates into the Yb–P bond was proposed to be the turnover limiting step during catalysis, which is followed by protonation by Ph_2PH and/or the liberated amine to form the phosphinoalkene. Takaki made a later report where similar lanthanide catalysts were explored with silyl phosphine substrates.[49]



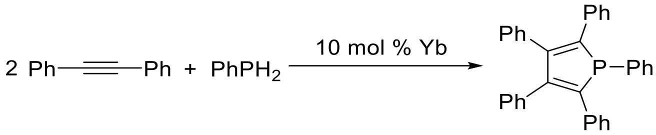
Scheme 19. Ytterbium-catalyzed hydrophosphination of alkynes.

The dual hydrophosphination of diynes was studied in depth by Takaki and coworkers using ytterbium(II) and (III) catalysts (Scheme 20).[50] Single hydrophosphination products would be isolated with a strong preference for the *Z* isomer through *anti*-addition. A second hydrophosphination event may then occur to yield a *Z,Z* isomer predominantly. Treating two equiv. of alkyne with one equiv. of $PhPH_2$ and 10 mol % catalyst with 20 mol % of aniline yields dual P–H activation products.



Scheme 20. Ytterbium catalyzed double P–H alkyne hydrophosphination.

The *Z,Z*, *Z,E*, and *E,E* isomers were produced, usually preferring the *Z,Z*. A similar reaction with diphenylacetylene and one equiv. of $PhPH_2$ in THF under reflux with 10 mol % catalyst gave cyclic phospholanes in low yield (Scheme 21). Aliphatic alkenes were tested under similar conditions but only double P–H bond activation was realized.



Scheme 21. Ytterbium catalyzed hydrophosphination/cyclization of diphenylacetylene with phenylphosphine.

Carpentier and Trifonov prepared heteroleptic ytterbium complexes with amidinate and carbazolyl ligands for the hydrophosphination of styrene (Figure 9).[51] With moderate heating and low catalyst loadings of 1–2 mol %, modest conversions were observed for Ph_2PH and $PhPH_2$, especially for shorter reaction times. The carbazolyl catalysts were found to be superior to amidinates for hydrophosphination catalysis. It was hypothesized to be a result of the lower formal coordination number in carbazolyl catalysts, which led to increased activity.

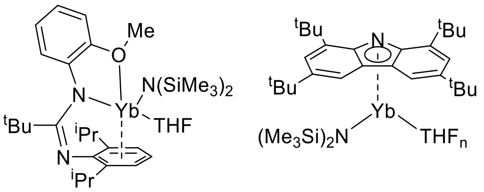


Figure 9. Carpentier and Trifonov's amidinate and carbazolyl ytterbium precatalysts.

Carpentier, Sarazin, and Trifonov went on to develop highly active, chemo- and regioselective ytterbium and samarium catalysts wielding aminoether-phenolate ligands for the hydrophosphination of styrene with $PhPH_2$ (Figure 10).[52] Three different ligand sets were prepared and tested with the two metals. As with other examples of rare earth catalyzed hydrophosphination, the reaction proceeds through insertion of the C=C double bond into the M–P bond of the catalytically active species. These catalysts were found to be very active, producing the anti-Markonikov products in quantitative conversions in as little as 30 min for some examples.

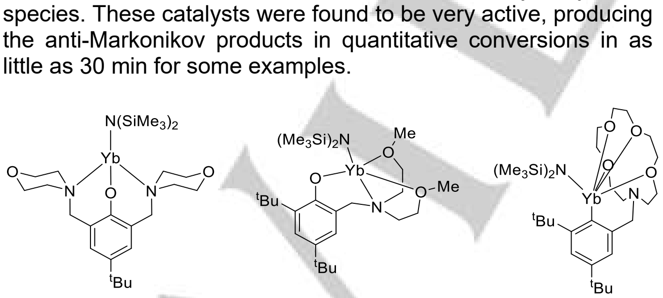


Figure 10. Carpentier, Sarazin, and Trifonov's ytterbium aminoether-phenolate hydrophosphination precatalysts.

Again employing aminoether phenolates, divalent rare earth and alkaline earth precatalysts were made by Carpentier, Sarazin, and Trifonov for the single and double P–H bond activation of $PhPH_2$ using alkene substrates.[53] Styrene derivatives were tested and the ytterbium catalysts were very competent for this reactivity. Conjugated dienes and isoprene were good substrates but less active. The hydrophosphination of 1-nonene was attempted but only reached 3% conversion after several days.

Cui and coworkers used an NHC ytterbium amide compounds (Figure 11) as precatalyst for the hydrophosphination of styrene derivatives, pyridines, dienes, and alkynes.[54] The Yb-NHC catalysts were active for hydrophosphination with loadings as low as 0.1–0.2 mol %. Similar to work reported by Marks, these could be used in the polymerization of styrene substrates where the polymer included a PPh_2 end group.

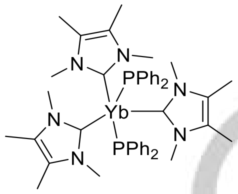
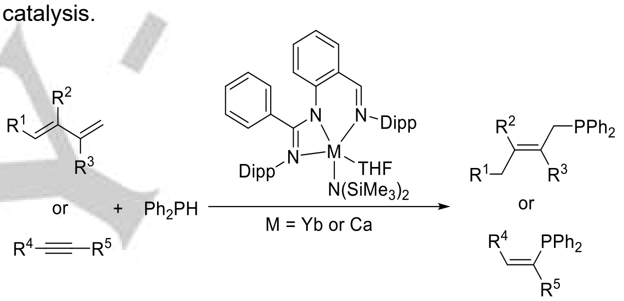


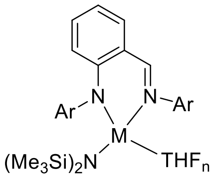
Figure 11. Cui's NHC ytterbium amide hydrophosphination and polymerization catalyst.

The hydrophosphination of alkenes, alkynes, and dienes using ytterbium and calcium compounds supported tridentate imino-amidinate ligands was tested by Cui and coworkers (Scheme 22).[55] High conversions were realized for each substrate and catalyst combination. Selectivity between *E* and *Z* isomers for the alkyne substrates would often vary. These ligands and metal types show promise of high selectivity with good conversion that could be further optimized for more efficient catalysis.



Scheme 22. Calcium and ytterbium catalyzed hydrophosphination of unsaturated substrates.

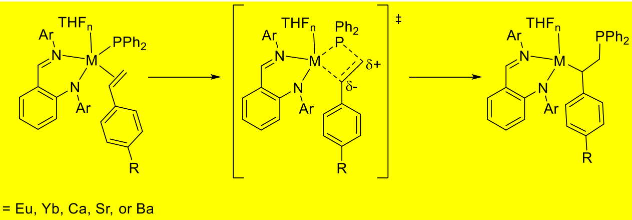
Carpentier and Sarazin studied heteroleptic alkyl and amide iminoanilide complexes of a variety of rare earth and alkaline earth elements (Eu, Yb, Ca, Sr, and Ba) for hydrophosphination reactions (Figure 12).[56]



M = Eu, Yb, Ca, Sr, or Ba

Figure 12. Carpentier and Sarazin's rare and alkaline earth amide iminoanilide complexes.

The hydrophosphination of *para*-substituted styrene derivatives with Ph_2PH and Cy_2PH was probed for three different ligand sets. Lower reactivity was observed with electron donating substituents. Isoprene and other dienes were also used as substrate. Similar to their hydroamination studies, the trend of reactivity for the metals was observed to be Ba > Sr(~Eu) > Ca(~Yb). The kinetic rate law was determined to be in orders of 0, 1, and 1 found for phosphine, styrene, and precatalyst, respectively. These results and the observed anti-Markovnikov selectivity are consistent with the transition state bearing a negative charge on the benzyl carbon atom that is stabilized with increasing efficiency upon introduction of *para*-substituents of higher electron-withdrawing strength. The rate determining step was proposed to be insertion of the polarized C=C double bond into the phosphido M–P bond (Scheme 23).



Scheme 23. Anti-Markovnikov P–C bond forming transition state.

Roesky developed chiral benzamidinate complexes of Eu, Yb, Ca, Sr, and Ba (Figure 13).[57] Styrene substrates were explored, and at 5 mol % loading with modest heating, good product conversions were observed after several hours. Though Roesky's catalysts are chiral, no clear enantioselectivites were obtained in this study.

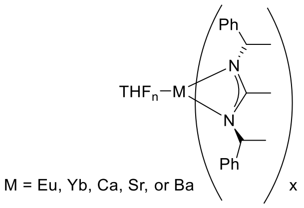


Figure 13. Roesky's chiral alkaline and rare earth benzamidinate hydrophosphination catalyst.

Trifonov further expanded the breadth of lanthanide hydrophosphination catalysts with bi- and tridentate amidinate ytterbium (Figure 14), samarium, and calcium compounds.[58] The hydrophosphination of alkenes and alkynes were tested with both primary and secondary phosphines. Reactions proceeded cleanly in toluene under mild conditions and afford good yields in most examples.

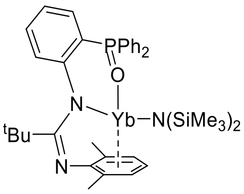


Figure 14. Trifonov's tridentate ytterbium hydrophosphination catalyst.

Trifonov and coworkers make another development with amidine-amidopyridinate ytterbium and calcium complexes for the catalytic hydrophosphination of alkenes (Figure 15).[59] In this report, additional phosphines beyond the typical set of Ph_2PH, Cy_2PH, and $PhPH_2$ were studied. Mesityl phosphine and 2-pyridyl phosphine, for example, were also used. Dramatic effects of steric and electronic properties of the ancillary ligand were realized with respect to both catalytic activity and selectivity in the reactions. For example, a fluorine atom at the *ortho*-position on one of the ligands leads to a noticeable increase in catalytic activity, but no change in chemoselectivity was observed. This was attributed to weak fluorine coordination to the metal ion. All compounds demonstrate high catalytic activity and regioselectivity in hydrophosphination with both $PhPH_2$ and Ph_2PH.

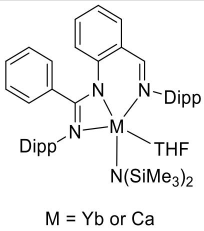


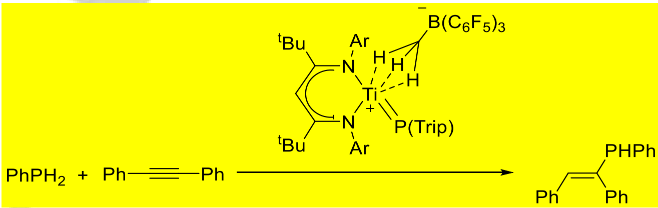
Figure 15. Trifonov's ytterbium and calcium amidine-amidopyridinate hydrophosphination precatalyst.

A final point about these elements is that their rich hydrophosphination chemistry is intimately related to that of the alkaline earth elements where the trajectory of rare earth hydrophosphination catalysis is echoed by the statements made in concluding the preceeding section.

5. Early Transition Metals

5.1. Titanium

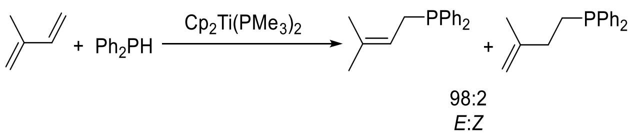
Mindiola reported an initial example of titanium-catalyzed hydrophosphination in 2006.[60] A family of titanium(IV) phosphinidene compounds based on the '(^{tBu}nacnac)Ti=P(Trip)' (^{tBu}nacnac = (Ar)NC(^{t}Bu)CHC(^{t}Bu)N(Ar), Ar = 2,6-$(CHMe_2)_2C_6H_3$, Trip = 2,4,6-$^iPr_3C_6H_2$) framework were prepared. Most germane, when (^{tBu}nacnac)Ti=P(Trip)CH_3 was reacted with $B(C_6F_5)_3$, methide abstraction to form the zwitterionic titanium(IV) phosphinidene compound (^{tBu}nacnac)Ti=P(Trip)($CH_3B(C_6F_5)_3$) was achieved. This compound was shown to catalyze the hydrophosphination of diphenylacetylene with $PhPH_2$ (Scheme 24).



Scheme 24. Mindiola's titanium-phosphinidene–catalyzed hydrophosphination of diphenylacetylene.

The reaction of (^{tBu}nacnac)Ti=P(Trip)($CH_3B(C_6F_5)_3$) with phenylacetylene produces a four-membered metallocycle through a [2 + 2] cycloaddition, presumably the first step during catalysis. An equivalent of phenylphosphine is proposed to then cleave the metallocycle and form a new Ti–P bond, which then releases the secondary vinyl phosphine product and restores the active phosphinidene compound catalyst. The vinyl phosphines are produced in a mixture of *E*/*Z* isomers in a ratio of 5:2, as determined by ^{31}P NMR spectroscopy.

