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Perspective

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Mechanisms of Metal-Catalyzed Hydrophosphination of Alkenes and Alkynes

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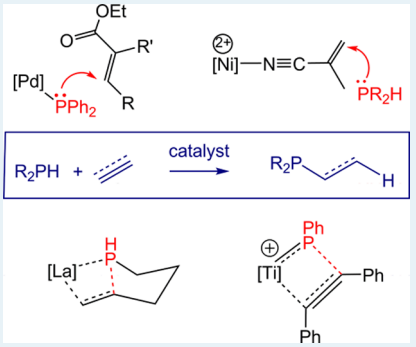
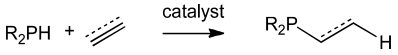
ABSTRACT: The elementary steps in proposed mechanisms for the hydrophosphination of alkenes or alkynes catalyzed by metal complexes are examined carefully with respect to the various potential roles of the metal center. This provides a context for understanding the unusually wide breadth of unsaturated substrates that participate in a P−C bond forming process mediated by a half-sandwich ruthenium system.



KEYWORDS: *alkenes, alkynes, secondary phosphines, primary phosphines, homogeneous catalysis, mechanism, P−H activation, P−C bond formation*

INTRODUCTION

This Perspective focuses on the metal-catalyzed hydrophosphination of carbon−carbon multiple bonds, using simple, unprotected primary or secondary phosphines, RPH_2 or R_2PH, where R are alkyl or aryl groups (eq 1). These are



[1]

challenging substrates for metal-catalyzed reactions since they, and the eventual hydrophosphination products, are good ligands that may poison catalysis. This issue is general for any heterofunctionalization reaction in which the heteroatom is a donor (e.g., hydroamination, hydrooxygenation, hydrothiolation); it is typically addressed in organophosphine synthesis either by protecting the phosphorus lone pair with coordinated borane or by working with phosphine oxide derivatives.[1] This can work well, but introduces additional synthetic steps (stoichiometric, posthydrophosphination deprotection or reduction, respectively) and reduces the atom economy of the transformation. An interesting challenge, then, is exploring the requisite P−H activation at or near a metal's coordination sphere while embracing the metal-ligating ability of the substrate primary and secondary phosphines, and ensuring the substitutional lability of the product phosphines.

There are obvious analogies between hydrophosphination and the more thoroughly studied hydroamination, the addition of N−H bonds in amines across multiple bonds.[2,3] A major difference, though, is that hydrophosphination reactions do not necessarily require a catalyst. The homolytic cleavage of P−H bonds (with subsequent 1,2-addition of the resulting radical partners to multiple bonds) can be effected by light, radical initiators, or even thermally, while heterolytic P−H activation can be mediated by either acid or base: these "uncatalyzed" P−H bond additions are part of the canon of routes to P−C bond formation in organophosphorus chemistry, along with metathetical routes involving P−Cl bonds or electropositive metal PR_2^- reagents.[4] So why bother developing metal catalysts for hydrophosphination? The main incentive is to introduce regio- and stereoselectivity in these addition reactions, through tuning and design of the metal catalyst's coordination sphere, thereby avoiding the time- and reagent-consuming separations that normally accompany the isolation of specific regioisomers or enantiopure chiral phosphines. Examples of desirable selectivity are shown in Figure 1. The prospect of enantioselective catalysis is particularly appealing in the context of catalytic asymmetric transformations used in the fine chemicals industry: the high cost of many homogeneous catalyst systems for these processes can derive as much from the preparation (or purchase) of chiral

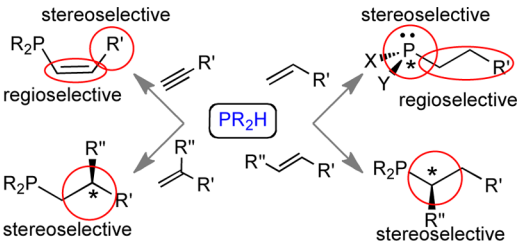


Figure 1. Examples of desirable selectivities in hydrophosphination reactions.

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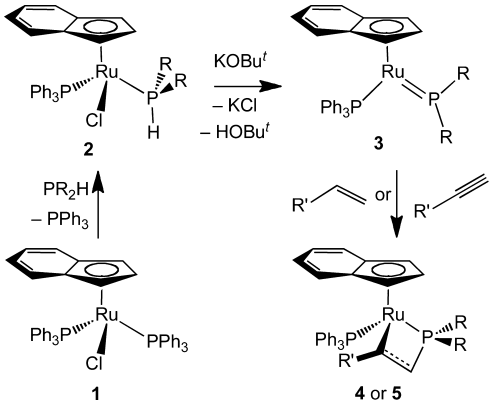
ligands as it does from the value of the precious metals often used, for example, in asymmetric hydrogenations.[5] In addition, though, there are many important achiral phosphine reagents whose current synthesis relies on the salt-elimination reactions of organophosphine halides or tosylates, or metal phosphido reagents such as $LiPR_2$, with the attendant workup, separations, and waste, because P−H addition routes have not been identified for their synthesis. Thus the development of metal-catalyzed hydrophosphination may provide general and clean alternatives for the preparation of even very simple phosphine reagents.

The topic of metal catalyzed hydrophosphination has been reviewed in a variety of formats;[6] these reviews typically encompass the addition of P−H bonds from a wider range of P(III) and P(V) substrates (e.g., hydrophosphinylation, hydrophosphorylation) than will be discussed here. Although systematic mechanistic studies of metal-catalyzed hydrophosphination are not yet plentiful, this Perspective highlights the catalytic cycles that have been proposed, with a particular focus on the various roles played by the metal.

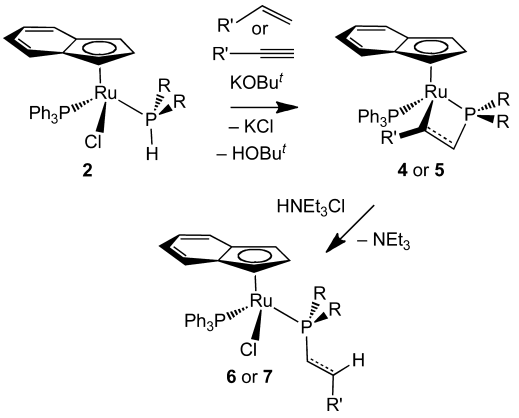
Stepwise Stoichiometric Hydrophosphination Mediated by a Ruthenium Complex. My co-workers and I have been studying reactions of a ruthenium half-sandwich system derived from commercially available Ru(η^5-indenyl)Cl(PPh_3)$_2$ (**1**) that are relevant to the hydrophosphination of alkenes and alkynes by secondary phosphines (Scheme 1). The major

Scheme 1



product resulting from the addition of an excess of secondary phosphine to complex **1** is the mixed phosphine complex **2**, which undergoes a dehydrohalogenation reaction with the addition of KOBu^t to yield the highly reactive terminal phosphido complex **3**.[7] The ruthenium center in **3**, which we have studied most thoroughly for R = cyclohexyl (Cy), is coordinatively unsaturated and is stabilized by π-donation of the phosphido lone pair; a formal Ru−P double bond results. The resulting "planar phosphido"[8] complex undergoes a number of interesting reactions, among them [2+2]-cycloadditions with alkenes and alkynes to give phospharuthenacyclobutanes (**4**) and -butenes (**5**), respectively.[9] Recently we have found that these cycloadducts form quantitatively from the direct addition of an excess of the unsaturated substrate to complex **2** in the presence of KOBu^t (Scheme 2), a "single pot" reaction that demonstrates both the P−H activation and the critical P−C bond forming step in a potential catalytic hydrophosphination cycle.[10a] We have also established that the Ru−C bond in the isolated metallacycles can be cleaved with the addition of acids as weak as [$HNEt_3$]Cl.[10b] This represents the final step of hydrophosphination, releasing

Scheme 2



novel tertiary phosphine products via the mixed phosphine complexes **6** or **7**. We are in the process of tuning this stepwise hydrophosphination process to allow it to occur catalytically.