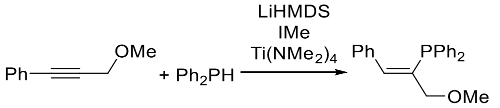
Le Gendre went on to expand the breadth of substrates for titanium-catalyzed hydrophosphination, investigating conjugated dienes.[61] In exploring the reactivity of $Cp_2Ti(PMe_3)_2$, Le Gendre and coworkers identified that 1,3-dienes undergo a 1,4-hydrophosphination. Isoprene was the first substrate tackled in this study, which yielded almost exclusively (98%) the 1,4-tail-addition (Scheme 25).



Scheme 25. Le Gendre's titanium-catalyzed hydrophosphination of terminal dienes.

Further studies with other titanium catalysts yielded mixed results with isoprene, and the best regioselectivity was observed with $Cp_2Ti(PMe_3)_2$ and $CpTiCl_2(\eta^5\text{-}C_5H_4(CH_2)_2PPh_2)$. A wider set of conjugated dienes was explored using $CpTiCl_2(\eta^5\text{-}C_5H_4(CH_2)_2PPh_2)$, including 1,3-cyclohecadiene, (1*R*)-nopadiene, and myrcene, which were all successful substrate candidates that underwent hydrophosphination with excellent regioselectivity. When using $CpTiCl_2(\eta^5\text{-}C_5H_4(CH_2)_2PPh_2)$, 20 mol % of ^nBuLi was necessary to activate the catalyst. Additionally, 1,3,5-cycloheptatriene underwent hydrophosphination in these studies. Unfortunately, efforts to extend this methodology to alkynes was unsuccessful. It was hypothesized that the mechanism involves the formation of a syn-π-allyl intermediate which forms as the major isomer, providing the high regioselectivity. A π/σ rearrangement is initiated by the re-coordination of the PR_2 moiety to the titanium center, where protonolysis of the resulting η^1-allyl complex with free phosphine leads to the 1,4-tail-addition and regenerates the active catalyst.

Takaki described the hydrophosphination of propargylic ethers with diphenylphosphine using $Ti(NMe_2)_4$, with added *N*-heterocyclic carbene (NHC) and lithium hexamethyldisilazide (LiHMDS).[62] Various catalyst systems were tested in this study, but the use of 10 mol % of $Ti(NMe_2)_4$, 1,3-dimethylimidazol-2-ylide (IMe) and LiHMDS was most effective, affording 97% conversion with a 97:3 *Z*/*E* ratio. Other propargylic alkynes with groups such as benzyl, *tert*-butyldimethylsilyl, and 2-tetrahydropyranyl were tested in this three-component catalysis with success (Scheme 26).



Scheme 26. Takaki's titanium-catalyzed hydrophosphination of propargylic ethers.

Although this methodology performed well, the role of the individual components was ultimately unclear. Sharp resonances at δ = –19 and –22 ppm in the ^{31}P NMR spectrum were observed upon reaction of LiHMDS/$Ti(NMe_2)_4$ and Ph_2PH in THF that were assigned to two phosphido species, which were posited to be responsible for the relatively high reaction rate and regioselectivity.

5.2. Zirconium

In 2010, Waterman and coworkers studied a triamidoamine-supported zirconium metallocycle, $(N_3N)Zr$ (Figure 16).[63]

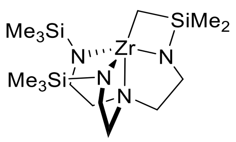


Figure 16. Waterman's triamidoamine zirconium catalyst.

Under mild conditions, $(N_3N)Zr$ reacts rapidly with P–H bonds to cleanly afford $(N_3N)ZrPRR'$ (R = alkyl, aryl; R' = R or H).[64] This compound formed vinyl phosphines from terminal alkynes with poor regioselectivity.[63] Those initial explorations of hydrophosphination catalysis were poor compared to contemporary catalysts for related substrates (e.g., Barrett and Hill),[13b, 17-18] and these reactions were largely ignored until 2014. At that time, significantly enhanced reactivity was observed with primary phosphine substrates in which unactivated alkenes were now reasonable, albeit challenging, substrates.[65] The continued exploration of $(N_3N)Zr$ led to the fortuitous discovery of photocatalysis while elaborating on the double hydrophosphination of internal alkenes in a complement to reactivity reported by Nakazawa.[66] That photocatalytic chemistry was leveraged to improve reactivity at $(N_3N)Zr$, affording both greater reactivity[67] and substrate scope.[68] Current evidence supports elongation of the Zr–P bond in the excited state, leading to more facile insertion. These studies have been described in greater detail recently and therefore not elaborated upon here.[69]

Yuan and Yao have advanced zirconium as a catalyst with a library of neutral and cationic zirconium compounds bearing multidentate aminophenolato ligands for the hydrophosphination of alkenes and heterocumulenes.[70] In one study, six distinct aminophenolato zirconium compounds exhibiting various substitution patterns were used for hydrophosphination. The hydrophosphination of styrene with diphenylphosphine was tested at 10 mol % catalyst loading at ambient temperature. Styrene derivatives with different substitution patterns and other activated alkenes were tested with the most active catalyst exhibiting moderate to excellent conversions for all substrates tested. Cationic zirconium complexes were prepared upon reaction of their neutral analogs with $(Ph_3C)[B(C_6F_5)_4]$ and screened as catalysts. A variety of carbodiimides and isocyanates were successfully tested with the most active cationic zirconium catalyst. It was noted that cationic species were more active for heterocumulenes (i.e., carbodiimides and isocyanates) to produce phosphaguanidines and phosphaureas. Cationic catalysts were found to be less active for alkene hydrophosphination which was proposed to be due to a stronger Zr–P bond for cationic species, increasing the barrier to migratory insertion.

Expanding on this work, Yuan and Yao explored their zirconium aminophenolato catalysts for the hydrophosphination of alkenes and alkynes with phenylphosphine.[71] While two of the catalysts used were present in their previous report, two new zirconium aminophenolato catalysts were explored. All catalysts were tested with styrene and phenylphosphine to undergo hydrophosphination with good selectivity for single P–H activation product. Cationic catalysts were found to be largely inactive in this report. Styrene derivatives and other unsaturated substrates were tested with their most active catalyst to afford products in good yields. Kinetic studies were undertaken to gain insight into their hydrophosphination reactions. A fractional order of 1.7 for $PhPH_2$ was determined where the rate law, rate = $\kappa[\text{styrene}]^1[\text{phenylphosphine}]^{1.7}[\text{catalyst}]^1$, was deduced.

In addressing whether photocatalytic hydrophosphination is a general phenomenon, Waterman and coworkers turned to determine if Yuan and Yao's aminophenolato zirconium catalysts could profit from improved reactivity under irradiation as was observed for $(N_3N)Zr$ (*vide supra*).[68a, 70-71] Using the most active alkene hydrophosphination catalyst with diphenylphosphine and another, less active counterpart from Yuan and Yao's work, hydrophosphination reactions were screened under irradiation, ambient light, and in the dark (Figure 17).

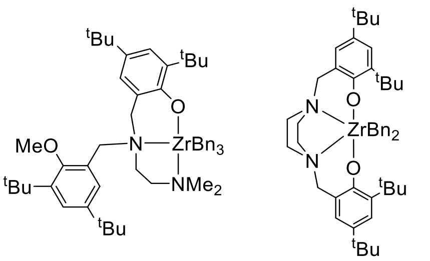


Figure 17. Two examples of Yuan and Yao's zirconium aminophenoxide hydrophosphination catalysts that are also photocatalytic.

Improved reactivity was observed for both diphenylphosphine and phenylphosphine, complementing Yuan and Yao's contribution to zirconium-catalyzed hydrophosphination. Using spectroscopic and structural data from one of the catalysts, a computational model for the putative active catalysts was produced. TDDFT results suggest the lowest lying excited state is populated by a charge transfer from the P 3 *p* orbital to the Zr 4 *d* orbital which are P *n* → Zr *d* transitions. Based on (N_3N)Zr, it was proposed that this charge transfer is correlated with weakening of the Zr–P bond in the lowest excited state, thereby facilitating insertion chemistry. Critically, the phenomenon of photocatalytic hydrophosphination appears to be independent of geometry and donor for these d^0 metals, suggesting this is a broad phenomenon, a notion being supported by recent late transition metal reactivity (*vide infra)*.

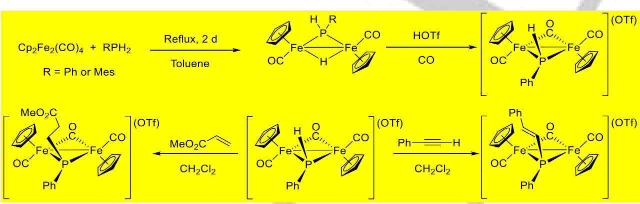
With these significant contributions, the trajectory for early metal hydrophosphination catalysis is promising. Improvement of activity through irradiation is likely to be general for d^0 metal in a way that may enhance already successful rare and alkali earth element catalysis. There is clearly significant growth possible in the scope of metals where group 4 metals have been the sole focus of these studies. While most of these catalysts have direct or indirect evidence to suggest insertion-based hydrophosphination, the cycloaddition at titanium as well as other interesting features of titanium-based catalysis indicate that unique discoveries are possible that can upend conceptions around selectivity. Overall the successes from the global community in this area continues to demonstrate opportunity as much as innovation in the field.

6. Mid Transition Metals

The mid transition metals are attractive targets for homogeneous catalysis. The 3 *d* elements in that set benefit from a generous abundance and potentially low toxicity, with iron at the fore of earth abundance. Many compounds, perhaps ironically with the exception of those containing 3 *d* metals, are most likely to exhibit classic, textbook-style organometallic reactions steps, and there are notable examples of metal-ligand cooperation that can facilitate catalysis in ways that may address latent challenges.

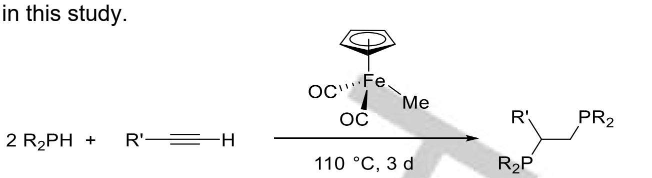
6.1. Iron

Initial stoichiometric iron chemistry that heralded later developments came from Hashimoto and Tobita in 2005 exploring a neutral phosphido-bridged diiron compound.[72] Hashimoto and Tobita's compound was prepared by treating $Cp_2Fe_2(CO)_4$ with $PhPH_2$ under reflux, and reaction with triflic acid under CO afforded [$Cp_2Fe_2(CO)_2$(μ-CO)(μ-PHPh)](OTf). This derivative was treated with a stoichiometric amount of phenylacetylene or methyl acrylate to afford the formal products of P–H bond insertion in quantitative yield. These transformations, whether or not catalytically relevant, demonstrated the key P–H bond activation and P–C bond formation steps essential to hydrophosphination catalysis (Scheme 27).



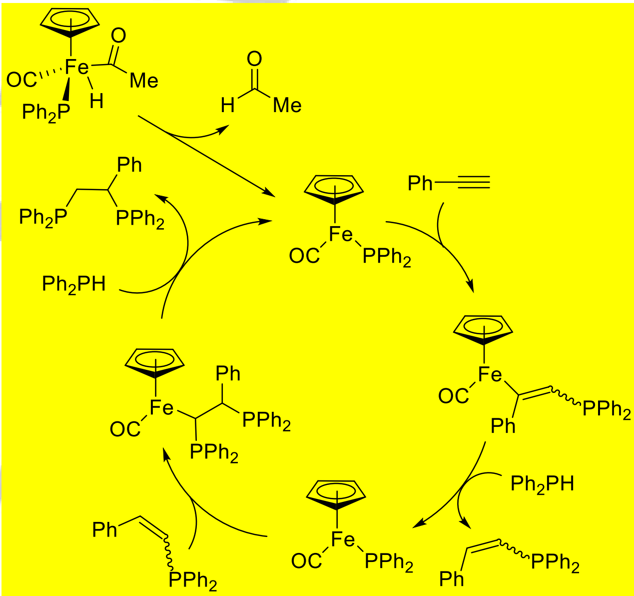
Scheme 27. Phosphido and insertion chemistry of cyclopentadienyl iron complexes.

The first iron hydrophosphination catalyst was reported by Nakazawa in 2012, undertaking the regioselective, 1,2-double hydrophosphination of terminal alkynes.[73] Nakazawa tested many iron catalysts, but the most active was the piano stool compound, $CpFe(CO)_2Me$, which could be used at 5 mol % loading. Heating at 110 °C for 3 days afforded 1,2-bis(diphenylphosphino)-1-phenylethane in 94% yield (Scheme 28). The length of reaction and temperature indicate the difficulty of this transformation to value-added products. Other diaryl phosphines and terminal aryl alkynes were successful substrates in this study.



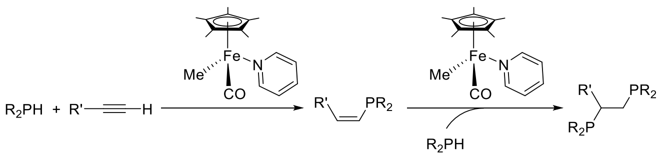
Scheme 28. Nakazawa's iron-catalyzed double hydrophosphination of terminal alkynes.

This is a key advance in which privileged diphosphinoethane ligands could be synthesized using an earth-abundant catalyst. A DFT study where a detailed mechanism was constructed suggested the reaction proceeded in three steps,[74] beginning with the formation of the active species via the elimination of an equivalent of acetaldehyde. A single hydrophosphination then occurs with *E* and *Z* configurations being formed at this step while the active species is regenerated once again. The regenerated active species reacts with the phosphinoalkene from the first hydrophosphination event, affording the double hydrophosphination product (Scheme 29). Part of the need for forcing conditions was indicated by coordination of the intermediate vinylphosphine during catalysis.



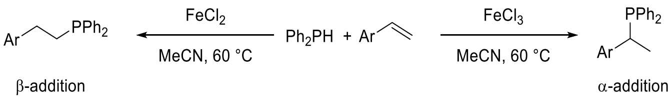
Scheme 29. Iron catalyzed double hydrophosphination of phenylacetylene.

In a follow on study, Itazaki and Nakazawa reported the synthesis of vinylphosphines and unsymmetrical diphosphinoethane derivatives using an iron piano stool complex, Cp*Fe(CO)(py)Me (Scheme 30).[75] Vinyl phosphines were prepared from diaryl phosphines and terminal alkynes, generally preferring the *Z* isomer. Vinyl phosphines were further reacted with diaryl phosphines to yield unsymmetric diphosphinoethane products using 5 mol % catalyst loading. Mechanistic studies determined that Cp*Fe(CO)($PHPh_2$)PPh_2 and a metallaphosphacyclobutene were the resting states in the cycle, which were isolated and fully characterized.



Scheme 30. Nakazawa iron-catalyzed hydrophosphination of terminal alkynes.

Taillefer and Gaumont identified a simpler catalyst system capable of selecting between Markovnikov and anti-Markovnikov addition to styrene substrates. Their use of simple iron salts began with iron(II) chloride as a catalyst that affords the β-addition product, whereas iron(III) chloride affords the α-adduct addition product (Scheme 31).[8] Access to both Markovnikov products via catalytic hydrophosphination was unprecedented and remains unmatched in simplicity of the catalyst. Thus, this remains a highly attractive methodology. The selectivity of iron(III) salts to produce Markovnikov products remains unclear and relatively rare for metal catalysts to date, but the investigators suggest this is due to the difference in Lewis acidity between the iron salts.



Scheme 31. Taillefer and Gaumont's Markovnikov vs. anti-Markovnikov iron-salt–catalyzed hydrophosphination.

Ambient temperature hydrophosphination catalyzed by iron salen compounds was later developed by Webster and coworkers (Figure 18).[76] At low catalyst loading of 0.5 mol %, hydrophosphination of styrene derivatives, vinylpyridines, and acrylates occurred in good yields with diphenylphosphine. The reaction was deemed to be radical driven, and the phosphine products were utilized as pro-ligands for the iron-mediated Negishi cross coupling of benzyl bromides and diaryl zinc reagents, demonstrating the synthetic application of the phosphines prepared by hydrophosphination.

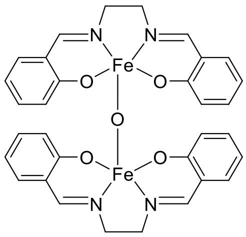


Figure 18. Webster's iron salen hydrophosphination catalyst.

Webster went on to report the catalytic dehydrocoupling of phosphines using β-diketiminate iron(II) compounds (Figure 19).[77] The hydrophosphination of alkenes with these iron compounds was also explored in this report. Substituted styrene derivatives and acrylate substrates were successfully utilized in good yields after 24 h with diphenylphosphine.

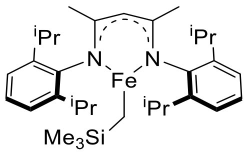


Figure 19. Webster's β-diketiminate iron(II) hydrophosphination catalyst.

Additional study of hydrophosphination using similar iron(II) β-diketiminate compounds using alkene and alkyne substrates has been reported.[78] In that work, intramolecular hydrophosphination of unactivated substrates yielded the cyclic products. The active catalyst was found to be a dimer bearing two bridging phosphido ligands. An in-depth study of the mechanism suggests that the transformation proceeds via a radical pathway in which one iron species and a phosphine molecule are involved. The catalyst resting state and the precise nature of the radicals involved in catalysis remained undetermined.

Mahon and Webster describe an air-stable, iron(III)-μ-oxo precatalyst bearing salen and tetraphenyl porphyrin ligands for the hydrophosphination of alkenes with phenylphosphine and diphenylphosphine (Figure 20).[79] Catalysis was performed with Ph_2PH to avail tertiary phosphines. Secondary phosphines were prepared through the hydrophosphination of vinyl phosphines with phenylphosphine, and similar reactions using two equiv. of $PhPH_2$ results in the double activation of the P–H bond activation to yield tertiary phosphines.

Webster demonstrated the utility of the hydrophosphination products using the iron(III)-μ-oxo-bridged salen dimer in cross-coupling reactions.[80] The hydrophosphination products of diphenylphosphine with 2-methyoxy styrene, 2-vinylpyridine, and methylacrylate were used as ligands in the palladium catalyzed cross coupling of aryl bromides with styrene, methylacrylate, methylmethacrylate, and 2-methoxyphenyl boronic acid. Suzuki-Miyaura cross-coupling was also explored using the same phosphine ligands with phenylboric acid along with aryl halide and amine cross-couplings. The three ligands were compared to PPh_3 in all these studies. The product of hydrophosphination between 2-methoxy styrene and diphenylphosphine, (2-methoxyphenethyl)diphenylphosphane, proved to be a good ligand across a wide range of cross-coupling reactions, outperforming PPh_3. Methyl 3-(diphenylphosphanyl)propanoate showed good reactivity as well. Surprisingly, 2-(2-(diphenylphosphanyl)ethyl)pyridine is not a good ligand for cross coupling. The pyridyl group was proposed to stabilize intermediates during catalysis but any such behavior proved inconsequential in practice.

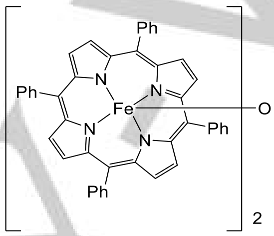
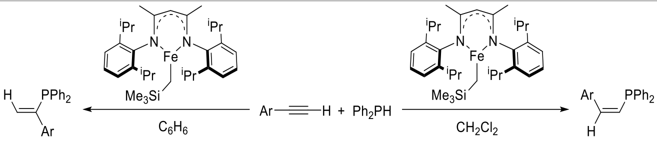


Figure 20. Mahon and Webster's air-stable iron(III)-μ-oxo catalyst for the hydrophosphination of primary and secondary phosphines.

Visible light photoactivation for hydrophosphination using the commercially available $[CpFe(CO)_2]_2$ was demonstrated by Waterman and coworkers, using styrene derivatives, vinylpyridines, and acrylates.[81] Upon irradiation of $(CpFe(CO)_2)_2$, two 17-electron compounds are formed that participate in cooperative P–H bond activation. Several alkenes were tested at ambient temperature with irradiation by >500 nm light to produce tertiary phosphines in good yield for activated substrates. Waterman and coworkers expand in this methodology in the visible-light and thermally driven double hydrophosphination of terminal alkynes using the same commercially available iron compound, $(CpFe(CO)_2)_2$.[82] Terminal aryl alkynes were used as substrate, similar to work done by Nakazawa in 2012, where photocatalysis reduced reaction times by about a third and thermal conditions reduced reaction times by about two thirds.[73] The increased activity of $(CpFe(CO)_2)_2$ was attributed to the additional CO ligand at iron, which is consistent with Nakazawa's mechanistic hypotheses for $CpFeMe(CO)_2$, where the additional CO ligand was lost during catalysis in his seminal report.

In a return to iron(II) β-diketiminate pre-catalysts, Webster demonstrated another rare system that can select between anti-Markovnikov and Markonikov products, in this instance based on the solvent used (Scheme 32).[83] Instead of alkenes, terminal aryl alkynes were used as substrates in this study. Catalysis done in benzene at 50 °C yielded Markovnikov addition in 3 h; whereas, catalysis done in CH_2Cl_2 at 70 °C yielded *Z* anti-Markovnikov products in 24 h. Large substrate scopes for both reactions were screened and several examples for each reaction was demonstrated with good yield and functional group tolerance. Preliminary mechanistic study suggests the source of divergent reactivity rises from the oxidation state and the mode of the P–C bond-forming process. Iron(II) and radicals are implicated in Markovnikov selective reactions, whereas in the anti-Markovnikov process, iron(III) is generated, and radicals appear not to be involved in the P–C bond forming step.



Scheme 32. Solvent-dependent regioselectivity of hydrophosphination as demonstrated by Webster using an iron(II) β-diketiminate compound.

Kays reported the hydrophosphination of isocyanates using $(2,6\text{-}Mes_2C_6H_3)_2Fe$ and $(2,6\text{-}Tmp_2C_6H_3)_2Fe(THF)$ (Tmp = 2,2,6,6-tetramethylpiperidine) under mild conditions.[84] The ease of reactivity was attributed to the low coordination number and the unique steric pocket created by bulky *m*-terphenyl ligands in $(2,6\text{-}Tmp_2C_6H_3)_2Fe(THF)$. Mono- or di-insertion products were obtained in high selectivity through simple modifications, such as the addition of weak acid to the reaction mixture or changes in solvent. For example, the addition of acid promoted the double insertion pathway, while switching the solvent from benzene-d_6 to THF affords the single insertion product almost exclusively.

6.2. Ruthenium

Ruthenium-catalyzed hydrophosphination has also been leveraged in recent times. The first example was described by Dixneuf and coworkers in 2003 for the hydrophosphination of propargyl alcohols.[85] Cp*Ru(cod)Cl (cod = 1,5-cyclooctadiene) was used along with other ruthenium piano stool complexes. Vinyl alcohols were prepared with a strong preference for the *Z* isomer.

Rosenberg reported the inner- and outer-sphere roles of ruthenium phosphido complexes in the hydrophosphination of alkenes (Figure 21).[86]

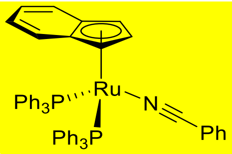


Figure 21. Rosenberg's original ruthenium phosphido hydrophosphination catalyst.

The proposed [2 + 2] cycloaddition at a coordinatively unsaturated $Ru{=}PR_2$ with alkenes is explored with prepared intermediates. New cationic ruthenium indenyl phosphine complexes were isolated and structurally characterized. An outer-sphere Michael addition process is also proposed to rationalize the observed selectivity for the hydrophosphination of activated alkenes. Detailed mechanistic study on these compounds has yielded substantial insight that has allowed Rosenberg and coworkers to leverage design principles that have substantially improved the activity of these compounds in the hydrophosphination of Michael acceptors.[87] Specifically, Replacing the indenyl ligand with Cp* (Figure 22) alters the turnover-limiting step, where a 30-fold increase in activity is observed. The turnover-limiting step in the Cp* ruthenium catalyzed process is suggested to be conjugate addition of the phosphido ligand to the substrate alkene. In the indenyl ruthenium catalyzed process, the turnover-limiting step is phosphine substitution during the product liberation step with Ph_2PH. The increased rate at the product liberation step is attributed to a more sterically conjested and labile ruthenium center when Cp* is used as a ligand.

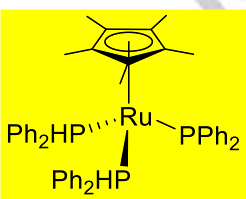


Figure 22. Ronsenberg's Cp* ruthenium hydrophosphination catalyst.

Waterman and coworkers further expanded on commercially available Group 8 catalysts by employing $[CpRu(CO)_2]_2$ for the hydrophosphination of alkenes and alkynes using phenylphosphine, diphenylphosphine, and cyclohexylphosphine.[88] Catalyst loadings as low as 0.1 mol % were used to yield phosphine products in good yield and reasonable reaction times. Three equiv. of $PhPH_2$ was necessary to avoid multiple P–H activations, however.

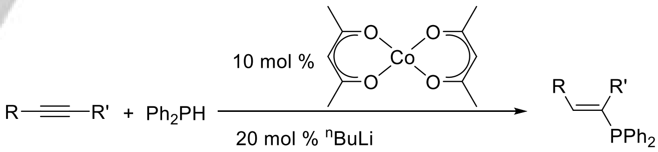
Mid-transition metals are enjoying a special status as not only highly active catalysts but as systems capable of unique reactivity and selectivity. This reactivity is also complemented by the high earth abundance of some of these metals. These developments and the strong connection of the hydrophosphination products to utility as ligands argue for a continued high pace of influential chemistry from these metals.