Although we have not yet observed catalytic turnover, these results are intriguing, because the P−C bond forming reactions shown in Schemes 1 and 2 occur for unsaturated substrates ranging from highly activated (e.g., acrylonitrile, phenylacetylene) through "mildly" activated (e.g., styrenes) to simple (e.g., ethylene, *n*-hexyne, acetylene) and even electron-rich (e.g., ethylvinylether). It is an exciting discovery because none of the known hydrophosphination catalyst systems have been shown to exhibit this sort of generality of substrate scope (vide infra). The discussion below of proposed mechanisms for established metal-catalyzed hydrophosphination reactions allows us to put the unusual behavior of this ruthenium system in context.

Overview of Known Catalyst Systems. Metals from the s-, d-, and f-blocks have all been reported to catalyze hydrophosphination reactions. Systems based on group 10 elements (Ni, Pd, Pt) or on group 3 and the lanthanides (Y, La, Sm, Yb) are the most common so far. In addition to alkenes and alkynes, unsaturated substrates for these reactions include conjugated dienes, enynes, allenes, the C=N bonds in various heterocumulenes, and formaldehyde. The most common phosphine used in hydrophosphination is diphenylphosphine, Ph_2PH; there are many fewer examples of alkylphosphine substrates than aryl, probably because the latter tend to exhibit lower pK_a values[11] (vide infra).

In general, late transition metal-mediated hydrophosphination works only for activated unsaturated substrates containing electron-withdrawing groups (eqs 2−5[13,14,15,3a]),[12] and many of these systems employ a base as cocatalyst (eq 5[3a]). Only late metal systems have been exploited in enantioselective synthesis of chiral phosphines, with increasingly impressive enantiomeric excesses (ee's), as shown in eqs 3−5[14,15,3a]. In contrast, the early transition metal, lanthanide, and alkaline earth catalysts do not require basic cocatalysts, and among these systems are the only examples of catalytic hydrophosphination of simple, unactivated alkenes or alkynes (eqs 6−8[3c,b,16]).

Late d-Block Metals. For late metal hydrophosphination catalysts the critical P−C bond forming step usually relies on attack of nucleophilic phosphorus at the alkene or alkyne; this is why only activated, Michael-type substrates containing electron-withdrawing groups participate in these reactions. Two outer-sphere mechanisms are possible. In some cases the metal directly or indirectly binds the unsaturated substrate,

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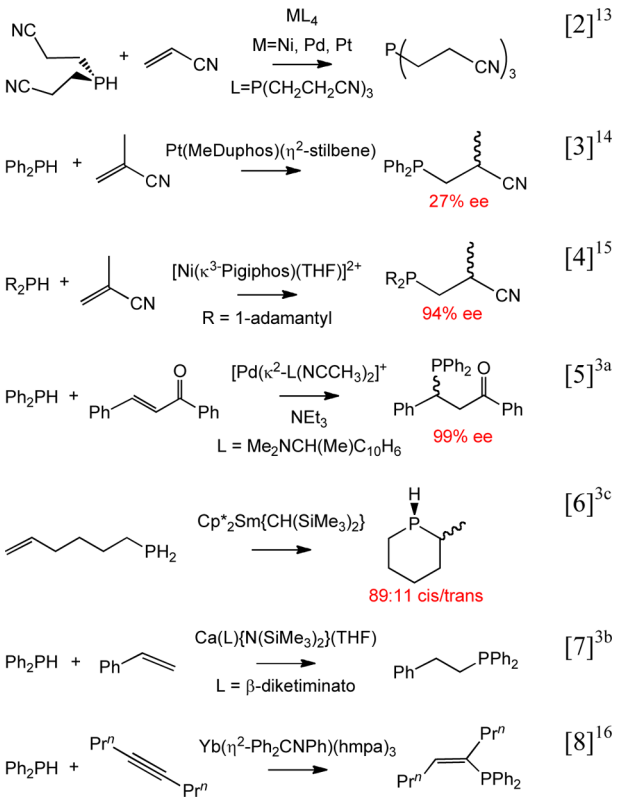


which is subsequently attacked by the free substrate phosphine, as shown in the example in Figure 2.[15,17] More often, though, late metal catalysts bind/activate the phosphine substrate to generate highly nucleophilic, terminal phosphido ligands.[18] In these cases, P−C bond formation occurs via the attack of the metal-bound phosphido lone pair at the electropositive carbon of the unsaturated substrate. This is the mechanism proposed

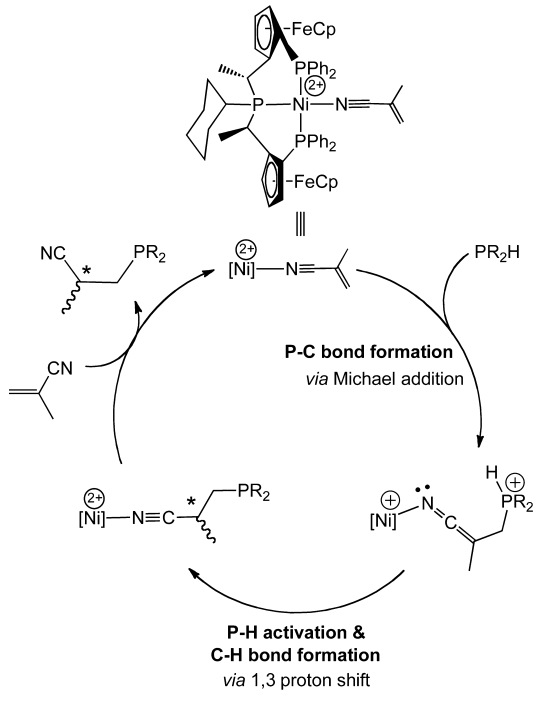


Figure 2. Proposed mechanism for hydrophosphination of methacrylonitrile catalyzed by a cationic nickel complex.[15]

by Leung and Pullarkat for the asymmetric synthesis of chiral phosphines via cationic palladacycle-mediated hydrophosphination of a wide range of activated alkenes,[3a,19] of which one example is shown in Figure 3. Notice that added base, NEt_3,