7. Late Transition Metals

Late transition metals have led in activity and selectivity for many catalytic transformations.[89] Although scarce, palladium and platinum maintain tremendous value as catalysts in a wide range of bulk and specialized transformations. With tuning by specified ligands, nickel and copper can facilitate similar chemistry to other noble metals with the added feature that these metals are available in far greater abundance. Since inception, catalytic hydrophosphination has had leading examples of reactivity or mechanistic understanding using late or noble metal catalysts, which has represented a great deal in the development of the transformation. Additionally, late metal catalysts have dominated asymmetric hydrophosphination, but that will be discussed in Section 10.

7.1. Cobalt

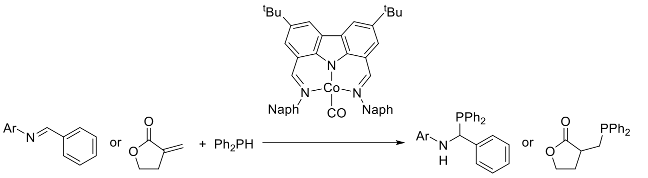
Group 9 metals have also garnered attention as catalysts for hydrophosphination. The first example came from Oshima and coworkers with their $Co(acac)_2$ catalyzed hydrophosphination of internal alkynes with Ph_2PH (Scheme 33).[90] These reactions largely yielded syn-addition products using 10 mol % catalyst loading, and 20 mol % $^{n}BuLi$ was necessary for catalyst activation.



Scheme 33. $Co(acac)_2$ catalyzed hydrophosphination of internal alkynes with diphenylphosphine.

Shanmugam later demonstrated the *E*-selective hydrophosphination of internal alkynes catalyzed by $Co(PMe_3)_4$.[91] A variety of functionalized alkynes, including very bulky functional groups were tested with good reactivity. The suprafacial addition of P–H across the alkyne in *syn*-fashion results in the regio- and stereoselective vinyl phosphine product, determined by deuterium labeling experiments. The active catalyst was proposed to be $CoH(PMe_3)_3(PPh_2)$, which forms upon oxidative addition of Ph_2PH to $Co(PMe_3)_4$.

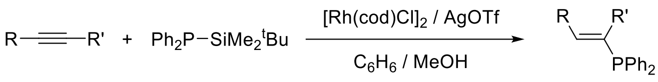
Kays reported a cobalt(I) *N,N,N*-pincer complex for the hydrophosphination of activated alkenes.[92] This example demonstrates good promise for cobalt(I) hydrophosphination catalysis and it is noteworthy that aromatic imines and lactones with terminal alkenes were used as substrates because they are uncommon in the literature (Scheme 34).



Scheme 34. Kay's cobalt-catalyzed hydrophosphination of imines and lactones.

7.2. Rhodium

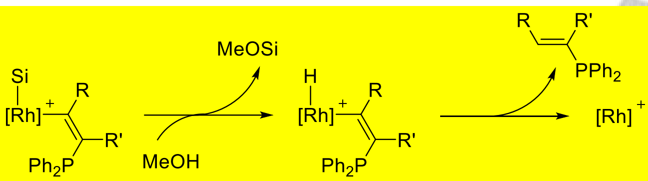
Rhodium has also been utilized in the hydrophosphination literature. The first report came from Hayashi and coworkers describing the hydrophosphination of internal and terminal alkynes using a silyl phosphine to afford the *E* product predominantly (Scheme 35).[93]



R = alkyl, aryl, or CO_2R''
R' = H, alkyl, or aryl

Scheme 35. Rhodium-catalyzed hydrophosphination of alkynes with silyl phosphines.

This methodology had a unique approach in employing silyl phosphines. It was proposed the silyl phosphine coordinated to the cationic rhodium(I) and oxidatively adds the P–Si bond to form a rhodium(III) intermediate. An alkene then coordinates and inserts into the Rh–P bond, which is subsequently cleaved of the Rh–Si bond via reaction with alcohol. The rhodium center then reductively eliminates the tertiary phosphine product (Scheme 36).



Scheme 36. Cleavage of Rh–Si bond and reductive elimination of product in rhodium catalyzed hydrophosphination of alkynes with silylphosphines.

Tejel reported the hydrophosphination of dimethyl fumarate with diphenylphosphine using $TpRhH(PMe_3)(PPh_2)$ (Tp = hydridotris(pyrazolyl)borate) (Scheme 37).[94] An isolable phosphido was prepared by treating TpRh $(C_2H_4)_2$ with Ph_2PH through oxidative addition. A further reaction with PMe_3 yields $TpRhH(PMe_3)(PPh_2)$. Similar reactions were attempted with phenylphosphine, but the products were too active to isolate, forming a bridged dimer species $\{TpRhH(\mu\text{-}PHPh)\}_2$.

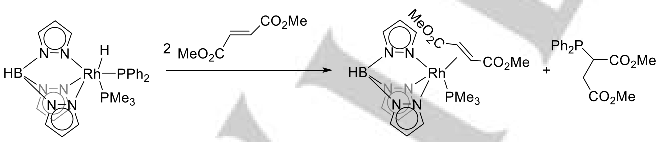
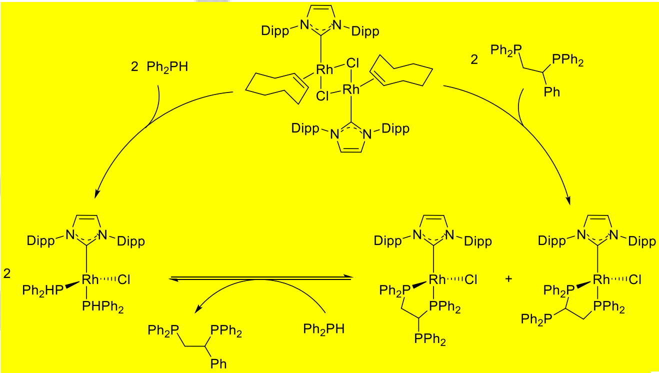


Figure 37. Rhodium catalyzed hydrophosphination of dimethylfumarate.

A later report by Tejel explains the role of the hydrido ligand in their catalysis.[95] Additionally, more substrates were tested such as acrylates, aldehydes, and enones. The activity was attributed to an outer-sphere P–C and C–H bond formation likely through a 1,3-dipolar cycloaddition. A displacement reaction of the functionalized phosphine with Ph_2PH, and facile P–H bond activation step regenerates the active species during catalysis. This supposition was supported by stoichiometric, kinetic, and DFT studies in which the critical P–C bond formation step takes place through intermediates where both the phosphido and hydride ligands interact with the α- and β-carbons of the alkene, respectively, in a cooperative way. It was also suggested the beneficial role of the Rh–H coordinating with a chloride anion avoids side reactions and facilitates hydrogen transfer from rhodium to the product. This was further supported by the poor activity of $Rh(Tp)Cl(PMe_3)(PPh_2)$, which lacks an electrophilic arm (i.e., the hydrido ligand).

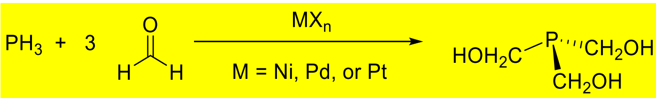
Di Giuseppe, Castarlenas, and Oro reported the double hydrophosphination of alkynes with a rhodium NHC compound, where the NHC ligand plays a pivotal role in catalysis.[96] Stochiometric reactions indicated that the mechanism proceeds through oxidative addition of the secondary phosphine, followed by migratory insertion and reductive elimination steps, first for the alkyne followed by the vinyl phosphine intermediate. It was suggested the enhanced activity of Nakazawa's double hydrophosphination system was attributed to the hard-soft mismatching of the iron and diphosphine and/or the bite angle of the catalyst. This was not the case for the soft rhodium(I) catalyst in Di Giuseppe's system. The NHC, however, plays a major role, enabling this catalysis by its stereoelectronic properties that prevent catalyst deactivation by coordination of the diphosphine products (i.e., product inhibition) as determined by stoichiometric reactions (Scheme 38).



Scheme 38. Intermediates in rhodium NHC catalyzed hydrophosphination determined by stoichiometric reactions.

7.3. Nickel

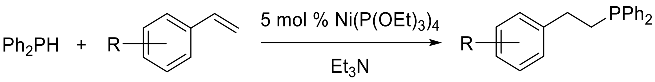
The hydrophosphination of formaldehyde catalyzed by tris(hydroxymethyl)phosphine nickel, palladium, and platinum salts was reported by Pringle and coworkers (Scheme 39).[97] Tertiary phosphines were prepared by the triple P–H bond activation of the parent phosphine substrate with formaldehyde in the presence of these group 10 metals. These reactions were performed in water due to the formaldehyde substrate, but that solvent choice foreshadowed later efforts for hydrophosphination catalysis in water. Palladium precatalysts proceeded 10x faster than nickel compounds under similar conditions. Interestingly, platinum compounds were found to demonstrate similar reactivity to palladium derivatives. The mechanism is proposed to proceed through oxidative addition of a phosphine P–H bond to the metal followed by the migratory insertion of an η^2-coordinated formaldehyde molecule, which is followed by product liberation via reductive elimination. It was believed phosphines in solution would inhibit product formation, but the catalyst still functioned efficiently despite the presence of phosphine and product. However, competitive, non-productive coordination of substrate and product remain a challenge for any catalysis involving phosphines as substrates or products.



Scheme 39. Group 10 metal catalyzed hydrophosphination of formaldehyde.

Beletskaya reported early examples of styrene hydrophosphination with late metal catalysts, namely nickel and palladium.[98] Nickel phosphine compounds such as $(PPh_3)_2NiBr_2$

would catalyze quantitative phosphine dehydrocoupling at 50 °C and afford product mixtures including hydrophosphination and dehydrocoupling at higher temperatures. The ideal nickel catalysts were found to be $Ni(P(OEt)_3)_4$, where one equiv. of Et_3N as an additive and two equiv. of styrene gave quantitative conversion in 20 h (Scheme 40). Phosphine dehydrcoupling has appeared as a competitive process in the literature and in empirical observations. While this study illustrates how this can be controlled in catalyst strcuture, design principles for differentiating these processes that both rely on P–H bond activation remain unknown.

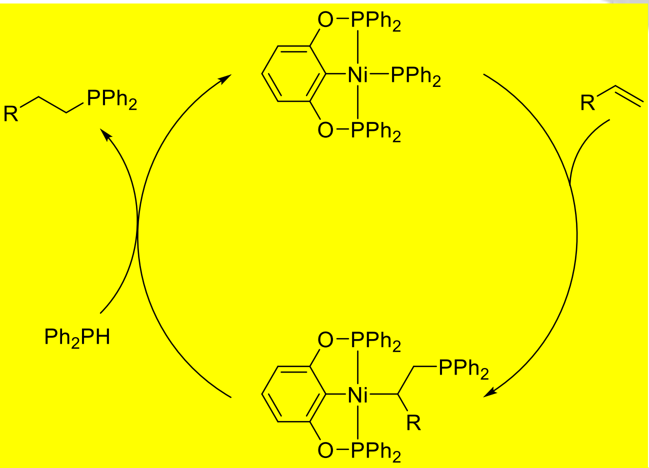


Scheme 40. Nickel-catalyzed hydrophosphination of styrene substrates.

Substituted alkenes and vinylpyridines were utilized as substrates as well in this study. Additional study of nickel and palladium hydrophosphination catalysts was undertaken by Beletskaya and coworkers.[99] Phenylacetylene was the substrate in this report where several palladium and nickel phosphine compounds were tested. In benzene solution, $Ni(acac)_2$ and $NiBr_2$ were among the most active precatalysts, and perfect selectivity for the *E* product phosphino alkene was achieved when using $NiBr_2$. This was the first reported catalytic hydrophosphination of a triple bond with diphenylphosphine.

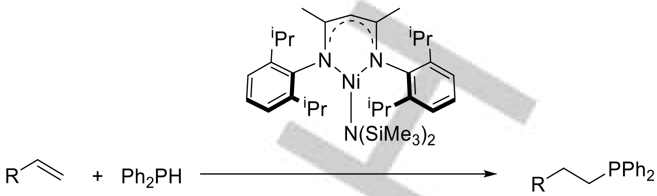
Alkoxyalkenes were used as substrates by Beletskaya and coworkers.[100] Similar to previous work, various nickel and palladium salts were tested for hydrophosphination catalysis, this time using butoxyethene as substrate. In toluene solution, $Ni(PPh_3)_2Br_2$ and $Ni(acac)_2$/HCl were among the most active precatalysts tested with quantitative conversion in 2 h with heating.

The notion that metal-phosphido compounds are nucleophilic with respect to hydrophosphination catalysis has assisted in development of new catalysts.[14, 101] A computational assessment of electron density in a nickel pincer complex with respect to the formation of P–C bonds was performed by Downey and coworkers.[102] The DFT analysis suggests catalysis proceeds through an insertion-based mechanism (Scheme 41). Pincer complexes were shown to be insensitive to solvent dielectric constants through the orbital energies and consequently the HOMO-LUMO gap.