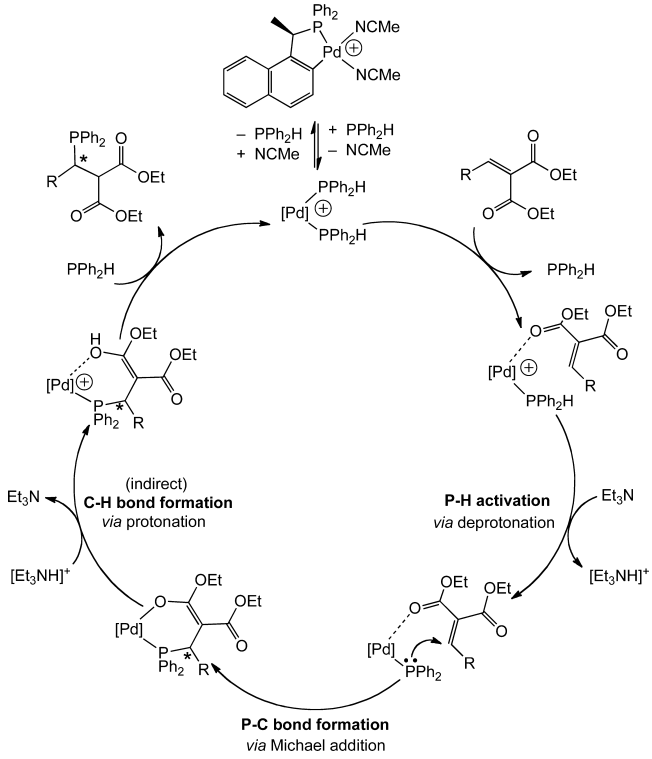
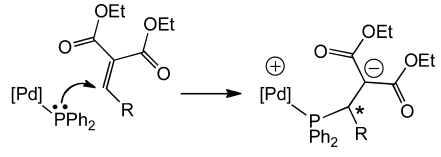


Figure 3. Proposed mechanism for enantioselective hydrophosphination of activated alkenes catalyzed by cationic palladacycles in the presence of base.[19a]

deprotonates the relatively acidic, Pd-coordinated Ph_2PH (P−H activation), to generate the reactive phosphido ligand. Later in the cycle the $[HNEt_3]^+$ delivers a proton to the oxygen of the beta-carbonyl group to give an overall 1,4-addition, though ultimately a keto−enol tautomerization gives an apparent 1,2-addition product. Presumably the authors propose Pd-coordination of this beta-carbonyl oxygen to rationalize the observed enantioselectivity, although no intermediates have been observed that show this interaction with the soft, albeit cationic, Pd^{2+} center. Eq 9 shows the zwitterionic intermediate that would result in a



1,2-addition, illustrating more clearly the overall regiochemistry of the P−H addition.

The cycle shown in Figure 3 illustrates that oxidative addition of the P−H bond at the metal is not required for catalytic hydrophosphination: the Pd stays in the +2 oxidation state throughout. Other late metal systems that do not involve P−H oxidative addition[20] also usually contain the metal in the +2 oxidation state, and many are cationic complexes, two features that enhance the acidity of the coordinated secondary phosphine. These systems inevitably require added base to act as a proton shuttle.[21] On the other hand, the Pt(0)-mediated hydrophosphination shown

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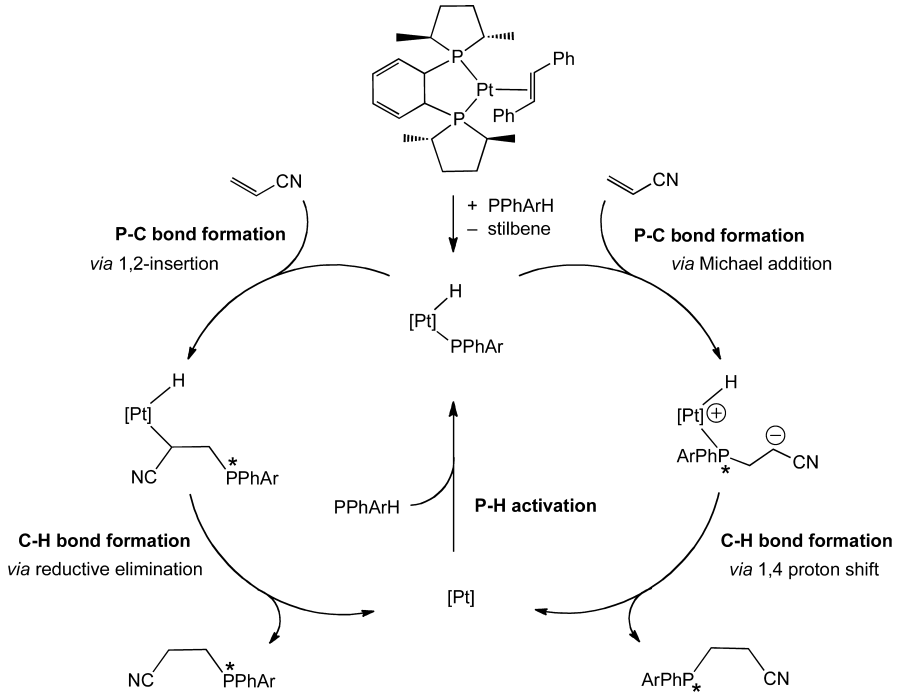
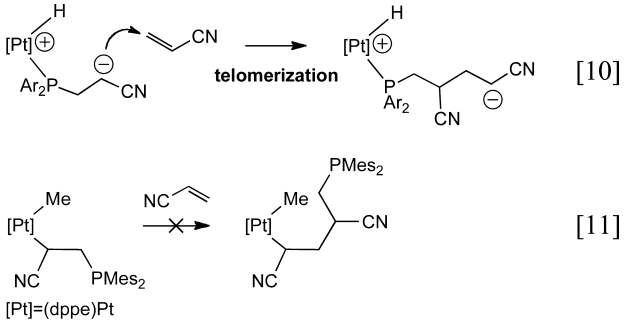


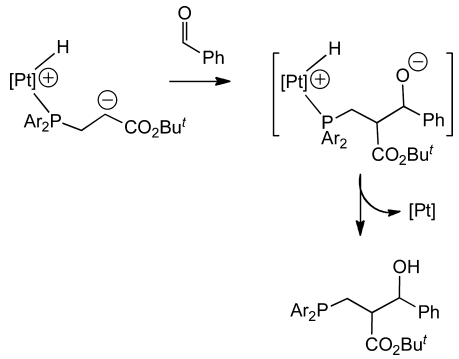
Figure 4. (left) Initially proposed mechanism for hydrophosphination of activated alkenes catalyzed by platinum, based on stoichiometric reactivity studies pointing to 1,2-insertion of alkene into the Pt–P bond.[14,22c] (right) Revised mechanism for Pt-mediated hydrophosphination of activated alkenes, invoking Michael-type outer-sphere nucleophilic attack by the phosphido ligand.[22a,b]

in Figure 4, which has been thoroughly investigated by Glueck and co-workers,[14,22] relies on oxidative addition of the P–H bond to generate a Pt^{2+}-phosphido intermediate.

The Glueck system is an interesting example of an outer-sphere P–C bond forming pathway that is apparently lower energy than an equally plausible inner-sphere, 1,2-insertion mechanism. Having identified $(P_2)Pt(H)(PR_2)$ as an active intermediate in catalysis, these researchers showed via the independent preparation of relevant phosphido complexes that (i) the substrate acrylonitrile inserts into the Pt–P bond, as opposed to the P–H bond, and (ii) C–H reductive elimination of the resulting insertion product is facile.[22c] This exciting evidence for alkene insertion into a metal-heteroatom bond seemed to point to the inner-sphere mechanism shown on the left in Figure 4. However, the simple hydrophosphination product was usually accompanied by telomerization products, *apparently* resulting from multiple 1,2-insertions of the acrylonitrile into new Pt–C bonds. In an effort to explain and avoid these byproducts, Glueck investigated the alternative, outer-sphere mechanism shown on the right in Figure 4, on the premise that the carbanion of the resulting zwitterionic intermediate was responsible for subsequent C–C bond formation to yield telomers (eq 10).[22a,b] Three findings in particular strongly support the importance of this outer-sphere P–C bond forming step: (i) independently prepared model alkyl complexes, including those with pendant phosphine groups, containing electron-withdrawing substituents on the carbon alpha to Pt did not react with additional equivalents of the appropriate activated alkenes (e.g., eq 11); (ii) telomerization was inhibited by the addition of weak acids such as H_2O or Bu^tOH, presumably because of fast protonation (quenching) of the putative intermediate carbanion, relative to carbanion attack on further equivalents of activated alkene; (iii) the putative carbanion was actually trapped through the addition of benzaldehyde, as shown in Scheme 3, under catalytic conditions.



Scheme 3



Glueck's painstaking studies, which targeted the synthesis of many possible intermediates from both pathways, clearly point to the importance of outer-sphere P–C bond formation. However, similar efforts to demonstrate outer sphere C–H bond formation via the putative zwitterionic intermediate (a proposed 1,4-proton transfer from Pt to the carbanion in the final step in the cycle) were frustrated by the inevitable appearance of an intermediate

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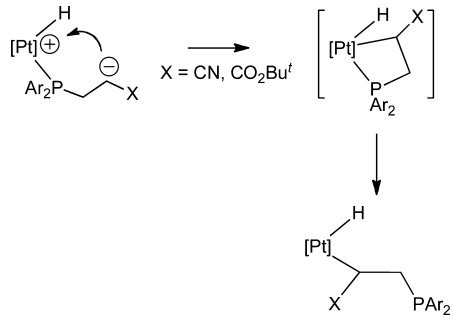
containing an alkyl ligand with pendant phosphine: if the zwitterion is forming in these reactions, it must rearrange quickly, presumably by attack of the carbanion at Pt, as shown in Scheme 4.

Scheme 4



One final point about the Glueck system is that no external base is required to shuttle a proton between P and C (although added HY/Y^- can play that role), because the Pt fragment acts as an internal base. Thus the introduction of the Pt−H bond as a hydride and its departure as a proton renders this formally a redox process at Pt, in contrast to the examples given above for which there is no change in oxidation state at the metal, and a basic cocatalyst is required.

An exception to the tenet that late metal complexes catalyze hydrophosphination via outer-sphere P−C bond formation is a series of Ni and Pd complexes shown by Beletskaya to catalyze the hydrophosphination of styrenes[23] and alkynes.[24] The proposed mechanism is shown in Figure 5 for the hydrophospination of

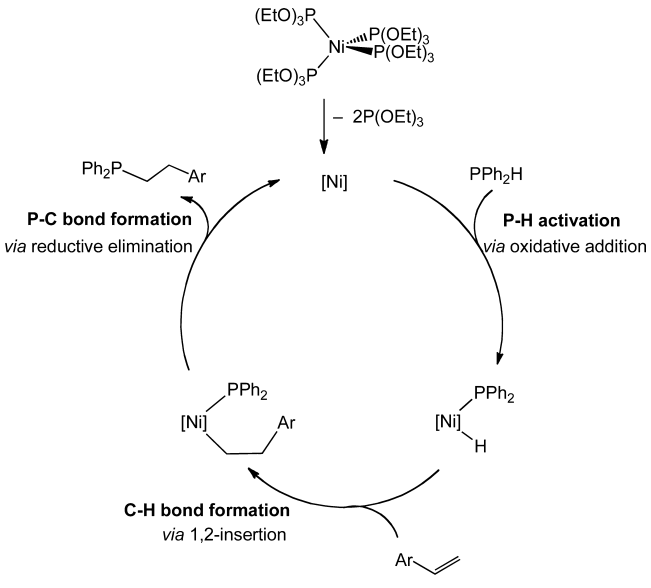
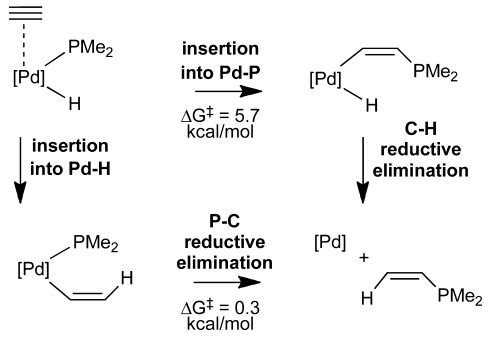


Figure 5. Proposed mechanism for hydrophosphination of styrenes by diphenylphosphine catalyzed by nickel(0).[23]

styrenes by diphenylphosphine, catalyzed by the M(0) complex $Ni\{P(OEt)_3\}_4$. As for Glueck's Pt(0) catalysts, this mechanism relies on oxidative addition of the P−H bond to give M^{2+} phosphido hydride complexes. These intermediates were not directly observed, but indirect evidence for their formation comes from the Ni^{2+}, Pd^{2+}, and Pd(0) systems studied, which tend to produce Ph_2P-PPh_2, along with the hydrophosphination products observed.[23b] This implies that catalytic oxidative dimerization of PPh_2H competes with hydrophosphination in these systems, presumably also via the formation of M-PPh_2 intermediates. Additional support for the intermediacy of a nickel phosphido hydride complex comes from the recent isolation of a bulky analogue of the proposed Ni^{2+} intermediate ([NiH{P(Dmp)H}-(dtbpe)], where Dmp = 2,6-dimesitylphenyl and dtbpe = 1,2-bis(di-*t*-butylphosphino)ethane), which was shown to react with 1-hexene to give the hydrophosphination product P(Hex)(Dmp)-H.[12a] The hydrophosphination mechanism shown in Figure 5 is considered general for both M(0) and M^{2+} precatalysts; it is postulated that MX_2 salts are reduced to M(0) in the presence of the secondary phosphines, with concurrent elimination of HX.[25]

The most interesting feature of Beletskaya's proposed inner-sphere mechanism, which is based on product distributions and stereo- and regiochemistry arguments, is that the critical P−C bond forming step involves reductive elimination of a P−C bond from an M^{2+} alkyl phosphido intermediate. This has limited precedent in stoichiometric chemistry,[26] although the preceding step, alkene or alkyne insertion into the M-H bond, certainly is a well-established and facile phenomenon.[27] Ananikov and Beletskaya's recent computational investigation of the hydrophosphination of acetylene by Me_2PH mediated by a Pd-PH_3 fragment focused specifically on the relative barriers to alkyne insertion into the M-H versus M-P bonds in a putative oxidative addition product (Scheme 5).[24a,c] They conclude that

Scheme 5



M-H insertion to give an alkyl (vinyl) phosphido intermediate is indeed favored ($\Delta G^{\ddagger}$ = 0.3 versus 5.7 kcal/mol for M-P insertion), but that the barriers to both insertions are sufficiently small that selectivity for M-H insertion over M-P insertion would be possible only at mild temperatures.