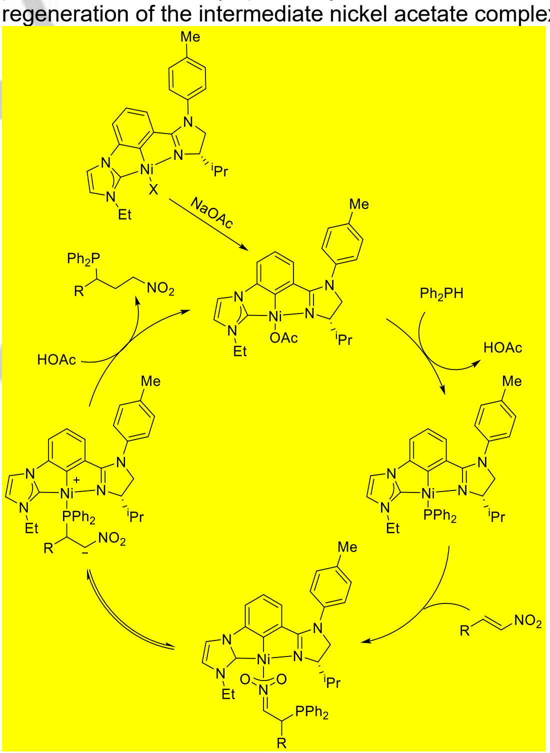
Scheme 41. Proposed mechanism for nickel PCP catalyzed hydrophosphination (R = alkyl, aryl).

In partial realization of these predictions, Webster reported the ambient temperature nickel catalyzed hydrophosphination and cyclotrimerization of alkynes.[103] Nickel β-diketiminate complexes were used as catalysts for internal alkynes, diynes, styrene derivatives, and acrylates (Scheme 42). Catalysis is assumed to proceed through a Michael addition mechanism, where telomerization is possible for some substrates. Under ideal conditions of 5 mol % of catalyst in acetonitrile solution, conversions in the 80% range were achieved in several hours.



Scheme 42. Nickel catalyzed hydrophosphination of alkenes.

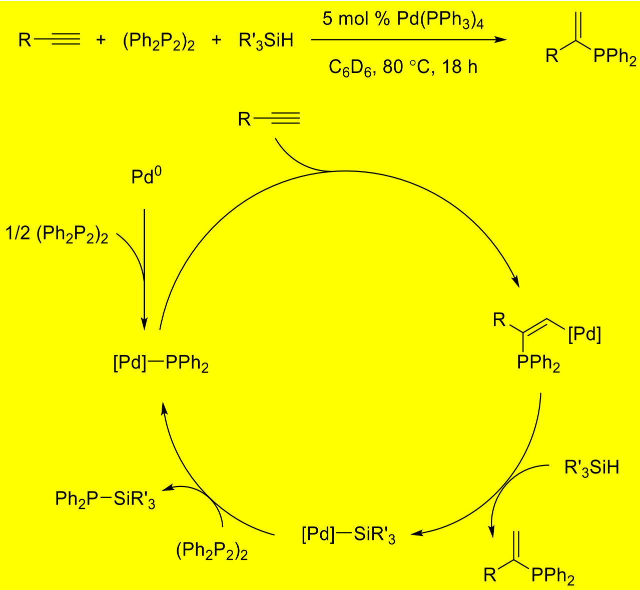
Zhu and Song reported the hydrophosphination of nitroalkene substrates with diphenylphosphine using nickel supported by a NCC pincer ligand.[104] This report marked the first use of nitroalkenes as substrate in the literature. Catalysis tolerated a wide range of functional groups on the nitroalkene, and Ad_2PH was successful in these reactions. Heteroaromatic and aliphatic nitroalkenes were tolerated and products were prepared in high yield. The reaction is proposed to proceed by activation of the nickel halide pre-catalyst complex with added sodium acetate, followed by a transphosphination with the secondary phosphine substrate to yield a phosphido intermediate. A nucleophilic attack of the nickel phosphido on the nitroalkene generates a neutral intermediate that might equilibrate with the zwitterionic nickel phosphido complex (Scheme 43). The added sodium acetate not only activates the catalyst but is proposed to be responsible for product liberation by protonolysis of the intermediate and regeneration of the intermediate nickel acetate complex.



Scheme 43. Proposed mechanism for the nickel catalyzed hydrophosphination of nitroalkenes.

7.4. Palladium

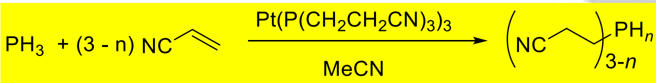
Ogawa and coworkers reported the regioselective hydrophosphination of alkynes using a palladium catalyst in a diphosphine-hydrosilane binary system (Scheme 44).[105] A palladium(0) precursor reacts with $(Ph_2P)_2$ to form a phosphido intermediate via oxidative addition. Terminal alkynes are proposed to react with the palladium phosphido complex to form an insertion product that reacts with R_3SiH to release the hydrophosphination product. The resultant palladium silyl complex then can react with another equivalent of $(Ph_2P)_2$ to regenerate the catalyst. Several functional groups were tested resulting in a range of low to excellent product yields with 5 mol % loading of $Pd(PPh_3)_4$.



Scheme 44. Mechanism of palladium catalyzed hydrophosphination of alkynes.

7.5. Platinum

In an early report by Pringle and coworkers, $Pt(P(CH_2CH_2CN)_3)_3$ was studied for the hydrophosphination of acrylonitrile with PH_3 or $(CH_2CH_2CN)_2PH$ (Scheme 45).[12] A mechanism was proposed where the alkene coordinates in an η^2-fashion to the platinum center, an intermediate that was identified through control reactions. Binuclear μ-phosphido compounds were suggested as possible intermediates because these were independently prepared and were successful precatalysts for the same reaction.



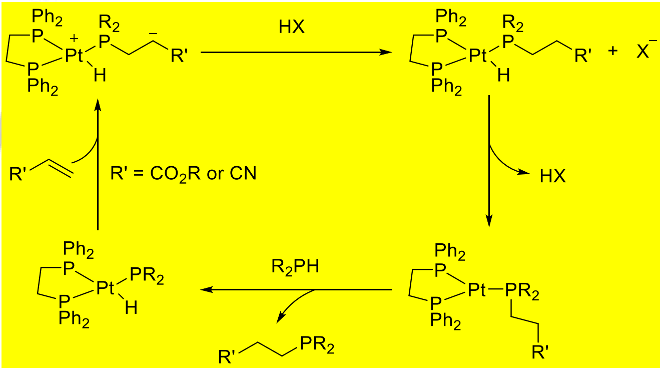
Scheme 45. Platinum catalyzed hydrophosphination of acrylonitrile.

Pringle continued to develop hydrophosphination, exploring the platinum(0) catalyzed P–H of PH_3 to ethyl acrylate.[106] The tertiary phosphine dominated the product distribution, representing more than 90% of the products, but the single- and double-addition products (i.e., primary and secondary phosphines) were present as well.

Glueck and coworkers looked at $Pt(dppe)(CH_2CHCN)$ (dppe = 1,2-bis(diphenylphosphino)ethane) catalyzed hydrophosphination of acrylonitrile with Mes^*PH_2 (Mes^* = 2,4,6-$^t Bu_3C_6H_2$) to yield $Mes^*(CH_2CHCN)PH$.[107] While these reactions were sluggish by modern standards (TOF = 1 per day) at a relatively high catalyst loading of 10 mol %, the advances in understanding would be of tremendous value. Study of the system revealed oxidative addition of the P–H bond at platinum generates a phosphido-hydride intermediate, and treatment of that compound with acrylonitrile affords the hydrophosphination product along with regeneration of the catalyst. Results from this system indicate selective insertion into the Pt–P bond occurs preferentially over the Pt–H bond. As a result, the hydrophosphination community has not been mired in distinguishing between Chalk-Harrod and the modified Chalk-Harrod mechanisms, a lá hydrosilylation.

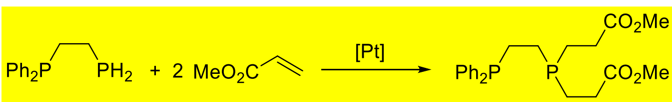
Further confirmation of this mechanistic view came from Glueck and coworkers' study of $Pt(dppe)(CH_2CHCN)$ as a catalyst precursor for the hydrophosphination acrylonitrile.[108] As before, the mechanism of catalysis was proposed to be oxidative addition of P–H to platinum, followed by insertion of coordinated acrylonitrile substrate into the Pt–P bond rather than the Pt–H bond, and a reductive elimination step to form the product C–H bond during product liberation. All intermediates were isolated or identified spectroscopically. Product forming reductive elimination was shown to be irreversible, while oxidative addition to platinum and insertion of acrylonitrile are reversible.

Glueck later used protic additives to suppress byproducts in platinum catalyzed hydrophosphination.[109] Two derivatives, Pt((*R,R*)-Me-Duphos)(*trans*-stilbene) and $Pt(norbornene)_3$, were tested as catalysts, and several secondary phosphine substrates were used in this report including Ph_2PH, iBu_2PH, Me(Is)PH (Is = 2,4,6-$(^iPr)_3C_6H_2$), and Ph(Cy)PH with acrylonitrile and *tert*-butylacrylate as unsaturated substrate. Some enantioselectivity was measured with the highest being an ee value of 56 % using Pt((*R,R*)-Me-Duphos)(*trans*-stilbene), Me(Is)PH, and *tert*-butylacrylate. Evidence was provided for an addition mechanism through the formation of byproducts containing two or more alkene-containing fragments, though contribution from coordination/insertion mechanisms could not be completely ruled out. Stoichiometric reactions with platinum phosphido complexes with more activated alkenes was done by Glueck and coworkers.[110] Form these studies, a new mechanism was proposed for platinum-catalyzed hydrophosphination where nucleophilic attack by the phosphido ligand of the intermediate hydride complex, $Pt(diphos)(PR_2)(H)$, gives a zwitterionic species, containing a cationic platinum compound and a phosphine ligand with a pendent stabilized carbanion (Scheme 46). Product C–H bond formation then proceeds through a platinum hydride and carbanion intermediate to yield the product phosphine and regenerate the catalyst. This mechanism explains the role of additives and is supported by stoichiometric reactions as well as the isolation of intermediate compounds.



Scheme 46. Mechanism for platinum catalyzed hydrophosphination of alkenes.

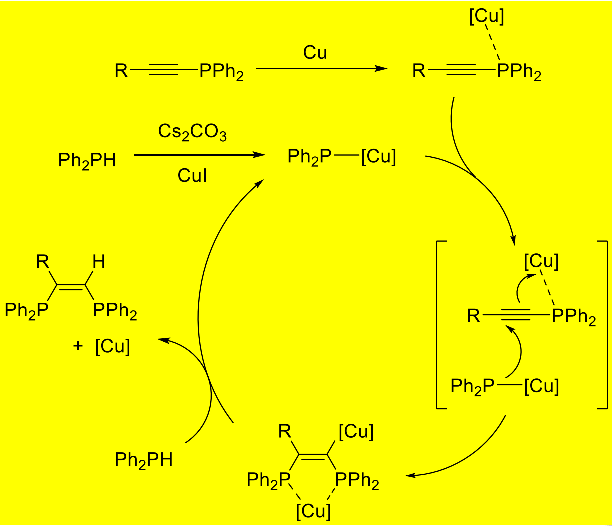
Pringle and coworkers developed a protocol for the self-replication of chelating diphosphines via platinum catalyzed hydrophosphination.[111] Bidentate phosphines such as $Ph_2PCH_2CH_2P(CH_2CH_2R)_2$ were prepared from the reaction of $Ph_2PCH_2CH_2PH_2$ with electron deficient alkenes (Scheme 47). The catalyst is very efficient despite the possibility of chelating diphosphines poisoning catalysis (i.e., product inhibition).



Scheme 47. Platinum catalyzed hydrophosphination of alkenes with $Ph_2PCH_2CH_2PH_2$.

7.6. Copper

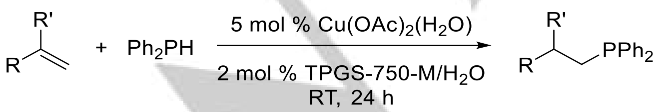
The first report of copper catalyzed hydrophosphination came from Yorimitsu and Oshima.[112] The preparation of *Z*-1,2-diphosphino-1-alkenes was achieved via copper catalyzed *anti*-selective hydrophosphination of 1-alkynylphosphines (Scheme 48). These 1-alkenyl phosphine substrates were synthesized through the nucleophilic substitution of chlorophosphines with lithiated alkynes. The diphosphinoalkene products could then be made into chiral bidentate phosphine ligands by treatment with an enantioselective hydrogenation catalyst. Products were oxidized with sulfur, which was unreactive during hydrogenations, but could be removed with $Cp_2Zr(H)Cl$ once stereochemistry has been established.



Scheme 48. Proposed mechanism of copper catalyzed hydrophosphination of phosphinoalkynes.