The possibility of competing Michael addition mechanisms such as those observed for the Glueck Pt hydrophosphination systems does not appear to have been investigated for the Beletskaya group 10 metal systems. However, support for the absence of an outer-sphere mechanism comes from their observation of hydrophosphination of some substrates that are less activated for Michael addition, including a simple alkyne, Bu^tCCH,[24b] and the relatively electron-rich *p*-methoxystyrene, using Ni and Pd catalysts.[23a] Also, these authors do not report observing telomeric products, as were observed for the Glueck Pt(0) systems, and which indicated the intermediacy of reactive carbanions. Nevertheless, it would be interesting to see computational and/or experimental investigation of a possible alternative outer-sphere mechanism for the Ni and Pd complexes studied.

f-, s- and Early d-Block Metals. Almost all electron-deficient metal complexes that have been reported to catalyze hydrophosphination of alkenes or alkynes are d^0, from groups

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1−4, including a range of lanthanide complexes. Typically the catalysis is proposed to involve inner-sphere P−C bond forming steps via metal-phosphido intermediates, as opposed to outer-sphere, Michael addition pathways. This may be because the phosphido ligands at these electron-poor metals are not expected to exhibit a "transition metal gauche effect" (dπ-pπ repulsions), although the M-P bonds should certainly be sufficiently polarized to impart strong P-nucleophilicity.[18]

Marks and co-workers reported the first examples of hydrophosphination of simple alkenes and alkynes, which are catalyzed by lanthanocene complexes (Figure 6).[3c,28] These

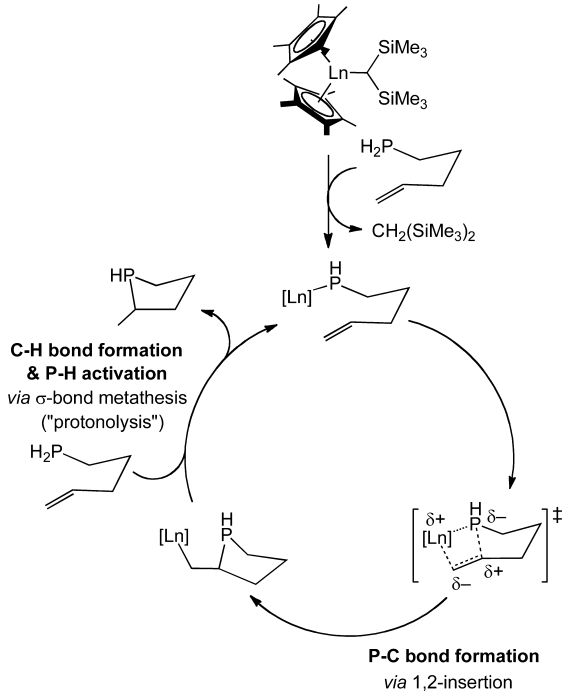

Figure 6. Proposed mechanism for hydrophosphination of α,ω-pentenylphosphine catalyzed by lanthanocenes, highlighting the transition state for the P−C bond forming step.[3c,28d]

reactions are intramolecular, employing bifunctional, α,ω-alkenyl- or alkynylphosphines that give cyclic phosphine products. There are some conformational constraints (and some kinetic advantages) associated with the use of such bifunctional substrates, but the fundamental nature of the proposed P−H bond-cleavage and P−C and C−H bond forming steps shown above are representative of most of the hydrophosphination mechanisms that have been proposed for electron-poor metals. In this mechanism, there is no formal oxidation state change at the Ln^{3+} ion. The P−H bond in the primary phosphine substrate is activated by σ-bond metathesis of an alkyl ligand via a four-center transition state that relies on the relative acidity of the P−H bond and the relative basicity of the alkyl fragment at the electropositive lanthanide: this is typically referred to as "protonolysis". P−C bond formation in these systems occurs via 1,2-insertion of the alkene (or alkyne) into the Ln-P bond. This generates a new Ln-alkyl ligand, and the final step of the cycle involves another protonolysis reaction to liberate the product phosphine and reinstall a reactive Ln phosphido ligand.

The catalytic cycle shown in Figure 6 is predicated on a well-established mechanism for the analogous hydroamination reaction.[29] It is considered general for the series of lanthanides studied, and is consistent with thermodynamic analysis of the relevant bonds purportedly made and broken at the metal, using available enthalpy data. The authors originally surmised, based on initial rates data including an estimated high negative entropy of activation,[3c] that the polar, highly ordered transition state associated with the concerted alkene insertion step was turnover-limiting, exactly as for the analogous hydroamination cycle. A re-evaluation of the reaction trajectory based on density functional theory (DFT) analysis of a simple Cp_2La fragment, however, suggests that it is the final protonolysis step of the cycle (which also involves a polar, highly ordered, concerted transition state, and is a bimolecular process) that is turnover-limiting for hydrophosphination.[28a] Support for this comes from the observation that protonolysis of the Ln-C bond in the catalyst precursor (Figure 6) occurs orders of magnitude more slowly for the primary phosphine substrate than for an analogous primary amine substrate, and is slow on the time scale of hydrophosphination catalysis.[30]

A feature of this lanthanocene hydrophosphination catalysis that is not obvious from the proposed catalytic cycle in Figure 6 is the importance of both substrate and product phosphine coordination at the coordinatively unsaturated metal intermediates. For example, variable temperature $^{31}P\{^1H\}$ and ^{31}P NMR monitoring of catalytic reaction mixtures and model stoichiometric reactions provide evidence for a catalyst resting state composed of several intermediates undergoing rapid exchange on the time scale of catalysis, each of which contains two distinct "P−H"-containing ligands.[3c] These are assigned to various adducts of the catalytically active phosphido complex: presumably these must dissociate to allow the pendant alkene close enough to the metal for productive catalysis to proceed. An alternative view of the catalytic cycle, shown in Figure 7, includes equilibria for this off-cycle resting state. It also shows details of the catalytically relevant intermediates uncovered by Marks and Fragalà's computational study of the simplified Cp_2La phosphido system, in which the lone pair of the newly formed cyclic alkylphosphine remains loosely coordinated to La after P−C bond formation and during the turnover-limiting La−C protonolysis step, and the lone pair of the substrate phosphine approaches the metal prior to the protonolysis step. Finally, the importance of phosphine adduct formation throughout this cycle is consistent with the authors' observation of product inhibition of catalysis at high conversions.[3c]

Protonolysis of polar M-C bonds by substrate phosphine is a key feature of the catalytic cycle for electron-poor metal hydrophosphination catalysts, whereas such concerted P−H activation/C−H bond formation typically is not seen for the less polar M-C bonds in late metal hydrophosphination catalysts—hence the frequent requirement of a basic cocatalyst to act as a proton shuttle (vide supra). As described above for Marks' lanthanocene systems, a protonolysis step is also usually required to generate the active phosphido catalyst from an alkyl, hydride, or amido precursor. This necessitates the use of well-anchored chelating or polyhapto ancillary ligands in these electron-deficient metal systems. A good example is the β-diketiminate-stabilized Ca^{2+} system reported by Barrett and Hill to catalyze the hydrophosphination of mildly activated alkenes (e.g., styrene, isoprene, and 1,3-cyclohexadiene): the catalyst precursor is an amido complex.[3b] The authors isolated the phosphido complex resulting from protonolysis of the amido ligand by the substrate diphenylphosphine, and showed its catalytic competence (eq 12[3b]). However they also note that the simpler bis(amido) precursor $[Ca\{N(SiMe_3)_2\}_2(THF)_2]$ showed low hydrophosphination activity, apparently because of

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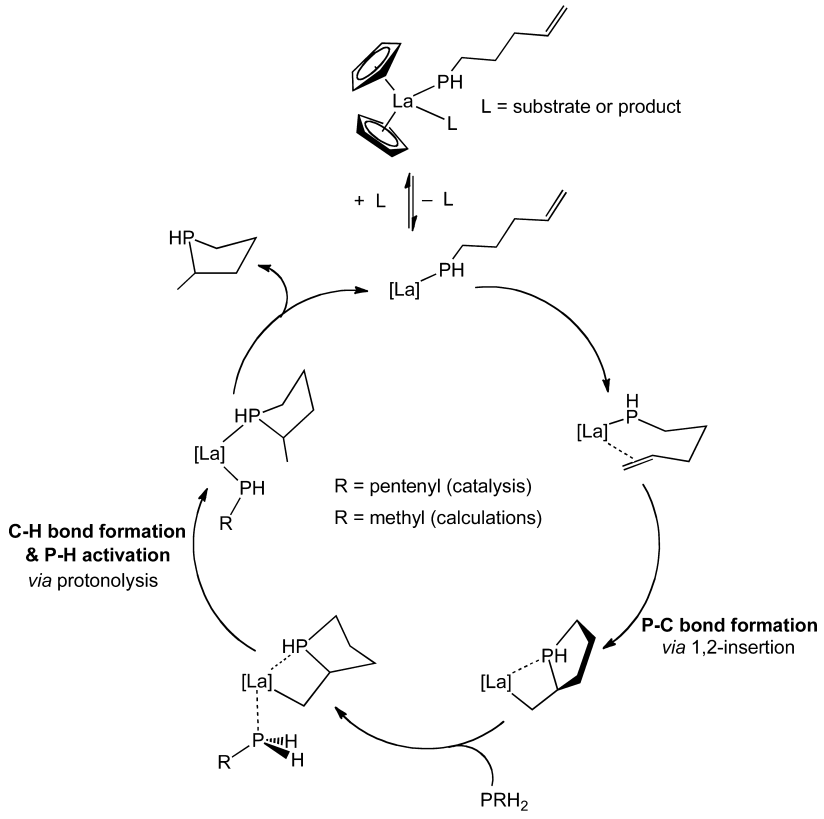
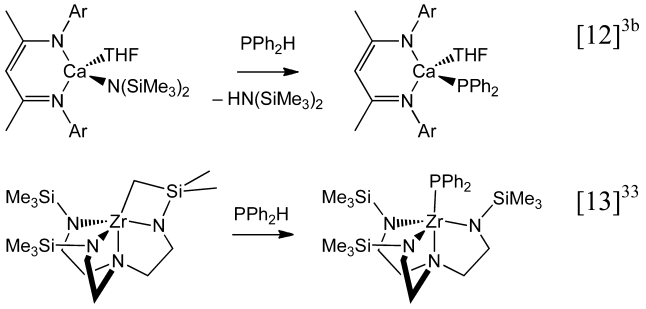


Figure 7. Further details of the proposed mechanism for hydrophosphination of α,ω-pentenylphosphine catalyzed by lanthanocenes, showing the probable importance of both product and substrate phosphine binding to coordinatively unsaturated intermediates.



precipitation of the bis(phosphido) complex $[Ca(PPh_2)_2(THF)_4]$ resulting from protonolysis of both amido ligands.[31] Similarly, Marks reported that moving from lanthanocenes to simpler homoleptic lanthanide alkyl or amido catalyst precursors complicated kinetic study of the catalysis, presumably because of the variety of active phosphido-containing species resulting from sequential protonolysis reactions.[28b] A complex reaction manifold established by Takaki for the hydrophosphination of alkynes catalyzed by an ytterbium imido complex derives from a number of competing protonolyses leading to both phosphido and amido complexes.[32] A tripodal triamidoamine zirconium complex reported by Waterman to catalyze hydrophospination of alkynes by diphenylphosphine is an interesting example of a polydentate ancillary ligand that further protects the active site by undergoing intramolecular metalation of a peripheral $N(SiMe_3)$ group (eq 13[33]): the resulting chelating alkyl group undergoes protonolysis by incoming phosphine to initiate catalysis.[33]

Another important feature in these electron-poor metal catalyzed hydrophosphinations is the degree of polarization in the proposed concerted transition state for P–C bond formation. Marks and Fragalà's computational results point to significant bond polarization around the four-centered transition state during alkene insertion into the Ln-P bond (Figure 6), despite the decidedly nonpolar nature of their simple alkene substrate.[28a] Presumably the charge separation in the substrate alkene is induced by the polarity of the Ln-P bond, driven in particular by the electropositive character of the metal ion.[34] Barrett and Hill also comment on the importance of this polar transition state, attributing the regioselectivity of P–H addition they observe for the Ca^{2+}-catalyzed hydrophosphination of styrene to the ability of the phenyl substitutent to stabilize the induced negative charge at the substituted carbon of this terminal alkene.[3b] So the success of these hydrophosphinations relies on polarization of the unsaturated substrate within the metal's coordination sphere, while most late metal catalysts, operating via outer-sphere P–C bond formation, require "pre-polarized" substrates. Interestingly, while Barrett and Hill do not report the participation of simple terminal alkenes or ethylene in their Ca^{2+}-mediated reactions, they note that moving from styrenes and other slightly activated alkenes to the more electrophilic vinylpyridine actually leads to telomeric products resulting from multiple insertions of the polar alkene: the rate of insertion of this activated alkene into the polar Ca–C bond becomes competitive with the (in this case) turnover-limiting protonolysis of the Ca–C bond by incoming substrate phosphine.[3b]

Almost all catalyst systems that participate in hydrophosphination through coordination/activation of the substrate phosphine involve "PR_2" phosphido intermediates. It is surprising that there are not more examples of the participation of metal phosphinidenes, M=PR, in catalytic hydrophosphination, particularly given the importance of [2+2]-cycloaddition of alkynes and alkenes at metal imido (M=NR) intermediates as an N–C bond forming step in early metal-catalyzed hydroamination.[35] Stoichio-

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metric [2+2]-cycloadditions of alkynes and alkenes at metal phosphinidene fragments are known,[36] and Mindiola has proposed such a mechanism for the Ti-catalyzed hydrophosphination of diphenylacetylene by phenylphosphine, $PPhH_2$ (Figure 8).[37] In this cycle, a cationic phosphinidene precursor complex, stabilized by