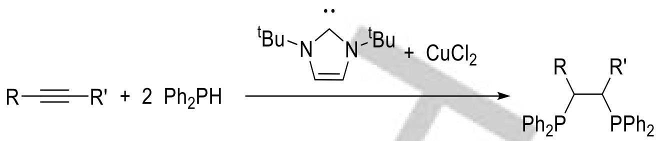
The copper(I) catalyzed hydrophosphination of styrenes was explored by Corma and coworkers.[113] This was the first hydrophosphination of styrene substrates using a simple metal salt (i.e., MX_n), where a $(CuOTf)_2$ was the optimal pre-catalyst. The active catalyst is generated via a redox reaction with diphenylphosphine. Unactivated substrates such as *trans*-stilbene and 1-octene were utilized, albeit at low conversions. Substituted styrenes were facile substrates, and kinetic studies demonstrated that the electronic density of the styrene ring influences the rate of reactivity.

Lipshutz and coworkers further enhanced copper catalyzed hydrophosphination of styrene derivatives by moving to aqueous solution in a green alternative for catalytic hydrophosphination (Scheme 49).[114] For full reactivity, a surfactant, TPGS-750-M was used. The surfactant spontaneously self-aggregates into nanometer-sized micelles. The reactions occur in the lipophilic cores, where water insoluble components such as the catalyst and substrate can react. This allowed reactions to take place at ambient temperature in water where $Cu(OAc)_2$ was applied to several styrene substrates. Control reactions to detect radicals supported a closed-shell pathway.



Scheme 49. Copper catalyzed hydrophosphination of alkenes in aqueous solution.

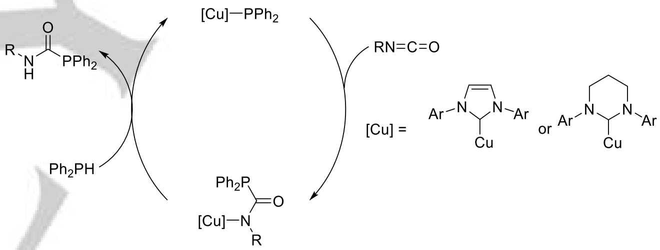
Cui and coworkers reported the copper catalyzed double hydrophosphination of terminal alkynes (Scheme 50).[115] Several precatalysts including NHC-copper phosphido complexes as well as $CuCl_2$/NHC mixtures were tested. These precatalysts were found to be highly efficient and selective catalysts for the double hydrophosphination of aryl- and alkyl-substituted terminal alkynes. The reaction was found to be more convenient with the in situ $CuCl_2$/NHC system, which performed better than the well-defined copper catalyst.



Scheme 50. Copper NHC catalyzed double hydrophosphination of alkynes with diphenylphosphine.

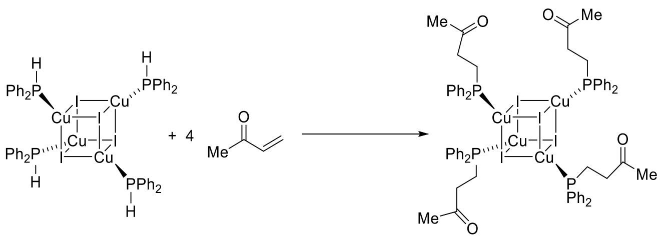
Independently, Waterman and coworkers investigated copper(II) acetylacetonate as a bench-stable catalyst for hydrophosphination.[116] Copper(II) acetylacetonate enjoys enhanced catalytic activity towards unactivated substrates with both primary and secondary phosphines under photocatalytic conditions. This catalyst exhibits high ease of use and substrate scope. Initial mechanistic investigation supports the formation of copper(I) active catalyst like Corma's study and a closed-shel pathway consistent with Lipshutz's study. With both some background reactivity in the dark and high activity under either UV or visible irradiation, this is an accessible catalyst that is ideal for screening reactions, even in more specialized synthetic applications.

Following on Cui's study, Liptrot and coworkers report the first ring-expanded NHC copper(I) phosphide catalyst for the selective hydrophosphination of isocyanates (Scheme 51).[117] Copper phosphides were easily prepared by treating (NHC)CuO^{t}Bu with Ph_2PSiMe_3. Intermediate compounds in the catalysis were obtained through stoichiometric insertion reactions of heterocumulenes into the Cu–P bond.



Scheme 51. Copper catalyzed hydrophosphination of isocyanates.

In a recent example from Bellemin-Laponnaz, the post functionalization of a copper-iodide phosphine complex was utilized for the formation of new carbon-phosphorus bonds through hydrophosphination (Scheme 52).[118] Methyl vinyl ketone, among other substrates was utilized in this study where the copper-iodide species was activated by UV light to mediate reactivity.

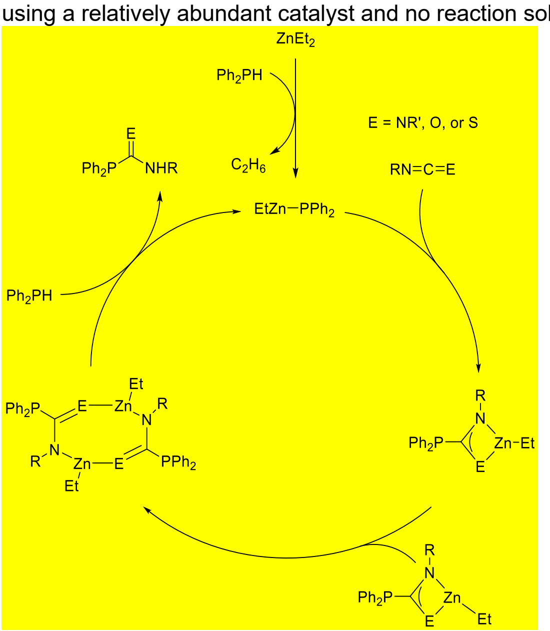


Scheme 52. Copper-iodide cubane mediated hydrophosphination of methyl vinyl ketone.

7.7. Zinc

Diethyl zinc was used as a precatalyst for the hydrophosphination of heterocumulenes under neat conditions (Scheme 53).[119] Activation of a P–H bond at a zinc-ethyl substituent to form $Zn(Et)PPh_2$ was identified in reaction of $ZnEt_2$

with Ph_2PH, akin to related zinc chemistry.[120] Addition of heterocumulene substrate resulted in the formation of the dimer $((PPh_2C(NR)_2)ZnEt)_2$ when heated for extended periods. Additional equivalents of Ph_2PH releases the hydrophosphination product by formal protonation to restore catalyst. Reactions could be performed neat at ambient temperature to prepare phosphaguanidines, phosphaureas, and phosphathioureas in good conversions. This is the only group 12 hydrophosphination catalyst representing an environmentally sustainable example, using a relatively abundant catalyst and no reaction solvent.



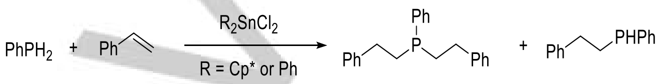
Scheme 53. Diethyl zinc catalyzed hydrophosphination of heterocumulenes.

Late transition metals started and subsequently dominated hydrophosphination catalysis. Activation of many substrates were achieved for the first time with late-metal catalysts, such as styrenes and alkynes, which are now benchmark substrates. Facing the scarcity of noble metals, 3d late metals such as copper and nickel have received increasing attention. There is also the possibility of development in zinc-based hydrophosphination catalysts.

8. P-block and Lewis Acid Catalysts

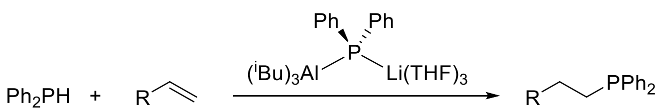
Though equally interesting, there have been fewer examples of p-block element and Lewis acid catalyzed hydrophosphination reactions in the literature than those of metals. Waterman and Wright reported the tin-catalyzed hydrophosphination using $Cp^*{}_2SnCl_2$.[121] Mainly a report for the dehydrocoupling of phosphines using $Cp^*{}_2SnCl_2$ and close derivatives, the hydrophosphination of styrene, 2,3-dimethylbutadiene, phenylacetylene, and diphenylacetylene with phenylphosphine was realized with relatively high catalyst loadings of 10 mol %. This marked the first example of a p-block hydrophosphination catalyst. It was observed in dehydrocoupling reactions that the tin compounds studied undergo facile P–H bond activation, which suggested other bond-forming reactions to phosphorus might be possible. Based on heightened reactivity with primary phosphines over secondary, those were chosen as substrate. Michael acceptor type substrates were deliberately excluded from this study to focus on insertion-based reactivity. Mixture of secondary and tertiary phosphine products was obtained with styrene as substate, demonstrating styrene as the limiting reagent. For diphenylacetylene as substrate, mixture of *E* and *Z* products were formed. Increasing the $PhPH_2$ to 2 equiv. resulted in significant improvements in selectivity, also granting quantitative conversion for styrene and 2,3-dimethylbutadiene under moderate heating. Temperature also had a large effect on the hydrophosphination of alkynes, where reactions done at 75 °C had a strong preference for the *E* isomer.

Waterman and coworkers returned to tin derivatives for hydrophosphination to explore Ph_2SnCl_2 as a catalyst (Scheme 54).[122] A wider range of alkene substrates were tested, along with diphenylphosphine and the previously studied phenylphosphine. Substituted styrenes, vinylpyridines, Michael acceptors, alkynes, and unactivated substrates were visited in this report. Reactions with Ph_2PH were initially sluggish compared to $PhPH_2$, and phosphine dehydrocoupling predominated under the reaction conditions. As a result, catalysis was conducted under a positive H_2 atmosphere to succesfully mitigate competitive dehydrocoupling. Styrenes and Michael acceptors were the most effective substrates. Unactivated alkenes and terminal alkynes were essentially unreactive. Hydrophosphination with other Lewis acids was tested. Tin(II) chloride and tin(IV) chloride were found to be unreactive at 10 mol % catalyst loading. Stalwart Lewis acid $B(C_6F_5)_3$ was used as a catalyst at 10 mol %, where product was only observed at high temperatures (100 °C), suggesting Lewis acidity was not the dominating pathway for catalysis with tin.



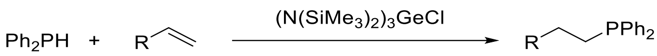
Scheme 54. Tin catalyzed hydrophosphination of styrene.

Mulvey reported the lithium-aluminate-catalyzed–hydrophosphination of alkynes, styrene derivatives, carbodiimides, and vinyl borane (Scheme 55).[123] Using 10 mol % of the dimeric $(^iBu_3AlHLi)_2$ as catalyst at 70 °C resulted in very low conversions. Increasing reaction temperatures afforded 72% conversion. Unactivated alkenes were not possible substrates under any conditions tested. Substituted styrene derivatives were facile substrates with no clear difference in electron withdrawing or donating substituents on the rate of catalysis. Vinyl boranes and carbodiimides achieved excellent conversions. Addition of a Lewis base was found to improve the relative rate of hydrophosphination while also enhancing selectivity for the *Z* isomer when using diphenylacetylene as substrate. A mechanism was proposed, supported by stoichiometric reactions, that proceeds via formation of a crystallographically determined lithium aluminum phosphide, $^iBu_3AlPPh_2Li(THF)_3$, followed by insertion of the substrate into the Al–P bond. Protonolysis by a second equiv. of phosphine generates the product and restores the catalyst. It was initially postulated the formation of an anionic aluminum center coordinated by four anionic ligands, as in this aluminate, would have insufficient Lewis acidity to participate in hydrophosphination catalysis. The results here using a variety of donor solvents in the presence of lithium serves to alleviate this issue and enable catalysis.



Scheme 55. Lithium-aluminate catalyzed hydrophosphination of alkenes.

The first example of a germanium hydrophosphination catalyst was described by Webster and coworkers (Scheme 56).[124] Indeed, germanium catalyzed reactions are rare, making this anti-Markonikov hydrophosphination using $GeCl(N(SiMe_3)_2)_3$ diphenylphosphine at ambient temperature a noteworthy achievement among even the limited examples of p-block catalysts. Substituted styrenes and alkynes were tested as successful substrates. A kinetic study of the reaction was undertaken via variable time normalization analysis, which implied the reaction is approximately first-order with respect to catalyst and Ph_2PH, and a more complex relationship with styrene (≤1, ≥0.5). The investigators proposed a complex reaction mixture where multiple species can propagate from one equivalent of germanium. $GeCl(N(SiMe_3)_2)_3$ reacts with Ph_2PH to form a bright yellow compound, where ^{1}H NMR DOSY experiments show fast diffusing $HN(SiMe_3)_2$ peaks and slower diffusing aryl resonances consistent with protonation of Ge-bound $N(SiMe_3)_2$ by Ph_2PH. A germanium phosphido compound was identified by ^{31}P NMR spectroscopy. These preliminary mechanistic studies imply the formation of a germanium (tris)phosphido species as the active catalyst, and a redox neutral mechanistic pathway is proposed.

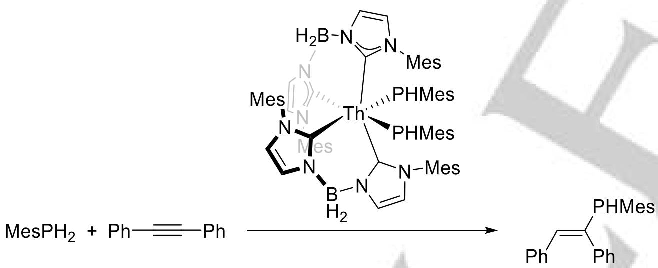


Scheme 56. Germanium catalyzed hydrophosphination of alkenes.

The main group has been a frontier in catalysis in the 21st century, and Lewis acids are a critical component of these advances. This pattern is true for hydrophosphination where some of the greatest potential for new discoveries and advances may lie with these elements and systems.

9. Actinides

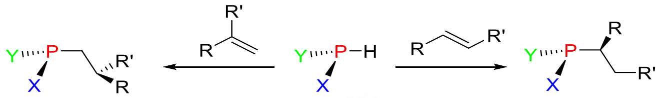
There has only been one example of actinide-catalyzed hydrophosphination in the literature, reported by Arnold and coworkers (Scheme 57).[125] This investigation arose from exploration of bis(NHC)borate-supported thorium(IV) bis(mesitylphosphido) compounds that undergo reversible intermolecular C–H bond activation. Treating the thorium bis(phosphido) compound with 2 equiv. of diphenylacetylene affords one equiv. of the anticipated vinyl phosphine and a thorium-NHC metallacycle in a 1:1 ratio. Further treatment of the thorium compound with excess $MesPH_2$ rapidly liberates an equivalent of vinyl phosphine and reforms the original phosphido complex. Reaction of $MesPH_2$ with 10 mol % of thorium allowed for the catalytic hydrophosphination of internal alkynes. Reactions provided the *E* isomer of in relatively high selectivity. Clearly, this is an area ripe for further development, technical challenges of actinide chemistry aside.



Scheme 57. Thorium catalyzed hydrophosphination of diphenylacetylene with mesitylphosphine.

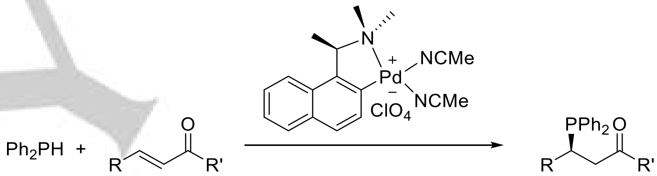
10. Asymmetric Hydrophosphination

In many regards, regioselectivity in hydrophosphination is well controlled. The field lacks design principles for new catalysts to be selective for particular regioisomers. However, most catalysts afford specific products with high enough selectivity that our empirical understanding of specific systems allows for the isolation of desired products. Enantioselectivity is a greater challenge for any chemical transformation, and it is of key importance in heterofunctionalizations. This is an issue of heightened interest for hydrophosphination, where the phosphine substrate can be pro-chiral as well as the unsaturated substrate. Simple examples of pro-chiral unsaturated and phosphine substrates in hydrophosphination reactions are shown in Scheme 58. The added complexity of chirality at phosphorus is interesting from both the potential products and modest energetics of inversion at phosphorus, particularly as facilitated by a metal.[126]



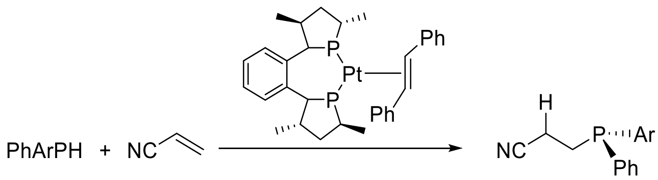
Scheme 58. Stereoselective hydrophosphination of pro-chiral alkenes.

The importance of chiral phosphines is undeniable. Historically, chiral phosphines have been prepared by means of stoichiometric chiral reagents or potentially complex or wasteful resolutions.[127] Asymmetric hydrophosphination serves as an atom economical path to prepare these value-added products. It is logical that such reactions were explored since the early days of hydrophosphination catalysis. Aspects of this area have been reviewed, and it is important to note that Leung and Pullarkat are the most prolific contributions to the field of asymmetric hydrophosphination, focusing on group 10 metal compounds as catalysts.[13e-g, 128] The majority of their work has been detailed in comprehensive reviews, outlining the evolution of their research.[13e-g] For that reason, this review will avoid reproducing what has been outlined so well in those reports and primarily focus on progress that has been made in since those accounts. In short summary, the bulk of their work involves using secondary aryl phosphines (Ar_2PH) and activated pro-chiral substrates such as *trans*-chalcone and a vast array of related Michael acceptors, with their highly active palladium metallocycle catalysts (Scheme 59). These products have realized unrivaled enantioselectivity and have been primarily employed as ligands for other asymmetric transformations alongside uses in other areas of chemistry.[13e]



Scheme 59. Leung's palladium catalyzed asymmetric hydrophosphination of enones.

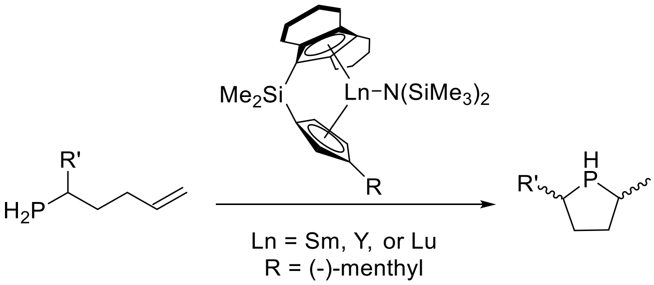
The first example of an enantioselective hydrophosphination dates back to 2000, where Glueck reported a platinum catalyst supported by DuPhos in the reaction of acrylonitrile to produce a P-chiral tertiary phosphine (Scheme 60).[129] Though ee values were modest in this report (maximum ee = 27%), this was the first report of metal-catalyzed asymmetric hydrophosphination in the literature.



Scheme 60. Glueck's platinum catalyzed asymmetric hydrophosphination of activated olefins.

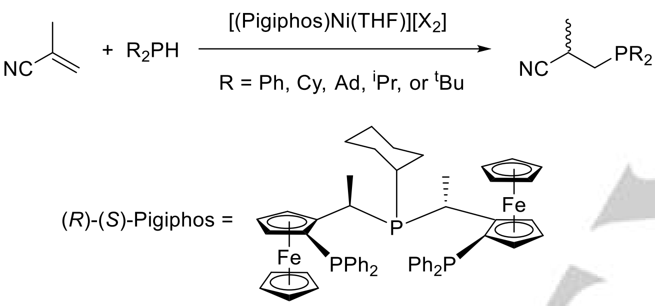
This work was later extended to dienes to form chiral bisphosphines through two subsequent 1,2-addition hydrophosphination events of *cis,cis*-muconitrile. Products were prepared as a 3:2 mixture of diastereomers.[130] Glueck summarizes his developments in the metal-catalyzed asymmetric synthesis of P-stereogenic phosphines in a detailed report as well.[101a]

Marks reported lanthanocene-catalyzed intramolecular hydrophosphination/cyclization of phosphinoalkenes and phosphinoalkynes to prepare substituted phospholanes (Scheme 61).[30] Using a chiral C_1-symmetric octahydrofluorenyl organolanthanide compound as catalyst, 91% diastereomeric purity was achieved with quantitative diastereomeric purity obtained after recrystallization.



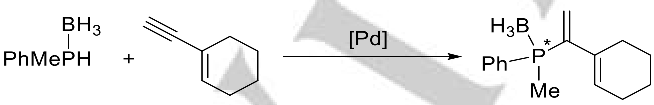
Scheme 61. Marks chiral *ansa*-lanthanocene catalyzed intramolecular hydrophosphination of phosphinoalkenes.

Togni and coworkers developed a nickel catalyzed asymmetric hydrophosphination of methacrylonitrile (Scheme 62).[131] Using a nickel Pigiphos compound, Togni achieved some of the best enantioselectivity to date, with ee values as high as 94% when using Ad_2PH as the phosphine substrate. Interestingly, Togni used many other phosphine substrates such as Cy_2PH, $^{i}Pr_2PH$, $^{t}Bu_2PH$, and the now ubiquitous Ph_2PH, which had yet to be reported in this context. The nickel catalyst operates via a 1,4-conjugate addition mechanism that was fully established in a later mechanistic, kinetic, and more structural study on the catalyst and intermediates.[132]



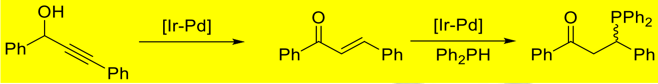
Scheme 62. Togni's nickel catalyzed asymmetric hydrophosphination of methacylonitrile.

Gaumont reported the palladium-catalyzed hydrophosphination of alkynes with P-chiral phosphine boranes (Scheme 63).[133] The borane auxiliary is rare in hydrophosphination reactions, but this feature allowed for control over the stereochemistry at phosphorus to be controlled. Using a variety of chiral diphosphine ligands and both palladium(0) and (II) precatalysts, 1-ethynylcyclohexene was utilized as unsaturated substrate with racemic methylphenylphosphine borane. For chiral catalysts, it was hypothesized that chirality would be transferred upon P–C bond formation. The highest ee value in the vinyl phosphine-borane products was reported to be 42% after a kinetic resolution with up to 70% conversion.



Scheme 63. Palladium catalyzed hydrophosphination of ethynylcyclohexene with a phosphine borane.

Mata and coworkers describe the preparation of heterobimetallic iridium-palladium compounds containing two axes of chirality and their use in the subsequent isomerization/hydrophosphination of 1,3-diphenylpropargylic alcohol (Scheme 64).[134] The palladium portion of the catalyst was very similar to the catalysts used by Leung.[13e] The iridium component of the complex isomerizes the propargylic alcohol into an enone that was subject to hydrophosphination by the palladium component of the compound. Despite this effort to innovate using a multifunctional bimetallic catalyst, the highest ee value measured was 17%. Mata went on to develop N-heterocyclic carbene ligands for asymmetric hydrophosphination using palladium, again bearing an amine containing metallocycle, similar to their iridium-palladium dual catalyst (Figure 23).[135] Higher ee values are reported using *trans*-chalcone and diphenylphosphine, up to 56%.



Scheme 64. Subsequent isomerization/asymmetric hydrophosphination of 1,3-diphenylpropargylic alcohol with an Ir-Pd dual catalyst.

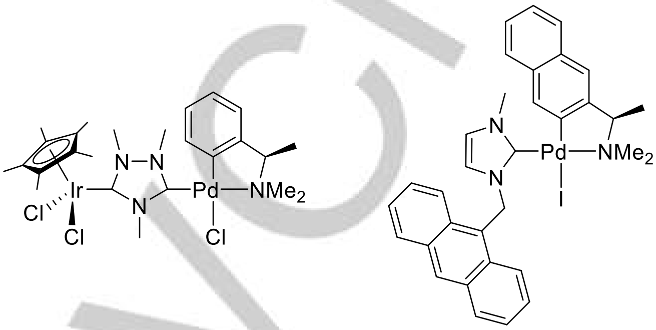


Figure 23. Mata's chiral palladium catalysts.

Gong and Song have made several contributions with palladium pincer complexes, which have been highlighted in a review.[13d] Their first contribution reports ee values up to 94% using a palladium pincer compound with secondary aryl phosphine and enone substrates.[136] Gong and Song go on to prepare pyridine-functionalized phosphine oxides as chiral ligands for other palladium catalyzed transformations.[137] Remarkable enantioselectivity is observed in this report, as high as 98% ee. A later report highlights similar reactivity with bis(imidazoline) NCN pincer palladium(II) compounds (Figure 24).[138]

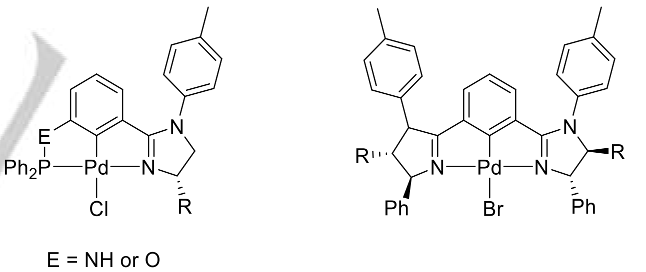
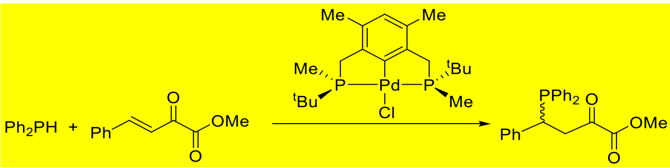


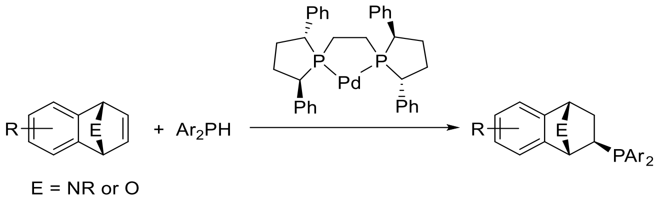
Figure 24. Gong and Song's bis(imidazoline) NCN pincer palladium(II) hydrophosphination catalysts.