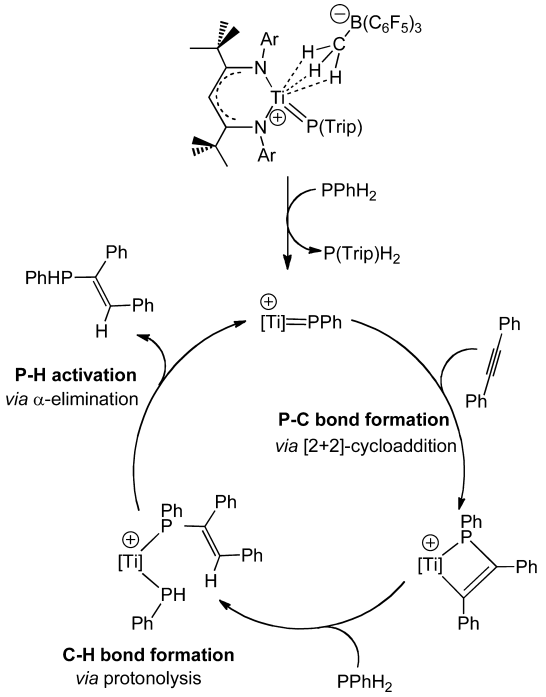
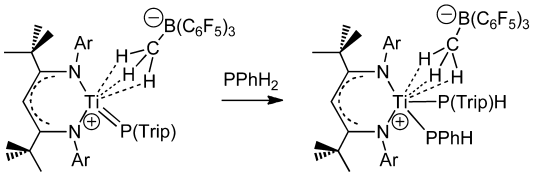


Figure 8. Proposed catalytic cycle for the hydrophosphination of diphenylacetylene by phenylphosphine, mediated by a cationic titanium phosphinidene complex.[37]

the bulky Trip (= 2,4,6-tris(isopropyl)phenyl) substituent at P and by the close association of a $[MeB(C_6F_5)_3]^-$ counteranion, undergoes facile exchange of the P(Trip) fragment with the corresponding PPh fragment in the presence of the primary phosphine. This can occur via two σ-bond metathesis steps: the first is a protonolysis of the Ti=P(Trip) double bond to give a mixed bis(phosphido) intermediate (eq 14[37]), and the second is an



[14][37]

α-elimination (or 1,3-proton transfer) to generate free Trip phosphine and a new, more reactive phenylphosphinidene complex. The Ti=PPh phosphinidene fragment then participates in [2+2] cycloaddition with the incoming diphenylacetylene to give a phosphatitanacyclobutene intermediate. Incoming $PPhH_2$ can protonolyze the Ti–C bond to generate another mixed bis(phosphido) intermediate, and a final 1,3-proton shift generates the product secondary phosphine and regenerates an active phosphinidene intermediate. The authors have isolated the P(Trip) analogue of the intermediate [2+2]-cycloadduct, and have shown that it can be protonolyzed (at least using more protic amines) to yield the corresponding secondary vinylphosphine. Further support for the importance of a phosphinidene intermediate in this catalysis (as opposed to one of the phosphido intermediates resulting from a single P–H activation step) comes from the observation that hydrophosphination does not occur when a secondary phosphine, PPh_2H is used instead of the primary phosphine $PPhH_2$.

Finally, the titanium-catalyzed 1,4-hydrophosphination of 1,3-dienes by PPh_2H reported by Le Gendre and co-workers (Figure 9) demonstrates yet another mode of metal catalyst

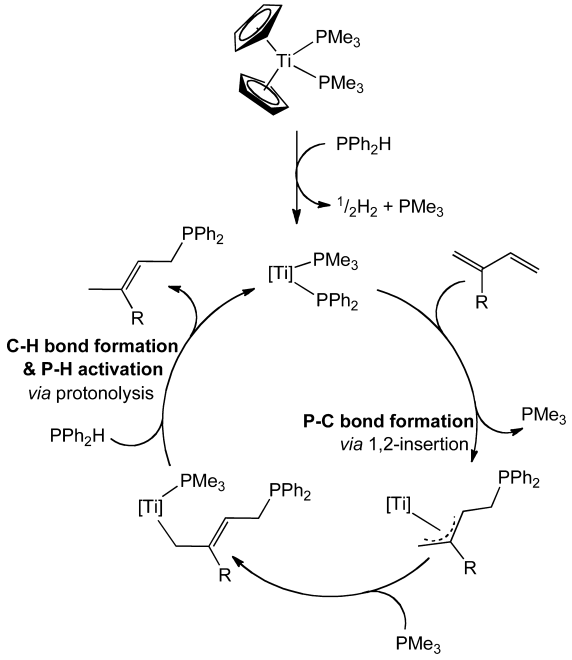


Figure 9. Proposed catalytic cycle for the 1,4-hydrophosphination of 1,3-dienes by diphenylphosphine, mediated by a titanium(III) phosphido complex.[38]

activation, and provides an unusual example of a non-d^0, early transition metal catalyst.[38] The Ti^{2+} precursor apparently undergoes oxidative addition of the P–H bond in PPh_2H, followed by H-atom transfer reactions that release H_2(g) and produce the active catalyst, which is a Ti^{3+} phosphido complex.[39] Support for this mechanism comes from electron paramagnetic resonance (EPR) analysis of the reaction mixture, which confirms the presence of one or more paramagnetic (presumably d^1) species. Also, the proposed active intermediate, $Cp_2Ti(PMe_3)PPh_2$, was prepared independently and shown to be catalytically competent. The rest of the catalytic cycle is typical for an electron-deficient metal complex, involving the "usual" P–C bond formation (1,2-insertion) and concerted C–H bond formation and P–H activation (protonolysis) steps.

Where Our Results Fit into This Picture. We have been considering the above proposed mechanisms for catalytic hydrophosphination in our efforts to understand the broad substrate scope of P–C bond formation we observe for the terminal phosphido ruthenium complex **2**, and to extend this promising stoichiometric chemistry to useful catalysis. This is an electron-rich, late-metal center that may be active for the catalytic hydrophosphination of not only traditional, activated "late-metal" substrates but also less activated and simple substrates whose hydrophosphination previously has been catalyzed only by electron-poor metal systems. A synthetic cycle based on observed stoichiometric steps is shown in Figure 10.

There is no formal oxidation state change for Ru in this cycle: deprotonation of a coordinated secondary phosphine by added base is responsible for P–H activation, and C–H bond

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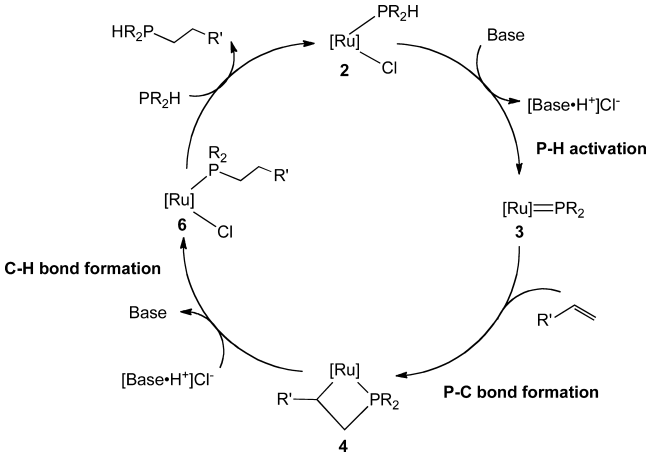


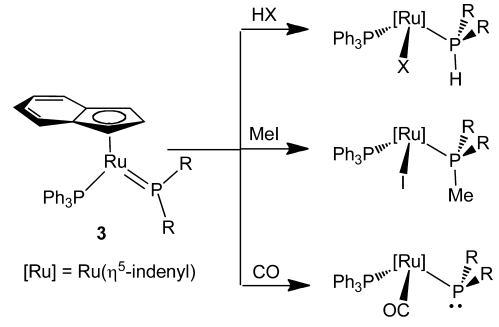
Figure 10. Synthetic cycle for the hydrophosphination of alkenes by a secondary phosphine, mediated by complex **2** ([Ru] = Ru(η^5-indenyl)PPh_3).