Imamoto and Zhang describe the asymmetric hydrophosphination of β,γ-unsaturated α-keto esters using a P-stereogenic pincer palladium compound (Scheme 65).[139] High enantioselectivity of 93% ee was proposed to be a result of a favorable *Si*-attack of a catalytic intermediate.



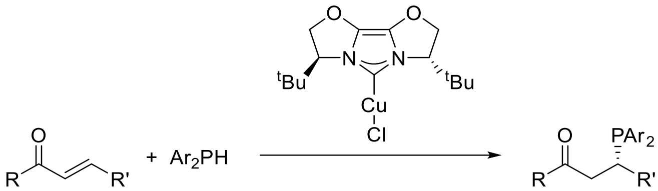
Scheme 65. Imamoto and Zhang's palladium pincer catalyzed asymmetric hydrophosphination of β,γ-unsaturated α-keto esters.

Wang recently reported a detailed study on the asymmetric hydrophosphination of bicyclic alkenes using a palladium precatalyst with chiral ancillary diphosphine ligands to prepare chiral phosphine ligands (Scheme 66).[140] This report of a value-added chiral bidentate ligand follows Leung's initial report and further demonstrates realized utility of asymmetric hydrophosphination for other fields, such as catalysis.



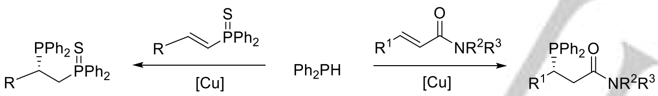
Scheme 66. Wang's palladium catalyzed asymmetric hydrophosphination of bicyclic alkenes.

The first copper-catalyzed asymmetric hydrophosphination was reported by Duan and coworkers.[141] In this work, Duan describes the asymmetric hydrophosphination of α,β-unsaturated ketones with a copper NHC complex (Scheme 67). Despite moderate ee values, high yields were obtained using mild conditions.



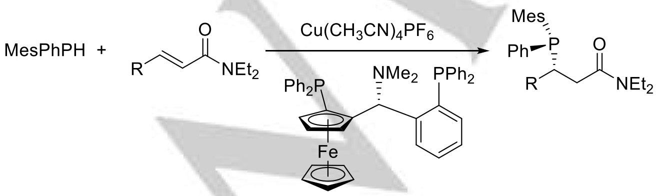
Scheme 67. Copper NHC catalyzed asymmetric hydrophosphination of α,β-unsaturated ketones.

Yin and coworkers have also been successful in copper(I) catalyzed asymmetric hydrophosphination of vinyl phosphine sulfides to form chiral 1,2-bisphosphine derivatives[142] and of α,β-unsaturated amides through a 1,4-conjugate addition mechanism (Scheme 68).[143]



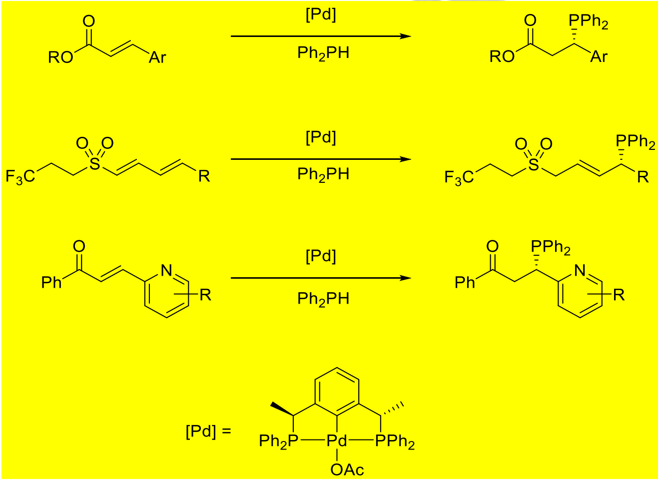
Scheme 68. Copper catalyzed asymmetric hydrophosphination of oxidized vinyl phosphines.

Phosphine sulfides were utilized in the former account, where a 'soft-soft' interaction between the copper and sulfide atoms led to high ee values with excellent reaction times. Additionally, dynamic kinetic resolutions of racemic phosphine mixtures were successful in affording high diastereo- and enantioselectivities. In Yin's work involving asymmetric phosphines, P-stereocenters were obtained with ee values as high as 98% using Mes(Ph)PH as the phosphine substrate (Scheme 69). Double asymmetric conjugate hydrophosphination was also achieved in this report. The highest ee values were observed with (R,R_P)-Taniaphos as the ancillary ligand in both accounts.



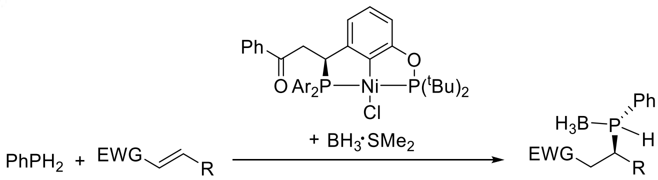
Scheme 69. Yin's copper catalyzed asymmetric hydrophosphination of α,β-unsaturated amides.

Duan and coworkers were early to adopt pincer-supported palladium derivatives for the asymmetric hydrophosphination of enones.[144] Using similar catalysts, this methodology was extended to α,β-unsaturated carboxylic esters,[145] α,β,γ,δ-unsaturated sulfonic esters,[146] and β-2 pyridyl substituted enones.[147] All reports demonstrate high enantioselectivity in these transformations. The mechanism either proceeds through a 1,4- or 1,6-conjugate addition depending on the substrate. Duan and coworkers have had their greatest success with a PCP-supported palladium acetate precatalyst (Scheme 70), despite studies of other palladium pincer complexes.



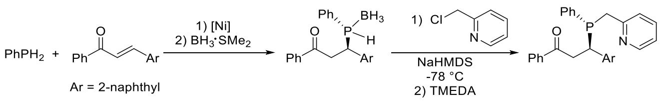
Scheme 70. Examples of Duan's palladium pincer catalyzed asymmetric hydrophosphination reactions.

Duan and Wang in 2021 made a particularly important contribution with the first reported primary phosphine in asymetric hydrophosphination (Scheme 71).[148] With a chiral nickel catalyst and the assistance of added borane, the hydrophosphination of electron deficient alkenes was achieved while preserving stereocenters at both phosphorus and carbon (*cf.* Scheme 58). They reported ee values in excess of 99% and dr values of 20:1, exhibiting remarkable selectivity.[148] While other catalysts have been successful with primary phosphine substrates, many examples of asymmetric hydrophosphination have relied on steric pressure from phosphorus. Stereoselectivity at the phosphorus atom is achieved by the clever use of a coordinating borane post P–C bond formation to prevent racemization. These results suggest that more general catalysts, those that do not rely on substrate properties, are indeed accessible.



Scheme 71. Duan and Wang's nickel-catalyzed asymmetric hydrophosphination with primary phosphines.

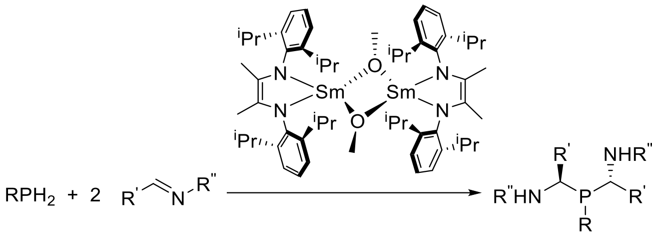
The use of primary phosphine as substrate is attractive due to the potential for further functionalization at the reactive P–H bond of the product. This was taken advantage of in Duan and Wang's study, where stereochemistry at carbon and phosphorus are retained in the preparation of a tertiary phosphine ligand following deprotection of phosphorus (Scheme 72).[148]



Scheme 72. Preparation of tertiary phosphines from asymmetric hydrophosphination using a primary phosphine substrate.

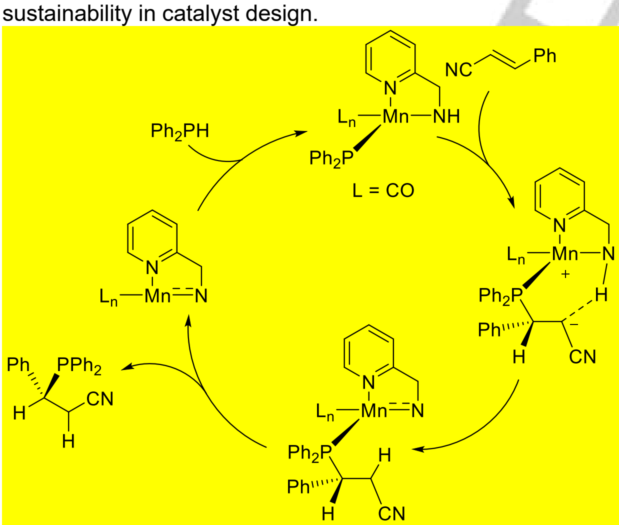
Zhang and coworkers reported the nickel catalyzed asymmetric hydrophosphination of unactivated alkynes.[149] Though this report is not fundamentally hydrophosphination as phosphine oxides are used as the starting substrate, it represents a useful method for preparing P-chiral products that are converted to phosphine sulfides or phosphine boranes with excellent enantioselectivity.

These recent examples have helped realize some of the synthetic utility of hydrophosphination catalysis through enantioselectivity. However, most work focused on enantioselectivity has been centered largely on group 10 and coinage metals. There has been increasing effort to develop hydrophosphination catalysts, and particularly enantioselective hydrophosphination catalysis, using many different metals. A key initial example of the potential for diversity of enatioselective hydrophosphination catalysis was demonstrated by Cui in 2017 with the diastereoselective hydrophosphination of imines through double P–H bond activation of a primary phosphine substrate to produce bis(α-amino) phosphine products with high yields and dr values of 99:1 (Scheme 73).[40] This study presents an unusual substrate for asymmetric hydrophosphination reactions, where the products can be aimed at more biologically relevant applications.



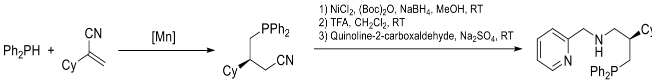
Scheme 73. Cui's samarium catalyzed double addition of primary phosphines to imines.

A recent advance was made by Ge and Harutyunyan employing a chiral manganese(I) catalyst for the asymmetric hydrophosphination of α,β-unsaturated nitriles.[150] Interestingly, this is a rare example of metal-ligand cooperation in hydrophospination catalysis where both the metal and ligand participated in P–H bond activation (Scheme 74). As the second most abundant transition metal, the use of manganese also represents both progress in asymmetric hydrophosphination and sustainability in catalyst design.



Scheme 74. Proposed mechanism for manganese catalyzed asymmetric hydrophosphination of α,β-unsaturated nitriles.

The utility of the nitrile group of the substrate provides access to chiral tridentate N,P-type ligands upon further functionalization (Scheme 75). This has been demonstrated by Ge and Harutyunyan, where the ligands have been used in manganese catalyzed asymmetric hydrophosphination followed by asymmetric hydrogen transfer reactions to produce value-added products.[150]



Scheme 75. Preparation of tridentate chiral phosphine ligand via manganese catalyzed asymmetric hydrophosphination of α,β-unsaturated nitriles.

Significant progress has been made since initial studies of asymmetric hydrophosphination catalysis. Beside the tremendous successes in selectivity achieved by a cadre of research teams around the world, there have been great developments in the substrates available for this transformation alongside the increasing use of more earth-abundant metals such as iron and manganese. Despite these steps forward, the pool of substrates is still limited, and many of the best studied catalysts are the least abundant. As the pursuit for catalytic asymmetric hydrophosphination continues, a greater understanding of these catalytic systems will be critical to fuel those advances. Such understanding may also aid in the development of sustainable catalytic systems for this transformation. Overall, the area has excellent future potential as a key area that connects the organophosphine products of hydrophosphination to a range of applications and other fields.

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Keywords: Hydrophosphination • Phosphines • Phosphorus • Catalysis • Ligands

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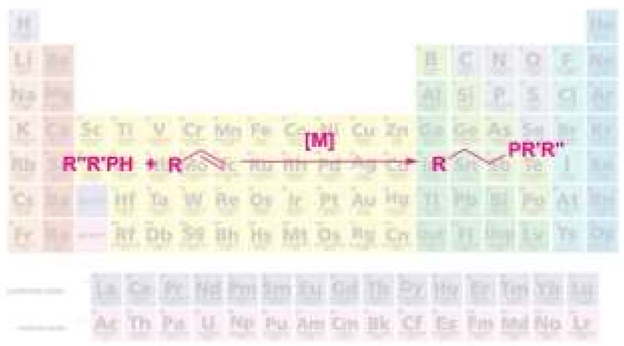

Hydrophosphination is an atom-economic method of readily preparing P–C bonds with high selectivity. This report gathers all accounts of metal catalyzed hydrophosphination since its inception in an organized and comprehensive form. Through this narrative, the evolution of the field is described highlighting the wide array of catalysts that have improved this reaction leading to high activity and broad substrate scope.

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