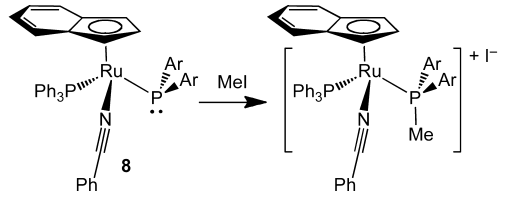
formation results from "redelivery" of the abstracted proton following the P−C bond forming step. Although this is formally a protonolysis of the Ru−C bond, similar to the proposed mechanism for hydrophosphination mediated by electron-poor metals (Figure 6), the fact that it relies on the base cocatalyst to act as a proton shuttle, instead of reacting directly with the P−H bond of the incoming substrate phosphine places this aspect of the mechanism firmly in the "late metal" camp, similar to the catalytic cycle proposed by Leung for the Pd-mediated hydrophosphination of activated alkenes (Figure 3).

It is trickier to decide whether the critical P−C bond forming step in Figure 10 is occurring via an inner sphere process such as cycloaddition or insertion,[40] or via outer sphere nucleophilic attack of the ruthenium phosphido ligand on the unsaturated substrate. Stereolabeling and kinetic studies of the formal [2+2]-cycloadditions of the simple alkenes ethylene and 1-hexene at **3** strongly support a concerted, inner sphere mechanism,[9a] rather than a stepwise Michael-type addition involving a zwitterionic intermediate such as that shown for Glueck's Pt-catalyzed hydrophosphination of activated alkenes (Figure 4). Comparable experiments using activated substrates such as acrylonitrile or styrenes are currently underway: preliminary kinetic studies examining the solvent dependence of cycloaddition rates for these substrates suggest the absence of zwitterionic intermediates, but we have not yet excluded the possibility that an outer sphere mechanism could be operative in these cases. Despite the fact that its lone pair is participating in π-donation to Ru, the terminal phosphido ligand in **3** certainly acts as a nucleophile in other reactions of the complex with polar substrates. For example, reagents such as HX or MeI undergo 1,2-addition reactions with the Ru=P bond in **3** that inevitably place the electropositive end (H^+, Me^+) of the addendum at phosphorus (Scheme 6).[7] Addition of donor ligands can disrupt the Ru−P π-bond to give formal six-coordinate adducts in which the phosphido has become pyramidal, and X-ray structural data showing unusually long Ru−P bonds are consistent with the importance of a "transition metal gauche effect" for these adducts.[7,41] For diaryl analogues of **3**, handled as their benzonitrile adducts **8**, we have actually isolated the cationic intermediates of outer sphere nucleophilic attack of the terminal phosphido ligands at MeI (eq 15).[41a]

Nevertheless, we are fairly certain that the reactions of at least the nonpolar alkenes and alkynes at the Ru=P bond in **3**

Scheme 6

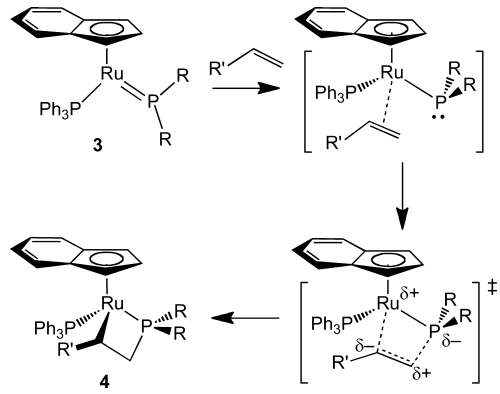




[15][41a]

are occurring in an inner sphere, concerted fashion. These reactions closely resemble those described for Marks' lanthanocene-catalyzed hydrophosphinations of simple alkenes, in that the initial product (complex **4** in our potential cycle (Figure 10) and the corresponding Cp_2La intermediate in Figure 7) is a κ^2-alkylphosphine complex, where the phosphorus is behaving as a neutral donor. This is distinct from Mindiola's proposed P−C bond forming step, in which [2+2]-cycloaddition of an alkyne at a Ti phosphinidene double bond gives a κ^2-alkylphosphido complex, where the phosphorus is acting as an anionic donor. Although our P−C bond forming reactions are overall [2+2]-cycloadditions, we presume at least weak interaction of the π-system of the unsaturated substrate with Ru occurs prior to the actual concerted bond forming step (Scheme 7).[42] This association (weak or strong) will reduce the

Scheme 7



Ru phosphido bond order such that the concerted, four-centered transition state does not involve a formal cyclic flow of π-electrons: this is a 1,2-insertion step. Given the sensitivity of **3** to adduct formation in the presence of donor ligands, this reaction trajectory seems reasonable. It also helps to explain why these P−C bond forming reactions are quite sensitive to the steric demands of the unsaturated substrate, since bulky substituents would hinder the requisite adduct formation.

The insertion of simple alkenes into an M-P bond has not been observed for other late metal complexes. What makes this

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Ru system different? The combined hemilability and nucleophilicity/basicity of the terminal phosphido ligand, constrained in the half-sandwich structure of complex **3**, seems to be critical. The d^6 Ru^{2+} in this complex is not electron-poor, but its reactivity is driven by the ready coordination of an extra ligand to achieve pseudo-octahedral geometry and an 18-electron count. The available coordination site is cis to the PR_2 ligand, which is sufficiently basic to deprotonate even acetonitrile, normally considered an aprotic solvent.[41b] Evidently these features provide a polarizing influence on the incoming unsaturated substrate that is comparable to that exhibited by d^0 or d^1 complexes, allowing the concerted insertion step to proceed. Another way to think about this behavior is in the context of a pervasive modern paradigm: the close pairing in this system of coordinatively unsaturated Ru and its strongly basic phosphido ligand provides an intramolecular "frustrated Lewis pair" that leads to unexpected modes of small molecule activation.[43]

CONCLUSIONS AND OUTLOOK

There is wide scope for the further development and application of metal-catalyzed hydrophosphination, given the breadth of mechanistic possibilities that have already been identified. For example, it is surprising that there are not more examples of the use of chiral metal fragments to effect enantioselectivity in the established early metal and lanthanide mediated processes. Wider exploration of the activities of mid-to-late transition metals that are not from Group 10 is certainly warranted, and a particular focus on these more electron-rich metals in low coordinate environments seems particularly promising as a means to expanding substrate scope and generality.

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Notes

The authors declare no competing financial interest.

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